聲明

本檔案之內容僅供下載人自學或推廣化學教育之非營利目的使用。並請於使用時註明出處。[如本頁取材自〇〇〇教授演講內容]。

2013 綠色/永續合成化學工作坊
暨南國際大學
2013/11/23

綠色溶劑

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Table 1.4 Some solvent applications.

Application	*Description*
Solvent extraction	In hydrometallurgy to recover metals from ores In nuclear fuel reprocessing In waste water treatment To recover natural products from plants or from fermentation liquors In organic synthesis and analytical chemistry As a degreaser and cleaning agent
Analytical chemistry and electrochemistry	Eluant in analytical and preparative chromatography, and in other separation techniques Dissolving the electrolyte to permit current to flow between the electrodes, without being oxidized or reduced itself As an oxidant or a reductant
Organic chemistry	As a reaction medium and diluent In separations and purification As a dehydrator (also in materials chemistry)
Polymer and materials chemistry	As a dispersant As a plasticizer As a blowing agent to create porosity As a binder to achieve cohesiveness in composite materials Production of powders, coatings, films, *etc.* As a developer in photoresist materials
Household and others	Fuels and lubricants Paints, varnishes, adhesives, dyes, *etc.* Antifreeze Cleaning fluids As a humectant (hydrating material) and in emulsions within cosmetics and pharmaceuticals

Kerton F.M. Alternative Solvents for Green Chemistry RSC 2009

Principle 3

Wherever practicable, synthetic methodologies should be designed to **use and generate substances that possess little or no toxicity** to human health and the environment.

Principle 5

The use of **auxiliary substances** (e.g. solvents, separation agents, etc.) should **be made unnecessary** whenever possible and, innocuous when used.

Traditional solvents

- **Volatile organic solvents (VOCs)**
  - **Chloroform, Carbon tetrachloride, Methylene chloride, Dichloroethylane**
  - **BTX: Benzene, Toluene, Xylene**
  - **Acetone, Methylethyl ketone (MEK), etc.**
- **CFCs**

PROBLEMS WITH CURRENTLY USED SOLVENTS

In the US in the early 1990's:

- solvent production was 26 million tons p.a.
- of tracked chemicals, many of the top chemicals released or disposed of were solvents (MeOH, toluene, xylene, CS_2, MEK, CH_2Cl_2)

Organic solvent hazards

- flammable (almost all except chlorinated solvents)
- carcinogenic (chlorinated solvents and aromatics)
- high vapour pressure (i.e. inhalation route)
- narcotic (ether, chloroform)
- toxic (MeOH, CS_2)
- mutagens/teratogens (toluene)
- peroxides (ethers)
- smog formation

How can we reduce the use of traditional solvents?

- **Solvent recovery and recycle**
- **Nontraditional reaction systems.**
  - **Solventless reaction systems.**

- **Green synthesis:**

- **Green solvents**

溶劑的回收與處理

- Chemical treatment technologies for **waste-water** recycling—an overview (*RCS Adv*. **2012**, *2*, 6380-6388)
- STEP wastewater treatment: A solar thermal electrochemical process for pollutant oxidation (*ChemSusChem* **2012**, *5*, 2000-2010)
- The importance of **acetonitrile** in the pharmaceutical industry and opportunities for its recovery from waste (*Org. Process Res. Dev*. **2012**, *16*, 612-624)
- Green design alternatives for **isopropanol** recovery in the celecoxib process (*Clean Techn. Environ. Policy* **2012**, *14*, 697-698)
- Pervaporation as a green drying process for **tetrhydrofuran** recovery in pharmaceutical synthesis (*Green Chem. Lett. Rev*. **2012**, *5*, 55-64)

Selection of greener solvents

- To choose solvent(s) that will lead to the lowest possible negative environmental impacts for a synthetic process.
- There is no such thing as a green solvent. The greenness of a solvent can only be considered in the context of the process in which it is being used.

Selection of Solvents

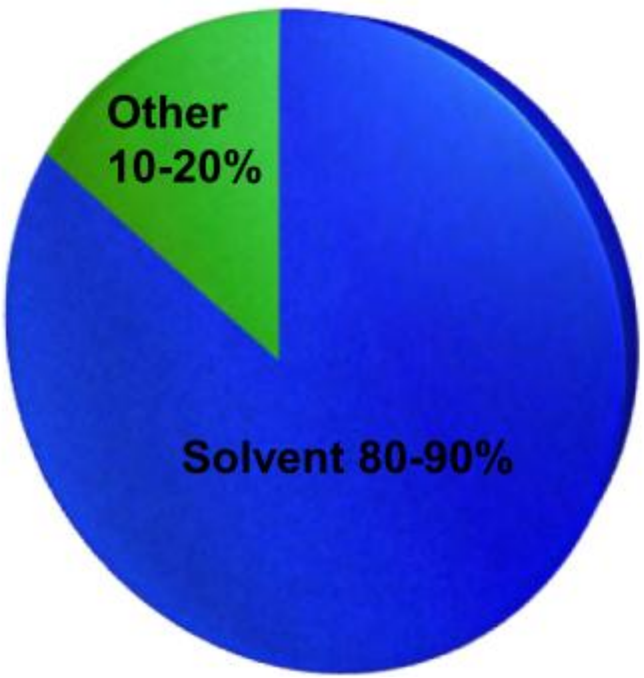
- It affects yields, selectivities, and the rate of reactions.
- The careful selection of the solvent can greatly reduce the wastefulness and the energy use of a synthetic process.

$$\text{"E" factor} = \frac{\text{Mass of waste}}{\text{Mass of product}}$$

Industry segment	Product tonnage	E factor
Bulk chemicals	10^4 - 10^6	<1 - 5
Fine chemicals	10^3 - 10^4	5 - 50
Pharmaceuticals	10 - 10^3	25 - over 100

R. Sheldon, CHEMTECH 1994, 38.

Mass utilization in fine chemical production



http://www.caraet.com/Waste_solvent.htm

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綠色量度

Sheldon E-factor = mass of waste produced/mass of desired product

環境因數

- The E-factor includes all auxiliary materials and takes into account the yields and selectivities of the reactions. However, it does not take into account the toxicities or other environmental hazards of the waste products, nor does it encompass the **energy** used in the process.
- Hence, changing solvents, leading to greater selectivities or more effective separation, can reduce (improve) the E-factor for the reaction. However, using a less toxic solvent or changing related reaction rates has no influence on the E-factor.

$$A + B \xrightarrow[\text{Solvent 14 g}]{\text{Catalyst 1 g}} C + D + E \xrightarrow[\text{純化過程用到的物質總重30 g}]{\text{Purification}} D$$

A	B	C	D	E	D
5 g	5 g	3 g	4 g	3 g	4 g

Yield = ?

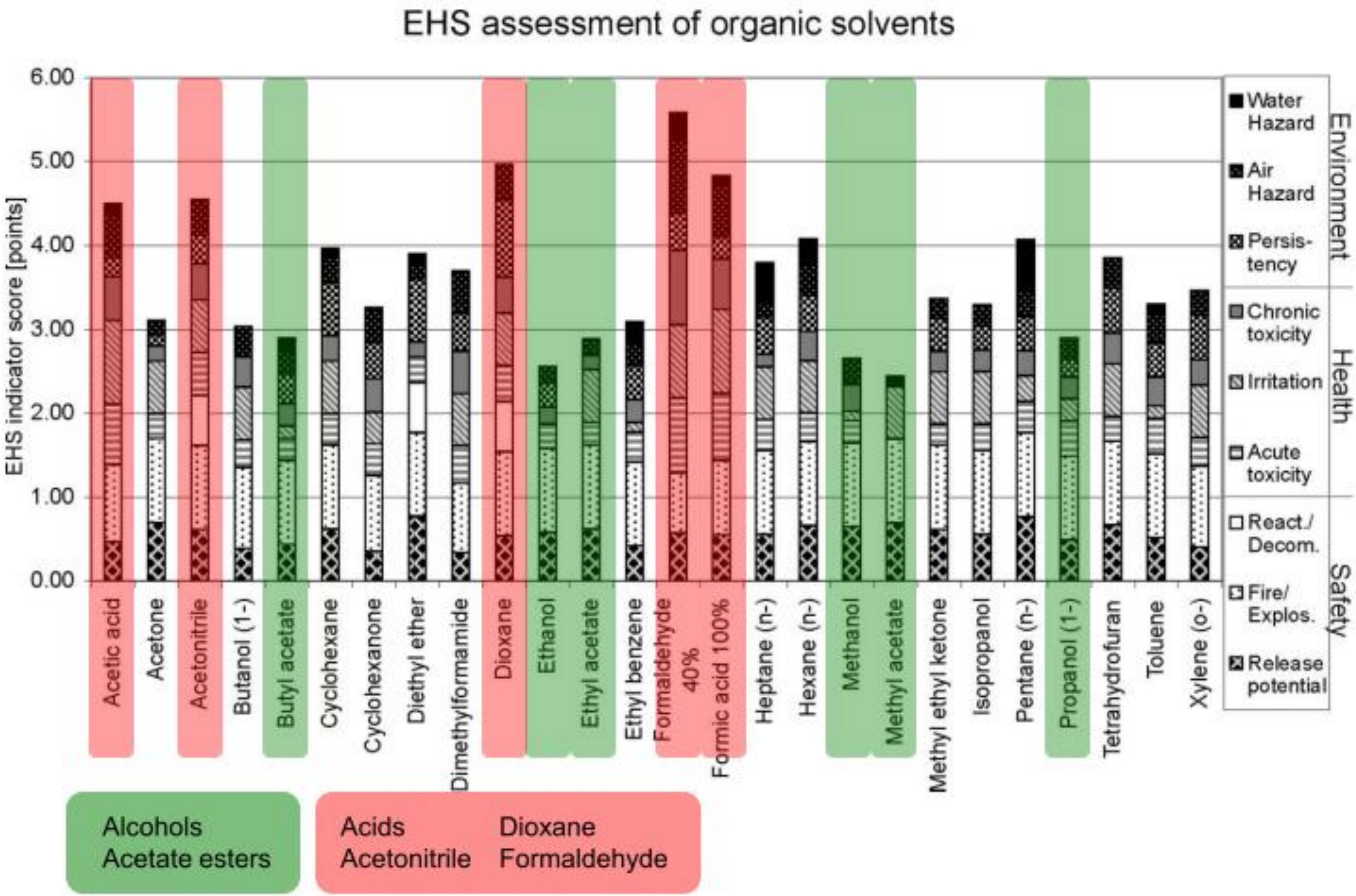
Atom Economy = ?

Process Mass Intensity = ?

Chemical's EHS file

- An Environmental Health and Safety (EHS) tool has been developed to assess the direct environmental risks of a chemical compound. The EHS profile is calculated by considering for the environmental persistency, air hazard, and water hazard; for safety: release potential, fire/explosion risk, and irritation. Any compound is given a score for each of these factors, which are then summed to give an overall EHS profile.

ENVIRONMENTAL AND HEALTH RISKS



Capello et al., *Green Chem* (2007) 9, 927

Which solvent is greener?

PFIZER SOLVENT SELECTION GUIDE

Water	Cyclohexane	Pentane
Acetone	Toluene	Hexane(s)
Ethanol	Methylcyclohexane	Di-isopropyl ether
2-Propanol	TBME	Diethyl ether
1-Propanol	Isooctane	Dichloromethane
Heptane	Acetonitrile	Dichloroethane
Ethyl Acetate	2-MeTHF	Chloroform
Isopropyl acetate	THF	NMP
Methanol	Xylenes	DMF
MEK	DMSO	Pyridine
1-Butanol	Acetic Acid	DMAc
t-Butanol	Ethylene Glycol	Dioxane
		Dimethoxyethane

Green Chem. 2008, 10, 31

Pfizer Solvent Replacement Table

Table 1. Solvent Replacement

nongreen solvent	alternative
pentane	heptane
hexane(s)	heptane
diisopropyl ether or ether	2-MeTHF or *tert*-butyl methyl ether
dioxane or dimethoxyethane	2-MeTHF or *tert*-butyl methyl ether
chloroform, dichloroethane, or carbon tetrachloride	DCM[51]
DMF or DMA or NMP	acetonitrile
pyridine	Et_3N (if pyridine used as base)
DCM (extractions)	EtOAc, MTBE, toluene, 2-MeTHF
DCM (chromatography)	EtOAc/heptanes
benzene	toluene

Green Chem. **2008**, *10*, 31. *J. Med. Chem.* **2013**, *56*, 6007.

Editorial Advisory Board of

Organic Process Research & Development

"Thus submissions including quantitative measures of green chemistry performance such as mass intensity/efficiency, atom economy, and E-factor are particularly welcome."

We warn that authors risk having papers rejected unless environmental impact and green chemistry principles are considered.

Papers containing strongly undesirable solvents (e.g., benzene, carbon tetrachloride, chloroform, carbon disulfide, etc.) will only be considered if accompanied by an analysis of alternatives or if a convincing justification for such use is presented."

Unconventional (Green) Solvents

- Water
- Switchable solvent
- Supercritical CO_2
- Ionic liquid
- Liquid polymer
- CO_2 expanded liquid

Water- A “green” solvent?

Advantage: the most environmentally benign solvent in terms of its direct impact in the environment.

Disadvantage: Its high heat of vaporization can lead to excess energy demands if it is removed from a product by evaporation, which in turn leads to the production of CO_2, hence it may be better to use a less apparently green solvent from which the desired product can be more easily produced.

Solvent properties

PROPERTIES OF CONCERN

For green-ness

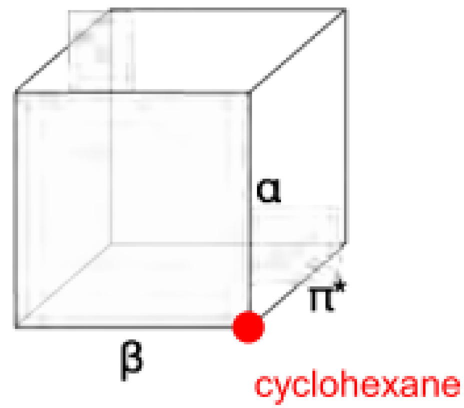
- boiling point / energy to distill
- flash point
- energy to distill
- cumulative energy demand

For utility

- polarity
- basicity / hydrogen-bond accepting ability
- acidity / hydrogen-bond donating ability
- viscosity

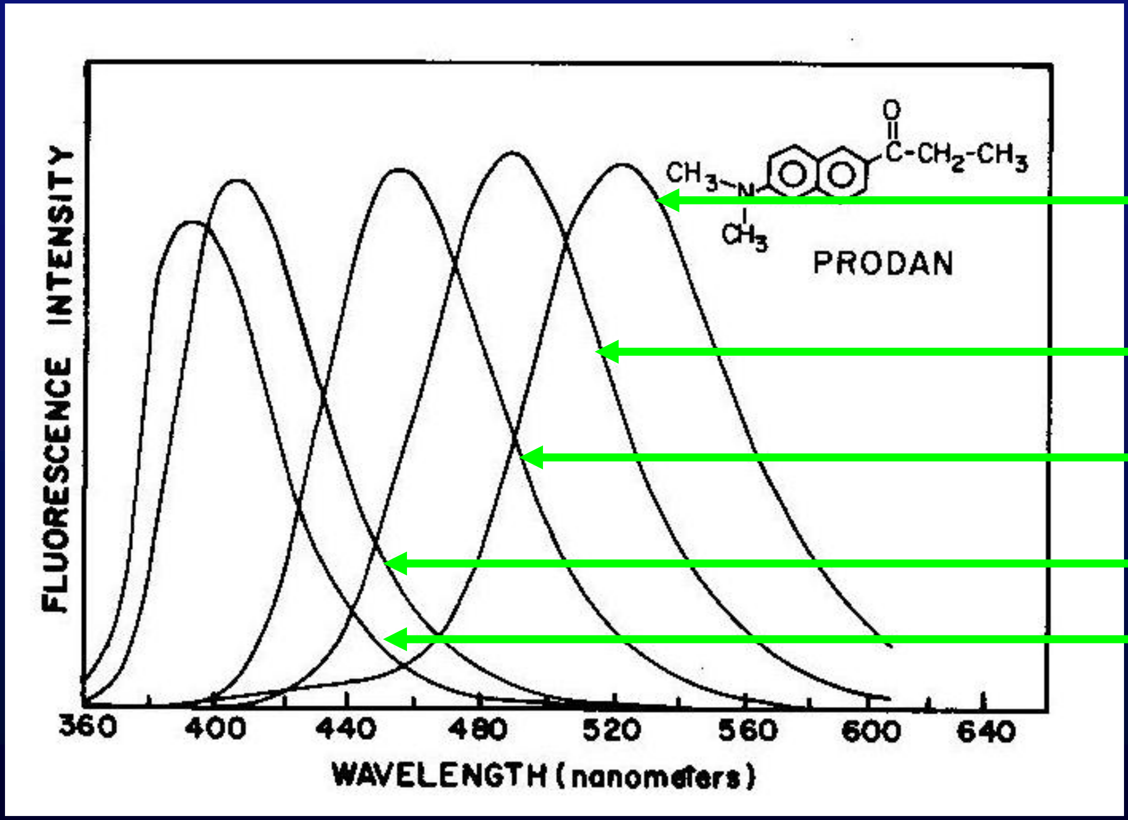
KAMLET-TAFT SOLVATOCHROMIC PARAMETERS

	acidity or proticity or H-bond donating ability	basicity or H-bond accepting ability	polarity & polarizability
Solvent	α	β	π*
cyclohexane	0	0	0
benzene	0	0.1	0.59
MeCN	0.19	0.31	0.75
NEt_3	0.14	0.71	0
water	1.17	0.47	1.09



●Shifting emission wavelengths

6-propionyl-2-(dimethylamino)naphthalene



solvent

Water

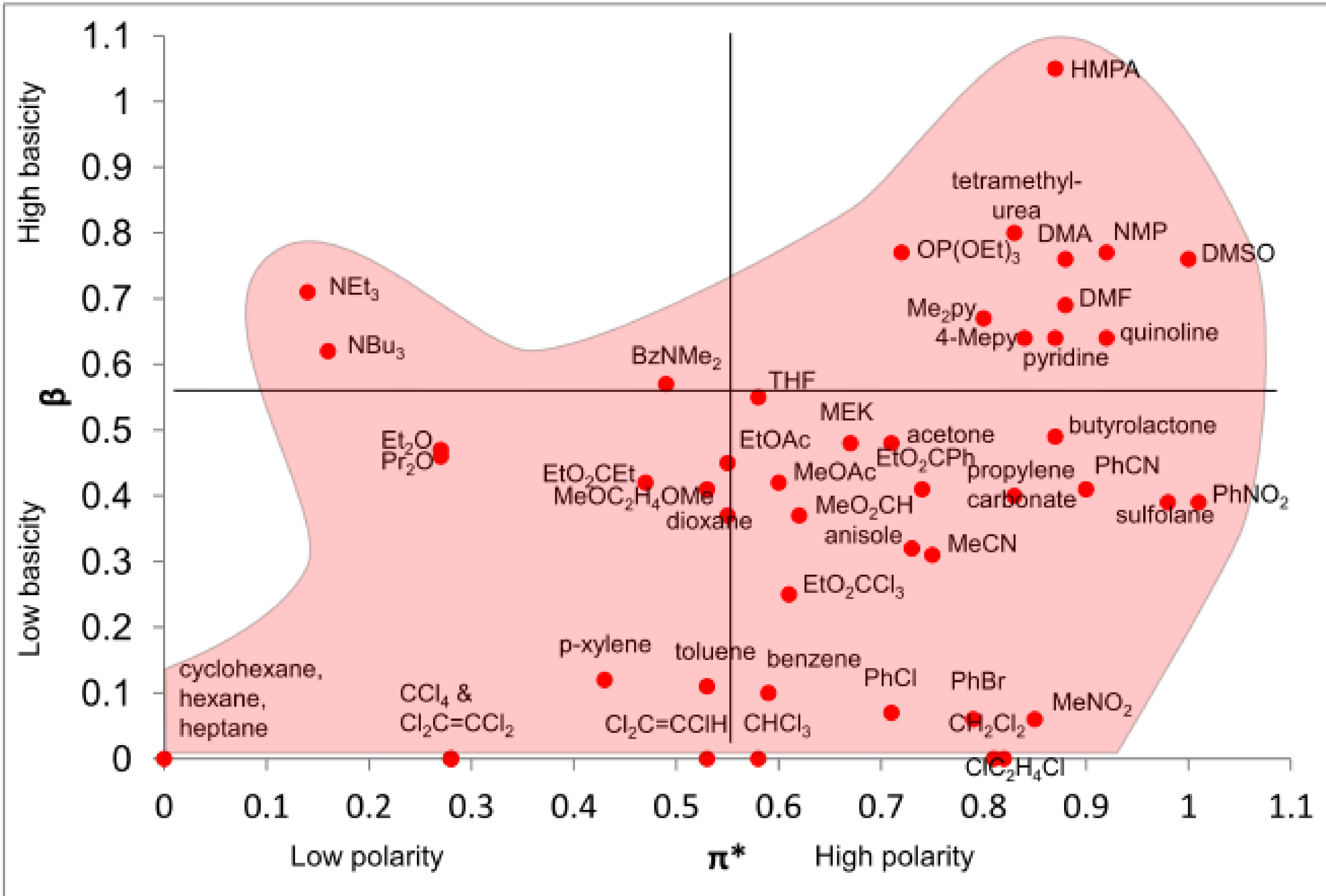
Ethanol

Dimethylformamide

Chlorobenzene

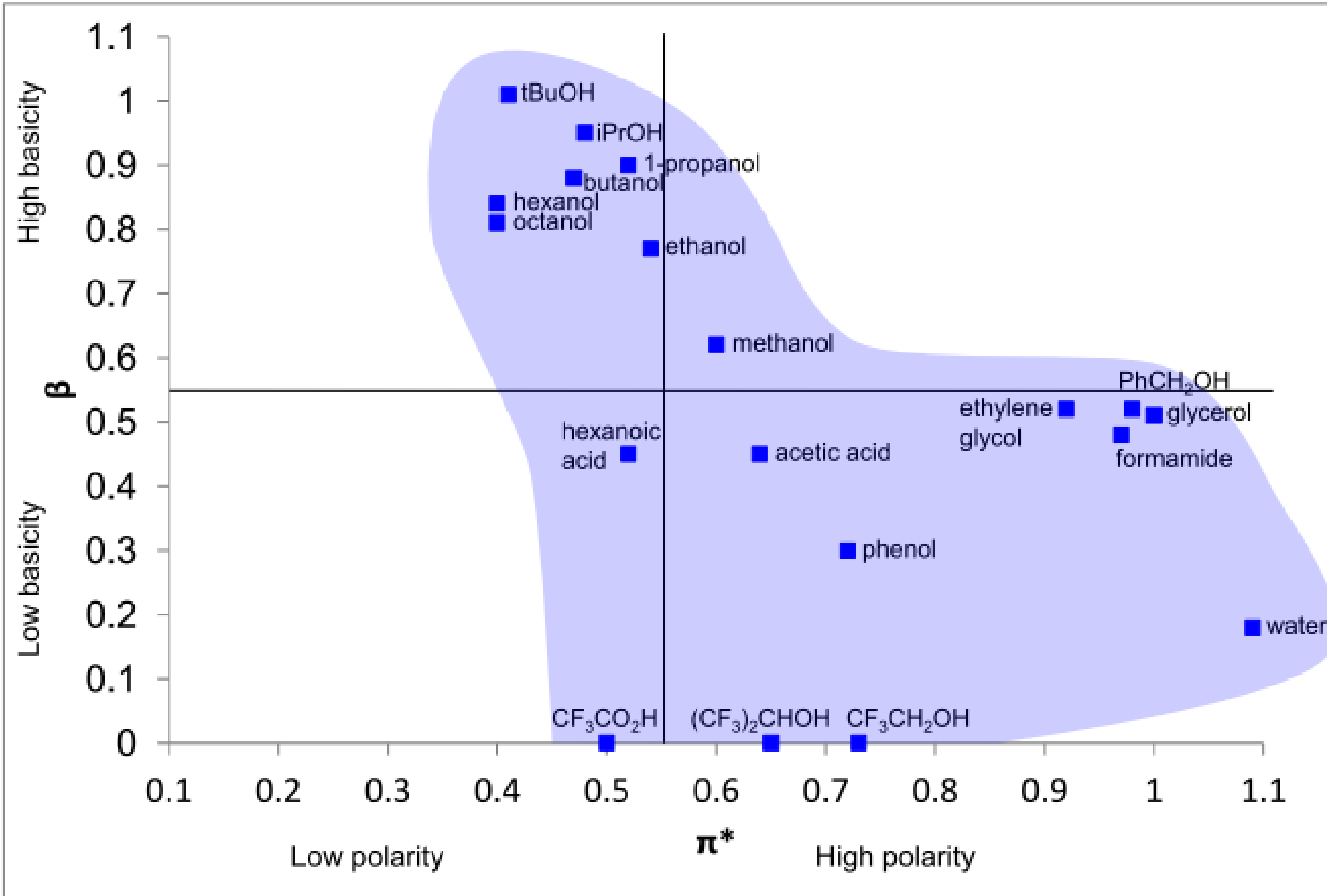
cyclohexane

SURVEY OF SOLVENTS (APROTIC)



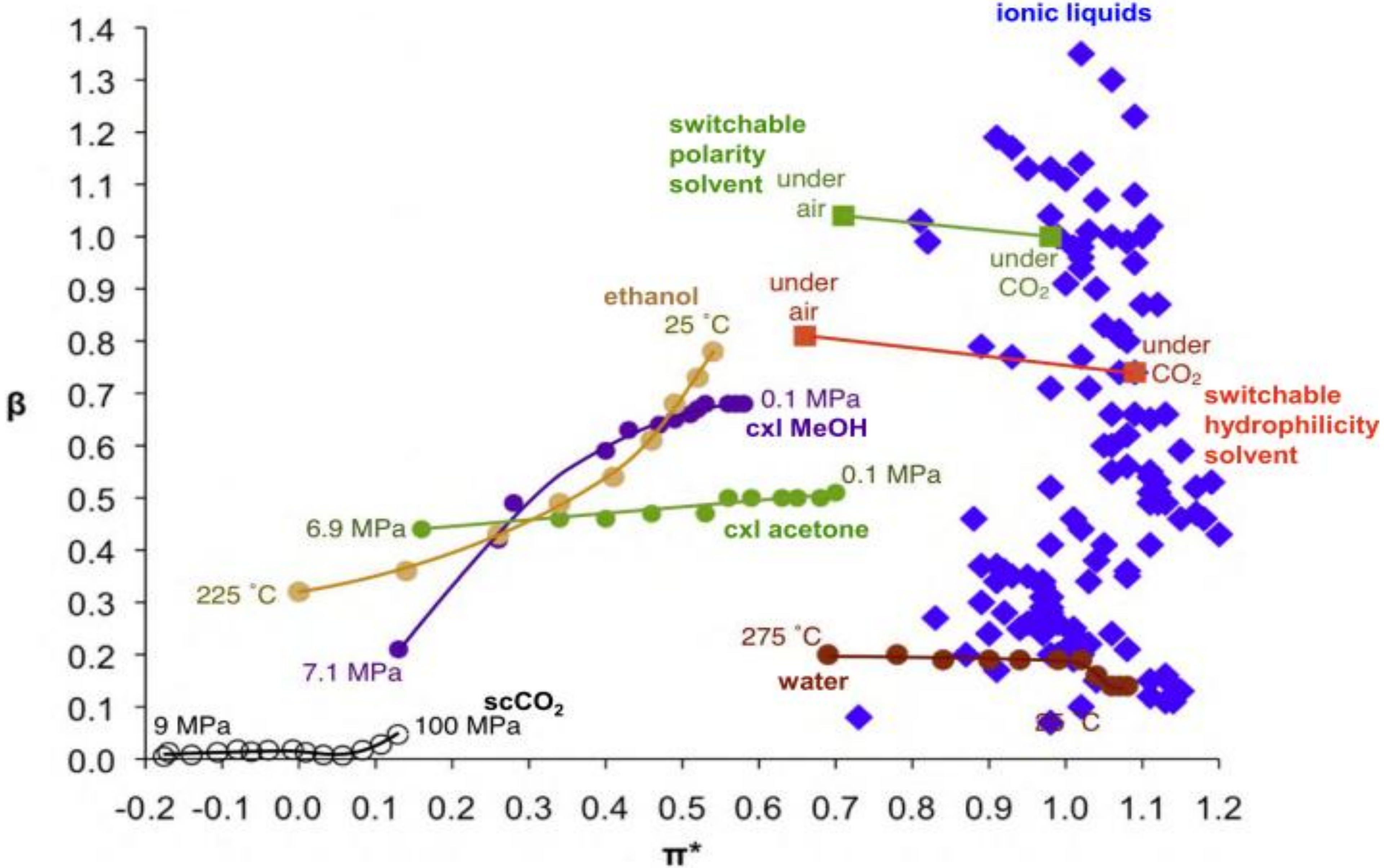
Jessop, *Green Chem* (2012) *14*, 1245

SURVEY OF SOLVENTS (PROTIC)



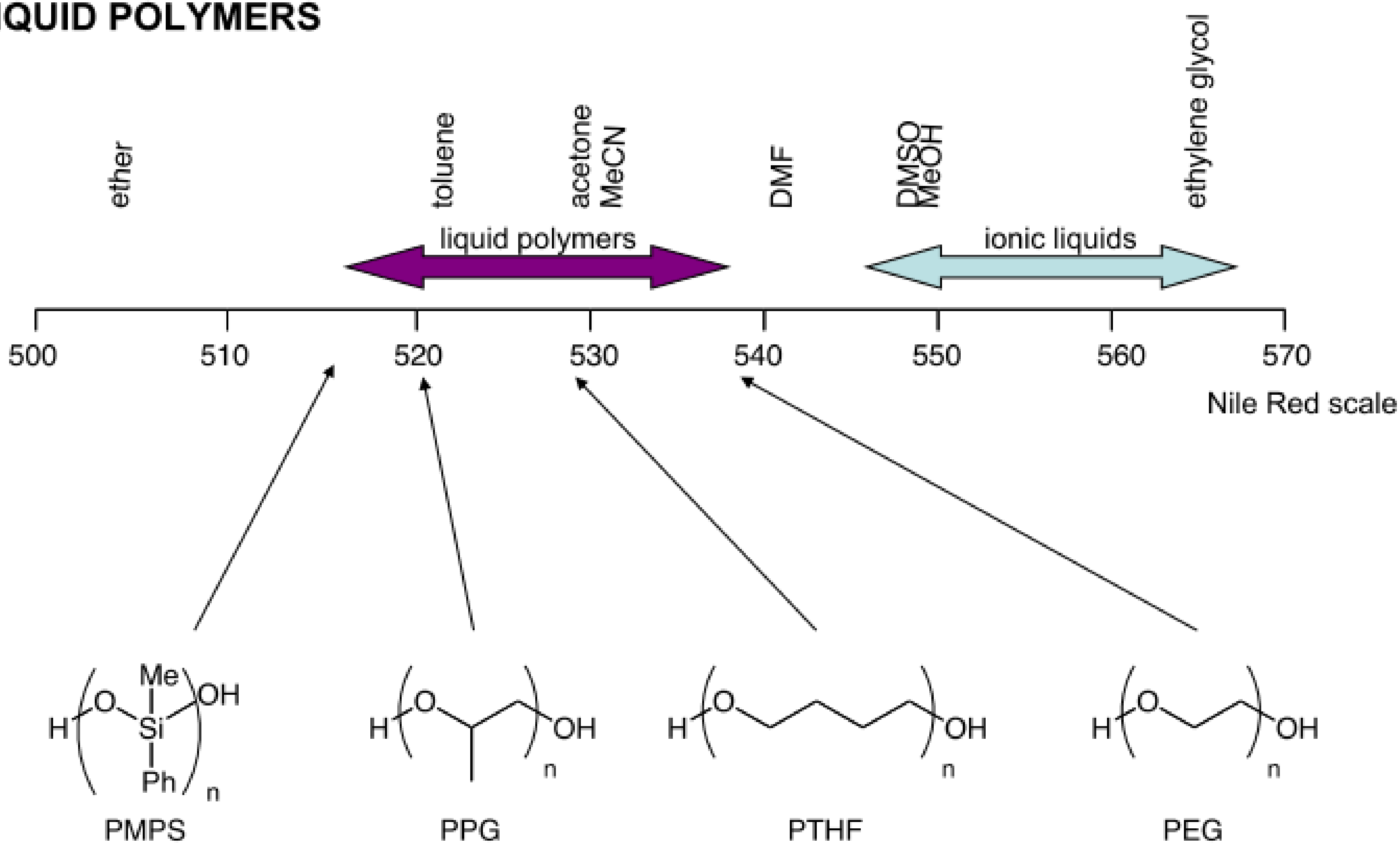
Jessop, *Green Chem* (2012) *14*, 1245

OVERVIEW OF UNCONVENTIONAL GREEN SOLVENTS



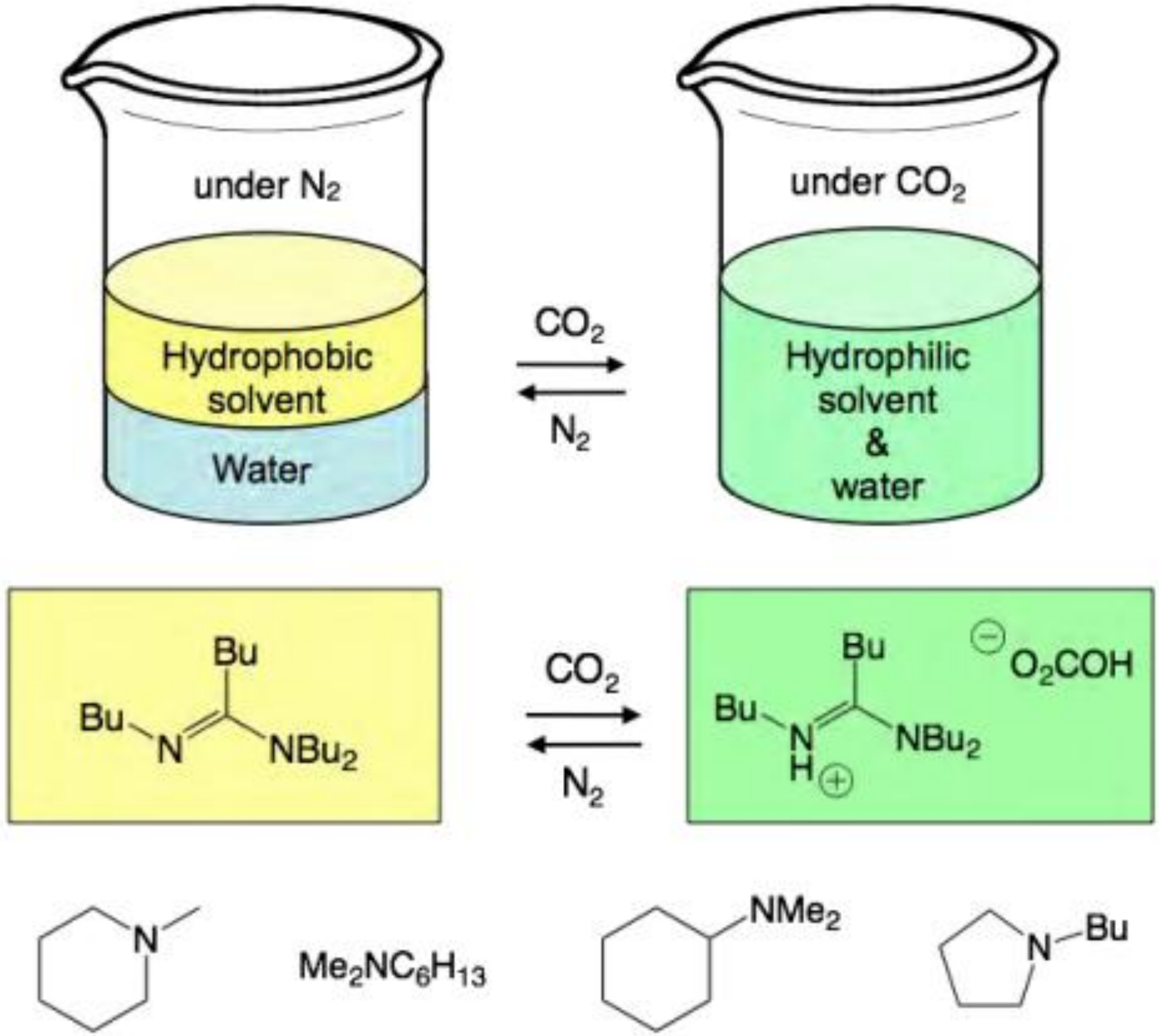
Dr. Tamer Andrea: Greener solvents

LIQUID POLYMERS



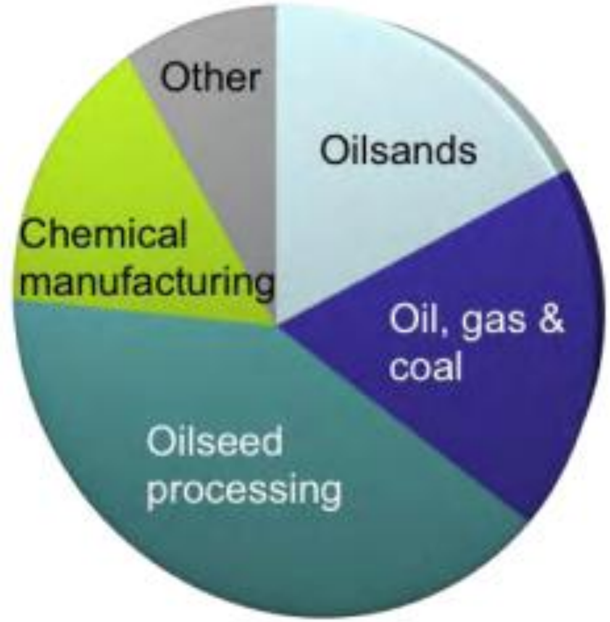
Heldebrant, Jessop et al. *Green Chem* (2006)

SWITCHABLE-HYDROPHILICITY SOLVENTS

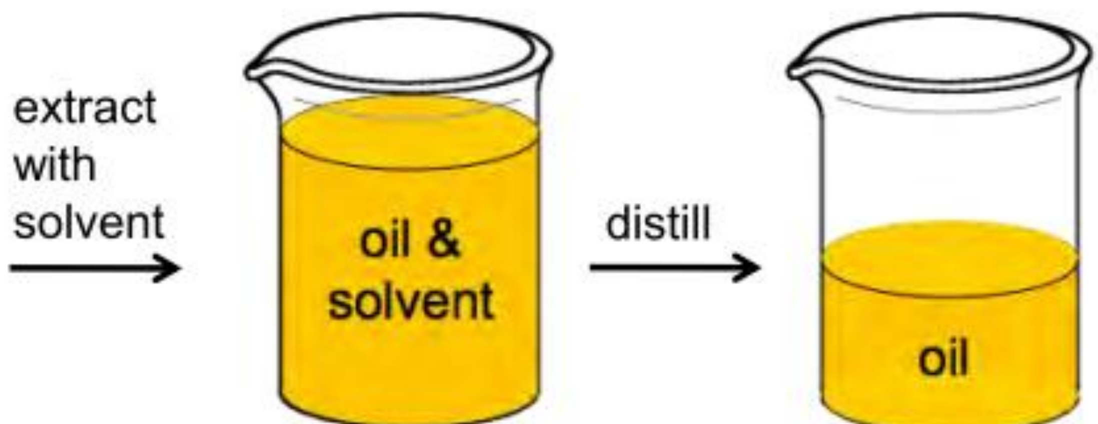


Green Chem (2010) *12*, 809
Green Chem (2011) *13*, 619

A REAL WORLD PROBLEM

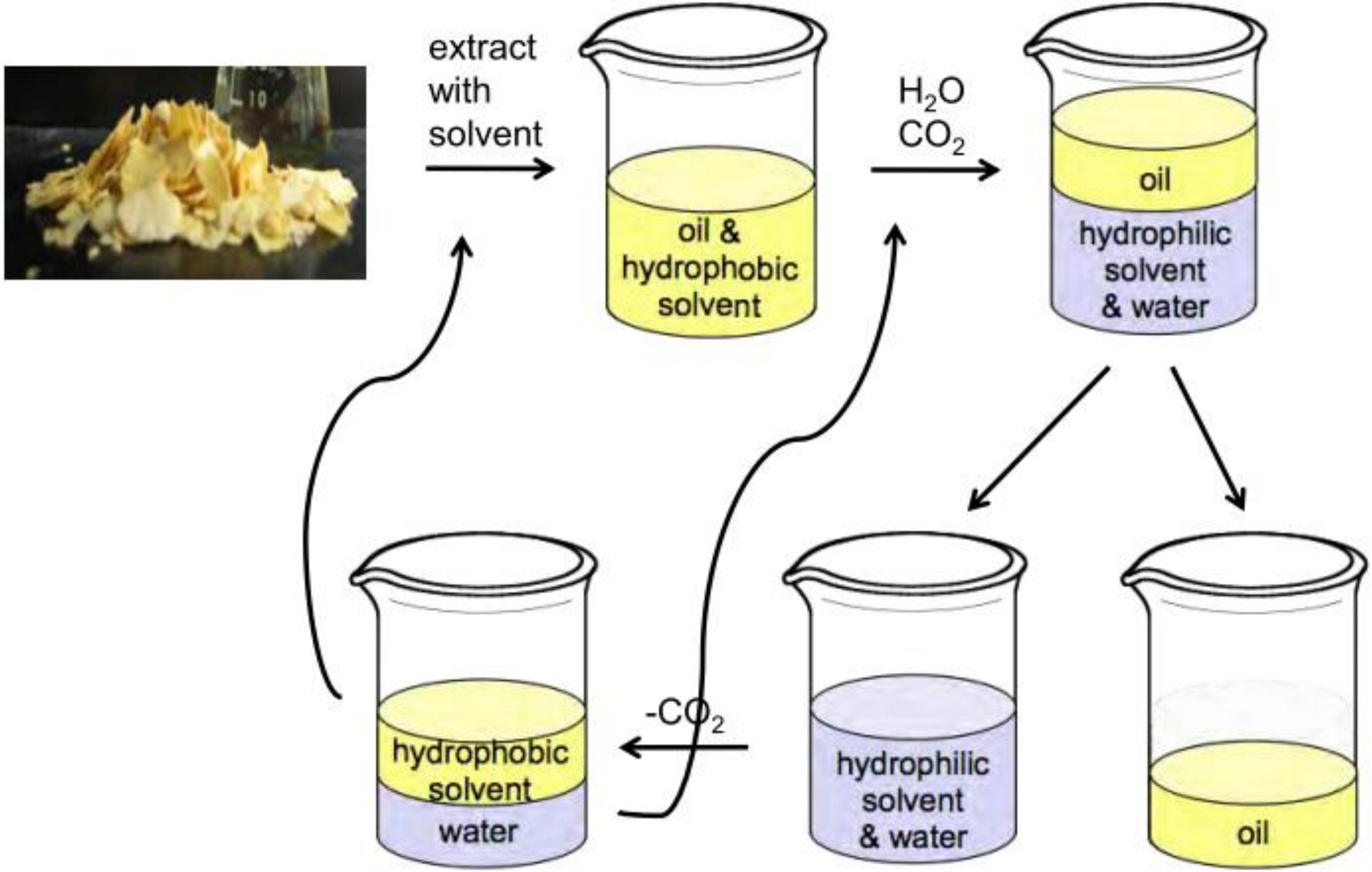


hexane emissions to air in Canada (NPRI, 2007)



Green Chem (2010) *12*, 809

SOY EXTRACTION WITHOUT DISTILLATION



Green Chem (2010) *12*, 809
Green Chem (2011) *13*, 619

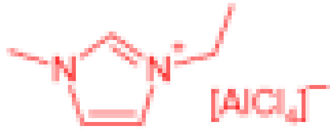
What is a Room Temperature Ionic Liquid (RTIL)? (室溫離子液體)

- Liquid salt consisting at least one organic component (cation or anion) with melting point below room temperature
- Properties:
  - –Negligible vapor pressure
  - –High thermal stability (~250-400°C)
  - –High viscosity
  - –Hydrophobic or hydrophilic
  - –Dissolve many organic, organometallic, and inorganic compounds

Ionic Liquids-Evolution

- 1980s: Chloroaluminate Ionic Liquids

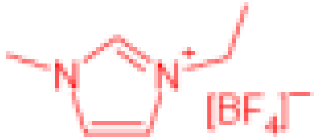
  1st generation



J.S. Wilkes, J.A. Levisky, R.A. Wilson and C.L. Hussey, *Inorg. Chem. 21* (**1982**) 1263-1264.

- 1990s: Air- and moisture-stable Ionic Liquids

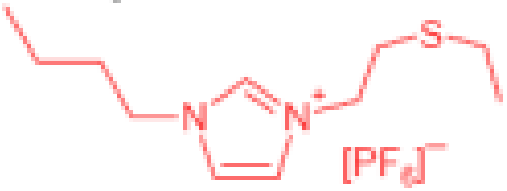
  2nd generation



J.S. Wilkes and M.J. Zaworotko, *J. Chem. Soc. Chem. Commun* (**1992**) 965-966.

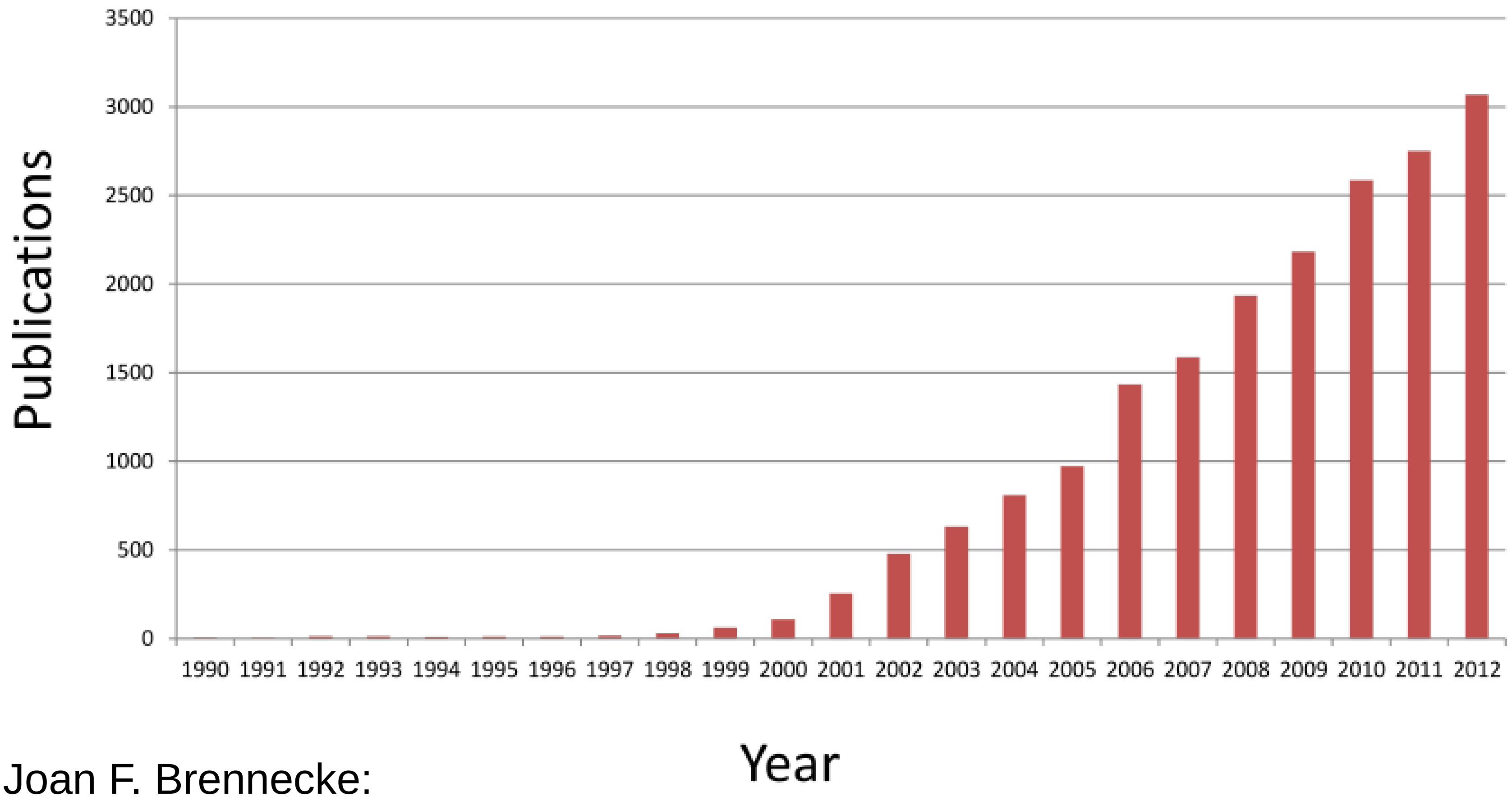
- 2000s: First examples of „Task Specific Ionic Liquids"

  3rd generation



A.E. Visser, R.P. Swatloski, W.M. Reichert, R. Mayton, S. Sheff, A. Wierzbicki, J.H. Davis, Jr. and R.D. Rogers, *Chem. Commun.* (**2001**) 135-136.

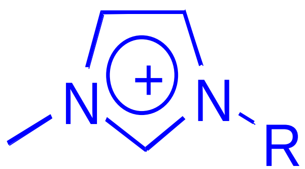
Growth in Publications



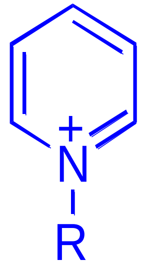
Joan F. Brennecke:
Energy Applications of Ionic Liquids

Structures of ILs

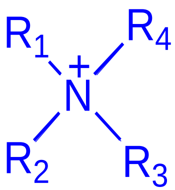
Most Commonly Used Cations



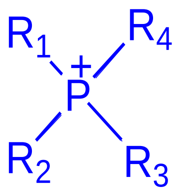
1-alkyl-3-methyl-imidazolium



N-alkyl-pyridinium



Tetraalkyl-ammonium



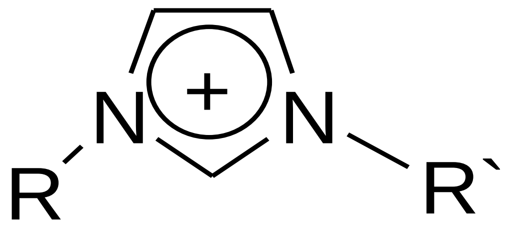
Tetraalkyl-phosphonium

Possible Anions

$[PF_6]^-$	$[CH_3CO_2]^-$
$[(CF_3SO_2)_2N]^-$ (NTf_2^-)	Cl^-, Br^-, I^-
$[CF_3SO_3]^-$(TfO^-)	$[BF_4]^-$, $FeCl_4^-$

Structures of Imidazolium ILs

- Cations



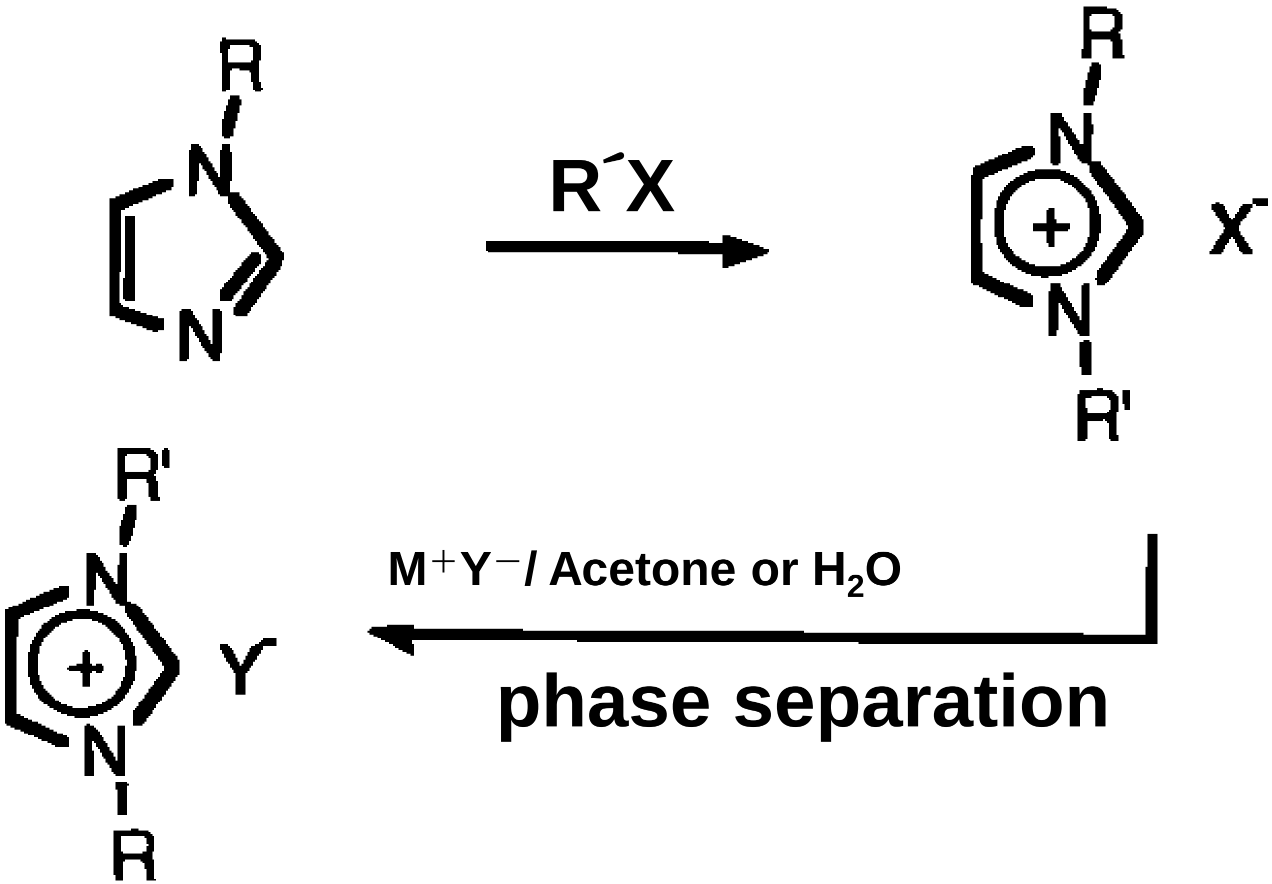
R: methyl;
R': n-butyl, n-octyl

1-butyl-3-methylimidazolium, BMIM, C_4MIM
1-octyl-3-methylimidazolium, OMIM, C_8MIM

- Anions
  - PF_6^-
  - $N(CF_3SO_2)_2^-$ (NTf_2)

-BF_4^-
-$CF_3SO_3^-$
-Cl^-

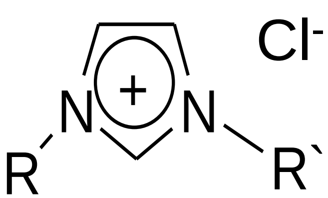
1-butyl-3-methylimidazolium hexafluorophosphate
[BMIM][PF_6]



R=CH_3 , R´=C_2H_5, C_4H_9 , C_6H_{13} , C_8H_{17} ;
X=Cl, Br ; M^+Y^- = $K^+PF_6^-$

Melting points of various chlorides

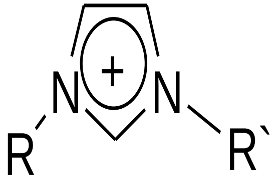
Salts	M.P. (^oC)
NaCl	802
KCl	772
$NaClO_4$	482(d)



R=R'=methyl	125
R= methyl, R'=ethyl	87
R= methyl, R'=butyl	65

Influence of different anions on the M.P. of imidazolium salts

Imidazolium Salts	M.P. (^oC)
[Emim]Cl	87
[Emim]NO_2	55
[Emim]NO_3	38
[Emim]$AlCl_4$	7
[Emim]BF_4	6
[Emim]CF_3SO_3	-9
[Emim]CF_3CO_2	-14



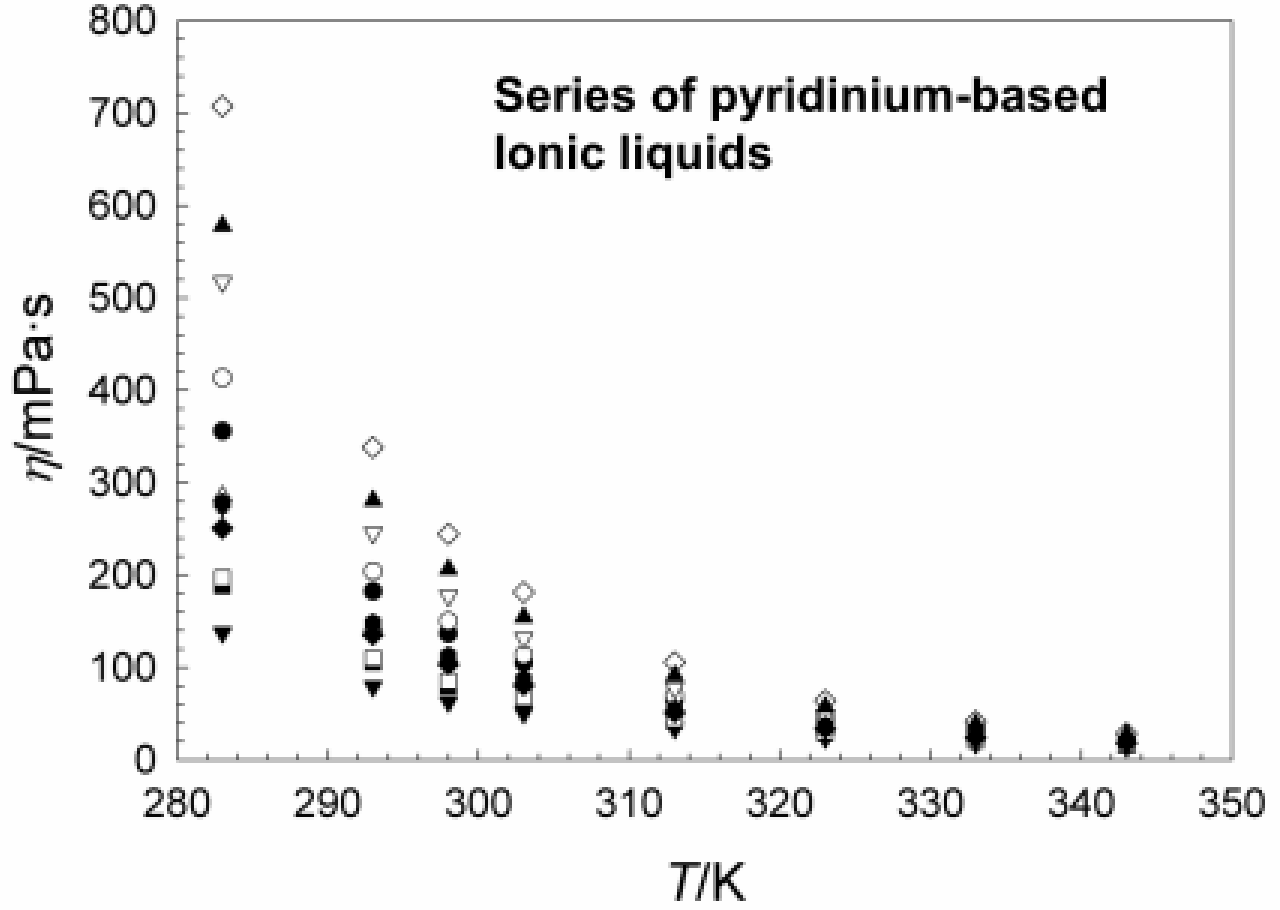
R =methyl, R'=ethyl

Viscosities

Ionic Liquid	Viscosity / mPa s
Diethyl ether	0.22
Water	1.00
Ethylene glycol	16
1-ethyl-3-methylimidazolium dicyanamide	21
1-ethyl-3-methylimidazolium tetracyanoborate	22
1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide	27
1-ethyl-3-methylimidazolium thiocyanate	38
1-ethyl-3-methylimidazolium tetrafluoroborate	38
1,2-propylene glycol	40
1-ethyl-3-methylimidazolium trifluoromethylsulfonate	43
1-ethyl-3-methylimidazolium tris(pentafluoroethyl)trifluorophosphate	44
1-ethyl-3-methylimidazolium methylsulfate	93
1-butyl-3-methylimidazolium tetrafluoroborate	154
1-hexyl-3-methylimidazolium tetrafluoroborate	224
4-methyl-*N*-butylpyridinium tetrafluoroborate	291
1-butyl-3-methylimidazolium hexafluorophosphate	371
1-octyl-3-methylimidazolium tetrafluoroborate	468
1-butyl-2,3-dimethylimidazolium tetrafluoroborate	932
Glycerol	934

W. Pitner – Merck KGaA

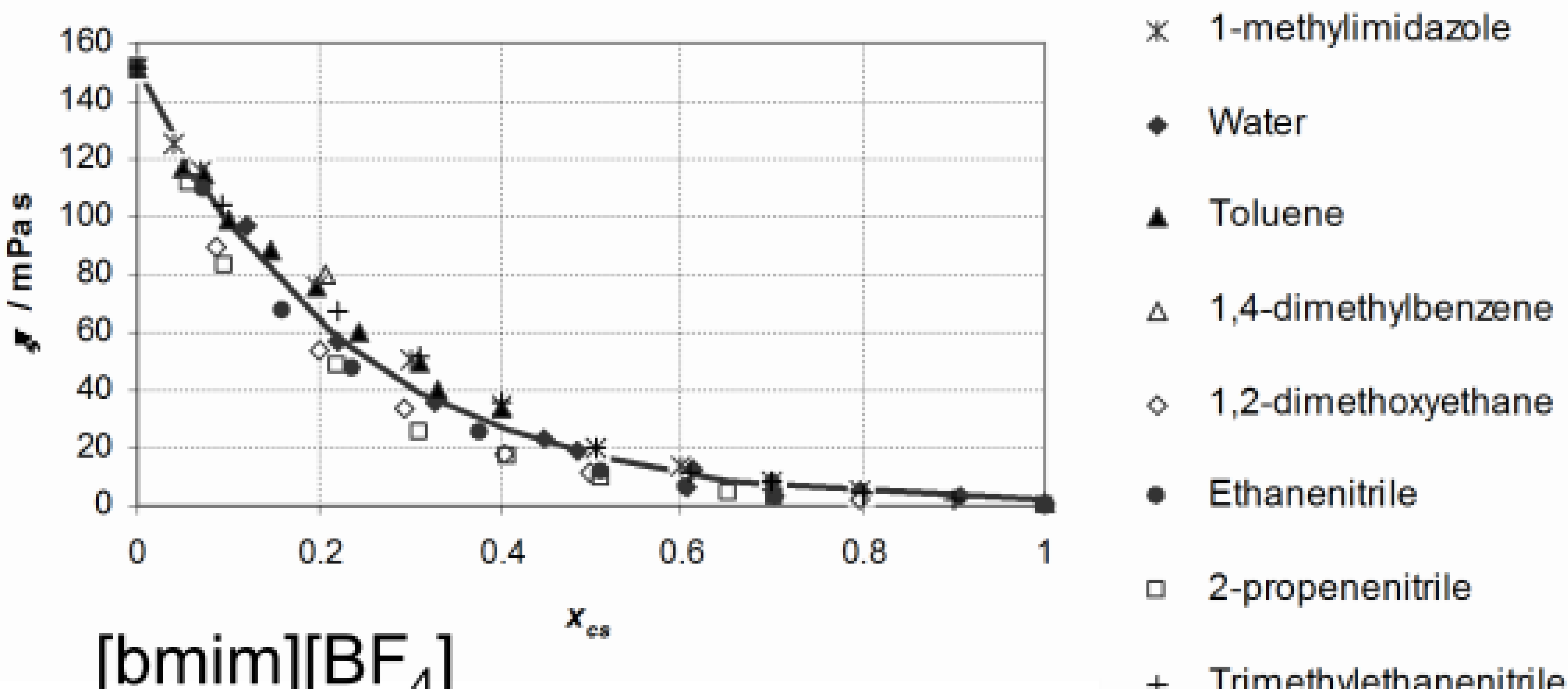
Viscosities



Joan F. Brennecke:
Energy Applications of Ionic Liquids

Properties Sensitive to Impurities!

- Presence of water, organics, etc. reduces viscosity, density, etc.

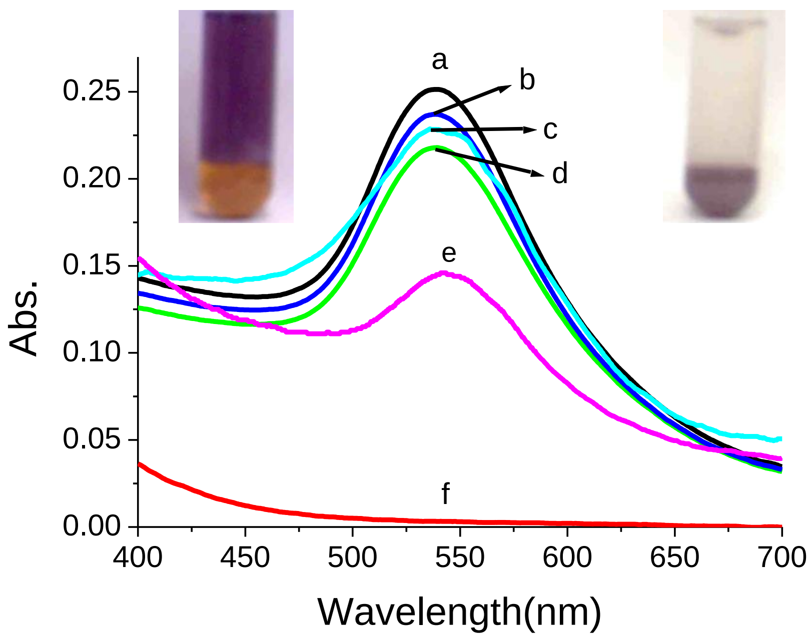


[bmim][BF_4]

Seddon et al., Pure Appl. Chem, 2000

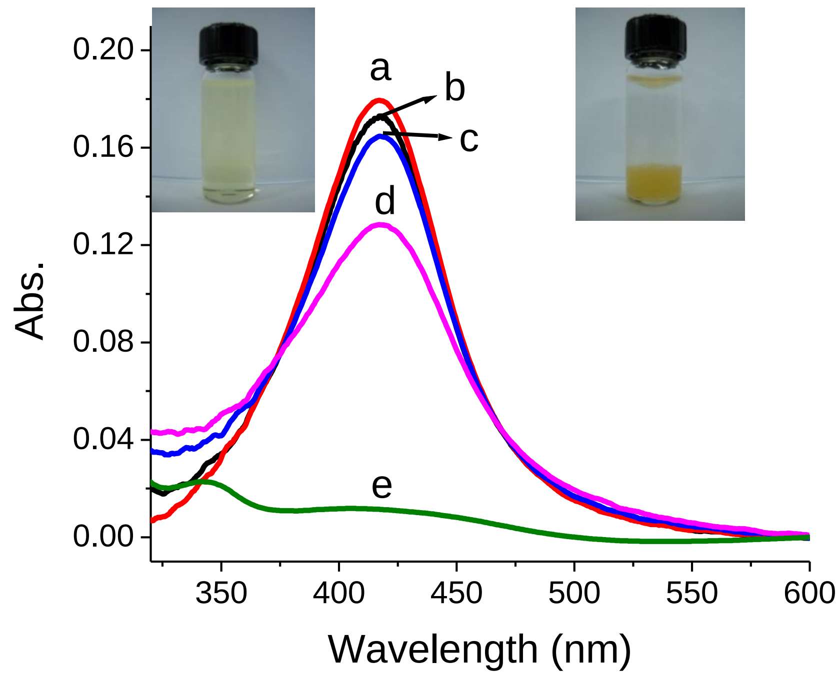
Phase transfer of metal nanopartilces with organic solvents

Au nanoparticles



(a) Au nanoparticle hydrosol, extracted with (b) benzene, (c) hexane, (d) chloroform, (e) 10-undecene-1-ol, (f) [BMIM][PF_6]

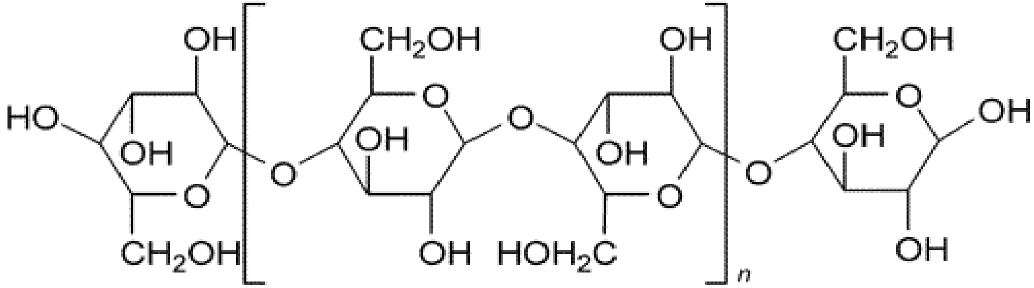
Ag nanoparticles



(a) Ag nanoparticle hydrosol, extracted with (b) benzene, (c) dichloromethane, (d) hexanol, (e) [BMIM][PF_6]

Wei et al., JACS 2004, 126, 5036.

Dissolution of Cellulose with Ionic Liquids



Solubility of Dissolving Pulp Cellulose in Ionic Liquids

ionic liquid	method	solubility (wt %)
$[C_4mim]Cl$	heat (100°C)	10%
	(70°C)	3%
$[C_4mim]Cl$	heat (80°C) + sonication	5%
$[C_4mim]Cl$	microwave heating	25%, clear
	3-5-s pulses	viscous solution
$[C_4mim]Br$	microwave	5-7%
$[C_4mim]SCN$	microwave	5-7%
$[C_4mim][BF_4]$	microwave	insoluble
$[C_4mim][PF_6]$	microwave	insoluble
$[C_6mim]Cl$	heat (100°C)	5%
$[C_8mim]Cl$	heat (100°C)	slightly soluble

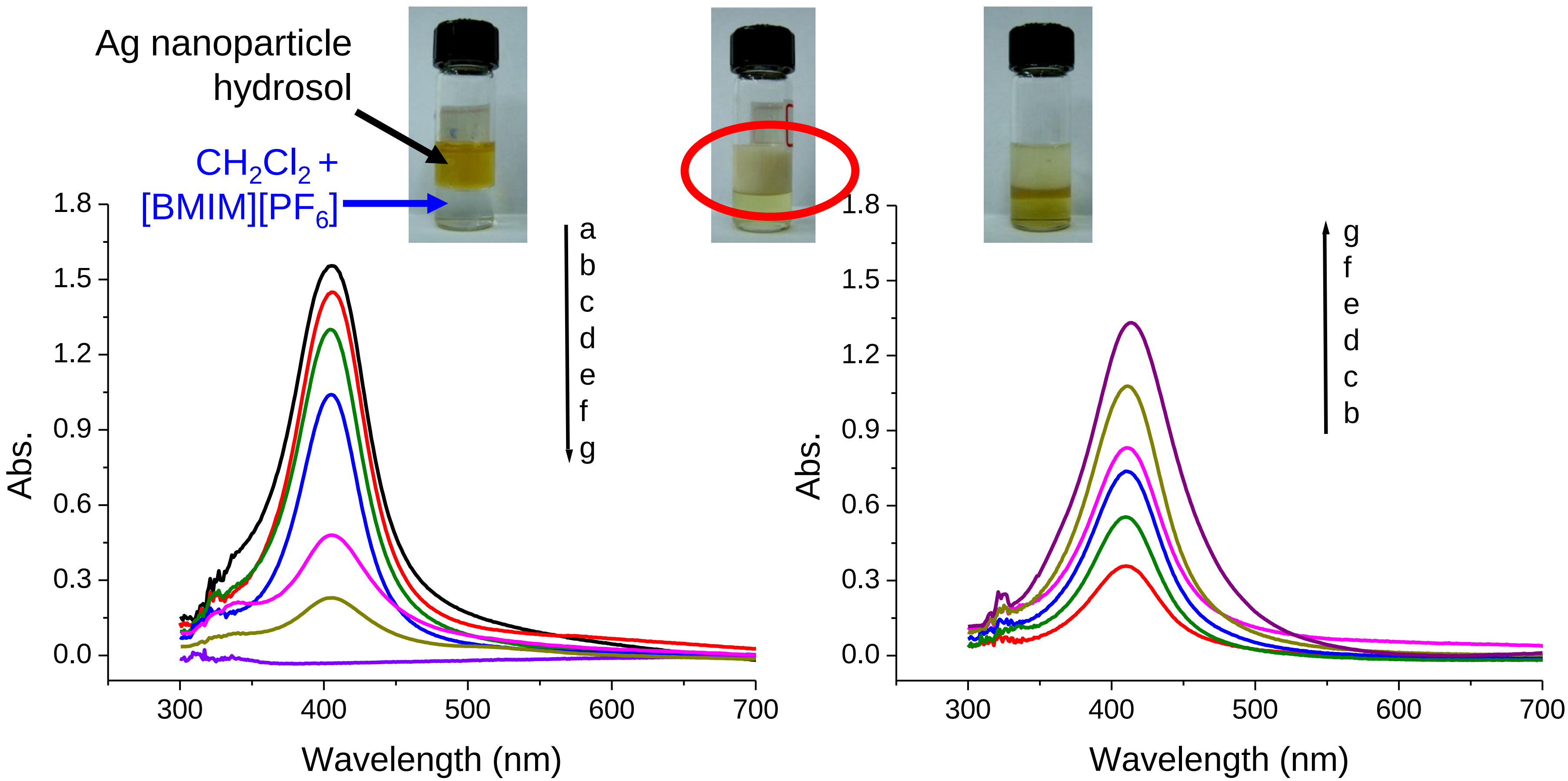
R.P. Swatloski, R.D. Rogers, et al. *J.A.C.S.* 124 (2002) 4974.

Presidential Green Chemistry Challenge Awards

Alternative Synthetic Pathways Award:
Alternative Solvents/Reaction Conditions Award:
Designing Safer Chemicals Award:
Small Business Award:
Academic Award : Robin D. Rogers, University of Alabama
A Platform Strategy Using Ionic Liquids to Dissolve and Process Cellulose for Advanced New Materials

Combining two major principles of green chemistry: developing environmentally preferable solvents and using biorenewable feedstocks to form advanced materials .

Phase transfer of Ag nanopartilcles with CH_2Cl_2 involving [BMIM][PF_6]

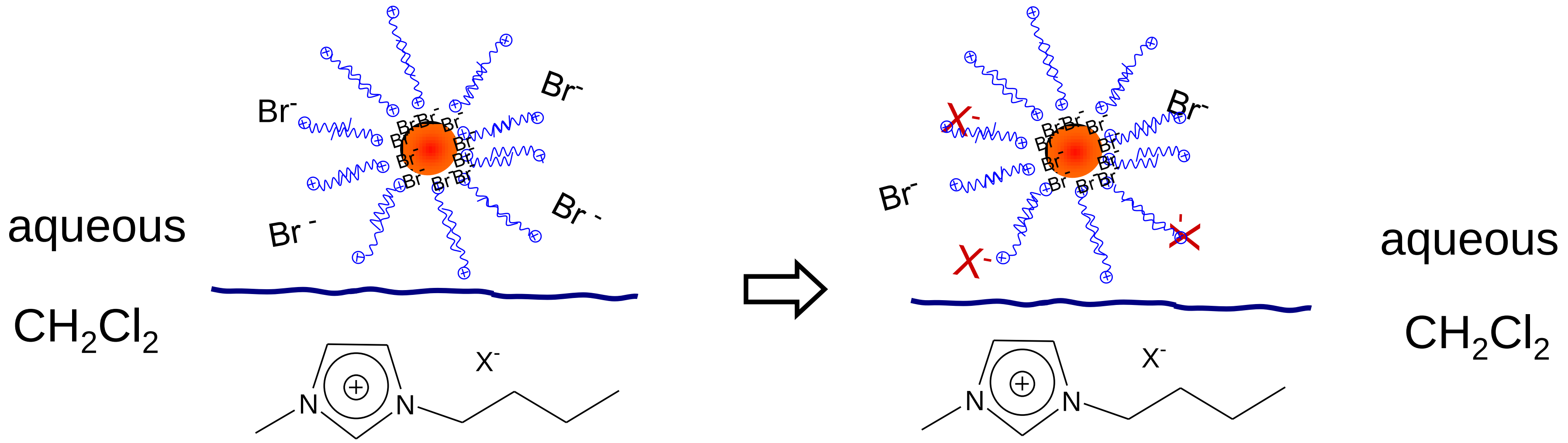


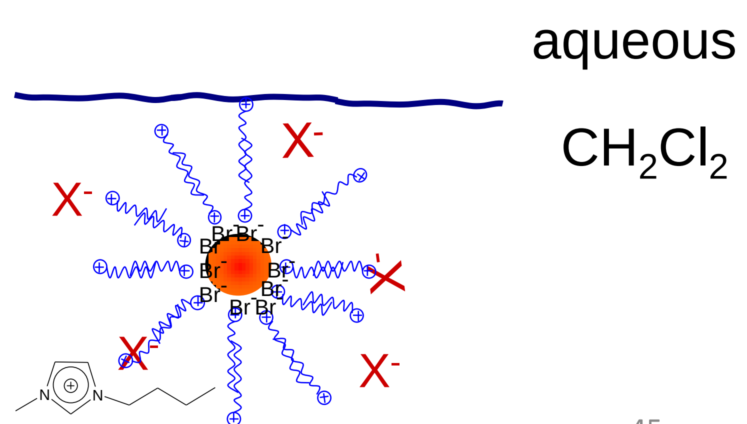
(A) Aqueous phase

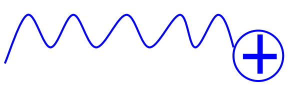
(B) Organic phase

Extracted for: (a) 10, (b) 20, (c) 30, (d) 40, (d) 50, (f) 60 minutes

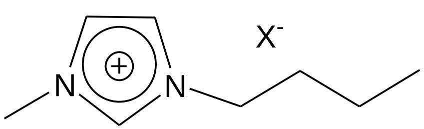
Schematic diagram of phase transferring of nanoparticles with IL







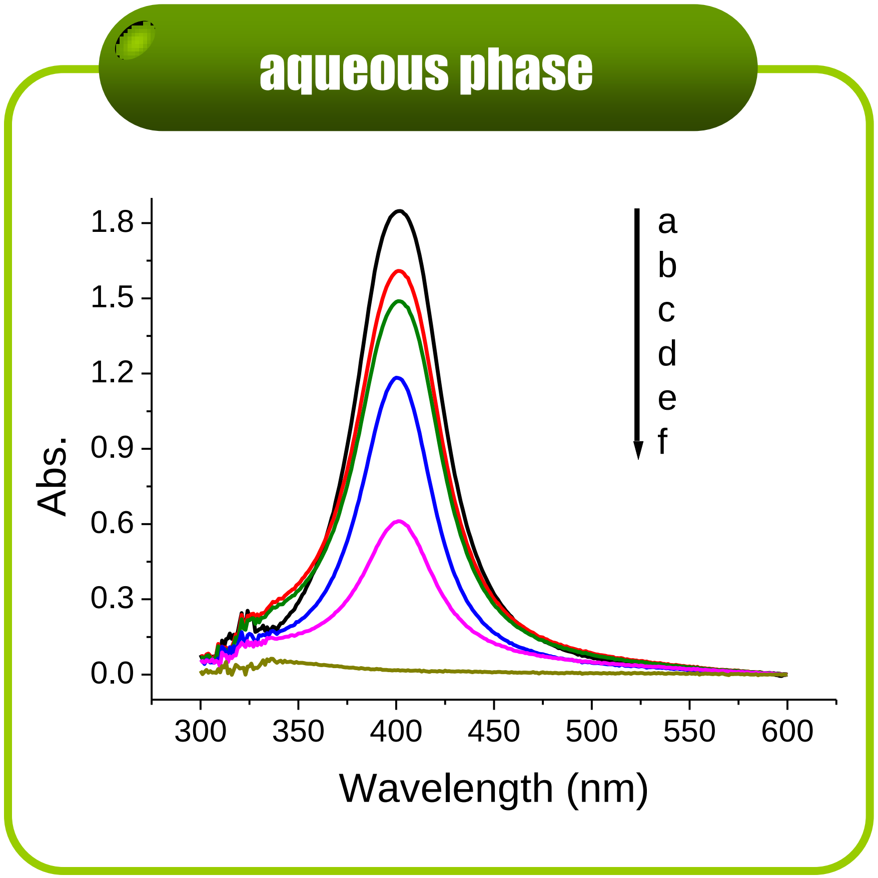
Br - = TTAB (stabilizer)

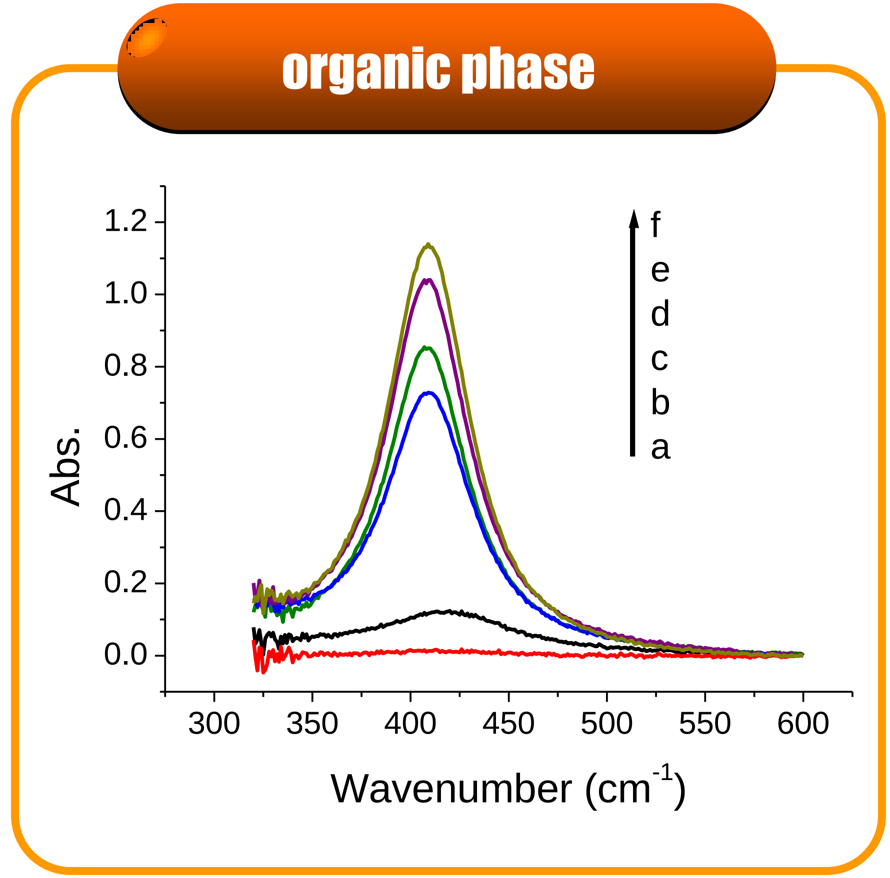


X-: PF_6^-, BF_4^-

= [BMIM][X]
(ionic liquid)

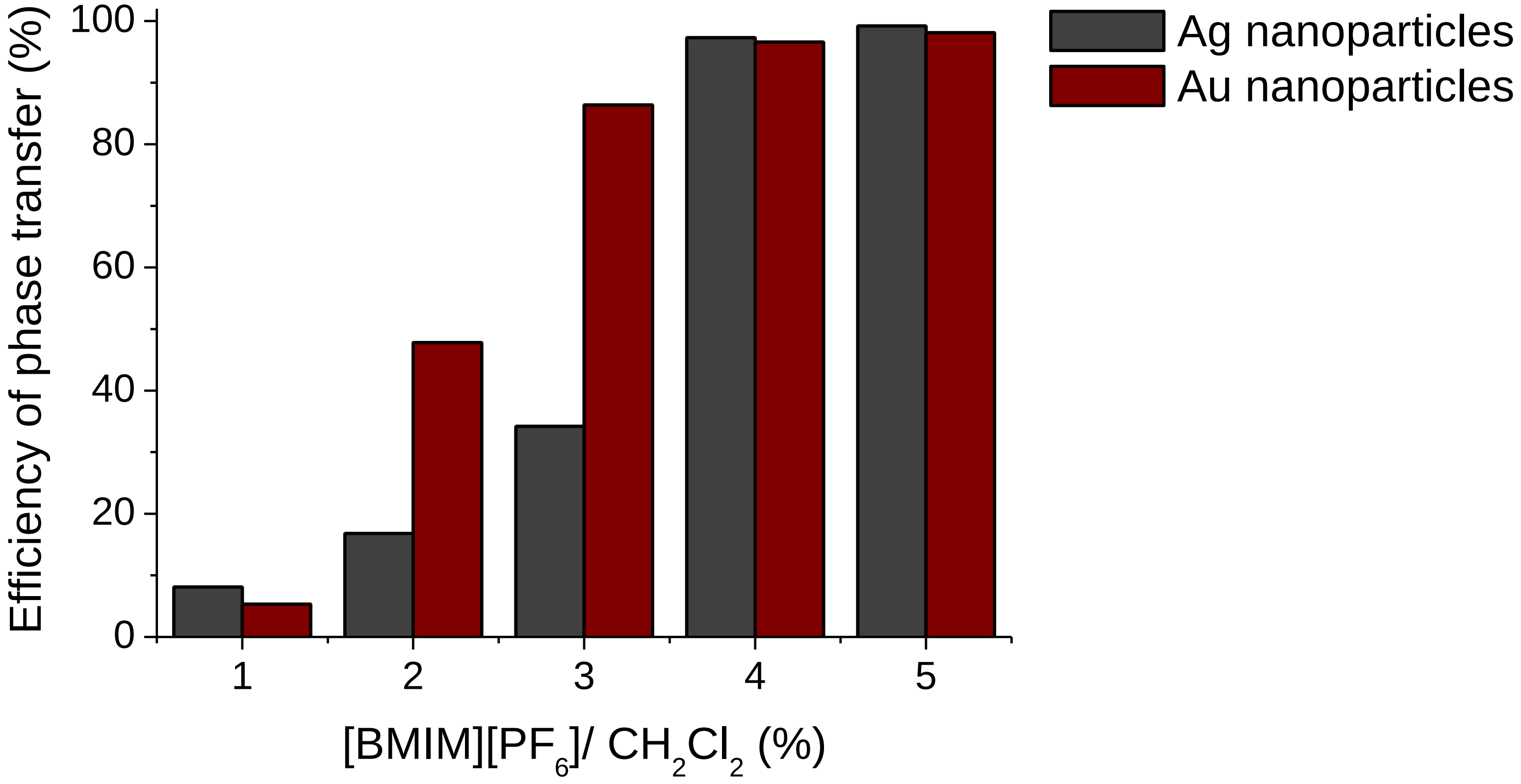
Phase transfer of Ag nanopartilcles with CH_2Cl_2 involving KPF_6





Extracted for: (a) 10, (b) 20, (c) 30, (d) 40, (d) 50, (f) 60 minutes

Effect of $[BMIM][PF_6]$ concentration

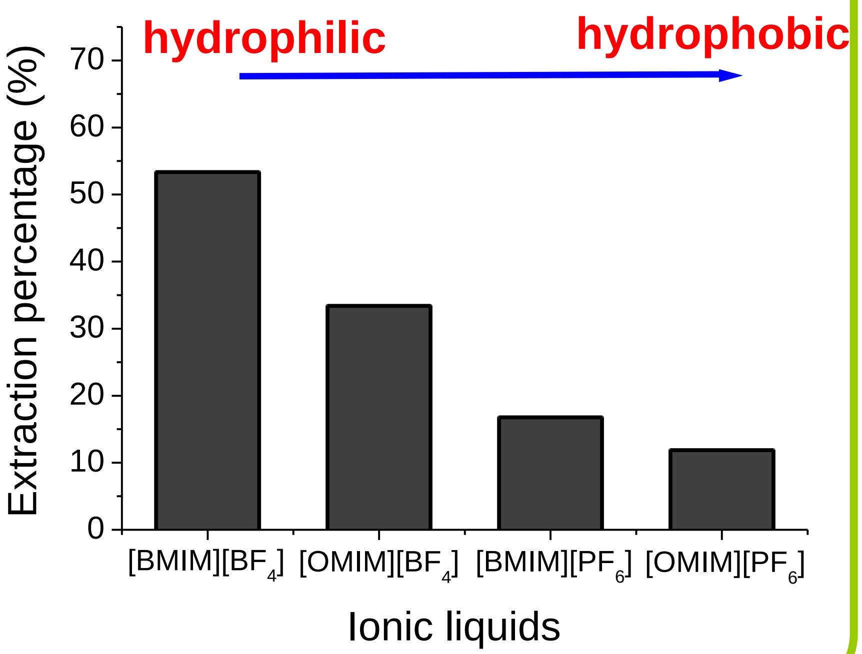


$[TTA]^+ + [PF_6]^- \rightarrow [TTA]^+[PF_6]^-$

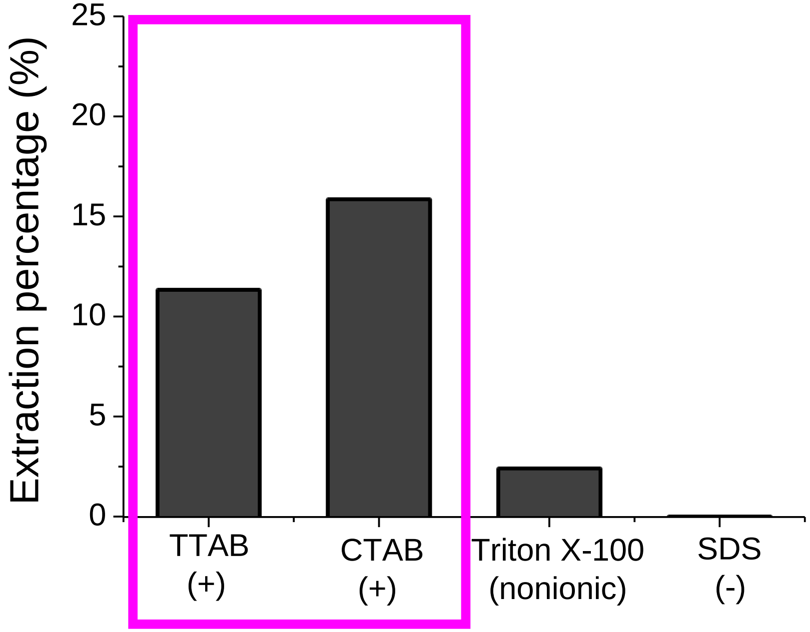
Lee et al., Colloids and Surface A 2010, 364, 24.

Effect of various ionic liquids and stabilizers

effect of ILs

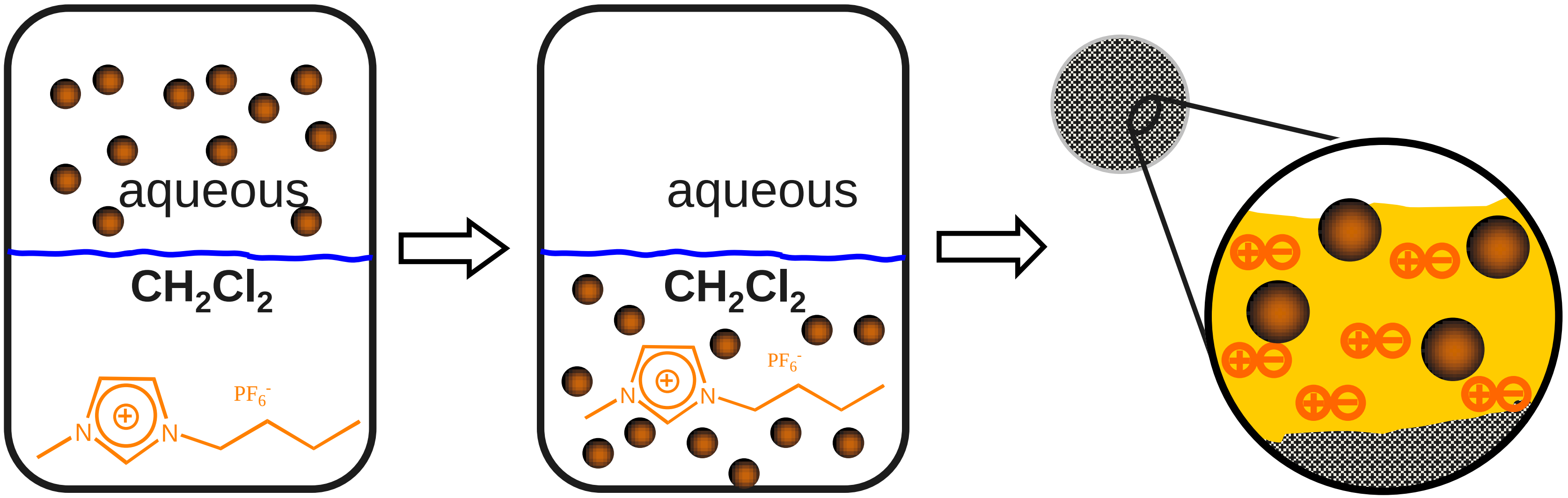


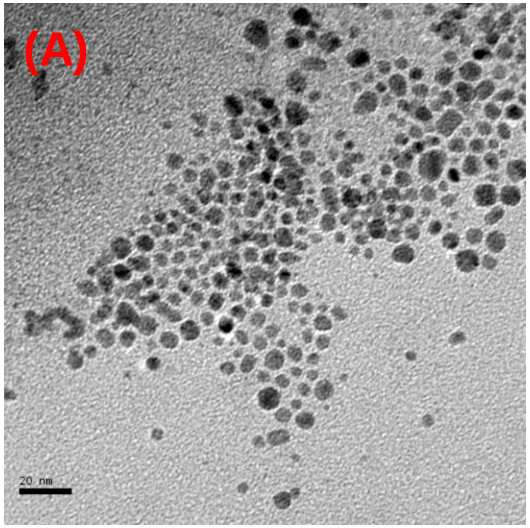
effect of stabilizers

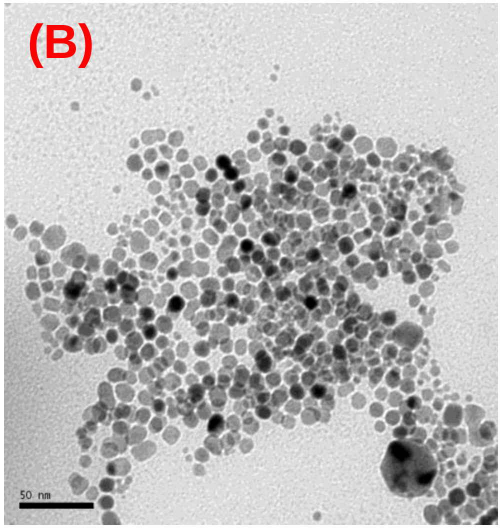


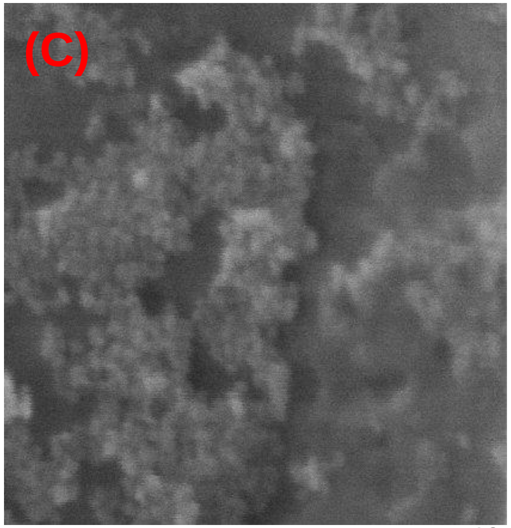
Lee et al., Colloids and Surface A 2010, 364, 24.

Preparation of Metal Nanoparticles/ ILs/ Support Catalyst

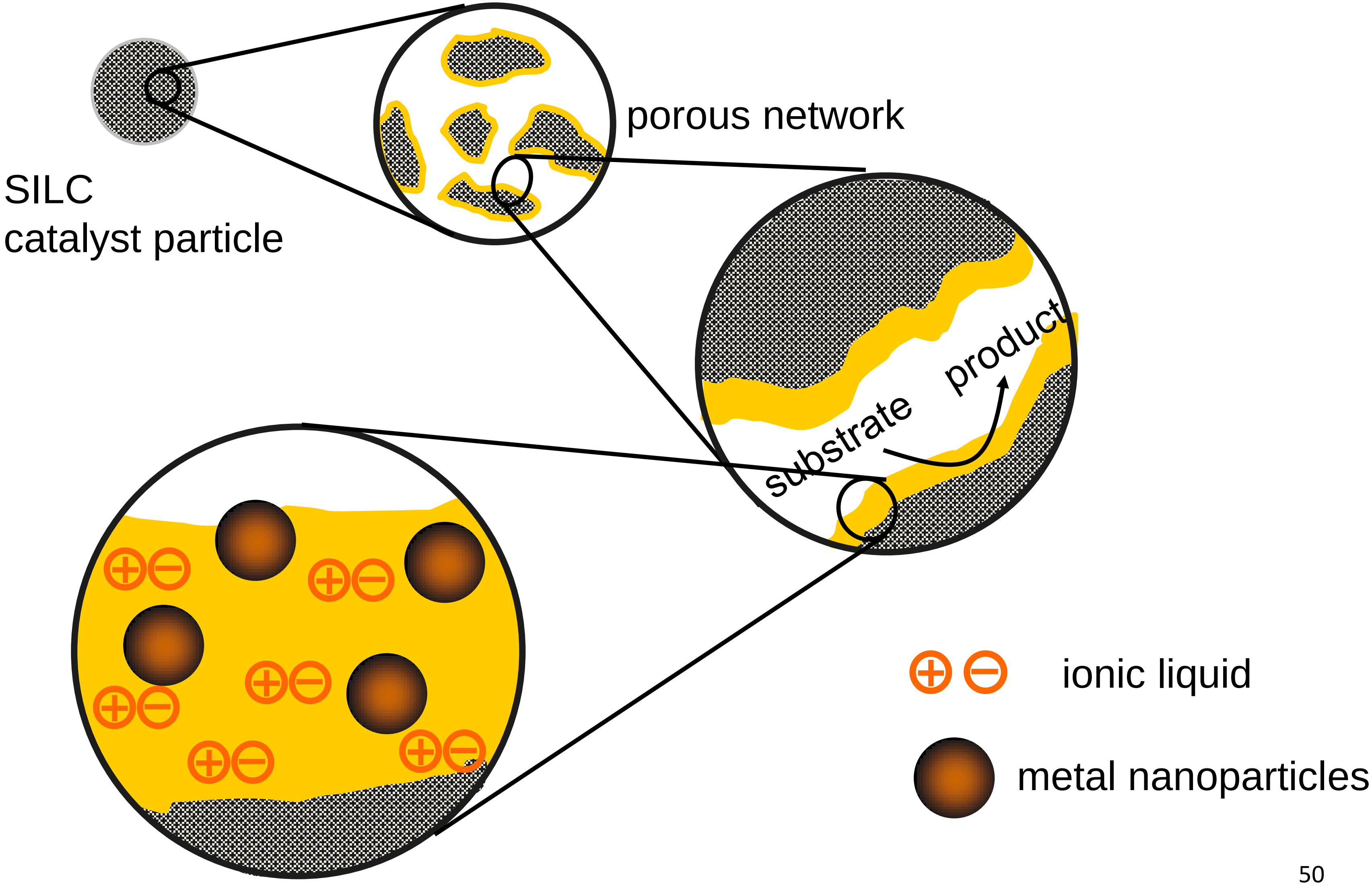




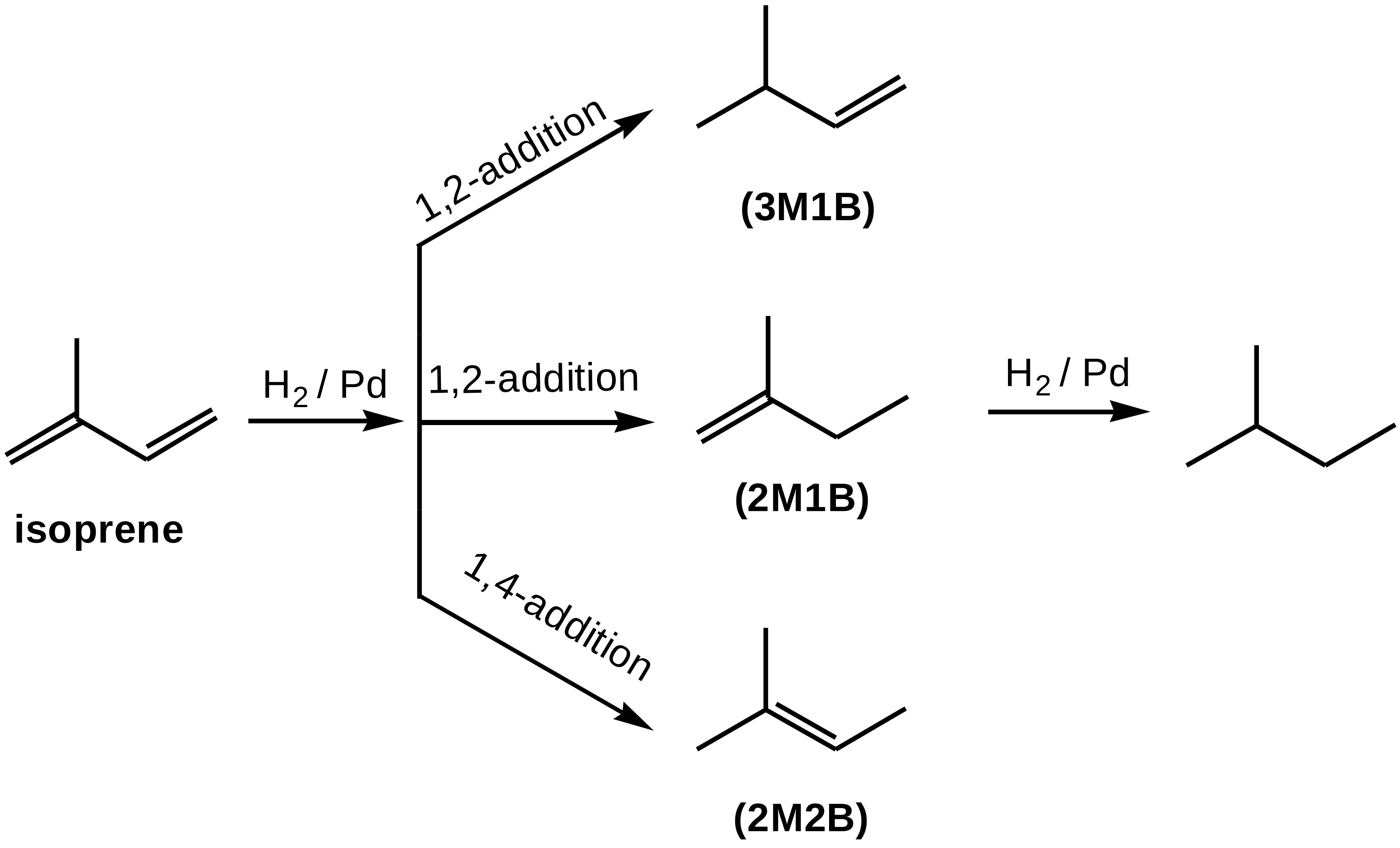




Metal Nanoparticles/ IL/ Support Catalytic System (SILC)



Selective Hydrogenation



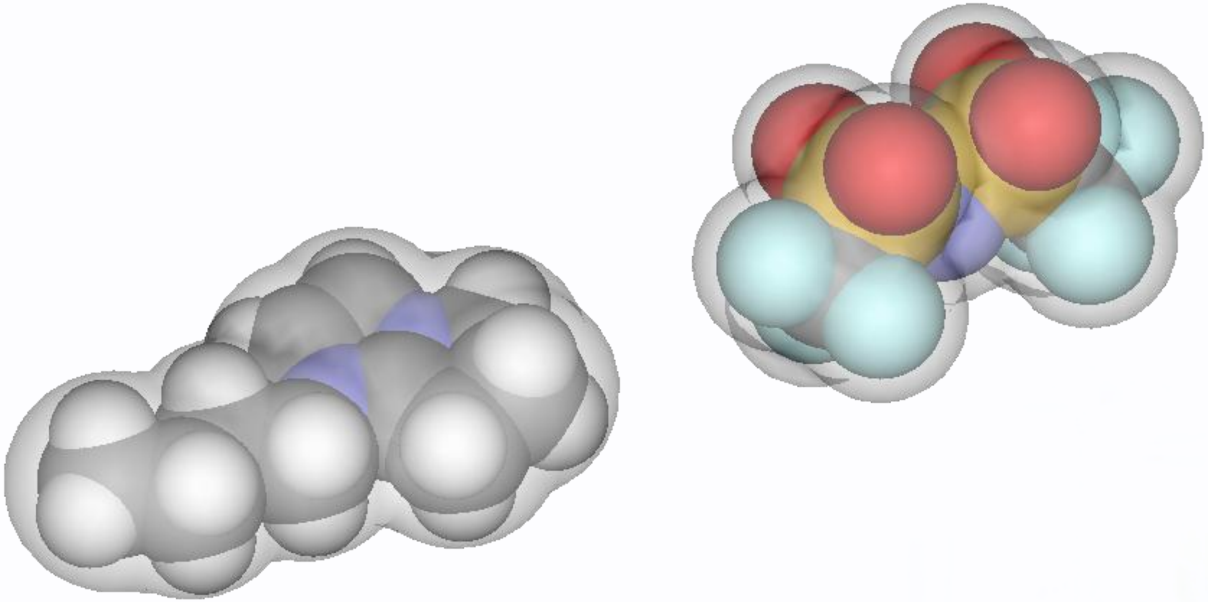
Selective hydrogenation of isoprene

Ionic Liquids for Organic Synthesis

Aldol reactions
Baylis-Hillman reactions
Claisen condensations/rearrangements
Diels-Alder cycloadditions
Friedel-Crafts reactions
Heck reactions
Pictet-Spengler condensations
Ring closing metathesis

and many others . . . .

Ionic Liquids for Green Organic Synthesis



Sowmiah, S.; Cheng, C. I.; Chu, Y.-H. *Curr. Org. Syn.* 2012, *9*, 74-95.
Tseng, M.-C.; Cheng, H.-T.; Shen, M.-J.; Chu, Y.-H. *Org. Lett.* 2011, *13*, 4434-4437.
Chen, C.-W.; Tseng, M.-C.; Hsiao, S.-K.; Chen, W.-H.; Chu, Y.-H. *Org. Biomol. Chem.* 2011, *9*, 4188-4193.
Sowmiah, S.; Srinivasadesikan, V.; Tseng, M.-C.; Chu, Y.-H. *Molecules* 2009, *14*, 3780-3813.
Tseng, M.-C.; Kan, H.-C.; Chu, Y.-H. *Tetrahedron Lett.* 2007, *48*, 9085-9089.
Lin, Y.-L.; Chang, J.-Y.; Chu, Y.-H. *Tetrahedron* 2007, *63*, 10949-10957.
Kan, H.-C.; Tseng, M.-C.; Chu, Y.-H. *Tetrahedron* 2007, *63*, 1644-1653.
Cheng, J.-Y.; Chu, Y.-H. *Tetrahedron Lett.* 2006, *47*, 1575-1579.
Tseng, M.-C.; Liang, Y.-M.; Chu, Y.-H. *Tetrahedron Lett.* 2005, *46*, 6131-6136.
Yen, Y.-H.; Chu, Y.-H. *Tetrahedron Lett.* 2004, *45*, 8137-8140.
Hsu, R.-C.; Yen, Y.-H.; Chu, Y.-H. *Tetrahedron Lett.* 2004, *45*, 4673-4676.

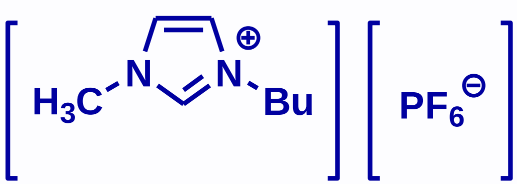
Are ionic liquids really stable chemically?

Ionic Liquids for Organic Synthesis

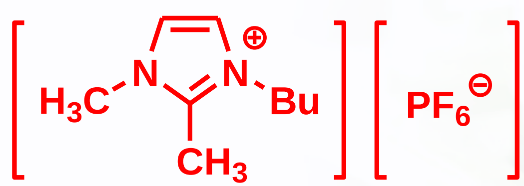
Baylis-Hillman reaction in [bmim][PF_6]:

lower yield contaminated with side products.

aliphatic aldehydes: 58-66%
aromatic aldehydes: 61-99%



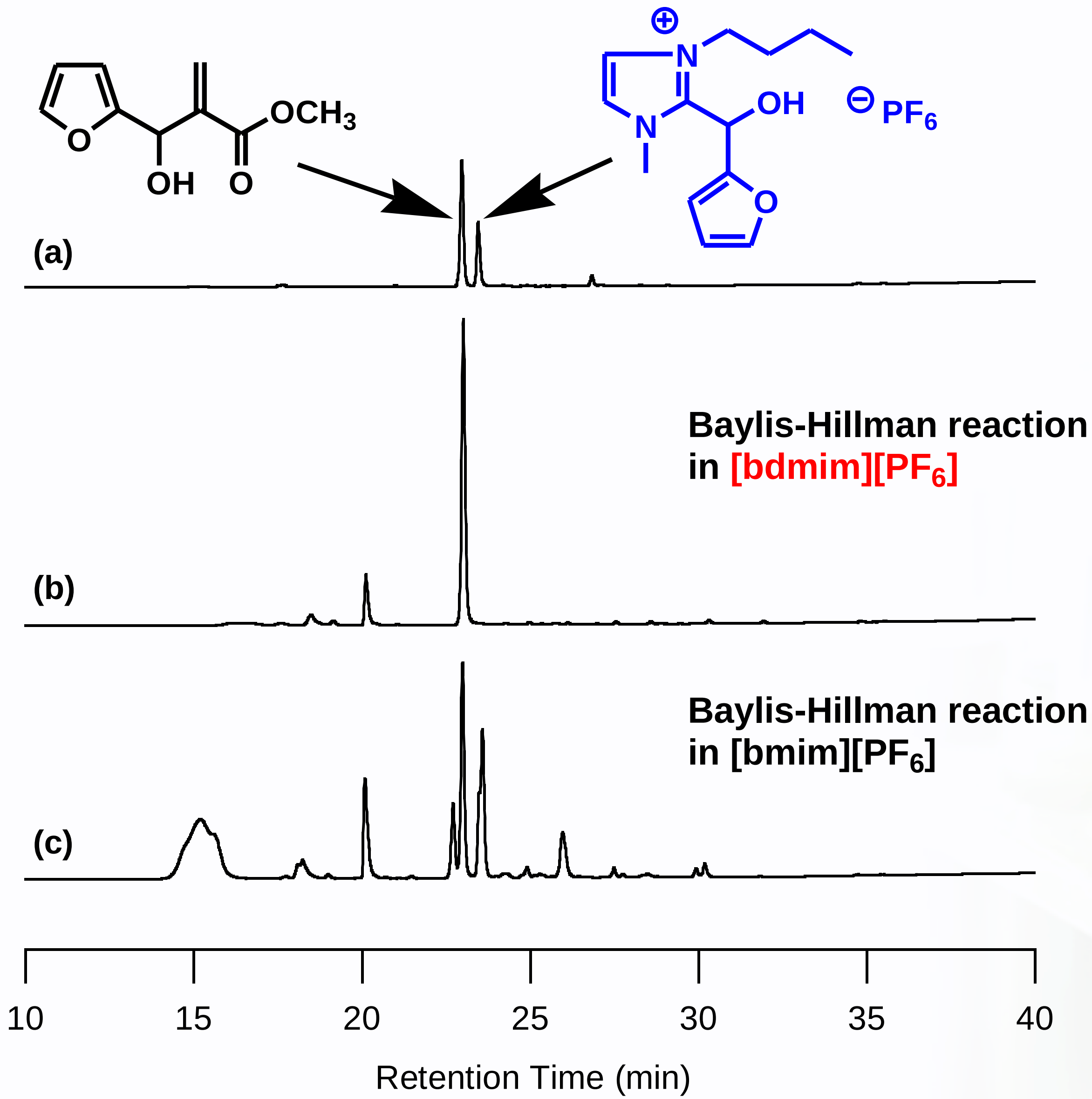
[bmim][PF_6]



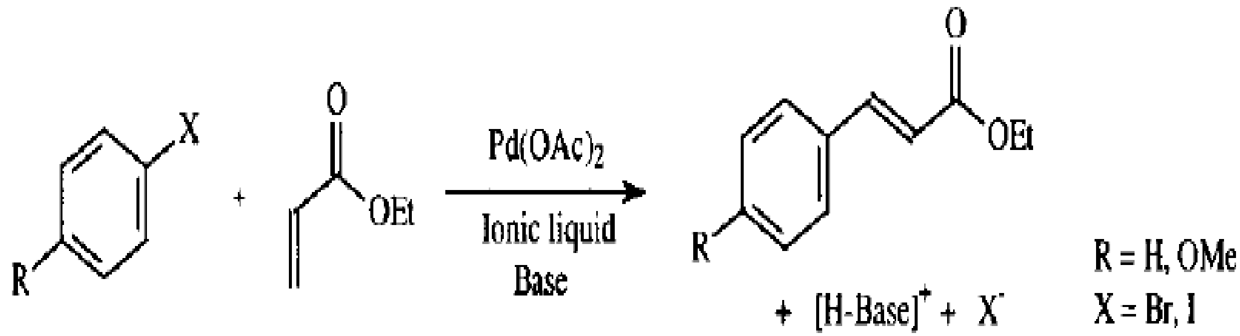
[bdmim][PF_6]

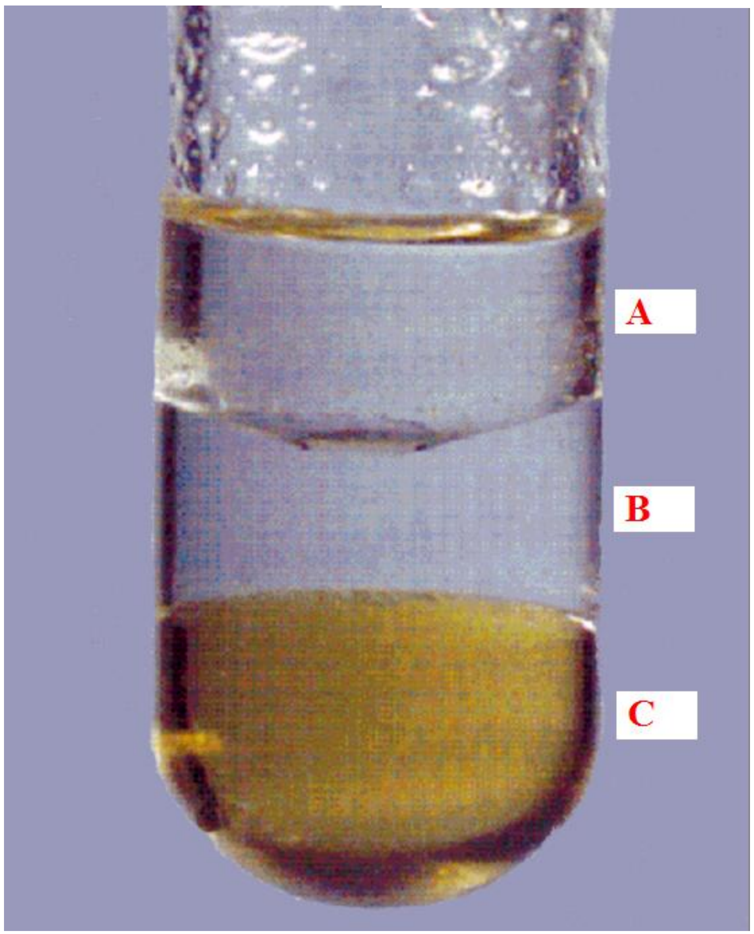
Aggarwal, V. K.; Emme, I.; Mereu, A. *Chem. Commun.* 2002, 1612-1613.
Hsu, R.-C.; Yen, Y.-H.; Chu, Y.-H. *Tetrahedron Lett.* 2004, *45*, 4673-4676.

Ionic Liquids for Organic Synthesis



Heck Reaction in Ionic Liquids : A Multiphasic Catalyst System



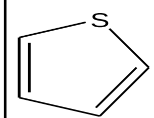
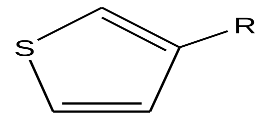
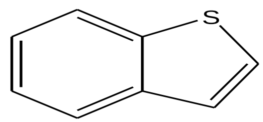
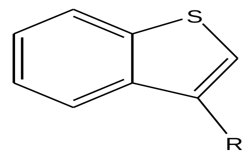
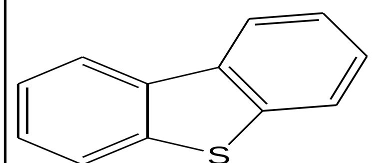
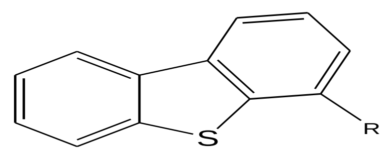
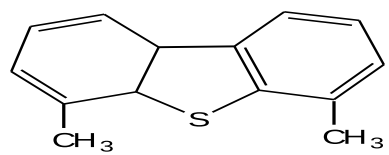
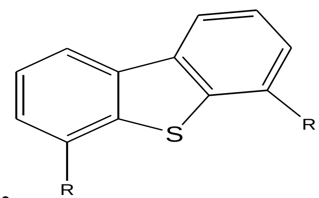
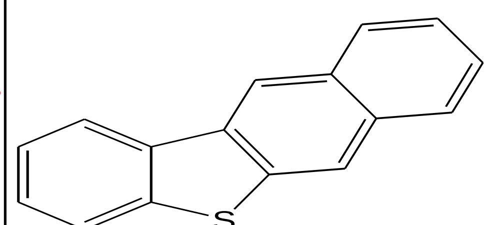


A ： Cyclohexane (product)
B ： Water (salt)
C ： Pd/phosphine ligand in [bmim][PF6]

A. J. Carmichael, et al., Org. Lett. 1,997, 1999.

Desulfurization of light oils by chemical oxidation/solvent extraction with RTILs

Wen-Hen Lo, Hsiao-Yen Yang and Guor-Tzo Wei* Green Chem. 2003, 5, 639.

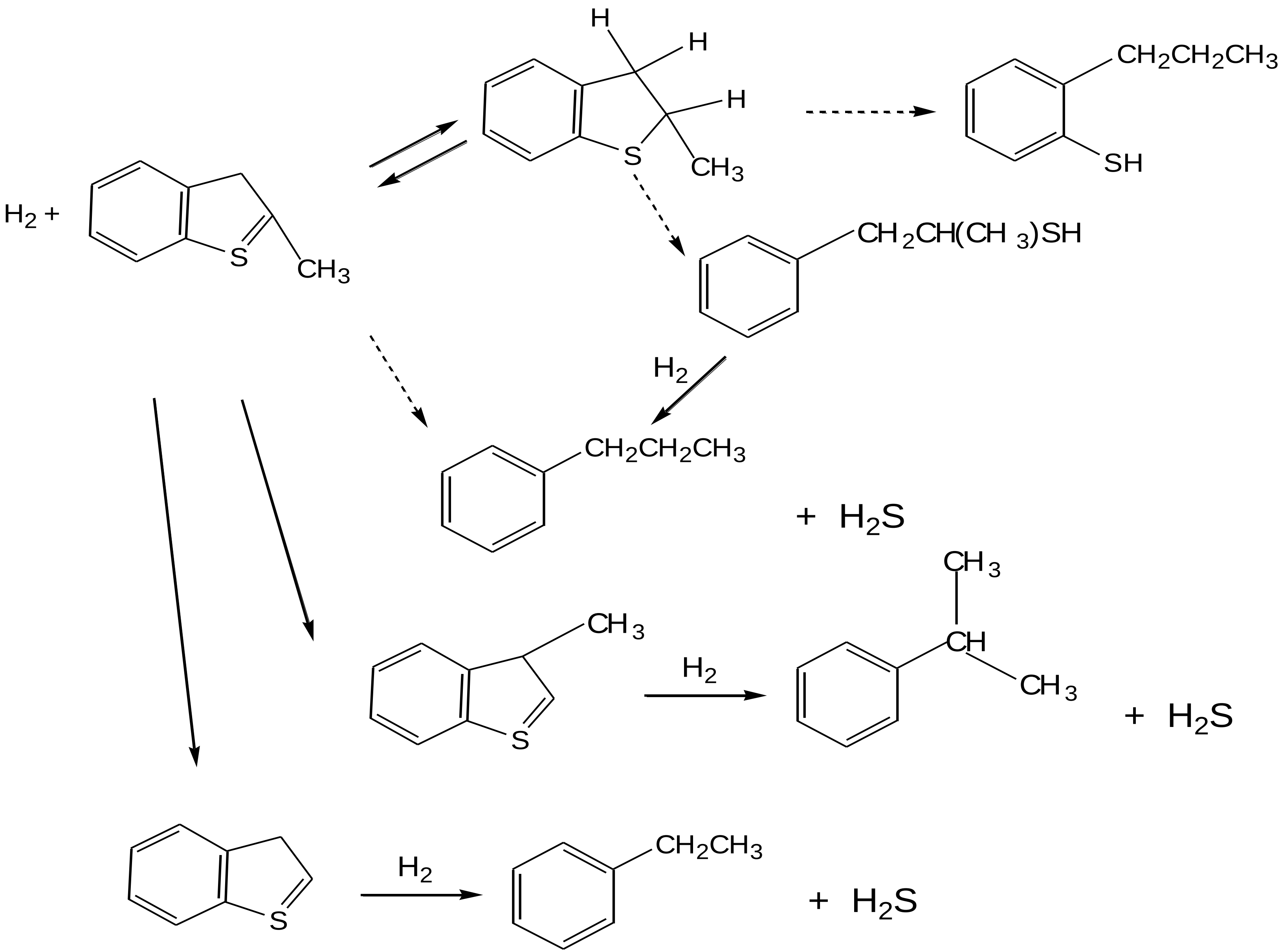
Thiols	R — SH
Disulfides	R — S — S — R`
Sulfides	R — S — R`
Thiophenes	  ,etc
Benzothiophenes	  ,etc.
Dibenzothiophenes (DBTs)	 
Alkyldibenzothiophene	 , 
Benzonaphthothiophenes	

柴油中含硫化合物之結構

各國實施低硫柴油規範的日期

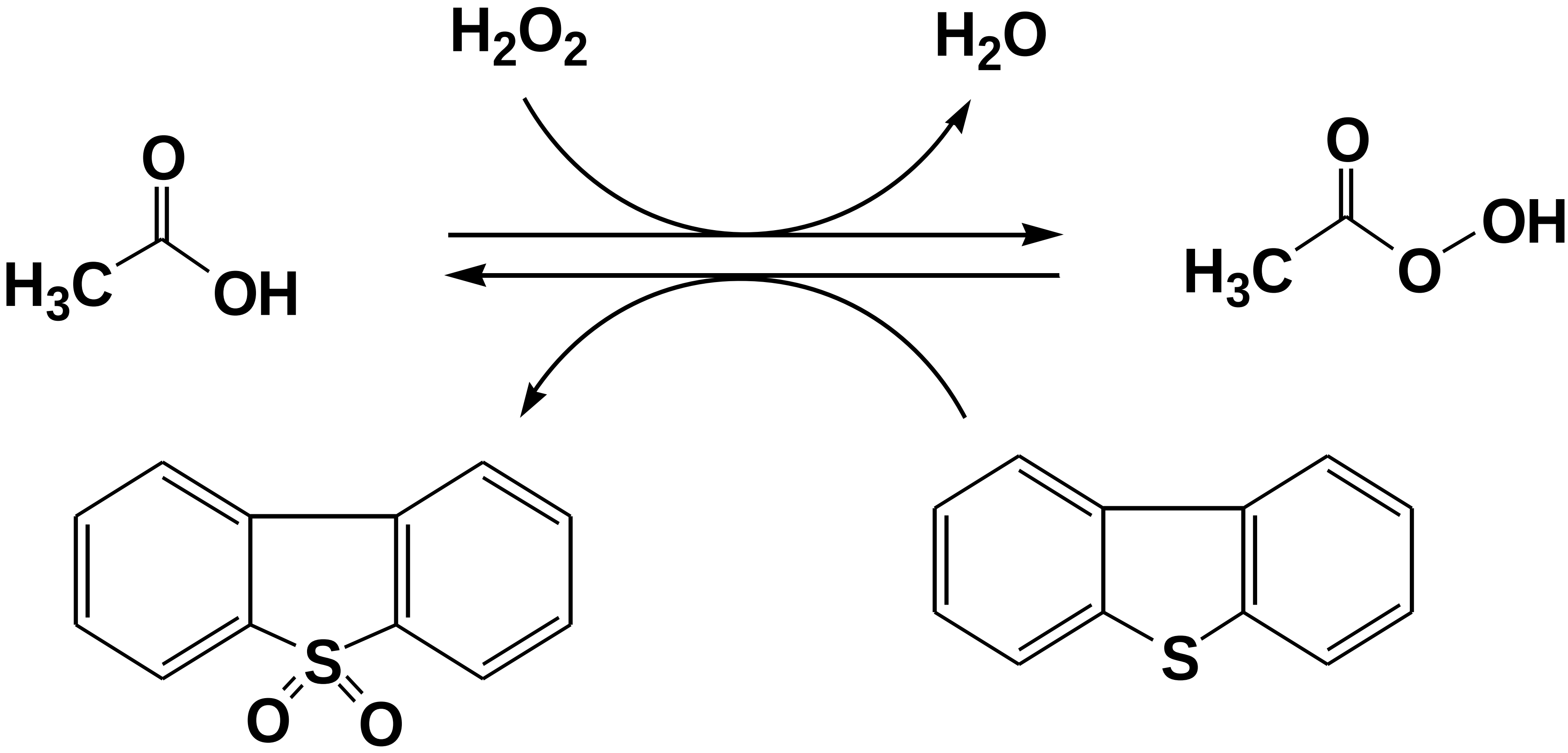
國家	柴油硫含量	開始實施日期
美國	500ppm→15ppm	2006年6月
加拿大	500ppm→15ppm	2007年1月
歐盟	300ppm→50~30ppm	2005年1月
日本	500ppm→50ppm	2005年1月
澳大利亞	500ppm→50ppm	2006年1月
台灣	500ppm→50ppm	2007年1月

工業上以Co-Mo/Al_2O_3催化之加氫脫硫(HDS)反應途徑



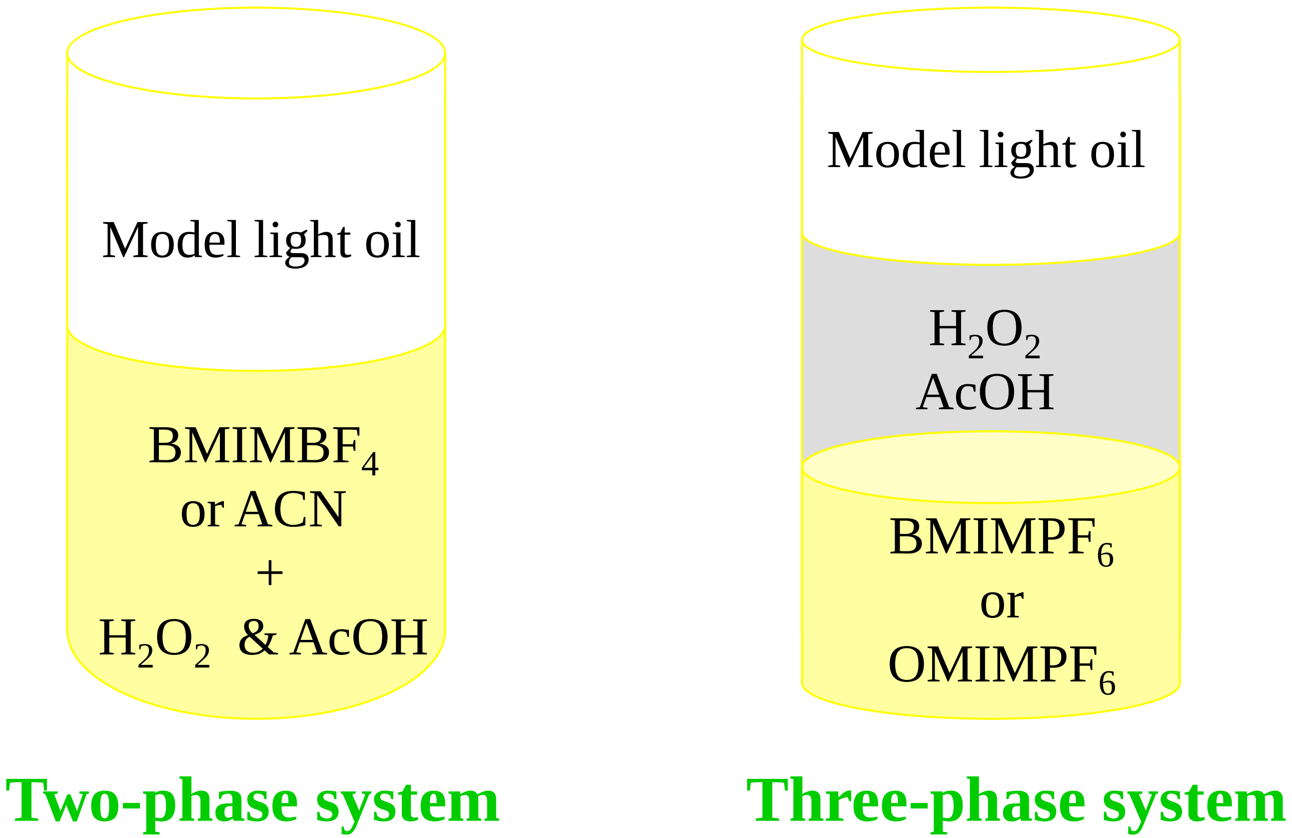
氫化脫硫(HDS)技術的缺點

- 反應需在高溫高壓下進行。
- 操作成本高且耗費能源 。
- 加氫作用使油品中烯烴類飽和，辛烷值減少而降低了燃料油之品質 。
- 對於benzothiophenes和dibenzothiophenes等硫化合物的脫硫效率較差，尤其是4,6-DMDBT 。



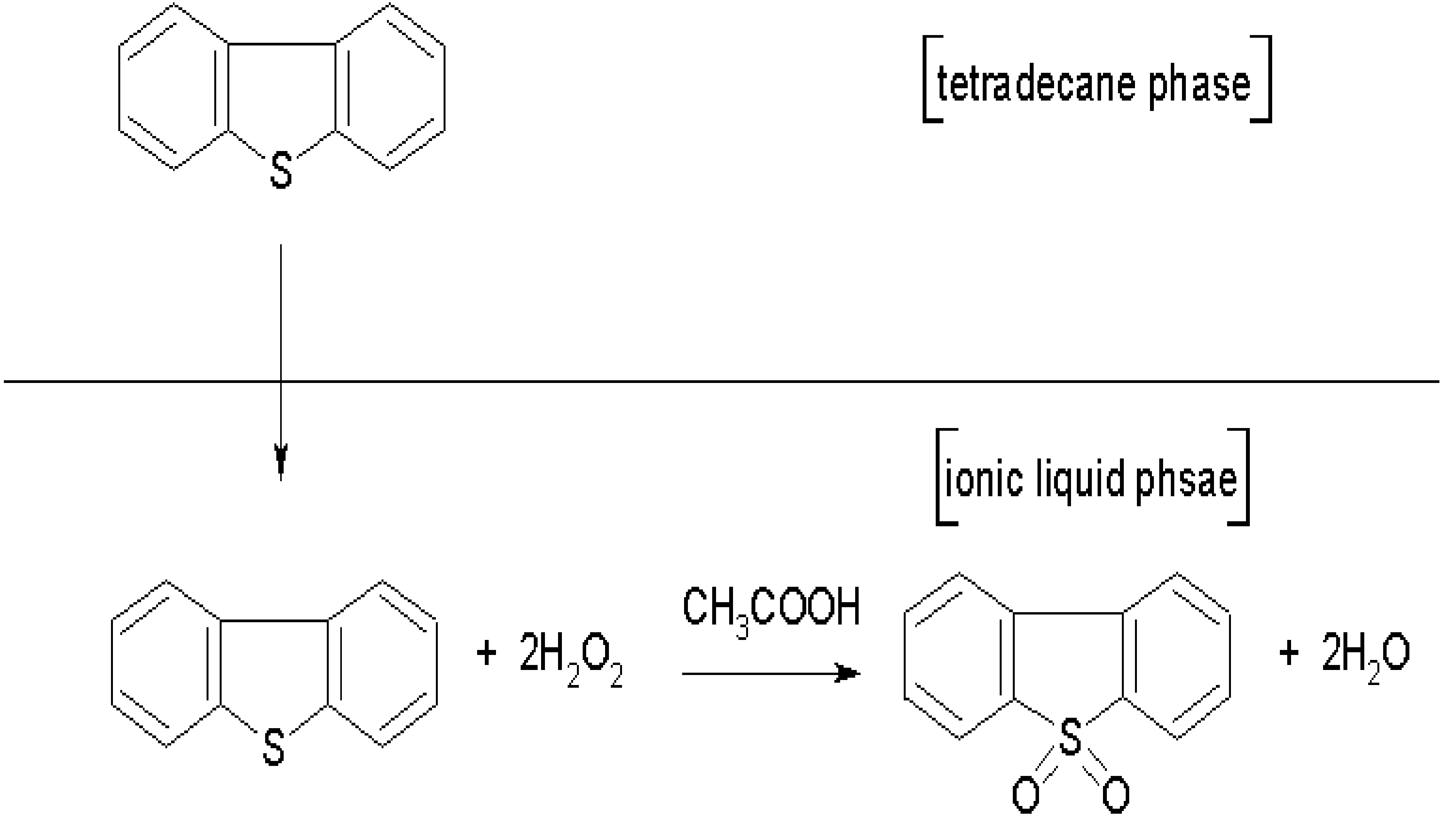
Chemical Oxidation Desulfurization (ODS)

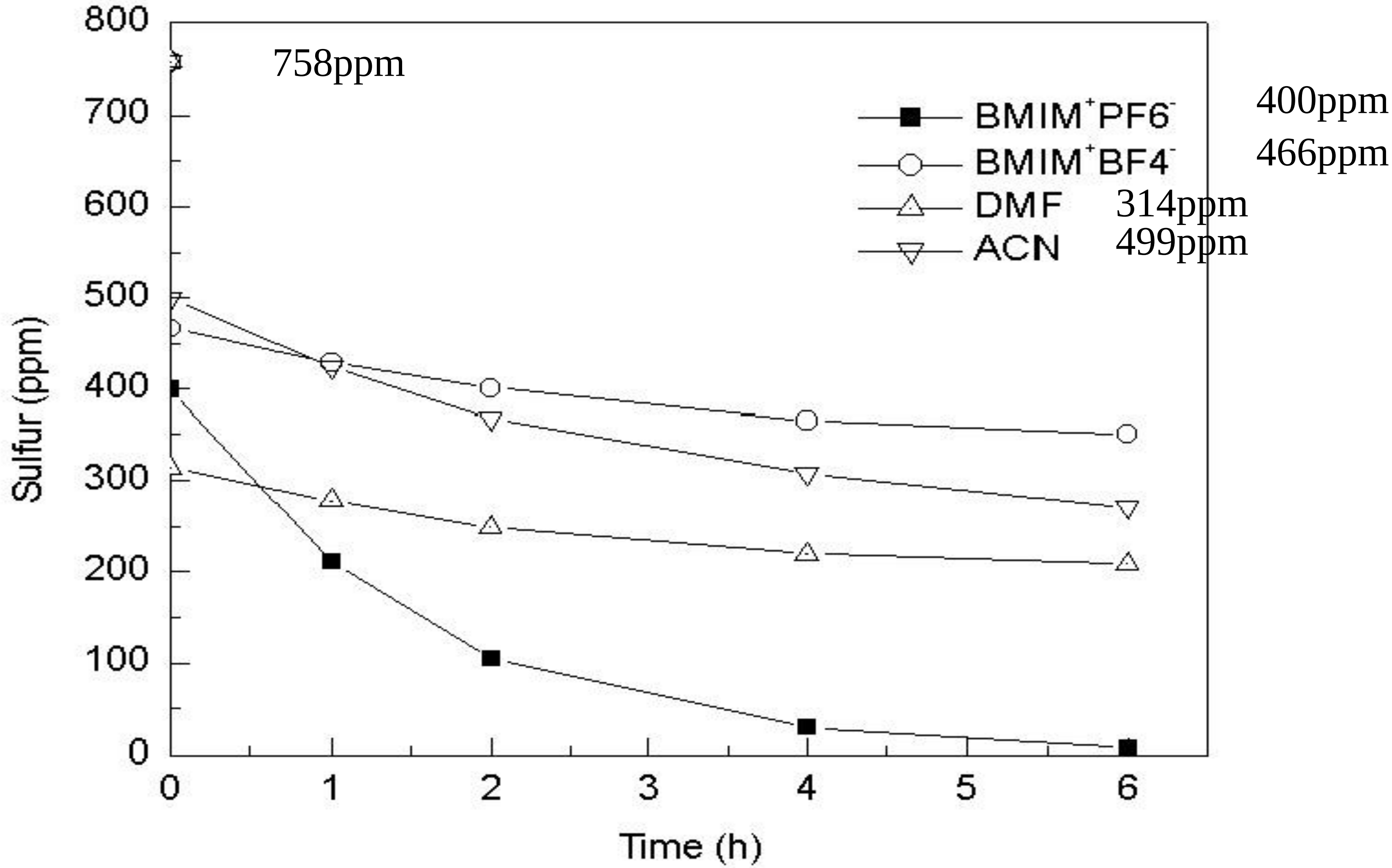
$$R = \frac{K[H_2O_2]^2[AcOH]}{[H_2O]}$$



B. N. Heimlich and T. J. Wallace, *Tetrahedron*, 1966, **22**, 3571.

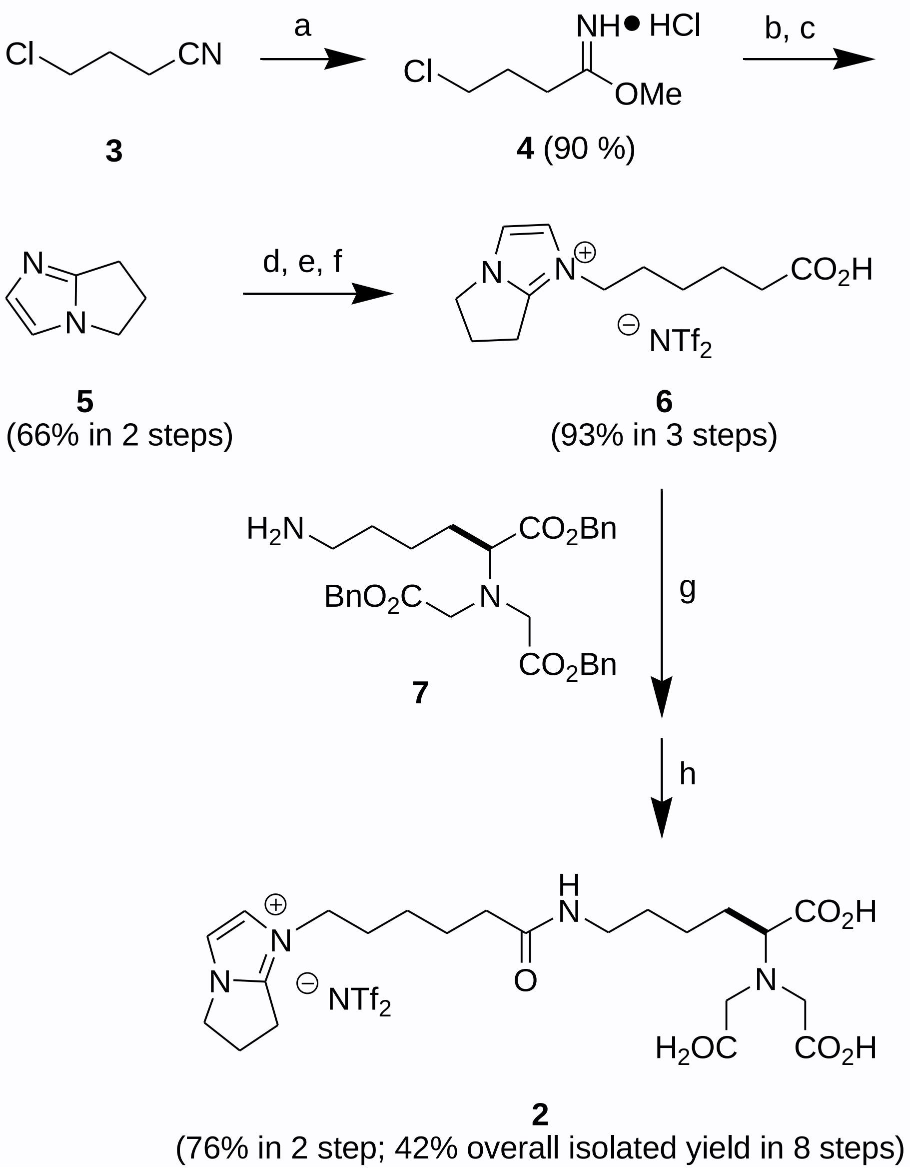
Extraction + Oxidation of DBT with an oil/IL system in One-pot operation





Sulfur content left in model light oil as a function of time with different solvents in the ODS/extraction system

Affinity Ionic Liquids for Biomolecular Interaction Analysis



Synthesis of AIL 2, [NTA-h-3C-im][NTf_2]

Experimental conditions:

(a) HCl, MeOH, ether, -20 ^{o}C, 24 h;

(b) $H_2NCH_2CH(OMe)_2$, Et_3N, CH_2Cl_2, reflux, 2 h;

(c) HCO_2H, reflux, 20 h;

(d) $Br(CH_2)_5CO_2Bn$, 80 ^{o}C, 2 h;

(e) H_2, $Pd(OH)_2/C$, MeOH, rt, 1 h;

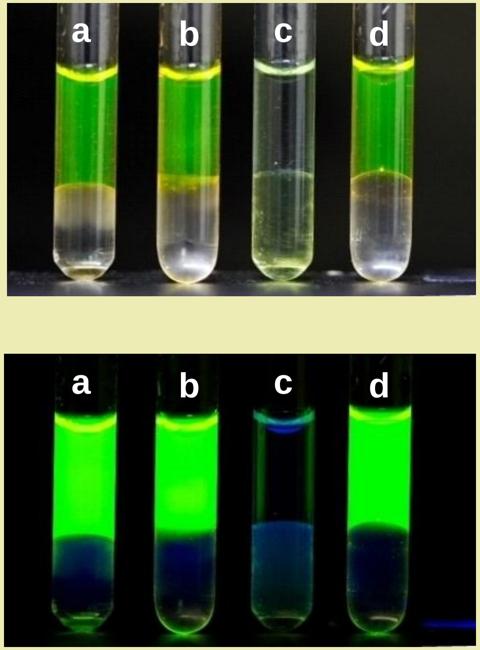
(f) $LiNTf_2$, H_2O, rt, 12 h;

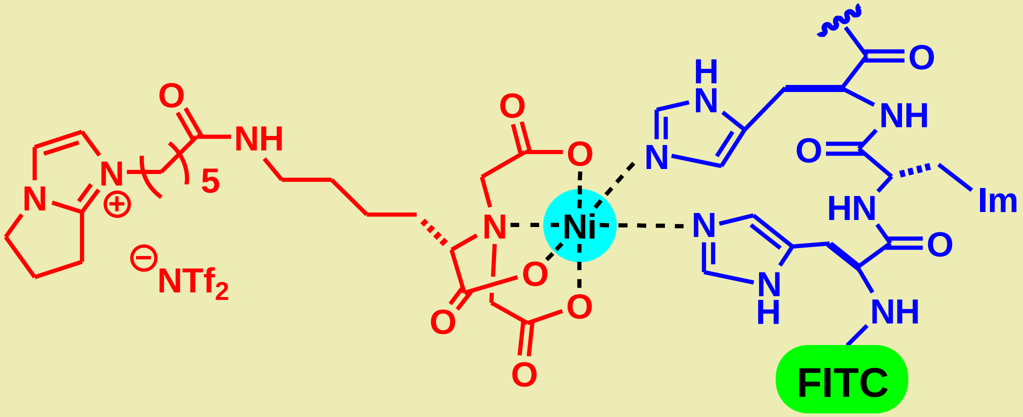
(g) EDC, DIEA, CH_2Cl_2, rt, 5 h;

(h) H_2, $Pd(OH)_2/C$, MeOH, rt, 1 h.

Affinity Ionic Liquids for Biomolecular Interaction Analysis

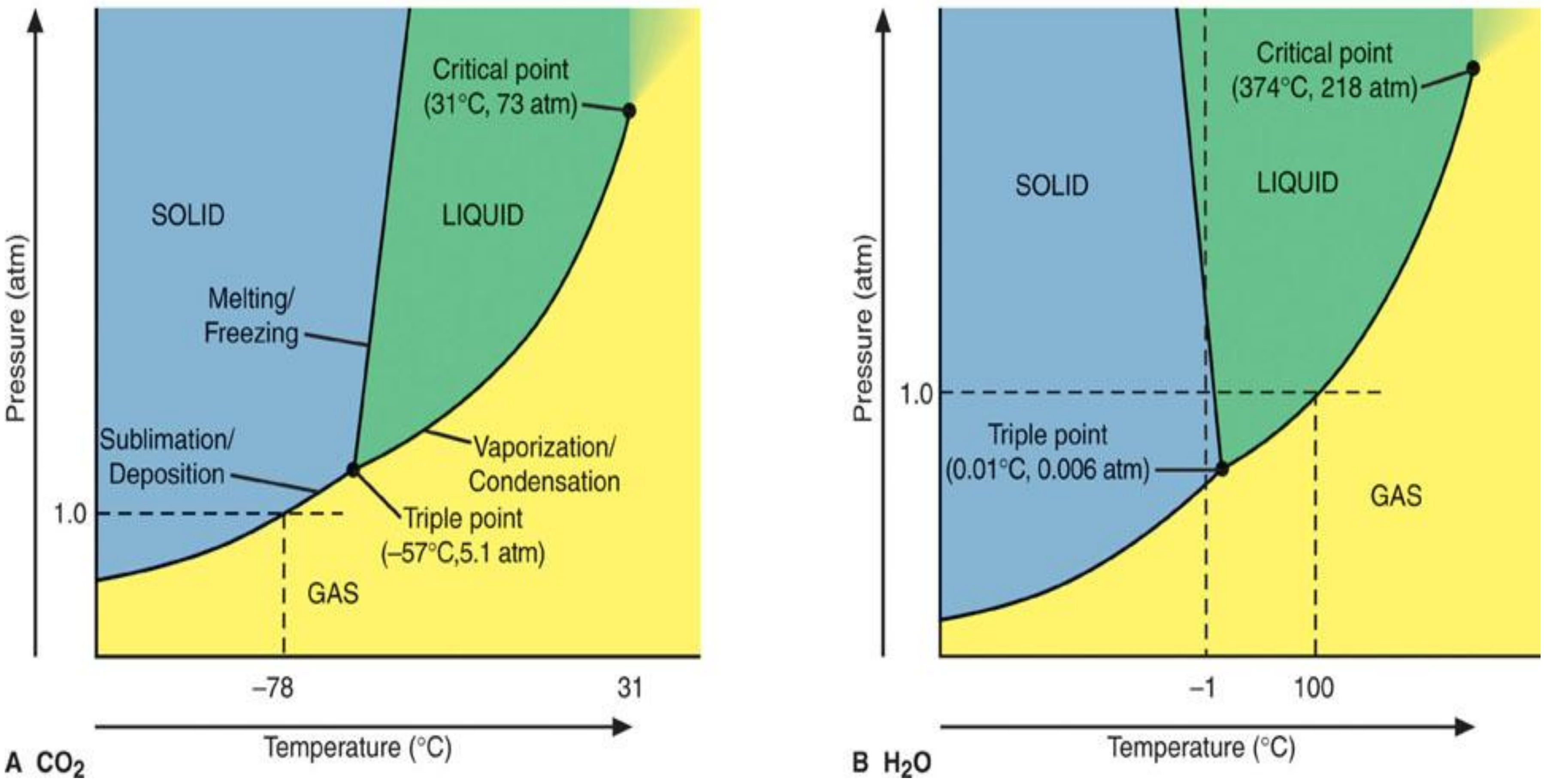
(A) (B)





Tseng, M.-C.; Tseng, M.-J.; Chu, Y.-H. *Chem. Commun.* 2009, 7503-7505.

Phase diagrams for CO_2 and H_2O



Physical Parameters of Selected Supercritical Fluids

Fluid	Dipole moment (debyes)[a]	T_c (°C)[a]	P_c (atm)[a]	ρ_c (g mL^{-1})[a]	ρ_{400} (g mL^{-1})[b]	ρ_l (g mL^{-1})[a,c]
CO_2	0.00	31.3	72.9	0.47	0.96	0.71 (63.4 atm)
N_2O	0.17	36.5	72.5	0.45	0.94	0.91 (0°C)
						0.64 (59 atm)
NH_3	1.47	132.5	112.5	0.24	0.40	0.68 (-33.7°C)
						0.60 (10.5 atm)
n-C_5	0.00	196.6	33.3	0.23	0.51	0.75 (1 atm)
n-C_4	0.00	152.0	37.5	0.23	0.50	0.58 (20°C)
						0.57 (2.6 atm)
SF_6	0.00	45.5	37.1	0.74	1.61	1.91 (-50°C)
Xe	0.00	16.6	58.4	1.10	2.30	3.08 (111.75°C)
CCl_2F_2	0.17	111.8	40.7	0.56	1.12	1.53 (-45.6°C)
						1.30 (6.7 atm)
CHF_3	1.62	25.9	46.9	0.52	1.15	1.51 (-100°C)
H2O		**374.2**	**220.5**	**0.34**		

[a] Data taken from Refs. 62 and 63.

[B] The density at 400 atm (p,,,,) end T, = 1.03 was calculated from compressibility data."

[C] measurements were made under saturated conditions if no pressure is specified or were performed at 25°C if no temperature is specified.

CO_2 as a Solvent

- Liquid (ca. 50-60 bar, t> rt)
  - Already found application in dry cleaning etc.
  - Relatively little studied for reactions, but still many potential benefits.
- Supercritical (>31 °C, >74 bar)
  - Usually involves higher pressures, but much more control over solvent properties
  - Used for decaffeination, natural product extraction
- Gas expanded liquids
  - Relatively little studied
  - Lower pressures, allow higher concentrations of light gases to be dissolved

Comparison of the properties of gas, Supercritical fluid and liquid

Mobile phase	Density (g／ml)	Viscosity (m^2／s)	Diffusion coefficient (cm^2／s)
Gas	0.6～2.0×10^{-3} (0.01)	0.5～3.5×10^{-4} (0.01)	0.01～1.0 (10,000)
Supercritical fluid	0.2～0.9 (~ 0.5)	2.0～9.9×10^{-4} (0.01)	0.5～3.3×10^{-4} (10-100)
Liquid	0.8～1.0 (1)	0.3～2.4×10^{-2} (1)	0.5～2.0×10^{-5} (1)

SCFs are used as extraction solvents (e.g. extracting caffeine from coffee beans, fats from potato chips), carrier medium for chromatography, and solvents for disposal of organic hazardous wastes

CO_2 as a Solvent

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  - Already found application in dry cleaning etc.
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  - Usually involves higher pressures, but much more control over solvent properties
  - Used for decaffeination, natural product extraction
- Gas expanded liquids
  - Relatively little studied
  - Lower pressures, allow higher concentrations of light gases to be dissolved

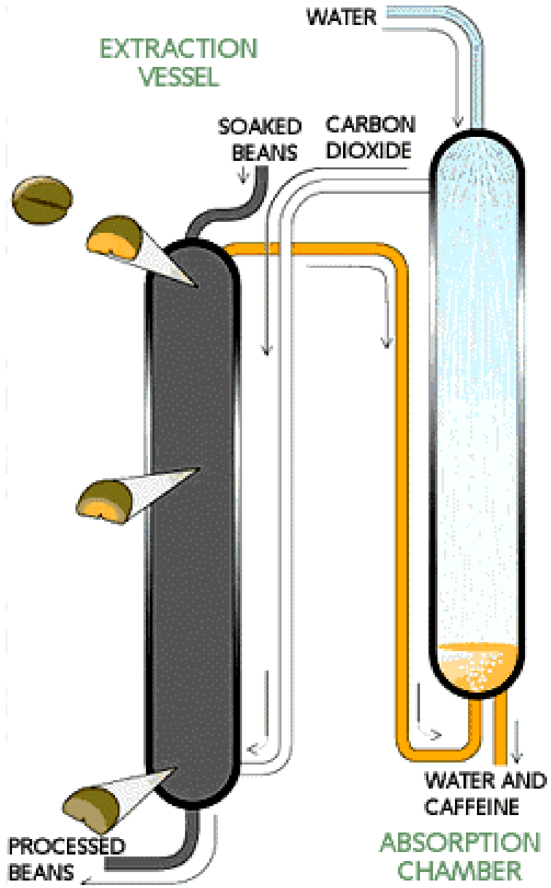
Benefits of supercritical carbon dioxide

- Moderate critical pressure (73.8 bar)
- Low critical temperature (31.1℃)
- Low toxicity and reactivity
- High purity at low cost
- Useful for extractions at temperature < 150℃

Liquid or supercritical CO_2 as Solvent

- Extraction.
- Cleaning.
- Material synthesis and catalyst: Exploring reaction kinetics and routes to new materials.
- Material processing for new materials.
- Supercritical fluid chromatography.

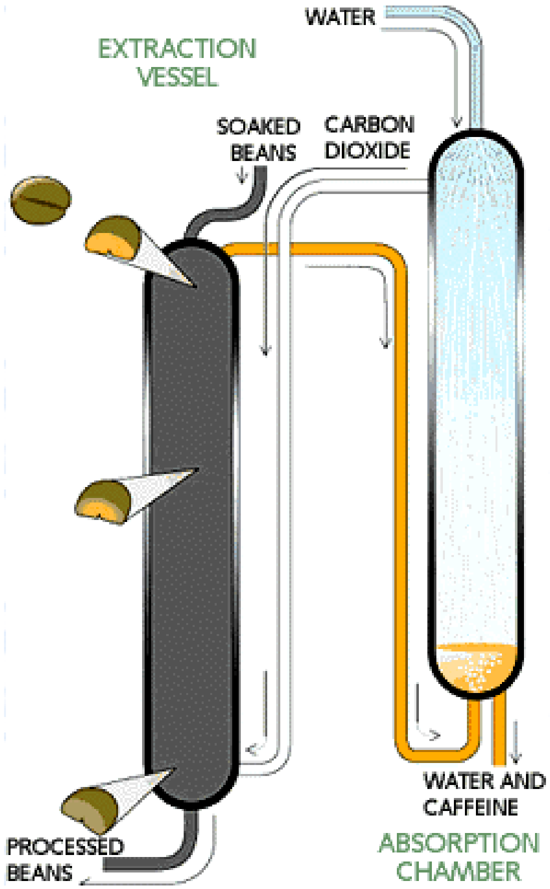
Decaffeination process



- **SOAKING** green coffee beans in water doubles their size, allowing the caffeine to dissolve into water inside the bean.
- **CAFFEINE REMOVAL** occurs in an extraction vessel. Caffeine diffuses into this supercritical carbon dioxide, along with some water.

Scientific American, June 1997

Decaffeination process



- **DECAFFEINATED BEANS** at the bottom of the vessel are removed, dried and roasted.
- **RECOVERY** of dissolved caffeine occurs in an absorption chamber. A shower of water droplets leaches the caffeine out of the supercritical carbon dioxide.

Scientific American, June 1997

Industrial extraction with supercritical CO_2

- Decaffeinating coffee and tea
- Extracting bitterness from hops to make beer
- Extracting spices and aromatic plants
- Defatting cocoa powder : Fat is precipitated from the supercritical fluid by dropping solution pressure, so precipitated fat can be dried and weighed
- Can be as efficient as solvent extraction (up to 98% of the available oil)

Techno Rice

Delicious Brown Rice

- **Brand: I-Mei Good for You Rice**
- Five King Cereals Industry Co., Ltd.
- Products: brown rice, white rice, and mixed
- Advantages:
  - pesticides and heavy metals are removed
  - germs and insect eggs are exterminated
  - waxy layer and fatty acid are removed; preventing rice from rancid and retrograded
  - cooking time is shortened by 25-33% for brown rice
  - shelf life of the bagged rice is extended
  - nutrients are preserved

五王糧食股份有限公司
『超臨界流體淨米技術』
Techno Rice

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- Five King Cereals Industry Co., Ltd.
- Products: brown rice, white rice, and mixed
- Advantages:
  - pesticides and heavy metals are removed
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  - nutrients are preserved

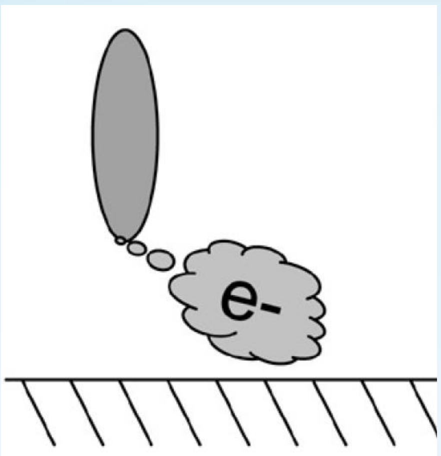
*嘉義縣義竹鄉義工三路**12**號*

SFC Commercial Instruments

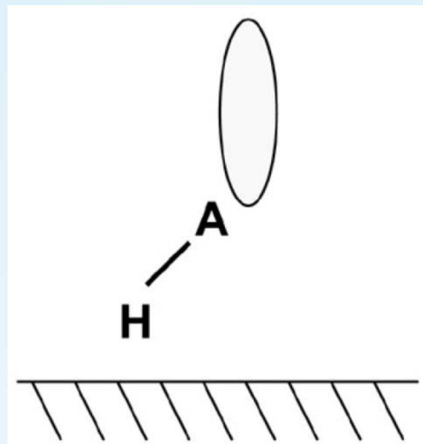
Jasco SFC/SFE system (packed column)

LSER equation

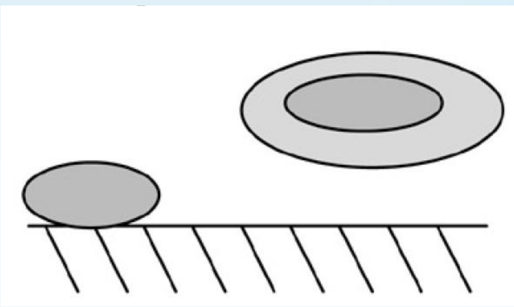
$$\log k = c_0 + eE + sS + aA + bB + vV$$



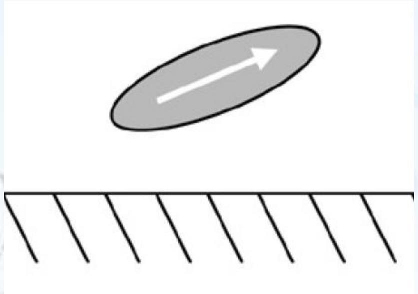
n – π & π – π interaction



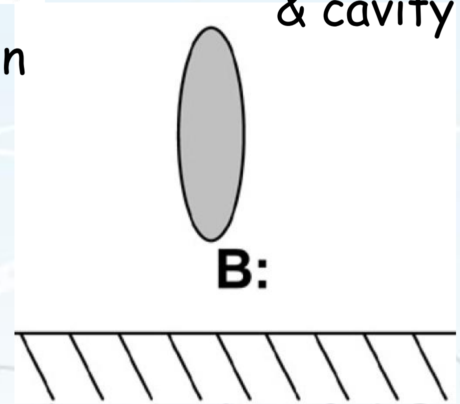
Acidic interaction



Dispersion interaction & cavity effect



Dipole-dipole interaction



Basic interaction

HPLC vs SFC

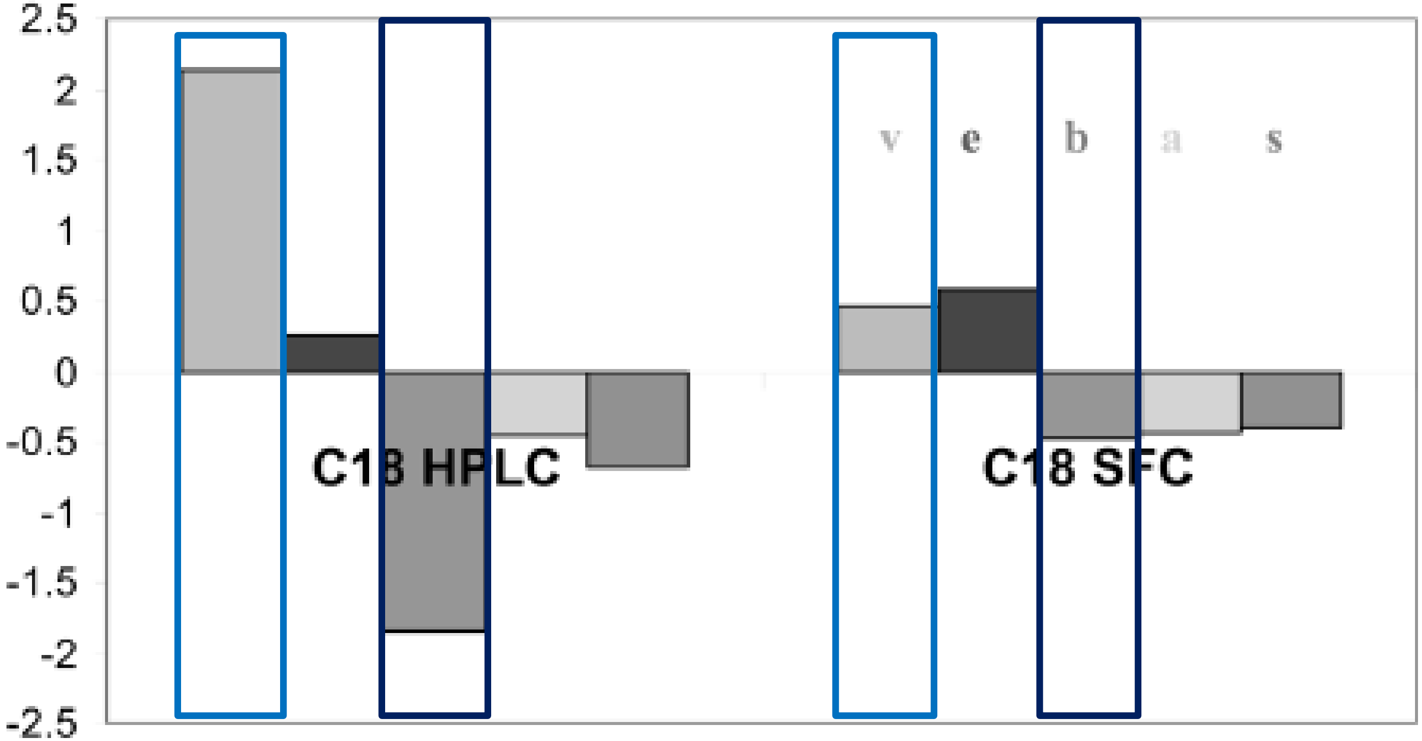


Figure 18. Values of the five coefficients (*v*, *e*, *b*, *a*, *s*) on a C18 stationary phase in HPLC chromatography (MeOH/H_2O 50:50 v/v) and in SFC (CO_2/MeOH 90:10 v/v).

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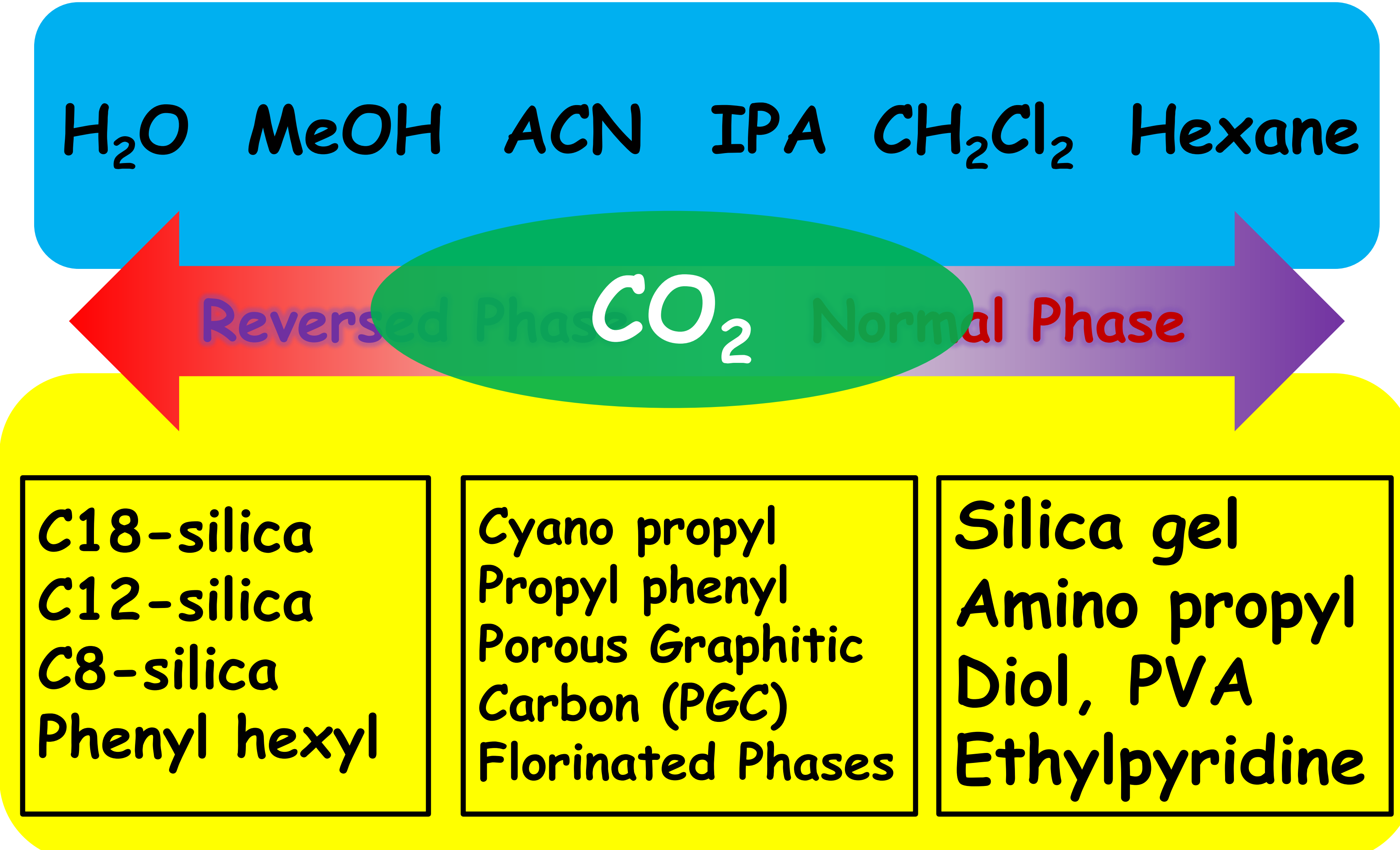
LC column

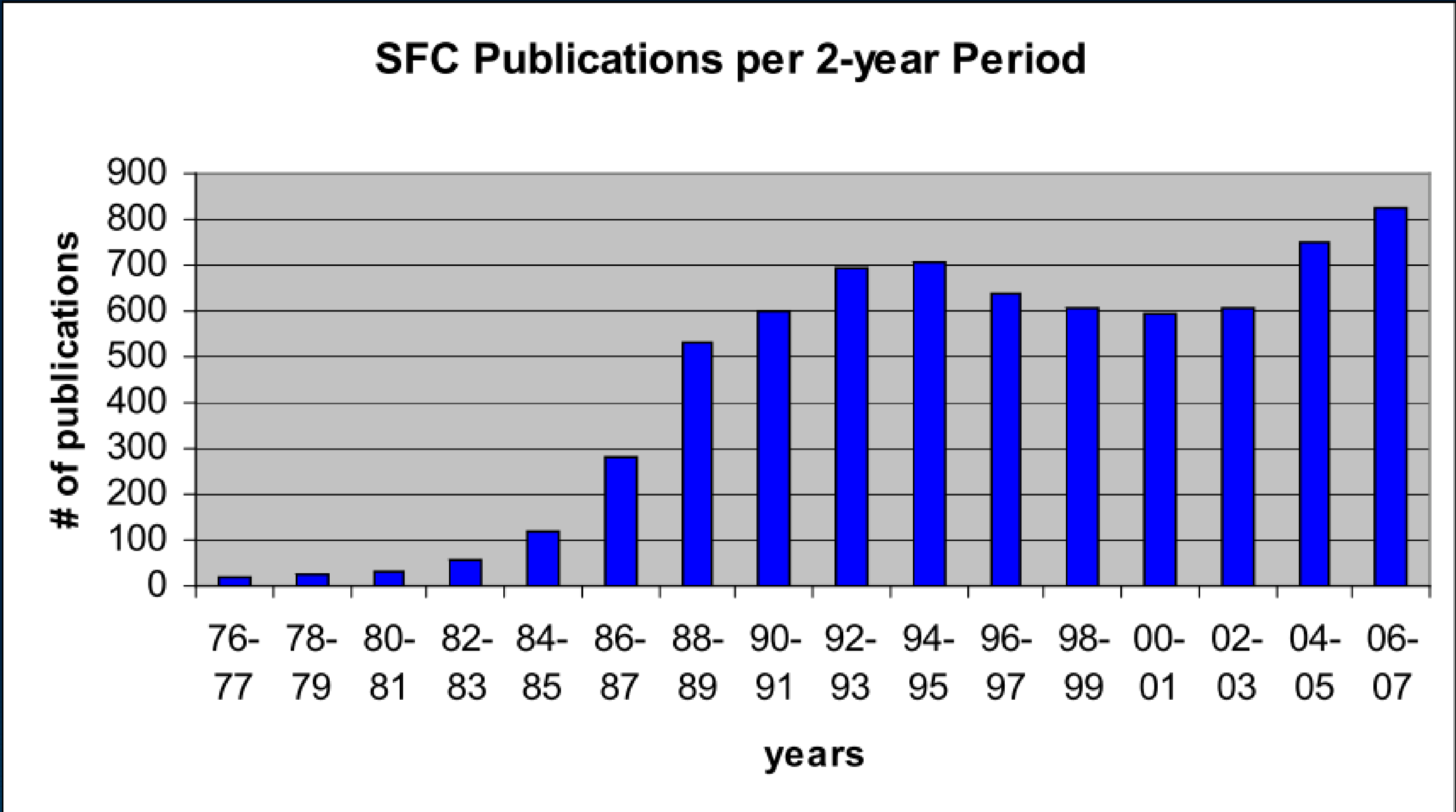
H_2O MeOH ACN IPA CH_2Cl_2 Hexane

Reversed Phase ⟷ Normal Phase

C18-silica C12-silica C8-silica Phenyl hexyl	Cyano propyl Propyl phenyl Porous Graphitic Carbon (PGC) Florinated Phases	Silica gel Amino propyl Diol, PVA Ethylpyridine

SFC column


H2O MeOH ACN IPA CH2Cl2 Hexane
Reversed Phase
CO2
Normal Phase
C18-silica
C12-silica
C8-silica
Phenyl hexyl
Cyano propyl
Propyl phenyl
Porous Graphitic
Carbon (PGC)
Florinated Phases
Silica gel
Amino propyl
Diol, PVA
Ethylpyridine



SciFinder search of “supercritical fluid chromatography” OR “subcritical fluid chromatography” OR “SFC”

Conclusions

- Ionic liquids have unique solvent properties that make them become attractive for specific function-task specified ionic liquids.
- Achiral separations of SFC will become attractive once the proper-designed columns are available.
- LESR is a useful tool to characterize SFC achiral column

Acknowledgement

$ Support:

National Science Council, Taiwan

National Chung Cheng University, Taiwan

Thank you for your time