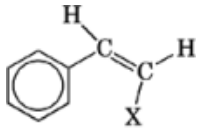
Kirk-Othmer Encyclopedia of Chemical Technology.

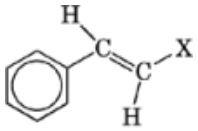
CINNAMIC ACID, CINNAMALDEHYDE, AND CINNAMYL ALCOHOL

The earliest references to cinnamic acid, cinnamaldehyde, and cinnamyl alcohol are associated with their isolation and identification as odor-producing constituents in a variety of botanical extracts. It is now generally accepted that the aromatic amino acid L-phenylalanine [63-91-2], a primary end product of the Shikimic Acid Pathway, is the precursor for the biosynthesis of these phenylpropanoids in higher plants (1, 2).

The widespread use of cinnamic derivatives has led to the pursuit of reliable methods for their direct synthesis. Commercial processes have focused on condensation reactions between benzaldehyde and a number of active methylene compounds for assembly of the requisite carbon skeleton. The presence of a disubstituted carbon–carbon double bond in the sidechain of these chemicals also gives rise to the existence of two distinct stereoisomers, the cis or (Z)-and trans or (E)-isomers:



(*Z*)-isomer



(*E*)-isomer

where X = COOH, CHO, or CH_2OH

A considerable range of products, including flavors, fragrances, agrochemicals, pharmaceuticals, and polymers, has been developed using these chemicals as either synthetic intermediates or ingredients (3).

1. Cinnamic Acid

3-Phenyl-2-propenoic acid [621-82-9], commonly referred to as cinnamic acid, is a white crystalline solid having a low intensity sweet, honeylike aroma. It has been identified as a principal constituent in the botanical exudates from Styrax (*Liquidamber orientalis*), Benzoin (*Styrax benzoin*), Peru Balsam (*Myroxylon pereirae*), and Tolu Balsam (*Myroxylon balsamum*) (4, 5). In these, as well as numerous other natural products, it exists both as the free acid and in the form of one or more of its esters, as for example, methyl cinnamate, benzyl cinnamate [103-41-3], and cinnamyl cinnamate.

Table 1. Properties of (*E*)-Cinnamic Acid

Property	Value
molecular formula	$C_9H_8O_2$
mol wt	148.2
melting point, °C	133
boiling point, °C at 101.3 kPa[a]	300
specific gravity at 25°C	1.245
solubility at 20°C	
g/L H_2O	0.5
g/L C_2H_5OH	189
dissociation constant, K_a, at 25°C	3.5×10^{-5}

[a] To convert kPa to mm Hg, multiply by 7.5.

1.1. Physical and Chemical Properties

Cinnamic acid is generally encountered as the thermodynamically favored (*E*)-isomer. (*E*)-Cinnamic acid [140-10-3] is an off-white solid having the properties outlined in Table 1 (6, 7).

For (*Z*)-cinnamic acid [102-94-3], three distinct polymorphic forms have been characterized. The most stable form, referred to as allocinnamic acid, has a melting point of 68°C, and the two metastable forms, isocinnamic acids, have melting points of 58°C and 42°C, respectively. (*E*)-Cinnamic acid can be converted to the (*Z*)-isomer photochemically through irradiation of a solution with ultraviolet light.

Cinnamic acid undergoes reactions that are typical of an aromatic carboxylic acid. Using standard methodology, simple esters are easily prepared and salts are formed upon neutralization with the appropriate base. Hydrogenation of cinnamic acid under mild conditions leads to 3-phenylpropanoic acid [501-52-0] whereas under forcing conditions, such as under high pressure in presence of a nickel catalyst, complete saturation to 3-cyclohexylpropanoic acid [701-97-3] is readily accomplished (8).

Decomposition to styrene and carbon dioxide has been observed upon heating the acid to temperatures in excess of 150°C. The decarboxylation process can be accelerated with the addition of a bicyclic amine base (9).

Selective oxidation of either the aromatic ring or the side chain can also be accomplished. For example, epoxidation of the double bond of cinnamic acid is effected in excellent yield by treatment with potassium hydrogen persulfate (10).

1.2. Manufacture

The most widely employed method for the commercial synthesis of (*E*)-cinnamic acid utilizes benzaldehyde, acetic anhydride, and anhydrous sodium or potassium acetate in a condensation reaction commonly referred to as the Perkin reaction1 (11).

$$C_6H_5CHO + (CH_3CO)_2O \xrightarrow{CH_3COONa} C_6H_5CH{=}CHCOOH + CH_3COOH$$

In a typical process, a mixture of acetic anhydride, anhydrous sodium acetate, and benzaldehyde in a ratio of 1.8:1:1 is charged into a reactor equipped with a column suitable for fractional distillation. The reaction mixture is heated to 180–190°C and acetic acid is continuously removed over an 8–10-h period. This process yields over 80% cinnamic acid based on consumed benzaldehyde. Other catalysts such as pyridine, potassium acetate, potassium carbonate, and sodium borate have been examined in an attempt to maximize the yield and reduce by-product formation. None of the alternative systems have given dramatically improved performance.

Treatment of benzal chloride [98-87-3] with anhydrous sodium acetate at 180–200°C provides another economically attractive route to cinnamic acid2.

$$C_6H_5CHCl_2 + 2CH_3COONa \longrightarrow C_6H_5CH{=}CHCOOH + 2\,NaCl + CH_3COOH$$

The chloride is readily available as a by-product of benzyl chloride [100-44-7] production (see Chlorocarbon and chlorohydrocarbons-benzyl chloride, benzal chloride, and benzotrichloride). The yield is comparable to the Perkin-based process, but the difficulty associated with removal of trace halogenated impurities makes the resultant cinnamic acid less desirable for many applications.

Another potentially valuable method for the preparation of cinnamic acid involves treatment of benzaldehyde with ketene (12). The initially formed oligomer of β-hydroxy-β-phenylpropionic acid is thermally decomposed at 100–250°C in the presence of an acid or base catalyst(**3**).

$$C_6H_5CHO + H_2C{=}C{=}O \longrightarrow \left(O{-}\overset{\displaystyle C_6H_5}{\overset{|}{C}}HCH_2\overset{\displaystyle O}{\overset{\|}{C}}\right)_n \longrightarrow C_6H_5CH{=}CHCOOH$$

Esters of cinnamic acid are used more extensively than the acid itself, and can be converted to the acid by standard hydrolysis protocols. The Claisen condensation between benzaldehyde and the appropriate acetate ester3 provides a direct, high yield route to the simple esters.

$$C_6H_5CHO + CH_3COOR \xrightarrow{NaOR} C_6H_5CH{=}CHCOOR$$

The catalyst of choice for this reaction is the corresponding sodium alkoxide.

Several newer methods take advantage of the highly selective nature of organopalladium reagents4. A palladium acetate-triarylphosphine catalytic system has been employed to induce the coupling of bromobenzene with the desired acrylate ester (13).

$$C_6H_5Br + CH_2{=}CHCOOR + R'_3N \xrightarrow[\text{phosphine}]{Pd(OOCCH_3)_2} C_6H_5CH{=}CHCOOR + R'_3NH^+Br^-$$

Cinnamate ester yields of 70–95% have been realized, but the substrates are expensive when compared with those employed in the standard Claisen approach.

The oxidative carbonylation5 of styrene with carbon monoxide, oxygen, and an aliphatic alcohol in the presence of a palladium salt, a copper salt, and sodium propionate also provides the requisite cinnamate.

$$C_6H_5CH{=}CH_2 + CO + \tfrac{1}{2}\,O_2 + ROH \longrightarrow C_6H_5CH{=}CHCOOR + H_2O$$

Conditions that give selectivity as high as 95% have been defined (14).

1.3. Economic Aspects

There are no published production figures for cinnamic acid. Most of the manufactured acid is consumed internally to generate a series of cinnamate esters for flavor and fragrance applications. With this in mind, it was possible to estimate a 1990 usage in the range of 175 metric tons. The cinnamic acid that does find its way into the marketplace has been sold for $12–14/kg in drum quantities.

1.4. Health and Safety

The Flavor and Extract Manufacturers' Association (FEMA) and the Research Institute for Fragrance Materials (RIFM) have developed procedures which employ expert panels to evaluate the safety in use of new and existing flavor and fragrance ingredients. The FEMA expert panel has given cinnamic acid GRAS (generally recognized as safe) status and FEMA No. 2288 has been assigned to this material (15). As a consequence, the FDA has approved it for food use. The acid is likewise devoid of any significant dermal irritation or sensitization and has been approved for fragrance use (16).

1.5. Uses

Although cinnamic acid is not considered an important odorant, it serves as a precursor for derivatives such as the esters (17) which have pleasant long-lasting aromas. Methyl cinnamate [103-26-4] enjoys the greatest usage and is found in flavor and fragrance compositions created for products which include soaps and cosmetics as well as beverages, baked goods, and convenience foods. Reported applications for cinnamic acid and its derivatives also include: use as a light penetration inhibitor in sunscreen formulations (18); for the preparation of herbicidal compositions (19); as a substrate in the formation of photopolymers (20–22); as a raw material in the synthesis of heterocyclic color complexes (23); and in the electroplating process for zinc (24).

One of the most interesting uses for cinnamic acid in recent years has been as a raw material in the preparation of L-phenylalanine [63-91-2], the key intermediate for the synthetic dipeptide sweetener aspartame (25). Genex has described a biosynthetic route to L-phenylalanine which involves treatment of immobilized cells of *R. rubra* containing the enzyme phenylalanine ammonia lyase (PAL) with ammonium cinnamate [25459-05-6] (26).

2. Cinnamaldehyde

3-Phenyl-2-propenal [104-55-2], also referred to as cinnamaldehyde, is a pale yellow liquid with a warm, sweet, spicy odor and pungent taste reminiscent of cinnamon. It is found naturally in the essential oils of Chinese cinnamon (*Cinnamomum cassia*, Blume) (75–90%) and Ceylon cinnamon (*Cinnamomum zeylanicum*, Nees) (60–75%) as the primary component in the steam distilled oils (27). It also occurs in many other essential oils at lower levels.

2.1. Physical and Chemical Properties

The (*E*)- and (*Z*)-isomers of cinnamaldehyde are both known. (*E*)-Cinnamaldehyde [14371-10-9] is generally produced commercially and its properties are given in Table 2. Cinnamaldehyde undergoes reactions that are typical of an α,β-unsaturated aromatic aldehyde. Slow oxidation to cinnamic acid is observed upon exposure to air. This process can be accelerated in the presence of transition-metal catalysts such as cobalt acetate (28). Under more vigorous conditions with either nitric or chromic acid, cleavage at the double bond occurs to afford benzoic acid. Epoxidation of cinnamaldehyde via a conjugate addition mechanism is observed upon treatment with a salt of *t*-butyl hydroperoxide (29).

Hydrogenation of cinnamaldehyde has been studied extensively since selectivity has often been an issue. Under mild conditions the carbonyl group is reduced giving cinnamyl alcohol, whereas at elevated temperatures complete reduction to 3-phenylpropanol [122-97-4] results. It is possible to saturate the double bond without concomitant reduction of the carbonyl group through selective hydrogenation with a ferrous chloride-activated palladium catalyst (30), thereby producing 3-phenylpropanol [104-53-0].

Table 2. Properties of (*E*)-Cinnamaldehyde

Property	Value
molecular formula	C_9H_8O
mol wt	132.2
boiling point, °C	
at 101 kPa[a]	252
at 1.3 kPa[a]	120
specific gravity at 20°C	1.049
refractive index at 20°C	1.6195
solubility	
in 50% C_2H_5OH	1:25
in ethyl ether	infinite

[a] To convert kPa to mm Hg, multiply by 7.5.

The formation of acetals with methanol, ethanol, or ethylene glycol in the presence of an acid catalyst such as hydrogen chloride or benzenesulfonic acid is straightforward. Sodium bisulfite and hydroxylamine form adducts with cinnamaldehyde that are used in typical quantitative analysis protocols.

Upon treatment with aluminum ethoxide, the aldehyde is converted to cinnamyl cinnamate [122-69-0] (Tishchenko reaction), a valuable perfumery ingredient.

2.2. Manufacture

Cinnamaldehyde is routinely produced by the base-catalyzed aldol addition of benzaldehyde [100-52-7] with acetaldehyde [75-07-0], a procedure which was first established in the nineteenth century (31). Formation of the (*E*)-isomer is favored by the transition-state geometry associated with the elimination of water from the intermediate. The commercial process is carried out in the presence of6 a dilute sodium hydroxide solution (ca 0.5–2.0%) with at least two equivalents of benzaldehyde and slow addition of the acetaldehyde over the reaction period (32).

$$C_6H_5CHO + CH_3CHO \xrightarrow{NaOH} C_6H_5CH{=}CHCHO + H_2O$$

In this manner, self-condensation of acetaldehyde is minimized and yields in the range of 77–85% are obtained. However, even with these precautions a detectable amount of 5-phenyl-2,4-pentadienal [13466-40-5] is invariably formed.

Another approach is based on the rearrangement7 of an acetylenic carbinol formed between benzaldehyde and acetylene.

$$C_6H_5CH(OH)C{\equiv}CH \longrightarrow C_6H_5CH{=}CHCHO$$

Isomerization catalyzed by silyl vanadates (33) gives cinnamaldehyde in high yield.

2.3. Economic Aspects

Since the 1970s cinnamaldehyde has been produced in significant quantities by Fritzsche Dodge & Olcott (FDO), Haarmann & Reimer (H&R), and Dutch State Mines (DSM). However, by the end of 1989 DSM was the only remaining producer for this material. Production statistics are listed in Table 3.

Table 3. Cinnamaldehyde Production

Year	Volume[a], 10^3t	Price,[b] $/kg
1970	685	2.30–2.60
1980	850	3.30–3.65
1990	975	3.50–4.00

[a] Estimates based on U.S. International Trade Commis-sion figures and unpublished data.
[b] Prices based on drum quantities.

2.4. Health and Safety

FEMA has examined cinnamaldehyde and established its GRAS status (No. 2286). The material has been used in some fragrance compositions, but RIFM (34) has noted its potential for sensitization and limited the use in perfumes for skin contact at 1% in the formula. Eugenol and limonene have been used in conjunction with cinnamaldehyde as quenchers to neutralize the irritation reaction that some individuals have toward this aldehyde.

2.5. Uses

Greater than 95% of the consumption of cinnamaldehyde occurs in flavor applications where a spicy, cinnamon character is required. It is used in a wide range of products including bakery goods, confection, and beverages as well as in toothpastes, mouthwashes,, and chewing gum. It is also used effectively in air fresheners where odor neutralization can be accomplished by reaction with sulfur and nitrogen malodorants.

In electroplating processes, cinnamaldehyde is utilized as a brightener (35). Other applications include its efficacy as an animal repellent (36), its use in compositions to attract insects (37), and demonstration of a positive antifungal activity (38).

Cinnamaldehyde has been efficiently isolated in high purity by fractional distillation from cassia and cinnamon bark essential oils. This material has been utilized in several manufacturing protocols (39–41) for the preparation of natural benzaldehyde through a retro-aldol process. Since the late 1970s the demand for natural flavors has increased dramatically. This demand has led to a corresponding requirement for a more extensive line of readily available natural aroma chemicals for flavor creation.

3. Cinnamyl Alcohol

3-Phenyl-2-propen-1-ol [104-54-1], commonly referred to as cinnamyl alcohol, is a colorless crystalline solid with a sweet balsamic odor that is reminiscent of hyacinth. Its occurrence in nature is widespread as, for example, in Hyacinth absolute (*Hyacinthus orientalis*) (42), the leaf and bark oils of cinnamon (*Cinnamomum cassia*, *Cinnamomum zeylancium*, etc), and Guava fruit (*Psidium guajava L.*) (43). In many cases it is also encountered as the ester or in a bound form as the glucoside.

3.1. Physical and Chemical Properties

Although both the (*E*)- and (*Z*) [4510-34-3] isomers of cinnamyl alcohol are known in nature, (*E*)-cinnamyl alcohol [4407-36-7] is the only isomer with commercial importance. Its properties are summarized in Table 4.

When heated in the presence of a carboxylic acid, cinnamyl alcohol is converted to the corresponding ester. Oxidation to cinnamaldehyde is readily accomplished under Oppenauer conditions with furfural as a

Table 4. Properties of (*E*)-Cinnamyl Alcohol

Property	Value
molecular formula	$C_9H_{10}O$
mol wt	134.2
boiling point, °C at 1.33 kPa	117–118
melting point, °C	33
density, g/mL at 20°C	1.044
refractive index at 20°C	1.5819
solubility in 60% C_2H_5OH	1:2

hydrogen acceptor in the presence of aluminum isopropoxide (44). Cinnamic acid is produced directly with strong oxidants such as chromic acid and nickel peroxide. The use of t-butyl hydroperoxide with vanadium pentoxide catalysis offers a selective method for epoxidation of the olefinic double bond of cinnamyl alcohol (45).

Halogens add to the double bond of the alcohol to afford the corresponding dihalo derivatives, eg, $C_6H_5CHXCHXCH_2OH$, where X = Cl or Br. The allylic chloride C_9H_9Cl [2687-12-9] can be obtained by treatment of the alcohol with hydrochloric acid, thionyl chloride, or carbon tetrachloride–triphenylphosphine as the halogen donor.

3.2. Manufacture

A limited amount of natural cinnamyl alcohol is produced by the alkaline hydrolysis of the cinnamyl cinnamate present in Styrax Oil. Thus treatment of the essential oil with alcoholic potassium hydroxide liberates cinnamyl alcohol of reasonable purity which is then subjected to distillation. This product is sometimes preferred in fine fragrance perfumery because it contains trace impurities that have a rounding effect in finished formulations.

One of the first practical methods for the manufacture of cinnamyl alcohol involved reduction of cinnamic aldehyde diacetate with iron filings in acetic acid. This approach suffered from low yields and liberation of a significant amount of the starting aldehyde.

The commercial production of cinnamyl alcohol is accomplished exclusively by the reduction of cinnamaldehyde8.

$$C_6H_5CH{=}CHCHO \longrightarrow C_6H_5CH{=}CHCH_2OH$$

The preferred method for many years has been the Meerwein-Ponndorf-Verley reaction (46). In a typical process, cinnamaldehyde is dissolved in two volumes of 2-propanol containing aluminum isopropoxide (5–8 mol %) and acetone formed is removed continuously at reflux. Purification affords the alcohol in 85–90% yield. The reduction is mild and highly chemoselective, attacking only the carbonyl group in an α,β-unsaturated aldehyde. A significant disadvantage of the Meerwein reduction is the waste treatment problem associated with disposal of large quantities of aluminum salts. Another process involves liquid-phase hydrogenation in the presence of a platinum catalyst. The reaction is carried out in a two-phase, eg, water-toluene, solvent system at 20–40°C and 3–6 MPa (435–870 psi) hydrogen pressure (47). The cinnamyl alcohol (ca 75–80% yield) is accompanied by 5–8% 3-phenylpropanol which must be removed by careful distillation.

3.3. Economic Aspects

The market prices for cinnamyl alcohol quoted in Table 5 have been adjusted to reflect an average price for the relative quantities of the different grades sold. As of this writing, DSM is the only significant supplier for this material.

Table 5. Cinnamyl Alcohol Production

Year	Volume[a], 10^3t	Price[b], $/kg
1970	95	3.50–3.85
1980	175	7.95–8.18
1990	260	7.70–8.55

[a] Estimate based on U.S. International Trade Commission figures and unpublished data.
[b] Based on drum quantities.

3.4. Health and Safety

Cinnamyl alcohol has been evaluated by FEMA and given GRAS status (FEMA No. 2294). Two of its esters, cinnamyl cinnamate (FEMA No. 2298) and cinnamyl acetate (FEMA No. 2293), are also used extensively in flavor and fragrance compositions. Cinnamyl alcohol has also been tested by RIFM (48) and found to be safe for use. There have been reported cases of irritation and several manufacturers market a desensitized alcohol for use in fragrance applications.

3.5. Uses

Cinnamyl alcohol and its esters, especially cinnamyl acetate, are widely employed in perfumery because of their excellent sensory and fixative properties. They are frequently used in blossom compositions such as lilac, jasmine, lily of the valley, hyacinth, and gardenia to impart balsamic and oriental notes to the fragrance. In addition, they are utilized as modifiers in berry, nut, and spice flavor systems. The value of cinnamyl alcohol has also been mentioned in a variety of applications which include the production of photosensitive polymers (49), the creation of inks for multicolor printing (50), the formulation of animal repellent compositions (51), and the development of effective insect attractants (52).

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