Faculty of Pharmacy

Menoufia University

Pharmaceutical Organic Chemistry (PC202)

For

First Year Pharmacy Students

Second Semester

By Staff Members Of

Pharmaceutical Chemistry Department

Course Specifications

University:	**Menoufia University**
Faculty:	**Faculty of Pharmacy**
Department:	**Pharmaceutical Chemistry**
Year:	**2019-2020**

A) Affiliation:	
Relevant program	**Bachelor of Pharmacy Pharm-D (Credit Hours)**

B) Basic information:	
Course Title	Pharmaceutical Organic Chemistry-2
Course Code	PC202
Level / Semester	Level 1 / Semester 2
Lecture	2 hrs
Tutorial/ Practical	1 hrs
Credit Hours	3 hrs / Week
Total academic hours	3 hrs / Week
Pre-requisite Course	Pharmaceutical Organic Chemistry-1

C) Professional information:

1. Course Description:

This course involves different classes of organic compounds: Benzene and aromaticity (Kekule structure, modern theories of benzene structures, aromaticity, electrophilic substitution reactions, Friedle-Craft alkylation and acylation), Arenes (structure, nomenclature, preparation, physical and chemical properties), Alcohols (classification, nomenclature, preparation, physical and chemical properties), Ethers (classification, nomenclature, preparation, chemical properties and ethers of pharmaceutical interest), Aldehydes and Ketones (classification, nomenclature, preparation, physical and chemical properties) .

2. Intended Learning Outcomes (ILO's):

a- Knowledge and understanding:

By the end of this course, the student should be able to:

a1	Recognize organic functional groups and their reactivity
a2	Understand the aromaticity and electrophilic substitution reactions on benzene ring
a3	Know the Chemical names, physical and chemical properties of different organic functional groups
a4	Understand the basic concepts of reaction mechanism

b- Intellectual skills:

By the end of this course, the student should be able to:

b1	Relate the compound structure to the possible identification and synthetic procedures.
b2	Demonstrate electron donating and withdrawing groups
b3	Distinguish different electrophilic substitution reactions mechanisms
b4	Appreciate the difference between aromatic and nonaromatic compounds.

c- Professional and practical skills:

By the end of this course, the student should be able to:

c1	Appraise the practical methods for identification and synthesis of different aliphatic and aromatic functional groups.
c2	Investigate the concept of aromaticity.
c3	Locate the mechanism of electrophilic substitution reactions.
c4	Safely handle basic laboratory equipments.

d- General and transferable skills:

By the end of this course, the student should be able to:

d1	Improve writing and oral communication skills.
d2	Work in a group and to take the appropriate decision in the appropriate time.
d3	Think logically about the daily life situations.

3. Teaching and Learning Methods:

No.	Methods	Applied Methods
1.	Lecture (PowerPoint presentation)	√
2.	Picture/Videos	√
3.	Interactive Discussions	-
4.	Tutorials	-
5.	Modeling and Simulation	-
6.	Problem solving/case study	-
7.	Practical	√
8.	Self-Learning	√
9.	Researches and Reports	√
10.	*Others:	-

4. Student Assessment:

Semester work (quizzes, Project)	5 Marks	To asses:	Knowledge, understanding, intellectual, professional, general and transferable skills
Practical exam	40 Marks	To asses:	Knowledge, intellectual and professional skills
Mid-term exam	15 Marks	To asses:	Knowledge and understanding and intellectual skills
Oral exam	15 Marks	To asses:	Knowledge, understanding, intellectual, general and transferable skills
Written exam	75 Marks	To asses:	Knowledge, understanding and intellectual, skills

5. List of references:

Type	Reference
a. Course notes:	Printed hand-outs and presentation files
b. Essential books:	1- Introduction to Organic Chemistry, 5th Edition, W. H. Brown & T. Poon. 2- Organic Chemistry, T.W. G. Solomon, C. B. Fryhle and S. A. Snyder, 11th Edition.
c. Recommended books:	Introduction to Organic Chemistry, 5th Edition, W. H. Brown & T. Poon.
d. Periodicals, Web sites, etc.:	https://www.coursera.org/

6. Course coordinators:

Dr. Mona Elzoghbi

Chemistry of aromatic compounds

Introduction

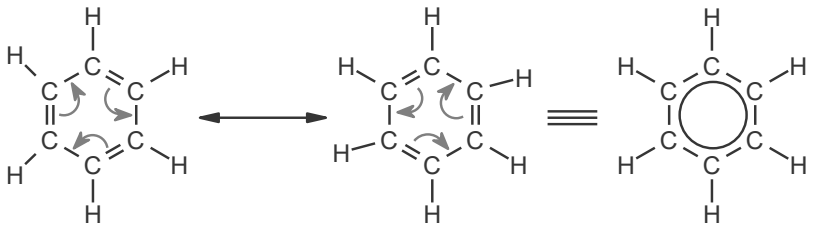
Aromatic originally referred to the aroma smell. Benzene is the parent of all aromatic compounds. The study of aromatic compounds began with the discovery in 1825 of benzene by the English chemist Michael Faraday. In 1834 a German chemist synthesized benzene by heating benzoic acid with calcium oxide.

$$C_6H_5CO_2H + CaO \quad \text{-------heat------>} \quad C_6H_6 + CaCO_3$$

To be classified as aliphatic the chemical behavior of the compound reacts like an alkane, an alkene, an alkyne, or one of their derivatives. To be classified as aromatic the compound had a low ratio of hydrogen-to-carbon and that it was "fragrant". Aromatic compounds are widely distributed in amino acids, hormones drugs. Examples include benzene, Aniline, tyrosine, phenylalanine, Ibuprofen, salbutamol, epinephrine and propranolol:

The Kekulé Structure for Benzene

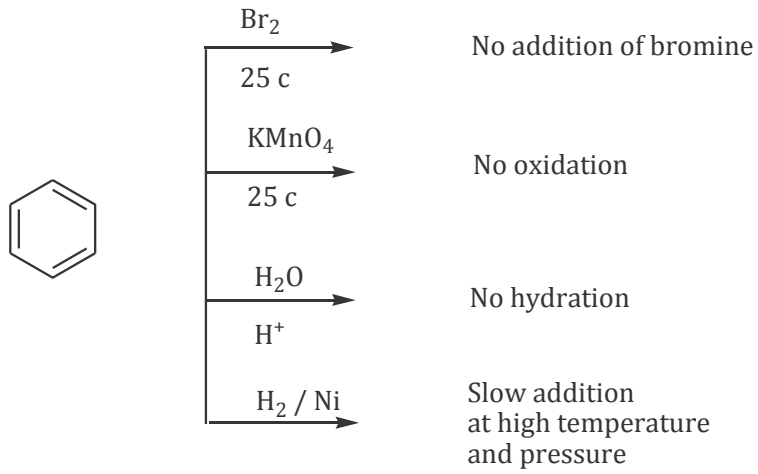
August Kekulé proposed the first definite structure for benzene which is still used today. Kekulé suggested that the carbon atoms of benzene are in a ring, that they are bonded to each other by alternating single and double bonds, and that one hydrogen atom is attached to each carbon atom.



This structure satisfied the requirements of the structural theory that carbon atoms form four bonds and that all the hydrogen atoms of benzene are equivalent and monovalent.

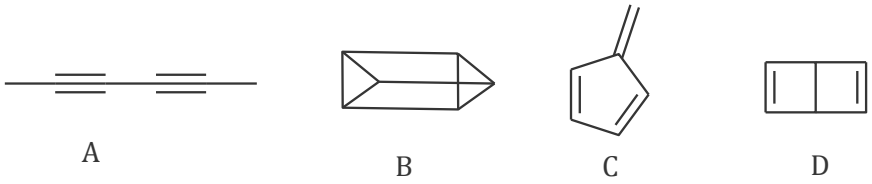
Reactions of Benzene

Benzene is highly unsaturated (C_6H_6), and expected to react like unsaturated compounds through addition. Benzene expected to react like an alkene by decolorizing bromine through addition. They expected that it would change the color of aqueous potassium permanganate by oxidation, that it would add hydrogen rapidly in the presence of a metal catalyst, and that it would add water in the presence of strong acids through hydrolysis but surprisingly, **Benzene does none of these**. Benzene does react with bromine but only in the presence of a Lewis acid catalyst such as ferric bromide. However, it reacts not by addition but by substitution.



Exercise

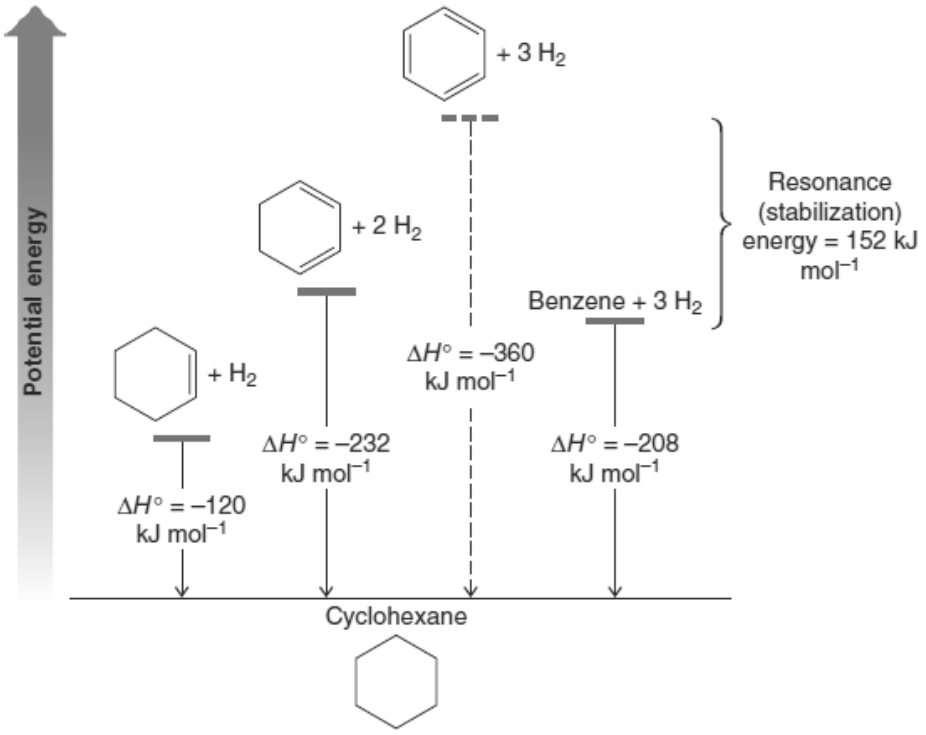
Listed below are four compounds that have the molecular formula C6H6. Which of these compounds would yield only one monosubstitution product if for example, one hydrogen was replaced by bromine?



The Thermodynamic Stability of Benzene

Cyclohexene, a six-membered ring containing one double bond, can be hydrogenated easily to cyclohexane. When the ΔH for this reaction is measured, it is found to be -120 kJ mol^{-1} (-28.6 Kcal/mole). We would expect that hydrogenation of 1,3-cyclohexadiene would liberate roughly twice as much heat and thus have a ΔH equal to about -240 kJ mol^{-1} (-57.2 Kcal/mole). When this experiment is done, the result is Δ H = -232 kJ mol^{-1}.(-55.4 Kcal/mole).

If we extend this kind of thinking, and if benzene is simply 1,3,5-cyclohexatriene, we would predict benzene to liberate approximately 360 kJ mol-1 [3 * (-120)] or (-85.8 Kcal/mole) when it is hydrogenated. When the experiment is actually done, the result is surprisingly different. The reaction is exothermic, but only by 208 kJ mol^{-1} (-49.8 Kcal/mole). The difference between theoretical amount of energy liberated and that actually observed is called **resonance energy** of benzene.



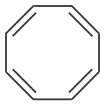
Relative stabilities of cyclohexene, 1,3-cyclohexadiene, 1,3,5-cyclohexatriene (hypothetical), and benzene.

Review problem

Based on the information in the diagram above, what is the resonance energy of 1,3-cyclohexadiene

Aromatic, non-aromatic and anti-aromatic compounds

A compound to be called aromatic, it has to react by substitution rather than addition even if it was highly unsaturated. Not all of cyclic compounds with alternating single and double bonds are aromatic. A compound like Cyclooctatetraene found not at all like benzene. Cyclooctatetraene reacts with bromine by addition, it adds hydrogen readily, it is oxidized by solutions of potassium permanganate, and thus it is clearly not aromatic.



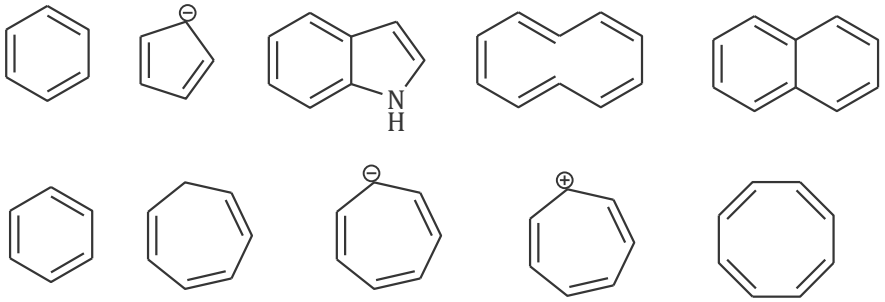
A compound to be aromatic it must be:

1. Cyclic
2. Planar

3. All atoms in the ring must be sp2 hybridized
4. Obey Huckel's rule

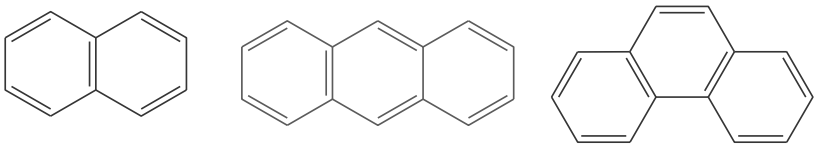
Hückel's Rule: The 4n + 2 = number of p Electron

Hückel's Rule in another words: Planar monocyclic rings with 2, 6, 10, 14, ..., delocalized electrons should be aromatic

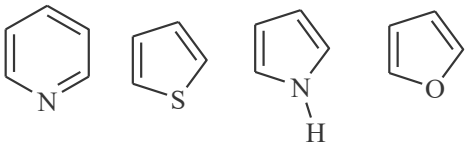


Assign each of these compounds with aromatic, non-aromatic or anti-aromatic

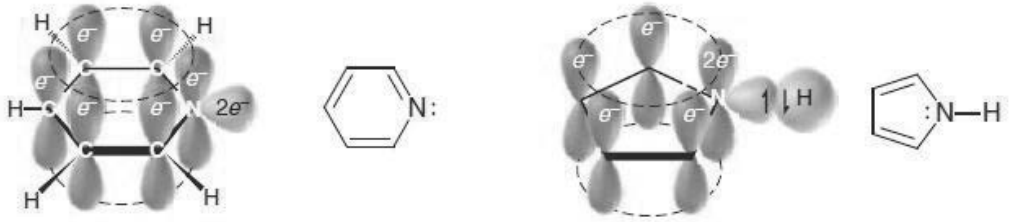
Polycyclic aromatic hydrocarbons



Heterocyclic aromatic compounds



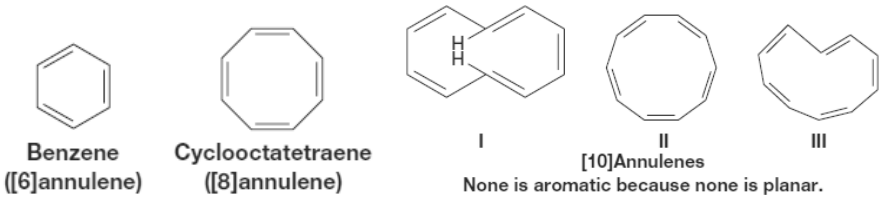
Pyridine Thiophene Pyrrole Furane



The annulenes

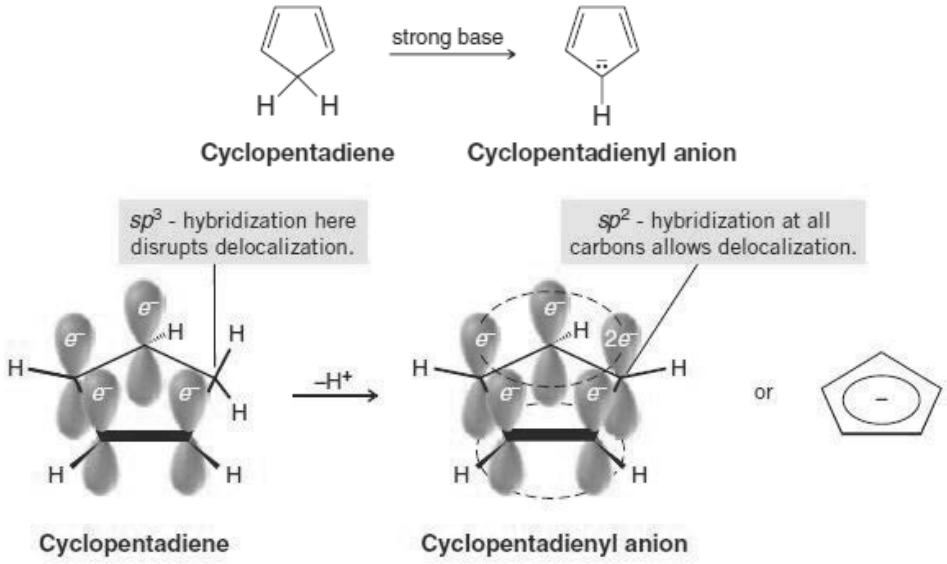
The word annulene is incorporated into the class of monocyclic fully conjugated compounds with the molecular formula of C_nH_n and can be represented by structures having alternating

single and double bonds. The ring size of an annulene is indicated by a number in brackets. Thus, benzene is [6]annulene and cyclooctatetraene is [8]annulene.

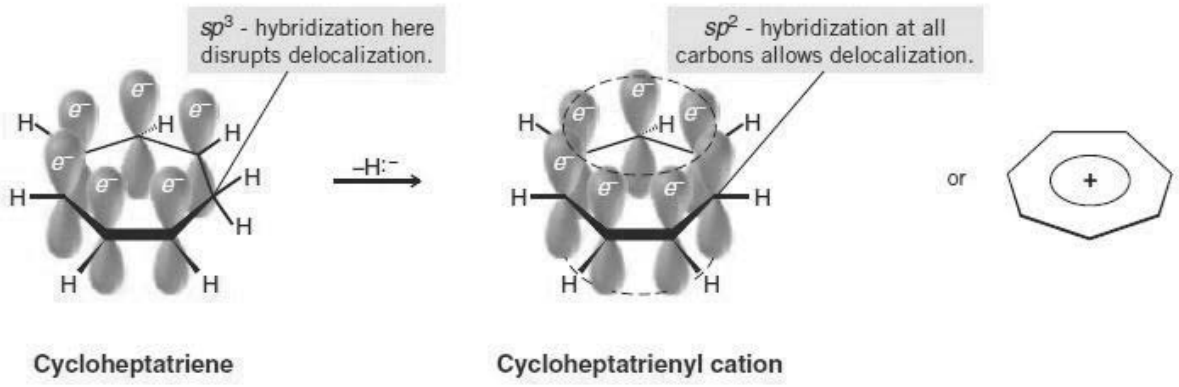


Aromatic Ions

There are a number of monocyclic species that bear either a positive or a negative charge. Some of these ions show unexpected stabilities that suggest that they are aromatic ions. Cyclopentadiene is not aromatic; however, it is unusually acidic Because of its acidity, cyclopentadiene can be converted to its anion by treatment with moderately strong bases. The cyclopentadienyl anion is unusually stable due to the aromatic nature of this anion.

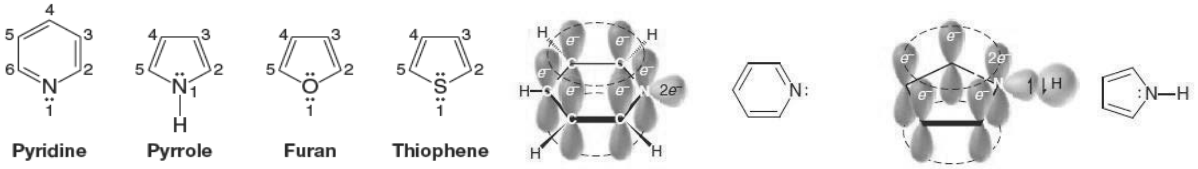


Cycloheptatriene has six p electrons. However, the six p electrons of cycloheptatriene cannot be fully delocalized because of the presence of the CH_2 group. When cycloheptatriene is converted to the cycloheptatrienyl (or tropylium) cation by loss of a hydride ion from cycloheptatriene, cycloheptatrienyl cation found highly stable and the hydride ion removed unexpectedly easy.



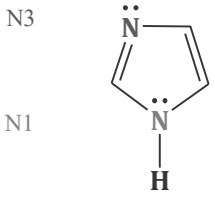
Heterocyclic Aromatic Compounds

Cyclic compounds that include an element other than carbon are called heterocyclic compounds. Pyridine is electronically related to benzene. Pyrrole, furan, and thiophene are related to the cyclopentadienyl anion.



Exercise

Imidazole has two nitrogens. N3 is relatively basic (like the nitrogen of pyridine). N1 is relatively nonbasic (like the nitrogen of pyrrole). Explain the different basicities of these two nitrogens.

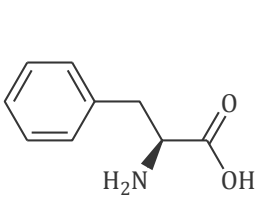


imidazole

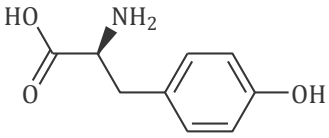
Aromatic Compounds in Biochemistry

Compounds with aromatic rings occupy numerous and important positions in reactions that occur in living systems. Two amino acids necessary for protein synthesis contain the benzene ring. A third aromatic amino acid, tryptophan, contains a benzene ring fused to a pyrrole ring. This aromatic ring system is called an indole system. In humans, no biochemical ability to synthesize the benzene ring. As a result, phenylalanine and tryptophan derivatives are essential in the human diet.

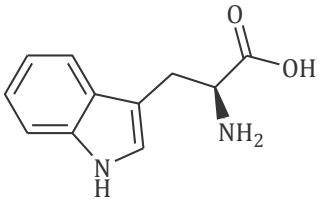
Because tyrosine can be synthesized from phenylalanine in a reaction catalyzed by an enzyme known as phenylalanine hydroxylase, it is not essential in the diet as long as phenylalanine is present. Derivatives of purine and pyrimidine are essential parts of DNA and RNA. DNA is the molecule responsible for the storage of genetic information. RNA is involved in the synthesis of enzymes and other proteins. 6-Mercaptopurine is used in the treatment of acute leukemia.



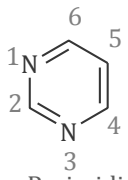
Phenylalanine



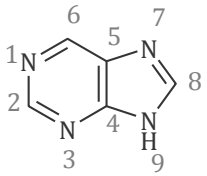
Tyrosine



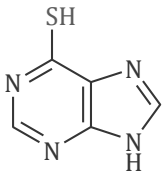
Tryptophan



Pyrimidine



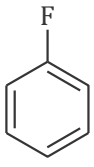
Purine



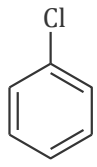
6-Mercaptopurine

Nomenclature of Benzene Derivatives

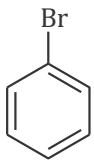
Two systems are used in naming monosubstituted benzenes. In many simple compounds, benzene is the parent name and the substituent is simply indicated by a prefix. For other simple and common compounds, the substituent and the benzene ring taken together may form a commonly accepted parent name. Methylbenzene is usually called toluene, hydroxybenzene is almost always called phenol, and aminobenzene is almost always called aniline.



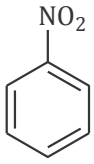
fluorobenzene



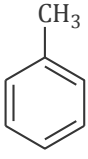
chlorobenzene



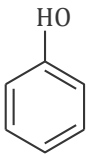
bromobenzene



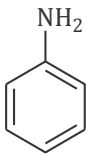
nitrobenzene



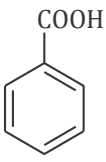
toluene



phenol

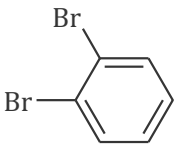


aniline

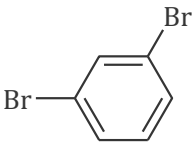


benzoic acid

When two substituents are present, their relative positions are indicated by the prefixes ortho-, meta-, and para- (abbreviated o-, m-, and p-) or by the use of numbers.



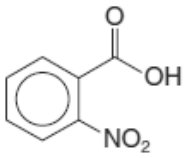
1,2-Dibromobenzene
(*o*-dibromobenzene)



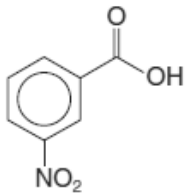
1,3-dibromobenzene
(*m*-dibromobenzene)

1,4-dibromobenzene
(*p*-dibromobenzene)

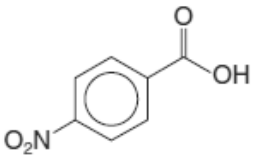
and for the nitrobenzoic acids



2-Nitrobenzoic acid
(*o*-nitrobenzoic acid)

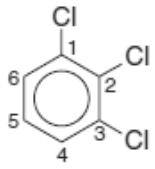


3-Nitrobenzoic acid
(*m*-nitrobenzoic acid)

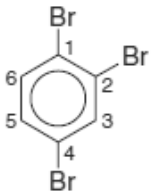


4-Nitrobenzoic acid
(*p*-nitrobenzoic acid)

If more than two groups are present on the benzene ring, their positions must be indicated by the use of numbers.



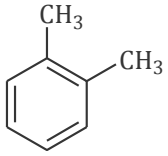
1,2,3-Trichlorobenzene



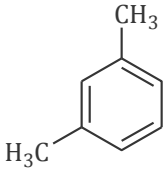
1,2,4-Tribromobenzene
(*not* 1,3,4-tribromobenzene)

The benzene ring is numbered so as to give the lowest possible numbers to the substituents. When more than two substituents are present and the substituents are different, they are listed in alphabetical order.

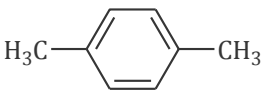
The dimethylbenzenes are called xylenes.



o-Xylene

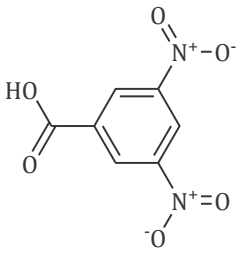


m-Xylene

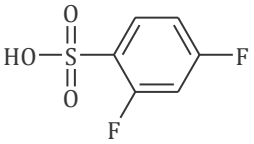


p-Xylene

When a substituent is one that together with the benzene ring gives a new base name, that substituent is assumed to be in position 1 and the new parent name is used.



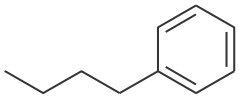
3,5-Dinitrobenzoic acid



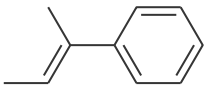
2,4-Difluorobenzenesulfonic acid

When the C_6H_5 group is named as a substituent, it is called a phenyl group. The phenyl group is often abbreviated as C_6H_5 or Ph

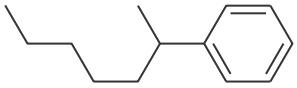
A hydrocarbon composed of one saturated chain and one benzene ring is usually named as a derivative of the larger structural unit. However, if the chain is unsaturated, the compound may be named as a derivative of that chain, regardless of ring size.



Butylbenzene

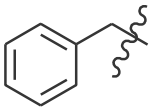


(E)-2-Phenyl-2-butene

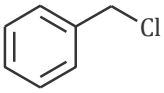


2-Phenylheptane

Benzyl is an alternative name for the phenylmethyl group while benzoyl is alternative name for the phenylcarbonyl.



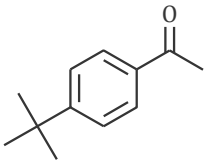
The benzyl group
(phenylmethyl)



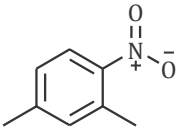
Benzyl chloride
(phenylmethyl chloride)

Exercise

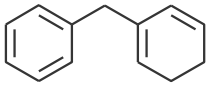
1. Provide a name for each of the following compounds



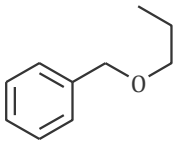
(a)



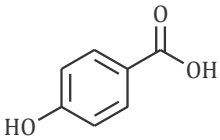
(b)



(c)



(d)



(e)

2. Draw chemical structures of the following chemical names

1. 3-Nitrobenzoic acid
2. *p*-Bromotoluene
3. o-Dibromobenzene
4. *m*-Dinitrobenzene
5. 3,5-Dinitrophenol
6. *p*-Nitrobenzoic acid
7. *p*-toluenesulfonate
8. Benzyl bromide
9. *p*-Nitroaniline
10. o-Xylene
11. *tert*-Butylbenzene
12. *p*-Methylphenol
13. *p*-Bromoacetophenone
14. 3-Phenylcyclohexanol
15. 2-Methyl-3-phenyl-1-butanol
16. *o*-Chloroanisole

Review problems

Write structural formulas and give acceptable names for all representatives of the following

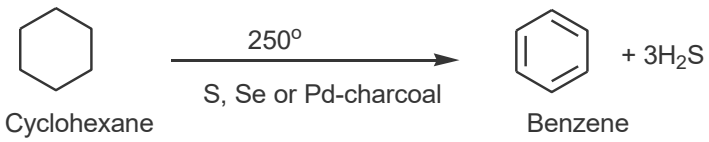
1. Tribromobenzenes
2. Nitroanilines
3. Isomers of C_6H_5-C_4H_9
4. Dichlorophenols

Sources of aromatic compounds

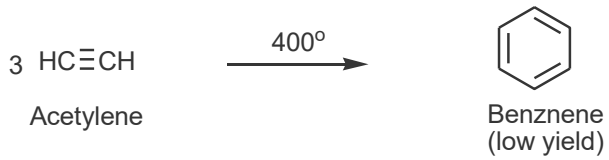
1- The principal source is the coal tar obtained by destructive distillation of coal.
2- Petroleum, since it contains varying quantities of aromatic hydrocarbons.
3- Plants, these are important sources for simple and fused ring aromatic compounds.

Synthesis of aromatic compounds

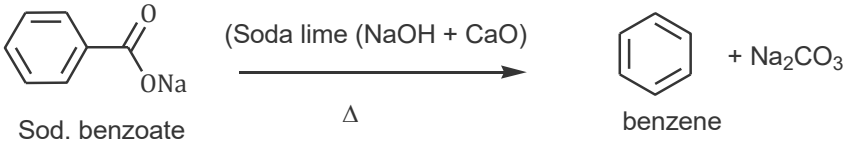
1. By dehydrogenation of cyclohexane derivatives.

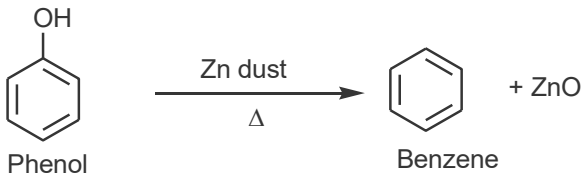


2. From acetylene



3. From sodium benzoate and phenol

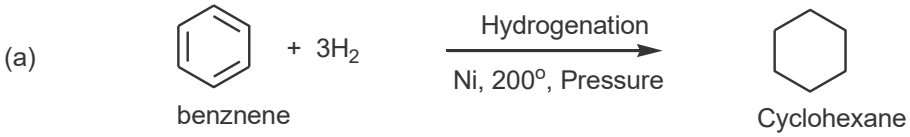




Reactions of aromatic compounds

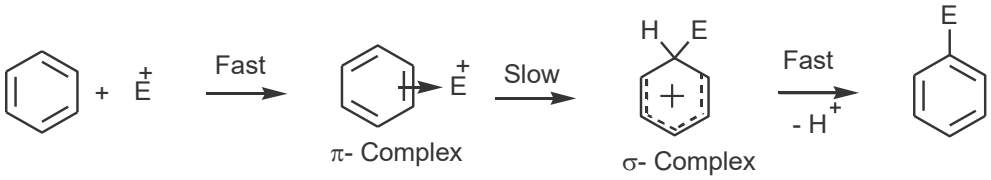
1- Addition reactions:

In contrast to alkenes and alkynes, which readily react by addition, benzene and other arenes undergo addition reactions to only a limited extent.

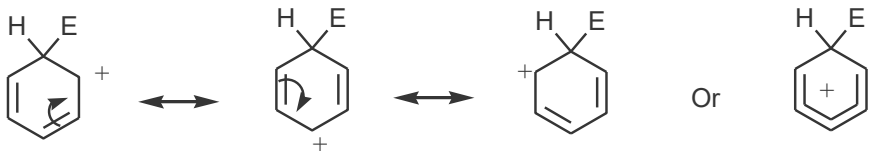


2- Substitution reactions:

The most important reactions of aromatic hydrocarbons are electrophilic aromatic substitution reactions (S_E2 aromatic), in which functional group replaces one of the hydrogen atoms on the aromatic ring. The reaction involves 3 steps: π- complex formation, σ- complex formation, and finally loss of a proton.



while the π- complex is hypothetical, σ- complex is a real intermediate, it is stabilized by resonance. e.g.



σ- Complex, stabilized by resonance

The σ- complex has been separated in some reactions.

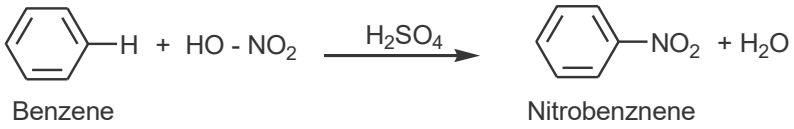
Some electrophilic substitution reactions are reversible e.g. sulfonation and Friedl-Craft's alkylation, however the majority of which are irreversible e.g. nitration and halogenation.

The rate determining step (slowest step in a chemical reaction) in electrophilic substitution is the step of σ- complex formation except in sulfonation where the RDS is the final step of the loss of a proton to afford the substitution product.

Benzene is a nucleophile and its nucleophilic characters (and its reactivity) is increased by the electron repelling atoms and groups. On the other hand the electron withdrawing atoms or groups decrease the reactivity of benzene toward electrophilic substitution reactions.

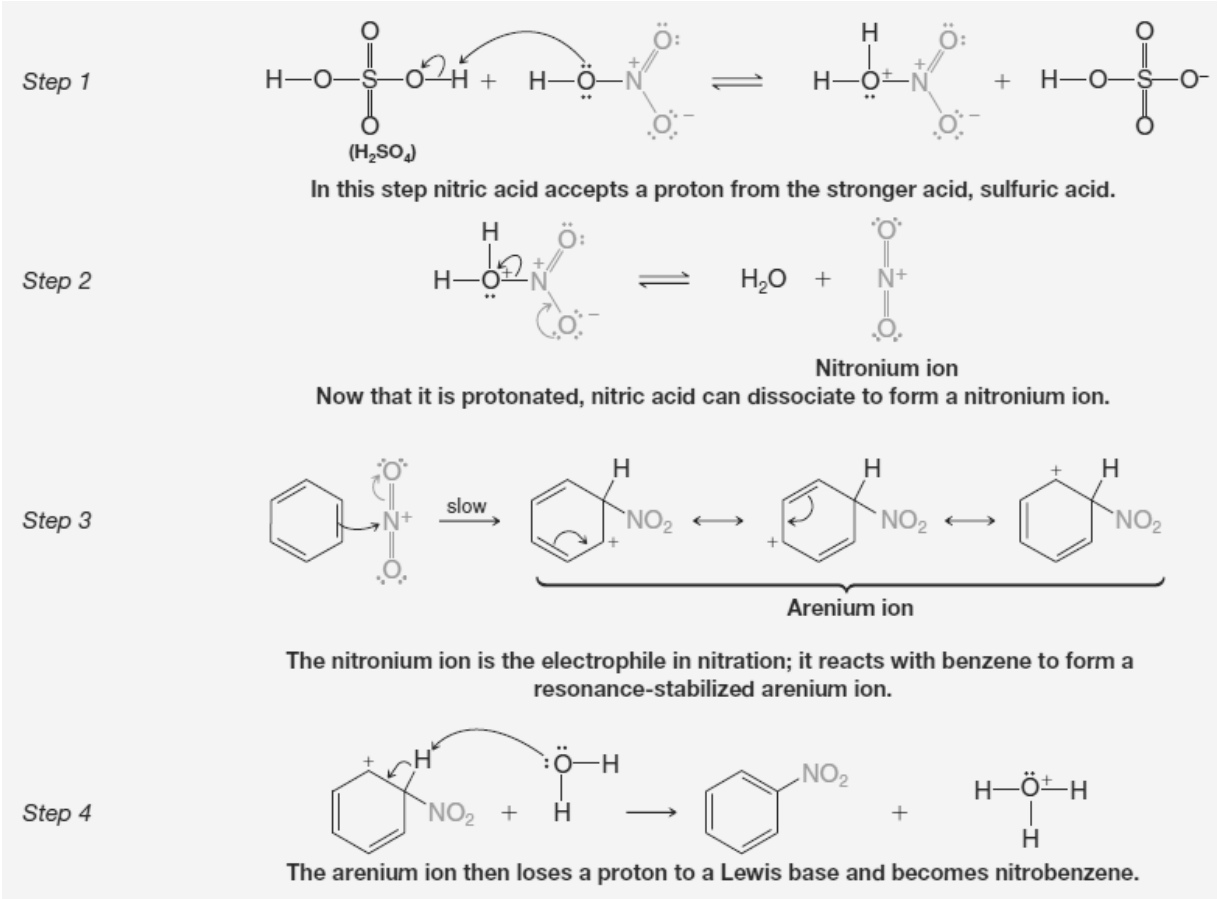
Examples of electrophilic substitution reactions:

1. Nitration**:**



Benzene Nitrobenznene

Mechanism of nitration by mixed acid

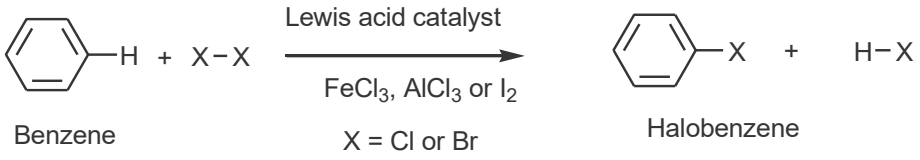


HNO_3 accepts a proton from the stronger acid, H_2SO_4

Obviously, the electrophile (N^+O_2) is attracted by π electrons cloud of the benzene ring forming resonance stabilized carbonium ion (carbocation)

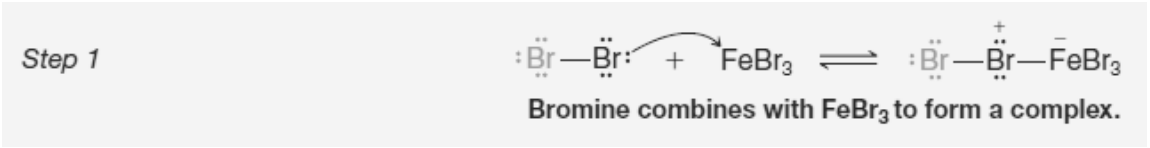
2. Halogenation

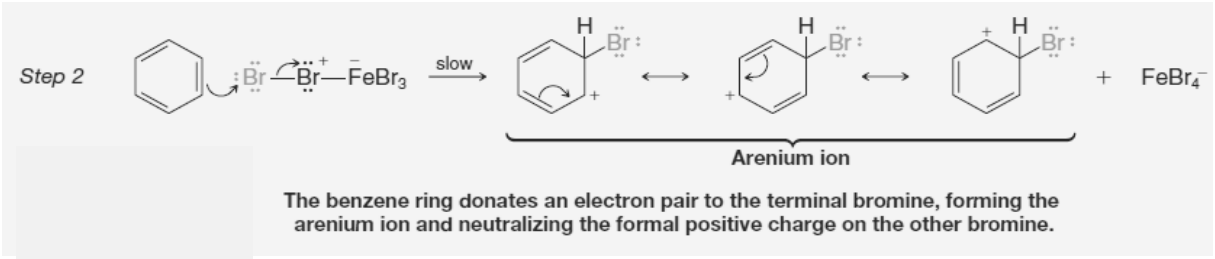
Halogen molecules alone are $F_2 > Cl_2 > Br_2 > I_2$ have insufficient electrophilicity to attack benzene and Lewis acid catalyst e.g. $FeCl_3$, $AlCl_3$ ....etc must be used. The catalyst facilitate the heterolysis of the halogen - halogen bond to produce the positive halonium ion which is the halogenating species in halogenation.

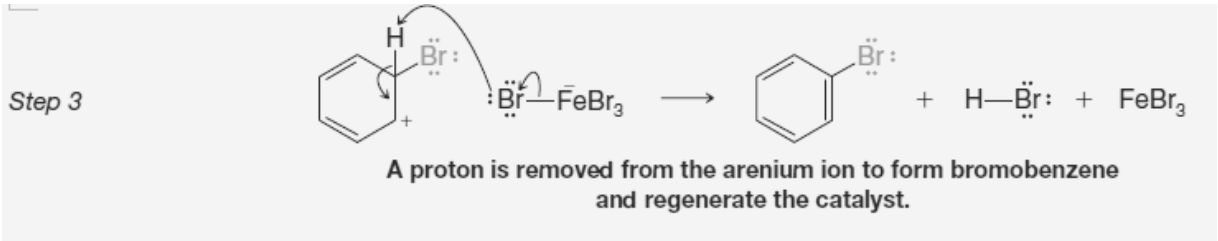


Benzene — Halobenzene

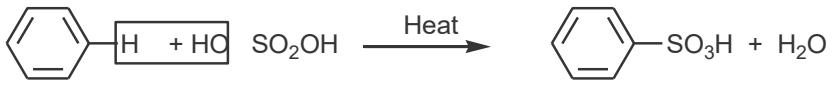
Mechanism of halogenation :





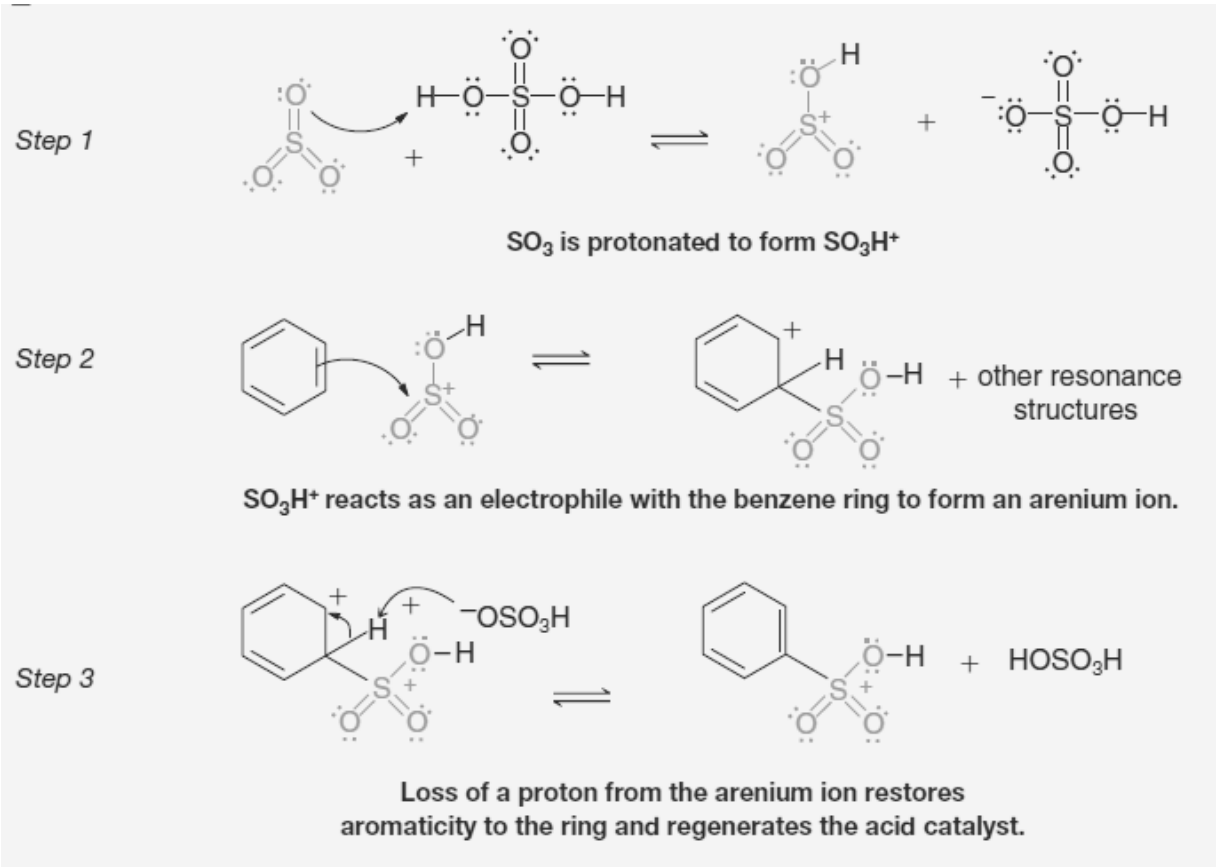


3. Sulfonation:



Benzenesulfonic acid

Mechanism of sulfonation:

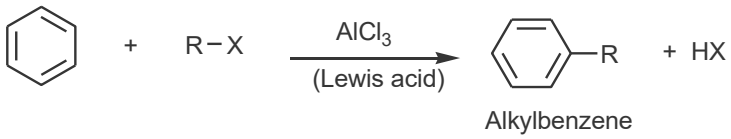


If we want to desulfonate benzenesulfonic acid, we employ dilute H_2SO_4 and usually pass steam through the mixture, where the equilibrium lies to the left and desulfonation occurs. The equilibrium is shifted even further to the left with volatile aromatic compounds because the aromatic compound distils with the steam.

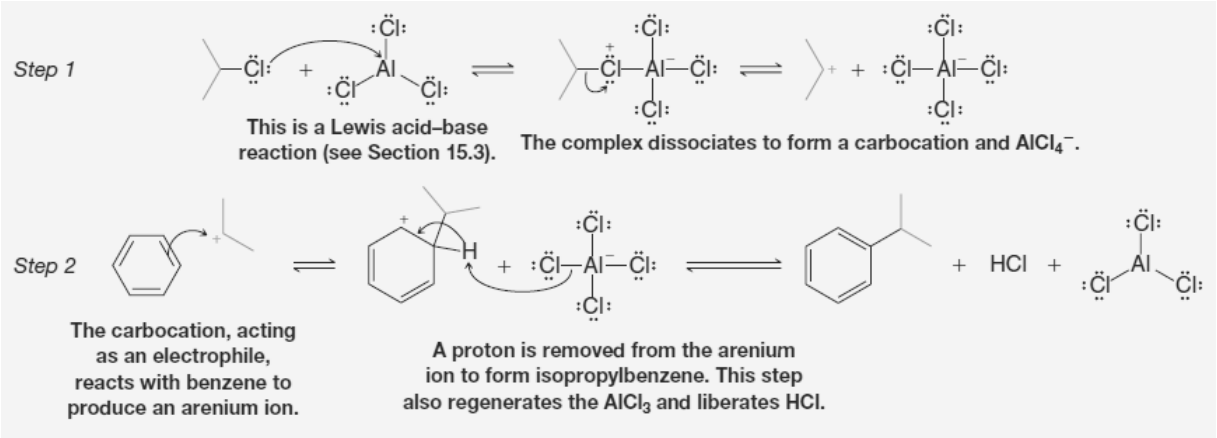
Sulfonation - desulfonation is a useful tool in syntheses involving electrophilic aromatic substitution.

We may, for example, sulfonate the benzene ring to influence the course of some further reaction. Later, we may remove the sulfonic acid group by desulfonation.

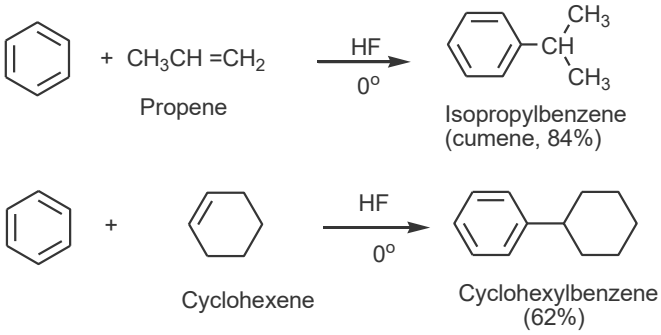
4. Friedel-Crafts Alkylation



Mechanism of Friedel-Crafts alkylation:



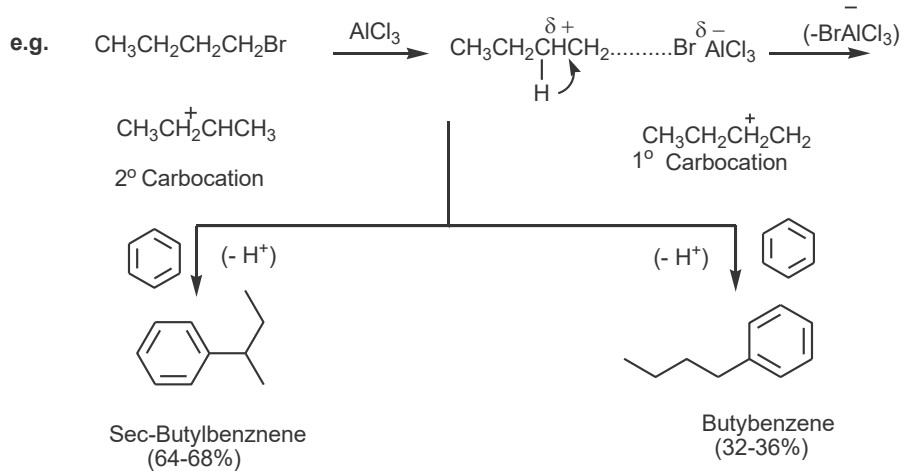
Alkylation with mixture of alkene and acid



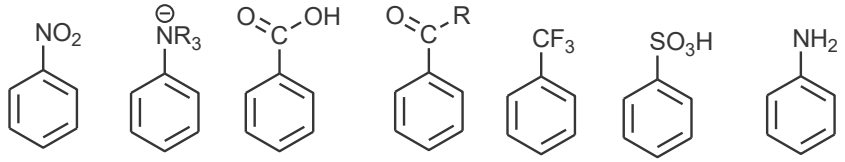
Limitations of Friedel-Crafts reactions

Several restrictions limit the usefulness of Friedel-Crafts alkylation.

1. Rearrangement of the carbocation formed from RX, alkene or alcohol to give the more stable carbocation

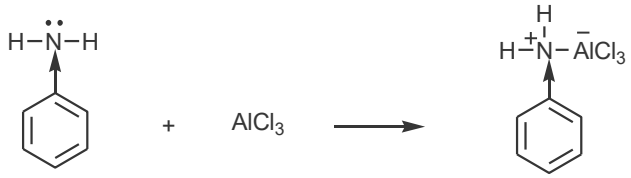


2. Friedel-Crafts reactions give poor yields when powerful electron with-drawing groups are present on the aromatic ring or when the ring bears $-NH_2$,-NHR, or NR_2 groups. This applies to both alkylation's and acylations. The following structures give poor yields in Friedel-Crafts reactions:



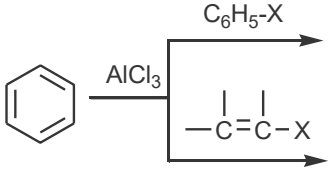
Electron-withdrawing groups make the aromatic ring too electron- deficient to undergo Friedl-Crafts reactions.

The amino groups, $-NH_2$, -NHR, and $-NR_2$ are changed into powerful electron-withdrawing groups by the Lewis acid used to catalyze Friedel-Crafts reactions.



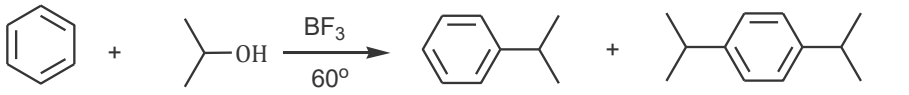
Does not undergo a *Friedel-Crafts* reaction

3. Aryl and vinylic halides cannot be used because they do not form carbocations.



No F*riedel- Crafts* reaction

4. Polyalkylations often occur.
Alkyl groups are electron-releasing and once one is introduced into the benzene ring, it activates the ring toward further substitution.



Isopropylbenzene (43%)

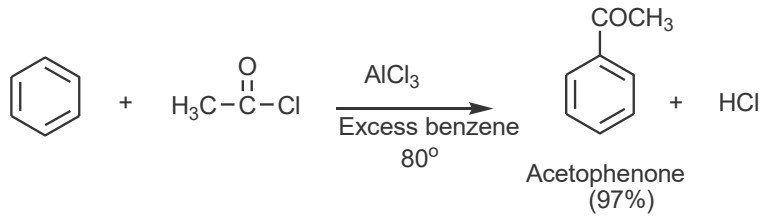
p-Diisopropylbenzene (14%)

Polyacylation is not a problem in Friedel-Crafts acylation.

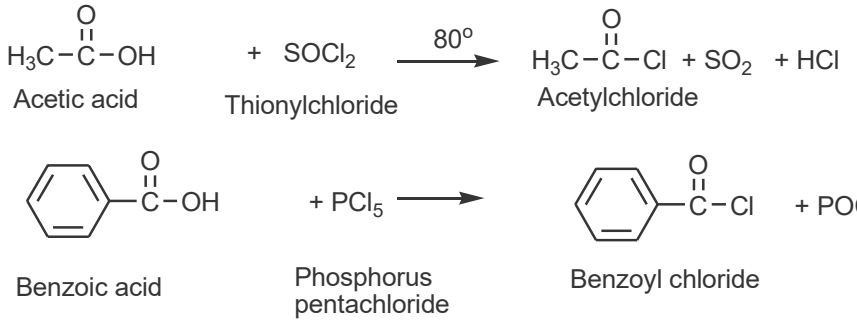
Friedel-Crafts acylation

Two common acyl groups are: the acetyl and the benzoyl groups. Acylation is the introduction of acyl group into a compound. Friedl-Crafts acylation is an effective means of

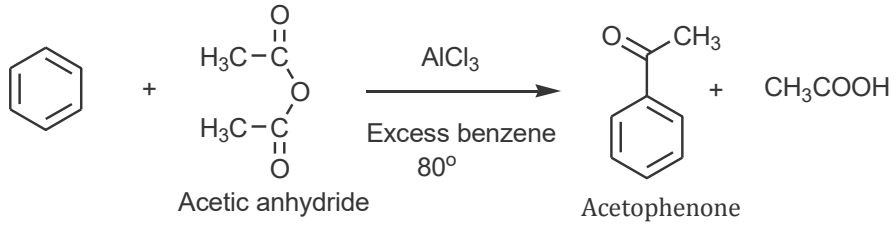
introducing an acyl group into the aromatic ring. The reaction is carried out by treating the aromatic compound with an acyl chloride. Unless the aromatic compound is highly reactive, the reaction requires the addition of a Lewis acid (such as $AlCl_3$). The product is an aryl ketone.



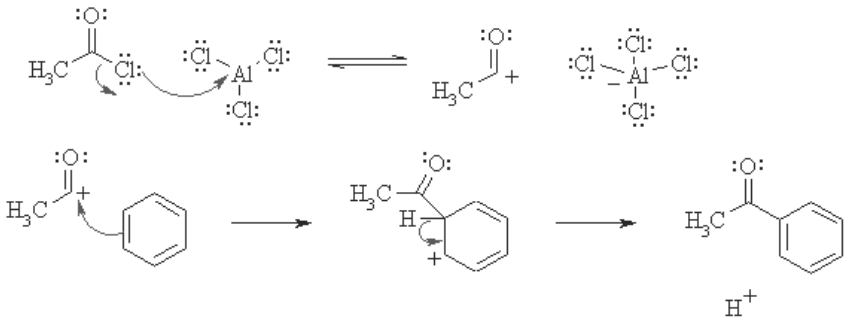
Acyl chlorides, also called acid chlorides, are easily prepared by treating carboxylic acids with thionyl chloride ($SOCl_2$) or phosphorus pentachloride (PCl_5).



Friedl-Crafts acylations can also be carried out using carboxylic acid anhydrides.



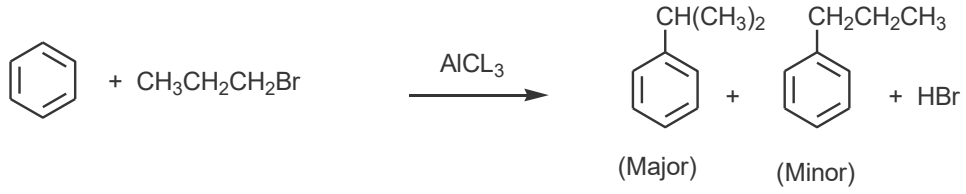
Mechanism for the reaction:

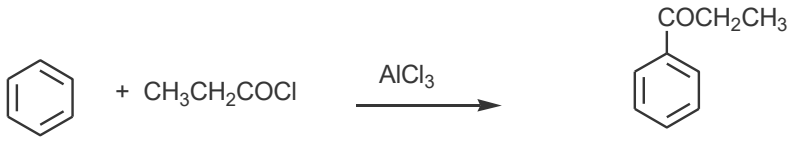


It should be noted that, in Friedel- Crafts acylation:

- No rearrangement occurs.
- Acylium ion is more stabilized (by resonance) than other carbocations:

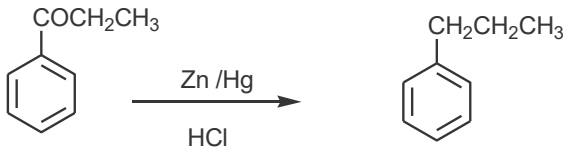
- It is a much better synthetic route to n-alkyl benzenes than Friedl-Crafts alkylation.





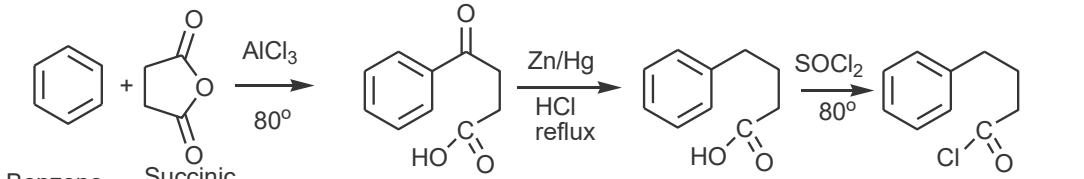
Ethylphenyl ketone (excellent yield, 90%)

This ketone can be reduced to propylbenzene by Clemmensen reduction (Zn/Hg + HCl) or Wolf-Kishner reduction (H_2NNH_2/OH^-).



n-Propylbenzene
(80%)

Friedel-Crafts acylation followed by ketone reduction is the synthetic equivalent of Friedl-Crafts alkylation. When cyclic anhydrides are used, Friedel-Crafts acylation provides a means of adding a new ring to an aromatic compound.



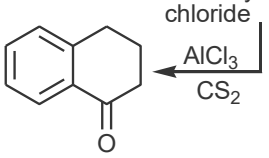
Benzene (excess)

Succinic anhydride

3-Benzoylpropanoic acid

4-Phenylbutanoic acid

4-Phenylbutanoyl chloride



α-Tetralone

Effect of substituents on reactivity and orientation

Substituent groups already on the ring affect both the rate of the reaction (reactivity) and the site of attack (orientation) in electrophilic aromatic substitution. They can be divided into two classes according to their influence on the reactivity of the ring:

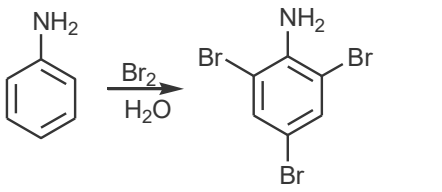
a. Activating groups, that cause the ring to be more reactive than benzene itself.
b. Deactivating groups, that cause the ring to be less reactive than benzene.

Substituent groups can also be classified into two classes according to the way they influence the orientation of attack by the incoming electrophile:

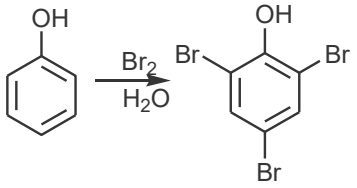
a- Ortho-para directors, that direct the incoming group into the ortho and para positions.
b- Meta directors, that direct the incoming electrophile to the meta position.

Activating groups: ortho - para directors:

All activating groups are ortho-para directors. Activating groups include alkyl groups, alkoxy groups, acetamido group, hydroxyl, and amino groups. OH and NH_2 groups are very powerful activating and o-p directors. Phenol and aniline react with Br_2 in water (No catalyst is required) to produce products in which both of the ortho positions and the para position are substituted. These tribromo products are obtained is nearly quantitative yield.



2,4,6-Tribromoaniline
(~ 100%)



2,4,6-Tribromophenol
(~ 100%)

Deactivating groups: meta directors:

All deactivating groups are meta directors except halogens which are ortho-para directors. All meta-directing groups have either a partial positive charge or a full positive charge on the atom directly attached to the ring. These include nitro, carboxyl (COOH), sulfo ($-SO_3H$), and trifluoromethyl group ($-CF_3$).

Halo substituents: Deactivating ortho-para directors:

Halogens are weak deactivating groups, but they are ortho-para directors.

Classification of substituents:

Ortho-para directors	Meta directors

A. Strongly activating

- $\ddot{N}H_2$, - $\ddot{N}HR$, - $\ddot{N}R_2$, - $\ddot{O}H$, -$\ddot{O}^-$

B. Moderately activating

- $NHCOCH_3$, - NHCOR, - OCOR

C. Weakly activating

-R, - C_6H_5

D. Weakly deactivating

-F , - Cl , -Br , - I

A. Strongly deactivating

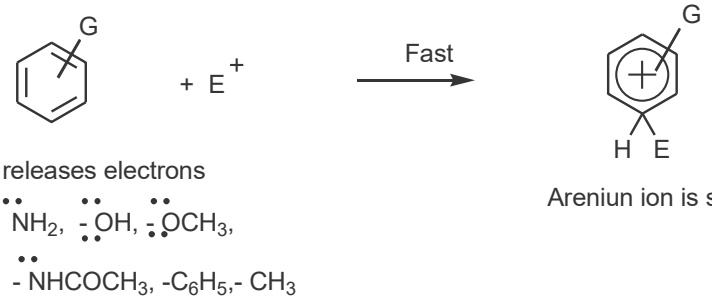
- NO_2, N^+R_3, - CF_3, -CCl_3

B. Moderately deactivating

- CN, -SO_3H, - COOH, - COOR, - CHO, - COR

Theory of substituent effects on electrophilic aromatic substitution:

The effect of electron-releasing and electron-withdrawing groups on reactivity:



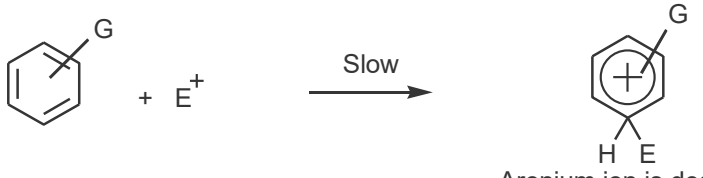
G releases electrons

G = $\ddot{N}H_2$, - $\ddot{O}H$, - $\ddot{O}CH_3$,

- $NHCOCH_3$, -C_6H_5,- CH_3

Areniun ion is stabilised

Reaction is faster.



G = Wilhdraws electrons

G = -$\overset{+}{N}(CH_3)_3$, - NO_2, - CN,

- SO_3H, - COOH, -CHO, -COR,-X

Arenium ion is destabilised

Reaction is slower.

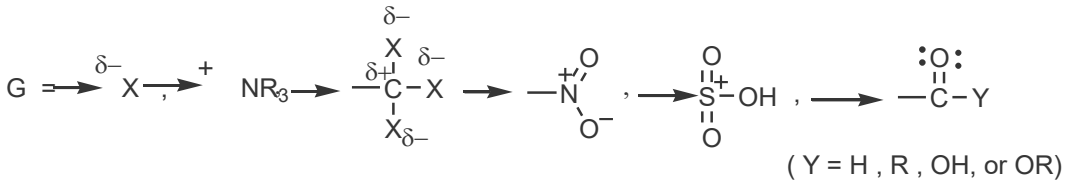
Reactivity, in EAS, depends upon the tendency of group G to release or withdraw electrons. A group that releases electrons activates the ring; a group that withdraws electrons deactivates.

Inductive and Resonance effects: Theory of orientation:

The electron-releasing and electron-withdrawing properties of substituent groups (G) are due to:

An inductive effect (I) and a resonance effect(M). These two factors determine the orientation in aromatic substitution reactions.

An inductive effect results from electronegativity differences between two groups. If, for example, G is a more electronegative atom or group than carbon, the ring will be at the positive end of the dipole.



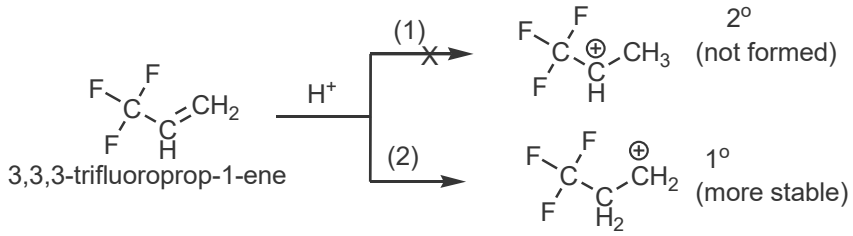
Electron-withdrawing groups with a full or partial charge on the atom attached to the ring.

The importance of inductive effect can be illustrated in the following reactions:

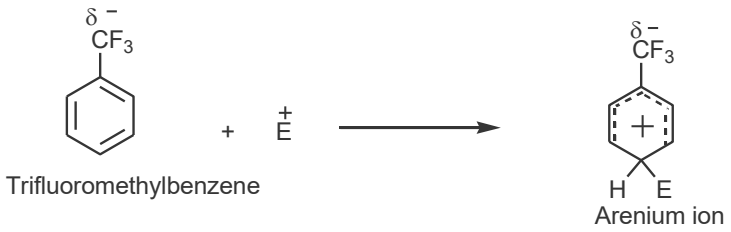
i) CF_3-CH=CH_2 + HCl → CF_3-CH_2CH_2Cl

3,3,3-Trifluoropropene

HCl adds to 3,3,3-trifluoropropene more slowly than to propene itself. The reaction may proceed as follows:



The trifluoromethyl group, because of the three highly electronegative fluorines, is strongly electron withdrawing. By path (1), the intermediate structure is highly unstable, because even though it is a 2° carbocation, the positive charge is on the C-atom adjacent to the highly electronegative trifluoromethyl group. Therefore, the reaction proceeds by path (2), where the intermediate is more stable even though it is a 1° carbocation, because the positive charge is separated from the trifluoromethyl group by methylene group, -CH_2-, and inductive effects are not transmitted very effectively through σ bonds.

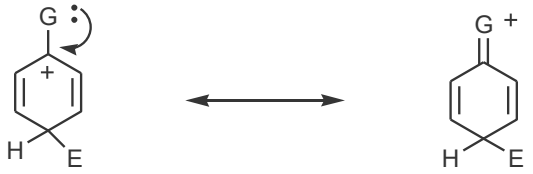


Trifluoromethylbenzene

Arenium ion

The arenium ion is highly unstable because trifluoromethyl group withdraws electrons from the developing carbocation, thus increasing the positive charge on the ring.

The resonance effect of substituent G refers to the increase or decrease of the resonance stabilization of the intermediate arenium ion. G may cause one of the contributors to the resonance hybrid for the arenium ion to be more stable or less stable than the case when G is H. Moreover, when G is an atom bearing one or more nonbonding electron pairs, it may give extra stability to the arenium ion by providing a fourth resonance contributor in which the positive charge residues on G.



This electron-donating resonance effect applies with decreasing strength in the following order:

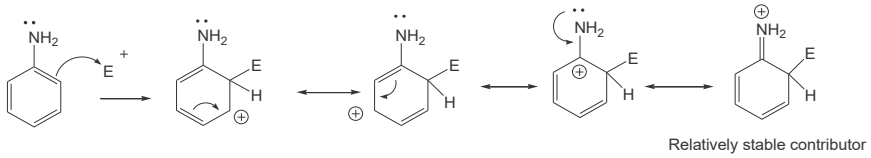
(Most e-donating) $-\ddot{N}H_2$, $-\ddot{N}R_2$ > $-\ddot{O}H$, $-\ddot{O}R$ > $-\ddot{X}$ (least e-donating)

This is also the order of the activating ability of these groups. The more electronegative the atom is, the less able it is to accept the positive charge. Fluorine is the most electronegative; nitrogen is the least.

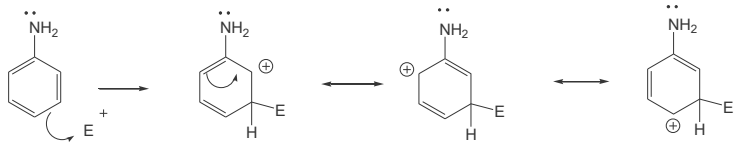
The resonance effects can be illustrated by the following examples:

a- The amino group is a powerful activating group and a powerful ortho-para director. Aniline, for example, reacts with bromine in aqueous solution at room temperature and in the absence of a catalyst to yield tribromoaniline. The inductive effect of NH_2 group makes it slightly electron withdrawing. N is more electronegative than C; the difference between electronegativities of N & C in aniline is not large. The resonance effect of NH_2 group is far more important than its inductive effect is EAS, and this resonance effect makes the amino group electron releasing. The resonance structures for the arenium ions arising from ortho, meta, and para attack on aniline can be written as follows:

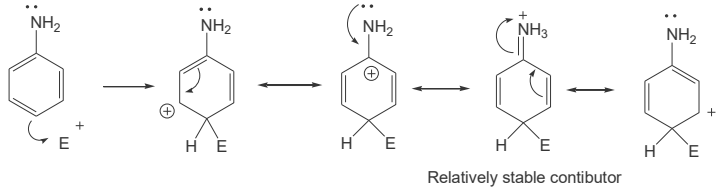
Ortho attack:



Meta attack:



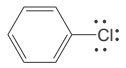
Para attack:



i.e. four resonance structures for the arenium ions result from ortho and para attack, whereas only three result from meta attack. This suggests that ortho-and para substituted arenium ions are more stable. Of great importance, however, are the relatively stable structures that contribute to the hybrid for the ortho-and para substituted arenium ions. In these structures, non-bonding pairs of electrons from N cause an extra bond which make these structures the most stable of all of the contributors.

Because these structures are unusually stable, they make a large and stabilizing contribution to the hybrid. Therefore, electrophiles react at ortho-and para-positions very rapidly.

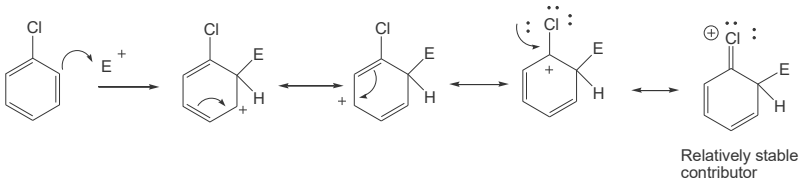
b- The halo groups are the only ortho-para directors that are deactivating groups. All other deactivating groups are meta directors. We can readily account for the behavior of halo substituents if we assume that their electron-withdrawing inductive effect influences reactivity and their electron-donating resonance effect governs orientation.



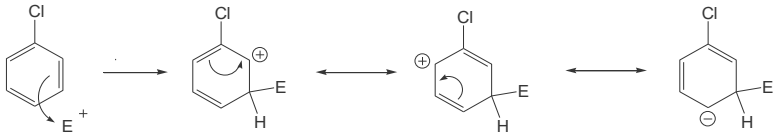
chlorobenzene

Inductive effect of Cl atom deactivates the ring.

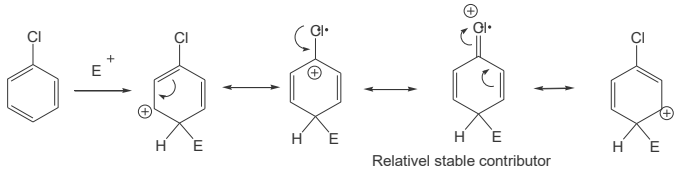
Ortho attack:



Meta attack:

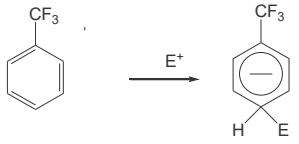


Para attack:

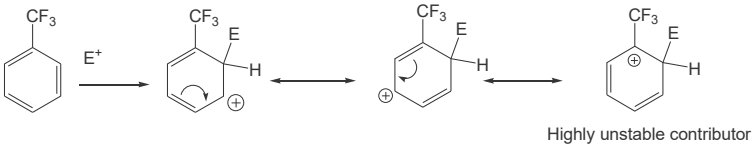


The inductive and resonance effects of halo substituents can be explained in the following way. X's make the ring more electron deficient than benzene, by electron-withdrawing inductive effect, i.e, X's are deactivating. Through their electron-donating resonance effect, halo substituents govern orientation and are ortho-para directors.

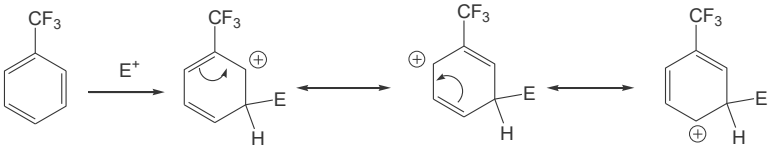
In trifluoromethylbenzene, the reactivity and directive effects of the trifluoromethyl group can be explained as follows:



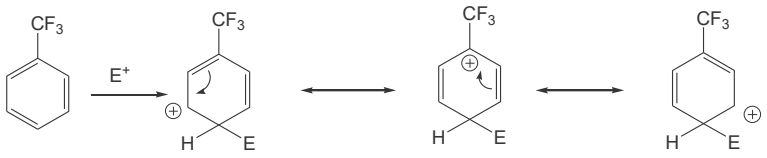
Ortho attack:



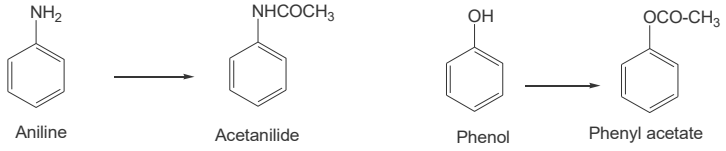
Meta attack:



Para attack:

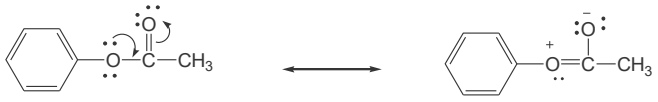


The resonance structures for the arenium ion arising from ortho and para attack have one highly unstable contributor, where the positive charge is located on the ring C-atom that bears the electron withdrawing group. This is absent in the resonance structures arising from meta attack. Therefore, trifluoromethyl group is a powerful meta director.



Phenyl acetate and acetanilide, although undergoing reactions at the ortho and para positions, are less reactive toward EAS than phenol and aniline, respectively. Explain, using resonance theory?

The following structures compete with the benzene ring for the oxygen electrons, making them less available to the benzene ring.



Similarly, the following structures compete with the benzene ring for the nitrogen electrons, making them less available to the benzene ring

Review problems:

Starting with benzene and the appropriate acyl chloride or acid anhydride, outline a synthesis of each of the following:

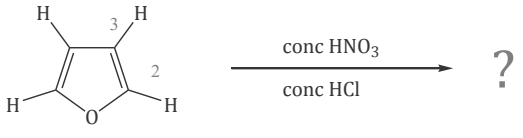
Butylbenzene Diphenylmethane 9,10-Dihydroanthracene

Starting with benzene, outline a synthesis of each of the following:

Isopropylbenzene Propylbenzene

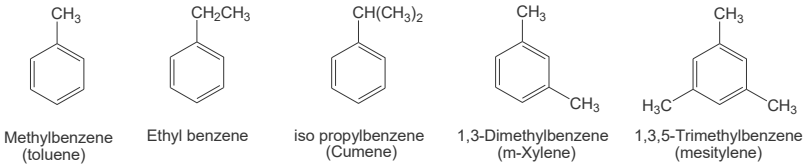
tert-Butylbenzene Butylbenzene

Furan undergoes electrophilic aromatic substitution. Use resonance structures for possible arenium ion intermediates to predict whether furan is likely to undergo nitration more rapidly at C2 or at C3.



Arenes

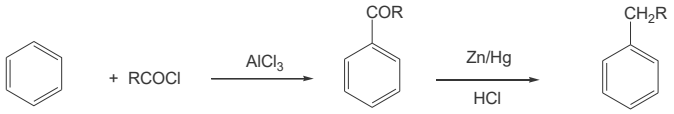
These are hydrocarbons consisting of aliphatic and aromatic groups. Ar-R; are called alkyl benzenes.



Preparation of alkyl benzenes:

1- Friedel-Crafts reactions:

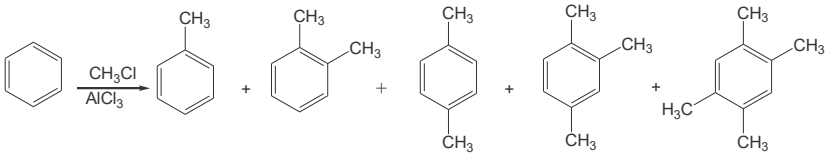
a- Acylation followed by reduction.



How could you prepare n-propylbenzene from benzene?

b- Alkylation:

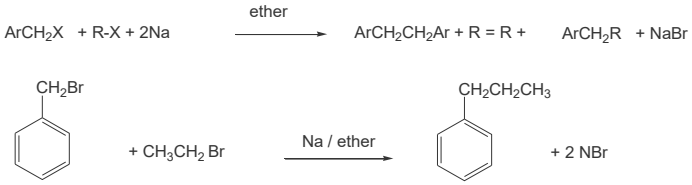
Friedel-Crafts alkylation reaction does not stop at the monoayklated stage, since the alkyl benzene is more readily alkylated than is benzene itself.



As shown, polyalkylation occurs, and purification must be undertaken to obtain a pure individual product.

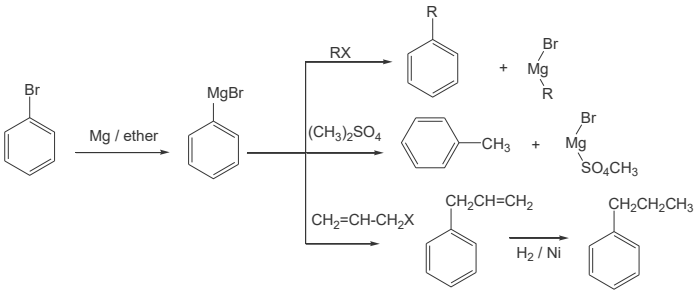
In Friedl-Crafts acylation, polysubstitution does not occur, since the acyl group is deactivating group. Direct alkylation of benzene is not a practical method for the preparation of alkyl benzene due to polyalkylation and rearrangement.

2- Wurtz- Fittig reaction:

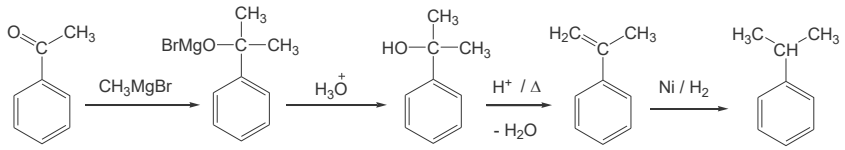


3- Grignard reagent:

a- By reaction of Ar Mg X with RX or R_2SO_4



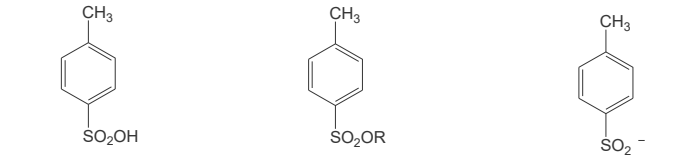
b- By reaction of R Mg X with acyl benzene.



Acetophenone

3° alcohol

c- By reaction of R Mg X with alkyl tosylate

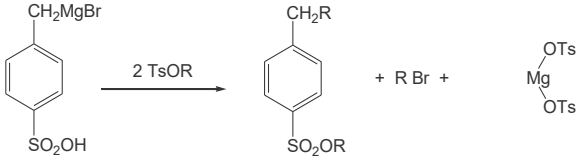


p-Toluenesulphonic acid

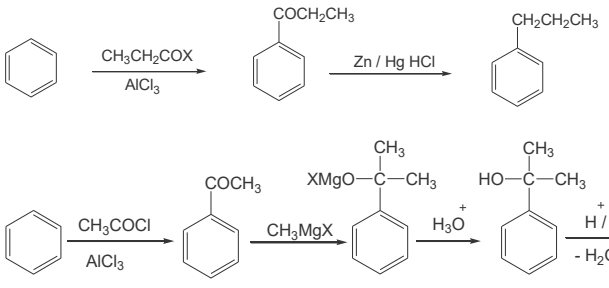
p-Toluensulphonate ester (or alkyl tosylate)

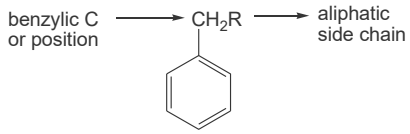
Tosyl radical (Ts)

Tosylate group (TsO) is a good leaving group and therefore the alkyl tosylate can be used as alkylating agent.



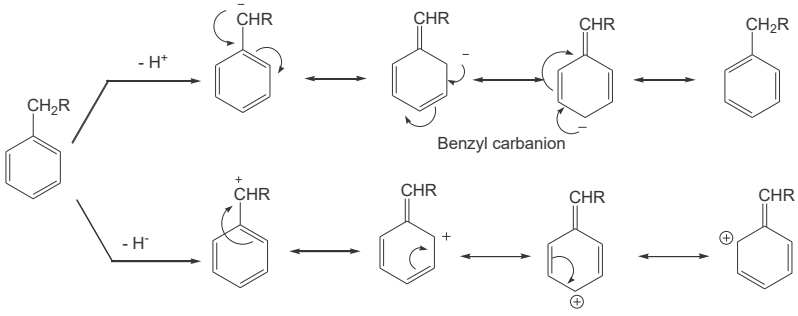
How can you convert benzene into n-propyl and isopropyl benzenes ?

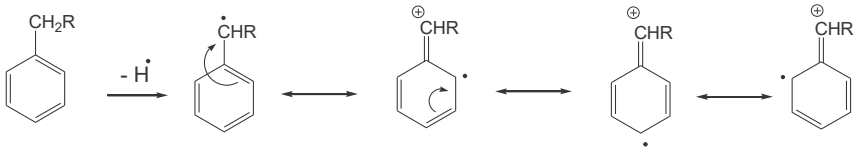




Reactions

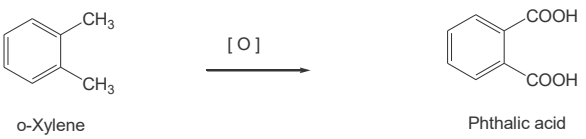
1- The benzylic position is the most active position in the aliphatic side chain since benzyl cation, benzyl anion, and benzyl free radical are all resonance stabilized.





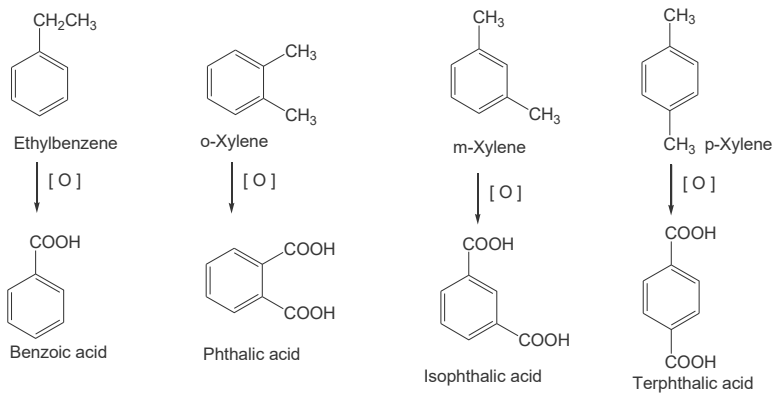
Benzyl free radical

Oxidation occurs to benzylic carbon by using $KMnO_4/OH^-$ or H^+, or by using $K_2Cr_2O_7/H^+$ as oxidizing agent.



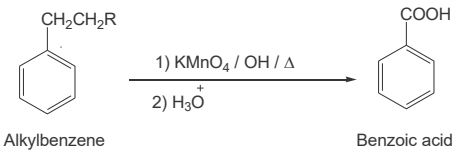
o-Xylene Phthalic acid

How could you differentiate between the following structures (all having C_8H_{10}) as molecular formulas??



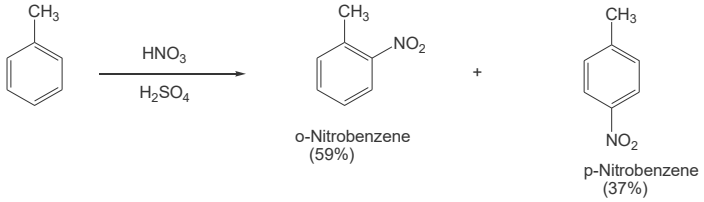
The resulting acids are identified by their melting points.

Oxidation takes place at the benzylic carbon, e.g.,



2- Electrophilic substitution (ES):

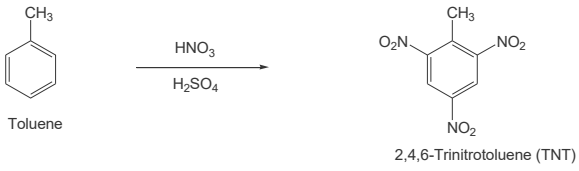
Alkyl benzene is more reactive than benzene toward ES, as the alkyl group has +I effect. Also, R is ortho-para director, e.g, milder conditions (lower temperatures and lower concentrations of the electrophile) can be used in ES of toluene than with benzene.



Bear in mind that alkyl groups are activating; methoxy group CH_3O-, and acetamido group CH_3CONH-are strong activating groups., the hydroxyl group and amino groups are very powerful activating groups. R, CH_3O-, CH_3CONH, -OH, and NH_2 are ortho-para directors.

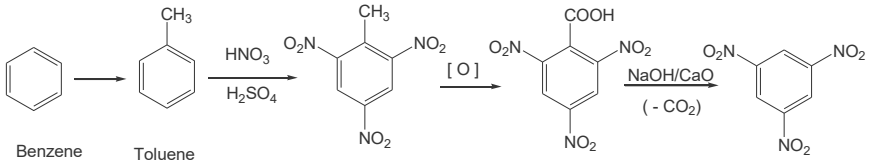
a- Nitration:

Toluene reacts 25 times as fast as benzene, under the same conditions.



How could you convert benzene into trinitrobenzene ??

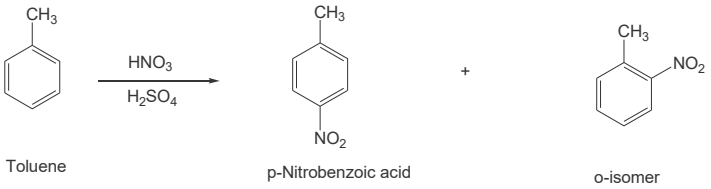
Direct nitration is not used because once NO_2 group is introduced, it will deactivate benzene nucleus for further nitration. So, indirect method is used.



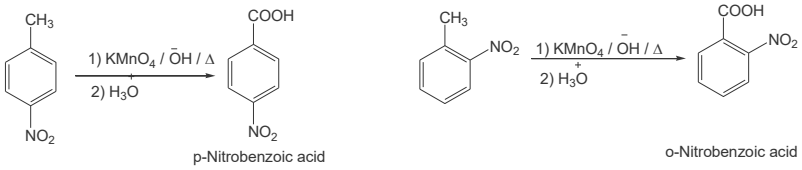
Starting from toluene, how could you synthesize:

o-, *m*-, and *p*-nitrobenzoic acids?

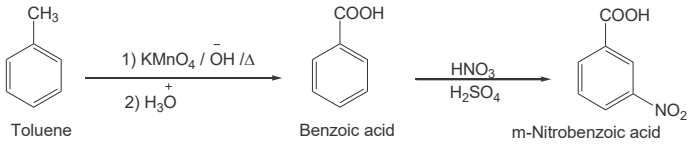
The proper order of reaction is important.



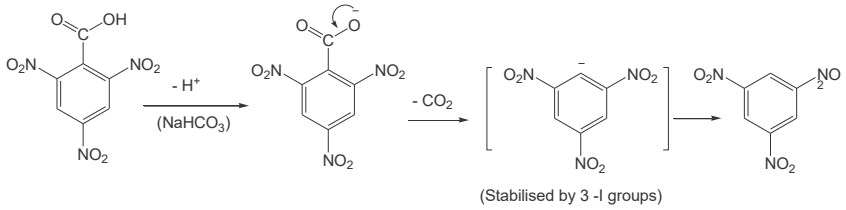
o- and p-isomers are separated.



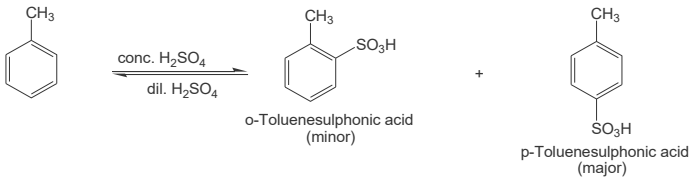
m-Nitro benzoic acid can be prepared by reversing the order of reactions:



2,4,6-Trinitrobenzoic acid undergoes facile decarboxylation, since -M (mesmeric effect) of three nitro groups creates partial positive charge on the carbon atom attached to the carboxylic acid group; this will facilitate elimination of a proton from COOH, and then decarboxylation.

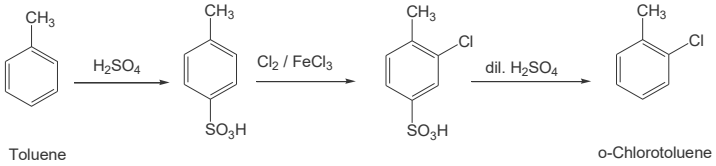


b- Sulphonation:



It is a reversible process.

How could you synthesise o-chlorotoluene from toluene ?



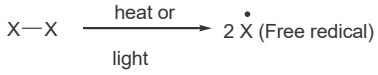
SO_3H group blocks para position.

c- Halogenation:

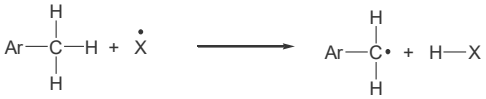
It occurs in the aromatic ring by EAS (ionic mechanism) or in benzylic position, i.e., benzylic halogenation (free radical mechanism).

Benzylic halogenation mechanism:

1- Initiation:

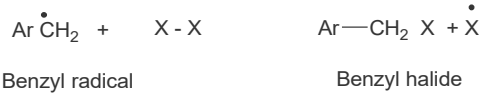


2- Chain propagation:



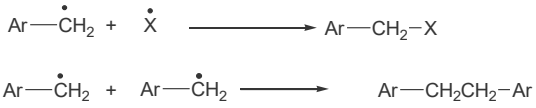
A halogen radical abstracts a benzylic hydrogen atom, forming a benzylic radical and hydrogen halide.

3.



The benzylic radical reacts with a halogen molecule to form benzylic halide and a halogen radical that propagates the chain.

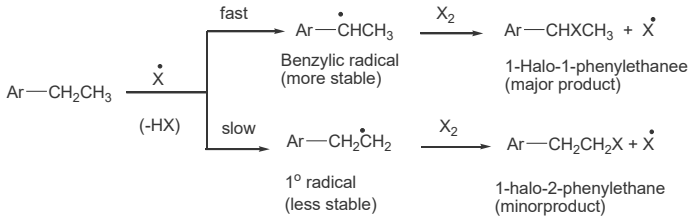
4.Chain termination:



All free radicals react with each other. The reaction may continue till all benzylic hydrogens are replaced by halogens.

Benzylic halogenations are similar to allylic halogenations, in that they involve the formation of unusually stable radicals which are even more stable than tertiary radicals.

The greater stability of benzylic radicals accounts for the fact that when ethyl benzene is halogenated, the major product is 1-halo-1-phenylethane. The benzylic radical is formed much faster than the 1° radical.

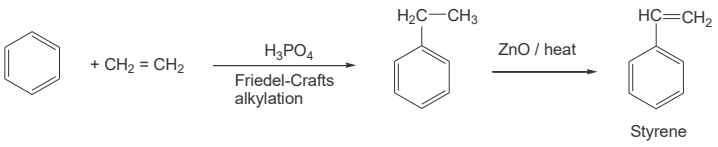


Alkenyl benzenes

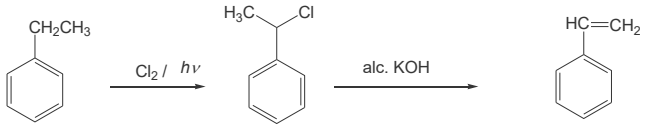
Aromatic compounds with side chain containing double bond.

Preparation:

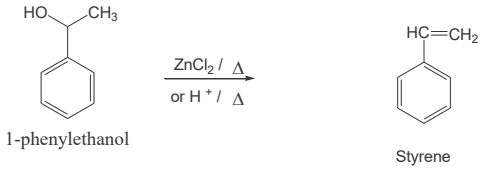
1. By dehydrogenation:



2. By dehydrohalogenation:



3. By dehydration of alcohols:



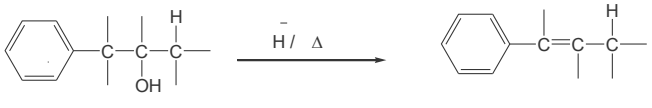
1-phenylethanol

Styrene

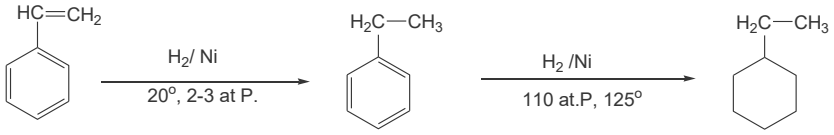
Reactions:

Alkenylbenzenes that have their side-chain double bond conjugated with the benzene ring are more stable than those that do not.

For example, acid-catalyzed dehydration of alcohols yield the most stable alkene; exclusively the conjugated system.

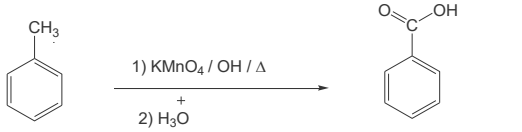


1- Reduction:



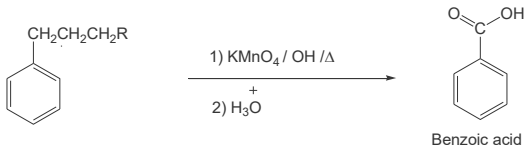
The alkene side chain is more reactive than benzene ring.

2- Oxidation:



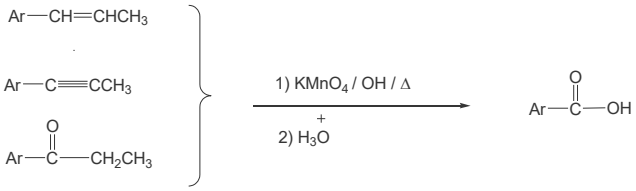
Toluene

Benzoic acid (~ 100%)



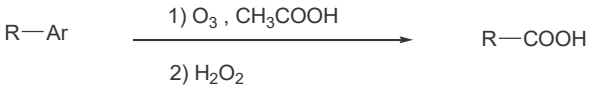
Benzoic acid

Oxidation takes place at benzylic carbon. Alkenyl, alkynyl, and acyl groups are oxidized by hot alkaline $KMnO_4$ in the same way:

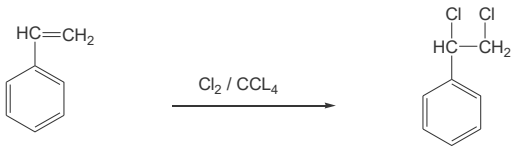


Oxidation of the benzene ring, how?

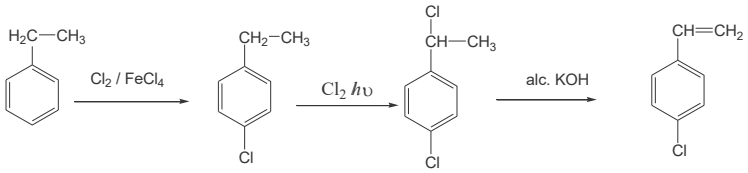
The benzene ring of Ar-R is converted to a carboxyl group by ozonolysis, followed by H_2O_2:



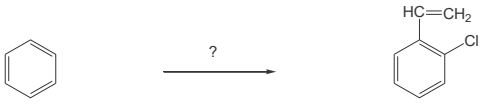
3-Halogenation:

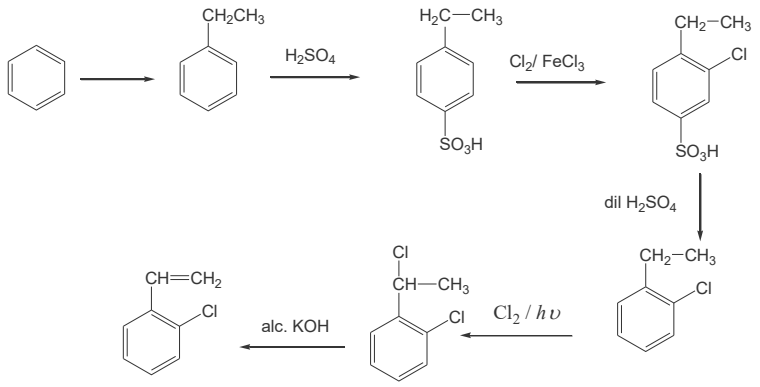


Alkenyl halobenzenes are prepared from alkyl halobenzenes as follows:



Starting from benzene, how could you prepare *o*-chlorostyrene?

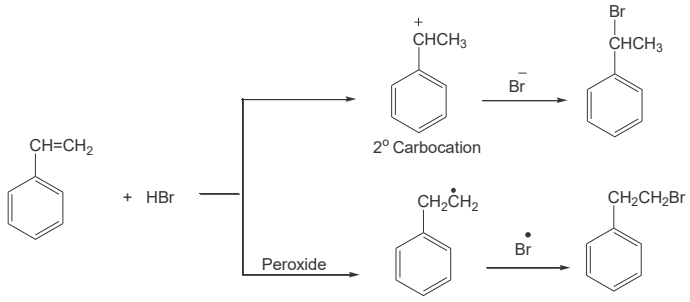


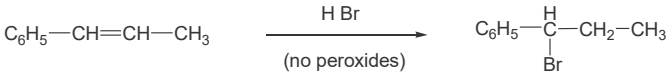


4. Addition of HBr:

In the absence of peroxide → benzylic cation (ionic mechanism), according to Markovnikoff's rule.

In the presence of peroxides → benzylic radical (free radical mechanism); Anti-Markovnikoff's rule.

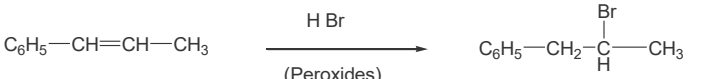




1- Phenylpropene

1-Bromo-1-phenylpropane (major)

The addition proceeds through benzylic cation in the absence of peroxides.



1- Phenylpropene

2-Bromo-1-phenylpropane (major)

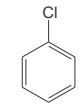
The addition of HBr proceeds through benzylic radical in the presence of peroxides.

Halogenated aromatic hydrocarbons

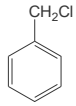
Nuclear substituted

(Aryl halides)

Side chain substituted



Chlorobenzene



Benzyl chloride

Halogenated hydrocarbons or organohalogen compounds can be classified into:

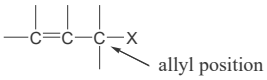
- ✓ According to X (F, CL, Br, or I): Fluoro-, chloro-, bromo-, or iodo compounds.
- ✓ According to hydrocarbon group:

a- Alkyl halides, R-X

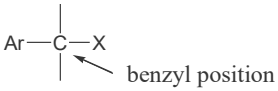
b- Aryl hides, Ar-X

c- Vinyl halides,

d- Allyl halides,

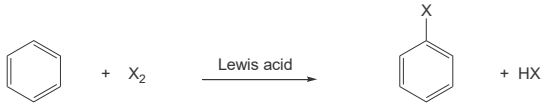


e- Benzyl halides



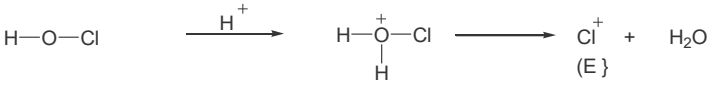
Preparation:

1- By direct halogenation, using Lewis acid catalyst such as $FeCl_3$, $AlCl_3$, or I_2

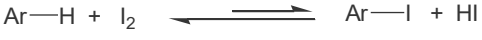


X = Cl or Br

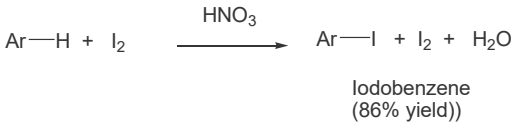
Chlorination could be done by hypochlorous acid:



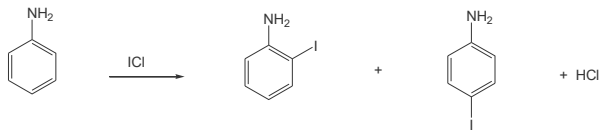
Iodination requires addition of an oxidizing agent:



HI should be simultaneously removed by oxidation.



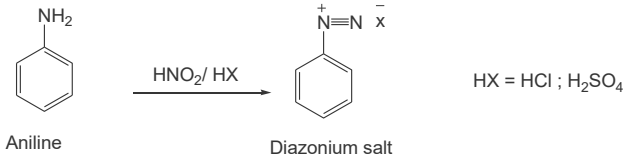
Iodination of highly activated rings, e.g. phenol or aniline, could be done by ICl:

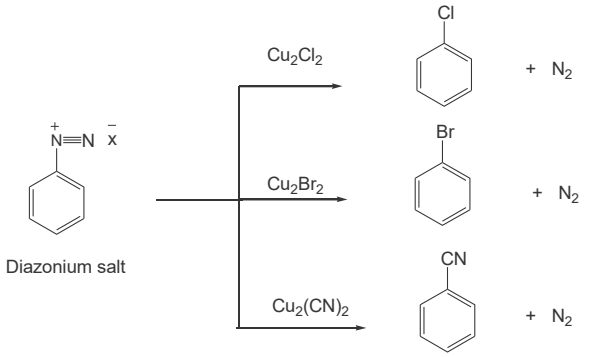


2- Indirect halogenation:

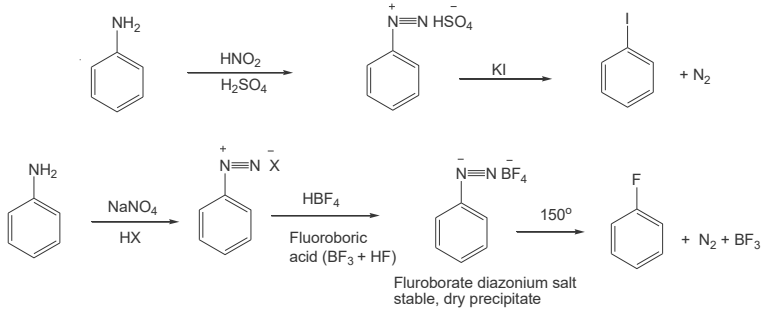
From amines through diazonium salts.

i- Sandmeyer reaction:



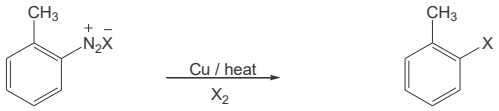


Iodobenzene and fluorobenzene can be prepared as follows:



ii- Gattermann reaction:

By heating the diazonium salt with copper powder:



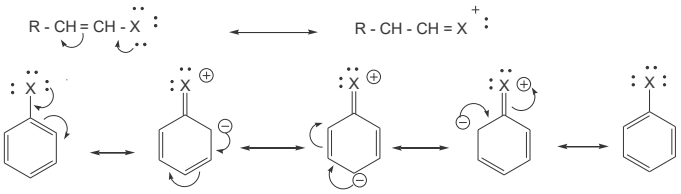
Reactions:

Like vinyl halides, aryl halides are unreactive toward nucleophilic substitution characteristic to alkyl halides.

Account for the inertness of aryl halides towards nucleophilic reagents?

This is due resonance.

$CH_2 = CHCl + NaOH \xrightarrow{\Delta}$ No substitution



Resonance structures of vinylic halides and aryl halide.

The C-X bonds of aryl and vinylic halides are shorter & stronger, due to:

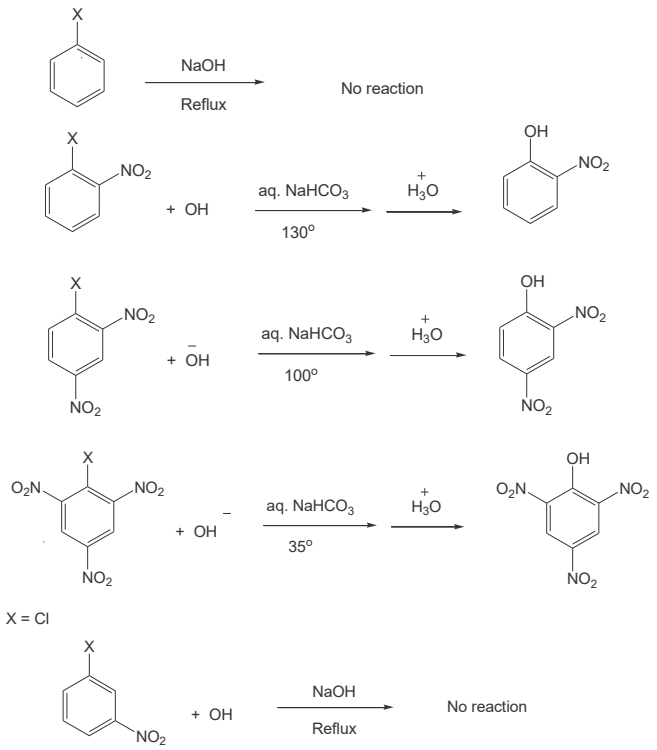
a) The C is SP-2 hybridized and so the electrons of the C orbital are closer to the nucleus than those of an SP-3 hybridized carbons
b) Resonance strengthens C-X bond by giving it double-bond character.

(1) Nucleophilic aromatic substitution by: addition-elimination mechanism:

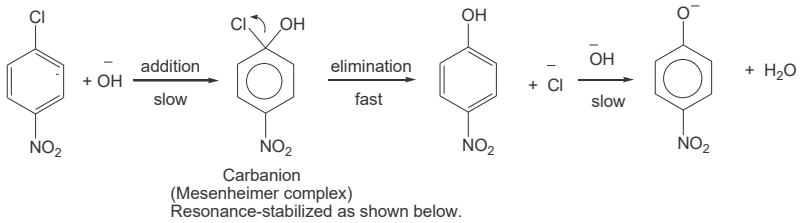
The following are common anions in decreasing basicity: -

$$\bar{C}H_3 > \bar{N}H_2 > \bar{O}R > \bar{O}H > \bar{I} > \bar{B}r > \bar{C}l > F$$

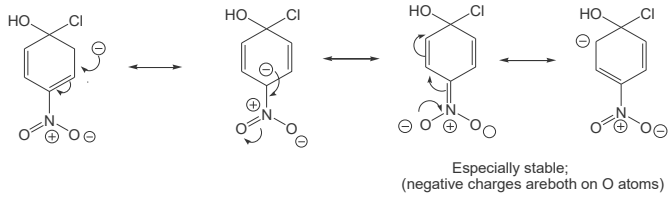
Nucleophilic substitution can occur when strong electron-withdrawing groups are ortho or para to X:



The mechanism involves addition-elimination mechanism involving formation of a carbanion called Meisenheimer complex:

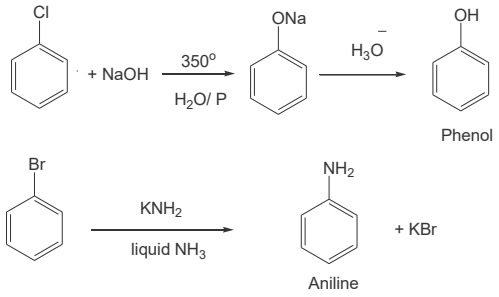


The carbanion is stabilized by electron-withdrawing groups in positions *ortho* and *para* to X.



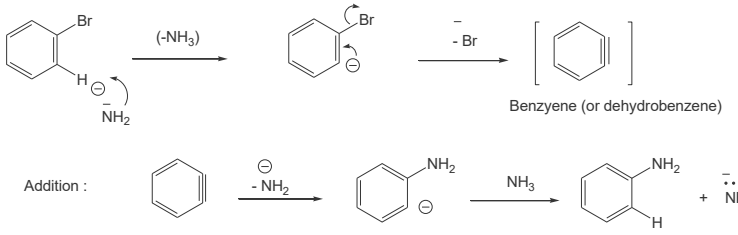
Nucleophilic aromatic substitution by: elimination-addition mechanism (Benzyne).

Ar-X (X = Cl or B) can react with nucleophiles under highly forcing conditions.

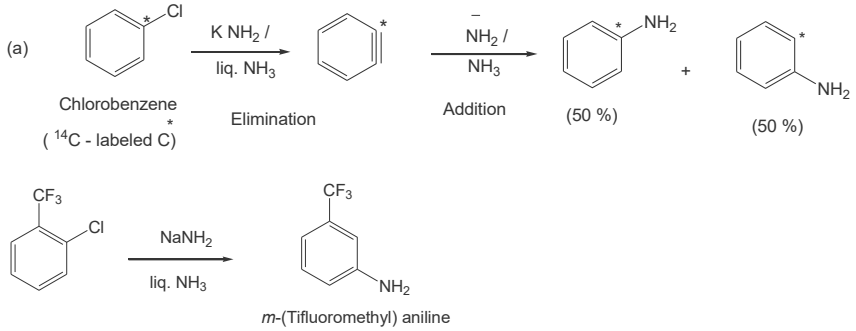


The benzyne elimination-addition mechanism:

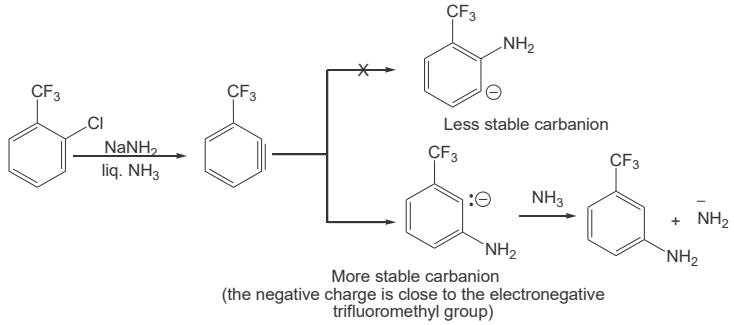
Elimination:



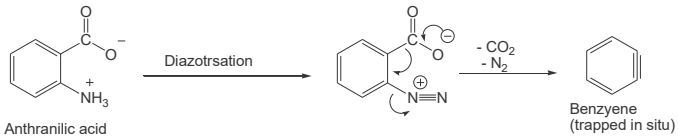
Evidence for an elimination-addition mechanism:



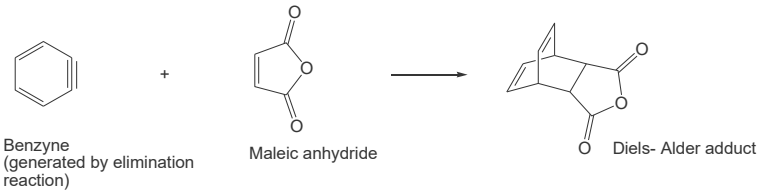
This product can be explained by an elimination-addition mechanism, as follows:

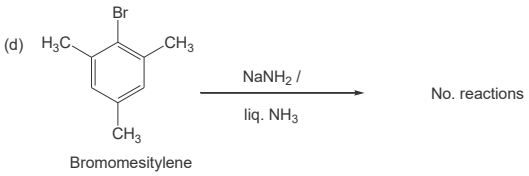


(c) Benzyne intermediate can be obtained by a convenient method via diazotization of anthranilic acid (2-aminobenzoic acid) followed by elimination of CO_2 and N_2:



When benzyne is generated in the presence of the diene maleic anhydride, the product is Diels-Alder adduct:

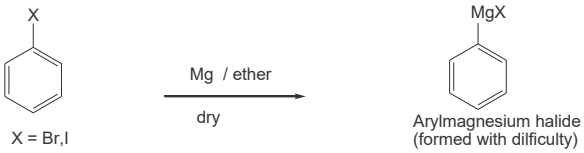


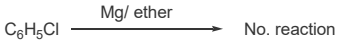


Since no H atom on the carbon adjacent to that bearing the halogen atom.

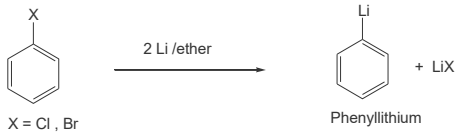
(2) Electrophilic substitution: X is deactivating, and ortho-para director.

(3) Formation of Grignard reagents:

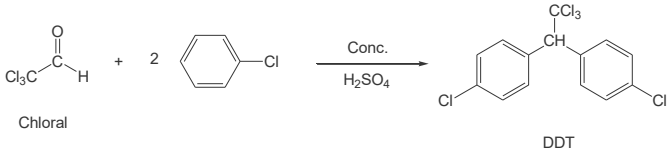




(4) Formation of aryl lithium:



Halogen compounds comprise many pesticides, e.g., DDT

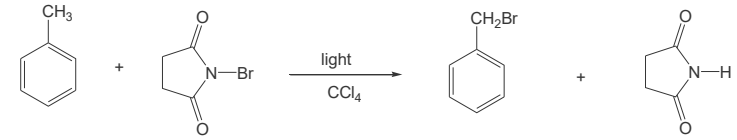


IUPAC name: 1,1,1-Trichloro-2,2-bis (p-chlorophenyl) ethane.

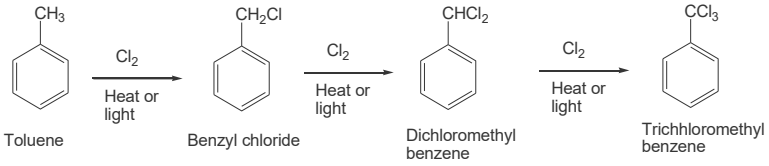
Common name: p,p'- Dichlorodiphenyl trichloroethane.

Side chain substituted aromatic hydrocarbons

Side-chain or benzylic halogenation takes place when the reaction is carried out in the absence of Lewis acids and under conditions that favor the formation of radicals.

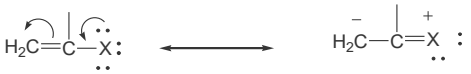


Side-chain chlorination occurs in the gas phase at 400-600^{o} or in the presence of UV light. Excess Cl_2 produces multiple chlorination.



Halogenation takes place via radical mechanism as in alkanes.

Allyl and benzyl halides react by S_N1, since their carbonium ions are resonance-stabilized.



Vinyl halide

Vinyl halides (sp^2 hybridized, shorter and stronger C-X bond)

Ar-X (sp^2 hybridized, shorter and stronger C-X bond)

R-X (sp^3 hybridized C-X bond).

Practice Problem

What reactant from each of the following pairs of compounds would easily transformed into the corresponding phenol?

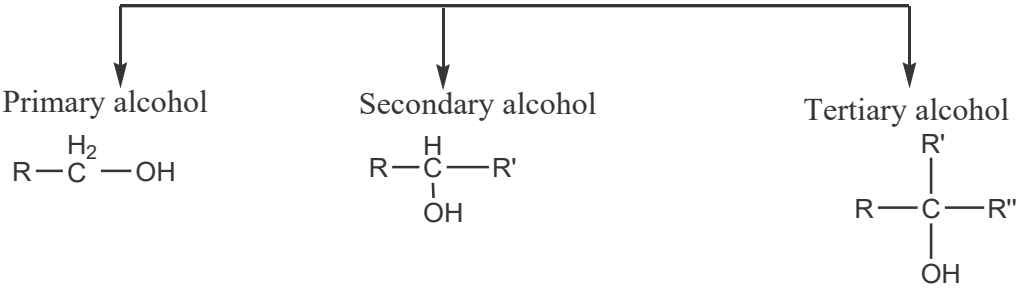
(a) chlorobenzene & 2-chloro nitrobenzene:

(b) 1-chloro-2,4,6-trinitrobenzene & 2-chloro benzonitrile:

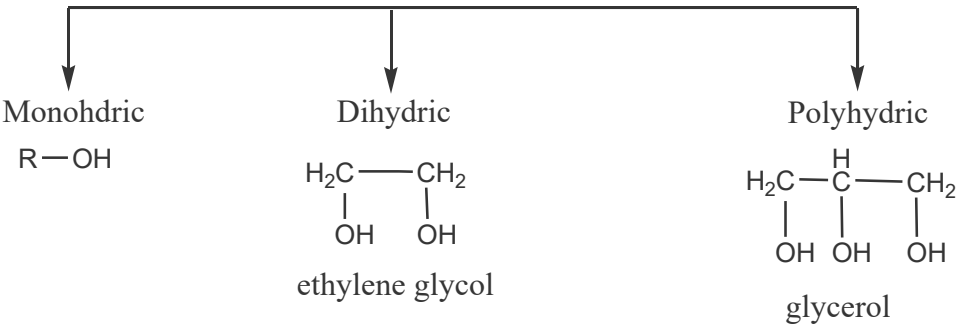
(c) 2-chloro anisol & 1-chloro-2,6-dinitrobenzene:

Alcohols

- Alcohols are compounds whose molecules have a hydroxyl group attached to a saturated carbon atoms.
- Classification of alcohols
  - According to the type of α-carbon



- According to the number of hydroxyl groups:

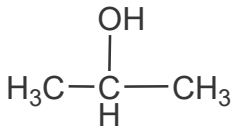


Nomenclature of alcohols

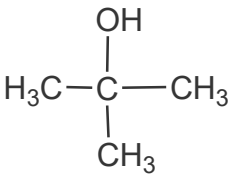
Common name

A) Monohydric alcohols: named as alkyl alcohol

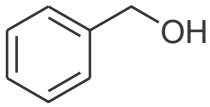
CH_3OH	CH_3CH_2OH
Methyl alcohol	Ethyl alcohol
(1°-alcohol)	(1°-alcohol)



isopropyl alcohol
(2^o-alcohol)

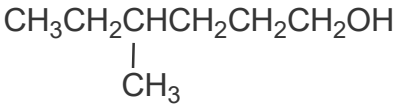


Tertiary butyl alchol
(3^o-alcohol)

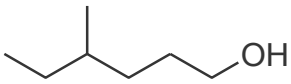


Benzyl alcohol

IUPAC name



or



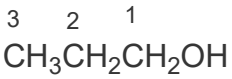
4- Methyl-1-hexanol or 4-methyl hexan-1-ol

Lacant prefix locant parent suffix

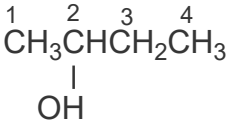
The following procedure should be followed in giving alcohols IUPAC names.

1- Select the longest continuous carbon chain to which hydroxyl group is directly attached, change the name of the corresponding alkane by dropping the final (e) and adding the suffix (ol).
2- Number the longest continuous carbon chain so as to give the carbon atom bearing the hydroxyl group the lowest possible number. Indicate the position of the hydroxyl group by using this number as a locant, indicate the positions of other substituents (as prefixes) by using numbers corresponding to their position along the chain as locants.

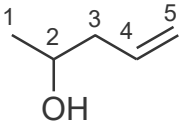
e.g.



1-propanol

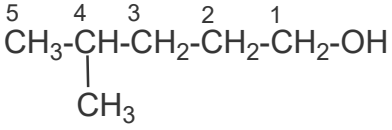


2-butanol

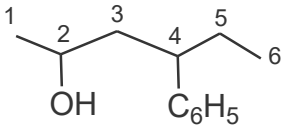


4-penten-2-ol

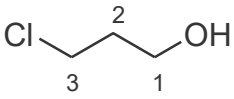
or Pent-4-en-2-ol



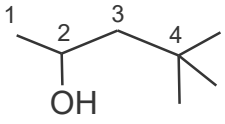
4-Methyl-1-pentanol
or 4-methyl pentan-1-ol
(not 2-methyl-5-pentanol)



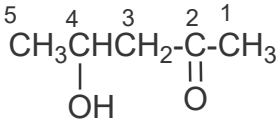
4-Phenyl-2-hexanol



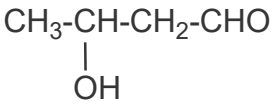
3-chloro-1-propanal



4,4-Dimethyl-2-pentanol



4-hydroxy-2-pentanone

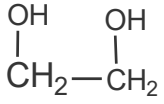


3-hydroxy-1-butanol

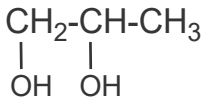
B) Dihydric alcohols

Common name : named as alkylene glycol

eg.

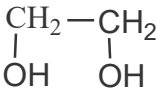


Ethylene glycol

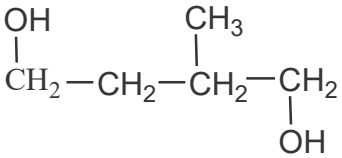


Propylene glycol

- **IUPAC name** named as alkane diol



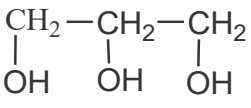
1,2-Ethylene diol
or ethane-1,2-diol



2-methyl butane-1,4-diol
or 2-methyl-1,4-dihydroxy butane

c) Trihydric alcohol

eg.

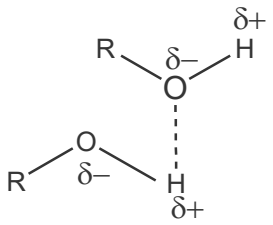


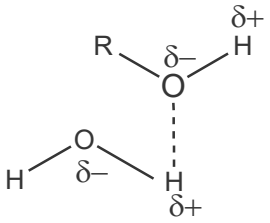
Common name : Glycerol

IUPAC name : Propane-1,2,3-triol

or 1,2,3-trihydroxypropane

Properties of alcohols





Most alcohols are miscible with water due to intermolecular hydrogen bonding between alcohol molecules and water molecules, however, as the number of carbon atoms increase, the solubility decrease.

Alcohol	Methanol	Ethanol	n-propanol	n-butanol	n-pentanol	n-hexanol
Solubility ($1g/100g\ H_2O$)	Miscible	Miscible	Miscible	7.9	2.7	0.59

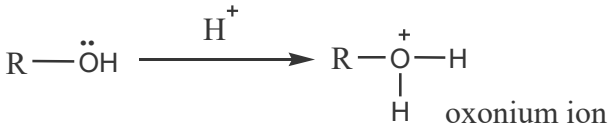
The difference in water-solubility of alcohols can be explained as follows:

The alcohol molecule is made of OH group and alkyl group R. The OH group confers polarity and water solubility upon the alcohol molecule. On the other hand, the alkyl portion confers non polarity and water-insolubility. In lower alcohol, the OH group comprises substantial portion of the total molecule to make it water-soluble. As the size of carbon chain increases. The water insoluble alkane portion increases.

In addition, the molecules of alcohol can associate with each of other through hydrogen bonding that give rise to the fact that alcohols have higher boiling point comparable to the corresponding alkane.

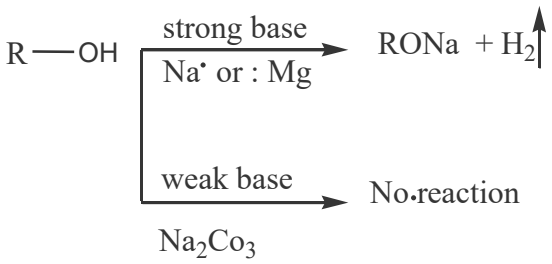
3- Basicity :

Alcohol act as weak bases



4- Acidity :

Alcohols act as very weak acids.

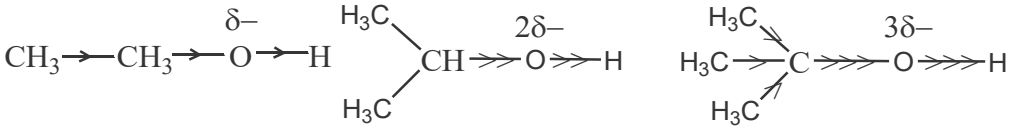


The order of relative acidity between water, alcohol and alkyne

$H_2O > ROH > R–C\equiv C–H$

Because the inductive effect of alkyl group (+I) decrease the electron withdrawing effect of oxygen atom towards hydrogen atom.

Moreover, since alkyl groups have +I effect, there will be an increased electron displacement toward oxygen atom in going from primary to tertiary alcohols.



The greater the negative charge on oxygen atom, the closer is the covalent pair in O–H bond driven to the hydrogen atom and separation of a proton became difficult. The order of acidity of alcohols will be as follows:

$$1° > 2° > 3°$$

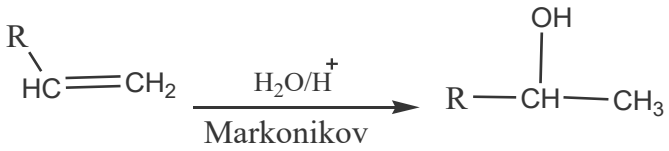
Preparation of monohydric alcohols

Alcohols can be prepared by the following general methods:

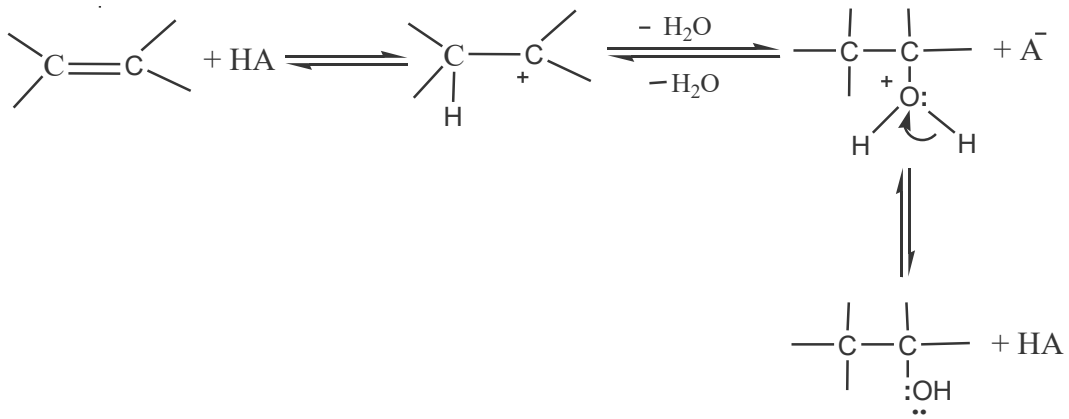
1) **Hydration of alkenes:**

   a) **Direct hydration**

Alkenes on treatment with concentrated sulphuric acid form alkyl hydrogen sulphates which on subsequent hydrolysis with water or steam yield alcohols.



Mechanism :

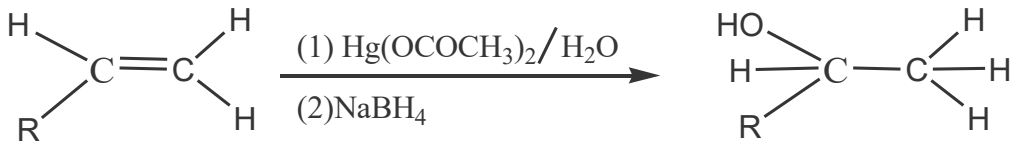


Acid catalyzed hydration of alkenes has limited synthetic utility because the carbocation intermediate may rearrange if a more stable carbocation is possible by hydride or alkanide migration. Thus, a mixture of isomeric alcohol products may result.

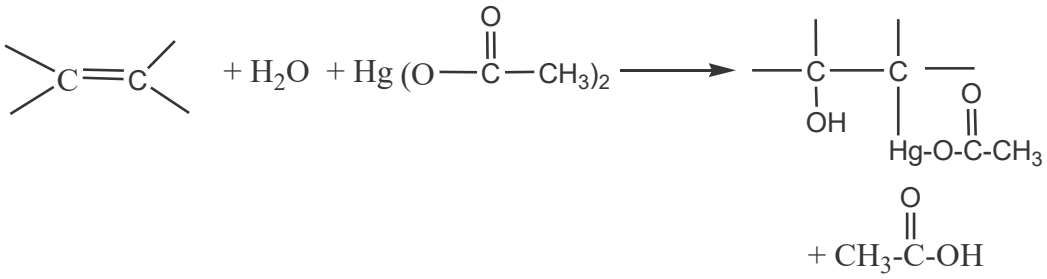
B- Indirect hydration :

1- Oxymercuration – Demercuration

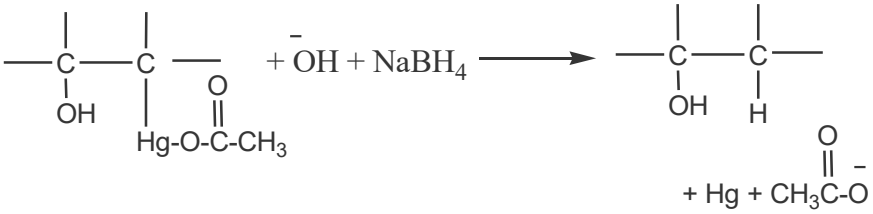
Alkenes react with mercuric acetate to produce (hydroxy alkyl) mercury compounds that can be reduced to alcohols with sodium borohydride and water.



Oxymercuration :



Demercuration :



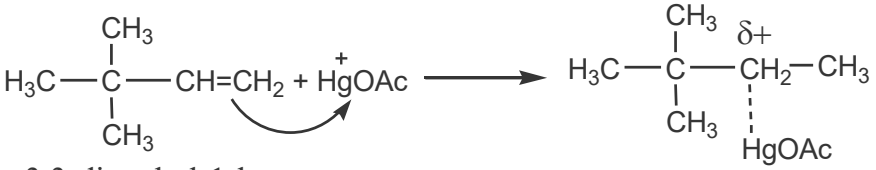
In the oxymercuration step, water and mercuric acetate add to the double bond, in the demercuration step, sodium borohydride reduces the acetoxy mercury group and replaces it with hydrogen. The net addition of –H and –OH takes place with Markonikov regioselectivity and generally without rearrangement.

- **Mechanism for oxymercuration reaction**

  Step (1) :

  $Hg(OAc)_2 \rightleftharpoons Hg^+OAc + OAc^-$

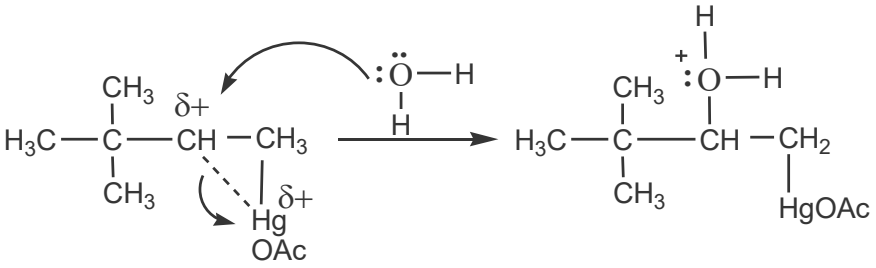
Step (2) :



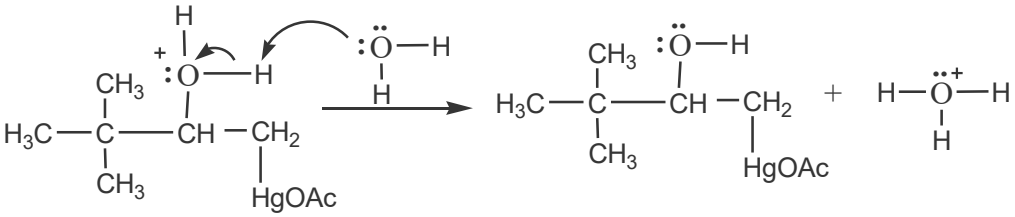
3,3-dimethyl-1-butene

Mercury-bridged carbocation

Step (3):

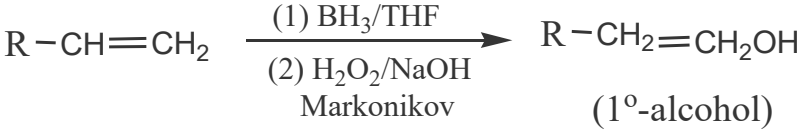


Step (4):



ii) <u>Hydroboration – oxidation :</u>

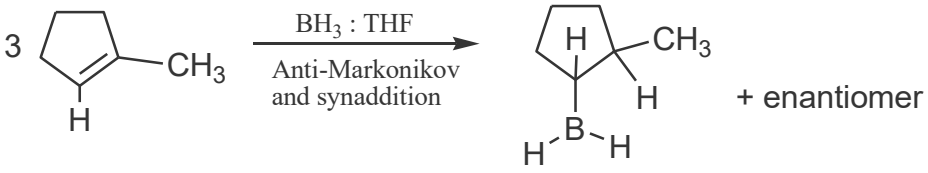
Alkene reacts with borane to produce an alkyl borane. Oxidation and hydrolysis of the alkyl borane, with hydrogen peroxide and base yield an alcohol.



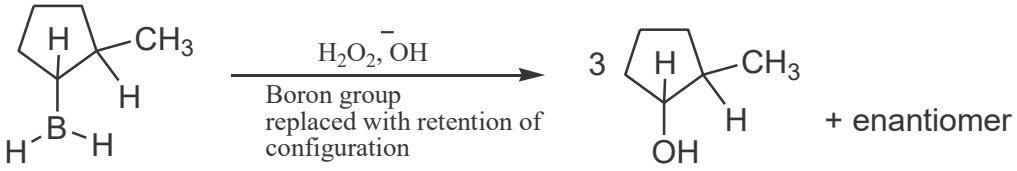
(1°-alcohol)

For an example

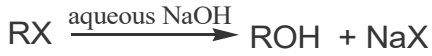
Hydroboration :



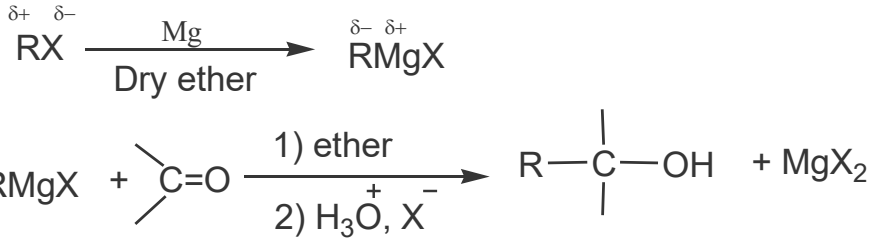
Oxidation



2) <u>Nucleophic substitution reaction of alkyl halide:</u>

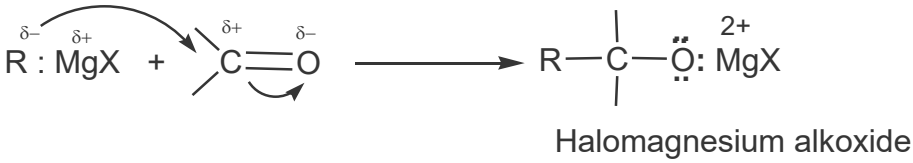


3) <u>Reaction of Grignard reagent with carbonyl compounds</u>



<u>Mechanisms</u>

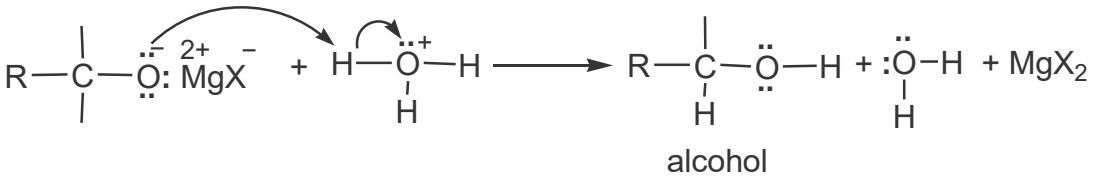
Step (1)



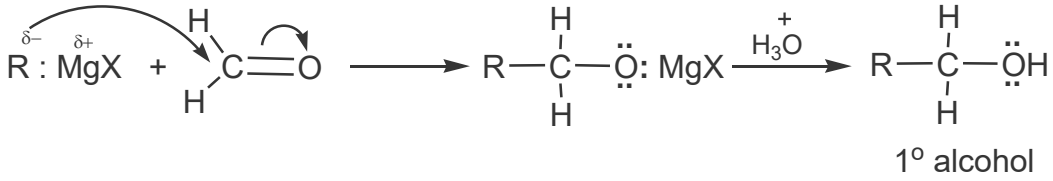
The strongly nucleophilic Grignard reagent uses its electron pair to form a bond to the carbon atom one electron pair of the carbonyl group shifts out to the

oxygen. This reaction is a nucleophilic addition reaction and its results in the formation of alkoxide ion associated with Mg^{2+} and X^{-}.

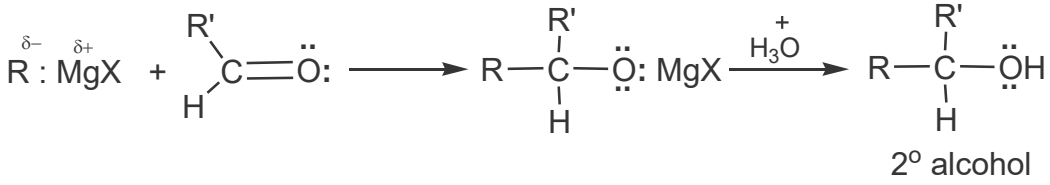
Step (2):



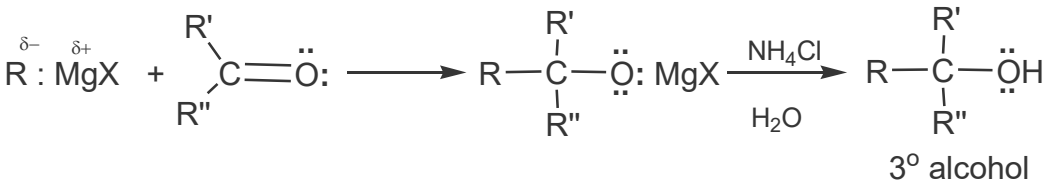
- In the second step, the addition of aqueous HX causes protonation of the alkoxide ion leading to the formation of alcohol.
- Grignard reagents react with formaldehyde to give a primary alcohol.



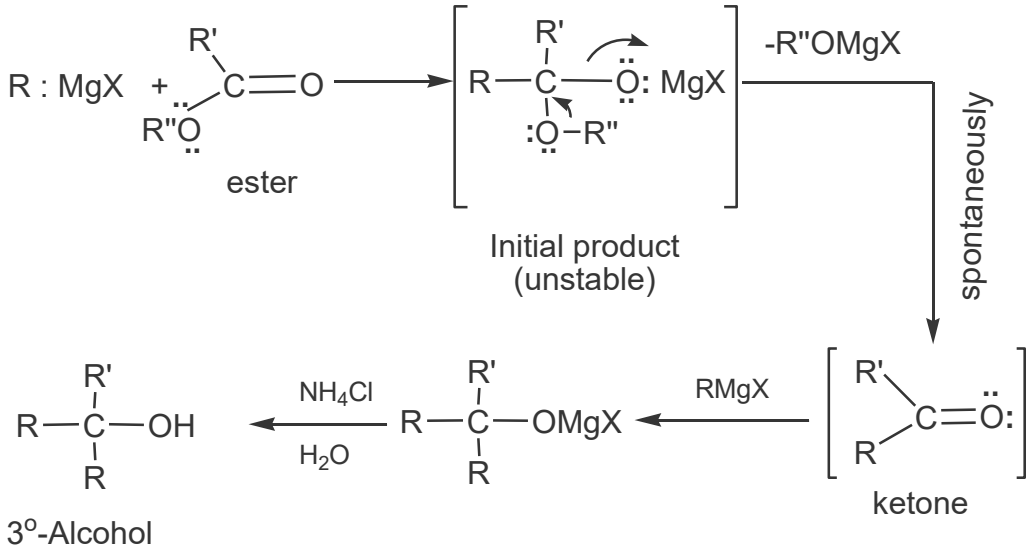
- Grignard reagents react with all other aldehydes to give secondary alcohols.



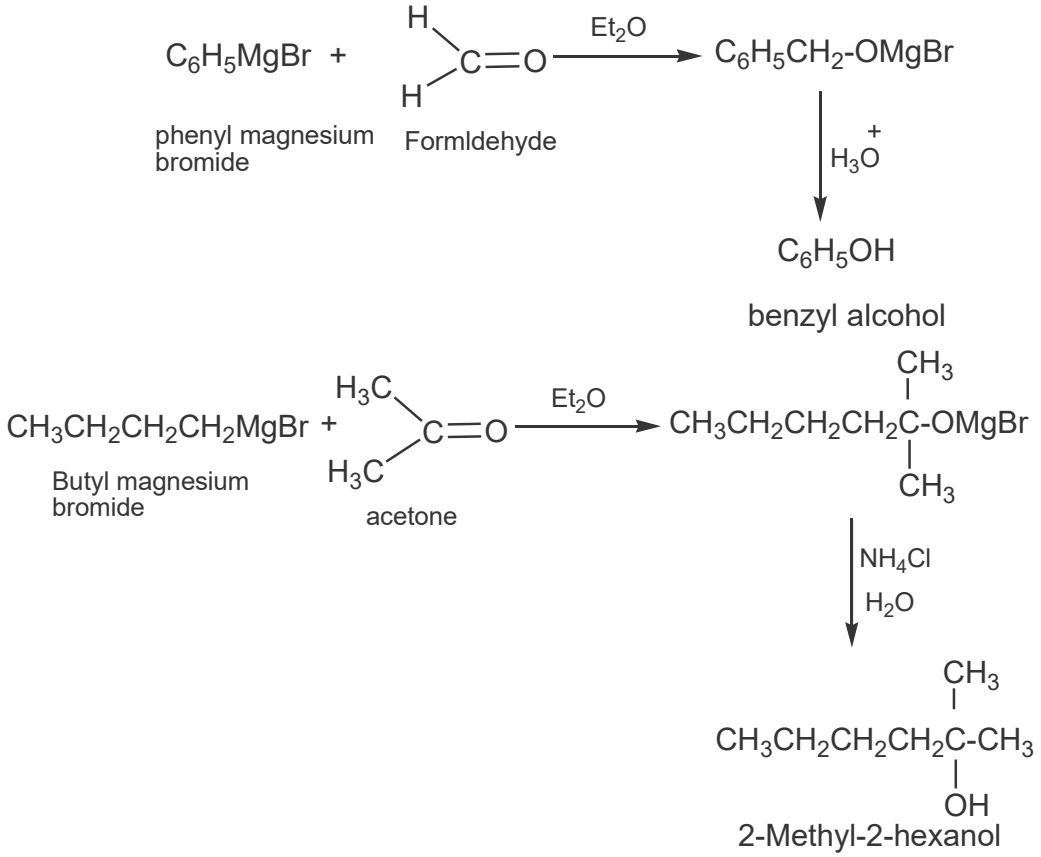
- Grignard reagents react with ketones to give tertiary alcohols.

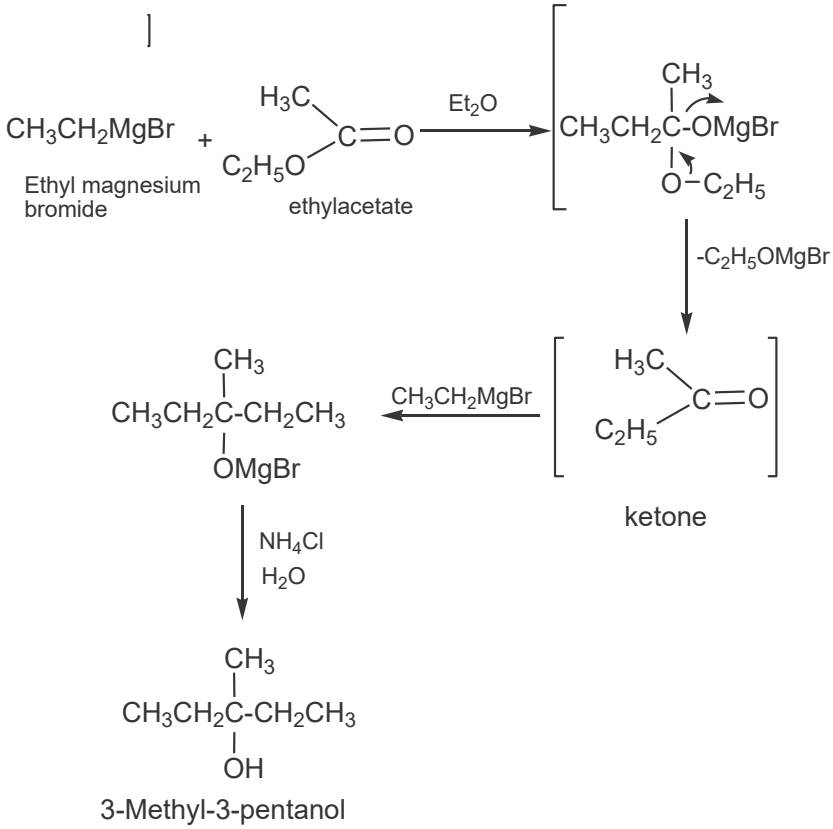


- Esters react with two equivalents of a Grignard reagent to form tertiary alcohols with two identical alkyl groups (corresponding to alkyl portion of Grignard reagent).


R : MgX
R'
C
O
R"O
ester
R
MgX
-R"OMgX
spontaneously
Initial product
(unstable)
ketone
RMgX
OMgX
NH4Cl
H2O
OH
3o-Alcohol

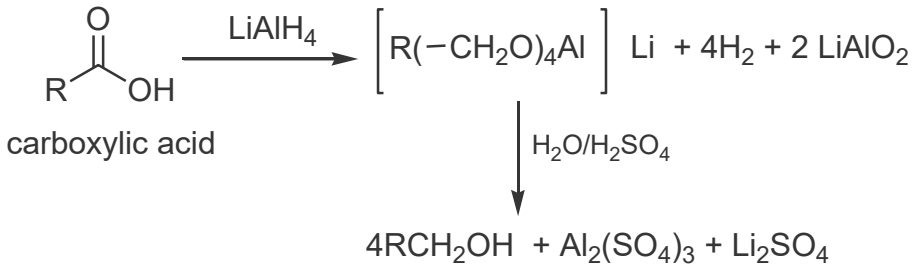
e.g.

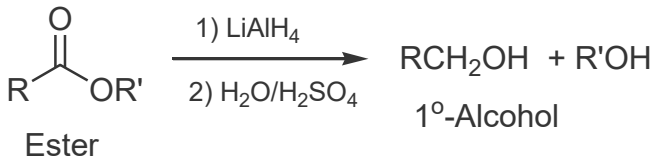

C6H5MgBr +
phenyl magnesium bromide
H
C
O
Formldehyde
Et2O
C6H5CH2-OMgBr
H3O+
C6H5OH
benzyl alcohol
CH3CH2CH2CH2MgBr +
Butyl magnesium bromide
H3C
acetone
Et2O
CH3CH2CH2CH2C-OMgBr
NH4Cl
H2O
CH3CH2CH2CH2C-CH3
OH
2-Methyl-2-hexanol

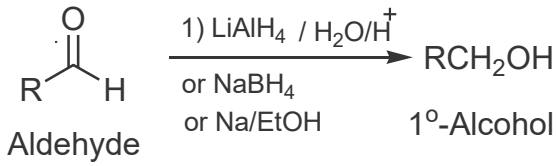


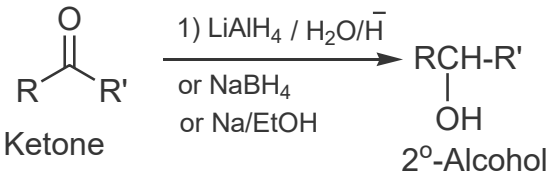
4) Reduction of carbonyl compounds

Primary and secondary alcohols can be synthesized by the reduction of a variety of compounds that contain carbonyl group.



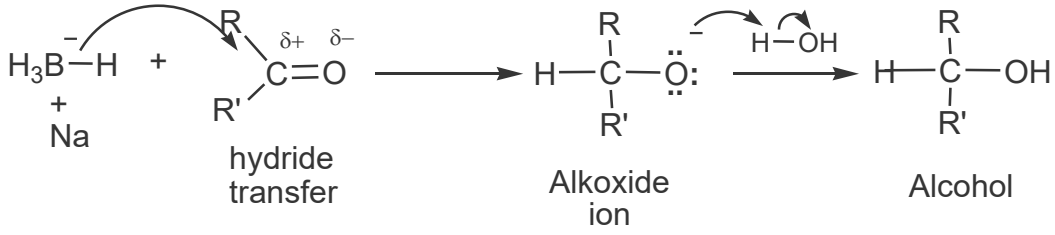




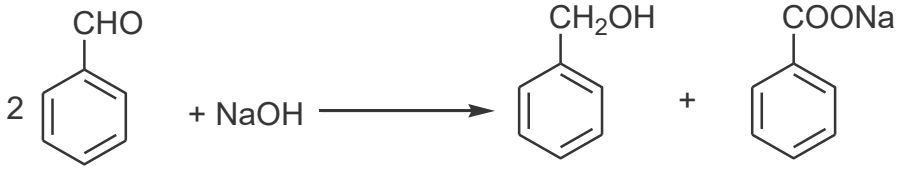


The key step in the reduction of a carbonyl compound by either lithium aluminium hydride or sodium borohydride is the transfer of a hydride ion from the metal to the carbonyl carbon and act as a nucleophile.

Mechanism:



5) Cannizzaro reaction



Reactions of Monohydric alcohols

1) Conversion of alcohol into alkyl halide

Alcohols react with a variety of reagents to yield alkyl halid. The most commonly used reagents are hydrogen halides (HCl, HBr and HI), phosphorus tribromide (PBr_3) and thionyl chloride ($SOCl_2$). Because the hydroxyl group is such a poor leaving group, it is first converted to a suitable leaving group.

a) By using hydrogen halide (HX)

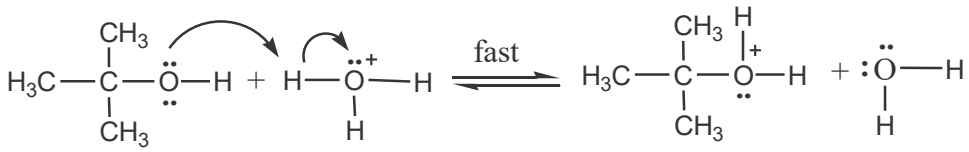
$$R–OH + HX \longrightarrow R–X + H_2O$$

The order of reactivity of the hydrogen halide is HI > HBr > HCl (HF is unreactive) while the order of reactivity of alcohols is 3°>2°>1°> methyl.

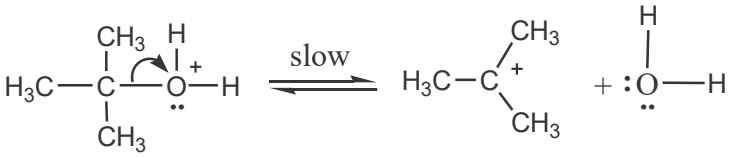
The reaction is acid catalyzed and involves the formation of carbocation (hence, rearrangement) in case of secondary, tertiary, allylic and benzylic alcohols.

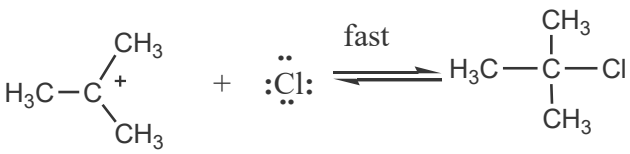
Mechanism : (SN^1)

Step 1 :

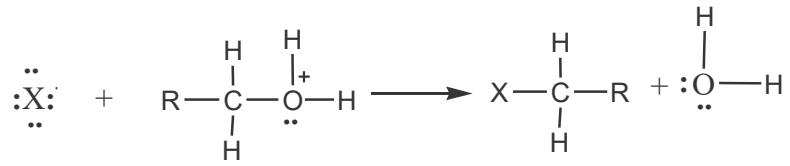


Step 2 :





Furthermore, primary alcohols and methanol react through a mechanism without formation of carbocation (SN^2). In these reactions, The function of the acid is to produce a protonated alcohol.

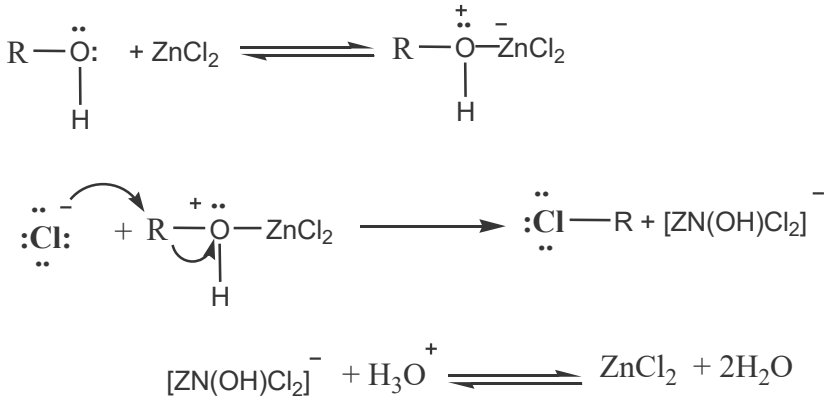


Protonated 1°-alcohol or methanol

good leaving group

We can see why the reaction of alcohols with hydrogen halides is acid promoted with tertiary and secondary alcohols, the function of the acid is to produce a carbocation. With methanol and primary alcohols, the function of the acid is to produce a substrate in which the leaving group is weakly basic water molecule rather than a strongly basic hydroxide ion.

In addition, because the chloride ion is a weaker nucleophile, hydrogen chloride doesn't react with 1° or 2° alcohols unless zinc chloride or some similar Lewis acid is added (Lucas test).



Lucas test can be used to differentiate between primary, secondary and tertiary alcohols as the order of reactivity directed from tertiary to primary alcohols. The differing reactivity reflects the differing ease of formation of the corresponding carbocations. Tertiary carbocations are far more stable than secondary carbocations, and primary carbocations are the least stable.

An equimolar mixture of $ZnCl_2$ and HCl is Lucas reagent. Tertiary alcohols react immediately with Lucas reagent as evidenced by turbidity owing to the

low solubility of the organic chloride in the aqueous mixture. Secondary alcohols react within five or so minutes (depending on their solubility). Primary alcohols do not react appreciably with Lucas reagent at room temperature. Hence, the time taken for turbidity to appear is a measure of the reactivity of the class of alcohol, and this time difference is used to differentiate among the three classes of alcohols.

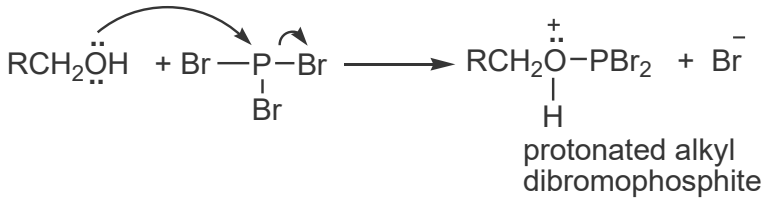
B) Using phosphorus tribromide (PBr_3)

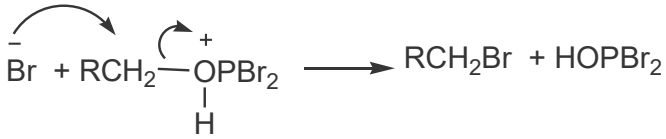
Unlike the reaction with HBr, the reaction of alcohol with PBr_3, PCl_3 or PCl_5 doesn't involve the formation of carbocation and occurs without rearrangement, consequently, it is preferred than hydrogen halide.

$$3\ R{-}OH\ +\ PBr_3 \longrightarrow 3R{-}Br\ +\ H_3PO_3$$

1° or 2°

Mechanism :



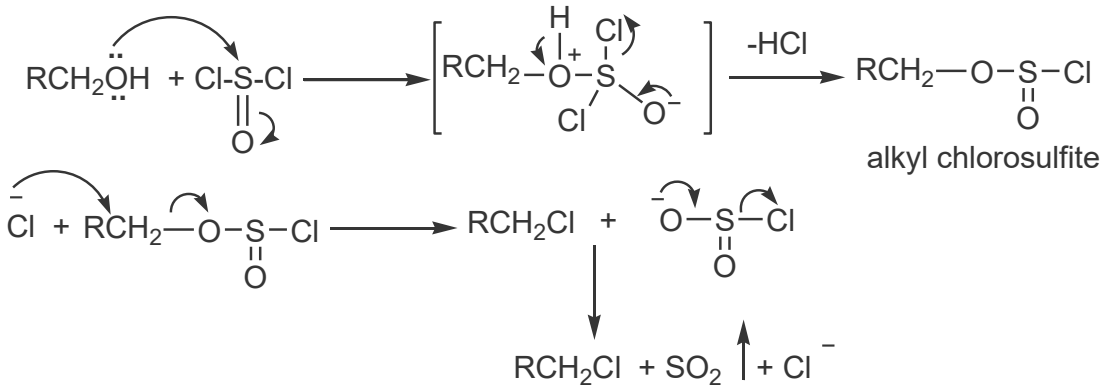


C) By using thionyl chloride ($SOCl_2$)

$SOCl_2$ converts 1° and 2° alcohols to alkyl chlorides without rearrangement.

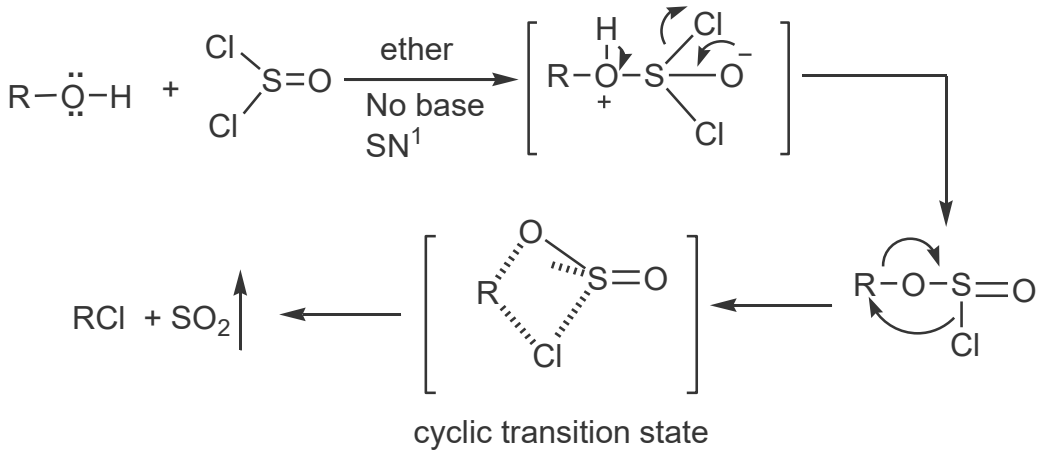
Often a tertiary amine is added to the reaction as a catalyst to promote the reaction by reacting with HCl .

Mechanism :

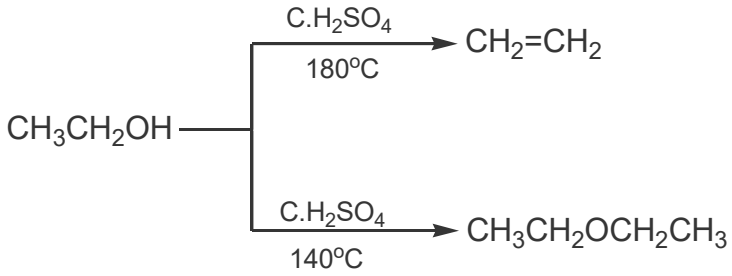


SO_2 and HCl are gases that can be easily removed which showed the reaction with $SOCl_2$ is preferable than PBr_3.

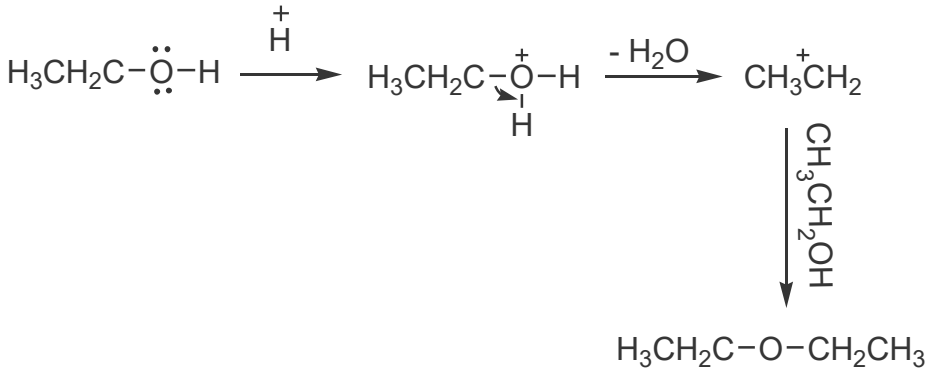
N.B. **:** Basic solvent provide the reaction with Cl^- that attack alkyl group from opposite site leading to inversion of configuration (SN^2). If a base wasn't added to the reaction, Cl^- is internal and attacks the alkyl group from the same site of leaving group. Therefore, the reaction is SN^1 and no inversion of configuration occur.



2) Dehydration of alcohol:



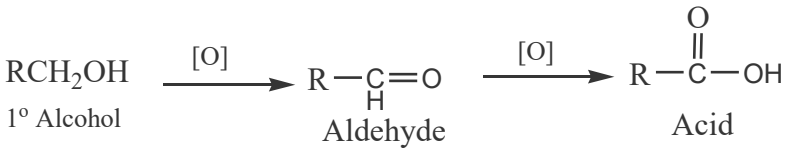
Mechanism :



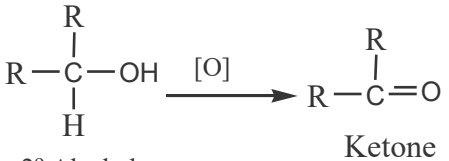
3) Oxidation of alcohols :

a) Non specific oxidizing agents:

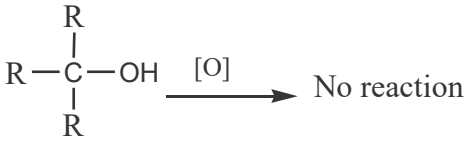
As $KMnO_4/H^+$, K_2Cr_2O7/ H^+ or $CrO_3/HOAc$



1° Alcohol Aldehyde Acid



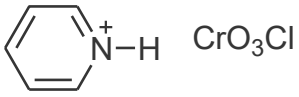
2° Alcohol Ketone



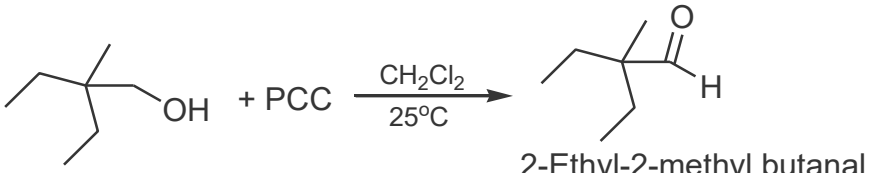
3° Alcohol

b) Specific oxidizing agent:

As pyridinium chlorochromate (PCC)

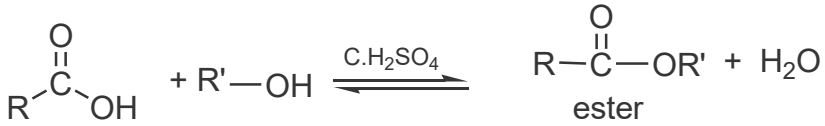


PCC will oxidize a primary alcohol to an aldehyde and stop at that stage.



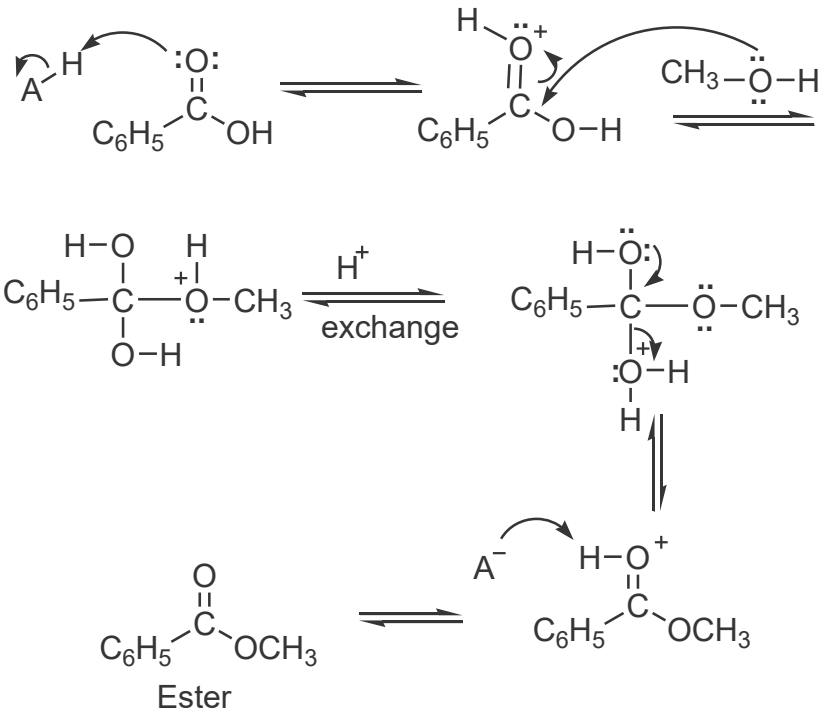
2-Ethyl-2-methyl butanol 2-Ethyl-2-methyl butanal

4) Esterification of alcohol



ester

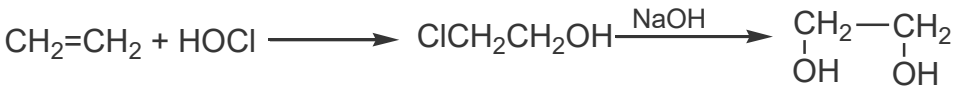
Mechanism


A
H
:O:
C
OH
C6H5
H
O+
C
O–H
C6H5
CH3–O–H
H–O
H
+
C6H5–C–O–CH3
O–H
H+
exchange
H–O:
C6H5–C–O–CH3
:O–H
H
A–
H–O+
C
C6H5
OCH3
O
C
C6H5
OCH3
Ester

Preparation of dihydric alcohols

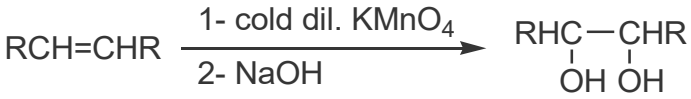
1- Reaction of alkene with hypochlorous acid:

By passing ethylene into hypochlorous acid and then hydrolyzing the chlorohydrin by boiling with sodium hydroxide.

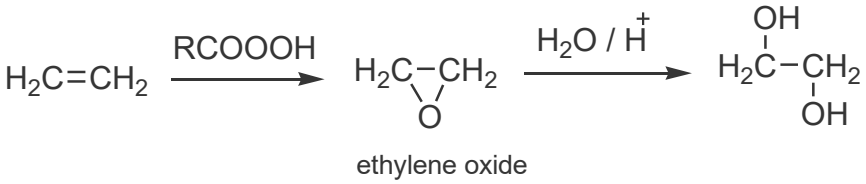


2- Hydroxylation of alkene:

a- Syn-hydroxylation:



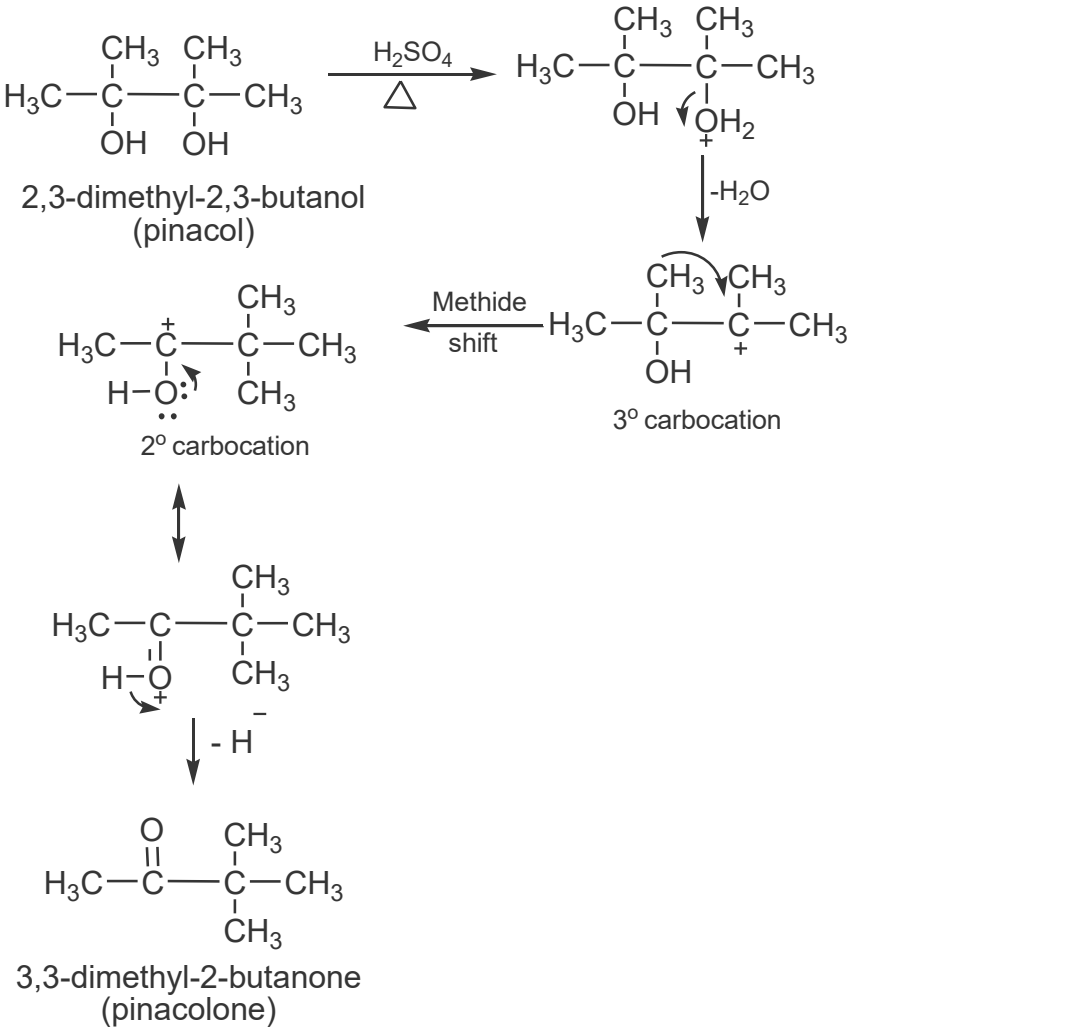
b- Anti-hydroxylation:



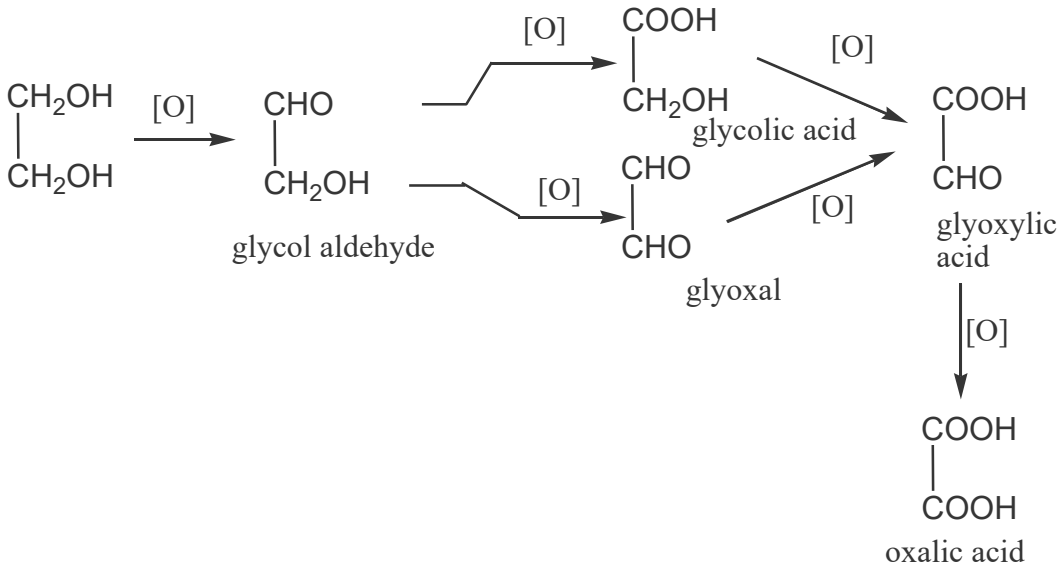
Reaction of dihydric alcohols :

1) Pinacol – Pinacolone rearrangement :

It occures with vicinal diols on heating with concentrated sulfuric acid.

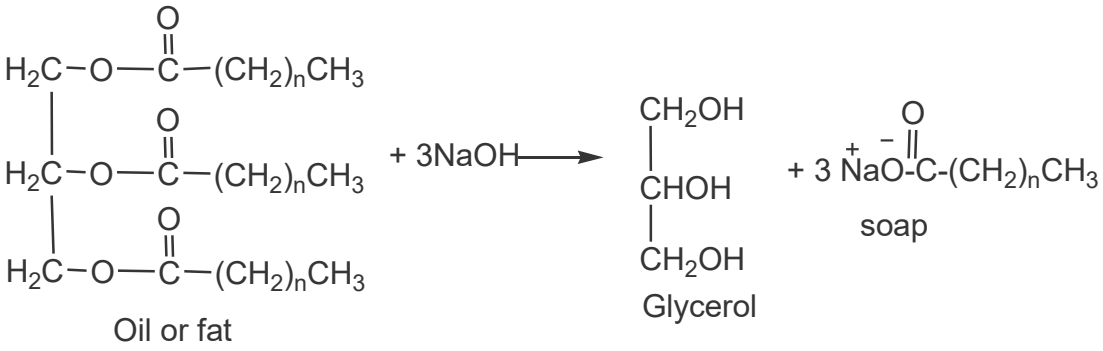


2) Oxidation of glycol :



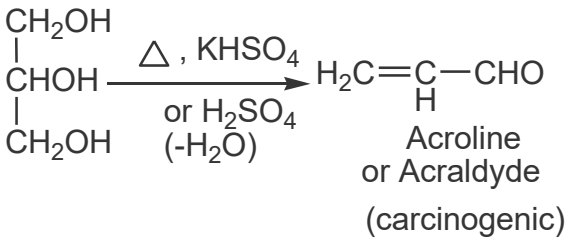
Preparation of trihydric alcohol (glycerol)

Glycerol is obtained as a by-product in the manufacture of soap (saponification). Soap can be made from the base hydrolysis of triglycerides (fat or oil).



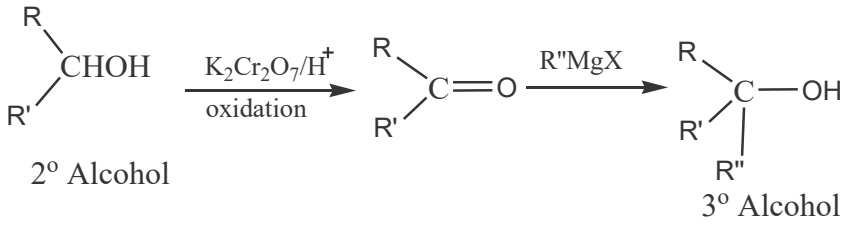
Reaction of trihydric alcohol (glycerol)

Acrolein test



Applications

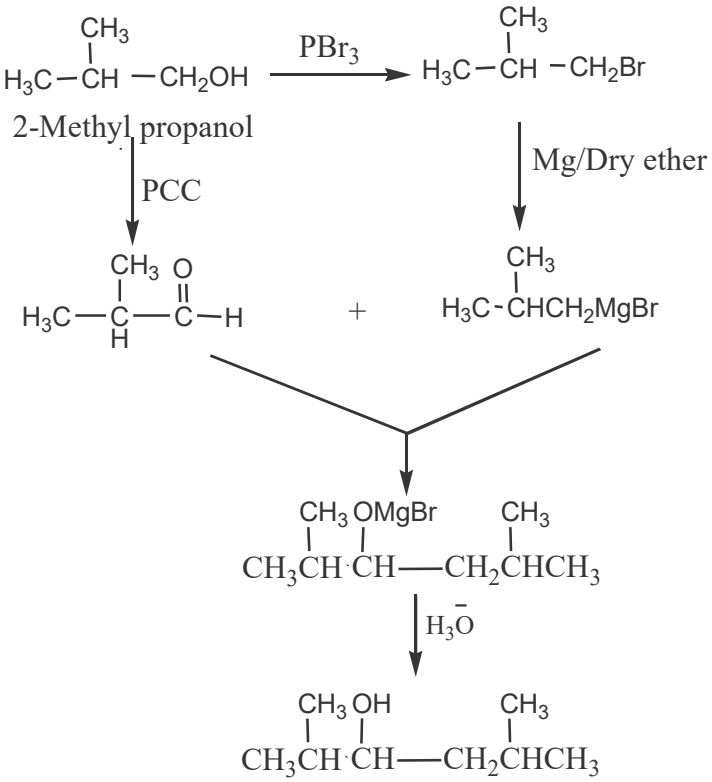
- **Synthesis of higher alcohol :**



2° Alcohol

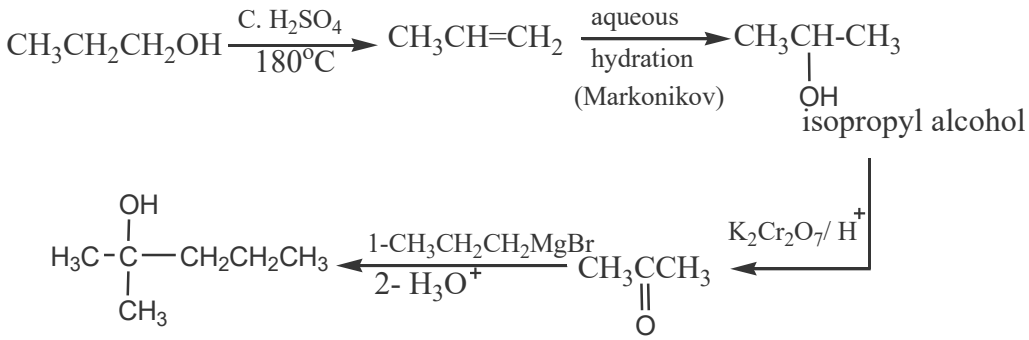
3° Alcohol

- **Conversion of 2-methyl propanol into 2,5-dimethyl-3-hexanol**



2,5-dimethyl-3-hexanol

- **Conversion of propanol into 2-methyl-2-pentanol**



2-methyl-2-pentanol

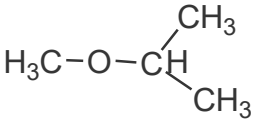
Ethers

General formula :R–O–R

Ether are classified into :

1- Symmetric ether : eg. $CH_3CH_2OCH_2CH_3$

Diethyl ether (common name)

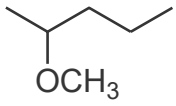
2- Unsymmetric ether : eg. 

Isopropyl methyl ether

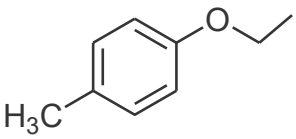
(Common name)

IUPAC Nomencloture :

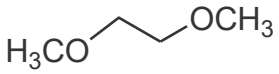
Ether are named as alkoxy alkanes , alkoxy alkenes and alkoxy arenes. The RO–group is an alkoxy group



2-Methoxy pentane



1-Ethoxy-4-methyl benzene



1,2-Dimethoxy ethane

Physical characters of ethers:

Ethers have boiling points that are roughly comparable with those of hydrocarbons of the same molecular weight for example, B.P. of diethyl ether (MW= 74) is 34.6°C while that of pentane (MW= 72) is 36°C.

Ethers are able to form hydrogen bonds with water therefore have solubilities in water

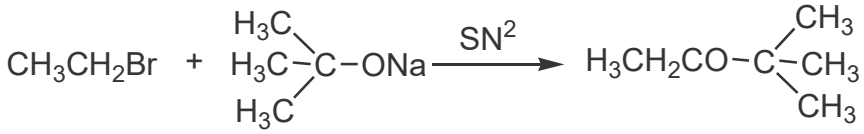
Preparation of ethers:

1) **Dehydration of alcohol:** as discussed before.
2) **Williamson Synthesis of ethers**

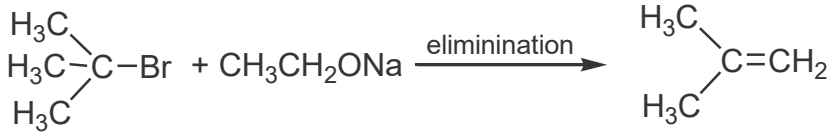
   SN^2 reaction of a sodium alkoxide with an alkyl/aryl halide; alkyl/ aryl sulfonate or alkyl/aryl sulfate.

   –L = –Br , –I, $–SO_2R''$ or $–SO_2OR''$

   Best results are obtained when the alkyl halide is primary . If the substrate is tertiary, elimination is the exclusive result.

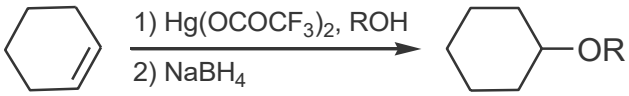


Ethyl-tert-butyl ether

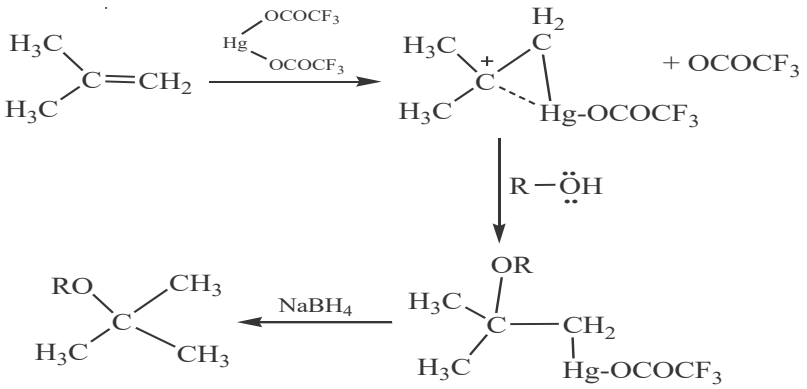


3° Alkyl halide

3) **Alkoxy mercuration – Demercurtion of alkene:**

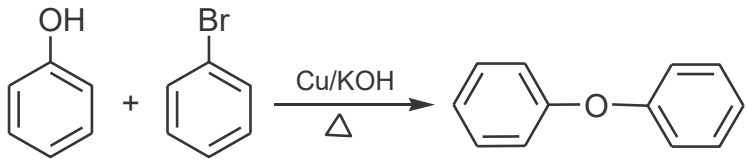


Mechanism :



4) Ulmann reaction

Used for preparation of diphenyl ethers which cannot be prepared by Williamson synthesis.

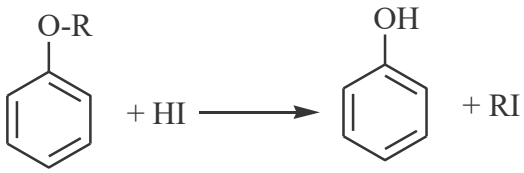


Reaction of ethers

Dialkyl ethers react with few reagents, this lack of reactivity coupled with the ability of ethers to solvate cations (by donating an electron pair from their oxygen atom) makes ethers especially useful as solvents for many reactions.

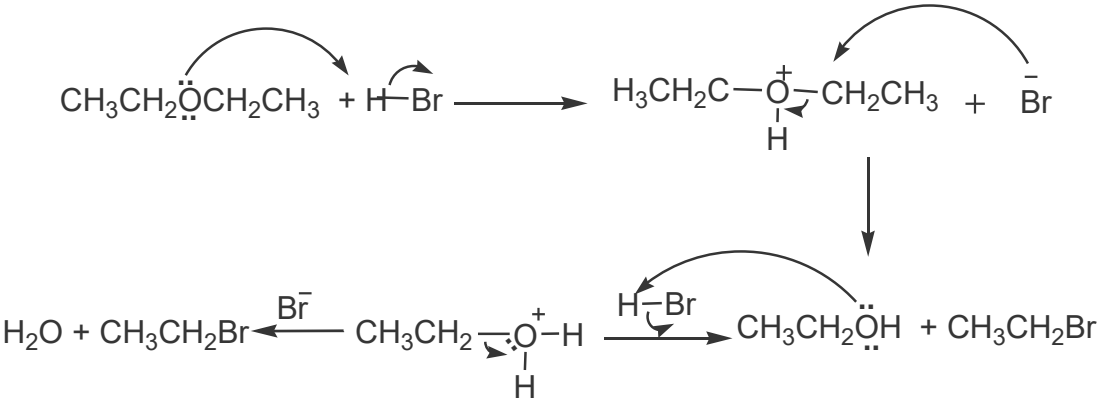
Cleavage of ethers :

Heating ethers with very strong acid (HI, HBr or H_2SO_4) causes them to undergo reaction in which the C–O bond breaks.

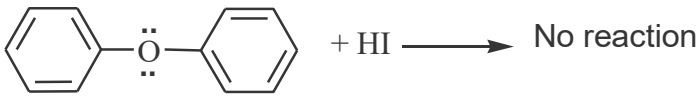


$CH_3CH_2OCH_2CH_3 + HBr \longrightarrow 2CH_3CH_2Br + H_2O$

Mechanism :

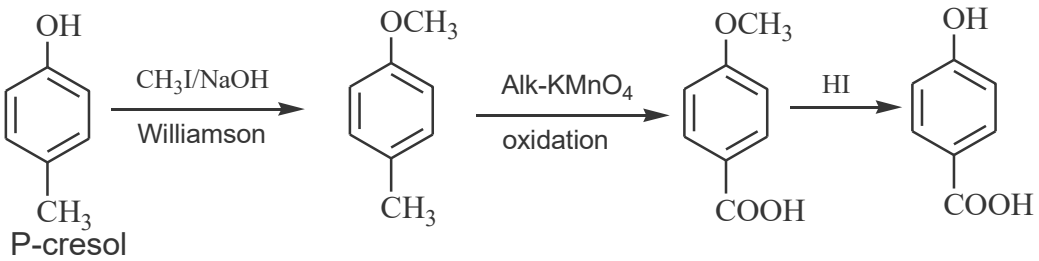


While diphenyl ethers are not cleaved by HI due to conjugation from both sides.



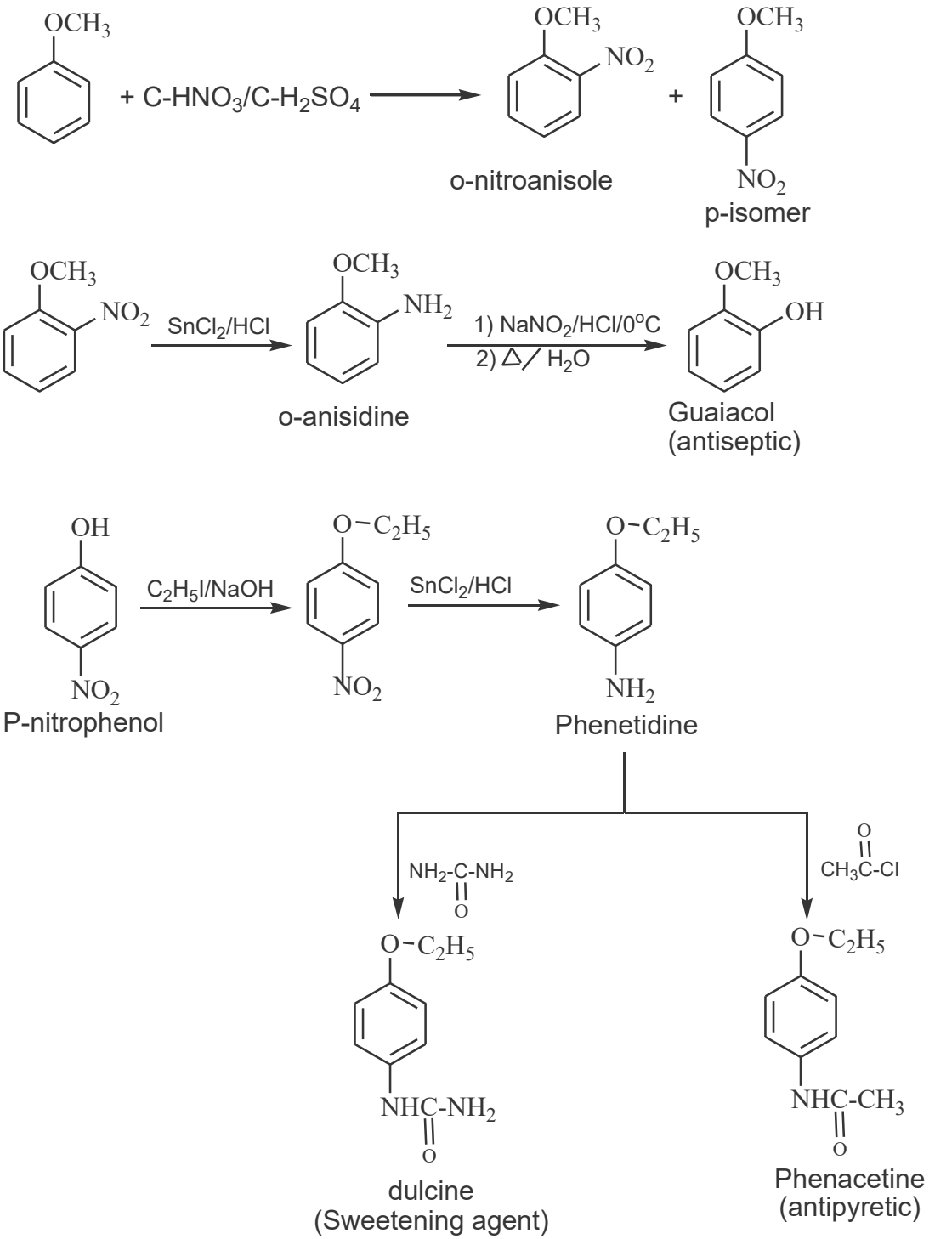
Ether formation acts as a protection means for alcoholic or phenolic function especially from oxidation and reduction reaction.

e.g. Convert p-cresol into p-hydroxy benzoic acid



Some important ether derivatives

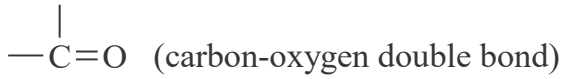
The –OR group of ethers is O–, P–directing towards EAS reaction as it activates the ring by positive mesomeric effect (+M).


OCH3
+ C-HNO3/C-H2SO4
OCH3
NO2
+
OCH3
NO2
o-nitroanisole
p-isomer
OCH3
NO2
SnCl2/HCl
OCH3
NH2
1) NaNO2/HCl/0°C
2) Δ / H2O
OCH3
OH
o-anisidine
Guaiacol
(antiseptic)
OH
NO2
P-nitrophenol
C2H5I/NaOH
O−C2H5
NO2
SnCl2/HCl
O−C2H5
NH2
Phenetidine
NH2-C-NH2
O
CH3C-Cl
O
O−C2H5
NHC-NH2
O
dulcine
(Sweetening agent)
O−C2H5
NHC-CH3
O
Phenacetine
(antipyretic)

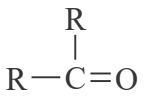
Aldehydes and Ketones.

The carbonyl Compounds

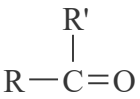
Aldehydes and ketones are classes of compounds both of which contain a carbon doubly bonded to oxygen,



The group C=O known as the *carbonyl group* determines, the chemistry of aldehydes and ketones, and hence these compounds are collectively called as Carbonyl Compounds. In aldehydes the carbonyl carbon is linked to one hydrogen atom and one alkyl group (formaldehyde in which CO is joined to two H atoms being an exception), while in ketones it is linked to two alkyl groups. Their type formulas are:

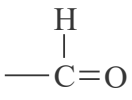


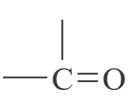
symmetrical ketone



unsymmetrical ketone

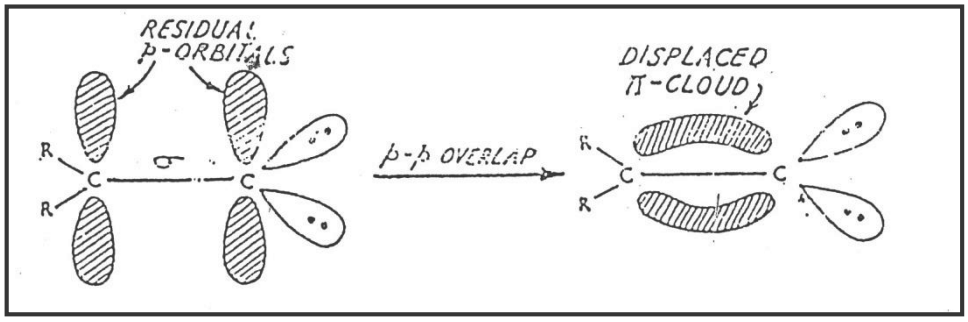
The functional groups characteristic of aldehydes and ketones respectively are



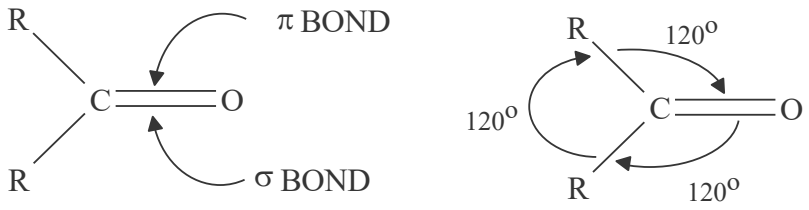


Structure

The carbon-oxygen double bond in aldehydes and ketones can be formulated in a manner similar to the carbon-carbon double bond in alkenes. Here we assume-that both the carbon and oxygen of the carbonyl group are sp^2 hybridized. One sp^2 orbital of carbon overlaps with a sp^2 orbital of oxygen to form a σ bond, while the residual *p* orbitals of the two atoms overlap in a sidewise fashion to from π bond. Therefore, a carbonyl double bond is, in fact, made of one σ bond and one π bond. Thus,



It may be noted that in the above model of a carbonyl compound, ell the three sp^2 orbitals of carbon form σ bonds. On the other hand, only one sp^2orbital of oxygen forms a σ bond and the two unused ones are occupied by pairs of electrons. Also, since the electronegativity of oxygen is much higher than that of carbon, the π electron cloud is displaced towards the oxygen as shown in the above model. This causes net polarisation of the bond. The carbon becomes slightly positive and oxygen slightly negative. Thus the carbonyl double bond can be represented as:



The carbonyl double bond thus differs from the carbon-carbon double bond of alkenes which is non-polar.

The above structure of carbonyl compounds accounts for their high dipole moment (2-3 to 2-8 D). The electron diffraction and spectroscopic studies reveal that the carbon, oxygen and the other two atoms or groups attached to carbonyl carbon lie in the same plane and have bond angles roughly 120°. These facts support the formulation of the structure of aldehydes and ketones described above.

Nomenclature

Aldehydes and ketones are named according to the Common and the IUPAC systems.

(1) Aldehydes. The common names of aldehydes are derived from those of the carboxylic acids to which they are oxidized. The portion '—*ic* acid' of the name of the corresponding acid is replaced by the suffix '—aldehyde'. Thus CH_3CHO is oxidized to acetic acid and is named as acetaldehyde.

Acetic acid — ic acid + aldehyde ⟶ acetaldehyde

In the IUPAC system, aldehydes are named as alkanals and the name of an individual aldehyde is obtained by dropping the terminal '*e*' of

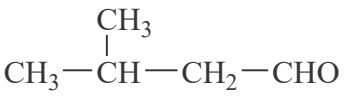
the name of the parent hydrocarbon (having same carbon skeleton) and adding the suffix '—al'. Thus HCHO is called methanal, the parent hydrocarbon being methane,

Methane — e + al $\longrightarrow$ methanal

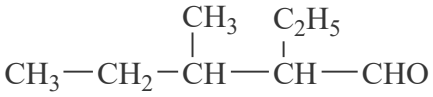
The common name of some aldehydes are given below.

Formula	***Common Name***	***IUPAC Name***
HCHO	formaldehyde	methanal
CH_3CHO	acetaldehyde	ethanal
CH_3CH_2CHO	propionaldehyde	propanal
$CH_3CH_3CH_2CHO$	butyraldehyde	butanal
CH_2=CHCHO	Acrylaldehyde	propenal

While assigning IUPAC names to complex aldehydes, the longest carbon chain including the —CHO group is selected as the parent chain. It is numbered from the carbon of the —CHO group which is assigned number (1). The substituents on the chain are given positional numbers and named in the usual fashion. Since the aldehydic group —CHO is always at the end of the chain, it is unnecessary to specify its position in the systematic-name. Thus,



3- methylbutanal



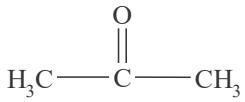
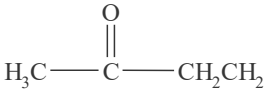
2-ethyl-3-methylpentanal

(2) Ketones. According to the COMMON SYSTEM, symmetrical ketones are named as dialkyl ketones: first member of the series CH_3COCH_3 is, however popularly called *acetone.*

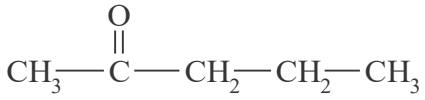
The common names of unsymmetrical ketones are obtained by naming the alkyl groups as separate words in alphabetic order and adding the third word 'ketone'.

The IUPAC name of ketones is *alkanones* and the name of an individual member one system is derived by dropping the final *'e'* of the parent hydrocarbon (containing same number of C-atoms) and adding the suffix *'one*'.

The common and systematic names of a few ketones are given below.

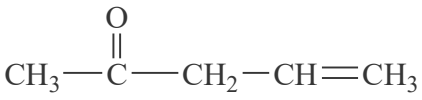
Formula	***Common Name***	***IUPAC Name***
	Acetone dimethyl ketone	Propanone
	Ethylmethyl ketone	Butanone

While naming higher ketones on IUPAC system, it becomes necessary to assign positional number to the carbonyl group.



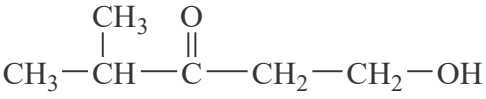
2-pentanone

In complex compounds, where prefixing of the positional number to the ketone name gives rise to confusion it is inserted before the suffix *one.*



4-penten-2-one

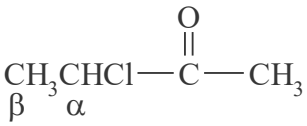
For naming a compound which in addition to carbonyl contains another functional group, the term *oxo* is also used to indicate the position of carbonyl on the hydrocarbon chain. For example,



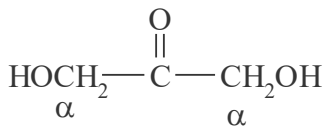
4-methyl-3-oxo-l-pentanol

Sometimes, while naming substituted ketones, the positions of the side -chains or substituents on the parent chain are denoted by Greek letters α , β , γ etc.

The carbon adjacent to the carbonyl group is called α, the one next to it β and so no. Thus,



α-chlorobutanone

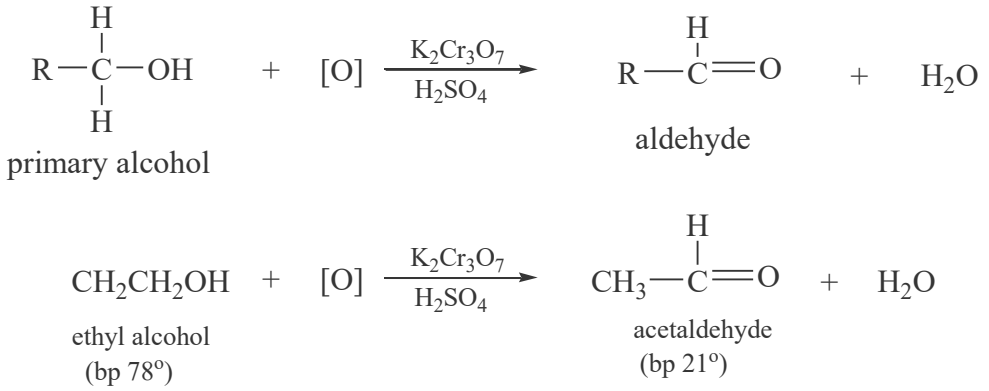


α,α'-dihydioxypropanone

Methods of Preparation

Aldehydes and ketones are similar in structure and there are several synthetic methods applicable to the preparation of these types of compounds. Also, there are methods useful for the preparation of aldehydes only and some for the preparation of ketones only.

(1) Direct Oxidation of Alcohols. Aldehydes are obtained by the direct oxidation of primary alcohols. The oxidants most commonly used are potassium dichromate in sulphuric acid or potassium permanganate in alkaline solution.



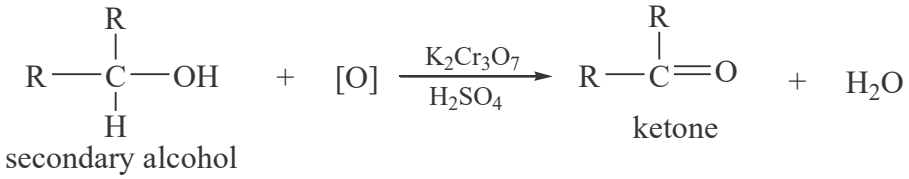
The aldehydes formed in the above process are readily-oxidized to carboxylic acid allowed to remain in the reaction mixture.

$$\underset{\text{Aldehyde}}{RCHO} + [O] \longrightarrow \underset{\text{acid}}{RCOOH}$$

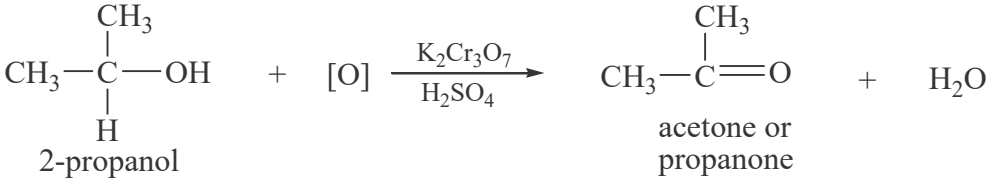
Therefore, the aldehyde formed must be removed from the reaction mixture before it gets opportunity to be oxidized to the acid. The aldehydes, however, have lower boiling points than the corresponding alcohols. Thus the reaction is carried at a temperature slightly above the

boiling point of the aldehyde when the latter can be distilled as it is formed. In the oxidation of ethyl alcohol (78°), if the reaction mixture is maintained at about 25°, the acetaldehyde (bp 21°) formed distils over leaving the alcohol behind.

Ketones also may be prepared by oxidation of secondary alcohols with potassium dichromate in sulphuric acid.

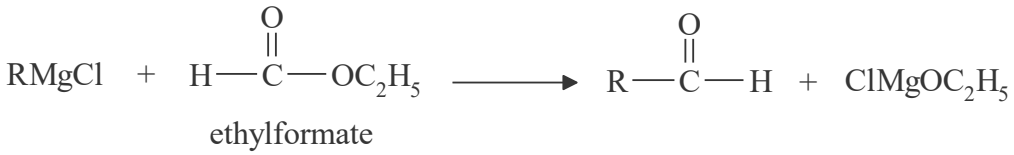


secondary alcohol ketone



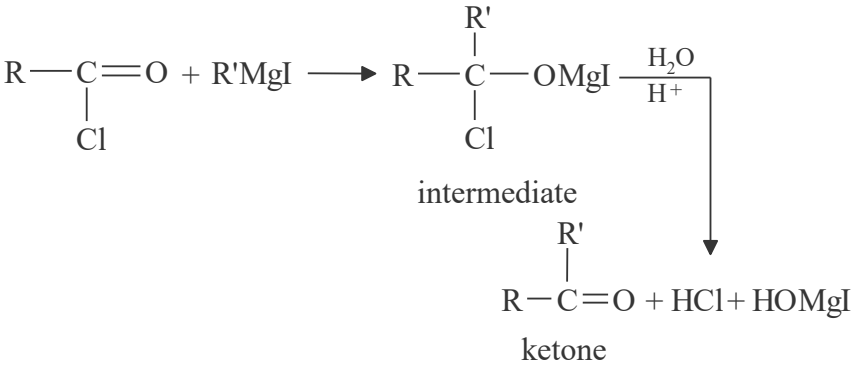
2-propanol acetone or propanone

(2) From Grighard Reagents. Aldehydes can be synthesized by the action of Grignard reagents with excess of formic ester.



ethylformate

Ketones are obtained by the addition of Grignard reagents to acid chlorides, and subsequent acid hydrolysis.

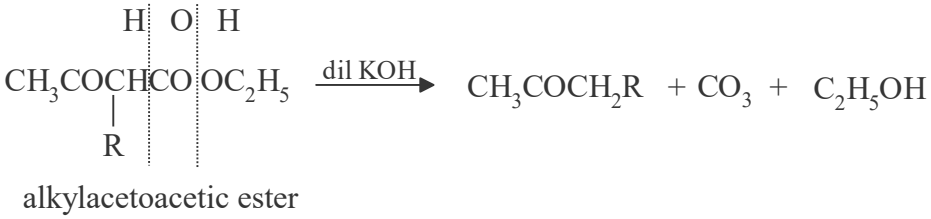


Recently organocadmium compounds have been used for the preparation of ketone from acid halides, in preference to Grignard reagents, since they do not react further with ketone product to from alcohol.

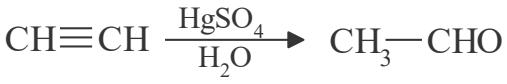
$$RMgCl + CdCl_2 \longrightarrow RCdCl + MgCl_2$$

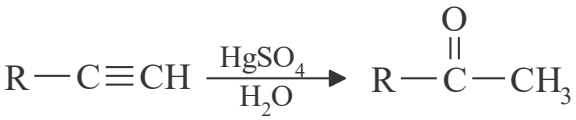
$$R'COCl + RCdCl \longrightarrow R'COR + CdCl_2$$

(3) From Acetoacetic esters. Alkyl derivatives of acetoacetic esters, $CH_3COCH_2COOC_2H_5$, on hydrolysis with dilute alkalis give the corresponding ketones.



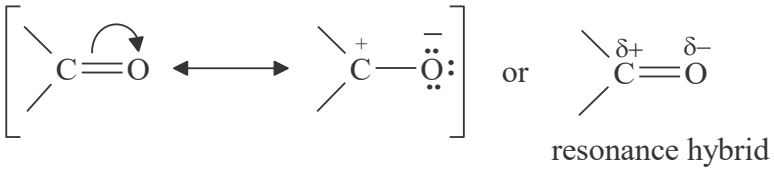
(4) Hydration of alkynes





Nature of reactions of carbonyl compounds

We have said earlier that the carbon-oxygen bond in aldehydes and ketones is polar. The greater electronegativity of oxygen than carbon shifts the electrons constituting the π bond partially towards oxygen. Thus carbon becomes slightly positive and oxygen slightly negative. Also, the carbonyl double bond can be represented as a resonance hybrid of the canonical forms I and II.



Hence, the carbon-oxygen, bond is highly polarised. It implies that the carbon atom of the carbonyl group is electron-deficient, while the oxygen atom is electron-rich. This makes the C=O groups an extremely reactive function in aldehydes and ketones. The basic principles involved in the general reactions of this class of compounds' are discussed below.

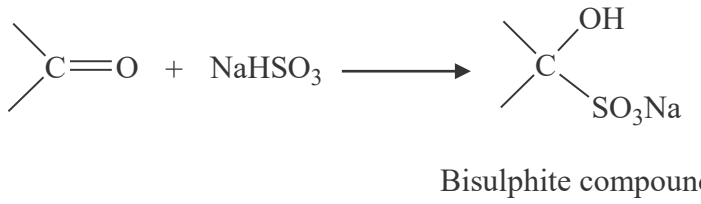
(1) Nucleophilic addition reactions.

The electron-deficient carbon of the carbonyl group is easily attacked by a nucleophile which then supplies an electron pair. Thus

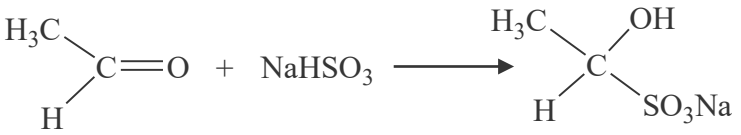
many addition reactions of the carbonyl compounds are initiated by nucleophiles. A general mechanism of such reactions is given on the next page.

(1) Nucleophilic addition reactions

(1) Addition of Sodium bisulphite. Saturated solution of sodium bisulphite ($NaHSO_3$) in water, when mixed with aldehydes and some ketones forms nicely crystalline bisulphate addition compounds. Thus,

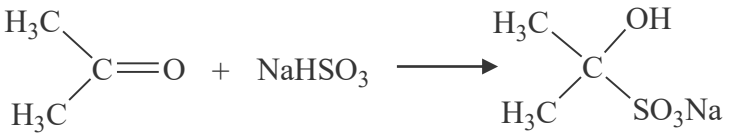


Bisulphite compound



acetaldehyde

Acetaldehyde bisulphite compound

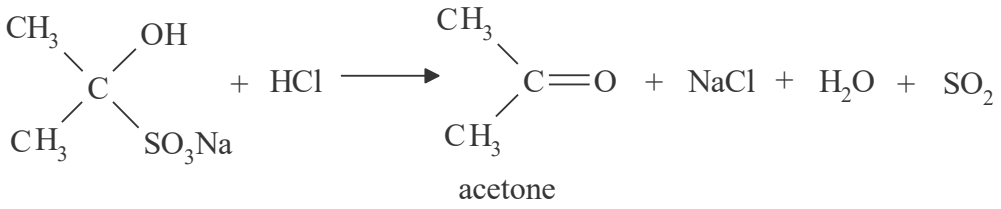


Acetone

Acetone bisulphite compound

Almost all aldehydes form bisulphite addition compounds but only a few ketone of the type CH_3COR, where R is a primary alkyl group up to C_3 in size, undergo this addition. Ketones with bulky alkyl groups fail to react with sodium bisulphite presumably because of steric hindrance and shielding the electrophilic carbon atom of the carbonyl group.

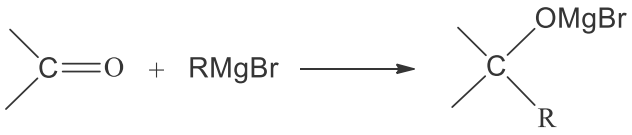
The bisulphite addition compounds get decomposed back to the original carbonyl compounds in presence of acids or alkalis. Thus,



acetone

Hence the formation and-decomposition of the bisulphite compounds serves as a powerful means of purification and separation of carbonyl compounds from non-carbonyl substances.

(2) Addition of Griguard Reagents. Almost all aldehydes and ketones react with Grignard reagent to form complex adducts,



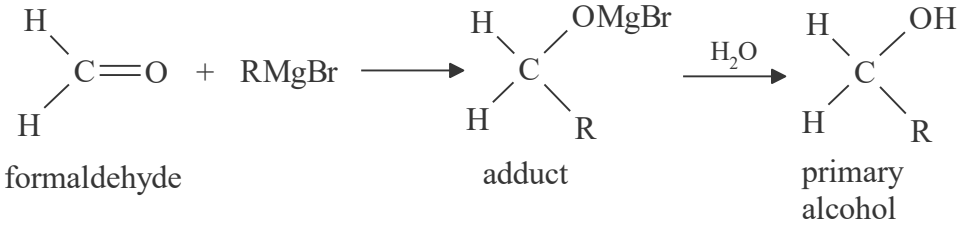
aldehyde or ketone

adduct

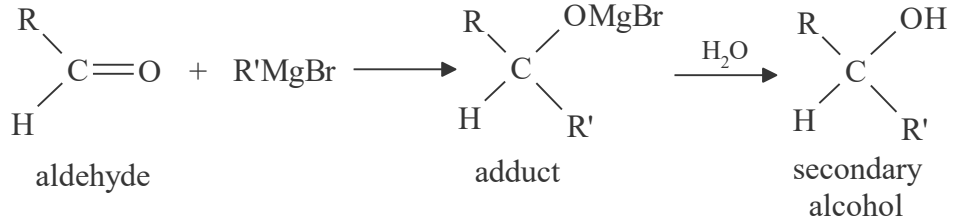
These upon hydrolysis with acid yield alcohols.

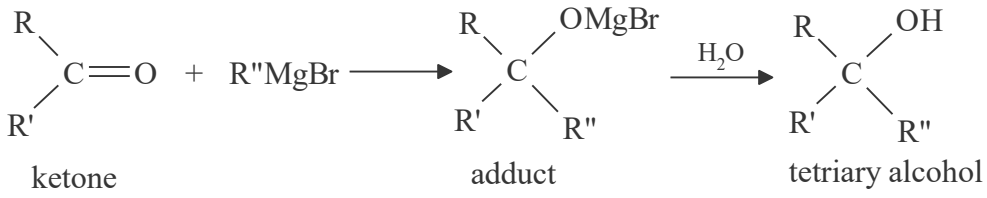
alcohol

Formaldehyde gives a primary alcohol and this reaction is particularly useful for increasing the carbon chain by one carbon.



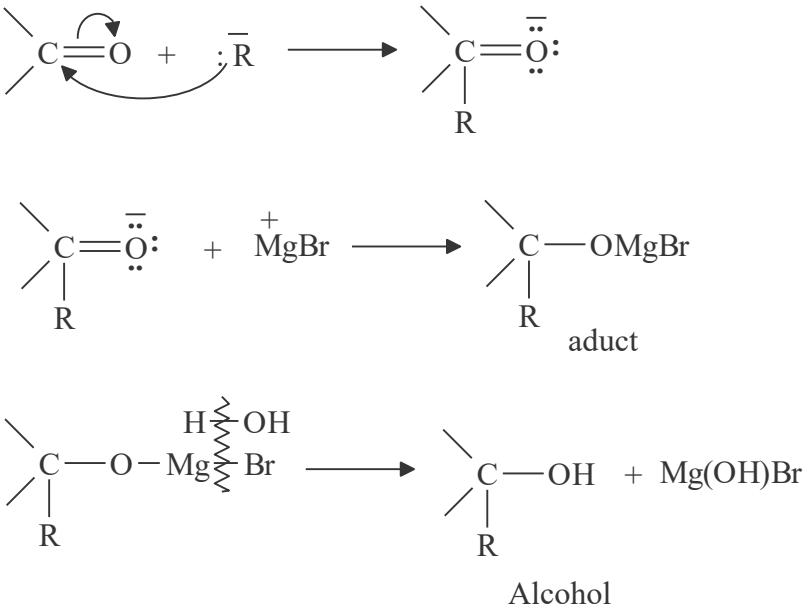
Other aldehydes yield secondary alcohols and ketones form tertiary alcohols.



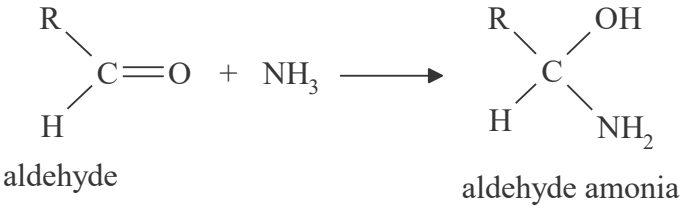


Mechanism.

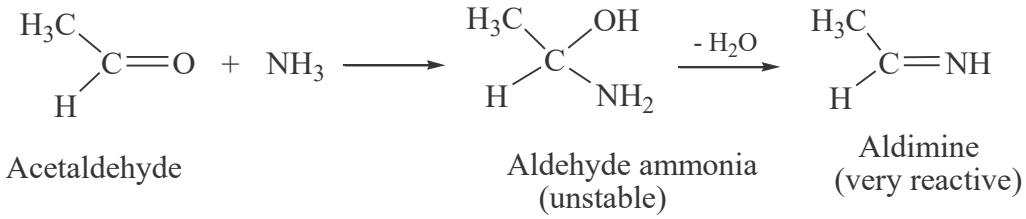
As we have pointed out earlier, Grignard reagents have considerable ionic character and may be represented as $R^{-}Mg^{+}Br$. The carbanion $:R^{-}$ is a powerful nucleophile and attacks the carbonyl carbon atom which is followed by the association of $Mg^{+}Br$ with the oxygen atom.



(4) Addition of Ammonia. Aldehydes react with ammonia to form aldehyde ammonias.



The aldehyde ammonias are unstable and lose water immediately to form aldimine. The dehydration product is not usually obtained because, in most cases, it immediately polymerises to form cyclic trimers. Thus for acetaldehyde,



The reaction product in each case is named *as oxime* (aldoxime or ketoxime), *phenylhdrazone* or *semicarbazone* of the carbonyl compound from which it was obtained. Thus the various ammonia derivatives react with acetaldehyde and acetone as follows.

(a) With hydroxylamine **H_2NOH**

$$CH_3CH{=}O + H_2NOH \longrightarrow CH_3CH{=}N{-}OH + H_2O$$

Acetaldehyde — Acetaldoxime

$$(CH_3)_2C{=}O + H_2NOH \longrightarrow (CH_3)_2C{=}N{-}OH + H_2O$$

Acetone — Acetone oxime

dimethyl ketoxime

(b) With phenylhydrazine; **$H_2NNHC_6H_5$**

$$CH_3CH{=}O + H_3NNHC_6H_5 \longrightarrow CH_3CH{=}NNHC_6H_5 + H_2O$$

Acetaldehyde phenylhydrazone

$$(CH_3)_2C{=}O + + H_3NNHC_6H_5 \longrightarrow (CH_3)_2C{=}NNHC_6H_5 + H_2O$$

Acetone phenylhydrazone

(c) With semicarbazide, **$H_2NNHCONH_3$**

$$CH_3CH{=}O + H_3NNHCONH_2 \longrightarrow CH_3CH{=}NNHCONH_2 + H_2O$$

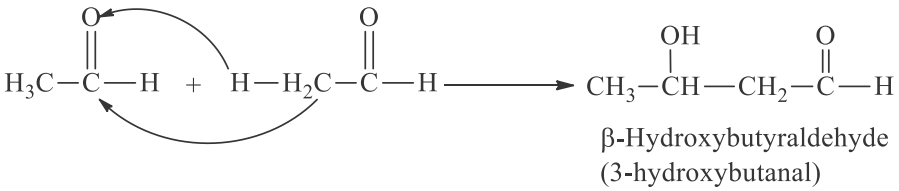
Acetaldehyde semicarbazone

$$(CH_3)_2C{=}O + + H_2NNHCONH_2 \longrightarrow (CH_3)_2C{=}NNHCONH_2 + H_2O$$

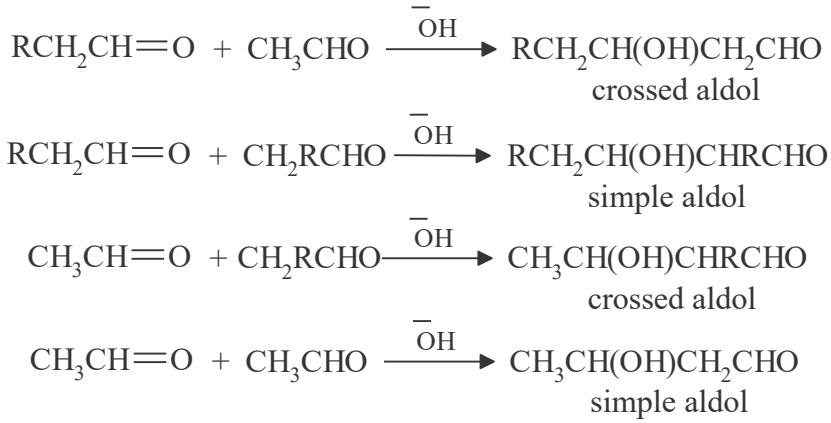
Acetone semicarbazone

Reactions involving alkyl group

(1) Aldol Condensation. Aldehydes undergo a reversible self addition in presence of dilute base to give condensation product which is both an aldehyde and alcohol. This is called aldol and the reaction is known as *aldol condensation.* It proceeds by addition of one molecule of aldehyde to the carbonyl group of another, with a simultaneous "cleavage of carbon-hydrogen bond in α position. Thus acetaldehyde when warmed with dilute sodium hydroxide gives hydroxyl butyraldehyde (acetaldol).



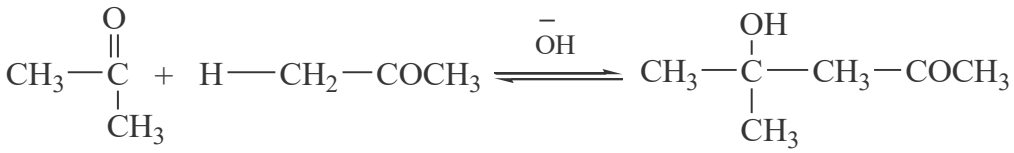
When a mixture of two different aldehydes, each possessing an α-hydrogen, treat with base, four different aldol products are formed; two from condensation of the two aldehyde with like molecules and two from condensation of two different aldehydes in two different way. Thus,



Because of the mixtures of aldols-obtained, the reactions between two different aldehyde are of little preparative value.

It is noteworthy that any aldol condensation takes place with aldehydes having at least one α-hydrogen but not at all with those having no α-hydrogen such as trimethylacetaldehyde $(CH_3)_3CCHO$.

Ketones containing α-hydrogen also undergo aldol condensation to a smaller extent to do aldehydes. This is presumably as a consequence of steric hindrance to the carbonyl addition. Thus acetone in the presence of a base would establish the following equilibrium.



Diacetone alcohol,

4-bydroxypentan-2-pentanone

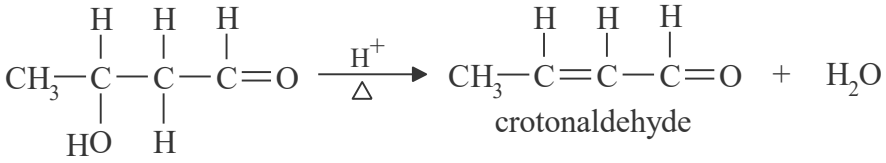
(aldol)

Aldol condensation is not confined to aldehydes alone but can also take place between an aldehyde and a ketone (Cross aldol condensation), thus acetaldehyde and acetone condensed in presence of KCN to form 4-hydroxypentan-2-one.

acetaldehyde acetone 4-hydroxypentan-2-one

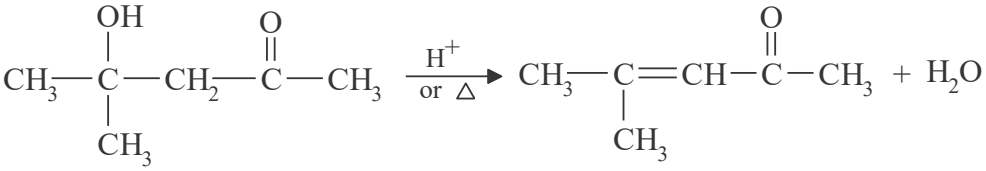
Dehydration of Aldols. Sometimes the aldol products are stable enough to be isolate. In other cases water may be lost spontaneously to

form unsaturated aldehyde or ketone. Acetaldol itself may undergo dehydration on warming or in the presence of an acid to form crotonaldehyde.



Acetaldol or aldol

Similarly, diacetone alcohol (aldol of acetone) upon heating or in the presence of dilute mineral acid, dehydrates to give mesityl oxide.

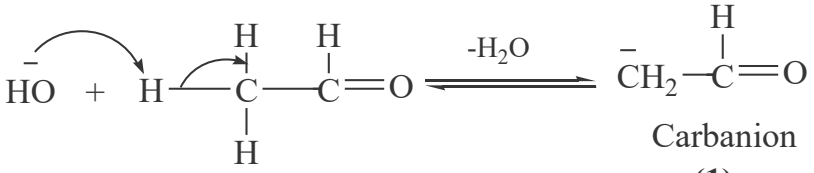


diacelone alcohol methyl oxide

Mechanism:

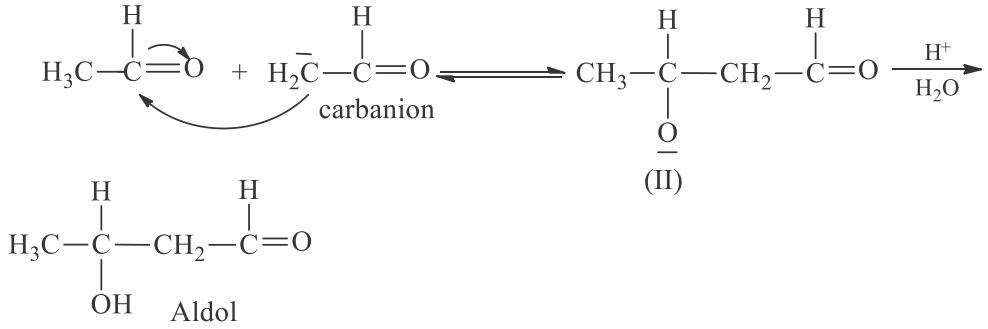
The aldol condensation in case of aldehydes will be illustrated by taking example of acetaldehyde.

(a) The base ionizes to form $^-$OH ion which removes a proton (H^+) from α-carbon forming a negatively charged residue or carbanion.



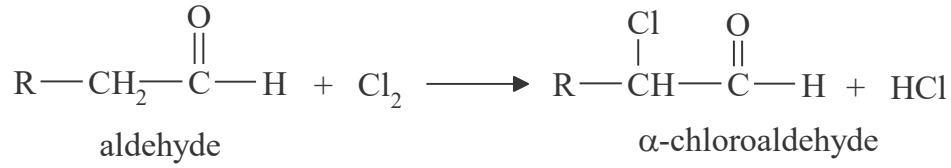
(1)

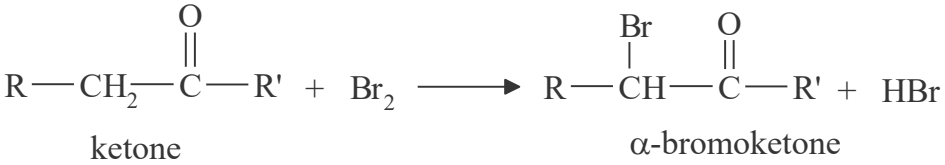
(b) The nucleophilic attach of the carbanion (I) on the carbonyl carbon results in the formation of anion (II) which picks up a proton from H_2O to form aldol.



(1) Halogenation.

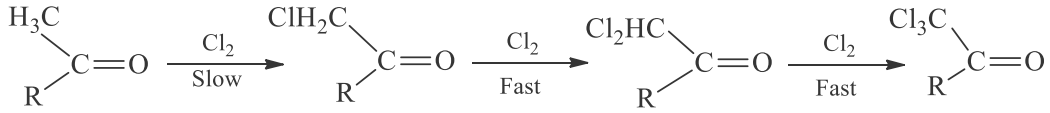
Aldehydes and ketones are readily halogenated whereby the hydrogen atoms on the carbon next to the carbonyl group are readily replaced by Cl, Br or I atoms.





Thus acetaldehyde upon chlorination yields α-chloroacetaldehyde, CH_2ClCHO, and acetone upon bromination gives α bromoacetone. $CH_2BrCOCH_2$.

The second and third α-hydrogens in a carbonyl compound can be substituted by halogen atoms depending on the reaction time and conditions.



The introduction of the first halogen atom is slow but further substitution takes place more rapidly due to the additional electron withdrawl of the halogen atom already present.

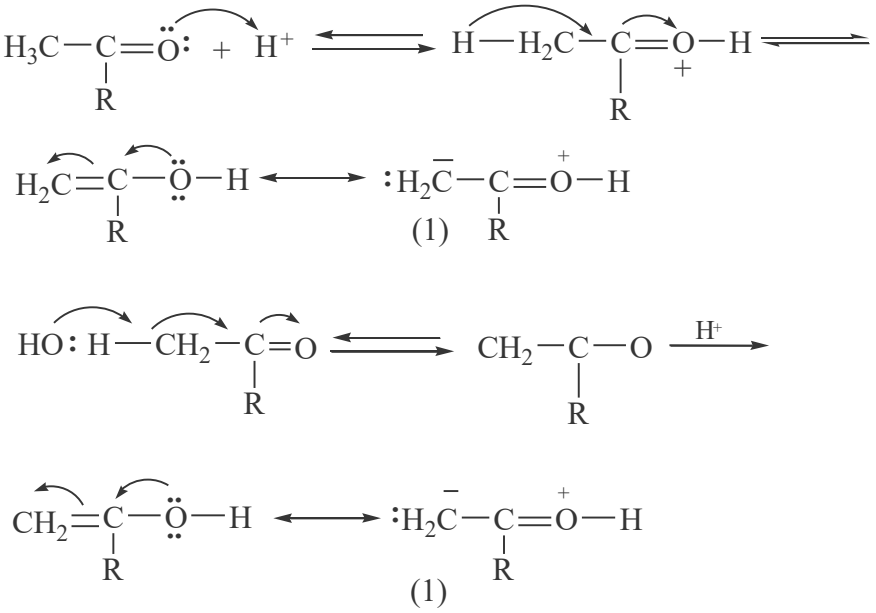
The halogenation of aldehydes and ketones is catalysed by acids and bases, but occur more rapidly with the latter. Acid catalysis is used if the monoketone is required as the overall rate of halogenation is slower than base catalysis.

<u>Mechanism</u>.

Acid catalysed and base catalysed halogenation of aldehydes and ketone takes place *via* enolic form. We will illustrate the mechanism of both types by taking example of bromination of a methyl ketone , $RCOCH_3$.

(a) Acid catalysed reaction :

(i) In the presence of acids (H^+) the ketone gives the enolic form (I).

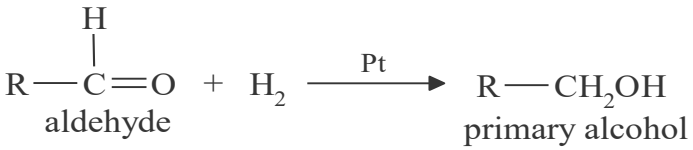


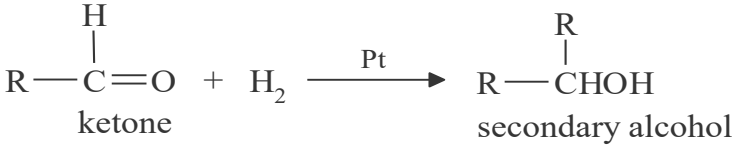
Enol form (1) then reacts in a fashion as described in step (ii) of acid catalysed mechanism to give α-bromoketone.

Reduction of carbonyl compounds

(1) Reduction to Alcohols.

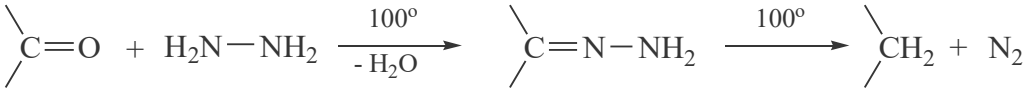
The carbony] group of aldehydes and ketones can be reduced to give a primary and secondary alcohol respectively. This reaction can be carried with hydrogen in the presence of metal catalysts such as platinum, palladium, nickel or copper chromite.





The catalytic hydrogenation of aldehydes and ketones to get alcohols, on account of drastic conditions of the reaction, is no longer used in the laboratory. However, the method remains useful on an industrial scale because hydrogen gas is quiet cheap.

According to *Huang-Minion modification* (1946) of this method, the hydrazone of carbonyl compound is prepared, and while still in solution, is heated in a high boiling solvent (diethylene glycol) with alkali until it is decomposed.

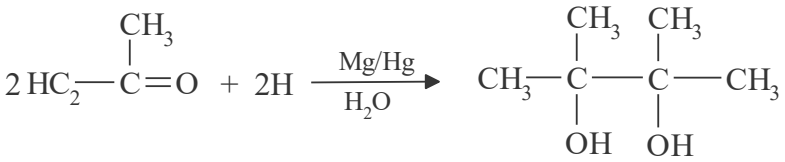


The advantage of this method is that it is convenient and the product is readily isolated in pure state.

Both Clemmensen method and Kishner method are widely used for converting aldehyde and ketones to hydrocarbons, the latter being preferable for aldehydes and the former for ketones.

(2) Reduction to Pinacols.

Ketones when reduced in neutral or alkaline medium, form 1,2-diols *or pinacols.* Thus with magnesium amalgam and water, acetone is reduced as follow;

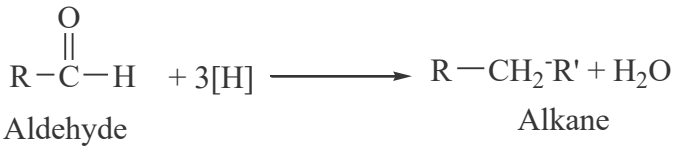


2,3-dimethylbutane,
2,3-diol (pinacol)

Aldehydes do not undergo pinacol reduction.

3) Reduction to Hydrocarbons

The carbonyl group of aldehydes and ketones may be reduced to methylene group, yielding hydrocarbons.

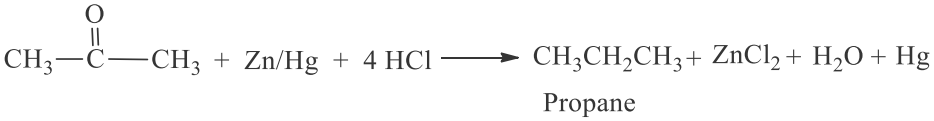


This is done by two .general methods:

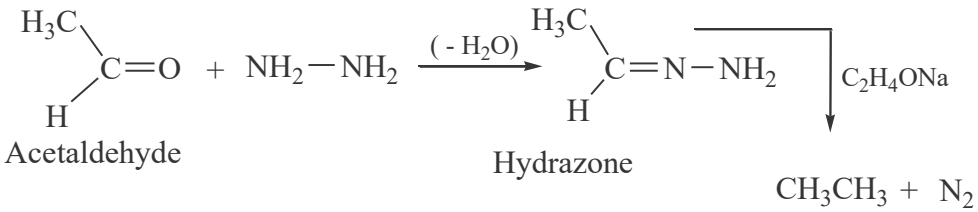
(i) The *Clemnenson reduction:*

(ii) The *Wolff-Kishner reduction,*

Clemmerson Reduction uses amalgamated zinc (Zn/Hg) and hydrochloric acid as the reducing agent. For illustration,



Wolff-Kishner reduction utilizes hydrazine (NH_2NH_3) as a reducing agent and sodium ethoxide as catalyst. First the aldehyde or ketone is converted to hydrazone which is then heated with sodium ethoxide (Na + C_2H_5OH) to give the hydrocarbon. Thus,



Individual Aldehydes

Formaldehyde: Methanal (H–CH=O)

It is the first member of the homologous series of aldehydes. Traces of formaldehyde are produced by the incomplete combustion of coal, wood, sugar, etc.

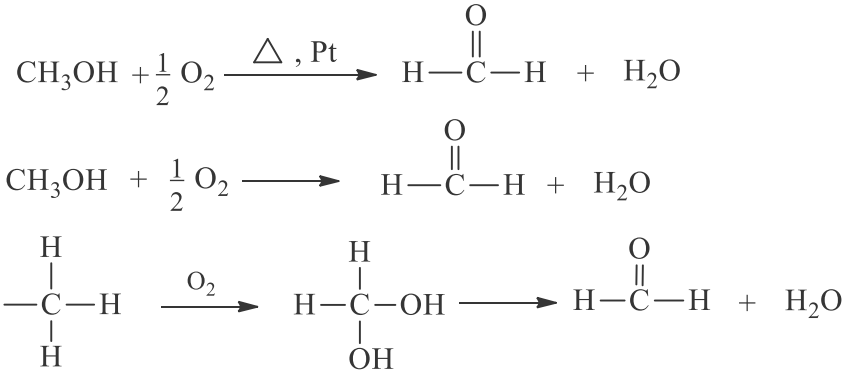
Preparation:

(1) By reduction of Carbon monoxide.

Formaldehyde is produced from carbon monoxide and hydrogen when a-mixture of these gases (water gas) is passed at low pressure through an electric discharge of low intensity.

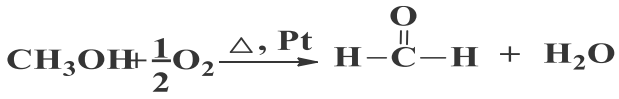
(2) By oxidation of methyl alcohol.

Large quantities of formaldehyde are prepared by passing a mixture of methyl alcohol vapour and air over heated copper or silver.



Laboratory method.

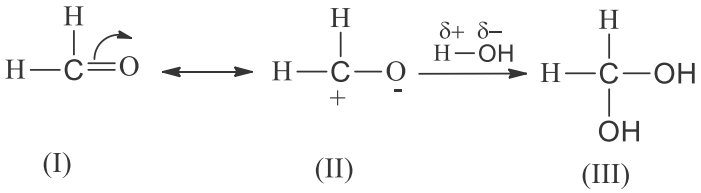
Formaldehyde is prepared in the laboratory by the oxidation of methyl alcohol in the presence of platinum.



Properties:

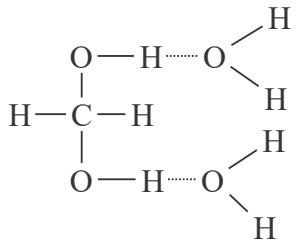
Physical Properties: Formaldehyde is a colourless gas at ordinary temperature and pressure. It is easily condensed to a liquid which boils at—21°. It has a very pungent and penetrating odour. It is readily soluble in water. In the gaseous state or when dissolved in water, formaldehyde is a powerful disinfectant.

Formaldehyde forms an unstable hydrate with water. It is decidedly more stable than the hydrate of acetaldehyde, the latter being unstable owing to the presence of the electron repelling methyl group; Mechanism of hydrate formation may be depicted as :



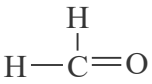
(I) (II) (III)

The presence of a methyl group in place of H-atom would exert its inductive effect *(electron repelling)* and reduce the magnitude of positive charge on C-atom in formula II). *(See acetaldehyde).*



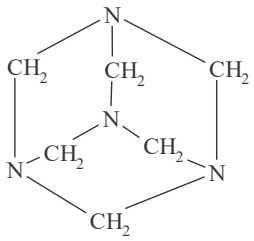
Chemical Properties

Structurally, formaldehyde differs from other aldehydes in that it has a hydrogen linked to the —CHO group instead of the alkyl group.



Consequently it does not duplicate all of the general reactions of the higher aldehydes and is actually more reactive. The following reactions of formaldehyde are noteworthy.

(1) Reaction with Ammonia. Unlike other aldehydes, it does not form aldehydeammonia but instead gives a white crystalline compound hexamethylenetetramine.



Hexamethylene tetramine

$$6CH_2O + 4NH_3 \longrightarrow (CH_2)_6N_4 + 6H_2O$$

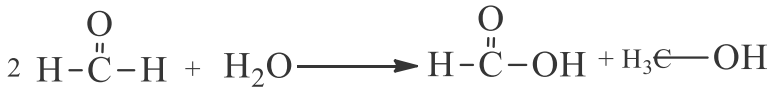
Hexamethylene

Tetramine

The proposed structural formula for the compound is indicated. It is used in medicine as a urinary antiseptic under the name Urotropine.

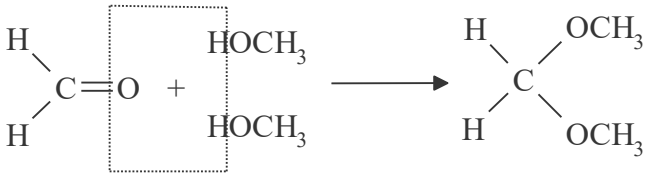
(2) Reaction with Sodium Hydroxide.

Formaldehyde differs from other aldehydes as it from a resin with dilute sodium hydroxide solution. However, when treated with alkali solution, it undergoes *Cannizzaro Reaction.*



(3) Reaction with Alcohols.

Like other aldehydes, it reacts with alcohols forming acetals in the presence of hydrogen chloride and fused chloride. Formaldehyde reacts with alcohol to form methylal.



Uses.

Formaldehyde is placed in the market as 40 percent aqueous solution under the name *'formalin'* and is used, as such for most purposes.

(1) The vapour of formaldehyde, produced by the action of heat on formalin is used as a disinfectant. Formalin is used for sterilizing surgical instruments.

(2) Formalin is used for preserving biological and anatomical specimens, since it makes the tissues hard and insoluble.

(3) On account of its hardening effect on hide-proteins formalin is used for tanning.

(4) Formalin is used in the production of plastics including well-known *'Bakelite'* which is obtained by heating phenol with formalin.

(5) Formalin is used as reducing agent for decolourizing of *vat* dyes and also making mirrors.

Tests:

Formaldehyde can be identified by usual reactions of aldehydes. It also gives the usual the following special test not given by other aldehydes.

A freshly prepared solution of pyrogallol is mixed with the solution of formaldehyde and excess of concentrated hydrochloric acid is added. In a few minutes a white precipitate is formed which rapidly turns pink and then deep red.

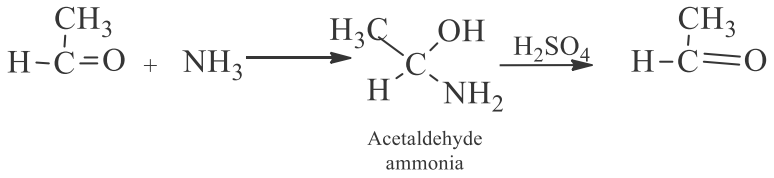
Acetaldehyde, Ethanal, $CH_3CH=O$

It is the second member of the aldehyde series. It is' formed as an intermediate compound in the alcoholic fermentation of glucose and is present in wines.

Acetaldehyde can be prepared by almost all the general methods of preparation described earlier.

Laboratory Method:

It is obtained in the laboratory by the oxidation of ethyl alcohol using a mixture of aqueous sodium or potassium dichromate and sulphuric acid as the oxidizing agent. Acetaldehyde, as soon as it is formed, is distilled away to avoid its oxidation to acetic acid. The crude substance thus formed is purified by converting it into acetaldehyde ammonia by treatment with ammonia. The crystals of acetaldehyde ammonia are dried and distilled with dilute sulphuric acid and the regenerated acetaldehyde is collected in an ice-cooled receiver.



Manufacture:

Acetaldehyde is obtained commercially:

(i) By the catalytic oxidation of ethyl alcohol with air in presence of

silver at 250º.

$$CH_3CH_2OH \xrightarrow[250^o]{Ag} CH_3CHO + H_2O$$

(ii) By passing ethyl alcohol vapours over copper at 300°.

$$CH_3CH_2OH \xrightarrow[300^o]{Cu} CH_3CHO + H_2$$

(iii) By the hydration of acetylene in presence of sulphuric acid and mercury salts.

$$HC\equiv CH + H_2O \xrightarrow[HgSO_4]{H_2SO_4} CH_3CHO$$

Properties:

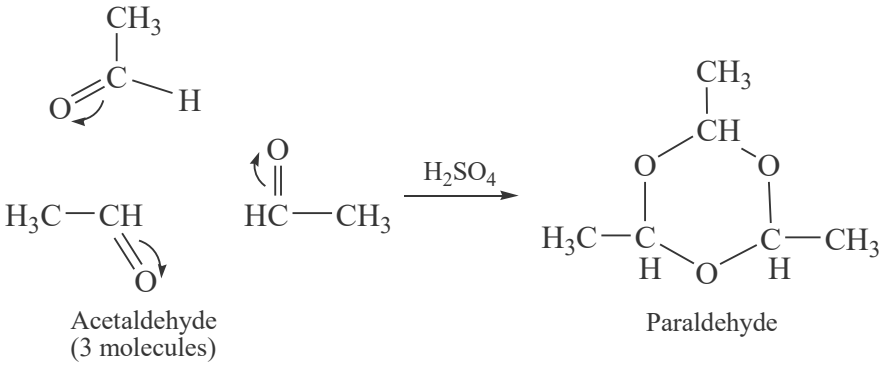
I- Physical Properties:

Acetaldehyde is a colourless volatile liquid, bp 21°. It has a characteristic pungent odour. It is readily soluble in water, alcohol, and ether. Its solutions; in water, have an agreeable fruit odour.

II-Chemical Properties:

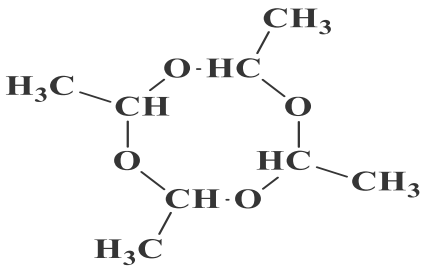
All the chemical properties of acetaldehyde have already been discussed under the **'General Reactions'** of aldehydes and ketones. Only a few polymerisation reactions will be described here.

(1) With a drop of concentrated sulphuric acid, acetaldehyde polymerises with explosive violence to form paraldehyde. Paraldehyde is a trimer and has and has a cyclic structure since it does not possess reducing properties.



Paraldehyde is sweet smelling liquid, bp 128°, and is used in medicine as hypnotic.

4) When acetaldehyde is treated with a few drops of cone H_3SO_4 at 0º, the tetramer, (CH_3CHO) methaldehyde is formed. This is a white solid, mp 246° and has the structure.



Both the polymers regenerate acetaldehyde on distilling with sulphoric acid.

Aromatic Aldehydes

Aromatic aldehydes fall into two groups:

a) Aromatic aldehydes, in which the aldehyde group is directly attached to the nucleus e.g. benzaldehyde.
b) Aryl-substituted aliphatic aldehydes, in which the aldehyde group is attached to the side chain.

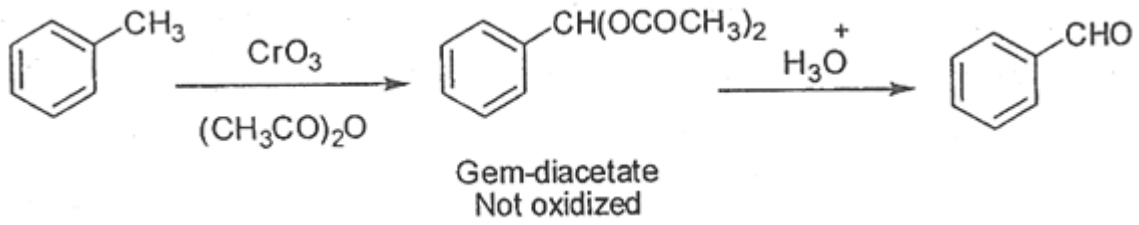
Benzaldehyde (benzenecarbonal): is found in the glycoside amygdalin occurs in bitter almond. Benzaldehyde has alimeted use as a flavoring and in the manufacture of dye-stuff.

Preparation:

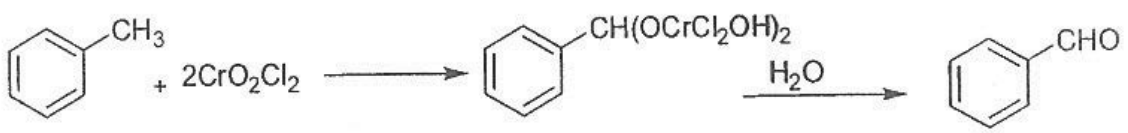
1) From toluene by oxidation:

Two methods are in common use in the laboratory for the oxidation of methylbenzene.

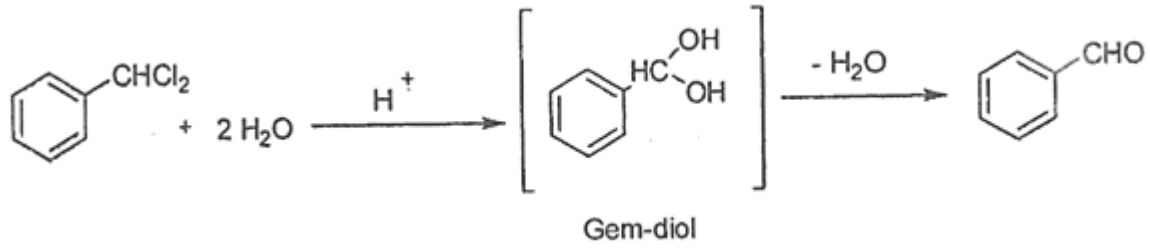
a) Oxidation of toluene with chromium trioxide in acetic anhydride. As the benzaldehyde is formed, it is converted into the non oxidizable derivative gem-diacetate (benzylidene acetate). Hydrolysis of the acetate with dilute sulphuric acid or hydrochloric acid gives benzaldehyde.



b) An interesting oxidizing agent is chromyl chloride (CrO_2Cl_2, Etard's reaction) in this method, toluene is treated with chromyl chloride in CCl_4 and the complex, which is precipitated, is decomposed with water.



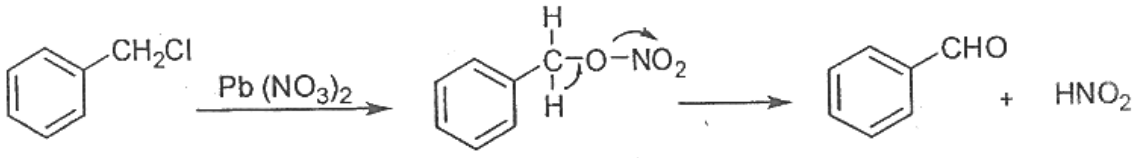
2) **From benzvlidene chloride;** by hydrolysis with aqueous acid (commercial method).



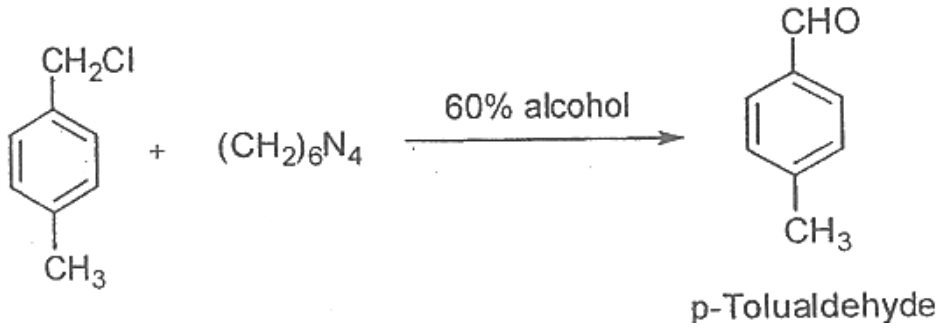
3) **From benzyl chloride:**

Benzaldehyde can be prepared from benzyl chloride via two methods:

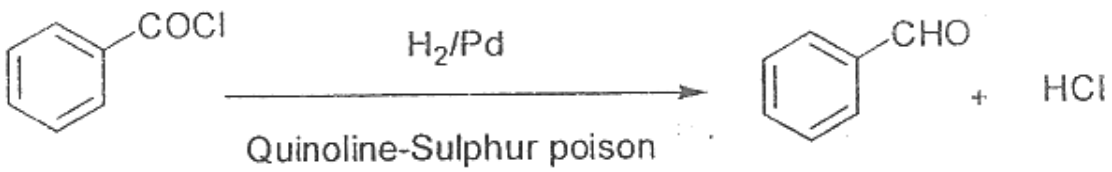
a) Oxidative hydrolysis: by boiling benzyl chloride with aqueous copper or lead nitrate in a current of carbon dioxide.



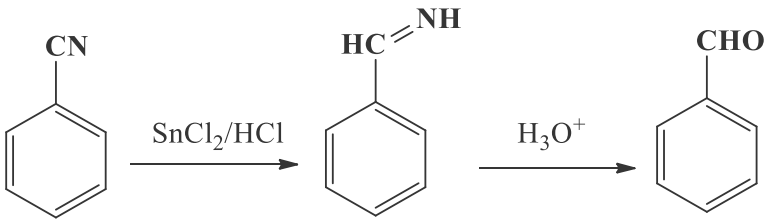
b) Sommelet's reaction: benzaldehyde is produced when benzyl chloride is refluxed with hexamethylenetetramine in aqueous ethanolic solution, followed by acid hydrolysis.



4) From acid chloride (Rosenmund reaction)



5)From nitriles (Stephen's method)



6) Direct formylation:

The formyl group may be introduced directly into an aromatic nucleus by:

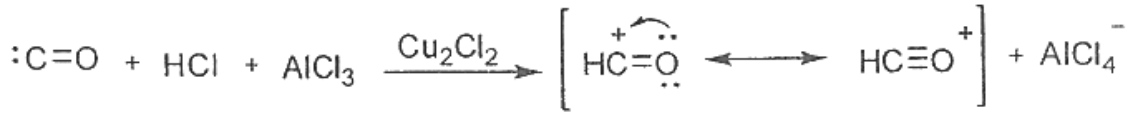
a) Gattermann-Koch aldehyde synthesis.

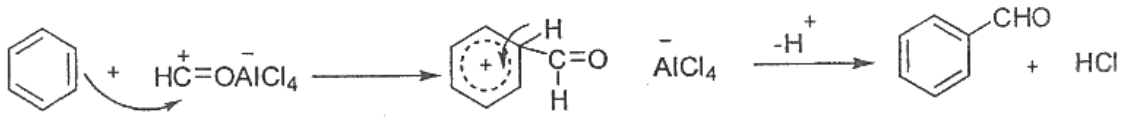
b) Gattermann aldehyde synthesis.

a) Gattermann-Koch aldehyde synthesis.

Benzaldehyde can be synthesized by passing a mixture of carbon monoxide and hydrogen chloride through a solution of benzene in ether or nitrobenzene in presence of aluminum chloride and small amount of cuprous chloride, in this reaction, the formyl cation is the active species ,

and cuprous chloride forms a complex with carbon monoxide, thereby increasing its local concentration.



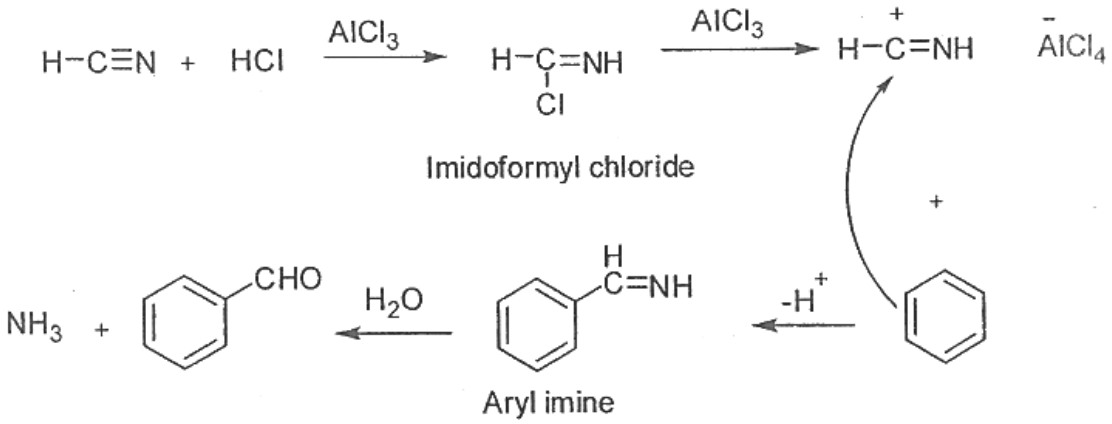


When there are substituents in the ring e.g. methyl group, the aldehyde group is introduced into the p-position only.

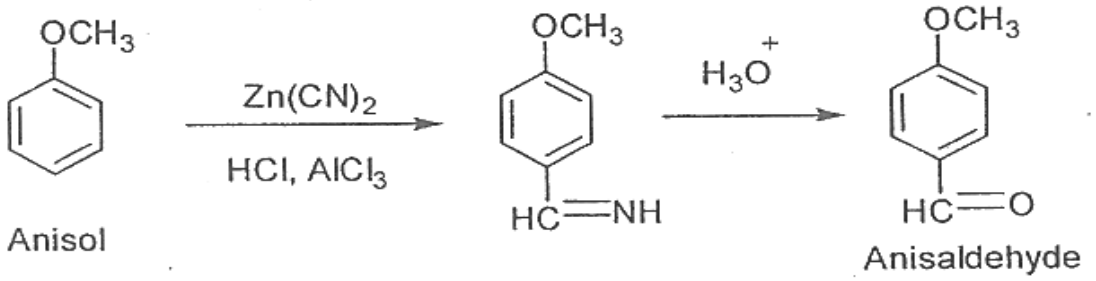
Gatterman-Koch aldehyde synthesis is not applicable to phenols and their ethers or when the substituent is strongly deactivating e.g. nitrobenzene (cf. Fridel-Grafts reaction).

b) <u>Gattermann aldehyde synthesis.</u>

By treating benzene with a mixture of hydrogen cyanide and hydrogen chloride in presence of aluminum chloride, and the complex so formed decomposed with water, benzaldehyde is produced.

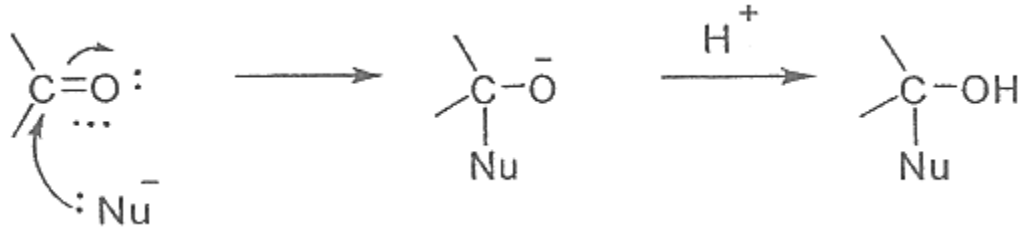


Instead of using poisonous hydrogen cyanide as such, a mixture of zinc cyanide and hydrogen chloride is employed. Gattermann aldehyde synthesis is applicable to phenols and phenolic ethers, but not to nitrobenzene.

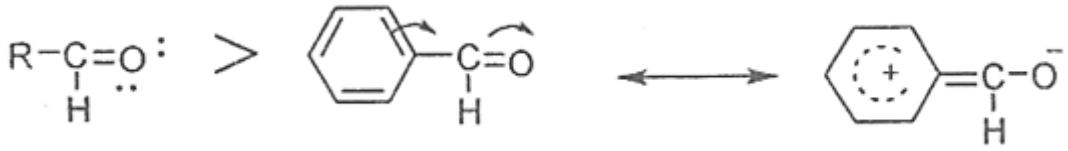


Structure of the carbonyl group;

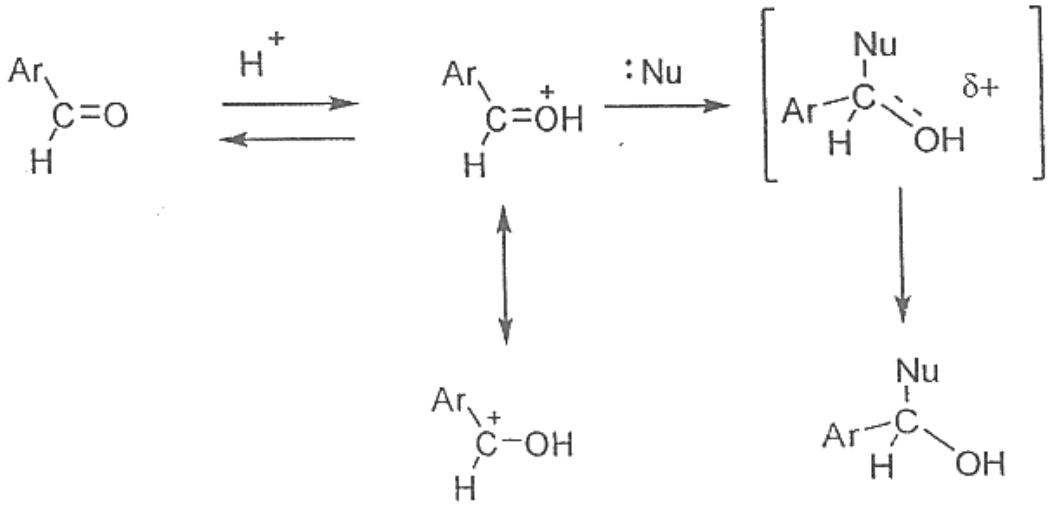
The carbonyl group, C=O, governs the chemistry of aldehydes, since the mobile π electrons are pulled strongly toward oxygen, the carbonyl carbon is electron deficient and carbonyl oxygen is electron rich. The carbonyl group is most susceptible to attack by electron-rich nucleophilic reagents that are by bases (nucleophilic addition).



Aromatic aldehydes is less reactive than aliphatic aldehydes, since the delocalized electrons of the benzene ring act as more readily available electron-source than is present in the alkyl group.



If acid is present, hydrogen ion becomes attached to carbonyl oxygen. This prior protonation lowers the E_{act} for nucleophilic attack, since it permits oxygen to acquire the π electrons without having to accept a negative charge. Thus "nucleophilic addition to aldehydes can be catalyzed by acids.



Reaction of aldehydes :

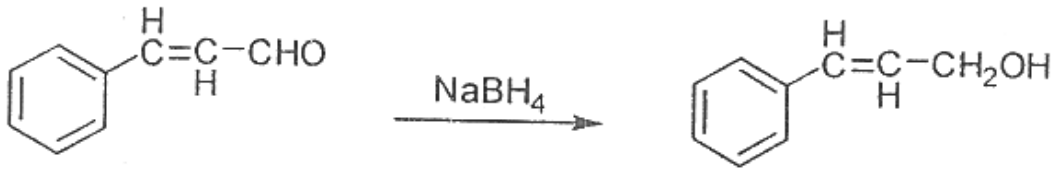
I- Oxidation:

Benzaldehyde is readily oxidized to benzoic acid even when exposed to air (autoxidation), i.e. it is strong reducing agent. The reducing power of benzaldehyde is clearly shown in the laboratory by the restoration of colour to Schiff s reagent and the production of silver mirror from an ammoniacal solution of silver nitrate. Benzaldehyde is not affected by Fehling's solution or Bendicts solution.

II-Reduction:

a- Reduction to alcohols:

Benzaldehyde can be reduced to benzyl alcohol, either by catalytic hydrogenation or by use of lithium aluminium hydride, $LiAlH_4$. Sodium borohydride, $NaBH_4$ does not reduce carbon-carbon double bonds, not even' those conjugated with carbonyl group and is thus useful for the reduction of such unsaturated carbonyl compounds to unsaturated alcohols.



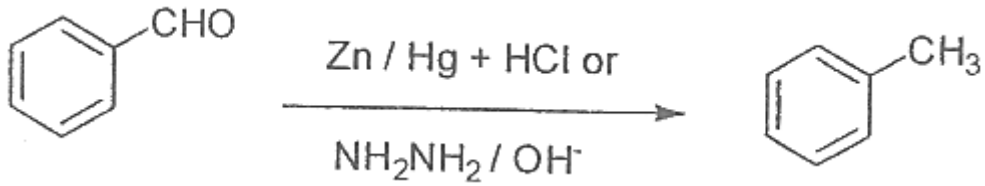
Cinnamaldehyde Cinnamyl alcohol

b- Reduction to hydrocarbons:

Benzaldehyde can be reduced to toluene by the action of:

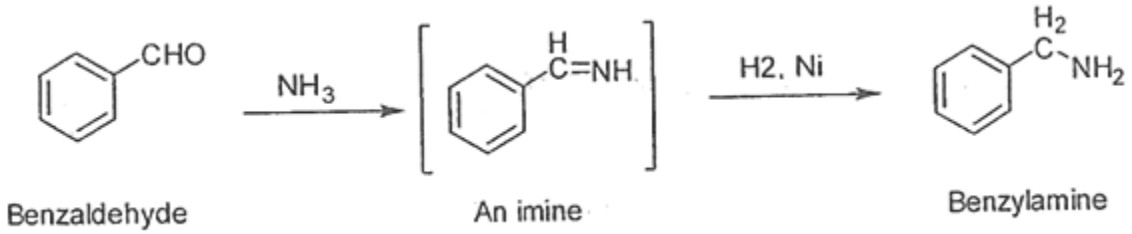
i- amalgamated zinc and conc. HCl (Clemensen reduction) or

ii- of hydrazine, NH_2NH_2 and KOH or Pot. ter. butoxide (Wolf-Kishner reduction).



c- Reductive amination:

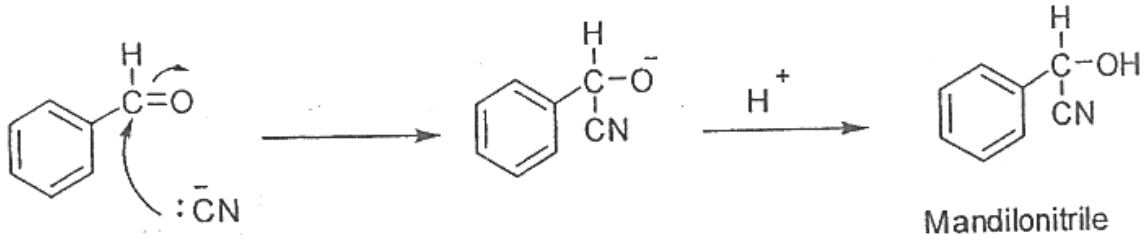
Many aldehydes are converted into amines by reductive animation: reduction in presence of ammonia. Reduction can be accomplished catalyticaily. The reaction involves reduction of intermediate compound (an imine, RCH=NH) that contains a carbon-nitrogen double bond.



III- Nucleophilic additions to the carbonyl group:

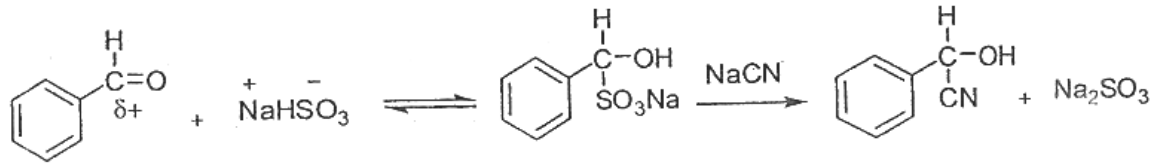
1) Addition of hydrogen cyanide:

Hydrogen cyanide is usually produced in situ by the action of dilute acid on a mixture of potassium or sodium cyanide solution and the carbonyl compound. The nucleophile which is the cyanide ion is added to the carbonyl group and the product is a hydroxynitrile (cyanohydrin).



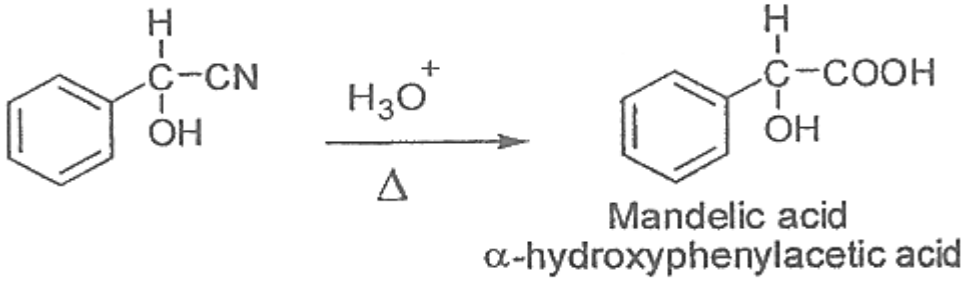
Mandilonitrile

A useful modification, cyanide is added to the bisulphite addition product of the carbonyl compound.



Mandilonitrile

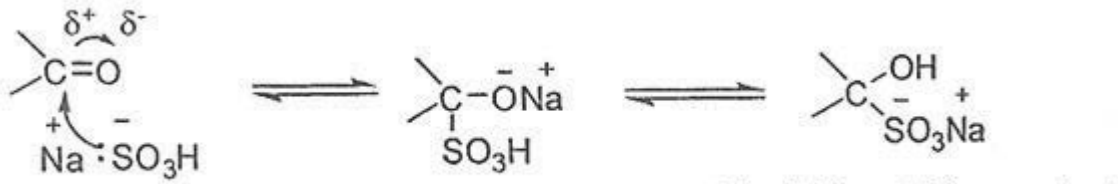
Subsequent hydrolysis of the cyanohydrin by boiling with dilute acid gives the α-hydroxy acid.



Mandelic acid
α-hydroxyphenylacetic acid

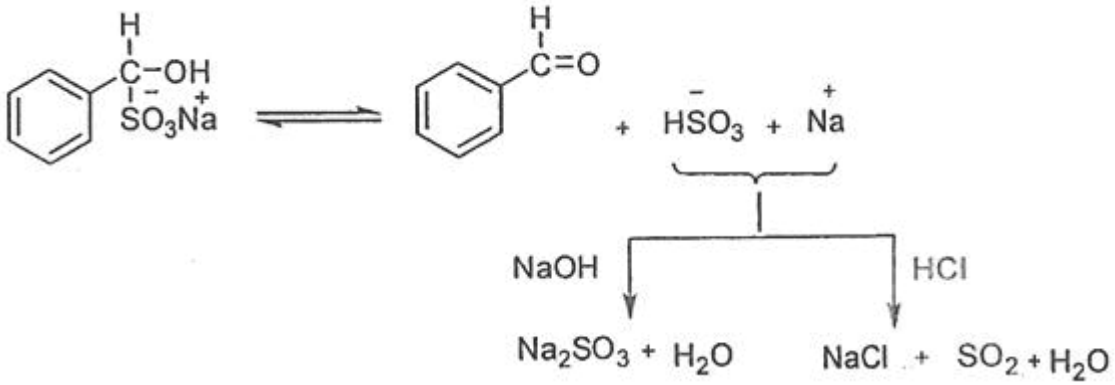
2) Addition of sodium bisulphite ($NaHSO_3$):

Saturated sodium bisulphite solution yields crystalline compounds, the nucleophile being the hydrogen sulphite in $^{-}SO_3H$.



Bisulphite addition product

This reaction can be reversed to form the original carbonyl compound by the action of dilute acid or base.

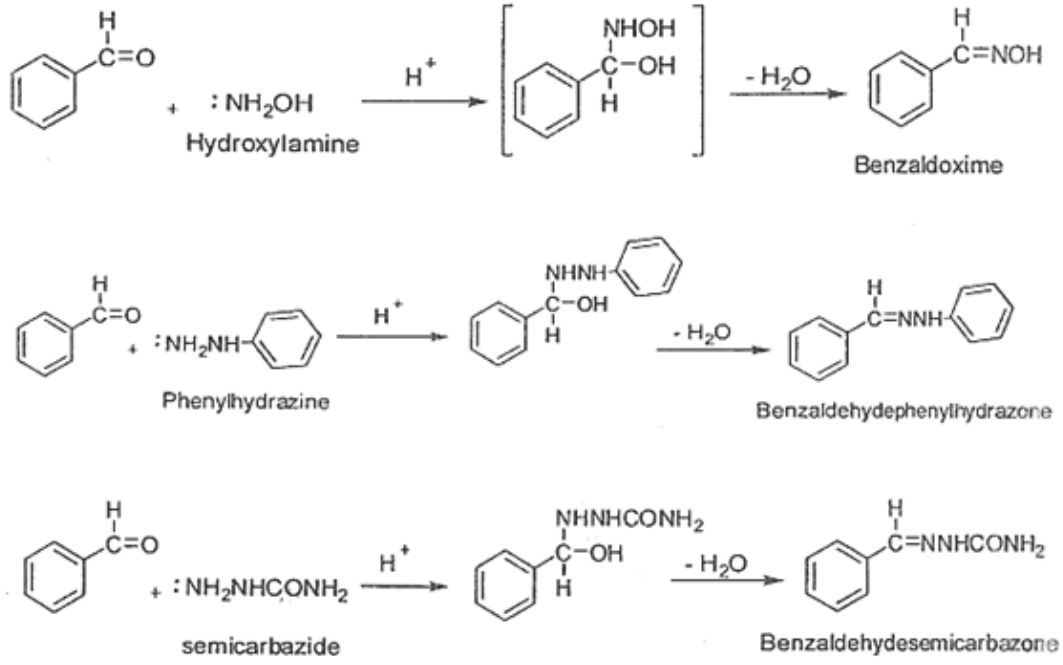


Bisulphite addition products are generally prepared for the purpose of separating a carbonyl compound from non-carbonyl compounds.

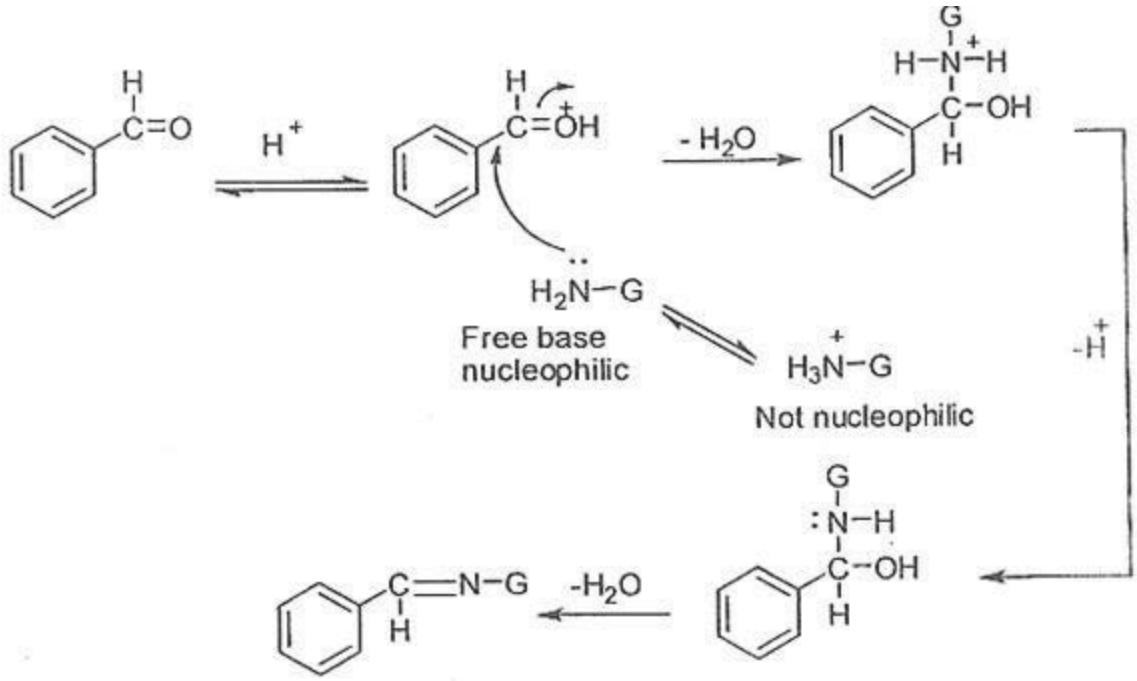
3) Addition of derivatives of ammonia:

Certain compounds related to ammonia add to the carbonyl group to form derivatives that are important chiefly for the characterization and identification of aldehydes. The products contain a carbon-nitrogen double bond resulting from elimination of a

molecule of water from the initial addition products. Some of these reagents and their products are:

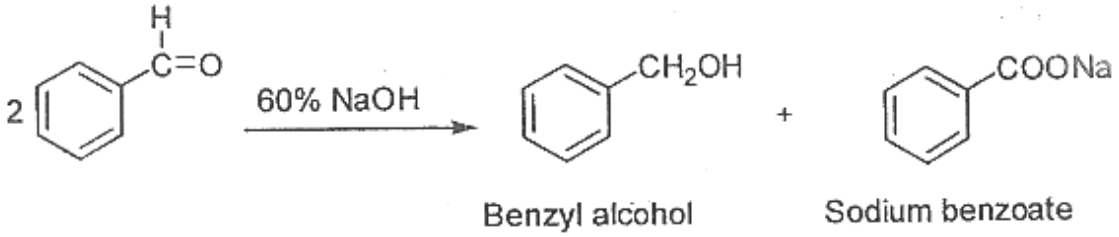


These additions involve nucleophilic attack by the basic nitrogen compounds on carbonyl carbon. Protonation of carbonyl oxygen makes carbon more susceptible to nucleophilic attack; in-so-far as the carbonyl compound is concerned, then addition, will be favoured by high acidity. But, the ammonia derivatives, H_2N-G can also undergo protonation to form the ion $^{+}H_2N$-G, which lacks unshared electrons and is no longer nucleophilic, in-so-far as the nitrogen compound is concerned, the addition is favoured by lower acidity. The solution must be acidic enough for an appreciable fraction of the carbonyl compound to be protonated, but not so acidic that the concentration of the free nitrogen compound is too low.



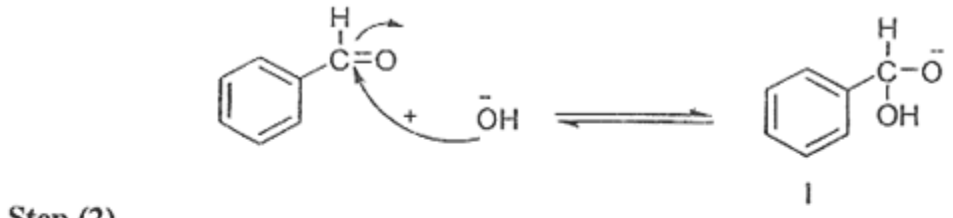
IV- <u>Action of alkali-Cannizzaro reaction:</u>

In the presence of conc. Aqueous sodium hydroxide aromatic aldehydes having no α-hydrogen atoms undergo self-oxidation and reduction (disproportionation) to yield a mixture of an alcohol and a salt of carboxylic acid.

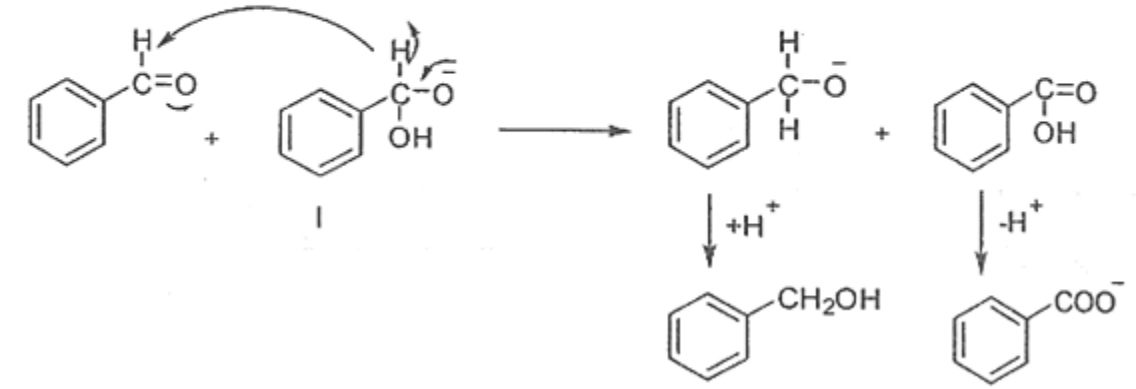


A likely mechanism for the cannizzaro reaction is the following:

Step (1)

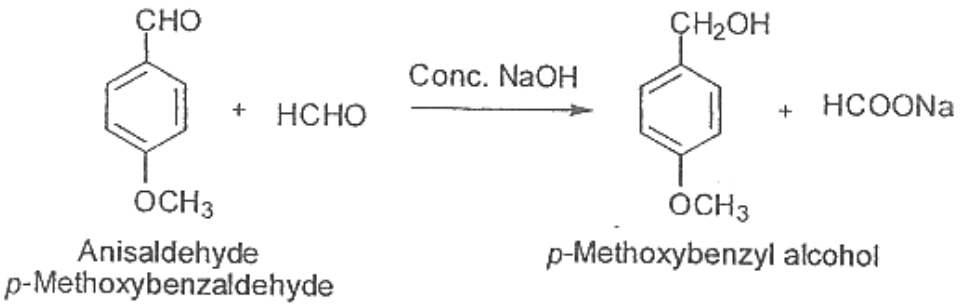


Step (2)



Two successive additions are involved; in step 1 addition of hydroxide ion to the carbonyl carbon to give intermediate I and in step 2 addition or transfer of a hydride ion from I to a second molecule of aldehyde. The presence of the negative charge on I aids in loss of hydride ion.

Cannizzaro reactions themselves are of little synthetic use since most aldehydes are expensive reducing agents. However, crossed Cannizzaro reactions, using inexpensive formaldehyde as one component (and in excess), are practical. Formaldehyde has the advantage, too, that it preferentially accepts the hydroxide ion in step 1 and thus acts as reducing agent in step 2. The reaction showed below illustrates this method.



Anisaldehyde
p-Methoxybenzaldehyde

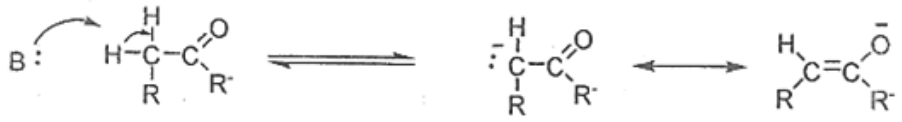
p-Methoxybenzyl alcohol

V- Condensation reactions of aromatic aldehydes:

Base catalytic addition of carbanion: (Crossed aldol condensation)

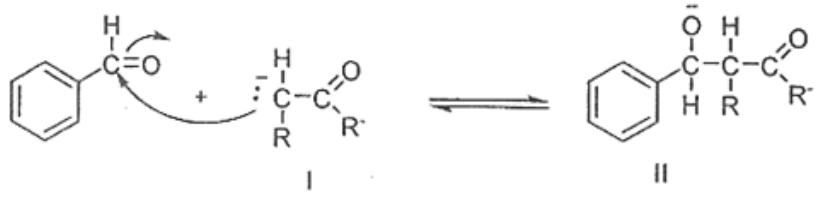
As those aromatic aldehydes e.g. benzaldehyde, lake α-hydrogen atoms, self-condensation reactions involving α-carbanion formation (aldol condensation) clearly cannot occur. There are a large number of condensations that are closely related to the aldol condensation. Each of these reactions has its own name. Claisen-Schmidt, Perkin, Knoevenagel, Doebner. In each case, the carbanion is generated in very much the same way. Different bases may be used sodium hydroxide, sodium ethoxide, sodium acetate, amines and the carbonyl group to which the hydrogen is alpha may vary aldehyde, ketone, ester, anhydride but the chemistry is essentially the same as that of aldol condensation.

Step (1)



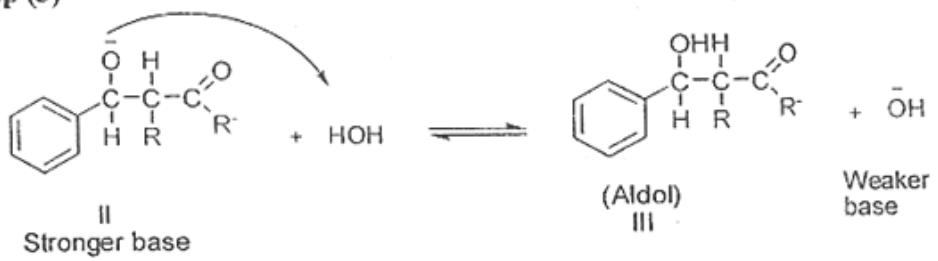
Resonance stabilized carbanion

Step (2)



I II

Step (3)

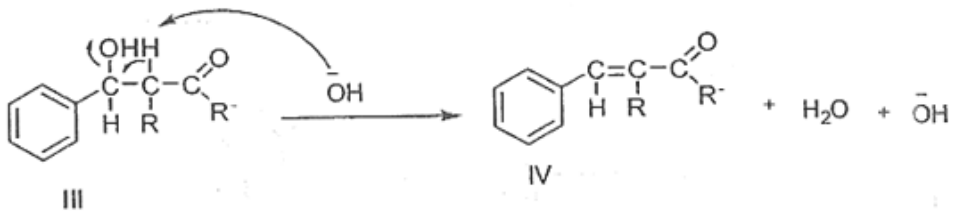


II
Stronger base

(Aldol)
III

Weaker
base

Step (4)



III IV

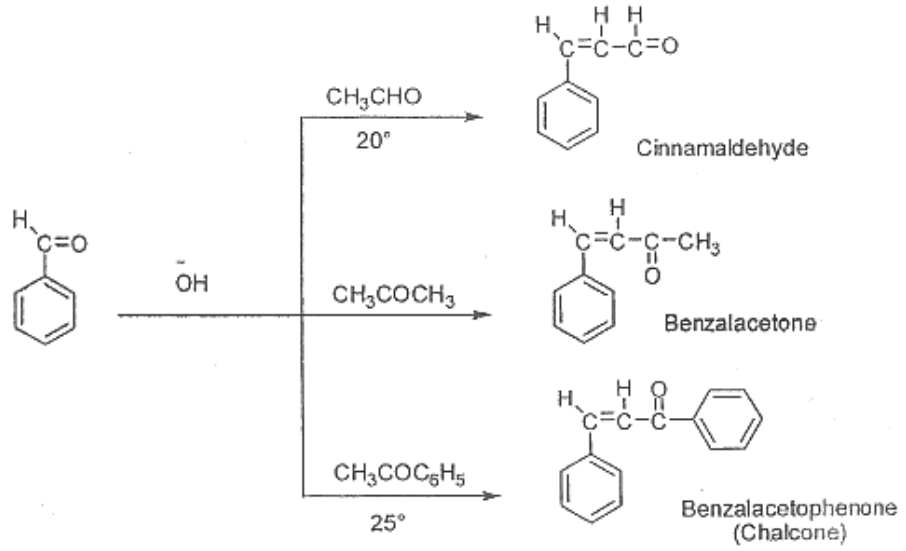
In step (1), the base abstracts a hydrogen ion the α-carbon of the carbonyl compound to form a resonance stabilized carbanion.

In step (2), the carbanion attacks the carbonyl carbon of benzaldehyde or any aromatic aldehyde to form ion II (alkoxide).

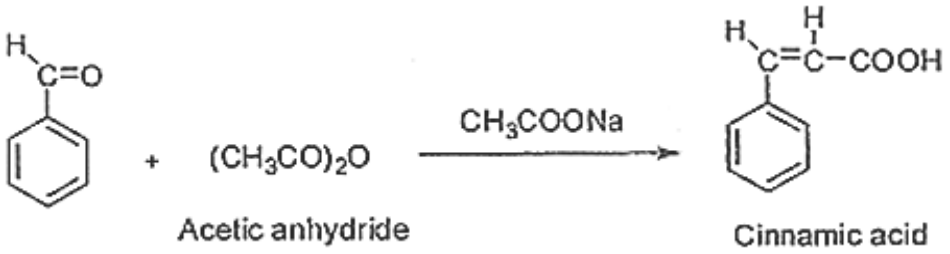
In step (3), the alkoxide (II) abstracts hydrogen from water to form the β-hydroxy derivative III (aldol).

In step (4), when aldol is heated dehydration takes place and *α,* β-unsaturated compound is formed.

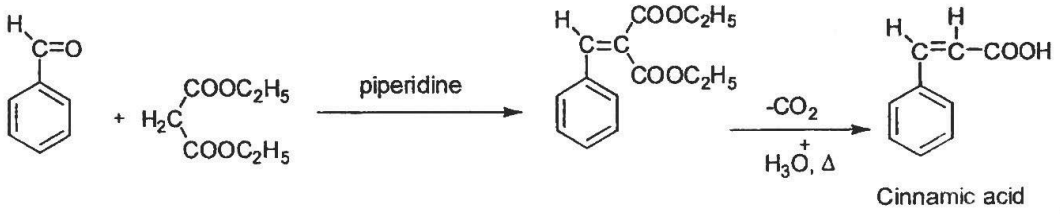
a- Claisen-Schmidt reaction:



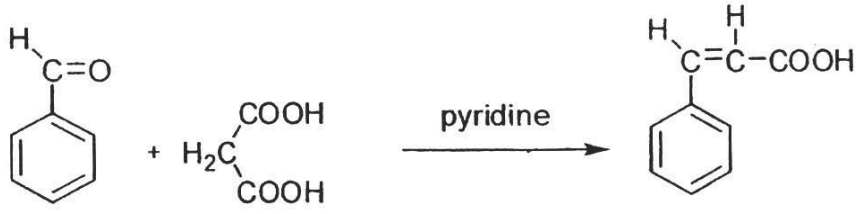
b- Perkin reaction:



c- <u>Knoevenagel reaction:</u>



d- <u>Doebner condensation:</u>

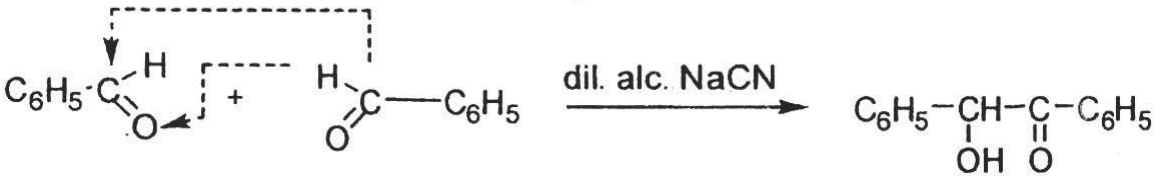


Malonic acid

Here decarboxylation usually occurs spontaneously.

VI- Benzoin condensation

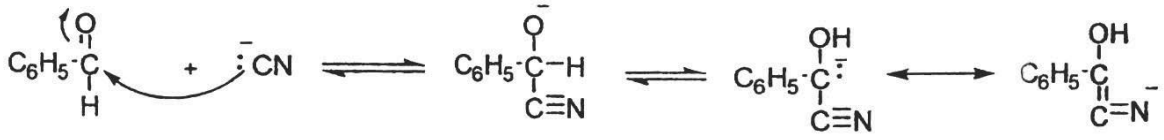
Benzaldehyde undergoes self-condensation reaction in presence of strong alcoholic potassium or sodium cyanide to form benzoin (α-hydroxy ketone).



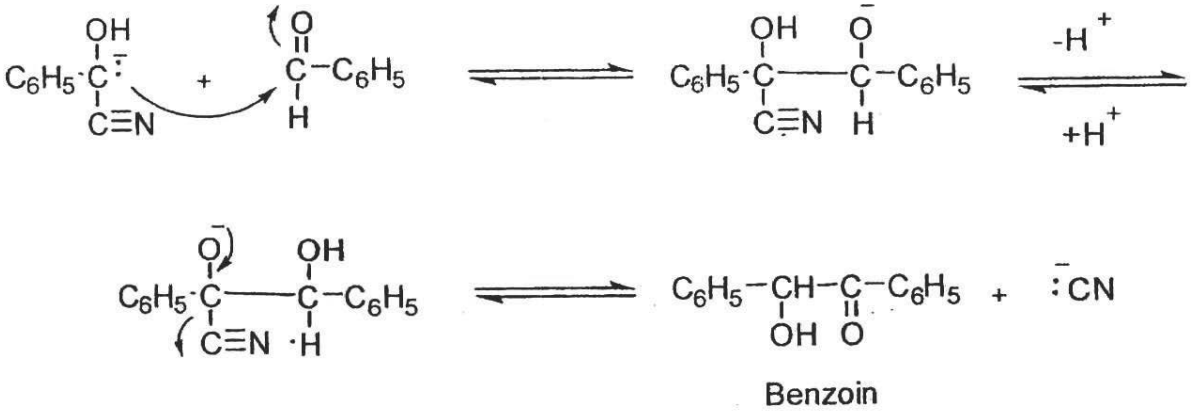
Benzoin

Mechanism of benzoin reaction:

Step (1)



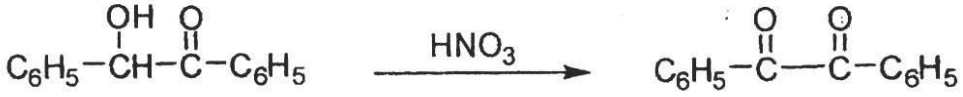
α-hydroxynitrile



Benzoin

The cyanide ion is highly specific catalyst for this reaction, its effectiveness depends on the ease with which it adds to benzaldehyde and with which it is finally expelled to yield benzoin, also the electron-withdrawing power of cyanide ion promotes the ready release-as proton- of the hydrogen atom attached to carbon to yield the carbanion (α-hydroxynitrile).

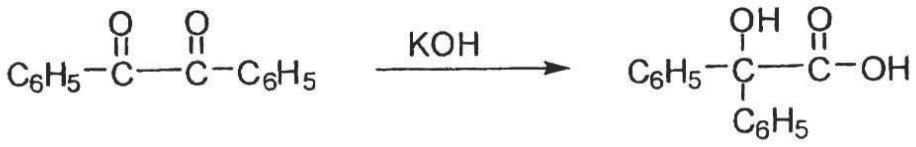
Benzoin is readily oxidized by nitric acid to benzil (a-diketone).



Benzoin

Benzil

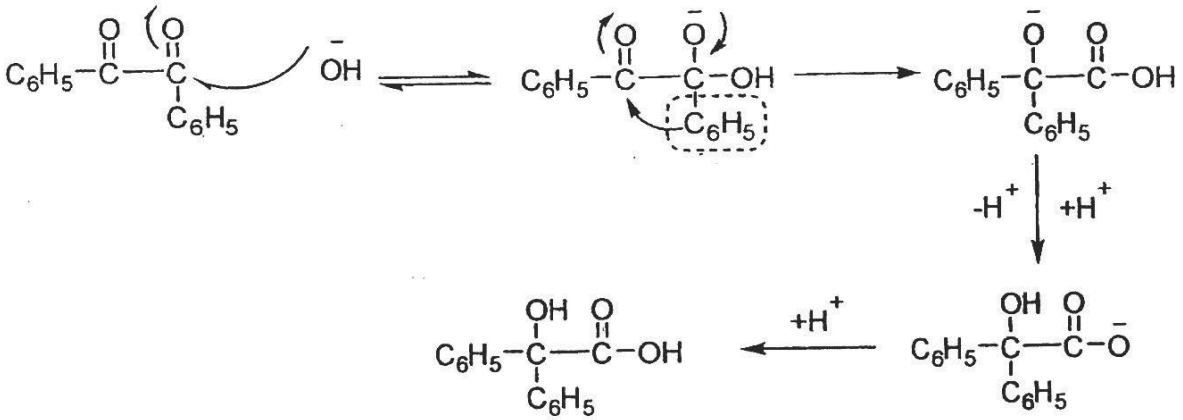
When benzil is treated with aqueous potassium hydroxide, it undergoes a peculiar rearrangement known as the benzilic acid rearrangement (intramolecular rearrangement) to give the potassium salt of benzilic acid.



Benzil

Benzilic acid

Mechanism of benzilic acid rearrangement:



The first step in this rearrangement is the rapid reversible addition of hydroxide ion to the benzyl followed by the migration of phenyl group with its electron pair to the slightly positive carbon atom of the adjacent carbonyl group. Benzilic acid rearrangement is an example of 1, 2-shift.

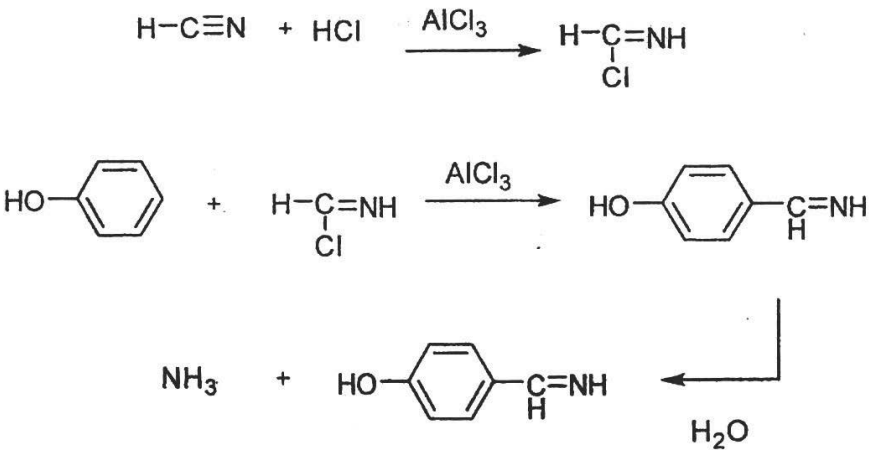
Phenolic aldehydes

Phenolic aldehydes contain an aldehyde group and one or more hydroxyl groups directly attached to the nucleus.

General methods of preparation:

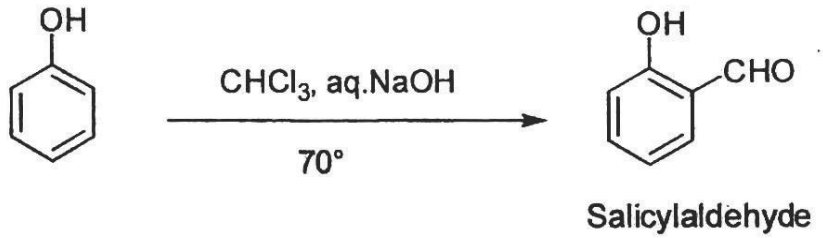
1) Gattermann's aldehyde synthesis:

When phenol or phenolic ether is treated with a mixture of hydrogen cyanide and hydrogen chloride in the presence of aluminium chloride, and the complex produced then decomposed with water p-hydroxy- (or alkoxy) benzaldehyde is the main product.



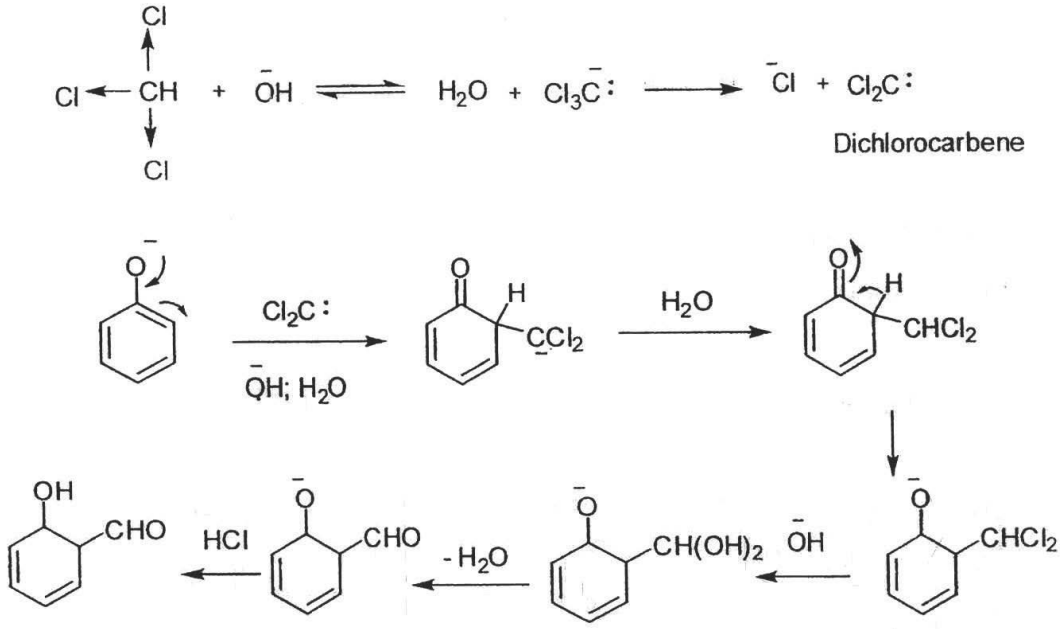
2) Reimer-Tiemann reaction:

Treatment of a phenol with chloroform and aqueous hydroxide introduces an aldehyde group, CHO, into the aromatic ring, generally ortho to the -OH group.



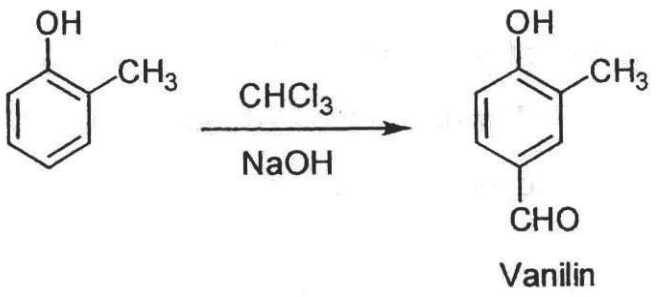
Salicylaldehyde

The mechanism of reaction involves electrophilic substitution on the highly reactive phenoxide ring. The electrophilic reagent is dichlorocarbene, $:CC1_2$ generated from chloroform by the action of base. Although electrically neutral, dichlorocarbene contains a carbon atom with only a sextet of electrons and hence is strongly electrophilic.



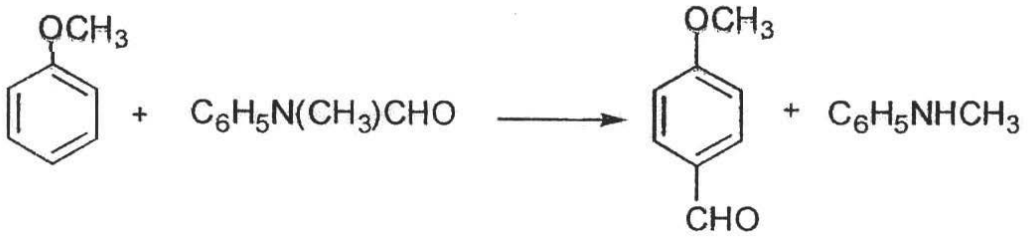
A substituted benzal chloride is initially formed, but is hydrolyzed by the alkaline reaction medium.

In the Reimer-Tiemann reaction, the o-isomer predominates, but if one of the o-position is occupied, the aldehyde group tends to go to the *p*-position; e.g., guaiacol forms vanillin.



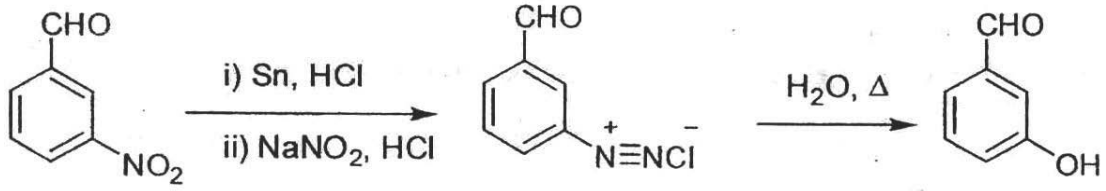
3) Formylation with *N*-methylformanilide:

This method works well for the *o*- and p-positions of phenolic ethers. The formylation is carried out by treating the compound with *N*-methylformanilide and phosphoryl chloride.



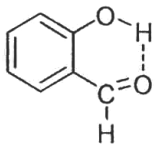
Dimethylformamide, $HCONMe_2$, is often used instead of *N*-methylformanilide.

4) *m*-Hvdroxybeitzaldehyde may be prepared by an indirect method as follows:

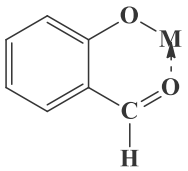


Many phenolic aldehydes occur in plant materials, they often have pleasant odour and are used as flavouring agents or as perfume (e.g. vanillin). The presence of the hydroxyl group in *o*- and p-hydroxybenzaldehyde lowers the electrophilic character of the carbonyl carbon atom to the extent that Cannizzaro reaction is inhibited.

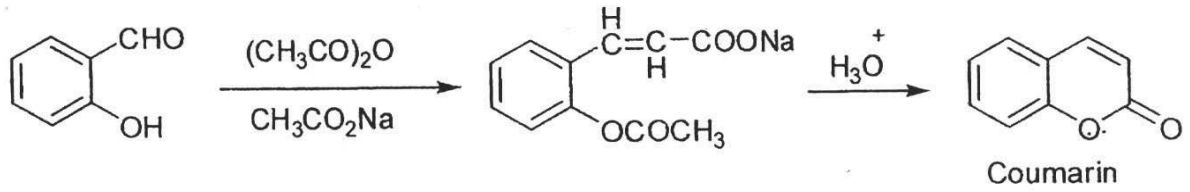
The hydroxyl group of salicylaldehyde is not so reactive as that in the *m*-and p-isomers. This is probably due to the hydrogen bonding, which also accounts for the high volatility of salicylaldehyde (compared with the *m*- and p-compound).



Salicylaldehyde gives violent colouration with ferric chloride solution and yield solution in alkali due to the chelation with metal ion.



Condensation reactions of salicylaldehyde are frequently accompanied by cyclization e.g. condensation with acetic anhydride (Perkin reaction) gives largely coumarin.



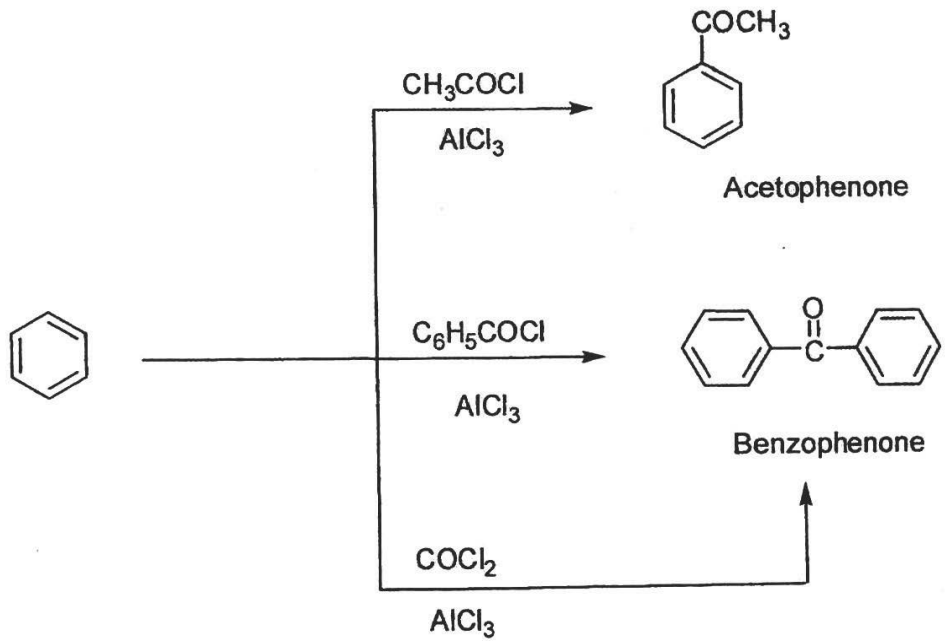
Coumarin

Aromatic Ketones

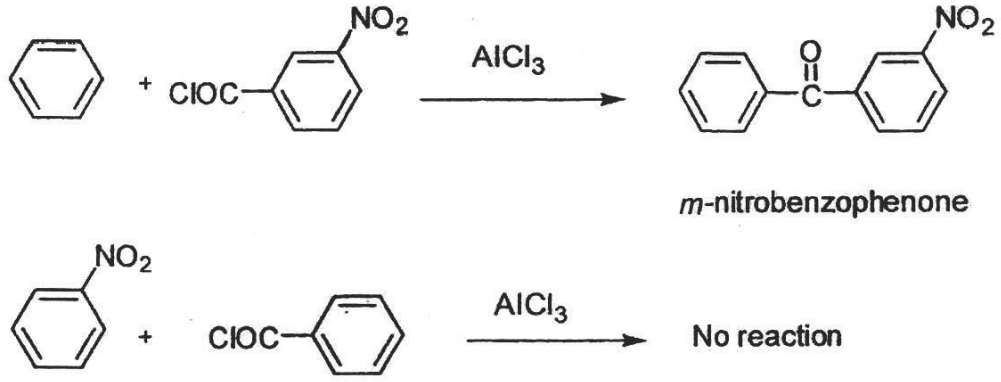
Aromatic ketones may be either aralkyl ketones (Ar.CO.R), e.g. acetophenone or diaryl ketones (Ar.CO.Ar), e.g. benzophenone.

Preparation:

1) Friedel-Crafts acylation: Benzene reacts with acetyl chloride to give acetophenone, and similarly, Friedel-Crafts of benzene with benzoyl chloride or with phosegene gives benzophenone.

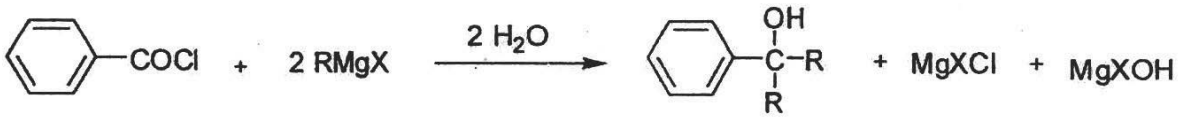


In planning the synthesis of diaryl ketones, Ar.CO.Ar, it is particularly important to select the right combination of ArCOCl and ArH. in the preparation of *m*-nitrobenzophenone, for example, the nitro group can be present in the acid chloride but not in the ring undergoing substitution, since a strongly deactivating group it prevents the Friedel-Crafts reaction.

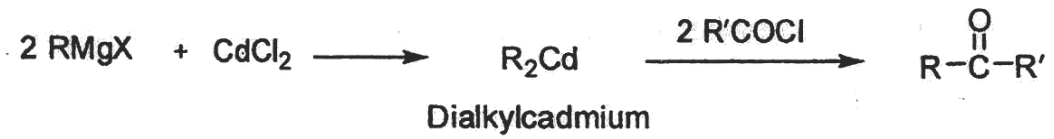


3) Preparation of ketones through the reaction of organocadmium compounds with acid chlorides:

Grignard reagents react readily with acid chloride, but the products are usually tertiary alcohols, these presumably results from reaction of the initially formed ketones with more Grignard reagent.



However, if Grignard reagent is first converted to a dialkylcadmium by treating it with anhydrous cadmium chloride, subsequent treatment with an acid chloride gives a ketone in good yield.

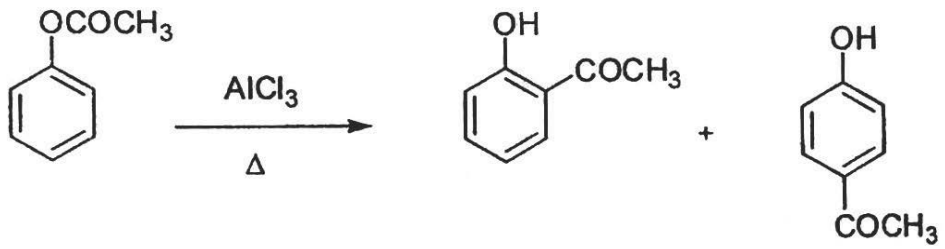


Organocadmium compounds, being less reactive, do not react with ketones. The comparatively low reactivity of organocadmium

compounds not only makes the synthesis of ketones possible, but in addition widens the applicability of the method. Organocadmium compounds do not react with many of the functional groups with which the Grignard reagent does react: $-NO_2$, -CN, -CO, -COOR, for example, consequently, the presence of one of these groups in the acid chloride molecule does not interfere with the synthesis of a ketone.

p-Nitroacetophenone
(methyl *p*-nitrophenyl ketone)

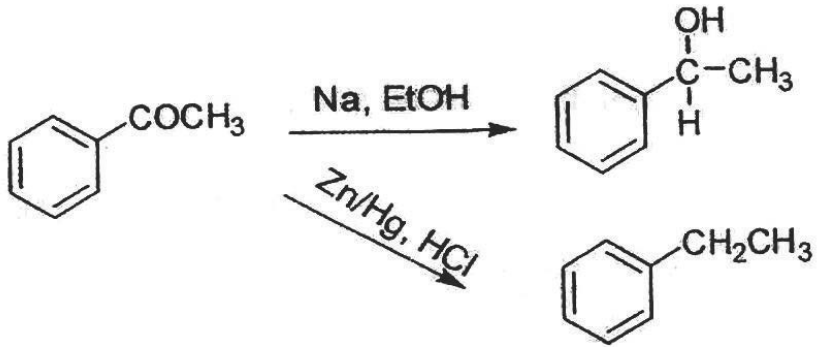
3) Several phenolic ketones are prepared by means of the Fries rearrangement, which consists of heating an acyl derivative of a phenol with aluminum chloride in an inert solvent. The acyl group can migrate to either the ortho or para isomer depends on the condition of the reaction as solvent, temperature, and amount of catalyst used.



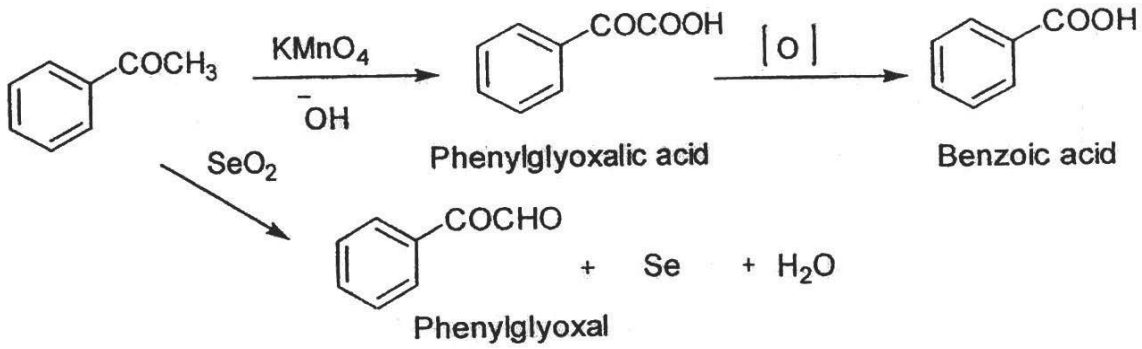
Chemical Reactions:

The reactions of typical aromatic ketones are illustrated by consideration of those of acetophenone. Acetophenone has been used in medicine as a hypnotic under the trade name Hypnone.

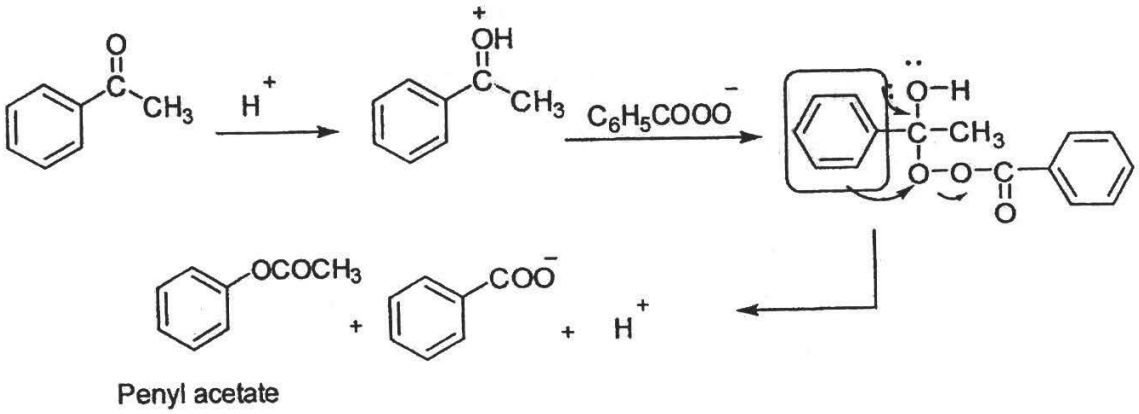
1) **Reduction:** when reduced with sodium and ethanol, acetophenone gives the secondary alcohol phenylmethylmethanol; reduction by Clemmensen's method gives ethyl benzene.



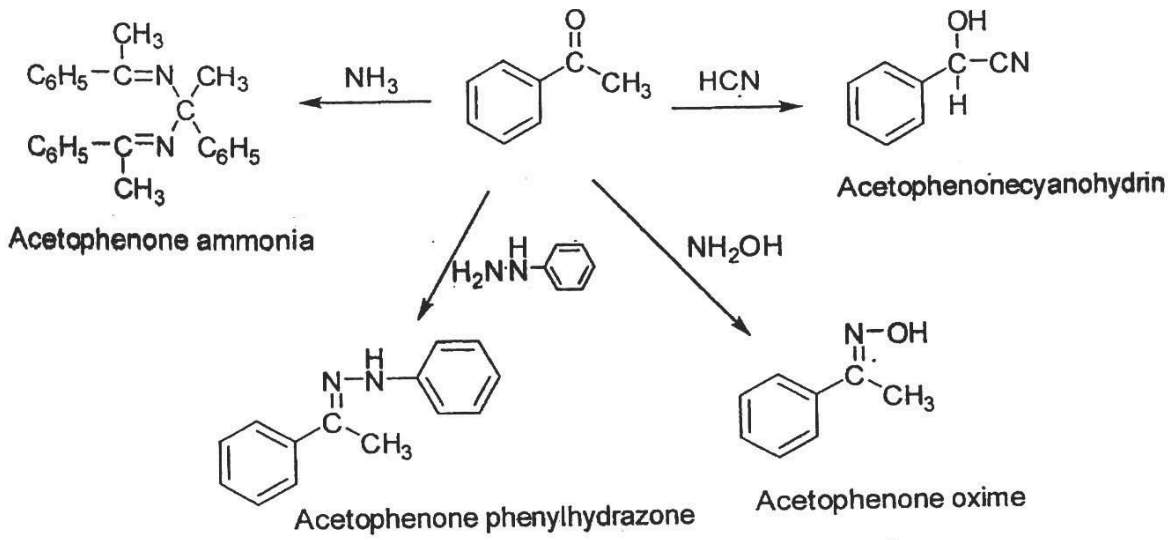
2) Oxidation: with cold potassium permanganate, acetophenone gives phenylglyoxalic acid (benzoylformic acid), which on further oxidation, is converted into benzoic acid. Acetophenone is oxidized by selenium oxide to phenyl glyoxal.



Bayer-Villiger oxidation: acetophenone undergoes oxidation with perbenzoic acid to form predominantly phenyl acetate according to the following mechanism:



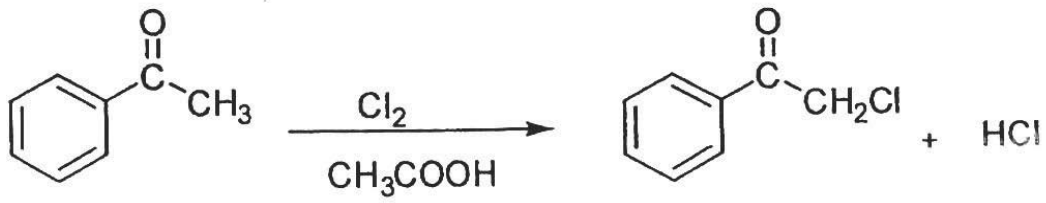
3) Addition reactions of the carbonvl group: acetophenone undergoes many of the addition reactions involving the carbonyl group.



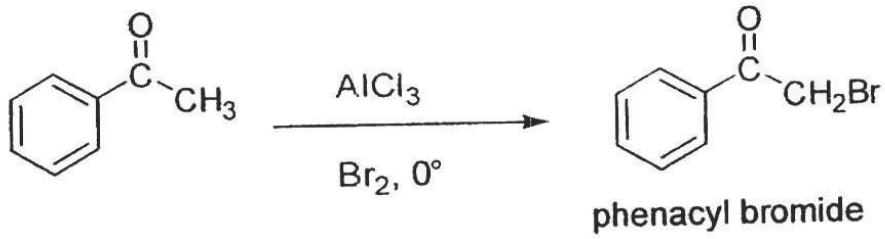
Although benzophenone forms an oxime and the usual substituted phenylhydrazines fairly readily, reactions with hydrogen cyanide or with sodium bisulphite is inhibited (the bisulphite addition is also inhibited with acetophenone), probably for steric reason.

4) <u>Reactivity of the α-hydrogen atoms of acetophenone;</u>

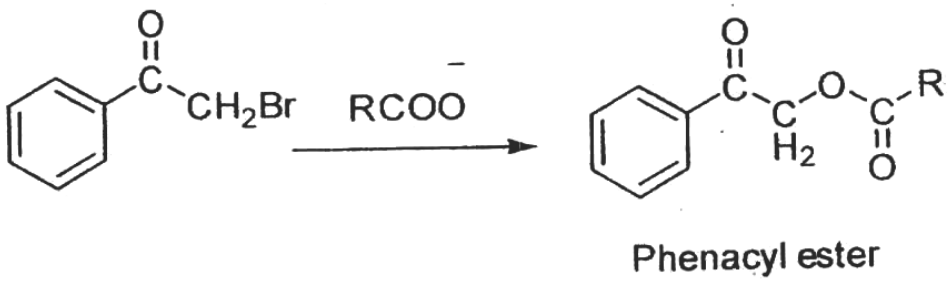
a) On chlorination in acetic acid solution, acetophenone gives phenacyl chloride, which is a powerful lachrymatory and is used as a tear gas in police work.



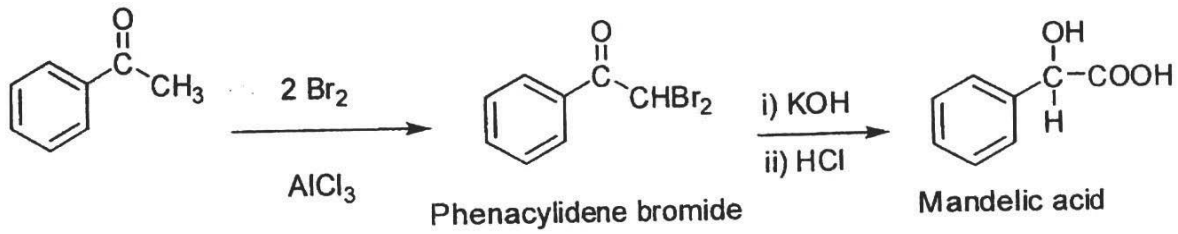
Bromination of acetophenone, similarly, furnishes phenacyl bromide (*ω*-bromoacetophenone).



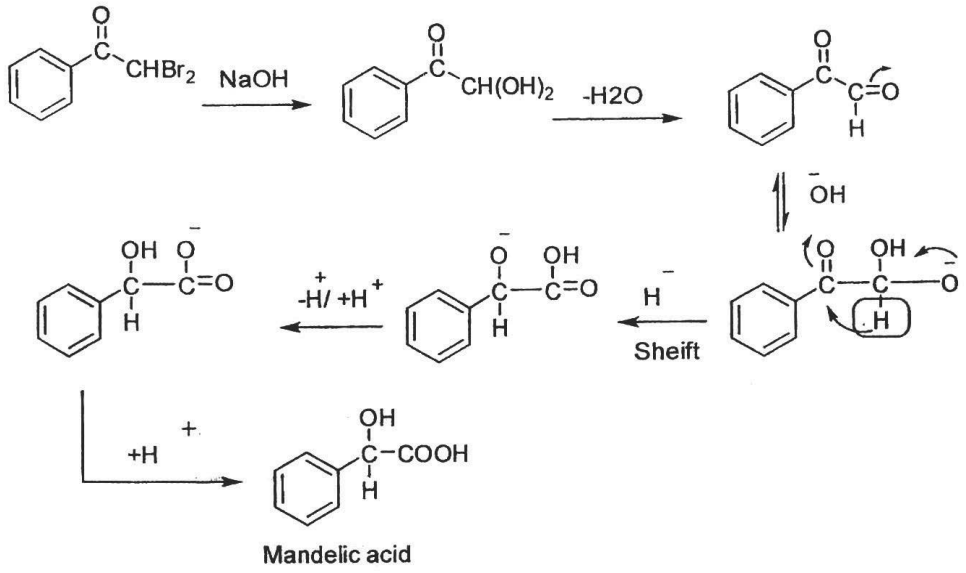
This side-chain atom is highly reactive and is readily replaced by nucleophilic reagents, phenacyl bromide reacts with a carboxylate ion to form the corresponding phenacyl ester as well-defined crystalline product, and this makes it suitable for identifying acids.



Treatment of acetophenone with two equivalents of bromine forms *ω,ώ*-dibromoacetophenone (phenacylidene bromide). This compound undergoes rearrangement on treatment with alkali to form mandilic acid.

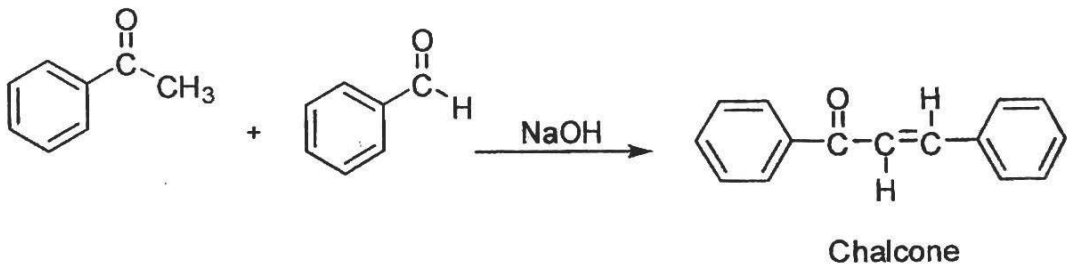


A probable mechanism of this rearrangement is one involving an intramolecular Cannizzaro reaction.



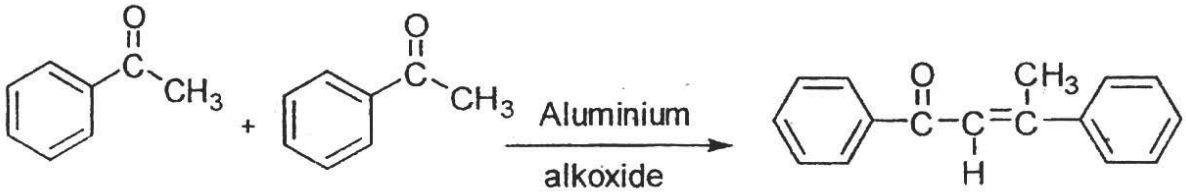
This rearrangement does not take place if both o-positions are occupied e.g. *ω,ώ*-dibromo-derivatives of mesitylene. This is probably due to steric factor.

b) Acetophenone readily condenses with benzaldehyde to give chalcone.



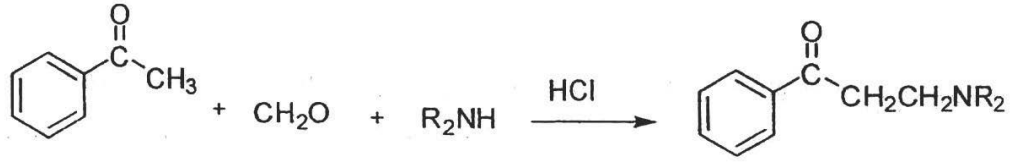
Chalcone

Acetophenone can also undergo self-condensation in the presence of mild alkaline catalyst.



Dypnone

c) <u>Mannich reaction:</u> acetophenone, being an active hydrogen containing compound, reacts with formaldehyde and a secondary amine (or less frequently, ammonia or a primary amine) to form Mannich bases.

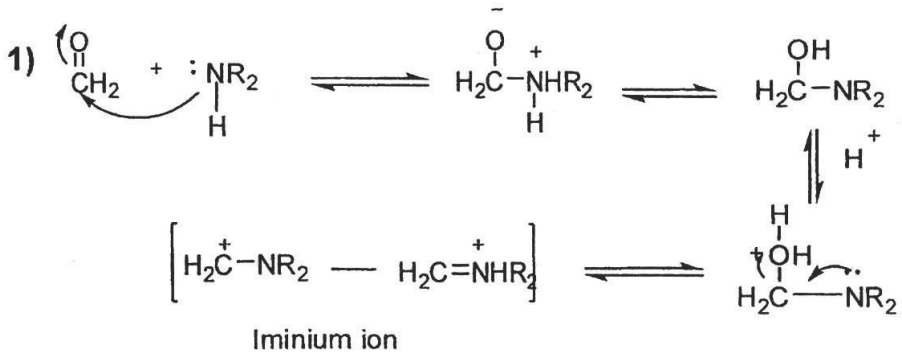


Mannich base

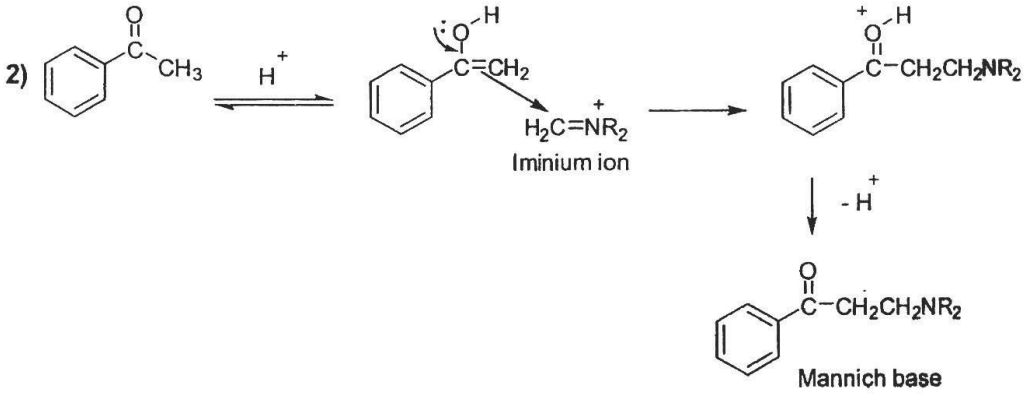
The mechanism that appears to operate in neutral or acidic media involves:

(1) Initial reaction of the secondary amine with formaldehyde to yield an iminium ion and

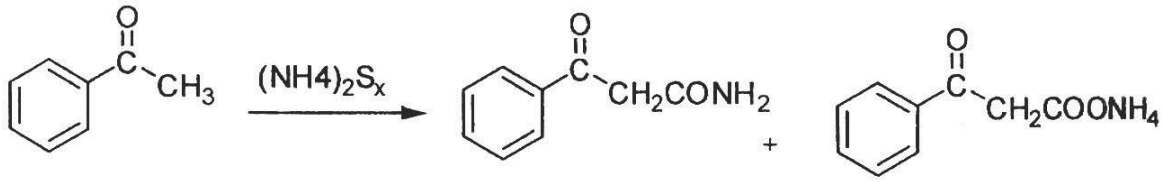
(2) Subsequent reaction of the iminium ion with the enol form of the active methylene compound.



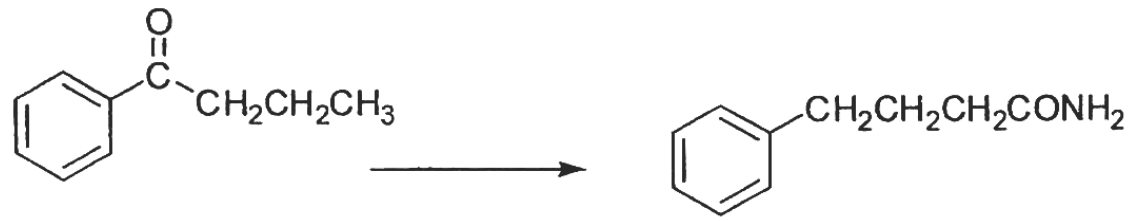
Iminium ion



5) **Willgerodt reaction:** this is the name given to these reactions in which a carbonyl compound is converted into an amide with the same number of carbon atoms. The reaction was originally carried out by heating an arylalkyl ketone with an aqueous solution of yellow ammonium poly sulphide; e.g. acetophenone forms the amide of phenylacetic acid, together with a small amount of the ammonium salt.

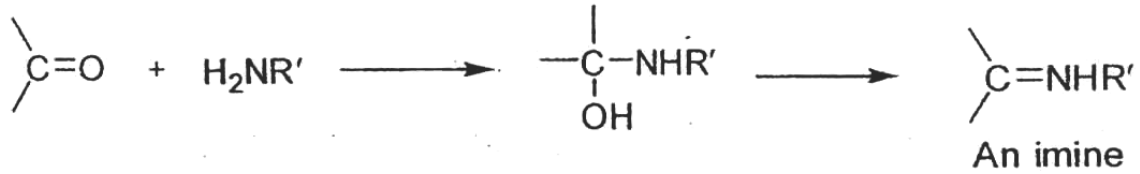


The amido group is always formed at the end of the chain whatever the size of the alkyl group in C_6H_5COR, e.g. buterophenone forms *γ*-phenylbutyramide.



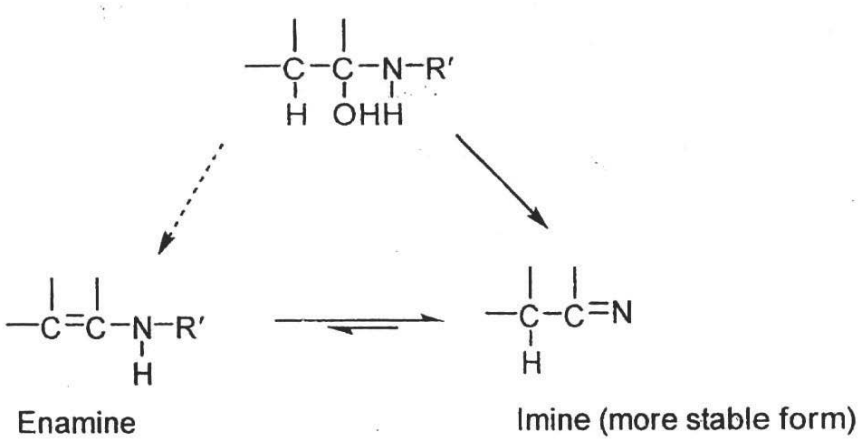
The Willgerodt reaction is very useful for preparing aryl substituted aliphatic acids.

6) Alkylation of carbonyl compounds via enamines: as we might expect, amines react with carbonyl compounds by nucleophilic addition. If the amine is primary, the initial addition product undergoes dehydration to form a compound containing a carbon-nitrogen double bond, an imine.



An imine

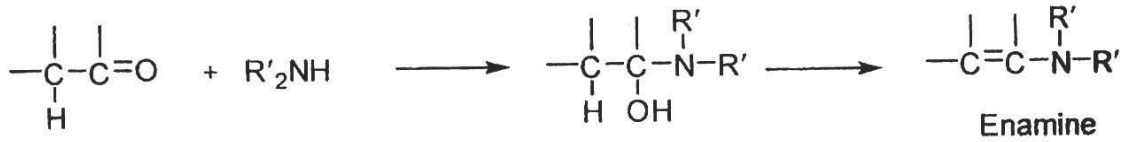
Elimination occurs with orientation even if the carbonyl contains α-hydrogen; that is, the preformed product is the imine rather than the enamine (ene for the carbon-carbon double bond amine for the amino group).



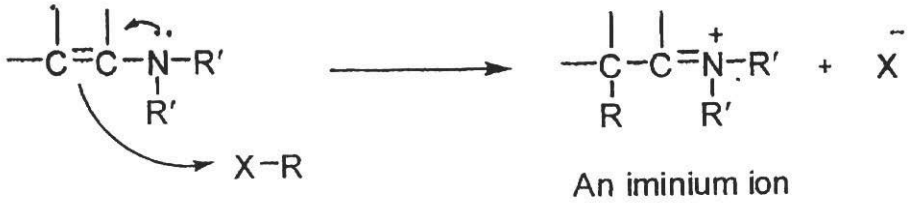
Imine-enamine tautomerism

If some enamine should be formed initially, it rapidly tautomerizes into the more stable imino form.

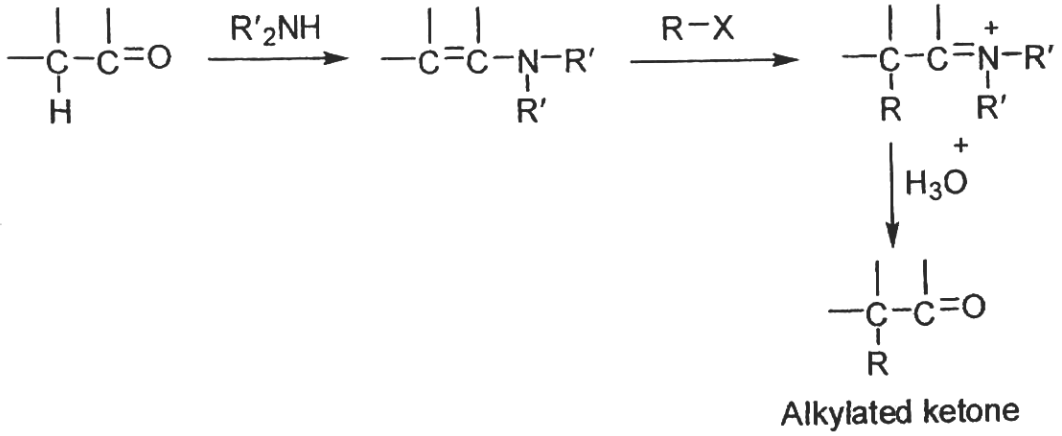
Now, a secondary amine too, can react with a carbonyl compound, and to yield the same kind of initial product. But here there is no hydrogen left on nitrogen; if dehydration is to occur, it must be in the other direction, to form a carbon-carbon double bond. A stable enamine is the product.



The usefulness of enamines stems from the fact that they contain nucleophilic carbon. The electrons responsible for this nucleophilicity are, in the unshared pair on nitrogen; but they are available for nucleophilic attack by carbon of the enamine. Thus, in alkylation:



The product of alkylation is an iminium ion, which is readily hydrolyzed to regenerate the carbonyl group. The overall process, then, is:

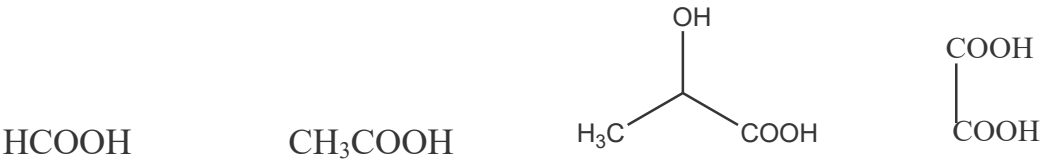


Practical part

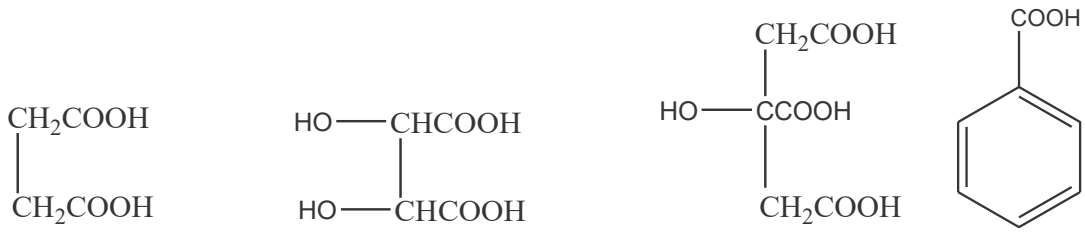
Identification of aliphatic and aromatic carboxylic acid

Generally carboxylic acids are classified into:

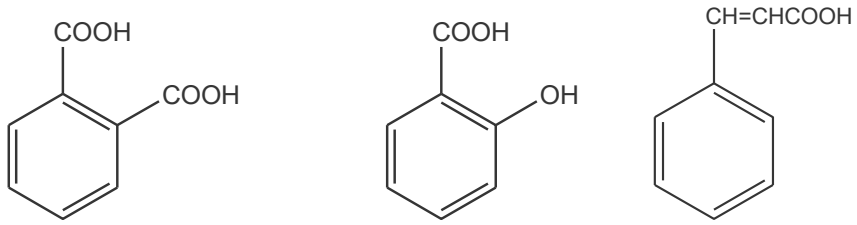
1- **Aliphatic acids**: formic, acetic, lactic, oxalic, citric, succinic and tartaric acids.
2- **Aromatic acids**: benzoic, salicylic, cinnamic and phthalic acids.



Formic acid acetic acid lactic acid oxalic acid



Succinic acid tartaric acid citric acid benzoic acid



Phthalic acid salicylic acid cinnamic acid

Physical properties:

1. **State**: All are solids except formic, acetic, lactic are liquids
2. **Colour**: Colourless
3. **Odour:** pungent odour: formic acid
   Vinegar like odour: acetic acid
   Sour milk like odour: lactic acid
4. **Miscibility and solubility**:

All aliphatic acids are miscible with or soluble in cold water.

All aromatic acids are soluble in hot water and recrystallize on cooling as colourless crystals.

5. **action on litmus paper**: acidic.

Chemical properties:

1- Na_2CO_3 test: effervescence

It is an acidic compound.

2- Dry ignition:

i- Inflammability:

Inflammable with non-smoky, non-luminous flame. It is an aliphatic acid.

In flammable with smoky, luminous flame. It is an aromatic acid.

ii- Odour:

-Pungent odour. Formic acid

- Vinegar like odour: acetic acid

-irritant odour oxalic or succinic acid

-burnt sugar odour hydroxyl acids as citric, tartaric, or lactic acid.

-phenolic odour salicylic acid

- sweet pleasant odour cinnamic acid.

- aromatic odour benzoic or phthalic acid.

iii- residue: no residue.

3- Soda lime (CaO/NaOH):

Carboxylic acids liberate carbon dioxide and give the parent hydrocarbon when heated with soda lime. Different products are formed depending on the nature of the acid.

In a test tube, a mixture of 0.2 gm or 0.2 ml acid and 0.5 gm of fine powdered soda lime is heated. The odour evolved is detected which is similar to that evolved in dry ignition.

4- Sod. Hydroxide 30%: all are soluble

5- Concentrated sulphuric acid:

In a dry test tube, 0.5 gm or 0.5 ml of the acid and 1 ml of conc. Sulphuric acid are heated gently on small direct flame for 30 seconds.

- Effervescence, gas evolved inflammable with blue flame (CO gas) and no blackening. **Oxalic, formic**
- Effervescence, gas evolved inflammable with blue flame and yellow solution. **Citric acid**
- Effervescence, gas evolved inflammable with blue flame and blackening **lactic or tartaric acid**
- No Effervescence no blackening acetic and succinic acid
- No action **aromatic acid**

6- Neutral ferric chloride test:

The test should be carried out on neutral solution of acid which is prepared as follows:

In a test tube, one or two drops of concentrated ammonium hydroxide (detected by the odour) is add to a solution of the acid (0.2 ml or 0.2 gm of the acid in 2 ml of water). Boil the solution till no ammonia odour is evolved

(this converts the acid into its ammonium salt). Cool, add 2ml of neutral ferric chloride.

Note: carry out blank test.

- Red colour **formic or acetic acid**
- Faint yellow colour **oxalic acid**
- Deep yellow colour **lactic, citric or tartaric**
- Buff precipitate **succinic, benzoic, phthalic, cinnamic acid**
- Violet colour **salicylic acid**

N.B. the neutral ferric chloride test can be done on salicylic acid without neutralization

Confirmatory test:

Formic acid:

i) Reduction of mercuric chloride:

Add 0.5 ml $HgCl_2$ to 0.5 ml of the acid and heat in boiling water bath for 2 minutes. White precipitate of mercurous chloride (Hg_2Cl_2) is formed which is insoluble in dilute hydrochloric acid.

$$HgCl_2 + HCOOH \longrightarrow Hg_2Cl_2 \downarrow$$

white ppt.

ii) Reduction of potassium permanganate:

1- In alkaline medium:

Add gradually 5 ml of 10% sodium carbonate solution to 0.5 ml of acid (till no effervescence). Add 5 drops of dilute solution of $KMnO_4$ (1ml $KMnO_4$ +5 ml H_2O). an immediate decolourization occurs with formation of brown precipitate of manganese dioxide (MnO_2).

$$KMnO_4 + HCOONa \xrightarrow{\text{water}} MnO_2\downarrow + CO_2 + KOH + NaOH$$

2- In acid medium

Add 1 ml of dilute sulphuric acid to 0.5 ml of formic acid. Warm in a water bath, then add 3 drops of dilute solution of $KMnO_4$. An immediate decolourization occurs.

$$KMnO_4 + HCOOH \xrightarrow{\text{sulphuric acid}} MnSO_4 + CO_2 + K_2SO_4 + H_2O$$

Acetic acid

Esterification:

In a dry test tube, add 2-3 drops of conc. sulphuric acid to a mixture of 1 ml of acetic acid and 1 ml of ethanol. Heat in boiling water bath for 2 minutes, pour the content of the test tube on to sodium carbonate solution in a beaker. A fruity odour of ethyl acetate is evolved.

$$CH_3COOH + C_2H_5OH \longrightarrow CH_3COOC_2H_5 + H_2O$$

Lactic acid:

Iodoform test:

To 1 ml of the acid, add 5 ml of iodine solution, then 30 % sod. hydroxide was added dropwise with shaking, fine pale yellow crystals of iodoform is formed

$$CH_3CH(OH)COONa + I_2 / NaOH \longrightarrow Na_2CO_3 + CHI_3$$

Succinic acid:

Fluorescein test:

In a dry test tube place few crystals of resorcinol and equal amount of the acid and moist the mixture with 2 drops of conc. Sulphuric. Heat on small flame till the mixture become red, cool, triturate the mixture with 1 ml water and add excess10% sod. Hydroxide, red colour with green florescence is formed.

Oxalic acid:

i- **Calcium chloride test:**
To 2 ml of the neutral solution of acid, add 1 ml $CaCl_2$ solution. A heavy white ppt. is formed insoluble in acetic acid but soluble in dil. HCl.

ii- **Reduction of acidic potassium permanganate:**
To 2 ml of the acid solution, add 0.5 ml dil. Sulphuric acid. Warm in a water bath then add few drops of dil. KMnO4 solution, decolourization occurs.

Tartaric acid:

i- **Fenton's test:**
To 2 ml of conc. Solution of the acid, add exactly 1 drop of freshly prepared ferrous sulphate solution and 1 drop hydrogen peroxide then add excess dilute sodium hydroxide, violet colour is formed.

ii- **Calcium chloride test**:
It gives white precipitate after scratching.

Citric acid:

i- **Dengie's test:**
To 2 ml of the acid solution (0.2 gm in 2 ml water), add 2 ml of mercuric sulphate. Boil the reaction mixture (the solution should be clear after boiling) and then add few drops of potassium permanganate solution while hot. Immediate decolourization and heavy white precipitate is formed.

ii- **Sodium nitroprusside test:**
In a dry test tube add 1 ml conc. Sulphuric acid to 0.5 g of acid, heat till a yellow solution is formed then cool. Few drops of the yellow solution are diluted with 1 ml water, cool then add drops of sodium nitroprusside solution and excess of 30% NaOH, blood red colour is formed.

Salicylic acid:

i- Esterification:

In a dry test tube, add 2-3 drops of conc. Sulphuric acid to a mixture of 0.2 g of acid and 1 ml of ethanol. Heat in boiling water bath for 2 minutes, pour the content of the test tube on to10% sodium carbonate solution in a beaker. Oil of winter green like odour is evolved.

ii- Phthalene test:

In a dry test tube place few crystals of phthalic anhydride and equal amount of the acid and moist the mixture with 2 drops of conc. Sulphuric. Heat on small flame till the mixture become red, cool, triturate the mixture with 1 ml water and add excess10% sod. hydroxide, pink colour is formed.

Phthalic acid:

i- Phthalene test:

In a dry test tube place 2 drops of phenol and equal amount of the acid and moist the mixture with 2 drops of conc. Sulphuric acid. Heat on small flame till the mixture become red, cool, triturate the mixture with 1 ml water and add excess10% sod. hydroxide, pink colour is formed.

ii- Fluorescein test:

In a dry test tube place few crystals of resorcinol and equal amount of the acid and moist the mixture with 2 drops of conc. Sulphuric acid. Heat on small flame till the mixture become red, cool, triturate the mixture with 1 ml water and add excess10% sod. Hydroxide, red colour with green florescence is formed.

Cinnamic acid:

i- Oxidation with alkaline potassium permanganate:

Dissolve 0.5 g of the acid in 5 ml sod. Carbonate solution then add 2 ml of potassium permanganate solution. Warm the mixture in water bath, brown precipitate is formed and bitter almond odour is evolved.

ii- Bromine water test:

Dissolve 0.5 g of acid in 5 ml sod. Carbonate solution then warm the solution and add bromine water dropwise. Decolourization with fragrant odour of bromostyrene and white emulsion is formed.

Benzoic acid:

There is no specific test for benzoic acid. It is confirmed when all the previous tests for phthalic and cinnamic acids are negative.

Scheme for acetic acid

Physical properties

1. **State**: Liquid
2. **Colour**: Colourless
3. **Odour**: vinegar like odour
4. **Miscibility**: miscible with water
5. **Effect on litmus paper**: acidic

Chemical properties

1- **Na_2CO_3 test**: effervescence it is an acidic compound

2- **Dry ignition:**

i- **Inflammability**: Inflammable with non smoky non luminous flame

ii- **Odour**: vinegar like odour

iii- **Residue**: No residue

it is an aliphatic compound

3- **Soda lime**: vinegar like odour

4- **Sod. Hydroxide 30%**: miscible

5- **Conc. Sulphuric acid**: no eff. and no blackening

It may be acetic acid

6- **Neutral ferric chloride**: red colour

It may be acetic acid

7- **Esterification with ethyl alcohol**: fruity odour of ethyl acetate ester

It is acetic acid

Scheme for citric acid

Physical properties

1. **State**: solid
2. **Colour**: white
3. **Odour**: odourless
4. **Solubility**: soluble in water
5. **Effect on litmus paper**: acidic

Chemical properties

1- **Na_2CO_3 test**: effervescence it is an acidic compound

2- **Dry ignition**:

i- **Inflammability**: Inflammable with non smoky non luminous flame

ii- **Odour**: burnt sugar odour

iii- **Residue**: No residue

it is an aliphatic compound

3- **Soda lime** : burnt sugar odour

4- **Sod. Hydroxide 30%**: soluble

5- **Conc. Sulphuric acid**: effervescence, gas evolved inflammable with blue flame and yellow solution

It may be citric acid

6- **Neutral ferric chloride**: yellow colour

It may be citric acid

7- **Dengie's test**: decolourization and immediate white ppt

8- **Sod. nitroprusside test**: red colour

It is citric acid

Scheme for benzoic acid

Physical properties

1. State: solid
2. Colour: white
3. Odour: odourless
4. Solubility: insoluble in cold water but soluble in hot water and recrystallize on cooling
5. Effect on litmus paper: acidic

Chemical properties

1- Na_2CO_3 test: slight effervescence it is an acidic compound

2- Dry ignition:

i- Inflammability: Inflammable with smoky luminous flame

ii- Odour: aromatic odour

iii- Residue: No residue , it is an aromatic compound

3- Soda lime: aromatic odour

4- Sod. Hydroxide 30%: soluble

5- Neutral ferric chloride: buff ppt.

It may be phthalic, cinnamic or benzoic acid

6- Phthalene test: no pink colour

7- Fluorescence test: no red colour with green fluorescence

It is not phthalic acid

8- Bromine water: no decolourization

9- Alkaline KMnO4 test: no decolourization and no brown ppt

It is not cinnamic acid

The unknown is benzoic acid

Scheme for unknown No.

Identification of aliphatic and aromatic acid salts

The following are examples of salts: sodium formate, potassium formate, sodium acetate, potassium acetate, copper acetate, lead acetate, sodium oxalate, potassium oxalate, ferrous oxalate, potassium sodium tartarate,(Rochelle), potassium hydrogen tartrate, calcium lactate, potassium citrate, sodium citrate, copper citrate, calcium gluconate, sodium benzoate, sodium salicylate, and bismuth salicylate.

Physical properties

1. State: all are solids
2. Colour: all colourless crystalline solids except copper salts are blue and iron salts are yellow.

N.B. acetate and formate salts are hygroscopic.

3. Odour: all are odourless
4. Solubility: all are soluble in cold water except:

potassium hydrogen tartrate, calcium salts are soluble in hot water

lead acetate, oxalate salts are soluble in distilled water

bismuth salicylate, ferrous oxalate are completely insoluble in water

6. Effect on litmus paper:
all are neutral except potassium hydrogen tartrate is slightly acidic

Chemical properties

1- Na_2CO_3 test:
no effervescence it is not an acidic compound

Effervescence it is an acidic compound (potassium hydrogen tartrate).

2- **Dry ignition**:

Dry ignition of carboxylic acid salts causes the organic parts to be consumed leaving an inorganic residue. The residue is either a metal oxide(group I-II or carbonate group IV-V).

i- Inflammability:

a) Inflammable with non-smoky non luminous flame It is salt of aliphatic acid.

b) Inflammable with smoky luminous flame It is salt of aromatic acid.

N.B. some salts are difficult to be ignited e.g. sodium benzoate, sodium oxalate.

ii **- Odour:**

Pungent odour. Formate

Vinegar like odour: acetate

irritant odour oxalate or succinate

burnt sugar odour hydroxyl acids salts as citrate, tartarate, lactate or gluconate.

phenolic odour salicylate

characteristic aromatic odour benzoate

ii- Residue:

- Black residue which give effervescence with dil. HCl

  It is an acid salt and the basic radical from group IV to V

(Ca^{+2}, K^{+}, Na^{+})

- Coloured residue gives no effervescence with dil. HCl

  It is an acid salt and the basic radical from group I to II

  Cu^{+2}(black), iron(brown), B^{+3}, Pb(yellowish orange)

N.B.:

Ca gluconate gives residue with enlargement like popcorn.

To differentiate between aliphatic and aromatic salts, especially those which are difficult to be ignited(if the unknown is soluble in water) add 1 ml of conc. HCl to 2 ml solution of salt.

White precipitate it is salt of aromatic acid

No precipitate it is salt of aliphatic acid

3- **Soda lime** : odour similar to that formed in dry ignition.

4- **Sod. Hydroxide 30%** :

Soluble . potassium hydrogen tartrate

White precipitate of metal hydroxide:

$Ca(OH)_2$ for calcium lactate or gluconate,

$Pb(OH)_2$ for lead acetate.

5- **Concentrated sulphuric acid**:

- Effervescence, gas evolved inflammable with blue flame (CO gas) and no blackening. Oxalate , formate
- Effervescence, gas evolved inflammable with blue flame and yellow solution. Citrate
- Effervescence, gas evolved inflammable with blue flame and blackening lactate , tartarate, or gluconate
- No Effervescence no blackening acetate and succinate
- No action aromatic acid salts

For white soluble salts:

6- Neutral ferric chloride test:

To 1 ml of solution of unknown add 2 drops of ferric chloride,

- Red colour **formate or acetate**
- Faint yellow colour **oxalate**
- Deep yellow colour **lactate, citrate, tartarate or gluconate**
- Buff precipitate **succinate, benzoate, phthalate, cinnamate**
- Violet colour **salicylate**

N.B. in case of lead acetate, a false buff precipitate is formed which on standing for a while white precipitate sediment of lead chloride and a red supernatant layer of ferric acetate.

A- confirmatory test for acidic radicals:

i- For calcium lactate or gluconate salts:

In order to do confirmatory test for lactic or gluconic acid part we have to remove calcium ion first (otherwise it will interfere with the test) as follows:

Add 5 ml of Na_2CO_3 solution 10% to 2 ml of concentrated solution of the salt. Filter the precipitate calcium carbonate and carry out the following confirmatory test on the filtrate.

a- Iodoform test: fine pale yellow crystals. It is lactate salt

b- Molisch test:

Add 2-3 drops of alcoholic alpha naphthol to 1 ml of filtrate and then add 1 ml conc. Sulphuric dropwise on the wall of test tube. A violet ring between the junction of the two layers is formed.

ii- For the other acidic radical:

carry out the same confirmatory test for the acids

B- tests for basic radical:

i- Test for calcium ion(Ca^{+2})

- ammonium oxalate test:

add 1 ml of ammonium oxalate solution to 1 ml unknown solution,

a heavy white ppt. insoluble in acetic acid is formed.

- **Flame test**: brick red colour.

ii- Test for potassium ion(K^+)

- **Sodium cobaltinitrite test**:

In watch glass, add 1 ml of sodium cobaltinitrite solution to 1 ml of unknown solution, a yellow precipitate is formed

- **Flame test**: violet colour

iii- Test for sodium ion(Na^+)

- **Potassium dihydrogen antimonite test**: in a watch glass, add 1 ml of Potassium dihydrogen antimonite solution to 1 ml of unknown solution , a white ppt. is formed.
- **Flame test**: golden yellow colour

iv- Test for lead ion(Pb^{+2})

Add 1 ml potassium chromate to 1 ml of unknown in distilled water, a yellow ppt. soluble in dilute sodium hydroxide.

For coloured and insoluble salts:

To perform neutral FeCl3 test or to make confirmation of acid and basic radicals we have to carry out sodium carbonate fusion test.

7- **Sodium carbonate fusion test**:

In a conical flask, put 1 gm unknown, 4 gm of sodium carbonate and 25 ml water then heat for 20 min. using a funnel(to decrease rate of evaporation , cool, then filter. The filtrate is used to identify the acid radical and precipitate is used to detect the basic radical(double exchange take place).

$$RCOOM + Na_2CO_3 \longrightarrow RCOONa + M_2CO_3$$

M= metal soluble ppt.

A- **Test for acid radical**:

To the filtrate add dilute hydrochloric acid till no more effervescence. Then prepare a neutral solution by addition of ammonia and boil. Test for acid radical by using neutral ferric chloride then do confirmatory tests.

B- **Test for basic radical**:

Test for copper ion(Cu^{+2}):

Dissolve $CuCO_3$ precipitate in dil. Nitric acid and add potassium ferrocyanide, a chocolate brown precipitate is formed.

Test for bismuth ion(Bi^{+3}):

Dissolve the precipitate bismuth carbonate in dil. Nitric acid then add conc. Ammonium hydroxide, a fine gelatinous precipitate of bismuth hydroxide is formed. Filter, add to the precipitate few drops of sodium stannite solution(prepared by adding excess sodium hydroxide to $SnCl_2$solution), ablack ppt. of bismuth metal is formed on the filter paper.

Scheme for roschelle salt

(potassium sodium tartrate)

Physical properties

1. State: solid
2. Colour: white
3. Odour: odourless
4. Solubility: soluble in cold water
5. Effect on litmus paper: neutral

Chemical properties

1- Na_2CO_3 test: no effervescence it is not an acidic compound

2- Dry ignition:

i- Inflammability: Inflammable with non smoky non luminous flame

ii- Odour: burnt sugar odour

iii- Residue: black residue which gives effervescence with dil. HCl

It is aliphatic salt and basic radical is from group IV to V.

3- Soda lime : burnt sugar odour

4- Sod. Hydroxide 30%: no reaction

5- Conc. Sulphuric acid: effervescence and blackening.

It may be lactate or tartarate

6- Neutral ferric chloride: yellow colour

It may be lactate or tartarate

7- Fenton's test: violet colour

8- calcium chloride: white ppt. after scratching.

It is tartrate salt.

8- Test for basic radical:

a- Ammonium oxalate test: no white ppt. it is not calcium ion.

b- Sodium cobaltinitrite test: yellow ppt it is potassium ion

c- Potassium di hydrogen antimonite test: white ppt it is sodium ion

d- Flame test: golden yellow

The unknown is pot. Sod. Tartrate.

Scheme for calcium gluconate

Physical properties

1. State: solid
2. Colour: white
3. Odour: odourless
4. solubility: soluble in hot water
5. Effect on litmus paper: neutral

Chemical properties

1- Na_2CO_3 test: noeffervescence it is not an acidic compound

2- Dry ignition:

i- Inflammability: Inflammable with non smoky non luminous flame

ii- Odour: burnt sugar odour

iii- Residue: black residue which gives effervescence with dil. HCl

It is aliphatic salt and basic radical is from group IVto V.

3- soda lime : burnt sugar odour

4- sod. Hydroxide 30% : white ppt. it may be calcium salt

5- conc. Sulphuric acid: effervescence and blackening.

It may be lactate or tartarate or gluconate

6- neutral ferric chloride: yellow colour

It may be lactate or tartarate or gluconate

7- molish's test: violet ring it is gluconate salt

9- Test for basic radical:

a- Ammonium oxalate test: heavy white ppt. it is calcium ion.

b- Flame test: brick red colour it is calcium ion

The unknown is calcium gluconate

Scheme for sodium salicylate

Physical properties

1. State: solid
2. Colour: white
3. Odour: odourless
4. Solubility: soluble in cold water
5. Effect on litmus paper: neutral

Chemical properties

1- Na_2CO_3 test: no effervescence it is not an acidic compound

2- Dry ignition:

i- Inflammability: Inflammable with smoky luminous flame

ii- Odour: phenolic odour

i- Residue: black residue which gives effervescence with dil. HCl

It is salt of aromatic acid and basic radical is from group IV to V.

3- Soda lime : phenolic odour

4- Sod. Hydroxide 30%: no reaction

5- Neutral ferric chloride: violet colour It may be salicylate salt

6- Esterification with ethyl alcohol: oil of winter green like odour

7- Phthalene test: pink colour it is salicylate salt

10- Test for basic radical:

a- Ammonium oxalate test: no white ppt. it is not calcium ion.

b- Sodium cobaltinitrite test: no white ppt it is not potassium ion

c- Potassium di hydrogen antimonite test: white ppt it is sodium ion

d- Flame test: golden yellow

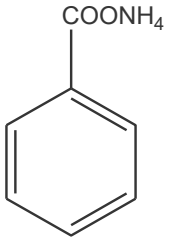
The basic radical is sodium

The unknown is sodium salicylate.

Scheme for unknown No.

Identification of aliphatic and aromatic ammonium salts

Ammonium formate ammonium acetate ammonium oxalate



Ammonium benzoate

Physical properties

1. State: crystalline solids.
   (amm.formate and amm.acetate are hygroscopic solids)
2. Colour: all are white
3. Odour: odourless except amm.formate and amm.acetate have ammonia odour(hygroscopic salts)
4. Solubility in distilled water: soluble in cold water
5. Effect on litmus paper: neutral

Chemical properties

1- Na_2CO_3 test: no effervescence it is not an acidic compound

2- Dry ignition:

i- Inflammability:

- Inflammable with non-smoky non luminous flame

It is an aliphatic compound.

- Inflammable with smoky luminous flame

It is an aromatic compound.

ii- Odour: ammonia odour

ii- Residue: no residue

3- Soda lime: ammonia odour **it may be ammonium salt**.

4- Sod. Hydroxide 30%: ammonia odour it is an ammonium salt.

5- Conc.sulphuric acid: as the scheme of acids

6- Neutral ferric chloride: as the scheme of acids

7- **confirmatory test for acidic radical:** as the scheme of acids

8- **Test for ammonium radical:**

$CaCl_2$ test:

To 1 ml of solution of unknown, add 1 ml calcium chloride solution, a white precipitate is formed.

Scheme for unknown No.

Scheme for ammonium oxalate

Physical properties

1- State: solid.

2. Colour: white

3. Odour: odourless

4. Solubility in distilled water: soluble in cold water

5. Effect on litmus paper: neutral

Chemical properties

1- Na_2CO_3 test: no effervescence it is not an acidic compound

2- Dry ignition:

i- Inflammability: Inflammable with non-smoky non luminous flame

ii- Odour: ammonia odour

ii- Residue: no residue

it is an aliphatic compound and may be ammonium oxalate

3- Soda lime : ammonia odour

4- Sod. Hydroxide 30%: ammonia odour it is an ammonium salt.

5- Conc. sulphuric acid: effervescence and no blackening

May be ammonium formate or oxalate

6- Neutral ferric chloride: yellow colour may be ammonium oxalate

7- Calcium chloride test: heavy white ppt

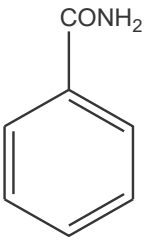
8- Oxidation with alkaline potassium permanganate: decolourization and brown ppt

9- oxidation with acidic potassium permanganate: decolourization occure

The unknown is ammonium oxalate

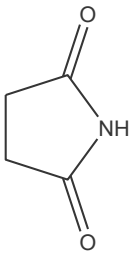
Scheme for unknown No.

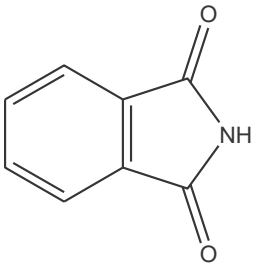
Identification of acid amides and imides



NH_2CONH_2 **CH_3CONH_2**

Urea (carbamide) **acetamide** **benzamide**





succinimide **phthalimide**

Physical properties

2- State: all are solids (acetamide is hygroscopic).

2. Colour: white

3. Odour: odourless except acetamide is mice like odour.

4. Solubility: all are soluble in cold water except benzamide and phthalimide which are soluble in hot water.

5. Effect on litmus paper: all are neutral except phthalimide and succinimide are slightly acidic.

Chemical properties

1- Na_2CO_3 test:

no effervescence it is not an acidic compound

slight effervescence(acid imide) it is an acidic compound

2- Dry ignition:

i- Inflammability:

- Inflammable with non-smoky non luminous flame it is an aliphatic compound
- Inflammable with smoky luminous flame it is an aromatic compound

ii- Odour: mice like odour acetamide

irritant odour succinimide

aromatic odour benzamide and phthalimide

ammonia odour urea

iii- Residue: no residue

N.B (during dry ignition of urea, it melts, gives ammonia odour and then solidifies leaving white residue of biuret).

3- soda lime: ammonia odour on hot. It is an acid imide or acid amide.

4-sodium hydroxide 30%: ammonia odour on hot.

It is an acid imide or acid amide.

5- Conc.sulphuric acid: no reaction

6- Neutral ferric chloride: no reaction

7- Hydrolysis with 30% NaOH:

In a conical flask, add 20 ml of 30% NaOH to 1 gm of the unknown. Heat under reflux for 20 minutes, cool then acidified with concentrated hydrochloric acid and cool again.

a- If effervescence with conc. HCl: it may be urea

b- If a precipitate is formed(aromatic acid), filter then wash with water and carry out neutral ferric chloride test on the neutral solution, buff precipitate is formed the unknown may be benzamide or phthalimide.

c- If no effervescence and no precipitate. The unknown may be acetamide or succinimide.

i- For acetamide:

The acidic solution after hydrolysis is distilled. Collect about 1 ml of acetic acid then carry out the following tests:

1- neutral ferric chloride on neutral solution red colour

2- esterification with ethyl alcohol fruity odour

ii- for succinimide:

carry out neutral ferric chloride test, buff ppt. is formed

confirmatory test:

1- succinimide:

fluorescein test on the original solid unknown.

2- benzamide:

test for benzoic acid on the precipitate formed upon acidification of the product of hydrolysis. Negative tests for phthalic and cinnamic acid

3- urea :

a- biuret test:

when urea is heated, ammonia is evolved giving biuret which reacts with copper sulphate in the presence of sodium hydroxide to give a purple or rose colour.

In a dry test tube, few crystals of urea are heated(it melts and solidify give white residue). Cool, dissolve the residue in 1 ml of sodium hydroxide solution(10%) and then add few drops of very dilute solution of copper sulphate(1 ml $CuSO_4$+ 10 ml water). A purple colour is formed.

b- Conc. Nitric acid test

Add 1 ml conc. nitric acid to 1 ml conc. solution of urea. A white ppt. of urea nitrate ($H_2NCONH_2.HNO_3$) is formed.

c- Oxalic acid test

Add 1 ml of oxalic acid solution to 1 ml of conc. solution of urea. A white ppt. of urea oxalate is formed.

Scheme for urea

Physical properties

1- State: solid

2- Colour: white

3- Odour: odourless

4- Solubility: soluble in cold water

5- Effect on litmus paper: neutral

Chemical properties

1- Na_2CO_3 test: no effervescence it is not an acidic compound

2- Dry ignition:

i- Inflammability: Inflammable with non-smoky non luminous flame

ii- Odour: ammonia odour

Residue: melts, gives and then solidifies leaving white residue

3- Soda lime: ammonia odour on hot.

4-Sodium hydroxide 30%: ammonia odour on hot. It is may be urea

5- Conc.sulphuric acid: no reaction

6- Neutral ferric chloride: no reaction

7- Hydrolysis with 30% NaOH: effervescence with conc. HCl: it may be urea

8- Biuret test: purple or rose colour it may be urea

9- Conc. Nitric acid test: white ppt. of urea nitrate

10- Oxalic acid test: white ppt. of urea oxalate

The unknown is urea

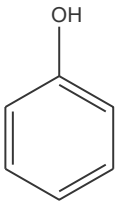
Scheme for unknown No.

Identification of phenol

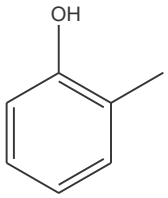
Phenols are compounds which have one or more hydroxyl groups attached directly to benzene ring.

A) Classification:

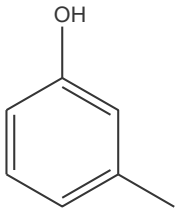
1- **Monohydric phenols**: contain one OH group



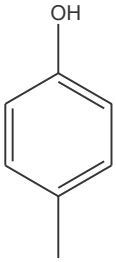
Phenol



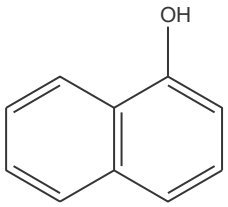
o-cresol



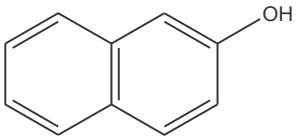
m-cresol



p-cresol

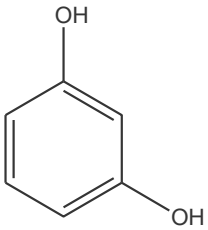


alpha naphthol

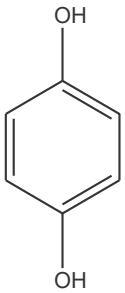


beta naphthol

2- **Dihydric phenols**: contain two OH groups



Resorcinol



hydroquinone

Physical properties

1- State:

Phenol, o-cresol and p-cresol are solids of low m.p (may be liquids at room temp), m-cresol is liquid.

Resorcinol, hydroquinone, alpha naphthol and beta naphthol are solids.

2- Colour:

In a pure form they are colourless crystalline solid but on standing due to auto-oxidation the compound acquire distinct colouration.

3- Odour: phenolic odour

4- Solubility or miscibility :

- Phenol, o-cresol and p-cresol are partially soluble or miscible with water.
- m-cresol is partially miscible with water.
- alpha naphthol and beta naphthol are insoluble in cold water and form oil globules on heating
- Resorcinol, hydroquinone are soluble in cold water

5- Effect on litmus paper: slightly acidic.

Chemical properties

1- Na_2CO_3 test: no effervescence acidic group is absent

2- Dry ignition:

i- Inflammability: Inflammable with smoky luminous flame

ii- Odour: phenolic odour

ii- Residue: no residue it is an aromatic phenolic compound

3- soda lime: phenolic odour. it is an aromatic phenolic compound

4-sodium hydroxide 30%: if soluble it is monohydric phenol

If soluble with darkening it is dihydric phenol

5- Conc. sulphuric acid: no characteristic reaction

6- Neutral ferric chloride: to a dil. solution of the unknown (1 drop + 5 ml water) add 2 drops of $FeCl_3$

- phenol, o,m,p-cresols and resorcinol give violet colour.
- Hydroquinone give red colour then green shiny crystals which with excess $FeCl_3$ give yellow solution.
- Alpha and beta naphthol ⟶ negative

7- Bromine water:

To a dil. solution of unknown (1 drop + 5 ml water) add 1-2 ml of bromine water:

- phenol, o,m,p-cresols and resorcinol result in decolourization with formation of white ppt.
- Hydroquinone gives red colour then green shiny crystals and then yelloW solution.
- Alpha and beta naphthol ⟶ decolourization only

8- Azodye:

a- in a test tube, place 1ml 20%$NaNO_2$

b- in second test tube add one drop aniline+ 1ml conc HCl + 2ml water

c- in third t.t add 2drops of unknown+ 3ml 10%NaOH

cool the three test tubes in an ice bath. Then add slowly the first to the second and the second to the third.

- phenol, o,m -cresols and resorcinol give orange to red ppt.
- Hydroquinone and p-cresol ……. negative
- Alpha naphthol gives reddish brown ppt.
- Beta naphthol ⟶ scarlet red ppt.

9- Phthalene test:

In a dry test tube, place equal amounts of the unknown and phthalic anhydride then add 2-3 drops conc. Sulphuric. Fuse the reaction mixture, cool, and add 1 ml of water and excess 10%NaOH.

- phenol,o -cresol red or pink colour
- m –cresol bluish purple colour
- resorcinol no characteristic odour
- Alpha naphthol green or blue colour
- beta naphthol faint green colour with slight blue fluorescence
- Hydroquinone purple colour

10- **Colouration with $CHCl_3$ and 30%NaOH**:

Place 0.2 gm of the unknown, 1 ml 30%NaOH, and 1 ml $CHCl_3$ in a test tube and heat in a water bath.

- phenol,p -cresol negative
- o,m –cresol and resorcinol red colour in the aqueous layer.
- Alpha naphthol and beta naphthol blue colour fading to green
- Hydroquinone brown colour

Scheme for unknown No.

Carbohydrates

A) Classification

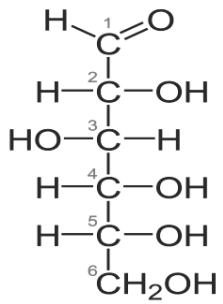
They are classified according to number of monosaccharide units present in the molecules:

1- **Monosaccharides**:- consists of unit of monosaccharide e.g. glucose fructose, galactose.
2- **Disaccharide**:- consists of two units of monosaccharides combined together e.g. maltose, lactose, sucrose
3- **Polysaccharides**:- consists of more than ten units of monosaccharides e.g. starch.

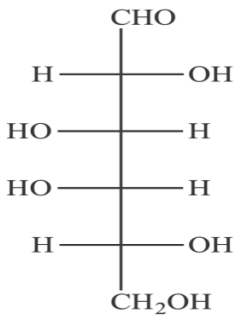
Monosaccharides are classified according to functional groups:

a- Aldoses having free aldehydic group as glucose.
b- Ketoses having free ketonic group as fructose

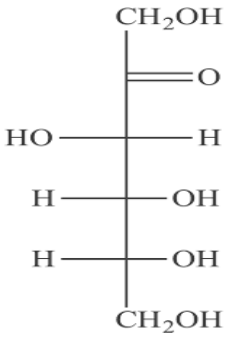
Both are hexoses containing six carbon atoms and having reducing properties.



Glucose



galactose



fructose

Disaccharides are classified as:

1- **Non reducing disaccharides** :
In which two molecule are linked through their two carbonyl groups e.g. sucrose.
2- **Reducing disaccharides**:
In which only one carbonyl group is involved in this linkage e.g.

Maltose and lactose

Maltose = 2 glucose	reducing disaccharide
Lactose = glucose + galactose	reducing disaccharide
Sucrose = glucose + fructose	non-reducing disaccharide

Polysaccharides e.g. starch which is polymer of glucose and is non-reducing

Physical properties

1- State: all are solid

2- Colour: white

3- Odour: odourless

4- Solubility: all are soluble in cold water except starch which is insoluble in cold water and form gelatinous matter on heating

5- Effect on litmus paper: all are neutral

Chemical properties

1- Na_2CO_3 test: no effervescence it is not an acidic compound

2- Dry ignition:

i- Inflammability: Inflammable with non-smoky non luminous flame

ii- Odour: characteristic burnt sugar odour

iii- Residue: melts, froth, chars and leave black residue which give no effervescence with dil. HCl.

3- Soda lime: burnt sugar odour it may be carbohydrate.

4 -Sodium hydroxide 30%:

if yellow solution turned to brown with caramel like odour by heating.

It may be monosaccharide or reducing disaccharide.

If yellow solution only

It may be non-reducing disaccharide or poly saccharide

5- Conc. sulphuric acid: effervescence and charring it may be carbohydrate

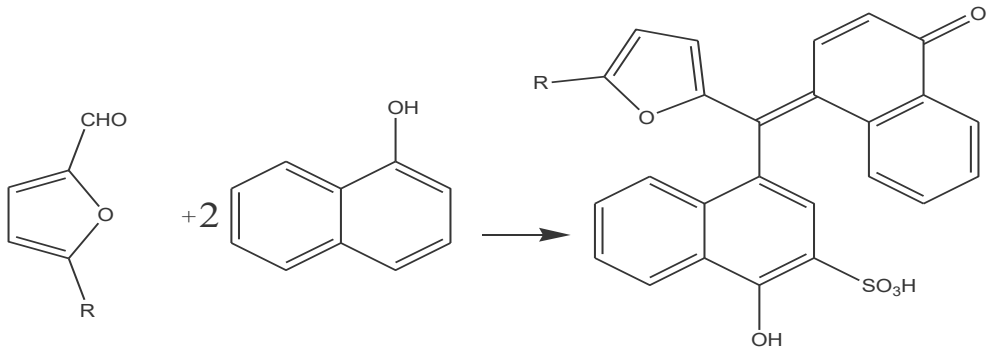
6- Neutral ferric chloride: no specific reaction

6- Molish test:

On 2 ml of solution or suspension of unknown, add 3-5 drops of alcoholic beta naphthol followed by 1-2 ml of conc. Sulphuric on the wall of the test tube to give two layer.

If violet ring is formed at junction between the two layer. It is carbohydrate

The carbohydrate is dehydrated by mineral acids to a furfural derivative, which condenses with beta naphthol to give violet colour.



7- Fehling reduction:

On 2 ml of solution or suspension of unknown, add equal volumes of fehling A and B. place the test tube in a boiling water bath for 2 min.

- If any change in colour

  It may be monosaccharide or reducing disaccharide
- If no change in colour
- It may be nonreducing disaccharide(sucrose) or poly saccharide(starch).

If Fehling is positive: carry out barfoed test.

8- Barfoed reduction:(barfoed reagent =Cu acetate /acetic acid)

Take equal amounts of unknown solution and barfoed reagent in a test tube and place the test tube in a boiling water bath for only 2 min.

- If red or brown ppt develops

  It may be monosaccharide(glucose and fructose)

- If no red or brown ppt. is obtained.

  It may be reducing disaccharide(lactose and maltose).

9- Osazone test:

Prepare a solution containing 0.6 gm phenylhydrazine hydrochloride and 0.3 gm sodium acetate in 2 ml water then add 2 ml conc. solution of sugar (0.25 gm). Place the test tube in a boiling water bath for 15-30 min.

- If yellow ppt. is formed while hot.

  It may be momosaccharide

  ❖ Microscopical examination : needle crystals it may be glucose or fructose

- If yellow ppt. is formed after cooling

  It is non-reducing disaccharide

  ❖ Microscopical examination:

  1- Plate- like crystals. Maltose

  2- Clusters of needle lactose

10- Resorcinol test (to differentiate between glucose and fructose)

1 ml of unknown is added to 2 ml of dil HCl and one crystal of resorcinol then heat in boiling water bath for 3 min.

- If wine red colour it is fructose.

- If no wine red colour it is glucose

If fehling is negative:

a- Hydrolysis with conc. HCl:
In a test tube, place 1 gm of solid unknown, then add 5 ml conc HCl then heat in a water bath for 20 min. then cool and neutralize with 30 % NaOH and carry out the following test on the hydrolytic products:
  a- Fehling test: change in colour
  b- Barfoed test: red ppt
  c- Osazone test: yellow ppt. is formed while hot and needle crystals are formed
  The hydrolytic product is glucose and the original product is starch or sucrose

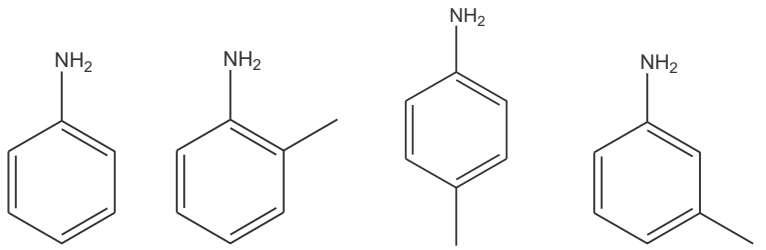
b- Iodine test:
to dil. Suspension of unknown add one drop of iodine solution

- If blue colour starch
- If no change in colour sucrose

Scheme for unknown No.

Identification of amines

1- Aromatic amines



Aniline o-toluidine p-toluidine m-toluidine

Physical properties

1- State :

- ❖ Aniline, o- and m-toluidine are liquids
- ❖ p-toluidine is solid

2- colour:

- ❖ Aniline, o- and m-toluidine are colourless liquid when pure. The change in colour due to oxidation
- ❖ p-toluidine is yellowish brown.

3- Odour: all have fishy odour

4- Solubility or miscibility:

- ❖ Liquids are immiscible and heavier than water.
- ❖ Solids are insoluble in water and form oil globules on heating

5- Action on litmus paper:

All amines have basic character.

Chemical properties

1- Sodium carbonate test: no effervescence it is not an acidic compound

2- Dry ignition

Inflammability: inflammable with smoky luminous flame

Odour: fishy odour

Residue: no residue it is an aromatic compound

3- Soda lime test: fishy odour

4- 30% NaOH: no reaction

5- Conc. H_2SO_4:

In a dry test tube, place one drop of unknown and one drop of conc. Sulphuric acid, a white ppt. is formed which is soluble in water and forms oil droplets on addition of dil NaOH.

It may be aromatic amine

6- Azo dye test:

d- in a test tube, place 1ml 20%$NaNO_2$

e- in second test tube add one drop unknown+ 1ml conc HCl + 2ml water

f- in third t.t add few crystal of beta naphthol + 5ml dil NaOH solution.

1- Diazotization

Cool in an ice bath to 0 °C, then add the first test tube to the second Clear diazonium salt solution is formed.

2- Coupling with beta naphthol

Add the formed diazonium salt solution to the third test tube scarlet red ppt. is formed. It is primary aromatic amine

7- **Reaction with oxidizing agent**:

a- **With bleaching powder**(calcium hypochloride):

On a very dilute solution of the unknown (1 drop or 1 crystal in 10 ml water)add few drops of bleaching powder(after shaking the bottle)

- ❖ Aniline give purple colour change in to brown.
- ❖ o-and m-toluidine give immediate brown colour.
- ❖ p-toluidine give a yellowish brown colour

b- **acidic FeCl3**:

to 2 drops or 2 crystals of unknown, add 3 ml dil. HCl and 0.5 drop of FeCl3 (warm gently if no colouration appears).

- ❖ Aniline give a pale green colour, changing into a dark green
- ❖ o-toluidine give a green colour changing into bluish green
- ❖ m-toluidine , no change in colour
- ❖ p-toluidine gives a reddish brown colour.

II- Aliphatic amines
e.g. hexamine

Physical properties

1- State: solid
2- colour: white
3- Odour: fishy
4- Solubility: soluble in cold water
5- Action on litmus paper: basic

Chemical properties

1- Sodium carbonate: no effervescence it is not aromatic compound
2- Dry ignition

- Inflammability: inflammable with non-smoky non luminous flame, sparks with blue candle shaped flame till complete exhaustion
- Odour: fishy
- Residue: no residue

3- Soda lime: fishy odour
4- 30% NaOH: fishy odour
5- Conc. H_2SO_4:

In a dry test tube, place few crystal of unknown and 1 ml conc. sulphuric warm gently, a pungent formalin odour is obtained.

6- **$FeCl_3$**: no colour

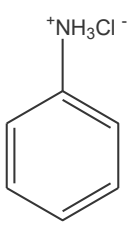
7- **HNO_2 test** :

Dissolve 0.5 gm of hexamine in 2 ml conc. HCl, then add 2 ml of 20% solution of $NaNO_2$ and cool in ice, a strong effervescence is observed with the separation of crystals of nitroso derivative.

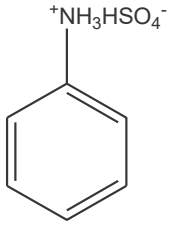
8- **Resorcinol or salicylic acid test**:

In dry test tube place equal amounts of salicylic acid or resorcinol and hexamine. then add few drops of conc. Sulphuric and warm. A wine red colour is formed.

Identification of amine salts



Aniline hydrochloride



aniline sulfate

Physical properties

1- State: solid

2- colour: Aniline hydrochloride is greyish white

aniline sulfate is yellowish white.

The changes according to purity of the compound.

3- Odour: slight fishy odour

4- Solubility: soluble in cold water

5- Action on litmus paper: acidic

Chemical properties

1- Sodium carbonate:
effervescence with formation of oily globules and fishy odour
it is an acidic compound and may be an amine salt.

2- Dry ignition

- Inflammability: inflammable with smoky luminous flame.

- Odour: fishy odour

- Residue: no residue

It is an aromatic compound may be amine salt

3- Soda lime: fishy odour

4- 30% NaOH:

Add 2 ml 30% NaOH to 0.5 gm of solid unknown, shake. An oily layer with a fishy odour is obtain

It may be an amine salt.

5- Azo dye test: scarlet red ppt. it is primary aromatic amine salt

5- $FeCl_3$:

Add few drops of $FeCl_3$ to solution of the unknown , apale green colour is formed, changing to dark green by heating

Aniline is present.

6- Bleaching powder:

Add few drops of bleaching powder to a dilute solution of the unknown , a transient purple colour is formed which turns to brown.

The basic radical is aniline

7- Test for acidic radical

a- With $BaCl_2$ /conc.HCl

To a solution of the unknown in distilled water add 1 ml conc. HCl and 1 ml $BaCl_2$, a white ppt is formed with aniline sulfate.

b- **With $AgNO_3$/conc. HNO_3**:

To a solution of the unknown in distilled water add 1 ml conc. HNO_3 and 1 ml $AgNO_3$, a white ppt. is formed with aniline hydrochloride

Scheme for unknown No.