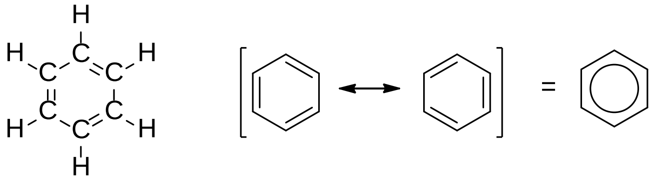
Module 7 Benzenes and Substituted Benzenes

Lecture 17 Benzene and Related Compounds

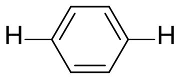
7.1 Introduction

Michael Faraday isolated a pure compound from the oily mixture in the year of 1825. Elemental analysis evidenced hydrogen-to-carbon ratio of 1:1, corresponding to an empirical formula of CH. In 1834, Eilhard Mitscherlich synthesized the same compound by heating benzoic acid, isolated from gum benzoin, in the presence of lime. Like Faraday, Mitscherlich found that the empirical formula was CH. A vapor-density measurement showed the molecular weight of about 78, for a molecular formula of C_6H_6. He named it as benzin, since it was derived from gum benzoin and now it is called, benzene. Many compounds discovered in the nineteenth century seemed to be related to benzene. These compounds also had low hydrogen-to-carbon ratios as well as pleasant aromas. This group of compounds was called aromatic because of their pleasant odors. Other organic compounds without these properties were called aliphatic, meaning "fatlike." August Kekulé, the originator of the structural theory, suggested that the carbon atoms of benzene are in a ring. They are bonded to each other by alternating single and double bonds, and one hydrogen atom is attached to each carbon atom.



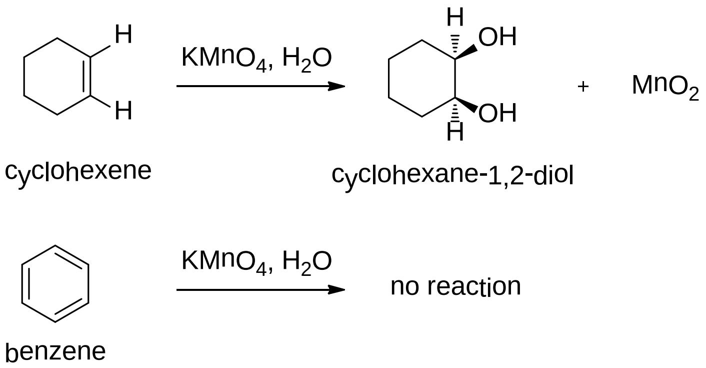
7.2 Structure

Benzene is a ring of six *sp*^{2} hybrid carbon atoms, each bonded to one hydrogen atom. It is a resonance hybrid of the two Kekule structures. The π-electrons are delocalized, with a bond order of 1.5 between adjacent carbon atoms. That is the carbon-carbon bond lengths in benzene are shorter than typical single-bond lengths, yet longer than typical double-bond lengths. All the carbon-carbon bonds are the same length, and all the bond angles are 120°. The unhybridized *p*-orbital of each *sp*^{2} carbon atom is perpendicular to the plane of the ring and overlap to form a ring.



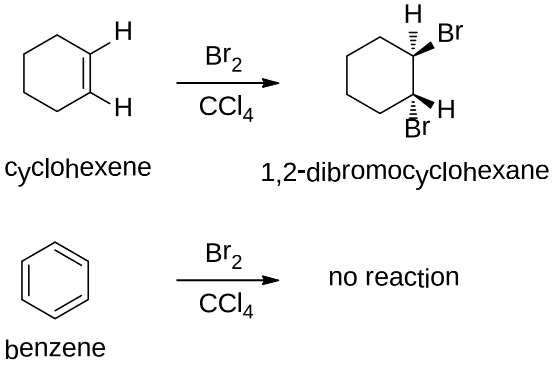
7.3 Properties

Benzene is a very stable than alkenes so benzenes do not undergo reaction that alkenes do. We know that an alkene decolorizes potassium permanganate by reacting to form a glycol. But when permanganate is added to benzene, no reaction occurs (Scheme 1).



Scheme 1

In the same way, most alkenes decolorize solutions of bromine in carbon tetrachloride. The red bromine color disappears as bromine adds across the double bond. When bromine is added to benzene, no reaction occurs, and the red bromine color remains unchanged (Scheme 2).



Scheme 2

By comparing heats of hydrogenation of benzene, cyclohexene, and cyclohexadiene, we can get an idea about the stability of benzene (Figure 1). On hydrogenation all these compounds give cyclohexane.

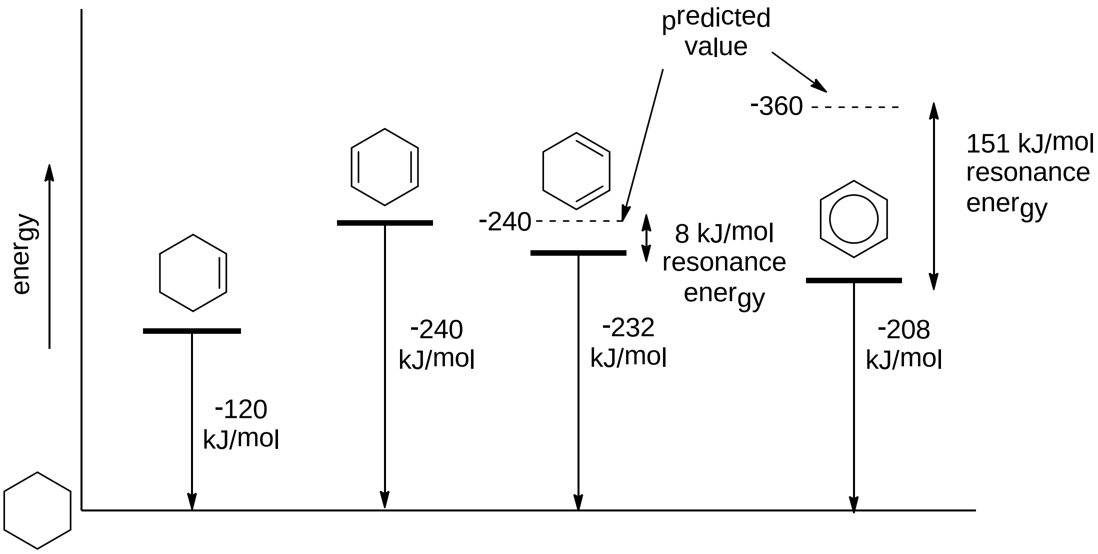


Figure 1

Hydrogenation of cyclohexene is exothermic by 120 kJ/mol. Hydrogenation of 1,4-cyclohexadiene is also exothermic by 240 kJ/mol which is about twice the value of the heat of hydrogenation of cyclohexene as predicted. So the resonance energy of the isolated double bonds in 1,4-cyclohexadiene is about zero.

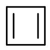
Hydrogenation of 1,3-cyclohexadiene is exothermic by 232 kJ/ which is about 8 kJ/mol less than the predicted value of 240 kJ/mol. So the resonance energy of the conjugated double bonds in 1,3-cyclohexadiene is 8 kJ/mol. Hydrogenation of benzene requires higher pressures of hydrogen and active catalysts. This hydrogenation is exothermic by 208 kJ/mol, which is about 151 kJ/mol less than the predicted value of 360 kJ/mol.

7.4 Aromaticity

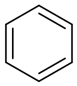
Aromatic compounds are those that meet the following criteria

- The structure must be cyclic and planar, containing conjugated π-bonds.
- Each atom in the ring must have an unhybridized *p*-orbital.
- The unhybridized *p*-orbitals must overlap to form a continuous ring of parallel orbitals.
- Delocalization of the π-electrons over the ring must lower the electronic energy.
- It should follow the Huckel's rule. The rule states that aromatic compounds must contain (4n+2) π-electrons, where n is any whole number. If it contains (4n) π-electrons, the compounds are *anti*-aromatic compound.
- Aromatic systems have 2, 6, or 10 π-electrons, for n = 0, 1, or 2 and antiaromatic systems have 4, 8, or 12 π-electrons, for n = 1, 2, or 3.

➢ Monocyclic hydrocarbons with alternating single and double bonds are called annulenes. A prefix in brackets denotes the number of carbons in the ring. Benzene is [6]-annulene, cyclic and planar, with a continuous ring of overlapping *p*-orbitals. Huckel's rule predicts that benzene is an aromatic compound as it has (4n+2) π-electron system. Cyclobutadiene ([4]-annulene) cyclic and it has a continuous ring of overlapping *p*-orbitals. But it has (4n) π-system so Huckel's rule predicts that cyclobutadiene is an antiaromatic compound.

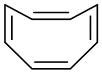


Cyclobutadiene
(antiaromatic)



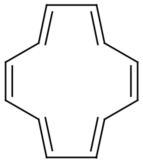
benzene
(aromatic)

- By Huckel’s rule one can predict that cyclooctatetraene ([8]-annulene) would be an antiaromatic as it has (4n) π-system. But it does not apply for cyclooctatetraene because it has the flexibility to adopt nonplanar “tub” shaped conformation. There is no continuous overlapping of *p*-orbital. Huckel’s rule applies to a compound only if there is a continuous ring of overlapping *p*-orbitals. So the compound is nonaromatic.

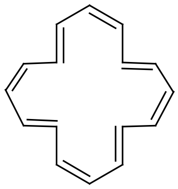


Cyclooctatetraene
(nonaromatic)

- Like cyclooctatetraene, larger annulenes such as [12]-annulene and [16]-annulene have (4n) π-systems and do not show antiaromaticity because they have the flexibility to adopt nonplanar conformations.

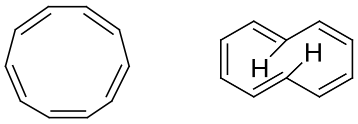


[12]-Annulene



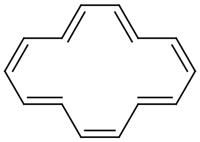
[16]-Annulene

- [10]-Annulene would be aromatic as it has (4n+2) but it is a nonaromatic compound. [10]-Annulene that has only *cis* double bonds cannot have the planar conformation because of angle strain. [10]-Annulene that has two *trans* double bonds cannot adopt a planar conformation either, because two hydrogen atoms interfere with each other.

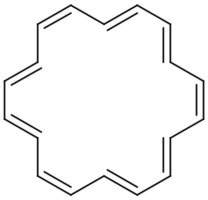


[10]-Annulene

- Some larger annulenes with (4n+2) π-electrons such as [14]-annulene and [18]-annulene can achieve planar conformations to have aromatic properties.



[14]-Annulene



[18]-Annulene

- Cyclopropene is not aromatic because one of its ring atoms is sp^3 hybridized so it does not fulfill the criterion for aromaticity. But the cyclopropenyl cation is aromatic because it has an uninterrupted ring of *p*-orbital and (4n+2) π-system. The cyclopropenyl anion is antiaromatic as it has (4n) π-system.

+ −

cyclopropene (nonaromatic)

cyclopropenyl cation (aromatic)

cyclopropenyl anion (antiaromatic)

Cyclopentadiene is not aromatic because of the presence of sp^3 hybridized carbon atom. The cyclopentadienyl anion is aromatic because it has an uninterrupted ring of *p*-orbital and (4n+2) π-system. The cyclopentadienyl cation is antiaromatic as it has (4n) π-system.

+ $\overset{-}{:}$

cyclopetadiene (nonaromatic)

cyclopentadienyl cation (antiaromatic)

cyclopentadienyl anion (aromatic)

Cycloheptatrienyl cation and cyclooctatetraene dianion are aromatic compounds because they have uninterrupted ring of *p*-orbital and (4n+2) π-system.

+

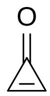
$:^{-}$

$\underset{-}{:}$

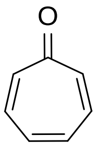
cycloheptatrienyl cation (aromatic)

cyclooctatetraene dianion (aromatic)

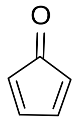
Cyclopropenone and cycloheptatrienone are stable aromatic compounds. We know that the double bond in carbonyl (C=O) group is polarized to give partial positive charge on the carbon atom and partial negative charge on the oxygen atom. So cyclopropenone and cycloheptatrienone are considered to be aromatic as it obeys (4n+2) π-rule. But the same reason makes cyclopentadienone to be antiaromatic and it is unstable, rapidly undergoes a Diels-Alder dimerization.



cyclopropenone
(aromatic)



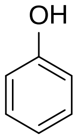
cycloheptatrienone
(aromatic)



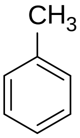
Cyclopentadienone
(antiaromatic)

7.5 Nomenclature

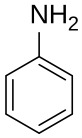
- Many benzene derivatives are called by their common historical names.



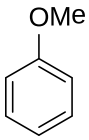
phenol



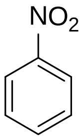
toluene



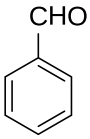
aniline



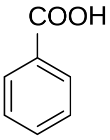
anisole



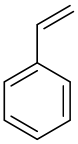
nitrobenzene



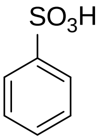
benzaldehyde



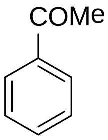
benzoic acid



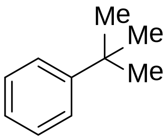
styrene



benzenesulfonic
acid

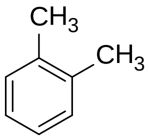


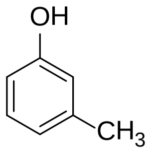
acetophenone

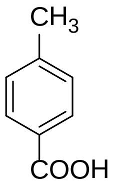


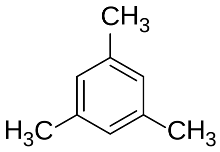
tert-butylbenzene

- Disubstituted benzenes can also called by historical names. They are named using the prefixes *ortho*-, *meta*-, and *para*- to specify the position of the substituents.

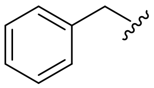

o-xylene

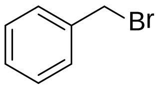

m-cresol

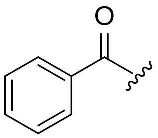

p-toluic acid

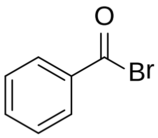

mesitylene

- The seven carbon unit consisting of a benzene ring and a methylene (-CH_2-) group is named as a benzyl group and the seven carbon unit consisting of a benzene ring and a carbonyl (C=O) group is named as a benzoyl group.

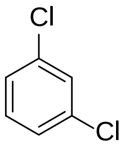

benzyl group

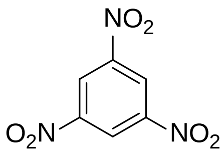

benzyl bromide

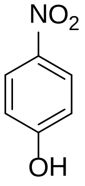

benzoyl group

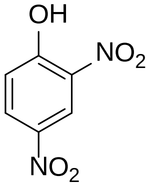

benzoyl bromide

- Numbers can also be used to specify the position of the substitution in disubstituted benzenes.


1,3-dichlorobenzene


1,3,5-trinitrobenzene

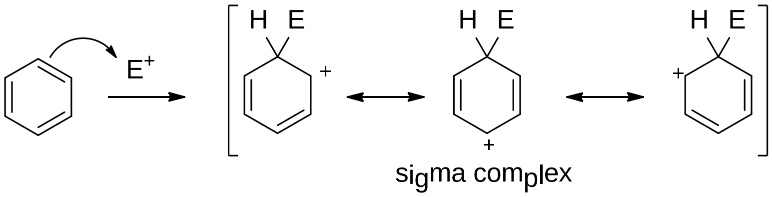

4-nitrophenol


2,4-dinitrophenol

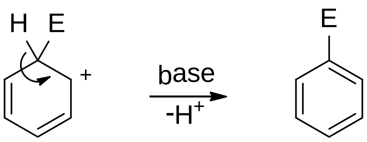
7.6 Electrophilic Substitution Reactions

The π-bond electrons in benzenes attack a strong electrophile and lose its aromaticity to give a resonance stabilized carbocation, called a sigma complex. Loss of the proton on the tetrahedral carbon atom of the sigma complex helps to regain the aromaticity. The overall reaction is the electrophilic aromatic substitution reaction (Scheme 3).

Step 1: Attack on the electrophile forms the sigma complex.



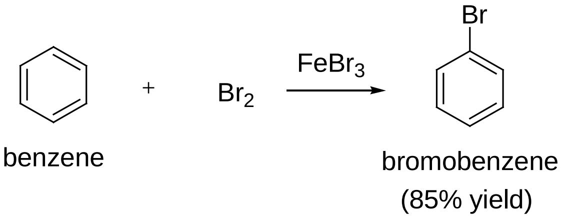
Step 2: Loss of a proton regains aromaticity



Scheme 3

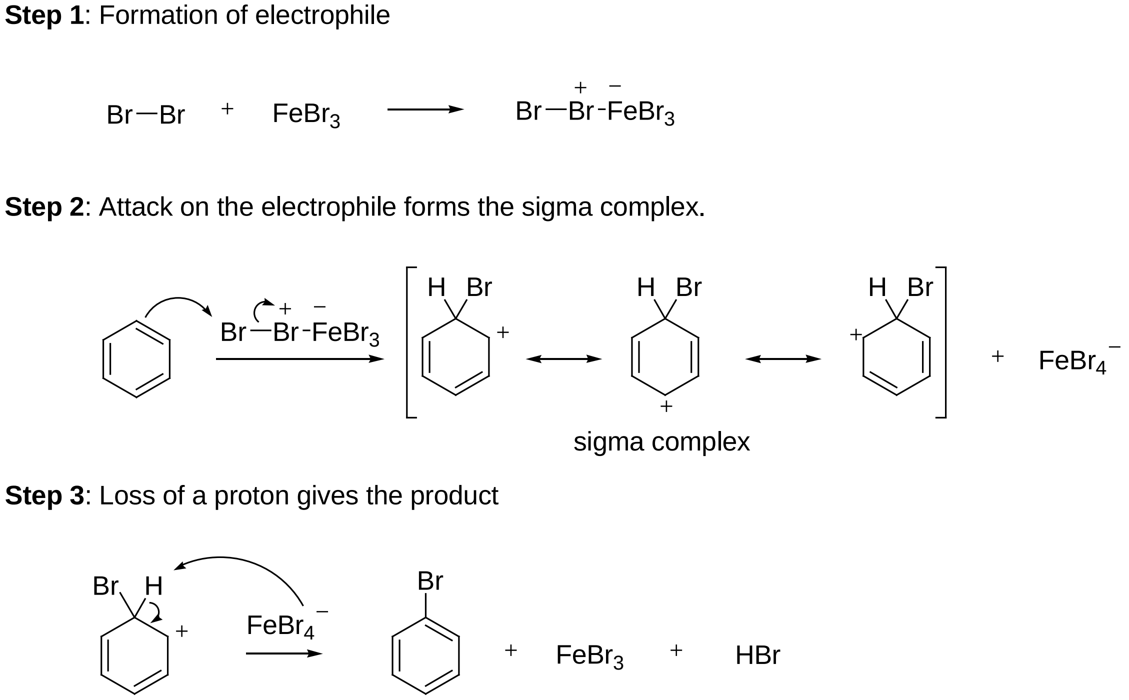
7.6.1 Halogenation

Halogens react with benzene in the presence of a strong Lewis acid such as $AlCl_3$ or $FeBr_3$ to give halobenzenes. For example, bromobenzene can be prepared with good yield as shown in Scheme 4.



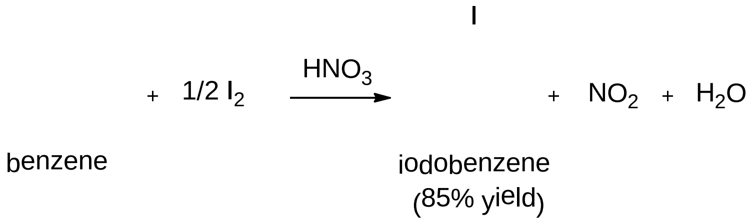
Scheme 4

Bromine itself is not sufficiently electrophilic to react with benzene so that a strong Lewis acid such as $FeBr_3$ used as a catalyst for the formation of Br^+ which attacks benzene to form the sigma complex. Bromide ion acts as a weak base to remove a proton from the sigma complex, giving the substituted benzene and HBr (Scheme 5).



Scheme 5

Chlorination of benzene works much like bromination. Aluminum chloride ($A1Cl_3$) is often used as the Lewis acid catalyst for chlorination of benzene. Iodination of benzene requires an acidic oxidizing agent, such as nitric acid. The iodine cation, an electrophile, results from oxidation of iodine by nitric acid (Scheme 6).



Scheme 6

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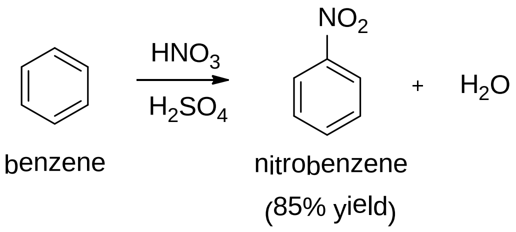
Lecture 18 Benzene and Related Compounds II

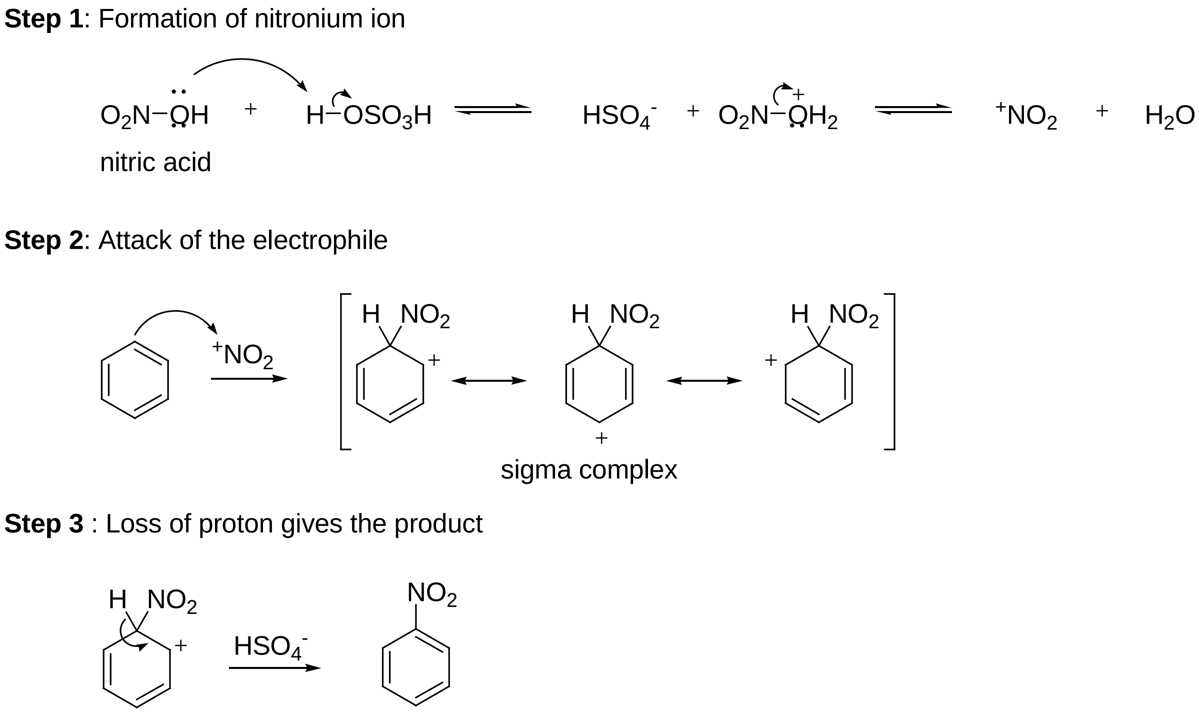
7.6.2 Nitration

Nitration of benzene using a mixture of HNO_3 and H_2SO_4 gives the target product rapidly at lower temperatures (Scheme 1).



Scheme 1

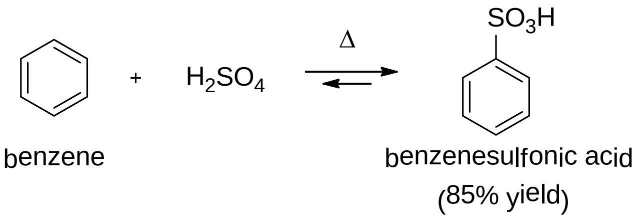
Sulfuric acid protonates the hydroxyl group of nitric acid, allowing it to leave as water and form a nitronium ion ($^+NO_2$), a powerful electrophile. The nitronium ion reacts with benzene to form a sigma complex. Loss of a proton from the sigma complex gives nitrobenzene (Scheme 2).



Scheme 2

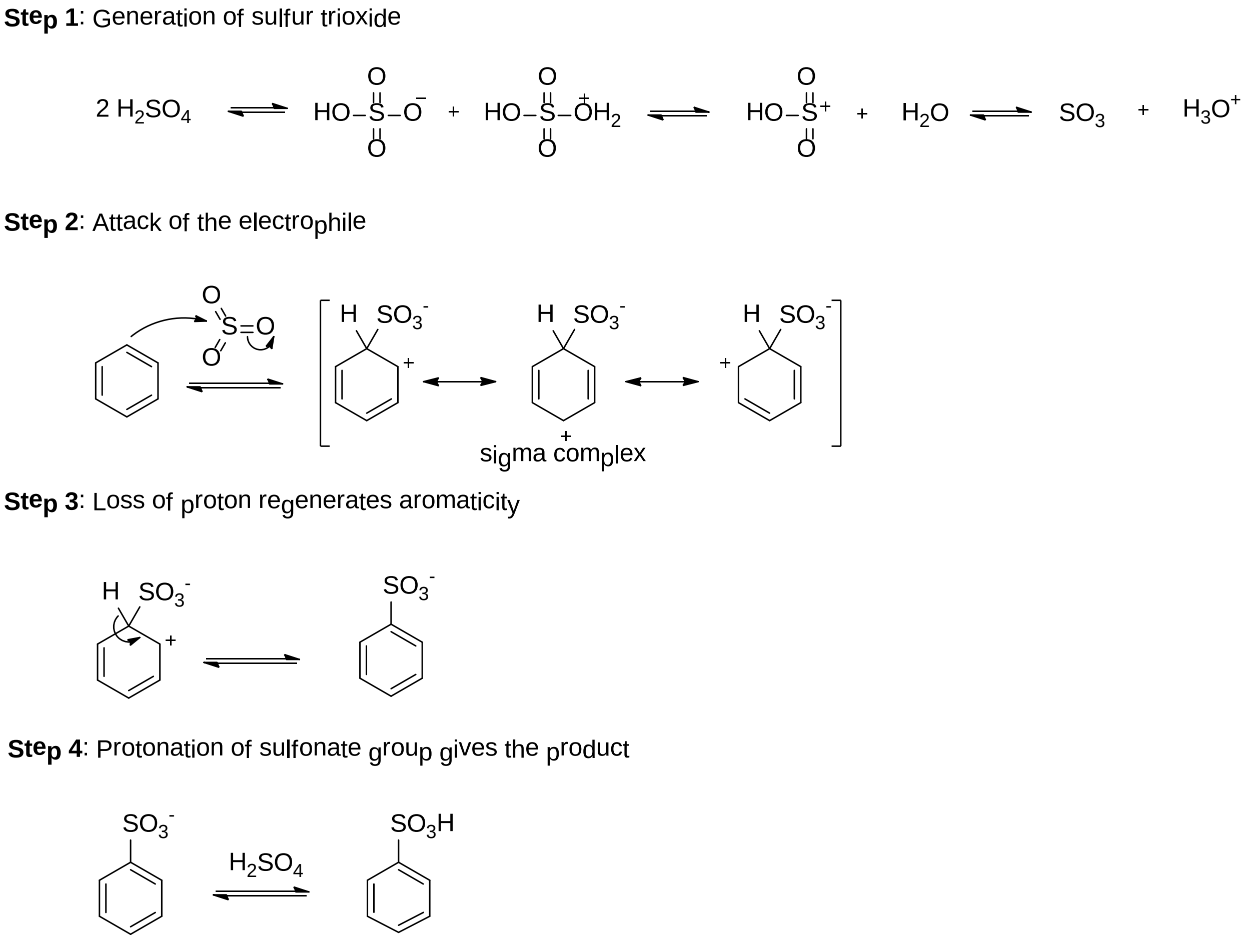
7.6.3 Sulfonation

Aryl sulfonic acid can be easily synthesized by an electrophilic aromatic substitution using sulfur trioxide (SO_3) as the electrophile (Scheme 3).



Scheme 3

Sulfur trioxide is the anhydride of sulfuric acid. Although sulfur trioxide is uncharged, it is a strong electrophile where three sulfonyl (S=O) bonds drawing electron density away from the sulfur atom. Benzene attacks sulfur trioxide, forming a sigma complex. Loss of a proton on the tetrahedral carbon and reprotonation on oxygen gives benzenesulfonic acid (Scheme 4).


Step 1: Generation of sulfur trioxide

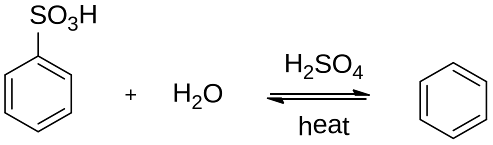
Step 2: Attack of the electrophile

Step 3: Loss of proton regenerates aromaticity

Step 4: Protonation of sulfonate group gives the product

Scheme 4

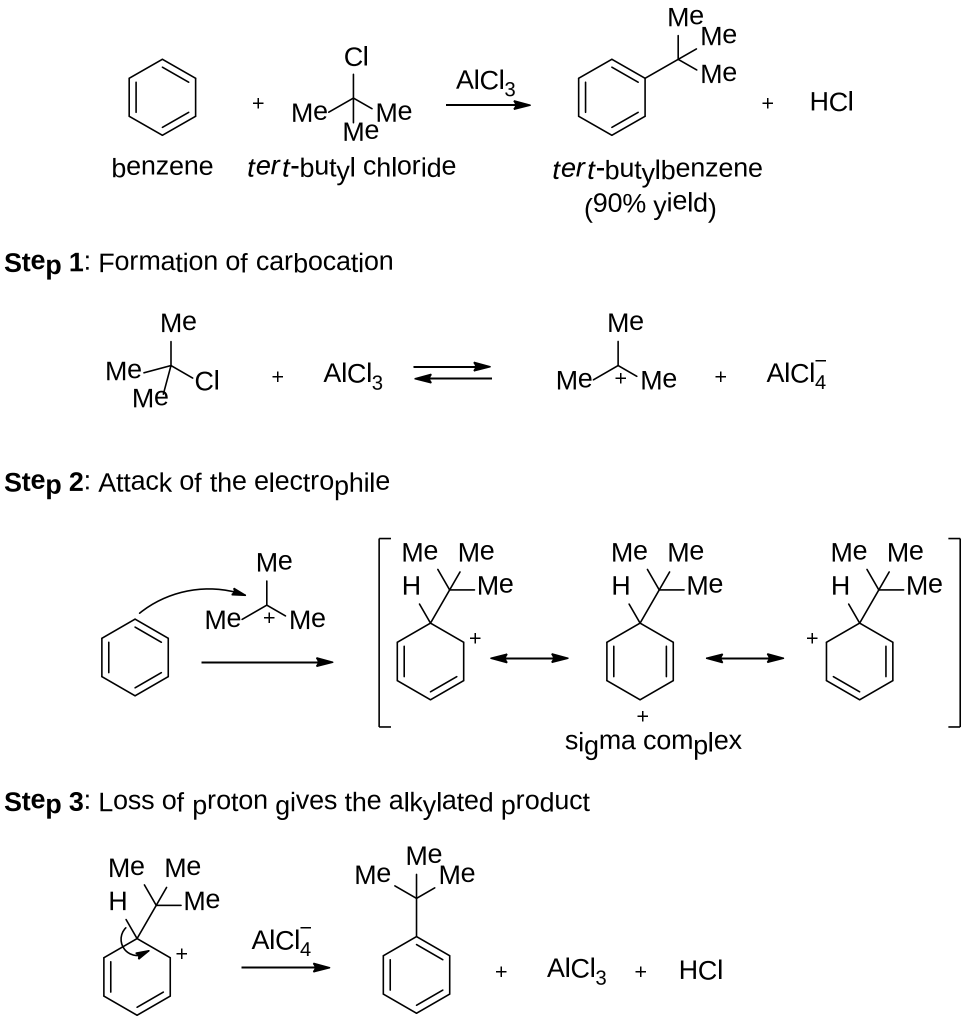
Sulfonation is reversible reaction, and a sulfonic acid group can be removed from an aromatic ring by heating in dilute sulfuric acid. Excess water removes SO_3 from the equilibrium by hydrating it to sulfuric acid (Scheme 5).



Scheme 5

7.6.4 The Friedel-Crafts Alkylation

In the presence of Lewis acid catalysts such as aluminum chloride ($AlCl_3$) or ferric chloride ($FeCl_3$), alkyl halides react with benzene to give alkyl benzenes (Scheme 6). This reaction is called the Friedel-Crafts alkylation.

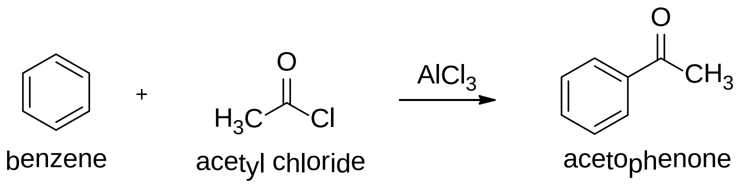


Scheme 6

This alkylation is an electrophilic aromatic substitution reaction where the *tert*-butyl cation acts as the electrophile. The *tert*-butyl cation is formed by the reaction of *tert*-butyl chloride with the catalyst, aluminum chloride. The *tert*-butyl cation reacts with benzene to form a sigma complex. Loss of a proton gives the product. The aluminum chloride catalyst is regenerated in the final step.

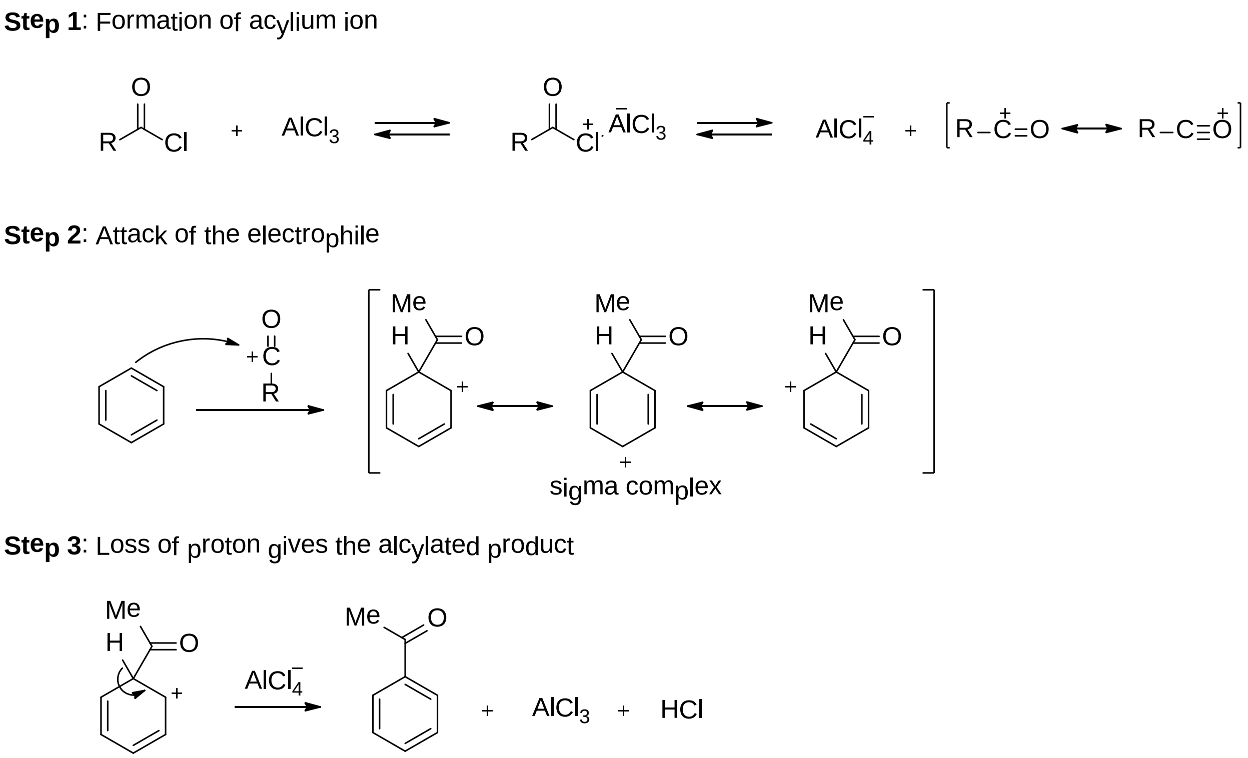
7.6.5 The Friedel-Crafts Acylation

In the presence of aluminum chloride, an acyl chloride reacts with benzene to give acyl benzene (Scheme 7). The Friedel-Crafts acylation is analogous to the Friedel-Crafts alkylation, except that the reagent is acyl chloride instead of an alkyl halide and the product is acyl benzene instead of alkyl benzene.



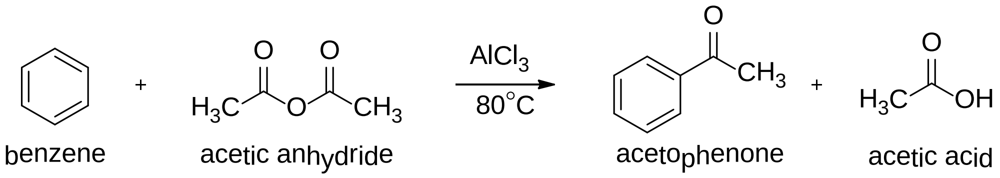
Scheme 7

In the first step a resonance-stabilized acylium ion formed which reacts with benzene via an electrophilic aromatic substitution reaction to form an acyl benzene. The carbonyl group in the product has nonbonding electrons that can form a complex with the Lewis acid ($AlCl_3$). Addition of water hydrolyzes this complex, giving the free acyl benzene (Scheme 8). Friedel-Crafts reactions do not occur on strongly deactivated rings, so the acylation stops after one substitution.



Scheme 8

Friedel-Crafts acylations can also be carried out using carboxylic acid anhydrides. For example, benzene reacts with acetic anhydride in the presence of Lewis acid to give acetophenone (Scheme 9). Excess of benzene is used in this reaction to get good yield.

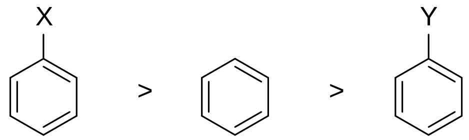


Scheme 9

7.7 Electrophilic Substitution Reactions with Substituted Benzenes

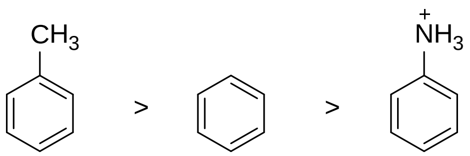
Substituted benzenes undergo the electrophilic aromatic substitution reactions such as halogenation, nitration, sulfonation, alkylation and acylation. Some substituents make the ring more reactive and some make it less reactive than benzene toward electrophilic aromatic substitution. The rate determining step of an electrophilic aromatic substitution reaction is the formation of a carbocation intermediate. So substituents that are capable of donating electrons into the benzene ring can stabilize the carbocation intermediate, thereby increasing the rate of electrophilic aromatic substitution.

- In contrast, substituents that withdraw electrons from the benzene ring will destabilize the carbocation intermediate, thereby decreasing the rate of electrophilic aromatic substitution. The relative rates of electrophilic aromatic substitution reaction of benzene and substituted benzenes are given below.



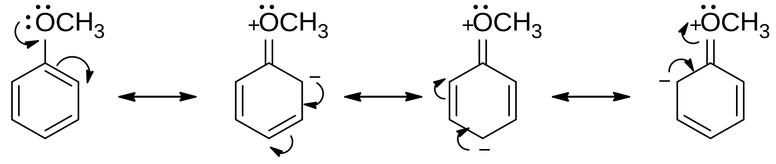
X = Electron donating group
Y = Electron withdrawing group

- Substituents can donate electrons into a benzene ring or can withdraw from benzene ring either by inductive effect or resonance effect. Alkyl substituents that are bonded to a benzene ring can donate electrons inductively. Donation of electrons through a σ-bond is called inductive electron donation. Withdrawal of electrons through a σ-bond is called inductive electron withdrawal. For example methyl group is an electron donating group because of hyperconjugation and NH_3^+ group is an electron withdrawing group because it is more electronegative than a hydrogen. The relative rates of electrophilic substitution decrease in the following order.

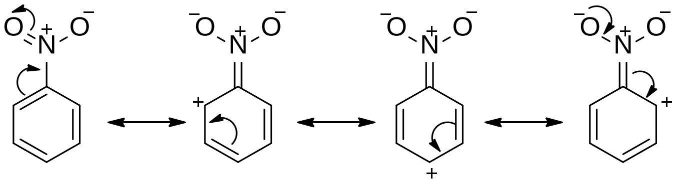


CH_3 = Electron donating group
NH_3^+ = Electron withdrawing group

- Substituents such as OH, OR and Cl have a lone pair on the atom that is directly attached to the benzene ring. This lone pair can be delocalized into the ring. These substituents also withdraw electrons inductively because the atom attached to the benzene ring is more electronegative than a hydrogen. But electron donation into the ring by resonance is more significant than inductive electron withdrawal from the ring.



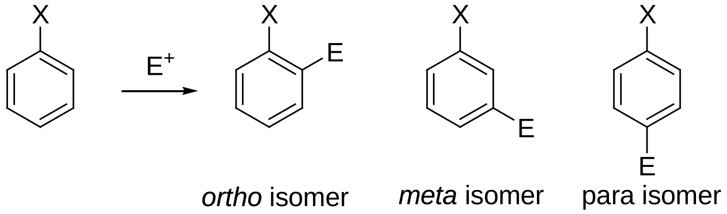
- Substituents such as C=O, C≡N and NO_2 withdraw electrons by resonance. These substituents also withdraw electrons inductively because the atom attached to the benzene ring is more electronegative than a hydrogen.



- Substituents that make the benzene ring more reactive toward electrophilic substitution, by donating electrons into the benzene ring, are called the ***activating groups***. In contrast, substituents that make the benzene ring less reactive toward electrophilic substitution, by withdrawing electrons from the benzene ring, are called the ***deactivating groups***.

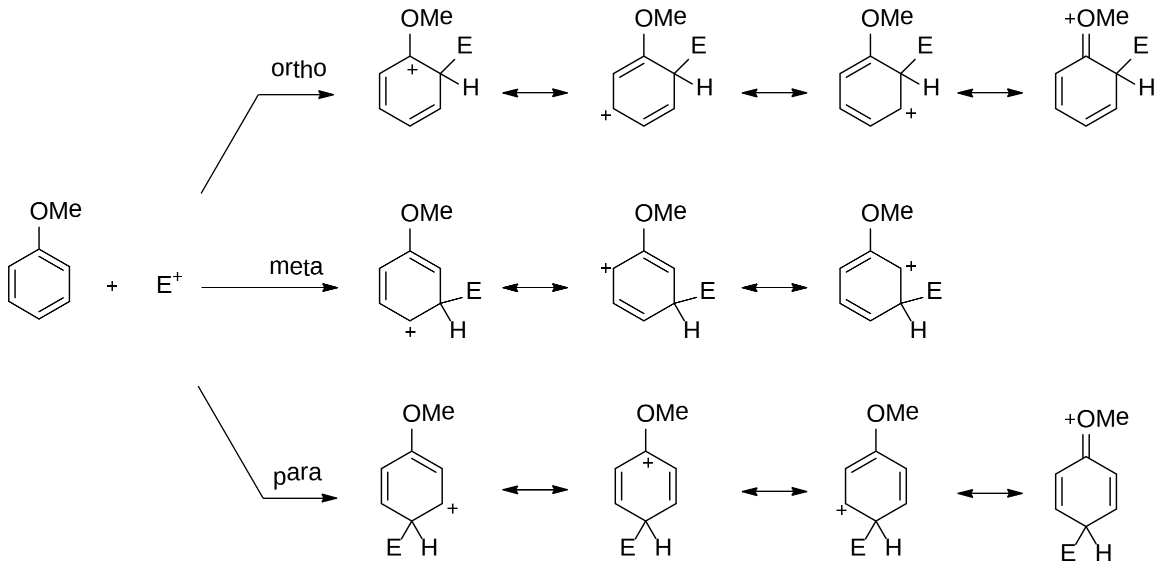
- Strongly activating substituents such as $-NH_2$, -NHR, $-NR_2$ -OR, and –OH make the benzene ring more reactive toward electrophilic substitution. The moderately activating substituents such as –NHCOR and –OCOR, also donate electrons into the ring by resonance less effectively than that of strongly activating substituents. Alkyl, aryl, and -CH=CHR groups are weakly activating substituents.

- Strongly deactivating substituents such as -C≡N, $-SO_3H$, $-NO_2$, and ammonium ions make the benzene ring less reactive toward electrophilic substitution. Carbonyl compounds are moderately deactivating substituents and the halogens are weakly deactivating substituents.
- Substituted benzene undergoes an electrophilic substitution reaction to give an *ortho*-isomer, a *meta*-isomer, a *para*-isomer or mixture of these isomers. The substituent already attached to the benzene ring determines the location of the new substituent.

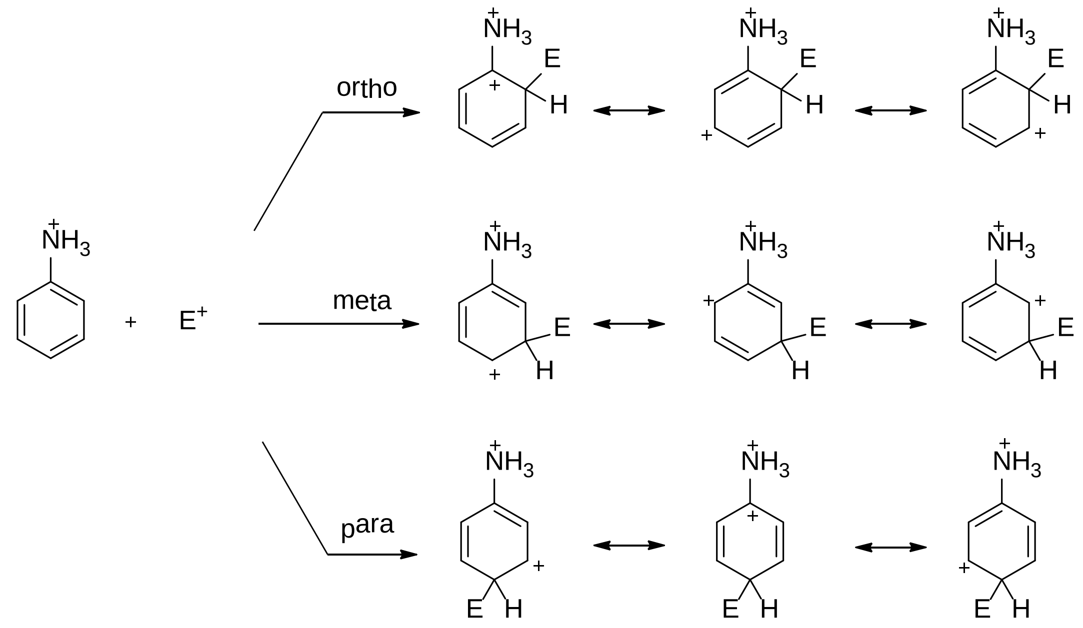


- All activating substituents and weakly deactivating halogens are *ortho*-*para* directors, and all substituents that are more deactivating are *meta* directors. When substituted benzene undergoes an electrophilic substitution reaction, an *ortho*-substituted carbocation, a *meta*-substituted carbocation, and a *para*-substituted carbocation can be formed. The relative stabilities of the three carbocations determine the preferred pathway of the reaction.

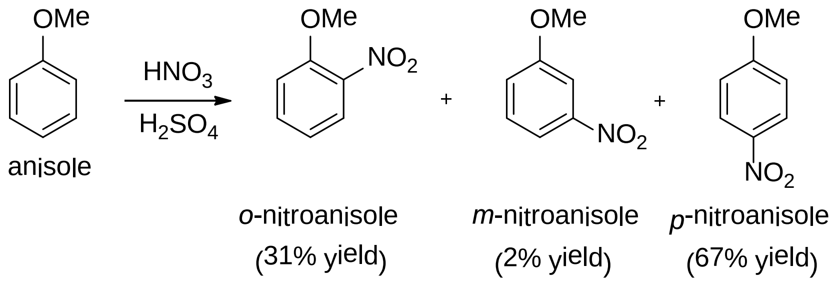
- The methoxy substituent (an activating group), for example, donates electron into the ring and stabilize the *ortho*- and *para*-substituted carbocations as shown. Therefore, the most stable carbocation is obtained by directing the incoming group to the *ortho* and *para* positions. Thus, any substituent that donates electrons is an *ortho-para* director.

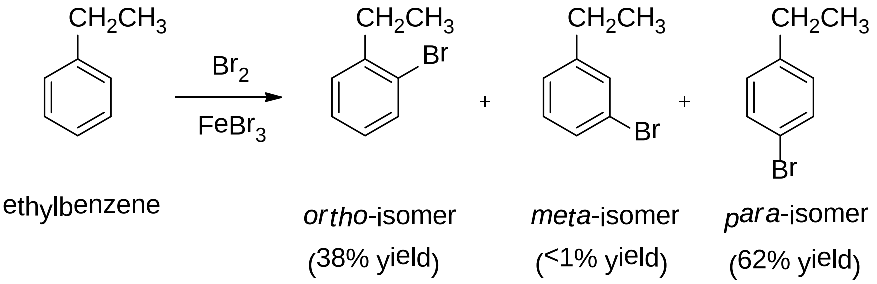


- In contrast, the ammonuium ion substituent (a deactivating group), for example, withdraws electron from the ring and destabilize the *ortho*- and *para*-substituted carbocations as shown. Therefore, the most stable carbocation is obtained by directing the incoming group to the *meta* position. Thus, any substituent that withdraws electrons is a *meta* director.

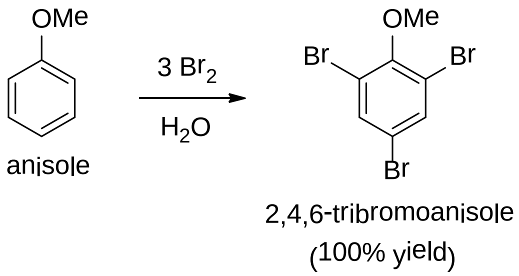


- In the following examples, the methoxy group and ethyl group are activating substituents which preferably direct the incoming electrophile to *ortho* and *para* position. These substituted benzenes undergo electrophilic aromatic substitution faster than benzene.





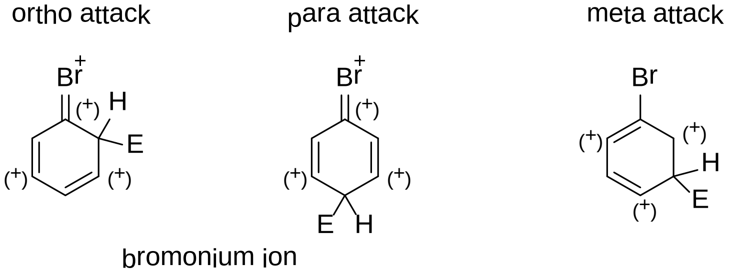
- A methoxy group is so strongly activating group so that anisole quickly brominates in water without a catalyst. In the presence of excess bromine, this reaction proceeds to give the tribromide substituted product.



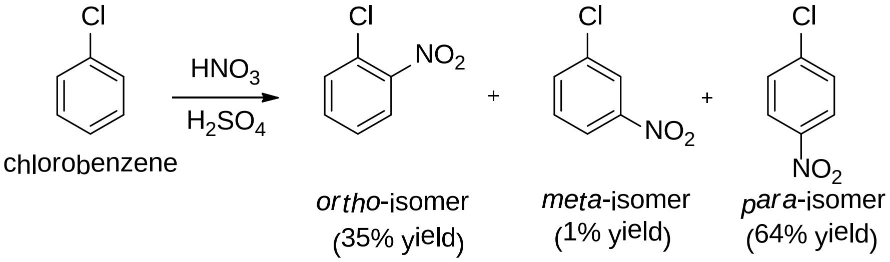
Module 7 Benzenes and Substituted Benzenes
Lecture 19 Benzene and Related Compounds III

7.7 Electrophilic Substitution Reactions of Substituted Benzenes

Halogens are deactivating groups, yet they are *ortho, para*-directors because the halogens are strongly electronegative, withdrawing electron density from a carbon atom through the σ-bond, and the halogens have nonbonding electrons that can donate electron density through π-bonding. If an electrophile reacts at the *ortho* or *para* position, the positive charge of the sigma complex is shared by the carbon atom bearing the halogen. The nonbonding electrons of the halogen can further delocalize the charge onto the halogen, giving a halonium ion structure. This resonance stabilization allows a halogen to be pi-donating, even though it is sigma-withdrawing.

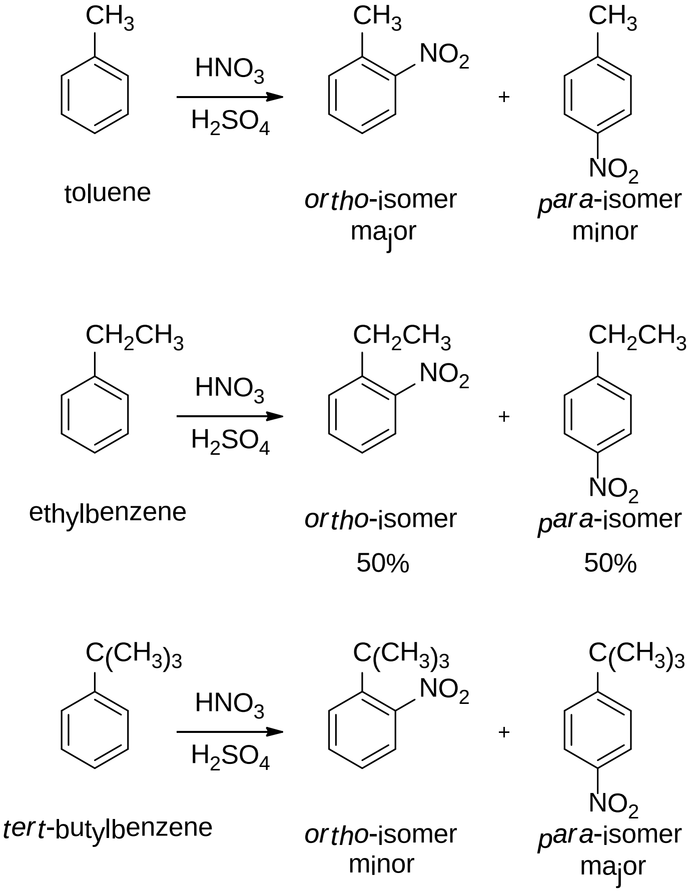


- Reaction at the *meta* position gives a sigma complex whose positive charge is not delocalized onto the halogen-bearing carbon atom. Therefore, the *meta* intermediate is not stabilized by the halonium ion structure. Scheme 1 illustrates the preference for *ortho* and *para* substitution in the nitration of chlorobenzene.



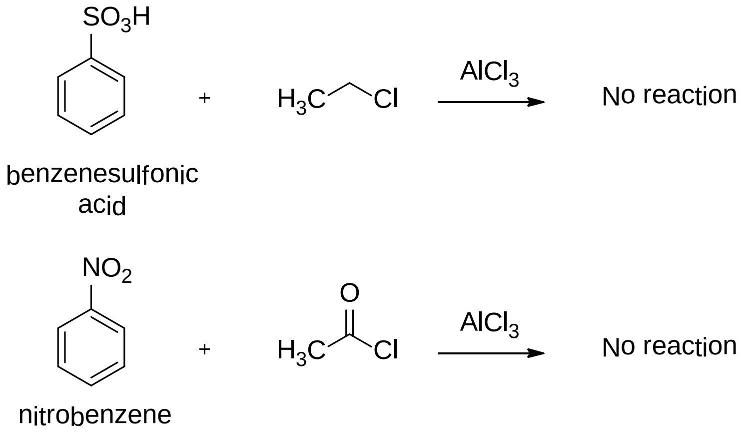
Scheme 1

- *Ortho-para* ratio differs with the size of the substituents. Nitration of toluene preferably gives *ortho* as the major product where the activating substituent is methyl group. Electrophilic substitution reaction of ethyl substituted benzene, however, gives *ortho* and *para* isomers equally. Bulky substituent such as *tert*-butyl benzene preferably gives *para*-isomer as the major product (Scheme 2).



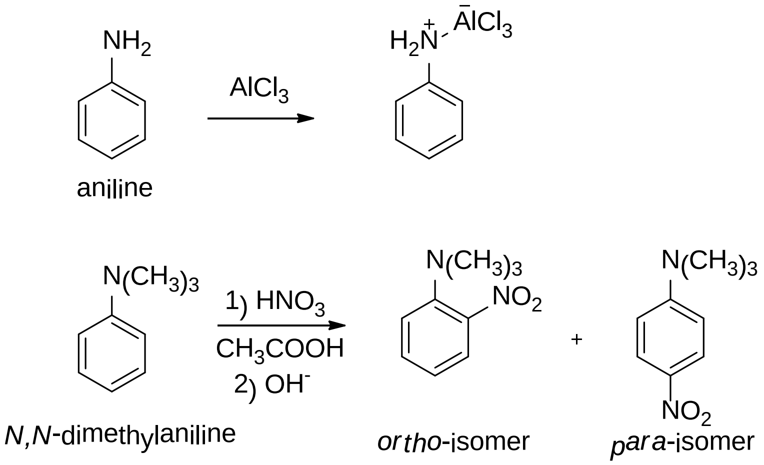
Scheme 2

- Benzenes which are having a *meta* director (a deactivating group) on the ring, will be too unreactive to undergo either Friedel-Crafts alkylation or Friedel-Crafts Acylation (Scheme 3).



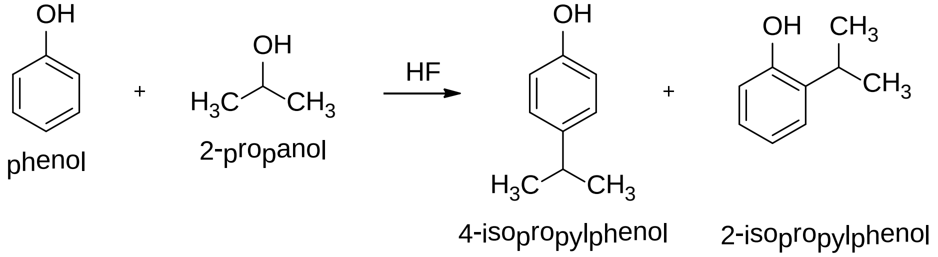
Scheme 3

- Aniline and *N*-substituted anilines also do not undergo Friedel-Crafts reactions because the lone pair on the amino group will form complex with the Lewis acid and converting the substituent into a deactivating *meta* director. Tertiary aromatic amines, however, can undergo electrophilic substitution because the tertiary amino group is a strong activator (Scheme 4).



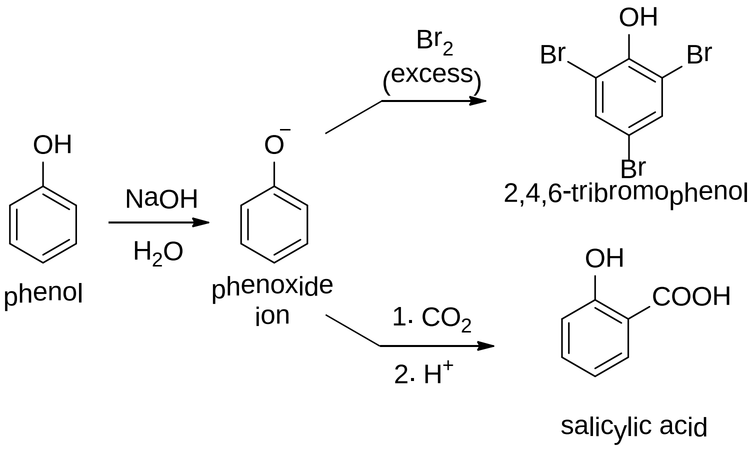
Scheme 4

- Phenols are highly reactive substrates for electrophilic aromatic substitution because of the presence of a strong activating group. So phenols can be alkylated or acylated using relatively weak Friedel-Crafts catalysts such as HF (Scheme 5).



Scheme 5

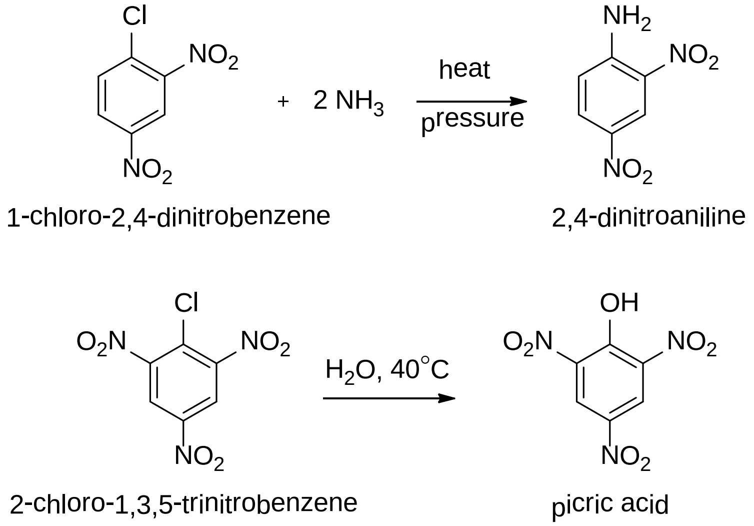
- Phenoxide ions, generated by treating a phenol with sodium hydroxide, are even more reactive than phenols toward electrophilic aromatic substitution. It gives tribromosubstituted phenol when reacts with excess bromine and salicylic acid when reacts with carbon dioxide (Scheme 6).



Scheme 6

7.8 Nucleophilic Substitution

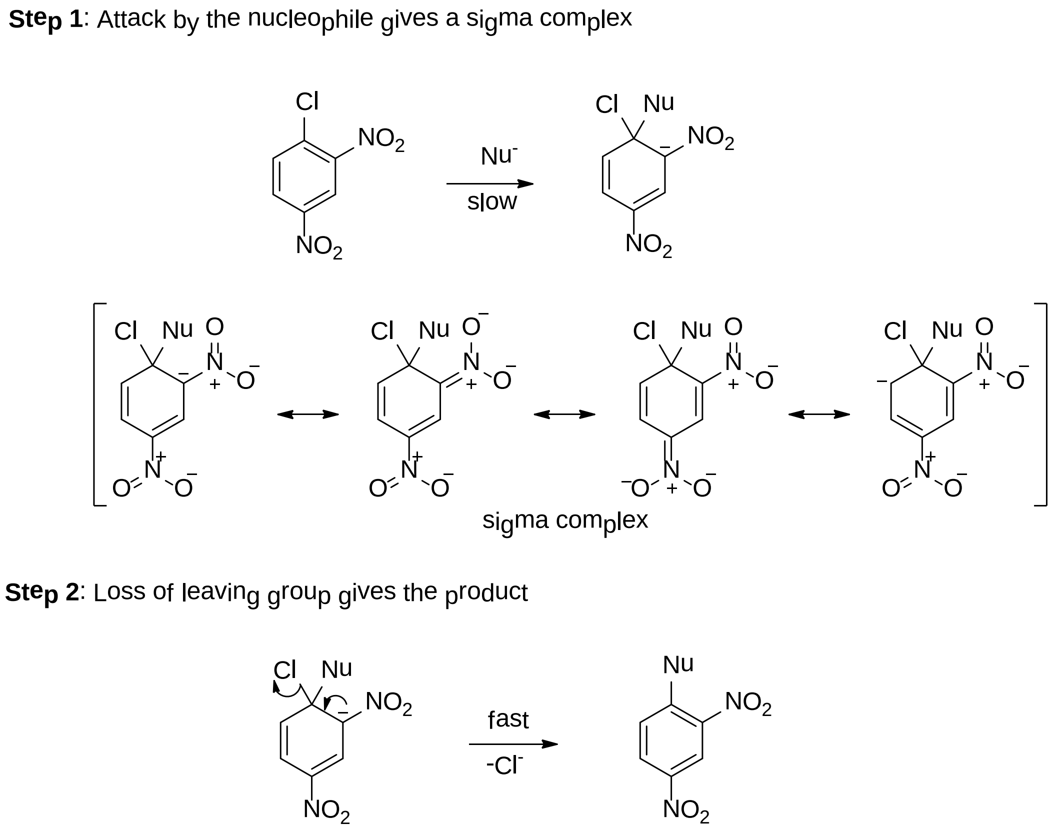
Aryl halides do not react with nucleophiles under the standard reaction conditions because the electron clouds of aryl ring repel the approach of a nucleophile. Nucleophiles can displace halide ions from aryl halides, if there are strong electron-withdrawing groups *ortho* or *para* to the halide. This class of reactions is called ***nucleophilic aromatic substitution reaction*** (Scheme 7).



Scheme 7

- Electron-withdrawing substituents such as nitro group make the ring reactive towards nucleophilic aromatic substitution but without at least one powerful electron-withdrawing group, the nucleophilic aromatic substitutions would be difficult. The mechanism of nucleophilic aromatic substitution cannot be the S_N2 mechanism because aryl halides cannot achieve the correct geometry for back-side approach of a nucleophile. The S_N1 mechanism also cannot be involved.

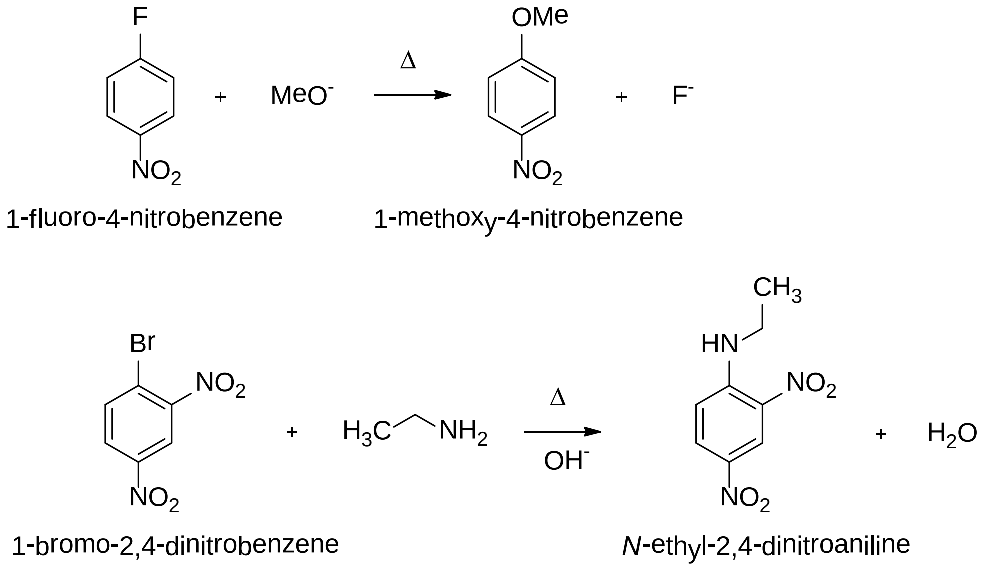
- Consider the reaction of 2,4-dinitrochlorobenzene with a nucleophile (Scheme 8). When a nucleophile attacks the carbon bearing the chlorine, a negatively charged sigma complex results. The negative charge is delocalized over the *ortho* and *para* carbons of the ring and further delocalized into the electron-withdrawing nitro groups. Loss of chloride from the sigma complex gives the nucleophilic substituted product.


Step 1: Attack by the nucleophile gives a sigma complex

Step 2: Loss of leaving group gives the product

Scheme 8

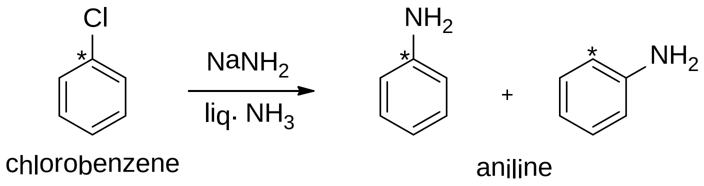
- The leaving group ability of halogen in nucleophilic aromatic substitution reaction is following the order: F > Cl > Br > I. The incoming group should be a stronger base than the group that is being replaced (Scheme 9).



Scheme 9

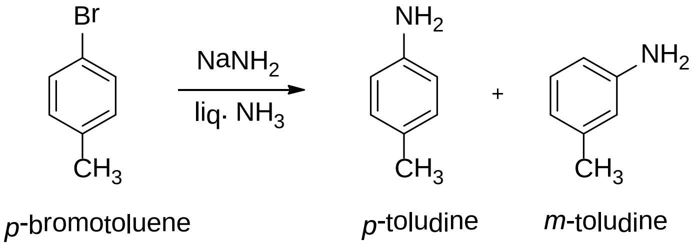
7.9 Benzyne Mechanism

Although chlorobenzene does not contain an electron-withdrawing group, it can undergo a nucleophilic substitution reaction in the presence of a very strong base but the incoming substituent does not always end up on the carbon vacated by the leaving group. For example, when chlorobenzene is treated with amide ion in liquid ammonia, aniline is obtained as the product. Half of the product has the amino group attached to the carbon vacated by the leaving group, but the other half has the amino group attached to the carbon adjacent to the carbon vacated by the leaving group. This is confirmed by isotopic labeling method (Scheme 11).



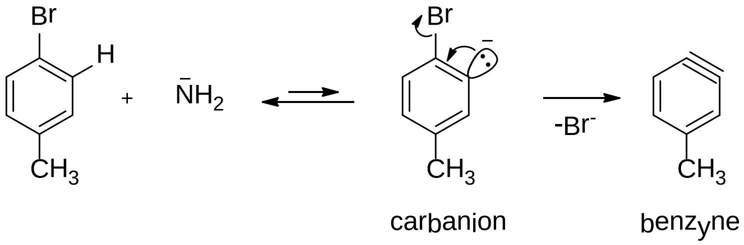
Scheme 11

When *p*-bromotoluene is treated with amide ion in liquid ammonia, 50:50 mixtures of *p*-toludine and *m*-toludine is obtained (Scheme 12).



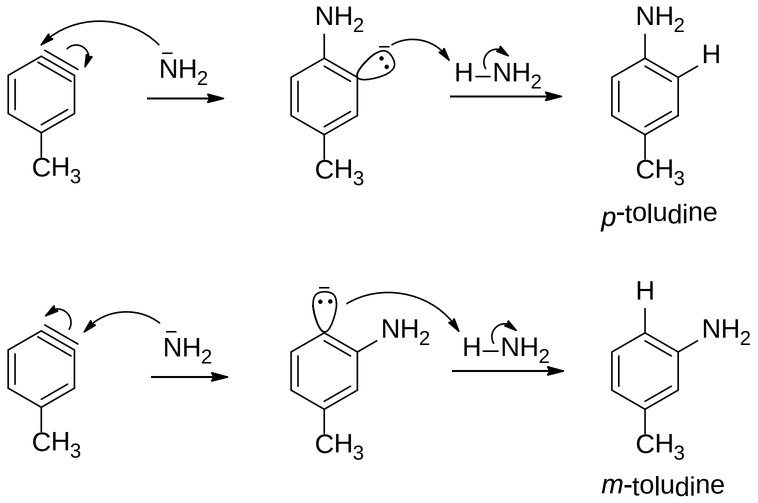
Scheme 12

- From the above examples one can conclude that the reaction takes place by a mechanism that forms an intermediate in which the two adjacent carbons are equivalent. The experimental observations evidence the formation of a **benzyne** intermediate where there is triple bond between the two adjacent carbons atoms of benzene. In the first step of the mechanism, the strong base removes a proton from the position *ortho* to the halogen. The resulting anion expels the halide ion, thereby forming benzyne (Scheme 13).



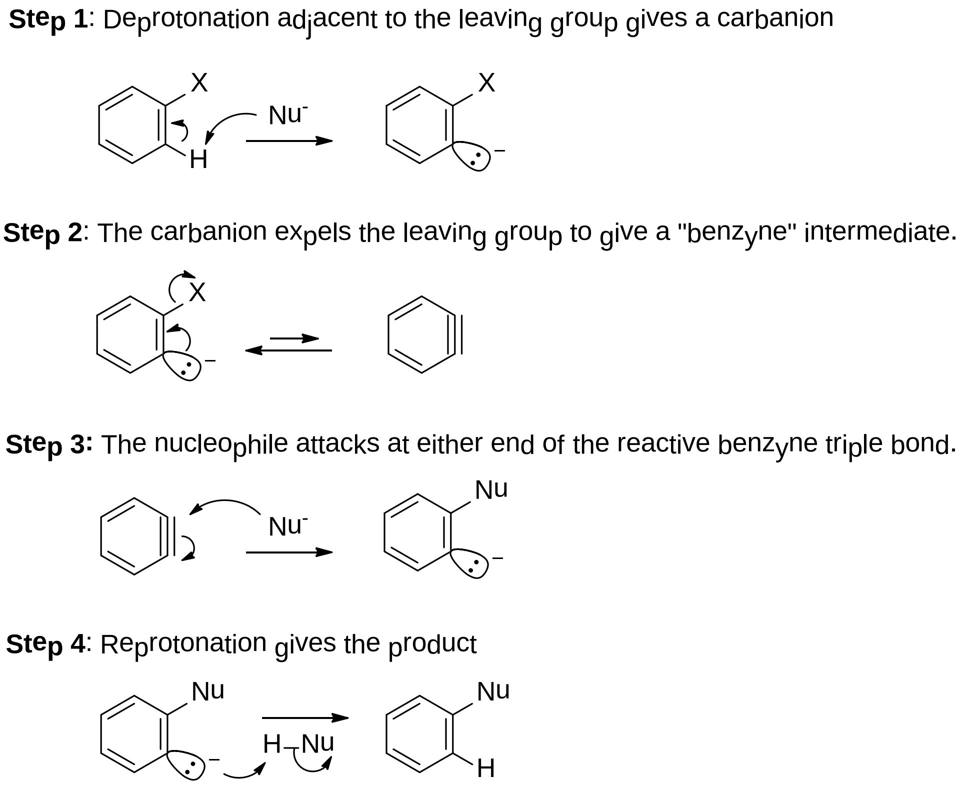
Scheme 13

- The incoming nucleophile can attack either carbons of the "triple bond" of benzyne (Scheme 14). Protonation of the resulting anion forms the substitution product. The overall reaction is an elimination-addition reaction. Substitution at the carbon that was attached to the leaving group is called **direct substitution**. Substitution at the adjacent carbon is called **cine** (Greek: movement) **substitution.**



Scheme 14

- As halide leaves with its bonding electrons from the carbanion, an empty *sp*^{2} orbital remains that overlaps with the filled orbital adjacent to it, giving additional bonding between these two carbon atoms. The two *sp*^{2} orbitals are directed 60° away from each other, so their overlap is not very effective. Triple bonds are usually linear but the triple bond in benzyne is a highly strained, so it is a very reactive intermediate. Amide ion is a strong nucleophile, attacking at either end of the benzyne triple bond. Subsequent protonation gives the product (Scheme 15).


Step 1: Deprotonation adjacent to the leaving group gives a carbanion

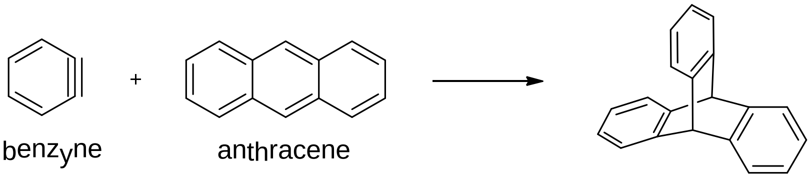
Step 2: The carbanion expels the leaving group to give a "benzyne" intermediate.

Step 3: The nucleophile attacks at either end of the reactive benzyne triple bond.

Step 4: Reprotonation gives the product

Scheme 15

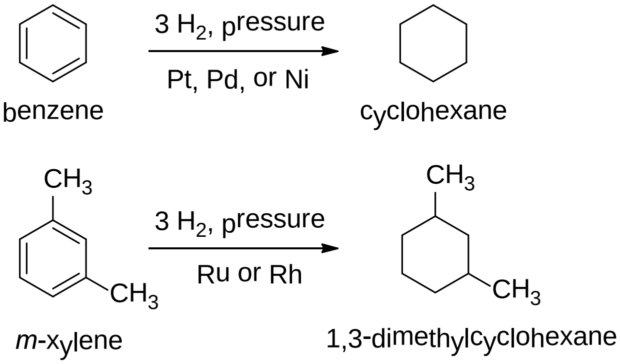
Benzyne is too unstable to be isolated but can be trapped by Diels-Alder reaction with anthracene or furan. For example, Anthracene reacts with benzyne to give a symmetrical cage structure (Scheme 16).



Scheme 16

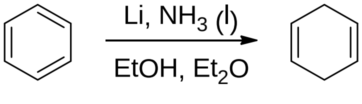
7.10 Reduction

Catalytic hydrogenation of benzene to cyclohexane takes place at high temperatures and pressures. Platinum, palladium, nickel, ruthenium or rhodium is used as catalyst. The reduction cannot be stopped at an intermediate stage as these alkenes are reduced faster than benzene (Scheme 17).



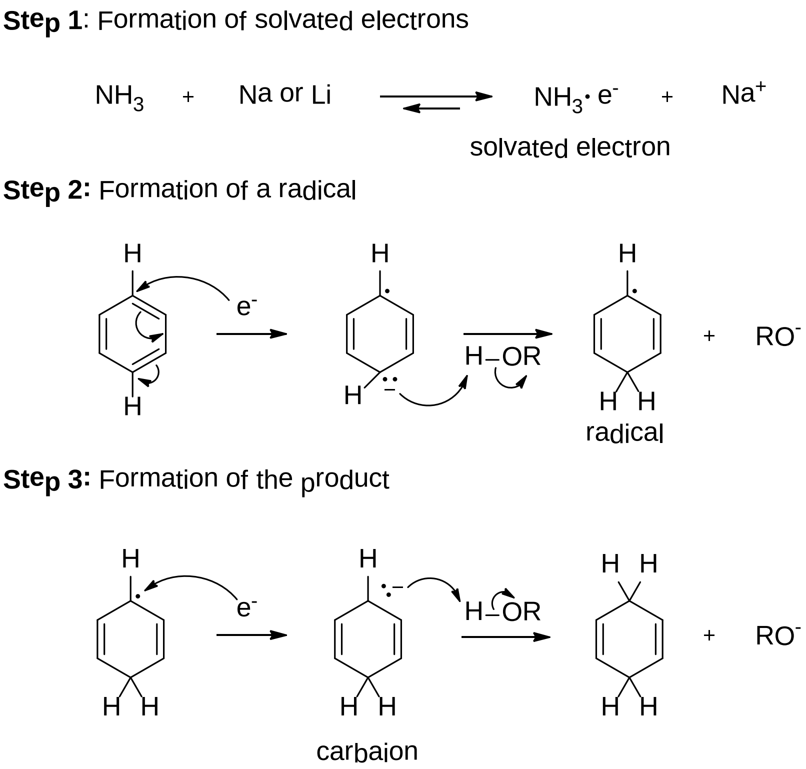
Scheme 17

Benzene and its derivatives can be reduced to nonconjugated cyclic dienes by treating sodium or lithium liquid ammonia (Scheme 18). This reduction is called **Birch reduction**.



Scheme 18

A solution of sodium or lithium in liquid ammonia contains solvated electrons that can add to benzene, forming a radical anion. The strongly basic radical anion abstracts a proton from the alcohol, giving a cyclohexadienyl radical. The radical quickly adds another solvated electron to form a cyclohexadienyl anion which is then protonated to give the reduced product (Scheme 19).



Scheme 19