# GREEN CHEMISTRY

## SEMESTER-VI
## DSE-A3

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# Polyethylene glycol (PEG)

**Polyethylene glycol**


- Polyethylene glycol is a polyether compound and it is an ethylene glycol polymer. PEGs are condensation polymers of ethylene oxide, available in variety of molecular weights. The properties of PEGs vary with their molecular weights. The PEGs are comparatively available in different grades such as PEG-400, PEG-600, PEG-1000.

- The number in the name of PEGs indicates their average molecular weights. For example, PEG-600 indicates that its average molecular weight is 600 dalton.

| Polyethylene glycol | |
|---|---|
| Molecular weight | State (at ambient temperature) |
| < 600 | Colourless viscous liquid |
| 600 - 800 | Semi-solid |
| > 800 | Waxy white solid |

- PEG-2000 is soluble to the extent of 60% in water at 20°. Lower molecular weight PEG can be used as solvents with or without the addition of water.

# Polyethylene glycol (PEG)

**Properties / Advantages of PEG**

(1) PEGs are neutral and low toxic.

(2) They are soluble in water and many organic solvents. it occurs because of strong H-bonding ability of PEGs with water or organic solvents.

(3) They have low flammability.

(4) PEG can be recovered from aqueous solution by extraction with a suitable solvent or by distillation of water or solvent. Due to this PEG can be recovered and recycled.

(5) They are stable to acid, base and high temperature.

(6) The PEGs of low molecular weight are non-volatile unlike VOCs.

(7) They are biodegradable.

(8) Low molecular weight PEGs are used as solvent with or without adding water.

(9) They have low cost and reduced environmental hazard.

(10) PEG is very weakly immunogenic. Due to this it is used by the drug companies.

(11) Aqueous solutions of PEG are biocompatible and are used in tissue culture media for the preservation of organs.

(12) PEG is not effected by $O_2$, $H_2O_2$, high oxidation systems and $NaBH_4$ reduction system.

# Polyethylene glycol (PEG)

**Advantages of PEG over water, Sc $CO_2$, ionic liquid and fluorous solvent**

- Water, Sc $CO_2$, ionic liquid and fluorous solvents have been chosen as green alternative to the common volatile organic solvents having toxic and circinogenic properties.

- In the context of green chemistry, PEGs have been considered as an effective green medium for organic synthesis. This is because:

(1) The poor solubility of organic reactants in water is the main limitation for the extensive use of water as solvent. Sc $CO_2$ can be obtained by applying high pressure, which needs special arrangement and special equipment.

(2) The preparation of ionic liquid is a costly process and ionic liquids are also suffers from the problem of toxicity.

(3) Fluorous solvents have limited miscibility with common organic solvents or organic reactants.

**Fluorous solvents**

- Solvents containing fluorine with a relatively large component in molecules are called fluorous solvents.
- Most fluorous solvents have high thermostability and chemostability and are low in toxicity.

# Polyethylene glycol (PEG)

**(1) Substitution reaction**

The reaction of alkyl halides, e.g., $RCH_2Br$ with nucleophiles like $CH_3CO_2^{\ominus}$, $I^{\ominus}$ and $CN^{\ominus}$ in PEG 400 give the corresponding substituted products.

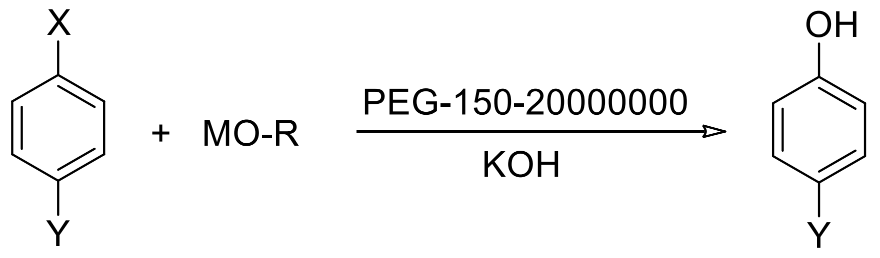
$$RCH_2Br + CH_3CO_2^{\ominus} \xrightarrow{\text{PEG-400}} RCH_2OCHOCH_3$$

$$RCH_2Br + I^{\ominus} \xrightarrow{\text{PEG-400}} RCH_2I$$

$$RCH_2Br + CN^{\ominus} \xrightarrow{\text{PEG-400}} RCH_2CN$$

R = $C_6H_5$, $C_3H_7$, etc.

Aromatic halogen compounds undergo aromatic nucleophilic substitution reaction with alkaline metal alkoxide ($RO^-M^+$) in PEG-150 solvent to give the substituted product.




X = Cl, Br

Y = H, Cl, Br

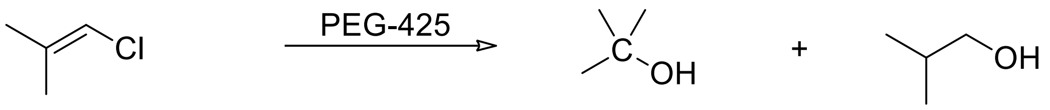
M = alkali metals

R = alkyl, aryl

# Polyethylene glycol (PEG)

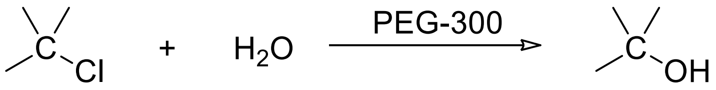
**(2) Hydrolysis reaction**

(a) The reaction of 1-chloro-2-methylpropene with $H_2O$ in PEG-425 gave a mixture of alcohols.




1-Chloro-2-methylprop-1-ene    *tert*-butyl alcohol    2-methylpropan-1-ol

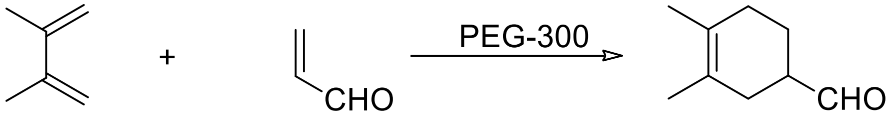
(b) The reaction of *tert*-butyl chloride with $H_2O$ in PEG-300 gives *tert*-butyl alcohol




*tert*-butyl chloride    *tert*-butyl alcohol

**(3) Diels-Alder reaction**

2,3-Dimethyl-1,3-butadiene adds to acrolein giving the adduct in good yield.




2,3-dimethylbuta-1,3-diene    acrolein

- In this reaction, the yield was 14-fold in comparison to the reaction carried out in methanol.

# Polyethylene glycol (PEG)

**(4) Oxidation reaction**

**Oxidation of benzyl bromide**

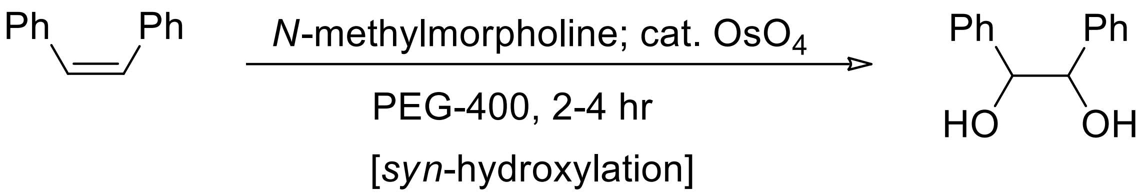
$K_2Cr_2O_7$ is soluble in PEG-400 and can oxidise benzyl bromide to benzaldehyde in good yield.

$$\underset{\text{benzyl bromide}}{PhCH_2Br} \xrightarrow[\text{oxidation}]{K_2Cr_2O_7\ /\ \text{PEG-400}} \underset{\text{benzaldehyde}}{PhCHO}$$

The above oxidation is similar to the reaction of $Na_2Cr_2O_7$ in hexamethyl phosphoramide (HMPA) and Crown ether using the same substrate.

**(5) Dihydroxylation of olefins**

Using PEG-400 as solvent and osmium tetroxide as catalyst gives high yield of diols.

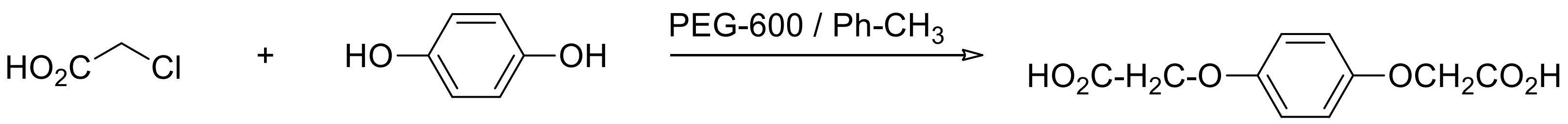


# Polyethylene glycol (PEG)

**(6) Substitution Reactions using PEGs as PTC**

- PEGs have been used as PTC in nucleophilic substitution reactions. The anionic nucleophilic reagents used are hydroxides, halides, sulfides, cyanides, cyanamides, carboxylates, etc.

- The synthesis of 1,4-phenylenedioxydiacetic acid can be obtained by using PEG-400 as PTC in good yields under mild conditions.




2-chloroacetic acid    Quinol    1,4-phenylenedioxydiacetic acid

- PEG as PTC is employed in a Sc $CO_2$ solvent to convert benzyl chloride to benzyl cyanide in presence of potassium cyanide. Use of PEG as PTC iprovides a method with a low cost, green reaction process.

$PhCH_2Cl$ + KCN $\xrightarrow{\text{PEG, Sc } CO_2}$ $PhCH_2CN$

benzyl chloride    benzyl cyanide

- Use of potassium sulphocyanide in the above reaction gives the corresponding sulphocyanide.

$PhCH_2Cl$ + KSCN $\xrightarrow{\text{PEG, Sc } CO_2}$ $PhCH_2SCN$

benzyl chloride    benzyl sulphocyanide

# Water as solvent in Organic Synthesis

**Introduction**

- Solvents which are normally used for carrying out organic reactions are extremely harmful.

(1) For example, benzene - a commonly used solvent is known to cause or promote cancer in humans and other animals.

(2) Aromatic hydrocarbons like toluene can damage the brain and may have adverse effects on speech, vision or cause liver and kidney problems.

(3) Halogenated solvents commonly used, e.g. methylene chloride, chloroform, polychloroethylene and carbon tetrachloride have been identified as suspected human carcinogens.

The halogenated solvents, being volatile, rise to the stratospheric region, where they get converted into chlorine free radicals by the action of UV light from the sun. The chlorine free radicals are responsible for depletion of ozone layer.

**Advantages of carrying out reactions using water as a solvent :**

(1) Water is comparatively a cheaper solvent which makes the chemical reactions economical.

(2) Water is a safe solvent. Unlike organic solvents, water is neither inflammable, potentially explosive, mutagenic and/or carcinogenic.

(3) Water-soluble substances, like carbohydrates, proteins, etc., can be used directly.

(4) In industrial process, the products can be isolated by simple phase separation. Also, it is easier to control the reaction temperature, since water has one of the largest heat capacities of all substances.

(5) The use of water as solvent may not cause problems of pollution, which is a major concern when volatile organic solvents are used.

(6) Water can be readily recycled.

# Water as solvent in Organic Synthesis

**Properties of water**

(1) **High dipole moment :** High dipole moment (1.85 D) of water makes it a good polar solvent.

(2) **High dielectric constant :** High dielectric constant (~ 80 at 25 $^oC$) makes it a good ionizing solvent.

(3) **High heat capacity :** Due to high heat capacity, water can store heat for long time which can help to control the reaction temperature for effective conversion of the reactant to the product.

(4) **Viscosity :** The moderately high value of viscority (1 centipoise at 20 $^oC$) heps water to act as a good reaction medium.

(5) **Ionic product :** The ionic product of water at 25 $^oC$ is 1 x $10^{-14}$ and makes water to act as a neutral medium.

(6) **Freezing point and boiling point :** The freezing and boiling points of water are 0 $^oC$ and 100 $^oC$ respectively which makes water to remain in the liquid state in a wide range of temperature.

(7) **Non-toxicity, non-volatility and non-flammability :** These properties make water as a safe and effective green solvent for organic synthesis.

(8) **Hydrogen bonding :** Water remains in the liquid state due to association of large number of molecules through hydrogen bonding. Hydrogen bonding ability helps water to dissolve many organic substances which are able to form H-bond with water molecules, e.g., sugars.

# Water as solvent in Organic Synthesis

**Factors on which rate of organic reactions in aqueous medium depends**

The organic reactions in water / aqueous medium depend on the following factors which inflence the rate of the reactions and selectivity. The factors are:

(1) Hydrophobic effect,

(2) Hydrogen bonding,

(3) Polarity effect,

(4) Trans-phase hydrogen bonding.

**Hydrophobic effect**

- The hydrophobic effect is the tendency of nonpolar substances to aggregate in an aqueous solution so as to decrease the hydrocarbon-water interfacial area and to be excluded by water.
- This allows the non-polar molecules to associate with other non-polar / hydrocarbon molecules instead of distributing in the aqueous medium to have a minimum contact with water.
- The word hydrophobic literally means "water-fearing", and it describes the segregation of water and nonpolar substances, which maximizes the entropy of water and minimizes the area of contact between water and nonpolar molecules.

# Hydrophobic Effect

- The hydrophobic effect is the free energy change of water surrounding a solute. A positive free energy change of the surrounding solvent indicates hydrophobicity, whereas a negative free energy change implies hydrophilicity.

**Examples:**

(1) The hydrophobic effect is responsible for the separation of a mixture of oil and water into its two components.

(2) The hydrophobic effect is essential to life. It is responsible for effects related to biology, including: cell membrane and vesicle formation, protein folding, insertion of membrane proteins into the nonpolar lipid environment and protein-small molecule associations.

(3) A droplet of water forms a spherical shape, minimizing contact with the hydrophobic leaf.

- The hydrophobic interaction (interaction between the hydrophobes) describes the relation between water and hydrophobes (low water-soluble molecules).

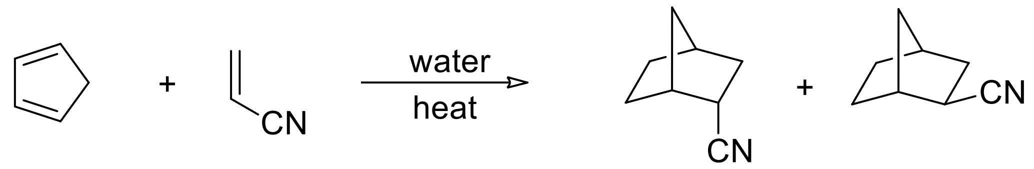
- Hydrophobes are non-polar molecules and usually have a long carbon chain that do not interact with water.

- The concept of hydrophobic effect was developed by Breslow to explain the rate acceleration and selectivity of Diels-Alder reactions in aqueous medium.

# Hydrogen bonding effect of water

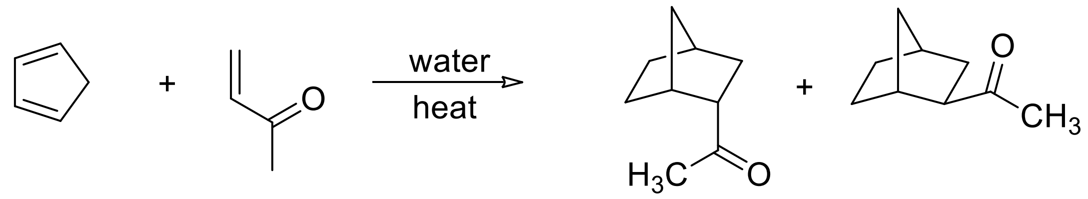
- The hydrophobic effect is the free energy change of water surrounding a solute. A positive free energy change of the surrounding solvent indicates hydrophobicity, whereas a negative free energy change implies hydrophilicity.

  The rate of Diels-Alder recation depends on the nature of solvents. The rate of Diels-Alder reaction remarkably accelerated in water. The hydrophobic effect was operating in water. In the transition state of the reaction, two hydrocarbon surfaces must aggregate with each each other which is favoured in water.




ratio of rate (methanol : isooctane) = 2

ratio of rate (water : methanol) = 15




ratio of rate (methanol : isooctane) = 12

ratio of rate (water : methanol) = 730

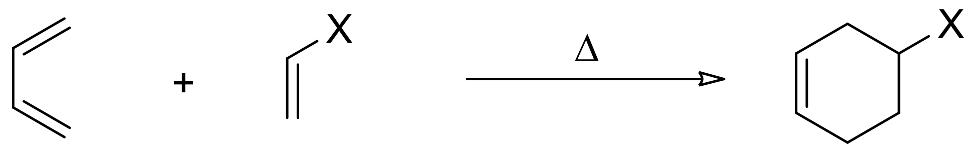
**HW:** Why are most of Diels-Alder reactions faster in water than in methanol? [2022]

# Hydrogen bonding effect of water

- A large number of water molecules remain in association through H-bonding, which has the ability to influence the rate of different types of reactions.

- The rate of Diels-Alder reactions are influenced by the hydrogen bonding effect. The effect of H-bonding in Diels-Alder reaction mostly depends on the nature of the dienophiles and their reaction centres. The dienophiles having site to form H-bond with water in aqueous medium can stabilize the transition state of a Diels-Alder reaction and hence lower the activation energy to accelerate the rate of reaction.

- The dienophiles having electron-attracting groups are most reactive and suitable for stabilizing the transition state through H-bonding. Thus, $\alpha,\beta$-unsaturated aldehyde, ketones, esters, nitriles, etc., are effective dienophiles for the such type of reactions.



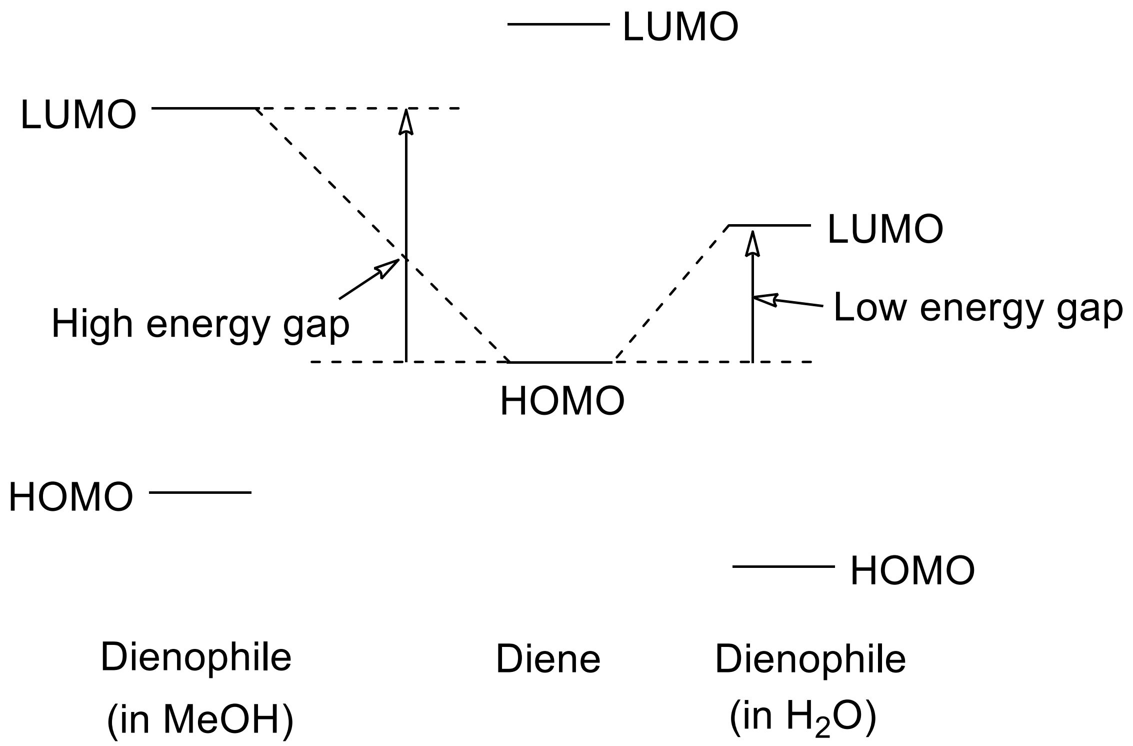

diene dienophile D. A. adduct

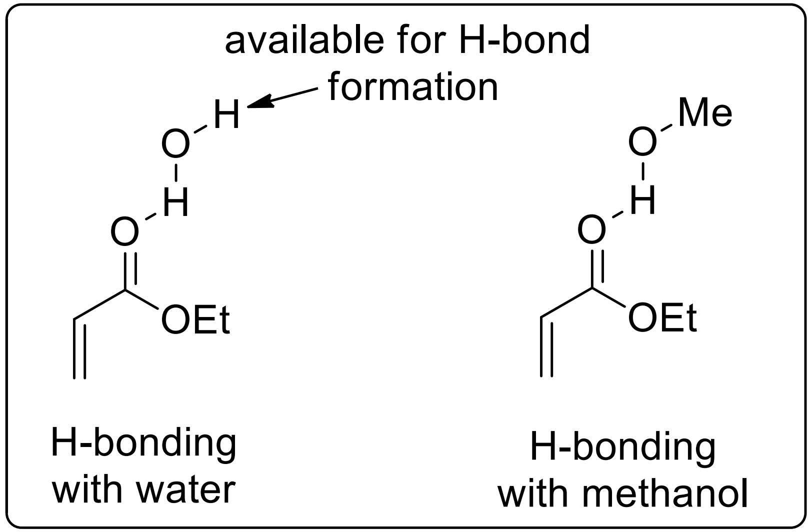
X = electron-withdrawing group
= -$COCH_3$, -CN

- The reaction between a diene and dienophile could be better understood by the HOMO-LUMO enegy gap between the diene and dienophile.

# Hydrogen bonding effect of water

The dienophiles having electron-attracting group are stablized by H-bonding with water and hence it's energy is lowered. Thus, the energy gap betwwen HOMO of diene and LUMO of dienophiles decreases, which accelerates the rate of reaction. The HOMO-LUMO energy diagram is shown below.



# Hydrogen bonding effect of water

**Classification of organic reaction in aqueous medium**

The organic reactions in aqueous medium are generally classified into the following three categories :

(1) **'In water' reaction:** The reactions where the reactants are soluble in water but products are water insoluble. Such reactions are called 'in water' reaction.

(2) **'On water' reaction:** The reactions where both the reactants and formed products are insoluble in water are called 'on water' reaction.

(3) **'With water' reaction:** The reactions where water acts as one of the reactant are called 'with water' reaction.

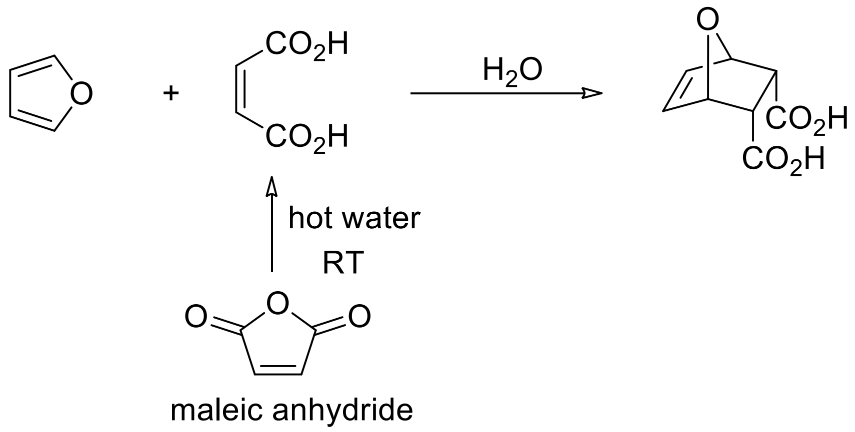
**Conclusion:**

Hydrophobic effect, hydrogen bonding and polarity effects are associated with 'in water' reactions and trans-phase hydrogen bonding effect is observed only for the 'on water' reactions.

# ‘In water’ Reactions

**'In water' reactions**

(1) The reaction of maleic anhydride with furan in hot water gives a Diels-Alder adduct. The formation of this dicarboxylic acid proceeds through hydrolysis of maleic anhydride to maleic acid. In this cas, the *endo*-productis the major product.




(2) The Baylis-Hillman reaction between aromatic aromatic aldehydes and a,b-unsaturated esters to produce the product in the presence of tertiary amine. The reaction rate is icreased in water and it does not depend on 'salting-in' or 'salting-out' conditions.