

PHARMACEUTICAL CHEMISTRY

Alkanes, Alkenes, Alkynes, Alkyl Halides, Alicyclic Hydrocarbons, Alcohols, Ethers and Epoxides, Aldehydes and Ketones, Carboxylic Acids and their Functional Derivatives

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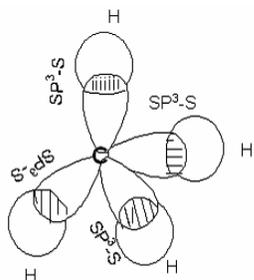
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Keywords

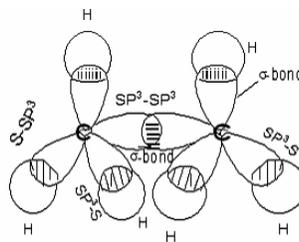
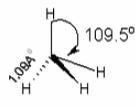
Alkanes, alkenes, alkynes, alkyl halides, alicyclic hydrocarbons, alcohols, ethers, epoxides, aldehydes, ketones and carboxylic acids

Alkanes

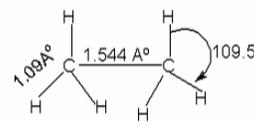
The alkanes are simplest and least reactive class of organic compounds, because they contain only carbon and hydrogen and they have no functional groups. They also referred to as Paraffins. Alkanes are the saturated hydrocarbon with general formula (C_nH_{2n+2}). Alkanes contain only single covalent carbon-carbon (C-C) and Carbon –Hydrogen(C-H) bonds. Each carbon atom of alkanes is sp^3 hybridized.



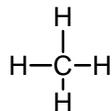
Structure of Methane



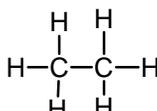
Structure of Ethane



All C-C and C-H bonds are σ bonds and every C-H and C-C bond lengths have the value $1.09A^\circ$ and $1.54A^\circ$ respectively. All bond angles are tetrahedral (109.5°) because of tetrahedral position of the four bonds of carbon, the C-C chain is zig-zag and not linear some examples of the alkanes are



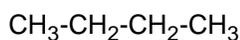
Methane [CH_4]



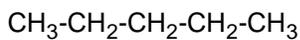
Ethane [C_2H_6]



Propane [C_3H_8]

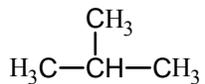


Butane [C_4H_{10}]

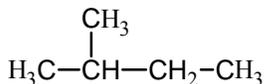


Pentane

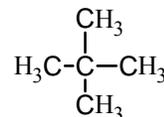
First three members do not exhibit isomerism but the higher members [butane and onwards] exhibit chain isomerism.



Iso butane [C_4H_{10}]



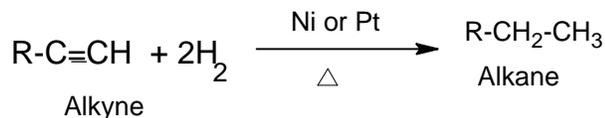
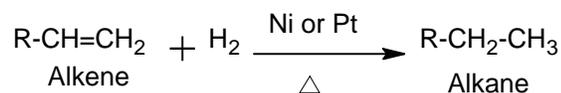
Iso pentane [C_5H_{12}]



Neo pentane [C_5H_{12}]

Methods of preparations:

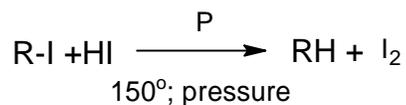
i) Hydrogenation of unsaturated hydrocarbons: Alkenes or alkynes react with hydrogen in presence of catalyst (Ni, Pt or Pd) at $200-300^\circ C$ to give alkanes. (Sabatier and Senderen's reaction).



ii) **Reduction of alkyl halide:** Alkyl halide on reduction gives alkanes. Reducing agents used for reduction are zinc and acetic acid; Zn-Cu couple in ethanol; or LiAlH₄, H₂ gas and Ni or Pt catalyst.



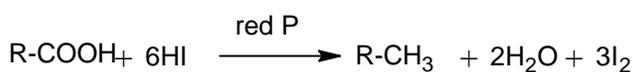
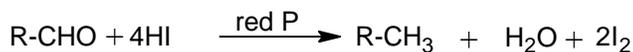
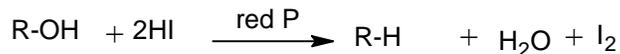
Alkyl iodides are conveniently reduced by heating with HI and red P in sealed tube.



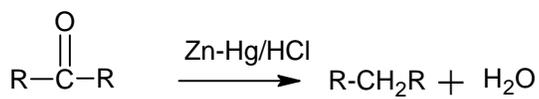
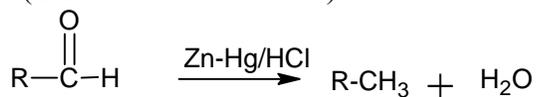
The function of red phosphorous is to remove the iodine formed by forming PI₃ otherwise it would react with alkane to give back alkyl iodide.

iii) Reduction of Alcohols, Aldehydes, Ketones and fatty acids:

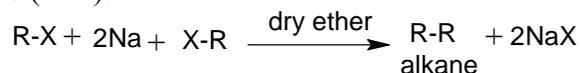
a) Alcohols, aldehydes, ketones and fatty acids can be reduced with hot hydroiodic acid and red phosphorous to give alkanes.



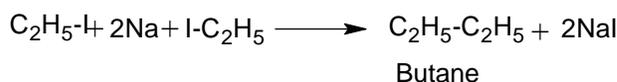
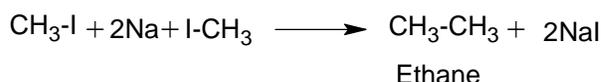
b) Aldehydes and ketones can also be reduced to alkanes by means of amalgamated zinc and Conc. Hydrochloric acid (Clemmensen reduction)



iii) Wurtz Reaction: Higher alkanes are produced by heating an alkyl halide with sodium metal in dry ether solution. Two molecules of alkyl halide (RX) condense with sodium metal to give symmetrical alkane (R-R).

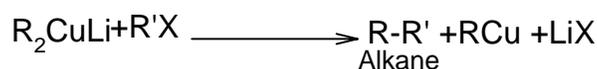


If two reacting alkyl halides are different, mixture of three alcohols are produced which is difficult to separate. For example methyl iodide and ethyl iodide gives the mixture of ethane, propane and butane.



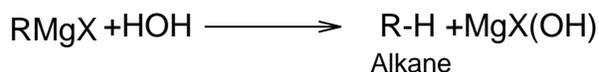
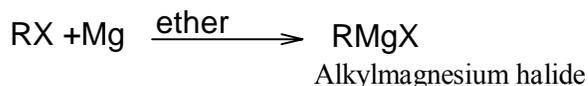
USE:-Therefore this method is useful only for the **preparation of symmetrical alkanes**.

v) Corey-House Alkane synthesis: This method is superior to Wurtz synthesis. It involves first conversion of alkyl halide to lithium dialkyl cuperate, LiR_2Cu and then coupling between lithium alkyl cuperate and an alkyl halide.

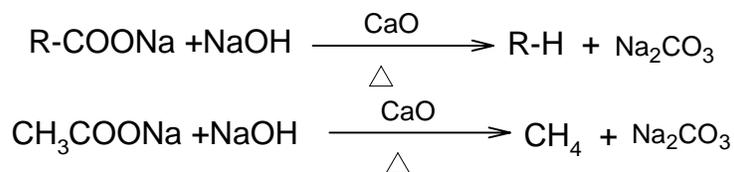


USE:-This method is suitable for **preparation unsymmetrical alkane**.

vi) Hydrolysis of Grignard Reagent: Alkyl magnesium halide which is prepared by treating alkyl halides with magnesium in dry ether, on hydrolysis yield alkane.



vii) Decarboxylation of Carboxylic acids: Salt of Carboxylic Acid when heated strongly with sodalime ($NaOH+CaO$), decarboxylate to give alkane.



USE:-The alkane produced has one carbon less in its structure as compared to parent.

viii) Kolbe's Synthesis: Alkane is collected at anode when a concentrated solution of sodium or potassium salt of carboxylic acid is electrolyzed using Platinum electrodes.



USE:-This method is also suitable for the **preparation of symmetrical alkanes**.

Properties of Alkanes:

Physical Properties:

- 1) First four members (methane to butane) are colourless, odourless gases, next thirteen (C_3 to C_{17}) are colourless, odourless liquids while higher alkanes are colourless wax like solids.
- 2) These are insoluble in water as they are nonpolar compounds but soluble in organic solvents like ether, benzene and acetone etc. Liquid alkanes are lighter than water.
- 3) In case of normal alkanes boiling points and specific gravities increase with rise in molecular weights. As a rule the boiling points of alkanes having branched carbon chain are lower than those of isomeric normal alkanes.
- 4) Variation in the melting point of alkanes is not regular. Alkanes with odd number of carbon atoms have lower melting point than the next lower and next higher alkanes having even number of carbon atoms. This is due to the greater inter molecular attraction in even numbered alkanes having end carbon on the opposite sides of the molecules.

Chemical properties:

- 1) Alkanes are extremely stable and inert substances. This is due to the fact that there is a small difference in the electro negativity of carbon (2.60) and hydrogen (2.10). Thus the bond electron in C-H bond are practically equally shared between them and the bond is almost non polar. The C-C bond is completely non polar. Therefore electrophilic or nucleophilic reagent find no site for attack on alkane molecules. Furthermore, the C-H and C-C bonds are strong bonds. Alkanes due to these types of strong bonds remain unaffected by acids, alkalis and oxidizing agents under ordinary conditions.

Lower alkanes undergo two types of reactions:

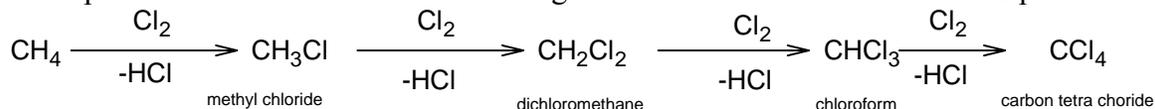
- i) Substitution Reaction
- ii) Thermal and catalytic Reactions

Some of the important reactions of alkanes are following.

1) Halogenations: This involves replacement of hydrogen atom by halogen atom.

a) Chlorination: Alkanes react with chlorine in presence U.V light or diffused sunlight or at temperature 300-400°C to form the corresponding substituted products.

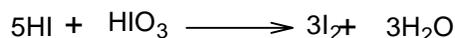
For example: Methane reacts with chlorine to give mixture of different substituted products.



It is difficult to stop this reaction at first step. However, the yield of CH₃Cl can be improved by taking excess of methane. Ethane and higher alkanes react with chlorine in a similar way and all possible substitution products are obtained.

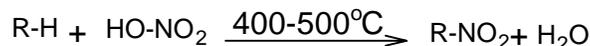
b) Bromination: Bromine reacts with alkanes in a similar way but slowly and at higher temperature.

c) Iodination: It is reversible. The hydrogen iodide formed during iodination reduces the product back to reactant hence it must be carried out in the presence of strong oxidizing agent like iodic acid or nitric acid which destroys the hydroiodic acid (HI) as it is formed.



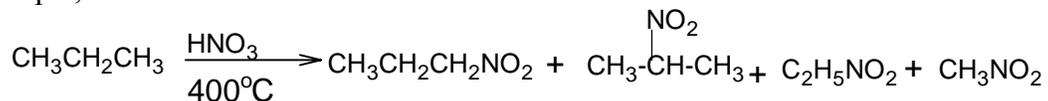
d) Fluorination: Since fluorine is most reactive, fluorination under ordinary condition accompanies by explosion. Fluoroalkane can however be obtained from alkane by action of fluorine diluted with Nitrogen.

2) Nitration: This involves replacement of hydrogen atom by –NO₂ group. Nitration is carried out by heating mixture of alkanes and nitric acid vapours at 400-500°C. The process is known as **Vapour Phase Nitration.**

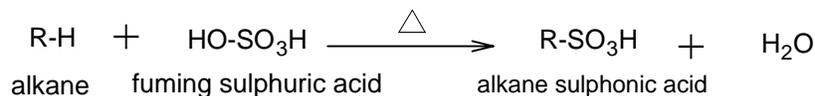


Since the reaction is carried out at high temperature, chain fusion also takes place during the reaction and mixture of all possible mono nitro derivatives are obtained.

For example,

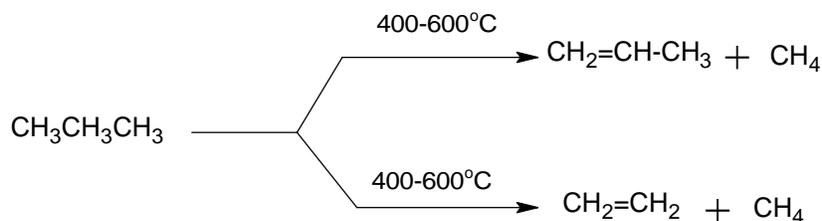


3) Sulphonation: This involves replacement of hydrogen atom by –SO₃H group. It is carried out by heating alkanes with fuming sulphuric acid or oleum at higher temperature.



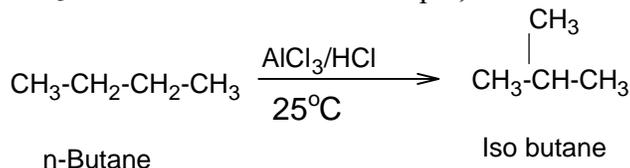
Lower alkanes do not give this reaction.

4) Thermal decomposition [Pyrolysis or Cracking]: The decomposition of compound by heat is known as pyrolysis. Thermal decomposition when applied to alkanes it is known as Cracking. This leads to the formation of lower alkanes, alkenes and hydrogen etc. For example

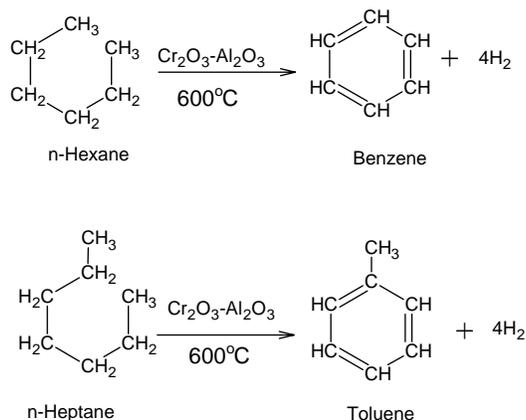


In presence of catalyst pyrolysis can be carried out at less higher temperature. This is called Catalytic Cracking.

5) Isomerisation: Conversion of alkanes to its chain isomer is carried out by heating normal alkane with anhydrous AlCl_3 and HCl at 25°C . For example,



6) Aromatisation: Conversion of aliphatic compound to aromatic compounds is known as aromatisation. Alkanes containing 6-10 carbon atoms are converted into benzene and its homologous at high temperature and in the presence of catalyst. For example:



7) Oxidation[Combustion]: When burnt in excess of air or oxygen alkanes form carbon dioxide and water with the evolution of heat.

For Example:



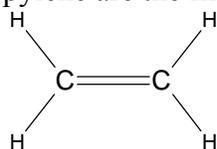
In general,



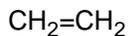
The evolution of heat in this reaction forms the basis of the use of these hydrocarbons as source of heat and power.

Alkenes or Olefins

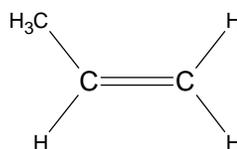
Alkenes are unsaturated hydrocarbons containing carbon-carbon double bond (C=C) in their molecules. General formula of alkene is C_nH_{2n} . They are commonly known as olefins because lower members form oil products with chlorine or bromine (Latin Oleum=Oil; ficane = to make). Ethylene and propylene are the first and second members of this series respectively.



or



Ethylene (C_2H_4)



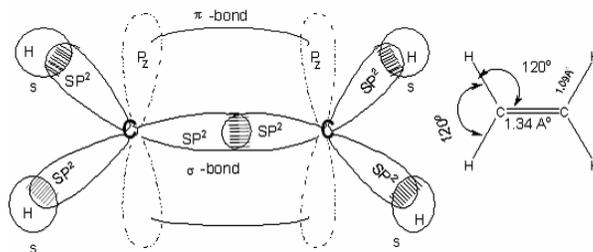
or



Propylene (C_3H_6)

Double bonded carbon in alkenes is sp^2 hybridised. The Carbon-Carbon double bond in alkene consists of one sigma (σ) and one pi (π) bond. Sigma bond is formed by overlapping of sp^2 hybrid orbital of each carbon and π bond is formed by overlapping of unhybridised p-orbitals. The two carbon atoms which are double bonded in alkenes are held more tightly together than in alkane with the result C=C bond length in alkene is less (1.34\AA) than C-C bond length in alkanes.

For example;

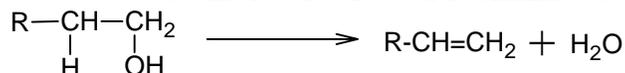


Orbital Structure of Ethene

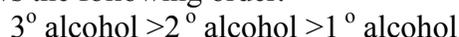
Alkenes are more reactive than alkanes this is due to the availability of more exposed π -electrons.

Methods of Preparations:

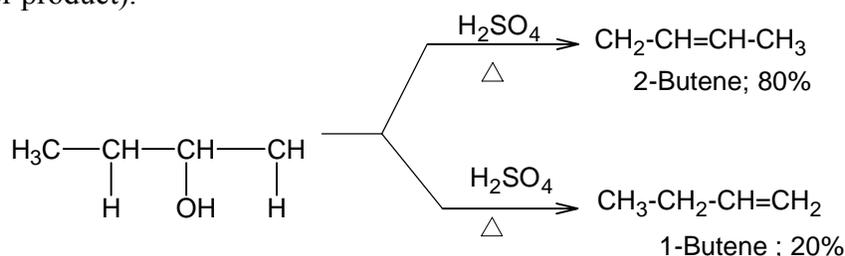
1) Dehydration of Alcohols: When an alcohol is heated with concentrated sulphuric acid at 100°C or with phosphoric acid at 200°C or by passing alcohol vapour over alumina, P_2O_5 or anhydrous zinc chloride at $350\text{-}400^{\circ}\text{C}$ a molecule of water is eliminated and alkene is formed.



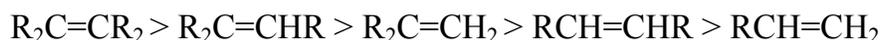
The ease of dehydration follows the following order.



Dehydration of unsymmetrical 2° or 1° alcohol can proceed in two ways and mixture of alkene is formed for example dehydration of 2-butanol yields mixture of 2-butene (major product) and 1-butene (minor product).

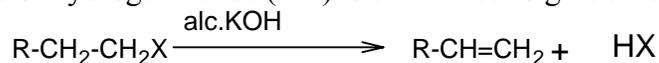


In such cases major products can be predicted by **Saytzeff's rule**. Which states that "Hydrogen is preferentially eliminated from the carbon atom with fewer number of hydrogen atoms." Thus 2-butene is the major product in above example. In other words Saytzeff's rule states that "Greater the number of alkyl groups attached to the double bonded carbon atoms, the more stable is the Alkene." Hence more substituted alkene is preferentially formed. The ease of formation of alkene is ,



This can be explained on the basis of more stability of more substituted carbonium ion formed.

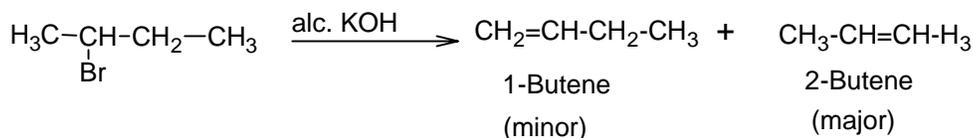
ii) By dehydrogenation of Alkyl halides: when an alkyl halide is heated with alcoholic NaOH or KOH, one molecule of hydrogen halide (HX) is eliminated to give alkene.



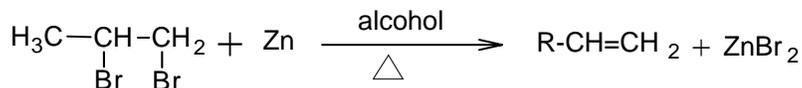
The ease of dehydrogenation of alkyl halide is



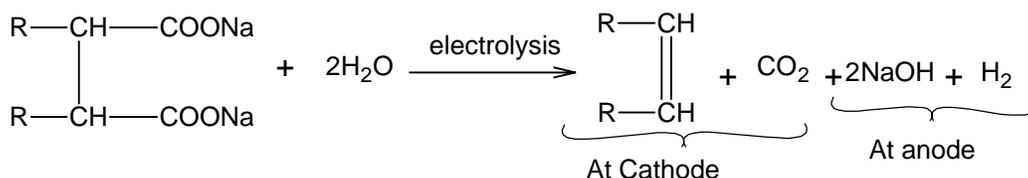
In case of dehydrogenation of 2° and 3° alkyl halides the major product can be predicted according to Saytzeff's rule. E.g.



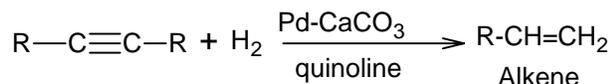
iii) **By Dehydro Halogenation of Vicinal Dihalide:** when vicinal dihalides (containing two halogen atoms at adjacent carbon) are heated with zinc dust in alcohol alkenes are produced.



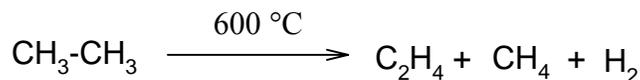
iv) **By Kolbe's electrolytic method:** electrolysis of aqueous solution of sodium or potassium salt of saturated dicarboxylic acids yields alkene.



v) **By controlled Hydrogenation of Alkyne:** Alkyne is presence of Lindlar Catalyst react with Hydrogen in controlled manners to give alkene. In Lindlar catalyst Pd is deactivated with CaCO_3 and quinoline.



vi) **Cracking of Alkanes:** Paraffins on heating at $500-800^\circ\text{C}$ in absence of air get decomposed to lower molecular weight alkene, alkanes and hydrogen.



Properties of Alkenes:

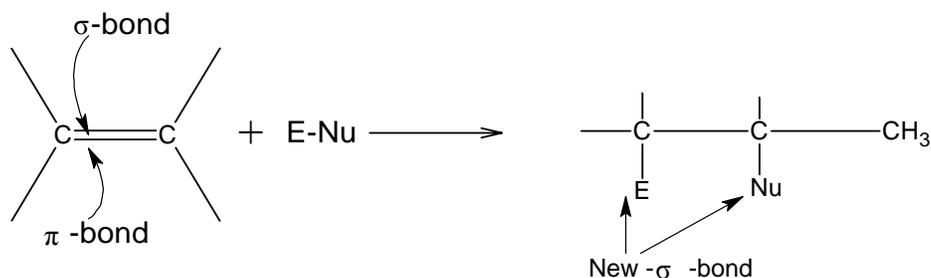
Physical properties:

- 1) The first three members are gases at ordinary temperature, next 14 are liquids and the higher ones are solids. Except ethylene all members are colourless and odorless. Ethylene is pleasant smelling gas.
- 2) Alkenes are only slightly soluble in water but soluble in non polar solvents.
- 3) Generally, their boiling points, melting points and specific gravities rise with increase of molecular weights. Further like alkanes, the branched chain alkenes have lower boiling points than the corresponding n-alkenes.
- 4) Like alkanes, alkenes are generally non polar, but certain alkenes due to their unsymmetrical structure are weakly polar. Trans alkene has a smaller dipole moment than cis-isomer because trans isomer is relatively more symmetrical than cis-alkene. Due to

poorer symmetry molecules of cis-alkenes do not fit into the crystal lattice so well as in the trans-isomer with the result cis alkenes have generally lower melting points than the trans.

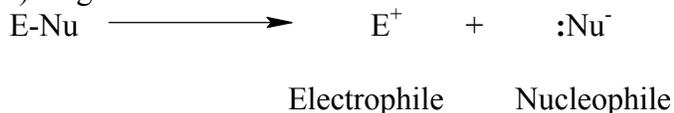
Chemical properties: Alkenes are more reactive than alkanes due to the presence of π -bond. The π electrons constituting π bond are located much farther the carbon nuclei and are easily available for reaction when needed. The overlap of atomic orbital forming π -bond is not as effective as that in σ bonds. Thus π bond is weaker than σ bond and can be easily broken.

Addition reactions are the most important reactions of the carbon-carbon double bond. π electrons of double bond are easily available to the reagent. Thus carbon-carbon double bond acts as a source of electrons for electrophilic reagents and undergoes electrophilic addition reaction.

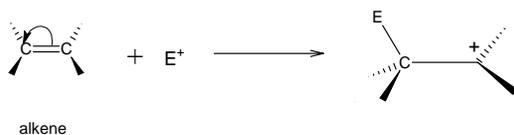


Mechanism of electrophilic addition to Carbon-Carbon double bond:

Step 1: Ionisation of (E-Nu) reagent

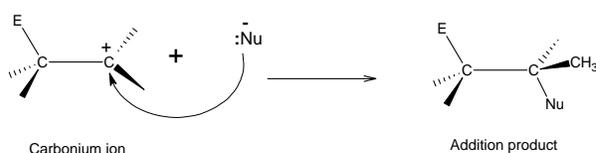


Step 2: Attack of electrophile (E^+) to Carbon- Carbon double bond.



The addition of electrophilic reagents relieves the strain of $\text{C}=\text{C}$ (bond angle 120°) by converting it to $\text{C}-\text{C}$ (bond angle 109.5°)

Step-3: The nucleophile (:Nu^-) attack the carbonium ion to give the addition product.



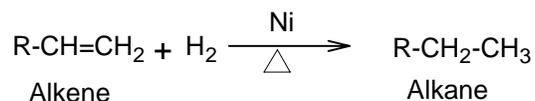
Because the addition reactions are initiated by electrophiles, they are referred to as electrophilic addition reactions.

E^+ is usually H^+ , Br^+ or Cl^+

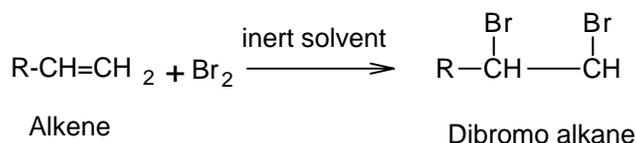
$:Nu^-$ is usually Br^- , Cl^- , OH^- or OSO_3H^-

Some of the important reactions of alkenes are following:

i) Addition of Hydrogen: Addition of hydrogen to alkenes takes place under pressure and in the presence of catalyst like Ni, Pt or Pd to produce saturated hydrocarbons. This is called catalytic hydrogenation.

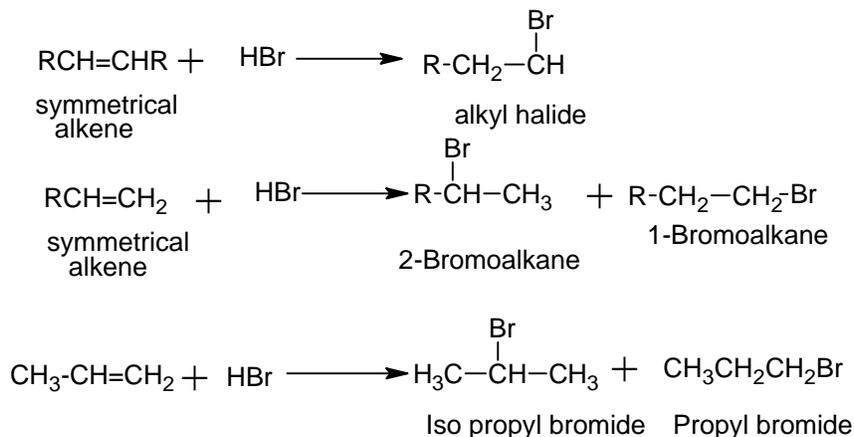


ii) Addition of Halogen: Alkenes reacts to halogen in presence of inert solvent to give dihalogen derivative for example.



iii) Addition of Hydrogen Halide-(Hydro halogenation) : Addition of Hydrogen halide to alkene produce alkyl halides. In case of symmetrical alkene only one alkyl halide is formed but when the olefin is unsymmetrical two products are possible.

For Example:

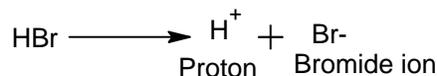


It has been found that isopropyl bromide is the major product. In such cases addition is governed by Markonikov's rule which states that,

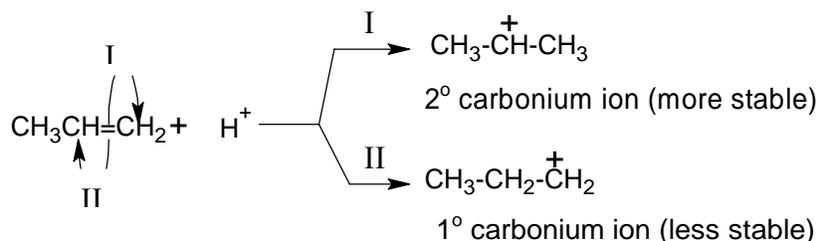
“When an unsymmetrical reagent (such as HX , H_2SO_4 , $HOCl$ etc) adds to an unsymmetrical alkene, then the negative part of the reagent is added to that carbon atom of the double bond which bears the least number of hydrogen atoms i.e which bears more substituents and positive part of the reagent is added to that carbon atoms which bears greatest number of hydrogen atoms i.e. which bears less substituents.”

The reaction take place through ionic mechanism. Markonikov's rule can be explained with the help of mechanism.

Step I: Isomerisation of reagent to give electrophile (H^+) and nucleophile (Br^-)

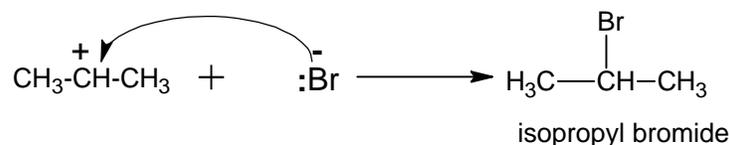


Step II: Attack of electrophile (H^+) to double bond to form more stable carbocation.

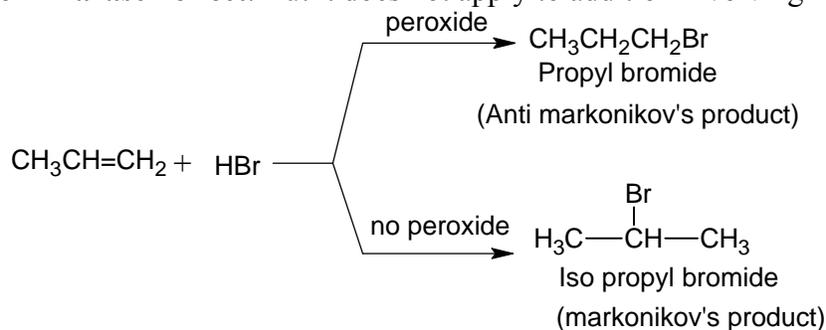


More stable carbocation is preferentially formed.

Step III: Attack of nucleophile (Br^-) to carbonium ion (more stable) to give major product.

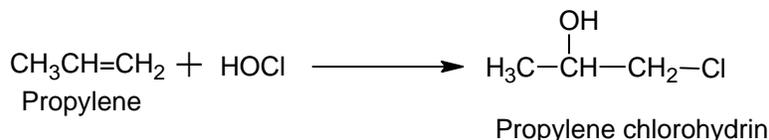


Peroxide Effect - Anti markovnikov addition: Kharasch and Mayo (1933) discovered that addition of HBr to propene or other unsymmetrical alkene in presence of organic peroxide ($R-O-O-R$) yields mainly n-alkyl bromide (anti markovnikov's product). This effect is known as peroxide effect or **Kharasch effect**. But it does not apply to addition involving HCl, HI or HF

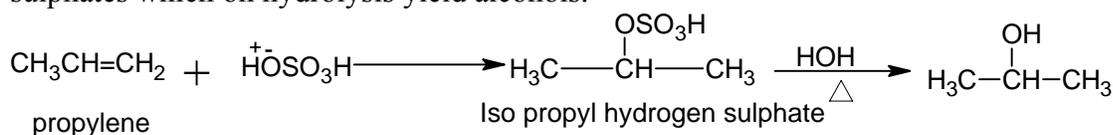


In presence of peroxide the addition takes place via a free radical mechanism rather than the ionic mechanism. This addition of free radical to double bond involves the intermediate formation of more stable free radical.

iv) Addition of Hypohalous acid: In hypohalous acid (HOX) $-OH$ is more negative part. They add to alkene to give halohydrin. In case of unsymmetrical alkene Markovnikov's rule is followed.

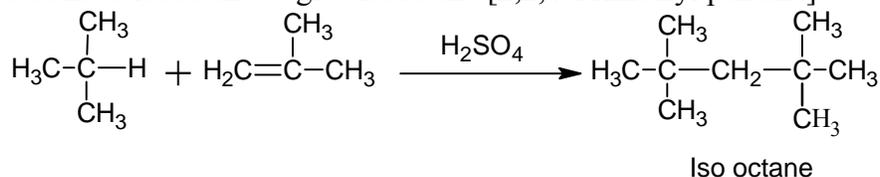


v) **Addition of sulphuric acid:** alkenes react with sulphuric acid to produce alkyl hydrogen sulphates which on hydrolysis yield alcohols.

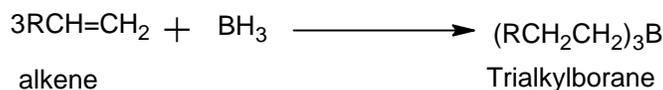


vi) **Addition of Alkene [Alkylation]:**

Some alkanes add to alkenes in the presence of H_2SO_4 or HF . The best example of this reaction is addition of isobutane to isobutene to give isooctane [2,2,4-Trimethyl pentane]

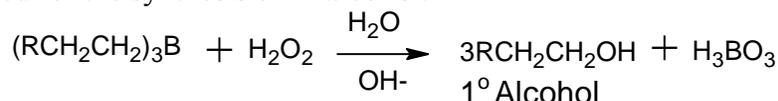


vii) **Addition of Diborane [Hydroboration]:** Diborane (B_2H_6) adds to the double bond as BH_3 to form trialkyl borane. The positive part of BH_3 is the boron, the negative part is hydrogen.



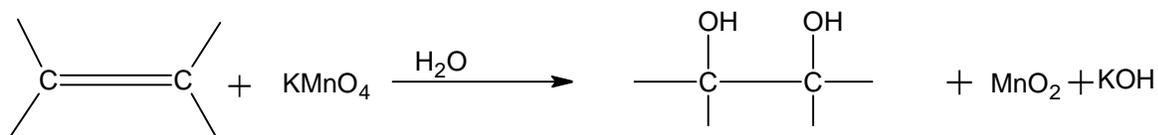
Try alkyl borane on treatment with alkaline aqueous solution of hydrogen peroxide are converted to alcohols.

USE: They are used for the synthesis of **1° alcohol**.



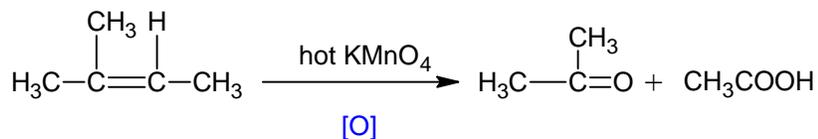
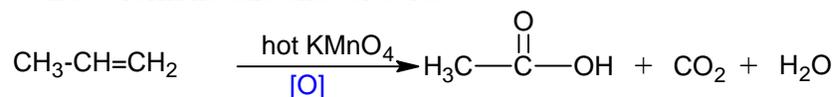
2) Oxidation: Alkane undergo oxidation reaction readily to form different compounds under different conditions.

i) Oxidation with dilute Cold KMnO_4 : On oxidation with cold alkaline KMnO_4 (Bayers's Reagent) alkenes give glycols.

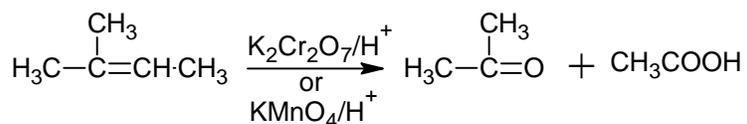
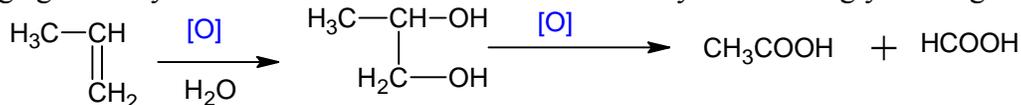


Since the bright purple colour of KMnO_4 disappears during the reaction, Bayer's reagent is used as a test for detecting the presence of Olefinic double bond.

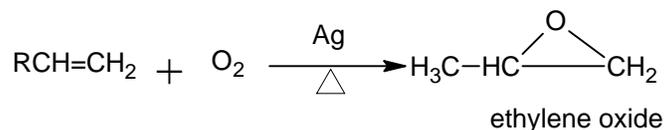
ii) Oxidation with Hot KMnO_4 : Alkene on treatment with hot potassium permanganate solution split at the double bond to form ketone and /or acids.



iii) Oxidation with acidic KMnO_4 or $\text{K}_2\text{Cr}_2\text{O}_7$: Alkenes when oxidized with these strong oxidizing agents they are converted to ketones and /or carboxylic acid via glycols. e.g.

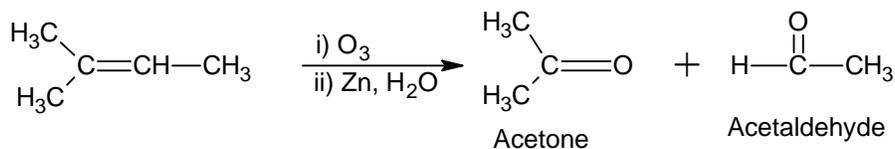
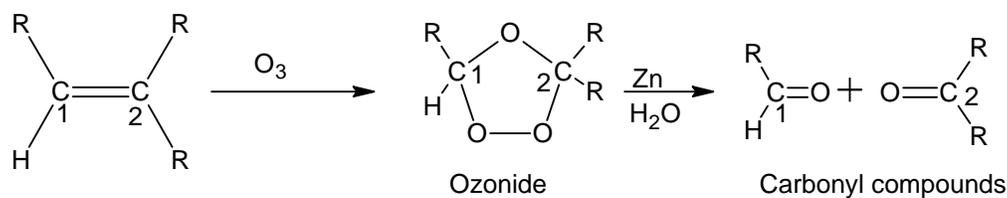


iv) Catalytic oxidation: Alkenes react with oxygen in presence of silver catalyst at $250\text{-}400^\circ\text{C}$ to form Epoxides.



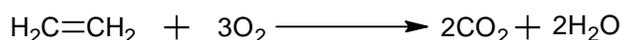
v) Oxidation with ozone: Ozone adds to an alkene molecule to form an **ozonide**. Ozonide on warming with zinc and water hydrolysed to yield smaller carbonyl fragments.

The process of preparing the Ozonide and then decomposing it to get the carbonyl compound is called Ozonolysis.

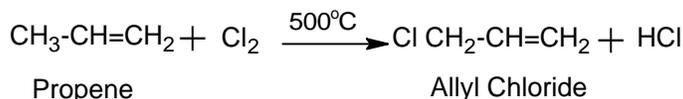


USE: This is the best method for location the position of the double bonds in unknown alkene with the help of products formed.

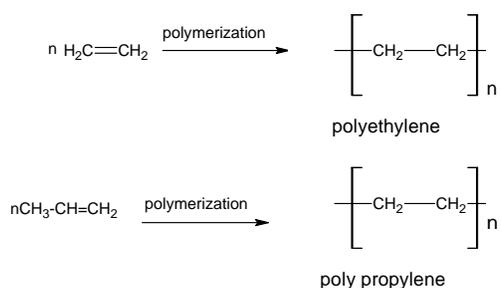
3) Combustion: Alkene are completely burnt in air to form CO_2 and H_2O



4) Substitution of Alkenes by Halogens: Alkenes having alkyl group undergo substitution, when treated Cl_2 or Br_2 at high temperature. One of the allylic hydrogen is replaced by halogen atom. For example



5) Polymerization: The process in which simple molecule join together to form a large molecule without the elimination of anything is known as polymerization. Simple alkene molecules undergo polymerization to form long chain polymers. For example



These reactions are catalyzed by HF , H_2SO_4 or organic peroxide and conditions of high temperature and pressure are generally required.

Alkynes

Alkynes are also unsaturated hydrocarbons but they are more unsaturated than alkenes. Alkynes are characterized by the presence of carbon-carbon triple bond ($C\equiv C$) in hydrocarbon molecule. The triple bond of alkynes consists of a strong sigma (σ) two weak pi (π) bonds. In alkynes triple bonded carbon atom are sp hybridized. The σ – bond is formed by the overlap of sp - hybrid orbitals and the π bonds are formed by the separated overlap of the two P-orbitals. Carbon-Carbon distance in acetylene is 1.20\AA and C-H bond length is 1.06\AA . As acetylene molecule is linear, the H-C-C bond angle is 180° .

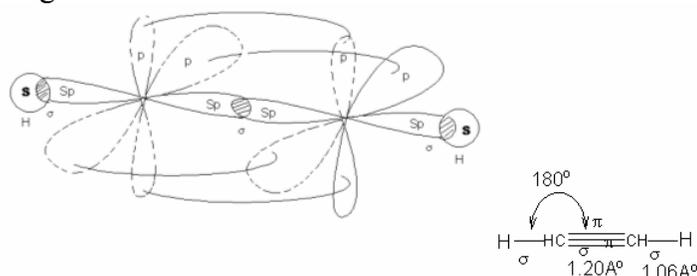
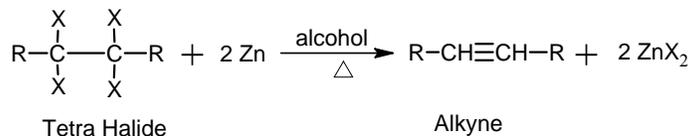


Figure-4: Structure of Acetylene

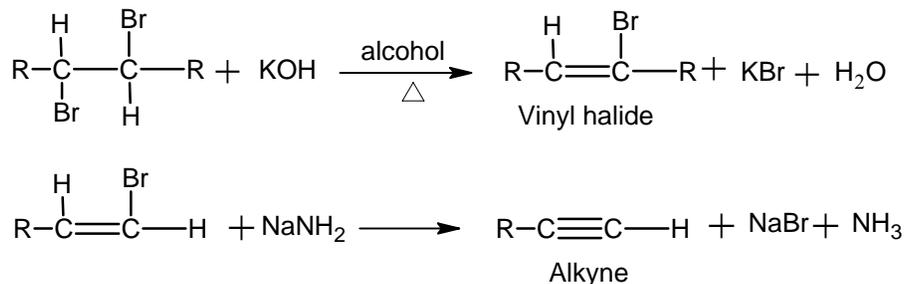
Acetylene and 1-alkynes are acidic in character this is because of more S-character of the C-H bond thus the electrons of the C-H bond in 1-alkynes are more strongly held by the carbon nucleus and hydrogen atom of $\equiv C-H$ can be easily removed.

Methods of Preparation:

i) Dehydrogenation of Tetra halides: When Vic –tetra halides are heated with zinc dust in alcohol, alkynes are produced.

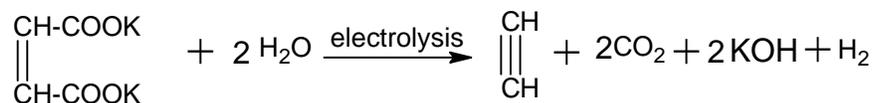


ii) Dehydro Halogenation of Vicinal Dihalides: When vicinal dihalides are heated with alcoholic KOH and then sodium amide (NaNH_2), alkynes are formed.

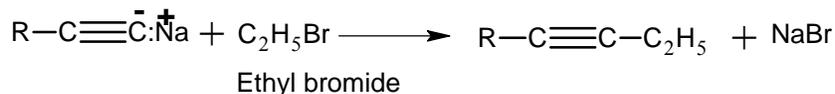
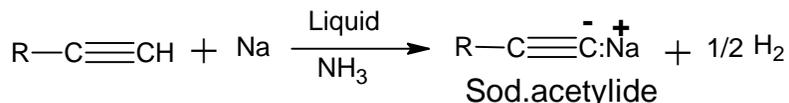


Vicinal dihalides may be directly treated with NaNH_2 to give alkynes.

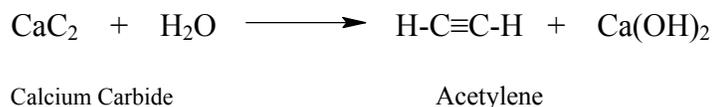
iii) By Kolbe electrolytic Method: Electrolyses of sodium or potassium salt of unsaturated dicarboxylic acid yields alkynes.e.g;



iv) Reaction of Sodium Acetylides with 1° Alkyl Halides: This reaction is useful for the preparation of higher alkynes. Sodium acetylides are prepared by treatment of acetylene or 1-alkynes with sodium in liquid ammonia



v) Reaction of Calcium Carbide with H₂O: This method is used for the preparation of acetylene.



Properties of Alkynes:

Physical Properties:

- i) The First three members are gases, next eight are liquids, and the higher members are solids.
- ii) Alkynes are colourless and odourless except acetylene which has garlic colour.
- iii) They are only slightly soluble in water but dissolve in organic solvents.
- iv) Their boiling points, melting points and specific gravities show a regular increase with the increase in molecular weights.

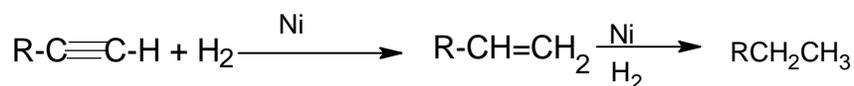
Chemical Properties: Due to the presence of pi-electrons alkynes give the same kind of addition reactions as do alkenes. In addition to **electrophilic additions**, alkynes also undergo **nucleophilic additions** with electron rich reagents.

Other reactions of alkynes result from acidic hydrogen atoms in acetylene and 1-alkynes, which can be easily removed by means of a strong base and hence acetylenes or 1-alkynes are considered as weak acids.

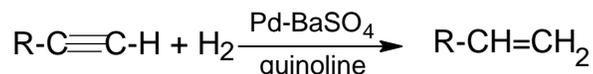


Following are some important general chemical reactions of alkynes,

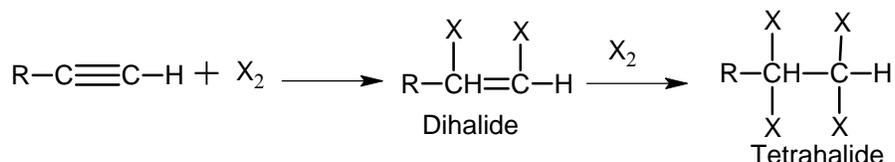
1) Addition of Hydrogen: In presence of catalyst like finely divided Ni, Pt, or Pd, alkynes add two molecules of hydrogen to give corresponding alkanes.



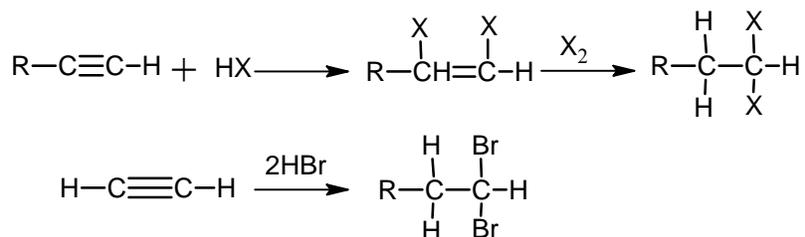
The reaction can be stopped at alkene stage by using **Lindlar's Catalyst** (Pd deactivated by BaSO₄ + quinoline)



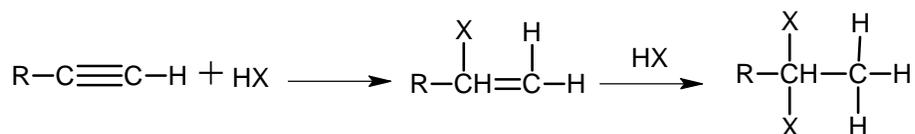
2) Addition of Halogen: Halogens add to alkyne to form first dihalide and then tetra halide.



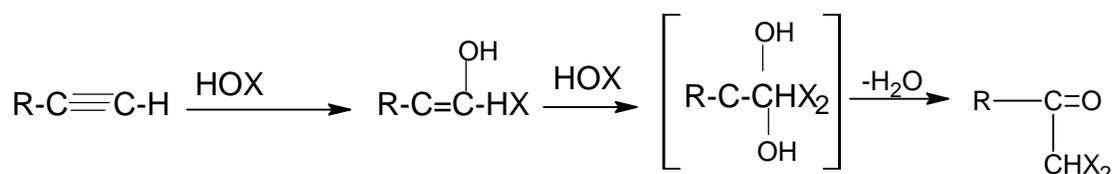
3) Addition of Halogen Acids: Two molecule of halogen acids can be added to symmetrical alkynes in two stages. After addition of one molecule alkyne become unsymmetrical derivative of alkene so that the addition of a second molecule takes place according to **Markonikov's rule**. Thus both the halogens become attached to the same carbon atom.



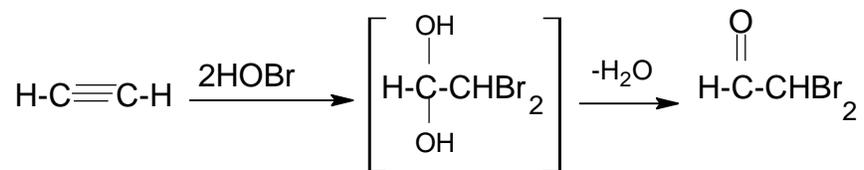
In case of unsymmetrical alkynes addition takes place in accordance with Markonikov's rule.



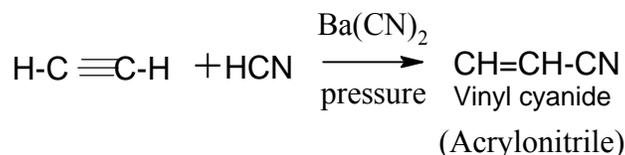
4) Addition of Hypo Halous acids: Addition of two molecules of hypohalous acids to alkynes takes place according to Markonikov's rule. Haloaldehyde or Haloketones are the final products.



For example, Acetylene with HOBr give dibromo acetaldehyde

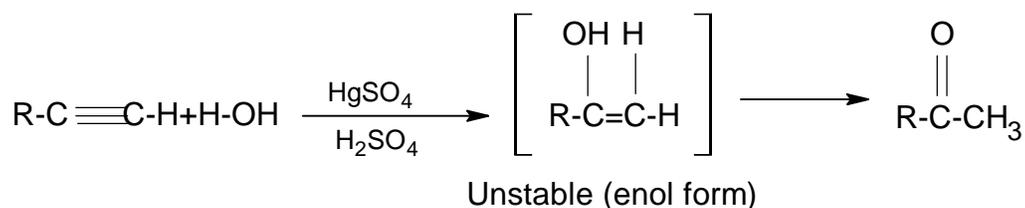


5) Addition of Hydrogen Cyanide: Alkynes react with hydrogen cyanide in presence of barium cyanide to give addition product alkenyl cyanide. For example, on addition of HCN acetylene gives vinyl cyanide or acrylonitrile.



USE: Acrylonitrile is used for the manufacture of synthetic rubber and synthetic fiber, **Orlon**.

6) Addition of Water(hydration): Alkyne react with water in presence of sulphuric acid and mercuric sulphate to form aldehyde or ketones.



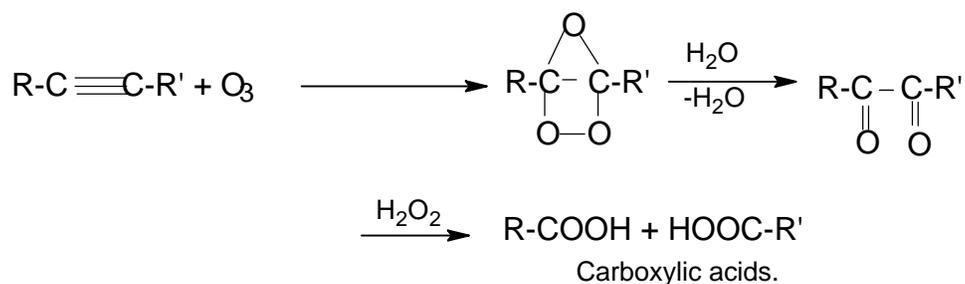
7) Addition of Arsenic Trichloride: Alkyne reacts with AsCl_3 in presence of AlCl_3 and HgCl_2 to form 2-chlorovinyl dichloroarsenic, which is commonly known as *Lewisite*.



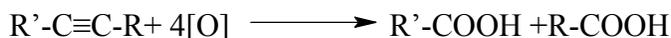
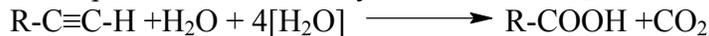
2-chlorovinyl dichloroarsenic(*Lewisite*)

NOTE: Lewisite is highly poisonous gas. It is four times active than the mustard gas.

8) Ozonolysis: Alkynes form addition products ozonides, with ozone. These ozonides on decomposition with water yield diketones, which are oxidized by hydrogen peroxide produced in the reaction to give carboxylic acids. e.g.



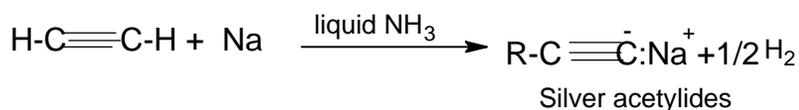
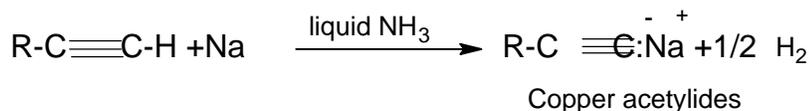
9) **Oxidation with KMnO_4 :** When alkynes are treated with alkaline KMnO_4 , cleavage at the site of the triple bond takes place to form carboxylic acids and CO_2 .



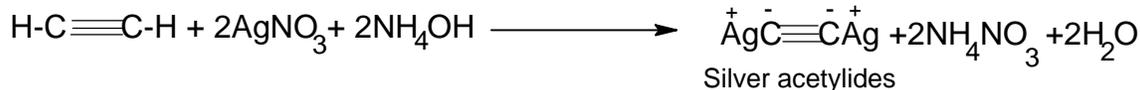
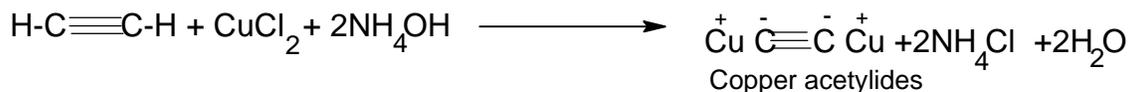
USE: This reaction is useful in determination of structure of alkynes.

10) **Salt formation:** As hydrogen in 1-alkyne and acetylene are acidic, they can form salts with metals by replacement of acidic hydrogen. These salts are known as *Acetylides*. For example;

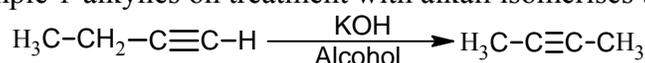
a) Formation of Copper and silver acetylides with sodium in liquid ammonia or sodium amide (NaNH_2)



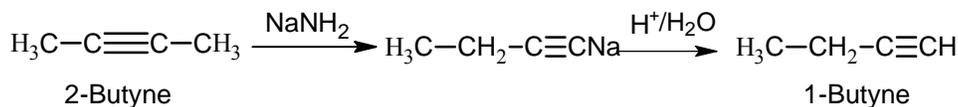
b) Formation of Copper and silver acetylides with ammonical solution of cuprous chloride and silver nitrate.



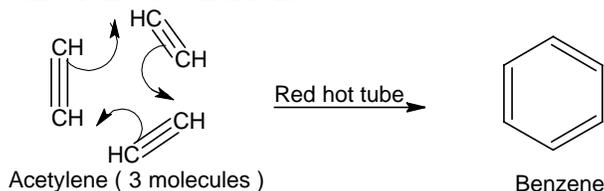
11) **Isomerisation:** Alkynes when treated with traces of alkali like alc.KOH and NaNH_2 undergo isomerisation, for example 1-alkynes on treatment with alkali isomerises to 2-alkyne.



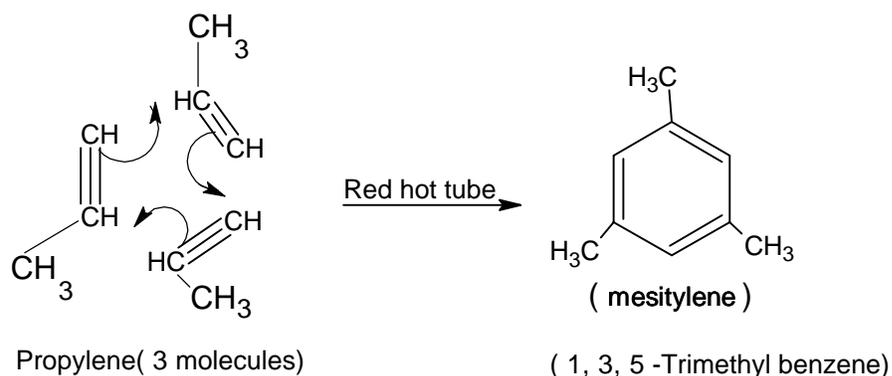
On the other hand 2-alkyne with NaNH_2 in inert solvent gives 1-alkyne.



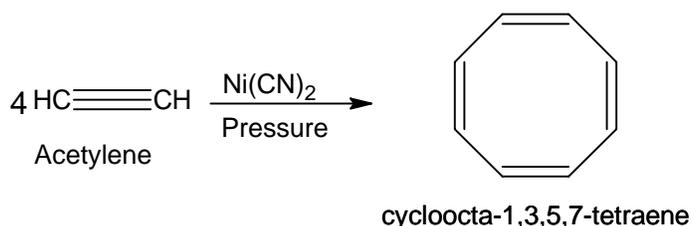
12) **Polymerization:** Alkynes, when passed through a red hot iron tube, undergo cyclic polymerization to form aromatic hydrocarbons. For example, three molecules of acetylene combine to give benzene under these conditions.



Under similar condition three molecules of propylene polymerizes to give mesitylene.

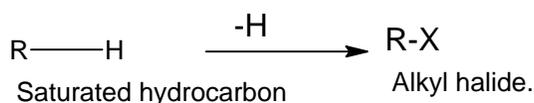


Acetylene with nickel cyanide under pressure gives cyclo-octa tetraene.

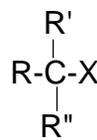
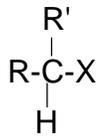
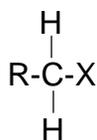


Alkyl Halides

Alkyl halides are the compounds derived from the saturated hydrocarbons by replacement of one of the hydrogen atom by halogen atom.



Thus they can be represented by general formula R-X where R= alkyl group; X= Cl, Br, I or F. Halogen atom may be attached to 1^o, 2^o or 3^o Carbon atom of alkyl group. Thus alkyl halide can be classified as primary (1^o), secondary(2^o) or tertiary (3^o) depending upon whether the halogen is attached to primary, secondary or tertiary carbon atom.



1^o - alkyl halide

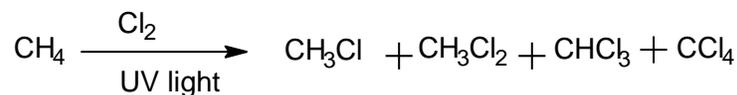
2^o - alkyl halide

3^o - alkyl halide

Alkyl halides are very useful organic compounds.

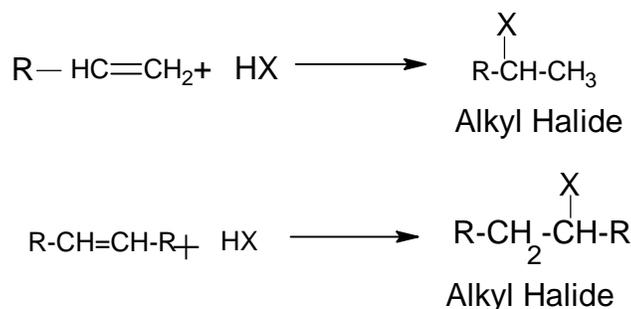
Methods of preparation:

1) By direct Halogenation of Alkanes: Alkanes when treated with chlorine or bromine in the presence of U.V light or at high temperature (400°C) gives alkyl chloride or alkyl bromide along with poly halogen derivatives. For example,



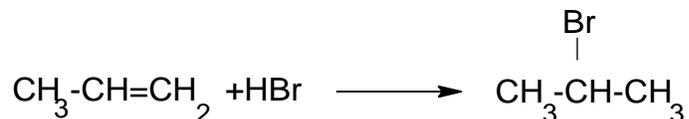
But iodoalkanes can be prepared only in the presence of oxidizing agents like HIO_3 , HIO_4 . Or Conc. HNO_3 etc. because HI formed during the reaction reduces back alkyl iodide to alkane. But the products are difficult to separate.

2) By addition of Hydrogen Halide to Alkene: When alkenes are treated with hydrogen halides, addition of hydrogen halide takes place in accordance with Markonikov's rule except the addition of HBr in presence of organic peroxide $[\text{R-O-O-R}]$.

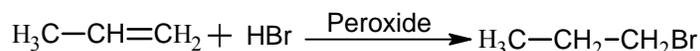


Addition of HBr to unsymmetrical alkene

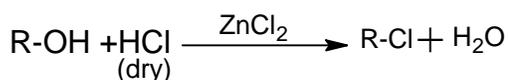
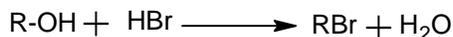
a) In absence of peroxide:



b) In presence of peroxide:



3) By treatment of Alcohol with Halogen Acid: Alcohols react with HBr or HI to give alkyl bromide or alkyl iodide. They react with HCl in presence of zinc chloride catalyst.

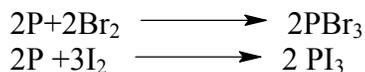


4) By treatment of Alcohol with Phosphorous Halides: Alcohols react with phosphorous halides (PX_5 or PX_3) to give alkyl halides.





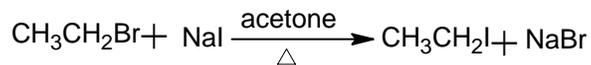
PBr₃ or PI₃ are produced *in situ* by the reaction of bromine or iodine with red phosphorus



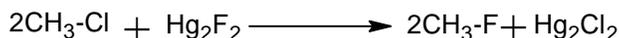
5) By treatment of Alcohol with Thionyl Chloride: Alcohols when treated with thionyl chloride in the presence of pyridine give alkyl chloride. Pyridine acts as scavenger for HCl formed.



6) By Halogen Exchange Reaction [Finkelstein reaction]: This method is suitable for the preparation of alkyl iodides and fluorides. This involves the treatment of alkyl bromide or chloride with concentrated solution of sodium iodide in acetone.



For the preparation of alkyl fluoride alkyl bromides or chlorides are heated with inorganic fluorides.



Properties of Alkyl halides:

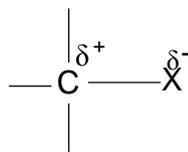
1) Physical Properties:

- i) Methyl chloride, Methyl bromide, Methyl fluoride and Ethyl chloride are gases at room temperature. Other alkyl halides up to C₁₈ are colourless liquids and beyond C₁₈ are colorless gases.
- ii) Although alkyl halides are polar in nature but they are insoluble in water but soluble in organic solvents. Insolubility in water is due to the inability to form hydrogen bonding with water and to break already existing hydrogen bonding in water molecule.
- iii) Their densities decrease in the following order; Iodide > bromide > Chloride > fluoride. Alkyl bromides and iodides are denser than water while alkyl chlorides and fluorides are lighter than water.
- iv) For a given alkyl group boiling points of alkyl halides follow the following order.
Alkyl iodide > Alkyl bromide > Alkyl Chloride > Alkyl fluoride.

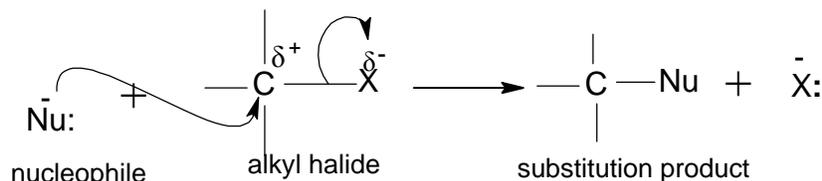
For a given halogen atom, the boiling points of alkyl halides increase with the increase in the size of the alkyl group.

Chemical Properties: In alkyl halides (C-X) bond is highly polar because of the high electronegativity of the halogen atom. Thus alkyl halides are very reactive compounds alkyl halides can be nearly all types of organic compounds and thus synthetically they are very important. They undergo **substitution**, **elimination**, and **reduction** reactions.

Substitution Reaction: The (C-X) bond is strongly polarized covalent bond due to the high electronegativity of halogen atom.



Thus carbon atom of C-X bond is therefore a good site for the attack of nucleophiles (electron rich species) and the nucleophilic substitution reactions are most common reactions of the alkyl halides.

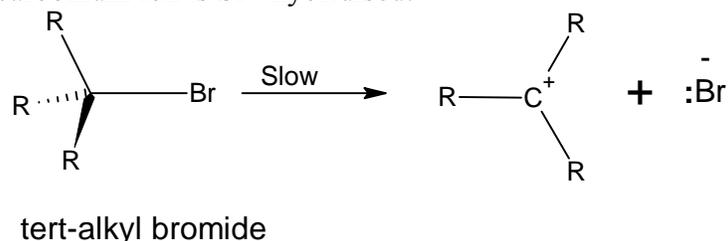


The common nucleophiles are OH^- , CN^- , SH^- , NO_2^- , NH_2^- and OR^- .

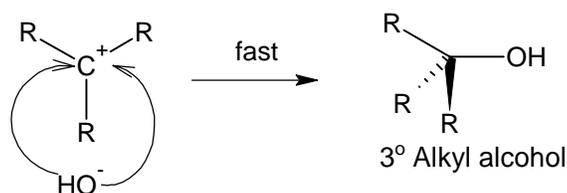
Nucleophilic substitution in alkyl halides takes place in two ways.

1) S_N^1 Mechanism (unimolecular nucleophilic substitution): In this mechanism substitution takes place in two steps. Let us consider the hydrolysis of bromide by aqueous NaOH.

Step-I: This involves the ionization of alkyl halide to give a planar carbonium ion in which central positively charged carbonium ion is sp^2 hybridised.



Step-II: This involves the attack of nucleophile on carbonium ion from either side to give the substitution product.

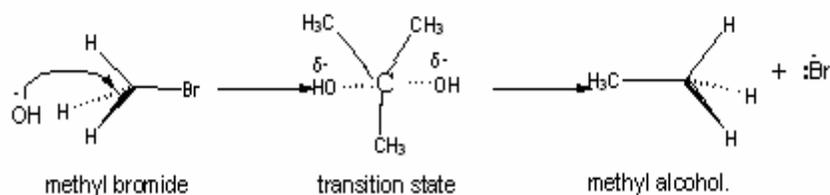


Remember that if alkyl halide is optically active then we will get the racemic mixture of two enantiomers. Tertiary alkyl halides undergo substitution by S_N^1 mechanism via formation of carbonium ion because the attack of the nucleophile on the crowded tertiary alkyl halide i.e. sterically hindered central carbon atom is difficult. The reactivity order for S_N^1 mechanism is 3° alkyl halide $>$ 2° alkyl halide $>$ 1° alkyl halide

1° alkyl halide undergoes substitution by S_N^2 mechanism and the 2° alkyl halide may undergo substitution by either S_N^2 or S_N^1 mechanism depending upon the solvent.

2) S_N^2 Mechanism [Bimolecular nucleophilic substitution]: 1° alkyl halides undergo substitution by S_N^2 mechanism. This is one step process in which the attack of the nucleophile

and the ejection of the halide ion takes place simultaneously. 1° alkyl halide undergoes substitution by SN¹ mechanism via formation of transition state. Let us consider the hydrolysis of methylbromide by aqueous NaOH.



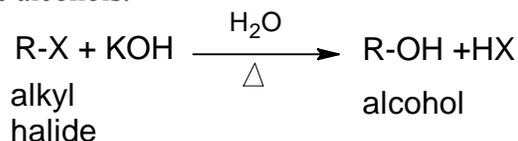
Bulkier the alkyl group, more is the steric hindrance in the formation of transition state and thus is the reactivity of alkyl halide.

The reactivity order for SN² mechanism is,

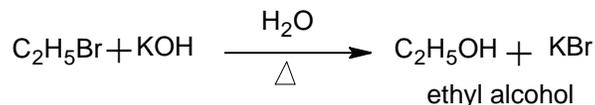


Some important substitution reactions of alkyl halides are given below:

i) Reaction with aqueous KOH: When alkyl halides react with aq.KOH, halogen is substituted by -OH group to give alcohols.



For example;



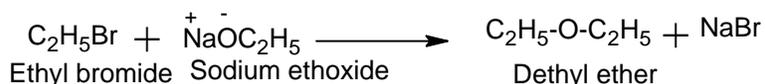
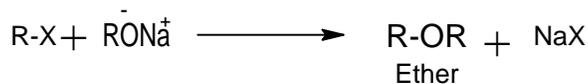
ii) Reaction with moist Silver Oxide: Alkyl halides on treatment with moist silver oxide also gives alcohols.



Example:



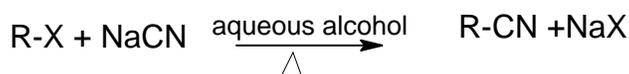
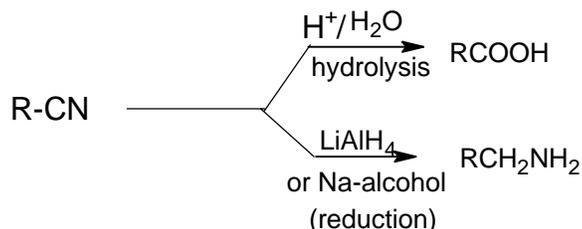
iii) Reaction with sodium Alkoxide: Alkyl halides on treatment with sodium alkoxide give ethers. This reaction is known as **Williamson ether Synthesis**.



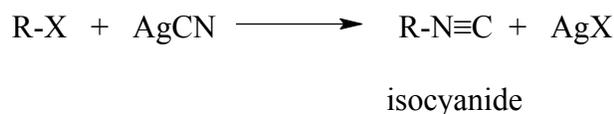
iv) Reaction with Dry Silver Oxide: Alkyl halides on heating with dry silver oxide give ethers.



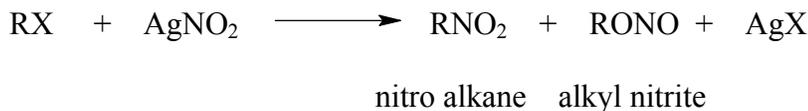
v) Reaction with Sodium or Potassium Cyanide: Alkyl halides react with sodium or potassium cyanide to give alkyl cyanides which are very important synthetic intermediates. They can be easily converted to carboxylic acids and primary amines.



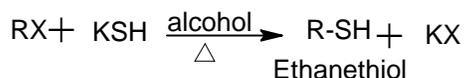
Alkyl halides when react with AgCN, isocyanides are formed.



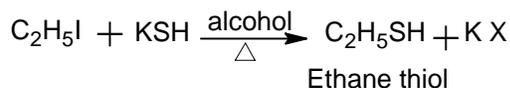
vi) Reaction with AgNO₂: Alkyl halides react with silver nitrite form nitro alkane. Some Alkyl nitrites are also formed.



viii) Reaction with KSH: On treatment with alcoholic potassium hydrosulphide, alkyl halides yield thiols.



e.g.



viii) **Reaction with K_2S :** Alcohols react with potassium sulphide to form alkyl sulphide



e.g.



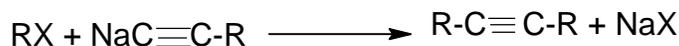
ix) **Reaction with $R-COOAg$:** When alkyl halide reacts with alcoholic solution of silver salt of carboxylic acid an ester is formed.



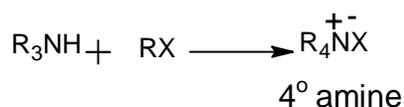
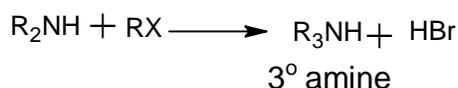
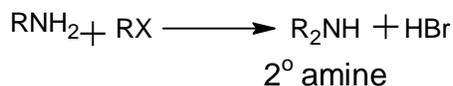
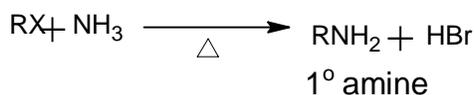
e.g



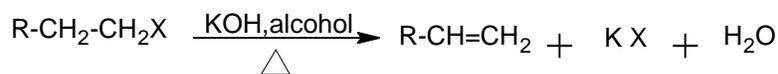
x) **Reaction with Acetylides:** Alkyl halides with sodium acetylides give higher alkyne.



xi) **Reaction with Ammonia:** Heating of alkyl halides with alcoholic solution of ammonia in a sealed tube results a mixture of different classes of amines.



xii) **Reaction with alcoholic KOH :** When alkyl halides are treated with alc. KOH , dehydrohalogenation takes place and alkenes are produced.



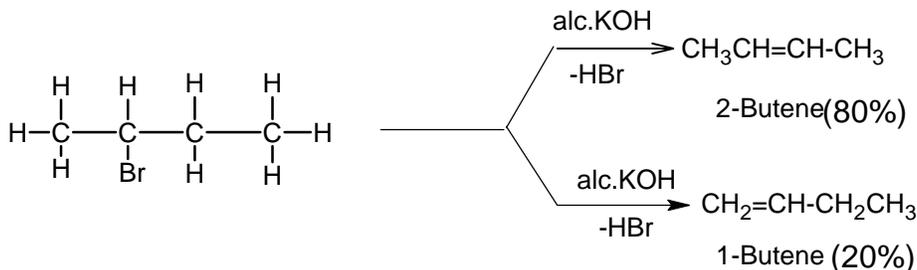
In alcohol, there is an equilibrium between the solvent and KOH



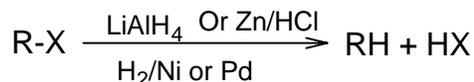
Sodium ethoxide is a strong base. It favours elimination more than substitution. The rate of elimination to substitution product depends on the structure of the alkyl halide and experiment condition. For example in case of 1° alcohol substitution product is also formed but in case of 2° and 3° alcohol elimination product predominates. 1° and 2° alkyl halides undergo dehydrohalogenation by E₂ mechanism and 3° alkyl halides do so by E₁ mechanism.

Saytzeff's Rule: *In case of unsymmetrical alkyl halide dehydro halogenation yield more than one alkene. One of them, the most highly substituted alkene, is the major product.* In such cases elimination of HX is governed by Saytzeff's rule. According to which the main product is the most highly substituted alkene. Or in other words Hydrogen is eliminated from the Carbon atom of alkyl halide which bears the least number of hydrogen atoms.

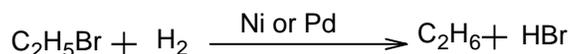
For example, when 2-bromobutane undergo elimination with alc. KOH, two alkenes are possible and major one is more substituted alkene. (In accordance with Saytzeff's rule).



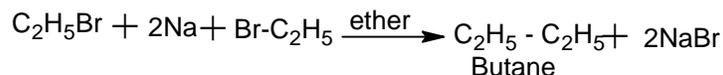
xiii) Reduction: Alkyl halides are reduced to alkanes by different reducing agents like LiAlH₄, Zn/HCl and H₂/Ni or Pd etc.



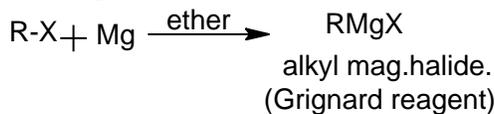
e.g.



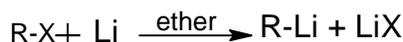
xiv) Wurtz Reaction: When alkyl halides react with metallic sodium in dry ether two molecules join together to give alkane with double number of carbon atoms.



xv) Reaction with Mg and Li: Alkyl halides react with Magnesium in dry ether to give alkyl magnesium halide, the Grignard reagent.

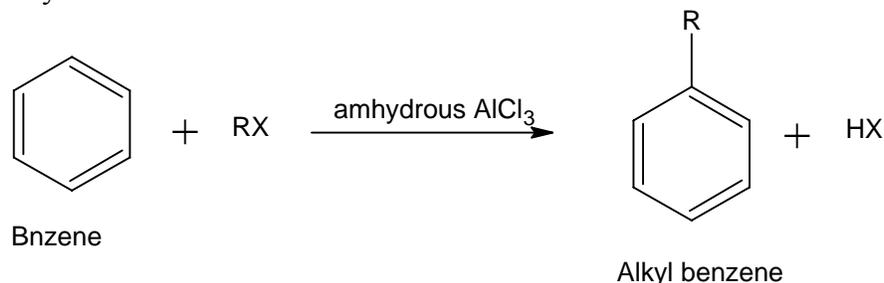


But with Lithium in dry ether alkyl halides give alkyl Lithium.



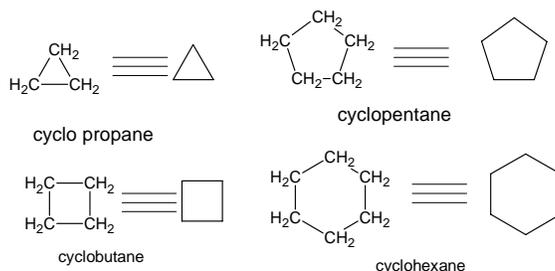
Grignard reagent is an important group of organometallic complex which has the great synthetic utility in organic chemistry. Alkyl Lithium behaves in the same way as Grignard reagent but with increase reactivity.

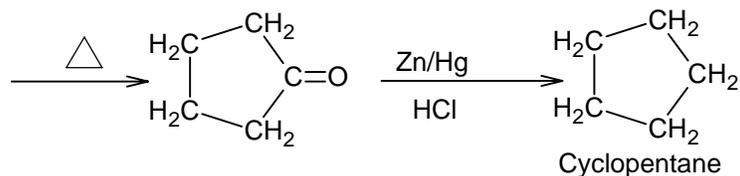
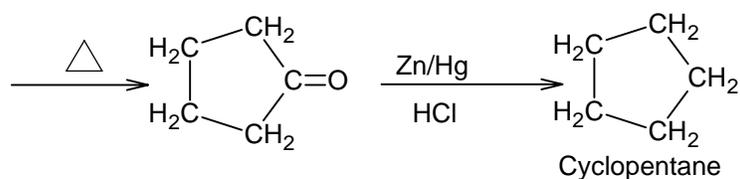
(xvi) Friedel Crafts Reaction: Alkyl halides react with Arenes in the presence of anhydrous AlCl_3 to form alkyl benzene.



Alicyclic Hydrocarbons or Cyclo Alkanes

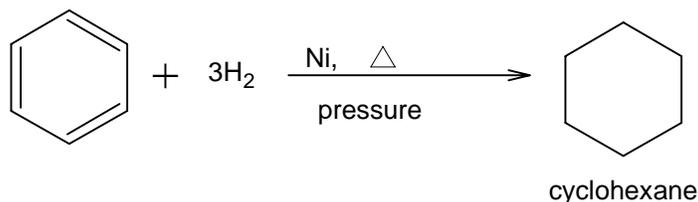
Alicyclic Hydrocarbons are those carboxylic compounds in which the carbon atoms are joined together to form a ring. In this carbon atoms are joined together to form a ring. In saturated alicyclic hydrocarbons methylene groups joined together to form a cyclic structure, hence they are also known as polymethylene. According to IUPAC system, they are named as cycloalkanes or cycloparaffins. They resemble with the aliphatic compound in their properties. Some example of cyclo alkanes are,



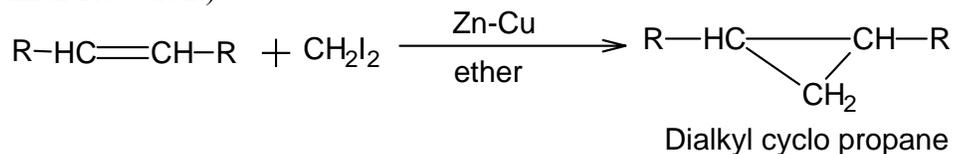


iv) **From Aromatic Hydrocarbons:** Benzene and its derivatives on catalytic reduction are converted to six membered cycloalkanes.

E.g.



v) **From Alkenes:** [preparation of cyclopropane derivatives]: Alkene when treated with methylene iodide in presence of Zn-Cu couple in ether, give cyclopropane derivatives. (Simmons-Smith Reaction)



Properties:

Physical Properties:

- 1) Cycloalkanes are liquids at room temperature except cyclopropane and cyclobutane which are gases at room temperature.
- 2) Their melting and boiling points are gradually increase with increase in molecular weights.

Compound	bp ^o C	mp ^o C
Cyclopropane	-32.8	-127.4
Cyclobutane	12.5	-90.7
Cyclopentane	49.3	-13.9
Cyclohexane	80.7	6.6

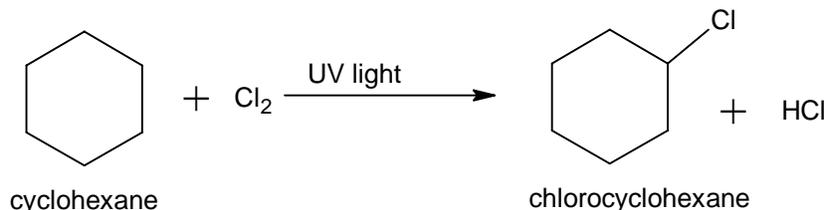
- 3) Cycloalkanes are insoluble in water but soluble in ethanol and ether.

Chemical Properties: Cycloalkanes resemble with alkanes in several chemical properties. But the lower members, cyclopropane and cyclobutene are the exceptions. They form addition compounds with the ring fusion. Thus cycloalkanes behave both like alkanes as well as alkenes.

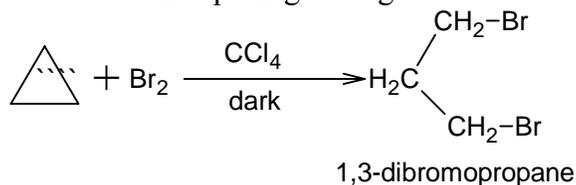
Important Reactions of Cycloalkanes are described below:

1) Substitution with Cl₂ and Br₂: In presence of UV light cycloalkane react with Cl₂ or Br₂ to give substitution products.

For example:

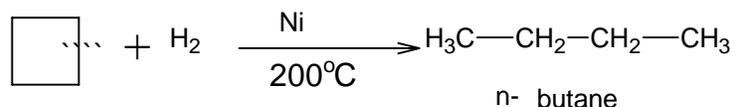
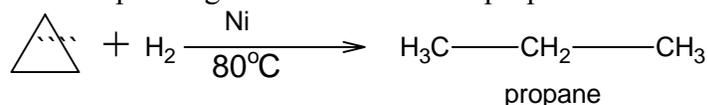


2) Addition of Cl₂ and Br₂: Cyclopropane reacts with Cl₂ or Br₂ in dark and in CCl₄ as a solvent to give addition product with the opening of ring.

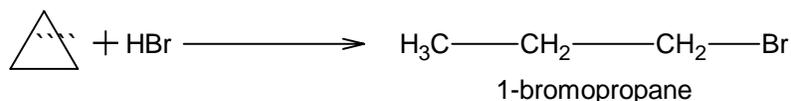


Cyclo butane and other higher members do not give this reaction.

3) Addition of Hydrogen: Cyclopropane and Cyclobutane react with Hydrogen in the presence of Ni Catalyst to give corresponding normal alkanes .i.e. propane and n-butane.



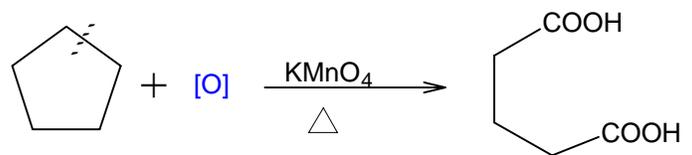
4) Addition of HBr and HI: Cyclopropane gives open chain addition product with concentrated HBr and HI.



Higher members do not give this reaction.

5) Oxidation: Cyclo alkanes when treated with hot alkaline KMnO₄ yield dicarboxylic acid with the cleavage of ring.

e.g.

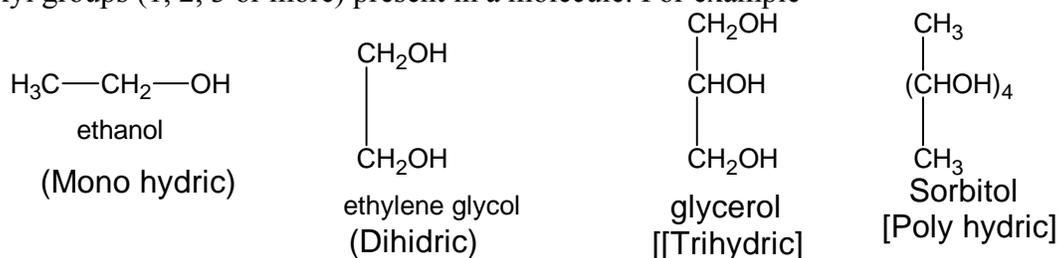


1,5-pentanedioic acid

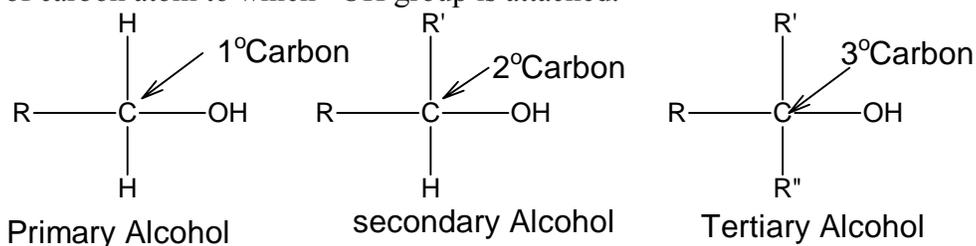
Alcohols

Alcohols are the hydroxyl derivatives of saturated hydrocarbon in which hydroxyl(-OH) group is attached to saturated carbon atom. All the chemical properties of alcohols are due to the presence of -OH group thus hydroxyl group is the functional group of alcohols. Alcohols can be represented by the general formula R-OH.

Alcohols can be classified as mono, di, tri and polyhydric alcohols depending on the number of hydroxyl groups (1, 2, 3 or more) present in a molecule. For example

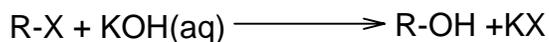


Monohydric alcohols [R-OH] are further subdivided into 1°, 2° and 3° alcohols depending upon the nature of carbon atom to which -OH group is attached.



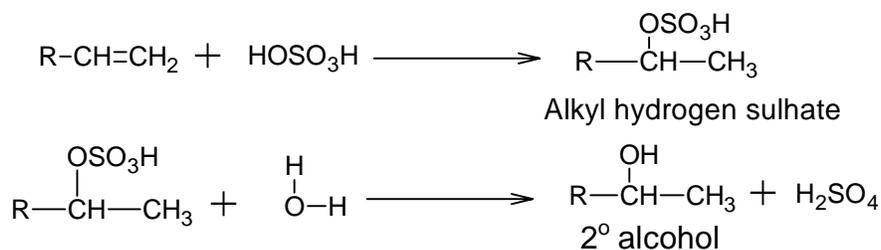
General Methods of preparation:

1) **By the Hydrolysis of alkyl halides:** Alkyl halides react with aq. KOH or moist silver oxide to give alcohols.

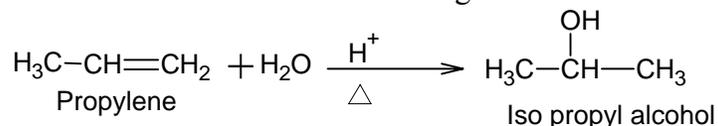


2) **By hydration of olefins:** Alkenes react with Sulphuric acid (98%) to give first addition product, alkyl hydrogen sulphates which on hydrolysis give alcohols.

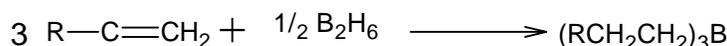
In case on unsymmetrical alkenes for addition, Markonikov's rule is followed.



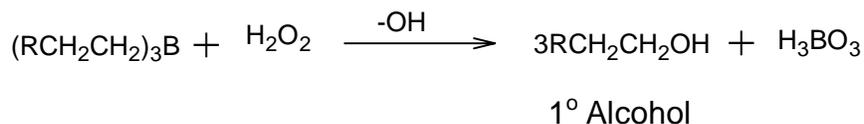
Except ethyl alcohols primary alcohols cannot be prepared by this method. Overall reaction is the Markonikov's addition of water to a double bond. e.g.



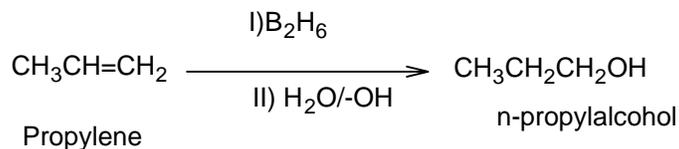
3)Hydroboration-Oxidation of Alkenes: When alkenes are treated with diborane, trialkyl boranes are formed. In this reaction diborane adds as borane (BH₃). The positive part of BH₃ is boron and negative part is hydrogen. e.g.



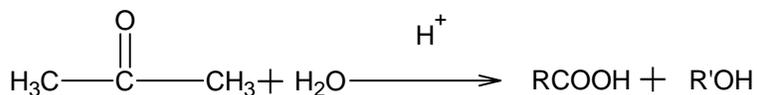
Trialkyl borane on treatment with alkaline aqueous solution of hydrogen peroxide gives 1°alcohols.



The overall reaction of hydroboration-oxidation results anti- Markonikov's addition of water to double bond. e.g.

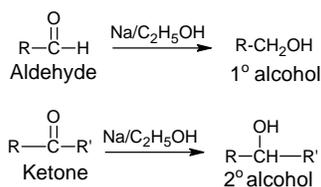


4) Hydrolysis of Esters: Acid hydrolysis of esters yield alcohols. e.g

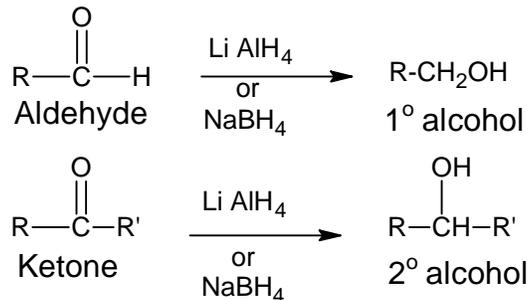


5)By catalytic Reduction of Carbonyl Compounds: Aldehydes on reduction give 1° alcohols and ketones give 2° alcohols. 3° Alcohols can't be prepared by this method.

i) Reduction by using alcoholic sodium[Bouveault-Blanc reduction]:

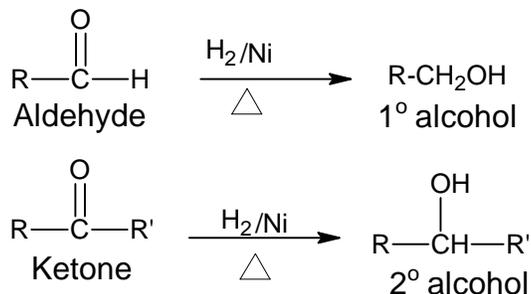


ii) Reduction by using LiAlH_4 or NaBH_4 :

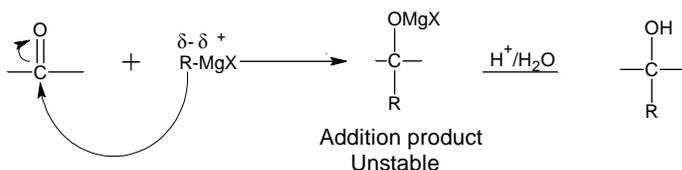


α,β -unsaturated carbonyl compounds may also be reduced by LiAlH_4 or NaBH_4 to give corresponding alcohols.

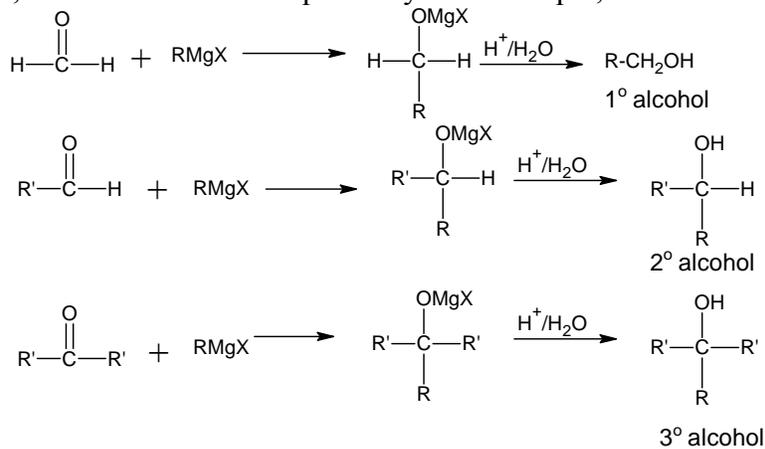
iii) Reduction with H_2/Ni :



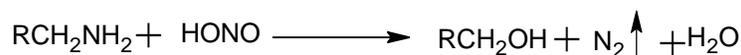
6) **From Grignard Reagent:** Grignard Reagent (RMgX) first react with carbonyl compound to give the addition product which on acid-hydrolysis gives corresponding alcohol.



Grignard reagent with formaldehyde, aldehydes other than formaldehyde and ketones leads to the formation of 1° , 2° and 3° alcohols respectively. For example,

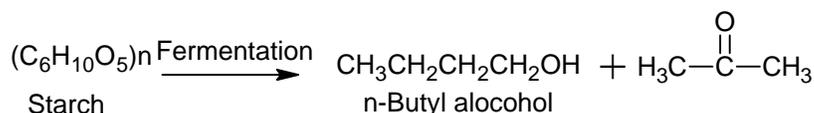
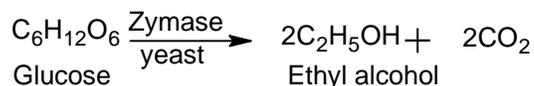


7) **By the reaction of aliphatic primary amine with nitrous acid:** Primary aliphatic amines react with nitrous acid to give alcohols.



8) **By Fermentation:** Fermentation is the slow decomposition of complex organic compounds into simple compound in the presence of enzymes obtained from microorganism. Fermentation of starch and sugars under the influence of suitable microorganism gives alcohols.

For example:



Properties:

Physical properties:

1) Lower alcohols are colourless, toxic liquids while higher having more than 12 carbon are solids. They have characteristic sweet alcoholic odour and burning taste.

2) Lower alcohols are easily soluble in water but solubility decreases with increase in molecular weight.

Solubility of lower alcohols in water is due to the Hydrogen bonding between highly polarized –OH groups present both in water and alcohols.

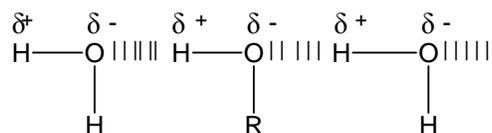
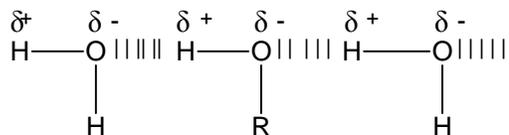


Figure-5: Hydrogen bonding between alcohol and water molecules.

But Higher alcohols have less tendency to form hydrogen bonds with water molecule because of the presence of non polar long hydrocarbon chain and hence the solubility in water decreases.

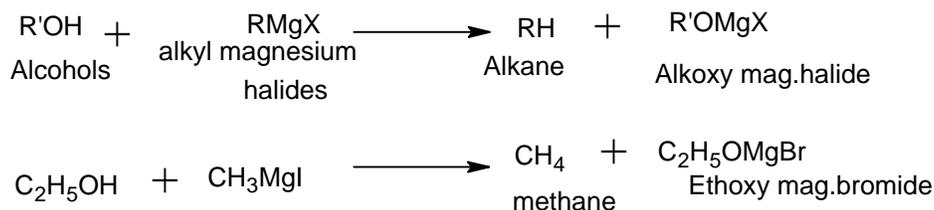
3) Boiling points of alcohol increase with the increase in number of carbon atoms but their boiling points are much higher than those of the corresponding alkanes. This is again because of intermolecular hydrogen bonding. Highly polar –OH groups of different alcohol molecule and partially negative oxygen in another alcohol molecule.



4) Among isomeric alcohols boiling and melting points decreases with branching.

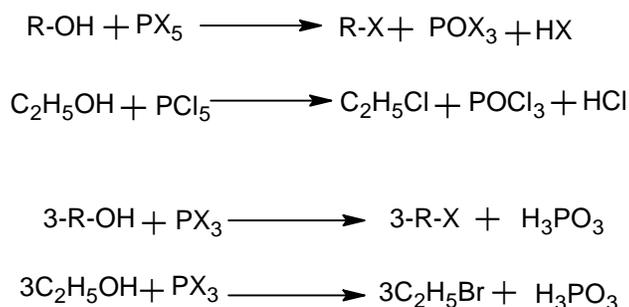
Primary > Secondary > Tertiary.

4) Reaction with Grignard Reagent: Alcohols react with Grignard reagent to give alkanes. This reaction is used for the estimation of alcoholic group [**Zerewitnoff reaction**]



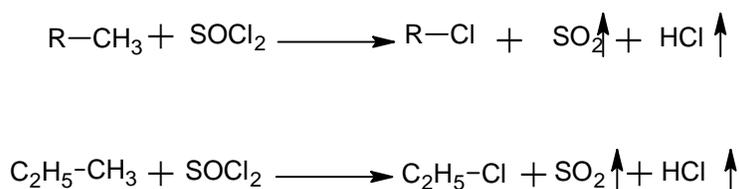
(B) Reaction involving $-\text{OH}$ group: These reaction involve cleavage of Carbon-oxygen bond $[-\overset{\cdot\cdot}{\text{C}}-\overset{\cdot\cdot}{\text{O}}\text{H}]$

5) Reaction with phosphorous Halides: When alcohols react with phosphorous penta halide $[\text{PX}_5]$ or phosphorous halide $[\text{PX}_3]$, replacement of $-\text{OH}$ group by halogen atom take place and alkyl halides are formed.

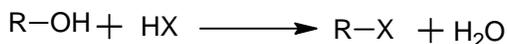


PBr_3 and PI_3 are usually prepared in situ.

6) Reaction with thionyl chloride: This involves replacement of $-\text{OH}$ group by chlorine atom.

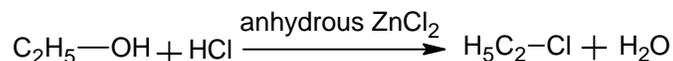


7) Reaction with halogen acids: Alcohols react with halogen acid to give corresponding alkyl halides.



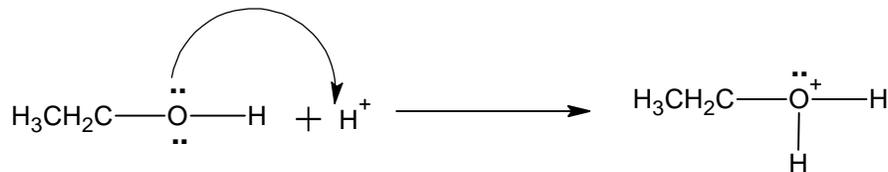
The reactivity of halogen acids are in the order,
 $\text{HI} > \text{HBr} > \text{HCl}$

No catalyst is required in case of HI and HBr but HCl reacts only in presence of anhydrous ZnCl_2 catalyst.

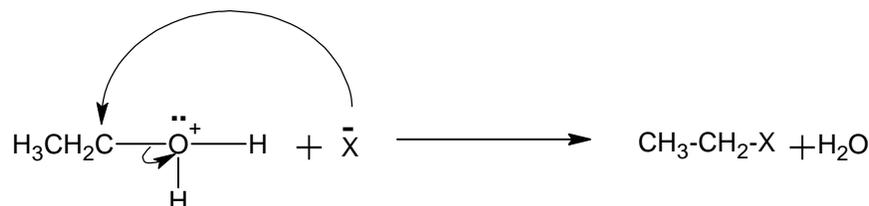


Mechanism: Primary alcohols follow SN^1 mechanism for the substitution of —OH group by halogen atom.

Step 1: Protonation of Alcohol



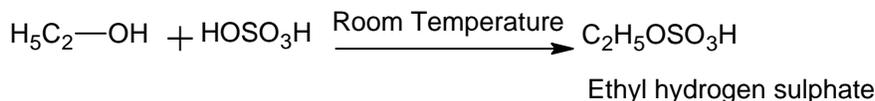
Step 2: Attach of nucleophile $[\text{X}^-]$



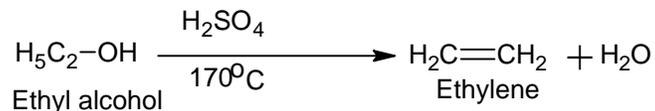
2° and 3° alcohols follow SN^2 mechanism.

8) Reaction with sulphuric acid: The action of concentrated sulphuric acid is of great interest as it gives different products under different conditions.

i) At room temperature, ethyl alcohol reacts with concentrated sulphuric acid to give ethyl hydrogen sulphate.



ii) When alcohols heated with concentrated H_2SO_4 , dehydration takes place to give alkenes. For example



Mechanism: Mechanism involve formation of carbocation.

Step 1: Protonation of alcohol.



Step 2: Elimination of water molecule to give carbocation.



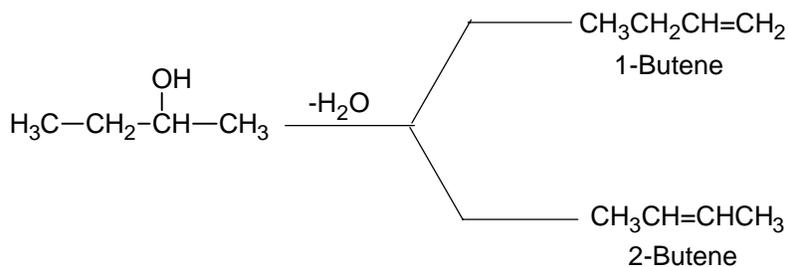
Step 3: Removal of proton from carbocation:



The ease of dehydration of alcohols follow the following order
 $3^\circ > 2^\circ > 1^\circ$

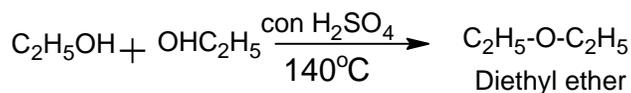
This is also the order of stability of carbocation.

With secondary and tertiary alcohols, dehydration may occur in two ways, e.g.:



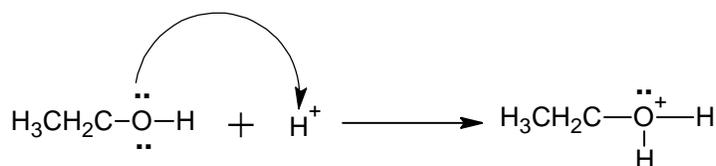
According to Saytzeff's rule more substituted alkene is the major product.

iii) When excess of ethyl alcohol is heated with concentrated sulphuric acid at 140°C , diethyl ether is formed.

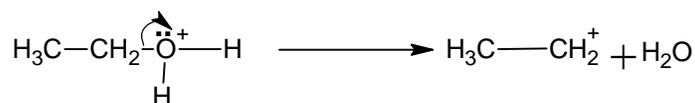


Mechanism: Mechanism involves the following steps.

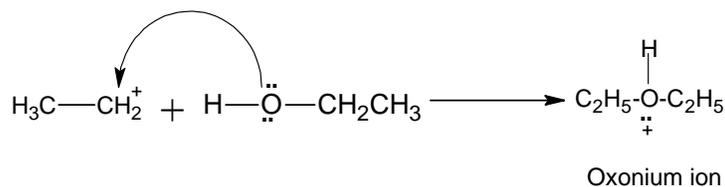
Step 1: Protonation of one Molecule.



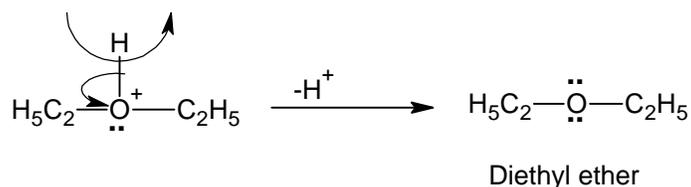
Step 2: Elimination of water molecule:



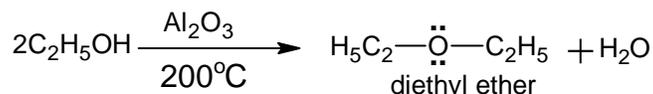
Step 3: Attach of carbocation to another molecule of alcohol.



Step 4: Removal of proton from Oxonium ion leads to the formation of ether.

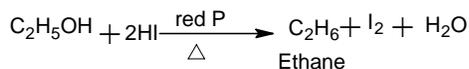


Alcohols can also be dehydrated by passing the vapours of alcohol over heated alumina to give ethers or alkenes e.g.



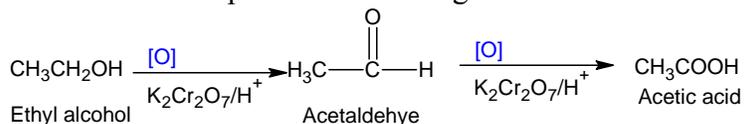
9) Reduction of Alcohols:

Alcohols are reduced to alkanes by concentrated HI and red phosphorous

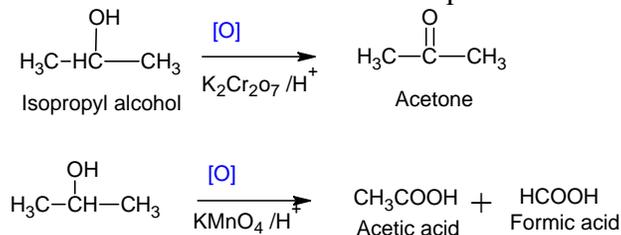


10) Oxidation: Nature of oxidation products of alcohols depend upon the nature of alcohols, oxidizing agent used and reaction conditions. Most commonly used oxidizing agents are acidic KMnO_4 and acidic $\text{Na}_2\text{Cr}_2\text{O}_7$.

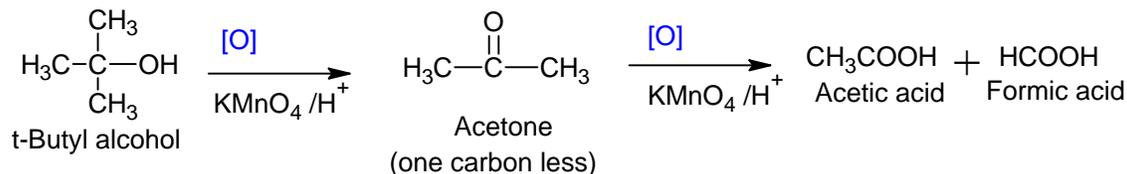
Primary alcohols are easily oxidized to aldehydes and then to carboxylic acids both with the same number of carbon atoms as the parent alcohol. E.g.:



Secondary alcohols oxidized to ketone with same number of carbon atoms, but these ketones can't be easily oxidized, these undergo oxidation under very drastic conditions to give mixture of carboxylic acid with lesser number of carbon atoms than parent alcohol. Eg:

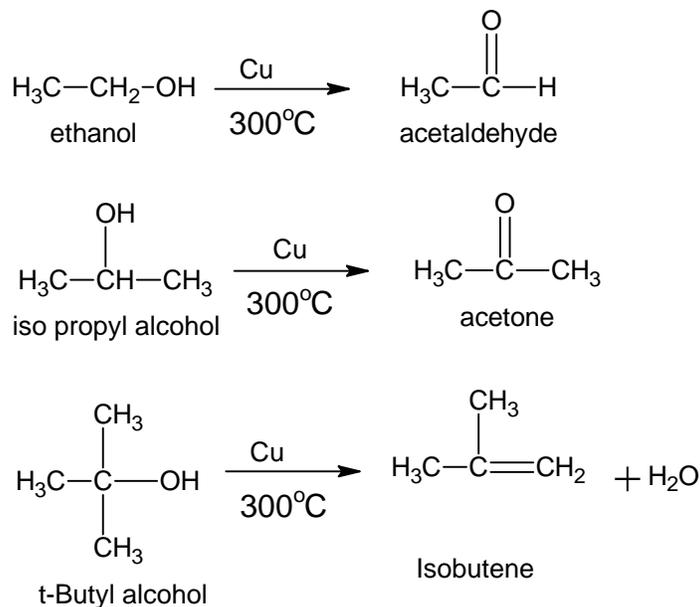


Tertiary alcohols are resistant to oxidation under normal conditions but under drastic conditions they oxidized to first form ketones and then carboxylic acid both having lesser number of carbon atoms.



USE: The oxidation reaction may also be used to distinguish between primary, secondary and tertiary alcohols.

11) Reaction with hot Copper: Primary and secondary alcohols dehydrogenated to form aldehyde and ketones respectively, Tertiary alcohols are not dehydrogenated but they dehydrated to give alkanes. e.g.



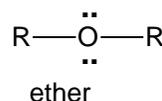
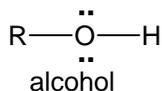
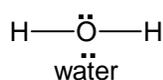
USE: The dehydrogenation with hot copper may also be used to distinguish between primary and secondary alcohols.

Ethers

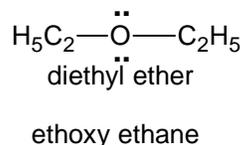
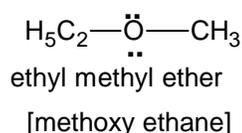
Ethers are the organic compounds in which an oxygen atom is bonded to alkyl groups. The functional group is [C-O-C]. If same alkyl groups are attached to central oxygen atom ethers are classified as symmetrical ethers. While ethers containing different alkyl groups attached with central oxygen atom are classified as unsymmetrical ethers.



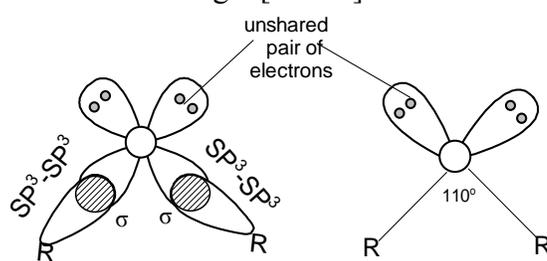
Ethers may be considered as derivatives of alcohol or water in which hydrogen atom /atoms have been replaced by alkyl group or groups.



Some common examples of ethers are



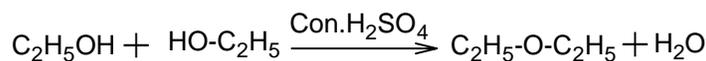
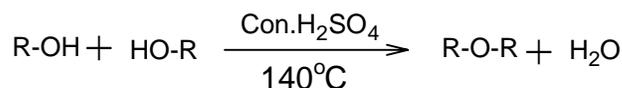
In ethers central oxygen atom is sp^3 hybridized. Thus two C-O, σ -bond are formed by the overlap of two half filled sp^3 hybrid orbitals of oxygen atom with the half filled sp^3 hybrid orbitals of two carbon atoms of two alkyl groups. Remaining two sp^3 hybrid orbitals of oxygen atoms are occupied by the two unshared pairs of electrons. Here the C-O-C bond angle is about 110° which is quite close to tetrahedral angle [109.5°]



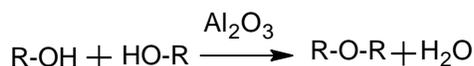
Structure of Ether

Methods of preparation:

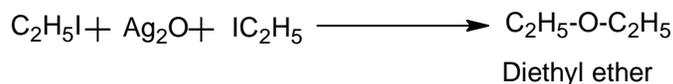
i) **Dehydration of alcohols:** By heating excess of alcohol with concentrated sulphuric acid at 140°C



ii) **By passing alcohol vapors over Al_2O_3 at 250°C :**

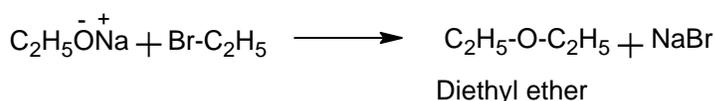
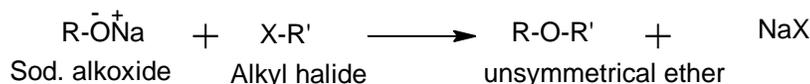


2) **By heating alkyl halides with silver oxide:** Ethers are obtained by heating alkyl halides with dry silver oxide.

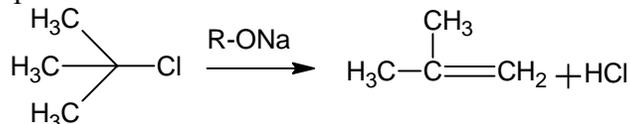


This method is useful for the preparation of simple ethers only.

3) Williamson Ether Synthesis: This is the most important industrial and laboratory method of preparation of ethers. It involves the treatment of sodium alkoxide with an alkyl halide. Both symmetrical unsymmetrical ethers can be prepared by this method.

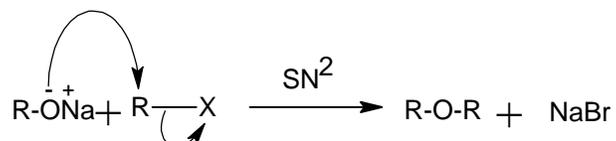


Tertiary and Secondary alkyl halides undergo elimination reaction with sodium alkoxide [strong base]. Thus to introduce a tertiary group it will be better to take this group as a base, not as a tertiary halide. For example



Thus for preparing $(\text{CH}_3)_3\text{C-O-C}_2\text{H}_5$, we should start with $(\text{CH}_3)_3\text{C-O}^-\text{Na}^+$ and $\text{C}_2\text{H}_5\text{Br}$.

Mechanism: It follows S_N^2 mechanism. Displacement of halide ion by alkoxide ion.



5) Action of Diazomethane on Alcohols: Ethers can be prepared by treatment of primary or secondary alcohols with diazomethane in presence of fluoboric acid as a catalyst.



But this method is only useful for the preparation of methyl ethers.

Properties:

Physical properties:

- 1) Ethers are highly volatile and inflammable substances.
- 2) Except dimethyl ether and ethyl methyl ether, which are gases all are pleasant smelling colourless liquids.
- 3) Their boiling points gradually increase with the increase in molecular weight. But ethers have lower boiling points than isomeric alcohols because they are incapable of forming inter molecular hydrogen bonds due to the absence of –OH groups.

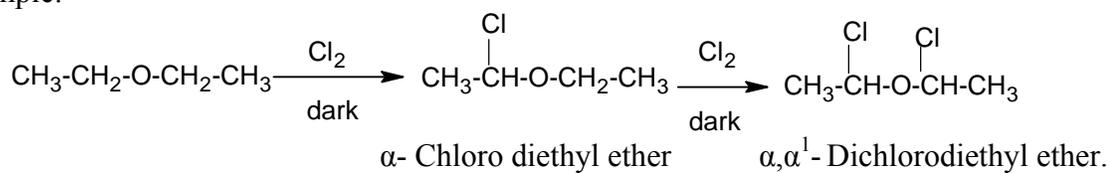
Ethers are sparingly soluble in water since their oxygen atom is not capable of forming H-bond with hydrogen with hydrogen atom of water molecule.

Chemical Properties:

Ethers are much less reactive compounds because they are quite stable. They do not react with active metals, strong bases like NaOH, reducing and oxidizing agents.

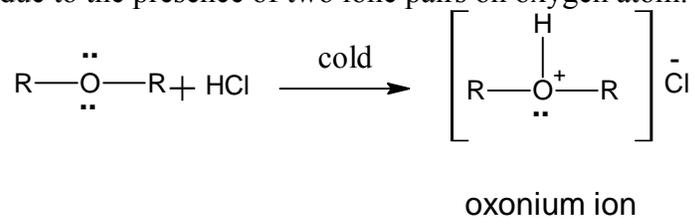
1) Halogenations: When ethers react with chlorine or bromine substitution preferentially at α -Carbon takes place.

For example:



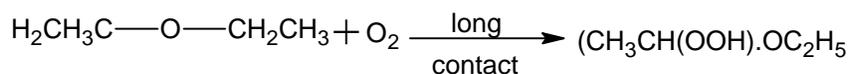
The extent of substitution depends on reaction conditions.

2) Basic Nature: Ethers react with cold concentrated sulphuric acid or HCl to give oxonium salt. Their basic nature is due to the presence of two lone pairs on oxygen atom.



This property is used to separate ethers from ethyl bromide and to distinguish from alkanes. Since alkanes do not react with acids.

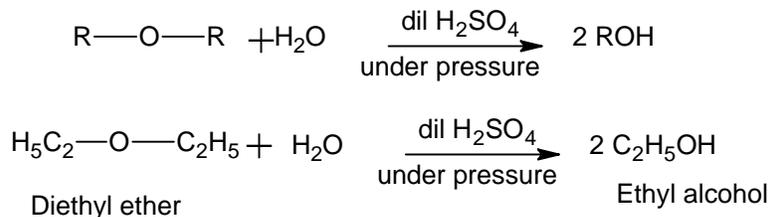
3) Formation of peroxides (Auto oxidation): On standing in contact with air ethers combine with oxygen to form peroxide which is highly explosive.



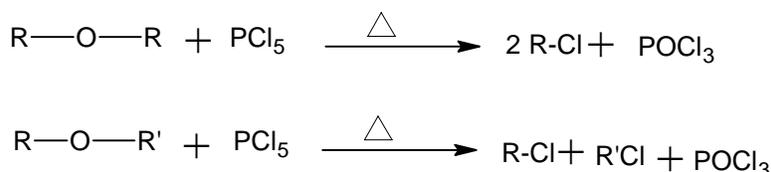
These peroxides decompose violently at high temperature. Thus ethers should be always be purified before distillation. When ethers that contains peroxide is distilled, at the end of

distillation residual peroxide may explode. Because of this ether should never be evaporated to dryness.

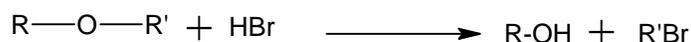
4) Hydrolysis: Ethers when treated with dilute sulphuric acid under pressure, they hydrolyse to give alcohols.



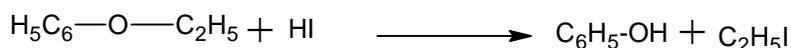
5) Reaction with Phosphorus Penta-chloride: With PCl_5 ether cleave to give alkyl chlorides



6) Reaction with HI and HBr: Ethers react with hot concentrated HI or HBr to give an alcohol and alkyl halide.



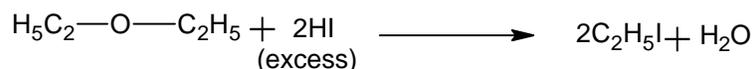
In case of mixed ethers the halogen atom attacks to the smaller alkyl groups, due to the steric effect. e.g.



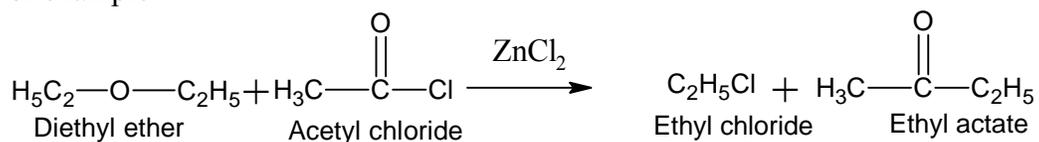
The order of reactivity of halogen acid is



With the excess of acid, the alcohol initially produced is also converted to alkyl halide. e.g.

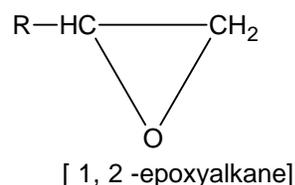
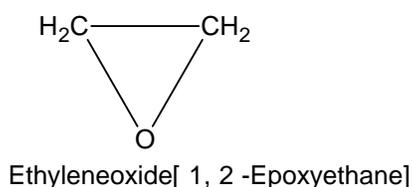
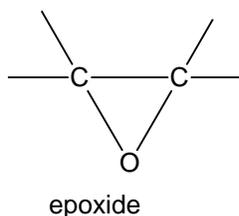


7) Reaction with acetyl chloride: Ethers react with acid chloride to give alkyl halides and esters. For example



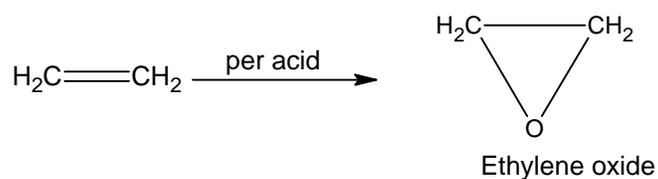
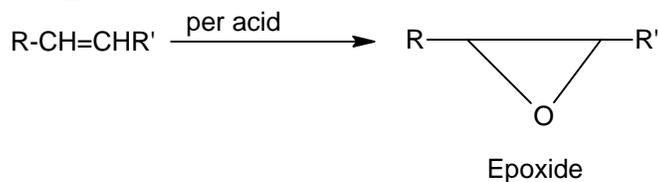
Epoxide

Epoxides are the cyclic ethers in which etheral oxygen is linked with two adjacent carbon to form three membered ring. i.e. oxiran (oxirane) ring. Epoxy compound contain oxirane ring. Oxiran compounds are also referred to as cyclic ethers or alkene oxides.



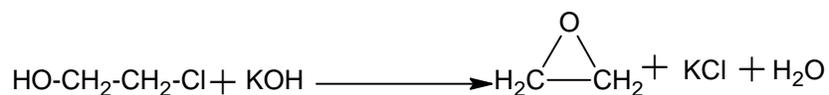
Epoxy ethane or ethylene oxide (oxiran) is the most important member of this group.

Method of preparation: Epoxides may, in general, be prepared by epoxidation of alkenes with peroxy acids. Perbenzoic acid C₆H₅COO₂H, monoperothalic acid, HOCC₆H₄COO₂H and P-nitro benzoic acid have been used.

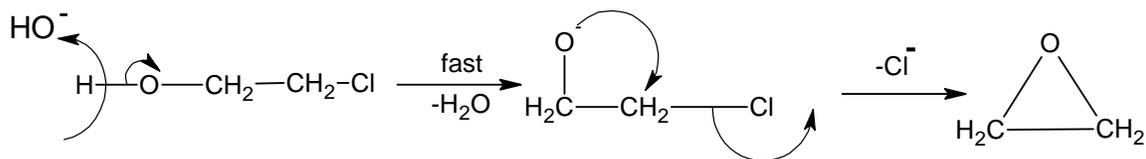


Ethylene oxide may be obtained:

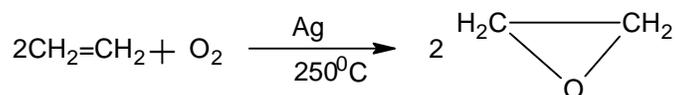
i) By Reaction of Chlorohydrin with base:



Possibly the mechanism is:

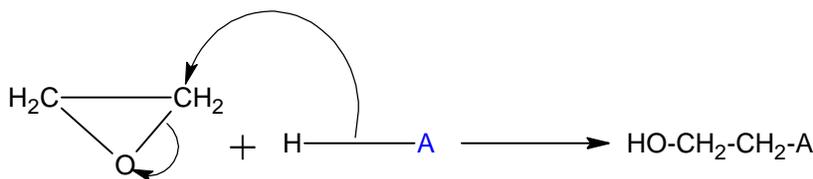


ii) By oxidation of ethylene with oxygen in the presence of silver catalyst.

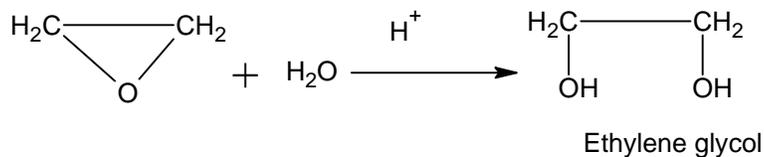


Properties:

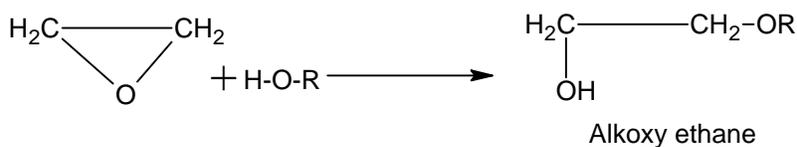
Ethylene oxide is toxic, flammable gas having b.p 10.7°C . generally epoxides are reactive compound, this is because to release their strain they have the tendency to open their ring. These oxygen atoms combine with the reactive hydrogen atom of various compounds to form hydroxyl group.



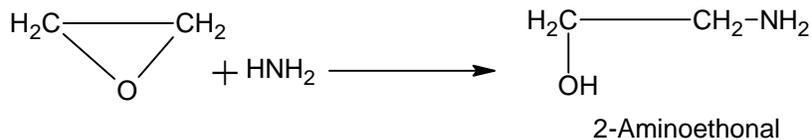
Reaction with HOH



Reaction with alcohols



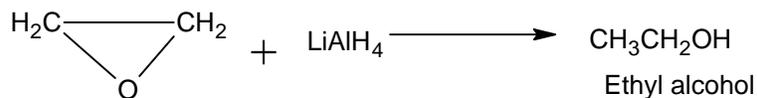
Reaction with Ammonia



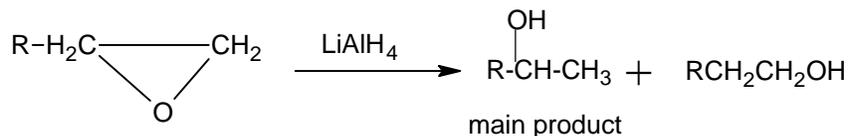
Reaction with halogenated, HBr:



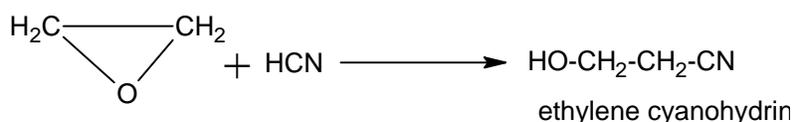
Reaction with LiAlH₄



Unsymmetrical epoxides give the more highly substituted alcohol with main product.

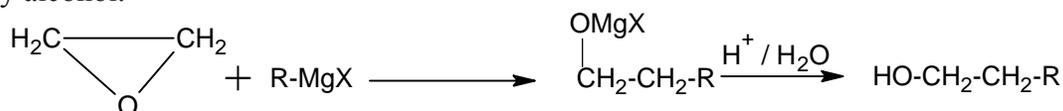


Reaction with HCN:



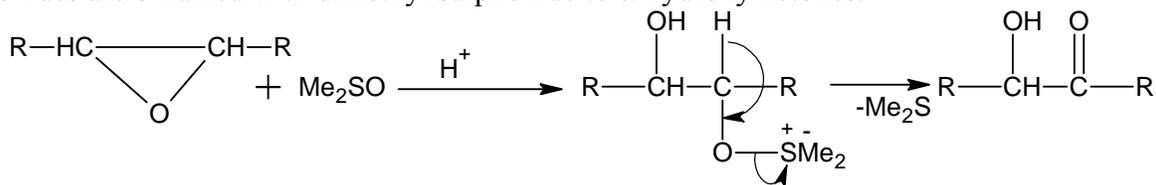
Reaction with Grignard Reagent:

Ethylene oxide reacts with Grignard Reagent to give addition product which on hydrolysis yield primary alcohol.



Oxidation:

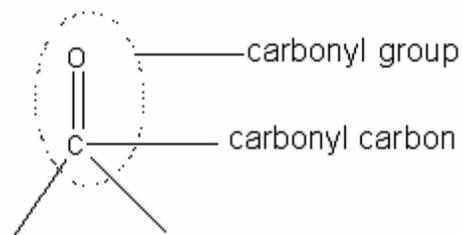
Epoxides are oxidized with dimethyl sulphoxide to α -hydroxy ketones.



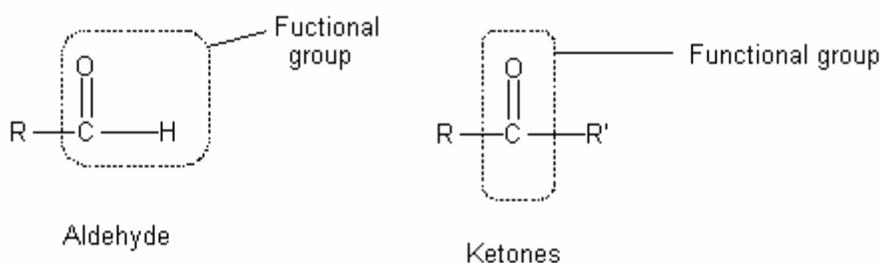
Aldehydes and Ketones

Aldehydes and ketones both contain oxo or carbonyl group ($>=O$). In aldehydes carbonyl carbon on one side attached to hydrogen atom and to carbon atom on other side, thus functional group of aldehydes is $-\text{CHO}$. This group occurs at the end of a chain. In ketones carbonyl carbon, on both sides attack to carbon atoms, thus the functional group in ketones occurs within a

chain. ($\text{c} \begin{array}{c} \text{O} \\ || \\ \text{c} \end{array} \text{c}$)



Aldehyde and ketones are collectively called carbonyl compounds.



Like carbon-carbon double bond, double bond between carbon and oxygen in carbonyl group is composed of one σ and one π bond. Carbonyl carbon is in a state of sp^2 hybridization. The carbon-oxygen σ bond is formed by the overlap of sp^2 orbital of carbon with sp^2 -orbital of oxygen atom. On the other hand the carbon oxygen π bond is formed by side wise overlap of unhybridised p-orbital of both atoms. Two unshared pairs of electron occupy the sp -hybrid orbitals of oxygen. since three σ -bond of carbonyl carbon utilize sp^2 orbitals, they lie in one plane. The bond angles between the attached atoms are approximately 120° .

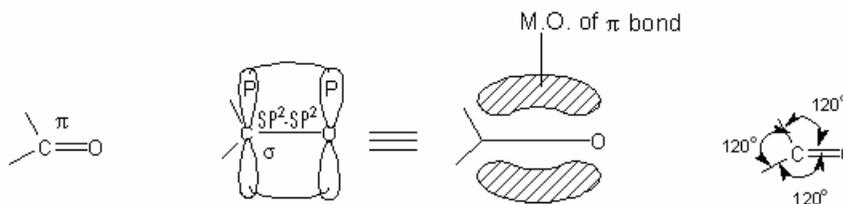
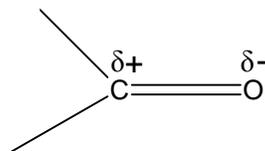


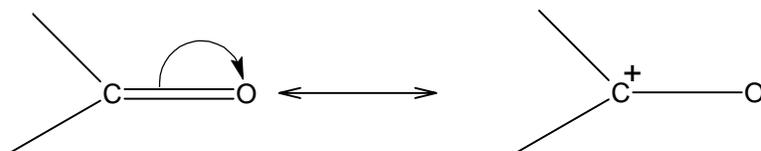
Figure-7: Structure of carbonyl group

But here π electrons are not equally shared by both carbon and oxygen atoms. This is because of the electronegativity. Due to the high electronegativity of oxygen atom, the π electron cloud is pulled more forward the oxygen atom. As result bond is polarized, oxygen attains a partial negative charge and carbon a partial positive charge.



polarity due to inductive effect

However the high values of dipole moments of aldehydes and ketones can't be accounted only by inductive effect but also by the resonance effect. Following resonance structures are possible.

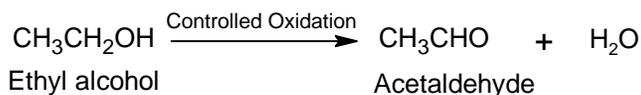
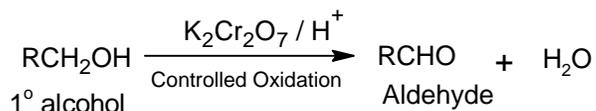


Carboxyl group is resonance hybrid of above two structures.

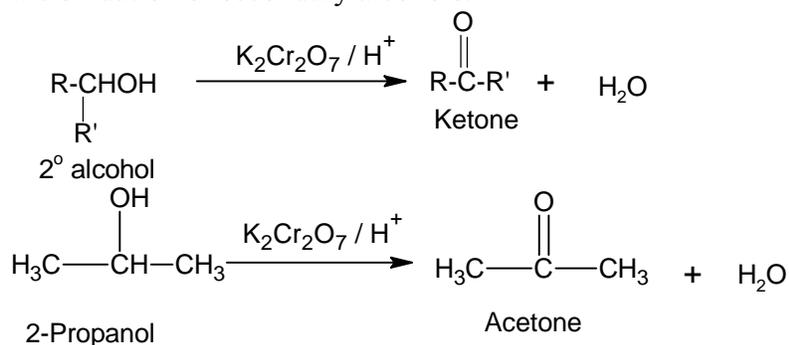
Methods of Preparation:

Both Aldehydes and ketones may be prepared by the following methods.

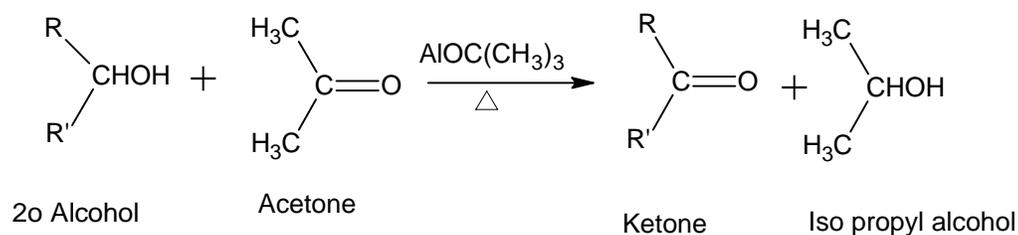
1) Oxidation of alcohols: Aldehydes are formed by the oxidation of primary alcohols.



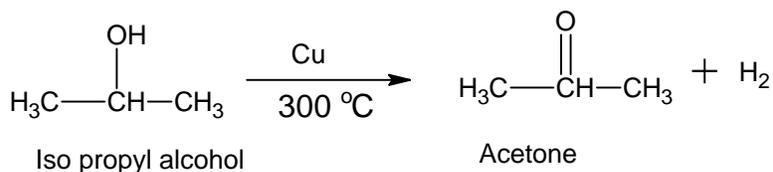
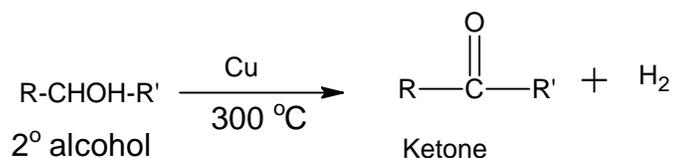
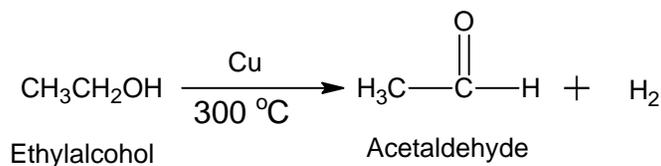
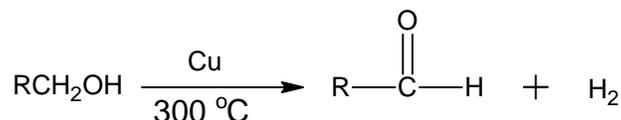
Controlled oxidation can also be carried out by using CrO_3 -pyridine [**Collin reagent**] Ketones are prepared by the oxidation of secondary alcohols.



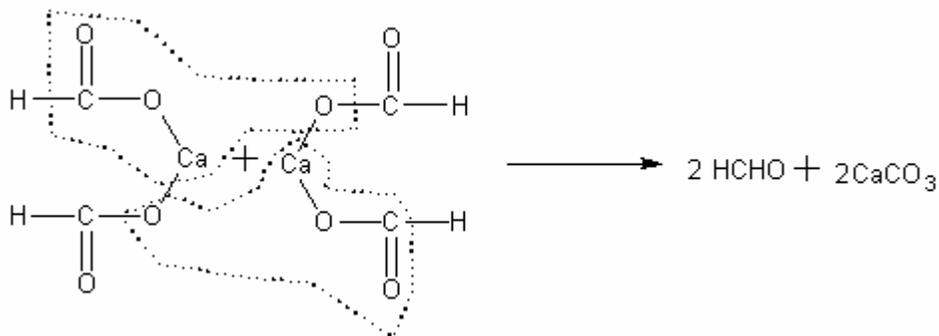
Ketones are not easily oxidized further. Ketones can also be obtained by **Oppenauer oxidation** of secondary alcohols, which involves refluxing of second alcohol with acetone in the presence of aluminium tertiary butoxide, $\text{AlOC}(\text{CH}_3)_3$, catalyst.

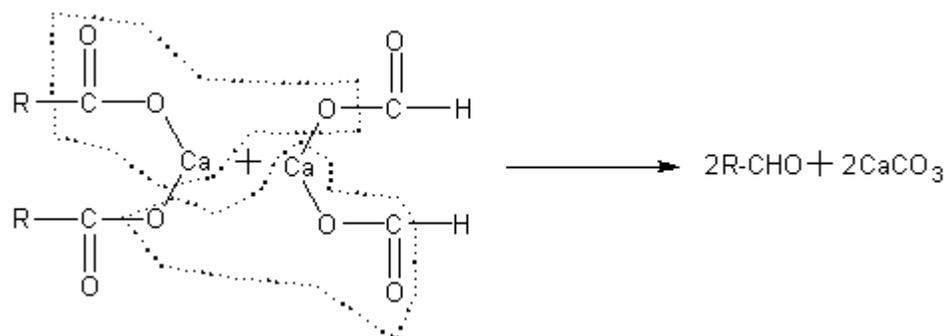


2) Dehydrogenation of alcohols: By passing the alcohol vapours over a copper catalyst heated to about 300°C, aldehydes and ketones are prepared. 1° alcohols give aldehydes while 2° give ketones.

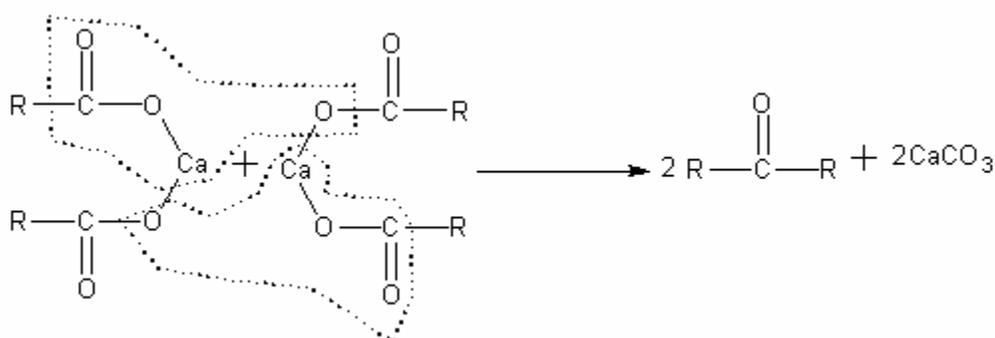


3. Dry distillation of calcium salts of Acids: Aldehydes are prepared by pyrolysis of calcium salt of fatty acid with Calcium formate. While calcium formate alone on heating gives formaldehyde.

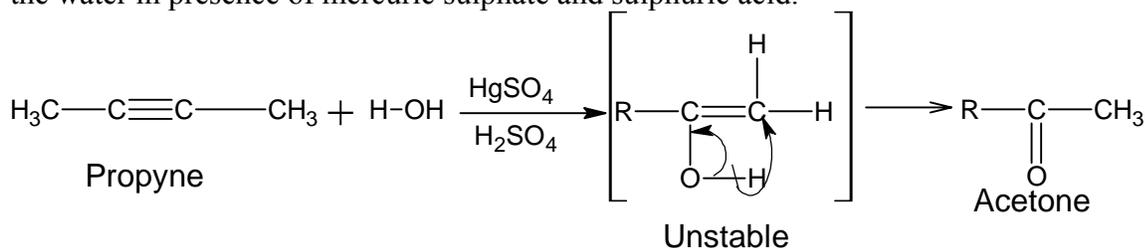




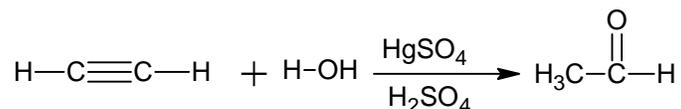
Ketones are obtained by heating calcium salt of fatty acid other than calcium formate.



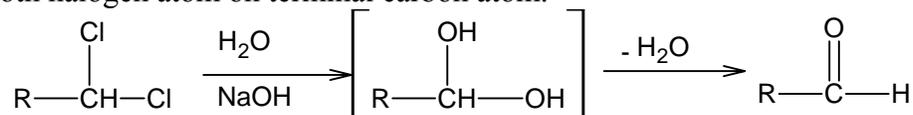
4) Hydration of alkynes: Aldehydes and ketones can be prepared by reactions of alkynes with the water in presence of mercuric sulphate and sulphuric acid.



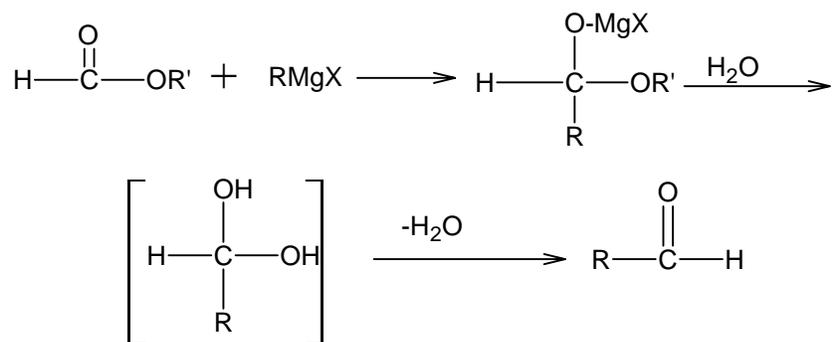
Acetylene give aldehyde under these conditions.



5) Hydrolysis of gem-Dihalides: Aldehydes are prepared by the hydrolysis of gem dihalides containing both halogen atom on terminal carbon atom.

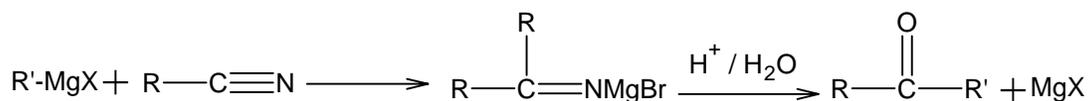


ii) From alkyl formates:

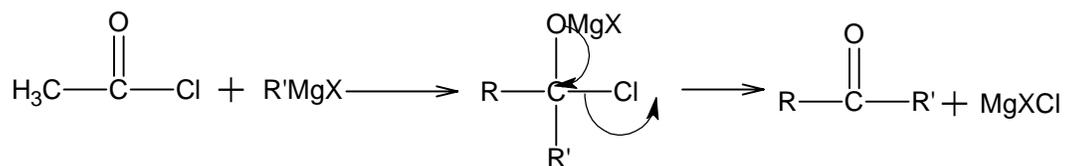


Ketones can also be prepared from Grignard reagent in two ways,

i) From alkyl cyanide:

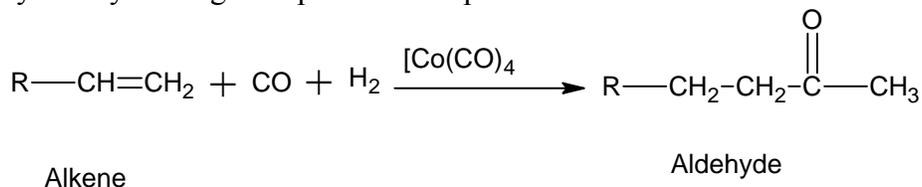


ii) From acid Chlorides:



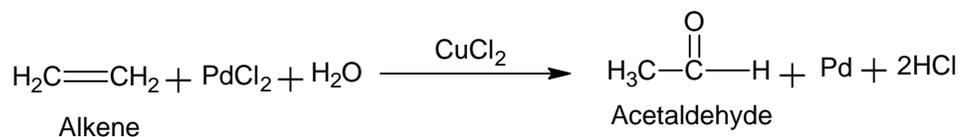
Aldehyde or ketones so formed, may further react with excess of the Grignard reagents to give alcohols.

9) Oxo process: This method is industrially important for the preparation of aldehydes. It involves the treatment of an alkene with carbon monoxide and hydrogen in the presence of cobalt carbonyl catalyst at high temperature and pressure.



Ketones cannot be prepared by this method.

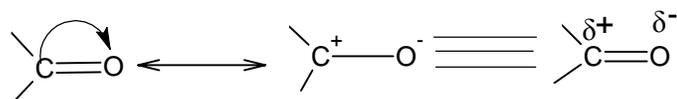
10) Wacker process: This method involves the treatment of alkene with acidified aqueous solution of palladium chloride, PdCl_2 and cupric chloride, CuCl_2 .



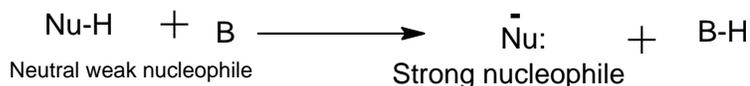
Properties:

- 1) Formaldehyde is gas at room temperature and other aldehydes and ketones are colourless liquids.
- 2) Lower aldehydes and ketones are soluble in water due to capability of forming hydrogen bonds with water molecules. But higher members containing more than five carbon atoms are insoluble in water and soluble in organic solvent.
- 3) Since aldehydes and ketones are polar compounds. Their boiling points are higher than corresponding non polar compounds. But these molecules are not capable of forming intermolecular hydrogen bonds. Their boiling points are lower than corresponding alcohols.
- 4) Density of aldehydes and ketones are lesser than that of water.

Chemical properties: Both aldehydes and ketones contain highly polar carbonyl group.

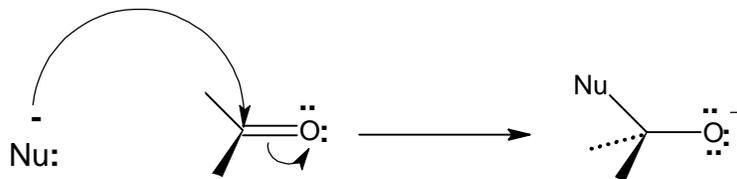


Carbonyl carbon is electron deficient and carbonyl oxygen is electron rich. The electron deficient carbon is readily attacked by electron rich nucleophiles and electron rich oxygen is attacked by electron deficient electrophiles. The typical reaction of aldehydes and ketones is nucleophilic addition. They undergo nucleophilic addition reaction by following general mechanism.

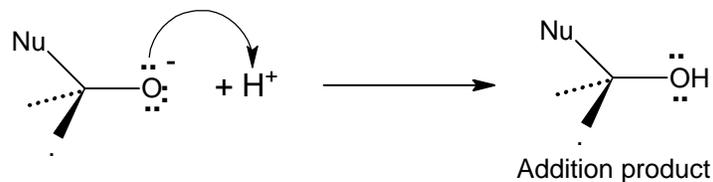


A: Base Catalysed Addition: Base convert weak nucleophile to strong one

Step 1: Attack of nucleophile at carbonyl carbon to form new σ -bond.

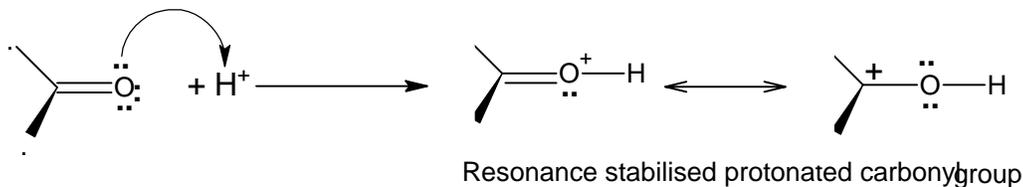


Step 2: Attack of electrophile (e.g., -H^+) at negatively charged oxygen to give addition product.

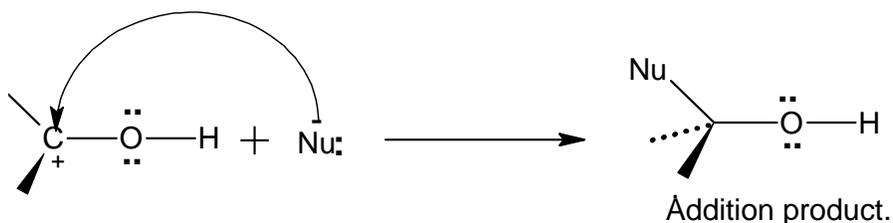


B) Acid Catalysed Addition:

Step 1: Protonation of carbonyl group.

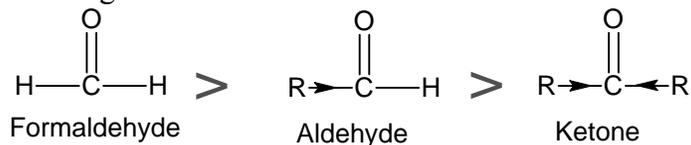


Step 2: Attack of nucleophile on protonated carbonyl carbon to give addition product.

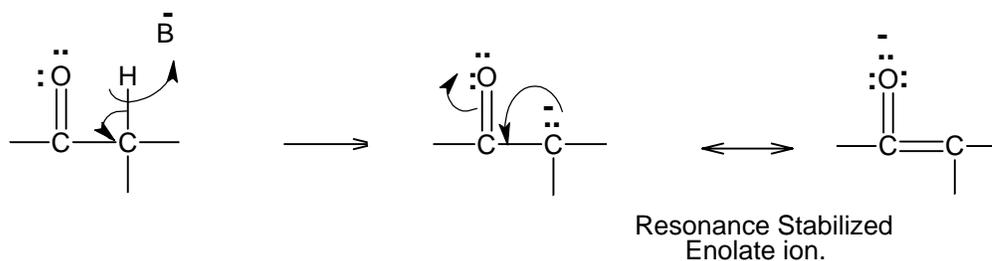


Addition products remains same in both acid and base catalysed reaction.

The reactivity of the carbonyl group towards the nucleophilic addition reactions depends upon the magnitude of the positive charge on the carbonyl carbon and also on crowding around the carbonyl carbon. (Steric factor). Alkyl groups of other electron donating that decreases the positive charge on the carbonyl carbon will decrease its reactivity towards the nucleophilic addition follows the following order.



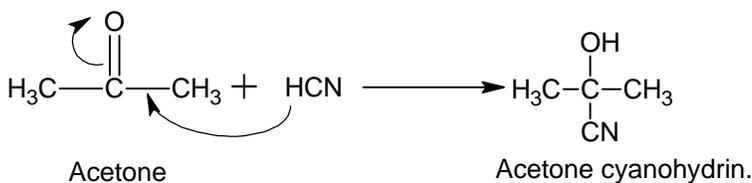
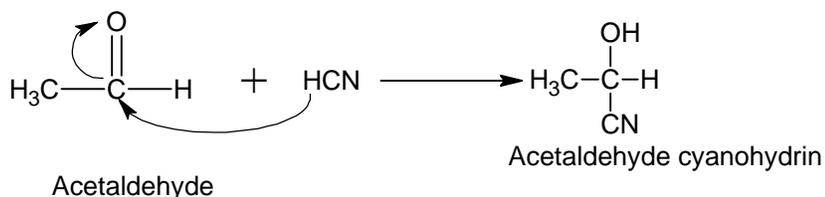
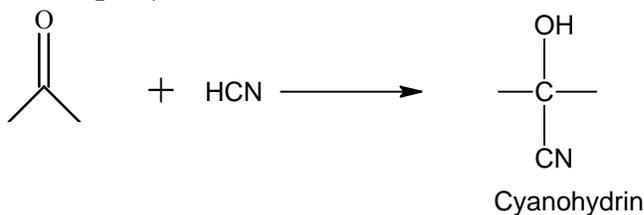
Acidity of α -Hydrogens: A carbon atom next to carbonyl group is α -carbon atom and hydrogens attached to this carbon are known as α - hydrogens. α - hydrogens in aldehydes and ketones are abstractable by base i.e; acidic in nature. this is due to the fact that carbanion formed the normal of hydrogen atom is stabilized by resonance. this ion is called **Enolate ion**.



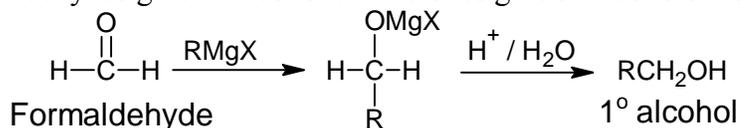
The negatively charged carbon of enolate ion act as a nucleophile. All condensation reaction involved formation of enolate ion and its addition to carbonyl group.

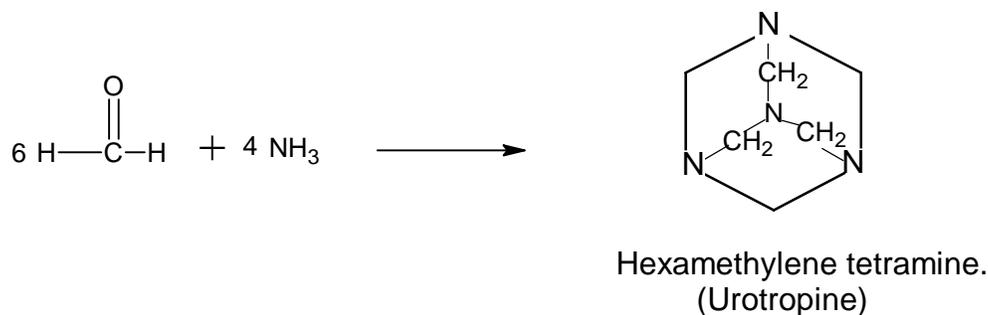
(A) Nucleophilic Addition Reactions of Aldehydes & Ketones

(1) Addition of Hydrogen Cyanide: Aldehydes and Ketones on addition of HCN give **cyanohydrins**. Reaction is carried out in the presence of basic catalyst. HCN is produced *in situ* by the action of dilute H_2SO_4 on KCN.

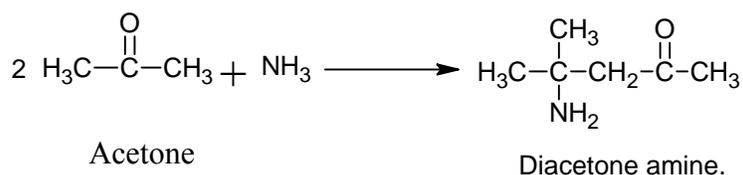


(2) Addition of Grignard reagent: Aldehydes and Ketones with Grignard reagent first give the addition product which can be hydrolysed with dilute acid to yield alcohol. Only formaldehyde gives 1° alcohols, other aldehydes give 2° alcohol and ketones give 3° alcohols. For example



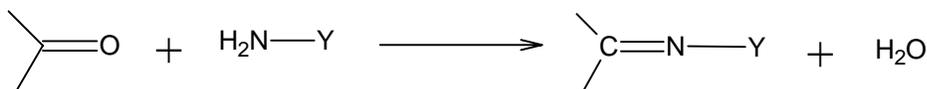


Urotropine is used as urinary antiseptic.



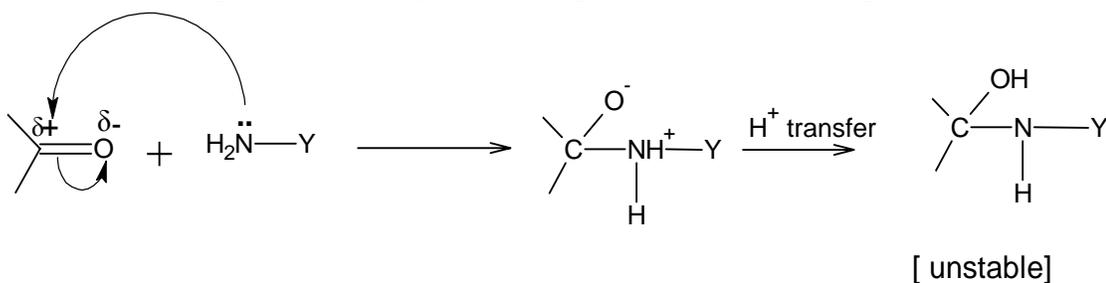
B) Reactions Involving addition followed by removal of water:

5) Reaction with Ammonia Derivatives: Reactions of Aldehyde and Ketones with ammonia derivatives are very important and characteristic reactions of carbonyl compounds. They react with ammonia derivatives ($\text{H}_2\text{N}-\text{Y}$) to form compounds containing carbon-nitrogen double bond ($\text{C}=\text{N}-$), with the elimination of water.

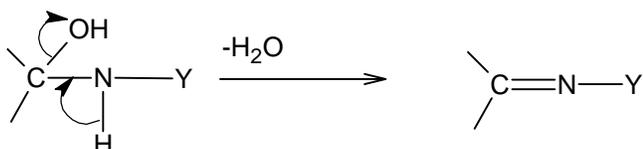


General mechanism of the reaction involve following steps.

Step 1: Attack of nucleophile on carbonyl carbon to give unstable addition product.

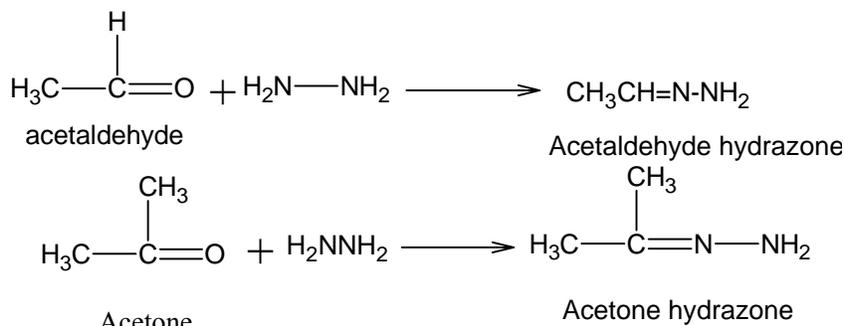


Step 2: Removal of water to give the final product.

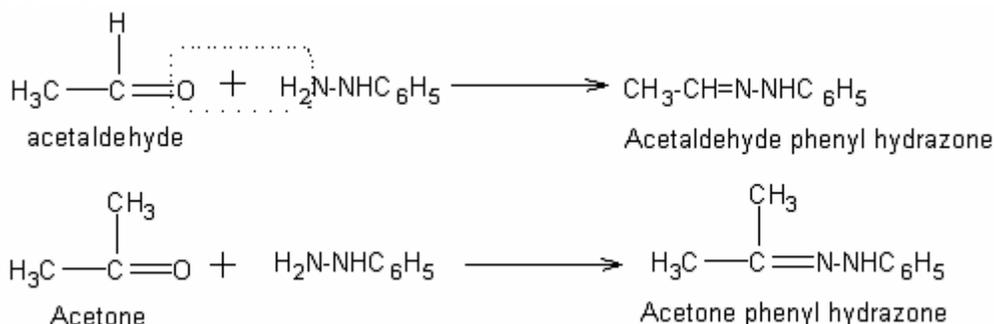


All the ammonia derivatives follow the same mechanism. The ammonia derivatives are hydrazine, phenyl hydrazine, 2,4-dinitrophenyl hydrazine, hydroxylamine, and semicarbazide.

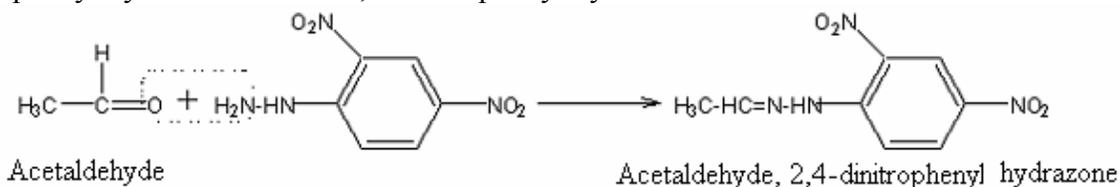
a) Reaction with Hydrazine: Aldehydes and ketones form hydrazones with hydrazine (NH_2NH_2)



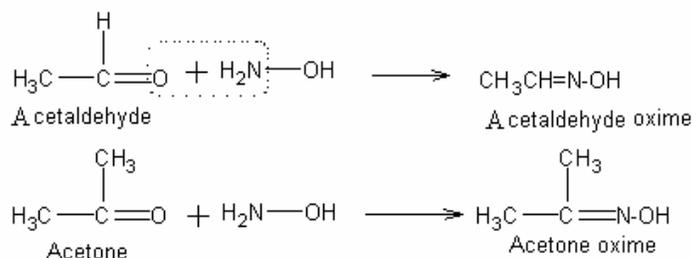
b) Reaction with phenyl hydrazine: Aldehydes and ketones form phenyl hydrazone with phenyl hydrazine.



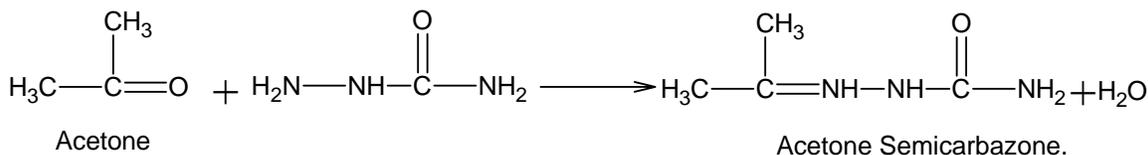
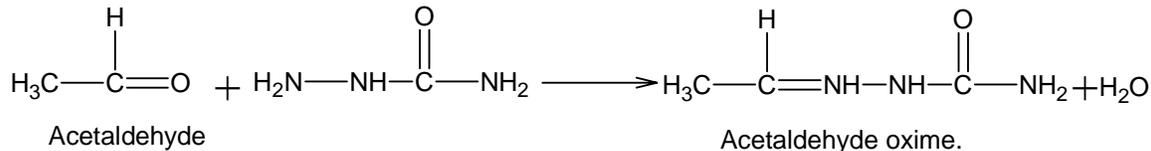
c) Reaction with 2,4-Dinitro phenyl hydrazine: Aldehydes and ketones react with 2,4-dinitrophenyl hydrazine to form 2,4-dinitrophenyl hydrazone.



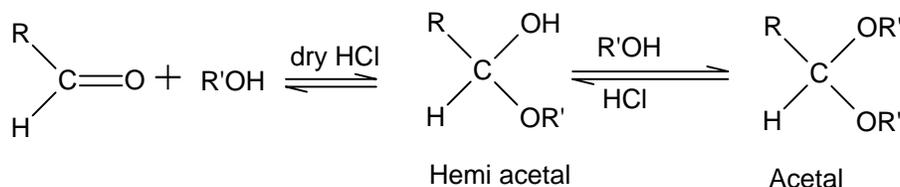
d) Reaction with Hydroxylamine: Aldehydes and ketones form oxime with hydroxylamine (NH_2OH).



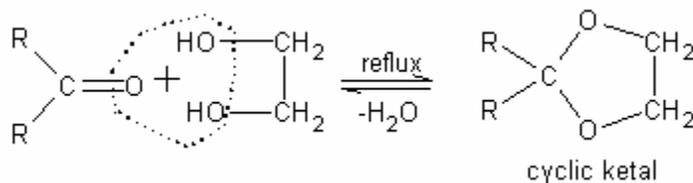
e) **Reaction with Semicarbazide:** Aldehydes and ketones give Semicarbazone with semicarbazide



6) **Reaction with alcohols:** Aldehyde react with alcohol in the presence of dry HCl gas to form Acetals e.g:

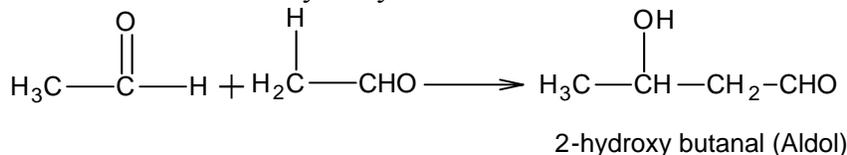


Acetals are readily cleaved by acids to give acetaldehydes, and are stable towards base. Ketones however, do not form ketals with monohydric alcohols, they react with dihydric alcohols to give cyclic ketals. e.g



(C) **Condensation Reactions:** These reactions involve formation of enolate ion which attack on carbonyl carbon of another molecule to give condensation product.

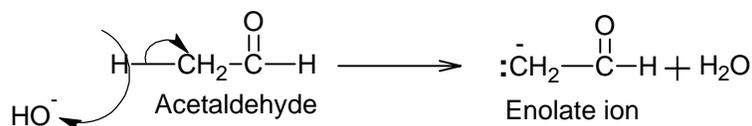
7) **Aldol condensation:** Aldehydes containing at least one α -hydrogen atom. When treated with dilute base like NaOH undergo condensation reaction to give products called **Aldols**. The reaction is known as aldol condensation. Aldols are the compounds containing both aldehydic and Alcoholic functional groups. For example two molecules of acetaldehyde combine in presence of dilute NaOH to form 3-hydroxy butanal.



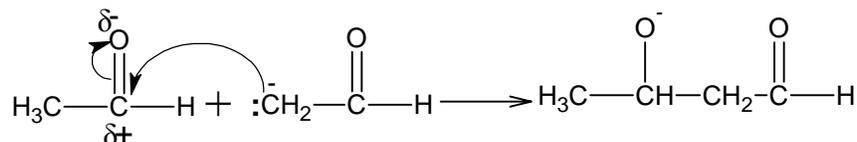
Mechanism:

Following steps are involved in the mechanism of aldol condensation reaction.

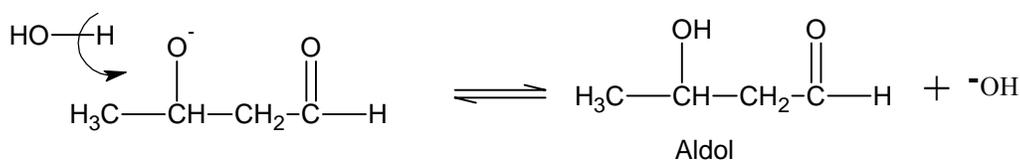
Step 1: Formation of enolate ion



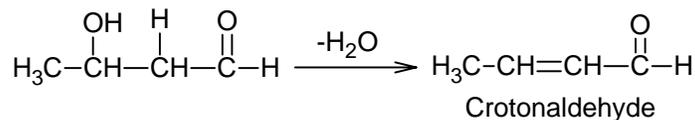
Step 2: Attack of enolate ion (nucleophile) on carbonyl carbon of another molecule of acetaldehyde.



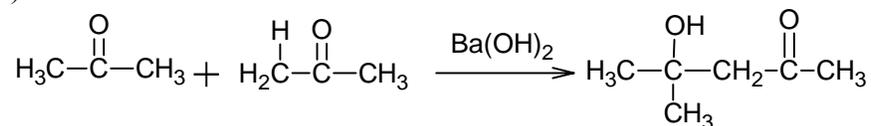
Step 3: Abstraction of proton from water molecule to give final product Aldol.



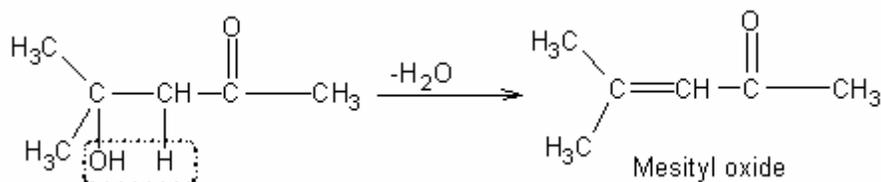
Aldol when heated easily loses a molecule of water to form α,β -unsaturated compound. For example



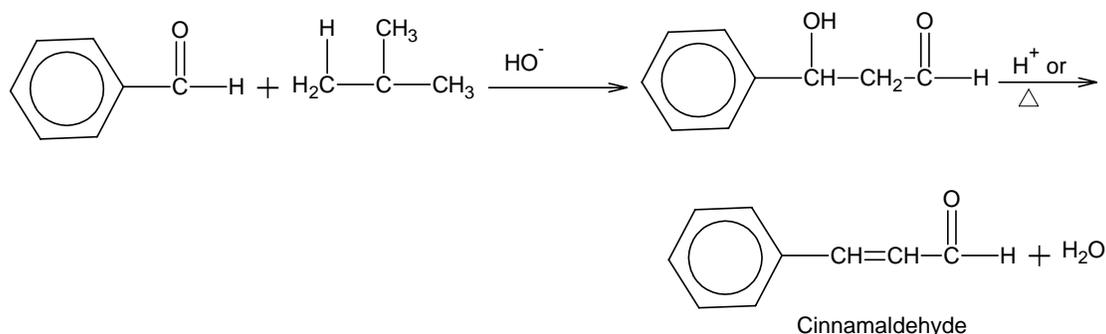
Ketones containing α -hydrogens also undergo condensation to give ketols. For examples, two molecule of acetone condense together in the presence of barium hydroxide to form diacetone alcohol (Ketol)



Diacetone alcohol on heating loses one molecule of water to form mesityl oxide.

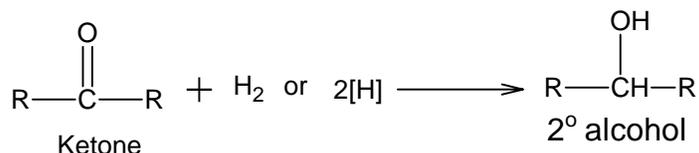
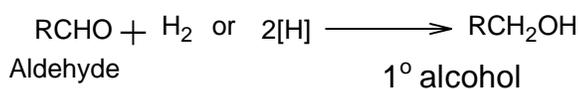


Mixed Aldol Condensation: Condensation that take place between two different molecules, one of which must have an α -hydrogen, in the presence of base is known as mixed aldol condensation. For example condensation of acetaldehyde with benzaldehyde.

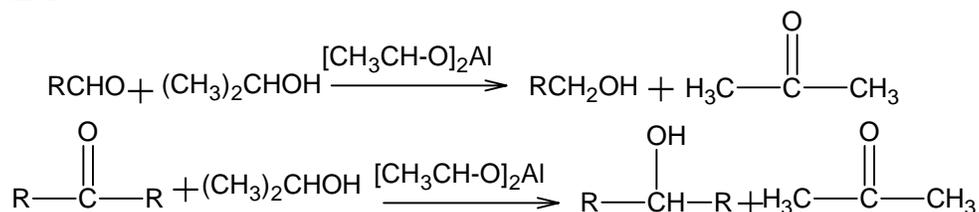


(D) Reduction Reactions:

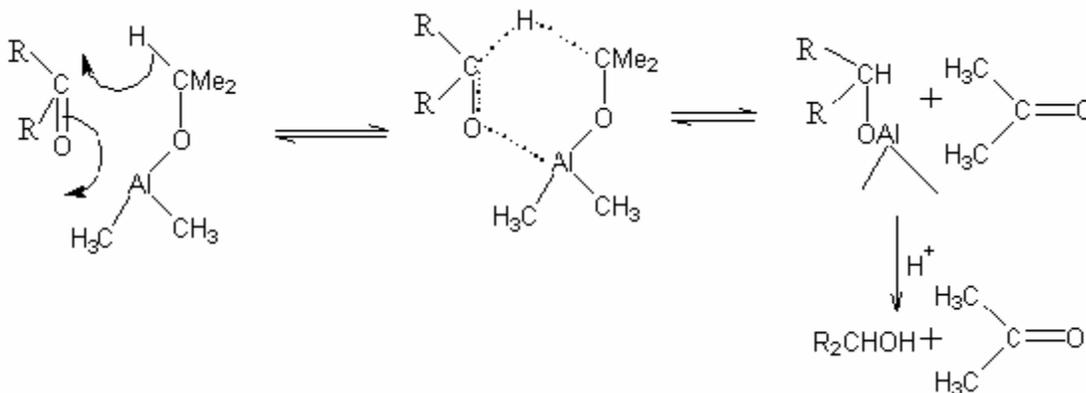
8) Reduction to Alcohols: Aldehydes and ketones are reduced to the primary and secondary alcohols respectively by catalytic hydrogenation (H_2/Ni or Pt), nascent hydrogen (Na-Hg or $\text{Na/C}_2\text{H}_2\text{OH}$), LiAlH_4 or NaBH_4



Reduction of both aldehydes and ketones to alcohols may be effected by means of Merwein-Ponndorf-Verley Reduction which involves the reduction by means of aluminum iso propoxide in isopropanol.

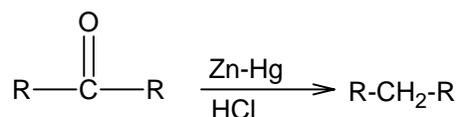
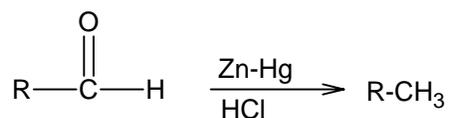


The reduction occurs by hydride ion transfer from aluminium isopropoxide to the carbonyl compound via a cyclic transition state.

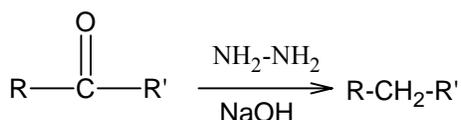
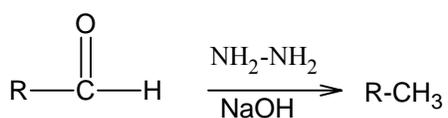


9) Reduction to Alkanes: Aldehydes and ketones are reduced to corresponding alkanes by means of zinc amalgam and hydrochloric acid [Clemensen reduction] or alkaline solution of hydrazine.[Wolf Kishner Reduction]

Clemmensen Reduction: This involves the use of zinc- mercury amalgam in hydrochloric acid as the reducing agent.

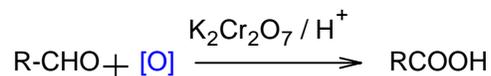


Wolf Kishner Reduction : This involves the use of basic solution of hydrazine as the reducing agent



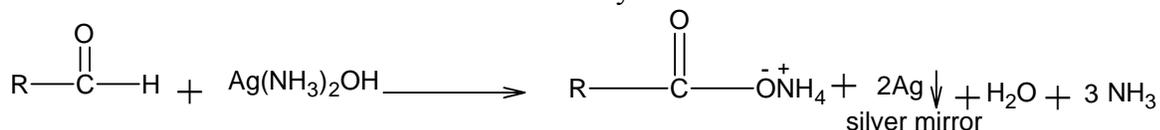
(E) Oxidation Reactions:

10) Aldehydes are easily oxidized to carboxylic acid by acidic $\text{Na}_2\text{Cr}_2\text{O}_7$ or $\text{K}_2\text{Cr}_2\text{O}_7$ or acidic KMnO_4 .



Aldehydes can also be oxidized by another oxidizing agents such as Tollen's reagent, Fehling's solution and Benedicts solution and thus act as a strong reducing agents.

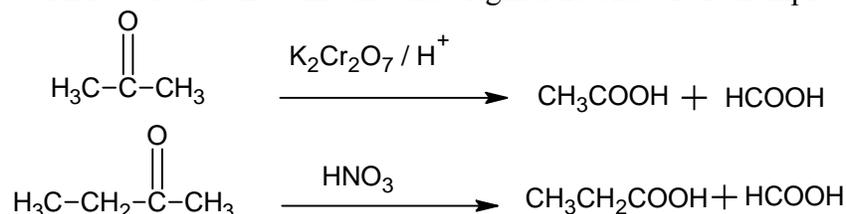
Tollen's Reagent:[Ammonical Silver nitrate Solution] : When Tollen's reagent is used to oxidize an aldehyde, the Silver ion is reduced to metallic form and deposits as a mirror on clean test tube. This reaction is used as a test of aldehyde and known as **Silver mirror test**.



Fehling solution: Blue coloured alkaline solution of cupric ion [Fehling Solution A] complexed with sodium potassium tartrate (Fehling Solution B) is also reduced by Aldehyde. The complexed cupric ion (deep blue) is reduced to Cuprous oxide.

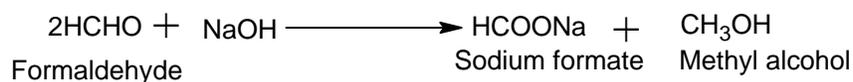
Benedict solution (alkaline solution of cupric ion complexed with citrate ions) reacts in the same way as Fehling Solution.

Ketones are not oxidized by milder oxidizing agents thus they do not reduce Tollen's reagent, Fehling solution and Benedicts solutions. However, ketones can be oxidized by stronger oxidizing agents such as acid dichromate, alkaline KMnO_4 and hot con. HNO_3 to form carboxylic acids with fewer carbon atoms than the original ketones. For example



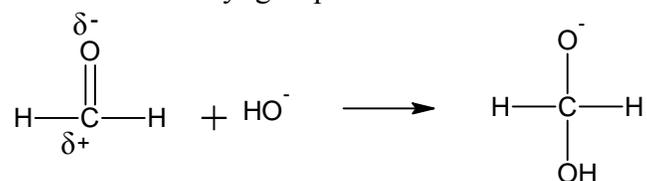
(F) Other important Reactions of Aldehydes and Ketones.

(11) Cannizzaro reaction: Aldehydes which do not have α -hydrogen atom, when treated with concentrated solution of NaOH undergo disproportionation reaction. One half of the aldehydes are oxidized to carboxylic acid and other half are reduced to alcohol. This reaction is known as **Cannizzaro reaction**.

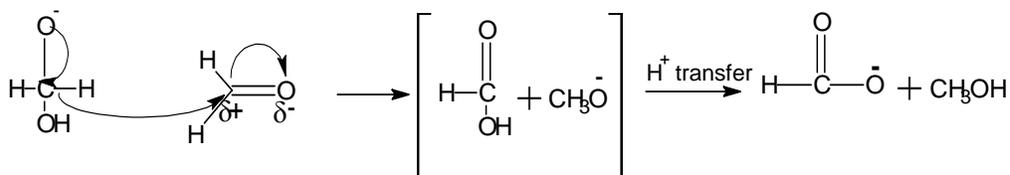


Mechanism: Following steps are involved

Step 1: Attack of the OH^- on the carbonyl group.

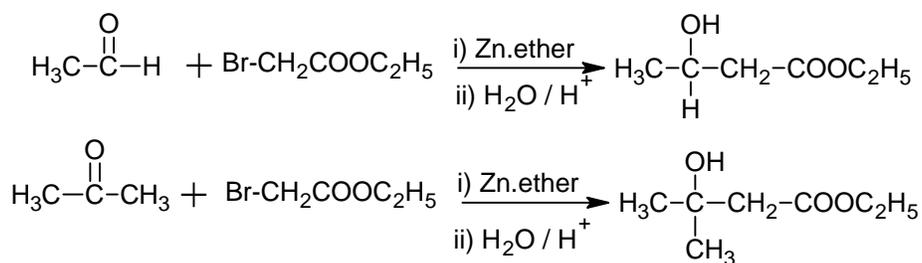


Step 2: Hydride transfer:



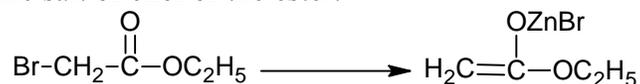
Ketones do not give this reaction.

12) Reformatsky Reaction: Reaction of aldehydes and ketones with α -bromoester in the presence of metallic zinc and ether to give β -hydroxy ester is known as Reformatsky reaction. e.g.

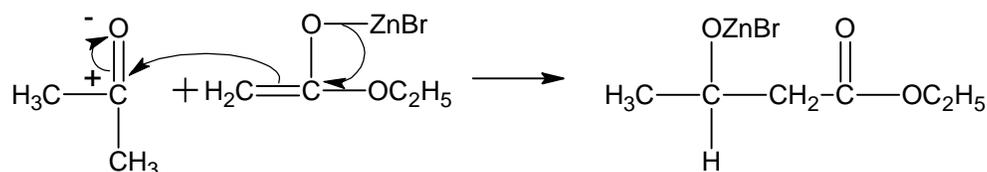


Mechanism: Three steps are involved.

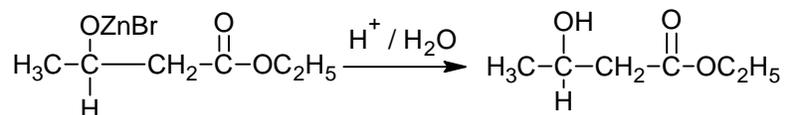
Step 1: Formation of zinc salt of enol of the ester.



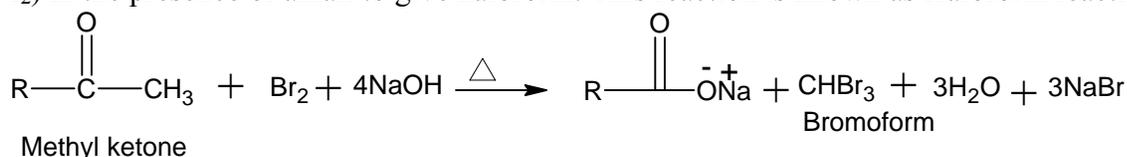
Step 2: The zinc salt reacts with the carbonyl compound.



Step 3: Acid hydrolysis



13) Haloform Reaction: Acetaldehyde and methyl ketones react rapidly with halogen (Cl_2, Br_2 or I_2) in the presence of alkali to give haloform. This reaction is known as Haloform reaction.

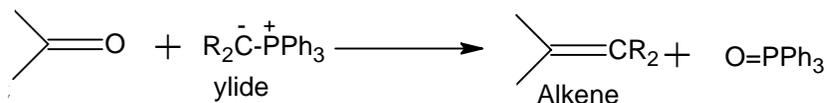


The reaction takes place in two steps.

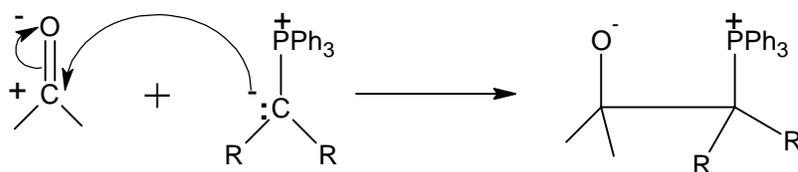


Haloform reaction is used as a diagnostic test for detecting the presence of $-\text{COCH}_3$ group in a compound. This reaction can also be used to distinguish methyl ketones. Ketone not containing $(-\text{CO}-\text{CH}_3)$ do not give this reaction.

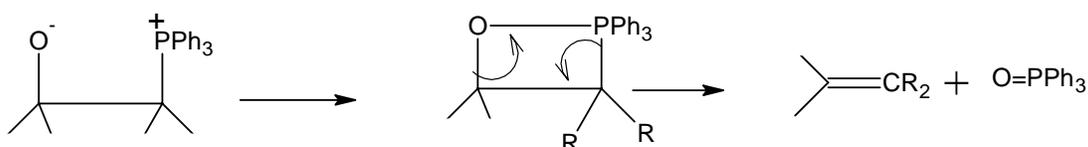
14) Wittig Reaction: Reaction between aldehydes and ketones with triphenyl phosphine alkylidenes or phosphorous ylide ($\text{Ph}_3\text{P}=\text{CR}_2$) to form alkene is known as Wittig reaction.



Mechanism: Attack of negative carbon of ylide on carbonyl carbon to form **betaine**,

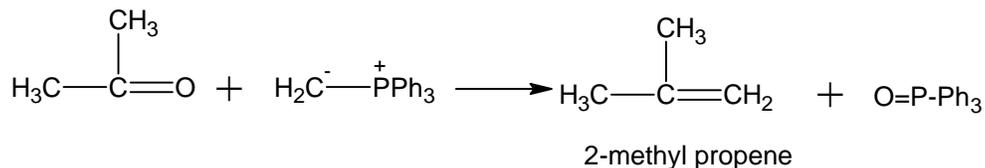


Betaine undergo elimination to give the alkene.

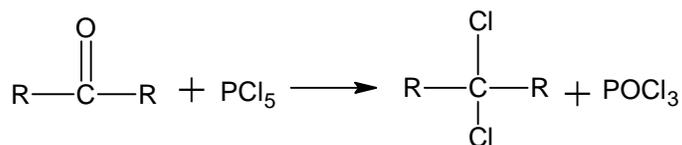
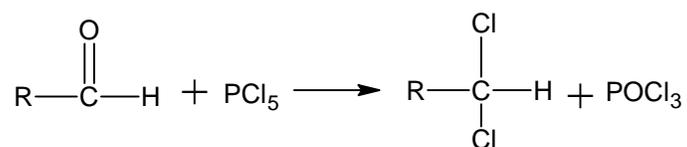


Betaine

Example:

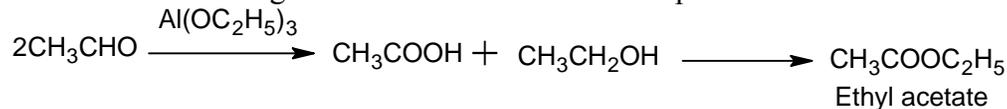


15) Reaction with PCl_5 : Aldehydes and ketones react with PCl_5 to give gem-dihalides.e.g.



Gem.dihalide

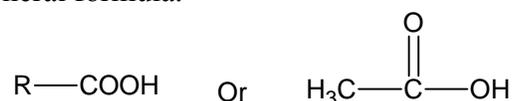
16) Tischenko Reaction: Aldehydes having α -hydrogen atom can also be made to undergo cannizzaro type reaction, if reaction is carried out in presence of aluminum ethoxide. But in such case, acid and alcohol react together to form ester as the final product.



17) Polymerization: Lower aldehydes undergo polymerization to form different products under different conditions. Ketones however, are not much susceptible to polymerization.

Carboxylic Acids and Their Functional Derivatives

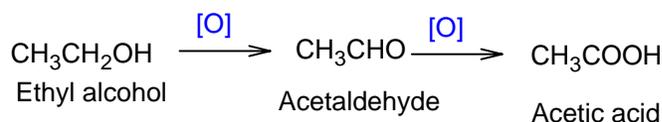
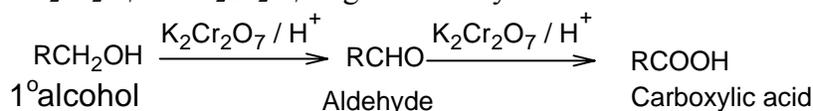
Organic compounds containing carboxyl group (-COOH) are known as carboxylic acids. They can be represented by the general formula.



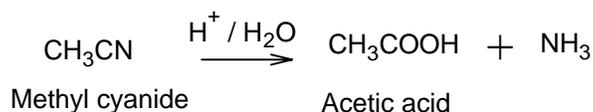
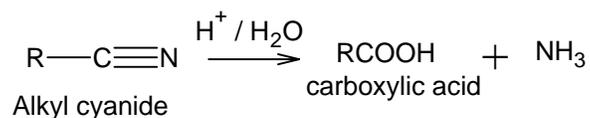
They are further classified as mono, di, tri etc., carboxylic acids, according to the number of carboxylic groups present in their molecules. The long chain monocarboxylic acids are also called fatty acids because many of them are obtained from fats.

Methods of Preparation

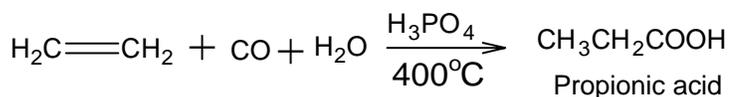
1) By the oxidation of primary alcohols or Aldehydes: Primary alcohols or aldehydes are oxidized by acidic $\text{K}_2\text{Cr}_2\text{O}_7$ or $\text{Na}_2\text{Cr}_2\text{O}_7$ to give carboxylic acids.



2) By the hydrolysis of alkyl cyanides or nitriles: Alkyl cyanide on acid hydrolysis give carboxylic acids.

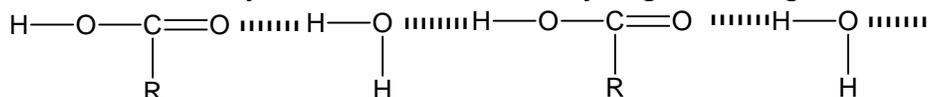


3) By the Hydrolysis of Ester: When esters are hydrolysed by alkali NaOH or KOH, sodium or potassium salt of carboxylic acids are formed which on treatment with dil HCl gives the corresponding carboxylic acids.



Properties:

- 1) The lower carboxylic acids (C₁ to C₁₀) are colourless pungent smelling liquids. Higher members are wax like solids and almost colourless.
- 2) First four members are freely soluble in water due to hydrogen bonding with water molecule.



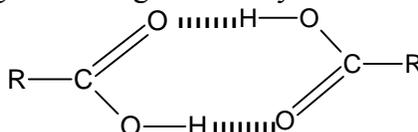
But the solubility of higher members decreases rapidly with the increase in the size of the alkyl group due to increased influence of the non-polar and hydrophobic hydrocarbon chain.

- 3) Melting points of carboxylic acids increase irregularly with increase in the molecular weight. The even members have markedly higher boiling points than the odd members.

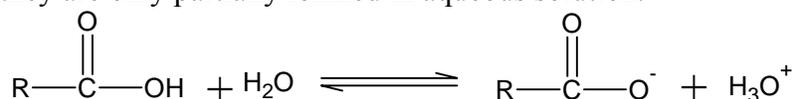
- 4) Boiling points of the carboxylic acids, particularly lower members higher than the alcohols of same molecular weight. e.g.

Acetic acid (CH ₃ COOH)	MW = 60	b.p. = 118°C
1-Propanol (CH ₃ CH ₂ CH ₂ OH)	MW = 60	b.p = 97°C

This is due to the strong hydrogen bonding in carboxylic acids than those in alcohols.

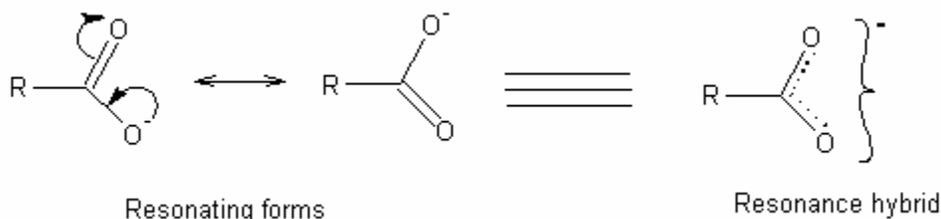


- 5) **Acidity of Carboxylic Acids:** Carboxylic acid are acidic in nature but they are weak acids as compared to inorganic acids (e.g. HCl or H₂SO₄). They can donate a proton and form salts with strong bases and they are only partially ionized in aqueous solution.

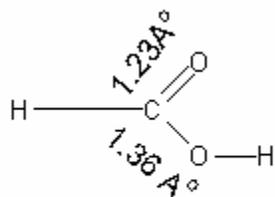


The acidic character of carboxylic acids decreases with increase in molecular weight. Formic acid is strongest of all fatty acids.

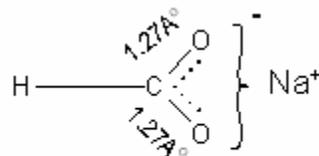
The acidic character of carboxylic acid is due to the resonance. The carboxylic ion form by ionization is stabilized by resonance.



Hence carboxylic ion is more stabilized than the acid itself. The equilibrium of the ionization of acids shifts to the right hand side. X-ray studies also support the existence of carboxylate ion as resonance hybrid for example bond lengths of carboxy oxygen have different values in formic acid. Where as in sodium formate the two carbon-oxygen bond lengths are identical.

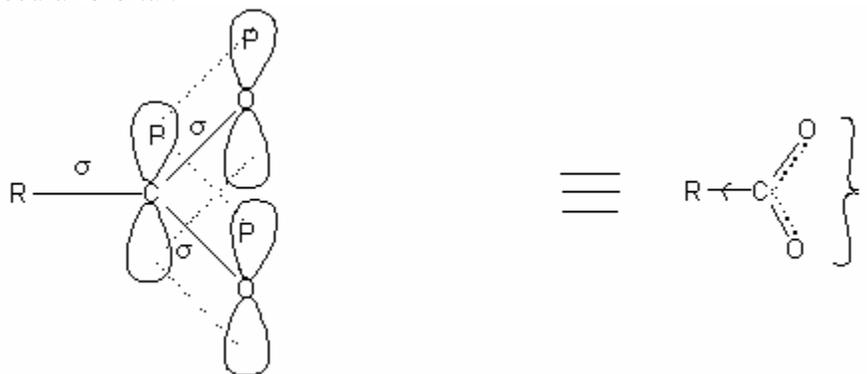


Formic acid

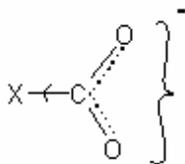


Sodium formate

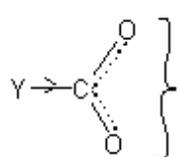
The stability of carboxylate ion can also be explained on the basis of its molecular orbital structure. The carbon atom of carboxyl group in sp^2 hybridised. In carboxylate ion the unhybridised P orbital of carbon overlaps with P orbital of both oxygen atom to form stable delocalized molecular orbital.



Effect of substituents on Acidity: Acidic character of carboxylic acid is due to the stabilization of carboxylate ion. So any factor which can enhance the dispersal of negative charge of the carboxylate ion will increase the acidity and vice versa. Inductive effect of the substituent on the α -carbon play very important role. Electron withdrawing substituents like Cl, Br, F, NO_2 , OH, CN etc. would disperse the negative charge and hence stabilize the carboxylic ion. On the other hand electron releasing substituents would increase the negative charge destabilizes the carboxylate ion and thus decrease acidity of the acid.



Electron withdrawing substituents
stabilise the carboxylate ion.



Electron releasing substituents
destabilise the carboxylate ion.

Alkyl groups are electron releasing group thus their presence in the molecule will decrease the acidity. Longer the lengths of alkyl chain, lower will the acidity of the acid. Since formic acid has no alkyl group, it is the strongest of all fatty acids. It is ten times stronger than acetic acid.



Similarly Chloroacetic acid is hundred times stronger than acetic acid because of the electron withdrawing nature of Cl group following order is observed in Chloro acetic acid.



Trichloroacetic acid is almost as strong as a mineral acid.

Chemical Properties:

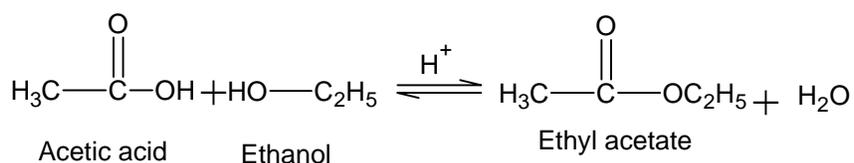
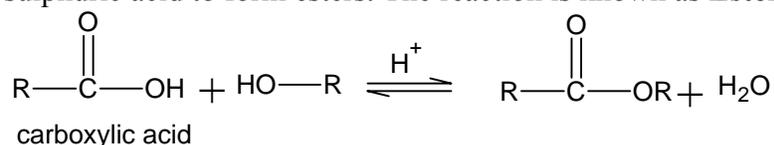
A) Reactions involving hydrogen atom of the -COOH group

1) **Reaction with metals and alkalis:** Carboxylic acids react with strongly positive metals with the liberation of hydrogen and form salt.



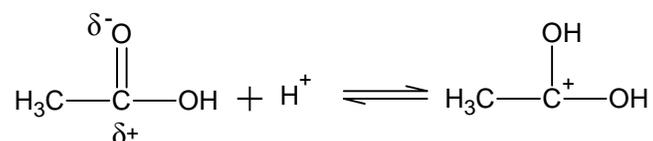
Carboxylic acids also form salts with metal hydroxides, carbonates and bicarbonates. For example

2) **Reaction with Alcohols:** Monocarboxylic acids react with alcohols in the presence of strong acid catalyst like sulphuric acid to form esters. The reaction is known as **Esterification**.

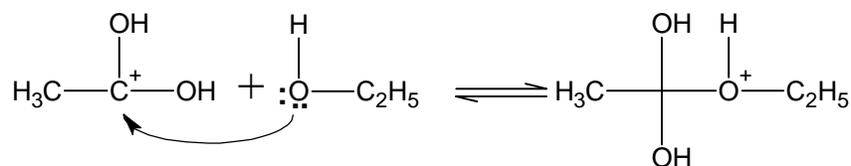


Following mechanism is suggested for the esterification

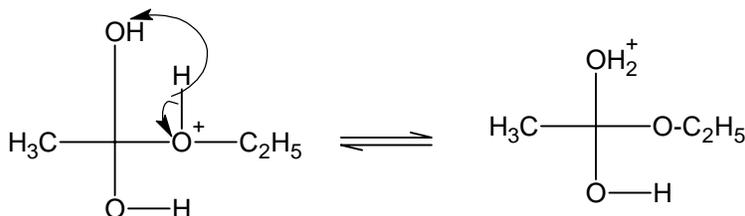
Step 1: Protonation of carboxylic acid.



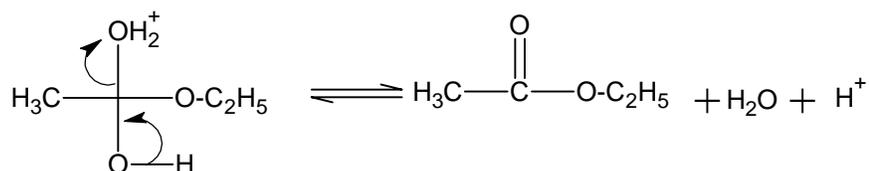
Step II: Attack of nucleophile, $\text{C}_2\text{H}_5\ddot{\text{O}}\text{H}$



Step III: Hydrogen ion transfer

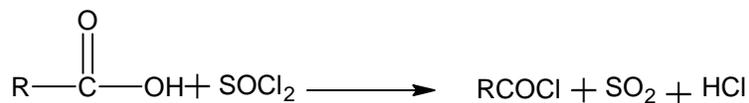


Step IV: Elimination of water and proton.

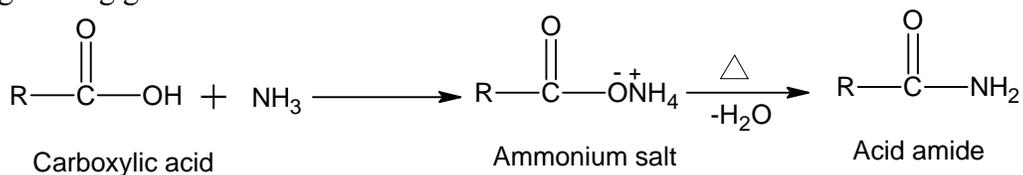


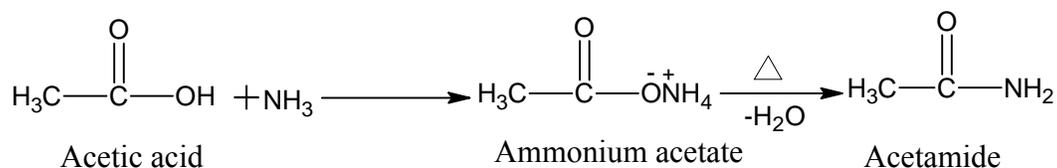
B) Reaction involving -OH part of the -COOH group

3) Reaction with Phosphorous Halides and Thionyl Chloride: Carboxylic acids react with phosphorous halides and thionyl chloride to form acid halides. For example.

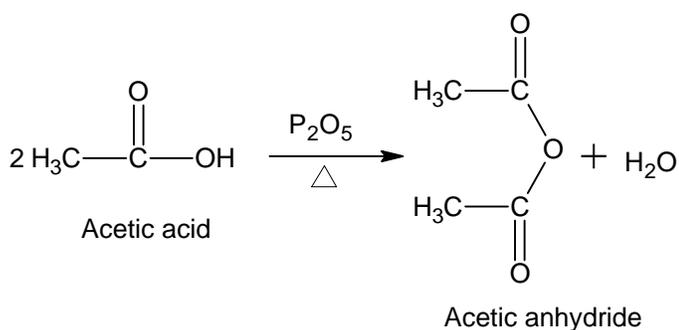
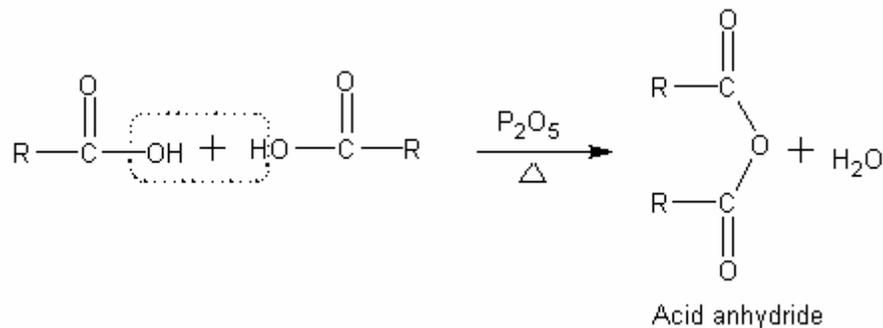


4) Reaction with ammonia: Carboxylic acid react with ammonia to form ammonium salt which on strong heating give acid amides with the elimination of water.

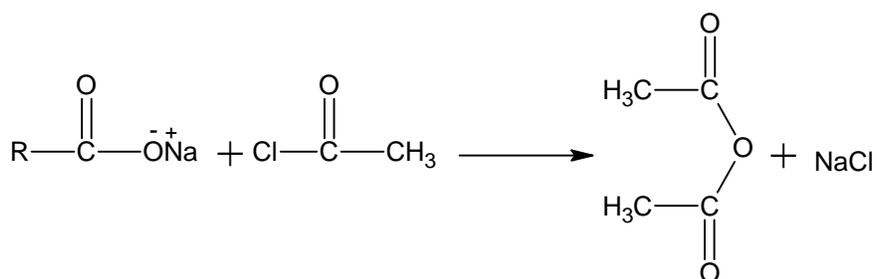




5) Dehydration: Carboxylic acid on dehydration with P_2O_5 (dehydrating agents) give acid anhydride.

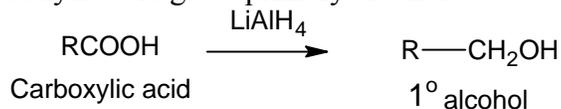


Acid anhydrides can also be prepared by heating sodium salt of acids with halides.

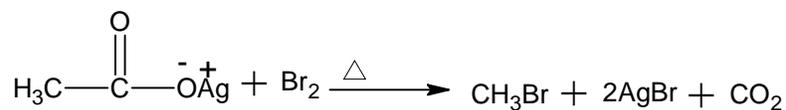


C) Some Other Reactions:

6) Reduction: Reduction of carboxylic acids depends on the nature of reducing agents. On reduction with LiAlH_4 , carboxylic acid gives primary alcohol.



Heating with HI / red Phosphorous, under pressure, or with hydrogen under pressure at elevated temperature in the presence of a nickel catalyst, produces an alkane.



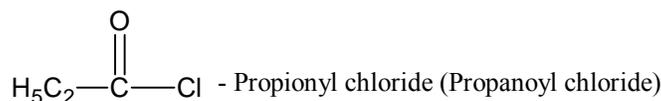
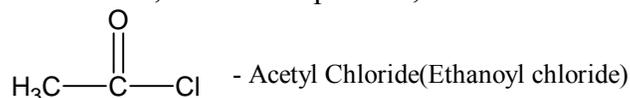
Carboxylic Acid Derivatives (Acid Derivatives): The compounds derived from the carboxylic acids by the replacement of $-\text{OH}$ function of Carboxyl group by another group are known as acid derivatives. All such derivatives upon hydrolysis generate the parent acid.

Different Acid derivatives are:

	Name	Formula
i)	Acid halides	$\text{H}_3\text{C}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_3 \quad \text{X} = \text{Cl, Br or I}$
ii)	Acid anhydride	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}$
iii)	Ester	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{OR}$
iv)	Amide	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$

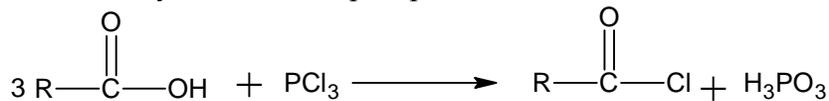
1. Acid Halides: Acid halides are the derivatives of acids in which the $-\text{OH}$ function of carboxyl group is replaced by a halogen atom. Acid halides are also known as **acyl halides**. Acid chlorides are most important of all the acid halides.

They are represented as $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{Cl}$, some examples are,

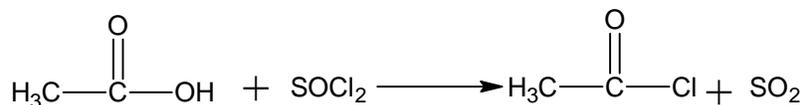


Methods of Preparation:

1) By the reaction of carboxylic acids with phosphorous halides



2) By the reaction of Carboxylic acids with thionyl chloride

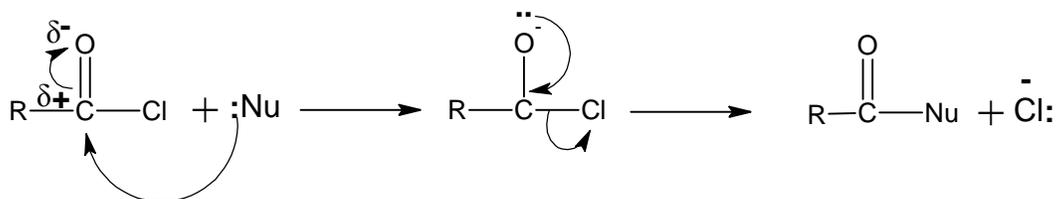


Properties:

Physical Properties:

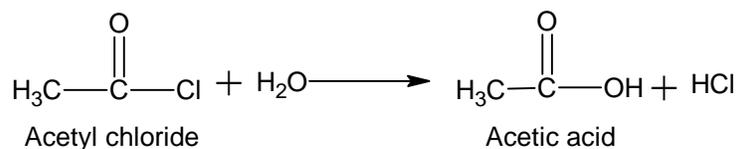
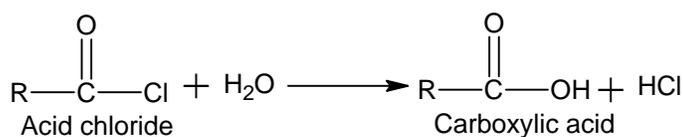
- i) All simple acid chlorides are pungent smelling colourless liquids of lower boiling points than the corresponding acid. They also have tear producing property. i.e lachrymators.
- ii) They are insoluble in water but slowly start to dissolve in it because of hydrolysis.

Chemical properties: Acid chlorides are very reactive compounds as they are more readily attacked by nucleophile because of the electron withdrawing effect of highly electronegative, chlorine atom attached to carbonyl carbon. This further diminishes the electron density on the carbonyl carbon. Cl atom is replaced by the nucleophile.



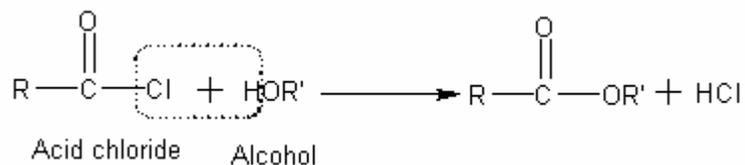
Some important reactions of acid chloride are following.

1)Hydrolysis: The acyl chlorides are readily hydrolysed by water to reform the original acid.

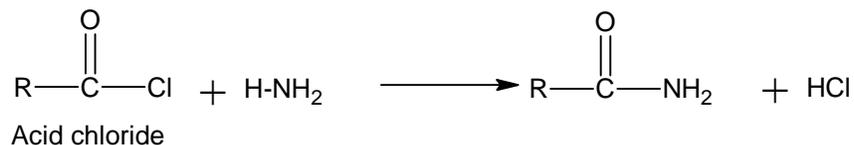


2) Acylation: Acid chlorides are important acylating reagent. Thus usually react rapidly with compounds containing active hydrogen atoms i.e. hydrogen attached to oxygen, nitrogen or sulphur. This active hydrogen is replaced by acyl group ($\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-$) of acid chloride.

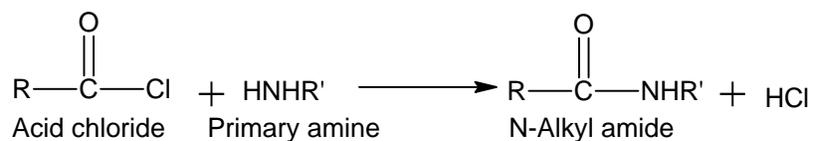
a) Reaction with alcohols (Alcoholysis): Esters are formed



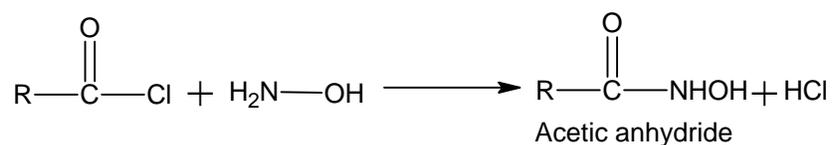
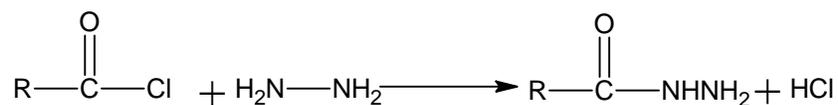
b) Reaction with Ammonia (Ammonolysis): Amides are formed.



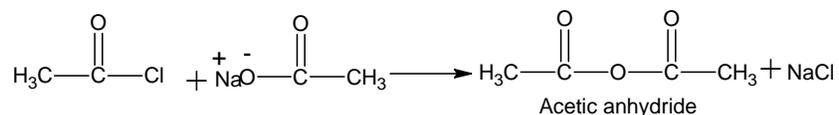
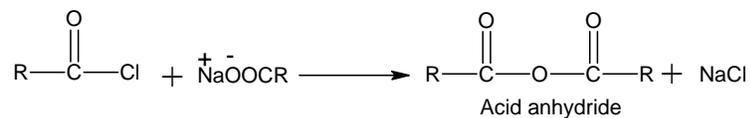
c) Reaction with Primary and Secondary Amines: N-substituted amides are formed.



d) Reaction with hydrazine and hydroxylamine: Hydrazides are formed.

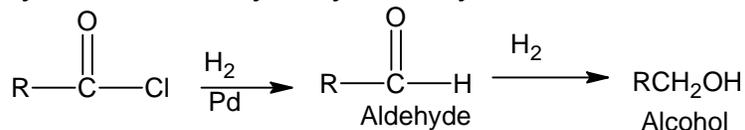


3) Reaction with salt of carboxylic acids: Anhydrides are formed.

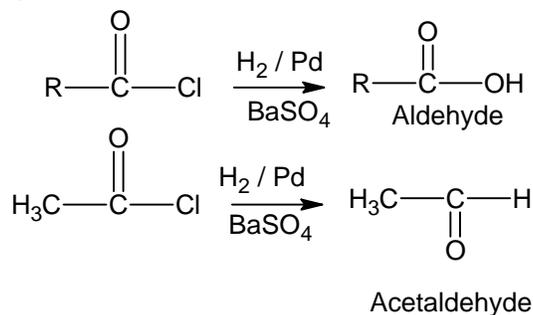


4) Reduction:

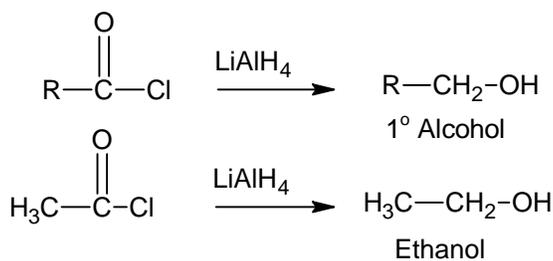
a) Acyl chlorides may be reduced catalytically to aldehydes or to alcohols.



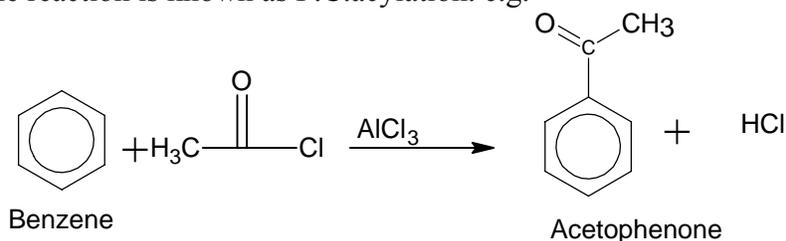
When reduced in presence of poisoned Palladium Catalyst, they form aldehyde. This reaction is called **Rosenmund Reduction**.



b) When reduced with LiAlH_4 , they form primary alcohols.



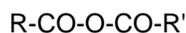
5) Friedel-Craft Acylation: Acyl chlorides react with aromatic hydrocarbon in presence of AlCl_3 catalyst. The reaction is known as F.C. acylation. e.g.



2. Acid Anhydrides: The compound derived from an acid by the removal of one water molecule from two molecule of the acid are called anhydrides.



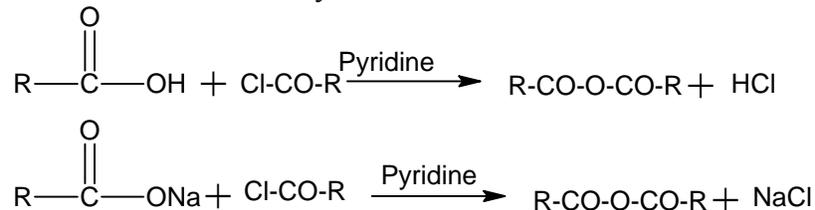
Anhydrides derived from two molecule of different acids are called mixed anhydride.



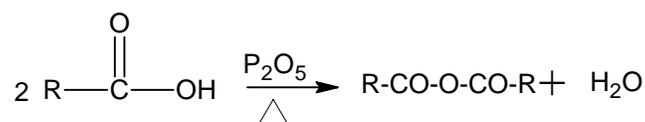
Methods of preparation:

Acid anhydrides may be prepared.

1) By reaction of acid halide with carboxylic acid or its Sodium salt.



2) By dehydration of Carboxylic acids in presence of P_2O_5 .

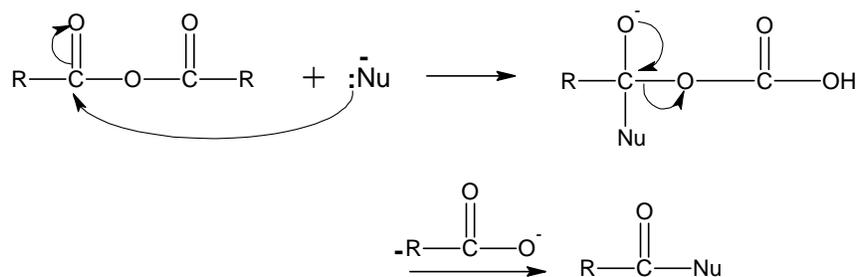


Properties:

Physical properties:

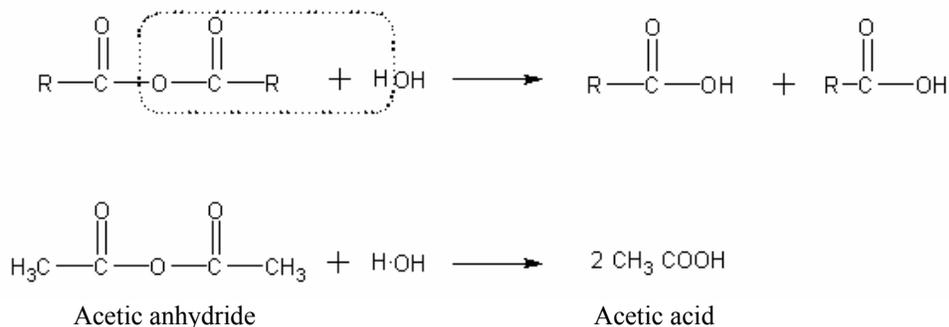
- The lower simple anhydrides are colourless liquids with an irritating smell.
- They are soluble in water but dissolve slowly because of the slow hydrolysis. They are soluble in ether and benzene.
- They have higher boiling points than the corresponding acids because of large size of molecule and enhanced van der Waals interactions.

Chemical Properties: In anhydrides $-\text{OCOR}$ group is replaced by nucleophile like acid chlorides but they are less reactive than acid chlorides because $-\text{OCOR}$ group is not as electronegative as Cl atom.

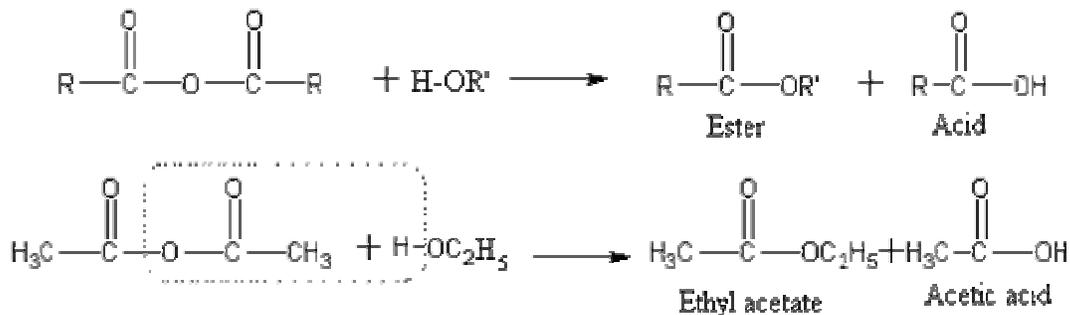


The anhydrides give all the nucleophilic substitution reaction given by acid chlorides but with less vigour.

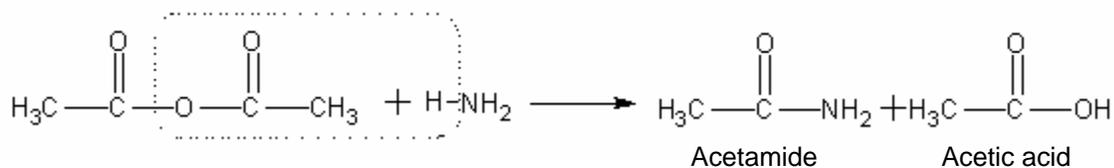
i) Hydrolysis:



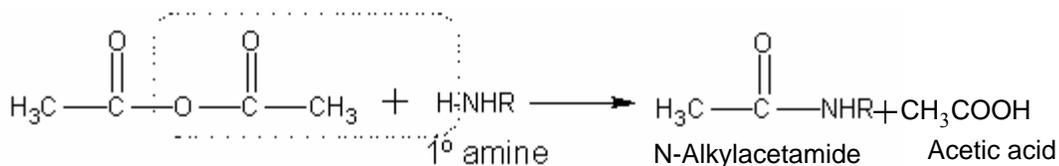
ii) Reaction with Alcohols:



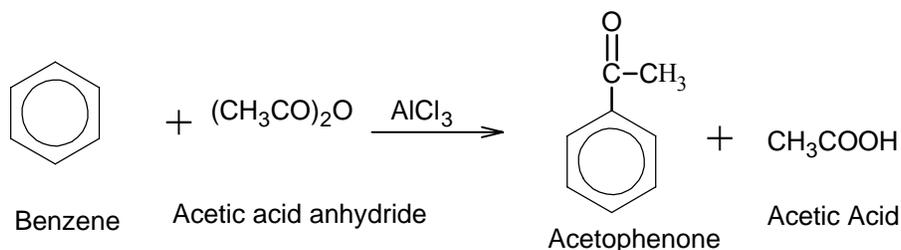
iii) Reaction with Ammonia:



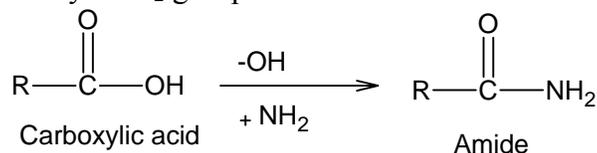
iv) Reaction with Amines:



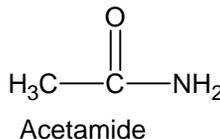
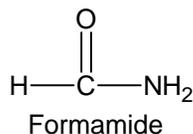
v) Friedel Crafts Reaction:



3. Acid Amides: These are the derivatives of carboxylic acids in which the $-\text{OH}$ function of carboxylic group is replaced by $-\text{NH}_2$ group.

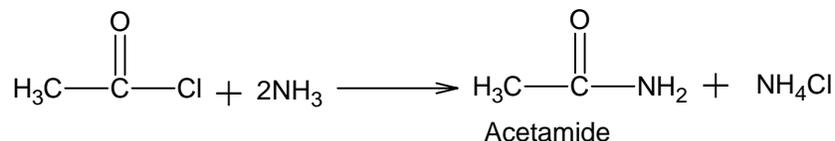


Functional group of amides is $-\text{CONH}_2$.

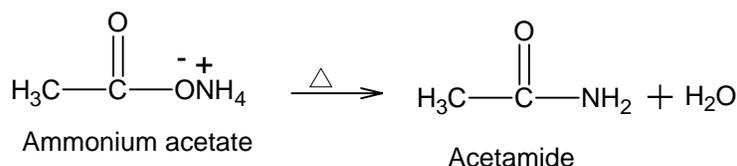


Methods of Preparation: Amides are prepared-

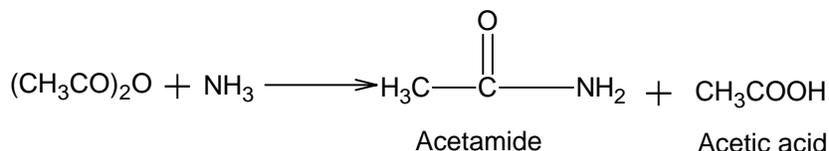
i) By the action of Ammonia on Acid Chlorides:



ii) By heating of Ammonia salts of Carboxylic acid:



iii) By the action of ammonia on Anhydrides:



Properties:

Physical Properties:

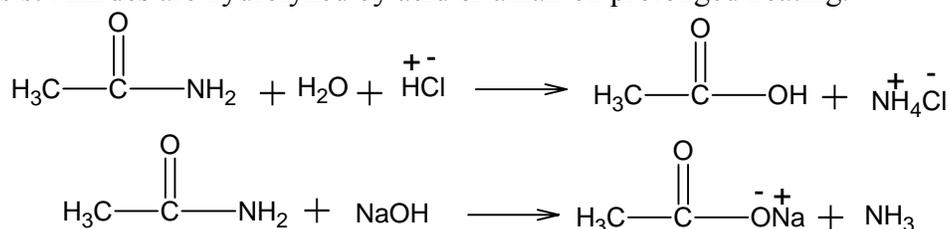
- i) All amides are white, odourless, crystalline solids.
- ii) Among the four derivatives of acids, only acid amides are capable of forming intermolecular hydrogen bonds due to which they have sharp melting points that are higher than those of corresponding acids.
- iii) Simple amides (up to C_6) are soluble in water but solubility in water decreases as we ascend the series.

Chemical Properties: Amides are stabilized by resonance.

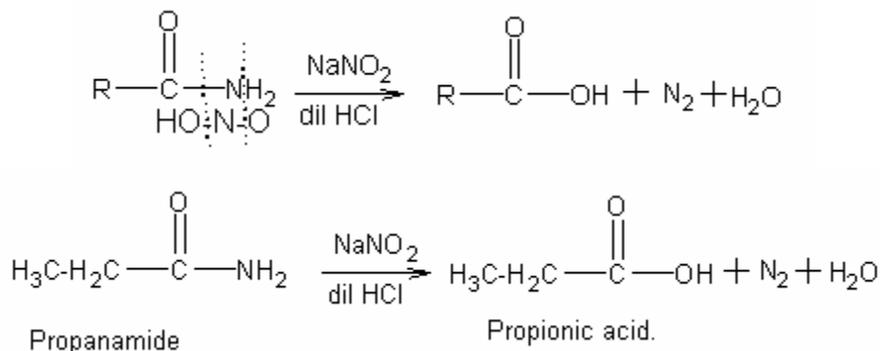


Since the electron pair on N-atom is not readily available to an acid amides are less basic than amines. Amides are least reactive of the acid derivatives. Important reactions of amides are given below.

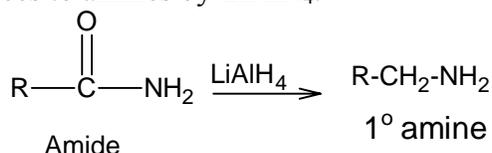
i) Hydrolysis: Amides are hydrolyzed by acid or alkali on prolonged heating.



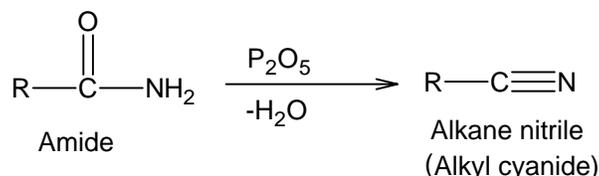
ii) Reaction with Nitrous Acid (HONO): Amides when heated with Nitrous acid ($\text{NaNO}_2 + \text{HCl}$) give carboxylic acids.



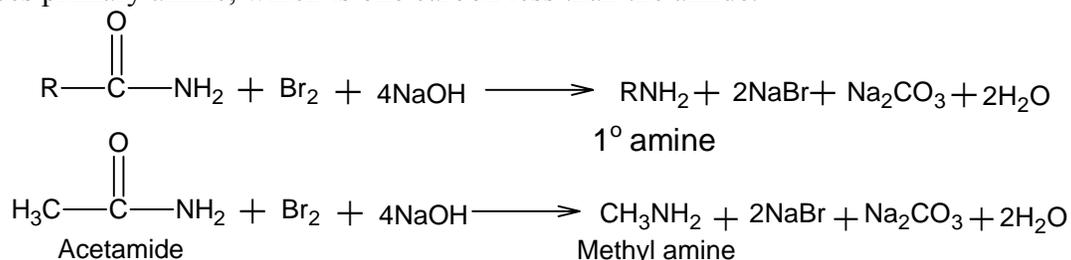
iii) Reduction: Amides reduce to amines by LiAlH_4 .



iv) Dehydration: When heated with strong dehydrating agent such as phosphorous pentoxide, they form nitriles.

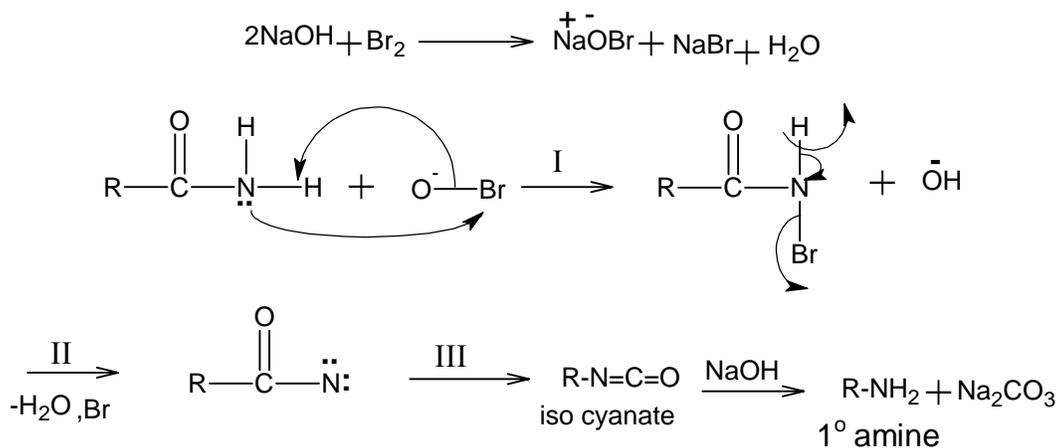


v) Hofmann's Degradation: Amides when treated with bromine and sodium hydroxide, they produce primary amine, which is one carbon less than the amide.

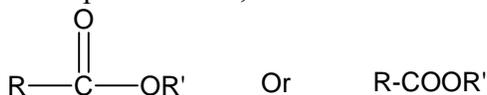


This reaction is also called **Hofmann's rearrangement**.

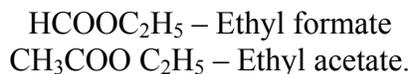
Mechanism: The Hofmann's degradation of amides involves the following steps.



4. Esters: Esters are carboxylic acid derivatives in which the $-\text{OH}$ group has been replaced by alkoxy ($-\text{OR}$) group. They can be represented as,



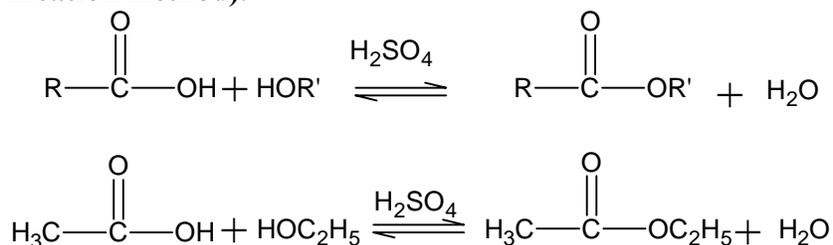
They are named as the alkyl salts of the acid e.g



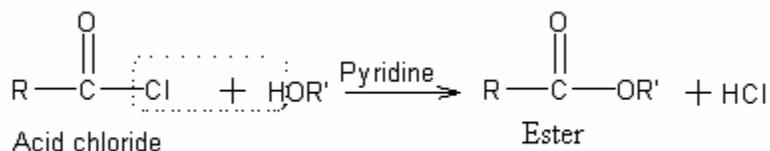
A large number of esters occur in flowers, fruits of the plants and provide the fragrance to flowers and fruits.

Method of Preparation: Generally esters are prepared by carboxylic acids and their other derivatives.

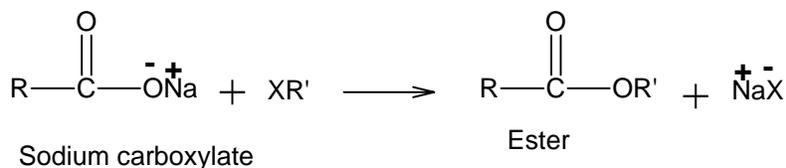
i) By the reaction of carboxylic acid with alcohols in presence of acid (Fischer's Esterification method).



ii) By the reaction of Acid Chlorides with Alcohols.



iii) By the reaction of Carboxylic salts with alkyl halide.

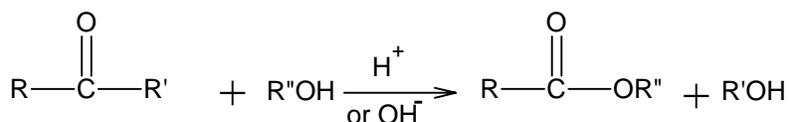


iv) By the reaction of carboxylic acid with Diazomethane.



But only methyl esters are formed by this method.

v) Transformation.



vi) By the reaction of alkyl halide with silver salt of carboxylic acid.

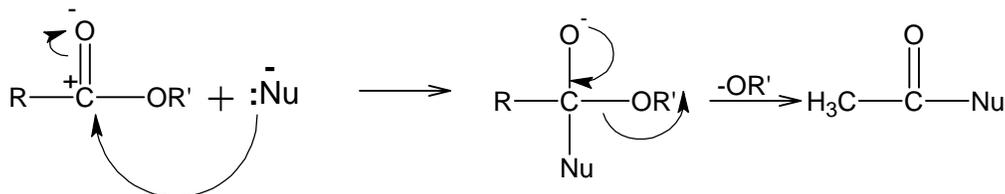


Properties:

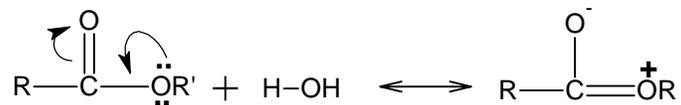
Physical Properties:

- 1) The carboxylic esters are pleasant smelling liquids or solids.
- 2) The boiling points of the straight chain isomers are higher than those of branched chain isomers. The boiling points of methyl and ethyl esters are lower than those of corresponding acid, this is due to their inability to form intermolecular hydrogen bonds.
- 3) They are generally insoluble in water and soluble in most organic solvents.

Chemical Properties: Esters give nucleophilic substitution reaction similar to acid halides because of the electron withdrawing effect of the $-\text{OR}'$ group.



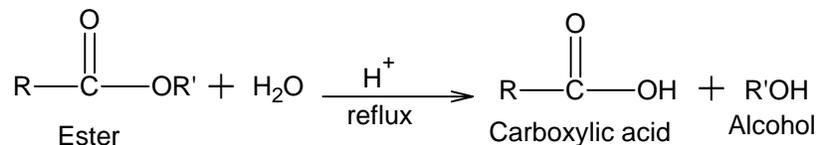
But esters are also stabilized by resonance thus they undergo nucleophilic substitution less readily than do acid halides.



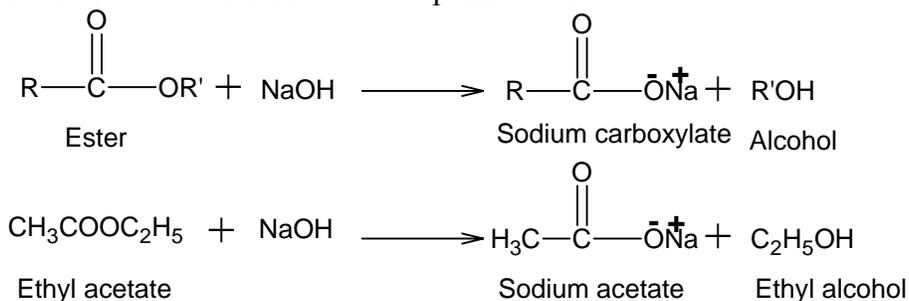
General reactions of esters are given below.

1) Hydrolysis:

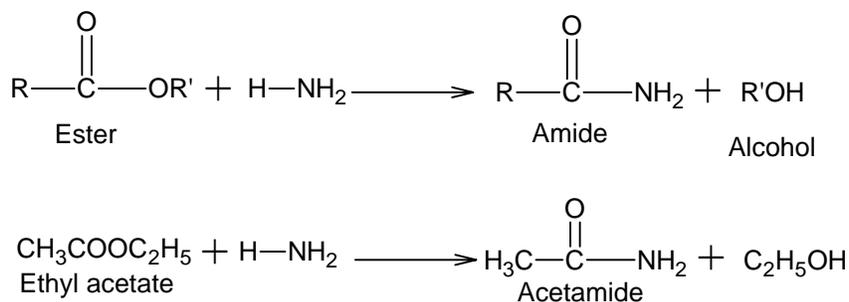
a) Acid hydrolysis: Esters are hydrolyzed in presence of acid catalyst (H_2SO_4) or HCl) to give parent carboxylic acid and alcohol.



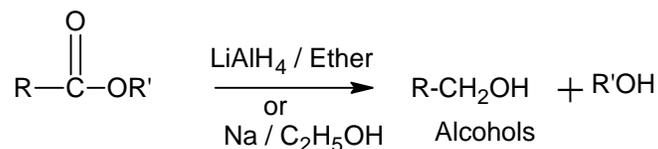
b) Alkaline hydrolysis: The alkaline hydrolysis of ester to form sodium or potassium salt of carboxylic acid and alcohol is referred to as Saponification.

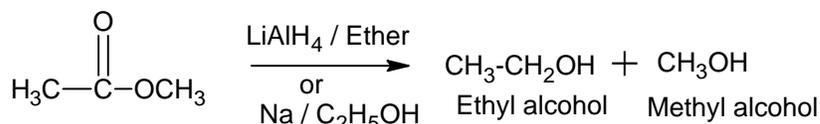


2) Reaction with Ammonia:

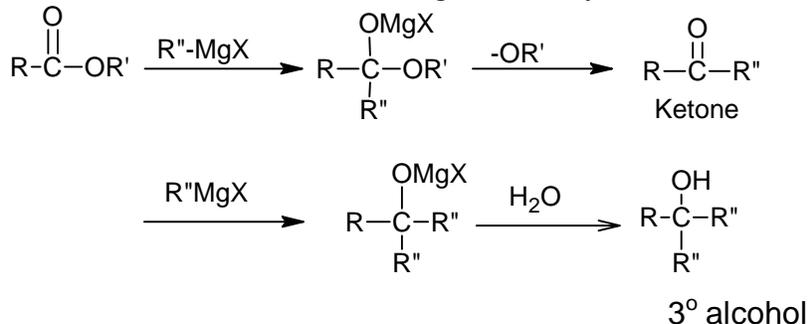


3) Reduction:

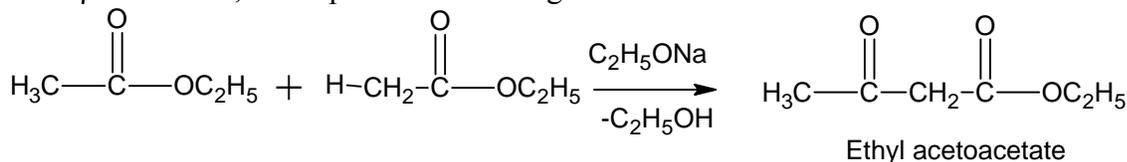




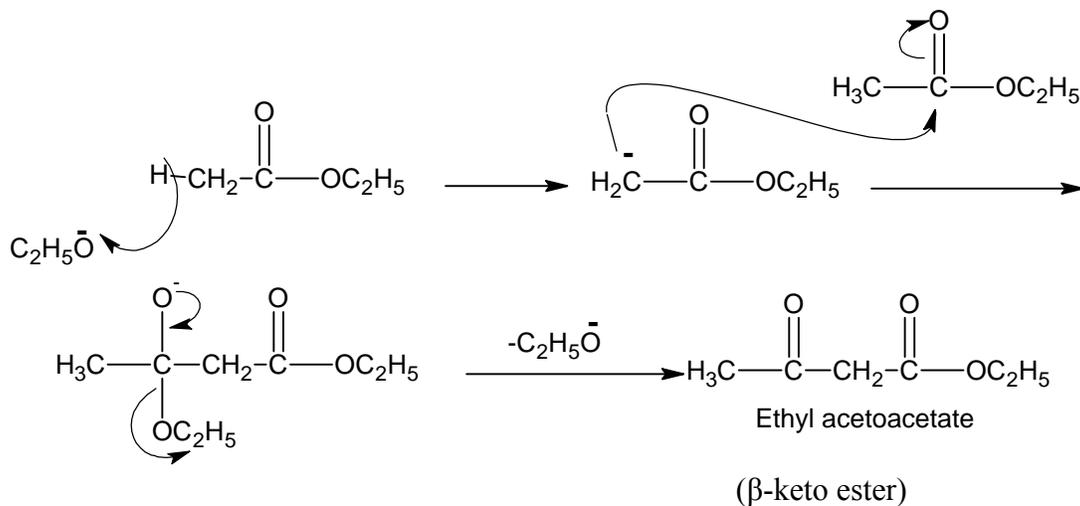
4) Reaction with Grignard Reagent: Esters with Grignard reagent first gives ketone which on further reacting with another molecule of the G.R gives tertiary alcohol.



5) Claisen Condensation: Esters containing α -hydrogen atom undergo condensation reactions to form β -ketoesters, in the presence of strong base. This reaction is known as .



Mechanism: Following steps are involved.



Suggested Readings:

- Organic Chemistry by I. L. Finar, vol. 1, 6th edition
- Organic Chemistry by Paula Yurkanis Bruice, 3rd edition.
- Organic Chemistry by Robert T. Morrison and Robert Neilson Boyd, 6th edition.
- Organic Chemistry by K. Peter C. Vollhardt and Neil E. Schore, 4th edition.