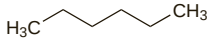
n-Hexane

n-Hexano.

н-Гексан

C_6H_{14} = 86.18.

CAS — 110-54-3.



Description. *n*-Hexane is a colourless, flammable, volatile liquid with a faint odour. Wt per mL about 0.66 g. B.p. about 69°. Store in airtight containers.

Adverse Effects

n-Hexane is irritant. Acute exposure to the vapour may result in CNS depression with headache, drowsiness, dizziness, and in severe cases unconsciousness. Chronic occupational exposure and abuse of *n*-hexane have been associated with the development of peripheral neuropathies. *n*-Hexane is a constituent of some adhesives and may be implicated in volatile substance abuse (p.2019). Some adverse effects of petrol have been attributed to its content of *n*-hexane.

◊ References.

1. Health and Safety Executive. *n*-Hexane. *Toxicity Review 18*. London: HMSO, 1987.
2. WHO. *n*-Hexane. *Environmental Health Criteria 122*. Geneva: WHO, 1991. Available at: http://www.inchem.org/documents/ehc/ehc/ehc122.htm (accessed 30/06/04)
3. WHO. *n*-Hexane health and safety guide. *IPCS Health and Safety Guide 59*. Geneva: WHO, 1991. Available at: http://www.inchem.org/documents/hsg/hsg/hsg059.htm (accessed 30/06/04)

Effects on the nervous system. There have been many reports of peripheral neuropathy attributed to the abuse of, and occupational exposure to, *n*-hexane, although symptoms tend to be milder in the latter.[1] Tetraplegia has occurred in severe cases. There is typically a clinical deterioration several weeks after exposure followed by a slow recovery which, in severe cases, may not be complete. It has been suggested that methyl ethyl ketone potentiates the peripheral neuropathy induced by *n*-hexane. Occupational exposure to *n*-hexane has also been associated with cranial nerve neuropathy.

Parkinsonism in a leather worker, possibly associated with exposure to solvents, mainly *n*-hexane, has been noted.[2]

For further discussion of neurotoxicity after occupational exposure to solvents including *n*-hexane, see under Toluene, p.2026.

1. Lolin Y. Chronic neurological toxicity associated with exposure to volatile substances. *Hum Toxicol* 1989; **8:** 293–300.
2. Pezzoli G, *et al.* Parkinsonism due to n-hexane exposure. *Lancet* 1989; **ii:** 874.

Pharmacokinetics

n-Hexane is absorbed after inhalation and to a limited extent through the skin. Oxidative metabolites, including 2,5-hexanedione are excreted in the urine largely as conjugates. Some unchanged *n*-hexane is excreted via the lungs.

Uses

n-Hexane is widely used as an industrial solvent, as a solvent in glues, and as an extraction solvent in food processing.

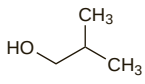
Isobutyl Alcohol

Alcohol isobutílico; Isobutanol.

Изобутиловый Спирт

$C_4H_{10}O$ = 74.12.

CAS — 78-83-1.



Profile

Isobutyl alcohol is used as an industrial solvent. It is also used as an anaesthetic in the American lobster, *Homarus americanus*.

◊ References.

1. WHO. Butanols—four isomers: 1-butanol, 2-butanol, tert-butanol, isobutanol. *Environmental Health Criteria 65*. Geneva: WHO, 1987. Available at: http://www.inchem.org/documents/ehc/ehc/ehc65.htm (accessed 30/06/04)
2. WHO. Isobutanol health and safety guide. *IPCS Health and Safety Guide 9*. Geneva: WHO, 1987. Available at: http://www.inchem.org/documents/hsg/hsg/hsg009.htm (accessed 30/06/04)

Kerosene

Kerosine; 'Paraffin'; Queroseno.

Керосин

CAS — 8008-20-6.

Description. Kerosene is a mixture of hydrocarbons, chiefly members of the alkane series, distilled from petroleum. It is a clear, colourless liquid with a characteristic odour. Sp. gr. about 0.8 g. B.p. 180° to 300°. An odourless grade is available. Store in airtight containers.

Adverse Effects

The chief danger from ingestion of kerosene is pneumonitis and attendant pulmonary complications resulting from aspiration. Spontaneous or induced vomiting increases the risk of aspiration. Ingestion of kerosene results in a burning sensation in the mouth and throat, gastrointestinal disturbances, and possibly cough, dyspnoea, and transient cyanosis. There may be excitation followed by CNS depression, with weakness, dizziness, drowsiness, confusion, incoordination, and restlessness progressing to convulsions, coma, and respiratory depression in severe cases. Cardiac arrhythmias have been reported.

The course of poisoning from inhalation is similar to that following ingestion although CNS and cardiac effects are more likely. Kerosene is irritant.

Abuse. A case of volatile substance abuse (p.2019) involving inhalation and ingestion of kerosene has been reported.[1]

1. Das PS, *et al.* Kerosene abuse by inhalation and ingestion. *Am J Psychiatry* 1992; **149:** 710.

Treatment of Adverse Effects

Treatment of kerosene poisoning is supportive and symptomatic. Every precaution should be taken to avoid aspiration of kerosene into the lungs. The UK National Poisons Information Service considers that gastric lavage should not be used. If large amounts have been taken or there is concern about another toxin, gastric aspiration may be considered if it can be carried out within 1 hour of ingestion and the airway can be protected. Adrenaline and other sympathomimetics should also be avoided because of the risk of precipitating cardiac arrhythmias.

Uses

Kerosene is used as a degreaser and cleaner and as an illuminating and fuel oil in kerosene ('paraffin') lamps and stoves. The odourless grade has been used as a solvent in the preparation of some insecticide sprays.

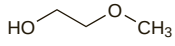
2-Methoxyethanol

Eter monometylowy glikolu etylenowego; Ethylene Glycol Monomethyl Ether; 2-Metoxietanol.

2-Метоксиэтанол

$C_3H_8O_2$ = 76.09.

CAS — 109-86-4.



Description. 2-Methoxyethanol is a clear, colourless to slightly yellow liquid. Wt per mL about 0.96 g. B.p. about 125°. Miscible with water, with alcohol, with acetone, with dimethylformamide, with ether, and with glycerol. Store in airtight containers.

Adverse Effects and Precautions

2-Methoxyethanol is irritant to mucous membranes. Ingestion may result in CNS depression with confusion, weakness, and in severe cases coma and death from respiratory depression. Nausea, metabolic acidosis, and renal damage may also occur. Prolonged industrial exposure to the vapour has been associated with severe effects on the CNS characterised by headache, dizziness, lethargy, weakness, ataxia, tremor, disorientation, mental changes, weight loss, and visual disturbances. Anaemia has also been reported. There has been concern about the potential for reproductive toxicity.

◊ References to the toxicity of 2-methoxyethanol and other glycol ethers.

1. Health and Safety Executive. Glycol ethers. *Toxicity Review 10*. London: HMSO, 1985.
2. WHO. 2-Methoxyethanol, 2-ethoxyethanol, and their acetates. *Environmental Health Criteria 115*. Geneva: WHO, 1990. Available at: http://www.inchem.org/documents/ehc/ehc/ehc115.htm (accessed 30/06/04)
3. Browning RG, Curry SC. Clinical toxicology of ethylene glycol monoalkyl ethers. *Hum Exp Toxicol* 1994; **13:** 325–35.
4. Johanson G. Toxicity review of ethylene glycol monomethyl ether and its acetate ester. *Crit Rev Toxicol* 2000; **30:** 307–45.
5. Bagchi G, Waxman DJ. Toxicity of ethylene glycol monomethyl ether: impact on testicular gene expression. *Int J Androl* 2008; **31:** 269–74.

Handling. Suitable precautions should be taken to avoid skin contact with 2-methoxyethanol as it can penetrate skin and produce systemic toxicity.

Uses

2-Methoxyethanol is used as an industrial solvent.

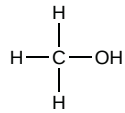
Methyl Alcohol

Metanol; Metanoli; Metanolis; Méthanol; Methanol; Methanolum.

Метиловый Спирт

CH_3OH = 32.04.

CAS — 67-56-1.



Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF*.

Ph. Eur. 6.2 (Methanol). A colourless, clear, volatile, hygroscopic liquid. It is flammable. B.p. about 64°. Relative density 0.791 to 0.793. Miscible with water and with dichloromethane. Store in airtight containers.

The BP 2008 gives Methyl Alcohol as an approved synonym.

USNF 26 (Methyl Alcohol). A clear, colourless, flammable liquid having a characteristic odour. Miscible with water, with alcohol, with ether, with benzene, and with most other organic solvents. Store in airtight containers remote from heat, sparks, and open flames.

Adverse Effects

Immediate signs of acute poisoning after ingestion of methyl alcohol resemble those of ethanol (alcohol; ethyl alcohol) intoxication (see p.1625), but are milder. Characteristic symptoms of methyl alcohol poisoning are caused by toxic metabolites and develop after a latent period of about 12 to 24 hours, or longer if taken with ethanol. The outstanding features of poisoning are metabolic acidosis with rapid, shallow breathing, visual disturbances which often proceed to irreversible blindness, and severe abdominal pain. Other symptoms include headache, gastrointestinal disturbances, pain in the back and extremities, and coma which in severe cases may result in death due to respiratory failure or, rarely, to circulatory collapse. Mania and convulsions occasionally occur. Individual response to methyl alcohol varies widely. Ingestion of 30 mL is considered to be potentially fatal.

Absorption of methyl alcohol through the skin or inhalation of the vapour may also lead to toxic systemic effects.

◊ References to the adverse effects of methyl alcohol.

1. Jacobsen D, McMartin KE. Methanol and ethylene glycol poisonings: mechanism of toxicity, clinical course, diagnosis and treatment. *Med Toxicol* 1986; **1:** 309–34.
2. Anderson TJ, *et al.* Neurologic sequelae of methanol poisoning. *Can Med Assoc J* 1987; **136:** 1177–9.
3. Cavalli A, *et al.* Severe reversible cardiac failure associated with methanol intoxication. *Postgrad Med J* 1987; **63:** 867–8.
4. Shapiro L, *et al.* Unusual case of methanol poisoning. *Lancet* 1993; **341:** 112.
5. Medinsky MA, Dorman DC. Recent developments in methanol toxicity. *Toxicol Lett* 1995; **82–83:** 707–11.
6. McKellar MJ, *et al.* Acute ocular methanol toxicity: clinical and electrophysiological features. *Aust N Z J Ophthalmol* 1997; **25:** 225–30.
7. Williams GF, *et al.* Methanol poisoning: a review and case study of four patients from central Australia. *Aust Crit Care* 1997; **10:** 113–18.
8. Shelby M, *et al.* NTP-CERHR expert panel report on the reproductive and developmental toxicity of methanol. *Reprod Toxicol* 2004; **18:** 303–90.
9. Hantson PE. Intoxication aiguë par le méthanol : physiopathologie, pronostic et traitement. *Bull Mem Acad R Med Belg* 2006; **161:** 425–34.

Handling. Suitable precautions should be taken to avoid skin contact with methyl alcohol as it can penetrate skin and produce systemic toxicity.

Treatment of Adverse Effects

Gastric aspiration may be considered if the patient presents within 1 hour of ingesting methyl alcohol. Activated charcoal is probably of little use as it does not absorb significant amounts of methyl alcohol. Metabolic acidosis (p.1667) should be corrected immediately with intravenous sodium bicarbonate. If significant amounts of methyl alcohol have been ingested, early treatment with an antidote (ethanol or fomepizole) is recommended. Ethanol delays the oxidation of methyl alcohol to its toxic metabolites formaldehyde and formic acid; dosage is adjusted to achieve and maintain a blood-ethanol concentration of 1 to 1.5 mg/mL. An **oral** dose for a 70-kg adult of about 150 mL of an ethanolic solution containing 40% v/v of C_2H_5OH has been suggested. Alcoholic spirits (such as whisky, gin, or vodka) may often be of the suitable strength. If required, an ethanolic **infusion** containing 10% v/v of C_2H_5OH may then be given as maintenance for which the following doses have been used:

- for an average adult, 1.38 mL/kg per hour
- for a non-drinker or child, 0.83 mL/kg per hour
- for a chronic drinker, 1.96 mL/kg per hour

The infusion should be continued until methyl alcohol concentrations are undetectable, or fall below 50 micrograms/mL with resolution of systemic toxicity.

Fomepizole (p.1446), an inhibitor of alcohol dehydrogenase, is also used; it inhibits the metabolism of methyl alcohol to its toxic metabolites.

Haemodialysis may be indicated to increase the removal of methyl alcohol and its toxic metabolites. Peritoneal dialysis has been used but is less efficient. Haemodialysis may be considered if the blood-methyl alcohol concentration is greater than 500 micrograms/mL, if there is severe metabolic acidosis unresponsive to sodium bicarbonate, or there is visual disturbance, CNS toxicity, renal failure, or severe electrolyte disturbance. If haemodialysis is used, a constant blood-ethanol concentration may be ensured either by increasing the ethanol infusion rate or by addition of ethanol to the dialysate fluid.

Treatment should not be stopped prematurely since oxidation and excretion of methyl alcohol may continue for several days; patients should, therefore, be closely observed and monitored. Suitable supportive treatment should be carried out as required.

Folinic acid and folic acid have been given in the treatment of methyl alcohol toxicity because they may enhance the metabolism of formic acid.

◊ References.

1. Barceloux DG, *et al.* American Academy of Clinical Toxicology Ad Hoc Committee on the Treatment Guidelines for Methanol Poisoning. American Academy of Clinical Toxicology practice guidelines on the treatment of methanol poisoning. *J Toxicol Clin Toxicol* 2002; **40:** 415–46.

Pharmacokinetics

Methyl alcohol is readily absorbed from the gastrointestinal tract and distributed throughout the body fluids. It may also be absorbed after inhalation or through large areas of skin. Oxidation by alcohol dehydrogenase with formation of formaldehyde and formic acid takes place mainly in the liver and also in the kidneys. These metabolites are thought to be largely responsible for the characteristic symptoms of methyl alcohol poisoning. Metabolism is much slower than for ethanol, which competitively inhibits the metabolism of methyl alcohol. Oxidation and excretion may continue for several days after ingestion. Elimination of unchanged methyl alcohol via the lungs and in the urine is a minor route of excretion.

Uses

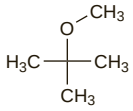
Methyl alcohol is used as a pharmaceutical and industrial solvent. It is also used as 'wood naphtha' to denature ethanol in the preparation of industrial methylated spirits. Methyl alcohol is also used as an extraction solvent in food processing.

Methyl *tert*-Butyl Ether

Éter metilterbutílico; Methyl Terbutyl Ether; Methyl Tertiary Butyl Ether; MTBE. 2-Methoxy-2-methylpropane.

Метил-трет-бутиловый Эфир

$C_5H_{12}O$ = 88.15.
CAS — 1634-04-4.



Description. Methyl *tert*-butyl ether is a volatile, flammable liquid. Wt per mL about 0.74 g. B.p. about 55°. Store in airtight containers.

Stability. Explosive peroxides may be generated by the atmospheric oxidation of methyl tert-butyl ether, but the risk is lower than with solvent ether.

Adverse Effects

Methyl *tert*-butyl ether is irritant and may cause CNS depression. Adverse effects that have been reported after use as a gallstone solvent are described under Uses and Administration, below.

Uses and Administration

Methyl *tert*-butyl ether is a solvent that has been used for the rapid dissolution of cholesterol gallstones.

Gallstones. An alternative to bile acid therapy in patients with gallstones (p.2409) who are not considered suitable for surgery is direct instillation of a solvent into the gallbladder.

Methyl *tert*-butyl ether has been used to dissolve cholesterol gallstones; stones rich in calcium or pigments are not dissolved.[1] Unfortunately incomplete dissolution and residual debris can lead to recurrence of stone formation.[2] The solvent is usually instilled via a percutaneous transhepatic catheter,[1,3] although other routes have been used.[4] Gallbladder stones were treated in 75 patients with continuous infusion and aspiration of methyl *tert*-butyl ether 4 to 6 times/minute for an average of 5 hours daily for 1 to 3 days.[1] At least 95% of the stone mass was dissolved in 72 patients. Gallbladder stones recurred in 4 patients between 6 and 16 months after the procedure; 7 of 51 patients with residual stone fragments had an episode of biliary colic during 6 to 42 months of follow-up. Nausea, sometimes with emesis, occurred in about one-third of patients. Overflow of solvent from the gallbladder can result in absorption from the gastrointestinal tract; methyl *tert*-butyl ether is detected on the breath and sedation can occur. One patient in whom overflow occurred developed ulcerative duodenitis and intravascular haemolysis. Coma and acute renal failure have also complicated treatment and have been attributed to leakage alongside the catheter rather than overflow of solvent.[5] Other workers[6,7] have obtained similar results for the dissolution of gallstones. One group[6] found that nausea and vomiting could be reduced if the treatment time was kept short and the perfusion volume was kept as low as possible; they also managed to prevent bile leakage and haemorrhage using a tissue adhesive or subcutaneous ceruletide to contract the gallbladder. Dissolution of gallbladder stones with methyl *tert*-butyl ether is likely to remain confined to specialist centres for use in patients unsuitable for surgical treatment.[1,8] A combination of litholytic modalities such as dissolution with solvents or bile acids, or lithotripsy may overcome some of the disadvantages of individual treatments.[9]

Methyl *tert*-butyl ether has been instilled via a nasobiliary catheter to dissolve stones in the common bile duct. Although effective in some cases,[10] further study has indicated disappointing overall results.[1,11]

Various combinations of drugs have been investigated to dissolve pigment-rich or mixed stones. For common bile-duct stones these include a cocktail of dimethyl sulfoxide 60%, methyl *tert*-butyl ether 20%, and sodium bicarbonate 20%, and a regimen of alternating infusions of pentyl ether and edetic acid-urea 10%.[12] A similar regimen of methyl hexyl ether and edetic acid-urea has been used successfully in 2 patients with calcified gallbladder stones.[13]

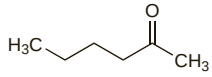
1. Bouchier IAD. Gall stones. *BMJ* 1990; **300:** 592–7.
2. Maudgal DP, Northfield TC. A practical guide to the nonsurgical treatment of gallstones. *Drugs* 1991; **41:** 185–92.
3. Thistle JL, *et al.* Dissolution of cholesterol gallbladder stones by methyl *tert*-butyl ether administered by percutaneous transhepatic catheter. *N Engl J Med* 1989; **320:** 633–9.
4. Foerster E-Ch, *et al.* Direct dissolution of gallbladder stones. *Lancet* 1989; **i:** 954.
5. Ponchon T, *et al.* Renal failure during dissolution of gallstones by methyl-*tert*-butyl ether. *Lancet* 1988; **ii:** 276–7.
6. Hellstern A, *et al.* Gall stone dissolution with methyl tert-butyl ether: how to avoid complications. *Gut* 1990; **31:** 922–5.
7. McNulty J, *et al.* Dissolution of cholesterol gall stones using methyltertbutyl ether: a safe effective treatment. *Gut* 1991; **32:** 1550–3.
8. Hetzer FH, *et al.* Kontaktlitholyse von Gallensteinen mit Methyltertbutyläther bei Risikopatienten—eine Fallbeschreibung. *Swiss Surg* 2001; **7:** 39–42.
9. Salen G, Tint GS. Nonsurgical treatment of gallstones. *N Engl J Med* 1989; **320:** 665–6.
10. Murray WR, *et al.* Choledocholithiasis—in vivo stone dissolution using methyl tertiary butyl ether (MTBE). *Gut* 1988; **29:** 143–5.
11. Neoptolemos JP, *et al.* How good is methyl tert-butyl (MTBE) for common bile duct (CBD) stone dissolution? *Gut* 1989; **30:** A736–7.
12. Anonymous. Gallstones, bile acids, and the liver. *Lancet* 1989; **ii:** 249–51.
13. Swobodnik W, *et al.* Dissolution of calcified gallbladder stones by treatment with methyl-hexyl ether and urea-EDTA. *Lancet* 1988; **ii:** 216.

Methyl Butyl Ketone

2-Hexanone; Methyl *n*-Butyl Ketone; Metilbutilcetona; Propylacetone. Hexan-2-one.

Метилбутилкетон

$C_6H_{12}O$ = 100.2.
CAS — 591-78-6.



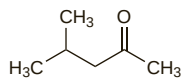
Description. Methyl butyl ketone is a colourless, volatile liquid. Wt per mL about 0.82 g. B.p. about 127°. Store in airtight containers.

Methyl Isobutyl Ketone

Hexone; Isobutilmetilcetona; Isopropylacetone; Metilisobutilcetona; MIBK. 4-Methylpentan-2-one.

Метилизобутилкетон

$C_6H_{12}O$ = 100.2.
CAS — 108-10-1.



Pharmacopoeias. In *USNF.*

USNF 26 (Methyl Isobutyl Ketone). A transparent, colourless, mobile, volatile liquid having a faint ketonic and camphoraceous odour. Sp. gr. not more than 0.799. Distilling range 114° to 117°. Slightly soluble in water; miscible with alcohol, with ether, and with benzene. Store in airtight containers.

Adverse Effects and Precautions

Methyl butyl ketone and methyl isobutyl ketone may depress the CNS in high concentrations. Their vapours are irritating to mucous membranes. Methyl isobutyl ketone may be implicated in volatile substance abuse (p.2019).

◊ References.

1. WHO. Methyl isobutyl ketone. *Environmental Health Criteria 117*. Geneva: WHO, 1990. Available at: http://www.inchem.org/documents/ehc/ehc/ehc117.htm (accessed 30/06/04)
2. WHO. Methyl isobutyl ketone health and safety guide. *IPCS Health and Safety Guide 58*. Geneva: WHO, 1991. Available at: http://www.inchem.org/documents/hsg/hsg/hsg058.htm (accessed 30/06/04)

Effects on the nervous system. Peripheral neuropathy[1] has occurred after occupational exposure to methyl butyl ketone, particularly an outbreak of neuropathy in a printing plant after the replacement of methyl isobutyl ketone by methyl butyl ketone in a solvent mixture with methyl ethyl ketone. Methyl ethyl ketone may have potentiated the neurotoxicity induced by methyl butyl ketone.

For further discussion of neurotoxicity after occupational exposure to solvents including methyl butyl ketone, see under Toluene, p.2026.

1. Lolin Y. Chronic neurological toxicity associated with exposure to volatile substances. *Hum Toxicol* 1989; **8:** 293–300.

Handling. Suitable precautions should be taken to avoid skin contact with methyl butyl ketone or methyl isobutyl ketone as they can penetrate skin and produce systemic toxicity.

Uses

Methyl isobutyl ketone is used as an industrial and pharmaceutical solvent and also as an alcohol denaturant. Methyl butyl ketone is used as an industrial solvent.

Methyl Chloride

Cloruro de metilo; Monochloromethane. Chloromethane.

Метилхлорид

CH_3Cl = 50.49.
CAS — 74-87-3.

Description. Methyl chloride is a colourless gas compressed to a colourless liquid with an ethereal odour. B.p. about –24°. Store in airtight containers.

Adverse Effects and Treatment

Symptoms of methyl chloride intoxication often appear after a latent period of several hours and are similar after acute or chronic exposure to the vapour. Symptoms include gastrointestinal disturbances such as nausea, vomiting, and abdominal pain, and signs of CNS depression including headache, weakness, drowsiness, confusion, visual disturbances, and incoordination progressing to convulsions, coma, and death from respiratory depression in severe cases. There have been a few reports of hepatic and renal damage.

Treatment consists of removal from exposure and supportive and symptomatic measures. Neurological effects may persist for many months.

◊ References to the toxicity of methyl chloride.

1. Repko JD, Lasley SM. Behavioral, neurological, and toxic effects of methyl chloride: a review of the literature. *CRC Crit Rev Toxicol* 1979; **6:** 283–302.

Uses

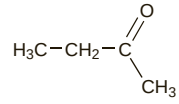
Methyl chloride is used as an industrial solvent. It has been used as an aerosol propellant and refrigerant and was formerly used as a local anaesthetic.

Methyl Ethyl Ketone

Ethyl Methyl Ketone; Etylometyloketon; MEK; Metiletilcetona; Metyloetyloketon. Butan-2-one.

Метилэтилкетон

C_4H_8O = 72.11.
CAS — 78-93-3.



Description. Methyl ethyl ketone is a colourless flammable liquid with an acetone-like odour. Wt per mL about 0.81 g. B.p. 79° to 81°. Soluble in water; miscible with alcohol and with ether. Store in airtight containers.

Adverse Effects

Methyl ethyl ketone is irritant. Inhalation may result in mild CNS effects including headache and dizziness; nausea and vomiting may also occur.