GREEN CHEMISTRY

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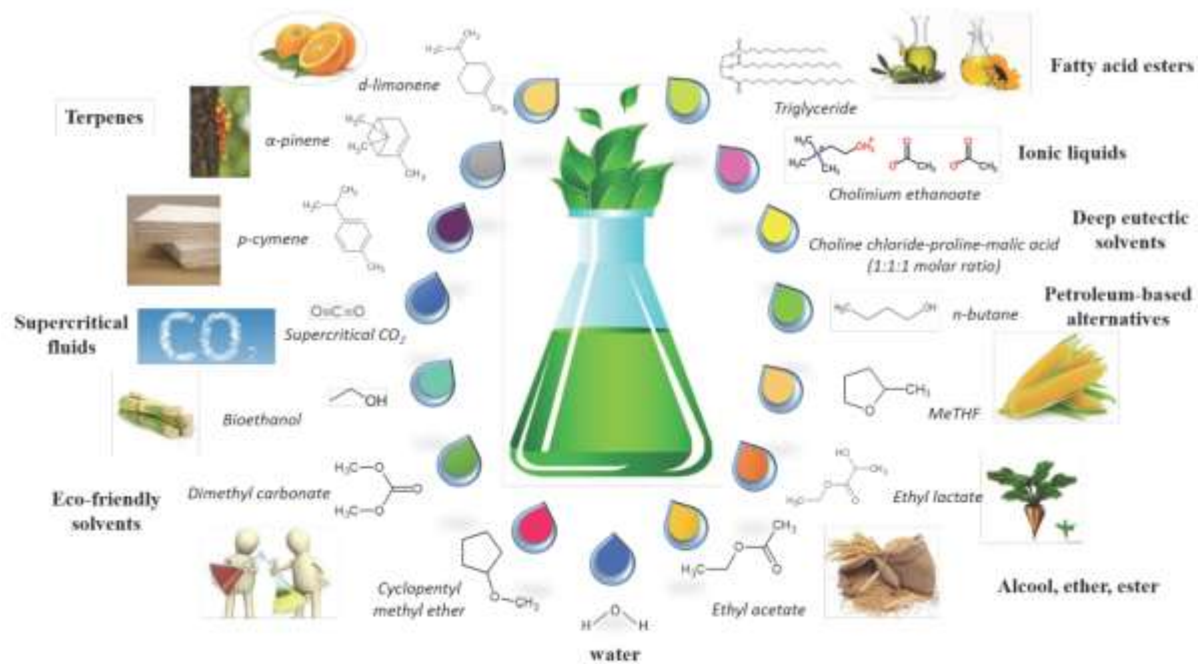
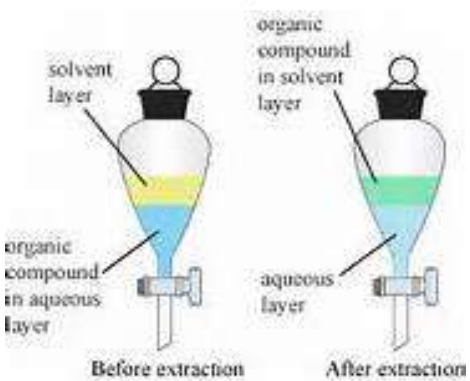
Outline

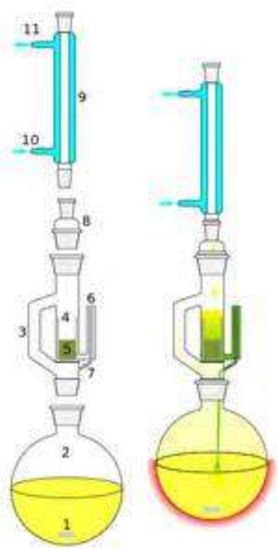
- Why we use solvents for chemical reaction?
- Problems with traditional organic solvents
- Green Solvents available for selection (water, supercritical fluids, ionic liquids, polyethylene glycol)



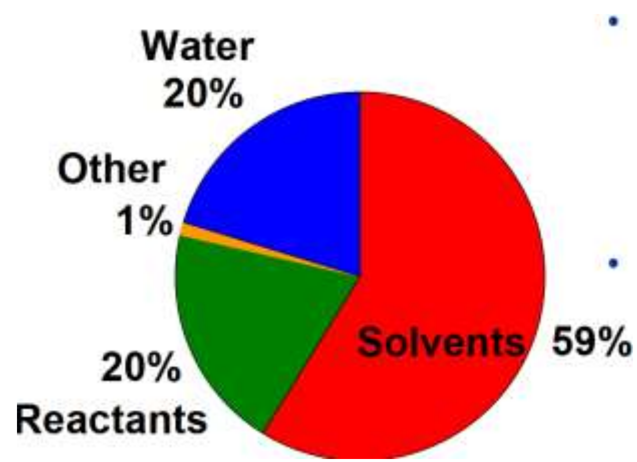
Why is Chemistry Performed Using Solvents?

- Efficient mixing and stirring
- Addition of solid reagents as a solution
- Used to bring reactants together at suitable concentrations
- Energy control
  - ✓ Endothermic reactions require energy – heat can be supplied by heating solution
  - ✓ Exothermic reactions – solvent acts as a heat sink preventing runaway reactions. Heat can be removed by allowing solvent to boil.





- Widely used throughout chemistry
  - Synthetic Chemistry
    - Reaction medium on laboratory and industrial scale
    - Extensively used in work-up and purification (usually more than for reaction medium)
  - Analytical Chemistry
    - Sample extraction and preparation (Spectroscopy)
    - Chromatography mobile phase (HPLC, TLC etc.)
  - Crystallisation
    - Recrystallization to purify compounds and prepare crystals suitable for analysis



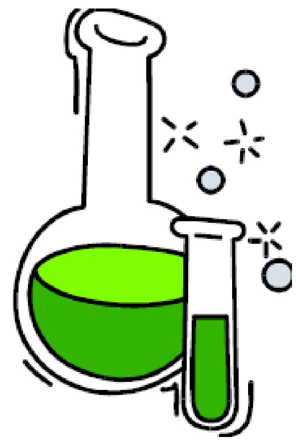
Other applications of solvents

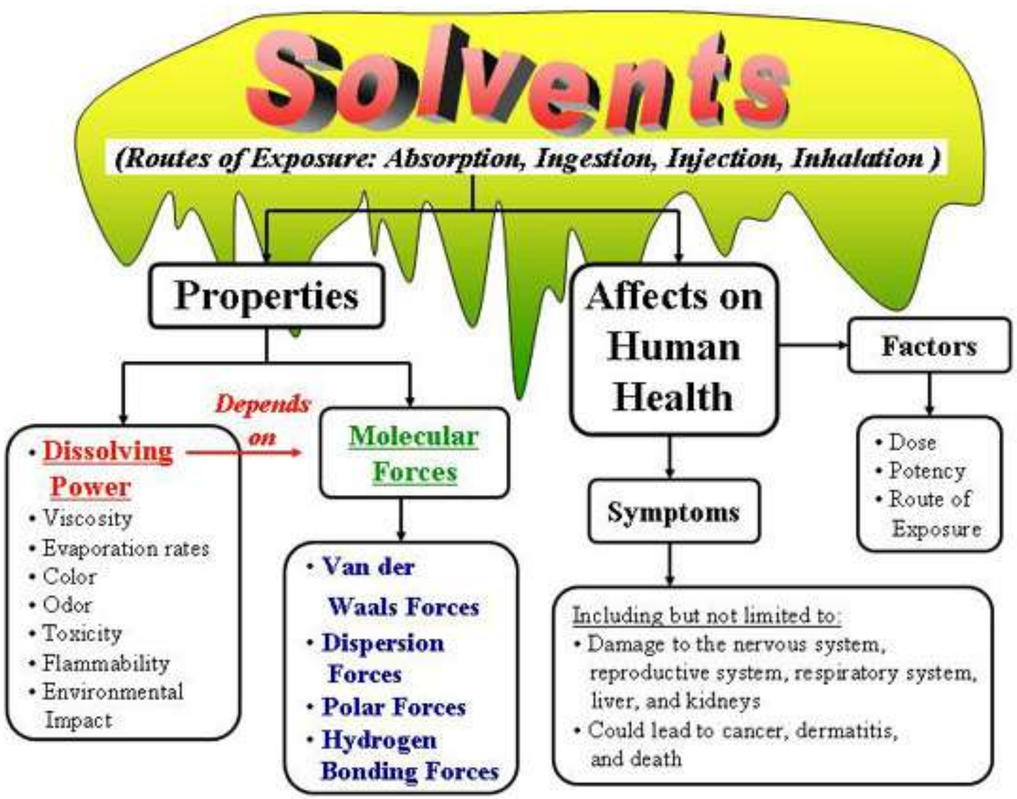
- Used much more widely than just synthetic chemistry
- Coatings:
  - Paints, adhesives
    - Solvent usually removed by evaporation after application leaving coating behind
    - Coating removal or cleaning
- Cleaning
  - E.g. Dry cleaning – extensive use of perchloroethylene, a known cancer suspect agent, which also contaminates groundwater supplies
- Extraction
  - E.g. Coffee decaffeination (benzene, CH_2Cl_2)

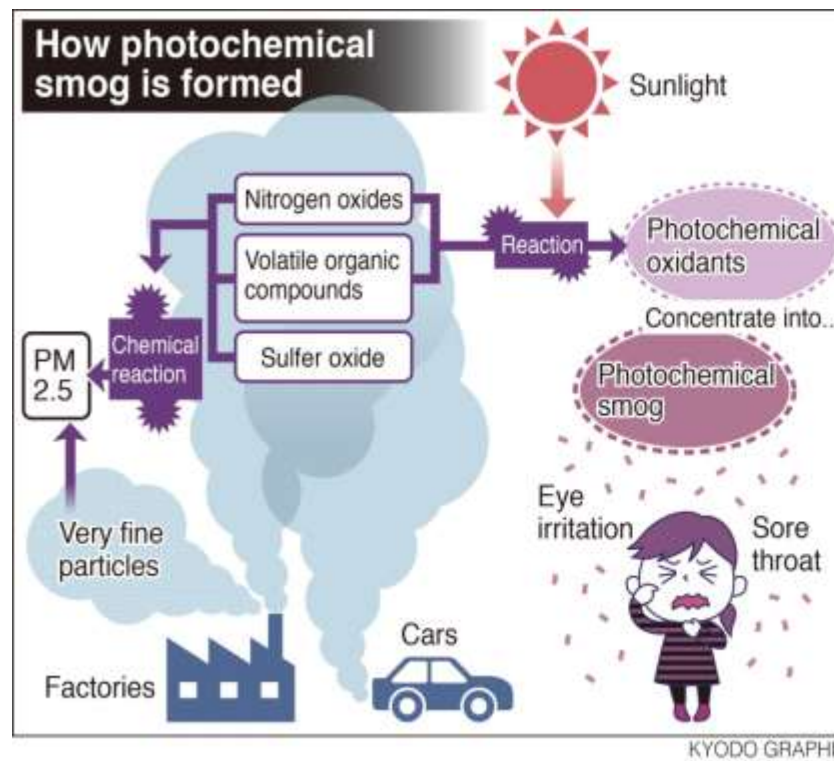
Issues with Organic Solvents

- Organic solvents are of concern to the chemical industry because of the sheer volume used in synthesis, processing, and separation (global demand was over 18,500 kilotons in 2015, 24,550 kilotons estimated in 2023).
- Organic solvents are expensive (USD 35 billion in 2015 and is expected to be worth more than USD 50 billion by 2023)
- Additional fees spent on environmental technology, much of which is end of pipe equipment and associated operating costs to clean up emissions and air.
- Organic solvents are highly regulated (e.g., glycerol, methanol, chloroform, acetone…).
- Many organic solvents are volatile, flammable, toxic, and carcinogenic (e.g., perchloroethylene).

- *Solvent use* (excluding incineration) is the *major contributor* to:
  - Energy (ca. 75%)
  - Resource utilisation (about 80%)
  - Photochemical Ozone Creation Potential (ca. 70%)
  - Green House Gases (about 50%)







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)

Butanone

Organic solvent hazards

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

Problems with VOC's

- Direct
  - Varying toxicity depending on nature of volatile organic compounds (VOC), exposure method and duration.
    - E.g. DMF (teratogenic易致畸形的), $CHCl_3$ (suspect carcinogen)
  - Flammability (fire hazards)
  - Peroxide formation (usually ethers)
- Indirect
  - Ozone depletion
    - Chlorofluorocarbons (CFC's) now phased out
      - E.g. CF_3Cl, lifetime in atmosphere 640 years, GWP 14,000
      - CCl_4 – now much more limited use (35yrs, GWP 1400)
  - Global warming potential (GWP)
    - Does not have to be ozone depleting to have GWP
      - E.g. CH_2FCF_3 used in refrigerants and air conditioning units, 14yrs, GWP 1300
  - Environmental persistence
- Use of less volatile solvents may improve environment as long as they do not lead to problems elsewhere.

Global warming potential (GWP)

- **Global warming potential** (GWP) is a relative measure of how much heat a greenhouse gas traps in the atmosphere over a specific time interval, commonly 20, 100, or 500 years.
- It compares the amount of heat trapped by a certain mass of **the gas** with the amount of heat trapped by a similar mass of **carbon dioxide**. GWP is expressed as a factor of carbon dioxide (whose GWP is standardized to 1).
- The GWP depends on the following factors:

  -the absorption of infrared radiation by a given species

  - the spectral location of its absorbing wavelengths

  -the atmospheric lifetime of the species
- Thus, a high GWP correlates with a large infrared absorption and a long atmospheric lifetime.

Current Approaches to Solvent Replacement

- Not a simple problem – usually cannot simply replace one solvent with another

- Consider process as a whole, not just one aspect (solvents used in work-up and purification not just reaction medium)

Solvent extraction

- Very important part of reaction sequence – need to consider whole process – NOT JUST REACTION ITSELF.
- Often more solvent is used in work-up than as reaction medium.
- Compounds dissolved in one solvent shaken with water to remove inorganic impurities, or other water soluble contaminants. Generates aqueous waste as well as organic waste, both of which will require disposal.
- Solutes usually remain in the non-aqueous solvent, which is then concentrated, and waste solvent discarded (often incinerated generating CO_2).

Strategies of solvent replacement

- Avoid or minimise solvents in first place
- Use less toxic solvents
- Use renewable solvents (not derived from petrochemicals)
- Avoid VOC's – solvents with low vapour pressure / high boiling points may be preferable as long as this does not lead to other complications.

Solvent replacement in synthetic chemistry

- Can be very difficult to replace solvents.
- As reaction media:
  - Solvents have a substantial effect on a reaction, allowing a degree of control not possible in its absence
  - Can affect:
    - Rates of reaction
    - Chemo-, regio- and stereoselectivity
    - Outcome of reaction – may not work at all, or may do something totally different!
- If can be exploited then may give extra incentive for adoption of new technology.

Commonly used solvents

Preferred	Usable	Undesirable
Water	Cyclohexane	Pentane
Acetone	Methylcyclohexane	Hexane(s)
Ethanol	Toluene	Di-isopropyl ether
2-propanol	Heptane	Diethyl ether
1-propanol	Methyl t-butyl ether	Dicholoromethane
Ethyl acetate/Ethyl lactate	Isooctane	Dicholoroethane
Iso-propyl acetate	Acetonitrile	Chloroform
Methanol	2-methyltetrahydrofuran	Dimethyl formamide
Methyl ethyl ketone	Tetrahydrofuran	N-methylpyrrolidinone
1-butanol	Xylenes	Pyridine
t-butanol	Dimethyl sulfoxide	Dimethyl acetamide

Red Category Solvents

Red Category Solvents	Flash Point (°C)	Reason
Pentane	-49	Very low flash point, good alternative available
Hexane(s)	-23	More toxic than the alternative heptane
Di-isopropyl ether	-12	Very low flash point, good alternative ethers available
Diethyl ether	-40	Very low flash point
Dicholoroethane	15	Carcinogen
Chloroform	N/A	Carcinogen
Dimethyl formamide	57	Toxic
N-methylpyrrolidinone	86	Toxic
Pyridine	20	carcinogen, toxicity, very low threshold limit value TLV for worker exposures
Dimethyl acetamide	70	Toxic
Benzene	-11	Carcinogen, toxic to humans and environment

Explosion, fire at Quebec plan
two; 19 more sent to hospital

SHERBROOKE, Que. — The Canadian Press
Published Thursday, Nov. 08 2012, 3:11 PM EST

Acetone reserves

Hexane Leak Cited for Explosions At Soybean Plant

Radio Iowa, Des Moines; Associated Press

February 2008

Streets explode in Louisville, Kentucky
13 Feb 1981

ignition of <u>hexane</u> <u>vapors</u>

Barton Solvents Plant, Jul 2007

nonconductive flammable liquid

Current approaches to solvent replacement in synthetic chemistry

- No solvent
- Greener conventional solvents
- Unconventional Solvents (Water, Carbon dioxide, Ionic liquids, Lactate esters)

All have advantages and disadvantages which need to be considered when assessing suitability for replacement

“No Coopora nisi Fluida”

- Aristotle believed that “No reaction occurs in the absence of solvent.”

(This is not true!)

Solvent alternatives

A. Use of solventless reactions

B. Use of “non-organic” solvents

C. Processing technology

Advantages to Solventless Organic Reactions

- There is no reaction medium to collect, purify, and recycle.
- Reaction times can be dramatically shortened.
- Lowered energy usage.
- Considerable reduction in batch size volume.
- Less expensive.

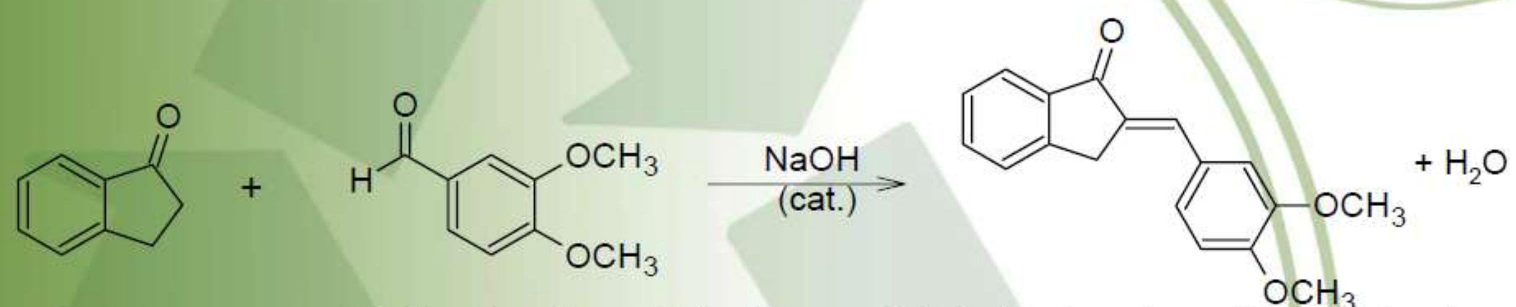
Ways to be Solvent-Free

- **Neat** – reagents react together in the liquid phase in the absence of a solvent.

- **Solid-state synthesis** – two macroscopic solids interact directly and form a third, solid product without the intervention of a liquid or vapor phase.

Neat, isn't it!

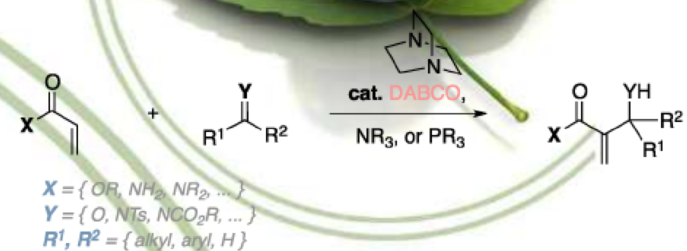
A Solventless Atom Efficient Reaction: The Crossed-Aldol Condensation



1-indanone	3,4-dimethoxybenzaldehyde	2-(3,4-dimethoxybenzylidene)indan-1-one
C_9H_8O = 132.16	$C_9H_{10}O_3$ = 166.18	$C_{18}H_{16}O_3$ = 280.32
m.p. 40-42°C	m.p. 42-45°C	m.p. 183 -185°C

Examples - Neat

- Baylis-Hillman reactions[1]
- Aldol additions[2]



1. For a review, see: Ciganek, E. *Organic Reactions*, **1997**, *51*, 201.,
2. For a review see: Tanaka, K.; Toda, F. "Solvent-Free Organic Synthesis" *Chem. Rev.* **2000**, *100*, 1025-1074.

Examples – Solid State

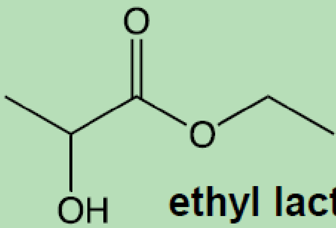
- Oxidations
- Reductions
- Halogenations and Hydrohalogenations
- Michael Additions and Aldol Additions
- Elimination Reactions
- [2+2], [4+2], and [6+2] Cycloaddition Reactions
- Aldol Condensation Reaction

For a review, see: Tanaka, K.; Toda, F. "Solvent-Free Organic Synthesis" *Chem. Rev.* **2000**, *100*, 1025-1074.

Limitations

- Not all reactions will work in the absence of solvent.
- Function of catalysts.
- Exothermic reactions are potentially dangerous.
- Specialized equipment needed for some procedures.
- If aqueous quench and organic extraction are performed, this reduces green benefits.

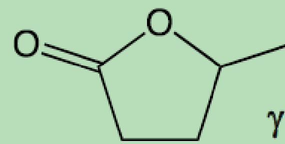
PROPOSED NEW GREEN ORGANIC SOLVENTS



ethyl lactate

low toxicity, biodegradable, renewable

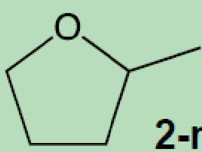
Aparicio, *Green Chem.* (2009) *11*, 65



γ-valerolactone

low toxicity, biodegradable, renewable

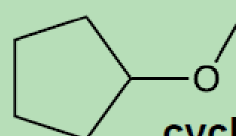
Horvath, *Green Chem.*, 2008, *10*, 238



2-methyltetrahydrofuran

renewable

Aycock, *Org. Process Res. Dev. 2007, 11, 156*

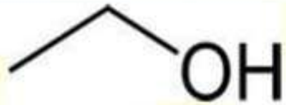
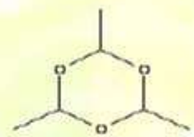
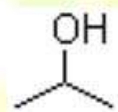
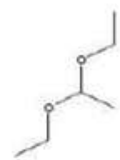
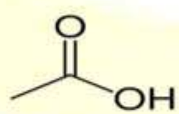
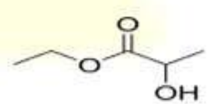
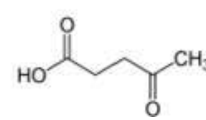


cyclopentylmethylether

doesn't form peroxides, low solubility in water

Watanabe, *Org. Process Res. Dev. 2007, 11, 251*

Green Solvents

- Ethanol 
- Ethyl Acetate 
- Paraldehyde 
- 1,3-Butanediol 
- Acetaldehyde diethyl acetal 
- 3-Ethoxy Butanol 
- Acetic Acid 
- Ethyl Lactate 
- Levulinic acid and esters 

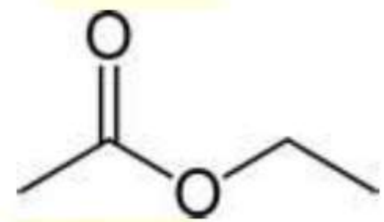
Ethyl Acetate

- ***One of the most popular Solvent***

糖浆

- Molasses $\longrightarrow$ Ethanol $\longleftrightarrow$ Ethyl Acetate
- Esterification reaction

$$CH_3CH_2OH + CH_3COOH \longleftrightarrow CH_3COOCH_2CH_3 + H_2O$$



- **Properties & Applications**
  - Low cost, low toxicity, and agreeable odour.
  - Present in confectionery, perfumes, and fruits.
  - In perfumes, it evaporates quickly, leaving only the scent of the perfume on the skin.
  - In paints act as an activator or hardener
  - As a solvent it is pretty harmless to the environment and to people too.
  - Non-carcinogenic

EA as alternative

Parameters	Ethyl Acetate	Dicholoromethane
Molecular weight (g/mol)	88.10	84.93
Density (20 ^{O}C){g/cm3}	0.897	1.33
Boling Point (^{O}C)	77.1	39.6
Melting Point (^{O}C)	-83.6	-96.7
Flash Point (^{O}C)	13	N/A
Viscosity (25 ^{O}C){cP}	0.426	0.44
n (refractive index) (20 ^{O}C)	1.3720	1.424
Dielectric constant (25 ^{O}C)	6.02	8.93
Azeotropic point with water (20 ^{O}C)	70.4	38.1
Solubility in water (20 ^{O}C){g/100g}	7.8	1.3
Explosion range (vol%)	2.2 to 11	14 to 22

Ethyl Lactate

- ***A renewable Solvent***

- Sugarcane/Molasses $\longrightarrow$ Lactic Acid $\longleftrightarrow$ Ethyl Lactate

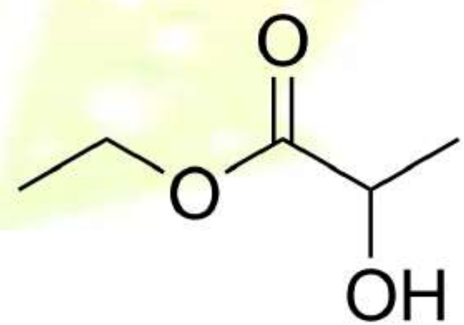
- It's an important organic ester

- Biodegradable solvent with excellent properties and low toxicity being produced by lactic acid aqueous solution and ethanol, via an esterification process

$$CH_3CH(OH)CO_2H + C_2H_5OH \longleftrightarrow CH_3CH(OH)CO_2C_2H_5 + H_2O$$

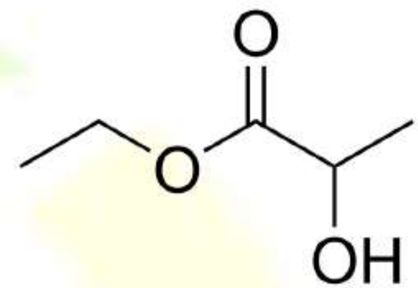
- Variety of lactate esters possible

- Renewable source (non-petrochemical)



Ethyl Lactate

- Attractive Solvent Properties
  - Biodegradable,
  - Easy to recycle,
  - Non-corrosive,
  - Non-carcinogenic
  - Non-ozone depleting
  - Good solvent for variety of processes
  - Low volatility & Non-toxic
  - Low-Cost and Environmentally Friendly



- Commonly used in the paint and coatings industry
  - Potentially has many other applications.

EL as alternative

Parameters	Ethyl Lactate	Methyl Ethyl Ketone
Molecular weight (g/mol)	118.13	72.11
Density (20 ^{O}C){g/cm3}	1.03	0.805
Boling Point (^{O}C)	151 – 155	79.64
Melting Point (^{O}C)	-26	-86
Flash Point (^{O}C)	46	-9
Viscosity (25 ^{O}C){cP}	2.8	0.43
n (refractive index) (20 ^{O}C)	1.4118	1.3788
Dielectric constant (25 ^{O}C)	18.5	8.93
Azeotropic point with water (20 ^{O}C)	No azeotrope 共沸的	73.4
Solubility in water (20 ^{O}C){g/100g}	Totally Soluble	27.5

Ethyl Lactate as an alternative

SOLVENTS	TOXIC RELEASE INVENTORY (TRI)	EVAPORATION RATE	EFFECTIVENESS XYLENE = 1
Xylene	Yes	0.86	1
Toluene	Yes	2.4	1.025
Acetone	Yes	7.7	1.375
N-methyl,1,2 pyrolidone (NMP)	Yes	0.03	3.5
Methyl Ethyl Ketone (MEK)	Yes	6	1.275
Ethyl Lactate	No	0.22	10

Ethyl Levulinate

- ***A renewable Solvent***

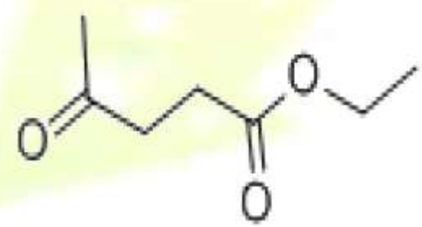
- Sugarcane/Molasses → Levulinic acid Acid → Ethyl Levulinate 乙酰丙酸乙酯

- It's an important organic ester

- Biodegradable solvent with excellent properties and low toxicity being produced by levulinic acid aqueous solution and ethanol, via an esterification process

- Variety of esters possible

- Renewable source (non-petrochemical)



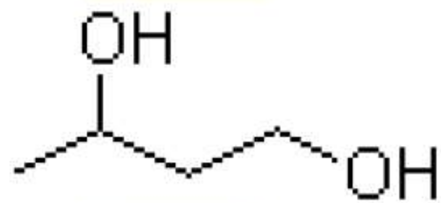
1,3-Butylene Glycol

- ***Solvent for food flavouring agents***

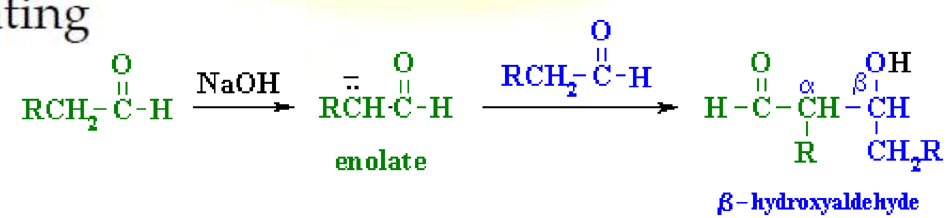
- Molasses ⟶ Ethanol ⟶ Aldehyde ⟶ Aldol ⟶ 1,3-BG

$$CH_3CH(OH)CH_2CHO + H_2 \longrightarrow CH_3CH(OH)CH_2CH_2(OH)$$

2-hydroxyl Buatanone



- **Properties & Applications**
  - Practically odourless, viscous,
  - Hygroscopic liquid of low toxicity.
  - Better efficacy of preservatives
  - Has anti-microbial effect itself
  - Contributes to the preservation of cosmetics against spoilage by micro-organisms.
  - Intermediate in the manufacture of polymeric plasticizers
  - Outstanding humectant
  - Non-irritating

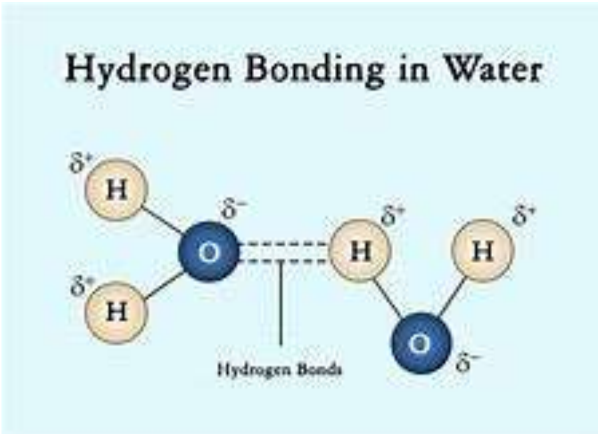


Different Solvents

	Ethyl Lactate	Ethyl Acetate	1,3-Butylene Glycol
Source	Molasses	Ethanol	Acetaldehyde
Application	Paint and coatings industry,	Paints and printing ink industry,	Cosmetic industry
Flash Point, °C **CC - Closed Cup** **OC - Open Cup**	46 CC 130 OC	–4 CC 13 OC	109 CC 115 OC
Solubility	Totally soluble	78 g/l @ 20 C	Totally soluble
Azetropic point with water, °C & composition	No azeotrope	70.4 91.5/8.5	No azeotrope

共沸点

Water as a reaction medium



IMPORTANCE OF WATER FOR LIFE

- 1. Source of H and O for chemical reactions
- 2. a medium for transporting foods, minerals and other substances in a living system
- 3. medium in which dissolvable materials are absorbed from the environment
- (“medium” means: method, material or way)

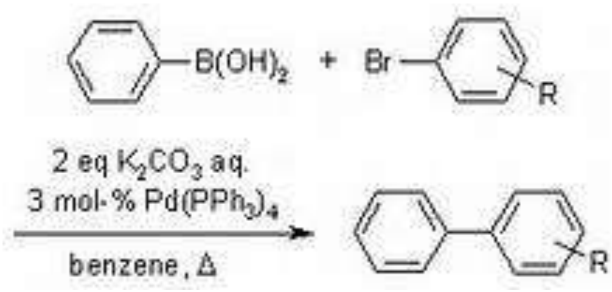
- One of the most obvious alternatives to VOCs.
- Cheap, readily available, and plentiful
- Useful for certain types of reaction but limited because of:
  - Low solubility of organic substrates
  - Compatibility with reagents

Clean up of aqueous waste difficult

Useful in biphasic processes in conjunction with other solvents

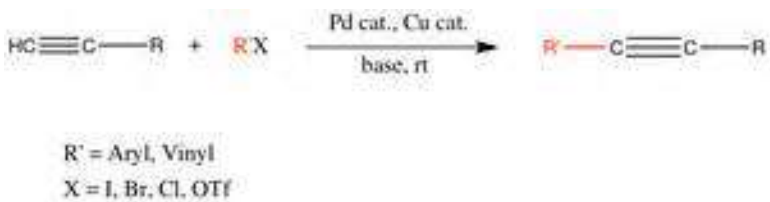
Water as solvent for chemical reactions

- ## Suzuki reaction



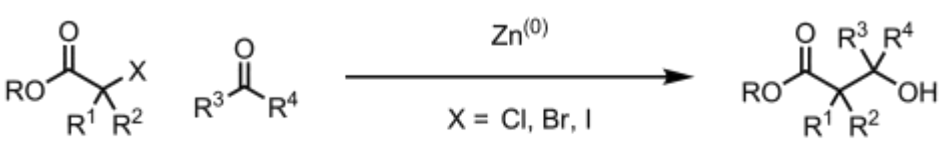
Suzuki reaction is an organic reaction,
where the coupling partners are a boronic acid
and an organohalide catalyzed by a palladium(0) complex.

- ## Sonogashira reaction



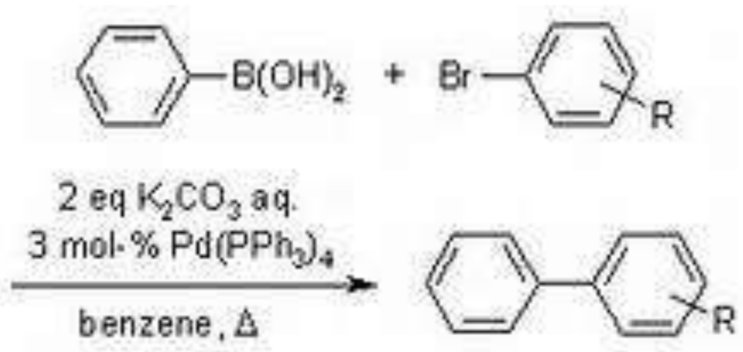
Sonogashira reaction is a cross-coupling reaction, which
employs a palladium catalyst to form a carbon–carbon
bond between a terminal Alkyne and an aryl or vinyl halide

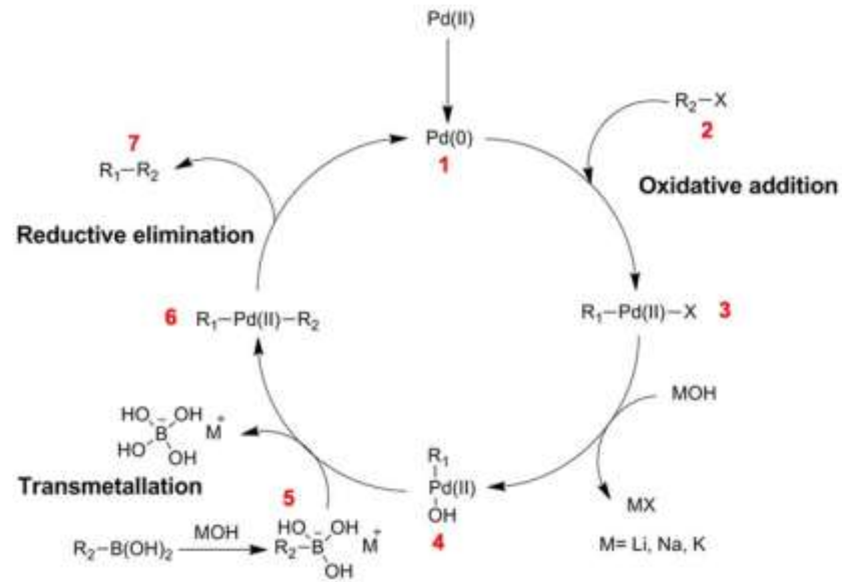
- ## Reformatsky reaction

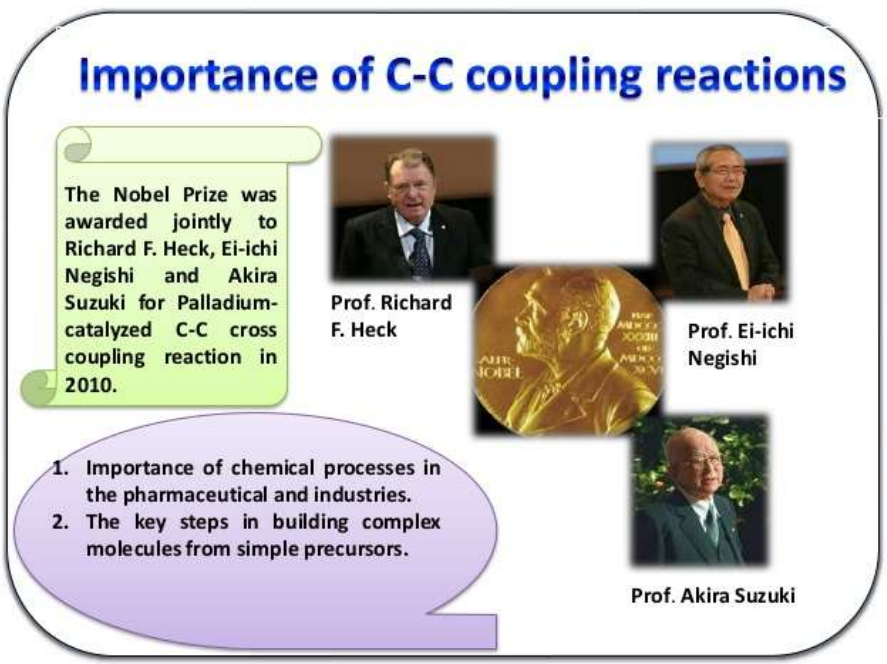


Reformatsky reaction is an organic reaction which
Condenses α-halo esters with aldehydes or ketones,
using a metallic zinc to form β-hydroxy-esters

Suzuki reaction

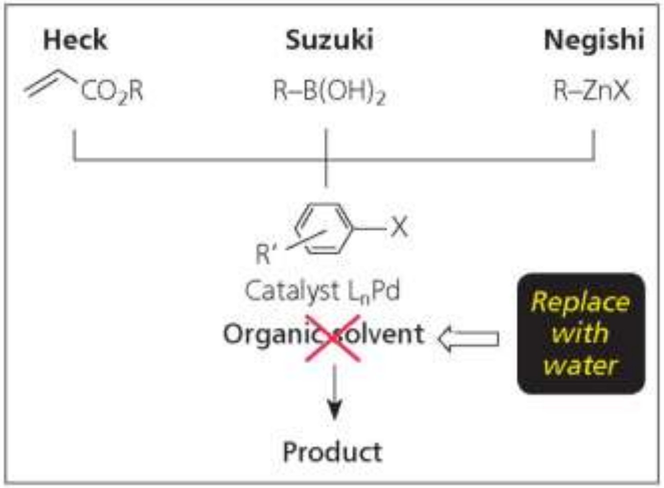


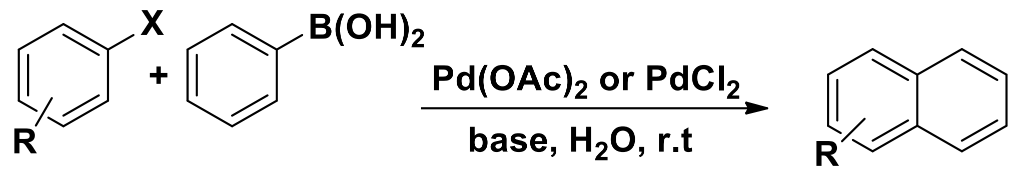




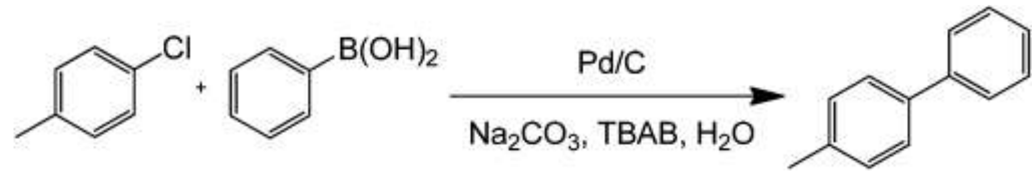
(i) The first step is the oxidative addition of palladium 1 to the halide 2, which further forms the organo-palladium complex 3.
(ii) After reaction with base, organo-palladium species 3 transforms to intermediate 4, a hydroxypalladium complex.
(iii) Intermediate 4 further reacts with the boronate complex 5 (produced by reaction of the boronic acid with base) via trans-metalation to form the organo-palladium species 6.
(iii) The desired product 7 was obtained via reductive elimination, and the original palladium catalyst 1 was restored after one catalytic cycle

Suzuki reaction





X=Br, I   R=*m*-,*p*-OH; *m*-, *p*-COOH



TBAB: tetra-n-butylammonium bromide

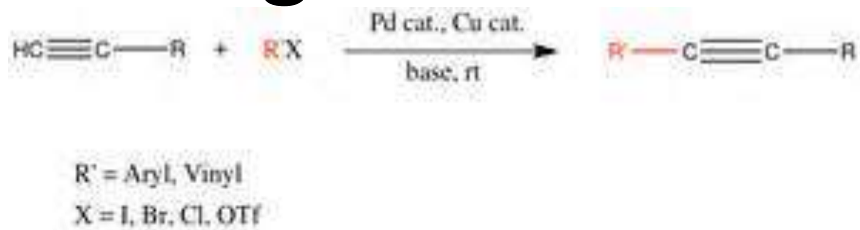
- Palladium acetate, palladium chloride as catalyst
- Sodium hydroxide, sodium carbonate, potassium carbonate as base.
- Then this reaction can take place at room temperature.
- For the reaction in water system, it requires the reactants water-soluble such as benzene bromide, benzene iodine.
- For the reactants with low water-solubility, we can add little organic solvent to increase their solubility such as alcohol.

Several Advantages of Suzuki Coupling Reactions:

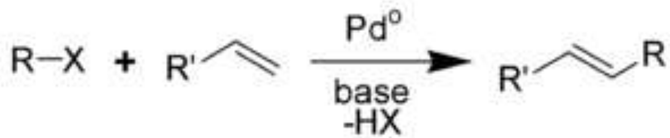
- Ready availability of reagents: hydroboration and transmetalation
- Mild reaction conditions
- Easy use of the reaction both in aqueous and heterogeneous conditions
- Toleration of a broad range of functional groups
- High regio- and stereoselectivity of the reaction
- Insignificant effect of the steric hindrance
- Use of a small amount of catalysts
- Application in one-pot synthesis
- Nontoxic reaction
- Easy separation of inorganic boron compounds

Sonogashira reaction

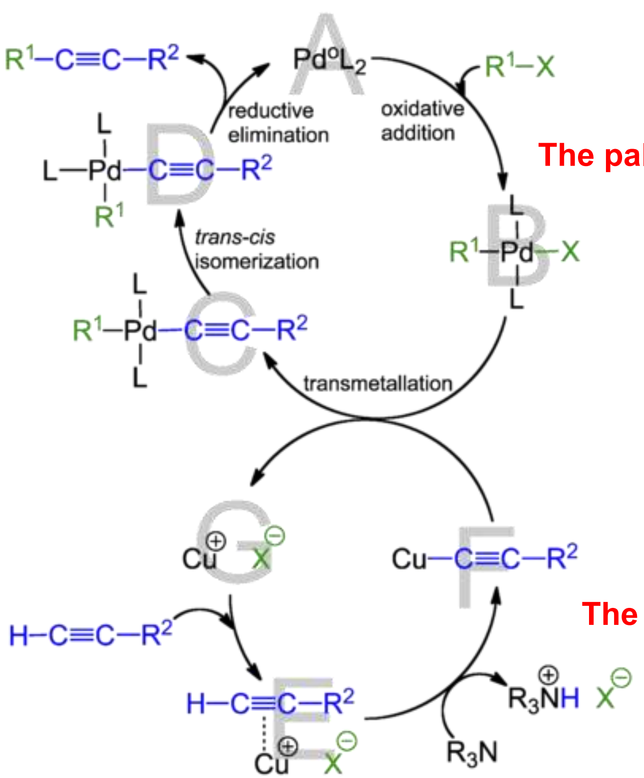
Sonogashira reaction



Heck reaction



Kenkichi Sonogashira



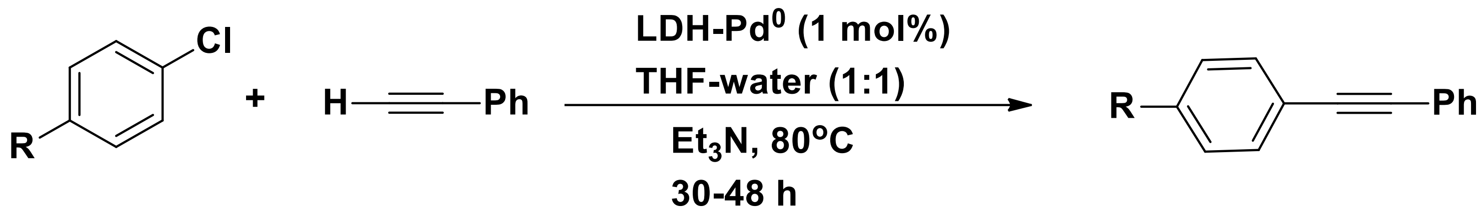
The palladium cycle

(i) The active palladium catalyst is Pd^0L_2, complex A, which reacts with the aryl or vinyl halide in an oxidative addition to produce a Pd^{II} intermediate, complex B.
(ii) Complex B reacts in a transmetallation with the copper acetylide, complex F, which is produced in the copper cycle, to give complex C, releasing the copper halide, complex G.
(iii) Both organic ligands are trans oriented and convert to cis in a trans-cis isomerization to produce complex D.
(iv) In the final step, complex D undergoes reductive elimination to produce the alkyne, with regeneration of the palladium catalyst.

The copper cycle

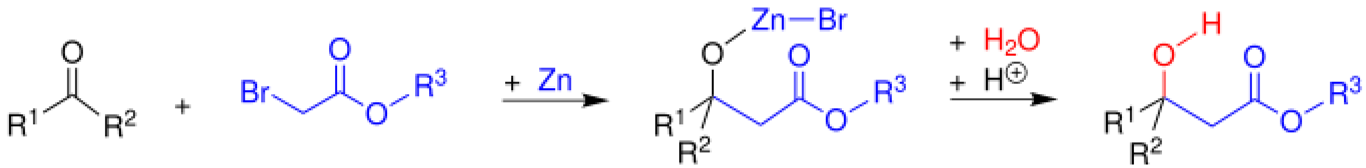
(i) The presence of base results in the formation of a pi-alkyne complex, complex E, which makes the terminal proton on the alkyne more acidic, leading to the formation of the copper acetylide, compound F.
(ii) Compound F continues to react with the palladium intermediate B, with regeneration of the copper halide, G.

Sonogashira reaction

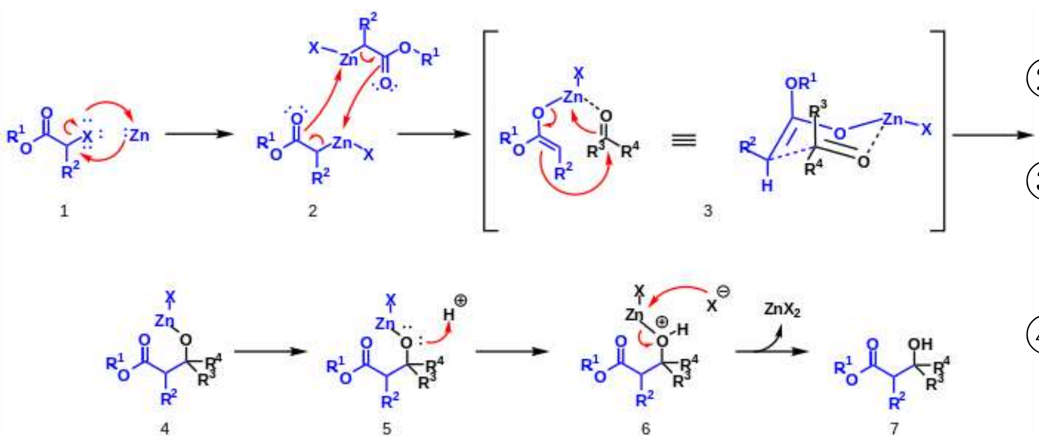


- The Sonogashira reaction is typically run under mild conditions.
- The cross-coupling is carried out at room temperature with a base, typically an amine, such as triethylamine, and water-mixed solution acts as the solvent.
- The reaction medium must be basic to neutralize the hydrogen halide produced as the byproduct of this coupling reaction
- Other bases such as potassium carbonate or cesium carbonate are occasionally used.
- In addition, de-aerated conditions are formally needed for Sonogashira coupling reactions because the palladium(0) complexes are unstable in the air, and oxygen promotes the formation of homo-coupled acetylenes.
- Recently, development of air-stable organo-palladium catalysts enable this reaction to be conducted in the ambient atmosphere.

Reformatsky reaction



The **Reformatsky reaction** is an organic reaction which condenses aldehydes or ketones, with α-halo esters, using a metallic zinc to form β-hydroxy-esters



① Zinc metal is inserted into the carbon-halogen bond of the α-haloester by oxidative addition **1**.

② This compound dimerizes and rearranges to form two zinc enolates **2**.

③ The oxygen on an aldehyde or ketone coordinates to the zinc to form the six-member chair like transition state **3**.

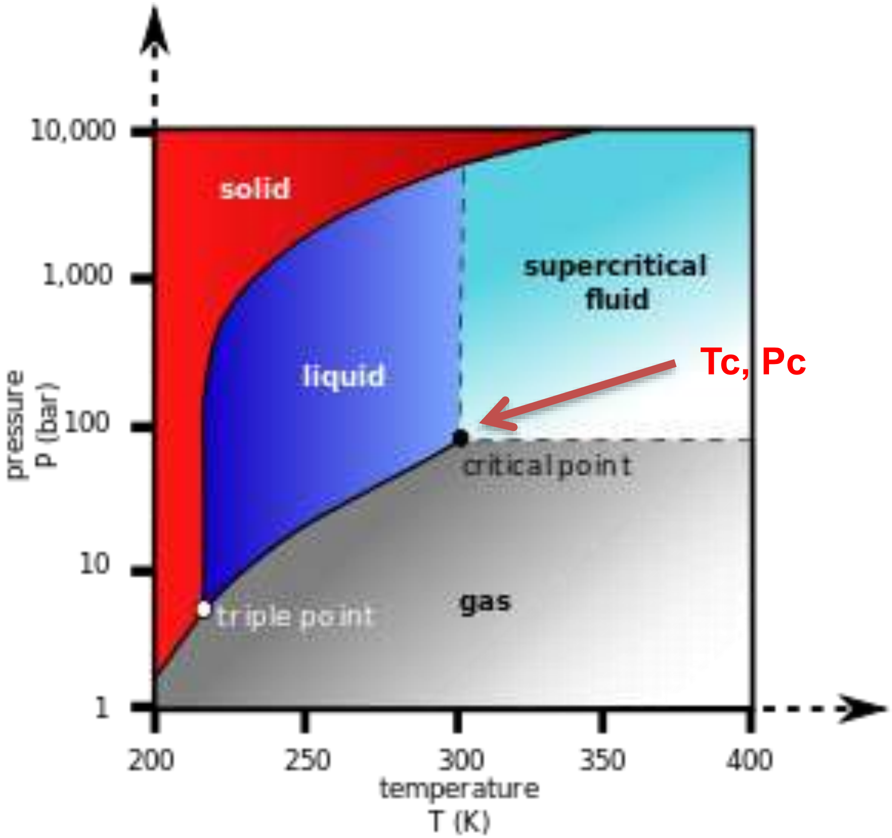
④ A rearrangement occurs in which zinc switches to the aldehyde or ketone oxygen and a carbon-carbon bond is formed **4**.

⑤ Acid workup **5**,**6** removes zinc to yield zinc(II) salts and a β-hydroxy-ester **7**.

Carbon Dioxide

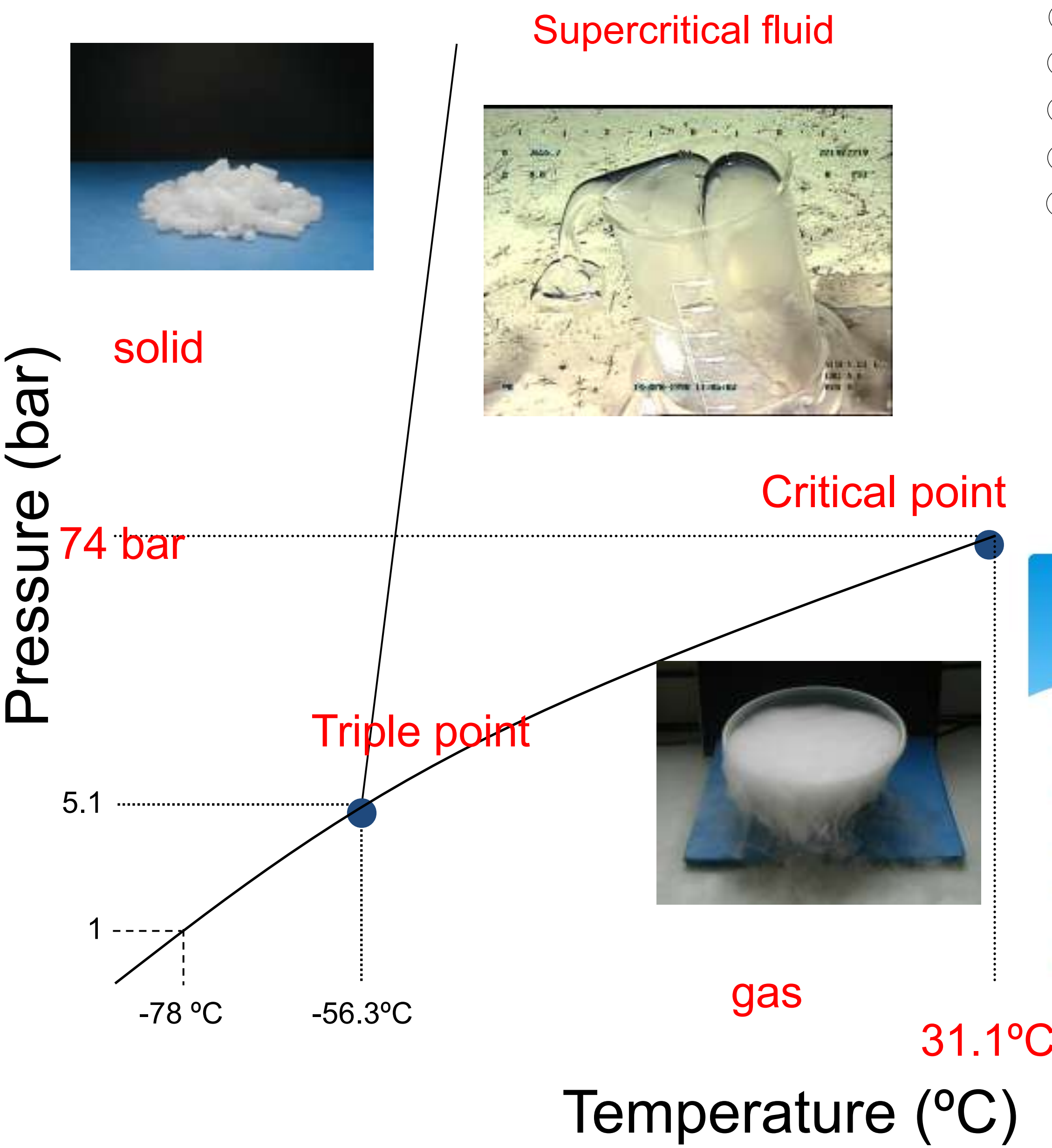
- Similar advantages to water
  – Natural, cheap, plentiful (too much of it!)
  – Available in >99.9% pure form, £70/$110 per 25kg.
  – By-product of brewing, ammonia synthesis, combustion
- Already being adopted in a variety of commercial processes (see later)
- Non-toxic and properties well understood
  – asphyxiant (窒息的) at high concentrations
- Easily removed and recycled, and can be disposed of with no net increase in global CO_2
  – Simple product isolation by evaporation, to 100% dryness.
- No organic solvent effluent
- Potential for product processing (extraction, particle formation, chromatography etc.)

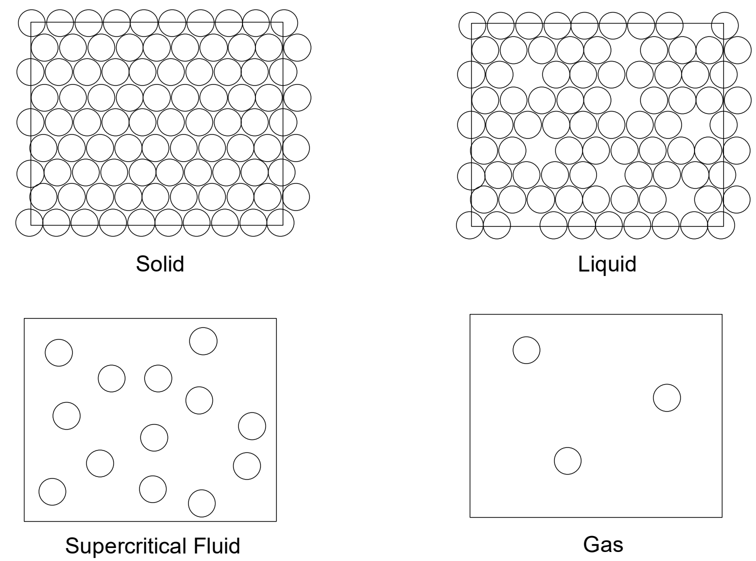
Supercritical fluids

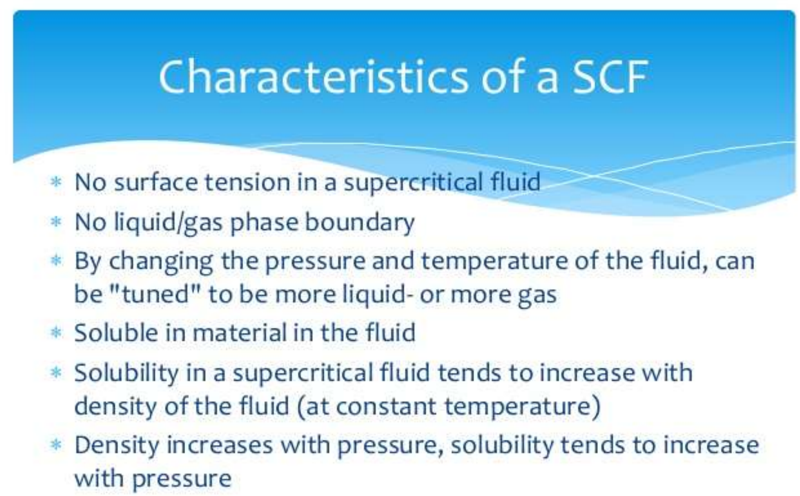


- A **supercritical fluid** is any substance at a temperature and pressure above its critical point, where distinct liquid and gas phases do not exist. It can effuse through solids like a gas, and dissolve materials like a liquid.
- The ***critical temperature*** of a substance is the temperature at and above which vapor of the substance cannot be liquefied, no matter how much pressure is applied.
- Every substance has a critical temperature.
- The ***critical pressure*** of a substance is the pressure required to liquefy a gas at its critical temperature.

Supercritical fluids are intermediate between liquids and gases







Characteristics of a SCF

- No surface tension in a supercritical fluid
- No liquid/gas phase boundary
- By changing the pressure and temperature of the fluid, can be "tuned" to be more liquid- or more gas
- Soluble in material in the fluid
- Solubility in a supercritical fluid tends to increase with density of the fluid (at constant temperature)
- Density increases with pressure, solubility tends to increase with pressure

Other advantages of supercritical fluid CO_2

- High diffusion rates offer potential for increased reaction rates.
- Potential for homogeneous catalytic processes.
  - High solubility of light gases, some catalysts and substrates; bring all together in single homogeneous phase
- Inert to oxidation; resistant to reduction
  - Excellent medium for oxidation and reduction reactions.
- Small amounts of co-solvents can further modify solvent properties
- High compressibility
  - Large change in solvent properties for relatively small change in pressure – infinite range of solvent properties available
  - Ability to tune solvent to favour a particular reaction pathway simply by optimising temperature or pressure.

Other advantages of supercritical fluid CO_2

- should be handled in standard high-pressure equipment on lab or industrial scale

- Non-toxic, non-flammable, and inexpensive.

- Non-protic and generally unreactive.

- Product isolation to total dryness is achieved by simple decompression.

- CO_2 can be recovered and reused

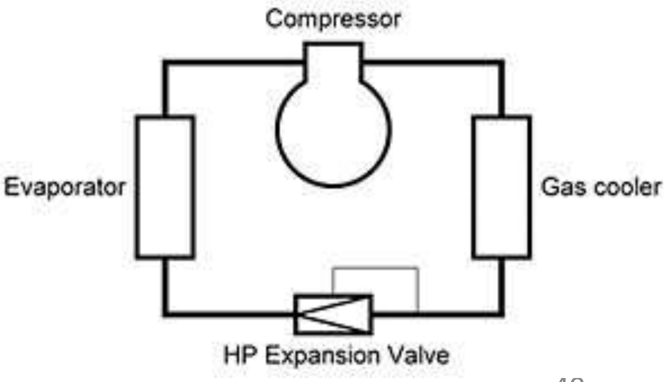
Current industrial applications of CO_2 technology

- Union Carbide, Unicarb Technology
  - Replaces 40-90% of VOCs with CO_2.
    - Coatings on aerospace parts
    - Chocolate biscuits (milk fat fractionation??)

Chem. Eng. News, June 14 1999, 77 (24), 13.

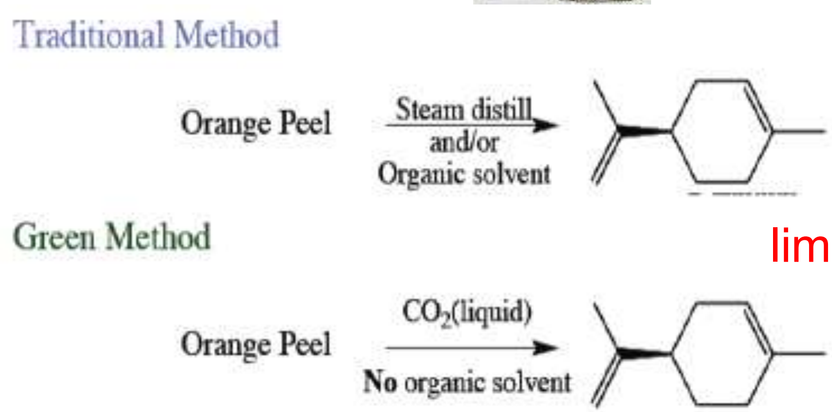
- CO_2 Refrigeration
  - Large scale units now in operation.
  - ASDA distribution centres in Falkirk and Skelmersdale (2003)
    - Amongst the biggest temperature controlled buildings in the UK (412,000m^3)

- No ozone depletion potential and insignificant global warming potential
- Carbon dioxide has a very high volumetric capacity, as much as 5 or 6 times hydrofluorocarbon at medium temperature, which means that the same volume of CO_2 can absorb much more heat than hydrofluorocarbon .



Extraction using $scCO_2$

- Extensively used for ‘natural’ coffee decaffeination; alternative uses CH_2Cl_2 (also tea)
- Extraction of hops（啤酒花）for Brewing
- Many other extraction processes
  - Often use liquid rather than supercritical CO_2.
  - Spices
  - Essential oils and fragrances
- Simple product isolation evaporation, to 100% dryness.
- No solvent residues or effluent



limonene

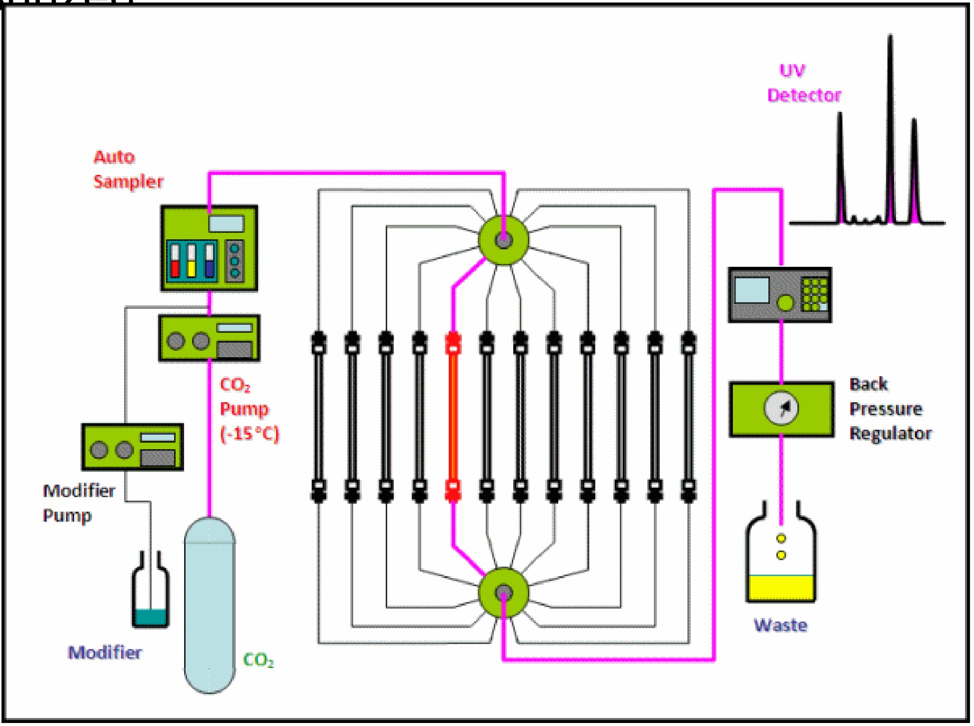
McKenzie, L. C.; Thompson, J. E.; Sullivan, R.; Hutchison, J. E. "Green chemical processing in the teaching laboratory: A convenient liquid CO2 extraction of natural products,“ *Green Chem.* **2004**, 355-358

SCF Chromatography

Supercritical Fluid Chromatography (SFC) is a form of normal phase chromatography, first used in 1962, that is used for the analysis and purification of low to moderate, thermally labile molecules.

Principles are similar to those of high performance liquid chromatography (HPLC), however SFC typically utilizes carbon dioxide as the mobile phase; therefore the entire chromatographic flow path must be pressurized.

- Widely used
  - Gives superior resolution
  - Solvent power modified by pressure
  - Easy product isolation
  - Negligible solvent waste



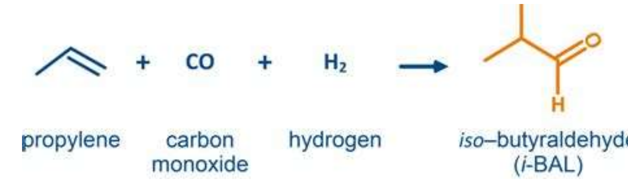
$scCO_2$ as a reaction medium

- Use of conventional organic solvents often leads to the formation of hazardous waste, the disposal of it is a matter of environmental concern.
- Carbon dioxide is a green reaction medium and can replace conventional organic solvents, because of:

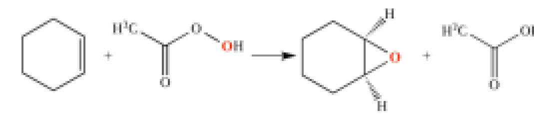
- It is benign and leads to elimination/reduction of hazardous wastes
- The reactions can be pressure-tuned to eliminate transport resistance, increase solvent power and heat capacity.
- The density, viscosity and diffusivity of $ScCO_2$ can be varied continuously between those of liquid and gaseous CO_2 by varying the temperature and/or pressure.
- Increased reaction rate, improved selectivity, and elimination of mass transfer problems

scCO$_2$ as a reaction medium

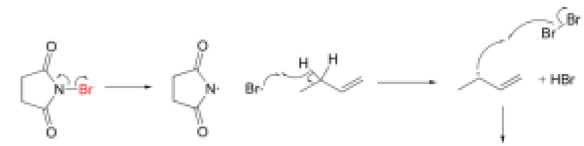
- Hydrogenation/hydroformylation



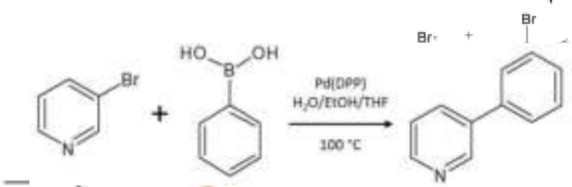
- Epoxidation



- Radical reactions

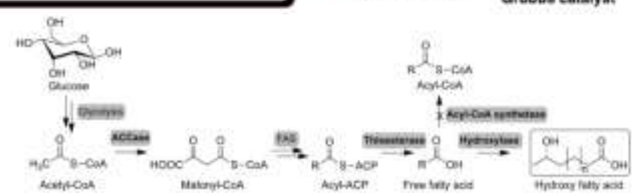


- Pd-mediated C-C bond formation



- Ring closing metathesis

- Biotransformations

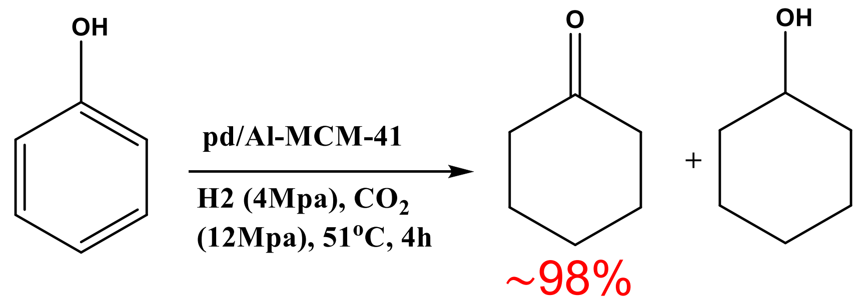


- Polymerisation

R.S. Oakes, A.A. Clifford and C.M. Rayner, *J. Chem. Soc., Perkin Trans. 1, 2001*, 917.

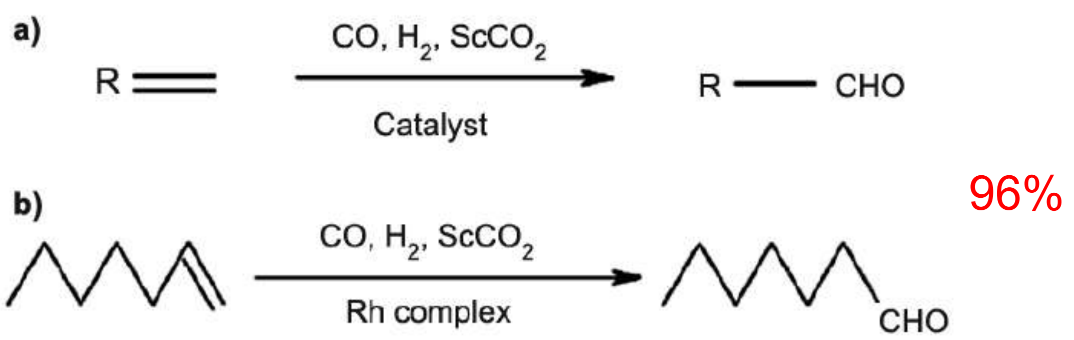
$scCO_2$ for chemical reactions

(1) Hydrogenation reaction



Advanced synthesis and catalysis, 2009, 351, 1912-1924

(2) Hydroformylation

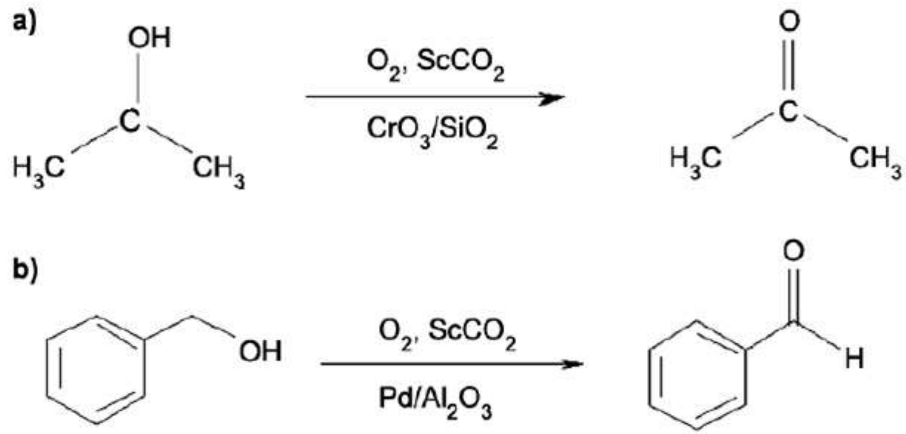


(a) Hydroformylation reaction; (b) hydroformylation of 1-hexene in ScCO2

Tadd A R, Marteel A, Mason M R, Davies J A & Abraham M A, *J Supercrit Fluids*, 25 (2003) 183.

$scCO_2$ for chemical reactions

3. Oxidation reaction

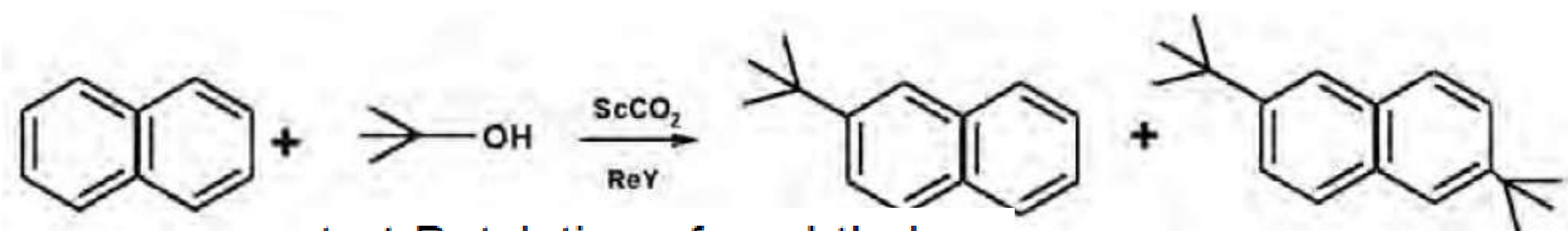


Oxidation reactions in $ScCO_2$

(a) Propanol to acetone; (b) Benzyl alcohol to benzaldehyde

Jenzer G, Mallat T & Baiker A, *Catal Lett,* 73 (2001) 5.
Glaser R, Josl R & Willardt J, *Topics Catal,* 22 (2003) 31

4. C-C bond formation reaction



tert-Butylation of naphthalene

Marathe R P, Mayadevi S, Pardhy S A, Sabne S M & Sivasanker S, *J Mol Catal,* 181 (2002) 201.

$scCO_2$ for chemical reactions

$scCO_2$ as reactants

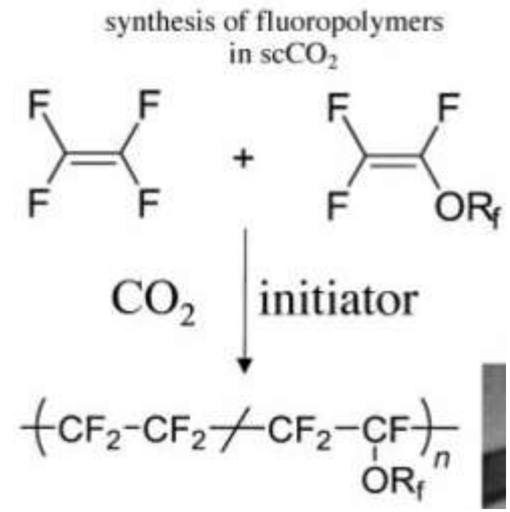
$$CO_2 + H_2 \xrightarrow[scCO_2,\ NEt3]{Ru\text{-}cat} HCOOH$$ formic acid

$$CO_2 + H_2 + CH_3OH \xrightarrow[scCO_2,\ NEt3]{Ru\text{-}cat} HCOOCH_3 + H_2O$$ methyl formate

$$CO_2 + H_2 + NH(CH_3)_2 \xrightarrow[scCO_2,\ NEt3]{Ru\text{-}cat} HCON(CH_3)_2 + H_2O$$ N,N-Dimethylformamide

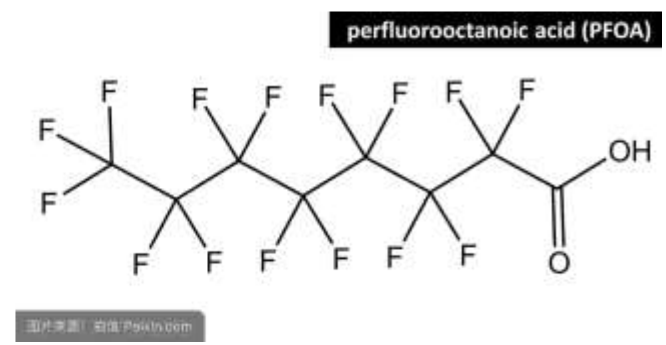
Chemical Synthesis

Tetrafluoroethylene



vinylidene fluoride

- Fluoropolymer synthesis
  - Dupont $275 million, 2.5 million lb/y
  - Replaces CFCs as solvents used previously (now banned by Montreal Protocol)
  - Easy polymer isolation and drying, and minimal waste,
  - inertness to chain transfer reactions,
  - its low viscosity to facilitates diffusion,
  - Effectively precipitating semicrystalline fluoropolymers and its high solubility for many amorphous fluoropolymers.



- Perfluorooctanoic acid
- its dominant use is as an emulsifier for the emulsion polymerization of fluoropolymers such as PTFE, polyvinylidene fluoride, and fluoroelastomers.

Angew. Chem. Int. Ed., 2001, 40, 518; *J. of Supercritical Fluids*, 2009, 47, 447–457

Problems using $scCO_2$

- Moderate pressures required
  - Standard HPLC apparatus used in lab, reactors made of stainless steel, many commercially available.
  - Can be expensive for large scale work
- Weak solvent
  - Relatively non-polar. Use of co-solvents (MeOH, MeCN, THF, toluene)
  - Simple modification of reagents to improve solubility
- Energy considerations
  - Compression of CO_2 requires energy
- Reacts in the presence of good nucleophiles
  - Often reversible, can be exploited synthetically

Supercritical fluids

Table 1. Critical properties of various solvents (Reid et al., 1987)

Solvent	Molecular weight	Critical temperature	Critical pressure	Critical density
	g/mol	K	MPa (atm)	g/cm^3
Carbon dioxide (CO_2)	44.01	304.1	7.38 (72.8)	0.469
Water (H_2O)	18.015	647.096	22.064 (217.755)	0.322
Methane (CH_4)	16.04	190.4	4.60 (45.4)	0.162
Ethane (C_2H_6)	30.07	305.3	4.87 (48.1)	0.203
Propane (C_3H_8)	44.09	369.8	4.25 (41.9)	0.217
Ethylene (C_2H_4)	28.05	282.4	5.04 (49.7)	0.215
Propylene (C_3H_6)	42.08	364.9	4.60 (45.4)	0.232
Methanol (CH_3OH)	32.04	512.6	8.09 (79.8)	0.272
Ethanol (C_2H_5OH)	46.07	513.9	6.14 (60.6)	0.276
Acetone (C_3H_6O)	58.08	508.1	4.70 (46.4)	0.278
Nitrous oxide (N_2O)	44.013	306.57	7.35 (72.5)	0.452

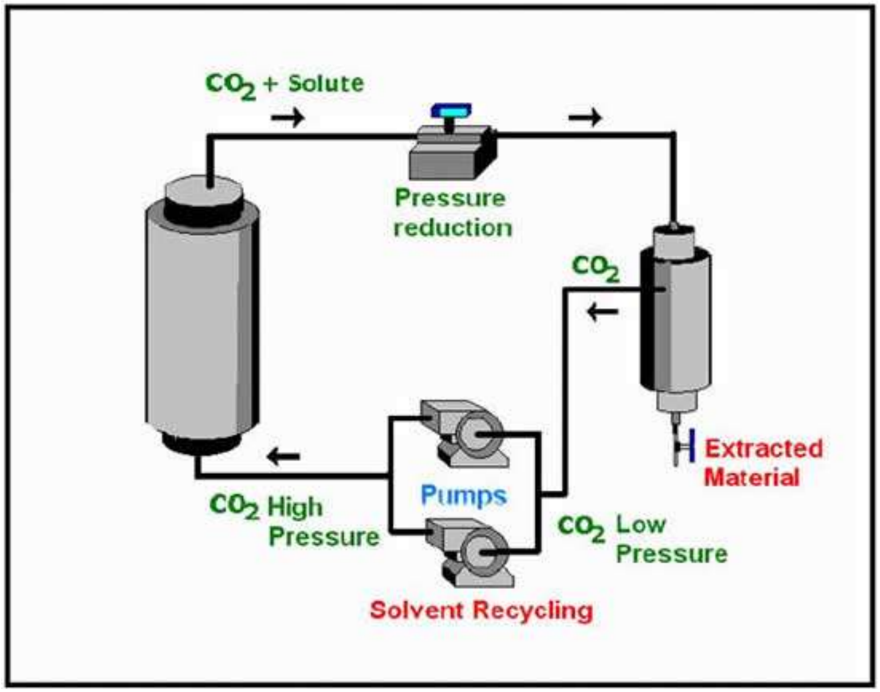
Properties of Supercritical fluids

- There is no surface tension in a supercritical fluid, as there is no liquid/gas phase boundary.
- One of the most important properties is the solubility of material in the fluid.
- All supercritical fluids are completely miscible with each other, so for a mixture, a single phase can be guaranteed if the critical point of the mixture is exceeded.

Supercritical fluids

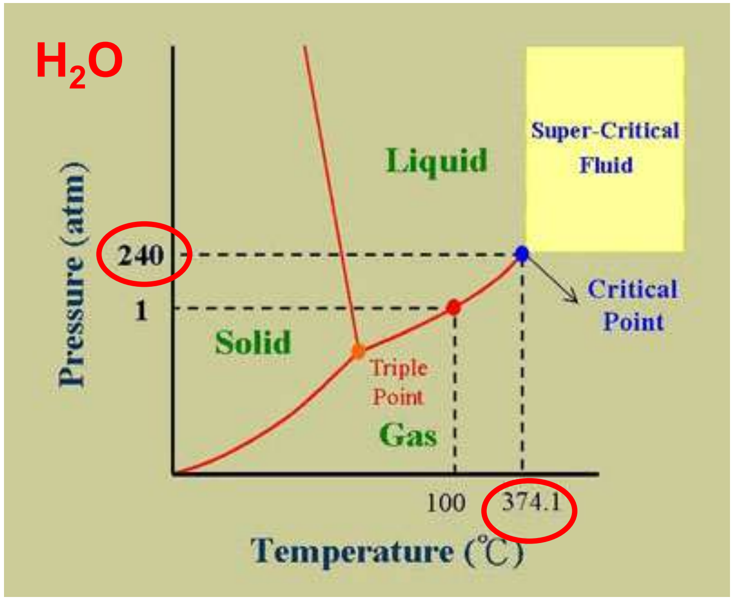
- Supercritical fluid extraction
- Supercritical fluid decomposition
- Dry-cleaning
- Supercritical fluid chromatography
- Chemical reactions
- Impregnation and dyeing
- Nano and micro particle formation
- Generation of pharmaceutical cocrystals
- Supercritical drying
- Supercritical water oxidation
- Supercritical water hydrolysis
- Supercritical water gasification
- Supercritical water gasification
- Biodiesel production
- Enhanced oil recovery and carbon capture and storage

Supercritical fluid extraction



- The advantages of supercritical fluid extraction (compared with liquid extraction) are that it is relatively rapid because of the low viscosities and high diffusivities associated with supercritical fluids.
- The extraction can be selective to some extent by controlling the density of the medium.
- The extracted material is easily recovered by simply depressurizing, allowing the supercritical fluid to return to gas phase and evaporate leaving little or no solvent residues.

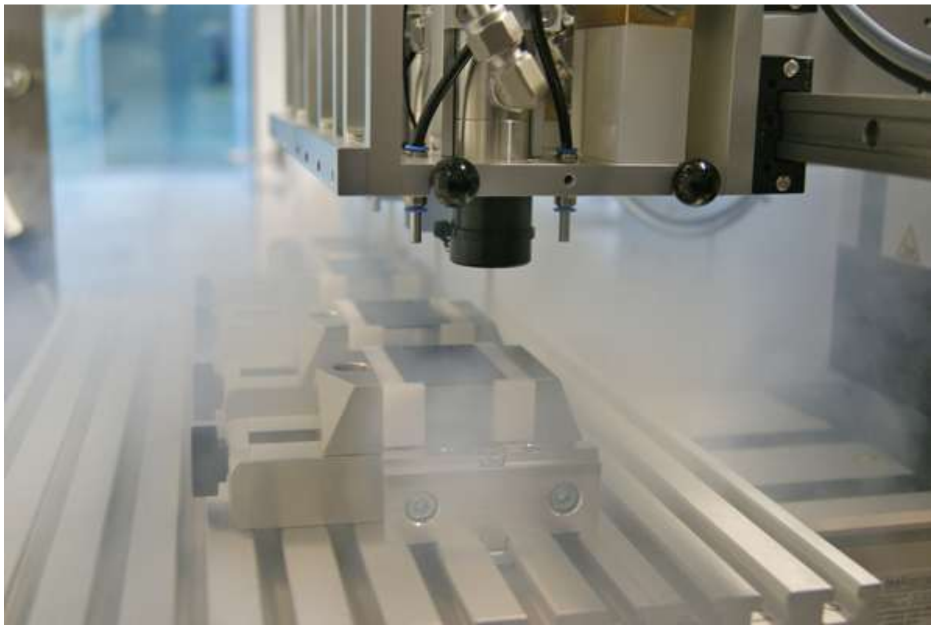
Supercritical fluid decomposition



$$C_nH_mO_k + (2n-k)H_2O \rightarrow nCO_2 + \left(2n + \frac{m}{2} - k\right)H_2$$

- Supercritical water can be used to decompose biomass via supercritical water gasification of biomass.
- Biomass gasification can be used to produce hydrocarbon fuels for use in an efficient combustion device or to produce hydrogen for use in a fuel cell.
- Hydrogen yield can be much higher than the hydrogen content of the biomass due to steam reforming where water is a hydrogen-providing participant in the overall reaction.

Other application of SCD

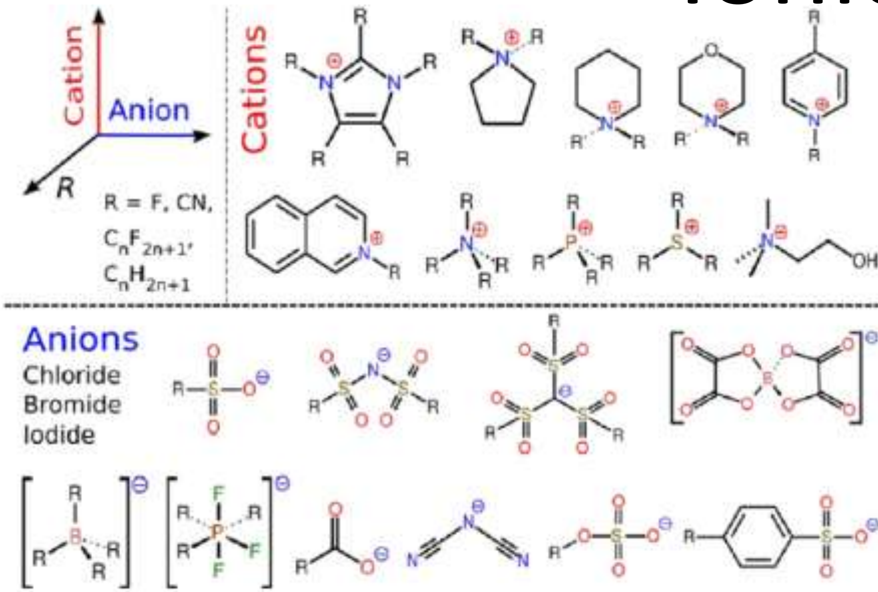


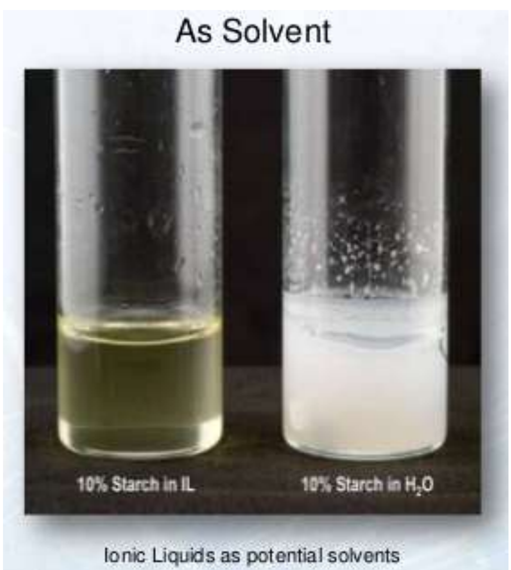
- Supercritical carbon dioxide (SCD) can be used instead of PERC (perchloroethylene) or other undesirable solvents for dry-cleaning.
- Supercritical carbon dioxide sometimes intercalates into buttons, and, when the SCD is depressurized, the buttons pop, or break apart.
- Detergents that are soluble in carbon dioxide improve the solvating power of the solvent.

Supercritical fluids for chemical reactions

- Changing the conditions of the reaction solvent can allow separation of phases for product removal, or single phase for reaction.
- Rapid diffusion accelerates diffusion controlled reactions. Temperature and pressure can tune the reaction down preferred pathways, e.g., to improve yield of a particular chiral isomer.
- There are also significant environmental benefits over conventional organic solvents.

Ionic liquids

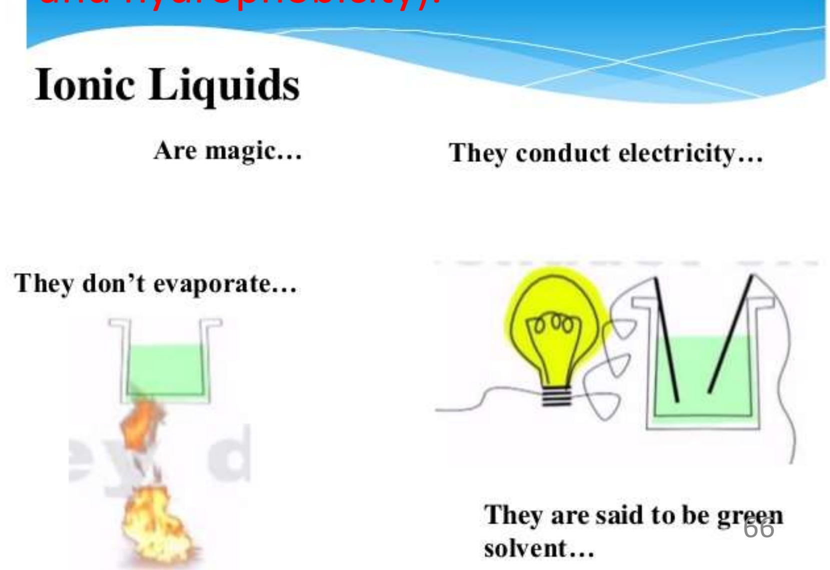




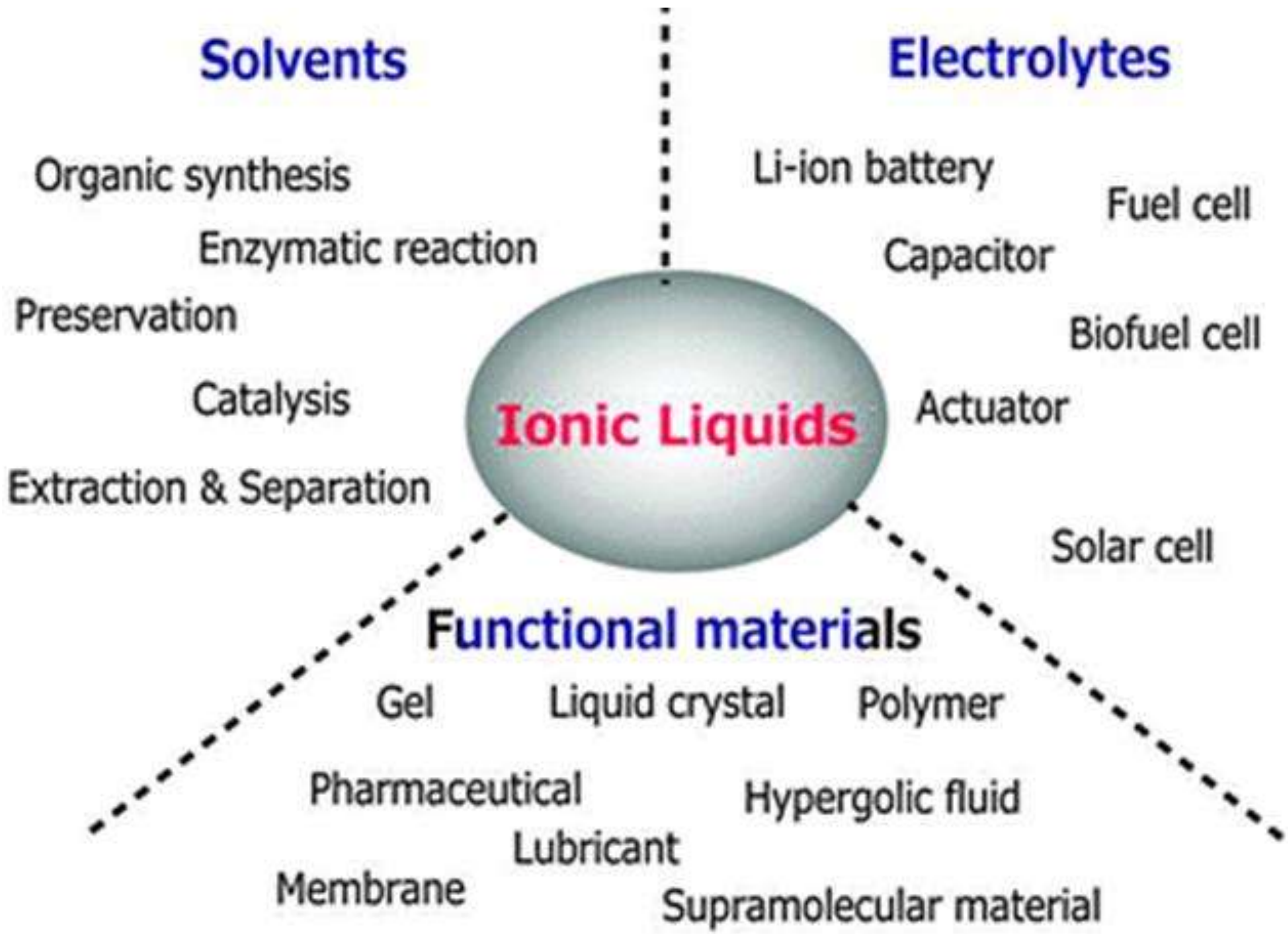
Ionic Liquids as potential solvents

Journal of Molecular Liquids, 2017, 227, 44–60.

- An **ionic liquid** is a salt in the liquid state, whose melting point is below 30 °C, with nonvolatility, nonflammability, thermal stability, and controlled miscibility) than from conventional solvents.
- Typically consist of organic cation (often ammonium or phosphonium salt) and inorganic anion.
- A wide diversity in ionic liquid structure is possible, and by altering either the cationic or anionic component of an IL, resulting varied physical properties (melting point, viscosity, density, solubility, and hydrophobicity).



Ionic liquids

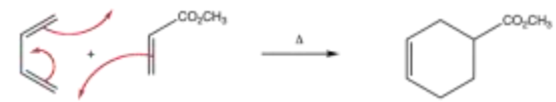


Properties of Ionic Liquids

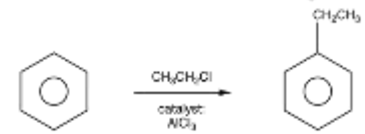
- Good solvents for a wide range of organic, inorganic and polymeric compounds
- Anion and cation can be fine tuned to give a wide range of solvent properties (e.g. melting point, viscosity, density, solubility, hydrophilicity, and hydrophobicity)
- Wide range of reactions already demonstrated in this medium
- Can be used in conjunction with other alternative solvents (particularly CO_2)
- Be recyclable (essential for widespread use) although there may be regulatory problems with this.
- Be effectively, properties similar to many other high boiling, polar solvents.

Ionic Liquids as Reaction Media

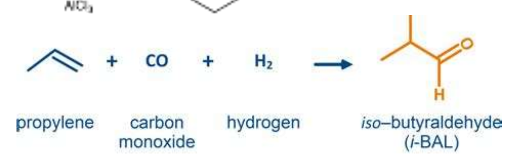
- Diels-Alder reactions



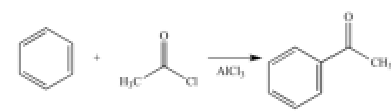
- Alkylation reactions



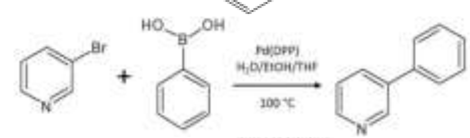
- Hydroformylation reactions



- Friedel Crafts reactions

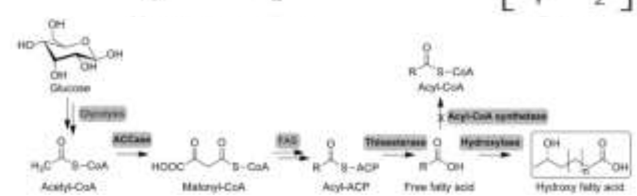


- Pd-mediated C-C bond formation



- Alkene polymerisation

- Biotransformations

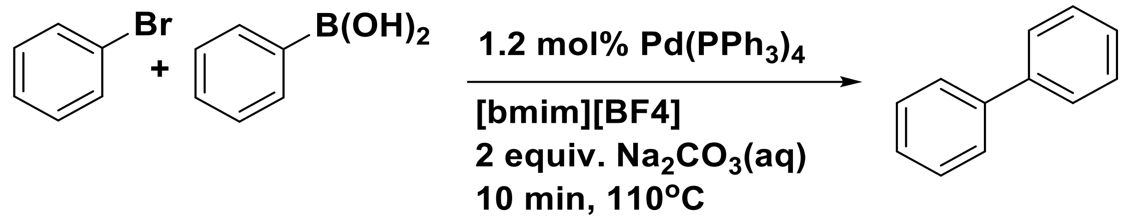


T. Welton, *Chem. Rev.*, **1999**, *99*, 2071.

Ionic liquids

6 h in toluene–ethanol

- Suzuki reaction

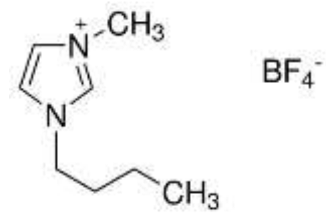


Shorter time

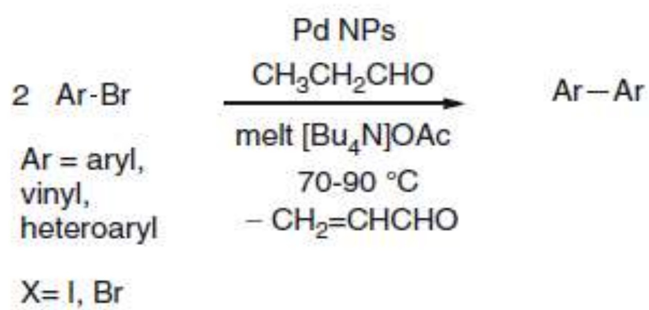
[bmim][BF_4]: 1-Butyl-3-methylimidazolium tetrafluoroborate

1-丁基-3-甲基咪唑四氟硼酸盐

Chem Commun., 2000, 1249–1250

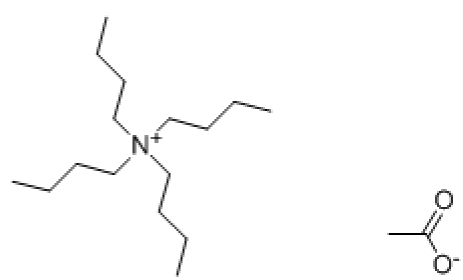


- Ullmannn Homo-Coupling



[Bu_4N]Oac: Tetrabutylammonium acetate

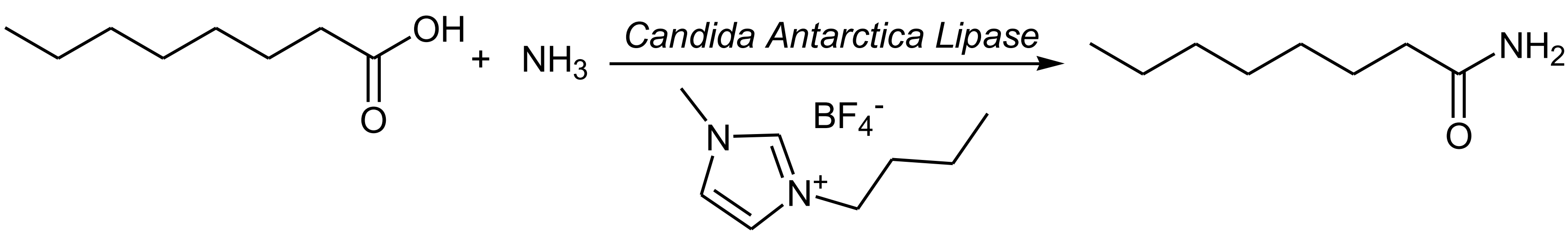
四丁基醋酸铵



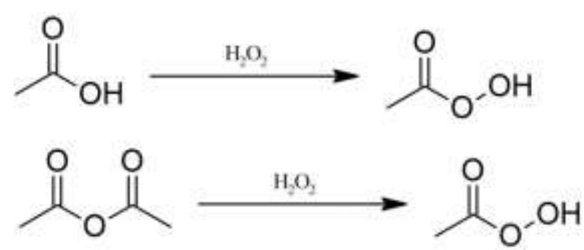
Chem Eur J, 2009, 15:1272–1279

Biotransformations in ILs

- *Candida Antarctica Lipase*(南极假丝酵母脂肪酶) catalyses alcoholysis, ammoniolysis, and perhydrolysis reactions in ILs:



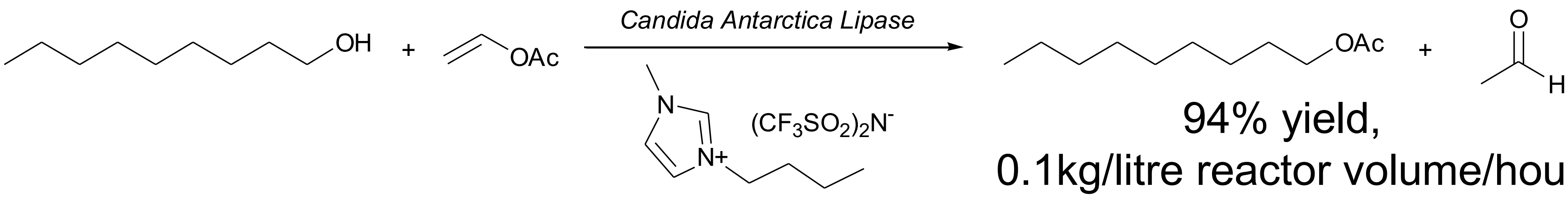
- Reaction rates comparable with or better than those observed in organic media.
- Products usually extracted with ether



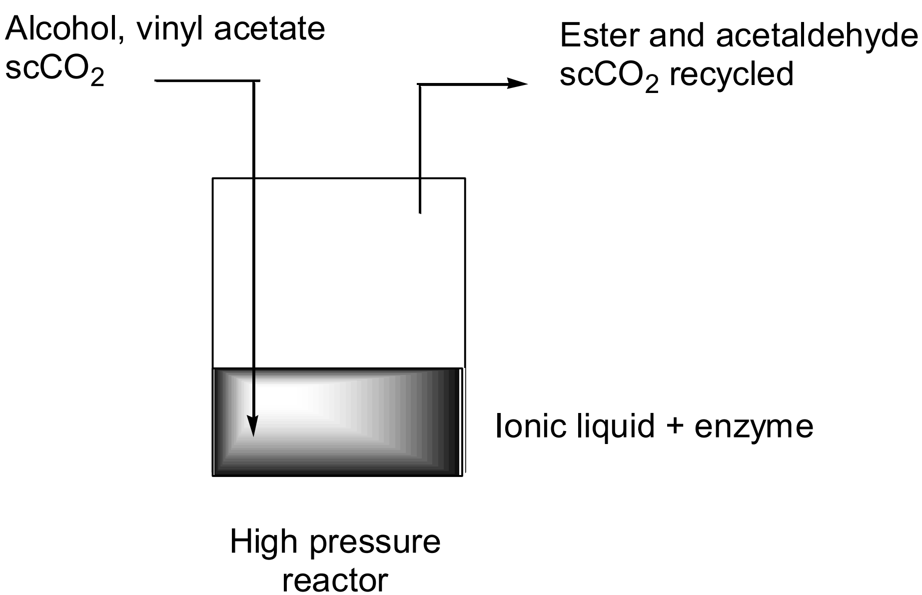
R.M. Lau, F. van Rantwijk, K.R. Seddon and R.A. Sheldon, *Org. Lett.*, 2000, 4189

Biocatalysis in Ionic Liquids using $scCO_2$ as mobile phase

- Continuous process reported by Reetz and Leitner, combines green solvents:



94% yield,
0.1kg/litre reactor volume/hour



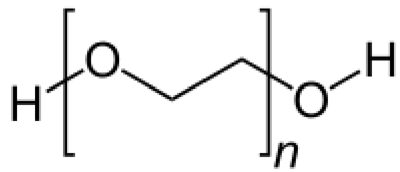
- Enzyme suspended in ionic liquid phase
- Substrates injected using flow of $scCO_2$
- Substrate more soluble in ionic liquid than in $scCO_2$
- Product has good solubility in $scCO_2$ and readily extracted
- Ionic liquid and enzyme reused
- Ionic liquid does not dissolve in $scCO_2$

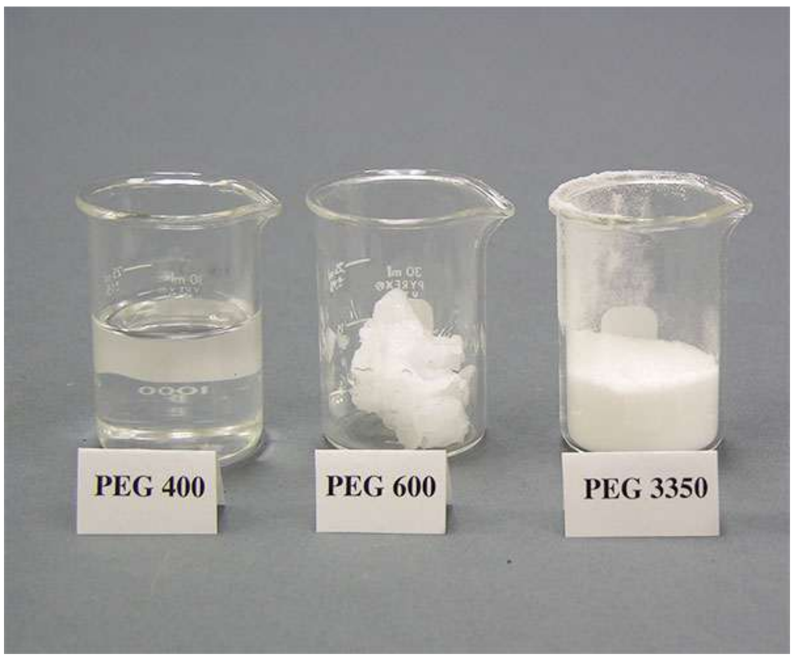
Chem. Commun., 2002, 992.

Problems with Ionic Liquids

- But…
  – Expensive compared to other solvents although cheaper versions are appearing
  – Have to be prepared
    - usually involved use of other solvents so must have real advantages
  – Work-up to separate/extract products usually involves other solvents
  – Recycling also usually involves other solvents to extract unwanted residues
  – Questionable toxicity – some certainly are toxic and have been shown to have a detrimental effect on aquatic life – problem as not VOC so will tend to persist in local environment, on land/sea etc.
  – Still require disposal at end of life (incineration?)

Polyethylene glycol (PEG)





- PEG, PEO, or POE refers to an oligomer or polymer of ethylene oxide, and is produced by the interaction of ethylene oxide with water, ethylene glycol, or ethylene glycol oligomers.
- Its properties is dependent on the molecular weight.
- PEG is soluble in water, methanol, ethanol, acetonitrile, benzene, and dichloromethane, and is insoluble in diethyl ether and hexane.

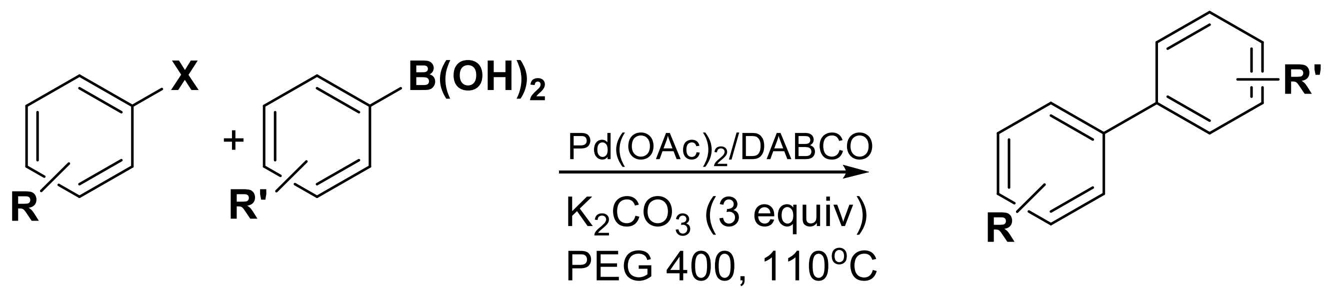
Polyethylene glycol (PEG)

- Reduction reaction

$$\mathrm{RCHXR'} \xrightarrow[70^{o}\mathrm{C}]{\mathrm{NaBH_4,\ PEG\text{-}400}} \mathrm{RCH_2R'}$$

R=aryl, alkyl R'=H, alkyl X=Cl, Br, I, OTs

- Suzuki reaction



Summary

- Variety of approaches to alternative solvents currently under investigation
  - Some are arguably more ‘green’ than others
- Must be financially beneficial for investment in new technology
- All have significant advantages, but also disadvantages
  - Whole life cycle of solvent needs to be considered
- One of most significant problems is getting industry to adopt to the new technology
  - Will only do this if it is commercially advantageous.
  - Education important to ensure industry is aware of possibilities

Home work

- **What is the critical temperature and critical pressure of supercritical fluid? Discuss what are the advantages of supercritical carbon dioxide in comparision with traditional organic solvents in chemical applications .**

Thank You!