

Chloroform

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Chloroform	
IUPAC name ^[hide] Chloroform	
Systematic name ^[hide] Trichloromethane	
Other names ^[hide] Formyl trichloride, Methane trichloride, Methyl trichloride, Methenyl trichloride, TCM, Freon 20, R-20, UN 1888	
Identifiers	
CAS number	67-66-3
PubChem	6212
ChemSpider	5977
UNII	7V31YC746X
EC number	200-663-8
KEGG	C13827
ChEBI	CHEBI:35255
ChEMBL	CHEMBL44618
RTECS number	FS9100000
SMILES [show]	
InChI [show]	
Properties	
Molecular formula	CHCl ₃
Molar mass	119.38 g/mol
Appearance	Colorless liquid
Density	1.483 g/cm ³
Melting point	-63.5 °C
Boiling point	61.2 °C
Solubility in water	0.8 g/100 ml (20 °C)

Refractive index (n_D)	1.4459
Structure	
Molecular shape	Tetrahedral
Hazards	
MSDS	External MSDS
R-phrases	R22 , R38 , R40 , R48/20/22
S-phrases	(S2) , S36/37
NFPA 704	0 2 0
Flash point	Non-flammable
U.S. Permissible exposure limit (PEL)	50 ppm (240 mg/m ³) (OSHA)
Supplementary data page	
Structure and properties	n , ϵ_r , etc.
Thermodynamic data	Phase behaviour Solid, liquid, gas
Spectral data	UV , IR , NMR , MS
(what is this?) (verify)	
Except where noted otherwise, data are given for materials in their standard state (at 25 °C, 100 kPa)	
Infobox references	



Chloroform in its liquid state shown in a test tube

Chloroform is the [organic compound](#) with [formula](#) CHCl_3 . The colorless, sweet-smelling, dense liquid is a [trihalomethane](#), and is considered somewhat

hazardous. Several million tons are produced annually as a precursor to [Teflon](#) and refrigerants, but its use for refrigerants is being phased out.^[1]

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[\[edit\]](#) Occurrence

CHCl₃ has a multitude of natural sources, both biogenic and abiotic. It is estimated that greater than 90% of atmospheric CHCl₃ is of natural origin.^[2]

[\[edit\]](#) Marine

In particular, chloroform is produced by brown seaweeds ([Laminaria digitata](#), [Laminaria saccharina](#), [Fucus serratus](#), [Pelvetia canaliculata](#), [Ascophyllum nodosum](#)), red seaweeds ([Gigartina stellata](#), [Corallina officinalis](#), [Polysiphonia lanosa](#)), and green seaweeds ([Ulva lactuca](#), [Enteromorpha](#) sp., [Cladophora albida](#)).^[3] Similarly, the macroalga *Euचेuma denticulatum*, which is cultivated and harvested on a large scale for [carrageenan](#) production, produces CHCl₃,^[4] as do *Hypnea spinella*, *Falkenbergia hillebrandii*, and *Gracilara cornea* along with seven indigenous macroalgae inhabiting a rock pool.^[5] These studies show increased CHCl₃ production with increased light intensity, presumably

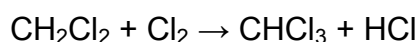
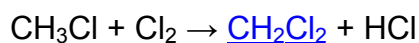
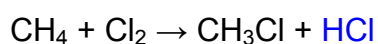
when photosynthesis is at a maximum. Chloroform is also produced by the brown alga [Fucus vesiculosus](#), the green algae *Cladophora glomerata*, *Enteromorpha ahneriana*, [Enteromorpha flexuosa](#), and *Enteromorpha intestinalis*, and the diatom *Pleurosira laevis*.^[6] Other studies observe CHCl₃ in [Fucus serratus](#), *Fucus vesiculosus*, *Corallina officinalis*, *Cladophora pellucida*, and *Ulva lactuca*,^[7] and *Desmarestia antarctica*, *Lambia antarctica*, *Laminaria saccharina*, [Neuroglossum ligulatum](#).^[8]

[\[edit\]](#) Production

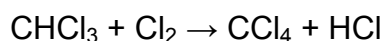
Chloroform was reported in 1831 by the French [chemist Eugène Soubeiran](#), who prepared it from [acetone](#) (2-propanone) as well as [ethanol](#) through the action of chlorine [bleach](#) powder ([calcium hypochlorite](#)).^[9] The American physician [Samuel Guthrie](#) prepared gallons of the material and described its "deliciousness of flavor."^[10] Independently, [Justus von Liebig](#) also described the same compound.^[11] All early preparations used variations of the [haloform reaction](#). Chloroform was named and chemically characterized in 1834 by [Jean-Baptiste Dumas](#).^[12]

[\[edit\]](#) Industrial routes

In industry, chloroform is produced by heating a mixture of [chlorine](#) and either [chloromethane](#) or [methane](#).^[1] At 400–500 °C, a [free radical halogenation](#) occurs, converting these precursors to progressively more chlorinated compounds:



Chloroform undergoes further chlorination to give [CCl₄](#):



The output of this process is a mixture of the four chloromethanes, chloromethane, dichloromethane, chloroform, and carbon tetrachloride, which are then separated by [distillation](#).^[1]

[\[edit\]](#) Deuteriochloroform

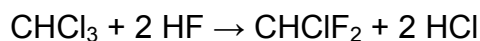
An archaic industrial route to chloroform involved the reaction of acetone (or ethanol) with [sodium hypochlorite](#) or calcium hypochlorite, the aforementioned [haloform reaction](#).^[1] The chloroform can be removed from the coproducts by distillation. A related reaction is still used in the production of [bromoform](#) and [iodoform](#). Although the haloform process is obsolete for the production of ordinary chloroform, it is used to produce CDCl_3 .^[citation needed] Deuteriochloroform can also be prepared by the reaction of sodium deuterioxide with [chloral hydrate](#),^[citation needed] or from ordinary chloroform.^[13]

[edit] Inadvertent formation of chloroform

The haloform reaction can also occur inadvertently in domestic settings. Sodium hypochlorite solution ([chlorine bleach](#)) mixed with common household liquids such as [acetone](#), [butanone](#), [ethanol](#), or [isopropyl alcohol](#) can produce some chloroform, in addition to other compounds such as [chloroacetone](#), or dichloroacetone.

[edit] Uses

The major use of chloroform today is in the production of the [chlorodifluoromethane](#) (R-22), a major precursor to [tetrafluoroethylene](#):



The reaction is conducted in the presence of a catalytic amount of [antimony pentafluoride](#). Chlorodifluoromethane is then converted into tetrafluoroethylene, the main precursor to [Teflon](#). Before the [Montreal Protocol](#), chlorodifluoromethane (R22) was also a popular refrigerant.

[edit] As a solvent

Chloroform is a common solvent in the laboratory because it is relatively unreactive, miscible with most organic liquids, and conveniently volatile. Chloroform is used as a [solvent](#) in the [pharmaceutical](#) industry and for producing [dyes](#) and [pesticides](#). Chloroform is an effective solvent for [alkaloids](#) in their base form and thus plant material is commonly extracted with chloroform for pharmaceutical processing. For example, it is used in commerce to extract [morphine](#) from [poppies](#) and [scopolamine](#) from [Datura](#) plants. Chloroform containing [deuterium](#) (heavy hydrogen), CDCl_3 , is a common solvent used in [NMR spectroscopy](#). It can be used to bond pieces of

[acrylic glass](#) (also known under the trade names Perspex and Plexiglas). A solvent of phenol:chloroform:isoamyl alcohol 25:24:1 is used to dissolve non-nucleic acid biomolecules in DNA and RNA extractions.

[edit] As a reagent in organic synthesis

As a [reagent](#), chloroform serves as a source of the dichlorocarbene CCl_2 group.^[14] It reacts with aqueous [sodium hydroxide](#) usually in the presence of a [phase transfer catalyst](#) to produce [dichlorocarbene](#), CCl_2 .^{[15][16]} This reagent affects ortho-formylation of activated [aromatic rings](#) such as [phenols](#), producing aryl [aldehydes](#) in a reaction known as the [Reimer-Tiemann reaction](#). Alternatively the [carbene](#) can be trapped by an [alkene](#) to form a [cyclopropane](#) derivative. In the [Kharasch addition](#) chloroform forms the CHCl_2 free radical in addition to alkenes.

[edit] As an anesthetic



Antique bottles of Chloroform

Chloroform was once a popular [anesthetic](#); its vapor depresses the [central nervous system](#) of a patient, allowing a doctor to perform various otherwise painful procedures. In 1847, the Scottish [obstetrician James Young Simpson](#) first used chloroform for [general anesthesia](#) during [childbirth](#). The use of chloroform during [surgery](#) expanded rapidly thereafter in Europe. In the United States, chloroform began to replace [ether](#) as an anesthetic at the beginning of the 20th century; however, it was quickly abandoned in favor of ether upon discovery of its toxicity, especially its tendency to cause fatal [cardiac arrhythmia](#) analogous to what is now termed "[sudden sniffer's death](#)". [Ether](#) is still the preferred anesthetic in some [developing nations](#) due to its high [therapeutic index](#) (~1.5–2.2)^[17] and low price. One possible mechanism of action for chloroform is that it increases movement of potassium ions through certain types of [potassium channels](#) in [nerve cells](#).^[18] Chloroform could also be

mixed with other anaesthetic agents such as [ether](#) to make C.E. mixture, or ether and [alcohol](#) to make [A.C.E. mixture](#).

[\[edit\]](#) **Veterinary use**

In veterinary medicine it is used externally to kill maggots in wounds.^{[\[citation needed\]](#)}

[\[edit\]](#) **Safety**

Fatal oral dose of chloroform may be as low as 10 mL (14.8 g), with death due to respiratory or cardiac arrest.^{[\[19\]](#)}

As might be expected for an [anesthetic](#), chloroform vapors depress the [central nervous system](#). It is [immediately dangerous to life and health](#) at approximately 500 [ppm](#), according to the [U.S. National Institute for Occupational Safety and Health](#). Breathing about 900 ppm for a short time can cause dizziness, fatigue, and headache. Chronic chloroform exposure can damage the [liver](#) (where chloroform is metabolized to [phosgene](#)) and to the [kidneys](#), and some people develop sores when the skin is immersed in chloroform.

[Animal studies](#) have shown that [miscarriages](#) occur in [rats](#) and [mice](#) that have breathed [air](#) containing 30 to 300 [ppm](#) of chloroform during [pregnancy](#) and also in rats that have ingested chloroform during pregnancy. [Offspring](#) of rats and mice that breathed chloroform during pregnancy have a higher incidence of [birth defects](#), and abnormal [sperm](#) have been found in male mice that have breathed air containing 400 ppm chloroform for a few days. The effect of chloroform on [reproduction](#) in humans is unknown.

Chloroform once appeared in [toothpastes](#), [cough syrups](#), [ointments](#), and other [pharmaceuticals](#), but it has been banned as a [consumer product](#) in the US since 1976.^{[\[20\]](#)} Cough syrups containing Chloroform can still be legally purchased in pharmacies and supermarkets in the UK.

The US National Toxicology Program's eleventh report on carcinogens^{[\[21\]](#)} implicates it as reasonably anticipated to be a human [carcinogen](#), a designation equivalent to [International Agency for Research on Cancer](#) class 2A. The IARC itself classifies chloroform as *possibly carcinogenic to humans*, a Group 2B designation.^{[\[22\]](#)} It has been most readily associated with

[hepatocellular carcinoma](#).^{[23][24]} Caution is mandated during its handling in order to minimize unnecessary exposure; safer alternatives, such as [dichloromethane](#), have resulted in a substantial reduction of its use as a solvent.

[edit] Conversion to phosgene

During prolonged storage in the presence of [oxygen](#) chloroform converts slowly to [phosgene](#). To prevent accidents, commercial chloroform is stabilized with [ethanol](#) or [amylene](#), but samples that have been recovered or dried no longer contain any stabilizer. Amylene has been found ineffective, and the phosgene can affect analytes in samples, lipids and nucleic acids dissolved in or extracted with chloroform.^[25] Dissolved phosgene cannot be removed by distillation or carbon filters, but is removed by calcium hydroxide or activated alumina.^[26] Suspicious samples can be tested for phosgene using filter paper (treated with 5% diphenylamine, 5% dimethylaminobenzaldehyde in alcohol, and then dried), which turns yellow in phosgene vapor. There are several colorimetric and fluorometric reagents for phosgene, and it can also be quantified with mass spectrometry.

[edit] References

- [^] [a](#) [b](#) [c](#) [d](#) M. Rossberg *et al.* "Chlorinated Hydrocarbons" in Ullmann's Encyclopedia of Industrial Chemistry, 2006, Wiley-VCH, Weinheim. [doi:10.1002/14356007.a06_233.pub2](https://doi.org/10.1002/14356007.a06_233.pub2)
- [^] <http://www.eurochlor.org/upload/documents/document56.pdf>
- [^] Nightingale PB, Malin G, Liss PS (1995). "[Production of Chloroform and Other Low- Molecular-Weight Halocarbons by Some Species of Macroalgae](#)". *Limnology and Oceanography* (American Society of Limnology and Oceanography) **40** (4): 680. <http://www.jstor.org/pss/2838303>.
- [^] Mtolera, Matern; Collén, Jonas; Pedersén, Marianne; Ekdahl, Anja; Abrahamsson, Katarina; Semesi, Adelaida (1996). "Stress-induced production of volatile halogenated organic compounds in *Eucheuma denticulatum* (Rhodophyta) caused by elevated pH and high light intensities". *European Journal of Phycology* **31**: 89. [doi:10.1080/09670269600651241](https://doi.org/10.1080/09670269600651241).
- [^] Ekdahl A, Pedersen M, Abrahamsson K (1998). "A Study of the Diurnal Variation of Biogenic Volatile Halocarbons". *Mar Chem* **63**: 1.

6. [^ Abrahamsson, K; Choo, KS; Pedersén, M; Johansson, G; Snoeijs, P \(2003\). "Effects of temperature on the production of hydrogen peroxide and volatile halocarbons by brackish-water algae." *Phytochemistry* **64** \(3\): 725–34. \[doi:10.1016/S0031-9422\\(03\\)00419-9\]\(https://doi.org/10.1016/S0031-9422\(03\)00419-9\). \[PMID 13679095\]\(https://pubmed.ncbi.nlm.nih.gov/13679095/\).](#)
7. [^ Baker JM, Sturges WT, Sugier J, Sunnenberg G, Lovett AA, Reeves CE, Nightingale PD, Penkett SA \(2001\). "Emissions of CH₃Br, Organochlorines, and Organoiodines from Temperate Macroalgae". *Chemosphere - Global Change Science* **3**: 93. \[doi:10.1016/S1465-9972\\(00\\)00021-0\]\(https://doi.org/10.1016/S1465-9972\(00\)00021-0\).](#)
8. [^ Laternus, F; Svensson, T; Wiencke, C; Oberg, G \(2004\). "Ultraviolet radiation affects emission of ozone-depleting substances by marine macroalgae: results from a laboratory incubation study." *Environmental science & technology* **38** \(24\): 6605–9. \[doi:10.1021/es049527s\]\(https://doi.org/10.1021/es049527s\). \[PMID 15669318\]\(https://pubmed.ncbi.nlm.nih.gov/15669318/\).](#)
9. [^ Eugène Soubeiran \(1831\). *Ann. Chim.* **48**: 131.](#)
10. [^ Samuel Guthrie \(1832\). "New mode of preparing a spirituous solution of Chloric Ether". *Am. J. Sci. And Arts* **21**: 64.](#)
11. [^ Justus Liebig \(1832\). "Ueber die Verbindungen, welche durch die Einwirkung des Chlors auf Alkohol, Aether, ölbildendes Gas und Essiggeist entstehen". *Annalen der Pharmacie* **1** \(2\): 182–230. \[doi:10.1002/jlac.18320010203\]\(https://doi.org/10.1002/jlac.18320010203\).](#)
12. [^ Jean-Baptiste Dumas \(1834\). "Untersuchung über die Wirkung des Chlors auf den Alkohol". *Annalen der Pharmacie* **107** \(41\): 650–656. \[doi:10.1002/andp.18341074103\]\(https://doi.org/10.1002/andp.18341074103\).](#)
13. [^ Canadian Patent 1085423](#)
14. [^ Srebnik, M.; Laloë, E. "Chloroform" Encyclopedia of Reagents for Organic Synthesis" 2001 John Wiley. \[doi:10.1002/047084289X.rc105\]\(https://doi.org/10.1002/047084289X.rc105\)](#)
15. [^ "1,6-Methano\[10\]annulene", *Org. Synth.*, 1988, <http://www.orgsyn.org/orgsyn/orgsyn/prepContent.asp?prep=cv6p0731>; *Coll. Vol. 6*: 731](#)
16. [^ Gokel, G. W.; Widera, R. P.; Weber, W. P. \(1988\), "Phase-Transfer Hofmann Carbylamine Reaction: tert-Butyl Isocyanide", *Org. Synth.*, <http://www.orgsyn.org/orgsyn/orgsyn/prepContent.asp?prep=cv6p0232>; *Coll. Vol. 6*: 232](#)
17. [^ Calderone, F.A. \(1935\). *J. Pharmacology Experimental Therapeutics* **55**: 24. <http://jpet.aspetjournals.org/cgi/reprint/55/1/24.pdf>.](#)
18. [^ Patel, Amanda J.; Honoré, Eric; Lesage, Florian; Fink, Michel; Romey, Georges; Lazdunski, Michel \(May 1999\). "Inhalational anesthetics](#)

- activate two-pore-domain background K⁺ channels". *Nature Neuroscience* **2** (5): 422–426. doi:[10.1038/8084](https://doi.org/10.1038/8084). PMID [10321245](https://pubmed.ncbi.nlm.nih.gov/10321245/).
19. [^ Chloroform](#), US Environmental Protection Agency
 20. [^ "The National Toxicology Program: Substance Profiles: Chloroform CAS No. 67-66-3" \(pdf\)](#).
<http://ntp.niehs.nih.gov/ntp/roc/eleventh/profiles/s038chlo.pdf>.
Retrieved 2007-11-02.
 21. [^ "11th Report on Carcinogens"](#).
<http://ntp.niehs.nih.gov/ntp/roc/toc11.html>. Retrieved 2007-11-02.
 22. [^ "International Agency for Research on Cancer \(IARC\) - Summaries & Evaluations: Chloroform"](#).
<http://www.inchem.org/documents/iarc/vol73/73-05.html>. Retrieved 2010-09-02.
 23. [^ "Centers for Disease Control and Prevention: Current Intelligence Bulletin 9"](#). http://www.cdc.gov/Niosh/78127_9.html.
 24. [^ "National Toxicology Program: Report on the carcinogenesis bioassay of chloroform"](#).
http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/trChloroform.pdf.
 25. [^](#) (Turk, Eric, "Phosgene from Chloroform", *Chemical & Engineering News* (2 March 1998) Vol. 76, No. 9, pp. 6.)
 26. [^](#) (Cone, Edward J., William F. Buckwald, and William D. Darwin, "Analytical controls in Drug Metabolic Studies, II Artifact formation During Chloroform Extraction of Drugs and Metabolites with Amine Substituents", *Drug Metabolism & Disposition* November 1982 vol. 10 no. 6 561-567)

[\[edit\]](#) **External links**