Name of Unit	Alkyl halides & Alcohol
Subject /Course	Pharmaceutical Organic Chemistry-I
Subject/Course ID	BP202T
Class: B.Pharm.Semester	II
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Learning Outcome of Module 03

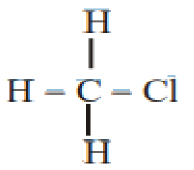
LO	Learning Outcome	Course Outcome Code
LO1	To gain the knowledge of classification of Alkyl halide and Alcohol .	BP202.1
LO2	To understand the nomenclature of Alkyl halide and Alcohols	BP202.1
LO3	To gain the knowledge of method of preparation of alkyl halide and alcohols	
LO4	To understand the Stereochemistry, orientation & Reactivity of Alkyl halide	BP202.2
LO5	To gain the knowledge Identification tests for Alcohols	BP202.3
LO6	To understand Physical & chemical properties of Alkyl halide and Alcohol	BP202.4
LO7	Structure and uses of some compounds	BP202.6

Content Table

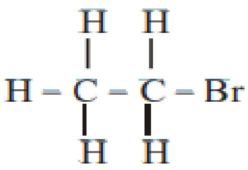
Topic
- Introduction of Alkyl halide and Alcohols. - Nomenclature and classification - Method of Preparation - Stereochemistry, orientation and reactivity - Identification test to distinguish 1^{o}, 2^{o},3^{o} alcohol - Physical properties & Chemical reactions - Structure and medicinal uses of some important compounds.

ALKYL HALIDES

Alkyl Halides are compounds in which a halogen atom is attached to carbon. For example, Methyl chloride and ethyl bromide



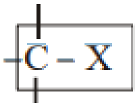
Methyl chloride



Ethyl bromide

They have the general formula

$R - X$ or

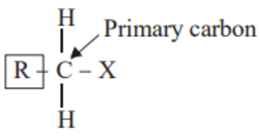


$\boxed{C - X}$

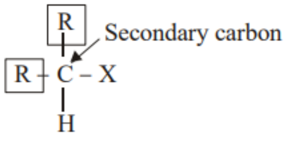
Where **R - alkyl group; X = Cl, Br, I or F**. The halogen atom bonded to carbon is the functional group of alkyl halides.

CLASSIFICATION

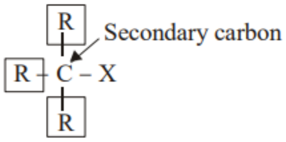
Alkyl halides are classified as ***Primary (1°), Secondary (2°), or Tertiary (3°),*** depending upon whether the X atom is attached to a primary, secondary, or a tertiary carbon.



1° Alkyl Halide



2° Alkyl Halide

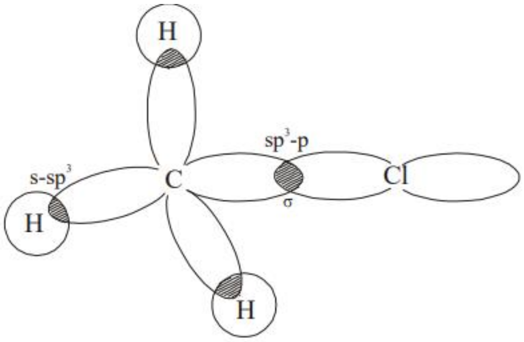


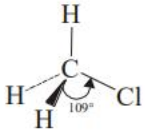
3° Alkyl Halide

Alkyl halides are among the most useful organic compounds. They are frequently used to introduce alkyl groups into other molecules.

STRUCTURE

Let us consider methyl chloride (CH_3Cl) for illustrating the orbital make up of alkyl halides in methyl chloride, the carbon atom is sp^3 hybridized. The chlorine atom has a half-filled p orbital in valence shell. The C- Cl bond is formed by the overlap of an sp^3 orbital of carbon and the half-filled p orbtial of chlorine atom shown in figure. Each C- H bond is formed by the overlap of an sp^3 orbital of carbon and the s orbital of hydrogen.





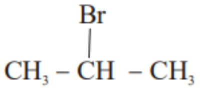
NOMENCLATURE

Alkyl halides are named in two ways

1. **Common system:** In this system the alkyl group attached to the halogen atom is named first. This is then followed by an appropriate word chloride, bromide, or fluoride. Notice that the common names of alkyl halides are TWO-WORD names.

$CH_3 - Br$ Methyl bromide

$CH_3CH_2 - Cl$ Ethyl chloride



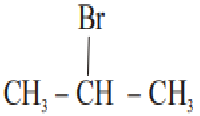
$$CH_3 - \overset{\overset{Br}{|}}{CH} - CH_3$$

Isopropyl bromide

2. **IUPAC system:** The IUPAC names of alkyl halides are obtained by using the following rules:
   a) Select the longest carbon chain containing the halogen atom and name the alkyl halides as a derivative of the corresponding hydrocarbon.
   b) Number the chain so as to give the carbon carrying the halogen atom the lowest possible number.
   c) Indicate the position of the halogen atom by a number and by the fluoro-, chloro-, bromo- or iodo-.
   d) Name other substituents and indicate their positions by numbers. The examples given below show how these rules are applied. Notice that the IUPAC names of alkyl halides are ONE-WORD names.

$CH_3 - Br$ Methyl bromide

$CH_3CH_2 - Cl$ Ethyl chloride



$$CH_3 - \overset{\overset{Br}{|}}{CH} - CH_3$$

Isopropyl bromide

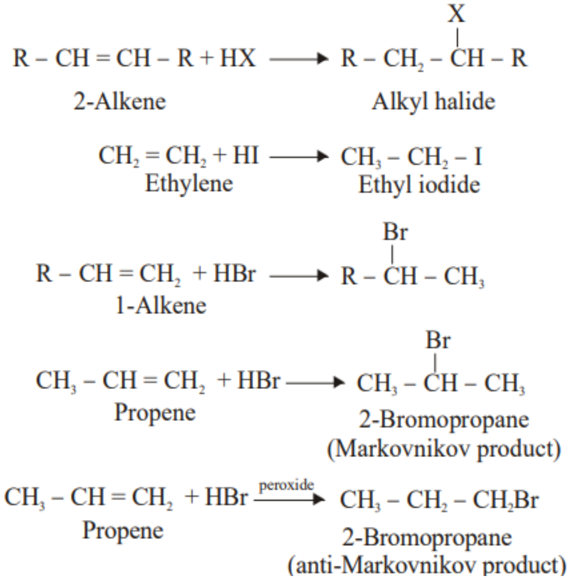
METHODS OF PREPARATION

Alkyl halides can be prepared by the following methods:

1. **Halogenation of Alkanes**: Alkanes react with Cl_2 or Br_2 in the presence of UV light or at high temperature (400°C) to give alkyl halides along with polyhalogen derivatives. This method is not used in the laboratory because of the difficulty of separating the products.

$$CH_4 \xrightarrow[\text{UV light}]{Cl_2} CH_3Cl + CH_2Cl_2 + CHCl_3 + CCl_4$$

2. **Addition of Halogen Acids to Alkenes:** Halogen acids (HCl, HBr, HI) add to alkenes to yield alkyl halides. The mode of addition follows Markovnikov rule, except for the addition of HBr in the presence of organic peroxides (R-O-O-R).



$$\underset{\text{2-Alkene}}{R-CH=CH-R+HX} \longrightarrow \underset{\text{Alkyl halide}}{R-CH_2-\overset{\overset{X}{|}}{C}H-R}$$

$$\underset{\text{Ethylene}}{CH_2=CH_2+HI} \longrightarrow \underset{\text{Ethyl iodide}}{CH_3-CH_2-I}$$

$$\underset{\text{1-Alkene}}{R-CH=CH_2+HBr} \longrightarrow R-\overset{\overset{Br}{|}}{C}H-CH_3$$

$$\underset{\text{Propene}}{CH_3-CH=CH_2+HBr} \longrightarrow \underset{\substack{\text{2-Bromopropane}\\ \text{(Markovnikov product)}}}{CH_3-\overset{\overset{Br}{|}}{C}H-CH_3}$$

$$\underset{\text{Propene}}{CH_3-CH=CH_2+HBr} \xrightarrow{\text{peroxide}} \underset{\substack{\text{2-Bromopropane}\\ \text{(anti-Markovnikov product)}}}{CH_3-CH_2-CH_2Br}$$

3. **Action of Halogen Acids on Alcohols**- Alcohols react with HBr or HI to produce alkyl bromides or alkyl iodides. Alkyl chlorides are produced by the action of dry HCl in the presence of zinc chloride catalyst.

$$\underset{\text{Alcohol}}{R-\boxed{OH + H}-X} \longrightarrow \underset{\text{Alkyl halide}}{R-X} + H_2O$$

$$\underset{\text{Ethyl alcohol}}{CH_3CH_2OH + HCl} \xrightarrow{ZnCl_2} \underset{\text{Ethyl chloride}}{CH_3CH_2Cl} + H_2O$$

$$\underset{\text{n-propyl alcohol}}{CH_3CH_2OH + HBr} \rightarrow \underset{\text{n-propyl bromide}}{CH_3CH_2Br} + H_2O$$

4. **Action of Phosphorus Halides on Alcohols**- Alcohols react with phosphorus halides (PX_5 or PX_3) to form alkyl halides.

$$\underset{\text{Alcohol}}{R-OH} + PX_5\ (\text{or } PX_3) \longrightarrow \underset{\text{Alkyl halide}}{R-X}$$

$$\underset{\text{Ethyl alcohol}}{2CH_3CH_2OH} + PCl_5 \longrightarrow \underset{\text{Ethyl chloride}}{2CH_3CH_2Cl} + POCl_3 + H_2O$$

$$3CH_3CH_2OH + PBr_3 \longrightarrow \underset{\text{Ethyl bromide}}{3CH_3CH_2Br} + H_3PO_3$$

$$3CH_3OH + PI_3 \longrightarrow \underset{\text{Methyl iodide}}{3CH_3I} + H_3PO_3$$

5. **Action of Thionyl chloride on alcohols**- Alcohols react with thionyl chloride (SOCl2) in the presence of pyridine to produce alkyl chlorides. Pyridine (C5H5N) absorbs hydrogen chloride as it is formed.

$$\underset{\text{Alcohol}}{R-OH} + \underset{\text{Thionyl chloride}}{SOCl_2} \xrightarrow{\text{pyridine}} \underset{\text{Alkyl chloride}}{R-Cl} + SO_2 + HCl$$

$$\underset{\text{Ethyl Alcohol}}{CH_3CH_2OH} + SOCl_2 \xrightarrow{\text{pyridine}} \underset{\text{Ethyl chloride}}{CH_3CH_2Cl} + SO_2 + HCl$$

6. **Halogen Exchange reaction**- This reaction is particularly suitable for preparing alkyl iodides. The alkyl bromide or chloride is heated with a concentrated solution of sodium iodide in acetone.

$$\underset{\text{Ethyl bromide}}{CH_3CH_2-Br} + NaI \xrightarrow[\Delta]{\text{acetone}} \underset{\text{Ethyl iodide}}{CH_3CH_2-I} + NaBr$$

Alkyl fluorides are also prepared by treating an alkyl chloride or bromide with inorganic fluorides.

$$\underset{\text{Methyl chloride}}{2CH_3-Cl} + Hg_2F_2 \xrightarrow[\Delta]{\text{acetone}} \underset{\text{Methyl fluoride}}{2CH_3-F} + Hg_2Cl_2$$

PHYSICAL PROPERTIES

1) CH_3Cl, CH_3Br, CH_3F and CH_3CH_2Cl are gases at room temperature. Other alkyl halides upto C18 are colourless liquids. Those beyond C_{18} are colourless solids.
2) Alkyl halides are insoluble in water but soluble in organic solvents. The insolubility in water is due to their inability to form hydrogen bonds with water.
3) Alkyl bromides and iodides are denser than water. Alkyl chlorides and fluorides are lighter than water.

4) Alkyl halides have higher boiling points than alkanes of comparable molecular weight. For a given halogen atom, the boiling points of alkyl halides increase with the increase in the size of the alkyl group. For a given alkyl group, the boiling points of alkyl halides follow the order RI>RBr>RCl>RF.

CHEMICAL PROPERTIES

Alkyl halides are very reactive compounds. They undergo substitution, elimination and reduction reactions. Alkyl halides also react with metals to form organometallic compounds.

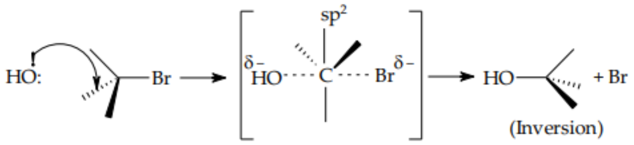
THE SN^2 REACTION MECHANISM AND KINETICS

The reaction between methyl bromide and hydroxide ion to yield methanol follows second order kinetics; that is, the rate depends upon the concentration of both reactants.

$$CH_3Br + \bar{O}H \longrightarrow CH_3OH + Br^-$$

$$\text{rate} = K[CH_3Br]\,[OH^-]$$

The simplest way to account for the kinetics is to assume that reaction requires a collision between a hydroxide ion and a methyl bromide molecule. In its attack, the hydroxide ion stays for away as possible from the bromine; i.e. it attacks the molecule from the rear and begins to overlap with the tail of the sp^3 hybrid orbital holding Br. The reaction is believed to take place as shown:

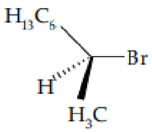


(T.S.)

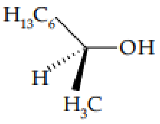
In the T.S. the carbon is partially bonded to both –OH and – Br; the C–OH bond is not completely formed, the C–Br bond is not yet completely broken. Hydroxide has a diminished – ve charge, since it has begun to share its electrons with carbon. Bromine has developed a partial negative charge, since it has partly removed a pair of electrons from carbon. At the same time, of course, ion dipole bonds between hydroxide ion and solvent are being broken and ion-dipole bonds between bromide ion and solvent are being formed. As the –OH becomes attached to C, 3 bonds are forced apart (120°) until they reach the spike arrangement of the T.S; then as bromide is expelled, they move on to the tetrahedral arrangement opposite to the original one.

STEREOCHEMISTRY

Both 2-bromo-octane and 2-octanol are chiral

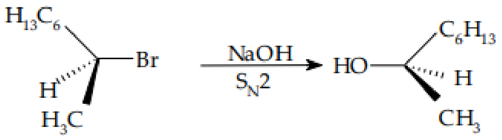


(2S)-2-bromooctane



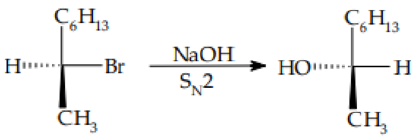
(2S)-octan-2-ol

The (–) bromide and the (–) alcohol have similar configurations, i.e. –OH occupies the same relative position in the (–) alcohol as –Br does in the bromide. When (–)-2-bromooctane is allowed to react with sodium hydroxide under SN^2 conditions, (+)-2-octanol is obtained.



(2S)-2-bromooctane (2R)-octan-2-ol

In Fisher projection the above reaction can be represented as follows.



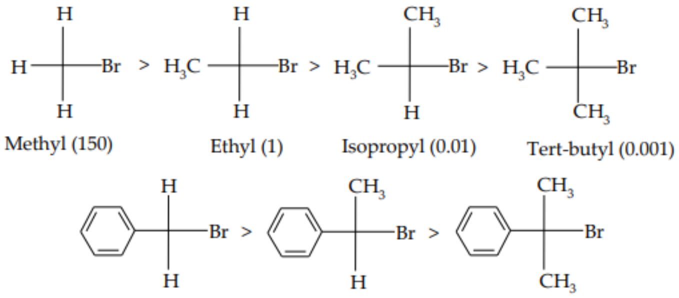
(2S)-2-bromooctane (2R)-octan-2-ol

We see that – OH group has not taken the position previously occupied by –Br; the alcohol obtained has a configuration opposite to the bromide. A reaction that yields a product whose configuration is opposite to that of the reactant is said to proceed with inversion of configuration.

REACTIVITY

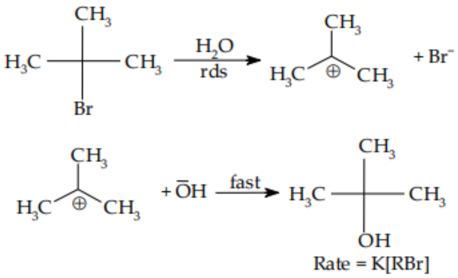
In SN^2 reactions the order of reactivity of RX is CH3X > 1° > 2° > 3°.

Difference in rate between two SN2 reactions seem to be chiefly due to steric factors (bulk of the substituents) and not due to electronic factors i.e. ability to withdraw or release electrons. Relative Reactivity Towards I^{-}.



THE SN^1 REACTION MECHANISM AND KINETICS

The reaction between tert-butyl and hydroxide ion to yield tert-butyl alcohol follows first order kinetics; i.e., the rate depends upon the concentration of only one reactant, tert-butyl bromide.



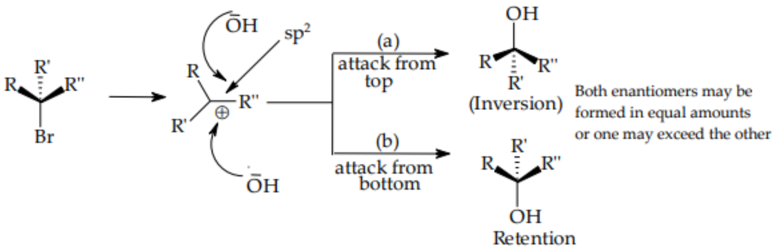
SN^1 reaction follows first order kinetics

STEREOCHEMISTRY

When (–)-2-bromo octane is converted into alcohol under conditions where first-order kinetics are followed, partial racemization is observed.

The optically active bromide ionizes to form bromide ion and the flat carbocation. The nucleophilic reagent then attaches itself to carbonium ion from either face of the flat ion. 68 If the attack were purely random, we would expect equal amounts of two isomers; i.e. we would expect ony the racemic modification. But the product is not completely racemized, for the inverted product exceeds its enantiomer.

We can say in contrast SN2 reaction, which proceeds with complete inversion; an SN1 reaction proceeds with racemization though may not be complete.



Both enantiomers may be formed in equal amounts or one may exceed the other

Reactivity of an alkyl halide depends upon the stable carbonium ion it can form. In SN1 reactions the order of reactivity of alkyl halides is Allyl, benzyl > 3° > 2° > 1° > CH_3X. Some of the important nucleophilic substitution reactions of alkyl halides are described below:

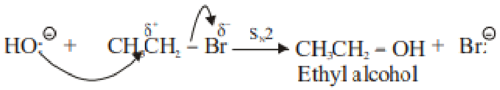
1. **Reaction with aqueous KOH**: Alkyl halides react with aqueous potassium hydroxide to form alcohols. The halogen atom is substituted by -OH group.

$$\underset{\text{Methyl iodide}}{CH_3I} + KOH \xrightarrow[\Delta]{H_2O} \underset{\text{Methyl alcohol}}{CH_3OH} + KI$$

$$\underset{\text{Ethyl bromide}}{CH_3CH_2Br} + KOH \xrightarrow[\Delta]{H_2O} \underset{\text{Ethyl alcohol}}{CH_3CH_2OH} + KBr$$

MECHANISM:

In the above reaction OH^- is the nucleophile



2. **Reaction with Moist Silver Oxide**: Alkyl halides on treatment with a suspension of silver oxide in moist ether produce alcohols. Halogen atom is substituted by -OH group.

$$Ag_2O + H_2O \longrightarrow 2AgOH$$

$$\underset{\text{Ethyl bromide}}{CH_3CH_2Br} + AgOH \xrightarrow{\Delta} \underset{\text{Ethyl alcohol}}{CH_3CH_2OH} + KBr$$

3. **Reaction with sodium alkoxides**: Alkyl halides react with sodium alkoxides (RONa) to form ethers. Sodium alkoxides are prepared by dissolving metallic sodium in excess of the appropriate alcohol. For example,

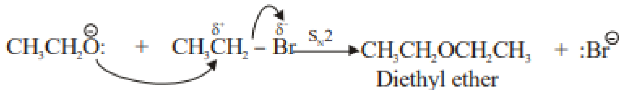
$$CH_3CH_2OH + Na \longrightarrow \underset{\text{Sodium ethoxide}}{CH_3CH_2ONa} + H_2$$

$$\underset{\text{Ethyl bromide}}{CH_3CH_2Br} + \overset{\oplus}{Na}\overset{\ominus}{O}CH_2CH_3 \longrightarrow \underset{\text{Diethyl ether}}{CH_3CH_2OCH_2CH_3} + NaBr$$

This method of making ethers is called Williamson Ether Synthesis

MECHANISM

In the above reactionCH_3CH_2O, is the nucleophile



Ethers can also be produced by heating an alkyl halide with dry silver oxide.

$$\underset{\text{Methyl iodide}}{2CH_3I} + Ag_2O \xrightarrow{\Delta} \underset{\text{Diethyl ether}}{CH_3 - O - CH_3} + 2AgI$$

4. **Reaction with Ammonia:** When an alkyl halide is heated with an alcoholic solution of ammonia in a sealed tube, alkylation of ammonia takes place. A mixture of different classes of amines results.

$$\underset{\text{Ethyl bromide}}{CH_3CH_2Br} + \underset{\text{(in ethanol)}}{NH_3} \xrightarrow{\Delta} \underset{\text{Ethylamine(1°)}}{CH_3 - O - CH_3 + 2AgI}$$

$$CH_3CH_2NH_2 + CH_3CH_2Br \longrightarrow \underset{\text{Diethylamine (2°)}}{(CH_3CH_2)_2NH + HBr}$$

$$CH_3CH_2)_2NH + CH_3CH_2Br \longrightarrow \underset{\text{Triethylamine (3°)}}{(CH_3CH_2)_3N + HBr}$$

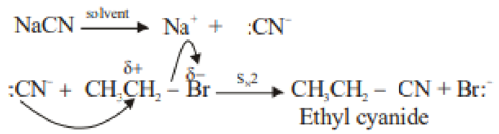
$$CH_3CH_2)_3N + CH_3CH_2Br \rightarrow \underset{\text{Tetraethylammonium bromide (4°)}}{(CH_3CH_2)_4\overset{+}{N}Br^-}$$

5. **Reaction with Sodium Cyanide:** Alkyl halides react with sodium cyanide in a suitable solvent (generally aqueous ethanol) to form alkyl cyanides or nitriles. Halogen atom is replaced by CN group.

$$\underset{\text{Ethyl bromide}}{CH_3CH_2 - Br} + NaCN \xrightarrow[\text{ethanol},\Delta]{\text{aqueous}} \underset{\text{Ethyl cyanide}}{CH_3CH_2 - CN} + NaBr$$

MECHANISM:

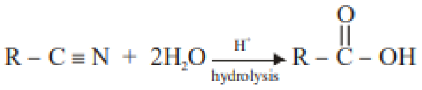
Cyanide ion is an excellent nucleophile. It attacks ethyl bromide by an SN2 mechanism to form ethyl cyanide.



$$NaCN \xrightarrow{\text{solvent}} Na^{+} + :CN^{-}$$

$$:CN^{-} + \overset{\delta+}{CH_3CH_2} - \overset{\delta-}{Br} \xrightarrow{S_N2} \underset{\text{Ethyl cyanide}}{CH_3CH_2 - CN} + Br:^{-}$$

Alkyl cyanides are useful synthetic reagents. They can be easily converted into carboxylic acids and 1° amines.



$$R - C \equiv N + 2H_2O \xrightarrow[\text{hydrolysis}]{H^{+}} R - \overset{\overset{\displaystyle O}{||}}{C} - OH$$

$$R - C \equiv N + 4[H] \xrightarrow[\text{reduction}]{LiAlH_4} \underset{1^\circ \text{ Amine}}{R - CH_2 - NH_2}$$

Alkyl halides react with silver cyanide to form isocyanides.

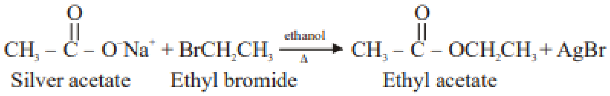
$$\underset{\text{Ethyl bromide}}{CH_3CH_2Br} + AgCN \longrightarrow \underset{\text{Ethyl isocyanide}}{CH_3CH_2NC} + AgBr$$

The explanation for this lies in the structure of silver cyanide which is thought to exist in the form of a chain.

$$Ag - C \equiv N : Ag - C \equiv N$$

Thus the silver atom is linked to both nitrogen and carbon atom. Accordingly both isomers are possible.

6. **Reaction with RCOOAg**: When an alkyl halide is heated with an alcoholic solution of the silver salt of a carboxylic acid, an ester is formed.



$$\underset{\text{Silver acetate}}{CH_3 - \overset{\overset{\displaystyle O}{||}}{C} - O^{-}Na^{+}} + \underset{\text{Ethyl bromide}}{BrCH_2CH_3} \xrightarrow[\Delta]{\text{ethanol}} \underset{\text{Ethyl acetate}}{CH_3 - \overset{\overset{\displaystyle O}{||}}{C} - OCH_2CH_3} + AgBr$$

7. **Reaction with Acetylides**: Alkyl halides react with sodium acetylides to form higher alkynes.

$$CH_3Br + \underset{\text{Sodium acetylide}}{^{-}CNa^{+} \equiv CH} \longrightarrow \underset{\text{Propyne}}{CH_3 - C \equiv CH} + NaBr$$

$$CH_3Br + \underset{\text{Sodium propynide}}{^{-}CNa^{+} \equiv CCH_3} \longrightarrow \underset{\text{2-Butyne}}{CH_3C \equiv CCH_3} + NaBr$$

8. **Reaction with KSH:** Alkyl halides react with alcoholic potassium hydrosulphide to form thiols. Halogen atom is substituted by -SH group.

$$\underset{\text{Ethyl iodide}}{CH_3CH_2 - I} + KSH \xrightarrow[\Delta]{\text{ethanol}} \underset{\text{Ethanethiol}}{CH_3CH_2 - SH} + KI$$

9. **Reaction with K_2S**: Alkyl halides react with potassium sulphide to form dialkyl sulphides.

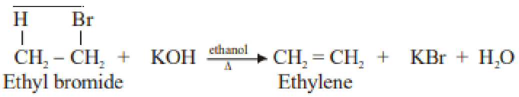
$$\underset{\text{Ethyl iodide}}{2CH_3CH_2-I} + K_2S \longrightarrow \underset{\text{Diethyl sulphide}}{CH_3CH_2-S-CH_2CH_3} + 2KI$$

10. **Reaction with $AgNO_2$:** Alkyl iodides react with silver nitrite to form nitroalkanes.

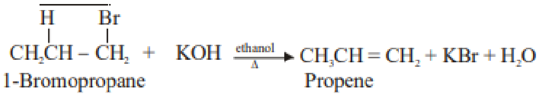
$$\underset{\text{Ethyl iodide}}{CH_3CH_2I} + AgNO_2 \xrightarrow[\Delta]{\text{ethanol}} \underset{\text{Nitroethane}}{CH_3CH_2NO_2} + AgI$$

ELIMINATION REACTIONS

Reaction with alcoholic KOH: Alkyl halides react with alcoholic potassium hydroxide to form alkenes. The reaction involves the elimination of HX from the alkyl halides and is called dehydrohalogenation reaction.



$$\underset{\text{Ethyl bromide}}{\overset{H}{CH_2}-\overset{Br}{CH_2}} + KOH \xrightarrow[\Delta]{\text{ethanol}} \underset{\text{Ethylene}}{CH_2=CH_2} + KBr + H_2O$$



$$\underset{\text{1-Bromopropane}}{CH_3\overset{H}{CH}-\overset{Br}{CH_2}} + KOH \xrightarrow[\Delta]{\text{ethanol}} \underset{\text{Propene}}{CH_3CH=CH_2} + KBr + H_2O$$

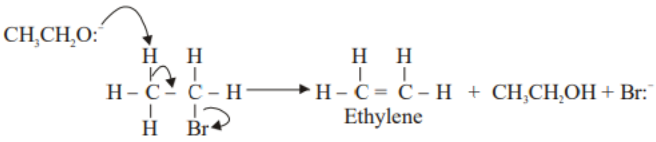
MECHANISM:

In ethanol an equilibrium occurs between the solvent and potassium hydroxide to produce potassium ethoxide.

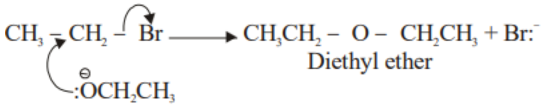
$$\underset{\text{Ethanol}}{CH_3CH_2OH} + KOH \rightleftharpoons CH_3CH_2O^-K^+ + H_2O$$

Potassium ethoxide is a strong base. It favours elimination and substitution reactions. There is always a competition between elimination and substitution reactions. For example, ethyl bromide on treatment with alcoholic KOH can give either ethylene or diethyl ether. The attacking nucleophile is CH_3CH_2O.

ELIMINATION

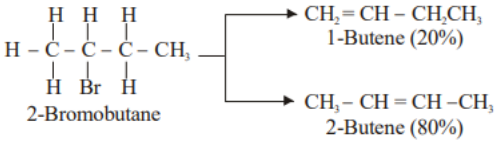


SUBSTITUTION



$$CH_3CH_2-Br + {}^{\ominus}:OCH_2CH_3 \longrightarrow \underset{\text{Diethyl ether}}{CH_3CH_2-O-CH_2CH_3} + Br:^-$$

The ratio of the elimination to substitution product depends on the structure of the alkyl halide and experimental conditions. Primary and secondary alkyl halides undergo dehydrohalogenation by E2 mechanism. Tertiary alkyl halides do so by E1 mechanism. Saytzeff Rule: If the dehydrohalogenation of an alkyl halide can yield more than one alkene, then according to the Saytzeff rule, the main product is the most highly substituted alkene. For example, two alkenes are possible when 2-bromobutane is heated with alcoholic KOH.



Notice that the major product is 2-butene, a disubstituted alkene.

Reaction with Mg- alkyl halides react with magnesium metal in dry ether to form Grignard reagents.

$$\underset{\text{Methyl iodide}}{CH_3I + Mg} \xrightarrow{\text{Ether}} \underset{\text{Methylmagnesium iodide}}{CH_3MgI}$$

$$\underset{\text{Ethyl bromide}}{CH_3CH_2Br + Mg} \xrightarrow{\text{Ether}} \underset{\text{Ethylmagnesium bromide}}{CH_3CH_3MgBr}$$

Reaction with Lithium-Alkyl halides react with lithium in dry ether to form alkyllithiums.

$$\underset{\text{Ethyl bromide}}{CH_3CH_2Br} + 2Li \xrightarrow{\text{Ether}} \underset{\text{Ethyllithium}}{CH_3CH_2Li} + LiBr$$

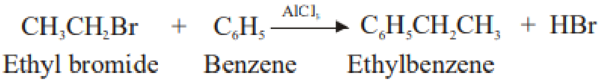
Alkyllithiums behave in the same way as Grignard reagents, but with increased reactivity. Wurtz reaction: Alkyl halides react with metallic sodium in dry ether to give alkanes with double the number of carbon atoms.

$$\underset{\text{Ethyl bromide}}{CH_3CH_2Br} + 2Na + BrCH_2CH_3 \xrightarrow{\text{Ether}} \underset{\text{n-Butane}}{CH_3CH_2CH_2CH_3} + 2NaBr$$

Halogenation: Alkyl halides react with Cl_2 or Br_2 in the presence of UV light or at high temperature to form polyhalogenation derivatives. For example, methyl chloride react with chlorine to yield a mixture of methylene dichloride, chloroform and carbon tetrachloride.

$$CH_3Cl \xrightarrow[\text{UV light}]{Cl_2} CH_2Cl_2 \xrightarrow{Cl_2} CHCl_3 \xrightarrow{Cl_2} CCl_4$$

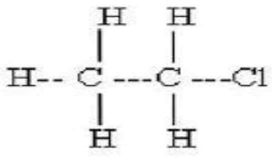
Friedel-Crafts Alkylation: Alkyl halides react with benzene in the presence of anhydrous AlCl3 to form alkylbenzenes.



$$\underset{\text{Ethyl bromide}}{CH_3CH_2Br} + \underset{\text{Benzene}}{C_6H_5} \xrightarrow{AlCl_3} \underset{\text{Ethylbenzene}}{C_6H_5CH_2CH_3} + HBr$$

STRUCTURE AND USES OF FOLLOWING COMPOUNDS

1. ETHYLCHLORIDE

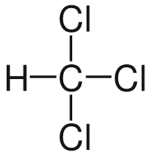


$$\begin{array}{ccccccc} & & H & & H & & \\ & & | & & | & & \\ H & -- & C & --- & C & --- & Cl \\ & & | & & | & & \\ & & H & & H & & \end{array}$$

USES

1. It was used to produce tetraethyllead which was an antiknock additive for gasoline.
2. It reacts with aluminium metal and give ethylaluminium sesquichloride which is a precursor for the synthesis of organometallic compounds.
3. It is also used as refrigerant, anesthetic and aerosol spray propellant.
4. In industry it is used to synthesize ethyl cellulose which is a thickening agent and used as binder in paints, cosmetics etc.
5. In dentistry, chloroethane is used to diagnose a dead tooth due to its chilling effect.
6. This is also used to prevent pain caused by injections and minor surgical procedures and also used for temporary relief of minor sports injuries.
7. It also helps to relieve deep muscle pain.

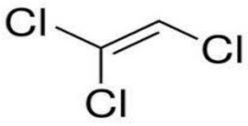
2. CHLOROFORM



USES

1. It is used as an anesthetic but it may cause cardiac and respiratory failure, so it has been replaced by other safe anesthetic.
2. With hydrogen fluoride it give monochloro-difluoromethane which is used in production of Teflon.
3. It is used as a solvent for fats, oils, rubber, alkaloids, waxes, resin and iodine.
4. It is used as cleansing agent in fire extinguisher and in rubber industry.
5. It is useful laboratory reagent for testing primary amines.
6. It is used in preparation of Chloropicrin and chloretone.
7. Chloroform contains deuterium $CDCl_3$ is common solvent in NMR.

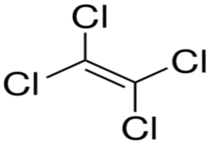
3. TRICHLOROETHYLENE



USES

1. It is used as solvent for variety of organic materials.
2. It is used to extract vegetable oils from plants.
3. It is used for decaffeination from coffee.
4. It is also used for the preparation of flavouring extract from spices.
5. It is used as cleaning agent to clean metal parts and electronic parts.
6. It is used in the synthesis of pesticides like trichlorfon and dimethoate.
7. It is used as extracting agent for purification of pharmaceutical intermediates-methoxy-phthalic acid.
8. It is used as solvent for waterless drying.

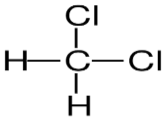
4. TETRACHLOROETHYLENE



USES

1. Due to its inflammability properties it is used as dry-cleaning solvents.
2. It is used for the production of chlorofluorocarbons and hydrofluorocarbons.
3. In textile industries, it is used to remove oils from fabrics after knitting and weaving operations and also used as solvent for sizing and desizing and water repellants.
4. It is used in neutrino detectors where a nuterino interacts with a neutron in the chlorine atom converts it to a proton to form argon.
5. In printing industries, TCE is used to clean unpolymerized coating fron the flexible film and used in printing inks.

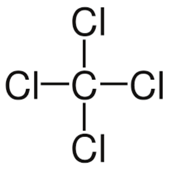
5. DICHLOROMETHANE



USES

1. It is used as a solvent due to its ability to dissolve wide range of organic compounds.
2. It is used as degreaser and paint strippers.
3. In food industry it is used in decaffeinate the coffee and tea.
4. It is used as aerosol spray propellant and as a blowing agent for polyurethane.
5. It is used in material testing in the field of civil engineering.

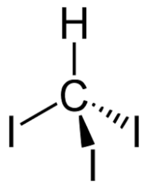
6. TETRACHLOROMETHANE



USES

1. It is used in fire extinguisher under the name pyrene. It gives dense, incombustible vapours which covers burning substance and prevent oxygen from reaching them and hence stop fire.
2. It is used as solvent for many organic compounds.
3. It is used as fumigants.
4. It is used for removing hook worms from the intestine of infected human.
5. Due to its good solvent property it is used in IR spectroscopy.
6. It is used as a source of chlorine in the Appel reaction.

7. IODOFORM

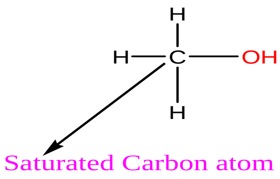


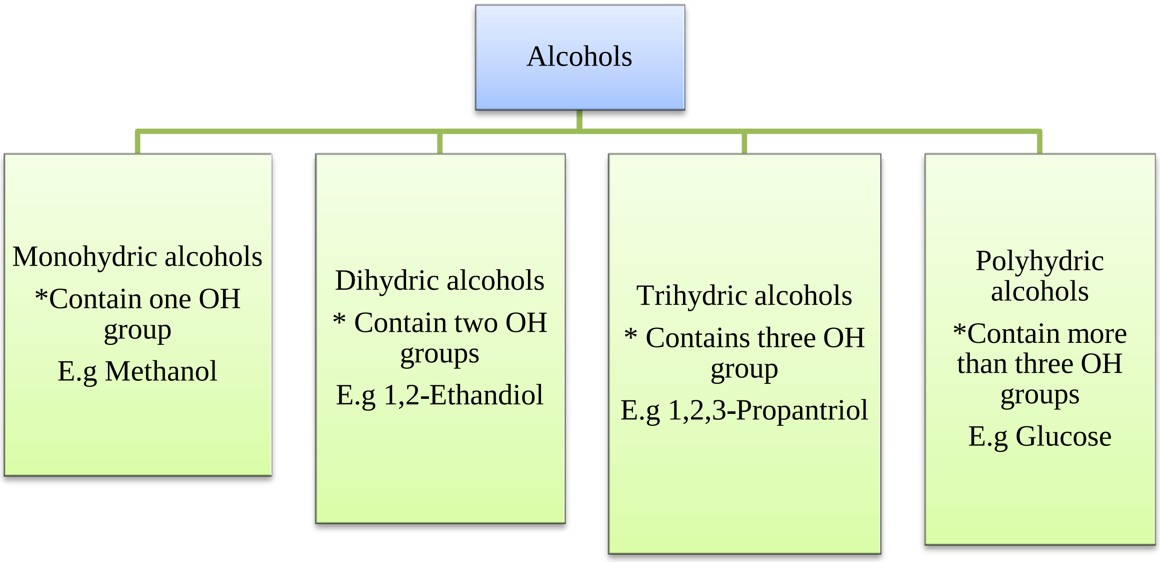
USES

1. It is used as disinfectant and Antiseptic
2. It was also used for sterilization of instruments which was used for surgery.
3. It is active ingredient in many ear powders for dogs and cats along with zinc oxide and propanoic acid which are used to prevent infection and facilitate removal of ear hairs

ALCOHOLS

The compounds in which a (-OH) group is attached to the saturated carbon atom with general formula R-OH.





Alcohols

Monohydric alcohols
*Contain one OH group
E.g Methanol

Dihydric alcohols
* Contain two OH groups
E.g 1,2-Ethandiol

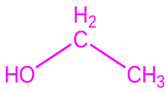
Trihydric alcohols
* Contains three OH group
E.g 1,2,3-Propantriol

Polyhydric alcohols
*Contain more than three OH groups
E.g Glucose

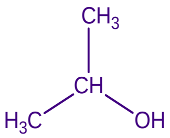
NOMENCLATURE

1. **Common System** – In this system, alcohols are named alkyl alcohol. The alkyl group attached to the OH group is named and alcohol is added as separate word. **E.g**

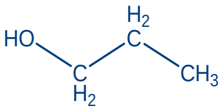
Methyl alcohol



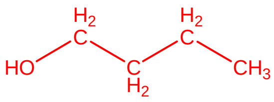
Ethyl alcohol



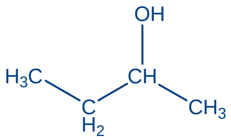
Isopropyl alcohol



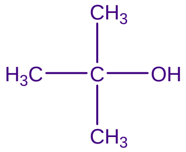
n-propyl alcohol



n-butyl alcohol



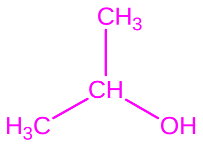
sec-butyl alcohol



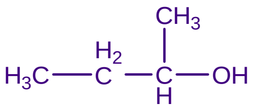
tert-butyl alcohol

2. **Carbinol System-** In this system alcohols are considered derivatives of Methyl alcohol which is called Carbinol.

Carbinol



Dimethyl carbinol (IPA)

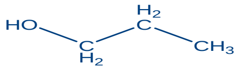


Ethyl methyl carbinol

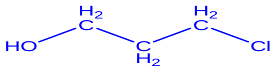
3. **IUPAC System** – In this system alcohols are named Alkanols.

- Select the longest chain containing the OH group.
- Drop the ending e in alkanes and replace with ol.
- Number the chain so as to give carbon carrying the OH group, the lowest possible number.
- Indicate the position of other substituent or multiple bonds by the number.

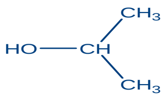
Methanol



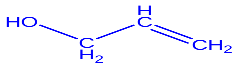
1-Propanol



3-Chloro-1-propanol



2-Propanol

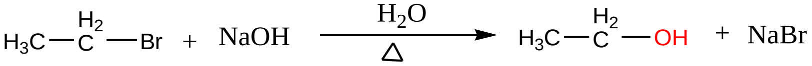


Prop-2-en-1-ol

Method of Preparation-

1. **Hydrolysis of alkyl halide**- Alkyl halide reacts with aqueous NaOH to form alcohol

$$R\text{-}X + NaOH \xrightarrow[\triangle]{H_2O} R\text{-}OH + NaX$$

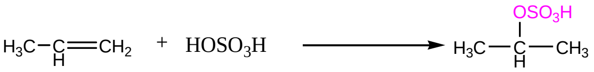


$$H_3C-\overset{H_2}{C}-Br + NaOH \xrightarrow[\triangle]{H_2O} H_3C-\overset{H_2}{C}-OH + NaBr$$

Ethylbromide

Ethanol

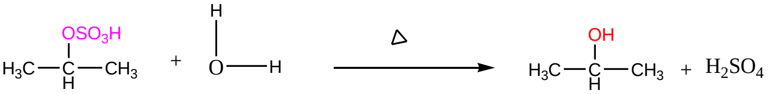
2. **Hydration of Alkenes-** Alkenes react with H_2SO_4 to produce alkyl hydrogen sulfate. Alkyl hydrogen sulfate on hydrolysis gives alcohol.



$$H_3C-\underset{H}{C}=CH_2 + HOSO_3H \longrightarrow H_3C-\underset{H}{\overset{OSO_3H}{C}}-CH_3$$

Propylene

Isopropylhydrogen sulphate

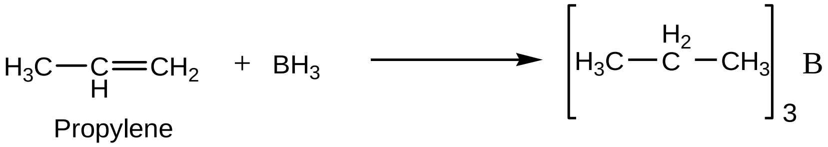


$$H_3C-\underset{H}{\overset{OSO_3H}{C}}-CH_3 + H-O-H \xrightarrow{\triangle} H_3C-\underset{H}{\overset{OH}{C}}-CH_3 + H_2SO_4$$

Isopropylhydrogen sulphate

Isopropyl Alcohol

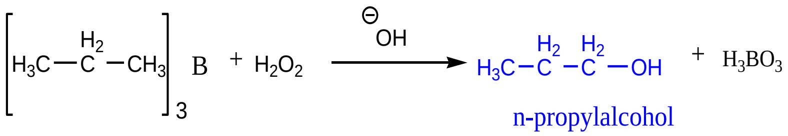
3. **Hydroboration Oxidation of Alkenes** – Alkenes react with diborane B_2H_6 to form trialkylborane. Diborane adds as borane, BH_3 the positive part is Boron and negative part is hydrogen.



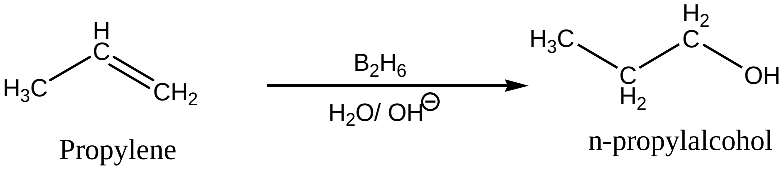
$$H_3C-\underset{H}{C}=CH_2 + BH_3 \longrightarrow \left[H_3C-\overset{H_2}{C}-CH_3\right]_3 B$$

Propylene

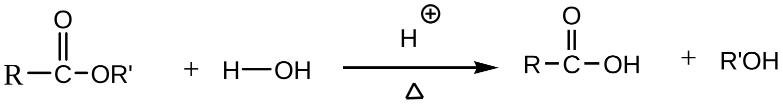
Trialkylborane used for making primary alcohols by reaction with alkaline aqueous solution of H_2O_2.

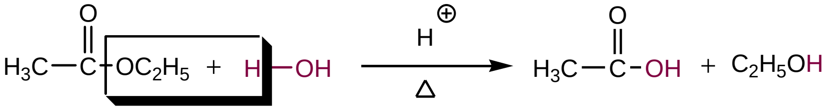


The overall result of the above reaction appears to be Anti-Markonikov's addition to water to double bond.

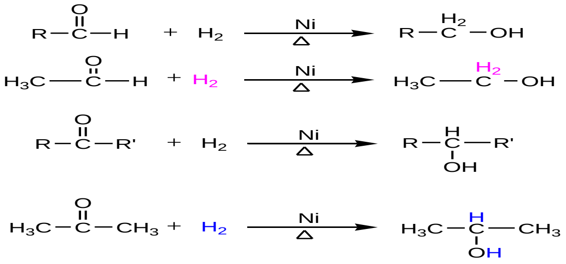


4. **Hydrolysis of Ester-** Alcohols may be prepared by base or acid catalysed hydrolysis of ester.

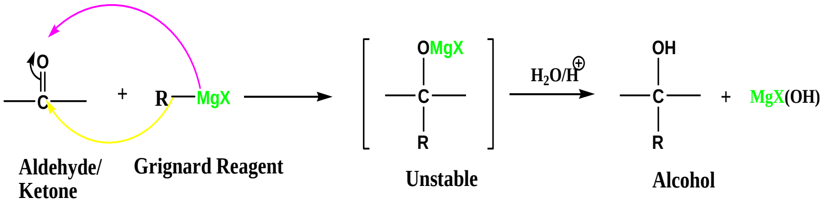




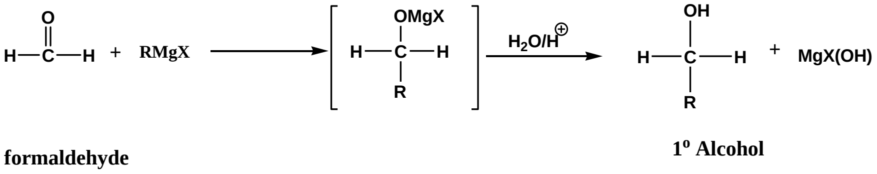
5. **Reduction of Aldehydes and Ketones –** Aldehydes and ketones can be reduced with H_2/Ni or Lithium aluminium hydride to form the corresponding alcohol. Aldehyde gives primary alcohol. Ketones give secondary alcohols.

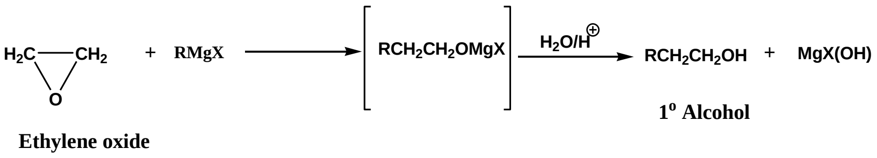


6. **Addition of Grignard reagent to aldehyde and Ketones-** Grignard reagent react with aldehyde and ketone to form an addition compound which on hydrolysis with dilute acid gives the corresponding alcohols.

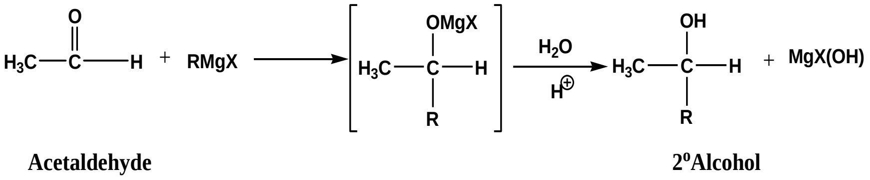


Primary alcohol are obtained by treating a Grignard reagent with formaldehyde or ethylene oxide

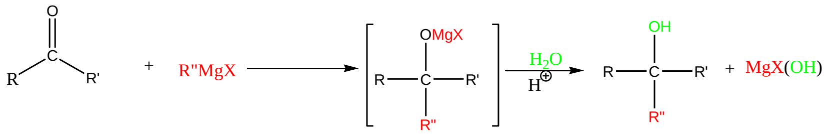




Secondary alcohols are obtained by treating a Grignard reagent with aldehyde other than formaldehyde.



Tertiary alcohols are obtained by treating reagents with ketones.



3^o Alcohol

7. Fermentation of Carbohydrates

Some alcohols can be prepared by fermentation of starches and sugar under the influence of suitable microorganism.E.g

$$\underset{\text{Glucose}}{C_6H_{12}O_6} + \text{Yeast} \xrightarrow{\text{Fermentation}} \underset{\text{Ethyl alcohol}}{2CH_3CH_2OH} + 2CO_2$$

Physical Properties of Alcohol

1. Lower alcohols are colourless,toxic liquids. They have a characteristic smell.
2. Boiling point of alcohols increase regularly with the increase in the number of carbon atoms

Name	Structure	No. of Carbon Atoms	Boiling point (^oC)
Methanol	CH_3OH	1	64.5
Ethanol	CH_3CH_2OH	2	78.3
1-Propanol	CH_3CH_2 CH_2OH	3	97.0
1-Butanol	CH_3CH_2 CH_2 CH_2OH	4	118.0
1-Pentanol	CH_3CH_2 CH_2 CH_2 CH_2OH	5	138.0

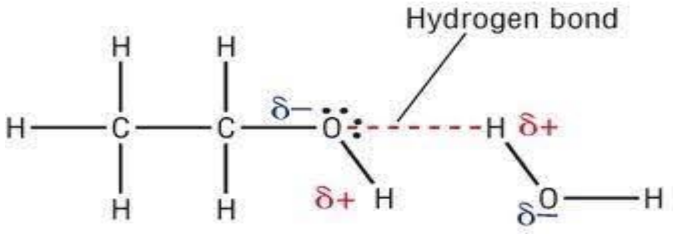
3. Among isomeric alcohol, as branching increase the boiling point decrease. E.g

Name	Boiling point (^oC)
1-Butanol	118
2-Butanol	99
2-Methyl-2-propanol	83

4. Boiling point of alcohols are much higher than that of alkanes.

EXPLANATION

The O-H bond of alcohols is highly polar because oxygen is electronegative. The oxygen carries a partial negative charge and hydrogen carries partial positive charge. This polarity gives rise to the force of attraction between partially positive and partially negative charges in another molecule of alcohol. This force of attraction is known as **Hydrogen bonding. The reason that alcohol has a higher boiling point is that great energy is required to overcome these attractive forces.**

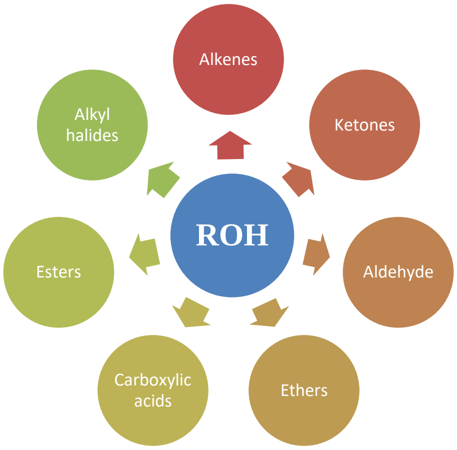


Lower alcohols are completely soluble in water. As we go higher in the series the water solubility falls rapidly.

EXPLANATION

A compound that forms hydrogen bonds between its own molecule can also form hydrogen bonds with water. These alcohol water bonds are the cause of high solubility of lower in water. In higher alcohols the nonpolar alkyl groups became more important. They have less tendency to form hydrogen bond with water.

CHEMICAL PROPERTIES



Reaction with Active metal- Alcohols react with sodium or potassium to form alkoxide with the liberation of hydrogen gas.

$$2ROH + 2Na \longrightarrow 2RONa^{+} + H_2$$

Sod.alkoxide

$$2CH_3CH_2OH + 2Na \longrightarrow 2CH_3CH_2ONa^{+} + H_2$$

Sod.ethoxide

The above reaction shows that alcohols are acidic in nature. The reason for this is that the O-H bond in alcohols is polar and allows the release of hydrogen atom as proton . However the alcohols are weaker acids than water. This is because the alkyl group in alcohols have a +I effect. They release electrons toward the oxygen atom so that it became negatively charged. This negative charge on oxygen make the release of positive proton more difficult.

Reaction with Phosphorus halide- Alcohols react with phosphorus pentahalide and phosphorus trihalide to form alkyl halide.

$$R{-}OH + PX_5 \longrightarrow R{-}X + POX_3 + HX$$

$$CH_3CH_2OH + PBr_5 \longrightarrow CH_3CH_2Br + PBr_3 + HBr$$

$$3\ R{-}OH + PX_3 \longrightarrow 3\ R{-}X + H_3PO_3$$

Reaction with Thionyl Chloride- Alcohol react with thionyl chloride to form alkyl chloride

$$R{-}OH + SOCl_2 \longrightarrow R{-}Cl + SO_2 + HCl$$

Reaction with hydrogen halides- Alcohols react with hydrogen halides (HX) to form the Corresponding alkyl halides.

$$R\text{-}OH + HX \longrightarrow R\text{-}X + HOH$$

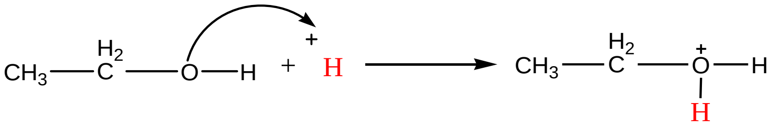
Where HX= HI, HBr, HCl

$$CH_3CH_2OH + HBr \longrightarrow CH_3CH_2Br + HOH$$

In general, tertiary alcohols react rapidly with hydrogen halides; secondary alcohols react Somewhat slower; and primary alcohols, even more slowly. The order of reactivity of hydrogen Halides is HI> HBr> HCl. HCl reacts only in the presence of a catalyst (anhydrous ZnCl,). No catalyst is required in the case of HBr or HI

MECHANISM. Primary alcohols react with hydrogen halides by an SNl mechanism. The Mechanism of the reaction between ethyl alcohol (1° alcohol) and hydrogen bromide is described below:

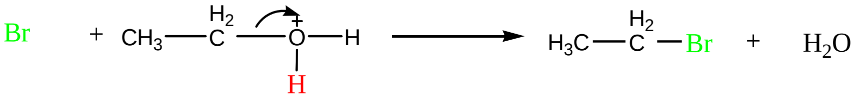
Step 1. Protonation of ethyl alcohol



Ethyl alcohol

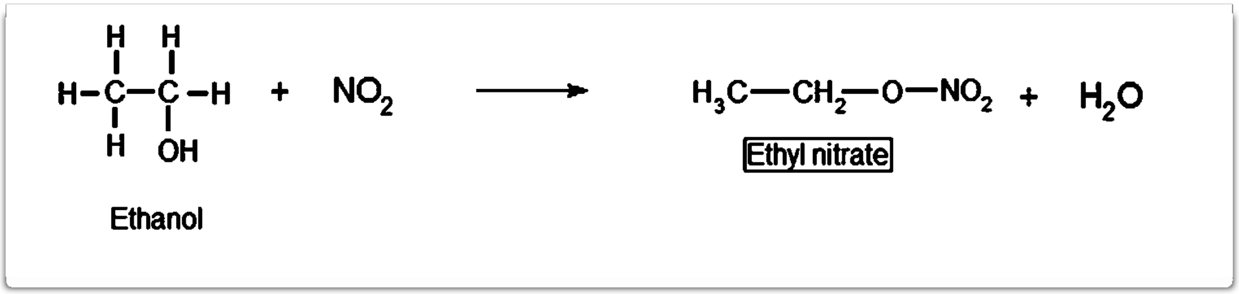
Protonated alcohol

Step 2- Nucleophile attack the carbon holding the protonated hydroxyl group to form ethyl bromide



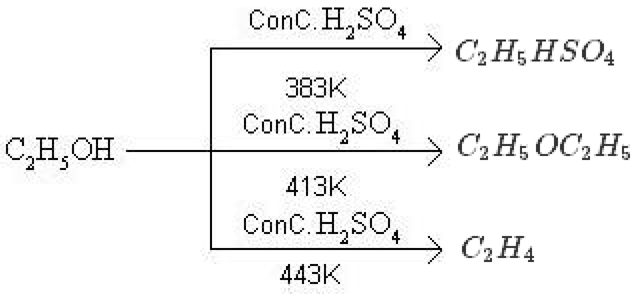
Protonated alcohol

Reaction with Nitric acid- Alcohol react with nitric acid to form alkyl nitrate. Eg.

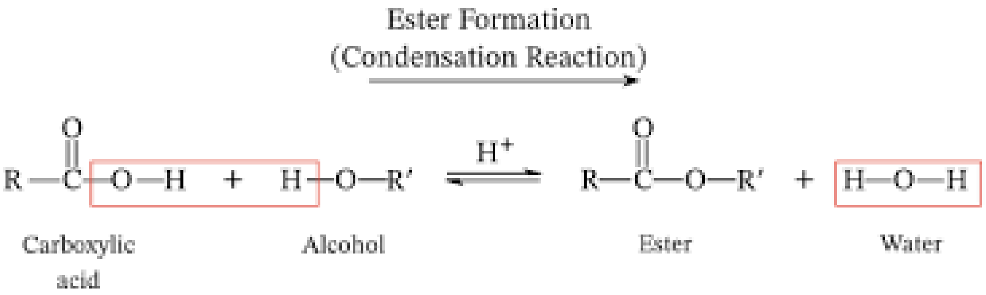


Reaction with sulphuric acid - The reaction of sulphuric acid is very sensitive to reaction condition. Eg.

- When ethyl alcohol is treated with conc. Sulphuric acid at room temperature, ethylhydrogen sulphate is produced.
- Dehydration of alcohol to ether- When excess of ethyl alcohol is treated with conc. Sulphuric acid at 140^{0}C, diethyl ether is formed. Two alcohol molecules are involved in the reaction.
- Dehydration of alcohols to alkenes- when ethyl alcohol is treated with conc. Sulphuric acid at 170^{0}C, ethylene is formed.

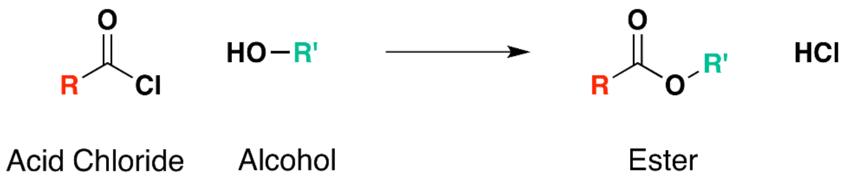


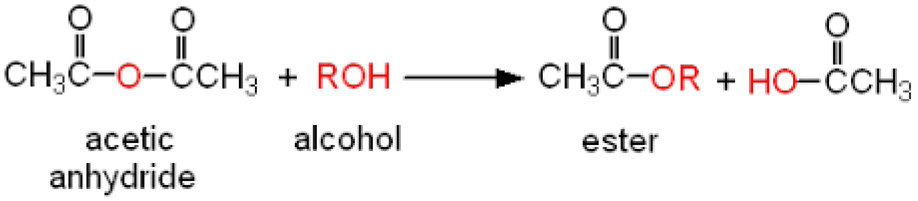
Reaction with carboxylic acid – Alcohol react with carboxylic acid to form ester. Conc. Sulphuric acid is used as catalyst. The reaction is reversible and can be shifted in the forward direction by removing water as soon as it is formed.



The reaction between alcohol and a carboxylic acid to form an ester is called as **Esterification reaction.**

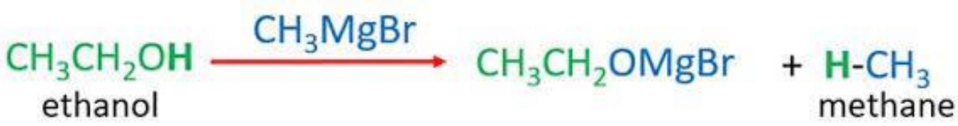
Reaction with Acid halides and anhydrides- Alcohols react with acid halides and anhydride to form esters.





$$CH_3COOCOCH_3 + ROH \rightarrow CH_3COOR + HOCOCH_3$$

Reaction with Grignard reagent- Alcohols react with Grignard reagent to form alkanes.



$$CH_3CH_2OH \xrightarrow{CH_3MgBr} CH_3CH_2OMgBr + H\text{-}CH_3$$

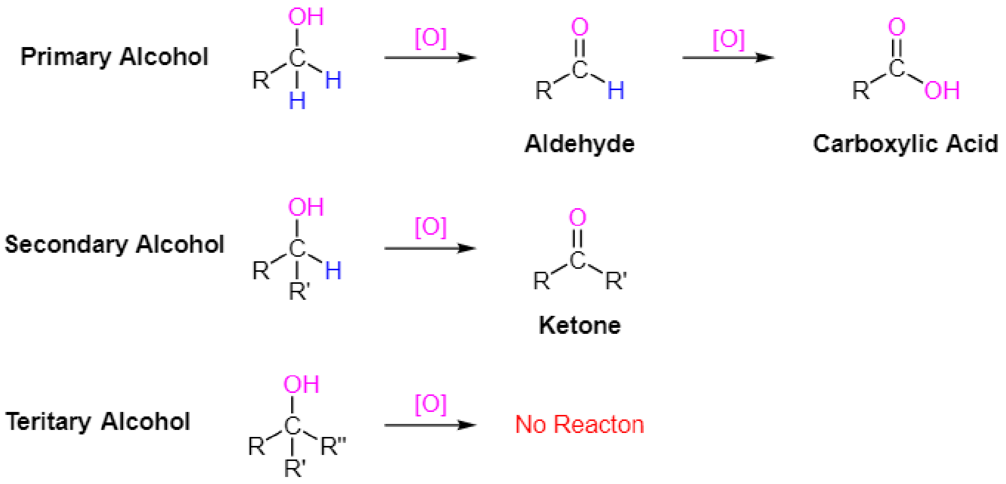
Reduction- Alcohol undergoes reduction with concentrated hydroiodic acid and red phosphorus to produce alkanes.

$$ROH + 2HI \xrightarrow[150^\circ C]{\text{Red P}} R\text{—}H + H_2O + I_2$$

Oxidation- Alcohols can be oxidized. The nature of product depends on type of alcohols and the condition of the reaction. Most widely used oxidizing agents are $KMnO_4$+ H_2SO_4 or $Na_2Cr_2O_7$+ H_2SO_4.Oxidation of alcohols can be used to distinguish between primary, secondary and tertiary alcohols.

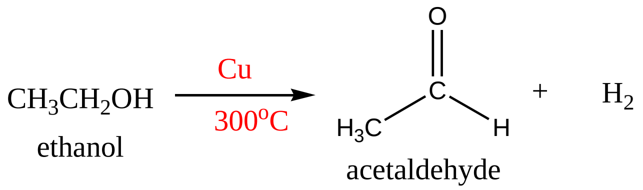
- Primary alcohols are first oxidized to aldehyde and then to acid.
- Secondary alcohols are oxidized to corresponding ketones.
- Tertiary alcohols are stable to oxidation under normal condition.

Under drastic condition , tertiary alcohols give ketones and acids, each contain less carbon than alcohols

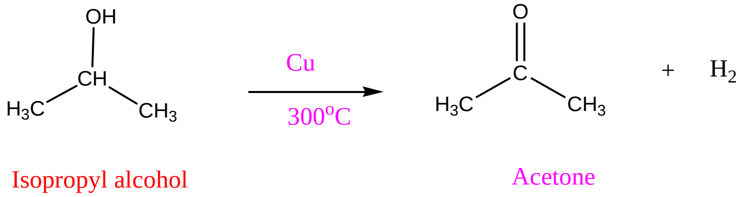


Reaction with the hot Copper- Dehydrogenation – Different types of alcohols give different products when their vapors are passed over coper guaze at 300^0C.

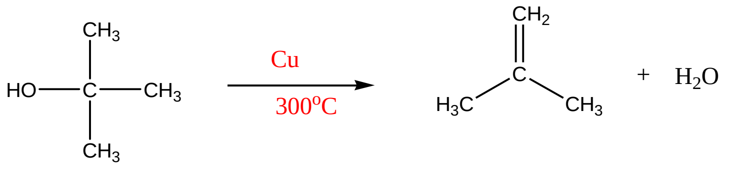
Primary alcohol lose hydrogen and give an aldehyde.



Secondary alcohol lose hydrogen and yield a ketone.



Tertiary alcohol are not dehydrogenated but lose a molecule of water to give alkenes



Tert-butylalcohol 2-Methylpropene

TESTS TO DISTINGUISH 1°,2°,3° ALCOHOLS

1. **LUCAS TEST –** In this test, alcohols are treated with solution of HCl and Zinc Chloride (Lucas Reagent) to form alkyl halide. Zinc Chloride serve as a catalyst.

$$R{-}OH + HCl \xrightarrow{ZnCl_2} R{-}Cl + H_2O$$

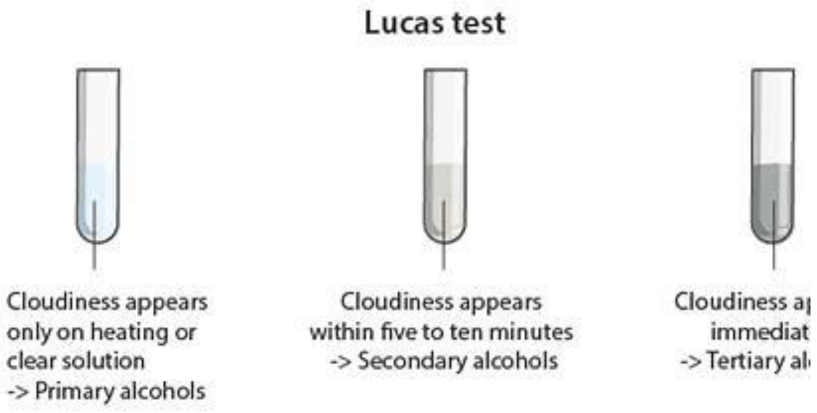
Three types of alcohols undergoes this reaction at different rates. Tertiary alcohol react with Lucas Reagent very rapidly. Secondary alcohols react somewhat slower. Primary alcohols react with lucas reagent somewhat more slower.

An alcohol is mixed at room temperature with conc. HCl and $ZnCl_2$. The alkyl chloride formed is insoluble in the medium it causes the solution to become cloudy before it separates as distinct layer.

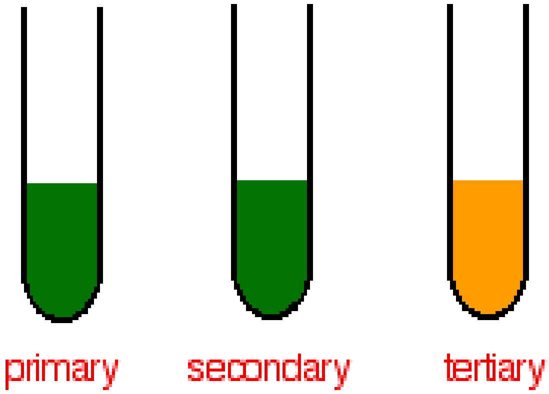
a) With Tertiary alcohols cloudiness appears immediately.

b) With Secondary alcohols cloudiness appears in 5 minutes.

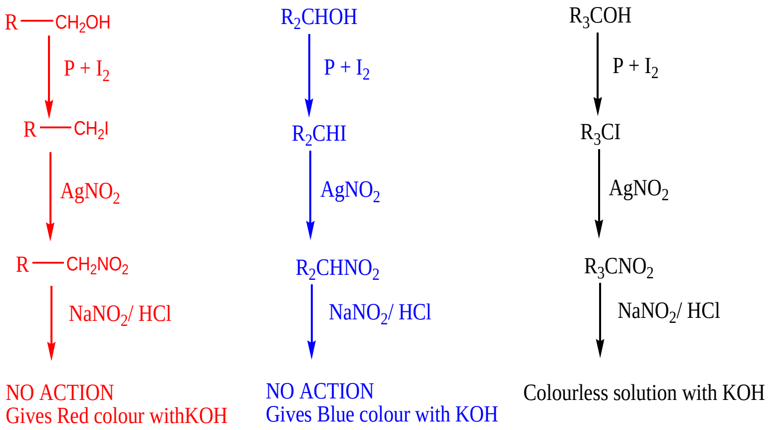
c) With Primary alcohols the solution remains clear. This is because primary alcohols do not react with Lucas reagent at room temperature.



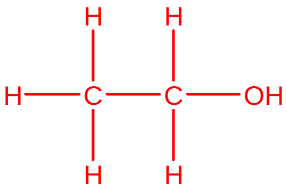
2. **DICHROMATE TEST-** This test is based on the fact that different types of alcohol gives different products on Oxidation. The alcohol is treated at room temperature with sodium dichromate in sulphuric acid. Identification of product gives us information regarding the type of alcohol
   a) **Primary alcohols** give a Carboxylic acid containing the same number of carbons. There will be a change in color of solution from orange to green.
   b) **Secondary alcohols** give a ketone containing the same number of carbon. There will be a change in color of solution from orange to green.
   c) **Tertiary alcohols** do not react under these conditions. Solution will remains orange.



3. **VICTOR MEYER'S METHOD-**The test is carried by the following sequence of reaction.
   - The alcohol is first treated with phosphorus and iodine to convert it into the corresponding iodide.
   - The iodide is then treated with silver nitrate to get corresponding nitroparaffin.
   - The nitroparaffin is finally treated with nitrous acid and then made alkaline, then primary alcohols give red colour, Secondary give blue colour and tertiary gives no colour.



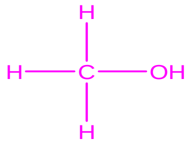
1. ETHANOL



USES

1. It is used to make alcoholic beverages- wine, Whiskey, Beer .
2. It is used as a medicine , as a topical antiinfective agent.
3. It is used in mouthwashes because of its antibacterial property.
4. It is used as Antidote for ethylene, glycol and methanol overdose.
5. It is used as road side breather test.
6. Medicinally it is used to depress CNS.
7. It is used for purification of DNA and RNA.

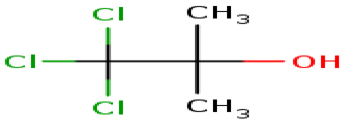
2. METHYL ALCOHOL



USES

1. It is also known as wood alcohol because it is obtained by destructive distillation of wood.
2. It is used as solvent in paints.
3. It is used as Antifreezer for automobile radiation.
4. It is also used to denature ethyl alcohol.
5. It is also used as motor fuel.
6. It is also used in the manufacturing of formaldehyde.

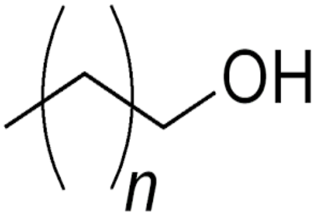
3. Chlorobutanol



USES

1. It is used as chemical preservative for eye drops, injectables, mouthwashes and cosmetic products.
2. It is used as weak local anesthetic .
3. It is used as sedative and hypnotics.
4. It has Antibacterial and fungicidal action.

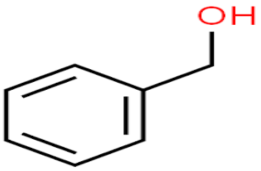
4. **Cetostearyl alcohol**- It is mixture of steryl and cetyl alcohol that can come from synthetic or vegetable sources.



USES

1. In pharmaceutical industry it functions as emulsion stabilizer, surfactant, foam booster and viscosity increasing agent.
2. It is often used in creams and lotions.

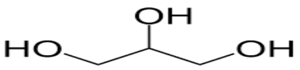
5. Benzyl alcohol



USES

1. It is used aginst head lice.
2. It is used as Antimicrobial preservative.
3. It is used as general solvent for inks, waxes, paints and epoxyresins, coating.
4. It has antipruritic activity to relieve itching.

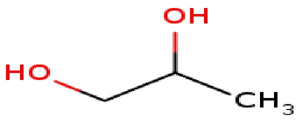
6. GLYCEROL -



USES

1. It is used as emollient, humectant and lubricant in personal care industry, shaving creams, soaps, mouth washes and tooth paste.
2. It is used as hair conditioner.
3. To make suppositories which acts as laxative.
4. As anti freezer in automobiles.

7. Propylene glycol



USES

1. Commonly used as food additives.
2. It helps to retain moisture as well as dissolve color and flavour.
3. It is used as humectant.
4. As a working fluid in hydraulic press.
5. In fragrance oil
6. As coolant in distilleries.
7. In hand sanitizers, antibacterial lotions and saline solution.

2 MARKS QUESTION

1. Define Alkyl Halides.
2. What is Saytzeff rule? Give example.
3. Although alkyl halides are polar yet insoluble in water.?
4. Why alkyl halides give alcohols with aq. KOH whereas with alcoholic KOH these give alkene?
5. What is Wurtz reaction? Give example.
6. Give structure and medicinal uses of Chloroform.
7. Give structure and medicinal uses of Dichloromethane.
8. Give structure and medicinal uses of Ethyl chloride.
9. Vinyl halides are less reactive than alkyl halides. Why?
10. Define Elimination reaction. Give example.
11. Give Classification of Alkyl Halides.
12. Give the tests to distinguish primary, secondary and tertiary alcohols.
13. What are alcohols give example of mono, di, trihydric alcohol with example?
14. What is carbinol?
15. Explain the structure of methanol.
16. Give the physical properties of alcohols.
17. Give the structure and uses of Benzyl alcohol.
18. Give the oxidation reaction of alcohols.
19. Why alcohols have higher boiling point than alkyl halides.
20. Draw structural formula of the followings.
    - 3-Phenyl-1-propanol
    - 2-Chloro-2,4-dimethyl-3-hexanol.
21. What happens when ethanol is reacted with thionyl chloride and phosphorus halide.

5 & 10 MARKS QUESTION

1. Discuss the mechanism of SN_1 and SN_2 reactions.
2. Discuss factors influencing SN_2 reaction.
3. Discuss factors influencing SN_1 reaction.
4. Discuss the stereochemistry of SN_1 and SN_2 reactions.
5. Explain the followings
    - Hydroboration oxidation
    - Hydrolysis of ester
6. What are Mono, di, trihydric alcohols? Give example of each class.
7. Give the method of preparation of alcohols.
8. Enlist various qualitative tests of alcohols.
9. Give the physical and chemical properties of alcohols.
10. Write the test to distinguish different types of alcohols.
11. Give the 4 methods of preparation of alcohols.
12. Write different chemical reactions of alcohols.
13. Write the structure and uses of the followings
    - Ethanol
    - Propylene glycol.
    - Benzyl Alcohol
    - Glycerol.
14. Write a detail note on alcohol and give method of preparation.