03 Alcohols and Ethers

Alcohol:

Hydroxy derivatives

↓

Aliphatic hydroxy derivatives | Aromatic hydroxy derivatives

(I) Aliphatic hydroxy derivatives :

Hydroxy derivatives in which —OH is directly attached to sp^3 C (Alcoholic compounds).

(II) Aromatic hydroxy derivatives :

Hydroxy derivatives in which —OH is directly attached to sp^2 C of benzene ring (Phenolic compounds).

(a) Classification according to number of —OH groups :

(i) Monohydric [one –OH] ⟶ CH_3CH_2—OH

(ii) Dihydric [two –OH] ⟶ $CH_2(OH)-CH_2(OH)$ Glycol

(iii) Trihydric [three –OH] ⟶ $CH_2(OH)-CH(OH)-CH_2(OH)$ Glycerol

(iv) Polyhydric [n –OH] ⟶ $CH_2OH-(CHOH)_4-CH_2OH$ Sorbitol

(b) Classification according to nature of carbon :

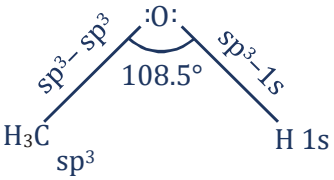
(i) primary (1°) alcohol ⟶ CH_3CH_2-OH

(ii) secondary (2°) alcohol ⟶ $(CH_3)_2CH-OH$

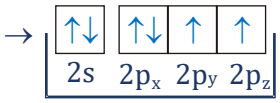
(iii) tertiary (3°) alcohol ⟶ $(CH_3)_3C-OH$

Structure of alcohol:

Alcohols are bent molecules. The carbon atom (linked with 'O' atom of –OH group) is sp^3 hybridised. The central 'O' atom is also in sp^3 state of hybridisation. The bond angle is 108.5°. In sp^3 hybridisation of O - $2s^2, 2p_x^2\ 2p_y^1\ 2p_z^1$ orbitals hybridised to form sp^3 orbitals



Structure of CH_3OH



sp^3 hybridisation

In these four orbitals two containing one electron each and two containing two electrons each. Orbitals containing two electrons do not take part in bonding. Other two half filled orbitals forms bond with s-orbitals of H -atom and hybridised orbital of C-atom (O—C). Due to lone pair effect the bond angle of tetrahedral oxygen atom is lesser than normal tetrahedral structure (109°28').

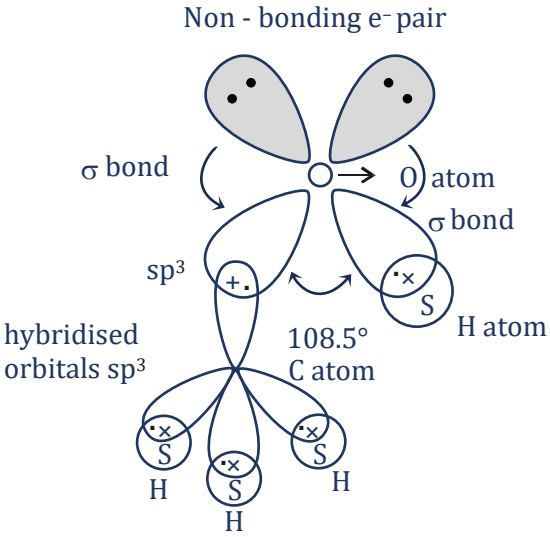
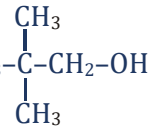


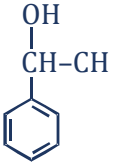
Illustration 1:

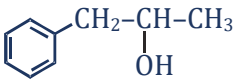
Classify the following as primary, secondary and tertiary alcohols :

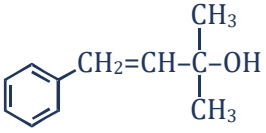
(i) 

(ii) $H_2C = CH - CH_2OH$

(iii) $CH_3–CH_2–CH_2–OH$

(iv) 

(v) 

(vi) 

Solution:

(i) Primary alcohol (ii) Primary alcohol (iii) Primary alcohol

(iv) Secondary alcohol (v) Secondary alcohol (vi) Tertiary alcohol

Ethers:

R—O—R (Dialkyl ether), alkoxy alkane. It's General formula is $C_nH_{2n+2}O$.

CH_3—O—CH_2CH_3 (Methoxy ethane) or ethyl methyl ether or 2–oxa butane.

Ether is monoalkyl derivative of R–OH and dialkyl derivative of H_2O

$$R—OH \xrightarrow[+R]{-H} R—O—R \xleftarrow[+2R]{-2H} H—O—H$$

Classification : They may be classified as :

(a) Simple or symmetrical ether. e.g. R–O–R

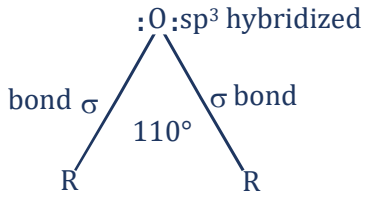
(b) Mixed or unsymmetrical ether e.g. R–O–R'

Structure :

The molecule of ether is bent due to lone pair of electron on oxygen atom- bond electron repulsion. The bond angle is 110°.

It is greater than that of water 105° due to the repulsion between bulky alkyl groups.

Due to bent structure, it posses dipole moment and hence are polar molecules



III Phenols :

Aromatic hydroxy compounds in which –OH group is bonded to benzene ring directly are called phenols. Monohydroxy benzene is called phenol. Phenol is also known as carbolic acid.

The simplest hydroxyl derivative of benzene is phenol which is also its accepted IUPAC name.

methyl phenols are called cresols.

dihydroxy derivatives of benzene are called benzene diols.

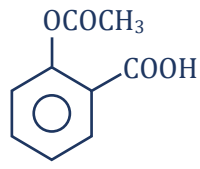
In phenols, the –OH group is attached to sp^2 hybridized carbon of an aromatic ring.

The bond angle of C—O—H in phenol is 109°.

The carbon–oxygen bond length is 136pm which is slightly less than that of methanol. This is due to partial double bond character on account of conjugation of unshared electron pair of oxygen with the aromatic ting.

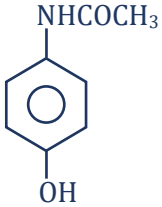
Some important phenolic compounds

(i)

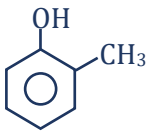
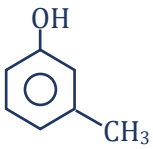
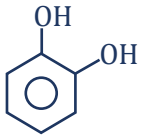
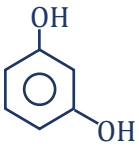
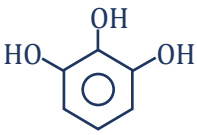
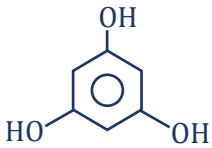
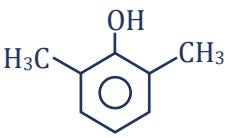


Aspirin (acetyl salicylic acid)

(ii)



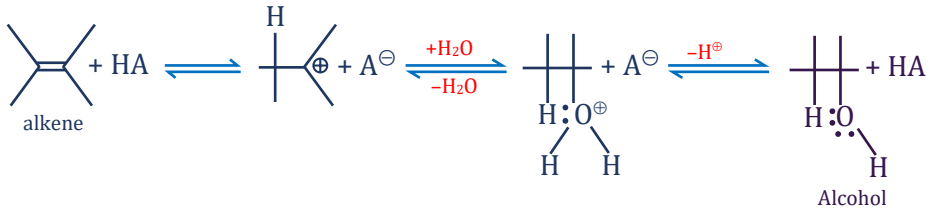
(ii)paracetamol

Molecule	Common name	IUPAC name
	Phenol	Phenol
	o–cresol	2–methyl phenol
	m–cresol	3–methyl phenol
	p–cresol	4–methyl phenol
	Catechol	Benzene–1,2–diol
	Resorcinol	Benzene–1,3–diol
	Hydroquinol	Benzene–1,4–diol
	Pyrogallol	(Benzene1,2,3–triol)
	Phloroglucinol	(Benzene–1,3,5–triol)
		2,6–dimethyl phenol

Preparation methods of Alcohols:

(i) Hydration of alkenes:

Alkenes add water in the presence of an acid catalyst to yield alcohol. The addition takes place according to Markovnikov regioselectivity. The reaction is reversible.

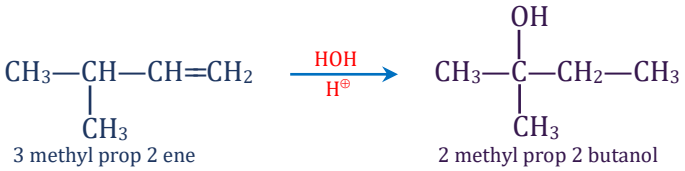


Acid catalysed hydration of alkene has limited synthetic utility because carbocation is the intermediate and rearrangement may take place.

Thus a mixture of isomeric alcohols may result, it is an electrophilic addition reaction.

$$H_2C{=}CH_2 + H_2O \xrightarrow{H^{\oplus}} CH_3{-}CH_2{-}OH$$

In this reaction there is a possibility of formation of carbocation.

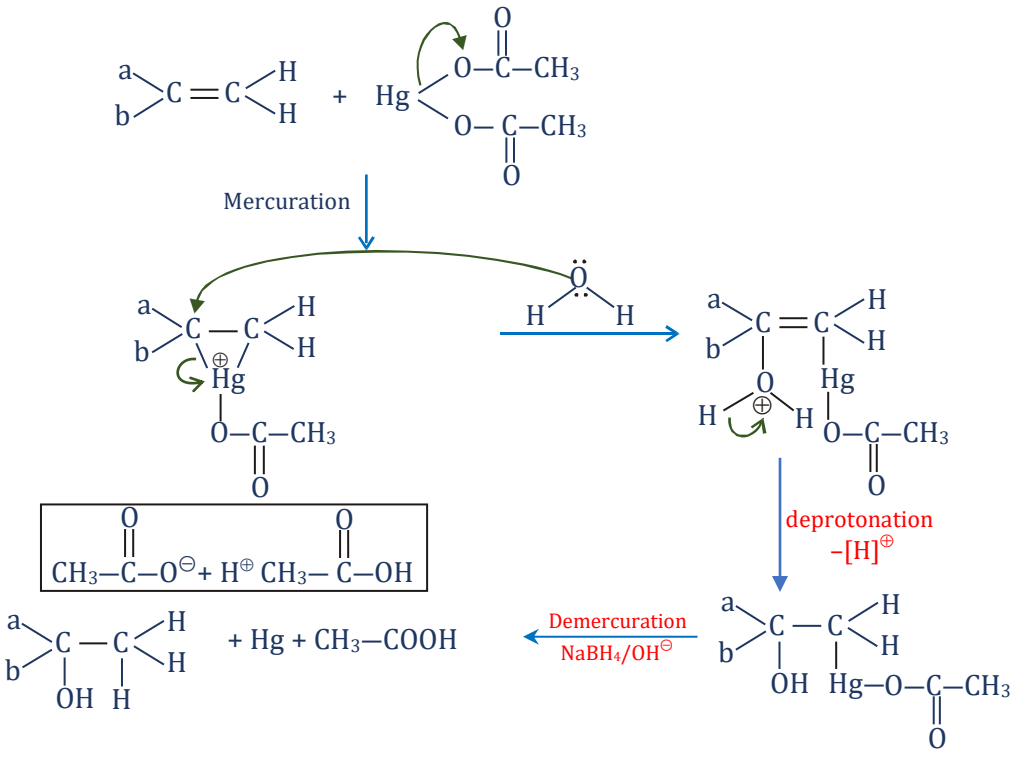


(ii) By oxymercuration demercuration of alkenes :

$$CH_3{-}CH{=}CH_2 \xrightarrow[(ii)\,NaBH_4,OH^{\ominus}]{(i)\,Hg(OAc)_2,H_2O} CH_3{-}\underset{\displaystyle OH}{\underset{|}{CH}}{-}CH_3$$

Mechanism

Take place by Markonikoff rule. No carbonium is formed during reaction hence no rearrangement takes place. Mercuration by $Hg(AcO)_2$ and demercuration by $NaBH_4/OH^{\ominus}$



If a = b = H ⇒ 1° alcohol

a = R b = H ⇒ 2° alcohol

a = R and b = R ⇒ 3° alcohol

(iii) By hydroboration oxidation of alkenes :

$$CH_3—CH=CH_2 \xrightarrow[(ii)H_2O_2/HO^{\ominus}]{(i)\ B_2H_6/THF} CH_3—CH_2—CH_2(OH)$$

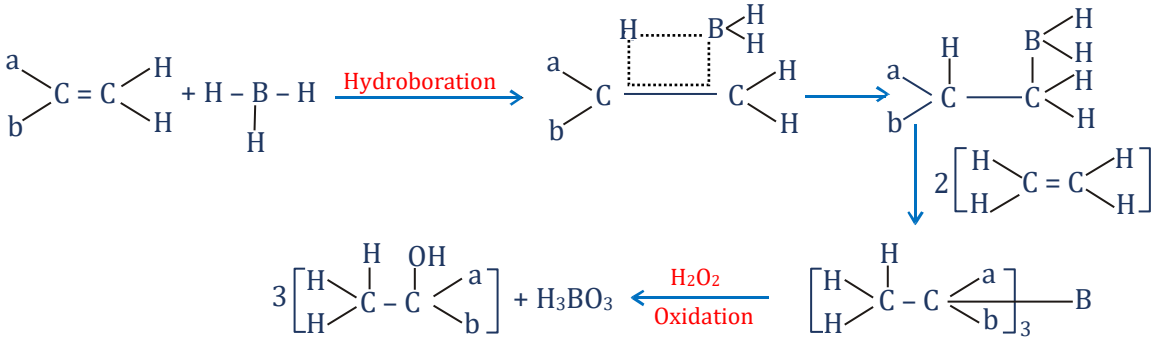
(1° alcohol)

Mechanism :

Takes place by Anti Markownikov Rule in presence of B_2H_6.

Firstly formed trialkyl borane by Cis cyclic addition which convert in alcohol by oxidation with $H_2O_2/OH^{\ominus}$

$B_2H_6 \rightarrow BH_3 + BH_3$



(iv) From carbonyl compounds (By reduction):

$$>C=O \xrightarrow{\text{Reducing agent}} >CH—OH$$

Reducing agents may be,

(a) $LiAlH_4$/protic solvent, $NaBH_4$/protic solvent

(b) Na + EtOH [Bouveault-blanc Reduction]

(c) Ni/H_2 etc.

$$R—CHO \xrightarrow[\text{protic solvent}]{LiAlH_4} R—CH_2—OH$$

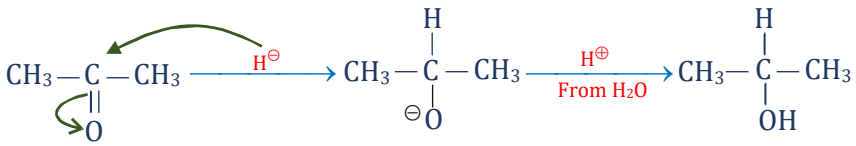
$$R—\underset{\underset{O}{\|}}{C}—R \xrightarrow[\text{protic solvent}]{NaBH_4} R—\underset{OH}{CH}—R$$

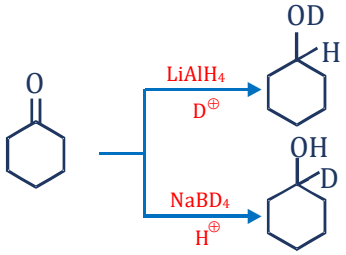
$$CH_3—\underset{\underset{O}{\|}}{C}—CH_3 \xrightarrow[\text{protic solvent}]{LiAlH_4} CH_3—\underset{OH}{CH}—CH_3$$

Mechanism :

$LiAlH_4 \rightarrow Li^+ + AlH_4^-$

$AlH_4^- \rightarrow AlH_3 + H^-$





$CH_3—CH=CH—CHO \xrightarrow[H^{\oplus}]{LiAlH_4} CH_3—CH=CH—CH_2—OH$

Crotonaldehyde

$Ph—CH=CH—CHO \xrightarrow[H^{\oplus}]{LiAlH_4} Ph—CH_2—CH_2—\ CH_2—OH$

Cinnamaldehyde

From acid and derivatives (By reduction):

$R—COOH \xrightarrow[H^{\oplus}]{LiAlH_4} R—CH_2—OH + H_2O$

$R—\underset{\underset{O}{\|}}{C}—Cl \xrightarrow[H^{\oplus}]{LiAlH_4} R—CH_2—OH + HCl$

$R—\underset{\underset{O}{\|}}{C}—OR \xrightarrow[H^{\oplus}]{LiAlH_4} R—CH_2—OH + R—OH$

$R—\underset{\underset{O}{\|}}{C}—O—\underset{\underset{O}{\|}}{C}—R \xrightarrow[H^{\oplus}]{LiAlH_4} R—CH_2—OH + R—CH_2—OH$

** $R—\underset{\underset{O}{\|}}{C}—NH_2 \xrightarrow[H^{\oplus}]{LiAlH_4} R—CH_2—NH_2 + H_2O$

NOTE : Amide gives amine (not alcohol) with $LiAlH_4$

(v) Synthesis of Alcohols using Grignard

There are following methods to obtain alcohols from Grignard reagent.

(i) From carbonyl compounds

$R - MgX + \diagup C=O \longrightarrow R—\underset{|}{\overset{|}{C}}—OMgX \xrightarrow{HOH} R—\underset{|}{\overset{|}{C}}—OH$ (alcohol)

This is nucleophilic addition reaction

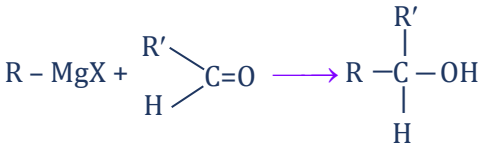
a. Primary (1°) Alcohols

Primary alcohols are formed on taking formaldehyde

$R - MgX + \begin{matrix} H \\ \diagup \\ H \end{matrix} C=O \longrightarrow R—\underset{H}{\overset{H}{C}}—OMgX \xrightarrow{HOH} R—\underset{H}{\overset{H}{C}}—OH$ (1° Alcohol)

b. Secondary (2°) alcohols :

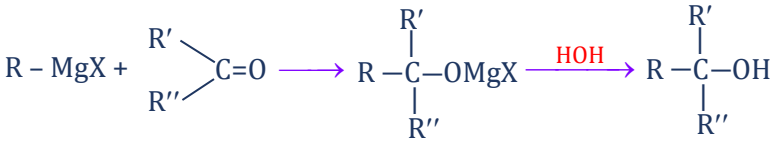
From RCHO Secondary alcohols are formed by the reaction of any aldehyde other than formaldehyde.



2° Alcohol

c. Tertiary (3°) alcohols

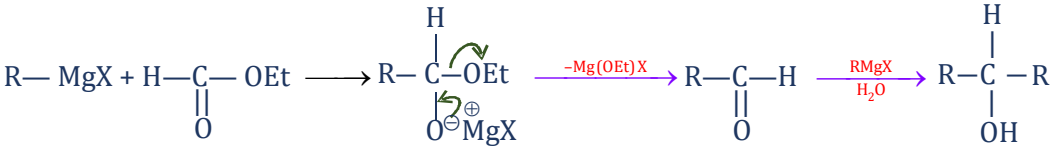
Tertiary alcohols are formed by taking any ketone



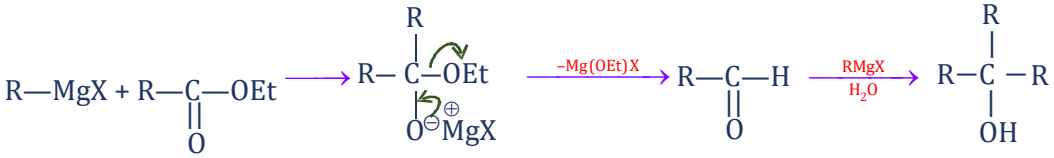
3° Alcohol

(ii) From Ester :

Secondary alcohols are obtained on hydrolysis of the product obtained by taking excess of Grignard reagent and adding formic ester to it.

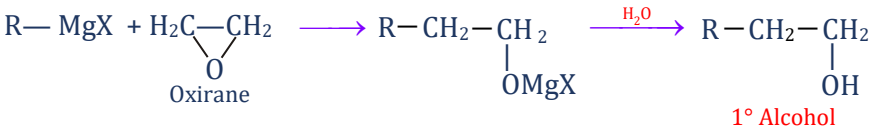


Tertiary alcohols are also obtained on hydrolysis of the product obtained by taking excess of Grignard reagent and an ester of a higher homologue of formic acid.



Various alcohols can be prepared by changing R in the above synthesis.

(iii) From Epoxides



Oxirane

1° Alcohol

(iv) From Oxygen

Synthesis of alcohol

$R - MgX + O = O \longrightarrow R - O - O - MgX$

$R - O - O - MgX + R - MgX \longrightarrow 2R - O - MgX$

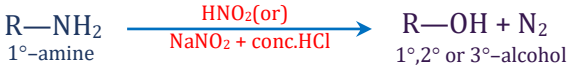
$R - O - MgX + HOH \longrightarrow R - O - H + Mg(OH)X$

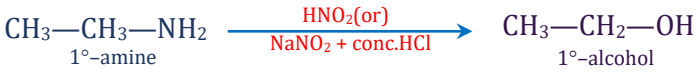
Primary, secondary and tertiary alcohols can be obtained by above reaction

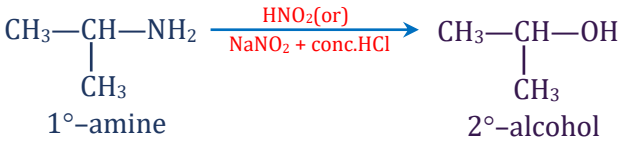
ADVANCE LEVEL ILLUSTRATIONS INVOLVING PREPARATION OF ALCOHOL

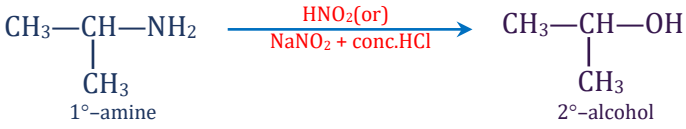
From aliphatic primary amines:

Primary amines react with nitrous acid to give alcohols





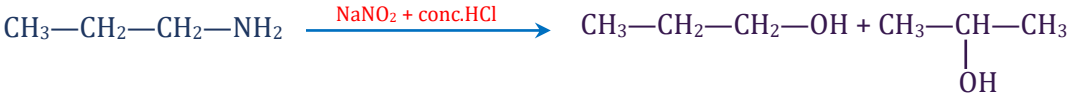




NOTE :

(1) Nature of alcohol depends on the nature of carbon having $-NH_2$ group.

(2) Reaction proceeds through carbocation hence rearrangement may take place and mixture of normal and rearranged alcohol is obtained, e.g.



(3) Methyl amine gives mixture of following four compounds:

(4) Other primary amines give alkenes, alkyl chloride and alkyl nitrite as minor by products.

Physical properties:

(i) C_1 to C_{11} are colourless liquids and higher alcohols are solids.

(ii) Density of monohydric alcohol is less than H_2O.

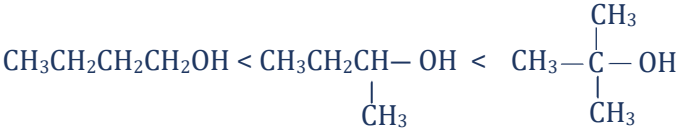
(iii) Density $\propto$ mol. wt. (for monohydric alcohol).

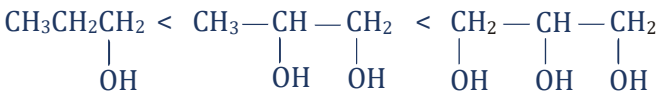
(iv) **Solubility :** C_1 to C_3 and t-butyl alcohol is completely soluble in H_2O due to H–bonding.

$$\text{solubility} \propto \text{No. of side chain} \propto \frac{1}{\text{Molecular weight}}$$

Order of solubility :

$C_4H_9OH > C_5H_{11}OH > C_6H_{13}OH$





[Number of —OH increases, H-bonding increases]

(v) **Boiling points :** B.P. $\propto$ molecular weight

If molecular wt. is same then B.P. $\propto \frac{1}{\text{branching}}$

Order of BP : $C_4H_9OH < C_5H_{11}OH < C_6H_{13}OH$

$CH_3CH_2CH_2CH_2OH > CH_3CH_2CH(CH_3)OH > CH_3C(CH_3)_2OH$

$CH_3CH_2CH_2OH < CH_3CH(OH)CH_2OH < CH_2(OH)CH(OH)CH_2OH$

[Number of OH increases, H-bonding increases]

Illustration 2 :

Boiling point of alcohol is more than corresponding ether. Why ?

Solution:

Reason : H-bonding in alcohol.

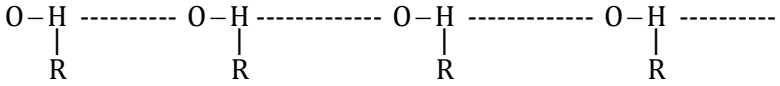


Illustration 3 :

Boiling point of alcohol is less than corresponding carboxylic acid. Why ?

Solution:

Reason : Dimer formation in carboxylic acid. 

KEY POINTS

1. Diols and triols have higher b.p's and are more water soluble
2. In Thiols, Hydrogen bonding is much weaker than that in alcohols.
3. Thiols have Lower boiling points than similar alcohols.
4. Thiols are much more acidic than similar alcohols

Chemical Reaction of alcohol:

The reaction of alcohols with HX (X=Cl, Br) is a general method to prepare primary, secondary and tertiary alkyl halide.

$CH_3—CH_2—OH \xrightarrow{HBr} CH_3CH_2Br + H_2O$

More substituted alcohols usually react more rapidly with HX.

Order of reactivity of alcohols with HX is **Tertiary > Secondary > Primary.**

Primary alcohols form R—X by S_N2 reaction while secondary and tertiary alcohols form R—X by S_N1 reaction.

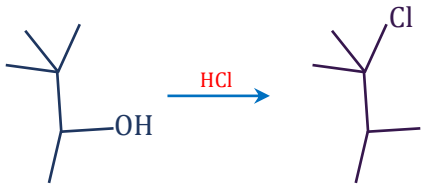
Because carbocation is formed in S_N1 reaction of secondary and tertiary alcohols with HX, carbocation rearrangement is also possible.

The reactivity of the hydrogen halide is HI > HBr > HCl (HF is generally unreactive) and the order of reactivity of alcohols is $3° > 2° > 1° > CH_3OH$.

The least reactive hydrogen halide i.e. HCl generally requires the presence of $ZnCl_2$ for reaction with 1° and 2° alcohols, however the highly reactive 3° alcohol do not require $ZnCl_2$.

$$CH_3—CH_2—\ CH_2—OH \xrightarrow[NaBr + H_2SO_4]{\text{dry HBr or}} CH_3—CH_2—CH_2—Br$$

Chloride ion is a weaker nucleophile than bromide and iodide ion. HCl does not react with less reactive 1°C and 2°C alcohol unless some good Lewis acid like $ZnCl_2$ is added to a reaction mixture. Primary alcohol being least reactive requires some heat in addition to $ZnCl_2$. Zinc chloride a good Lewis acid to form a complex with alcohol. This complex provides a better leaving group for the reaction than H_2O. But for primary alcohols, rearrangement of the alkyl group occurs.



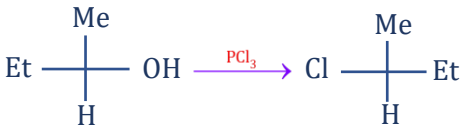
Reaction with phosphorous halides:

a. Reaction of alcohol with PCl_3

$$3R—OH + PCl_3 \longrightarrow 3RCl + H_3PO_3$$

NOTE : Reaction follow S_N2 path, thus inversion product can be obtained.

EX.

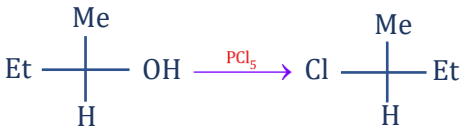


b. Reaction of alcohol with PCl_5

$$R—OH + PCl_5 \longrightarrow R—Cl + POCl_3 + HCl$$

NOTE : Reaction follow S_N2 path, thus inversion product can be obtained.

EX.



Esterification reaction :

Treatment of a carboxylic acids with an alcohol in presence of an acid catalyst forms an ester. This reaction is called a Fischer esterification.

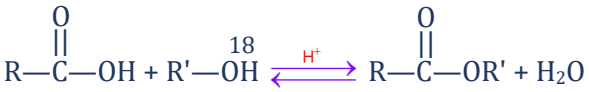
$$R—COOH + R'—OH \underset{}{\overset{H_2SO_4}{\rightleftharpoons}} RCOOR' + H_2O$$

This reaction is an equilibrium. According to Lechatilier's principle, it is driven to the right excess of alcohol or by removing the water is it is formed.

NOTE :

Esterification of a carboxylic acids occur in the presence of acid but not in the presence of base. Base removes a proton from the carboxylic acids forming a carboxylate anion, which do not react with an electron rich nucleophile.

Advance concept of Esterification:



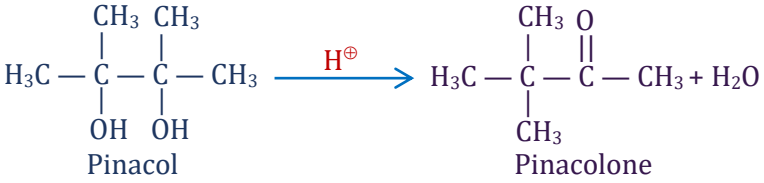
Pinacol-Pinacolone Rearrangement :

Pinacol is a compound which has two hydroxyl groups, each attached to a vicinal carbon atom. It is a solid organic compound which is white.

The IUPAC name of pinacolone is 3, 3-dimethyl-2-butanone. It has a peppermint like or camphor like odour and appear as to be a colourless liquid.

The pinacol pinacolone rearrangement proceeds through the formation of an intermediate which is positively charged. The methyl group in this intermediate proceeds to migrate from one carbon to another.

This reaction can be given by



Pinacol pinacolone rearrangement Mechanism

The pinacol pinacolone rearrangement mechanism proceeds via four steps.

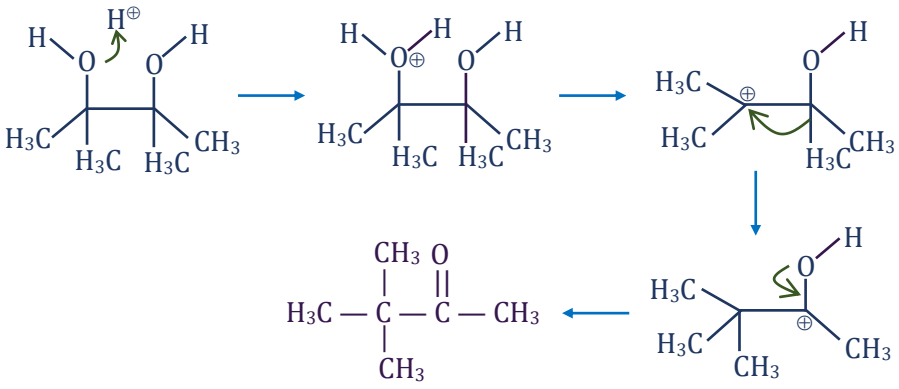
Step : 1 Since the reaction is carried out in an acidic medium, the hydroxide group of the pinacol is protonated by the acid.

Step : 2 Water is now removed from the compound, leaving behind a carbocation. This carbocation is tertiary.

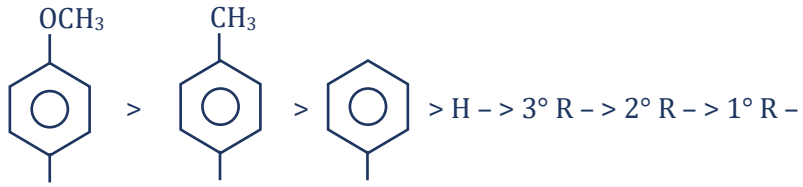
Step -3 : The methyl group shifts to the positively charged carbon in a rearrangement of the compound.

Step – 4 : The oxygen atom which is doubly bounded to the carbon is now deprotonated, giving rise to the required pinacolone.

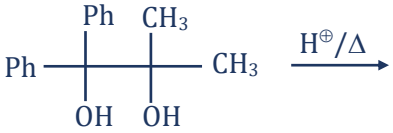
This reaction mechanism can be illustrated as



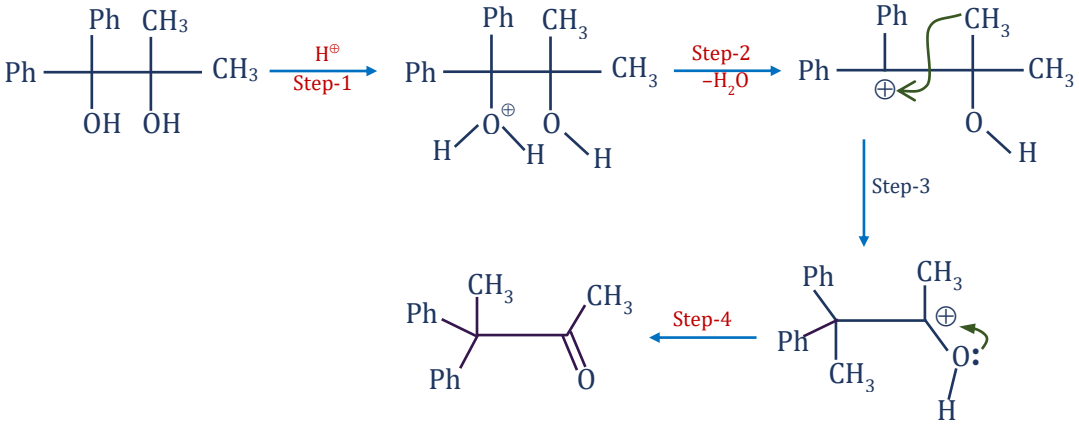
Migration ability orders



Example :-

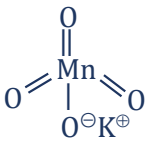


Solution:



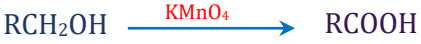
Oxidation of alcohols :

(a) Oxidation of alcohol by $KMnO_4$:

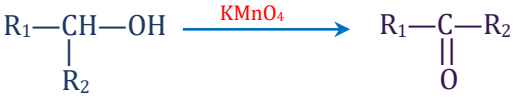


1. $KMnO_4$ is a very strong oxidising agent.
2. It never depends upon the type of medium used.

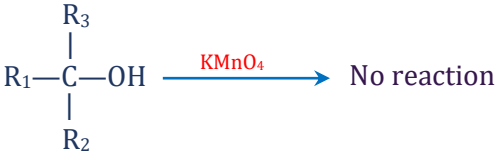
i. Primary alcohol



ii. Secondary alcohol



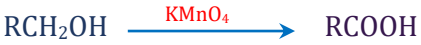
iii. Tertiary alcohol



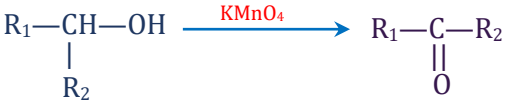
(b) Oxidation of alcohol by (CrO_3 + H_2SO_4) :

1. (CrO_3 + H_2SO_4) is called of Jones reagent.
2. It is strong oxidising agent.

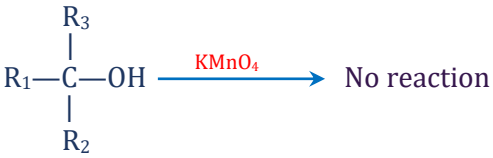
i. Primary alcohol



ii. Secondary alcohol



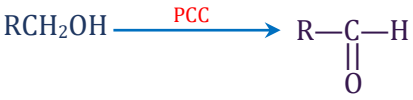
iii. Tertiary alcohol



(c) Oxidation of alcohol by PCC (Pyridinium chloro chromate) :

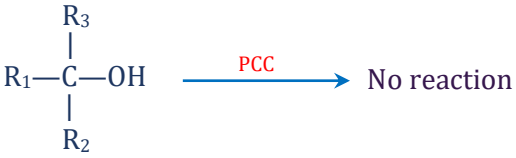
1. It is milder oxidising agent.
2. It is efficient reagent to produce aldehydes/ketones from primary/secondary alcohols.

i. Primary alcohol



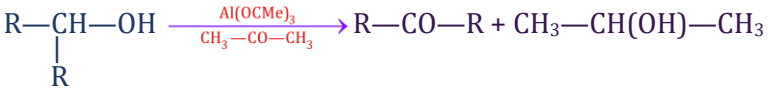
ii. Secondary alcohol

iii. Tertiary alcohol



(d) Oppenaur oxidation

The reaction involves the oxidation of secondary alcohols with a ketone and a base to the corresponding ketone of the alcohol.



Two structural requirements for the oxidation to carbonyl products are

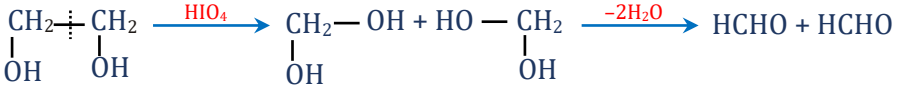
i. The carbon atom bonded to oxygen must also bear a hydrogen atom. Tertiary alcohols (R_3C—OH) cannot be oxidized in this fashion.

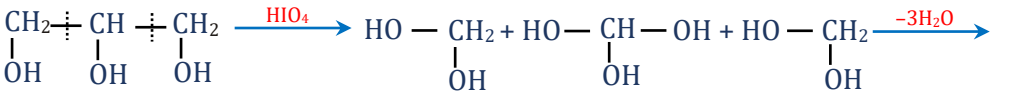
ii. The oxygen atom must be bonded to a hydrogen atom so that a chromate ester intermediate (or other suitable leaving group) may be formed. Ethers (R—O—R) cannot be oxidized in this fashion.

(e) Oxidation by HIO_4 [per iodic acid] :

When diols reacts with HIO_4 [Periodic acid]. Those diols/ Polyols in which –OH group attached to vicinal C-atom after reaction with HIO_4 forms aldehyde and ketone.

This reaction is also used in identification of no. of OH group in polyol.

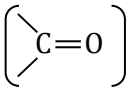
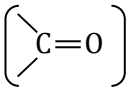




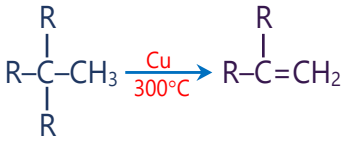
(Glycerol)

$HCHO + HCOOH + HCHO$

Condition for oxidation by HIO_4 :

At least 2 —OH or 2  or 1—OH and 1  should be at adjacent carbons.

Test for alcohols:

Test	Primary alcohol	Secondary alcohol	Tertiary alcohol
Luca's reagent Testing with a mixture of conc. HCl and anhyd. $ZnCl_2$	Does not from turbidity at room temperature (turbidity is obtained only upon heating)	Turbidity formed in 5 to 10 minutes	Turbidity is formed immediately
Catalytic dehydrogenation (Vapours of alcohol are passed over hot metal)	$RCH_2OH \xrightarrow[300°C]{Cu} RCHO$ An aldehyde is obtained	$RCHOHR \xrightarrow[300°C]{Cu} RCOR$ A ketone is obtained	 An alkene is obtained
Oxidation (with acidified permanganate or dichromate solution)	RCH_2OH ↓ RCHO ↓ RCOOH	RCHOHR ↓ RCOR ↓ Two acids	R_3COH ↓ RCOR ↓ Two acids

	(same number of carbon atoms in the three compounds)	(with less number of carbon atoms)	(with less number of carbon atoms under drastic conditions)
Victor Meyer test Alcohol ↓ HI Alkyl iodide ↓ $AgNO_2$ Nitro compounds ↓ (i) HNO_2 ↓ (ii) NaOH	Nitrolic acid gives red colour RCH_2OH ↓ HI RCH_2I ↓ $AgNO_2$ RCH_2NO_2 ↓ HNO_2 $R-\underset{\underset{NO}{|}}{C}-NO_2$ $R-\underset{\underset{NOH}{||}}{C}-NO_2$ ↓ NaOH $R-\underset{\underset{\overset{-}{N}O\overset{+}{N}a}{||}}{C}-NO_2$ Red colour	Pseudonitrol gives blue colour R_2CHOH ↓ HI R_2CHI ↓ $AgNO_2$ R_2CHNO_2 ↓ HNO_2 $R_2\underset{\underset{NO}{|}}{C}-NO_2$ ↓ NaOH Blue colour	No colour is obtained R_3COH ↓ HI R_2CI ↓ $AgNO_2$ R_2CNO_2 ↓ HNO_2, NaOH No reaction

(1) Lucas test : A mixture of HCl(conc.) and anhydrous $ZnCl_2$ is called Lucas reagent.

Primary alcohol $\xrightarrow{ZnCl_2 + HCl}$ No turbidity at room temp. [On heating within 30 minutes.]

Secondary alcohol $\xrightarrow{ZnCl_2 + HCl}$ Turbidity appears within 5 minutes.

Tertiary alcohol $\xrightarrow{ZnCl_2 + HCl}$ Turbidity appears within 1 minute.

This test is used to differentiate 1°, 2° and 3° alcohols,

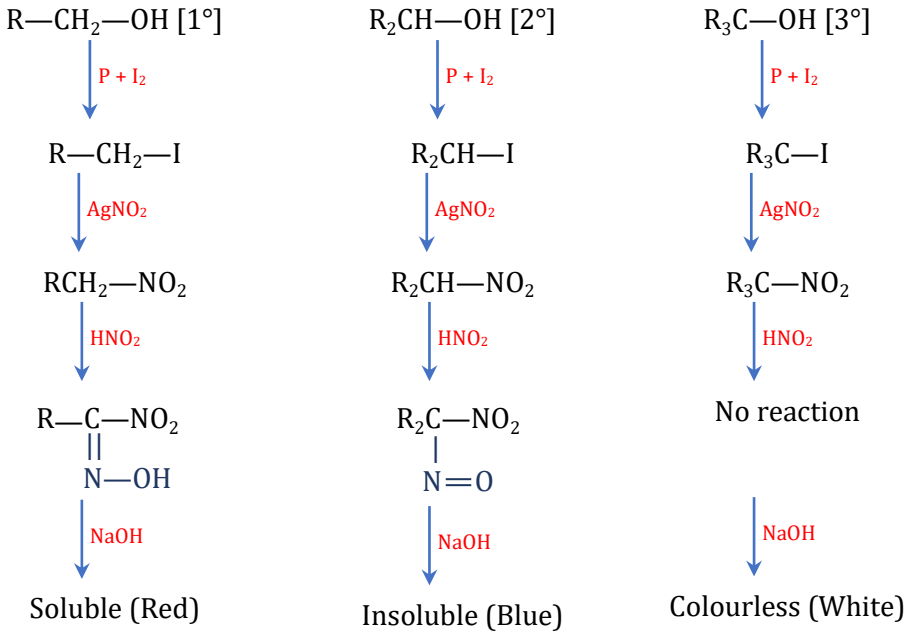
(2) Victor - Meyer test : This is colour test for alcohol (primary, secondary & tertiary) .

Primary alcohol ⟶ Red colour

Secondary alcohol ⟶ Blue colour

Tertiary alcohol ⟶ No colour

This test is used to differentiate 1°, 2° and 3° alcohols,



(3) Dichromate test:

1° Alcohol $\xrightarrow[\text{orange}[Cr^{+6}]]{H^{\oplus}/K_2Cr_2O_7}$ Acid + Cr^{+3} [green]

2° Alcohol $\xrightarrow[\text{orange}[Cr^{+6}]]{H^{\oplus}/K_2Cr_2O_7}$ Ketone + Cr^{+3} [green]

3° Alcohol $\xrightarrow[\text{orange}[Cr^{+6}]]{H^{\oplus}/K_2Cr_2O_7}$ No oxidation, No green

3° Alcohol $\xrightarrow[\text{orange}[Cr^{+6}]]{H^{\oplus}/K_2Cr_2O_7}$ No oxidation, No green

(4) Ceric Ammonium Nitrate test:

Alcohol on reaction with ceric ammonium nitrate forms a pink or red colour precipitate due to the formation of a complex compound and ammonium nitrate.

The chemical reaction is given below :

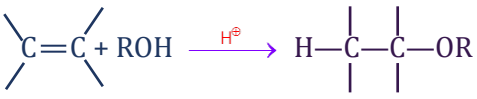
$(NH_4)_2[Ce(NO_3)_6] + 3ROH \longrightarrow [Ce(NO_3)_4(ROH)_3] + 2NH_4NO_3$

$(NH_4)_2[Ce(NO_3)_6] + 3CH_3OH \longrightarrow [Ce(NO_3)_4(CH_3OH)_3] + 2NH_4NO_3$

Note : The appearance of wine red colour precipitate shows the presence of alcoholic group.

Preparation of ethers from hydro carbon :

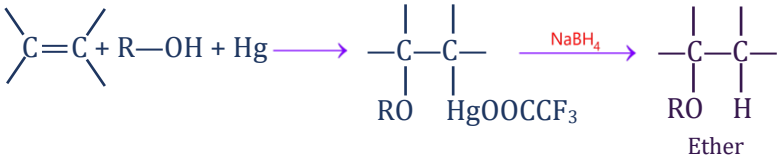
(A) Addition of alcohols to alkenes

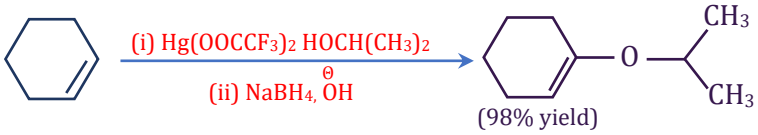


Ex. $H_2C{=}CH_2 + EtOH \xrightarrow{H^{\oplus}} Et{-}O{-}Et$

(B) Alkoxy mercuration demercuration :

Alkoxy mercuration demercuration is another method for synthesising ethers. The reaction of an alkene with an alcohol in the presence of mercury salts such as mercuric acetate or trifluoro acetate leads to an alkoxy mercuric intermediate which upon reaction with sodium borohydride yields an ether.



Ex. 

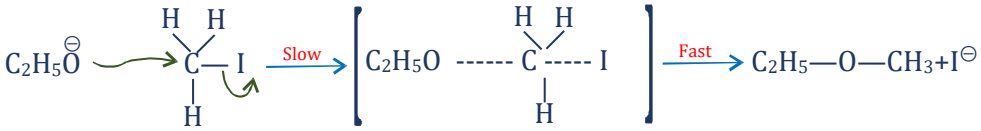
Ex. $H_2C{=}CH_2 + EtOH \xrightarrow{H^{\oplus}} Et{-}O{-}Et$

Preparations of open chain ether by Williamson's synthesis :

$R{-}X + Na{-}O{-}R \longrightarrow R{-}O{-}R + NaX$ [Reaction]

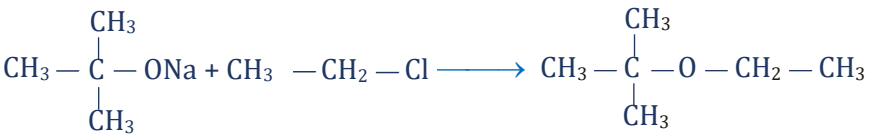
Ex. $CH_3{-}I + C_2H_5O\text{-}Na^{+} \longrightarrow CH_3{-}CH_2{-}O{-}CH_3 + NaI$

Mechanism : [S_N2 Reaction]



$Na^{\oplus} + I^{\ominus} \longrightarrow NaI$

Ex. 

Ex. 

Ex. $CH_2 = CH{-}Cl + CH_3CH_2{-}ONa \longrightarrow$ No reaction

By dehydration of alcohols:

Alcohols undergo dehydration in the presence of protic acids (H_2SO_4, H_3PO_4). The formation of product alkene or ether depends on the reaction conditions.

Ethanol is dehydrated to ethene in the presence of sulphuric acid at 443 K and at 413 K ethoxyethane is the main product

$$C_2H_5OH + HOC_2H_5 \xrightarrow[413\ K]{Conc.H_2SO_4} C_2H_5OC_2H_5 + H_2O$$

$$C_2H_5OH \xrightarrow[443\ K]{H_2SO_4} CH_2 = CH_2$$

The catalytic dehydration of ethanol with Al_2O_3 at 250 – 260°C also gives diethyl ether

$$2C_2H_5OH \xrightarrow[260°C]{Al_2O_3} C_2H_5OC_2H_5 + H_2O$$

The formation of ether is a nucleophilic bimolecular substitution reaction (S_N2) involving the attack of alcohol molecule on a protonated alcohol, as indicated below :

Step-i $CH_3—CH_2—O—H + H^+ \longrightarrow CH_3—CH_2—\overset{\oplus}{O}\begin{matrix}H\\H\end{matrix}$

Step-ii $CH_3CH_2—OH + CH_3—CH_2—\overset{\oplus}{O}\begin{matrix}H\\H\end{matrix} \longrightarrow CH_3CH_2\overset{\oplus}{O}CH_2CH_3$ (H)

Step-iii $CH_3CH_2\overset{\oplus}{O}CH_2CH_3$ (H) $\longrightarrow CH_3CH_2—O—CH_2CH_3 + H^{\oplus}$

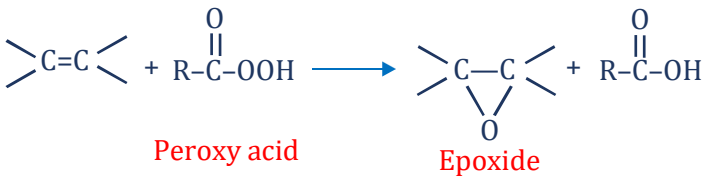
Above method is suitable for the preparation of ethers having primary alkyl groups only and alkyl group should be un hindered, temperature be kept low.

If alcohol is secondary or tertiary, elimination competes over substitution, which forms alkene.

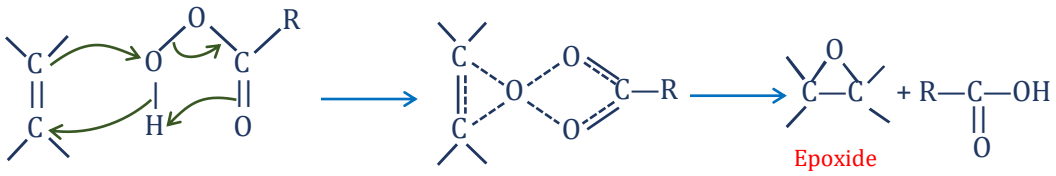
Ethers having different alkyl groups are never prepared by this method, as a mixture of different ethers are formed.

$$R—OH + R'—OH \xrightarrow{Conc.H_4SO_4} R—O—R + R'—O—R' + R—O—R'$$

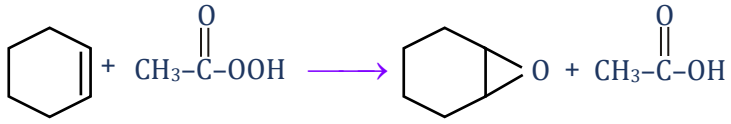
Epoxidation of alkenes by reaction with peroxy acids:



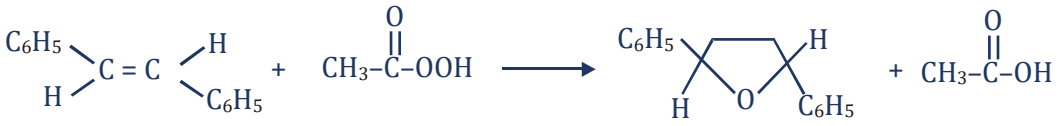
Mechanism:



Ex. $CH_2= CH-(CH_2)_9CH_3 + CH_3-\overset{O}{\overset{\|}{C}}-OOH \longrightarrow CH_2-CH-(CH_2)_9CH_3 + CH_3-\overset{O}{\overset{\|}{C}}-OH$



NOTE: Epoxidation is a stereospecific syn addition :



(E) -1,2-diphenyl ethene

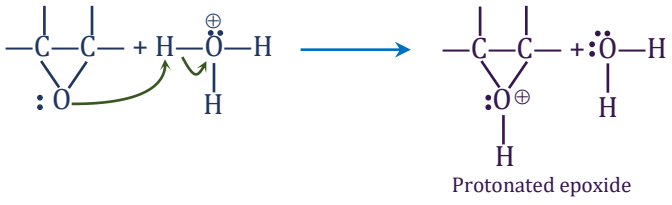
trans -2,3-diphenyl oxirane

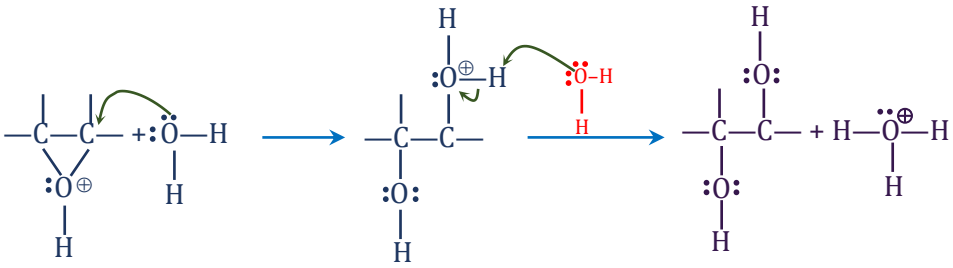
Reaction of Epoxides:

The highly strained three membered ring molecules of epoxides make them much more reactive towards nucleophilic substitution than other ethers.

(i) Acid catalysed ring opening of Epoxide:

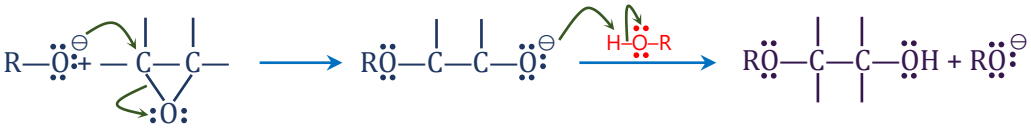
Acid catalysis assists epoxide ring opening by providing a better leaving group at the carbon atom undergoing nucleophilic attack



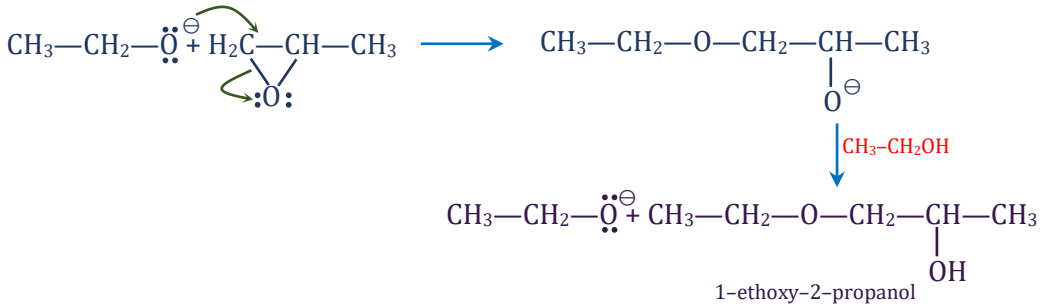


(ii) Base catalysed ring opening of Epoxide:

Epoxides can also undergo base catalysed ring opening such reactions do not occur with other ethers provided that the attacking nucleophile is also a strong base such as alkoxide ion or hydroxide ion.



If the epoxide is unsymmetrical, in base catalysed ring opening attack by the alkoxide ions occurs primarily at the less substituted carbon atom.

Ex. 

Reaction involving cleavage of C–O bond in Ethers:

(a) Ethers are almost as inert as alkanes. Under ordinary conditions, they are stable to dilute acids, bases, catalytic hydrogenation, as well as to most other reducing agents because the functional group $\left(-\ddot{O}-\right)$ does not have any active site as compared to (—OH) groups of alcohols and phenols even though O atom in both these functional groups has 2 LP of $\bar{e}$'s.

The cleavage of (C—O) bond in ethers takes place under drastic conditions with excess of HX, i.e., with conc. HI or HBr at high temperature (373K).

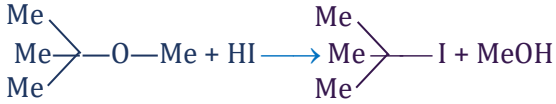
$$R—O—R + HX \longrightarrow RX + ROH \xrightarrow{HX} R — X + H_2O$$

(b) Alkyl are ethers are cleaved at the $(R \overset{\vdots}{-} O)$ bond because (Ar — O) bond is more stable, for example,

$$Ph—\underset{H}{O}\overset{\vdots}{-}\underset{X}{R} + H—X \longrightarrow PhOH + R — X$$

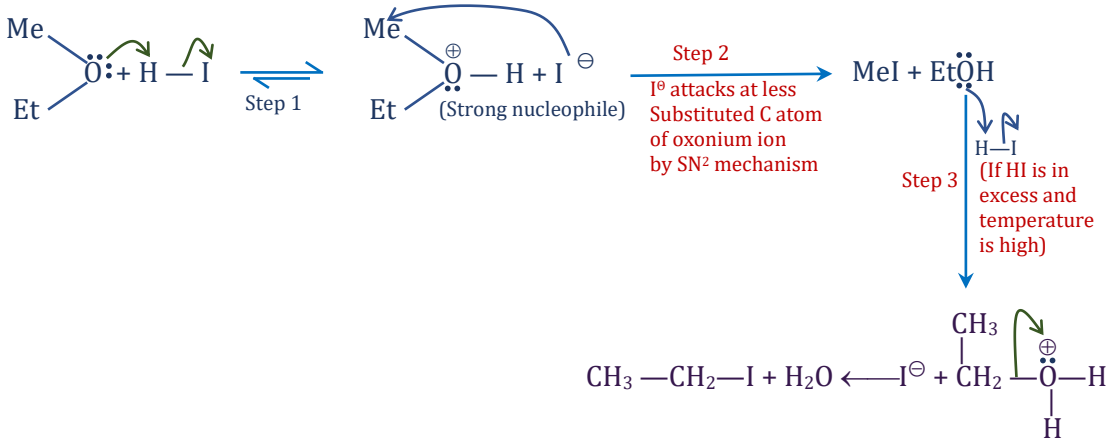
(c) When ethers with two different 1° alkyl groups are cleaved, the halide formed is with smaller alkyl group. When one of the (R—) group is 3°, the halide formed is 3° RI, for example

i. $Me — O — Et + HI \longrightarrow MeI + EtOH$

ii. 

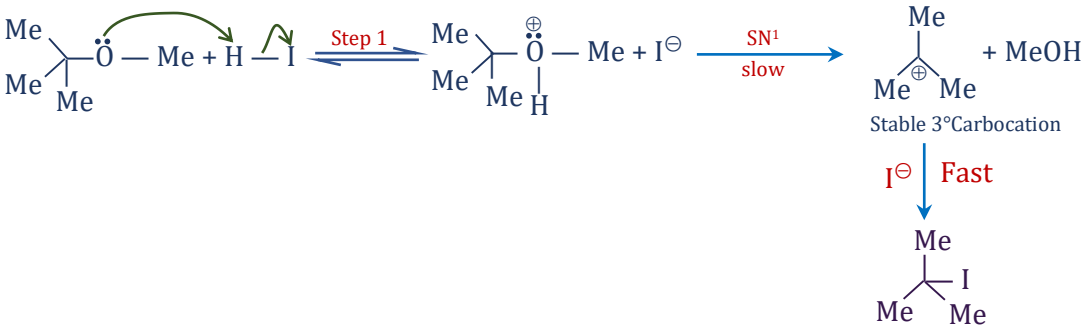
Mechanism (When both alkyl groups are 1°, The Halide formed is with Smaller Alkyl group)

The cleavage of ethers takes place with conc. HI or HBr because these reagents are sufficiently acidic.



Mechanism when one of the Alkyl groups is 3°

The halide formed is 3° RI because in step 2 of the reaction, the departure of leaving group (CH_3 — OH) Produces more stable 3° $C^{\oplus}$ and the reaction follows S_N1 mechanism, for example,



In case of aryl ether, RI and ArOH are formed.

In case of benzyl ether, $PhCH_2I$ and ROH are formed.

i. $Ph—O—Me + HI \longrightarrow MeI + PhOH$
Anisole

ii. $PhCH_2—O—Me + HI \longrightarrow PhCH_2I + MeOH \xrightarrow[\text{High temp.}]{\text{Excess of HI}} MeI + H_2O$
Benzyl methyl ether

iii. $O_2N-C_6H_4-O—Me + HI \longrightarrow MeI + O_2N-C_6H_4-OH \xrightarrow{\text{Excess of HI}} O_2N-C_6H_4-I + H_2O$

Mechanism in case of Anisole

Methyl phenyloxonium ion (Ph — $\overset{\oplus}{O}$(H) —Me) is formed by protonation of ether with HI. The (Me — O) bond is weaker than (Ph —O) bond because the (C—) of phenyl group is sp^2 – hybridised and there is partial double character due to resonance. Therefore, $I^{\ominus}$ attacks Methyl group and breaks (Me — O) bond to form MeI and PhOH. Phenols do not react further with HI to form PhI because the sp2-hybridised (C—) of phenol does not undergo ArSN reaction unless it is activated by EWG (e.g., (NO_2) group.

i. $Ph-\overset{\oplus}{O}(H)-Me + I^{\ominus} \xrightarrow[\text{Step 2}]{SN^2} PhOH + MeI$

ii. $O_2N-C_6H_4-\overset{\oplus}{O}(H)-Me + I^{\ominus} \xrightarrow[\text{Step 2}]{SN^2} O_2N-C_6H_4-OH + MeI$

iii. In case of benzyl methyl ether, benzyl methyl oxonium ion (Ph —CH_2 — $\overset{\oplus}{O}$(H) —Me) is formed protonation of ether with HI. In step 2 of the reaction, the departure of leaving group (Me —OH) produces more stable benzyl carbonium ion $\left(Ph\overset{\oplus}{C}H_2\right)$ and the reaction follows S_NI mechanism, e.g.,

$$PhCH_2-\ddot{O}-Me + H-I \rightleftharpoons PhCH_2-\overset{\oplus}{O}(H)-Me + H-I^{\ominus} \xrightarrow[\text{Slow}]{S_N1} Ph\overset{\oplus}{C}H_2 + MeOH \xrightarrow{I^{\ominus}} PhCH_2I$$

Reaction of Ether by Aqueous HI and Anhydrous HI

t-Buty methyl ether with aqueous or conc. HI undergoes cleavage by S_NI mechanism and with anhydrous HI/ether, cleavage takes place by S_N2 mechanism, e.g.,

$$Me_3C-\ddot{O}-Me \xrightarrow[H^{\oplus}I^{\ominus}\ \text{Ether}]{\text{anhydrous}} Me_3C-\overset{\oplus}{O}(H)-Me + I^{\ominus} \xrightarrow{SN^2} Me_3C-OH + MeI$$

(Reaction I)

(Reaction 2) aq $H^{\oplus}I^{\ominus}$

$$Me_3C-\overset{\oplus}{O}(H)-Me \xrightarrow{SN^1} Me_3C^{\oplus} + MeOH \xrightarrow{I^{\ominus}} Me_3C-I$$

(CO) bond cleavage by $H_3O^{\oplus}$

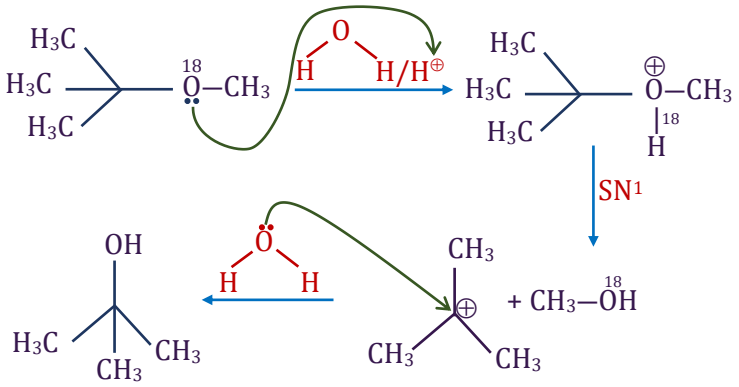
$$R-O-R' \xrightarrow[\text{Or Dil . } H_2SO_4 \text{ or } H_3O^{\oplus}]{H^{\oplus}/H_2O} R-OH + R'-OH$$

(A)

Case (I)	Case (II)
R and R'	R and R'
3° 3°	3° 3°
or 3° 2°	or 2° 3°
or 3° 1°	or 1° 3°
or 2° 2°	or 2° 2°
or 2° 1°	or 1° 2°

In all above cases cleavage of open chain ether follow S_N1 pathway.

Ex.



(B) If R and R'

1° 1°

then in such case cleavage of open chain ether follow SN^2 pathway.

Ex. $CH_3-O-CH_3 \xrightarrow{H^{\oplus}/H_2O} CH_3-\overset{\overset{H}{|}}{\underset{\oplus}{O}}-CH_3 \xrightarrow[H_2O:]{SN^2} 2CH_3OH$