



Laboratory Safety Guideline

Dichloromethane Substitutes

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Introduction

The Environmental Protection Agency (EPA) regulates dichloromethane (DCM), also called methylene chloride, under the [Toxic Substances Control Act \(TSCA\)](#) due to its potential impacts on public health and the environment.

Personnel using DCM in lab settings must assess alternatives and only use DCM if an acceptable alternative doesn't exist.

For additional resources and sources about DCM substitutes, contact EHS.



Dichloromethane Substitutes by Activity

These alternative solvents can potentially be effective replacements for DCM in critical research activities.

DCM Activity	DCM Substitutes	References
Biphasic reactions such as alkylation, amidation, or nucleophilic substitution	2-Methyltetrahydrofuran	Sigma Aldrich (2015). Green Chemistry. Greener Solvent Alternatives.
Bonding, such as connecting sawn edges or making T joints	ACRIFIX® 1S 0116 Pure-V	Recommendation from Harvard University makerspace personnel.
Chromatography	Ethyl Acetate, Heptane, or Methyl Tertiary-Butyl Ether (MTBE)	Taygerly, J. P., Miller, L. M., Yee, A., & Peterson, E. A. (2012). A convenient guide to help select replacement solvents for dichloromethane in chromatography, Green Chemistry, 14, 3020-3025.
Extractions and purifications	Ethyl Acetate and Ethanol (3:1 ratio), MTBE, Toluene, or 2-Methyltetrahydrofuran	Jordan, A., Stoy, P., & Sneddon, H. F. (2020). Chlorinated Solvents: Their Advantages, Disadvantages, and Alternatives in Organic and Medicinal Chemistry, Chemical Reviews, 121, 1582-1622.



DCM Activity	DCM Substitutes	References
Paint stripping	Dimethyl Sulfoxide (DMSO)	Morose, G., Marshall, J., McCarthy A. (2020). Assessment of Safer and Effective Alternatives for Coating Removal Products, TURI Report 2020-001.
Tissue clearing	N,N,N',N'-Tetrakis (2-hydroxyethyl) ethylenediamine	Recommendation from Harvard University biology lab personnel.

Regrettable Substitutes

Regrettable substitutes are chemical replacements that increase risks to health, safety, or the environment.

Avoid replacing DCM with chemicals that are similarly hazardous but unregulated.

Many regrettable solvents, particularly chlorinated ones, can cause even greater harm. For example:

- Chloroform is unsuitable due to its toxicity and because it is reasonably anticipated as a human carcinogen.
- Trichloroethylene (TCE) and n-propyl bromide (nPB) are poor alternatives because they can cause serious health issues, including carcinogenicity, reproductive toxicity, and neurotoxicity.
- Hydrochlorofluorocarbons (HCFCs) contribute to ozone depletion and global warming.

Before selecting a substitute, thoroughly review data on the health, safety, and environmental impacts of the chemical. Contact your [Laboratory Safety Advisor](#) with questions or to discuss your lab's experimental processes or setups.



Solvent Alternatives

When choosing a solvent alternative, use a preferred alternative whenever possible. If no preferred alternatives meet your requirements, choose a usable alternative. Avoid undesirable alternatives whenever possible.

This section includes three solvent lists organized by polarity in ascending order, beginning with non-polar and ending with polar. These lists were originally developed by Pfizer's Environmental, Health and Safety group based on worker safety, process safety, and environmental and regulatory considerations.

Preferred Solvent Alternatives

These preferred solvent alternatives are organized by polarity in ascending order, beginning with non-polar and ending with polar.

Use these solvent alternatives whenever possible:

- Water
- Methanol
- Acetone
- Dimethyl carbonate
- Ethyl acetate
- Propyl acetate
- 1-propanol
- 2-Butanol
- 2-propanol
- t-Butanol
- Toluene



Usable Solvent Alternatives

These usable solvent alternatives are organized by polarity in ascending order, beginning with non-polar and ending with polar.

If you can't use a preferred solvent alternative, use these solvent alternatives:

- Dimethyl sulfoxide
- Acetic acid
- Acetonitrile
- Tetrahydrofuran
- Ethylene glycol
- 2-MethylTHF
- Methyl-t-butyl-ether
- Methylcyclohexane
- Xylenes
- Cyclohexane
- Isooctane
- Heptane

Undesirable Solvent Alternatives

These undesirable solvent alternatives are organized by polarity in ascending order, beginning with non-polar and ending with polar.

Avoid using these solvent alternatives whenever possible:

- N-methylpyrrolidone
- Dimethyl formamide



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- Pyridine
- 1,4-Dioxane
- Chloroform
- Dichloromethane
- Dichloroethane
- Benzene
- Carbon tetrachloride
- Di-isopropyl ether
- Dimethyl acetate
- Diethyl ether
- Hexane
- Pentane

Resources

- Agency for Toxic Substances and Disease Registry (ATSDR) (2020) [Public Health Statement: Trichloroethylene](#).
- Alfonsi, Kim *et al.* (2008) [Green chemistry tools to influence a medicinal chemistry and research chemistry based organization](#). *Green Chemistry* 10(1).
- [DCM Safety Data Sheet](#): Safety Data Sheet for Dichloromethane (Methylene Chloride).
- EPA, [Ongoing and Completed Chemical Risk Evaluations under TSCA](#).
- Ichihara, G. (2005) [Neuro-reproductive toxicities of 1-bromopropane and 2-bromopropane](#). *International Archives of Occupational and Environmental Health* 78(2):79-96.
- Jordan, A., Stoy, P., & Sneddon, H. F. (2020) [Chlorinated Solvents: Their Advantages, Disadvantages, and Alternatives in Organic and Medicinal Chemistry](#). *Chemical Reviews* 121(3).



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- Morose, G., Marshall, J., McCarthy A. (2020) [Assessment of Safer and Effective Alternatives for Coating Removal Products](#). *Toxics Use Reduction Institute Report 2020-2021*.
- National Toxicology Program, “15th Report on Carcinogens: Chloroform” (2021) [15th Report on Carcinogens \[Internet\]](#).
- Sigma Aldrich (2015) [Green Chemistry. Greener Solvent Alternatives](#).
- Taygerly, J. P., Miller, L. M., Yee, A., & Peterson, E. A. (2012) [A convenient guide to help select replacement solvents for dichloromethane in chromatography](#). *Green Chemistry* 14(11).
- Toxics Use Reduction Institute (2014) [Massachusetts Chemical Fact Sheet: Methylene Chloride](#).
- Tsai, W.T. (2005) [An overview of environmental hazards and exposure risk of hydrofluorocarbons](#). *Chemosphere* 61(11):1539-47.

Solvent Resources

Use these resources to help select and replace solvents and transition to safer chemical practices. They provide structured frameworks for selecting and replacing solvents, emphasizing safety, health, and environmental considerations.

- [American Chemical Society: Solvents](#): Strategies for solvent replacement.
- [American Chemical Society: Solvent Selection Guides](#): Guides for solvent selection.
- [American Chemical Society: Solvent Tool](#): Interactive tool for choosing solvents based on physical properties.
- [American Chemical Society: The CHEM21 Solvent Selection Guide](#): Consolidated solvent guide that includes less-classical (bio-derived) solvents, developed by CHEM21, a consortium of European organizations and companies. This includes a link to a [solvent ranking Excel file](#) to help rank other solvents based on safety, health, and environmental risks.
- [Occupational Safety and Health Administration: Transitioning to Safer Chemicals](#): Step-by-step framework and resources for employers and workers.



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- [Sanofi: Solvent Selection Guide](#): Evaluates safety, health, and environmental risks.
- [The Royal Society of Chemistry: Solvent Guide for Chromatography](#): Chromatography guide for selecting a solvent to replace DCM/methanol mixtures.
- [Toxics Use Reduction Institute \(TURI\): Database of Safer Solvents \(DOSS\)](#): Hansen Solubility Parameters-based database for replacing highly hazardous chemicals (includes bulk cost estimates).