UNIT I

Benzene and its derivatives

Sub Topic: Reactions of benzene [Electrophilic aromatic substitution reactions and Mechanisms]

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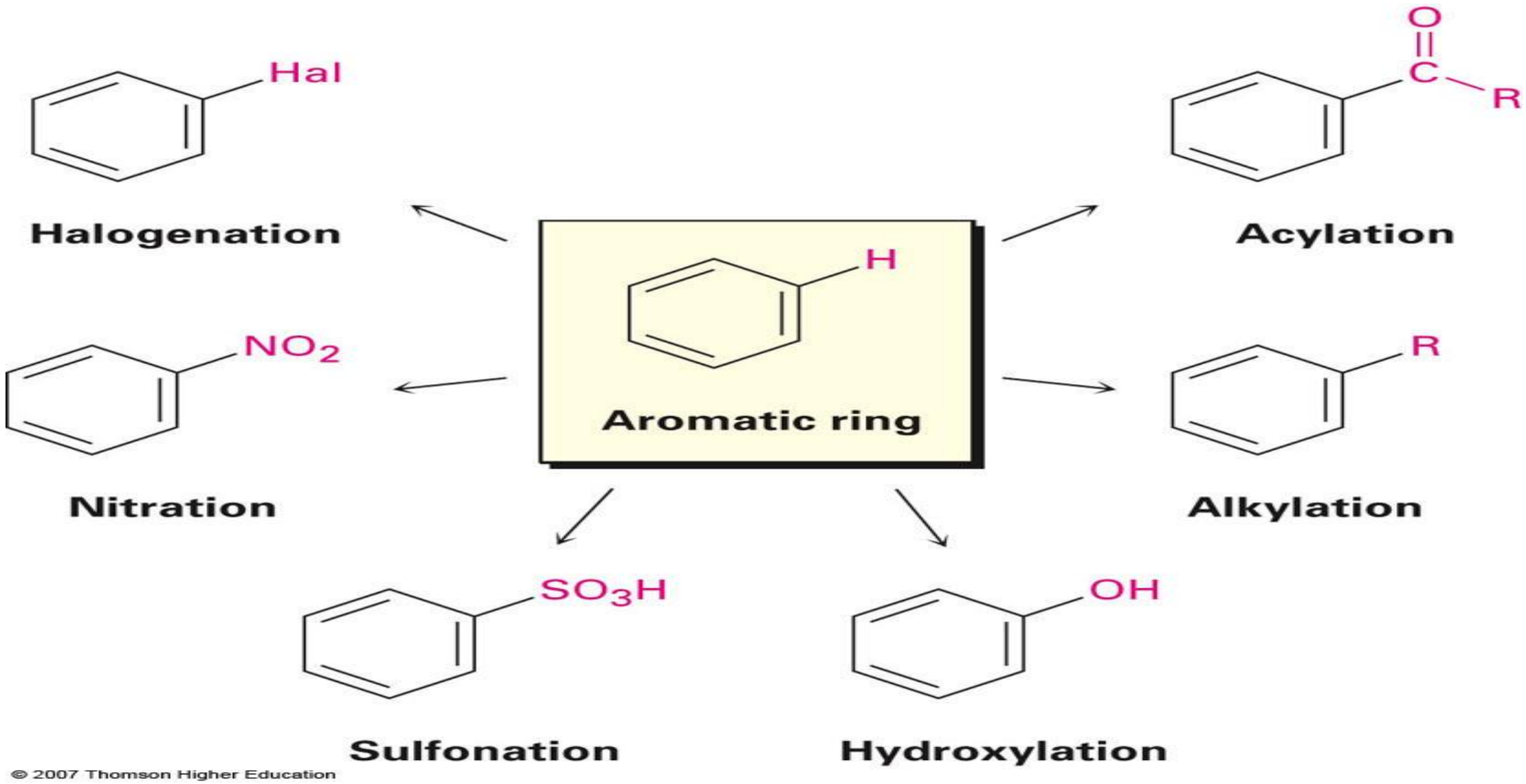
Reactions of Benzene and Its Derivatives

- Benzene **does not** undergo electrophilic addition
- It undergoes electrophilic aromatic substitution maintaining the aromatic core
- Electrophilic aromatic substitution replaces a proton on benzene with another Nucleophile

Electrophilic Aromatic Substitution



General electrophilic Aromatic Substitution rn of benzene:

$$E-NU \longrightarrow E^{+} + NU^{-}$$

Benzene Eg: E^{+} Electrophilic Aromatic Sub. product.

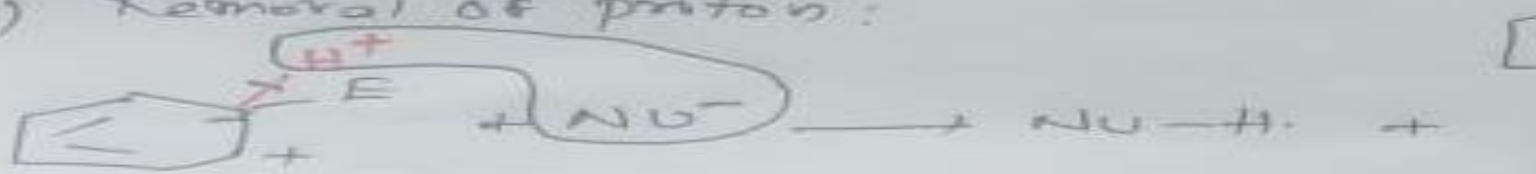
Mechanism:

i) Generation of electrophile.

$$E-NU \longrightarrow \underset{\text{electrophile}}{E^{+}} + NU^{-} \longrightarrow \text{Nucleophile}.$$

ii) Formation of Stable Carbocation.

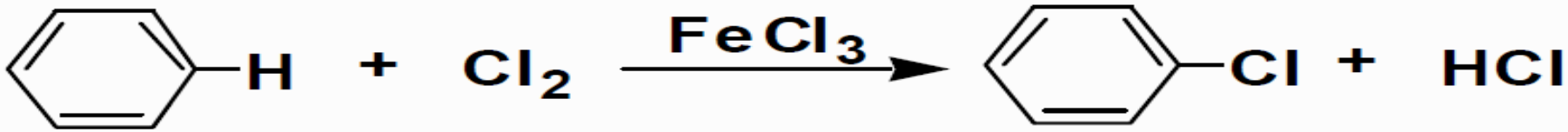
iii) Removal of proton:



Reactions of Benzene

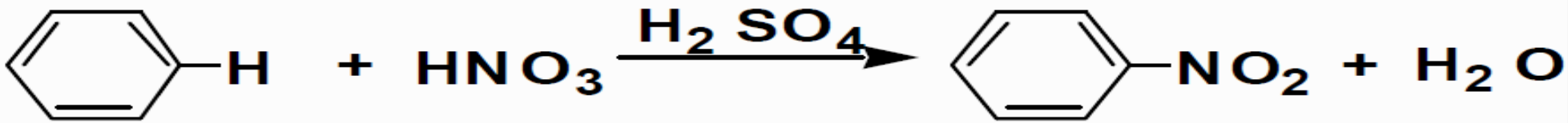
The most characteristic reaction of aromatic compounds is substitution at a ring carbon:

Halogenation:



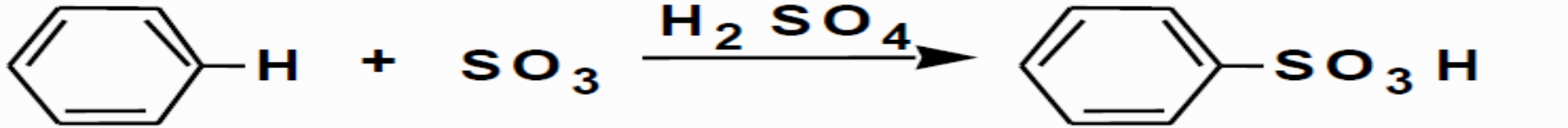
Chlorobenzene

Nitration:



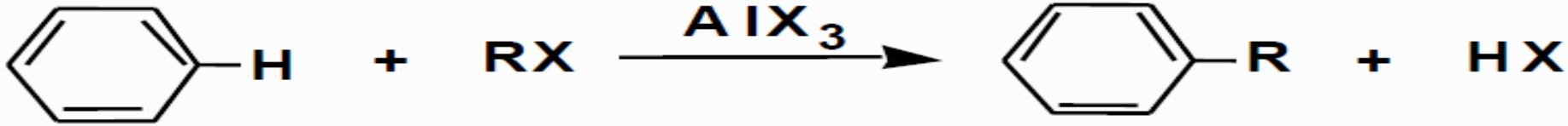
Nitrobenzene

Sulfonation:



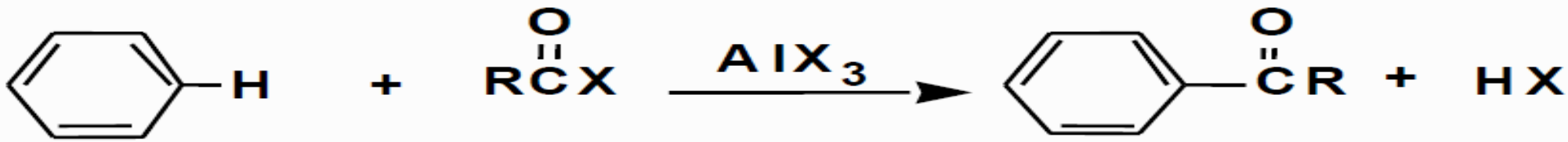
Benzenesulfonic acid

Alkylation:



An alkylbenzene

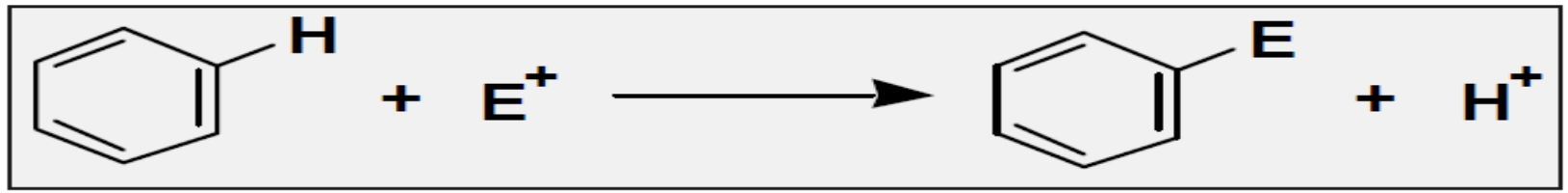
Acylation:



An acylbenzene

Electrophilic Aromatic Substitution

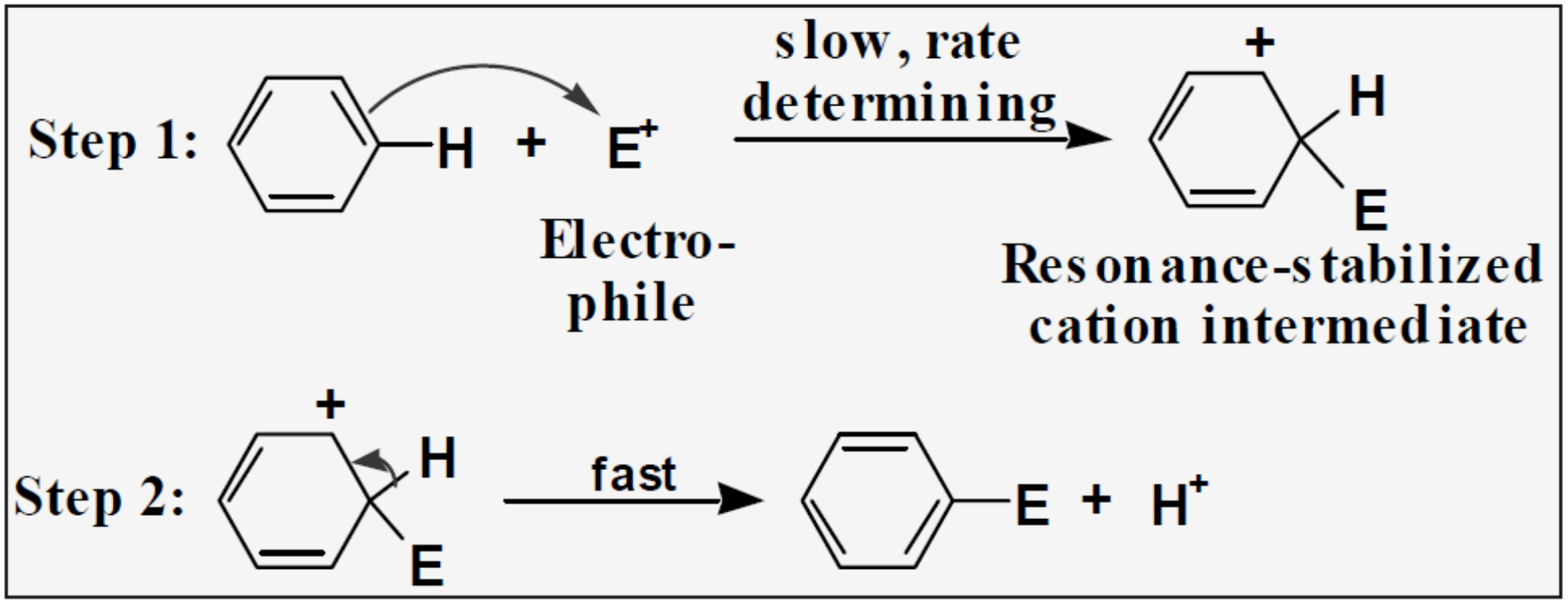
- Electrophilic aromatic substitution: a reaction in which a hydrogen atom of an aromatic ring is replaced by an electrophile



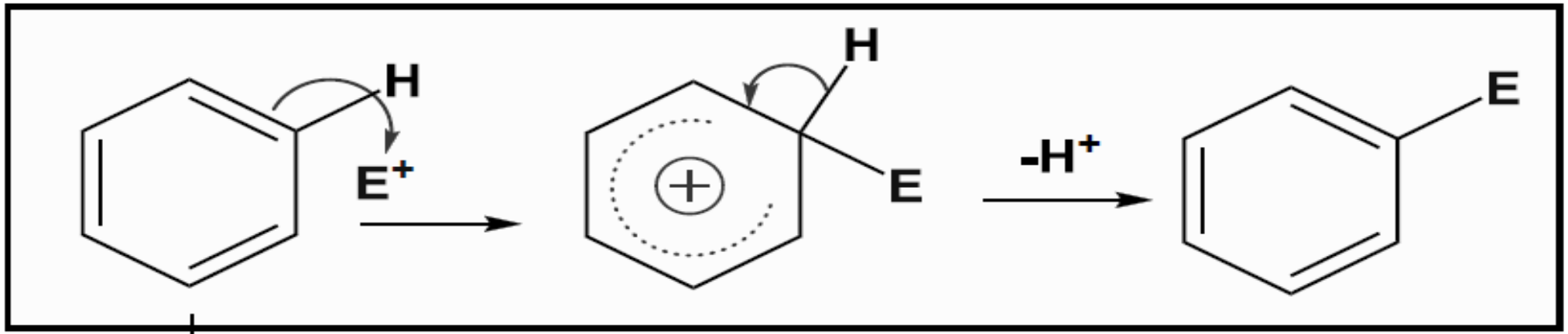
- In this section:
  - several common types of electrophiles
  - how each is generated
  - the mechanism by which each replaces hydrogen

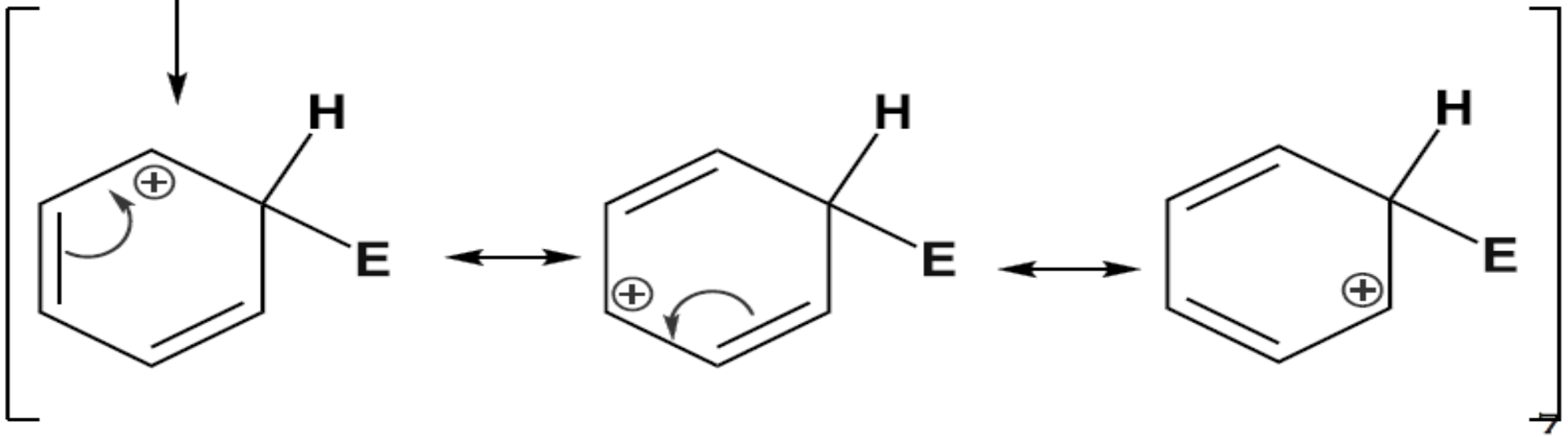
EAS: General Mechanism

- A general mechanism



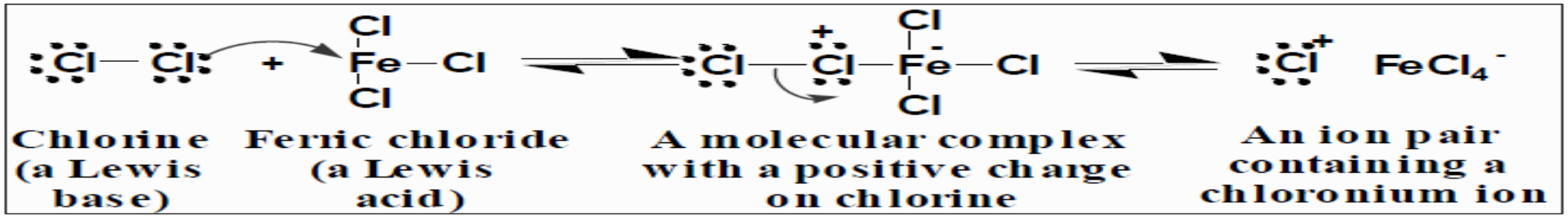
Electrophilic Aromatic Substitution (EAS)



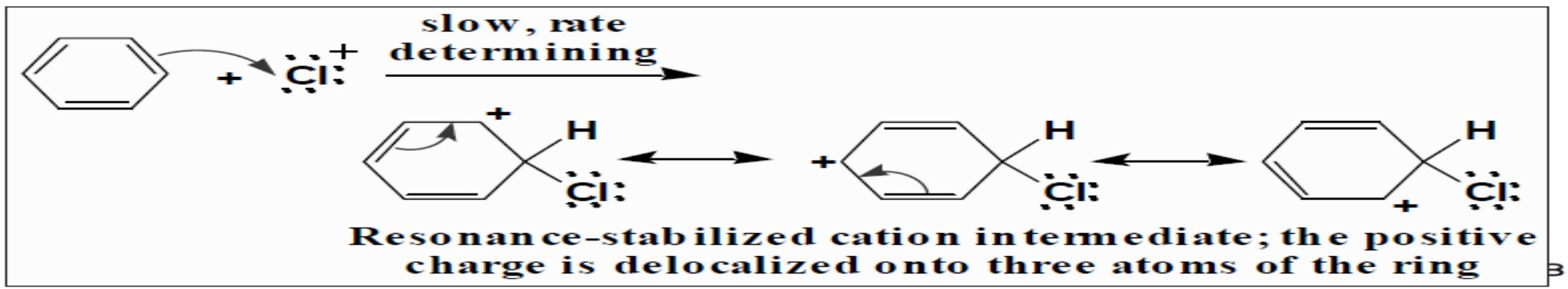


Chlorination

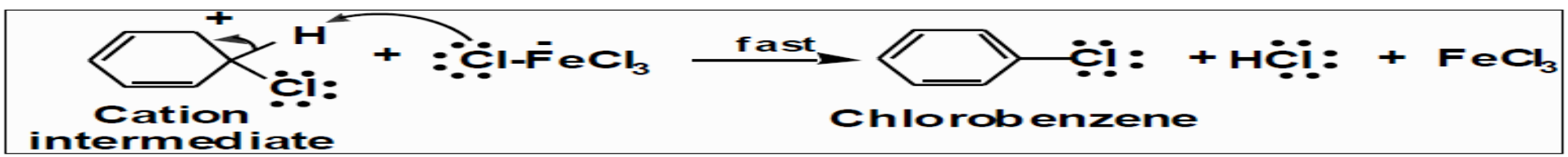
Step 1: formation of a chloronium ion



Step 2: attack of the chloronium ion on the ring



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



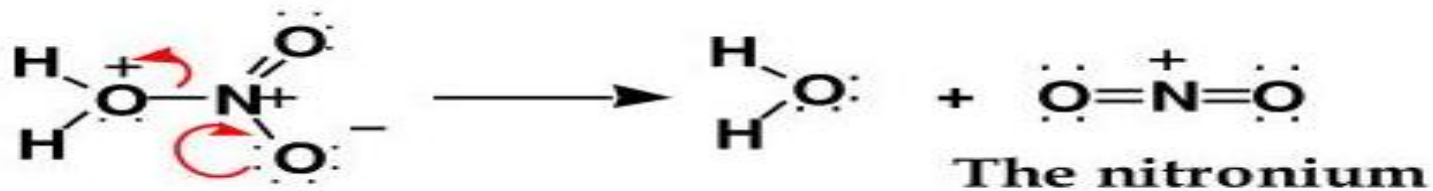
Nitration:

Generation of the nitronium ion, NO_2^+ :

- **Step 1: proton transfer to nitric acid.**

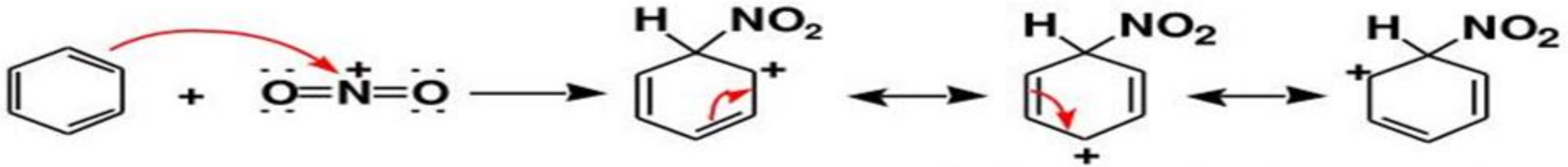
Sulfuric acid — Nitric acid — Conjugate acid of nitric acid

- **Step 2: loss of H_2O gives the nitronium ion, a very strong electrophile.**

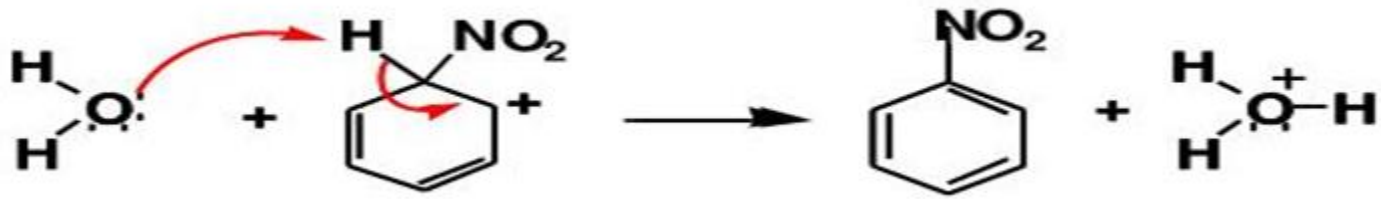


The nitronium ion

Step : attack of the nitronium ion (an electrophile) on the aromatic ring (a nucleophile).

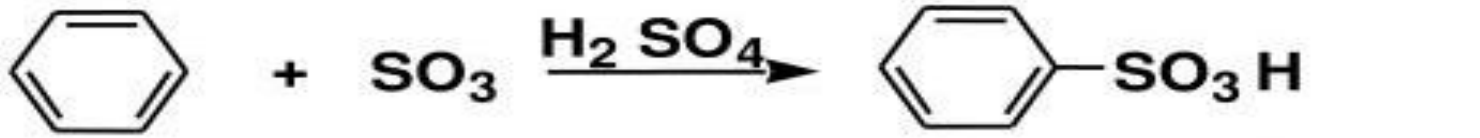


Step : proton transfer regenerates the aromatic ring.



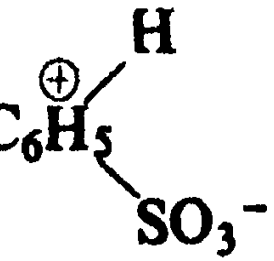
HSO4 - +H H2SO4

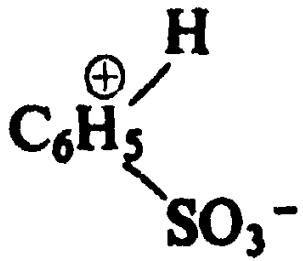
Sulphonation of benzene



Benzene — Benzenesulfonic acid

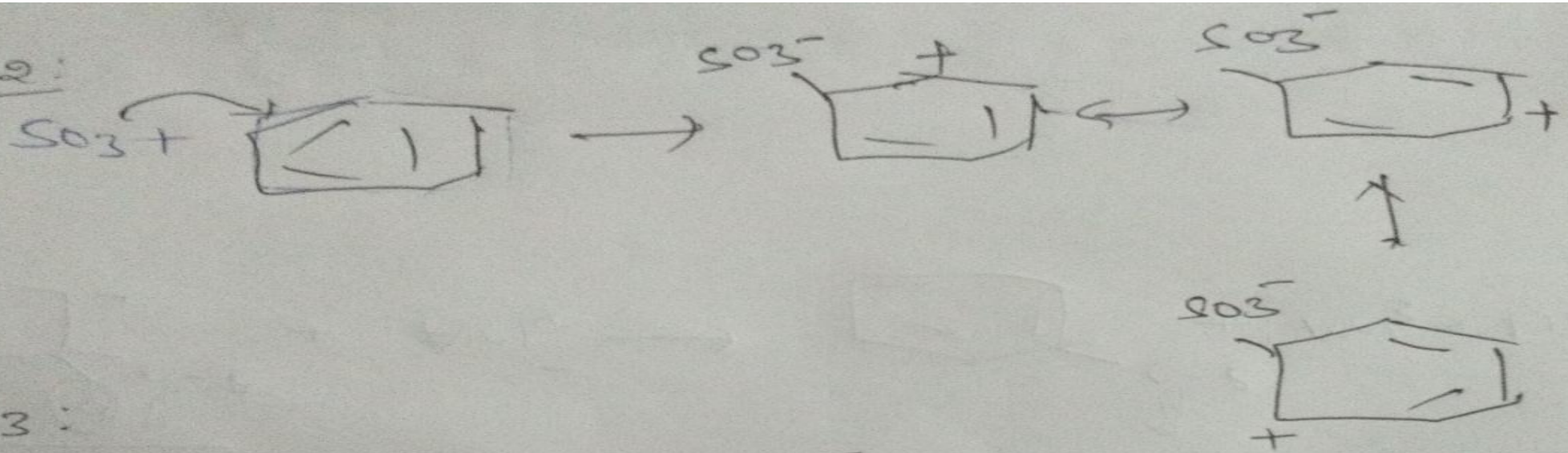
(1) $2H_2SO_4 \rightleftharpoons H_3O^+ + HSO_4^- + SO_3$

(2) $SO_3 + C_6H_6 \rightleftharpoons$  *Slow*

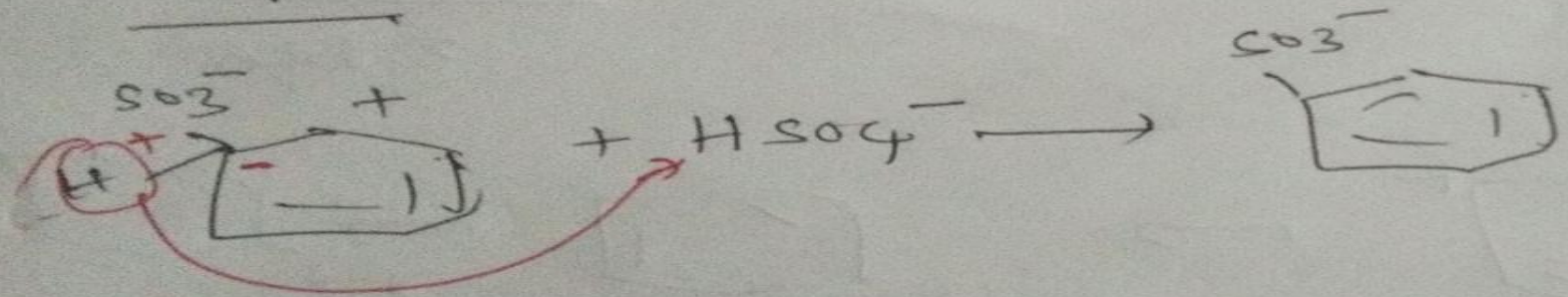
(3)  $+ HSO_4^- \rightleftharpoons C_6H_5SO_3^- + H_2SO_4$ *Fast*

(4) $C_6H_5SO_3^- + H_3O^+ \rightleftharpoons C_6H_5SO_3H + H_2O$ *Equilibrium far to the left*

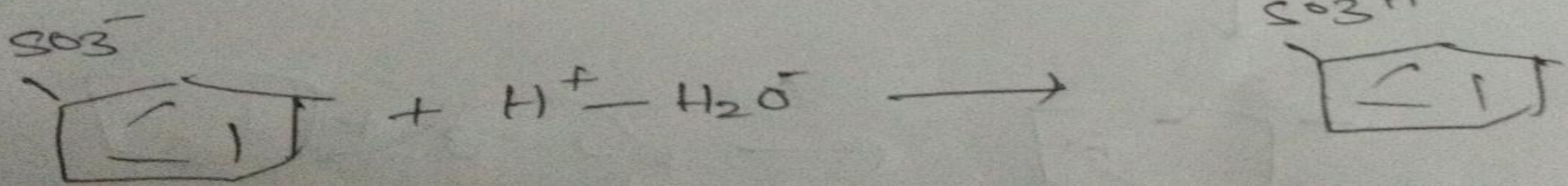
Step 2:



Step 3:

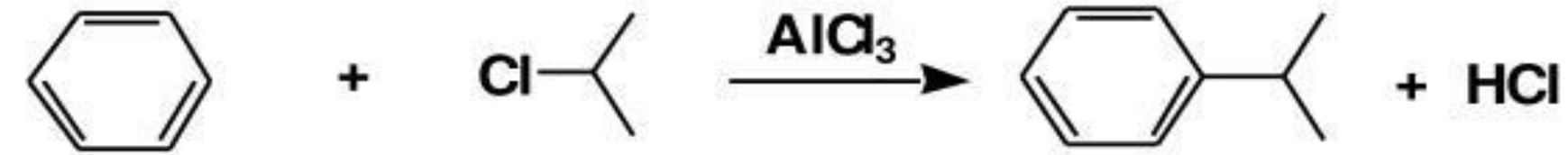


Step 4:



C. Friedel-Crafts Alkylation of Benzene

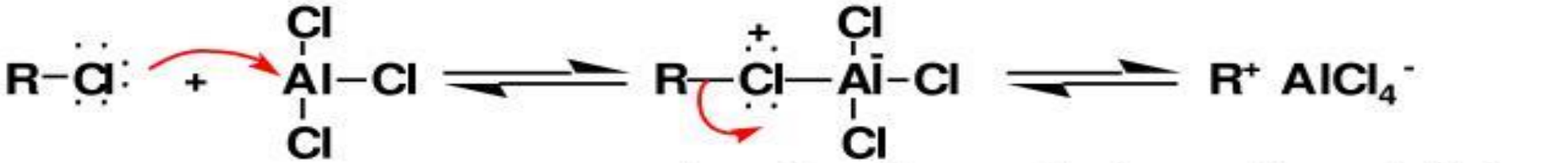
- **Friedel-Crafts alkylation forms a new C-C bond between an aromatic ring and an alkyl group.**



Benzene 2-Chloropropane (Isopropyl chloride) Cumene (Isopropylbenzene)

Friedel-Crafts Alkylation

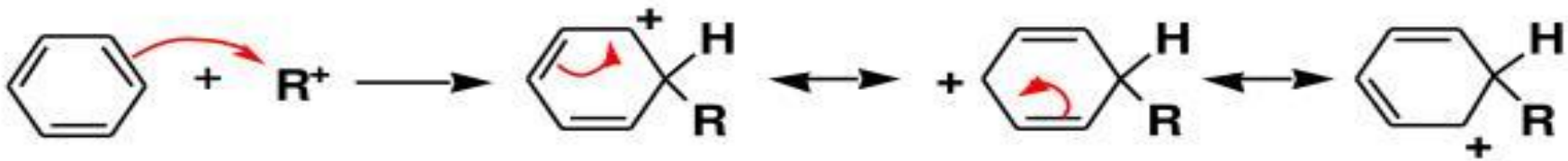
Step 1: formation of an alkyl cation as an ion pair.



A molecular complex

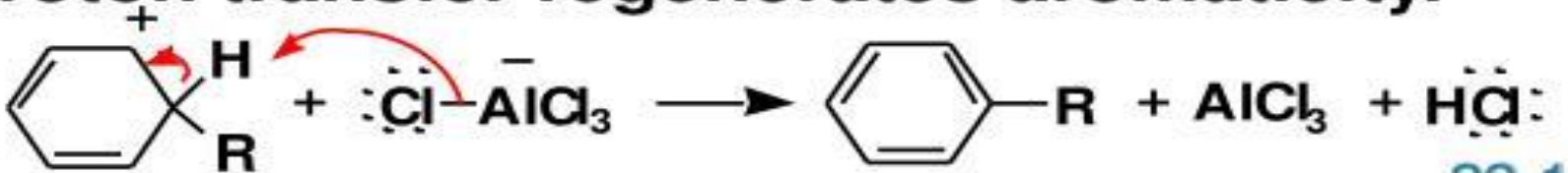
An ion pair containing a carbocation

Step 2: attack of the alkyl cation on the ring.



A resonance-stabilized cation

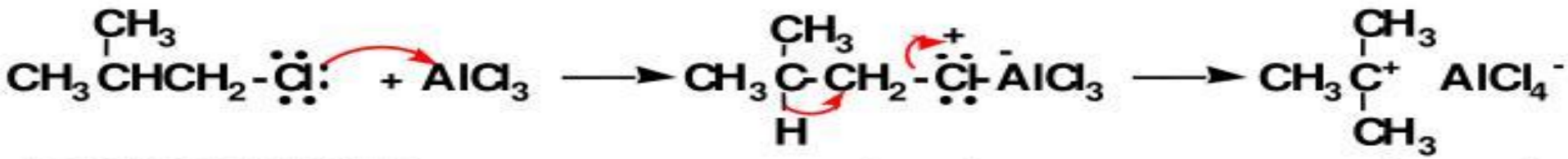
Step 3: proton transfer regenerates aromaticity.



Limitations on Friedel-Crafts Alkylation

- There are three major limitations on Friedel-Crafts alkylations.
  1. carbocation rearrangements are common.

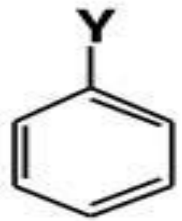
Benzene | Isobutyl chloride | *tert*-Butylbenzene



Isobutyl chloride | a molecular complex | an ion pair

Limitations on Friedel-Crafts Alkylation

2. F-C alkylation fails on benzene rings bearing one or more of these strongly electron-withdrawing groups.



$$\text{+ RX} \xrightarrow{AlCl_3} \text{No reaction}$$

When Y Equals Any of These Groups, the Benzene Ring Does Not Undergo Friedel-Crafts Alkylation

$-\overset{O}{\overset{\|}{C}}H$	$-\overset{O}{\overset{\|}{C}}R$	$-\overset{O}{\overset{\|}{C}}OH$	$-\overset{O}{\overset{\|}{C}}OR$	$-\overset{O}{\overset{\|}{C}}NH_2$
$-SO_3H$	$-C\equiv N$	$-NO_2$	$-NR_3^+$	
$-CF_3$	$-CCl_3$			

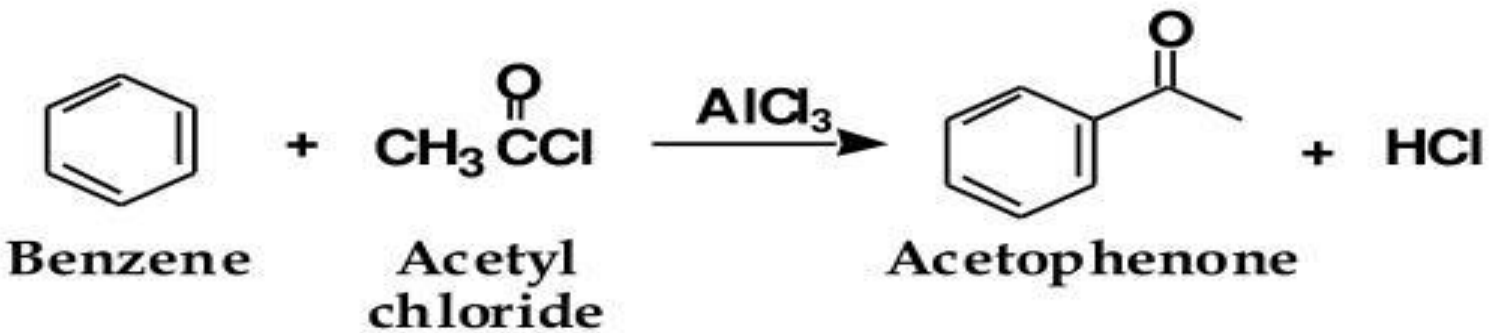
Limitations on Friedel-Crafts Alkylation

- **3. Polyalkylation: An alkyl group added to the ring activates the ring and further alkylation occurs.**

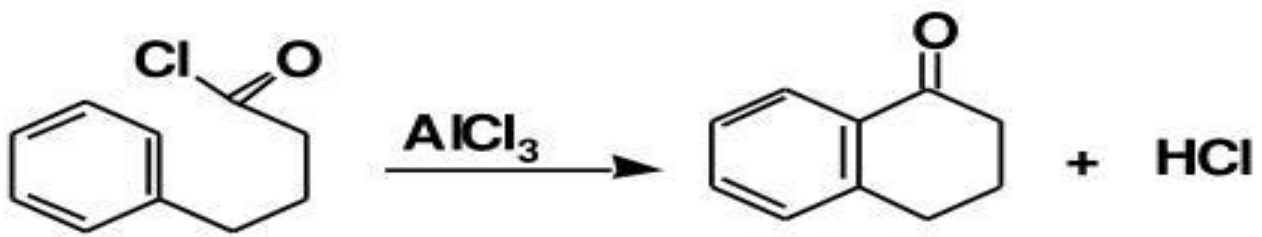
- **Limitations 1 & 3 do not apply to Friedel-Crafts Acylation reactions.**

Friedel-Crafts Acylation of Benzene

- **Friedel-Crafts acylation forms a new C-C bond between a benzene ring and an acyl group.**



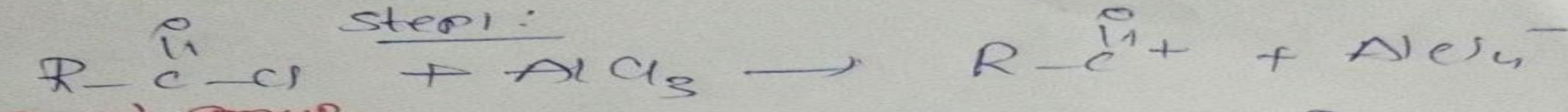
Benzene + Acetyl chloride → Acetophenone + HCl



4-Phenylbutanoyl chloride → α-Tetralone + HCl

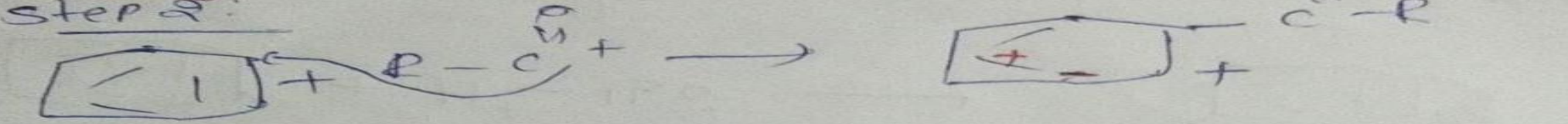
Mechanism:

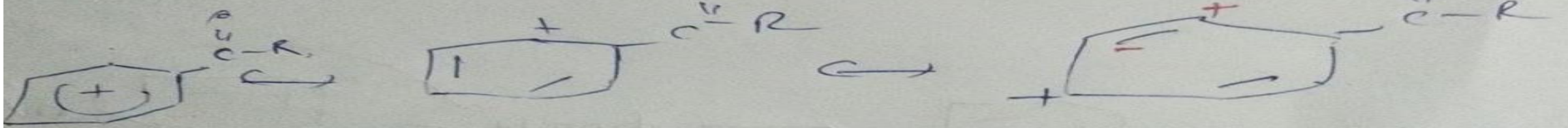
Step 1:



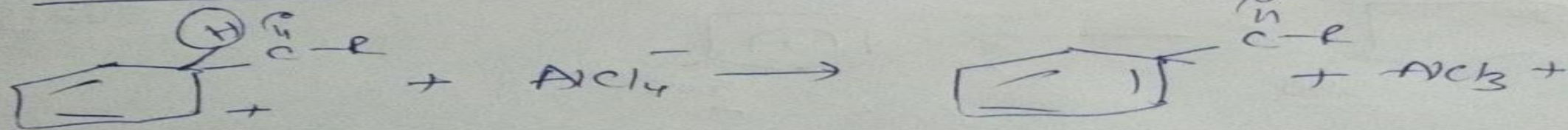
*Acyl group.

Step 2:

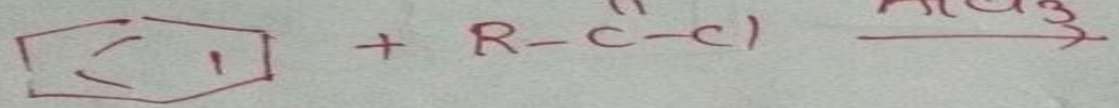




Step 3.

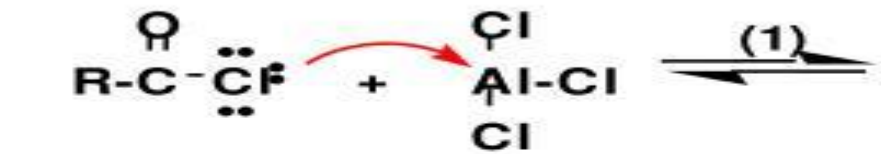


Reaction:



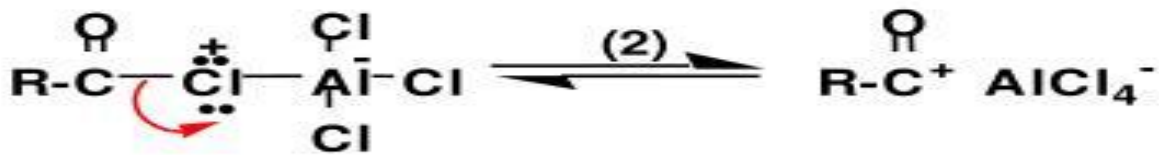
Friedel-Crafts Acylation

- The electrophile is an acylium ion.



An acyl chloride

Aluminum chloride

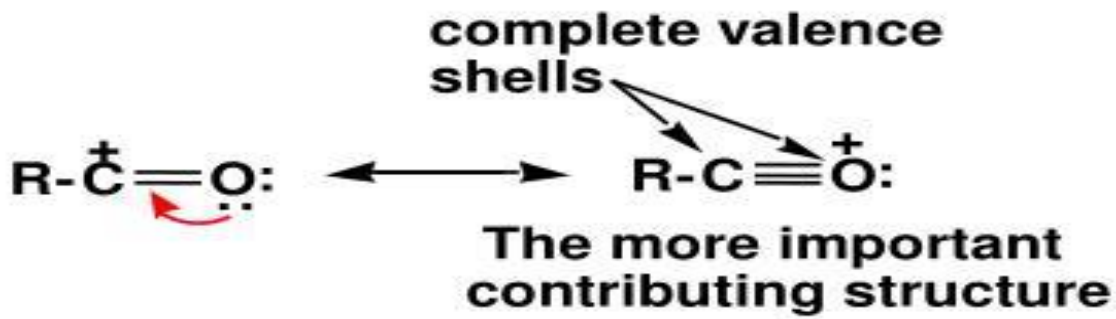


A molecular complex with a positive charge charge on chlorine

A n ion pair containing an acylium ion

Friedel-Crafts Acylation

- an acylium ion is a resonance hybrid of two major contributing structures.



- F-C acylations are free of two major limitation of F-C alkylations; acylium ions do not rearrange nor do they polyacylate.