

# Unit 1. The Chemistry of Aromatic Compounds

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## Learning Objectives

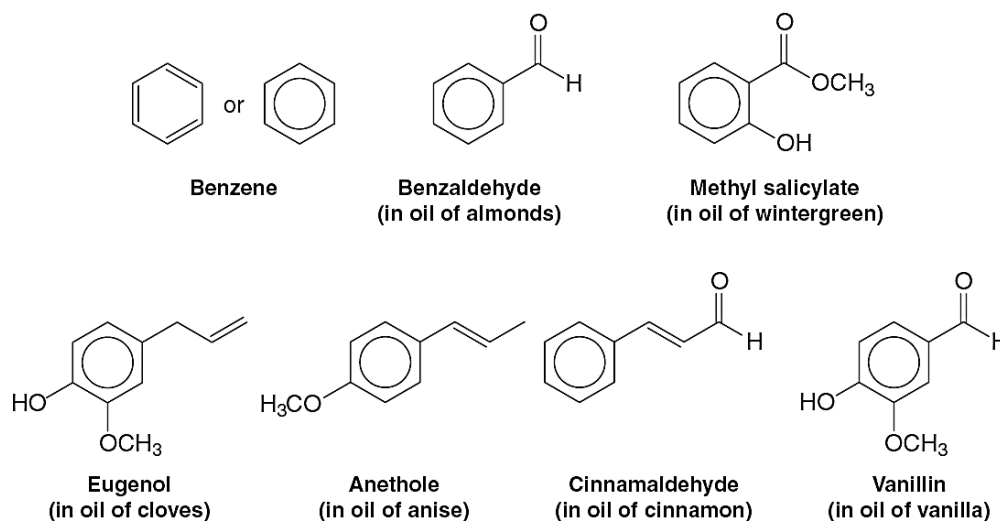
After completing this unit the student should be able to:

- Understand the concept of the aromaticity, antiaromaticity and nonoaromaticity
- recognize the structural features that cause a compound to be aromatic, antiaromatic and nonaromatic.
- know about the effect of aromaticity on the physical and chemical properties of the compound.

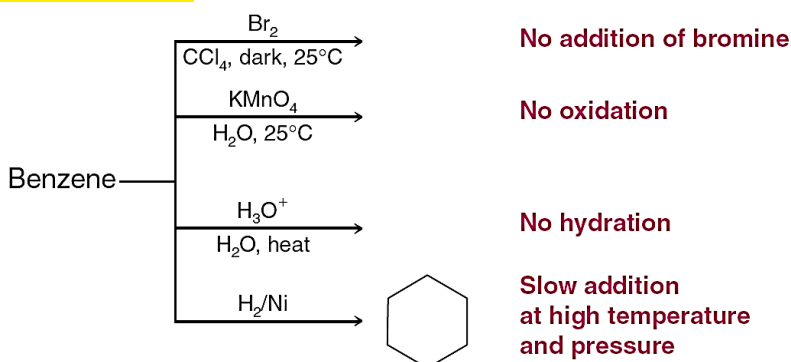
- discuss the mechanisms of electrophilic and nucleophilic substitution in aromatic compounds including heteroaromatic compounds.
- classify various functional groups as either electron-donating or withdrawing and predict their effects on the rates of electrophilic aromatic substitution (EAS) reactions,
- explain the factors that cause meta- versus *ortho/para*- substitution in EAS reactions, and predict the course of nucleophilic aromatic substitution (S<sub>N</sub>Ar) reactions based on mechanistic considerations.
- Explain the structure and chemistry of the heterocyclic systems, furan, thiophene and pyrrole as five-member ring heterocyclic compounds, as well as pyridine (six-member ring heterocyclic compound).
- change functional groups from one to another.
- describe the usefulness of diazotization of aromatic amines in synthetic chemistry.

## Aromatic Compounds

Early in the history of organic chemistry (late 18th, early 19th century) a class of compounds were isolated which had a distinct odour (aroma). These were typically found in oils produced by trees and other plants. Hence these compounds were called “**aromatic**”, for example **benzaldehyde** (from cherries, peaches, and almonds), **toluene** (from Tolu balsam), and **benzene** (from coal distillate). Although benzene and toluene are not particularly fragrant compounds themselves, their origins in aromatic plant extracts led them and compounds related to them to be classified as *aromatic compounds*.



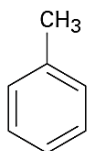
Later it was found that these compounds differed from most other organic compounds in their chemical behaviour. Aromatic compounds were distinguished from **aliphatic compounds**, with higher hydrogen-to-carbon ratios. **These compounds, though are highly unsaturated, are very stable. Unlike alkenes, they do not undergo addition, oxidation and reduction reactions. Today the classification of organic compounds as aromatic is not based on aroma but on structure and reactivity of the compounds. Aromatic compounds, unlike acyclic and cyclic dienes, do not show addition and oxidation reactions:**



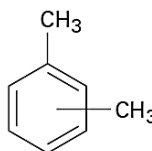
The term '**arene**' is used to describe aromatic hydrocarbons, by analogy with alkane, alkene, and alkyne. The main sources of simple aromatic hydrocarbons are coal and petroleum. Thermal breakdown of coal at 1000°C in the absence of air produces *coal tar*. Fractional distillation of coal tar yields benzene, xylene, phenanthrene, etc.



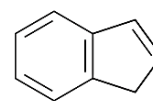
**Benzene**  
(bp 80 °C)



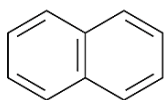
**Toluene**  
(bp 111 °C)



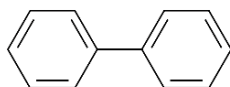
**Xylene**  
(bp: ortho, 144 °C;  
meta, 139 °C; para, 138 °C)



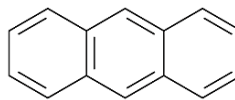
**Indene**  
(bp 182 °C)



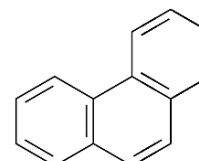
**Naphthalene**  
(mp 80 °C)



**Biphenyl**  
(mp 71 °C)



**Anthracene**  
(mp 216 °C)



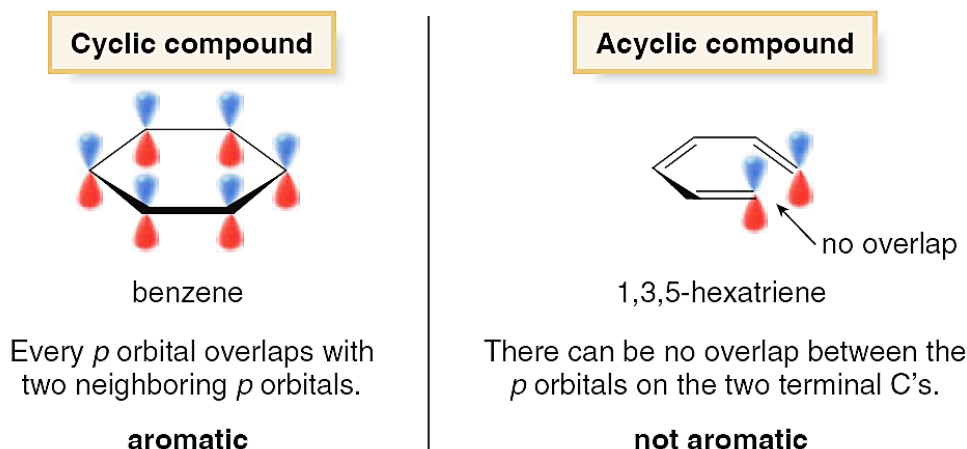
**Phenanthrene**  
(mp 101 °C)

## 1.1. Aromaticity

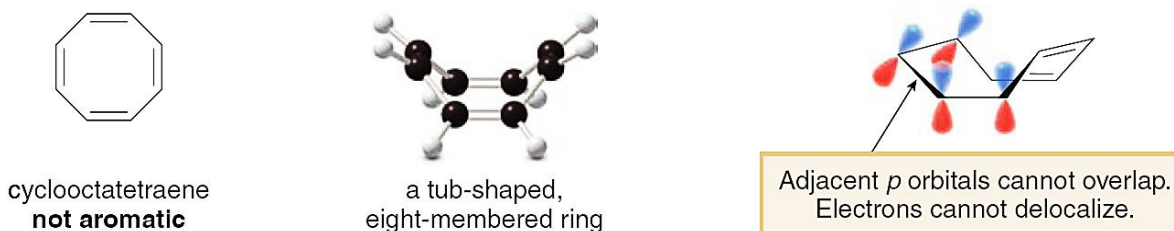
In 1931 Erich Huckel's realized that an aromatic compound must have an odd number of pairs of electrons. He stated that the cyclic compounds containing  $(4n+2)$  delocalized  $\pi$  electrons exhibit aromatic character; where  $n$  is zero or a whole number. Hence the system containing 2, 6, 10, 14 and so on, delocalized  $\pi$  electrons show aromatic behaviour.

For a compound to be aromatic, four following structural criteria must be satisfied simultaneously:

- A molecule must be **cyclic**. Each  $p$  orbital must overlap with  $p$  orbitals on two adjacent atoms. For example, the  $p$  orbitals on all six carbons of benzene continuously overlap, so benzene is aromatic. 1,3,5-Hexatriene has six  $p$  orbitals, too, but the two on the terminal carbons cannot overlap with each other, so **1,3,5-hexatriene is not aromatic**.

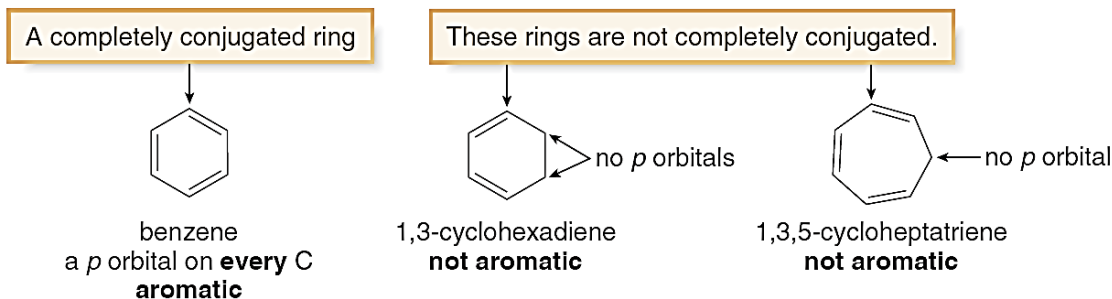


- b. The molecule must be planar. All adjacent  $p$  orbitals must be aligned so that the  $\pi$  electron density can be delocalized. For example, cyclooctatetraene resembles benzene in that it is a cyclic molecule with alternating double and single bonds. Cyclooctatetraene is tub shaped, however, **not planar**, so overlap between adjacent  $\pi$  bonds is impossible.



**Cyclooctatetraene, therefore, is not aromatic**, so it undergoes addition reactions like those of other alkenes.

- c. The molecule must be completely conjugated. It means an aromatic compound must have a  $p$  orbital on every atom.



- d. The molecule should follow Huckel's rule, that is, it should contain  $(4n+2)$  number of delocalized  $\pi$  electrons where  $n$  is zero or a whole number. The compounds which are cyclic, planar and completely conjugated but contain  $4n$   $\pi$  electrons are especially unstable and are called **antiaromatic**.

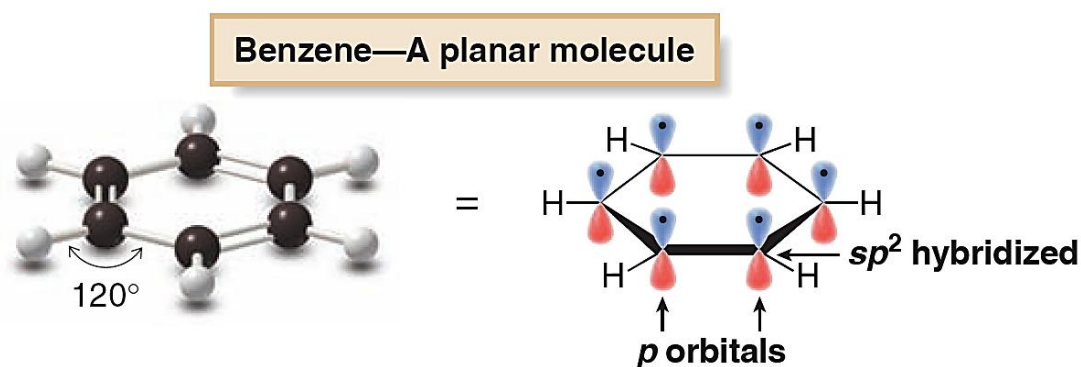
Thus cyclic compounds can be classified into three categories:

- (i) **Aromatic:** A cyclic, planar, completely conjugated compound with  $4n + 2 \pi$  electrons.
- (ii) **Antiaromatic:** A cyclic, planar, completely conjugated compound with  $4n \pi$  electrons.
- (iii) **Not aromatic (or non-aromatic):** A compound that lacks one (or more) of the four requirements to be aromatic or antiaromatic.

## Aromaticity in Benzene and other cyclic systems

### A. Benzene:

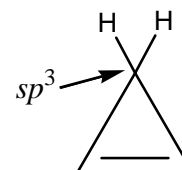
- (i) It is cyclic.
- (ii) It is planar.
- (iii) It **exhibits continuous delocalisation**. All the carbons in cyclic system are  $sp^2$  hybridized and thus,  $p$  orbital is available on all carbons for delocalisation.
- (iv) The number of delocalized  $\pi$  electrons is 6 which follows Huckel's rule of  $(4n+2)$   $\pi$  electrons. Here  $n$  is one.



**Thus, benzene is aromatic as it satisfies all the conditions of aromaticity simultaneously.**

### B. Cyclopropene:

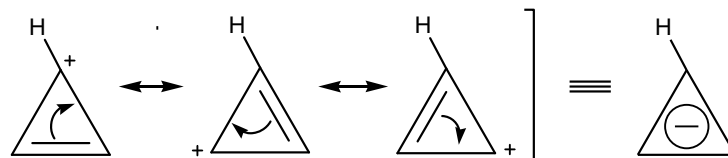
- (i) It is cyclic.
- (ii) It is planar.
- (iii) The number of delocalized  $\pi$  electrons is 2 which follows Huckel's rule of  $(4n+2)$   $\pi$  electrons. Here  $n$  is zero.
- (iv) However, it **does not exhibit continuous delocalisation**. One of the carbons in cyclic system is  $sp^3$  hybridized and thus,  $p$  orbital is not available on that carbon for delocalisation.



**Hence, cyclopropene is not aromatic (or non-aromatic).**

### Cyclopropenyl cation:

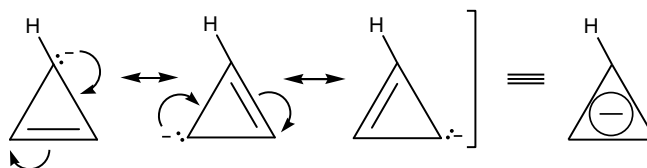
- (i) It is cyclic.
- (ii) It is planar.
- (iii) The number of delocalized  $\pi$  electrons is 2 which follows Huckel's rule of  $(4n+2)$   $\pi$  electrons. Here  $n$  is zero.
- (iv) It exhibits continuous delocalisation. All the carbons in cyclic system are  $sp^2$  hybridized and thus,  $p$  orbital is available for delocalisation.



**Hence, cyclopropenyl cation is aromatic, as all the conditions are simultaneously satisfied.**

#### Cyclopropenyl anion:

- (i) It is cyclic.
- (ii) It is planar.
- (iii) It exhibits continuous delocalisation. All the carbons in cyclic system are  $sp^2$  hybridized and thus,  $p$  orbital is available for delocalisation.
- (iv) However, the number of delocalized  $\pi$  electrons is 4. Lone pair of electrons participate in delocalization with  $\pi$  electrons of the ring resulting the total number of  $\pi$  electrons to 4, which does not follow Huckel's rule of  $(4n+2)$   $\pi$  electrons.



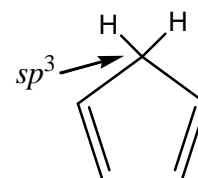
**Therefore, cyclopropenyl anion is not aromatic; it is antiaromatic.**

#### C. Cyclobutadiene:

Cyclobutadiene is cyclic and planar. It exhibits continuous delocalisation. All the carbons of the cyclic system are  $sp^2$  hybridized, and thus  $p$  orbitals are available for delocalization. However, it does not follow  $(4n + 2)$  Huckel's rule, as the number of delocalized  $\pi$  electrons is 4. Thus, cyclobutadiene is not aromatic; it is antiaromatic.



#### D. Cyclopentadiene:



Like cyclopropene, cyclopentadiene is also not aromatic. It is cyclic and planar. However, one of the carbons in cyclic system is  $sp^3$  hybridized, and thus the  $p$  orbital is not available on that carbon for delocalization. So the continuous delocalization is broken. In addition, it does not obey  $(4n + 2)$  Huckel's rule as the number of  $\pi$  electrons is 4.

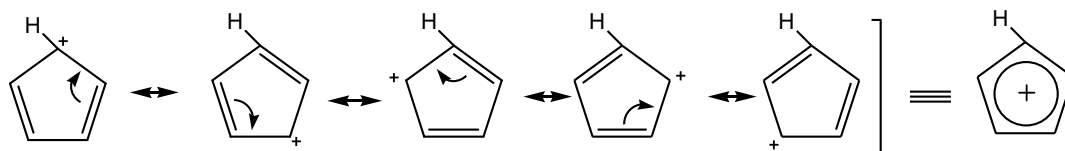
### Cyclopentadienyl anion:

Cyclopentadienyl anion is aromatic as it follows all conditions of aromaticity simultaneously. It is cyclic, planar and exhibits continuous delocalisation as all the carbons of the ring are  $sp^2$  hybridized and have a  $p$  orbital for overlapping with the neighbouring carbons. It also obeys Huckel's rule as the number of  $\pi$  electrons is 6 as the lone pair of electrons participate in delocalization with  $\pi$  electrons of the ring. So the total number of  $\pi$  electrons is 6. Cyclopentadiene is more acidic than many hydrocarbons because its conjugate base (i.e. cyclopentadienyl anion) is aromatic.



### Cyclopentadienyl cation:

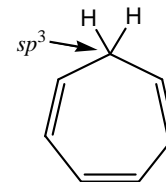
Cyclopentadienyl cation is cyclic, planar and exhibits continuous delocalization of  $p$  electrons. However, the number of  $p$  electrons is 4, which does not obey the Huckel's rule. Therefore, cyclopentadienyl cation is not aromatic; rather it is antiaromatic.



### E. Cycloheptatriene:

Cycloheptatriene is cyclic, planar and follows Huckel's rule as it contains six delocalized  $\pi$  electrons. However, as in cyclopropene and cyclopentadiene, one of the carbons in the ring in cycloheptatriene is  $sp^3$  hybridized which interrupts the continuous delocalization of  $\pi$  electrons in the ring.

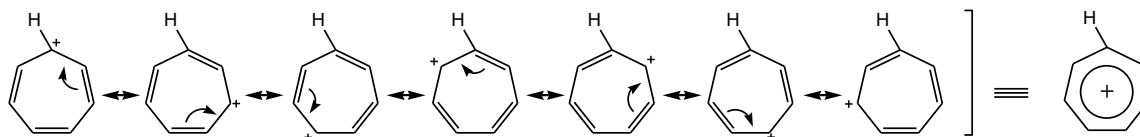
Hence, **cycloheptatriene is not aromatic.**



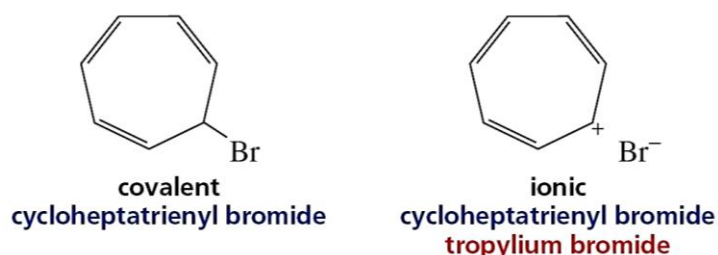
### Cycloheptatrienyl cation (Tropylium ion):



Cycloheptatrienyl cation satisfies all conditions of aromaticity. It is cyclic, planar, exhibits continuous delocalization of  $\pi$  electrons as well as it obeys Huckel's rule of  $(4n + 2)$   $\pi$  electrons (i.e. 6) in the ring. Therefore, **it is aromatic**.

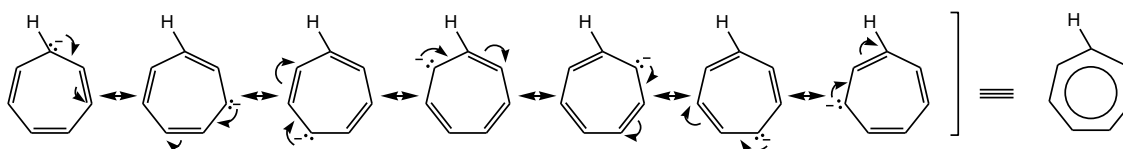


- *Cycloheptatrienyl halide is not aromatic in covalent form because it contains one  $sp^3$  hybridized carbon. But it is aromatic in ionic form because cycloheptatrienyl cation has all the carbons  $sp^2$  hybridized. The stability associated with the aromatic cation causes the tropylium halide to exist in the ionic form. Therefore, tropylium bromide is insoluble in nonpolar solvents, but readily soluble in water unlike other alkyl halides which are soluble in nonpolar solvents and insoluble in water.*



### Cycloheptatrienyl anion:

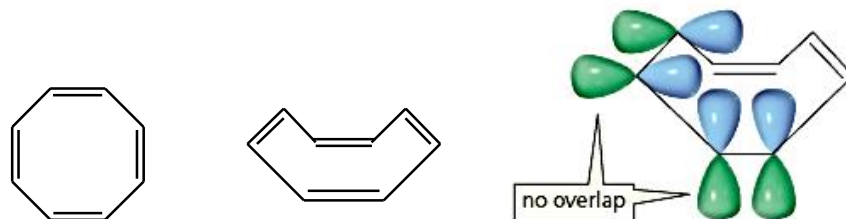
Cycloheptatrienyl anion is cyclic, planar and exhibits continuous delocalization of  $\pi$  electrons. However, it does not obey Huckel's rule as it contains 8 electrons. The lone pair of electrons participates with the  $\pi$  electrons of the ring in delocalization, so the total number of  $\pi$  electrons is 8. Hence, cycloheptatrienyl anion is not aromatic; it is rather **antiaromatic**.



### F. Cyclooctatetraene:

Cyclooctatetraene is cyclic and all the carbons are  $sp^2$  hybridized and thus a  $p$  orbital is available on all carbons for overlapping with the  $p$  orbitals on the neighbouring carbons. However, it exists as non-planar tub shaped structure. The overlapping of  $p$  orbitals for the delocalization of  $\pi$  electrons is possible only when the  $p$  orbitals are in the same plane. Any deviation from planarity in a molecule retards the delocalization process and thus reduces the aromaticity. Thus the coplanarity is essential for aromaticity. As

explained earlier the overlapping of  $p$  orbitals is difficult in tub shaped molecule of cyclooctatetraene. In addition cyclooctatetraene does not follow Huckel's rule as the number of  $\pi$  electrons is 8.



Therefore, cyclooctatetraene is not aromatic as the structure is not planar, and it does not obey Huckel's rule

### G. Annulenes:

Monocyclic systems with conjugated double bonds are called annulenes. A number in bracket denotes the ring size. For example benzene is [6]annulene. Generally, the term annulene is used for large size monocyclic systems of  $C_{10}$  and more.

#### [10]Annulene:

It is cyclic, all carbons are  $sp^2$  hybridized and it obeys Huckel's rule as it contains 10  $\pi$  electrons. However, due to steric hindrance of central hydrogens, the molecule is non-planar. Due the lack of coplanarity, it loses aromaticity. Hence [10]annulene is not aromatic.

#### [14]Annulene:

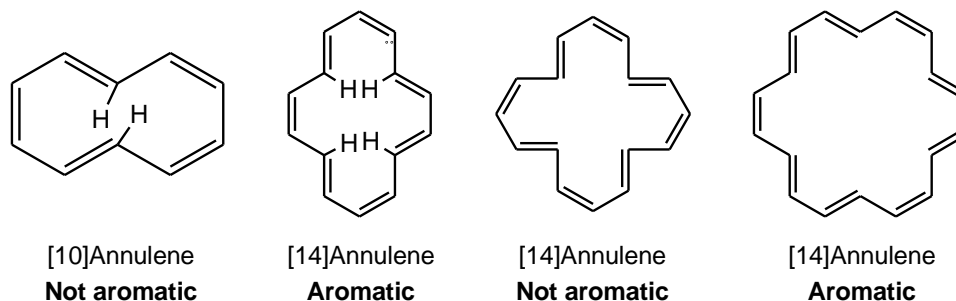
It is nearly planar and obeys Huckel's rule as the number of  $\pi$  electrons are 14. Therefore, it is aromatic.

#### [16]Annulene:

It is planar. However does not follow Huckel's rule. Thus it is not aromatic.

#### [18]Annulene:

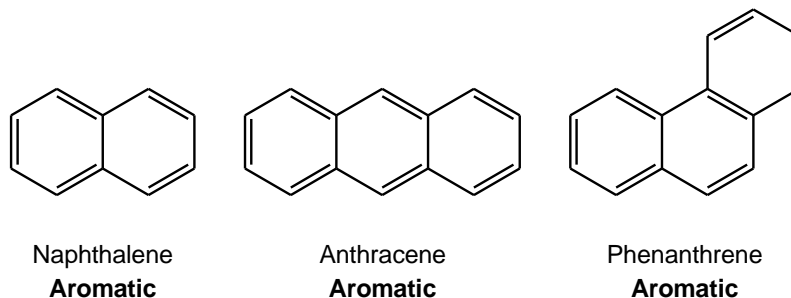
It is planar and obeys Huckel's rule also. Hence it is aromatic.



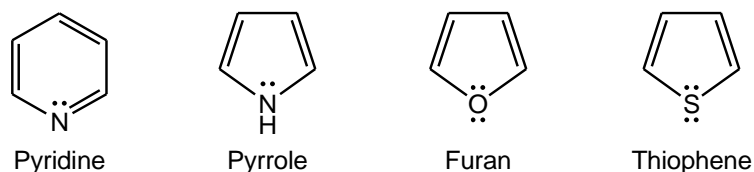
### H. Other ring systems:

**(i) Fused ring system:**

For example, in naphthalene, anthracene and phenanthrene, all carbons are  $sp^2$  hybridized and  $\pi$  electrons are continuously delocalized among all carbons of the rings. All obeys Huckel's rule. Therefore all are aromatic.

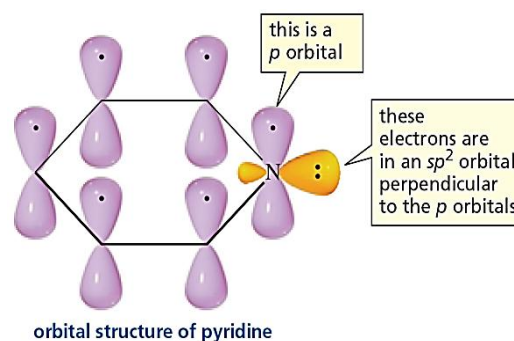
**(ii) Aromatic Heterocyclic compounds:**

A heterocycle is a cyclic compound that contains atoms of two or more elements in its ring, usually carbon along with nitrogen, oxygen, or sulfur. Pyridine, for example, is six-membered heterocycles with nitrogen in its ring, and pyrrole, furan and thiophene are five-membered heterocycles with nitrogen, oxygen and sulfur, respectively, in their rings. All these heterocyclic compounds are aromatic.

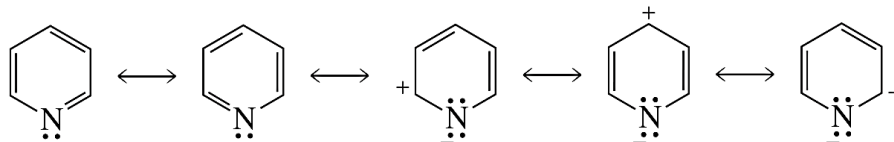
**Pyridine:**

Pyridine is aromatic because:

- It contains  $6\pi$  electrons (i.e.  $4n+2$   $\pi$  electrons).
- Pyridine is cyclic, planar, and completely conjugated, because the three single and double bonds alternate around the ring.
- Each of the six ring atoms of pyridine is  $sp^2$  hybridized, which means that each has a  $p$  orbital.
- Because nitrogen is  $sp^2$  hybridized, it has three  $sp^2$  orbitals and a  $p$  orbital. The  $p$  orbital is used to form the  $\pi$  bond. Two of nitrogen's  $sp^2$  orbitals overlap the  $sp^2$  orbitals of adjacent carbon atoms, and nitrogen's third  $sp^2$  orbital contains the lone pair.



- The lone pair on N resides in a  $sp^2$  hybridized orbital that is perpendicular to the delocalized  $\pi$  electrons and thus is not part of the delocalized  $\pi$  electron system of the aromatic ring.

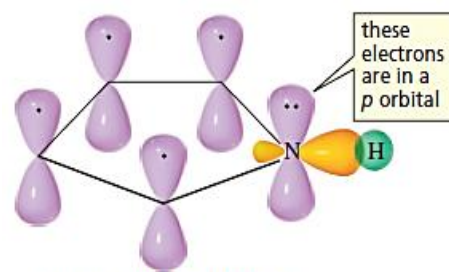


resonance contributors of pyridine

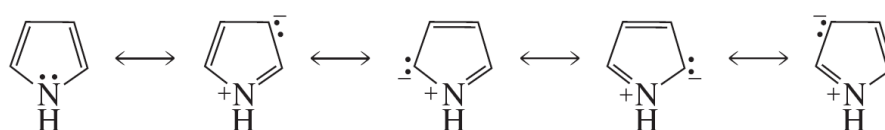
**Pyrrole:**

Pyrrole is aromatic because:

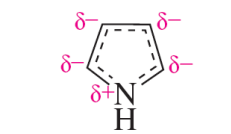
- It contains  $4n + 2$   $\pi$  electrons—four from the two  $\pi$  bonds and two from the lone pair on nitrogen. The nitrogen atom is  $sp^2$  hybridized and uses its three  $sp^2$  orbitals to bond to two carbons and one hydrogen. The lone-pair electrons are in a p orbital that overlaps the p orbitals on adjacent carbons, forming a  $\pi$  bond—thus, they are  $\pi$  electrons. Pyrrole, therefore, has three pairs of  $\pi$  electrons.
- It is cyclic, planar and completely conjugated because it has a p orbital on every adjacent atom.



orbital structure of pyrrole



resonance contributors of pyrrole



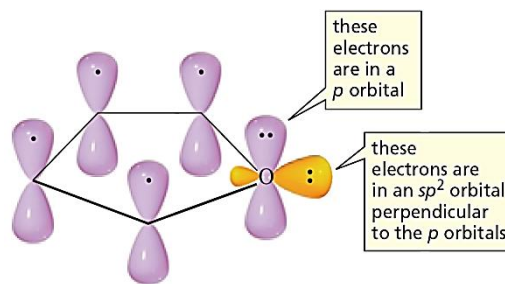
resonance hybrid

*Pyrrole is aromatic but not basic. It does not have any unshared electron pairs. The electron pair on nitrogen is part of the aromatic system.*

**Furan and thiophene:**

Furan and thiophene are aromatic because:

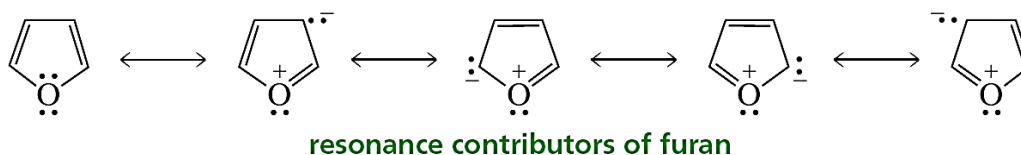
- Furan and thiophene are oxygen and sulfur analogs of pyrrole, respectively. The oxygen atom in furan and the sulfur atom in thiophene are  $sp^2$  hybridized. These  $sp^2$  orbitals make sigma bonds with neighboring carbons. The remaining p orbital of oxygen in furan and of sulfur in



orbital structure of furan

thiophene is in the same plane as  $p$  orbitals of carbon and contain a lone pair of electrons. This  $p$  orbital overlaps with the  $p$  orbitals of neighboring carbons. Thus overlapping of five  $p$  orbitals (one of oxygen/sulfur and four of carbons) results in delocalization of six  $\pi$  electrons (one lone pair + 4 single electrons) which follows Huckel's rule of  $(4n + 2)$   $\pi$  electrons.

- In each case, the heteroatom provides a pair of electrons to the aromatic system, but each also has an unshared electron pair in a  $sp^2$  orbital that is perpendicular to the plane of  $p$  orbitals and is not part of the aromatic system.



Various approaches have been taken to estimate the aromaticity of these compounds. The aromatic stabilization of pyridine is similar to that of benzene. Typically the five-membered compounds are found to be somewhat less stabilized than benzene. The order of aromaticity is:

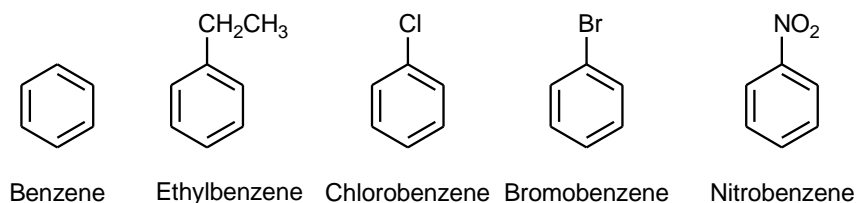


The resonance energy of benzene is  $36 \text{ kcal mol}^{-1}$  while that of thiophene, pyrrole and furan is  $29 \text{ kcal mol}^{-1}$ ,  $22 \text{ kcal mol}^{-1}$  and  $16 \text{ kcal mol}^{-1}$ , respectively. Due to the less electronegativity of sulfur as compared to oxygen and nitrogen, the electrons on sulfur in thiophene are easily available to participate in delocalization while the high electronegativity of oxygen in comparison to nitrogen and sulfur reduces the ease of delocalization of electrons in furan.

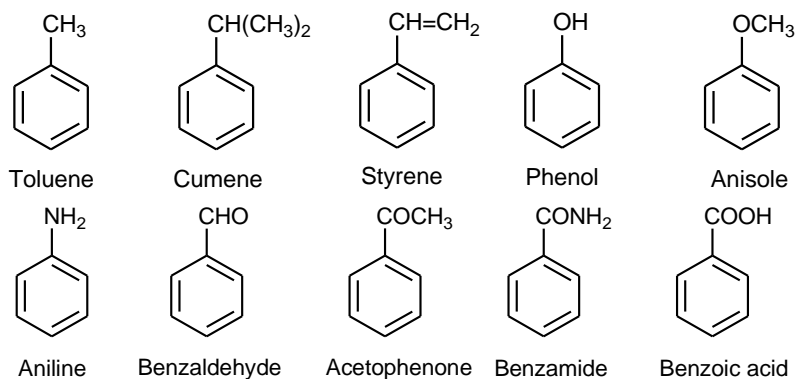
## 1.2. Properties of Benzene and its Derivatives

### 1.2.1. Nomenclature:

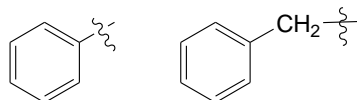
- Mono-substituted benzenes are named as derivatives of benzene:



- Many simple mono-substituted derivatives of benzene have common names which are accepted by IUPAC:

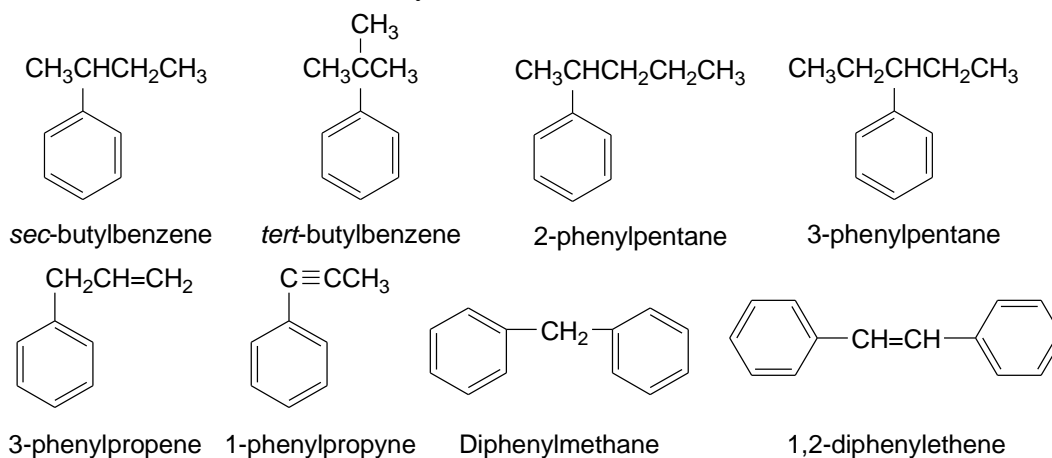


- The name 'phenyl' is used for  $\text{-C}_6\text{H}_5$  group and 'benzyl' is used for  $\text{C}_6\text{H}_5\text{CH}_2\text{-}$  group.

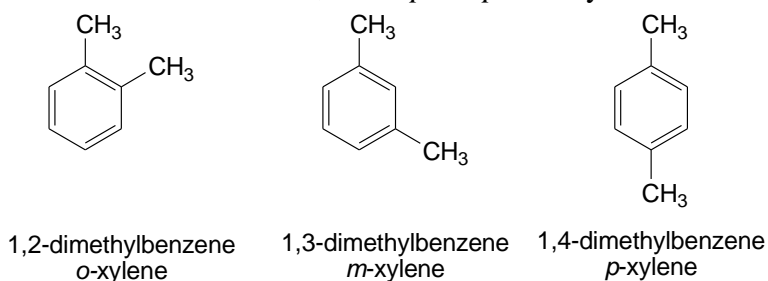


A Phenyl group      A benzyl group

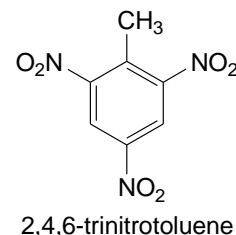
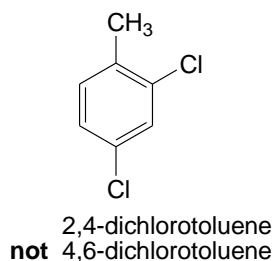
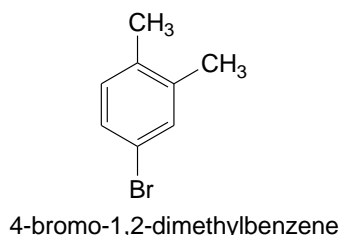
- Alkyl substituted benzenes are named in different ways depending on the size of alkyl group. If the alkyl group is small, it is named as alkyl-substituted benzene. If the alkyl group is large and in case of unsaturated side chain, it is named as a phenyl-substituted alkane, alkene or alkyne.



- Disubstituted benzenes are designated by prefixes *ortho-* for the substituents at 1,2-positions, *meta-* for substituents at 1,3-positions and *para-* for substituents at 1,4-positions. These are abbreviated as *o-*, *m-* or *p-* respectively.

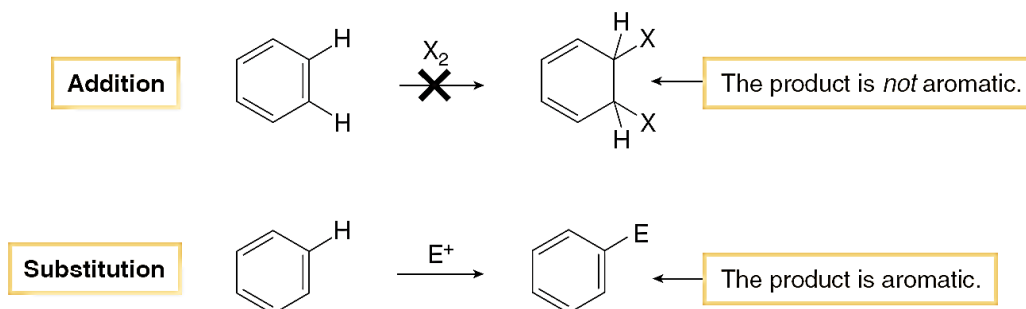


- If more than two substituents are present, their position is designated by numbering the ring in such a way that all the substituents get the minimum possible number. The substituents are listed in alphabetical order. If monosubstituted aromatic compound serves as parent name, the principal substituent will be on C-1 position on the ring.

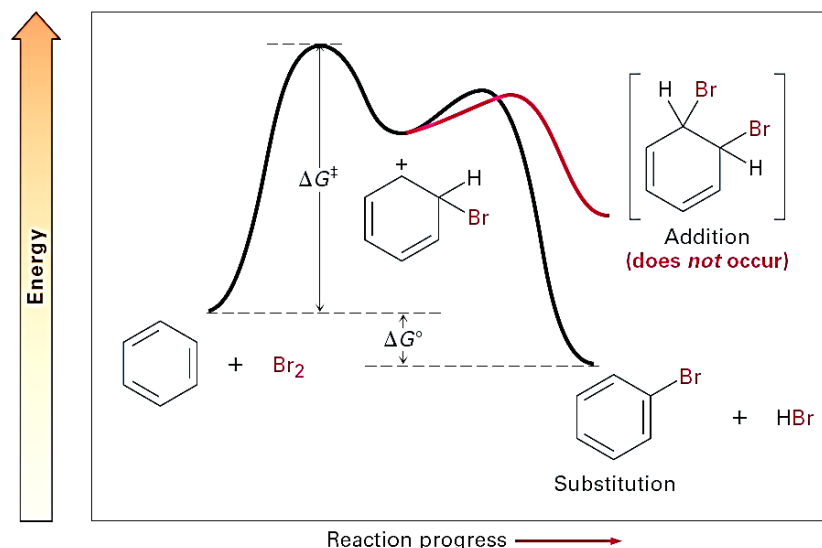


### 1.2.2. Physical properties:

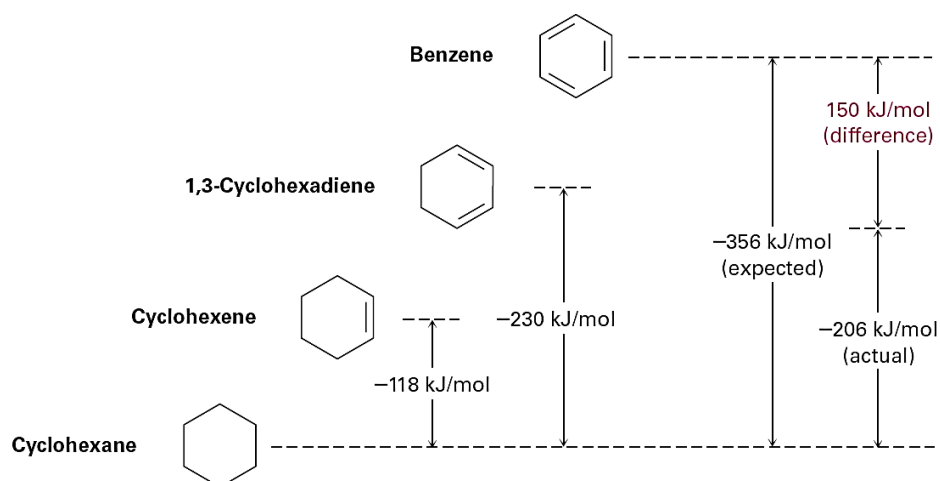
- The physical properties of substituted benzenes resemble those of alkanes and alkenes of similar shape and molecular weight.
- Arenes (aromatic hydrocarbons) are nonpolar, insoluble in water and less dense than water.
- Due to high carbon content aromatic compounds burn with sooty flame.
- All the carbon-carbon bonds in benzene are equal and are intermediate (1.39 Å) between single (1.47 Å) and double bonds (1.34 Å).
- They do not undergo usual addition reactions of alkenes because addition reaction would yield a product that is not aromatic.



The energy profile of reactions of aromatic compounds favours substitution over addition reactions.

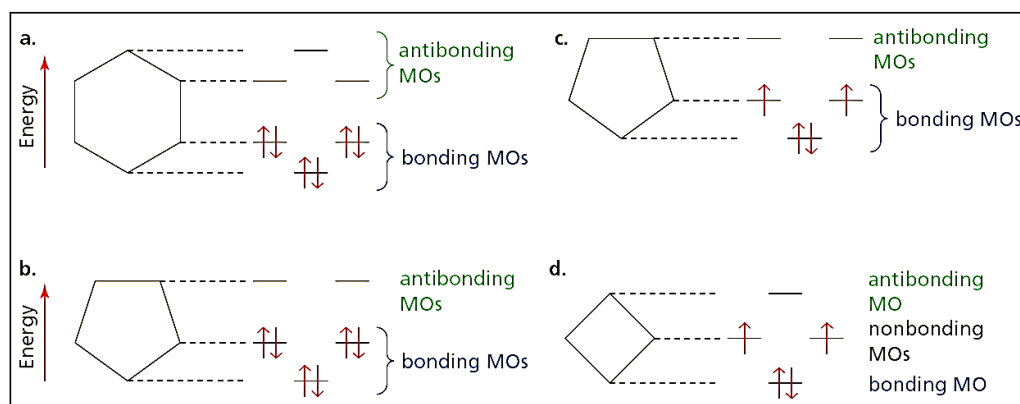


- They are unusually stable, heat of hydrogenation is much less than expected, given the number of unsaturation. The heat of hydrogenation of cyclohexene is 28.6 kcal/mole (118 kJ/mole). Benzene has three double bonds, so the expected heat of hydrogenation should have been  $28.6 \times 3 = 85.8$  kcal/mole (356 kJ/mole). However the heat of hydrogenation of benzene is only 49.8 kcal/mole (206 kJ/mole). Therefore, benzene is stabilized by  $85.8 - 49.8 = 36$  kcal/mole (150 kJ/mole).



- All bonding Molecular Orbitals and Highest Occupied Molecular Orbitals (HOMO) are completely filled and no electrons occupy antibonding orbitals. For example, 'a' (benzene) and 'b' (cyclopentadienyl anion) have HOMO completely filled and there is no electron in antibonding orbitals. Hence these are aromatic. On the other hand, 'c' (cyclopentadienyl cation) and 'd' (cyclobutadiene) have unfilled HOMO and nonbonding molecular orbitals, therefore, these are antiaromatic.



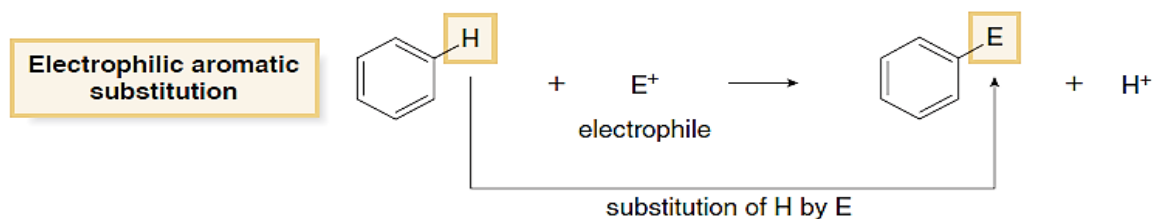


The relative energies of the  $p$  molecular orbitals in a cyclic compound correspond to the relative levels of the vertices. Molecular orbitals below the midpoint of the cyclic structure are bonding, those above the midpoint are antibonding, and those at the midpoint are nonbonding.

- The conjugated  $\pi$  electrons of a benzene ring give characteristic ultraviolet absorptions that indicate the presence of benzene ring in an unknown compound. One absorption band of moderate intensity occurs near 205 nm and another, less intense band appears in the 250-275 nm range.
- The ring hydrogens of benzene derivatives absorb downfield in the region between  $\delta$  6.0 and  $\delta$  9.5 of  $^1\text{H}$  NMR spectra.
- The carbon atoms of benzene rings generally absorb in  $\delta$  100-170 region of  $^{13}\text{C}$  NMR spectra.

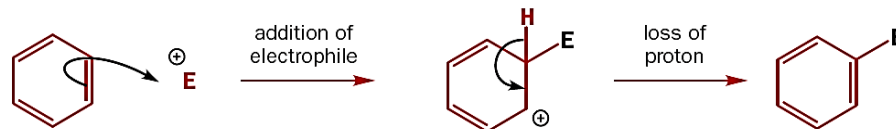
### 1.3. Aromatic Substitution Reactions and their Mechanism:

Aromatic compounds having delocalized  $\pi$  electrons are susceptible to react with electron deficient species called electrophiles. As discussed earlier, the addition of electrophile results in loss of aromaticity while the substitution reactions retain the aromaticity. Therefore, aromatic compounds prefer to undergo electrophilic substitution reactions. These reactions are carried out in presence of catalyst which promotes the generation of electrophiles.

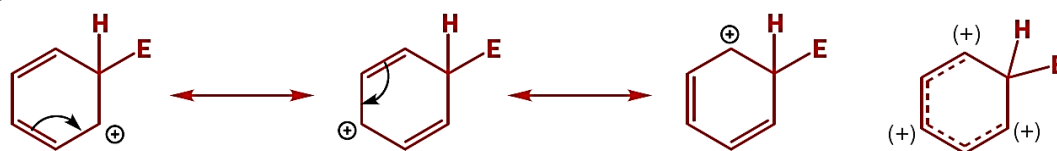


**Mechanism:**

Aromatic substitution is a three step process. In first step, electrophile is generated. In second step, the electrophile attacks on the  $\pi$ -electron rich aromatic system to give an intermediate cation; and in the last step a proton is lost to restore the aromaticity.



The cationic intermediate is, of course, less stable than the starting materials or the product but, as a cation, it is reasonably stable because of delocalization around the six-membered ring.

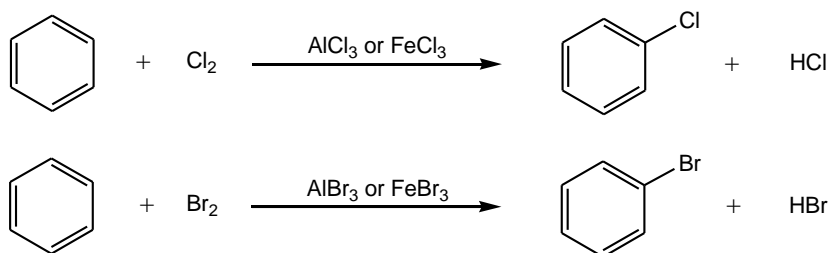


Halogenation, nitration, sulphonation, alkylation and acylation of aromatic compounds are the examples of aromatic substitution:

### 1.3.1. Halogenation:

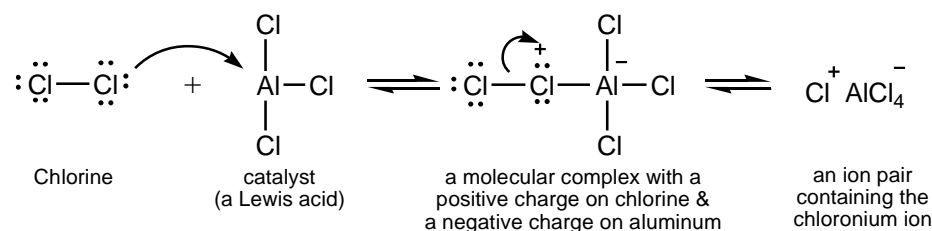
#### Chlorination and Bromination:

Benzene reacts with  $\text{Cl}_2$  or  $\text{Br}_2$  in the presence of a Lewis acid catalyst, such as  $\text{FeCl}_3$ ,  $\text{AlCl}_3$ ,  $\text{FeBr}_3$  or  $\text{AlBr}_3$  etc. to produce chlorobenzene or bromobenzene, respectively. The catalyst initiates the reaction by generating the electrophile i.e. chloronium ( $\text{Cl}^+$ ) or bromonium ( $\text{Br}^+$ ) ions.

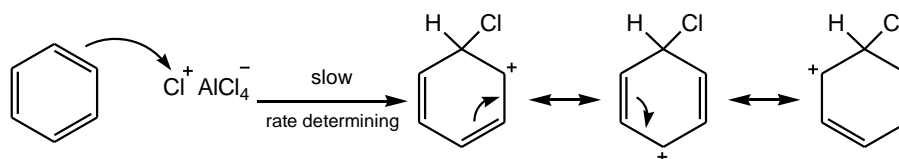


#### Mechanism:

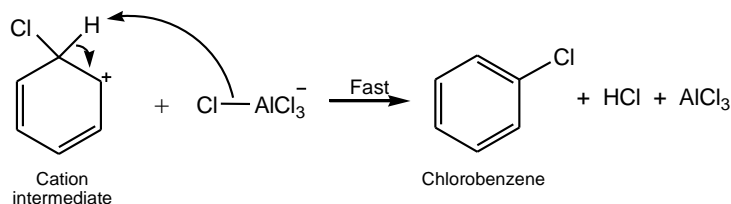
**Step 1: Generation of electrophile.** Chlorine reacts with Lewis acid catalyst ( $\text{AlCl}_3$ ) to produce a molecular complex with a positive charge on chlorine and a negative charge on aluminum. Redistribution of electrons in this complex generates a chloronium ion,  $\text{Cl}^+$ , a very strong electrophile, as part of an ion pair.



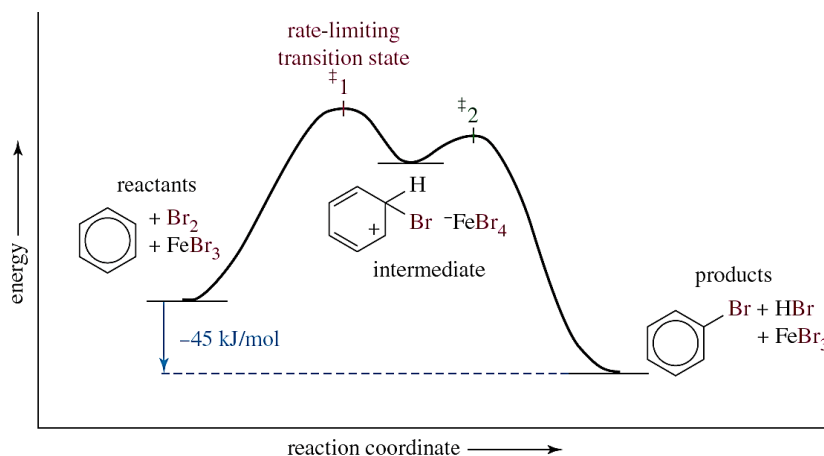
**Step 2: Bond formation between aromatic compound and chloronium ion.** A pair of  $\pi$  electrons of aromatic ring attacks the positively polarized chloronium ion (a strong electrophile) and produces a resonance-stabilized carbocation intermediate (arenium ion). This arenium ion is nonaromatic as one of the carbons becomes  $sp^3$  hybridized. The four  $\pi$ -electrons in arenium ion are delocalized among five  $sp^2$  hybridized carbons.



**Step 3: Loss of proton (formation of chlorobenzene and regeneration of catalyst).** A proton is lost from  $sp^3$  carbon of arenium ion in order to regain aromaticity. This proton is captured by  $\text{AlCl}_4^-$  (formed in previous step) to regenerate the catalyst ( $\text{AlCl}_3$ ) with simultaneous formation of chlorobenzene and  $\text{HCl}$ .



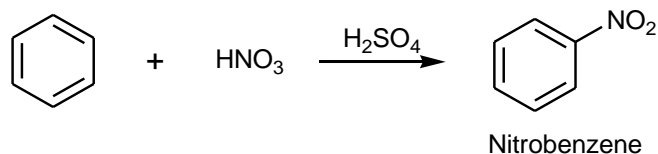
The energy diagram of aromatic substitution reactions shows that formation of arenium ion is endothermic, slow and rate determining step while the formation of chlorobenzene from arenium ion is an exothermic process. Resonance energy is regained in this process.



Treating benzene with bromine in the presence of ferric chloride or aluminum chloride gives bromobenzene and HBr. The mechanism of this reaction is the same as above.

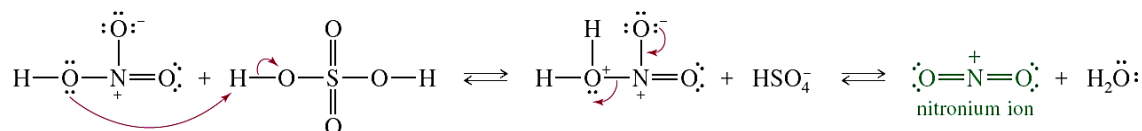
### 1.3.2. Nitration:

The reaction of benzene with fuming nitric acid (conc.HNO<sub>3</sub> + conc.H<sub>2</sub>SO<sub>4</sub>) produces nitrobenzene. Sulfuric acid acts as catalyst and helps in generating nitronium ion, an electrophile.

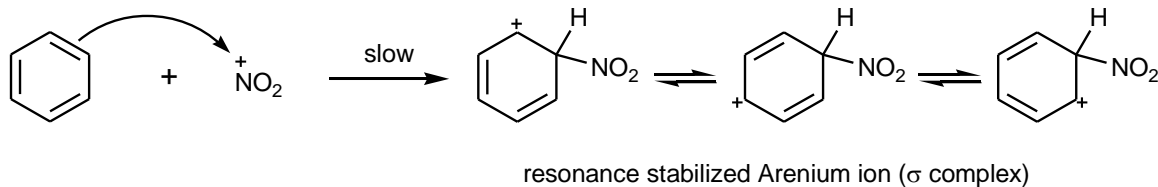


#### Mechanism:

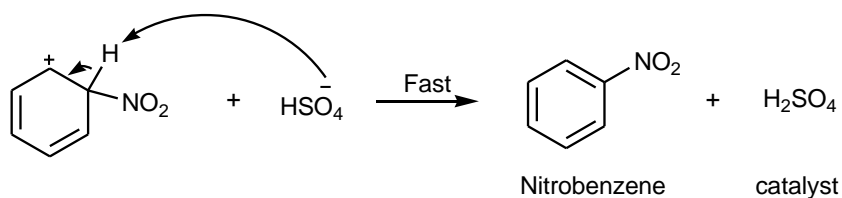
**Step 1: Generation of nitronium ion (electrophile).** The sulfuric acid, a stronger acid, donates a proton to nitric acid. Protonated nitric acid on dissociation produces a water molecule and nitronium ion.



**Step 2: Reaction of nitronium ion (electrophile) with benzene, a nucleophile (formation of arenium ion).** This step is same as in halogenations. Nitronium ion attacks on the  $\pi$  system of benzene to form a carbocation (arenium ion) which is stable due to resonance. The formation of arenium ion is slow, endothermic and rate determining step. The aromaticity is lost at this stage as one of the carbons becomes  $sp^3$  hybridized. The four  $\pi$  electrons of the ring are delocalized on five  $sp^2$  hybridized carbons of the arenium ion.

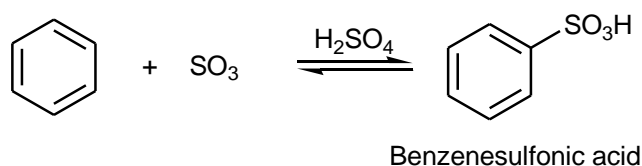


**Step 3: Loss of proton to form nitrobenzene and regeneration of catalyst:** In order to regain aromaticity, the arenium ion transfers a proton from  $sp^3$  hybridized carbon to  $\text{HSO}_4^-$  (formed in earlier step) which regenerates the catalyst with the formation of nitrobenzene simultaneously. The formation of nitrobenzene from arenium ion is exothermic as resonance energy is regained in this process.



### 1.3.3. Sulfonation:

Benzene is sulfonated by reaction with fuming sulfuric acid (7%  $\text{SO}_3$  in conc.  $\text{H}_2\text{SO}_4$ ) to produce benzenesulfonic acid. The reactive electrophile is either  $\text{HSO}_3^+$  or neutral  $\text{SO}_3$ , depending on reaction condition.

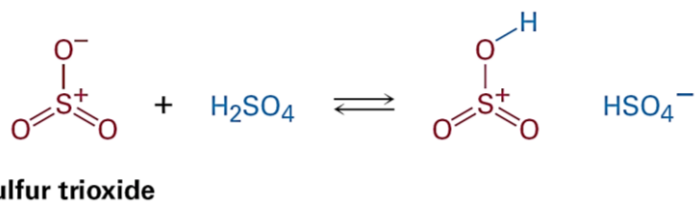


The sulfonation is reversible reaction; it can occur either forward or backward, depending on the reaction conditions. Sulfonation is favoured in strong acid, but desulfonation is favoured in hot, dilute aqueous acid. For sulfonation, conc.  $\text{H}_2\text{SO}_4$  or – better – fuming sulfuric acid is used, which shifts the equilibrium to right side and benzenesulfonic acid is obtained. For desulfonation (removal of sulfonic group), dilute sulfuric acid is used and steam is passed through the mixture. Under these conditions, with high concentration of water, the equilibrium shifts to the left and benzenesulfonic acid is desulfonated to produce benzene.

Sulfonation-desulfonation is useful tool in syntheses involving aromatic substitution reactions. Sulfonate group is used as a protecting or a directing group to influence the position of another substituent. Later it is removed by desulfonation.

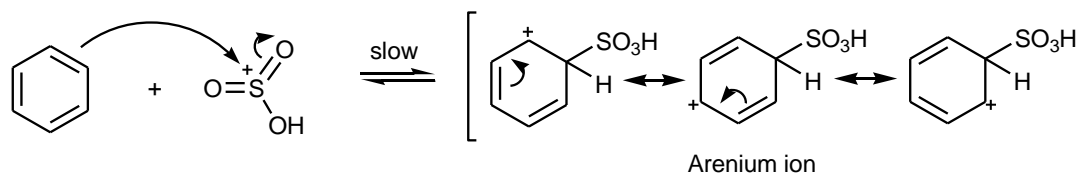
**Mechanism:** Mechanism of sulfonation is almost same as of nitration.

**Step 1: Generation of electrophile.** Sulfur trioxide is itself a strong electrophile. Alternatively, sulfuric acid donates proton to sulfur trioxide to produce  $\text{HSO}_3^+$  which act as electrophile.

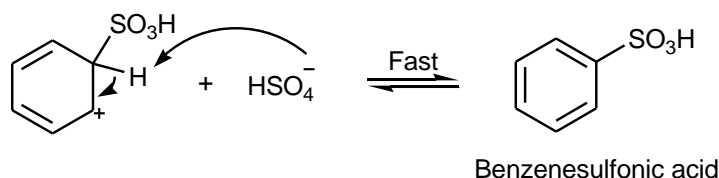


**Step 2: Reaction of electrophile with aromatic  $\pi$  system (formation of arenium ion).**

The electrophile (either sulfur trioxide or  $\text{HSO}_3^+$ ) attacks on the  $p$  system of benzene to form arenium ion as in nitration reaction. The arenium ion ( $\sigma$  complex) so formed is resonance stabilized. This step is slow and rate determining process. The aromaticity is lost in this step.

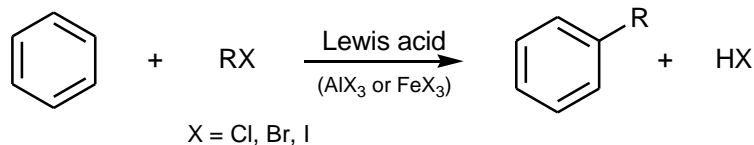


**Step 3: Loss of proton (formation of benzenesulfonic acid).** This step is fast. The aromaticity is regenerated in this step.

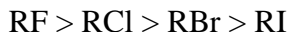


### 1.3.4. Friedel-Crafts Alkylation:

Benzene reacts with alkyl halides in presence of Lewis acid ( $\text{AlX}_3$ ,  $\text{FeX}_3$ ) which acts as catalyst and produces alkylbenzene. The alkyl halides are not strong electrophiles. The catalyst enhances the electrophilicity of alkyl halides.



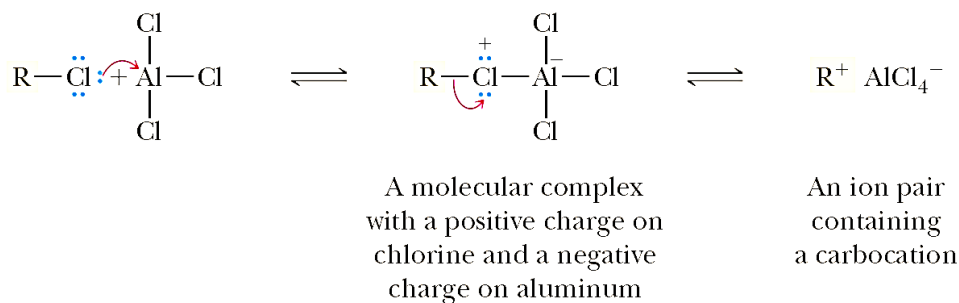
The reactivity of alkyl halides increases as the polarity of C-X bond increases. Thus the order of reactivity is:



This is one of the most important methods for making new carbon-carbon bond in aromatic compounds. Halogen atoms on  $sp^2$ -hybridized carbons (vinylic and aryl halides) do not react to produce electrophiles under conditions of the Friedel-Crafts alkylation because of the high activation energy required to form these carbocations.

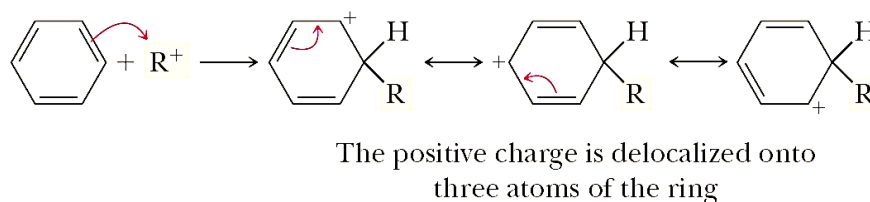
#### Mechanism:

**Step 1: Generation of electrophile (carbocation).** The alkyl halide reacts with Lewis acid (aluminum halide) to form a complex in which aluminum carries a negative charge and the halogen of the alkyl halide possesses a positive charge. This complex is dissociated to produce carbocation, if the carbocation, so formed, is stable as in case of secondary or tertiary alkyl halides. In case of primary alkyl halides, where the carbocation is relatively unstable, the complex directly attacks on aromatic ring as electrophile.



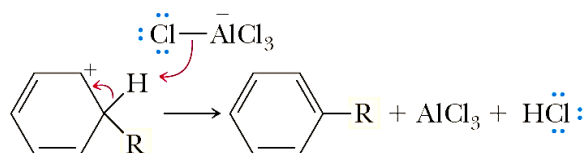
**Step 2: Attack of carbocation on  $\pi$  system of benzene (formation of arenium ion).**

Reaction of the carbocation (a strong electrophile) with the  $\pi$  electrons (a weak nucleophile) of the aromatic ring gives a resonance-stabilized cation intermediate (arenium ion).

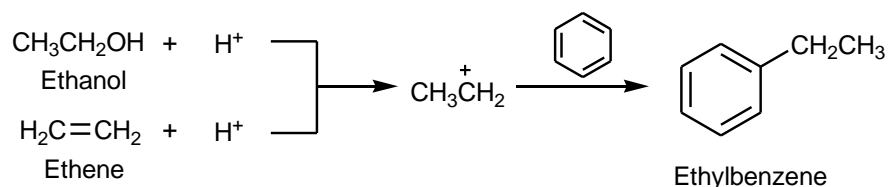


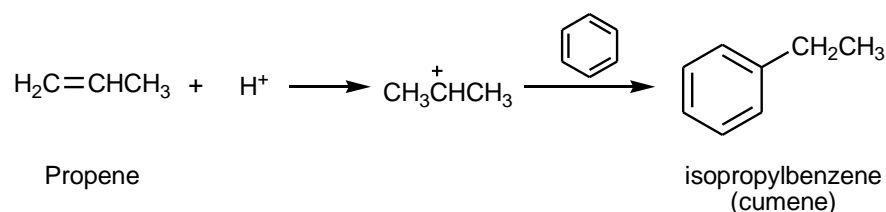
This is slow, endothermic and rate determining step of the reaction. Aromaticity is lost in this step as one of the carbons in the ring becomes  $sp^3$  hybridized. The four  $\pi$ -electrons are delocalized among five  $sp^2$  hybridized carbons of the ring.

**Step 3: Loss of proton (formation of alkylbenzene and regeneration of catalyst).** A proton is transferred from the arenium ion to  $\text{AlCl}_4^-$  so as to regain the aromaticity, formation of alkylbenzene and regeneration of catalyst with the simultaneous loss of  $\text{HCl}$ .



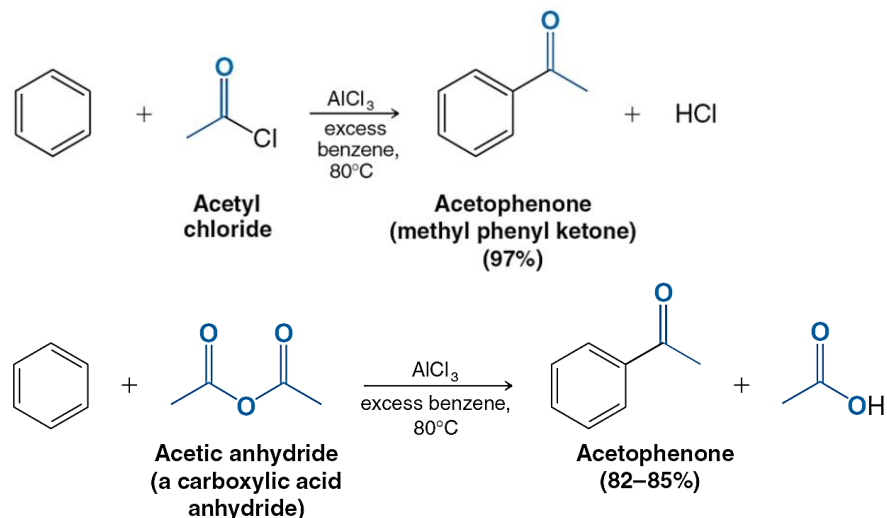
**Alkylation of aromatic compounds by other alkylating agents:** The Friedel-Craft alkylation proceeds through the formation of carbocation. Therefore, the reagents which can produce carbocations can also be used for alkylation. Alkenes and alcohols in presence of acidic catalyst produce carbocation; thus can be used for alkylation of aromatic compounds. For example, ethanol and ethene produce ethyl carbocation in presence of acid, which alkylates benzene to produce ethylbenzene. Similarly, propene reacts with benzene in presence of acid ( $\text{H}_3\text{PO}_4$ ) to produce cumene (isopropyl benzene).





### 1.3.5. Friedel-Craft Acylation

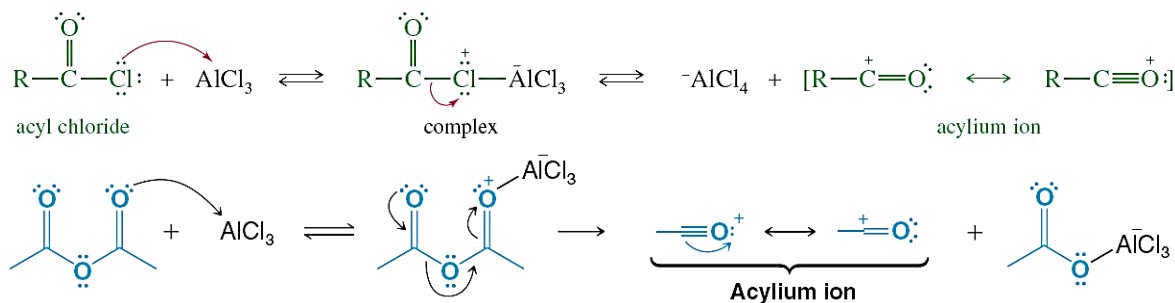
Benzene reacts with acid halide or acetic anhydride in presence of a Lewis acid ( $\text{AlCl}_3$ ) to produce arylketone. The reaction is called Friedel-Craft Acylation and is carried out in the presence of a solvent like  $\text{CS}_2$  or nitrobenzene.



#### Mechanism:

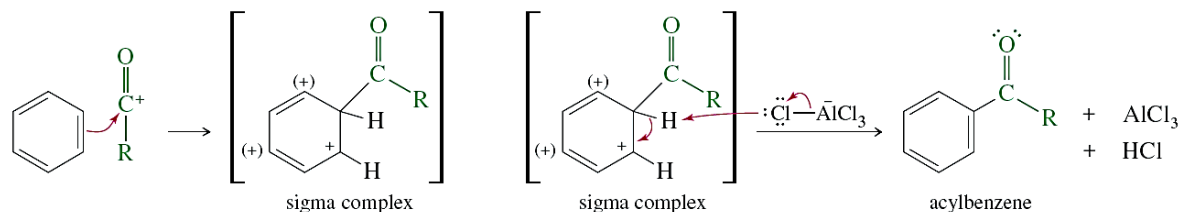
The mechanism of Friedel-Craft acylation is similar to that of alkylation. Here the electrophile is an acylium ion.

**Step 1: Generation of electrophile (acylium ion).** The reaction of acid chloride or acid anhydride with a Lewis acid ( $\text{AlCl}_3$ ) forms a molecular complex with a positive charge on chlorine and negative charge on aluminum. The cleavage of C–Cl bond results in the formation of an ion pair containing acylium ion. The acid chloride is prepared by the reaction of carboxylic acid with thionyl chloride.

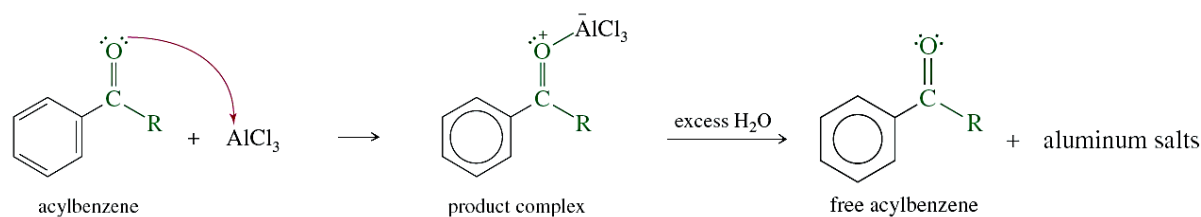




**Step 2 and 3: Attack of acylium ion on  $\pi$  system of benzene (formation of arenium ion) and loss of proton.** The reaction of acylium ion with the  $\pi$  electrons of benzene ring produces a resonance stabilized arenium ion ( $\sigma$  complex). A proton is transferred from the arenium ion to  $\text{AlCl}_4^-$  to produce acylbenzene. Aromaticity is lost in step 2 and regenerated in step 3.

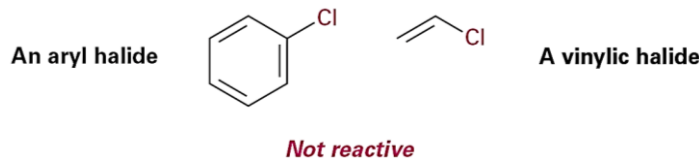


**Step 4: Complexation.** The ketone group of acylbenzene has nonbonding electrons that make a complex with the Lewis acid ( $\text{AlCl}_3$ ) which is hydrolyzed by addition of water to give free acylbenzene.

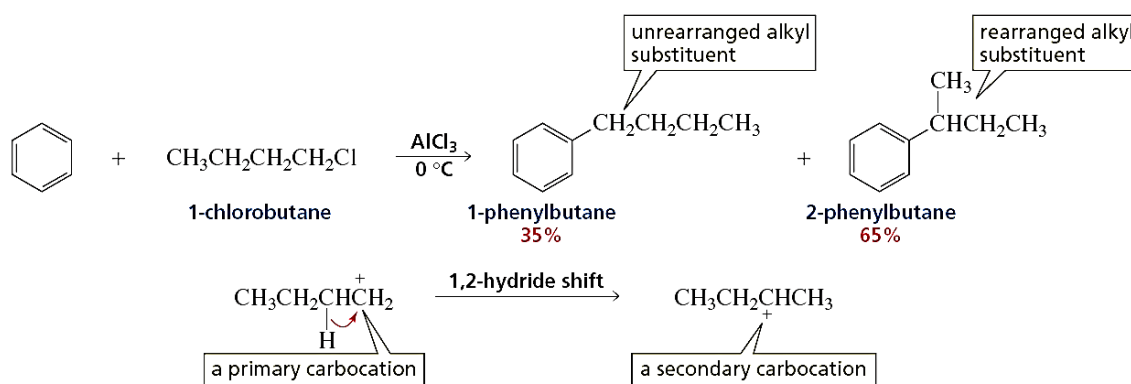


### Limitations of Friedel-Craft Reactions:

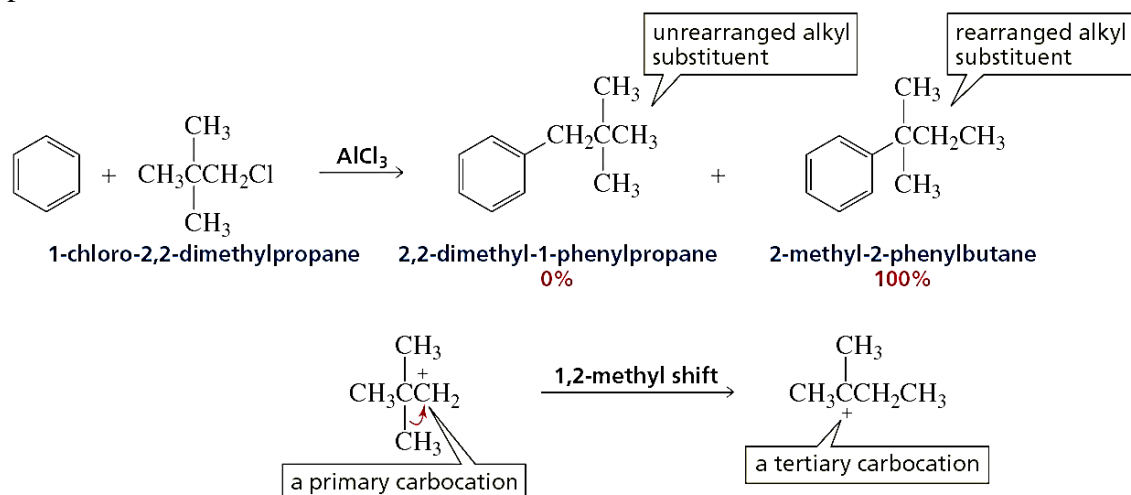
- a. Halogen atoms on  $sp^2$ -hybridized carbons (vinylic and aryl halides) do not react to produce electrophiles under conditions of the Friedel-Crafts alkylation because of the high activation energy required to form these carbocations.



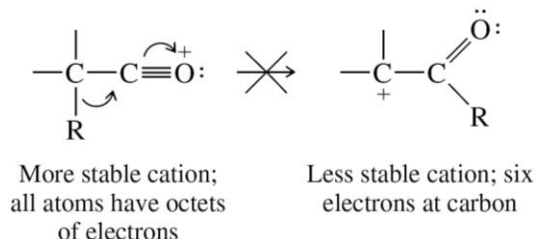
- b. **Rearrangement:** The carbocation formed in Friedel-Craft reactions may undergo rearrangement to form a more stable carbocation, especially when primary alkyl halides are used. The major product will be the product with the rearranged alkyl group on the benzene ring. The relative amounts of rearranged and un-rearranged product depend on the increase in carbocation stability achieved as a result of the rearrangement. For example, when benzene reacts with 1-chlorobutane, a primary carbocation rearranges to a secondary carbocation, and 60–80% of the product (the actual percentage depends on the reaction conditions) is the rearranged product.



As the stability of carbocation increases, the percentage of rearranged product also increases. For example in case of reaction of benzene with 1-chloro-2,2-dimethylpropane, the primary carbocation rearranges to tertiary carbocation which is even more stable than secondary carbocation. Thus the final product is 100% rearranged product.

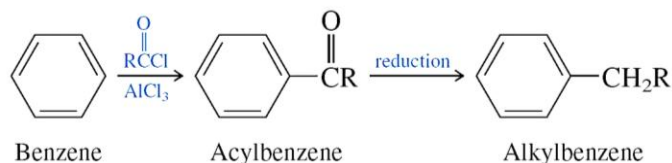


**However, Friedel-Craft acylation undergoes without rearrangement.** Acylium ion formed in Friedel-Craft acylation is more stabilized by resonance than any carbocation expected to be formed by hydride or alkyl shift. Thus, there is no driving force for a rearrangement.

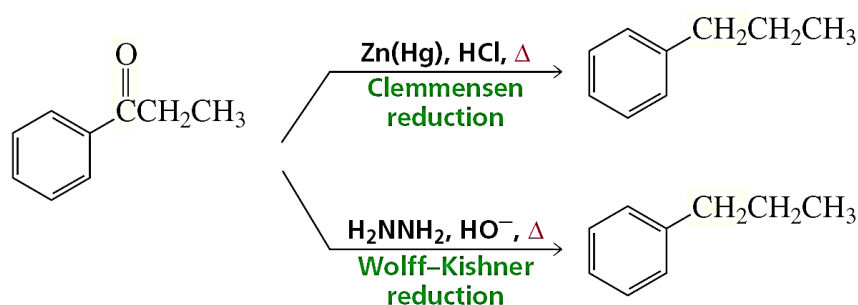


Therefore, Friedel-Craft acylation followed by reduction of  $>\text{C}=\text{O}$  group to  $-\text{CH}_2$  group is preferred to introduce unbranched alkyl group on benzene ring than Friedel-Craft

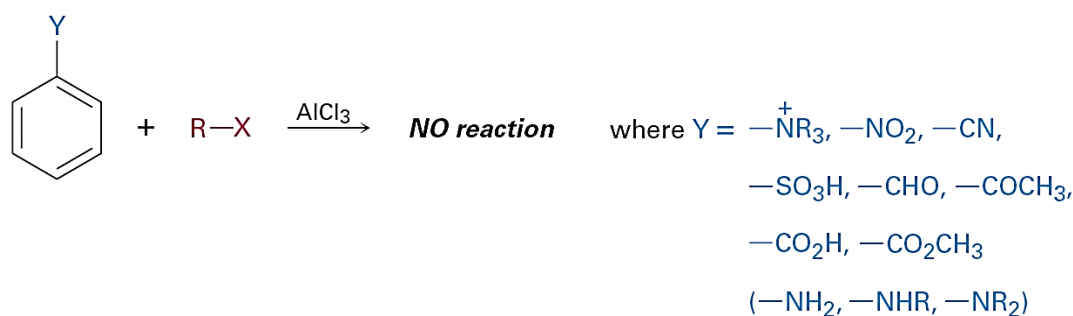
alkylation which would produce branched alkylbenzene because of rearrangement of carbocation.



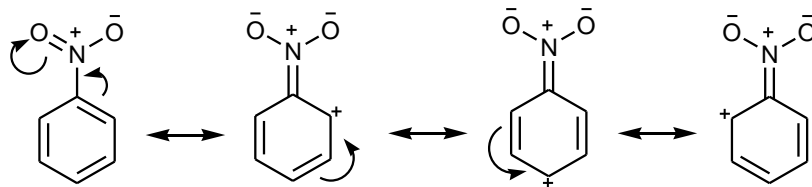
The reduction of acylbenzene to alkylbenzene can be done by **Clemmensen reduction** which is carried out by zinc–mercury amalgam in concentrated hydrochloric acid. Alternatively, it can be done by Wolff-Kishner reduction, which involves the reaction with hydrazine under basic conditions.



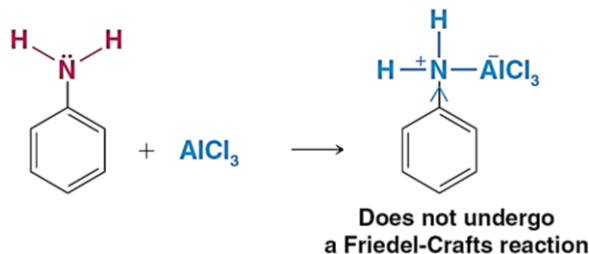
- c. **Friedel-Craft alkylation and acylation fail if electron-withdrawing group is present in the ring.** Friedel-Craft reaction works only with benzene, activated benzene derivatives, and halobenzenes. An aromatic system bearing electron-withdrawing groups ( $-\text{NO}_2$ ,  $>\text{C}=\text{O}$ ,  $-\text{CHO}$ ,  $-\text{COOH}$ ,  $-\text{SO}_3$ ) or amino group do not undergo this reaction.



The electron-withdrawing groups attached to benzene ring make the ring electron deficient (carrying positive charge); thereby the attack of electrophile becomes difficult.



Although  $\text{-NH}_2$ ,  $\text{-NHR}$ ,  $\text{-NR}_2$  are electron-releasing groups, but when they make a complex with the Lewis acid ( $\text{AlCl}_3$ ), a positive charge is developed on nitrogen, which makes these groups electron-withdrawing.



- d. **Polyalkylation:** The Friedel-Craft alkylation is hard to stop at monoalkylation because the alkylated product is more reactive than benzene itself. The alkyl group, being electron releasing in nature, increases the electron density in the benzene ring and thus activates the ring towards further electrophilic substitution resulting to polyalkylation. To obtain high yield of monoalkylation product, a large excess of benzene is used, which acts as the solvent as well as the reactant. When large excess of benzene is used, the electrophile (carbocation) is more likely to react with benzene than with monoalkylated product which is very less.

**Polyalkylation is not a problem in Friedel-Craft acylation, however.** The acyl group is electron-withdrawing and its complex with  $\text{AlCl}_3$  is even more electron-withdrawing which deactivates the ring and strongly inhibits further substitution. Thus, acylation is preferred than alkylation, if mono-substituted product is required.

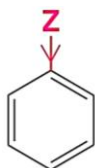
### 1.3.6. Directing Effects of Substituents

The nature of the substituent already present on benzene ring affects both the reactivity of the benzene ring and the placement of an incoming substituent for further substitution:

- 1. Substituents affect the reactivity of the aromatic ring.** Some substituents **activate** the ring, making it more **reactive than benzene**, and some **deactivate** the ring, making it less reactive than benzene. For instance, an  **$\text{-OH}$  substituent** makes the ring **1000 times** more reactive than **benzene**, while a  **$\text{-NO}_2$  substituent** makes the ring more than **10 million times less reactive**. Toluene undergoes nitration some 20–25 times faster than benzene. Because toluene is more reactive than benzene, we say that a methyl group activates the ring toward electrophilic aromatic substitution. (Trifluoromethyl) benzene, on the other hand, undergoes nitration about 40,000 times more slowly than benzene. We say that a trifluoromethyl group deactivates the ring toward electrophilic aromatic substitution.

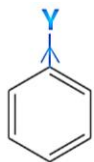
- ✓ The rate of electrophilic aromatic substitution is increased by electron-donating substituents and decreased by electron-withdrawing substituents.
- ✓ Substituents can donate or withdraw electrons due to **inductive effect** or due to **resonance**.

- ✓ The groups like  $-\text{OH}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}$ ,  $-\text{NR}_2$ ,  $-\text{CH}_3$ ,  $-\text{OCH}_3$ ,  $\text{Cl}$ ,  $\text{Br}$ ,  $\text{I}$ ,  $\text{F}$  have (+)-inductive and (+)-resonance effect and release electrons toward benzene ring. This increases the electron density on benzene ring and thus, electrophile reacts faster. These groups are called **ring activators** or **activating groups** for further substitution.



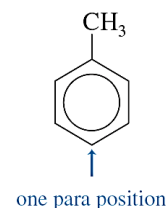
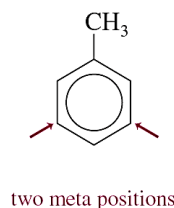
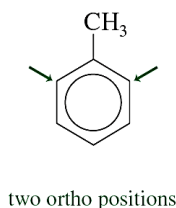
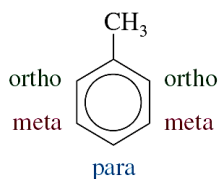
If **Z** donates electrons the ring is more electron rich and it reacts faster with an electrophile.

- ✓ The groups like  $-\text{NO}_2$ ,  $-\text{CN}$ ,  $-\text{CHO}$ ,  $>\text{C}=\text{O}$ ,  $-\text{COOH}$ ,  $-\text{COOR}$ ,  $-\text{SO}_3\text{H}$  have (−)-inductive and (−)-resonance effect and withdraw electrons from benzene ring which reduces the electron density on benzene ring and thus makes the electrophile attack difficult which slows down the further substitution. These groups are called **ring deactivators** or **deactivation groups**.



If **Y** withdraws electrons the ring is electron poor and it reacts more slowly with an electrophile.

2. The **nature of the substituent** already present on the **benzene ring determines** the position of the **second substitution**. For instance an  $-\text{OH}$  group directs substitution toward the *ortho* and *para* positions, while a **carbonyl** group such as  $-\text{CHO}$  directs substitution primarily toward the *meta* position.

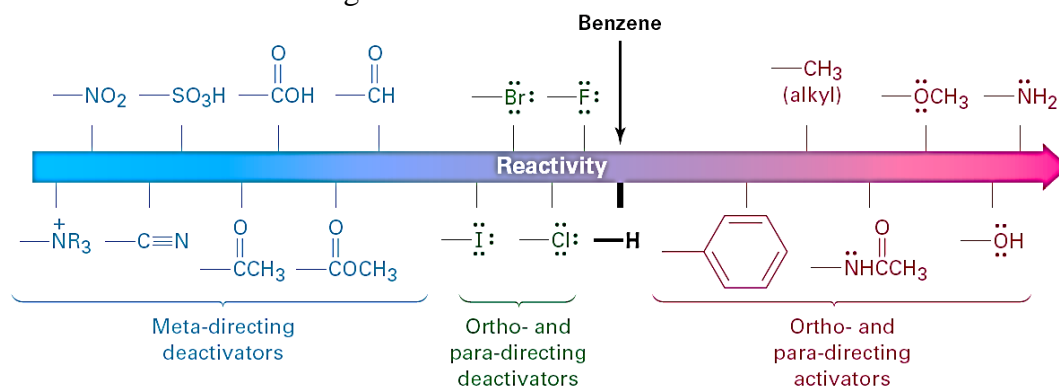


- ✓ The groups that direct the electrophile at positions *ortho* and *para* to itself are called ***ortho, para directing groups***.
- ✓ The groups that direct the electrophile at a position *meta* to itself are called ***meta directing groups***.

Therefore, substituents can be classified into three categories:

- (i) *Electron releasing* groups are **ring activators** and ***ortho, para directors***.
- (ii) *Electron withdrawing* groups are **ring deactivators** and ***meta directors***.

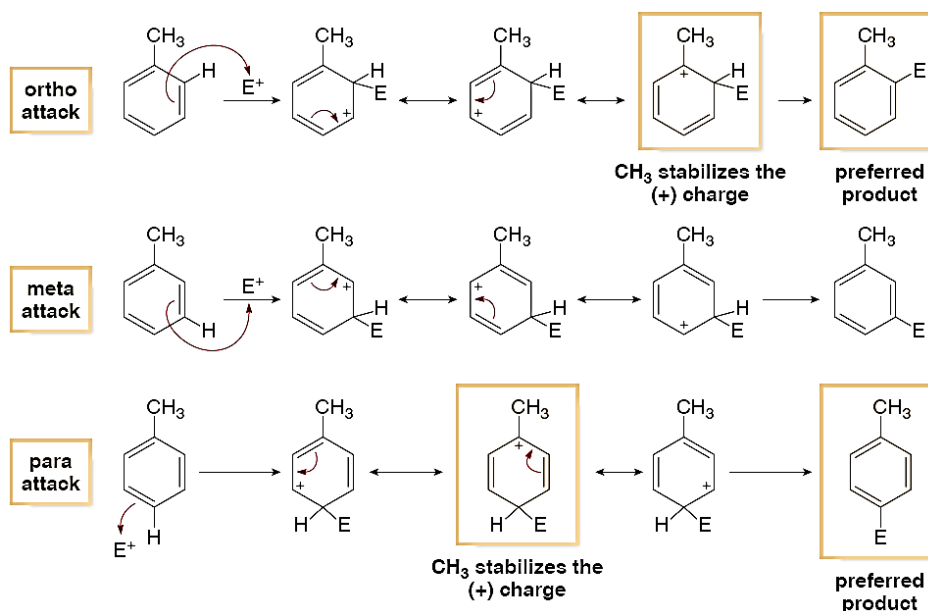
- (iii) Exceptions are halogens, which *withdraw electron* due to inductive effect while *donate electrons* due to resonance. Hence they are **ortho, para director** but **deactivate** the benzene ring.



### Ortho, para directing activators:

Electron releasing groups activate the ring and direct the electrophile towards *ortho* and *para* positions. The group may release the electrons through inductive or resonance effect. The most favourable site of attack is decided from the stability of the carbocation formed in each case. Let us consider some examples.

**Toluene:** The attack of electrophile (e.g. nitronium ion) may occur at *ortho*, *meta* and *para* positions, producing the three carbocations:

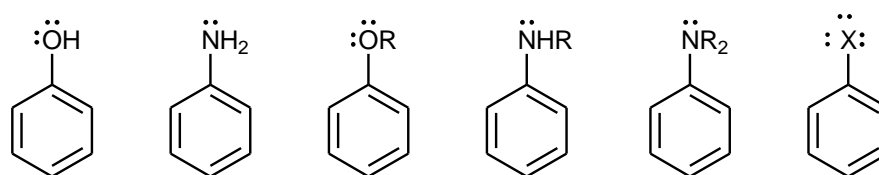


In all the three cases, each carbocation is a hybrid of three resonating structures. However, the *ortho* and *para* intermediates are more stable than the *meta* intermediate because one of the contributing structures of *ortho* and *para* intermediates carry positive charge directly on

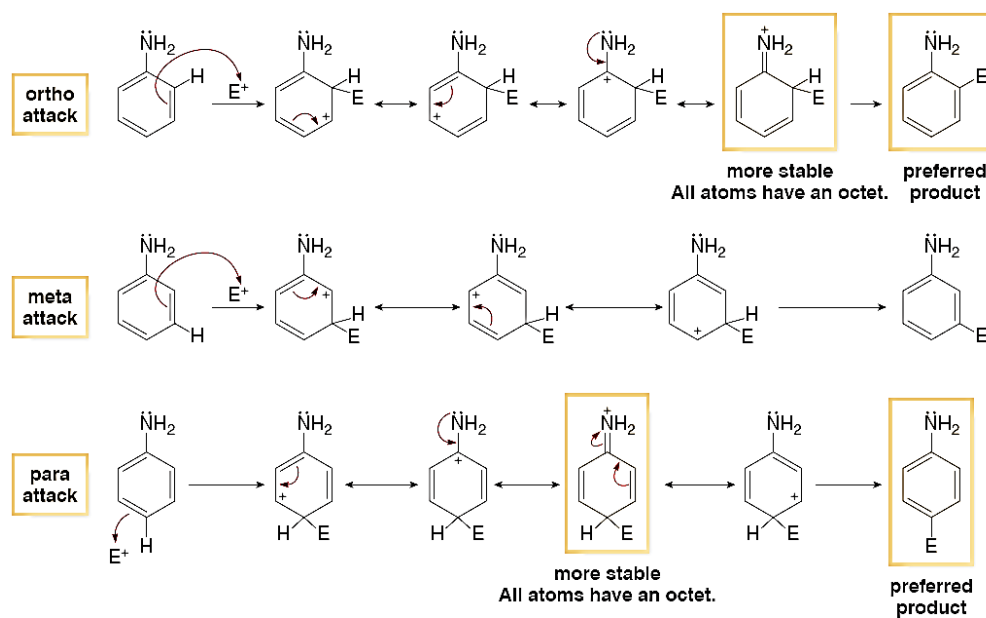
the methyl-substituted carbon, where it is stabilized by the electron-donating inductive effect of the methyl group. Further, the positive charge in *ortho* and *para* intermediates is at the tertiary carbon. Tertiary carbocation is more stable than the secondary carbocation. Therefore, *ortho* and *para* intermediates are lower in energy and preferred than the *meta* intermediate.

### Aniline:

Nitrogen, oxygen, and halogens are electronegative in nature and withdraw electrons through inductive effect (-I effect). However, the lone pair present on these atoms participates in an extended delocalisation with the  $\pi$ -electrons of the benzene ring. Due to this strong resonance effect, these groups behave as electron-releasing groups towards benzene ring.



Let us take an example of aniline. The electrophile may attack at *ortho*, *meta* and *para* positions. In case of *meta* attack three structures are contributing for  $\sigma$ -complex while in case of *ortho* and *para* attack there is one additional structure because the lone pair on nitrogen is participating in  $\pi$ -electron delocalisation, and this structure is more stable because all atoms in this have octet. Therefore,  $-\text{NH}_2$  is *ortho*, *para* directing.



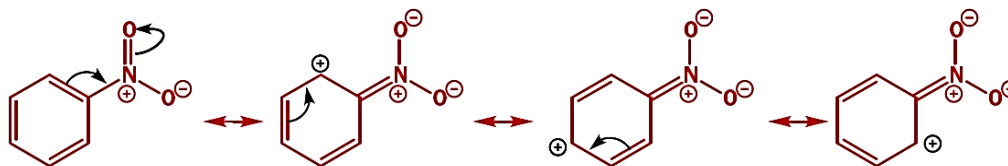
Similarly, other groups like  $\text{-NHR}$ ,  $\text{-NR}_2$ ,  $\text{-OR}$ ,  $\text{-OCOR}$ ,  $\text{-NHCOR}$  and halogens are electron releasing groups and thus are *ortho*, *para* directors.

### **Meta directors deactivators:**

A substituent on a benzene ring has its greatest effect on the carbon atoms *ortho* and *para* to the substituent. An electron-donating substituent activates primarily the *ortho* and *para* positions. An electron-withdrawing substituent (such as a nitro group) deactivates primarily the *ortho* and *para* positions, thus directs the substitution at relatively less deactivated *meta* position. The groups that withdraw electrons through inductive or resonance effect deactivate the ring. For example:

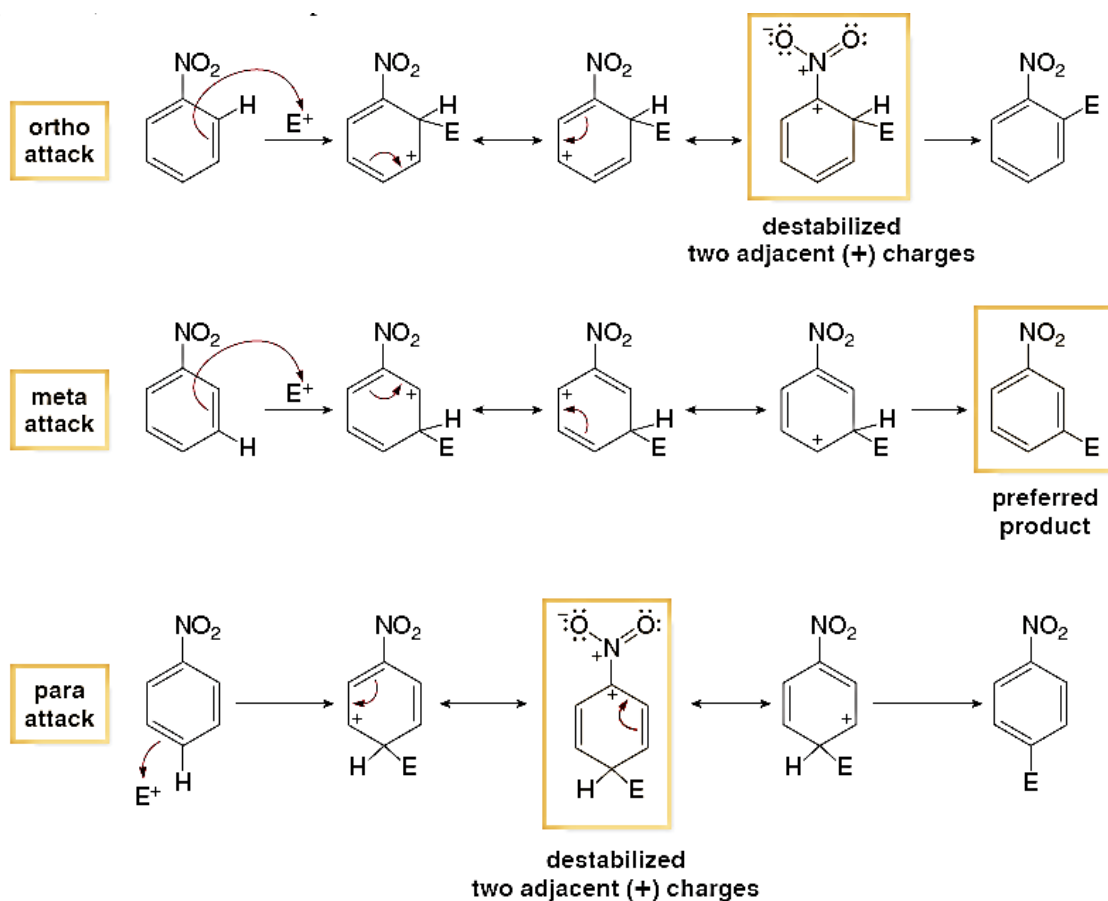
#### **Nitrobenzene:**

The nitro group withdraws electron density from the  $\pi$  system of the ring thereby making the ring electron deficient. Hence the nitro group is deactivating towards electrophilic attack. Since electron density is removed from the *ortho* and *para* positions, comparatively more electron density is available at the *meta* position for an electrophile. Hence the nitro group is *meta* directing. In the nitration of benzene, it is much harder to nitrate a second time.



Moreover, let us compare the stability of the resonating structures of the  $\sigma$ -complex (arenium ion) when electrophile attacks at *ortho*, *meta* and *para* positions.

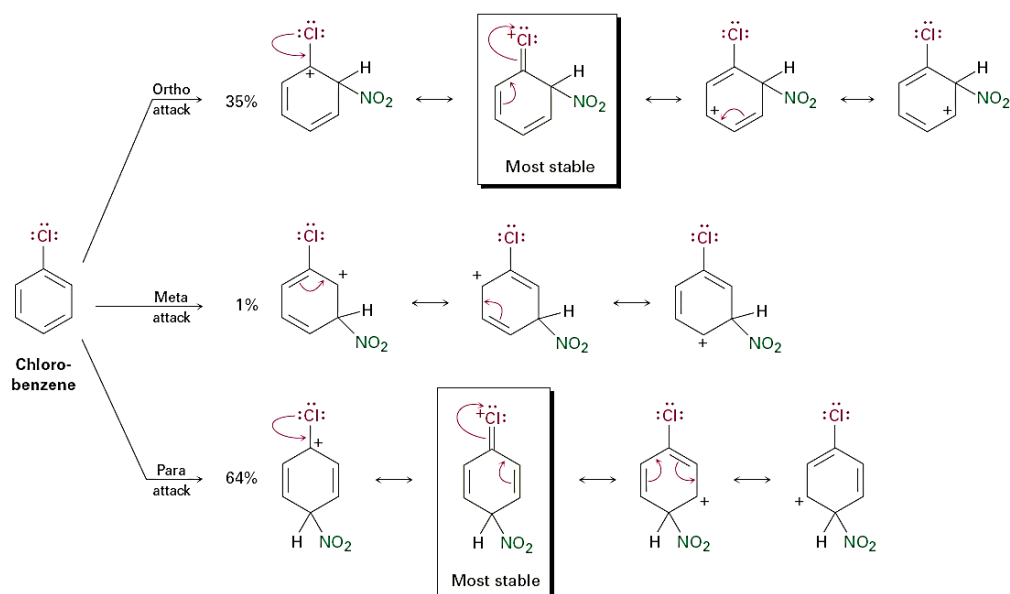




In all the three cases, the number of contributing structures is three. However, in case of *ortho* and *para* attack, one of the contributing structures is highly unstable because it contains a positive charge on adjacent atoms. Attack at *meta* position does not generate any unstable structure. Therefore, the attack of electrophile is favoured at relatively stable *meta* position. Similarly, the groups like  $-\text{CN}$ ,  $-\text{CF}_3$ ,  $-\text{CHO}$ ,  $-\text{CO}$ ,  $-\text{COOH}$ ,  $-\text{SO}_3\text{H}$  etc. are *meta* directing deactivators.

### ***Ortho, para* directing deactivators:**

Halogens being most electronegative withdraw electrons through inductive effect, and thus deactivate the ring for electrophilic substitution. On the other hand, halogens possess lone pair of electrons which participate in delocalization with the  $\pi$ -electrons of the benzene ring through resonance effect, thus release electrons towards the ring. This release of electrons through resonance (+R effect), stabilizes the carbocations formed by *ortho* and *para* attack. Thus, the resonance effect (+R effect) governs the orientation towards *ortho* and *para* positions, whereas inductive effect (-I effect) governs the reactivity of the ring. Therefore, halogens are *ortho, para* directing deactivators.

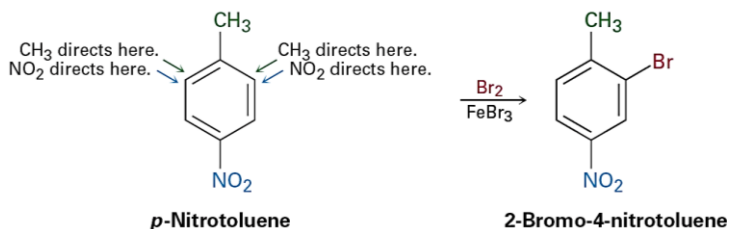


- **Note:** Halogens, hydroxyl, alkoxyl, and amino groups all withdraw electrons through inductive effect (-I effect) and donate electrons by resonance. All are *ortho* and *para* directors because of the lone pair of electrons on the atom bonded to the aromatic ring. However, hydroxyl, alkoxyl, and amino groups have a weaker electron-withdrawing inductive effect but a stronger electron donating resonance effect and are thus activators, while halogens have a stronger electron-withdrawing inductive effect but a weaker electron-donating resonance effect and are thus deactivators.

### Orientation in disubstituted benzene

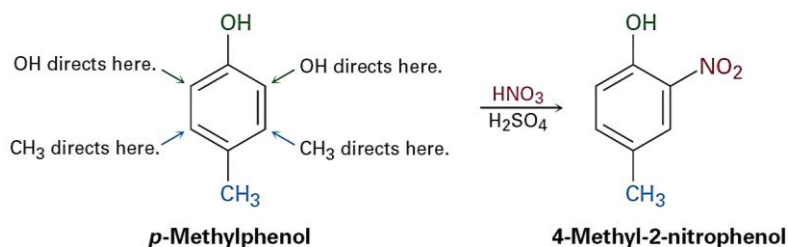
Electrophilic substitution of a disubstituted benzene ring is governed by the same resonance and inductive effects that affect mono substituted rings. The only difference is the **additive effects** of two different groups. It follows **three rules**:

1. If the **directing effects** of the **two groups** reinforce each other, only one product will be formed and that can easily be predicted. For example, in case of bromination of nitrotoluene,  $-\text{CH}_3$  group is *o*-, *p*-director whereas  $-\text{NO}_2$  group is *m*-director. But both the positions are same. Therefore, it produces only 2-bromo-4-nitrotoluene.



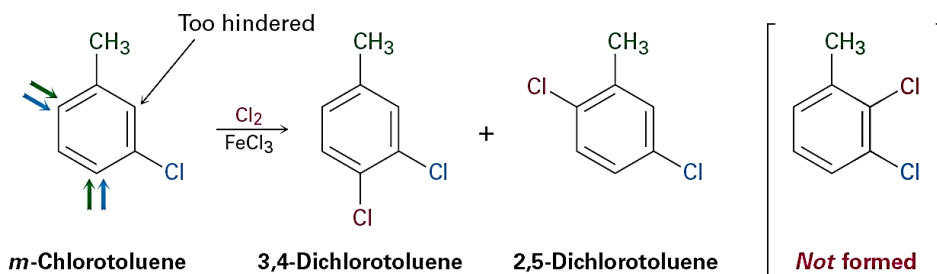
2. If the **directing effects** of the **two groups** oppose each other, the more powerful activating group has the dominant influence, but mixtures of products are often formed.

For example, bromination of *p*-methylphenol yields primarily 2-bromo-4-methylphenol because -OH is a more powerful activator than -CH<sub>3</sub>.

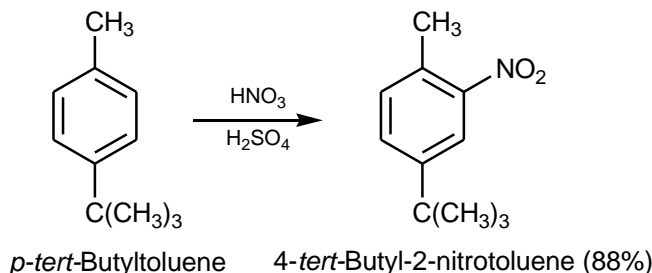


### 3. Steric hindrance:

- a. Due to steric hindrance, the electrophilic substitution is not favoured between two groups which are positioned *meta* to each other.



- b. When two positions are comparably activated by alkyl groups, substitution usually occurs at the less hindered site. For example, due to steric hindrance, nitration of *p*-*tert*-butyltoluene takes place at positions *ortho* to the methyl group in preference to those *ortho* to the larger *tert*-butyl group.



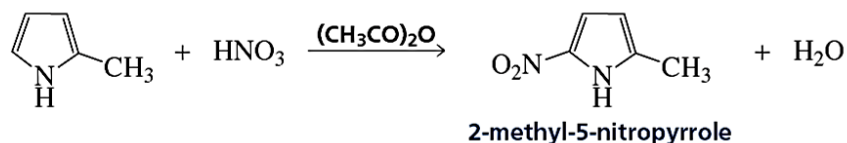
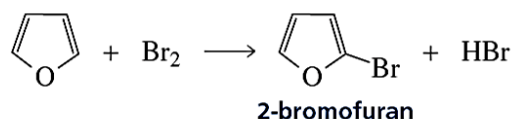
### 1.3.7. Representative Reactions of pyrrole, furane, thiophen and pyridine

As we have seen earlier that heterocyclic compounds, like pyridine, pyrrole, furan and thiophene, are aromatic in nature. Therefore, they also undergo electrophilic substitution reactions – halogenations, sulfonation, and nitration. In fact, heterocycles, in general, are more reactive towards electrophiles than benzene is, and low temperatures are often required to accomplish the reaction. Friedel-Craft alkylation is not generally practicable in heterocyclic compounds. However, many heterocyclic systems, including furans,

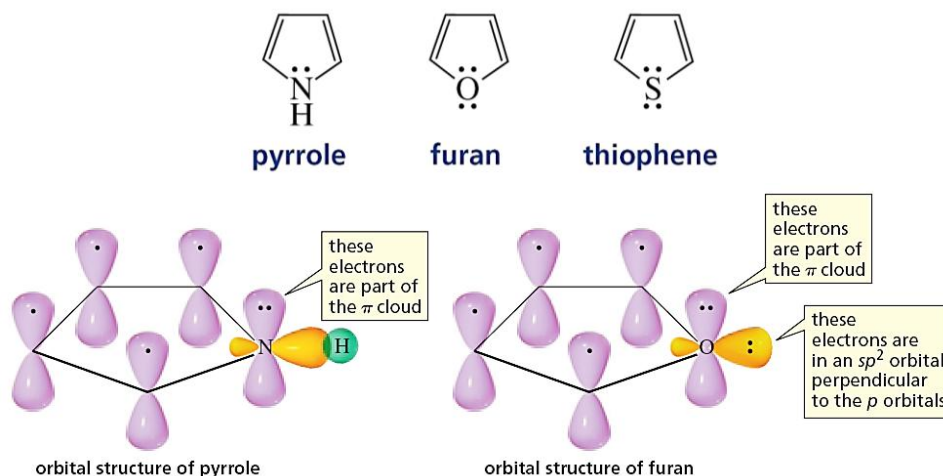
thiophenes, pyrans, and pyrroles but not pyridines, can be acylated in good yield by Friedel Craft acylation.

### Electrophilic substitution Reactions of pyrrole, furan and thiophene:

Pyrrole, furan, and thiophene are aromatic and more reactive toward electrophilic aromatic substitution – more like phenol and aniline than benzene.

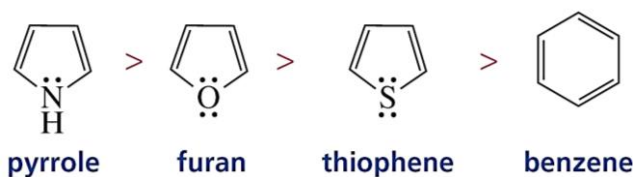


Because of the lone pair of electrons on the heteroatom they can donate electrons into the ring by resonance and thus are better able to stabilize the positive charge on the carbocation intermediate.



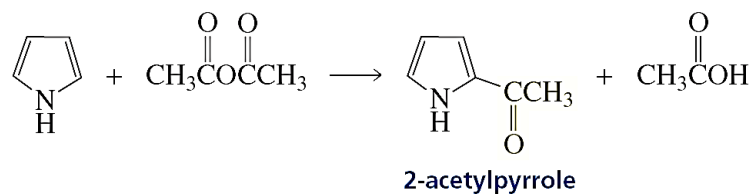
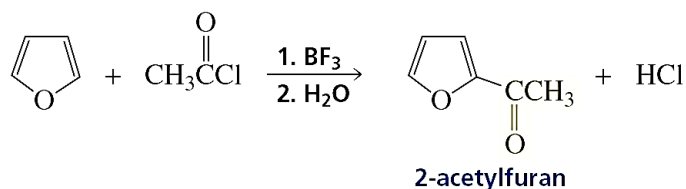
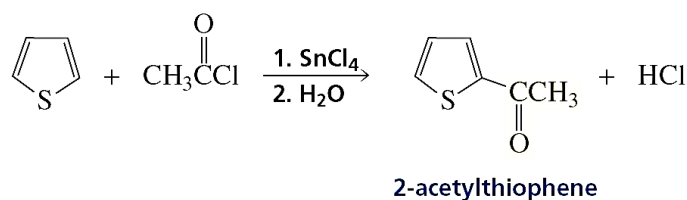
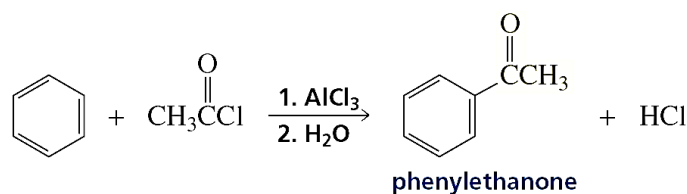
Furan is not as reactive as pyrrole in electrophilic aromatic substitution reactions. The oxygen of furan is more electronegative than the nitrogen of pyrrole, so the oxygen is not as effective as nitrogen in stabilizing the carbocation. Thiophene is less reactive than furan toward electrophilic substitution because sulfur's electrons are in a 3p orbital, which overlaps less effectively than the 2p orbital of nitrogen or oxygen with the 2p orbital of carbon.

### Relative reactivity toward electrophilic aromatic substitution



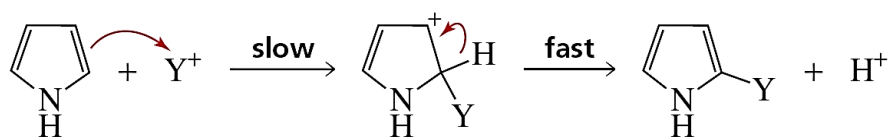
For such highly reactive heteroaromatic systems, mild non-acidic reagents are commonly used for electrophilic substitution. The relative reactivities of the five-membered-ring heterocycles are reflected in the Lewis acid required to catalyze a Friedel–Crafts acylation reaction:

- Benzene requires  $\text{AlCl}_3$ , a relatively strong Lewis acid.
- Thiophene is more reactive than benzene, so it can undergo a Friedel–Crafts reaction using  $\text{SnCl}_4$ , a weaker Lewis acid.
- Furan requires  $\text{BF}_3$ , an even weaker Lewis acid.
- Pyrrole is so reactive that an anhydride is used instead of a more reactive acyl chloride, and no catalyst is necessary.

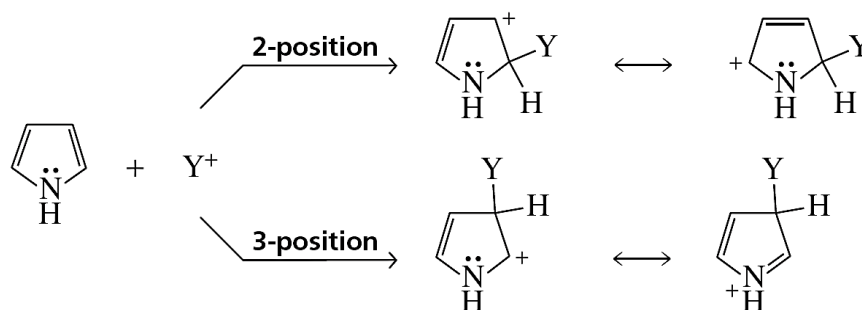


### Mechanism of electrophilic substitution:

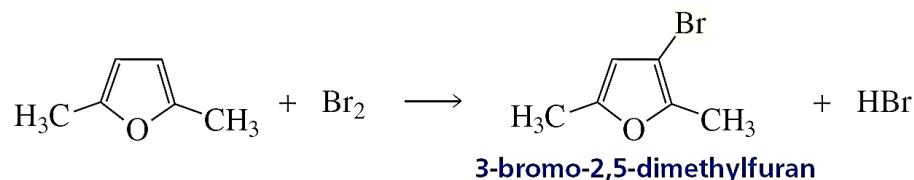
The mechanism of electrophilic substitution in heterocyclic compounds is same as in benzene. The electrophilic attack on the  $\pi$ -electrons of the ring generates a nonaromatic  $\sigma$ -complex. This is slow and rate determining step. A proton is lost from the  $\sigma$ -complex to give a substituted product with the regeneration of aromaticity.



Substitution occurs preferentially at C-2 because the intermediate obtained by attaching a substituent at this position is more stable than the intermediate obtained by attaching a substituent at C-3. The intermediate resulting from C-2 substitution of pyrrole has three resonance contributors. The intermediate resulting from C-3 substitution, however, has two resonance contributors.

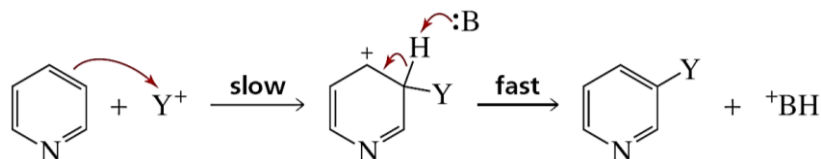


When both positions adjacent to the heteroatom are occupied, electrophilic substitution occurs at C-3.

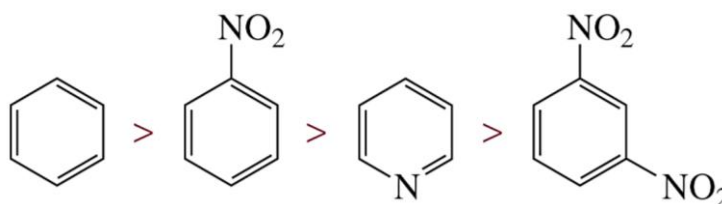


### Electrophilic substitution Reactions of pyridine:

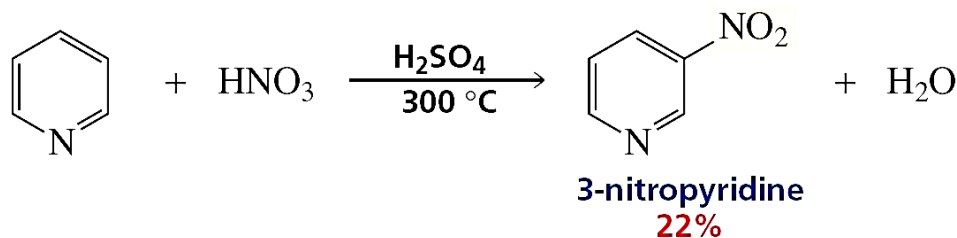
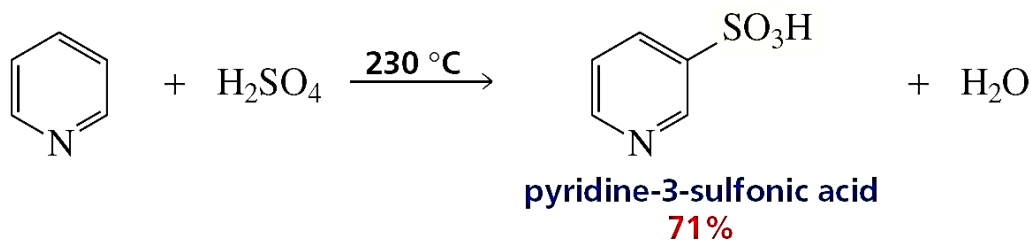
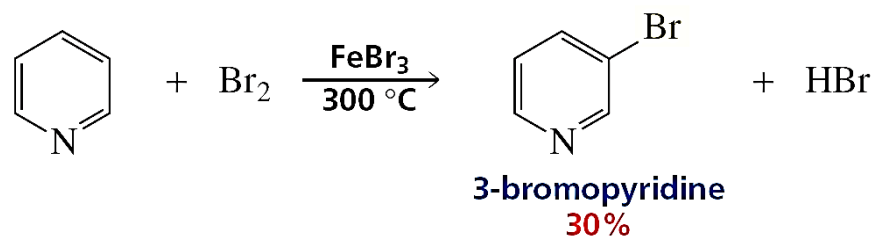
Being aromatic, pyridine undergoes electrophilic substitution reactions with the same mechanism like in benzene.



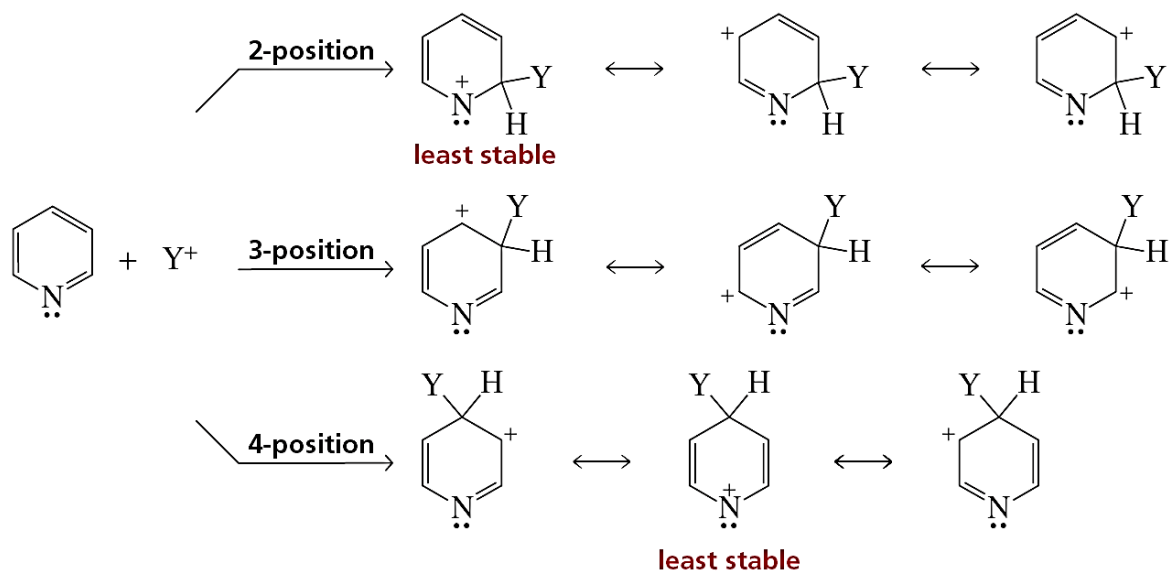
Pyridine deactivates the ring for electrophilic substitution. The deactivation is due to the presence of electronegative nitrogen which pulls the electron from the ring and thus decreases the electron density in the ring. The carbocation intermediate obtained from electrophilic aromatic substitution of pyridine becomes less stable than the carbocation intermediate obtained from electrophilic aromatic substitution of benzene. Therefore pyridine is less reactive than benzene, even **less reactive than nitrobenzene**.



**Pyridine** undergoes electrophilic aromatic substitution reactions only under vigorous conditions, and the yields of these reactions are often quite low. It undergoes halogenations, nitration, and sulfonation. However, Friedel-Craft **alkylation and acylation are not possible**. If the nitrogen becomes protonated under the reaction conditions, the reactivity is further decreased because a positively charged nitrogen is more electron withdrawing than a neutral nitrogen.



The substitution occurs preferably at 3-position ( $\beta$ -position) as it results in the formation of a more resonance-stabilized intermediate. The intermediate formed by the attack of electrophile at 2- and 4-position are less stabilized because one of the contributing structures in both cases carries positive charge on electronegative nitrogen; therefore, it is high-energy structure.



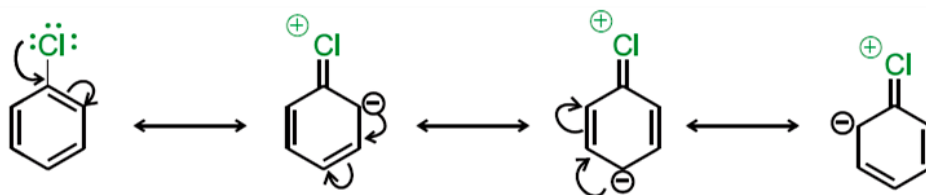
## 1.4. Nucleophilic Aromatic Substitution Reactions

Nucleophilic aromatic substitution reactions are far less common than electrophilic aromatic substitution reactions and have only limited application for the synthesis of organic compounds. Nucleophiles can displace halide ions from aryl halides, particularly if there are strong electron-withdrawing groups *ortho* or *para* to the halide. Because a nucleophile substitutes for a leaving group on an aromatic ring, this class of reactions is called nucleophilic aromatic substitution.

### Reactions of Aryl halides:

Aryl halides are extremely less reactive towards nucleophilic substitution reactions due to the following reasons:

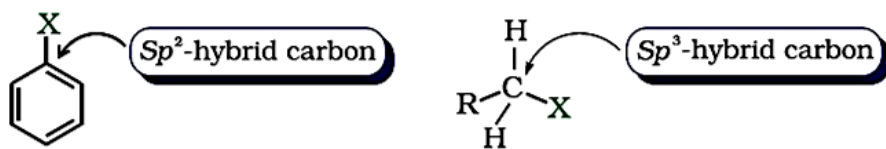
- (i) *Resonance effect:* In aryl halides, the electron pairs on halogen atom are in conjugation with  $\pi$ -electrons of the ring and the following resonating structures are possible.



C—Cl bond acquires a partial double bond character due to resonance. As a result, the bond cleavage in aryl halides is difficult than alkyl halides and therefore, they are less reactive towards nucleophilic substitution reaction.

- (ii) *Difference in hybridisation of carbon atom in C—X bond:* In alkyl halides, the carbon atom attached to halogen is  $sp^3$  hybridised while in case of aryl halides, the carbon atom attached to halogen is  $sp^2$  hybridised.



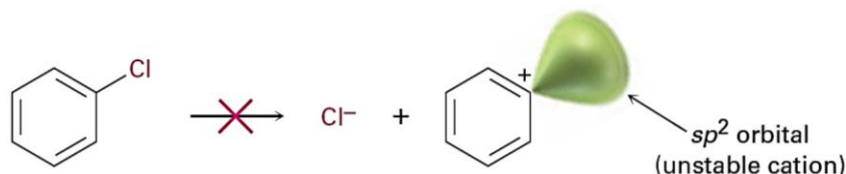


The  $sp^2$  hybridised carbon with a greater  $s$ -character is more electronegative and can hold the electron pair of C—X bond more tightly than  $sp^3$  hybridised carbon in alkyl halides with less  $s$ -character. The electrons of  $sp^2$  hybridized carbon, being more close to the nucleus compared to  $sp^3$  hybridized carbon, form a stronger bond. Therefore, aryl halides are less reactive than alkyl halides towards nucleophilic substitution reaction.

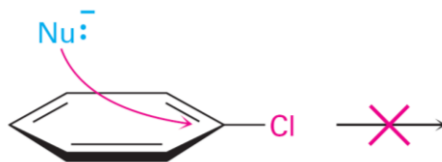
#### 1.4.1. Mechanisms of Nucleophilic Aromatic Substitution Reactions:

Aryl halides undergo **nucleophilic aromatic substitution** under certain conditions but by mechanisms quite different from those for nucleophilic aliphatic substitutions. They do not follow  $S_N1$  or  $S_N2$  mechanisms unlike alkyl halides because:

- In both  $S_N1$  and  $S_N2$  mechanisms, the C—X bond cleavage requires a very high energy due to high bond strength of C—X bond.
- The  $S_N1$  mechanism is not favoured because the phenyl cation formed by the removal of halide from aryl halides is highly unstable.

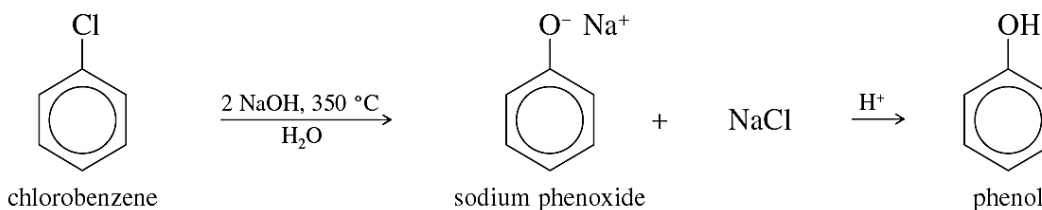


- The  $S_N2$  reactions undergo by the nucleophilic attack from the back (rear) side of the molecule to form a product with inversion of configuration. In aryl halides, back (rear) side attack is not favoured due to steric hindrance by aromatic ring.



Therefore, the substitution in aryl halides occurs through the following two mechanisms:

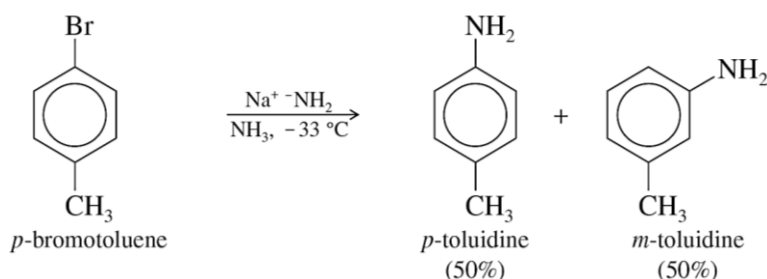
**Elimination-addition mechanism (via benzyne intermediate):** Unactivated aryl halides react with strong bases by nucleophilic substitution reaction under drastic conditions such as high temperature, high pressure, and strong concentrated reagent. For example, a commercial synthesis of phenol (the “Dow process”) involves treatment of chlorobenzene with sodium hydroxide and a small amount of water in a pressurized reactor at 350 °C:



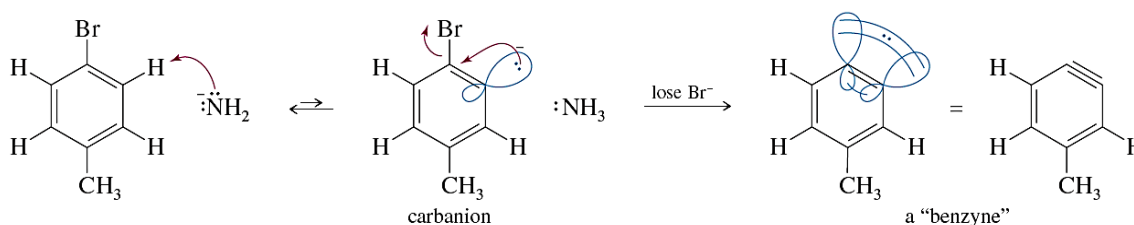
Similarly, chlorobenzene reacts with sodium amide ( $\text{NaNH}_2$ , an extremely strong base) in presence of liquid ammonia to produce aniline ( $\text{Ph-NH}_2$ ) at  $-33^\circ\text{C}$ . The reaction does not require high temperature.

### Mechanism:

The elimination-addition nucleophilic substitution reaction undergo through benzyne intermediate. Let us consider the reaction of *p*-bromotoluene with  $\text{NaNH}_2$ .



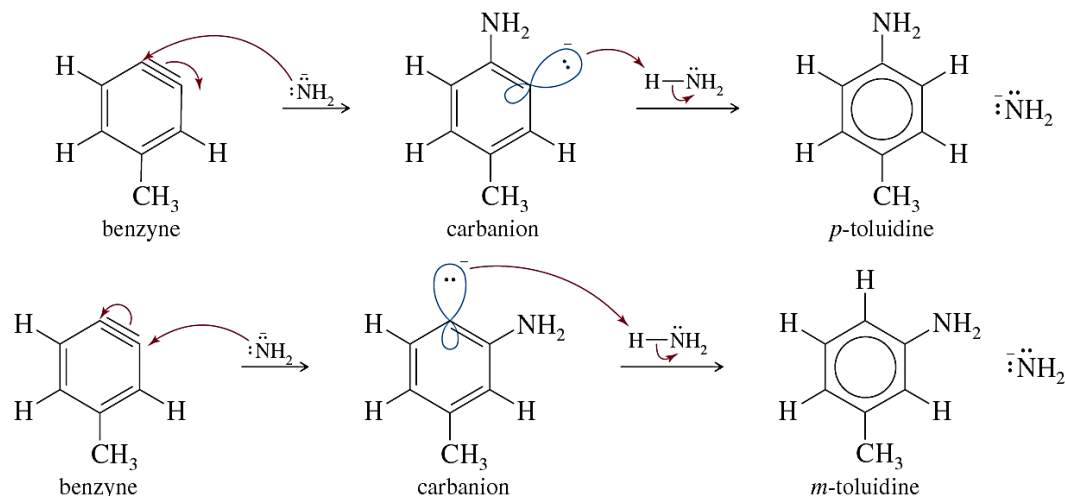
**Steps 1 & 2: Abstraction of *ortho*-proton of *p*-bromotoluene (formation of carbanion) followed by elimination of Chloride ion (formation of benzyne intermediate).** Highly electronegative bromine makes the *ortho*-proton acidic, which can easily be abstracted by a strong base like amide ion ( $\text{:NH}_2^-$ ) to produce carbanion. The electronegative bromine stabilizes the carbanion through its  $-I$  effect. Loss of bromide ion from carbanion results in the formation of highly reactive benzyne intermediate.



Bromide comes out with its bonding electrons leaving behind an empty orbital. This orbital overlaps with the filled orbital adjacent to it, giving additional bonding between these two carbon atoms. The two orbitals are directed  $60^\circ$  away from each other, so their overlap is not very effective due to improper orientation. So this is a very reactive, highly strained triple bond. This reactive intermediate is called a **benzyne**; it can be symbolized by drawing a triple bond between these two carbon atoms.

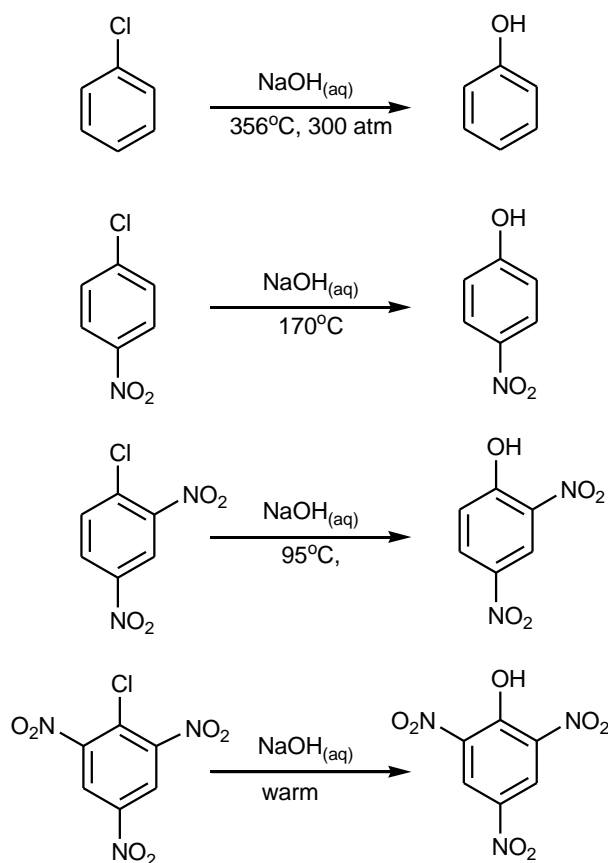
**Step 3 & 4: Addition of  $\text{:NH}_2^-$  to benzyne (formation of carbanion) followed by proton abstraction by carbanion (formation of substituted product).** Amide ion, a strong

nucleophile, attacks at either end of the weak, reactive benzyne triple bond. Subsequent protonation gives toluidine. About half of the product results from attack by the amide ion at the *meta* carbon, and about half from attack at the *para* carbon.



#### Addition-elimination mechanism:

The presence of electron-withdrawing groups (such as nitro group) on benzene ring activates the rate of nucleophilic substitution reactions. More the number of electron-withdrawing substituents present at *ortho* or *para* positions, the nucleophilic substitution reaction will be faster. For example, chlorobenzene can be converted into phenol by heating in aqueous sodium hydroxide solution at a temperature of  $356^\circ\text{C}$  and 300 atm. pressure while 2,4,6-trinitrophenol can be prepared from 2,4,6-trinitrochlorobenzene in alkaline medium at room temperature.



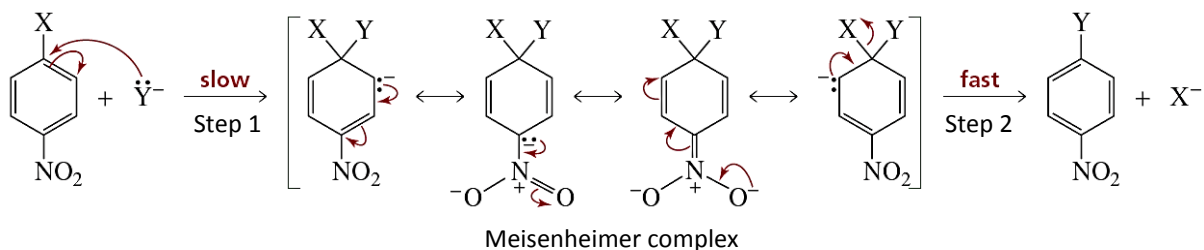
In the presence of electron-withdrawing groups the nucleophilic substitution reaction follows addition-elimination mechanism.

### Mechanism:

The addition-elimination substitution reaction occurs in two steps.

**Step 1: Addition of nucleophile (formation of Meisenheimer-complex).** The nucleophile adds to the carbon bearing the leaving group (i.e. halide) to produce negatively charged  $\sigma$ -complex. This complex is called Meisenheimer complex. The presence of electron withdrawing groups at *ortho* or *para* positions stabilize the Meisenheimer complex by delocalization of the negative charge. This is slow and rate determining step.

**Step 2: Elimination of leaving group (formation of substituted product).** Elimination of halide ion regenerates the aromatic ring and produces the substituted product. This step is fast.



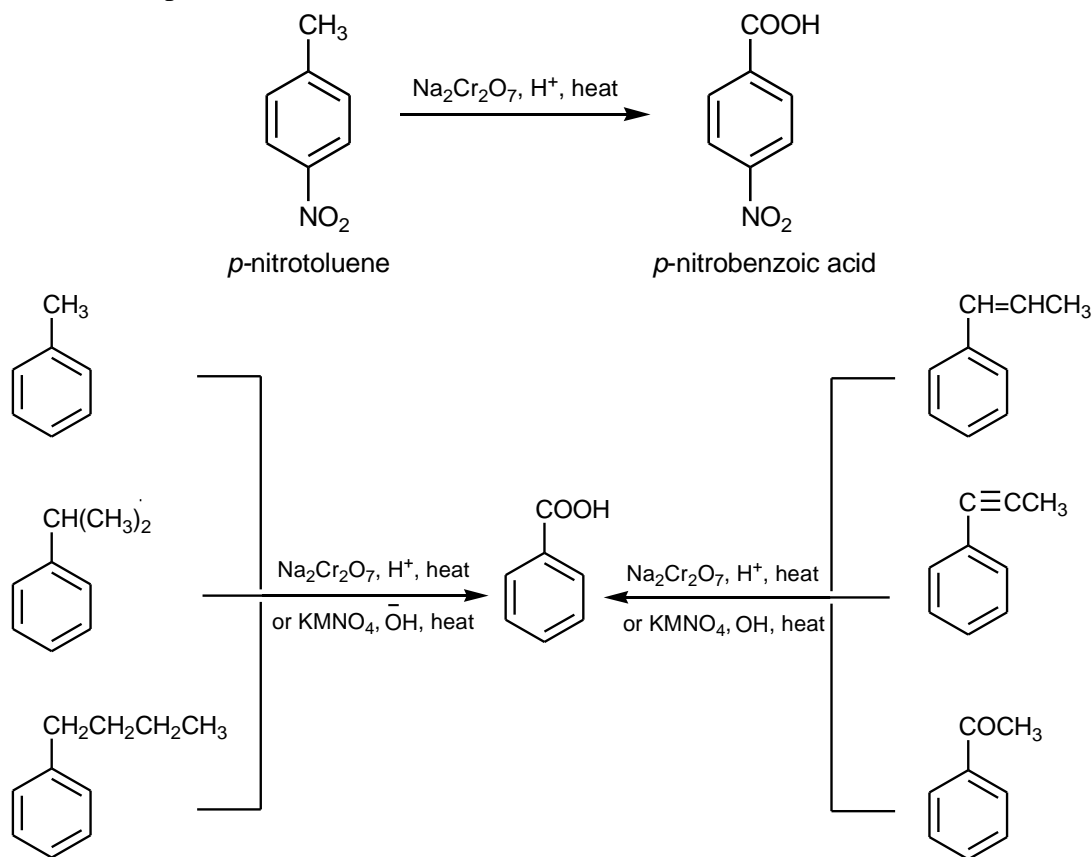
In nucleophilic substitution reaction, the nucleophile must be a stronger base than the leaving group, because the weaker of the two bases will be the one eliminated from the intermediate.

## 1.5. Reactions of Aromatic Side Chains

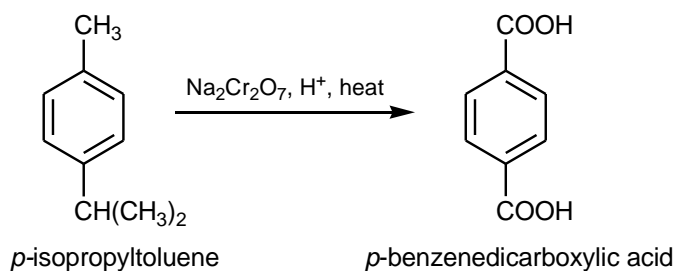
### 1.5.1. Oxidation and Substitution of Alkyl Side-Chains

#### Oxidation:

The oxidation of alkylbenzenes, irrespective of the side chain, with acidified dichromate or alkaline potassium permanganate produces benzoic acid or substituted derivative of benzoic acid as the final product.



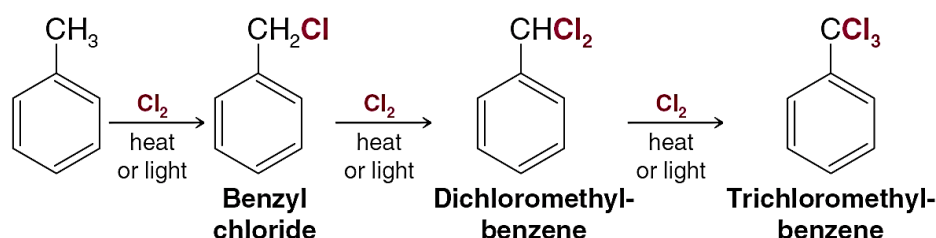
If two alkyl groups are present on the ring, both are oxidized.



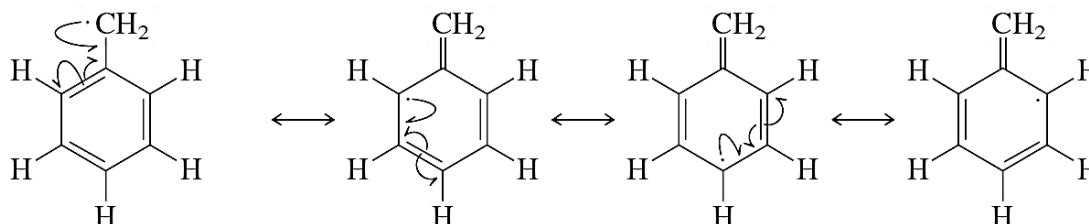
The oxidation occurs at the benzylic carbon. However, it is necessary that benzylic carbon should have at least one hydrogen atom attached to it, for example, the oxidation does not occur in *tert*-butylbenzene. Functional groups such as  $-\text{NO}_2$ ,  $-\text{COOH}$ , halogens, and  $-\text{SO}_3\text{H}$  usually are not affected under these conditions.

### Halogenation:

Toluene reacts with chlorine in presence of light (in the absence of Lewis acid) which results in substitution in the side chain ( $-\text{CH}_3$ ) like substitution reaction in alkanes. The reaction produces, subsequently, benzyl chloride, benzal chloride (dichloromethylbenzene) and finally trichloromethylbenzene.

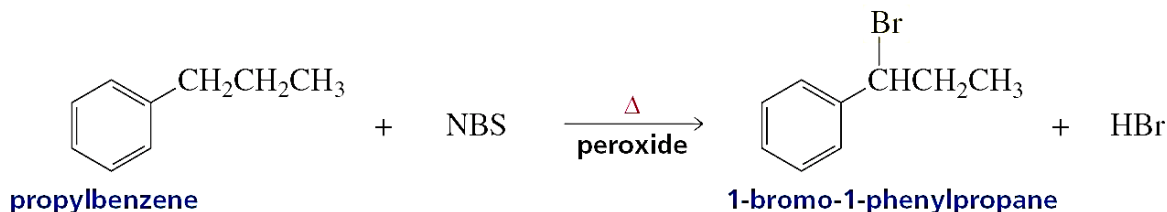


The reaction undergoes through free radical mechanism and the substitution occurs exclusively at the benzylic position because benzyl radical is stabilized by electron delocalization and thus weakens the benzylic C–H bond. The unpaired electron is shared by the benzylic carbon as well as the ring carbons that are *ortho* and *para* to it.



Most stable Lewis structure  
of benzyl radical

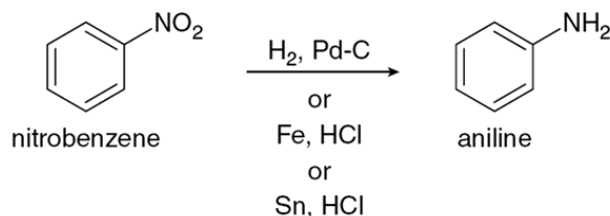
Benzylic bromination is a more commonly used laboratory procedure than chlorination. *N*-bromosuccinimide (NBS) in the presence of peroxides is generally used as free-radical brominating agent. Peroxides acts as initiators.



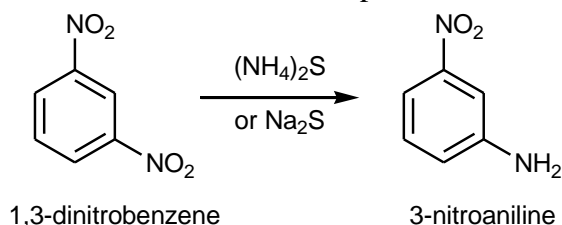
### 1.5.2. Reduction of Nitro Groups and Aryl Ketones

#### Reduction of nitro groups:

The nitro group can easily be reduced to an amino group ( $-\text{NH}_2$ ) by  $\text{H}_2$  and a catalyst, or a metal (e.g. Fe or Sn) and a strong acid like HCl.



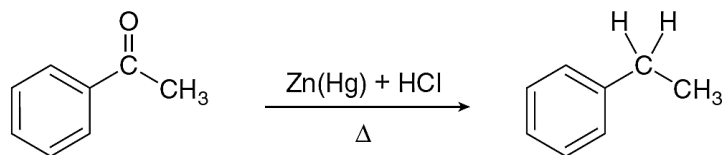
The dinitro compounds can undergo selective reduction of one of the nitro groups in the presence of ammonium or sodium sulfide. For example



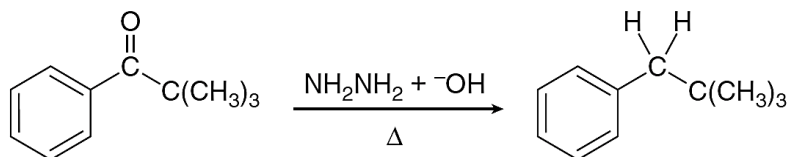
#### Reduction of aryl ketones:

The aryl ketones can be reduced by two methods:

- (i) **Clemmensen reduction:** The carbonyl group ( $>\text{C}=\text{O}$ ) of aromatic ketones can be reduced to methylene ( $>\text{CH}_2$ ) group by using zinc and mercury (zinc amalgam) in presence of acid. This method is used for reducing carbonyl compounds that are sensitive to alkali.

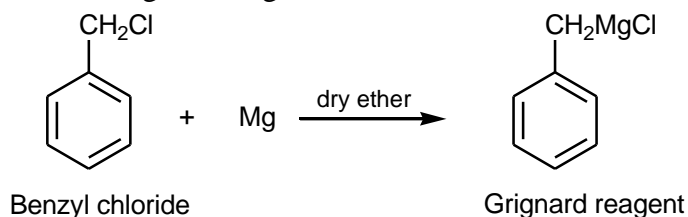


- (ii) **Wolff-Kishner reduction:** The carbonyl group ( $>\text{C}=\text{O}$ ) of aromatic ketones can be reduced to methylene ( $>\text{CH}_2$ ) group by reaction with hydrazine followed by hydrolysis in presence of strong base. This method is used for reducing carbonyl compounds that are sensitive to acids.



### 1.5.3. Conversion of Halogens to organometallic Reagents

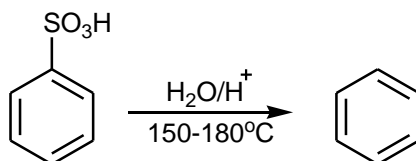
The reaction of benzyl chloride with magnesium in dry ether produces organometallic reagent. This is also called Grignard reagent.



### 1.5.4. Hydrolysis and Fusion of Sulfonic Acids

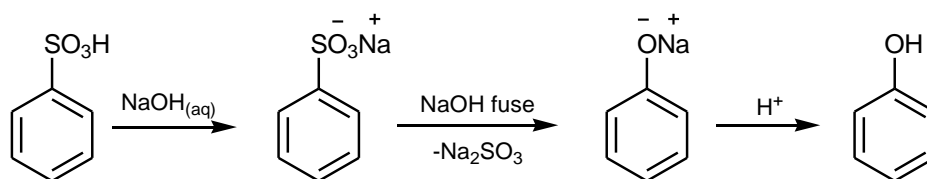
#### Hydrolysis of arylsulfonic acids:

Benzenesulfonic acid on heating in aqueous acidic medium at  $150\text{--}180^\circ\text{C}$  undergoes desulfonation to produce benzene.



#### Fusion of arylsulfonic acid:

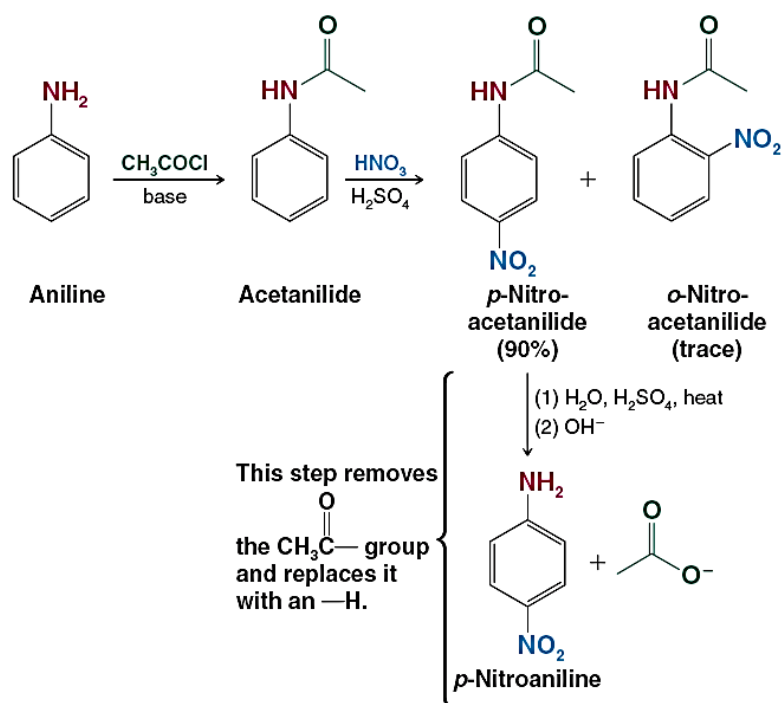
Fusion of sodium salt of arylsulfonic acid with sodium hydroxide results in the formation of phenol.



### 1.5.5. Modifying the Influence of Strong Activating Groups

The strong activating groups like amino and hydroxyl groups make the benzene ring so reactive that the electrophilic substitution is difficult to stop at the stage of monosubstitution; the reaction generally gives polysubstituted product. To overcome this problem, the amino group is converted to acetanilide by acetylation, and hydroxyl group is converted to methoxy group by methylation. Amide and methoxy groups are moderate activators, therefore, the monosubstituted product can be achieved in good yield. For example nitration of aniline can be done by protecting the amino group by acetylation with acetic anhydride or acetyl chloride followed by substitution using nitrating reagent. The reaction gives *p*-nitroacetanilide in excellent yield with only a trace amount of *ortho* isomer because the *ortho* position is sterically hindered by large acetomido group ( $-\text{NHCOCH}_3$ ). Acidic hydrolysis of *p*-nitroacetanilide removes the acetyl group and gives *p*-nitroaniline, also in good yield.





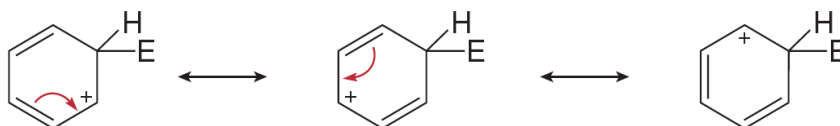
### 1.5.6. Diazotization of Primary Aromatic Amines and their Usefulness in Synthesis of Aromatic Derivatives

It will be discussed in Unit 2

## 1.6. Summary

- A cyclic, planar, completely conjugated compound containing  $4n + 2$   $\pi$ -electrons (where  $n = 0, 1, 2, 3$ , and so on) is called **aromatic compound**. This aromaticity provides more stability to the compound than a similar acyclic compound with the same number of  $\pi$ -electrons.
- A cyclic, planar, completely conjugated compound containing  $4n$   $\pi$ -electrons (where  $n = 0, 1, 2, 3$ , and so on) is called **antiaromatic compound**. An antiaromatic compound is less stable than a similar acyclic compound with the same number of  $\pi$ -electrons.
- A compound lacking one (or more) of the four requirements to be aromatic is called **nonaromatic**.
- In aromatic compounds, every atom in the ring contains a  $p$ -orbital to delocalize electron density. All bonding MOs and HOMOs are completely filled and no electron occupies antibonding orbitals.
- The resonance energy for benzene is large (36.0 kcal/mol) meaning that the  $\pi$  system of benzene is extremely stable.
- Aromatic compounds are named according to IUPAC rules, although many common names of the simpler benzene derivatives are retained in IUPAC e.g. to cumene, styrene, xylene, phenol, aniline, benzoic acid, and anisole.

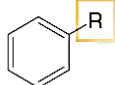
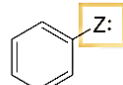
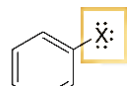
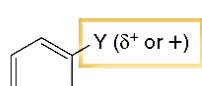
- Substituted benzenes are named by adding prefixes or suffixes to the word *benzene*. Disubstituted systems are named as **ortho** (1, 2-disubstituted), **meta** (1, 3-disubstituted), and **para** (1, 4-disubstituted) compounds, depending on the location of the substituents. These are abbreviated as ***o*-**, ***m*-**, and ***p*-**, respectively.
- The parent aryl substituent,  $-\text{C}_6\text{H}_5$ , is called **phenyl group**; its homolog  $\text{C}_6\text{H}_5\text{CH}_2-$  is named **benzyl group**.
- If a compound with any substituent has a common name (e.g. aniline contains  $-\text{NH}_2$ ), the molecule is named after that parent molecule and the key group is assigned the number 1.
- When none of the groups impart a *special* name, the substituents are listed in alphabetical order followed by the word *benzene*. For example, 1-chloro-4-ethylbenzene or *p*-chloroethylbenzene.
- A **heterocyclic compound** is a cyclic compound containing one or more **heteroatom** (e.g. **O, N, S**) in the ring. Pyridine, pyrrole, furan, and thiophene follow Huckel's rule, therefore, they are aromatic heterocyclic compounds.
- Because of stability due to aromaticity, benzene does not undergo addition reaction unlike simple alkenes. Rather it undergoes electrophilic substitution reactions.
- The most common electrophilic aromatic substitution reactions include halogenation, nitration, sulfonation, and Friedel–Crafts acylation and alkylation.
- After the electrophile is generated, all electrophilic aromatic substitution reactions follow the same two step mechanism i.e. the attack of electrophile on the aromatic  $\pi$ -system to generate resonance stabilized nonaromatic carbocation intermediate, called **arenium ion** followed by removal of proton to produce the final product with regeneration of aromaticity.



- Halogenation takes place in presence of a Lewis acid catalyst ( $\text{FeX}_3$  or  $\text{AlX}_3$ ) to give aryl halides.
- Nitration proceeds with nitric acid in presence of sulfuric acid as catalyst and produce nitroarenes.
- In a sulfonation reaction, aromatic rings react with  $\text{SO}_3$  in the presence of sulfuric acid to yield arylsulfonic acids.
- **Friedel-Crafts acylation** takes place with acid chlorides in the presence of a Lewis acid like  $\text{AlCl}_3$  to produce acylbenzenes.
- In a **Friedel-Crafts alkylation**, aromatic rings react with alkyl halides in the presence of a Lewis acid like  $\text{AlCl}_3$  to produce alkylbenzenes. Polyalkylation and carbocation rearrangements often occur in Friedel–Crafts alkylation. The major product will be the product with the rearranged alkyl group. A straight-chain alkyl group can be placed on a benzene ring via a Friedel–Crafts acylation reaction, followed by reduction of the carbonyl

group by catalytic hydrogenation, a **Clemmensen reduction**, or a **Wolff–Kishner reduction**.

- Substituent groups, other than hydrogen, on an aromatic ring influence the reaction rate and substitution pattern of electrophilic aromatic substitution reactions.
- Substituents can be divided into three broad classes:
  - (a) Alkyl groups and all groups in which the atom bonded to the ring has an unshared pair of electrons are *ortho-para* directing and most are electron releasing; therefore they **activate** the ring toward electrophilic aromatic substitution
  - (b) Halogens are exceptions. They are *ortho-para* directing, but electron withdrawing; therefore they weakly deactivate the ring toward electrophilic aromatic substitution.
  - (c) All groups with a partial positive charge on the atom attached to the ring are *meta* directing and electron withdrawing; therefore they are **deactivators** toward electrophilic aromatic substitution.
- Aromatic compounds containing two or more substituents already on ring, the orientation of the incoming substituent will be governed according to the more activating group.
- Summary of substituent's effects in electrophilic substitution reactions in aromatic compounds:

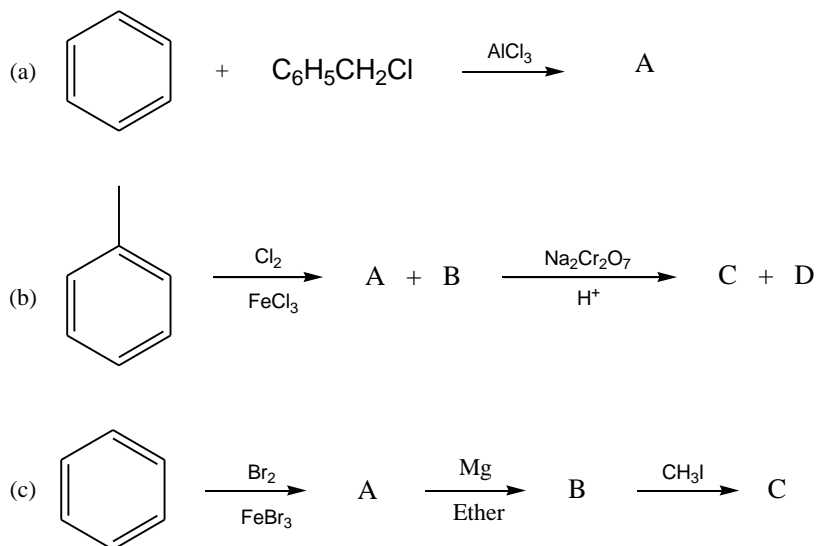
	Substituent	Inductive effect	Resonance effect	Reactivity	Directing effect
[1]	 R = alkyl	donating	none	activating	ortho, para
[2]	 Z = N or O	withdrawing	donating	activating	ortho, para
[3]	 X = halogen	withdrawing	donating	deactivating	ortho, para
[4]	 Y ( $\delta^+$ or +)	withdrawing	withdrawing	deactivating	meta

- Aromatic compounds also react with nucleophile under certain reaction conditions. For example, aryl halides react with very strong bases ( $\text{NaNH}_2$ ) or moderate bases ( $\text{NaOH}$ ) at high temperature ( $300^\circ\text{C}$  to  $500^\circ\text{C}$ ) to yield products in which the halogen is replaced by the nucleophile.
- The nucleophilic aromatic reactions take place through a benzyne intermediate, or a carbanion ion intermediate.
- Substitution is also possible at the benzylic position of aromatic hydrocarbons because benzyliccation and radical intermediates are stabilized through delocalization into the aromatic ring. For example:

- (i) Benzylic hydrogens can be replaced by bromine or chlorine in the presence of light or heat.
- (ii) The whole side chain is oxidized to  $-\text{COOH}$ .

### 1.7.Exercises

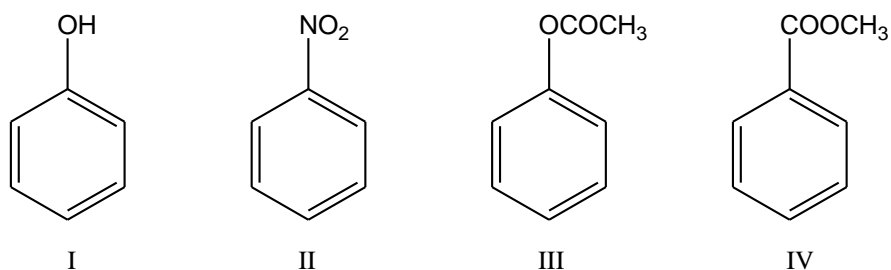
Q. 1. Predict the products in the following reactions:



Q. 2. Giving suitable explanation, classify the following compounds as aromatic, non-aromatic, and anti-aromatic.

- |                             |                             |
|-----------------------------|-----------------------------|
| (a) Cyclobutadiene          | (b) Cyclopentadienyl cation |
| (c) Cyclopentadiene         | (d) Cyclopropenyl anion     |
| (e) Cycloheptatrienyl anion | (f) Tropylium ion           |
| (g) Cyclooctatetraene       | (h) Benzene                 |

Q. 3. Arrange the following compounds in the increasing order of their reactivity towards electrophilic substitution reactions.



Q. 4. Indicate the position of the entering electrophile  $\text{NO}_2^+$  in the following compounds.

