

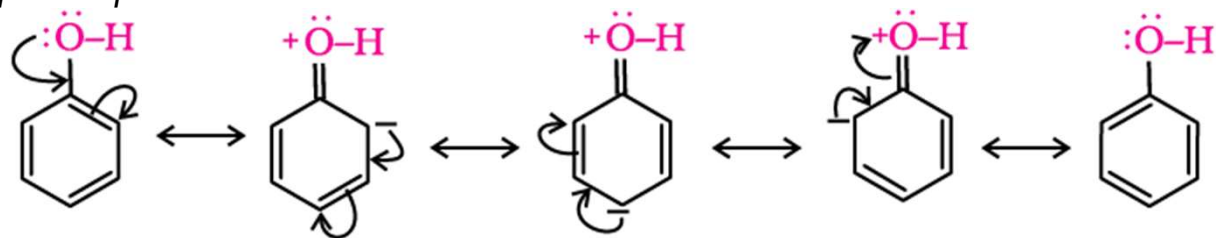
Chemical Reactions of Alcohols and Phenols

(a) Reactions involving cleavage of O–H bond

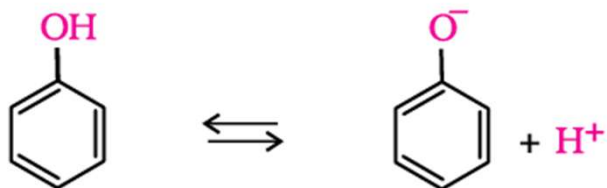
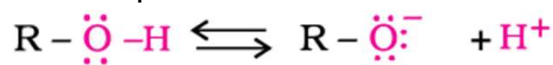
1. Acidity of alcohols and phenols

(iii) **Acidity of phenols:** reactions of phenol with metals (e.g., sodium, aluminium) and sodium hydroxide indicate its acidic nature.

The hydroxyl group, in phenol is directly attached to the sp^2 hybridized carbon of benzene ring which acts as an electron withdrawing group. Due to this, the charge distribution in phenol molecule, as depicted in its resonance structures, causes the oxygen of –OH group to be positive.



- The reaction of phenol with aqueous sodium hydroxide indicates that **phenols are stronger acids than alcohols and water**.
- The ionization of an alcohol and a phenol takes place as follows:

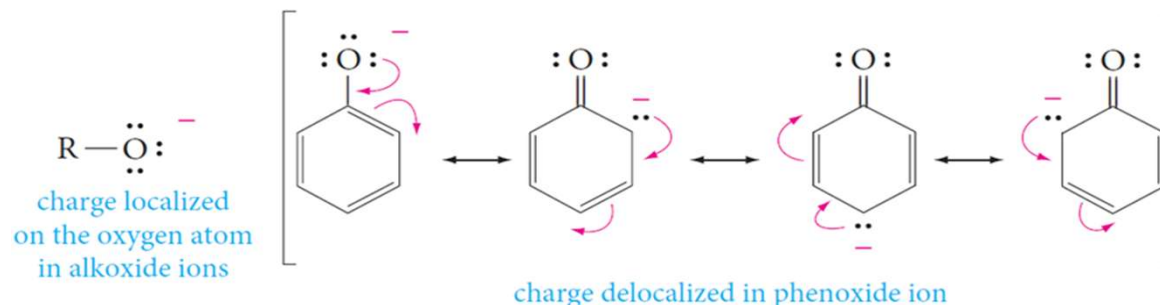


Chemical Reactions of Alcohols and Phenols

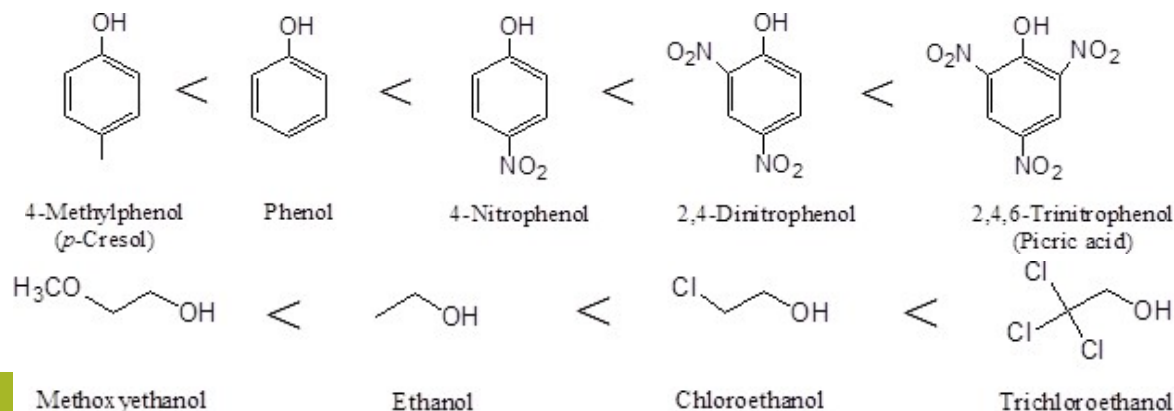
(a) Reactions involving cleavage of O–H bond

1. Acidity of alcohols and phenols

- The stabilities of alkoxide and phenoxide ions. In alkoxide ion, the negative charge is localized on oxygen while in phenoxide ion, the charge is delocalized which makes phenoxide ion more stable and favors the ionization of phenol.



- Electron-withdrawing groups increase acidity by stabilizing the conjugate base.
- Electron-donating groups decrease acidity because they destabilize the conjugate base.

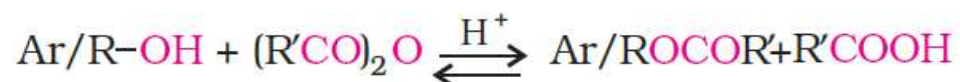


Chemical Reactions of Alcohols and Phenols

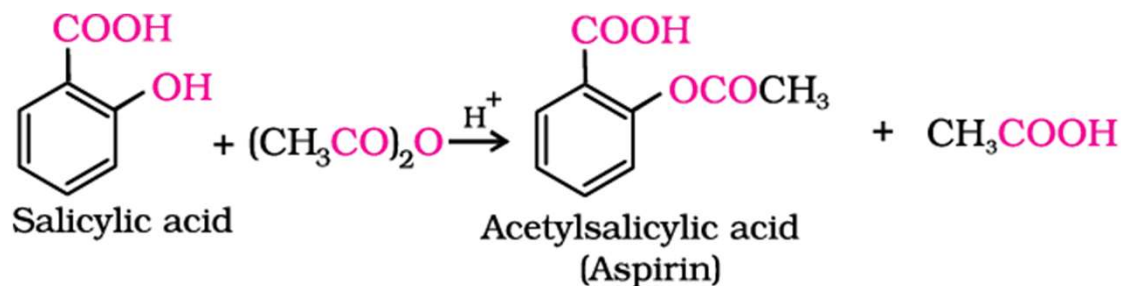
(a) Reactions involving cleavage of O–H bond

2. Esterification

- Alcohols and phenols react with carboxylic acids, acid chlorides and acid anhydrides to form esters.



- Acetylation;** The introduction of acetyl (CH_3CO) group in alcohols or phenols.
Example: Acetylation of salicylic acid produces aspirin.



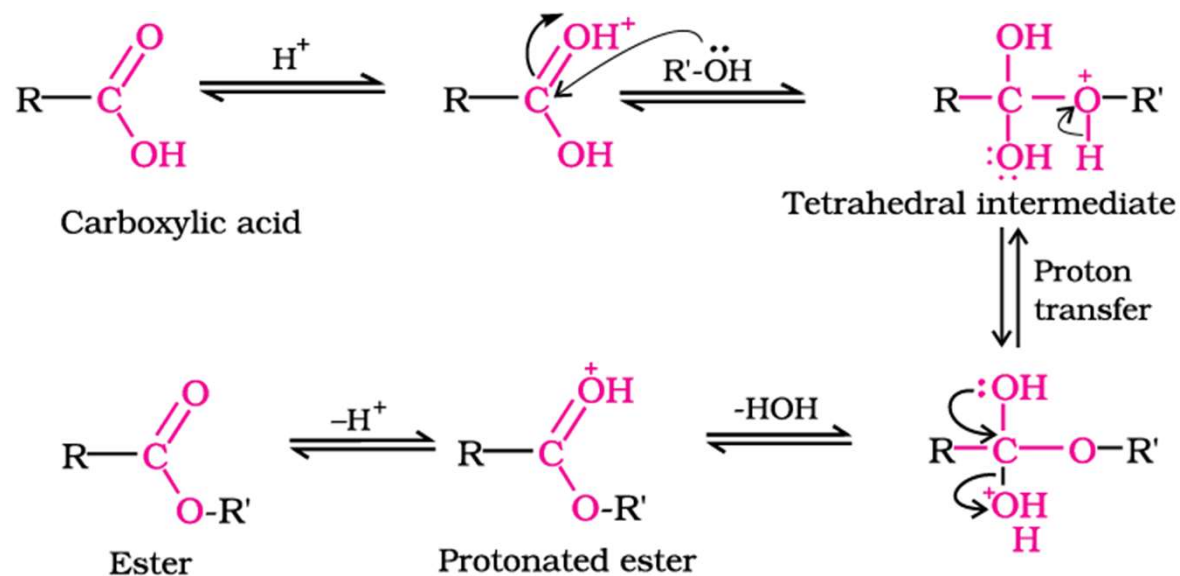
Chemical Reactions of Alcohols and Phenols

(a) Reactions involving cleavage of O–H bond

2. Esterification

Mechanism of esterification of carboxylic acids:

- The esterification of carboxylic acids with alcohols is a kind of *nucleophilic acyl substitution*.
 - Protonation of the carbonyl oxygen activates the carbonyl group towards nucleophilic addition of the alcohol.
 - Proton transfer in the tetrahedral intermediate converts the hydroxyl group into $-^+\text{OH}_2$ group (leaving group).
 - The protonated ester so formed finally loses a proton to give the ester.

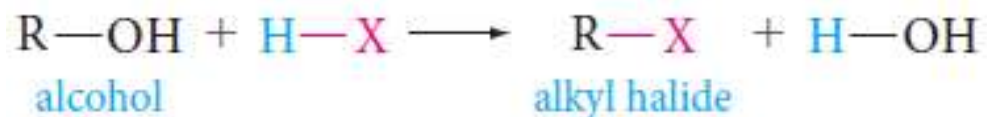


Chemical Reactions of Alcohols and Phenols

(b) Reactions involving cleavage of carbon – oxygen (C–O) bond in alcohols

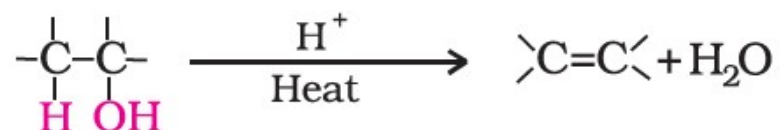
1. Reaction with hydrogen halides: **Nucleophilic Substitution Reaction**

Alcohols react with hydrogen halides (*HCl*, *HBr* and *HI*) to form alkyl halides.

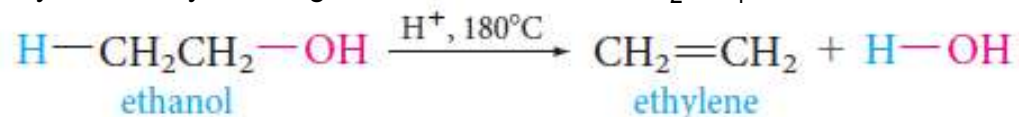


2. Dehydration: **Formation of Alkenes**

Alcohols undergo dehydration (removal of a molecule of water) to form alkenes on treating with protic acid (concentrated H_2SO_4 or H_3PO_4 , or catalysts such as anhydrous zinc chloride or alumina)



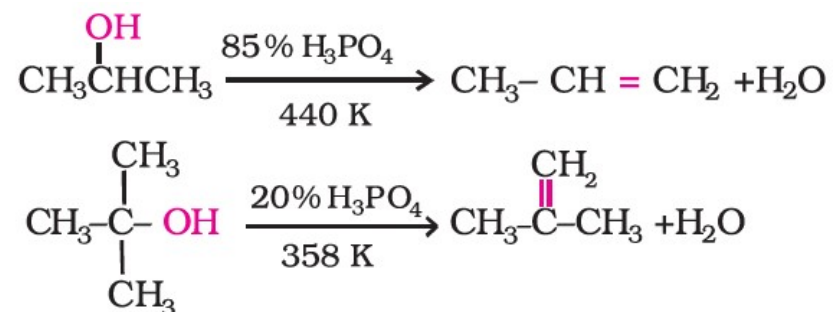
- Ethanol undergoes dehydration by heating it with concentrated H_2SO_4 at 180°C .



Chemical Reactions of Alcohols and Phenols

(b) Reactions involving cleavage of carbon – oxygen (C–O) bond in alcohols

- **Secondary and tertiary alcohols** are dehydrated under milder conditions.



- The relative ease of dehydration of alcohols follows the following order:

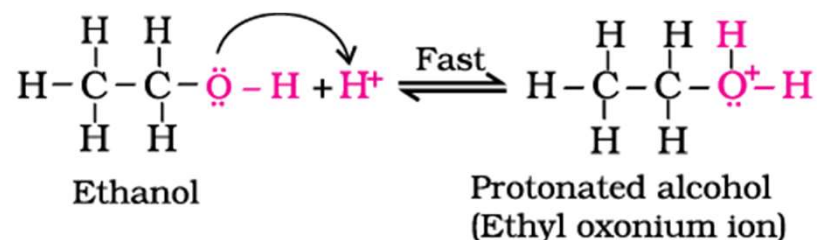
Tertiary > Secondary > Primary

Chemical Reactions of Alcohols and Phenols

(b) Reactions involving cleavage of carbon – oxygen (C–O) bond in alcohols

Dehydration of ethanol; Mechanism:

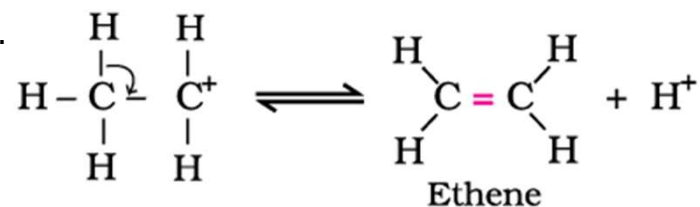
Step 1: Formation of protonated alcohol.



Step 2: Formation of carbocation: It is the slowest step and hence, the rate determining step of the reaction.



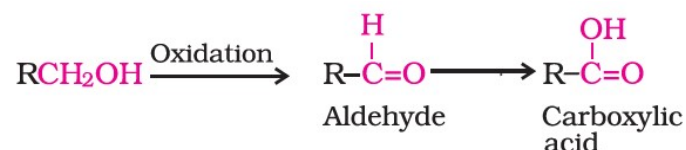
Step 3: Formation of ethene by elimination of a proton.



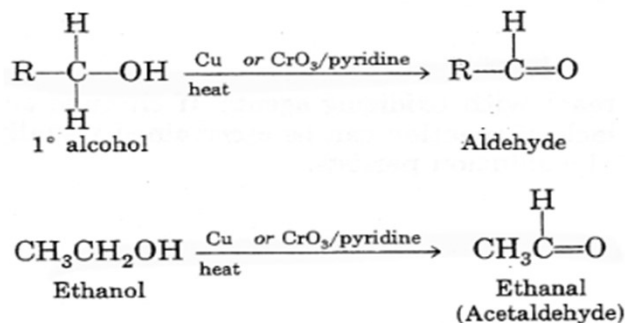
Chemical Reactions of Alcohols and Phenols

(b) Oxidation of alcohols

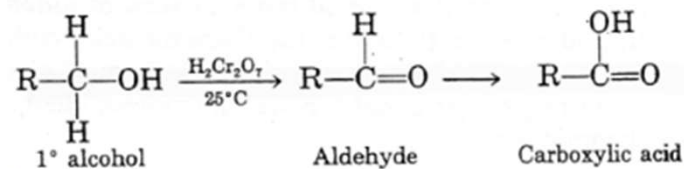
- Depending on the oxidizing agent used, a **primary alcohol** is oxidized to an aldehyde which in turn is oxidized to a carboxylic acid.



- **Primary alcohols** yield **aldehydes** when treated with **mild oxidizing agents** such as **hot metallic copper** or **CrO₃ in pyridine**.



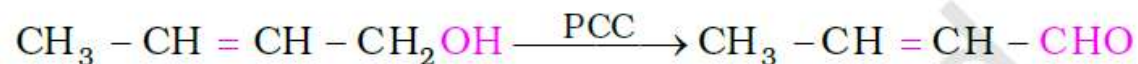
- **Primary alcohols**; when treated with **stronger oxidizing agents**, such as **chromic acid, H₂Cr₂O₇**, or **neutral potassium permanganate, KMnO₄**, the **intermediate aldehydes** formed initially are oxidized further to **carboxylic acids**.



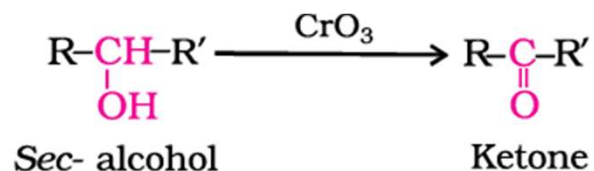
Chemical Reactions of Alcohols and Phenols

(b) Oxidation of alcohols

- A better reagent for oxidation of primary alcohols to aldehydes in good yield is **pyridinium chlorochromate (PCC)**, a complex of chromium trioxide with pyridine and HCl.



- **Secondary alcohols** are oxidized to ketones by chromic anhydride (CrO_3).



- **Tertiary alcohols** do not undergo oxidation reaction.

Chemical Reactions of Alcohols and Phenols

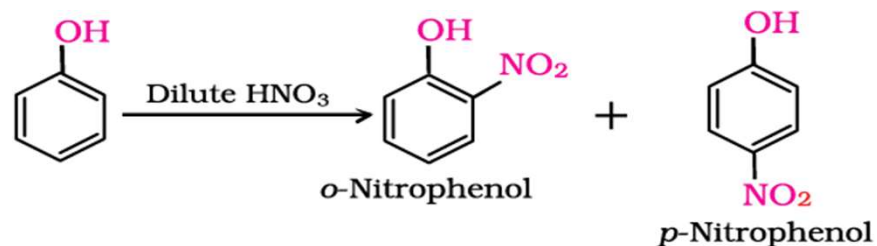
(c) Reactions of Phenols

1. Electrophilic aromatic substitution

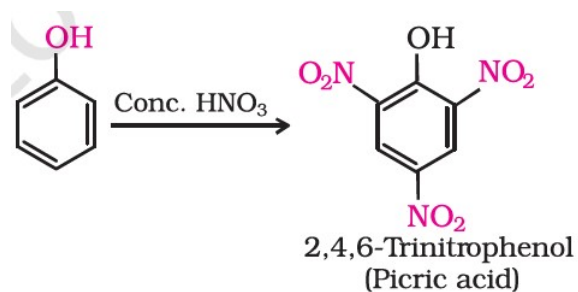
- The $-OH$ group attached to the benzene ring activates it towards electrophilic substitution.
- Also, it directs the incoming group to *ortho* and *para* positions in the ring.

(i) Nitration:

- With dilute nitric acid at low temperature (298 K), phenol yields a mixture of *ortho* and *para*-nitrophenols.



- With concentrated nitric acid, phenol is converted to 2,4,6-trinitrophenol (picric acid).



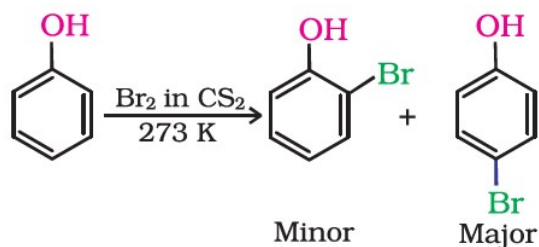
Chemical Reactions of Alcohols and Phenols

(c) Reactions of Phenols

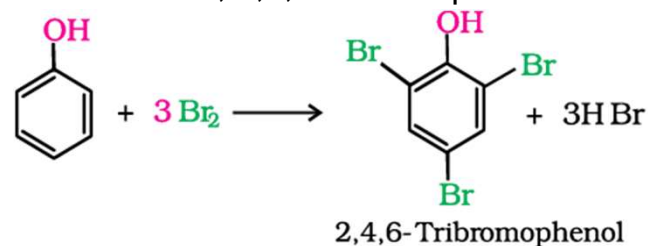
1. Electrophilic aromatic substitution

(ii) Halogenation:

- (a) When the reaction is carried out in solvents of low polarity such as CHCl_3 or CS_2 and at low temperature, monobromophenols are formed.



- (b) When phenol is treated with bromine water, 2,4,6-tribromophenol is formed as white precipitate.



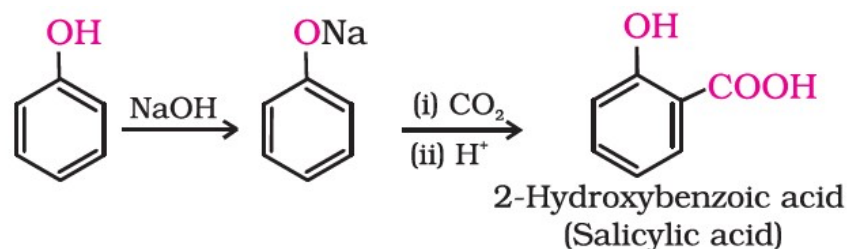
In case of phenol, the polarization of bromine molecule takes place even in the absence of Lewis acid due to the highly activating effect of $-\text{OH}$ group attached to the benzene ring.

Chemical Reactions of Alcohols and Phenols

(c) Reactions of Phenols

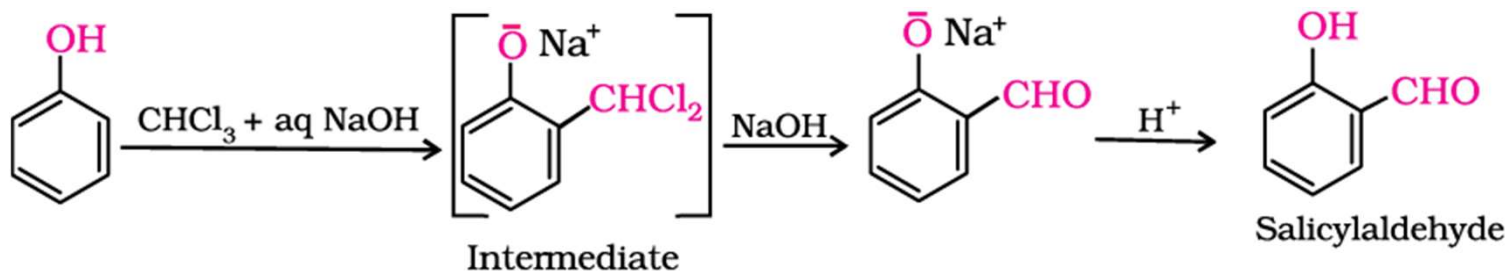
2. Kolbe's reaction

The **synthesis of salicylic acid** by heating a mixture of sodium phenoxide and carbon dioxide under pressure at 180° - 200°C, then treating the product with sulfuric acid.



3. Reimer-Tiemann reaction

- Treatment of phenol with chloroform in the presence of sodium hydroxide, a -CHO group is introduced at *o*- position of benzene ring.
- The intermediate substituted benzal chloride is hydrolyzed in the presence of alkali to produce salicylaldehyde.

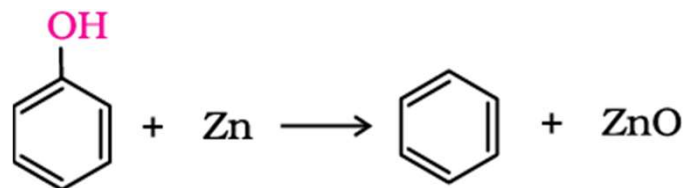


Chemical Reactions of Alcohols and Phenols

(c) Reactions of Phenols

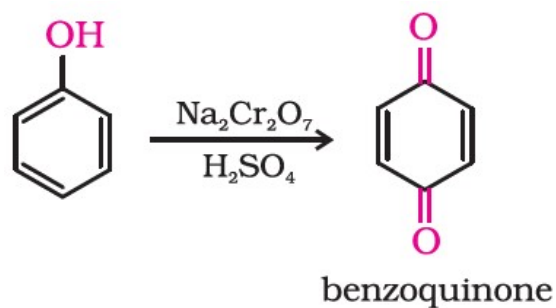
4. Reaction of phenol with zinc dust

Phenol is converted to benzene on heating with zinc dust.



5. Oxidation

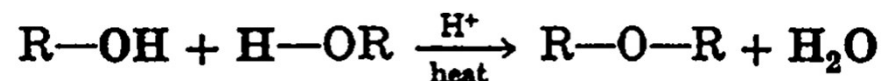
- Oxidation of phenol with chromic acid produces a conjugated diketone known as benzoquinone.
- In the presence of air, phenols are slowly oxidized to dark colored mixtures containing quinones.



Preparation of Ethers

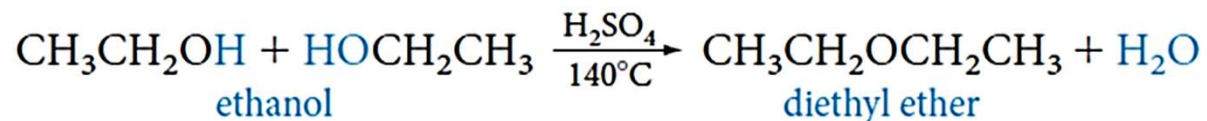
1. Dehydration of Alcohols

- It takes place in the presence of acid catalysts (H_2SO_4 , H_3PO_4) (intermolecular reaction)

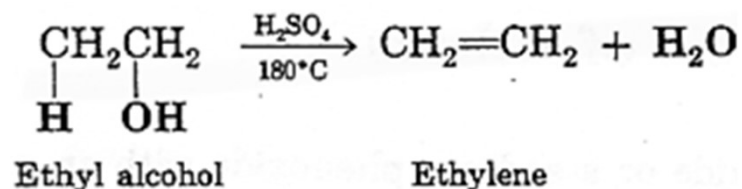


- **Example;**

The most important commercial ether is diethyl ether. It is prepared from ethanol and sulfuric acid.



- When ethyl alcohol is dehydrated by **sulfuric acid at 180°C** , the dominant product is **ethylene**.



Preparation of Ethers

2. Williamson Synthesis

- It is an important laboratory method for the **preparation of symmetrical and unsymmetrical ethers**.
- In this method, an *alkyl halide* is allowed to react with *sodium alkoxide*.
- **This method has two steps;**

1) An alcohol is converted to its alkoxide by treatment with a reactive metal (sodium or potassium).



2) Displacement is carried out between the alkoxide and an alkyl halide.



- To obtain the best yields of mixed dialkyl ethers, we select a 1° rather than a 2° or 3° alkyl halide and react it with a sodium alkoxide
- To prepare an alkyl aryl ether, we must be careful **not to pick a combination in which one of the reagents has a halogen directly attached to an aromatic ring**.

Preparation of Ethers

2. Williamson Synthesis

○ **Example 1;** Preparation of *t*-butyl methyl ether, $(\text{CH}_3)_3\text{C-O-CH}_3$.

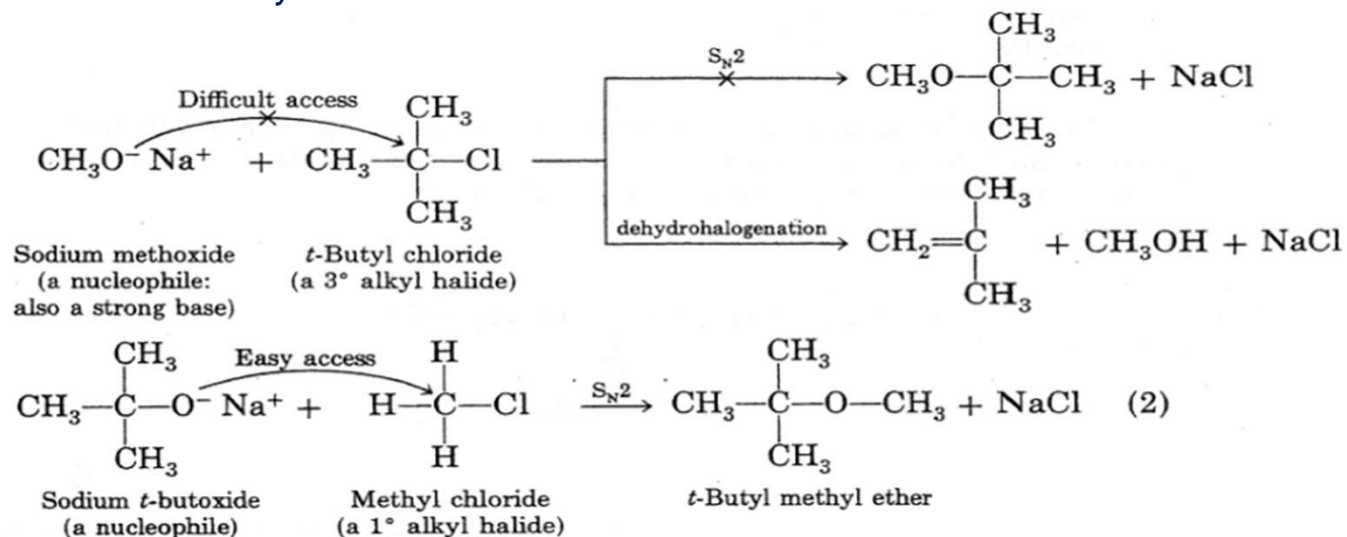
▪ In theory, this could be done by either of two reactions.

1. You could react sodium methoxide, $\text{CH}_3\text{O}^-\text{Na}^+$, with *t*-butyl chloride, $(\text{CH}_3)_3\text{C-Cl}$.

This combination leads to dehydrohalogenation to an alkene, an elimination reaction.

2. You could react sodium *t*-butoxide, $(\text{CH}_3)_3\text{C-O}^-\text{Na}^+$, with methyl chloride, CH_3Cl .

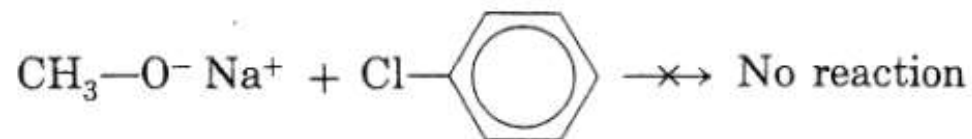
This route gives the desired ether by substitution.



Preparation of Ethers

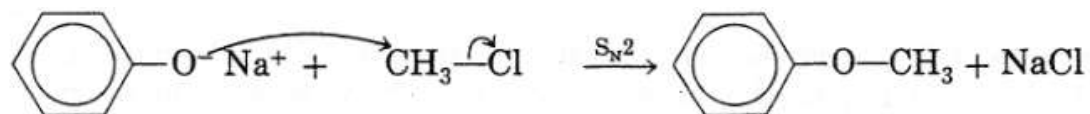
2. Williamson Synthesis

- **Example 2;** Assume you need to synthesize methyl phenyl ether (anisole), $\text{CH}_3\text{-O-C}_6\text{H}_5$, by the Williamson method.
 - *In theory, you could obtain anisole in either of two ways.*



Sodium methoxide
(a nucleophile)

Chlorobenzene
(an aryl halide)



Sodium phenoxide
(a nucleophile)

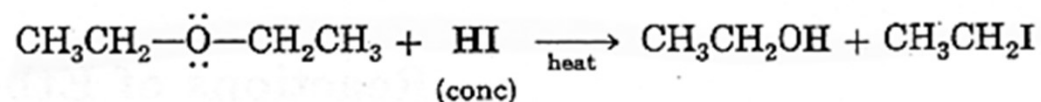
Methyl chloride
(a 1° alkyl halide)

Anisole

Chemical Reactions of Ethers

1. Cleavage of C–O bond in ethers

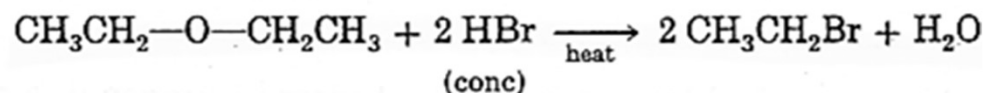
- Ethers are the **least reactive** of the functional groups.
- When **ethers** are heated in concentrated acid solutions, the ether linkage is broken.



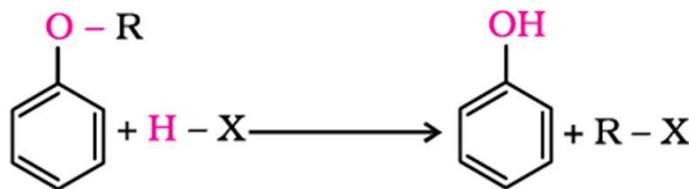
- The acids most often used in this reaction are $\text{HI} > \text{HBr} > \text{HCl}$.
- If an **excess of acid** is present, the alcohol initially produced is converted into an alkyl halide by the reaction.



For example,



- **Alkyl aryl ethers** are cleaved at the alkyl-oxygen bond due to the more stable aryl-oxygen bond. The reaction yields *phenol* and *alkyl halide*.



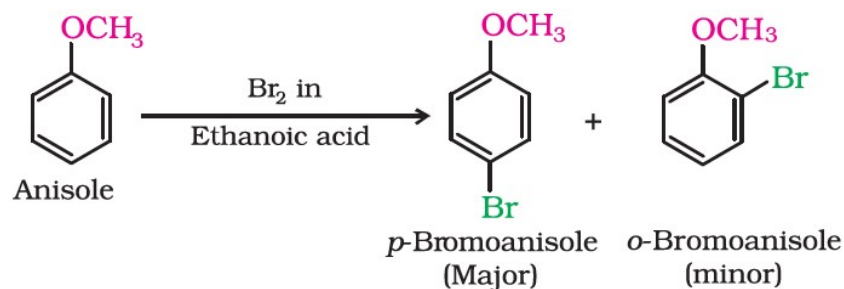
Chemical Reactions of Ethers

2. Electrophilic substitution

- The alkoxy group (-OR) is *ortho*, *para* directing and activates the aromatic ring towards electrophilic substitution.

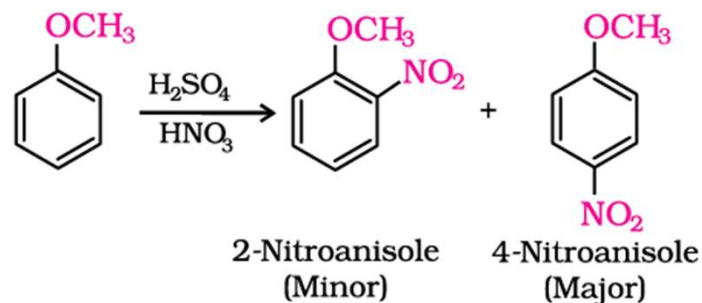
(i) Halogenation:

Anisole undergoes bromination with bromine in ethanoic acid even in the absence of iron (III) bromide catalyst. It is due to the activation of benzene ring by the methoxy group. *Para* isomer is obtained in 90% yield.



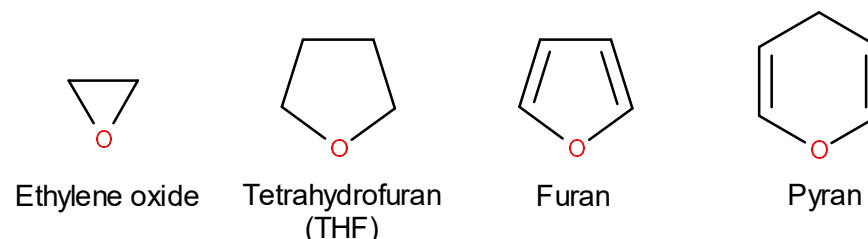
(ii) Nitration:

Anisole reacts with a mixture of concentrated sulphuric and nitric acids to yield a mixture of *ortho* and *para* nitroanisole.



Cyclic Ethers

- **Cyclic ethers** are similar to cycloalkanes/cycloalkenes, but possess an O- atom as part of the ring.



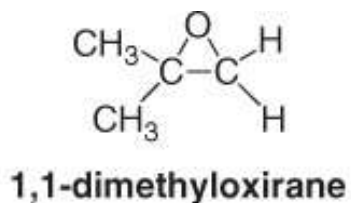
- **Epoxides** are ethers having the oxygen atom in a **three-membered ring**.
- **Epoxides** are also called **oxiranes**.



- The C-O-C bond angle for an epoxide must be 60° , a considerable deviation from the tetrahedral bond angle of 109.5° . Thus, epoxides have **angle strain**, making them **more reactive** than other ethers.

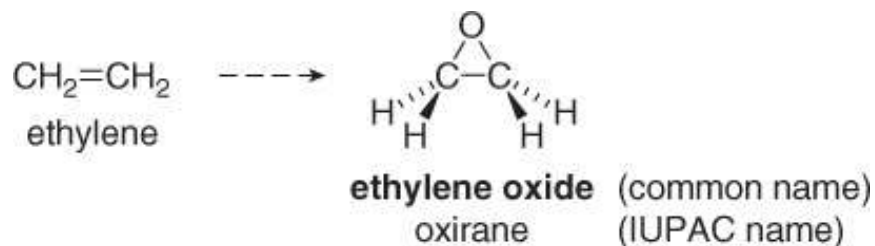
Nomenclature of Epoxides

- **Epoxides** bonded to a chain of carbon atoms are named as **derivatives of oxirane**.
- When an epoxide is bonded to a ring, the O atom is considered a substituent, called an epoxy group, bonded to a cycloalkane, and two numbers are used to designate the atoms to which the O atoms are bonded.



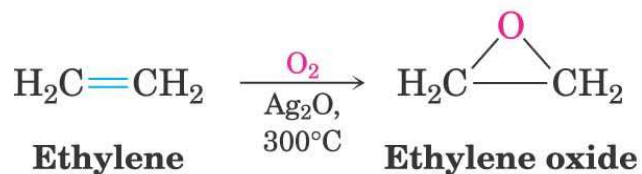
- **Epoxides** are also named as **alkene oxides**, because they are often prepared by adding an O atom to an alkene.
- **To name an epoxide in this way:**

- Mentally replace the epoxide oxygen by a double bond.
- Name the alkene.
- Add the word oxide.



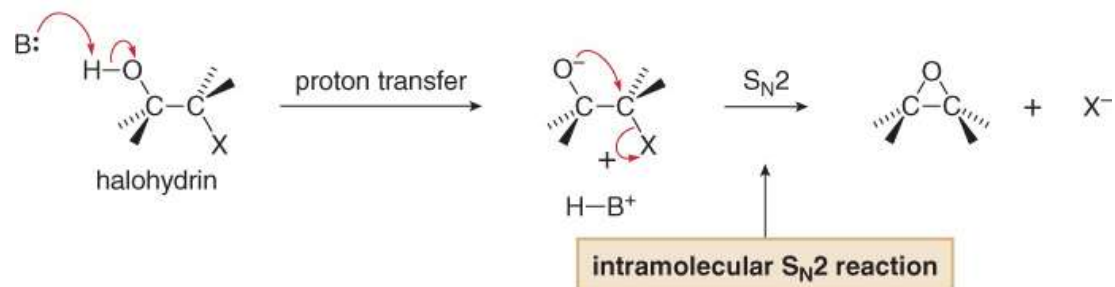
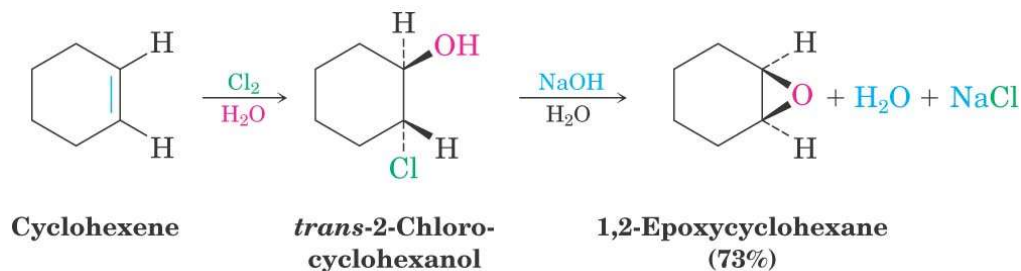
Preparation of Epoxides

- **Ethylene oxide** is prepared commercially by air oxidation of ethylene.



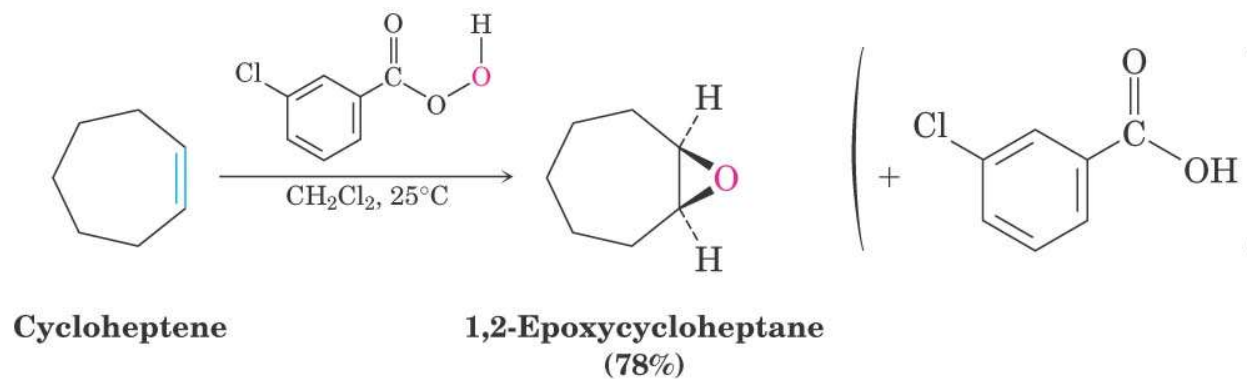
- **Epoxides from Halohydrins**

- Addition of HO-X to an alkene gives a halohydrin
- Treatment of a halohydrin with base gives an epoxide

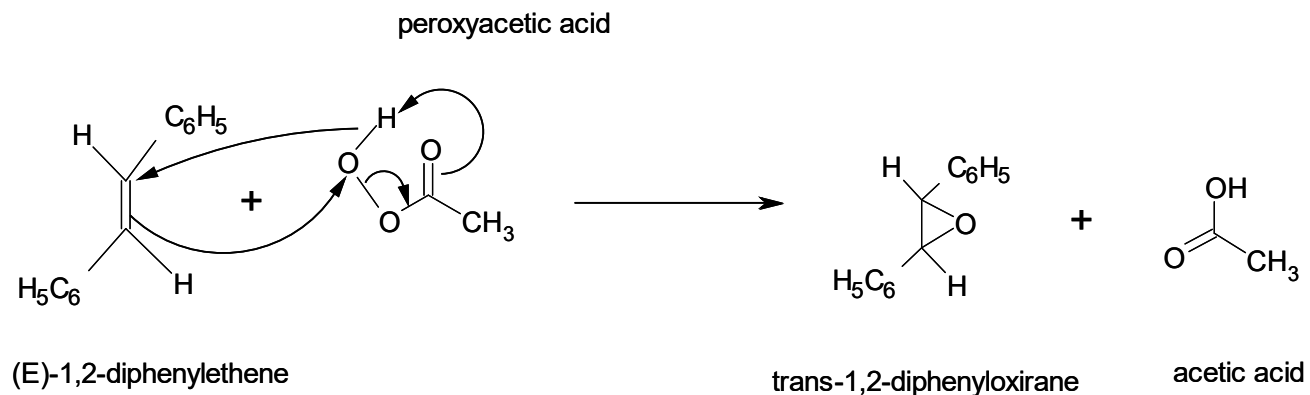


Preparation of Epoxides

○ Preparation of Epoxides Using a Peroxyacid

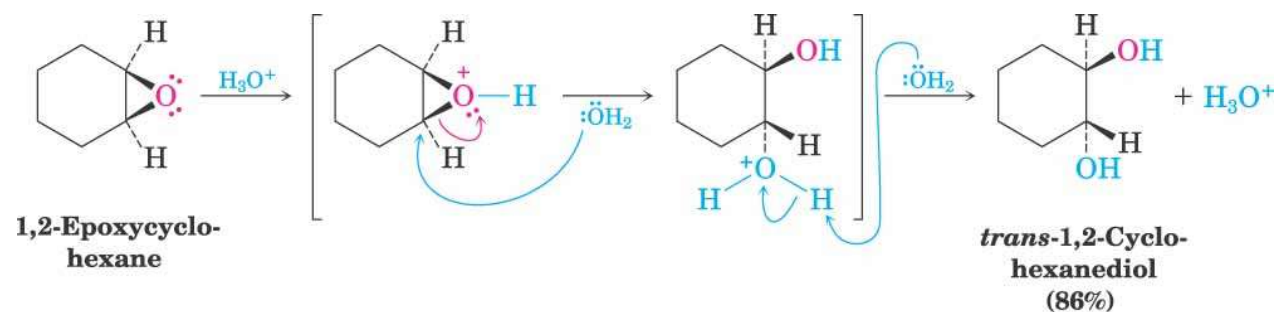


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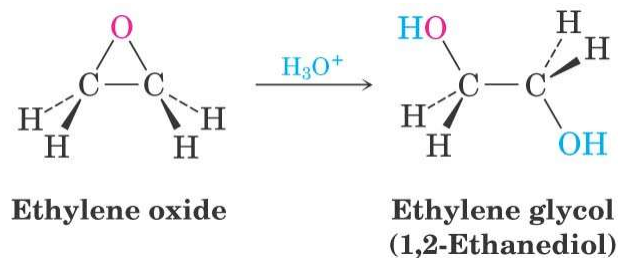


Ring-Opening Reactions of Epoxides

- Common nucleophiles that open the epoxide ring include OH^- , OR^- , CN^- , SR^- and NH_3 .
- With these strong nucleophiles, the reaction occurs by an $\text{S}_{\text{N}}2$ mechanism
- **Water** adds to epoxides with dilute acid at room temperature
 - Product is a 1,2-diol (on adjacent C's: *vicinal*)
 - Mechanism: acid protonates oxygen and water adds to opposite side (anti-addition)



- **Example;** 1,2-ethanediol from acid catalyzed hydration of ethylene



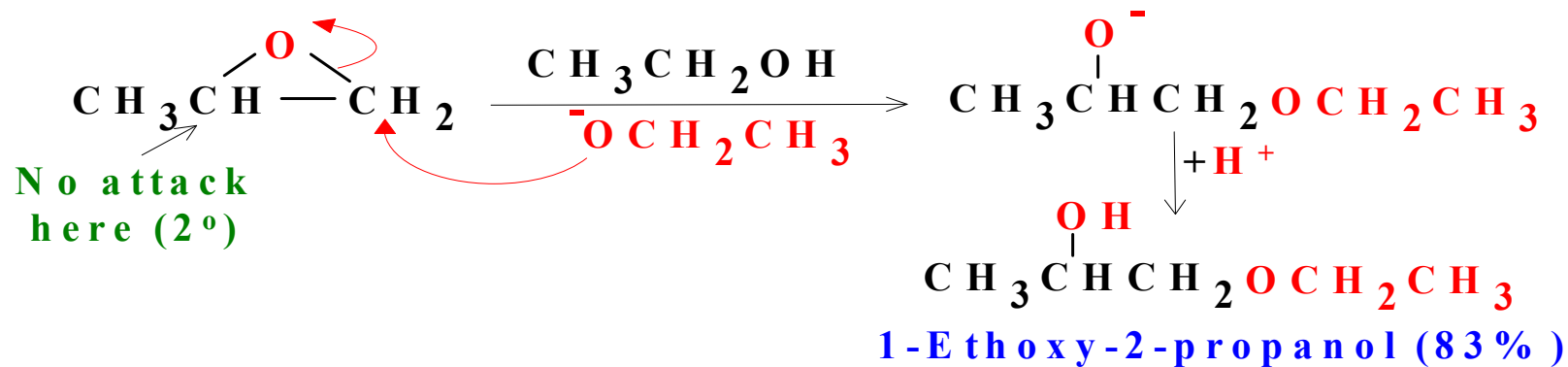
Ring-Opening Reactions of Epoxides

الانتقائية الموضعية لتفاعل فتح الحلقة

Regioselectivity of ring opening

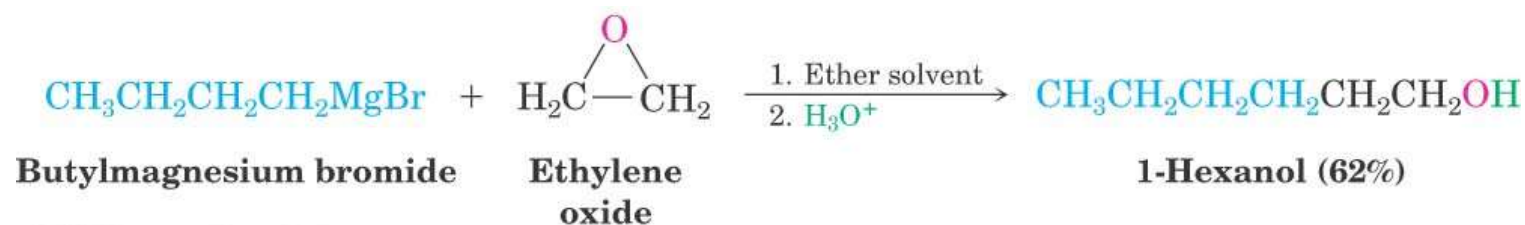
تختلف ميكانيكية تفاعل فتح حلقة الايبوكسيدات باختلاف وسط التفاعل ففي الوسط القاعدي يقوم الكاشف النيوكليوفيلي بمهاجمة ذرة الكربون الاقل اعاقاة فراغية

○ Base-Catalyzed Epoxide Opening



Ring-Opening Reactions of Epoxides

○ Addition of Grignard to Ethylene Oxide



○ Acid-Catalyzed Epoxide Opening

- Hydroxide cleaves epoxides at elevated temperatures to give trans 1,2-diols.

اما في الوسط الحمضي يقوم الكاشف النيوكليوفيلي بمهاجمة ذرة الكربون الاكثر اعاقا فراغية حيث يتكون ايون الكربونيوم الاكثر استقرارا

