UNIT – I BENZENE AND ITS DERIVATIVES

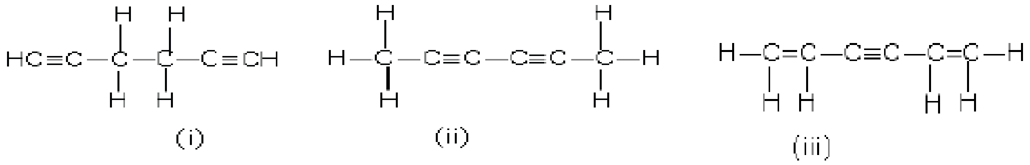
Aromaticity and Electrophilic Aromatic Substitution: Benzene, aromaticity, and other aromatic systems, Nomenclature of benzene derivatives, Other aromatic systems Electron donating and withdrawing groups, Inductive vs. resonance effects; effects of substituents, General mechanism of electrophilic aromatic substitution, Halogenation, Nitration, Sulfonation, Friedel-Crafts Alkylation and Acylation, Directing and activating effects in electrophilic aromatic substitution, Use of electrophilic aromatic substitution in synthesis, Nucleophilic substitution of aryl halides (benzyne and addition-elimination mechanisms).

➢ Structure of Benzene

The molecular formula of benzene has been found from analytical data, to be C_6H_6. Relatively higher proportion of carbon and addition of chlorine to benzene molecule indicate it to be an unsaturated compound. Depending on the various facts available to scientists from time to time, many structures for benzene had been proposed. Some are described below.

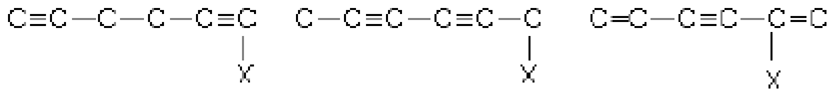
❖ Open Chain Structure

- Based upon observable facts given above and the tetravalency of carbon, the following open chain structures were proposed for benzene.



❖ Drawbacks of open chain structure: The open chain structure for benzene was rejected due to the following reasons:

- Addition reactions usually given by alkenes and alkynes are not given by benzene.
- Benzene forms only one kind of mono-substituted product.
- An open chain structure however, can form more than one kind of monosubstituted product as shown below:



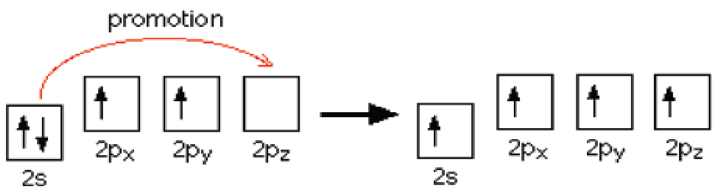
- The open chain compounds do, not give reactions such as FriedelCraft reaction, nitration, sulphonation.
- On reduction with hydrogen in the presence of Ni at 200°C, actually a cyclic compound cyclohexane is obtained.

❖ An orbital model for the benzene structure

✓ ***Building the orbital model***

- Benzene is built from hydrogen atoms (**$1s^1$**) and carbon atoms (**$1s^2 2s^2 2px^1 2py^1$**).
- Each carbon atom has to join to three other atoms (one hydrogen and two carbons) and doesn't have enough unpaired electrons to form the required number of bonds, so it needs to promote one of the **$2s^2$** pair into the empty **2pz** orbital.

✓ ***Promotion of an electron***

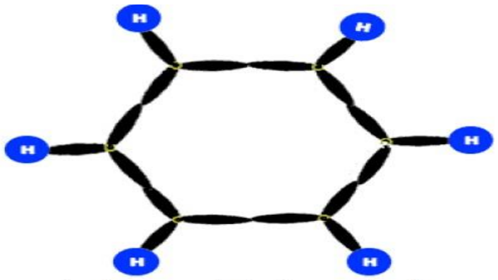


- There is only a small energy gap between the **2s** and **2p** orbitals, and an electron is promoted from the **2s** to the empty **2p** to give 4 unpaired electrons. The extra energy released when these electrons are used for bonding more than compensates for the initial input. The carbon atom is now said to be in an excited state.

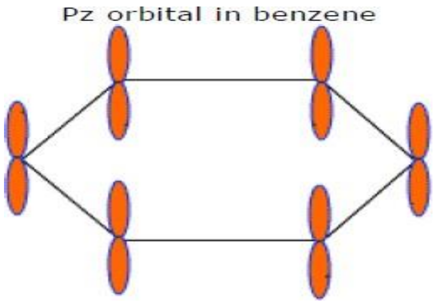
✓ ***Hybridisation***

Because each carbon is only joining to three other atoms, when the carbon atoms hybridise their outer orbitals before forming bonds, they only need to hybridise *three* of the orbitals rather than all four. They use the **2s** electron and two of the 2p electrons, but leave the other **2p** electron unchanged.

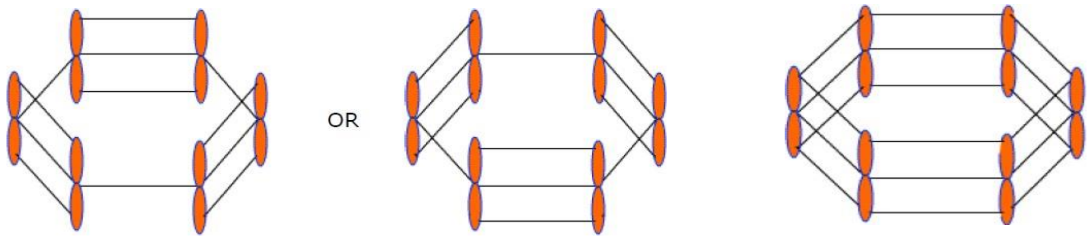
- The new orbitals formed are called **sp^2** *hybrids*, because they are made by an **s** orbital and two **p** orbitals reorganizing themselves.
- The three **sp^2** hybrid orbitals arrange themselves as far apart as possible which is at 120° to each other in a plane. The remaining **p** orbital is at right angles to them.
- Each carbon atom now looks like the diagram on the right. This is all exactly the same as happens in ethene.
- The difference in benzene is that each carbon atom is joined to two other similar carbon atoms instead of just one. Each carbon atom uses the **sp^2** hybrids to form sigma bonds with two other carbons and one hydrogen atom.
- The next diagram shows the sigma bonds formed, but for the moment leaves the **p** orbitals alone.



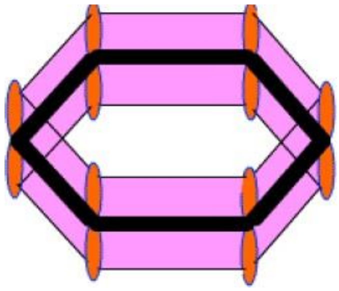
*Since sigma bond results from the overlap of above said planar orbital, all **H** and **C** atoms are in the same plane and their generate a hexagonal ring of **C** atoms.*



*Each **C** atom in benzene also has an unhybrid **2pz** orbital containing one electron. These **2pz** orbital are perpendicular to the plane of sigma bonds.*



*Actually these **2pz** orbital produce a **π (pi)** molecular orbital containing six electrons. One half of this **π (pi)** molecular orbital lies above the plane of hexagonal ring and remaining half below the ring like a sandwich.*



*The overlap of these **2pz** orbital results in the formation of a fully delocalized **π (pi)** bond, which extends all over the six **C** atoms of benzene nucleus. The molecular orbital approach clearly indicates that these six electrons could be found anywhere in highly delocalized manner. As a result of delocalization, a stronger **π (pi)** bond and a more* *stable benzene molecule is obtained which undergo substitution reactions more frequently than addition reactions.*

Bond Length Analysis in Benzene C-C
length in alkane = 1.54°A **C=C** length in
alkene = 1.34°A

But in benzene,

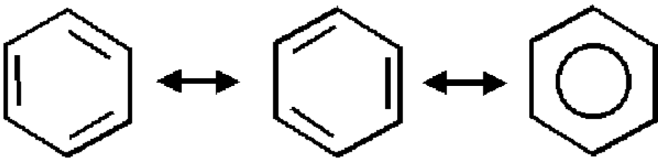
C-C length = 1.397°A

C=C length = 1.397°A

- This shows that in benzene single and double bonds have quite extraordinary character as they do not resemble to alkane and alkene in bond lengths.
- That is why benzene shows a behavior of saturated as well as an unsaturated hydrocarbon simultaneously.

❖ **Modern Representation of Benzene**

- With the help of molecular orbital behavior we conclude that benzene has
  - ✓ A regular hexagonal structure with an inscribed circle.
  - ✓ A hexagon with alternate double and single bonds.



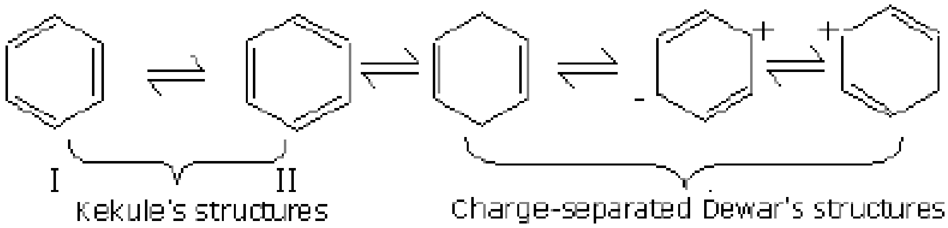
QUESTION: WRITE A NOTE ON THE STABILITY OF BENZENE RING.

ANSWER:

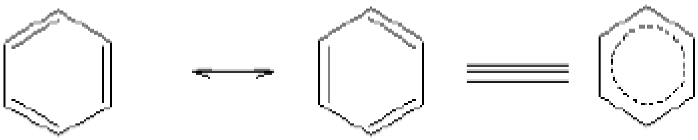
- In benzene ring ***π (pi)*** molecular orbital is in a state of vibration due to this vibration resonance is produced. The stability of benzene ring is due to resonance energy of the system. The resonance energy is the difference in energy content of benzene compared with that of a formal written structure. The Kekule's structure requires localization of **2p**-electrons as specific ***π (pi)*** bonds alternately between particular **C** atoms.
- The actual resonance hybrid structure has these electrons delocalized spread over the whole ring. Hence, ***π (pi)*** electrons of benzene are not readily available at particular positions as in alkenes, and so do not assist the attack of a weak electrophile in the same way as in alkenes. On the other hand the reactivity of benzene ring is also affected by the presence of annular ***π (pi)*** electronic cloud which acts as a repelling shield to any nucleophilic attack. Thus electrophilic substitution is more common in benzene but for a powerful electrophile reagent.

❖ Resonance hybrid structure of benzene

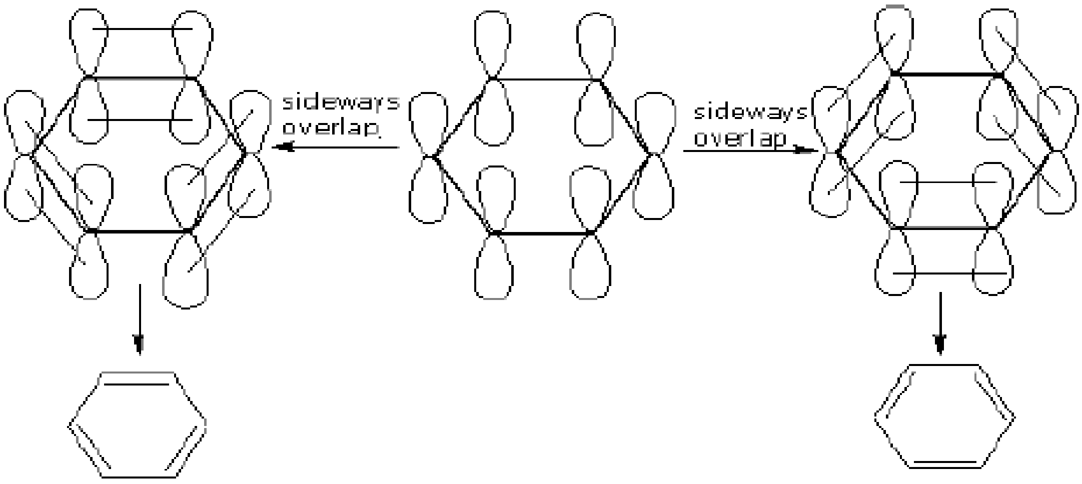
- ✓ The currently accepted structure was developed by the application of the theory of resonance proposed in 1933. This theory states that benzene is a resonance hybrid of the following canonical forms.



- ✓ Since, the forms I and II are the most contributing, hence benzene is represented as a hybrid structure of these two structures, i.e.,



Resonance hybrid

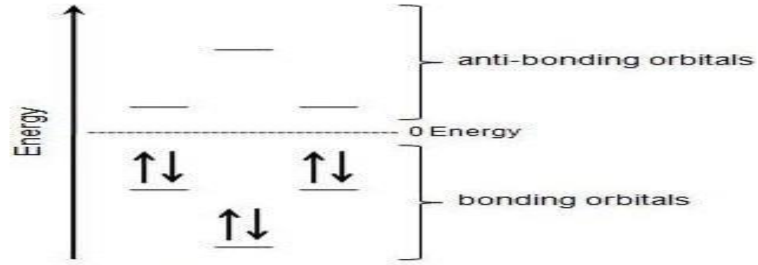


SIR ERICH ARMAND ARTHUR JOSEPH HUCKEL (August 9, 1896, Berlin – February 16, 1980, Marburg) was a German physicist and physical chemist. He is known for two major contributions:

i. The Debye–Huckel theory of electrolytic solutions
ii. The Huckel method of approximate molecular orbital (MO) calculations on π electron systems.

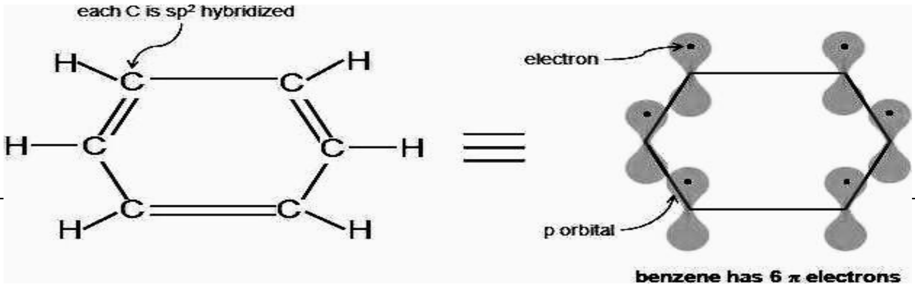
➢ HUCKEL'S RULE

- In 1931, *Sir Erich Huckel* proposed a rule to determine if a planar ring molecule would have aromatic properties. This rule states that if a cyclic, planar molecule has **4n+2 *π-electrons***, it is aromatic. This rule would come to be known as **Huckel's Rule**.
- ***Four Criteria for Aromaticity***
  i. The molecule is cyclic (a ring of atoms)
  ii. The molecule is planar (all atoms in the molecule lie in the same plane)
  iii. The molecule is fully conjugated (p orbitals at every atom in the ring)
  iv. The molecule has 4n+2 *π-electrons* (n=0 or any positive integer)
- **Why 4n+2 *π-Electrons*?**
  - According to Hückel's Molecular Orbital Theory, a compound is particularly stable if all of its bonding molecular orbitals are filled with paired electrons.
  - This is true of aromatic compounds, meaning they are quite stable.
  - With aromatic compounds, 2 electrons fill the lowest energy molecular orbital, and 4 electrons fill each subsequent energy level (the number of subsequent energy levels is denoted by **π**), leaving all bonding orbitals filled and no anti-bonding orbitals occupied.
  - This gives a total of **4n+2** *π-electrons*.
  - The molecular orbital diagram for the aromatic compound, benzene, below.



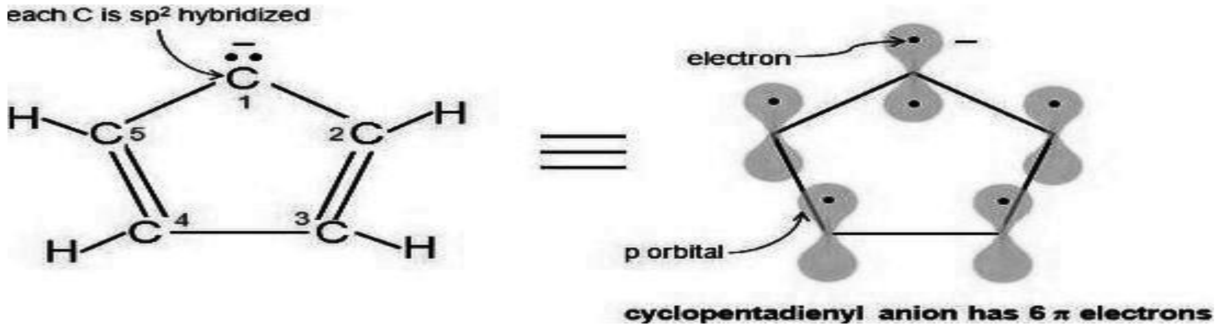
Molecular Orbitals levels of Benzene

  - Benzene has ***6π- electrons***. Its first 2π-electrons fill the lowest energy orbital, and it has ***4π-electrons*** remaining. These 4 fill in the orbitals of the succeeding energy level. Notice how all of its bonding orbitals are filled, but none of the anti-bonding orbitals have any electrons.
- **Which Electrons are π -Electrons**
  - **Huckel's Rule** is figuring out which electrons in the compound are actually **π-electrons**.
  - The rule is quite straight forward; **π-electrons** lie in **p orbitals**.
  - **Sp^2 hybridized** atoms have **1 p orbital** each.
  - So if every molecule in the cyclic compound is **sp^2 hybridized**, this means the molecule is fully conjugated (has **1 p orbital** at each atom), and the electrons in these **p orbitals** are the **π-electrons**.
  - A simple way to know if an atom is **sp^2 hybridized** is to see if it has 3 attached atoms and no lone pairs of electrons.
  - In a cyclic hydrocarbon compound with alternating single and double bonds, each carbon is attached to **1 hydrogen** and **2 other carbons**. Therefore, each carbon is **sp2 hybridized** and has a p orbital.
  - As for example, benzene:

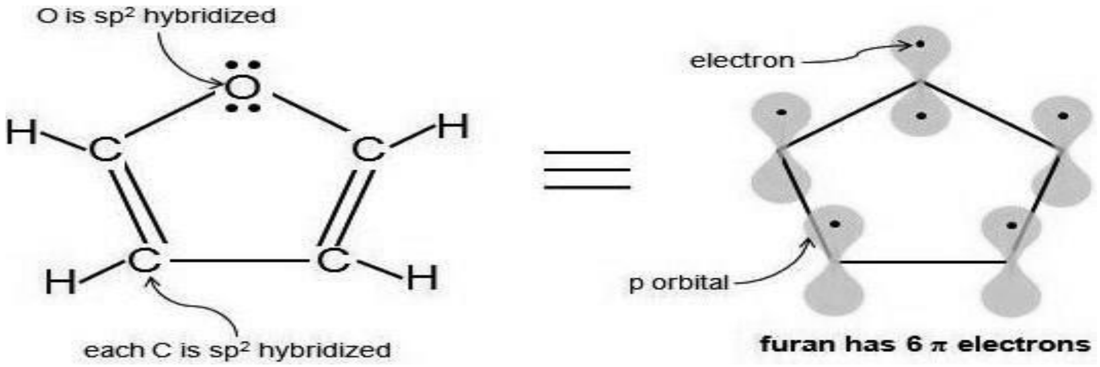


Each double bond (π bond) always contributes 2 π electrons. Benzene has 3 double bonds, so it has 6 π electrons.

- **Aromatic Ions**
  - Hückel's Rule also applies to ions. As long as a compound has 4n+2 π electrons, it does not matter if the molecule is neutral or has a charge.
  - ***For example, cyclopentadienyl anion is an aromatic ion***: **Carbons 2-5** are **sp2 hybridized** because they have 3 attached atoms and have no lone electron pairs. Whereas about **carbon-1** another simple rule to determine if an atom is **sp2 hybridized** is if an atom has 1 or more lone pairs and is attached to an sp2 hybridized atom, then that atom is **sp2 hybridized** also. Therefore, carbon 1 has a **p orbital**. ***Cyclopentadienyl anion*** has **6 π electrons** and fulfills the **4n+2 rule**.

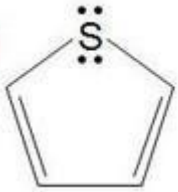


- **Heterocyclic Aromatic Compounds**
  - Compounds with elements other than carbon in the ring can also be aromatic, as long as they fulfill the criteria for aromaticity. These molecules are called heterocyclic compounds because they contain 1 or more different atoms other than carbon in the ring.
  - **A common example in furan:** This contains an oxygen atom. All carbons in furan are **sp2 hybridized**. The oxygen has at least 1 lone electron pair and is attached to an **sp2 hybridized** atom, so it is **sp2 hybridized** as well. Notice how oxygen has 2 lone pairs of electrons. An **sp2 hybridized** atom only has **1 p orbital**, which can only hold **2 electrons**, while the other pair is in an **sp2 orbital**. So, only 1 of oxygen's **2 lone electron pairs** are **π electrons**. Furan has **6 π electrons** and fulfills the **4n+2** rule.

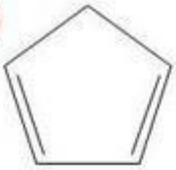


QUESTION: Using the criteria for aromaticity, determine if the following molecules are aromatic.

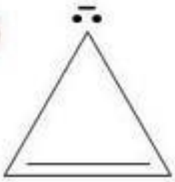
1)



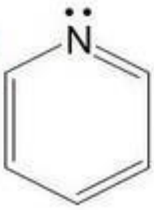
2)



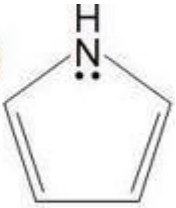
3)



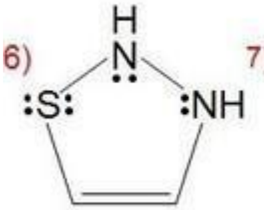
4)



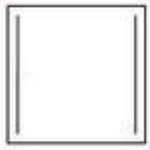
5)



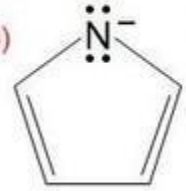
6)



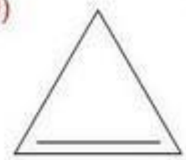
7)



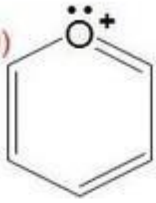
8)



9)



10)



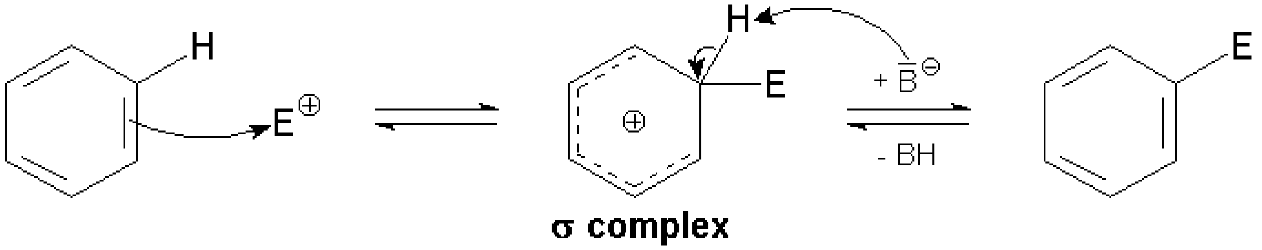
ANSWER:

1. **Aromatic** - only 1 of S's lone pairs counts as π electrons, so there are 6 π electrons, n=1
2. **Not aromatic** - not fully conjugated, top C is sp^3 hybridized
3. **Not aromatic** - top C is sp^2 hybridized, but there are 4 π electrons, n=1/2
4. **Aromatic** - N is using its 1 p orbital for the electrons in the double bond, so its lone pair of electrons are not π electrons, there are 6 π electrons, n=1
5. **Aromatic** - there are 6 π electrons, n=1
6. **Not aromatic** - all atoms are sp^2 hybridized, but only 1 of S's lone pairs counts as π electrons, so there 8 π electrons, n=1.5
7. **Not aromatic** - there are 4 π electrons, n=1/2
8. **Aromatic** - only 1 of N's lone pairs counts as π electrons, so there are 6 π electrons, n=1
9. **Not aromatic** - not fully conjugated, top C is sp^3 hybridized
10. **Aromatic** - O is using its 1 p orbital for the elections in the double bond, so its lone pair of electrons are not π electrons, there are 6 π electrons, n=1

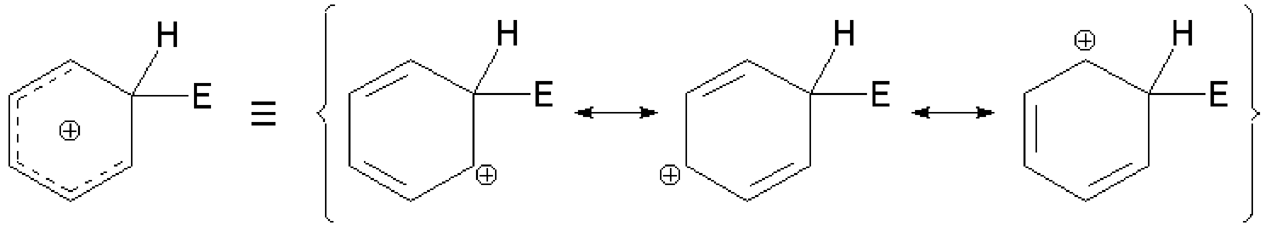
❖ THE ELECTROPHILIC SUBSTITUTION REACTION BETWEEN BENZENE

➢ Mechanism of Electrophilic Aromatic Substitution (Ar-SE)

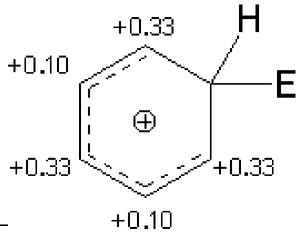
- Electrophilic aromatic substitution is a multistep process.
- In the first step, the addition of an electrophile yields a high-energy carbocation in which the aromatic **π system** has been broken. Subsequently, the aromatic system is recovered by splitting off a proton. Therefore, the mechanism of an **electrophilic aromatic substitution** (**Ar-SE**) may be classified as an ***addition-elimination mechanism***.



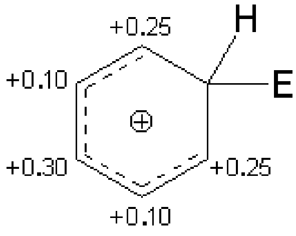
- Initially, the approaching electrophile interacts with the nucleophilic, **aromatic π electron cloud**. The so-called **π complex**.
- The **π complex** that is initially generated by the **aromatic π system's** nucleophilic attack on the electrophile is then rapidly converted into a **cyclohexadienyl cation** known as either the **Wheland complex** or **the σ complex**, or **the arenium ion**. In the **σ complex**, the electrophile is connected to one of the aromatic ring carbons by a **σ bond**.
- *In the second step*, a proton is eliminated from the **σ complex** and then accepted by a base. The base is frequently the counterion of the electrophile; occasionally, the solvent acts as the base. The first step of **Ar-SE** reaction, that is, the formation of the **σ complex**, requires a particularly high amount of energy, as the aromatic π system is broken. In the second step, that is, in the deprotonation, the **aromatic π system** is recovered.
- *In some cases*, it is not a proton but another cation that is eliminated from the **σ complex**. As a result, the aromatic compound is defunctionalized - it loses a functional group. Such a reaction is called an ***Ipso Attack***.
- In the **cyclohexadienyl cation** (**σ complex**), the **positive charge** is delocalized - that is, it is shared by several carbon atoms.



- If the three resonance structures of the **σ complex** are simply superposed, the positive charge in each ***ortho*** and ***para*** position would amount to **+0.33**. In an improved model, the ***meta*** position also carries a small positive charge (+0.10).

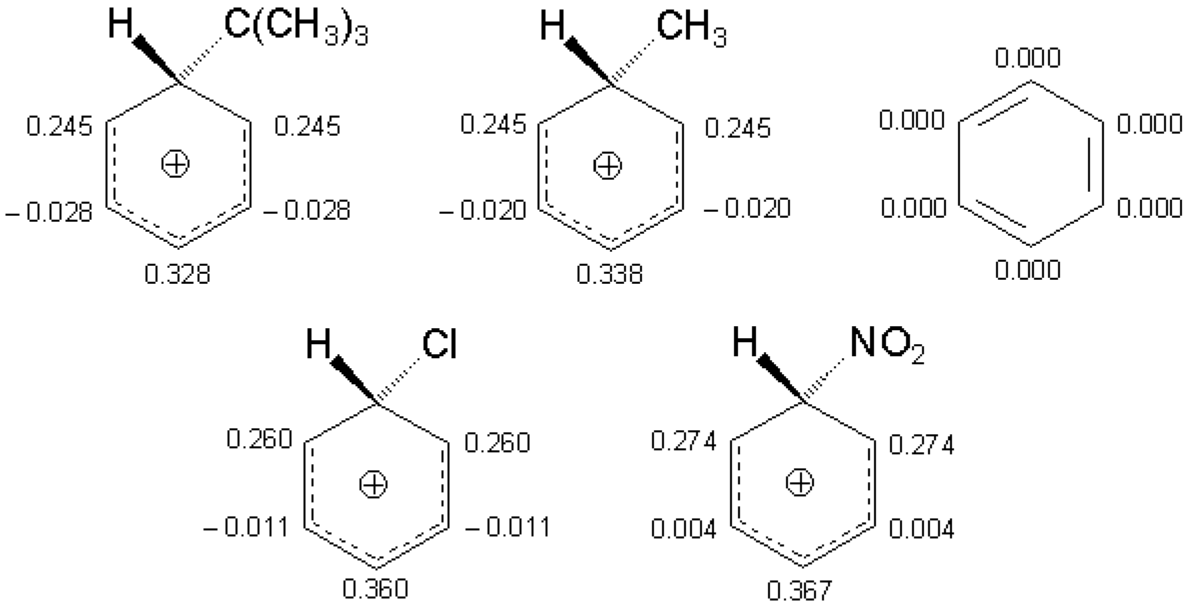


simple model



improved model

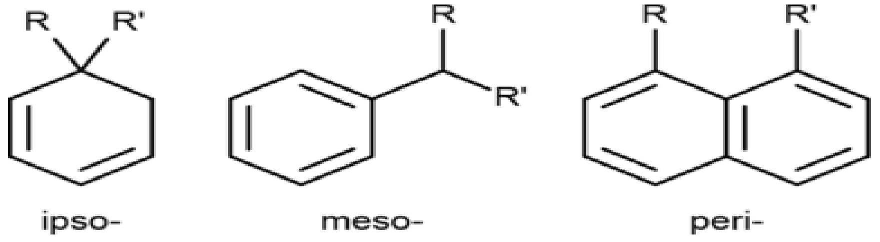
- Atom’s electric charges of several σ complexes



QUESTION: WHAT ARE *IPSO*, *MESO*, AND *PERI* SUBSTITUTIONS IN ORGANIC CHEMISTRY?

ANSWER:

- ***Ipso Substitution:*** The *ipso*- prefix is used when two substituents share the same ring position in an intermediate compound. This could occur in an electrophilic aromatic ring substitution.
- ***Meso Substitution:*** The *meso*- prefix is used when substituents occupy a benzylic position, when the first carbon covalently bonds adjacent to benzene or other aromatic ring. It is seen in acridines and calixarenes.
- ***Peri Substitution:*** The *peri*- prefix is used to describe substituents at the 1 and 8 positions. It is seen specifically in naphthalenes**.**



- According to the considerations above, substituents may be classified into two main groups:
  1. ACTIVATING SUBSTITUENTS: Those are capable of stabilizing the positive charge of the **σ complex**. Compared to benzene, such substituents result in a higher reaction rate of (a second) electrophilic aromatic substitution.

     Examples of activating groups in the relative order from the most activating group to the least activating:

     $$-NH_2, -NR_2 > -OH, -OR > -NHCOR > -CH_3 \text{ and other alkyl groups}$$

     [**R** as alkyl groups (C_nH2_{n+1})]

  2. DEACTIVATING SUBSTITUENTS: Those additionally destabilize the positive charge of the **σ complex**. Compared to benzene, such substituents characteristically result in a lower reaction rate of (a second) electrophilic aromatic substitution.

     Examples of deactivating groups in the relative order from the most deactivating to the least deactivating:

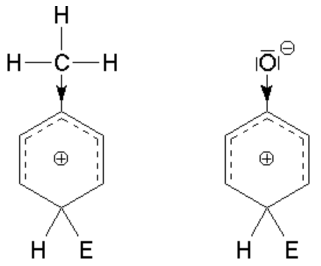
     $$-NO_2, -CF_3 > -COR, -CN, -CO_2R, -SO_3H > \text{Halogens}$$

     [**R** as alkyl groups (C_nH_{2n+1})]

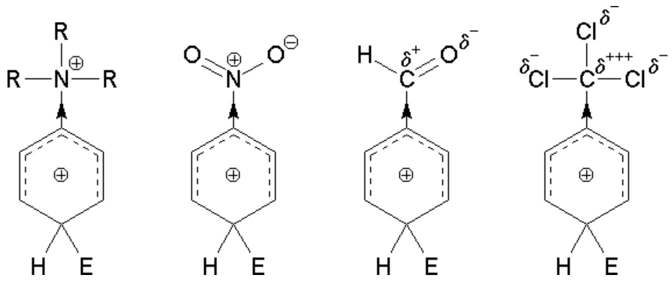
     The order of reactivity among Halogens from the more reactive (least deactivating substituent) to the least reactive (most deactivating substituent) halogen is: $F > Cl > Br > I$

- Halogen substituents are a little unusual in that they are deactivating but still direct **ortho/ para**. The reason is that they are both inductive electron withdrawing (electronegativity) and resonance donating (lone pair donation). The inductive effect lowers the reactivity but the resonance effect controls the regiochemistry due to the stability of the intermediates.

- The stabilization as well as the destabilization of the **σ complex** may be the outcome of two different effects.
  1. *Inductive increase or decrease, respectively, in the aromatic system's electron density through polarization of the σ bond between the substituent and the aromatic ring. This quality of substituents is known as the* ***electron-donating inductive effect*** *(****+I effect****) or* ***electron-withdrawing inductive effect****(****-I effect****), respectively.*

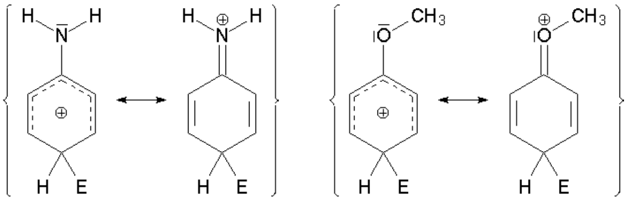


Alkyl groups and the negatively charged oxygen of a phenolate anion are examples of substituents with a **+I effect**

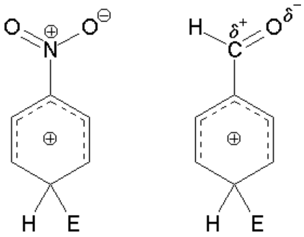


The atom of a substituent with a -I effect that is directly bound to the aromatic ring carbon carries a partially positive charge. R_3N^+- and SO_3H- are examples of substituents with a **-I effect**

An increase or decrease of the aromatic system's electron density through ***resonance*** *(****mesomerism****). That is, the substituent participates in the aromatic π electron system either by donating* ***π electron density (lone electron pair****) or by accepting* ***π electron density****. These qualities of a substituent are called* ***electron-donating mesomeric effect*** *(****+M effect****) or* ***electron-withdrawing mesomeric effect*** *(****-M effect****),respectively. In Lewis formulas, the mesomeric effect of a substituent is illustrated by several possible resonance structures of the σ complex.* *<u>Mesomeric effects are usually much stronger than inductive effects</u>.*

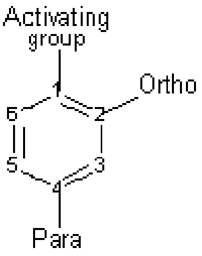


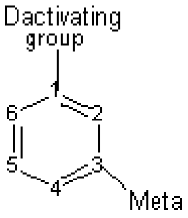
Substituents such as the amino group (NH_2-) of aminobenzene (aniline) or the methoxy group (OCH_3-) of methoxybenzene (anisole) show a considerable **+M effect.**



The nitro group and carboxyl groups are examples of substituents with a **-M effect.**

- The ***activating group*** directs the reaction to the ortho or para position, which means the electrophile substitute the hydrogen that is on **carbon 2** or **carbon 4**.
- The ***deactivating group*** directs the reaction to the meta position, which means the electrophile substitute the hydrogen that is on **carbon 3** <u>with the exception of the halogens that is a deactivating group but directs the ortho or para substitution</u>.



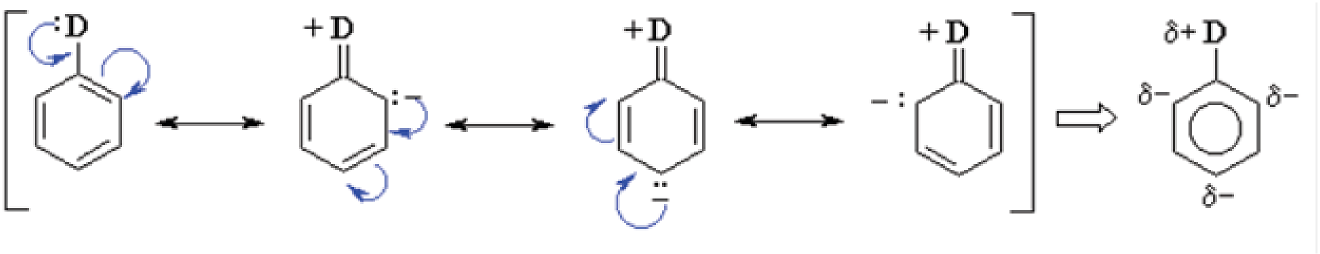


1. ACTIVATING GROUPS *(ortho or para directors)*

- When the substituents like OH have an unshared pair of electrons, the resonance effect is stronger than the inductive effects which make these substituents stronger activators, since this resonance effect direct the electron toward the ring. In cases where the subtituents is esters or amides, they are less activating because they form resonance structure that pull the electron density away from the ring.

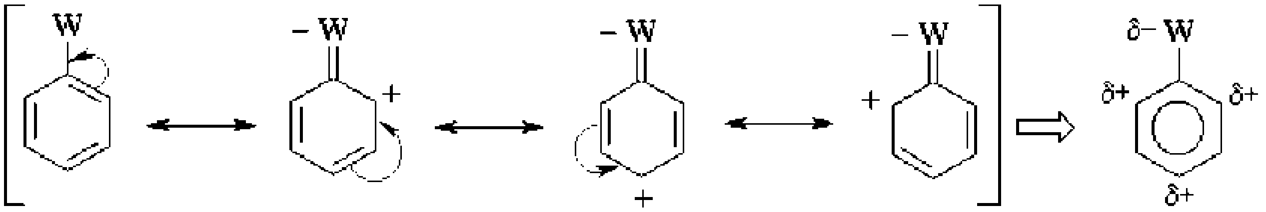
OR

- **Electron Donating Groups** (**EDG**) with lone pairs (*e.g.* :O:Me, **:**NH_2) on the atoms adjacent to the **π** system activate the aromatic ring by increasing the electron density on the ring through a resonance donating effect. The resonance only allows electron density to be positioned at the **ortho** and **para** positions. Hence these sites are more nucleophilic, and the system tends to react with electrophiles at these **ortho** and **para** sites.



2. DEACTIVATING GROUP *(meta directors)*

- The deactivating groups deactivate the ring by the inductive effect in the presence of an electronegative atom that withdraws the electrons away from the ring.
- **Electron Withdrawing Groups** (**EWG**) with π bonds to electronegative atoms (e.g. C=O, NO_2) adjacent to the **π system** deactivate the aromatic ring by decreasing the electron density on the ring through a resonance withdrawing effect. The resonance only decreases the electron density at the ortho and para positions. Hence these sites are less nucleophilic, and so the system tends to react with electrophiles at the **Meta** sites.



✓ ***There are two main electronic effects that substituents can exert:***

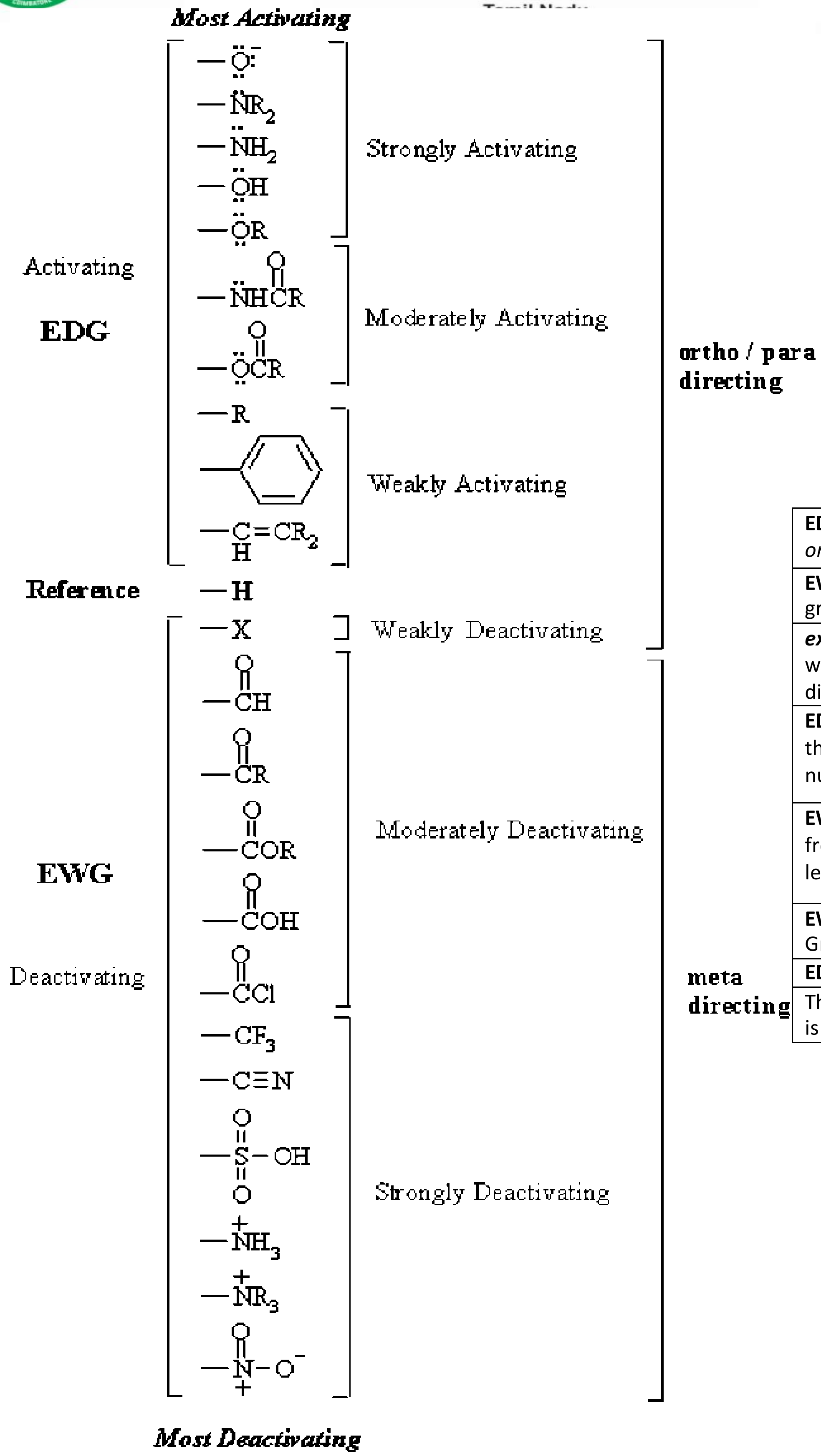
- **RESONANCE** effects are those that occur through the π system and can be represented by resonance structures. These can be either electron donating (e.g. **OMe**) where π electrons are pushed toward the arene or electron withdrawing (e.g. **C=O**) where **π electrons** are drawn away from the **arene**.
- **INDUCTIVE** effects are those that occur through the π system due to electronegativity type effects. These too can be either electron donating (e.g. **Me**) where π electrons are pushed toward the arene or electron withdrawing (e.g. **CF_3**, **$+NR_3$**) where **π electrons** are drawn away from the **arene**.

NOTE BY:

WHAT ARE ARENES?

Arenes are aromatic hydrocarbons. The term "aromatic" originally referred to their pleasant smells, but now implies a particular sort of delocalised bonding.

The **arene**s are likely to meet at this level are based on benzene rings. The simplest of them is benzene itself, C_6H_6. The next simplest is methylbenzene (old name: toluene) which has one of the hydrogen atoms attached to the ring replaced by a methyl group - $C_6H_5CH_3$.



EDG / activating groups direct *ortho / para*

EWG / deactivating groups direct *meta*

***except* halogens (X)** which are deactivating but direct *ortho / para*

EDG add electron density to the p system making it more nucleophilic

EWG remove electron density from the p system making it less nucleophilic

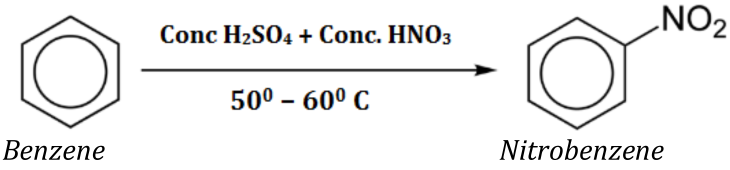
EWG = Electron Withdrawing Group

EDG = Electron Donating Group

The **H atom** is the standard and is regarded as having no effect.

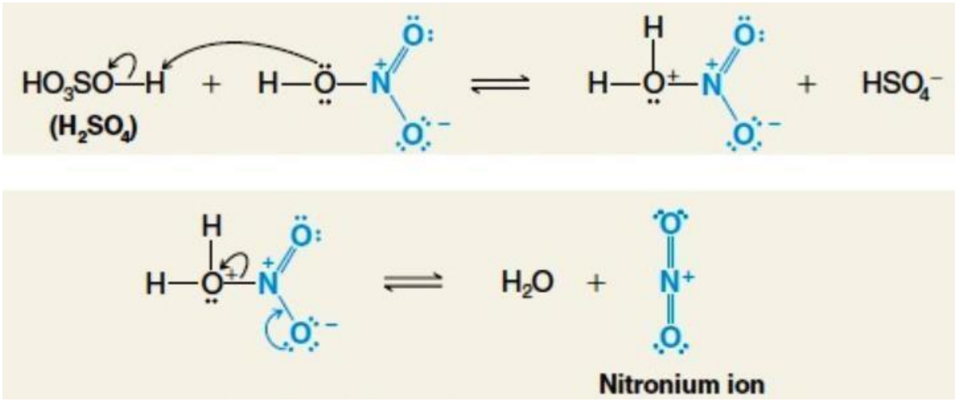
1. NITRATION OF BENZENE

- Benzene reacts with concentrated nitric acid at 50^0 – 60^0 C in the presence of concentrated sulphuric acid to form nitrobenzene. This reaction is known as nitration of benzene.
- ***Reaction type***: *Electrophilic Aromatic Substitution*
- **General Reaction**

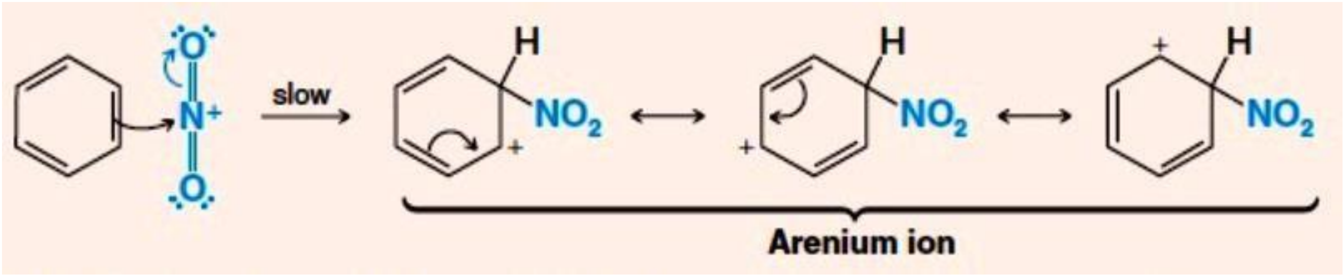


- ***Reaction Mechanism***

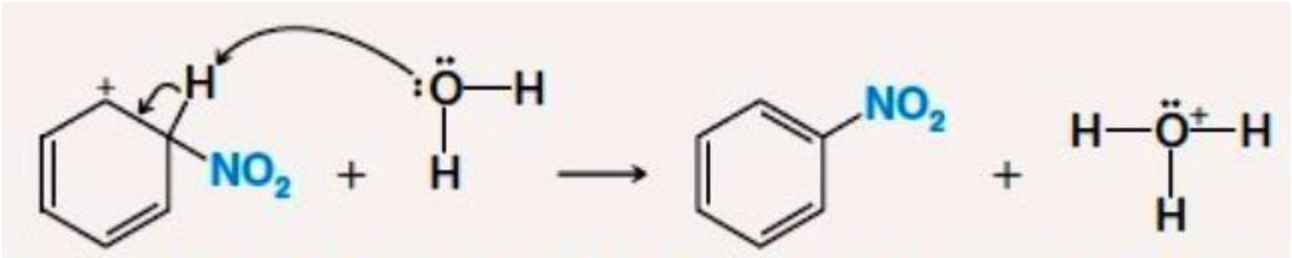
Step 1: Nitric acid accepts a proton from sulphuric acid and then dissociates to form **nitronium ion**.



Step 2: The **nitronium ion** acts as an **electrophile** in the process which further reacts with benzene to form **arenium ion.**

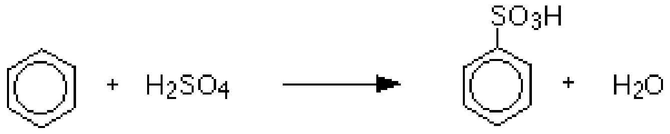


Step 3: The **arenium** ion then loses its proton to Lewis base forming nitrobenzene.



2. SULFONATION OF BENZENE

- Sulfonation of benzene is a process of heating benzene with fuming sulphuric acid (**H_2SO_4 +SO_3**) to produce **benzenesulfonic acid**. The reaction is reversible in nature.
- Sulphonation of benzene requires "***fuming sulphuric acid***", which is sulphuric acid with extra **SO_3** added. The sulphuric acid produces even more **SO_3**, which is the electrophile in this reaction.
- **Reaction type:** *Electrophilic Aromatic Substitution*
- **General Reaction**

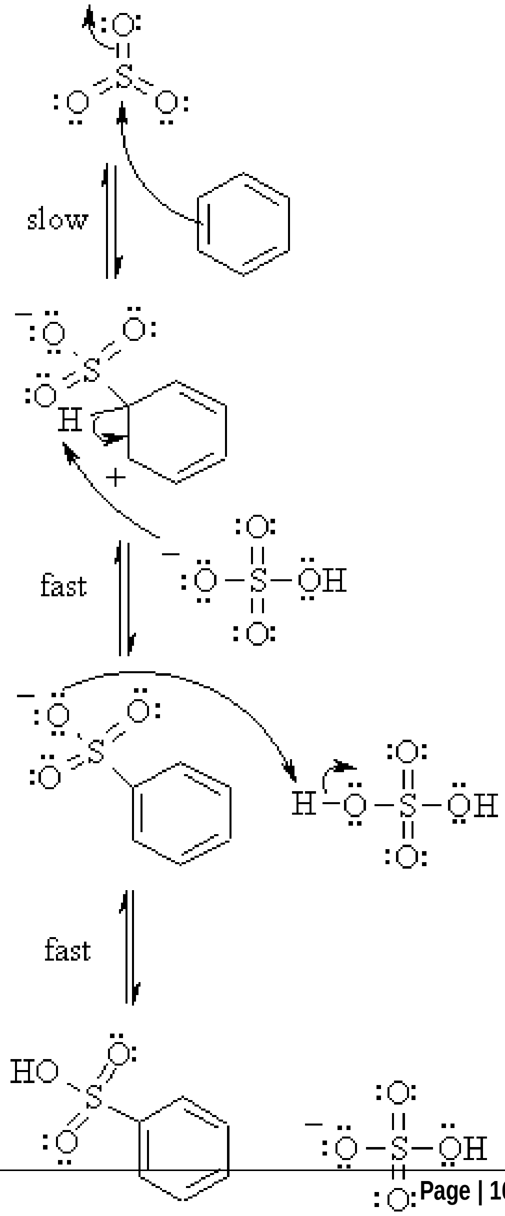


Benzene *Sulphuric Acid* *Benzenesulfonic Acid*

- ***Reaction Mechanism***

Step I: Formation of Electrophilic species, **SO_3** which can be formed by the loss of water from the sulfuric acid

$$2\ H_2SO_4 \rightleftharpoons SO_3 + H_3O^+ + HSO_4^-$$



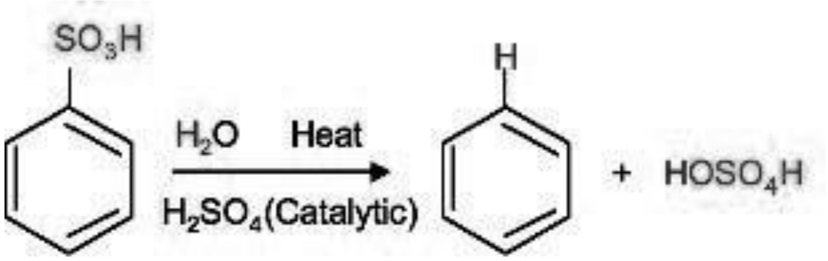
Step 2:
The **π electrons** of the aromatic **C=C** act as a nucleophile, attacking the electrophilic S, pushing charge out onto an electronegative O atom. This destroys the aromaticity giving the **cyclohexadienyl cation** intermediate.

Step 3:
Loss of the proton from the **sp3 C** bearing the **sulfonyl-group** reforms the **C=C** and the aromatic system.

Step 3:
Protonation of the conjugate base of the sulfonic acid by sulfuric acid produces the sulfonic acid.

3. REVERSE SULFONATION

- Sulfonation of benzene is a reversible reaction. Sulfur trioxide readily reacts with water to produce sulfuric acid and heat. Therefore, by adding heat to benzenesulfonic acid in diluted aqueous sulfuric acid the reaction is reversed.



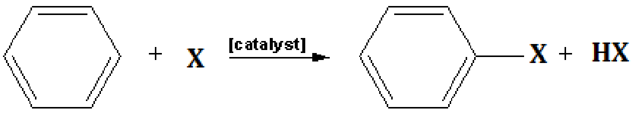
❖ Applications of Nitration and Sulfonation

- **Nitration** is used to add nitrogen to a benzene ring, which can be used further in substitution reactions. The nitro group acts as a ring deactivator. Having nitrogen present in a ring is very useful because it can be used as a directing group as well as a masked amino group. The products of aromatic nitrations are very important intermediates in industrial chemistry.

- Because **sulfonation** is a **reversible reaction**, it can also be used in further substitution reactions in the form of a directing blocking group because it can be easily removed. The sulfonic group blocks the carbon from being attacked by other substituents and after the reaction is completed it can be removed by reverse sulfonation. Benzenesulfonic acids are also used in the synthesis of detergents, dyes, and sulfa drugs. Bezenesulfonyl Chloride is a precursor to sulfonamides, which are used in chemotherapy.

4. HALOGENATION OF BENZENE

- **Reaction type:** *Electrophilic Aromatic Substitution*
- An electrophilic aromatic halogenation is a type of electrophilic aromatic substitution. This organic reaction is typical of aromatic compounds and a very useful method for adding substituents to an aromatic system.
- A few types of aromatic compounds, such as phenol, will react without a catalyst, but for typical benzene derivatives with less reactive substrates, a Lewis acid catalyst is required. Typical **Lewis acid catalysts** include **$AlCl_3$, $FeCl_3$, $FeBr_3$,** and **$ZnCl_2$**. These work by forming a highly electrophilic complex which is attacked by the benzene ring.
- ***Electrophilic species***: the halonium ion (i.e. **X^+;** **X =** Cl_2 and Br_2) formed by the removal of a halide ion by the Lewis acid catalyst
- Restricted for **I^-** or **F^-** are usually introduced using alternative methods
- **General Reaction:**

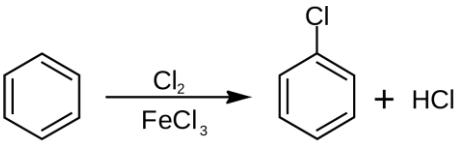


X = Halogen

CATALYSTS = Lewis acid catalysts ($AlCl_3$, $FeCl_3$, $FeBr_3$, and $ZnCl_2$)

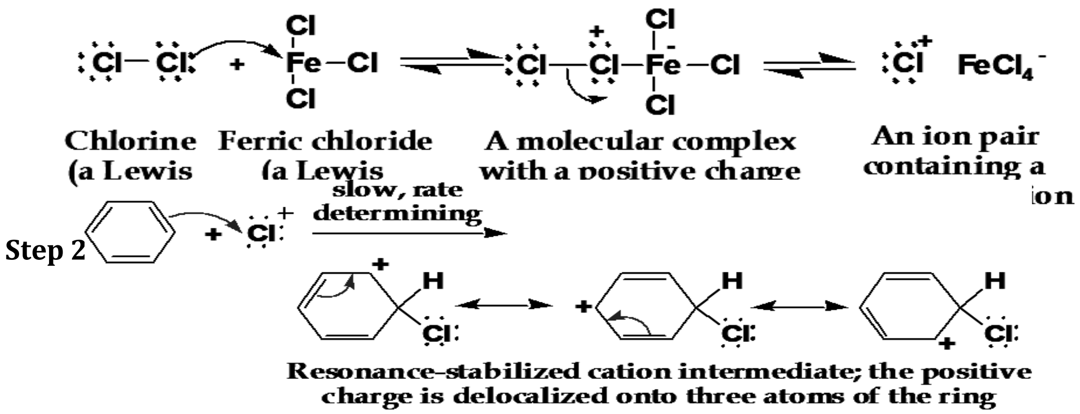
A. Chlorination of Benzene

- **General Reaction:**

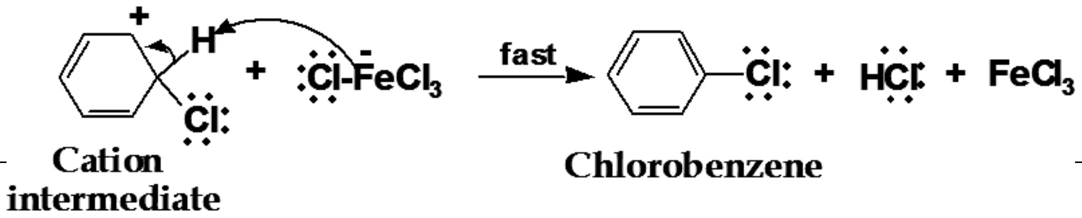


- ***Mechanism of Chlorination of Benzene***

Step 1: *formation of a chloronium ion.*

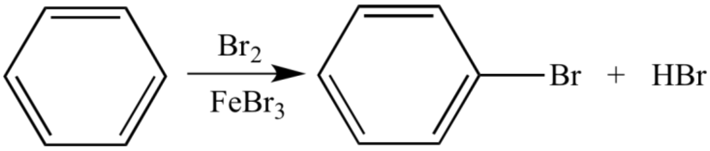


Step 3: *proton transfer regenerates the aromatic character of the ring.*



B. Bromination of benzene

- **General Reaction:**



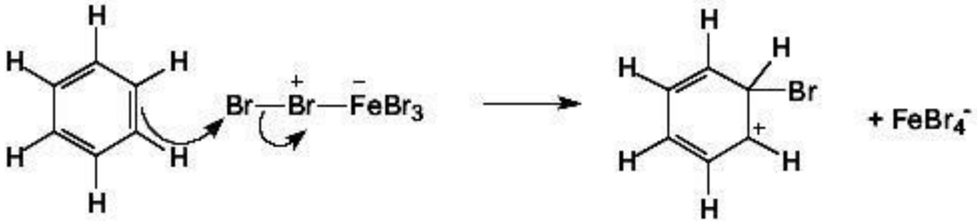
- ***Mechanism of Bromination of benzene***

Step 1: Generate of Electrophile

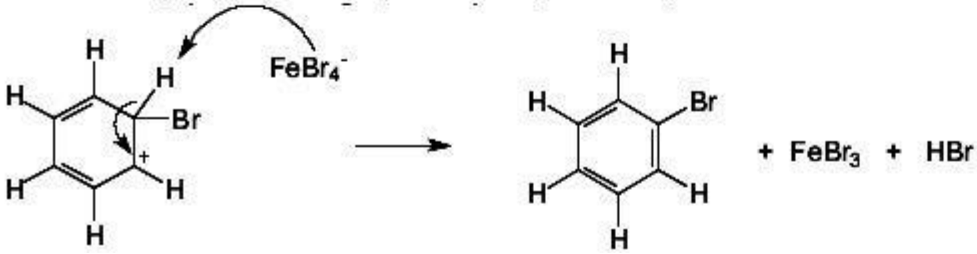
(stronger electrophile than Br_2)

- Before the electrophilic aromatic substitution can take place, the electrophile must be activated.
- A strong Lewis acid catalyst, such as $FeBr_3$, should be used.

Step 2: Electrophilic attack and formation of the sigma complex.



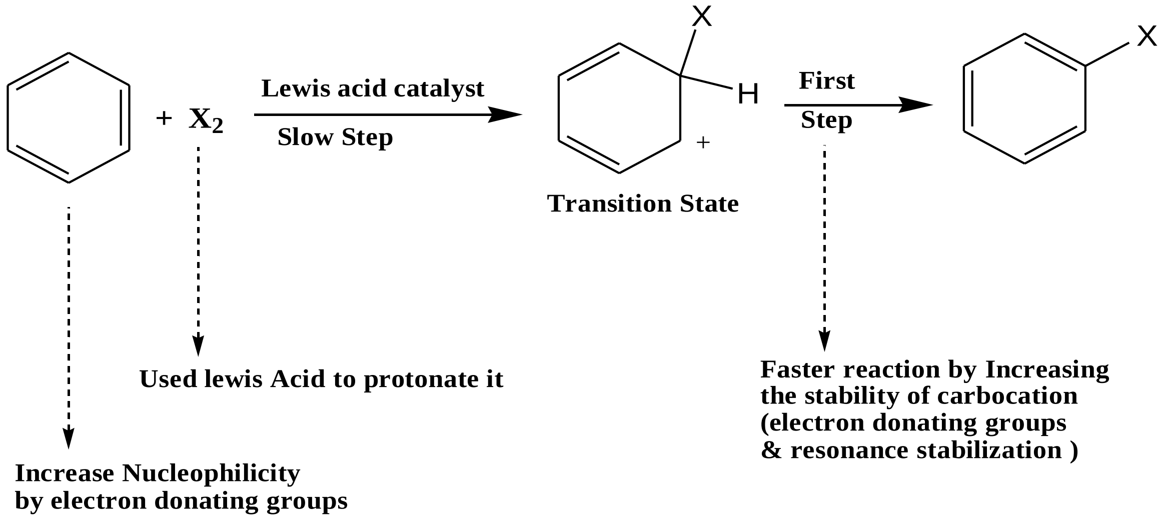
Step 3: Loss of a proton to give the products.



QUESTION: WHY IODINATION AND FLUORINATION OF BENZENE DIFFICULT?

ANSWER:

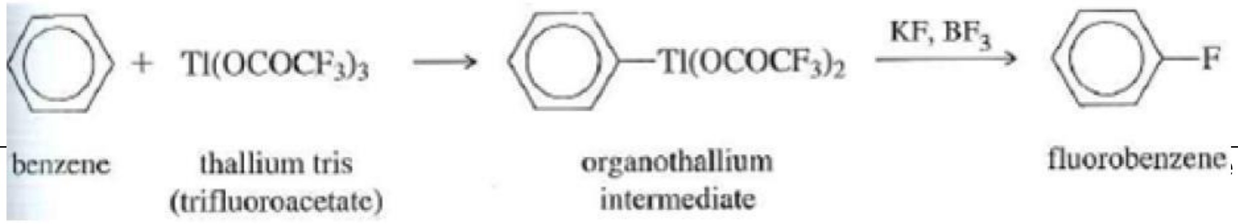
- When Benzene or the halogen in the starting material has to be slightly more reactive than the other.
- For satisfying this condition, electron donating groups attached to the phenyl ring making it more nucleophilic are preferred over unsubstituted Benzene. Also, the electrophilicity of the halogen is increased by using a Lewis acid catalyst thereby making it more reactive.
- These changes in turn help to achieve transition state faster and stabilize it better.
- **Electrophilic aromatic substitution reaction**

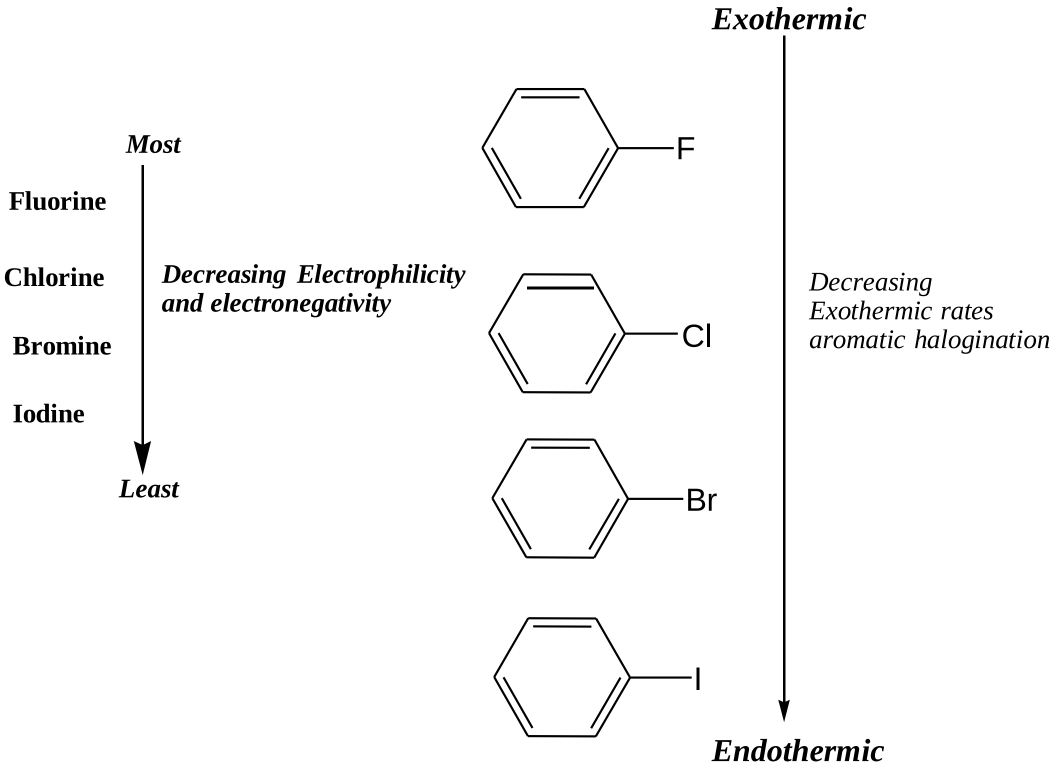


- In case of the halogens, the electronegativity and electrophilicity decrease from **F** to **I** in the periodic table. **Fluorine** is most **electrophilic**, and **Iodine** is least. Therefore, **Fluorination** is highly reactive, and **Iodination** is highly unreactive for electrophilic aromatic substitution reactions.
- The exothermic rates of aromatic halogenation also decrease from **Fluorine** to **Iodine**. Fluorination reaction being highly exothermic and explosive, the reaction cannot be controlled resulting in polyfluorinated products. For Iodination, the reaction is endothermic with 12kJ/mol of energy absorbed. Therefore, it cannot be done using the conventional method using Lewis acid catalyst and requires strong oxidizing agents.

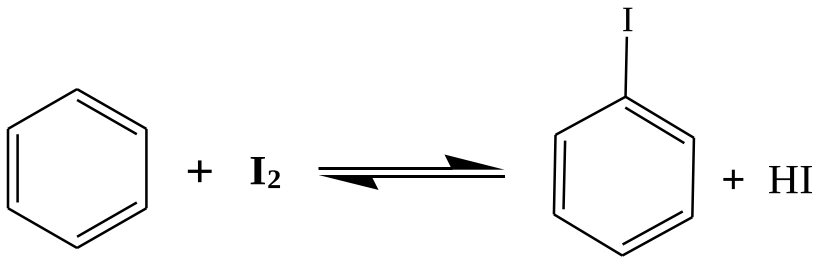
Atom	**Electronegativity**	**Electrophilicity**	**First Ionization Energy (kJ/mol)**
Fluorine	4.0	3.86	1681
Chlorine	3.0	3.67	1251
Bromine	2.8	3.40	1140
Iodine	2.5	3.09	1008

- Controlled fluorination of benzene is difficult, but it can be accomplished by a two-step **THALLATION PROCEDURE**. Benzene reacts with **thallium tris** [**trifluoroacetate, Tl(OCOCF$_3$)$_3$**] to give an **organothallium** intermediate. Further reaction with **potassium fluoride** and **boron trifluoride** gives the **aryl fluoride.**





- This is because, when **Iodine** adds to the **Benzene** reversibly generating **HI**. **HI** being a strong reducing agent regenerates "**I**" from **aryl iodide** giving back the **aromatic hydrocarbon**. However, in the presence of oxidizing agents such as **HIO_3**, **HI** is converted back to **Iodine** thereby increasing the concentration of **Iodine** in the reaction mixture. According to *Le-Chatelier's principle*, if the concentration of one of the reagents is increased then the equilibrium shifts in the forward direction to give aryl iodide as the desired product.



a) Oxidizing agents (HIO_3, HNO_3) reconverts **HI** to **I_2**

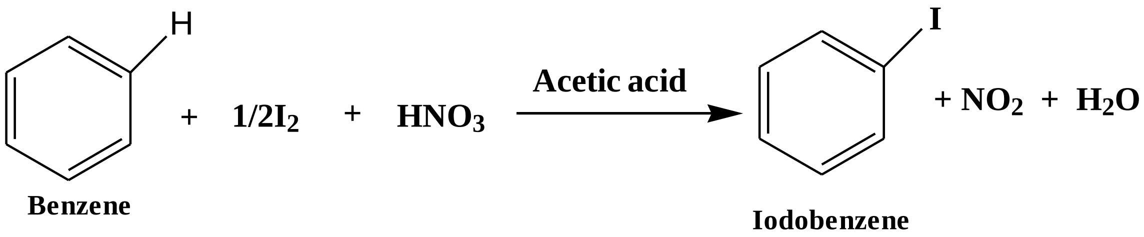
$$5HI + HIO_3 \longrightarrow 3I_2 + 3H_2O \quad\Big|\quad 2HI + 2HNO_3 \longrightarrow I_2 + 2H_2O + 2NO_2$$

- Another way to obtain aryl iodide is to remove HI as soon as it is formed in the reaction mixture, by forming salts. For example, when the Mercuric oxide is used, it converts Hydrogen Iodide to Mercuric Iodide that is then discarded.

b) Salt formation (alkali hydroxide, carbonate or hydrogen carbonate, borax, HgO, Hg-acetate or aliphatic amine or Ammonia)

$$2HI + HgO \longrightarrow HgI_2 + H_2O$$

- **The reaction mechanism of Iodination of benzene**
  - Oxidizing agents, when used, **Iodine** (**I_2**) get oxidize to **iodonium ion** (**I^+**) by using **HNO_3** or **H_2SO_4** in the presence of **Acetic acid** and this reaction was called **Tronov-Novikov reaction**.
  - **Iodine** can be easily oxidized by using **nitric acid** (**HNO_3**) in the presence of an **Acetic acid** and **Iodine** generates **Iodine cation** that reacts with Benzene giving **Iodobenzene**, **Nitrogen dioxide**, and **water**.
  - Here **HNO_3** is consumed in the reaction; hence it is a **reagent** and not a **catalyst**.
  - Reaction mechanism:



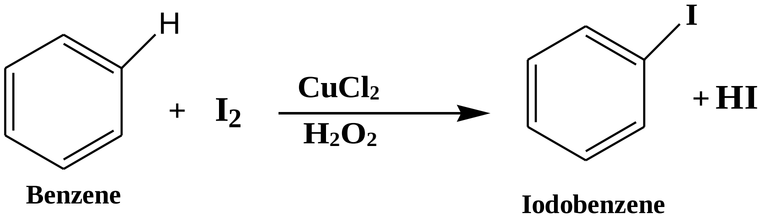
Generate of iodonium ion (I^+)

$$H^+ + HNO_3 + 1/2I_2 \longrightarrow I^+ + NO_2 + H_2O$$

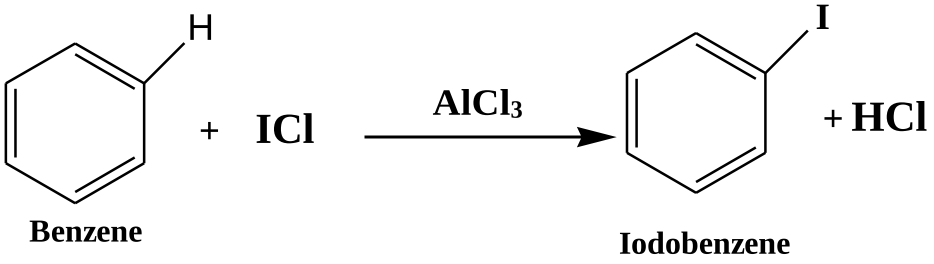
Iodine cation

$$\boxed{I_2 + HNO_3 + \text{Acetic acid }(H^+)} \longrightarrow$$ ***Tronov-Novikov Method***

- A similar mechanism is seen for **Cupric Chloride** and **Hydrogen peroxide** for generation of Iodine cation.

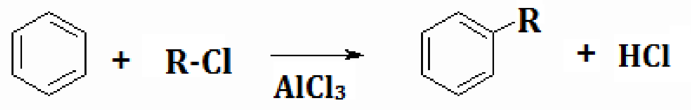


- The best reagent for Iodination is **Iodine monochloride** (**ICl**) an interhalogen compound. **Chlorine** is more electronegative and pulls the electron cloud towards itself giving **Iodine** a (delta) positive charge. The Benzene ring can pick up this quickly than Iodine from the non-polar I bond thereby giving **aryl iodide** as the desired product.

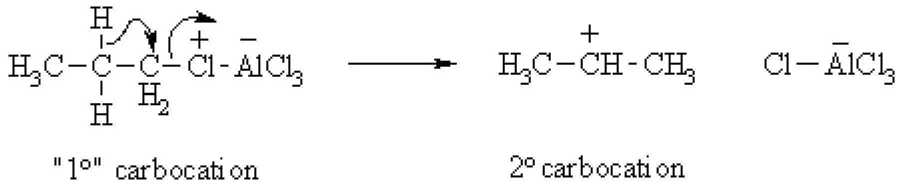


5. FRIEDEL-CRAFTS ALKYLATION OF BENZENE

- Alkylation means substituting an alkyl group into something - in this case into a benzene ring. A hydrogen on the ring is replaced by a group like methyl or ethyl and so on. Benzene is treated with a chloroalkane (for example, chloromethane or chloroethane) in the presence of aluminium chloride as a catalyst.
- **Reaction type:** Electrophilic Aromatic Substitution
- **General Reaction:**



- Named after **Friedel** and **Crafts** who discovered the reaction in 1877.
- **Reagent:** normally the alkyl halide (e.g. R-Br or R-Cl) with aluminum trichloride, $AlCl_3$, a Lewis acid catalyst
- The $AlCl_3$ enhances the electrophilicity of the alkyl halide by complexing with the halide
- **Electrophilic species:** the carbocation (**R^+**) formed by the "removal" of the halide by the Lewis acid catalyst
- The reactive electrophile, the carbocation is prone to rearrangement to a more stable carbocation which will then undergo the alkylation reaction.

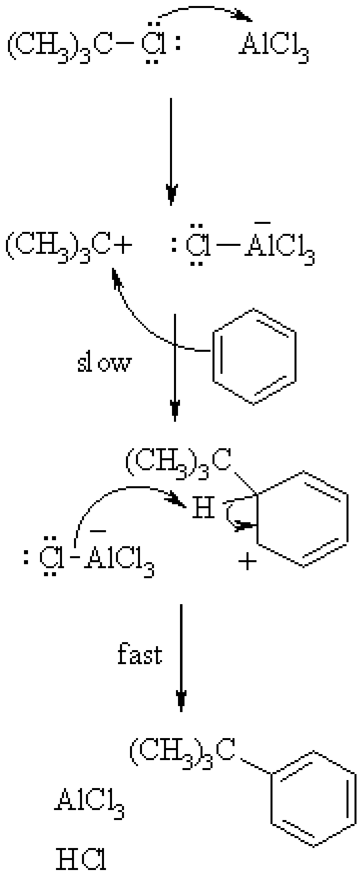


- **Mechanism for the Friedel-Crafts Alkylation of Benzene**

Step 1:
The alkyl halide reacts with the Lewis acid to form a more electrophilic a **carbocation**

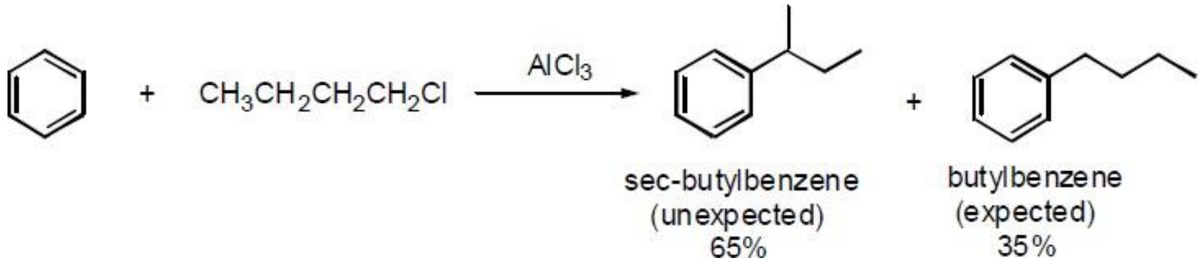
Step 2:
The **p** electrons of the aromatic **C=C** act as a nucleophile, attacking the electrophilic **C^+**. This step destroys the aromaticity giving the cyclohexadienyl cation intermediate.

Step 3:
Removal of the proton from the **sp^3 C** bearing the alkyl-group reforms the **C=C** and the aromatic system, generating **HCl** and regenerating the active catalyst.

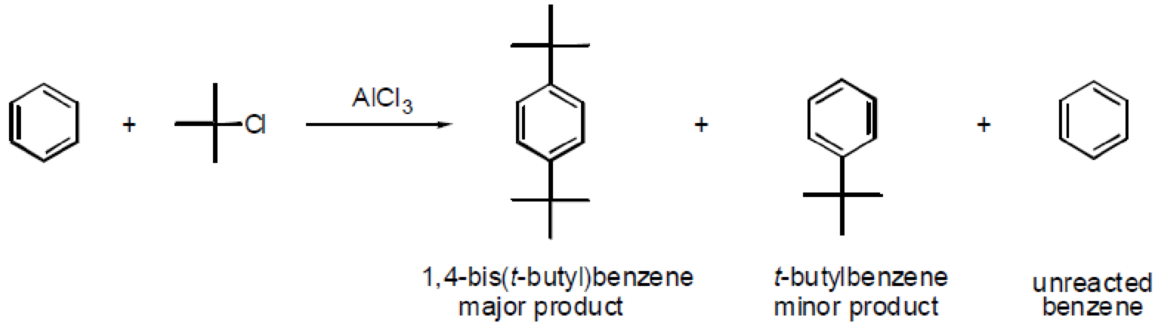


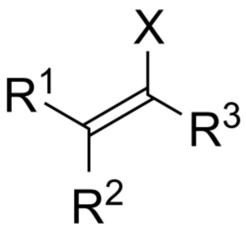
- **THE FRIEDEL-CRAFTS ALKYLATION AND ITS LIMITATIONS**

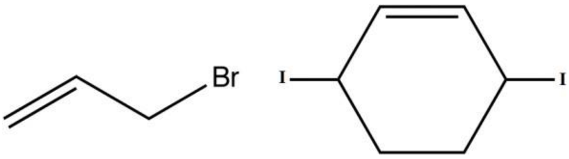
- The Friedel-Crafts reaction is a convenient way to introduce alkyl groups in the benzene ring. It is a typical electrophilic substitution process, in which the electrophile is (in most cases) a carbocation.
- There are three ways to generate the carbocationic species:
  i. *Via preliminary reaction* of an alkyl chloride with $AlCl_3$.
  ii. *Via preliminary reaction* of an alcohol with a Lewis acid (such as BF_3) or a Bronsted acid (usually H_3PO_4).
  iii. *Via preliminary reaction* of an alkene with a Bronsted acid, whose anion is a weak nucleophile (HF)
- Four strict limitations for Friedel-Crafts Alkylation:
  i. The reaction works only with benzene or ACTIVATED benzene derivatives. It will not occur if the benzene ring is DEACTIVATED.
  ii. The reaction works only with ALKYL halides (i.e. chlorides, bromides or iodides), but it does not work with VINYL or ARYL halides.
  iii. Because of the intermediate formation of carbocations, product mixtures might be obtained, due to rearrangements of the carbocations.



  iv. The Friedel-Crafts reaction often leads to the introduction of more than one alkyl group in the molecule. The reason for such undesired polyalkylation

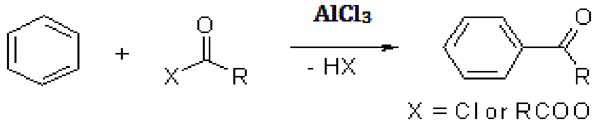




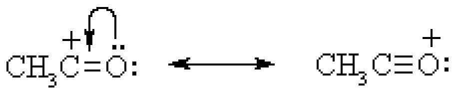
Note By: **VINYL HALIDE:** In organic chemistry, a vinyl halide is any alkene with at least one halide substituent bonded directly on one of the alkene carbons.	An **ALLYLIC HALIDE** is an alkyl halide in which there is one or more halogen atoms on an allylic carbon. Allylic carbons are carbons bonded to carbon atoms that are doubly bonded to other carbon atoms 

6. FRIEDEL-CRAFTS ACYLATION OF BENZENE

- **Friedel-Crafts Acylation** allows to synthesis of **monoacylated products** from the reaction between **arenes** and **acyl chlorides** or anhydrides. The products are deactivated, and do not undergo a **second substitution**.
- **General Reaction:**

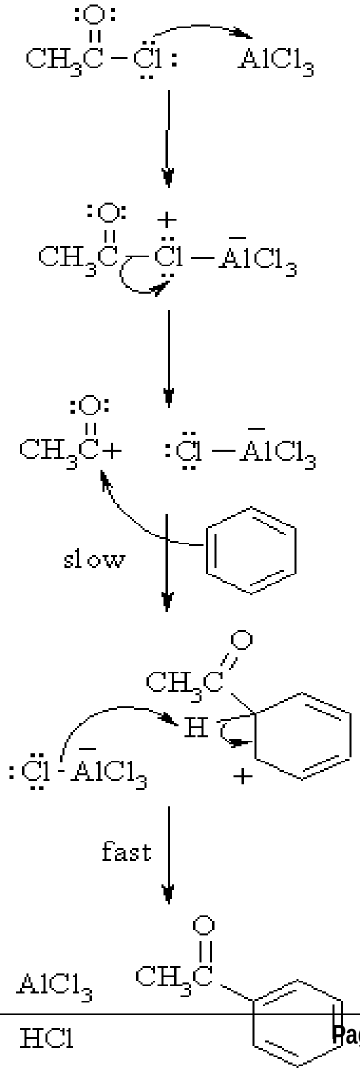


- **Reaction type:** Electrophilic Aromatic Substitution.
- **Reagent:** normally the **acyl halide** (**RCOCl**) with **aluminum trichloride** (**$AlCl_3$**) which acts as a Lewis acid catalyst.
- Alternatively, the **acid anhydride [$(RCO)_2O$]** can be used instead of the **acyl halide**.
- The **$AlCl_3$** enhances the electrophilicity of the acyl halide by complexing with the halide.
- **Electrophilic species:** the **acyl cation** or **acylium ion** (**RCO^+**) formed by the "removal" of the halide by the *Lewis acid catalyst*
- The **acylium ion** is stabilized by resonance as shown below. This extra stability prevents the problems associated with the rearrangement of simple **carbocations**:



acylium ion

- **Mechanism for the Friedel-Crafts Acylation of Benzene**

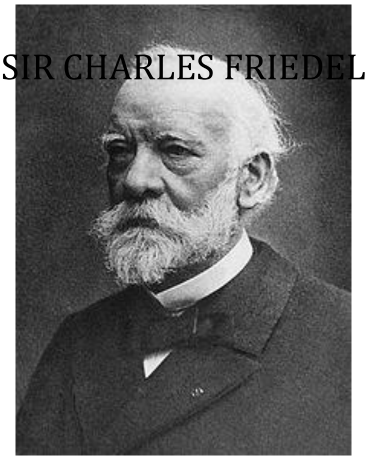


Step 1:
The acyl halide reacts with the Lewis acid to form a complex.

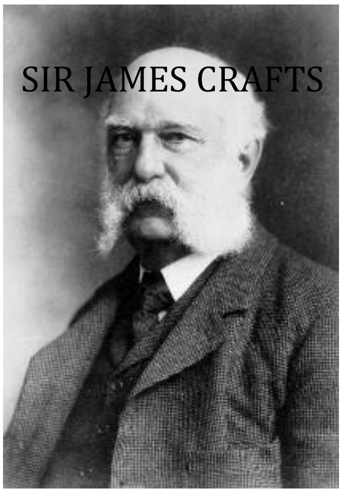
Step 2:
Loss of the halide to the Lewis acid forms the electrophilic acylium ion.

Step 3:
The ***p electrons*** of the aromatic **C=C** act as a nucleophile, attacking the electrophilic **C^+**. This step destroys the aromaticity giving the cyclohexadienyl cation intermediate.

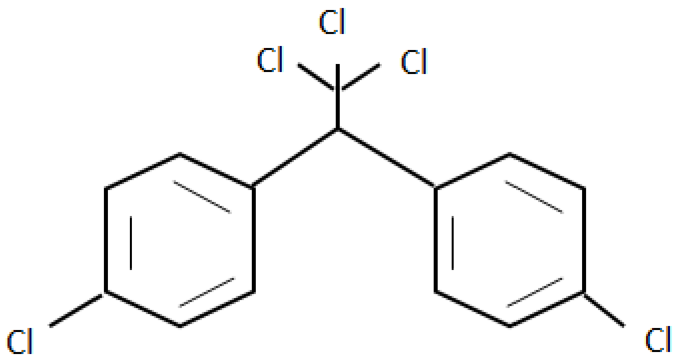
Step 4:
Removal of the proton from the sp3 C bearing the acyl- group reforms the **C=C** and the aromatic system, generating HCl and regenerating the active catalyst.



SIR CHARLES FRIEDEL



SIR JAMES CRAFTS

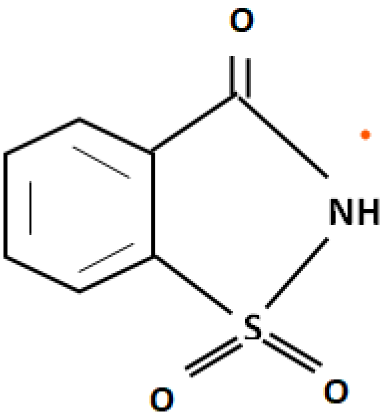


DDT

Dichlorodiphenyltrichloroethane

Uses:

1. It is an effective insecticide, particularly for mosquito, flies.
2. Responsible for the almost complete eradication of malaria-carrying mosquito.
3. DDT is still being widely used in poor country due to non-availability of other cheaper insecticides.



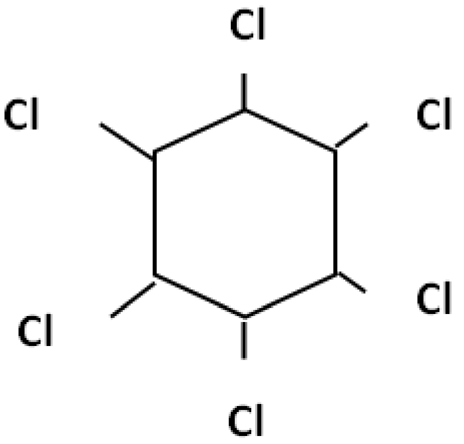
Saccharin

Benzoic sulfimide

Uses:

1. It is generally used as artificial sweetner.
2. It is used in different vitamin supplement.

3. Saccharin is used to sweeten products such as drinks, candies, cookies, and medicines.
4. Saccharin can be used to prepare exclusively disubstituted amines from alkyl halides also.

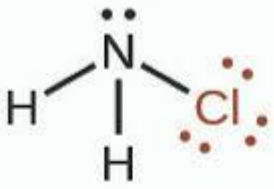


BHC

Benzene Hexa Chloride

Uses:

1. Benzene hexachloride is used as an insecticide on crops, in forestry, for seed treatment.
2. It is used in the treatment of head and body lice.
3. It is used in pharmaceuticals.
4. It is used to treat scabies.
5. It is used in shampoo.



chloramine

Uses:

1. It is used as a disinfectant.