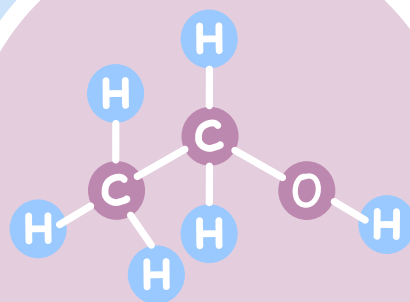
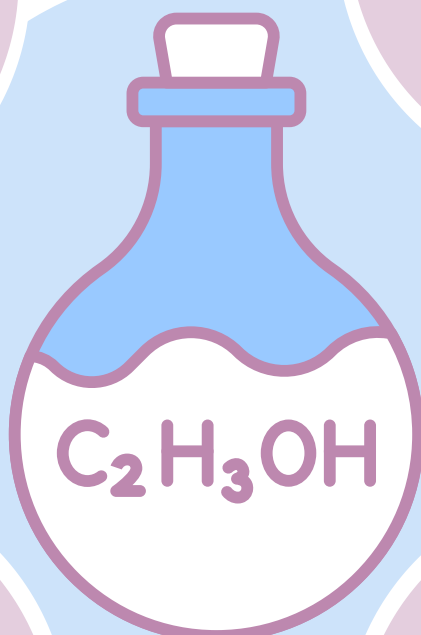
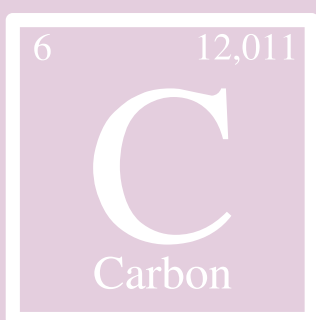


ALCOHOLS, PHENOLS, ETHER

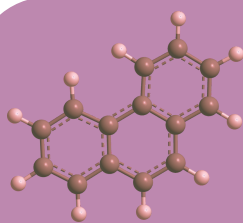


The Vision

behind PreMed Notes



PreMed.PK is on a mission to provide the most authentic and up-to-date MDCAT resources to the aspiring medical students of Pakistan. These Revision Notes have been specifically designed by toppers to make learning all the difficult content of the MDCAT super easy and effective for our students. Have fun learning with PreMed.PK!



NOTES ALCOHOLS, PHENOLS, ETHER

ALCOHOLS:

Hydroxyl derivatives of alkane, alkene or cycloalkane.

C attached to OH group is alpha carbon, also called alcoholic carbon.

Hybridization of C is sp^3 , or can be sp^2 if present in cycle.

If the chain is having double bonds then they are termed as Alkenols.

They can be mono-hydric, di-hydric or polyhydric according to the number of OH groups attached.

MONOHYDRIC ALCOHOL:

The alcohols which have only one OH group attached are termed as monohydric alcohol.

They are classified into Primary, Secondary and Tertiary depending upon the number of Carbon attached to alcoholic Carbon.

Primary Alcohol: When OH group is attached to Primary Carbon then it is termed as primary alcohol.

Secondary alcohol: When OH group is attached to secondary carbon then it is termed as secondary alcohol.

Tertiary alcohol: When OH group is attached to tertiary carbon then it is termed as tertiary alcohol.

DIHYDRIC ALCOHOLS (GLYCOLS)

Alcohols with two hydroxyl groups. Examples include ethylene glycol ($HO-CH_2-CH_2-OH$).

POLYHYDRIC ALCOHOLS

Alcohols with more than two hydroxyl groups.

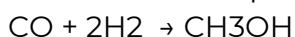
Examples include glycerol ($HO-CH_2-CH(OH)-CH_2-OH$).

Hydroxyl derivatives of alkanes, alkenes, and cycloalkanes, known as alcohols, are classified based on the carbon structure to which the hydroxyl group is attached. They can be mono-hydric, di-hydric, or polyhydric depending on the number of hydroxyl groups. Monohydric alcohols are further categorized into primary, secondary, and tertiary alcohols based on the type of carbon to which the hydroxyl group is bonded. Understanding these classifications helps in predicting the physical and chemical behavior of alcohols.

PREPARATION OF ALCOHOL

By methanol:

Alcohols can be prepared by methanol/ methyl alcohol/ carbinol/ wood spirit.

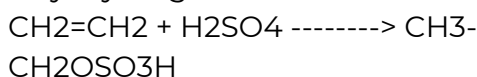


(ZnO + Cr₂O₃/450C, 200 atm)

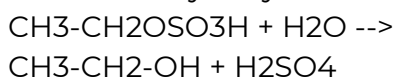
Hydration of Alkenes.

Alcohols can be prepared by adding water to alkenes, which is carried out in two steps:

Preparation of alkyl hydrogen sulfate : Alkene are dissolved in concentrated H₂SO₄ to form alkyl hydrogen sulfate.



Hydrolysis of alkyl hydrogen sulfate: On dilution with water and heating of alkyl hydrogen sulfate are hydrolyzed to alcohol.



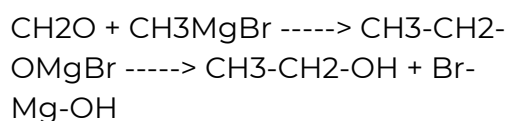
Hydrolysis of alkyl halides:

When alkyl halides are mixed with water they form alcohols
 $\text{R-X} + \text{H-OH} \rightarrow \text{R-OH} + \text{HX}$
 Water or OH acts as Nucleophile. The mechanism is called single Nucleophilic substitution

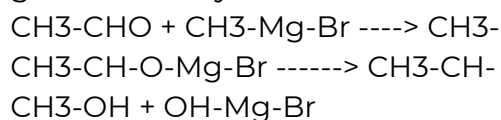
Reaction of RMgX with aldehydes and Ketones:

When Grignard reagents reacts with aldehydes or ketones it gives primary, secondary or tertiary alcohols. The process is hydrolysis.

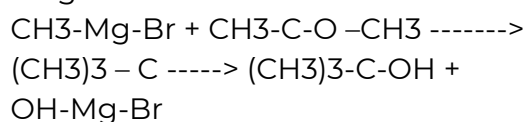
Primary alcohol formation: Formaldehyde when reacts with Grignard reagent it gives primary alcohol.



Secondary alcohol: Except formaldehyde all other aldehydes give secondary alcohol.



Tertiary alcohol: They are formed when ketones reacts with grignard reagent



From Ethanol:

Alcohol can be prepared from ethanol/ C₂H₅OH/ spirit of wine/ green alcohol/ ethyl alcohol.

By process of fermentation.

This is biochemical process, ferver means to boil

Occurs in presence of enzyme secreted by yeast

It is anaerobic process

Necessary condition for fermentation are:

Proper aeration, if excess air given then oxidation occurs.

Solution should be diluted, if concentrated then enzymes won't work

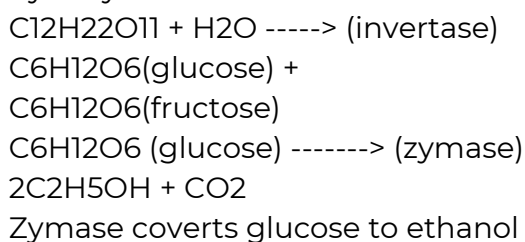
Temperature should be (25C-35C), fermentation is fast at this temperature

Absence of preservatives, because preservatives kill yeast

NOTES

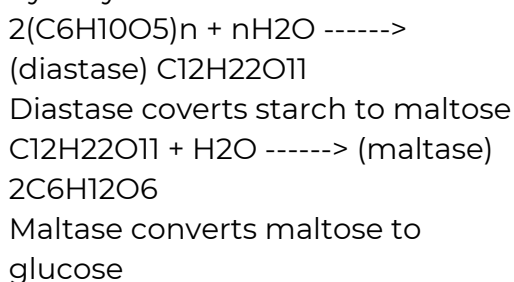
From Molasses:

Alcohol can be formed from hydrolysis of molasses.



From Starch:

Alcohol can be prepared from hydrolysis of starch.

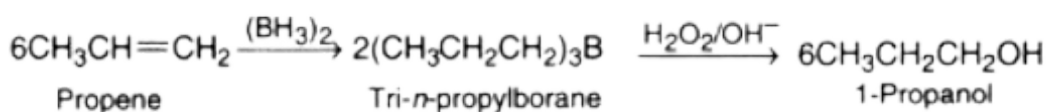
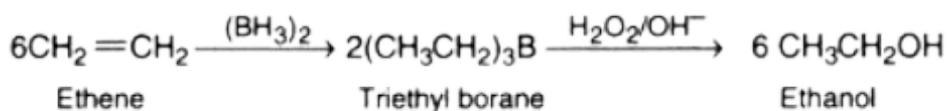


From reduction of aldehydes and ketones:

Reduction of carbonyl compounds in presence of Ni, Pd, or Pt gives alcohol
 $COOR \xrightarrow{(H^+)} R-CHOH-R$
LiAlH₄ reduces carboxylic acids too

Reaction of MgX with esters:

Esters reacts with grignard reagent to gives aldehydes.
Aldehyde reacts with grignard reagent to give alcohol
Esters gives secondary and tertiary alcohols when reacted with grgnard reagent
 $CH_3-Mg-Br + HCOOC_2H_5 \xrightarrow{\quad} CH_3-O-CH + OC_2H_5-Mg-Br \xrightarrow{\quad} C_2H_5OH + Br-Mg-OH$



REACTIVITY OF ALCOHOL

- Reactions of alcohol depends on breaking of OH and CO bonds and breaking of these bonds depends of nature of attacking reagent.

BREAKING OF O-H BONDS:	Breaking of C-O bonds:
If a Nu ⁻ attacks then C-O bonds breaks and carbocation is formed	If a electrophile attacks then O-H bonds breaks and alkoxide is formed
Nu ⁻ substitution reaction	Electrophile substitution reaction
$\text{CH}_3\text{-CH}_2\text{-OH} \text{ ----> } \text{CH}_3\text{-CH}_2^+ + \text{OH}^-$	$\text{CH}_3\text{-CH}_2\text{-OH} \text{ -----> } \text{CH}_3\text{-CH}_2\text{-O}^- + \text{H}^+$
Order of reactivity: ter: alcohol > secondary alcohol > primary alcohol	Order of reactivity: CH_3OH > pri: alcohol > sec: alcohol > Ter: alcohol

Esterification:

Formation of ester

During esterification, O-H bonds breaks of ethanol.

During this process, CH_3OH gives fastest reaction

Acid + alcohol -----> (H⁺) ester + H₂O

$\text{CH}_3\text{-COOH} + \text{C}_2\text{H}_5\text{OH} \rightleftharpoons \text{CH}_3\text{-COO-C}_2\text{H}_5 + \text{H}_2\text{O}$

Oxidation:

Alcohol can be oxidized by $\text{KMnO}_4/\text{K}_2\text{Cr}_2\text{O}_7 + \text{H}_2\text{SO}_4$.

Oxidation means addition of Oxygen, Loss of electron, removal of H₂.

Primary alcohol: primary alcohol is first oxidized to aldehyde and then to carboxylic acid

$\text{CH}_3\text{-CH}_2\text{-OH} + [\text{O}] \text{ -----> } \text{CH}_3\text{-COH}$

Secondary alcohol: secondary alcohol is oxidized to ketone which is not further oxidized

$2(\text{CH}_2)\text{-CH-OH} + [\text{O}] \text{ -----> } \text{CH}_3\text{-CO-CH}_3$

Tertiary alcohol: tertiary alcohol are resistant to oxidation

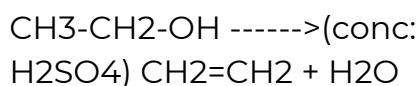
$3(\text{CH}_3)\text{-C-OH} \text{ -----> } 2(\text{CH}_2)\text{-C-CH}_3$

NOTES

Dehydration:

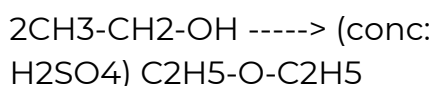
During dehydration first process occurs is elimination reaction:

Which is unimolecular dehydration, C-O and C-H bonds break



Second process: condensation reaction

Which is bimolecular dehydration



Temperature used in second reaction is less because OH bond breaking energy is comparatively less than C-H bond

Lucas Test:

The Lucas Test, also known as the Lucas Reagent Test or Lucas Test for distinguishing between primary, secondary, and tertiary alcohols. It is a qualitative test.

Lucas reagent is a solution of concentrated hydrochloric acid, HCl, and zinc chloride, ZnCl₂.

1. Primary alcohols when heated gently, they eventually form alkyl chlorides (halides) after some time. This reaction can take several minutes to hours.

2. Secondary alcohols react relatively quickly with the Lucas reagent at room temperature to form alkyl chlorides. This reaction typically occurs within a few minutes.

3. Tertiary alcohols react very rapidly with the Lucas reagent at room temperature, often producing an immediate cloudy or milky solution due to the formation of alkyl chlorides.

The rate of reaction can be used to distinguish between the different types of alcohols:

Primary alcohols require heating and a longer time to react.

Secondary alcohols react at room temperature within minutes.

Tertiary alcohols react almost instantly at room temperature.

USES OF ALCOHOL

Alcohol has wide range of uses which includes:

Beverages: Ethanol, is the primary component in alcoholic beverages.

Disinfectants and Antiseptics: Ethanol and isopropyl alcohol are commonly used as disinfectants and antiseptics to kill microorganisms on surfaces, skin, and medical instruments.

Solvents: ethanol and methanol, are used as solvents in various industries. They dissolve a wide range of substances, making them valuable for processes such as extraction, cleaning, and formulation of products like paints, inks, and perfumes.

Fuel: Ethanol, derived from renewable sources like corn or sugarcane, is blended with gasoline to create ethanol fuel

Pharmaceuticals: Alcohols are used as solvents in the manufacture of pharmaceuticals and as components in medications

Perfumes and Fragrances: Alcohol is used as a carrier for many fragrances and perfumes. It helps disperse and deliver the scent when applied to the skin.

Cleaning Products: Alcohol-based cleaning products are used to clean surfaces, glass, and electronics due to their ability to evaporate quickly without leaving residue.

Preservatives: Some alcohols, like phenethyl alcohol, are used as preservatives in cosmetics and personal care products.

Cooling Agent: Ethanol and isopropanol have cooling properties when they evaporate, making them useful for cooling purposes in applications like heat exchangers.

Laboratory and Research: Alcohol is used in laboratories as a solvent, reagent, and for cleaning glassware due to its relatively low toxicity and wide solubility range.

Alcohol-Based Hand Sanitizers: alcohol-based hand sanitizers with a high concentration of ethanol or isopropyl alcohol are used to disinfect hands when soap and water are not available.

Food Industry: Some alcohols, like glycerol, are used in the food industry as humectants, thickeners, and stabilizers in various food products.

PHENOL

Hydroxy derivatives of benzene
 The compound in which OH group is directly attached to sp^2 hybridized carbon of aromatic ring
 First isolated from coal tar
 First prepared by Runge
 Melting point = 41°C
 Boiling point = 182°C
 Simple example phenol = carbolic acid ($\text{C}_6\text{H}_5\text{OH}$)
 Name of phenol is derived from old name of benzene which is phen.

Nomenclature:

Phenol is an important aromatic compound with a hydroxyl group (-OH) attached to a benzene ring. The systematic IUPAC (International Union of Pure and Applied Chemistry) name for phenol is "benzenol." However, phenol is more commonly known by its common name, which is simply "phenol."

These are the rules for naming phenol using the IUPAC system:

1. Identify the parent hydrocarbon: In the case of phenol, the parent hydrocarbon is benzene, which consists of a six-membered carbon ring with alternating single and double bonds.

2. Locate and name the substituent: In phenol, the substituent is the hydroxyl group (-OH) attached to one of the carbon atoms in the benzene ring. The carbon atom to which the hydroxyl group is attached is typically assigned the position number 1.

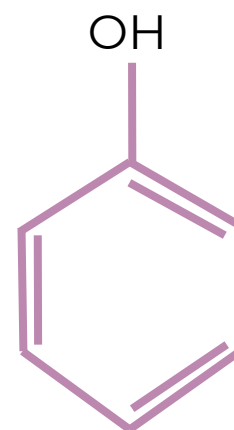
3. Combine the parent hydrocarbon and substituent names: Since the substituent is an -OH group, you simply attach it as a prefix to the parent hydrocarbon name. In this case, you get "benzenol."

So, using the IUPAC system, phenol is named as "benzenol."

Structure of Phenol:

The chemical structure of phenol is simple. Phenol is an aromatic organic compound consisting of a benzene ring (a six-membered carbon ring with alternating single and double bonds) with a hydroxyl group (-OH) attached to one of the carbon atoms in the ring. Here is the structural formula for phenol.

STRUCTURE OF PHENOL:



In this structural formula:

- The six carbon atoms in the benzene ring are represented by the letter "C."
- The hydroxyl group (-OH) is attached to one of the carbon atoms in the benzene ring.
- Hydrogen atoms (H) are attached to the remaining carbon atoms in the benzene ring.

NOTES

Phenol is a colorless or white crystalline solid at room temperature and is commonly found in nature as well as in various industrial processes. It has a distinct odor and is both a valuable chemical reagent and an important precursor in the synthesis of various chemicals and pharmaceuticals.

Classification of phenol:

Phenols can be mono-hydric, dihydric or trihydric
Monohydric alcohol includes o-cresol, m-cresol, p-cresol
Dihydric alcohol includes catechol, resorcinol, quinol
Tri-hydric alcohol includes pyragallol, hydroxy quinol and phlorogucinol

Physical Properties:

Phenol is a white crystalline solid at room temperature.

It has a distinctive sweet and tarry odor.

It is slightly soluble in water and more soluble in organic solvents like ethanol and ether.

Acidity:

Phenol is more acidic than alcohols due to the resonance stabilization of its conjugate base (phenoxide ion, $\text{C}_6\text{H}_5\text{O}^-$).

The hydroxyl group donates a hydrogen ion (proton), making phenol weakly acidic.

Reactivity:

Phenol undergoes electrophilic aromatic substitution reactions more readily than benzene due to the activating effect of the hydroxyl group.

Common reactions include nitration, halogenation, sulfonation, and Friedel-Crafts alkylation/acylation.

Uses:

Phenol is used in the production of plastics, such as Bakelite.

It is a precursor for the synthesis of drugs, dyes, and other industrial chemicals.

Phenol is used in the manufacture of resins and as a disinfectant.

Toxicity and Safety:

Phenol is toxic and can cause severe burns upon contact with the skin.

Inhalation or ingestion of phenol can be harmful and potentially fatal.

Proper safety precautions, including gloves and eye protection, are necessary when handling phenol.

Natural Occurrence:

Phenol is found in small amounts in nature, including in some essential oils and as a metabolic product in plants.

ACIDIC NATURE OF PHENOL

- Acidic nature of phenol:
- Acid strength order:
- Carboxylic acid > phenol > water > alcohol
- K_a : $1.75 \times 10^{-5} > 1.3 \times 10^{-10} > 1.8 \times 10^{-16} > 10^{-16} - 10^{-18}$
- Pka : $5 > 10 > 16 > 16-18$
- Acidity of all these substances are determined by K_a and pka values.
- Greater the K_a value, greater will be acidic strength
- Greater the K_a , lesser will be pka value.

COMPARISON OF ACIDITY OF PHENOL AND ALCOHOL

Acidity of phenol	Acidity of alcohol
They have benzene ring attached to OH	They have alkyl or aryl group attached to OH
They have phenoxide ion as conjugate base ($C_6H_5O^-$)	They have Alkoxide ion or aryloxide ion (RO^- or ArO^-) as conjugate base
Conjugate base stability is high due to resonance in benzene ring	Conjugate base stability is lower as compared to phenol due to lack of resonance
Pka : approx 9.95	Pka value: 15-18
They are moderately strong acid	They are weak acids

COMPARISON OF ACIDITY OF PHENOL AND CARBOXYLIC ACID:

Acidity of phenol	Acidity of carboxylic acid
They have benzene ring attached to OH	They contain COOH functional group
They have phenoxide ion as conjugate base (C ₆ H ₅ O ⁻)	They are relatively strong acids due to presence of carboxylic group. They can donate proton to form carboxylate ion (RCOO ⁻)
Conjugate base stability is high due to resonance in benzene ring	Carboxylate ion is present as conjugate base which is very highly stable conjugate base due to resonance between oxygen atoms, which delocalise negative charge
Pka: approx 9.95	Pka : 3-5
They are moderately strong acid	Carboxylic acids are widely used in various chemical reactions, including in the synthesis of esters, amides, and other organic compounds.

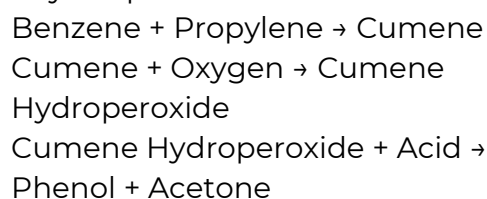
- **STABILITY ORDER OF ION:**
- carboxylate ion > phenoxide ion > alkoxide ion
- Carboxylate ion is most stable due to -ve charge which resonates between both O.
- Alkoxide ion is least stable due to -ve charge on O is localized making it unstable

PREPARATION OF PHENOL

Phenol can be prepared through various methods. Here are some common methods for preparing phenol:

1. Cumene Process:

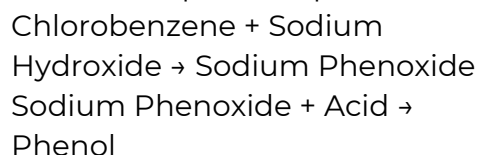
In this industrial process, benzene is alkylated with propylene to form cumene (isopropylbenzene). Cumene is then oxidized using air or oxygen, often in the presence of a catalyst like a metal complex, to form cumene hydroperoxide. Cumene hydroperoxide is cleaved in the presence of acid to yield phenol and acetone.



2. Dow Process:

Chlorobenzene is treated with a concentrated aqueous sodium hydroxide (NaOH) solution at high temperature and pressure. This process is known as hydrolysis.

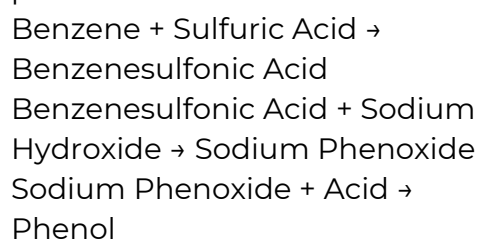
Hydrolysis of chlorobenzene results in the formation of sodium phenoxide, which is then acidified to produce phenol.



3. Hock Process:

Benzene is sulfonated with concentrated sulfuric acid to form benzenesulfonic acid.

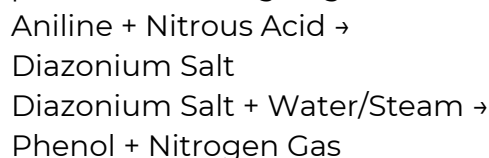
Benzenesulfonic acid is then heated with aqueous sodium hydroxide, leading to the formation of sodium phenoxide, which is then acidified to obtain phenol.



4. Diazotization Process:

Aniline is diazotized using nitrous acid (HNO₂) to form a diazonium salt.

The diazonium salt is then treated with water or steam to produce phenol and nitrogen gas.



Effect of substituents on acidity of phenol:

1) e⁻ withdrawing group:

They include -X, -NO₂, -SO₃H, -CN

They tend to disperse -ve charge on phenoxide ion

They stabilize phenoxide ion

They increase acidity

2) e⁻ donating group:

They include -NH₂, -OR, R

They tend to intensify -ve charge on phenoxide ion

They destabilize phenoxide ion

They decrease acidity

REACTION OF PHENOL

Phenols are very reactive towards electrophilic substitution reaction because of hydroxyl group which is strongly activating ortho or para directing substituent.

Electrophilic Aromatic Substitution:

Substitution occurs mostly at para position, but if para position is blocked then it is substituted at ortho position,
Phenols are so activated that polysubstitution may cause a problem

Reaction	Phenol	Benzene
nitration	Dil HNO_3 in H_2O or $\text{CH}_3\text{CO}_2\text{H}$	Conc $\text{H}_2\text{SO}_4/\text{HNO}_3$
sulphonation	Conc H_2SO_4	H_2SO_4 or SO_3
halogenation	X_2	X_2/Fe or FeX_3
alkylation	ROH/H^+ or RCI/AlCl_3	RCl/AlCl_3
acylation	$\text{RCOCl}/\text{AlCl}_3$	$\text{RCOCl}/\text{AlCl}_3$
nitrosation	Aq. NaNO_2/H^+	

REACTION WITH SODIUM:

It is also called Kolbe-Schmitt reaction, carboxylation of phenol. The reaction of sodium salt with CO_2 is called the Kolbe reaction. It is the carbonation of phenol.

Carbon of CO_2 acts as an electrophilic centre.

Acidification of salt gives corresponding hydroxyl acid

NOTES

OXIDATION OF PHENOL:

Phenols are very reactive towards oxidizing agent

Oxidation takes place by destroying the ring structure

Alcohol	Phenol
Hydroxy derivatives of alkane, alkenes or cyclo alkane	Hydroxy derivatives of benzene
Lower alcohols (generally colourless liquids)	Colourless crustalline deliquescent solid
Less acidic (Pka = 16-20)	More acidic (pka = 10)
Sweet smell	Phenolic smell
No reaction with Br ₂ water	Gives white ppt with Br ₂ water
No reaction with NaOH	React with NaOH to form salt
Readily soluble in water	sparingly soluble in water at room temperature

ETHERS

NOMENCLATURE

Ethers are commonly named by first taking names of alkyl groups attached to oxygen, followed by class name ether

According to IUPAC, the ethers are regarded as alkanes in which a hydrogen atom is replaced by an alkoxy (-OR) group.

In mixed ethers, the larger alkyl group is chosen as the alkane.

e.g: $(\text{CH}_3)_2\text{CH-O-CH}_3$ = isopropyl methyl ether or 2-methoxy propane

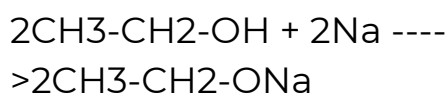
PREPARATION

Ethers are prepared from following reactions:

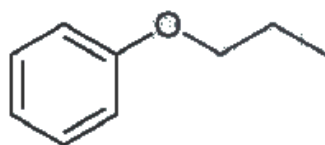
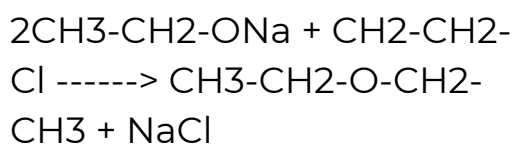
1) Williamson synthesis:

In this reaction alcohols are converted to ether

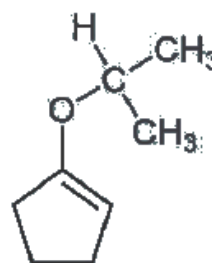
When primary alcohol reacts with sodium it gives an alkoxide



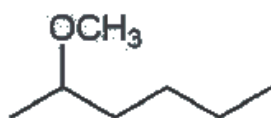
Then alkoxide reacts with alkyl halide it forms ether.



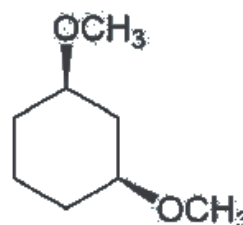
Propoxybenzene



1-Isopropoxycyclopentene



2-Methoxyhexane



Cis-1,3-Dimethoxycyclohexane

PHYSICAL PROPERTIES OF ETHERS

Physical properties of ethers are:

Odor: ethers have a characteristic, sweet, and pleasant odor.

Physical State: Ethers can exist in various physical states at room temperature, ranging from gases to liquids and solids.

Boiling Point: Ethers generally have lower boiling points compared to alcohols and water.

Solubility: Ethers are typically soluble in organic solvents like acetone, chloroform, and alcohols.

Density: Ethers are less dense than water, so they tend to float on the surface of water.

Flammability: Ethers can be highly flammable in the presence of air and an open flame.

Boiling Point Range: The boiling points of ethers generally increase with an increase in molecular weight and the presence of polar groups.

Anaesthetic: Ether is an effective anesthetic.

Viscosity:

Ethers typically have low viscosity, meaning they flow easily. This low viscosity is due to the weak intermolecular forces present in ethers.

Volatility:

Ethers are generally quite volatile, meaning they readily evaporate at room temperature. This property is particularly true for low molecular weight ethers like diethyl ether.

Refractive Index:

Ethers have a refractive index, which measures how much they bend light. This property varies depending on the structure and composition of the ether but generally falls between 1.3 and 1.5.

Polarizability:

Ethers have moderate polarizability due to the presence of the oxygen atom, which allows the electron cloud to be distorted more easily compared to hydrocarbons. This polarizability contributes to the solubility of ethers in various organic solvents.

Dielectric Constant:

Ethers have a relatively low dielectric constant, indicating they are poor conductors of electricity. This property makes them useful as non-polar solvents in various chemical reactions.

REACTIVITY OF ETHERS

Reactivity of ether can be better understood by concept of electrostatic potential of dimethyl ether.

The red area indicates higher electron density

The blue area indicates lower electron density

The ethereal O atom is region of high electron density (red) due to lone pairs

Ether oxygen atoms are lewis base

RESISTANT TO OXIDATION:

Ethers are resistant to attack by usual chemical oxidizing agent

REACTION WITH HI:

The O atom of ether possess unshared paired electron, which accepts proton of HI to form oxonium ion, which reacts with I to form R-OH and RI.

REACTION WITH HBr:

O atom of an ether possess unshared electron pair, which accepts proton of HBr to form oxonium ion.

FORMATION OF PEROXIDES:

Ethers can form peroxides upon prolonged exposure to air and light, leading to the formation of explosive peroxides.

This is a notable exception to their general resistance to oxidation and poses a significant safety hazard.

CLEAVAGE BY ACID HALIDES:

Ethers can undergo cleavage reactions with acid halides (e.g., acyl chlorides).

The oxygen atom of the ether donates an electron pair to the electrophilic carbon of the acid halide, leading to cleavage of the ether bond.

COMPLEX FORMATION:

Ethers can form coordination complexes with various metal ions. The lone pairs on the oxygen atom can coordinate to metal centers, stabilizing various metal ions in solution.

REACTION WITH GRIGNARD REAGENTS:

Ethers are commonly used as solvents for Grignard reagents because they can stabilize the organomagnesium compounds. The lone pairs on the ether oxygen atoms help solvate and stabilize the Grignard reagent.

Reaction with Strong Acids:

Ethers can react with strong acids such as sulfuric acid (H_2SO_4) to form oxonium ions.

This reaction can lead to the cleavage of the ether bond under strong acidic conditions

EXPERT REVIEW:



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