MilliporeSigma

The Future of Solvents:

BIO

RENEWABLE

MilliporeSigma is the U.S. and Canada Life Science business of Merck KGaA, Darmstadt, Germany.

Sigma-Aldrich®

Lab & Production Materials

Dedicated to supporting all your explorations RESPONSIBLY.

Why should you have to choose between solvents that are ecological and those that are reliable? Enjoy both at once with our BioRenewable and greener solutions. Thanks to their origin, they won't compromise the environment. And thanks to their high quality, they won't compromise your work.

In addition to our familiar greener solvents, such as water and ethanol, you also have the option of other innovative solutions that are made from biological sources, have higher recovery rates, or are safer for handling and disposal. Many of them are bio-based, sourced from non-food materials, so they don't depend on petroleum sources or deplete food supplies. Certain solvents are still essential for scientific work.

But, here too, we're investing in promising research to find optimal, safer alternatives for you. Explore our latest range of greener and BioRenewable solvents, and see how your explorations go even further through sustainability.

Learn more about our dedication to green chemistry on:
SigmaAldrich.com/greener

12 Principles of Green Chemistry

In 1998, Paul Anastas and John Warner proposed a framework to change how scientists thought about their work by making environmentally friendly chemical processes and products top of mind.

Their 12 principles are represented by the icons below, which provide a **quick reference for the classification of our greener substitutes and BioRenewable solvents.**

Use of Renewable Feedstocks

Safer Solvents and Auxiliaries

Design for Degradation

Prevention of Waste

Designing Safer Chemicals

Inherently Safer Chemistry for Accident Prevention

Design for Energy Efficiency

Reduced Derivates

Catalysis

Atom Economy

Less Hazardous Chemical Syntheses

Real-Time Analysis for Pollution Prevention

Explore our complete range of solvents on:
SigmaAldrich.com/solvents

BioRenewable solvents. A simple switch.

It's now easy for everyone – from the smallest universities to the largest pharmaceutical and technology companies – to implement greener chemistry. Simply replace classic petroleum solvents in your current workflows with our bio-based alternatives and proceed as you always have.

These solvents are free of the many by-products of petroleum manufacturing, such as benzene, aldehydes, and ethers. What's more, each solvent is verified as renewable through ASTM testing (ASTM Standard D6866), which verifies the percentage of new carbon.

Acetone (904082)			
Property Tested	**BioRenewable Acetone**	**Non-Renewable Acetone**	**Test Method**
Total purity	≥ 99.5%	≥ 99.5%	**GC**
Water	≤ 0.3%	≤ 0.5%	**ASTM D1364**
Benzene	Not Detected	0.003%	**GC**
Aldehydes	Not Detected	≤ 0.002%	**GC**
Methanol	≤ 0.05%	≤ 0.05%	**GC**
Isopropanol	≤ 0.05%	≤ 0.05%	**GC**
Nonvolatile Matter wt%	≤ 1 mg / 100 mL	≤ 0.001%	**ASTM D1353**
Renewable Carbon wt%	100%	0%	**ASTM D6866**

Glycerol (911046)			
Property Tested	**BioRenewable Glycerol**	**Non-Renewable Glycerol**	**Test Method**
Total purity	≥99.5%	≥99.5%	**CG**
Water	≤0.5%	≤0.5%	**Karl Fischer**
Residue in ignition (Ash)	≤0.005%	≤0.005%	**ACS methodology**
Heavy Metals	≤ 2ppm	≤ 2ppm	**ACS methodology**
Sulfate (SO4)	≤0.001%	≤0.001%	**ACS methodology**
Fatty Acid Esters	≤0.05%	≤0.05%	**Titration**
Renewable Carbon wt%	100%	0%	**ASTM D6866**

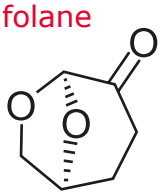
Cat. No.	Product Description
904082	Acetone, BioRenewable, ACS Reagent, ≥ 99.5%
911038	Glycerol, BioRenewable, ACS reagent, ≥99.5%
911046	Glycerol, BioRenewable, ≥99.5%

It may seem like a small change but by choosing a greener alternative you are joining thousands of scientists who are designing a new future that uses resources more responsibly. One small change early on has the potential to help make the world better for the generations to come.

Join us in taking giant steps toward creating smaller footprints.
To find out more visit **SigmaAldrich.com/biorenewable-solvents**

Cyrene™

CAS No.: 53716-82-8
Alternative for: NMP, DMF, and sulfolane



Features & benefits

Cyrene™ is a new dipolar aprotic alternative to common REACH-restricted solvents, such as N-methyl-2-pyrrolidone (NMP). One of the first true greener solvents, it is produced from renewable resources, and safe for end of life disposal, decomposing into CO_2 and H_2O. Cyrene™ is also safer to handle, with no mutagenic or genotoxic concerns.

- 99% biodegradation in 28 days
- Stable during incineration
- Not mutagenic or genotoxic

Applications:

- Exceeds NMP's dispersive ability for graphene solutions by an order of magnitude[1]
- Used as an alternative to DMF in synthesis of metal-organic frameworks[2]
- Comparable replacement for DMF in amide and dipeptide coupling reactions[3]

Reactions:

- Sonogashira
- Cacchi-type annulation
- Synthesis of metal-organic frameworks
- Suzuki-Miyaura coupling reaction
- Synthesis of ureas

Cat. No.	Product Description
807796	Cyrene™, BioRenewable

1 Identification of high performance solvents for the sustainable processing of graphene, Salavagoine, H., Sherwood, J., De bruyn, M., Budarin, V., Ellis, G., Clark, J., Shuttleworth, P., Green Chem, 2017, 11, 2550-2560

2 Dihydrolevoglucosenone (Cyrene) as a Green Alternative to N,N-Dimethylfomamide (DMF) in MOF Synthesis, Zhang, J., White, G., Ryha, M., Hunt, A., Katz, J., ACS Sustainable Chem Eng., 2016, 4(12), 7186-7192

3 Cyrene as a bio-based solvent for HATU mediated amide coupling, Wilson, K., Murray, J., Jamieson, C., Watson, A., Org Biol. Chem, 2018, 16, 2851-2854

Cyrene™ γ-Valerolactone & Cyrene™ 2-MeTHF blends

Features & benefits

Cyrene™ 2-Methyltetrahydrofuran Blend and Cyrene™ γ-Valerolactone Blend combine the benefits of classic Cyrene™ with those of two BioRenewable solvents. While they maintain the excellent efficacy of Cyrene™, the new blends offer considerably lower viscosity.

This greatly simplifies their handling and broadens their applicability, leading to even higher product yields in automated processes. Experience greater performance with lower environmental impact by switching from NMP and DMF to our new Cyrene™ Blends.

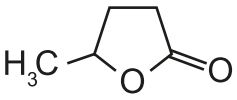
- Independently certified as 100% renewable carbon
- Sustainably produced and less hazardous for the environment
- Non-toxic, much safer to handle than petroleum-based aprotic solvents
- Physical properties more analogous to those of NMP and DMF
- Same high reaction yields as traditional solvents
- Optimized for automated processes due to lower viscosity
- Lower boiling point facilitates removal from automated systems

Cat. No.	Product Description
920193	Cyrene™ 2-Methyltetrahydrofuran Blend, BioRenewable
920207	Cyrene™ γ-Valerolactone Blend, BioRenewable

Read our tech article to learn how the the Cyrene™ blends performed in cross-coupling reactions.

γ-Valerolactone (GVL)

CAS No.: 108-29-2
Alternative for: NMP, DMF and DMA



Features & benefits

γ-Valerolactone is a dipolar aprotic, BioRenewable, fully degradable and non-toxic green solvent. It is completely miscible in water, has low volatility (VOC), good thermal stability and does not form peroxide or hydrolyses under ambient conditions. It is considered a sustainable alternative to traditional solvents such as NMP and DMF.

- Non-toxic solvent
- Biodegradable
- Low vapor pressure
- Safer Solvent and Auxiliar

Applications:

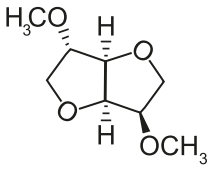
- Cross-coupling reactions[4]
- ATRP polymerization[5]
- Replacement of DCM in peptide synthesis[6]

Cat. No.	Product Description
918660	γ-Valerolactone, BioRenewable

4. γ-Valerolactone as a Renewable Dipolar Aprotic Solvent Deriving from Biomass Degradation for the Hiyama Reaction, Ismalaj, E.; Strappaveccia, G.; Ballerini, E.; Elisei, F.; Piermatti, O.; Gelman, D.; Vaccaro. L.; ACS Sustainable Chem. Eng.; 2014 2 (10), 2461-2464.
5. γ-valerolactone (GVL) as a bio-based green solvent and ligand for iron-mediated AGET ATRP, Shen, X.; Xia, D.; Xiang, Y.; Gao, J.; e-Polymers; 2019, 19, 323 – 329.
6. γ-Valerolactone (GVL): An eco-friendly anchoring solvent for solid-phase peptide synthesis, Musaimi, O. A.; El-Faham, A.; Basso, A.; de la Torre, B. G.; Albericio, F.; Tetrahedron Letters; 2019, 60, 151058

Dimethyl isosorbide (DMI)

CAS No.: 5306-85-4
Alternative for: NMP and DMF



Features & benefits

Dimethyl isosorbide (DMI) is a BioRenewable green solvent used notably cosmetic formulation. Its high solubilization capacity when used as co-solvent for nonpolar drugs, make it an interesting compound for pharmaceutical industries as well. DMI is also a sustainable alternative to NMP and DMF, and suitable in organic synthesis, such as Baylis–Hillman reaction.

- Derived from renewable feedstocks
- High solubility potential
- High boiling point

Applications:

- Used in polymer membranes preparation[7]
- Solvent in Baylis Hillman reactions
- Used as co-solvent to improve solubility of nonpolar compounds[8]
- Potential substitutes to short-chain glycol ethers[8]

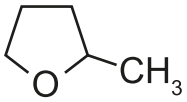
Cat. No.	Product Description
906832	Dimethyl isosorbide, BioRenewable

7. Dimethyl Isosorbide as a Green Solvent for Sustainable Ultrafiltration and Microfiltration Membrane Preparation, Russo, F., Galiano, F.; Pedace, F.; Arico, F.; Figoli, A., ACS Sustainable Chem. Eng, 2020, 8, 659–668.
8. Cosolvency of Dimethyl Isosorbide for Steroid Solubility, Zia, H., Ma, J.K.H., O'Donnell, J.P.; 1991, 8, 502-504.

Looking to further reduce your environmental impact?
Explore more green solvent alternatives on:
SigmaAldrich.com/greensolvents

2-Methyltetrahydrofuran (2-MeTHF)

CAS No.: 96-47-9
Alternative for: THF, diethyl ether, and DCM



Features & benefits

2-Methyltetrahydrofuran is an environmentally favorable alternative to tetrahydrofuran (THF), 1,4 dioxane (dioxane), and dichloromethane (DCM) for most industrial applications.

- High boiling point: Processes may be run at higher temperatures, decreasing reaction time
- Organic water-phase separation: Limits need for extraction solvents, lowers solvent and water waste
- Reduced energy to recover: Standard distillation is sufficient for solvent recovery
- No risk of genotoxicity or mutagenicity from exposure

Other applications:

Forms organic (non-crystalline) glass for low temperature (-196°C) spectroscopic studies

Alternative for THF in organometallic reactions:

- Grignard
- Reformatsky
- Lithiation
- Hydride reduction
- Metal-catalyzed coupling (Heck, Stile, Suzuki)

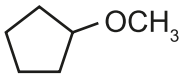
Alternative for dichloromethane in biphasic reactions:

- Alkylation
- Amidation
- Nucleophilic substitution

Cat. No.	Product Description
155810	2-Methyltetrahydrofuran, BioRenewable, ReagentPlus®, ≥99.5%, contains 150-400 ppm BHT as stabilizer
414247	2-Methyltetrahydrofuran, BioRenewable, anhydrous, ≥99.0%, contains 250 ppm BHT as stabilizer
673277	2-Methyltetrahydrofuran, BioRenewable, anhydrous, ≥99%, Inhibitor-free
900520	2-Methyltetrahydrofuran, anhydrous, contains 250 ppm BHT as stabilizer, ZerO2®, ≥99.0%

Cyclopentyl methyl ether (CPME)

CAS No.: 5614-37-9
Alternative for: THF, t-butyl methyl ether (MTBE), dioxane, and other ether solvents



Features & benefits

Cyclopentyl methyl ether (CPME) is a hydrophobic ether solvent with a high boiling point, making it an optimal substitute for many ether solvents, such as MTBE and THF. CPME has a synthetic origin, and offers other benefits, including significantly safer handling.

- Low peroxide formation[9]
- High hydrophobicity[9]
- High boiling point, low melting point[9]
- Narrow explosion area[9]

Applications:

- Crystallization[10]
- Polymerization
- Coatings

Reactions:

- Alkali agent (nucleophilic substitution of heteroatoms)
- Azeotropic removal of water
- Transition metal catalysis
- Organometallic
- Lewis acid mediated reactions

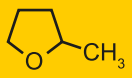
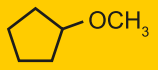
Cat. No.	Product Description
675989	CPME, contains 50 ppm BHT as inhibitor, *ReagentPlus*®, ≥ 99.9%
675970	CPME, contains 50 ppm BHT as inhibitor, anhydrous, ≥ 99.9%
791962	CPME, inhibitor-free, anhydrous, ≥ 99.9%

Looking to further reduce your environmental impact?
Explore more green solvent alternatives on:
SigmaAldrich.com/greensolvents

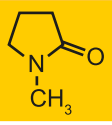
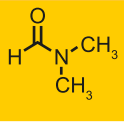
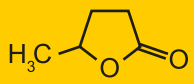
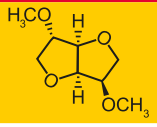
9. The toxicological assessment of cyclopentyl methyl ether (CPME) as a green solvent. Watanabe, K., Molecules 2013, 18(3), 3183-94
10. Cyclopentyl Methyl Ether: An Elective Eco-Friendly Etheral Solvent in Classical and Modern Organic Chemistry, Azena, U., Carraro, M., Pisano, L., Monticelli, S., Barolotta, R., Pace, V., Chem Sus. 2018

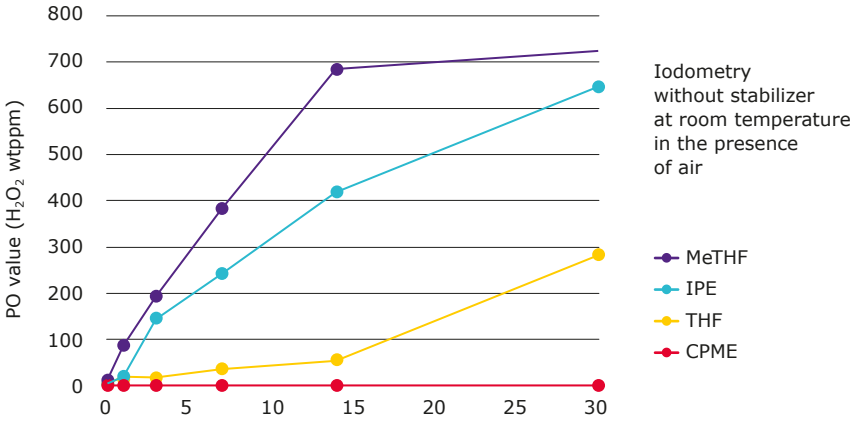
Greener alternative solvents at a glance

THF alternatives

Solvent	*THF*	*MeTHF*	*CPME*
Structure			
CAS No.	109-99-9	96-47-9	5614-37-9
Density (g/mL)	0.928	0.85	0.86
Boiling Point (°C)	65.8	80	106
Melting Point (°C)	-108	-136	< -140
Dielectric Constant	7.58	7	4.76
Dipole Moment (D)	1.7	1.38	1.27
Solubility in Water (mol/L)	13.9	14	0.226
Viscosity (cP)	0.589	0.6	0.55
Surface Tension (dyn/cm)	27.4	25.9	25.17
Vaporization Energy (kJ/mol)	98.1	89.7	69.2
Flash Point (°C)	-14.5	-11	-1
Ignition point (°C)	205	270	180

NMP and DMF alternatives

Solvent	*NMP*	*DMF*	*Cyrene™*	*GVL*	*DMI*
Structure					
CAS No.	872-50-4	68-12-2	53716-82-8	108-29-2	5306-85-4
Density (g/mL)	1.028	0.994	1.250	1.05 g/mL	1.15 g/mL
Boiling Point (°C)	204	153	227	~207 °C	~94 °C
Melting Point (°C)	-24	-61	< -20	-31 °C	-70 °C
Dielectric Constant	32.2	38.25	~3.4	36.5	36.5
Dipole Moment (D)	12.26	3.8	Unknown	4.3	4.3
Solubility in Water (mol/L)	10.1	13.7	∞	∞	∞
Viscosity (cP)	1.65	0.805	14.5	2.18	Unknown
Surface Tension (dyn/cm)	40.79	37.10	72.5	30	Unknown
Vaporization Energy (kJ/mol)	61.9	47.6	Unknown	Unknown	Unknown
Flash Point (°C)	91	58	108	96	108
Ignition point (°C)	245	445	296	Unknown	Unknown

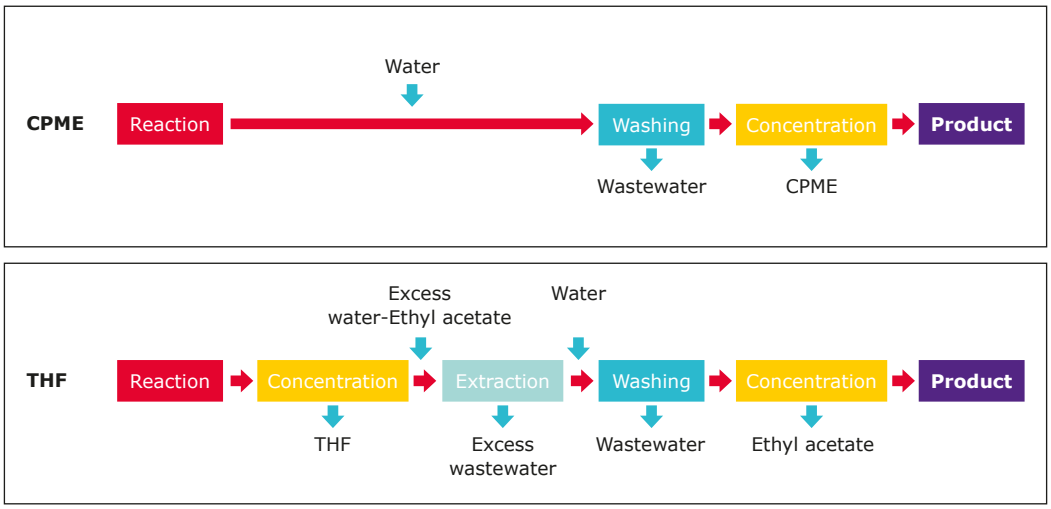


The product is stabilized with approximate 50 ppm of BHT

Peroxide formation comparison of MeTHF, isopropyl ether (IPE), THF, and CPME over 25 days.

Stabilized THF: 102 days to reach 100ppm

Stabilized CPME:
683 days to reach 100 ppm



CPME vs. THF process flow.

CPME reduces the number of steps required for production. It reduces the amount of water that is required for washing and eliminates the need for co-solvents for product recovery.

Sigma-Aldrich®

Lab & Production Materials

MilliporeSigma
400 Summit Drive
Burlington, MA 01803

SigmaAldrich.com

Lit. No. MS_BR3670EN Ver. 2.0 47432 08/2023