Organic Acid

By

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1 - Introduction To Organic Acid

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1 - Introduction

An organic acid is an organic compound with acidic properties. The most common organic acids are the carboxylic acids, whose acidity is associated with their carboxyl group – COOH. Sulfonic acids, containing the group – SO_2OH, are relatively stronger acids. Alcohols, with – OH, can act as acids but they are usually very weak. The relative stability of the conjugate base of the acid determines its acidity. Other groups can also confer acidity, usually weakly: the thiol group –SH, the enol group, and the phenol group. In biological systems, organic compounds containing these groups are generally referred to as organic acids.

2 - Characteristics

In general, organic acids are weak acids and do not dissociate completely in water, where as the strong mineral acids do. Lower molecular mass organic acids such as formic and lactic acids are miscible in water, but higher molecular mass organic acids, such as benzoic acid, are insoluble in molecular (neutral) form.

On the other hand, most organic acids are very soluble in organic solvents. *p*-Toluene sulfonic acid is a comparatively strong acid used in organic chemistry often because it is able to dissolve in the organic reaction solvent.

Exceptions to these solubility characteristics exist in the presence of other substituents that affect the polarity of the compound.

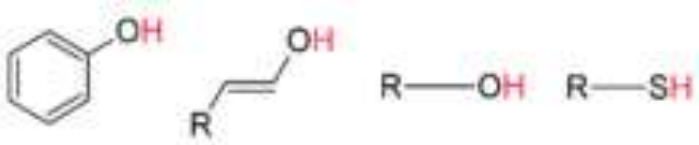
3 - Applications

Simple organic acids like formic or acetic acids are used for oil and gas well stimulation treatments. These organic acids are much less reactive with metals than are strong mineral acids like hydrochloric acid (HCl) or mixtures of HCl and hydrofluoric acid (HF). For this reason, organic acids are used at high temperatures or when long contact times between acid and pipe are needed .

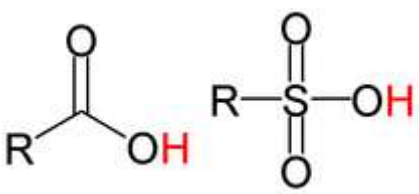
The conjugate bases of organic acids such as citrate and lactate are often used in biologically- compatible buffer solutions.

Citric and oxalic acids are used as rust removal. As acids, they can dissolve the iron oxides, but without damaging the base metal as do stronger mineral acids. In the dissociated form, they may be able to chelate the metal ions, helping to speed removal .

Biological systems create many and more complex organic acids such as L-lactic, citric, and D- glucuronic acids that contain hydroxyl or carboxyl groups. Human blood and urine contain these plus organic acid degradation products of amino acids, neurotransmitters, and intestinal bacterial action on food components. Examples of these categories are alpha – ketoisocaproic vanilmandelic, and D-lactic acids, derived from catabolism of L-leucine and epinephrine (adrenaline) by human tissues and catabolism of dietary carbohydrate by intestinal bacteria, respectively.



The general structure of a few weak organic acids.
From left to right: phenol, enol, alcohol, thiol.
The acidic hydrogen in each molecule is colored red.



The general structure of a few organic acids. From left to right: carboxylic acid, sulfonic acid. The acidic hydrogen in each molecule is colored red.

3 - Application in food

Organic acids are used in food preservation because of their effects on bacteria. The key basic principle on the mode of action of organic acids on bacteria is that non-dissociated (non-ionized) organic acids can penetrate the bacteria cell wall and disrupt the normal physiology of certain types of bacteria that we call *pH-sensitive*, meaning that they cannot tolerate a wide internal and external pH gradient. Among those bacteria are *Escherichia coli*, *Salmonella* spp., *C. perfringens*, *Listeria mono cytogenes*, and *Campylobacter* species.

Upon passive diffusion of organic acids into the bacteria, where the pH is near or above neutrality, the acids will dissociate and lower the bacteria internal pH, leading to situations that will impair or stop the growth of bacteria. On the other hand, the anionic part of the organic acids that cannot escape the bacteria in its dissociated form will accumulate within the bacteria and disrupt many metabolic functions, leading to osmotic pressure increase, incompatible with the survival of the bacteria.

It has been well demonstrated that the state of the organic acids (undissociated or dissociated) is extremely important to define their capacity to inhibit the growth of bacteria, compared to undissociated acids.

Lactic acid and its salts sodium lactate and potassium lactate are widely used as antimicrobials in food products, in particular, meat and poultry such as ham and sausages.

4 - Application in nutrition and animal feeds

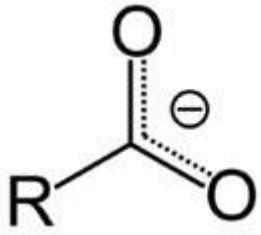
Organic acids have been used successfully in pig production for more than 25 years. Although less research has been done in poultry, organic acids have also been found to be effective in poultry production.

Organic acids ($C_1 - C_7$) are widely distributed in nature as normal constituents of plants or animal tissues. They are also formed through microbial fermentation of carbohydrates mainly in the large intestine. They are sometimes found in their sodium, potassium, or calcium salts, or even stronger double salts.

Organic acids added to feeds should be protected to avoid their dissociation in the crop and in the intestine (high pH segments) and reach far into the gastrointestinal tract, where the bulk of the bacteria population is located.

From the use of organic acids in poultry and pigs, one can expect an improvement in performance similar to or better than that of antibiotic growth promoters, without the public health concern, a preventive effect on the intestinal problems like necrotic enteritis in chickens and *Escherichia coli* infection in young pigs. Also one can expect a reduction of the carrier state for *Salmonella* species and *Campylobacter* species.

2 - Introduction To Carboxylic Acid



Carboxylate ion

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1 - Introduction

A carboxylic acid is an organic acid characterized by the presence of at least one carboxyl group . The general formula of a carboxylic acid is R- COOH, where R is some monovalent functional group. A carboxyl group (or carboxy) is a functional group consisting of a carbonyl (RR'C= O) and a hydroxyl (R- O -H), which has the formula - C(= O)OH, usually written as - COOH or - CO_2H.

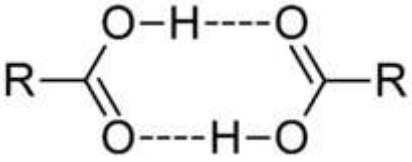
Carboxylic acids are Brønsted-Lowry acids because they are proton (H+) donors. They are the most common type of organic acid.

Among the simplest examples are formic acid H-COOH, which occurs in ants, and acetic acid CH3- COOH, which gives vinegar its sour taste. Acids with two or more carboxyl groups are called dicarboxylic, tricarboxylic, etc. The simplest dicarboxylic example is oxalic acid $(COOH)_2$, which is just two connected carboxyls. Mellitic acid is an example of a hexacarboxylic acid. Other important natural examples are citric acid (in lemons) and tartaric acid (in tamarinds).

Salts and esters of carboxylic acids are called carboxylates. When a carboxyl group is deprotonated, its conjugate base forms a carboxylate anion. Carboxylate ions are resonance stabilized and this increased stability makes carboxylic acids more acidic than alcohols. Carboxylic acids can be seen as reduced or alkylated forms of the Lewis acid carbon dioxide; under some circumstances they can be decarboxylated to yield carbon dioxide.

2 - Physical properties

2 – 1 - Solubility



Carboxylic acid dimers

Carboxylic acids are polar. Because they are both hydrogen-bond acceptors (the carbonyl) and hydrogen-bond donors (the hydroxyl), they also participate in hydrogen bonding. Together the hydroxyl and carbonyl group forms the functional group carboxyl. Carboxylic acids usually exist as dimeric pairs in nonpolar media due to their tendency to "self-associate." Smaller carboxylic acids (1 to 5 carbons) are soluble in water, whereas higher carboxylic acids are less soluble due to the increasing hydrophobic nature of the alkyl chain. These longer chain acids tend to be rather soluble in less-polar solvents such as ethers and alcohols.

2 – 2 - Boiling points

Carboxylic acids tend to have higher boiling points than water, not only because of their increased surface area, but because of their

tendency to form stabilised dimers. Carboxylic acids tend to evaporate or boil as these dimers. For boiling to occur, either the dimer bonds must be broken, or the entire dimer arrangement must be vaporised, both of which increase enthalpy of vaporization requirements significantly.

2 – 3 - Acidity

Carboxylic acids are typically weak acids, meaning that they only partially dissociate into H+ cations and RCOO – anions in neutral aqueous solution. For example, at room temperature, only 0.4% of all acetic acid molecules are dissociated. Electronegative substituents give stronger acids.

Carboxylic acid	Forula	pKa
Formic acid	H COOH	3.75
Acetic acid	CH_3 COOH	4.76
Chloro acetic acid	CH_2 ClCOOH	2.86
Oxalic acid	HOOC- COOH	1.27
Benzoic acid	C_6H_5 COOH	4.2

Deprotonation of carboxylic acids gives carboxylate anions, which is resonance stabilized because the negative charge is delocalized between the two oxygen atoms increasing its stability. Each of the carbon - oxygen bonds in carboxylate anion has partial double-bond character.

2 - 4 - Odor

Carboxylic acids often have strong odors, especially the volatile derivatives. Most common are acetic acid (vinegar) and butanoic acid (rancid butter). On the other hand, esters of carboxylic acids tend to have pleasant odors and many are used in perfumes.

3 - Characterization

Carboxylic acids are most readily identified as such by infrared spectroscopy. They exhibit a sharp band associated with vibration of the C- O vibration bond (νC = O) between 1680 and 1725 cm−1. A characteristic νO-H band appears as a broad peak in the 2500 to

3000 cm−1 region. By 1H NMR spectrometry, the hydroxyl hydrogen appears in the 10 - 13 ppm region, although it is often either broadened or not observed owing to exchange with traces of water.

4 - Occurrence and applications

Many carboxylic acids are produced industrially on a large scale. They are also pervasive in nature. Esters of fatty acids are the main components of lipids and polyamides of aminocarboxylic acids are the main components of proteins.

Carboxylic acids are used in the production of polymers, pharmaceuticals, solvents, and food additives. Industrially important carboxylic acids include acetic acid (component of vinegar, precursor to solvents and coatings), acrylic and methacrylic acids (precursors to polymers, adhesives), adipic acid (polymers), citric acid (beverages), ethylenediaminetetraacetic acid (chelating agent), fatty acids (coatings), maleic acid (polymers), propionic acid (food preservative), terephthalic acid (polymers).

5 - Synthesis

5 – 1 - Industrial routes

Industrial routes to carboxylic acids generally differ from those used on smaller scale because they require specialized equipment.

Oxidation of aldehydes with air using cobalt and manganese catalysts. The required aldehydes are readily obtained from alkenes by hydroformylation.

Oxidation of hydrocarbons using air. For simple alkanes, the method is nonselective but so inexpensive to be useful. Allylic and benzylic compounds undergo more selective oxidations. Alkyl groups on a benzene ring oxidized to the carboxylic acid, regardless of its chain length. Benzoic acid from toluene and terephthalic acid from para - xylene, and phthalic acid from ortho-xylene are illustrative large-scale conversions. Acrylic acid is generated from propene.

Base - catalyzed dehydrogenation of alcohols.

Carbonylation is versatile method when coupled to the addition of water. This method is effective for alkenes that generate secondary and tertiary carbocations, e.g. isobutylene to pivalic acid. In the Koch reaction, the addition of water and carbon monoxide to alkenes is catalyzed by strong acids. Acetic acid and formic acid are produced by the carbonylation of methanol, conducted with iodide and alkoxide promoters, respectively and often with high pressures of carbon monoxide, usually involving additional hydrolytic steps. Hydro carboxylations involve the simultaneous addition of water and CO. Such reactions are some times called "Reppe chemistry" :

$$HC{=}CH + CO + H_2O \rightarrow CH_2 = CHCO_2H$$

Some long chain carboxylic acids are obtained by the hydrolysis of triglycerides obtained from plant or animal oils. These methods are related to soap making.

fermentation of ethanol is used in the production of vinegar.

5 – 2 - Laboratory methods

Preparative methods for small scale reactions for research or for production of fine chemicals often employ expensive consumable reagents.

oxidation of primary alcohols or aldehydes with strong oxidants such as potassium dichromate , Jones reagent , potassium permanganate , or sodium chlorite. The method is amenable to laboratory conditions compared to the industrial use of air, which is “greener” since it yields less inorganic side products such as chromium or manganese oxides.

Oxidative cleavage of olefins by ozonolysis, potassium permanganate, or potassium dichromate.

Carboxylic acids can also be obtained by the hydrolysis of nitriles, esters, or amides, generally with acid- or base-catalysis.

Carbonation of a Grignard and organolithium reagents :

$RLi + CO_2 \; RCO_2Li$
$RCO_2Li + HCl \; RCO_2H + LiCl$

Halogenation followed by hydrolysis of methyl ketones in the haloform reaction

The Kolbe-Schmitt reaction provides a route to salicylic acid, precursor to aspirin.

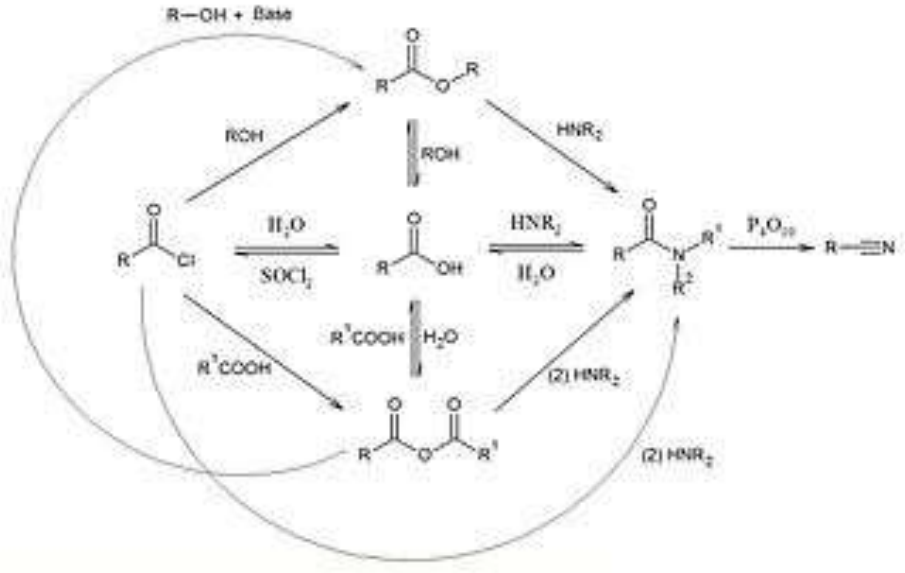
5 – 1 – Less - common reactions

Many reactions afford carboxylic acids but are used only in specific cases or are mainly of academic interest:

Disproportionation of an aldehyde in the Cannizzaro reaction

Rearrangement of diketones in the benzilic acid rearrangement involving the generation of benzoic acids are the von Richter reaction from nitrobenzenes and the Kolbe-Schmitt reaction from phenols.

6 - Reactions



Carboxylic acid Organic Reactions

The most widely practiced reactions convert carboxylic acids into esters, amides, carboxylate salts, acid chlorides, and alcohols.

Carboxylic acids react with bases to form carboxylate salts, in which the hydrogen of the hydroxyl (-OH) group is replaced with a metal cation. Thus, acetic acid found in vinegar reacts with sodium bicarbonate (baking soda) to form sodium acetate, carbon dioxide, and water:

$$CH_3COOH + NaHCO_3 \rightarrow CH_3COO{-}Na+ + CO_2 + H_2O$$

Carboxylic acids also react with alcohols to give esters. This process is heavily used in the production of polyesters. Similarly carboxylic acids are converted into amides, but this conversion typically does not occur by direct reaction of the carboxylic acid and the amine. Instead esters are typical precursors to amides. The conversion of amino acids into peptides is a major biochemical process that requires ATP.

The hydroxyl group on carboxylic acids may be replaced with a chlorine atom using thionyl chloride to give acyl chlorides. In nature, carboxylic acids are converted to thioesters.

Carboxylic acid can be reduced to the alcohol by hydrogenation or using stoichiometric hydride reducing agents such as lithium aluminium hydride.

N,N- dimethyl chloro methyl enammonium chloride is a highly chemoselective agent for carboxylic acid reduction. It selectively activate the carboxylic acid and is known to tolerate active functionalities such as ketone as well as the moderate ester, olefin, nitrile and halide moeties.

6 – 1 - Specialized reactions

As with all carbonyl compounds, the protons on the α-carbon are labile due to keto-enol tautomerization. Thus the α- carbon is easily halogenated in the Hell-Volhard-Zelinsky halogenation.

The Schmidt reaction converts carboxylic acids to amines.

Carboxylic acids are decarboxylated in the Hunsdiecker reaction.

The Dakin-West reaction converts an amino acid to the corresponding amino ketone.

In the Barbier-Wieland degradation, the alpha-methylene bridge in an aliphatic carboxylic acid is removed in a sequence of reaction steps, effectively a chain-shortening . The inverse procedure is the Arndt-Eistert synthesis, where an acid is converted into acyl halide and reacts with diazomethane to give the highest homolog.

Many acids undergo oxidative decarboxylation. Enzymes that catalyze these reactions are known as carboxylases (EC 6.4.1) and decarboxylases (EC 4.1.1).

Carboxylic acids are reduced to aldehydes via the ester and DIBAL, via the acid chloride in the Rosenmund reduction and via the thioester in the Fukuyama reduction.

In ketonic decarboxylation carboxylic acids are converted to ketones.

7 - Nomenclature and examples

Carboxylic acids are commonly named as indicated in the table below. Although rarely used, IUPAC-recommended names also exist. For example, butyric acid ($C3H_7CO_2H$) is, according to IUPAC guidelines, also known as butanoic acid.

The carboxylate anion R-COO – is usually named with the suffix -ate, so acetic acid, for example, becomes acetate ion. In IUPAC nomenclature, carboxylic acids have an -oic acid suffix (e.g., octadecanoic acid). In common nomenclature, the suffix is usually -ic acid (e.g., stearic acid).

Straight - chained, saturated carboxylic acids

Carbon atoms	Common name	IUPAC name	Chemical formula	Common location or use
1	Formic acid	Methanoic acid	$HCOOH$	Insect stings
2	Acetic acid	Ethanoic acid	CH_3COOH	Vinegar
3	Propionic acid	Propanoic acid	CH_3CH_2COOH	Preservative for stored grains
4	Butyric acid	Butanoic acid	$CH_3(CH_2)_2COOH$	Rancid butter
5	Valeric acid	Pentanoic acid	$CH_3(CH_2)_3COOH$	Valerian
6	Caproic acid	Hexanoic acid	$CH_3(CH_2)_4COOH$	Goat fat
7	Enanthic acid	Heptanoic acid	$CH_3(CH_2)_5COOH$	
8	Caprylic acid	Octanoic acid	$CH_3(CH_2)_6COOH$	Coconuts and breast milk
9	Pelargonic acid	Nonanoic acid	$CH_3(CH_2)_7COOH$	Pelargonium
10	Capric acid	Decanoic acid	$CH_3(CH_2)_8COOH$	
11	Undecylic acid	Undecanoic acid	$CH_3(CH_2)_9COOH$	
12	Lauric acid	Dodecanoic acid	$CH_3(CH_2)_{10}COOH$	Coconut oil and hand wash soaps.
13	Tridecylic acid	Tridecanoic acid	$CH_3(CH_2)_{11}COOH$	
14	Myristic acid	Tetradecanoic acid	$CH_3(CH_2)_{12}COOH$	Nutmeg
15		Pentadecanoic acid	$CH_3(CH2)_{13}COOH$	
16	Palmitic acid	Hexadecanoic acid	$CH_3(CH_2)_{14}COOH$	Palm oil
17	Margaric acid	Heptadecanoic acid	$CH_3(CH_2)_{15}COOH$	
18	Stearic acid	Octadecanoic acid	$CH_3(CH_2)_{16}COOH$	Chocolate, waxes, soaps, and oils
20	Arachidic acid	Icosanoic acid	$CH_3(CH_2)_{18}COOH$	Peanut oil

Other carboxylic acids

Compound class	Members
unsaturated monocarboxylic acids	acrylic acid (2-propenoic acid) – CH_2=CHCOOH, used in polymer synthesis
Fatty acids	medium to long-chain saturated and unsaturated monocarboxylic acids, with even number of carbons examples docosahexaenoic acid and eicosapentaenoic acid (nutritional supplements)
Amino acids	the building blocks of proteins
Keto acids	acids of biochemical significance that contain a ketone group e.g. acetoacetic acid and pyruvic acid
Aromatic carboxylic acids	benzoic acid, the sodium salt of benzoic acid is used as a food preservative, salicylic acid – a beta hydroxy type found in many skin care products
Dicarboxylic acids	containing two carboxyl groups examples adipic acid the monomer used to produce nylon and aldaric acid – a family of sugar acids
Tricarboxylic acids	containing three carboxyl groups example citric acid – found in citrus fruits and isocitric acid
Alpha hydroxy acids	containing a hydroxy group example glyceric acid, glycolic acid and lactic acid (2-hydroxypropanoic acid) – found in sour milk tartaric acid – found in wine

8 - Carboxyl radical

The radical · COOH has only a separate fleeting existence.[10] The acid dissociation constant of · COOH has been measured using electron paramagnetic resonance spectroscopy. The carboxyl group tends to dimerise to form oxalic acid.

- Volume One –

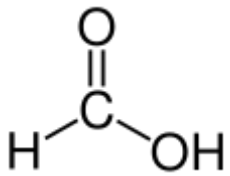
Aliphatic Organig Acids

Section - 1 -

Aliphatic Carboxylic Organic Acids

Part - 1 - Aliphatic Acids Mono Carboxylic

Formic Acid



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1 - Introduction

Formic acid (also called methanoic acid) is the simplest carboxylic acid. Its chemical formula is HCOOH or HCO_2H. It is an important intermediate in chemical synthesis and occurs naturally, most notably in the venom of bee and ant stings. In fact, its name comes from the Latin word for ant, formica, referring to its early isolation by the distillation of ant bodies. Esters, salts, and the anion derived from formic acid are referred to as formates.

IUPAC name : Formic acid

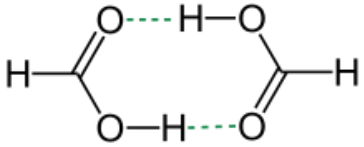
Systematic name : Methanoic Acid

Other names :

Aminic acid ;
Formylic acid ;
Hydrogen carboxylic acid ; Hydroxymethanone;
Hydroxy(oxo) methan ;
Meta carbonoic acid ;
Oxocarbinic acid ; Oxo methanol

Molecular formula	C H_2 O_2
Molar mass	46 g mol−1
Appearance	Colorless liquid
Density	1.22 g / mL
Melting point	8.4 °C
Boiling point	100.8 °C
Solubility in water	Miscible
Acidity (pKa)	3.77
Viscosity	1.57 cP at 26 °C
Main hazards	Corrosive ; irritant ; sensitizer.
Flash point	69 °C
Auto ignition temperature	601 °C
Structure and properties	n , εr , etc .
Thermo dynamic data	Phase behaviour Solid , liquid , gas
Spectral data	UV, IR , NMR , MS

2 - Properties



Cyclic dimer of formic acid ;
dashed green lines represent hydrogen bonds

Formic acid is a colorless liquid having a highly pungent, penetrating odor at room temperature. It is miscible with water and most polar organic solvents, and is somewhat soluble in hydrocarbons. In hydrocarbons and in the vapor phase, it consists of hydrogen-bonded dimers rather than individual molecules . Owing to

its tendency to hydrogen - bond, gaseous formic acid does not obey the ideal gas law. Solid formic acid (two polymorphs) consists of an effectively endless network of hydrogen - bonded formic acid molecules. This relatively complicated compound also forms a low-boiling azeotrope with water (22.4 %) and liquid formic acid also tends to supercool.

3 - Natural occurrence

In nature, it is found in the stings and bites of many insects of the order Hymenoptera, mainly ants. Formic acid is a naturally occurring component of the atmosphere due primarily to forest emissions.

4 - Production

In 2009, the world wide capacity for producing this compound was 720,000 tones / annum, with production capacity roughly equally divided between Europe (350,000, mainly in Germany) and Asia (370,000, mainly in China), while production was below 1000 tonnes/annum in all other continents. It is commercially available in solutions of various concentrations between 85 and 99 w/w %.[4] As of 2009[update], the largest producers are BASF, Kemira and Feicheng Acid Chemicals, with the largest production facilities in Ludwigshafen (200,000 tones / annum, BASF, Germany), Oulu (105,000, Kemira, Finland) and Feicheng (100,000, Feicheng, China). 2010 Prices ranged from circa € 650 / tonne in Western Europe and $ 1250/tonne in the United States.

4 – 1 - From methyl formate and formamide

When methanol and carbon monoxide are combined in the presence of a strong base, the acid derivative methyl formate results, according to the chemical equation:

$$CH_3OH + CO \rightarrow HCO_2CH_3$$

In industry, this reaction is performed in the liquid phase at elevated pressure. Typical reaction conditions are 80 °C and 40 atm.

The most widely-used base is sodium methoxide. Hydrolysis of the methyl formate produces formic acid:

$$HCO_2CH_3 + H_2O \rightarrow HCO_2H + CH_3OH$$

Efficient hydrolysis of methyl formate requires a large excess of water. Some routes proceed indirectly by first treating the methyl formate with ammonia to give formamide, which is then hydrolyzed with sulfuric acid:

$$HCO_2CH_3 + NH_3 \rightarrow HC(O)NH_2 + CH_3OH$$
$$2\ HC(O)NH_2 + 2\ H_2O + H_2SO_4 \rightarrow 2HCO_2H + (NH_4)_2SO_4$$

This approach suffers from the need to dispose of the ammonium sulfate byproduct. This problem has led some manufacturers to develop energy efficient means for separating formic acid from the large excess amount of water used in direct hydrolysis. In one of these processes (used by BASF) the formic acid is removed from the water via liquid-liquid extraction with an organic base.

4 – 2 - By - product of acetic acid production

A significant amount of formic acid is produced as a by product in the manufacture of other chemicals. At one time, acetic acid was produced on a large scale by oxidation of alkanes, via a process that cogenerates significant formic acid. This oxidative route to acetic acid is declining in importance, so that the aforementioned dedicated routes to formic acid have become more important.

4 – 3 - Hydrogenation of carbon dioxide

The catalytic hydrogenation of CO2 has long been studied. This reaction can be conducted homogeneously.

4 – 4 - Laboratory methods

In the laboratory, formic acid can be obtained by heating oxalic acid in glycerol and extraction by steam distillation . Glycerol acts as a catalyst, as the reaction proceeds through a glyceryl oxalate intermediary. If the reaction mixture is heated to higher temperatures, allyl alcohol results. The net reaction is thus:

$$C_2O_4H_2 \rightarrow CO_2H_2 + CO_2$$

Another preparation (which must be performed under a fume hood) is the acid hydrolysis of ethyl isonitrile (C_2H_5NC) using HCl solution.

$$C_2H_5NC + 2\ H_2O \rightarrow C_2H_5NH_2 + HCO_2H$$

The isonitrile can be obtained by reacting ethyl amine with chloroform (note that the fume hood is required because of the overpoweringly objectionable odor of the isonitrile).

5 - Uses

A major use of formic acid is as a preservative and antibacterial agent in livestock feed. In Europe, it is applied on silage (including fresh hay) to promote the fermentation of lactic acid and to suppress the formation of butyric acid; it also allows fermentation to occur quickly, and at a lower temperature, reducing the loss of nutritional value. Formic acid arrests certain decay processes and causes the feed to retain its nutritive value longer, and so it is widely used to preserve winter feed for cattle. In the poultry industry, it is sometimes added to feed to kill E. coli bacteria . Use as preservative for silage and (other) animal feed constituted 30 % of the global consumption in 2009.

Formic acid is also significantly used in the production of leather, including tanning (23 % of the global consumption in 2009[7]), and in dyeing and finishing of textile (9 % of the global consumption in 2009) because of its acidic nature. Use as a coagulant in the production of rubber constituted in 2009 6 % of the global consumption.

Formic acid is also used in place of mineral acids for various cleaning products, such as limescale remover and toilet bowl cleaner. Some formate esters are artificial flavorings or perfumes. Beekeepers use formic acid as a miticide against the tracheal mite (Acarapis woodi) and the Varroa mite. The use of formic acid in fuel cells is also under investigation.

5 – 1 - Laboratory use

Formic acid is a source for a formyl group for example in the formylation of methylaniline to N-methylformanilide in toluene. In synthetic organic chemistry, formic acid is often used as a source of hydride ion. The Eschweiler-Clarke reaction and the Leuckart-Wallach reaction are examples of this application. It, or more commonly its azeotrope with triethylamine, is also used as a source of hydrogen in transfer hydrogenation.

Like acetic acid and trifluoroacetic acid, formic acid is commonly used as a volatile pH modifier in HPLC and capillary electrophoresis.

As mentioned below, formic acid may serve as a convenient source of carbon monoxide by being readily decomposed by sulfuric acid.

6 - Reactions

Formic acid shares most of the chemical properties of other carboxylic acids. Reflecting its high acidity, its solutions in alcohols form esters spontaneously. Formic acid shares some of the reducing properties of aldehydes, reducing solutions of gold, silver, and platinum to the metals.

6 – 1 - Decomposition

Heat and especially acids cause formic acid to decompose to carbon monoxide (CO) and water (dehydration). Treatment of formic acid with sulfuric acid is a convenient laboratory source of CO.

In the presence of platinum, it decomposes with a release of hydrogen and carbon dioxide. Soluble ruthenium catalysts are also effective . Carbon monoxide free hydrogen has been generated in a very wide pressure range (1- 600 bar). Formic acid has even been considered as a material for hydrogen storage. The co - product of this decomposition, carbon dioxide, can be rehydrogenated back to formic acid in a second step. Formic acid contains 53 g L^{-1} hydrogen at room temperature and atmospheric pressure, which is three and a

half times as much as compressed hydrogen gas can attain at 350 bar pressure (14.7 g L−1). Pure formic acid is a liquid with a flash point of + 69 °C, much higher than that of gasoline (– 40 °C) or ethanol (+ 13 °C).

6 – 2 - Addition to alkenes

Formic acid is unique among the carboxylic acids in its ability to participate in addition reactions with alkenes. Formic acids and alkenes readily react to form formate esters. In the presence of certain acids, including sulfuric and hydrofluoric acids, however, a variant of the Koch reaction occurs instead, and formic acid adds to the alkene to produce a larger carboxylic acid.

6 – 3 - Formic acid anhydride

An unstable formic anhydride, H (C= O) – O - (C= O) H, can be obtained by dehydration of formic acid with N,N'-Dicyclo hexyl carbo diimide in ether at low temperature.

7 - History

Some alchemists and naturalists were aware that ant hills give off an acidic vapor as early as the 15th century. The first person to describe the isolation of this substance (by the distillation of large numbers of ants) was the English naturalist John Ray, in 1671. Ants secrete the formic acid for attack and defense purposes. Formic acid was first synthesized from hydrocyanic acid by the French chemist Joseph Gay-Lussac. In 1855, another French chemist, Marcellin Berthelot, developed a synthesis from carbon monoxide that is similar to that used today.

Formic acid was long considered a chemical compound of only minor interest in the chemical industry. In the late 1960s, however, significant quantities of it became available as a byproduct of acetic acid production. It now finds increasing use as a preservative and antibacterial in livestock feed.

8 - Safety

Formic acid has low toxicity (hence its use as a food additive), with an LD50 of 1.8 g / kg (oral, mice). The concentrated acid is, however, corrosive to the skin.

Formic acid is readily metabolized and eliminated by the body. Nonetheless, it has specific toxic effects; the formic acid and formaldehyde produced as metabolites of methanol are responsible for the optic nerve damage, causing blindness seen in methanol poisoning. Some chronic effects of formic acid exposure have been documented. Some experiments on bacterial species have demonstrated it to be a mutagen. Chronic exposure to humans may cause kidney damage. Another effect of chronic exposure is development of a skin allergy that manifests upon re-exposure to the chemical.

Concentrated formic acid slowly decomposes to carbon monoxide and water, leading to pressure buildup in the container it is kept in. For this reason, 98 % formic acid is shipped in plastic bottles with self-venting caps.

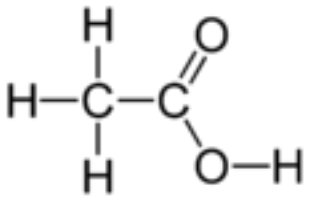
The hazards of solutions of formic acid depend on the concentration. The following table lists the EU classification of formic acid solutions:

Concentration (weight percent)	Classification
2 % – 10 %	Irritant (Xi)
10 % – 90 %	Corrosive (C)
> 90 %	Corrosive (C)

An assay for formic acid in body fluids, designed for determination of formate after methanol poisoning, is based on the reaction of formate with bacterial formate dehydrogenase.

Formic acid in 85 % concentration is not flammable, and diluted formic acid is on the US Food and Drug Administration list of food additives . The principal danger from formic acid is from skin or eye contact with the concentrated liquid or vapors. The US OSHA Permissible Exposure Level (PEL) of formic acid vapor in the work environment is 5 parts per million parts of air (ppm).

Acetic Acid



Contents

1 - Introduction

cetic acid pron.: (systematically named ethanoic acid pron) is an organic compound with the chemical formula CH_3CO_2H (also written as CH_3COOH or $C_2H_4O_2$). It is a colourless liquid that when undiluted is also called glacial acetic acid. Acetic acid is the main component of vinegar (apart from water; vinegar is roughly 8% acetic acid by volume), and has a distinctive sour taste and pungent smell. Besides its production as household vinegar, it is mainly produced as a precursor to polyvinylacetate and cellulose acetate. Although it is classified as a weak acid, concentrated acetic acid is corrosive and attacks the skin.

Acetic acid is one of the simplest carboxylic acids. It is an important chemical reagent and industrial chemical, mainly used in the production of cellulose acetate mainly for photographic film and polyvinyl acetate for wood glue, as well as synthetic fibres and fabrics. In households, diluted acetic acid is often used in descaling agents. In the food industry, acetic acid is used under the food additive code E 260 as an acidity regulator and as a condiment. As a food additive it is approved for usage in the EU, USA and Australia and New Zealand.

The global demand of acetic acid is around 6.5 million tonnes per year (Mt/a), of which approximately 1.5 Mt/a is met by recycling; the remainder is manufactured from petrochemical feedstock.[9] As a chemical reagent, biological sources of acetic acid are of interest but generally uncompetitive. Vinegar is dilute acetic acid, often produced by fermentation and subsequent oxidation of ethanol.

IUPAC name : Acetic acid
Systematic name : Ethanoic acid
Other names : Methane carboxylic acid

Molecular formula	$C_2 H_4 O_2$
Molar mass	60 g mol−1
Appearance	Colourless liquid
Density	1.049 g cm-3
Melting point	16 - 17 °C

Boiling point	118 - 119 °C
Solubility in water	Miscible
Viscosity	1.22 mPa s
Specific heat capacity, C	123.1 J K-1 mol-1
GHS pictograms	
GHS signal word	Danger
EU classification	 C
Flash point	40 °C
Autoignition temperature	400 °C
LD50	3.31 g kg-1, oral (rat)
Structure and properties	n, εr, etc.
Thermodynamic data	Phase behaviour Solid, liquid, gas
Spectral data	UV, IR, NMR, MS

2 - Nomenclature

The trivial name acetic acid is the most commonly used and preferred IUPAC name. The systematic name ethanoic acid, a valid IUPAC name, is constructed according to the substitutive nomenclature . The name acetic acid derives from acetum, the Latin word for vinegar, and is related to the word acid itself.

Glacial acetic acid is a trivial name for water-free (anhydrous) acetic acid. Similar to the German name Eisessig (ice-vinegar), the name comes from the ice - like crystals that form slightly below room temperature at 16.6 °C (the presence of 0.1 % water lowers its melting point by 0.2 °C).

A common abbreviation for acetic acid is AcOH, where Ac stands for the acetyl group $CH_3-C(=O)-$. Acetate (CH_3COO-) is abbreviated AcO–. The Ac is not to be confused with the abbreviation for the chemical element actinium. To better reflect its structure, acetic acid is often written as $CH_3-C(O)OH$, $CH_3-C(=O)OH$,

CH_3COOH, and CH_3CO_2H. In the context of acid-base reactions, the abbreviation HAc is sometimes used, where Ac instead stands for acetate. Acetate is the ion resulting from loss of H+ from acetic acid. The name acetate can also refer to a salt containing this anion, or an ester of acetic acid.

3 - History

Vinegar was known early in civilization as the natural result of air exposure to beer and wine, because acetic acid-producing bacteria are present globally. The use of acetic acid in alchemy extends into the 3rd century BC, when the Greek philosopher Theophrastus described how vinegar acted on metals to produce pigments useful in art, including white lead (lead carbonate) and verdigris, a green mixture of copper salts including copper(II) acetate. Ancient Romans boiled soured wine to produce a highly sweet syrup called sapa. Sapa that was produced in lead pots was rich in lead acetate, a sweet substance also called sugar of lead or sugar of Saturn, which contributed to lead poisoning among the Roman aristocracy.

In the Renaissance, glacial acetic acid was prepared through the dry distillation of certain metal acetates (the most noticeable one being copper(II) acetate). The 16th-century German alchemist Andreas Libavius described such a procedure, and he compared the glacial acetic acid produced by this means to vinegar. The presence of water in vinegar has such a profound effect on acetic acid's properties that for centuries chemists believed that glacial acetic acid and the acid found in vinegar were two different substances. French chemist Pierre Adet proved them identical.

In 1847 German chemist, Hermann Kolbe synthesized acetic acid from inorganic compounds for the first time. This reaction sequence consisted of chlorination of carbon disulfide to carbon tetrachloride, followed by pyrolysis to tetrachloroethylene and aqueous chlorination to trichloroacetic acid, and concluded with electrolytic reduction to acetic acid.

By 1910, most glacial acetic acid was obtained from the "pyroligneous liquor" from distillation of wood. The acetic acid was isolated from this by treatment with milk of lime, and the resulting calcium acetate was then acidified with sulfuric acid to recover acetic acid. At that time, Germany was producing 10,000 tons of glacial acetic acid, around 30 % of which was used for the manufacture of indigo dye.

Because both methanol and carbon monoxide are commodity raw materials, methanol carbonylation long appeared to be an attractive precursors to acetic acid. Henry Dreyfus at British Celanese developed a methanol carbonylation pilot plant as early as 1925.[15] However, a lack of practical materials that could contain the corrosive reaction mixture at the high pressures needed (200 atm or more) discouraged commercialization of these routes. The first commercial methanol carbonylation process, which used a cobalt catalyst, was developed by German chemical company BASF in 1963. In 1968, a rhodium-based catalyst (cis−[Rh(CO)2I2]−) was discovered that could operate efficiently at lower pressure with almost no by-products. US chemical company Monsanto Company built the first plant using this catalyst in 1970, and rhodium-catalysed methanol carbonylation became the dominant method of acetic acid production (see Monsanto process). In the late 1990s, the chemicals company BP Chemicals commercialized the Cativa catalyst ([Ir(CO)2I2]−), which is promoted by ruthenium for greater efficiency. This iridium-catalysed Cativa process is greener and more efficient and has largely supplanted the Monsanto process, often in the same production plants.

3 - 1 - In the interstellar medium

Acetic acid was discovered in interstellar medium in 1996 by a team led by David Mehringer who detected it using the former Berkeley-Illinois-Maryland Association array at the Hat Creek Radio Observatory and the former Millimeter Array located at the Owens Valley Radio Observatory. It was first detected in the Sagittarius B2 North molecular cloud (also known as the Sgr B2 Large Molecule Heimat source). Acetic acid has the distinction of being the first molecule discovered in the interstellar medium using solely radio

interferometers; in all previous ISM molecular discoveries made in the millimeter and centimeter wavelength regimes, single dish radio telescopes were at least partly responsible for the detections.

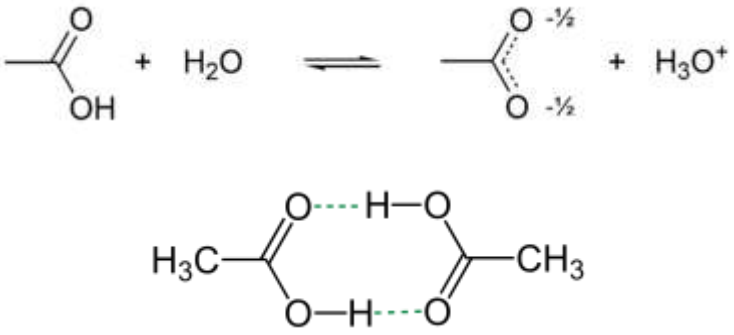
4 - Chemical properties

4 – 1 - Acidity

The hydrogen center in the carboxyl group (− COOH) in carboxylic acids such as acetic acid can separate from the molecule by ionization:

$$CH_3CO_2H \rightarrow CH_3CO_2^- + H+$$

Because of this release of the proton (H+), acetic acid has acidic character. Acetic acid is a weak monoprotic acid. In aqueous solution, it has a pKa value of 4.75. Its conjugate base is acetate ($CH3COO^-$). A 1.0 M solution (about the concentration of domestic vinegar) has a pH of 2.4, indicating that merely 0.4% of the acetic acid molecules are dissociated.



Cyclic dimer of acetic acid;
dashed green lines represent hydrogen bonds

4 – 2 - Structure

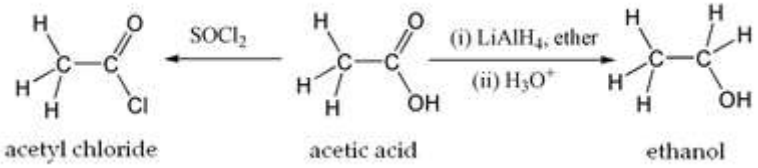
In solid acetic acid, the molecules form pairs (dimers), being connected by hydrogen bonds . The dimers can also be detected in the vapour at 120 °C . Dimers also occur in the liquid phase in dilute solutions in non - hydrogen-bonding solvents, and a certain extent in pure acetic acid , but are disrupted by hydrogen - bonding solvents. The dissociation enthalpy of the dimer is estimated at 65.0 –66.0 kJ / mol, and the dissociation entropy at 154 –157 J mol−1 K−1. Other lower carboxylic acids dimerize in a similar fashion.

4 – 3 - Solvent properties

Liquid acetic acid is a hydrophilic (polar) protic solvent, similar to ethanol and water. With a moderate relative static permittivity (dielectric constant) of 6.2, it dissolves not only polar compounds such as inorganic salts and sugars, but also non-polar compounds such as oils and elements such as sulfur and iodine. It readily mixes with other polar and non-polar solvents such as water, chloroform, and hexane. With higher alkanes (starting with octane), acetic acid is not completely miscible anymore, and its miscibility continues to decline with longer n-alkanes . This dissolving property and miscibility of acetic acid makes it a widely used industrial chemical. Its solvent properties are mainly of value in the production of dimethyl terephthalate.

4 - 4 – Chemical reactions

4 - 4 – 1 - Organic chemistry



Acetic acid undergoes the typical chemical reactions of a carboxylic acid. Upon treatment with a standard base, it converts to metal acetate and water. With strong bases (e.g., organolithium reagents), it can be doubly deprotonated to give LiCH2CO2Li. Reduction of acetic acid gives ethanol. The OH group is the main site of reaction, as illustrated by the conversion of acetic acid to acetyl chloride. Other substitution derivatives include acetic anhydride; this anhydride is produced by loss of water from two molecules of acetic acid. Esters of acetic acid can likewise be formed via Fischer esterification, and amides can be formed. When heated above 440 °C acetic acid decomposes to produce carbon dioxide and methane, or to produce ketene and water.

4 - 4 – 2 - Reactions with inorganic compounds

Acetic acid is mildly corrosive to metals including iron, magnesium , and zinc , forming hydrogen gas and salts called acetates:

$$Mg + 2\ CH_3COOH \rightarrow (CH_3COO)_2Mg + H_2$$

Because aluminium forms a passivating acid - resistant film of aluminium oxide, aluminium tanks are used to transport acetic acid.

Metal acetates can also be prepared from acetic acid and an appropriate base, as in the popular "baking soda + vinegar" reaction:

$$NaHCO_3 + CH_3COOH \rightarrow CH_3COONa + CO_2 + H_2O$$

A colour reaction for salts of acetic acid is iron (III) chloride solution, which results in a deeply red colour that disappears after acidification. Acetates when heated with arsenic trioxide form cacodyl oxide, which can be detected by its malodorous vapours.

4 - 5 - Biochemistry

At physiological pHs, acetic acid is usually fully ionized to acetate. In biochemistry, acetate and acetic acid are equivalent.

The acetyl group, derived from acetic acid, is fundamental to all forms of life. When bound to coenzyme A, it is central to the metabolism of carbohydrates and fats. Unlike longer-chain carboxylic acids (the fatty acids), acetic acid does not occur in natural triglycerides. However, the artificial triglyceride triacetin (glycerine triacetate) is a common food additive and is found in cosmetics and topical medicines.

Acetic acid is produced and excreted by acetic acid bacteria, notable ones being the Acetobacter genus and Clostridium acetobutylicum. These bacteria are found universally in foodstuffs, water, and soil, and acetic acid is produced naturally as fruits and other foods spoil. Acetic acid is also a component of the vaginal

lubrication of humans and other primates, where it appears to serve as a mild antibacterial agent.

5 - Production

Acetic acid is produced industrially both synthetically and by bacterial fermentation. About 75 % of acetic acid made for use in the chemical industry is made by the carbonylation of methanol, explained below.[9] Alternative methods account for the rest. The biological route accounts for only about 10 % of world production, but it remains important for the production of vinegar, as many food purity laws stipulate that vinegar used in foods must be of biological origin. As of 2003 - 2005, total worldwide production of virgin acetic acid was estimated at 5 Mt/a (million tonnes per year), approximately half of which was then produced in the United States. European production stood at approximately 1 Mt/a and was declining, and 0.7 Mt/a were produced in Japan. Another 1.5 Mt were recycled each year, bringing the total world market to 6.5 Mt/a.[23][24] Since then the global production has increased to 10.7 Mt/a (in 2010), and further, however, slowing increase in production is predicted.[25] The two biggest producers of virgin acetic acid are Celanese and BP Chemicals. Other major producers include Millennium Chemicals, Sterling Chemicals, Samsung, Eastman, and Svensk Etanolkemi.

5 – 1 - Methanol carbonylation

Most acetic acid is produced by methanol carbonylation. In this process, methanol and carbon monoxide react to produce acetic acid according to the equation:

$$CH_3OH + CO \rightarrow CH_3COOH$$

The process involves iodomethane as an intermediate, and occurs in three steps. A catalyst, metal carbonyl, is needed for the carbonylation (step 2).

$$CH_3OH + H\,I \rightarrow CH_3\,I + H_2O$$
$$CH_3\,I + CO \rightarrow CH_3CO\,I$$
$$CH_3CO\,I + H_2O \rightarrow CH_3COOH + H\,I$$

By altering the process conditions, acetic anhydride may also be produced on the same plant.

5 – 2 - Acetaldehyde oxidation

Prior to the commercialization of the Monsanto process, most acetic acid was produced by oxidation of acetaldehyde. This remains the second-most-important manufacturing method, although it is usually uncompetitive with the carbonylation of methanol.

The acetaldehyde may be produced via oxidation of butane or light naphtha, or by hydration of ethylene. When butane or light naphtha is heated with air in the presence of various metal ions, including those of manganese, cobalt, and chromium, peroxides form and then decompose to produce acetic acid according to the chemical equation

$$2\ C_4H_{10} + 5\ O_2 \rightarrow 4\ CH_3COOH + 2\ H_2O$$

The typical reaction is conducted at temperatures and pressures designed to be as hot as possible while still keeping the butane a liquid. Typical reaction conditions are 150 °C and 55 atm. Side - products may also form, including butanone, ethyl acetate, formic acid, and propionic acid. These side-products are also commercially valuable, and the reaction conditions may be altered to produce more of them where needed. However, the separation of acetic acid from these by-products adds to the cost of the process.

Under similar conditions and using similar catalysts as are used for butane oxidation, the oxygen in air to produce acetic acid can oxidize acetaldehyde.

$$2\ CH_3CHO + O_2 \rightarrow 2\ CH_3COOH$$

Using modern catalysts, this reaction can have an acetic acid yield greater than 95 %. The major side-products are ethyl acetate, formic acid, and formaldehyde, all of which have lower boiling points than acetic acid and are readily separated by distillation.

5 – 3 - Ethylene oxidation

Acetaldehyde may be prepared from ethylene via the Wacker process, and then oxidized as above . In more recent times, chemical company Showa Denko, which opened an ethylene oxidation plant in Ōita, Japan, in 1997, commercialized a cheaper single-stage conversion of ethylene to acetic acid.[28] The process is catalysed by a palladium metal catalyst supported on a heteropoly acid such as tungstosilicic acid. It is thought to be competitive with methanol carbonylation for smaller plants (100 – 250 kt / a) , depending on the local price of ethylene.

5 – 4 - Oxidative fermentation

For most of human history, acetic acid bacteria of the genus Acetobacter have made acetic acid, in the form of vinegar. Given sufficient oxygen, these bacteria can produce vinegar from a variety of alcoholic foodstuffs. Commonly used feeds include apple cider, wine, and fermented grain, malt, rice, or potato mashes. The overall chemical reaction facilitated by these bacteria is:

$$C_2H_5OH + O_2 \rightarrow CH_3COOH + H_2O$$

A dilute alcohol solution inoculated with Acetobacter and kept in a warm, airy place will become vinegar over the course of a few months. Industrial vinegar-making methods accelerate this process by improving the supply of oxygen to the bacteria.

The first batches of vinegar produced by fermentation probably followed errors in the winemaking process. If must is fermented at too high a temperature, acetobacter will overwhelm the yeast naturally occurring on the grapes. As the demand for vinegar for culinary, medical, and sanitary purposes increased, vintners quickly learned to use other organic materials to produce vinegar in the hot summer months before the grapes were ripe and ready for processing into wine. This method was slow, however, and not always successful, as the vintners did not understand the process.

One of the first modern commercial processes was the "fast method" or "German method", first practised in Germany in 1823. In this process, fermentation takes place in a tower packed with wood shavings or charcoal. The alcohol - containing feed is trickled into the top of the tower, and fresh air supplied from the bottom by either natural or forced convection. The improved air supply in this process cut the time to prepare vinegar from months to weeks.

Nowadays, most vinegar is made in submerged tank culture, first described in 1949 by Otto Hromatka and Heinrich Ebner.[31] In this method, alcohol is fermented to vinegar in a continuously stirred tank, and oxygen is supplied by bubbling air through the solution. Using modern applications of this method, vinegar of 15% acetic acid can be prepared in only 24 hours in batch process, even 20% in 60-hour fed-batch process.

5 – 5 - Anaerobic fermentation

Species of anaerobic bacteria, including members of the genus Clostridium or Acetobacterium can convert sugars to acetic acid directly, without using ethanol as an intermediate. The overall chemical reaction conducted by these bacteria may be represented as:

$$C_6H_{12}O_6 \rightarrow 3\ CH_3COOH$$

These acetogenic bacteria produce acetic acid from one-carbon compounds, including methanol, carbon monoxide, or a mixture of carbon dioxide and hydrogen:

$$2\ CO_2 + 4\ H_2 \rightarrow CH_3COOH + 2\ H_2O$$

This ability of Clostridium to utilize sugars directly, or to produce acetic acid from less costly inputs, means that these bacteria could potentially produce acetic acid more efficiently than ethanol-oxidizers like Acetobacter. However, Clostridium bacteria are less acid-tolerant than Acetobacter. Even the most acid-tolerant Clostridium strains can produce vinegar of only a few per cent acetic acid, compared to Acetobacter strains that can produce vinegar of up

to 20% acetic acid. At present, it remains more cost-effective to produce vinegar using Acetobacter than to produce it using Clostridium and then concentrate it. As a result, although acetogenic bacteria have been known since 1940, their industrial use remains confined to a few niche applications.

6 - Uses

Acetic acid is a chemical reagent for the production of chemical compounds. The largest single use of acetic acid is in the production of vinyl acetate monomer, closely followed by acetic anhydride and ester production. The volume of acetic acid used in vinegar is comparatively small.

6 – 1 - Vinyl acetate monomer

The major use of acetic acid is for the production of vinyl acetate monomer (VAM). This application consumes approximately 40 % to 45 % of the world's production of acetic acid. The reaction is of ethylene and acetic acid with oxygen over a palladium catalyst.

$$2\ H_3C{-}\ COOH + 2\ C_2H_4 + O_2 \rightarrow$$
$$2\ H_3C{-}\ CO - O - CH = CH_2 + 2\ H_2O$$

Vinyl acetate can be polymerized to polyvinyl acetate or to other polymers, which are components in paints and adhesives.

6 – 2 - Ester production

The major esters of acetic acid are commonly used solvents for inks, paints and coatings. The esters include ethyl acetate, n-butyl acetate, isobutyl acetate, and propyl acetate. They are typically produced by catalysed reaction from acetic acid and the corresponding alcohol:

$$H_3C\text{-}\ COOH + HO\ \text{-}\ R \rightarrow$$
$$H3C\text{-}\ CO\ \text{-}\ O\ \text{-}\ R + H_2O,$$

(R = a general alkyl group)

Most acetate esters, however, are produced from acetaldehyde using the Tishchenko reaction. In addition, ether acetates are used as solvents for nitrocellulose, acrylic lacquers, varnish removers, and wood stains. First, glycol monoethers are produced from ethylene oxide or propylene oxide with alcohol, which are then esterified with acetic acid. The three major products are ethylene glycol monoethyl ether acetate (EEA), ethylene glycol monobutyl ether acetate (EBA), and propylene glycol monomethyl ether acetate (PMA, more commonly known as PGMEA in semiconductor manufacturing processes, where it is used as a resist solvent). This application consumes about 15 % to 20 % of worldwide acetic acid. Ether acetates, for example EEA, have been shown to be harmful to human reproduction.

6 – 3 - Acetic anhydride

The product of the condensation of two molecules of acetic acid is acetic anhydride. The worldwide production of acetic anhydride is a major application, and uses approximately 25 % to 30 % of the global production of acetic acid. The main process involves dehydration of acetic acid to give ketene, which condenses with acetic acid to give the anhydride:

$CH_3CO_2H \rightarrow CH_2= C= O + H_2O$

$CH_3CO_2H + CH2= C= O \rightarrow (CH_3CO)_2O$

Acetic anhydride is an acetylation agent. As such, its major application is for cellulose acetate, a synthetic textile also used for photographic film. Acetic anhydride is also a reagent for the production of heroin and other compounds.

6 – 4 - Vinegar

Vinegar is typically 4 - 18 % acetic acid by mass. Vinegar is used directly as a condiment, and in the pickling of vegetables and other foods. Table vinegar tends to be more diluted (4 % to 8 % acetic acid), while commercial food pickling employs solutions that are more concentrated. The amount of acetic acid used as vinegar on a worldwide scale is not large, but is by far the oldest and best-known application.

6 – 5 - Use as solvent

Glacial acetic acid is an excellent polar protic solvent, as noted above. It is frequently used as a solvent for recrystallization to purify organic compounds. Acetic acid is used as a solvent in the production of terephthalic acid (TPA), the raw material for polyethylene terephthalate (PET). In 2006, about 20 % of acetic acid is used for TPA production.

Acetic acid is often used as a solvent for reactions involving carbocations, such as Friedel-Crafts alkylation. For example, one stage in the commercial manufacture of synthetic camphor involves a Wagner-Meerwein rearrangement of camphene to isobornyl acetate; here acetic acid acts both as a solvent and as a nucleophile to trap the rearranged carbocation. Acetic acid is the solvent of choice when reducing an aryl nitro-group to aniline using palladium-on-carbon.

Glacial acetic acid is used in analytical chemistry for the estimation of weakly alkaline substances such as organic amides. Glacial acetic acid is a much weaker base than water, so the amide behaves as a strong base in this medium. It then can be titrated using a solution in glacial acetic acid of a very strong acid, such as perchloric acid.

6 – 6 - Niche applications

Dilute solutions of acetic acids are also used as a stop bath during the development of photographic films, and in descaling agents to remove limescale from taps and kettles. In the clinical laboratory dilute acetic acid lyse red blood cells in order to facilitate microscopic examination.

Acetic acid in the form of household vinegar is often used to clean indoor climbing holds of chalk (magnesium carbonate).

The acidity is also used for treating the sting of the box jellyfish by disabling the stinging cells of the jellyfish, preventing serious injury or death if applied immediately, and for treating outer ear infections in people in preparations such as Vosol. In this manner, acetic acid is used as a spray-on preservative for livestock silage, to

discourage bacterial and fungal growth. Acetic acid vapour is used for the fumigation of bee hives to control Nosema and other pests.

Glacial acetic acid is also used as a wart and verruca remover.

Organic or inorganic salts are produced from acetic acid, including:

Sodium acetate, used in the textile industry and as a food preservative (E262) .

Copper (II) acetate, used as a pigment and a fungicide.

Aluminium acetate and iron (II) acetate — used as mordants for dyes.

Palladium (II) acetate, used as a catalyst for organic coupling reactions such as the Heck reaction.

Silver acetate, used as a pesticide.

Substituted acetic acids produced include :

Chloroacetic acid (monochloroacetic acid, MCA), dichloroacetic acid (considered a by-product), and trichloroacetic acid. MCA is used in the manufacture of indigo dye.

Bromoacetic acid, which is esterified to produce the reagent ethyl bromoacetate.

Trifluoroacetic acid, which is a common reagent in organic synthesis.

Amounts of acetic acid used in these other applications together (apart from TPA) account for another 5–10 % of acetic acid use worldwide. These applications are, however, not expected to grow as much as TPA production. Diluted acetic acid is also used in physical therapy to break up nodules of scar tissue via iontophoresis.

7 - Safety

Concentrated acetic acid is corrosive to skin and must, therefore, be handled with appropriate care, since it can cause skin burns, permanent eye damage, and irritation to the mucous membranes. These burns or blisters may not appear until hours after exposure. Latex gloves offer no protection, so specially resistant gloves, such as those made of nitrile rubber, are worn when handling the compound. Concentrated acetic acid can be ignited with difficulty in the laboratory. It becomes a flammable risk if the ambient temperature exceeds 39 °C . and can form explosive mixtures with air above this temperature (explosive limits: 5.4 – 16%).

The hazards of solutions of acetic acid depend on the concentration. The following table lists the EU classification of acetic acid solutions:

Safety symbol

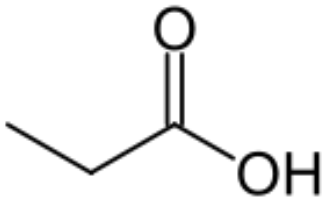
Concentration by weight	Classification
10 –25 %	Irritant (Xi)
25 – 90 %	Corrosive (C)
> 90 %	Corrosive (C) Flammable (F)

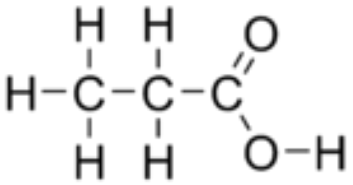
Solutions at more than 25% acetic acid are handled in a fume hood because of the pungent, corrosive vapour. Dilute acetic acid, in the form of vinegar, is harmless. However, ingestion of stronger solutions is dangerous to human and animal life. It can cause severe

damage to the digestive system, and a potentially lethal change in the acidity of the blood.

Due to incompatibilities, it is recommended to keep acetic acid away from chromic acid, ethylene glycol, nitric acid, perchloric acid, permanganates, peroxides and hydroxyls.

Propanoic Acid





Contents

1 - Introduction

Propanoic acid (also known as propionic acid from the Greek words protos = "first" and pion = "fat) is a naturally occurring carboxylic acid with chemical formula CH3CH2COOH. It is a clear liquid with a pungent odor. The anion CH3CH2COO− as well as the salts and esters of propanoic acid are known as propanoates (or propionates).

IUPAC name ; propanoic acid	
Other names : ethane carboxylic acid , propionic acid	
Molecular formula	$C_3 H_6 O_2$
Molar mass	74 g mol−1
Appearance	colourless liquid
Odor	slightly rancid
Density	0.99 g/cm³
Melting point	−21 °C
Boiling point	141 °C
Solubility in water	miscible

Viscosity	10 mPa·s
Main hazards	Corrosive
Flash point	54 °C
Auto ignition temperature	512 °C

2 - History

Propanoic acid was first described in 1844 by Johann Gottlieb, who found it among the degradation products of sugar. Over the next few years, other chemists produced propanoic acid in various other ways, none of them realizing they were producing the same substance. In 1847, the French chemist Jean-Baptiste Dumas established that all the acids were the same compound, which he called propionic acid, from the Greek words protos = "first" and pion = "fat", because it was the smallest H(CH2)nCOOH acid that exhibited the properties of the other fatty acids, such as producing an oily layer when salted out of water and having a soapy potassium salt.

3 - Properties

Propanoic acid has physical properties intermediate between those of the smaller carboxylic acids, formic and acetic acids, and the larger fatty acids. It is miscible with water, but can be removed from water by adding salt. As with acetic and formic acids, it consists of hydrogen bonded pairs of molecules both as the liquid and vapor.

Propanoic acid displays the general properties of carboxylic acids: it can form amide, ester, anhydride, and chloride derivatives. It can undergo alpha-halogenation with bromine in the presence of PBr3 as catalyst (the HVZ reaction) to form CH3CHBrCOOH.

4 - Production

In industry, propanoic acid is mainly produced by the hydrocarboxylation of ethylene using nickel carbonyl as the catalyst:

$$H_2C{=}\ CH_2 + H_2O + CO \rightarrow CH_3CH_2CO_2H$$

It is also produced by the aerobic oxidation of propionaldehyde. In the presence of cobalt or manganese ions, this reaction proceeds rapidly at temperatures as mild as 40 –50 °C:

$$CH_3CH_2CHO + ½\ O_2 \rightarrow CH_3CH_2COOH.$$

Large amounts of propanoic acid were once produced as a byproduct of acetic acid manufacture. Currently the world's largest producer of propanoic acid is BASF, with approximately 80 kt/a production capacity.

Propanoic acid is produced biologically as its coenzyme A ester, propionyl-CoA, from the metabolic breakdown of fatty acids containing odd numbers of carbon atoms, and also from the breakdown of some amino acids. Bacteria of the genus Propionibacterium produce propanoic acid as the end product of their anaerobic metabolism. This class of bacteria is commonly found in the stomachs of ruminants and the sweat glands of humans, and their activity is partially responsible for the odor of both Swiss cheese and sweat.

5 - Uses

Propanoic acid inhibits the growth of mold and some bacteria at the levels between 0.1 and 1% by weight. As a result, most propanoic acid produced is consumed as a preservative for both animal feed and food for human consumption. For animal feed, it is used either directly or as its ammonium salt. The antibiotic Monensin is added to cattle feed to favor propionibacteria over acetic acid producers in the rumen; this produces less carbon dioxide and feed conversion is better. This application accounts for about half of the world production of propanoic acid. Another major application is as a preservative in baked goods, which use the sodium and calcium salts. As a food additive it is approved for use in the EU, USA and Australia and New Zealand . It is listed by its INS number (280) or E number E280.

Propanoic acid is also useful as an intermediate in the production of other chemicals, especially polymers. Cellulose-acetate-propionate is a useful thermoplastic. Vinyl propionate is also used. In more specialized applications, it is also used to make pesticides and pharmaceuticals. The esters of propanoic acid have fruit-like odors and are sometimes used as solvents or artificial flavorings.

6 - Metabolism

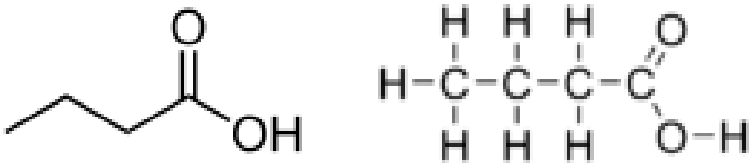
The metabolism of propanoic acid begins with its conversion to propionyl coenzyme A (propionyl- CoA), the usual first step in the metabolism of carboxylic acids. Since propanoic acid has three carbons, propionyl-CoA cannot directly enter either beta oxidation or the citric acid cycles. In most vertebrates, propionyl-CoA is carboxylated to D-methylmalonyl - CoA , which is isomerised to L-methylmalonyl- CoA. A vitamin B12- dependent enzyme catalyzes rearrangement of L-methylmalonyl- CoA to succinyl-CoA, which is an intermediate of the citric acid cycle and can be readily incorporated there.

In propanoic acidemia, a rare inherited genetic disorder, propionate acts as a metabolic toxin in liver cells by accumulating in mitochondria as propionyl-CoA and its derivative, methylcitrate, two tricarboxylic acid cycle inhibitors. Propanoate is metabolized oxidatively by glia, which suggests astrocytic vulnerability in propanoic acidemia when intramitochondrial propionyl-CoA may accumulate. Propanoic acidemia may alter both neuronal and glial gene expression by affecting histone acetylation.[6][7] When propanoic acid is infused directly into rodents brains it produces reversible behavior (e.g., hyperactivity, dystonia, social impairment, perseveration) and brain (e.g., innate neuroinflammation, glutathione depletion) changes that may be used as a means to model autism in rats.

6 – 1 - Human occurrence

The human skin is host of several species of bacteria known as Propionibacteria, which are named after their ability to produce propanoic acid. The most notable one is the Propionibacterium acnes, which lives mainly in the sebaceous glands of the skin and is one of the principal causes of acne.

Butyric Acid



Contents

1 - Introduction

Butyric acid (from Greek meaning "butter"), also known under the systematic name butanoic acid, is a carboxylic acid with the structural formula $CH_3CH_2CH_2$-COOH. Salts and esters of butyric acid are known as butyrates or butanoates. Butyric acid is found in milk, especially goat, sheep and buffalo's milk, butter, Parmesan cheese, and as a product of anaerobic fermentation (including in the colon and as body odor). It has an unpleasant smell and acrid taste, with a sweetish aftertaste (similar to ether). It can be detected by mammals with good scent detection abilities (such as dogs) at 10 ppb, whereas humans can detect it in concentrations above 10 ppm.

Butyric acid was first observed (in impure form) in 1814 by the French chemist Michel Eugène Chevreul. By 1818, he had purified it sufficiently to characterize it . The name of butyric acid comes from the Latin word for butter, butyrum (or buturum), the substance in which butyric acid was first found.

IUPAC name ; Butanoic acid	
Other names : Butyric acid ; 1-Propanecarboxylic acid ; Propane carboxylic acid ; C4 : 0 (Lipid numbers)	
Molecular formula	$C_4 H_8 O_2$
Molar mass	88 g mol−1
Appearance	Colorless liquid
Density	0.9595 g / mL
Melting point	− 7.9 °C
Boiling point	163.5 °C
Solubility in water	miscible
Acidity (pKa)	4.82
Refractive index (nD)	1.3980 (19 °C)
Viscosity	0.1529 cP
EU classification	 Xn  C
Flash point	72 °C
Auto ignition temperature	452 °C

2 - Chemistry

Butyric acid is a fatty acid occurring in the form of esters in animal fats. The triglyceride of butyric acid makes up 3% to 4% of butter. When butter goes rancid, butyric acid is liberated from the glyceride by hydrolysis, leading to the unpleasant odor. It is an important member of the fatty acid subgroup called short- chain fatty acids. Butyric acid is a medium-strong acid that reacts with bases and strong oxidants, and attacks many metals.

The acid is an oily, colorless liquid that is easily soluble in water, ethanol, and ether, and can be separated from an aqueous phase by saturation with salts such as calcium chloride. It is oxidized to carbon dioxide and acetic acid using potassium dichromate and sulfuric acid, while alkaline potassium permanganate oxidizes it to

carbon dioxide. The calcium salt, $Ca(C_4H_7O_2)_2 \cdot H_2O$, is less soluble in hot water than in cold.

Butyric acid has a structural isomer called isobutyric acid (2-methylpropanoic acid).

3 - Production

It is industrially prepared by the fermentation of sugar or starch, brought about by the addition of putrefying cheese, with calcium carbonate added to neutralize the acids formed in the process. The butyric fermentation of starch is aided by the direct addition of Bacillus subtilis. Salts and esters of the acid are called butyrates or butanoates.

Butyric acid or fermentation butyric acid is also found as a hexyl ester hexyl butyrate in the oil of Heracleum giganteum (a type of hogweed) and as the octyl ester octyl butyrate in parsnip (Pastinaca sativa); it has also been noticed in skin flora and perspiration.

4 - Uses

Butyric acid is used in the preparation of various butyrate esters. Low-molecular-weight esters of butyric acid, such as methyl butyrate, have mostly pleasant aromas or tastes. As a consequence, they find use as food and perfume additives. It is also used as an animal feed supplement, due to the ability to reduce pathogenic bacterial colonization.[3] It is an approved food flavoring in the EU FLAVIS database (number 08.005).

Due to its powerful odor, it has also been used as a fishing bait additive . Many of the commercially available flavors used in carp (Cyprinus carpio) baits use butyric acid as their ester base; however, it is not clear whether fish are attracted by the butyric acid itself or the substances added to it. Butyric acid was, however, one of the few organic acids shown to be palatable for both tench and bitterling.

The substance has also been used as a stink bomb by Sea Shepherd Conservation Society to disrupt Japanese whaling crews, as well as by anti-abortion protesters to disrupt abortion clinics.

5 - Biochemistry

5 – 1 - Biosynthesis

Butyrate is produced as end - product of a fermentation process solely performed by obligate anaerobic bacteria. Fermented Kombucha "tea" includes butyric acid as a result of the fermentation. This fermentation pathway was discovered by Louis Pasteur in 1861. Examples of butyrate-producing species of bacteria :

Clostridium butyricum
Clostridium kluyveri
Clostridium pasteurianum
Fusobacterium nucleatum
Butyrivibrio fibrisolvens
Eubacterium limosum

The pathway starts with the glycolytic cleavage of glucose to two molecules of pyruvate, as happens in most organisms. Pyruvate is then oxidized into acetyl coenzyme A using a unique mechanism that involves an enzyme system called pyruvate - ferredoxin oxidoreductase. Two molecules of carbon dioxide (CO2) and two molecules of elemental hydrogen (H2) are formed as waste products from the cell. Then,

Action	Responsible enzyme
Acetyl coenzyme A converts into acetoacetyl coenzyme A	acetyl-CoA-acetyl transferase
Acetoacetyl coenzyme A converts into β-hydroxybutyryl CoA	β-hydroxybutyryl-CoA dehydrogenase
β-hydroxybutyryl CoA converts into crotonyl CoA	crotonase
Crotonyl CoA converts into butyryl CoA (CH3CH2CH2C=O-CoA)	butyryl CoA dehydrogenase
A phosphate group replaces CoA to form butyryl phosphate	phosphobutyrylase
The phosphate group joins ADP to form ATP and butyrate	butyrate kinase

ATP is produced, as can be seen, in the last step of the fermentation. Three molecules of ATP are produced for each glucose molecule, a relatively high yield. The balanced equation for this fermentation is

$$C_6H_{12}O_6 \rightarrow C_4H_8O_2 + 2CO_2 + 2H_2.$$

Several species form acetone and n-butanol in an alternative pathway, which starts as butyrate fermentation. Some of these species are :

Clostridium acetobutylicum, the most prominent acetone and propianol producer, used also in industry
Clostridium beijerinckii
Clostridium tetanomorphum
Clostridium aurantibutyricum

These bacteria begin with butyrate fermentation, as described above, but, when the pH drops below 5, they switch into butanol and acetone production to prevent further lowering of the pH. Two molecules of butanol are formed for each molecule of acetone.

The change in the pathway occurs after acetoacetyl CoA formation. This intermediate then takes two possible pathways:

acetoacetyl CoA → acetoacetate → acetone
acetoacetyl CoA → butyryl CoA → butanal → butanol

Highly-fermentable fiber residues, such as those from resistant starch, oat bran, pectin, and guar are transformed by colonic bacteria into short-chain fatty acids (SCFA) including butyrate, producing more SCFA than less fermentable fibers such as celluloses.[8] One study found that resistant starch consistently produces more butyrate than other types of dietary fiber. The production of SCFA from fibers in ruminant animals such as cattle is responsible for the butyrate content of milk and butter.

5 – 2 - Cancer

The role of butyrate changes differs between normal and cancerous cells. This is known as the "butyrate paradox". Butyrate inhibits colonic tumor cells, and promotes healthy colonic epithelial cells;[11] but the signaling mechanism is not well understood.[12] A review suggested the chemopreventive benefits of butyrate depend in part on amount, time of exposure with respect to the tumorigenic process, and the type of fat in the diet. The production of volatile fatty acids such as butyrate from fermentable fibers may contribute to the role of dietary fiber in colon cancer.

Butyric acid can act as an HDAC inhibitor, inhibiting the function of histone deacetylase enzymes, thereby favoring an acetylated state of histones in the cell. Acetylated histones have a lower affinity for DNA than nonacetylated histones, due to the neutralization of electrostatic charge interactions. In general, it is thought that transcription factors will be unable to access regions where histones are tightly associated with DNA (i.e., nonacetylated, e.g., heterochromatin). Therefore, butyric acid is thought to enhance the transcriptional activity at promoters, which are typically silenced or downregulated due to histone deacetylase activity.

Two HDAC inhibitors, sodium butyrate (NaB) and trichostatin A (TSA), increase lifespan in experimental animals.

Butyrate is a major metabolite in colonic lumen arising from bacterial fermentation of dietary fiber and has been shown to be a critical mediator of the colonic inflammatory response. Butyrate possesses both preventive and therapeutic potential to counteract inflammation-mediated ulcerative colitis (UC) and colorectal cancer. One mechanism underlying butyrate function in suppression of colonic inflammation is inhibition of the IFN-γ/STAT1 signaling pathways at least partially through acting as a histone deacetylase (HDAC) inhibitor. While transient IFN-γ signaling is generally associated with normal host immune response, chronic IFN-γ signaling is often associated with chronic inflammation. It has been shown that Butyrate inhibits activity of HDAC1 that is bound to the

Fas gene promoter in T cells, resulting in hyperacetylation of the Fas promoter and up-regulation of Fas receptor on the T cell surface.[14] It is thus suggested that Butyrate enhances apoptosis of T cells in the colonic tissue and threby eliminates the source of inflammation (IFN-γ production).

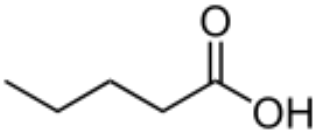
6 - Safety

The United States Environmental Protection Agency rates and regulates butyric acid as a toxic substance.

Personal protective equipment such as rubber or PVC gloves, protective eye goggles, and chemical-resistant clothing and shoes are used to minimize risks when handling butyric acid.

Inhalation of butyric acid may result in soreness of throat, coughing, a burning sensation and laboured breathing. Ingestion of the acid may result in abdominal pain, shock, and collapse. Physical exposure to the acid may result in pain, blistering and skin burns, while exposure to the eyes may result in pain, severe deep burns and loss of vision.

Valeric Acid



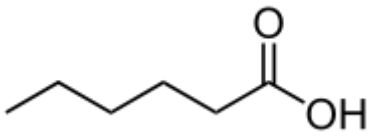
1 – Introduction ;

Valeric acid, or pentanoic acid, is a straight - chain alkyl carboxylic acid with the chemical formula $C_5H_{10}O_2$. Like other low-molecular-weight carboxylic acids, it has a very unpleasant odor. It is found naturally in the perennial flowering plant valerian (Valeriana officinalis), from which it gets its name. Its primary use is in the synthesis of its esters. Volatile esters of valeric acid tend to have pleasant odors and are used in perfumes and cosmetics. Ethyl valerate and pentyl valerate are used as food additives because of their fruity flavors.

Valeric acid appears similar in structure to GHB and the neurotransmitter GABA in that it is a short-chain carboxylic acid, although it lacks the alcohol and amine functional groups that contribute to the biological activities of GHB and GABA, respectively. It differs from valproic acid simply by lacking a 3-carbon side - chain.

IUPAC name : Pentanoic acid	
Other names :	
Valeric	acid
Butane-1-carboxylic	acid
Valerianic acid	
Molecular formula	$C_5 H_{10} O_2$
Molar mass	102 g mol−1
Appearance	Colorless liquid
Density	0.930 g / cm³
Melting point	−34.5 °C
Boiling point	186 - 187 °C,
Solubility in water	4.97 g / 100 mL
Flash point	86 °C

Hexanoic Acid



Hexanoic acid (caproic acid), is the carboxylic acid derived from hexane with the general formula $C_5H_{11}COOH$. It is a colorless oily liquid with an odor that is fatty, cheesy, waxy, and like that of goats[1] or other barnyard animals. It is a fatty acid found naturally in various animal fats and oils, and is one of the chemicals that give the decomposing fleshy seed coat of the ginkgo its characteristic unpleasant odor. The primary use of hexanoic acid is in the manufacture of its esters for artificial flavors, and in the manufacture of hexyl derivatives, such as hexylphenols.

The salts and esters of this acid are known as hexanoates or caproates.

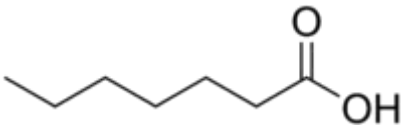
Two other acids are named after goats: caprylic (C8) and capric (C10). Along with hexanoic acid, these total 15% in goat milk fat.

Caproic, caprylic, and capric acids (capric is a crystal- or wax-like substance, whereas the other two are mobile liquids) are not only used for the formation of esters, but also commonly used "neat" in: butter, milk, cream, strawberry, bread, beer, nut, and other flavors.

IUPAC name ; Hexanoic acid	
Other names : Caproic acid ; n - Caproic acid ; C6:0 (Lipid numbers)	
Molecular formula	$C_6 H_{12} O_2$
Molar mass	116 g mol−1
Appearance	Oily liquid
Odor	goat-like

Density	0.929 g / cm3
Melting point	− 3.4 °C
Boiling point	205.8 °C
Solubility in water	1.082 g / 100 mL
Solubility	soluble in ethanol , ether
Refractive index (nD)	1.4170
Viscosity	3.1 mP
Flash point	103 °C
Auto ignition temperature	380 °C
Explosive limits	1.3 - 9.3 %
LD50	3000 mg / kg (rat , oral)

Heptanoic Acid



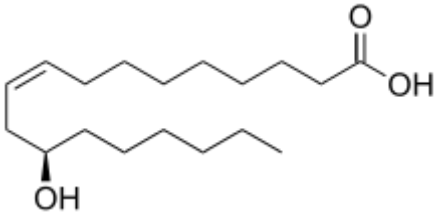
1 - Introduction

Heptanoic acid, also called enanthic acid, is an organic compound composed of a seven - carbon chain terminating in a carboxylic acid. It is an oily liquid with an unpleasant, rancid odor. It contributes to the odor of some rancid oils. It is slightly soluble in water, but very soluble in ethanol and ether.

IUPAC name : Heptanoic acid	
Other names : Enanthic acid ; Oenanthic acid; n-Heptylic acid ; n-Heptoic acid	
Molecular formula	$C_7 H_{14} O_2$
Molar mass	130 g mol−1
Appearance	Oily liquid
Density	0.9181 g / cm3 (20 °C)
Melting point	-7.5 °C
Boiling point	223 °C
Solubility in water	0.2419 g / 100 mL (15 °C)

2 - Production and uses

The methyl ester of ricinoleic acid, obtained from castor bean oil is the main commercial precursor to heptanoic acid. It is hydrolyzed to the methyl ester of [[undecenoic acid]] and heptanal, which is then air oxidized to the carboxylic acid. Approximately 20,000 tons were consumed in Europe and US in 1980.

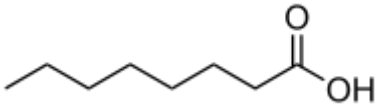


Ricinoleic acid is the main precursor to heptanoic acid.

Heptanoic acid is used in the preparation of esters, such as ethyl heptanoate, which are used in fragrances and as artificial flavors.

Heptanoic acid is used to esterify steroids in the preparation of drugs such as as testosterone enanthate, trenbolone enanthate, drostanolone enanthate and methenolone enanthate (Primobolan). It is also one of many additives in cigarettes.

Caprylic Acid



1 - Introduction

Caprylic acid is the common name for the eight-carbon saturated fatty acid known by the systematic name octanoic acid. It is found naturally in the milk of various mammals, and it is a minor constituent of coconut oil and palm kernel oil.[3] It is an oily liquid that is minimally soluble in water with a slightly unpleasant rancid-like smell and taste.

Two other acids are named after goats: caproic (C6) and capric (C10). Along with caprylic acid these total 15 % in goat milk fat.

IUPAC name : Octanoic Acid	
Other names ; C8 : 0 (Lipid numbers)	
Molecular formula	$C_8 H_{16} O_2$
Molar mass	144 g / mol
Appearance	Oily colorless liquid
Density	0.910 g / cm3
Melting point	16.7 °C
Boiling point	239.7 °C
Solubility in water	0.068 g /100 mL
LD50	10.08 g / kg (orally in rats)

2 - Uses

Caprylic acid is used commercially in the production of esters used in perfumery and also in the manufacture of dyes.

Caprylic acid is also used in the treatment of some bacterial infections. Due to its relatively short chain length it has no difficulty in penetrating fatty cell wall membranes, hence its effectiveness in

combating certain lipid-coated bacteria, such as Staphylococcus aureus and various species of Streptococcus.

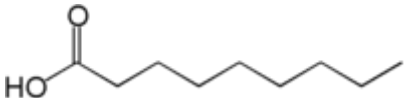
Caprylic acid is an antimicrobial pesticide used as a food contact surface sanitizer in commercial food handling establishments on dairy equipment, food processing equipment, breweries, wineries, and beverage processing plants. It is also used as disinfectant in health care facilities, schools/colleges, animal care/veterinary facilities, industrial facilities, office buildings, recreational facilities, retail and wholesale establishments, livestock premises, restaurants, and hotels/motels. In addition, caprylic acid is used as an algaecide, bactericide, and fungicide in nurseries, greenhouses, garden centers, and interiorscapes on ornamentals. Products containing caprylic acid are formulated as soluble concentrate/liquids and ready-to-use liquids.

For ghrelin to have a hunger-stimulating action on a hypothalamus, caprylic acid must be linked to a serine residue at the 3-position of ghrelin. To cause hunger, it must acylate a - OH group. Other fatty acids in the same position have similar effects on hunger.

The octanoic acid breath test is used to measure gastric emptying. Some potential benefit is possible from administration of octanoic acid for patients with essential tremor.

The acid chloride of caprylic acid is used in the synthesis of perfluorooctanoic acid.

Nonanoic Acid



Nonanoic acid , also called pelargonic acid, is an organic compound composed of a nine - carbon chain terminating in a carboxylic acid with structural formula CH3(CH2)7COOH. Nonanoic acid forms esters—nonanoates. It is a clear, oily liquid with an unpleasant, rancid odor. It is nearly insoluble in water, but very soluble in chloroform, ether, and hexane.

Its refractive index is 1.4322. Its critical point is at 712 K (439 °C) and 2.35 MPa.

IUPAC name : Nonanoic Acid	
Other names ; Pelargonic acid , 1- Octane carboxylic acid	
Molecular formula	$C_9 H_{18} O_2$
Molar mass	158 g / mol
Appearance	Clear to yellowish oily liquid
Density	0.900 g / cm3
Melting point	12.5 °C
Boiling point	254 °C
Solubility in water	0.3 g / l
Main hazards	Corrosive (C)
Flash point	114 °C
Auto ignition temperature	405 °C

2 - Occurrence and uses

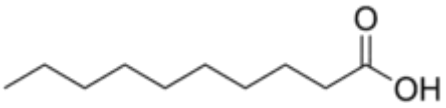
Nonanoic acid is a fatty acid which occurs naturally as esters in the oil of pelargonium. Synthetic esters, such as methyl nonanoate, are used as flavorings.

Nonanoic acid is also used in the preparation of plasticizers and lacquers.

The derivative 4-nonanoylmorpholine is an ingredient in some pepper sprays.

The ammonium salt of nonanoic acid, ammonium nonanoate, is used as an herbicide.

Decanoic Acid



Contents

1 - Introduction

Decanoic acid, or capric acid, is a saturated fatty acid. Its formula is CH3(CH2)8COOH. Salts and esters of decanoic acid are called decanoates or "caprates". The term capric acid arises from the Latin "capric" which pertains to goats due to their olfactory similarities.

Capric acid occurs naturally in coconut oil (about 10%) and palm kernel oil (about 4 %), otherwise it is uncommon in typical seed oils.[4] It is found in the milk of various mammals and to a lesser extent in other animal fats.

Two other acids are named after goats: caproic (a C6 fatty acid) and caprylic (a C8 fatty acid). Along with decanoic acid, these total 15 % in goat milk fat.

IUPAC name : Decanoic acid

Other names :
Capric acid
n - Capric acid
n- Decanoic acid
Decylic acid
n- Decylic acid
C10 : 0 (Lipid numbers)

Molecular formula $C_{10}H_{20}O_2$

Molar mass	172 g mol−1
Appearance	White crystals with strong smell
Density	0.893 g / cm3
Melting point	31.6 °C
Boiling point	269 °C
Solubility in water	immiscible
Main hazards	Medium toxicity May cause respiratory irritation May be toxic on ingestion May be toxic on skin contact

2 - Production

Decanoic acid can be prepared from oxidation of primary alcohol decanol, by using chromium trioxide (CrO3) oxidant under acidic conditions.

Neutralization of decanoic acid or saponification of its esters, typically triglycerides, with sodium hydroxide will give sodium decanoate. This salt (CH3(CH2)8COO-Na+) is a component of some types of soap.

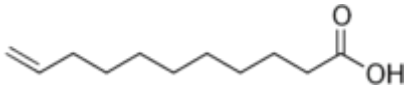
3 - Use

Manufacturing of esters for artificial fruit flavors and perfumes. Also as an intermediate in chemical syntheses. It is used in organic synthesis and industrially in the manufacture of perfumes, lubricants, greases, rubber, dyes, plastics, food additives and pharmaceuticals.

3 – 1 - Pharmaceuticals

Decanoate salts and esters of various drugs are available. Since decanoic acid is a fatty acid, forming a salt or ester with a drug will increase its lipophilicity and its affinity for fatty tissue. Since distribution of a drug from fatty tissue is usually slow, one may develop a long-acting injectable form of a drug (called a Depot injection) by using its decanoate form. Some examples of drugs available as a decanoate ester or salt include nandrolone, fluphenazine, bromperidol, haloperidol and vanoxerine.

Undecylenic Acid



Contents

1 - Introduction

Undecylenic acid is an organic unsaturated fatty acid derived from castor oil. It is the common name of 10-undecenoic acid, ($CH_2CH(CH_2)_8COOH$). It is used in the manufacture of pharmaceuticals, cosmetics and perfumery, including antidandruff shampoos , antimicrobial powders and as a musk in perfumes and aromas. Undecylenic acid is produced by cracking of castor oil under pressure.

IUPAC name : undec – 10 - enoic acid	
Molecular formula	$C_{11}H_{20}O_2$
Molar mass	184 g mol−1

2 - Medicinal uses

Undecylenic acid is also FDA - approved for over-the-counter use on skin disorders or skin problems. Castor oil penetrates deep into the skin due to its molecular mass, which is low enough to penetrate into the stratum corneum. Castor isostearate succinate is a polymeric mixture of esters with isostearic acid and succinic acid used for skin conditioning, such as in shampoo, lipstick and lip balm.

Undecylenic acid is the active ingredient in medications for skin infections, and relieves itching, burning, and irritation. For example, it is used against fungal skin infections, such as athlete's foot, ringworm, jock itch or Candida albicans.[5] When used for jock itch, it can result in extreme burning, as the skin is rather sensitive. It is also used in the

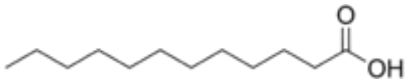
treatment of psoriasis. Undecylenic acid has antiviral properties that are effective on skin infections such as herpes simplex.

At least one of the mechanisms underlying its antifungal effects observed is its inhibition of morphogenesis of Candida albicans. In a study on denture liners, undecylenic acid in the liners was found to inhibit conversion of yeast to the hyphal form. Hyphae were associated with active infection. The mechanisms of action appear to be interference with fatty acid biosynthesis, which can inhibit germ tube (hyphae) formation. Medium-chain fatty acids have also been shown to disrupt the pH of the cell cytoplasm by being proton carriers, which interferes with viral replication mechanisms in infected cells. The mechanism of action and effectiveness in fatty acid based antifungals is dependent on the number of carbon atoms in the chain, being more effective as the number of atoms in the chain increases (Undecylenic acid has 11).

3 - Other uses

Undecylenic acid can be used in silicon-based biosensors. Monolayers can be made on bare silicon transducer surfaces with the help of covalent bonds between silicon atom and the double bonds of undecylenic acid. The carboxylic acid groups remain available for the conjugation of biomolecules such as DNA or proteins.

Lauric Acid



Contents

1 - Introduction

Lauric acid (systematically: dodecanoic acid) , the saturated fatty acid with a 12-carbon atom chain, thus falling into the medium chain fatty acids, is a white, powdery solid with a faint odor of bay oil or soap.

IUPAC name ; dodecanoic acid	
Other names : n-Dodecanoic acid ; Dodecylic acid ; Dodecoic acid ; Lauro stearic acid;Vulvic acid ; 1- Undecane carboxylic acid ; Duodecylic acid; C12:0 (Lipid numbers)	
Molecular formula	$C_{12}H_{24}O_2$
Molar mass	200
Appearance	white powder
Odor	slight odor of bay oil
Density	0.880 g / cm3
Melting point	43.2 °C

Boiling point	298.9 °C
Solubility in water	0.006 g / 100 mL (20 °C)
Refractive index (nD)	1.423
Viscosity	7.30 mPa·s at 323 K
Flash point	≥ 110 °C

2 - Occurrence

Lauric acid, as a component of triglycerides, comprises about half of the fatty acid content in coconut oil, laurel oil, and in palm kernel oil (not to be confused with palm oil) , Otherwise it is relatively uncommon. It is also found in human breast milk (6.2 % of total fat), cow's milk (2.9%), and goat's milk (3.1 %).

3 - Properties

Like many other fatty acids, lauric acid is inexpensive, has a long shelf-life, and is non-toxic and safe to handle. It is mainly used for the production of soaps and cosmetics. For these purposes, lauric acid is neutralized with sodium hydroxide to give sodium laurate, which is a soap. Most commonly, sodium laurate is obtained by saponification of various oils, such as coconut oil. These precursors give mixtures of sodium laurate and other soaps.

3 – 1 - Niche uses

In the laboratory, lauric acid is often used to investigate the molar mass of an unknown substance via the freezing-point depression. Lauric acid is convenient because its melting point when pure is relatively high (43.2 °C). Its cryoscopic constant is 3.9 K·kg/mol. By melting lauric acid with the unknown substance, allowing it to cool, and recording the temperature at which the mixture freezes, the molar mass of the unknown compound may be determined.

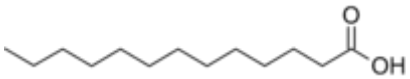
3 – 2 - Potential medicinal properties

Lauric acid has been claimed to have antimicrobial properties.

Lauric acid has been found to increase total cholesterol the most of all fatty acids. But most of the increase is attributable to an increase

in high-density lipoprotein (HDL) "good" cholesterol. As a result, lauric acid has "a more favorable effect on total:HDL cholesterol than any other fatty acid, either saturated or unsaturated";[9] a lower total / HDL cholesterol ratio suggests a decrease in atherosclerotic risk.

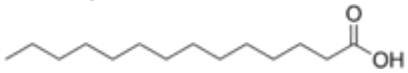
Tridecylic Acid



Tridecylic acid, or tridecanoic acid, is a 13 - carbon saturated fatty acid with the chemical formula CH3(CH2)11COOH. It is commonly found in dairy products.

IUPAC name : Tridecanoic acid	
Molecular formula	$CH_3(CH_2)_{11}COOH$
Molar mass	214 g / mol
Appearance	White crystals or powder
Melting point	40 - 45°C
Boiling point	236°C (100 mmHg)
Main hazards	Irritant (Xi)

Myristic Acid



IUPAC name : tetradecanoic acid	
Other names : C14:0 (Lipid numbers)	
Molecular formula	$C_{14}H_{28}O_2$
Molar mass	228
Density	0.8622 g / cm3
Melting point	54.4 °C
Boiling point	250.5 °C at 100 mmHg

Myristic acid, also called tetradecanoic acid , is a common saturated fatty acid with the molecular formula $CH_3(CH_2)_{12}COOH$. A myristate is a salt or ester of myristic acid.

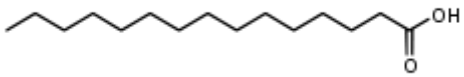
Myristic acid is named after the nutmeg Myristica fragrans. Nutmeg butter is 75 % trimyristin, the triglyceride of myristic acid. Besides nutmeg, myristic acid is also found in palm kernel oil, coconut oil, butter fat and is a minor component of many other animal fats. It is also found in spermaceti, the crystallized fraction of oil from the sperm whale.

Myristic acid is also commonly added co-translationally to the penultimate, nitrogen-terminus, glycine in receptor-associated kinases to confer the membrane localisation of the enzyme. The myristic acid has a sufficiently high hydrophobicity to become incorporated into the fatty acyl core of the phospholipid bilayer of the plasma membrane of the eukaryotic cell. In this way, myristic acid acts as a lipid anchor in biomembranes.

The ester isopropyl myristate is used in cosmetic and topical medicinal preparations where good absorption through the skin is desired.

Reduction of myristic acid yields myristyl aldehyde and myristyl alcohol.

Penta Decanoic Acid

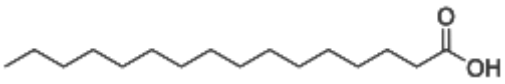


IUPAC name : pentadecanoic acid	
Other names : *n*-Pentadecanoic acid ; Pentadecylic acid	
Molecular formula	$C_{15}H_{30}O_2$
Molar mass	242 g mol^{-1}
Density	0.842 g/cm^3
Melting point	51 - 53 °C
Boiling point	257 °C (100 mmHg)

Pentadecanoic acid is a saturated fatty acid. Its molecular formula is $CH_3(CH_2)_{13}COOH$. It is rare in nature, being found at the level of 1.2 % in the milk fat from cows . The butterfat in cows milk is its major dietary source and it is used as a marker for butterfat consumption . Pentadecanoic acid also occurs in hydrogenated mutton fat.

Pentadecanoic acid may increase mother-to-child transmission of HIV through breastfeeding.

Palmitic Acid



Contents

1 - Intoduction

Palmitic acid, or hexadecanoic acid in IUPAC nomenclature, is the most common fatty acid found in animals, plants and microorganisms. Its molecular formula is $CH_3(CH_2)_{14}CO_2H$. As its name indicates, it is a major component of the oil from palm trees (palm oil, palm kernel oil, and coconut oil), but can also be found in meats, cheeses, butter, and dairy products. Palmitate is a term for the salts and esters of palmitic acid. The palmitate anion is the observed form of palmitic acid at basic pH.

Rats fed on a diet of 20 % palmitic acid and 80 % carbohydrate showed alterations in central nervous system control of insulin secretion, and suppression of the body's natural appetite - suppressing signals from leptin and insulin (the key hormones involved in weight regulation).

Aluminium salts of palmitic acid and naphthenic acid were combined during World War II to produce napalm. The word "napalm" is derived from the words naphthenic acid and palmitic acid.

IUPAC name : Hexa decanoic acid
Other names : C16:0 (Lipid numbers) , palmic acid

Molecular formula	$C_{16}H_{32}O_2$
Molar mass	256 g / mol
Appearance	White crystals
Density	0.853 g /cm3 at 62 °C
Melting point	62.9 °C
Boiling point	351-352 °C 215 °C at 15 mmHg
Solubility in water	Insoluble

2 - Occurrence and production

Palmitic acid mainly occurs as its ester in triglycerides (fats), especially palm oil but also tallow. The cetyl ester of palmitic acid (cetyl palmitate) occurs in spermaceti. It was discovered by Edmond Frémy in 1840, in saponified palm oil. Butter, cheese, milk and meat also contain this fatty acid.

Palmitic acid is prepared by treating fats and oils with water at a high pressure and temperature (above 200 °C), leading to the hydrolysis of triglycerides. The resulting mixture is then distilled.

3 - Biochemistry

Excess carbohydrates in the body are converted to palmitic acid. Palmitic acid is the first fatty acid produced during fatty acid synthesis and the precursor to longer fatty acids. Palmitate negatively feeds back on acetyl-CoA carboxylase (ACC), which is responsible for converting acetyl-CoA to malonyl-CoA, which in turn is used to add to the growing acyl chain, thus preventing further palmitate generation.[8] In biology, some proteins are modified by the addition of a palmitoyl group in a process known as palmitoylation. Palmitoylation is important for membrane localisation of many proteins.

4 - Applications

Palmitic acid is mainly used to produce soaps, cosmetics, and release agents. These applications utilize sodium palmitate, which is commonly obtained by saponification of palm oil. To this end, palm

oil, rendered from the coconut palm nut, is treated with sodium hydroxide (in the form of caustic soda or lye), which causes hydrolysis of the ester groups. This procedure affords glycerol and sodium palmitate.

Because it is inexpensive and adds texture to processed foods (convenience food), palmitic acid and its sodium salt find wide use including foodstuffs. Sodium palmitate is permitted as a natural additive in organic products.

Hydrogenation of palmitic acid yields cetyl alcohol, which is used to produce detergents and cosmetics.

Recently, a long-acting antipsychotic medication, paliperidone palmitate (marketed as INVEGA Sustenna), used in the treatment of schizophrenia, has been synthesized using the oily palmitate ester as a long-acting release carrier medium when injected intramuscularly. The underlying method of drug delivery is similar to that used with decanoic acid to deliver long-acting depot medication, in particular, neuroleptics such as haloperidol decanoate.

5 - Dietary effect

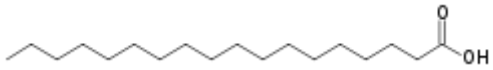
According to the World Health Organization, evidence is "convincing" that consumption of palmitic acid increases risk of developing cardiovascular diseases, placing it in the same evidence category as trans fatty acids.[10] Retinyl palmitate is an antioxidant and a source of vitamin A added to low fat milk to replace the vitamin content lost through the removal of milk fat. Palmitate is attached to the alcohol form of vitamin A, retinol, to make vitamin A stable in milk.

Hepta Decanoic Acid

Heptadecanoic acid, or margaric acid, is a saturated fatty acid. Its molecular formula is CH3(CH2)15COOH. It occurs as a trace component of the fat and milkfat of ruminants, but it does not occur in any natural animal or vegetable fat at concentrations over half a percent. Salts and esters of heptadecanoic acid are called heptadecanoates.

IUPAC name : Hepta decanoic Acid	
Other names : Margaric acid n-Margaric acid n-Heptadecanoic acid Hepta decylic acid n-Hepta decylic acid 17:0 (Lipid numbers)	
Molecular formula	$C_{17}H_{34}O_2$
Molar mass	270 g / mol
Appearance	White crystals
Density	0.853 g / cm3
Melting point	61.3 °C
Boiling point	227 °C (100 mmHg)
Solubility in water	insoluble

Stearic Acid



Contents

1 - Introduction

Stearic acid (STAIR-ik or STEER-ik) is the saturated fatty acid with an 18 carbon chain and has the IUPAC name octadecanoic acid. It is a waxy solid, and its chemical formula is $CH_3(CH_2)_{16}CO_2H$. Its name comes from the Greek word στέαρ "stéar", which means tallow. The salts and esters of stearic acid are called stearates. Stearic acid is one of the most common saturated fatty acids found in nature following palmitic acid.

IUPAC name : Octa decanoic acid	
Other names : C18:0 (Lipid numbers)	
Molecular formula	C_{18} H_{36} O_2
Molar mass	284 g mol−1
Appearance	white solid
Density	0.847 g/cm3 at 70 °C
Melting point	69.6 °C
Boiling point	383 °C
Solubility in water	3 mg / L (20 °C)
Refractive index (nD)	1.4299
Flash point	110

2 - Production

It occurs in many animal and vegetable fats and oils, but it is more abundant in animal fat (up to 30 %) than vegetable fat (typically < 5 %) . The important exceptions are cocoa butter and shea butter where the stearic acid content (as a triglyceride) is 28 – 45 %.

Stearic acid is prepared by treating these fats and oils with water at a high pressure and temperature (above 200 °C), leading to the hydrolysis of triglycerides. The resulting mixture is then distilled.[4] Commercial stearic acid is often a mixture of stearic and palmitic acids, although purified stearic acid is available.

In terms of its biosynthesis, stearic acid is produced from carbohydrates via the fatty acid synthesis machinery via acetyl-CoA .

3 - Uses

Generally applications of stearic acid exploit its bifunctional character, with a polar head group that can be attached to metal cations and a nonpolar chain that confers solubility in organic solvents. The combination leads to uses as a surfactant and softening agent. Stearic acid undergoes the typical reactions of saturated carboxylic acids, notably reduction to stearyl alcohol, and esterification with a range of alcohols.

3 – 1 - Soaps , cosmetics , detergents

Stearic acid is mainly used in the production of detergents, soaps, and cosmetics such as shampoos and shaving cream products. Soaps are not made directly from stearic acid, but indirectly by saponification of triglycerides consisting of stearic acid esters. Esters of stearic acid with ethylene glycol; glycol stearate and glycol distearate, are used to produce a pearly effect in shampoos, soaps, and other cosmetic products. They are added to the product in molten form and allowed to crystallize under controlled conditions. Detergents are obtained from amides and quaternary alkylammonium derivatives of stearic acid.

3 – 2 - Lubricants , softening and release agents

In view of the soft texture of the sodium salt, which is the main component of soap, other salts are also useful for their lubricating properties. Lithium stearate is an important component of grease. The stearate salts of zinc, calcium, cadmium, and lead are used to soften PVC. Stearic acid is used along with castor oil for preparing softeners in textile sizing. They are heated and mixed with caustic potash or caustic soda. Related salts are also commonly used as release agents, e.g. in the production of automobile tires.

3 – 3 - Niche uses

Being inexpensively available and chemically benign, stearic acid finds many niche applications. When making plaster castings from a plaster piece mold or waste mold and when making the mold from a shellacked clay original. In this use, powdered stearic acid is mixed in water and the suspension is brushed onto the surface to be parted after casting. This reacts with the calcium in the plaster to form a thin layer of calcium stearate which functions as a release agent. When reacted with zinc it forms zinc stearate which is used a lubricant for playing cards (fanning powder) to ensure a smooth motion when fanning. In compressed confections, it is used as a lubricant to keep the tablet from sticking to the die.

Fatty acids are classic components of candle - making. Stearic acid is used along with simple sugar or corn syrup as a hardener in candies.

Stearic acid is used to produce dietary supplements.

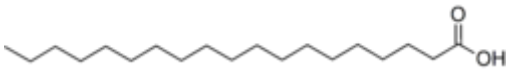
In fire works, stearic acid is often used to coat metal powders such as aluminium and iron. This prevents oxidation, allowing compositions to be stored for a longer period of time.

Stearic acid is a common lubricant during injection molding and pressing of ceramic powders. It is also used as a mold release for foam latex that is baked in stone molds.

4 - Metabolism

An isotope labeling study in humans concluded that the fraction of dietary stearic acid oxidatively desaturated to oleic acid was 2.4 times higher than the fraction of palmitic acid analogously converted to palmitoleic acid. Also, stearic acid was less likely to be incorporated into cholesterol esters. In epidemiologic and clinical studies stearic acid was associated with lowered LDL cholesterol in comparison with other saturated fatty acids.[7] These findings may indicate that stearic acid is healthier than other saturated fatty acids.

Nona Decylic Acid

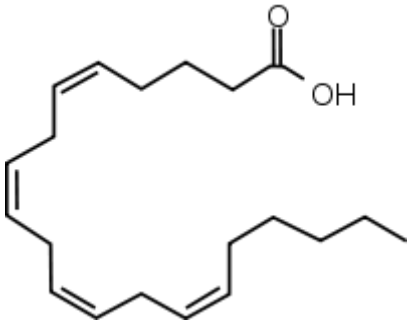


IUPAC name : Nonadecanoic acid	
Molecular formula	$CH_3\ (CH_2)_{17}\ COOH$
Molar mass	298 g/mol
Appearance	White flakes or powder
Melting point	68 -70°C
Boiling point	236°C (10 mmHg) 297°C (100 mmHg)
Solubility in water	Insoluble
Main hazards	Irritant (**Xi**)

Nonadecyclic acid, or nonadecanoic acid, is a 19-carbon long-chain saturated fatty acid with the chemical formula $CH_3(CH_2)_{17}COOH$. It forms salts called *nonadecylates*.

Nonadecylic acid can be found in fats and vegetable oils. It is also used by insects as pheromones.

Arachidonic Acid



Contents

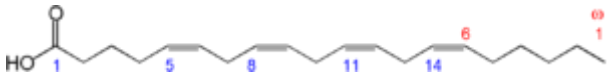
1 - Introduction

Arachidonic acid (AA, sometimes ARA) is a polyunsaturated omega-6 fatty acid 20:4(ω-6). It is the counterpart to the saturated arachidic acid found in peanut oil, (L. arachis – peanut.)

IUPAC name : Eicosatetraenoic acid	
Systematic name : tetra enoic acid	
Other names : 5,8,11,14-all-cis-Eicosatetraenoic acid ; Arachidonate	
Molecular formula	$C_{20}\ H_{32}\ O_2$
Molar mass	304 g mol−1
Density	0.922 g / cm3

Melting point	- 49 °C
Boiling point	169 -171 °C (at 0.15 mm Hg)
Flash point	113 °C (235 °F)

2 - Chemistry



In chemical structure, arachidonic acid is a carboxylic acid with a 20-carbon chain and four cis-double bonds; the first double bond is located at the sixth carbon from the omega end.

Some chemistry sources define 'arachidonic acid' to designate any of the eicosatetraenoic acids. However, almost all writings in biology, medicine and nutrition limit the term to all-cis-5,8,11,14-eicosatetraenoic acid.

3 - Biology

Arachidonic acid is a poly unsaturated fatty acid present in the phospholipids (especially phosphatidyl ethanol amine, phosphatidyl choline , and phosphatidyl inositides) of membranes of the body's cells, and is abundant in the brain, muscles, liver.

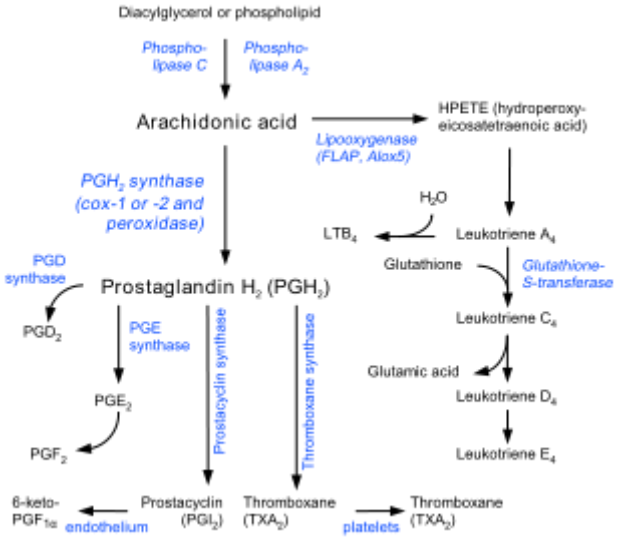
In addition to being involved in cellular signaling as a lipid second messenger involved in the regulation of signaling enzymes, such as PLC- γ, PLC- δ, and PKC- α, - β, and - γ isoforms, arachidonic acid is a key inflammatory intermediate and can also act as a vasodilator. (Note separate synthetic pathways, as described in section below)

4 - Essential fatty acid

Arachidonic acid is not one of the essential fatty acids. However, it does become essential if there is a deficiency in linoleic acid or if there is an inability to convert linoleic acid to arachidonic acid, which is required by most mammals. Some mammals lack the ability to—or have a very limited capacity to—convert linoleic acid

into arachidonic acid, making it an essential part of their diets. Since little or no arachidonic acid is found in common plants, such animals are obligate carnivores; the cat is a common example.[4][5] A commercial source of arachidonic acid has been derived, however, from the fungus Mortierella alpina.

5 - Synthesis and cascade



Eicosanoid synthesis.

Arachidonic acid is freed from a phospholipid molecule by the enzyme phospholipase A2 (PLA2), which cleaves off the fatty acid, but can also be generated from DAG by diacylglycerol lipase.

Arachidonic acid generated for signaling purposes appears to be derived by the action of a phosphatidylcholine-specific cytosolic phospholipase A2 (cPLA2, 85 kDa), whereas inflammatory arachidonic acid is generated by the action of a low-molecular-weight secretory PLA2 (sPLA2, 14-18 kDa).

Arachidonic acid is a precursor in the production of eicosanoids:

The enzymes cyclooxygenase and peroxidase lead to prostaglandin H2, which in turn is used to produce the prostaglandins, prostacyclin, and thromboxanes.

The enzyme 5-lipoxygenase leads to 5-HPETE, which in turn is used to produce the leukotrienes.

Arachidonic acid is also used in the biosynthesis of anandamide.

Some arachidonic acid is converted into hydroxyeicosatetraenoic acids (HETEs) and epoxyeicosatrienoic acids (EETs) by epoxygenase.

The production of these derivatives and their action in the body are collectively known as the "arachidonic acid cascade"; see essential fatty acid interactions for more details.

6 - Arachidonic acid in the body

6 – 1 - Muscle growth

Through its conversion to active components such as the prostaglandin PGF2 alpha, arachidonic acid is necessary for the repair and growth of skeletal muscle tissue. This role makes ARA an important dietary component in support of the muscle anabolic process. One of the lead researchers of the Baylor study (see Bodybuilding section) on arachidonic acid, Mike Roberts MS, CSCS, has authored an article published under the title Arachidonic Acid, The New Mass Builder explaining the role of this nutrient in muscle anabolism, and its potential for the enhancement of muscle size and strength . The paper explains that for optimal muscle growth, a training stimulus must elicit localized inflammation and soreness. It explains that arachidonic acid (AA, 20:4n-6) is an essential omega-6 (1-6) polyunsaturated fatty acid that is abundant in skeletal muscle membrane phospholipids (figure 2). It is also the body's principal building block for the production of prostaglandins, which are known to have various physiological roles, including a close involvement in inflammation. Also, the prostaglandin isomer PGF2a has a potent ability to stimulate muscle growth. As such, arachidonic acid is a regulator of localized muscle inflammation, and may be a central nutrient controlling the intensity of the anabolic/tissue-rebuilding response to weight training.

6 – 2 - Brain

Arachidonic acid is one of the most abundant fatty acids in the brain, and is present in similar quantities to docosahexaenoic acid

(DHA). The two account for approximately 20% of its fatty acid content. Like DHA, neurological health is reliant upon sufficient levels of arachidonic acid. Among other things, arachidonic acid helps to maintain hippocampal cell membrane fluidity.[13] It also helps protect the brain from oxidative stress by activating peroxisome proliferator-activated receptor gamma.[14] ARA also activates syntaxin-3 (STX-3), a protein involved in the growth and repair of neurons.

Arachidonic acid is also involved in early neurological development. In one study funded by the U.S. National Institute of Child Health and Human Development, infants (18 months) given supplemental arachidonic acid for 17 weeks demonstrated significant improvements in intelligence, as measured by the Mental Development Index. This effect is further enhanced by the simultaneous supplementation of ARA with DHA.

In adults, the disturbed metabolism of ARA contributes to neurological disorders such as Alzheimer's disease and Bipolar disorder. This involves significant alterations in the conversion of arachidonic acid to other bioactive molecules (overexpression or disturbances in the ARA enzyme cascade).

6 – 3 - Alzheimer's disease

Studies on arachidonic acid and the pathogenesis of Alzheimer's disease is mixed with one study of AA and its metabolites suggests they are associated with the onset of Alzheimer's disease,[18] whereas another study suggests that the supplementation of arachidonic acid during the early stages of this disease may actually be effective in reducing symptoms and slowing the disease progress. Additional studies on arachidonic acid supplementation for Alzheimer's patients are needed.

6 – 4 - Bodybuilding supplement

Arachidonic acid is marketed as an anabolic bodybuilding supplement in a variety of products. The first clinical study concerning the use of arachidonic acid as a sport supplement found that arachidonic acid has a possible enhancement of anaerobic

capacity. A significant group–time interaction effect was observed in Wingate relative peak power (AA: 1.2 ± 0.5; P: -0.2 ± 0.2 W•kg-1, p=0.015). Statistical trends were also seen in bench press 1RM (AA: 11.0 ± 6.2; P: 8.0 ± 8.0 kg, p=0.20), Wingate average power (AA:37.9 ± 10.0; P: 17.0 ± 24.0 W, p=0.16), and Wingate total work (AA: 1292 ± 1206; P: 510 ± 1249 J, p=0.087). AA supplementation during resistance-training promoted significant increases in relative peak power with other performance related variables approaching, but not reaching, significance. These findings provide some preliminary evidence to support the use of AA as an ergogenic.

7 - Dietary arachidonic acid and inflammation

Under normal metabolic conditions, the increased consumption of arachidonic acid is unlikely to increase inflammation. ARA is metabolized to both proinflammatory and anti-inflammatory molecules . Studies giving between 840 mg and 2,000 mg per day to healthy individuals for up to 50 days have shown no increases in inflammation or related metabolic activities. Increased arachidonic acid levels are actually associated with reduced pro-inflammatory IL-6 and IL-1 levels, and increased anti-inflammatory tumor necrosis factor- beta. This may result in a reduction in systemic inflammation.

Arachidonic acid does still play a central role in inflammation related to injury and many diseased states. How it is metabolized in the body dictates its inflammatory or anti-inflammatory activity. Individuals suffering from joint pains or active inflammatory disease may find that increased arachidonic acid consumption exacerbates symptoms, presumably because it is being more readily converted to inflammatory compounds. Likewise, high arachidonic acid consumption is not advised for individuals with a history of inflammatory disease, or who are in compromised health. Of note, while ARA supplementation does not appear to have proinflammatory effects in healthy individuals, it may counter the anti-inflammatory effects of omega-3 fatty acid supplementation.

8 - Health effects of arachidonic acid supplementation

Arachidonic acid supplementation in daily dosages of 1,000–1,500 mg for 50 days has been well tolerated during several clinical studies, with no significant side effects reported. All common markers of health, including kidney and liver function, serum lipids,[27] immunity, and platelet aggregation appear to be unaffected with this level and duration of use. Furthermore, higher concentrations of ARA in muscle tissue may be correlated with improved insulin sensitivity.[29] Arachidonic acid supplementation of the diets of healthy adults appears to offer no toxicity or significant safety risk.

A scientific advisory from the American Heart Association has favorably evaluated the health impact of dietary omega-6 fats, including arachidonic acid. The group does not recommend limiting this essential fatty acid. In fact, the paper recommends individuals follow a diet that consists of at least 5 – 10 % of calories coming from omega - 6 fats, including arachidonic acid. Dietary ARA is not a risk factor for heart disease, and may play a role in maintaining optimal metabolism and reduced heart disease risk. It is, therefore, recommended to maintain sufficient intake levels of both omega-3 and omega-6 essential fatty acids for optimal health.

Arachidonic acid is not carcinogenic, and studies show dietary level is not associated (positively or negatively) with risk of cancers. ARA remains integral to the inflammatory and cell growth process, however, which is disturbed in many types of disease including cancer. Therefore, the safety of arachidonic acid supplementation in patients suffering from cancer, inflammatory, or other diseased states is unknown, and supplementation is not recommended.

Part - 2 –

Aliphatic Acids

Di & Tri Carboxylic

Di Carboxylic Acid

Contents

1 - Introduction

Dicarboxylic acids are organic compounds that contain two carboxylic acid functional groups. In molecular formulae for dicarboxylic acids, these groups are sometimes written as HOOC-R-COOH. Dicarboxylic acids are be used to prepare copolymers such as polyamides and polyesters.

In general, dicarboxylic acids show similar chemical behaviour and reactivity as monocarboxylic acids. The ionization of the second carboxyl group occurs less readily than the first. This effect arises because more energy is required to deprotonate anions than neutral molecules.

A mnemonic to aid in remembering the order of the common nomenclature for the first six dicarboxylic acids is "Oh my, such great apple pie!" (oxalic, malonic, succinic, glutaric, adipic, pimelic). A variant adds "Sweet as sugar!" (suberic, azelaic, sebacic) to the end of the mnemonic. An additional way of remembering the first six dicarboxylic acids is by simply recalling the acronym OMSGAP,

which is a simplification of the previously described mnemonic device.

When one of the carboxy groups is replaced with an aldehyde group, the resulting structure is called a "aldehydic acid".

2 – Examples

Elementary saturated dicarboxylic acids

Common name	IUPAC name	Chemical formula
Oxalic acid	ethanedioic acid	HOOC- COOH
Malonic acid	propanedioic acid	HOOC-(CH_2)-COOH
Succinic acid	butanedioic acid	HOOC-(CH_2)$_2$-COOH
Glutaric acid	pentanedioic acid	HOOC-(CH_2)$_3$-COOH
Adipic acid	hexanedioic acid	HOOC-(CH_2)$_4$-COOH
Pimelic acid	heptanedioic acid	HOOC-(CH_2)$_5$-COOH
Suberic acid	octanedioic acid	HOOC-(CH_2)$_6$-COOH
Azelaic acid	nonanedioic acid	HOOC-(CH_2)$_7$-COOH
Sebacic acid	decanedioic acid	HOOC-(CH_2)$_8$-COOH

Elementary aromatic dicarboxylic acids

Common name	IUPAC name	Chemical formula
(Ortho-)Phthalic acid	benzene-1,2-dicarboxylic acid o-phthalic acid	$C_6H_4(COOH)_2$
Isophthalic acid	benzene-1,3-dicarboxylic acid m-phthalic acid	$C_6H_4(COOH)_2$
Terephthalic acid	benzene-1,4-dicarboxylic acid p-phthalic acid	$C6H_4(COOH)_2$

Elementary unsaturated dicarboxylic acids

Type	Common name	IUPAC name	Chemical formula
Monounsaturated: two isomeric forms: cis and trans	Maleic acid (cis form) and Fumaric acid (trans form)	(Z)-Butenedioic acid and (E)-Butenedioic acid	$HO_2CCH=CHCO_2H$
	Glutaconic acid	Pent-2-enedioic acid	$HO_2CCH=CHCH_2CO_2H$
	Traumatic acid	Dodec-2-enedioic acid	$HO_2C(CH_2)_8CH=CHCO_2H$
Diunsaturated: three isomeric forms: trans,trans, cis,trans and cis,cis	Muconic acid	(2E,4E)-Hexa-2,4-dienedioic acid	$HO_2CCH=CHCH=CHCO_2H$

3 - More on Dibasic or Dicarboxylic Acids

Although the dicarboxylic acids do not occur in appreciable amounts as components of animal or vegetal lipids, they are in general important metabolic products of fatty acids since they originate from byoxidation. Dicarboxylic acids are suitable substrates for preparation of organic acids for the pharmaceutical and food industries. Furthermore, they are useful materials for the preparation of fragrances, polyamides, adhesives, lubricants, and polyesters.

They have the general type formula HOOC-(CH2)n-COOH In vegetal, a great variety of molecular forms of dicarboxylic acids are found :

simple forms with a straight carbon chain or a branched chain

complex forms with a dicarboxylic acid and an alkyl side chain like alkylitaconates

4 - Simple forms of dicarboxylic acids

Short - chain dicarboxylic acids are of great importance in the general metabolism and up to n = 3 they cannot be considered as lipids since their water solubility is important. The simplest of these

intermediates is oxalic acid (n = 0) , the others are malonic (n = 1) , succinic (n = 2) and glutaric (n = 3) acids.

The other lipid members of the group found in natural products or from synthesis have a "n" value from 4 up to 21.

Adipic acid (n = 4) : Despite its name (in Latin adipis is fat), this acid (hexanedioic acid) is not a normal constituent of natural lipids but is a product of oxidative rancidity (lipid peroxidation). It was obtained by oxidation of castor oil with nitric acid (splitting of the carbon chain close to the OH group). Synthesized in 1902 from tetramethylene bromide, it is now obtained by oxidation of cyclohexanol or cyclohexane. It has several industrial uses in the production of adhesives, plasticizers, gelatinizing agents, hydraulic fluids, lubricants, emollients, as an additive in the manufacture of some form of nylon (nylon-6,6), polyurethane foams, leather tanning, urethane and also as an acidulant in foods. Adipic acid is used after esterification with various groups such as dicapryl, di(ethylhexyl), diisobutyl, and diisodecyl.

Pimelic acid (n = 5) : this acid (heptanedioic acid), from the Greek pimelh (pimele fat), as adipic acid, was isolated from oxidized fats. It was obtained in 1884 by Ganttner F et al. as a product of ricinoleic acid (hydroxylated oleic acid) from castor oil.

Suberic acid (n = 6) : it was firstly produced by nitric acid oxidation of cork (Latin suber) material and then from castor oil.[4] The oxidation of ricinoleic acid produces, by splitting at the level of the double bond and at the level of the OH group, at the same time, suberic acid (octanedioic acid) and the next homologue azelaic acid. Suberic acid was used in the manufacture of alkyd resins and in the synthesis of polyamides leading to nylon.

Azelaic acid (n = 7) : nonanedioic acid is the best known dicarboxylic acid. Its name stems from the action of nitric acid (azote, nitrogen, or azotic, nitric) oxidation of oleic or elaidic acid. It was detected among products of rancid fats. Its origin explains for its

presence in poorly preserved samples of linseed oil and in specimens of ointment removed from Egyptian tombs 5000 years old.[6] Azelaic acid was prepared by oxidation of oleic acid with potassium permanganate, but now by oxidative cleavage of oleic acid with chromic acid or by ozonolysis. Azelaic acid is used, as simple esters or branched-chain esters) in the manufacture of plasticizers (for vinyl chloride resins, rubber), lubricants and greases. Azelaic acid is now used in cosmetics (treatment of acne). It displays bacteriostatic and bactericidal properties against a variety of aerobic and anaerobic micro-organisms present on acne-bearing skin. . Azelaic acid was identified as a molecule that accumulated at elevated levels in some parts of plants and was shown to be able to enhance the resistance of plants to infections.

Sebacic acid (n = 8) : decanedioic acid was named by Thenard LJ (1802) from the Latin sebaceus(tallow candle) or sebum (tallow) in reference to its use in the manufacture of candles. Thenard LJ isolated this compound from distillation products of beef tallow. In 1954, it was reported that it was produced in excess of 10,000 tons annually by alkali fission of castor oil. Sebacic acid and its derivatives, as azelaic acid, have a variety of industrial uses as plasticizers, lubricants, diffusion pump oils, cosmetics, candles, etc. It is also used in the synthesis of polyamide, as nylon, and of alkyd resins. An isomer, isosebacic acid, has several applications in the manufacture of vinyl resin plasticizers, extrusion plastics, adhesives, ester lubricants, polyesters, polyurethane resins and synthetic rubber.

Dodecanedioic acid (n = 10) : that acid is used in the production of nylon (nylon - 6,12), polyamides, coatings, adhesives, greases, polyesters, dyestuffs, detergents, flame retardants, and fragrances. It is now produced by fermentation of long-chain alkanes with a specific strain of Candida tropicalis. Its monounsaturated analogue (traumatic acid) is described below.

It was shown that all these dicarboxylic acids are formed during the drying process of paint oils and that the determination of these

decomposition products may be of value in determining the age of old samples.

The higher weight dicarboxylic acids (n = 10 - 21) are found in different plant lipids, particularly in what was named erroneously Japan wax (triglycerides containing C20 , C21, C22 and C23 dicarboxylic acids besides normal fatty acids) from the sumac tree (Rhus sp.). Among them, Thapsic acid (n=14) was isolated from the dried roots of the Mediterranean "deadly carrot", Thapsia garganica (Umbelliferae), but others, as Brassylic acid (n=11), were prepared chemically from different sources. Brassylic acid can be produced chemically from erucic acid by ozonolysis but also by microorganisms (Candida sp.) from tridecane. This diacid is produced on a small commercial scale in Japan for the manufacture of fragrances.

A large survey of the dicarboxylic acids present in Mediterranean nuts revealed unusual components. A total of 26 minor acids (from 2 in pecan to 8% in peanut) were determined : 8 species derived from succinic acid, likely in relation with photosynthesis, and 18 species with a chain from 5 to 22 carbon atoms.

Higher weight acids (> C20) are found in suberin present at vegetal surfaces (outer bark, root epidermis). C16 to C26 a, ω-dioic acids are considered as diagnostic for suberin. With C18:1 and C18:2, their content amount from 24 to 45% of whole suberin. They are present at low levels (< 5 %) in plant cutin, except in Arabidopsis thaliana where their content can be higher than 50 %.

The first allenic dicarboxylic acid, named glutinic acid (2,3-pentadienedioic acid) was isolated from Alnus glutinosa (Betulaceae).

It was shown that hyperthermophilic microorganisms specifically contained a large variety of dicarboxylic acids.[15] This is probably the most important difference between these micro organisms and other marine bacteria. Dioic fatty acids from C16 to

C22 were found in an hyperthermophilic archaeon, Pyrococcus furiosus. Short and medium chain (up to 11 carbon atoms) dioic acids have been discovered in Cyanobacteria of the genus Aphanizomenon.

A mono unsaturated dicarboxylic acid, traumatic acid, (10E-dodeca-1,12-dicarboxylic acid), was among the first biologically active molecules isolated from plant tissues. That dicarboxylic acid was shown to be a potent wound healing agent in plant that stimulates cell division near a wound site, it derives from 18:2 or 18:3 fatty acid hydroperoxides after conversion into oxo fatty acids. While polyunsaturated fatty acids are unusual in plant cuticles, a diunsaturated dicarboxylic acid has been reported as a component of the surface waxes or polyesters of some plant species. Thus, octadeca-c6,c9-diene-1,18-dioate, a derivative of linoleic acid, is present in Arabidopsis and Brassica napus cuticle.

Dicarboxylic acids were shown in 1934 to be produced by ω-oxidation of fatty acids during their catabolism.[20] It was discovered that these compounds appeared in urine after administration of tricaprin and triundecylin. Although the significance of their biosynthesis remains poorly understood, it was demonstrated that ω-oxidation occurs in rat liver but at a low rate, needs oxygen, NADPH and cytochrome P450. It was later shown that this reaction is more important in starving or diabetic animals where 15 % of palmitic acid is subjected to ω-oxidation and then tob-oxidation, this generates malonyl-coA which is further used in saturated fatty acid synthesis.

It was proposed recently that dicarboxylic acids are alternate lipid substrates in parenteral nutrition . Basically, they are water soluble, undergo b - oxidation, do not induce ketogenesis but rather promote gluconeogenesis. They could represent an immediately available form of energy. Thus, inorganic salts of sebacic (C10) and lauric (C12) acids were firstly proposed, but now, triglycerides containing these fatty acids are under investigation. Treatment of rats with derivatives of C16 dioic acid have shown that this compound markedly improved lipid metabolism and inhibited the development of advanced cardiovascular disease.

It must be recalled that the determination of the dicarboxylic acids generated by permanganate-periodate oxidation of monoenoic fatty acids was useful to study the position of the double bond in the carbon chain.

5 - Branched - chain diacids

Long-chain dicarboxylic acids containing vicinal dimethyl branching near the centre of the carbon chain have been discovered in the genus Butyrivibrio, bacteria which participate in the digestion of cellulose in the rumen. These fatty acids, named diabolic acids, have a chain length depending on the fatty acid used in the culture medium. The most abundant diabolic acid inButyrivibrio had a 32 - carbon chain length.

Diabolic acid (15,16 – dimethyl tri acontanedioic acid) These diacids were also detected in the core lipids of the genus Thermotoga of the order Thermotogales, bacteria living in solfatara springs, deep-sea marine hydrothermal systems and high-temperature marine and continental oil fields. It was shown that about 10% of their lipid fraction were symmetrical C30 to C34 diabolic acids. The C30 (13,14-dimethyl octa cosanedioic acid) and C32 (15,16-dimethyl tri acontanedioic acid) diabolic acids have been described in Thermotoga maritima. Some parent C29 to C32 diacids but with methyl groups on the carbons C-13 and C-16 have been isolated and characterized from the lipids of thermophilic anaerobic eubacterium Themanaerobacter ethanolicus. The most abundant diacid was the C30 a,ω-13,16-dimethyloctacosanedioic acid.

Biphytanic diacids are present in geological sediments and are considered as tracers of past anaerobic oxidation of methane.[31] Several forms without or with one or two pentacyclic rings have been detected in Cenozoic seep limestones. These lipids may be unrecognized metabolites from Archaea.

Crocetin is the core compound of crocins (crocetin glycosides) which are the main red pigments of the stigmas of saffron (Crocus

sativus) and the fruits of gardenia (Gardenia jasminoides). Crocetin is a 20-carbon chain dicarboxylic acid which is a diterpenenoid and can be considered as a carotenoid. It was the first plant carotenoid to be recognized as early as 1818 while the history of saffron cultivation reaches back more than 3,000 years. The major active ingredient of saffron is the yellow pigment crocin 2 (three other derivatives with different glycosylations are known) containing a gentiobiose (disaccharide) group at each end of the molecule.

A simple and speccific HPLC-UV method has been developed to quantify the five major biologically active ingredients of saffron, namely the four crocins and crocetin.

6 - Alkylitaconates

Several dicarboxylic acids having an alkyl side chain and an itaconate core have been isolated from lichens and fungi, itaconic acid (methylenesuccinic acid) being a metabolite produced by filamentous fungi.

Among these compounds, several analogues, called chaetomellic acids with different chain lengths and degrees of unsaturation have been isolated from various species of the lichen Chaetomella.

These molecules were shown to be valuable as basis for the development of anticancer drugs due to their strong farnesyl trans ferase inhibitory effects.

In 1999, a series of new fungal alkyl- and alkenyl-itaconates, ceriporic acids, were found in cultures of a selective lignin-degrading fungus (white rot fungus), Ceriporiopsis subvermispora.

It was determined that these ceriporic acids suppressed iron redox reactions to attenuate • OH production by the Fenton reaction in the presence of iron reductants such as hydroquinone and cysteine. It was proposed that the suppression of the cellulolytic active oxygen species, • OH, by this metabolite contributes to the selective lignin-degradation with a minimum loss of cellulose. The absolute

configuration of ceriporic acids, their stereoselective biosynthetic pathway and the diversity of their metabolites have been largely discussed.

7 - Fatty acid carbonates

Carbonates (esters of carbonic acid, H_2CO_3) are well known to chemists as they represent an important class of organic compounds and among them oleochemical carbonates have interesting characteristics which make them candidates for many industrial applications.

The most common carbonates have the following structure : RO - CO – OR . R is a linear chain with 8 to 18 carbon atoms, saturated or with one double bond (dioleyl carbonate), or a branched chain (ethylhexyl, butyloctyl, or hexyldecyl).

They are miscible in organic solvents but insoluble in water. Unsaturation or branching on the alkyl chain lowers their melting point.The condensation of phosgene (ClCOCl) with an alcohol appears the most commonly used procedure to synthesize oleochemical carbonates.

The polar nature of the carbonate moiety enables it to adhere strongly to metal surfaces. Thus, they are used as lubricant components which have a protective property for metal corrosion. Some C8 to C18 carbonates have been exploited in personal-care products (sunscreen, cosmetics), dioctyl carbonate being also used as emollient or solvent in UV-filter solutions. Extraction of metal ions (gold, silver, platinum) is improved by the use of the chelating properties of oleochemical carbonates when mixed with the metal-containing aqueous phase. Future developments will ensure a growing interest in these molecules.

8 - Phenyl and benzoic alkanoic acids

Short chain ω-phenylalkanoic acids have long been known to occur in natural products. Phenylacetic, 3-phenylpropanoic and 3-phenylpropenoic (cinnamic) acids were found in propolis, mammalian

exocrine secretions or plant fragrances. During a systematic study of the lipids from seeds of the plant Araceae, the presence of 13 - phenyltridecanoic acid as a major component (5-16 % of total fatty acids) was discovered. Other similar compounds but with 11 and 15 carbon chain lengths and saturated or unsaturated were shown to be also present but in lower amounts. At the same time, the even carbon chain ω-phenylalkanoic acids of C10 up to C16 were discovered in halophilic bacteria.

8 – 1 - ω-phenylalkanoic acid (x = 1 to 17)

Later, an exhaustive study of 17 genus of the subfamily Aroideae of Araceae revealed the presence of three major acids, 11-phenylundecanoic acid, 13- phenyltridecanoic acid and 15-phenylpentadecanoic acid in seed lipids. Other odd carbon number acids from C7 to C23 were detected but in trace amounts. Similarly, two series of homologous odd carbon number monounsaturated ω-phenylalkanoic acids were found. Thus, it can be stated that all odd carbon chain ω-phenylalkanoic acids from C1 through C23 have been found in nature. Furthermore, even carbon chain ω-phenylalkanoic acids from C10 through C16 were also detected.

Substituted phenylalkenoic acids are periodically encountered in nature. As an example, rubrenoic acids were purified from Alteromonas rubra, compounds which showed bronchodilatatoric properties.

Methyl phenylalkenoic acids (5 carbon chain) have been described from a terrestrial Streptomycete.[42] Serpentene, a similar polyunsaturated phenylalkenoic acid, is also produced by Streptomyces and was shown to have some antibacterial properties.

Several serpentene - like compounds have also been isolated from the same bacterial source.

Several bicyclic derivatives of linolenic acid were shown to be generated by alkali isomerization.

8 – 2 - Bicyclic hexahydroindenoic acid

Some others (alkyl-phenyl)-alkanoic acids) are formed when linolenic acid is warmed at 260 – 270 °C .

Several forms with 16, 18 and 20 carbon atoms were identified in archaeological pottery vessels and were presumed to have been generated during heating triunsaturated fatty acids. They were used as biomarkers to trace the ancient processing of marine animal in these vessels.

Several benzoic acid derivatives have been described in leaves of various Piperaceae species. Thus, a prenylated benzoic acid acid derivative, crassinervic acid, has been isolated from Piper crassinervium.

8 – 3 - Crassinervic acid

Similar compounds were isolated from Piper aduncum (aduncumene) and Piper gaudichaudianum(gaudichaudianic acid). All these molecules showed high potential as antifungal compounds. A prenylated benzoic acid with a side chain formed of two isoprene units has also been isolated from the leaves of Piper aduncum. More recently, three prenylated benzoic acid derivatives with four isoprene units have been extracted from the leaves of Piper heterophyllum and Piper aduncum.These compounds displayed moderate anti plasmodial (against Plasmodium falciparum) and trypanocidal (against Trypanosoma cruzi) activities.

9 - Fatty acyl - CoA esters

These fatty acid derivatives may be considered as complex lipids since they are formed of one fatty acid, a 3'-phospho-AMP linked to phosphorylated pantothenic acid (Vitamin F) and cysteamine. However, to simplify the nomenclature and taking into account their metabolism, we classify them within the big group of the fatty acids and their simple derivatives rather than within the complex and phosphorylated lipids. Long-chain acyl-CoA esters are substrates for a number of important enzymatic reactions and play a central role in the regulation of metabolism as allosteric regulators of

several enzymes. To participate in specific metabolic processes, fatty acids must first be activated by being joined in thioester linkage (R-CO - SCoA) to the -SH group of coenzyme A. The thioester bond is a high energy bond.

9 – 1 - R = fatty carbon chain

The activation reaction normally occurs in the endoplasmic reticulum or the outer mitochondrial membrane. This is an ATP-requiring reaction (fatty acyl - CoA synthase), yielding AMP and pyrophosphate (PPi). Different enzymes are specific for fatty acids of different chain length. Then, the acyl CoA esters are transported in mitochondria. They are converted to fatty acyl carnitine by carnitine acyl transferase I, an enzyme of the inner leaflet of the outer mitochondrial membrane. Fatty acyl carnitine is then transported by an antiport in exchange for free carnitine to the inner surface of the inner mitochondrial membrane. There carnitine acyl transferase II reverses the process, producing fatty acyl-CoA and carnitine. This shuttle mechanism is required only for longer chain fatty acids. Once inside the mitochondrial matrix, the fatty acyl-CoA derivatives are degraded by a series of reactions that release acetyl-CoA and leads to the production of NADH and FADH2. There are four steps in fatty acid oxidation pathway; oxidation, hydration, oxidation, and thiolysis. It requires 7 rounds of this pathway to degrade palmitate (a C16 fatty acid).

10 - Divinyl ether fatty acids

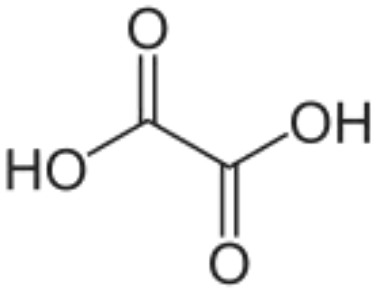
Fatty acid hydroperoxides generated by plant lipoxygenases from linoleic and linolenic acids are known to serve as substrates for a divinyl ether synthase which produces divinyl ether fatty acids. Up to date divinyl ethers were detected only within the plant kingdom. The discovery of that class of compounds dates back to 1972, when the structures of two ether C18 fatty acids generated by homogenates of the potato tuber wee described. These compounds, named colneleic acid (from linoleic acid) and colnelenicacid (from linolenic acid), could be also produced in potato leaves and tomato roots by rearrangement of 9 - hydroperoxides.

Isomers of colneleic and colnelenic acids were isolated from homogenates of leaves of Clematis vitalba (Ranunculaceae).

Similarly, 13- lipoxygenase-generated hydroperoxides serve as precursor of other divinyl ether fatty acids which are produced in bulbs of garlic or Ranunculus leaves. These compounds were named etheroleic and etherolenic acids.

The physiological significance of divinyl ethers is still not fully studied. As infection of potato leaves leads to increased levels of divinyl ether synthase, it was suggested that this pathway could be of importance in the defense of plants against attacking pathogens. Similar structures have been discovered in the brown alga Laminaria sinclairii, with 18 or 20 carbons and 4 , 5 or 6 double bonds , and in the red alga Polyneura latissima, with 20 carbons and 5 double bonds.

Oxalic Acid



Contents

1 - Introduction

Oxalic acid is an organic compound with the formula $H_2C_2O_4$. It is a colorless crystalline solid that dissolves in water to give colorless solutions. It is classified as a dicarboxylic acid. In terms of acid strength, it is much stronger than acetic acid. Oxalic acid is a reducing agent and its conjugate base, known as oxalate ($C_2O_4^{2-}$), is a chelating agent for metal cations. Typically, oxalic acid occurs as the dihydrate with the formula $H_2C_2O_4 \cdot 2H_2O$. Ingestion of oxalic acid through skin contact or orally is dangerous.

IUPAC name : Ethanedioic acid
Other names : Oxalic acid

Molecular formula	$C_2 H_2 O_4$
Molar mass	90. g mol^{-1} (anhydrous) 126 g mol^{-1} (dihydrate)
Appearance	White crystals
Density	1.90 g cm^{-3} (anhydrous) 1.653g cm^{-3} (dihydrate)
Melting point	189-191 °C (anhydrous) (101.5 °C (d ihydrate)
Solubility in water	14.3 g/100ml (25 °C)
Solubility	23.7 g /100 ml (15 °C) in ethanol 1.4 g / 100 ml (15 °C) in diethyl ether
Main hazards	Toxic
Flash point	166 °C

2 - Preparation

Oxalic acid is mainly manufactured by the oxidation of carbohydrates or glucose using nitric acid or air in the presence of vanadium pentoxide. A variety of precursors can be used including glycolic acid and ethylene glycol. A newer method entails oxidative carbonylation of alcohols to give the diesters of oxalic acid:

$$4\ ROH + 4\ CO + O_2 \rightarrow 2\ (CO_2R)_2 + 2\ H_2O$$

These diesters are subsequently hydrolyzed to oxalic acid. Approximately 120,000 metric tons are produced annually.

2 – 1 - Laboratory methods

Although it can be readily purchased, oxalic acid can be prepared in the laboratory by oxidizing sucrose using nitric acid in the presence of a small amount of vanadium pentoxide as a catalyst.

The hydrated solid can be dehydrated with heat or by azeotropic distillation.

Of historical interest, Wöhler prepared oxalic acid by hydrolysis of cyanogen in 1824. This experiment may represent the first synthesis of a natural product.

3 - Structure

Anhydrous oxalic acid exists as two polymorphs; in one the hydrogen - bonding results in a chain-like structure whereas the hydrogen bonding pattern in the other form defines a sheet-like structure . Because the anhydrous material is both acidic and hydrophilic (water seeking), it is used in esterifications.

4 - Reactions

Oxalic acid is a relatively strong acid, despite being a carboxylic acid :

$C_2O_4H_2 \rightarrow C_2O_4H^- + H^+$; $pK_a = 1.27$

$C_2O_4H^- \rightarrow C_2O_4^{2-} + H^+$; $pK_a = 4.27$

Oxalic acid undergoes many of the reactions characteristic of other carboxylic acids. It forms esters such as dimethyl oxalate (m.p. 52.5–53.5 °C). It forms an acid chloride called oxalyl chloride.

Oxalate, the conjugate base of oxalic acid, is an excellent ligand for metal ions, e.g. the drug oxaliplatin.

Oxalic acid and oxalates can be oxidized by permanganate in an autocatalytic reaction.

5 - Occurrence

5 – 1 - Biosynthesis

At least two pathways exist for the enzyme-mediated formation of oxalate. In one pathway, oxaloacetate, a component of the Krebs citric acid cycle, is hydrolyzed to oxalate and acetic acid by the enzyme oxaloacetase:

$[O_2CC(O)CH_2CO_2]^{2-} + H_2O \rightarrow C_2O_4^{2-} + CH_3CO_2^-$

It also arises from the dehydrogenation of glycolic acid, which is produced by the metabolism of ethylene glycol.

5 – 2 - Occurrence in foods and plants

Calcium oxalate is the most common component of kidney stones. Early investigators isolated oxalic acid from wood-sorrel (*Oxalis*). Its presence makes it dangerous to eat unripe carambola or monstera fruits. Members of the spinach family are high in oxalates, as is sorrel. Rhubarb leaves contain about 0.5% oxalic acid and jack-in-the-pulpit (*Arisaema triphyllum*) contains calcium oxalate crystals. Bacteria produce oxalates from oxidation of carbohydrates.

5 – 3 - Other

Oxidized bitumen or bitumen exposed to gamma rays also contains oxalic acid among its degradation products. Oxalic acid may increase the leaching of radionuclides conditioned in bitumen for radioactive waste disposal.

6 - Biochemistry

The conjugate base of oxalic acid (oxalate) is a competitive inhibitor of the lactate dehydrogenase(LDH) enzyme.[12] LDH catalyses the conversion of pyruvate to lactic acid (End product of the Fermentation (Anaerobic) Process) oxidising the coenzyme NADH to NAD+ and H+ concurrently. Restoring NAD+ levels are essential to the continuation of anaerobic energy metabolism through glycolysis. As cancer cells preferentially use anaerobic metabolism (see Warburg effect) inhibition of LDH has been shown to inhibit tumor formation and growth, thus is an interesting potential course of cancer treatment.

7 - Applications

About 25 % of produced oxalic acid is used as a mordant in dyeing processes. It is used in bleaches, especially for pulp wood. It is also used in baking powder.

7 – 1 - Cleaning

Oxalic acid's main applications include cleaning or bleaching, especially for the removal of rust (iron complexing agent), e.g. Bar Keepers Friend is an example of a household cleaner containing

oxalic acid. Its utility in rust removal agents is due to its forming a stable, water soluble salt with ferric iron, ferrioxalate ion.

7 – 2 - Extractive metallurgy

Oxalic acid is an important reagent in lanthanide chemistry. Hydrated lanthanide oxalates form readily in strongly acidic solutions in a densely crystalline, easily filtered form, largely free of contamination by nonlanthanide elements. Thermal decomposition of these oxalate gives the oxides, which is the most commonly marketed form of these elements.

7 – 3 - Niche uses

Vaporized oxalic acid, or a 3.2 % solution of oxalic acid in sugar syrup, is used by some beekeepers as a miticide against the parasitic varroa mite.

Oxalic acid is rubbed onto completed marble sculptures to seal the surface and introduce a shine.

8 - Content in food items

This table was originally published in *Agriculture Handbook No. 8-11, Vegetables and Vegetable Products*, 1984.

Vegetable	Oxalic acid (g / 100 g)
Amaranth	1.09
Asparagus	.13
Beans, snap	.36
Beet leaves	.61
Broccoli	.19
Brussels sprouts	.36
Cabbage	.10
Carrot	.50
Cassava	1.26
Cauliflower	.15
Celery	.19
Chicory	.21

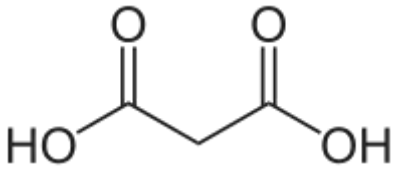
Chives	1.48
Collards	.45
Coriander	.01
Corn, sweet	.01
Cucumbers	.02
Eggplant	.19
Endive	.11
Garlic	.36
Kale	.02
Lettuce	.33
Okra	.05
Onion	.05
Parsley	1.70
Parsnip	.04
Pea	.05
Bell pepper	.04
Potato	.05
Purslane	1.31
Radish	.48
Rutabaga	.03
Spinach	.97
Squash	.02
Sweet potato	.24
Tomato	.05
Turnip	.21
Turnip greens	.05
Water cress	.31

7 - Toxicity and safety

In humans, oxalic acid has an oral LD_{Lo} (lowest published lethal dose) of 600 mg / kg.

The toxicity of oxalic acid is due to kidney failure, which arises because it causes precipitation of solid calcium oxalate, the main component of kidney stones. Oxalic acid can also cause joint pain due to the formation of similar precipitates in the joints. Ingestion of ethylene glycol results in oxalic acid as a metabolite which can also cause acute kidney failure.

Malonic Acid



Contents

1 - Introduction

Malonic acid (IUPAC systematic name: propanedioic acid) is a dicarboxylic acid with structure $CH_2(COOH)_2$. The ionized form of malonic acid, as well as its esters and salts, are known as malonates. For example, diethyl malonate is malonic acid's diethyl ester. The name originates from the Greek word (malon) meaning 'apple'.

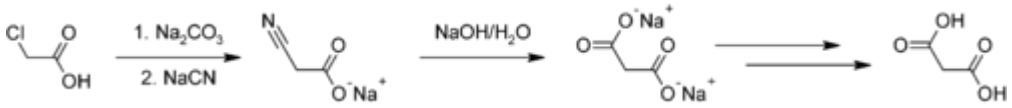
IUPAC name : propanedioic acid	
Other names : methane dicarboxylic acid	
Molecular formula	$C_3 H_4 O_4$
Molar mass	104 g mol−1
Density	1.619 g / cm3
Melting point	135 – 136 °C
Boiling point	decomposes
Solubility in water	Miscible

2 - Biochemistry

The calcium salt of malonic acid occurs in high concentrations in beetroot. It exists in its normal state as white crystals. Malonic acid is the classic example of a competitive inhibitor: It acts against succinate dehydrogenase (complex II) in the respiratory electron transport chain.

3 - Preparation

A classical preparation of malonic acid starts from chloroacetic acid :

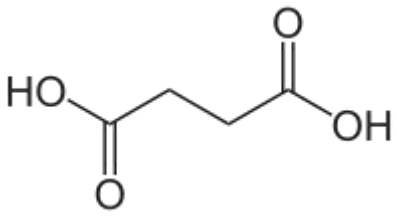


Sodium carbonate generates the sodium salt, which is then reacted with sodium cyanide to provide the cyano acetic acid salt via a nucleophilic substitution. The nitrile group can be hydrolyzed with sodium hydroxide to sodium malonate, and acidification affords malonic acid.

4 - Organic reactions

In a well - known reaction, malonic acid condenses with urea to form barbituric acid. Malonic acid is also frequently used as an enolate in Knoevenagel condensations or condensed with acetone to form Meldrum's acid. The esters of malonic acid are also used as a - CH_2COOH synthon in the malonic ester synthesis.

Succinic Acid



Contents

1 - Introduction

Succinic acid (IUPAC systematic name: butanedioic acid; historically known as spirit of amber) is a diprotic, dicarboxylic acid with chemical formula $C_4H_6O_4$ and structural formula HOOC-$(CH_2)_2$-COOH. It is a white , odorless solid. Succinate plays a role in the citric acid cycle, an energy - yielding process. The name derives from Latin succinum, meaning amber, from which the acid may be obtained.

IUPAC name ; Butanedioic acid	
Other names ; ethane -1,2- dicarboxylic acid	
Molecular formula	C_4 H_6 O_4
Molar mass	118 g mol −1
Density	1.56 g / cm3
Melting point	184 °C
Boiling point	235 °C
Solubility in water	58 g / L (20 °C) [
Flash point	206 °C (403 °F)

2 - Production and reactions

Spirit of amber was originally obtained from amber by pulverising and distilling it using a sand bath. In the past it was chiefly used externally for rheumatic aches and pains, and internally in inveterate gleets.

Succinic acid is produced by several methods. Common industrial routes include hydrogenation of maleic acid, oxidation of 1,4-butanediol, and carbonylation of ethylene glycol.

Succinic acid can be converted into fumaric acid by oxidation. The diethyl ester is a substrate in the Stobbe condensation. Dehydration of succinic acid gives succinic anhydride.

3 - Applications

Succinic acid is a precursor to some specialized polyesters. It is also a component of some alkyd resins.

Succinic acid is used in the food and beverage industry, primarily as an acidity regulator . Global production is estimated at 16,000 to 30,000 tonnes a year, with an annual growth rate of 10 %.

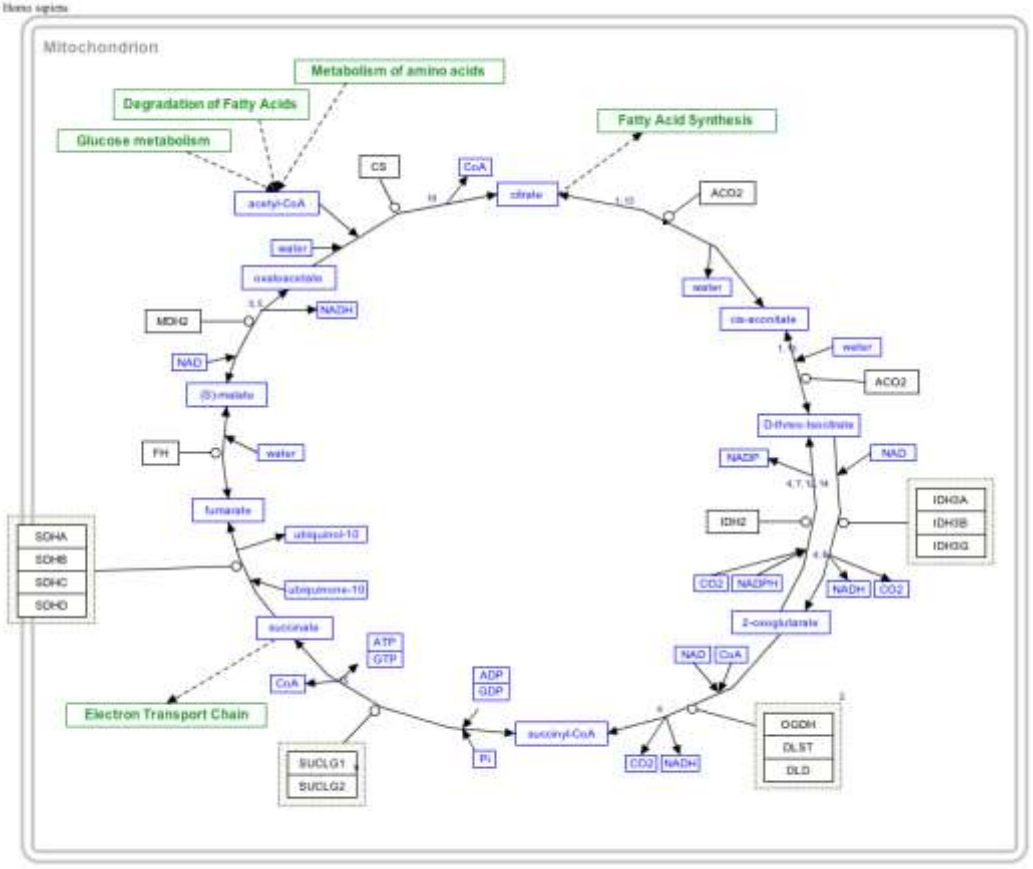
In nutraceutical form as a food additive and dietary supplement, is safe and approved by the U.S. Food and Drug Administration.[6] As an excipient in pharmaceutical products it is used to control acidity[7] and, more rarely, in effervescent tablets.

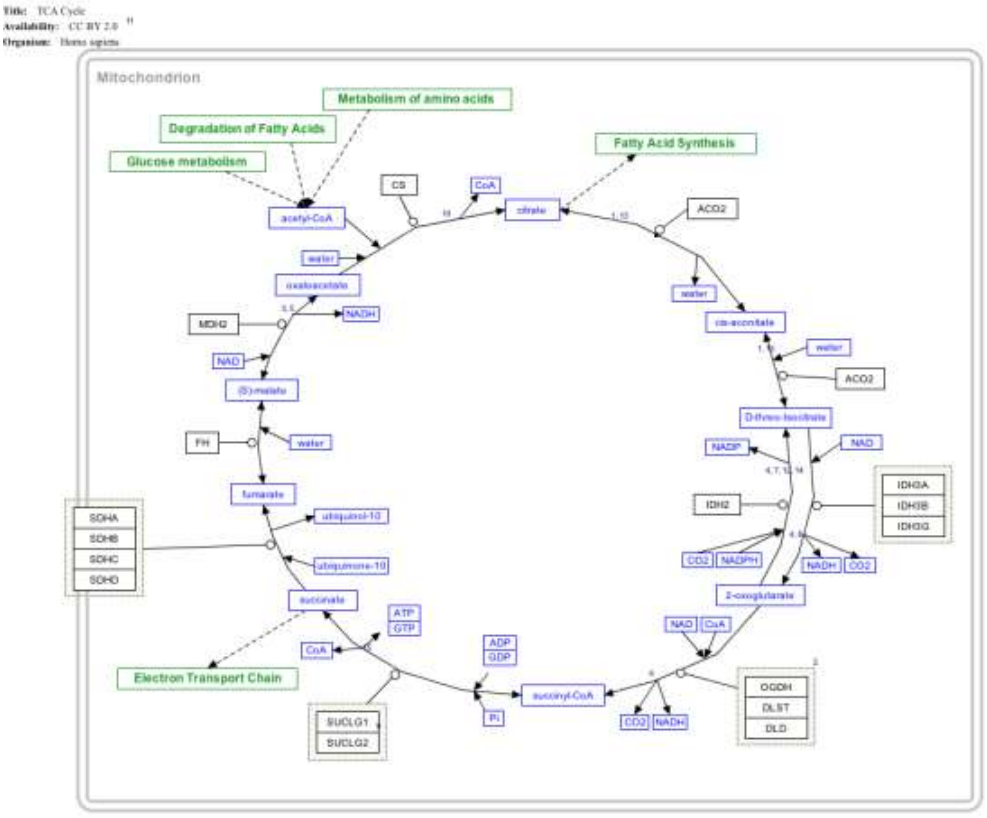
4 - Biochemistry

Succinate is an intermediate in the citric acid cycle and is capable of donating electrons to the electron transport chain by the reaction :

succinate + FAD $\rightarrow$ fumarate + $FADH_2$.

Title: TCA Cycle
Availability: CC BY 2.0
Organism: Homo sapiens





This conversion is catalysed by the enzyme succinate dehydrogenase (or complex II of the mitochondrial ETC). The complex is a 4 subunit membrane-bound lipoprotein which couples the oxidation of succinate to the reduction of ubiquinone. Intermediate electron carriers are FAD and three 2Fe-2S clusters part of subunit B.

4 – 1 - Fermentation

Succinic acid is created as a byproduct of the fermentation of sugar. It lends to fermented beverages such as wine and beer a common taste that is a combination of saltiness, bitterness and acidity.

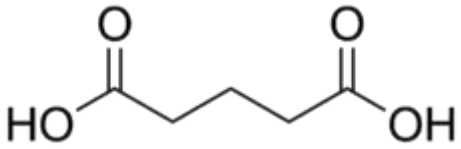
5 - Succinates

Salts formed by neutralizing succinic acid are called succinates. One example is sodium succinate, a white, water-soluble salt. Esters of succinic acid are also called succinates, one example being dimethylsuccinate with the formula $(CH^2CO^2CH^3)^2$.

6 - Safety

Succinic acid is an important biochemical intermediate that occurs in all living creatures. Like other simple mono- and dicarboxylic acids, it is not considered dangerous, although it is a skin irritant.

Glutaric Acid Type 1



Contents

1 - Introduction

Glutaric acidemia type 1 (or "Glutaric Aciduria", "GA1", or "GAT1") is an inherited disorder in which the body is unable to break down completely the amino acids lysine, hydroxylysine and tryptophan. Excessive levels of their intermediate breakdown products (glutaric acid, glutaryl- CoA , 3- hydroxyglutaric acid, glutaconic acid) can accumulate and cause damage to the brain (and also other organs[1]), but particularly the basal ganglia, which are

regions that help regulate movement. GA1 causes secondary carnitine deficiency, as glutaric acid, like other organic acids, is detoxified by carnitine. Mental retardation may also occur.

2 - Signs and symptoms

The severity of glutaric acidemia type 1 varies widely; some individuals are only mildly affected, while others have severe problems. GA1 can be defined as two clinical entities: GA1 before the encephalopathic crisis and GA1 after the encephalopathic crisis.

2 – 1 - GA1 before the encephalopathic crisis

2 – 1 – 1 - Macrocephaly

Babies with glutaric acidemia type 1 often are born with unusually large heads (macrocephaly). Macrocephaly is amongst the earliest signs of GA1. It is thus important to investigate all cases of macrocephaly of unknown origins for GCDH deficiency, given the importance of the early diagnosis of GA1. Macrocephaly is a "pivotal clinical sign" of many neurological diseases. Physicians and parents should be aware of the benefits of investigating for an underlying neurological disorder, particularly a neurometabolic one, in children with head circumferences in the highest percentiles.

2 – 2 – GA1 after the encephalopathic crisis

2 – 2 – 1 - Neuromotor aspects

Affected individuals may have difficulty moving and may experience spasms, jerking, rigidity or decreased muscle tone and muscle weakness (which may be the result of secondary carnitine deficiency). Glutaric aciduria type 1, in many cases, can be defined as a cerebral palsy of genetic origins.

2 – 2 - 1 – 1 - Occupational therapy

Parents and caregivers can provide a more interactive occupational therapy by enabling the child to use his or her own excessive postural muscle tone to his or her own advantage (see picture; note the care with which minimal pressure is applied while ensuring safety).

The excessive tone can also be managed with "jolly jumpers" and other aids to the upright stance that do not constrain the child but help him or her gradually tone down the rigidity.

2 – 2 – 2 - Bleeding abnormalities

Some individuals with glutaric acidemia have developed bleeding in the brain or eyes that could be mistaken for the effects of child abuse.

2 – Treatment

3 – 1 – Correction of secondary carnitine depletion

Like many other organic acidemias, GA1 causes carnitine depletion . Whole - blood carnitine can be raised by oral supplementation . However, this does not significantly change blood concentrations of glutarylcarnitine or esterified carnitine , suggesting that oral supplementation is suboptimal in raising tissue levels of carnitine. In the field of clinical nutrition, researchers come to the same conclusion, that oral carnitine raises plasma levels but doesn't affect muscle carnitine, where most of it is stored and used.

In contrast, regular intravenous infusions of carnitine caused distinct clinical improvements: "decreased frequency of decompensations, improved growth, improved muscle strength and decreased reliance on medical foods with liberalization of protein intake " .

Choline increases carnitine uptake and retention . Choline supplements are inexpensive, safe (probably even in all children requiring anti cholinergics) and can provide spectacular evidence of the suboptimal efficiency of carnitine supplementation by increasing exercise tolerance, truncal tone and general well - being.

3 – 2 - Precursor restriction

Dietary control may help limit progression of the neurological damage.

3 – 2 – 1 - Selective precursor restriction

3 – 2 – 1 – 1 -Tryptophan

Formulas such as XLys, XTrp Analog, XLys, XTrp Maxamaid, XLys, XTrp Maxamum or Glutarex 1 are designed to provide amino acids other than lysine and tryptophan, in order to tentatively prevent protein malnutrition.

The entry of tryptophan to the brain is crucial in the proper synthesis of the neurotransmitter serotonin in the brain. One way to acutely cause depression or bulimia or anxiety in humans, in order to assess an individual's vulnerability to those disorders, is to supplement with a formula with all or most amino acids except tryptophan. The protein synthesis elicited by the amino acids leads circulating amino acids, including tryptophan, to be incorporated into proteins. Tryptophan thus lowers in the brain as a result of the protein synthesis enhancement (causing circulating tryptophan to lower more than other amino acids) , and perhaps also competition of large neutral amino acids for transport across the blood–brain barrier through the large neutral amino acid transporter 1 (LNAA1). The consequence is acute tryptophan depletion (ATD) in the brain and a consecutive lowering of serotonin synthesis. ATD, which is basically a diagnostic procedure, is not a treatment for GA1.

In the Amish community, where GA1 is overrepresented (Morton, 2003), patients with GA1 did not and still don't receive tryptophan-free formulas, neither as the sole source of amino acids, nor as a supplement to protein restriction. Doctor D. Holmes Morton, the 1993 Albert Schweitzer Prize for Humanitarianism laureate, is taking care of patients affected with GA1 and other metabolic diseases in this community in his Clinic for Special Children.

5- hydroxy try ptophan, the precursor of serotonin that is not metabolized to glutaryl-CoA, glutaric acid and secondary metabolites, could be used as an adjunct to selective tryptophan restriction, considering the risks associated with the procedure. However, the evidence in favour of selective tryptophan restriction remains

insufficient and the consensus evolves towards the restriction of lysine only .

3 – 2 – 1 - 2 - Lysine

Lysine restriction, as well as carnitine supplementation, are considered the best predictors of a good prognosis for GA1 (Kolker & al., 2006). This excludes, however, patients who already suffered an encephalopathic crisis, for whom the prognosis is more related to the treatment of their acquired disorder (striatal necrosis, frontotemporal atrophy).

3 – 2 – 2 - Protein restriction

Vegetarian diets and, for younger children, breastfeeding[9] are common ways to limit protein intake without endangering tryptophan transport to the brain.

3 – 3 - Enhancement of precursor's anabolic pathway

3 – 3 – 1 - Lysine and hydroxylysine anabolic pathway enhancement

A possible way to prevent the build-up of metabolites is to limit lysine and hydroxylysine degradation, as lysine is one of the most abundant amino acids and tryptophan is one the least abundant amino acids.

3 – 3 – 1 – 1 - Interaction of GCDH deficiency with GLO deficiency

While GCDH deficiency is a rare disease, GLO deficiency is the most common of metabolic diseases affecting Humanity, limiting ascorbic acid biosynthesis to a minute fraction of what other non-primate species synthesize. It was thus called by OMIM (Online Mendeleian Inheritance in Man) a "public" error of metabolism. Ascorbic acid (Vitamin C) is a necessary cofactor for the utilization of lysine in collagen synthesis. Collagen, the most abundant protein in the human body, requires great amounts of lysine, the most abundant amino acids in proteins. Ascorbic acid, the main hydroxyl radical quencher, works as the cofactor providing the hydroxyl radical

required to collagen cross-linking; lysine thus becomes hydroxylysine.

GA1 worsens during stresses and catabolic episodes, such as fasts and infections. Endogenous catabolism of proteins could be an important route for glutaric acid production. It thus follows that collagen breakdown (and protein breakdown in general) should be prevented by all possible means.

Ascorbic acid is used to prevent multiple organ failure and to lessen mortality and morbidity in intensive care units.[10] It thus appears reasonable to include sufficient doses of ascorbic acid to the treatment protocol during stresses and other challenges to growth in order to stimulate collagen synthesis and thus prevent lysine breakdown.

3 – 3 – 2 - Tryptophan anabolic pathway enhancement

The conversion of tryptophan to serotonin and other metabolites depends on vitamin B6. If tryptophan catabolism has any impact on brain glutaric acid and other catabolite levels, vitamin B6 levels should be routinely assayed and normalized in the course of the treatment of GA1.

3 – 3 – 3 - Management of intercurrent illnesses

Stress caused by infection, fever or other demands on the body may lead to worsening of the signs and symptoms, with only partial recovery.

4 - Genetics

The condition is inherited in an autosomal recessive pattern: mutated copies of the gene GCDH must be provided by both parents to cause glutaric acidemia type 1. The GCDH gene encodes the enzyme glutaryl-CoA dehydrogenase. This enzyme is involved in degrading the amino acids lysine, hydroxylysine and tryptophan. Mutations in the GCDH' gene prevent production of the enzyme or result in the production of a defective enzyme with very low residual activity, or an enzyme with relatively high residual activity but still

phenotypic consequences . This enzyme deficiency allows glutaric acid, 3- hydroxyglutaric acid and (to a lesser extent) glutaconic acid to build up to abnormal levels, especially at times when the body is under stress. These intermediate breakdown products are particularly prone to affect the basal ganglia, causing many of the signs and symptoms of glutaric acidemia type 1.

Glutaric acidemia type 1 occurs in approximately 1 of every 30,000 to 40,000 births. It is much more common in the Amish community and in the Ojibway population of Canada, where up to 1 in 300 newborns may be affected.

Relatives of children with GA1 can have very low GCDH activity: in an early study of GA1, GCDH activity was found to be 38%, 42%, and 42% of controls in three of the four relatives tested.[14] Those levels are close to those found by Christensen & al[12] in some heavily symptomatic GA1-affected children.

5 - Epistemology

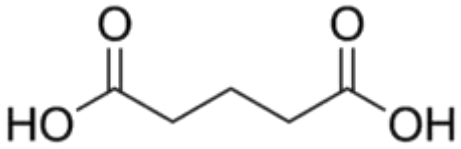
GA1 can be described as a metabolic disease, a neurometabolic disease, a cerebral palsy or a basal ganglia disorder (it is also misdiagnosed as shaken baby syndrome). Depending on the paradigm adopted, GA1 will mostly be managed with precursor restriction or with neurorehabilitation (or with incarceration of the parents in the case of presumed shaken baby syndrome).

So - called "orphan diseases", such as GA1, can be adopted into wider groups of diseases (such as carnitine deficiency diseases, cerebral palsies of diverse origins, basal ganglia disorders, and others); Morton at al. (2003b) emphasize that acute striatal necrosis is a distinctive pathologic feature of at least 20 other disorders of very different etiologies (e.g. HIV encephalopathy-AIDS dementia complex, pneumococcal meningitis, hypoadrenal crisis, methyl malonic acidemia, propionic acidemia, middle cerebral artery occlusion, hypertensive vasculopathy, acute mycoplasma pneumoniae infection, 3-nitropropionic acid intoxication, late onset familial

dystonia, cerebrovascular abrupt and severe neonatal asphyxia ("selective neuronal necrosis")).

Amongst 279 patients who had been reported to have GA1, 185 were symptomatic (two thirds); being symptomatic was seen as an indication of "low treatment efficacy". High risk screening, neonatal screening and a diagnosis of macrocephaly were the ways to identify bearers of the GCDH' defective gene who weren't frankly symptomatic. Macrocephaly remains the main sign of GA1 for those who aren't related to GA1 in any way or benefit from no screening program. GA1 was considered as a "treatable disease".[15] Two thirds of the patients who have GA1 will receive little benefit from the treatment for GA1 but can benefit from treatments given to victims of middle cerebral artery occlusion, AIDS dementia and other basal ganglia disorders: brain implants, stem cell neurorestauration, growth factors, monoaminergic agents, and many other neurorehabilitation strategies.

Glutaric Acid Type 2



Contents

1 - Introduction

Glutaric acidemia type 2 is an autosomal recessive metabolic disorder that is characterised by defects in the ability of the body to use proteins and fats for energy. Incompletely processed proteins and fats can build up, leading to a dangerous chemical imbalance called acidosis.

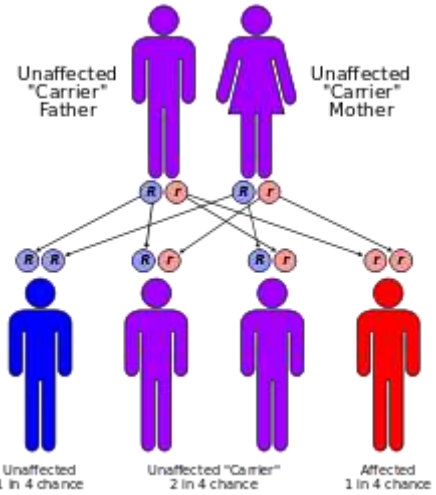
2 - Diagnosis

Glutaric acidemia type 2 often appears in infancy as a sudden metabolic crisis, in which acidosis and low blood sugar (hypoglycemia) cause weakness, behavior changes, and vomiting. There may also be enlargement of the liver, heart failure, and a characteristic odor resembling that of sweaty feet. Some infants with glutaric acidemia type 2 have birth defects, including multiple fluid-filled growths in the kidneys (polycystic kidneys). Glutaric acidemia type 2 is a very rare disorder. Its precise incidence is unknown. It has been reported in several different ethnic groups.

3 - Genetics

Mutations in the ETFA, ETFB, and ETFDH genes cause glutaric acidemia type II. Glutaric acidemia type 2 is caused by a deficiency in either of two enzymes, called electron transfer flavoprotein and electron transfer flavoprotein dehydrogenase. These enzymes are normally active in the mitochondria, which are the energy-producing centers of cells. When one of these enzymes is defective or missing,

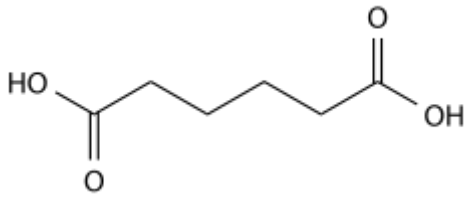
partially broken-down nutrients accumulate in the cells and damage them, causing the signs and symptoms of glutaric acidemia type II.



Glutaric acidemia type 2 has an autosomal recessive pattern of inheritance.

This condition is inherited in an autosomal recessive pattern, which means the defective gene is located on an autosome, and two copies of the gene - one from each parent - are needed to inherit the disorder. The parents of an individual with an autosomal recessive disorder are carriers of one copy of the defective gene, but do not show signs and symptoms of the disorder themselves.

Adipic Acid



Contents

1 - Introduction

Adipic acid is the organic compound with the formula $(CH_2)_4(COOH)_2$. From the industrial perspective, it is the most important dicarboxylic acid: About 2.5 billion kilograms of this white crystalline powder are produced annually, mainly as a precursor for the production of nylon. Adipic acid otherwise rarely occurs in nature.

IUPAC name : hexanedioic acid	
Other names . hexane-1,6- dioic acid	
Molecular formula	$C_6 H_{10} O_4$
Molar mass	146 g mol−1
Appearance	White crystals (monoclinic)
Density	1.36 g / cm3
Melting point	152.1 °C
Boiling point	337.5 °C
Solubility in water	fairly soluble

EU classification	Irritant (Xi)
Flash point	196 °C
Auto ignition temperature	422 °C
LD50	3600 mg / kg (rat)

2 - Preparation and reactivity

Adipic acid is produced from a mixture of cyclohexanol and cyclohexanone called "KA oil", the abbreviation of "ketone-alcohol oil." The KA oil is oxidized with nitric acid to give adipic acid, via a multistep pathway. Early in the reaction the cyclohexanol is converted to the ketone, releasing nitrous acid:

$HOC_6H_{11} + HNO_3 \rightarrow OC_6H_{10} + HNO_2 + H_2O$

Among its many reactions, the cyclohexanone is nitrosated, setting the stage for the scission of the C- C bond:

$HNO_2 + HNO_3 \rightarrow NO^+NO_3^- + H_2O$

$OC_6H_{10} + NO^+ \rightarrow OC_6H_9{}^{-2} - NO + H^+$

Side products of the method include glutaric and succinic acids.

Related processes start from cyclohexanol, which is obtained from the hydrogenation of phenol.

2 – 1 - Alternative methods of production

Several methods have been developed by carbonylation of butadiene. For example, the hydrocarboxylation proceeds as follows:

$CH_2= CHCH = CH_2 + 2\ CO + 2\ H_2O \rightarrow HO_2C(CH_2)_4CO_2H$

A method that utilizes principles of green chemistry in that water is the only by-product. Cyclohexene is oxidized with hydrogen peroxide using a tungstate - based catalyst and a phase transfer catalyst. The waste product is water. Historically, adipic acid was prepared by oxidation of various fats.

2 – 2 - Reactions

Adipic acid is a dibasic acid (can be deprotonated twice). Its pKa's are 4.41 and 5.41.

With the carboxylate groups separated by four methylene groups, adipic acid is suited for intramolecular condensation reactions. Upon treatment with barium hydroxide at elevated temperatures, it undergoes ketonization to give cyclopentanone.

3 - Uses

The great majority of the 2.5 billion kg of adipic acid produced annually is used as monomer for the production of nylon by a polycondensation reaction with hexamethylene diamine forming 6,6-nylon. Other major applications also involve polymers: it is a monomer for production of Poly urethane and its esters are plasticizers , especially in PVC.

3 – 1 - In medicine

Adipic acid has been incorporated into controlled-release formulation matrix tablets to obtain pH-independent release for both weakly basic and weakly acidic drugs. It has also been incorporated into the polymeric coating of hydrophilic monolithic systems to modulate the intragel pH, resulting in zero-order release of a hydrophilic drug. The disintegration at intestinal pH of the enteric polymer shellac has been reported to improve when adipic acid was used as a pore-forming agent without affecting release in the acidic media. Other controlled-release formulations have included adipic acid with the intention of obtaining a late-burst release profile.

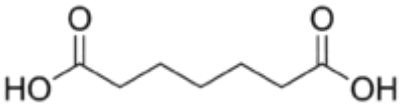
3 – 2 - In foods

Small but significant amounts of adipic acid are used as a food ingredient as a flavorant and gelling aid . It is used in some calcium carbonate antacids to make them tart.

4 - Safety

Adipic acid, like most carboxylic acids, is a mild skin irritant. It is mildly toxic, with an LD50 of 3600 mg/kg for oral ingestion by rats.

Pimelic Acid

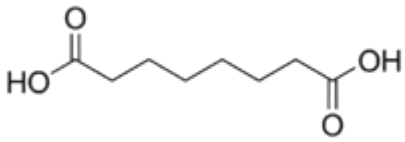


Pimelic acid is the organic compound with the formula $HO_2C(CH_2)_5CO_2H$. Derivatives of pimelic acid are involved in the biosynthesis of the amino acid called lysine. Pimelic acid is one CH_2 unit longer than a related dicarboxylic acid, adipic acid, a precursor to many polyesters and polyamides. It is the final member of the mnemonic used to aid recollection of the order of the first six dicarboxylic acids using their common (not IUPAC) nomenclature: Dicarboxylic acid

Pimelic acid has been synthesized from cyclohexanone and from salicylic acid. In the former route, the additional carbon is supplied by dimethyloxalate, which reacts with the enolate.

IUPAC name[hide] heptanedioic acid	
Molecular formula	$C_7H_{12}O_4$
Molar mass	160 g / mol
Density	1.28 g / cm3
Melting point	103 – 105 °C
Boiling point	Decomposes

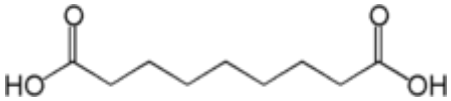
Suberic Acid



Suberic acid, also octanedioic acid, is a dicarboxylic acid, with formula $C_8H_{14}O_4$. It is a colorless crystalline solid used in drug syntheses and plastics manufacture.

IUPAC name :	Octa nedioic acid
Molecular formula	$C_8H_{14}O_4$
Molar mass	174 g / mol
Density	1.272 g / cm^3 (25 °C)
Melting point	141–144 °C
Boiling point	230 °C at 15 mmHg
Solubility in water	2.46 g /L

Azelaic Acid



Contents

1 - Introduction

Azelaic acid is an organic compound with the formula $(CH_2)_7(CO_2H)_2$. This saturated dicarboxylic acid exists as a white powder. It is found in wheat, rye, and barley. It is a component of a number of hair and skin conditioners.

IUPAC name : nona nedioic acid	
Molecular formula	$C_9H_{16}O_4$
Molar mass	188 g mol−1
Melting point	109 -111 °C
Boiling point	286 °C at 100 mmHg
Solubility in water	2.14 g / L

2 - Production

Azelaic acid is industrially produced by the ozonolysis of oleic acid. The side product is nonanoic acid. It is produced naturally by Malassezia furfur (also known as Pityrosporum ovale), a yeast that lives on normal skin. The bacterial degradation of nonanoic acid gives azelaic acid.

3 - Biological function

In plants, azelaic acid serves as a "distress flare" involved in defense responses after infection . It serves as a signal that induces the accumulation of salicylic acid , an important component of a plant's defensive response.

4 - Applications

4 – 1 - Polymers and related materials

Esters of this dicarboxylic acid find applications in lubrication and plasticizers. With hexamethylenediamine azelaic acid forms Nylon - 6,9, which finds specialized uses as a plastic.

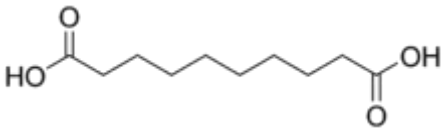
4 – 2 - Medical

Azelaic acid is used to treat mild to moderate acne, both comedonal acne and inflammatory acne . It belongs to a class of medication called dicarboxylic acids. It works by killing acne bacteria that infect skin pores. It also decreases the production of keratin, which is a natural substance that promotes the growth of acne bacteria Azelaic acid is also used as a topical gel treatment for rosacea, due to its ability to reduce inflammation . It clears the bumps and swelling caused by Rosacea. Azelaic acid has been used for treatment of skin pigmentation including melasma and post inflammatory hyper pigmentation , particularly in those with darker skin types. It has been recommended as an alternative to hydroquinone (HQ). As a tyrosinase inhibitor, azelaic acid reduces synthesis of melanin.

4 – 3 - Brand names

AzClear Action (20 % lotion, Ego Pharmaceuticals), Azelex (20% cream, Allergan), White Action cream (20 % cream ,2 % glycolic acid), SynCare), Finacea (15 % gel, Intendis/Berlex Laboratories, subsidiaries of Bayer AG), Finevin (20 % cream, Intendis / Berlex Laboratories), Skinoren (20 % cream or 15% gel, Intendis), Melazepam, Strata Dermatologics, 2oz, Mixed Dicarboxylic Acids 20 % Azelaic Acid Cream.,and Azaclear (azelaic acid and niacinamide, Epikinetics LLC).

Sebacic Acid



Sebacic acid is a dicarboxylic acid with structure $(HOOC)(CH_2)_8(COOH)$, and is naturally occurring.

In its pure state it is a white flake or powdered crystal. The product is described as non-hazardous, though in its powdered form it can be prone to flash ignition (a typical risk in handling fine organic powders).

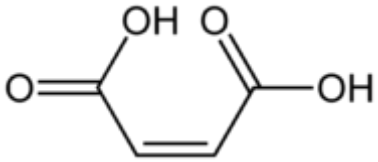
Sebaceus is Latin for tallow candle, sebum (tallow) is Latin for tallow, and refers to its use in the manufacture of candles.

Sebacic acid is a derivative of castor oil, with the vast majority of world production occurring in China which annually exports over 20,000 metric tonnes, representing over 90 % of global trade of the product .

In the industrial setting, sebacic acid and its homologues such as azelaic acid can be used in plasticizers, lubricants, hydraulic fluids, cosmetics, candles, etc. Sebacic acid is also used as an intermediate for aromatics, antiseptics, and painting materials.

IUPAC name : decanedioic acid	
Other names : 1,8 - octanedicarboxylic acid	
Molecular formula	$C_{10}H_{18}O_4$
Molar mass	202 g / mol
Density	1.209 g / cm^3 (25 °C)
Melting point	131–134.5 °C
Boiling point	294.4 °C at 100 mmHg
Solubility in water	0.25 g / L

Maleic Acid



Contents

1 - Introduction

Maleic acid is an organic compound that is a dicarboxylic acid, a molecule with two carboxyl groups. Its chemical formula is $HO_2CCHCHCO_2H$. Maleic acid is the cis-isomer of butenedioic acid, where as fumaric acid is the trans-isomer. It is mainly used as a precursor to fumaric acid, and relative to its parent maleic anhydride, maleic acid has few applications.

IUPAC name : Maleic acid (Z)-Butenedioic acid	
Other names : (Z)-butenedioic acid, cis-butenedioic acid, malenic acid, maleinic acid, toxilic acid	
Molecular formula	$C_4H_4O_4$
Molar mass	116 g mol−1
Appearance	White solid
Density	1.59 g/cm³

Melting point	135 °C (decomposes)
Solubility in water	788 g / L
EU classification	Harmful (Xn)

2 - Physical properties

Maleic acid is a less stable molecule than fumaric acid. The difference in heat of combustion is 22.7 kJ·mol−1. The heat of combustion is -1355 kJ / mole. Maleic acid is more soluble in water than fumaric acid. The melting point of maleic acid (135 °C) is also much lower than that of fumaric acid (287 °C). Both properties of maleic acid can be explained on account of the intramolecular hydrogen bonding that takes place in maleic acid at the expense of intermolecular interactions, and that are not possible in fumaric acid for geometric reasons.

3 - Production and industrial applications

In industry, maleic acid is derived by hydrolysis of maleic anhydride, the latter being produced by oxidation of benzene or butane.

Maleic acid is an industrial raw material for the production of glyoxylic acid by ozonolysis.

Maleic acid may be used to form acid addition salts with drugs to make them more stable, such as indacaterol maleate.

3 – 1 - Isomerization to fumaric acid

The major industrial use of maleic acid is its conversion to fumaric acid. This conversion, an isomerization, is catalysed by a variety of reagents, such as mineral acids and thiourea. Again, the large difference in water solubility makes fumaric acid purification easy.

The isomerization is a popular topic in schools. Maleic acid and fumaric acid do not spontaneously interconvert because rotation around a carbon carbon double bond is not energetically favourable. However, conversion of the cis isomer into the trans isomer is possible by photolysis in the presence of a small amount of bromine.[8] Light converts elemental bromine into a bromine radical, which attacks the alkene in a radical addition reaction to a bromo-

alkane radical; and now single bond rotation is possible. The bromine radicals recombine and fumaric acid is formed. In another method (used as a classroom demonstration), maleic acid is transformed into fumaric acid through the process of heating the maleic acid in 12 M hydrochloric acid solution. Reversible addition (of H+) leads to free rotation about the central C- C bond and formation of the more stable and less soluble fumaric acid.

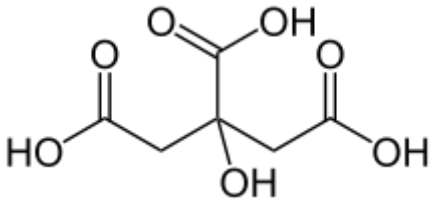
4 - Other reactions

Although not practised commercially, maleic acid can be converted into maleic anhydride by dehydration, to malic acid by hydration, and to succinic acid by hydrogenation (ethanol / palladium on carbon).[9] It reacts with thionyl chloride or phosphorus pentachloride to give the maleic acid chloride (it is not possible to isolate the mono acid chloride). Maleic acid, being electrophilic, participates as a dienophile in many Diels - Alder reactions.

5 - Maleates

The maleate ion is the ionized form of maleic acid. The maleate ion is useful in biochemistry as an inhibitor of transaminase reactions. Maleic acid esters are also called maleates, for instance dimethyl maleate.

Tri Carboxylic Acid



Citric acid

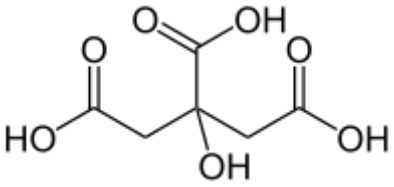
1 - Introduction

A tri carboxylic acid is an organic carboxylic acid whose chemical structure contains three carboxyl functional groups (-COOH) The best-known example of a tricarboxylic acid is citric acid.

2 - Examples

Citric acid
Aconitic acid

Citric Acid



Contents

1 - Introduction

Citric acid is a weak organic acid with the formula $C_6H_8O_7$. It is a natural preservative / conservative and is also used to add an acidic, or sour, taste to foods and soft drinks. In biochemistry, the conjugate base of citric acid, citrate, is important as an intermediate in the citric acid cycle, which occurs in the metabolism of all aerobic organisms.

Citric acid is a commodity chemical, and more than a million tonnes are produced every year by fermentation. It is used mainly as an acidifier, as a flavoring, and as a chelating agent.

IUPAC name :
2-hydroxypropane-1,2,3-tricarboxylic acid
Other names :
3-carboxy-3- hydroxypentanedioic acid
2-hydroxy-1,2,3 - propanetricarboxylic acid[1]

Molecular formula	$C_6H_8O_7$
Molar mass	192 g/mol (anhydrous) 210 g / mol (monohydrate)
Appearance	crystalline white solid
Density	1.665 g /cm^3 (1.5 g / cm^3 for mono hydrate)
Melting point	153 °C
Boiling point	175 °C (decomposes)
Solubility in water	73 g/100 ml (20 °C)
Main hazards	skin and eye irritant

2 - Properties

At room temperature, citric acid is a white crystalline powder. It can exist either in an anhydrous (water-free) form or as a monohydrate. The anhydrous form crystallizes from hot water, while the monohydrate forms when citric acid is crystallized from cold water. The monohydrate can be converted to the anhydrous form by heating above 78 °C. Citric acid also dissolves in absolute (anhydrous) ethanol (76 parts of citric acid per 100 parts of ethanol) at 15 °C.

In chemical structure, citric acid shares the properties of other carboxylic acids. When heated above 175 °C, it decomposes through the loss of carbon dioxide and water (see decarboxylation).

Citric acid is a slightly stronger acid than typical carboxylic acids because the anion can be stabilized by intramolecular hydrogen-bonding from other protic groups on citric acid.

3 - Discovery and production

The discovery of citric acid has been credited to the 8th century Persian alchemist Jābir ibn Hayyān (Geber) . Medieval scholars in

Europe were aware of the acidic nature of lemon and lime juices; such knowledge is recorded in the 13th century encyclopedia *Speculum Maius* (*The Great Mirror*), compiled by Vincent of Beauvais.[*citation needed*] Citric acid was first isolated in 1784 by the Swedish chemist Carl Wilhelm Scheele, who crystallized it from lemon juice.[6][7] Industrial-scale citric acid production began in 1890 based on the Italian citrus fruit industry.

In 1893, C. Wehmer discovered *Penicillium* mold could produce citric acid from sugar. However, microbial production of citric acid did not become industrially important until World War I disrupted Italian citrus exports. In 1917, the American food chemist James Currie discovered certain strains of the mold *Aspergillus niger* could be efficient citric acid producers, and the pharmaceutical company Pfizer began industrial-level production using this technique two years later, followed by Citrique Belge in 1929.

In this production technique, which is still the major industrial route to citric acid used today, cultures of *A. niger* are fed on a sucrose or glucose-containing medium to produce citric acid. The source of sugar is corn steep liquor, molasses, hydrolyzed corn starch or other inexpensive sugary solutions.[8] After the mold is filtered out of the resulting solution, citric acid is isolated by precipitating it with lime (calcium hydroxide) to yield calcium citrate salt, from which citric acid is regenerated by treatment with sulfuric acid.

3 – 1 - Other methods

Prior to the fermentative process, citric acid was isolated from citrus fruits. The juice was treated with lime ($Ca(OH)_2$) to precipitate calcium citrate, which was isolated and converted back to the acid.

In 2007, world wide annual production stood at approximately 1,600,000 tonnes. More than 50 % of this volume was produced in China. More than 50 % was used as acidulent in beverages, some 20% in other food applications, 20 % for detergent applications and 10% for related applications other than food, such as cosmetics, pharmaceutics and in the chemical industry.

4 - Occurrence

Citric acid exists in greater than trace amounts in a variety of fruits and vegetables, most notably citrus fruits. Lemons and limes have particularly high concentrations of the acid; it can constitute as much as 8 % of the dry weight of these fruits (about 47 g/L in the juices) . The concentrations of citric acid in citrus fruits range from 0.005 mol/L for oranges and grapefruits to 0.30 mol/L in lemons and limes. Within species, these values vary depending on the cultivar and the circumstances in which the fruit was grown.

5 - Biochemistry

5 – 1 - Citric acid cycle

Citrate, the conjugate base of citric acid is one of a series of compounds involved in the physiological oxidation of fats, proteins, and carbohydrates to carbon dioxide and water.

This series of chemical reactions is central to nearly all metabolic reactions, and is the source of two-thirds of the food-derived energy in higher organisms. Hans Adolf Krebs received the 1953 Nobel Prize in Physiology or Medicine for the discovery. The series of reactions is known by various names, including the "citric acid cycle", the "Krebs cycle" or "Szent-Györgyi — Krebs cycle", and the "tricarboxylic acid (TCA) cycle".

5 – 2 - Other biological roles

Citrate is a critical component of bone, helping to regulate the size of calcium crystals.

6 - Applications

The dominant use of citric acid is as a flavoring and preservative in food and beverages, especially soft drinks . Within the European Union it is denoted by E number E330. Citrate salts of various metals are used to deliver those minerals in a biologically available form in many dietary supplements. The buffering properties of citrates are used to control pH in household cleaners and pharmaceuticals. In the United States the purity requirements for citric acid as a food additive

are defined by the Food Chemicals Codex, which is published by the United States Pharmacopoeia (USP).

6 – 1 - Foods , other

Citric acid can be added to ice cream as an emulsifying agent to keep fats from separating, to caramel to prevent sucrose crystallization, or to recipes in place of fresh lemon juice. Citric acid is used with sodium bicarbonate in a wide range of effervescent formulae, both for ingestion (*e.g.*, powders and tablets) and for personal care (*e.g.*, bath salts, bath bombs, and cleaning of grease). Citric acid is also often used in cleaning products and sodas or fizzy drinks.

Citric acid sold in a dry powdered form is commonly sold in markets and groceries as "sour salt", due to its physical resemblance to table salt. It has use in culinary applications where an acid is needed for either its chemical properties or for its sour flavor, but a dry ingredient is needed and additional flavors are unwanted (e.g., instead of vinegar or lemon juice).

6 – 2 - Cleaning and chelating agent

Citric acid is an excellent chelating agent, binding metals. It is used to remove limescale from boilers and evaporators . It can be used to soften water, which makes it useful in soaps and laundry detergents. By chelating the metals in hard water, it lets these cleaners produce foam and work better without need for water softening. Citric acid is the active ingredient in some bathroom and kitchen cleaning solutions. A solution with a 6% concentration of citric acid will remove hard water stains from glass without scrubbing. In industry, it is used to dissolve rust from steel. Citric acid can be used in shampoo to wash out wax and coloring from the hair.

Illustrative of its chelating abilities, citric acid was the first successful eluant used for total ion - exchange separation of the lanthanides, during the Manhattan Project in the 1940s. In the 1950s, it was replaced by the far more efficient EDTA. It can be used to slow setting of Portland cement. It can delay setting time substantially.

6 – 3 - Cosmetics and pharmaceuticals

Citric acid is widely used as a pH adjusting agent in creams and gels of all kinds. In this role, it is classified in most jurisdictions as a processing aid and so does not need to be listed on ingredient lists.

Citric acid is an alpha hydroxy acid and used as an active ingredient in chemical peels.

Citric acid is commonly used as a buffer to increase the solubility of brown heroin. Single-use citric acid sachets have been used as an inducement to get heroin users to exchange their dirty needles for clean needles in an attempt to decrease the spread of AIDS and hepatitis . Other acidifiers used for brown heroin are ascorbic acid, acetic acid, and lactic acid; in their absence, a drug user will often substitute lemon juice or vinegar.

Citric acid is used as one of the active ingredients in the production of antiviral tissues.

6 – 4 - Dyeing

Citric acid can be used in food coloring to balance the pH level of a normally basic dye. It is used as an odorless alternative to white vinegar for home dyeing with acid dyes.

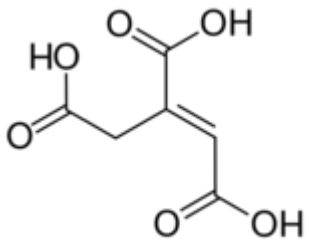
6 – 5 - Industrial and construction

Citric acid can be used as a successful alternative to nitric acid in passivation of stainless steel.

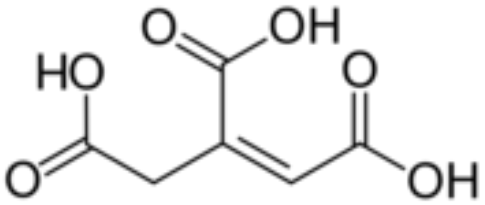
6 – 6 - Photography

Citric acid can be used as a lower-odor stop bath as part of the process for developing photographic film. Photographic developers are alkaline, so a mild acid is used to neutralize and stop their action quickly, but commonly used acetic acid leaves a strong vinegar odor in the darkroom.

Aconitic Acid



trans-Aconitic acid



cis-Aconitic acid

Aconitic acid is an organic acid. The two isomers are *cis*-aconitic acid and *trans*-aconitic acid. The conjugate base of *cis*-aconitic acid, *cis*-aconitate is an intermediate in the isomerization of citrate to isocitrate in the citric acid cycle. It is acted upon by the enzyme aconitase.

Aconitic acid can be synthesized by dehydration of citric acid using sulfuric acid :

$$(HO_2CCH_2)_2COH(CO_2H) \rightarrow HO_2CCH{=}C(CO_2H)CH_2CO_2H + H_2O$$

It was first prepared by thermal dehydration.

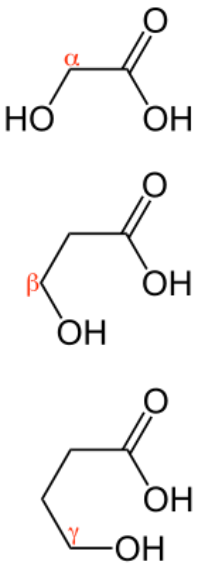
IUPAC name :
Prop-1-ene-1,2,3-tricarboxylic acid
Other names :
Achilleic acid ; Equisetic acid ;
Citridinic acid ; Pyrocitric acid

Molecular formula	$C_6H_6O_6$
Molar mass	174 g mol^{-1}
Appearance	Colorless crystals
Melting point	190 °C (decomp) (*trans isomer*), 122 °C (*cis isomer*)

Part - 3 -

Aliphatic Hydroxy Carboxy Acid

Alpha Hydroxy Acid



A - , β - and γ - Hydroxy Acids

Contents

1 - Introduction

α-Hydroxy acids, or alpha hydroxy acids (AHAs), are a class of chemical compounds that consist of a carboxylic acid substituted with a hydroxyl group on the adjacent carbon. They may be either naturally occurring or synthetic. AHAs are well known for their use in the cosmetics industry. They are often found in products claiming to reduce wrinkles or the signs of aging, and improve the overall look and feel of the skin. They are also used as chemical peels available in a dermatologist's office, beauty and health spas and home kits, which usually contain a lower concentration of around 4 %. Although their effectiveness is documented numerous cosmetic products have appeared on the market with unfounded claims of performance. Many

well - known α-hydroxy acids are useful building blocks in organic synthesis: the most common and simple are glycolic acid, lactic acid, citric acid, mandelic acid.

2 - Cosmetic applications

Understanding skin structure and cutaneous aging is helpful to a discussion of the topical action of AHAs. Human skin has two principal components, the avascular epidermis and the underlying vascular dermis. Cutaneous aging, while having epidermal concomitants , seems to involve primarily the dermis and is caused by intrinsic and extrinsic aging factors.

AHAs are a group of organic carboxylic compounds. AHAs most commonly used in cosmetic applications are typically derived from food products including glycolic acid (from sugar cane), lactic acid (from sour milk), malic acid (from apples), citric acid (from citrus fruits) and tartaric acid (from grape wine). For any topical compound to be effective, including AHA, it must penetrate into the skin where it can act on living cells. Bioavailability (influenced primarily by small molecular size) is an important factor in a compound's ability to penetrate the top layer of the skin. Glycolic acid, having the smallest molecular size, is the AHA with greatest bioavailability and penetrates the skin most easily; this largely accounts for the popularity of this product in cosmetic applications.

2 – 1 - Epidermal effect

AHAs have a profound effect on keratinization; which is clinically detectable by the formation of a new stratum corneum. It appears that AHAs modulate this formation through diminished cellular cohesion between corneocytes at the lowest levels of the stratum corneum.

2 – 2 - Dermal effects

AHAs with greater bioavailability appear to have deeper dermal effects. Glycolic acid, lactic acid and citric acid, on topical application to photodamaged skin, have been shown to produce increased amounts of mucopolysaccharides and collagen and increased skin

thickness without detectable inflammation, as monitored by skin biopsies

3 - Alpha hydroxy acids at different concentrations

In low concentrations, 5 – 10 %, as is found in many over-the-counter products, glycolic acid reduces cell adhesion in the top layer of the skin. This action promotes exfoliation of the outermost layer of the skin accounting for smoother texture following regular use of topical glycolic acid (GA). This relatively low concentration of GA lends itself to daily use as a monotherapy or a part of a broader skin care management for such conditions as acne, photo-damage, wrinkling as well as melasma . Care needs to be taken to avoid irritation as this may result in worsening of melasma or other pigmentary problems. Newer formulations combine glycolic acid with an amino acid such as arginine and form a time-release system that reduces the risk of irritation without affecting glycolic acid efficacy.[6] The use of an anti-irritant like allantoin is also helpful. Because of its safety, glycolic acid at the concentrations below 10 % can be used daily by most people except those with very sensitive skin.

In higher concentrations, between 10 and 50 %, its benefits are more pronounced but are limited to temporary skin smoothing without much long lasting results. This is still a useful concentration to use as it can prepare the skin for stronger glycolic acid concentrations (50 - 70%) as well as prime the skin for deeper chemical peels such as TCA peel (trichloroacetic acid).

At highest concentrations, 50 - 70 % applied for 3 to 8 minutes under the supervision of a physician, glycolic acid promotes slitting between the cells and can be used to treat acne or photo-damage (such as mottled dyspigmentation, melasma or fine wrinkles). The benefits from such short contact application (chemical peels) depend on the pH of the solution (the more acidic the product, or the lower the pH, the more pronounced the results), the concentration of GA (higher concentrations produce more vigorous response), the length of application and prior skin conditioning such as prior use of topical vitamin A products. Although single application of 50 - 70% GA will

produce beneficial results, multiple treatments every 2 to 4 weeks are required for optimal results . It is important to understand that glycolic acid peels are chemical peels with similar risks and side effects as other peels. Some of the side effects of AHAs chemical peeling can include hyper-pigmentation, persistent redness, scarring, as well as flare up of facial herpes infections ("cold sores").

4 - Chemical acidity

Although these compounds are related to the ordinary carboxylic acids, and therefore are weak acids, their chemical structure allows for the formation of an internal hydrogen bond between the hydrogen at the hydroxyl group and one of the oxygen atoms of the carboxylic group. Two effects emerge from this situation :

Due to the "occupation" of electrons of the carboxylic oxygens in the hydrogen bonding, the acidic proton is held less strongly, as the same electrons are used in bonding that hydrogen too. So the pK_a of 2-hydroxypropanoic acid (lactic acid) is a full unit lower compared to that of propionic acid itself (3.86 versus 4.87)

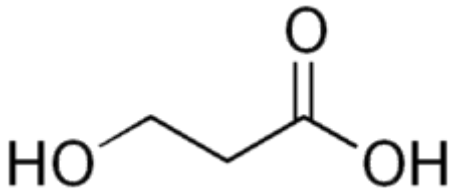
The internal bridging hydrogen is locked in its place on the NMR timescale: in mandelic acid (2- hydroxy - 2 - phenylacetic acid) this proton couples to the one on carbon in the same way and magnitude as hydrogens on geminal carbon atoms.

5 - Safety

AHAs are generally safe when used on the skin as a cosmetic agent using the recommended dosage. The most common side-effects are mild skin irritations, redness and flaking. The severity usually depends on the pH and the concentration of the acid used. Chemical peels tend to have more severe side - effects including blistering, burning and skin discoloration, although they are usually mild and go away a day or two after treatment.

The FDA has also warned consumers that care should be taken when using AHAs after an industry- sponsored study found that they can increase photosensitivity to the sun.

Beta Hydroxy Acid



3-Hydroxypropionic acid, a simple beta hydroxy acid

1 – Introductıon

A beta hydroxy acid or β -hydroxy acid (BHA) is an organic compound that contains a carboxylic acid functional group and hydroxy functional group separated by *two* carbon atoms. They are closely related to alpha hydroxy acids, in which the two functional groups are separated by *one* carbon atom.

In cosmetics, the term *beta hydroxy acid* refers specifically to salicylic acid, which is used in some "anti-aging" creams and acne treatments.

Upon dehydration, beta-hydroxy acids yield an alpha-beta unsaturated acid.

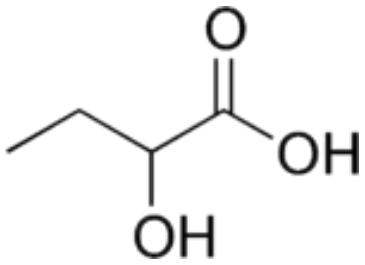
2 - Acidic properties

Compared to non - hydroxylated carboxylic acids, this group of acids is stronger, although less strong than the alpha hydroxy acids. Due to the larger distance, the intramolecular hydrogen bridge is less easily formed compared to the alpha hydroxy acids.

3 - Other beta hydroxy acids include :

beta-Hydroxy Butyric Acid
beta-Hydroxy *beta*-Methyl Butyrate
Carnitine

2 - Hydroxy Butyric Acid

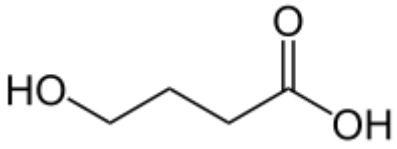


2-Hydroxybutyric acid (or alpha - hydroxy butyrate) is a hydroxy butyric acid with the hydroxyl group on the carbon adjacent to the carboxyl. It is a chiral compound having two enantiomers, D-2-hydroxybutyric acid and L-2-hydroxybutyric acid.

2-Hydroxy butyrate, the conjugate base of 2-hydroxy butyric acid, is produced in mammalian tissues (principally hepatic) that catabolize L-threonine or synthesize glutathione. Oxidative stress or detoxification demands can dramatically increase the rate of hepatic glutathione synthesis. Under such metabolic stress conditions, supplies of L-cysteine for glutathione synthesis become limiting, so homocysteine is diverted from the transmethylation pathway forming methionine into the transsulfuration pathway forming cystathionine. 2-Hydroxybutyrate is released as a byproduct when cystathionine is cleaved to cysteine that is incorporated into glutathione. Chronic shifts in the rate of glutathione synthesis may be reflected by urinary excretion of 2-hydroxybutyrate.

IUPAC name : 2-Hydroxybutanoic acid	
Other names : alpha – hydroxy butyrate	
Molecular formula	$C_4H_8O_3$
Molar mass	104 g mol−1

Gamma – Hydroxy Butyric Acid



Contents

1 - Introduction

γ-Hydroxybutyric acid (GHB), also known as 4-hydroxybutanoic acid, is a naturally occurring substance found in the human central nervous system, as well as in wine, beef, small citrus fruits, and almost all animals in small amounts. It is also categorized as an illegal drug in many countries. It is currently regulated in Australia and New Zealand, Canada, most of Europe and in the US. GHB as the sodium salt, known as sodium oxybate (INN) or by the trade name Xyrem, is used to treat cataplexy and excessive daytime sleepiness in patients with narcolepsy.

2 - Medical use

The only common medical applications for GHB today are in the treatment of narcolepsy and more rarely alcoholism.

GHB is the active ingredient in the prescription medication sodium oxybate (Xyrem). Sodium oxybate is approved by the U.S. Food and Drug Administration (FDA) for the treatment of cataplexy associated with narcolepsy and Excessive Daytime Sleepiness (EDS) associated with narcolepsy.

3 - Recreational use

GHB is a central nervous system depressant used as an intoxicant. It has many street names, including "Georgia Home Boy","Lollipops", "Juice", "Liquid Ecstasy", "Mils", "G", "Liquid X", and "Liquid G", as well as "Fantasy". Its effects have been described anecdotally as comparable with alcohol and ecstasy use, such as euphoria, disinhibition, enhanced sensuality and empathogenic states. At higher doses, GHB may induce nausea, dizziness, drowsiness, agitation, visual disturbances, depressed breathing, amnesia, unconsciousness, and death. The effects of GHB can last from 1.5 to 3 hours, or even longer if large doses have been consumed. Consuming GHB with alcohol is dangerous as it can lead to vomiting in combination with unrouseable sleep, a potentially lethal combination.

In general, the doses used recreationally are between 500 mg and 3,000 mg. When used as a recreational drug, GHB may be found as the sodium or potassium salt, which is a white crystalline powder, or as GHB salt dissolved in water to form a clear solution. The sodium salt of GHB has a salty taste. Other salt forms such as calcium GHB and magnesium GHB have also been reported, but the sodium salt is by far the most common.

Some chemicals convert to GHB in the stomach and blood stream. GBL, or gamma - butyrolactone, is one such prodrug. Other prodrugs include 1,4- butanediol. There may be additional toxicity concerns with these precursors. 1,4-B and GBL are normally found as pure liquids, though they may be mixed with other more harmful

solvents when intended for industrial use, e.g., as paint stripper or varnish thinner.

GHB can be easily manufactured at home with very little knowledge of chemistry, as it only involves the mixing of its two precursors, GBL and an alkali hydroxide (such as sodium hydroxide) to form the resulting GHB salt. Due to the ease of manufacture and the availability of its precursors, its production is not done in relatively few illicit laboratories like most other synthetic drugs, but in private homes by low level producers instead. While available as a prescription for rare and severe forms of sleep disorders such as narcolepsy in some other countries, notably most of Europe, GHB was banned (in the U.S.) by the FDA in 1990. However, on 17 July 2002, GHB was approved for treatment of cataplexy, often associated with narcolepsy. GHB is "colourless and odorless".

3 – 1 - Club and rave scene use

GHB is often taken because users find that it enhances their experiences of being in a club, party, or rave; small doses of GHB can act as a stimulant and aphrodisiac. GHB is sometimes referred to as liquid ecstasy, liquid X or liquid E due to its tendency to produce euphoria and sociability and its use in the dance party scene.[14] Despite this nickname, GHB has entirely separate chemical and pharmacological modes of action compared to MDMA (ecstasy).

3 – 2 - Sports and athletics

Some athletes also use GHB, as GHB has been shown to elevate human growth hormone in vivo . The growth hormone elevating effects of GHB are mediated through muscarinic acetylcholine receptors and can be prevented by prior administration of pirenzepine, a muscarinic acetylcholine receptor blocking agent.

As certain succinate salts have been shown to elevate growth hormone in vitro , and because GHB is metabolized into succinate some people have suggested this may play a role in the growth hormone elevations from GHB. There is however currently no evidence to show that succinate plays any role in the growth hormone elevations from GHB.

4 - As a date rape drug

Like alcohol and potent benzodiazepines such as flunitrazepam (Rohypnol), GHB has been labeled as a date rape drug . The sodium form of GHB has an extremely salty taste but, as it is colourless and odorless , it has been described as "very easy to add to drinks" that mask the flavor. Allegedly, GHB has been used in cases of drug-related sexual assault, usually when the victim is vulnerable due to intoxication with a sedative, generally alcohol . It is difficult to establish how often GHB is used to facilitate rape as it is difficult to detect in a urine sample after a day, and many victims may not recall the rape until some time after this , although GHB can be detected in hair.[21] Hair testing can be a useful tool in court cases and/or for the victim's own information. Over – the - counter urine test kits only test for date rape drugs that are benzodiazepines, which GHB is not. To detect GHB in urine, the sample must be taken within 8 – 12 hours of GHB ingestion, and cannot be tested at home. GHB can be detected in hair for months after GHB ingestion. Other drugs, such as muscle relaxers (Carisoprodol for example), are sometimes mixed with GHB. Therefore, it can be beneficial to request that the hair sample be tested for multiple drugs.

There have been several high profile cases of GHB as a date rape drug that received national attention in the United States. In early 1999 a 15 year old girl, Samantha Reid of Rockwood, MI, died from GHB poisoning. Reid’s death inspired the legislation titled the "Hillory J. Farias and Samantha Reid Date-Rape Drug Prohibition Act of 2000." This is the law that made GHB a schedule 1 controlled substance.

GHB produced as a sodium salt (sodium oxybate) may provide a noticeable salty character to the drink, though individual sensitivity to the taste of salt varies. GHB can also be produced as different salts, some of which may not have a taste as distinctive as the sodium salt (e.g., magnesium oxybate), or much less commonly in the unstable free-acid form.

5 - Adverse effects

5 – 1 - Combination with alcohol

In humans, GHB has been shown to inhibit the elimination rate of alcohol. This may explain the respiratory arrest that has been reported after ingestion of both drugs. A review of the details of 194 deaths attributed to or related to GHB over a ten - year period found that most were from respiratory depression caused by interaction with alcohol or other drugs.

5 – 2 - Reported deaths

One report has suggested that sodium oxybate overdose may be fatal, based on deaths of three patients who had been prescribed the drug . However, for two of the three cases, post-mortem GHB concentrations were 141 and 110 mg / L, which is within the expected range of concentrations for GHB after death, and the third case was a patient with a history of intentional drug overdose.

One publication has investigated 226 deaths attributed to GHB. Of 226 deaths included, 213 suffered cardiorespiratory arrest and 13 suffered fatal accidents. Seventy-one deaths (34 %) had no co-intoxicants. Postmortem blood GHB was 18 – 4400 mg / L (median = 347) in deaths negative for co - intoxicants.

GHB is produced in the body in very small amounts, and blood levels may climb after death to levels in the range of 30–50 mg/L.[30] Levels higher than this are found in GHB deaths. Levels lower than this may be due to GHB or to postmortem endogenous elevations.

A UK parliamentary committee commissioned report found the use of GHB to be less dangerous than tobacco and alcohol in social harms, physical harm and addiction.

5 – 3 - Treatment of overdose

Overdose of GHB can be difficult to treat because of its multiple effects on the body. GHB tends to cause rapid unconsciousness at doses above 3500 mg, with single doses over 7000 mg often causing life-threatening respiratory depression, and higher doses still inducing

bradycardia and cardiac arrest. Other side - effects include convulsions (especially when combined with stimulants), and nausea/vomiting (especially when combined with alcohol).

The greatest life threat due to GHB overdose (with or without other substances) is respiratory arrest . Other relatively common causes of death due to GHB ingestion include aspiration of vomitus, positional asphyxia, and trauma sustained while intoxicated (e.g., motor vehicle accidents while driving under the influence of GHB). The risk of aspiration pneumonia and positional asphyxia risk can be reduced by laying the patient down in the recovery position. People are most likely to vomit as they become unconscious, and as they wake up. It is important to keep the patient/friend awake and moving, plus do not allow them to be alone as death through vomiting can easily happen. Frequently they will be in a good mood but this does not mean they are not in danger. GHB overdose is a medical emergency and immediate assessment in an emergency department is needed.

Convulsions from GHB can be treated with diazepam or lorazepam , even though these are also CNS depressants they are GABAA agonists, whereas GHB is primarily a GABAB agonist, so the benzodiazepines do not worsen CNS depression as much as might be expected.

Because of the faster and more complete absorption of GBL relative to GHB, its dose-response curve is steeper, and overdoses of GBL tend to be more dangerous and problematic than overdoses involving only GHB or 1,4-B. Any GHB/GBL overdose is a medical emergency and should be cared for by appropriately trained personnel.

A newer synthetic drug SCH-50911, which acts as a selective GABAB antagonist, quickly reverses GHB overdose in mice.[34] However, this treatment has yet to be tried in humans, and it is unlikely that it will be researched for this purpose in humans due to the illegal nature of clinical trials of GHB, and the lack of medical indemnity coverage inherent in using an untested treatment for a life-threatening overdose .

5 – 4 - Detection of use

GHB may be quantitated in blood or plasma to confirm a diagnosis of poisoning in hospitalized patients, provide evidence in an impaired driving arrest or to assist in a medicolegal death investigation. Blood or plasma GHB concentrations are usually in a range of 50 – 250 mg / L in persons receiving the drug therapeutically (during general anesthesia), 30 – 100 mg / L in those arrested for impaired driving, 50 – 500 mg / L in acutely intoxicated patients and 100 – 1000 mg / L in victims of fatal overdosage. Urine is often the preferred specimen for routine drug abuse monitoring purposes. Both gamma-butyrolactone (GBL) and 1,4- butanediol are converted to GHB in the body.

5 – 5 - Neurotoxicity

In multiple studies, GHB has been found to impair spatial and working learning and memory in rats with chronic administration. These effects are associated with decreased NMDA receptor expression in the cerebral cortex and possibly other areas as well.

Pedraza et al. (2009) found that repeated administration of GHB to rats for 15 days drastically reduced the number of neurons and non-neuronal cells in the CA1 region of the hippocampus and in the prefrontal cortex. With doses of 10 mg/kg of GHB, they were decreased by 61 % in the CA1 region and 32 % in the prefrontal cortex, and with 100 mg/kg, they were decreased by 38 % and 9 %, respectively. It is interesting to note that GHB has biphasic effects on neuronal loss, with lower doses (10 mg/kg) producing the most neurotoxicity, and higher doses (100 mg/kg) producing less.

Pretreatment with NCS - 382, a GHB receptor antagonist, prevents both learning/memory deficits and neuronal loss in GHB-treated animals, suggesting that GHB's neurotoxic actions are mediated via activation of the GHB receptor. In addition, the neurotoxicity appears to be caused by oxidative stress.

5 – 6 - Addiction

Although there have been reported fatalities due to GHB withdrawal, reports are inconclusive and further research is needed. Addiction occurs when repeated drug use disrupts the normal balance of brain circuits that control rewards, memory and cognition, ultimately leading to compulsive drug taking.

Colombo reports that rats forced to consume massive doses of GHB will intermittently prefer GHB solution to water, but notes that "no rat showed any sign of withdrawal when GHB was finally removed at the end of the 20 - week period" or during periods of voluntary abstinence.

5 – 7 - Withdrawal

GHB has also been associated with a withdrawal syndrome of insomnia, anxiety, and tremor that usually resolves within three to twenty- one days . The withdrawal syndrome can be severe producing acute delirium and may require hospitalization in an intensive care unit for management . The mainstay of treatment for severe with drawal is supportive care and benzo diazepines for control of acute delirium, but larger doses are often required compared to acute delirium of other causes (e.g . > 100 mg / d of diazepam). Baclofen has been suggested as an alternative or adjunct to benzodiazepines based on anecdotal evidence and some animal data. However, there is less experience with the use of baclofen for GHB withdrawal, and additional research in humans is needed. Baclofen was first suggested as an adjunct because benzodiazepines do not affect GABAB receptors and thus have no cross - tolerance with GHB while baclofen, which works via GABAB receptors, is cross-tolerant with GHB and may be more effective in alleviating withdrawal effects of GHB.

GHB withdrawal is not widely discussed in text books and some psychiatrists, general practitioners, and even hospital emergency physicians may not be familiar with this withdrawal syndrome.

6 - Endogenous production

Cells produce GHB by reduction of succinic semialdehyde via the enzyme succinic semialdehyde dehydrogenase. This enzyme appears to be induced by cAMP levels , meaning substances that elevate cAMP, such as forskolin and vinpocetine, may increase GHB synthesis and release. People with the disorder known as succinic semialdehyde dehydrogenase deficiency, also known as gamma-hydroxybutyric aciduria, have elevated levels of GHB in their urine, blood plasma and cerebrospinal fluid.

The precise function of GHB in the body is not clear. It is known, however, that the brain expresses a large amount of receptors that are activated by GHB . These receptors are excitatory and not responsible for the sedative effects of GHB – they have been shown to elevate the principle excitatory neuro transmitter — glutamate . The benzamide antipsychotics — amisulpride, sulpiride — have been shown to bind to this receptor in vivo . Other antipsychotics were tested and were not found to have an affinity for this receptor.

It is a precursor to GABA, glutamate, and glycine in certain brain areas.

GHB has neuroprotective properties and has been found to protect cells from hypoxia.

7 - Natural fermentation by- product

GHB is also produced as a result of fermentation and so is found in small quantities in some beers and wines, in particular fruit wines. However, the amount of GHB found in wine is insignificant and not sufficient to produce any effects.

8 - Pharmacology

GHB has at least two distinct binding sites[61] in the central nervous system. GHB is an agonist at the newly characterized GHB receptor, which is excitatory , and it is a weak agonist at the GABAB receptor, which is inhibitory. GHB is a naturally occurring substance that acts in a similar fashion to some neurotransmitters in the

mammalian brain . GHB is probably synthesized from GABA in GABAergic neurons, and released when the neurons fire.

If taken orally, GABA itself does not effectively cross the blood-brain - barrier.

GHB induces the accumulation of either a derivative of tryptophan or tryptophan itself in the extracellular space, possibly by increasing tryptophan transport across the blood – brain barrier. The blood content of certain neutral amino-acids, including tryptophan, is also increased by peripheral GHB administration. GHB-induced stimulation of tissue serotonin turnover may be due to an increase in tryptophan transport to the brain and in its uptake by serotonergic cells. As the serotonergic system may be involved in the regulation of sleep, mood, and anxiety, the stimulation of this system by high doses of GHB may be involved in certain neuropharmacological events induced by GHB administration.

How ever, at therapeutic doses, GHB reaches much higher concentrations in the brain and activates GABAB receptors, which are primarily responsible for its sedative effects . GHB's sedative effects are blocked by GABAB antagonists.

The role of the GHB receptor in the behavioural effects induced by GHB is more complex. GHB receptors are densely expressed in many areas of the brain, including the cortex and hippocampus, and these are the receptors that GHB displays the highest affinity for. There has been somewhat limited research into the GHB receptor; however, there is evidence that activation of the GHB receptor in some brain areas results in the release of glutamate, the principal excitatory neurotransmitter. Drugs that selectively activate the GHB receptor cause absence seizures in high doses, as do GHB and GABA(B) agonists.

Activation of both the GHB receptor and GABA(B) is responsible for the addictive profile of GHB. GHB's effect on dopamine release is biphasic. Low concentrations stimulate

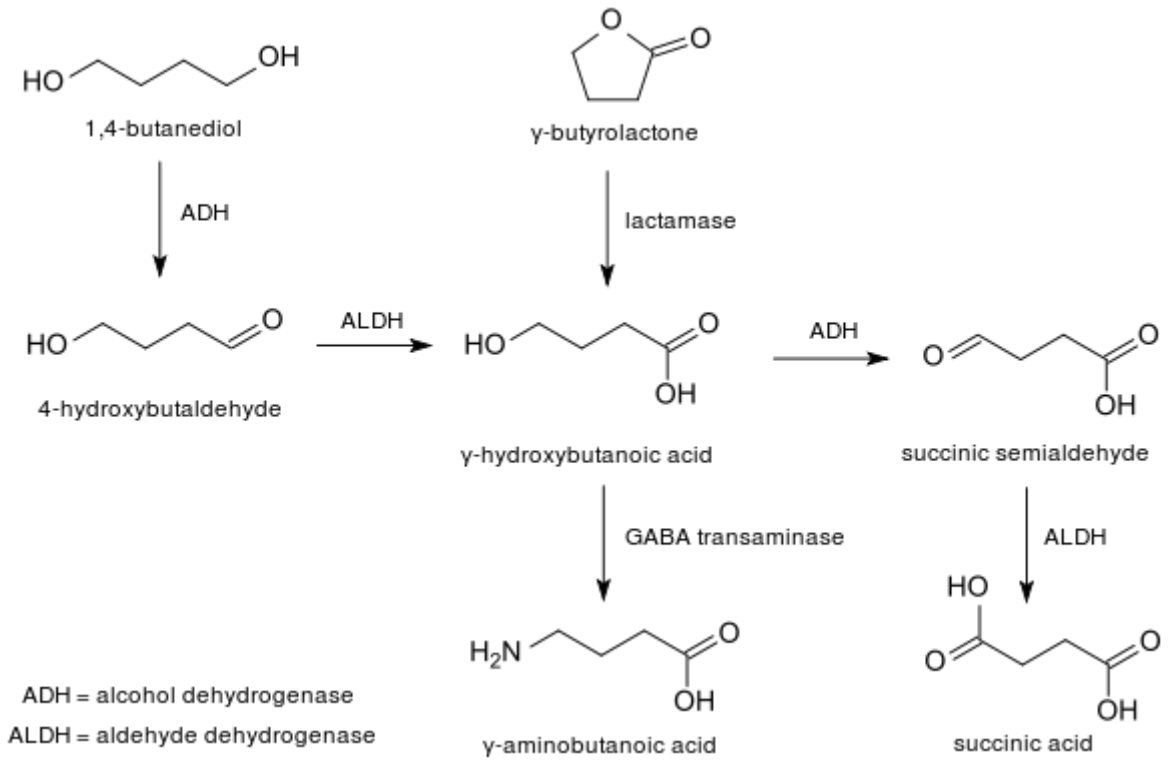
dopamine release via the GHB receptor. Higher concentrations inhibit dopamine release via GABA(B) receptors as do other GABA(B) agonists such as baclofen and phenibut. After an initial phase of inhibition, dopamine release is then increased via the GHB receptor. Both the inhibition and increase of dopamine release by GHB are inhibited by opioid antagonists such as naloxone and naltrexone. Dynorphin may play a role in the inhibition of dopamine release via kappa opioid receptors.

This explains the paradoxical mix of sedative and stimulatory properties of GHB, as well as the so-called "rebound" effect, experienced by individuals using GHB as a sleeping agent, wherein they awake suddenly after several hours of GHB-induced deep sleep. That is to say that, over time, the concentration of GHB in the system decreases below the threshold for significant GABAB receptor activation and activates predominantly the GHB receptor, leading to wakefulness.

Recently, analogs of GHB, such as 4 - hydroxy- 4 –methyl pentanoic acid have been synthesised and tested on animals, in order to gain a better understanding of GHB's mode of action . Analogues of GHB such as 3- methyl-GHB, 4- methyl- GHB and 4-phenyl-GHB have been shown to produce similar effects to GHB in some animal studies, but these compounds are even less well researched than GHB itself. Of these analogues, only 4 - methyl- GHB (γ - hydroxyvaleric acid, GHV) and its prodrug form gamma-valerolactone (GVL) have been reported as drugs of abuse in humans, and on the available evidence seem to be less potent but more toxic than GHB, with a particular tendency to cause nausea and vomiting.

Other prodrug ester forms of GHB have also rarely been encountered by law enforcement, including 1,4-diacetoxybutane, methyl - 4 - acetoxy butanoate, and ethyl-4-acetoxybutanoate, but these are, in general, covered by analogue laws in jurisdictions where GHB is illegal, and little is known about them beyond their delayed onset and longer duration of action. The intermediate compound 4-hydroxybutaldehyde is also a prodrug for GHB; however, as with all

aldehydes this compound is caustic and is strong-smelling and foul-tasting; actual use of this compound as an intoxicant is likely to be unpleasant and result in severe nausea and vomiting.



Metabolic pathway of GHB.

Also note that both of the metabolic breakdown pathways shown for GHB can run in either direction, depending on the concentrations of the substances involved, so the body can make its own GHB either from GABA or from succinic semialdehyde. Under normal physiological conditions, the concentration of GHB in the body is rather low, and the pathways would run in the reverse direction to what is shown here to produce endogenous GHB. However, when GHB is consumed for recreational or health promotion purposes, its concentration in the body is much higher than normal, which changes the enzyme kinetics so that these pathways operate to metabolise GHB rather than producing it.

9 - History

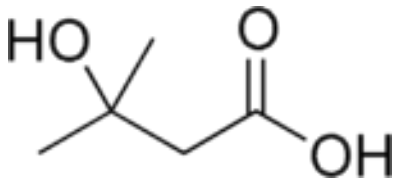
Synthesis of the chemical GHB was first reported in 1874 by Alexander Zaytsev , but the first major research into its use in

humans was conducted in the early 1960s by Dr. Henri Laborit to use in studying the neurotransmitter GABA . It quickly found a wide range of uses due to its minimal side - effects and short duration of action, the only difficulties being the narrow therapeutic dosage range and the dangers presented by its combination with alcohol and other nervous system depressants.

GHB was widely used in France, Italy, and other European countries for several decades as a sleeping agent and an anesthetic in childbirth but problems with its abuse potential and development of newer drugs have led to a decrease in legitimate medical use of GHB in recent times. In the Netherlands, GHB could be bought as aphrodisiac and euphoriant in a smartshop for several years, until several incidents caused it to become regulated. The only common medical applications for GHB today are in the treatment of narcolepsy and more rarely alcoholism. In the typical scenario, GHB has been synthesized from γ-butyrolactone (GBL) by adding sodium hydroxide (lye) in ethanol or water.

A popular children's toy, Bindeez (also known as Aqua Dots, in the United States), produced by Melbourne company Moose, was banned in Australia in early November 2007 when it was discovered that 1,4-butanediol (1,4-B), which is metabolized into GHB, had been substituted for the non-toxic plasticiser 1,5-pentanediol in the bead manufacturing process. Three young children were hospitalized as a result of ingesting a large number of the beads, and the toy was recalled.

Beta - Hydroxy *beta* –Methyl Butyric Acid



Contents

1 - Introduction

β-Hydroxy β-methylbutyric acid (HMB), or β-hydroxy β-methylbutyrate, is a metabolite of the essential amino acid leucine and is synthesized in the human body. It plays a part in protein synthesis and was discovered by Dr. Steven L. Nissen at Iowa State University. It has been used in scientific studies to purportedly increase muscle mass and decrease muscle breakdown. Nissen held the original patent on the metabolite as a nutritional supplement. It was discovered in pigs, and small quantities can also be found in grapefruit, alfalfa, and catfish. As a supplement it is usually sold as a calcium salt.

Research published in the Journal of Applied Physiology has shown that HMB may have an effect on increasing muscle weight and strength.[4] A review in Nutrition & Metabolism provides an in depth and objective analysis of HMB research . The same study lists as HMB' s proposed mechanisms of action the following:

Increased sarcolemmal integrity via conversion to HMG-CoA
Enhanced protein synthesis via the mTOR pathway
Depression of protein degradation through inhibition of the ubiquitin pathway

Three grams of Calcium beta-hydroxy-beta-methylbutyrate per day may help muscles combat protein breakdown, assist in muscle repair and support increased endurance. Studies suggest its benefits may be greater for the untrained. Also, well-controlled scientific studies have found increases in muscle mass and decreases in body fat

in 70 year old men. It has helped patients with chronic obstructive pulmonary disease in hospital intensive care units, muscle wasting associated with HIV or AIDS and with cancer, and trauma victims with severe injuries.

The human body produces about 0.2 - 0.4 grams per day. Standard doses in research studies have been 1.5 to 3.0 grams per day, usually divided into two doses.

IUPAC name : 3-hydroxy-3-methylbutanoic acid	
Other names . β-Hydroxy iso valeric acid 3- Hydroxy iso valeric acid	
Molecular formula	$C_5 H_{10} O_3$
Molar mass	118 g / mol
Density	0.938 g / mL
Melting point	− 80 °C
Boiling point	88 °C at 1 mmHg

2 - Multiple carboxylase disorders

In multiple carboxylase deficiency, individuals have low or non-existent activity in one or more of the enzymes that facilitate recycling of biotin, a nutrient referred to as vitamin B7 or vitamin H. In such individuals, hydroxyisovaleric acid (or hydroxy iso valerate) accumulates as a consequence of incomplete leucine metabolism. The presence of hydroxy iso valerate is there fore a sensitive marker of biotin deficiency and may indicate the presence of a genetic disorder such as biotinidase deficiency or holocarboxylase synthetase deficiency.

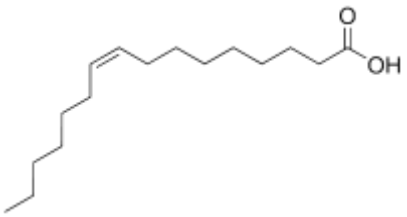
Part - 4 -

An Saturated

Carboxylic Acids

(An Saturated Fatty Acids)

Palmitoleic Acid



Contents

1 - Introduction

Palmitoleic acid, or (*Z*)-9-hexadecenoic acid, is an omega - 7 mono unsaturated fatty acid with the formula $CH_3(CH_2)_5CH=CH(CH_2)_7COOH$ that is a common constituent of the glycerides of human adipose tissue. It is present in all tissues, but generally found in higher concentrations in the liver. It is biosynthesized from palmitic acid by the action of the enzyme delta-9 desaturase. A beneficial fatty acid, it has been shown to increase insulin sensitivity by suppressing inflammation, as well as inhibit the destruction of insulin-secreting pancreatic beta cells.

IUPAC name : hexadec-9-enoic acid
Other names :
Palmitoleic acid
cis-Palmitoleic acid
9-*cis*-Hexadecenoic acid
C16:1 (Lipid numbers)

Molecular formula	$C_{16}\ H_{30}\ O_2$
Molar mass	254
Density	0.894 g / cm³
Melting point	- 0.1 °C

2 - Sources

Palmitoleic acid can be abbreviated as $16{:}1\Delta^9$. Dietary sources of palmitoleic acid include a variety of animal oils, vegetable oils, and marine oils. Macadamia oil (*Macadamia integrifolia*) and sea buckthorn oil (*Hippophae rhamnoides*) are botanical sources with high concentrations, containing 17 % and 40 % of palmitoleic acid, respectively.

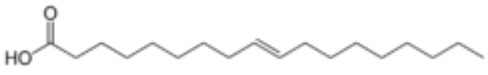
3 - Potential biological effects

In an analysis of numerous fatty acids, palmitoleate was shown to possibly influence fatty liver deposition/production, insulin action, palmitate, and fatty acid synthase, leading to proposal of a new term, "lipokine" having hormone-like effects.

As one such effect may include improved insulin sensitivity, palmitoleic acid (C16:1 n-7) was shown in diabetic mice to attenuate hyperglycemia and hypertriglyceridemia by increasing insulin sensitivity, in part owing to suppression of pro-inflammatory gene expressions and improving hepatic lipid metabolism.

Other preliminary research indicated that palmitoleic acid could have a role as a signaling molecule affecting body weight , a finding consistent with previous observations that palmitoleic acid, among other fatty acids available in the diet, may be used by enzymes affecting fat oxidation . Consequently, oil types manufactured with high palmitoleic acid content may have a role in addressing obesity.[8]

Elaidic Acid



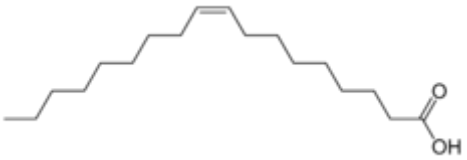
IUPAC name: (*E*)- octadec-9-enoic acid

Molecular formula	$C_{18}H_{34}O_2$
Molar mass	282 g / mol

Elaidic acid is the major trans fat found in hydrogenated vegetable oils and occurs in small amounts in caprine and bovine milk (very roughly 0.1% of the fatty acids) and some meats. It is the trans isomer of oleic acid. The name of the elaidinization reaction comes from elaidic acid.

Elaidic acid increases CETP activity, which in turn raises VLDL and lowers HDL cholesterol.

Oleic Acid



Contents

1 - Introduction

Oleic acid is a fatty acid that occurs naturally in various animal and vegetable fats and oils. It is an odorless, colourless oil, although commercial samples may be yellowish. In chemical terms, oleic acid is classified as a monounsaturated omega-9 fatty acid, abbreviated with a lipid number of 18:1 cis-9. It has the formula $CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$. The term "oleic" means related to, or derived from, oil or olive, the oil that is predominantly composed of oleic acid.

IUPAC name : (9*Z*)-Octadec-9-enoic acid
Other names :
(9*Z*)-Octadecenoic acid
(*Z*)-Octadec-9-enoic acid
cis-9-Octadecenoic acid
cis-Δ^9-Octadecenoic acid
Oleic acid
18:1 cis-9

Molecular formula	$C_{18}H_{34}O_2$
Molar mass	282 g mol^{-1}
Appearance	Pale yellow or brownish

	yellow oily liquid with lard - like odor
Density	0.895 g / mL
Melting point	13-14 °C
Boiling point	360 °C
Solubility in water	Insoluble
Solubility in methanol	Soluble

2 - Occurrence

Fatty acids (or as their salts) do not often occur as such in biological systems. Instead fatty acids like oleic acid occur as their esters, commonly the triglycerides, which are the greasy materials in many natural oils. Via the process of saponification, the fatty acids can be obtained.

Triglycerides of oleic acid compose the majority of olive oil, although there may be less than 2.0% as free acid in the virgin olive oil, with higher concentrations making the olive oil inedible. It also makes up 59 -75 % of pecan oil, 61 % of canola oil,[4] 36 - 67 % of peanut oil , 60 % of macadamia oil, 20 - 85 % of sunflower oil (the latter in the high oleic variant), 15-20 % of grape seed oil, sea buckthorn oil, and sesame oil, and 14 % of poppyseed oil. It is abundantly present in many animal fats, constituting 37 to 56% of chicken and turkey fat and 44 to 47 % of lard.

Oleic acid is the most abundant fatty acid in human adipose tissue.

2 – 1 - As an insect pheromone

Oleic acid is emitted by the decaying corpses of a number of insects, including bees and *Pogonomyrmex* ants, and triggers the instincts of living workers to remove the dead bodies from the hive. If a live bee[10] or ant[11][12] is daubed with oleic acid, it is dragged off for disposal as if it were dead. The oleic acid smell also may indicate danger to living insects, prompting them to avoid others who have succumbed to disease or places where predators lurk.

3 - Production and chemical behavior

The biosynthesis of oleic acid involves the action of the enzyme stearoyl - CoA 9 - desaturase acting on stearoyl- CoA . In effect, stearic acid is dehydrogenated to give the monounsaturated derivative oleic acid.

Oleic acid undergoes the reactions of carboxylic acids and alkenes. It is soluble in aqueous base to give soaps called oleates. Iodine adds across the double bond. Hydrogenation of the double bond yields the saturated derivative stearic acid. Oxidation at the double bond occurs slowly in air, and is known as rancidification in foodstuffs or drying in coatings. Reduction of the carboxylic acid group yields oleyl alcohol. Ozonolysis of oleic acid is an important route to azelaic acid. The coproduct is nonanoic acid :

$H_{17}C_8CH{=}CHC_7H_{14}CO_2H + 4"O" \rightarrow$

$H_{17}C_8CO_2H + HO_2CC_7H_{14}CO_2H$

Esters of azelaic acid find applications in lubrication and plasticizers.

The *trans* isomer of oleic acid is called elaidic acid (hence the name elaidinization for a reaction that converts oleic acid to elaidic acid.

4 - Uses

Oleic acid (in triglyceride form) is included in normal human diet as part of animal fats and vegetable oil.

Oleic acid as its sodium salt is a major component of soap as an emulsifying agent. It is also used as emollient.[15] Small amounts of oleic acid are used as an excipient in pharmaceuticals, oleic acid is used as an emulsifying or solubilizing agent in aerosol products.

Oleic acid is also used to induce lung damage in certain types of animals, for the purpose of testing new drugs and other means to treat lung diseases. Specifically in sheep, intravenous administration of oleic acid causes acute lung injury with corresponding pulmonary edema . This sort of research has been of particular benefit to

premature newborns, for whom treatment for underdeveloped lungs (and associated complications) often is a matter of life and death.

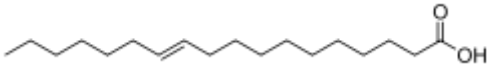
5 - Health effects

Oleic acid is a common monounsaturated fat in human diet. Monounsaturated fat consumption has been associated with decreased low-density lipoprotein (LDL) cholesterol, and possibly increased high-density lipoprotein (HDL) cholesterol . However, its ability to raise HDL is still debated.

Oleic acid may hinder the progression of adrenoleukodystrophy (ALD), a fatal disease that affects the brain and adrenal glands.

Oleic acid may be responsible for the hypotensive (blood pressure reducing) effects of olive oil. Adverse effects also have been documented, however, since both oleic and monounsaturated fatty acid levels in the membranes of red blood cells have been associated with increased risk of breast cancer.

Vaccenic Acid



1 - Introduction

Vaccenic acid is an omega-7 fatty acid. It is a naturally occurring trans-fatty acid found in the fat of ruminants and in dairy products such as milk, butter, and yogurt. It is also the predominant fatty acid comprising trans fat in human milk.

Its IUPAC name is (*E*)-11-octadecenoic acid, and its lipid shorthand name is 18:1 *trans*-11. The name was derived from the Latin *vacca* (cow).

Vaccenic acid was discovered in 1928 in animal fats and butter. It is the main *trans* fatty acid isomer present in milk fat.[4] Mammals convert it into rumenic acid, a conjugated linoleic acid,[5][6] where it shows anticarcinogenic properties.

Its stereoisomer, cis-vaccenic acid, also an omega-7 fatty acid, is found in Sea Buckthorn (*Hippophae rhamnoides*) oil. Its IUPAC name is (*Z*)-11-octadecenoic acid, and its lipid shorthand name is 18:1 *cis*-11.

IUPAC name : (E)-Octadec-11-enoic acid

Molecular formula	$C_{18}H_{34}O_2$
Molar mass	282 g / mol

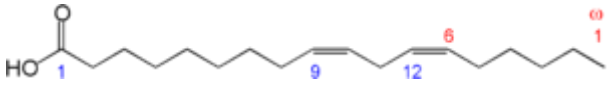
2 - Health

A 2008 study at the University of Alberta suggests that vaccenic acid feeding in rats over 16 weeks resulted in lowered total cholesterol, lowered LDL cholesterol and lower triglyceride levels. The researchers are preparing to conduct further research, including human clinical trials.

Vaccenic acid is also found in human orbitofrontal cortex of patients with bipolar disorder and schizophrenia.[10][11]

Oxidation of omega-7 unsaturated fatty acids on the skin surface, such as palmitoleic acid and vaccenic acid, may be the cause of the phenomenon commonly known as old person smell.

Linoleic Acid



Contents

1 - Introduction

Linoleic acid (LA) is an unsaturated omega-6 fatty acid. It is a colorless liquid at room temperature. In physiological literature, it has a lipid number of 18:2 cis,cis-9,12. Chemically, linoleic acid is a carboxylic acid with an 18-carbon chain and two *cis* double bonds; the first double bond is located at the sixth carbon from the methyl end.

Linoleic acid belongs to one of the two families of essential fatty acids. The body cannot synthesize linoleic acid from other food components.

The word "linoleic" comes from the Greek word *linon* (flax). *Oleic* means "of, relating to, or derived from oil of olive" or "of or relating to oleic acid" because saturating the omega-6 double bond produces oleic acid.

IUPAC name :
(9*Z*,12*Z*)-9,12-Octadecadienoic acid
Other names :
C18:2 (Lipid numbers)
Molecular formula $C_{18}H_{32}O_2$
Molar mass 280 g mol^{-1}

Appearance	Colorless oil
Density	0.9 g / cm^3
Melting point	−5 °C
Boiling point	230 °C at 16 mm Hg
Solubility in water	0.139 mg / L
Vapor pressure	16 Torr at 229 °C
Flash point	112 °C

2 - In physiology

LA is a polyunsaturated fatty acid used in the biosynthesis of arachidonic acid (AA) and thus some prostaglandins. It is found in the lipids of cell membranes. It is abundant in many vegetable oils, comprising over half (by weight) of poppy seed, safflower, sunflower, and corn oils.

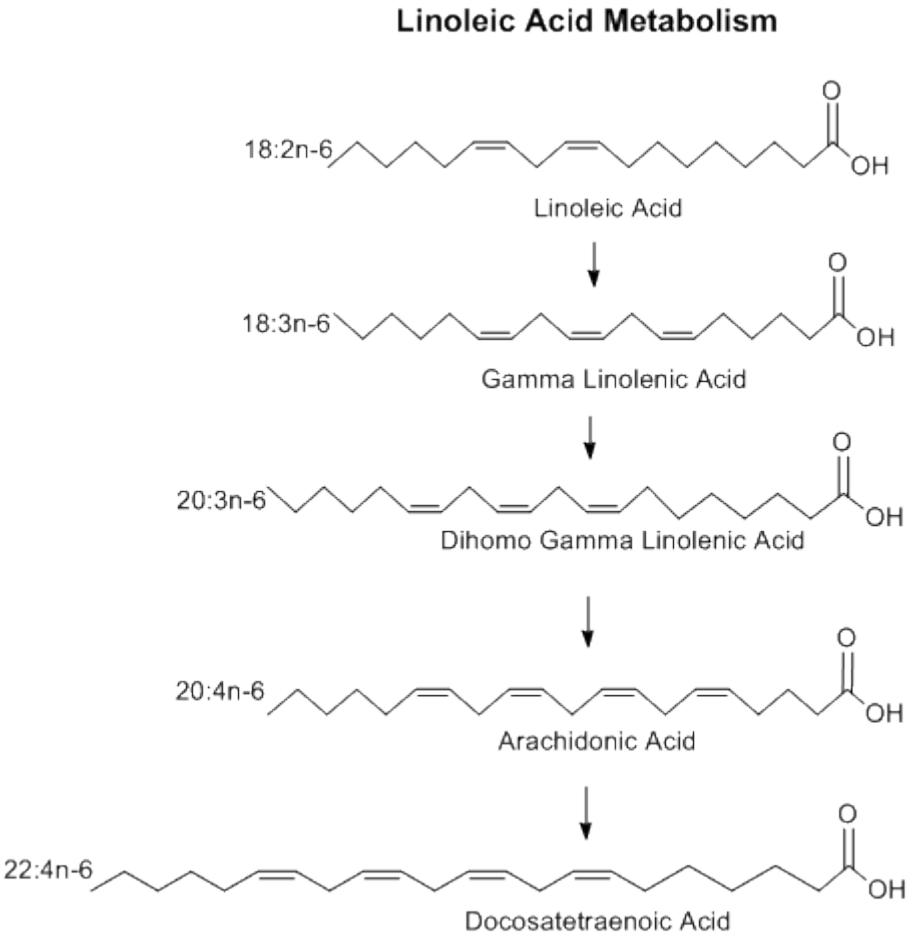
Linoleic acid is an essential fatty acid that must be consumed for proper health. A diet only deficient in linoleate causes mild skin scaling, hair loss, and poor wound healing in rats . However, achieving a deficiency in linoleic acid is nearly impossible consuming any normal diet and is thus not considered to be of clinical concern.

Along with oleic acid, linoleic acid is released by cockroaches upon death which has the effect of preventing other roaches from entering the area. This is similar to the mechanism found in ants and bees, in which oleic acid is released upon death.

2 – 1 - Metabolism and eicosanoids

The first step in the metabolism of LA is performed by Δ^6desaturase, which converts LA into gamma-linolenic acid (GLA).

There is evidence suggesting that infants lack Δ^6 desaturase of their own, and must acquire it through breast milk. Studies show that breast-milk fed babies have higher concentrations of GLA than formula-fed babies, while formula-fed babies have elevated concentrations of LA.



GLA is converted to dihomo-gamma-linolenic acid (DGLA), which in turn is converted to arachidonic acid (AA). One of the possible fates of AA is to be transformed into a group of metabolites called eicosanoids, a class of paracrine hormones. The three types of eicosanoids are prostaglandins, thromboxanes, and leukotrienes. Eicosanoids produced from AA tend to be inflammatory.[10] For example, both AA-derived thrombaxane and leukotriene$_{B4}$ are proaggretory and vasoconstrictive eicosanoids. The oxidized metabolic products of linoleic acid, such as 9-hydroxyoctadecanoic acid and 13-hydroxyoctadecanoic acid, have also been shown to activate TRPV1, the capsaicin receptor, and through this might play a major role in hyperalgesia and allodynia.

n increased intake of certain omega–3 fatty acids with a decrease in omega-6 fatty acids has been shown to attenuate inflammation due to reduced production of these eicosanoids.

One study monitoring two groups of survivors of myocardial infarction concluded “the concentration of alpha-linolenic acid was increased by 68 %, in the experimental group, and that of linoleic acid reduced by 7 %...the survivors of a first myocardial infarction, assigned to a Mediterranean alpha-linolenic acid rich diet, had a markedly reduced rate of recurrence, other cardiac events and overall mortality.”

3 - Uses

3 – 1 - Industrial uses

Linoleic acid is used in making quick- drying oils, which are useful in oil paints and varnishes. These applications exploit the easy reaction of the linoleic acid with oxygen in air, which leads to crosslinking and formation of a stable film.

Reduction of linoleic acid yields linoleyl alcohol.

Linoleic acid has become increasingly popular in the beauty products industry because of its beneficial properties on the skin. Research points to linoleic acid's anti-inflammatory, acne reductive, and moisture retentive properties when applied topically on the skin.

3 – 2 - Use in research

Linoleic acid can be used to show the antioxidant effect of natural phenols. Experiments on linoleic acid subjected to 2,2′-azobis (2-amidinopropane) dihydrochloride-induced oxidation with different combinations of phenolics show that binary mixtures can lead to either a synergetic antioxidant effect or to an antagonistic effect.

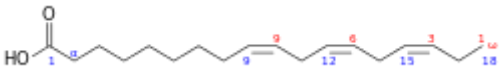
Linoleic acid may be linked to obesity by promoting overeating and damaging the arcuate nucleus in the brain's hypothalamus.

4 - Dietary sources

Name	% LA[†]
Salicornia oil	75 %
Safflower oil	74 %
Evening Primrose oil	73 %

Poppyseed oil	70 %
Grape seed oil	69 %
Sunflower oil	65 %
Hemp oil	60 %
Corn oil	59 %
Wheat germ oil	55 %
Cottonseed oil	54 %
Soybean oil	51 %
Walnut oil	51 %
Sesame oil	45 %
Rice bran oil	39 %
Argan oil	37 %
Pistachio oil	32.7%
Peanut oil	32 %
Almonds	24 %
Canola oil	21 %
Chicken fat	18 - 23 %
Egg yolk	16 %
Linseed oil	15 %
Lard	10 %
Olive oil	10 %
Palm oil	10 %
Cocoa butter	3 %
Macadamia oil	2 %
Butter	2 %
Coconut oil	2 %

Alpha - Linolenic Acid



Contents

1 - Introduction

α-Linolenic acid (ALA) is an organic compound found in many common vegetable oils. In terms of its structure, it is named *all-cis*-9,12,15-octadecatrienoic acid. In physiological literature, it is given the name 18:3 (*n*−3).

α-Linolenic acid is a carboxylic acid with an 18-carbon chain and three *cis* double bonds. The first double bond is located at the third carbon from the methyl end of the fatty acid chain, known as the *n* end. Thus, α-linolenic acid is a polyunsaturated *n*−3 (omega-3) fatty acid. It is an isomer of gamma-linolenic acid, a polyunsaturated *n*−6 (omega-6) fatty acid.

IUPAC name :
(9*Z*,12*Z*,15*Z*)-9,12,15-Octa deca tri enoic acid
Other names :
ALA;
Linolenic acid;
cis,*cis*,*cis*-9,12,15- Octa deca tri enoic acid;
(9*Z*,12*Z*,15*Z*)-octa deca-9,12,15-trienoic acid;
Industrene 120

Molecular formula	$C_{18}H_{30}O_2$
Molar mass	278 g mol^{-1}

2 - History

Alpha-linolenic acid was first isolated by Rollett as cited in J. W. McCutcheon's synthesis in 1942 , and referred to in Green and Hilditch's 1930's survey. It was first artificially synthesized in 1995 from C6 homologating agents. A Wittig reaction of the phosphonium salt of [(*Z*-*Z*)-nona-3,6-dien-1-yl]triphenylphosphonium bromide with methyl 9-oxononanoate, followed by saponification, completed the synthesis.

3 - Dietary sources

Seed oils are the richest sources of α-linolenic acid, notably those of chia, perilla, flaxseed (linseed oil), rapeseed (canola), and soybeans. Alpha-Linolenic acid is also obtained from the thylakoid membranes in the leaves of *Pisum sativum* (pea leaves).[7] ALA is not suitable for baking, as it will polymerize with itself, a feature exploited in paint with transition metal catalysts. Some ALA will also oxidize at baking temperatures. % ALA in the table below is for the oil extracted from each item.

Common name	Alternate name	Linnaean name	% ALA†
Chia	chia sage	*Salvia hispanica*	64 %
Kiwifruit seeds	Chinese gooseberry	*Actinidia chinensis*	62 %
Perilla	shiso	*Perilla frutescens*	58 %
Flax	linseed	*Linum usatissimum*	55 %
Lingonberry	cowberry	*Vaccinium vitis-idaea*	49 %
Camelina	camelina	*Camelina sativa*	35-45 %
Purslane	portulaca	*Portulaca oleracea*	35 %
Sea buckthorn	seaberry	*Hippophae rhamnoides L.*	32 %
Hemp	cannabis	*Cannabis sativa*	20 %
Rapeseed	canola	*Brassica napus*	10 %
Soybean	soya	*Glycine max*	8 %

4 - Potential role in nutrition and health

Flax is a rich source of α-linolenic acid.

α-Linolenic acid, an *n*−3 fatty acid, is a member of the group of essential fatty acids (EFAs), so called because they cannot be produced within the body and must be acquired through diet. Most seeds and seed oils are much richer in an *n*−6 fatty acid, linoleic acid. Linoleic acid is also an EFA, but it, and the other *n*−6 fatty acids, compete with *n*−3s for positions in cell membranes and have very different effects on human health.

α-Linolenic acid can only be obtained by humans through their diets because the absence of the required 12- and 15-desaturase enzymes makes *de novo* synthesis from stearic acid impossible. Eicosapentaenoic acid (EPA; 20:5, *n*−3) and docosahexaenoic acid (DHA; 22:6, *n*−3) are readily available from fish and algae oil and play a vital role in many metabolic processes. These can also be synthesized by humans from dietary α-linolenic acid, but with an efficiency of only a few percent . Because the efficacy of *n*−3 long-chain polyunsaturated fatty acid (LC-PUFA) synthesis decreases down the cascade of α-linolenic acid conversion, DHA synthesis from α-linolenic acid is even more restricted than that of EPA.

Linoleic acid (LA; 18:2, *n*−6) is generally assumed to reduce EPA synthesis because of the competition between α-linolenic acid and LA for common desaturation and elongation enzymes.

Preliminary research has found evidence that α-linolenic acid is related to a lower risk of cardiovascular disease.

A 2005 study found that daily administration of α-linolenic acid significantly reduced both self-reported anxiety, stress levels, and objective measured cortisol levels in college age students.

A large 2006 study found no association between total α-linolenic acid intake and overall risk of prostate cancer.[17] Multiple studies have shown a relationship between alpha-linolenic acid (ALA), which is abundant in linseed oil, and an increased risk of prostate cancer. This risk was found to be irrespective of source of origin (e.g., meat, vegetable oil) . A recent (2009) meta - analysis, however, found evidence of publication bias in earlier studies, and concluded that if ALA contributes to increased prostate cancer risk, the increase in risk is quite small. In contrast, alpha-linoleic acid was recently shown to negatively regulate the growth of cancer cells, but not healthy cells, in vitro.

Basic research has also suggested a major neuroprotective effect of α-linolenic acid in *in vivo* models of both global ischemia and kainate-induced epilepsy; however, if sourced from flax seed oil, residues may have adverse effect due to its content of neurotoxic cyanogen glycosides and immunosuppressive cyclic nonapeptides.

A 2011 longitudinal study of over 50,000 women, conducted at Harvard University, over a period of ten years, found that a higher intake of α-linolenic acid (combined with a lower intake of linoleic acid) was positively associated with a significant reduction in depression in the same group (the same study also found that by contrast an intake of EPA and DHA found in fish oils did not reduce depression).

4 – 1 - Stability and Hydrogenation

Alpha-linolenic acid is relatively more susceptible to oxidation and will become rancid more quickly than many other oils. Oxidative instability of α-linolenic acid is one reason why producers choose to partially hydrogenate oils containing α-linolenic acid, such as soybean

oil . Soybeans are the largest source of edible oils in the U.S., and 40 % of soy oil production is partially hydrogenated.

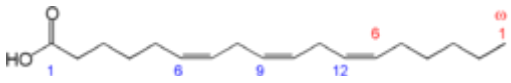
However, when partially hydrogenated, part of the unsaturated fatty acids become unhealthy trans fats. Consumers are increasingly avoiding products that contain trans fats, and governments have begun to ban trans fats in food products. These regulations and market pressures have spurred the development of low-α-linolenic acid soybeans. These new soybean varieties yield a more stable oil that doesn't require hydrogenation for many applications, thus providing trans fat-free products, such as frying oil.

Several consortia are bringing low-α-linolenic acid soy to market. DuPont's effort involves silencing the FAD2 gene that codes for Δ^6-desaturase, giving a soy oil with very low levels of both α-linolenic acid and linoleic acid. Monsanto Company has introduced to the market Vistive, their brand of low α-linolenic acid soybeans, which is less controversial than GMO offerings, as it was created via conventional breeding techniques.

4 – 2 - Cardiovascular

Dietary α-linolenic acid has been assessed for its role in cardiovascular health. Clinical benefits have been seen in some, but not all, studies. Still, a review in 2005 concluded "The weight of the evidence favors recommendations for modest dietary consumption of α-linolenic acid (2 to 3 g per day) for the primary and secondary prevention of coronary heart disease."

Gamma - Linolenic Acid



Contents

1 - Introduction

γ-Linolenic acid (gamma-linolenic acid or GLA, INN and USAN gamolenic acid) is a fatty acid found primarily in vegetable oils. It is sold as a dietary supplement for treating problems with inflammation and auto-immune diseases, although its efficacy is disputed.

IUPAC name :
all-*cis*-6,9,12- octa deca tri enoic acid
Other names :
Gamma-linolenic acid,
gamolenic acid,
GLA

Molecular formula	$C_{18}H_{30}O_2$
Molar mass	278 g mol^{-1}
Appearance	Colorless oil

2 - Chemistry

GLA is categorized as an *n*−6 (also called ω−6 or omega-6) fatty acid, meaning that the first double bond on the methyl end (designated with *n* or ω) is the sixth bond. In physiological literature, GLA is designated as 18:3 (*n*−6). GLA is a carboxylic acid with an 18-carbon chain and three *cis* double bonds. It is an isomer of α-

linolenic acid, which is a polyunsaturated n−3 (omega-3) fatty acid, found in rapeseed canola oil, soy beans, walnuts, flax seed (linseed oil), perilla, chia, and hemp seed.

3 - History

GLA was first isolated from the seed oil of evening primrose. This herbal plant was grown by Native Americans to treat swelling in the body. In the 17th century, it was introduced to Europe and became a popular folk remedy, earning the name *king's cure-all.* in 1919, Heiduschka and Lüft extracted the oil from evening primrose seeds and described an unusual linolenic acid, which they name γ-. Later, the exact chemical structure was characterized by Riley.

Although there are α- and γ- forms of linolenic acid, there is no β- form. One was once identified, but it turned out to be an artifact of the original analytical process.

4 - Dietary sources

GLA is obtained from vegetable oils such as GLA safflower oil (*Carthamus tinctorius*), evening primrose (*Oenothera biennis*) oil, blackcurrant seed oil, borage oil, and hemp seed oil. GLA is also found in edible hemp seeds, oats, barley, and spirulina. Each contains varying amounts of the fatty acid, with GLA safflower oil at 40% GLA being a novel concentrated form. This is a new genetically modified oil and has been available in commercial quantities since 2011. It should be noted that conventional safflower oils have zero GLA. Borage oil ranges from 15 % to 20 % and evening primrose oil ranges from 8 % to 10 % GLA.

The human body produces GLA from linoleic acid (LA). This reaction is catalyzed by Δ^6 - desaturase (D6D), an enzyme that allows the creation of a double bond on the sixth carbon counting from the carboxyl terminus. LA is consumed sufficiently in most diets, from such abundant sources as cooking oils and meats. However, a lack of GLA can occur when there is a reduction of the efficiency of the D6D conversion (for instance, as people grow older or when there are specific dietary deficiencies) or in disease states wherein there is excessive consumption of GLA metabolites.

5 - Source of eicosanoids

From GLA, the body forms dihomo-*γ*-linolenic acid (DGLA). This is one of the body's three sources of eicosanoids (along with AA and EPA.) DGLA is the precursor of the prostaglandin PGH_1, which in turn forms PGE_1 and the thromboxane TXA_1. PGE_1 has a role in regulation of immune system function and is used as the medicine alprostadil. TXA_1 modulates the pro-inflammatory properties of the thromboxane TXA_2.

Unlike AA and EPA, DGLA cannot yield leukotrienes. However it can inhibit the formation of pro-inflammatory leukotrienes from AA.

Although GLA is an *n*−6 fatty acid, a type of acid that is, in general, pro-inflammatory, it has anti-inflammatory properties .

6 - Health and medicine

The seed oil of Oenothera biennis (evening primrose) is a source of GLA

GLA is sometimes prescribed in the belief that it has anti-inflammatory properties lacking some of the common side-effects of other anti - inflammatory drugs. Herbal medicine advocates recommend GLA for autoimmune disorders, arthritis, eczema, and PMS, with noticeable results not expected for months. Research is ongoing, investigating GLA as a potential anticancer agent.[8] GLA is unique among the omega-6 polyunsaturated fatty acids (linoleic acid, GLA and arachidonic acid) in its potential to suppress tumor growth and metastasis.

GLA can also form a lithium salt, increasing its solubility in water. The resulting compound is Li-GLA, also called lithium gammalinolenate. Li-GLA is currently in phase II clinical trials to determine whether it is useful in the treatment of HIV infections, since it has the ability to destroy HIV-infected T cells *in vitro*. It has a number of side-effects, including a reduction in hemoglobin, hematuria, gastrointestinal disturbance, fatigue, and headache.

6 – 1 - Atopic eczema

Conflicting data are found for GLA in the treatment of eczema. The UK's Medicines and Healthcare products Regulatory Agency has withdrawn GLA's product licence for atopic eczema . Still, the US National Institute of Health's MedlinePlus states that there is 'B' grade evidence ('good scientific evidence') for the efficacy of evening primrose oil in the treatment of eczema and skin irritation. But it cautions that large well-designed studies are still needed.

A controlled study of borage oil for eczema found no benefit to GLA; it underperformed placebo.

A small Finnish study on Hempseed oil (which contains GLA) demonstrated that it relieved the symptoms of eczema (atopic dermatitis).

7 - History

The medical use of GLA has been controversial. David Horrobin published much research on the use of GLA (as evening primrose oil) as a dietary supplement for treating atopic eczema. He also founded Scotia Pharmaceuticals, which sold this oil as a pharmaceutical, which led to controversy even after his death.

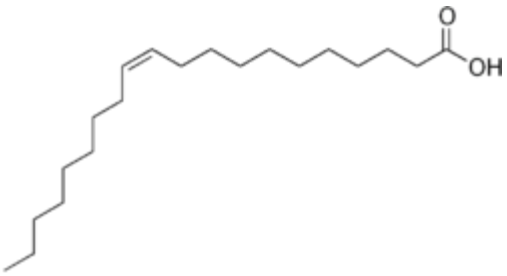
Stearidonic Acid

IUPAC name:
(6Z,9Z,12Z,15Z)-6,9,12,15-octa deca tetra enoic acid

Molecular formula	$C_{18}H_{28}O_2$
Molar mass	276 g / mol

Stearidonic acid (SDA) is an ω-3 fatty acid, sometimes called moroctic acid. It is biosynthesized from alpha-linolenic acid by the enzyme delta-6-desaturase. Natural sources of this fatty acid are the seed oils of hemp, blackcurrant, corn gromwell[1] and echium, and the cyanobacterium *Spirulina*.

Gondoic Acid

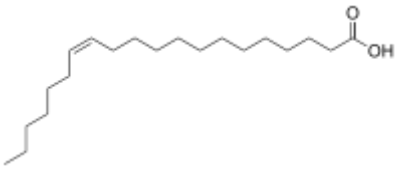


Gondoic acid is a mono unsaturated omega-9 fatty acid found in a variety of plant oils and nuts. It is the main acid component of jojoba oil

IUPAC name : (*Z*)-Eicos-11-enoic acid
Other names :
Gondoic acid
cis-Gondoic acid
cis-11-Eicosenoic acid
11-Eicosenoic acid
11*Z*-Eicosenoic acid
cis-11-Icosenoic acid
(11*Z*)-Icos-11-enoic acid

Molecular formula	$C_{20}H_{38}O_2$
Molar mass	310 g/mol
Density	0.883 g /mL
Melting point	23 - 24 °C
Flash point	110 °C

Paullinic Acid



Paullinic acid is an omega-7 fatty acid find in a variety of plant sources , including guarana (*Paullinia cupana*) from which it gets its name.

IUPAC name :
(13*Z*)-13-Eicosenoic acid

Other names :
Eicos-13-enoic acid;
cis-13-Eicosenoic acid;
(*Z*)-Icos-13-enoic acid

Molecular formula $C_{20}H_{38}O_2$

Molar mass 310 g mol^{-1}

Dihomo – *gamma* - linolenic Acid

Contents

1 - Introductıon

Dihomo-γ-linolenic acid (DGLA) is a 20-carbon ω−6 fatty acid. In physiological literature, it is given the name 20:3 (ω−6). DGLA is a carboxylic acid with a 20-carbon chain and three *cis* double bonds; the first double bond is located at the sixth carbon from the omega end. DGLA is the elongation product of γ-linolenic acid (GLA; 18:3, ω−6). GLA, in turn, is a desaturation product of linoleic acid (18:2, ω−6). DGLA is made in the body by the elongation of GLA, by an efficient enzyme which does not appear to suffer any form of (dietary) inhibition. DGLA is an extremely uncommon fatty acid, found only in trace amounts in animal products.

Other names :
cis,*cis*,*cis*-8,11,14-Eicosatrienoic acid
DGLA

Molecular formula	$C_{20}H_{34}O_2$
Molar mass	306.48 g mol^{-1}

2 - Biological effects

The eicosanoid metabolites of DGLA are:

Series-1 thromboxanes (thromboxanes with 1 double-bond), via the COX-1 and COX-2 pathways.

Series-1 prostanoids, via the COX-1 and COX-2 pathways.[3]

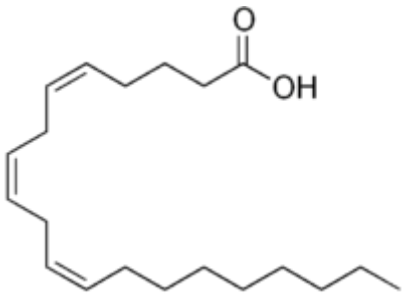
A 15-hydroxyl derivative that blocks the transformation of arachidonic acid to leukotrienes.

All of these effects are anti-inflammatory. This is in marked contrast with the analogous metabolites of arachidonic acid (AA), which are the series-2 thromboxanes and prostanoids and the series-4 leukotrienes. In addition to yielding anti-inflammatory eicosanoids, DGLA competes with AA for COX and lipoxygenase, inhibiting the production of AA's eicosanoids.

Taken orally in a small study, DGLA produced antithrombotic effects.[5] Supplementing dietary GLA increases serum DGLA, as well as serum AA levels.[6] Cosupplementation with GLA and EPA lowers serum AA levels by blocking Δ-5-desaturase activity, while also lowering leukotriene synthesis in neutrophils.

Borage is a rich source of γ-linolenic acid—the dietary precursor to DGLA.

Mead Acid



Contents

Mead acid is an omega-9 fatty acid, first characterized by James F. Mead. Like some other omega-9 polyunsaturated fatty acids animals can make Mead acid *de novo*. Its elevated presence in the blood is an indication of essential fatty acid deficiency . Mead acid is found in large quantities in cartilage.

IUPAC name:
(5Z,8Z,11Z)-Eicosa-5,8,11-tri enoic acid

Molecular formula	$C_{20}H_{34}O_2$
Molar mass	306.48276

2 - Chemistry

Mead acid, also referred to as eicosatrienoic acid, is chemically a carboxylic acid with a 20-carbon chain and three methylene-interrupted *cis* double bonds. The first double bond is located at the ninth carbon from the omega end. In physiological literature, it is given the name 20:3(n-9) b. Mead acid can form various hydroxy (HETE) and hydoperoxy (HpETE) products .

3 - Physiology

Two fatty acids, linoleic acid and alpha-linolenic acid, are considered essential fatty acids (EFAs) in humans and other

mammals. Both are 18 carbon fatty acids unlike mead acid, which has 20 carbons. Linoleic is an ω-6 fatty acid whereas linolenic is ω-3 and mead is ω-9. One study examined patients with intestinal fat malabsorption and suspected EFA deficiency. They were found to have blood-levels of Mead acid 1263 % higher than reference subjects. Under severe conditions of essential fatty acid deprivation, mammals will elongate and desaturate oleic acid to make mead acid, (20:3, $n - 9$). This has been documented to a lesser extent in vegetarians and semi-vegetarians following an unbalanced diet.

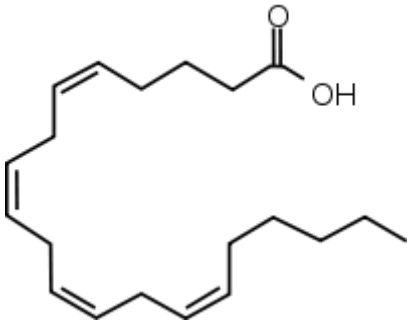
Mead acid has been found to decrease osteoblastic activity. This may be important in treating conditions where inhibition of bone formation is desired.

4 - Role in inflammation

Prostaglandin H synthases (also known as COX) are enzymes known to play a large role in inflammatory processes through oxidation of unsaturated fatty acids. Most notably, the formation of Prostaglandin H2 from arachidonic acid which is very similar in structure to mead acid. When physiological levels of arachidonic acid are low, other unsaturated fatty acids including mead and linoleic acid are oxidized by COX.

Mead acid is also converted to Leukotrienes C3 and D3.

Arachidonic Acid



Contents

1 - Introduction

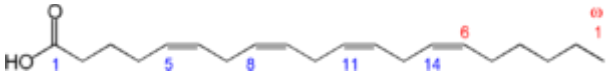
Arachidonic acid (AA, sometimes ARA) is a polyunsaturated omega-6 fatty acid 20:4(ω-6). It is the counterpart to the saturated arachidic acid found in peanut oil, (*L. arachis* – peanut.)

IUPAC name :
(5*Z*,8*Z*,11*Z*,14*Z*)-5,8,11,14-Eicosa tetra enoic acid
Systematic name :
(5*Z*,8*Z*,11*Z*,14*Z*)-Icosa-5,8,11,14- tetra enoic acid
Other names :
5,8,11,14-all-*cis*-Eicosatetraenoic acid;

all-*cis*-5,8,11,14-Eicosatetraenoic acid;
Arachidonate

Molecular formula	$C_{20}H_{32}O_2$
Molar mass	304 g mol^{-1}
Density	0.922 g/cm^3
Melting point	-49 °C
Boiling point	169-171 °C (at 0.15 mmHg)
log P	6.994
Acidity (pK_a)	4.752
Flash point	113 °C

2 - Chemistry



In chemical structure, arachidonic acid is a carboxylic acid with a 20-carbon chain and four *cis*-double bonds; the first double bond is located at the sixth carbon from the omega end.

Some chemistry sources define 'arachidonic acid' to designate any of the eicosatetraenoic acids. However, almost all writings in biology, medicine and nutrition limit the term to all-*cis*-5,8,11,14-eicosatetraenoic acid.

3 - Biology

Arachidonic acid is a polyunsaturated fatty acid present in the phospholipids (especially phosphatidyl ethanolamine , phosphatidyl choline , and phosphatidylinositides) of membranes of the body's cells, and is abundant in the brain, muscles, liver.

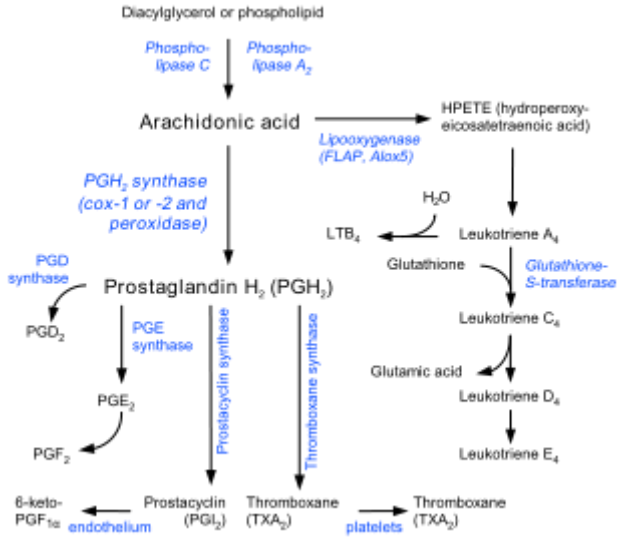
In addition to being involved in cellular signaling as a lipid second messenger involved in the regulation of signaling enzymes, such as PLC-γ, PLC- δ, and PKC- α , - β, and -γ isoforms, arachidonic acid is a key inflammatory intermediate and can also act as a vasodilator . (Note separate synthetic pathways, as described in section below)

4 - Essential fatty acid

Arachidonic acid in the human body usually comes from dietary animal sources—meat, eggs, dairy — or is synthesized from linoleic acid.

Arachidonic acid is not one of the essential fatty acids. However, it does become essential if there is a deficiency in linoleic acid or if there is an inability to convert linoleic acid to arachidonic acid, which is required by most mammals. Some mammals lack the ability to — or have a very limited capacity to — convert linoleic acid into arachidonic acid, making it an essential part of their diets. Since little or no arachidonic acid is found in common plants, such animals are obligate carnivores; the cat is a common example.[4][5] A commercial source of arachidonic acid has been derived, however, from the fungus *Mortierella alpina*.

5 - Synthesis and cascade



Eicosanoid synthesis.

Arachidonic acid is freed from a phospholipid molecule by the enzyme phospholipase A2 (PLA_2), which cleaves off the fatty acid, but can also be generated from DAG by diacylglycerol lipase.

Arachidonic acid generated for signaling purposes appears to be derived by the action of a phosphatidylcholine-specific cytosolic phospholipase A2 ($cPLA_2$, 85 kDa), whereas inflammatory arachidonic acid is generated by the action of a low-molecular-weight secretory PLA_2 ($sPLA_2$, 14-18 kDa).

Arachidonic acid is a precursor in the production of eicosanoids:
The enzymes cyclooxygenase and peroxidase lead to prostaglandin H2, which in turn is used to produce the prostaglandins, prostacyclin, and thromboxanes.

The enzyme 5-lipoxygenase leads to 5-HPETE, which in turn is used to produce the leukotrienes.

Arachidonic acid is also used in the biosynthesis of anandamide.
Some arachidonic acid is converted into hydroxy eicosa tetra enoic acids (HETEs) and epoxy eicosa tri enoic acids (EETs) by epoxygenase.

The production of these derivatives and their action in the body are collectively known as the "arachidonic acid cascade";

5 – 1 - PLA_2 activation

Further information: Phospholipase_A2 # Regulation

PLA_2, in turn, is activated by ligand binding to receptors, including :

5 - HT2 receptors
mGLUR1
bFGF receptor
IFN - α receptor
IFN - γ receptor

Furthermore, any agent increasing intracellular calcium may cause activation of some forms of PLA_2.

5 – 2 - PLC activation

Further information: Phospholipase C#Activation

Alternatively, arachidonic acid may be cleaved from phospholipids by phospholipase C (PLC), yielding diacylglycerol (DAG), which subsequently is cleaved by DAG lipase to yield arachidonic acid.

Receptors that activate this pathway include :

A1 receptor

D2 receptor

α - 2 adrenergic receptor

5 - HT1 receptor

PLC may also be activated by MAP kinase. Activators of this pathway include PDGF and FGF.

6 - Arachidonic acid in the body

6 – 1 - Muscle growth

Through its conversion to active components such as the prostaglandin PGF2alpha, arachidonic acid is necessary for the repair and growth of skeletal muscle tissue . This role makes ARA an important dietary component in support of the muscle anabolic process. One of the lead researchers of the Baylor study (see Bodybuilding section) on arachidonic acid, Mike Roberts MS, CSCS, has authored an article published under the title *Arachidonic Acid, The New Mass Builder* explaining the role of this nutrient in muscle anabolism, and its potential for the enhancement of muscle size and strength. The paper explains that for optimal muscle growth, a training stimulus must elicit localized inflammation and soreness. It explains that arachidonic acid (AA, 20:4n-6) is an essential omega-6 (1-6) polyunsaturated fatty acid that is abundant in skeletal muscle membrane phospholipids (figure 2). It is also the body's principal building block for the production of prostaglandins, which are known to have various physiological roles, including a close involvement in inflammation. Also, the prostaglandin isomer PGF2a has a potent ability to stimulate muscle growth. As such, arachidonic acid is a regulator of localized muscle inflammation, and may be a central nutrient controlling the intensity of the anabolic/tissue-rebuilding response to weight training.

6 – 2 - Brain

Arachidonic acid is one of the most abundant fatty acids in the brain, and is present in similar quantities to docosahexaenoic acid (DHA). The two account for approximately 20 % of its fatty acid content . Like DHA, neurological health is reliant upon sufficient levels of arachidonic acid. Among other things, arachidonic acid helps to maintain hippocampal cell membrane fluidity. It also helps protect the brain from oxidative stress by activating peroxisome proliferator-activated receptor gamma. ARA also activates syntaxin-3 (STX-3), a protein involved in the growth and repair of neurons.

Arachidonic acid is also involved in early neurological development. In one study funded by the U.S. National Institute of Child Health and Human Development, infants (18 months) given supplemental arachidonic acid for 17 weeks demonstrated significant improvements in intelligence, as measured by the Mental Development Index . This effect is further enhanced by the simultaneous supplementation of ARA with DHA.

In adults, the disturbed metabolism of ARA contributes to neurological disorders such as Alzheimer's disease and Bipolar disorder. This involves significant alterations in the conversion of arachidonic acid to other bioactive molecules (over expression or disturbances in the ARA enzyme cascade) .

6 - 3 - Alzheimer's disease

Studies on arachidonic acid and the pathogenesis of Alzheimer's disease is mixed with one study of AA and its metabolites suggests they are associated with the onset of Alzheimer's disease , whereas another study suggests that the supplementation of arachidonic acid during the early stages of this disease may actually be effective in reducing symptoms and slowing the disease progress. Additional studies on arachidonic acid supplementation for Alzheimer's patients are needed.

6 - 4 - Bodybuilding supplement

Arachidonic acid is marketed as an anabolic bodybuilding supplement in a variety of products. The first clinical study

concerning the use of arachidonic acid as a sport supplement found that arachidonic acid has a possible enhancement of anaerobic capacity. A significant group–time interaction effect was observed in Wingate relative peak power (AA: 1.2 ± 0.5; P: -0.2 ± 0.2 W•kg-1, p=0.015). Statistical trends were also seen in bench press 1RM (AA: 11.0 ± 6.2; P: 8.0 ± 8.0 kg, p=0.20), Wingate average power (AA:37.9 ± 10.0; P: 17.0 ± 24.0 W, p=0.16), and Wingate total work (AA: 1292 ± 1206; P: 510 ± 1249 J, p=0.087). AA supplementation during resistance-training promoted significant increases in relative peak power with other performance related variables approaching, but not reaching, significance. These findings provide some preliminary evidence to support the use of AA as an ergogenic.

7 - Dietary arachidonic acid and inflammation

Under normal metabolic conditions, the increased consumption of arachidonic acid is unlikely to increase inflammation. ARA is metabolized to both proinflammatory and anti-inflammatory molecules . Studies giving between 840 mg and 2,000 mg per day to healthy individuals for up to 50 days have shown no increases in inflammation or related metabolic activities . Increased arachidonic acid levels are actually associated with reduced pro-inflammatory IL-6 and IL-1 levels, and increased anti-inflammatory tumor necrosis factor-beta. This may result in a reduction in systemic inflammation.

Arachidonic acid does still play a central role in inflammation related to injury and many diseased states. How it is metabolized in the body dictates its inflammatory or anti-inflammatory activity. Individuals suffering from joint pains or active inflammatory disease may find that increased arachidonic acid consumption exacerbates symptoms, presumably because it is being more readily converted to inflammatory compounds. Likewise, high arachidonic acid consumption is not advised for individuals with a history of inflammatory disease, or who are in compromised health. Of note, while ARA supplementation does not appear to have proinflammatory effects in healthy individuals, it may counter the anti-inflammatory effects of omega-3 fatty acid supplementation.

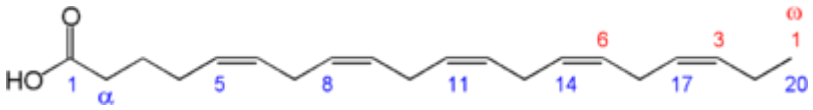
8 - Health effects of arachidonic acid supplementation

Arachidonic acid supplementation in daily dosages of 1,000–1,500 mg for 50 days has been well tolerated during several clinical studies, with no significant side effects reported. All common markers of health, including kidney and liver function , serum lipids,[27] immunity, and platelet aggregation appear to be unaffected with this level and duration of use. Furthermore, higher concentrations of ARA in muscle tissue may be correlated with improved insulin sensitivity. Arachidonic acid supplementation of the diets of healthy adults appears to offer no toxicity or significant safety risk.

A scientific advisory from the American Heart Association has favorably evaluated the health impact of dietary omega-6 fats, including arachidonic acid. The group does not recommend limiting this essential fatty acid. In fact, the paper recommends individuals follow a diet that consists of at least 5 – 10 % of calories coming from omega-6 fats, including arachidonic acid. Dietary ARA is not a risk factor for heart disease, and may play a role in maintaining optimal metabolism and reduced heart disease risk. It is, therefore, recommended to maintain sufficient intake levels of both omega-3 and omega-6 essential fatty acids for optimal health.

Arachidonic acid is not carcinogenic, and studies show dietary level is not associated (positively or negatively) with risk of cancers. ARA remains integral to the inflammatory and cell growth process, however, which is disturbed in many types of disease including cancer. Therefore, the safety of arachidonic acid supplementation in patients suffering from cancer, inflammatory, or other diseased states is unknown, and supplementation is not recommended.

Eicosa Pentaenoic Acid



Contents

1 - Introduction

Eicosa pentaenoic acid (EPA or also icosapentaenoic acid) is an omega-3 fatty acid. In physiological literature, it is given the name 20:5(n-3). It also has the trivial name timnodonic acid. In chemical structure, EPA is a carboxylic acid with a 20-carbon chain and five *cis* double bonds; the first double bond is located at the third carbon from the omega end.

EPA is a polyunsaturated fatty acid (PUFA) that acts as a precursor for prostaglandin-3 (which inhibits platelet aggregation), thromboxane-3, and leukotriene-5 groups (all eicosanoids).

IUPAC name :
(5*Z*,8*Z*,11*Z*,14*Z*,17*Z*)-5,8,11,14,17-icosapentaenoic acid

Molecular formula	$C_{20}H_{30}O_2$
Molar mass	302. g / mol

2 - Sources

It is obtained in the human diet by eating oily fish or fish oil — e.g., cod liver, herring, mackerel, salmon, menhaden and sardine, and various types of edible seaweed. It is also found in human breast milk.

However, fish do not naturally produce EPA, but obtain it from the algae they consume. It is available to humans from some non - animal sources (e.g., commercially, from microalgae). Microalgae are

being developed as a commercial source. EPA is not usually found in higher plants, but it has been reported in trace amounts in purslane.

The human body converts alpha-linolenic acid (ALA) to EPA. ALA is itself an essential fatty acid, an appropriate supply of which must be ensured. The efficiency of the conversion of ALA to EPA, however, is much lower than the absorption of EPA from food containing it. Because EPA is also a precursor to docosahexaenoic acid (DHA), ensuring a sufficient level of EPA on a diet containing neither EPA nor DHA is harder both because of the extra metabolic work required to synthesize EPA and because of the use of EPA to metabolize DHA. Medical conditions like diabetes or certain allergies may significantly limit the human body's capacity for metabolization of EPA from ALA.

3 - Clinical significance

Salmon is a rich source of EPA.

The US National Institute of Health's MedlinePlus lists medical conditions for which EPA (alone or in concert with other ω-3 sources) is known or thought to be an effective treatment. Most of these involve its ability to lower inflammation.

Among omega-3 fatty acids, it is thought that EPA in particular may possess some beneficial potential in mental conditions, such as schizophrenia. Several studies report an additional reduction in scores on symptom scales used to assess the severity of symptoms, when additional EPA is taken.

Studies have suggested that EPA may be efficacious in treating depression. One 2004 study, took blood samples of 100 suicide attempt patients and compared the blood samples to those of controls and found that levels of eicosapentaenoic acid were significantly

lower in the washed red blood cells of the suicide-attempt patients. A 2009 metastudy found that patients taking omega-3 supplements with a higher EPA:DHA ratio experienced less depressive symptoms.

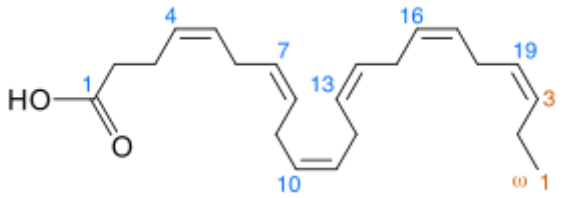
EPA has an inhibitory effect on CYP2C9 and CYP2C19 hepatic enzymes. At high dose, it may also inhibit the activity of CYP2D6 and CYP3A4, important enzymes involved in drug metabolism.

Research suggests that EPA improves the response of patients to chemotherapy, possibly by modulating the production of eicosanoid.

In a study published in 2011, EPA was shown to be significantly more effective than placebo for treating hyperactivity and attention symptoms, both together and separately.

A 2011 study describes, for the first time, a prominent protection by EPA against valproate (VPA)-induced hepatic dysfunction, necrosis, and steatosis. Given that VPA is commonly used in mood disorders, this may offer protection against intentional or unintentional overdose. Further, this same study showed a synergistic effect on raising seizure threshold (in pentylenetetrazol mouse convulsion model) when EPA and VPA are used concomitantly.

Docosa Hexaenoic Acid



Contents

1 - Introduction

Docosa Hexaenoic acid (DHA) is an omega-3 fatty acid that is a primary structural component of the human brain, cerebral cortex, skin, sperm, testicles and retina. It can be synthesized from alpha-linolenic acid or obtained directly from maternal milk or fish oil.[1] DHA's structure is a carboxylic acid(~oic acid) with a 22-carbon chain (*docosa-* is Greek for 22) and six (Greek "hexa") *cis* double bonds (-en~); the first double bond is located at the third carbon from the omega end.[3] Its trivial name is cervonic acid, its systematic name is *all-cis*-docosa-4,7,10,13,16,19-hexa-enoic acid, and its shorthand name is 22:6(n-3) in the nomenclature of fatty acids.

Cold-water oceanic fish oils are rich in DHA. Most of the DHA in fish and multi-cellular organisms with access to cold-water oceanic

foods originates from photosynthetic and heterotrophic microalgae, and becomes increasingly concentrated in organisms the further they are up the food chain. DHA is also commercially manufactured from microalgae; *Crypthecodinium cohnii* and another of the genus *Schizochytrium*. DHA manufactured using microalgae is vegetarian.

Some animals with access to seafood make very little DHA through metabolism, but obtain it in the diet. How ever, in strict herbivores, and carnivores that do not eat seafood, DHA is manufactured internally from α-linolenic acid, a shorter omega -3 fatty acid manufactured by plants (and also occurring in animal products as obtained from plants). Eicosa pentaenoic and docosa pentaenoic acids are the principal products of α-linolenic acid metabolism in young men and illustrates the importance of DHA production for the developing fetus and healthy breast milk. Giltay, Gooren, Toorians, and Katan (2004) found rates of conversion 15% higher for women, and that those taking oral contraceptives demonstrated 10 % higher DHA levels. Administration of testosterone or the aromatase inhibitor anastrozole, which blocks conversion of testosterone to estradiol, reduces DHA conversion. DHA is a major fatty acid in sperm and brain phospholipids and in the retina. Dietary DHA may reduce the risk of heart disease by reducing the level of blood triglycerides in humans. Below- normal levels of DHA have been associated with Alzheimer's disease. A low level of DHA is also spotted in patients with retinitis pigmentosa.

IUPAC name:
(4*Z*,7*Z*,10*Z*,13*Z*,16*Z*,19*Z*)-docosa- 4,7,10,13,16,19-hexaenoic acid;
Doconexent

Other names:
cervonic acid ,
DHA

Molecular formula	$C_{22}H_{32}O_2$
Molar mass	328 g / mol
Density	0.943 g / cm^3
Melting point	- 44 °C
Boiling point	446.7 °C

2 - Central nervous system constituent

DHA is the most abundant omega-3 fatty acid in the brain and retina. DHA comprises 40 % of the polyunsaturated fatty acids (PUFAs) in the brain and 60 % of the PUFAs in the retina. Fifty percent of the weight of a neuron's plasma membrane is composed of DHA. DHA is richly supplied during breastfeeding, and DHA levels are high in breastmilk regardless of dietary choices.

DHA modulates the carrier-mediated transport of choline, glycine, and taurine, the function of delayed rectifier potassium channels, and the response of rhodopsin contained in the synaptic vesicles, among many other functions.

DHA deficiency is associated with cognitive decline.[11] Phosphatidylserine (PS) controls apoptosis, and low DHA levels lower neural cell PS and increase neural cell death. DHA are reduced in the brain tissue of severely depressed patients.

3 - Metabolic synthesis

In humans, DHA is either obtained from the diet or synthesized from eicosapentaenoic acid (EPA, 20:5, ω-3) via docosapentaenoic acid (DPA, 22:5 ω-3) as an intermediate. This synthesis had been thought to occur through an elongation step followed by the action of Δ4-desaturase. It is now considered more likely that DHA is biosynthesized via a C24 intermediate followed by beta oxidation in peroxisomes. Thus, EPA is twice elongated, yielding 24:5 ω-3, then desaturated to 24:6 ω-3, then shortened to DHA (22:6 ω-3) via beta oxidation. This pathway is known as **Sprecher's shunt**.

4 - Potential health effects

4 – 1 - Attention deficit hyperactivity disorder (ADHD)

Research on DHA supplementation and attention deficit hyperactivity disorder (ADHD) have shown mixed results. One study of pure DHA supplementation on children with ADHD found no behavioral improvements, while another study found fish oil containing both EPA and DHA did improve behavior, though these studies and most others regarding the influence of DHA on behavior are confounded by not controlling for gender differences.

4 – 2 - Alzheimer's disease and decline of mental health

Preliminary studies indicated that DHA can slow the progression of Alzheimer's disease in mice , sparking interest in additional research. However, the first large - scale human trials showed that DHA did not slow decline of mental function in elderly people with mild to moderate Alzheimer's disease. These trials were part of a large US National Institutes of Health (NIH) intervention study to evaluate DHA in Alzheimer's disease.

Researchers from the National Institute on Aging-supported Alzheimer's Disease Cooperative Study conducted a double-blind, randomized, placebo-controlled clinical trial comparing DHA and placebo over 18 months in 402 people (average age =76) diagnosed with mild to moderate Alzheimer's at 51 sites. According to this study, treatment with DHA increased blood levels of DHA, and appeared to increase brain DHA levels, based on a measured increase of DHA in study participants' cerebrospinal fluid.

However, DHA treatment did not slow the rate of change on tests of mental function, global dementia severity status, activities of daily living, or behavioral symptoms in the study population as a whole. Treatment effects did not differ between the mild and moderate Alzheimer's patients, leading study authors to conclude that the results do not support the routine use of DHA for patients with Alzheimer's.

Animal studies in the TG3 transgenic mouse model of Alzheimer's disease had linked dietary DHA to decreases in amyloid plaques and tau. Animal studies also showed, when DHA was combined with arachidonic acid (also present in fish oil), plaque formation was greater with the arachidonic acid compared to DHA alone.

DHA deficiency likely plays a role in decline of mental function in healthy adults, which is indicated in a study from 2010 conducted at 19 U.S. clinical sites on 485 subjects aged 55 and older who met criteria for age-associated memory impairment. The study found algal

DHA taken for six months decreased heart rate and improved memory and learning in healthy, older adults with mild memory complaints. These findings indicate the importance of early DHA intervention and provided a statistically significant benefit to cognitive function in individuals over 50 years of age. Higher DHA levels in middle-aged adults is related to better performance on tests of nonverbal reasoning and mental flexibility, working memory, and vocabulary.

4 – 3 - Cancer

In mice, DHA was found to inhibit growth of human colon carcinoma cells, more than other omega-3 PUFAs. The cytotoxic effect of DHA was not caused by increased lipid peroxidation or any other oxidative damage, but rather a decrease in cell growth regulators. However, different cancer lines may handle PUFAs differently and display different sensitivities toward them.

Such preliminary findings point to the need for further research, and are not proof DHA does or does not provide any benefit for intended treatment, cure, or mitigation of cancer. However, DHA was shown to increase the efficacy of chemotherapy in prostate cancer cells in vitro,[28] and a chemoprotective effect in a mouse model was reported.[29] By contrast, one case-control study nested within a clinical trial originally designed to test the effect of finasteride on prostate cancer occurrence, the "Prostate Cancer Prevention Trial", found that DHA measured in blood serum was associated with an *increase* in high-grade prostate cancer risk. In addition to DHA's possible anticancer effect, it may also be used as a non-toxic adjuvant to increase the efficacy of chemotherapy.

4 – 4 - Pregnancy and lactation

DHA concentrations in breast milk range from 0.07 % to greater than 1.0% of total fatty acids, with a mean of about 0.34 %. DHA levels in breast milk are higher if a mother's diet is high in fish. The Food and Drug Administration has noted specific concerns for women who are pregnant or might become pregnant, nursing mothers, and young children regarding mercury levels in fish and shellfish.

DHA has recently gained attention as a supplement for pregnant women, noting studies of improved attention and visual acuity. Given the recently gained attention, the majority of pregnant women in the U.S. fail to get the recommended amount of DHA in their diets.[33] One recent study indicated low levels of plasma and erythrocyte DHA were associated with poor retinal development, low visual acuity, and poor cognitive development. In that same study, alpha-linolenic acid was shown as a source of fetal DHA, but preformed DHA was more readily accredited . A working group from the International Society for the Study of Fatty Acids and Lipids recommended 300 mg/day of DHA for pregnant and lactating women, whereas the average consumption was between 45 mg and 115 mg per day of the women in the study. The March of Dimes recommends pregnant women consume at least 200 mg DHA per day. Other requirements are available from other sources.

Docosahexaenoic acid single-cell oil (DHASCO) has been an ingredient in several brands of premium infant formula sold in North America since 2001 after Mead Johnson, the first infant formula manufacturer to add DHASCO and arachidonic acid single-cell organism oil to its Enfamil Lipil product, received a "Generally Regarded As Safe" status by the Food and Drug Administration and Health Canada. Several past and recent studies indicate supplementation with arachidonic acid (omega-6) may be unsuitable for some infants and toddlers as it may potentiate the inflammatory response.

DHASCO does not make infant formulas more like human milk than "conventional" formula containing alpha-linolenic acid and linoleic acid, which are precursors to DHA. Formula sold in North America uses lipids from microorganisms grown in bioreactors as sources of DHA. Some doubt that DHA additives benefit brain development of term infants, as formula makers claim in their advertisements, which has led some public interest groups to file complaints with the Federal Trade Commission of the United States, alleging false and misleading advertising. There is some obvious debate about the safety of single cell DHA and AA as compared to natural sources, but origanal studies on the increase of the Mental

Development Index were based on single cell DHA and AA added to preformed Enfamil. The following is a good review of that study: "The study tested the intelligence scores of 56 infants, 18 months old. One group received formula containing only DHA, while another received one containing DHA and AA. The control group's commercial formula did not contain either substance. All three groups of infants were enrolled in the study within five days of their birth, and for 17 weeks received one of the three formulas.

When the children's overall intelligence was tested, they differed significantly on the Mental Development Index (MDI) that measures young children's memory, their ability to solve simple problems, and their language capabilities.

The children in the control group received an average MDI score of 98 – slightly below the national average of 100 for U.S. children. The DHA group received an average score of 102.4, and the DHA plus AA group received an average score of 105."

A study found that preterm infants fed baby formulas fortified with DHASCO provided better developmental outcomes than formulas not containing the supplement.

A study sponsored by March of Dimes and National Institutes of Health suggests that women who take DHA supplements during pregnancy give their babies some degree of added protection against getting common colds. The babies whose mothers had taken DHA supplements seemed to get over cold symptoms faster when they did get sick.

4 – 5 - Current research

Although most studies demonstrate positive effects of dietary DHA on human health, contrary results exist. For example, one study found that the use of DHA - rich fish oil capsules did not reduce postpartum depression in mothers or improve cognitive and language development in their offspring during early childhood (though this is not a negative effect, only shows no effect).

Additional studies confirmed DHA benefits for other nervous system functions, cardiovascular health, and potentially other organs. In one study, men who took DHA supplements for 6 –12 weeks decreased the concentrations of several inflammatory markers in their blood by approximately 20 %. It has been shown that heart disease patients with higher intakes of DHA and EPA survived longer .A new study found that higher intake of DHA was associated with slower rates of telomere shortening, which is a basic DNA-level marker of aging. Preliminary studies showed that a high intake of DHA was associated with reduced risk for developing Alzheimer's disease and reduced symptoms of depression in Parkinson's Disease consistent with DHA being the most abundant omega-3 fatty acid in the brain. It is now considered so important to brain and eye development that DHA is included in most infant formulas. Lastly, in preliminary research, it was found that a diet rich in DHA might protect stroke victims from brain damage and disability and aid in a speedier recovery.

According to a new study, DHA is very likely important in the formation of the acrosome, an arc-like structure on the top of sperm, which is critical in fertilization because it houses a variety of enzymes that sperm use to penetrate an egg . Because humans and other mammals are able to make their own DHA from other fatty acids, DHA deficiency isn't very common. But, if that DHA-synthesizing enzyme is defective, it could lead to problems with infertility.

Researchers in Norway are testing a treatment for psoriasis with a synthesised molecule based on DHA.

5 - Nutrition

Ordinary types of cooked salmon contain 500 – 1500 mg DHA and 300–1000 mg EPA per 100 grams.(USDA) Additional top fish sources of DHA are: tuna, bluefish, mackerel, swordfish, anchovies, herring, sardines, and caviar.

5 – 1 - The discovery of algae - based DHA

In the early 1980s, NASA sponsored scientific research in search of a plant-based food source that could generate oxygen and

nutrition on long-duration space flights. The researchers discovered that certain species of marine algae produced rich nutrients. This research led to the development of an algae-based, vegetable-like oil that contains two essential polyunsaturated fatty acids: DHA and ARA (Arachidonic acid).

5 – 2 - Use as a food additive

DHA is widely used as a food supplement. It was first used primarily in infant formulas. In 2004, the US Food and Drug Administration endorsed qualified health claims for DHA , and by 2007 DHA - fortified dairy items (milk, yogurt, cooking oil) started to appear in grocery stores.

DHA is believed to be helpful to people with a history of heart disease, for premature infants, and to support healthy brain development especially in young children along with supporting retinal development. Some manufactured DHA is a vegetarian product extracted from algae, and it competes on the market with fish oil that contains DHA and other omega-3's such as EPA. Both fish oil and DHA are odorless and tasteless after processing as a food additive

5 – 3 - Studies of vegetarians and vegans

Vegetarian diets typically contain limited amounts of DHA, and vegan diets typically contain no DHA. Vegetarians and vegans have substantially lower levels of DHA in their bodies, and short-term supplemental ALA has been shown to increase EPA, but not DHA. However, supplemental preformed DHA, available in algae-derived oils or capsules, has been shown to increase DHA levels. While there is little evidence of adverse health or cognitive effects due to DHA deficiency in adult vegetarians or vegans, fetal and breast milk levels remain a concern.

5 – 4 - DHA and EPA in fish oils

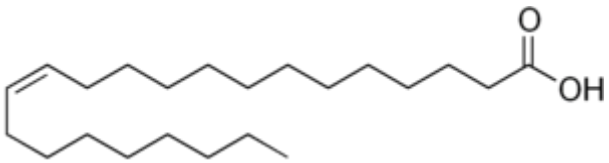
Fish oil is widely sold in gelatin capsules containing a mixture of omega-3 fatty acids including EPA and smaller quantities of DHA. One study found fish oil higher in DHA than EPA lowered inflammatory cytokines, such as IL-6 and IL-1β, associated with neurodegenerative and autoimmune diseases. They note the brain

normally contains DHA, but not EPA, though both DHA and EPA plasma concentrations increased significantly for participants.

6 - Hypothesized role in human evolution

An abundance of DHA in seafood has been suggested as being helpful in the development of a large brain,[59] though other researchers claim a terrestrial diet could also have provided the necessary DHA.

Erucic Acid



Contents

1 - Introduction

Erucic acid is a monounsaturated omega-9 fatty acid, denoted 22:1ω9. It has the formula $CH_3(CH_2)_7CH{=}CH(CH_2)_{11}COOH$. It is prevalent in wallflower seed, makes up 4.1% of rapeseed oil,[1] and makes up 42% of mustard oil. Erucic acid is also known as *cis*-13-docosenoic acid and the trans isomer is known as brassidic acid.

IUPAC name:
(*Z*)-Docos-13-enoic acid

Molecular formula	$C_{22}H_{42}O_2$
Molar mass	338 g mol^{-1}
Appearance	White waxy solid
Density	0.860 g / cm^3
Melting point	33.8 °C
Boiling point	381.5 °C (decomposes)
Solubility in water	Insoluble
Solubility in methanol and ethanol	Soluble
Flash point	349.9 °C

2 - Uses

Erucic acid has many of the same uses as mineral oils, but it is more readily biodegradable than some. It has limited ability to polymerize and dry for use in oil paints. Like other fatty acids, it can be converted into surfactants or lubricants, and can be used as a precursor to bio-diesel fuel.

Derivatives of erucic acid have many further uses, such as behenyl alcohol ($CH_3(CH_2)_{21}OH$) , a pour point depressant (enabling liquids to flow at a lower temperature), and silver behenate, for use in photography. It is also used as an ingredient in appetite suppressants.

3 - Sources of erucic acid

The seed oil of the rape plant is rich in erucic acid.

The name *erucic* means: of or pertaining to eruca; which is a genus of flowering plants in the family Brassicaceae. It is also the Latin for colewort, which today is better known as kale

.

Erucic acid is produced naturally (together with other fatty acids) across a great range of green plants, but especially so in members of the brassica family. It is highest in some of the rapeseed varieties of brassicas, kale and mustard being some of the highest, followed by Brussels sprouts and broccoli. For industrial purposes, a *Low-Erucic Acid Rapeseed* (LEAR) has been developed, which contains fats derived from oleic acid instead of erucic acid.

4 - Biochemistry

Erucic acid is produced by elongation of oleic acid via oleoyl-coenzyme A and malonyl- CoA. Erucic acid is broken down into shorter- chain fatty acids in the human liver by the long - chain Acyl CoA dehydrogenase enzyme.

5 - Health effects

The effects of erucic acid from edible oils on human health are controversial. However no negative health effects have ever been documented in humans.

Mustard oil was once considered unsuitable for human consumption in the United States, Canada, and the European Union due to the high content of erucic acid. This is because of early studies in rats. Subsequent studies on rats have shown that they are less able to digest vegetable fats (whether they contain erucic acid or not) than humans and pigs . Chariton *et al.* suggests that in rats: "Inefficient activation of erucic acid to erucyl - CoA and a low level of activity of triglyceride lipase and enzymes of betaoxidation for erucic acid probably contribute to the accumulation and retention of cardiac lipid."[9] Before this process was fully understood it led to the belief that erucic acid and mustard oil were both highly toxic to humans. The high percentage of erucic acid in mustard oil has led to the latter being banned for food use in the European Union and other countries.

Epidemiological studies suggest that, in regions where mustard oil is still used in a traditional manner, mustard oil may afford some protection against cardiovascular diseases. In this sense "traditional" means that :

(a) the oil is used fresh; and

(b) vegetable fats count only as a small percentage of the total caloric intake.

Whether this effect is due to the nature of erucic acid *per se* to make the blood platelets less sticky, or to the presence of a reasonably high percentage of α-linolenic acid, or to a combination of properties of fresh unrefined oil, is as yet uncertain. Care needs to be taken with such epidemiological studies to exclude the possibility of early deaths

from other causes skewing the results. The fact that early asymptomatic coronary disease is readily detectable post mortem and is absent in the mustard oil cohorts tends to add weight to the hypothesis that mustard oil is protective.

A four - to - one mixture of erucic acid and oleic acid constitutes Lorenzo's oil; an experimental treatment for the rare neurobiology disorder adrenoleukodystrophy. Thrombocytopenia has been seen in patients treated with Lorenzo’s oil, probably related to its erucic acid content.

However, for the reasons given above, it is not advisable for nursing mothers or babies to eat food containing erucic acid.

6 - Health concerns

Before genetic engineering, plant breeders were aiming to produce a less-bitter-tasting multi - purpose oil from rapeseed that would appeal to a larger market by making it more palatable for cattle and other livestock. While it was possible to breed out much of the pungent-tasting glucosinolates, one of the dominant erucic acid genes would get stripped out of the genome as well, greatly reducing its valuable erucic acid content . Studies on rats show lipidosis problems when fed high quantities of erucic acid, however, so this did not hinder saleability. Later trials showed that rats had the same problems with other vegetable fatty acids, because rats are poor at metabolising some fats. The plant breeding industry later changed "low erucic acid" to be its unique selling proposition over that of its competitors.

There are not many studies done on humans with erucic acid; the majority are carried out by the food science industry on animals. Animal studies failed to show negative events occurring from feeding of erucic acid, and the studies were repeated under increasingly unnatural scenarios. In one case, neonate piglets that have a limited ability to absorb these fats had their normal sow's milk replaced solely with rapeseed oil for one hundred percent of their calorific needs.[14] The studies showed that lipidoses suffered by the piglets proved to be only a transient effect; the liver automatically responded by increasing enzyme levels to cope with the unusual diet, and the lipidoses subsided.

A 2006 study reported higher rates of lung cancer in countries with populations that cook over solid fuel wood and biomass fires and stoves. The possibility of production of smoke from heated oil was also considered, and it was established that rapeseed oil, which contains erucic acid, can cause increased lung carcinomas through emissions under high heat. However, the report also showed a variety of other cooking oils also did this at similar heats.

6 – 1 - Cardiac concerns

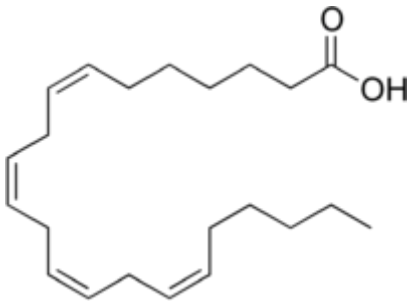
The levels of erucic acid in human foods are restricted, in part, over concerns that it may adversely affect heart tissue. Erucic acid is preferentially absorbed in myocardium tissue but is not metabolized there.

In 2003 Food Standards Australia set a Provisional Tolerable Daily Intake (PTDI) of about 500 mg/day of erucic acid, based on "the level that is associated with increased myocardial lipidosis in nursling pigs." "There is a 120-fold safety margin between this level and the level that is associated with increased myocardial lipidosis in nursling pigs. The dietary exposure assessment has concluded that the majority of exposure to erucic acid by the general population would come from the consumption of canola oil. The dietary intake of erucic acid by an individual consuming at the average level is well below the PTDI, therefore, there is no cause for concern in terms of public health and safety. However, the individual consuming at a high level has the potential to approach the PTDI. This would be particularly so if the level of erucic acid in canola oil was to exceed 2% of the total fatty acids."

7 - Low erucic acid rapeseed

Food grade rapeseed oil (also known as canola oil, rapeseed 00 oil, low erucic acid rapeseed oil, LEAR oil, and rapeseed canola-equivalent oil) is regulated to a maximum of 2% erucic acid by weight in the USA. and 5 % in the EU,] with special regulations for infant food.

Adrenic Acid



IUPAC name :
7*Z*,10*Z*,13*Z*,16*Z*-docosa tetra enoic acid

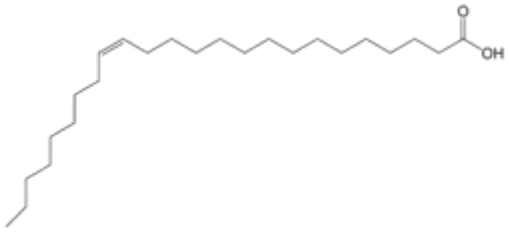
Molecular formula	$C_{22}H_{36}O_2$
Molar mass	332 g / mol

Docosa tetra enoic acid designates any straight chain 22:4 fatty acid.

One isomer is of particular interest :

all-*cis*-7,10,13,16-docosa tetra enoic acid is an ω-6 fatty acid with the trivial name adrenic acid. This is a naturally occurring polyunsaturated fatty acid formed through a 2-carbon chain elongation of arachidonic acid. It is one of the most abundant fatty acids in the early human brain.

Nervonic Acid



1 - Introduction

Nervonic acid is a monounsaturated omega-9 fatty acid. Nervonic acid has been identified as important in the biosynthesis of nerve cell myelin. It is found in the sphingolipids of white matter in human brain.

Nervonic acid is used in the treatment of disorders involving demyelination, such as adrenoleukodystrophy and multiple sclerosis where there is a decreased level of nervonic acid in sphingolipids.

IUPAC name :
(*Z*)-Tetracos-15-enoic acid
Other names :
cis-15-Tetracosenoic acid 24:1 cis, delta 9 or 24:1 omega 9

Molecular formula	$C_{24}H_{46}O_2$
Molar mass	366 g / mol
Melting point	42 – 43 °C

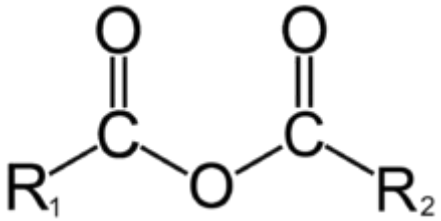
2 - Dietary sources

Nervonic acid is abundant in King Salmon (Chinook) with 140 mg / 100g, yellow mustard seed 83 mg/100 g , flax seed 64 mg / 100g, Sockeye salmon 40 mg / 100g, sesame seed 35 mg/100g, and macademia nuts 18 mg / 100g.

Part - 5 -

Aliphatic Anhydrous Carboxylic Acids

Acid Anhydride



Generic example of an acid anhydride.

Contents

1 - Introduction

Commonly an acid anhydride is an organic compound that has two acyl groups bound to the same oxygen atom. Most commonly, the acyl groups are derived from the same carboxylic acid, the formula of the anhydride being $(RC(O))_2O$. Symmetrical acid anhydrides of this type are named by replacing the word *acid* in the name of the parent carboxylic acid by the word *anhydride*. Thus, $(CH_3CO)_2O$ is called *acetic anhydride*. Mixed (or unsymmetrical) acid anhydrides, such as acetic formic anhydride (see below), are known.

One or both acyl groups of an acid anhydride may also be derived from another type of organic acid, such as sulfonic acid or a phosphonic acid. One of the acyl groups of an acid anhydride can be derived from an inorganic acid such as phosphoric acid. The mixed anhydride 1,3- bi sphospho glycerate is an intermediate in the formation of ATP via glycolysis, is the mixed anhydride between 3 – phospho glyceric acid and phosphoric acid. Acidic oxides are often classified as acid anhydrides.

2 - Preparation

Acid anhydrides are prepared in industry by diverse means. Acetic anhydride is mainly produced by the carbonylation of methyl acetate. Maleic anhydride is produced by the oxidation of benzene or

butane. Laboratory routes emphasize the dehydration of the corresponding acids. The conditions vary from acid to acid, but phosphorus pentoxide is a common dehydrating agent:

$2\ CH_3COOH + P_4O_{10} \rightarrow CH_3C(O)OC(O)CH_3 + "(HO)_2P_4O_9"$

Acid chlorides are also effective precursors:

$CH_3C(O)Cl + HCO_2Na \rightarrow HCO_2COCH_3 + NaCl$

Mixed anhydrides containing the acetyl group are prepared from ketene:

$RCO_2H + H_2C{=}\ C{=}\ O \rightarrow RCO_2C(O)CH_3$

3 - Reactions

Acid anhydrides are a source of reactive acyl groups, and their reactions and uses resemble those of acyl halides. In reactions with protic substrates, the reactions afford equal amounts of the acylated product and the carboxylic acid:

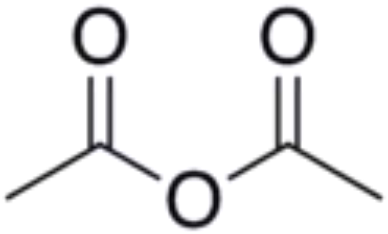
$RC(O)OC(O)R + HY \rightarrow RC(O)Y + RCO_2H$

for HY = HOR (alcohols), HNR'_2 (ammonia, primary, secondary amines), aromatic ring .

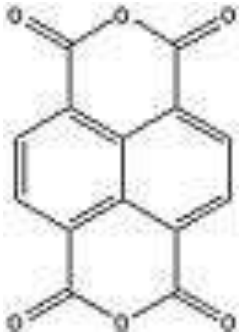
Acid anhydrides tend to be less electrophilic than acyl chlorides, and only one acyl group is transferred per molecule of acid anhydride, which leads to a lower atom efficiency. The low cost, however, of acetic anhydride makes it a common choice for acetylation reactions.

4 - Applications and occurrence of acid anhydrides

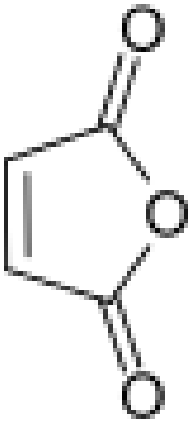
Illustrative acid anhydrides



Acetic anhydride is produced on a large scale for many applications.



Naphthalene tetra carboxylic dianhydride, a building block for complex organic compounds, is an example of a dianhydride.

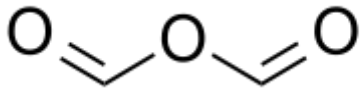


Maleic anhydride is a cyclic anhydride, widely used to make industrial coatings.

Acetic anhydride is a major industrial chemical widely used for preparing acetate esters, e.g. cellulose acetate. Maleic anhydride is the precursor to various resins by copolymerization with styrene. Maleic anhydride is a dienophile in the Diels-Alder reaction.

Dianhydrides, molecules containing two acid anhydride functions, are used to synthesize polyimides and sometimes polyesters and polyamides. Examples of dianhydrides: pyromellitic dianhydride (PMDA), 3,3', 4,4' – oxy diphtalic dianhydride (ODPA), 3,3', 4,4'-benzophenone tetra carboxylic dianhydride (BTDA), 4,4'-diphtalic (hexa fluoro is opropylidene) anhydride (6FDA), benzo quinone tetra carboxylic dianhydride , ethylene tetra carboxylic dianhydride. Poly anhydrides are a class of polymers characterized by anhydride bonds that connect repeat units of the polymer backbone chain.

Formic Anhydride



Formic anhydride, also called methanoic anhydride, is a chemical compound with formula $C_2H_2O_3$ or $(H(C{=}O)\text{-})_2O$. It can be viewed as the anhydride of formic acid (HCOOH).

Formic anhydride is a liquid with boiling point 24 °C at 20 mmHg. It is stable in diethyl ether solution. It can be isolated by low-temperature, low - pressure distillation, but decomposes on heating above room temperature. It decomposes into formic acid and carbon monoxide.

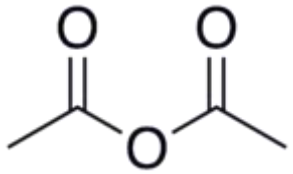
Formic anhydride can be obtained by reaction of formyl fluoride with sodium formate in ether at −78 °C.[3] It can also be produced by reacting formic acid with *N*,*N*′- di cyclo hexyl carbo di imide $((C_6H_{11}\text{-}N{=})_2C)$ in ether at -10 °C. It can also be obtained by disproportionation of acetic formic anhydride.

The decomposition of formic anhydride may be catalyzed by formic acid.

Formic anhydride can be detected in the gas phase reaction of ozone with ethylene. The molecule is planar in the gas phase.

IUPAC name : Formyl oxy methanone	
Other names : Methanoic anhydride	
Molecular formula	$C_2H_2O_3$
Molar mass	74 g mol^{-1}
Appearance	Colorless gas
Boiling point	24 °C (at 20 mmHg)

Acetic Anhydride



Contents

1 - Introduction

Acetic anhydride, or ethanoic anhydride, is the chemical compound with the formula $(CH_3CO)_2O$. Commonly abbreviated Ac_2O, it is the simplest isolatable acid anhydride and is a widely used reagent in organic synthesis. It is a colorless liquid that smells strongly of acetic acid, formed by its reaction with the moisture in the air.

Formic anhydride is an even simpler acid anhydride, but it spontaneously decomposes, especially once removed from solution.

IUPAC name : acetic anhydride	
Systematic name ; ethanoic anhydride	
Other names : Ethanoyl ethanoate Acetic acid anhydride Acetyl acetate Acetyl oxide Acetic oxide	
Molecular formula	$C_4H_6O_3$
Molar mass	102 g mol^{-1}

Appearance	colorless liquid
Density	1.082 g cm^{-3}, liquid
Melting point	−73.1 °C
Boiling point	139.8 °C
Solubility in water	2.6 g / 100 mL,
Refractive index (n_D)	1.3901
EU classification	Corrosive (C)
Flash point	49 °C
Auto ignition temperature	316 °C
Explosive limits	2.7 – 10.3 %

2 - Structure and properties

Contrary to what its Lewis structure seems to predict, acetic anhydride, like many other acid anhydrides that are free to rotate, has experimentally been found to be aplanar. The pi system linkage through the central oxygen offers very weak resonance stabilization compared to the dipole-dipole repulsion between the two carbonyl oxygens. However, the energy barriers to bond rotation between each of the optimal aplanar conformations are quite low.

Like most acid anhydrides, the carbonyl carbon of acetic anhydride is a potent electro phile as the leaving group for each carbonyl carbon (a carboxylate) is a good electron-withdrawing leaving group. The internal asymmetry may contribute to acetic anhydride's potent electro philicity as the asymmetric geometry makes one side of a carbonyl carbon more reactive than the other, and in doing so tends to consolidate the electro positivity of a carbonyl carbon to one side .

3 - Production

Acetic anhydride is produced by carbonylation of methyl acetate :

$CH_3CO_2CH_3 + CO \rightarrow (CH_3CO)_2O$

This process involves the conversion of methyl acetate to methyl iodide and an acetate salt. Carbonylation of the methyl iodide in turn affords acetyl iodide, which reacts with acetate salts or acetic

acid to give the product. Rhodium iodide and lithium iodide are employed as catalysts. Because acetic anhydride is not stable in water, the conversion is conducted under anhydrous conditions. In contrast, the Monsanto acetic acid process, which also involves a rhodium catalyzed carbonylation of methyl iodide, is at least partially aqueous.

To a decreasing extent, acetic anhydride is also prepared by the reaction of ethenone (ketene) with acetic acid at 45–55 °C and low pressure (0.05–0.2 bar).

$$H_2C{=}\ C{=}\ O + CH_3COOH \rightarrow (CH_3CO)_2O\ (\Delta H = -63\ \text{kJ/mol})$$

Ketene is generated by dehydrating acetic acid at 700–750 °C in the presence of triethyl phosphate as a catalyst or (in Switzerland and the CIS) by the thermolysis of acetone at 600–700 °C in the presence of carbon disulfide as a catalyst.

$$CH_3COOH \rightleftharpoons H_2C{=}\ C{=}\ O + H_2O\ (\Delta H = +147\ \text{kJ/mol})$$
$$CH_3COCH_3 \rightarrow H_2C{=}\ C{=}\ O + CH_4$$

The route from acetic acid to acetic anhydride via ketene was developed by Wacker Chemie in 1922, when the demand for acetic anhydride increased due to the production of cellulose acetate.

Due to its low cost, acetic anhydride is purchased, not prepared, for use in research laboratories.

4 - Reactions

Acetic anhydride is a versatile reagent for acetylations, the introduction of acetyl groups to organic substrates . In these conversions, acetic anhydride is viewed as a source of CH_3CO^+. Alcohols and amines are readily acetylated. For example, the reaction of acetic anhydride with ethanol yields ethyl acetate:

$$(CH_3CO)_2O + CH_3CH_2OH \rightarrow CH_3CO_2CH_2CH_3 + CH_3COOH$$

Often a base such as pyridine is added to function as catalyst. In specialized applications, Lewis acidic scandium salts have also proven effective catalysts.

Aromatic rings are acetylated, usually in the presence of an acid catalyst. Illustrative is the conversion of benzene to aceto phenone:

$(CH_3CO)_2O + C_6H_6 \rightarrow CH_3COC_6H_5 + CH_3CO_2H$

Ferrocene can be acetylated as well:

$Cp_2Fe + (CH_3CO)_2O \rightarrow CpFe(C_5H_4COCH_3)$

4 – 1 - Hydrolysis

Acetic anhydride dissolves in water to approximately 2.6% by weight.[10] Aqueous solutions have limited stability because, like most acid anhydrides, acetic anhydride hydrolyses to give carboxylic acids. In this case, acetic acid is formed :

$(CH_3CO)_2O + H_2O \rightarrow 2\ CH_3CO_2H$

5 - Applications

As indicated by its organic chemistry, Ac_2O is mainly used for acetylations leading to commercially significant materials. Its largest application is for the conversion of cellulose to cellulose acetate, which is a component of photographic film and other coated materials. Similarly it is used in the production of aspirin (acetylsalicylic acid), which is prepared by the acetylation of salicylic acid.[12] It is also used as a wood preservative via autoclave impregnation to make a longer lasting timber.

In starch industry, acetic anydride is a common acetylation compound, used for the production of modified starches (E1414, E1420, E1422)

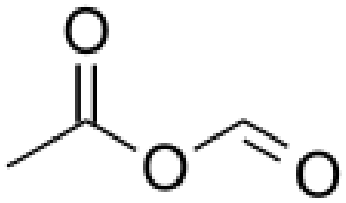
Because of its use for the synthesis of heroin by the diacetylation of morphine, acetic anhydride is listed as a U.S. DEA List II precursor, and restricted in many other countries.

6 - Safety

Acetic anhydride is an irritant and flammable. Because of its reactivity toward water, alcohol foam or carbon dioxide are preferred for fire suppression. The vapour of acetic anhydride is harmful.

When mixed with hydrogen peroxide, an excess of acetic anhydride reacts with one of the reaction products per acetic acid and forms highly shock sensitive and explosive di acetyl peroxide.

Acetic Formic Anhydride

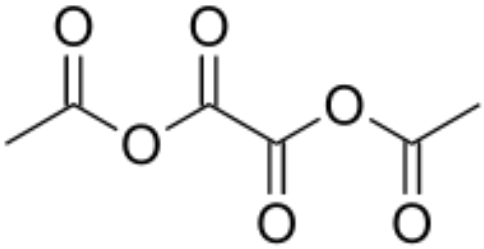


Acetic formic anhydride, or ethanoic methanoic anhydride is a chemical compound with formula $C_3H_4O_3$, or H_3C-(C=O)-O-(C=O)H. It can be viewed as the mixed anhydride of acetic acid (H_3C-(C=O)OH) and formic acid (H(C= O)OH) by removal of a molecule of water.

It can be produced by reaction between sodium formate and acetyl chloride in anhydrous diethyl ether, at 23–27 °C.[2] Among other uses, it is a formylation agent for amines, amino acids, and alcohols, and a starting material for formyl fluoride.

IUPAC name : Acetyl oxy methanone	
Systematic name : Formyl acetate	
Other names : Formic acetic anhydride	
Molecular formula	$C_3H_4O_3$
Molar mass	88.06 g mol^{-1}

Acetic Oxalic Anhydride



Acetic oxalic anhydride is an organic compound with formula $C_6H_6O_6$ or $(H_3C\text{-}(C{=}O)\text{-}O\text{-}(C{=}O)\text{-})_2$. It can be viewed as a mixed anhydride, formally derived from acetic acid ($H_3C\text{-}(C{=}O)OH$) and oxalic acid ($(\text{-}(C{=}O)OH)_2$), in 2:1 molecular ratio, by the loss of two water molecules.

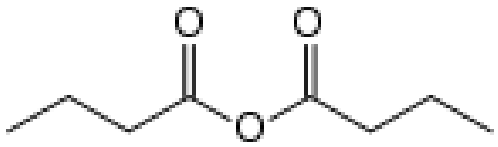
Molecular formula	$C_6H_6O_6$
Molar mass	174 g mol^{-1}

It is an unstable colorless crystalline solid, soluble in diethyl ether, that decomposes at about −3 °C into acetic anhydride ($H_3C\text{-}(C{=}O)\text{-})_2O$, carbon dioxide ($CO_2$) and carbon monoxide (CO). It is hydrolyzed by water into acetic and oxalic acids.

Unlike some other anhydrides, it cannot be obtained directly from the acids. It was synthesized in 1953 by W. Edwards and W. M. Henley, by reacting silver oxalate ($Ag_2C_2O_4$) suspended in diethyl ether with acetyl chloride at temperatures below −5 °C and distilling off the solvent under low pressure. It can also be obtained by reacting anhydrous oxalic acid with ketene ($H_2C{=}C{=}O$).

Acetic oxalic anhydride was conjectured to be an intermediate in the decomposition of anhydrous oxalic acid by acetic anhydride.[1]

Butyric Anhydride



1 – Introduction :

Butyric anhydride, or Butanoic anhydride, is a chemical compound with the formula $(CH_3CH_2CH_2CO)_2O$.It is a colorless liquid that smells strongly of butyric acid, formed by its reaction with the moisture in the air.

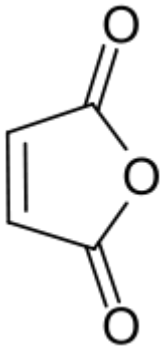
2 - Applications

Because of its odor, butyric anhydride has use as a fumigant to drive bees from their hives in products such as Bee - Go.

3 - Safety

Butyric anhydride is a combustible, corrosive liquid. It is considered water sensitive.

Maleic Anhydride



1 - Introduction

Maleic anhydride (butenedioic anhydride , toxilic anhydride , 2,5- dioxofuran) is an organic compound with the formula $C_2H_2(CO)_2O$. It is the acid anhydride of maleic acid and in its pure state it is a colourless or white solid with an acrid odour.

IUPAC name : Furan-2,5-dione	
Molecular formula	$C_4 H_2 O_3$
Molar mass	98 g/mol
Appearance	White crystals
Density	1.48 g / cm^3
Melting point	52.8 °C
Boiling point	202 °C
Solubility in water	Reacts
EU classification	Corrosive (C)
Flash point	102 °C

2 - Production

Maleic anhydride was traditionally manufactured by the oxidation of benzene or other aromatic compounds. As of 2006, only a few smaller plants continue to use benzene; due to rising benzene prices, most maleic anhydride plants now use n-butane as a feedstock.

In both cases, benzene and butane are fed into a stream of hot air, and the mixture is passed through a catalyst bed at high

temperature. The ratio of air to hydrocarbon is controlled to prevent the mixture from catching on fire. Vanadium pentoxide and molybdenum trioxide are the catalysts used for the benzene route, whereas vanadium and phosphorus oxides are used for the butane route.

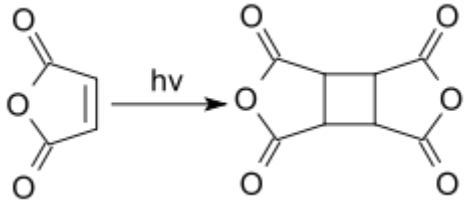
$$2\ CH_3CH_2CH_2CH_3 + 7\ O_2 \rightarrow 2\ C_2H_2(CO)_2O + 8\ H_2O$$

3 - Reactions

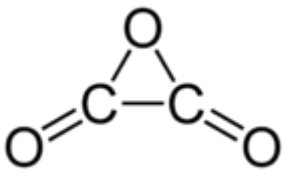
The chemistry of maleic anhydride is very rich, reflecting its ready availability and bifunctional reactivity. It hydrolyzes, producing maleic acid, *cis*-HOOC–CH=CH–COOH. With alcohols, the half-ester is generated, e.g., *cis*-HOOC–CH=CH–$COOCH_3$.

Maleic anhydride is a potent dienophile in Diels-Alder reactions. It is also a ligand for low-valent metal complexes, examples being $Pt(PPh_3)_2$(MA) and $Fe(CO)_4$(MA).

Maleic anhydride dimerizes in a photochemical reaction to form cyclo butane tetra carboxylic dianhydride (CBTA). This compound is used in the production of polyimides and as an alignment film for liquid crystal displays.



Oxalic Anhydride



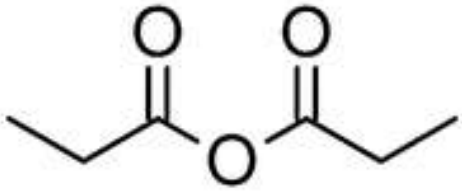
Oxalic anhydride or ethanedioic anhydride, also called oxiranedione, is a hypothetical organic compound with the formula C_2O_3, which can be viewed as the anhydride of oxalic acid or the two - fold ketone of ethylene oxide. It is an oxide of carbon (an oxocarbon).

The simple compound apparently has yet to be observed (as of 2009). In 1998, however, P. Strazzolini and others have claimed the synthesis of dioxane tetraketone (C_4O_6), which can be viewed as the cyclic dimer of oxalic anhydride.

It has been conjectured to be a fleeting intermediate in the thermal decomposition of certain oxalates and certain chemo luminescent reactions of oxalyl chloride.

IUPAC name : oxiranedione	
Other names : oxalic anhydride ethanedioic anhydride	
Molecular formula	C_2O_3
Molar mass	72 g mol^{-1}

Propionic Anhydride



1 - Introduction

Propanoic anhydride is an organic compound with the formula $(CH_3CH_2CO)_2O$. This simple acid anhydride is a colourless liquid. It is a widely used reagent in organic synthesis.

2 - Synthesis

Propanoic anhydride has been prepared by dehydration of propanoic acid using ketene :

$$2\ CH_3CH_2CO_2H + CH_2{=}\ C{=}\ O \rightarrow (CH_3CH_2CO)_2O + CH_3CO_2H$$

3 - Safety

Propanoic anhydride is strong smelling and corrosive, and will cause burns on contact with skin. Vapour can burn eyes and lungs.

Succinic Anhydride

1- Introduction

Succinic anhydride, also called di hydro - 2,5- furandione , is an organic compound with the molecular formula $C_4H_4O_3$. This colorless solid is the acid anhydride of succinic acid.

IUPAC name : Oxolane-2,5-dione	
Other names : Succinic acid anhydride Succinyl oxide Dihydro-2,5-furandione	
Molecular formula	$C_4 H_4 O_3$
Molar mass	100 g mol^{-1}
Appearance	Colorless crystalline needles
Density	1.23 g / cm^3
Melting point	119 –120 °C
Boiling point	261 °C
Solubility in water	Decomposes
Flash point	147 °C[4]
LD_{50}	1510 mg / kg (oral, rat)

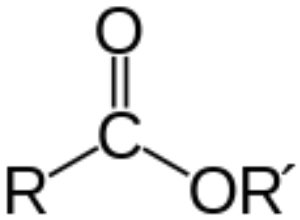
2 - Applications

Alkyl succinic anhydride (ASA) is used as a sizing agent or wet strength additive in paper production.

Part - 6 -

Aliphatic Ester

Ester



A carboxylate ester. R and R' denote any alkyl or aryl group

Contents

1 - Introduction

Esters are chemical compounds consisting of a carbonyl adjacent to an ether linkage. They are derived by reacting an oxoacid with a hydroxyl compound such as an alcohol or phenol.[1] Esters are usually derived from an inorganic acid or organic acid in which at least one -OH (hydroxyl) group is replaced by an -O-alkyl (alkoxy) group, and most commonly from carboxylic acids and alcohols. That is, esters are formed by condensing an acid with an alcohol.

Esters are ubiquitous. Most naturally occurring fats and oils (e.g. triglycerides) are the fatty acid esters of glycerol. Esters with low molecular weight are commonly used as fragrances and found in essential oils and pheromones. Phospho esters form the backbone of DNA molecules. Nitrate esters, such as nitroglycerin, are known for their explosive properties, while polyesters are important plastics, with monomers linked by ester moieties.

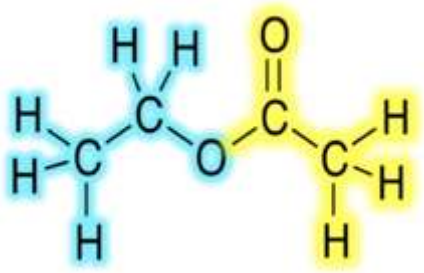
2 - Nomenclature

2 – 1 - Etymology

The word 'ester' was coined in 1848 by German chemist Leopold Gmelin , probably as a contraction of the German Essigäther - acetic ether.

2 – 2 - IUPAC nomenclature of Esters

Ester names are derived from the parent alcohol and the parent acid, where the latter may be an organic or an inorganic acid. Esters derived from the simplest carboxylic acids are commonly named according to the more traditional, so-called "trivial names" e.g. as formate, acetate, propionate, and butyrate, as opposed to the IUPAC nomenclature methanoate, ethanoate, propanoate and butanoate. Esters derived from more complex carboxylic acids are, on the other hand, more frequently named using the systematic IUPAC name, based on the name for the acid followed by the suffix *-oate*. For example the ester hexyl octanoate, also known under the trivial name hexyl caprylate, has the formula $CH_3(CH_2)_6CO_2(CH_2)_5CH_3$.



Ethyl acetate derived from an alcohol (blue- lift) and an acyl group (yellow -right) derived from a carboxylic acid.

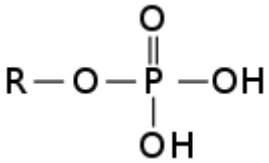
The chemical formulas of organic esters are typically written in the format of RCO_2R', where R and R' are the hydrocarbon parts of the carboxylic acid and alcohol, respectively. For example butyl acetate (systematically butyl ethanoate), derived from butanol and acetic acid (systematically ethanoic acid) would be written $CH_3CO_2C_4H_9$. Alternative presentations are common including BuOAc and $CH_3COOC_4H_9$.

Cyclic esters are called lactones, regardless of whether they are derived from an organic or an inorganic acid. One example of a (organic) lactone is *gamma*-valerolactone.

2 – 3 - Ortho esters

An uncommon class of organic esters are the orthoesters, which have the formula $RC(OR')_3$. Triethylorthoformate ($HC(OC_2H_5)_3$) is derived, in terms of its name (but not its synthesis) from orthoformic acid ($HC(OH)_3$) and ethanol.

2 – 4 - "Inorganic esters"



A phosphoric acid ester

Ester is a general term for the product derived from the condensation of an acid and an alcohol. Thus, the nomenclature

extends to inorganic oxo acids, e.g. phosphoric acid, sulfuric acid, nitric acid and boric acid. For example, triphenyl phosphate is the ester derived from phosphoric acid and phenol. Organic carbonates, such as ethylene carbonate, are derived from carbonic acid and ethylene glycol.

3 - Structure and bonding

Esters contain a carbonyl center, which gives rise to 120°C-C-O and O - C - O angles. Unlike amides, esters are structurally flexible functional groups because rotation about the C - O - C bonds has a low barrier. Their flexibility and low polarity is manifested in their physical properties; they tend to be less rigid (lower melting point) and more volatile (lower boiling point) than the corresponding amides. The pKa of the alpha-hydrogens on esters is around 25.

4 - Physical properties and characterization

Esters are more polar than ethers but less polar than alcohols. They participate in hydrogen bonds as hydrogen-bond acceptors, but cannot act as hydrogen - bond donors, unlike their parent alcohols. This ability to participate in hydrogen bonding confers some water-solubility. Because of their lack of hydrogen - bond - donating ability, esters do not self-associate. Consequently esters are more volatile than carboxylic acids of similar molecular weight.

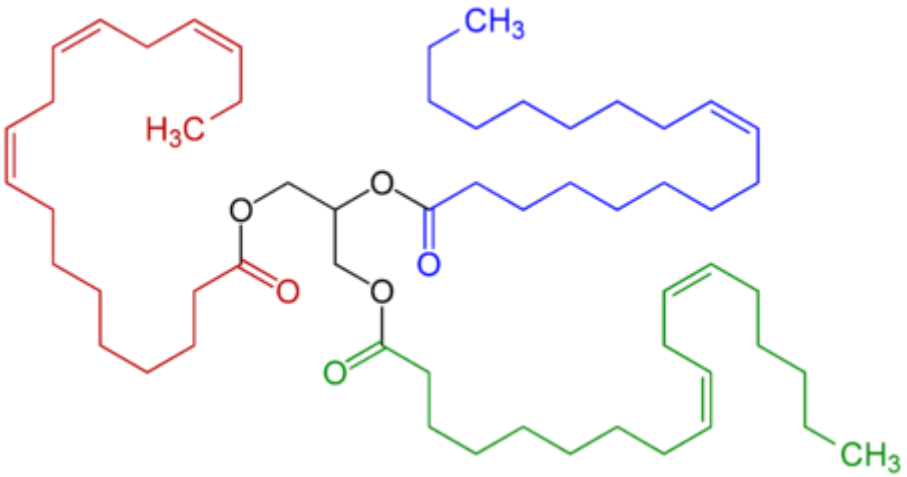
4 – 1 - Characterization and analysis

Esters are usually identified by gas chromatography, taking advantage of their volatility. IR spectra for esters feature an intense sharp band in the range 1730 – 1750 cm^{-1} assigned to $\nu_{C=O}$. This peak changes depending on the functional groups attached to the carbonyl. For example, a benzene ring or double bond in conjugation with the carbonyl will bring the wave number down about 30 cm^{-1}.

5 - Applications and occurrence

Esters are widespread in nature and are widely used in industry. In nature, fats are, in general, tri esters derived from glycerol and fatty acids.[5] Esters are responsible for the aroma of many fruits, including apples, durians, pears, bananas, pineapples, and strawberries.[6] Several billion kilograms of polyesters are produced industrially

annually, important products being polyethylene terephthalate, acrylate esters, and cellulose acetate.



Representative triglyceride found in a linseed oil , a tri glyceride derived of ***linoleic acid***, ***alpha - linolenic acid***, *and* ***oleic acid***.

6 - Preparation

Esterification is the general name for a chemical reaction in which two reactants (typically an alcohol and an acid) form an ester as the reaction product. Esters are common in organic chemistry and biological materials, and often have a characteristic pleasant, fruity odor. This leads to their extensive use in the fragrance and flavor industry. Ester bonds are also found in many polymers.

6 – 1 - Esterification of carboxylic acids

The classic synthesis is the Fischer esterification, which involves treating a carboxylic acid with an alcohol in the presence of a dehydrating agent:

$$RCO_2H + R'OH \rightleftharpoons RCO_2R' + H_2O$$

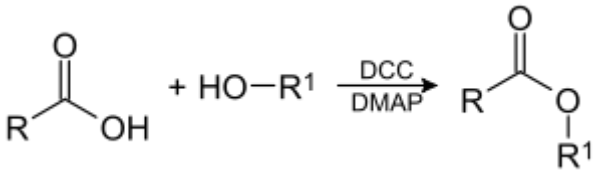
The equilibrium constant for such reactions is about 5 for typical esters, e.g., ethyl acetate. The reaction is slow in the absence of a catalyst. Sulfuric acid is a typical catalyst for this reaction. Many other acids are also used such as polymeric sulfonic acids. Since esterification is highly reversible, the yield of the ester can be improved using Le Chatelier's principle:

using the alcohol in large excess (i.e., as a solvent)

using a dehydrating agent: sulfuric acid not only catalyzes the reaction but sequesters water (a reaction product). Other drying agents such as molecular sieves are also effective.

removal of water by physical means such as distillation as a low - boiling azeotropes with toluene, in conjunction with a Dean-Stark apparatus.

Reagents are known that drive the dehydration of mixtures of alcohols and carboxylic acids. One example is the Steglich esterification, which is a method of forming esters under mild conditions. The method is popular in peptide synthesis, where the substrates are sensitive to harsh conditions like high heat. DCC (di cyclo hexyl carbo di imide) is used to activate the carboxylic acid to further reaction. DMAP (4- di methyl amino pyridine) is used as an acyl-transfer catalyst.



Another method for the dehydration of mixtures of alcohols and carboxylic acids is the Mitsunobu reaction:

$$RCO_2H + R'OH + P(C_6H_5)_3 + R_2N_2 \rightarrow RCO_2R' + OP(C_6H_5)_3 + R_2N_2H_2$$

Carboxylic acids can be esterified using diazomethane:

$$RCO_2H + CH_2N_2 \rightarrow RCO_2CH_3 + N_2$$

Using this diazomethane, mixtures of carboxylic acids can be converted to their methyl esters in near quantitative yields, e.g., for analysis by gas chromatography. The method is useful in specialized organic synthetic operations but is considered too expensive for large scale applications.

6 – 2 - Alcoholysis of acyl chlorides and acid anhydrides

Alcohols react with acyl chlorides and acid anhydrides to give esters:

$RCOCl + R'OH \rightarrow RCO_2R' + HCl$
$(RCO)_2O + R'OH \rightarrow RCO_2R' + RCO_2H$

The reactions are irreversible simplifying work-up. Since acyl chlorides and acid anhydrides also react with water, anhydrous conditions are preferred. The analogous acylations of amines to give amides are less sensitive because amines are stronger nucleophiles and react more rapidly than does water. This method is employed only for laboratory-scale procedures, as it is expensive.

6 – 3 - Alkylation of carboxylate salts

Although not widely employed for esterifications , salts of carboxylate anions can be alkylating agent with alkyl halides to give esters. In the case that an alkyl chloride is used, an iodide salt can catalyze the reaction (Finkelstein reaction). The carboxylate salt is often generated *in situ*. In difficult cases, the silver carboxylate may be used, since the silver ion coordinates to the halide aiding its departure and improving the reaction rate. This reaction can suffer from anion availability problems and, therefore, can benefit from the addition of phase transfer catalysts or highly polar aprotic solvents such as DMF.

6 – 4 - Trans esterification

Trans esterification, which involves changing one ester into another one, is widely practiced:

$RCO_2R' + CH_3OH \rightarrow RCO_2CH_3 + R'OH$

Like the hydrolysation , trans esterification is catalyzed by acids and bases. The reaction is widely used for degrading triglycerides, e.g. in the production of fatty acid esters and alcohols. Poly(ethylene terephthalate) is produced by the trans esterification of dimethyl terephthalate and ethylene glycol :

$(C_6H_4)(CO_2CH_3)_2 + 2\ C_2H_4(OH)_2 \rightarrow$
$1/n\ \{(C_6H_4)(CO_2)_2(C_2H_4)\}_n + 2\ CH_3OH$

6 – 5 - Carbonylation

Alkenes undergo "hydro esterification" in the presence of metal carbonyl catalysts. Esters of propionic acid are produced commercially by this method:

$$C_2H_4 + ROH + CO \rightarrow C_2H_5CO_2R$$

The carbonylation of methanol yields methyl formate, which is the main commercial source of formic acid. The reaction is catalyzed by sodium methoxide:

$$CH_3OH + CO \rightarrow CH_3O_2CH$$

6 – 6 - Addition of carboxylic acids to alkenes

In the presence of palladium-based catalysts, ethylene, acetic acid, and oxygen react to give vinyl acetate:

$C_2H_4 + CH_3CO_2H + 1/2\ O_2 \rightarrow C_2H_3O_2CCH_3 + H_2O$

Direct routes to this same ester are not possible because vinyl alcohol is unstable.

6 – 7 - Other methods

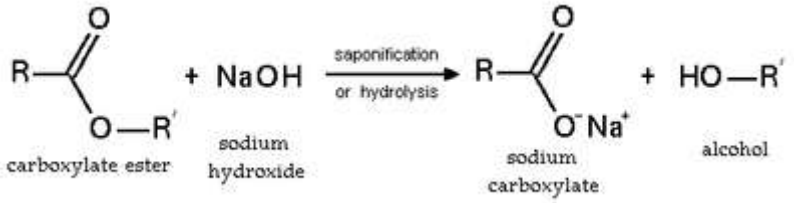
Favorskii rearrangement of α-haloketones in presence of base
Baeyer-Villiger oxidation of ketones with peroxides
Pinner reaction of nitriles with an alcohol
Nucleophilic abstraction of a metal-acyl complex
Hydrolysis of ortho esters in aqueous acid

7 - Reactions

Esters react with nucleo philes at the carbonyl carbon. The carbonyl is weakly electro philic but is attacked by strong nucleo philies (amines, alkoxides, hydride sources, organo lithium compounds, etc.). The C- H bonds adjacent to the carbonyl are weakly acidic but undergo deprotonation with strong bases. This process is the one that usually initiates condensation reactions. The carbonyl oxygen is weakly basic (less so than in amides) but forms adducts.

7 – 1 - Addition of nucleophiles at carbonyl

Esterification is a reversible reaction. Esters undergo hydrolysis under acid and basic conditions. Under acidic conditions, the reaction is the reverse reaction of the Fischer esterification. Under basic conditions, hydroxide acts as a nucleophile, while an alkoxide is the leaving group. This reaction, saponification, is the basis of soap making.



The alkoxide group may also be displaced by stronger nucleophiles such as ammonia or primary or secondary amines to give amides:

$RCO_2R' + NH_2R'' \rightarrow RCONHR'' + R'OH$

This reaction is not usually reversible. Hydrazines and hydroxylamine can be used in place of amines. Esters can be converted to iso cyanates through intermediate hydroxamic acids in the Lossen rearrangement.

Sources of carbon nucleo philes, e.g., Grignard reagents and organo lithium compounds, add readily to the carbonyl.

7 – 2 - Reduction

Compared to ketones and aldehydes, esters are relatively resistant to reduction. The introduction of catalytic hydrogenation in the early part of the 20th century was a breakthrough; esters of fatty acids are hydrogenated to fatty alcohols.

$RCO_2R' + 2\ H_2 \rightarrow RCH_2OH + R'OH$

A typical catalyst is copper chromite. Prior to the development of catalytic hydrogenation, esters were reduced on a large scale using the Bouveault-Blanc reduction. This method, which is largely obsolete, uses sodium in the presence of proton sources.

Especially for fine chemical syntheses, lithium aluminium hydride is used to reduce esters to two primary alcohols. The related reagent sodium boro hydride is slow in this reaction. DIBAH reduces esters to aldehydes.

7 – 3 - Claisen condensation and related reactions

As for aldehyde and aldehydes, the hydrogen atoms on the carbon adjacent ("α to") the carboxyl group in esters are sufficiently acidic to undergo deprotonation, which in turn leads to a variety of useful reactions. Deprotonation requires relatively strong bases, such as alkoxides. Deprotonation gives a nucleo philic enolate , which can further react, e.g., the Claisen condensation and its intramolecular equivalent, the Dieckmann condensation. This conversion is exploited in the malonic ester synthesis, wherein the diester of malonic acid reacts with an electrophile (e.g., alkyl halide), and is subsequently decarboxylated. Another variation is the Fráter – Seebach alkylation.

7 – 4 - Other reactions

Phenyl esters react to hydroxy aryl ketones in the Fries rearrangement.

Specific esters are functionalized with an α-hydroxyl group in the Chan rearrangement.

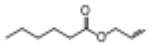
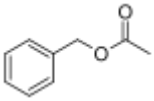
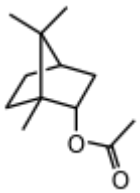
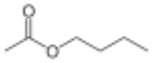
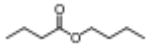
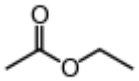
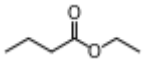
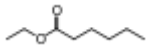
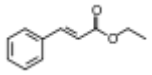
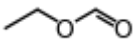
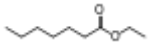
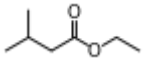
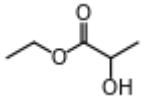
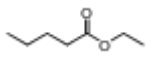
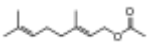
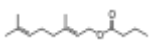
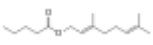
Esters with β-hydrogen atoms can be converted to alkenes in ester pyrolysis.

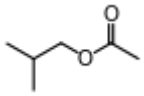
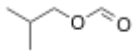
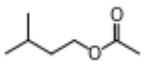
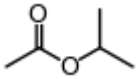
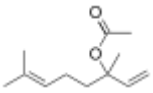
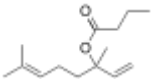
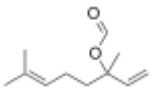
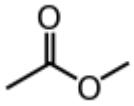
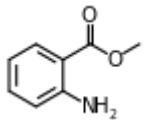
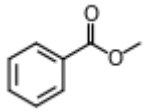
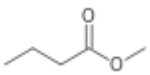
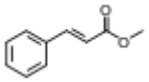
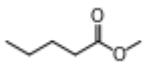
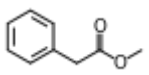
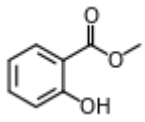
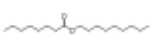
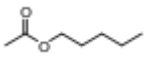
7 – 5 - Protecting groups

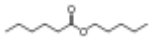
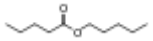
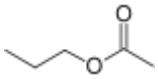
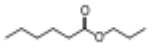
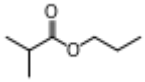
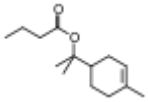
As a class, esters serve as protecting groups for carboxylic acids. Protecting a carboxylic acid is useful in peptide synthesis, to prevent self-reactions of the bi functional amino acids. Methyl and ethyl esters are commonly available for many amino acids; the *t*-butyl ester tends to be more expensive. However, *t*-butyl esters are particularly useful because, under strongly acidic conditions, the *t*-butyl esters undergo elimination to give the carboxylic acid and isobutylene, simplifying work-up.

7 - List of ester odorants

Many esters have distinctive fruit-like odors, and many occur naturally in the essential oils of plants. This has also led to their commonplace use in artificial flavorings and fragrances when those odors aim to be mimicked.

Ester Name	Formula	Odor or occurrence
Allyl hexanoate		pineapple
Benzyl acetate		pear, strawberry, jasmine
Bornyl acetate		pine
Butyl acetate		apple, honey bee
Butyl butyrate		pineapple
Ethyl acetate		nail polish remover, model paint, model airplane glue
Ethyl butyrate		banana, pineapple, strawberry
Ethyl hexanoate		pineapple, waxy-green banana
Ethyl cinnamate		cinnamon
Ethyl formate		lemon, rum, strawberry
Ethyl heptanoate		apricot, cherry, grape, raspberry
Ethyl isovalerate		apple
Ethyl lactate		butter, cream
Ethyl nonanoate		grape
Ethyl pentanoate		apple
Geranyl acetate		geranium
Geranyl butyrate		cherry
Geranyl pentanoate		apple

Isobutyl acetate		cherry, raspberry, strawberry
Isobutyl formate		raspberry
Isoamyl acetate		pear, banana (flavoring in Pear drops)
Isopropyl acetate		fruity
Linalyl acetate		lavender, sage
Linalyl butyrate		peach
Linalyl formate		apple, peach
Methyl acetate		glue
Methyl anthranilate		grape, jasmine
Methyl benzoate		fruity, ylang ylang, feijoa
Methyl butyrate (methyl butanoate)		pineapple, apple, strawberry
Methyl cinnamate		strawberry
Methyl pentanoate (methyl valerate)		flowery
Methyl phenylacetate		honey
Methyl salicylate (oil of wintergreen)		Modern root beer, wintergreen, Germolene and Ralgex ointments (UK)
Nonyl caprylate		orange
Octyl acetate		fruity-orange
Octyl butyrate		parsnip
Amyl acetate		apple, banana

(pentyl acetate)		
Pentyl butyrate (amyl butyrate)		apricot, pear, pineapple
Pentyl hexanoate (amyl caproate)		apple, pineapple
Pentyl pentanoate (amyl valerate)		apple
Propyl acetate		pear
Propyl hexanoate		blackberry, pineapple, cheese, wine
Propyl isobutyrate		rum
Terpenyl butyrate		cherry

Trans Esterification

In organic chemistry, trans esterification is the process of exchanging the organic group R″ of an ester with the organic group R′ of an alcohol. These reactions are often catalyzed by the addition of an acid or base catalyst. The reaction can also be accomplished with the help of enzymes (biocatalysts) particularly lipases (E.C.3.1.1.3).

Trans esterification: alcohol + ester →
different alcohol + different ester

Contents

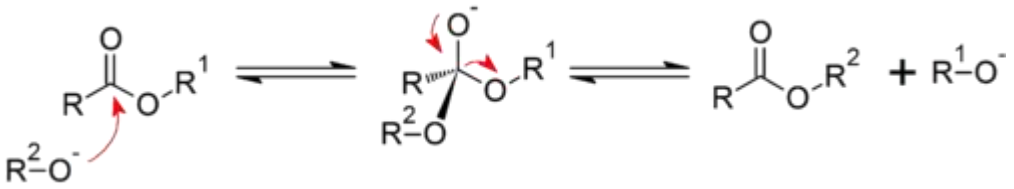
1 - Introduction

Strong acids catalyze the reaction by donating a proton to the carbonyl group, thus making it a more potent electro phile, whereas bases catalyze the reaction by removing a proton from the alcohol, thus making it more nucleo philic. Esters with larger alkoxy groups can be made from methyl or ethyl esters in high purity by heating the mixture of ester, acid / base, and large alcohol and evaporating the small alcohol to drive equilibrium.

2 - Mechanism

In the trans esterification mechanism, the carbonyl carbon of the starting ester ($RCOOR^1$) undergoes nucleo philic attack by the incoming alkoxide (R^2O^-) to give a tetrahedral intermediate, which either reverts to the starting material, or proceeds to the trans

esterified product ($RCOOR^2$). The various species exist in equilibrium, and the product distribution depends on the relative energies of the reactant and product.



3 - Applications

3 – 1 - Polyester production

The largest scale application of trans esterification is in the synthesis of polyesters. In this application di esters undergo trans esterification with diols to form macromolecules. For example, dimethyl terephthalate and ethylene glycol react to form polyethylene terephthalate and methanol, which is evaporated to drive the reaction forward.

3 – 2 - Methanolysis and biodiesel production

The reverse reaction, methanolysis, is also an example of trans esterification. This process has been used to recycle polyesters into individual monomers (see plastic recycling). It is also used to convert fats (triglycerides) into biodiesel. This conversion was one of the first uses. Transesterified vegetable oil (biodiesel) was used to power heavy-duty vehicles in South Africa before World War II.

It was patented in the U.S. in the 1950s by Colgate, though Bio lipid trans esterification may have been discovered much earlier. In the 1940s, researchers were looking for a method to more readily produce glycerine, which was used to produce explosives for World War II. Many of the methods used today by producers and homebrewers have their origin in the original 1940s research.

Bio lipid trans esterification has also been recently shown by Japanese researchers to be possible using a super-critical methanol methodology, whereby high temperature, high-pressure vessels are

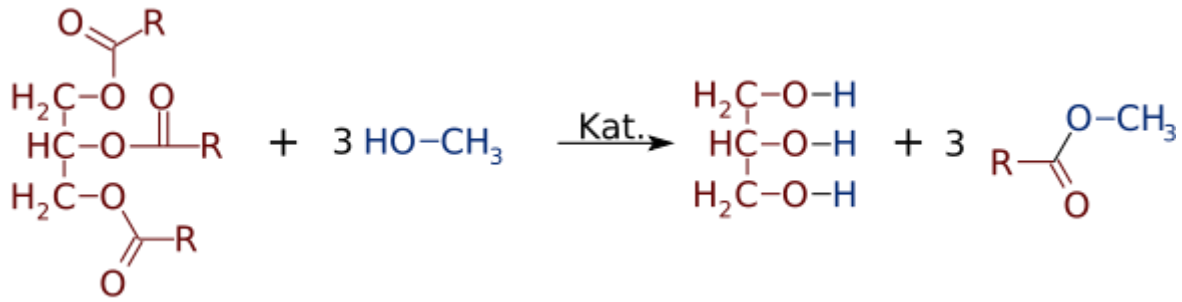
used to physically catalyze the Bio lipid / methanol reaction into fatty-acid methyl esters.

3 – 3 – High - pressure trans esterification

Base - catalyzed trans esterification is characterized by a negative activation volume (approx. -12 cm^3) and therefore it proceeds faster under high-pressure conditions. It has been shown that amine-catalyzed alcoholysis of sterically hindered esters (e.g. protecting groups, [[chiral auxiliary|chiral auxiliaries) proceeds rapidly at room temperature under 10 kbar pressure, giving quantitative yields.

Fatty Acid Methyl Ester

Fatty acid methyl esters (FAME) are a type of fatty acid ester that can be produced by an alkali-catalyzed reaction between fats or fatty acids and methanol. The molecules in biodiesel are primarily FAMEs, usually obtained from vegetable oils by trans esterification.



Since every microorganism has its specific FAME profile (microbial fingerprinting), it can be used as a tool for microbial source tracking (MST). The types and proportions of fatty acids present in cytoplasm membrane and outer membrance (gram negative) lipids of cells are major phenotypic traits.

Clinical analysis can determine the lengths, bonds, rings and branches of the FAME. To perform this analysis, a bacterial culture is taken, and the fatty acids extracted and used to form methyl esters. The volatile derivatives are then introduced into a gas chromatagraph, and the patterns of the peaks help identify the organism. This is widely used in characterizing new species of bacteria, and is useful for identifying pathogenic strains.

Biodiesel

Contents

1 - Introduction

Biodiesel refers to a vegetable oil - or animal fat - based diesel fuel consisting of long - chain alkyl (methyl, propyl or ethyl) esters. Biodiesel is typically made by chemically reacting lipids (e.g., vegetable oil, animal fat (tallow)) with an alcohol producing fatty acid esters.

Biodiesel is meant to be used in standard diesel engines and is thus distinct from the vegetable and waste oils used to fuel *converted* diesel engines. Biodiesel can be used alone, or blended with petro diesel. Biodiesel can also be used as a low carbon alternative to heating oil.

The National Biodiesel Board (USA) also has a technical definition of "biodiesel" as a mono-alkyl ester.

2 - Blends

Blends of biodiesel and conventional hydrocarbon-based diesel are products most commonly distributed for use in the retail diesel fuel marketplace. Much of the world uses a system known as the "B" factor to state the amount of biodiesel in any fuel mix :

100% biodiesel is referred to as **B100**, while

20% biodiesel, 80% petrodiesel is labeled **B20**

5% biodiesel, 95% petrodiesel is labeled **B5**
2% biodiesel, 98% petrodiesel is labeled **B2**.

Blends of 20 % biodiesel and lower can be used in diesel equipment with no, or only minor modifications, although certain manufacturers do not extend warranty coverage if equipment is damaged by these blends. The B6 to B20 blends are covered by the ASTM D7467 specification. Biodiesel can also be used in its pure form (B100), but may require certain engine modifications to avoid maintenance and performance problems. Blending B100 with petroleum diesel may be accomplished by:

Mixing in tanks at manufacturing point prior to delivery to tanker truck

Splash mixing in the tanker truck (adding specific percentages of biodiesel and petroleum diesel)

In-line mixing, two components arrive at tanker truck simultaneously.

Metered pump mixing, petroleum diesel and biodiesel meters are set to X total volume, transfer pump pulls from two points and mix is complete on leaving pump.

3 - Applications

Biodiesel can be used in pure form (B100) or may be blended with petroleum diesel at any concentration in most injection pump diesel engines. New extreme high-pressure (29,000 psi) common rail engines have strict factory limits of B5 or B20, depending on manufacturer . Biodiesel has different solvent properties than petro diesel, and will degrade natural rubber gaskets and hoses in vehicles (mostly vehicles manufactured before 1992), although these tend to wear out naturally and most likely will have already been replaced with FKM, which is nonreactive to biodiesel. Biodiesel has been known to break down deposits of residue in the fuel lines where petro diesel has been used . As a result, fuel filters may become clogged with particulates if a quick transition to pure biodiesel is made. Therefore, it is recommended to change the fuel filters on engines and heaters shortly after first switching to a biodiesel blend.

4 - Historical back ground

Trans esterification of a vegetable oil was conducted as early as 1853 by scientists E. Duffy and J. Patrick, many years before the first diesel engine became functional . Rudolf Diesel's prime model, a single 3 m iron cylinder with a flywheel at its base, ran on its own power for the first time in Augsburg, Germany, on 10 August 1893 running on nothing but peanut oil. In remembrance of this event, 10 August has been declared "International Biodiesel Day".

It is often reported that Diesel designed his engine to run on peanut oil, but this is not the case. Diesel stated in his published papers, "at the Paris Exhibition in 1900 (*Exposition Universelle*) there was shown by the Otto Company a small Diesel engine, which, at the request of the French government ran on arachide (earth-nut or pea-nut) oil (see biodiesel), and worked so smoothly that only a few people were aware of it. The engine was constructed for using mineral oil, and was then worked on vegetable oil without any alterations being made. The French Government at the time thought of testing the applicability to power production of the Arachide, or earth-nut, which grows in considerable quantities in their African colonies, and can easily be cultivated there." Diesel himself later conducted related tests and appeared supportive of the idea. In a 1912 speech Diesel said, "the use of vegetable oils for engine fuels may seem insignificant today but such oils may become, in the course of time, as important as petroleum and the coal-tar products of the present time."

Research into the use of transesterified sunflower oil, and refining it to diesel fuel standards, was initiated in South Africa in 1979. By 1983, the process for producing fuel-quality, engine-tested biodiesel was completed and published internationally.[37] An Austrian company, Gaskoks, obtained the technology from the South African Agricultural Engineers; the company erected the first biodiesel pilot plant in November 1987, and the first industrial-scale plant in April 1989 (with a capacity of 30,000 tons of rapeseed per annum).

Throughout the 1990s, plants were opened in many European countries, including the Czech Republic, Germany and Sweden.

France launched local production of biodiesel fuel (referred to as *diester*) from rapeseed oil, which is mixed into regular diesel fuel at a level of 5%, and into the diesel fuel used by some captive fleets (e.g. public transportation) at a level of 30%. Renault, Peugeot and other manufacturers have certified truck engines for use with up to that level of partial biodiesel; experiments with 50 % biodiesel are underway. During the same period, nations in other parts of the world also saw local production of biodiesel starting up: by 1998, the Austrian Biofuels Institute had identified 21 countries with commercial biodiesel projects. 100 % biodiesel is now available at many normal service stations across Europe.

5 - Properties

Biodiesel has better lubricating properties and much higher cetane ratings than today's lower sulfur diesel fuels. Biodiesel addition reduces fuel system wear , and in low levels in high pressure systems increases the life of the fuel injection equipment that relies on the fuel for its lubrication. Depending on the engine, this might include high pressure injection pumps, pump injectors (also called *unit injectors*) and fuel injectors.

The calorific value of biodiesel is about 37.27 MJ / kg. This is 9 % lower than regular Number 2 petro diesel. Variations in biodiesel energy density is more dependent on the feedstock used than the production process. Still, these variations are less than for petrodiesel.[40] It has been claimed biodiesel gives better lubricity and more complete combustion thus increasing the engine energy output and partially compensating for the higher energy density of petro diesel.

Biodiesel is a liquid which varies in color —between golden and dark brown —depending on the production feedstock. It is immiscible with water, has a high boiling point and low vapor pressure. *The flash point of biodiesel > 130 °C is significantly higher than that of petroleum diesel 64 °C or gasoline − 45 °C. Biodiesel has a density of ~ 0.88 g/cm³, higher than petro diesel (~ 0.85 g / cm³).

6 - Technical standards

Biodiesel has a number of standards for its quality including European standard EN 14214, ASTM International D 6751, and others.

7 - Low temperature gelling

When biodiesel is cooled below a certain point, some of the molecules aggregate and form crystals. The fuel starts to appear cloudy once the crystals become larger than one quarter of the wavelengths of visible light - this is the cloud point (CP). As the fuel is cooled further these crystals become larger. The lowest temperature at which fuel can pass through a 45 micro metre filter is the cold filter plugging point (CFPP). As biodiesel is cooled further it will gel and then solidify. Within Europe, there are differences in the CFPP requirements between countries. This is reflected in the different national standards of those countries. The temperature at which pure (B100) biodiesel starts to gel varies significantly and depends upon the mix of esters and therefore the feedstock oil used to produce the biodiesel. For example, biodiesel produced from low erucic acid varieties of canola seed (RME) starts to gel at approximately −10 °C (14 °F). Biodiesel produced from tallow tends to gel at around +16 °C (61 °F). There are a number of commercially available additives that will significantly lower the pour point and cold filter plugging point of pure biodiesel. Winter operation is also possible by blending biodiesel with other fuel oils including #2 low sulfur diesel fuel and #1 diesel / kerosene.

Another approach to facilitate the use of biodiesel in cold conditions is by employing a second fuel tank for biodiesel in addition to the standard diesel fuel tank. The second fuel tank can be insulated and a heating coil using engine coolant is run through the tank. The fuel tanks can be switched over when the fuel is sufficiently warm. A similar method can be used to operate diesel vehicles using straight vegetable oil.

8 - Contamination by water

Biodiesel may contain small but problematic quantities of water. Although it is not miscible with water it is hygroscopic. One of the reasons biodiesel can absorb water is the persistence of mono and diglycerides left over from an incomplete reaction. These molecules can act as an emulsifier, allowing water to mix with the biodiesel . In addition, there may be water that is residual to processing or resulting from storage tank condensation. The presence of water is a problem because:

Water reduces the heat of fuel combustion, causing smoke, harder starting, and reduced power.

Water causes corrosion of fuel system components (pumps, fuel lines, etc.)

Microbes in water cause the paper-element filters in the system to rot and fail, causing failure of the fuel pump due to ingestion of large particles.

Water freezes to form ice crystals that provide sites for nucleation, accelerating gelling of the fuel.

Water causes pitting in pistons.

Previously, the amount of water contaminating biodiesel has been difficult to measure by taking samples, since water and oil separate. However, it is now possible to measure the water content using water-in-oil sensors.

Water contamination is also a potential problem when using certain chemical catalysts involved in the production process, substantially reducing catalytic efficiency of base (high pH) catalysts such as potassium hydroxide. However, the super-critical methanol production methodology, whereby the transesterification process of oil feedstock and methanol is effectuated under high temperature and pressure, has been shown to be largely unaffected by the presence of water contamination during the production phase.

9 - Production

Biodiesel is commonly produced by the trans esterification of the vegetable oil or animal fat feedstock. There are several methods for carrying out this trans esterification reaction including the

common batch process, supercritical processes, ultrasonic methods, and even microwave methods.

Chemically, trans esterified biodiesel comprises a mix of mono-alkyl esters of long chain fatty acids. The most common form uses methanol (converted to sodium methoxide) to produce methyl esters (commonly referred to as Fatty Acid Methyl Ester - FAME) as it is the cheapest alcohol available, though ethanol can be used to produce an ethyl ester (commonly referred to as Fatty Acid Ethyl Ester - FAEE) biodiesel and higher alcohols such as isopropanol and butanol have also been used. Using alcohols of higher molecular weights improves the cold flow properties of the resulting ester, at the cost of a less efficient trans esterification reaction. A lipid trans esterification production process is used to convert the base oil to the desired esters. Any free fatty acids (FFAs) in the base oil are either converted to soap and removed from the process, or they are esterified (yielding more biodiesel) using an acidic catalyst. After this processing, unlike straight vegetable oil, biodiesel has combustion properties very similar to those of petroleum diesel, and can replace it in most current uses.

The methanol used in most biodiesel production processes is made using fossil fuel inputs. However, there are sources of renewable methanol made using carbon dioxide or biomass as feedstock, making their production processes free of fossil fuels.

A by - product of the trans esterification process is the production of glycerol. For every 1 tone of biodiesel that is manufactured, 100 kg of glycerol are produced. Originally, there was a valuable market for the glycerol, which assisted the economics of the process as a whole. However, with the increase in global biodiesel production, the market price for this crude glycerol (containing 20% water and catalyst residues) has crashed. Research is being conducted globally to use this glycerol as a chemical building block. One initiative in the UK is The Glycerol Challenge.

Usually this crude glycerol has to be purified, typically by performing vacuum distillation. This is rather energy intensive. The refined glycerol (98 %+ purity) can then be utilised directly, or converted into other products. The following announcements were made in 2007: A joint venture of Ashland Inc. and Cargill announced plans to make propylene glycol in Europe from glycerol[50] and Dow Chemical announced similar plans for North America.[51] Dow also plans to build a plant in China to make epichlorhydrin from glycerol. Epichlorhydrin is a raw material for epoxy resins.

9 – 1 - Biodiesel feed stocks

A variety of oils can be used to produce biodiesel. These include:

Virgin oil feed stock – rapeseed and soybean oils are most commonly used, soybean oil accounting for about half of U.S. production . It also can be obtained from Pongamia, field pennycress and jatropha and other crops such as mustard, jojoba, flax, sunflower, palm oil, coconut, hemp (see list of vegetable oils for biofuel for more information);

Waste vegetable oil (WVO);

Animal fats including tallow, lard, yellow grease, chicken fat,[61] and the by-products of the production of Omega-3 fatty acids from fish oil.

Sewage Sludge - The sewage-to-biofuel field is attracting interest from major companies like Waste Management and startups like InfoSpi, which are betting that renewable sewage biodiesel can become competitive with petroleum diesel on price.[64]

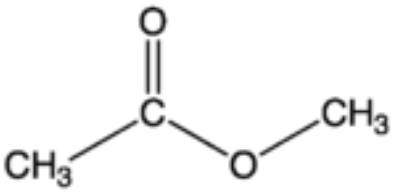
Many advocates suggest that waste vegetable oil is the best source of oil to produce biodiesel, but since the available supply is drastically less than the amount of petroleum-based fuel that is burned for transportation and home heating in the world, this local solution could not scale to the current rate of consumption.

Animal fats are a by-product of meat production and cooking. Although it would not be efficient to raise animals (or catch fish) simply for their fat, use of the by-product adds value to the livestock industry (hogs, cattle, poultry). Today, multi-feedstock biodiesel facilities are producing high quality animal-fat based biodiesel.

10 - Fuel Viscosity

One of the main concerns regarding biodiesel is its viscosity. The viscosity of diesel is 2.5–3.2 cSt at 40°C and the viscosity of biodiesel made from soybean oil is between 4.2 and 4.6 cSt [130] The viscosity of diesel must be high enough to provide sufficient lubrication for the engine parts but slow enough to flow at operational temperature. High viscosity can plug the fuel filter and injection system in engines.[130] Vegetable oil is composed of lipids with long chains of hydrocarbons, to reduce its viscosity the lipids are broken down into smaller molecules of esters. This is done by converting vegetable oil and animal fats into alkyl esters using trans esterification to reduce their viscosity Nevertheless, biodiesel viscosity remains higher than that of diesel, and the engine may not be able to use the fuel at low temperatures due to the slow flow through the fuel filter.

Methyl Acetate



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Contents

1 - Introduction

Methyl acetate, also known as Me O Ac , acetic acid methyl ester or methyl ethanoate, is a carboxylate ester with the formula CH_3COOCH_3. It is a flammable liquid with a characteristically pleasant smell reminiscent of some glues and nail polish removers. Methyl acetate is occasionally used as a solvent, being weakly polar and lipophilic, but its close relative ethyl acetate is a more common solvent being less toxic and less soluble in water. Methyl acetate has a solubility of 25% in water at room temperature. At elevated temperature its solubility in water is much higher. Methyl acetate is not stable in the presence of strong aqueous bases or aqueous acids. Methyl acetate is VOC exempt.

IUPAC name : Methyl acetate	
Systematic name : Methyl ethanoate	
Molecular formula	$C_3H_6O_2$
Molar mass	74 g mol^{-1}
Density	0.932 g cm^{-3}
Melting point	- 98 °C
Boiling point	56.9 °C

Solubility in water	~ 25 % (20 °C)
Refractive index (n_D)	1.361
Flash point	−9 °C

2 - Preparation and reactions

Methyl acetate is produced industrially via the carbonylation of methanol as a byproduct of the production of acetic acid.[3] Methyl acetate also arises by esterification of acetic acid with methanol in the presence of strong acids such as sulfuric acid, this production process is famous because of Eastman Kodak's intensified process using a reactive distillation.

2 – 1 - Reactions

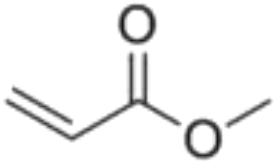
In the presence of strong bases such as sodium hydroxide or strong acids such as hydrochloric acid or sulfuric acid it is hydrolyzed back into methanol and acetic acid, especially at elevated temperature. The conversion of methyl acetate back into its components, by an acid , is a first-order reaction with respect to the ester. The reaction of methyl acetate and a base, for example sodium hydroxide, is a second-order reaction with respect to both reactants.

3 - Applications

A major use of methyl acetate is as a volatile low toxicity solvent in glues, paints, and nail polish removers.

Acetic anhydride is produced by carbonylation of methyl acetate in a process that was inspired by the Monsanto acetic acid synthesis.[4]

Methyl Acrylate



Contents

1 - Introduction

Methyl acrylate is an organic compound with the formula $CH_2CHCO_2CH_3$. It is the methyl ester of acrylic acid. It is a colourless liquid with a characteristic acrid odor. It is mainly produced to make acrylate fiber, which is used to weave synthetic carpets. It is also a reagent in the synthesis of various pharmaceutical intermediates.

IUPAC name ; Methyl prop-2-enoate	
Other names : Methyl acrylate Methyl propenoate Methoxy carbonyl ethylene Curithane 103	
Molecular formula	$C_4H_6O_2$
Molar mass	86 g mol^{-1}
Appearance	Colorless liquid
Density	0.95 g / cm^3
Melting point	-74 °C
Boiling point	80 °C
Solubility in water	5 g / 100 mL
Main hazards	Harmful (Xn) ; Highly flammable (F+)
Flash point	− 3 °C

2 - Production, reactions, and uses

It is produced by acid- catalyzed esterification of acrylic acid, which in turn is produced by oxidation of propylene. Owing to its tendency to polymerize, samples typically contain an inhibitor such as hydroquinone.

The compound undergoes trans esterification to give a variety of other acrylate esters. The trans esterification is facilitated because methanol and methyl acrylate form a low boiling azeotrope (b.p. 62-63 °C). Several other esters are precursors to useful polymers.

Methyl acrylate is a classic Michael acceptor, which means that it adds nucleophiles at its terminus. For example in the presence of a base catalyst, it adds hydrogen sulfide to give the thio ether :

$$2\ CH_2CHCO_2CH_3 + H_2S \rightarrow S\ (CH_2CH_2CO_2CH_3)_2$$

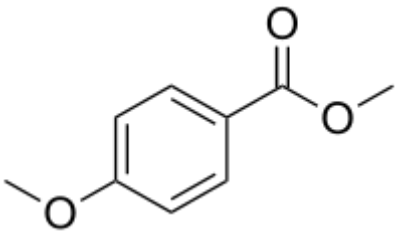
It is also a good dienophile.

Methyl acrylate is the precursor to fibers that are woven to make carpets. Acrylates are also used in the preparation of poly amido amine (PAMAM) dendrimers typically by Michael addition with a primary amine.

3 - Safety

It is an acute toxin with an LD_{50} (rats, oral) of 300 mg/kg and a TLV of 10 ppm.

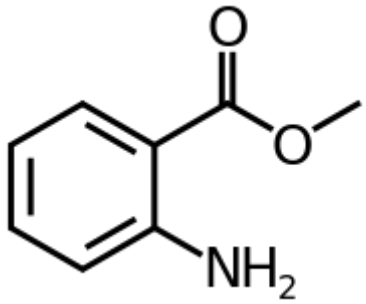
Methyl Anisate



Methyl anisate is the methyl ester of *p*-anisic acid.

IUPAC name : Methyl 4-methoxy benzoate	
Other names : p-Anisic acid methyl ester; 4-(Methoxycarbonyl)anisole; 4-Methoxybenzoic acid methyl ester; Methyl *p*-anisate; Methyl *p*-methoxy benzoate; *p*-Methoxybenzoic acid methyl ester	
Molecular formula	$C_9H_{10}O_3$
Molar mass	166.17 g mol^{-1}
Melting point	48-51 °C[1]
Boiling point	244-245 °C[1]

Methyl Anthranilate



Molecular formula	$C_8 H_9 N O_2$
Molar mass	151
Melting point	24 °C
Boiling point	256 °C
Flash point	104 °C

Contents

1 - Introduction

Methyl anthranilate, also known as MA, methyl 2-amino benzoate or carbo methoxy aniline, is an ester of anthranilic acid. Its chemical formula is $C_8H_9NO_2$.

2 - Chemical properties

It is a clear to pale yellow liquid with melting point 24 °C and boiling point 256 °C. It shows a light blue fluorescence. It is very slightly soluble in water, and soluble in ethanol and propylene glycol. It is insoluble in paraffin oil . It is combustible, with flash point at 104 °C. At full concentration, it has a fruity grape smell; at 25 ppm it has a sweet fruity concord grape like smell with a musty and berry nuance.

3 - Uses

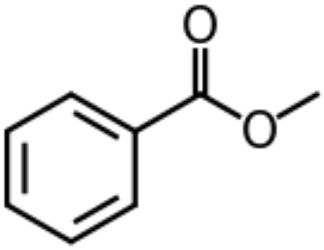
Methyl anthranilate acts as a bird repellent. It is food-grade and can be used to protect corn, sunflowers, rice, fruit, and golf courses. Dimethyl anthranilate (DMA) has a similar effect. It is also used for the flavor of grape Kool Aid. It is used for flavoring of candy, soft drinks (e.g. grape soda), gums, and drugs.

Methyl anthranilate both as a component of various natural essential oils and as a synthesised aroma-chemical is used extensively in modern perfumery . It is also used to produce Schiff's Bases with aldehydes, many of which are also used in perfumery. In a perfumery context the most common Schiff's Base is known as aurantiol - produced by combining methyl anthranilate and hydroxyl citronellal.

4 - Occurrence

Methyl anthranilate naturally occurs in the Concord grapes and other Vitis labrusca grapes or hybrids thereof, and in bergamot, black locust, champaca , gardenia, jasmine, lemon, mandarin, neroli, oranges, rue oil, strawberry, tuberose, wisteria, galangal and ylang ylang. It is also a primary component of the essential apple flavor, along with ethyl acetate and ethyl butyrate.[5] It is also secreted by the musk glands of foxes and dogs, and lends a "sickly sweetness" to the smell of rotting flesh.

Methyl Benzoate



Contents

1 - Introduction

Methyl benzoate is an organic compound. It is an ester with the chemical formula $C_6H_5CO_2CH_3$. It is a colorless liquid that is poorly soluble in water, but miscible with organic solvents. Methyl benzoate has a pleasant smell, strongly reminiscent of the fruit of the feijoa tree, and it is used in perfumery. It also finds use as a solvent and as a pesticide used to attract insects.

IUPAC name : Methyl benzoate	
Molecular formula	$C_8H_8O_2$
Molar mass	136 g mol^{-1}
Density	1.0837 g / cm^3
Melting point	-12.5 °C
Boiling point	199.6 °C
Refractive index (n_D)	1.5164
Flash point	82 °C

2 - Synthesis and reactions

Methyl benzoate is formed by the condensation of methanol and benzoic acid, in presence of a strong acid such as hydrochloric acid . It reacts both at the ring and the ester. Illustrative of its ability to

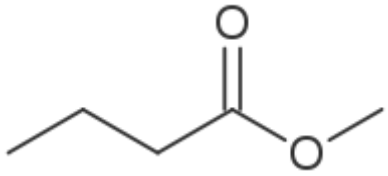
undergo electrophilic substitution, methyl benzoate undergoes acid-catalysed nitration with nitric acid to give methyl 3-nitrobenzoate. It also undergoes hydrolysis with addition of aqueous NaOH to give methanol and sodium benzoate, which can be acidified with aqueous HCl to form benzoic acid.

3 - Occurrence

Methyl benzoate can be isolated from the freshwater fern *Salvinia molesta*. It is one of many compounds that is attractive to males of various species of orchid bees, which apparently gather the chemical to synthesize pheromones; it is commonly used as bait to attract and collect these bees for study.

Cocaine hydrochloride hydrolyzes in moist air to give methyl benzoate; drug - sniffing dogs are thus trained to detect the smell of methyl benzoate.

Methyl Butyrate



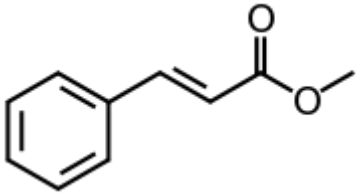
Methyl butyrate, also known under the systematic name methyl butanoate , is the methyl ester of butyric acid. Like most esters, it has a fruity odor, in this case resembling apples or pineapples. At room temperature, it is a colorless liquid with low solubility in water, upon which it floats to form an oily layer. Although it is flammable, it has a relatively low vapor pressure (40 mm Hg at 30 °C), so it can be safely handled at room temperature without special safety precautions.

Methyl butyrate is present in small amounts in several plant products, especially pineapple oil. It can be produced by distillation from essential oils of vegetable origin, but is also manufactured on a small scale for use in perfumes and as a food flavoring.

IUPAC name : Methyl butanoate	
Other names : Butyric acid methyl ester	
Molecular formula	$C_5H_{10}O_2$
Molar mass	102 g mol^{-1}
Appearance	Colorless liquid
Density	0.898 g / cm^3
Melting point	- 95 °C
Boiling point	102 °C
Solubility in water	1.5 g /100 mL (22 °C)
Refractive index (n_D)	1.386
Flash point	12 °C

Methyl butyrate has been used in combustion studies as a surrogate fuel for the larger fatty acid methyl esters found in biodiesel. However , studies have shown that, due to its short-chain length, methyl butyrate does not reproduce well the negative temperature coefficient (NTC) behaviour and early CO_2 formation characteristics of real biodiesel fuels. Therefore, methyl butyrate is not a suitable surrogate fuel for biodiesel combustion studies.

Methyl Cinnamate



Contents

1 - Introduction

Methyl cinnamate is the methyl ester of cinnamic acid and is a white or transparent solid with a strong, aromatic odor. It is found naturally in a variety of plants, including in fruits, like strawberry, and some culinary spices, such as Sichuan pepper and some varieties of basil.[3] *Eucalyptus olida* has the highest known concentrations of methyl cinnamate (98 %) with a 2 - 6 % fresh weight yield in the leaf and twigs.

Methyl cinnamate is used in the flavor and perfume industries. The flavor is fruity and strawberry-like; and the odor is sweet, balsamic with fruity odor, reminiscent of cinnamon and strawberry.

It is known to attract males of various orchid bees, such as *Aglae caerulea*.

Methyl cinnamate crystals extracted using steam distillation from Eucalyptus olida.

IUPAC name :	
Methyl (*E*)-3-Phenylprop-2-enoate	
Molecular formula	$C_{10}H_{10}O_2$
Molar mass	162 g mol^{-1}
Density	1.092 g / cm^3

Melting point	34-38 °C
Boiling point	261-262 °C
Solubility in water	Insoluble
Flash point	> 110 °C

2 - List of plants that contain the chemical

Eucalyptus olida 'Strawberry gum'

Ocimum americanum cv.Purple Lovingly (Querendona Morada)

Ocimum americanum cv. Purple Castle (Castilla Morada)

Ocimum americanum cv. Purple Long-legged (Zancona morada)

Ocimum americanum cv. Clove (Clavo)

Ocimum basilicum cv. Sweet Castle (Dulce de Castilla)

Ocimum basilicum cv. White Compact (Blanca compacta)

Ocimum basilicum cv. large green leaves (Verde des horjas grandes)

Ocimum micranthum cv. Cinnamon (Canela)

Ocimum minimum cv. Little Virgin (Virgen pequena)

Ocimum minimum cv. Purple Virgin (Virgen morada)

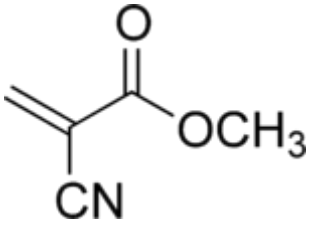
Ocimum sp. cv. Purple ruffle (Crespa morada)

Ocimum sp. cv. White Ruffle (Crespa blanca)

3 - Toxicology and safety

Moderately toxic by ingestion . The oral LD_{50} for rats is 2610 mg / kg . It is combustible as a liquid, and when heated to decomposition it emits acrid smoke and irritating fumes.

Methyl Cyanoacrylate



Contents

1 - Introduction

Methyl cyanoacrylate (MCA) is an organic compound that contains several functional groups, a methyl ester, a nitrile, and an alkene. It is a colorless liquid with low viscosity. Its chief use is as the main component of cyanoacrylate glues.[1] It can be encountered under many trade names. Methyl cyanoacrylate is less commonly encountered than ethyl cyanoacrylate.

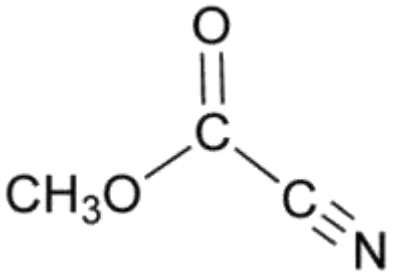
It is soluble in acetone, methyl ethyl ketone, nitro methane, and dichloromethane. MCA polymerizes rapidly in presence of moisture.

IUPAC name :Methyl 2-cyanopropenoate	
Molecular formula	$C_5 H_5 NO_2$
Molar mass	111 g / mol
Density	1.1
Melting point	- 40 °C
Boiling point	48- 49°C (2.5-2.7 mm Hg)

2 - Safety

Heating the polymer causes depolymerization of the cured MCA, producing gaseous products strongly irritant to lungs and eyes.

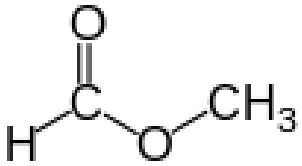
Methyl Cyanoformate



Methyl cyanoformate is the organic compound with the formula $CH_3OC(O)CN$. It is used as a reagent in organic synthesis as a source of the methoxy carbonyl group , in which context it is also known as Mander's reagent. It was also the active ingredient in the pesticide product Zyklon A.

IUPAC name : Methyl cyanoformate	
Molecular formula	$C_3H_3NO_2$
Molar mass	85 g mol^{-1}
Appearance	colorless liquid
Density	1.072 g / cm^3
Boiling point	100 °C
Main hazards	toxic

Methyl Formate



Contents

1 - Introduction

Methyl formate , also called methyl methanoate, is the methyl ester of formic acid. The simplest example of an ester, it is a clear liquid with an ethereal odour, high vapor pressure, and low surface tension.

IUPAC name : methyl methanoate	
Other names : R- 611	
Molecular formula	$C_2H_4O_2$
Molar mass	60 g mol^{-1}
Density	0.98 g / cm^3
Melting point	-100 °C
Boiling point	32 °C
EU classification	Highly flammable (F+); Harmful (Xn)

2 - Production

In the laboratory, methyl formate can be produced by the condensation reaction of methanol and formic acid, as follows:

$HCOOH + CH_3OH \rightarrow HCOOCH_3 + H_2O$

Industrial methyl formate, however, is usually produced by the combination of methanol and carbon monoxide (carbonylation) in the presence of a strong base, such as sodium methoxide :

$CH_3OH + CO \rightarrow HCOOCH_3$

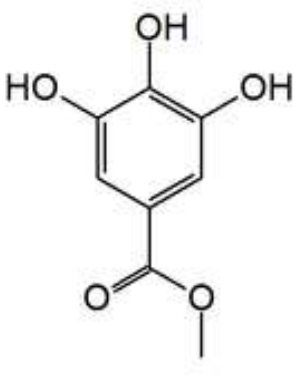
This process, practiced commercially by BASF among other companies gives 96 % selectivity toward methyl formate, although it can suffer from catalyst sensitivity to water, which can be present in the carbon monoxide feedstock, commonly derived from synthesis gas. Very dry carbon monoxide is, therefore, an essential requirement.

3 - Uses

Methyl formate is used primarily to manufacture formamide, dimethyl formamide, and formic acid. Because of its high vapor pressure, it is used for quick - drying finishes. It is also used as an insecticide and to manufacture certain pharmaceuticals. Foam Supplies, Inc. has trademarked Ecomate, which is used as a blowing agent for foam insulation, as a replacement for CFC, HCFC, or HFCs, with zero ozone depletion potential and < 25 global warming potential.

A historical use of methyl formate, which sometimes brings it attention, was in refrigeration. Before the introduction of less-toxic refrigerants, methyl formate was used as an alternative to sulfur dioxide in domestic refrigerators, such as some models of the famous GE Monitor Top. Owners of methyl formate refrigerators should keep in mind that, even though they operate below atmospheric pressure, if evidence of a leak develops, they should take measures to avoid exposure to the ether-smelling liquid and vapor.

Methyl Gallate

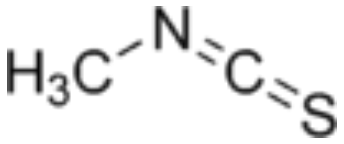


Methyl gallate is a phenolic compound found in *Terminalia myriocarpa* and *Geranium niveum*. It is also found in wine.

It is the methyl ester of gallic acid.

IUPAC name : Methyl 3,4,5-trihydroxybenzoate	
Other names : Methylgallate Gallic acid methyl ester	
Molecular formula	$C_8H_8O_5$
Molar mass	184 g mol^{-1}

Methyl Iso Thio Cyanate



Contents

1 - Introduction

Methyl iso thio cyanate is the organo sulfur compound with the formula $CH_3N = C = S$. This low melting colorless solid is a powerful lachrymator. As a precursor to a variety of valuable bioactive compounds, it is the most important organic iso thio cyanate in industry.

IUPAC name :Methyl iso thio cyanate	
Other names : MITC	
Molecular formula	$C_2 H_3 N S$
Molar mass	73 g mol^{-1}
Appearance	colourless solid
Density	1.07 g cm^{-3}
Melting point	31 °C
Boiling point	117 °C
Solubility in water	8.2 g / L

2 - Synthesis

It is prepared industrially by two routes. Annual production in 1993 was estimated to be 4M kg. The main method involves the thermal rearrangement of methyl thio cyanate :

$$CH_3 S - C \equiv N \rightarrow CH_3 N = C = S$$

It is also prepared via with the reaction of methylamine with carbon disulfide followed by oxidation of the resulting dithio carbamate with hydrogen peroxide. A related method is useful to prepare this compound in the laboratory.

MITC forms naturally upon the enzymatic degradation of gluco capparin , a modified sugar found in capers.

3 - Reactions

A characteristic reaction is with amines to give methyl thioureas:

$$CH_3NCS + R_2NH \rightarrow R_2NC(S)NHCH_3$$

Other nucleophiles add similarly.

4 - Applications

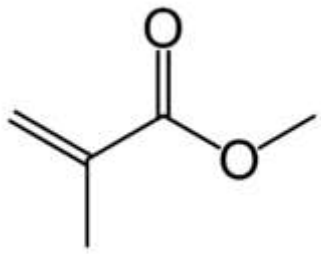
Solutions of MITC are used in agriculture as soil fumigants, mainly for protection against fungi and nematodes.

MITC is a building block for the synthesis of 1,3,4 - thiadiazoles, which are heterocyclic compounds used as herbicides. Commercial products include "Spike", "Ustilan," and "Erbotan." Well known pharmaceuticals prepared using MITC include Zantac and Tagamet.

5 - Safety

MITC is a dangerous lachrymator as well as being poisonous.

Methyl Methacrylate



Contents

1 - Introduction

Methyl methacrylate is an organic compound with the formula $CH_2=C(CH_3)COOCH_3$. This colourless liquid, the methyl ester of methacrylic acid (MAA) is a monomer produced on a large scale for the production of poly(methyl methacrylate) (PMMA).

IUPAC name : methyl 2-methylpropenoate	
Other names : MMA, 2-(methoxy carbonyl) -1- propene	
Molecular formula	$C_5 H_8 O_2$
Molar mass	100 g mol^{-1}
Appearance	Colorless liquid
Density	0.94 g / cm^3
Melting point	- 48 °C
Boiling point	101 °C
Solubility in water	1.5 g / 100 ml
Viscosity	0.6 cP at 20 °C
Main hazards	Flammable

Flash point	2 °C
Autoignition temperature	435 °C
Structure and properties	*n*, ε_r, etc.
Thermo dynamic data	Phase behaviour Solid, liquid, gas
Spectral data	UV, IR, NMR, MS

2 - Production

The compound is manufactured by several methods, the principal one being the acetone cyanohydrin (ACH) route, using acetone and hydrogen cyanide as raw materials. The intermediate cyanohydrin is converted with sulfuric acid to a sulfate ester of the methacrylamide, methanolysis of which gives ammonium bisulfate and MMA. Although widely used, the ACH route coproduces substantial amounts of ammonium sulfate. Some producers start with an isobutylene or, equivalently, *tert*-butanol, which is sequentially oxidized first to methacrolein and then to methacrylic acid, which is then esterified with methanol. Propene can be carbonylated in the presence of acids to iso butyric acid, which undergoes subsequent dehydrogenation . The combined technologies afford more than 3 billion kilograms per year. MMA can also be prepared from methyl propionate and formaldehyde.

3 - Uses

The principal application, consuming approximately 80% of the MMA, is the manufacture of poly methyl methacrylate acrylic plastics (PMMA). Methyl methacrylate is also used for the production of the co-polymer methyl methacrylate-butadiene-styrene (MBS), used as a modifier for PVC. Another application is as cement used in total hip replacements as well as total knee replacements. Used as the "grout" by orthopedic surgeons to make the bone inserts fix into bone, it greatly reduces post-operative pain from the insertions but has a finite lifespan. Typically the lifespan of methyl methacrylate as bone cement is 20 years before revision surgery is required. Cemented implants are usually only done in elderly populations that require

more immediate short term replacements. In younger populations, cementless implants are used because their lifespan is considerably longer. Also used in fracture repair in small exotic animal species using internal fixation.

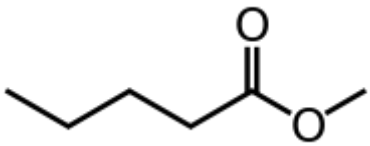
4 - Initiators

Initiators for methyl methacrylate polymerization include AIBN, dilauroyl peroxide (LPO), and 2,2'-Azobis[2-(2-imidazolin-2-yl)propane].

5 - Shortage

In 2010 the world experienced an MMA shortage, believed to be due to production facilities shutting down for economic reasons. One of the largest producers, Dow Chemical, surprised many purchasers when they announced a six month shut down of their plant that produced 60 % of MMA.

Methyl Pentanoate



Methyl pentanoate, commonly known as methyl valerate, is the methyl ester of pentanoic acid (valeric acid) with a fruity odor.

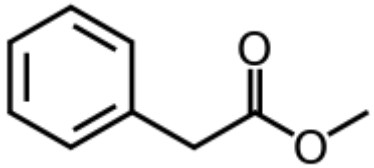
Methyl pentanoate is commonly used in fragrances, beauty care, soap, laundry detergents at levels of 0.1 – 1 % .

In a very pure form (greater than 99.5 %) it is used as a plasticizer in the manufacture of plastics.

It is also used as an insecticide.

IUPAC name : Methyl pentanoate	
Other names : Methyl valerate Mentholum valerianicum	
Molecular formula	$C_6H_{12}O_2$
Molar mass	116 g / mol
Density	0.89 g / cm^3
Melting point	< 25 °C
Boiling point	126 °C

Methyl Phenyl Acetate



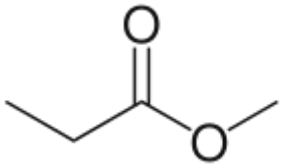
IUPAC name :Methyl 2-phenylacetate	
Other names : Methyl 2-phenyl acetate , Methyl benzene acetate	
Molecular formula	$C_9H_{10}O_2$
Molar mass	150 g mol^{-1}
Appearance	Colorless liquid
Density	1.055 g / cm^3
Melting point	50 °C
Boiling point	218 °C
Solubility in water	2070 mg / L
Vapor pressure	17.3 Pa
Refractive index (n_D)	1.505 at 20 °C
Flash point	90.6 °C

Methyl phenyl acetate is an organic compound that is the ester formed from methanol and phenyl acetic acid, with the structural formula $C_6H_5CH_2COOCH_3$. It is a clear colorless liquid that is only slightly soluble in water, but very soluble in most organic solvents.

Methyl phenyl acetate has a strong odor similar to honey. The odor is so strong that recommended smelling is of a solution with 10% or less methyl phenyl acetate. This compound also naturally occurs in brandy, capsicum, coffee, honey, pepper and some wine.

Methyl phenyl acetate is used in the flavor industry and in perfumes to impart honey scents.

Methyl propionate



Contents

1 - Introduction

Methyl propionate, also known as methyl propanoate, is a chemical compound with the molecular formula $C_4H_8O_2$. It is a volatile ester with a sweet, fruity, rum-like odor.

IUPAC name : Methyl propanoate	
Other names : Propanoic acid, methyl ester Propionic acid, methyl ester	
Molecular formula	$C_4H_8O_2$
Molar mass	88 g mol^{-1}
Appearance	Colorless liquid
Density	0.915 g / mL
Melting point	-88 °C
Boiling point	80 °C
Solubility in water	72 g / L (20 °C)
Flash point	− 2 °C
Auto ignition temperature	465 °C

2 - Preparation

Methyl propionate can be prepared by esterification of propionic acid with methanol. Industrially, it is prepared by the reaction of

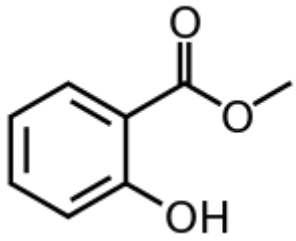
ethylene with carbon monoxide and methanol in the presence of nickel carbonyl

3 - Uses

Methyl propionate is used as a solvent for cellulose nitrate and lacquers, and as a raw material for the production of paints, varnishes and other chemicals such as methyl methacrylate.[2][3]

Due to its fruity smell and taste, it is also used in fragrances and flavoring.

Methyl Salicylate



Contents

1 - Introduction

Methyl salicylate (oil of wintergreen or wintergreen oil) is an organic ester that is naturally produced by many species of plants. Some of the plants which produce it are called wintergreens, hence the common name. This compound is used as a fragrance. It is also found in liniments (rubbing ointments).

2 - Natural occurrence

Wintergreen plants (Gaultheria procumbens)

Numerous plants produce methyl salicylate in very small amounts. Some plants, such as the following, produce more:

Some species of the genus *Gaultheria* in the family Ericaceae, including Gaultheria procumbens, the wintergreen or eastern teaberry;

Some species of the genus *Betula* in the family Betulaceae, particularly those in the subgenus *Betulenta* such as *B. lenta*, the black birch;

All species of the genus *Spiraea* in the family Rosaceae, also called the meadowsweets.

This compound is produced most likely as an anti-herbivore defense. If the plant is infected with herbivorous insects, the release of methyl salicylate may function as an aid in the recruitment of beneficial insects to kill the herbivorous insects.[1] Aside from its toxicity, methyl salicylate may also be used by plants as a pheromone to warn other plants of pathogens such as tobacco mosaic virus.

3 - Commercial production

Methyl salicylate can be produced by esterifying salicylic acid with methanol. Commercial methyl salicylate is now synthesized, but in the past, it was commonly distilled from the twigs of *Betula lenta* (sweet birch) and *Gaultheria procumbens* (eastern teaberry or winter green).

4 - Uses

In high concentrations as a rubefacient in deep heating liniments (such as Bengay) to treat joint and muscular pain. Randomised double blind trial reviews report evidence of its effectiveness that is weak, but stronger for acute pain than chronic pain, and that effectiveness may be due entirely to counter-irritation. However, in the body it metabolizes into salicylates, including salicylic acid, a known NSAID.

In low concentrations as a flavoring agent (no more than 0.04%; it is toxic).

providing fragrance to various products and as an odor-masking agent for some organophosphate pesticides. If used excessively, it can cause stomach and kidney problems.

Attracting male orchid bees, who apparently gather the chemical to synthesize pheromones; it is commonly used as bait to attract and collect these bees for study.

Clear plant or animal tissue samples of color, and as such is useful for microscopy and immunohistochemistry when excess pigments obscure structures or block light in the tissue being examined. This clearing generally only takes a few minutes, but the tissue must first be dehydrated in alcohol.

A mint flavoring in some kinds of chewing gum and candy, as an alternative to the more common peppermint and spearmint oils. It can also be found as a flavoring of root beer. It is also a potentially entertaining source of tri boluminescence ; when mixed with sugar and dried, it gains the tendency to build up electrical charge when crushed or rubbed. This effect can be observed by crushing wintergreen Life Savers candy in a dark room.

As a transfer agent, to produce a manual copy of an image on a surface.

In small amounts, to lower the freezing point of glacial acetic acid for transport.

A simulant or surrogate for the research of chemical warfare agent sulfur mustard, due to its similar chemical and physical properties.

An antiseptic in Listerine mouthwash produced by the Johnson & Johnson company.

Restoring (at least temporarily) the elastomeric properties of old rubber rollers, especially in printers.

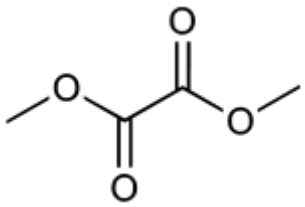
5 - Safety and toxicity

In pure form, methyl salicylate is toxic, especially when taken internally. A single teaspoon (5ml) of methyl salicylate contains 7g of salicylate, which is equivalent to more than twenty- three 300 mg

aspirin tablets. The lowest published lethal dose is 101 mg / kg body weight in adult humans , (or 7.07 grams for a 70 - kg adult). It has proven fatal to small children in doses as small as 4 ml.[6] A seventeen-year- old cross - country runner at Notre Dame Academy on Staten Island, died in April 2007, after her body absorbed methyl salicylate through excessive use of topical muscle-pain relief products.

Most instances of human toxicity due to methyl salicylate are a result of over-application of topical analgesics, especially involving children. Some people have intentionally ingested large amounts of oil of wintergreen. Salicylate, the major metabolite of methyl salicylate, may be quantitated in blood, plasma or serum to confirm a diagnosis of poisoning in hospitalized patients or to assist in an autopsy.

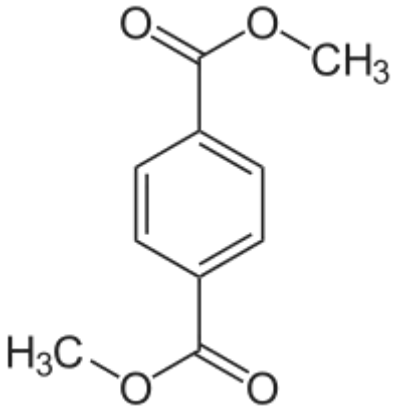
Dimethyl Oxalate



Dimethyl oxalate is a chemical compound with formula $(CH_3)_2(COO)_2$. It is the dimethyl ester of oxalic acid.

IUPAC name : Dimethyl oxalate	
Molecular formula	$C_4H_6O_4$
Molar mass	118 g mol^{-1}

Dimethyl Terephthalate



Contents

1 - Introduction

Dimethyl terephthalate (DMT) is an organic compound with the formula $C_6H_4(CO_2CH_3)_2$. It is the diester formed from terephthalic acid and methanol. It is a white solid that melts to give a distillable colourless liquid.

Preferred IUPAC name : Dimethyl terephthalate	
Systematic name : 1,4-Dimethyl benzene-1,4-dicarboxylate	
Other names : 1,4-Benzenedicarboxylic acid dimethyl ester Dimethyl 4-phthalate Dimethyl-p-phthalate Di-Me terephthalate Methyl 4 – carbo methoxy benzoate Methyl-p- (methoxy carbonyl) benzoate Methyl terephthalate Terephthalic acid methyl ester	
Molecular formula	$C_{10}H_{10}O_4$
Molar mass	194 g mol^{-1}

Appearance	white solid
Density	1.2 g / cm^3
Melting point	142 °C
Boiling point	288 °C

2 - Production

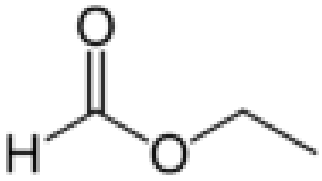
DMT has been produced in a number of ways. Conventionally and still of commercial value is the direct esterification of terephthalic acid. Alternatively, it can be prepared by alternating oxidation and methyl-esterification steps from p-xylene via methyl- p - toluate .

3 - Use

DMT is used in the production of polyesters, including polyethylene terephthalate (PET) and poly trimethylene terephthalate. It consists of benzene substituted with carboxy methyl groups (CO_2CH_3) at the 1 and 4 positions. Because DMT is volatile, it is an intermediate in some schemes for the recyclic of PET, e.g. from plastic bottles.

Hydrogenation of DMT affords the diol cyclo hexane dimethanol , which is a useful monomer.

Ethyl Formate



Contents

1 - Introduction

Ethyl formate is an ester formed when ethanol (an alcohol) reacts with formic acid (a carboxylic acid). It is also known as ethyl methanoate because formic acid is also known as methanoic acid. Ethyl formate has the characteristic smell of rum and is also partially responsible for the flavor of raspberries.

IUPAC name : Ethyl formate	
Systematic name : Ethyl methanoate	
Molecular formula	$C_3H_6O_2$
Molar mass	74 g mol^{-1}
Density	0.917 g / cm^3
Melting point	-80 °C
Boiling point	54.0 °C

2 - Exposure

Ethyl methanoate is generally recognized as safe by the U.S. Food and Drug Administration.

According to the U.S Occupational Safety and Health Administration (OSHA), ethyl formate can irritate eyes, skin, mucous membranes, and the respiratory system of humans and other animals; it is also a central nervous system depressant.[3] In industry, it is used as a solvent for cellulose nitrate, cellulose acetate, oils, and greases. It

can be used as a substitute for acetone; workers may also be exposed to it under the following circumstances:

during spray, brush, or dip applications of lacquers

during the manufacture of safety glass

When fumigating tobacco, cereals, and dried fruits (as an alternative to methyl bromide under the U.S. Department of Agriculture quarantine system)

OSHA considers a time-weighted average of 100 parts per million (300 milligrams per cubic meter) over an eight-hour period as the permissible exposure limit.

3 In space

Astronomers have identified ethyl formate in dust clouds in an area of the Milky Way galaxy called Sagittarius B2. The astronomers, from the Max Planck Institute for Radio Astronomy in Bonn, Germany, used the 30 meter IRAM radio telescope in Spain to analyze the spectra of radiation emitted from hot regions near a new star. It is among 50 molecules identified by the astronomers.

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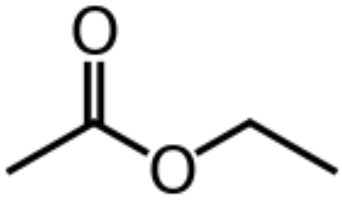
Ethyl Acetate



Contents

1 - Introduction

Ethyl acetate (systematically, ethyl ethanoate, commonly abbreviated EtOAc or EA) is the organic compound with the formula $CH_3COOCH_2CH_3$. This colorless liquid has a characteristic sweet smell (similar to pear drops) and is used in glues, nail polish removers, decaffeinating tea and coffee, and cigarettes (see list of additives in cigarettes). Ethyl acetate is the ester of ethanol and acetic acid; it is manufactured on a large scale for use as a solvent. The combined annual production in 1985 of Japan, North America, and Europe was about 400,000 tons. In 2004, an estimated 1.3M tons were produced worldwide.

IUPAC name : Ethyl acetate	
Systematic name : Ethyl ethanoate	
Molecular formula	$C_4H_8O_2$
Molar mass	88 g mol^{-1}
Appearance	Colorless liquid

Density	0.897 g /cm³
Melting point	−83.6 °C
Boiling point	77.1 °C
Solubility in water	8.3 g /100 mL (20 °C)
Solubility in ethanol , acetone , diethyl ether, benzene	Miscible
Refractive index (n_D)	1.3720
Viscosity	0.426 cP at 25 °C
Main hazards	Flammable (F), Irritant (Xi)
Flash point	− 4 °C
LD_{50}	11.3 g / kg, rat
Structure and properties	n, ε_r, etc.
Thermo dynamic data	Phase behaviour Solid, liquid, gas
Spectral data	UV, IR, NMR, MS

2 - Production

Ethyl acetate is synthesized in industry mainly via the classic Fischer esterification reaction of ethanol and acetic acid. This mixture converts to the ester in about 65% yield at room temperature:

$$CH_3CH_2OH + CH_3COOH \rightleftharpoons CH_3COOCH_2CH_3 + H_2O$$

The reaction can be accelerated by acid catalysis and the equilibrium can be shifted to the right by removal of water. It is also prepared in industry using the Tishchenko reaction, by combining two equivalents of acetaldehyde in the presence of an alkoxide catalyst:

$$2\ CH_3CHO \rightarrow CH_3COOCH_2CH_3$$

2 – 1 - By dehydrogenation of ethanol

A specialized industrial route entails the catalytic dehydrogenation of ethanol. This method is less cost effective than

the esterification but is applied with surplus ethanol in a chemical plant. Typically, dehydrogenation is conducted with copper at an elevated temperature but below 250 °C. The copper may have its surface area increased by depositing it on zinc, promoting the growth of snowflake, fractal like structures (dendrites). Surface area can be again increased by deposition onto a zeolite, typically ZSM-5. Traces of rare earth and alkali metals are beneficial to the process. Byproducts of the dehydrogenation include diethyl ether, which is thought to arise primarily due to aluminum sites in the catalyst, acetaldehyde and its aldol products, higher esters, and ketones. Separations of the byproducts are complicated by the fact that ethanol forms an azeotrope with water, as does ethyl acetate with ethanol and water, and methyl ethyl ketone (MEK, which forms from 2-butanol) with both ethanol and ethyl acetate. These azeotropes are "broken" by pressure swing distillation or membrane distillation.

3 - Uses

Ethyl acetate is used primarily as a solvent and diluent, being favored because of its low cost, low toxicity, and agreeable odor. For example, it is commonly used to clean circuit boards and in some nail varnish removers (acetone and acetonitrile are also used). Coffee beans and tea leaves are decaffeinated with this solvent.[3] It is also used in paints as an activator or hardener.[*citation needed*] Ethyl acetate is present in confectionery, perfumes, and fruits. In perfumes, it evaporates quickly, leaving only the scent of the perfume on the skin.

3 – 1 - Laboratory uses

In the laboratory, mixtures containing ethyl acetate are commonly used in column chromatography and extractions. Ethyl acetate is rarely selected as a reaction solvent because it is prone to hydrolysis and trans esterification.

Ethyl acetate is very volatile and has a boiling point of 77 °C. Due to these properties, it can be removed from a sample by heating in a hot water bath and providing ventilation with compressed air.

3 – 2 - Occurrence in wines

Ethyl acetate is the most common ester in wine, being the product of the most common volatile organic acid — acetic acid, and the ethyl alcohol generated during the fermentation. The aroma of ethyl acetate is most vivid in younger wines and contributes towards the general perception of "fruitiness" in the wine. Sensitivity varies, with most people having a perception threshold around 120 mg/L. Excessive amounts of ethyl acetate are considered a wine fault. Exposure to oxygen can exacerbate the fault due to the oxidation of ethanol to acetaldehyde, which leaves the wine with a sharp vinegar-like taste.

3 – 3 - Entomological killing agent

In the field of entomology, ethyl acetate is an effective asphyxiant for use in insect collecting and study. In a killing jar charged with ethyl acetate, the vapors will kill the collected (usually adult) insect quickly without destroying it. Because it is not hygroscopic, ethyl acetate also keeps the insect soft enough to allow proper mounting suitable for a collection.

4 - Reactions

Ethyl acetate can be hydrolyzed in acidic or basic conditions to regain acetic acid and ethanol. The use of an acid catalyst accelerates the hydrolysis, which is subject to the Fischer equilibrium mentioned above. In the laboratory, and usually for illustrative purposes only, ethyl esters are typically hydrolyzed in a two step process starting with a stoichiometric amount of strong base, such as sodium hydroxide. This reaction gives ethanol and sodium acetate, which is unreactive toward ethanol:

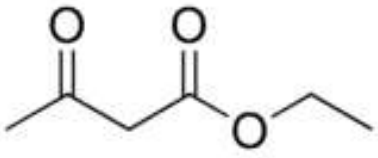
$$CH_3CO_2C_2H_5 + Na\ OH \rightarrow C_2H_5OH + CH_3CO_2Na$$

The rate constant is 0.111 dm^3 / mol.sec at 25 °C.

6 - Safety

The LD_{50} for rats is 11.3 g / kg, indicating low toxicity.

Ethyl Acetoacetate



Contents

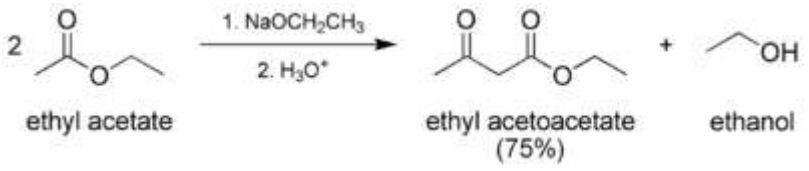
1 - Introduction

The organic compound ethyl acetoacetate (EAA) is the ethyl ester of acetoacetic acid. It is mainly used as a chemical intermediate in the production of a wide variety of compounds, such as amino acids, analgesics, antibiotics, antimalarial agents, antipyrine and amino pyrine, and vitamin B_1; as well as the manufacture of dyes, inks, lacquers, perfumes, plastics, and yellow paint pigments. Alone, it is used as a flavoring for food.

2 - Preparation

Ethyl acetoacetate is produced industrially by treatment of diketene with ethanol.

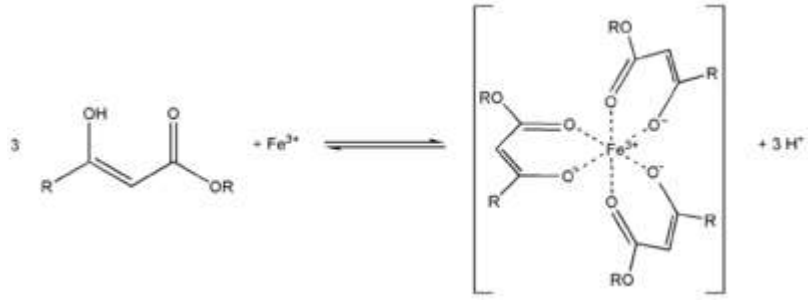
The preparation of ethyl acetoacetate is a classic laboratory procedure . It is prepared via the Claisen condensation of ethyl acetate. Two moles of ethyl acetate condense to form one mole each of ethyl acetoacetate and ethanol.



3 - Reactivity

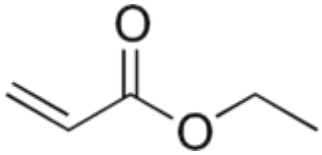
Ethyl acetoacetate is subject to Keto - enol tautomerism. Ethyl acetoacetate is often used in the acetoacetic ester synthesis similar to diethyl malonate in the malonic ester synthesis or the Knoevenagel

condensation. The protons alpha to carbonyl groups are acidic, and the resulting carbanion can undergo nucleophilic substitution. A subsequent thermal decarboxylation is also possible.[3] Similar to the behavior of acetylacetone, the enolate of ethyl acetoacetate can also serve as a bidentate ligand. For example, it forms purple coordination complexes with iron (III) salts :



Ethyl acetoacetate can also be reduced to ethyl 3-hydroxy butyrate.

Ethyl Acrylate



Contents

1 - Introduction

Ethyl acrylate is an organic compound with the formula $CH_2CHCO_2CH_2CH_3$. It is the ethyl ester of acrylic acid. It is a colourless liquid with a characteristic acrid odor. It is mainly produced for paints, textiles, and non-woven fibers .. It is also a reagent in the synthesis of various pharmaceutical intermediates.

IUPAC name :Ethyl propenoate	
Other names : Acrylic acid ethyl ester Ethyl propenoate	
Molecular formula	$C_5H_8O_2$
Molar mass	100 g mol^{-1}
Appearance	Clear liquid
Density	0.9405 g / mL
Melting point	-71 °C
Boiling point	99.4 °C
Solubility in water	1.5 g / 100 mL
Flash point	15 °C

2 - Production, reactions, and uses

It is produced by acid-catalysed esterification of acrylic acid, which in turn is produced by oxidation of propylene. It may also be

prepared from acetylene, carbon monoxide and ethanol by a "Reppe reaction."

Owing to its tendency to polymerize, samples typically contain an inhibitor such as hydroquinone. Ethyl acrylate is a Michael acceptor and a good dienophile.

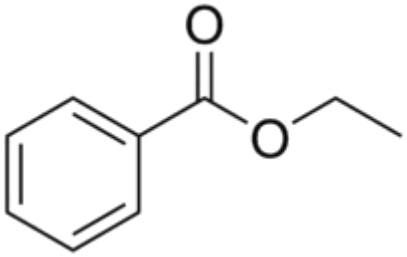
Ethyl acrylate is used in the production of polymers including resins, plastics, rubber, and denture material .

3 - Safety

It is an acute toxin with an LD50 (rats, oral) of 1020 mg / kg and a TLV of 5 ppm. The International Agency for Research on Cancer stated, "Overall evaluation, Ethyl acrylate is possibly carcinogenic to humans (Group 2B)." The United States Environmental Protection Agency (EPA) states, "Human studies on occupational exposure to ethyl acrylate... have suggested a relationship between exposure to the chemical(s) and colorectal cancer, but the evidence is conflicting and inconclusive. In a study by the National Toxicology Program (NTP), increased incidences of squamous cell papillomas and carcinomas of the fore stomach were observed in rats and mice exposed via gavage (experimentally placing the chemical in the stomach). However, the NTP recently determined that these data were not relevant to human carcinogenicity since humans do not have a fore stomach, and removed ethyl acrylate from its list of carcinogens." (Occupational exposure generally involves exposure that occurs regularly, over an extended period of time.)

One favorable safety aspect is that ethyl acrylate has good warning properties; the odor threshold is much lower than any level of health concern. In other words, the bad odor warns people of ethyl acrylate's presence long before the concentration reaches a level capable of creating a serious health risk. Reports of the exact levels vary somewhat, but, for example, the U.S. E.P.A. reports an odor threshold of 0.0012 parts per million (ppm) , but the E.P.A.'s lowest level of health concern, the Acute Exposure Guideline Level-1 (AEGL-1) is 8.3 ppm, which is almost 7000 times the odor threshold.

Ethyl Benzoate

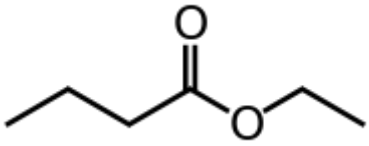


Ethyl benzoate, $C_9H_{10}O_2$, is the ester formed by the condensation of benzoic acid and ethanol. It is a colorless liquid that is almost insoluble in water, but miscible with most organic solvents.

As with many volatile esters, ethyl benzoate has a pleasant odor which could be described similar to wintergreen mint. It is a component of some artificial fruit flavors.

IUPAC name : Ethyl benzoate	
Molecular formula	$C_9 H_{10} O_2$
Molar mass	150 g / mol
Density	1.050 g/cm^3
Melting point	- 34 °C
Boiling point	211– 213 °C

Ethyl Butyrate



Contents

1 - Introduction

Ethyl butyrate, also known as ethyl butanoate, or butyric ether, is an ester with the chemical formula $CH_3CH_2CH_2COO.CH_2CH_3$. It is soluble in propylene glycol, paraffin oil, and kerosene. It has a fruity odor, similar to pineapple.

IUPAC name : Ethyl butanoate	
Other names : Ethyl n - butanoate , Ethyl n-butyrate, Butanoic acid ethyl ester, Butyric acid ethyl ester, Butyric ether, UN 1180	
Molecular formula	$C_6 H_{12} O_2$
Molar mass	116 g mol^{-1}
Appearance	Colorless liquid with fruity odor (typically pineapple)
Density	0.879 g / cm^3
Melting point	- 93 °C
Boiling point	120 -121 °C
Solubility in water	Soluble in 150 parts
Main hazards	Irritant (Xi)
Flash point	26 °C c.c.

Auto ignition temperature	463 °C
LD_{50}	13050 mg / kg (oral , rat)
Structure and properties	*n*, ε_r, etc.
Thermo dynamic data	Phase behaviour Solid, liquid, gas
Spectral data	UV, IR, NMR, MS

2 - Uses

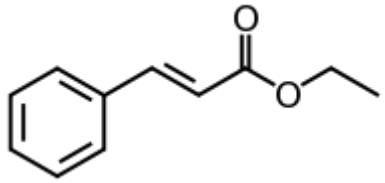
It is commonly used as artificial flavoring resembling orange juice[2] or pineapple in alcoholic beverages (e.g. martinis, daiquiris etc.), as a solvent in perfumery products, and as a plasticizer for cellulose. In addition, ethyl butyrate is often also added to orange juice, as most associate its odor with that of fresh orange juice.

Ethyl butyrate is one of the most common chemicals used in flavors and fragrances. It can be used in a variety of flavors: orange (most common), cherry, pineapple, mango, guava, bubblegum, peach, apricot, fig, and plum. In industrial use, it is also one of the cheapest chemicals, which only adds to its popularity.

3 - Production

It can be synthesized by reacting ethanol and butyric acid. This is a condensation reaction, meaning water is produced in the reaction as a byproduct.

Ethyl Cinnamate

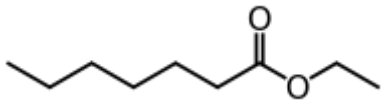


Ethyl cinnamate is the ester of cinnamic acid and ethanol. It is present in the essential oil of cinnamon. Pure ethyl cinnamate has a "fruity and balsamic odor, reminiscent of cinnamon with an amber note".

The *p*-methoxy derivative is reported to be a mono amine oxidase inhibitor.

IUPAC name : Ethyl 3-phenylprop-2-enoate	
Molecular formula	$C_{11}H_{12}O_2$
Molar mass	176 g / mol
Density	1.046 g / cm^3
Melting point	6.5 - 8 °C
Boiling point	271 °C, 544 K, 520 °F

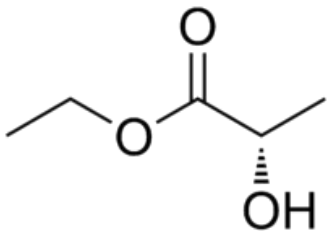
Ethyl Heptanoate



Ethyl heptanoate is the ester resulting from the condensation of heptanoic acid and ethanol. It is used in the flavor industry because of its odor that is similar to grape.

IUPAC name : Ethyl heptanoate	
Other names : Ethyl enanthate, Ethyl heptylate, Heptanoic acid ethyl ester, Enanthic acid ethyl ester	
Molecular formula	$C_9H_{18}O_2$
Molar mass	158 g / mol
Density	0.860 g / cm^3
Melting point	− 66 °C
Boiling point	188 −189 °C

Ethyl Lactate



IUPAC name : Ethyl (*S*)-2-hydroxypropanoate	
Other names : Ethyl lactate; Lactic acid ethyl ester; 2-Hydroxypropanoic acid ethyl ester; Actylol; Acytol	
Molecular formula	$C_5H_{10}O_3$
Molar mass	118 g mol^{-1}
Appearance	Clear to slightly yellow liquid
Density	1.03 g / cm^3
Melting point	- 26 °C
Boiling point	151-155 °C
Solubility in water	Miscible
Solubility in ethanol and most alcohols	Miscible
Chiral rotation $[\alpha]_D$	−11.3°
Main hazards	Irritant (Xi)
Flash point	46 °C

- **Introduction**

Ethyl lactate, also known as lactic acid ethyl ester, is a monobasic ester formed from lactic acid and ethanol, commonly used as a solvent. This compound is considered biodegradable and can be used as a water- rinsible degreaser. Ethyl lactate is found naturally in

small quantities in a wide variety of foods including wine, chicken, and various fruits. The odor of ethyl lactate when dilute is mild, buttery, creamy, with hints of fruit and coconut.

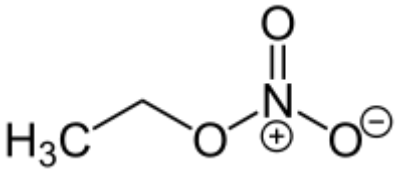
Ethyl lactate is produced from biological sources, and can be either the levo (*S*) form or dextro (*R*) form, depending on the organism that is the source of the lactic acid. Most biologically sourced ethyl lactate is ethyl (-)-L-lactate (ethyl (*S*)-lactate). Ethyl lactate is also produced industrially from petrochemical stocks, and this ethyl lactate consists of the racemic mixture of levo and dextro forms. In some jurisdictions, the *natural* product is exempt from many restrictions placed upon use and disposal of solvents. Because both enantiomers are found in nature, and because ethyl lactate is easily biodegradable, it is considered to be a *green* solvent.

Due to its relatively low toxicity, ethyl lactate is used commonly in pharmaceutical preparations, food additives,[2] and fragrances. Ethyl lactate is also used as solvent for nitrocellulose, cellulose acetate, and cellulose ethers.

Ethyl lactate hydrolyzes in the presence of water and acids or bases into lactic acid and ethanol.

Ethyl lactate can be used as a cosolvent to produce suitable conditions for the formation of aryl aldimines.

Ethyl Nitrate



1 - Introduction

Ethyl nitrate has formula $C_2H_5NO_3$. It is used in organic synthesis and as an intermediate in the preparation of some drugs, dyes, and perfumes.

Ethyl nitrate is found in the atmosphere, where it can react with other gases to form smog. Originally thought to be a pollutant, formed mainly by the combustion of fossil fuels, recent analysis of ocean water samples reveal that in places where cool water rises from the deep, the water is saturated with alkyl nitrates, likely formed by natural processes.

IUPAC name :Ethyl nitrate	
Other names : Nitric acid ethyl ester	
Molecular formula	$C_2H_5NO_3$
Molar mass	91 g / mol
Appearance	Liquid
Melting point	− 102 °C
Boiling point	87 °C

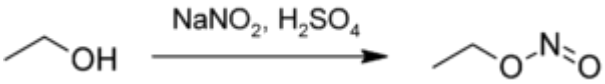
2 - Preparation

Ethyl nitrate has been prepared by bubbling gaseous nitryl fluoride through ethanol at −10 °C . The reaction was subsequently studied in detail.

Ethyl Nitrite

IUPAC name ; 1-Nitroso oxy ethane	
Other names : Ethyl alcohol nitrite; Nitrous acid, ethyl ester; Nitrethyl	
Molecular formula	$C_2H_5NO_2$
Molar mass	75 g mol^{-1}
Boiling point	17 °C

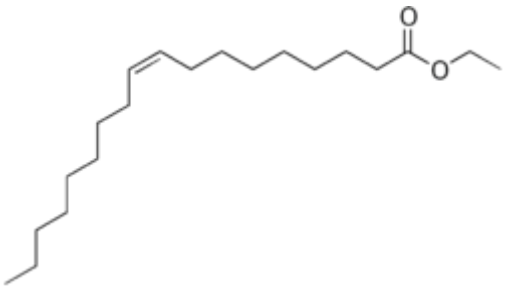
The chemical compound ethyl nitrite is an alkyl nitrite. It may be prepared from ethanol



Ethyl nitrite is the main ingredient in a traditional ethanol-based South African remedy for colds and flu known as Witdulsies and sold in pharmacies. It is known as a traditional Afrikaans remedy and may have Dutch roots, as the same remedy is apparently made by the Germano-Dutch Amish people in the USA. However FDA has blocked over-the-counter sales of this same remedy, known in the USA as *sweet nitrite* or *sweet spirit of nitre* since 1980 .

Alkyl nitrites ("**Poppers**")
Amyl nitrite (iso amyl nitrite, iso pentyl nitrite)
Butyl nitrite
Cyclo hexyl nitrite
Ethyl nitrite
Hexyl nitrite
Isobutyl nitrite (2- methyl propyl nitrite)
Iso propyl nitrite
Methyl nitrite

Ethyl Oleate



Ethyl oleate is a fatty acid ester formed by the condensation of oleic acid and ethanol. It is a colorless to light yellow liquid. Ethyl oleate is produced by the body during ethanol intoxication.

Ethyl oleate is used as a solvent for pharmaceutical drug preparations involving lipophilic substances such as steroids.[2] It also finds use as a lubricant and a plasticizer.

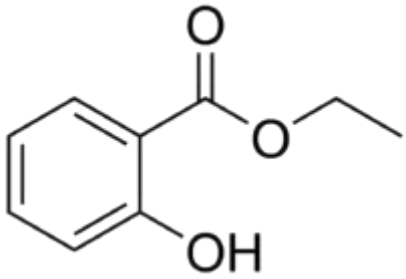
Ethyl oleate is regulated as a food additive by the Food and Drug Administration under "Food Additives Permitted for Direct Addition to Food for Human Consumption", 21CFR172.515.

Ethyl oleate has been identified as a primer pheromone in honeybees.

Ethyl oleate is one of the fatty acid ethyl esters (FAEE) that is formed in the body after ingestion of ethanol. There is a growing body of research literature that implicates FAEEs such as ethyl oleate as the toxic mediators of ethanol in the body (pancreas, liver, heart, and brain). Among the speculations is that ethyl oleate may be the toxic mediator of alcohol in fetal alcohol syndrome. The oral ingestion of ethyl oleate has been carefully studied and due to rapid degradation in the digestive tract it appears safe for oral ingestion. Ethyl oleate is not currently approved by the U.S. Food and Drug Administration for any injectable use. However, it is used by compounding pharmacies as a vehicle for intramuscular drug delivery, in some cases to prepare the daily doses of progesterone in support of pregnancy. Studies which document the safe use of ethyl oleate in pregnancy for both the mother and the fetus have never been performed.

IUPAC name : Ethyl (*Z*)-octadec-9-enoate	
Other names : Oleic acid ethyl ester	
Molecular formula	$C_{20}H_{38}O_2$
Molar mass	310 g mol^{-1}
Appearance	Colorless to light yellow liquid
Density	0.87 g / cm^3
Melting point	- 32 °C
Boiling point	210 °C
Solubility in water	Insoluble

Ethyl Salicylate



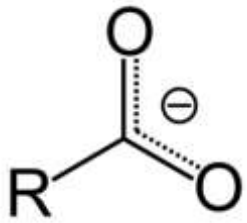
Ethyl salicylate is the ester formed by the condensation of salicylic acid and ethanol. It is a clear liquid that is sparingly soluble in water, but soluble in alcohol and ether. It has a pleasant odor resembling wintergreen and is used in perfumery and artificial flavors.

IUPAC name : Ethyl 2-hydroxy benzoate	
Molecular formula	$C_9H_{10}O_3$
Molar mass	166 g / mol
Density	1.131 g / cm^3
Melting point	1 °C
Boiling point	231–234 °C

Part -7 –

Carboxylic Acids Salts

Carboxylate



Carboxylate ion

Contents

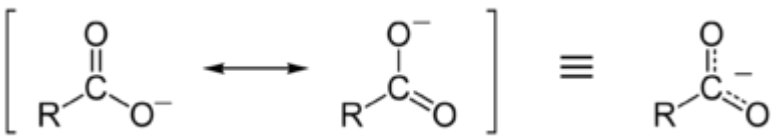
1 -Introduction

Carboxylate is a salt or ester of a carboxylic acid. *Carboxylate salts* have the general formula $M(RCOO)_n$, where M is a metal and *n* is 1,2,...; *carboxylate esters* have the general formula RCOOR'. R and R' are organic groups; R'≠H.

A carboxylate ion is the conjugate base of a carboxylic acid, $RCOO^-$. It is an ion with negative charge.

2 - Resonance stabilization of the carboxylate ion

Carboxylic acids easily dissociate into a carboxylate anion and a positively charged hydrogen ion (proton), much more readily than alcohols do (into an alkoxide ion and a proton), because the carboxylate ion is stabilized by resonance. The negative charge that is left after deprotonation of the carboxyl group is delocalized between the two electronegative oxygen atoms in a resonance structure.



This delocalization of the electron cloud means that either of the oxygen atoms is less strongly negatively charged; the positively charged proton is therefore less strongly attracted back to the carboxylate group once it has left. In contrast, an alkoxide ion, once formed, would have a strong negative charge on the oxygen atom, which would make it difficult for the proton to escape. Thus, the carboxylate ion is more stable and carboxylic acids have a lower pH than alcohols: the higher the number of protons in solution, the lower the pH.

3 - Uses

Polycarboxylate ethers serve as the main component of superplasticizers, admixtures used in the construction industry.

4 - Examples

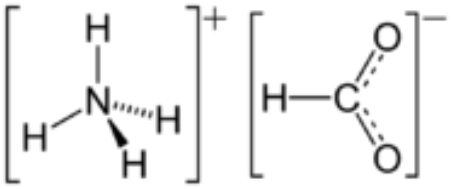
Formate ion, $HCOO^-$
Acetate ion, CH_3COO^-
Lactate ion, $CH_3CH(OH)COO^-$
Oxalate ion, $(COO)_2^{2-}$
Citrate ion, $C_3H_5O(COO)_3^{3-}$

Aluminium Formate

Aluminium formate is the formate of aluminium, with the chemical formula $Al(HCOO)_3$. It can be produced via the reaction of aluminium soaps and formic acid.

IUPAC name : Aluminium triformate
Molecular formula $(HCOO)_3Al$
Molar mass 162 g / mol

Ammonium Formate



Contents

1- Introduction

Ammonium formate, NH_4HCO_2, is the ammonium salt of formic acid. It is a colorless, hygroscopic, crystalline solid.

Molecular formula	HCOO NH_4
Molar mass	63 g / mol
Appearance	white monoclinic crystals deliquescent
Density	1.280 g / cm^3
Melting point	116 °C
Boiling point	decomposes
Solubility in water	102 g/100 mL (0 °C) 143 g/100 mL (20 °C) 531 g/100 mL (80 °C)
Solubility	soluble in liquid ammonia, alcohol and diethyl ether
LD_{50}	2250 mg/kg, oral (mouse)

2 - Uses

Pure ammonium formate decomposes into formamide and water when heated, and this is its primary use in industry. Formic acid can also be obtained by reacting ammonium formate with a dilute acid, and since ammonium formate is also produced from formic acid, it can serve as a way of storing formic acid.

Ammonium formate can also be used in palladium on carbon (Pd / C) reduction of functional groups. In the presence of Pd / C, ammonium formate decomposes to hydrogen, carbon dioxide, and ammonia. This hydrogen gas is adsorbed onto the surface of the palladium metal, where it can react with various functional groups. For example, alkenes can be reduced to alkanes, or formaldehyde to methanol. Activated single bonds to heteroatoms can also be replaced by hydrogens (hydrogenolysis).

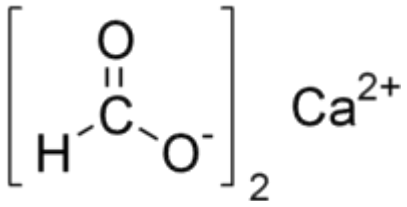
Ammonium formate can be used for reductive amination of aldehydes and ketones (Leuckart reaction)

Ammonium formate can be used as a buffer in high performance liquid chromatography (HPLC), and is suitable for use with liquid chromatography/mass spectrometry (LC/MS). The pK_a values of formic acid and the ammonium ion are 3.8 and 9.2, respectively.

3 - Reactions

When heated, ammonium formate eliminates water, forming formamide. Upon further heating it forms to HCN and H_2O. A side reaction of this is the decomposition of formamide to CO and NH_3.

Calcium Formate

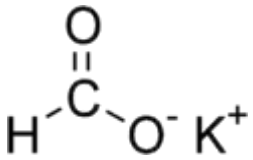


Calcium formate, $Ca(HCOO)_2$, is the calcium salt of formic acid, HCOOH. It is also known as food additive E238 in food industry. The mineral form is very rare and called formicaite. It is known from a few boron deposits. It may be produced synthetically by reacting calcium oxide or calcium hydroxide with formic acid.

Other names :
formic acid calcium salt,
calcoform

Molecular formula	$Ca (HCOO)_2$
Molar mass	130 g / mol
Appearance	white powder
Odor	weak, caramel-like odor
Density	2.009 g / cm^3
Melting point	decomposes at 300°C
Solubility in water	16.1 g /100 mL (0 °C) 16.6 g /100 mL (20°C) 18.4 g /100 mL (100 °C)
Solubility	insoluble in alcohol
Other anions	Calcium acetate
Other cations	Sodium formate

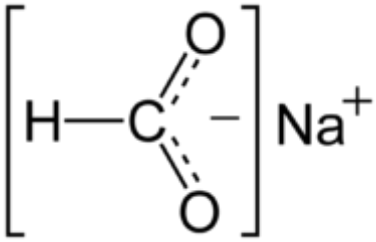
Potassium Formate



Potassium formate is the potassium salt of formic acid. It is an intermediate in the formate potash process for the production of potassium . Potassium formate has also been studied as a potential environmentally friendly deicing salt for use on roads.

IUPAC name :	
Potassium formate	
Molecular formula	HCOO K
Molar mass	84 g mol^{-1}
Appearance	colorless crystals deliquescent
Density	1.908 g / cm^3
Melting point	167.5 °C
Boiling point	Decomposes
Solubility in water	32.8 g / 100 mL (0 °C) 331 g / 100 mL (25°C) 657 g / 100 mL (80 °C)
Solubility	soluble in alcohol insoluble in ether
LD_{50}	5500 mg/kg (oral, mouse)

Sodium Formate



Contents

1 - Introduction

Sodium formate, HCOONa, is the sodium salt of formic acid, HCOOH. It usually appears as a white deliquescent powder.

Other names : formic acid , sodium salt	
Molecular formula	HCOO Na
Molar mass	68.007 g / mol
Appearance	white granules deliquescent
Density	1.92 g /cm^3 (20 °C)
Melting point	253 °C
Boiling point	decomposes
Solubility in water	97.2 g / 100 mL (20 °C) 160 g / 100 mL (100 °C)
Solubility	insoluble in ether soluble in glycerol, alcohol

2 - Uses

Sodium formate is used in several fabric dyeing and printing processes. It is also used as a buffering agent for strong mineral acids to increase their pH, and as a food additive (E237) .

3 - Preparation

Sodium formate can be prepared in the laboratory by neutralizing formic acid with sodium carbonate. It can also be obtained by reacting chloroform with an alcoholic solution of sodium hydroxide.

$CHCl_3 + 4NaOH \rightarrow HCOONa + 3NaCl + 2H_2O$

or by reacting sodium hydroxide with chloral hydrate.

$C_2HCl_3(OH)_2 + NaOH \rightarrow CHCl_3 + HCOONa + H_2O$

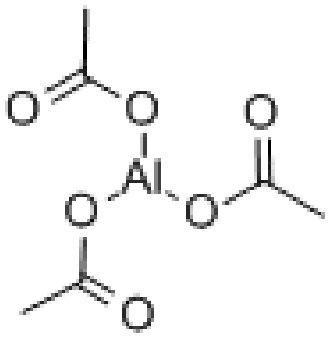
The latter method is, in general, preferred to the former because the low aqueous solubility of $CHCl_3$ makes it easier to separate out from the sodium formate solution, by fractional crystallization, than the soluble NaCl would be.

For commercial use, sodium formate is produced by absorbing carbon monoxide under pressure in solid sodium hydroxide at 160 °C.

$CO + NaOH \rightarrow HCOONa$

Sodium formate may also be created via the haloform reaction between ethanol and sodium hypochlorite in the presence of a base. This procedure is well documented for the preparation of chloroform.

Aluminium Acetate



Chemical formula of aluminum acetate

Contents

1 - Introduction

Aluminum acetate is a chemical compound and is a salt which can be produced by the reaction of aluminum hydroxide and acetic acid. The compound formula for Aluminum Acetate is $Al(CH_3COO)_3$.

Molecular formula: $C_6H_9AlO_6$
Three such salts exist:
Neutral Aluminum triacetate, $Al(C_2H_3O_2)_3$
Basic Aluminum diacetate, $HOAl(C_2H_3O_2)_2$
Basic Aluminum monoacetate, $(HO)_2AlC_2H_3O_2$

2 - Synthesis

The triacetate forms when aluminum sulfate is mixed with barium acetate. Another synthetic method is by bringing together aluminum hydroxide, acetic anhydride and glacial acetic acid in water, forming the basic aluminum monoacetate

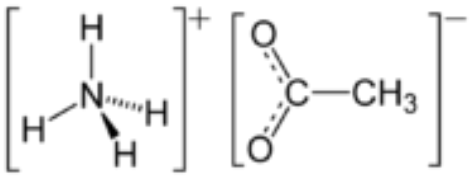
The diacetate is prepared in a reaction of sodium aluminate ($NaAlO_2$) with acetic acid.

3 - Applications

The diacetate is used as an antiseptic. The Aluminum Acetate compound can be used medicinally to treat infections in the outer ear canal. It is used in the name brand drug Domeboro, which contains acetic acid/aluminum acetate.This medication kills the infectious bacteria and fungus as well as drying out the ear canal.

Since it acts as a drying agent, it can also be used in the treatment of severe rashes, such as poison ivy, poison oak, and poison sumac.

Ammonium Acetate



Contents

1 - Introduction

Ammonium acetate is a chemical compound with the formula $NH_4C_2H_3O_2$ (or $C_2H_4O_2.NH_3$ or $C_2H_7NO_2$). It is a white solid and can be derived from the reaction of ammonia and acetic acid. It is available commercially and, depending on grade, can be rather inexpensive.

3 - Uses and distinctive properties

As the salt of a weak acid and a weak base, ammonium acetate has a number of distinctive properties.

$NH_4C_2H_3O_2$ is occasionally employed as a biodegradable de-icing agent.

It is often used with acetic acid to create a buffer solution, one that can be thermally decomposed to non-ionic products

Ammonium acetate is useful as a catalyst in the Knoevenagel condensation and as a source of ammonia in the Borch reaction in organic synthesis.

It is a relatively unusual example of a salt that melts at low temperatures.

Can be used with distilled water to make a protein precipitating reagent.

Is often used as an aqueous buffer for ESI mass spectrometry of proteins and other molecules.

Ammonium acetate is volatile at low pressures. Because of this it has been used to replace cell buffers with non-volatile salts, in preparing samples for mass spectrometry.[3] It is also popular as a buffer for mobile phases for HPLC with ELSD detection for this reason. Other volatile salts that have been used for this include ammonium formate.

2 – 1 - Food Additive

Ammonium acetate is also used as a food additive as an acidity regulator; INS number 264. It is approved for usage in Australia and New Zealand.

3 - Properties

CH_3COONH_4 is hygroscopic and decomposes easily to acetamide if heated above 165 °C.

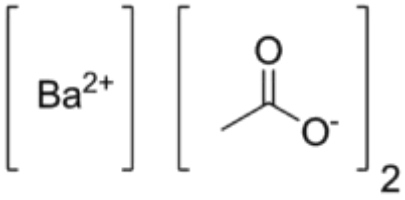
$$CH_3COONH_4 \rightarrow CH_3C(O)NH_2 + H_2O$$

In this reaction, a salt is converted to two molecular species, which is a relatively uncommon conversion at mild temperatures.

4 - Production

Ammonium acetate is produced by the neutralization of acetic acid with ammonium carbonate or by saturating glacial acetic acid with dry ammonia gas. Obtaining crystalline ammonium acetate is difficult on account of its aqueous solution giving off ammonia when evaporated.

Barium Acetate



Contents

1 - Introduction

Barium acetate ($Ba(C_2H_3O_2)_2$) is the salt of barium (II) and acetic acid.

2 - Preparation

Barium acetate is generally produced by the reaction of acetic acid with barium carbonate :

$$BaCO_3 + 2\,CH_3COOH \rightarrow (CH_3COO)_2Ba + CO_2 + H_2O$$

The reaction is performed in solution and the barium acetate crystallizes out. Alternatively, barium sulfide can be used :

$$BaS + 2\,CH_3COOH \rightarrow (CH_3COO)_2Ba + H_2S$$

Again, the solvent is evaporated off and the barium acetate crystallized.

3 - Properties

Barium acetate is a white powder, which is highly soluble: at 0 °C, 55.8 g of barium acetate can be dissolved in 100 g of water. It decomposes upon heating into barium carbonate .

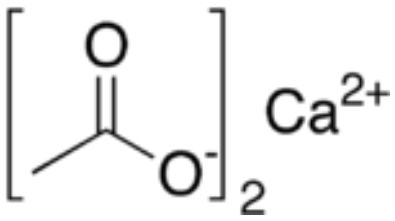
4 - Reactions

When heated in air, barium acetate decomposes to the carbonate. It reacts with acids: reaction with sulfuric acid, hydrochloric acid and nitric acid give the sulfate, chloride and nitrate respectively.

5 - Uses

Barium acetate is used as a mordant for printing textile fabrics, for drying paints and varnishes and in lubricating oil. In chemistry, it is used in the preparation of other acetates; and as a catalyst in organic synthesis.

Calcium Acetate



Contents

1 - Introduction

Calcium acetate is a chemical compound which is calcium salt of acetic acid. It has the formula $Ca(C_2H_3O_2)_2$. Its standard name is calcium acetate, while calcium ethanoate is the systematic name. An older name is acetate of lime. The anhydrous form is very hygroscopic; therefore the monohydrate ($Ca(CH_3COO)_2 \cdot H_2O$) is the common form.

IUPAC name : Calcium acetate

Other names :
Acetate of lime
Calcium ethanoate
Calcium diacetate

Abbreviations	$Ca(OAc)_2$
Molecular formula	$C_4 H_6 Ca O_4$
Molar mass	158 g mol^{-1}
Appearance	White solid hygroscopic
Odor	slight acetic acid odor
Density	1.509 g / cm^3
Melting point	160 °C (decomposition to acetone)
Solubility in water	37.4 g/100 mL (0 °C) 34.7 g/100 mL (20 °C) 29.7 g/100 mL (100 °C)
Solubility	slightly soluble in methanol

	insoluble in acetone, ethanol and benzene
Refractive index (n_D)	1.55
Auto ignition temperature	680 -730 °C
LD_{50}	4280 mg/kg (oral, rat)

2 Production

Calcium acetate can be prepared by soaking calcium carbonate (found in eggshells, or in common carbonate rocks such as lime stone or marble) in vinegar:

$$CaCO_3 + 2CH_3COOH \rightarrow Ca(CH_3COO)_2 + H_2O + CO_2$$

Since both reagents would have been available pre-historically, the chemical would have been observable as crystals then.

Copper (II) Acetate

Small crystals of copper(II) acetate

Contents

1 - Introduction

Copper (II) acetate, also referred to as cupric acetate, is the chemical compound with the formula $Cu(OAc)_2$ where OAc^- is acetate ($CH_3CO_2^-$). The hydrated derivative, which contains one molecule of water for each Cu atom, is available commercially. Anhydrous $Cu(OAc)_2$ is a dark green crystalline solid, whereas $Cu_2(OAc)_4(H_2O)_2$ is more bluish-green. Since ancient times, copper acetates of some form have been used as fungicides and green pigments. Today, copper acetates are used as reagents for the synthesis of various inorganic and organic compounds.[2] Copper acetate, like all copper compounds, emits a blue-green glow in a flame.

IUPAC name :
Tetra-μ2-acetatodiaqua dicopper (II)
Other names ;
Copper (II) ethanoate,
Cupric acetate,
Copper Acetate

Molecular formula	$Cu(CH_3COO)_2$
Molar mass	181 g / mol (anhydrous)

	199 g / mol (monohydrate)
Appearance	Dark green crystalline solid
Odor	odorless (monohydrate)
Density	1.882 g/cm^3 (monohydrate)
Melting point	115 °C
Boiling point	240 °C
	monohydrate:
Solubility in water	7.2 g / 100 mL (cold water) 20 g / 100 mL (hot water)
Solubility	Soluble in alcohol Slightly soluble in ether and glycerol
Refractive index (n_D)	1.545 (monohydrate)
Flash point	Non-flammable
LD_{50}	710mg/kg oral rat [1]

2 - Structure

Copper acetate monohydrate adopts the "paddle-wheel" structure seen also for related Rh (II) and Cr (II) tetra acetates. One oxygen atom on each acetate is bound to one copper at 1.97 Å (197 pm. Completing the coordination sphere are two water ligands, with Cu-O distances of 2.20 Å (220 pm). The two five-coordinate copper atoms are separated by only 2.65 Å (265 pm), which is close to the Cu—Cu separation in metallic copper.[5] The two copper centers interact resulting in a diminishing of the magnetic moment such that near 90 K, $Cu_2(OAc)_4(H_2O)_2$ is essentially diamagnetic due to cancellation of the two opposing spins. $Cu_2(OAc)_4(H_2O)_2$ was a critical step in the development of modern theories for antiferromagnetic coupling.

3 - Synthesis

Copper (II) acetate synthesized by the method described in the history section leads to impure samples. It is prepared industrially by heating copper (II) hydroxide or copper (II) carbonate with acetic acid.

A second method of copper acetate production is to electrolyze a concentrated aqueous solution of calcium acetate with copper electrodes. As the reaction proceeds the anode oxidizes to produce copper acetate which adheres to its surface and can be removed as

crystals. At the cathode calcium ions are reduced to calcium atoms and would be deposited, but due to the water content of the solution the calcium is converted to insoluble calcium hydroxide. The drawback with this setup is that the cathode gets coated with an insulating layer of calcium hydroxide, which gradually slows the process. To negate this hydroxide buildup mercury is utilized as the cathode; therefore as the process takes place the calcium formed immediately reacts with the mercury to make a calcium-mercury amalgam and the copper acetate formed at the anode is removed periodically. This process generally yields suitably pure copper acetate, on a small scale, with slight traces of calcium acetate.

Copper (II) acetate also forms by treating copper metal with a solution of acetic acid and hydrogen peroxide.

4 - Related compounds

Heating a mixture of anhydrous copper (II) acetate and copper metal affords cuprous acetate:

$$2\ Cu + Cu_2(OAc)_4 \rightarrow 4\ CuOAc$$

The hydrate form can be dehydrated by heating at 100 °C in a vacuum. Unlike the copper (II) derivative, copper (I) acetate is colourless and diamagnetic.

Basic copper acetate is prepared by neutralizing an aqueous solution of copper(II) acetate. The basic acetate is poorly soluble. This material is a component of verdigris, the blue-green substance that forms on copper during long exposures to atmosphere.

5 - Uses in chemical synthesis

The uses for copper (II) acetate are more plentiful as a catalyst or oxidizing agent in organic syntheses. For example, $Cu_2(OAc)_4$ is used to couple two terminal alkynes to make a 1,3-diyne:

$$Cu_2(OAc)_4 + 2\ RC \equiv CH \rightarrow 2\ CuOAc + RC \equiv C\text{-}C \equiv CR + 2\ HOAc$$

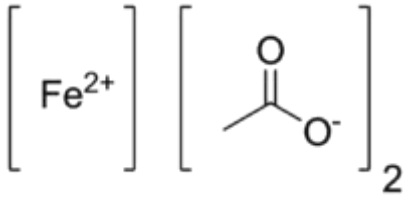
The reaction proceeds via the intermediacy of copper(I) acetylides, which are then oxidized by the copper(II) acetate, releasing the acetylide radical. A related reaction involving copper acetylides is the synthesis of ynamines, terminal alkynes with amine groups using $Cu_2(OAc)_4$.

6 - History

Copper (II) acetate was historically prepared in vineyards, since acetic acid is a byproduct of fermentation. Copper sheets were alternately layered with fermented grape skins and dregs left over from wine production and exposed to air. This would leave a blue substance on the outside of the sheet. This was then scraped off and dissolved in water. The resulting solid was used as a pigment, or combined with arsenic trioxide to form copper acetoarsenite, a powerful insecticide and fungicide called Paris Green or Schweinfurt Green.

During the Second World War copper acetate was used as shark repellent . Under war conditions, before adoption it has been tested only very briefly (while in general successfully). The source says copper acetate does repel sharks in some situations but not in all.

Iron (II) Acetate

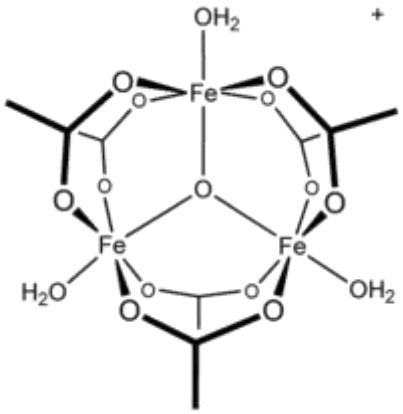


Iron (II) acetate is an off-white or light brown solid ionic compound of iron. It is highly soluble in water and it forms a light green tetrahydrate. Iron (II) acetate is manufactured from scrap iron and acetic acid, and it is used as a mordant by the dye industry. Ebonizing wood is one such process.

It can also be made by the reaction of ferrous oxide or ferrous hydroxide with concentrated acetic acidز

Other names : Ferrous acetate	
Molecular formula	Fe $(C_2H_3O_2)_2$
Molar mass	17 4 g / mol
Melting point	190 – 200 °C (dec)
Solubility in other solvents	Very soluble
LD_{50}	492 mg / kg scu-rat

Iron (III) Acetate



Contents

1 - Introduction

Ferric acetate is the coordination compound more commonly known as "basic iron acetate". With the formula $[Fe_3O(OAc)_6(H_2O)_3]OAc$ (OAc is $CH_3CO_2^-$), it is a salt, composed of the cation $[Fe_3(\mu^3\text{-}O)(OAc)_6(H_2O)_3]^+$ and an acetate anion . The formation of the red-brown complex has long been used as a test for ferric ions.

IUPAC name : Iron (III) acetate
Other names :
basic iron (III) acetate ,
iron (III) oxy acetate,
iron (III) Acetate

Molecular formula	$C_{14}H_{27}Fe_3O_{18}$
Molar mass	651 g / mol
Appearance	Brownish - red amorphous powder
Solubility in water	soluble
Solubility	soluble in ethanol
LD_{50}	Acute : 3250 mg / kg [Rat]

2 - Structure and synthesis

Basic iron acetate forms on treating aqueous solutions of iron (III) sources with acetate salts.

Early work showed that it is trinuclear.[7] The Fe centres are equivalent, each being octahedral, being bound to six oxygen ligands, including a triply bridging oxide at the center of the equilateral triangle.[8] The compound was an early example of a molecular compound of iron that features an oxide ligand. Ignoring its 24 hydrogen centres, the cation has D_{3h} symmetry.

3 - Reactions

The terminal aqua ligands on the trimetallic frame work can be substituted with other ligands, such as pyridine and dimethyl formamide . Many different salts are known by exchanging the anion, e.g. $[Fe_3(\mu^3\text{-}O)(OAc)_6(H_2O)_3]Cl$. Reduction of the cation affords the neutral mixed-valence derivative that contains one ferrous and two ferric centers. Mixed metal species are known such as $[Fe_2CoO(OAc)_6(H_2O)_3]$.

4 - Related compounds

Chromium (III), ruthenium (III), vanadium (III), and rhodium (III) form analogous compounds. Iron (III) acetate (lacking the oxo ligand) has been claimed as a red coloured compound from the reaction of silver acetate and iron (III) chloride.

5 - Uses

Materials prepared by heating iron, acetic acid, and air, loosely described as basic iron acetates, are used as dyes and mordants.

Lead (II) Acetate

Contents

1 - Introduction

Lead (II) acetate (Pb $(CH_3COO)_2$), also known as lead acetate, lead diacetate, plumbous acetate, sugar of lead, lead sugar, salt of **Saturn**, and **Goulard's** powder, is a white crystalline chemical compound with a sweetish taste. It is made by treating lead(II) oxide with acetic acid. Like other lead compounds, it is toxic. Lead acetate is soluble in water and glycerin. With water it forms the trihydrate, $Pb(CH_3COO)_2 \cdot 3H_2O$, a colorless or white efflorescent monoclinic crystalline substance.

The substance is used as a reagent to make other lead compounds and as a fixative for some dyes. In low concentrations, it is the principal active ingredient in progressive types of hair coloring dyes.[*citation needed*] Lead(II) acetate is also used as a mordant in textile printing and dyeing, as a drier in paints and varnishes, and in preparing other lead compounds.

IUPAC name : Lead (II) ethanoate
Systematic name ; Lead(II) ethanoate
Other names ;
Plumbous acetate,
Salt of Saturn,
Sugar of Lead,
lead diacetate

Molecular formula	Pb $(C_2H_3O_2)_2$
Molar mass	325 g / mol (anhydrous) 379 g / mol (trihydrate)

Appearance	White powder or colorless, efflorescent crystals
Odor	slight acetic
Density	3.25 g/cm^3 (anhydrous) 2.55 g/cm^3 (trihydrate) 1.69 g/cm^3 (decahydrate)
Melting point	280 °C (anhydrous) 75 °C (trihydrate) 22 °C (decahydrate)
Solubility in water	44.39 g/100 mL (20 °C) 211 g/100 mL (50 °C)[1]
Solubility	anhydrous soluble in alcohol hydrates insoluble in alcohol
Refractive index (n_D)	1.567 (trihydrate)
Main hazards	Neurotoxic, Probable Human Carcinogen
Flash point	Nonflammable

2 - Uses

2 – 1 - Sweetener

Like other lead (II) salts, lead (II) acetate has a sweet taste, which has led to its use as a sugar substitute throughout history. The ancient Romans, who had few sweeteners besides honey, would boil must (grape juice) in lead pots to produce a reduced sugar syrup called *defrutum*, concentrated again into *sapa*. This syrup was used to sweeten wine and to sweeten and preserve fruit. It is possible that lead(II) acetate or other lead compounds leaching into the syrup might have caused lead poisoning in anyone consuming it . Lead acetate is no longer used in the production of sweeteners in most of the world because of its recognized toxicity. Modern chemistry can easily detect it, which has all but stopped the illegal use that continued decades after legal use as a sweetener was banned .

2 – 1 – 1 - Resultant deaths

Pope Clement II died in October 1047. A toxicologic examination of his remains conducted in the mid – 20 th century

confirmed centuries-old rumors that he had been poisoned with lead sugar.[3] It is not clear if he was assassinated.

In 1787 painter Albert Christoph Dies swallowed, by accident, approximately 21 g of lead acetate. His recovery from this poison was slow and incomplete. He lived with illnesses until his death in 1822 .

Although the use of lead (II) acetate as a sweetener was already illegal at that time, composer Ludwig van Beethoven may have died of lead poisoning caused by wines adulterated with lead acetate.

Mary Seacole applied lead (II) acetate, among other remedies, against an epidemic of cholera in Panama.

3 - Production

Lead acetate can be made by boiling elemental lead in acetic acid and hydrogen peroxide. It's also possible to create with lead carbonate or lead oxide.

3 – 1 - Other uses

Lead (II) acetate, as well as white lead, have been used in cosmetics throughout history, though this practice has ceased in Western countries . It is still used in men's hair coloring products[9] like Grecian Formula.

Lead (II) acetate paper is used to detect the poisonous gas hydrogen sulfide. The gas reacts with lead (II) acetate on the moistened test paper to form a grey precipitate of lead (II) sulfide.

Lead (II) acetate solution was a commonly used folk remedy for sore nipples . In modern medicine, for a time, it was used as an astringent, in the form of Goulard's Extract.

An aqueous solution of lead (II) acetate is the by product of the 50 / 50 mixture of hydrogen peroxide and white vinegar used in the cleaning and maintenance of stainless steel fire arm suppressors (silencers) and compensators. The solution is agitated by the bubbling action of the hydrogen peroxide, and the main reaction is the

dissolution of lead deposits within the suppressor by the acetic acid, which forms lead acetate. Because of its high toxicity, this chemical solution must be appropriately disposed by a chemical processing facility or hazardous materials center. Alternatively, the solution may be reacted with sulfuric acid to precipitate nearly insoluble lead(II) sulfate. The solid may then be removed by mechanical filtration and is safer to dispose of than aqueous lead acetate.

It was also used in making of slow matches during the Middle Ages. It was made by mixing natural form of lead (II) oxide called litharge and vinegar.

Lead (II) acetate has also been used to treat poison ivy

4 - Precautions

Lead (II) acetate, as with any other lead salts, causes lead poisoning.

Lead (IV) Acetate

Contents

1 - Introduction

Lead (IV) acetate or lead tetraacetate is a chemical compound with chemical formula $Pb(C_2H_3O_2)_4$ and is a lead salt of acetic acid. It is commercially available often stabilized with acetic acid.

IUPAC name : Lead (IV) acetate
Other names : Lead tetra acetate

Molecular formula	$Pb(C_2H_3O_2)_4$
Molar mass	443 g / mol
Appearance	colorless or pink crystals
Odor	vinegar
Density	2.228 g / cm^3 (17 °C)
Melting point	175 °C
Boiling point	decomposes
Solubility in water	reacts with water
Solubility	reacts with ethanol soluble in chloroform, benzene, nitrobenzene, hot acetic acid, HCl, tetra chloro ethane
Main hazards	Toxic

2 - Preparation

It can be prepared by reaction of red lead with acetic acid The other main lead acetate is lead (II) acetate.

3 - Reagent in organic chemistry

Lead tetraacetate is a strong oxidizing agent, a source of acetyloxy groups and a general reagent for the introduction of lead into organolead compounds. Some of its many uses in organic chemistry :

* Acetoxylation of benzylic, allylic and α-oxygen ether C-H bonds, for example the photochemical conversion of dioxane to 1,4-dioxene through the *2-acetoxy-1,4-dioxane* intermediate and the conversion of α-pinene to verbenone

* Oxidation of hydrazones to diazo compounds for example that of *hexafluoroacetone hydrazone* to *bis(trifluoromethyl)diazomethane*

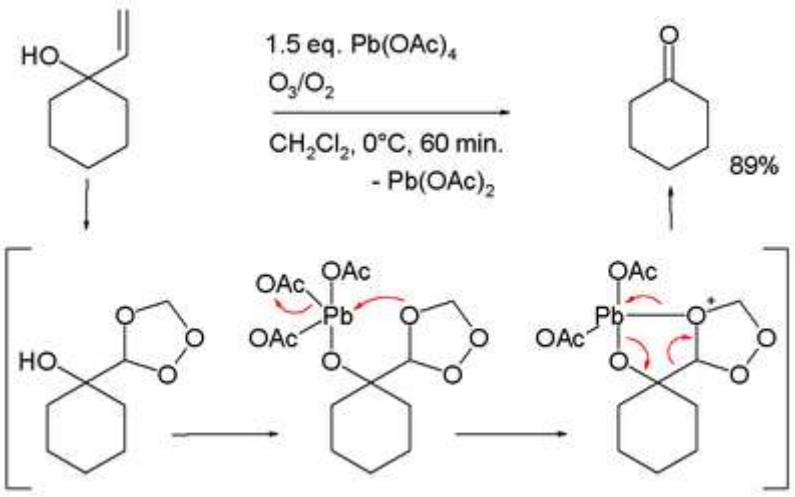
* Aziridine formation, for example the reaction of N-aminophthalimide and stilbene

* Cleavage of 1,2-diols to the corresponding aldehydes or ketones often replacing ozonolysis, for instance the oxidation of di-n-butyl d-tartrate to n-butyl glyoxylate

* Reaction with alkenes to γ-lactones

* Oxidation of alcohols carrying a δ-proton to cyclic ethers.

* Oxidative cleavage of certain allyl alcohols in conjunction with ozone :

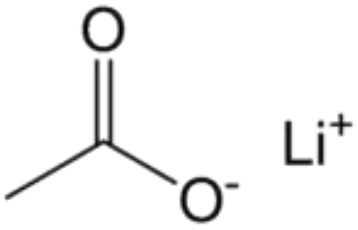


conversion of aceto phenones to phenyl acetic acids

4 - Safety

Lead (IV) acetate may be fatal if ingested, inhaled, or absorbed through skin. It causes irritation to skin, eyes, and respiratory tract. It is a neurotoxin. It affects the gum tissue, central nervous system, kidneys, blood, and reproductive system.

Lithium Acetate



IUPAC name :Lithium Acetate

Molecular formula	CH_3 COO Li
Molar mass	6 6 g mol^{-1}
Appearance	crystal
Density	1.26 g / cm^3
Melting point	286 °C
Solubility in water	45.0 g/100 mL

Contents

1 - Introduction

Lithium acetate (CH_3COOLi) is a salt of lithium and acetic acid.

2 - Uses

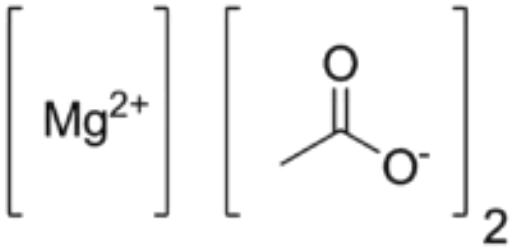
Lithium acetate is used in the laboratory as buffer for gel electrophoresis of DNA and RNA. It has a lower electrical conductivity and can be run at higher speeds than can gels made from TAE buffer (5-30V/cm as compared to 5 - 10 V / cm). At a given voltage, the heat generation and thus the gel temperature is much lower than with TAE buffers, therefore the voltage can be increased to speed up electrophoresis so that a gel run takes only a fraction of the usual time. Downstream applications, such as isolation of DNA from a gel slice or Southern blot analysis, work as expected when using lithium acetate gels.

Lithium boric acid or sodium boric acid are usually preferable to lithium acetate or TAE when analyzing smaller fragments of DNA

(less than 500 bp) due to the higher resolution of borate-based buffers in this size range as compared to acetate buffers.

Lithium acetate is also used to permeabilize the cell wall of yeast for use in DNA transformation. It is believed that the beneficial effect of LiAc is caused by its chaotropic effect denaturing both DNA, RNA and proteins.

Magnesium Acetate



Contents

1 - Introduction

Anhydrous Magnesium Acetate has the chemical formula $Mg(CH_3COO)_2$ and in its hydrous form, Magnesium Acetate Tetrahydrate, it has the chemical formula $Mg(CH_3COO)_2 \cdot 4H_2O$. In this compound the magnesium metal has an oxidation state of 2^+. Magnesium acetate is the magnesium salt of acetic acid.[1] It is deliquescent and upon heating, it decomposes to form magnesium oxide.[2] Magnesium acetate is commonly used as a source of magnesium or as a chemical reagent.

IUPAC name :	
Magnesium acetate	
Molecular formula	$Mg(CH_3COO)_2$
Molar mass	142.394 (anhydrous) 214 (tetrahydrate)
Appearance	White hygroscopic crystals
Density	1.45 g / cm^3
Melting point	80 °C (tetrahydrate)
Solubility in water	Soluble

2 - Physical properties

Magnesium acetate appears as white hygroscopic crystals. It smells like acetic acid and is soluble in water. When it is in an aqueous solution its pH can be considered to be neutral.

3 - Storage

Due to the fact that it is very hygroscopic, it must be stored away from water. It is also incompatible with strong oxidizers and should not be mixed with them.

4 - Synthesis

Synthesis of magnesium acetate from the reaction of magnesium hydroxide with acetic acid.

$$2CH_3COOH + Mg(OH)_2 \rightarrow (CH_3COO)_2Mg + 2H_2O$$

Magnesium carbonate suspended in distilled water with 20 % acetic acid solution.

$$2CH_3COOH + MgCO_3 \rightarrow Mg(CH_3COO)_2$$

Reacting metallic magnesium with acetic acid dissolved in dry nitrogen benzene causes Magnesium Acetate to form along with the release a gas, presumably hydrogen.

$$Mg + 2CH_3COOH \rightarrow Mg(CH_3COO)_2 + H_2$$

5 - Uses and applications

In 1881 Charles Clamond invented the Clamond basket, one of the first effective gas mantles. The reagents used in this invention included magnesium acetate, magnesium hydroxide and water.

Magnesium acetate is commonly used as a source of magnesium or for the acetate ion in chemistry experiments. One example of this is when magnesium acetate and magnesium nitrate were both used to perform molecular dynamics simulations and surface tension measurements. In the experiment the authors found that the acetate had a stronger affinity for the surface compared to the nitrate ion and

that the Mg^{2+} strongly repelled away from the air/liquid interference. They also found that the Mg^{2+} had a stronger tendency to bind with the acetate ion compared to the nitrate.

One of the more prevalent uses of magnesium acetate is in the mixture called calcium magnesium acetate (CMA). It is a mixture of calcium acetate and magnesium acetate. CMA is thought of as an environmentally friendly alternative deicer to NaCl and $CaCl_2$. CMA also acts as a powerful SO_2, NO_x, and toxic particulate emission control agent in coal combustion processes to reduce acid rain, and as an effective catalyst for the facilitation of coal combustion.

Magnesium acetate has been found to cause a conformational change in *Escherichia coli* Primase. In this experiment $Mg(OAc)_2$, $MnCl_2$, $CaCl_2$, NaOAc, LiCl, $MgSO_4$ and $MgCl_2$ were all compared to see what effect they had on the *Escherichia coli* Primase. The experimenters found that $Mg(OAc)_2$ caused the best conformational change. $MgSO_4$ and $MgCl_2$ induced the effect slightly while the rest did not.

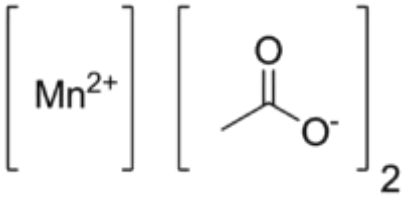
When Magnesium acetate is mixed with hydrogen peroxide it acts as a bactericidal.

Magnesium Acetate has been shown to be effective at ashing organic compounds in preparation for a fluorine analysis when high or low concentrations of fluorine are present.

6 - Safety

Magnesium Acetate is a relatively safe compound to handle and has been given a health hazard rating of zero. However, it should always be handled with gloves and safety goggles. If it is gets in the eyes, the skin, ingested, or inhaled it will cause irritation in the respective areas: eyes, skin, gastrointestinal system, and lungs.[14]

Manganese (II) Acetate



Contents

1 - Introduction

Manganese (II) acetate is the chemical compound with the formula $Mn(CH_3COO)_2$. It is used as a desiccant, a catalyst, and as fertilizer.

IUPAC name : Manganese (II) acetate

Other names : Manganese diacetate

Molecular formula	$Mn(CH_3COO)_2$ (anhydrous) $Mn(CH_3COO)_2 \cdot 4H_2O$ (tetrahydrate)
Molar mass	173 g / mol (anhydrous) 245 g / mol (tetrahydrate)
Appearance	red crystals (anhydrous) red monoclinic crystals (tetrahydrate)
Density	1.74 g / cm^3 (anhydrous) 1.59 g / cm^3 (tetrahydrate)
Melting point	210°C (anhydrous) 80°C (tetrahydrate)
Solubility	soluble in water, methanol, acetic acid (anhydrous) soluble in water, ethanol (tetrahydrate)
Flash point	> 130°C (tetrahydrate)

2 - Reactions

Manganese (II) acetate can be formed by reacting acetic acid with either manganese (II,III) oxide or manganese (II) carbonate :

$$Mn_3O_4 + 2CH_3COOH \rightarrow Mn(CH_3COO)_2 + Mn_2O_3 + H_2O$$

If manganese (II,III) oxide is used , manganese (III) oxide is produced as a byproduct.

If the anhydrous form needs to be produced, manganese (II) nitrate can be reacted with acetic anhydride.[2]

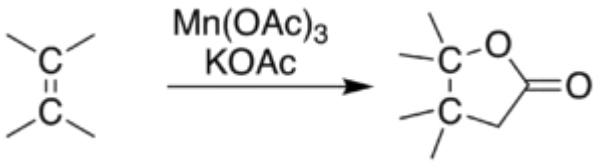
Manganese (III) Acetate

IUPAC name : Manganese triacetate
Other names :
Manganese triacetate dihydrate;
Manganese (III) acetate dihydrate

Molecular formula	$C_6H_9\,Mn\,O_6 \bullet 2H_2O$
Molar mass	268 g / mol (dihydrate)
Appearance	Brown powder
Density	1.049 g cm^{-3}, liquid; 1.266 g cm^{-3}, solid

Manganese (III) acetate is an inorganic compound that is used as an oxidizing agent in organic synthesis and materials science. Like the analogous acetates of iron and chromium, it is an oxygen-centered coordination complex containing three manganese atoms bridged by acetate units. The anhydrous form of this compound crystallizes as a linear coordination polymer, with an additional acetic acid molecule bridging between manganese atoms on consecutive three-manganese clusters.[3] The chemical is therefore not a simple metal acetate ionic compound nor does the actual structure of it reflect the simple "$Mn(OAc)_3$" chemical formula that is commonly given. It is usually used as the dihydrate, though the anhydrous form is also used in some situations. The dihydrate is prepared by reacting potassium permanganate and manganese (II) acetate in acetic acid; addition of acetic anhydride to the reaction produces the anhydrous form.

Mangese triacetate has been used as a single electron oxidant. It can oxidize alkenes via addition of acetic acid to form lactones.



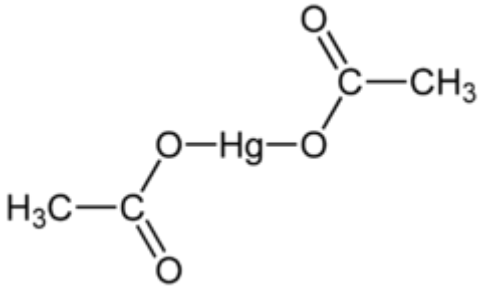
This process is thought to proceed via the formation of a $\bullet CH_2CO_2H$ radical intermediate, which then reacts with the alkene,

followed by additional oxidation steps and finally ring closure.[1] When the alkene is not symmetric, the major product depends on the nature of the alkene, and is consistent with initial formation of the more stable radical (among the two carbons of the alkene) followed by ring closure onto the more stable conformation of the intermediate.

When reacted with enones, the carbon on the other side of the carbonyl reacts rather than the alkene portion, leading to α'-acetoxy enones.[5] In this process, the carbon next to the carbonyl is oxidized by the manganese, followed by transfer of acetate from the manganese to it.

It can similarly oxidize β-ketoesters at the α carbon, and this intermediate can react with various other structures, including halides and alkenes (see: manganese-mediated coupling reactions). One extension of this idea is the cyclization of the ketoester portion of the molecule with an alkene elsewhere in the same structure.[7]

Mercury (II) Acetate



Contents

1 - Introduction

Mercury (II) acetate is the chemical compound with the formula $Hg(O_2CCH_3)_2$. Commonly abbreviated Hg $(OAc)_2$, this compound is employed as a reagent to generate organomercury compounds from unsaturated organic precursors.

Other names : mercuric acetate mercuri acetate	
Molecular formula	$C_4H_6O_4Hg$
Molar mass	318 g /mol
Appearance	White – yellow crystals
Odor	mild vinegar odor
Density	3.28 g / cm³, solid
Melting point	179 °C (decomposes)
Solubility in water	25 g / 100 mL (10 °C) 100 g / 100 mL (100 °C)
Solubility	soluble in alcohol , diethyl ether

2 - Structure

Mercury(II) acetate is a crystalline solid consisting of isolated $Hg(OAc)_2$ molecules with Hg-O distances of 2.07 Å. Three long, weak intermolecular Hg···O bonds of about 2.75 Å are also present,

resulting in a slightly distorted square pyramidal coordination geometry at Hg.

3 - Reactions

Arenes undergo "mercuration" upon treatment with $Hg(OAc)_2$. The one acetate group that remains on mercury can be displaced by chloride :

$$C_6H_5OH + Hg(OAc)_2 \rightarrow C_6H_4(OH)\text{-}2\text{-}HgOAc + HOAc$$
$$C_6H_4(OH)\text{-}2\text{-}HgOAc + NaCl \rightarrow C_6H_4(OH)\text{-}2\text{-}HgCl + NaOAc$$

The Hg^{2+} center binds to alkenes, inducing the addition of hydroxide and alkoxide. For example, treatment of methylacrylate with mercuric acetate in methanol gives an α - mercuri ester :

$$Hg(OAc)_2 + CH_2 = CHCO_2CH_3 + CH_3OH \rightarrow$$
$$CH_3OCH_2CH(HgOAc)CO_2CH_3 + HOAc$$

Mercury(II) has a high affinity for sulfur ligands. $Hg(OAc)_2$ can be used as a reagent to remove the acetamidomethyl protecting group, which is used to "protect" thiol groups in organic synthesis. Similarly $Hg(OAc)_2$ is a standard reagent to convert thiocarbonate esters into dithiocarbonates:

$$(RS)_2C=S + H_2O + Hg(OAc)_2 \rightarrow (RS)_2C=O + HgS + 2\ HOAc$$

Mercury (II) acetate is used for oxymercuration reactions.

Molybdenum (II) Acetate

Contents

1 - Introduction

Molybdenum (II) acetate is a coordination compound with the formula $Mo_2(O_2CCH_3)_4$. It is a yellow, diamagnetic, air-stable solid that is slightly soluble in organic solvents. Molybdenum(II) acetate is an iconic example of a compound with a metal-metal quadruple bond.

Other names :
Dimolybdenum tetra acetate,
tetra (aceto) dimolybdenum ,
Molybdenum (II) acetate dimer,

Molecular formula	$C_8H_{12}Mo_2O_8$
Molar mass	428 g / mol
Appearance	Yellow solids
Boiling point	decomposes
Solubility in water	not soluble

2 - Structure and bonding

It adopts the same Chinese lantern structure as related acetate dimers such as rhodium (II) acetate, copper (II) acetate, and chromium (II) acetate. Each Mo(II) center in $Mo_2(O_2CCH_3)_4$ has four d valence electrons. These eight d-electrons form one σ, two π bonds, and one δ bond, creating a bonding electron configuration of $\sigma^2\pi^4\delta^2$. Each of these bonds are formed by the overlapping of pairs of d orbitals.[3] The four acetate groups bridge the two metal centers. The Mo-O bond between each Mo(II) center and O atom from acetate has a distance of 2.119 Å, and the Mo-Mo distance between the two metal centers is 2.0934 Å.

3 - Preparation

$Mo_2(O_2CCH_3)_4$is prepared by treating molybdenum hexa carbonyl (Mo $(CO)_6$) with acetic acid. The process strips CO ligands from hexacarbonyl results in the oxidation of Mo (0) to Mo (II).

$$2\ Mo(CO)_6 + 4\ HO_2CCH_3 \rightarrow Mo_2(O_2CCH_3)_4 + 12\ CO + 2\ H_2$$

Trinuclear clusters are byproducts.

The reaction of HO_2CCH_3 and $Mo(CO)_6$ was first investigated by Bannister et al. in 1960. At the time, quadruple metal-metal bonds had not yet been discovered, so these authors proposed that "$Mo(O_2CCH_3)_2$ was tetrahedral . This perspective changed with Mason's characterization .

4 - Applications

$Mo_2(O_2CCH_3)_4$ is generally used as an intermediate compound in a process to form other quadruply bonded molybdenum compounds The acetate ligands can be replaced to give new compounds such as $[Mo_2Cl_8]^{4-}$ and $Mo_2Cl_4[P(C_4H_9)_3]_4$.

Nickel (II) Acetate

Contents

1 - Introduction

Nickel (II) acetate (Ni $(CH_3COO)_2$) is an inorganic compound of nickel and acetic acid. This inorganic compound is usually found as the tetrahydrate. It is used for electroplating.

It can be made by reacting nickel or nickel (II) carbonate with acetic acid.

$$Ni + 2\ CH_3COOH \rightarrow C_4H_6NiO_4 + H_2$$
$$NiCO_3 + 2\ CH_3COOH \rightarrow C_4H_6NiO_4 + CO_2 + H_2O$$

The green tetrahydrate has been determined by X-ray crystallography to be octahedral about the central nickel atom, coordinated by four water molecules and two acetate fragments.[3] It may be dehydrated *in vacuo*, by reaction with acetic anhydride,[4] or by heat.

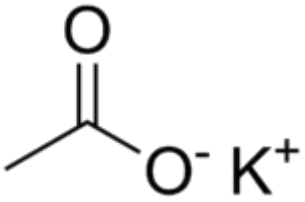
Systematic name :
Nickel (2+) diacetate

Molecular formula	$C_4\,H_6\,Ni\,O_4$
Molar mass	177 g mol^{-1}
Appearance	Green Solid
Odor	slight acetic acid
Density	1.798 g / cm^3 (anyhdrous) 1.744 g / cm^3 (tetrahydrate)
Melting point	decomposes when heated
Solubility in water	Easily soluble in cold water, hot water
Solubility	Soluble in methanol insoluble in diethyl ether, n-octanol

2 - Safety

Nickel salts are carcinogenic and irritate the skin.

Potassium Acetate



Contents

1 - Introduction

Potassium acetate (CH_3CO_2K) is the potassium salt of acetic acid.

Other names :
Potassium salt ;
E261

Molecular formula	CH_3CO_2K
Molar mass	98 g / mol
Appearance	White deliquescent crystalline powder
Density	1.57 g / cm^3
Melting point	292 °C
Solubility in water	253 g / 100 mL (20 °C) 492 g / 100 mL (62 °C)
Solubility	soluble in methanol, ethanol, liquid ammonia insoluble in ether, acetone
LD_{50}	3250 mg / kg (oral, rat)

2 - Preparation

It can be prepared by treating a potassium-containing base such as potassium hydroxide or potassium carbonate with acetic acid:

$2\ CH_3COOH + K_2CO_3 \rightarrow 2\ CH_3CO_2K + CO_2 + H_2O$

This sort of reaction is known as an acid-base neutralization reaction. Potassium acetate is the salt that forms along with water as acetic acid and potassium hydroxide are neutralized together.

Conditions/substances to avoid are: moisture, heat, flames, ignition sources, and strong oxidizing agents.

3 - Applications

Potassium acetate is used as a catalyst in the production of polyurethanes.

Potassium acetate can be used as a deicer instead of chloride salts such as calcium chloride or magnesium chloride. It offers the advantage of being less aggressive on soils and much less corrosive, and for this reason is preferred for airport runways. It is, however, more expensive. Potassium acetate is also the extinguishing agent used in class K fire extinguishers because of its ability to cool and form a crust over burning oils.

3 – 1 - Food additive

Potassium acetate is used as a food additive as a preservative and acidity regulator. In the European Union, it is labeled by the E number E261 ; it is also approved for usage in the USA and Australia and New Zealand. Potassium diacetate (CAS # 4251-29-0) with formula $KH(O_2CCH_3)_2$ is a related food additive with the same E number as potassium acetate.

3 – 2 - Medicine and biochemistry

In medicine, potassium acetate is used as part of replacement protocols in the treatment of diabetic ketoacidosis because of its ability to break down into bicarbonate and help neutralize the acidotic state.

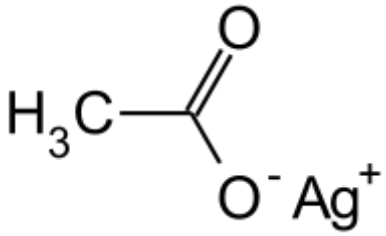
In molecular biology, potassium acetate is used to precipitate dodecyl sulfate (DS) and DS-bound proteins, allowing the removal of proteins from DNA. It is also used as a salt for the ethanol precipitation of DNA.

Potassium acetate is used in mixtures applied for tissue preservation, fixation, and mummification. Most museums today use the formaldehyde-based method recommended by Kaiserling in 1897 which contains potassium acetate.[5] For example, Lenin's mummy was soaked in a bath containing potassium acetate.

4 - Historical

Potassium acetate was originally used in the preparation of Cadet's fuming liquid, the first organometallic compound produced. It is used as diuretic and urinary alkaliser, and acts by changing the physical properties of the body fluids and by functioning as an alkali after absortion.

Silver Acetate



Contents

1 - Introduction

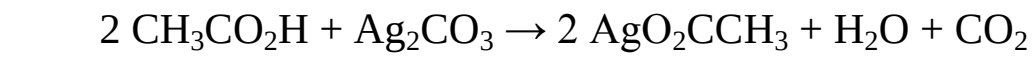
Silver acetate is an organic compound with the empirical formula CH_3COOAg (or $AgC_2H_3O_2$). It is a photosensitive, white crystalline solid. It is a useful reagent in the laboratory as a water soluble source of silver lacking an oxidizing anion. It has been used in some antismoking drugs.

Other names :
Acetic acid , silver (1+) salt
Silver ethanoate

Molecular formula	Ag $C_2H_3O_2$
Molar mass	167 g / mol
Appearance	white to slightly grayish powder slightly acidic odor
Density	3.26 g / cm^3 , solid
Boiling point	decomposes at 220 °C
Solubility in water	1.02 g /100 mL (20 °C)

2 - Synthesis and structure

The silver acetate salt can be synthesized by the reaction of acetic acid and silver carbonate at 45 – 60 °C. After allowing cooling to room temperature, the solid product precipitates.



$$2\ CH_3CO_2H + Ag_2CO_3 \rightarrow 2\ AgO_2CCH_3 + H_2O + CO_2$$

It can also be precipitated from concentrated aqueous solutions of silver nitrate by treatment with a solution of sodium acetate.

The structure of silver acetate consists of 8-membered $Ag_2O_4C_2$ rings formed by a pair of acetate ligands bridging a pair of silver centres.

3 - Reactions

3 – 1 - Carbonylation

Silver acetate, when combined with carbon monoxide (CO), can induce the carbonylation of primary and secondary amines. Other silver salts can be used but the acetate gives the best yield.

$$2\ R_2NH + 2\ AgOAc + CO \rightarrow [R_2N]_2CO + 2\ HOAc + 2\ Ag$$

3 – 2 - Hydrogenation

Silver acetate in a solution of pyridine absorbs hydrogen and is reduced to metallic silver.

3 – 3 - Direct *ortho* - arylation

Silver acetate is a useful reagent for direct *ortho*-arylation (to install two adjacent substituents on an aromatic ring) for of benzylamines and N-methylbenzylamines. The reaction is palladium-catalized and requires a slight excess of silver acetate.[4] This reaction is shorter than previous *ortho*-arylation methods.

4 - Uses

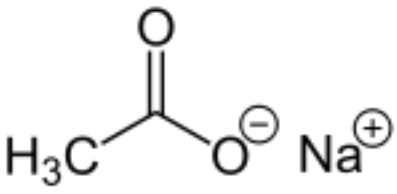
In the health field, silver acetate-containing products have been used in gum, spray, and lozenges to deter smokers from smoking. The silver in these products, when mixed with smoke, creates an unpleasant metallic taste in the smoker's mouth, thus deterring them

from smoking. Lozenges containing 2.5 mg of silver acetate showed "modest efficacy" on 500 adult smokers tested over a three-month period. However, over a period of 12 months, prevention failed. In 1974, silver acetate was first introduced in Europe as an over-the-counter smoking-deterrent lozenge (Repaton) and then three years later as a chewing gum (Tabmint).

5 - Safety

The LD_{50} of silver acetate in mice is 36.7 mg/kg. Low doses of silver acetate in mice produced hyper-excitability, ataxia, central nervous system depression, labored breathing, and even death.[6] The U.S. FDA recommends that silver acetate intake be limited to 756 mg over a short period of time; excessive intake may cause argyria.[5][7]

Sodium Acetate



Contents

1 - Introduction

Sodium acetate, CH_3COONa, also abbreviated NaOAc , also sodium ethanoate, is the sodium salt of acetic acid. This colourless salt has a wide range of uses.

IUPAC name ; Sodium acetate
Systematic name : Sodium ethanoate
Other names :Hot ice (Sodium acetate trihydrate)

Molecular formula	$C_2 H_3 Na O_2$
Molar mass	82 g mol^{-1}
Appearance	White deliquescent powder
Odor	vinegar
Density	1.528 g / cm^3 1.45 g / cm^3 (trihydrate)
Melting point	324 °C (anhydrous) 58 °C (trihydrate)
Boiling point	881.4 °C (anhydrous) 122 °C (trihydrate)(decomposes)
Solubility in water	36.2 g/100 ml (0 °C)

Solubility	46.4 g/100 mL (20 °C) 139 g/100 mL (60 °C) 170.15 g/100 mL (100 °C) soluble in ethanol (5.3 g/100 mL (trihydrate)
Refractive index (n_D)	1.464
Main hazards	Irritant
Flash point	250 °C
Autoignition temperature	607 °C

2 - Applications

2 - 1 - Industrial

Sodium acetate is used in the textile industry to neutralize sulfuric acid waste streams, and as a photoresist while using aniline dyes. It is also a pickling agent in chrome tanning, and it helps to retard vulcanization of chloroprene in synthetic rubber production. In processing cotton for disposable cotton pads, sodium acetate is used to eliminate the buildup of static electricity.

2 - 2 - Concrete longevity

Sodium acetate is used to reduce the damage water can potentially do to concrete by acting as a concrete sealant, while also being environmentally benign and cheaper than the epoxy alternative that is usually employed for sealing concrete against water permeation.

2 - 3 - Food

Sodium acetate may be added to foods as a seasoning. It may be used in the form of sodium diacetate — a 1:1 complex of sodium acetate and acetic acid, given the E-number E262. A frequent use is to impart a salt and vinegar flavor to potato chips.

2 - 4 - Buffer solution

As the conjugate base of acetic acid, a solution of sodium acetate and acetic acid can act as a buffer to keep a relatively constant pH.

This is useful especially in biochemical applications where reactions are pH dependent in a mildly acidic range (pH 4 - 6).

2 - 5 - Heating pad

Sodium acetate is also used in consumer heating pads or hand warmers and is also used in hot ice. Sodium acetate trihydrate crystals melt at 58.4°C , (to 58°C) dissolving in their water of crystallization. When they are heated to around 100°C, and subsequently allowed to cool, the aqueous solution becomes supersaturated. This solution is capable of cooling to room temperature with out forming crystals. By clicking on a metal disc in the heating pad, a nucleation centre is formed which causes the solution to crystallize into solid sodium acetate trihydrate again. The bond-forming process of crystallization is exothermic . The latent heat of fusion is about 264 – 289 kJ / kg . Unlike some other types of heat packs that depend on irreversible chemical reactions, sodium acetate heat packs can be easily recharged by placing in boiling water for a few minutes until all crystals are dissolved; they can be reused many times .

3 - Preparation

For laboratory use, sodium acetate is very inexpensive, and is usually purchased instead of being synthesized. It is sometimes produced in a laboratory experiment by the reaction of acetic acid (ethanoic acid) with sodium carbonate, sodium bicarbonate, or sodium hydroxide. These reactions produce aqueous sodium acetate and water. Carbon dioxide is produced in the reaction with sodium carbonate and bicarbonate, and it leaves the reaction vessel as a gas (unless the reaction vessel is pressurized). This is the well-known "volcano" reaction between baking soda (sodium bicarbonate) and vinegar.

$$CH_3COOH + NaHCO_3 \rightarrow CH_3COONa + H_2O + CO_2$$

Industrially, sodium acetate is prepared from glacial acetic acid and sodium hydroxide.

$$CH_3COOH + NaOH \rightarrow CH_3COONa + H_2O$$

4 - Reactions

Sodium acetate can be used to form an ester with an alkyl halide such as bromo ethane:

$$CH_3COONa + Br\,CH_2CH_3 \rightarrow CH_3COOCH_2CH_3 + NaBr$$

Caesium salts catalyze this reaction.

Zinc Acetate

Contents

1 - Introduction

Zinc acetate is the chemical compound with the formula $Zn(O_2CCH_3)_2$, which commonly occurs as a dihydrate $Zn(O_2CCH_3)_2(H_2O)_2$. Both the hydrate and the anhydrous forms are colorless solids that are commonly used in chemical synthesis and as dietary supplements. Zinc acetates are prepared by the action of acetic acid on zinc carbonate or zinc metal. When used as a food additive, it has the E number E650.

IUPAC name : Zinc acetate
Other names :
Acetic acid, Zinc salt
Acetic acid, Zinc (II) salt
Dicarbomethoxyzinc
Zinc diacetate

Molecular formula	$C_4H_{10}O_6Zn$ (dihydrate)
Molar mass	219.50 g/mol (dihydrate) 183.48 g/mol (anhydrous)
Appearance	White solid (all forms)
Density	1.735 g/cm^3 (dihydrate)
Melting point	Decomposes 237 °C (dihydrate loses water at 100 °C)
Boiling point	decomp.
Solubility in water	43 g / 100 mL (20 °C, dihydrate)
Solubility	soluble in alcohol
Main hazards	mildly toxic

2 - Basic properties and structures

The acetate group is capable of binding to metal ions in a variety of ways through its two oxygen atoms and several connectivities are observed for the various hydrates of zinc acetate. Anhydrous zinc acetate adopts a polymeric structure consisting of zinc coordinated to four oxygen atoms in a tetrahedral environment, each tetrahedron being connected to neighbors by the acetate groups . The acetate ligands are not bidentate. In contrast, most metal diacetates feature metals in octahedral coordination with bidentate acetate groups. In zinc acetate dihydrate the zinc is octahedral, wherein both acetate groups are bidentate.

2 – 1 - Basic zinc acetate

Heating $Zn(CH_3CO_2)_2$ in a vacuum results in loss of acetic anhydride, leaving a residue of "basic zinc acetate," with the formula $Zn_4O(CH_3CO_2)_6$. This cluster compound has the tetrahedral structure shown below. This species closely resembles the corresponding beryllium compound, although it is slightly expanded with Zn-O distances ~1.97 vs ~1.63 Å for $Be_4O(OAc)_6$.

3 - Applications

3 – 1 - Dietary and medicinal applications

Zinc acetate is used as a dietary supplement and in lozenges used to treat the common cold. Zinc acetate alone is thought to be a more effective treatment than zinc gluconate.

Zinc acetate can also be used to treat zinc deficiencies. As an oral daily supplement it is used to inhibit the body's absorption of copper as part of the treatment for Wilson's disease. Zinc acetate is also sold as an astringent in the form of an ointment, a topical lotion; or combined with an antibiotic such as erythromycin for the topical treatment of acne. Furthermore Zinc acetate is commonly sold as a topical anti-itch ointment.

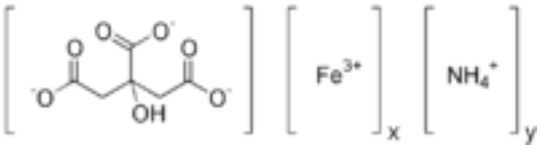
In chewing gum , zinc acetate is a breath freshener and plaque inhibitor.

3 – 2 - Industrial applications

Industrial applications include wood preserving, manufacturing other zinc salts, polymers, manufacture of ethylene acetate, as a dye mordant, and analytical reagent.

Zinc acetate is a precursor via a sol-gel route to the transparent semi conductor zinc oxide.

Ammonium Ferric Citrate



Ammonium ferric citrate is a food additive with E number E381 used as an acidity regulator. It is a green or reddish-brown powder which is very soluble in water.

The molecular formula of ammonium iron (III) citrate is variable. It can be prepared by adding $Fe(OH)_3$ to an aqueous solution of citric acid and ammonia . The brown form is approximately 9% NH_3, 16.5 – 18.5 % Fe , and 65 % hydrated citric acid; the green form is approximately 7.5 % NH_3 , 14.5 – 16 % Fe, and 75% hydrated citric acid. The green type is more readily reduced by light than the brown.

Other uses for ammonium ferric citrate include water purification and printing (cyano type). It is used as a reducing agent of metal salts of low activity like gold and silver and is also in a commonly used recipe with potassium ferricyanide to make cyanotype prints. Ammonium ferric citrate is also used in Kligler iron deeps to determine hydrogen sulfide production in microbial metabolism.

In medicine, ammonium ferric citrate is used as a contrast medium. It is also used as a hematinic.

IUPAC name :
2-Hydroxy propane-1,2,3-tricarboxylate, ammonium iron (3+) salt
Other names :
Ferric ammonium citrate;
Ammonium Iron(III) Citrate; Ammonium ferric citrate;
Iron ammonium citrate;
Prothoate+

Molecular formula	$C_6H_{5+4y}Fe_xN_yO_7$
Molar mass	Variable
Appearance	Reddish-brown powder

Calcium Citrate

Contents

1 - Introduction

Calcium citrate is the calcium salt of citric acid. It is commonly used as a food additive (E333), usually as a preservative, but sometimes for flavor. In this sense, it is similar to sodium citrate. Calcium citrate is also used as a water softener because the citrate ions can chelate unwanted metal ions. Calcium citrate is also found in some dietary calcium supplements (e.g. Citracal). Calcium makes up 21% of calcium citrate by weight.

IUPAC name ;
2-hydroxy-1,2,3-propane- tricarboxylic acid calcium salt (2:3)
Other names : E333

Molecular formula	$Ca_3(C_6H_5O_7)_2$
Molar mass	498 g / mol (anhydrous) 570 g / mol (tetrahydrate)
Appearance	White powder
Odor	odorless
Density	1.63 g /cm^3, solid
Melting point	120 °C (loses water)
Boiling point	Decomposes
Solubility in water	0.085 g /100 mL (18 °C) 0.095 g /100 mL (25 °C)
Solubility	insoluble in alcohol

2 - Chemical properties

Calcium citrate is an odorless white powder, practically insoluble in cold water.

Like citric acid, calcium citrate has a sour taste. Like other salts, however, it also has a salty taste. This should not be confused with the product commonly found in grocery stores labeled as "sour salt", which is simply powdered citric acid (which only resembles salt superficially).

3 - Production

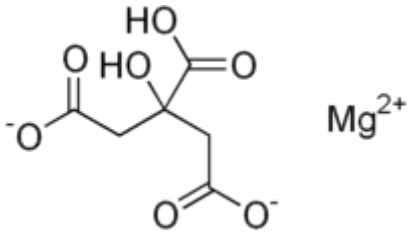
Calcium citrate is an intermediate in the isolation of citric acid from the fermentation process by which citric acid is produced industrially. The citric acid in the broth solution is neutralized by calcium hydroxide, precipitating insoluble calcium citrate. This is then filtered off from the rest of the broth and washed to give clean calcium citrate.

The calcium citrate thus produced may be sold as-is, or it may be converted to citric acid using dilute sulfuric acid.

4 - Biological role

In many individuals, bioavailability of calcium citrate is found to be equal to that of the cheaper calcium carbonate.[2] However, alterations to the digestive tract may change how calcium is digested and absorbed. Unlike calcium carbonate, which is basic and neutralizes stomach acid, calcium citrate has no effect on stomach acid. Individuals who are sensitive to antacids or who have difficulty producing adequate stomach acid should choose calcium citrate over calcium carbonate for supplementation. According to recent research into calcium absorption after gastric bypass surgery , calcium citrate may have improved bioavailability over calcium carbonate in Roux-en-Y gastric bypass patients who are taking calcium citrate as a dietary supplement after surgery. This is mainly due to the changes related to where calcium absorption occurs in the digestive tract of these individuals.

Magnesium Citrate



Contents

1 - Introduction

Magnesium citrate , a magnesium preparation in salt form with citric acid, is a chemical agent used medicinally as a saline laxative and to completely empty the bowel prior to a major surgery or colonoscopy. It is available without a prescription, both as a generic or under the brand name *Citromag* or *Citroma*. It is also used in pill form as a magnesium dietary supplement. The magnesium content of magnesium citrate corresponds to about 11 % by mass.

As a food additive, magnesium citrate is used to regulate acidity and is known as E number E345.

IUPAC name :
Magnesium 2- hydroxypropane -1,2,3 - tricarboxylate

Molecular formula	$C_6 H_6 Mg O_7$
Molar mass	214 g mol^{-1}
Solubility in water	20 g / 100 ml

2 - Mechanism of action

Magnesium citrate works by attracting water through the tissues by a process known as osmosis. Once in the intestine, it can attract enough water into the intestine to induce defecation. The additional water stimulates bowel motility. This means it can also be used to treat rectal and colon problems. Magnesium citrate functions best on an empty stomach, and should always be followed with a full (eight

ounce) glass of water or juice to help the magnesium citrate absorb properly and help prevent any complications. Magnesium citrate is generally not a harmful substance, but care should be taken by consulting a health-care professional if any adverse health problems are suspected or experienced.

3 - Use and dosage

The maximum Upper Tolerable Limit for magnesium in supplement form for adults is 350 mg per day of elemental magnesium according to the National Institutes of Health (NIH).[1] In addition, according to the NIH, total dietary requirements for magnesium from all sources (i.e. food and supplements) is 320–420 mg of elemental magnesium per day, though there is no upper tolerance limit (UTL) for dietary Magnesium. As a laxative syrup with a concentration of 1.745 g of magnesium citrate per fl. oz, a typical dose for adults and children twelve years or older is between 7 and 10 US fluid ounces (210 and 300 ml; 7.3 and 10 imp fl oz), followed immediately with a full 8 US fluid ounces (240 ml; 8.3 imp fl oz) glass of water. Consuming an adult dose of 10 oz of laxative syrup (@ 1.745 g / oz) implies a consumption of 17.45 g of magnesium citrate in a single 10 oz dose resulting in a consumption of approximately 2.0 g of elemental magnesium per single dose. Given that this laxative dose contains five times the recommended nutritional dose for magnesium, caution should be taken to avoid prolonged usage (i.e. over five days) and to follow the manufacturer's instructions strictly . For children between three and twelve years of age, the typical dose is roughly half that , based on physician recommendation. Magnesium citrate is not recommended for use in children and infants two years of age or less .

Although less common, as a magnesium supplement the citrate form is sometimes used due to its increased bio-availability to other common pill forms, such as magnesium oxide . However, according to one study, magnesium gluconate is marginally more bio-available than magnesium citrate.

Magnesium citrate, as a supplement in pill form, is useful for the prevention of kidney stones.

4 - Side effects

It is always important to correctly follow the prescribed doses; extreme magnesium overdose can result in serious complication such as slow heart beat, low blood pressure, nausea, drowsiness, etc. If severe enough, an overdose can even result in coma or death.[5] However, a moderate overdose will be excreted through the kidneys, unless one suffers from serious kidney problems.

Magnesium citrate solutions generally produce bowel movement in one half to six hours. Rectal bleeding or failure to have a bowel movement after use could be signs of a serious condition.

Potassium Citrate

Contents

1 - Introduction

Potassium citrate is a potassium salt of citric acid with the molecular formula $C_6H_5K_3O_7$. It is a white, slightly hygroscopic crystalline powder. It is odorless with a saline taste.

As a food additive, potassium citrate is used to regulate acidity and is known as E number E332. Medicinally, it may be used to control kidney stones derived from either uric acid or cystine.

IUPAC name ; tripotassium citrate

Molecular formula	$C_6H_5K_3O_7$
Molar mass	306 g / mol
Appearance	white powder hygroscopic
Odor	odorless
Density	1.98 g / cm^3
Melting point	180 °C
Boiling point	230 °C
Solubility in water	soluble
Solubility	soluble in glycerin insoluble in ethanol (95%)
LD_{50}	170 mg/kg (IV, dog)

2 -Production

Potassium citrate is produced by adding potassium bicarbonate or potassium carbonate to a solution of citric acid until effervescence ceases, filtering the solution and evaporating to granulation.

3 - Uses

Potassium citrate is rapidly absorbed when given by mouth and is excreted in the urine. Since it is an alkaline salt it is effective in

reducing the pain and frequency of urination when these are caused by highly acidic urine . It is used for this purpose in dogs and cats, but is chiefly employed as a non-irritating diuretic.

Potassium citrate is an effective way to treat/manage gout and arrhythmia, if the patient is hypokalemic.

It is widely used to treat urinary calculi (kidney stones) and is often used by patients with cystinuria . A study of 500 patients with recurrent stones found that it reduced the frequency of stones from 2 per year to a half per year.

It is also used as an alkanizing agent in the treatment of mild urinary tract infections such as cystitis.

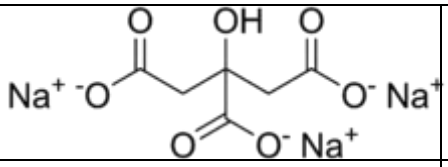
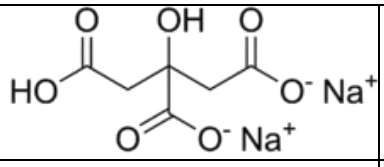
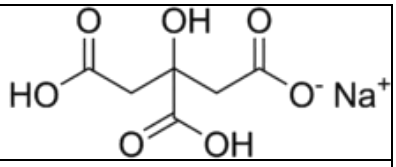
It is also used in many soft drinks as a buffering agent.

4 - Administration

Potassium citrate is usually administered by mouth in dilute aqueous solution. This is because of its somewhat caustic effect on the stomach lining, and the potential for other mild health hazards.

In states where non-prescription potassium citrate is legal, the maximum allowable over-the-counter (OTC) dose for elemental potassium is regulated by the FDA to be no more than 100 mg (approximately 3 % of the daily allowance) . Pure potassium citrate contains 38.28 % potassium.

Sodium Citrate

		
Trisodium citrate	*Disodium citrate*	*Monosodium citrate*

Contents

1 - Introduction

Sodium citrate may refer to any of the sodium salts of citric acid (though most commonly the third):

Mono sodium citrate
Di sodium citrate
Tri sodium citrate

As food additives, the 3 forms of the salt are also collectively known by the E number E331.

2 - Food and Drink

Sodium citrate is some times used as an acidity regulator in drinks, and also as an emulsifier for oils when making cheese. It allows the cheeses to melt with out becoming greasy. Consider the following quote from *Modernist Cuisine*:

Our modernist version of mac and cheese owes its chemistry to James L. Kraft, who in 1916 patented the first American cheese slice. He showed that sodium phosphate keeps the water and fat droplets mixed when the cheese is melted. We use sodium citrate, which has the same effect and is easier to find. The resulting texture is as smooth as melted American cheese, but as complex and intense in flavor as any of your favorite cheeses.

Mono Sodium Citrate

Contents

1 – Introduction

Other names :
sodium dihydrogen 2-hydroxy propane-1,2,3-tricarboxylate
Molecular formula $C_6H_7NaO_7$
Molar mass 214 g mol^{-1}

Mono sodium citrate, or sodium dihydrogen citrate, is an acid salt with the chemical formula $NaH_2C_6H_5O_7$, or $C_3H_4OH(COOH)_2COONa$. Since it has two remaining open spots on the citrate anion, it is used as a relatively strong sequestrant. It is used to prevent platelet clumping in blood samples. It is one of the 3 citric acid salts.

2 - Preparation

Monosodium citrate can be prepared by the direct reaction of sodium carbonate or bicarbonate with citric acid:

$$NaHCO_3\ (s) + C_6H_8O_7\ (aq) \rightarrow NaC_6H_7O_7\ (aq) + CO_2\ (g) + H_2O\ (l)$$

3 - Uses

Monosodium citrate is used as an anticoagulant in donated blood
.

Di Sodium Citrate

Contents

1 - Introduction

IUPAC name :
disodium hydrogen 2-hydroxypropane-1,2,3-tricarboxylate
Molecular formula $C_6H_6Na_2O_7$
Molar mass 236 g mol^{-1}

Disodium citrate, or disodium hydrogen citrate, is a sodium acid salt of citric acid (sodium citrate) with the chemical formula $Na_2HC_6H_5O_7$, or $Na_2H(C_3H_5O(COO)_3)$. It is used as an antioxidant in food as well as to improve the effects of other antioxidants. It is also used as an acidity regulator and sequestrant.

Typical products include gelatin, jam, sweets, ice cream, carbonated beverages, milk powder, wine, and processed cheeses.

2 - As Medicine

Disodium citrate may be used in patients to alleviate discomfort from urinary tract infections.

Tri Sodium Citrate

Contents

1 - Introduction

Trisodium citrate has the chemical formula of $Na_3C_6H_5O_7$. It is some times referred to simply as *sodium citrate*, though sodium citrate can refer to any of the three sodium salts of citric acid. It possesses a saline, mildly tart flavor. For this reason, citrates of certain alkaline and alkaline earth metals (e.g. sodium and calcium citrates) are commonly known as "sour salt" (occasionally citric acid is erroneously termed sour salt).

IUPAC name :
Trisodium citrate
Trisodium 2-hydroxypropane-1,2,3-tricarboxylate
Other names :
Citrosodine
Citric acid, trisodium salt
Sodium citrate

Molecular formula	$Na_3C_6H_5O_7$
Molar mass	258 g / mol (water free), 294 g / mol (dihydrate)
Appearance	White crystalline powder
Density	1.7 g/cm^3
Melting point	> 300 °C hydrates lose water ca. 150 C
Boiling point	Decomposes
Solubility in water	42.5 g / 100 ml (25 °C)
Main hazards	Irritant

2 - Applications

2 – 1 - Food

Sodium citrate is chiefly used as a food additive E331, usually for flavor or as a preservative. Sodium citrate is employed as a flavoring agent in certain varieties of club soda. Sodium citrate is common as an ingredient in Bratwurst, and is also used in commercial ready to drink beverages and drink mixes, contributing a tart flavour.

2 – 2 - Buffer

As a conjugate base of a weak acid, citrate can perform as a buffering agent or acidity regulator, resisting changes in pH. Sodium citrate is used to control acidity in some substances, such as gelatin desserts. It can be found in the mini milk containers used with coffee machines. The compound is the product of antacids, such as Alka-Seltzer, when they are dissolved in water.

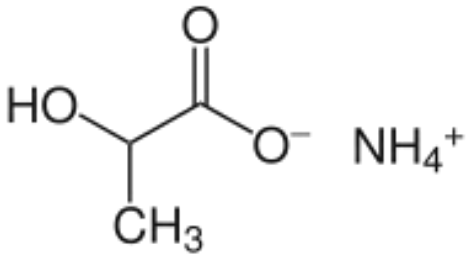
2 – 3 - Medical uses

In 1914, the Belgian doctor Albert Hustin and the Argentine physician and researcher Luis Agote successfully used sodium citrate as an anticoagulant in blood transfusions. It continues to be used today in blood collection tubes and for the preservation of blood in blood banks. The citrate ion chelates calcium ions in the blood by forming calcium citrate complexes, disrupting the blood clotting mechanism.

Sodium citrate is used to relieve discomfort in urinary tract infections, such as cystitis, to reduce the acidosis seen in distal renal tubular acidosis, and can also be used as an osmotic laxative. It is a major component of the WHO Oral Rehydration Solution.

It is used as an antacid, especially prior to anaesthesia, for caesarian section procedures to reduce the risks associated with the aspiration of gastric contents.

Ammonium Lactate



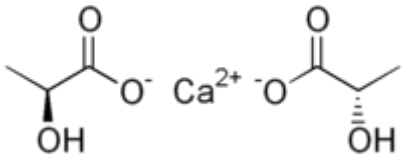
Ammonium lactate is a compound with formula $NH_4(C_2H_4(OH)COO)$. It is the ammonium salt of lactic acid.

It has E number "E328" and is the active ingredient of the skin lotions Amlactin and Lac-Hydrin.

IUPAC name :
azanium 2-hydroxypropanoate
Other names :
Ammonium lactate
Lac-hydrin

Molecular formula	$C_3H_9O_3N$
Molar mass	107.06 g/mol

Calcium Lactate



Calcium lactate is a black or white crystalline salt made by the action of lactic acid on calcium carbonate. It is used in foods (as an ingredient in baking powder) and given medicinally. Its E number is E327. It is created by the reaction of lactic acid with calcium carbonate or calcium hydroxide.

Calcium lactate is often found in aged cheeses. Small crystals of it precipitate out when lactic acid is converted into a less soluble form by the bacteria active during the ripening process.

In medicine, calcium lactate is most commonly used as an antacid and also to treat calcium deficiencies. Calcium lactate can be absorbed at various pHs and does not need to be taken with food for absorption for these reasons.

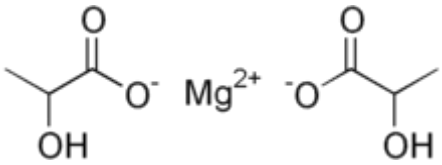
Calcium lactate is added to sugar-free foods to prevent tooth decay. When added to chewing gum containing xylitol, it increases the remineralization of tooth enamel.[1] It is also added to fresh-cut fruits such as cantaloupes to keep them firm and extend their shelf life, without the bitter taste caused by calcium chloride, which can also be used for this purpose.

It is also found in some over the counter (OTC) mouth washes.

IUPAC name :
calcium 2-hydroxy propanoate
Other names :
calcium lactate 5-hydrate,
calcium lactate,
2- hydroxy propanoic acid
calcium salt pentahydrate

Molecular formula	$C_6H_{10}CaO_6$
Molar mass	218 g / mol
Appearance	white or off-white powder
Odor	slightly efflorescent
Density	1.494 g/cm^3
Melting point	240 °C (anhydrous) 120 °C (pentahydrate)
Solubility in water	7.9 g / 100 mL (30 °C)
Solubility	very soluble in ethanol
Refractive index (n_D)	1.470
Flash point	Not applicable
Auto ignition temperature	No data

Magnesium Lactate

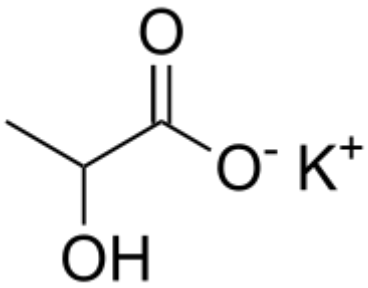


Systematic (**IUPAC**) name	
magnesium 2-hydroxy propanoate	
Metabolism	256 g / mol
Formula	$C_6 H_{10} Mg O_6$
Mol. mass	202 g / mol

Magnesium lactate, the magnesium salt of lactic acid, is a mineral supplement.

Added to some food and beverages as an acidity regulator and labeled as E329.

Potassium Lactate



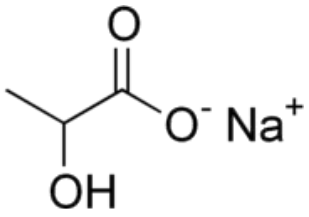
IUPAC name :
Potassium 2-hydroxy propanoate
Molecular formula $C_3H_5KO_3$
Molar mass 128 g / mol

Potassium lactate is a compound with formula $KC_3H_5O_3$, or H3C-CHOH-COOK. It is the potassium salt of lactic acid. It is produced by neutralizing lactic acid which is fermented from a sugar source. It has E number "E326". Potassium lactate is a liquid product that is usually 60% solids but is available at up to 78 % solids.

Potassium lactate is commonly used in meat and poultry products to extend shelf life and increase food safety as it has a broad antimicrobial action and is effective at inhibiting most spoilage and pathogenic bacteria.

Potassium lactate is also used as an extinguishing media in the First Alert Tundra fire extinguishers.

Sodium Lactate



Contents

1 - Introduction

Sodium lactate is the sodium salt of lactic acid that has a mild saline taste. It is produced by fermentation of a sugar source, such as corn or beets, and then, by neutralizing the resulting lactic acid[3] to create a compound having the formula $NaC_3H_5O_3$

As early as 1836, sodium lactate was recognized as a salt of a weak acid rather than being a base, and it was then known that the lactate had to be metabolized in the liver before the sodium could have any titrating activity.

IUPAC name :
Sodium 2-hydroxypropanoate
Other names :
Sodium DL-lactate;
Lactic acid sodium salt;
E325

Molecular formula	$C_3 H_5 Na O_3$
Molar mass	112 g mol^{-1}
Appearance	White powder
Density	1.33 g / mL, 1.31 g/ml (60 % syrup)
Melting point	161–162 °C 17 °C (60 % syrup)
Boiling point	113 °C (60 % syrup)
Solubility in water	> 1.5 g/mL

2 - Usage

As a food additive, sodium lactate has the E number E325 and is naturally a liquid product, but also is available in powder form. It acts as a preservative, acidity regulator, and bulking agent.

Sodium lactate is sometimes used in shampoo products and other similar items such as liquid soaps as it is an effective humectant and moisturizer.

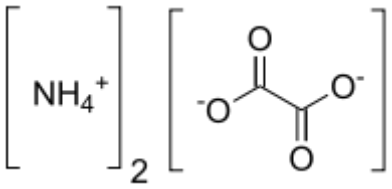
Sodium lactate is used to treat arrhythmias caused by overdosing of class I antiarrythmics, as well as pressor sympathomimetics which can cause hypertension.

It also can be given intravenously as a source of bicarbonate for preventing or controlling mild to moderate metabolic acidosis in patients with restricted oral intake (for sodium bicarbonate) whose oxidative processes are not seriously impaired. However, the use in lactic acidosis is contraindicated.

3 - Regarding milk

Sodium lactate need not be restricted by someone avoiding milk or those with a milk allergy.[3][9] In general, lactates such as sodium, calcium, and potassium lactate are salts derived from the neutralization of lactic acid and most commercially used lactic acids are fermented from dairy - free products such as cornstarch, potatoes, or molasses. Sugar or tapioca additionally may be used. However some lactic acid is fermented from dairy products such as whey[3] and lactose . Whey is made of up 6.5 % solids of which 4.8% is solid lactose . Waste whey typically is used to produce lactic acid when the whey itself is produced as waste during the manufacture of certain dairy products . As a result, such dairy-type lactic acid generally goes back into dairy products, such as ice cream and cream cheese,[10] rather than into non - dairy products. Moreover, although the lactic-acid starter culture to ferment corn or beets may contain milk,[3] sodium lactate does not contain milk protein and need not be restricted by someone avoiding milk or those with a milk allergy.

Ammonium Oxalate

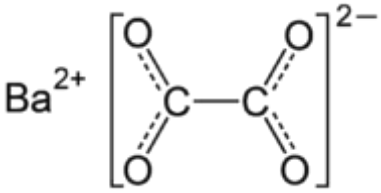


IUPAC name :
Diammonium ethanedioate
Other names :
Diammonium oxalate

Molecular formula	$C_2H_8N_2O_4$
Molar mass	124.10 g mol^{-1}
Appearance	White solid

Ammonium oxalate, $C_2H_8N_2O_4$ (some times written as $(NH_4)_2C_2O_4$), is an oxalate salt with ammonium (sometimes as a monohydrate). It is a constituent of some types of kidney stone.[1][2] Found also in guano.

Barium Oxalate



Barium **oxalate**, a Barium salt of oxalic acid, is a white odourless powder that is sometimes used as a green pyrotechnic colorant generally in specialized pyrotechnic compositions containing magnesium.

Though largely stable, it can be reactive with strong acids. A mild skin irritant, the substance is considered toxic when ingested, causing nausea, vomiting, renal failure and injury to the gastrointestinal tract. Its molecular structure is written as *C2BaO4*. The raw materials that are required to prepare Barium oxalate are oxalic acid, Barium hydroxide octahydrate, and Barium hydroxide.

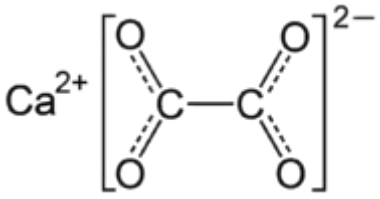
It can also be prepared alternatively by using an oxalic acid solution and a Barium chloride solution, with the reaction as follows:

$$BaCl_2 + (COOH)_2 \ > \ BaC_2O_4 + HCl$$

It is different from most pyrotechnic colorants in that it is a reducing agent, and not an oxidizing agent. It is extremely insoluble in water and converts to the oxide form when heated.

Molecular formula	Ba C_2O_4
Molar mass	225 g / mol
Density	2.658 g / cm^3
Melting point	400 °C (decomp)
Solubility in water	0.9290 mg / L

Calcium Oxalate



Contents

1 - Introduction

Calcium oxalate (in archaic terminology, **oxalate** of lime) is a chemical compound that forms envelope-shaped crystals, known in plants as raphides. A major constituent of human kidney stones, the chemical is also found in beerstone, a scale that forms on containers used in breweries. Its chemical formula is CaC_2O_4 or $Ca(COO)_2$.

IUPAC name :
calcium ethanedioate

Molecular formula	$Ca\ C_2O_4$
Molar mass	128 g / mol, anhydrous 146 g / mol, mono hydrate
Appearance	white solid
Density	2.12 g / cm^3, anhydrous 2.12 g / cm^3, mono hydrate
Melting point	200 °C , decomposes (mono hydrate)
Solubility in water	6.7 mg / L (20 °C)

2 - Occurrence

Many plants are accumulating calcium oxalate (it has been reported in 1000 genera of tree). The calcium oxalate accumulation is linked to the detoxification of calcium (Ca^{2+}) in the plant.

Calcium oxalate is a poisonous substance that can produce sores and numbing on ingestion and could even be fatal.

The poisonous plant dumb cane (*Dieffenbachia*) contains the substance and on ingestion can prevent speech and be suffocating. It is also found in rhubarb (in large quantities in the leaves) and in species of *Oxalis*, Araceae, taro, kiwifruit, tea leaves, agaves, and *Alocasia* and in spinach in varying amounts. Insoluble calcium oxalate crystals are found in plant stems, roots, and leaves and produced in idioblasts.

Calcium oxalate, as ' beer stone ', is a brownish precipitate that tends to accumulate within vats, barrels and other containers used in the brewing of beer. If not completely removed in a cleaning process, beerstone will leave an unsanitary surface that can harbour microorganisms . Beerstone is composed of calcium and magnesium salts and various organic compounds left over from the brewing process; it promotes the growth of unwanted microorganisms that can adversely affect or even ruin the flavor of a batch of beer.

Calcium oxalate crystals in the urine are the most common constituent of human kidney stones, and calcium oxalate crystal formation is also one of the toxic effects of ethylene glycol poisoning.

Hydrated forms of the compound occur naturally as three mineral species: whewellite (monohydrate, known from some coal beds), weddellite (dihydrate) and a very rare trihydrate called caoxite.

3 - Morphology

Most crystals look like a 6 sided prism and often look like a pointed picket from a wooden fence. More than 90 % of the crystals in a urine sediment will have this type of morphology. These other shapes are less common than the 6 sided prism, however it is important to be able to quickly identify them in case of emergency.[4]

4 - Effects of ingestion

Even a small dose of calcium oxalate is enough to cause intense sensations of burning in the mouth and throat, swelling, and choking that could last for up to two weeks . In greater doses it can cause

severe digestive upset, breathing difficulties, coma or even death. Recovery from severe oxalate poisoning is possible, but permanent liver and kidney damage may have occurred.

The stalks of plants in the *Dieffenbachia* genus produce the most severe oxalate reactions. The needle - like oxalate crystals produce pain and swelling when they contact lips, tongue, oral mucosa, conjunctiva, or skin. Edema primarily is due to direct trauma from the needle-like crystals and, to a lesser extent, by other plant toxins (e.g., bradykinins, enzymes).

Depending on the plant ingested, mild (Elephant Ear *Colocasia esculenta*) to more severe (Jack in the Pulpit, *Arisaema*) can cause compromised airways. One bite on the *Arisaema* seed pod will result in immediate swelling and burning. It will take over 12 hours for the swelling to subside .

4 – 1 - Treatment

Medication administered at the emergency room may include diphenhydramine, epinephrine, or famotidine, all intravenously. Although this most likely will be a localized reaction, it will be treated by the ER as an anaphylactic reaction.

5 - Applications

Calcium oxalate is used in the manufacture of ceramic glazes.

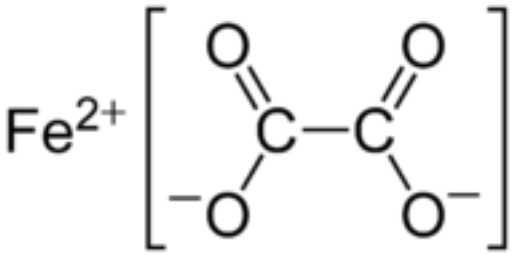
Ferric Ammonium Oxalate

Ferric ammonium oxalate is a chemical compound. It is mostly used for the manufacture of blueprint paper .

IUPAC name :
ammonium iron (3+) ethanedioate (3:1:3)
Systematic name :
ammonium iron (3+) ethanedioate (3:1:3)

Molecular formula	$C_6H_{12}FeN_3O_{12}$
Molar mass	374
Appearance	Green crystals
Solubility in water	Soluble
Solubility in Ethanol	Insoluble

Iron (II) Oxalate



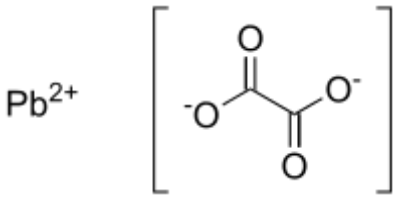
Other names :	
Iron oxalate	
Molecular formula	Fe $C_2 O_4$
Molar mass	144 g / mol
Appearance	yellow powder
Odor	odorless
Density	2.28 g/cm^3 (dihydrate)
Melting point	150-160 °C, decomp (dihydrate)
Solubility in water	slightly soluble

Ferrous oxalate, or iron (II) oxalate, is a chemical compound consisting of one iron (II) ion (Fe^{2+}) and one oxalate ion ($C_2O_4^{2-}$). It has the chemical formula FeC_2O_4.

Iron(II) oxalate is more commonly encountered as the dihydrate, $FeC_2O_4 \cdot 2H_2O$. Its crystal structure consists of chains of oxalate-bridged iron atoms, capped by water molecules .

When heated, it dehydrates and decomposes into carbon dioxide, carbon monoxide, iron oxides and pyrophoric black iron.

Lead (II) Oxalate



Contents

1 - Introduction

Lead(II) oxalate is an inorganic compound with the formula PbC_2O_4. It is naturally found as a heavy white solid.

UN number	2291
Molecular formula	Pb C_2 O_4
Molar mass	295
Appearance	White Powder
Density	5.28 g / cm^3
Melting point	327.4°C
Boiling point	1740°C
GHS pictograms	
Main hazards	Highly Toxic
Eye hazard	Causes irritation.
Skin hazard	Harmful if absorbed in the skin. Causes irritation.
U.S. Permissible exposure limit (PEL)	0.05 mg / m^3, as Pb

2 - Preparation

This compound is commercially available. It may be prepared by the metathesis reaction between lead(II) nitrate and sodium oxalate:[3]

$Pb^{2+}(aq) + C_2O_4^{2-} \rightarrow PbC_2O_4\ (s)$

3 - Solubility

Lead (II) oxalate is sparingly soluble in water. Its solubility is increased in presence of excess oxalate anions, due to the formation of the $Pb(C_2O_4)_2^{2-}$ complex ion.

Potassium Ferri Oxalate

Contents

1 - Introduction

Potassium ferri oxalate , is a chemical compound with the formula $K_3[Fe(C_2O_4)_3]$, where iron is in the +3 oxidation state. It is an octahedral transition metal complex in which three bidentate oxalate ions are bound to an iron center. Potassium acts as a counterion, balancing the -3 charge of the complex. Crystals of the trihydrated form of the complex, $K_3[Fe(C_2O_4)_3]\cdot 3H_2O$, are emerald green in color. In solution, the salt ionizes to give the ferrioxalate anion, $[Fe(C_2O_4)_3]^{3-}$, which appears fluorescent green in color. Potassium ferrioxalate is often used in chemical actinometry.

IUPAC name :
Potassium iron (III) oxalate
Other names :
potassium ferri oxalate

Molecular formula	$K_3[Fe(C_2O_4)_3]$ $K_3[Fe(C_2O_4)_3]\cdot 3H_2O$
Molar mass	437 g / mol - anhydrous 491 g / mol - trihydrate
Appearance	emerald green hydrated crystals
Density	2.13 g /cm^3
Melting point	230 °C
Main hazards	Corrosive. Eye, respiratory and skin irritant.

2 - Preparation

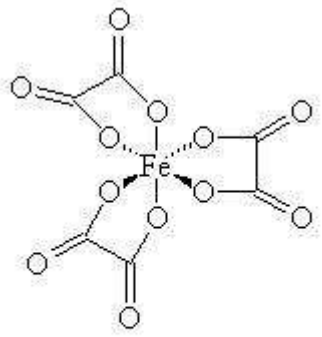
The complex can be synthesized from the reaction between iron (III) sulfate, barium oxalate and potassium oxalate :

$$Fe_2(SO_4)_3 + 3\ BaC_2O_4 + 3\ K_2C_2O_4 \rightarrow 2\ K_3[Fe(C_2O_4)_3] + 3\ BaSO_4$$

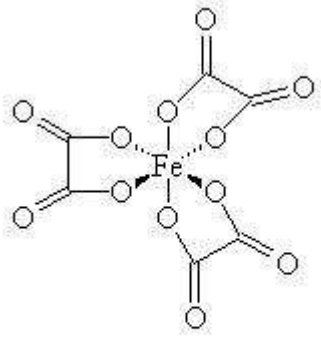
The reactants are dissolved in water and heated for around 1.5 hours. $BaSO_4$ precipitates out leaving behind the newly formed complex in solution. The complex can then be obtained by filtering off the $BaSO_4$ and cooling the solution so that it crystallizes out.

3 - Iso merism

The ferrioxalate complex exhibits optical activity since there are two non-superimposable stereoisomers of the complex. In accordance with the IUPAC convention, the isomer with the left-handed screw axis is assigned the Greek symbol Λ (lambda). Its mirror image with the right-handed screw axis is given the Greek symbol Δ (delta).



Λ-$[Fe(C_2O_4)_3]^{3-}$



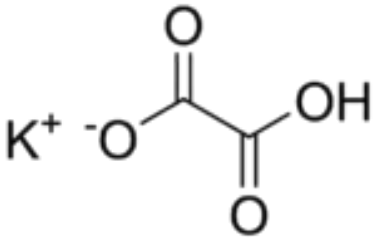
Δ-$[Fe(C_2O_4)_3]^{3-}$

4 - Photoreduction

In solution, the ferrioxalate complex undergoes photoreduction. In this process, the complex absorbs a photon of light and subsequently decomposes to form $Fe(C_2O_4)_2^{2-}$ and CO_2. The iron centre is reduced (gains an electron) from the +3 to the +2 oxidation state while an oxalate ion is oxidised to carbon dioxide :

$$2\ [Fe(C_2O_4)_3]^{3-} + h\nu \rightarrow 2\ [Fe(C_2O_4)_2]^{2-} + C_2O_4^{2-} + 2\ CO_2$$

Potassium Hydrogen Oxalate



Contents

1 Introduction

Potassium hydrogen oxalate, also known as *potassium bioxalate*, is a salt with formula KHC_2O_4 or $K^+ \cdot HO_2C\text{-}CO_2^-$. It is one of the most common salts of the hydrogenoxalate anion, and can be obtained by reacting potassium hydroxide with oxalic acid in 1:1 mole ratio.

The salt is also known as potassium hydrogen oxalate , acid potassium oxalate, or monobasic potassium oxalate. In older literature, it was also called sorrel salt, *sal acetosella* ,

Potassium hydrogen oxalate occurs in some plants, notably sorrel. It is a commercial product, used in photography, marble grinding, and to remove ink stains.

IUPAC name :
Potassium 2-hydroxy-2-oxo acetate
Other names :
Potassium bi oxalate

Molecular formula	C_2HKO_4
Molar mass	128 g mol^{-1}
Appearance	White crystalline solid
Odor	odorless
Density	2.0 g /cm^3
Solubility in water	2.5 g / 100 g
Solubility	slightly soluble in alcohol

2 - Properties

The anhydrous product is a white, odorless, crystalline solid, hygroscopic and soluble in water (2.5 g / 100 g at room temperature). The solutions are basic. Below 50 °C the much less soluble potassium tetraoxalate forms and precipitates out of solution.

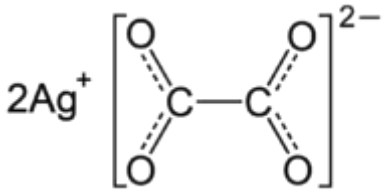
The monohydrate $KHC_2O_4 \cdot H_2O$ starts losing the water at 100 °C.

The anhydrous salt was found to have remarkable elastic anisotropy, due to its crystal structure that consists of relatively rigid columns of hydrogen-bonded hydrogenoxalate anions, joined into sheets by ionic K – O bonds.

3 - Toxicity

Potassium hydrogen oxalate is strongly irritating to eyes, mucoses and gastrointestinal tract. It may cause cardiac failure and death .

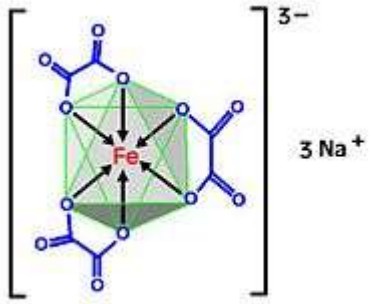
Silver Oxalate



Silver oxalate ($Ag_2C_2O_4$) is commonly employed in experimental petrology to add carbon dioxide (CO_2) to experiments as it will break down to silver (Ag) and the carbon dioxide under geologic conditions . It is explosive upon heating , shock or friction .

Other names :	
Silver Ethane dioate	
Molecular formula	$Ag_2 C_2O_4$
Molar mass	303.755 g/mol
Appearance	white powder
Density	5 g / cm^3
Melting point	140 °C decomp.
Solubility in water	$3.270*10^{-3}$ g / 100mL

Sodium Ferri Oxalate

	
Sodium Ferri tri Oxalate crystals	*Sodium Ferri Oxalate*

Contents

1 - Introduction

Sodium ferri oxalate, also known as sodium oxalatoferrate, is a chemical compound with the formula $Na_3[Fe(C_2O_4)_3]$, where iron is in the +3 oxidation state. It is an octahedral transition metal complex in which three bidentate oxalate ions act as ligands bound to an iron centre. Sodium acts as a counterion, balancing the -3 charge of the complex. Crystals of the hydrated form of the complex, $Na_3[Fe(C_2O_4)_x].xH_2O$, are lime green in colour. In solution the complex dissociates to give the ferrioxalate anion, $[Fe(C_2O_4)_3]^{3-}$, which appears a deep apple green in colour.

IUPAC name :
Sodium ferric (III) oxalate
Other names :
Sodium ferri oxalate
Sodium tri oxalat ferrate (III)

Molecular formula	$Na_3[Fe(C_2O_4)_3]$ $Na_3[Fe(C_2O_4)_3].xH_2O$
Molar mass	389 g / mol - anhydrous 389 + x (18) g / mol - hydrated
Appearance	lime green hydrated crystals
Density	1.97 g / cm^3 at 17 °C
Solubility in water	32.5 pts per 100 pts , cold water, 182 pts per 100pts , boiling water
Main hazards	Corrosive. Eye, respiratory and skin irritant.

2 - Bonding

The bonds to the iron atom are dative covalent bonds where the ligands, (oxalate ions, blue), donate a lone pair into the empty p and d orbitals of the transition metal (iron, red), atom. The three oxalate ions donate 12 electrons in all and Fe-III has three electrons in the d orbitals leaving 13 empty places in the remaining d and p orbitals.

3 - Solubility

This compound is very soluble in hot water, (182 parts per 100 parts solvent by mass), but a lot less soluble in cold water, (32 parts per 100 parts solvent), about the solubility of sodium chloride. It is not appreciably soluble in ethanol or ethanol water mixtures which are more than 50% ethanol by mass. It is somewhat more soluble in water than the corresponding potassium salt.

4 - Preparation

The crystals pictured were synthesised by mixing solutions of sodium oxalate and ferric oxalate and waiting a few hours for the brown colour of the ferric oxalate to be replaced with the green colour of the complex anion. This complex is relatively inert and the equilibrium is attained only slowly at room temperature. The ferric oxalate was made by dissolving rust in oxalic acid and filtering off any residual insolubles. The solution was evaporated at just below boiling until small crystals appeared on the bottom indicating the solution was then hot and saturated. The solution was allowed to cool in a beaker sitting on a large aluminium block. The thermal mass of

the block allowed sufficiently slow cooling over night to produce crystals a few milimetres long. These larger crystals are pictured at the upper left.

$$Fe_2(C_2O_4)_3 + 3\ Na_2(C_2O_4) \rightarrow 2\ Na_3[Fe(C_2O_4)_3]$$

Stoichiometry was not worried about and an excess of sodium oxalate was added, this is a lot less soluble in hot water than the ferrioxalate and crystallizes out first. The intensity of the green colour was used as a guide to concentration of the solution with respect to the complex. A few drops of 100 vol hydrogen peroxide were periodically added during the evaporation to maintain the iron in the III oxidation state and any insoluble ferrous oxalate was removed if it precipitated out.

The smaller crystals were recovered from the solution by placing it in the freezer after the large crystals had been removed. The smallest crystals, pictured at the lower right were precipitated from the cold solution by addition of methylated spirit.

5 - Iso merism

The ferri oxalate complex demonstrates optical activity since there are two non-superimposable stereoisomers of the complex. This is described in more detail under potassium ferrioxalate. Theoretically the two stereoisomers could be separated by crystallization of a diastereomeric salt of the optically inactive racemic mixture of ferrioxalate ions with an optically active cation, such as methylethylpropylammonium ion which is one pure enantomer. Thus methylethylpropylammonium ferrioxalate should crystallize out to produce crystals which are non superimposable mirror images. These would be Λ-methyl ethyl propyl ammonium Λ-ferri oxalate and Λ-methyl ethyl propyl ammonium Δ-ferri oxalate.

6 - Photo reduction

In solution the ferrioxalate complex is decomposed by light. This is described in more detail under potassium ferrioxalate. Some samples of the crystals were exposed to direct sunlight for a few hours, the larger crystals did not appear to be affected, however

solutions and small crystals so exposed did change colour to a different shade of green.

If a solution containing both green ferrioxalate ions and colourless free oxalate ions is exposed to strong light, such as direct sunlight, the light allows the Iron-III to oxidize one of the oxalate ligands to carbon dioxide and gives the orange-brown ferrooxalate complex ion which is coordinated around an Iron-II centre, however, when placed in the dark the Iron - II is re - oxidized to Iron-III by the oxygen in the atmosphere and the green ferrioxalate complex ion re-forms. The orange - brown Iron - II complex starts to appear after around ten minutes exposure and after the passage of a few hours in direct sunlight more than half of the green Iron - III complex had been reduced. The re-oxidation in the dark is equally slow and observable under ambient electric lighting. If this process is allowed to repeat over many months, such as leaving a container outside where it is exposed to the sun each day, eventually almost all of the oxalate ions present are oxidized to carbonate and the iron remains as Ferric Hydroxide, $Fe(OH)_3$.

This indicates that when exposed to the environment, particularly if that environment is damp the ferrioxalate ion is quite unstable and gradually decomposes via the above redox processes into much more stable and common compounds.

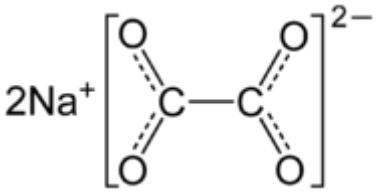
This light catalyzed redox reaction once formed the basis of some photographic processes, however due to their insensitivity and the ready availability of digital photography these processes have become obsolete and all but forgotten.

7 - Uses

In contemporary times ferrioxalate salts, usually the potassium salt, are used as exampls of a transition metal ligand complexes which can be easily synthesized by high school, college or undergraduate university students to introduce them to transition metal ligand chemistry, as well as to redox chemistry in now-obsolete photographic processes.

The process of blueprint making, now also nearly obsolete, makes use of Iron-cyanide ligand complexes such as Ferricyanide and Ferrocyanide and redox reactions related to them. The presence of free Iron-II ions and oxalate ions gives rise to a whole family of Iron centered ligand complexes exhibiting intense blue colours. The best known of these is Prussian Blue, Potassium Ferrous Ferrocyanide.[2]

Sodium Oxalate



Contents

1 - Introduction

Sodium oxalate, or disodium oxalate, is the sodium salt of oxalic acid with the molecular formula $Na_2C_2O_4$. It is usually a white, crystalline, odorless powder, that decomposes at 250 – 270 °C.

Disodium oxalate can act as a reducing agent, and it may be used as a primary standard for standardizing potassium permanganate ($KMnO_4$) solutions.

The mineral form of sodium oxalate is natroxalate. It is only very rarely found and restricted to extremely sodic conditions of ultra-alkaline pegmatites.

IUPAC name :
Sodium ethane dioate
Other names :
Oxalic acid di sodium salt

Molecular formula	$Na_2 C_2O_4$
Molar mass	134 g mol^{-1}
Density	2.34 g cm^{-3}
Solubility in water	3.7 g /100 mL (20 °C) 6.25 g/100 mL (100 °C)
Solubility	insoluble in alcohol
EU classification	 Xn

2 - Preparation

Sodium oxalate can be prepared through the neutralization of oxalic acid with sodium hydroxide (NaOH) in a 1:2 acid-to-base molar ratio. Half-neutralization can be accomplished with NaOH in a 1:1 ratio which produces $NaHC_2O_4$, monobasic sodium oxalate or sodium hydrogenoxalate.

3 - Reactions

Sodium oxalate is used to standardize potassium permanganate solutions. It is desirable that the temperature of the titration mixture is greater than 60 °C to ensure that all the permanganate added reacts quickly. The kinetics of the reaction is complex, and the manganate (II) ions formed catalyze the further reaction between permanganate and oxalic acid (formed *in situ* by the addition of excess sulfuric acid). The final equation is as follows:

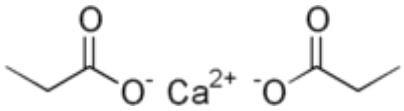
$$5Na_2C_2O_4 + 2KMnO_4 + 8H_2SO_4 \rightarrow K_2SO_4 + 2MnSO_4 + 10CO_2 + 8H_2O$$

4 -Biological activity

Like several other oxalates, sodium oxalate is toxic to humans. It can cause burning pain in the mouth, throat and stomach, bloody vomiting, headache, muscle cramps, cramps and convulsions, drop in blood pressure, heart failure, shock, coma, and possible death. Mean lethal dose by ingestion of oxalates is 10 -15 grams (per MSDS).

Sodium oxalate, like citrates, can also be used to remove calcium ions (Ca^{2+}) from blood plasma. It also prevents blood from clotting. Note that by removing calcium ions from the blood, sodium oxalate can impair brain function, and deposit calcium oxalate in the kidneys.

Calcium Propanoate



Contents

1 - Introduction

Calcium propanoate or calcium propionate has the formula $Ca(C_2H_5COO)_2$. It is the calcium salt of propanoic acid.

IUPAC name :	
Calcium propanoate	
Other names :	
Calcium propionate	
Mycoban	
Molecular formula	$C_6H_{10}CaO_4$
Molar mass	186 g / mol
Appearance	White crystalline solid
Solubility in water	49 g /100 mL (0 °C) 55.8 g /100 mL (100 °C)
Solubility	slightly soluble in methanol, ethanol insoluble in acetone , benzene

2 - Uses

As a food additive, it is listed as E number 282 in the Codex Alimentarius. Calcium propanoate is used as a preservative in a wide variety of products, including but not limited to bread, other baked goods, processed meat, whey, and other dairy products. In agriculture, it is used, amongst other things, to prevent milk fever in cows and as a feed supplement Propanoates prevent microbes from producing the energy they need, like benzoates do. However, unlike benzoates, propanoates do not require an acidic environment.

Calcium propanoate is used in bakery products as a mold inhibitor, typically at 0.1- 0.4 % (though animal feed may contain up to 1 %) . Mold contamination is considered a serious problem amongst bakers, and conditions commonly found in baking present near-optimal conditions for mold growth.

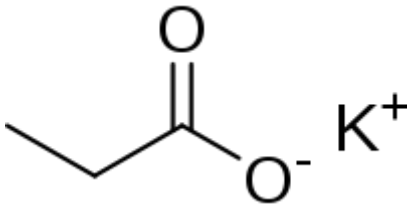
A few decades ago, *Bacillus mesentericus* (rope), was a serious problem , but today's improved sanitary practices in the bakery, combined with rapid turnover of the finished product, have virtually eliminated this form of spoilage . Calcium propanoate and sodium propanoate are effective against both *B. mesentericus* rope and mold.

Metabolism of propanoate begins with its conversion to propionyl coenzyme A (propionyl – Co A), the usual first step in the metabolism of carboxylic acids. Since propanoic acid has three carbons, propionyl - CoA can directly enter neither beta oxidation nor the citric acid cycles. In most vertebrates, propionyl-CoA is carboxylated to D- methyl malonyl - CoA , which is isomerised to L-methylmalonyl - CoA. A vitamin B_{12}-dependent enzyme catalyzes rearrangement of L-methylmalonyl - CoA to succinyl- CoA, which is an intermediate of the citric acid cycle and can be readily incorporated there.

When propanoic acid is infused directly into rodents' brains, it produces reversible behavior changes (e.g. hyperactivity, dystonia, social impairment, perseveration) and brain changes (e.g. innate neuroinflammation, glutathione depletion) that may be used as a model of human autism in rats.

According to the Pesticide Action Network North America, calcium propionate is slightly toxic . This rating is not uncommon for food products; vitamin C is also rated by the same standards as being slightly toxic . Calcium propanoate can be used as a fungicide on fruit.

Potassium Propanoate



Contents

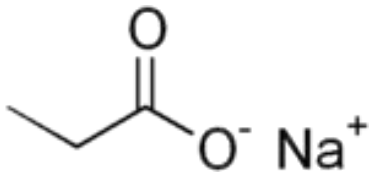
Potassium propanoate or potassium propionate has formula $K(C_2H_5COO)$. Its melting point is 410 °C. It is the potassium salt of propanoic acid.

Other names :	
Potassium propionate ;	
E283	
Molecular formula	$C_3 H_5 K O_2$
Molar mass	112 g / mol
Appearance	Colorless crystalline platelets
Melting point	> 300 °C
Solubility in water	soluble
Solubility in ethanol	soluble

2 - Use

It is used as a food preservative and is represented by the food labeling E number E283 in Europe and by the INS number 283 in Australia and New Zealand.

Sodium Propionate



Contents

1 - Introduction

Sodium propanoate or sodium propionate is the sodium salt of propionic acid which has the chemical formula $Na(C_2H_5COO)$.

IUPAC name :
Sodium propanoate
Other names :
Sodium propionate
Napropion

Molecular formula	$C_3 H_5 Na O_2$
Molar mass	96 g / mol
Appearance	Transparent crystals
Odor	faint acetic - butyric odor
Melting point	289 °C
Solubility in water	~ 1 g / mL

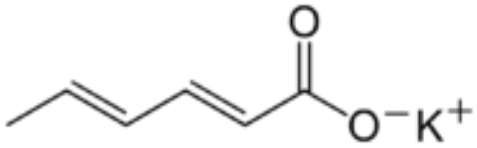
2 - Reactions

It is produced by the reaction of propionic acid and sodium carbonate or sodium hydroxide.

3 - Uses

It is used as a food preservative and is represented by the food labeling E number E281 in Europe; it is used primarily as a mold inhibitor in bakery products. It is approved for use as a food additive in the EU, USA and Australia and New Zealand (where it is listed by its INS number 281) .

Potassium Sorbate



Contents

1 - Introduction

Potassium sorbate is the potassium salt of sorbic acid, chemical formula $C_6H_7KO_2$. Its primary use is as a food preservative (E number 202).[3] Potassium sorbate is effective in a variety of applications including food, wine, and personal care products. Commercial sources are now produced by the condensation of crotonaldehyde and ketene (Ashford, 1994).

IUPAC name :
Potassium (2*E*,4*E*)-hexa-2,4-dienoate
Other names :
E202
Sorbistat-K
Sorbistat potassium

Molecular formula	$C_6 H_7 K O_2$
Molar mass	150 g mol^{-1}
Appearance	White crystals
Odor	yes
Density	1.363 g / cm^3
Melting point	270 °C (decomp.)
Solubility in water	58.5 g/100 mL (100 °C)
Solubility in other solvents	Soluble in ethanol, propylene glycol Slightly soluble in acetone

	Very slightly soluble in chloroform , corn oil , ether Insoluble in benzene
LD_{50}	4920 mg/kg (rat, oral)

2 - Properties

Potassium sorbate is produced by neutralizing potassium hydroxide with sorbic acid, an unsaturated carboxylic acid that occurs naturally in some berries. The colourless salt is very soluble in water (58.2% at 20 °C).

3 -Production

Potassium sorbate is produced by reacting sorbic acid with an equimolar portion of potassium hydroxide. The resulting potassium sorbate may be crystallized from aqueous ethanol.

Most of the sorbic acid is generally prepared by a process comprising the steps of reacting crotonaldehyde with ketene in the presence of a catalyst (e.g., a fatty acid salt of zinc) to yield a polyester, and hydrolyzing the polyester with an acid or an alkali, or decomposing the polyester in a hot water.

4 - Uses

Potassium sorbate is used to inhibit molds and yeasts in many foods, such as cheese, wine, yogurt, dried meats, apple cider, soft drinks and fruit drinks, and baked goods.[6] It can also be found in the ingredients list of many dried fruit products. In addition, herbal dietary supplement products generally contain potassium sorbate, which acts to prevent mold and microbes and to increase shelf life, and is used in quantities at which there are no known adverse health effects, over short periods of time.[7] Labeling of this preservative on ingredient statements reads as "potassium sorbate" and or "E202". Also, it is used in many personal care products to inhibit the development of microorganisms for shelf stability. Some manufacturers are using this preservative as a replacement for parabens.

Also known as "wine stabilizer", potassium sorbate produces sorbic acid when added to wine. It serves two purposes. When active fermentation has ceased and the wine is racked for the final time after clearing, potassium sorbate will render any surviving yeast incapable of multiplying. Yeast living at that moment can continue fermenting any residual sugar into CO_2 and alcohol, but when they die no new yeast will be present to cause future fermentation. When a wine is sweetened before bottling, potassium sorbate is used to prevent refermentation when used in conjunction with potassium metabisulfite. It is primarily used with sweet wines, sparkling wines, and some hard ciders but may be added to table wines which exhibit difficulty in maintaining clarity after fining.

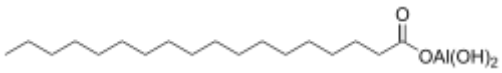
Some molds (notably some *Trichoderma* and *Penicillium* strains) and yeasts are able to detoxify sorbates by decarboxylation, producing piperylene (1,3-pentadiene). The pentadiene manifests as a typical odor of kerosene or petroleum.

5 - Toxicology

Potassium sorbate is a skin, eye and respiratory irritant.[9] Although some research implies it has a long term safety record,[10] in vitro studies have shown that it is both genotoxic and mutagenic to human blood cells. Potassium sorbate is found to be toxic to human DNA in peripheral blood lymphocytes (type of white blood cells), and hence found that it negatively affects immunity.[11] It is often used with ascorbic acid and iron salts as they increase its effectiveness but this tends to form mutagenic compounds that damage DNA molecules.

Potassium sorbate exhibits low toxicity with LD_{50} (rat, oral) of 4.92 g / kg, similar to that of table salt . Typical usage rates of potassium sorbate are 0.025 % to 0.1 % (see sorbic acid), which in a 100 g serving yields intake of 25 mg to 100 mg. Acceptable daily intakes for human is 12.5 mg / kg, or 875 mg daily for an average adult (70 kg), according to FAO/World Health Organization Expert Committee on Food Additives.

Aluminium Mono Stearate



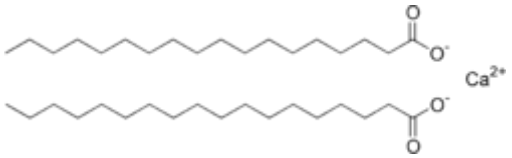
Aluminium mono stearate is an organic compound which is a salt of stearic acid and aluminium. It has the molecular formula $Al(OH)_2C_{18}H_{35}O_2$. It is also referred to as dihydroxy(octa decanoato -O-)aluminium or dihydroxy(stearato) aluminium.

It is used to form gels in the packaging of pharmaceuticals, and in the preparation of colors for cosmetics. It is usually safe in commercial products, but aluminium may accumulate in the body.

IUPAC name :
Dihydroxy(stearoyloxy) aluminium
Other names :
Aluminum mono stearate;
Dibasic aluminum stearate;
Dihydroxy aluminum stearate;
Dihydroxy(octa decanoato-O-)aluminium;
Dihydroxy (stearato) aluminium

Molecular formula	$C_{18}H_{37}AlO_4$
Molar mass	344 g mol^{-1}

Calcium Stearate



Contents

1 - Introduction

Calcium stearate is carboxylate of calcium that is found in some lubricants and surfactants. It is a white waxy powder.

IUPAC name :
Calcium octa decanoate
Other names :
E 470

Molecular formula	$C_{36}H_{70}CaO_4$
Molar mass	607 g mol^{-1}
Appearance	white to yellowish-white powder
Density	1.08 g / cm^3
Melting point	155 °C
Solubility in water	0.004 g /100 mL (15 °C)
	soluble in hot pyridine
Solubility	slightly soluble in oil
	insoluble in alcohol, ether

2 - Production and occurrence

Calcium stearate is produced by heating stearic acid, a fatty acid, and calcium oxide:

$$2\ C_{17}H_{35}COOH + CaO \rightarrow (C_{17}H_{35}COO)_2Ca + H_2O$$

It is also the main component of soap scum, a white solid that forms when soap is mixed with hard water. Unlike soaps containing sodium and potassium, calcium stearate is insoluble in water and does

not lather well . Commercially it is sold as a 50 % dispersion in water or as a spray dried powder. As a food additive it is known by the generic E number E470.

3 - Applications

Calcium stearate is used as a flow agent in powders including some foods (such as Smarties), a surface conditioner in hard candies such as Sprees, a waterproofing agent for fabrics, a lubricant in pencils and crayons.

The concrete industry uses calcium stearate for efflorescence control of cementitious products used in the production of concrete masonry units i.e. paver and block, as well as waterproofing.

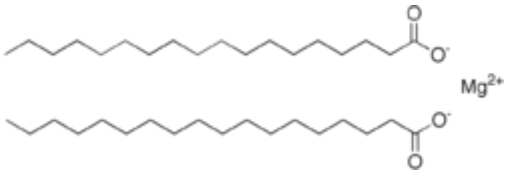
In paper production, calcium stearate is used as a lubricant to provide good gloss, preventing dusting and fold cracking in paper and paperboard making.

In plastics, it can act as an acid scavenger or neutralizer at concentrations up to 1000ppm, a lubricant and a release agent. It may be used in plastic colorant concentrates to improve pigment wetting. In rigid PVC, it can accelerate fusion, improve flow, and reduce die swell.

Applications in the personal care and pharmaceutical industry include tablet mold release, anti-tack agent, and gelling agent.

Calcium stearate is a component in some types of defoamers.

Magnesium Stearate



Contents

1 - Introduction

Magnesium stearate, also called *octa decanoic acid, magnesium salt*, is a white substance, powder which becomes solid at room temperature. It has the chemical formula $Mg(C_{18}H_{35}O_2)_2$. It is a salt containing two equivalents of stearate (the anion of stearic acid) and one magnesium cation (Mg^{2+}). Magnesium stearate melts at about 120 °C, is not soluble in water, and is generally considered safe for human consumption at levels below 2500 mg/kg per day.[1] In 1979, the FDA's Subcommittee on GRAS (generally recognized as safe) Substances (SCOGS) reported, "There is no evidence in the available information on ... magnesium stearate ... that demonstrates, or suggests reasonable grounds to suspect, a hazard to the public when they are used at levels that are now current and in the manner now practiced, or which might reasonably be expected in the future."

IUPAC name :
Magnesium octa decanoate

Molecular formula	$Mg\ (\ C_{18}H_{35}O_2\ )_2$
Molar mass	591 g / mol
Appearance	light white powder
Odor	slight
Density	1.026 g / cm^3
Melting point	88.5 °C
Solubility in water	0.003 g /100 mL (15 °C
Solubility	negliglble in ether and alcohol slightly soluble in benzene

Flash point	250 °C
LD_{50}	> 1000 mg / kg (oral, rat)

2 - Manufacturing

Magnesium stearate is created by the reaction of sodium stearate with magnesium sulfate.

3 - Uses

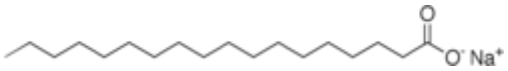
Magnesium stearate is often used as a anti-adherent[3] in the manufacture of medical tablets, capsules and powders.[4] In this regard, the substance is also useful, because it has lubricating properties, preventing ingredients from sticking to manufacturing equipment during the compression of chemical powders into solid tablets; magnesium stearate is the most commonly used lubricant for tablets.[5] Studies have shown that magnesium stearate may affect the release time of the active ingredients in tablets, etc., but not that it reduces the overall bioavailability of those ingredients. As a food additive or pharmaceutical excipient, its E number is E470b.

Magnesium stearate is also used to bind sugar in hard candies like mints, and is a common ingredient in baby formulas. In pure powder form, the substance can be a dust explosion hazard, although this issue is effectively insignificant beyond the manufacturing plants using it.

Magnesium stearate is manufactured from both animal and vegetable oils. Some nutritional supplements specify that the magnesium stearate used is sourced from vegetables.

Magnesium stearate is a major component of "bathtub rings." When produced by soap and hard water, magnesium stearate and calcium stearate both form a white solid insoluble in water, and are collectively known as "soap scum."

Sodium Stearate



Contents

1 - Introduction

Sodium stearate is the sodium salt of stearic acid. This white solid is the most common soap. It is found in many types of solid deodorants, rubbers, latex paints, and inks. It is also a component of some food additives and food flavorings.

IUPAC name :
sodium octa deca noate

Molecular formula	$C_{18}H_{35}NaO_2$
Molar mass	306 g mol^{-1}
Appearance	Yellow / white solid
Melting point	245 - 255 °C
Solubility in water	soluble
Flash point	176 °C (348.8°F)

2 - Use

Characteristic of soaps, sodium stearate has both hydrophilic and hydrophobic parts, the carboxylate and the long hydrocarbon chain, respectively. These two chemically different components induce the formation of micelles, which present the hydrophilic heads outwards and their hydrophobic (hydrocarbon) tails inwards, providing a lipophilic environment for hydrophobic compounds. It is also used in the pharmaceutical industry as a surfactant to aid the solubility of hydrophobic compounds in the production of various mouth foams.

3 - Production

Sodium stearate is produced as a major component of soap upon saponification of oils and fats. The percentage of the sodium stearate depends on the ingredient fats. Tallow is especially high in stearic acid content (as the triglyceride), whereas most fats only contain a few percent. The idealized equation for the formation of sodium stearate from stearin (the triglyceride of stearic acid) follows :

$$(C_{18}H_{35}O_2)_3C_3H_5 + 3\ NaOH \rightarrow C_3H_5(OH)_3 + 3\ C_{17}H_{35}CO_2Na$$

Purified sodium stearate can be made by neutralizing stearic acid with sodium hydroxide.

Zinc Stearate

Contents

1 - Introduction

Zinc stearate is a "zinc soap" that is widely used industrially. In this context, soap is used in its formal sense, a metal "salt" of a fatty acid. It is a white solid that repels water. It is insoluble in polar solvents such as alcohol and ether but soluble in aromatic hydrocarbons (e.g., benzene and chlorinated hydrocarbons) when heated. It is the most powerful mold release agent among all metal soaps. It contains no electrolyte and has a hydrophobic effect. Its main application areas are the plastics and rubber industry where it is used as a releasing agent and lubricant which can be easily incorporated.

Zinc carboxylates, e.g. basic zinc acetate, adopt complex formulas, and are not simply dicarboxylates of zinc. Instead the formula for most zinc carboxylates is $Zn_4O(O_2CR)_6$, consisting of a Zn_4O^{6+} core with carboxylate ligands spanning the edges.

IUPAC name :
zinc octa deca noate
Other names :
zinc distearate

Molecular formula	$C_{36}H_{70}O_4Zn$
Molar mass	632 g mol^{-1}
Appearance	soft, white powder
Density	1.095 g / cm^3, solid
Melting point	120 –130 °C
Boiling point	decomposes
Solubility in water	insoluble
Solubility in benzene	slightly soluble
Flash point	277 °C
Auto ignition temperature	420 °C

2 - Applications

It is widely used as a release agent for the production of many kinds of objects rubber, poly urethane, poly ester processing system, powder metallurgy. These applications exploit its "non-stick" properties . In cosmetics, zinc stearate is a lubricant and thickening to improve texture.

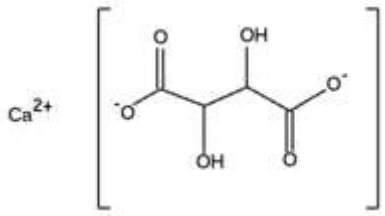
It is an "activator" for rubber vulcanization by sulfur and accelerators. As discovered in the early days of vulcanization, zinc has a beneficial effect on the reaction of the sulfur with the polyolefin. The stearate is a form of zinc that is highly soluble in the nonpolar medium of the poly olefins.

Being lipophilic, it functions as a phase transfer catalyst for the saponification of fats.

3 - Niche uses

It is a component of some paints, imparting gloss. As a chief ingredient in "fanning powder", it is used by magicians performing card manipulation to decrease the friction between the cards.

Calcium Tartrate

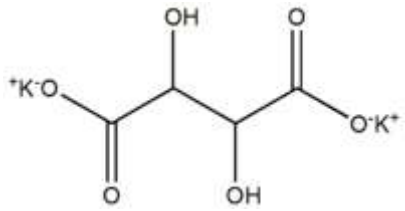


Calcium tartrate is a by product of the wine industry, prepared from wine fermentation dregs. It is the calcium salt of tartaric acid, an acid most commonly found in ripe grapes. Its solubility decreases with colder temperature, which results in the forming of whitish (in red wine often reddish) crystalline clusters as it precipitates. It finds use as a food preservative and acidity regulator. Like tartaric acid, calcium tartrate has two asymmetric carbons, hence it has two chiral isomers and a non-chiral isomer (meso-form). Most calcium tartrate of biological origin is the chiral levorotatory (–) isomer.

IUPAC name :
2,3-Dihydroxy butane dioic acid calcium salt

Molecular formula	$CaC_4H_4O_6$
Molar mass	190 g / mol (anhydrous) 260 g / mol (tetrahydrate)
Appearance	hygroscopic white powder or colorless crystals
Density	1.817 g / cm^3 (tetrahydrate)
Melting point	tetrahydrate decomposes at 160 °C anhydrous decomposes at 650 °C
Solubility in water	0.037 g/100 ml (0 °C)

Potassium Tartrate



Contents

1 - Introduction

Potassium tartrate, dipotassium tartrate or argol has formula $K_2C_4H_4O_6$. It is the potassium salt of tartaric acid. It is often confused with potassium bitartrate, also known as cream of tartar. As a food additive, it shares the E number E336 with potassium bitartrate.

IUPAC name :
Dipotassium 2,3-dihydroxy butanedioate
Other names :
Dipotassium tartrate;
Argol;
E336

Molecular formula	$C_4H_4K_2O_6$
Molar mass	226 g / mol
Appearance	colorless, slightly opaque crystals
Density	1.984 g / cm^3
Solubility	insoluble in alcohol
Refractive index (n_D)	1.550

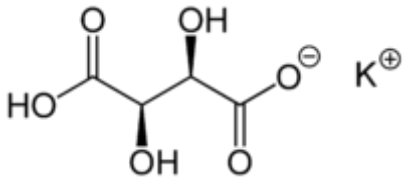
2 - Manufacturing

Potassium tartrate is produced by the reaction of tartaric acid with potassium sodium tartrate (rochelle salt), and potassium sulfate, followed by filtration, purification, precipitation and drying.

3 - Other compounds

Tartar emetic is produced when potassium tartrate is heated with antimony trioxide. Tartar emetic causes intense nausea, prostration and vomiting by irritating the gastrointestinal mucosa.[*citation needed*]

Potassium Bitartrate



Contents

1 - Introduction

Potassium bitartrate, also known as potassium hydrogen tartrate, has formula $KC_4H_5O_6$, is a byproduct of winemaking. In cooking it is known as cream of tartar. It is the potassium acid salt of tartaric acid, a carboxylic acid.

Other names “ potassium hydrogen tartrate cream of tartar potassium acid tartrate monopotassium tartrate	
Molecular formula	$K\,C_4\,H_5\,O_6$
Molar mass	188
Appearance	white crystalline powder
Density	1.05 g / cm^3 (solid)
Solubility	soluble in acid, alkali insoluble in acetic acid, alcohol
Refractive index (n_D)	1.511

2 - Occurrence

Potassium bitartrate crystallizes in wine casks during the fermentation of grape juice, and can precipitate out of wine in bottles.

The crystals (wine diamonds) will often form on the underside of a cork in wine-filled bottles that have been stored at temperatures below 10 °C , and will seldom, if ever, dissolve naturally into the wine.

These crystals also precipitate out of fresh grape juice that has been chilled or allowed to stand for some time. To prevent crystals forming in homemade grape jam or jelly, fresh grape juice should be chilled overnight to promote crystallisation. The potassium bitartrate crystals are removed by filtering through two layers of cheesecloth. The filtered juice may then be made into jam or jelly.[2] In some cases they adhere to the side of the chilled container, making filtering unnecessary.

The crude form (known as beeswing) is collected and purified to produce the white, odorless, acidic powder used for many culinary and other household purposes.

3 – Applications

3 – 1 - In food

In food, potassium bitartrate is used for:

Stabilizing egg whites, increasing their heat tolerance and volume

Stabilizing whipped cream, maintaining its texture and volume

Preventing sugar syrups from crystallising

Reducing discolouration of boiled vegetables

Thickening Tartar sauce

Additionally it is used as a component of:

Baking powder, as an acid ingredient to activate baking soda

Sodium-free salt substitutes, in combination with potassium chloride

A similar acid salt, sodium acid pyrophosphate, can be confused with cream of tartar because of their common function as a component of baking powder.

3 – 2 – House hold use

Potassium bitartrate can be mixed with an acidic liquid such as lemon juice or white vinegar to make a paste - like cleaning agent for metals such as brass, aluminum or copper, or with water for other

cleaning applications such as removing light stains from porcelain.[3] This mixture is sometimes mistakenly made with vinegar and sodium bicarbonate (baking soda), which actually react to neutralise each other, creating carbon dioxide and a sodium acetate solution.

Cream of tartar was often used in traditional dyeing where the complexing action of the tartrate ions were used to adjust the solubility and hydrolysis of mordant salts such as tin chloride and alum.

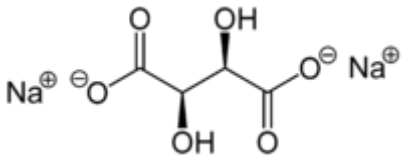
Cream of tartar, when mixed into a paste with hydrogen peroxide, can be used to clean rust from some hand tools, notably hand files. The paste is applied and allowed to set for a few hours and then washed off with a baking soda/water solution. Another rinse with water, a thorough drying and a thin application of oil will protect the file from further rusting.

3 – 3 - Chemistry

Potassium acid tartrate, also known as potassium hydrogen tartrate, is, according to NIST, used as a primary reference standard for a pH buffer. Using an excess of the salt in water, a saturated solution is created with a pH of 3.557 at 25 °C . Upon dissolution in water, potassium bitartrate will dissociate into acid tartrate, tartrate, and potassium ions. Thus, a saturated solution creates a buffer with standard pH. Before use as a standard, it is recommended that the solution be filtered or decanted between 22 °C and 28 °C

Potassium carbonate can be made by igniting cream of tartar producing "pearl ash". This process is now obsolete but produced a higher quality (reasonable purity) than "potash" extracted from wood or other plant ashes.

Sodium Tartrate



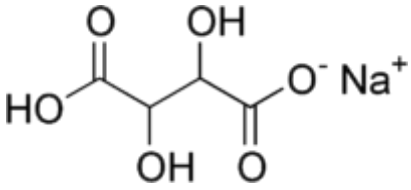
IUPAC name :
disodium (2*R*,3*R*)-2,3-dihydroxy butanedioate
Other names :
Sal tartar ;
Disodium tartrate;
Bisodium tartrate;
Sodium L-(+)-tartrate;
E335

Molecular formula	$C_4H_4Na_2O_6$ (anhydrous) $C_4H_8Na_2O_8$ (dihydrate)
Molar mass	194 g / mol (anhydrous) 230 g / mol (dihydrate)
Appearance	white crystals
Density	1.545 g / cm^3 (dihydrate)
Solubility in water	soluble
Solubility	insoluble in ethanol

Sodium tartrate ($Na_2C_4H_4O_6$) is used as an emulsifier and a binding agent in food products such as jellies, margarine, and sausage casings. As a food additive, it is known by the E number E335.

Because its crystal structure captures a very precise amount of water, it is also a common primary standard for Karl Fischer titration, a common technique to assay water content.

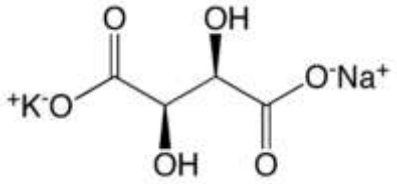
Mono Sodium Tartrate



IUPAC name :
Sodium 3-carboxy-2,3- dihydroxy propionate
Other names :
Sodium bitartrate;
E335
Molecular formula $C_4H_5NaO_6$
Molar mass 172.07 g/mol

Mono sodium tartrate or sodium bitartrate is a sodium salt of tartaric acid. As a food additive it is used as an acidity regulator and is known by the E number E335.

Potassium sodium tartrate



Contents

1 - Introduction

Potassium sodium tartrate is a double salt first prepared (in about 1675) by an apothecary, Pierre Seignette, of La Rochelle, France. As a result the salt was known as Seignette's salt or Rochelle salt. Rochelle salt is not to be confused with *rock salt*, which is simply the mineral form of sodium chloride. Potassium sodium tartrate and mono potassium phosphate were the first materials discovered to exhibit piezo electricity. This property led to its extensive use in "crystal" gramophone (phono) pick-ups, micro phones and earpieces during the post-War consumer electronics boom of the mid-20 th Century. Such transducers had an exceptionally high output with typical pick-up cartridge outputs as much as 2 volts or more. Rochelle salt is deliquescent so any transducers based on the material deteriorated if stored in damp conditions.

It is a colorless to blue - white salt crystallizing in the orthorhombic system. Its molecular formula is K Na $C_4H_4O_6 \cdot 4H_2O$. It is slightly soluble in alcohol but more completely soluble in water. It has a specific gravity of about 1.79, a melting point of approximately 75 °C, and has a saline, cooling taste. As a food additive, its E number is E337.

It has been used medicinally as a laxative. It has also been used in the process of silvering mirrors. It is an ingredient of Fehling's solution, formerly used in the determination of reducing sugars in solutions.

In organic synthesis, it is used in aqueous workups to break up emulsions, particularly for reactions in which an aluminium-based hydride reagent was used.

It is a common precipitant in protein crystallography and is also an ingredient in the Biuret reagent which is used to measure protein concentration. This ingredient maintains cupric ions in solution at an alkaline pH.

IUPAC name :
Potassium sodium tartrate
Other names :
E337

Molecular formula	K Na $C_4H_4O_6 \cdot 4H_2O$
Molar mass	282 g / mol
Melting point	75 °C
Boiling point	220 °C
Solubility in water	630 g / L (20 °C)

2 - Preparation

Potassium sodium tartrate, ($NaKC_4H_4O_6$) may be prepared by adding 0.5 mole sodium carbonate to heated solution containing 1 mole potassium bitartrate($KHC_4H_5O_6$). (1M $KHC_4H_4O_6$: 0.5M Na_2CO_3). The solution is filtered while hot. This solution is then dried to precipitate solid potassium sodium tartrate, as small crystallites.

Larger crystals of Rochelle salt have been grown under conditions of reduced gravity and convection on board Skylab .

Part - 8 –

Sugar Acids

Sugar Acid

Contents

1 - Introdution

Sugar acids are mono saccharides with a carboxyl group.

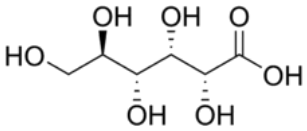
Main classes of sugar acids include :

Aldonic acids, in which the aldehyde functional group of an aldose is oxidized

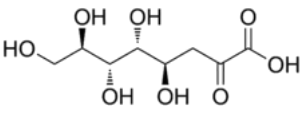
Ulosonic acids, in which the first hydroxyl group of a 2-ketose is oxidised creating an α- keto acid.

Uronic acids, in which the terminal hydroxyl group of an aldose or ketose is oxidized

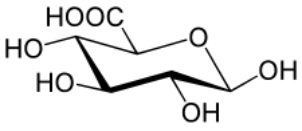
Aldaric acids, in which both ends of an aldose are oxidized



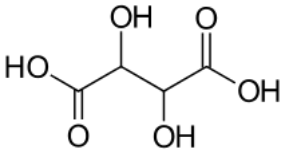
Aldonic acid



Ulosonic acid



Uronic acid



Aldaric acid

2 - Examples

Examples of sugar acids include :

Aldonic acids

Glyceric acid (3C)

Xylonic acid (5C)

Gluconic acid (6C)

Ascorbic acid (6C, unsaturated lactone)

Ulosonic acids

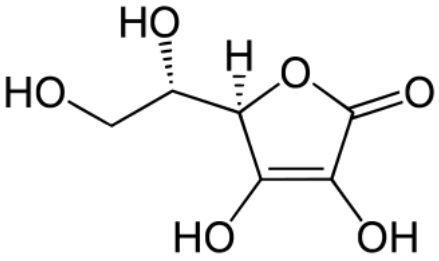
Neuraminic acid (5-amino-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-ulosonic acid)

Ketodeoxyoctulosonic acid (KDO or 3-deoxy-D-*manno*-oct-2-ulosonic acid)

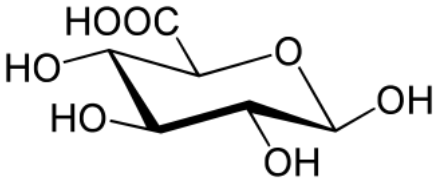
Uronic acids

Glucuronic acid (6C)

Galacturonic acid (6C)
Iduronic acid (6C)
Aldaric acids
Tartaric acid (4C)
meso-Galactaric acid (Mucic acid) (6C)
D-Glucaric acid (Saccharic acid) (6C)

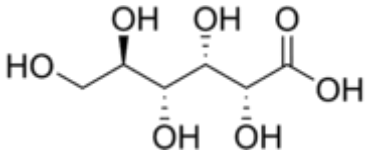


Ascorbic acid (Vitamin C)



The β-D form of glucuronic acid

Aldonic Acid



Chemical structure of gluconic acid ,
the aldonic acid derived from glucose.

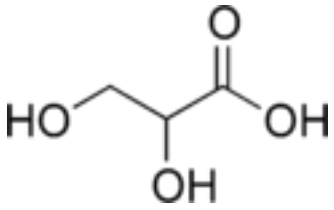
An aldonic acid is any of a family of sugar acids obtained by oxidation of the aldehyde functional group of an aldose to form a carboxylic acid functional group.[1] Thus, their general chemical formula is $HOOC\text{-}(CHOH)_n\text{-}CH_2OH$. Oxidation of the terminal hydroxyl group instead of the terminal aldehyde yields a uronic acid, while oxidation of both terminal ends yields an aldaric acid.

Aldonic acids are typically prepared by oxidation of the sugar with bromine. They are generally found in their lactone form, with the ring structure essentially the same as in the original sugar's cyclic hemiacetal form, which is the form the sugar is usually found in. However, unlike hemiacetals, lactones do not have a chiral anomeric carbon, and they cannot form glycosidic linkages.

Aldonic acids are found in many biological systems, and are the products of the oxidation of aldoses by Benedict's or Fehling's reagents. Their lactones are key intermediates in the Kiliani-Fischer synthesis of sugars.

Nomenclature of aldonic acids and their lactones is based on replacing the suffix "-ose" with "onic acid" or "onolactone" respectively; hence D-glucose is oxidized to D-gluconic acid and D-gluconolactone.

Glyceric Acid



Contents

1 - Introduction

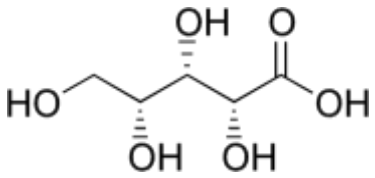
Glyceric acid is a natural three - carbon sugar acid . Salts and esters of glyceric acid are known as glycerates.

IUPAC name :	
2,3-Di hydroxy propanoic acid	
Other names ;	
Glycerate	
Molecular formula	$C_3H_6O_4$
Molar mass	106 g / mol

2 - Biochemistry

Several phosphate derivatives of glyceric acid, including 2-phospho glyceric acid, 3-phosphoglyceric acid, 2,3-bi sphospho glyceric acid, and 1,3-bi sphospho glyceric acid, are important biochemical intermediates in Glycolysis.

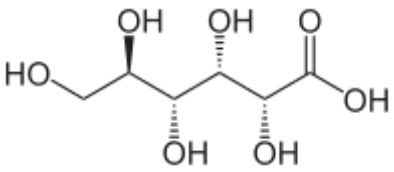
Xylonic Acid



IUPAC name : (2*R*,3*S*,4*R*)-2,3,4,5-tetra hydroxyl pentanoic acid	
Other names : Lyxonic acid; Xylonate	
Molecular formula	$C_5H_{10}O_6$
Molar mass	166.13 g/mol

Xylonic acid is a sugar acid that can be obtained by mild oxidation of xylose.

Gluconic Acid



Contents

1 - Introduction

Gluconic acid is an organic compound with molecular formula $C_6H_{12}O_7$ and condensed structural formula HO CH_2 $(CHOH)_4$ COOH. It is one of the 16 stereoisomers of 2,3,4,5,6-penta hydroxy hexanoic acid.

In aqueous solution at neutral pH, gluconic acid forms the gluconate ion. The salts of gluconic acid are known as "gluconates". Gluconic acid, gluconate salts, and gluconate esters occur widely in nature because such species arise from the oxidation of glucose. Some drugs are injected in the form of gluconates.

IUPAC name : D - Gluconic acid	
Other names : Dextronic acid	
Molecular formula	$C_6H_{12}O_7$
Molar mass	196 g / mol
Appearance	Colorless crystals
Melting point	131 °C
Solubility in water	Good
Acidity (pK_a)	3.86

2 - Chemical structure

The chemical structure of gluconic acid consists of a six-carbon chain with five hydroxyl groups terminating in a carboxylic acid

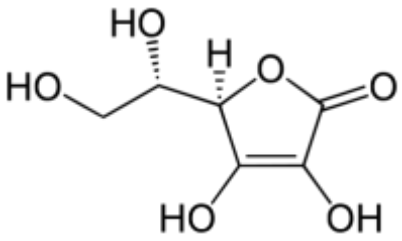
group. In aqueous solution, gluconic acid exists in equilibrium with the cyclic ester glucono delta-lactone.

3 - Occurrence and uses

Gluconic acid occurs naturally in fruit, honey, kombucha tea, and wine. As a food additive (E574), it is an acidity regulator. It is also used in cleaning products where it dissolves mineral deposits especially in alkaline solution. The gluconate anion chelates Ca^{2+}, Fe^{2+}, Al^{3+}, and other metals. In 1929 Horace Terhune Herrick developed a process for producing the salt by fermentation.

Calcium gluconate, in the form of a gel, is used to treat burns from hydrofluoric acid; calcium gluconate injections may be used for more severe cases to avoid necrosis of deep tissues. Quinine gluconate is a salt between gluconic acid and quinine, which is used for intramuscular injection in the treatment of malaria. Zinc gluconate injections are used to neuter male dogs. Iron gluconate injections have been proposed in the past to treat anemia.

Ascorbic Acid



Contents

1 - Introduction

Ascorbic acid is a naturally occurring organic compound with antioxidant properties. It is a white solid, but impure samples can appear yellowish. It dissolves well in water to give mildly acidic solutions. Ascorbic acid is one form ("vitamer") of vitamin C. It was originally called L-hexuronic acid, but when it was found to have vitamin C activity in animals ("vitamin C" being defined as a vitamin activity, not then a specific substance), the suggestion was made to rename L-hexuronic acid. The new name for L-hexuronic acid is derived from *a-* (meaning "no") and *scorbutus* (scurvy), the disease caused by a deficiency of vitamin C. Because it is derived from glucose, many animals are able to produce it, but humans require it as part of their nutrition. Other vertebrates lacking the ability to produce ascorbic acid include other primates, guinea pigs, teleost fishes, bats,

and birds, all of which require it as a dietary micronutrient (that is, a vitamin).

Chemically, there exists a D-ascorbic acid which does not occur in nature. It may be synthesized artificially. It has identical antioxidant properties to L-ascorbic acid, yet has far less vitamin C activity (although not quite zero).[3] This fact is taken as evidence that the antioxidant properties of ascorbic acid are only a small part of its effective vitamin activity. Specifically, L-ascorbate is known to participate in many specific enzyme reactions which require the correct epimer (L-ascorbate and not D-ascorbate).

IUPAC name : (5*R*)-[(1*S*)-1,2-dihydroxy ethyl]-3,4-dihydroxy furan-2(5*H*)-one	
Other names : Vitamin C	
Molecular formula	$C_6H_8O_6$
Molar mass	176 g mol^{-1}
Appearance	White or light yellow solid
Density	1.65 g/cm^3
Melting point	190-192 °C (decomposes)
Solubility in water	330 g / L
Solubility in ethanol	20 g / L
Solubility in glycerol	10 g / L
Solubility in propylene glycol	50 g/L
Solubility in other solvents	insoluble in diethyl ether, chloroform, benzene, petroleum ether, oils, fats
LD_{50}	11.9 g / kg (oral, rat)

2 – History

From the middle of the 18th century, it was noted that lemon juice could prevent sailors from getting scurvy. At first, it was supposed that the acid properties were responsible for this benefit; however, it soon became clear that other dietary acids, such as

vinegar, had no such benefits. In 1907, two Norwegian physicians reported an essential disease-preventing compound in foods that was distinct from the one that prevented beriberi. These physicians were investigating dietary deficiency diseases using the new animal model of guinea pigs, which are susceptible to scurvy. The newly discovered food-factor was eventually called vitamin C.

From 1928 to 1932, the Hungarian research team led by Albert Szent-Györgyi, as well as that of the American researcher Charles Glen King, identified the antiscorbutic factor as a particular single chemical substance. At the Mayo clinic, Szent-Györgyi had isolated the chemical hexuronic acid from animal adrenal glands. He suspected it to be the antiscorbutic factor, but could not prove it without a biological assay. This assay was finally conducted at the University of Pittsburgh in the laboratory of King, which had been working on the problem for years, using guinea pigs. In late 1931, King's lab obtained adrenal hexuronic acid indirectly from Szent-Györgyi and using their animal model, proved that it is vitamin C, by early 1932.

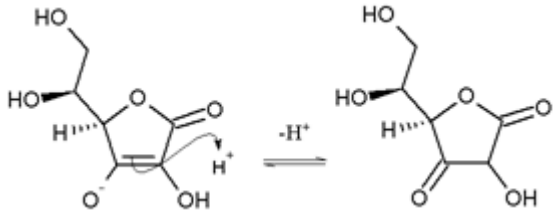
This was the last of the compound from animal sources, but, later that year, Szent-Györgyi's group discovered that paprika pepper, a common spice in the Hungarian diet, is a rich source of hexuronic acid. He sent some of the now-more-available chemical to Walter Norman Haworth, a British sugar chemist.[4] In 1933, working with the then-Assistant Director of Research (later Sir) Edmund Hirst and their research teams, Haworth deduced the correct structure and optical-isomeric nature of vitamin C, and in 1934 reported the first synthesis of the vitamin.[5] In honor of the compound's antiscorbutic properties, Haworth and Szent-Györgyi now proposed the new name of "a-scorbic acid" for the compound. It was named L-ascorbic acid by Haworth and Szent-Györgyi when its structure was finally proven by synthesis.

In 1937, the Nobel Prize for chemistry was awarded to Norman Haworth for his work in determining the structure of ascorbic acid (shared with Paul Karrer, who received his award for work on vitamins), and the prize for Physiology or Medicine that year went to Albert Szent-Györgyi for his studies of the biological functions of L-

ascorbic acid. The American physician Fred R. Klenner M.D. promoted vitamin C as a cure for many diseases in the 1950s by elevating the dosages greatly to as much as tens of grams vitamin C daily by injection. From 1967 on, Nobel prize winner Linus Pauling recommended high doses of ascorbic acid (he himself took 18 grams daily) as a prevention against cold and cancer. The results of Klenner have been controversial as yet, since his investigations do not meet the modern methodologic standards.

3 – Reactions

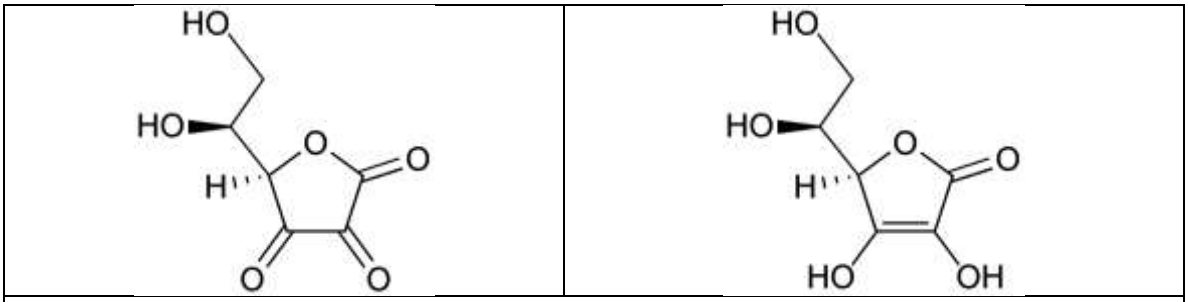
Ascorbic acid resembles the sugar from which it is derived, being a ring with many oxygen-containing functional groups. The molecule exists in equilibrium with two ketone tautomers, which are less stable than the enol form . In solutions, these forms of ascorbic acid rapidly interconvert.



Nucleophilic attack of ascorbic enol on proton to give 1,3-diketone

4 - Antioxidant mechanism

As a mild reducing agent, ascorbic acid degrades upon exposure to air, converting the oxygen to water. The redox reaction is accelerated by the presence of metal ions and light. It can be oxidized by one electron to a radical state or doubly oxidized to the stable form called dehydroascorbic acid.



Right: ascorbic acid(reduced form of Vitamin C)
Lefet: dehydroascorbic acid(nominal oxidized form of Vitamin C)

Ascorbate usually acts as an antioxidant. It typically reacts with oxidants of the reactive oxygen species, such as the hydroxyl radical formed from hydrogen peroxide. Such radicals are damaging to animals and plants at the molecular level due to their possible interaction with nucleic acids, proteins, and lipids. Sometimes these radicals initiate chain reactions. Ascorbate can terminate these chain radical reactions by electron transfer. Ascorbic acid is special because it can transfer a single electron, owing to the stability of its own radical ion called "semidehydroascorbate", dehydroascorbate. The net reaction is :

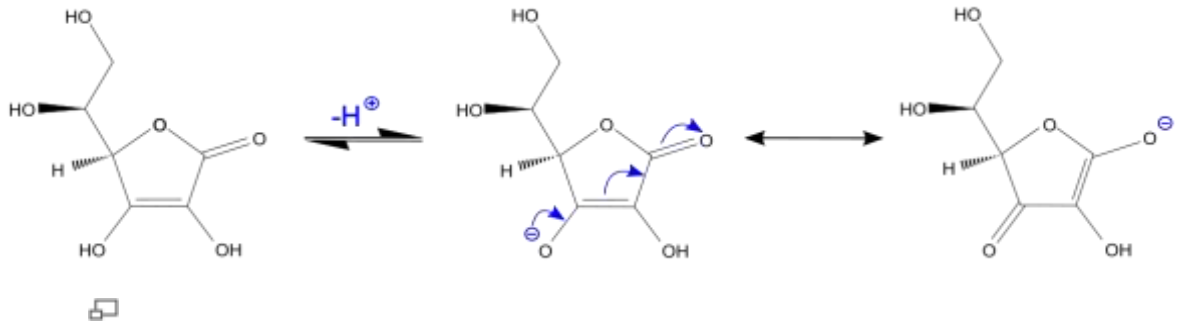
$$RO\bullet + C_6H_7O_6^- \rightarrow ROH + C_6H_6O_6^{\bullet -}$$

The oxidized forms of ascorbate are relatively unreactive, and do not cause cellular damage.

However, being a good electron donor, excess ascorbate in the presence of free metal ions can not only promote but also initiate free radical reactions, thus making it a potentially dangerous pro-oxidative compound in certain metabolic contexts.

4 – 1 – Acidity

Ascorbic acid, a reductone, behaves as a vinylogous carboxylic acid wherein the electrons in the double bond, hydroxyl group lone pair, and the carbonyl double bond form a conjugated system. Because the two major resonance structures stabilize the deprotonated conjugate base of ascorbic acid, the hydroxyl group in ascorbic acid is much more acidic than typical hydroxyl groups. In other words, ascorbic acid can be considered an enol in which the deprotonated form is a stabilized enolate.



Electron pushing for major contributing structures in conjugate base of ascorbic acid

5 - Food chemistry[edit source

Ascorbic acid and its sodium, potassium, and calcium salts are commonly used as antioxidant food additives. These compounds are water-soluble and thus cannot protect fats from oxidation: For this purpose, the fat-soluble esters of ascorbic acid with long-chain fatty acids (ascorbyl palmitate or ascorbyl stearate) can be used as food antioxidants. Eighty percent of the world's supply of ascorbic acid is produced in China. this is very bad for you espetially when heaed in food .

The relevant European food additive E numbers are :
E300 ascorbic acid
E301 sodium ascorbate
E302 calcium ascorbate
E303 potassium ascorbate
E304 fatty acid esters of ascorbic acid (i) ascorbyl palmitate (ii) ascorbyl stearate.

It creates volatile compounds when mixed with glucose and amino acids in 90 °C.
It is a cofactor in tyrosine oxidation

6 - Niche , non-food uses

Ascorbic acid is easily oxidized and so is used as a reductant in photographic developer solutions (among others) and as a preservative.

In fluorescence microscopy and related fluorescence - based techniques, ascorbic acid can be used as an antioxidant to increase fluorescent signal and chemically retard dye photobleaching.

It is also commonly used to remove dissolved metal stains, such as iron, from fiberglass swimming pool surfaces.

In plastic manufacturing, ascorbic acid can be used to assemble molecular chains more quickly and with less waste than traditional synthesis methods.

Heroin users are known to use ascorbic acid to convert heroin base to a water soluble salt, so that it can be injected.

Incidentally, as justified by its reaction with iodine, it is used to negate the effects of iodine tablets in water purification. It reacts with

the sterilized water removing the taste, color and smell of the iodine. This is why it is often sold as a second set of tablets in most sporting goods stores as Portable Aqua Neutralizing Tablets, along with the potassium iodide tablets.

7 – Biosynthesis

Ascorbic acid is found in plants and animals where it is produced from glucose. Animals must either produce it or digest it, otherwise a lack of vitamin C may cause scurvy which may eventually lead to death. Reptiles and older orders of birds make ascorbic acid in their kidneys. Recent orders of birds and most mammals make ascorbic acid in their liver where the enzyme L-gulono lactone oxidase is required to convert glucose to ascorbic acid. Humans, some other primates, and guinea pigs are not able to make L-gulono lactone oxidase because of a genetic mutation and are therefore unable to make ascorbic acid. Synthesis and signalling properties are still under investigation.

7 – 1 - Animal ascorbic acid biosynthesis pathway

The biosynthesis of ascorbic acid starts with the formation of UDP-glucuronic acid. UDP-glucuronic acid is formed when UDP-glucose undergoes two oxidations catalyzed by the enzyme UDP-glucose 6- dehydrogenase. UDP-glucose 6- dehydrogenase uses the co-factor NAD^+ as the electron acceptor. The transferase UDP-glucuronate pyro phosphorylase removes a UMP and glucuronokinase, with the cofactor ADP, removes the final phosphate leading to D-glucuronic acid. The aldehyde group of this is reduced to a primary alcohol using the enzyme glucuronate reductase and the cofactor NADPH yielding L-gulonic acid. This is followed by lactone formation with the hydrolase gluconolactonase between the carbonyl on C1 and hydroxyl group on the C4. L-gulonolactone then reacts with oxygen, catalyzed by the enzyme L-gulonolactone oxidase (which is nonfunctional in humans and other primates) and the cofactor FAD+. This reaction produces 2-oxogulonolactone which spontaneously undergoes enolization to form ascorbic acid.

7 – 2 - Plant ascorbic acid biosynthesis pathway

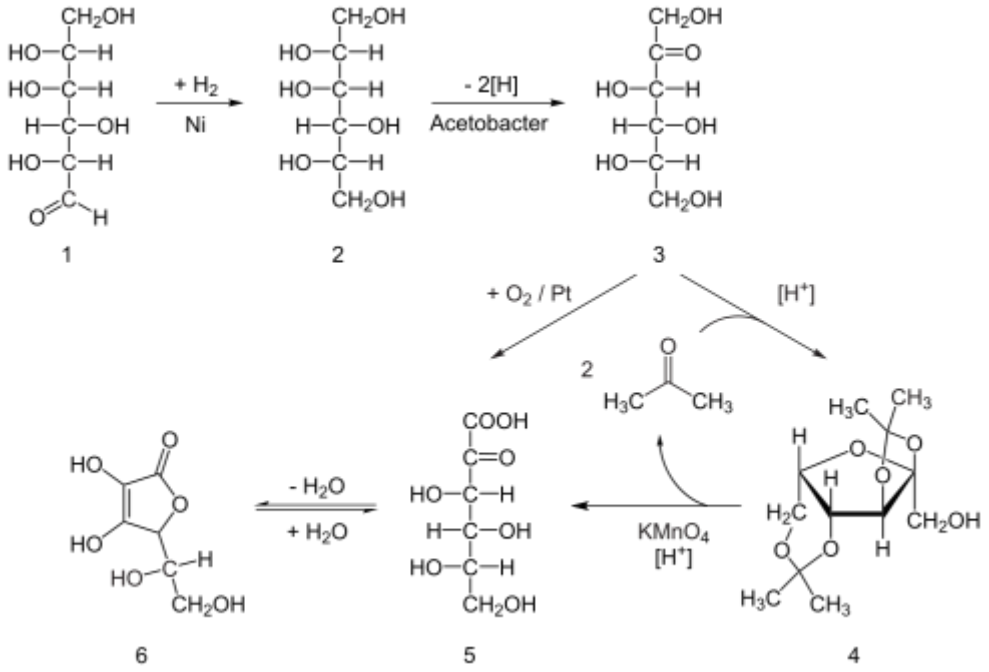
There are many different biosynthesis pathways for ascorbic acid in plants. Most of these pathways are derived from products found in glycolysis and other pathways. For example, one pathway goes through the plant cell wall polymers . The Plant Ascorbic Acid Biosynthesis Pathway most principal seems to be L-galactose. L-galactose reacts with the enzyme L-galactose dehydrogenase where the lactone ring opens and forms again but with between the carbonyl on C1 and hydroxyl group on the C4 resulting in L-galactonolactone. L-galactonolactone then reacts with the mitochondrial flavoenzyme L-galactonolactone dehydrogenase.[21] to produce ascorbic acid.[20] An interesting fact about L-ascorbic acid is that it has shown to have a negative feedback on L-galactose dehydrogenase in spinach.

8 - Industrial preparation

Ascorbic acid is prepared industrially from glucose in a method based on the historical Reichstein process. In the first of a five-step process, glucose is catalytically hydrogenated to sorbitol, which is then oxidized by the microorganism *Acetobacter suboxydans* to sorbose. Only one of the six hydroxy groups is oxidized by this enzymatic reaction. From this point, two routes are available. Treatment of the product with acetone in the presence of an acid catalyst converts four of the remaining hydroxyl groups to acetals. The unprotected hydroxyl group is oxidized to the carboxylic acid by reaction with the catalytic oxidant TEMPO (regenerated by sodium hypochlorite — bleaching solution). (Historically, industrial preparation via the Reichstein process used potassium permanganate.) Acid-catalyzed hydrolysis of this product performs the dual function of removing the two acetal groups and ring-closing lactonization. This step yields ascorbic acid. Each of the five steps has a yield larger than 90 %.

A more biotechnological process, first developed in China in the 1960s but further developed in the 1990s, bypasses the use of acetone protecting groups. A second genetically-modified microbe species (such as mutant *Erwinia*, among others) oxidises sorbose into 2-ketogluconic acid (2-KGA), which can then undergo ring-closing lactonization via dehydration. This method is used in the predominant

process used by the ascorbic acid industry in China, which supplies 80% of world's ascorbic acid . American and Chinese researchers are competing to engineer a mutant which can carry out a one-pot fermentation directly from glucose to 2-KGA, bypassing both the need for a second fermentation and the need to reduce glucose to sorbitol.



The outdated but historically-important industrial synthesis of ascorbic acid from glucose via the Reichstein process.

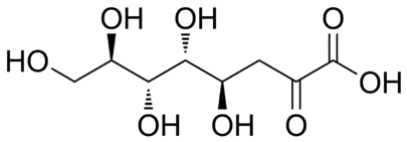
9 – Determination

The traditional way to analyze the ascorbic acid content is titration with an oxidizing agent, and several procedures have been developed, mainly relying on iodometry. Iodine is used in the presence of a starch indicator. Iodine is reduced by ascorbic acid, and, when all the ascorbic acid has reacted, the iodine is then in excess, forming a blue-black complex with the starch indicator. This indicates the end-point of the titration. As an alternative, ascorbic acid can be treated with iodine in excess, followed by back titration with sodium thiosulfate using starch as an indicator . The preceding iodometric method has been revised to exploit reaction of ascorbic acid with iodate and iodide in acid solution. Electrolyzing the solution of potassium iodide produces iodine, which reacts with ascorbic acid. The end of process is determined by potentiometric titration in a

manner similar to Karl Fischer titration. The amount of ascorbic acid can be calculated by Faraday's law.

An uncommon oxidising agent is *N*-bromosuccinimide, (NBS). In this titration, the NBS oxidizes the ascorbic acid in the presence of potassium iodide and starch. When the NBS is in excess (i.e., the reaction is complete), the NBS liberates the iodine from the potassium iodide, which then forms the blue-black complex with starch, indicating the end-point of the titration.

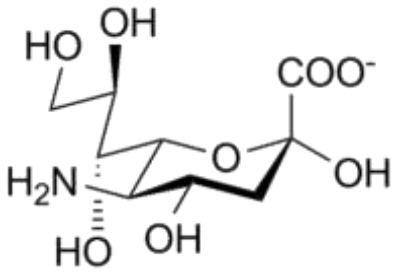
Ulosonic Acid



The ulosonic acid 3- Deoxy –D -manno- oct-2-ulosonic acid.

An ulosonic acid is a sugar acid obtained by the oxidation of the 1-hydroxyl group of a ketose to a carboxylic acid, creating an alpha-keto acid. An example of an ulosonic acid is 3-Deoxy-D-manno-oct-2-ulosonic acid.

Neuraminic Acid



IUPAC name :(4S,5R,6R,7S,8R)-5-amino-4,6,7,8,9-penta hydroxy-2-oxo-onanoic acid	
Molecular formula	$C_9 H_{17} N O_8$
Molar mass	267 g / mol

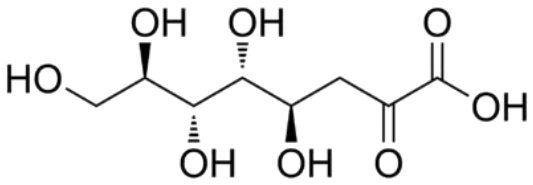
Neuraminic acid (5-amino-3,5-dideoxy-D-*glycero*-D-*galacto*-non-2-ulosonic acid) is a 9-carbon monosaccharide, a derivative of a ketononose. Neuraminic acid may be visualized as the product of an aldol-condensation product of pyruvic acid and D-mannosamine (2-amino-2-deoxy-mannose). Neuraminic acid does not occur naturally, but many of its derivatives are found widely distributed in animal tissues and in bacteria, especially in glycoproteins and gangliosides. The *N*- or *O*-substituted derivatives of neuraminic acid are collectively known as sialic acids, the predominant form in mammalian cells being *N*-acetylneuraminic acid. The amino group bears either an acetyl or a glycolyl group. The hydroxyl substituents may vary considerably: acetyl, lactyl, methyl, sulfate and phosphate groups have been found.

The name "neuraminic acid" was introduced by German scientist E. Klenk in 1941, in reference to the brain lipids from which it was derived as a cleavage product.

The symbol commonly used for neuraminic acid is Neu, and the residue is typically found with additional chemical modifications in biological systems. As a family, these residues are known as sialic acids. For example, N-acetyl-neuraminic acid, Neu5Ac, is typical in human glycoproteins.

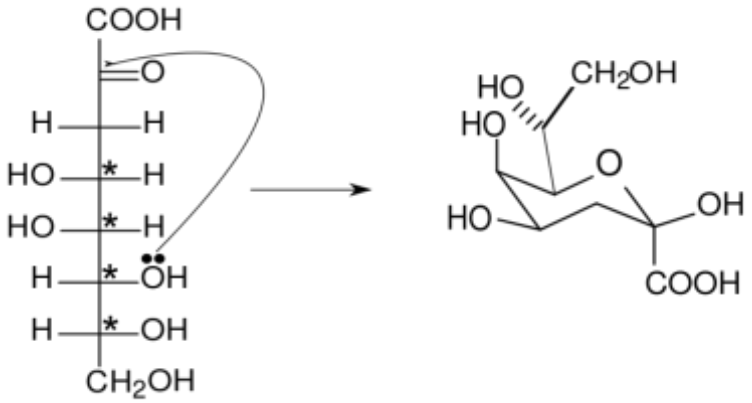
Among their many biological functions, these structures are substrates for neuraminidase enzymes which cleave neuraminic acid residues. Human flu viruses have a neuraminidase enzyme, signified in the name "H#N#", where the H refers to an isoform of hemaglutinin and N refers to an isoform of viral neuraminidase.

3-Deoxy-D-*manno*-oct-2-ulosonic acid



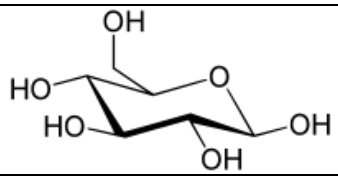
IUPAC name : (4*R*,5*R*,6*R*,7*R*)-4,5,6,7,8-penta hydroxy-2-oxo octanoic acid	
Other names : 2-Oxo-3-deoxy-D-mannooctonic acid; 2-Keto-3-Deoxy-D-*manno*-octonate; 2-Keto-3-deoxy-D-mannooctanoic acid; 3-Deoxy-D-manno-2-octulosonic acid; 3-Deoxy-D-*manno*-octulosonic acid	
Molecular formula	$C_8H_{14}O_8$
Molar mass	238 g mol^{-1}

3-Deoxy-D-*manno*-oct-2-ulosonic acid or KDO is an ulosonic acid of a 2-keto octose which is used by bacteria in the synthesis of lipo poly saccharides. The D-*manno* prefix indicates that four chiral centers have the same configuration as D-mannose.

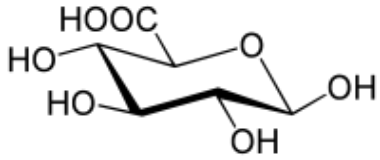


The cyclization of 3-deoxy-D-manno-oct-2-ulosonic acid to the β-anomer. The chiral centers are indicated by asterisks.

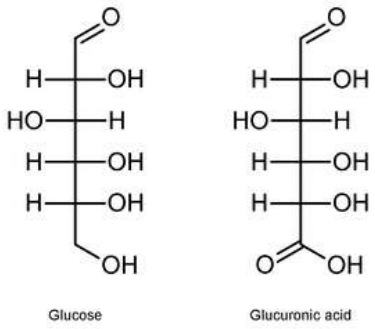
Uronic Acid



Glucose (before oxidization. Note difference at "6".)



The β-D form of glucuronic acid (after oxidization)



The Fischer projections of glucose and glucuronic acid. Glucose's terminal carbon's primary alcohol group has been oxidized to a carboxylic acid.

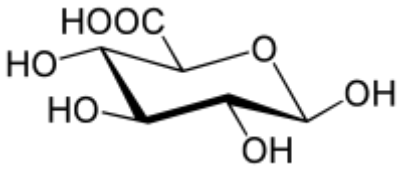
1 - Introduction

Uronic acids are a class of sugar acids with both carbonyl and carboxylic acid functional groups. They are sugars in which the terminal carbon's hydroxyl group has been oxidized to a carboxylic acid. Oxidation of the terminal aldehyde instead yields an aldonic acid, while oxidation of both the terminal hydroxyl group and the aldehyde yields an aldaric acid. The names of uronic acids are generally based on their parent sugars, however some of the most common do not have direct parents, and are formed by epimerization (e.g., iduronic acid is an epimer of glucuronic acid). Uronic acids that have six carbons are called hexuronic acids.

2 - Examples

Some of these compounds have important biochemical functions; for example, many wastes in the human body are excreted in the urine as their glucuronate salts, and iduronic acid is a component of some structural complexes such as proteoglycans.

Glucuronic Acid



Contents

1 - Introduction

Glucuronic acid (from Ancient Greek *γλυκύς* "sweet" + οὖρον "urine") is a carboxylic acid. Its structure is similar to that of glucose. However, glucuronic acid's sixth carbon is oxidized to a carboxylic acid. Its formula is $C_6H_{10}O_7$.

The salts and esters of glucuronic acid are known as glucuronates; the anion $C_6H_9O_7^-$ is the glucuronate ion.

Glucuronic acid should not be confused with gluconic acid, a linear carboxylic acid resulting from the oxidation of a different carbon of glucose. Both glucuronic acid and gluconic acid are reported to be found in kombucha.

IUPAC name :
(2*S*,3*S*,4*S*,5*R*,*6*R)-3,4,5,6-Tetra hydroxy oxane-2-carboxylic acid
Other names : β-D-gluco pyranuronic acid

Molecular formula	$C_6H_{10}O_7$
Molar mass	194 g mol^{-1}
Melting point	159 –161 °C

2 - Functions

2 – 1 - Proteoglycans

Glucuronic acid is common in carbohydrate chains of proteoglycans. It is part of mucous animal secretions (such as saliva), cell glycocalyx and intercellular matrix (for instance hyaluronan))

2 – 2 - Glucuronidation of toxic substances

In the animal body, glucuronic acid is often linked to the xenobiotic metabolism of substances such as drugs, pollutants, bilirubin, androgens, estrogens, mineralocorticoids, glucocorticoids, fatty acid derivatives, retinoids, and bile acids. These linkages involve glycosidic bonds, and this linkage process is known as glucuronidation. Glucuronidation occurs mainly in the liver, although the enzyme responsible for its catalysis, UDP-glucuronyltransferase, has been found in all major body organs, e.g., intestine, kidneys, brain, adrenal gland, spleen, and thymus.

The substances resulting from glucuronidation are known as glucuronides (or glucuronosides) and are typically much more water-soluble than the non-glucuronic acid-containing substance from which they were originally synthesised. The human body uses glucuronidation to make a large variety of substances more water-soluble, and, in this way, allow for their subsequent elimination from the body through urine or faeces (via bile from the liver). Hormones may also be glucuronidated to allow for easier transport around the body. Pharmacologists have linked drugs to glucuronic acid to allow for more effective delivery of a broad range of substances. Sometimes toxic substances are also less toxic after glucuronidation.

The conjugation of xenobiotic molecules with hydrophilic molecular species such as glucuronic acid is known as phase II metabolism.

3 - Use

Determination of urinary steroids and of steroid conjugates in blood.

Contained in some commercially available brands of Kombucha as an antioxidant & organic acid

In all plants and mammals - other than guinea pigs and primates- glucuronic acid is a precursor of ascorbic acid , also known as vitamin c.

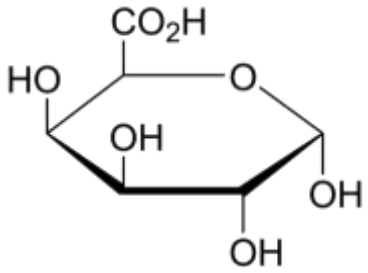
4 - Conformation

Unlike its C5 epimer iduronic acid, which may occur in a number of conformations, glucuronic acid occurs in predominantly the $^4C_1$ conformation.

5 - Glucuronidases

Glucuronidases are those enzymes that hydrolyze the glycosidic bond between glucuronic acid and some other compound.

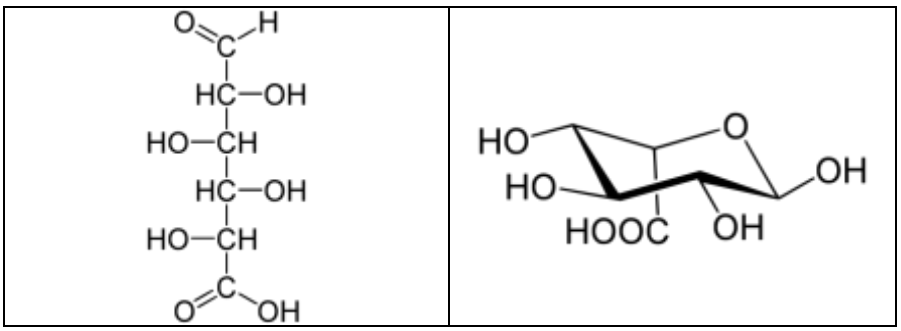
D - Galacturonic Acid



IUPAC name : (*2S,3R,4S,5R*)-2,3,4,5-Tetrahydroxy-6-oxo-hexanoic acid	
Molecular formula	$C_6H_{10}O_7$
Molar mass	194.139

D-Galacturonic acid is a sugar acid, an oxidized form of D-galactose. It is the main component of pectin, in which it exists as the polymer polygalacturonic acid.[1] It has an aldehyde group at C1 and a carboxylic acid group at C6. Other oxidized forms of D-galactose are D-galactonic acid (carboxylic group at C1) and *meso*-galactaric acid (mucic acid) (carboxylic groups at C1 and C6). It is also a uronic acid or hexuronic acid. Naturally occurring uronic acids are D-glucuronic acid, D-galacturonic acid, L-iduronic acid and D-mannuronic acid.

Iduronic Acid



IUPAC name : L-idopyranuronic acid	
Other names : L-Iduronic acid, D-ido-Hexuronic acid, IdoA	
Molecular formula	$C_6H_{10}O_7$
Molar mass	194.14 g mol^{-1}

L-Iduronic acid (IdoA) is the major uronic acid component of the glycosaminoglycans (GAGs) dermatan sulfate, and heparin. It is also present in heparan sulfate although here in a minor amount relative to its carbon-5 epimer glucuronic acid.

IdoA is a hexapyranose sugar. Most hexapyranoses are stable in one of two chair conformations $^1C_4$ or $^4C_1$. L-iduronate is different and adopts more than one solution conformation, with an equilibrium existing between three low-energy conformers. These are the $^1C_4$ and $^4C_1$ chair forms and an additional $^2S_0$ skew-boat conformation.

IdoA may be modified by the addition of an O-sulfate group at carbon position 2 to form 2-O-sulfo-L-iduronic acid (IdoA2S).

In 2000, LK Hallak described the importance of this sugar in respiratory syncytial virus infection. Dermatan sulfate and heparan

sulfate were the only GAGs containing IdoA, and they were the only ones that inhibited RSV infection in cell culture.

When internally positioned within an oligosaccharide, the $^{1}C_{4}$ and $^{2}S_{0}$ conformations (shown below for IdoA2S) predominate.

Proton NMR spectroscopy can be used to track changes in the balance of this equilibrium.

Aldaric Acid

Contents

1 - Introduction

Aldaric acids are a group of sugar acids, where the terminal hydroxyl groups of the sugars have been replaced by terminal carboxylic acids, and are characterised by the formula HOOC-$(CHOH)_n$-COOH.

2 - Synthesis

Aldaric acids are usually synthesized by the oxidation of aldoses with nitric acid. In this reaction it is the open-chain (poly hydroxy aldehyde) form of the sugar that reacts.

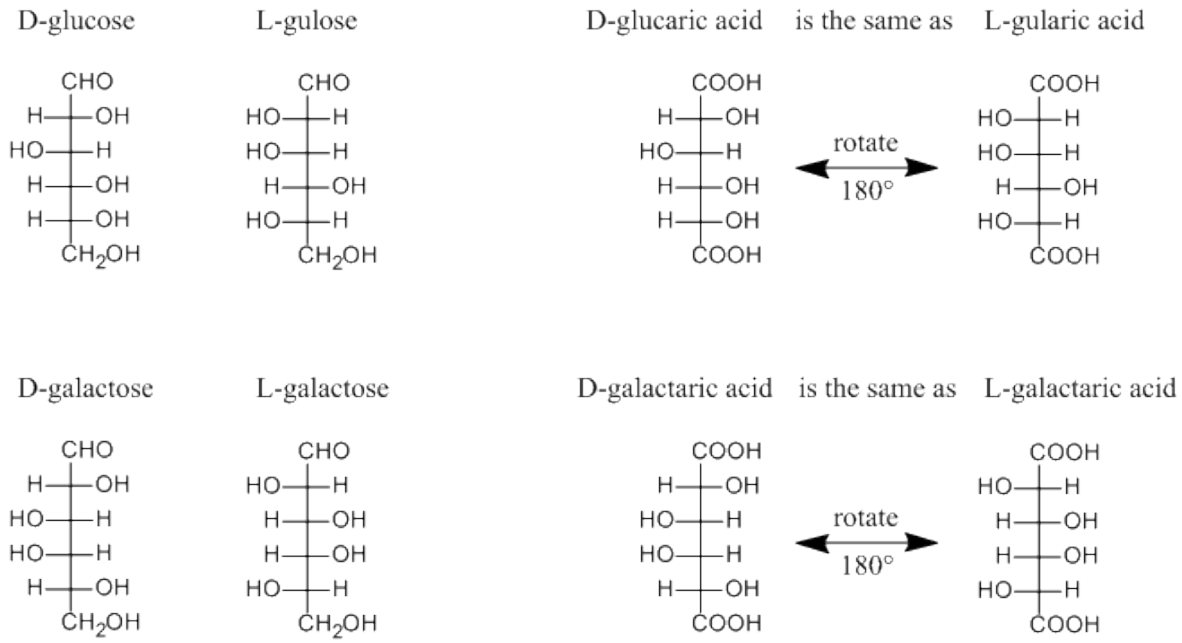
An aldaric acid is an aldose in which both the hydroxyl function of the terminal carbon and the aldehyde function of the first carbon have been fully oxidized to carboxylic acid functions. (Oxidation of just the aldehyde yields an aldonic acid while oxidation of just the terminal hydroxyl group yields an uronic acid.) Aldaric acids cannot form cyclic hemiacetals like unoxidized sugars, but they can sometimes form lactones.

3 - Structure

Nomenclature of the aldaric acids is based on the sugars from which they are derived; for example, glucose is oxidized to glucaric acid and xylose to xylaric acid.

Unlike their parent sugars, aldaric acids have the same functional group at both ends of their carbon chain; therefore, two different sugars can yield the same aldaric acid (this can be understood by looking at the Fischer projection of a sugar upside down—with normal aldoses, this is a different compound due to the aldehyde function at the top and the hydroxyl function at the bottom, but with

aldaric acids, there is a carboxylic acid function on both ends, so upside down and right side up do not matter). For example, D-glucaric acid and L-gularic acid are the same compound. A consequence of this is that some aldaric acids are meso forms with no optical activity despite their multiple chiral centers — this occurs if a sugar and its enantiomer oxidize to the same aldaric acid. An example is D-galactose — it has four chiral centers, but D-galactaric and L-galactaric acids, which have the opposite configuration at each chiral center and therefore would be expected to be enantiomers, are actually the same compound; therefore, galactaric acid is an achiral meso form with no optical activity. Again, this can be understood by taking the Fischer projection of either acid and looking at it upside down—the configuration is now switched at every carbon.



Adipic acid, HOOC- $(CH_2)_4$-COOH, is not an aldaric acid, though it is structurally similar. In fact, six-carbon aldaric acids can be considered tetrahydroxyl derivatives of adipic acid.

Tartaric Acid

Contents

1 - Introduction

Tartaric acid is a white crystalline diprotic aldaric acid. It occurs naturally in many plants, particularly grapes, bananas, and tamarinds, is commonly combined with baking soda to function as a leavening agent in recipes, and is one of the main acids found in wine. It is added to other foods to give a sour taste, and is used as an antioxidant. Salts of tartaric acid are known as tartrates. It is a dihydroxyl derivative of succinic acid.

Tartaric acid was first isolated from potassium tartrate, known to the ancients as tartar, *circa* 800 AD, by the alchemist Jabir ibn Hayyan The modern process was developed in 1769 by the Swedish chemist Carl Wilhelm Scheele.

Tartaric acid played an important role in the discovery of chemical chirality. This property of tartaric acid was first observed in 1832 by Jean Baptiste Biot, who observed its ability to rotate polarized light. Louis Pasteur continued this research in 1847 by investigating the shapes of ammonium sodium tartrate crystals, which he found to be chiral. By manually sorting the differently shaped crystals under magnification, Pasteur was the first to produce a pure sample of levotartaric acid.

IUPAC name :
2,3- dihydroxy butanedioic acid

Other names :
2,3-dihydroxy succinic acid
threaric acid
racemic acid
uvic acid

para tartaric acid	
Molecular formula	$C_4H_6O_6$ (Basic formula) $HO_2CCH(OH)CH(OH)CO_2H$ (Structural formula)
Molar mass	150 g / mol
Appearance	white powder
Density	1.79 g / mL (H_2O)
Melting point	171–174 °C (*L or D*-tartaric; pure) 206 °C (*DL*, racemic) 165-166°C ("meso-anhydrous") 146 –148 °C (*meso-hydrous*)
Solubility in water	133 g / 100ml (20 °C)
EU classification	Irritant(Xi)

2 – Stereo chemistry

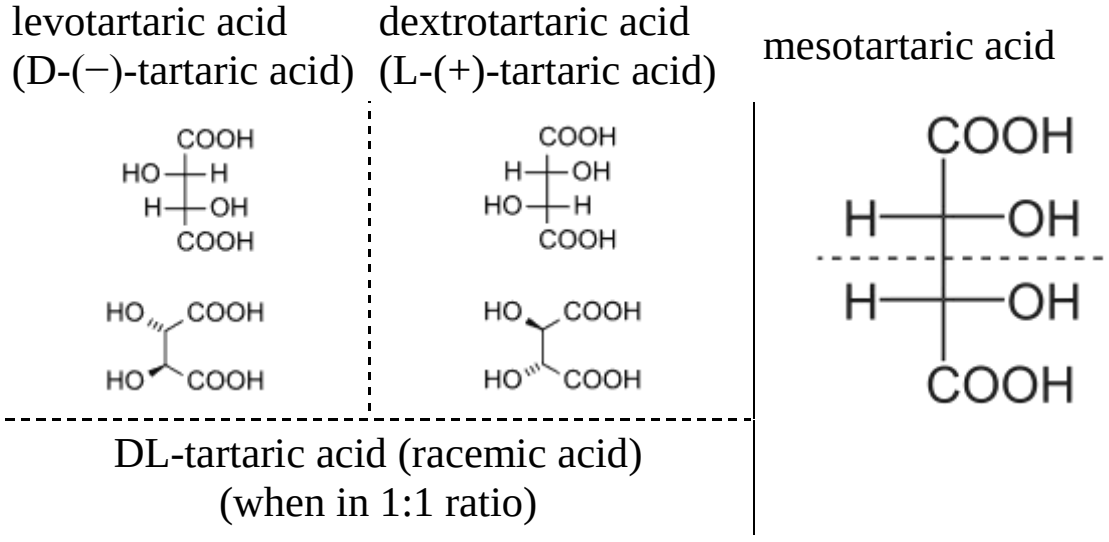
Tartaric acid crystals drawn as if seen through an optical microscope

Naturally occurring tartaric acid is chiral, meaning it has molecules that are not superimposable on their mirror images. It is a useful raw material in organic chemistry for the synthesis of other chiral molecules. The naturally occurring form of the acid is L-(+)-tartaric acid or dextrotartaric acid. The mirror-image (enantiomeric) form, levotartaric acid or D-(−)-tartaric acid, and the achiral form, mesotartaric acid, can be made artificially. The *dextro* and *levo* prefixes are not related to the D/L configuration (which is derived rather indirectly[8] from their structural relation to D- or L-

glyceraldehyde), but to the orientation of the optical rotation, (+) = dextrorotatory, (−) = levorotatory. Sometimes, instead of capital letters, small italic *d* and *l* are used. They are abbreviations of *dextro*- and *levo*- and, nowadays, should not be used. Levotartaric and dextrotartaric acid are enantiomers, mesotartaric acid is a diastereomer of both of them.

A rarely occurring, optically inactive form of tartaric acid, DL-tartaric acid is a 1:1 mixture of the *levo* and *dextro* forms. It is distinct from mesotartaric acid and was called racemic acid (from Latin *racemus* – "a bunch of grapes"). The word racemic later changed its meaning, becoming a general term for 1:1 enantiomeric mixtures – racemates.

Tartaric acid is used to prevent copper(II) ions from reacting with the hydroxide ions present in the preparation of copper(I) oxide. Copper(I) oxide is a reddish-brown solid, and is produced by the reduction of a Cu(II) salt with an aldehyde, in an alkaline solution.



3 – Derivatives

Important derivatives of tartaric acid include its salts, cream of tartar (potassium bitartrate), Rochelle salt (potassium sodium tartrate, a mild laxative), and tartar emetic (antimony potassium tartrate). Diisopropyl tartrate is used as a catalyst in asymmetric synthesis.

Tartaric acid is a muscle toxin, which works by inhibiting the production of malic acid, and in high doses causes paralysis and death. The median lethal dose (LD_{50}) is about 7.5 grams / kg for a human, ~5.3 grams/kg for rabbits and ~4.4 grams/kg for mice . Given this figure, it would take over 500 g to kill a person weighing 70 kg , and so it may be safely included in many foods, especially sour-tasting sweets. As a food additive, tartaric acid is used as an antioxidant with E number E334, tartrates are other additives serving as antioxidants or emulsifiers.

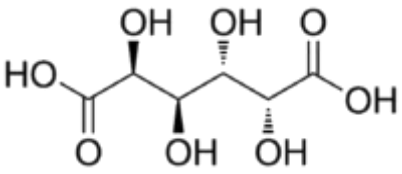
When cream of tartar is added to water, a suspension results which serves to clean copper coins very well, as the tartrate solution can dissolve the layer of copper(II) oxide present on the surface of the coin. The resulting copper(II)-tartrate complex is easily soluble in water.

4 - Tartaric acid in wine

Tartaric acid may be most immediately recognizable to wine drinkers as the source of "wine diamonds", the small potassium bitartrate crystals that sometimes form spontaneously on the cork. These "tartrates" are harmless, despite sometimes being mistaken for broken glass, and are prevented in many wines through cold stabilization. The tartrates remaining on the inside of aging barrels were at one time a major industrial source of potassium bitartrate.

However, tartaric acid plays an important role chemically, lowering the pH of fermenting "must" to a level where many undesirable spoilage bacteria cannot live, and acting as a preservative after fermentation. In the mouth, tartaric acid provides some of the tartness in the wine, although citric and malic acids also play a role.

Mucic Acid



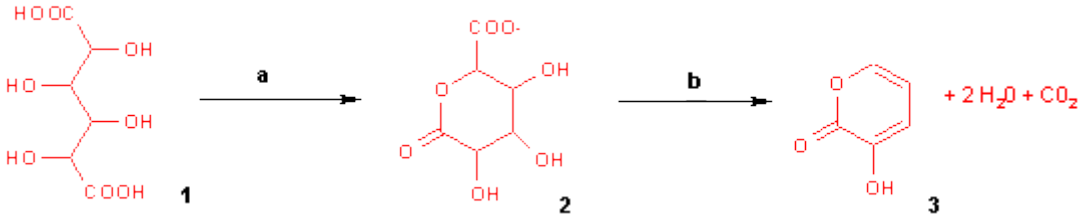
Contents

1 - Introduction

Mucic acid, $C_6H_{10}O_8$ or HOOC-$(CHOH)_4$-COOH, (also known as galactaric or meso - galactaric acid) is an aldaric acid obtained by nitric acid oxidation of galactose or galactose - containing compounds like lactose, dulcite, quercite, and most varieties of gum.

It forms a crystalline powder, which melts at 230 °C. It is insoluble in alcohol, and nearly insoluble in cold water. Due to the symmetry in the molecule, it is optically inactive even though it has chiral carbon atoms (i.e., it is a meso compound). When heated with pyridine to 140 °C, it is converted into allommic acid. When digested with fuming hydrochloric acid for some time it is converted into a furfural dicarboxylic acid while on heating with barium sulfide it is transformed into athiophene carboxylic acid. The ammonium salt yields on dry distillation carbon dioxide, ammonia, pyrrol and other substances. The acid when fused with caustic alkalis yields oxalic acid.

With potassium bisulfate mucic acid forms 3-hydroxy-2-pyrone by dehydration and decarboxylation.



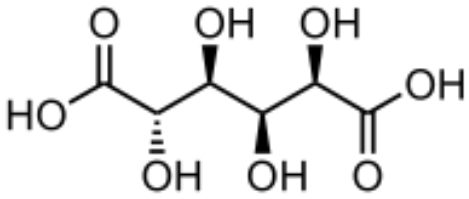
Reaction of mucic acid to 3-hydroxy-2-pyrone with a) potassium bisulfate 160 °C / 4 hrs. b) hydrochloric acid to pH = 7

IUPAC name :
(2*S*,3*R*,4*S*,5*R*)-2,3,4,5-tetra hydroxy hexanedioic acid
Other names :
Galactaric acid
Molecular formula $C_6H_{10}O_8$
Molar mass 210.1388

2 - Use

Mucic acid can be used to replace tartaric acid in self-rising flour or fizzies.

Saccharic Acid



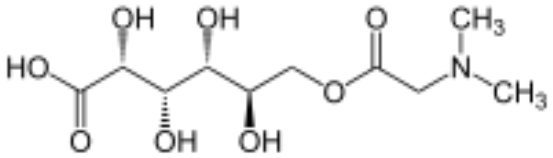
IUPAC name :
D - glucaric acid
Other names :
(2*S*,3*S*,4*S*,5*R*)-2,3,4,5-tetra hydroxy hexa nedioic acid

Molecular formula	$C_6H_{10}O_8$
Molar mass	210 g mol^{-1}

Saccharic acid, also called glucaric acid, is a chemical compound with the formula $C_6H_{10}O_8$. It is derived by oxidizing a sugar such as glucose with nitric acid.

The salts of saccharic acid are called saccharates.

Pangamic Acid



Contents

1 - Introduction

Pangamic acid, also called pangamate, is the name given to the chemical compound described as *d-glucono dimethyl amino acetic acid*, initially promoted by Ernst T. Krebs, Sr. and his son Ernst T. Krebs, Jr. as a medicinal compound for use in treatment of a wide range of diseases. They also termed this chemical "Vitamin B_{15}", though it is not a true vitamin, has no nutritional value, has no known use in the treatment of any disease and has been called a "quack remedy." Although a number of compounds labelled "pangamic acid" have been studied or sold, no chemical compound, including those claimed by the Krebses to be pangamic acid, has been scientifically verified to have the characteristics that defined the original description of the compound.

The Krebses derived the term "pangamic" to describe this compound which they asserted to be ubiquitous and highly concentrated in seeds (*pan* meaning "universal" and *gamic* meaning "seed").

IUPAC name :
6-(2-Dimethyl amino-acetoxy)-2,3,4,5-tetra hydroxy-hexanoic acid
Other names :
Vitamin B_{15};
D – glucono dimethyl amino acetic acid

Molecular formula	$C_{10}H_{19}NO_8$
Molar mass	281 g / mol

2 - Chemistry

Pangamic acid is the name given to the chemical compound with the empirical formula $C_{10}H_{19}O_8N$ and a molecular weight of 281 which appeared to be an ester derived from d-gluconic acid and dimethylglycine. In 1943, the Krebses applied for a patent for a process for extracting this chemical compound which they reported had been previously isolated from apricot seeds, and received the patent in 1949. A 1951 paper by the Krebses reported the first isolation of this compound using this patented process, but did not include enough information to confirm that this compound was actually isolated. In 1955, the Krebses received a patent for another synthesizing process for "N-substituted glycine esters of gluconic acid," but the patent contained no supporting data to confirm the process was able to synthesize compounds described by the patent, including pangamic acid.

Subsequent attempts at synthesizing this ester by other researchers found Krebs' purported methods of producing pangamic acid were not reproducible, and research into pangamic acid have focused on compounds of various chemical compositions. A review noted that of all the chemicals described in research about pangamic acid, "[n]ot a single product labeled "pangamate" or "B_{15}" has been established in a scientifically verifiable manner to conform to the empiric formula" described by the Krebses. Analysis of a sample of a compound called "pangamic acid" which was provided by a co-worker of the Krebses in the 1950s showed only lactose upon further evaluation by nuclear magnetic resonance spectroscopy. Thus, "pangamic acid" is more a label used to describe one of any number of chemical compounds rather than a particular substance.

Chemical compounds sold as "pangamic acid" for medicinal purposes have also had various chemical compositions, and suppliers of "pangamic acid" have regularly changed the chemical composition of the compounds sold under this label. One anecdote noted that the FDA has seized lots of calcium pangamate sold by General Nutrition Center (GNC), which agreed to stop selling the compound in those bottles after the FDA filed suit to stop sales. Afterwards, it was noted that GNC was still selling something in the same bottles with the same

labels, likely a different compound. Due to ambiguity in situations like this, the Food and Drug Administration (FDA) considers it "not an identifiable substance."

3 - Clinical claims and research

The Krebses' original patent claimed pangamic acid could be used for detoxification as well as treatment of asthma, skin conditions, joint pain, and nerve pain, with none of these claims supported by evidence in the patent application. Early promotion for pangamic acid included use by race horses as well as humans. Although given the name "Vitamin B_{15}" by the Krebses, there is no evidence that it meets the definition of a vitamin as there is no evidence it is a nutrient needed by the body.

Much of the clinical research on pangamic acid took place in the former Soviet Union, though that research often did not describe which of the many compounds called "pangamic acid" was used in the study. This research was also of limited quality due to being overwhelmingly anecdotal in nature (as opposed to controlled experimentation) and ignoring short and long term safety in human use.

Although more recent claims include treatment of a wide variety of conditions including cancer, heart disease, schizophrenia as well as providing improvement in oxygen utilization, there is no significant evidence for any of these claims or that it is safe for human use. One review noted that it meets "the criteria that define a quack remedy."

4 - Safety

Positive results from mutagenicity analysis via the Ames test of compounds commonly found in preparations labelled "pangamic acid" including diisopropylamine dichloroacetate, diisopropylamine,[4] dichloroacetate, as well as dimethylglycine mixed with sodium nitrite suggests there may be concern for the development of cancer with the use of these substances.

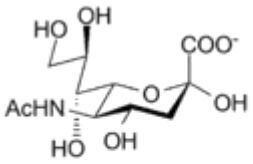
Sialic Acid

Contents

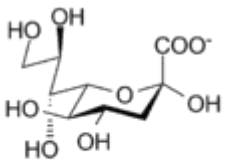
1 - Introduction

Sialic acid is a generic term for the *N*- or *O*-substituted derivatives of neuraminic acid, a monosaccharide with a nine-carbon backbone . It is also the name for the most common member of this group, N- acetylneuraminic acid (Neu 5Ac or NANA). Sialic acids are found widely distributed in animal tissues and to a lesser extent in other species, ranging from plants and fungi to yeasts and bacteria, mostly in glycoproteins and gangliosides. The amino group generally bears either an acetyl or glycolyl group, but other modifications have been described. The hydroxyl substituents may vary considerably; acetyl, lactyl, methyl, sulfate, and phosphate groups have been found. The term "sialic acid" (from the Greek for saliva, *σίαλον*/*sialon*) was first introduced by Swedish biochemist Gunnar Blix in 1952.

2 - Structure



N-Acetylneuraminic acid
Neu5Ac

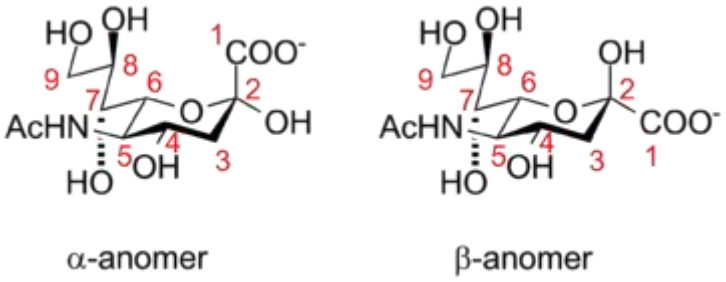


2-Keto-3-deoxynonic acid
Kdn

The numbering of the sialic acid structure begins at the carboxylate carbon and continues around the chain. The configuration which places the carboxylate in the axial position is the alpha-anomer.

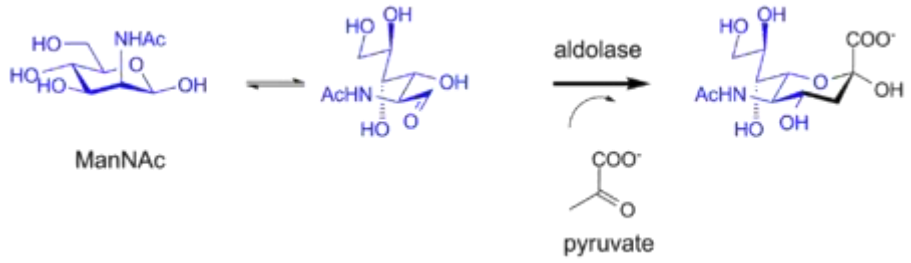
The alpha-anomer is the form that is found when sialic acid is bound to glycans, however, in solution it is mainly (over 90 %) in the beta-anomeric form. A bacterial enzyme with sialic acid mutarotase activity, NanM, has been discovered which is able to rapidly

equilibrate solutions of sialic acid to the resting equilibrium position of around 90 % beta 10 % alpha



3 - Biosynthesis

In bacterial systems, sialic acids are biosynthesized by an aldolase enzyme. The enzyme uses a mannose derivative as a substrate, inserting three carbons from pyruvate into the resulting sialic acid structure. These enzymes can be used for chemoenzymatic synthesis of sialic acid derivatives.



4 - Function

Sialic acid-rich glycoproteins (sialoglycoproteins) bind selectin in humans and other organisms. Metastatic cancer cells often express a high density of sialic acid-rich glycoproteins. This overexpression of sialic acid on surfaces creates a negative charge on cell membranes. This creates repulsion between cells (cell opposition) and helps these late-stage cancer cells enter the blood stream.

Sialic acid also plays an important role in human influenza infections. The influenza viruses (*Ortho myxoviridae*) have hemagglutinin activity (HA) glycoproteins on their surfaces that bind to sialic acids found on the surface of human erythrocytes and on the cell membranes of the upper respiratory tract. This is the basis of hemagglutination when viruses are mixed with blood cells, and entry of the virus into cells of the upper respiratory tract. Widely-used anti-

influenza drugs (oseltamivir and zanamivir) are sialic acid analogs that interfere with release of newly-generated viruses from infected cells by inhibiting the viral enzyme neuraminidase.

Many bacteria also use sialic acid in their biology, although this is usually limited to bacteria that live in association with higher animals (deuterostomes). Many of these incorporate sialic acid into cell surface features like their lipopolysaccharide and capsule, which helps them evade the innate immune response of the host.[6] Other bacteria simply use sialic acid as a good nutrient source, as it contains both carbon and nitrogen and can be converted to fructose-6-phosphate, which can then enter central metabolism.

Sialic acid-rich oligo saccharides on the glyco conjugates (glyco lipids, glyco proteins, proteoglycans) found on surface membranes help keep water at the surface of cells . The sialic acid - rich regions contribute to creating a negative charge on the cells' surfaces. Since water is a polar molecule with partial positive charges on both hydrogen atoms, it is attracted to cell surfaces and membranes. This also contributes to cellular fluid uptake.

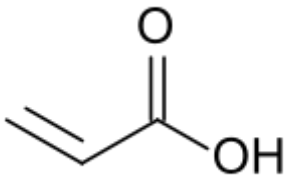
Sialic acid can "hide" mannose antigens on the surface of host cells or bacteria from mannose - binding lectin . This prevents activation of complement.

Sialic acid in the form of poly sialic acid is an unusual posttranslational modification that occurs on the neural cell adhesion molecules (NCAMs). In the synapse, the strong negative charge of the polysialic acid prevents NCAM cross-linking of cells.

Part -9 –

Aliphatic Acrylic Acid

Acrylic acid



Contents

1 - Introduction

Acrylic acid (IUPAC: prop-2-enoic acid) is an organic compound with the formula $CH_2 = CH\ CO_2H$. It is the simplest unsaturated carboxylic acid, consisting of a vinyl group connected directly to a carboxylic acid terminus. This colorless liquid has a characteristic acrid or tart smell. It is miscible with water, alcohols, ethers, and chloroform. More than one billion kilograms are produced annually.

IUPAC name : Prop-2-enoic acid
Other names :
acroleic acid
ethylene carboxylic acid
propene acid
propenoic acid
vinyl formic acid

Molecular formula	$C_3H_4O_2$
Molar mass	72 g mol^{-1}
Appearance	clear, colorless liquid
Density	1.051 g / mL
Melting point	14 °C
Boiling point	141 °C

Solubility in water	Miscible
Acidity (pK_a)	4.35
Viscosity	1.3 cP at 20 °C
Main hazards	Corrosive (C), Dangerous for the environment (N)
Flash point	68 °C
Autoignition temperature	429 °C

2 - Production

Acrylic acid is produced from propene which is a by product of ethylene and gasoline production.

$$CH_2 = CHCH_3 + 1.5\ O_2 \rightarrow CH_2 = CHCO_2H + H_2O$$

Because acrylic acid and its esters have long been valued commercially, many other methods have been developed but most have been abandoned for economic or environmental reasons. An early method was the hydrocarboxylation of acetylene ("Reppe chemistry") :

$$HCCH + CO + H_2O \rightarrow CH_2 = CHCO_2H$$

This method requires nickel carbonyl and high pressures of carbon monoxide. It was once manufactured by the hydrolysis of acrylonitrile which is derived from propene by ammoxidation, but was abandoned because the method cogenerates ammonium derivatives. Other now abandoned precursors to acrylic acid include ethenone and ethylene cyanohydrin.

Dow Chemical Company and a partner, OPX Bio technologies, are investigating using fermented sugar to produce 3-hydroxy propionic acid (3HP), an acrylic acid precursor. The goal is to reduce greenhouse gas emissions.

3 - Reactions and uses

Acrylic acid undergoes the typical reactions of a carboxylic acid and, when reacted with an alcohol, it will form the corresponding

ester. The esters and salts of acrylic acid are collectively known as acrylates (or propenoates). The most common alkyl esters of acrylic acid are methyl-, butyl-, ethyl-, and 2-ethylhexyl-acrylate.

Acrylic acid and its esters readily combine with themselves (to form polyacrylic acid) or other monomers (e.g. acrylamides, acrylonitrile, vinyl, styrene, and butadiene) by reacting at their double bond, forming homopolymers or copolymers which are used in the manufacture of various plastics, coatings, adhesives, elastomers, as well as floor polishes, and paints.

4 - Substituents

As a substituent acrylic acid can be found as an acyl group or a carboxyalkyl group depending on the removal of the group from the molecule. More specifically these are :

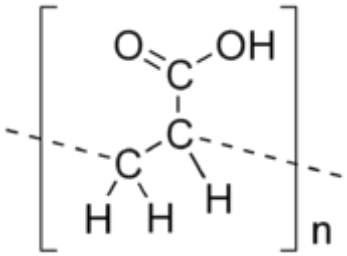
The acryloyl group, with the removal of the -OH from carbon-1.

The 2-carboxy ethenyl group, with the removal of a -H from carbon-3. This substituent group is found in chlorophyll.

5 - Safety

Acrylic acid is severely irritating and corrosive to the skin and the respiratory tract. Eye contact can result in severe and irreversible injury. Low exposure will cause minimal or no health effects, while high exposure could result in pulmonary edema. The LD_{50} is 340 mg/kg (rat, oral).

Poly Acrylic Acid



IUPAC name : Poly acrylic acid
Other names :
PAA , PAAc , Acrysol , Acumer , Alcosperse , Aquatreat , Carbomer , Sokalan
Molecular formula $(C_3H_4O_2)_n$
Molar mass variable
EU classification  Xi

1 - Introduction

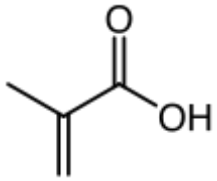
For a description of unrelated compounds expanded by two-carbon units,

Poly acrylic acid (PAA or Carbomer) is generic name for synthetic high molecular weight polymers of acrylic acid. They may be homopolymers of acrylic acid, crosslinked with an allyl ether pentaerythritol, allyl ether of sucrose or allyl ether of propylene. In a water solution at neutral pH, PAA is an anionic polymer, i.e. many of the side chains of PAA will lose their protons and acquire a negative charge. This makes PAAs polyelectrolytes, with the ability to absorb and retain water and swell to many times their original volume. Dry PAAs are found in the market as white and fluffy powders. Carbomer codes (910, 934, 940, 941 and 934P) are an indication of molecular weight and the specific components of the polymer. For many applications PAAs are used in form of alkali metal or amonium salts e.g. sodium polyacrylate.

2 - Applications

Poly acrylic acid and its derivatives are used in disposable diapers,[1] ion exchange resins and adhesives. They are also popular as a thickening, dispersing, suspending and emulsifying agents in pharmaceuticals, cosmetics and paints. PAA inactivates the antiseptic chlorhexidine gluconate.

Methacrylic Acid



IUPAC name :
2-methyl propenoic acid
Other names :
MAA ,
2-methyl-2-propenoic acid

Molecular formula	$C_4H_6O_2$
Molar mass	86 g / mol
Density	1.015 g / cm^3
Melting point	14 - 15 °C
Boiling point	161 °C

1 - Introduction

Methacrylic acid, abbreviated MAA, is an organic compound. This colourless, viscous liquid is a carboxylic acid with an acrid unpleasant odor. It is soluble in warm water and miscible with most organic solvents. Methacrylic acid is produced industrially on a large scale as a precursor to its esters, especially methyl methacrylate (MMA) and poly(methyl methacrylate) (PMMA). The methacrylates have numerous uses, most notably in the manufacture of polymers with trade names such as Lucite and Plexiglas. MAA occurs naturally in small amounts in the oil of Roman chamomile.

2 - Production and properties

More than 3 million tons of methyl methacrylate (MMA) are produced annually. In one route, acetone cyanohydrin is converted to methacrylamide sulfate using sulfuric acid. That compound is hydrolyzed to methacrylic acid, or it can be converted into methyl methacrylate in one step. In the second route, isobutylene or *tert*-butanol are oxidized to methacrolein, then methacrylic acid.

Methacrolein for this purpose can also be obtained from formaldehyde and ethylene. Isobutyric acid can also be dehydrogenated to methacrylic acid.

Methacrylic acid was first obtained in the form of its ethyl ester by treating phosphorus pentachloride with oxyisobutyric ester.[2] It is, however, more readily obtained by boiling citra- or meso-brompyrotartaric acids with alkalis. It crystallizes in prisms. When fused with an alkali, it forms propanoic acid. Sodium amalgam reduces it to isobutyric acid. A polymeric form of methacrylic acid was described in 1880.

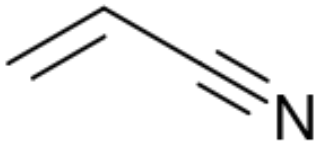
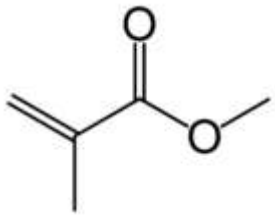
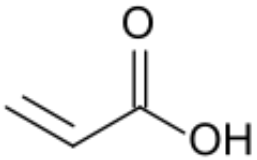
Acrylate Polymer

Contents

1 - Introduction

An acrylate polymer belongs to a group of polymers which could be referred to generally as plastics. They are noted for their transparency and resistance to breakage and elasticity. Also commonly known as acrylics or polyacrylates.

2 – Monomers

		
Acrylonitrile	*Methyl meth acrylate*	*Acrylic acid*

Acrylate monomers used to form acrylate polymers are based on the structure of acrylic acid, which consists of a vinyl group and a carboxylic acid terminus. Other typical acrylate monomers are derivatives of acrylic acid, such as methyl methacrylate in which one vinyl hydrogen and the carboxylic acid hydrogen are both replaced by methyl groups, and acrylonitrile in which the carboxylic acid group is replaced by the related nitrile group.

Other examples of acrylate monomers are :
Methacrylates
methyl acrylate
ethyl acrylate
2 - chloro ethyl vinyl ether
2 - ethyl hexyl acrylate,
hydroxy ethyl methacrylate

butyl acrylate
butyl methacrylate
TMPTA.

3 - Acrylic elastomers

Acrylic elastomer is a general term for a type of synthetic rubber whose main component is acrylic acid alkylester (ethyl or butyl ester). Acrylic elastomer has characteristics of heat and oil resistance.

It is divided into old type and new type: Old types include ACM (copolymer of acrylic acid ester and 2-chloroethyl vinyl ether) containing chlorine and ANM (copolymer of acrylic acid ester and acrylo nitrile) without chloride. Other than the slightly better water resistance of ANM, there are no physical differences; even process ability is poor for both types. Since prices are also high, demand is not so high vis-à-vis the characteristics. On the other hand, the new type of acrylic rubber does not contain any chlorine despite its unclear chemical composition. Processability has been improved, and most of tackiness to rolls as well as staining problems related to molds have been solved.

Major characteristics of acrylic rubber include heat resistance and oil resistance; it can endure a temperature of 170 ~ 180℃ under dry heat or in oil. Since it does not have a double bond, acrylic rubber also boasts of good weatherability and ozone resistance.

Its cold resistance is not that good, however. The saturation point is -15℃ for the old type and -28 ~ -30℃ for the new type. In terms of vulcanization, the standard method for the old type is amine vulcanization. To minimize permanent deformation, the old type requires curing for 24 hours under a temperature of 150℃. On the other hand, for the new type, the press curing time and follow-up vulcanization time are significantly reduced by combining metal soap and sulfur. It has no special characteristics. The rebound resilience and abrasion resistance of the new type are poor, and even its electrical characteristics are considerably poor compared with acrylonitrile-butadiene rubber and butyl rubber.

The materials are used mainly for oil seals and packagings related to automobiles.

4 - Other acrylic polymers

Polymethyl methacrylate, an acrylate polymer familiar to consumers is the clear break resistant glass or sheeting sold in hardware stores as acrylic glass or under the trade name Plexiglas.

Poly acrylate emulsion, water-born coating, are used as binder for outdoor and indoor "latex" house paints

Acrylic paints as artist paints

Acrylic fibre

Sodium poly acrylate water soluble thickeners, a polymer for the production of the Super absorbent polymer (SAP) used in disposable diapers due to its high absorbency per unit mass

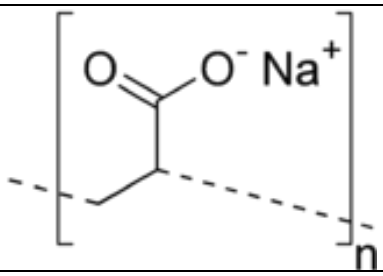
Acrylic resin as pressure - sensitive adhesive

"Super glue" is a formulation of cyano acrylate.

PVAc copolymer emulsion adhesive of vinyl acetate (VAM) and acrylic acid (VAA)

Polyacrylamide copolymer used as floculation agent in water treatment

Sodium Poly Acrylate



Molecular formula	$(C_3H_3NaO_2)_n$
Molar mass	Variable
Density	1.22 g/cm^3

1 - Introduction

Sodium polyacrylate, also known as waterlock, is a sodium salt of poly acrylic acid with the chemical formula $[-CH_2-CH(COONa)-]_n$ and broad application in consumer products. It has the ability to absorb as much as 200 to 300 times its mass in water. Sodium polyacrylate is anionic polyelectrolytes with negatively charged carboxylic groups in the main chain. While sodium neutralized poly acrylic acids are the most common form used in industry, there are also other salts available including potassium, lithium and ammonium.

2 - Applications

Sodium poly acrylate and other derivatives of polyacrylic acid have a wide variety of commercial and industrial uses that include:

Sequestering agents in detergents. (By binding hard water elements such as calcium and magnesium, the surfactants in detergents work more efficiently.)

3 - Thickening agents

Coatings

Artificial snow

Bath time recreational gel. (such as *Gellibaff* or *Squishybaff*)

Super absorbent polymers. These cross-linked acrylic polymers are referred to as "Super Absorbents" and "Water Crystals", and are

used in baby diapers . Copolymer versions are used in agriculture and other specialty absorbent applications. The origins of super absorbent polymer chemistry trace back to the early 1960 s when the U.S. Department of Agriculture developed the first super absorbent polymer materials . This chemical is featured in the Maximum Absorbency Garment used by NASA.

Acrylic Resin

Contents

1 - Introduction

Acrylic resins are a group of related thermoplastic or thermosetting plastic substances derived from acrylic acid, methacrylic acid or other related compounds.[1] Polymethyl acrylate is an acrylic resin used in an emulsed form for lacquer, textile finishes, adhesives and, mixed with clay, to gloss paper. Another acrylic resin is polymethyl methacrylate which is used to make hard plastics with various light transmitting properties.

2 - Formulae

Acrylic resin is a general term for any one of the plastics (resin) generated through chemical reaction by applying polymerization initiator and heat to a monomer.

The chemical name for the resin produced from the methyl methacrylate monomer (MMA) is polymethyl methacrylate (PMMA). MMA is a transparent and colorless fluid substance.[2] One of the main characteristic features of PMMA is its high transparency. With its high weather resistance, it has been known to last over 30 years, it does not easily turn yellow or crumble when exposed to sunlight. Polymethyl methacrylate is used not only for transparent windows in aquariums but also for various items such as signboards in places like convenience stores, taillights of automobiles, bathtub liners, sinks, cell phone display screens, backlight optical waveguides for liquid crystal displays (LCD) and so on.

3 - Advantages

The advantages of acrylic resins are :
Better stain protection (wash ability)
Water resistance

Better adhesion
Better blocking ('strap down')
Resist cracking and blistering better
Resistance to alkali cleaners

4 - Current market and forecast

The global demand on acrylic resin approached roughly US $ 14.5 billion in 2011. With an annual growth rate of 4 - 5 % , the acrylic resin market is expected to reach US $ 16.6 billion by 2014 and US$22 billion by 2020. Acrylic resins are used in a wide range of applications for the outstanding chemical characteristics and unique aesthetic properties. Currently, the strongest demand comes from automotive and medical device markets, and paints & coatings, adhesive & sealant and construction & architecture are the major application markets for acrylic resin.

Acrylic Fiber

Contents

1 Intrpduction

Acrylic fibers are synthetic fibers made from a polymer (poly acrylo nitrile) with an average molecular weight of ~100,000, about 1900 monomer units. To be called acrylic in the U.S, the polymer must contain at least 85% acrylonitrile monomer. Typical comonomers are vinyl acetate or methyl acrylate. The Dupont Corporation created the first acrylic fibers in 1941 and trademarked them under the name Orlon.

2 - Production

The polymer is formed by free - radical polymerization in aqueous suspension. The fiber is produced by dissolving the polymer in a solvent such as N,N-dimethyl formamide or aqueous sodium thiocyanate, metering it through a multi-hole spinnerette and coagulating the resultant filaments in an aqueous solution of the same solvent (wet spinning) or evaporating the solvent in a stream of heated inert gas (dry spinning). Washing, stretching, drying and crimping complete the processing. Acrylic fibers are produced in a range of deniers, typically from 0.9 to 15, as cut staple or as a 500,000 to 1 million filament tow. End uses include sweaters, hats, hand-knitting yarns, socks, rugs, awnings, boat covers, and upholstery; the fiber is also used as "PAN" precursor for carbon fiber. Production of acrylic fibers is centered in the Far East, Turkey, India, Mexico, and South America, though a number of European producers still continue to operate, including Dralon, Montefibre, and Fisipe. US producers have ended production, though acrylic tow and staple are still spun into yarns in the USA. Former U.S. brands of acrylic were Acrilan (Monsanto), Creslan (American Cyanamid), and Orlon (DuPont). Other brand names that are still in use include Dralon (Dralon GmbH).

3 - Textile uses

Acrylic is lightweight, soft, and warm, with a wool-like feel. It can also be made to mimic other fibers, such as cotton, when spun on short staple equipment. Some acrylic is extruded in colored or pigmented form; other is extruded in "ecru", otherwise known as "natural," "raw white," or "undyed." Pigmented fiber has highest light-fastness. Its fibers are very resilient compared to both other synthetics and natural fibers. Some acrylic is used in clothing as a less expensive alternative to cashmere, due to the similar feeling of the materials. Some acrylic fabrics may fuzz or pill easily. Other fibers and fabrics are designed to minimize pilling. Acrylic takes color well, is washable, and is generally hypoallergenic. End-uses include socks, hats, gloves, scarves, sweaters, home furnishing fabrics, and awnings.

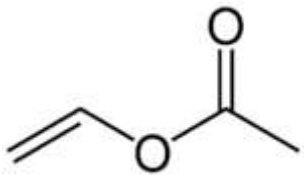
Acrylic is resistant to moths, oils, chemicals, and is very resistant to deterioration from sunlight exposure. However, static and pilling can be a problem in certain fabrications.

Acrylic is the "workhorse" hand-crafting fiber for crafters who knit or crochet; acrylic yarn may be perceived as "cheap" because it is typically priced lower than its natural-fiber counterparts, and because it lacks some of their properties, including softness and the ability to felt or take acid dyes. The fiber requires heat to "kill" or set the shape of the finished garment, and it isn't as warm as alternatives like wool. Some knitters also complain that the fiber "squeaks" when knitted, or that it is painful to knit with because of a lack of "give" or stretch in the yarn. On the other hand, it can be useful in certain items, like garments for babies, which require constant washing, because it is machine - washable and extremely color-fast.

Acrylic can irritate the skin of people with dermatological conditions such as eczema but this is unusual.

Leading US spinners include National Spinning Co., Inc. Leading acrylic fiber producers include Aksa (Turkey) , Montefibre (Spain) , Dralon (Germany) , Kaltex (Mexico) , and Birla Acrylic (Thailand & Egypt).

Vinyl Acetate



Contents

1 - Introduction

Vinyl acetate is an organic compound with the formula $CH_3COO\ CH = CH_2$. A colorless liquid with a pungent odor, it is the precursor to polyvinyl acetate, an important polymer in industry.

IUPAC name : Ethenyl acetate
Systematic name ; Ethenyl ethanoate
Other names :
Acetic acid vinyl ester, Acetoxy ethene, VyAc, VAM, zeset T, VAM vinyl acetate monomer, acetic acid ethenyl ester, 1-acetoxy ethylene

Molecular formula	$C_4 H_6 O_2$
Molar mass	86 g / mol
Appearance	Colorless liquid
Density	0.934 g / cm^3
Melting point	-93 °C
Boiling point	72.7 °C
Flash point	− 8 °C
Autoignition temperature	427 °C
Explosive limits	2.6 –13.40 %

2 - Production

The worldwide production capacity of vinyl acetate monomer (VAM) was estimated at 6,154,000 tonnes/annum in 2007, with most capacity concentrated in the United States (1,585,000 all in Texas), China (1,261,000), Japan (725,000) and Taiwan (650,000) . The average list price for 2008 was $1600/tonne. Celanese is the largest producer (ca 25% of the worldwide capacity), while other significant producers include China Petrochemical Corporation (7 %), Chang Chun Group (6%) and LyondellBasell (5%).

It is a key ingredient in furniture - glue.

3 - Preparation

The major industrial route involves the reaction of ethylene and acetic acid with oxygen in the presence of a palladium catalyst.

$$\text{Ethylene + acetic acid + 1/2 } O_2 \rightarrow \text{Vinyl acetate + } H_2O$$

But by products are also generated:

$$\text{Ethylene + 3 } O_2 \rightarrow 2\ CO_2 + 2\ H_2O$$

Vinyl acetate is also prepared by the gas-phase addition of acetic acid to acetylene.

4 - Polymerization

It can be polymerized, either by itself to make polyvinyl acetate or with other monomers to prepare copolymers such as ethylene-vinyl acetate (EVA), vinyl acetate-acrylic acid (VA / AA), polyvinyl chloride acetate (PVCA), and polyvinylpyrrolidone (Vp / Va Copolymer, used in hair gels). Due to the instability of the radical, attempts to control the polymerization via most 'living/controlled' radical processes have proved problematic. However, RAFT (or more specifically MADIX) polymerization offers a convenient method of controlling the synthesis of PVA by the addition of a xanthate or a dithiocarbamate chain transfer agent.

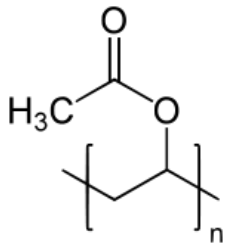
5 - Other reactions

Vinyl acetate undergoes many of the reactions anticipated for an alkene and an ester. Bromine adds to give the dibromide. Hydrogen halides add to give 1-haloethyl acetates, which cannot be generated by other methods because of the non - availability of the corresponding halo-alcohols. Acetic acid adds in the presence of palladium catalysts to give ethylidene diacetate, $CH_3CH(OAc)_2$. It undergoes transesterification with a variety of carboxylic acids.[6] The alkene also undergoes Diels - Alder and 2 + 2 cycloadditions.

6 - Toxicity evaluation

On January 31, 2009, the Government of Canada's final assessment concluded that exposure to vinyl acetate is not considered to be harmful to human health . This decision under the Canadian Environmental Protection Act (CEPA) was based on new information received during the public comment period, as well as more recent information from the risk assessment conducted by the European Union.

Poly Vinyl Acetate



Contents

1 - Introduction

Poly vinyl acetate, **PVA**, **PVAc**, **poly(ethenyl ethanoate)**, is a rubbery synthetic polymer with the formula $(C_4H_6O_2)_n$. It belongs to the polyvinyl esters family with the general formula -[$RCOOCHCH_2$]-. It is a type of thermoplastic.

It should not be confused with the related polymer polyvinyl alcohol, which is also called PVA.

Polyvinyl acetate is a component of a widely used glue type, commonly referred to as **wood glue**, **white glue**, **carpenter's glue**, **school glue**, **Elmer's glue** (in the US), or **PVA glue**.

IUPAC name : poly (1-acetyl oxi ethylene)
Other names : PVAc , PVA
Molecular formula $(C_4 H_6 O_2)_n$
Molar mass 86 g / mol / unit

2 - Preparation

PVAc is a vinyl polymer. Polyvinyl acetate is prepared by polymerization of vinyl acetate monomer (free radical vinyl polymerization of the monomer vinyl acetate).

3 - Discovery

Polyvinyl acetate was discovered in Germany in 1912 by Fritz Klatte.

The monomer, vinyl acetate, was first produced on an industrial scale by addition of acetic acid to acetylene with a mercury(I) salt[3] but it is now primarily made by palladium catalyzed oxidative addition of acetic acid to ethylene.

4 - Properties

The degree of polymerization of polyvinyl acetate typically is 100 to 5000. The ester groups of the polyvinyl acetate are sensitive to base hydrolysis and will slowly convert PVAc into polyvinyl alcohol and acetic acid.

Under alkaline conditions, boron compounds such as boric acid or borax cause the polymer to cross-link, forming tackifying precipitates or slime.

5 - Applications and uses

As an emulsion in water, aPVAc emulsions are used as adhesives for porous materials, particularly for wood, paper, and cloth, and as a consolidant for porous building stone, in particular sandstone . Uses :

As wood glue PVAc is known as "white glue" and the yellow "carpenter's glue" or PVA glue.

As paper adhesive during paper packaging converting

In bookbinding and book arts, due to its flexible strong bond and non-acidic nature (unlike many other polymers). The use of PVAC on the Archimedes Palimpsest during the 20th century greatly hindered the task of disbinding the book and preserving and imaging the pages in the early 21st century, in part because the glue was stronger than the parchment it held together.

In hand crafts

As envelope adhesive

As wall paper adhesive

The stiff homopolymer PVAc, but mostly the more soft copolymer a combination of vinyl acetate and ethylene, vinyl acetate ethylene (VAE), is used also in paper coatings, paint and other industrial coatings, as binder in nonwovens in glass fibers. sanitary napkins, filter paper and in textile finishing

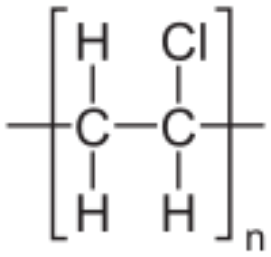
PVAc can also be used as coating to protect cheese from fungi and humidity.

Polyvinyl acetate is also the raw material to make other polymers like :

Polyvinyl alcohol -[$HOCHCH_2$]-: Polyvinyl acetate is partially or completely hydrolysed to give polyvinyl alcohol. This reversible saponification and esterification reaction was a strong hint for Hermann Staudinger in the formulation of his theory of macro molecules.

Polyvinyl acetate phthalate (PVAP): Polyvinyl acetate is partially hydrolyzed and then esterified with phthalic acid.

Poly Vinyl Chloride



PVC is used extensively in sewage pipe due to its low cost , chemical resistance and ease of jointing

Contents

1 - Introdution

Poly vinyl chloride, commonly abbreviated **PVC**, is the third-most widely produced plastic, after polyethylene and polypropylene.[4] PVC is used in construction because it is more effective than traditional materials such as copper, iron or wood in pipe and profile applications. It can be made softer and more flexible by the addition of plasticizers, the most widely used being phthalates. In this form, it is also used in clothing and upholstery, electrical cable insulation, inflatable products and many applications in which it replaces rubber.

Pure polyvinyl chloride is a white, brittle solid. It is insoluble in alcohol, but slightly soluble in tetrahydrofuran.

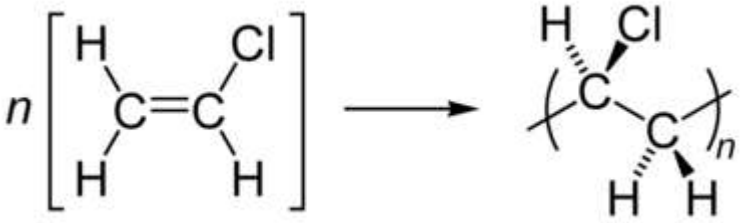
IUPAC name : Poly (1- chloro ethylene)	
Other names : Poly chloro ethylene	
Molecular formula	$(C_2H_3Cl)_n$
Mechanical properties	
Elongation at break	20 – 40 %
Notch test	2 – 5 kJ / m^2
Glass temperature	82 °C
Melting point	100–260 °C[3]
Effective heat of combustion	17.95 MJ / kg
Specific heat (*c*)	0.9 kJ / (kg·K)

Water absorption (ASTM)	0.04 – 0.4
Dielectric Breakdown Voltage	40 MV/ m

2 - Discovery and production

PVC was accidentally discovered at least twice in the 19th century, first in 1835 by French chemist Henri Victor Regnault and then in 1872 by German chemist Eugen Baumann. On both occasions the polymer appeared as a white solid inside flasks of vinyl chloride that had been left exposed to sunlight. In the early 20th century the Russian chemist Ivan Ostromislensky and Fritz Klatte of the German chemical company Griesheim-Elektron both attempted to use PVC in commercial products, but difficulties in processing the rigid, sometimes brittle polymer blocked their efforts. Waldo Semon and the B.F. Goodrich Company developed a method in 1926 to plasticize PVC by blending it with various additives. The result was a more flexible and more easily processed material that soon achieved widespread commercial use.

Polyvinyl chloride is produced by polymerization of the monomer vinyl chloride (VCM), as shown.



About 80 % of production involves suspension polymerization. Emulsion polymerization accounts for about 12 % and bulk polymerization accounts for 8 %. Suspension polymerizations affords particles with average diameters of 100 – 180 μm, whereas emulsion polymerization gives much smaller particles of average size around 0.2 μm. VCM and water are introduced into the reactor and a polymerization initiator, along with other additives. The reaction vessel is pressure tight to contain the VCM. The contents of the reaction vessel are continually mixed to maintain the suspension and

ensure a uniform particle size of the PVC resin. The reaction is exothermic, and thus requires cooling. As the volume is reduced during the reaction (PVC is denser than VCM), water is continually added to the mixture to maintain the suspension.

The polymerization of VCM is started by compounds called initiators that are mixed into the droplets. These compounds break down to start the radical chain reaction. Typical initiators include dioctanoyl peroxide and dicetyl peroxydicarbonate, both of which have fragile O - O bonds. Some initiators start the reaction rapidly but decay quickly and other initiators have the opposite effect. A combination of two different initiators is often used to give a uniform rate of polymerization. After the polymer has grown by about 10x, the short polymer precipitates inside the droplet of VCM, and polymerization continues with the precipitated, solvent-swollen particles. The weight average molecular weights of commercial polymers range from 100,000 to 200,000 and the number average molecular weights range from 45,000 to 64,000.

Once the reaction has run its course, the resulting PVC slurry is degassed and stripped to remove excess VCM, which is recycled. The polymer is then passed though a centrifuge to remove water. The slurry is further dried in a hot air bed, and the resulting powder sieved before storage or pelletization. Normally, the resulting PVC has a VCM content of less than 1 part per million. Other production processes, such as micro-suspension polymerization and emulsion polymerization, produce PVC with smaller particle sizes (10 μm vs. 120–150 μm for suspension PVC) with slightly different properties and with somewhat different sets of applications.

2 – 1 - Microstructure

The polymers are linear and are strong. The monomers are mainly arranged head-to-tail, meaning that there are chlorides on alternating carbon centres. PVC has mainly an atactic stereochemistry, which means that the relative stereochemistry of the chloride centres are random. Some degree of syndiotacticity of the chain gives a few percent crystallinity that is influential on the properties of the material. About 57 % of the mass of PVC is chlorine. The presence of chloride

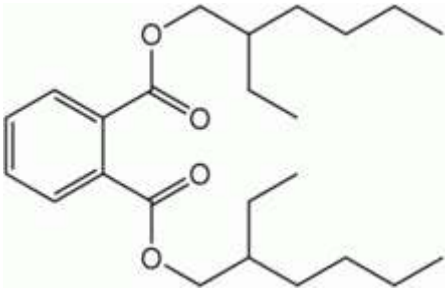
groups gives the polymer very different properties from the structurally related material polyethylene.

3 - Additives to finished polymer

The product of the polymerization process is unmodified PVC. Before PVC can be made into finished products, it always requires conversion into a compound by the incorporation of additives such as heat stabilizers, UV stabilizers, lubricants, plasticizers, processing aids, impact modifiers, thermal modifiers, fillers, flame retardants, biocides, blowing agents and smoke suppressors, and, optionally pigments.[8] The choice of additives used for the PVC finished product is controlled by the cost performance requirements of the end use specification e.g. underground pipe, window frames, intravenous tubing and flooring all have very different ingredients to suit their performance requirements.

3 – 1 - Phthalate plasticizers

Most vinyl products contain plasticizers which dramatically improve their performance characteristic. The most common plasticizers are derivatives of phthalic acid. The materials are selected on their compatibility with the polymer, their low volatility, their low toxicity, and their cost. These materials are usually oily colourless substances that mix well with the PVC particles. 90% of the plasticizer market, estimated to be millions of tons per year worldwide, is dedicated to PVC.



Bis(2-ethylhexyl) phthalate is a common plasticizer for PVC.

3 – 1 – 1 - High and low molecular weight phthalates

Phthalates can be divided into two groups: high and low molecular weight, with high molecular weight phthalates now

representing over 80 percent of European market for plasticisers. Low molecular weight phthalates include those with 3-6 carbon atoms in their chemical backbone; the most common types being Di(2-ethylhexyl) phthalate (DEHP), Di-butyl phthalate (DBP), Di- isobutyl phthalate (DIBP) and Butyl benzyl phthalate (BBP). Because of possible health effects of low phthalates in the environment, including Di(2-ethylhexyl) phthalate, there is movement to replace them with safer alternatives in Canada, the European Union, and the United States. They represent about 15% of the European market. High molecular weight phthalates include those with 7-13 Carbon atoms in their chemical backbone, which gives them increased permanency and durability. The most common types of high phthalates include di-isononyl phthalate (DINP) and di-isodecyl phthalate (DIDP). The European market has been shifting in the last decade from low to high phthalates, which today represent over 80% of all the phthalates currently being produced in Europe.

3 – 2 - Heat stabilizers

One of the most crucial additives are heat stabilizers. These agents minimize loss of HCl, a degradation process that starts above 70 °C. Once dehydrochlorination starts, it is autocatalytic. Many diverse agents have been used including, traditionally, derivatives of heavy metals (lead, cadmium). Increasingly, metallic soaps (metal "salts" of fatty acids) are favored, species such as calcium stearate.

4 - Physical properties

PVC is a thermoplastic polymer. Its properties for PVC are usually categorized based on rigid and flexible PVCs.

Property	**Rigid PVC**	**Flexible PVC**
Density [g / cm^3]	1.3 – 1.45	1.1 – 1.35
Thermal conductivity [W/(m·K)]	0.14 – 0.28	0.14 – 0.17
Yield strength [psi]	4500 - 8700	1450 - 3600
Young's modulus [psi]	490,000	
Flexural strength (yield) [psi]	10,500	
Compression strength [psi]	9500	

Coefficient of thermal expansion (linear) [mm/(mm °C)]	5×10^{-5}	
Resistivity [Ω m]	10^{16}	$10^{12} – 10^{15}$
Surface resistivity [Ω]	$10^{13} – 10^{14}$	$10^{11} – 10^{12}$

4 – 1 - Mechanical properties

PVC has high hardness and mechanical properties. The mechanical properties enhance with the molecular weight increasing, but decrease with the temperature increasing. The mechanical properties of rigid PVC (uPVC) is very good, the elastic modulus can reach to 1500-3,000 MPa. The soft PVC (Flexible PVC) elastic is 1.5-15 MPa. However, elongation at break is up to 200% -450%. PVC friction is ordinary, the static friction factor is 0.4-0.5, the dynamic friction factor is 0.23.

4 – 2 - Thermal properties

The heat stability of PVC is very poor, when the temperature reaches 140 °C PVC starts to decompose. Its melting temperature is 160 °C. The linear expansion coefficient of the PVC is small and has flame retardancy, the oxidation index is up to 45 or more. Therefore, the addition of a heat stabilizer during the process is necessary in order to ensure the product's properties.

4 – 3 - Electrical properties

PVC is a polymer with good insulation properties but because of its higher polar nature the electrical insulating property is inferior to non polar polymers such as poly ethylene and poly propylene.

As the dielectric constant, dielectric loss tangent value and volume resistivity are high, the corona resistance is not very good, it is generally suitable for medium or low voltage and low frequency insulation materials.

5 - Applications

PVC's relatively low cost, biological and chemical resistance and workability have resulted in it being used for a wide variety of applications. It is used for sewerage pipes and other pipe applications

where cost or vulnerability to corrosion limit the use of metal. With the addition of impact modifiers and stabilizers, it has become a popular material for window and door frames. By adding plasticizers, it can become flexible enough to be used in cabling applications as a wire insulator. It has been used in many other applications.

5 – 1 - Pipes

Roughly half of the world's polyvinyl chloride resin manufactured annually is used for producing pipes for municipal and industrial applications . In the water distribution market it accounts for 66 % of the market in the US, and in sanitary sewer pipe applications, it accounts for 75 % . Its light weight, low cost, and low maintenance make it attractive. However, it must be carefully installed and bedded to ensure longitudinal cracking and overbelling does not occur. Additionally, PVC pipes can be fused together using various solvent cements, or heat-fused (butt-fusion process, similar to joining HDPE pipe), creating permanent joints that are virtually impervious to leakage.

In February, 2007 the California Building Standards Code was updated to approve the use of chlorinated polyvinyl chloride (CPVC) pipe for use in residential water supply piping systems. CPVC has been a nationally accepted material in the US since 1982; California, however, has permitted only limited use since 2001. The Department of Housing and Community Development prepared and certified an environmental impact statement resulting in a recommendation that the Commission adopt and approve the use of CPVC. The Commission's vote was unanimous and CPVC has been placed in the 2007 California Plumbing Code.

In the United States and Canada, PVC pipes account for the largest majority of pipe materials used in buried municipal applications for drinking water distribution and wastewater mains.[17] Buried PVC pipes in both water and sanitary sewer applications that are 4 inches (100 mm) in diameter and larger are typically joined by means of a gasket-sealed joint. The most common type of gasket utilized in North America is a metal reinforced elastomer, commonly referred to as a Reiber sealing system.

5 – 2 - Electric cables

PVC is commonly used as the insulation on electrical cables; PVC used for this purpose needs to be plasticized.

In a fire, PVC-coated wires can form HCl fumes; the chlorine serves to scavenge free radicals and is the source of the material's fire retardance. While HCl fumes can also pose a health hazard in their own right, HCl dissolves in moisture and breaks down onto surfaces, particularly in areas where the air is cool enough to breathe, and is not available for inhalation. Frequently in applications where smoke is a major hazard (notably in tunnels and communal areas) PVC-free cable insulation is preferred, such as low smoke zero halogen (LSZH) insulation. Any metal parts must not be mixed together during the raw material stage, as it may lead to EMI.

5 – 3 - Unplasticized polyvinyl chloride (uPVC) for construction

"A modern Tudorbethan" house with uPVC gutters and downspouts, fascia, decorative imitation "half-timbering", windows, and doors

uPVC, also known as rigid PVC, is extensively used in the building industry as a low-maintenance material, particularly in Ireland, the United Kingdom, and in the United States. In the USA it is known as vinyl, or vinyl siding . The material comes in a range of colors and finishes, including a photo - effect wood finish, and is used as a substitute for painted wood, mostly for window frames and sills when installing double glazing in new buildings, or to replace older single-glazed windows. Other uses include fascia, and siding or weatherboarding. This material has almost entirely replaced the use of cast iron for plumbing and drainage, being used for waste pipes, drainpipes, gutters and downspouts. uPVC does not contain

phthalates, since those are only added to flexible PVC, nor does it contain BPA. uPVC is known as having strong resistance against chemicals, sunlight, and oxidation from water.

Double glazed units

5 – 4 - Signs

Poly vinyl chloride is formed in flat sheets in a variety of thicknesses and colors. As flat sheets, PVC is often expanded to create voids in the interior of the material, providing additional thickness without additional weight and minimal extra cost (see Closed-cell PVC foamboard). Sheets are cut using saw and rotary cutting equipment. Plasticized PVC is also used to produce thin, colored, or clear, adhesive - backed films referred to simply as vinyl. These films are typically cut on a computer-controlled plotter or printed in a wide-format printer. These sheets and films are used to produce a wide variety of commercial signage products and markings on vehicles, e.g. car body stripes.

5 – 5 - Clothing and furniture

PVC has become widely used in clothing, to either create a leather-like material or at times simply for the effect of PVC. PVC clothing is common in Goth, Punk, clothing fetish and alternative fashions. PVC is cheaper than rubber, leather, and latex which it is therefore used to simulate.

PVC fabric has a sheen to it and is waterproof so is used in coats, skiing equipment, shoes, jackets, aprons, and bags.

5 – 6 - Sport

Due to its versatility PVC has also developed quite a few uses within the sporting area. In the UK the British Plastics Federation has

produced a novel and interesting YouTube video covering the particular use of PVC coated fabric at recent sporting events in 2012. .

5 – 7 - Healthcare

The two main application areas for medically approved PVC compounds are flexible containers and tubing: containers used for blood and blood components for urine or for ostomy products and tubing used for blood taking and blood giving sets, catheters, heart-lung bypass sets, haemodialysis set etc. In Europe the consumption of PVC for medical devices is approximately 85.000 tons every year. Almost one third of plastic based medical devices are made from PVC.

5 – 8 - Flooring

Flexible PVC flooring is inexpensive and used in a variety of buildings covering the home, hospitals, offices, schools, etc. Complex and 3D designs are possible due to the prints that can be created which are then protected by a clear wear layer. A middle vinyl foam layer also gives a comfortable and safe feel. The smooth, tough surface of the upper wear layer prevents the build up of dirt which prevents microbes from breeding in areas that need to be kept sterile, such as hospitals and clinics.

5 – 8 - Other applications

PVC has been used for a host of consumer products of relatively smaller volume compared to the industrial and commercial applications described above. Another of its earliest mass-market consumer applications was to make vinyl records. More recent examples include wallcovering, greenhouses, home playgrounds, foam and other toys, custom truck toppers (tarpaulins), ceiling tiles and other kinds of interior cladding.

6 - Chlorinated PVC

PVC can be usefully modified by chlorination, which increases its chlorine content to 67 %. The new material has a higher heat resistance so is primarily used for hot water pipe and fittings, but it is more expensive and it is found only in niche applications, such as certain water heaters and certain specialized clothing. An extensive

market for chlorinated PVC is in pipe for use in office building, apartment and condominium fire protection. CPVC, as it is called, is produced by chlorination of aqueous solution of suspension PVC particles followed by exposure to UV light which initiates the free-radical chlorination.

7 - Health and safety

7 – 1 - Degradation

Plastics, like most materials, degrade, albeit slowly, in all environmental settings by means of bio-degradation, photo-degradation, thermo-oxidative degradation or hydrolysis. Degradation is a chemical change that drastically reduces the average molecular weight of the polymer. Since the mechanical integrity of plastics invariably depends on their high average molecular-weight, any significant extent of degradation inevitably weakens the material. Weathering degradation of plastics results in their surface embrittlement and microcracking, yielding microparticles that continue on in the environment, known as *microplastics*. Microplastics concentrate Persistent Organic Pollutants (POPs). The relevant distribution coefficients for common POPs are several orders of magnitude in favor of the plastic medium. Consequently, the microparticles laden with high levels of POPs can be ingested by organisms in the biosphere. Given the increased levels of plastic pollution of the environment, this is an important concept in understanding the food web.

7 – 2 - Plasticizers

It has been claimed that some plasticizers leach out of PVC products. However, it has been difficult to prove that plasticizers readily migrate and leach into the environment from flexible vinyl articles because they are physically and tightly bound into the plastic as a result of the heating process used to make PVC particles. Vinyl products are pervasive — including toys,[25] car interiors, shower curtains, and flooring — and initially release chemical gases into the air. Some studies indicate that this outgassing of additives may contribute to health complications, and have resulted in a call for banning the use of DEHP on shower curtains, among other uses.[26]

The Japanese car companies Toyota, Nissan, and Honda have eliminated PVC in their car interiors starting in 2007.

One niche area in which this has become of particular concern is in PC Water Cooling applications. Over the past year (beginning in early 2012), reports began to surface at the Enthusiast Computing Forum Overclock.net that the tubing used in many peoples' water loops had a strange, white powdery substance stuck to it. This was discovered after a great number of people had noticed their clear tubing begin to "haze" significantly and in a very short period of time.[27] Primochill, a company specializing in the production of water cooling equipment, had a line of tubing called "PrimoFlex Pro LRT" that was widely used due to its flexibility (low-radius bends possible without kinking), ease of use, and selection of colors which negated the need for dyes (potentially unreliable at best and damaging to components at worst). However, while this company was hit the hardest, likely due to their efforts to put the blame on the users, they were far from the only manufacturer whose tubing was having issues. Recently, new lines of tubing have been released that are alleged to use less or even "no" plasticizer, and while reception so far has been favorable in the community, many are still skeptical.

In 2004 a joint Swedish-Danish research team found a statistical association between allergies in children and indoor air levels of DEHP and BBzP (butyl benzyl phthalate), which is used in vinyl flooring.[28] In December 2006, the European Chemicals Bureau of the European Commission released a final draft risk assessment of BBzP which found "no concern" for consumer exposure including exposure to children.

7 – 2 - 1 - EU decisions on phthalates

Risk assessments have led to the classification of low molecular weight and labeling as Category 1B Reproductive agents. Three of these phthalates, DBP, BBP and DEHP were included on annex XIV of the REACH regulation in February 2011 and will be phased out by the EU by February 2015 unless an application for authorisation is made before July 2013 and an authorisation granted. DIBP is still on the REACH Candidate List for Authorisation. The European Union

has confirmed that DEHP poses no general risk to human health. The summary of a comprehensive European risk assessment, involving nearly 15 years of extensive scientific evaluation by EU regulators, was published in the EU Official Journal on February 7, 2008[30] The assessment demonstrated that DEHP poses no risk to the general population and that no further measures need to be taken to manage the substance in any of its key end-use applications. This confirms an earlier opinion of member state experts and an opinion from the EU Scientific Committee for Toxicity, Ecotoxicity and the Environment (CSTEE) adopted in 2004. The only areas of possible risk identified in the assessment relate to :

The use of DEHP in children's toys. Under regulations introduced in January 2007 DEHP is no longer permitted in toys and childcare articles in the EU.

Possible exposure of workers in factories. Adequate precautions are already taken based on occupational exposure limit values and some localised environmental exposure near to factories.

The use of DEHP in certain medical devices. An EU Scientific Review was requested to determine whether there may be any risk from the use of DEHP in certain medical applications (children and neonates undergoing long-term blood transfusion and adults undergoing long-term haemodialysis).

In 2008 the European Union's Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) reviewed the safety of DEHP in medical devices. The SCENIHR report states that certain medical procedures used in high risk patients result in a significant exposure to DEHP and concludes there is still a reason for having some concerns about the exposure of prematurely born male babies to medical devices containing DEHP . The Committee said there are some alternative plasticizers available for which there is sufficient toxicological data to indicate a lower hazard compared to DEHP but added that the functionality of these plasticizers should be assessed before they can be used as an alternative for DEHP in PVC medical devices. Risk assessment results have shown positive results

regarding the safe use of High Molecular Weight Phthalates. They have all been registered for REACH and do not require any classification for health and environmental effects, nor are they on the Candidate List for Authorisation. High phthalates are not CMR (carcinogenic, mutagenic or toxic for reproduction), neither are they considered endocrine disruptors.

In the EU Risk Assessment the European Commission has confirmed that Di-isononyl phthalate (DINP) and Di-isodecyl phthalate (DIDP) pose no risk to either human health or the environment from any current use. The European Commission's findings (published in the EU Official Journal on April 13, 2006)[32] confirm the outcome of a risk assessment involving more than 10 years of extensive scientific evaluation by EU regulators. Following the recent adoption of EU legislation with the regard to the marketing and use of DINP in toys and childcare articles, the risk assessment conclusions clearly state that there is no need for any further measures to regulate the use of DINP. In Europe and in some other parts of the world, the use of DINP in toys and childcare items has been restricted as a precautionary measure. In Europe, for example, DINP can no longer be used in toys and childcare items that can be put in the mouth even though the EU scientific risk assessment concluded that its use in toys does not pose a risk to human health or the environment. The rigorous EU risk assessments, which include a high degree of conservatism and built-in safety factors, have been carried out under the strict supervision of the European Commission and provide a clear scientific evaluation on which to judge whether or not a particular substance can be safely used.

The FDA Paper titled "Safety Assessment of Di(2-ethylhexyl)phthalate (DEHP)Released from PVC Medical Devices" states that [3.2.1.3] Critically ill or injured patients may be at increased risk of developing adverse health effects from DEHP, not only by virtue of increased exposure relative to the general population, but also because of the physiological and pharmacodynamic changes that occur in these patients compared to healthy individuals.

7 – 3 - Vinyl chloride monomer

In the early 1970s, the carcinogenicity of vinyl chloride (usually called vinyl chloride mononomer or VCM) was linked to cancers in workers in the polyvinyl chloride industry. Specifically workers in polymerization section of a B.F. Goodrich plant near Louisville, Kentucky (US) were diagnosed with liver angiosarcoma also known as hemangiosarcoma, a rare disease.[34] Since that time, studies of PVC workers in Australia, Italy, Germany, and the UK have all associated certain types of occupational cancers with exposure to vinyl chloride, and it has become accepted that VCM is a carcinogen.[4] Technology for removal of VCM from products have become stringent commensurate with the associated regulations.

7 – 3 - Dioxins

PVC produces HCl upon combustion almost quantitatively related to its chlorine content. Extensive studies in Europe indicate that the chlorine found in emitted dioxins is not derived from HCl in the flue gases. Instead, most dioxins arise in the condensed solid phase by the reaction of inorganic chlorides with graphitic structures in char-containing ash particles. Copper acts as a catalyst for these reactions.

Studies of household waste burning indicate consistent increases in dioxin generation with increasing PVC concentrations.[36] According to the EPA dioxin inventory, landfill fires are likely to represent an even larger source of dioxin to the environment. A survey of international studies consistently identifies high dioxin concentrations in areas affected by open waste burning and a study that looked at the homologue pattern found the sample with the highest dioxin concentration was "typical for the pyrolysis of PVC". Other EU studies indicate that PVC likely "accounts for the overwhelming majority of chlorine that is available for dioxin formation during landfill fires."

The next largest sources of dioxin in the EPA inventory are medical and municipal waste incinerators . Various studies have been conducted that reach contradictory results. For instance a study of commercial - scale incinerators showed no relationship between the PVC content of the waste and dioxin emissions . Other studies have

shown a clear correlation between dioxin formation and chloride content and indicate that PVC is a significant contributor to the formation of both dioxin and PCB in incinerators.

In February 2007, the Technical and Scientific Advisory Committee of the US Green Building Council (USGBC) released its report on a PVC avoidance related materials credit for the LEED Green Building Rating system. The report concludes that "no single material shows up as the best across all the human health and environmental impact categories, nor as the worst" but that the "risk of dioxin emissions puts PVC consistently among the worst materials for human health impacts."

In Europe the overwhelming importance of combustion conditions on dioxin formation has been established by numerous researchers. The single most important factor in forming dioxin-like compounds is the temperature of the combustion gases. Oxygen concentration also plays a major role on dioxin formation, but not the chlorine content.

The design of modern incinerators minimises PCDD / F formation by optimising the stability of the thermal process. To comply with the EU emission limit of 0.1 ng I-TEQ / m3 modern incinerators operate in conditions minimising dioxin formation and are equipped with pollution control devices which catch the low amounts produced. Recent information is showing for example that dioxin levels in populations near incinerators in Lisbon and Madeira have not risen since the plants began operating in 1999 and 2002 respectively.

Several studies have also shown that removing PVC from waste would not significantly reduce the quantity of dioxins emitted. The European Union Commission published in July 2000 a Green Paper on the Environmental Issues of PVC. " The Commission states (page 27) that it has been suggested that the reduction of the chlorine content in the waste can contribute to the reduction of dioxin formation, even though the actual mechanism is not fully understood. The influence on the reduction is also expected to be a second or third order relationship. It is most likely that the main incineration parameters,

such as the temperature and the oxygen concentration, have a major influence on the dioxin formation". The Green Paper states further that at the current levels of chlorine in municipal waste, there does not seem to be a direct quantitative relationship between chlorine content and dioxin formation.

A study commissioned by the European Commission on "Life Cycle Assessment of PVC and of principal competing materials" states that "Recent studies show that the presence of PVC has no significant effect on the amount of dioxins released through incineration of plastic waste."

7 – 5 - End – of - life

The European waste hierarchy refers to the 5 steps included in the article 4 of the Waste Framework Directive:

Prevention - preventing and reducing waste generation.

Reuse and preparation for reuse - giving the products a second life before they become waste.

Recycle - any recovery operation by which waste materials are reprocessed into products, materials or substances whether for the original or other purposes. It includes composting and it does not include incineration.

Recovery - some waste incineration based on a political non-scientific formula that upgrades the less inefficient incinerators.

Disposal - processes to dispose of waste be it landfilling, incineration, pyrolysis, gasification and other finalist solutions. Landfill is restricted in some EU-countries through Landfill Directives and there is a debate about Incineration E.g. original plastic which contains a lot of energy is just recovered in energy and not recycled. According to the Waste Frame work Directive the European Waste Hierarchy is legally binding except in cases that may require specific waste streams to depart from the hierarchy. This should be justified on the basis of life - cycle thinking.

The European Commission has set new rules to promote the recovery of PVC waste for use in a number of construction products. It says: "The use of recovered PVC should be encouraged in the manufacture of certain construction products because it allows the reuse of old PVC [..] This avoids PVC being discarded in landfills or incinerated causing release of carbon dioxide and cadmium in the environment".

7 – 5 - 1 - Industry initiatives

In Europe, developments in PVC waste management have been monitored by Vinyl 2010, established in 2000. Vinyl 2010's objective was to recycle 200,000 tonnes of post-consumer PVC waste per year in Europe by the end of 2010, excluding waste streams already subject to other or more specific legislation (such as the European Directives on End-of-Life Vehicles, Packaging and Waste Electric and Electronic Equipment).

Since June 2011, it is followed by Vinylplus, a new set of targets for sustainable development . Its main target is to recycle 800,000 tonnes/year of PVC by 2020 including 100,000 tonnes of *difficult to recycle* waste. One technology for collection and recycling of PVC waste is Recovinyl which reported the recycled tonnage as follows: pipe 25 kT, profile 107 kT, rigid film 6 kT, flexible cables 79 kt and mixed flexible 38 kT.

One approach to address the problem of waste PVC is through the process called Vinyloop. It is a mechanical recycling process using a solvent to separate PVC from other materials. This solvent turns in a closed loop process in which the solvent is recycled. Recycled PVC is used in place of virgin PVC in various applications: coatings for swimming pools, shoe soles, hoses, diaphragms tunnel, coated fabrics, PVC sheets . This recycled PVC's primary energy demand is 46 percent lower than conventional produced PVC. So the use of recycled material leads to a significant better ecological footprint. The global warming potential is 39 percent lower.

7 – 5 - 2 - Restrictions

In November, 2005 one of the largest hospital networks in the U.S., Catholic Healthcare West, signed a contract with B. Braun Melsungen for vinyl-free intravenous bags and tubing.

In January, 2012 a major U.S. West Coast healthcare provider, Kaiser Permanente, announced that it will no longer buy intravenous (IV) medical equipment made with polyvinyl chloride (PVC) and DEHP (di-2-ethyl hexyl phthalate) type plasticizers.

8 - Sustainability

The Olympic Delivery Authority (ODA) has chosen PVC as material for different temporary venues of the London Olympics 2012. The ODA want to ensure to meet the highest environmental and social standards for the PVC materials. E.g. temporary parts like Roofing covers of the Olympic Stadium, the Water Polo Arena and the Royal Artillery Barracks will be deconstructed and a part will be recycled in the Vinyloop process.

As we have done in the past with materials such as timber and concrete, we want to use the opportunity of hosting the London 2012 Games to work with industry to set new standards. In this case this may help move the industry towards more sustainable manufacture, use and disposal of PVC fabrics.

Dan Epstein Head of Sustainable Development at Olympic Delivery Authority (ODA)

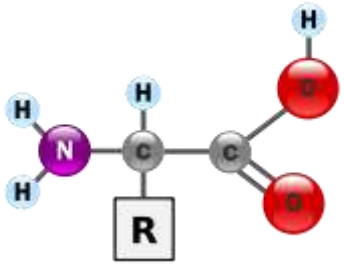
The ODA after initially rejecting PVC as material has reviewed its decision and develop a policy for the use of PVC. The PVC policy has focused attention on the use of PVC across the project and highlighted that the functional properties of PVC make it the most appropriate material in certain circumstances. Environmental and social impacts across the whole life cycle played an important role, with e.g. the rate for recycling or re-use and the percentage of recycled content.

Part – 10 –

Aliphatic Amino Acid

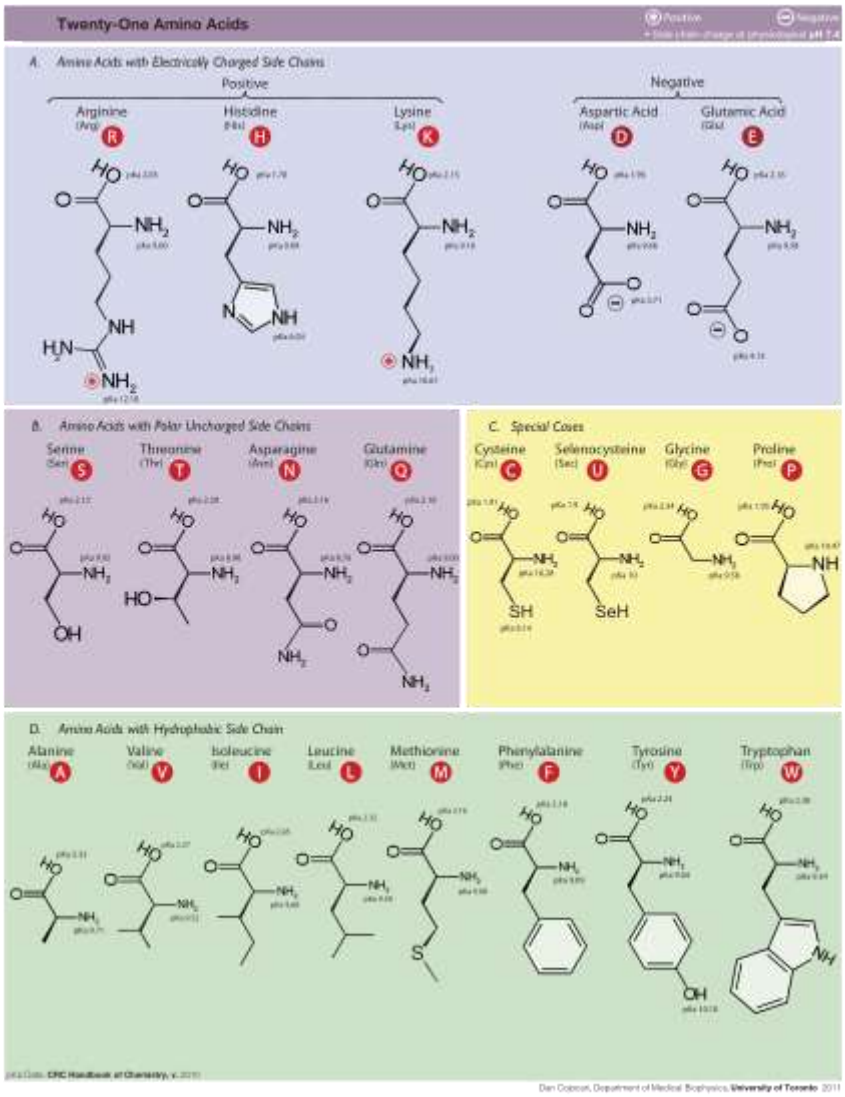
Amino Acid

This article is about the class of chemicals. For the structures and properties of the standard proteinogenic amino acids, see Proteinogenic amino acid.



The generic structure of an alpha amino acid in its un-ionized form

Contents



The 21 amino acids found in eukaryotes, grouped according to their side - chains' pK_a values and charges carried at physiological pH 7.4

1 - Introduction

Amino acids are biologically important organic compounds made from amine (-NH_2) and carboxylic acid (- COOH) functional groups, along with a side-chain specific to each amino acid. The key elements of an amino acid are carbon, hydrogen, oxygen, and nitrogen, though other elements are found in the side-chains of certain amino acids. About 500 amino acids are known[1] and can be classified in many ways. Structurally they can be classified according to the functional groups' locations as alpha- (α-), beta- (β-), gamma- (γ-) or delta- (δ-) amino acids; other categories relate to polarity, pH level, and side chain group type (aliphatic, acyclic, aromatic,

containing hydroxyl or sulfur, etc. In the form of proteins, amino acids comprise the second largest component (after water) of human muscles, cells and other tissues. Outside proteins, amino acids perform critical roles in processes such as neurotransmitter transport and biosynthesis.

Amino acids having both the amine and carboxylic acid groups attached to the first (alpha-) carbon atom have particular importance in biochemistry. They are known as **2-, alpha-,** or **α-amino acids** (generic formula $H_2NCHRCOOH$ in most cases where R is an organic substituent known as a "side-chain"); often the term "amino acid" is used to refer specifically to these. They include the 23 proteinogenic ("protein-building") amino acids which combine into peptide chains ("poly peptides") to form the building blocks of a vast array of proteins . These are all L-stereoisomers ("left-handed" isomers) although a few D-amino acids ("right-handed") occur in bacterial envelopes and some antibiotics . 20 of the 23 proteinogenic amino acids are encoded directly by triplet codons in the genetic code and are known as "standard" amino acids. The other three ("non-standard" or "non-canonical") are pyrrolysine (found in methanogenic organisms and other eukaryotes), selenocysteine (present in many noneukaryotes as well as most eukaryotes), and N-Formylmethionine.

For example, 25 human proteins include selenocysteine (Sec) in their primary structure, and the structurally characterized enzymes (selenoenzymes) employ Sec as the catalytic moiety in their active sites. Pyrollysine and selenocysteine are encoded via variant codons; for example, selenocysteine is encoded by stop codon and SECIS element . Codon–tRNA combinations not found in nature can also be used to "expand" the genetic code and create novel proteins known as alloproteins incorporating non - proteinogenic amino acids.

Many important proteinogenic and non-proteinogenic amino acids also play critical non-protein roles within the body. For example: in the human brain, glutamate (standard glutamic acid) and gamma-amino-butyric acid ("GABA", non-standard gamma-amino acid) are respectively the main excitatory and inhibitory neuro transmitters ; hydroxyproline (a major component of the connective

tissue collagen) is synthesised from proline; the standard amino acid glycine is used to synthesise porphyrins used in red blood cells; and the non-standard carnitine is used in lipid transport.

9 of the 20 standard amino acids are called "essential" for humans because they cannot be created from other compounds by the human body, and so must be taken in as food. Others may be conditionally essential for certain ages or medical conditions. Essential amino acids may also differ between species.

Because of their biological significance, amino acids are important in nutrition and are commonly used in nutritional supplements, fertilizers, and food technology. Industrial uses include the production of drugs, biodegradable plastics and chiral catalysts.

2 - History

The first few amino acids were discovered in the early 19th century. In 1806, French chemists Louis-Nicolas Vauquelin and Pierre Jean Robiquet isolated a compound in asparagus that was subsequently named asparagine, the first amino acid to be discovered. Cystine was discovered in 1810, although its monomer, cysteine, remained undiscovered until 1884. Glycine and leucine were discovered in 1820. Usage of the term *amino acid* in the English language is from 1898. Proteins were found to yield amino acids after enzymatic digestion or acid hydrolysis. In 1902, Emil Fischer and Franz Hofmeister proposed that proteins are the result of the formation of bonds between the amino group of one amino acid with the carboxyl group of another, in a linear structure which Fischer termed peptide.

3 - General structure

In the structure shown at the top of the page, **R** represents a side-chain specific to each amino acid. The carbon atom next to the carboxyl group is called the α–carbon and amino acids with a side-chain bonded to this carbon are referred to as *alpha amino acids*. These are the most common form found in nature. In the alpha amino acids, the α–carbon is a chiral carbon atom, with the exception of glycine. In amino acids that have a carbon chain attached to the α–

carbon (such as lysine, shown to the right) the carbons are labeled in order as α, β, γ, δ, and so on. In some amino acids, the amine group is attached to the β or γ-carbon, and these are therefore referred to as *beta* or *gamma amino acids*.

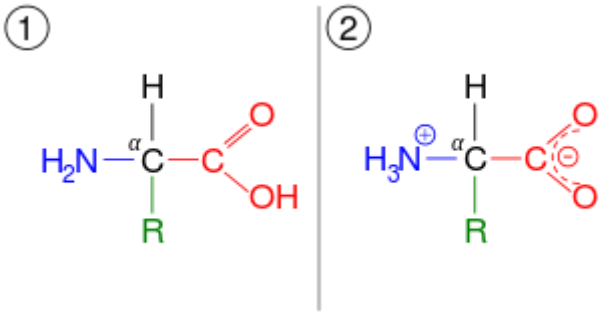
Amino acids are usually classified by the properties of their side-chain into four groups. The side-chain can make an amino acid a weak acid or a weak base, and a hydrophile if the side-chain is polar or a hydrophobe if it is nonpolar. The chemical structures of the 22 standard amino acids, along with their chemical properties, are described more fully in the article on these proteinogenic amino acids.

The phrase "branched - chain amino acids" or BCAA refers to the amino acids having aliphatic side-chains that are non-linear; these are leucine, isoleucine, and valine. Proline is the only proteinogenic amino acid whose side-group links to the α-amino group and, thus, is also the only proteinogenic amino acid containing a secondary amine at this position.[25] In chemical terms, proline is, therefore, an imino acid, since it lacks a primary amino group, although it is still classed as an amino acid in the current biochemical nomenclature, and may also be called an "N-alkylated alpha-amino acid".

3 – 1 - Isomerism

Of the standard α-amino acids, all but glycine can exist in either of two enantiomers, called L or D amino acids, which are mirror images of each other (*see also Chirality*). While L-amino acids represent all of the amino acids found in proteins during translation in the ribosome, D-amino acids are found in some proteins produced by enzyme post translational modifications after translation and translocation to the endoplasmic reticulum, as in exotic sea-dwelling organisms such as cone snails. They are also abundant components of the peptidoglycan cell walls of bacteria , and D-serine may act as a neurotransmitter in the brain. The L and D convention for amino acid configuration refers not to the optical activity of the amino acid itself, but rather to the optical activity of the isomer of glyceraldehyde from which that amino acid can, in theory, be synthesized (D-glyceraldehyde is dextrorotary; L-glyceraldehyde is levorotatory). In alternative fashion, the *(S)* and *(R)* designators are used to indicate the

absolute stereochemistry. Almost all of the amino acids in proteins are *(S)* at the α carbon, with cysteine being *(R)* and glycine non-chiral.[33] Cysteine is unusual since it has a sulfur atom at the second position in its side-chain, which has a larger atomic mass than the groups attached to the first carbon, which is attached to the α-carbon in the other standard amino acids, thus the *(R)* instead of *(S)*.



An amino acid in its (1) un-ionized and (2) zwitterionic forms

3 – 2 - Zwitterions

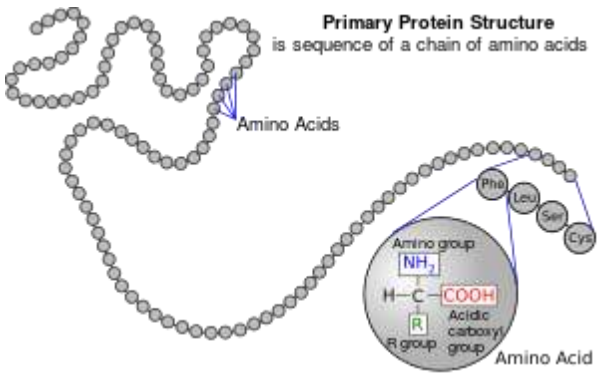
The amine and carboxylic acid functional groups found in amino acids allow them to have amphiprotic properties . Carboxylic acid groups ($-CO_2H$) can be deprotonated to become negative carboxylates ($-CO_2^-$), and α-amino groups (NH_2-) can be protonated to become positive α-ammonium groups ($^+NH_3-$). At pH values greater than the pKa of the carboxylic acid group (mean for the 20 common amino acids is about 2.2, see the table of amino acid structures above), the negative carboxylate ion predominates. At pH values lower than the pKa of the α - ammonium group (mean for the 20 common α-amino acids is about 9.4), the nitrogen is predominantly protonated as a positively charged α-ammonium group. Thus, at pH between 2.2 and 9.4, the predominant form adopted by α-amino acids contains a negative carboxylate and a positive α-ammonium group, as shown in structure (2) on the right, so has net zero charge. This molecular state is known as a zwitterion, from the German **Zwitter** meaning *hermaphrodite* or *hybrid* . Below pH 2.2, the predominant form will have a neutral carboxylic acid group and a positive α-ammonium ion (net charge +1), and above pH 9.4, a negative carboxylate and neutral α-amino group (net charge −1). The fully neutral form (structure (1) on the right) is a very minor species in aqueous solution throughout the pH range (less than 1 part in 10^7).

Amino acids also exist as zwitterions in the solid phase, and crystallize with salt-like properties unlike typical organic acids or amines.

3 – 3 – Iso electric point

At pH values between the two pKa values, the zwitterion predominates, but coexists in dynamic equilibrium with small amounts of net negative and net positive ions. At the exact midpoint between the two pKa values, the trace amount of net negative and trace of net positive ions exactly balance, so that average net charge of all forms present is zero . This pH is known as the isoelectric point pI, so pI = ½(pKa_1 + pKa_2). The individual amino acids all have slightly different pKa values, so have different isoelectric points. For amino acids with charged side - chains, the pKa of the side - chain is involved. Thus for Asp, Glu with negative side-chains, pI = ½ (pKa_1 + pKa_R), where pKa_R is the side-chain pKa. Cysteine also has potentially negative side-chain with pKa_R = 8.14, so pI should be calculated as for Asp and Glu, even though the side-chain is not significantly charged at neutral pH. For His, Lys, and Arg with positive side-chains, pI = ½ (pKa_R + pKa_2). Amino acids have zero mobility in electrophoresis at their isoelectric point, although this behaviour is more usually exploited for peptides and proteins than single amino acids. Zwitterions have minimum solubility at their isolectric point and some amino acids (in particular, with non-polar side-chains) can be isolated by precipitation from water by adjusting the pH to the required isoelectric point.

4 - Occurrence and functions in biochemistry



A polypeptide is an unbranched chain of amino acids.

4 – 1 - Standard amino acids

Amino acids are the structural units (monomers) that make up proteins. They join together to form short polymer chains called peptides or longer chains called either polypeptides or proteins. These polymers are linear and unbranched, with each amino acid within the chain attached to two neighboring amino acids. The process of making proteins is called *translation* and involves the step-by-step addition of amino acids to a growing protein chain by a ribozyme that is called a ribosome.[36] The order in which the amino acids are added is read through the genetic code from an mRNA template, which is a RNA copy of one of the organism's genes.

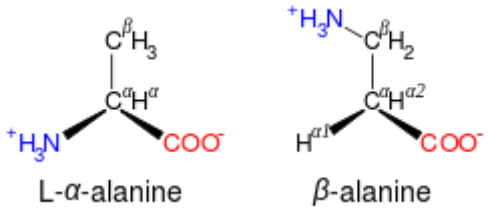
Twenty - two amino acids are naturally incorporated into polypeptides and are called proteinogenic or natural amino acids.[25] Of these, 20 are encoded by the universal genetic code. The remaining 2, selenocysteine and pyrrolysine, are incorporated into proteins by unique synthetic mechanisms. Selenocysteine is incorporated when the mRNA being translated includes a SECIS element, which causes the UGA codon to encode selenocysteine instead of a stop codon.[37] Pyrrolysine is used by some methanogenic archaea in enzymes that they use to produce methane. It is coded for with the codon UAG, which is normally a stop codon in other organisms. This UAG codon is followed by a PYLIS downstream sequence.

4 – 2 - Non-standard amino acids

Aside from the 22 standard amino acids, there are many other amino acids that are called *non-proteinogenic* or *non - standard*. Those either are not found in proteins (for example carnitine, GABA), or are not produced directly and in isolation by standard cellular machinery (for example, hydroxyproline and selenomethionine).

Non-standard amino acids that are found in proteins are formed by post - translational modification, which is modification after translation during protein synthesis. These modifications are often essential for the function or regulation of a protein; for example, the carboxylation of glutamate allows for better binding of calcium cations , and the hydroxylation of proline is critical for maintaining connective tissues . Another example is the formation of hypusine in

the translation initiation factor EIF5A, through modification of a lysine residue.[42] Such modifications can also determine the localization of the protein, e.g., the addition of long hydrophobic groups can cause a protein to bind to a phospholipid membrane.



β-alanine and its α-alanine isomer

Some nonstandard amino acids are not found in proteins. Examples include lanthionine, 2-amino isobutyric acid, dehydro alanine, and the neuro transmitter gamma – amino butyric acid. Nonstandard amino acids often occur as intermediates in the metabolic pathways for standard amino acids — for example, ornithine and citrulline occur in the urea cycle, part of amino acid catabolism (see below) . A rare exception to the dominance of α-amino acids in biology is the β-amino acid beta alanine (3-aminopropanoic acid), which is used in plants and microorganisms in the synthesis of pantothenic acid (vitamin B_5), a component of coenzyme A.

4 – 3 - In human nutrition

When taken up into the human body from the diet, the 22 standard amino acids either are used to synthesize proteins and other biomolecules or are oxidized to urea and carbon dioxide as a source of energy. The oxidation pathway starts with the removal of the amino group by a transaminase, the amino group is then fed into the urea cycle. The other product of transamidation is a keto acid that enters the citric acid cycle. Glucogenic amino acids can also be converted into glucose, through gluconeogenesis.

Pyrrolysine trait is restricted to several microbes, and only one organism has both Pyl and Sec. Of the 22 standard amino acids, 9 are called essential amino acids because the human body cannot synthesize them from other compounds at the level needed for normal growth, so they must be obtained from food . In addition, cysteine, taurine, tyrosine, and arginine are considered semiessential amino-

acids in children (though taurine is not technically an amino acid), because the metabolic pathways that synthesize these amino acids are not fully developed. The amounts required also depend on the age and health of the individual, so it is hard to make general statements about the dietary requirement for some amino acids.

Essential	**Non essential**
Histidine	Alanine
Isoleucine	Arginine
Leucine	Asparagine
Lysine	Aspartic acid
Methionine	Cysteine
Phenyl alanine	Glutamic acid
Threonine	Glutamine
Tryptophan	Glycine
Valine	Ornithine
	Proline
	Serine
	Tyrosine

5 - Classification of Amino Acids

Although there are many ways to classify amino acids, these molecules can be assorted into six main groups, on the basis of their structure and the general chemical characteristics of their R groups.

Class	**Name of the amino acids**
Aliphatic	Glycine, Alanine, Valine, Leucine, Isoleucine
Hydroxyl or Sulfur-containing	Serine, Cysteine, Threonine, Methionine
Cyclic	Proline
Aromatic	Phenylalanine, Tyrosine, Tryptophan
Basic	Histidine, Lysine, Arginine
Acidic and their Amide	Aspartate, Glutamate, Asparagine, Glutamine

5 – 1 – Non - protein functions

In humans, non-protein amino acids also have important roles as metabolic intermediates, such as in the biosynthesis of the neurotransmitter gamma-aminobutyric acid. Many amino acids are used to synthesize other molecules, for example:

Tryptophan is a precursor of the neurotransmitter serotonin.[54]

Tyrosine (and its precursor phenylalanine) are precursors of the catecholamine neuro transmitters dopamine , epinephrine and norepinephrine.

Glycine is a precursor of porphyrins such as heme.

Arginine is a precursor of nitric oxide.

Ornithine and S-adenosylmethionine are precursors of polyamines.

Aspartate, glycine, and glutamine are precursors of nucleotides.

Phenylalanine is a precursor of various phenylpropanoids, which are important in plant metabolism.

How ever, not all of the functions of other abundant non-standard amino acids are known.

Some non - standard amino acids are used as defenses against herbivores in plants. For example canavanine is an analogue of arginine that is found in many legumes, and in particularly large amounts in *Canavalia gladiata* (sword bean). This amino acid protects the plants from predators such as insects and can cause illness in people if some types of legumes are eaten without processing.[62] The non-protein amino acid mimosine is found in other species of legume, particularly *Leucaena leucocephala*. This compound is an analogue of tyrosine and can poison animals that graze on these plants.

6 - Uses in technology

Amino acids are used for a variety of applications in industry, but their main use is as additives to animal feed. This is necessary, since many of the bulk components of these feeds, such as soybeans, either have low levels or lack some of the essential amino acids: Lysine, methionine, threonine, and tryptophan are most important in the production of these feeds . In this industry, amino acids are also

used to chelate metal cations in order to improve the absorption of minerals from supplements, which may be required to improve the health or production of these animals.

The food industry is also a major consumer of amino acids, in particular, glutamic acid, which is used as a flavor enhancer,[66] and Aspartame (aspartyl-phenyl alanine-1- methyl ester) as a low-calorie artificial sweetener . Similar technology to that used for animal nutrition is employed in the human nutrition industry to alleviate symptoms of mineral deficiencies, such as anemia, by improving mineral absorption and reducing negative side effects from inorganic mineral supplementation.

The chelating ability of amino acids has been used in fertilizers for agriculture to facilitate the delivery of minerals to plants in order to correct mineral deficiencies, such as iron chlorosis. These fertilizers are also used to prevent deficiencies from occurring and improving the overall health of the plants. The remaining production of amino acids is used in the synthesis of drugs and cosmetics.

Amino acid derivative	**Pharmaceutical application**
5-HTP (5-hydroxy try ptophan)	Experimental treatment for depression.
L-DOPA (L-di hydroxy phenyl alanine)	Treatment for Parkinsonism.
Eflornithine	Drug that inhibits ornithine decarboxylase and is used in the treatment of sleeping sickness.

6 – 1 - Expanded genetic code

Since 2001, 40 non-natural amino acids have been added into protein by creating a unique codon (recoding) and a corresponding transfer-RNA:aminoacyl – tRNA-synthetase pair to encode it with diverse physicochemical and biological properties in order to be used as a tool to exploring protein structure and function or to create novel or enhanced proteins.

6 – 2 - Chemical building blocks

Amino acids are important as low - cost feed stocks. These compounds are used in chiral pool synthesis as enantiomerically pure building blocks.

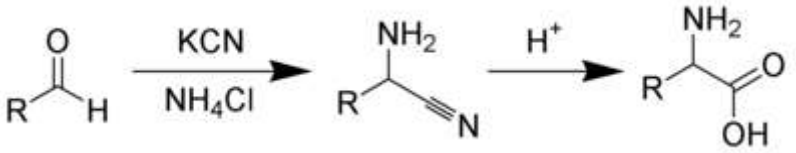
Amino acids have been investigated as precursors chiral catalysts, e.g., for asymmetric hydrogenation reactions, although no commercial applications exist.

6 – 3 - Biodegradable plastics

Amino acids are under development as components of a range of biodegradable polymers. These materials have applications as environmentally friendly packaging and in medicine in drug delivery and the construction of prosthetic implants. These polymers include polypeptides, polyamides, polyesters, polysulfides, and polyurethanes with amino acids either forming part of their main chains or bonded as side-chains. These modifications alter the physical properties and reactivities of the polymers. An interesting example of such materials is polyaspartate, a water-soluble biodegradable polymer that may have applications in disposable diapers and agriculture.[76] Due to its solubility and ability to chelate metal ions, polyaspartate is also being used as a biodegradeable anti-scaling agent and a corrosion inhibitor. In addition, the aromatic amino acid tyrosine is being developed as a possible replacement for toxic phenols such as bisphenol A in the manufacture of polycarbonates.

7 - Reactions

As amino acids have both a primary amine group and a primary carboxyl group, these chemicals can undergo most of the reactions associated with these functional groups. These include nucleophilic addition, amide bond formation and imine formation for the amine group and esterification, amide bond formation and decarboxylation for the carboxylic acid group. The combination of these functional groups allow amino acids to be effective polydentate ligands for metal - amino acid chelates. The multiple side-chains of amino acids can also undergo chemical reactions. The types of these reactions are determined by the groups on these side - chains and are, therefore, different between the various types of amino acid.



The Strecker amino acid synthesis

7 – 1 - Chemical synthesis

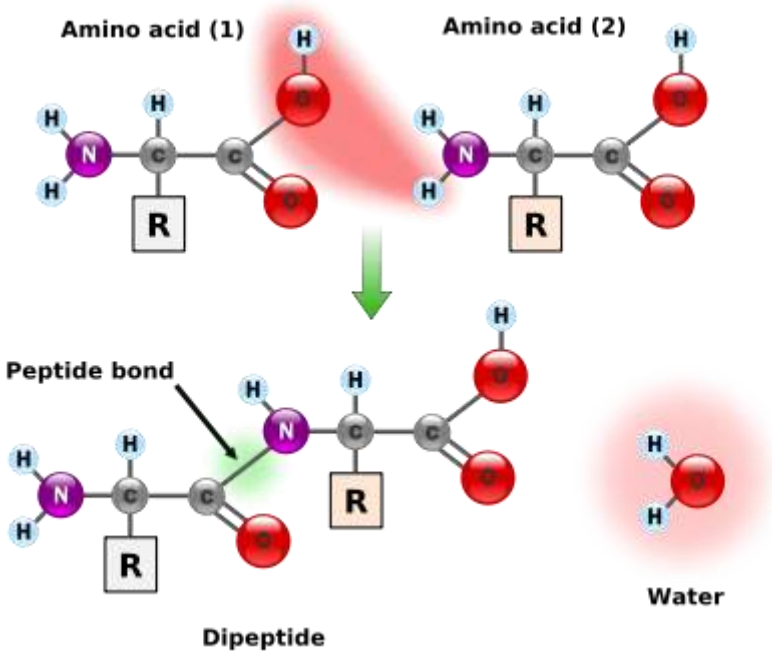
Several methods exist to synthesize amino acids. One of the oldest methods begins with the bromination at the α-carbon of a carboxylic acid. Nucleophilic substitution with ammonia then converts the alkyl bromide to the amino acid. In alternative fashion, the Strecker amino acid synthesis involves the treatment of an aldehyde with potassium cyanide and ammonia, this produces an α-amino nitrile as an intermediate. Hydrolysis of the nitrile in acid then yields a α-amino acid. Using ammonia or ammonium salts in this reaction gives unsubstituted amino acids, while substituting primary and secondary amines will yield substituted amino acids.[85] Likewise, using ketones, instead of aldehydes, gives α,α-disubstituted amino acids . The classical synthesis gives racemic mixtures of α-amino acids as products, but several alternative procedures using asymmetric auxiliaries or asymmetric catalysts have been developed.

At the current time, the most-adopted method is an automated synthesis on a solid support (e.g., polystyrene beads), using protecting groups (e.g., Fmoc and t-Boc) and activating groups (e.g., DCC and DIC).

7 – 2 - Peptide bond formation

As both the amine and carboxylic acid groups of amino acids can react to form amide bonds, one amino acid molecule can react with another and become joined through an amide linkage. This polymerization of amino acids is what creates proteins. This condensation reaction yields the newly formed peptide bond and a molecule of water. In cells, this reaction does not occur directly; instead the amino acid is first activated by attachment to a transfer RNA molecule through an ester bond. This aminoacyl-tRNA is produced in an ATP-dependent reaction carried out by an aminoacyl tRNA synthetase. This amino acyl - tRNA is then a substrate for the

ribosome, which catalyzes the attack of the amino group of the elongating protein chain on the ester bond. As a result of this mechanism, all proteins made by ribosomes are synthesized starting at their N-terminus and moving towards their C - terminus.



The condensation of two amino acids to form a dipeptide through a peptide bond

How ever, not all peptide bonds are formed in this way. In a few cases, peptides are synthesized by specific enzymes. For example, the tripeptide glutathione is an essential part of the defenses of cells against oxidative stress. This peptide is synthesized in two steps from free amino acids . In the first step gamma-glutamylcysteine synthetase condenses cysteine and glutamic acid through a peptide bond formed between the side-chain carboxyl of the glutamate (the gamma carbon of this side-chain) and the amino group of the cysteine. This dipeptide is then condensed with glycine by glutathione synthetase to form glutathione.

In chemistry, peptides are synthesized by a variety of reactions. One of the most-used in solid-phase peptide synthesis uses the aromatic oxime derivatives of amino acids as activated units. These are added in sequence onto the growing peptide chain, which is attached to a solid resin support. The ability to easily synthesize vast

numbers of different peptides by varying the types and order of amino acids (using combinatorial chemistry) has made peptide synthesis particularly important in creating libraries of peptides for use in drug discovery through high-throughput screening.

7 – 3 - Biosynthesis

In plants, nitrogen is first assimilated into organic compounds in the form of glutamate, formed from alpha-ketoglutarate and ammonia in the mitochondrion. In order to form other amino acids, the plant uses transaminases to move the amino group to another alpha-keto carboxylic acid. For example, aspartate aminotransferase converts glutamate and oxaloacetate to alpha-ketoglutarate and aspartate. Other organisms use transaminases for amino acid synthesis, too.

Non standard amino acids are usually formed through modifications to standard amino acids. For example, homocysteine is formed through the transsulfuration pathway or by the demethylation of methionine via the intermediate metabolite S-adenosyl methionine, while hydroxyproline is made by a posttranslational modification of proline.

Microorganisms and plants can synthesize many uncommon amino acids. For example, some microbes make 2-amino isobutyric acid and lanthionine, which is a sulfide-bridged derivative of alanine. Both of these amino acids are found in peptidic lantibiotics such as alamethicin. While in plants, 1-aminocyclopropane-1-carboxylic acid is a small disubstituted cyclic amino acid that is a key intermediate in the production of the plant hormone ethylene.

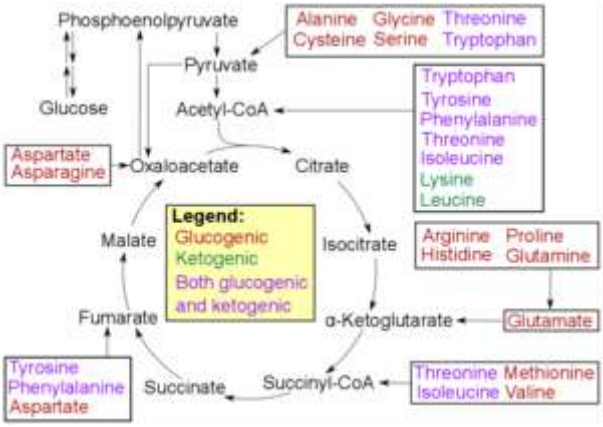
7 – 4 - Catabolism

Amino acids can be classified according to the properties of their main products as either of the following:

* *Glucogenic*, with the products having the ability to form glucose by gluconeogenesis

* *Ketogenic*, with the products not having the ability to form glucose. These products may still be used for ketogenesis or lipid synthesis.

* Amino acids catabolized into both glucogenic and ketogenic products.



Catabolism of proteinogenic amino acids.

Degradation of an amino acid often involves deamination by moving its amino group to alpha-ketoglutarate, forming glutamate. This process involves transaminases, often the same as those used in amination during synthesis. In many vertebrates, the amino group is then removed through the urea cycle and is excreted in the form of urea. However, amino acid degradation can produce uric acid or ammonia instead. For example, serine dehydratase converts serine to pyruvate and ammonia. After removal of one or more amino groups, the remainder of the molecule can sometimes be used to synthesize new amino acids, or it can be used for energy by entering glycolysis or the citric acid cycle, as detailed in image at right.

8 - Physicochemical properties of amino acids

The 20 amino acids encoded directly by the genetic code can be divided into several groups based on their properties. Important factors are charge, hydrophilicity or hydrophobicity, size, and functional groups . These properties are important for protein structure and protein – protein interactions. The water-soluble proteins tend to have their hydrophobic residues , buried in the middle of the protein, whereas hydrophilic side-chains are exposed to the aqueous solvent. The integral membrane proteins tend to have outer rings of exposed hydrophobic amino acids that anchor them into the lipid bilayer. In the case part-way between these two extremes, some peripheral membrane proteins have a patch of hydrophobic amino acids on their surface that locks onto the membrane. In similar fashion, proteins that have to bind to positively charged molecules have surfaces rich with negatively charged amino acids like glutamate

and aspartate, while proteins binding to negatively charged molecules have surfaces rich with positively charged chains like lysine and arginine. There are different hydrophobicity scales of amino acid residues.

Some amino acids have special properties such as cysteine, that can form covalent disulfide bonds to other cysteine residues, proline that forms a cycle to the polypeptide backbone, and glycine that is more flexible than other amino acids.

Many proteins undergo a range of posttranslational modifications, when additional chemical groups are attached to the amino acids in proteins. Some modifications can produce hydrophobic lipoproteins, or hydrophilic glycoproteins.[106] These type of modification allow the reversible targeting of a protein to a membrane. For example, the addition and removal of the fatty acid palmitic acid to cysteine residues in some signaling proteins causes the proteins to attach and then detach from cell membranes.

8 – 1 - Table of standard amino acid abbreviations and properties

Amino Acid	3-Letter	1-Letter[	Side-chain polarity[	Side-chain charge (pH 7.4)	Hydropathy index	Absorbance λ_{max}(nm)	ε at λ_{max} ($x10^{-3}$ M^{-1} cm^{-1})
Alanine	Ala	A	nonpolar	neutral	1.8		
Arginine	Arg	R	Basic polar	positive	−4.5		
Asparagine	Asn	N	polar	neutral	−3.5		
Aspartic acid	Asp	D	acidic polar	negative	−3.5		
Cysteine	Cys	C	nonpolar	neutral	2.5	250	0.3
Glutamic acid	Glu	E	acidic polar	negative	−3.5		
Glutamine	Gln	Q	polar	neutral	−3.5		
Glycine	Gly	G	nonpolar	neutral	−0.4		
Histidine	His	H	Basic polar	positive(10%) neutral(90%)	−3.2	211	5.9
Isoleucine	Ile	I	nonpolar	neutral	4.5		
Leucine	Leu	L	nonpolar	neutral	3.8		
Lysine	Lys	K	Basic polar	positive	−3.9		
Methionine	Met	M	nonpolar	neutral	1.9		
Phenylalanine	Phe	F	nonpolar	neutral	2.8	257, 206, 188	0.2, 9.3, 60.0
Proline	Pro	P	nonpolar	neutral	−1.6		
Serine	Ser	S	polar	neutral	−0.8		

Threonine	Thr	T	polar	neutral	−0.7		
Tryptophan	Trp	W	nonpolar	neutral	−0.9	280, 219	5.6, 47.0
Tyrosine	Tyr	Y	polar	neutral	−1.3	274, 222, 193	1.4, 8.0, 48.0
Valine	Val	V	nonpolar	neutral	4.2		

Two additional amino acids are in some species coded for by codons that are usually interpreted as stop codons:

21st and 22nd amino acids	**3-Letter**	**1-Letter**
Selenocysteine	Sec	U
Pyrrolysine	Pyl	O

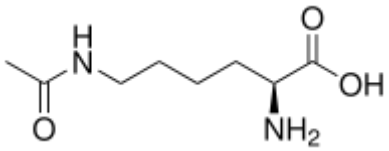
In addition to the specific amino acid codes, placeholders are used in cases where chemical or crystallographic analysis of a peptide or protein cannot conclusively determine the identity of a residue.

Ambiguous Amino Acids	**3-Letter**	**1-Letter**
Asparagine or aspartic acid	Asx	B
Glutamine or glutamic acid	Glx	Z
Leucine or Isoleucine	Xle	J
Unspecified or unknown amino acid	Xaa	X

Unk is sometimes used instead of **Xaa**, but is less standard.

In addition, many non-standard amino acids have a specific code. For example, several peptide drugs, such as Bortezomib and MG132, are artificially synthesized and retain their protecting groups, which have specific codes. Bortezomib is Pyz-Phe-boroLeu, and MG132 is Z-Leu-Leu-Leu-al. To aid in the analysis of protein structure, photocrosslinking amino acid analogues are available. These include photoleucine (**pLeu**) and photomethionine (**pMet**).

Acetyllysine



Other names :
6-Acetamido-2-amino hexanoic acid
2-Azaniumyl-6-acetamido hexanoate

Molecular formula	$C_8H_{16}N_2O_3$
Molar mass	188.22 g mol^{-1}
Appearance	White crystals
Odor	Odourless
Density	1.139 g / mL
Melting point	250 °C
Boiling point	442 °C
log P	− 0.961

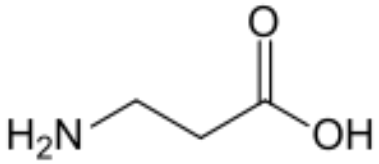
Acetyllysine (or acetylated lysine) is an acetyl-derivative of the amino acid lysine. There are multiple forms of acetyllysine - this article refers to *N*-ε-acetyl-L-lysine. The other form is *N*-α-acetyl-L-lysine.

In proteins, the acetylation of lysine residues is an important mechanism of epigenetics. It functions by regulating the binding of histones to DNA in nucleosomes and thereby controlling the expression of genes on that DNA. Non-histone proteins are acetylated as well. Unlike the functionally similar methyllysine, acetyllysine does not carry a positive charge on its side chain.

Histone acetyltransferases (HATs) catalyze the addition of acetyl groups from acetyl-CoA onto certain lysine residues of histones and non-histone proteins. Histone deacetylases (HDACs) catalyze the removal of acetyl groups from acetylated lysines.

Acetyllysine can be synthesized from lysine by the selective acetylation of the terminal amine group.

Alanine



IUPAC name :
3-Amino propanoic acid
Other names :
β-Alanine

Molecular formula	$C_3H_7NO_2$
Molar mass	89 g mol^{-1}
Appearance	Bipyramidal crystals
Density	1.437 g / cm^3 (19 °C)
Melting point	decomposes at 207 °C
Solubility in water	soluble

β-Alanine (or ***beta*-alanine**) is a naturally occurring beta amino acid, which is an amino acid in which the amino group is at the β-position from the carboxylate group (i.e., two atoms away. The IUPAC name for β-alanine is **3-amino propanoic acid**. Unlike its counterpart α-alanine, β-alanine has no stereocenter.

β-Alanine is not used in the biosynthesis of any major proteins or enzymes. It is formed in vivo by the degradation of dihydrouracil and carnosine. It is a component of the naturally occurring peptides carnosine and anserine and also of pantothenic acid (vitamin B_5), which itself is a component of coenzyme A. Under normal conditions, β-alanine is metabolized into acetic acid.

β-Alanine is the rate-limiting precursor of carnosine, which is to say carnosine levels are limited by the amount of available β-alanine. Supplementation with β-alanine has been shown to increase the concentration of carnosine in muscles, decrease fatigue in athletes and increase total muscular work done.

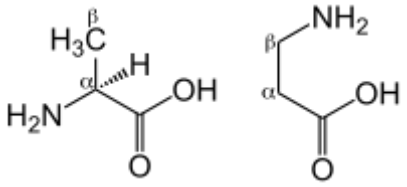


Figure 1: Comparison of β-alanine (right) with the more customary (chiral) amino acid, L-α-alanine (left)

Typically, studies have used supplementing strategies of multiple doses of 400 mg or 800 mg, administered at regular intervals for up to eight hours, over periods ranging from 4 to 10 weeks . After a 10 - week supplementing strategy, the reported increase in intramuscular carnosine content was an average of 80.1% (range 18 to 205%).

A study conducted at Adams State College, Alamosa, Colorado, compared the effects of β-alanine to a placebo group in two sports: wrestling and American football. The subjects taking β-alanine achieved more desirable results on all tests compared to placebo. The wrestlers, both placebo and supplement lost weight; however, the supplement group increased lean mass by 1.1 lb., while the placebo group lost lean mass (-0.98 lb). Both American football groups gained weight; however, the supplement group gained an average 2.1 lb lean mass compared to 1.1 lb for placebo

L-Histidine, with a pKa of 6.1 is a relatively weak buffer over the physiological intramuscular pH range. However, when bound to other amino acids, this increases nearer to 6.8 - 7.0. In particular, when bound to β-alanine, the pKa value is 6.83, making this a very efficient intramuscular buffer. Furthermore, because of the position of the beta amino group, β-alanine dipeptides are not incorporated proteins and thus can be stored at relatively high concentrations (millimolar). Occurring at 17-25 mmol / kg (dry muscle), carnosine (β-alanyl-L-histidine) is an important intramuscular buffer, constituting 10 - 20 % of the total buffering capacity in type I and II muscle fibres.

β-Alanine, provided in solution or as powder in gelatine capsules, however, causes paraesthesia when ingested in amounts

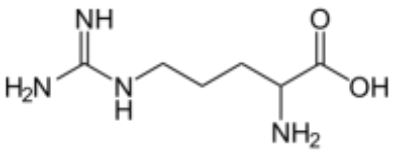
above 10 mg per kg body weight (bwt) . This is variable between individuals. Symptoms may be experienced by some individuals as mild even at 10 mg per kg bwt, in a majority as significant at 20 mg per kg bwt, and severe at 40 mg per kg bwt. However, an equivalent amount (equimolar) to 40 mg per kg bwt, ingested in the form of histidine containing dipeptides in chicken broth extract, did not cause paraesthesia.

It is probable that the paraesthesia, a form of neuropathic pain, results from high peak blood-plasma concentrations of β-alanine, since greater quantities, ingested in the form of the β-alanine/histidine (or methyl histidine) - containing dipeptides (i.e., carnosine and anserine) in meat, do not cause the same symptoms. In this case the β-alanine absorption profile is flattened but sustained for a longer period of time , whereas the β-alanine samples in the studies were administered as gelatine capsules containing powder. This resulted in the rapid rise of plasma concentrations, peaking within 30 to 45 minutes, and being eliminated after 90 to 120 minutes. The paraesthesia caused is no indication of efficacy, since the published studies undertaken so far have utilised doses of 400 mg or 800 mg at a time to avoid the paraesthesia. Furthermore, excretion of β-alanine in urine accounted for 0.60 % (+/- 0.09) , 1.50 % (+ / -0.40), or 3.64 % (+ / - 0.47) of the administered doses of 10, 20, or 40 mg per kg body weight, indicating greater losses occurring with increasing dosage.

Even though much weaker than glycine (and, thus, with a debated role as a physiological transmitter), β-alanine is an agonist next in activity to the cognate ligand glycine itself, for strychnine-sensitive inhibitory glycine receptors (GlyRs) (the agonist order: glycine >> β-alanine > taurine >> alanine, L-serine > proline).

A high-potency artificial sweetener, called suosan, is derived from beta-alanine.

Arginine



Contents

1 - Introduction

Arginine (abbreviated as Arg or R) is an α-amino acid. It was first isolated in 1886 . The L - form is one of the 20 most common natural amino acids. At the level of molecular genetics, in the structure of the messenger ribonucleic acid mRNA, CGU, CGC, CGA, CGG, AGA, and AGG, are the triplets of nucleotide bases or codons that code for arginine during protein synthesis. In mammals, arginine is classified as a semiessential or conditionally essential

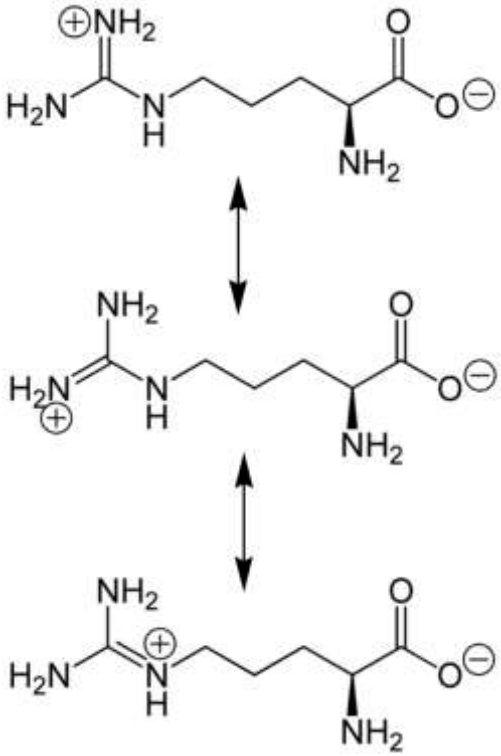
amino acid, depending on the developmental stage and health status of the individual. Preterm infants are unable to synthesize or create arginine internally, making the amino acid nutritionally essential for them. There are some conditions that put an increased demand on the body for the synthesis of L-arginine, including surgical or other trauma, sepsis and burns . Arginine was first isolated from a lupin seedling extract in 1886 by the Swiss chemist Ernst Schultze.

In general, most people do not need to take arginine supplements because the body usually produces enough.

Other names : 2- Amino - 5 - guanidino pentanoic acid	
Molecular formula	$C_6H_{14}N_4O_2$
Molar mass	174 g mol^{-1}
Appearance	White crystals
Odor	Odourless
Melting point	260 °C
Boiling point	368 °C
Solubility in water	14.87 g/100 mL (20 °C)
Solubility	slightly soluble in ethanol insoluble in ethyl ether
GHS signal word	WARNING
EU classification	 Xi
Thermo dynamic data	Phase behaviour Solid, liquid, gas
Spectral data	UV, IR, NMR, MS

2 – Structure

The amino acid side-chain of arginine consists of a 3-carbon aliphatic straight chain, the distal end of which is capped by a complex guanidinium group.



Delocalization of charge in guanidinium group of L-Arginine

With a pK_a of 12.48, the guanidinium group is positively charged in neutral, acidic and even most basic environments, and thus imparts basic chemical properties to arginine. Because of the conjugation between the double bond and the nitrogen lone pairs, the positive charge is delocalized, enabling the formation of multiple H-bonds

.

3 – Sources

3 – 1 - Dietary sources

Arginine is a conditionally nonessential amino acid, meaning most of the time it can be manufactured by the human body, and does not need to be obtained directly through the diet. The biosynthetic pathway however does not produce sufficient arginine, and some must still be consumed through diet. Individuals who have poor nutrition or certain physical conditions may be advised to increase their intake of foods containing arginine. Arginine is found in a wide variety of foods, including :

Animal sources

dairy products (e.g., cottage cheese, ricotta, milk, yogurt, whey protein drinks), beef, pork (e.g., bacon, ham), gelatin , poultry (e.g.

chicken and turkey light meat), wild game (e.g. pheasant, quail), seafood (e.g., halibut, lobster, salmon, shrimp, snails, tuna)

Plant sources

wheat germ and flour, buckwheat, granola, oatmeal, peanuts, nuts (coconut, pecans, cashews, walnuts, almonds, Brazil nuts, hazelnuts, pinenuts), seeds (pumpkin, sesame, sunflower), chickpeas, cooked soybeans, *Phalaris canariensis* (canaryseed or ALPISTE)

3 – 2 – Biosynthesis

Arginine is synthesized from citrulline by the sequential action of the cytosolic enzymes argininosuccinate synthetase (ASS) and argininosuccinate lyase (ASL). In terms of energy, this is costly, as the synthesis of each molecule of argininosuccinate requires hydrolysis of adenosine tri phosphate (ATP) to adenosine mono phosphate (AMP), i.e., two ATP equivalents. Taking an excess of arginine essentially gives more energy by saving ATPs that can be used elsewhere.

Citrulline can be derived from multiple sources:
from arginine via nitric oxide synthase (NOS)
from ornithine via catabolism of proline or glutamine/glutamate
from asymmetric dimethylarginine (ADMA) via DDAH

The pathways linking arginine, glutamine, and proline are bidirectional. Thus, the net utilization or production of these amino acids is highly dependent on cell type and developmental stage.

On a whole-body basis, synthesis of arginine occurs principally via the intestinal–renal axis, wherein epithelial cells of the small intestine, which produce citrulline primarily from glutamine and glutamate, collaborate with the proximal tubule cells of the kidney, which extract citrulline from the circulation and convert it to arginine, which is returned to the circulation. As a consequence, impairment of small bowel or renal function can reduce endogenous arginine synthesis, thereby increasing the dietary requirement.

Synthesis of arginine from citrulline also occurs at a low level in many other cells, and cellular capacity for arginine synthesis can be markedly increased under circumstances that also induce iNOS. Thus, citrulline, a coproduct of the NOS-catalyzed reaction, can be recycled

to arginine in a pathway known as the citrulline-NO or arginine-citrulline pathway. This is demonstrated by the fact that in many cell types, citrulline can substitute for arginine to some degree in supporting NO synthesis. However, recycling is not quantitative because citrulline accumulates along with nitrate and nitrite, the stable end-products of NO, in NO-producing cells.

4 – Function

Arginine plays an important role in cell division, the healing of wounds, removing ammonia from the body, immune function, and the release of hormones.

The benefits and functions attributed to oral supplementation of L-arginine include:

Precursor for the synthesis of nitric oxide (NO)
Reduces healing time of injuries (particularly bone)
Quickens repair time of damaged tissue
Helps decrease blood pressure in clinical hypertensive subjects

4 – 1 – Proteins

The distributing basics of the moderate structure found in geometry, charge distribution and ability to form multiple H-bonds make arginine ideal for binding negatively charged groups. For this reason, arginine prefers to be on the outside of the proteins where it can interact with the polar environment.

Incorporated in proteins, arginine can also be converted to citrulline by PAD enzymes. In addition, arginine can be methylated by protein methyltransferases.

4 – 2 – Precursor

Arginine is the immediate precursor of nitric oxide (NO), urea, ornithine, and agmatine; is necessary for the synthesis of creatine; and can also be used for the synthesis of polyamines (mainly through ornithine and to a lesser degree through agmatine), citrulline, and glutamate. As a precursor of nitric oxide, arginine may have a role in the treatment of some conditions where vasodilation is required . The

presence of asymmetric dimethyl arginine (ADMA), a close relative, inhibits the nitric oxide reaction; therefore, ADMA is considered a marker for vascular disease, just as L-arginine is considered a sign of a healthy endothelium.

4 – 3 – Treatment of dentin hypersensitivity

Arginine (8 %) in dental products (e.g., toothpaste) provides effective relief from sensitive teeth by depositing a dentin-like mineral, containing calcium and phosphate, within the dentin tubules and in a protective layer on the dentin surface.

4 – 4 – Treatment of herpes simplex virus

An unproven claim is that a low ratio of arginine to lysine may be of benefit in the treatment of herpes simplex virus. For more information, refer to Herpes - Treatment also see journal article.

4 – 5 – Possible increased risk of death after supplementation following heart attack

A clinical trial found that patients taking an L-arginine supplement following a heart attack found no change in the heart's vascular tone or decrease in the symptoms of congestive heart failure (the heart's ability to pump). In fact, six more patients who were taking L-arginine died than those taking a placebo resulting in early termination of the study with the recommendation that the supplement not be used by heart attack patients. These findings suggest L-arginine is not beneficial post - heart - attack.

5 - Potential medical uses

5 – 1 – Lung inflammation and asthma

Inhalation of L-arginine can increase lung inflammation and worsen asthma.

5 – 2 – Growth hormone

Intravenously-administered arginine stimulates the secretion of growth hormone , and is used in growth hormone stimulation tests. Two studies have found that oral L-arginine supplementation is also effective at increasing resting GH levels. The first study found that oral preparations of L-arginine are effective at increasing growth hormone levels. In fact, the 9g dose resulted in mean peak GH levels

of 6.4 (+/- 1.3) microg / L versus placebo levels of 2.9 (+/- 0.7).[21] Another study found similar results. It included resting versus exercise and oral L-arginine versus oral placebo. The authors concluded that "Oral arginine alone (7 g) stimulated GH release, but a greater GH response was seen with exercise alone. The combined effect of arginine before exercise attenuates the GH response... GH production: Ex > Arg + Ex > Arg > placebo" suggesting against supplementing with arginine alone prior to exercise if the goal is to raise GH levels, but concurring with the previous study that oral L-arginine increases GH on days free of significant exercise. In contrast to these two studies that found increased resting GH due to oral arginine supplementation, a third study did not find increase in resting GH levels from oral supplementation. In that study, oral preparations of L-arginine were ineffective at increasing growth hormone levels despite being effective at increasing plasma levels of L-arginine.

5 – 3 – MELAS syndrome

Several trials delved into effects of L-arginine in MELAS syndrome, a mitochondrial disease.

5 – 4 – Sepsis

Cellular arginine biosynthetic capacity determined by activity of argininosuccinate synthetase (AS) is induced by the same mediators of septic response — endotoxin and cytokines — that induce nitric oxide synthase (NOS), the enzyme responsible for nitric oxide synthesis.[27]

5 – 5 – Malate salt

The malate salt of arginine can also be used during the treatment of alcoholic hepatitis and advanced cirrhosis.

5 – 6 – Pre – eclampsia

A preliminary study of supplementation with L-arginine and antioxidant vitamins showed that this combination may help to combat abnormally high blood pressure during high risk pregnancies.

5 – 7 – Hypertension

Intravenous infusion of arginine reduces blood pressure in patients with hypertension as well as normal subjects.

A recent meta-analysis showed that L-arginine reduces blood pressure with pooled estimates of 5.4 / 2.7 mmHg for SBP / DBP.

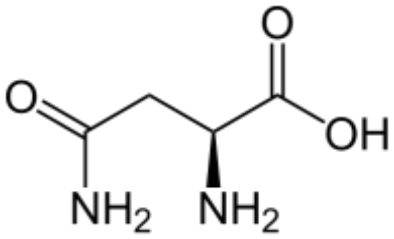
5 – 8 – Erectile dysfunction

Arginine taken in combination with proanthocyanidins or yohimbine, has also been used as a treatment for erectile dysfunction.

5 – 9 – Anxiety

Dietary supplementation of L-arginine taken in combination with L-lysine has been shown potentially useful in treating people subjected to high levels of mental stress and anxiety, in a double-blind, placebo controlled and randomized study, involving 108 Japanese adults. Trait anxiety and state anxiety induced by cognitive stress battery was significantly reduced, and basal levels of the stress hormone cortisol were decreased. The study was funded by Ajinomoto, Co. Inc., an industrial manufacturer of lysine and arginine.

Asparagine



Contents

1 - Introduction

Asparagine (abbreviated as Asn or N) is one of the 20 most common natural amino acids on Earth. It has carboxamide as the side-chain's functional group. It is not an essential amino acid. Its codons are AAU and AAC.

A reaction between asparagine and reducing sugars or reactive carbonyls produces acrylamide (acrylic amide) in food when heated to sufficient temperature. These products occur in baked goods such as French fries, potato chips, and toasted bread.

IUPAC name : Asparagine	
Other names : 2-Amino-3-carbamoyl propanoic acid	
Molecular formula	$C_4H_8N_2O_3$
Molar mass	132 g mol^{-1}
Appearance	white crystals
Density	1.543 g / cm^3

Melting point	234 °C
Boiling point	438 °C
Solubility in water	2.94 g / 100 mL
Solubility	soluble in acid, alkali negligible in : methanol, ethanol, ether, benzene
Flash point	219 °C
Spectral data	UV, IR, NMR, MS

2 – History

Asparagine was first isolated in 1806, under a crystalline form, by French chemists Louis Nicolas Vauquelin and Pierre Jean Robiquet (then a young assistant) from asparagus juice, in which it is abundant — hence, the name they chose for that new matter — becoming the first amino acid to be isolated.

A few years later, in 1809, Pierre Jean Robiquet again identified, this time from liquorice root, a substance with properties he qualified as very similar to those of asparagine, that Plisson in 1828 identified as asparagine itself.

3 - Structural function in proteins

Since the asparagine side-chain can form hydrogen bond interactions with the peptide backbone, asparagine residues are often found near the beginning and the end of alpha-helices, and in turn motifs in beta sheets. Its role can be thought as "capping" the hydrogen bond interactions that would otherwise be satisfied by the polypeptide back bone. Glutamines, with an extra methylene group, have more conformational entropy and thus are less useful in this regard.

Asparagine also provides key sites for N-linked glycosylation, modification of the protein chain with the addition of carbohydrate chains.

4 – Sources

4 – 1 - Dietary sources

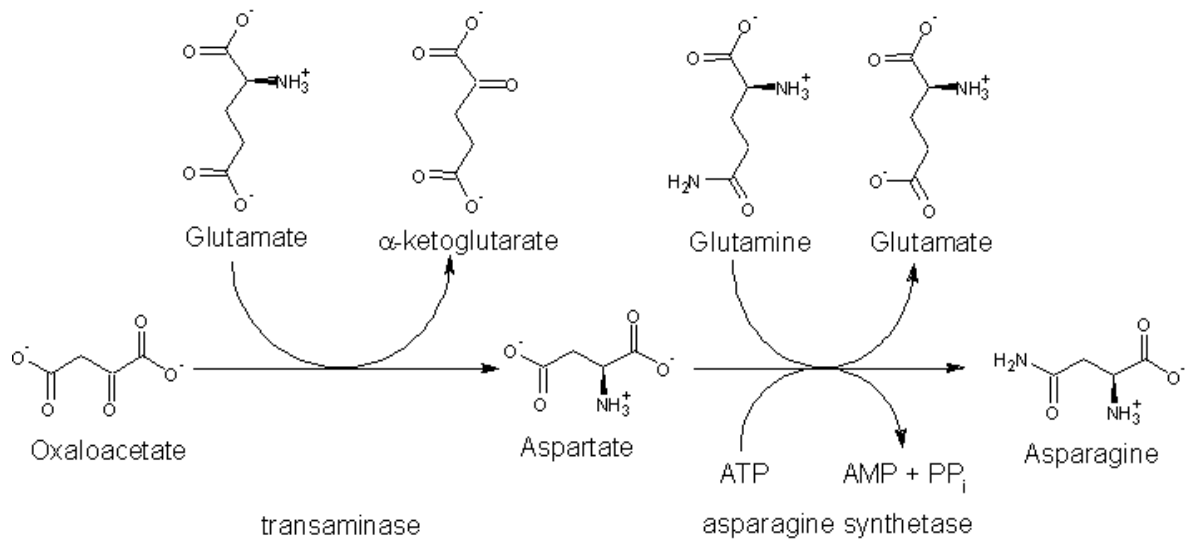
Asparagine is not essential for humans, which means that it can be synthesized from central metabolic pathway intermediates and is not required in the diet. Asparagine is found in :

Animal sources : dairy, whey, beef, poultry, eggs, fish, lactalbumin , sea food

Plant sources : asparagus, potatoes, legumes, nuts, seeds, soy, whole grains

4 – 2 - Biosynthesis

The precursor to asparagine is oxaloacetate. Oxaloacetate is converted to aspartate using a transaminase enzyme. The enzyme transfers the amino group from glutamate to oxaloacetate producing α-ketoglutarate and aspartate. The enzyme asparagine synthetase produces asparagine, AMP, glutamate, and pyrophosphate from aspartate, glutamine, and ATP. In the asparagine synthetase reaction, ATP is used to activate aspartate, forming β-aspartyl-AMP. Glutamine donates an ammonium group, which reacts with β-aspartyl-AMP to form asparagine and free AMP.



The biosynthesis of asparagine from oxaloacetate

5 – Degradation

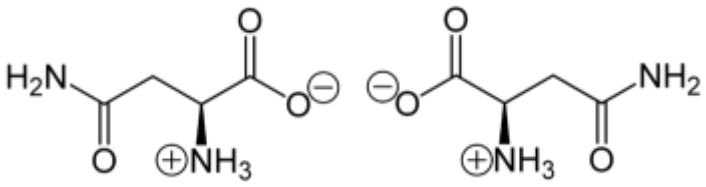
Aspartate is a glucogenic amino acid. L-asparaginase hydrolyzes the amide group to form aspartate and ammonium. A transaminase converts the aspartate to oxaloacetate, which can then be metabolized in the citric acid cycle or gluconeogenesis.

6 - Function

The nervous system requires asparagine. It also plays an important role in the synthesis of ammonia.

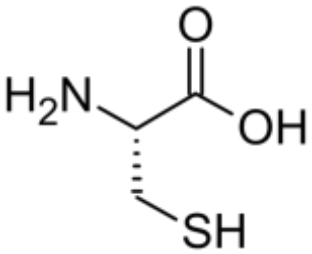
The addition of N-acetyl glucosamine to asparagine is performed by oligosaccharyltransferase enzymes in the endoplasmic reticulum.[6] This glycosylation is important both for protein structure and protein function.

7 - Betaine structure



(S)-Asparagine (left) and (R)-asparagine (right) in zwitterionic form at neutral pH.

Cysteine



Contents

1 - Introduction

Cysteine (abbreviated as Cys or C) is an α-amino acid with the chemical formula $HO_2CCH(NH_2)CH_2SH$. It is a semi - essential amino acid, which means that it can be biosynthesized in humans. The thiol side chain in cysteine often participates in enzymatic reactions, serving as a nucleophile. The thiol is susceptible to oxidization to give the disulfide derivative cystine, which serves an important structural role in many proteins. When used as a food additive, it has the E number E920.

IUPAC name : Cysteine
Other names : 2-Amino-3-sulfhydryl propanoic acid

Molecular formula	$C_3 H_7 N O_2 S$
Molar mass	121 g mol^{-1}
Appearance	white crystals or powder
Melting point	240 °C decomp.
Solubility in water	soluble
Solubility	1.5g / 100g ethanol 19 ^{o} C
Chiral rotation $[\alpha]_D$	+ 9.4° (H_2O, *c* = 1.3)
Thermo dynamic data	Phase behaviour Solid, liquid, gas
Spectral data	UV, IR, NMR, MS

2 – Sources

2 – 1 - Dietary sources

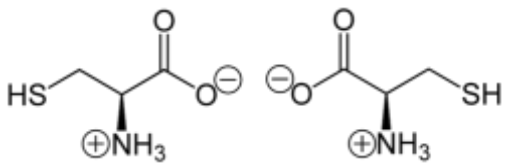
Although classified as a non - essential amino acid, in rare cases, cysteine may be essential for infants, the elderly, and individuals with certain metabolic disease or who suffer from malabsorption syndromes. Cysteine can usually be synthesized by the human body under normal physiological conditions if a sufficient quantity of methionine is available. Cysteine is catabolized in the gastrointestinal tract and blood plasma . In contrast, cystine travels safely through the GI tract and blood plasma and is promptly reduced to the two cysteine molecules upon cell entry.

Cysteine is found in most high-protein foods, including :

Animal sources: pork, sausage meat, chicken, turkey, duck, luncheon meat, eggs, milk, whey protein, ricotta, cottage cheese, yogurt

Plant sources: red peppers, garlic, onions, broccoli, brussels sprout, oats, granola, wheat germ, sprouted lentils.

Like other amino acids, cysteine has an amphoteric character.

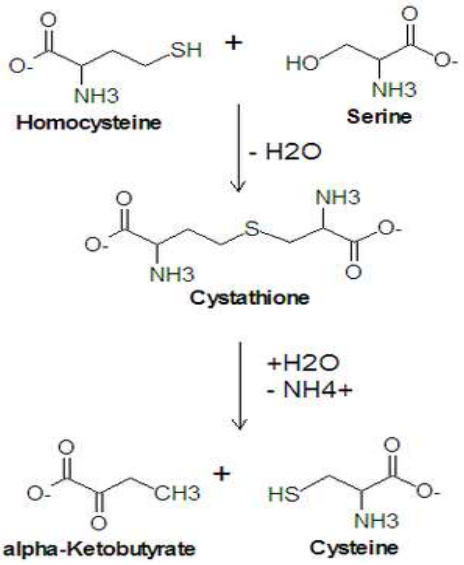


(R)-Cysteine (left) and (S)-Cysteine (right) in zwitterionic form at neutral pH

2 – 2 - Industrial sources

The majority of L- cysteine is obtained industrially by hydrolysis of poultry feathers or human hair. Synthetically produced L-cysteine, compliant with Jewish Kosher and Muslim Halal rules, is also available, albeit at a higher price . The synthetic route involves fermentation utilizing a mutant of *E. coli*. Degussa introduced a route from substituted thiazolines. Following this technology, L-cysteine is produced by the hydrolysis of racemic 2-amino-Δ^2-thiazoline-4-carboxylic acid using *Pseudomonas thiazolinophilum*.

2 – 3 – Biosynthesis



Cysteine synthesis. Cystathionine beta synthase catalyzes the upper reaction and cystathionine gamma-lyase catalyzes the lower reaction.

In animals, biosynthesis begins with the amino acid serine. The sulfur is derived from methionine, which is converted to homocysteine through the intermediate S- adenosylmethionine. Cystathionine beta-synthase then combines homocysteine and serine to form the asymmetrical thioether cystathionine. The enzyme cystathionine gamma-lyase converts the cystathionine into cysteine and alpha-ketobutyrate. In plants and bacteria, cysteine biosynthesis again starts from serine, which is converted to *O*-acetylserine by the enzyme serine transacetylase. The enzyme O-acetylserine (thiol)-lyase, using sulfide sources, converts this ester into cysteine, releasing acetate.

3 – Biological functions

The cysteine thiol group is nucleophilic and easily oxidized. The reactivity is enhanced when the thiol is ionized, and cysteine residues in proteins have pK_a values close to neutrality, so are often in their reactive thiolate form in the cell. Because of its high reactivity, the thiol group of cysteine has numerous biological functions.

3 – 1 - Precursor to the antioxidant glutathione

Due to the ability of thiols to undergo redox reactions, cysteine has antioxidant properties. Cysteine's antioxidant properties are typically expressed in the tripeptide glutathione, which occurs in humans as well as other organisms. The systemic availability of oral glutathione (GSH) is negligible; so it must be biosynthesized from its constituent amino acids, cysteine, glycine, and glutamic acid. Glutamic acid and glycine are readily available in most Western diets, but the availability of cysteine can be the limiting substrate.

3 – 2 - Precursor to iron-sulfur clusters

Cysteine is an important source of sulfide in human metabolism. The sulfide in iron-sulfur clusters and in nitrogenase is extracted from cysteine, which is converted to alanine in the process.

3 – 3 - Metal ion binding

Beyond the iron-sulfur proteins, many other metal cofactors in enzymes are bound to the thiolate substituent of cysteinyl residues. Examples include zinc in zinc fingers and alcohol dehydrogenase, copper in the blue copper proteins, iron in cytochrome P450, and nickel in the [NiFe]-hydrogenases. The thiol group also has a high affinity for heavy metals, so that proteins containing cysteine, such as metallothionein, will bind metals such as mercury, lead, and cadmium tightly.

3 – 4 - Roles in protein structure

In the translation of messenger RNA molecules to produce polypeptides, cysteine is coded for by the UGU and UGC codons.

Cysteine has traditionally been considered to be a hydrophilic amino acid, based largely on the chemical parallel between its thiol

group and the hydroxyl groups in the side-chains of other polar amino acids. However, the cysteine side chain has been shown to stabilize hydrophobic interactions in micelles to a greater degree than the side chain in the non-polar amino acid glycine, and the polar amino acid serine. In a statistical analysis of the frequency with which amino acids appear in different chemical environments in the structures of proteins, free cysteine residues were found to associate with hydrophobic regions of proteins. Their hydrophobic tendency was equivalent to that of known non-polar amino acids such as methionine and tyrosine, and was much greater than that of known polar amino acids such as serine and threonine. Hydrophobicity scales, which rank amino acids from most hydrophobic to most hydrophilic, consistently place cysteine towards the hydrophobic end of the spectrum, even when they are based on methods that are not influenced by the tendency of cysteines to form disulfide bonds in proteins. Therefore, cysteine is now often grouped among the hydrophobic amino acids, though it is sometimes also classified as slightly polar, or polar.

While free cysteine residues do occur in proteins, most are covalently bonded to other cysteine residues to form disulfide bonds. Disulfide bonds play an important role in the folding and stability of some proteins, usually proteins secreted to the extracellular medium. Since most cellular compartments are reducing environments, disulfide bonds are generally unstable in the cytosol with some exceptions as noted below.

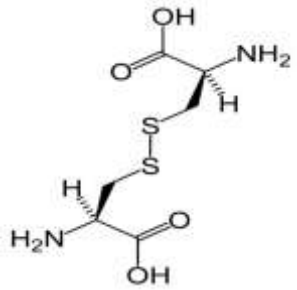


Figure 2: Cystine (shown here in its neutral form), two cysteines bound together by a disulfide bond.

Disulfide bonds in proteins are formed by oxidation of the thiol groups of cysteine residues. The other sulfur-containing amino acid, methionine, cannot form disulfide bonds. More aggressive oxidants convert cysteine to the corresponding sulfinic acid and sulfonic acid.

Cysteine residues play a valuable role by crosslinking proteins, which increases the rigidity of proteins and also functions to confer proteolytic resistance (since protein export is a costly process, minimizing its necessity is advantageous). Inside the cell, disulfide bridges between cysteine residues within a polypeptide support the protein's tertiary structure. Insulin is an example of a protein with cystine crosslinking, wherein two separate peptide chains are connected by a pair of disulfide bonds.

Protein disulfide isomerases catalyze the proper formation of disulfide bonds; the cell transfers dehydroascorbic acid to the endoplasmic reticulum, which oxidises the environment. In this environment, cysteines are, in general, oxidized to cystine and are no longer functional as a nucleophiles.

Aside from its oxidation to cystine, cysteine participates in numerous posttranslational modifications. The nucleophilic thiol group allows cysteine to conjugate to other groups, e.g., in prenylation. Ubiquitin ligases transfer ubiquitin to its pendant, proteins, and caspases, which engage in proteolysis in the apoptotic cycle. Inteins often function with the help of a catalytic cysteine. These roles are typically limited to the intracellular milieu, where the environment is reducing, and cysteine is not oxidized to cystine.

4 – Applications

Cysteine, mainly the L - enantiomer, is a precursor in the food, pharmaceutical, and personal care industries. One of the largest applications is the production of flavors. For example, the reaction of cysteine with sugars in a Maillard reaction yields meat flavors.[21] L-cysteine is also used as a processing aid for baking.

In the field of personal care, cysteine is used for permanent wave applications predominantly in Asia. Again the cysteine is used for breaking up the disulfide bonds in the hair's keratin.

Cysteine is a very popular target for site-directed labeling experiments to investigate biomolecular structure and dynamics. Maleimides will selectively attach to cysteine using a covalent

Michael addition. Site-directed spin labeling for EPR or paramagnetic relaxation enhanced NMR also uses cysteine extensively.

In a 1994 report released by five top cigarette companies, cysteine is one of the 599 additives to cigarettes. Like most cigarette additives, however, its use or purpose is unknown.[23] Its inclusion in cigarettes could offer two benefits: Acting as an expectorant, since smoking increases mucus production in the lungs; and increasing the beneficial antioxidant glutathione (which is diminished in smokers).

5 - Sheep

Cysteine is required by sheep in order to produce wool: It is an essential amino acid that must be taken in as food from grass. As a consequence, during drought conditions, sheep stop producing wool; however, transgenic sheep that can make their own cysteine have been developed.

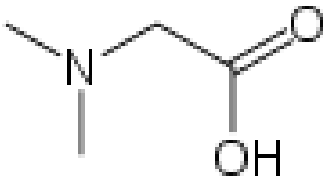
6 - Reducing toxic effects of alcohol

Cysteine has been proposed as a preventative or antidote for some of the negative effects of alcohol, including liver damage and hangover. It counteracts the poisonous effects of acetaldehyde, which is the major by-product of alcohol metabolism and is responsible for most of the negative aftereffects and long-term damage associated with alcohol use (but not the immediate effects of drunkenness). Cysteine supports the next step in metabolism, which turns acetaldehyde into the relatively harmless acetic acid. In a rat study, test animals received an LD_{50} dose of acetaldehyde. Those that received cysteine had an 80 % survival rate; when both cysteine and thiamine were administered, all animals survived.[25] There is not yet direct evidence for or against its effectiveness in humans who consume alcohol at normal levels.

6 – 1 - *N*-Acetylcysteine

N-Acetyl-L-cysteine (NAC) is a derivative of cysteine wherein an acetyl group is attached to the nitrogen atom. This compound is sold as a dietary supplement and used as an antidote in cases of acetaminophen overdose, and obsessive compulsive disorders such as trichotillomania

Dimethyl Glycine



Contents

1 - Introduction

Dimethyl glycine (DMG) is a derivative of the amino acid glycine with the structural formula $(CH_3)_2NCH_2COOH$. It can be found in beans and liver. It can be formed from trimethylglycine upon the loss of one of its methyl groups. It is also a byproduct of the metabolism of choline.

When DMG was first discovered, it was referred to as vitamin B_{16}, but, unlike true B vitamins, deficiency of DMG in the diet does not lead to any ill-effects meaning it does not meet the definition of a vitamin.

IUPAC name :
2 - (Dimethyl amino) acetic acid
Other names : *N*,*N*-Dimethyl glycine

Molecular formula	$C_4 H_9 N O_2$
Molar mass	103 g mol^{-1}
Appearance	White crystals
Odor	Odourless
Density	1.069 g / mL
Melting point	178-182 °C
Boiling point	175.2 °C
GHS signal word	WARNING

LD_{50}	650 mg kg^{-1} (oral, rat)
Related compounds	Dimethylacetamide

2 - Uses

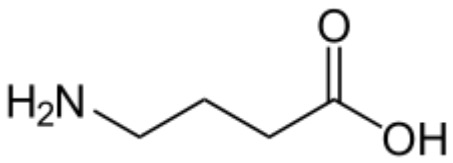
Dimethylglycine has been suggested for use as an athletic performance enhancer, immunostimulant, and a treatment for autism, epilepsy, or mitochondrial disease . Published studies on the subject have shown little to no difference between DMG treatment and placebo in autism spectrum disorders.

3 - Preparation

This compound is commercially available as the free form amino acid, and as the hydrochloride salt [2491-06-7]. DMG may be prepared by the alkylation of glycine *via* the Eschweiler–Clarke reaction. In this reaction, glycine is treated with aqueous formaldehyde in formic acid that serves as both solvent and reductant. Hydrochloric acid is added thereafter to give the hydrochloride salt. The free amino acid may been obtained by neutralization of the acid salt, which has been performed with silver oxide.

$$H_2NCH_2COOH + 2\ CH_2O + 2\ HCOOH \rightarrow (CH_3)_2NCH_2COOH + 2\ CO_2 + 2\ H_2O$$

Gamma – Amino Butyric Acid



Contents

1 - Introduction

γ-Amino butyric acid is the chief inhibitory neurotransmitter in the mammalian central nervous system. It plays a role in regulating neuronal excitability throughout the nervous system. In humans, GABA is also directly responsible for the regulation of muscle tone.

Although chemically it is an amino acid, GABA is rarely referred to as such in the scientific or medical communities, because the term "amino acid," used without a qualifier, conventionally refers to the alpha amino acids, which GABA is not, nor is it ever incorporated into a protein.

In spastic diplegia in humans, GABA absorption becomes impaired by nerves damaged from the condition's upper motor neuron

lesion, which leads to hypertonia of the muscles signaled by those nerves that can no longer absorb GABA.

IUPAC name : 4-amino butanoic acid	
Molecular formula	$C_4H_9NO_2$
Molar mass	103 g / mol
Appearance	white micro crystalline powder
Density	1.11 g / mL
Melting point	203.7 °C
Boiling point	247.9 °C
Solubility in water	soluble
Main hazards	Irritant, Harmful

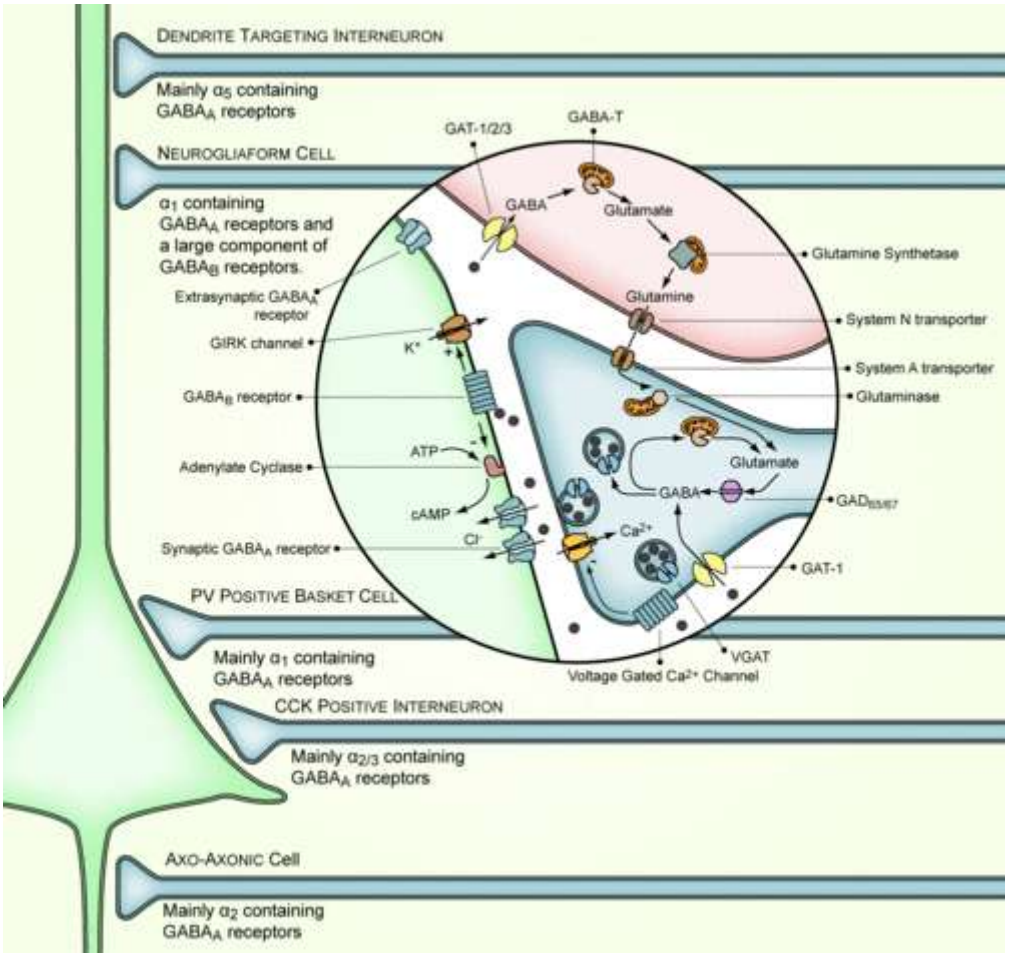
2 - Function

2 – 1 – Neuro transmitter

In vertebrates, GABA acts at inhibitory synapses in the brain by binding to specific transmembrane receptors in the plasma membrane of both pre- and postsynaptic neuronal processes. This binding causes the opening of ion channels to allow the flow of either negatively charged chloride ions into the cell or positively charged potassium ions out of the cell. This action results in a negative change in the transmembrane potential, usually causing hyperpolarization. Two general classes of GABA receptor are known: $GABA_A$ in which the receptor is part of a ligand-gated ion channel complex, and $GABA_B$ metabotropic receptors, which are G protein-coupled receptors that open or close ion channels via intermediaries (G proteins).

Neurons that produce GABA as their output are called GABAergic neurons, and have chiefly inhibitory action at receptors in the adult vertebrate. Medium Spiny Cells are a typical example of inhibitory CNS GABAergic cells. In contrast, GABA exhibits both excitatory and inhibitory actions in insects, mediating muscle activation at synapses between nerves and muscle cells, and also the stimulation of certain glands.[3] In mammals, some GABAergic

neurons, such as chandelier cells, are also able to excite their glutamatergic counterparts.



The production, release, action, and degradation of GABA at a stereotyped GABAergic synapse

$GABA_A$ receptors are ligand-activated chloride channels; that is, when activated by GABA, they allow the flow of chloride ions across the membrane of the cell. Whether this chloride flow is excitatory/depolarizing (makes the voltage across the cell's membrane less negative), shunting (has no effect on the cell's membrane) or inhibitory/hyperpolarizing (makes the cell's membrane more negative) depends on the direction of the flow of chloride. When net chloride flows out of the cell, GABA is excitatory or depolarizing; when the net chloride flows into the cell, GABA is inhibitory or hyperpolarizing. When the net flow of chloride is close to zero, the action of GABA is shunting. Shunting inhibition has no direct effect on the membrane potential of the cell; however, it minimizes the

effect of any coincident synaptic input essentially by reducing the electrical resistance of the cell's membrane (in essence, equivalent to Ohm's law). A developmental switch in the molecular machinery controlling concentration of chloride inside the cell – and, hence, the direction of this ion flow – is responsible for the changes in the functional role of GABA between the neonatal and adult stages. That is to say, GABA's role changes from excitatory to inhibitory as the brain develops into adulthood.

2 – 2 - Brain development

While GABA is an inhibitory transmitter in the mature brain, its actions are primarily excitatory in the developing brain.[5][6] The gradient of chloride is reversed in immature neurons, and its reversal potential is higher than the resting membrane potential of the cell; activation of a GABA-A receptor thus leads to efflux of Cl- ions from the cell, i.e. a depolarizing current. The differential gradient of chloride in immature neurons is primarily due to the higher concentration of NKCC1 co-transporters relative to KCC2 co-transporters in immature cells. GABA itself is partially responsible for orchestrating the maturation of ion pumps . GABA-ergic interneurons mature faster in the hippocampus and the GABA signalling machinery appears earlier than glutamatergic transmission. Thus, GABA is the major excitatory neurotransmitter in many regions of the brain before the maturation of glutamateergic synapses.

However, this theory has been questioned based on results showing that in brain slices of immature mice incubated in artificial cerebrospinal fluid (ACSF) (modified in a way that takes into account the normal composition of the neuronal milieu in sucklings by adding an energy substrate alternative to glucose, beta-hydroxybutyrate) GABA action shifts from excitatory to inhibitory mode .

This effect has been later repeated when other energy substrates, pyruvate and lactate, supplemented glucose in the slices' media.[9] Later investigations of pyruvate and lactate metabolism found that the original results were not due to energy source issues but to changes in pH resulting from the substrates acting as "weak acids". These arguments were later rebutted by further findings showing that

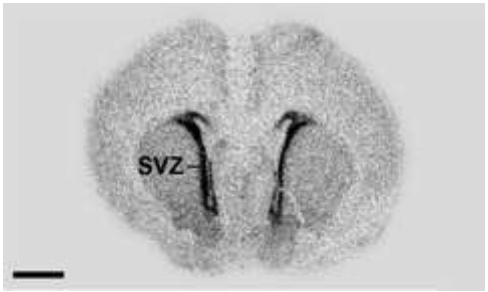
changes in pH even greater than that caused by energy substrates do not affect the GABA-shift described in the presence of energy substrate-fortified ACSF and that the mode of action of beta-hydroxybutyrate, pyruvate and lactate (assessed by measurement NAD(P)H and oxygen utilization) was energy metabolism-related.

In the developmental stages preceding the formation of synaptic contacts, GABA is synthesized by neurons and acts both as an autocrine (acting on the same cell) and paracrine (acting on nearby cells) signalling mediator . The ganglionic eminences also contribute greatly to building up the GABAergic cortical cell population.

GABA regulates the proliferation of neural progenitor cells[18][19] the migration and differentiation the elongation of neurites[22] and the formation of synapses.

GABA also regulates the growth of embryonic and neural stem cells. GABA can influence the development of neural progenitor cells via brain-derived neurotrophic factor (BDNF) expression . GABA activates the $GABA_A$ receptor, causing cell cycle arrest in the S-phase, limiting growth.

2 – 3 - Beyond the nervous system



GABA-producing GAD67 enzyme in the brain slice at 1st postnatal day, with the highest expression in subventricular zone (svz).

GABAergic mechanisms have been demonstrated in various peripheral tissues and organs including, but not restricted to the intestine, stomach, pancreas, Fallopian tube, uterus, ovary, testis, kidney, urinary bladder, lung, and liver.

In 2007, an excitatory GABAergic system was described in the airway epithelium. The system activates following exposure to allergens and may participate in the mechanisms of asthma.[28] GABAergic systems have also been found in the testis[29] and in the eye lens.

3 - Structure and conformation

GABA is found mostly as a zwitterion, that is, with the carboxy group deprotonated and the amino group protonated. Its conformation depends on its environment. In the gas phase, a highly folded conformation is strongly favored because of the electrostatic attraction between the two functional groups. The stabilization is about 50 kcal/mol, according to quantum chemistry calculations. In the solid state, a more extended conformation is found, with a trans conformation at the amino end and a gauche conformation at the carboxyl end. This is due to the packing interactions with the neighboring molecules. In solution, five different conformations, some folded and some extended, are found as a result of solvation effects. The conformational flexibility of GABA is important for its biological function, as it has been found to bind to different receptors with different conformations. Many GABA analogues with pharmaceutical applications have more rigid structures in order to control the binding better.

4 - History

Gamma – amino butyric acid was first synthesized in 1883, and was first known only as a plant and microbe metabolic product. In 1950, however, GABA was discovered to be an integral part of the mammalian central nervous system.

5 - Bio - synthesis

GABA does not penetrate the blood – brain barrier; it is synthesized in the brain. It is synthesized from glutamate using the enzyme L-glutamic acid decarboxylase and pyridoxal phosphate (which is the active form of vitamin B6) as a cofactor via a metabolic pathway called the GABA shunt. This process converts glutamate, the principal excitatory neurotransmitter, into the principal inhibitory neurotransmitter (GABA).

6 - Catabolism

GABA transaminase enzyme catalyzes the conversion of 4-aminobutanoic acid and 2-oxoglutarate into succinic semialdehyde and glutamate. Succinic semialdehyde is then oxidized into succinic acid by succinic semialdehyde dehydrogenase and as such enters the citric acid cycle as a usable source of energy.

7 - Pharmacology

Drugs that act as allosteric modulators of GABA receptors (known as GABA analogues or *GABAergic* drugs) or increase the available amount of GABA typically have relaxing, anti-anxiety, and anti-convulsive effects. Many of the substances below are known to cause anterograde amnesia and retrograde amnesia.

In general, GABA does not cross the blood–brain barrier,[40] although certain areas of the brain that have no effective blood–brain barrier, such as the periventricular nucleus, can be reached by drugs such as systematically injected GABA. At least one study suggests that orally administered GABA increases the amount of Human Growth Hormone. GABA directly injected to the brain has been reported to have both stimulatory and inhibitory effects on the production of growth hormone, depending on the physiology of the individual.

8 – GABA ergic drugs

Agonists / Positive allosteric modulators : ethanol , barbiturates , benzo diazepines , carisoprodol , chloral hydrate , etaqualone, etomidate , glutethimide , kava , methaqualone , muscimol , neuroactive steroids , z-drugs , propofol , scullcap , valerian , volatile / inhaled anaesthetics.

Antagonists / Negative allosteric modulators: bicuculline, cicutoxin, flumazenil, furosemide, gabazine, oenanthotoxin, picrotoxin, Ro15-4513, thujone.

$GABA_B$ receptor ligands

Agonists: baclofen, GBL, propofol, GHB, phenibut.Antagonists: phaclofen, saclofen.

GABA reuptake inhibitors: deramciclane, hyperforin, tiagabine.
GABA-transaminase inhibitors: gabaculine, phenelzine, valproate, vigabatrin, Lemon balm (Melissa officinalis).

GABA analogues: pregabalin, gabapentin.
Others: GABA (itself), L-glutamine, picamilon, progabide, tetanospasmin.

9 - GABA as a supplement

A number of commercial sources sell formulations of GABA for use as a dietary supplement, sometimes for sublingual administration. These sources typically claim that the supplement has a calming effect. These claims are not yet scientifically proven. For example, there is evidence stating that the calming effects of GABA can be seen observably in the human brain after administration of GABA as an oral supplement. However, there is also evidence that GABA does not cross the blood – brain barrier at significant levels.

There are some over-the-counter supplements such as phenylated GABA itself directly, or Phenibut; and Picamilon (both Soviet cosmonaut products) – Picamilon combines niacin and phenylated GABA and crosses the blood–brain barrier as a prodrug that later hydrolyzes into GABA and niacin.

10 - In plants

GABA is also found in plants, where it is the most abundant amino acid in the apoplast of tomatoes.[50] It may also have a role in cell signalling in plants.

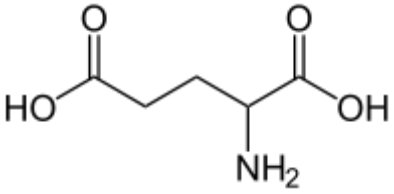
Glucogenic Amino Acid

A glucogenic amino acid is an amino acid that can be converted into glucose through gluconeogenesis . This is in contrast to the ketogenic amino acids, which are converted into ketone bodies.

The production of glucose from glucogenic amino acids involves these amino acids' being converted to alpha keto acids and then to glucose, with both processes occurring in the liver. This mechanism predominates during catabolysis, rising as fasting and starvation increase in severity.

In humans, the glucogenic amino acids are :
Glycine
Serine
Valine
Histidine
Arginine
Cysteine
Proline
Alanine
Glutamate
Glutamine
Aspartate
Asparagine
Methionine
Amino acids that are both glucogenic and ketogenic:
Isoleucine
Threonine
Phenyl alanine
Tyrosine
Tryptophan
Only leucine and lysine are not glucogenic.

Glutamic Acid



Contents

1 - Introduction

Glutamic acid (abbreviated as Glu or E) is one of the 20-22 proteinogenic amino acids, and its codons are GAA and GAG. It is a non-essential amino acid. The carboxylate anions and salts of glutamic acid are known as glutamates. In neuro science, glutamate is an important neuro transmitter that plays a key role in long-term potentiation and is important for learning and memory.

Systematic name :
2 - Amino penta nedioic acid
Other names :
2 – Amino glutaric acid
Molecular formula $C_5 H_9 N O_4$
Molar mass 147 g mol^{-1}

Appearance	white crystalline powder
Density	1.4601 (20 °C)
Melting point	199 °C decomp.
Solubility in water	8.64 g / l (25 °C)
Thermodynamic data	Phase behaviour Solid , liquid , gas
Spectral data	UV , IR , NMR , MS

3 - Chemistry

The side chain carboxylic acid functional group has a pK_a of 4.1 and therefore exists almost entirely in its negatively charged deprotonated carboxylate form at pH values greater than 4.1; therefore, it is negatively charged at physiological pH ranging from 7.35 to 7.45.

3 - History

Although they occur naturally in many foods, the flavour contributions made by glutamic acid and other amino acids were only scientifically identified early in the twentieth century. The substance was discovered and identified in the year 1866, by the German chemist Karl Heinrich Leopold Ritthausen who treated wheat gluten (for which it was named) with sulfuric acid. In 1908 Japanese researcher Kikunae Ikeda of the Tokyo Imperial University identified brown crystals left behind after the evaporation of a large amount of kombu broth as glutamic acid. These crystals, when tasted, reproduced the ineffable but undeniable flavour he detected in many foods, most especially in seaweed. Professor Ikeda termed this flavour umami. He then patented a method of mass-producing a crystalline salt of glutamic acid, monosodium glutamate.

4 - Biosynthesis

Reactants	Products	Enzymes
Glutamine + H_2O	→ Glu + NH_3	GLS, GLS2
NAcGlu + H_2O	→ Glu + Acetate	(unknown)
α-ketoglutarate + NADPH +	→ Glu + $NADP^+$ +	GLUD1,

NH_4^+	H_2O	GLUD2
α-ketoglutarate + α-amino acid	→ Glu + α-keto acid	transaminase
1-Pyrroline-5-carboxylate + NAD^+ + H_2O	→ Glu + NADH	ALDH4A1
N-formimino-L-glutamate + FH_4	→ Glu + 5-formimino-FH_4	FTCD
NAAG	→ Glu + NAA	GCPII

5 - Function and uses

5 - 1 - Metabolism

Glutamate is a key compound in cellular metabolism. In humans, dietary proteins are broken down by digestion into amino acids, which serve as metabolic fuel for other functional roles in the body. A key process in amino acid degradation is transamination, in which the amino group of an amino acid is transferred to an α-ketoacid, typically catalysed by a transaminase. The reaction can be generalised as such :

R_1-amino acid + R_2-α-ketoacid ⇌ R_1-α-ketoacid + R_2-amino acid

A very common α-keto acid is α-ketoglutarate, an intermediate in the citric acid cycle. Transamination of α-ketoglutarate gives glutamate. The resulting α-ketoacid product is often a useful one as well, which can contribute as fuel or as a substrate for further metabolism processes. Examples are as follows :

Alanine + α-ketoglutarate ⇌ pyruvate + glutamate
Aspartate + α-ketoglutarate ⇌ oxaloacetate + glutamate

Both pyruvate and oxaloacetate are key components of cellular metabolism, contributing as substrates or intermediates in fundamental processes such as glycolysis, gluconeogenesis, and the citric acid cycle.

Glutamate also plays an important role in the body's disposal of excess or waste nitrogen. Glutamate undergoes deamination, an oxidative reaction catalysed by glutamate dehydrogenase, as follows :

$$\text{glutamate} + H_2O + NADP^+ \rightarrow$$
$$\alpha\text{-keto glutarate} + NADPH + NH_3 + H^+$$

Ammonia (as ammonium) is then excreted predominantly as urea, synthesised in the liver. Transamination can, thus, be linked to deamination, effectively allowing nitrogen from the amine groups of amino acids to be removed, via glutamate as an intermediate, and finally excreted from the body in the form of urea.

5 – 2 - Neurotransmitter

Glutamate is the most abundant excitatory neurotransmitter in the vertebrate nervous system. At chemical synapses, glutamate is stored in vesicles. Nerve impulses trigger release of glutamate from the pre-synaptic cell. In the opposing post - synaptic cell, glutamate receptors, such as the NMDA receptor, bind glutamate and are activated. Because of its role in synaptic plasticity, glutamate is involved in cognitive functions like learning and memory in the brain.[10] The form of plasticity known as long-term potentiation takes place at glutamatergic synapses in the hippocampus, neocortex, and other parts of the brain. Glutamate works not only as a point-to-point transmitter but also through spill - over synaptic crosstalk between synapses in which summation of glutamate released from a neighboring synapse creates extrasynaptic signaling / volume transmission.

Glutamate transporters are found in neuronal and glial membranes . They rapidly remove glutamate from the extracellular space. In brain injury or disease, they can work in reverse, and excess glutamate can accumulate outside cells. This process causes calcium ions to enter cells via NMDA receptor channels, leading to neuronal damage and eventual cell death, and is called excitotoxicity. The mechanisms of cell death include

Damage to mitochondria from excessively high intracellular Ca^{2+}

Glu / Ca^{2+}-mediated promotion of transcription factors for pro-apoptotic genes, or down regulation of transcription factors for anti-apoptotic genes

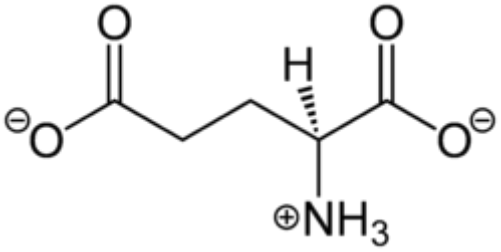
Excitotoxicity due to excessive glutamate release and impaired uptake occurs as part of the ischemic cascade and is associated with stroke and diseases like amyotrophic lateral sclerosis, lathyrism, autism, some forms of mental retardation, and Alzheimer's disease. In contrast, decreased glutamate release is observed under conditions of classical phenylketonuria leading to developmental disruption of glutamate receptor expression.

Glutamic acid has been implicated in epileptic seizures. Microinjection of glutamic acid into neurons produces spontaneous depolarisations around one second apart, and this firing pattern is similar to what is known as paroxysmal depolarizing shift in epileptic attacks. This change in the resting membrane potential at seizure foci could cause spontaneous opening of voltage - activated calcium channels, leading to glutamic acid release and further depolarization

Experimental techniques to detect glutamate in intact cells include using a genetically engineered nanosensor. The sensor is a fusion of a glutamate-binding protein and two fluorescent proteins. When glutamate binds, the fluorescence of the sensor under ultraviolet light changes by resonance between the two fluorophores. Introduction of the nanosensor into cells enables optical detection of the glutamate concentration. Synthetic analogs of glutamic acid that can be activated by ultraviolet light and two - photon excitation microscopy have also been described . This method of rapidly uncaging by photostimulation is useful for mapping the connections between neurons, and understanding synapse function.

Evolution of glutamate receptors is entirely the opposite in invertebrates, in particular, arthropods and nematodes, where glutamate stimulates glutamate - gated chloride channels . The beta subunits of the receptor respond with very high affinity to glutamate and glycine. Targeting these receptors has been the therapeutic goal of

anthelmintic therapy using avermectins. Avermectins target the alpha-subunit of glutamate-gated chloride channels with high affinity. These receptors have also been described in arthropods, such as *Drosophila melanogaster* and *Lepeophtheirus salmonis*. Irreversible activation of these receptors with avermectins results in hyperpolarization at synapses and neuromuscular junctions resulting in flaccid paralysis and death of nematodes and arthropods.



L-Glutamate at physiological conditions

5 – 3 - Brain nonsynaptic glutamatergic signaling circuits

Extracellular glutamate in *Drosophila* brains has been found to regulate postsynaptic glutamate receptor clustering, via a process involving receptor desensitization . A gene expressed in glial cells actively transports glutamate into the extracellular space,[23] while, in the nucleus accumbens-stimulating group II metabotropic glutamate receptors, this gene was found to reduce extracellular glutamate levels.[24] This raises the possibility that this extracellular glutamate plays an "endocrine-like" role as part of a larger homeostatic system.

5 – 3 – 1 - GABA precursor

Glutamate also serves as the precursor for the synthesis of the inhibitory GABA in GABA - ergic neurons. This reaction is catalyzed by glutamate decarboxylase (GAD), which is most abundant in the cerebellum and pancreas.

Stiff-man syndrome is a neurologic disorder caused by anti-GAD antibodies, leading to a decrease in GABA synthesis and, therefore, impaired motor function such as muscle stiffness and spasm. Since the pancreas is also abundant for the enzyme GAD, a direct immunological destruction occurs in the pancreas and the patients will have diabetes mellitus.

5 – 4 - Flavor enhancer

Glutamic acid, being a constituent of protein, is present in every food that contains protein, but it can only be tasted when it is present in an unbound form. Significant amounts of free glutamic acid are present in a wide variety of foods, including cheese and soy sauce, and is responsible for umami, one of the five basic tastes of the human sense of taste. Glutamic acid is often used as a food additive and flavour enhancer in the form of its salt, known as monosodium glutamate (MSG).

5 – 5 - Nutrient

All meats, poultry, fish, eggs, dairy products, and kombu are excellent sources of glutamic acid. Some protein-rich plant foods also serve as sources. Thirty to 35 % of the protein in wheat is glutamic acid. Ninety-five percent of the dietary glutamate is metabolized by intestinal cells in a first pass.

5 – 6 - Plant growth

Auxigro is a plant growth preparation that contains 30 % glutamic acid.

5 – 7 - NMR spectroscopy

In recent years, there has been much research into the use of RDCs in NMR spectroscopy. A glutamic acid derivative, poly-γ-benzyl-L-glutamate (PBLG), is often used as an alignment medium to control the scale of the dipolar interactions observed.

6 - Production

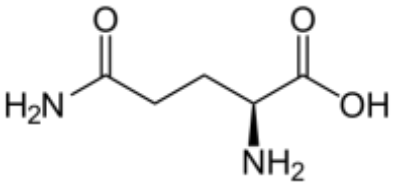
China-based Fufeng Group Limited is the largest producer of glutamic acid in the world, with capacity increasing to 300,000 tons at the end of 2006 , Meihua is the second - largest Chinese producer. Together, the top-five producers have roughly 50 % share in China. Chinese demand is roughly 1.1 million tons per year,

7 - Pharmacology

The drug phencyclidine (more commonly known as PCP) antagonizes glutamic acid non-competitively at the NMDA receptor. For the same reasons, dextromethorphan and ketamine also have

strong dissociative and hallucinogenic effects. Glutamate does not easily pass the blood brain barrier, but , instead, is transported by a high - affinity transport system . It can also be converted into glutamine.

Glutamine



Contents

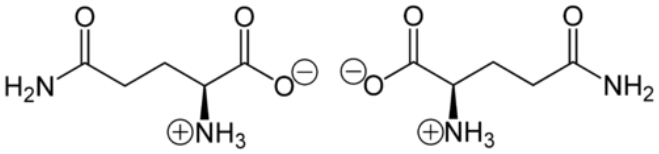
1 - Introduction

Glutamine (abbreviated as Gln or Q) is one of the 20 amino acids encoded by the standard genetic code. It is not recognized as an essential amino acid, but may become conditionally essential in certain situations, including intensive athletic training or certain gastrointestinal disorders . Its side-chain is an amide formed by replacing the side - chain hydroxyl of glutamic acid with an amine functional group, making it the amide of glutamic acid. Its codons are CAA and CAG. In human blood, glutamine is the most abundant free amino acid, with a concentration of about 500 – 900 µmol / l .

IUPAC name : Glutamine
Other names : L-Glutamine (levo) glutamide 2-Amino - 4 - carbamoyl butanoic acid

Molecular formula	$C_5H_{10}N_2O_3$
Molar mass	146 g mol^{-1}
Melting point	decomposes around 185°C
Solubility in water	soluble
Chiral rotation $[\alpha]_D$	+ 6.5º (H_2O, *c* = 2)
Thermodynamic data	Phase behaviour Solid , liquid , gas
Spectral data	UV, IR, NMR, MS

2 – Structure



Glutamine zwitterionic forms at neutral pH:
L-glutamine (left) and D-glutamine (right)

3 – Functions

Glutamine plays a role in a variety of biochemical functions, including :

Protein synthesis, as any other of the 20 proteinogenic amino acids

Regulation of acid-base balance in the kidney by producing ammonium

Cellular energy, as a source, next to glucose

Nitrogen donation for many anabolic processes, including the synthesis of purines

Carbon donation , as a source , refilling the citric acid cycle

Nontoxic transporter of ammonia in the blood circulation

3 – 1 - Producing and consuming organs

3 – 1 – 1 – Producers

Glutamine is synthesized by the enzyme glutamine synthetase from glutamate and ammonia. The most relevant glutamine-producing

tissue is the muscle mass, accounting for about 90% of all glutamine synthesized. Glutamine is also released, in small amounts, by the lung and the brain. Although the liver is capable of relevant glutamine synthesis, its role in glutamine metabolism is more regulatory than producing, since the liver takes up large amounts of glutamine derived from the gut.

3 – 1 – 2 - Consumers

The most eager consumers of glutamine are the cells of intestines, the kidney cells for the acid - base balance, activated immune cells, and many cancer cells. In respect to the last point mentioned, different glutamine analogues, such as DON, Azaserine or Acivicin, are tested as anticancer drugs.

3 – 2 - Examples for the usage of glutamine

In catabolic states of injury and illness, glutamine becomes conditionally essential (requiring intake from food or supplements).[8] Glutamine has been studied extensively over the past 10–15 years, and has been shown to be useful in treatment of injuries, trauma, burns, and treatment - related side effects of cancer, as well as in wound healing for postoperative patients. Glutamine is also marketed as a supplement used for muscle growth in weight lifting , body building, endurance, and other sports. Evidence indicates glutamine, when orally loaded, may increase plasma HGH levels by stimulating the anterior pituitary gland. In biological research, L-glutamine is commonly added to the media in cell culture. However, the high level of glutamine in the culture media may inhibit other amino acid transport activities.

3 –2 - 1 - Aiding recovery after surgery

Glutamine is also known to have various effects in reducing healing time after operations. Hospital-stay times after abdominal surgery can be reduced by providing parenteral nutrition regimens containing high amounts of glutamine to patients. Clinical trials have revealed patients on supplementation regimens containing glutamine have improved nitrogen balances, generation of cysteinyl - leukotrienes from polymorphonuclear neutrophil granulocytes, and improved lymphocyte recovery and intestinal permeability (in

postoperative patients), in comparison to those that had no glutamine within their dietary regimen, all without any side effects.

4 – Nutrition

4 – 1 - Occurrences in nature

Glutamine is the most abundant naturally occurring, nonessential amino acid in the human body, and one of the few amino acids that can directly cross the blood – brain barrier.[14] In the body, it is found circulating in the blood, as well as stored in the skeletal muscles. It becomes conditionally essential (requiring intake from food or supplements) in states of illness or injury.

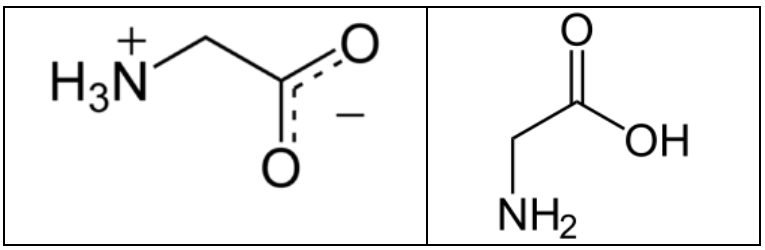
4 –1 - 2 - Dietary sources

Dietary sources of L-glutamine include beef, chicken, fish, eggs, milk, dairy products, wheat, cabbage, beets, beans, spinach, and parsley. Small amounts of free L-glutamine are also found in vegetable juices.

4 – 2 - Aiding gastrointestinal function

Glutamine-enriched diets have been linked with maintenance of gut barrier function and cell differentiation, suggesting glutamine may help to protect the lining of the gastrointestinal tract or mucosa.[16] People who have inflammatory bowel disease (ulcerative colitis and Crohn' s disease) may not have enough glutamine, but two clinical trials found taking glutamine supplements did not improve symptoms of Crohn' s disease.

Glycine



Contents

1 - Introduction

Glycine (abbreviated as Gly or G) is an organic compound with the formula NH_2CH_2COOH. Having a hydrogen substituent as its side-chain, glycine is the smallest of the 20 amino acids commonly found in proteins. Its codons are GGU, GGC, GGA, GGG of the genetic code.

Glycine is a colourless, sweet-tasting crystalline solid. It is unique among the proteinogenic amino acids in that it is not chiral. It can fit into hydrophilic or hydrophobic environments, due to its minimal side chain of only one hydrogen atom. Glycine is also the genus name of the Soybean plant (species name = Glycine max).

IUPAC name : Glycine	
Other names : Amino ethanoic acid Amino acetic acid	
Molecular formula	$C_2 H_5 N O_2$
Molar mass	75 g mol^{-1}
Appearance	white solid
Density	1.607 g / cm^3
Melting point	233 °C (decomposition)
Solubility in water	25 g / 100 mL (25 °C)
Solubility	soluble in ethanol, pyridine insoluble in ether
LD_{50}	2600 mg/kg (mouse, oral)
Thermodynamic data	Phase behaviour Solid, liquid, gas
Spectral data	UV, IR, NMR, MS

2 - Production and key properties

Glycine was discovered in 1820, by Henri Braconnot who boiled gelatin with sulfuric acid.

Glycine is manufactured industrially by treating chloroacetic acid with ammonia :

$$ClCH_2COOH + 2\ NH_3 \rightarrow H_2NCH_2COOH + NH_4Cl$$

About 15 million kg are produced annually in this way.

In the USA (by GEO Specialty Chemicals, Inc.) and in Japan (by Shoadenko), glycine is produced via the Strecker amino acid synthesis.

There are two producers of glycine in the United States: Chattem Chemicals, Inc., a subsidiary of Mumbai - based Sun Pharmaceutical, and GEO Specialty Chemicals, Inc., which purchased the glycine and

naphthalene sulfonate production facilities of Hampshire Chemical Corp, a subsidiary of Dow Chemical.

Chattem's manufacturing process ("MCA" process) occurs in batches and results in a finished product with some residual chloride but no sulfate, while GEO's manufacturing process is considered a semi-batch process and results in a finished product with some residual sulfate but no chloride.

Its pK_A values are 2.35 and 9.78, so above pH 9.78, most of the glycine exists as the anionic amine, $H_2NCH_2CO_2^-$. Below pH 2.35, its solutions contain mostly the cationic carboxylic acid $H_3N^+CH_2CO_2H$. Its isoelectric point (pI) is 6.06.

Glycine exists in zwitterionic form in solution. In this form, the partial charges on different atoms as determined using Gasteiger charge method are given as follows: N (+0.2358), H (attached to N) (+0.1964), alpha-C (+0.001853), H (attached to alpha-C) (+ 0.08799), carbonyl C (+0.085) and carbonyl O (-0.5445).

3 – Biosynthesis

Glycine is not essential to the human diet, as it is biosynthesized in the body from the amino acid serine, which is in turn derived from 3-phospho glycerate. In most organisms, the enzyme Serine hydroxy methyl transferase catalyses this transformation via the cofactor pyridoxal phosphate :

serine + tetra hydro folate →
glycine + N^5,N^{10}-Methylene tetrahydrofolate + H_2O

In the liver of vertebrates, glycine synthesis is catalyzed by glycine synthase (also called glycine cleavage enzyme). This conversion is readily reversible :

$CO_2 + NH_4^+ +$ N^5,N^{10}-Methylene tetra hydro folate + NADH + H^+ →
Glycine + tetrahydrofolate + NAD^+

Glycine is coded by codons GGU, GGC, GGA and GGG. Most proteins incorporate only small quantities of glycine. A notable exception is collagen, which contains about 35 % glycine.

4 – Degradation

Glycine is degraded via three pathways. The predominant pathway in animals and plants involves the glycine cleavage enzyme

Glycine + tetra hydro folate + $NAD^+ \rightarrow$

$CO_2 + NH_4^+ + N^5,N^{10}$-Methylene tetra hydrofolate + NADH + H^+

In the second pathway, glycine is degraded in two steps. The first step is the reverse of glycine biosynthesis from serine with serine hydroxymethyl transferase. Serine is then converted to pyruvate by serine dehydratase.

In the third pathway of glycine degradation, glycine is converted to glyoxylate by D - amino acid oxidase. Glyoxylate is then oxidized by hepatic lactate dehydrogenase to oxalate in an NAD^+-dependent reaction.

The half-life of glycine and its elimination from the body varies significantly based on dose. In one study, the half-life was between 0.5 and 4.0 hours.

5 - Physiological function

The principal function of glycine is as a precursor to proteins. It is also a building block to numerous natural products.

5 – 1 - As a biosynthetic intermediate

In higher eukaryotes, D-Aminolevulinic acid, the key precursor to porphyrins, is biosynthesized from glycine and succinyl-CoA. Glycine provides the central C_2N subunit of all purines.

5 – 2 - As a neurotransmitter

Glycine is an inhibitory neurotransmitter in the central nervous system, especially in the spinal cord, brainstem, and retina. When glycine receptors are activated, chloride enters the neuron via ionotropic receptors, causing an Inhibitory postsynaptic potential

(IPSP). Strychnine is a strong antagonist at ionotropic glycine receptors, whereas bicuculline is a weak one. Glycine is a required co-agonist along with glutamate for NMDA receptors. In contrast to the inhibitory role of glycine in the spinal cord, this behaviour is facilitated at the (NMDA) glutaminergic receptors which are excitatory. The LD_{50} of glycine is 7930 mg / kg in rats (oral), and it usually causes death by hyperexcitability.

There is some evidence showing that 3000 milligrams of glycine before bedtime improves sleep quality.

6 - Commercial uses

In the US, glycine is typically sold in two grades: United States Pharmacopeia ("USP"), and technical grade. Most glycine is manufactured as USP grade material for diverse uses. USP grade sales account for approximately 80 to 85 percent of the U.S. market for glycine.

Pharmaceutical grade glycine is produced for some pharmaceutical applications, such as intravenous injections, where the customer's purity requirements often exceed the minimum required under the USP grade designation. Pharmaceutical grade glycine is often produced to proprietary specifications and is typically sold at a premium over USP grade glycine.

Technical grade glycine, which may or may not meet USP grade standards, is sold for use in industrial applications; e.g., as an agent in metal complexing and finishing. Technical grade glycine is typically sold at a discount to USP grade glycine.

6 – 1 - Animal and human foods

Other markets for USP grade glycine include its use an additive in pet food and animal feed. For humans, glycine is sold as a sweetener/taste enhancer. Certain food supplements and protein drinks contain glycine.[18] Certain drug formulations include glycine to improve gastric absorption of the drug.

6 – 2 - Cosmetics and miscellaneous applications

Glycine serves as a buffering agent in antacids, analgesics, antiperspirants, cosmetics, and toiletries.

Many miscellaneous products use glycine or its derivatives, such as the production of rubber sponge products, fertilizers, metal complexants.

Zwitterionic salt (right) of glycine at neutral pH

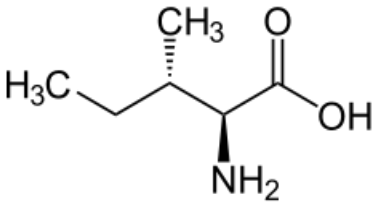
6 – 3 - Chemical feed stock

Glycine is an intermediate in the synthesis of a variety of chemical products. It is used in the manufacture of the herbicide glyphosate. Glyphosate is a non-selective systemic herbicide used to kill weeds, especially perennials and broadcast or used in the cut-stump treatment as a forestry herbicide.

7 - Presence in space

The detection of glycine in the interstellar medium has been debated . In 2008, the glycine - like molecule amino aceto nitrile was discovered in the Large Molecule Heimat, a giant gas cloud near the galactic center in the constellation Sagittarius by the Max Planck Institute for Radio Astronomy . In 2009, glycine sampled in 2004 from comet Wild 2 by the NASA spacecraft Stardust was confirmed, the first discovery of extraterrestrial glycine. That mission's results bolstered the theory of panspermia, which claims that the "seeds" of life are widespread throughout the universe.

Isoleucine



Contents

1 - Introduction

Isoleucine (abbreviated as Ile or I) is an α - amino acid with the chemical formula $HO_2CCH(NH_2)CH(CH_3)CH_2CH_3$. It is an essential amino acid, which means that humans cannot synthesize it, so it must be ingested. Its codons are AUU, AUC and AUA.

With a hydrocarbon side chain, isoleucine is classified as a hydrophobic amino acid. Together with threonine, isoleucine is one of two common amino acids that have a chiral side chain. Four stereoisomers of isoleucine are possible, including two possible diastereomers of L-isoleucine. However, isoleucine present in nature exists in one enantiomeric form, (2*S*,3*S*)-2-amino-3-methylpentanoic acid.

IUPAC name : Isoleucine	
Other names : 2-Amino-3-methyl pentanoic acid	
Molecular formula	$C_6H_{13}NO_2$
Molar mass	131 g mol^{-1}
Thermodynamic data	Phase behaviour Solid , liquid , gas
Spectral data	UV , IR , NMR , MS

2 – Biosynthesis

As an essential nutrient, it is not synthesized in the body, hence it must be ingested, usually as a component of proteins. In plants and microorganisms, it is synthesized via several steps, starting from pyruvic acid and alpha - keto glutarate. Enzymes involved in this biosynthesis include :

Aceto lactate synthase (also known as aceto hydroxy acid synthase)

Aceto hydroxy acid iso meroreductase

Dihydroxy acid dehydratase

Valine amino transferase

3 – Catabolism

Isoleucine is both a glucogenic and a ketogenic amino acid. After transamination with alpha-ketoglutarate the carbon skeleton can be converted into either Succinyl CoA, and fed into the TCA cycle for oxidation or converted into oxaloacetate for gluconeogenesis (hence glucogenic). It can also be converted into Acetyl CoA and fed into the TCA cycle by condensing with oxaloacetate to form citrate. In mammals Acetyl CoA cannot be converted back to carbohydrate but can be used in the synthesis of ketone bodies or fatty acids, hence ketogenic.

Biotin, sometimes referred to as Vitamin B7 or Vitamin H, is an absolute requirement for the full catabolism of isoleucine (as well as leucine). Without adequate biotin, the human body will be unable to fully break down isoleucine and leucine molecules . This can lead to numerous physiological issues (related to muscle maintenance and protein synthesis, lipid metabolism, and fatty acid metabolism) as well as cognitive issues resulting from general metabolic pathway failure and the irritating effects of hydroxy isovalerate, a byproduct of incomplete isoleucine catabolism. Isovaleric acidemia is an example of a disorder caused by incomplete catabolism of leucine.

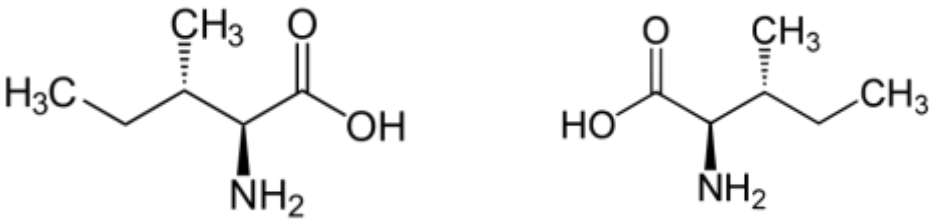
4 - Nutritional Sources

Even though this amino acid is not produced in animals, it is stored in high quantities. Foods that have high amounts of isoleucine

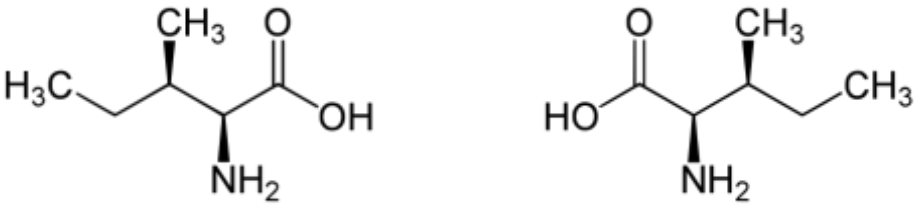
include eggs, soy protein, seaweed, turkey, chicken, lamb, cheese, and fish.

5 - Isomers of isoleucine

Forms of Isoleucine							
Common name:	isoleucine	D-isoleucine	L-isoleucine	DL-isoleucine	allo-D-isoleucine	allo-L-isoleucine	allo-DL-isoleucine
Synonyms:		(*R*)-Isoleucine	L(+)-Isoleucine	(*R**,*R**)-isoleucine		alloisoleucine	
PubChem:	CID 791	CID 94206	CID 6306	CID 76551			
EINECS number:	207-139-8	206-269-2	200-798-2		216-143-9	216-142-3	221-464-2
CAS number:	443-79-8	319-78-8	73-32-5		1509-35-9	1509-34-8	3107-04-8



L-isoleucine (2S,3S) and D-isoleucine (2R,3R)



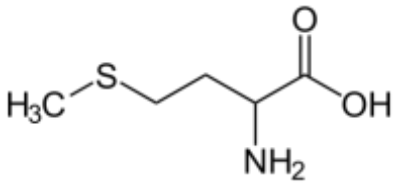
L-allo-isoleucine (2S,3R) and D-allo-isoleucine (2R,3S)

6 – Synthesis

Isoleucine can be synthesized in a multistep procedure starting from 2-bromobutane and diethylmalonate.[5] Synthetic isoleucine was originally reported in 1905.

German chemist Felix Ehrlich discovered isoleucine in hemoglobin in 1903.

Methionine



Contents

1 - Introduction

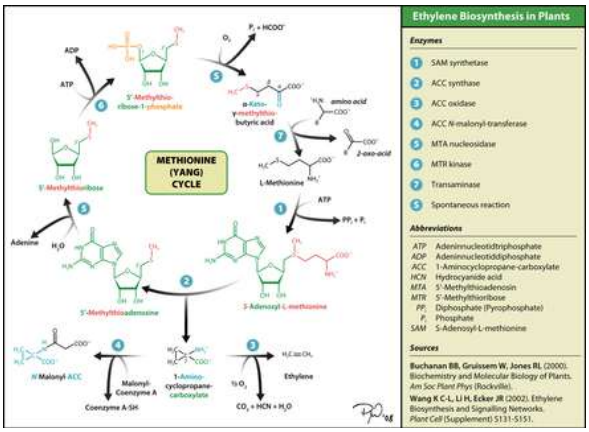
Methionine is an α-amino acid with the chemical formula $HO_2CCH\ (NH_2)\ CH_2CH_2SCH_3$. This essential amino acid is classified as nonpolar. This amino-acid is coded by the initiation codon AUG which indicates mRNA's coding region where translation into protein begins.

IUPAC name : Methionine	
Other names : 2 - amino - 4 - (methyl thio) butanoic acid	
Molecular formula	$C_5 H_{11} N O_2 S$
Molar mass	149 g mol^{-1}
Appearance	White crystalline powder

Density	1.340 g / cm^3
Melting point	281 °C decomp.
Solubility in water	Soluble
Thermo dynamic data	Phase behaviour Solid , liquid , gas
Spectral data	UV, IR, NMR, MS

2 – Function

Together with cysteine, methionine is one of two sulfur-containing proteinogenic amino acids. Its derivative *S*-adenosyl methionine (SAM) serves as a methyl donor. Methionine is an intermediate in the biosynthesis of cysteine, carnitine, taurine, lecithin, phosphatidylcholine, and other phospholipids. Improper conversion of methionine can lead to atherosclerosis.



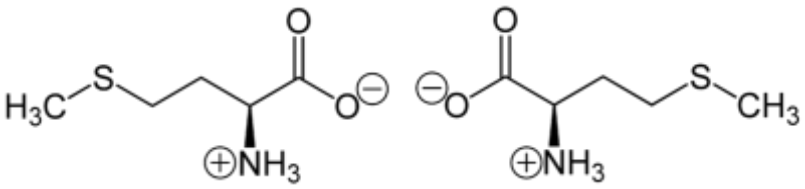
The Yang cycle

This amino acid is also used by plants for synthesis of ethylene. The process is known as the Yang Cycle or the methionine cycle.

Methionine is one of only two amino acids encoded by a single codon (AUG) in the standard genetic code (tryptophan, encoded by UGG, is the other). The codon AUG is also the most common eukaryote "Start" message for a ribosome that signals the initiation of protein translation from mRNA when the AUG codon is in a Kozak consensus sequence. As a consequence, methionine is often incorporated into the N-terminal position of proteins in eukaryotes and archaea during translation, although it can be removed by post-

translational modification. In bacteria, the derivative N-formylmethionine is used as the initial amino acid.

3 – Zwitterions



(S)-Methionine (left) and (R)-methionine (right) in zwitterionic form at neutral pH

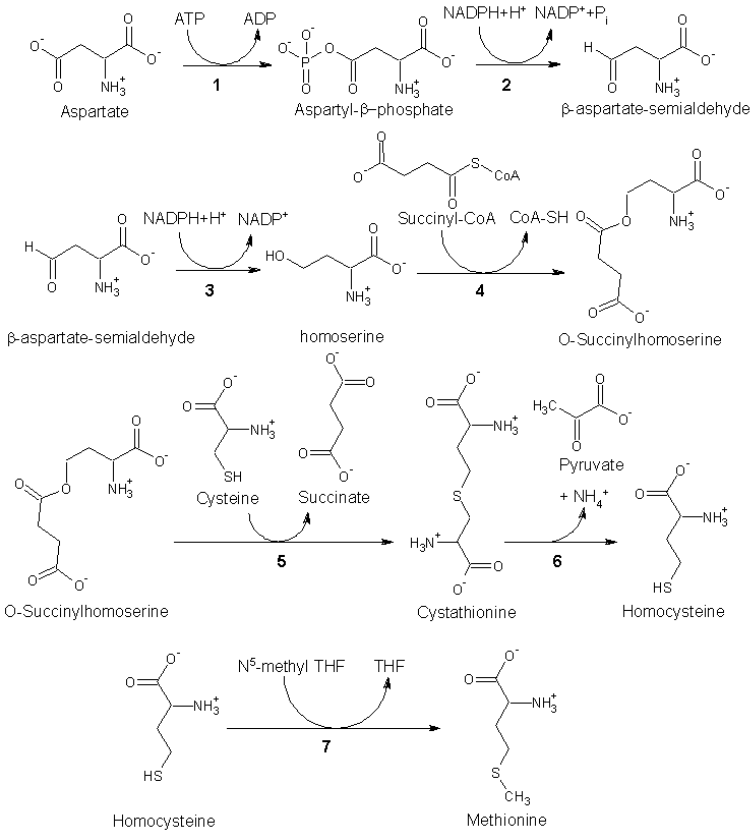
4 – Biosynthesis

As an essential amino acid, methionine is not synthesized de novo in humans, who must ingest methionine or methionine-containing proteins. In plants and microorganisms, methionine is synthesized via a pathway that uses both aspartic acid and cysteine. First, aspartic acid is converted via β-aspartyl-semialdehyde into homoserine, introducing the pair of contiguous methylene groups. Homoserine converts to *O*-succinyl homoserine, which then reacts with cysteine to produce cystathionine, which is cleaved to yield homocysteine. Subsequent methylation of the thiol group by folates affords methionine. Both cystathionine-γ-synthase and cystathionine-β-lyase require pyridoxyl-5'-phosphate as a cofactor, whereas homocysteine methyltransferase requires vitamin B_{12} as a cofactor.

Enzymes involved in methionine biosynthesis :

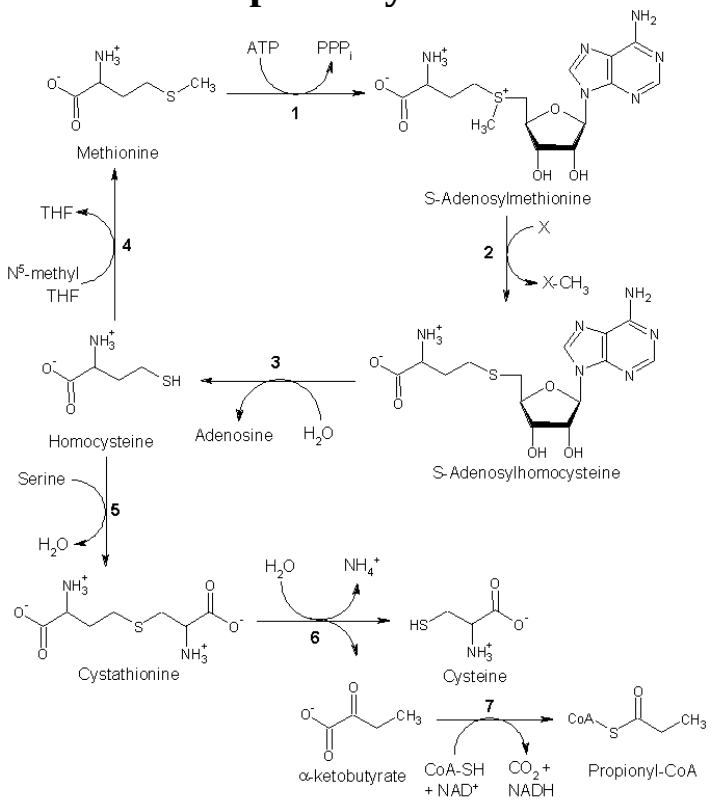
Aspartokinase
Aspartate-semialdehyde_dehydrogenase
Homoserine dehydrogenase
Homoserine O-transsuccinylase
Cystathionine-γ-synthase
Cystathionine-β-lyase

Methionine synthase (in mammals, this step is performed by Homocysteine methyltransferase or Betaine—homocysteine S-methyltransferase)



Methionine biosynthesis

5 - Other biochemical pathways



Fates of methionine

Although mammals cannot synthesize methionine, they can still use it in a variety of biochemical pathways:

5 – 1 - Generation of homocysteine

Methionine is converted to S-adenosyl methionine (SAM) by (1) methionine adenosyltransferase.

SAM serves as a methyl-donor in many (2) methyl transferase reactions, and is converted to *S*-adenosylhomocysteine (SAH).

(3) Adenosyl homocysteinase converts SAH to homocysteine.

There are two fates of homocysteine: it can be used to regenerate methionine, or to form cysteine.

5 – 2 - Regeneration of methionine

Methionine can be regenerated from homocysteine via (4) methionine synthase in a reaction that requires Vitamin B_{12} as a cofactor.

Homocysteine can also be remethylated using glycine betaine (NNN-trimethyl glycine, TMG) to methionine via the enzyme betaine-homocysteine methyltransferase (E.C.2.1.1.5, BHMT). BHMT makes up to 1.5% of all the soluble protein of the liver, and recent evidence suggests that it may have a greater influence on methionine and homocysteine homeostasis than methionine synthase.

5 – 3 - Conversion to cysteine

Homocysteine can be converted to cysteine.

(5) Cystathionine-β-synthase (a PLP-dependent enzyme) combines homocysteine and serine to produce cystathionine. Instead of degrading cystathionine via cystathionine-β-lyase, as in the biosynthetic pathway, cystathionine is broken down to cysteine and α-ketobutyrate via (6) cystathionine-γ-lyase.

(7) The enzyme α-ketoacid dehydrogenase converts α-ketobutyrate to propionyl-CoA, which is metabolized to succinyl-CoA in a three-step process .

6 – Synthesis

Racemic methionine can be synthesized from diethyl sodium phthalimidomalonate by alkylation with chloroethylmethylsulfide ($ClCH_2CH_2SCH_3$) followed by hydrolysis and decarboxylation.

Food sources of Methionine

Food	G / 100 g
Egg, white, dried, powder, glucose reduced	3.204
Sesame seeds flour (low fat)	1.656
Egg, whole, dried	1.477
Cheese, Parmesan, shredded	1.114
Brazil nuts	1.008
Soy protein concentrate	0.814
Chicken, broilers or fryers, roasted	0.801
Fish, tuna, light, canned in water, drained solids	0.755
Beef, cured, dried	0.749
Bacon	0.593
Beef, ground, 95 % lean meat / 5% fat, raw	0.565
Pork, ground, 96 % lean / 4 % fat, raw	0.564
Wheat germ	0.456
Oat	0.312
Peanuts	0.309
Chickpea	0.253
Corn, yellow	0.197
Almonds	0.151
Beans, pinto, cooked	0.117
Lentils, cooked	0.077
Rice, brown, medium-grain, cooked	0.052

m

7 - Dietary sources

High levels of methionine can be found in eggs, sesame seeds, Brazil nuts, fish, meats and some other plant seeds; methionine is also found in cereal grains. Most fruits and vegetables contain very little of it. Most legumes are also low in methionine. Racemic methionine is sometimes added as an ingredient to pet foods.

8 - Methionine restriction

There is scientific evidence that restricting methionine consumption can increase lifespans in some animals.

A 2005 study showed methionine restriction without energy restriction extends mouse lifespan.

A study published in *Nature* showed adding just the essential amino acid methionine to the diet of fruit flies under dietary restriction, including restriction of essential amino acids (EAAs), restored fecundity without reducing the longer lifespans that are typical of dietary restriction, leading the researchers to determine that methionine "acts in combination with one or more other EAAs to shorten lifespan."

Several studies showed that methionine restriction also inhibits aging-related disease processes in mice and inhibits colon carcinogenesis in rats.

A 2009 study on rats showed "methionine supplementation in the diet specifically increases mitochondrial ROS production and mitochondrial DNA oxidative damage in rat liver mitochondria offering a plausible mechanism for its hepatotoxicity".

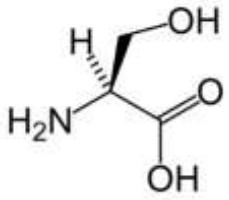
However, since methionine is an essential amino acid, it should not be entirely removed from animal diets without disease or death occurring over time. For example, rats fed a diet without methionine developed steatohepatitis (fatty liver), anemia and lost two thirds of their body weight over 5 weeks. Administration of methionine ameliorated the pathological consequences of methionine deprivation.

9 - Other uses

DL-Methionine is sometimes given as a supplement to dogs; it helps keep dogs from damaging grass by reducing the pH of the urine.

Methionine is allowed as a supplement to organic poultry feed under the US certified organic program.

Serine



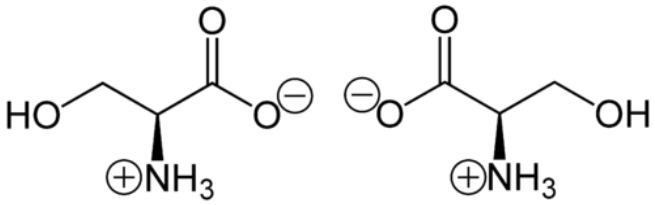
Contents

1 - Introduction

Serine (abbreviated as Ser or S) is an amino acid with the formula $HO_2CCH(NH_2)CH_2OH$. It is one of the proteinogenic amino acids. Its codons in the genetic code are UCU, UCC, UCA, UCG, AGU and AGC. By virtue of the hydroxyl group, serine is classified as a polar amino acid.

IUPAC name : Serine	
Other names : 2-Amino-3-hydroxy propanoic acid	
Molecular formula	$C_3 H_7 N O_3$
Molar mass	105 g mol^{-1}
Appearance	white crystals or powder
Density	1.603 g / cm^3 (22 °C)
Melting point	246 °C decomp.
Solubility in water	soluble
Thermo dynamic data	Phase behaviour Solid , liquid , gas
Spectral data	UV , IR , NMR , MS

2 - Occurrence and biosynthesis



(S)-Serine (left) and (R)-serine (right) in zwitterionic form at neutral pH

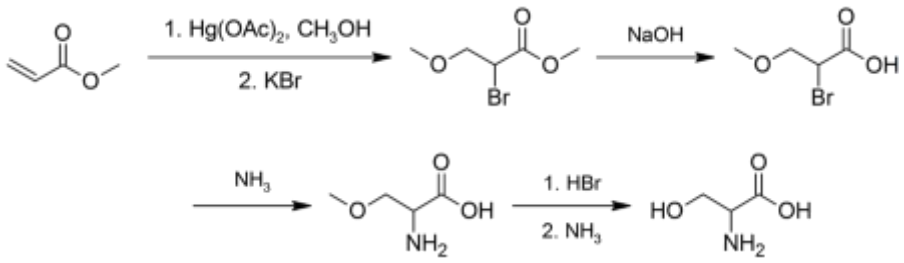
This compound is one of the naturally occurring proteinogenic amino acids. Only the L-stereoisomer appears naturally in proteins. It is not essential to the human diet, since it is synthesized in the body from other metabolites, including glycine. Serine was first obtained from silk protein, a particularly rich source, in 1865. Its name is derived from the Latin for silk, *sericum*. Serine's structure was established in 1902.

The biosynthesis of serine starts with the oxidation of 3-phosphoglycerate to 3-phosphohydroxypyruvate and NADH. Reductive amination of this ketone followed by hydrolysis gives serine. Serine hydroxymethyltransferase catalyzes the reversible, simultaneous conversions of L-serine to glycine (retro-aldol cleavage) and 5,6,7,8-tetra hydrofolate to 5,10-methylene tetra hydrofolate (hydrolysis).

This compound may also be naturally produced when UV light illuminates simple ices such as a combination of water, methanol, hydrogen cyanide, and ammonia, suggesting that it may be easily produced in cold regions of space.

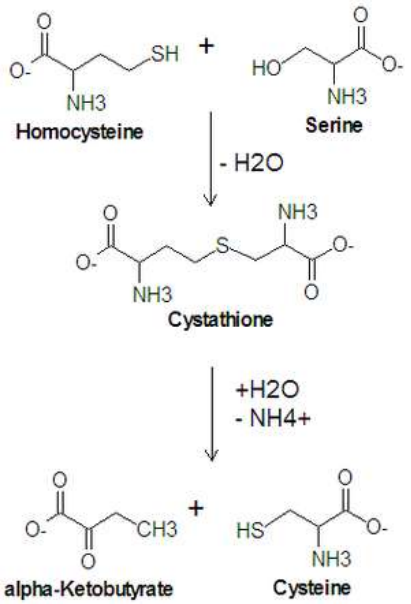
3 – Production

Industrially , L - serine is produced by fermentation, with an estimated 100 - 1000 tonnes per year produced . In the laboratory, racemic serine can be prepared from methyl acrylate via several steps:



4 - Biological function

4 - 1 - Metabolic



Cysteine synthesis from serine.
Cystathionine beta synthase catalyzes the upper reaction and cystathionine gamma-lyase catalyzes the lower reaction.

Serine is important in metabolism in that it participates in the biosynthesis of purines and pyrimidines. It is the precursor to several amino acids including glycine and cysteine, and tryptophan in bacteria. It is also the precursor to numerous other metabolites, including sphingolipids and folate, which is the principal donor of one-carbon fragments in biosynthesis.

4 – 2 - Structural role

Serine plays an important role in the catalytic function of many enzymes. It has been shown to occur in the active sites of chymotrypsin, trypsin, and many other enzymes. The so - called nerve gases and many substances used in insecticides have been shown to

act by combining with a residue of serine in the active site of acetylcholine esterase, inhibiting the enzyme completely.

As a constituent (residue) of proteins, its side chain can undergo *O*-linked glycosylation, which may be functionally related to diabetes.

It is one of three amino acid residues that are commonly phosphorylated by kinases during cell signaling in eukaryotes. Phosphorylated serine residues are often referred to as phosphoserine.

Serine proteases are a common type of protease.

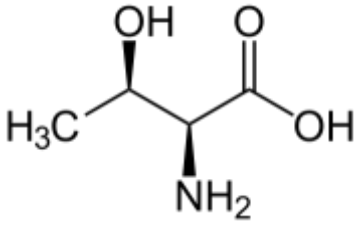
4 – 3 – Signaling

D-Serine, synthesized in the brain by serine racemase from L-serine (its enantiomer), serves as both a neuro transmitter and a gliotransmitter by coactivating NMDA receptors, making them able to open if they then also bind glutamate. D-serine is a potent agonist at the glycine site of the NMDA-type glutamate receptor. For the receptor to open, glutamate and either glycine or D-serine must bind to it. In fact, D-serine is a more potent agonist at the glycine site on the NMDAR than glycine itself. D-serine was only thought to exist in bacteria until relatively recently; it was the second D amino acid discovered to naturally exist in humans, present as a signalling molecule in the brain, soon after the discovery of D-aspartate. Had D amino acids been discovered in humans sooner, the glycine site on the NMDA receptor might instead be named the D-serine site.

4 – 4 - Gustatory sensation

Pure D-Serine is an off-white crystalline powder with a very faint funky or dirty aroma. L-Serine is sweet with minor umami and sour tastes at high concentration. D-Serine is sweet with an additional minor sour taste at medium and high concentrations.

Threonine



Contents

1 - Introduction

Threonine (abbreviated as Thr or T) is an α-amino acid with the chemical formula $HO_2CCH(NH_2)CH(OH)CH_3$. Its codons are ACU, ACA, ACC, and ACG. This essential amino acid is classified as polar. Together with serine, threonine is one of two proteinogenic amino acids bearing an alcohol group (tyrosine is not an alcohol but a phenol, since its hydroxyl group is bonded directly to an aromatic ring, giving it different acid/base and oxidative properties). It is also one of two common amino acids that bear a chiral side chain, along with isoleucine.

The threonine residue is susceptible to numerous posttr anslational modifications. The hydroxy side-chain can undergo *O*-linked glycosylation. In addition, threonine residues undergo phospho rylation through the action of a threonine kinase. In its phosphorylated form, it can be referred to as phospho threonine.

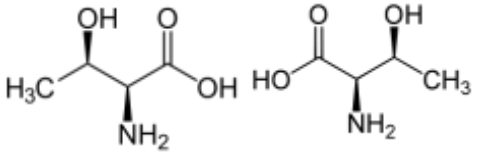
IUPAC name :Threonine
Other names : 2-Amino-3-hydroxy butanoic acid
Molecular formula $C_4 H_9 N O_3$

Molar mass	119.12 g mol^{-1}
Solubility in water	g / dl 10.6 (30°) , 14.1 (52°)
Thermo dynamic data	Phase behaviour Solid , liquid , gas
Spectral data	UV , IR , NMR , MS

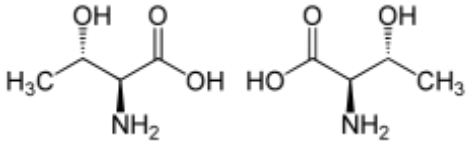
2 – History

Threonine was discovered as the last of the 20 common proteinogenic amino acids in the 1930s by William Cumming Rose.

3 – Stereoisomerism



L-Threonine (2*S*,3*R*) and D-Threonine (2*R*,3*S*)



L-*allo*-Threonine (2*S*,3*S*) and D-*allo*-Threonine (2*R*,3*R*)

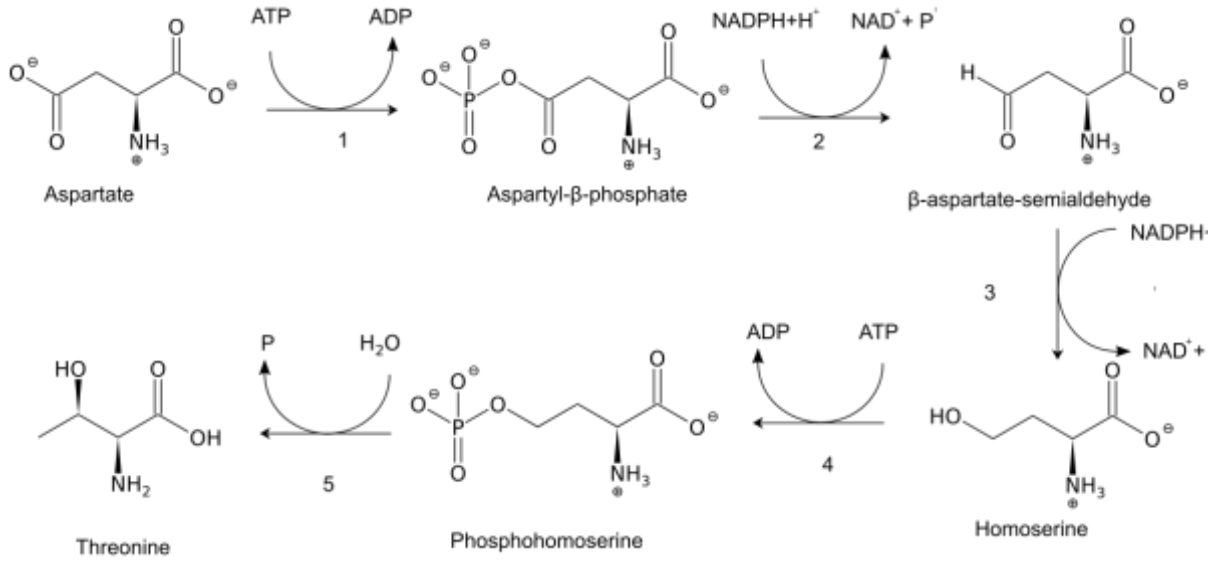
Threonine is one of two proteinogenic amino acids with two chiral centers. Threonine can exist in four possible stereo isomers with the following configurations: (2*S*,3*R*), (2*R*,3*S*), (2*S*,3*S*) and (2*R*,3*R*). However, the name L-threonine is used for one single diastereomer, (2*S*,3*R*)-2-amino-3-hydroxybutanoic acid. The second stereoisomer (2*S*,3*S*), which is rarely present in nature, is called L-*allo*-threonine. The two stereo isomers (2*R*,3*S*)- and (2*R*,3*R*)-2-amino-3-hydroxy butanoic acid are only of minor importance.

4 – Biosynthesis

As an essential amino acid, threonine is not synthesized in humans, hence we must ingest threonine in the form of threonine-containing proteins. In plants and microorganisms, threonine is

synthesized from aspartic acid via α-aspartyl-semialdehyde and homoserine. Homoserine undergoes *O*-phosphorylation; this phosphate ester undergoes hydrolysis concomitant with relocation of the OH group. Enzymes involved in a typical biosynthesis of threonine include :

aspartokinase
β-aspartate semialdehyde dehydrogenase
homoserine dehydrogenase
homoserine kinase
threonine synthase.



Threonine biosynthesis

5 – Metabolism

Threonine is metabolized in two ways:

It is converted to pyruvate via threonine dehydrogenase. An intermediate in this pathway can undergo thiolysis with CoA to produce acetyl-CoA and glycine.

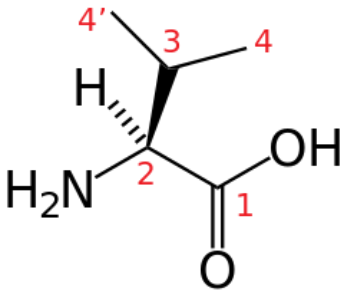
In humans, it is converted to α-ketobutyrate in a less common pathway via the enzyme serine dehydratase, and thereby enters the pathway leading to succinyl-CoA.

6 – Sources

Foods high in threonine include cottage cheese, poultry, fish, meat, lentils, Black turtle bean and Sesame seeds.[5]

Racemic threonine can be prepared from crotonic acid by alpha-functionalization using mercury (II) acetate.

Valine



Contents

1 - Introduction

Valine (abbreviated as Val or V) is an α-amino acid with the chemical formula $HO_2CCH(NH_2)CH(CH_3)_2$. L-Valine is one of 20 proteinogenic amino acids. Its codons are GUU, GUC, GUA, and GUG. This essential amino acid is classified as nonpolar. Human dietary sources are any proteinaceous foods such as meats, dairy products, soy products, beans and legumes.

Along with leucine and isoleucine, valine is a branched-chain amino acid. It is named after the plant valerian. In sickle-cell disease, valine substitutes for the hydrophilic amino acid glutamic acid in hemoglobin. Because valine is hydrophobic, the hemoglobin is prone to abnormal aggregation.

Valine	
IUPAC name : Valine	
Other names : 2 - amino - 3 - methyl butanoic acid	
Molecular formula	$C_5 H_{11} N O_2$
Molar mass	117 g mol^{-1}
Density	1.316 g / cm^3

Melting point	298 °C (decomposition)
Solubility in water	soluble
Thermo dynamic data	Phase behaviour Solid , liquid , gas
Spectral data	UV , IR , NMR , MS

2 – Nomenclature

According to IUPAC, carbon atoms forming valine are numbered sequentially starting from 1 denoting the carboxyl carbon, whereas 4 and 4' denote the two terminal methyl carbons.

3 – Biosynthesis

Valine is an essential amino acid, hence it must be ingested, usually as a component of proteins. It is synthesized in plants via several steps starting from pyruvic acid. The initial part of the pathway also leads to leucine. The intermediate α-ketoisovalerate undergoes reductive amination with glutamate. Enzymes involved in this biosynthesis include :

Acetolactate synthase
Acetohydroxy acid isomeroreductase
Dihydroxyacid dehydratase
Valine aminotransferase

4 – Synthesis

Racemic valine can be synthesized by bromination of isovaleric acid followed by amination of the α-bromo derivative

$$HO_2CCH_2CH(CH_3)_2 + Br_2 \rightarrow HO_2CCHBrCH(CH_3)_2 + HBr$$

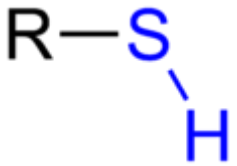
$$HO_2CCHBrCH(CH_3)_2 + 2\ NH_3 \rightarrow HO_2CCH(NH_2)CH(CH_3)_2 + NH_4Br$$

Part – 11 –

Aliphatic Thiol Acids

(Merceptanic Acids)

Thiol



*Thiol with a **blue** highlighted sulfhydryl group.*

Contents

1 - Introduction

In organic chemistry, a **thiol** is an organosulfur compound that contains a carbon-bonded sulfhydryl (–C–SH or R–SH) group (where R represents an alkane, alkene, or other carbon-containing group of atoms). Thiols are the sulfur analogue of alcohols (that is, sulfur takes the place of oxygen in the hydroxyl group of an alcohol), and the word is a portmanteau of "thio" + "alcohol", with the first word deriving

from Greek ("thion") = "sulfur". The –SH functional group itself is referred to as either a *thiol group* or a *sulfhydryl group*.

Many thiols have strong odors resembling that of garlic. Thiols are used as odorants to assist in the detection of natural gas (which in pure form is odorless), and the "smell of natural gas" is due to the smell of the thiol used as the odorant.

Thiols are often referred to as *mercaptans*. The term *mercaptan* is derived from the Latin *mercurium captans* (capturing mercury)[6] because the thiolate group bonds so strongly with mercury compounds.[7] Thiols react with mercury to form *mercaptides*.

2 - Structure and bonding

Thiols and alcohols have similar molecular structure. The major difference is the size of the chalcogenide, C–S bond lengths being around 180 picometers in length. The C–S–H angles approach 90°. In the solid or molten liquids, the hydrogen-bonding between individual thiol groups is weak, the main cohesive force being van der Waals interactions between the highly polarizable divalent sulfur centers.

Due to the lesser electronegativity difference between sulfur and hydrogen compared to oxygen and hydrogen, an S–H bond is less polar than the hydroxyl group. Thiols have a lower dipole moment relative to the corresponding alcohol.

3 - Nomenclature

There are several ways to name the alkylthiols:

The preferred method (used by the IUPAC) is to add the suffix -*thiol* to the name of the alkane. The method is nearly identical to naming an alcohol. Example: CH_3SH would be *methanethiol*.

An older method, the word *mercaptan* replaces *alcohol* in the name of the equivalent alcohol compound. Example: CH_3SH would be methyl mercaptan, just as CH_3OH is called methyl alcohol.

As a prefix, the terms *sulfanyl* or *mercapto* are used. Example: mercaptopurine.

4 - Physical properties

4 – 1 - Odor

Many thiols have strong odors resembling that of garlic. The odors of thiols are often strong and repulsive, particularly for those of low molecular weight. The spray of skunks consists mainly of low-molecular-weight thiols and derivatives . These compounds are detectable by the human nose at concentrations of only 10 parts per billion. Human sweat contains (*R*)/(*S*)-3-methyl-3-sulfanylhexan-1-ol (MSH), detectable at 2 parts per billion and having a fruity, onion-like odor. Women liberate significantly more MSH than men.[15] (Methylthio)methanethiol ($MeSCH_2SH$; MTMT) is a strong-smelling volatile thiol, also detectable at parts per billion levels, found in male mouse urine. Lawrence C. Katz and coworkers showed that MTMT functioned as a semiochemical, activating certain mouse olfactory sensory neurons, attracting female mice. Copper has been shown to be required by a specific mouse olfactory receptor, MOR244-3, which is highly responsive to MTMT as well as to various other thiols and related compounds.

Thiols are also responsible for a class of wine faults caused by an unintended reaction between sulfur and yeast and the "skunky" odor of beer that has been exposed to ultraviolet light.

Not all thiols have unpleasant odors. For example, furan-2-ylmethanethiol contributes to the aroma of roasted coffee while grapefruit mercaptan, a monoterpenoid thiol, is responsible for the characteristic scent of grapefruit. The effect of the latter compound is present only at low concentrations. The pure mercaptan has an unpleasant odor.

Natural gas distributors were required to add thiols, originally ethanethiol, to natural gas (which is naturally odorless) after the deadly New London School explosion in New London, Texas, in 1937. Many gas distributors were odorizing gas prior to this event. Most gas odorants utilized currently contain mixtures of mercaptans and sulfides, with t-butyl mercaptan as the main odor constituent. In situations where thiols are used in commercial industry, such as liquid petroleum gas tankers and bulk handling systems, an oxidizing

catalyst is used to destroy the odor. A copper-based oxidation catalyst neutralizes the volatile thiols and transforms them into inert products.

4 – 2 - Boiling points and solubility

Thiols show little association by hydrogen bonding, with both water molecules and among themselves. Hence, they have lower boiling points and are less soluble in water and other polar solvents than alcohols of similar molecular weight. Thiols and thioethers have similar solubility characteristics and boiling points.

5 - Characterization

Volatile thiols are easily and almost unerringly detected by their distinctive odor. S-specific analyzers for gas chromatographs are useful. Spectroscopic indicators are the D_2O-exchangeable S*H* signal in the ^{1}H NMR spectrum (^{33}S is NMR active but signals for divalent sulfur are very broad and of little utility). The ν_{SH} band appears near 2400 cm^{-1} in the IR spectrum.[3] In a colorimetric test, thiols react with nitroprusside.

6 - Preparation

In industry, methanethiol is prepared by the reaction of hydrogen sulfide with methanol. This method is employed for the industrial synthesis of methanethiol :

$$CH_3OH + H_2S \rightarrow CH_3SH + H_2O$$

Such reactions are conducted in the presence of acidic catalysts. The other principal route to thiols involves the addition of hydrogen sulfide to alkenes. Such reactions are usually conducted in the presence of an acid catalyst or UV light. Halide displacement, using the suitable organic halide and sodium hydrogen sulfide has also been utilized.

6 – 1 - Laboratory methods

On the typical laboratory scale, the direct reaction of a halogenoalkane with sodium hydrosulfide is generally *in*efficient owing to the competing formation of thioethers:

$$CH_3CH_2Br + NaSH \rightarrow CH_3CH_2SH + NaBr$$

$CH_3CH_2Br + CH_3CH_2SH \rightarrow (CH_3CH_2)_2S + HBr$

Instead, alkyl halides are converted to thiols via a S-alkylation of thiourea. This multistep, one-pot process proceeds via the intermediacy of the isothiouronium salt, which is hydrolyzed in a separate step :

$CH_3CH_2Br + SC(NH_2)_2 \rightarrow [CH_3CH_2SC(NH_2)_2]Br$
$[CH_3CH_2SC(NH_2)_2]Br + NaOH \rightarrow$
$CH_3CH_2SH + OC(NH_2)_2 + NaBr$

The thiourea route works well with primary halides, especially activated ones. Secondary and tertiary thiols are less easily prepared. Secondary thiols can be prepared from the ketone via the corresponding dithioketals.

Organolithium compounds and Grignard reagents react with sulfur to give the thiolates, which are readily hydrolyzed:

$RLi + S \rightarrow RSLi$
$RSLi + HCl \rightarrow RSH + LiCl$

Phenols can be converted to the thiophenols via rearrangement of their O-aryl dialkylthiocarbamates.

Many thiols are prepared by reductive dealkylation of thioethers, especially benzyl derivatives and thioacetals.

7 - Reactions

Akin to the chemistry of alcohols, thiols form thioethers, thioacetals and thioesters, which are analogous to ethers, acetals, and esters. Thiols and alcohols are also very different in their reactivity, thiols being easily oxidized and thiolates being highly potent nucleophiles.

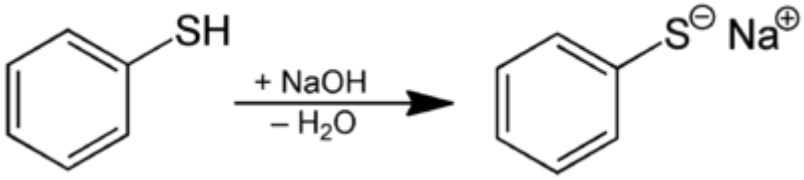
7 – 1 - S - alkylation

Thiols, or more particularly their conjugate bases, are readily alkylated to give thioethers :

$$RSH + R'Br + \textit{base} \rightarrow RSR' + [H\textit{base}]Br$$

7 – 2 - Acidity

Relative to the alcohols, thiols are fairly acidic. Butanethiol has a pK_a of 10.5 vs 15 for butanol. Thiophenol has a pK_a of 6 vs 10 for phenol. Thus, thiolates can be obtained from thiols by treatment with alkali hydroxides.



Synthesis of thiophenolate from thiophenol

7 – 3 - Redox

Thiols, especially in the presence of base, are readily oxidized by reagents such as iodine to give an organic disulfide (R–S–S–R).

$$2\ R–SH + Br_2 \rightarrow R–S–S–R + 2\ HBr$$

Oxidation by more powerful reagents such as sodium hypochlorite or hydrogen peroxide yields sulfonic acids (RSO_3H).

$$R–SH + 3H_2O_2 \rightarrow RSO_3H + 3H_2O$$

Oxidation by oxygen in the presence of heterogeneous [25] catalysts :

$$2R–SH + 1/2O_2 \rightarrow RS–SR + H_2O$$

Thiols participate in thiol-disulfide exchange:

$$RS–SR + 2\ R'SH \rightarrow 2\ RSH + R'S–SR'$$

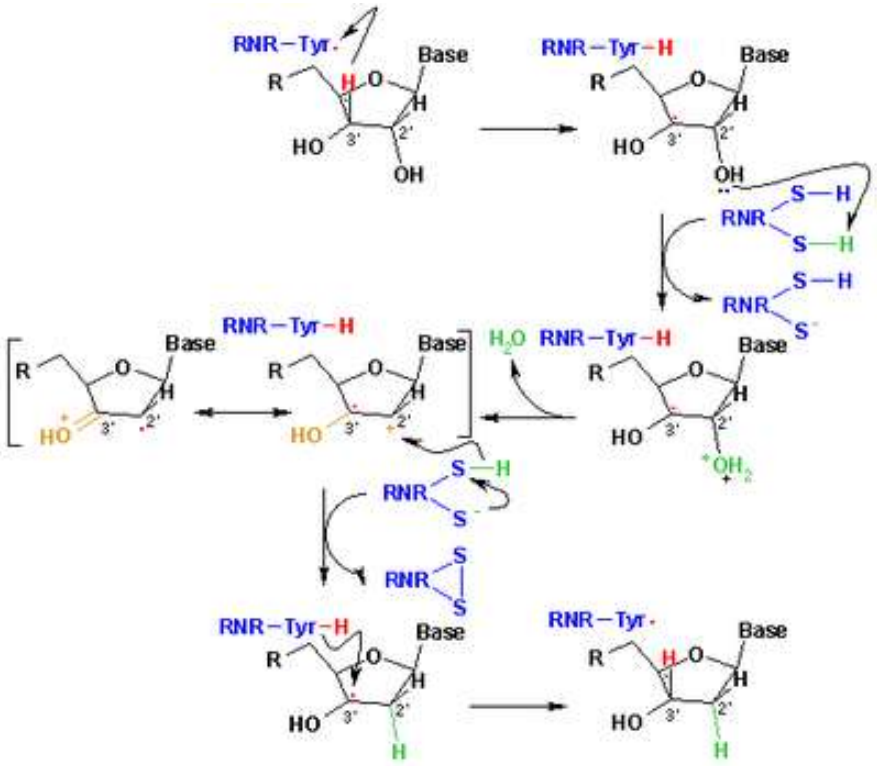
This reaction is especially important in nature.

7 – 4 - Metal ion complexation

Thiolates, the conjugate bases derived from thiols, form strong complexes with many metal ions, especially those classified as soft. The term *mercaptan* is derived from the Latin *mercurium captans* (capturing mercury)[6] because the thiolate group bonds so strongly with mercury compounds. The stability of metal thiolates parallels that of the corresponding sulfide minerals.

8 - Thiyl radicals

Free radicals derived from mercaptans, called thiyl or thiol radical or mercapto radical, are commonly invoked to explain reactions in organic chemistry and biochemistry. They have the formula RS where R is an organic substituent such as alkyl or aryl.[4] They arise from or can be generated by a number of routes, but the principal method is H-atom abstraction from thiols. Another method involves homolysis of organic disulfides. In biology thiyl radicals are responsible for the formation of the deoxyribonucleic acids, building blocks for DNA. This conversion is catalysed by ribonucleotide reductase (see figure). Thiyl intermediates also are produced by the oxidation of glutathione, an antioxidant in biology. Thiyl radicals are also intermediates in the vulcanization process. For example, the vulcanization of polyisoprene results when mercapto radicals couple forming disulfide and polysulfide crosslinks. Thiyl radicals (sulfur-centred) can transform to carbon-centred radicals *via* hydrogen atom exchange equilibria. The formation of carbon-centred radicals could lead to protein damage via the formation of C—C bonds or backbone fragmentation.[28]



The catalytic cycle for ribonucleotide reductase, demonstrating the role of thiyl radicals in producing the genetic machinery of life.

9 - Biological importance

9 – 1 - Cysteine and cystine

As the functional group of the amino acid cysteine, the thiol group plays a very important role in biology. When the thiol groups of two cysteine residues (as in monomers or constituent units) are brought near each other in the course of protein folding, an oxidation reaction can generate a cystine unit with a disulfide bond (-S-S-). Disulfide bonds can contribute to a protein's tertiary structure if the cysteines are part of the same peptide chain, or contribute to the quaternary structure of multi-unit proteins by forming fairly strong covalent bonds between different peptide chains. A physical manifestation of cysteine - cystine equilibrium is provided by hair straightening technologies.

Sulfhydryl groups in the active site of an enzyme can form noncovalent bonds with the enzyme's substrate as well, contributing to catalytic activity. Active site cysteine residues are the functional unit in cysteine proteases. Cysteine residues may also react with heavy metal ions (Zn^{2+}, Cd^{2+}, Pb^{2+}, Hg^{2+}, Ag^{+}) because of the high affinity between the soft sulfide and the soft metal (see hard and soft acids and bases). This can deform and inactivate the protein, and is one mechanism of heavy metal poisoning.

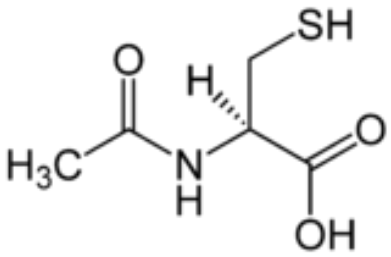
9 – 2 - Cofactors

Many cofactors (non - protein - based helper molecules) feature thiols. The biosynthesis and degradation of fatty acids and related long-chain hydrocarbons is conducted on a scaffold that anchors the growing chain through a thioester derived from the thiol Coenzyme A. The biosynthesis of methane, the principal hydrocarbon on earth, arises from the reaction mediated by coenzyme M, 2-mercaptoethyl sulfonic acid. Thiolates, the conjugate bases derived from thiols, form strong complexes with many metal ions, especially those classified as soft. The stability of metal thiolates parallels that of the corresponding sulfide minerals.

10 - Examples of thiols

Methanethiol – CH_3SH [m-mercaptan]
Ethanethiol – C_2H_5SH [e- mercaptan]
1-Propanethiol – C_3H_7SH [n-P mercaptan]
2-Propanethiol – $CH_3CH(SH)CH_3$ [2C3 mercaptan]
Butanethiol – C_4H_9SH [n-butyl mercaptan]
tert-Butyl mercaptan – $C(CH_3)_3SH$ [t-butyl mercaptan]
Pentanethiols – $C_5H_{11}SH$ [pentyl mercaptan]
Thiophenol – C_6H_5SH
Dimercaptosuccinic acid
Thioacetic acid
Coenzyme A
Glutathione
Cysteine
2-Mercaptoethanol
Dithiothreitol/dithioerythritol (an epimeric pair)
2-Mercaptoindole
Grapefruit mercaptan
Furan-2-ylmethanethiol
3-Mercaptopropane-1,2-diol

Acetyl cysteine



Contents

1 - Introduction

Acetylcysteine also known as ***N*-acetylcysteine** or ***N*-acetyl-*L*-cysteine** (abbreviated **NAC**), is a pharma ceutical drug and nutritional supplement used primarily as a mucolytic agent and in the management of paracetamol (acetaminophen) overdose. Other uses include sulfate repletion in conditions, such as autism, where cysteine and related sulfur amino acids may be depleted.

Acetylcysteine is a derivative of cysteine; an acetyl group is attached to the nitrogen atom. This compound is sold as a dietary supplement commonly claiming antioxidant and liver protecting effects. It is used as a cough medicine because it breaks disulfide

bonds in mucus and liquefies it, making it easier to cough up. It is also this action of breaking disulfide bonds that makes it useful in thinning the abnormally thick mucus in cystic and pulmonary fibrosis patients. In India it is marketed by Intas under the trade name '**Efetil**'.

IUPAC name :
2-Acetamido-3-sulfanyl propanoic acid

Molecular formula	$C_5 H_9 N O_3 S$
Molar mass	163 g mol^{-1}
Appearance	White , opaque crystals
Melting point	106 - 108 °C
Bioavailability	6 – 10 % (oral) < 3 % (inhalational)
LD_{50}	5050 mg kg^{-1} (oral, rat)

2 - Medical uses

2 – 1 - Paracetamol overdose

Intravenous acetylcysteine is indicated for the treatment of paracetamol (acetaminophen) overdose. When paracetamol is taken in large quantities, a minor metabolite called *N*-acetyl-*p*-benzoquinone imine (NAPQI) accumulates within the body. It is normally conjugated by glutathione, but when taken in excess, the body's glutathione reserves are not sufficient to inactivate the toxic NAPQI. This metabolite is then free to react with key hepatic enzymes, therefore damaging hepatocytes. This may lead to severe liver damage and even death by fulminant liver failure.

For this indication, acetylcysteine acts to augment the glutathione reserves in the body and, together with glutathione, directly bind to toxic metabolites. These actions serve to protect hepatocytes in the liver from NAPQI toxicity.

Although both IV and oral acetylcysteine are equally effective for this indication, oral administration is poorly tolerated because high oral doses are required due to low oral bioavailability,[3] because of its very unpleasant taste and odour, and because of adverse effects,

particularly nausea and vomiting. Studies conducted by Baker and Dilger suggest that the prior pharmacokinetic studies of acetylcysteine did not include acetylation as a reason for the low bioavailability of acetylcysteine. In the research conducted by Baker, it was concluded that oral acetylcysteine was identical in bioavailability to Cysteine precursors. However, 3 % to 6 % of people given intravenous acetylcysteine show a severe, anaphylaxis-like allergic reaction, which may include extreme breathing difficulty (due to bronchospasm), a decrease in blood pressure, rash, angioedema, and sometimes also nausea and vomiting . Repeated doses of intravenous acetylcysteine will cause these allergic reactions to progressively worsen in these people.

Several studies have found this anaphylaxis-like reaction to occur more often in people given IV acetylcysteine despite serum levels of paracetamol not high enough to be considered toxic.

In some countries, a specific intravenous formulation does not exist to treat paracetamol overdose. In these cases, the formulation used for inhalation may be used intravenously.

2 – 2 - Mucolytic therapy [edit]

Inhaled acetylcysteine is indicated for mucolytic ("mucus-dissolving") therapy as an adjuvant in respiratory conditions with excessive and / or thick mucus production. Such conditions include emphysema, bronchitis, tuberculosis, bronchiectasis, amyloidosis, pneumonia, cystic fibrosis, chronic obstructive pulmonary disease, and pulmonary fibrosis. It is also used post-operatively, as a diagnostic aid, and in tracheotomy care. It may be considered ineffective in cystic fibrosis. However, a recent paper in the Proceedings of the National Academy of Sciences reports that high-dose oral acetylcysteine modulates inflammation in cystic fibrosis and has the potential to counter the intertwined redox and inflammatory imbalances in CF. Oral acetylcysteine may also be used as a mucolytic in less serious cases.

For this indication, acetylcysteine acts to reduce mucus viscosity by splitting disulfide bonds linking proteins present in the mucus (mucoproteins).

2 – 3 - Nephroprotective agent

Oral acetylcysteine is used for the prevention of radiocontrast-induced nephropathy (a form of acute renal failure). Some studies show that prior administration of acetylcysteine markedly decreases radiocontrast nephropathy,[12] whereas others appear to cast doubt on its efficacy. Data published in two papers in the *New England Journal of Medicine* and the *Journal of the American Medical Association.* Conclude :

"Intravenous and oral N-acetyl cysteine may prevent contrast-medium–induced nephropathy with a dose-dependent effect in patients treated with primary angioplasty and may improve hospital outcome."

"Acetylcysteine protects patients with moderate chronic renal insufficiency from contrast-induced deterioration in renal function after coronary angiographic procedures, with minimal adverse effects and at a low cost"

A clinical trial from 2010, however, found that acetylcysteine is ineffective for the prevention of contrast-induced nephropathy. This trial, involving 2,308 patients, found that acetylcysteine was no better than placebo; whether acetylcysteine or placebo was used, the incidence of nephropathy was the same — 13 %.

Acetylcysteine continues to be commonly used in individuals with renal impairment to prevent the precipitation of acute renal failure .

2 – 4 - Treatment of cyclo phosphamide - induced hemorrhagic cystitis

Acetylcysteine has been used for cyclophosphamide-induced hemorrhagic cystitis, although mesna is generally preferred due to the ability of acetylcysteine to diminish the effectiveness of cyclophosphamide.

2 – 5 - Microbiological use [edit]

Acetylcysteine can be used in Petroff's method i.e. liquefaction and decontamination of sputum, in preparation for diagnosis of tuberculosis.

2 – 6 - Interstitial lung disease [edit]

Acetylcysteine is used in the treatment of interstitial lung disease to prevent disease progression.

2 – 7 - Psychiatry

Acetylcysteine has been shown to reduce the symptoms of both schizophrenia[24] and bipolar disorder in two placebo controlled trials conducted at Melbourne University. It is thought to act via modulation of NMDA glutamate receptors or by increasing glutathione. Pilot data suggests potential efficacy in autism, cocaine craving, smoking, and obsessive symptoms . Replicatory trials in bipolar disorder, schizophrenia, and depression are currently under way in Geelong, Australia conducted by Dr. Michael Berk of Barwon Health & Deakin University.

2 – 8 – Poly cystic ovary syndrome [edit]

In a small prospective trial comparing acetylcysteine to metformin (which is the standard drug treatment for PCOS), both treatments resulted in a significant decrease in body mass index, hirsutism score, fasting insulin, HOMA index, free testosterone and menstrual irregularity compared with baseline values, and both treatments had equal efficacy.

3 - Adverse effects

Researchers at the University of Virginia reported in 2007 study using very large doses in a mouse model that acetylcysteine could potentially cause damage to the heart and lungs. They found that acetyl cysteine was metabolized to *S*-nitroso-*N*-acetyl cysteine (SNOAC), which increased blood pressure in the lungs and right ventricle of the heart (pulmonary artery hypertension) in mice treated with acetylcysteine. The effect was similar to that observed following a 3-week exposure to an oxygen - deprived environment (chronic hypoxia). The authors also found that SNOAC induced a hypoxia-like response in the expression of several important genes both *in vitro* and *in vivo*.

The implications of these findings for long-term treatment with acetylcysteine have not yet been investigated. The dose used by

Palmer and colleagues was dramatically higher than that used in humans; nonetheless, positive effects on age-diminished control of respiration (the hypoxic ventilatory response) have been observed previously in human subjects at more moderate doses.

4 - Complexing agent

Acetyl cysteine has been used to complex palladium, to help it dissolve in water. This helps to remove palladium from drugs or precursors synthesized by palladium-catalyzed coupling reactions.

5 - Chemistry

Acetylcysteine is the *N*-acetyl derivative of the amino acid L-cysteine, and is a precursor in the formation of the antioxidant glutathione in the body. The thiol (sulfhydryl) group confers antioxidant effects and is able to reduce free radicals.

6 - Dosage forms

Acetylcysteine is available in different dosage forms for different indications :

Solution for inhalation (Assist,Mucomyst, Mucosil) – inhaled for mucolytic therapy or ingested for nephroprotective effect (to protect the kidneys)

IV injection (Assist,Parvolex, Acetadote) – treatment of paracetamol/acetaminophen overdose

Oral solution – various indications.

Effervescent Tablets (200 mg) - Reolin (Hochland Pharma Germany), Solmucol (600 mg)(IBSA, Switzerland), Cystaline (Thailand), Mucinac (Cipla India), Siran (MegaPharm, Israel / Temmler Pharma, Germany), Amuco200 (Camox Pharmaceuticals, South Africa), ACC200 (Hexal Pharma, South Africa).

Ocular solution - for mucolytic therapy

Sachet (600 mg) - Bilim Pharmaceuticals, trebon N (Uni-Pharma Greece)

CysNAC (900 mg) – NeuroScience Inc.

PharmaNAC Effervescent Tablets (900 mg) - Bioadvantex Pharma.

The IV injection and inhalation preparations are, in general, prescription only, whereas the oral solution and the effervescent tablets are available over the counter in many countries.

7 - Research

The following uses have not been well-established or investigated :

Acetylcysteine has been successfully used to aid in the treatment of cannabis dependence in adolescents.[34]

Acetylcysteine has had anecdotal reports and some research suggesting efficacy in preventing nail biting.[35]

Acetylcysteine is being tested in a double blind trial in Systemic Lupus Erythematosus.[36] The objective is to correct mitochondrial dysfunction.

Acetylcysteine has been shown to reduce cravings associated with chronic cocaine use in a study conducted at the Medical University of South Carolina.[37][38]

It may reduce the incidence of chronic obstructive pulmonary disease (COPD) exacerbations.[39]

In the treatment of AIDS, acetylcysteine has been shown to cause a "marked increase in immunological functions and plasma albumin concentrations".[40] Albumin concentration are inversely correlated with muscle wasting (cachexia), a condition associated with AIDS.

A human study of 262 primarily elderly individuals indicates that acetylcysteine may decrease influenza symptoms. In the study, 25% of virus-infected subjects who received acetylcysteine treatment developed symptoms whereas 79% in the placebo group developed symptoms.

It has been suggested that acetylcysteine may help sufferers of Samter's triad by increasing levels of glutathione allowing faster breakdown of salicylates, though there is no evidence that it is of benefit.

There are claims that acetylcysteine taken together with vitamin C and B_1 can be used to prevent and relieve symptoms of veisalgia (hangover following ethanol (alcohol) consumption). The claimed mechanism is through scavenging of acetaldehyde, a toxic intermediate in the metabolism of ethanol.

It has been shown to help women with PCOS (polycystic ovary syndrome) to reduce insulin problems and possibly improve fertility.

Small studies have shown acetylcysteine to be of benefit to sufferers of blepharitis.

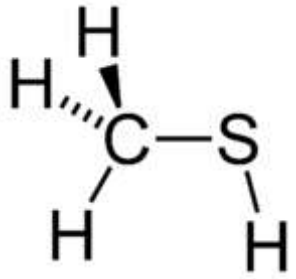
It has been shown to help trichotillomania , a condition causing compulsive hair-pulling as well as compulsive nailbiting.

It has been shown effective in the treatment of Unverricht-Lundborg disease in an open trial in 4 patients. A marked decrease in myoclonus and some normalization of somatosensory evoked potentials with acetylcysteine treatment has been documented.

Results of a research study published in the *New England Journal of Medicine* in November 2011, tested the effect of acetylcysteine in combination with glucocorticoids (combination group) for patients suffering from severe alcoholic hepatitis. The data showed that the combination of acetylcysteine with prednisolone decreased mortality significantly at one month compared to the prednisolone - only group (8 % vs 24 % , P = 0.006). However, the improvement was not as significant at 3 months or 6 months (22 % vs 34 % , P = 0.06) and (27 % vs 38 %, P = 0.07). Factors that were associated with increased 6-month survival included younger age, shorter prothrombin time, lower levels of bilirubin in baseline studies, and decrease in bilirubin on day 14, all (P<0.001). Death due to hepatorenal syndrome occurred less frequently for the combination group at 6 months (9 % vs 22 %, P = 0.02) and infections were also less frequent in the combination group as well (P=0.001). Six-month survival, the primary outcome, was not improved in conclusion.[49]

Acetylcysteine appears to improve the clinical efficacy of B vitamins in patients with raised homocysteine and memory disorders, including dementia.

Methane thiol



Contents

1 - Introduction

Methanethiol (also known as **methyl mercaptan**) is a colorless gas with a smell like rotten cabbage. It is a natural substance found in the blood and brain of humans and other animals as well as plant tissues. It is disposed of through animal feces. It occurs naturally in certain foods, such as some nuts and cheese. It is also one of the main chemicals responsible for bad breath and the smell of flatus. The chemical formula for methanethiol is CH_3SH; it is classified as a thiol. It is sometimes abbreviated as **MeSH**. It is very flammable.

IUPAC name : Methanethiol

Other names :
methyl mercaptan
mercapto methane
thio methyl alcohol

Molecular formula	CH_4S
Molar mass	48 $g \cdot mol^{-1}$
Melting point	- 123 °C
Boiling point	5.95 °C
Solubility in	2 %

water	
Solubility	Alcohol , ether
EU classification	 **F +**  **T**  N

2 - Occurrence

Methanethiol is released from decaying organic matter in marshes and is present in the natural gas of certain regions, in coal tar, and in some crude oils.

In surface seawater, methanethiol is the primary breakdown product of the algal metabolite dimethylsulfoniopropionate (DMSP). Marine bacteria appear to obtain most of their protein sulfur by the breakdown of DMSP and incorporation of methanethiol, despite the fact that methanethiol is present in seawater at much lower concentrations than sulfate (~0.3 nM vs. 28 mM). Bacteria in oxic and anoxic environments can also convert methanethiol to dimethyl sulfide (DMS), although most DMS in surface seawater is produced by a separate pathway. Both DMS and methanethiol can be used by certain microbes as substrates for methanogenesis in some anaerobic soils.

Methanethiol is a weak acid, with a pKa of ~10.4. This acidic property makes it reactive with dissolved metals in aqueous solutions. The environmental chemistry of these interactions in seawater or fresh water environments such as lakes has yet to be fully investigated.

A material safety data sheet (MSDS) lists methanethiol as a colorless, flammable gas with an extremely strong and repulsive smell. At very high concentrations it is highly toxic and affects the central nervous system. Its penetrating odor provides warning at dangerous concentrations. An odor threshold of 1 ppb has been reported. The United States OSHA Ceiling Limit is listed as 10 ppm.

3 - Preparation

Methanethiol is prepared commercially by the reaction of methanol with hydrogen sulfide gas over an acidic solid catalyst, such

as alumina. It can be prepared by the reaction of methyl iodide with thiourea.

4 - Uses

Cylinder of methanethiol gas

Methanethiol is mainly used to produce methionine, which is used as a dietary component in poultry and animal feed. Methanethiol is also used in the plastics industry and as a precursor in the manufacture of pesticides. It is released as a by-product of wood pulping in pulp mills.

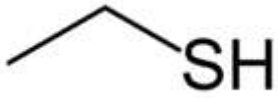
Methanethiol is also used for communication in mining operations . Releasing the substance into the ventilation system is generally the most efficient and reliable means to alert all workers of an emergency , and is referred to as "releasing the pest" .This substance's strong odor alerts the miners to immediately go to a saferoom .

Since natural gas and propane are colorless and odorless, a small amount of methyl mercaptan or ethyl mercaptan is added to make it easy to detect a gas leak.

5 - Asparagus

Methanethiol is a byproduct produced by the metabolism of asparagus.[4] The ability to produce methanethiol in urine after eating asparagus was once thought to be a genetic trait. However recent research suggests that the peculiar odor is in fact produced by all humans after consuming asparagus, while the ability to detect it (methanethiol being one of many components in "asparagus pee") is in fact the genetic trait.[5] The chemical components responsible for the change in the odor of urine show as soon as 15 minutes after eating asparagus.

Ethane thiol



Contents

1 - Introduction

Ethane thiol, commonly known as **ethyl mercaptan**, is a colorless gas or clear liquid with a distinct odor. It is an organosulfur compound with the formula CH_3CH_2SH. Abbreviated EtSH, it consists of an ethyl group (Et), CH_3CH_2, attached to a thiol group, SH. Its structure parallels that of ethanol, but with S instead of O. The odor of EtSH is infamous. Ethanethiol is more volatile than ethanol due to a diminished ability to engage in hydrogen bonding. Ethanethiol is toxic. It occurs naturally as a minor component of petroleum, and may be added to other wise odorless gaseous products such as liquefied petroleum gas (LPG) to help warn of gas leaks. At these concentrations, ethanethiol is not harmful.

IUPAC name ; Ethane thiol	
Other names : Ethyl mercaptan	
Molecular formula	$C_2 H_6 S$
Molar mass	62 $g \cdot mol^{-1}$
Density	0.8617 $g \cdot cm^{-3}$
Melting point	- 148 °C
Boiling point	35 °C
EU classification	 **F**  Xn  N

2 - Preparation

Ethanethiol is prepared by the reaction of ethylene with hydrogen sulfide over a catalyst. The various producers utilize different catalysts in this process. It is also be prepared commercially

by the reaction of ethanol with hydrogen sulfide gas over an acidic solid catalyst, such as alumina.

Ethanethiol was originally reported by Zeiss in 1834 . Zeise treated calcium ethyl sulfate with a suspension of barium sulfide saturated with hydrogen sulfide. He is credited with naming the C_2H_5S- group as mercaptum.

Ethanethiol can also be prepared by a halide displacement reaction, where ethyl halide is reacted with aqueous sodium bisulfide. This conversion was demonstrated as early as 1840 by Henri Victor Regnault.

3 - Odor

Ethanethiol has a strongly disagreeable odor that humans can detect in minute concentrations. The threshold for human detection is as low as one part in 2.8 billion parts of air. Its odor resembles that of leeks, onions or cooked cabbage, but is quite distinct. Ethanethiol is intentionally added to butane and propane (see: LPG) to impart an easily noticed smell to these normally odorless fuels that pose the threat of fire, explosion, and asphyxiation.

4 - Reactions

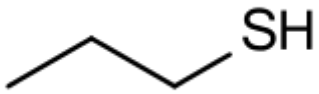
Ethane thiol is a valued reagent in organic synthesis. In the presence of sodium hydroxide, it gives the powerful nucleophile SEt^-. The salt can be generated quantitatively by reaction with sodium hydride.

Ethane thiol can be oxidized to ethyl sulfonic acid, using bleach and related strong aqueous oxidants. Weaker oxidants, such as ferric oxide give the disulfide, diethyl disulfide :

$$2\ EtSH + H_2O_2 \rightarrow EtS\text{-}SEt + 2\ H_2O$$

Like other thiols, it behaves comparably to hydrogen sulfide. For example, it binds, concomitant with deprotonation to "soft" transition metal cations, such as Hg^{2+}, Cu^+, and Ni^{2+} to give polymeric thiolato complexes, $Hg(SEt)_2$, CuSEt, and $Ni(SEt)_2$, respectively.

Propane thiol



Contents

1 - Introduction

Propane thiol is an organic compound with the molecular formula C_3H_8S. It belongs to the group of thiols. It is a colorless liquid with a strong, offensive odor. It is moderately toxic and is less dense than water and slightly soluble in water. It is used as a chemical intermediate and a herbicide . It is highly flammable and it gives off irritating or toxic fumes (or gases) in a fire. Heating it will cause rise in pressure with risk of bursting.

IUPAC name : Propane-1-thiol
Other names :
MERCAPTAN C3
n-Propyl thiol
1-Propane thiol
Propan-1- thiol
Propyl mercaptan

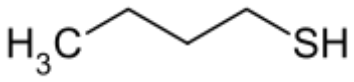
Molecular formula	$C_3 H_8 S$
Molar mass	76 g mol^{-1}
Appearance	Colorless to pale yellow liquid with cabbage-like, sulfur aceous odor
Density	0.84 g / mL
Melting point	- 113 °C
Boiling point	67-68 °C
Solubility in water	Slightly[*vague*]

2 - Chemistry

Propanethiol is chemically classified among the thiols, which are organic compounds with molecular formulas and structural formulas

similar to alcohols, except that sulfur-containing sulfhydryl group (-SH) replaces the oxygen - containing hydroxyl group in the molecule. Propanethiol's basic molecular formula is C_3H_7SH, and its structural formula is similar to that of the alcohol *n*-propanol.

Butane thiol



Contents

1 - Introduction

Butane thiol, also known as **butyl mercaptan**, is a volatile, clear to yellowish liquid with a fetid (extremely foul-smelling) odor, commonly described as "skunk" odor. In fact, butanethiol is structurally similar to several major constituents of a skunk's defensive spray but is not actually present in the spray.[1] The scent of butanethiol is so strong that the human nose can easily detect it in the air at concentrations as low as 10 parts per billion. The threshold level for 1-butane thiol is reported as 1.4 ppb

IUPAC name : Butane-1-thiol

Other names :
Butyl mercaptan
n-Butyl mercaptan
1-Butanethiol
Thiobutyl alcohol
Mercaptobutane

Molecular formula	$C_4H_{10}S$
Molar mass	90 g mol^{-1}
Appearance	Nauseating clear liquid
Density	0.83679 g / mL
Melting point	- 115.8 °C
Boiling point	98.2 °C
Solubility in water	Slightly soluble

2 - Chemistry

Butanethiol is chemically classified among the thiols, which are organic compounds with molecular formulas and structural formulas similar to alcohols, except that sulfur-containing sulfhydryl group (-SH) replaces the oxygen-containing hydroxyl group in the molecule. Butanethiol's basic molecular formula is C_4H_9SH, and its structural formula is similar to that of the alcohol *n*-butanol. Butanethiol is prepared by the free radical catalyzed addition of hydrogen sulfide to 1-butene. Commercially, this is performed using ultraviolet light. Butanethiol is a thiol of low molecular weight, and it is highly flammable.

3 - Uses

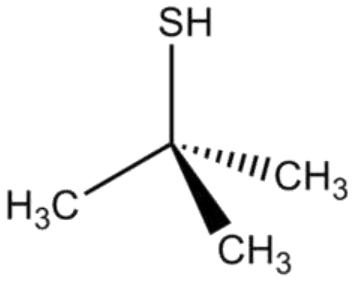
Butanethiol is used as an industrial solvent , and as an intermediate for cotton defoliants. It is some times placed in the "stink bombs" and "stink perfumes" for prankster

4 - Safety

Butanethiol is a very noxious and caustic chemical compound, and at sufficiently high concentrations, it produces serious health effects in both humans and animals, especially as a result of prolonged exposure. Higher concentrations can lead to unconsciousness and coma after prolonged exposure. Contact with the skin and mucous membranes causes burns, and contact with the eyes can lead to blurred vision or complete blindness.

Inhalation may cause weakness, confusion, cough, dizziness, drowsiness, headache, nausea, vomiting, and shortness of breath. The substance irritates the eyes, the skin, and the respiratory tract. It may cause effects on the thyroid and the nervous system and could cause lowering of consciousness.

tert-Butyl thiol



Contents

1 - Introduction

***tert*-Butylthiol**, also known as **2-methyl propane-2-thiol**, **2-methyl-2-propane thiol**, **tert-butyl mercaptan (TBM)**, and ***t*-BuSH**, is an organo sulfur compound with the formula $(CH_3)_3CSH$. This thiol may have been used as a flavoring agent, as an odorant for natural gas (which is odorless), and also in a wide range of organic reactions.

IUPAC name : 2-Methyl propane-2-thiol
Other names :
t-BuSH,
2-methyl propane-2-thiol,
2-methyl -2-propanethiol,
tert-butyl mercaptan, TBM

Molecular formula	$C_4H_{10}S$
Molar mass	90 g mol^{-1}
Appearance	Colorless, clear liquid
Density	0.8 g/mL (25 °C)
Melting point	- 0.50 °C
Boiling point	62 - 65 °C

2 - Preparation

tert-Butyl thiol likely does not occur naturally, but at least one publication has listed it as a very minor component of cooked potatoes.[2] The compound was first prepared in 1890 by Leonard Dobbin[3] by the reaction of zinc sulfide and *t*-butyl chloride.

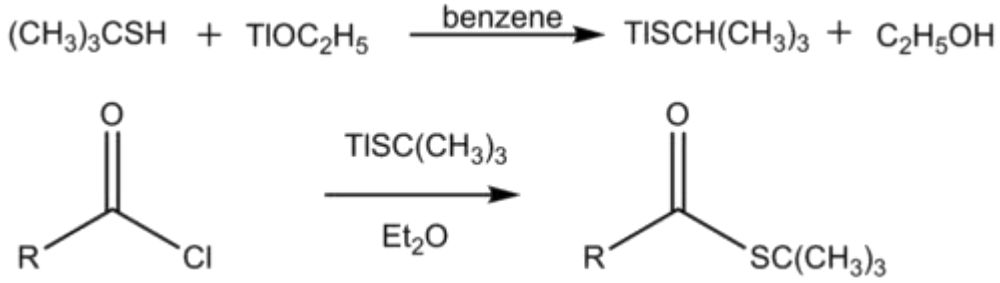
The compound was later prepared in 1932 by the reaction of the Grignard reagent, *t*-BuMgCl, with sulfur to give the corresponding thiolate, followed by hydrolysis. This preparation is shown below:

t-Bu Mg Cl + S → *t*-Bu S Mg Cl
t-Bu S Mg Cl + H_2O → *t*-Bu S H + Mg (OH) Cl

It is currently prepared industrially by the reaction of isobutylene with hydrogen sulfide over a clay (silica alumina) catalyst.

3 –Reactions

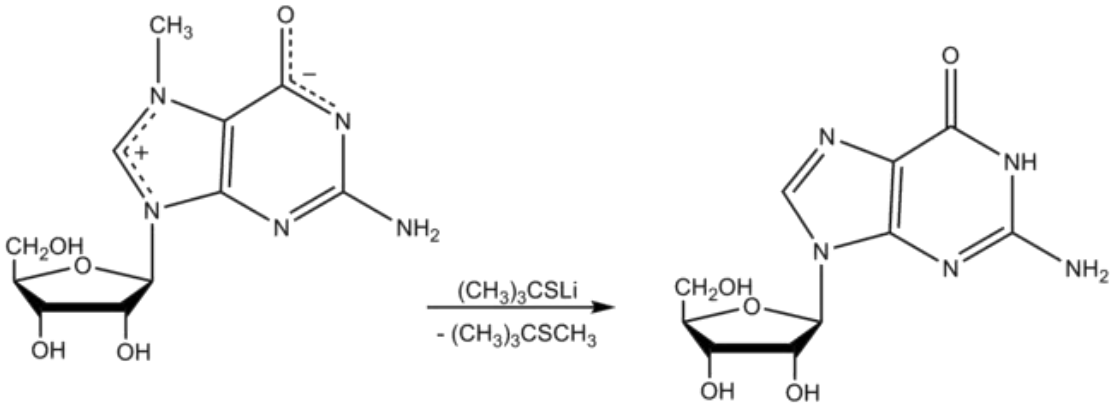
tert-Butylthiol can react with metal alkoxides and acyl chlorides to form thiol esters, as shown in the equation :



In the reaction above, thallium (I) ethoxide converts to thallium (I) *t*-butyl thiolate. In the presence of diethyl ether, thallium (I) *t*-butylthiolate reacts with acyl chlorides to give the corresponding tert-butyl thioesters. Like other thio esters, it reverts back to tert-butylthiol by hydrolysis.

Lithium 2-methyl propane-2-thiolate can be prepared by treatment of *tert*-butyl thiol with lithium hydride in an aprotic solvent such as hexa methyl phosphorous triamide (HMPT). The resulting thiolate salt is a useful demethylating reagent. For example, treatment

with 7- methyl guanosine gives guanosine. Other N-methylated nucleosides in tRNA are not demethylated by this reagent .

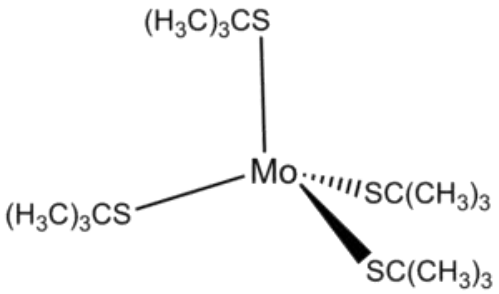


4 - Metal complexes

The anion derived from tert – butyl thiol forms complexes with various metals. One example is tetra kis (tert-butyl thiolato) molybdenum (IV), Mo(*t*-BuS)$_4$. This complex was prepared by treating $MoCl_4$ with *t*-BuSLi :

$$Mo\ Cl_4 + 4t\text{-}Bu\ S\ Li \rightarrow Mo\ (t\text{-}Bu\ S\ )_4 + 4Li\ Cl$$

Mo(*t*-BuS)$_4$ is a dark red diamagnetic complex that is sensitive to air and moisture. The molybdenum center has a distorted tetra hedral coordination to four sulfur atoms, with overall D_2 symmetry.



5 - Safety

Even in well ventilated areas, extreme caution must be made when handling *tert*-butylthiol as it is a highly odorous chemical with an odor threshold of < 0.33 ppb. Extreme caution is not due to toxicity, but due to the significant odor and concerns that this odor would cause to the many individuals that might be exposed. The PEL for thiols of most types is 500 ppb, primarily due to reaction of nausea

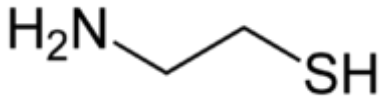
at levels of 2–3 ppm. The LC_{50} of tert-butylthiol is much, much higher.

6 - Commercial use

Tert-Butylthiol is the main ingredient in many gas odorant blends. It is always utilized as a blend of other compounds, typically dimethyl sulfide, methyl ethyl sulfide, tetrahydrothiophene or other mercaptans (isopropyl mercaptan, sec-butyl mercaptan and/or n-butyl mercaptan, due to its rather high melting point of 273 K. These blends are used only with natural gas and not propane, as the boiling points of these blends and propane are quite different. As propane is delivered as a liquid and vaporizes to gas when being delivered to the appliance, the vapor liquid equilibrium would substantially reduce the amount of odorant blend in the vapor.

Tert - Butyl thiol has been listed on the European Food Safety Authority (FL-no: 12.174) as a flavor additive. There is no indication of what flavor or flavors it may have been used in. It has been removed from this list.

Cysteamine



Contents

1 - Introduction

Cysteamine is the chemical compound with the formula $HSCH_2CH_2NH_2$. It is the simplest stable aminothiol and a degradation product of the amino acid cysteine. It is often used as the hydrochloride salt, $HSCH_2CH_2NH_3Cl$. The comparatively high melting point of cysteamine (95-97 °C), indicates that exists in a salt form.

IUPAC name : 2-amino ethane thiol
Other names :
β-mercapto ethylamine
2-amino ethane thiol
2-mercapto ethylamine
decarboxy cysteine
thio ethanol amine
mercaptamine

Molecular formula	$C_2 H_7 N S$
Molar mass	77 g mol^{-1}
Melting point	95 - 97 °C
EU classification	 Xn

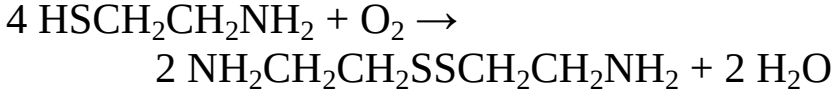
2 -Preparation

It can also be prepared by the reaction of ethylenimine with hydrogen sulfide.

$$(NHCH_2CH_2) + H_2S \rightarrow HSCH_2CH_2NH_2$$

3 - Reactions

It is used as the hydrochloride salt, as it readily oxidizes to the corresponding disulfide, in the presence of air. The amine portion of the molecule serves as a catalyst for this reaction.



$$4\ HSCH_2CH_2NH_2 + O_2 \rightarrow 2\ NH_2CH_2CH_2SSCH_2CH_2NH_2 + 2\ H_2O$$

4 -Biochemical and pharmaceutical applications

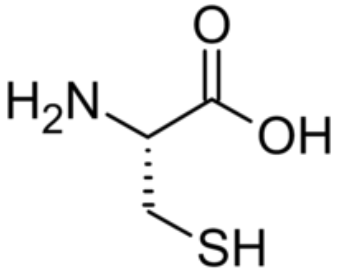
Under the trade name Cystagon, cysteamine is used in the treatment of disorders of cystine excretion. Cysteamine cleaves the disulfide bond with cystine to produce molecules that can escape the metabolic defect in cystinosis and cystinuria.

It is also used for treatment of radiation sickness.

Cysteamine is used in the body to form the essential biochemical coenzyme A by combining with pantothenate and adenosine triphosphate.

In 2008, Raptor Pharmaceuticals started phase II clinical trials testing a delayed release (DR) preparation of cysteamine bitartrate for Huntington's disease. DR Cysteamine is also being investigated as a treatment for cystinosis, Batten disease, and non-alcoholic steatohepatitis.

Cysteine



Contents

1 - Introduction

Cysteine (abbreviated as **Cys** or **C**) is an α-amino acid with the chemical formula $HO_2CCH(NH_2)CH_2SH$. It is a semi - essential amino acid, which means that it can be biosynthesized in humans. The thiol side chain in cysteine often participates in enzymatic reactions, serving as a nucleophile. The thiol is susceptible to oxidization to give the disulfide derivative cystine, which serves an important structural role in many proteins. When used as a food additive, it has the E number **E920**.

IUPAC name : Cysteine

Other names :

2-Amino-3-sulfhydryl propanoic acid

Molecular formula $C_3H_7NO_2S$

Molar mass	121 g mol^{-1}
Appearance	white crystals or powder
Melting point	240 °C decomp.
Solubility in water	soluble
Solubility	1.5g / 100g ethanol 19 degC
Chiral rotation $[\alpha]_D$	+9.4° (H_2O, *c* = 1.3)
Thermodynamic data	Phase behaviour Solid, liquid, gas
Spectral data	UV, IR, NMR, MS

2 - Sources

2 – 1 - Dietary sources

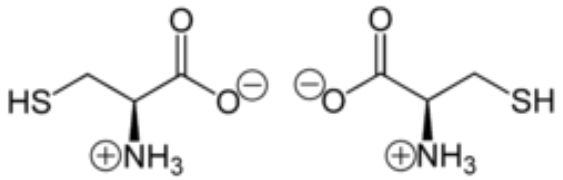
Although classified as a non-essential amino acid, in rare cases, cysteine may be essential for infants, the elderly, and individuals with certain metabolic disease or who suffer from malabsorption syndromes. Cysteine can usually be synthesized by the human body under normal physiological conditions if a sufficient quantity of methionine is available. Cysteine is catabolized in the gastrointestinal tract and blood plasma. In contrast, cystine travels safely through the GI tract and blood plasma and is promptly reduced to the two cysteine molecules upon cell entry.

Cysteine is found in most high-protein foods, including :

Animal sources : pork, sausage meat, chicken, turkey, duck, luncheon meat, eggs, milk, whey protein, ricotta, cottage cheese, yogurt

Plant sources: red peppers, garlic, onions, broccoli, brussels sprout, oats, granola, wheat germ, sprouted lentils.

Like other amino acids, cysteine has an amphoteric character.

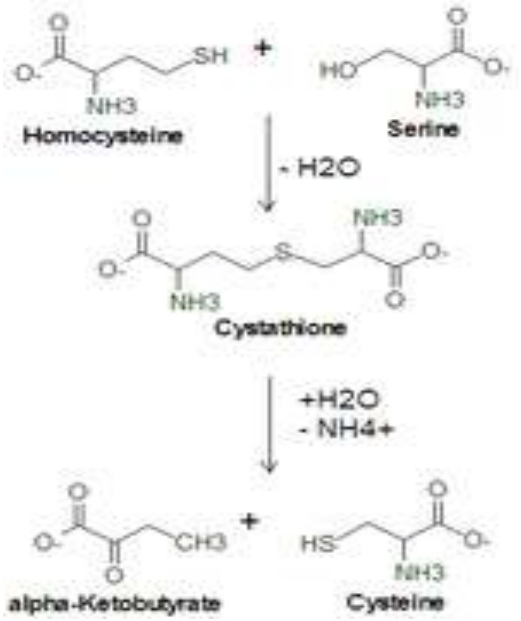


(R)-Cysteine (left) and (S)-Cysteine (right) in zwitterionic form at neutral pH

2 – 2 - Industrial sources

The majority of L - cysteine is obtained industrially by hydrolysis of poultry feathers or human hair. Synthetically produced L-cysteine, compliant with Jewish Kosher and Muslim Halal rules, is also available, albeit at a higher price. The synthetic route involves fermentation utilizing a mutant of *E. coli*. Degussa introduced a route from substituted thiazolines. Following this technology, L-cysteine is produced by the hydrolysis of racemic 2-amino-Δ^2-thiazoline-4-carboxylic acid using *Pseudomonas thiazolinophilum*.

2 – 3 - Biosynthesis



Cysteine synthesis. Cystathionine beta synthase catalyzes the upper reaction and cystathionine gamma-lyase catalyzes the lower reaction.

In animals, biosynthesis begins with the amino acid serine. The sulfur is derived from methionine, which is converted to homocysteine through the intermediate S- adenosylmethionine. Cystathionine beta-synthase then combines homocysteine and serine to form the asymmetrical thioether cystathionine. The enzyme cystathionine gamma-lyase converts the cystathionine into cysteine and alpha-ketobutyrate. In plants and bacteria, cysteine biosynthesis again starts from serine, which is converted to *O*-acetylserine by the enzyme serine transacetylase. The enzyme O-acetylserine (thiol)-lyase, using sulfide sources, converts this ester into cysteine, releasing acetate.

3 - Biological functions

The cysteine thiol group is nucleophilic and easily oxidized. The reactivity is enhanced when the thiol is ionized, and cysteine residues in proteins have pK_a values close to neutrality, so are often in their reactive thiolate form in the cell.[11] Because of its high reactivity, the thiol group of cysteine has numerous biological functions.

3 – 1 - Precursor to the antioxidant glutathione

Due to the ability of thiols to undergo redox reactions, cysteine has antioxidant properties. Cysteine's antioxidant properties are typically expressed in the tripeptide glutathione, which occurs in humans as well as other organisms. The systemic availability of oral glutathione (GSH) is negligible; so it must be biosynthesized from its constituent amino acids, cysteine, glycine, and glutamic acid. Glutamic acid and glycine are readily available in most Western diets, but the availability of cysteine can be the limiting substrate.

3 – 2 - Precursor to iron-sulfur clusters

Cysteine is an important source of sulfide in human metabolism. The sulfide in iron-sulfur clusters and in nitrogenase is extracted from cysteine, which is converted to alanine in the process.

3 – 3 - Metal ion binding

Beyond the iron - sulfur proteins, many other metal cofactors in enzymes are bound to the thiolate substituent of cysteinyl residues. Examples include zinc in zinc fingers and alcohol dehydrogenase, copper in the blue copper proteins, iron in cytochrome P450, and nickel in the [NiFe]-hydrogenases . The thiol group also has a high affinity for heavy metals, so that proteins containing cysteine, such as metallothionein, will bind metals such as mercury, lead, and cadmium tightly.

3 – 4 - Roles in protein structure

In the translation of messenger RNA molecules to produce polypeptides, cysteine is coded for by the UGU and UGC codons.

Cysteine has traditionally been considered to be a hydrophilic amino acid, based largely on the chemical parallel between its thiol

group and the hydroxyl groups in the side-chains of other polar amino acids. However, the cysteine side chain has been shown to stabilize hydrophobic interactions in micelles to a greater degree than the side chain in the non-polar amino acid glycine, and the polar amino acid serine . In a statistical analysis of the frequency with which amino acids appear in different chemical environments in the structures of proteins, free cysteine residues were found to associate with hydrophobic regions of proteins. Their hydrophobic tendency was equivalent to that of known non-polar amino acids such as methionine and tyrosine, and was much greater than that of known polar amino acids such as serine and threonine.[16] Hydrophobicity scales, which rank amino acids from most hydrophobic to most hydrophilic, consistently place cysteine towards the hydrophobic end of the spectrum, even when they are based on methods that are not influenced by the tendency of cysteines to form disulfide bonds in proteins. Therefore, cysteine is now often grouped among the hydrophobic amino acids, though it is sometimes also classified as slightly polar, or polar.

While free cysteine residues do occur in proteins, most are covalently bonded to other cysteine residues to form disulfide bonds. Disulfide bonds play an important role in the folding and stability of some proteins, usually proteins secreted to the extracellular medium.[20] Since most cellular compartments are reducing environments, disulfide bonds are generally unstable in the cytosol with some exceptions as noted below.

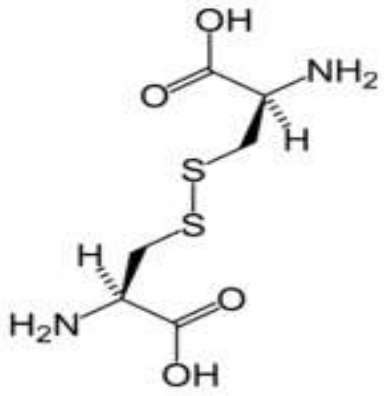


Figure 2: Cystine (shown here in its neutral form), two cysteines bound together by a disulfide bond.

Disulfide bonds in proteins are formed by oxidation of the thiol groups of cysteine residues. The other sulfur-containing amino acid, methionine, cannot form disulfide bonds. More aggressive oxidants convert cysteine to the corresponding sulfinic acid and sulfonic acid. Cysteine residues play a valuable role by crosslinking proteins, which increases the rigidity of proteins and also functions to confer proteolytic resistance (since protein export is a costly process, minimizing its necessity is advantageous). Inside the cell, disulfide bridges between cysteine residues within a polypeptide support the protein's tertiary structure. Insulin is an example of a protein with cystine crosslinking, wherein two separate peptide chains are connected by a pair of disulfide bonds.

Protein disulfide isomerases catalyze the proper formation of disulfide bonds; the cell transfers dehydroascorbic acid to the endoplasmic reticulum, which oxidises the environment. In this environment, cysteines are, in general, oxidized to cystine and are no longer functional as a nucleophiles.

Aside from its oxidation to cystine, cysteine participates in numerous posttranslational modifications. The nucleophilic thiol group allows cysteine to conjugate to other groups, e.g., in prenylation. Ubiquitin ligases transfer ubiquitin to its pendant, proteins, and caspases, which engage in proteolysis in the apoptotic cycle. Inteins often function with the help of a catalytic cysteine. These roles are typically limited to the intracellular milieu, where the environment is reducing, and cysteine is not oxidized to cystine.

4 - Applications

Cysteine, mainly the L-enantiomer, is a precursor in the food, pharmaceutical, and personal care industries. One of the largest applications is the production of flavors. For example, the reaction of cysteine with sugars in a Maillard reaction yields meat flavors.[21] L-cysteine is also used as a processing aid for baking.

In the field of personal care, cysteine is used for permanent wave applications predominantly in Asia. Again the cysteine is used for breaking up the disulfide bonds in the hair's keratin.

Cysteine is a very popular target for site-directed labeling experiments to investigate biomolecular structure and dynamics. Maleimides will selectively attach to cysteine using a covalent Michael addition. Site- directed spin labeling for EPR or paramagnetic relaxation enhanced NMR also uses cysteine extensively.

In a 1994 report released by five top cigarette companies, cysteine is one of the 599 additives to cigarettes. Like most cigarette additives, however, its use or purpose is unknown.[23] Its inclusion in cigarettes could offer two benefits: Acting as an expectorant, since smoking increases mucus production in the lungs; and increasing the beneficial antioxidant glutathione (which is diminished in smokers).

5 - Sheep

Cysteine is required by sheep in order to produce wool: It is an essential amino acid that must be taken in as food from grass. As a consequence, during drought conditions, sheep stop producing wool; however, transgenic sheep that can make their own cysteine have been developed.

6 - Reducing toxic effects of alcohol

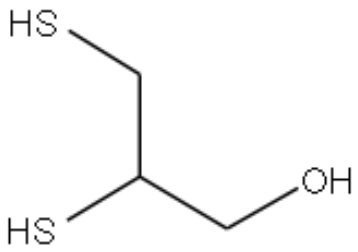
Cysteine has been proposed as a preventative or antidote for some of the negative effects of alcohol, including liver damage and hangover. It counteracts the poisonous effects of acetaldehyde, which is the major by - product of alcohol metabolism and is responsible for most of the negative aftereffects and long - term damage associated with alcohol use (but not the immediate effects of drunkenness). Cysteine supports the next step in metabolism, which turns acetaldehyde into the relatively harmless acetic acid. In a rat study, test animals received an LD_{50} dose of acetaldehyde. Those that received cysteine had an 80 % survival rate; when both cysteine and thiamine were administered, all animals survived . There is not yet direct evidence for or against its effectiveness in humans who consume alcohol at normal levels.

6 – 1 - *N*-Acetylcysteine

N - Acetyl - L - cysteine (NAC) is a derivative of cysteine wherein an acetyl group is attached to the nitrogen atom. This

compound is sold as a dietary supplement and used as an antidote in cases of acetaminophen overdose, and obsessive compulsive disorders such as trichotillomania.

Dimercaprol



Contents

1 - Introduction

Dimercaprol (INN) or **British anti - Lewisite** (abbreviated **BAL**), is a compound developed by British biochemists at Oxford University during World War II . It was developed secretly as an antidote for lewisite, the now - obsolete arsenic - based chemical warfare agent . Today, it is used medically in treatment of arsenic, mercury , gold, lead, antimony, and other toxic metal poisoning . In addition , it has in the past been used for the treatment of Wilson's disease, a genetic disorder in which the body tends to retain copper.

IUPAC name :
2,3 - Disulfanyl propan -1- ol
Other names :
2,3-Dimercapto propanol
British anti - Lewisite

Molecular formula	$C_3H_8S_2O$
Molar mass	124 g mol^{-1}
Density	1.239 g cm^{-3}
Boiling point	120 °C
Refractive index (n_D)	1.573
EU classification	 Xn
Flash point	112 °C

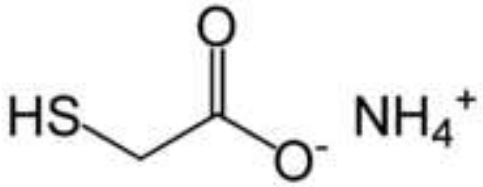
2 - Biochemical function

Arsenic and some other heavy metals act by chemically reacting with adjacent thiol residues on metabolic enzymes, creating a chelate complex that inhibits the affected enzyme's activity.[6] Dimercaprol competes with the thiol groups for binding the metal ion, which is then excreted in the urine .

Dimercaprol is itself toxic, with a narrow therapeutic range and a tendency to concentrate arsenic in some organs. Other drawbacks include the need to administer it by painful intramuscular injection.[7] Serious side effects include nephrotoxicity and hypertension.

Dimercaprol has been found to form stable chelates in vivo with many other toxic metals including inorganic mercury, antimony, bismuth, cadmium, chromium, cobalt, gold, and nickel. However, it is not necessarily the treatment of choice for toxicity to these metals. Dimercaprol has been used as an adjunct in the treatment of the acute encephalopathy of lead toxicity. It is a potentially toxic drug, and its use may be accompanied by multiple side effects. Although treatment with dimercaprol will increase the excretion of cadmium, there is a concomitant increase in renal cadmium concentration, so that its use in case of cadmium toxicity is to be avoided. It does, however, remove inorganic mercury from the kidneys; but is not useful in the treatment of alkylmercury or phenyl mercury toxicity. Dimercaprol also enhances the toxicity of selenium and tellurium, so it is not to be used to remove these elements from the body.

Ammonium thioglycolate



Other names : Perm salt

Molecular formula	$C_2 H_7 N O_2 S$
Molar mass	109 g / mol

Contents

1 - Introduction

Ammonium thioglycolate, also known as **perm salt**, is the chemical compound with the formula $HSCH_2CO_2NH_4$.

Being the salt of a weak acid and weak base, ammonium thioglycolic acid exists in solution as an equilibrium mixture of the salt itself as well as the free carboxylic acid thioglycolic acid ($HSCH_2CO_2H$) and ammonia :

$$HSCH_2COO^- + NH_4^+ \rightleftharpoons HSCH_2COOH + NH_3$$

2 - Chemical concepts related to perms

When discussing the chemistry of perms, one should consider two chemical facts. First is the thiol-disulfide equilibrium:

$$RSH + R'SSR' \rightleftharpoons R'SH + RSSR'$$

where R and R' are organic substituents such as methyl ($-CH_3$), ethyl ($-C_2H_5$), or $-CH_2COO^-$.

The thiol-disulfide exchange reaction is accelerated by bases such as ammonia, because the base generates some thiolate anion (RS^-

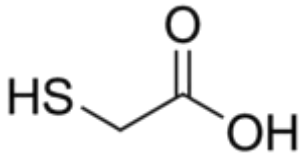
), which attacks the disulfide. Thus the ammonia plays multiple roles (and more, see below) in this application.

The second chemical fact is that polar molecules are less volatile than nonpolar ones. So the glycolate substituent makes the thiol non-volatile and hence non-odorous. An added advantage is that the glycolate confers some solubility in water. One could almost certainly use $HSCH_3$ and ammonia to give a perm, but there would be serious olfactory consequences.

3 - The actual chemistry of perms

A solution containing ammonium thioglycolate contains a lot of free ammonia, which swells hair, rendering it permeable. The thioglycolic acid in the perm solution reduces the disulfide cystine bonds in the cortex of the hair. In a sense, the thioglycolate removes crosslinks. After washing, the hair is treated with a mild solution of hydrogen peroxide, which oxidizes the cysteines back to cystine. These new chemical bonds impart the structural rigidity necessary for a successful perm. The rigidification process is akin to the vulcanization of rubber, where commonly polysulfide linkages are used to crosslink the polymer chains. However, not as many disulfide bonds are reformed as there were before the permanent. As a result, the hair is weaker than before the permanent was applied and repeated applications over the same spot may eventually cause strand breakage.

Thio Glycolic Acid



IUPAC name : 2-Sulfanylacetic acid
Other names :
Mercapto acetic acid
Thioglycolic acid

Molecular formula	$C_2H_4O_2S$
Molar mass	92.12 g mol^{-1}
Density	1.32 g/cm^3
Melting point	-16 °C, 257 K, 3 °F
Boiling point	96 °C at 5 mmHg

Thio glycolic acid (**TGA**) is the organic compound $HSCH_2CO_2H$. It contains both a thiol (mercaptan) and a carboxylic acid. It is a clear liquid with a strong unpleasant odor. It is readily oxidized by air to the corresponding disulfide $[SCH_2CO_2H]_2$.

TGA was developed in the 1940s for use as a chemical depilatory and is still used as such, especially in salt forms, including calcium thioglycolate and sodium thioglycolate. TGA is the precursor to ammonium thioglycolate that is used for permanents. TGA and its derivatives break the disulfide bonds in the cortex of hair. One reforms these broken bonds in giving hair a "perm." Alternatively and more commonly, the process leads to depilation as is done commonly in leather processing. It is also used as an acidity indicator, manufacturing of thioglycolates, and in bacteriology for preparation of thioglycolate media.

TGA is also used in the making of tin stabilizers often used in certain polyvinyl chloride products (such as vinyl siding).

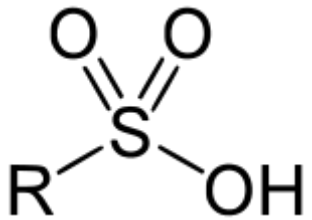
TGA, usually as its dianion, forms complexes with metal ions. Such complexes have been used for the detection of iron, molybdenum, silver, and tin.

Thioglycolic acid is used as nucleophile in thioglycolysis reactions used on condensed tannins to study their structure.

Part – 12 –

Aliphatic Sulfonic Acid

Aliphatic Sulfonic Acid



General structure of a sulfonic acid

Contents

1 - Introduction

Sulfonic acid (or sulphonic acid) refers to a member of the class of organosulfur compounds with the general formula $RS(=O)_2–OH$, where *R* is an organic alkyl or aryl group and the $S(=O)_2–OH$ group a sulfonyl hydroxide.[1] A sulfonic acid can be thought of as sulfuric acid with one hydroxyl group replaced by an organic substituent. The parent compound (with the organic substituent replaced by hydrogen) is the hypothetical compound sulfurous acid. Salts or esters of sulfonic acids are called sulfonates.

2 - Preparation

Sulfonic acid is produced by the process of sulfonation. Usually the sulfonating agent is sulfur trioxide. A particularly large scale application of this method is the production of alkylbenzenesulfonic acids:

$$RC_6H_5 + SO_3 \rightarrow RC_6H_4SO_3H$$

In this reaction, sulfur trioxide is an electrophile and the arene undergoes electrophilic aromatic substitution.

Thiols can be oxidized to sulfonic acids:

$$RSH + 3/2\ O_2 \rightarrow RSO_3H$$

Certain sulfonic acids, such as perfluoro octane sulfonic acid are prepared by electrophilic fluorination of preformed sulfonic acids. The net conversion can be represented simplistically:

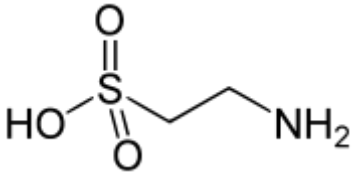
$$C_8H_{17}SO_3H + 17\ F_2 \rightarrow C_8F_{17}SO_3H + 17\ HF$$

3 - Properties

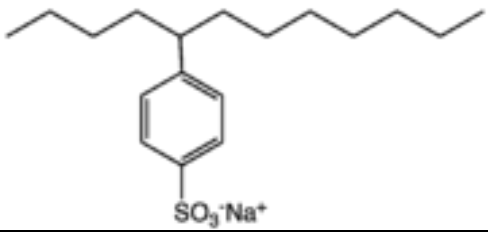
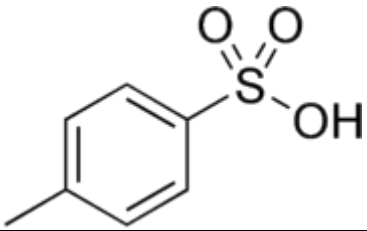
Sulfonic acids are much stronger acids than the corresponding carboxylic acids. *p*-Toluenesulfonic acid, with a pK_a of -2.8, is about a million times stronger acid than benzoic acid, with a pK_a of 4.2. Similarly, methanesulfonic acid, pK_a = -1.9, is also about one million times stronger acid than acetic acid. Because of their polarity, sulfonic acids tend to be crystalline solids. They are also usually colourless and nonoxidizing, which is convenient. Because of their high acidity, sulfonic acids are often soluble in water or exhibit detergent-like properties.

The structure of sulfonic acids is illustrated by the prototype, methanesulfonic acid. The sulfonic acid group, RSO_2OH features a tetrahedral sulfur centre, meaning that sulfur is at the center of four atoms: three oxygens and one carbon. The overall geometry of the sulfur centre is reminiscent of the shape of sulfuric acid.

Representative sulfonic acids and derivatives.



Taurine, a bile acid, and one of the few naturally occurring sulfonic acids (shown in uncommon tautomer).

	
Sodium dodecyl benzene sulfonate, an alkyl benzene sulfonate surfactant used in laundry detergents.	*Toluene sulfonic acid, a widely used reagent in organic synthesis.*

4 - Applications

Although both alkyl and aryl sulfonic acids are known, most of the applications are associated with the aromatic derivatives.

4 – 1 - Detergents and surfactants

Detergents and surfactants are molecules that combine highly nonpolar and highly polar groups. Traditionally, soaps are the popular surfactants, being derived from fatty acids. Since the mid-20th century, the usage of sulfonic acids has surpassed soap in advanced societies. For example, an estimated 2 billion kilograms of alkylbenzenesulfonates are produced annually for diverse purposes. Lignin sulfonates, produced by sulfonation of lignin are components of drilling fluids and additives in certain kinds of concrete.

4 – 2 - Dyes

Many if not most of the anthroquinone dyes are produced or processed via sulfonation.[3] Sulfonic acids tend to bind tightly to proteins and carbohydrates. Most "washable" dyes are sulfonic acids (or have the functional sulfonyl group in them) for this reason. p-Cresidinesulfonic acid is used to make food dyes.

4 – 3 - Acid catalysts

Being strong acids, sulfonic acids are also used as catalysts. The simplest examples are methanesulfonic acid, CH_3SO_2OH and *p*-toluenesulfonic acid, which are regularly used in organic chemistry as acids that are lipophilic (soluble in organic solvents). Polymeric sulfonic acids are also useful. Dowex resin are sulfonic acid derivatives of polystyrene and is used as catalysts and for ion

exchange (water softening).Nafion, a fluorinated polymeric sulfonic acid is a component of proton exchange membranes in fuel cells.

4 – 4 - Drugs

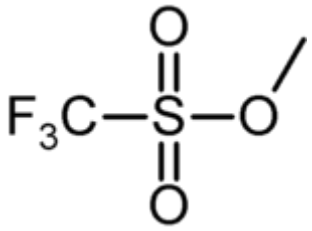
Antibacterial drugs sulfa drugs are produced from sulfonic acids.

5 - Reactions

5 – 1 - Esterification

Sulfonic acids can be converted to esters. This class of organic compounds has the general formula R-SO_2-OR. Sulfonic esters such as methyl triflate are considered good alkylating agents in organic synthesis. Such sulfonate esters are often prepared by alcoholysis of the sulfonyl chlorides:

$$RSO_2Cl + R'OH \rightarrow RSO_2OR' + HCl$$



Methyl triflate

5 – 2 - Chlorination

Sulfonyl halide groups occur when a sulfonyl functional group is singly bonded to a halogen atom. They have the general formula R-SO_2-X where X is a halide, almost invariably chloride. They are produced by chlorination of sulfonic acids using thionyl chloride and related reagents.

5 – 3 - Displacement

Although the C-SO_3H bond is strong, the (aryl)C-SO_3 bond can be cleaved by certain nucleophiles. Of historic and continuing significance is the α-sulfonation of anthroquinone followed by displacement of the sulfonate group by other nucleophiles, which cannot be installed directly.[3] An early method for producing phenol involved the base hydrolysis of sodium benzenesulfonate, which can be generated readily from benzene.

$C_6H_5SO_3Na + 2\ NaOH \rightarrow C_6H_5ONa + Na_2SO_3 + H_2O$

6 - Environmental concerns

Sulfonic acid derivatives are generally not derived from natural precursors and tend to biodegrade slowly. Some, such as perfluorooctane sulfonic acid, have been detected in the serum of humans. This should be not surprising as all organic fluorine compounds have extreme stability, and low to zero biodegradability. Many are intended to withstand harshest chemical conditions, for example teflon. The nonfluorinated sulfonic acids tend to have low toxicities.

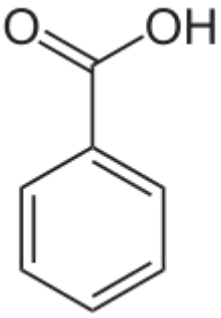
Volume Two

Aromatic Organic Acids

Part – 1 –

Aromatic Organic Acids And Their Compounds

Benzoic Acid



Contents

1 - Introduction

Benzoic acid (pronunciation : $C_7H_6O_2$ or C_6H_5COOH , is a colorless crystalline solid and a simple aromatic carboxylic acid. The name derived from gum benzoin, which was for a long time the only source for benzoic acid. Its salts are used as a food preservative and benzoic acid is an important precursor for the synthesis of many other

organic substances. The salts and esters of benzoic acid are known as benzoates .

IUPAC name : Benzoic acid
Other names :
Carboxy benzene;
E210 ;
Dracylic acid

Molecular formula	$C_7 H_6 O_2$
Molar mass	122 g mol −1
Appearance	Colorless crystalline solid
Density	1.27 g / cm^3
Melting point	122.41 °C
Boiling point	249.2 °C
Solubility in water	2.9 g / L
Refractive index (nD)	1.5397
Main hazards	Irritant
Flash point	121.5 °C
Auto ignition temperature	570 °C

2 - History

Benzoic acid was discovered in the sixteenth century. The dry distillation of gum benzoin was first described by Nostradamus (1556), and then by Alexius Pedemontanus (1560) and Blaise de Vigenère (1596).

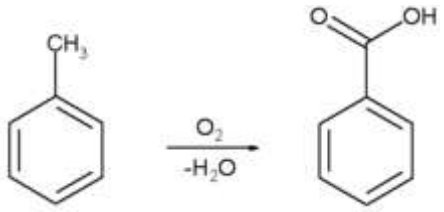
Pioneer work in 1830 through a variety of experiences based on amygdalin, obtained from bitter almonds (the fruit of Prunus dulcis) oil by Pierre Robiquet and Antoine Boutron - Charlard, two French chemists, had produced benzaldehyde but they failed in working out a proper interpretation of the structure of amygdalin that would account for it, and thus missed the identification of the benzoyl radical C7H5O. This last step was achieved some few months later (1832) by Justus von Liebig and Friedrich Wöhler, who determined the composition of benzoic acid . These latter also investigated how hippuric acid is related to benzoic acid.

In 1875 Salkowski discovered the antifungal abilities of benzoic acid, which was used for a long time in the preservation of benzoate-containing cloudberry fruits.

3 - Production

3 – 1 - Industrial preparations

Benzoic acid is produced commercially by partial oxidation of toluene with oxygen. The process is catalyzed by cobalt or manganese naphthenates. The process uses cheap raw materials, proceeds in high yield, and is considered environmentally green.



U.S. production capacity is estimated to be 126,000 tonnes per year (139,000 tons), much of which is consumed domestically to prepare other industrial chemicals.

3 – 2 - Laboratory synthesis

Benzoic acid is cheap and readily available, so the laboratory synthesis of benzoic acid is mainly practiced for its pedagogical value. It is a common undergraduate preparation.

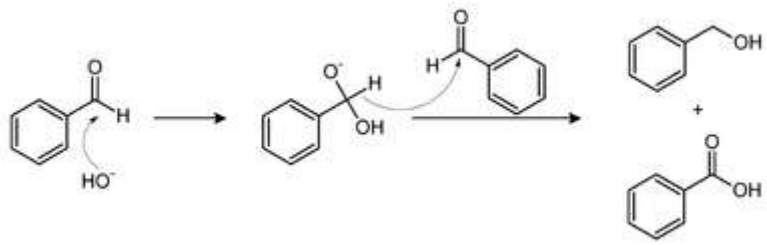
For all syntheses, benzoic acid can be purified by recrystallization from water because of its high solubility in hot water and poor solubility in cold water. The avoidance of organic solvents for the recrystallization makes this experiment particularly safe. Other possible recrystallization solvents include acetic acid (anhydrous or aqueous), benzene, acetone, petroleum ether, and a mixture of ethanol and water.[8] The solubility of benzoic acid in over 40 solvents with references to original sources can be found as part of the Open Notebook Science Challenge

3 – 2 - 1 - By hydrolysis

Like any other nitrile or amide, benzo nitrile and benzamide can be hydrolyzed to benzoic acid or its conjugate base in acid or basic conditions.

3 – 2 - 2 - From benzaldehyde

The base-induced disproportionation of benzaldehyde, the Cannizzaro reaction, affords equal amounts of benzoate and benzyl alcohol; the latter can be removed by distillation.



3 – 2 - 3 - From bromo benzene

Bromo benzene can be converted to benzoic acid by "carbonation" of the intermediate phenyl magnesium bromide:

$C_6H_5MgBr + CO_2 \rightarrow C_6H_5CO_2MgBr$
$C_6H_5CO_2MgBr + H\,Cl \rightarrow C_6H_5CO_2H + MgBrCl$

3 – 2 - 4 - From benzyl alcohol

Benzyl alcohol is refluxed with potassium permanganate or other oxidizing reagents in water. The mixture is hot filtered to remove manganese dioxide and then allowed to cool to afford benzoic acid.

3 – 2 - 5 - From benzyl chloride

Benzoic acid can be prepared by oxidation of benzyl chloride in the presence of alkaline KMnO4:

$C_6H_5CH_2Cl + 2\,KOH + 2\,[O] \rightarrow C_6H_5COOK + KCl + H_2O$

3 – 2 - 6 - Historical preparation

The first industrial process involved the reaction of benzo tri chloride (tri chloro methyl benzene) with calcium hydroxide in water, using iron or iron salts as catalyst. The resulting calcium benzoate is converted to benzoic acid with hydrochloric acid. The product contains significant amounts of chlorinated benzoic acid derivatives. For this reason, benzoic acid for human consumption was obtained by dry distillation of gum benzoin. Food-grade benzoic acid is now produced synthetically.

4 - Uses

4 – 1 - Calorimetry

Benzoic acid is the most commonly used chemical standard to determine the heat of capacity of a bomb calorimeter.

4 – 2 - Feed stock

Benzoic acid is used to make a large number of chemicals, important examples of which are :

Benzoyl chloride, $C_6H_5C(O)Cl$, is obtained by treatment of benzoic with thionyl chloride, phosgene or one of the chlorides of phosphorus. $C_6H_5C(O)$ Cl is an important starting material for several benzoic acid derivates like benzyl benzoate, which is used in artificial flavours and insect repellents.

Benzoate plasticizers, such as the glycol-, di ethylene glycol - , and tri ethylene glycol esters, are obtained by trans esterification of methyl benzoate with the corresponding diol. Alternatively these species arise by treatment of benzoyl chloride with the diol. These plasticizers are used similarly to those derived from terephthalic acid ester.

Phenol, C_6H_5OH, is obtained by oxidative decarboxylation at 300 − 400 °C . The temperature required can be lowered to 200 °C by the addition of catalytic amounts of copper (II) salts. The phenol can be converted to cyclo hexanol, which is a starting material for nylon synthesis.

4 – 3 - Food preservative

Benzoic acid and its salts are used as a food preservatives, represented by the E-numbers E210 , E211 , E212 , and E213 . Benzoic acid inhibits the growth of mold, yeast and some bacteria. It is either added directly or created from reactions with its sodium, potassium, or calcium salt. The mechanism starts with the absorption of benzoic acid in to the cell. If the intracellular pH changes to 5 or lower, the anaerobic fermentation of glucose through phospho - fructokinase is decreased by 95 %. The efficacy of benzoic acid and benzoate is thus dependent on the pH of the food. Acidic food and beverage like fruit juice (citric acid), sparkling drinks (carbon dioxide), soft drinks (phosphoric acid), pickles (vinegar) or other acidified food are preserved with benzoic acid and benzoates.

Typical levels of use for benzoic acid as a preservative in food are between 0.05 – 0.1 %. Foods in which benzoic acid may be used and maximum levels for its application are controlled by international food law.

Concern has been expressed that benzoic acid and its salts may react with ascorbic acid (vitamin C) in some soft drinks, forming small quantities of benzene.

4 – 4 - Medicinal

Benzoic acid is a constituent of Whitfield's ointment which is used for the treatment of fungal skin diseases such as tinea, ringworm, and athlete's foot. As the principal component of benzoin resin, benzoic acid is also a major ingredient in both tincture of benzoin and Friar's balsam. Such products have a long history of use as topical antiseptics and inhalant decongestants.

Benzoic acid was used as an expectorant, analgesic, and antiseptic in the early 20th century.

5 - Biology and health effects

Benzoic acid occurs naturally free and bound as benzoic acid esters in many plant and animal species. Appreciable amounts have

been found in most berries (around 0.05 %). Ripe fruits of several Vaccinium species (e.g., cranberry, V. vitis idaea; bilberry, V. macrocarpon) contain as much as 0.03 – 0.13 % free benzoic acid. Benzoic acid is also formed in apples after infection with the fungus Nectria galligena. Among animals, benzoic acid has been identified primarily in omnivorous or phytophageous species, e.g., in viscera and muscles of the Rock Ptarmigan (Lagopus muta) as well as in gland secretions of male muskoxen (Ovibos moschatus) or Asian bull elephants (Elephas maximus).

Gum benzoin contains up to 20 % of benzoic acid and 40% benzoic acid esters.

Cryptanaerobacter phenolicus is a bacterium species that produces benzoate from phenol via 4-hydroxy benzoate

Benzoic acid is present as part of hippuric acid (N-benzoyl glycine) in urine of mammals, especially herbivores (Gr. hippos = horse; ouron = urine). Humans produce about 0.44 g/L hippuric acid per day in their urine, and if the person is exposed to toluene or benzoic acid, it can rise above that level.

For humans, the World Health Organization's International Programme on Chemical Safety (IPCS) suggests a provisional tolerable intake would be 5 mg/kg body weight per day.[20] Cats have a significantly lower tolerance against benzoic acid and its salts than rats and mice. Lethal dose for cats can be as low as 300 mg/kg body weight. The oral LD50 for rats is 3040 mg / kg, for mice it is 1940 –2263 mg / kg.

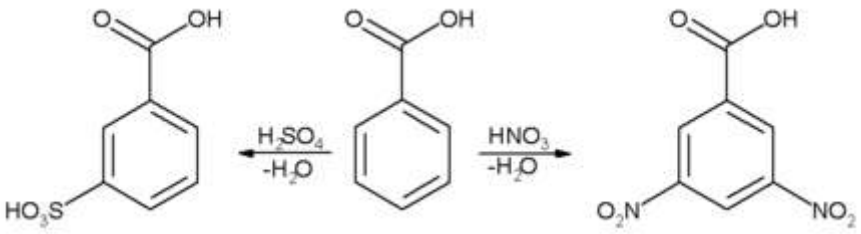
In Taipei, Taiwan, a city health survey in 2010 found 30 % of tested dried and pickled food products failed a test having too much benzoic acid, which is known to affect the liver and kidney, along with more serious issues like excessive cyclamate.

6 - Chemistry

Reactions of benzoic acid can occur at either the aromatic ring or the carboxyl group :

6 – 1 - Aromatic ring

Electrophilic aromatic substitution reaction will take place mainly in 3- position due to the electron-withdrawing carboxylic group; i.e. benzoic acid is meta directing.



The second substitution reaction (on the right) is slower because the first nitro group is deactivating. Conversely, if an activating group (electron - donating) was introduced (e.g., alkyl), a second substitution reaction would occur more readily than the first and the disubstituted product might accumulate to a significant extent.

6 – 2 - Carboxyl group

All the reactions mentioned for carboxylic acids are also possible for benzoic acid.

Benzoic acid esters are the product of the acid catalysed reaction with alcohols.

Benzoic acid amides are more easily available by using activated acid derivatives (such as benzoyl chloride) or by coupling reagents used in peptide synthesis like DCC and DMAP.

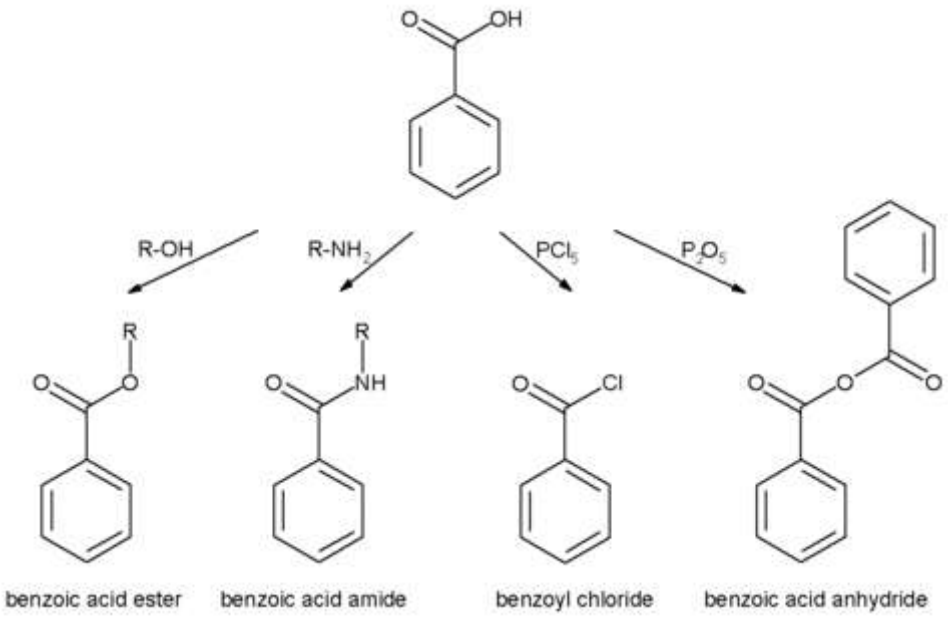
The more active benzoic anhydride is formed by dehydration using acetic anhydride or phosphorus pentoxide.

Highly reactive acid derivatives such as acid halides are easily obtained by mixing with halogenation agents like phosphorus chlorides or thionyl chloride.

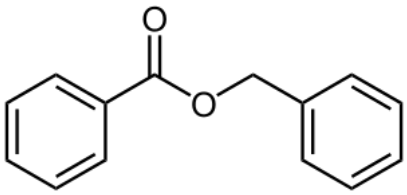
Ortho esters can be obtained by the reaction of alcohols under acidic water free conditions with benzonitrile.

Reduction to benzaldehyde and benzyl alcohol is possible using DIBAL- H , Li Al H_4 or sodium boro hydride.

The copper catalyzed decarboxylation of benzoate to benzene may be effected by heating in quinoline. Also, Hunsdiecker decarboxylation can be achieved by forming the silver salt and heating. Benzoic acid can also be decarboxylated by heating with an alkali hydroxide or calcium hydroxide.



Benzyl Benzoate



Contents

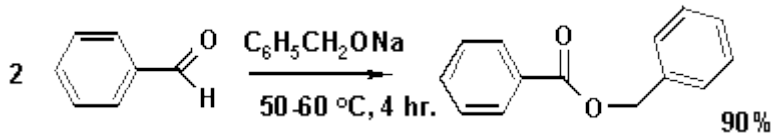
1 - Introduction

Benzyl benzoate is the ester of benzyl alcohol and benzoic acid, with the formula $C_6H_5CH_2O_2CC_6H_5$. This easily prepared compound with a mild balsamic odor has a variety of uses.

Molecular formula	$C_{14}H_{12}O_2$
Molar mass	212 g mol^{-1}
Appearance	Colorless liquid
Odor	faint aromatic
Density	1.118 g / cm^3
Melting point	18 °C
Boiling point	323 °C
Solubility	insoluble in water , glycerol miscible in alcohol, chloroform, ether, oils soluble in acetone, benzene
Refractive index (n_D)	1.5681 (21 °C)
Flash point	158 °C (closed cup)
Auto ignition temperature	481 °C
LD_{50}	1700 mg / kg (rat , oral)

2 – Synthesis

This colorless liquid is formally the condensation product of benzoic acid and benzyl alcohol. It can also be generated from benzaldehyde by the Tishchenko reaction.



3 - Uses[edit source

Benzyl benzoate, as a topical solution, may be used as an antiparasitic insecticide to kill the mites responsible for the skin condition scabies , for example as a combination drug of benzyl benzoate/disulfiram.

It has other uses :

a fixative in fragrances to improve the stability and other characteristics of the main ingredients

a food additive in artificial flavors

a plasticizer in cellulose and other polymers

a solvent for various chemical reactions

a treatment for sweet itch in horses[4]

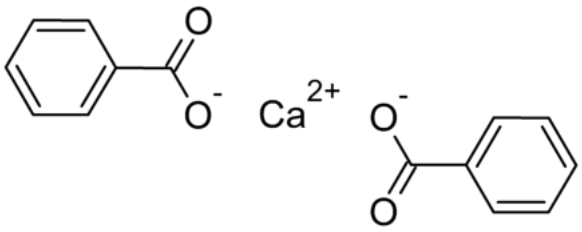
a treatment for scaly leg mites in chickens

4 - List of plants that contain the chemical

Kaempferia rotunda

Zingiber cassumunar

Calcium Benzoate

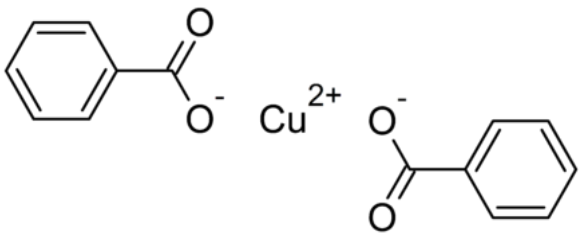


IUPAC name : Calcium di benzoate	
Other names : E213 Benzoic acid calcium salt	
Molecular formula	$Ca(C_7H_5O_2)_2$
Molar mass	282 g / mol
Solubility in water	2.32 g / 100 mL (0 °C) 2.72 g / 100 mL (20 °C) 8.7 g / 100 mL (100 °C)

Calcium benzoate refers to the calcium salt of benzoic acid. When used in the food industry as a preservative, its E number is E213 (INS number 213); it is approved for use as a food additive in the EU, USA and Australia and New Zealand.

The formulas and structures of calcium carboxylate derivatives of calcium and related metals are complex. Generally the coordination number is eight and the carboxylates form Ca-O bonds. Another variable is the degree of hydration.

Copper Benzoate



Contents

1 - Introduction

Copper benzoate is the chemical compound with the formula $Cu(C_6H_5CO_2)_2$. This coordination complex is derived from the cupric ion and the conjugate base of benzoic acid. Because copper emits blue in a flame, this salt has found some use as a source of blue light in fireworks.

IUPAC name : copper di benzoate	
Other names : cupric benzoate	
Molecular formula	$C_{14}H_{10}CuO_4$
Molar mass	305.5 g / mol
Appearance	blue solid
Density	1.197 g / cm^3
Boiling point	249.3°C @760 mmHg
Flash point	111.4°C

2 - Preparation

In laboratory, copper benzoate can be made by combining aqueous solutions of potassium benzoate with copper sulfate. Copper benzoate precipitates as a pale blue solid :

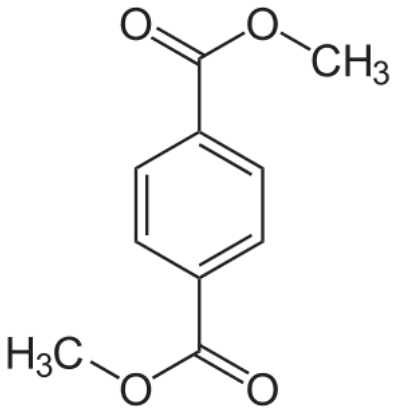
$$2\ C_6H_5COOK + CuSO_4 \rightarrow Cu(C_6H_5COO)_2 + K_2SO_4$$

The primary use of this of this compound is in production of blue flame in fireworks. Copper benzoate made from sodium benzoate for use in fireworks may result in strong yellow dilution of the flame unless the precipitate is carefully washed to remove sodium ion (which emits brightly yello). Emission from potassium does not complicate the emission spectrum.

3 - Structure

Copper (II) benzoates exists in at least two structural forms , depending on the degree of hydration. As for copper (II) acetate , the benzoate adopts a "Chinese lantern" structure, wherein a pair of copper centers are linked by four bridging carboxylate ligands. Typically one site on each copper center is occupied by water, which can be replaced by other ligands . A hydrated form is also known, wherein each Cu (II) center is bound to four water ligands and benzoate .

Dimethyl Terephthalate



Contents

1 - Introduction

Dimethyl terephthalate (DMT) is an organic compound with the formula $C_6H_4(CO_2CH_3)_2$. It is the diester formed from terephthalic acid and methanol. It is a white solid that melts to give a distillable colourless liquid.

Preferred IUPAC name ; Dimethyl terephthalate
Systematic name : 1,4-Dimethyl benzene -1,4- dicarboxylate
Other names : 1,4-Benzene dicarboxylic acid dimethyl ester, Dimethyl 4-phthalate , Dimethyl-p-phthalate , Di-Me terephthalate , Methyl 4- carbo methoxy benzoate , Methyl-p-(methoxy carbonyl) benzoate , Methyl terephthalate , Terephthalic acid methyl ester
Molecular formula $C_{10}H_{10}O_4$

Molar mass	194 g mol^{-1}
Appearance	white solid
Density	1.2 g / cm^3, ?
Melting point	142 °C
Boiling point	288 °C

2 – Production

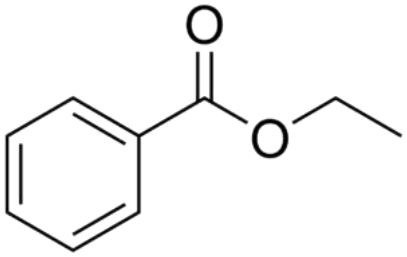
DMT has been produced in a number of ways. Conventionally and still of commercial value is the direct esterification of terephthalic acid. Alternatively, it can be prepared by alternating oxidation and methyl-esterification steps from p - xylene via methylp - toluate.

3 – Use

DMT is used in the production of polyesters, including polyethylene terephthalate (PET) and poly trimethylene terephthalate. It consists of benzene substituted with carboxy methyl groups (CO_2CH_3) at the 1 and 4 positions. Because DMT is volatile, it is an intermediate in some schemes for the recyclic of PET, e.g. from plastic bottles.

Hydrogenation of DMT affords the diol cyclohexanedimethanol, which is a useful monomer.

Ethyl Benzoate

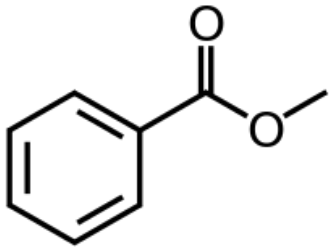


IUPAC name : Ethyl benzoate	
Molecular formula	$C_9H_{10}O_2$
Molar mass	150 g / mol
Density	1.050 g / cm^3
Melting point	-34 °C
Boiling point	211– 213 °C

Ethyl benzoate, $C_9H_{10}O_2$, is the ester formed by the condensation of benzoic acid and ethanol. It is a colorless liquid that is almost insoluble in water, but miscible with most organic solvents.

As with many volatile esters, ethyl benzoate has a pleasant odor which could be described similar to wintergreen mint. It is a component of some artificial fruit flavors.

Methyl Benzoate



Contents

1 - Introduction

Methyl benzoate is an organic compound. It is an ester with the chemical formula $C_6H_5CO_2CH_3$. It is a colorless liquid that is poorly soluble in water, but miscible with organic solvents. Methyl benzoate has a pleasant smell, strongly reminiscent of the fruit of the feijoa tree, and it is used in perfumery. It also finds use as a solvent and as a pesticide used to attract insects such as orchid bees.

IUPAC name : Methyl benzoate	
Molecular formula	$C_8H_8O_2$
Molar mass	136 g mol^{-1}
Density	1.0837 g / cm^3
Melting point	-12.5 °C
Boiling point	199.6 °C
Refractive index (n_D)	1.5164
Flash point	82 °C

2 Synthesis and reactions

Methyl benzoate is formed by the condensation of methanol and benzoic acid, in presence of a strong acid such as hydrochloric acid . It reacts both at the ring and the ester. Illustrative of its ability to undergo electrophilic substitution, methyl benzoate undergoes acid-

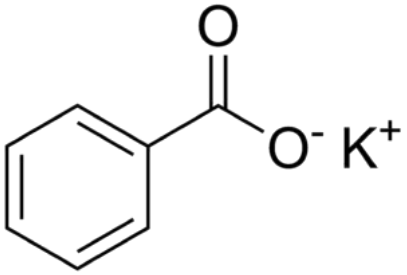
catalyzed nitration with nitric acid to give methyl 3- nitro benzoate. It also undergoes hydrolysis with addition of aqueous Na OH to give methanol and sodium benzoate, which can be acidified with aqueous HCl to form benzoic acid.

3 – Occurrence

Methyl benzoate can be isolated from the freshwater fern *Salvinia molesta* . It is one of many compounds that is attractive to males of various species of orchid bees, which apparently gather the chemical to synthesize pheromones; it is commonly used as bait to attract and collect these bees for study.

Cocaine hydrochloride hydrolyzes in moist air to give methyl benzoate ; drug-sniffing dogs are thus trained to detect the smell of methyl benzoate .

Potassium Benzoate



Contents

1 - Introduction

Potassium benzoate (**E212**) , the potassium salt of benzoic acid, is a food preservative that inhibits the growth of mold, yeast and some bacteria. It works best in low-pH products, below 4.5, where it exists as benzoic acid.

Acidic foods and beverages such as fruit juice (citric acid), sparkling drinks (carbonic acid), soft drinks (phosphoric acid), and pickles (vinegar) may be preserved with potassium benzoate. It is approved for use in most countries including Canada, the U.S., and the EU, where it is designated by the E number E212. In the EU, it is not recommended for consumption by children.

IUPAC name : Potassium benzoate	
Other names : Benzoic acid potassium salt	
Molecular formula	$C_7 H_5 K O_2$
Molar mass	160 g mol^{-1}

Appearance	White hygroscopic solid
Odor	Odorless
Density	1.5 g / cm^3
Melting point	> 300 °C
Solubility in water	65 g/100 mL (20 °C)
Solubility	Soluble in ethanol Slightly soluble in methanol Insoluble in ether
Auto ignition temperature	> 950 °C

2 - Synthesis[edit source

One very common way to make potassium benzoate is by oxidizing toluene.

Another way to synthesize potassium benzoate in the lab setting is by reacting methyl benzoate with potassium thio acetate.

3 - Mechanism of food preservation

The mechanism of food preservation begins with the absorption of benzoic acid into the cell. If the intracellular pH changes to 5 or lower, the anaerobic fermentation of glucose through phosphofructokinase is decreased by 95 %.

4 - Safety and health[edit source

Potassium benzoate was recently described by the Food Commission, who campaign for 'safer, healthier food in the UK', as "mildly irritant to the skin, eyes and mucous membranes".

Cats have a significantly lower tolerance to benzoic acid and its salts than rats and mice.

5 - Spectra[edit source

5 – 1 - Carbon 13 NMR[edit source

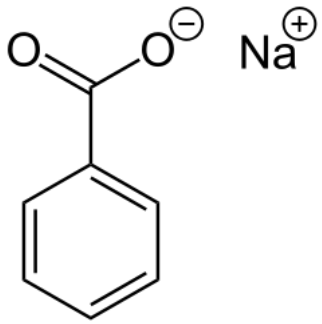
The carbon NMR shows 5 unique peaks. There are four peaks between 130 - 140 ppm from the carbons in the benzene ring. There is

an additional carbon peak around 178 ppm representing the carbon from the carbonyl.

5 – 2 - Infrared spectrum

The following are the main peaks in the IR spectrum.
1610: C=O from carbonyl
1580: C=C from benzene ring

Sodium Benzoate



Contents

1 - Introduction

Sodium benzoate has the chemical formula $NaC_7H_5O_2$; it is a widely used food preservative, with E number **E211**. It is the sodium salt of benzoic acid and exists in this form when dissolved in water. It can be produced by reacting sodium hydroxide with benzoic acid.

IUPAC name : sodium benzoate	
Other names : E211, benzoate of soda	
Molecular formula	$Na\ C_6\ H_5\ C\ O_2$
Molar mass	144 g / mol
Appearance	white or colorless crystalline powder
Odor	odorless
Density	1.497 g / cm^3
Melting point	300 °C
Solubility in water	62.9 g / 100 ml

Solubility	1.33g / 100ml ethanol
Flash point	100 °C
Auto ignition temperature	500 °C
LD_{50}	4100 mg / kg (oral, rat)

2 – Uses

Sodium benzoate is a preservative. It is bacteriostatic and fungistatic under acidic conditions. It is most widely used in acidic foods such as salad dressings (vinegar), carbonated drinks (carbonic acid), jams and fruit juices (citric acid), pickles (vinegar), and condiments. It is also used as a preservative in medicines and cosmetics. As a food additive, sodium benzoate has the E number E211.

It is also used in fireworks as a fuel in whistle mix, a powder that emits a whistling noise when compressed into a tube and ignited. The fuel is also one of the fastest burning rocket fuels and provides a lot of thrust and smoke. It does have its downsides: there is a high danger of explosion when the fuel is sharply compressed because of the fuel's sensitivity to impact.

Sodium benzoate is produced by the neutralization of benzoic acid with sodium hydroxide . Benzoic acid is detectable at low levels in cranberries, prunes, greengage plums, cinnamon, ripe cloves, and apples. Concentration as a preservative is limited by the FDA in the U.S. to 0.1% by weight. The International Programme on Chemical Safety found no adverse effects in humans at doses of 647–825 mg/kg of body weight per day.

Cats have a significantly lower tolerance against benzoic acid and its salts than rats and mice. Sodium benzoate is, however, allowed as an animal food additive at up to 0.1 %, according to AFCO's official publication.

3 - Mechanism of food preservation

The mechanism starts with the absorption of benzoic acid into the cell. If the intracellular pH changes to 5 or lower, the anaerobic

fermentation of glucose through phosphofructokinase is decreased by 95 %, thereby inhibiting the growth and survival of micro-organisms that cause food spoilage.

4 - Production[edit source

Sodium benzoate is prepared by adding benzoic acid to a hot concentrated solution of sodium carbonate until effervescence ceases. The solution is then evaporated, cooled and allowed to crystallize or evaporate to dryness, and then granulated.

5 - Safety and health[edit source

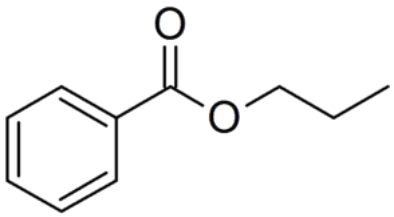
In combination with ascorbic acid (vitamin C, E300), sodium benzoate and potassium benzoate form benzene, a known carcinogen. However, in most beverages that contain both, the benzene levels are below those considered dangerous for consumption.[10] Heat, light and shelf life can affect the rate at which benzene is formed.

5 – 1 - Hyperactivity[edit source

Research published in 2007 for the UK's Food Standards Agency (FSA) suggests that certain artificial colors, when paired with sodium benzoate (E211) may be linked to hyperactive behaviour. The results were inconsistent regarding sodium benzoate, so the FSA recommended further study.

Professor Jim Stevenson from Southampton University, and author of the report, said: "This has been a major study investigating an important area of research. The results suggest that consumption of certain mixtures of artificial food colours and sodium benzoate preservative are associated with increases in hyperactive behaviour in children. However, parents should not think that simply taking these additives out of food will prevent hyperactive disorders. We know that many other influences are at work but this at least is one a child can avoid."

Propyl Benzoate



Contents

1 - Introduction

Propyl benzoate is an organic chemical compound used as a food additive. It is an ester.

IUPAC name : Propyl benzoate	
Other names : *n*-propyl benzoate, benzoic acid propyl ester	
Molecular formula	$C_{10}H_{12}O_2$
Molar mass	164. g / mol
Appearance	colorless oily liquid , nutty odor
Density	1.0230 g / cm^3 at 20 °C
Melting point	− 51.6 °C
Boiling point	230 °C
Solubility in water	insoluble
Solubility	miscible with ethanol, diethyl ether
Flash point	98 °C

2 - Uses

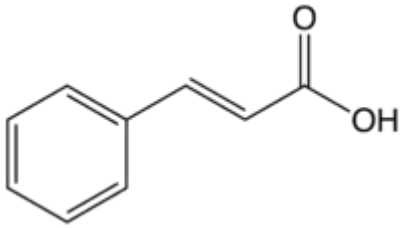
Propyl benzoate has a nutty odor and sweet fruity or nut-like taste, and as such, it is used as a synthetic flavoring agent in foods. It

also has antimicrobial properties and is used as a preservative in cosmetics. It occurs naturally in the sweet cherry and in clove stems, as well as in butter.

3 – Reactions

Propyl benzoate can be synthesized by the transesterification of methyl benzoate with propanol.

Cinnamic Acid



Contents

1 - Introduction

Cinnamic acid is a white crystalline organic acid, which is slightly soluble in water.

It is obtained from oil of cinnamon, or from balsams such as storax. It is also found in shea butter and is the best indication of its environmental history and post-extraction conditions. It can also be made synthetically.

Cinnamic acid is used in flavors, synthetic indigo, and certain pharmaceuticals, though its primary use is in the manufacturing of the methyl, ethyl, and benzyl esters for the perfume industry. Cinnamic acid has a honey- like odor; it and its more volatile ethyl ester (ethyl cinnamate) are flavor components in the essential oil of cinnamon, in which related cinnamaldehyde is the major constituent. Cinnamic acid is also part of the biosynthetic shikimate and phenyl propanoid pathways. Its biosynthesis is performed by action of the enzyme phenylalanine ammonia - lyase (PAL) on phenylalanine.

Cinnamic acid is freely soluble in benzene, diethyl ether, acetone, and it is insoluble in hexane.

Cinnamic acid is also a kind of self-inhibitor produced by fungal spore to prevent germination.

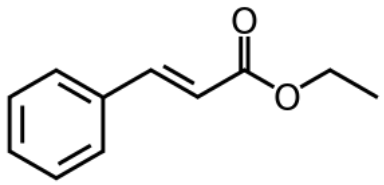
IUPAC name :
(E)-3-phenylprop-2-enoic acid
Other names :
Cinnamic Acid
trans - Cinnamic Acid
Phenyl acrylic acid
Cinnamylic acid
3-Phenyl acrylic acid
(E) - Cinnamic acid
Benzene propenoic acid
Iso cinnamic acid

Molecular formula	$C_9 H_8 O_2$
Molar mass	148 g mol−1
Appearance	White monoclinic crystals
Density	1.2475 g / cm^3
Melting point	133 °C
Boiling point	300 °C
Solubility in water	500 mg / L
Acidity (pKa)	4.44
EU classification	Irritant (Xi)
Flash point	>100 °C (212 °F)[1]

2 . Chemical synthesis

Rainer Ludwig Claisen (1851–1930), German chemist, described for the first time in 1890 the synthesis of cinnamates by reacting aromatic aldehydes with esters. The reaction is known as the Claisen condensation.

Ethyl Cinnamate



IUPAC name :	
Ethyl 3- phenyl prop-2- enoate	
Molecular formula	$C_{11}H_{12}O_2$
Molar mass	176 g / mol
Density	1.046 g / cm^3
Melting point	6.5 - 8 °C
Boiling point	271 °C

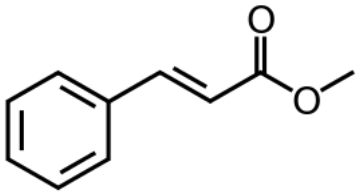
Ethyl cinnamate is the ester of cinnamic acid and ethanol. It is present in the essential oil of cinnamon . Pure ethyl cinnamate has a "fruity and balsamic odor, reminiscent of cinnamon with an amber note".

The *p*-methoxy derivative is reported to be a mono amine oxidase inhibitor.

List of plants that contain the chemical

Kaempferia galanga

Methyl Cinnamate



Contents

1 - Introduction

Methyl cinnamate is the methyl ester of cinnamic acid and is a white or transparent solid with a strong, aromatic odor. It is found naturally in a variety of plants, including in fruits, like strawberry, and some culinary spices, such as Sichuan pepper and some varieties of basil . *Eucalyptus olida* has the highest known concentrations of methyl cinnamate (n98 %) with a 2 - 6 % fresh weight yield in the leaf and twigs.

Methyl cinnamate is used in the flavor and perfume industries. The flavor is fruity and strawberry-like; and the odor is sweet, balsamic with fruity odor, reminiscent of cinnamon and strawberry.

It is known to attract males of various orchid bees , such as *Aglae caerulea*.

Methyl cinnamate crystals extracted using steam distillation from Eucalyptus olida.

IUPAC name :	
Methyl (*E*)-3-Phenyl prop-2- enoate	
Molecular formula	$C_{10}H_{10}O_2$
Molar mass	162 g mol^{-1}
Density	1.092 g / cm^3
Melting point	34-38 °C
Boiling point	261-262 °C
Solubility in water	Insoluble
Flash point	> 110 °C

2 - List of plants that contain the chemical

Eucalyptus olida 'Strawberry gum'

Ocimum americanum cv.Purple Lovingly (Querendona Morada)

Ocimum americanum cv. Purple Castle (Castilla Morada)

Ocimum americanum cv. Purple Long-legged (Zancona morada)

Ocimum americanum cv. Clove (Clavo)

Ocimum basilicum cv. Sweet Castle (Dulce de Castilla)

Ocimum basilicum cv. White Compact (Blanca compacta)

Ocimum basilicum cv. large green leaves (Verde des horjas grandes)

Ocimum micranthum cv. Cinnamon (Canela)

Ocimum minimum cv. Little Virgin (Virgen pequena)

Ocimum minimum cv. Purple Virgin (Virgen morada)

Ocimum sp. cv. Purple ruffle (Crespa morada)

Ocimum sp. cv. White Ruffle (Crespa blanca)

Vanilla

3 - Toxicology and safety

Moderately toxic by ingestion . The oral LD_{50} for rats is 2610 mg / kg . It is combustible as a liquid, and when heated to decomposition it emits acrid smoke and irritating fumes.

Eucalyptus Oil

Contents

1 - Introduction

Eucalyptus oil is the generic name for distilled oil from the leaf of *Eucalyptus*, a genus of the plant family Myrtaceae native to Australia and cultivated worldwide. Eucalyptus oil has a history of wide application, as a pharmaceutical, antiseptic, repellent, flavoring, fragrance and industrial uses. The leaves of selected Eucalyptus species are steam distilled to extract eucalyptus oil.

2 - Types and production

Eucalyptus oils in the trade are categorized into three broad types according to their composition and main end-use: medicinal, perfumery and industrial . The most prevalent is the standard cineole-based "oil of eucalyptus", a colourless mobile liquid (yellow with age) with a penetrating, camphoraceous, woody-sweet scent.

China produces about 75 % of the world trade, but most of this is derived from camphor oil fractions rather than being true eucalyptus oil . Significant producers of true eucalyptus oil include South Africa, Portugal, Spain, Brazil, Australia, Chile and Swaziland.

Global production is dominated by *Eucalyptus globulus*. However, *Eucalyptus kochii* and *Eucalyptus polybractea* have the highest cineole content, ranging from 80-95%. The British

Pharmacopoeia states that the oil must have a minimum cineole content of 70% if it is pharmaceutical grade. Rectification is used to bring lower grade oils up to the high cineole standard required. Global annual production of eucalyptus oil is estimated at 3,000 tones. The eucalyptus genus also produces non-cineole oils, including piperitone, phellandrene , citral, methyl cinnamate and geranyl acetate.

Eucalyptus oil should not be confused with the term "eucalyptol", another name for cineole.

Eucalyptus poly bractea or Blue-leaf Mallee, a species yielding high quality eucalyptus oil

3 – Uses

3 – 1 - Medicinal and antiseptic

The cineole-based oil is used as component in pharmaceutical preparations to relieve the symptoms of influenza and colds, in products like cough sweets, lozenges, ointments and inhalants. Eucalyptus oil has antibacterial effects on pathogenic bacteria in the respiratory tract . Inhaled eucalyptus oil vapor is a decongestant and treatment for bronchitis . Cineole controls airway mucus hyper secretion and asthma via anti - inflammatory cytokine inhibition . Eucalyptus oil also stimulates immune system response by effects on the phagocytic ability of human monocyte derived macrophages.

Eucalyptus oil also has anti-inflammatory and analgesic qualities as a topically applied liniment ingredient.

Eucalyptus oil is also used in personal hygiene products for antimicrobial properties in dental care and soaps. It can also be applied to wounds to prevent infection.

3 – 2 - Repellent and bio pesticide

Cineole - based eucalyptus oil is used as an insect repellent and bio pesticide. In the U.S., eucalyptus oil was first registered in 1948 as an insecticide and miticide.

3 – 3 – Flavoring

Eucalyptus oil is used in flavoring. Cineole - based eucalyptus oil is used as a flavoring at low levels (0.002 %) in various products, including baked goods, confectionery, meat products and beverages . Eucalyptus oil has antimicrobial activity against a broad range of foodborne human pathogens and food spoilage microorganisms . Non - cineole peppermint gum, strawberry gum and lemon ironbark are also used as flavoring.

3 – 4 – Fragrance

Eucalyptus oil is also used as a fragrance component to impart a fresh and clean aroma in soaps, detergents, lotions and perfumes.

3 – 5 – Industrial

Research shows that cineole - based eucalyptus oil (5% of mixture) prevents the separation problem with ethanol and petrol fuel blends. Eucalyptus oil also has a respectable octane rating and can be used as a fuel in its own right. However, production costs are currently too high for the oil to be economically viable as a fuel.

Phellandrene - and piperitone - based eucalyptus oils have been used in mining to separate sulfide minerals via flotation.

4 - Safety and toxicity

If consumed internally at low dosage as a flavoring component or in pharmaceutical products at the recommended rate, cineole-based 'oil of eucalyptus' is safe for adults. However, systemic toxicity can result from ingestion or topical application at higher than recommended doses.

The probable lethal dose of pure eucalyptus oil for an adult is in the range of 0.05 mL to 0.5 mL / per kg of body weight . Because of their high body surface area to mass ratio, children are more

vulnerable to poisons absorbed trans dermally. Severe poisoning has occurred in children after ingestion of 4 mL to 5 mL of eucalyptus oil.

5 – History

Australian Aboriginals use eucalyptus leaf infusions (which contain eucalyptus oil) as a traditional medicine for treating body pains, sinus congestion, fever, and colds.

Dennis Considen and John White, surgeons on the First Fleet, distilled eucalyptus oil from *Eucalyptus piperita* found growing on the shores of Port Jackson in 1788 to treat convicts and marines. Eucalyptus oil was subsequently extracted by early colonists, but was not commercially exploited for some time.

Baron Ferdinand von Mueller, Victorian botanist, promoted the qualities of Eucalyptus as a disinfectant in "fever districts", and also encouraged Joseph Bosisto, a Melbourne pharmacist, to investigate the commercial potential of the oil . Bosisto started the commercial eucalyptus oil industry in 1852 near Dandenong, Victoria, Australia, when he set up a distillation plant and extracted the essential oil from the cineole chemo type of *Eucalyptus radiata*. This resulted in the cineole chemo type becoming the generic 'oil of eucalyptus', and "Bosisto's Eucalyptus Oil" still survives as a brand.

French chemist, F.S. Cloez, identified and ascribed the name *eucalyptol* — also known as cineole — to the dominant portion of *E. globulus* oil. By the 1870s oil from *Eucalyptus globulus*, Tasmanian blue gum, was being exported worldwide and eventually dominated world trade, while other higher quality species were also being distilled to a lesser extent. Surgeons were using eucalyptus oil as an antiseptic during surgery by the 1880s.

The Australian eucalyptus oil industry peaked in the 1940s, the main area of production being the central goldfields region of Victoria, particularly Inglewood; then the global establishment of eucalyptus plantations for timber resulted in increased volumes of eucalyptus oil as a plantation by-product. By the 1950s the cost of

producing eucalyptus oil in Australia had increased so much that it could not compete against cheaper Spanish and Portuguese oils (closer to European Market there fore less costs). Non-Australian sources now dominate commercial eucalyptus oil supply, although Australia continues to produce high grade oils, mainly from blue mallee (*E. polybractea*) stands.

6 - Species utilized

Commercial cineole - based eucalyptus oils are produced from several species of *Eucalyptus*:

Eucalyptus cneorifolia
Eucalyptus dives
Eucalyptus dumosa
Eucalyptus globulus
Eucalyptus goniocalyx
Eucalyptus horistes
Eucalyptus kochii
Eucalyptus leucoxylon
Eucalyptus oleosa
Eucalyptus polybractea
Eucalyptus radiata
Eucalyptus sideroxylon
Eucalyptus smithii
Eucalyptus tereticornis
Eucalyptus viridis

Phenolic Acid

Contents

1 - Introduction

Phenolic acids (phenol carboxylic acids) are a type of organic compounds. Included in that class are substances containing a phenolic ring and an organic carboxylic acid function (C6 - C1 skeleton). There are several categories of phenolic acids including:

mono hydroxy benzoic acids: salicylic acid, 3-Hydroxy benzoic acid, 4- Hydroxy benzoic acid

Some esters of this group include paraben, methyl paraben, propyl paraben

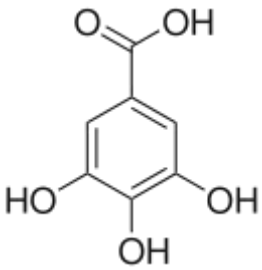
di hydroxy benzoic acids: (gentisic acid, protocatechuic acid)
tri hydroxy benzoic acids: (gallic acid, phloroglucinol carboxylic acid)
This type
of phenolic acids (especially gallic acid) is a component of hydrolysable tannins.
Syringic acid , eudesmic acid are other phenolic acids.

2 - Occurrences

Phenolic acids can be found in many plant species. Their content in dried fruits can be high.
Natural phenols in horse grams (Macrotyloma uniflorum) are mostly phenolic acids, namely, 3, 4-dihydroxy benzoic, p-hydroxy benzoic , vanillic , caffeic , p- coumaric , ferulic , syringic and sinapic acids.

Phenolic acids can be found in mushroom basidiomycetes species. It is also a part of the humic substances, which are the major organic constituents of soil humus.
Many phenolic acids can be found in human urine

Gallic Acid



Contents

1 - Introduction

Gallic acid is a tri hydroxy benzoic acid, a type of phenolic acid, a type of organic acid, also known as 3,4,5- tri hydroxy benzoic acid, found in gallnuts, sumac, witch hazel, tea leaves, oak bark, and other plants. The chemical formula is $C_6H_2(OH)_3COOH$. Gallic acid is found both free and as part of hydrolyzable tannins.

Salts and esters of gallic acid are termed 'gallates'. Despite its name, it does not contain gallium.

Gallic acid is commonly used in the pharmaceutical industry.[2] It is used as a standard for determining the phenol content of various analytes by the Folin - Ciocalteau assay; results are reported in *gallic acid equivalents*. Gallic acid can also be used as a starting material in the synthesis of the psychedelic alkaloid mescaline.

Gallic acid seems to have anti-fungal and anti - viral properties. Gallic acid acts as an antioxidant and helps to protect human cells against oxidative damage. Gallic acid was found to show cytotoxicity against cancer cells, without harming healthy cells. Gallic acid is used as a remote astringent in cases of internal haemorrhage. Gallic acid is also used to treat albuminuria and diabetes. Some ointments to treat psoriasis and external haemorrhoids contain gallic acid.

IUPAC name :
3,4,5-trihydroxybenzoic acid
Other names .
Gallic acid
Gallate
3,4,5-trihydroxy benzoate

Molecular formula	$C_7 H_6 O_5$
Molar mass	170 g / mol
Appearance	White, yellowish - white , or pale fawn - colored crystals.
Density	1.7 g / cm^3 (anhydrous)
Melting point	250 °C
Solubility in water	1.1 g / 100 ml water @ 20°C (anhydrous) 1.5 g / 100 ml water @ 20 °C (monohydrate)
Main hazards	Irritant

2 - Historical context and uses

Gallic acid is an important component of iron gall ink, the standard European writing and drawing ink from the 12 th to 19th century with a history extending to the Roman empire and the Dead Sea Scrolls. Pliny the Elder (23-79 AD) describes his experiments with it and writes that it was used to produce dyes. Galls (also known as oak apples) from oak trees were crushed and mixed with water, producing tannic acid (a macromolecular complex containing gallic acid). It could then be mixed with green vitriol (ferrous sulfate) — obtained by allowing sulfate - saturated water from a spring or mine drainage to evaporate — and gum arabic from acacia trees; this combination of ingredients produced the ink.

Gallic acid was one of the substances used by Angelo Mai (1782–1854), among other early investigators of palimpsests, to clear the top layer of text off and reveal hidden manuscripts underneath. Mai was the first to employ it, but did so "with a heavy hand", often rendering manuscripts too damaged for subsequent study by other researchers.

Gallic acid was first studied by the Swedish chemist Carl Wilhelm Scheele in 1786. In 1818 the French chemist and pharmacist Henri Braconnot (1780 –1855) devised a simpler method of purifying gallic acid from galls ; gallic acid was also studied by the French chemist Théophile-Jules Pelouze (1807–1867), among others.

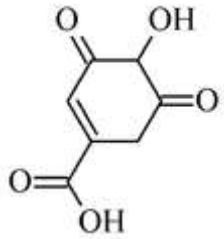
Early photographers, including Joseph Bancroft Reade (1801–1870) and William Fox Talbot (1800 – 1877), used gallic acid for developing latent images in calotypes. It has also been used as a coating agent in zincography.

George Washington used gallic acid to communicate with spies during the American Revolutionary War, according to the miniseries *America: The Story of Us* .

Gallic acid is a component of some pyrotechnic whistle mixtures.

3 - Metabolism

3 – 1 – Biosynthesis



Chemical structure of 3,5- didehydro shikimate

Gallic acid is formed from 3-dehydro shikimate by the action of the enzyme shikimate dehydro genase to produce 3,5-didehydro shikimate. This latter compound tautomerizes to form the redox equivalent gallic acid, where the equilibrium lies essentially entirely

toward gallic acid because of the coincidently occurring aromatization.

3 – 2 - Degradation

Gallate dioxygenase is an enzyme found in *Pseudomonas putida* that catalyzes the reaction :

gallate + O_2 → (1E)-4-oxobut-1-ene-1,2,4-tri carboxylate.

Gallate decarboxylase is another enzyme in the degradation of gallic acid.

3 – 3 - Conjugation

Gallate 1-beta-glucosyltransferase is an enzyme that uses UDP-glucose and gallate, whereas its two products are UDP and 1-galloyl-beta-D-glucose.

4 - Natural occurrences

Gallic acid is found in a number of land plants. It is also found in the aquatic plant *Myriophyllum spicatum* and shows an allelopathic effect on the growth of the blue-green alga *Microcystis aeruginosa*.

4 – 1 - List of plants that contain the chemical

Gallic acid is found in oaks species like the North American white oak (*Quercus alba*) and European red oak (*Quercus robur*).

Caesalpinia mimosoides,
stem bark of *Boswellia dalzielii*,
Drosera (sundew)
Rhodiola rosea (Golden root)
Triphala (Ayurvedic herbal rasayana formula)
Toona sinensis

4 – 2 - In food

Areca nut
Bearberry (*Arctostaphylos sp*)
Bergenia sp
Blackberry

Hot chocolate
Juglans regia (Common walnut)
Mango in peels and leaves
Phyllanthus emblica (Indian gooseberry) in fruits
Raspberry
Syzygium aromaticum (clove)[16]
Vinegar
wine
Witch hazel (*Hamamelis virginiana*)
White tea

5 - Esters

Also known as galloylated esters:
Methyl gallate
Ethyl gallate, a food additive with E number E313
Propyl gallate, or propyl 3,4,5-trihydroxybenzoate, an ester formed by the condensation of gallic acid and propanol
Octyl gallate, the ester of octanol and gallic acid
Dodecyl gallate, or lauryl gallate, the ester of dodecanol and gallic acid
Epicatechin gallate, a flavan-3-ol, a type of flavonoid, present in green tea
Epigallocatechin gallate (EGCG), also known as epigallocatechin 3-gallate, the ester of epigallocatechin and gallic acid, and a type of catechin
Gallocatechin gallate (GCG), the ester of gallocatechin and gallic acid and a type of flavan-3ol
Theaflavin-3-gallate, a theaflavin derivative

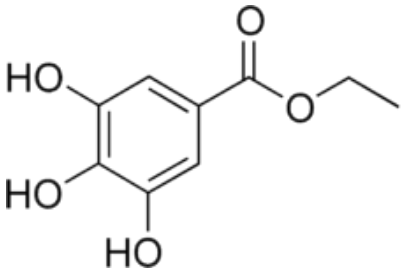
6 - Health effects

It is a weak carbonic anhydrase inhibitor.

7 - Potential uses

It can be used to produce polyesters based on phloretic acid and gallic acid.

Ethyl Gallate



IUPAC name : Ethyl 3,4,5-tri hydroxy benzoate	
Other names : Phyllemblin gallic acid ethyl ester	
Molecular formula	$C_9H_{10}O_5$
Molar mass	198 g / mol
Melting point	149 – 153 °C

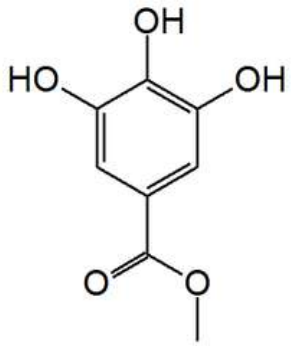
Ethyl gallate is a food additive with E number E313. It is the ethyl ester of gallic acid. Ethyl gallate is added to food as an antioxidant.

Though found naturally in a variety of plant sources including walnuts

Terminalia myriocarpa[3] or chebulic myrobolan (*Terminalia chebula*).

Ethyl gallate is produced from gallic acid and ethanol.[5] It can be found in wine.

Methyl Gallate

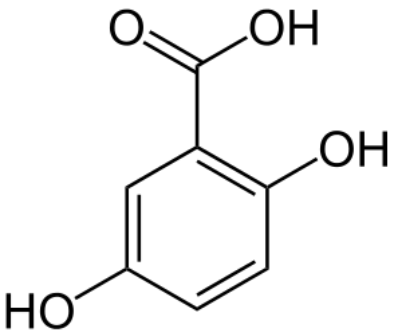


IUPAC name : Methyl 3,4,5-tri hydroxy benzoate	
Other names : Methyl gallate Gallic acid methyl ester	
Molecular formula	$C_8 H_8 O_5$
Molar mass	184 g mol^{-1}

Methyl gallate is methyl ester of gallic acid .

And it is a phenolic compound found in *Terminalia myriocarpa* and *Geranium niveum* . and wine.

Gentisic Acid



Contents

1 - Introduction

Gentisic acid is a dihydroxy benzoic acid. It is a derivative of benzoic acid and a minor (1 %) product of the metabolic break down of aspirin, excreted by the kidneys

It is also found in the African tree *Alchornea cordifolia* and in wine.

IUPAC name : 2,5- di hydroxy benzoic acid	
Other names : DHB 2,5 - di hydroxy benzoic acid 5- Hydroxy salicylic acid Gentianic acid Carboxyhydroquinone 2,5 - Dioxy benzoic Acid Hydro quinone carboxylic acid	
Molecular formula	$C_7H_6O_4$
Molar mass	154 g/mol
Appearance	white to yellow powder
Melting point	200 - 205 C (Sublimes)

2 - Production

Gentisic acid is produced by carboxylation of hydroquinone.

$C_6H_4(OH)_2 + CO_2 \rightarrow C_6H_3(CO_2H)(OH)_2$

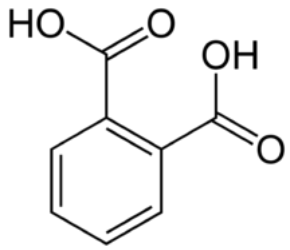
This conversion is an example of a Kolbe–Schmitt reaction.

3 - Applications

As a hydroquinone , gentisic acid is readily oxidized and is used as an antioxidant excipient in some pharmaceutical preparations.

In the laboratory, it is used as a sample matrix in matrix-assisted laser desorption/ionization (MALDI) mass spectrometry , and has been shown to conveniently detect peptides incorporating the boronic acid moiety by MALDI .

Phthalic Acid



Contents

1 - Introduction

Phthalic acid is an aromatic dicarboxylic acid, with formula $C_6H_4(CO_2H)_2$. It is an isomer of isophthalic acid and terephthalic acid. Although phthalic acid is of modest commercial importance, the closely related derivative phthalic anhydride is a commodity chemical produced on a large scale.

IUPAC name : Benzene -1,2- dicarboxylic acid	
Other names : benzene-1,2-dioic acid , phthalic acid , ortho-phthalic acid	
Molecular formula	$C_8H_6O_4$
Molar mass	166 g / mol
Appearance	white solid
Density	1.593 g / cm^3, solid
Melting point	191−230 °C
Solubility in water	0.6 g / 100 mL

2 – Production

Phthalic acid is produced by the catalytic oxidation of naphthalene directly to phthalic anhydride and a subsequent hydrolysis of the anhydride.

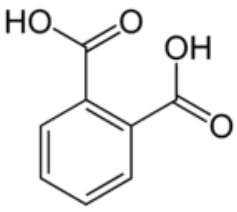
Phthalic acid was first obtained by French chemist Auguste Laurent in 1836 by oxidizing naphthalene tetrachloride. Believing the resulting substance to be a naphthalene derivative, he named it "naphthalic acid". After the Swiss chemist Jean Charles Galissard de Marignac determined its correct formula,[7] Laurent gave it its present name.[8] Manufacturing methods in the nineteenth century included oxidation of naphthalene tetrachloride with nitric acid, or, better, oxidation of the hydrocarbon with fuming sulfuric acid, using mercury or mercury(II) sulfate as a catalyst.

3 - Reactions and uses

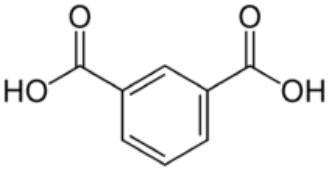
It is a dibasic acid, with pK_a's of 2.89 and 5.51. The mono potassium salt, potassium hydrogen phthalate is a standard acid in analytical chemistry. Typically phthalate esters are prepared from the widely available phthalic anhydride. Reduction of phthalic acid with sodium amalgam in the presence of water gives the 1,3-cyclohexadiene derivative.

4 – Isomers

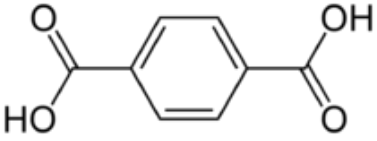
Phthalic acid is one of three isomers of benzene dicarboxylic acid, the others being iso phthalic acid and terephthalic acid. Sometimes the term "phthalic acids" is used to refer to this family of isomers, but in the singular, "phthalic acid", refers exclusively to the *ortho*- isomer.



phthalic acid (ortho-phthalic acid)



Iso phthalic acid (meta-phthalic acid)

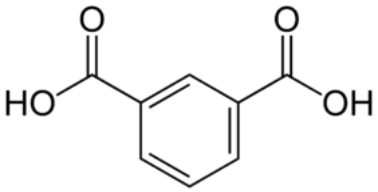


terephthalic acid (para-phthalic acid)

5 - Safety[edit source

The toxicity of phthalic acid is low with LD_{50} (mouse) of 550 mg/kg. However, many phthalate esters have been implicated as endocrine disruptors.

Iso Phthalic Acid



Contents

1 - Introduction

Iso phthalic acid is an organic compound with the formula $C_6H_4(CO_2H)_2$. This colourless solid is an isomer of phthalic acid and terephthalic acid. These aromatic dicarboxylic acids are used as precursors (in form of acyl chlorides) to commercially important polymers, e.g. the fire-resistant material Nomex. Mixed with terephthalic acid, iso phthalic acid is used in the production of resins for drink bottles. The high-performance polymer poly benzimidazole is produced from iso phthalic acid.

Other names :	
Benzene-1,3-dicarboxylic acid *meta*-Phthalic acid	
Molecular formula	$C_6H_4(COOH)_2$
Molar mass	166 g / mol
Appearance	White crystalline solid
Density	1.526 g / cm^3, Solid
Solubility in water	Insoluble in water
Acidity (pK_a)	3.46, 4.46

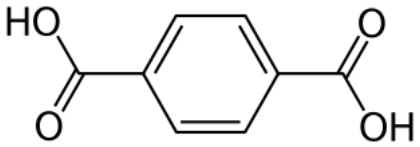
2 - Preparation

Iso phthalic acid is produced on the billion kilogram per year scale by oxidizing meta-xylene using oxygen . The process employs a cobalt-manganese catalyst. In the laboratory, chromic acid can be

used as the oxidant. It also arises by fusing potassium meta-sulpho benzoate , or meta - brom benzoate with potassium formate (terephthalic acid is also formed in the last case).

The barium salt (as its hexa hydrate) is very soluble (a distinction between phthalic and terephthalic acids). Uvitic acid, 5-methylisophthalic acid, is obtained by oxidizing mesitylene or by condensing pyroracemic acid with baryta water.

Terephthalic Acid



Contents

1 - Introduction

Terephthalic acid is the organic compound with formula $C_6H_4(COOH)_2$. This colourless solid is a commodity chemical, used principally as a precursor to the polyester PET, used to make clothing and plastic bottles. Several million tones are produced annually. It is one of three isomeric phthalic acids.

Other names :	
Benzene -1,4- dicarboxylic acid *para*-Phthalic acid TPA PTA BDC	
Molecular formula	$C_8H_6O_4$
Molar mass	166 g / mol
Appearance	white crystals or powder
Density	1.522 g / cm³
Melting point	300°C in a sealed tube (sublimes at 402°C (in air)
Boiling point	sublimes
Solubility in water	0.0017 g / 100 mL at 25°C

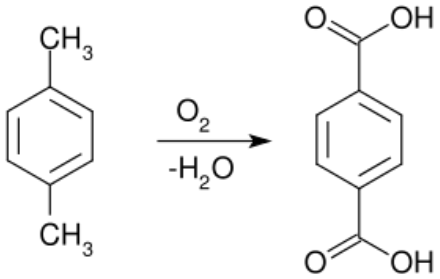
Solubility	polar organic solvents aqueous base
Thermo dynamic data	Phase behaviour Solid, liquid, gas
Spectral data	UV, IR, NMR, MS

2 – Properties

Terephthalic acid is poorly soluble in water and alcohols, consequently up until around 1970 most crude terephthalic acid was converted to the dimethyl ester for purification. It sublimates when heated.

3 – Production

Terephthalic acid is produced by oxidation of *p*-xylene by oxygen in air:



This reaction proceeds through a *p*-toluic acid intermediate which is then oxidized to terephthalic acid. In *p*-toluic acid, deactivation of the methyl by the electron withdrawing carboxylic acid group makes the methyl one tenth as reactive as xylene itself, making the second oxidation significantly more difficult . The commercial process utilizes acetic acid as solvent and a catalyst composed of cobalt and manganese salts, with a bromide promoter. The yield is nearly quantitative. The most problematic impurity is 4-formylbenzoic acid (commonly known in the field as 4-carboxybenzaldehyde or 4- CBA) , which is removed by hydrogenation of a hot aqueous solution. This solution is then cooled in a stepwise manner to crystallize highly pure terephthalic acid.

Despite optimized yields greater than 95 % with excellent purity, the synthesis has proven to have shortcomings. Due to high

reaction temperature, approximately 5 % of the acetic acid solvent is lost by decomposition or 'burning'. Solvent burning is a significant economic factor in the oxidation process. In addition, product loss by decarboxylation to benzoic acid is common. The high temperature diminishes oxygen solubility in an already oxygen starved system. Pure oxygen cannot be used in the traditional system due to hazards of flammable organic-O_2 mixtures. Atmospheric air can be used in its place, but once reacted needs to be purified of toxins and ozone depleters such as methylbromide before being released. Additionally, the corrosive nature of bromides at high temperatures requires the reaction be run in expensive titanium reactors.

Alternatively, but not commercially significant, is the so-called "Henkel process" or "Raecke process", named after the company and patent holder, respectively. This process involves the rearrangement of phthalic acid to terephthalic acid via the corresponding potassium salts.[5][6] Terephthalic acid can be prepared in the laboratory by oxidizing various para - disubstituted derivatives of benzene, including caraway oil or a mixture of cymene and cuminol with chromic acid.

3 – 1 – Advancements

The use of CO_2 overcomes many of the problems with the original industrial process. Because CO_2 is a better flame inhibitor than nitrogen gas, a CO_2 environment allows for the use of pure oxygen directly, instead of air, with reduced flammability hazards. The solubility of molecular oxygen in solution is also enhanced in the CO_2 environment. Because more oxygen is available to the system, supercritical carbon dioxide (Tc = 31 ^{0}C) has more complete oxidation with fewer byproducts, lower CO production, less decarboxylation and higher purity than the commercial process.

When reaction run is in supercritical water can be effectively catalyzed by $MnBr_2$ with pure O_2 in a medium-high temperature. Use of supercritical water instead of acetic acid as a solvent diminishes environmental impact and offers a cost advantage. However, the scope of such reaction systems is limited by the even harsher conditions than the industrial process (T = 300−400 °C, P > 200 bar).

Ketones have been found to act as promoters for formation of the active Co(III) catalyst. In particular, ketones with a-methylene groups oxidize to hydro peroxides that are known to oxidize Co (II). Viable ketones were butanone, tri acetyl methane (TAM), 2,3-pentanedione (2,3-PD), and acetyl acetone; all of which can stabilize radical formation through resonance.

Reactions run at temperatures as low as 100 ^{0}C are possible by using zirconium salts as a cocatalyst in place of bromide and manganese acetate. It is thought that the Zr(IV) acts to oxidize Co(II) to the active Co(III). This alone shortens the induction period, and has been shown to have a synergistic effect with ketones. However, a greater amount of cobalt acetate is required than the common industrial process and is ineffective over 160 ^{0}C.

The addition of a small portion of metalloporphyrin, in particular T(*p*-Cl) PPMnCl, has a cocatalytic effect with the traditional Co $(OAc)_2$ catalyst. This requires less acetic acid and does not require bromides. The catalytic effect has been attributed to the ease of peroxide formation over the metalloporphyrin.

3 – 2 – Mechanism

The autoxidation of *p*-xylene is known to proceed through a free radical process. The Mn (III) and Co (III) metals alone are not strong enough oxidizers to start the radical chain reaction, but instead initiate it by forming bromine radicals from the ions in solution. These bromine radicals then decompose hydroperoxides that are ligated to the metals as well as abstract hydrogens from the methyl groups on p-xylene to form free radicals and propagate the reaction. The following are the proposed initiation, propagation and terminations steps for the first of four oxidations involved in the autoxidation:

Oxidation of p-xylene to p-tolualdehyde

Initiation

$Mn(III)/Co(III) + Br^- \longrightarrow Mn(II)/Co(II) + Br^{\cdot}$

Propagation

$Br^{\cdot} + H_3C-Ph-CH_3 \longrightarrow HBr + H_3C-Ph-CH_2^{\cdot}$

$H_3C-Ph-CH_2^{\cdot} + O_2 \longrightarrow H_3C-Ph-CH_2O_2^{\cdot}$

$H_3C-Ph-CH_2O_2^{\cdot} + Mn(II)/Co(II) + H^+ \longrightarrow H_3C-Ph-CHO + Mn(III)/Co(III) + H_2O$

$H_3C-Ph-CH_2O_2^{\cdot} + Mn(II)/Co(II) + H^+ \longrightarrow H_3C-Ph-CH_2OOH + Mn(III)/Co(III)$

$H_3C-Ph-CH_2OOH + Mn(II)/Co(II) + H^+ \longrightarrow H_3C-Ph-CHO^{\cdot} + Mn(III)/Co(III) + H_2O$

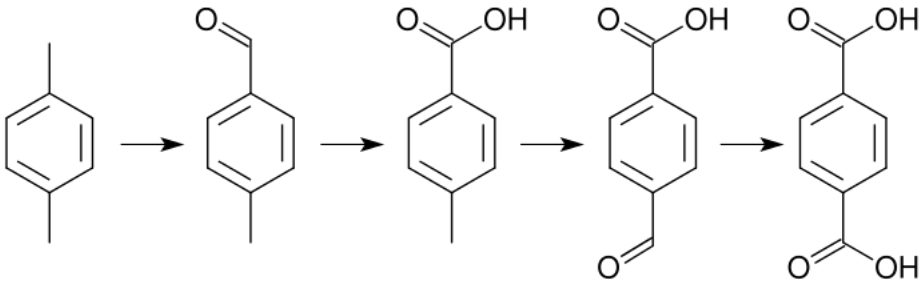
Termination

$Br^{\cdot} + H_3C-Ph-CH_2^{\cdot} \longrightarrow H_3C-Ph-CH_2Br$

$Br^{\cdot} + H_3C-Ph-CH_2O_2^{\cdot} \longrightarrow H_3C-Ph-CH_2O_2Br$

Mn()/Co() - either manganese or cobalt could be involved in the reaction

The radical chain reaction proceeds through a series of intermediates, starting with the oxidation of *p*-xylene to *p*-tolualdehyde (TALD), then *p*-toluic acid (PT), 4-carboxybenzaldehyde (4-CBA), and finally to the terephthalic acid (TA) product.



The kinetics of the oxidation are exceedingly complex, but a general understanding of the mechanism has been established.

4 - Applications[edit source

Virtually the entire world's supply of terephthalic acid and dimethyl terephthalate are consumed as precursors to polyethylene terephthalate (PET). World production in 1970 was around 1.75 million tones. By 2006, global purified terephthalic acid (PTA) demand had exceeded 30 million tonnes.

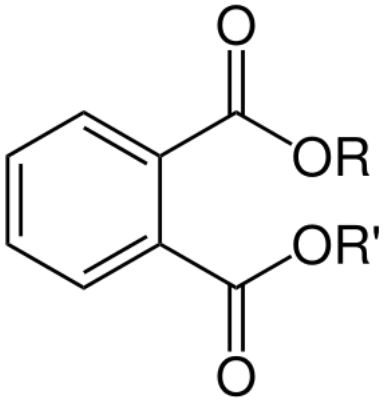
There is a smaller, but nevertheless significant, demand for terephthalic acid in the production of poly butylene terephthalate and several other engineering polymers.

In the research laboratory, terephthalic acid has been popularized as a component for the synthesis of metal - organic frameworks.

The analgesic drug oxycodone occasionally comes as a terephthalate salt; however, the more usual salt of oxycodone is the hydrochloride. Pharmacologically, one milligram of *terephthalas oxycodonae* is equivalent to 1.13 mg of *hydrochloridum oxycodonae*.

Terephthalic acid is used as a filler in some military smoke grenades, most notably the American M83 smoke grenade, producing a thick white smoke when burned.

Phthalate



General chemical structure of phthalates.
(R and R' are general placeholders)

Contents

1 - Introduction

Phthalates (pronounced or **phthalate esters**, are esters of phthalic acid and are mainly used as plasticizers (substances added to plastics to increase their flexibility, transparency, durability, and longevity). They are used primarily to soften polyvinyl chloride (PVC). Phthalates are being phased out of many products in the United States, Canada, and European Union over health concerns.

Phthalates are used in a large variety of products, from enteric coatings of pharmaceutical tablets and nutritional supplements to viscosity control agents, gelling agents, film formers, stabilizers, dispersants, lubricants, binders, emulsifying agents, and suspending agents. End-applications include adhesives and glues, electronics, agricultural adjuvants, building materials, personal-care products, medical devices, detergents and surfactants, packaging, children's toys, modeling clay, waxes, paints, printing inks and coatings, pharmaceuticals, food products, and textiles.

Phthalates are easily released into the environment because there is no covalent bond between the phthalates and plastics in which they are mixed. As plastics age and break down, the release of phthalates accelerates. People are commonly exposed to phthalates, and most Americans tested by the Centers for Disease Control and Prevention have metabolites of multiple phthalates in their urine. Because phthalate plasticizers are not chemically bound to PVC, they can easily leach and evaporate into food or the atmosphere. Phthalate exposure can be through direct use or by indirect means through leaching and general environmental contamination. Diet is believed to be the main source of di (2-ethyl hexyl) phthalate (DEHP) and other phthalates in the general population. Fatty foods such as milk, butter, and meats are a major source.

In studies of rodents exposed to certain phthalates, high doses have been shown to change hormone levels and cause birth defects.[2]

2 – Uses

Phthalates are used in a large variety of products, from enteric coatings of pharmaceutical pills and nutritional supplements to viscosity control agents, gelling agents, film formers, stabilizers, dispersants, lubricants, binders, emulsifying agents, and suspending agents. End-applications include adhesives and glues, agricultural adjuvants, building materials, personal-care products, medical devices, detergents and surfactants, packaging, children's toys, modeling clay, waxes, paints, printing inks and coatings, pharmaceuticals, food products, and textiles. Phthalates are also

frequently used in soft plastic fishing lures, caulk, paint pigments, and sex toys made of so-called "jelly rubber". Phthalates are used in a variety of household applications such as shower curtains, vinyl upholstery, adhesives, floor tiles, food containers and wrappers, and cleaning materials. Personal-care items containing phthalates include perfume, eye shadow, moisturizer, nail polish, liquid soap, and hair spray.[3] They are also found in modern electronics and medical applications such as catheters and blood transfusion devices. The most widely used phthalates are the di (2-ethyl hexyl) phthalate (DEHP), the di iso decyl phthalate (DIDP), and the di iso nonyl phthalate (DINP). DEHP is the dominant plasticizer used in PVC due to its low cost. Benzyl butyl phthalate (BBP) is used in the manufacture of foamed PVC, which is mostly used as a flooring material. Phthalates with small R and R' groups are used as solvents in perfumes and pesticides.

Globally, approximately six million tonnes of plasticizers are consumed every year, of which European consumption accounts for approximately 1 million tones. They contribute 10-60% of plastic products by weight . More recently in Europe, regulatory developments have resulted in a change in phthalate consumption, with the higher phthalates (DINP and DIDP) replacing DEHP as the plasticizer of choice because DIDP and DIP are not classified as hazardous. DEHP, although most applications are shown to pose no risk when studied using recognized methods of risk assessment, has been classified as a Category 1A reprotoxin and is now on the Annex XIV of the European Union's REACH legislation which means that producers and users will need to submit authorization requests to the European Chemicals Agency in Helsinki to continue to use DEHP. Analysis of such applications will involve studies on alternatives and, given the wide number of compounds that have been used as plasticizers, such evaluations are likely to be far reaching.

3 – History

The development of cellulose nitrate in 1846 led to the patent of castor oil in 1856 for use as the first plasticizer. In 1870, camphor became the more favored plasticizer for cellulose nitrate. Phthalates

were first introduced in the 1920s and quickly replaced the volatile and odorous camphor. In 1931, the commercial availability of polyvinyl chloride and the development of di(2-ethylhexyl) phthalate began the boom of the plasticizer PVC industry.

4 – Properties

Phthalate esters are the di alkyl or alkyl aryl esters of phthalic acid (also called 1,2-benzenedicarboxylic acid, not be confused with the structurally isomeric terephthalic or iso phthalic acids); the name *phthalate* derives from phthalic acid, which itself is derived from word "naphthalene". When added to plastics, phthalates allow the long polyvinyl molecules to slide against one another. The phthalates have a clear syrupy liquid consistency and show low water solubility, high oil solubility, and low volatility. The polar carboxyl group contributes little to the physical properties of the phthalates, except when R and R' are very small (such as ethyl or methyl groups). They are colorless, odorless liquids produced by reacting phthalic anhydride with an appropriate alcohol (usually 6- to 13-carbon).

The mechanism by which phthalates and other molecules afford plasticization to polar polymers has been a subject of intense study since the 1960s. The mechanism is one of a polar interactions between the polar centers of the phthalate molecule (the C=O functionality) and the positively charged areas of the vinyl chain, typically residing on the carbon atom of the carbon-chlorine bond. In order for this to be established, the polymer needs to be heated in the presence of the plasticizer, first above the Tg of the polymer and then into a melt state. This enables an intimate mix of polymer and plasticizer to be formed, and for these interactions to occur. When cooled, these interactions remain and the network of PVC chains cannot reform (as is present in un plasticized PVC, or PVC-U). The alkyl chains of the phthalate then screen the PVC chains from each other as well. This explains why small changes in the length of these chains produce small changes in the level of plasticization.

5 - Table of the most common phthalates

Name	Abbreviation	Structural formula
Di methyl hthalate	DMP	$C_6H_4(COOCH_3)_2$
Di ethyl phthalate	DEP	$C_6H_4(COOC_2H_5)_2$
Di allyl phthalate	DAP	$C_6H_4(COOCH_2CH=CH_2)_2$
Di-n-propyl phthalate	DPP	$C_6H_4[COO(CH_2)_2CH_3]_2$
Di-n-butyl phthalate	DBP	$C_6H_4[COO(CH_2)_3CH_3]_2$
Di iso butyl phthalate	DIBP	$C_6H_4[COOCH_2CH(CH_3)_2]_2$
Butyl cyclohexyl phthalate	BCP	$CH_3(CH_2)_3OOCC_6H_4COOC_6H_{11}$
Di-n-pentyl phthalate	DNPP	$C_6H_4[COO(CH_2)_4CH_3]_2$
Dicyclohexyl phthalate	DCP	$C_6H_4[COOC_6H_{11}]_2$
Butyl benzyl phthalate	BBP	$CH_3(CH_2)_3OOCC_6H_4COOCH_2C_6H_5$
Di-n-hexyl phthalate	DNHP	$C_6H_4[COO(CH_2)_5CH_3]_2$
Di iso hexyl phthalate	DIHxP	$C_6H_4[COO(CH_2)_3CH(CH_3)_2]_2$
Diisoheptyl phthalate	DIHpP	$C_6H_4[COO(CH_2)_4CH(CH_3)_2]_2$
Butyl decyl phthalate	BDP	$CH_3(CH_2)_3OOCC_6H_4COO(CH_2)_9CH_3$
Di (2- ethyl hexyl) phthalate	DEHP, DOP	$C_6H_4[COOCH_2CH(C_2H_5)(CH_2)_3CH_3]_2$
Di (n - octyl) phthalate	DNOP	$C_6H_4[COO(CH_2)_7CH_3]_2$
Di iso octyl phthalate	DIOP	$C_6H_4[COO(CH_2)_5CH(CH_3)_2]_2$
n-Octyl n-decyl phthalate	ODP	$CH_3(CH_2)_7OOCC_6H_4COO(CH_2)_9CH_3$
Di iso nonyl phthalate	DINP	$C_6H_4[COO(CH_2)_6CH(CH_3)_2]_2$
Di (2- propyl	DPHP	$C_6H_4[COOCH_2CH(CH_2CH_2CH_3)(CH_2)_4$

heptyl) phthalate		$CH_3]_2$
Di iso decyl phthalate	DIDP	$C_6H_4[COO(CH_2)_7CH(CH_3)_2]_2$
Di undecyl phthalate	DUP	$C_6H_4[COO(CH_2)_{10}CH_3]_2$
Di iso undecyl phthalate	DIUP	$C_6H_4[COO(CH_2)_8CH(CH_3)_2]_2$
Di tridecyl phthalate	DTDP	$C_6H_4[COO(CH_2)_{12}CH_3]_2$
Di iso tridecyl phthalate	DIUP	$C_6H_4[COO(CH_2)_{10}CH(CH_3)_2]_2$

6 - Health effects

6 – 1 – Exposure

Phthalates are easily released into the environment because there is no covalent bond between the phthalates and plastics in which they are mixed. As plastics age and break down, the release of phthalates accelerates. Phthalates in the environment are subject to bio degradation, photo degradation, and anaerobic degradation; therefore, in general, they do not persist in the outdoor environment. Outdoor air concentrations are higher in urban and suburban areas than in rural and remote areas.

In general, indoor air concentrations are higher than outdoor air concentrations due to the nature of the sources. Because of their volatility, DEP and DMP are present in higher concentrations in air in comparison with the heavier and less volatile DEHP. Higher air temperatures result in higher concentrations of phthalates in the air. PVC flooring leads to higher concentrations of BBP and DEHP, which are more prevalent in dust . A 2012 Swedish study of children found that phthalates from PVC flooring was taken up into their bodies, showing that children can ingest phthalates not only from food but also by breathing and through the skin .

People are commonly exposed to phthalates, and most people in the US tested by the Centers for Disease Control and Prevention have metabolites of multiple phthalates in their urine. Recent human bio monitoring data shows that the tolerable intake of children is

exceeded to a considerable degree, in some instances up to 20-fold. Because phthalate plasticizers are not chemically bound to PVC, they can easily leach and evaporate into food or the atmosphere. Phthalate exposure can be through direct use or by indirect means through leaching and general environmental contamination. Diet is believed to be the main source of DEHP and other phthalates in the general population. Fatty foods such as milk, butter, and meats are a major source. Low - molecular - weight phthalates such as DEP, DBP, BBzP may be dermally absorbed. Inhalational exposure is also significant with the more volatile phthalates.

In a 2008 Bulgarian study, higher dust concentrations of DEHP were found in homes of children with asthma and allergies, compared with healthy children's homes . The author of the study stated, "The concentration of DEHP was found to be significantly associated with wheezing in the last 12 months as reported by the parents."[7] Phthalates were found in almost every sampled home in Bulgaria. The same study found that DEHP, BBzP , and DnOP were in significantly higher concentrations in dust samples collected in homes where polishing agents were used. Data on flooring materials was collected, but there was not a significant difference in concentrations between homes where no polish was used that have balatum (PVC or linoleum) flooring and homes with wood. High frequency of dusting did decrease the concentration.

In general, children's exposure to phthalates is greater than that of adults. In a 1990s Canadian study that modeled ambient exposures, it was estimated that daily exposure to DEHP was 9 μg / kg bodyweight / day in infants, 19 μg / kg bodyweight / day in toddlers, 14 μg / kg bodyweight / day in children, and 6 μg / kg body weight / day in adults . Infants and toddlers are at the greatest risk of exposure, because of their mouthing behavior. Body-care products containing phthalates are a source of exposure for infants. The authors of a 2008 study "observed that reported use of infant lotion, infant powder, and infant shampoo were associated with increased infant urine concentrations of [phthalate metabolites], and this association is strongest in younger infants. These findings suggest that dermal exposures may contribute significantly to phthalate body burden in

this population." Though they did not examine health outcomes, they noted that "Young infants are more vulnerable to the potential adverse effects of phthalates given their increased dosage per unit body surface area, metabolic capabilities, and developing endocrine and reproductive systems."

Infants and hospitalized children are particularly susceptible to phthalate exposure. Medical devices and tubing may contain 20-40% Di(2-ethylhexyl) phthalate (DEHP) by weight, which "easily leach out of tubing when heated (as with warm saline/blood) ".[9] Several medical devices contain phthalates including, but not limited to, IV tubing, gloves, nasogastric tubes and respiratory tubing. The Food and Drug Administration did an extensive risk assessment of phthalates in the medical setting and found that neonates may be exposed to five times greater than the allowed daily tolerable intake. This finding led to the conclusion by the FDA that, "Children undergoing certain medical procedures may represent a population at increased risk for the effects of DEHP."

In 2008, the Danish Environmental Protection Agency (EPA) found a variety of phthalates in erasers and warned of health risks when children regularly suck and chew on them. The European Commission Scientific Committee on Health and Environmental Risks (SCHER), however, considers that, even in the case when children bite off pieces from erasers and swallow them, it is unlikely that this exposure leads to health consequences.

Phthalates are also found in medications, where they are used as inactive ingredients in producing enteric coatings. It is not known how many medications are made using phthalates, but some include omeprazole, didanosine , mesalamine , and theophylline. A recent study found that urinary concentrations of mono butyl phthalate, the DBP metabolite, of Asacol (a particular formulation of mesalamine) users was 50 times higher than the mean of nonusers . The study showed that exposures from phthalate-containing medications can far exceed population levels from other sources . DBP in medications raises concern about health risks due to the high level of exposures

associated with taking these medications, especially in vulnerable segments of the population, including pregnant women and children.

In 2008, the United States National Research Council recommended that the cumulative effects of phthalates and other anti androgens be investigated. It criticized US EPA guidances, which stipulate that, when examining cumulative effects, the chemicals examined should have similar mechanisms of action or similar structures, as too restrictive. It recommended instead that the effects of chemicals that cause similar adverse outcomes should be examined cumulatively . Thus, the effect of phthalates should be examined together with other anti androgens, which otherwise may have been excluded because their mechanisms or structure are different.

6 – 2 – Breast cancer

Much of the current research on effects of phthalate exposure has been focused towards children and men's health,[13] however, women may be at higher risk for potential adverse health effects of phthalates due to increased cosmetic use. Diethyl phthalate and dibutyl phthalate are especially ubiquitous in cosmetics and personal care products.[13] According to *in vivo* and observational studies by Davis *et al.* (1994) and Lopez-Carillo *et al.* (2010), there is an association between phthalate exposure and endocrine disruption leading to development of breast cancer. Furthermore, it has been well documented that endocrine disruptors such as phthalates can be additive, so even very small amounts can interact with other chemicals to have cumulative, adverse "cocktail effects"

Phthalate parent compounds and/or their metabolites have recently been implicated as a cause of breast cancer (BC). A 2010 study published in Environmental Health Perspectives for the first time implicated that the exposure to diethyl phthalates (DEP), a parent compound of the mono ethyl phthalate (MEP) metabolite, may be associated with increased risk of BC (Odds Ratio of 2.20, p value for trend, $p < 0.003$). The case-control study was age matched to 233 BC cases residing in northern Mexico. The phthalate level was determined in urine samples collected pretreatment from the cases. This is only a preliminary finding therefore additional research is

required. Interestingly, exposure to the parent phthalate, butylbenzyl phthalate (BBzP) of the mono benzyl phthalate (MBzP) metabolite showed a negative association with breast cancer (Odds ratio=0.46, p value for trend, p<.008). This finding may be associated with the demethylation of the estrogen receptor complex in breast cancer cells of this particular phthalate resulting in a negative effect . This explanation will require further confirmatory research since confounders may be playing an unknown role. It is also known that DEP is found in a high proportion of personal care products, deodorants and perfumes whereas in contrast, BBzP is not detected in most deodorants and hair products and in less than one-third of all products tested , so degree of exposure may also be influencing results. A higher phthalate tertile (microgram / g creatinine) of DEP/MEP was compared to a lower phthalate tertile of BBzP/MBzP in this study. In most cases of breast cancer the cause is unknown and less than 25 % of patients have a history of commonly associated risk factors . such as: early menarche, later age at first childbirth, nulliparity, family history of BC, or history of benign breast biopsy

6 – 3 – Endocrine disruption

In studies of rodents exposed to certain phthalates, high doses have been shown to change hormone levels and cause birth defects.[2] A recent British study showed that the phthalate di(n-butyl) phthalate (DBP) or its metabolite mono butyl phthalate (MBP) suppresses steroidogenesis by fetal-type Leydig cells in primates as in rodents.

In a study published in 2005, lead investigator Dr. Shanna Swan reported in the "Swan Study" that human phthalate exposure during pregnancy results in decreased anogenital distance among baby boys. In this study, phthalate metabolites were measured in urine samples collected from the pregnant women who gave birth to the infants. After birth, the genital features and anogenital distance of these women's babies were measured and correlated with the residue levels in the mother's urine. Boys born to mothers with the highest levels of phthalates were 7 times more likely to have a shortened anogenital distance. An editorial concerning this paper in the same volume stated that the study population was small, and "needs to be

investigated more thoroughly in a larger, more diverse population".[18] While anogenital distance is routinely used as a measure of fetal exposure to endocrine disruptors in animals,[19] this parameter is rarely assessed in humans, and its significance is unknown.[20] One paper states that "Whether anogenital distance measurements in humans relate to clinically important outcomes remains to be determined," and a National Toxicology Program expert panel concluded that anogenital distance is a "'novel index' whose relevance in humans 'has not been established,'" and that there is "insufficient evidence in humans" that DEHP causes harm . The Swan study is thought by some to "suggest that male reproductive development in humans could be affected by prenatal exposure to environmentally relevant levels of phthalates". Authors of a 2006 study of boys with undescended testis hypothesized that exposure to a combination of phthalates and anti-androgenic pesticides may have contributed to that condition.

In contrast to the Swan study, an earlier study found that "adolescents exposed to significant quantities of DEHP as neonates showed no significant adverse effects on their physical growth and pubertal maturity ." This study, however, examined children exposed intravenously to phthalate di esters, and intravenous exposure results in little metabolic conversion of the relatively nontoxic phthalate diester to its more toxic monoester metabolite.

6 – 4 – Other effects

There may be a link between the obesity epidemic and endocrine disruption and metabolic interference. Studies conducted on mice exposed to phthalates in utero did not result in metabolic disorder in adults . However, "in a national cross-section of U.S. men, concentrations of several prevalent phthalate metabolites showed statistically significant correlations with abnormal obesity and insulin resistance."[29] Mono- ethyl hexyl-phthalate (MEHP), a metabolite of DEHP, has been found to interact with all three peroxisome proliferator-activated receptors (PPARs) . PPARs are members of the nuclear receptor superfamily. The author of the study stated "The roles of PPARs in lipid and carbohydrate metabolism raise the question of their activation by a sub-class of pollutants, tentatively

named metabolic disrupters."[29] Phthalates belong to this class of metabolic disruptors. It is a possibility that, over many years of exposure to these metabolic disruptors, they are able to deregulate complex metabolic pathways in a subtle manner. A 2011 study of New York City children found an association between phthalate metabolite urinary concentrations and larger body size measurements. A 2012 study suggested that high levels of phthalates may be connected to the current obesity epidemic in children. It was found that obese children show greater exposure to phthalates than nonobese children. It was reported that the obesity risk increases according to the level of the chemical found in the children's bloodstream.

Large amounts of specific phthalates fed to rodents have been shown to damage their liver and testes , and initial rodent studies also indicated hepatocarcinogenicity. Following this result, di(2-ethylhexyl) phthalate was listed as a possible carcinogen by IARC, EC, and WHO. Later studies on primates showed that the mechanism is specific to rodents - humans are resistant to the effect. The carcinogen classification was subsequently withdrawn.

In 2004, a joint Swedish-Danish epidemiologic team found a link between allergies in children and the phthalates DEHP and BBzP. Their review article and meta-analysis of published data relating to phthalates and asthma found an association between phthalates in the home and asthma, especially in children, but this evidence was limited by imprecise data on levels of exposure.

In 2007, a cross - sectional study of U.S. males concluded that urine concentrations of four phthalate metabolites correlate with waist size and three phthalate metabolites correlate with the cellular resistance to insulin, a precursor to Type II diabetes. The authors note the need for follow-up longitudinal studies, as waist size is known to correlate with insulin resistance. A 2012 study found that people with elevated phthalate levels had roughly twice the risk of developing diabetes compared with those with lower levels. They also found that phthalates were associated with disrupted insulin production.

A 2009 study published in the Journal of Pediatrics found that prenatal phthalate exposure was related to low birth weight in infants. Low birth weight is the leading cause of death in children under 5 years of age and increases the risk of cardiovascular and metabolic disease in adulthood . Researchers at the University of Michigan School of Public Health found that women who deliver prematurely have, on average, up to three times the phthalate level in their urine compared to women who carry to term.

In 2009, South Korean scientists reported findings of a statistically significant correlation between urine phthalate concentrations in children and symptoms of ADHD. Although more research is needed in order to conclusively determine the relationship between phthalate and ADHD, the article suggests that consumers should be aware of its potential effects on behavior and neurological disorders . The findings were replicated in The Mount Sinai Children's Environmental Health Study, which enrolled a multiethnic prenatal population in New York City between 1998 and 2002 (n = 404), published in Jan 2010. There was an association of prenatal phthalate exposure with offspring behavior and executive functioning at ages 4 to 9 years . A study published in 2011 followed the children of 319 women who gave birth between 1999 and 2006 to evaluate possible associations between prenatal exposures to phthalates and possible adverse effects in development at age 3 years. The results suggested that prenatal exposure to phthalates had affected the children's mental, motor and behavioral development during the preschool years. The senior epidemiologist on the study stated, "The results are concerning since increasing exposures from the lowest 25% to the highest 25 % among the women in our study was associated with a doubling or tripling in the odds of motor and/or behavioral problems in the children".

6 – 5 – Biological alternatives

There are numerous biological alternatives on the market. The problem is that they are typically expensive and not compatible as a primary plasticizer.

A plasticizer based on vegetable oil has been developed which uses single reactor synthesis and is compatible as a primary plasticizer. It is a ready substitute for di octyl phthalate.

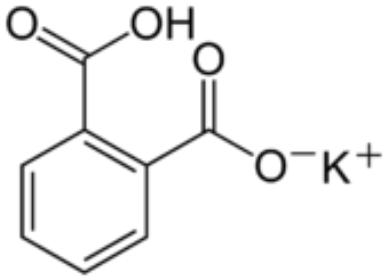
7 - Identification in plastics

Some type 3 plastics may leach phthalates.

Phthalates are used in some but not all PVC formulations, and there are no specific labeling requirements for phthalates. PVC plastics are typically used for various containers and hard packaging, medical tubing, and bags, and are labeled "Type 3" for recycling reasons. However, the presence of phthalates rather than other plasticizers is not marked on PVC items. Only un plasticized PVC (uPVC), which is mainly used as a hard construction material, has no plasticizers. If a more accurate test is needed, chemical analysis, for example by gas chromatography or liquid chromatography, can establish the presence of phthalates.

Polyethylene terephthalate (PETE) is the main substance used to package bottled water and many sodas. Products containing PETE are labeled "Type 1" (with a "1" in the recycle triangle) for recycling purposes. Although the word "phthalate" appears in the name, PETE does not use phthalates as plasticizers. The terephthalate polymer PETE and the phthalate ester plasticizers are chemically different substances . Despite this, however, a number of studies have found phthalates such as DEHP in bottled water and soda. One hypothesis is that these may have been introduced during plastics recycling. Several studies tested the liquids before they were bottled, in order to make sure the phthalates came from the bottles rather than already being in the water.

Potassium Hydrogen Phthalate



IUPAC name : Potassium hydrogen phthalate	
Other names : hydrogen potassium phthalate; phthalic acid potassium salt; potassium bi phthalate; potassium acid phthalate; 1,2-benzene di carboxylic acid , mono potassium salt; KHP; KHPh	
Molecular formula	$C_8 H_5 K O_4$
Molar mass	204 g mol^{-1}
Appearance	White or colorless solid
Density	1.636 g / cm^3
Melting point	~ 295 °C (decomposes)
Solubility in water	25 g / 100 ml
Solubility	slightly soluble in alcohol
Main hazards	Irritant to eyes, skin, and respiratory system
Flash point	Non - flammable

Potassium hydrogen phthalate, often called simply **KHP**, is an acidic salt compound. It forms white powder, colorless crystals, a colorless solution, and an ionic solid that is the mono potassium salt of phthalic acid. The hydrogen is slightly acidic, and it is often used

as a primary standard for acid-base titrations because it is solid and air-stable, making it easy to weigh accurately. It is not hygroscopic. It is also used as a primary standard for calibrating pH meters because, besides the properties just mentioned, its pH in solution is very stable.

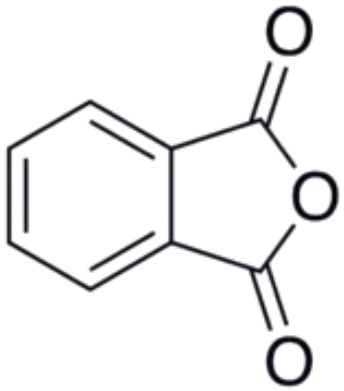
In water KHP dissociates completely giving the potassium cation (K^+) and hydrogen phthalate anion (HP^- or Hphthalate$^-$). As a weak acid hydrogen phthalate reacts reversibly with water to give hydronium (H_3O^+) and phthalate ions.

$$HP^- + H_2O \rightleftharpoons P^{2-} + H_3O^+$$

KHP can be used as a buffering agent (in combination with hydrochloric acid (HCl) or sodium hydroxide (Na OH) depending on which side of pH 4.0 the buffer is to be) but should not be used as a buffer for decarboxylation reactions, as these will degrade the KHP and mop up the conjugation groups.

KHP is also a useful standard for total organic carbon (TOC) testing. Most TOC analyzers are based on the oxidation of organics to carbon dioxide and water, with subsequent quantitation of the carbon dioxide. Many TOC analyzers suggest testing their instruments with two standards: one typically easy for the instrument to oxidize (KHP), and one more difficult to oxidize. For the latter, benzoquinone is suggested.

Phthalic Anhydride



Contents

1 - Introduction

Phthalic anhydride is the organic compound with the formula $C_6H_4(CO)_2O$. It is the anhydride of phthalic acid. This colourless solid is an important industrial chemical, especially for the large-scale production of plasticizers for plastics. In 2000, the world wide production volume of phthalic anhydride is estimated to be about 3 232 000 tones per year.

IUPAC name : 2-benzo furan-1,3-dione	
Other names : Iso benzo furan-1,3-dione	
Molecular formula	$C_8H_4O_3$
Molar mass	148 g / mol
Appearance	white flakes
Density	1.53 g/cm^3, solid

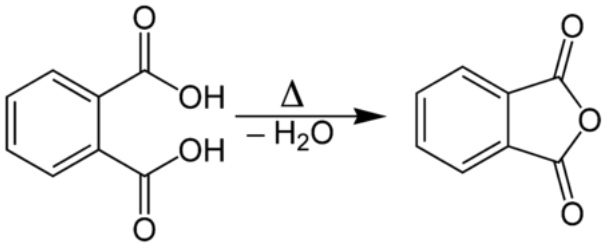
Melting point	131 °C
Boiling point	295 °C *subl.*
Solubility in water	0.62 g / 100g (20—25 °C); 19.0 g / 100g (100 °C); reacts slowly
Flash point	152 °C

2 - Synthesis and production

Phthalic anhydride was first reported in 1836 by Auguste Laurent. It is presently obtained by catalytic oxidation of *ortho*-xylene and naphthalene ("Gibbs phthalic anhydride process"):

$$C_6H_4(CH_3)_2 + 3\ O_2 \rightarrow C_6H_4(CO)_2O + 3\ H_2O$$
$$C_{10}H_8 + 4.5\ O_2 \rightarrow C_6H_4(CO)_2O + 2\ H_2O + 2\ CO_2$$

The catalyst that is used for the oxidation of xylene is a modified vanadium pent oxide (V_2O_5). When separating the phthalic anhydride from byproducts such as *o*-xylene in water, or maleic anhydride, a series of “switch condensers” is required. Phthalic anhydride can also be prepared from phthalic acid:



3 - Applications in industry and organic synthesis

Phthalic anhydride is a versatile intermediate in organic chemistry, in part because it is bi functional and cheaply available. It undergoes hydrolysis and alcoholysis. Hydrolysis by hot water forms *ortho*-phthalic acid. This process is reversible: Phthalic anhydride re-forms upon heating the acid above 180 °C.[3] Hydrolysis of anhydrides is not typically a reversible process. However, phthalic acid is easily dehydrated to form phthalic anhydride due to the creation of a thermo dynamically favorable 5-membered ring.

4 - Preparation of phthalate esters

As with other anhydrides, the alcoholysis reaction is the basis of the manufacture of phthalate esters, which are widely used (and controversial - see endocrine disruptor) plasticizers. In the 1980s, approximately 6.5×10^9 kg of these esters were produced annually, and the scale of production was increasing each year, all from phthalic anhydride. The process begins with the reaction of phthalic anhydride with alcohols, giving the monoesters:

$$C_6H_4(CO)_2O + ROH \rightarrow C_6H_4(CO_2H)CO_2R$$

The second esterification is more difficult and requires removal of water:

$$C_6H_4(CO_2H)CO_2R + ROH \rightleftarrows C_6H_4(CO_2R)_2 + H_2O$$

The most important di ester is bis (2-ethyl hexyl) phthalate ("DEHP"), used in the manufacture of polyvinyl chloride.

5 - Organic synthesis

Phthalic anhydride is a precursor to a variety of reagents useful in organic synthesis. Important derivatives include phthalimide and its many derivatives. Chiral alcohols form half-esters (see above), and these derivatives are often resolvable because they form diastereomeric salts with chiral amines such as brucine. A related ring - opening reaction involves peroxides to give the useful peroxy acid:

$$C_6H_4(CO)_2O + H_2O_2 \rightarrow C_6H_4(CO_3H)CO_2H$$

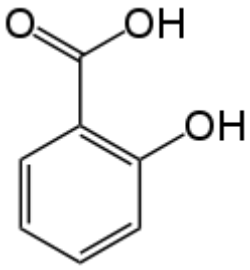
6 - Precursor to dyestuffs

Phthalic anhydride is widely used in industry for the production of certain dyes. A well-known application of this reactivity is the preparation of the anthroquinone dye quinizarin by reaction with para-chloro phenol followed by hydrolysis of the chloride.

7 - Pharmaceutical applications

Phthalic anhydride reacted with cellulose acetate forms cellulose acetate phthalate (CAP), a common enteric coating excipient that has also been shown to have antiviral activity. Phthalic anhydride is a degradation product of CAP.

Salicylic Acid



Contents

1 - Introduction

Salicylic acid (from Latin salix, willow tree, from the bark of which the substance used to be obtained) is a mono hydroxy benzoic acid, a type of phenolic acid and a beta hydroxy acid. This colorless crystalline organic acid is widely used in organic synthesis and functions as a plant hormone. It is derived from the metabolism of salicin. In addition to being an important active metabolite of aspirin (acetylsalicylic acid), which acts in part as a prod rug to salicylic acid, it is probably best known for its use in anti-acne treatments. The salts and esters of salicylic acid are known as salicylates.

IUPAC name : 2-Hydroxybenzoic acid	
Molecular formula	$C_7 H_6 O_3$
Molar mass	138 g mol−1
Density	1.443 g / cm^3
Melting point	159.0 °C

Boiling point	211 °C (20 mmHg)
Solubility in water	2 g / L (20 °C)
Acidity (pKa)	2.97
EU classification	Harmful (Xn)
Flash point	157 °C
Auto ignition temperature	545 °C

2 - Chemistry

Salicylic acid has the formula C_6H_4 (OH) COOH, where the OH group is ortho to the carboxyl group. It is also known as 2-hydroxybenzoic acid. It is poorly soluble in water (2 g / L at 20 °C). Aspirin (acetyl salicylic acid or ASA) can be prepared by the esterification of the phenolic hydroxyl group of salicylic acid with the acetyl group from acetic anhydride or acetyl chloride.

3 - Plant hormone

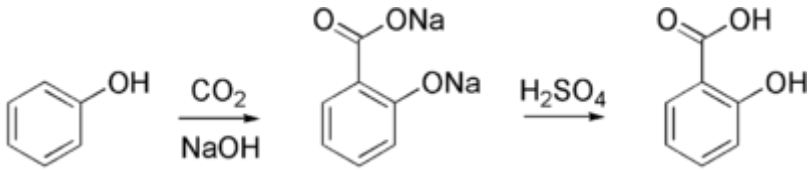
Salicylic acid (SA) is a phenolic phytohormone and is found in plants with roles in plant growth and development, photosynthesis, transpiration, ion uptake and transport. SA also induces specific changes in leaf anatomy and chloroplast structure. SA is involved in endogenous signaling, mediating in plant defense against pathogens. It plays a role in the resistance to pathogens by inducing the production of pathogenesis-related proteins . It is involved in the systemic acquired resistance (SAR) in which a pathogenic attack on one part of the plant induces resistance in other parts. The signal can also move to nearby plants by salicylic acid being converted to the volatile ester, methyl salicylate.

4 - Production

Salicylic acid is biosynthesized from the amino acid phenylalanine. In Arabidopsis thaliana it can also be synthesized via a phenylalanine - independent pathway.

Sodium salicylate is commercially prepared by treating sodium phenolate (the sodium salt of phenol) with carbon dioxide at high pressure (100 atm) and high temperature (390K) -a method known as

the Kolbe-Schmitt reaction. Acidification of the product with sulfuric acid gives salicylic acid :



It can also be prepared by the hydrolysis of aspirin (acetylsalicylic acid) or methyl salicylate (oil of winter green) with a strong acid or base.

5 - History

White willow (Salix alba) is a natural source of salicylic acid

The Greek physician Hippocrates wrote in the 5th century BC about a bitter powder extracted from willow bark that could ease aches and pains and reduce fevers . This remedy was also mentioned in texts from ancient Sumer , Lebanon , and As syria . The Cherokee and other Native Americans used an infusion of the bark for fever and other medicinal purposes for centuries . The medicinal part of the plant is the inner bark and was used as a pain reliever for a variety of ailments. The Reverend Edward Stone, a vicar from Chipping Norton,

Oxford shire, England, noted in 1763 that the bark of the willow was effective in reducing a fever.

The active extract of the bark, called salicin, after the Latin name for the white willow (Salix alba), was isolated and named by the German chemist Johann Andreas Buchner in 1826. A larger amount of the substance was isolated in 1828 by Henri Leroux, a French pharmacist. Raffaele Piria, an Italian chemist was able to convert the substance into a sugar and a second component, which on oxidation becomes salicylic acid.

Salicylic acid was also isolated from the herb meadowsweet (Filipendula ulmaria, formerly classified as Spiraea ulmaria) by German researchers in 1839. While their extract was somewhat effective, it also caused digestive problems such as gastric irritation, bleeding, diarrhea, and even death when consumed in high doses.

6 - Dietary sources

Unripe fruits and vegetables are natural sources of salicylic acid, particularly blackberries, blueberries, cantaloupes, dates, raisins, kiwi fruits, guavas, apricots, green pepper, olives, tomatoes, radish and chicory; also mushrooms. Some herbs and spices contain quite high amounts, although meat, poultry, fish, eggs and dairy products all have little to no salicylates. Of the legumes, seeds, nuts, and cereals, only almonds, water chestnuts and peanuts have significant amounts.

7 - Medicinal and cosmetic uses

Salicylic acid is known for its ability to ease aches and pains and reduce fevers. These medicinal properties, particularly fever relief, have been known since ancient times, and it is used as an anti-inflammatory drug.

In modern medicine, salicylic acid and its derivatives are used as constituents of some rubefacient products. For example, methyl salicylate is used as a liniment to soothe joint and muscle pain, and choline salicylate is used topically to relieve the pain of mouth ulcers.

As with other beta hydroxy acids, salicylic acid is a key ingredient in many skin-care products for the treatment of seborrhoeic dermatitis, acne, psoriasis, calluses, corns, keratosis pilaris, and warts. The standard treatment for calluses is a 6% aspirin suspension in petroleum jelly, applied on the callus for one hour and then removed with washing. It works as a keratolytic , bacteriocide and comedolytic agent by causing the cells of the epidermis to shed more readily, opening clogged pores and neutralizing bacteria within, preventing pores from clogging up again by constricting pore diameter, and allowing room for new cell growth . Because of its effect on skin cells, salicylic acid is used in several shampoos to treat dandruff. Use of concentrated solutions of salicylic acid may cause hyper - pigmentation on un pretreated skin for those with darker skin types (Fitzpatrick photo types IV, V, VI) , as well as with the lack of use of a broad spectrum sunblock.

Bismuth subsalicylate, a salt of bismuth and salicylic acid, is the active ingredient in stomach relief aids such as Pepto - Bismol .

8 - Mechanism of action

Salicylic acid has been shown to work through several different pathways. It produces its anti - inflammatory effects via suppressing the activity of cyclo oxygenase (COX), an enzyme which is responsible for the production of pro - inflammatory mediators such as the prostaglandins. Notably, it does this not by direct inhibition of COX, unlike most other non-steroidal anti-inflammatory drugs (NSAIDs), but instead by suppression of the expression of the enzyme (via a yet-un elucidated mechanism) . Salicylic acid has also been shown to activate adenosine monophosphate-activated protein kinase (AMPK), and it is thought that this action may play a role in the anticancer effects of the compound and its prod rugs aspirin and salsalate. In addition, the anti diabetic effects of salicylic acid are likely mediated by AMPK activation primarily through allosteric conformational change that increases levels of phosphorylation.[17] Salicylic acid also uncouples oxidative phosphorylation which leads to increased ADP:ATP and AMP:ATP ratios in the cell. Consequently, salicylic acid may alter AMPK activity and

subsequently exert its anti-diabetic properties through altered energy status of the cell. Even in AMPK knock - out mice, however, there is an anti-diabetic effect demonstrating that there is at least one additional, yet - unidentified action of the compound.

9 - Other uses

Although toxic in large quantities, salicylic acid is used as a food preservative and as bactericidal and an antiseptic . For some people with salicylate sensitivity even these small doses can be harmful .

Sodium salicylate is a useful phosphor in the vacuum ultraviolet with nearly flat quantum efficiency for wavelengths between 10 to 100 nm . It fluoresces in the blue at 420 nm. It is easily prepared on a clean surface by spraying a saturated solution of the salt in methanol followed by evaporation.

10 - Safety

Topically, as a beta-hydroxy acid (and unlike alpha-hydroxy acids) salicylic acid is capable of penetrating and breaking-down fats and lipids, making it capable of causing moderate chemical burns of the skin if at very high concentrations. It is capable of damaging the lining of pores in such cases if the solvent is alcohol, acetone, or an oil. Over-the-counter limits are set at 2 % for topical left on the face and 3% for those expected to be washed off, such as acne cleansers or shampoo. Caution should be exercised when handling large volumes of salicylic acid, and protective gloves are recommended for any repeat, prolonged exposure. 17 % salicylic acid, which is often sold for wart removal, should not be applied to the face and should not be used for acne treatment. Even for wart removal, such a solution should only be applied twice a day – more frequent use may lead to an increase in side effects without an increase in efficacy.

When ingested, salicylic acid has a possible ototoxic effect by inhibiting prestin. It can induce transient hearing loss in zinc-deficient individuals. This finding is based on clinical studies with rats. An injection of salicylic acid induced hearing loss in zinc -

deficient rats, while a simultaneous injection of zinc reversed the hearing loss. An injection of magnesium in the zinc-deficient rats did not reverse the salicylic acid-induced hearing loss.

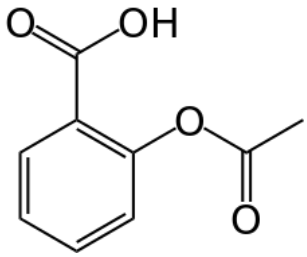
There are no studies specifically looking at topical salicylic acid in pregnancy. Oral salicylic acid has not been associated with an increase in malformations if used during the first trimester, but use in late pregnancy has been associated with bleeding, especially intracranial bleeding . The risks of aspirin late in pregnancy are probably not relevant for a topical exposure to salicylic acid, even late in the pregnancy, because of its low systemic levels. Topical salicylic acid is common in many over-the-counter dermatological agents, and the lack of adverse reports suggests a low teratogenic potential.

Salicylic acid over dose can lead to salicylate intoxication, which often presents clinically in a state of metabolic acidosis with compensatory respiratory alkalosis. In patients presenting with an acute overdose, a 16 % morbidity rate and a 1 % mortality rate are observed .

Some people are hypersensitive to salicylic acid and related compounds.

The United States Food and Drug Administration recommends the use of sun protection when using skincare products containing salicylic acid (or any other BHA) on sun-exposed skin areas.

Acetyl Salicylic Acid
(Aspirin)



Contents

1 - Introduction

Aspirin (USAN), also known as acetyl salicylic acid (abbreviated ASA) , is a salicylate drug, often used as an analgesic to relieve minor aches and pains, as an antipyretic to reduce fever, and as an anti - inflammatory medication. Aspirin was first isolated by Felix Hoffmann, a chemist with the German company Bayer in 1897.

Salicylic acid, the main metabolite of aspirin, is an integral part of human and animal metabolism. While in humans much of it is attributable to diet, a substantial part is synthesized endogenously.

Aspirin also has an antiplatelet effect by inhibiting the production of thromboxane, which under normal circumstances binds platelet molecules together to create a patch over damaged walls of blood vessels. Because the platelet patch can become too large and also block blood flow, locally and downstream, aspirin is also used long-term, at low doses, to help prevent heart attacks, strokes, and blood clot formation in people at high risk of developing blood clots.[4] It has also been established that low doses of aspirin may be given immediately after a heart attack to reduce the risk of another heart attack or of the death of cardiac tissue.[5][6] Aspirin may be effective at preventing certain types of cancer, particularly colorectal cancer.

The main undesirable side effects of aspirin taken by mouth are gastrointestinal ulcers, stomach bleeding, and tinnitus, especially in higher doses. In children and adolescents, aspirin is no longer indicated to control flu - like symptoms or the symptoms of chickenpox or other viral illnesses, because of the risk of Reye's syndrome.

Aspirin is part of a group of medications called non steroidal anti - inflammatory drugs (NSAIDs), but differs from most other NSAIDs in the mechanism of action. Though it, and others in its group called the salicylates, have similar effects (antipyretic, anti-inflammatory, analgesic) to the other NSAIDs and inhibit the same enzyme cyclooxygenase, aspirin (but not the other salicylates) does so in an irreversible manner and, unlike others, affects more the COX-1 variant than the COX-2 variant of the enzyme.

Today, aspirin is one of the most widely used medications in the world, with an estimated 40,000 tonnes of it being consumed each year . In countries where Aspirin is a registered trademark owned by Bayer, the generic term is acetylsalicylic acid (ASA).

Systematic (IUPAC) name : 2-acetoxy benzoic acid	
Bioavailability	Rapidly and completely absorbed
Protein binding	99.6 %
Metabolism	Hepatic
Half - life	300 – 650 mg dose: 3.1–3.2 h 1 g dose: 5 h 2 g dose: 9 h
Synonyms	2-acetyl oxy benzoic acid acetyl salicylate acetyl salicylic acid O - acetyl salicylic acid
Chemical data	
Formula	$C_9 H_8 O_4$
Mol. mass	180 g / mol
Density	1.40 g / cm³
Melt. point	136 °C
Boiling point	140 °C (decomposes)
Solubility in water	3 mg / mL (20 °C)

2 - Medical use

Aspirin is used in the treatment of a number of conditions, including fever, pain, rheumatic fever, and inflammatory diseases, such as rheumatoid arthritis, pericarditis, and Kawasaki disease.[14] Lower doses of aspirin have also shown to reduce the risk of death from a heart attack, or the risk of stroke in some circumstances. There is some evidence that aspirin is effective at preventing colorectal cancer, though the mechanisms of this effect are unclear.

2 – 1 - Pain[edit source

Asprin 325 MG for pain

In most cases, aspirin is considered inferior to ibuprofen for the alleviation of pain, because aspirin is more likely to cause gastrointestinal bleeding . Aspirin is generally ineffective for those pains caused by muscle cramps, bloating, gastric distension, or acute skin irritation.[20] As with other NSAIDs, combinations of aspirin and caffeine provide slightly greater pain relief than aspirin alone.[21] Effervescent formulations of aspirin, such as Alka - Seltzer or Blowfish,[22] relieve pain faster than aspirin in tablets , which makes them useful for the treatment of migraines.

Topical aspirin may be effective for treating some types of neuropathic pain.

2 – 2 – Headache

Aspirin, either by itself or in combined formulation, effectively treats some types of headache, but its efficacy may be questionable for others. Secondary headaches, meaning those caused by another disorder or trauma, should be promptly treated by a medical provider.

Among primary headaches, the International Classification of Headache Disorders distinguishes between tension headache (the most common), migraine, and cluster headache. Aspirin or other over-the-counter analgesics are widely recognized as effective for the treatment of tension headache. Aspirin, especially as a component of an acetaminophen/aspirin/caffeine formulation (e.g., Excedrin Migraine), is considered a first - line therapy in the treatment of migraine, and comparable to lower doses of sumatriptan. It is most effective at stopping migraines when they are first beginning . There is little data that suggest the aspirin is an effective treatment for cluster headache.

2 – 3 – Fever

Like its ability to control pain, aspirin's ability to control fever is due to its action on the prostaglandin system through its irreversible inhibition of COX . Although aspirin's use as an antipyretic in adults is well - established, many medical societies and regulatory agencies (including the American Academy of Family Physicians, the American Academy of Pediatrics, and the United States Food and Drug Administration) strongly advise against using aspirin for treatment of fever in children because of the risk of Reye's syndrome, a rare but often fatal illness associated with the use of aspirin or other salicylates in children during episodes of viral or bacterial infection. Because of the risk of Reye's syndrome in children, in 1986, the FDA required labeling on all aspirin - containing medications advising against its use in children and teenagers.

2 – 4 - Heart attacks and strokes

For a subset of the population, aspirin may help prevent heart attacks and strokes. In lower doses, aspirin has been known to prevent the progression of existing cardiovascular disease, and reduce the frequency of these events for those with a history of them . (This is known as *secondary prevention*.)

Aspirin appears to offer little benefit to those at lower risk of heart attack or stroke — for instance, those without a history of these events or with pre - existing disease. (This is called *primary prevention.*) Some studies recommend aspirin on a case-by-case basis,

while others have suggested that the risks of other events, such as gastrointestinal bleeding, were significant enough to outweigh any potential benefit, and recommended against using aspirin for primary prevention entirely.

Complicating the use of aspirin for prevention is the phenomenon of aspirin resistance . For patients who are resistant, aspirin's efficacy is reduced, which can cause an increased risk of stroke . Some authors have suggested testing regimes to identify those patients who are resistant to aspirin or other anti-thrombotic drugs (such as clopidogrel).

Aspirin has also been suggested as a component of a polypill for prevention of cardiovascular disease.

2 – 5 - Post – surgery

After percutaneous coronary interventions (PCIs), such as the placement of a coronary artery stent, a US Agency for Healthcare Research and Quality guideline recommends that aspirin be taken indefinitely.[44] Frequently, aspirin is combined with an ADP receptor inhibitor, such as clopidogrel, prasugrel or ticagrelor to prevent blood clots. This is called *dual anti-platelet therapy (DAPT)*. US and EU guidelines disagree somewhat about how long, and for what indications this combined therapy should be continued post-surgery. US guidelines recommend DAPT for at least 12 months while EU guidelines recommend DAPT for 6–12 months after drug eluting stent.[45] However, they agree that aspirin be continued indefinitely after DAPT is complete.

2 – 6 - Cancer prevention

Aspirin's effect on cancer has been widely studied, particularly its effect on colorectal cancer (CRC). Multiple meta-analyses and reviews have concluded that regular use of aspirin reduces the long-term risk of CRC incidence and mortality.[18][46][47][48] However, the relationships of aspirin dose and duration of use to the various types of CRC risk, including mortality, progression, and incidence, are not well-defined. While the majority of data on aspirin and CRC risk comes from observational studies, rather than randomized controlled

trials (RCTs), the available data from RCTs suggests that long-term use of low dose aspirin may be effective at preventing some types of CRC.[49] In the 2007 United States Preventive Services Task Force (USPSTF) guidelines on this topic, use of aspirin for prevention of CRC was given a "D" rating,[50] advising healthcare practitioners against routinely using aspirin for this purpose.

An online news story posted and accessed on Tuesday, June 18, 2013 by Jeffrey Norris at the University of California at San Francisco (UCSF) stated: "Aspirin is known to lower risk for some cancers, and a new study led by a UC San Francisco scientist points to a possible explanation, with the discovery that aspirin slows the accumulation of DNA mutations in abnormal cells in at least one pre-cancerous condition. 'Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs), which are commonly available and cost-effective medications, may exert cancer-preventing effects by lowering mutation rates,' said Dr. Carlo Maley, Ph.D., a member of the UCSF Helen Diller Family Comprehensive Cancer Center, and an expert on how cancers evolve in the body over time. In the study, published June 13 in the online journal PLOS Genetics, Maley – working with gastroenterologist and geneticist Dr. Brian Reid, M.D., Ph.D., of the Fred Hutchinson Cancer Research Center– analyzed biopsy samples from 13 patients with a pre-cancerous condition called Barrett's esophagus who were tracked for six to 19 years. In an 'observational crossover' study design, some patients started out taking daily aspirin for several years, and then stopped, while others started taking aspirin for the first time during observation. The goal was to track the rate of mutations in tissues sampled at different times. The researchers found that biopsies taken while patients were on an aspirin regimen had on average accumulated new mutations about 10 times more slowly than biopsies obtained during years when patients were not taking aspirin. 'This is the first study to measure genome-wide mutation rates of a pre-malignant tissue within patients for more than a decade, and the first to evaluate how aspirin affects those rates,' Maley said. Gender and ethnic distribution of study patients reflected the known demographics of esophageal cancer, which predominantly

affects white, middle-aged and elderly men, he said. Barrett's esophagus only occasionally progresses to esophageal cancer."

2 – 7 - Other uses

Aspirin is a first-line treatment for the fever and joint pain symptoms of acute rheumatic fever. The therapy often lasts for one to two weeks, and is rarely indicated for longer periods. After fever and pain have subsided, the aspirin is no longer necessary, since it does not decrease the incidence of heart complications and residual rheumatic heart disease. Naproxen has been shown to be as effective as aspirin and less toxic, but due to the limited clinical experience, naproxen is recommended only as a second-line treatment.

Along with rheumatic fever, Kawasaki disease remains one of the few indications for aspirin use in children in spite of a lack of high quality evidence for its effectiveness.

Low dose aspirin supplementation has moderate benefits when used for prevention of pre- eclampsia.

2 – 8 – Resistance

For some people, aspirin does not have as strong an effect on platelets as for others, an effect known as aspirin resistance or insensitivity. One study has suggested women are more likely to be resistant than men , and a different, aggregate study of 2,930 patients found 28 % were resistant . A study in 100 Italian patients, on the other hand, found that, of the apparent 31 % aspirin - resistant subjects, only 5 % were truly resistant, and the others were noncompliant . Another study of 400 healthy volunteers found no subjects who were truly resistant, but some had "pseudo resistance, reflecting delayed and reduced drug absorption."

2 – 9 – Dosage

Adult aspirin tablets are produced in standardized sizes, which vary slightly from country to country, for example 300 mg in Britain and 325 mg in the USA. Smaller doses are based on these standards (e.g., 75 mg and 81 mg tablets.) The 81 mg tablets are called "baby-strength." There is no medical significance in the slight difference in

dosage between the 75 mg and the 81 mg tablets. Of historical interest, in the US, a 325 mg dose is equivalent to the historic 5 grain aspirin tablet in use prior to the metric system.

In general, for adults, doses are taken four times a day for fever or arthritis , with doses near the maximal daily dose used historically for the treatment of rheumatic fever . For the prevention of myocardial infarction in someone with documented or suspected coronary artery disease, much lower doses are taken once daily.

Recommendations from the USPSTF on the use of aspirin for the primary prevention of coronary heart disease encourage men aged 45–79 and women aged 55–79 to use aspirin when the potential benefit of a reduction in myocardial infarction (MI) for men or stroke for women out weighs the potential harm of an increase in gastrointestinal hemorrhage . The WHI study said regular low dose (75 or 81 mg) aspirin female users had a 25 % lower risk of death from cardiovascular disease and a 14 % lower risk of death from any cause.[66] Low dose aspirin use was also associated with a trend toward lower risk of cardiovascular events, and lower aspirin doses (75 or 81 mg/day) may optimize efficacy and safety for patients requiring aspirin for long-term prevention.

In children with Kawasaki disease, aspirin is taken at dosages based on body weight, initially four times a day for up to two weeks and then at a lower dose once daily for a further six to eight weeks.

3 - Adverse effects

3 – 1 – Contraindications

Aspirin should not be taken by people who are allergic to ibuprofen or naproxen , or who have salicylate intolerance[70][71] or a more generalized drug intolerance to NSAIDs, and caution should be exercised in those with asthma or NSAID - precipitated bronchospasm. Owing to its effect on the stomach lining, manufacturers recommend people with peptic ulcers, mild diabetes, or gastritis seek medical advice before using aspirin . Even if none of these conditions is present, the risk of stomach bleeding is still increased when aspirin is taken with alcohol or warfarin. Patients

with hemophilia or other bleeding tendencies should not take aspirin or other salicylates . Aspirin is known to cause hemolytic anemia in people who have the genetic disease glucose - 6 - phosphate dehydrogenase deficiency, particularly in large doses and depending on the severity of the disease. Use of aspirin during dengue fever is not recommended owing to increased bleeding tendency.[74] People with kidney disease, hyperuricemia , or gout should not take aspirin because it inhibits the kidneys' ability to excrete uric acid, and thus may exacerbate these conditions. Aspirin should not be given to children or adolescents to control cold or influenza symptoms, as this has been linked with Reye's syndrome.

3 – 2 – Gastrointestinal

Aspirin use has been shown to increase the risk of gastrointestinal bleeding . Although some enteric-coated formulations of aspirin are advertised as being "gentle to the stomach", in one study, enteric coating did not seem to reduce this risk. Combining aspirin with other NSAIDs has also been shown to further increase this risk.[75] Using aspirin in combination with clopidogrel or warfarin also increases the risk of upper gastrointestinal bleeding.

It appears that blockade of COX-1 by aspirin results in the up regulation of COX-2 as part of a gastric defense and that taking COX-2 inhibitors concurrently with aspirin increases the gastric mucosal erosion . Therefore, caution should be exercised if combining aspirin with any "natural" supplements with COX-2 inhibiting properties, such as garlic extracts , curcumin, bilberry, pine bark, ginkgo, fish oil, resveratrol, genistein, quercetin, resorcinol, and others.

In addition to enteric coating, "buffering" is the other main method companies have used to try to mitigate the problem of gastrointestinal bleeding. Buffering agents are intended to work by preventing the aspirin from concentrating in the walls of the stomach, although the benefits of buffered aspirin are disputed. Almost any buffering agent used in antacids can be used; Bufferin, for example, uses MgO . Other preparations use Ca CO_3.

Taking it with vitamin C is a more recently investigated method of protecting the stomach lining. Taking equal doses of vitamin C and aspirin may decrease the amount of stomach damage that occurs compared to taking aspirin alone.

3 – 3 - Central effects

Large doses of salicylate, a metabolite of aspirin, have been proposed to cause tinnitus (ringing in the ears) based on experiments in rats, via the action on arachidonic acid and NMDA receptors cascade.

3 – 4 - Reye's syndrome

Reye's syndrome, a rare but severe illness characterized by acute encephalopathy and fatty liver, can occur when children or adolescents are given aspirin for a fever or other illnesses or infections. From 1981 through 1997, 1207 cases of Reye's syndrome in under-18 patients were reported to the US Centers for Disease Control and Prevention. Of these, 93 % reported being ill in the three weeks preceding onset of Reye's syndrome, most commonly with a respiratory infection, chickenpox, or diarrhea. Salicylates were detectable in 81.9 % of children for whom test results were reported.[83] After the association between Reye's syndrome and aspirin was reported, and safety measures to prevent it (including a Surgeon General's warning, and changes to the labeling of aspirin-containing drugs) were implemented, aspirin taken by children declined considerably in the United States, as did the number of reported cases of Reye's syndrome; a similar decline was found in the United Kingdom after warnings against pediatric aspirin use were issued.[83] The US Food and Drug Administration now recommends aspirin (or aspirin-containing products) should not be given to anyone under the age of 12 who has a fever,[10] and the British Medicines and Healthcare products Regulatory Agency recommends children who are under 16 years of age should not take aspirin, unless it is on the advice of a doctor.

3 – 5 - Hives and swelling

For a small number of people, taking aspirin can result in symptoms resembling an allergic reaction, including hives, swelling

and headache. The reaction is caused by salicylate intolerance and is not a true allergy, but rather an inability to metabolize even small amounts of aspirin, resulting in an overdose.

3 – 6 - Other adverse effects

Aspirin can induce angioedema (swelling of skin tissues) in some people. In one study, angioedema appeared one to six hours after ingesting aspirin in some of the patients. However, when the aspirin was taken alone, it did not cause angioedema in these patients; the aspirin had been taken in combination with another NSAID-induced drug when angioedema appeared.

Aspirin causes an increased risk of cerebral microbleeds having the appearance on MRI scans of 5 to 10 mm or smaller, hypointense (dark holes) patches . Such cerebral micro bleeds are important, since they often occur prior to ischemic stroke or intracerebral hemorrhage, Binswanger disease and Alzheimer's disease .

A study of a group with a mean dosage of aspirin of 270 mg per day estimated an average absolute risk increase in intra cerebral hemorrhage (ICH) of 12 events per 10,000 persons. In comparison, the estimated absolute risk reduction in myocardial infarction was 137 events per 10,000 persons, and a reduction of 39 events per 10,000 persons in ischemic stroke. In cases where ICH already has occurred, aspirin use results in higher mortality, with a dose of approximately 250 mg per day resulting in a relative risk of death within three months after the ICH of approximately 2.5 (95 % confidence interval 1.3 to 4.6).

Aspirin and other NSAIDs can cause hyperkalemia by inducing a hyporenin hypoaldosteronic state via inhibition of prostaglandin synthesis; however, these agents do not typically cause hyperkalemia by themselves in the setting of normal renal function and euvolemic state.

Aspirin can cause prolonged bleeding after operations for up to 10 days. In one study, 30 of 6499 elective surgical patients required reoperations to control bleeding. Twenty had diffuse bleeding and 10

had bleeding from a site. Diffuse, but not discrete, bleeding was associated with the preoperative use of aspirin alone or in combination with other NSAIDS in 19 of the 20 diffuse bleeding patients.

3 – 7 – Over dose

Aspirin overdose can be acute or chronic. In acute poisoning, a single large dose is taken; in chronic poisoning, higher than normal doses are taken over a period of time. Acute overdose has a mortality rate of 2 %. Chronic overdose is more commonly lethal, with a mortality rate of 25 % ; chronic overdose may be especially severe in children . Toxicity is managed with a number of potential treatments, including activated charcoal, intravenous dextrose and normal saline, sodium bicarbonate, and dialysis . The diagnosis of poisoning usually involves measurement of plasma salicylate, the active metabolite of aspirin, by automated spectrophotometric methods. Plasma salicylate levels in general range from 30–100 mg/l after usual therapeutic doses, 50 – 300 mg / l in patients taking high doses and 700 – 1400 mg / l following acute overdose. Salicylate is also produced as a result of exposure to bismuth subsalicylate, methyl salicylate and sodium salicylate.

3 – 8 – Interactions

Aspirin is known to interact with other drugs. For example, acetazolamide and ammonium chloride are known to enhance the intoxicating effect of salicyclates , and alcohol also increases the gastrointestinal bleeding associated with these types of drugs.[68][69] Aspirin is known to displace a number of drugs from protein-binding sites in the blood, including the antidiabetic drugs tolbutamide and chlorpropamide, the immunosuppressant methotrexate, phenytoin, probenecid, valproic acid (as well as interfering with beta oxidation, an important part of valproate metabolism) and any NSAID. Corticosteroids may also reduce the concentration of aspirin. Ibuprofen can negate the antiplatelet effect of aspirin used for cardio protection and stroke prevention. The pharmacological activity of spironolactone may be reduced by taking aspirin, and aspirin is known to compete with penicillin G for renal tubular secretion.[98] Aspirin may also inhibit the absorption of vitamin C.

4 - Chemical properties

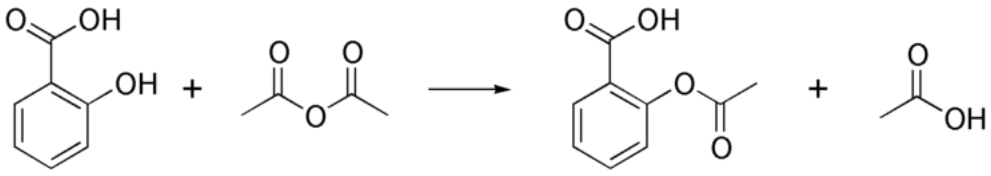
Acetyl salicylic acid (ASA) decomposes rapidly in solutions of ammonium acetate or of the acetates, carbonates, citrates or hydroxides of the alkali metals. ASA is stable in dry air, but gradually hydrolyses in contact with moisture to acetic and salicylic acids. In solution with alkalis, the hydrolysis proceeds rapidly and the clear solutions formed may consist entirely of acetate and salicylate.

5 - Physical properties

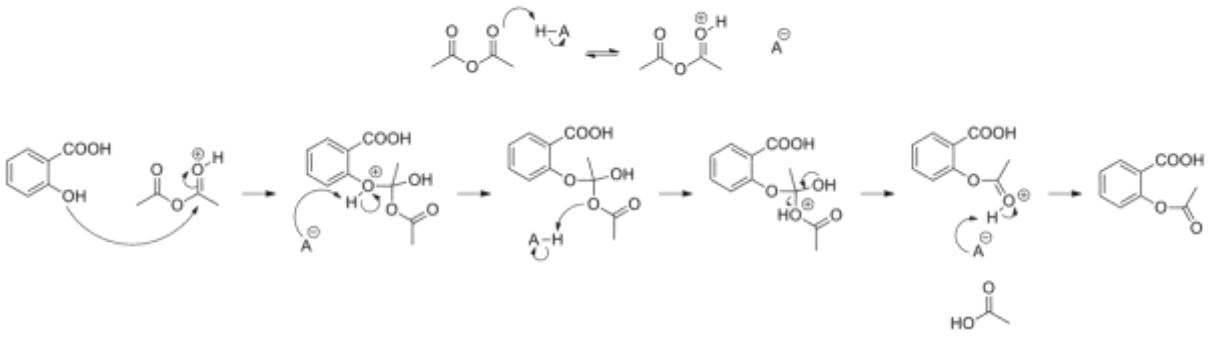
Aspirin, an acetyl derivative of salicylic acid, is a white, crystalline, weakly acidic substance, with a melting point of 136 °C , and a boiling point of 140 °C .

5 – 1 – Synthesis

The synthesis of aspirin is classified as an esterification reaction. Salicylic acid is treated with acetic anhydride, an acid derivative, causing a chemical reaction that turns salicylic acid's hydroxyl group into an ester group (R-OH → R-$OCOCH_3$). This process yields aspirin and acetic acid, which is considered a byproduct of this reaction. Small amounts of sulfuric acid (and occasionally phosphoric acid) are almost always used as a catalyst. This method is commonly employed in undergraduate teaching labs.



Reaction Mechanism



Formulations containing high concentrations of aspirin often smell like vinegar because aspirin can decompose through hydrolysis in moist conditions, yielding salicylic and acetic acids .

5 – 2 – Polymorphism

Polymorphism, or the ability of a substance to form more than one crystal structure, is important in the development of pharmaceutical ingredients. Many drugs are receiving regulatory approval for only a single crystal form or polymorph. For a long time, only one crystal structure for aspirin was known. That aspirin might have a second crystalline form was suspected since the 1960s. The elusive second polymorph was first discovered by Vishweshwar and coworkers in 2005 , and fine structural details were given by Bond *et al.* A new crystal type was found after attempted cocrystallization of aspirin and levetiracetam from hot acetonitrile. The form II is only stable at 100 K and reverts to form I at ambient temperature. In the (unambiguous) form I, two salicylic molecules form centrosymmetric dimers through the acetyl groups with the (acidic) methyl proton to carbonyl hydrogen bonds, and in the newly claimed form II, each salicylic molecule forms the same hydrogen bonds with two neighboring molecules instead of one. With respect to the hydrogen bonds formed by the carboxylic acid groups, both polymorphs form identical dimer structures.

6 - Mechanism of action

6 – 1 - Discovery of the mechanism

In 1971, British pharmacologist John Robert Vane, then employed by the Royal College of Surgeons in London, showed aspirin suppressed the production of prostaglandins and thromboxanes. For this discovery he was awarded the 1982 Nobel Prize in Physiology or Medicine, jointly with Sune K. Bergström and Bengt I. Samuelsson. In 1984 he was made a Knight Bachelor.

6 – 2 - Suppression of prostaglandins and thromboxanes

Aspirin's ability to suppress the production of prostaglandins and thromboxanes is due to its irreversible inactivation of the cyclo oxygenase (PTGS) enzyme required for prostaglandin and thromboxane synthesis. Aspirin acts as an acetylating agent where an acetyl group is covalently attached to a serine residue in the active site of the PTGS enzyme. This makes aspirin different from other NSAIDs

Low - dose, long-term aspirin use irreversibly blocks the formation of thromboxane A_2 in platelets, producing an inhibitory effect on platelet aggregation. This antithrombotic property makes aspirin useful for reducing the incidence of heart attacks. 40 mg of aspirin a day is able to inhibit a large proportion of maximum thromboxane A_2 release provoked acutely, with the prostaglandin I2 synthesis being little affected; however, higher doses of aspirin are required to attain further inhibition.

Prostaglandins, local hormones produced in the body, have diverse effects, including the transmission of pain information to the brain, modulation of the hypothalamic thermostat, and inflammation. Thromboxanes are responsible for the aggregation of platelets that form blood clots. Heart attacks are caused primarily by blood clots, and low doses of aspirin are seen as an effective medical intervention for acute myocardial infarction. An unwanted side effect of the effective anticlotting action of aspirin is that it may cause excessive bleeding.

6 – 3 - COX-1 and COX-2 inhibition

There are at least two different types of cyclooxygenase: COX-1 and COX-2. Aspirin irreversibly inhibits COX-1 and modifies the enzymatic activity of COX-2. COX-2 normally produces prostanoids, most of which are proinflammatory. Aspirin-modified PTGS2 produces lipoxins, most of which are anti-inflammatory.[115] Newer NSAID drugs, COX-2 inhibitors (coxibs), have been developed to inhibit only PTGS2, with the intent to reduce the incidence of gastrointestinal side effects.

However, several of the new COX-2 inhibitors, such as rofecoxib (Vioxx), have been withdrawn recently, after evidence emerged that PTGS2 inhibitors increase the risk of heart attack and stroke . Endothelial cells lining the microvasculature in the body are proposed to express PTGS2, and, by selectively inhibiting PTGS2, prostaglandin production (specifically, PGI2; prostacyclin) is down regulated with respect to thromboxane levels, as PTGS1 in platelets is unaffected. Thus, the protective anti coagulative effect of PGI2 is removed, increasing the risk of thrombus and associated heart attacks

and other circulatory problems. Since platelets have no DNA, they are unable to synthesize new PTGS once aspirin has irreversibly inhibited the enzyme, an important difference with reversible inhibitors.

6 – 4 - Additional mechanisms

Aspirin has been shown to have at least three additional modes of action. It uncouples oxidative phosphorylation in cartilaginous (and hepatic) mitochondria, by diffusing from the inner membrane space as a proton carrier back into the mitochondrial matrix, where it ionizes once again to release protons . In short, aspirin buffers and transports the protons. When high doses of aspirin are given, it may actually cause fever, owing to the heat released from the electron transport chain, as opposed to the antipyretic action of aspirin seen with lower doses. In addition, aspirin induces the formation of NO-radicals in the body, which have been shown in mice to have an independent mechanism of reducing inflammation. This reduced leukocyte adhesion, which is an important step in immune response to infection; however, there is currently insufficient evidence to show that aspirin helps to fight infection.[119] More recent data also suggest salicylic acid and its derivatives modulate signaling through NF-κB.[120] NF-κB, a transcription factor complex, plays a central role in many biological processes, including inflammation.

Aspirin is readily broken down in the body to salicylic acid, which itself has anti-inflammatory, antipyretic, and analgesic effects. In 2012, salicylic acid was found to activate AMP-activated protein kinase, and this has been suggested as a possible explanation for some of the effects of both salicylic acid and aspirin . The acetyl portion of the aspirin molecule is not without its own targets. Acetylation of cellular proteins is a well-established phenomenon in the regulation of protein function at the posttranslational level. Recent studies have reported aspirin is able to acetylate several other targets in addition to COX isoenzymes . These acetylation reactions may explain many hitherto unexplained effects of aspirin.

6 – 5 – Hypothalamic - pituitary - adrenal activity

Aspirin, like other medications affecting prostaglandin synthesis, has profound effects on the pituitary gland, which indirectly affects a number of other hormones and physiological functions. Effects on growth hormone, prolactin, and TSH (with relevant effect on T3 and T4) were observed directly. Aspirin reduces the effects of vasopressin[127] and increases those of naloxone upon the secretion of ACTH and cortisol by the hypothalamic-pituitary-adrenal axis (HPA axis), which has been suggested to occur through an interaction with endogenous prostaglandins and their role in regulating the HPA axis.

7 – Pharmacokinetics

Salicylic acid is a weak acid, and very little of it is ionized in the stomach after oral administration. Acetylsalicylic acid is poorly soluble in the acidic conditions of the stomach, which can delay absorption of high doses for eight to 24 hours. The increased pH and larger surface area of the small intestine causes aspirin to be absorbed rapidly there, which in turn allows more of the salicylate to dissolve. Owing to the issue of solubility, however, aspirin is absorbed much more slowly during overdose, and plasma concentrations can continue to rise for up to 24 hours after ingestion.

About 50 – 80 % of salicylate in the blood is bound to albumin protein, while the rest remains in the active, ionized state; protein binding is concentration - dependent. Saturation of binding sites leads to more free salicylate and increased toxicity. The volume of distribution is 0.1 – 0.2 l / kg. Acidosis increases the volume of distribution because of enhancement of tissue penetration of salicylates.

As much as 80% of therapeutic doses of salicylic acid is metabolized in the liver. Conjugation with glycine forms salicyluric acid, and with glucuronic acid it forms salicyl acyl and phenolic glucuronide. These metabolic pathways have only a limited capacity. Small amounts of salicylic acid are also hydroxylated to gentisic acid. With large salicylate doses, the kinetics switch from first order to zero order, as metabolic pathways become saturated and renal excretion becomes increasingly important.

Salicylates are excreted mainly by the kidneys as salicyluric acid (75 %), free salicylic acid (10 %), salicylic phenol (10 %), and acyl glucuronides (5 %), gentisic acid (< 1%), and 2,3-dihydroxybenzoic acid . When small doses (less than 250 mg in an adult) are ingested, all pathways proceed by first-order kinetics, with an elimination half-life of about 2.0 to 4.5 hours. When higher doses of salicylate are ingested (more than 4 g), the half-life becomes much longer (15 – 30 hours), because the biotransformation pathways concerned with the formation of salicyluric acid and salicyl phenolic glucuronide become saturated.[136] Renal excretion of salicylic acid becomes increasingly important as the metabolic pathways become saturated, because it is extremely sensitive to changes in urinary pH. A 10- to 20 - fold increase in renal clearance occurs when urine pH is increased from 5 to 8. The use of urinary alkalinization exploits this particular aspect of salicylate elimination.

8 – History

1923 advertisement

Plant extracts, including willow bark and spiraea, of which salicylic acid was the active ingredient, had been known to help alleviate headaches, pains, and fevers since antiquity. The father of modern medicine, Hippocrates, who lived some time between 460 BC

and 377 BC, left historical records describing the use of powder made from the bark and leaves of the willow tree to help these symptoms.

A French chemist, Charles Frederic Gerhardt, was the first to prepare acetylsalicylic acid in 1853. In the course of his work on the synthesis and properties of various acid anhydrides, he mixed acetyl chloride with a sodium salt of salicylic acid (sodium salicylate). A vigorous reaction ensued, and the resulting melt soon solidified.[139] Since no structural theory existed at that time, Gerhardt called the compound he obtained "salicylic-acetic anhydride" (*wasserfreie Salicylsäure-Essigsäure*). This preparation of aspirin ("salicylic-acetic anhydride") was one of the many reactions Gerhardt conducted for his paper on anhydrides and he did not pursue it further.

Six years later, in 1859, von Gilm obtained analytically pure acetylsalicylic acid (which he called *acetylierte Salicylsäure*, acetylated salicylic acid) by a reaction of salicylic acid and acetyl chloride.[140] In 1869, Schröder, Prinzhorn and Kraut repeated both Gerhardt's (from sodium salicylate) and von Gilm's (from salicylic acid) syntheses and concluded both reactions gave the same compound — acetylsalicylic acid. They were first to assign to it the correct structure with the acetyl group connected to the phenolic oxygen.

In 1897, chemists working at Bayer AG produced a synthetically altered version of salicin, derived from the species *Filipendula ulmaria* (meadowsweet), which caused less digestive upset than pure salicylic acid. The identity of the lead chemist on this project is a matter of controversy. Bayer states the work was done by Felix Hoffmann, but the Jewish chemist Arthur Eichengrün later claimed he was the lead investigator and records of his contribution were expunged under the Nazi regime . The new drug, formally acetylsalicylic acid, was named Aspirin by Bayer AG after the old botanical name for meadowsweet, *Spiraea ulmaria*. By 1899, Bayer was selling it around the world.[144] The name Aspirin is derived from "acetyl" and *Spirsäure*, an old German name for salicylic acid.[145] The popularity of aspirin grew over the first half of the 20th century, spurred by its supposed effectiveness in the wake of the Spanish flu

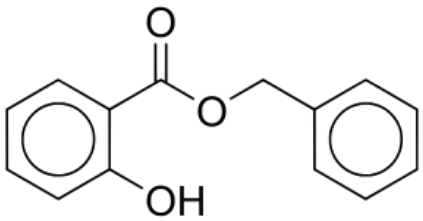
pandemic of 1918. However, recent research suggests the high death toll of the 1918 flu was partly due to aspirin, as the doses used at times can lead to toxicity, fluid in the lungs, and, in some cases, contribute to secondary bacterial infections and mortality.[146] Aspirin's profitability led to fierce competition and the proliferation of aspirin brands and products, especially after the American patent held by Bayer expired in 1917.

The popularity of aspirin declined after the market releases of paracetamol (acetaminophen) in 1956 and ibuprofen in 1969 . In the 1960s and 1970s, John Vane and others discovered the basic mechanism of aspirin's effects, while clinical trials and other studies from the 1960s to the 1980s established aspirin's efficacy as an anticlotting agent that reduces the risk of clotting diseases . Aspirin sales revived considerably in the last decades of the 20th century, and remain strong in the 21st century, because of its widespread use as a preventive treatment for heart attacks and strokes.

8 – 1 – Trademark

As part of war reparations specified in the 1919 Treaty of Versailles following Germany's surrender after World War I, Aspirin (along with heroin) lost its status as a registered trademark in France, Russia, the United Kingdom, and the United States, where it became a generic name. Today, *aspirin* is a generic word in Australia, France, India, Ireland, New Zealand, Pakistan, Jamaica, Colombia, the Philippines, South Africa, the United Kingdom and the United States. Aspirin, with a capital "A", remains a registered trademark of Bayer in Germany, Canada, Mexico, and in over 80 other countries, where the trademark is owned by Bayer, using acetylsalicylic acid in all markets, but using different packaging and physical aspects for each.

Benzyl Salicylate



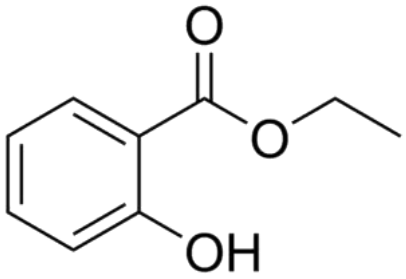
IUPAC name :	
Benzyl 2- hydroxy benzoate	
Molecular formula	$C_{14}H_{12}O_3$
Molar mass	228 g mol^{-1}
Appearance	Colorless liquid
Density	1.17 g / cm^3

Benzyl salicylate is a salicylic acid benzyl ester, a chemical compound most frequently used in cosmetics. It appears as an almost colorless liquid with a mild odor described as "very faint, sweet-floral, slightly balsamic" by those who can smell it, but many people either can't smell it at all or describe its smell as "musky". Trace impurities can have a significant influence on the odour.[1] It occurs naturally in a variety of plants and plant extracts and is widely used in blends of fragrance materials.

There is some evidence that people can become sensitized to this material and as a result there is a restriction standard concerning the use of this material in fragrances by the International Fragrance Association.

It is used as a solvent for crystalline synthetic musks and as a component and fixative in floral perfumes such as carnation, jasmine, lilac, and wallflower.

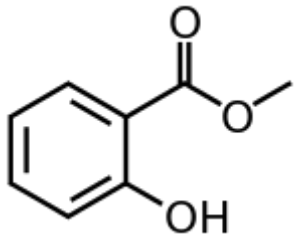
Ethyl Salicylate



IUPAC name : Ethyl 2- hydroxy benzoate	
Molecular formula	$C_9H_{10}O_3$
Molar mass	166 g / mol
Density	1.131 g / cm^3
Melting point	1 °C
Boiling point	231 – 234 °C

Ethyl salicylate is the ester formed by the condensation of salicylic acid and ethanol. It is a clear liquid that is sparingly soluble in water, but soluble in alcohol and ether. It has a pleasant odor resembling winter green and is used in perfumery and artificial flavors.

Methyl Salicylate



Contents

1 - Introductıon

Methyl salicylate (oil of winter green or winter green oil) is an organic ester that is naturally produced by many species of plants. Some of the plants which produce it are called wintergreens, hence the common name. This compound is used as a fragrance. It is also found in liniments (rubbing ointments).

IUPAC name :
Methyl 2-hydroxy benzoate
Other names :
Salicylic acid methyl ester ;
Oil of wintergreen ;
Betula oil ;
Methyl 2-hydroxybenzoate

Molecular formula	$C_8 H_8 O_3$
Molar mass	152 g / mol
Density	1.174 g / cm³
Melting point	- 9 °C
Boiling point	220 - 224 °C
Main hazards	Harmful
Flash point	101 °C

2 - Natural occurrence

Winter green plants (Gaultheria procumbens)

Numerous plants produce methyl salicylate in very small amounts. Some plants, such as the following, produce more:

some species of the genus Gaultheria in the family Ericaceae, including Gaultheria procumbens, the wintergreen or eastern teaberry;

some species of the genus Betula in the family Betulaceae, particularly those in the subgenus Betulenta such as B. lenta, the black birch;

all species of the genus Spiraea in the family Rosaceae, also called the meadowsweets.

This compound is produced most likely as an anti-herbivore defense. If the plant is infected with herbivorous insects, the release of methyl salicylate may function as an aid in the recruitment of beneficial insects to kill the herbivorous insects. Aside from its toxicity, methyl salicylate may also be used by plants as a pheromone to warn other plants of pathogens such as tobacco mosaic virus.

3 - Commercial production

Methyl salicylate can be produced by esterifying salicylic acid with methanol. Commercial methyl salicylate is now synthesized, but in the past, it was commonly distilled from the twigs of Betula lenta (sweet birch) and Gaultheria procumbens (eastern teaberry or winter green).

4 - Uses

Methyl salicylate is used in high concentrations as a rubefacient in deep heating liniments (such as Bengay) to treat joint and muscular pain. Randomised double blind trial reviews report evidence of its effectiveness that is weak, but stronger for acute pain than chronic pain, and that effectiveness may be due entirely to counter-irritation. However, in the body it metabolizes into salicylates, including salicylic acid, a known NSAID.

It is used in low concentrations as a flavoring agent (no more than 0.04 %; it is toxic). It is also used to provide fragrance to various products and as an odor-masking agent for some organophosphate pesticides . If used excessively, it can cause stomach and kidney problems.

Methyl salicylate is among the compounds that attract male orchid bees, who apparently gather the chemical to synthesize pheromones; it is commonly used as bait to attract and collect these bees for study.

Methyl salicylate has the ability to clear plant or animal tissue samples of color, and as such is useful for microscopy and immunohistochemistry when excess pigments obscure structures or block light in the tissue being examined. This clearing generally only takes a few minutes, but the tissue must first be dehydrated in alcohol.

Methyl salicylate, though its source plants are not true mints, is used as a mint in some kinds of chewing gum and candy, as an alternative to the more common peppermint and spearmint oils. It can also be found as a flavoring of root beer. It is also a potentially entertaining source of triboluminescence ; when mixed with sugar and dried, it gains the tendency to build up electrical charge when crushed or rubbed. This effect can be observed by crushing wintergreen Life Savers candy in a dark room.

Methyl salicylate can be used as a transfer agent, to produce a manual copy of an image on a surface.

Methyl salicylate is added in small amounts to glacial acetic acid to lower its freezing point for transport in cold countries.

Methyl salicylate is used as a simulant or surrogate for the research of chemical warfare agent sulfur mustard, due to its similar chemical and physical properties.

Methyl salicylate is one of several antiseptic ingredients in Listerine mouthwash produced by the Johnson & Johnson company.

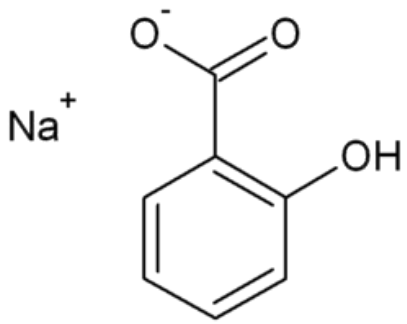
Methyl salicylate can also be effectively used to restore (at least temporarily) the elastomeric properties of old rubber rollers, especially in printers.

5 - Safety and toxicity

In pure form, methyl salicylate is toxic, especially when taken internally. A single teaspoon (5ml) of methyl salicylate contains 7g of salicylate , which is equivalent to more than twenty- three 300 mg aspirin tablets. The lowest published lethal dose is 101 mg/kg body weight in adult humans , (or 7.07 grams for a 70 - kg adult). It has proven fatal to small children in doses as small as 4 ml.[6] A seventeen-year - old cross-country runner at Notre Dame Academy on Staten Island, died in April 2007, after her body absorbed methyl salicylate through excessive use of topical muscle-pain relief products.

Most instances of human toxicity due to methyl salicylate are a result of over-application of topical analgesics, especially involving children. Some people have intentionally ingested large amounts of oil of winter green. Salicylate, the major metabolite of methyl salicylate, may be quantitated in blood, plasma or serum to confirm a diagnosis of poisoning in hospitalized patients or to assist in an autopsy.

Sodium Salicylate



Contents

1 - Introduction

Sodium salicylate is a sodium salt of salicylic acid. It can be prepared from sodium phenolate and carbon dioxide under higher temperature and pressure. Historically, it has been synthesized from methyl salicylate (found in wintergreen plants or the bark of sweet birch tree) by reacting it with an excess of sodium hydroxide and heating it under reflux.

IUPAC name : Sodium salicylate

Other names :
Salsonin,
Mono sodium salicylate,
Sodium o - hydroxy benzoate,
Sodium 2 - hydroxy benzoate,
Salicylic acid sodium salt,
Mono sodium 2-hydroxy benzoate, Diuratin,

Molecular formula	$C_7 H_5 Na O_3$
Molar mass	160 g / mol
Appearance	White crystals
Melting point	200 °C
Solubility in water	~ 660 g / l at 20 °C
Auto ignition temperature	> 250 °C

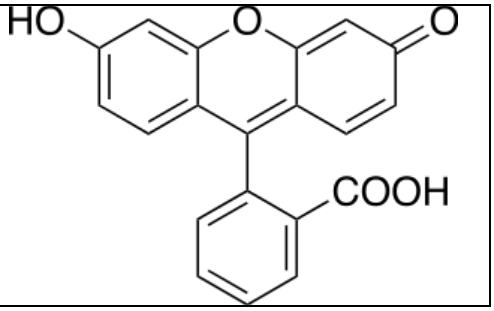
2 – Properties

Sodium salicylate is of the salicylate family and this compound is known to trigger Reye's Syndrome in children and adults, usually following a viral infection such as influenza or chicken pox. Products containing such salicylates should not be given to children under the age of 19.

3 – Uses

It is used in medicine as an analgesic and antipyretic. Sodium salicylate also acts as non - steroidal anti - inflammatory drug (NSAID), and induces apoptosis in cancer cells and also necrosis. It is also a potential replacement for aspirin for people sensitive to it. It may also be used as a phosphor for the detection of vacuum ultra violet radiation and electrons.

Fluorescein



Contents

1 - Introduction

Fluorescein is a synthetic organic compound available as a dark orange/red powder slightly soluble in water and alcohol. It is widely used as a fluorescent tracer for many applications.

Fluorescein is a fluorophore commonly used in microscopy, in a type of dye laser as the gain medium, in forensics and serology to detect latent blood stains, and in dye tracing. Fluorescein has an absorption maximum at 494 nm and emission maximum of 521 nm (in water). The major derivatives are fluorescein isothiocyanate (FITC) and, in oligonucleotide synthesis, 6-FAM phosphoramidite.

Fluorescein also has an isosbestic point (equal absorption for all pH values) at 460 nm. Fluorescein is also known as a color additive

(D&C Yellow no. 7). The disodium salt form of fluorescein is known as uranine or D&C Yellow no. 8.

The color of its aqueous solution varies from green to orange as a function of the way it is observed: by reflection or by transmission, as it can be noticed in bubble levels in which fluorescein is added as a colorant to the alcohol filling the tube to increase the visibility of the air bubble and the precision of the instrument. More concentrated solutions of fluorescein can even appear red.

Other names : Fluorescein, Resorcinol phthalein , C.I. 45350 , Solvent yellow 94, D & C yellow no. 7, Angiofluor, Japan yellow 201, Soap yellow	
Molecular formula	$C_{20}H_{12}O_5$
Molar mass	332 g mol^{-1}
Density	1.602 g / mL
Melting point	314 - 316 °C
Solubility in water	Slightly

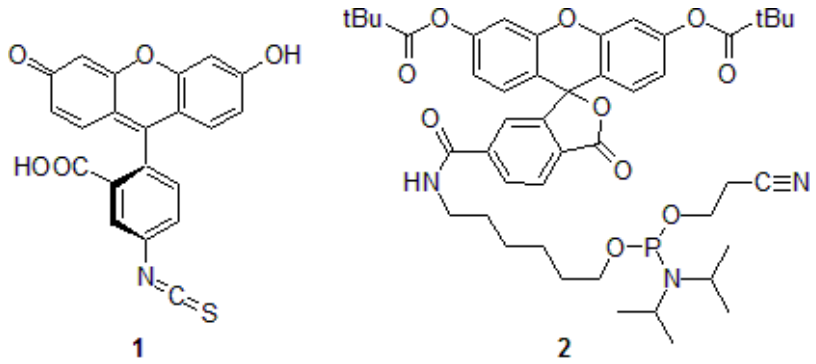
2 - Chemical and physical properties

Fluorescein under UV illumination

The fluorescence of this molecule is very intense; peak excitation occurs at 494 nm and peak emission at 521 nm.

Fluorescein has a pK_a of 6.4, and its ionization equilibrium leads to pH-dependent absorption and emission over the range of 5 to 9. Also, the fluorescence lifetimes of the protonated and deprotonated forms of fluorescein are approximately 3 and 4 ns, which allows for pH determination from non intensity based measurements. The lifetimes can be recovered using time-correlated single photon counting or phase-modulation fluorimetry.

3 – Derivatives



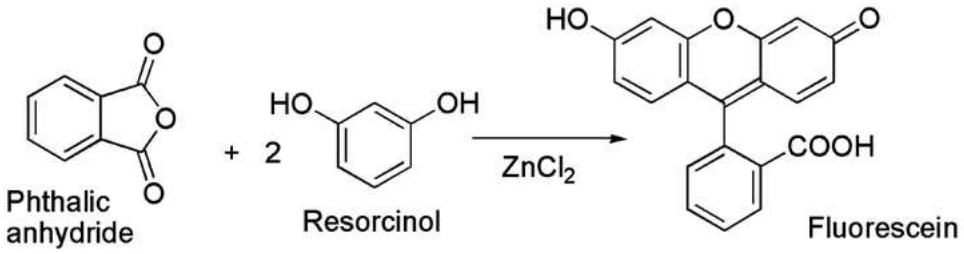
Fluorescein isothiocyanate and 6 - FAM phosphoramidite

There are many fluorescein derivatives. For example, fluorescein isothiocyanate 1, often abbreviated as FITC, is the original fluorescein molecule functionalized with an isothiocyanate group (- N = C = S) , replacing a hydrogen atom on the bottom ring of the structure. This derivative is reactive towards primary amine groups of biologically relevant compounds including intracellular proteins to form a thiourea linkage. A succinimidyl ester functional group attached to the fluorescein core, creating NHS-fluorescein, forms another common amine-reactive derivative, yielding more stable amide adducts. Penta fluoro phenyl esters (PFP) and tetra fluoro phenyl esters (TFP) are other useful reagents. In oligonucleotide synthesis, several phosphoramidite reagents containing protected fluorescein, *e.g.* 6-FAM phosphoramidite 2,[1] are widely used for the preparation of fluorescein-labeled oligonucleotides.

Other green dyes include Oregon Green, Tokyo Green, SNAFL, and carboxy naphtho fluorescein. These dyes, along with newer fluoro phores such as Alexa 488, Fluo Probes 488 and DyLight 488, have been tailored for various chemical and biological applications where higher photo stability, different spectral characteristics, or different attachment groups are needed.

4 – Synthesis

Fluorescein was first synthesized by Adolf von Baeyer in 1871. It can be prepared from phthalic anhydride and resorcinol in the presence of zinc chloride via the Friedel - Crafts reaction.



A second method to prepare fluorescein uses methanesulfonic acid as a Brønsted acid catalyst. This route has a high yield under milder conditions.

5 – Applications

5 – 1 - Biochemical research

In cellular biology, the isothiocyanate derivative of fluorescein is often used to label and track cells in fluorescence microscopy applications (for example, flow cytometry). Additional biologically active molecules (such as antibodies) may also be attached to fluorescein, allowing biologists to target the fluorophore to specific proteins or structures within cells. This application is common in yeast display.

Fluorescein can also be conjugated to nucleoside triphosphates and incorporated into a probe enzymatically for in situ hybridisation. The use of fluorescein amidite shown above allows one to synthesize labeled oligonucleotides for the same purpose. Yet another technique termed molecular beacons makes use of synthetic fluorescein-labeled

oligonucleotides. Fluorescein - labeled probes can be imaged using FISH, or targeted by antibodies using immunohisto chemistry. The latter is a common alternative to digoxigenin, and the two are used together for labelling two genes in one sample.

5 – 2 - Health care applications

Fluorescein drops being inserted for an eye examination

Fluorescein sodium", the sodium salt of fluorescein, is used extensively as a diagnostic tool in the field of ophthalmology and optometry, where topical fluorescein is used in the diagnosis of corneal abrasions, corneal ulcers and herpetic corneal infections. It is also used in rigid gas permeable contact lens fitting to evaluate the tear layer under the lens. It is available as sterile single-use sachets containing lint - free paper applicators soaked in fluorescein sodium.

Intravenous or oral fluorescein is used in fluorescein angiography in research and to diagnose and categorize vascular disorders in e.g. legs, including retinal disease macular degeneration, diabetic retinopathy, inflammatory intraocular conditions, and intraocular tumors, and, increasingly, during surgery for brain tumors.

5 – 3 - Air Sea Rescue

During World War 2, German aircrew carried small containers of fluorescein. In the event of parachuting into the sea after being shot down, the dye would be released into the water. This produced a vivid marking that could be seen from the air over long distances and aided the Air - sea rescue of the downed crew. This was later adopted by other air forces.

The Gemini 4 spacecraft releases dye into the water, to aid location after splashdown, June 1965

5 – 4 - Uses in river systems

One of its more recognizable uses was in the Chicago River, where fluorescein was the first substance used to dye the river green on St. Patrick's Day in 1962. In 1966, environmentalists forced a change to a vegetable-based dye to protect local wildlife.

Other uses of fluorescein include using it as a water-soluble dye added to rainwater in environmental testing simulations to aid in locating and analyzing any water leaks, and in Australia and New Zealand as a methylated spirit dye.

5 – 5 - Oil field application

Fluorescein dye solutions, typically 15 % active, are commonly used as an aid to leak detection during hydrostatic testing of sub sea oil and gas pipelines and other subsea infrastructure. Leaks can be detected by divers carrying ultraviolet lights.

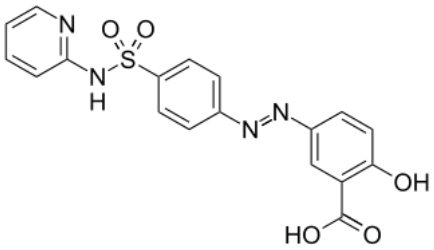
6 – Safety

Topical, oral, and intravenous use of fluorescein can cause adverse reactions, including nausea, vomiting, hives, acute hypotension, anaphylaxis and related anaphylactoid reaction, causing cardiac arrest and sudden death due to anaphylactic shock.

The most common adverse reaction is nausea, due to a difference in the pH from the body and the pH of the sodium fluorescein dye; a number of other factors , however, are considered contributors as well. The nausea usually is transient and subsides quickly. Hives can range from a minor annoyance to severe, and a single dose of antihistamine may give complete relief. Anaphylactic shock and subsequent cardiac arrest and sudden death are very rare, but because they occur within minutes, a health care provider who uses fluorescein should be prepared to perform emergency resuscitation.

Intravenous use has the most reported adverse reactions, including sudden death, but this may reflect greater use rather than greater risk. Both oral and topical uses have been reported to cause anaphylaxis,[11][12] including one case of anaphylaxis with cardiac arrest (resuscitated) following topical use in an eye drop. Reported rates of adverse reactions vary from 1 % to 6 %. The higher rates may reflect study populations that include a higher percentage of persons with prior adverse reactions. The risk of an adverse reaction is 25 times higher if the person has had a prior adverse reaction.[15] The risk can be reduced with prior (prophylactic) use of antihistamines[17] and prompt emergency management of any ensuing anaphylaxis.[18] A simple prick test may help to identify persons at greatest risk of adverse reaction.

Sulfasalazine



Contents

1 - Introduction

Sulfasalazine (brand name Azulfidine in the U.S., Salazopyrin and Sulazine in Europe and Hong Kong) was developed in the 1950s specifically to treat rheumatoid arthritis. It was believed at the time that bacterial infections were the cause of rheumatoid arthritis. Sulfasalazine is a sulfa drug, (a derivative of mesalazine) and is formed by combining sulfa pyridine and salicylate with an azo bond. It may be abbreviated SSZ.

Systematic (IUPAC) name : 2-hydroxy-5-[(*E*)-2-{4-[(pyridin-2-yl) sulfamoyl] phenyl} diazen-1-yl] benzoic acid	
Trade names	Azulfidine
Bioavailability	< 15%
Half-life	5-10 hours
Formula	$C_{18}H_{14}N_4O_5S$
Mol. mass	398 g / mol

2 – Indications

Sulfasalazine is used in the treatment of inflammatory bowel disease, including ulcerative colitis and Crohn's disease. It is also indicated for use in rheumatoid arthritis and used in other types of inflammatory arthritis (e.g. psoriatic arthritis) where it has a beneficial effect. It is often well tolerated compared to other DMARDS.

In clinical trials for the treatment of chronic alcoholics, sulfasalazine has been found to reverse the scarring associated with cirrhosis of the liver . Cells called myofibroblasts, which contribute to scar tissue in a diseased liver, also appear to secrete proteins that prevent the breakdown of the scar tissue. Sulfasalazine appears to retard this secretion.

A study at University of Newcastle found that the drug may also act to aid the healing of cirrhosis of the liver.

It is usually not given to children under 2 years of age.

The use of sulfasalazine in inflammatory bowel disease has declined due mainly to the fact that it yields the metabolite sulfapyridine which gives rise to side-effects such as agranulocytosis and hypospermia. However, the other metabolite of sulfasalazine, 5-aminosalicylic acid (5-ASA) is attributed to the drug's therapeutic effect. Therefore, 5-ASA and other derivatives of 5-ASA, are now usually preferred and given alone (as mesalazine), despite their increased cost, due to their more favour able side-effect profile.

Sulfasalazine has also been used successfully to treat cases of idiopathic urticaria that do not respond to antihistamines.

3 - Mode of action

Sulfasalazine, and its metabolite 5-ASA, are poorly absorbed from the gut. Its main mode of action is therefore believed to be inside the intestine.

3 – 1 - Bowel disease

In Crohn's disease and ulcerative colitis, it is thought to be an antinflammatory drug that is essentially providing topical relief inside

the intestine. It does this via a number of mechanisms such as reducing the synthesis of inflammatory mediators known as eicosanoids and inflammatory cytokines. However, unlike glucocorticoids (another class of drug used in the treatment in inflammatory bowel disease), sulfasalazine is a mild immunosuppressant.

3 – 2 – Arthritis

When treatment for arthritis is successful, pain, joint swelling and stiffness will be reduced and this may slow down or stop the development of joint damage. The precise reasons why sulfasalazine are effective in various forms of arthritis is not clearly understood.

Because sulfasalazine and its metabolite 5-ASA are poorly absorbed into the bloodstream, it is surprising that the drug is effective against symptoms outside of the intestine. One possible explanation is that, given that ulcerative colitis produces arthritic symptoms, the arthritic symptoms are actually a product of unrecognized ulcerative colitis , which is effectively treated with sulfazalazine.

The other metabolite, sulfa pyridine, is absorbed into the blood, and is believed to be the source of the side-effects discussed below. It is possible that the sulfa pyridine is responsible for some of the anti-arthritic effects of sulfasalazine.

4 - Side effects

Sulfsalazine metabolizes to sulfa pyridine. Serum levels should be monitored every three months, and more frequently at the outset. Serum levels above 50 μg / l are associated with side effects. In rare cases, Sulfasalazine can cause severe depression in young males. It can also cause temporary infertility. Immune thrombocytopenia has been reported.

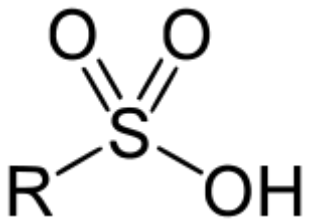
Sulfasalazine inhibits dihydrofolate reductase, and can cause folate deficiency and megaloblastic anemia.

Sulfasalazine can cause hemolytic anemia in people with G6PD deficiency

Part - 2 -

Aromatic Sulphonic Acids

Aromatic Sulfonic Acid



General structure of a sulfonic acid

Contents

1 - Introduction

A sulfonic acid (or sulphonic acid) refers to a member of the class of organo sulfur compounds with the general formula $RS(=O)_2-OH$, where *R* is an organic alkyl or aryl group and the $S(=O)_2-OH$ group a sulfonyl hydroxide . A sulfonic acid can be thought of as sulfuric acid with one hydroxyl group replaced by an organic substituent. The parent compound (with the organic substituent replaced by hydrogen) is the hypothetical compound sulfurous acid. Salts or esters of sulfonic acids are called sulfonates.

2 - Preparation

Sulfonic acid is produced by the process of sulfonation. Usually the sulfonating agent is sulfur trioxide. A particularly large scale

application of this method is the production of alkylbenzenesulfonic acids:

$$RC_6H_5 + SO_3 \rightarrow RC_6H_4SO_3H$$

In this reaction, sulfur trioxide is an electrophile and the arene undergoes electrophilic aromatic substitution.

Thiols can be oxidized to sulfonic acids :

$$RSH + 3/2\ O_2 \rightarrow RSO_3H$$

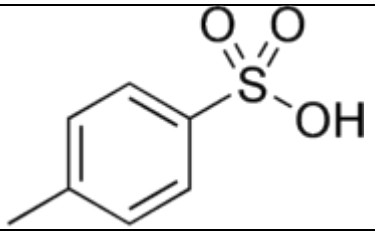
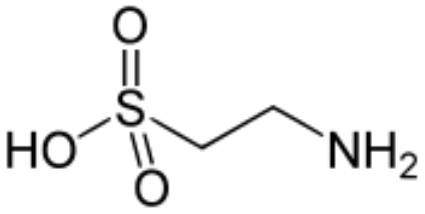
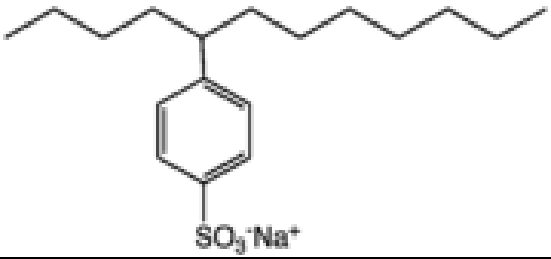
Certain sulfonic acids, such as per fluoro octane sulfonic acid are prepared by electrophilic fluorination of preformed sulfonic acids. The net conversion can be represented simplistically:

$$C_8H_{17}SO_3H + 17\ F_2 \rightarrow C_8F_{17}SO_3H + 17\ HF$$

3 - Properties

Sulfonic acids are much stronger acids than the corresponding carboxylic acids. *p*-Toluene sulfonic acid, with a pK_a of -2.8, is about a million times stronger acid than benzoic acid, with a pK_a of 4.2. Similarly, methane sulfonic acid, pK_a = -1.9, is also about one million times stronger acid than acetic acid. Because of their polarity, sulfonic acids tend to be crystalline solids. They are also usually colourless and non oxidizing, which is convenient. Because of their high acidity, sulfonic acids are often soluble in water or exhibit detergent-like properties.

The structure of sulfonic acids is illustrated by the prototype, methane sulfonic acid. The sulfonic acid group, RSO_2OH features a tetrahedral sulfur center, meaning that sulfur is at the center of four atoms: three oxygens and one carbon. The overall geometry of the sulfur center is reminiscent of the shape of sulfuric acid.

	
Toluene sulfonic acid, a widely used reagent in organic synthesis.	*Taurine, a bile acid, and one of the few naturally occurring sulfonic acids (shown in uncommon tautomer).*
	
Sodium do decyl benzene sulfonate, an alkyl benzene sulfonate surfactant used in laundry detergents.	

4 - Applications

Although both alkyl and aryl sulfonic acids are known, most of the applications are associated with the aromatic derivatives.

4 – 1 - Detergents and surfactants

Detergents and surfactants are molecules that combine highly nonpolar and highly polar groups. Traditionally, soaps are the popular surfactants, being derived from fatty acids. Since the mid-20th century, the usage of sulfonic acids has surpassed soap in advanced societies. For example, an estimated 2 billion kilograms of alkyl benzene sulfonates are produced annually for diverse purposes. Lignin sulfonates, produced by sulfonation of lignin are components of drilling fluids and additives in certain kinds of concrete.

4 – 2 - Dyes

Many if not most of the anthro quinone dyes are produced or processed via sulfonation . Sulfonic acids tend to bind tightly to proteins and carbohydrates. Most "washable" dyes are sulfonic acids (or have the functional sulfonyl group in them) for this reason. p-Cresidine sulfonic acid is used to make food dyes.

4 – 3 - Acid catalysts

Being strong acids, sulfonic acids are also used as catalysts. The simplest examples are methane sulfonic acid, CH_3SO_2OH and *p*-toluene sulfonic acid, which are regularly used in organic chemistry as acids that are lipophilic (soluble in organic solvents). Polymeric sulfonic acids are also useful. Dowex resin are sulfonic acid derivatives of polystyrene and is used as catalysts and for ion exchange (water softening).Nafion, a fluorinated polymeric sulfonic acid is a component of proton exchange membranes in fuel cells.

4 – 4 – Drugs

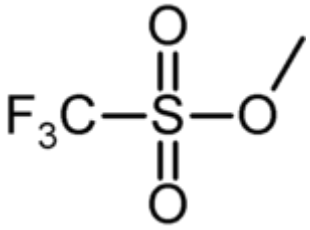
Antibacterial drugs sulfa drugs are produced from sulfonic acids.

5 – Reactions

5 – 1 - Esterification

Sulfonic acids can be converted to esters. This class of organic compounds has the general formula $R\text{-}SO_2\text{-}OR$. Sulfonic esters such as methyl triflate are considered good alkylating agents in organic synthesis. Such sulfonate esters are often prepared by alcoholysis of the sulfonyl chlorides:

$$RSO_2Cl + R'OH \rightarrow RSO_2OR' + HCl$$



Methyl triflate

5 – 2 - Chlorination

Sulfonyl halide groups occur when a sulfonyl functional group is singly bonded to a halogen atom. They have the general formula $R\text{-}SO_2\text{-}X$ where X is a halide, almost invariably chloride. They are produced by chlorination of sulfonic acids using thionyl chloride and related reagents.

5 – 3 - Displacement

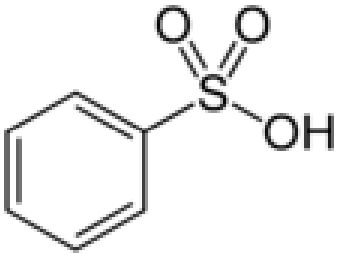
Although the C- SO_3H bond is strong, the (aryl) C- SO_3 bond can be cleaved by certain nucleophiles. Of historic and continuing significance is the α-sulfonation of anthroquinone followed by displacement of the sulfonate group by other nucleophiles, which cannot be installed directly. An early method for producing phenol involved the base hydrolysis of sodium benzene sulfonate, which can be generated readily from benzene.

$$C_6H_5SO_3Na + 2\ Na\ OH \rightarrow C_6H_5ONa + Na_2SO_3 + H_2O$$

6 - Environmental concerns

Sulfonic acid derivatives are generally not derived from natural precursors and tend to biodegrade slowly. Some, such as perfluoro octane sulfonic acid, have been detected in the serum of humans. This should be not surprising as all organic fluorine compounds have extreme stability, and low to zero biodegradability. Many are intended to withstand harshest chemical conditions, for example teflon . The non fluorinated sulfonic acids tend to have low toxicities.

Benzene Sulfonic Acid



Contents

1 - Introduction

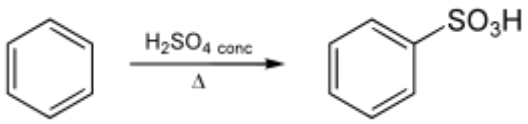
Benzene sulfonic acid is an organo sulfur compound with the formula $C_6H_5SO_3H$. It is the simplest aromatic sulfonic acid. It forms colorless deliquescent sheet crystals or a white waxy solid that is soluble in water and ethanol, slightly soluble in benzene and insoluble in carbon disulfide and diethyl ether. It is often stored in the form of alkali metal salts. Its aqueous solution is strongly acidic.

Other names:	
Benzene sulphonic acid;	
Benzene sulphonic acid;	
Phenyl sulfonic acid	
Molecular formula	$C_6 H_6 O_3 S$
Molar mass	158 g mol^{-1}
Appearance	Colorless crystalline solid
Density	1.32 g / cm^3 (47 °C)
Melting point	44 °C (hydrate) 51 °C (anhydrous)
Boiling point	190 °C, 463 K, 374 °F
Solubility in water	Soluble
Solubility in other	Soluble in alcohol,

solvents	insoluble in non-polar solvents
Main hazards	Corrosive
Flash point	> 113 °C

2 - Preparation

Benzene sulfonic acid is prepared from the sulfonation of benzene using concentrated sulfuric acid :



This conversion illustrates aromatic sulfonation, which has been called "one of the most important reactions in industrial organic chemistry."

3 - Reactions

Benzene sulfonic acid exhibits the reactions typical of other aromatic sulfonic acids, forming sulfonamides , sulfonyl chloride, and esters. The sulfonation is reversed above 220 °C. Dehydration with phosphorus pentoxide gives benzene sulfonic acid anhydride ($(C_6H_5SO_2)_2O$). Conversion to the corresponding benzene sulfonyl chloride ($C_6H_5SO_2Cl$) is effected with phosphorus penta chloride.

It is a strong acid, being dissociated in water.

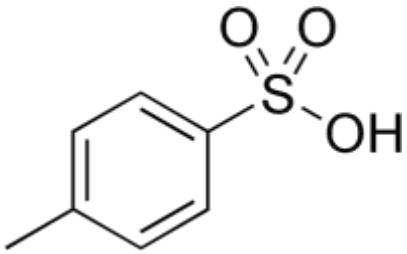
4 - Applications

The alkali metal salt of benzene sulfonic acid was once widely used in the production of phenol :

$$C_6H_5SO_3Na + 2\ Na\ OH \rightarrow C_6H_5ONa + Na_2SO_3$$
$$C_6H_5ONa + HCl \rightarrow C_6H_5OH + NaCl$$

The process has been largely displaced by the Hock process, which generates less waste. Benzene sulfonic acid is mainly consumed by conversion to other specialty chemicals. A variety of pharmaceutical drugs are prepared as salts of benzene sulfonic acid and are known as besylates or besilates.

p-Toluene Sulfonic Acid



Contents

1 - Introduction

p-Toluene sulfonic acid (PTSA) or tosylic acid (TsOH) is an organic compound with the formula $CH_3C_6H_4SO_3H$. It is a white solid that is soluble in water, alcohols, and other polar organic solvents. The 4-$CH_3C_6H_4SO_2$- group is known as tosyl group and is often abbreviated as Ts or Tos. Most often, TsOH refers to the monohydrate, $TsOH \cdot H_2O$.

TsOH is a strong organic acid, about a million times stronger than benzoic acid. It is one of the few strong acids that is solid and, hence, conveniently weighed. Also, unlike some strong mineral acids (especially nitric acid, sulfuric acid, and per chloric acid), TsOH is non - oxidizing.

IUPAC name :
4-methyl benzene sulfonic acid
Other names :
Tosylic acid
tosic acid
PTSA
Molecular formula $C H_3 C_6 H_4 S O_3 H$
Molar mass 172 g / mol (anhydrous)

	190 g / mol (monohydrate)
Appearance	colorless (white) solid
Density	1.24 g/cm^3
Melting point	38 °C (anhydrous) 103-106 °C, (monohydrate)
Boiling point	140 °C (at 20 mm Hg)
Solubility in water	67 g / 100 mL
Main hazards	skin irritant

2 - Preparation and handling

TsOH is prepared on an industrial scale by the sulfonation of toluene. It hydrates readily. Common impurities include benzene sulfonic acid and sulfuric acid. Impurities can be removed by recrystallization from its concentrated aqueous solution followed by azeotropic drying with toluene.

Toluene sulfonic acid finds use in organic synthesis as an "organic - soluble" acid catalyst. Examples of uses :

Acetalization of an aldehyde.

Esterification of carboxylic acids.

Trans esterification of an ester.[8]

3 - Tosylate esters

Tosylate esters are used as alkylating agents because the tosyl group is electron – with drawing, which makes the tosylate anion a good leaving group. The tosyl group is also a protecting group for alcohols and amines, prepared by combining the alcohol with 4-toluenesulfonyl chloride, usually in an aprotic solvent, often pyridine, the basicity of which activates the reaction.[9] Toluenesulfonate esters undergo nucleophilic attack or elimination. Reduction of tosylate esters gives the hydrocarbon. Thus, tosylation followed by reduction allows for the deoxygenation of alcohols.

4 - Reactions

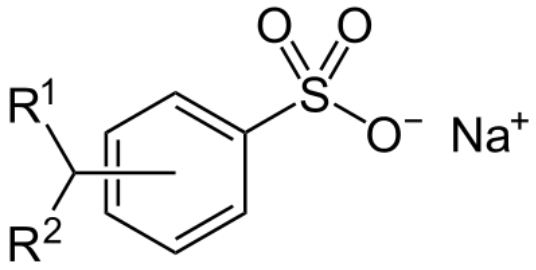
p-Toluene sulfonic acid may be converted to *p*-toluene sulfonic anhydride by heating with phosphorus pentoxide.

When TsOH is heated with acid and water, a hydrolysis reaction takes place and toluene is formed:

$$CH_3C_6H_4SO_3H + H_2O \rightarrow C_6H_5CH_3 + H_2SO_4$$

This reaction is general for aryl sulfonic acids, but the rate at which it occurs depends upon the structure of the acid, the temperature and the nature of the catalyzing acid. For example p-TsOH is unaffected by cold concentrated hydrochloric acid, but hydrolyzes when heated to 186°C in concentrated phosphoric acid.

Sodium Dodecyl Benzene Sulfonate



$$R^1 + R^2 = C_{11}H_{24}$$

Contents

1 - Introduction

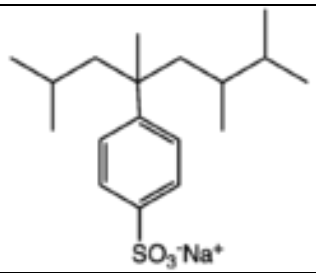
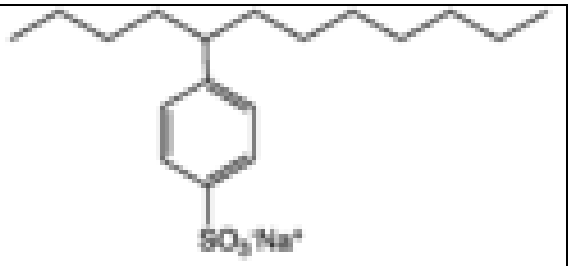
Sodium dodecyl benzene sulfonate is a series of organic compounds with the formula $C_{12}H_{25}C_6H_4SO_3Na$. It is a colourless salt with useful properties as a surfactant. It is usually produced as a mixture of related sulfonates. It is a major component of laundry detergent.

IUPAC name : sodium dodecyl benzene sulfonate	
Other names : Dodecyl benzene sulfonic acid, sodium salt; LAS; linear alkyl benzene sulfonate	
Molecular formula	$C_{18}H_{29}NaO_3S$
Molar mass	348 g mol^{-1}
Solubility in water	20 %

2 – Alkyl benzene sulfonates

Most sodium dodecyl benzene sulfonates are a member of the *linear* alkyl benzene sulfonates, meaning that the dodecyl group

($C_{12}H_{25}$) is un branched. This dodecyl chain is attached at the 4-position of the benzene sulfonate group. Linear dodecyl-4-benzene sulfonate anions can exist in six isomers (ignoring optical isomers), depending on the carbon of the dodecyl group that is attached to the benzene ring. The isomer shown below left is 4-(5-dodecyl) benzene sulfonate (4 indicating the position of the benzene ring, 5 indicating the position on the dodecane chain). Branched isomers, e.g. those derived from tetramerized propylene, are also known (below right) but are not as widely used because they biodegrade too slowly.

	
A branched dodecyl benzene sulfonate, which has been phased out in developed countries.	*A Linear dodecyl benzene sulfonate*

Further complicating the description of the commercial materials, sodium dodecyl benzene sulfonate is one component of a mixture of compounds that feature variable alkyl chain lengths aside from C12, mainly ranging from C10-C16. Dodecyl benzene sulfonate is considered representative of the entire class of compounds, since the mean number of alkyl carbon atoms in the alkyl benzene sulfonates is 12.

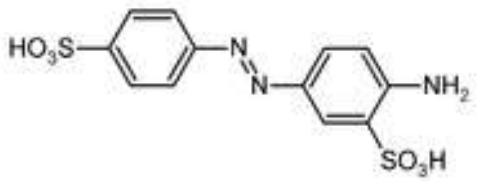
2 – 1 - Production[edit source

Trillions of kilograms are produced annually. Given the large scale of the application, the alkyl benzene sulfonates have been prepared by many methods. In the most common route, benzene is alkylated by long chain mono alkenes (e.g. dodecene) using hydrogen fluoride as a catalyst. The purified dodecyl benzenes (and related derivatives) are then sulfonated with sulfur trioxide to give the sulfonic acid. The sulfonic acid is subsequently neutralized with sodium hydroxide.

3 - Environmental considerations

Biodegradability has been well studied , and is affected by the isomerization (branching). The salt has an LD_{50} of 2.3 mg / liter for fish , about 4x more toxic than the branched tetra propylene benzene sulfonate. It is however biodegraded more rapidly. Oxidative degradation initiates at the alkyl chain.

Fast Yellow AB



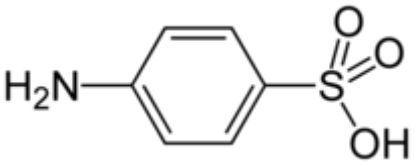
IUPAC name :
2-amino-5-[(*E*)-(4-sulfophenyl) diazenyl] benzene sulfonic acid

Other names :
Fast Yellow
Acid Yellow
Food Yellow 2
C.I. 13015

Molecular formula	$C_{12}H_{11}N_3O_6S_2$
Molar mass	357

Fast Yellow AB is an azo dye. It used to be used as a food dye, designated in Europe by the E number E105. It is now delisted in both Europe and USA and is forbidden if used in foods and drinks, as toxicological data has shown it is harmful. E105 has been implicated in non-atopic asthma.

Sulfanilic Acid



IUPAC name :
p-amino benzene sulphonic acid
Other names :
Sulphanilic acid

Molecular formula	$C_6H_7NO_3S$
Molar mass	173
Density	1.485
Melting point	288 °C
Solubility in water	> 20 g/l
Acidity (pK_a)	3.01

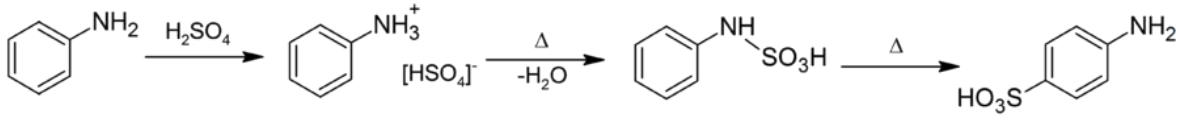
Contents

1 - Introduction

Sulfanilic acid (4-amino benzene sulfonic acid) is an off-white crystalline solid which finds application in quantitative analysis of nitrate and nitrite ions. The solid acid exists as a zwitterion, and has an unusually high melting point.

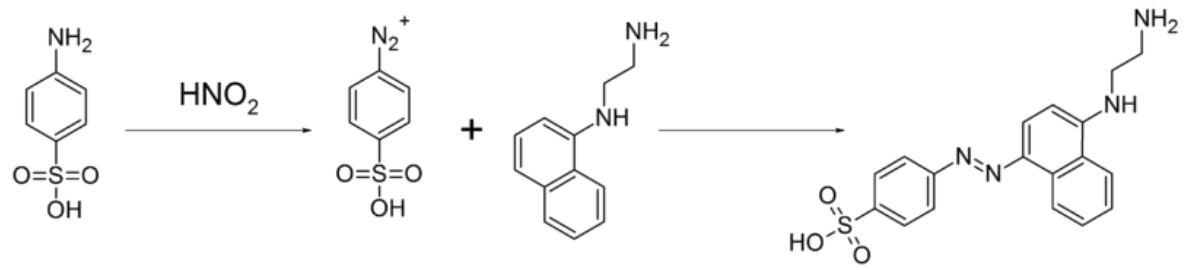
2 - Synthesis

Sulfanilic acid can be produced by sulfonation of aniline :



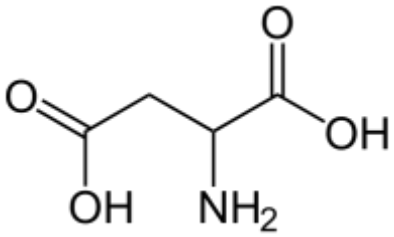
3 Applications

As the compound readily form diazo compounds, it is used to make dyes and sulpha drugs . This property is also used for the quantitative analysis of nitrate and nitrite ions by diazonium coupling reaction with N-(1-Naphthyl) ethylene diamine , resulting in an azo dye, and the concentration of nitrate or nitrite ions were deduced from the color intensity of the resulting red solution by colorimetry.



It is also used as a standard in combustion analysis.

Aspartic Acid



Contents

1 - Introduction

Aspartic acid (abbreviated as Asp or D) is an α-amino acid with the chemical formula $HOOCCH(NH_2)CH_2COOH$. The carboxylate anion, salt, or ester of aspartic acid is known as aspartate. The L-isomer of aspartate is one of the 20 proteinogenic amino acids, i.e., the building blocks of proteins. Its codons are GAU and GAC.

Aspartic acid is, together with glutamic acid, classified as an acidic amino acid with a pK_a of 3.9, however in a peptide the pK_a is highly dependent on the local environment. A pK_a as high as 14 is not at all uncommon. Aspartate is pervasive in biosynthesis. As with all amino acids, the presence of acid protons depends on the residue's local chemical environment and the pH of the solution.

IUPAC name : *Trivial:* Aspartic acid *Systematic:* 2-Amino butanedioic acid

Other names : Amino succinic acid, asparagic acid, asparaginic acid	
Molecular formula	$C_4H_7NO_4$
Molar mass	133 g mol^{-1}
Appearance	colourless crystals
Density	1.7 g / cm^3
Melting point	270 °C
Boiling point	324 °C (decomposes)
Solubility in water	4.5 g / L
EU Index	not listed
Thermo dynamic data	Phase behaviour Solid , liquid , gas
Spectral data	UV , IR , NMR , MS

2 – Discovery

Aspartic acid was first discovered in 1827 by Plisson, derived from asparagine, which had been isolated from asparagus juice in 1806, by boiling with a base.

3 - Forms and nomenclature

There are two forms or enantiomers of aspartic acid. The name "aspartic acid" can refer to either enantiomer or a mixture of two.[3] Of these two forms, only one, "L - aspartic acid", is directly incorporated into proteins. The biological roles of its counterpart, "D-aspartic acid" are more limited. Where enzymatic synthesis will produce one or the other, most chemical syntheses will produce both forms, "DL-aspartic acid," known as a racemic mixture.

4 - Role in biosynthesis of amino acids

Aspartate is non - essential in mammals, being produced from oxaloacetate by transamination. It can also be generated from ornithine and citrulline in the urea cycle. In plants and

microorganisms, aspartate is the precursor to several amino acids, including four that are essential for humans: methionine, threonine, isoleucine, and lysine. The conversion of aspartate to these other amino acids begins with reduction of aspartate to its "semi aldehyde," $O_2CCH(NH_2)CH_2CHO$. Asparagine is derived from aspartate via trans amidation :

$$-O_2CCH(NH_2)CH_2CO_2^- + GC(O)NH_3^+$$
$$O_2CCH(NH_2)CH_2CONH_3^+ + GC(O)O$$

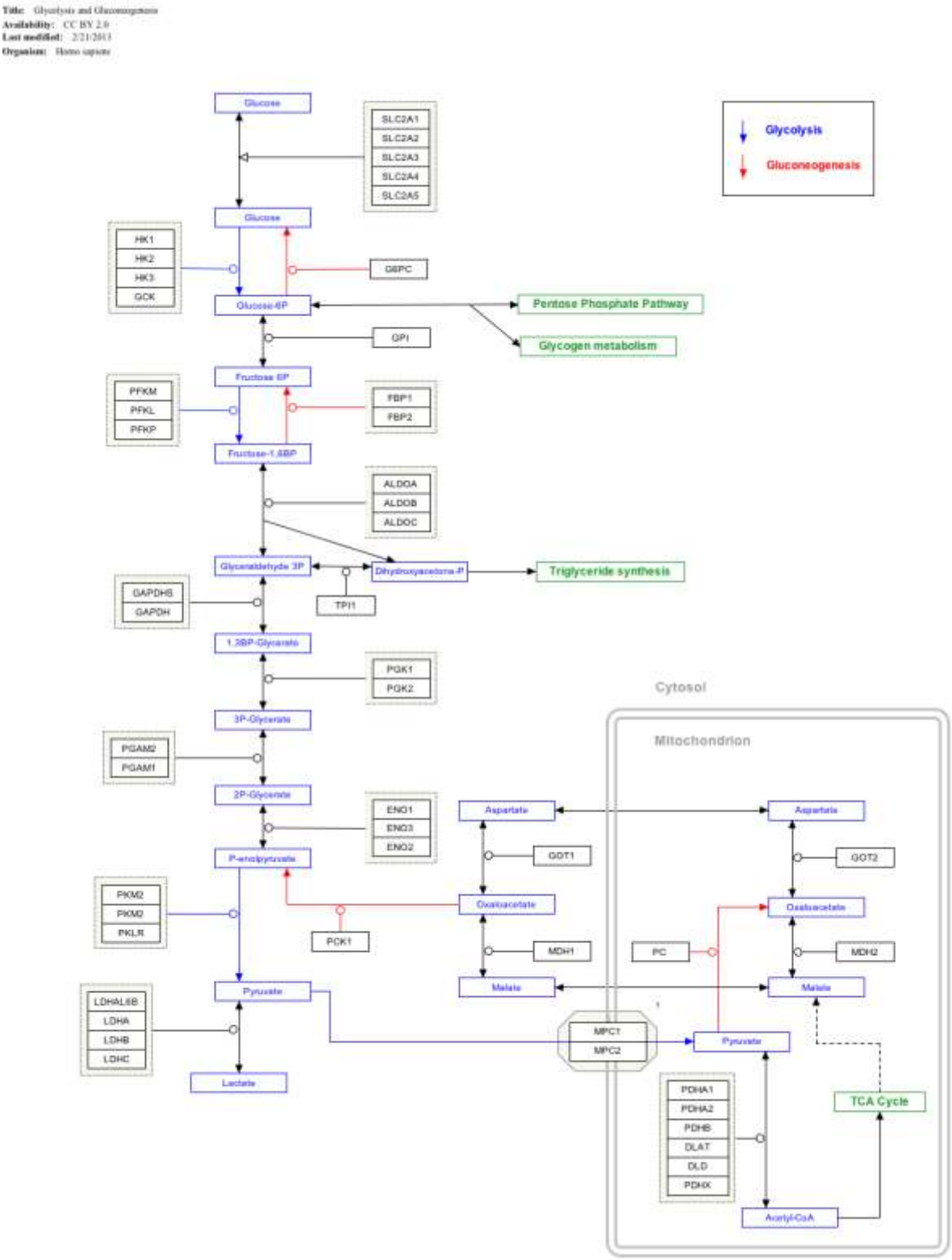
(where $GC(O)NH_2$ and $GC(O)OH$ are glutamine and glutamic acid, respectively)

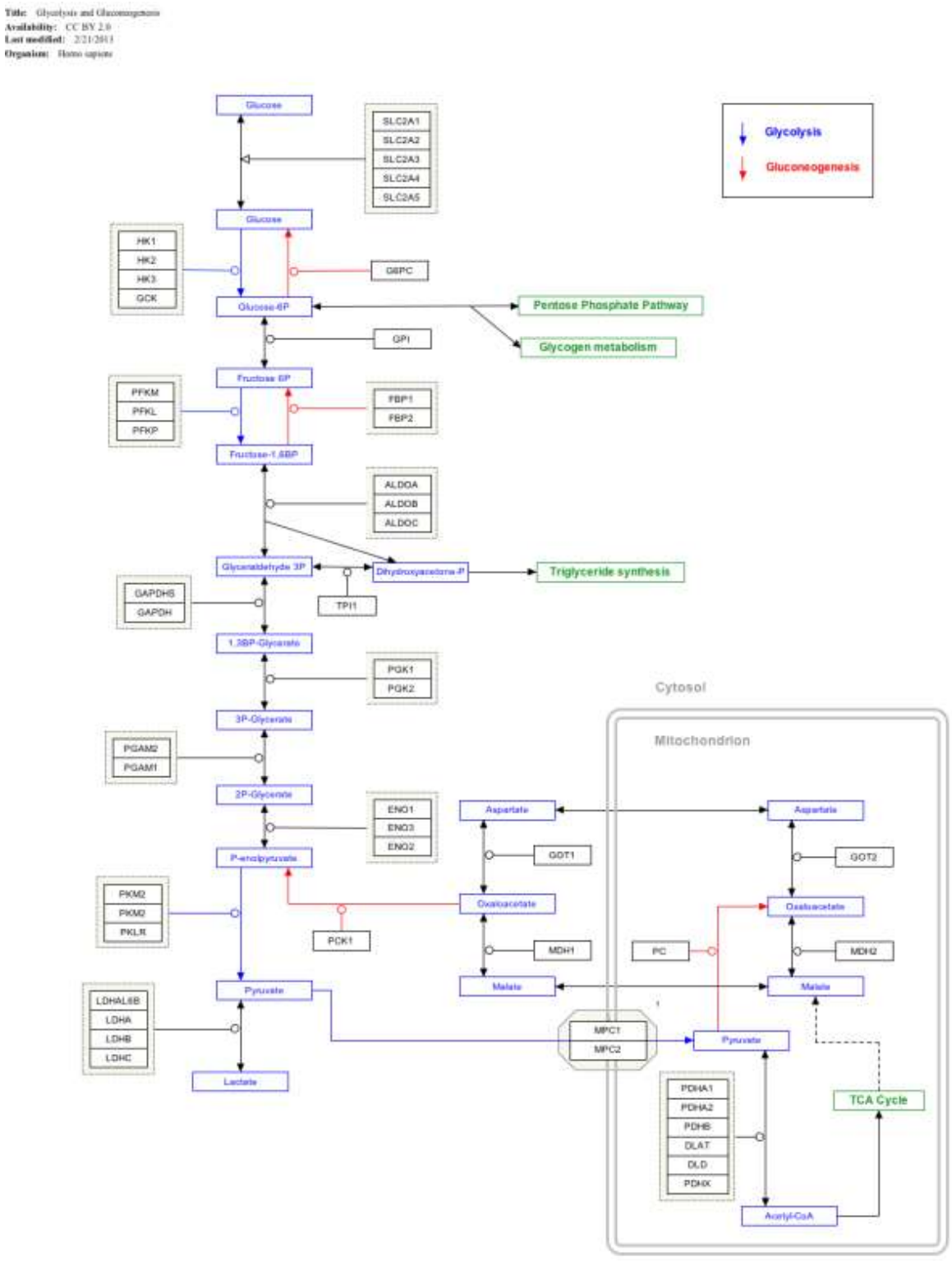
5 - Other biochemical roles

Aspartate is also a metabolite in the urea cycle and participates in gluconeogenesis. It carries reducing equivalents in the malate-aspartate shuttle, which utilizes the ready inter conversion of aspartate and oxaloacetate, which is the oxidized (dehydrogenated) derivative of malic acid. Aspartate donates one nitrogen atom in the biosynthesis of inosine, the precursor to the purine bases. In addition, aspartic acid acts as hydrogen acceptor in a chain of ATP synthase.

5 – 2 - Interactive pathway map

Click on genes, proteins and metabolites below to link to respective articles.





6 – Sources

6 – 1 - Dietary sources

Aspartic acid is not an essential amino acid, which means that it can be synthesized from central metabolic pathway intermediates in humans. Aspartic acid is found in :

Animal sources : luncheon meats, sausage meat, wild game

Vegetable sources: sprouting seeds, oat flakes, avocado, asparagus ' young sugarcane, and molasses from sugar beets.

Dietary supplements, either as aspartic acid itself or salts (such as magnesium aspartate)

The sweetener aspartame (NutraSweet, Equal, Canderel, etc.)

6 – 2 - Chemical synthesis

Racemic aspartic acid can be synthesized from diethyl sodium phthalimido malonate, ($C_6H_4(CO)_2NC(CO_2Et)_2$).

The major disadvantage of the above technique is that equimolar amounts of each enantiomer are made. Using biotechnology it is now possible to use immobilized enzymes to create just one type of enantiomer owing to their stereo specificity. Aspartic acid is made synthetically using ammonium fumarate and aspartase from *E.coli*, *E.coli* usually breaks down the aspartic acid as a nitrogen source but using excess amounts of ammonium fumarate a reversal of the enzyme's job is possible, and so aspartic acid is made to very high yields, 98.7 mM from 1 M.

LIST