

SUPPLEMENTARY INFORMATION

How do you (dis)solve a problem like methylene chloride?

James Sherwood

Green Chemistry Centre of Excellence, University of York

Table S1	Online resources for organisations reducing or eliminating methylene chloride use (compiled April 2025)	2
Table S2	Composition of modern paint remover products referenced in the main article	2
Table S3	Toxic Release Inventory (TRI) organized by sector for the years 2020-2023	3
Table S4	Toxic Release Inventory (TRI) organized by environmental fate for the years 2020-2023	3
Table S5	Chlorinated solvents: Safe and Sustainable by Design (SSbD) hierarchy of hazards and corresponding CHEM21 solvent selection scores (three tier scoring, high scores are worse)	4
Table S6	Alternative solvents: Safe and Sustainable by Design (SSbD) hierarchy of hazards and corresponding CHEM21 solvent selection scores (three tier scoring, high scores are worse)	5
Table S7	Journal survey: methylene chloride (DCM) as a solvent, total original research articles, and usage ratio (2020–2023)	6
Table S8	Methylene chloride uses from OPRD (Jan–Mar 2025, 79 articles). Absolute values	7
Table S9	Methylene chloride (DCM) uses (of 1,627,689 examples) as recorded in SciFinder	9
Table S10	Dependency on methylene chloride for common reactions	9
Scheme S1	Reactions illustrating major uses of methylene chloride in organic synthesis	10

Table S1. Online resources for organisations reducing or eliminating methylene chloride use (compiled between April and July 2025).

Organisation	Link	Content
EPA	https://communities.acs.org/t5/GCI-Nexus-Blog/The-EPA-s-DCM-Restriction-and-What-You-Need-to-Know-to-Comply/ba-p/98225	Compliance advice
GreenScreen	https://www.newmoa.com/prevention/ic2/projects/assessments/DCM_GreenScreen_Assessment.pdf	Assessment of methylene chloride
GreenScreen	https://www.theic2.org/wp-content/uploads/2023/08/141-78-6-Ethyl-acetate-GS-348-v-1.4-Certified-March-2023.pdf	Assessment of ethyl acetate (alternative to methylene chloride)
California Department of Toxic Substances Control	https://dtsc.ca.gov/wp-content/uploads/sites/31/2022/05/DTSC_Final_Quant_AA_pilot_UCSB-1_accessible.pdf	Alternative paint removers
GreenScreen	https://www.greenscreenchemicals.org/resources/entry/resource-methylene	Alternative paint removers
ACS	https://www.acs.org/green-chemistry-sustainability/research-innovation/solvents/dcm.html	Alternative solvents
OSHA	https://www.osha.gov/methylene-chloride	Exposure monitoring advice
OSHA	https://www.osha.gov/sites/default/files/publications/OSHA3883.pdf	Incident report
GCTLC	https://vimeo.com/1013658714/0e32147bb6	Alternative solvents (webinar)

Table S2. Composition of modern paint remover products referenced in the main article.

Ingredients	SDS
3-Butoxypropan-2-ol, potassium hydroxide, 2-aminoethanol.	[S1]
Methanol, ethanol, MEK, dimethyl succinate, light alkanes, 1-methoxy-2-propanol.	[S2]
Hydrocarbons (C9-11 isoalkanes), 1,3-dioxolane and ammonia.	[S3]

Table S3. Toxic Release Inventory (TRI) organized by sector for the years 2020-2023.

Methylene chloride emissions /L	2020	2021	2022	2023
Chemicals	670946	934170	839324	544286
Polymers	84227	62888	162712	60782
Metals and minerals	67274	57715	68694	47370
Machinery	98720	109448	7815	886
Other industry	126862	144940	131252	124604
Waste management	29927	32570	13017	29325

Table S4. Toxic Release Inventory (TRI) organized by environmental fate for the years 2020-2023.

Methylene chloride emissions /L	2020	2021	2022	2023
Landfill	52096	217047	98464	68204
Air	896873	985419	976806	682900
Other	129505	139265	147547	56149

Table S5. Chlorinated solvents: Safe and Sustainable by Design (SSbD) hierarchy of hazards (three tier scoring, worst hazards at the top) and the corresponding and CHEM21 solvent selection scores (three tier scoring, high scores are worse).

Solvent	Health	Environment	Physical	Regulations	S	H	E
Methylene chloride				TSCA		7	7
	H351						
	H315 H319 H336				1		
Chloroform	H372					7	
	H351 H361						5
	H302 H315 H319 H331				2		
Carbon tetrachloride	H372			TSCA and Montreal protocol		7	10
	H351	H412 H420					
	H301 H311 H317 H331				2		
1,2-DCE	H350			REACH		10	
						4	
	H302 H304 H315 H319 H331 H335		H225				3
Trichloroethylene	H350			TSCA		9	
	H341	H412					5
	H315 H317 H319 H336				1		
Perchloroethylene				TSCA			7
	H351	H411				6	
	H315 H317 H319 H336				1		

Table S6. Alternative solvents: Safe and Sustainable by Design (SSbD) hierarchy of hazards and the corresponding and CHEM21 solvent selection scores.

Solvent	Health	Environment	Physical	Regulations	S	H	E
Ethyl acetate							
					5		
	H319 H336		H225			3	3
Dimethyl carbonate							
					4		
			H225			1	3
Cyrene							7
	H319				1	2	
Acetonitrile							
					4		
	H302 H312 H219 H332		H225			3	3
2-Methyl tetrahydro-furan							
					6	5	
	H302 H315 H318		H225				3
Methyl <i>t</i> -butyl ether					8		
							5
	H315		H225			3	
Cyclopentyl methyl ether					7		
							5
	H302 H315 H319		H225			2	

Table S7. Journal survey recording the uses of methylene chloride (DCM) as a solvent, total original research articles, and the ratio for the years 2020 to 2023.

Journal	Survey	2020	2021	2022	2023
<i>J. Org. Chem. (JOC)</i>	Uses of DCM	9543	9703	10012	11771
	Articles	1451	1519	1514	1667
	Ratio	6.6	6.4	6.6	7.1
<i>Green Chem.</i>	Uses of DCM	602	787	909	1404
	Articles	701	749	735	808
	Ratio	0.9	1.1	1.2	1.7
<i>J. Am. Chem. Soc. (JACS)</i>	Uses of DCM	9084	9862	8446	8645
	Articles	2397	2221	2220	2804
	Ratio	3.8	4.4	3.8	3.1
<i>J. Med. Chem.</i>	Uses of DCM	8769	10366	10113	9927
	Articles	725	805	766	839
	Ratio	12.1	12.9	13.2	11.8
<i>Org. Process Res. Dev. (OPRD)</i>	Uses of DCM	366	247	328	120
	Articles	270	178	60	127
	Ratio	1.4	1.4	5.5	0.9
<i>Angew. Chemie Int. Ed.</i>	Uses of DCM	11702	12232	11672	11904
	Articles	3033	3286	3109	3703
	Ratio	3.9	3.7	3.8	3.2
<i>ACS Sustainable Chem. Eng.</i>	Uses of DCM	145	158	166	84
	Articles	1825	1545	1583	1619
	Ratio	0.1	0.1	0.1	0.1

Table S8. Methylene chloride uses from OPRD (Jan-Mar 2025, 79 articles). Absolute values.

Solvent	Reactions	Work-up (separations and recrystallisation)	Column chromatography
Methanol	28	12	2
Ethyl acetate	8	25	8
Methylene chloride	18	19	5
Tetrahydrofuran	25	2	0
Ethanol	13	11	2
Toluene	14	7	0
Methyl t-butyl ether	9	14	0
Acetonitrile	14	9	0
2-Propanol	7	12	0
Heptane	0	10	5
Acetone	4	7	1
DMF	10	2	0
Hexane(s)	3	6	4
2-MeTHF	5	3	0
Pet. ether	0	4	3
DMAc	6	0	0
DMSO	6	0	0
Acetic acid	3	1	0
t-Butanol	2	0	0
Trifluoroethanol	2	0	0

Table S8. Continued.

Solvent	Reactions	Work-up (separations and recrystallisation)	Column chromatography
Dimethyl carbonate	2	0	0
Pentane	0	1	2
1-Butanol	0	2	0
Chloroform	1	1	0
Butanone	0	1	0
Methyl isobutyl ketone	1	1	0
Isooctane	0	1	0
Cyclopentyl methyl ether	1	0	0
Anisole	1	0	0
Ethyl formate	0	1	0
Cyclohexane	0	0	1
Nitrobenzene	1	0	0
Methylcyclohexane	0	1	0
Diphenyl ether	1	0	0
Carbon dioxide	0	0	1

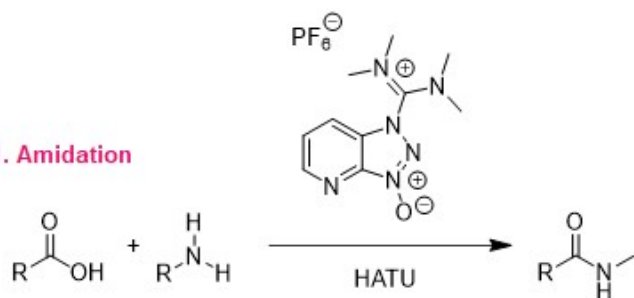
Table S9. Methylene chloride (DCM) uses (of 1627689 examples) as recorded in SciFinder.

Reaction	DCM uses	Use distribution
Amidation	389253	24%
Amide hydrolysis	152857	9%
Esterification	77457	5%
Aromatic nucleophilic substitution	60951	4%
Sulfonamidation	57175	4%
Reductive amination	42008	3%
Ether hydrolysis	41641	3%
Ester hydrolysis	41601	3%

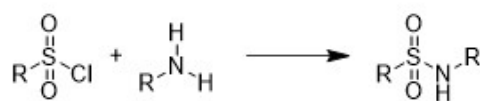
Table S10. Dependency on methylene chloride for common reactions.

Reaction	Total reactions	Reactions using methylene chloride	Dependency on methylene chloride	Other notable solvent(s)
Amidation	151007	27206	18%	DMF (74%)
Amide hydrolysis	221849	97092	44%	Dioxane (23%)
Esterification	22598	18658	83%	-
Aromatic nucleophilic substitution	30848	291	1%	DMSO (33%) and DMF (26%)
Sulfonamidation	242909	163367	67%	THF (39%) and DMF (28%)
Reductive amination	39938	16918	42%	DCE (25%)
Ether hydrolysis	19149	13868	72%	-
Ester hydrolysis	29679	24086	81%	-

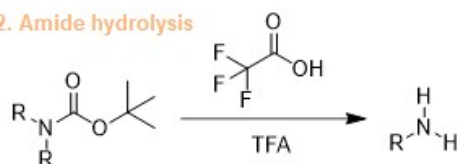
1. Amidation



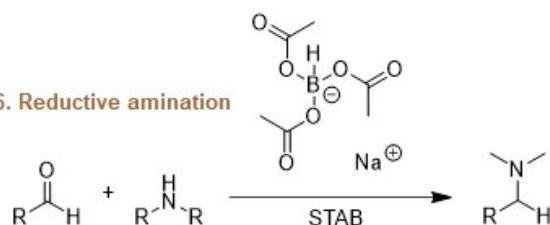
5. Sulphonamidation



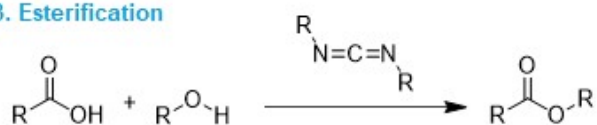
2. Amide hydrolysis



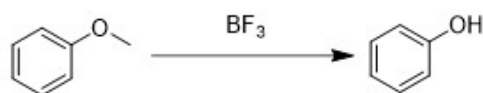
6. Reductive amination



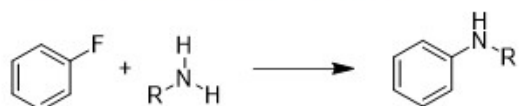
3. Esterification



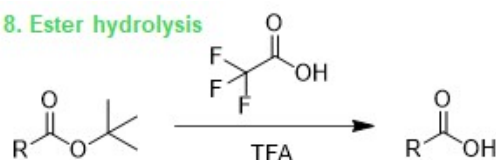
7. Ether hydrolysis



4. Aromatic nucleophilic substitution



8. Ester hydrolysis



Scheme S1. Reactions representing major uses of methylene chloride in organic synthesis.