Kirk-Othmer Encyclopedia of Chemical Technology.

CYCLOHEXANOL AND CYCLOHEXANONE

Cyclohexanol [108-93-0] is a colorless, viscous liquid with a camphoraceous odor. It is used chiefly as a chemical intermediate, a stabilizer, and a homogenizer for various soap detergent emulsions, and as a solvent for lacquers and varnishes. Cyclohexanol was first prepared by the treatment of 4-iodocyclohexanol with zinc dust in glacial acetic acid, and later by the catalytic hydrogenation of phenol at elevated temperatures and pressures.

Cyclohexanone [108-94-1] is a colorless, mobile liquid with an odor suggestive of peppermint and acetone. Cyclohexanone is used chiefly as a chemical intermediate and as a solvent for resins, lacquers, dyes, and insecticides. Cyclohexanone was first prepared by the dry distillation of calcium pimelate [19455-79-9], $^{-}OOC(CH_2)_5COO^{-}Ca^{2+}$, and later by Bouveault by the catalytic dehydrogenation of cyclohexanol.

1. Physical Properties

Important physical properties of cyclohexanol and cyclohexanone are shown in Table 1. Cyclohexanol is miscible in all proportions with most organic solvents, including those customarily used in lacquers. It dissolves many oils, waxes, gums, and resins.

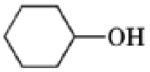
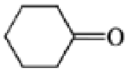
Cyclohexanone is miscible with methanol, ethanol, acetone, benzene, *n*-hexane, nitrobenzene, diethyl ether, naphtha, xylene, ethylene glycol, isoamyl acetate, diethylamine, and most organic solvents. This ketone dissolves cellulose nitrate, acetate, and ethers, vinyl resins, raw rubber, waxes, fats, shellac, basic dyes, oils, latex, bitumen, kaure, elemi, and many other organic compounds.

2. Manufacture

2.1. Cyclohexanol

This alcohol is produced commercially by the catalytic air oxidation of cyclohexane or the catalytic hydrogenation of phenol. The oxidation of cyclohexane to a mixture of cyclohexanol and cyclohexanone, known as KA-oil (ketone–alcohol, cyclohexanone–cyclohexanol crude mixture), is used for most production (1). The earlier technology that used an oxidation catalyst such as cobalt naphthenate at 180–250°C at low conversions (2) has been improved. Cyclohexanol can be obtained through a boric acid-catalyzed cyclohexane oxidation at 140–180°C with up to 10% conversion (3). Unreacted cyclohexane is recycled and the product mixture is separated by vacuum distillation. The hydrogenation of phenol to a mixture of cyclohexanol and cyclohexanone is usually carried out at elevated temperatures and pressure in either the liquid (4) or in the vapor phase (5) catalyzed by nickel.

Table 1. Properties of Cyclohexanol and Cyclohexanone

Property	Cyclohexanol	Cyclohexanone
		
mp, °C	25.15	−47
bp, °C	161.1	156.7
d_4^{20}, g/mL	0.9493	0.9478
n_D^{25}	1.4648	
n_D^{20}		1.4507
vapor pressure, kPa[a]		
25°C	0.15	
20°C		0.53
sp heat, 15–18°C, J/g[b]	1.75	1.81
viscosity, 25°C, mPa·s(= cP)	4.6	2.2
flash point, open cup, °C	67.2	54
solubility in water, g/100 g		
10°C	4.2	15
30°C	4.3	5
solubility of water in compound, g/100 g, 20°C	12.6	9.5

[a] To convert kPa to mm Hg, multiply by 7.5.
[b] T convert J to cal, divide by 4.184.

3. Cyclohexanone

The ketone is produced commercially by the catalytic hydrogenation of phenol or by the catalytic air-oxidation of cyclohexane; and may be prepared by either the catalytic dehydrogenation or oxidative dehydration of cyclochexanol. The hydrogenation of phenol to cyclohexanone is the most efficient route. This process can be carried out either in the liquid phase, catalyzed by palladium on carbon (6), or in the vapor phase, catalyzed by palladium on alumina (7). Of the two processes, the liquid phase is more selective and requires much less catalyst inventory. Allied Signal Corp. operates an inherently safe liquid-phase phenol hydrogenation process at temperatures below the atmospheric boiling point of the reaction liquids, permitting over 99% selectivity at 90% conversion (8).

Vapor-phase oxidation of cyclohexane is commercially feasible, but the preferred route is liquid-phase cyclohexane oxidation (2). In the latter process, conversions are usually below 10%. The product is a mixture of cyclohexanone and cyclohexanol which may be separated by distillation (2) or converted to cyclohexanone by dehydrogenation over either zinc oxide (5) or nickel or magnesium oxide (9). Mild oxidation of cyclohexanol to cyclohexanone can be carried out with (10) or without (11) catalyst.

4. Reactions, Derivatives, and Uses

Cyclohexanol shows most of the typical reactions of secondary alcohols. It reacts with organic acids to form esters, and with halogen acids to form the corresponding halides. Dehydrating agents convert cyclohexanol into cyclohexene [110-83-8]. Catalytic dehydrogenation or mild oxidation of cyclohexanol yields cyclohexanone. Strong oxidizing agents such as nitric acid or alkaline potassium permanganate convert cyclohexanol into adipic acid [124-04-9], $HOOC(CH_2)_4COOH$. Oxidation of cyclohexanol to adipic acid (qv) is the most important

Table 2. Boiling Points of Methylcyclohexanols

Isomer	CAS Registry Number	Boiling point, °C
2-methylcyclohexanol	[583-59-5]	164.5–165.5[a]
3-methylcyclohexanol	[591-23-1]	173.7–174[b]
4-methylcyclohexanol	[589-91-9]	172.5–173[a]

[a] At 99.3 kPa = 745 mm Hg.
[b] At 102.5 kPa = 769 mm Hg.

use; fully 90% of adipic acid produced in the United States is used in the manufacture of nylon-6,6, a polymer of adipic acid and hexamethylenediamine. Adipic acid may also be used to produce the hexamethylenediamine. The next important usage of cyclohexanol, pure or admixed with cyclohexanone as KA-oil, is in the production of caprolactam (qv), which is used in the manufacture of nylon-6 polymer (see Polyamides).

One principal use of cyclohexanol has been in the manufacture of esters for use as plasticizers (qv), ie, cyclohexyl and dicyclohexyl phthalates. In the finishes industry, cyclohexanol is used as a solvent for lacquers, shellacs, and varnishes. Its low volatility helps to improve secondary flow and to prevent blushing. It also improves the miscibility of cellulose nitrate and resin solutions and helps maintain homogeneity during drying of lacquers. Reaction of cyclohexanol with ammonia produces cyclohexylamine [108-91-8], a corrosion inhibitor. Cyclohexanol is used as a stabilizer and homogenizer for soaps and synthetic detergent emulsions. It is used also by the textile industry as a dye solvent and kier-boiling assistant (see Dye carriers).

Commercial methylcyclohexanol, $CH_3C_6H_{10}OH$, is a slightly viscous, straw-colored liquid which is a mixture of isomers listed in Table 2. The commercial product, made by the catalytic hydrogenation of mixed cresols, has a boiling range of 155–180°C, $d_{15.5}^{15.5}$, 0.924 ± 0.003 g/mL, and n_{D}^{20}, 1.461. It is used as a solvent in lacquers, as an ingredient in soap-based spot removers, as a blending agent for special textile soaps and detergents, and in the manufacture of lubricating-oil additives.

Cyclohexanone shows most of the typical reactions of aliphatic ketones. It reacts with hydroxylamine, phenylhydrazine, semicarbazide, Grignard reagents, hydrogen cyanide, sodium bisulfite, etc, to form the usual addition products, and it undergoes the various condensation reactions that are typical of ketones having α-methylene groups. Reduction converts cyclohexanone to cyclohexanol or cyclohexane, and oxidation with nitric acid converts cyclohexanone almost quantitatively to adipic acid.

The most important use of cyclohexanone is as a chemical intermediate in nylon manufacture; 97% of all cyclohexanone output is used either to make caprolactam for nylon-6, or adipic acid for nylon-6,6. In the caprolactam process cyclohexanone is converted to cyclohexanone oxime (mp, 89–90)°C), which is rearranged with sulfuric acid to ϵ-caprolactam [105-60-2] (mp, 69°C). The overall efficiency is $>97\%$. In the production of adipic acid, cyclohexanone is oxidized with nitric acid in the presence of catalysts. Cyclohexanone is also used as a solvent and thinner for lacquers, especially those containing nitrocellulose or vinyl chloride polymer and copolymers and as a general solvent for synthetic resins and polymers. Cyclohexanone is an excellent solvent for insecticides and many other similar materials. Cyclohexanone is used as a building block in the synthesis of many organic compounds, such as pharmaceuticals, insecticides, and herbicides. Cyclohexanone is used in the manufacture of magnetic and video tapes (see Magnetic tape). Cyclohexanone is not restricted under California Rule 66 and has, therefore, found use as a substitute for isophorone [78-59-1] as a solvent for resins and polymers (12) (see Air pollution).

5. Economic Aspects

Estimated annual cyclohexanone production capacities are shown in Table 3; the production is greater than 90% captive for caprolactam production (13). The annual cyclohexanol production is only 10 thousand metric

Table 3. Estimated U.S. Annual Production Capacity of Cyclohexanone

Producer	Location	Annual capacity,[a] 10^3 t
Allied Signal, Fibers Division	Hopewell, Virginia	330
BASF Corp., Chemicals Division	Freeport, Texas	180
DSM Chemicals North America, Inc.	Augusta, Georgia	155

[a] 1992.

tons. These production figures do not include KA-oil (cyclohexanol-cyclohexanone) production for adipic acid. Worldwide annual capacity for cyclohexanone is approximately 3.0 million metric tons, also primarily for caprolactam production. Projected new capacity for caprolactam could add 0.5 million metric tons worldwide in this decade.

6. Specifications and Analysis

Commercial cyclohexanol is offered in two grades, ie, technical and high grade. Typical specifications are as follows (14).

	Technical	High Grade
mp, °C min	−10	18
distillation range	10–19% within 1.5°C of 161.7°C	100% 159–163°C, 5–95% within 1.5°C of 161.7°C
$d_{15.5}^{25}$, g/mL	0.9375–0.9405	0.9425–0.9455
phenol content	none to trace	none
n_{D}^{25}	1.4575–1.4605	1.463–1.465

Some cyclohexanol is shipped with 2.25% of methanol [67-56-1] as antifreeze.

Cyclohexanol purity is best determined by gas–liquid chromatography using a DC-710 or carbowax 20M-on-chromosorb column. Impurities such as cyclohexane, benzene, cyclohexanone, and phenol do not interfere. Other analytical procedures include acylation with acetyl chloride and pyridine at elevated temperatures. Following hydrolysis, the excess acid is titrated with sodium hydroxide solution (15). Aldehydes and easily hydrolyzed esters interfere with this method. For samples containing high concentrations of acids and easily hydrolyzed esters but no aldehydes or ketones, an alternative procedure is used (16). This procedure involves treatment at elevated temperatures of the sample containing cyclohexanol with acetic acid containing boron trifluoride catalyst. The water formed in the esterification reaction is then determined by the Karl Fischer method. For analyses based on micro procedures, acetic anhydride is the preferred acetylating agent (17).

Cyclohexanol can be determined colorimetrically by reaction with *p*-hydroxy-benzaldehyde in sulfuric acid (18). This method can be used in the presence of cyclohexanone and cyclohexane. Cyclohexanol and cyclohexanone both show a maximum absorbency at 535 nm but at 625 nm the absorption by cyclohexanone is negligible, whereas cyclohexanol shows appreciable absorption.

Cyclohexanol and cyclohexanone are shipped in 208-L (55-gal) drums, in tank cars, and tank trucks. DOT regulations classify both cyclohexanol and cyclohexanone as combustible liquids. Drums containing less than 416-L (110 gal) do not require hazardous material labeling. Larger quantities must be labeled “Combustible Liquid” (19). The price in 1990 (for Technical, tank trucks, delivered) (13), was $1.87/kg for cyclohexanol and $1.70/kg for cyclohexanone.

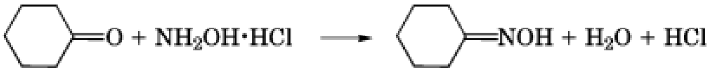
Commercial cyclohexanone is offered in various grades. The specifications of two typical grades are listed in Table 4 (14).

Table 4. Specifications of Two Typical Cyclohexanones

Property	Commercial grade	High purity
appearance	colorless liquid	colorless liquid
$d_{15.5}^{15.5}$, g/mL		0.950–9.951
d_{20}^{20}, g/mL	0.940–0.950	
distillation range, 95% at 101.3 kPa[a]	152–157°C	152–157°C
ash, % max	0.01	0.01
acidity, % max	none	0.03
alkalinity to phenolphthalein	none	none
ketone content, % min	89	99.5
soly in water at 20°C, %		5
water content, % max	0.2	0.2
flash point		
(Abel closed cup), °C		42
(Cleveland open cup), °C	46	
evaporation rate (ether = 1)	38	40

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

Cyclohexanonepurity is most readily determined by gas-liquid chromatography over DC-710 or carbowax 20M-on-chromosorb. Impurities such as cyclohexane, benzene, cyclohexanol, and phenol do not interfere. In the absence of other carbonyl compounds cyclohexanone may be determined by treatment with hydroxylamine hydrochloride, which forms the oxime, as follows:



With materials containing low concentrations of acids, the liberated hydrogen chloride is titrated with sodium hydroxide, either electrometrically (20) or with an indicator (21).

7. Health and Safety Factors

Cyclohexanol is slightly toxic by the oral route of exposure and is slightly irritating to the skin (22). It can cause severe eye irritation and transient corneal injury (23). The vapor is irritating to the eyes of humans at 100 ppm (24). Inhalation of high concentrations (~1000 ppm) of cyclohexanol in rabbits for 6 h/day, 5 days/wk for about 10 weeks induced effects including conjunctival congestion and irritation, lacrimation, salivation, lethargy, incoordination, narcosis, and mild convulsions.

After pregnant female mice were fed a diet containing 1% cyclohexanol during gestation, the offspring were observed to have an increased mortality during the first 21 days of life (25). Since only one dose (1%) was employed, a no-observable-effect level (NOEL) could not be determined from this study. The ability of cyclohexanol to cause testicular atrophy resulting in loss of spermatogonia, spermatocytes, and spermatozoa with shrinkage of seminiferous tubules and Leidig cells was reported upon repeated subcutaneous administration of 15 mg/kg/day in rats (for 37 days) and gerbils (for 21 days) (26). Similar signs were observed in rabbits after repeated oral administration of 25 mg/kg/day for a period of 40 days. Normal spermatogenesis returned after a 70 day recovery period (27). However, in one other reported study, testicular atrophy was not observed in rats administered cyclohexanol at a dose of 455 mg/kg/day by daily gastric intubation for 7 days (28).

The ACGIH threshold limit value (TLV), time-weighted average for an 8 hour workday, 40 hour workweek, was set at 50 ppm (~200 mg/m^3) with a notation for skin absorption (29).

Precautions that should be observed as a matter of course in using cyclohexanol include adequate and proper ventilation, avoidance of prolonged breathing of vapor or contact of the liquid with the skin, avoidance of ingestion, and protection of the eyes against splashing liquids.

Cyclohexanone has only slight toxicity by the oral, dermal, and inhalation routes of exposure. Liquid or vapor exposures may result in transient corneal injury (23). Primary irritation and defatting of the skin can result from substantial or prolonged contact with cyclohexanone. Exposure to high vapor concentrations can cause central nervous system (CNS) depression, an effect which can also occur after ingestion or repeated dermal exposure. Both positive and negative results have been reported for the genetic activity of cyclohexanone (30). The preponderance of the negative data stems from *in vivo* assay systems with positive results obtained with *in vitro* assay systems. Convincing evidence for carcinogenicity has not been provided, however (30, 31). Cyclohexanone has been reported to be nonteratogenic in both rats and mice (32, 33). Results of a two-generation inhalation reproduction study in rats indicate that the growth, development, or reproductive performance of animals exposed to 1000 ppm for one generation, or exposed to 250 or 500 ppm for two generations, was not adversely affected. When the progeny derived from parental animals (previously exposed to 100 ppm cyclohexanone) were exposed to 1400 ppm cyclohexanone for one generation, effects observed included lethargy, male body weight depressions, reduced male fertility, reduced progeny survival, and progeny body weight depression. These effects were found to be reversible during a post-exposure recovery period. Furthermore, there was no evidence of a dominant lethal effect resulting from the exposures. A no-observable-effect level (NOEL) of at least 500 ppm cyclohexanone vapor was determined from this study (34).

The time-weighted average OSHA permissible exposure limit (PEL), as well as the ACGIH threshold limit value (TLV), for cyclohexanone is 25 ppm (100 mg/m^3) with a notation for skin absorption (29, 35).

The precautions usually observed when handling volatile solvents should be observed as a matter of course with cyclohexanone. These include adequate and proper ventilation, avoidance of prolonged breathing of vapor or contact of the liquid with the skin, avoidance of internal consumption, and protection of the eyes against splashing liquids.

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