

B.Sc SEM-VI Chemistry (Honours)

PAPER-DSE-3

# Green Solvent for Organic Synthesis



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# Topic Covered.....



**Water as green solvent**

**Supercritical carbon dioxide**

**Ionic liquids**

**Solvent free reaction**

**Fluorous biphasic solvent**

**PEG**

**Immobilized solvents**

# **Water as a Solvent for Organic Synthesis**

# Water as a Solvent for Organic Synthesis

In view of the environmental pollutions caused by organic solvents, scientists all over the world are carrying out the experiments in aqueous phase.

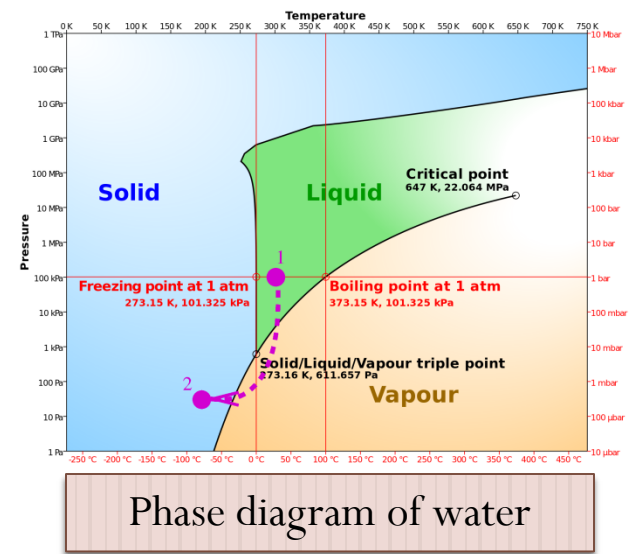
## *Potential Advantages:*

1. Water is comparatively a cheaper solvent available. Chemical Reaction should be economical using water as solvent.
2. Unlike organic solvents (inflammable, explosive, carcinogenic), water is free of all disadvantages and safe.
3. In large industrial process, the product can be isolated by simple phase separation. It is easier to control the reaction temperature.
4. The use of it may not cause problems of pollution, which is a major concern in using volatile organic solvents.
5. Water can be readily recycled.



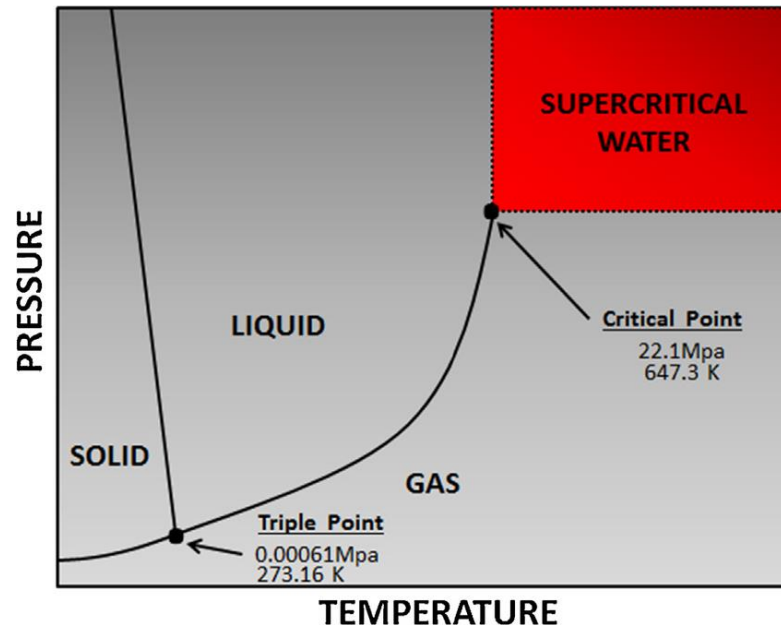
# The Principal Physical Properties of water:

- ❑ The **peak density** of water is 3.98 °C, the density decrease as the temp falls to 0 °C. Also density decrease when the temp exceeds 3.98 °C. It reaches the same density of ice at about 70 °C.
- ❑ The **viscosity** of the water inversely proportional to the rise in temp because no. of H-bonding decrease. The viscosity of the water affect the movement of solute and sedimentation rate of suspended solids.
- ❑ **Specific heat** of water is highest as compare to other substances due to heat capacity of water mass. This effect is advantageous to control temp both endo- and exothermic reactions in large scale industrial process.
- ❑ Water has highest **surface tension** of all liquids. The surface tension decreases with temp and also by addition of surface-active agents (surfactants).
- ❑ Many substances soluble in water. However, the **solubility** is dependent on the temp. solubility of gases like O<sub>2</sub>, N<sub>2</sub>, CO<sub>2</sub> is decreases with rise in temp but some gases like He the solubility increases. In case of solids, the solubility of AgNO<sub>3</sub> increases with rise in temp but for NaCl, slight increase in solubility. **Polar Compounds (hydrophilic)** are readily soluble in water but **Hydrophobic** substances have very low solubility in water.



# The Principal Physical Properties of water:

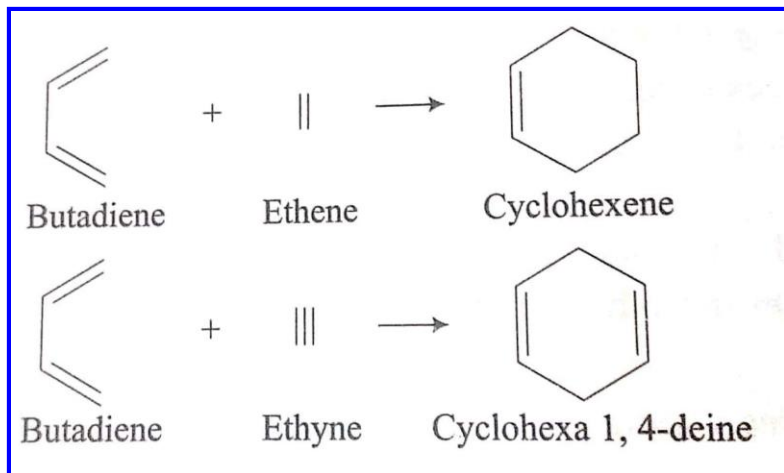
- Ordinary water behaves very differently under high temperature and pressure. Electrolytic conductance of aqueous solutions increases with increase pressure and this effect is more pronounced at lower temp. For all other solvents, the electrical conductivity of solutions decreases with increase in pressure.
- Thermal expansion causes liquid water to become less dense as the temp decreases. Also the liquid vapour density increases as the pressure rises. The density of water varies from 1.0 g/cm<sup>3</sup> at RT to 7.0 g /cm<sup>3</sup> at about 300 °C. The densities of two phases become a single fluid called **Supercritical fluid**. The phase diagram of water around the super critical is given below.....



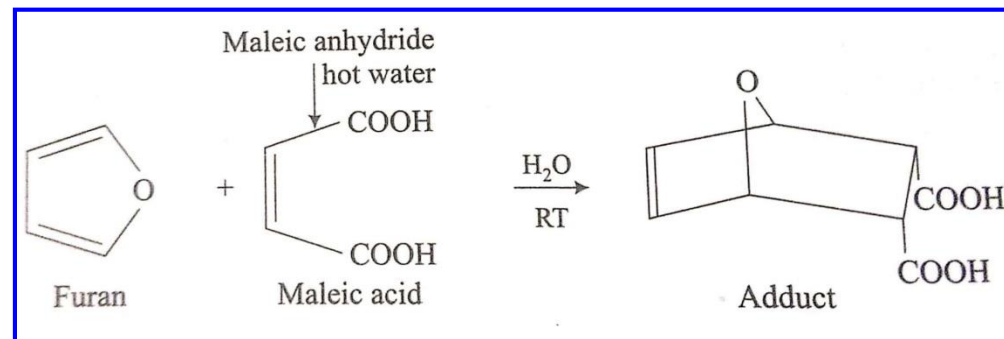
Phase diagram of water in supercritical fluid

# REACTION IN AQUEOUS PHASE

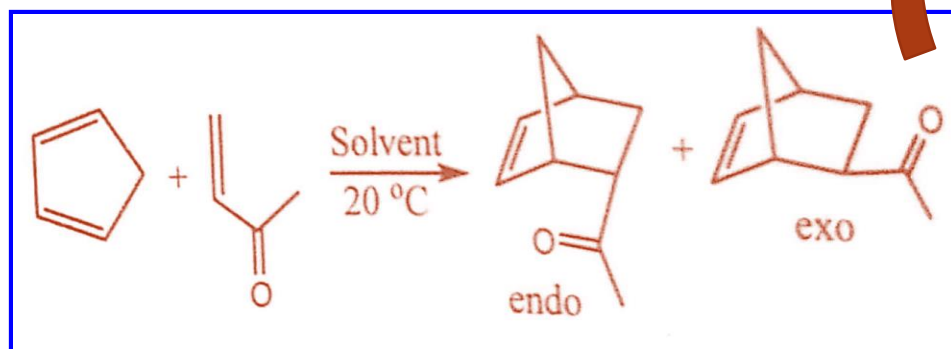
## 1. Diels-Alder Reaction:



Scheme-1



Scheme-2



Scheme-3

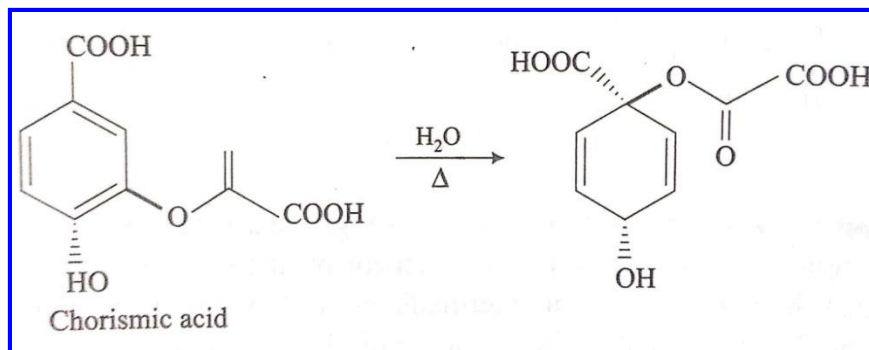
Table 1. Relative rate of Diels-Alder reaction between cyclopentadiene and butenone

Entry	Solvent	Relative rate of reaction
1	Isooctane	1
2	MeOH	12.7
3	H <sub>2</sub> O	740
4	H <sub>2</sub> O (4.86 M LiCl)	1818

## 2. Claisen Rearrangement:

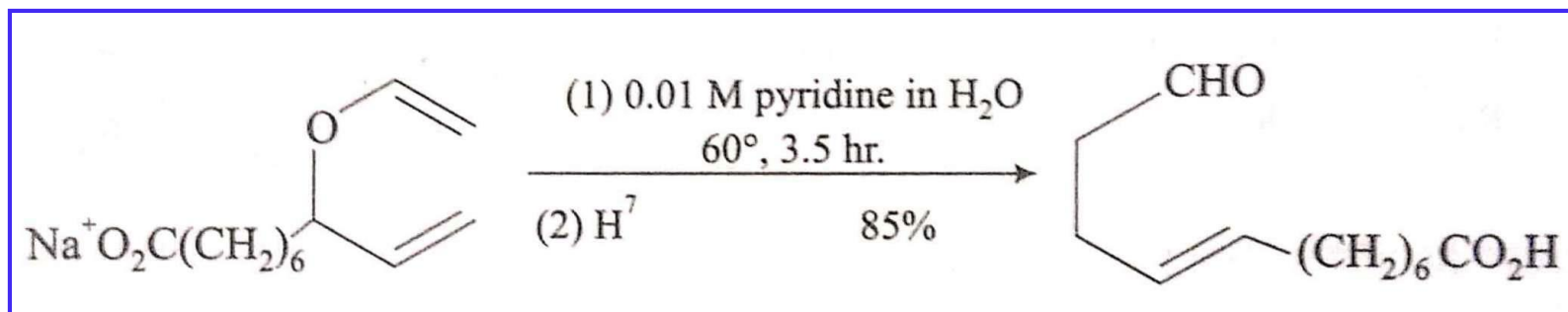
Allyl phenyl ether on heating to 200 °C undergo intramolecular reaction called Claisen Rearrangement. Both the aliphatic and aromatic Claisen rearrangement involve a 3,3-sigmatropic shift.

It is found that polar solvents have been known to increase the rate of the reaction. The first reported use of water in promoting Claisen rearrangement was 1970.



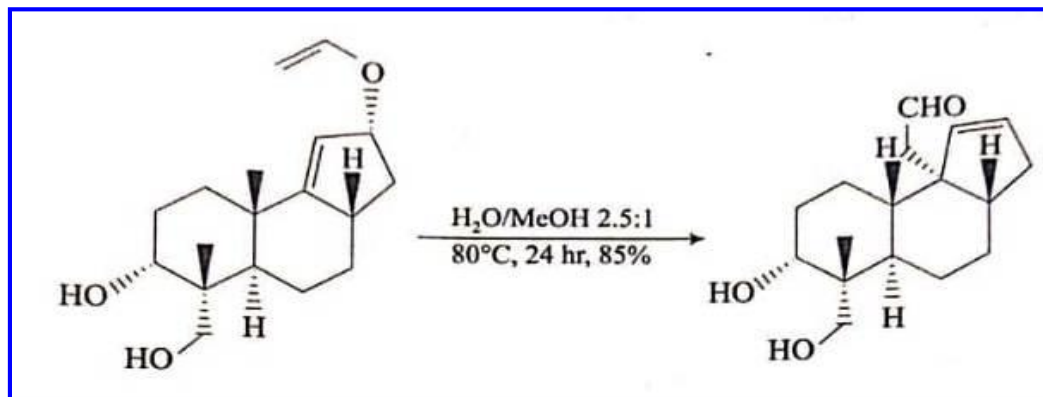
Scheme-1

Some other example:

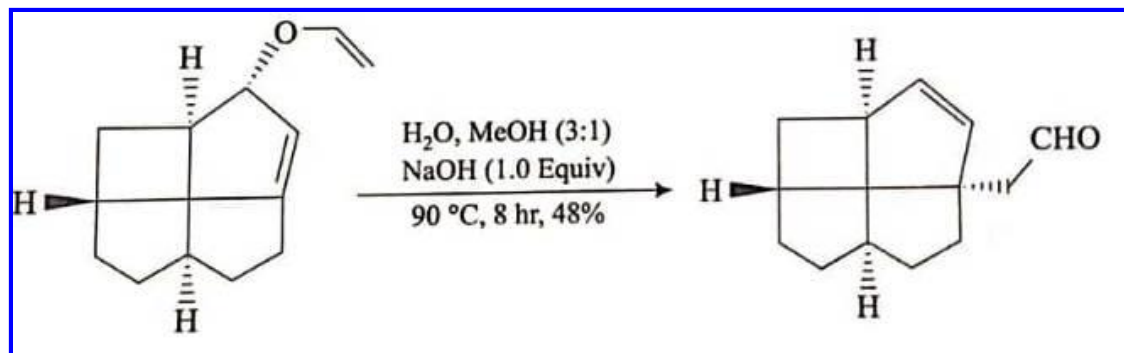


Scheme-2

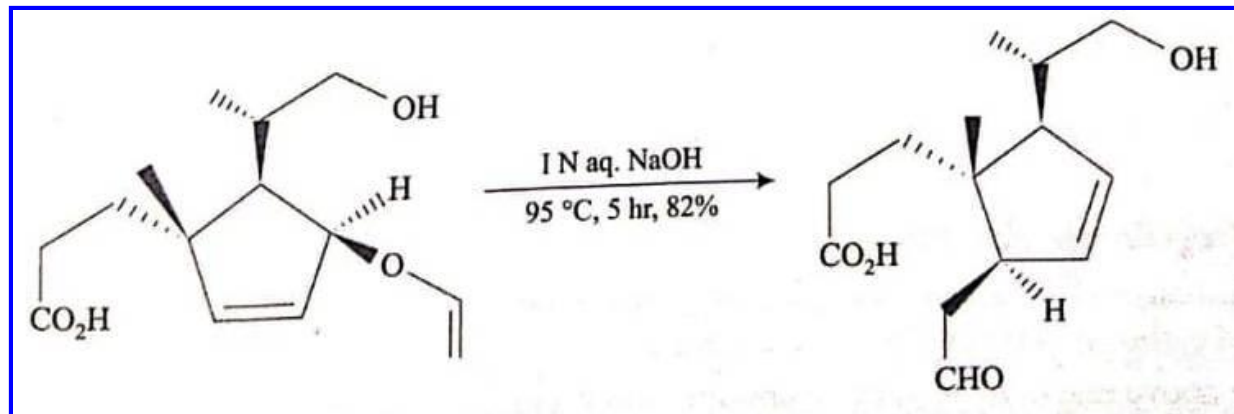
Some other example:



Scheme-3

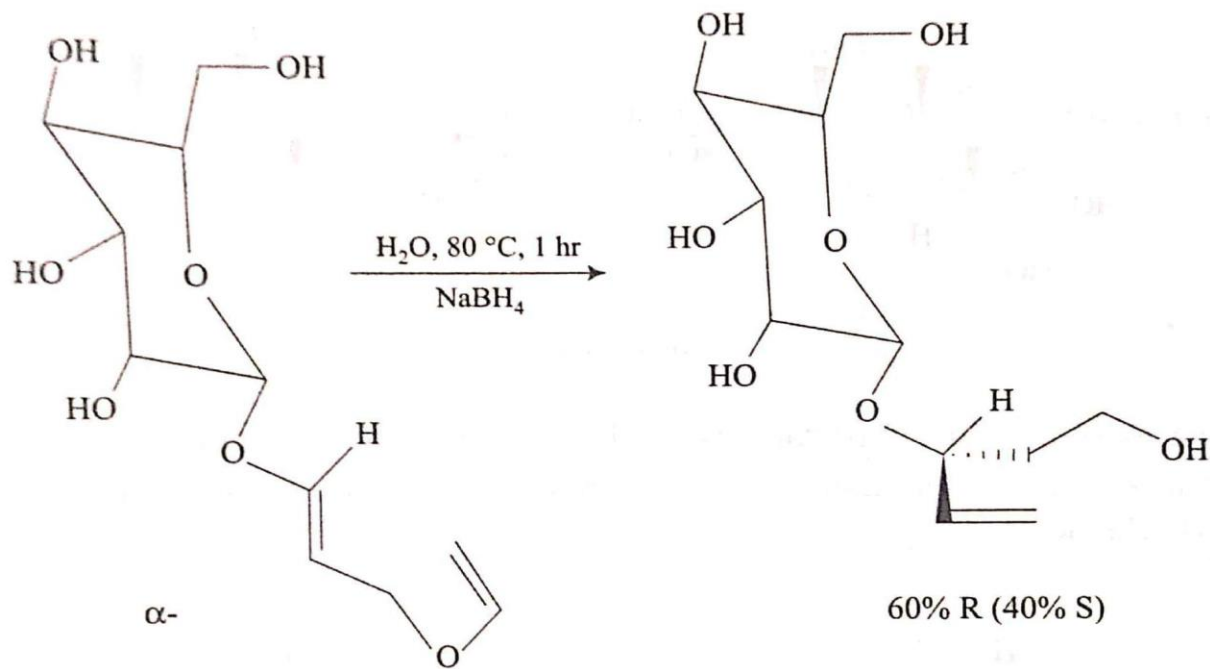


Scheme-4

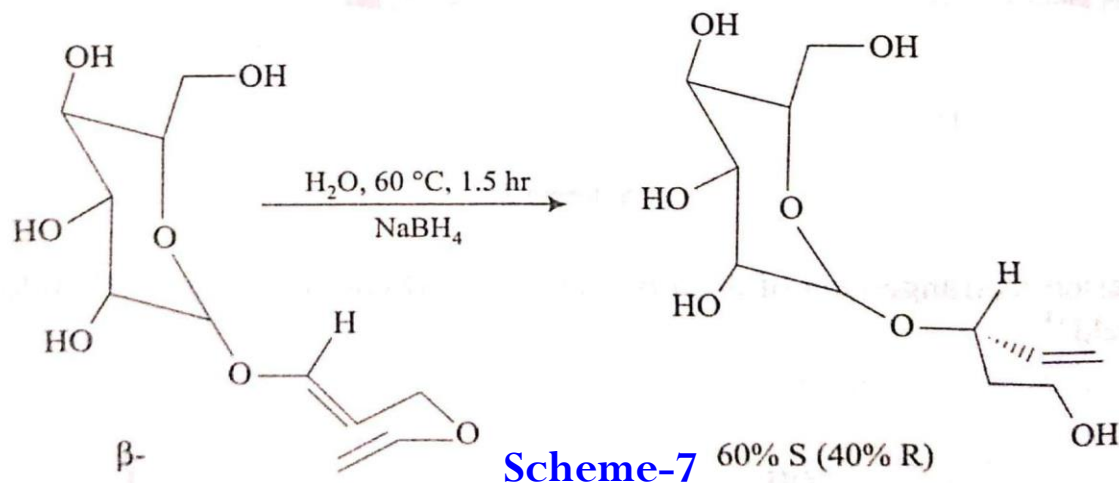


Scheme-5

Some other example:



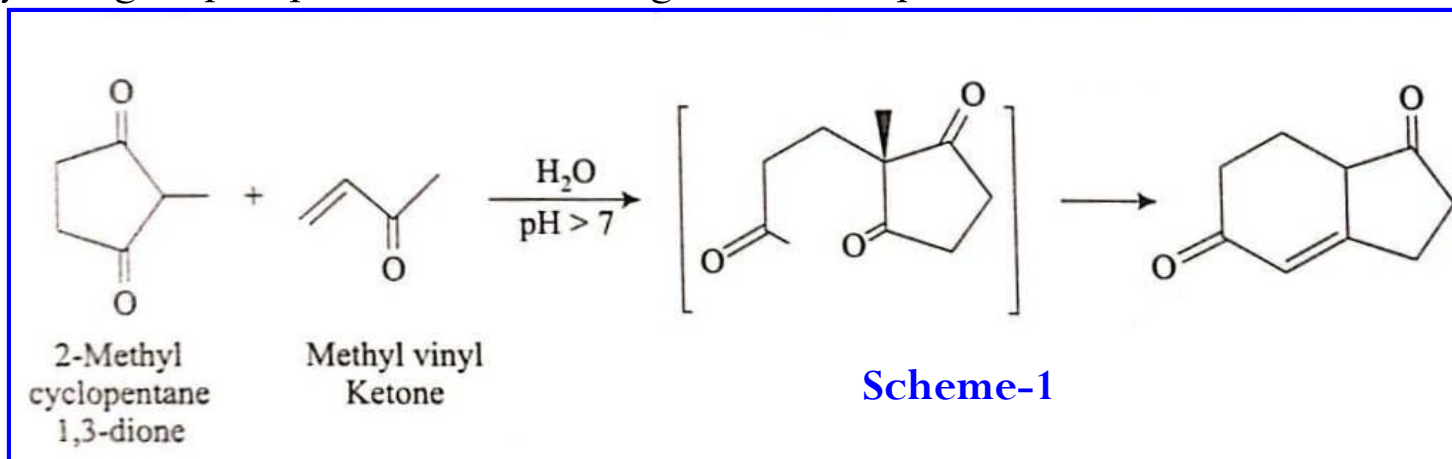
Scheme-6



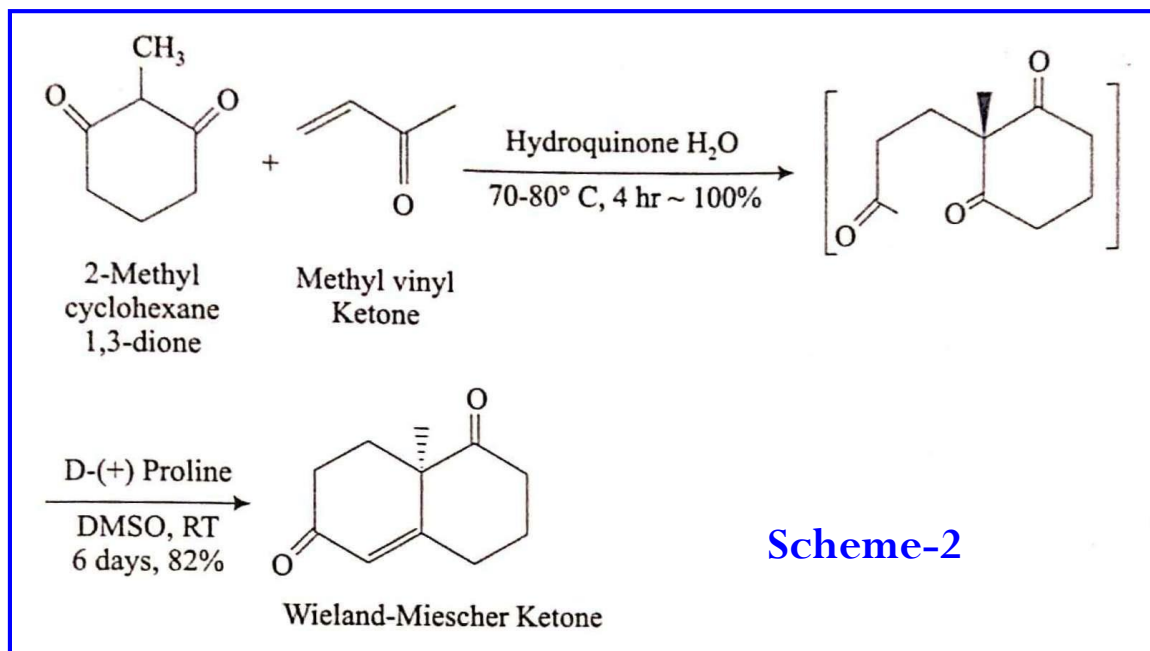
Scheme-7 60% S (40% R)

### 3. Michael Reaction:

The reaction between an  $\alpha, \beta$ -unsaturated carbonyl compound and a compound with an active methylene group in presence of base e.g. NaOEt/Piperidine is known as Michael Reaction.

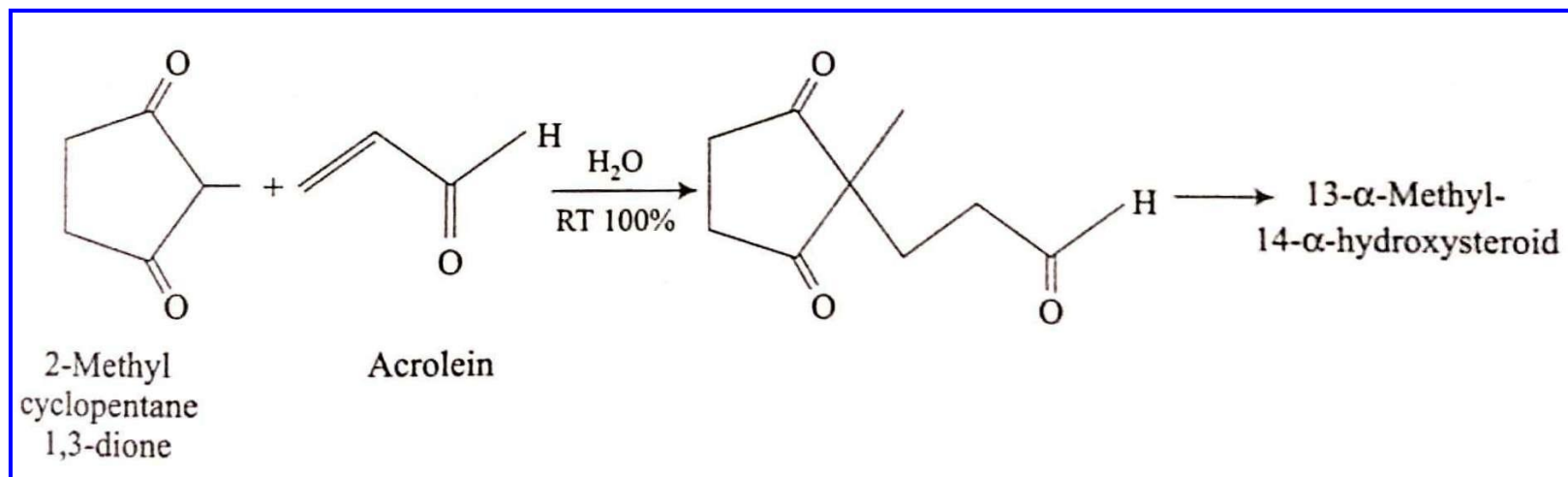


Some other example:

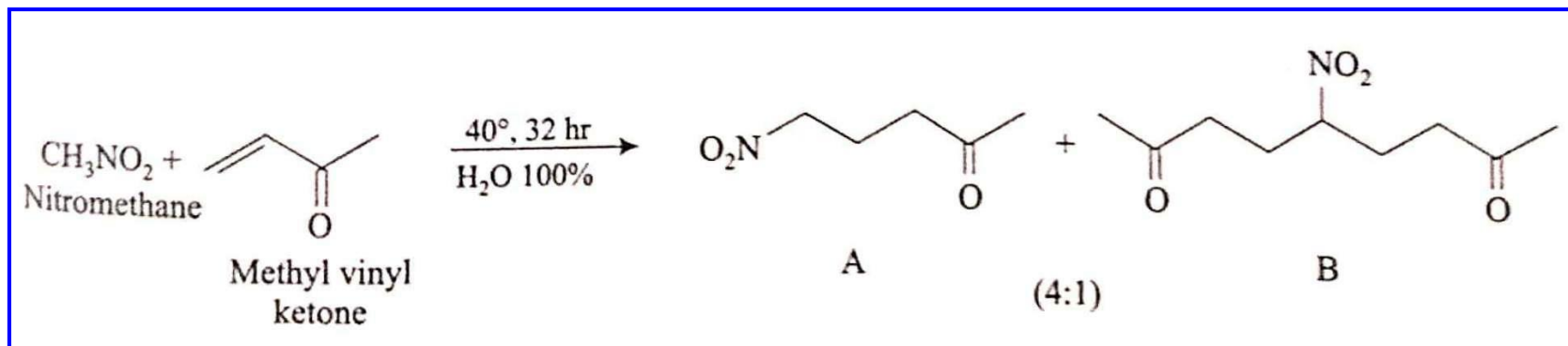




*Some other example:*



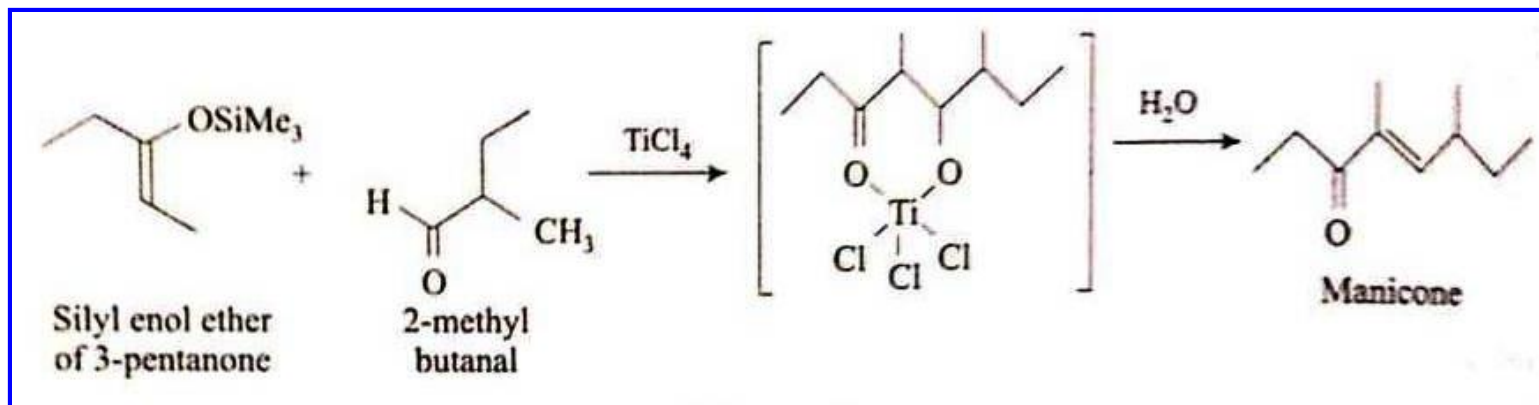
Scheme-3



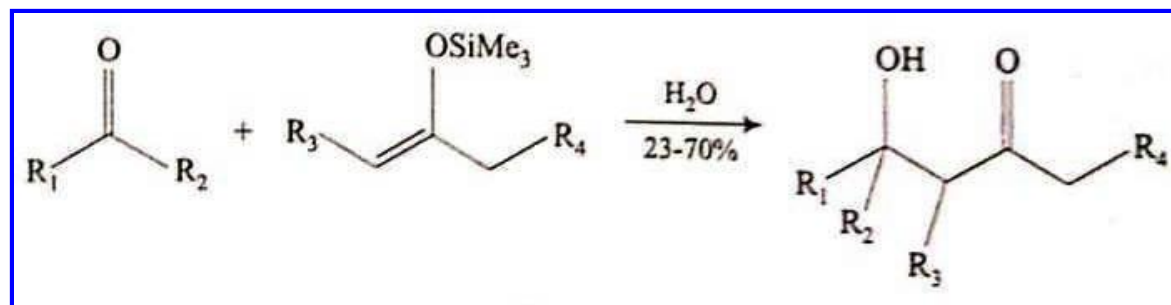
Scheme-4

## 4. Aldol Condensation:

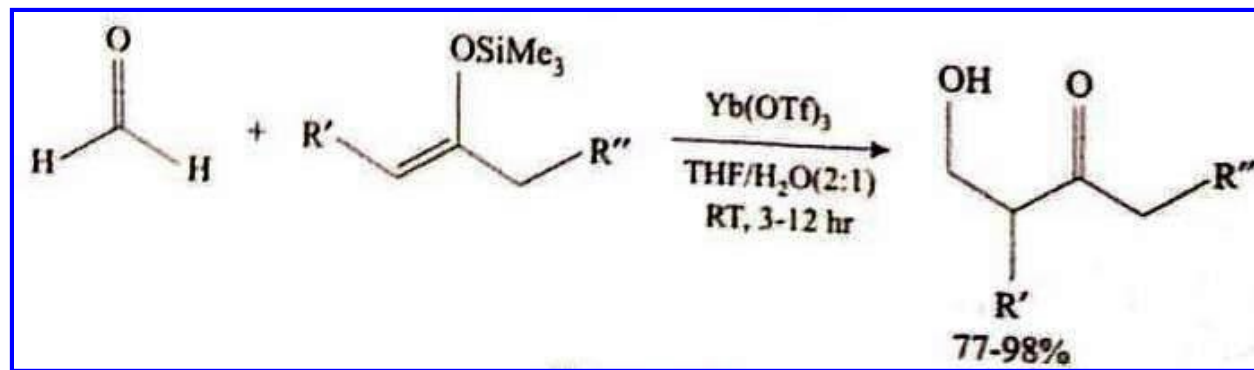
Scheme-1



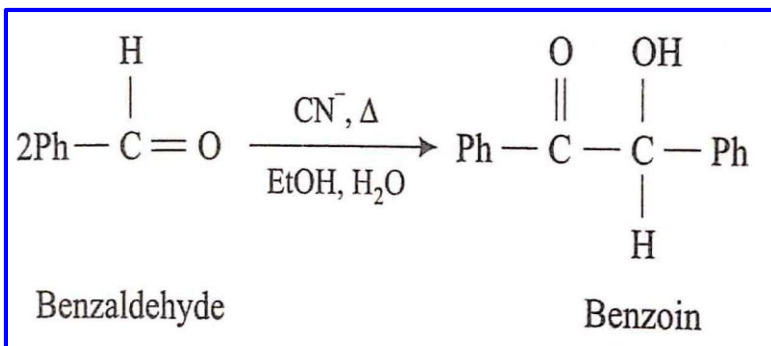
Scheme-2



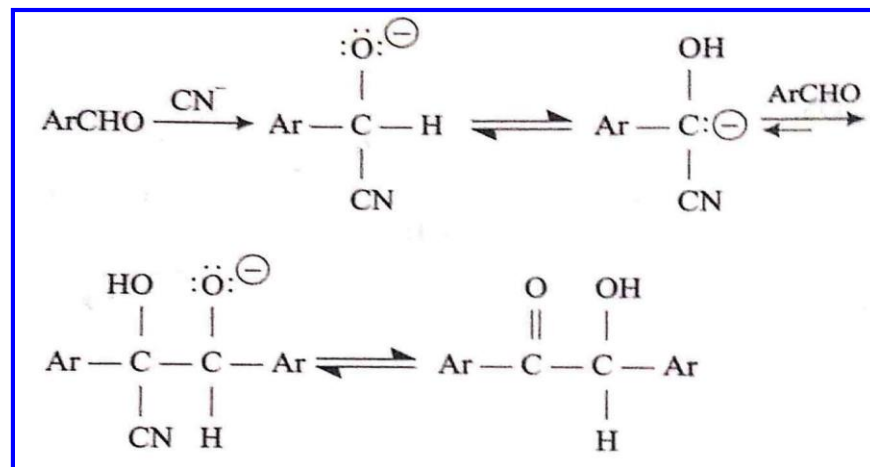
Scheme-3



## 5. Benzoin Condensation:

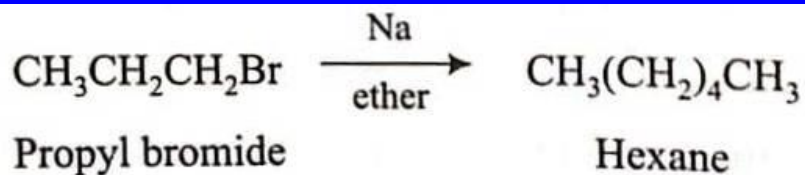


Scheme-1



Mechanism of Benzoin Condensation

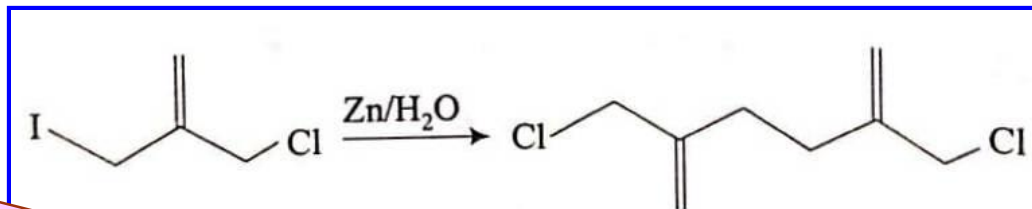
## 6. Wurtz Reaction:



Scheme-1

Coupling of alkyl halides with sodium in dry ether to give hydrocarbon is known as Wurtz Reaction

It has been shown that Wurtz coupling can be achieved by  $\text{Zn}/\text{H}_2\text{O}$

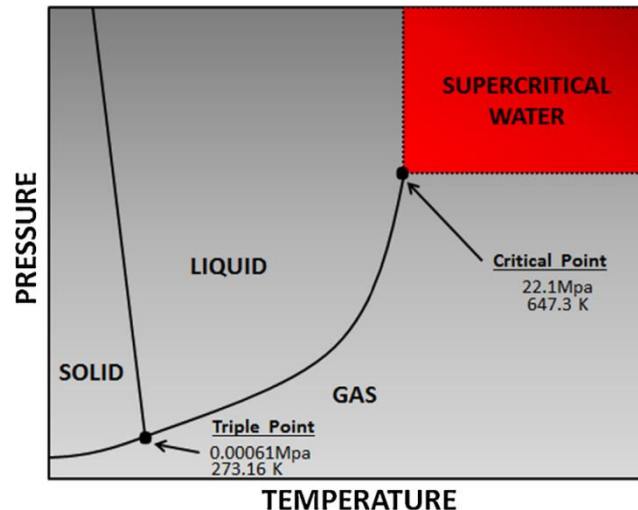


Scheme-2

# REACTION IN SUPER CRITICAL WATER/NEAR CRITICAL WATER (NCW) REGION

**Super critical water (SC-H<sub>2</sub>O)**, the critical temperature of which are 374 °C nad 22.1 Mpa has been attracting attention of synthetic organic chemists because of its unique physical and chemical properties that are quite different from those of ambident water. For example , because the dielectric constant of SC-H<sub>2</sub>O is much lower, a number of organic compounds are soluble in it.

**The near critical water (NCW)** region is describe as 205-300<sup>0</sup>C at pressures 100-80 bar. NCW also process properties very different from those of ambident water.



Phase diagram of water in supercritical fluid

## ORGANIC REACTION IN SC-H<sub>2</sub>O

1. Cyclohexane, Cyclohexene and cyclohexanol in Sc – H<sub>2</sub>O in presence of PtO<sub>2</sub> catalyst yielded<sup>4</sup> benzene as the major product.
2. Dibenzothiophene in Sc – H<sub>2</sub>O on treatment with the catalyst NiMo/Al<sub>2</sub>O<sub>3</sub> resulted<sup>5</sup> in desulphurisation. Higher yields were obtained in CO – Sc – H<sub>2</sub>O and HCOOH – Sc – H<sub>2</sub>O than in H<sub>2</sub> – Sc – H<sub>2</sub>O. This showed that hydrosulfurization could be achieved without the addition of expensive H<sub>2</sub> gas as is the normal practice in industry.
3. Heck-coupling reaction could be conducted<sup>6,7</sup> in Sc – H<sub>2</sub>O.
4. Friedel-crafts alkylation reactions have been accomplished<sup>8,9</sup> in high temperature water.

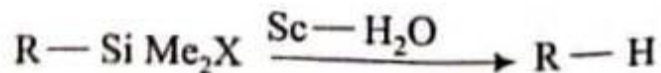


## ORGANIC REACTION IN SC-H<sub>2</sub>O

5. Phenol and p-cresol could be alkylated in Sc – H<sub>2</sub>O with tert. butyl alcohol and 2-propanol at 275° in the absence of any added catalyst to produce sterically hindered phenols<sup>9</sup>.
6. Diels-Alder cycloaddition reactions have also been conducted<sup>10</sup> in Sc – H<sub>2</sub>O. A number of different diene/dienophiles have been used.
7. Aldol condensation reactions can be accomplished in high temperature water. Though, 2, 5-hexanedione is unreactive in pure water, but it undergoes intramolecular aldol condensation in presence of small amount of base (NaOH) to form 3-methylcyclopent-2-enone in 81% yield<sup>11</sup>.
8. 2, 5-Dimethyl furan on treatment with Sc – H<sub>2</sub>O at 250° produced quantitatively 2, 5-hexanedione<sup>12</sup>.
9. Pinacol could be arranged<sup>13</sup> to pinacolone in Sc – H<sub>2</sub>O at 275°.
10. Cyclohexene on treatment with Sc – H<sub>2</sub>O rearranged to methyl cyclopentene<sup>4</sup> in presence of mineral acid or acidic metal salts.
11. Claisen, Rupe and Meyer-Schuster rearrangements have also been reported<sup>11</sup> in Sc – H<sub>2</sub>O at elevated temperature.

## ORGANIC REACTION IN Sc-H<sub>2</sub>O

12. Dehydration of tert. butyl alcohol to isobutylene in Sc – H<sub>2</sub>O at 250° was reported<sup>14,15</sup> in the absence of any added catalyst. However addition of acid or base did accelerate the reaction rate.
13. The dehydration of alcohols such as cyclohexanol<sup>4,12</sup>, 2-methylcyclohexanol<sup>12</sup> and 2-phenylethanol<sup>7</sup> have also been reported in Sc – H<sub>2</sub>O.
14. Carboxylic acids, eg, formic acid<sup>16</sup>, citric acid and itaconic acids<sup>17</sup> and cinnamic acid and indole 2-carboxylic acid<sup>11</sup> undergo facile decarboxylation in Sc – H<sub>2</sub>O.
15. Esters undergo hydrolysis in Sc – H<sub>2</sub>O to form carboxylic acids and alcohols; the acid produced catalyses the hydrolysis. This is referred to as autocatalysis<sup>8,11</sup> Nitriles also undergo hydrolysis to form the corresponding amide and then get further hydrolysed to the corresponding acid.
16. The action of Sc – H<sub>2</sub>O has been examined<sup>18</sup> on a large number of other compounds like hydrocarbons, 1-nitrobutane, butyronitrile, nitroanilines, benzyl sulfide, a large number of oxygen containing compounds and chlorine and fluoroine containing compounns. The results obtained are still in explarotary stage.
17. A facite carbon-silicon bond cleavase of organoailicon compounds in Sc – H<sub>2</sub>O has been reported<sup>19</sup> (Scheme 1)

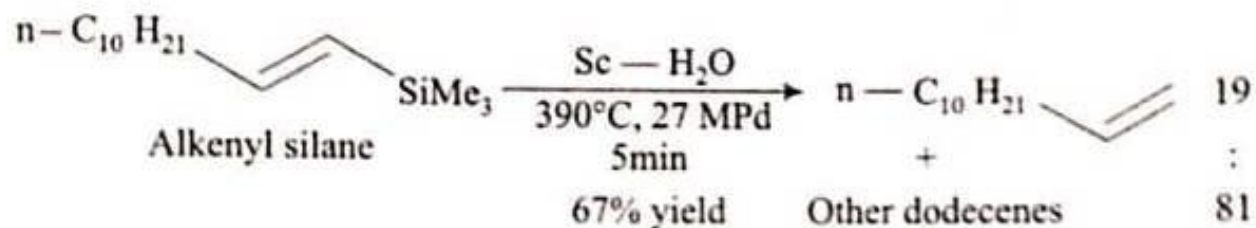


R = aryl, allkenyl, allyl and alkyl

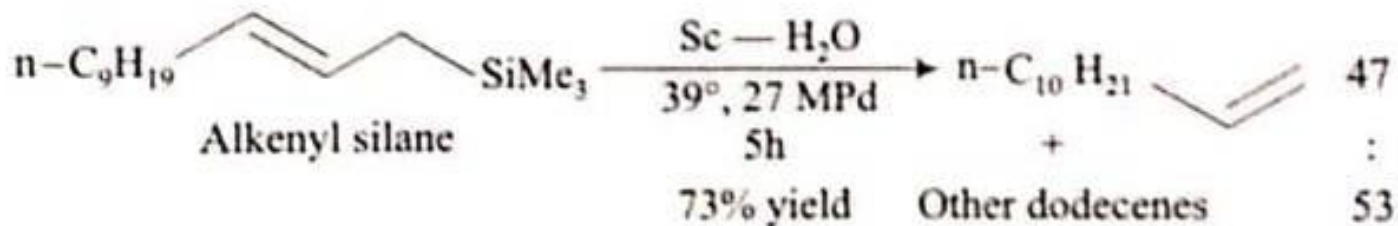
X = OH, Cl, OEt, OSi R'<sub>3</sub>, SiMe<sub>3</sub>, Me



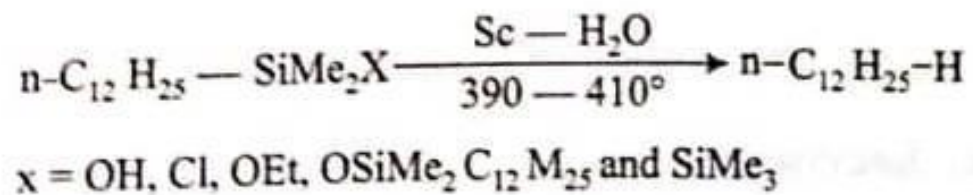
# ORGANIC REACTION IN SC-H<sub>2</sub>O



Scheme 3



Scheme 4

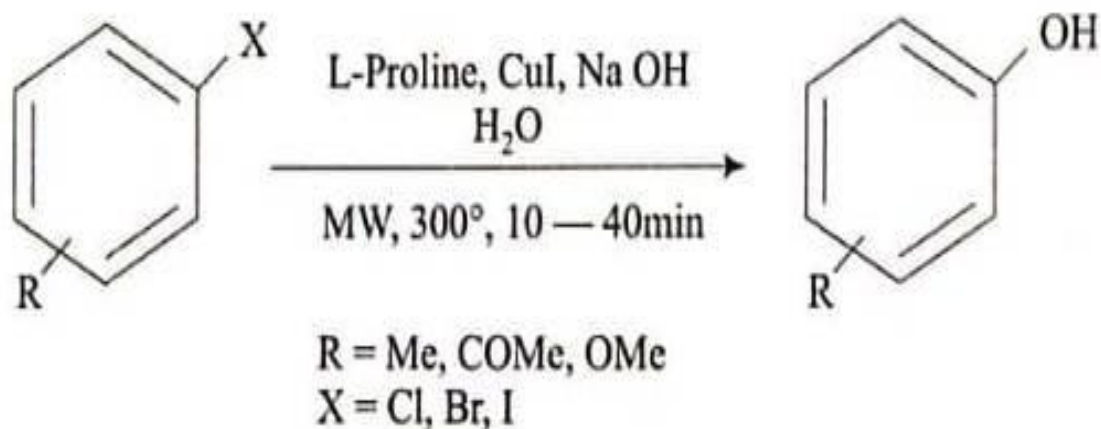


Scheme 5

# ORGANIC REACTION IN NCW REGION

## 3.1 Conversion of Aryl Halides into Phenols

The reaction of aryl halides in water at 300° with L-proline and sodium hydroxide in presence of CuI (catalyst) gave the corresponding phenol<sup>23</sup> (Scheme 6)



Scheme 6

# ORGANIC REACTION IN NCW REGION

## 3.2 Claisen Rearrangement

The Claisen rearrangement of allyl phenyl ether to 2-allyl phenol was performed in near critical water at 240° in a MW oven to give 84% yield. However, at 200° only 10% yield was obtained<sup>24,25</sup>. It was also shown<sup>26</sup> that by increasing the reaction temperature to 250° and time to 1 hr, a cyclic product, dihydrobenzofuran was produced in 72% yield (Scheme 7)

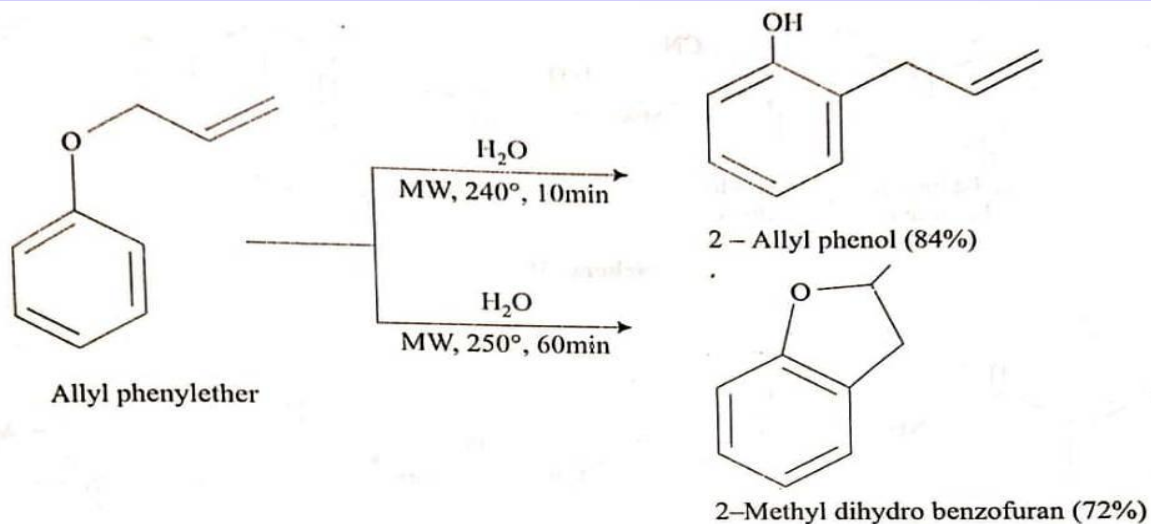
## 3.3 Pinacol-pinacolone Rearrangement

Pinacol on heating with water in MW oven at 270° gave pinacolone<sup>27</sup> in 76% yield. Pinacolone was isolated by converting it into the 2, 4-dinitrophenyl hydrazone. Pinacolone-pinacolone rearrangement generally proceeds in presence of acid catalyst. It was therefore assumed<sup>27</sup> that here NCW acts as an acid catalyst itself (Scheme 8)

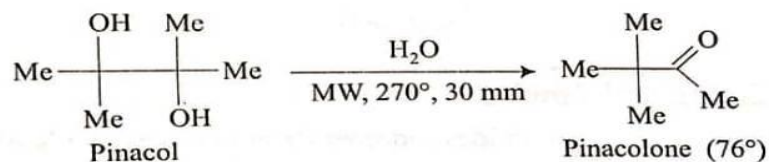
## 3.4 Hydration of Alkenes: Synthesis of Carvacrol from Carvone

Carvone [(+)-isomer] on heating with water in MW oven at 210° for 10 min give (S) – (+) – 8-hydroxy-p-6-menthen 2 one as an intermediate (isolated in 20% yield), which isomerises quantitatively (95% yield) to carvacrol (Scheme 9)

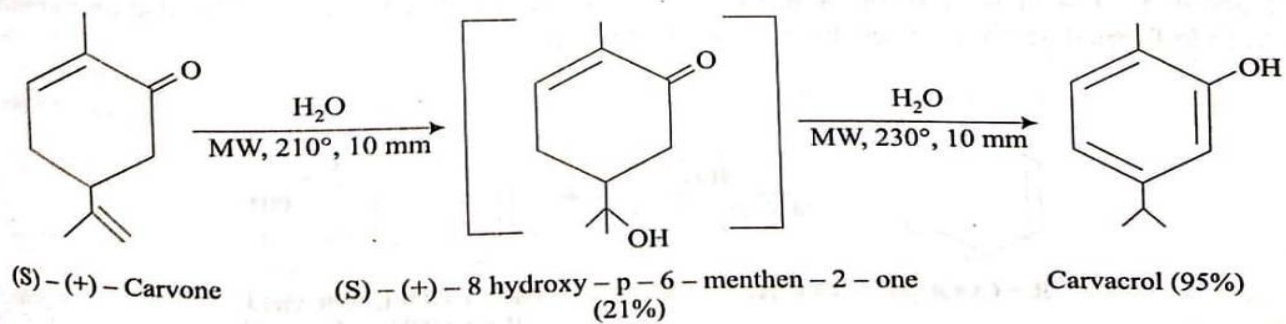
# ORGANIC REACTION IN NCW REGION



Scheme 7



Scheme 8



Scheme 9

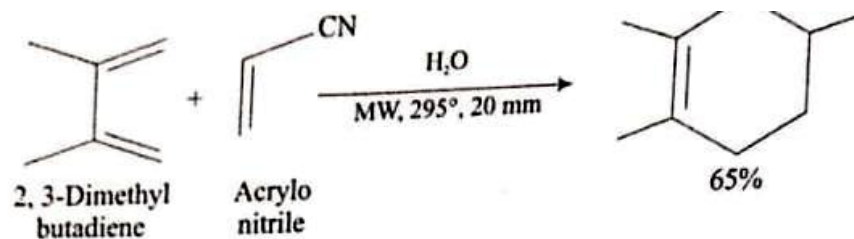
# ORGANIC REACTION IN NCW REGION

## 3.5 Diels-Alder Cycloaddition Reaction

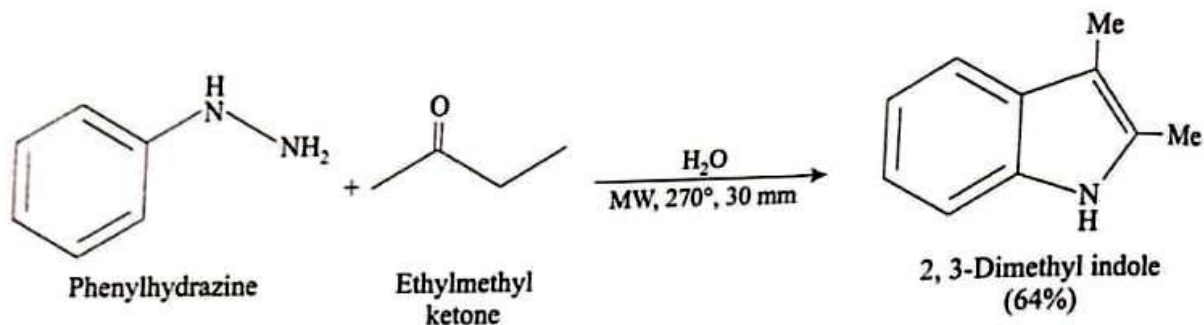
A simple Diels-Alder Cycloaddition reaction was reported<sup>27</sup> by reacting 2, 3-dimethyl butadiene and acrylonitrile by heating with water in a MW oven at 295° for 20 min (using microwave generated NCW) (Scheme 10)

## 3.6 Fischer Indole Synthesis

The reaction of phenylhydrazine with ethyl methyl ketone by heating with water in a microwave oven at 270° for 30 min gave<sup>28,29</sup> 64% yield of the indole derivative (Scheme 11)



Scheme 10



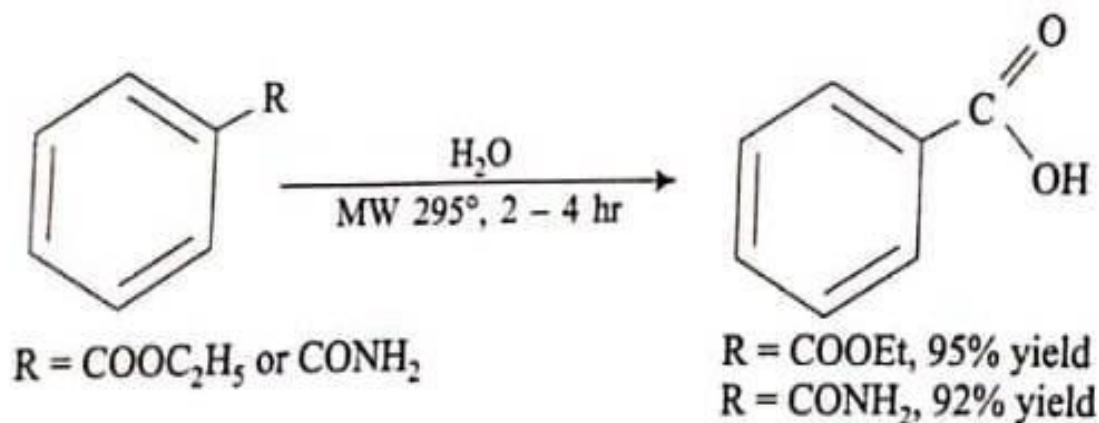
Scheme 11



# ORGANIC REACTION IN NCW REGION

## 3.7 Hydrolysis of Esters and Amides

Normally, the hydrolysis of esters and amides requires strong mineral acids or bases. However, in the NCW region no addition of any catalyst is necessary. Ethyl benzoate hydrolysed to benzoic acid in MW at 295° for 2 hr. In case of benzamide, complete hydrolysis under NCW conditions (295°) was achieved in 4 hr without the addition of catalyst. It is believed that in this case ammonium hydroxide formed acetocatalyzes this reaction<sup>27</sup> (Scheme 12)



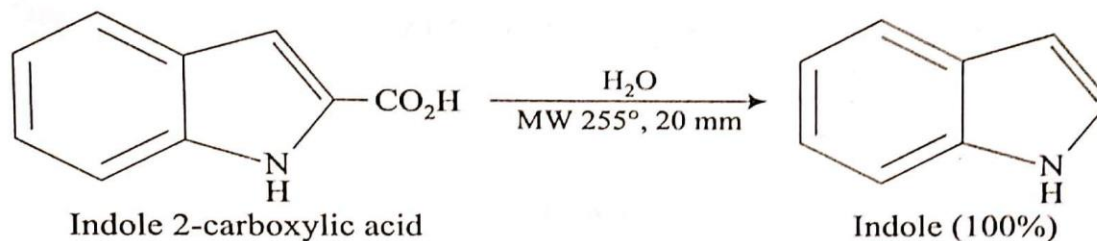
Scheme 12

# ORGANIC REACTION IN NCW REGION

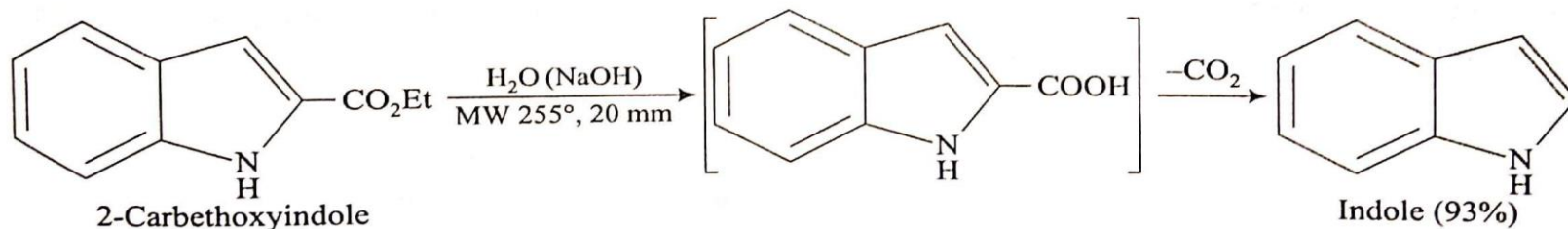
## 3.8 Decarboxylation

Indole-2-carboxylic acid could be decarboxylated<sup>25</sup> to give indole. This decarboxylation was quantitative in 20 min at 255° in near critical region (Scheme 13)

2-Carboethoxy indole on similar hydrolysis gave<sup>25</sup> only 20% yield of the decarboxylated product. This problem could be overcome by heating with 0.2 M aqueous NaOH solution; in the latter case the ester group is first deesterified to the acid, which undergoes decarboxylation to give indole (Scheme 14)



Scheme 13



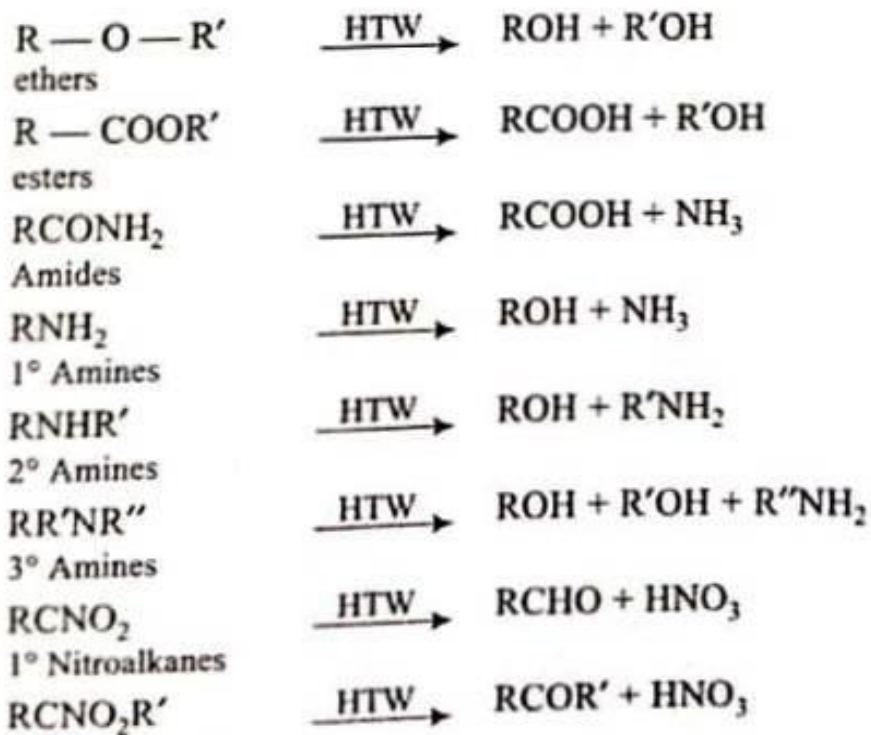
HTW  $\rightarrow$



# ORGANIC REACTION IN NCW REGION

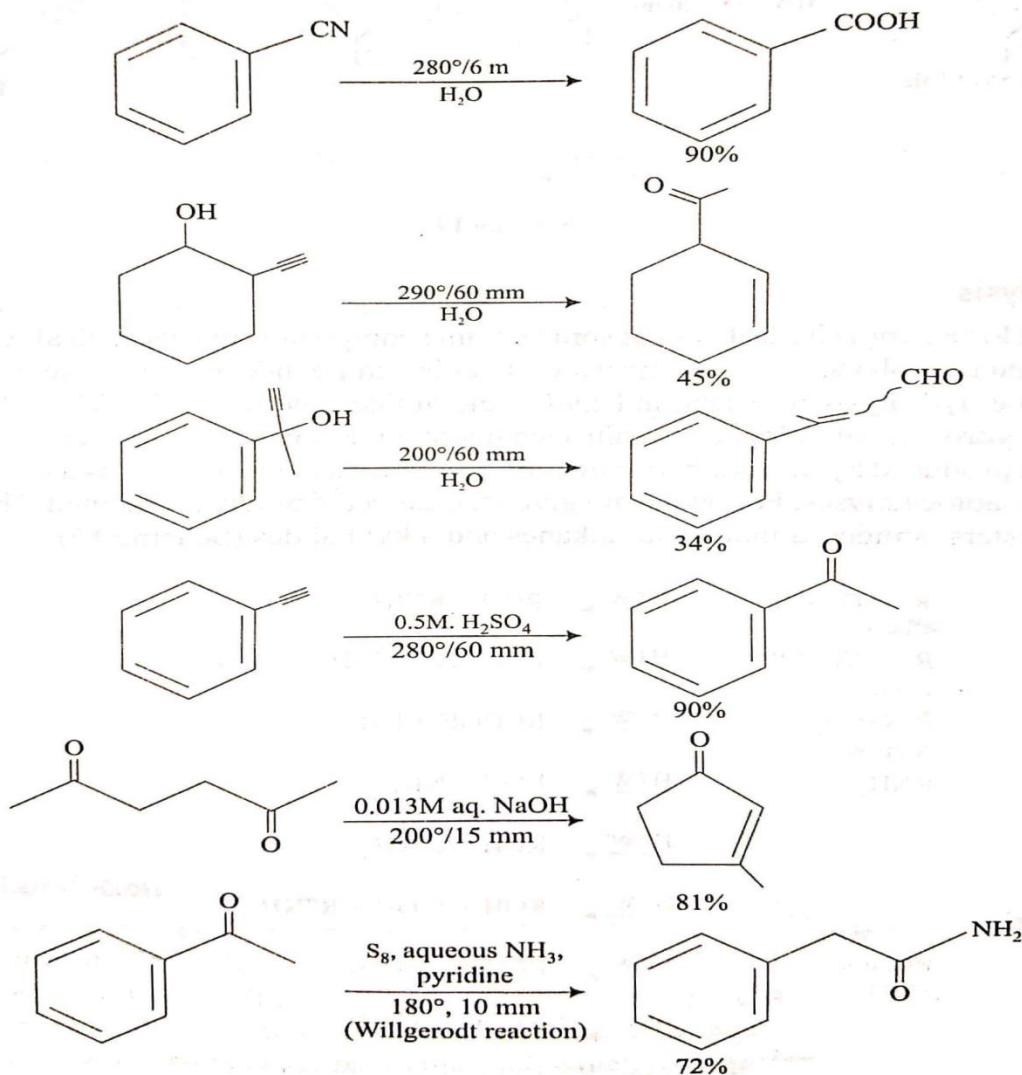
## 9 Autocatalysis

The reactivity (for example hydrolysis) of some organic compounds in near critical region or in high temperature water is enhanced<sup>30</sup> by some water-soluble compounds. For example, carboxylic acids produced by the hydrolysis of esters, aldehydes and amines and mineral acids (HX, HNO<sub>3</sub>) produced by the hydrolysis of halogen and nitrogen compounds can act as acid catalyst. In a similar way, ammonia produced by the hydrolysis of amines, amides and nitriles acts as a base catalyst. This is referred to as autocatalyses. Following are given the expected products obtained<sup>30</sup> by the hydrolysis of ethers, esters, amides, amines, nitroalkanes and alkyl halides (Scheme 15).



# ORGANIC REACTION IN NCW REGION

## 10. Miscellaneous Reactions



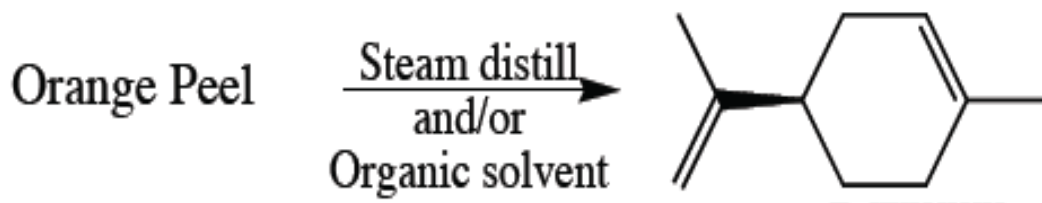
### Conclusion:

Super critical water or high temperature water is a good medium for organic chemical reaction. In addition, it can serve as a reactant and catalyst. These properties have been utilised for conducting chemical synthesis.

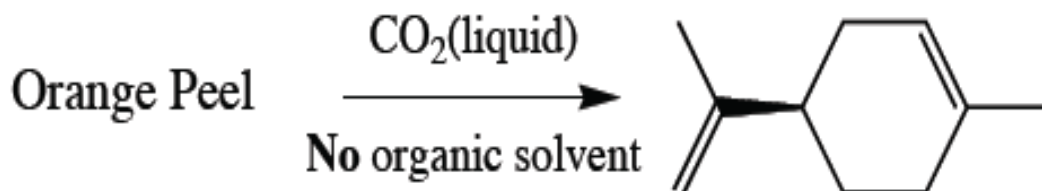
# Supercritical carbon dioxide for Organic Synthesis

# Liquid CO<sub>2</sub> as a green extraction solvent

## Traditional Method



## Green Method



### Chemical Concepts:

Solid/liquid extraction  
Natural products (terpenes)  
Spectroscopy  
Phase transitions

### Green Lessons:

Use of safer solvents  
Prevention of waste  
Green materials processing

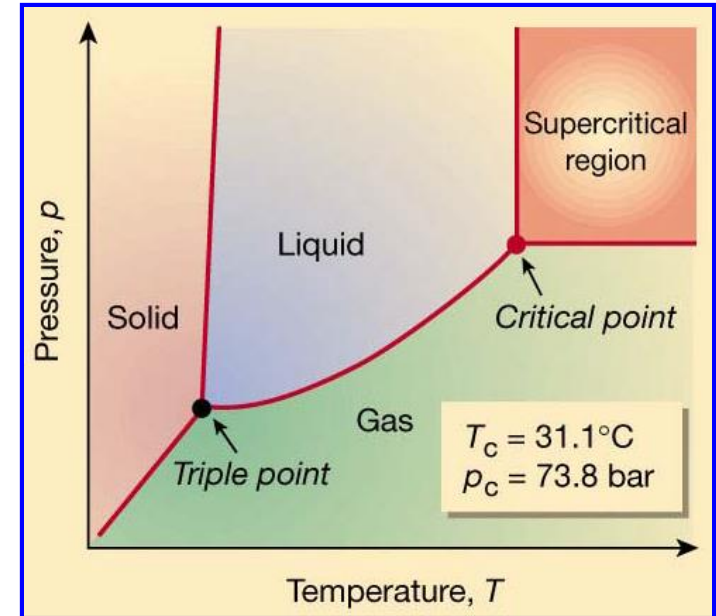
# Supercritical CO<sub>2</sub> (scCO<sub>2</sub>)

## ❑ *What does it mean to be supercritical?*

Till the early sixteen century CO<sub>2</sub> was not known to people. It was in 1823 when Faraday introduced the existence of various liquefied gases including CO<sub>2</sub>. Gore in 1961 gave the process of preparing liquid CO<sub>2</sub>.

### Properties of scCO<sub>2</sub>

- Combination of properties from both the liquid and gas state.
- At liquid-like densities, scCO<sub>2</sub> exhibits low viscosity and high diffusion rates.
- High compressibility of the supercritical phase allows for solvent properties to be varied by small changes in temperature and pressure.
- Can 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<sub>2</sub> can be recovered and reused.



# Commercial Applications of scCO<sub>2</sub>

- ❖ **Natural Product Extraction**
- ❖ **Polymer Synthesis**
- ❖ **Dry Cleaning**

## Natural Product Extraction

The extraction of natural products with classical organic solvents is an important procedure for obtaining 'Lippophilic' plant components. It is on record that the most common organic solvents which have been used for the extraction of natural products are alcohol (methyl and ethyl alcohol), benzene, chloroform, methylene chloride, ether and petroleum ether. We find that some of the solvents are carcinogenic (particularly benzene) and a large number are volatile solvents and are harmful for the environment.

### Advantages of using $s_c\text{CO}_2$ over conventional solvent extracts are:

- (1) No thermal degradation product
- (2) No hydrolysis as occurs in steam distillation
- (3) No loss of volatile components
- (4) High concentration of valuable ingredients
- (5) No solvent residue
- (6) Free of inorganic salts or heavy metals (these are insoluble in SCC)



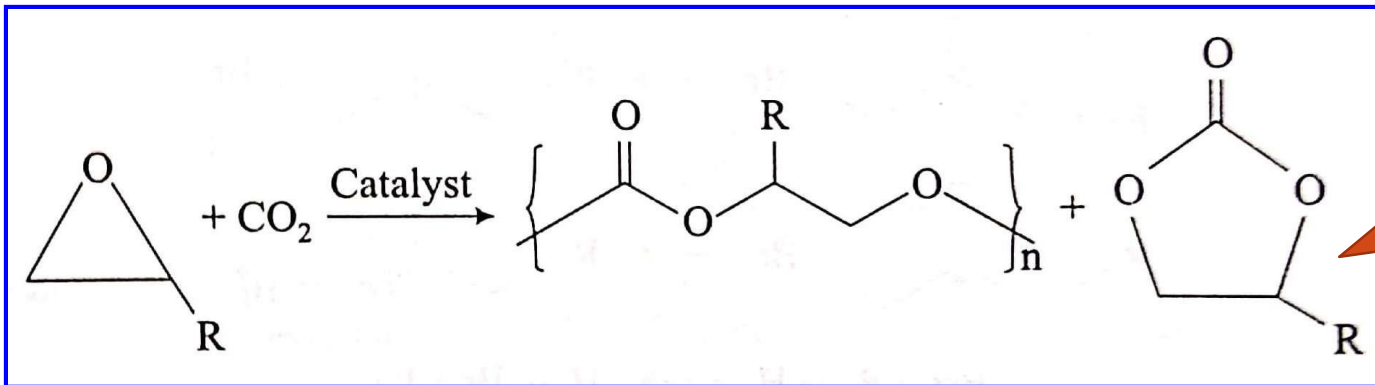
## Advantages of using $s_c\text{CO}_2$ over conventional solvent extracts are:

- (7) Free of any microbial life.
- (8) Meets legal requirement of being environmentally benign.
- (9) High extraction yields.
- (10) High solubility towards lipophilic molecules, hydrocarbons, ethers, esters, ketones, lactones, alcohols (mono and sesquiterpenes).
- (11) Polar substances like sugars, glycosides, amino acids and tannins are insoluble in SCC.

## Applications of using $s_c\text{CO}_2$ :

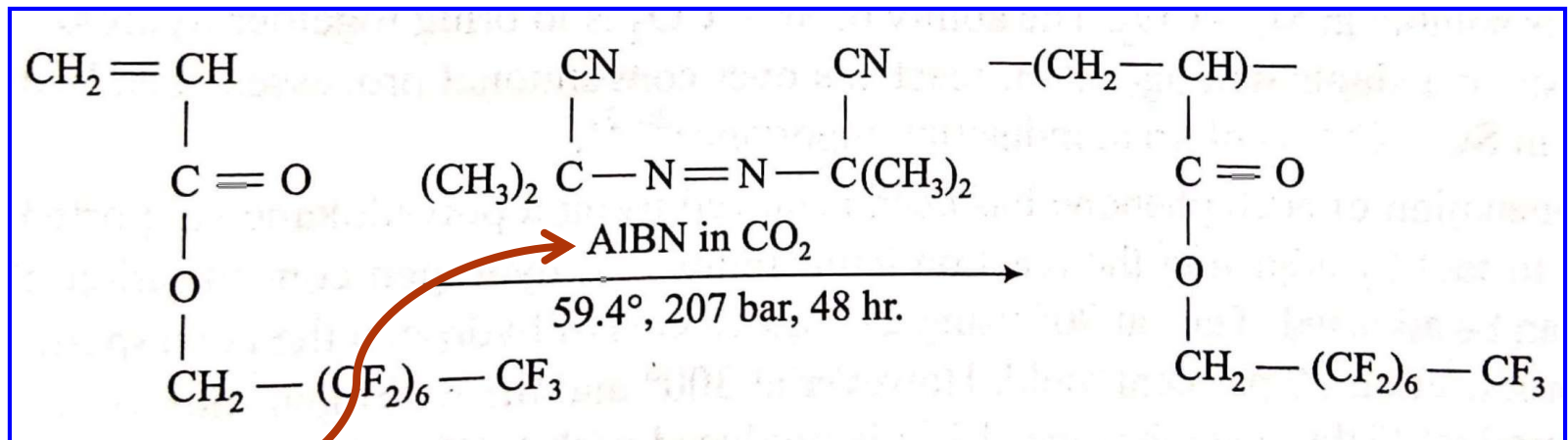
- (i) Essential oils from crushed/prepared Ajowan, Turmeric, Ginger and Caraway have been isolated.
- (ii) A number of food products including spices like pepper, ginger, cumin, cardamom, cloves and decaffeination of coffee and Tea, oils from ground nuts, rice bran, wheat germ etc. have been isolated.
- (iii) Essential oils from *Acorus calamus*, *Angelica sp.*, *Costus sp.*, Turmeric, coriander and bottle brush have been extracted with SCC.
- (iv) Vegetable Tannin materials, which find extensive applications in leather processing, ink manufacture, engraving and in the preparation of formulation of drugs have been isolated using SCC extraction procedure .
- (v) Pyrethrin – a naturally occurring insecticide found in flowers of a variety of chrysanthemum can be a product at lower capital and operating costs than by conventional organic solvent molecules.

# Polymer Synthesis

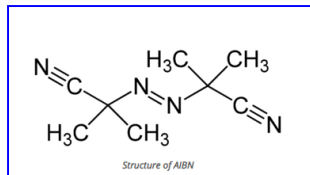


Scheme-1

Sc-CO<sub>2</sub>  
containing  
a  
surfactant:  
'Soapy CO<sub>2</sub>'



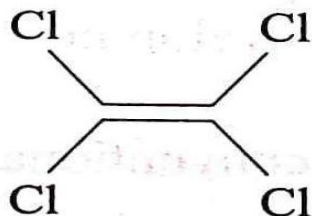
Scheme-2



Azobisisobutyronitrile

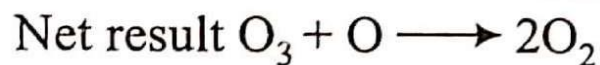
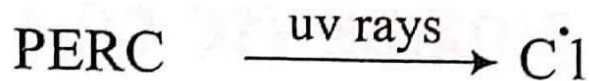
## Dry Cleaning

Articles of clothing made from fabrics cannot be washed in water and require a dry – cleaning process. In fact, the term dry cleaning is somewhat misleading, because a liquid solvent is actually used for removing dirt and stains. Most of the drycleaners use the solvent perchloroethylene, or PERC.



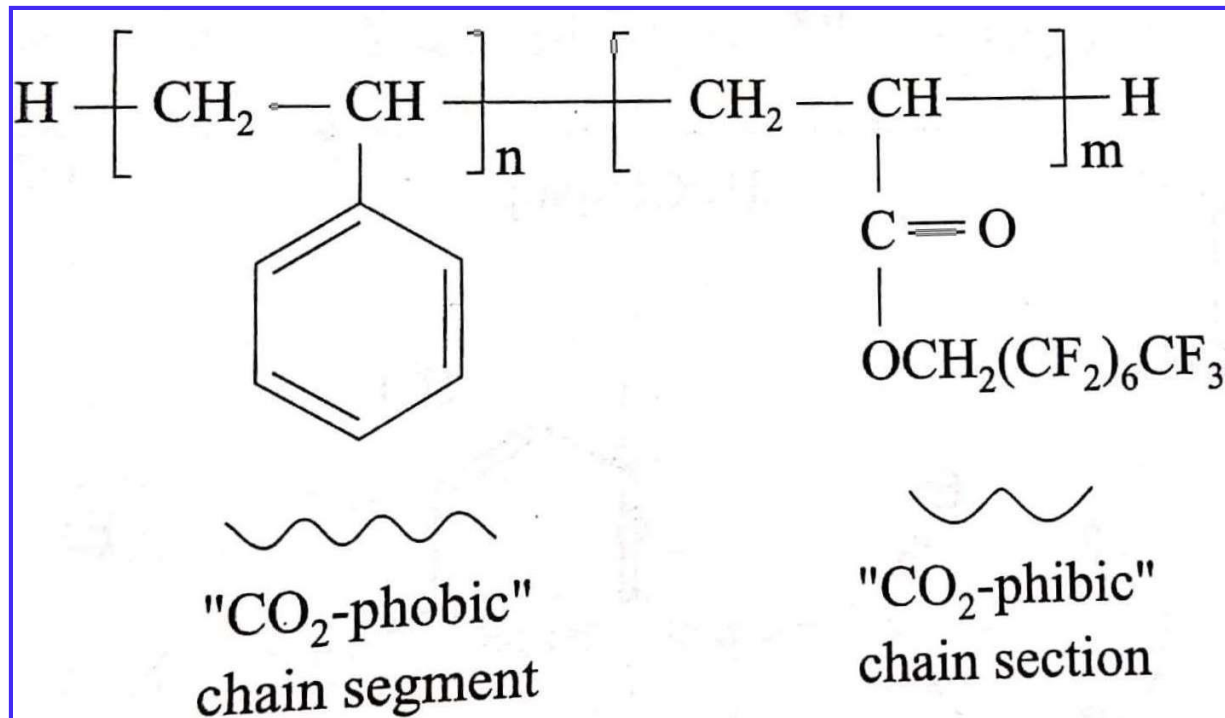
**Perchloroethylene**

Disposal of perchloroethylene, a suspected carcinogen, can contaminate ground water. Besides this, PERC when released into the atmosphere rises to the stratosphere region, where it gets decomposed into chlorine radical by the action of UV rays of the sun. The chlorine radicals, as we know are responsible for depleting the ozone layer.



# Dry Cleaning

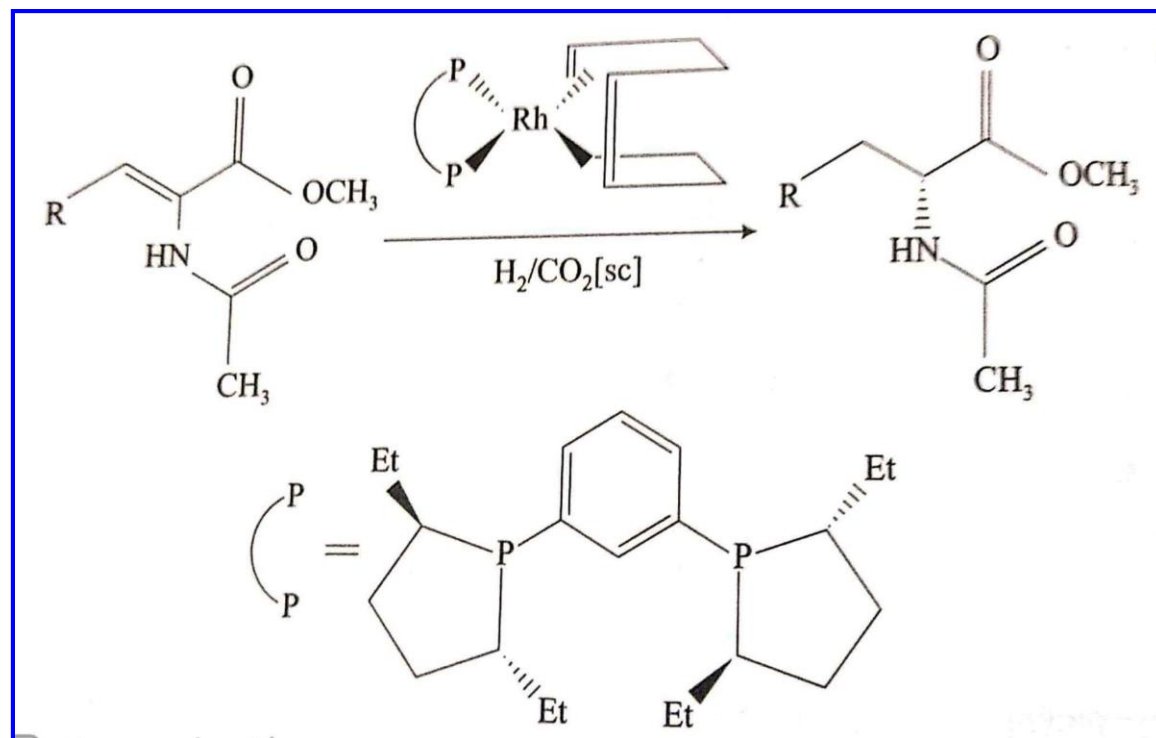
De Simone has developed polymers that acts as surfactants so that liquid CO<sub>2</sub> can be used more effectively as a dry-cleaning solvent. The surfactant is a polymer composed of 'CO<sub>2</sub>-philic' segments (which are attracted to CO<sub>2</sub>) and 'CO<sub>2</sub>-phobic' segments (which are not attracted to CO<sub>2</sub>)



# Use of sc-CO<sub>2</sub> as Solvent for Organic Reaction

## 1. Asymmetric Catalyst:

It has been found that asymmetric catalytic reductions, particularly hydrogenation and hydrogen transfer reactions can be carried out in super critical carbon dioxide with selectivity comparable or superior to those observed in conventional organic solvent (Scheme-1)



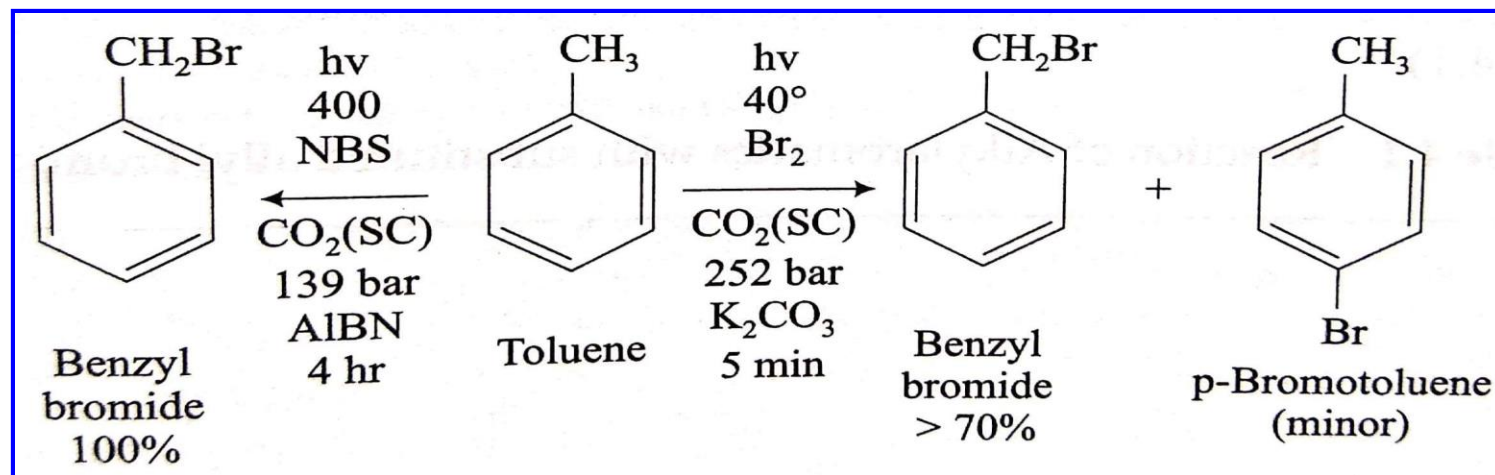
Scheme-1



# Use of sc-CO<sub>2</sub> as Solvent for Organic Reaction

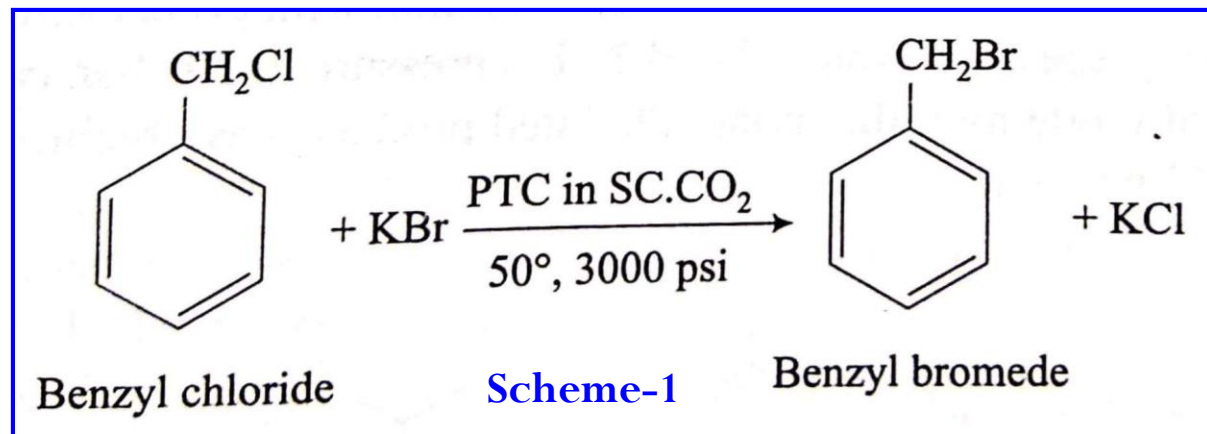
## 2. Free Radical Bromination:

Scheme-1



## 3. Bromination: Displacement of a Chlorinated Aromatics:

This a phase transfer catalysed reaction in presence of PTC: tetra-n-heptommonium bromide / 18-crown-6

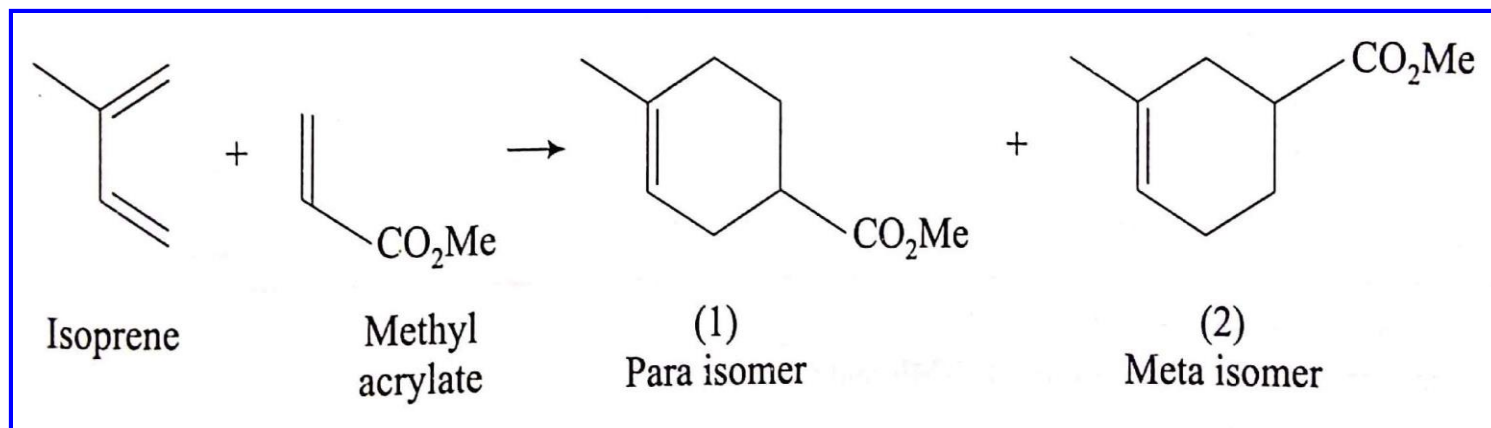




# Use of sc-CO<sub>2</sub> as Solvent for Organic Reaction

## 4. Diels-Alder Reaction:

Scheme-1

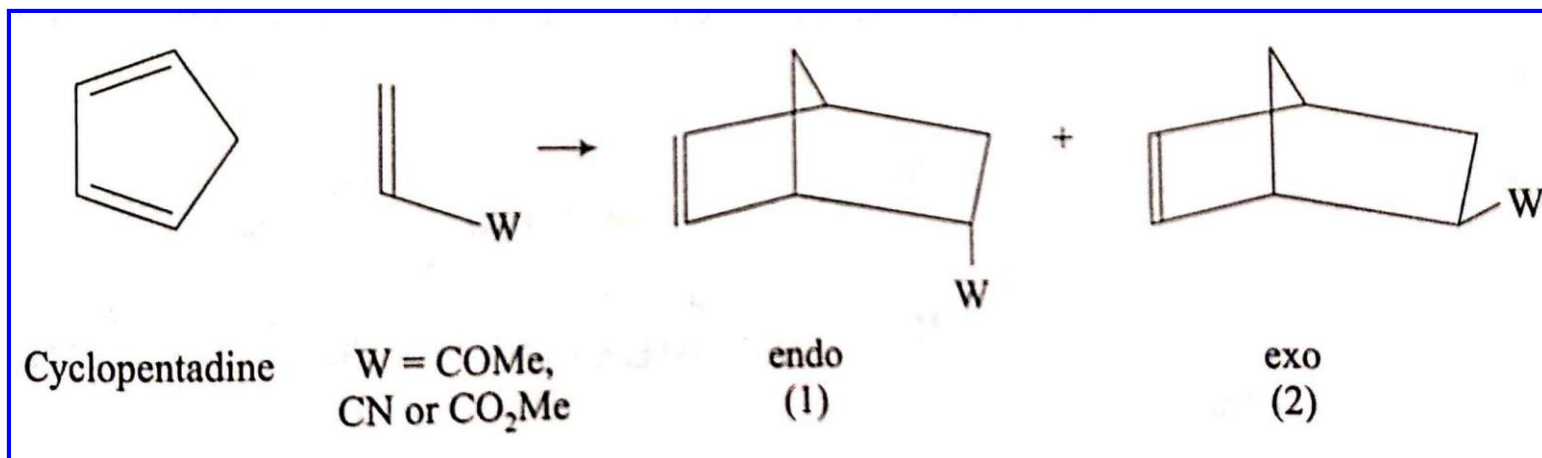


Condition	Yield (%) <sup>a</sup>	Ratio <sup>b</sup> 1 : 2
PhCH <sub>3</sub> , 145°, 15hr	78	71 : 29 (71 : 29)
PhCH <sub>3</sub> , 50°, 3d	(7)	69 : 31 (72 : 28)
CO <sub>2</sub> , 49.5 bar, 50°, 4d	(11)	69 : 31 (73 : 27)
CO <sub>2</sub> , 74.5 bar, 50°, 4d	(5)	67 : 33 (73 : 27)
CO <sub>2</sub> , 95.2 bar, 50°, 7d	(4)	71 : 19 (73 : 27)
CO <sub>2</sub> , 117 bar, 50°, 3d	(3)	70 : 30 (72 : 28)

# Use of sc-CO<sub>2</sub> as Solvent for Organic Reaction

## 4. Diels-Alder Reaction:

Scheme-2

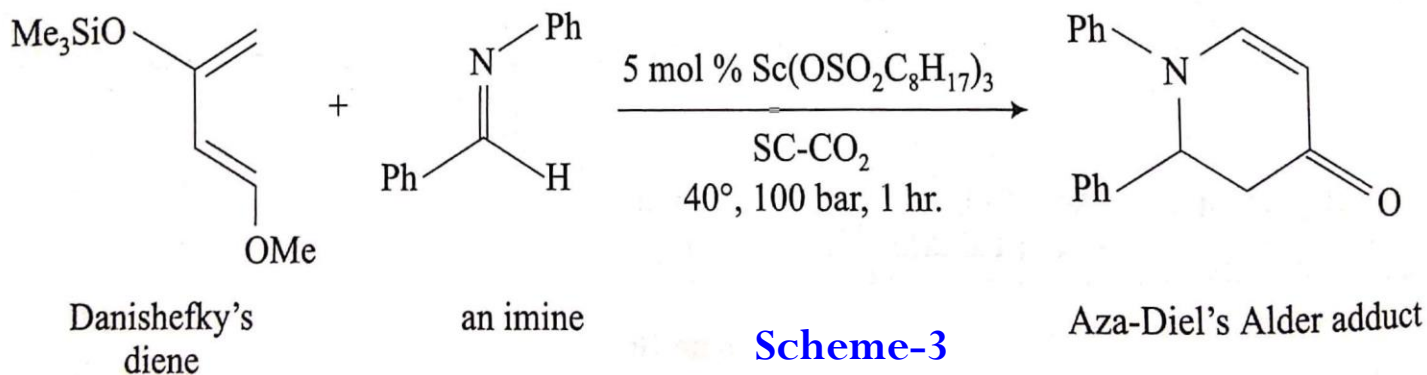


Conditions	Promolar	yield %	Endo : Exo (1 : 2)
W = COMe			
CO <sub>2</sub> , 50°, 4h	none	29	82 : 18
CO <sub>2</sub> , 50°, 4hr	0.5 g SiO <sub>2</sub>	82	92 : 8
W = CN			
CO <sub>2</sub> , 50°, 4h	none	5	57 : 43
CO <sub>2</sub> , 50°, 4hr	0.5 g SiO <sub>2</sub>	14	59 : 41
W = CO <sub>2</sub> Me			
CO <sub>2</sub> , 50°, 4hr	none	5	72 : 28
CO <sub>2</sub> , 50°, 4hr	0.5 g SiO <sub>2</sub>	21	85 : 15

# Use of sc-CO<sub>2</sub> as Solvent for Organic Reaction

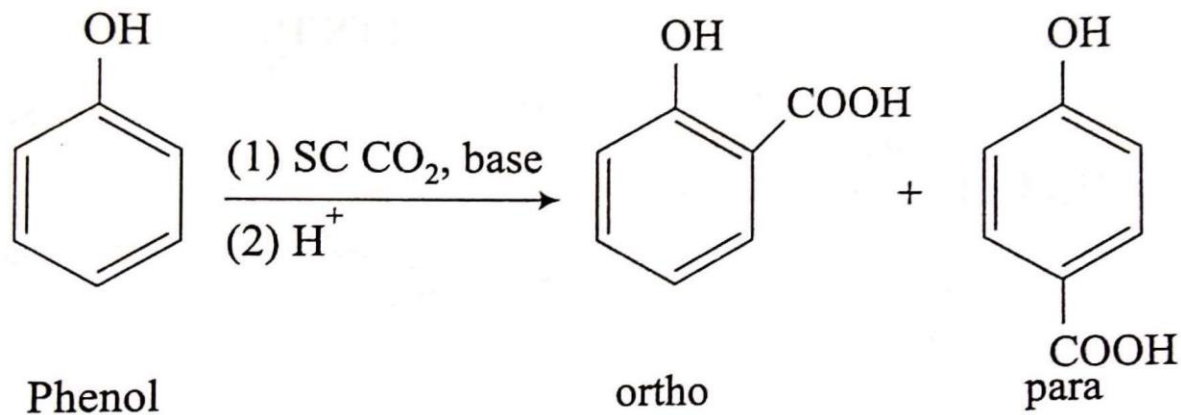
## 4. Diels-Alder Reaction:

This is an aza-Diels-Alder Reaction; Here Silica gel acts as efficient catalyst



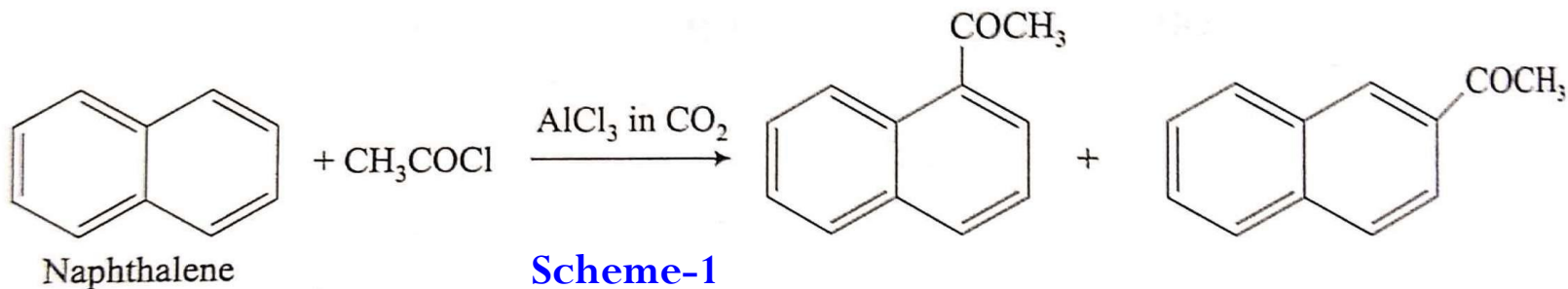
## 5. Kolbe-Schmitt Synthesis:

Scheme-1



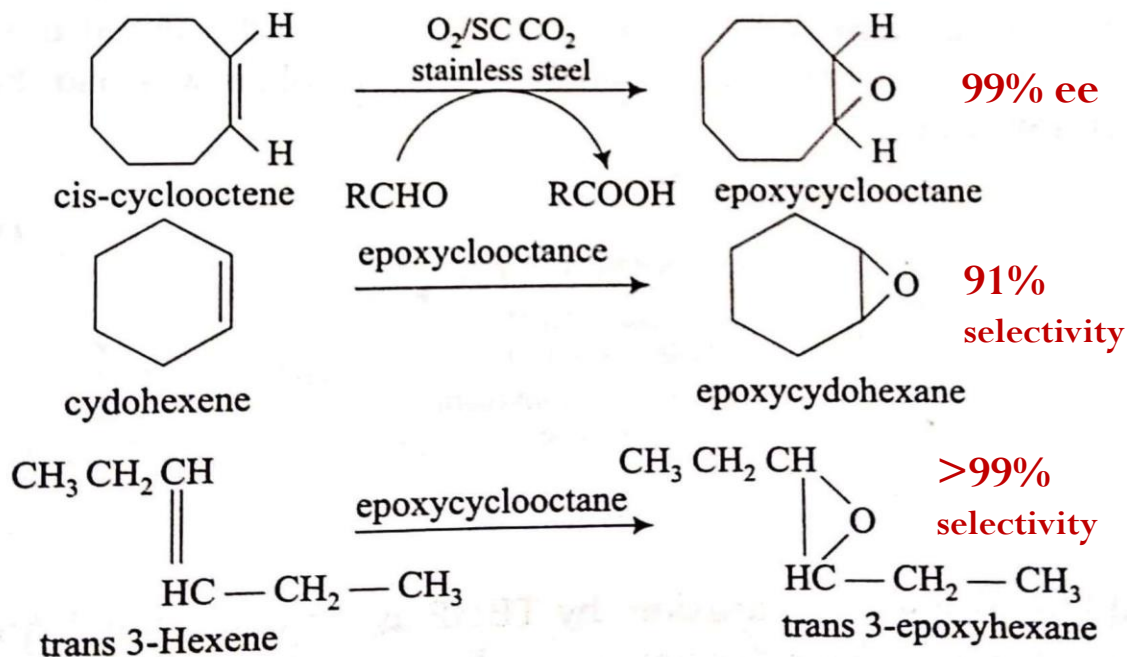
# Use of sc-CO<sub>2</sub> as Solvent for Organic Reaction

## 6. Freidel-Crafts Reaction:



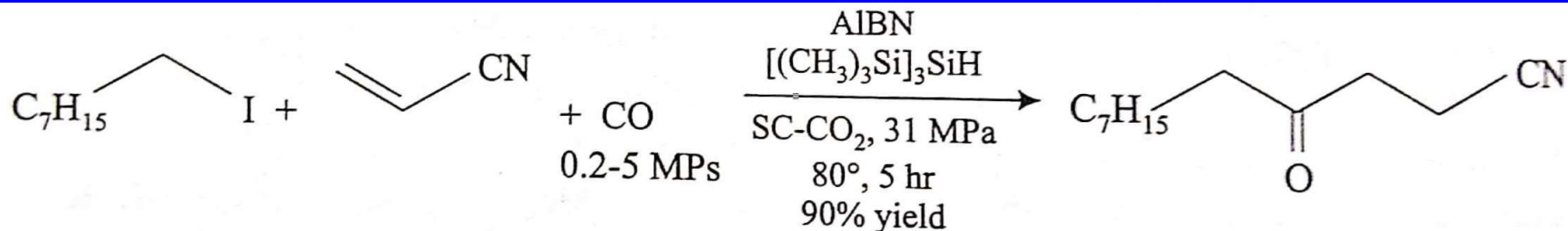
## 7. Oxidation in SC-CO<sub>2</sub>:

**Scheme-1**



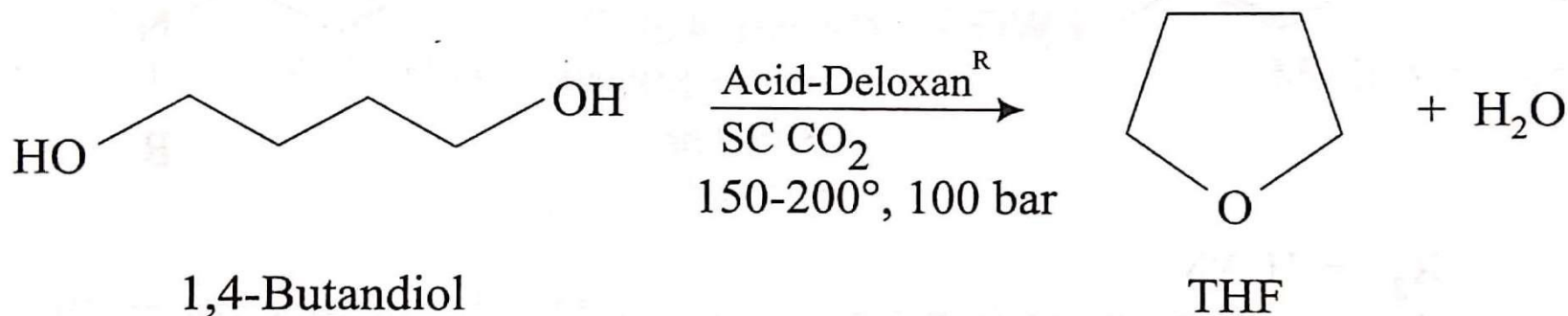
# Use of sc-CO<sub>2</sub> as Solvent for Organic Reaction

## 8. Radical Reactions in SC-CO<sub>2</sub>:



Scheme-1

## 9. Acid-Catalysed Reaction:

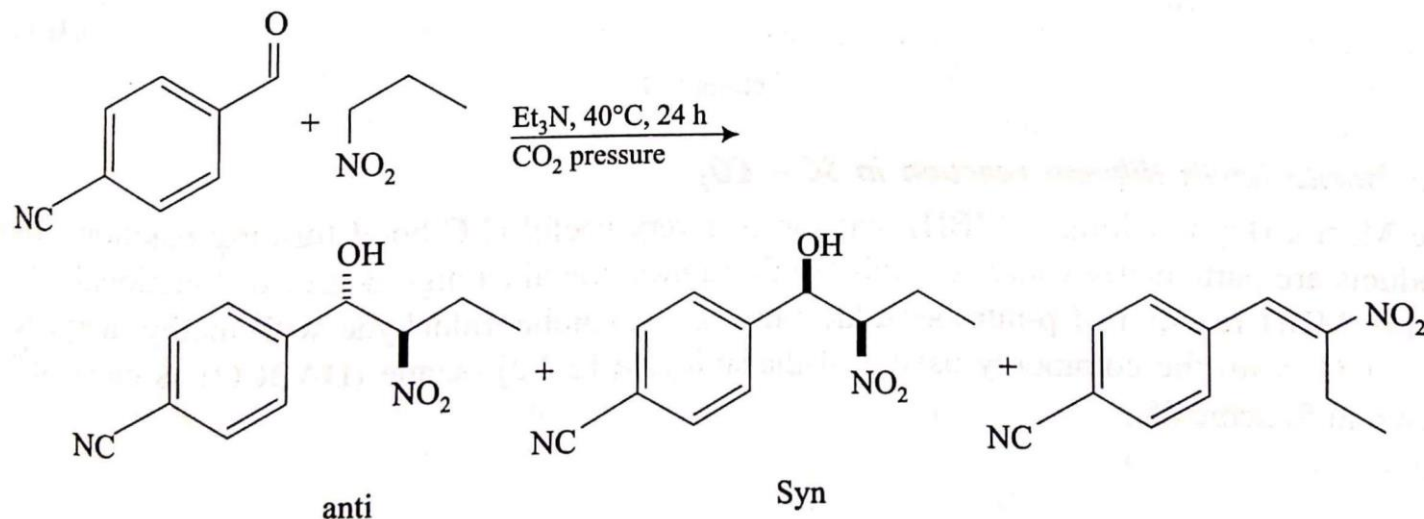


Scheme-1



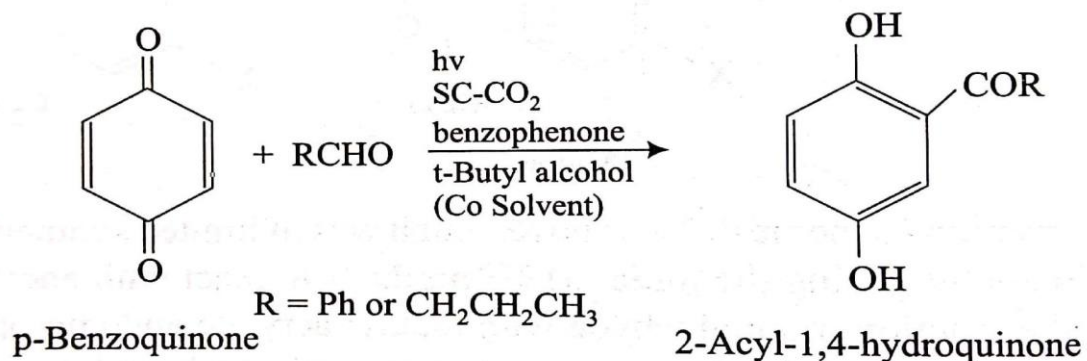
# Use of sc-CO<sub>2</sub> as Solvent for Organic Reaction

## 10. Stereochemical Control Reaction in SC-CO<sub>2</sub>:



Scheme-1

## 11. Photochemical Reaction:

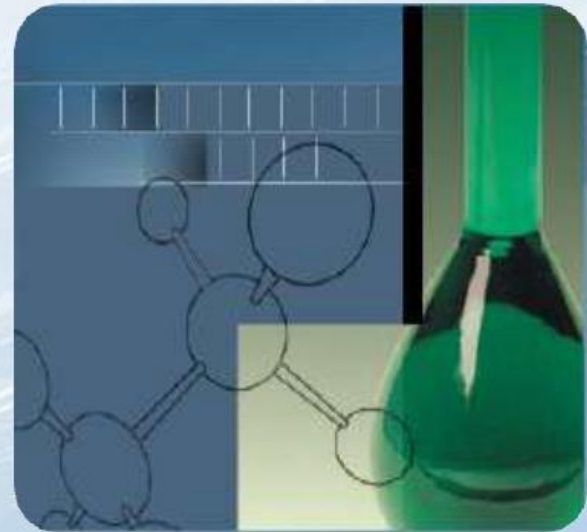


Scheme-1

**Organic Synthesis  
Using  
Ionic Liquids**

# What is Ionic Liquid (IL) ?

- ❖ Salts with melting point close or below room temperature , hence called RTILs.
- ❖ Salts with melting point lower than  $30^{\circ}\text{C}$
- ❖ Entirely made up of equal number of positive & negative ions.
- ❖ So, entire system is neutral.



## PROPERTIES OF RTILs

A salt	<i>Cation and or anion quite large</i>
Freezing point	<i>Preferably below 100°C</i>
Liquidus range	<i>Often &gt; 200°C</i>
Thermal stability	<i>Usually high</i>
Viscosity	<i>Normally &lt; 100 cP, workable</i>
Dielectric constant	<i>Implied &lt; 30</i>
Polarity	<i>Moderate</i>
Specific conductivity	<i>Usually &lt; 10 mScm<sup>-1</sup>, “<b>Good</b>”</i>
Molar conductivity	<i>&lt; 10 Scm<sup>2</sup> mol<sup>-1</sup></i>
Electrochemical window	<i>&gt; 2V, even 4.5 V, except for <b>Brønsted acidic systems</b></i>
Solvent and/or catalyst	<i>Excellent for many organic reactions</i>
Vapor pressure	<i>Usually negligible</i>

# Ionic Liquids

## SALIENT FEATURES

Vapour Pressure

Melting Point

Viscosity

Miscibility with water

Thermal Decomposition



# Vapour Pressure of Ionic Liquids

1

They have small or negligible vapour pressure

2

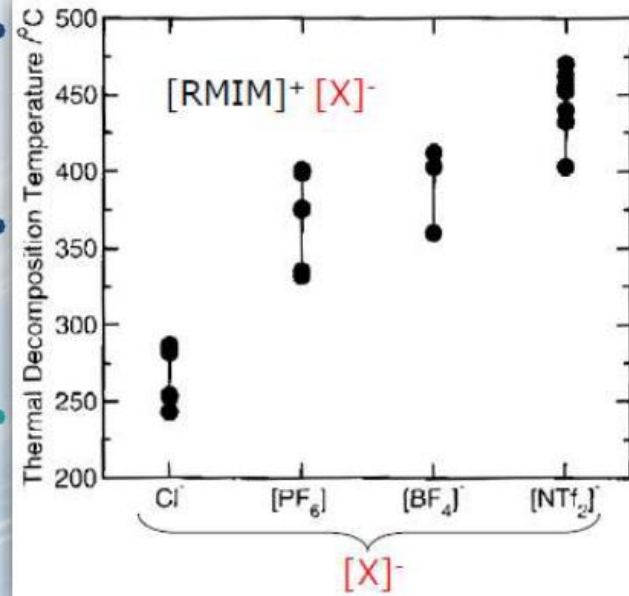
Higher thermal decomposition point

3

Ecological Solvents

4

Unique solvent



# Melting Points of ILs

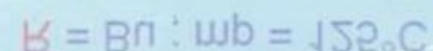
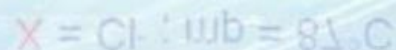
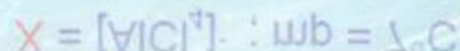
Large range of temperature (-90°C to 150°C)

Modulation of melting point with variation of anion &/or cation size.

## Generally :

size of cation or/and anion increases → melting point decreases

## Examples :



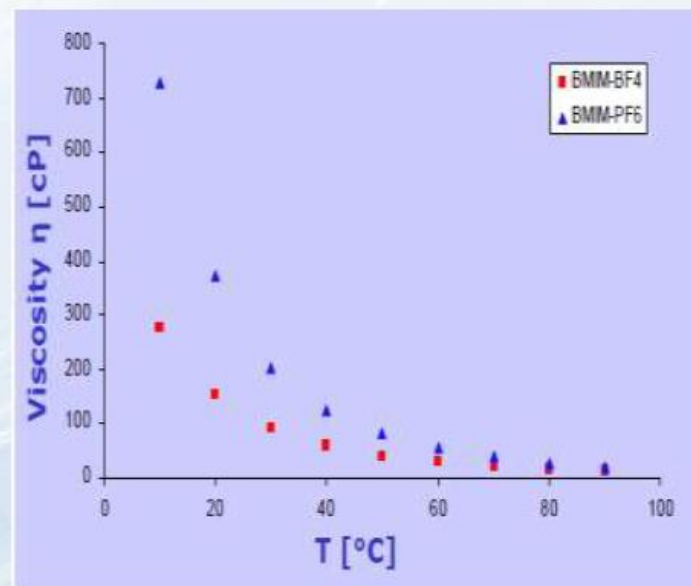
## Examples :



# VISCOSITY OF ILs

They are usually more viscous than classical solvents.

Product	Viscosity [cP] 20°C
Water	1.0
Toluene	0.6
DMF	0.8
[bmim] [BF <sub>4</sub> ]	154
[bmim] [PF <sub>6</sub> ]	371



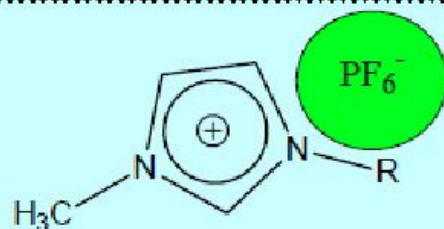
One of the major demerit of ILs



# Miscibility with Water

By changing the nature of ions, It is possible to change miscibility with water.

**IL water  
no soluble**

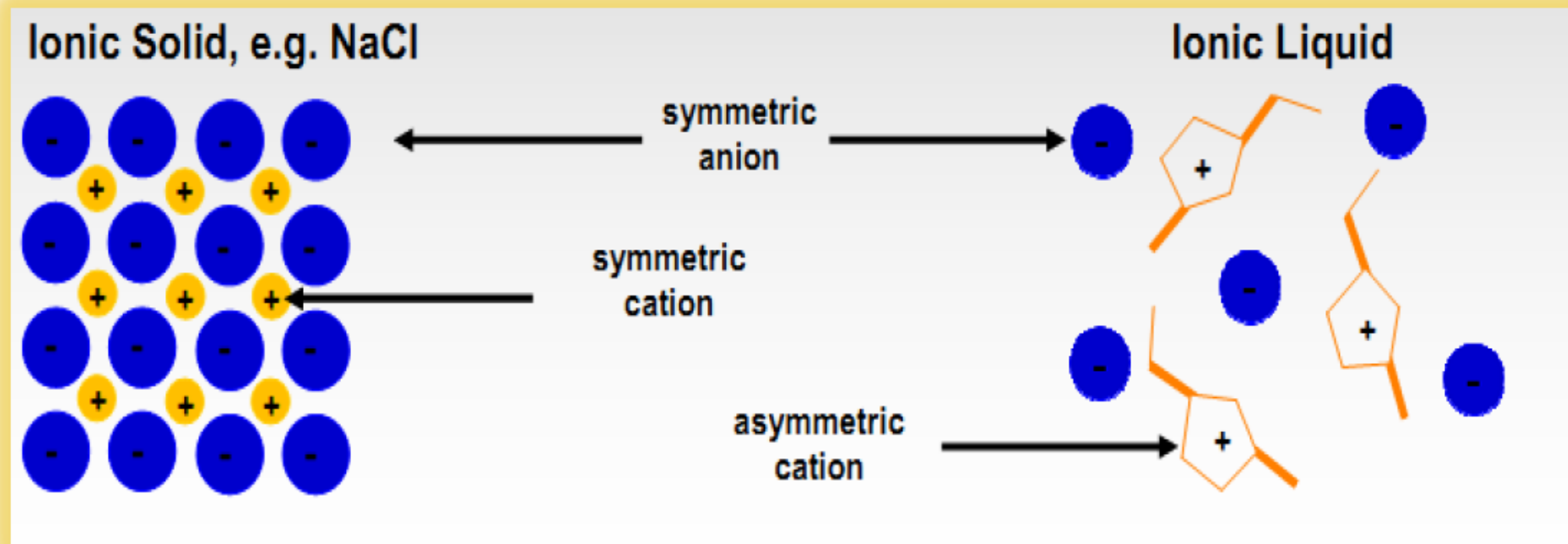


**IL water  
soluble**



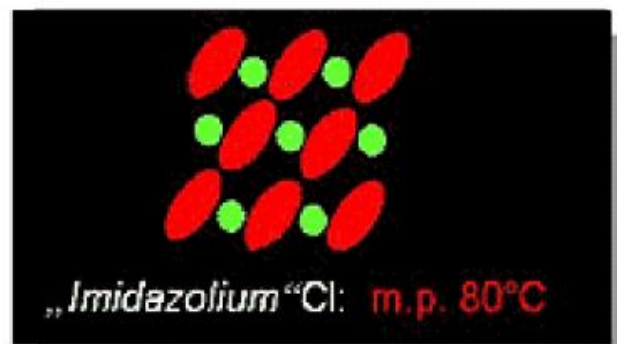
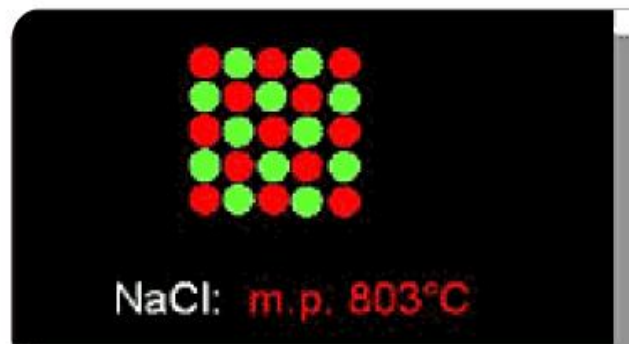
# The 'Ionic State'

- Class of materials-consisting entirely of ions and being liquid below 100°C.

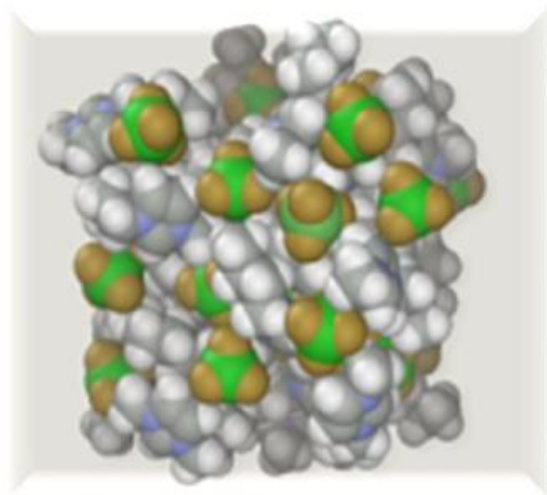




# Why are ionic liquids “liquids”?



- Traditional salts like sodium chloride pack efficiently to form a crystal lattice



- Ionic Liquids-cations are asymmetrically substituted with different **Bulky groups**- to **weaken** this ionic interactions
- prevents packing of the cations/anions into a crystal lattice

A simulated model of an Ionic Liquid

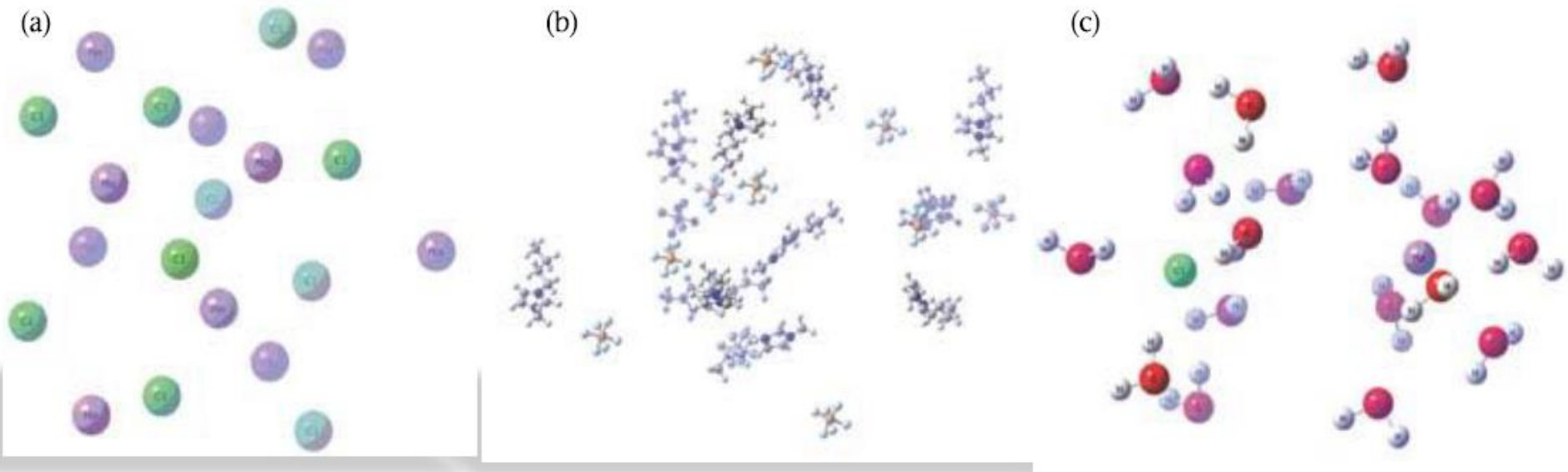
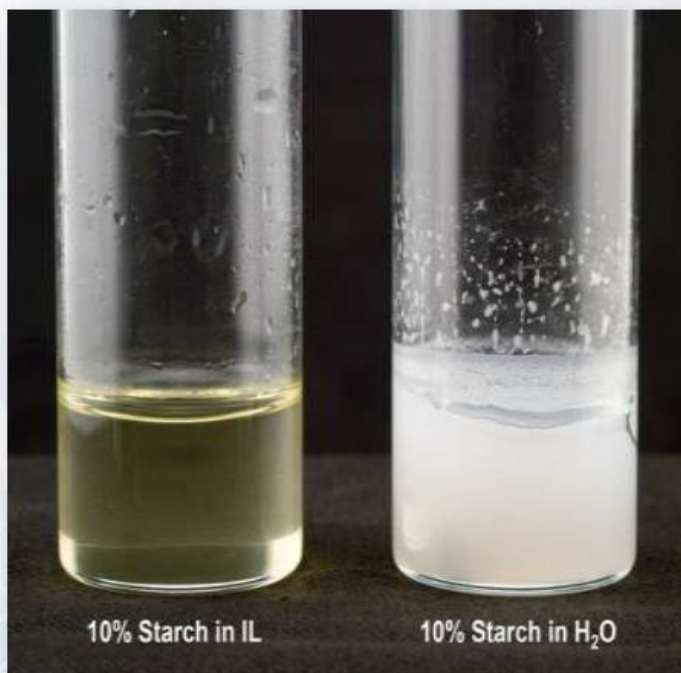


Fig. 1. Representation of (a) liquid NaCl, (b) molten BMIM PF<sub>6</sub>, and (c) aqueous NaCl.



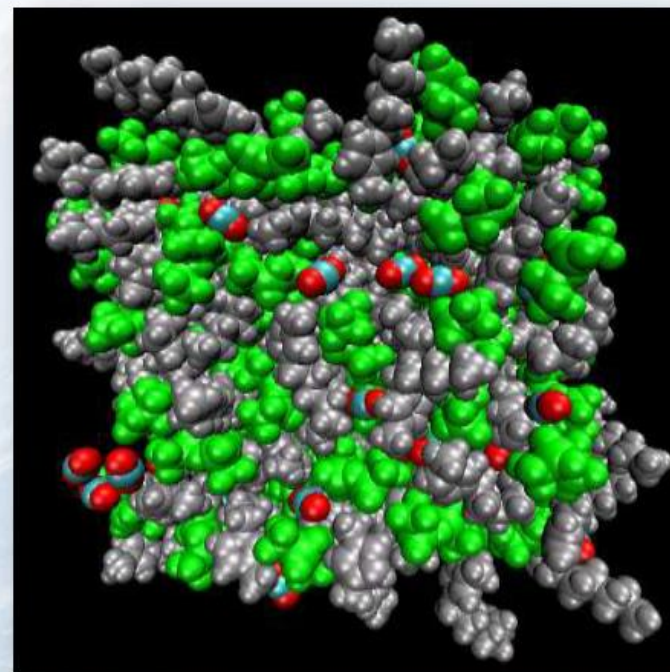
# FEW EXAMPLES OF APPLICATIONS

As Solvent



Ionic Liquids as potential solvents

As Absorbent



*Model of CO<sub>2</sub> absorption by an ionic liquid.  
The model shows that the anions are controlling absorption in ionic liquids. The green units represent anions and the grey units represent cations.*



# FEW Magic fluids...examples...

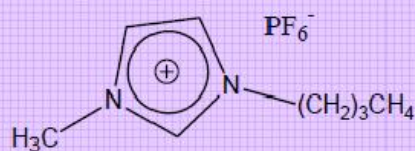
## structures of cations



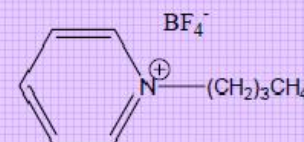
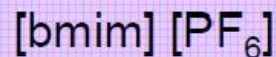
tetraalkylammonium



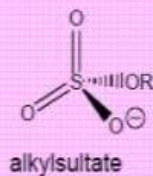
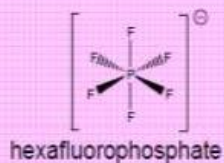
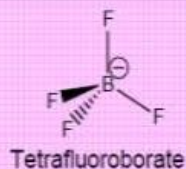
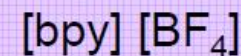
trihexyl(tetradecyl)phosphonium



1-butyl-3-methyl-imidazolium  
hexafluorophosphate



1-butyl-pyridinium tetrafluoroborate



## structures of anions

# HOW TO FORMULATE THIS MAGICAL LIQUID?

1) ALKYLATION  
FOLLOWED BY  
METATHESIS

2) ACID BASE  
NEUTRALIZATION



1) ALKYLATION  
FOLLOWED BY  
METATHESIS

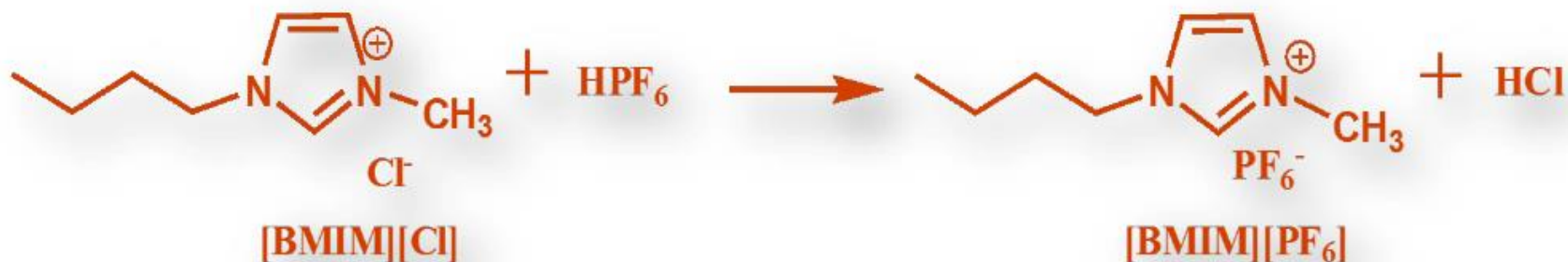
ELEVATED TEMPERATURE & REFLUXING  
SOLVENT APPROACH

MICROWAVE OR ULTRASONIC  
SYNTHESIS

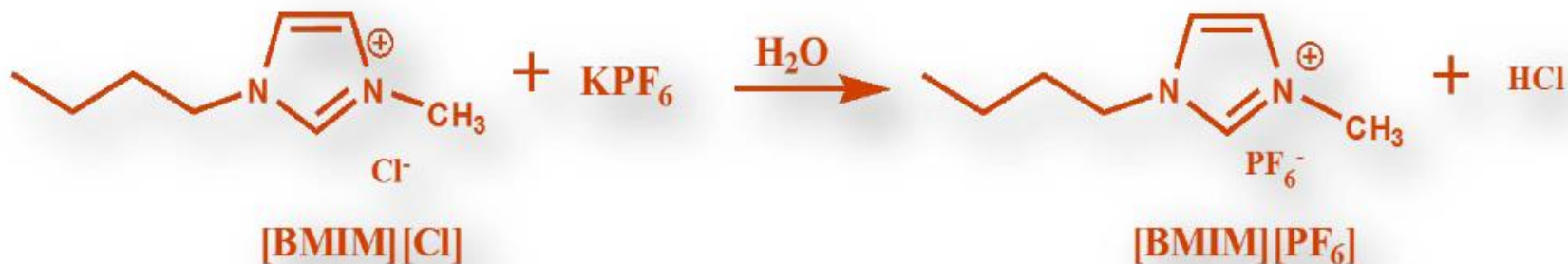
ROOM TEMPERATURE "WAIT & SEE"  
SOLVENT FREE APPROACH.

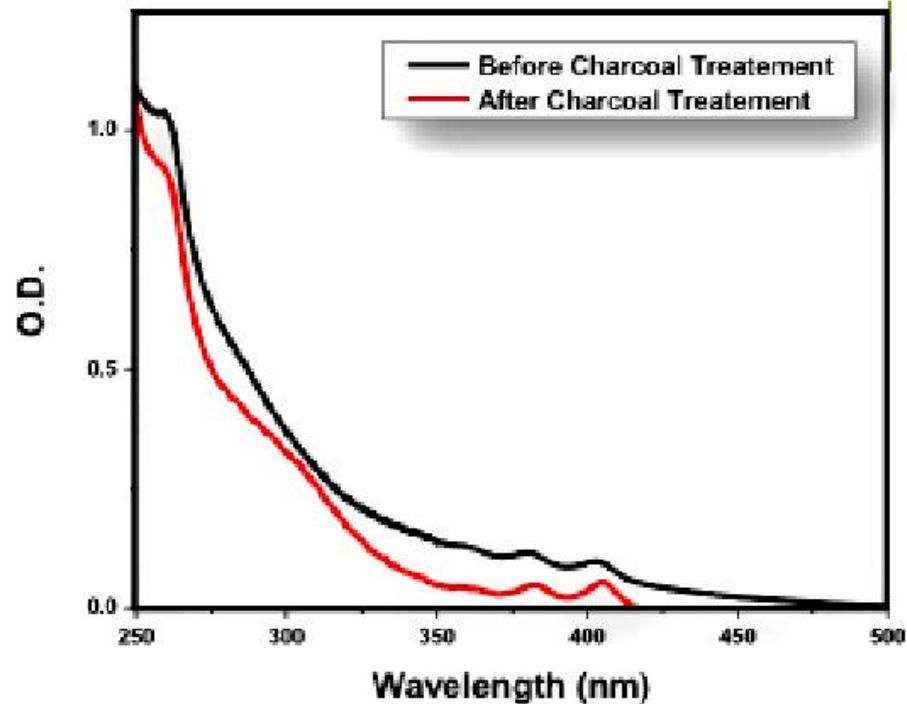
## Metathesis reaction

Using  $\text{HPF}_6$ :



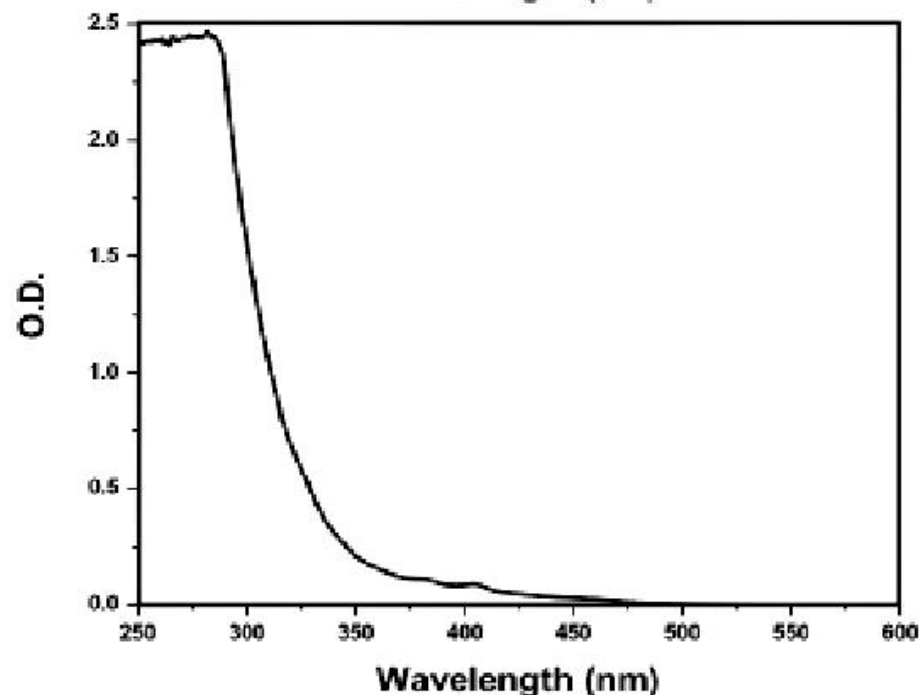
Using  $\text{KPF}_6$ :





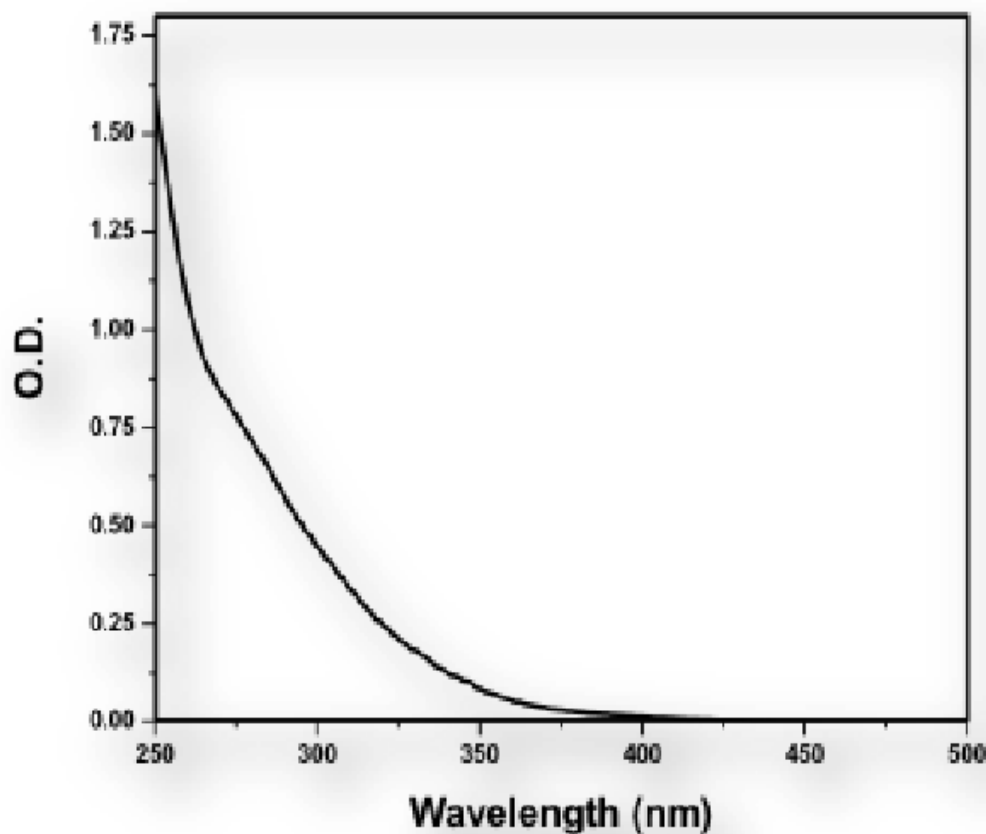
**Figure 1:** Absorption spectrum of [BMIM][PF<sub>6</sub>] before and after charcoal treatment.

Two additional peaks were also observed at 404 nm and 383 nm.



**Figure 2 :** Absorption spectrum of [BMIM][PF<sub>6</sub>] after passing through specially designed celite column. 383nm and 404nm peak persisted.

## Metathesis Reaction using $\text{KPF}_6$

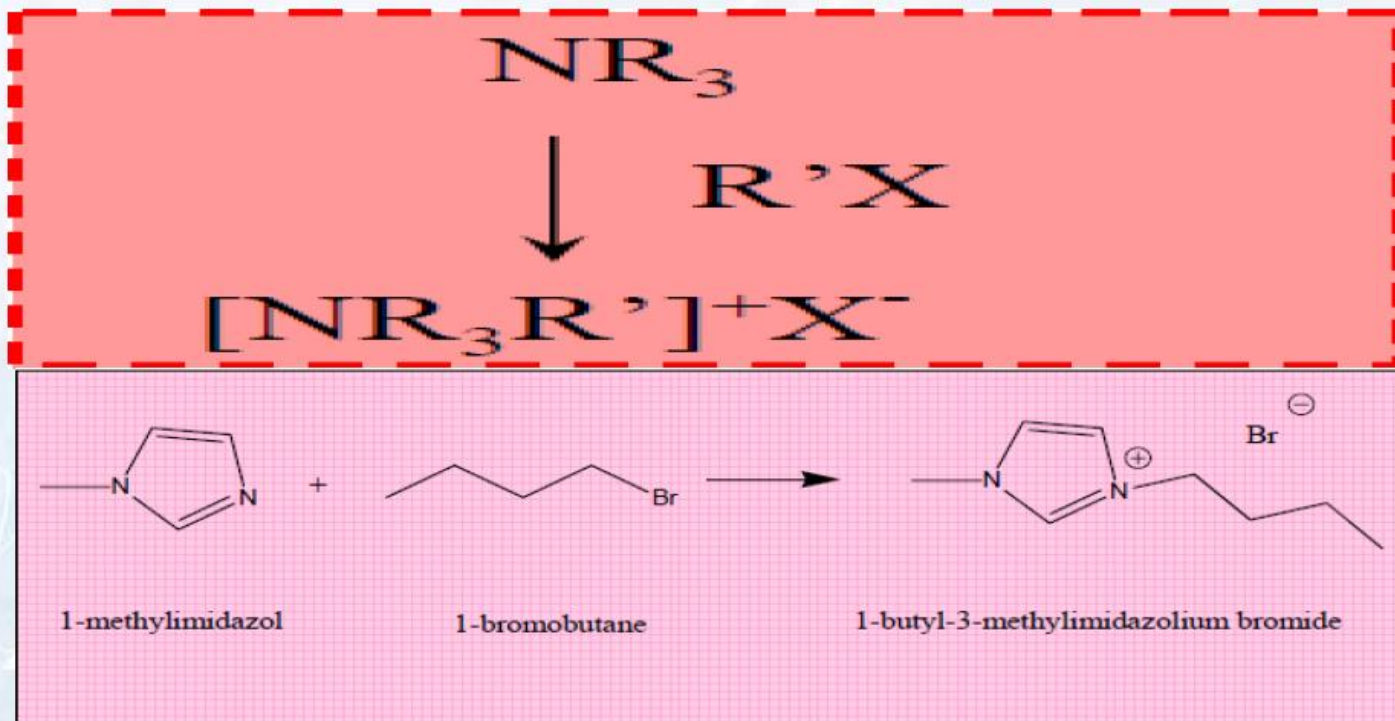


**Figure 3:** Absorption Spectrum of  $[\text{BMIM}][\text{PF}_6]$  prepared by using  $\text{KPF}_6$

The impurities that came along the preparation of ionic liquid with  $\text{HPF}_6$  might be result of products obtained by this corrosive nature of  $\text{HPF}_6$  on glass.



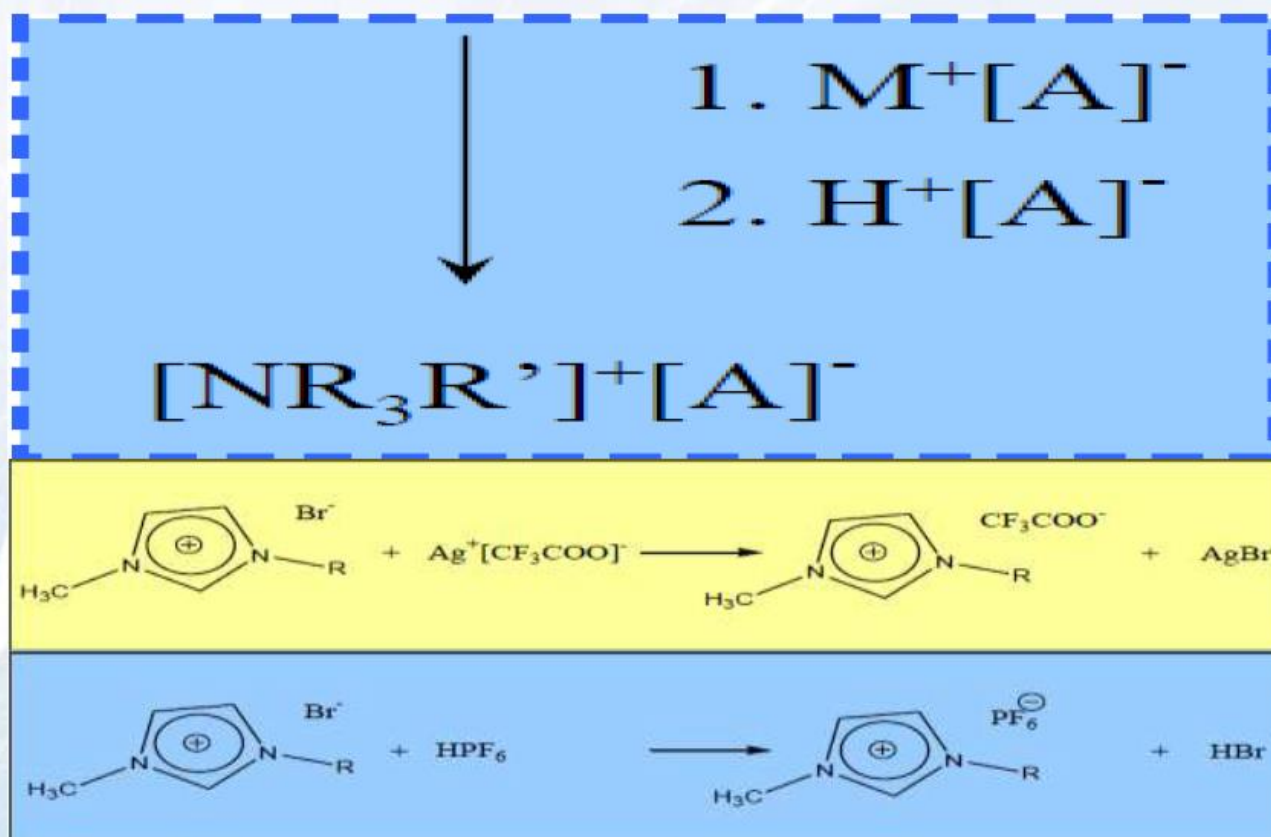
# QUATERNIZATION REACTION



**Quaternization reaction**

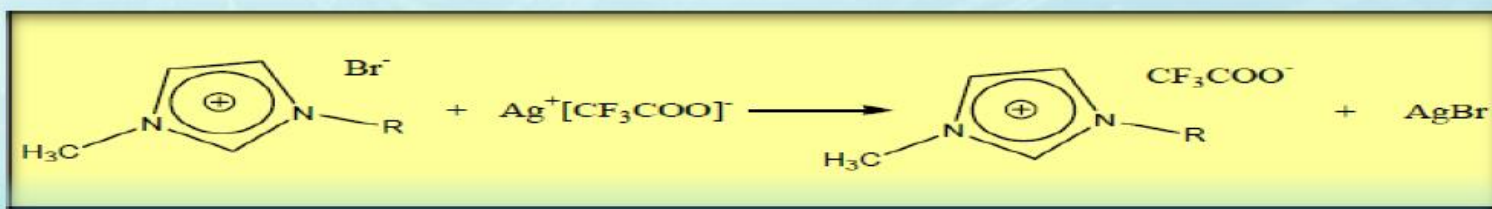
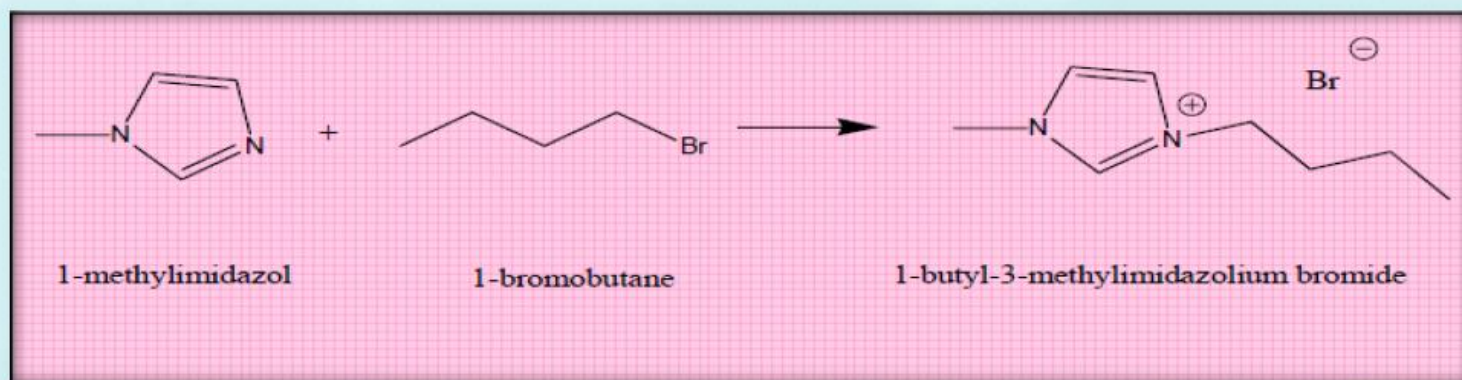


# Anion Exchange



# SYNTHESIS cont....

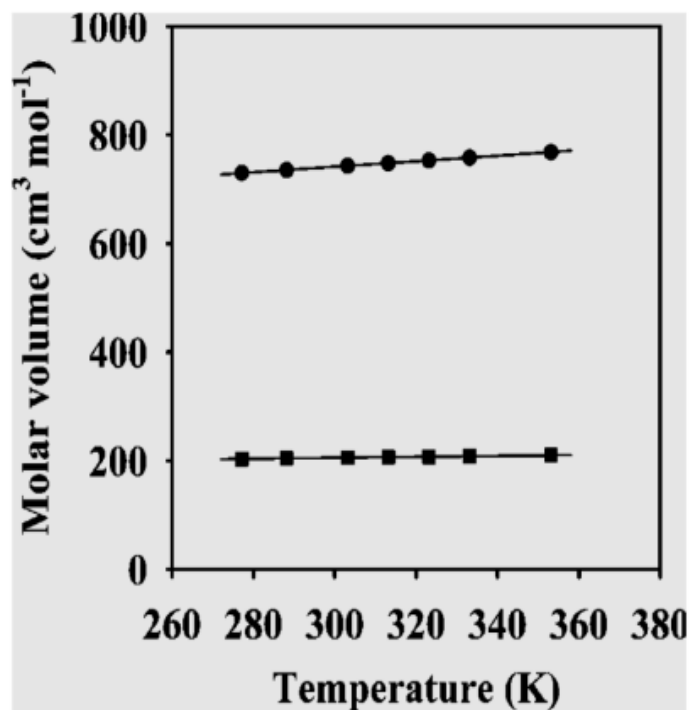
## QUATERNIZATION REACTION



## ANIONIC EXCHANGE REACTION

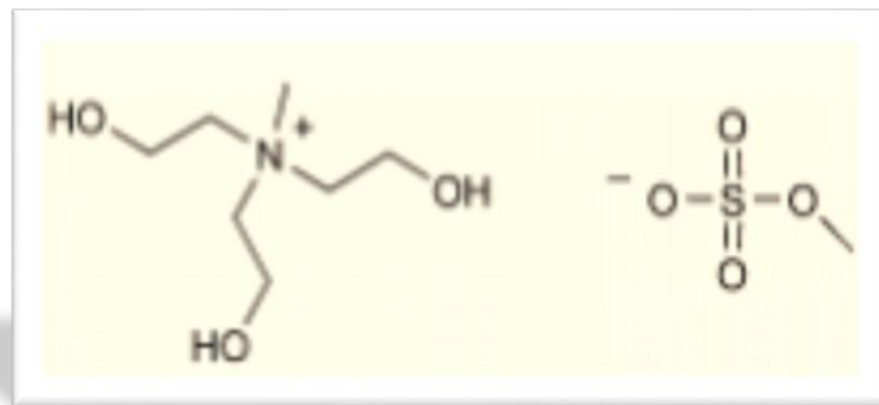
# Ionic liquids for liquid-in-glass thermometers

- Tris(2-hydroxyethyl) methylammonium methylsulphate ([TEMA][MeSO<sub>4</sub>]).



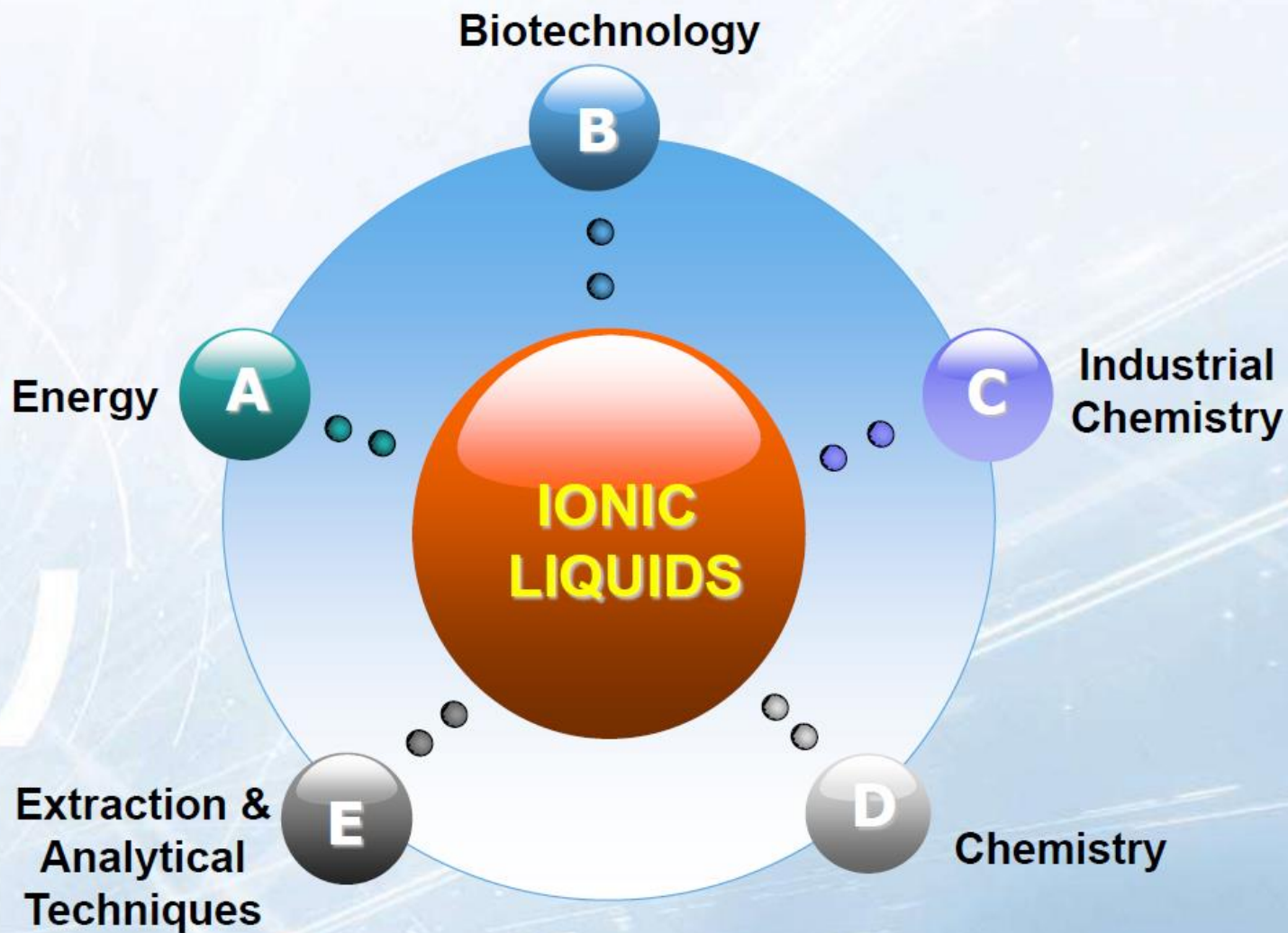
**Fig. 1** Molar volume  $V$  as a function of temperature  $T$  for [TEMA][MeSO<sub>4</sub>] (squares) and [P<sub>66614</sub>][NTf<sub>2</sub>] (circles). The solid lines represent the linear regressions.

- Range: -50 °C to 140 °C
- Glass transition temperature  $T_g = -81$  °C
- Stable up to 200 °C



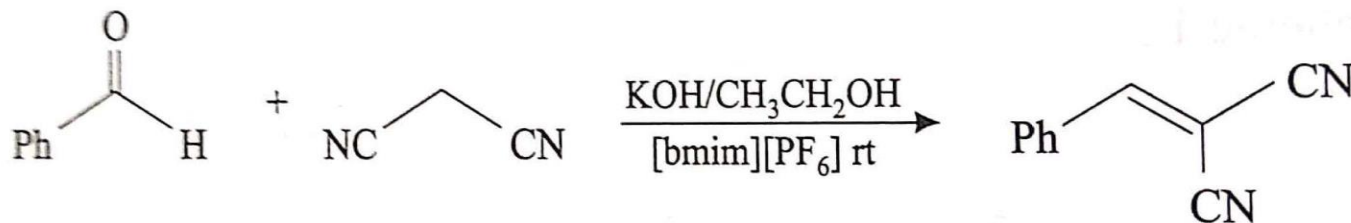


# Applications



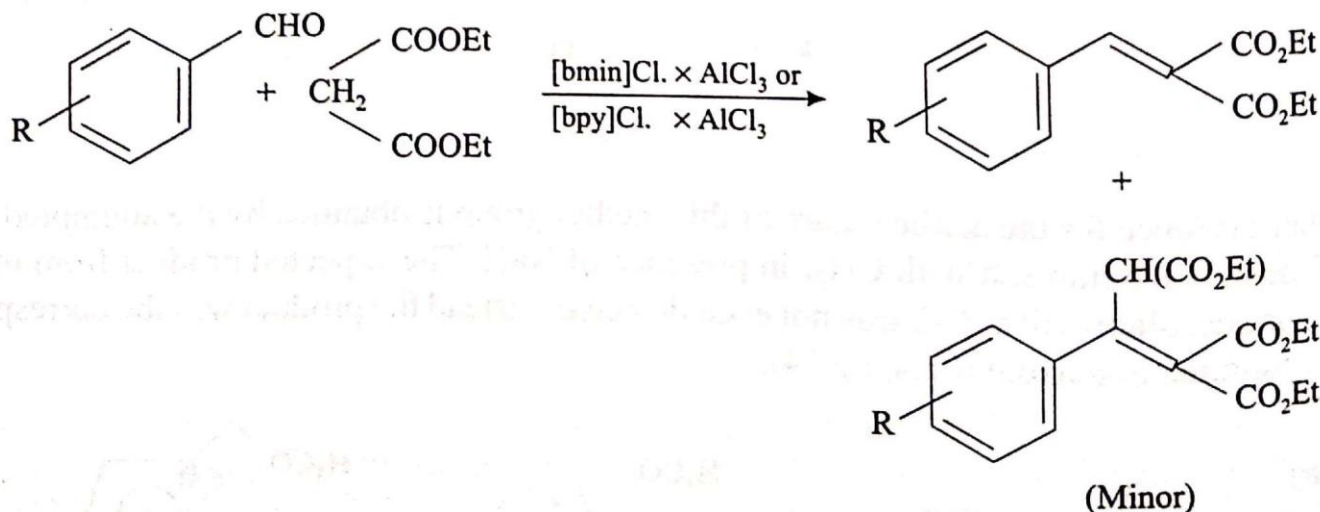
# Organic Reactions Using Ionic Liquid

## 1. The Knoevenagel Condensation:



Scheme-1

Here low yield due to the solubility of the formed product in the IL

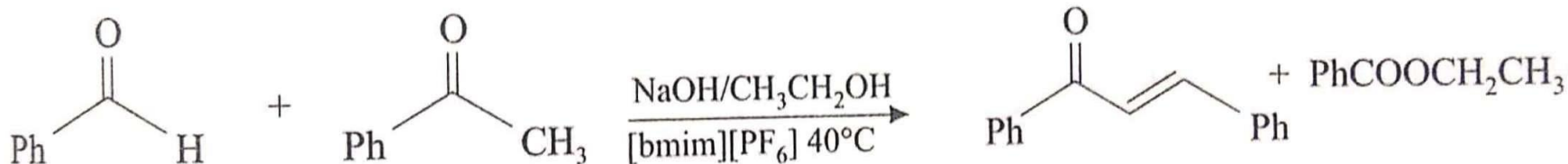


Scheme-2

In scheme-2 yield increase due to ILs works as Lewis acid catalyst.

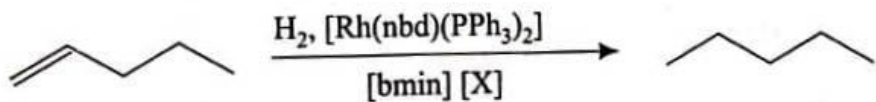


## 2. Claisen-Schmidt Condensation:



Scheme-1

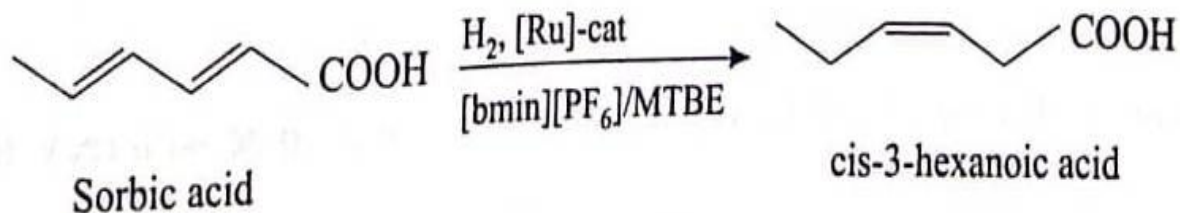
## 3. Hydrogenation:



X = BF<sub>4</sub><sup>-</sup>, PF<sub>6</sub><sup>-</sup>, Sb F<sub>6</sub><sup>-</sup>, nbd = norboranadiene

Using Wilkinson's Catalyst  
in this reaction

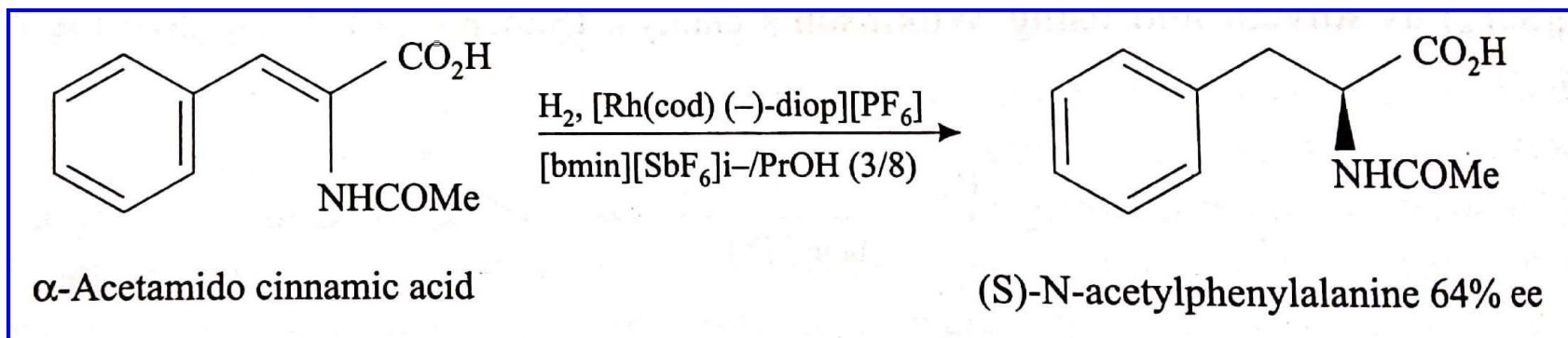
Scheme-1



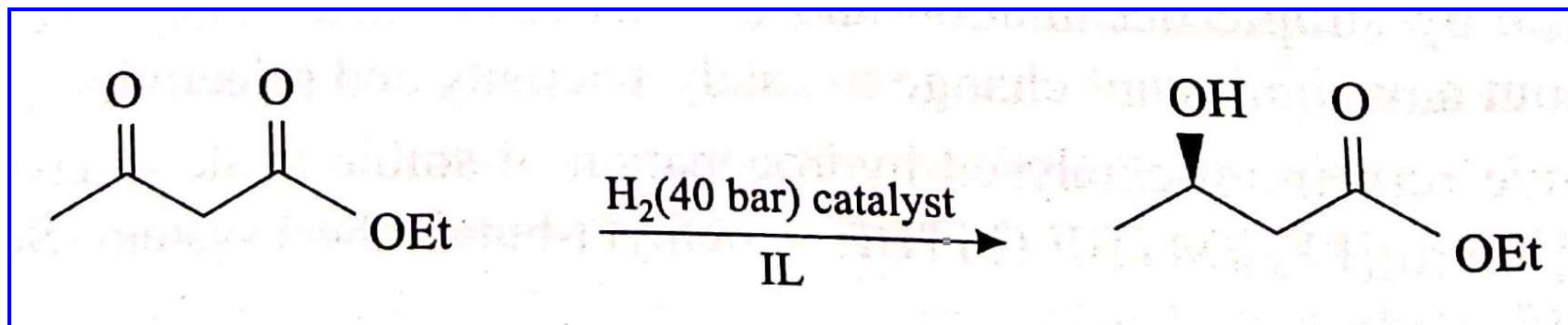
An example of  
stereoselective  
ruthenium-catalysed  
hydrogenation

Scheme-2

### 3. Hydrogenation:

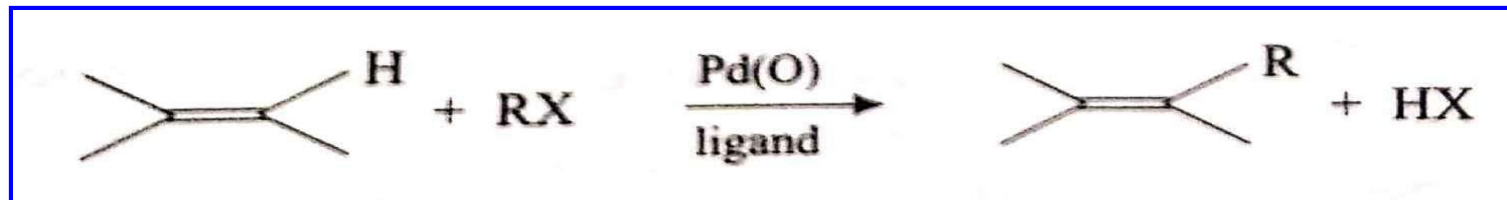


Scheme-3: An example of enantioselective hydrogenation



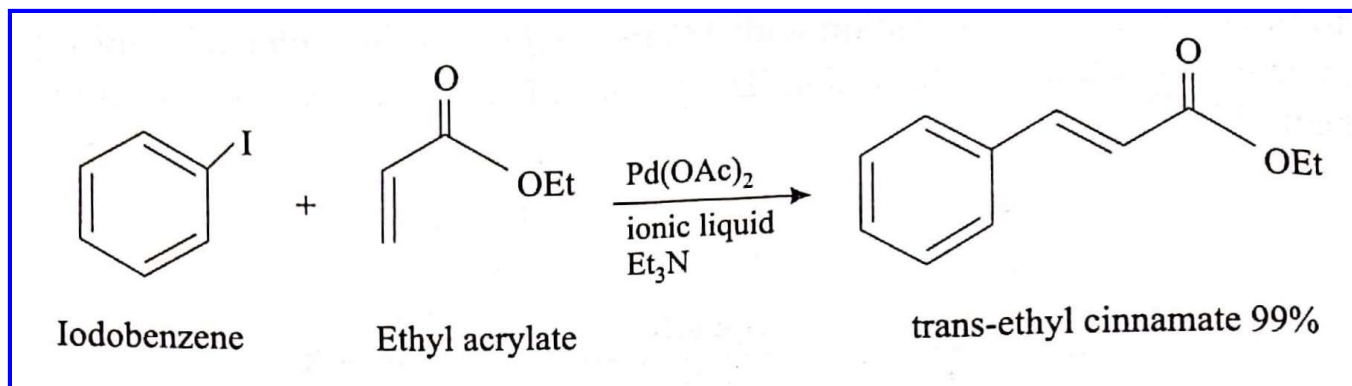
Scheme-4: In this reaction IL allowed the catalyst to be recycled with an increased in ee with recycle number.

## 4. Heck Reaction:



Scheme-1

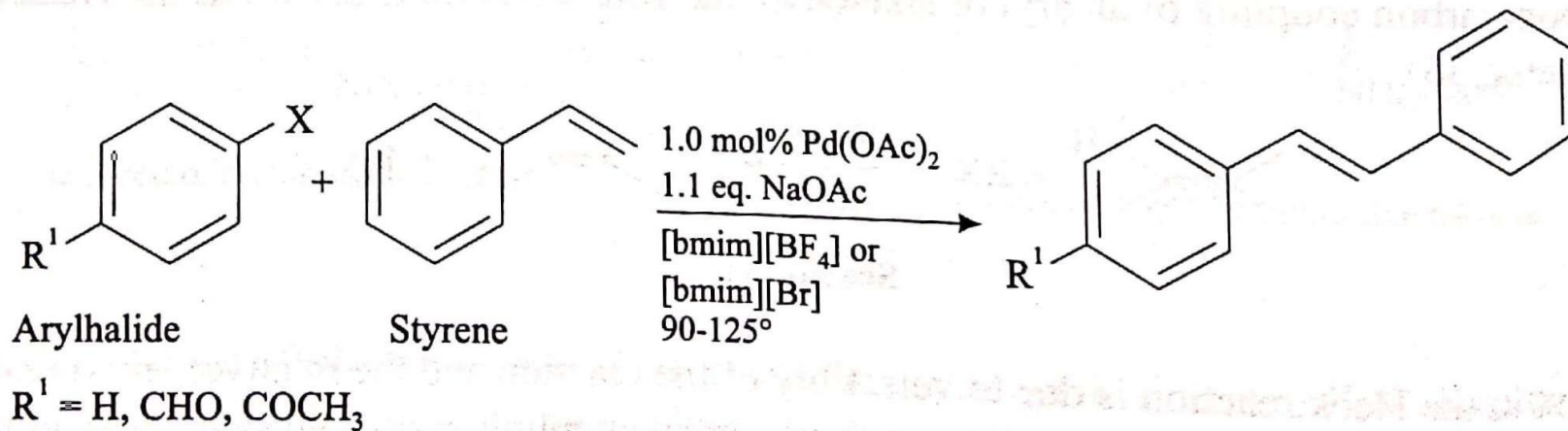
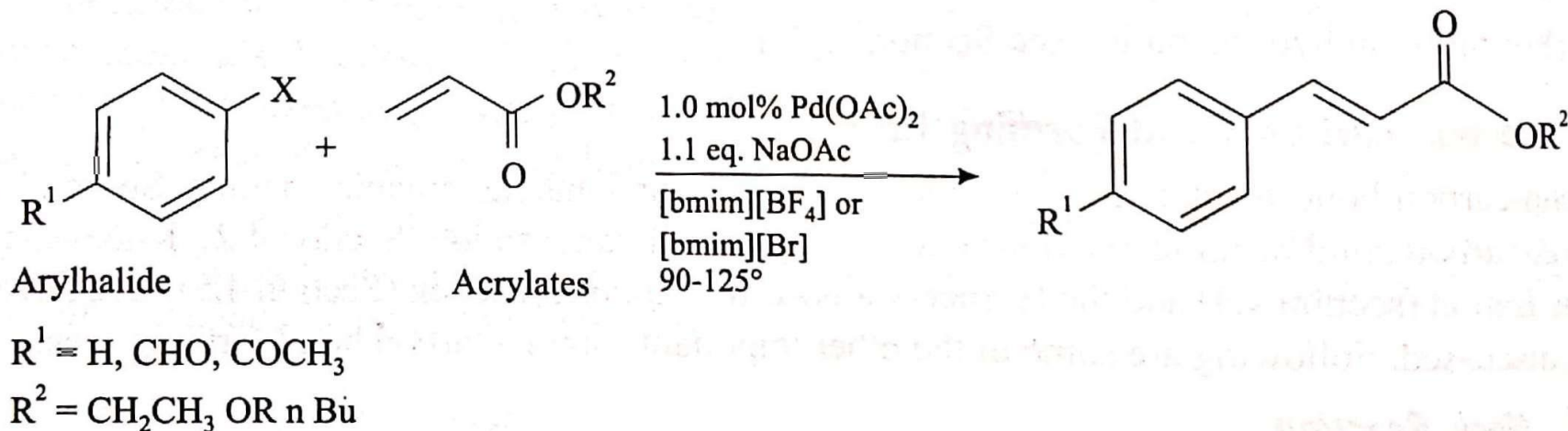
It has been found that the Heck Reaction with less reactive halides (bromides and chlorides) require the use of Phosphine liquids to stabilize the active palladium species. A drawback of the Heck Reaction is that the palladium catalyst can not be recovered and reused.



Scheme-2

Higher yield were obtained in presence of IL

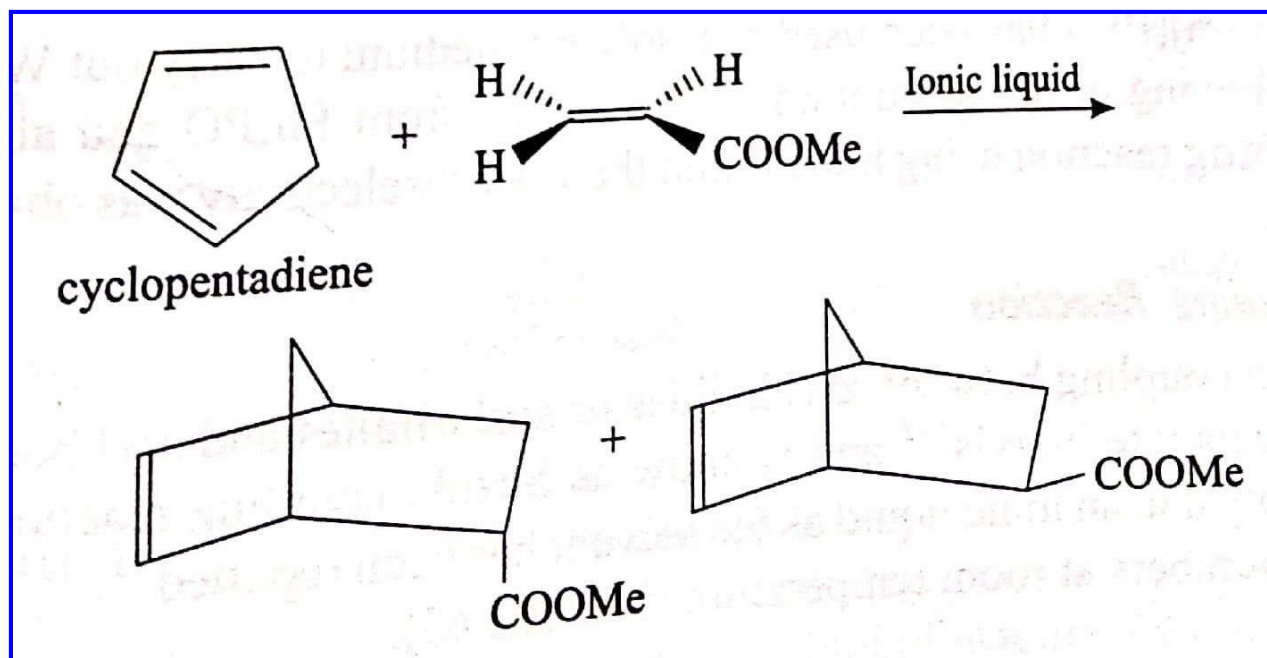
## 4. Heck Reaction:



Scheme-3

## 5. Diels-Alder Reaction:

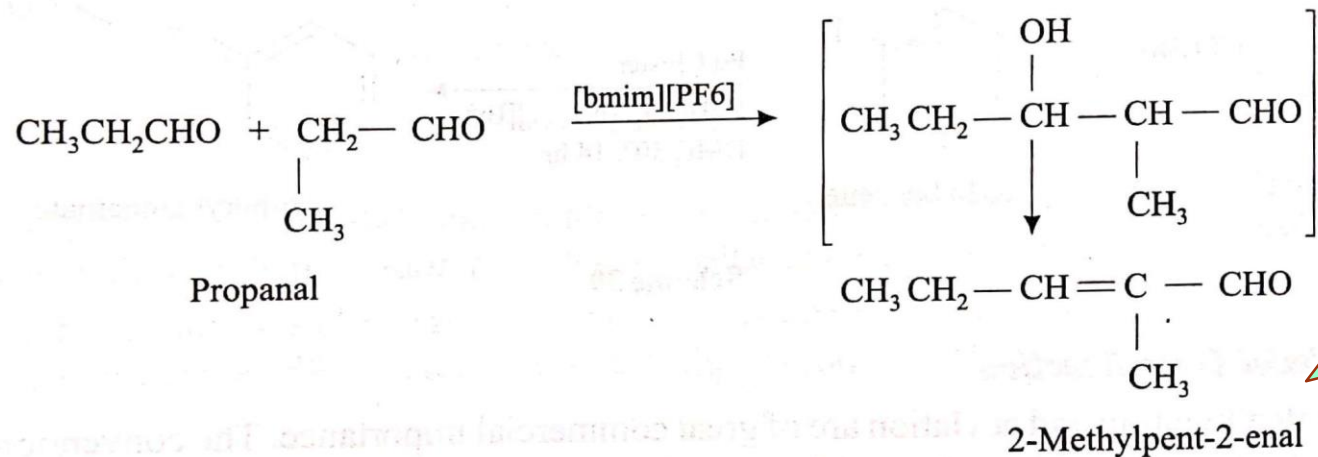
The great usefulness of Diels-Alder reaction lies in its high yield and high stereospecificity. Use of ionic liquids such as [bmim][BF<sub>4</sub>], [bmin][ClO<sub>4</sub>], [emin][CF<sub>3</sub>SO<sub>3</sub>] and [emin][PF<sub>6</sub>] for Diels-Alder reaction between cyclopentadiene and methyl acrylate result in rate enhancement, high yields and strong endoselectivities.



Scheme-1



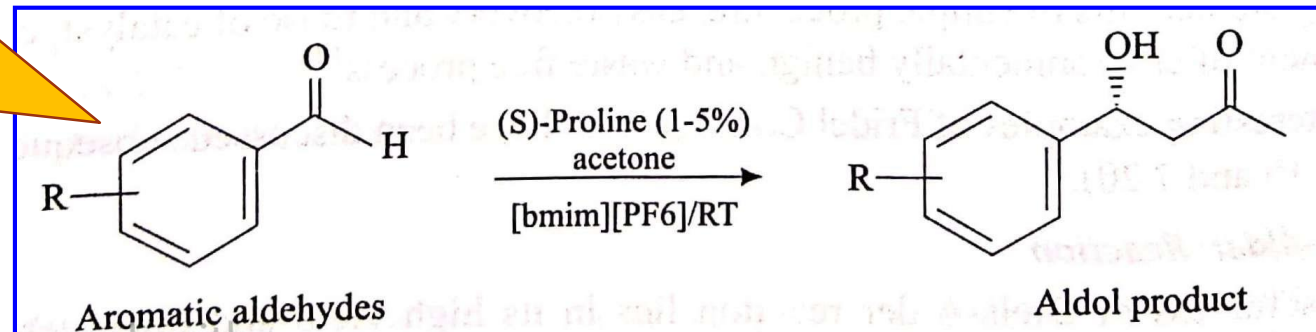
## 6. Aldol Condensation:



This is the self-condensation reaction where highest product selectivity was found for that IL

Scheme-1

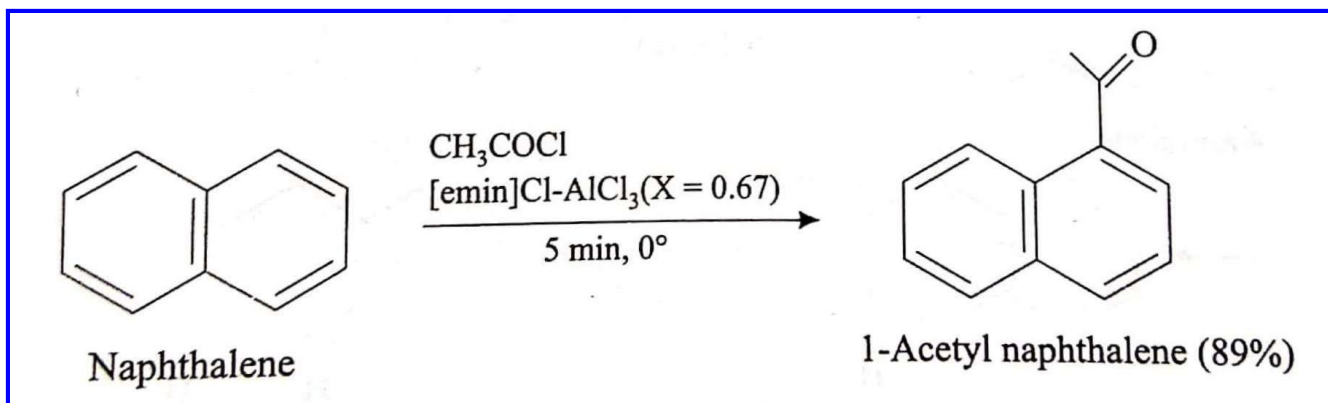
The proline-catalyst asymmetric direct aldol reaction gave good yield with reasonable enantioselective.



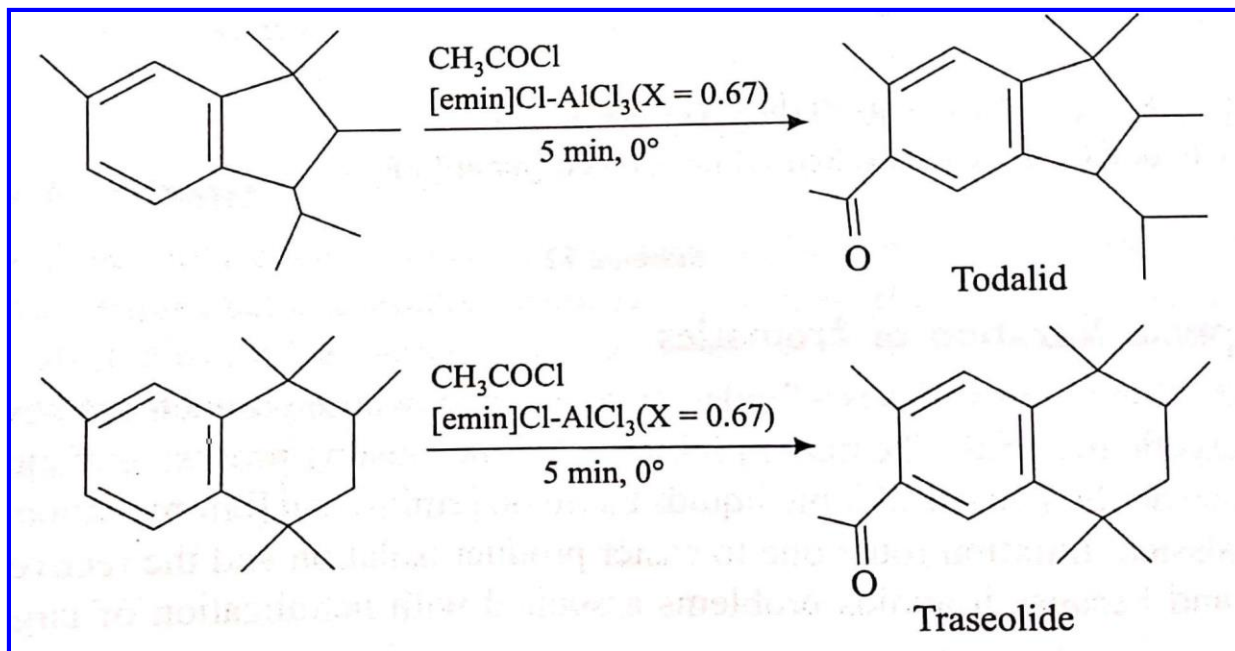
Scheme-2

## 7. Friedel-Craft Reaction:

Scheme-1



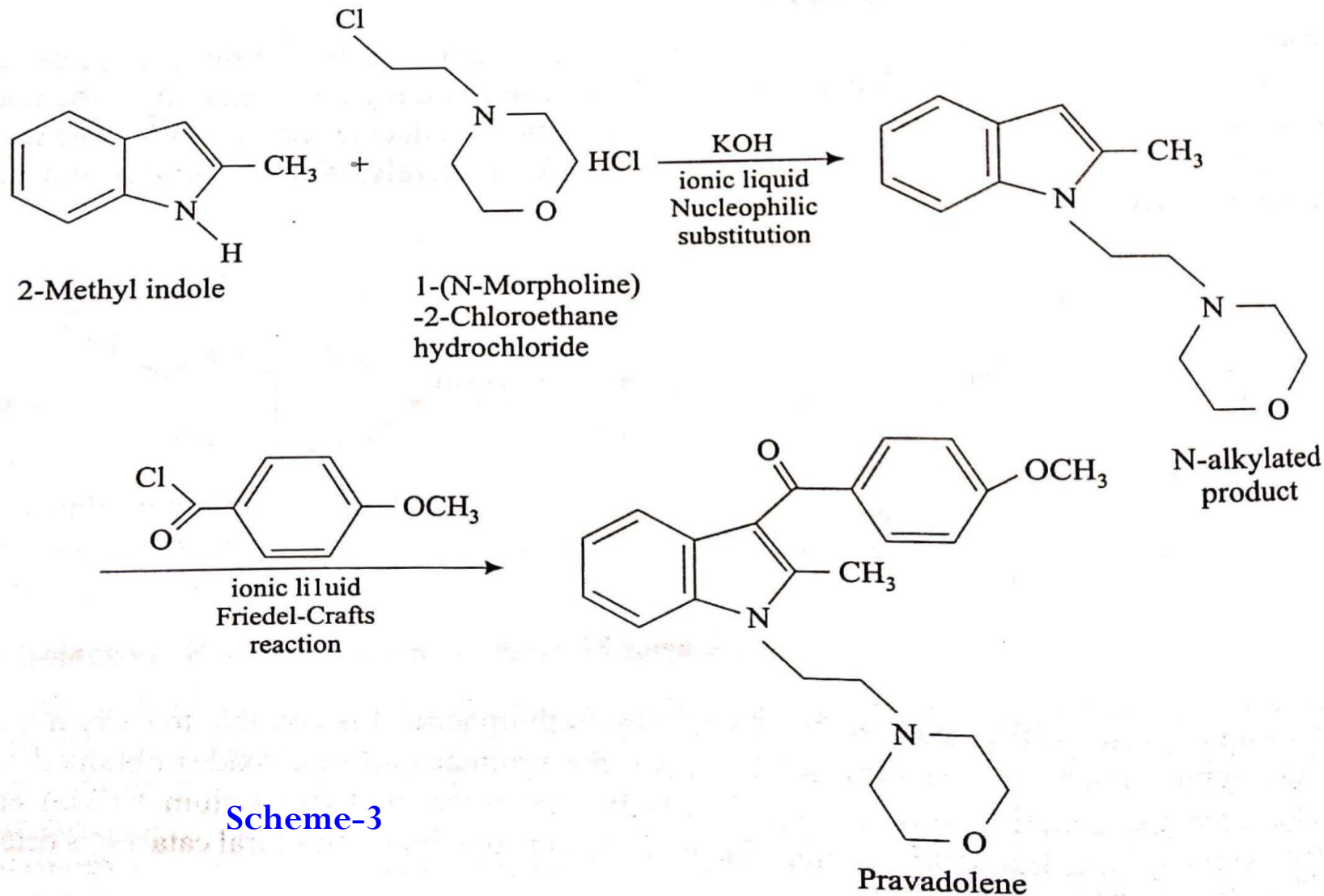
Synthesis of 1-Acetylnaphthalene



Scheme-2

Synthesis of Tonalid and Traseolide

## 7. Friedel-Craft Reaction:



## Synthesis of Pravadolene

# Limitations of Ionic liquids



- Very expensive compared to organic solvents (100 to 1000 x).
- Have to be made, often using solvent.
- Products have to be extracted from ionic liquid using solvent.
- May have to wash with water prior to reuse.

# **SOLVENTLESS REACTIONS**



# Why Are Reactions Performed Using Solvents?

- To dissolve reactants.
- To slow or increase the rate of reactions.
- To act as a heat sink or heat transfer agent.
- To prevent hot spots and run-away reactions.

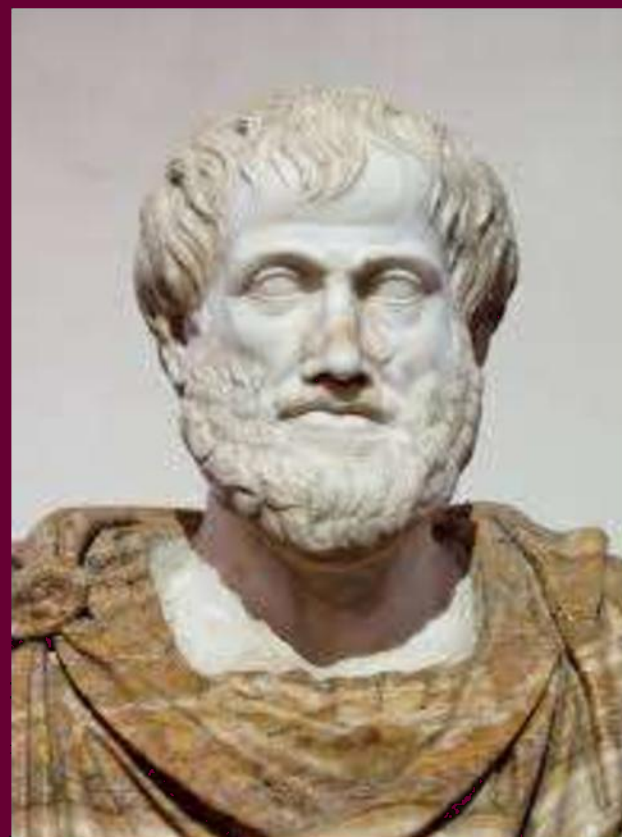
# Issues with Organic Solvents

- **Organic solvents are of concern to the chemical industry because of the sheer volume used in synthesis, processing, and separation.**
- **Organic solvents are expensive**
- **Organic solvents are highly regulated.**
- **Many organic solvents are volatile, flammable, toxic, and carcinogenic.**

# “No Coopora nisi Fluida”

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

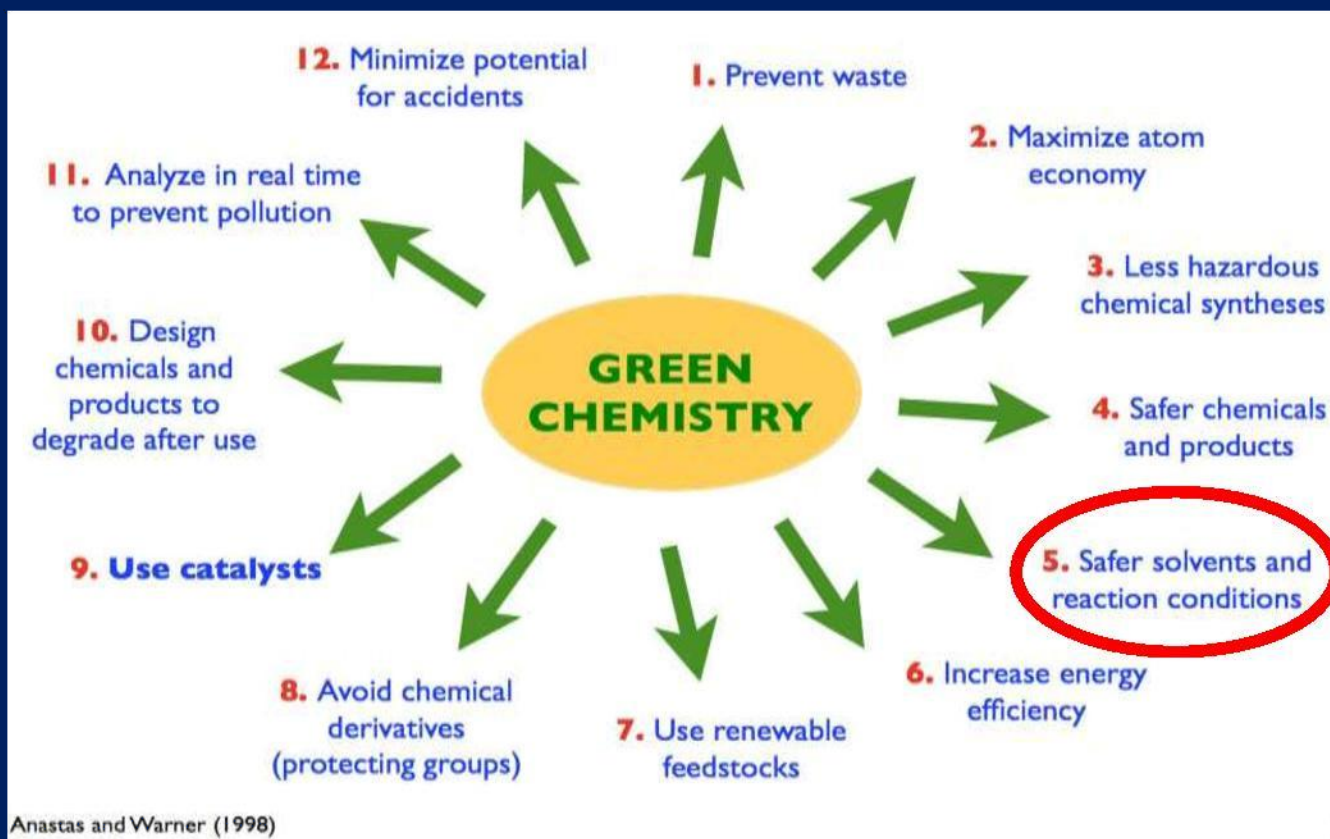
(This is not true!)



# SOLVENTLESS REACTIONS

- ✓ A dry media reaction or solid-state reaction or **solventless reaction** is a chemical reaction system in the absence of a solvent.
- ✓ The **drive** for the development of dry media reactions in chemistry is:
  - **Economics** (save money on solvent)
  - **Not required to remove a solvent** after reaction completion ultimately purification step not required
  - **Reaction rate is high** due more availability of reactants.
  - **Environmentally friendly** because solvent is not required.

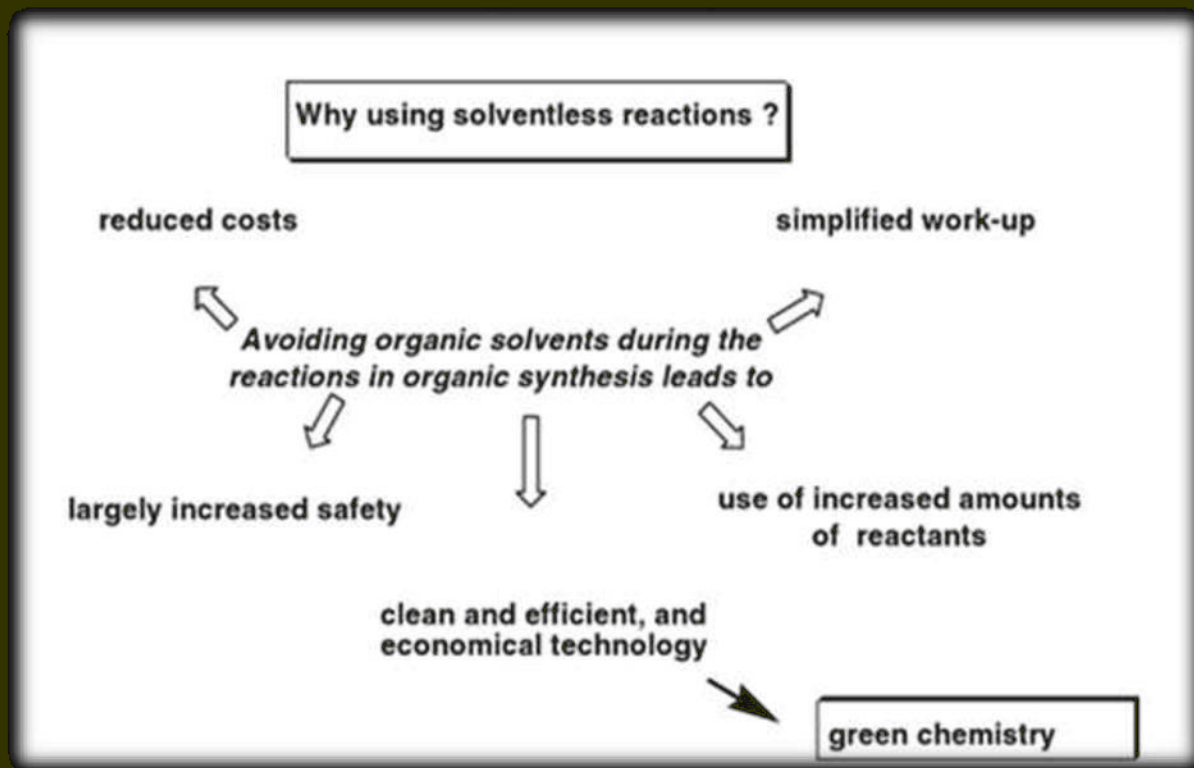
**Solid state** reaction follows the **fifth principle** of green chemistry which avoid using toxic solvents in the chemical reaction.





# ADVANTAGES

- More efficient **with** more selectivity **compared to reactions carried out in solvents.**
- **Reactions are simple to handle, reduce pollution, comparatively.**
- **Cheaper to operate and are especially important in industry.**



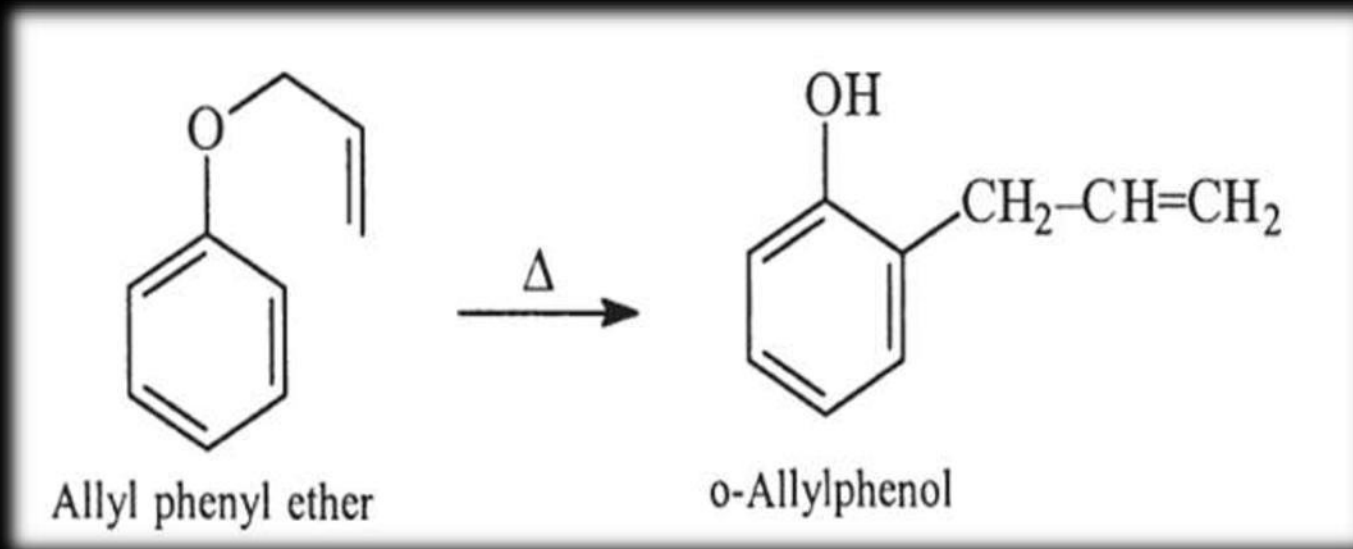
**Solvent  
Free**

**•Organic  
Reaction**

- **Halogenation**
- **Michael Addition**
- **Aldol Condensation**
- **Grignard Reaction**
- **Reformatsky Reaction**
- **Pinacol-Pinacolone Rearrangement**
- **Benzil-benzilic acid rearrangement**
- **Beckmann Rearrangement**
- **Aromatic Substitution Reactions**
- **Oxidative coupling of phenols**

# Solid phase organic synthesis without using any solvent

- The earliest record of an organic reaction in dry state is the **Claisen rearrangement** of allyl phenyl ether to o-allyl phenol.

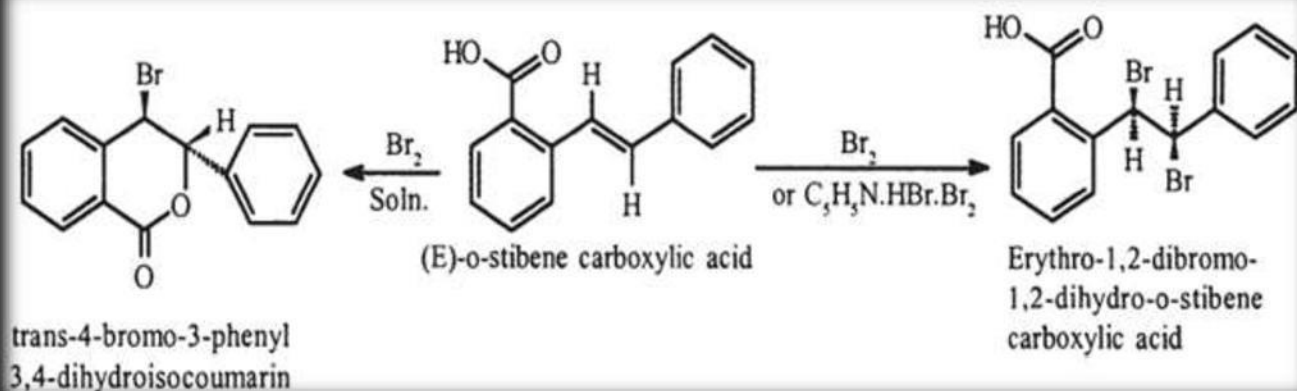


# HALOGENATION

## Bromination of powdered (E)-o-stilbene carboxylic acid

- Bromination with bromine in solution gives 1,2,4-bromo-3-phenyl-3,4-dihydroisocoumarin as the major product.

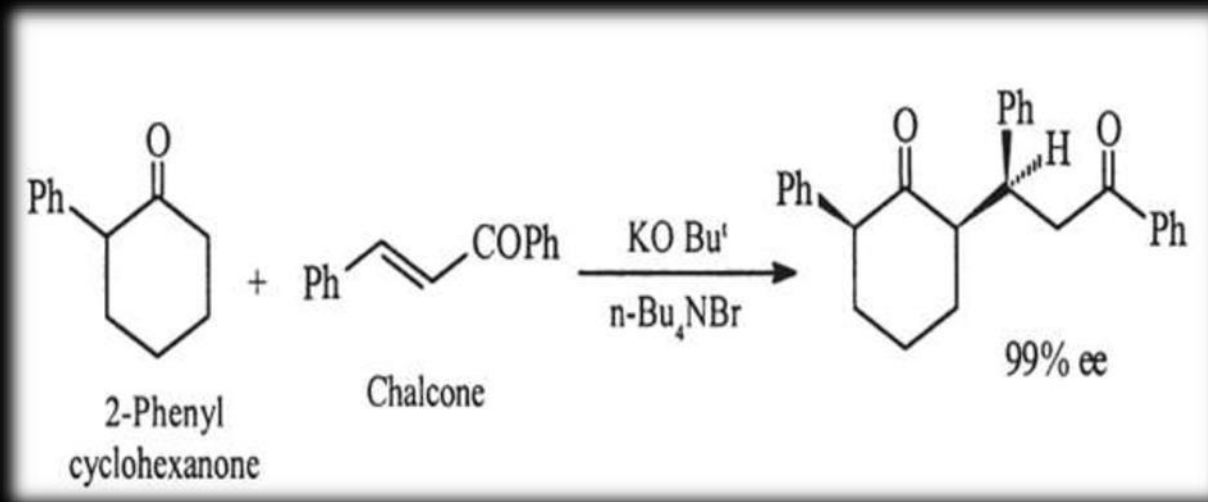
- HBr.Br<sub>2</sub> complex in solid state at room temperature gave 12 selectively erythro-1,2-dibromo-1,2-dihydrostilbene carboxylic acid.





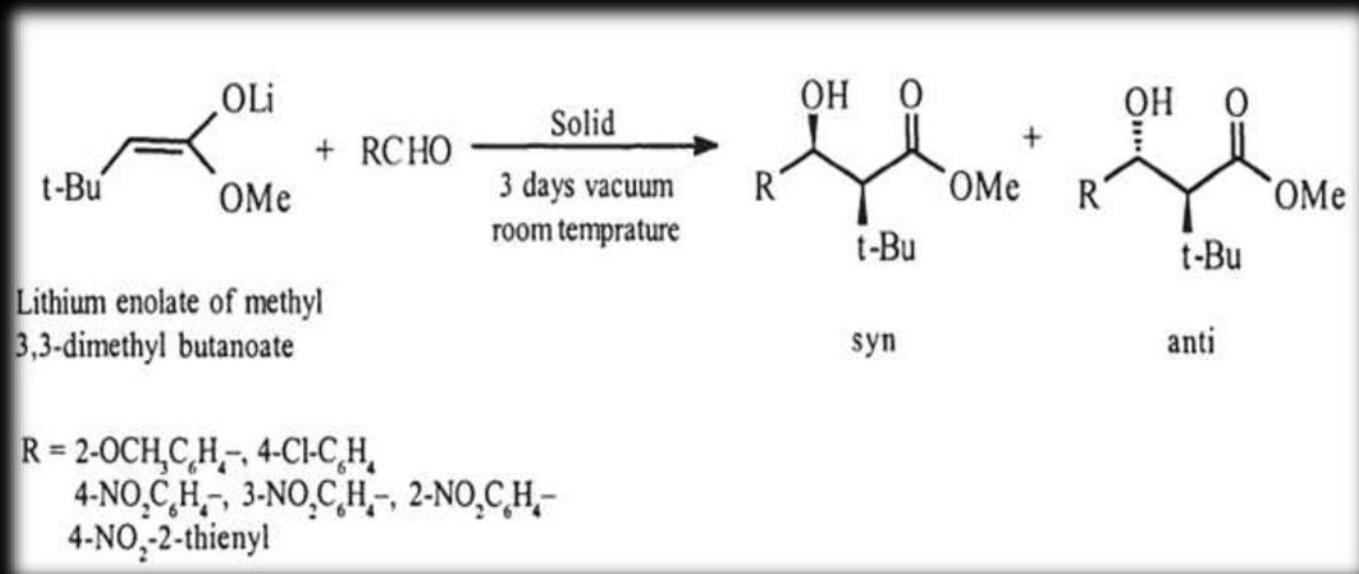
# MICHAEL ADDITION

- The Michael addition of chalcone to 2-phenyl cyclohexanone give 2,6-disubstituted cyclohexanone derivative in **high distereoselectivity**.



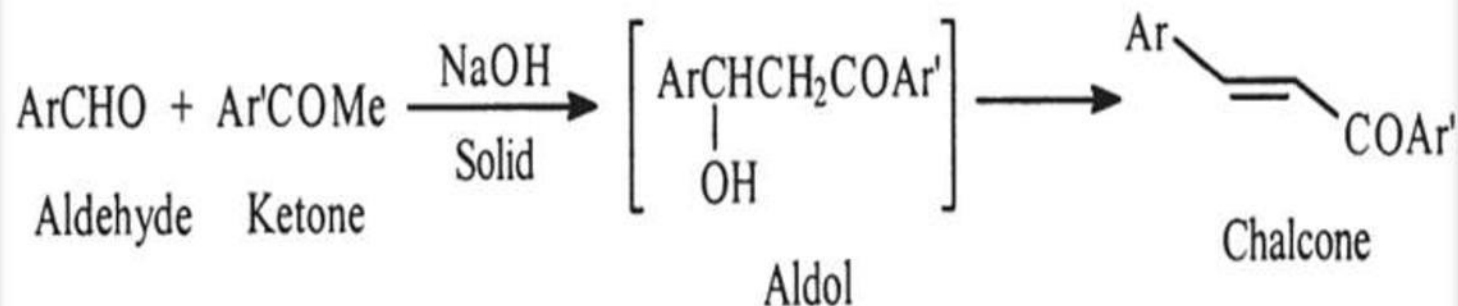
# ALDOL CONDENSATION

- The aldol condensation of the lithium enolate of methyl 3,3-dimethyl butanoate with aromatic aldehydes gives mixture of the syn and anti products in 70% yield.



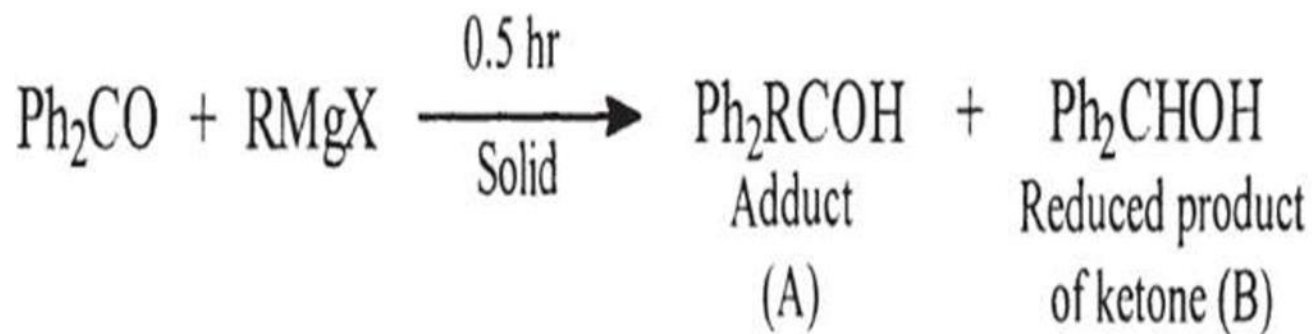
## FROM ALDOL TO CHALCONES:

- The aldehyde and ketone and NaOH is grounded in a pestle and mortar at room temperature for 5 min.
- The product obtained is the corresponding chalcone.
- The formed aldol dehydrates more easily to the chalcone in the absence of solvent.



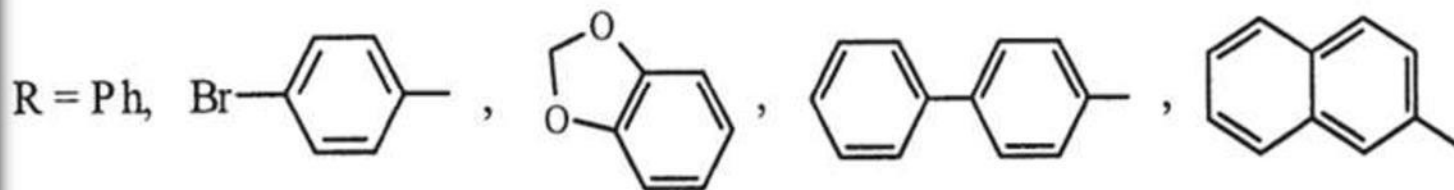
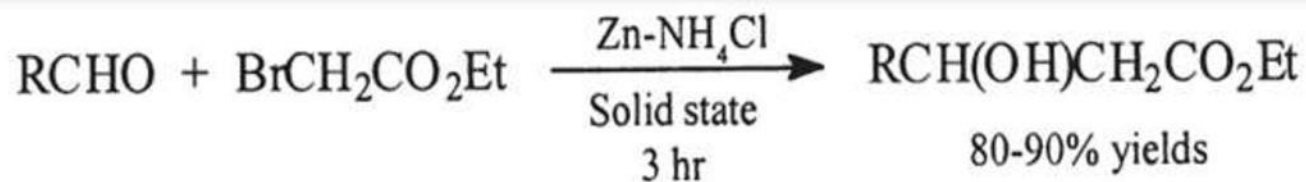
# GRIGNARD REACTION

- The reaction of benzophenone with powdered Grignard reagent gives more of the reduced product of the ketone than the adduct.



# REFORMATSKY REACTION

Treatment of aromatic aldehydes with ethyl bromoacetate and Zn-NH<sub>4</sub>Cl in the solid state give the corresponding Reformatsky reaction products.





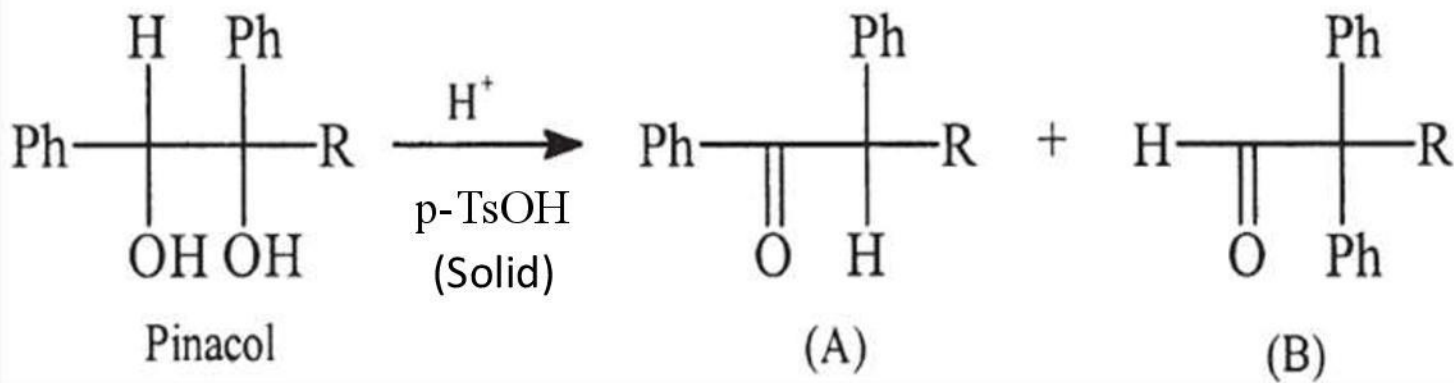
# Pinacol-Pinacolone Rearrangement

## USUAL TREATMENT

- In the presence of  $\text{CCl}_3\text{CO}_2\text{H}$  (in place of  $p\text{-TsOH}$ ) gives major amount of the isomeric product (B).

## GREEN SYNTHESIS

- Pinacol-pinacolone rearrangements proceed faster and more selectively in solid state.



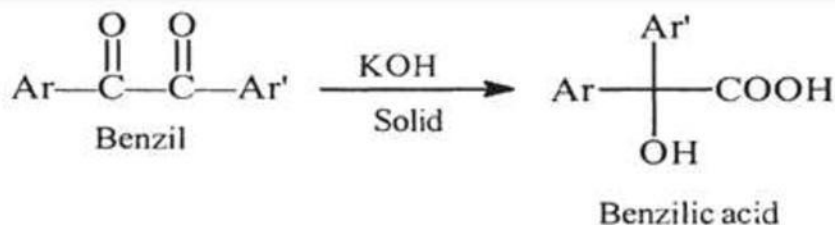
# BENZIL-BENZILIC ACID REARRANGEMENT

## USUAL TREATMENT

- This rearrangement is carried out by heating benzil and alkali metal hydroxides in aqueous organic solvent.

## GREEN SYNTHESIS

- It is found that this reaction proceeds more efficiently and faster in the **solid state**. The reaction takes 0.1 to 6 hr and the yields are 70-93 %



Ar = Ar' = Ph  
Ar = Ar' = p-ClC<sub>6</sub>H<sub>4</sub>  
Ar = Ar' = p-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>  
Ar = Ph; Ar' = p-ClC<sub>6</sub>H<sub>4</sub>  
Ar = Ph; Ar' = p-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>  
Ar = Ph; Ar' = p-MeOC<sub>6</sub>H<sub>4</sub>

# AROMATIC SUBSTITUTION REACTIONS

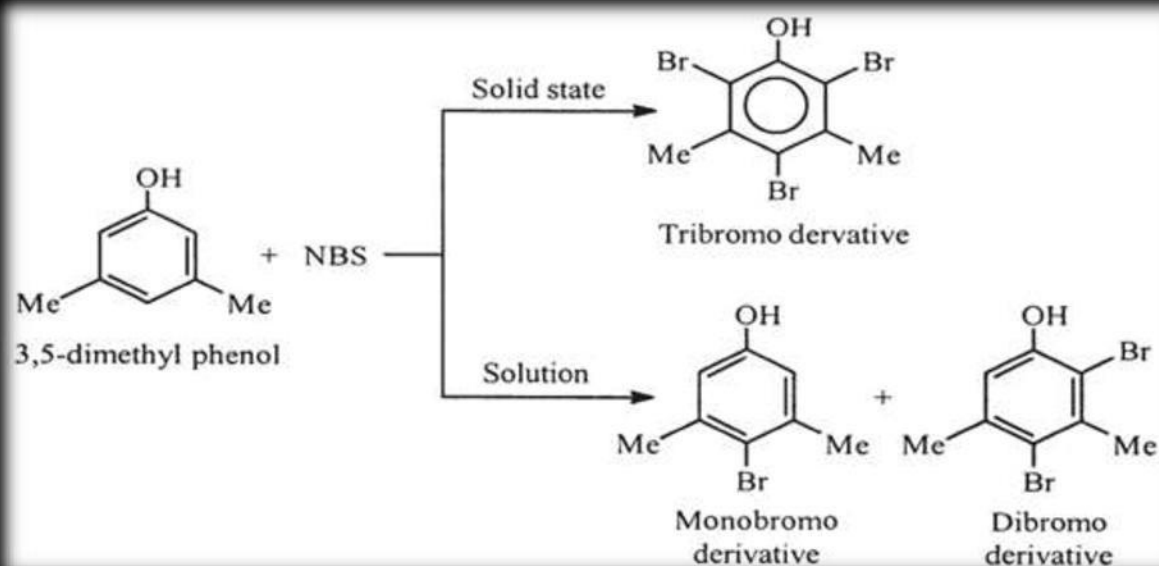
## Nuclear bromination of phenols with (NBS)

### USUAL TREATMENT

- In solution a mixture of mono and dibromo derivatives is obtained.

### GREEN SYNTHESIS

- The reaction of 3,5-dimethylphenol with NBS in the solid state for 1 min gave the tribromo derivative in 45% yield.



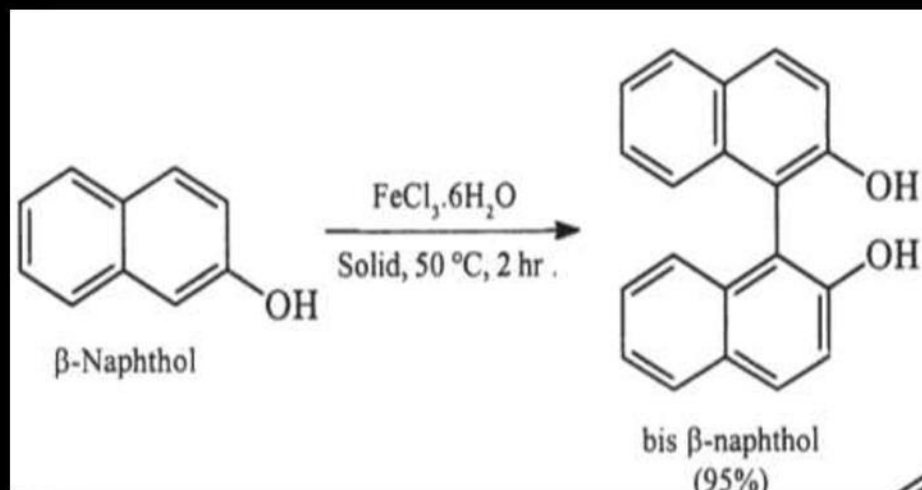
# OXIDATIVE COUPLINGS OF PHENOLS

## USUAL TREATMENT

- Oxidative couplings of phenols in solution with metal salts such as  $\text{FeCl}_3$  or Manganese tris(acetylacetonate), although the latter one is too expensive to use in a large quantity.

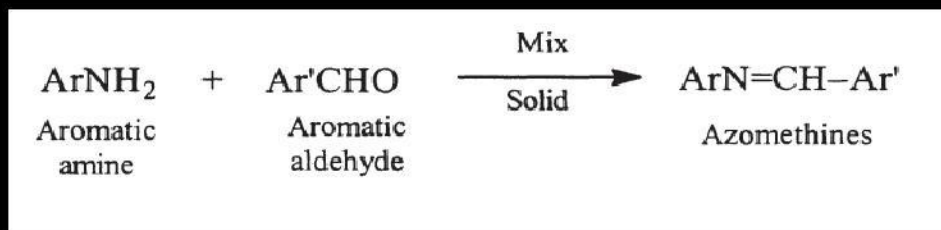
## GREEN SYNTHESIS

- In 1989, Toda et al., have reported, Oxidative coupling of phenols in presence of  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$  proceed much faster in the solid state than in solution.

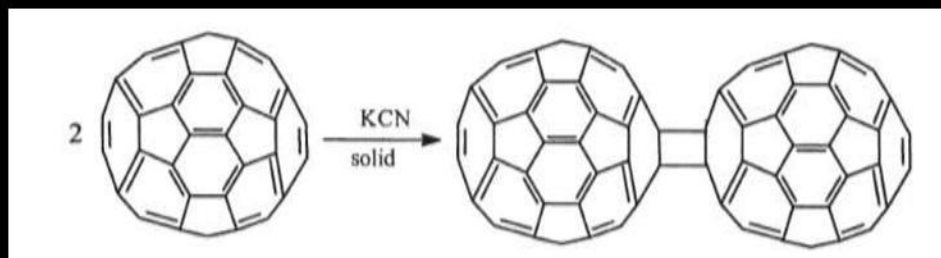




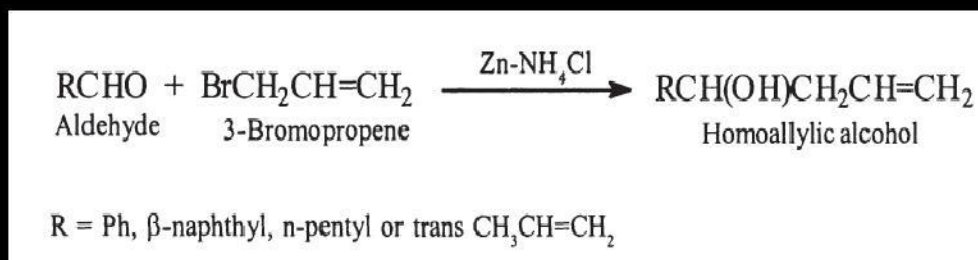
- Synthesis of Azomethines



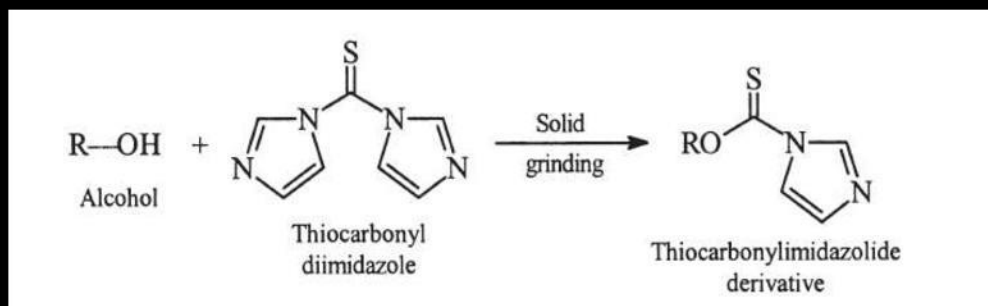
- Dimerisation of [60] fullerene



- Synthesis of Homoallylic Alcohols



- Synthesis of Thio carbonylimidazolidine Derivatives





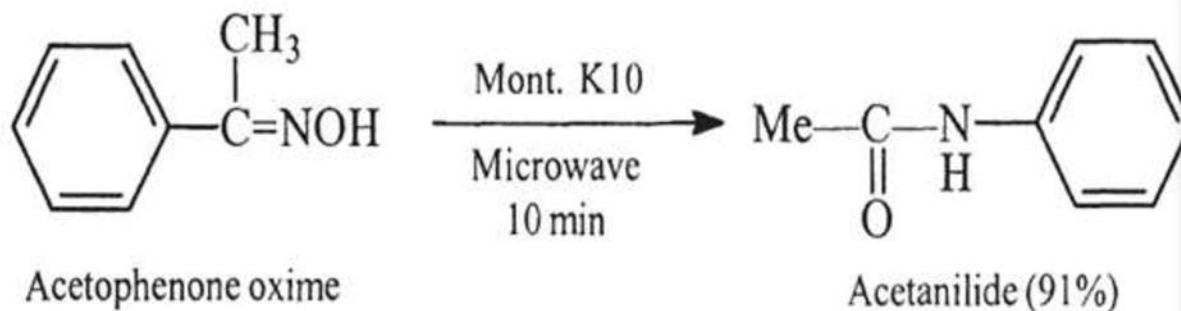
# BECKMANN REARRANGEMENT

## USUAL TREATMENT

- Beckmann rearrangement of oximes of ketones are converted into anilides by heating with acidic reagents like  $\text{PCl}_5$ ,  $\text{HCOOH}$ ,  $\text{SOCl}_2$  etc.

## GREEN SYNTHESIS

- Oxime of a ketone is mixed with **montmorillonite** and irradiated for 7 min in microwave oven to give corresponding anilide in **91 % yield**



- **Solventless reactions of organic compounds** has gained much popularity.
- It is the one of the best techniques in green chemistry by which many important compounds can be synthesized in an efficient & environment friendly manner.

# DRAWBACKS

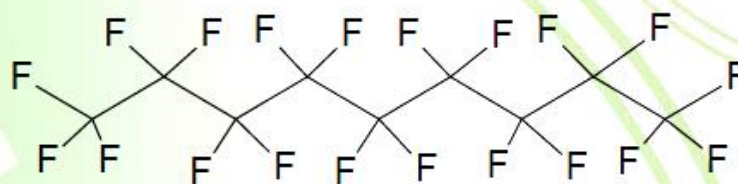
- Homogenous reactants should mix to a system.
- Solvents are often still required during work-up (e.g. extraction)
- Unsuitable for solvent assisted chemical reactions.

**Organic Synthesis  
Using  
Fluorous Phase  
Techniques**

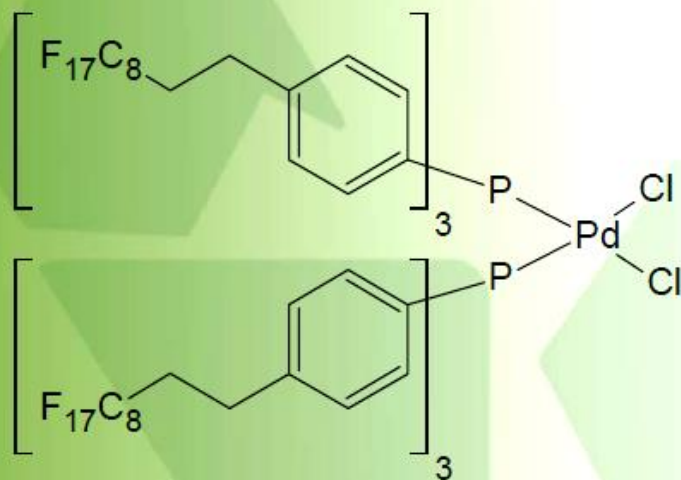
# Check out all the fluorine!



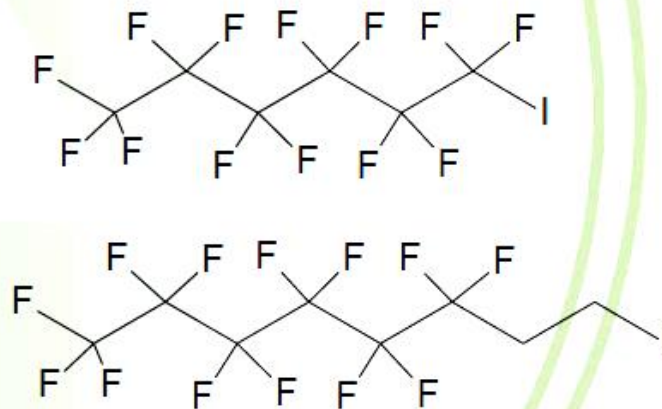
## Perfluorous Solvents



## Perfluorous Catalyst



## Perfluorous Tags





# Physical Properties of Perfluorinated Organic Compounds



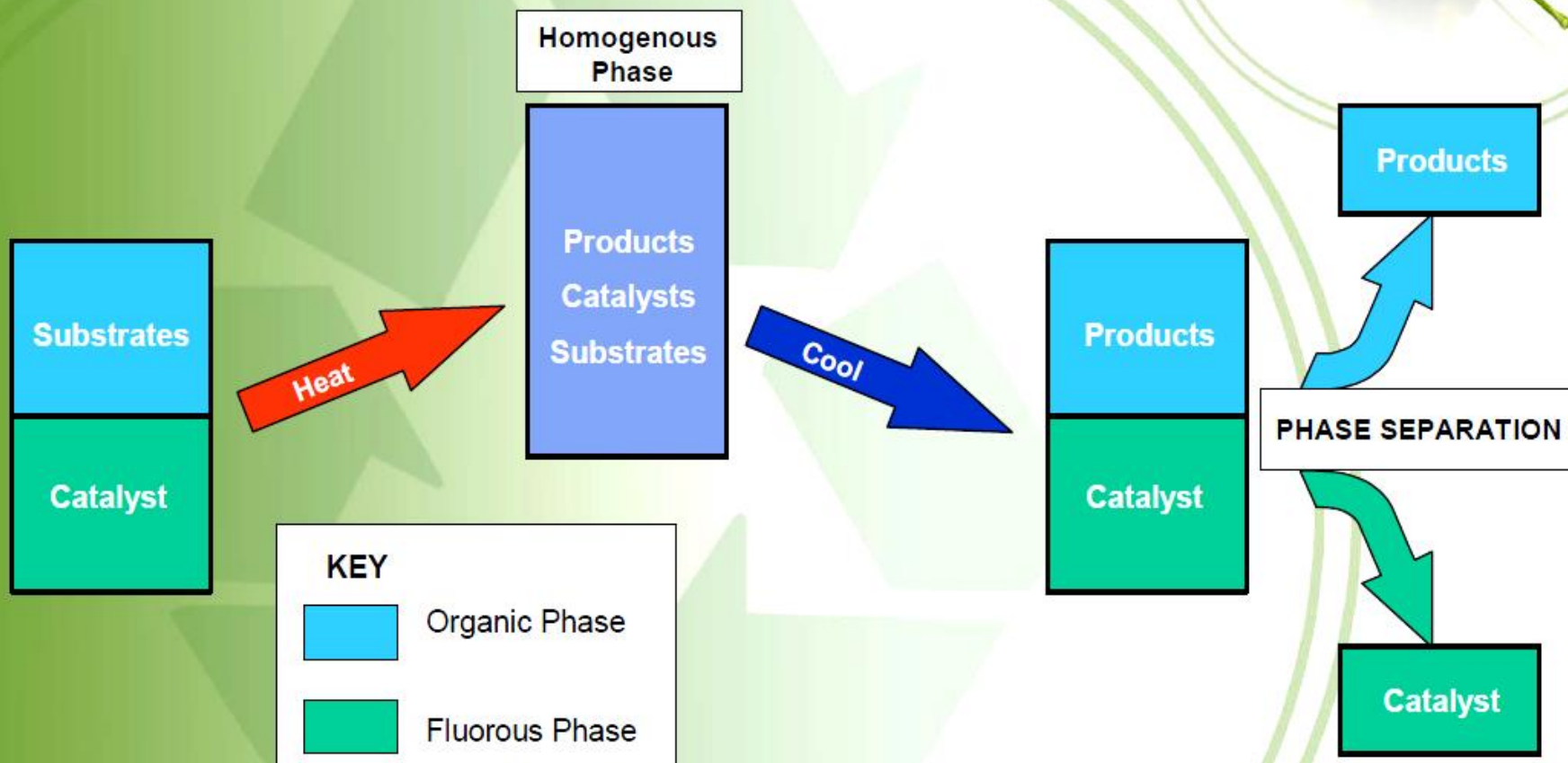
- High affinity for other fluorinated compounds.
- High solubility in  $scCO_2$ .
- Immiscible in water and most common organic solvents at room temperature.
- Forms homogenous solutions at elevated temperatures with many of these solvents.
- Chemically inert.
  - Is this good or bad?

# Uses for Fluorous Chemistry



- For the recovery and recycling of fluorous catalysts and fluorous reagents.
- Fluorous biphasic organic synthesis.

# Principle of Fluorous Biphase Catalysis



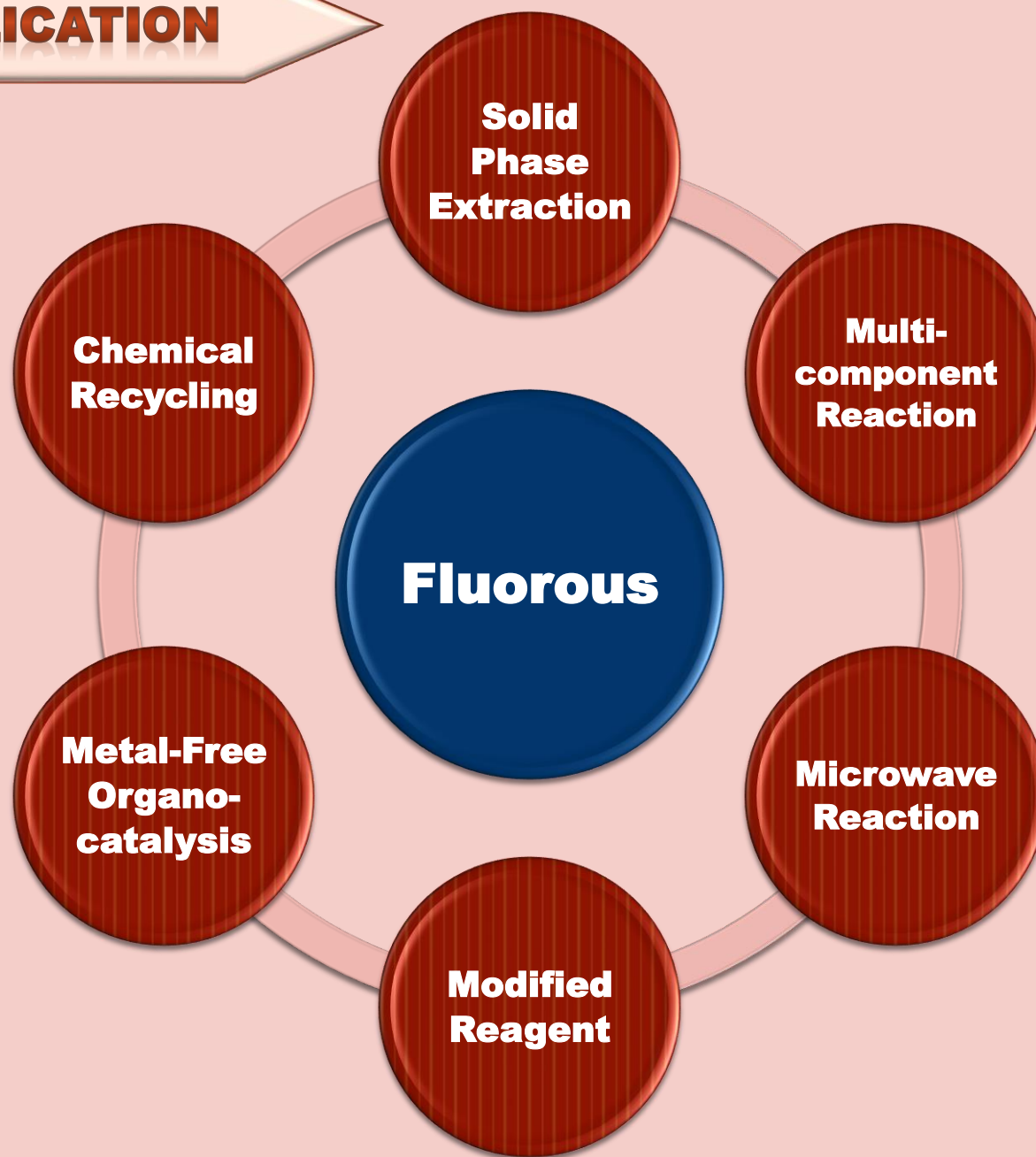


# Advantages



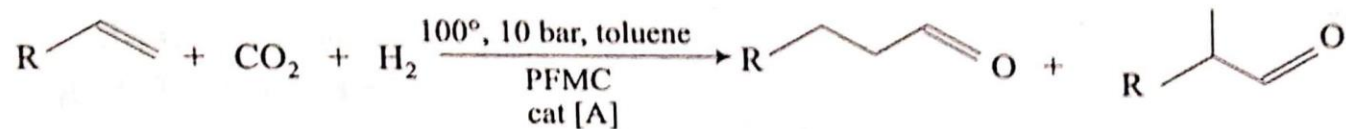
- Facile recovery of expensive catalysts.
- Complementary to other biphase chemistries.
- More facile separation.
- Design of novel catalysts and reagents.
- Alternative to the solid phase in combinatorial chemistry.
- Non-toxic?

# APPLICATION

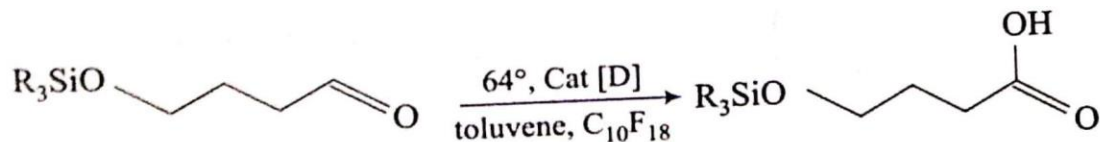
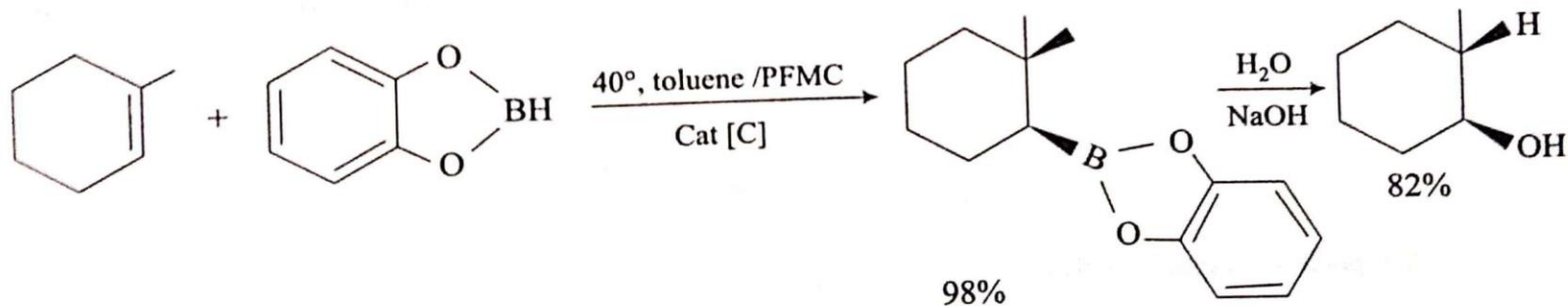
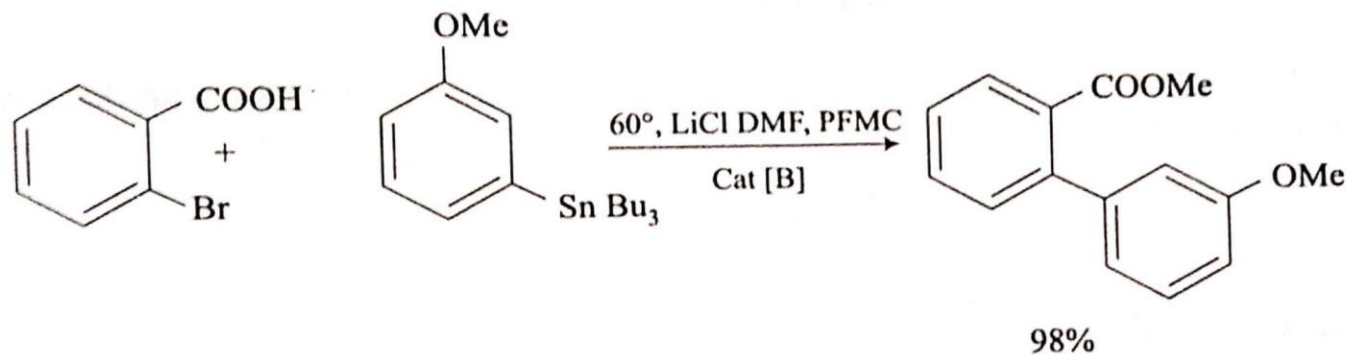




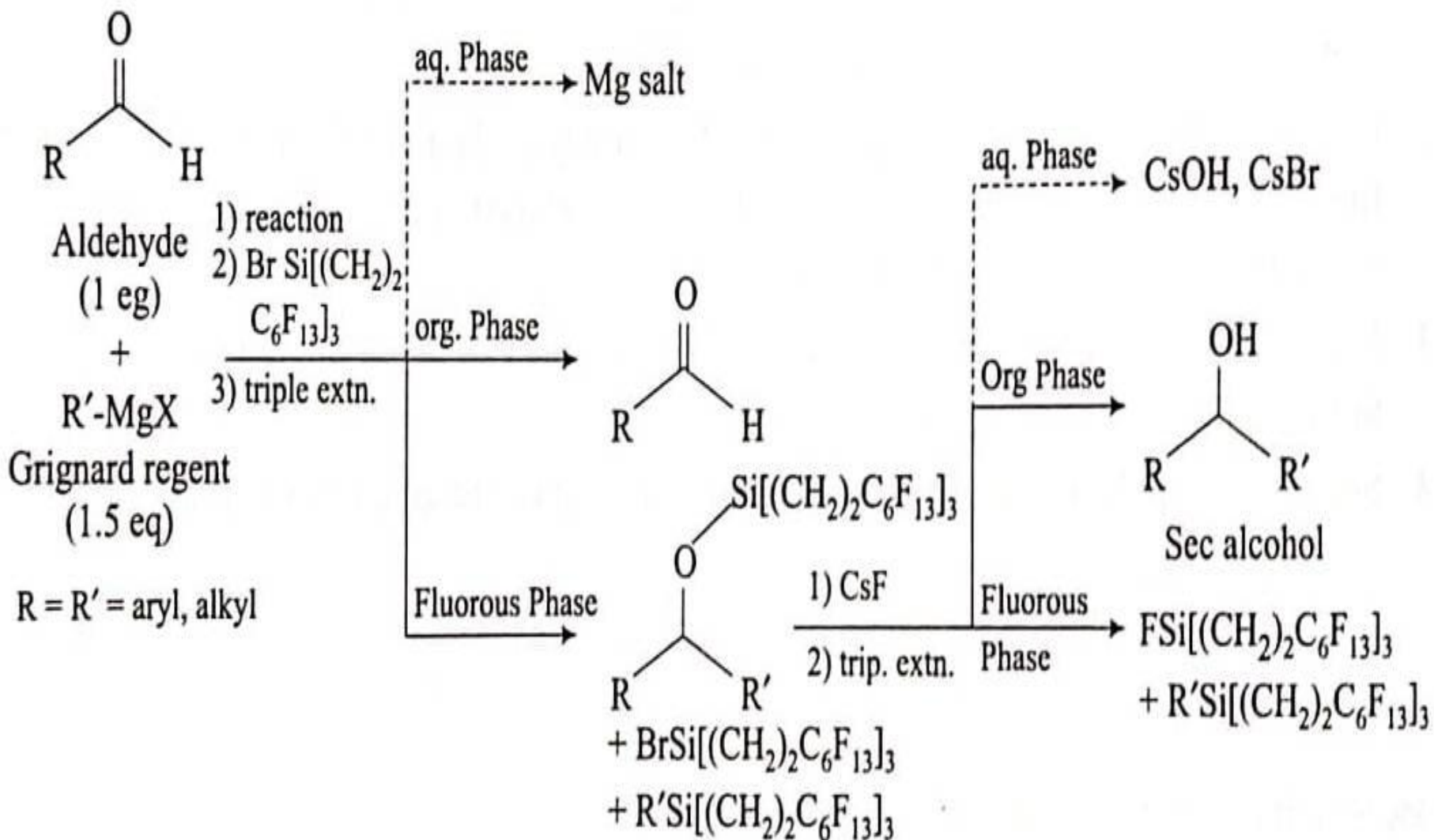
# 1. Some Applications of Fluorous Phase Techniques:



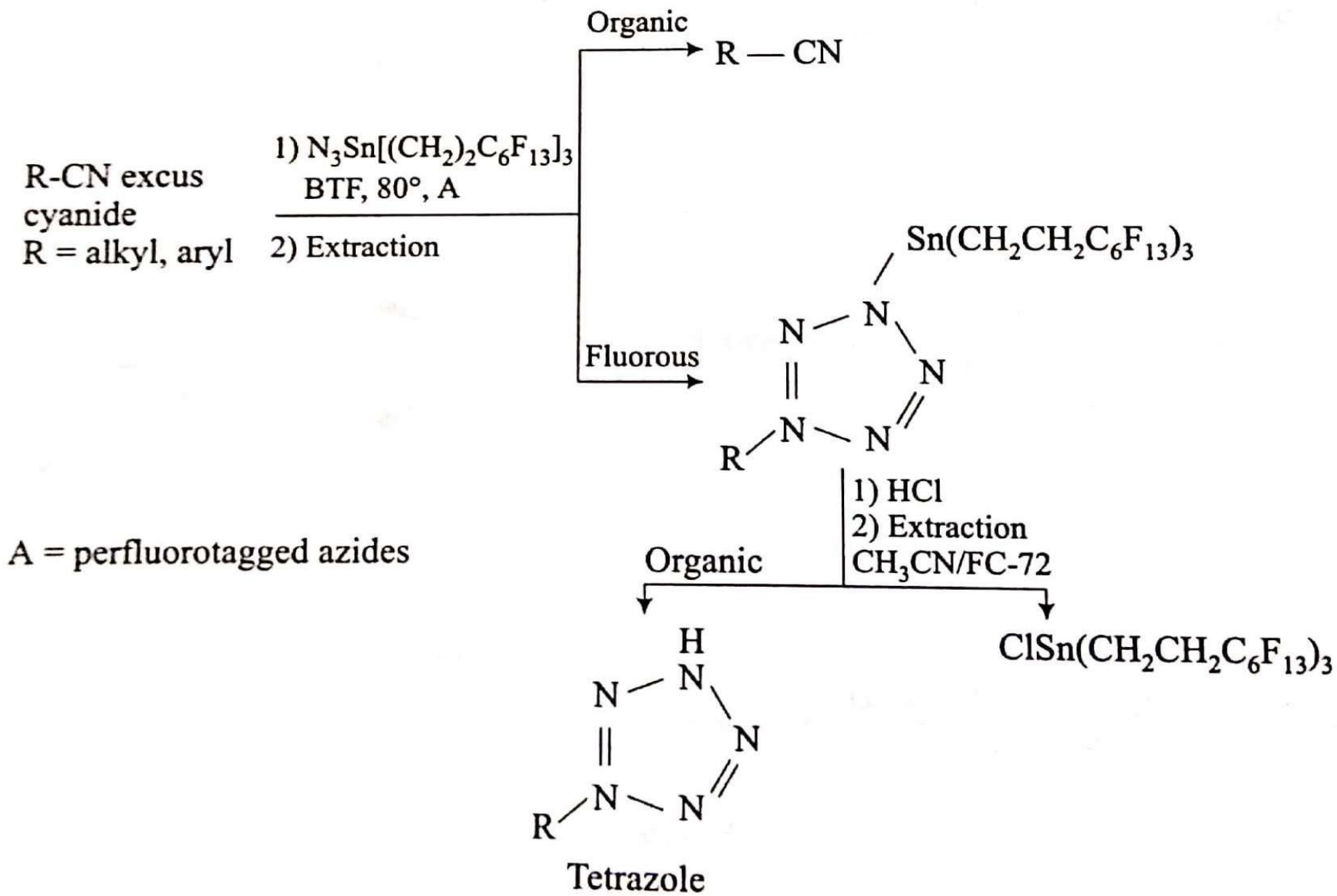
PFMC = Perfluoro (methylcyclohexane)



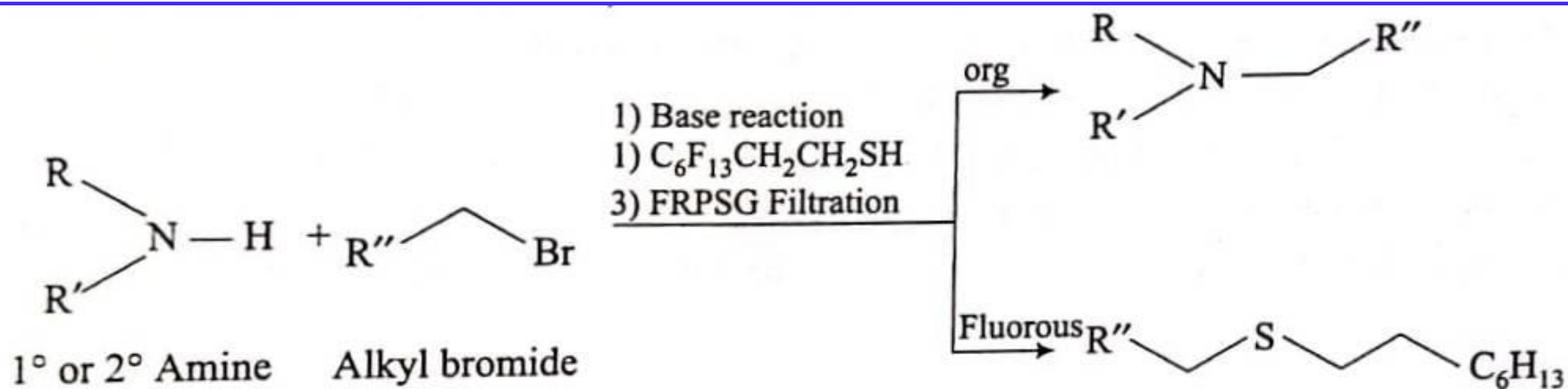
## 2. Reaction of Aldehyde with Grignard Reagent:



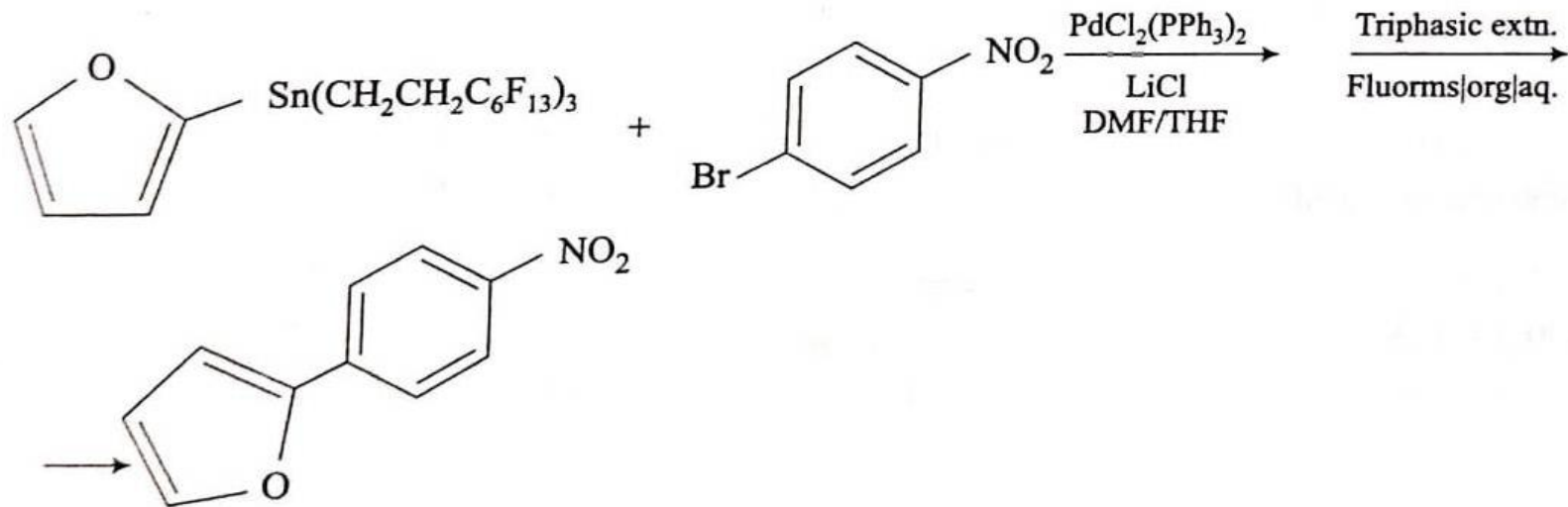
### 3. Synthesis of Tetrazole:



## 4. N-Alkylation of Primary and Secondary Amines:



## 5. Still Coupling:



# Limitations



- Fluorous solvents and reagents are very expensive.
- 60% fluorine is usually considered the lower cutoff point for efficient fluorous extraction.
- Still requires use of a second solvent for biphasic.





**‘PEG (Polyethyl Glycol)’  
as Green Solvent**



## Polyethylene glycol (PEG)

**Polyethylene glycol (PEG)** is a polyether compound with many applications, from industrial manufacturing to medicine. PEG is also known as polyethylene oxide (PEO) or polyoxyethylene (POE), depending on its molecular weight **(200 to Tens Thousands)**. The structure of PEG is commonly expressed as  **$H-(O-CH_2-CH_2)_n-OH$** .

The numerical designation of PEG indicates the number of **average molecular weight** (e.g. PEG-5000; PEG-2000; PEG-900; PEG-425; **PEG-400**; PEG-350 & PEG-300 etc).

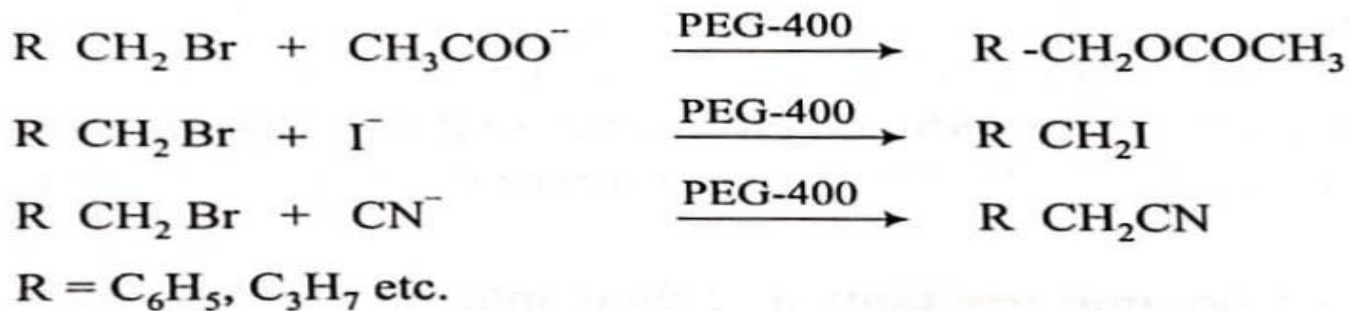
### Advantages of PEG as Green Solvent:

1. **Inexpensive and Significantly less hazardous than other common organic solvents.**
2. **PEGs have negligible vapour pressure and stable at ambient temperature.**
3. **Soluble in polar and non-polar solvents**
4. **Insoluble in aliphatic hydrocarbons and  $scCO_2$  .**
5. **Good stability towards acidic and basic media.**
6. **Least affected by most common oxidizing and reducing agents.**

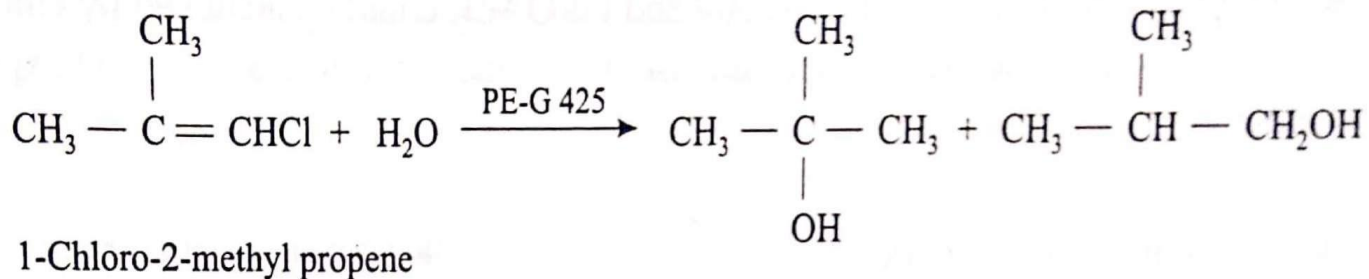
# USE OF PEG IN ORGANIC REACTIONS

## 1. Substitution Reactions:

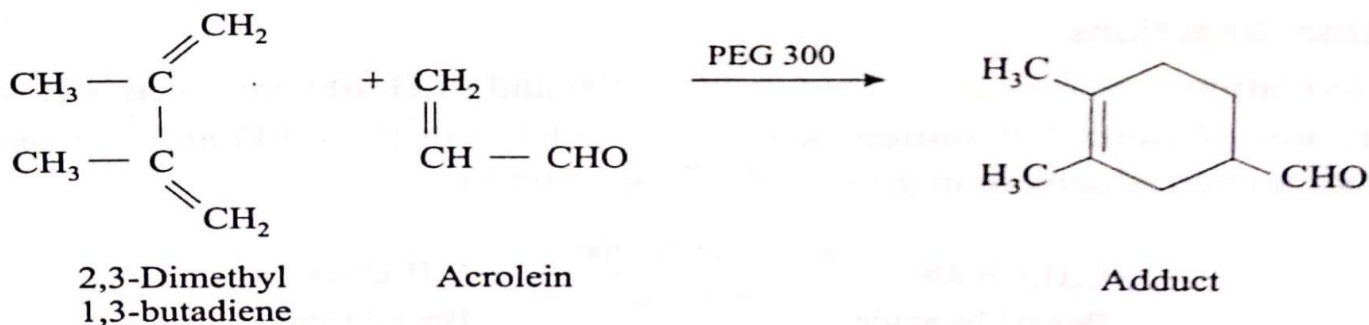
Scheme-1



Scheme-2



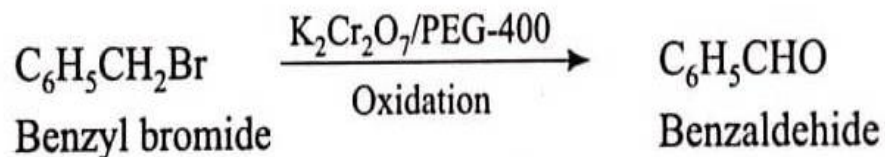
Scheme-3



# USE OF PEG IN ORGANIC REACTIONS

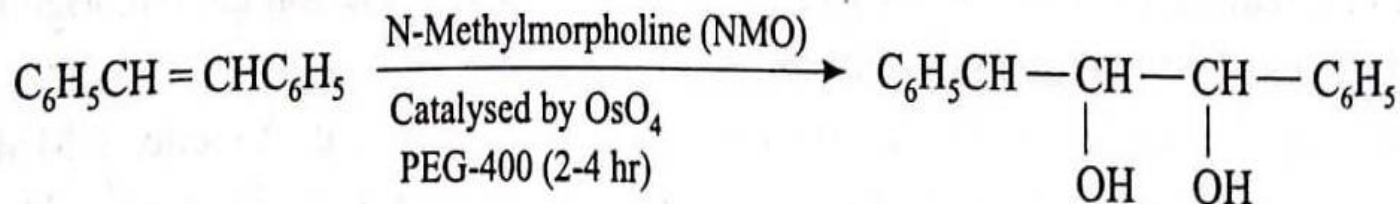
## 2. Oxidation Reactions:

- (i) **Oxidation of Benzyl Bromide.**  $K_2Cr_2O_7$  is soluble in PEG-400 and can oxidize benzyl bromide to benzaldehyde in good yield.



**Scheme-1**

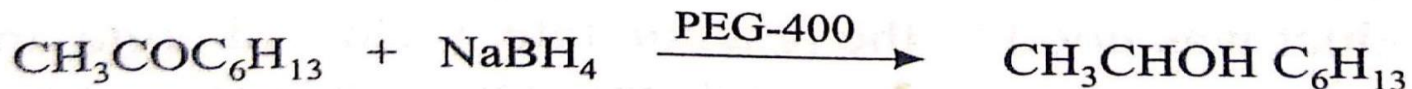
- (ii) **Dihydroxylation of olefins.** Using PEG-400 as solvent and osmium tetroxide as catalyst gives high yield of diols.



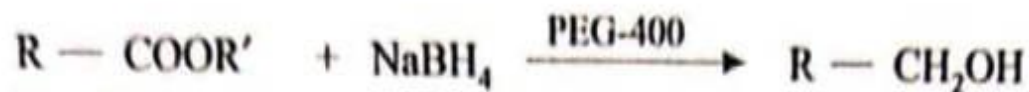
**Scheme-2**

# USE OF PEG IN ORGANIC REACTIONS

## 3. Reduction Reactions:



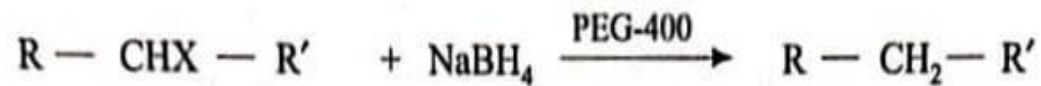
Scheme-1



R = alkyl, aryl

R' = CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>

Scheme-2

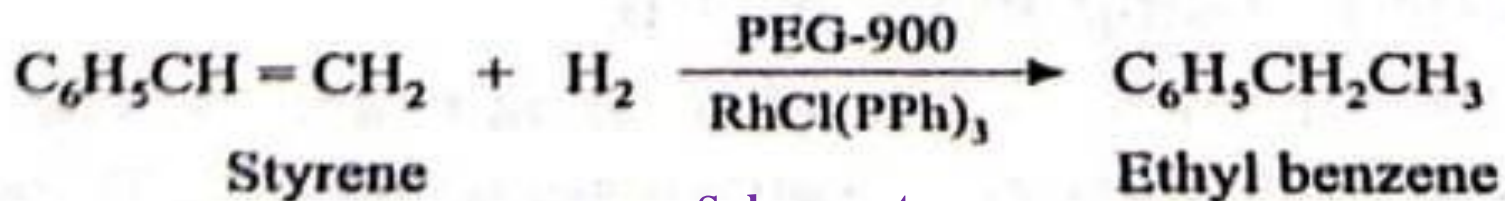


R = alkyl, aryl

X = Cl, Br, I

R' = H, CH<sub>3</sub>, C<sub>4</sub>H<sub>9</sub>

Scheme-3



Scheme-4



# USE OF PEG AS PHASE-TRANSFER CATALYST (PTC)

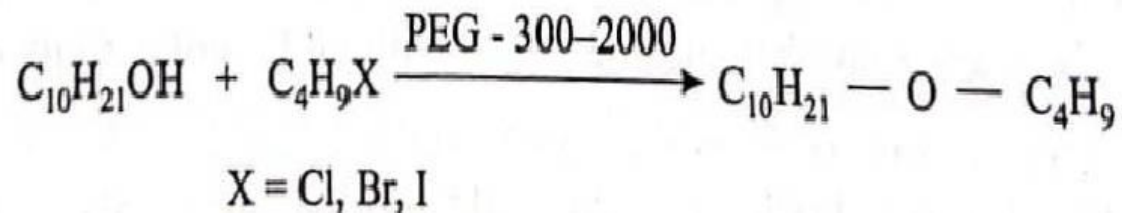
## 1. Williamson Ether Synthesis:

Williamson Ether synthesis is an important nucleophilic substitution reaction ( $S_N2$ ) and involves the synthesis of ether using alkyl halides and an alkoxide in an alcoholic solution .



Scheme-1

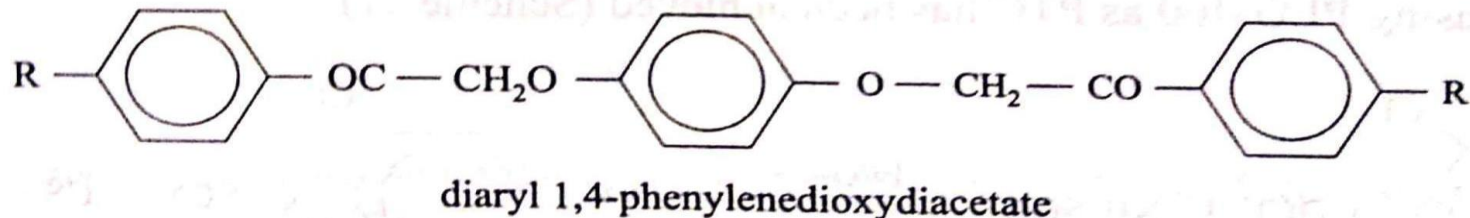
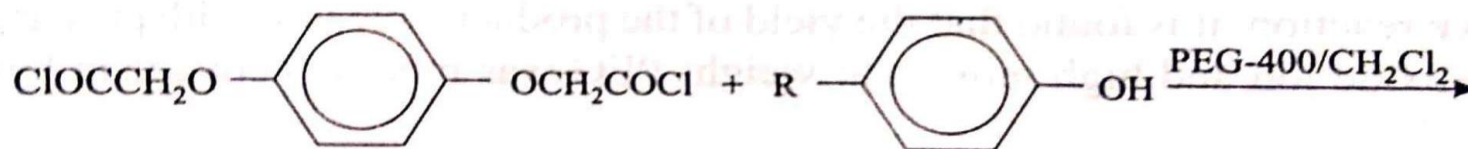
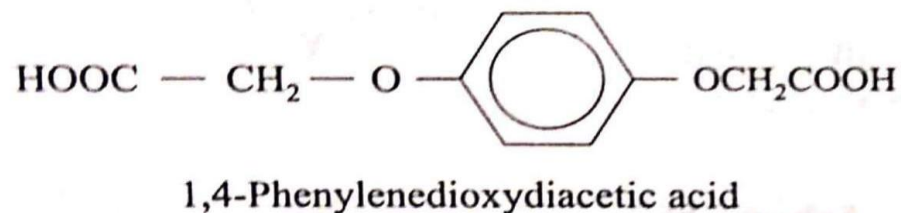
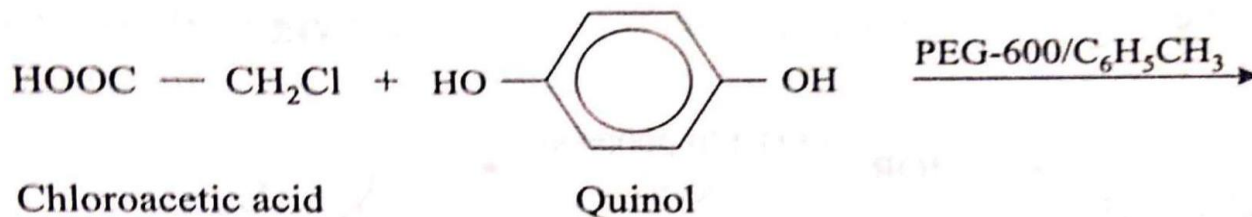
The yield of decan-1-ol during etherification in using PEG-2000 as PTC is 84%, which is comparable to that found by using 18-Crown-6 and higher than 72% yield found using kryptofix 222 (cryptand) .



Scheme-2

# USE OF PEG AS PHASE-TRANSFER CATALYST (PTC)

## 2. Substitution Reaction Using PEGs as PTC:

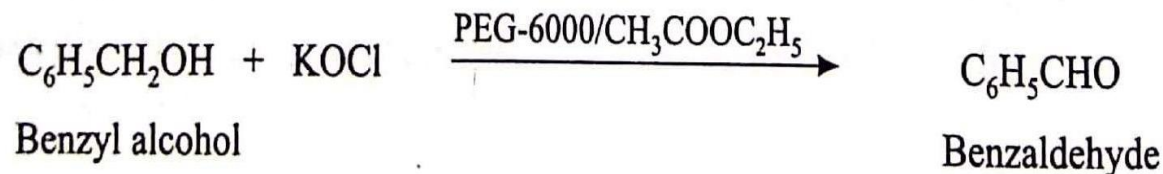


Scheme-1

# USE OF PEG AS PHASE-TRANSFER CATALYST (PTC)

## 3. Oxidation Reaction Using PEGs as PTC:

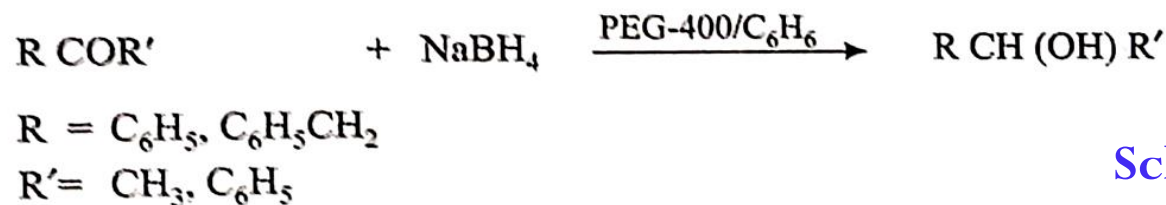
PEG has been used with success in many oxidation reactions. Thus benzylalcohol on oxidation with potassium hypochlorite in PEG-6000 and ethyl acetate yields benzaldehyde.



**Scheme-1**

## 4. Reduction Reaction Using PEGs as PTC:

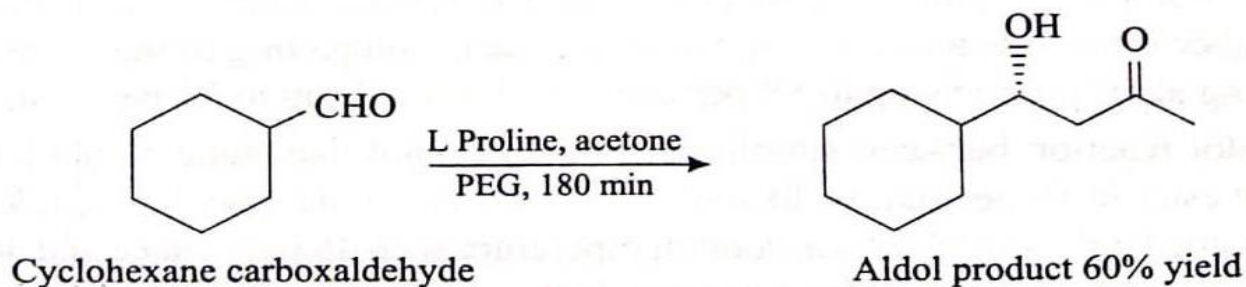
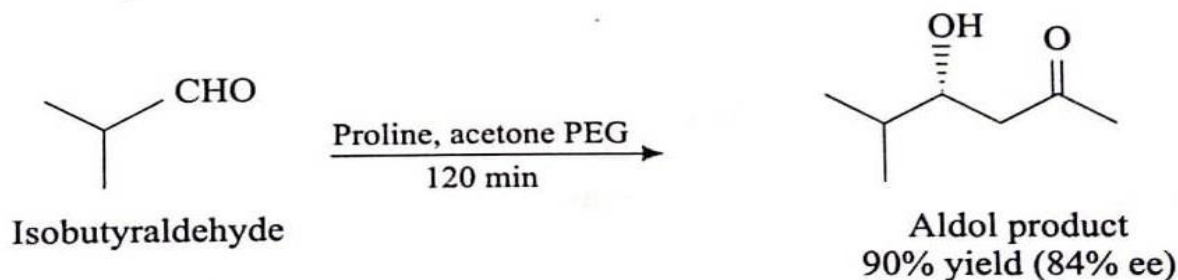
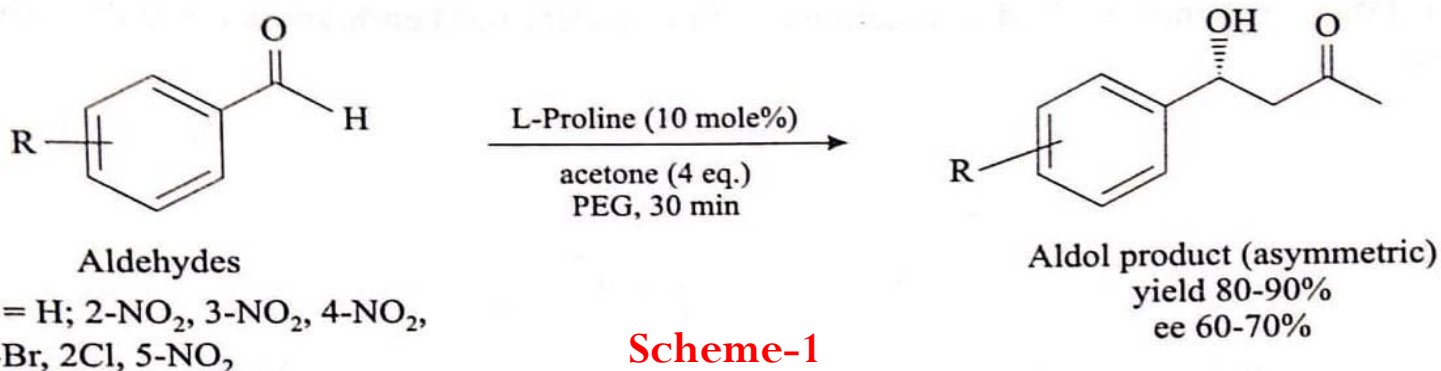
The reduction of ketones and aldehydes can be effected with PEG and  $\text{NaBH}_4$  and PEG- $\text{NaBH}_4$  complexes.



**Scheme-2**

# USE OF PEG AS PHASE-TRANSFER CATALYST (PTC)

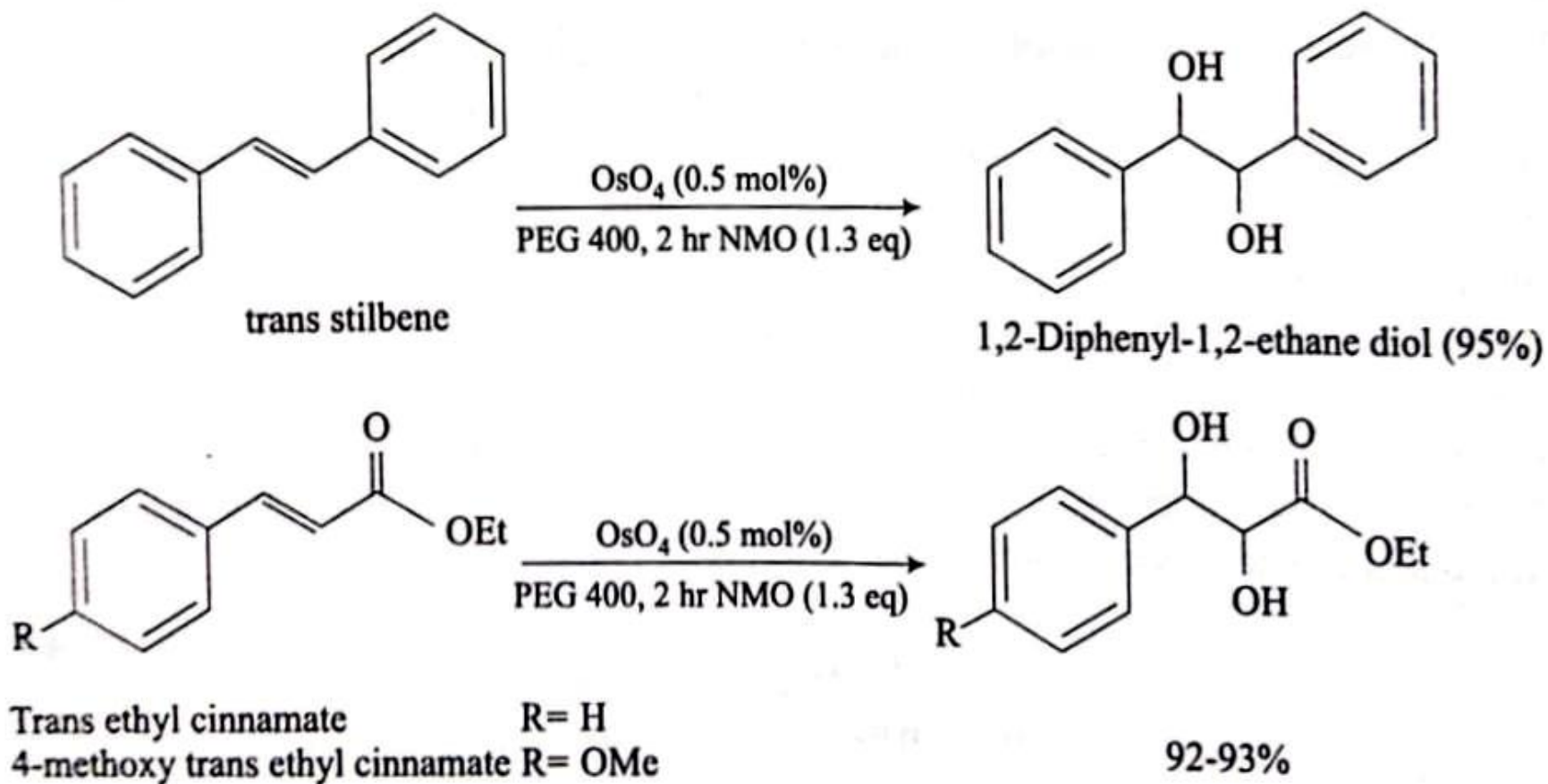
## 5. *L*-Proline Catalysed Asymmetric Aldol Reactions:



**Scheme-2**

# USE OF PEG AS PHASE-TRANSFER CATALYST (PTC)

## 6. Asymmetric Dihydroxylation of Olefins:

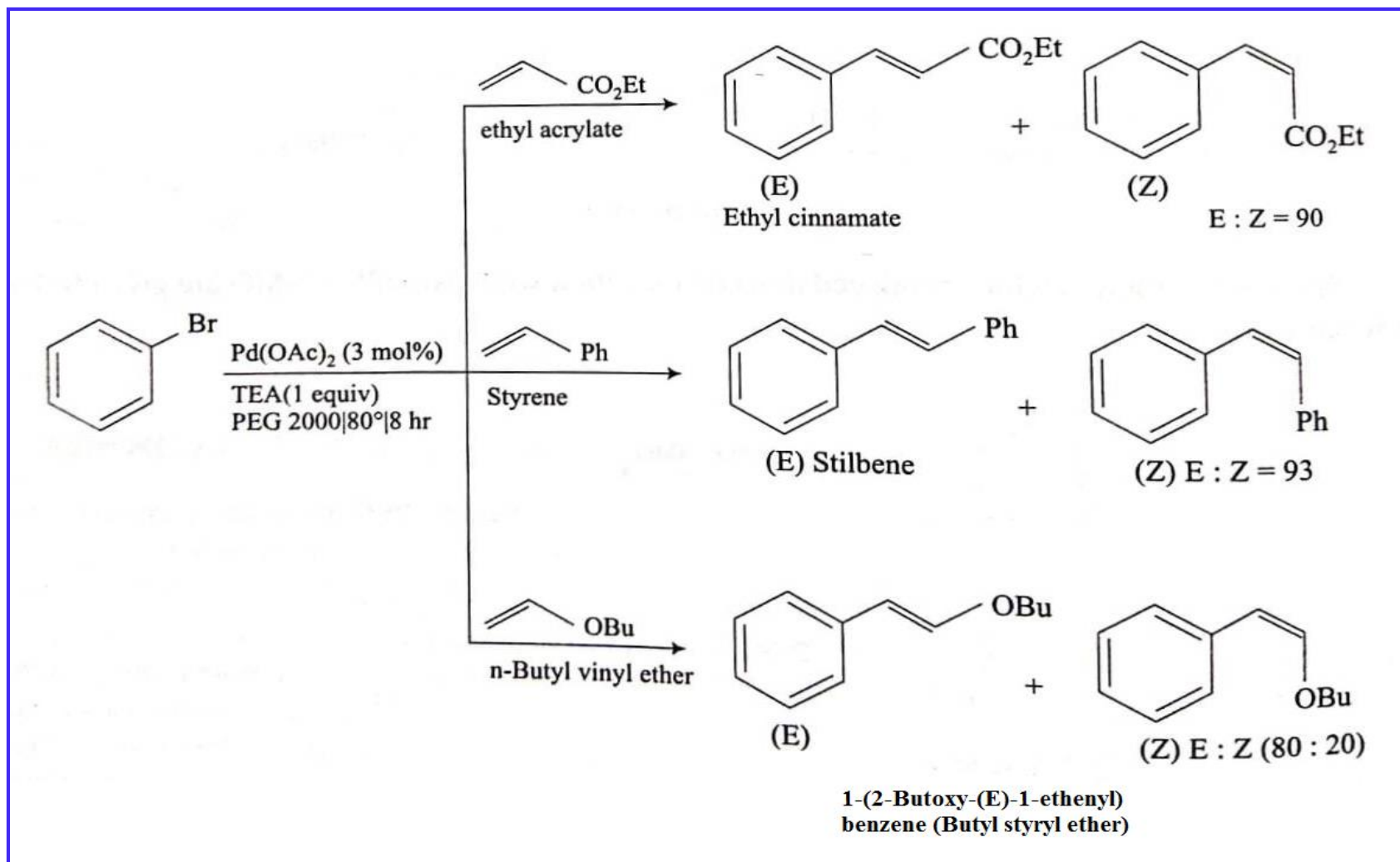


Scheme-1



# USE OF PEG AS PHASE-TRANSFER CATALYST (PTC)

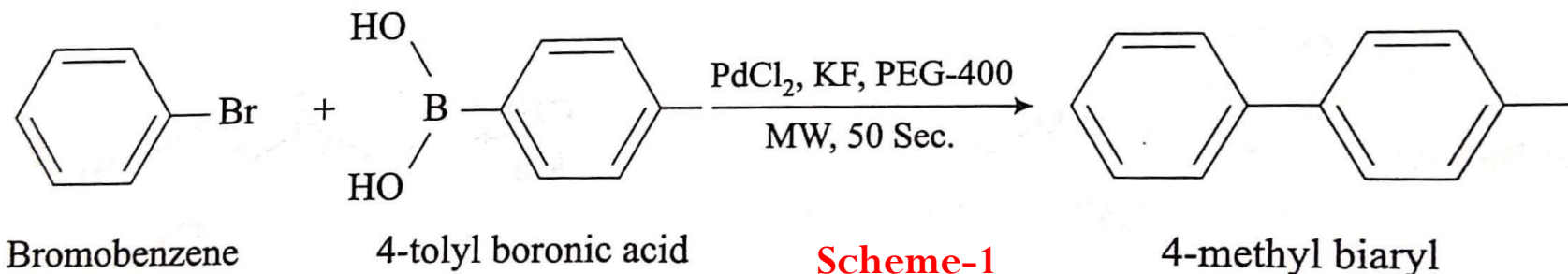
## 7. Regioselective Heck Reaction:




Scheme-1

# USE OF PEG AS PHASE-TRANSFER CATALYST (PTC)

## 8. Suzuki Cross-Coupling Reaction in PEG:



Polyethylene glycol (PEG) and its aqueous solutions have been used in many different types of reaction systems. The special feature of PEGs is their low toxicity, low volatility and biodegradability and relatively low cost as a bulk commodity chemical.

A large, horizontally-oriented oval with a dark red, slightly textured background. The oval is centered on a light gray, textured background. The text is written in a blue, serif font with a white outline and a drop shadow effect.

**Immobilized  
Solvents in Green  
Chemistry**

## What is an immobilized liquid?

The concept of “**immobilized**” or “heterogenised” **liquids** is well-known from supported **liquid** phase catalysts. ... Supported ionic **liquid** phase (SILP) materials, combining ILs with heterogeneous support materials, are a recent concept where a film of ionic **liquid** is **immobilized** on a solid phase.

Some examples are given earlier.....



A lush green landscape with a row of trees in the foreground and a grassy field in the background. The trees are tall and leafy, creating a canopy effect. The grass is vibrant green and appears to be a mix of grass and small white flowers. The overall scene is bright and sunny, suggesting a healthy, green environment.

**Thank You for Your  
Attention**

**Lets Make Green...This is our Future...**