

# ***ELECTROPHILIC AROMATIC SUBSTITUTION II***

*Department of Pharmaceutical Chemistry*

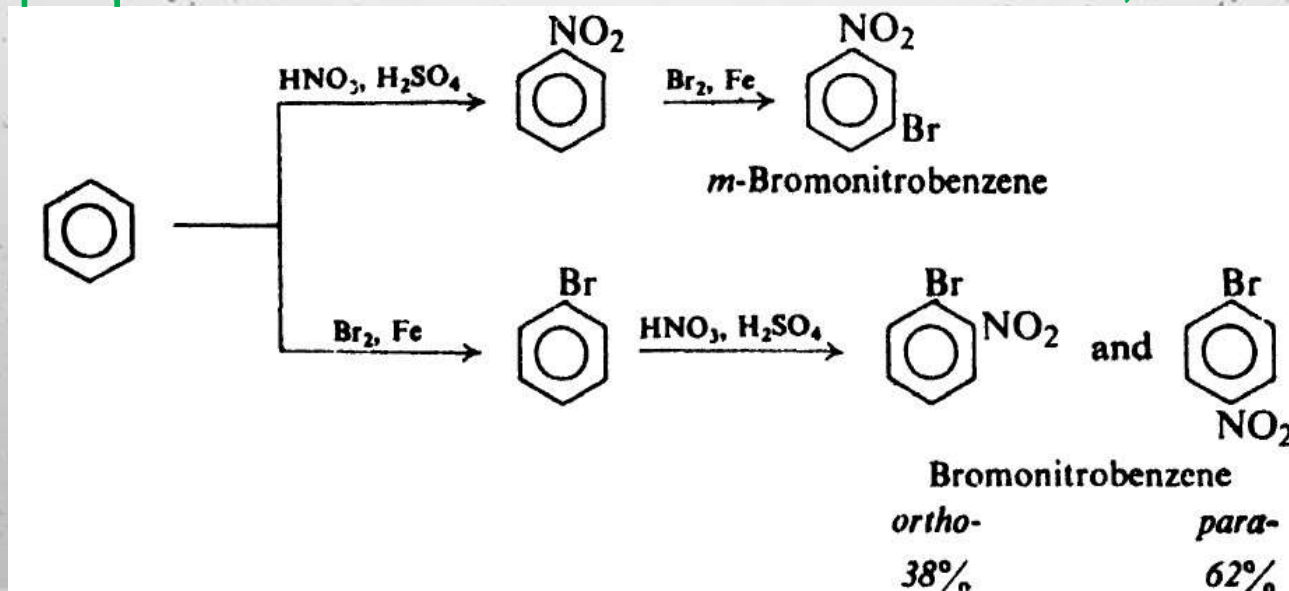
*Dr. Husam Hamza*

# Orientation and synthesis

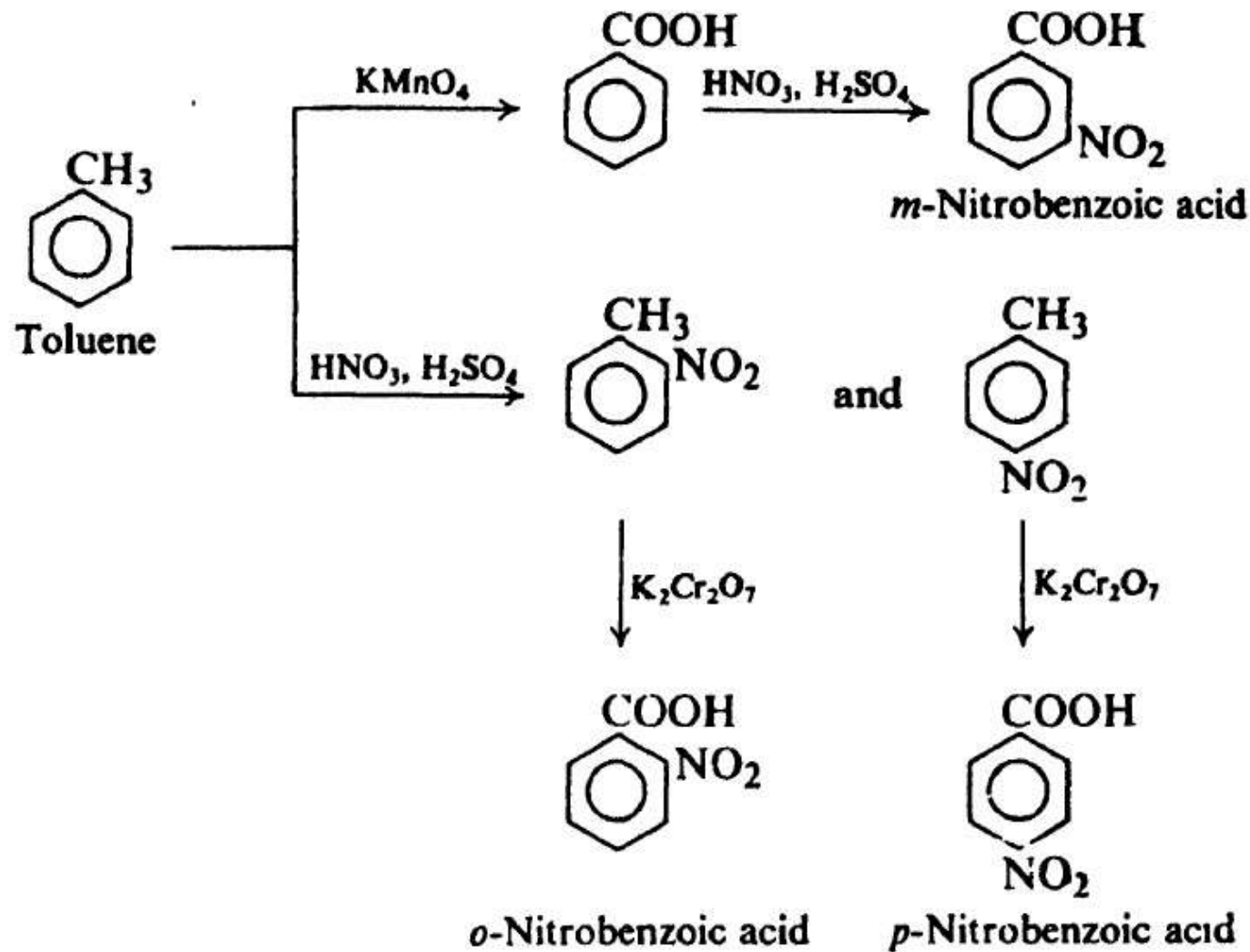
A laboratory synthesis is generally aimed at obtaining a single, pure compound. ➤

**A goal of aromatic synthesis is control of orientation:** the preparation, at will and from the same substrate, of a pure *ortho*, a pure *meta*, or a pure *para* isomer. ➤

First of all, *we must consider the order in which we introduce these various substituents into the ring.* In the preparation of the bromonitrobenzenes, for example: ➤



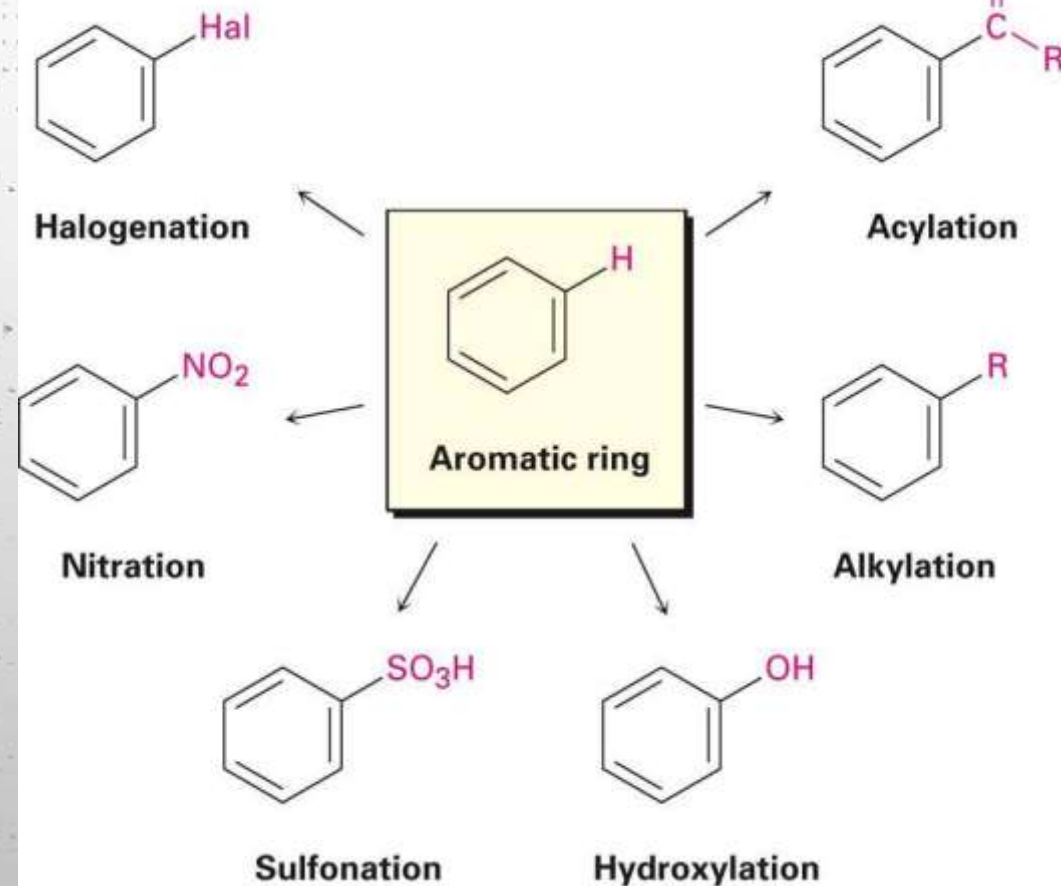
If our synthesis involves conversion of one group into another, For example, oxidation of a methyl group yields a carboxyl group. ➤



# Substitution Reactions of Benzene and Its Derivatives

Benzene is aromatic: a cyclic conjugated compound with  $6\pi$  electrons

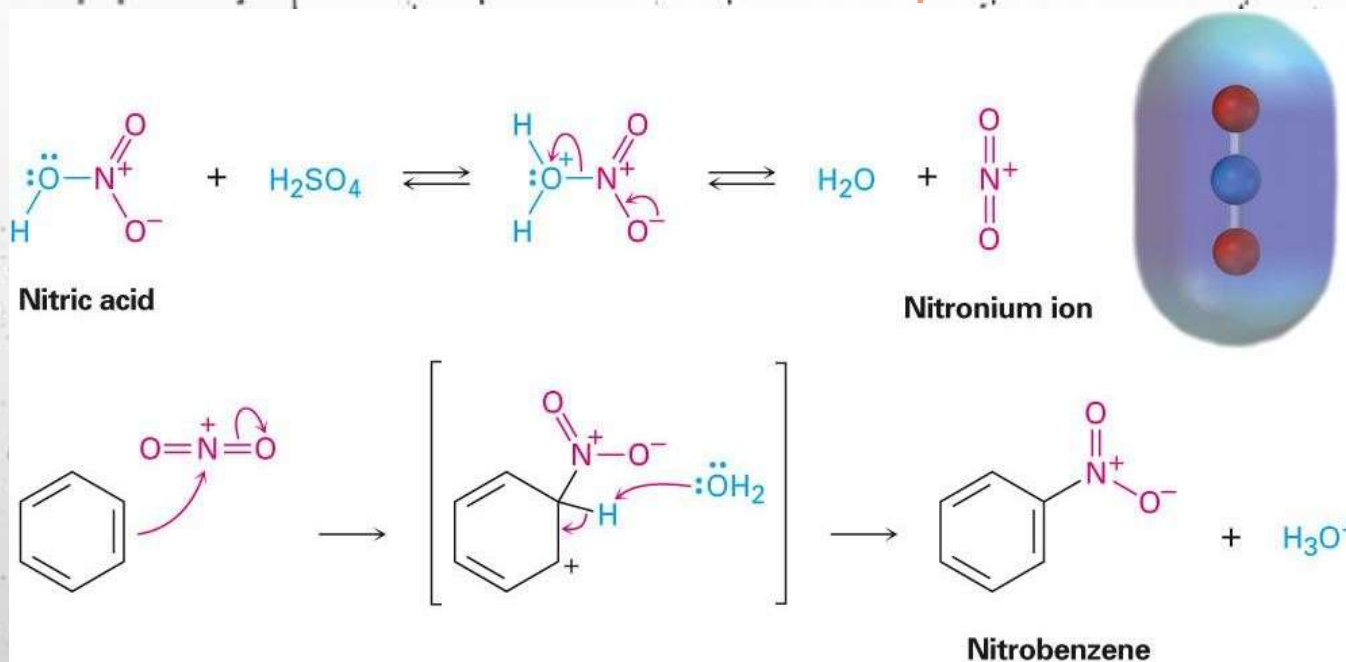
the of retentionthe to lead benzeneofReactions aromatic core



# Mechanism of nitration

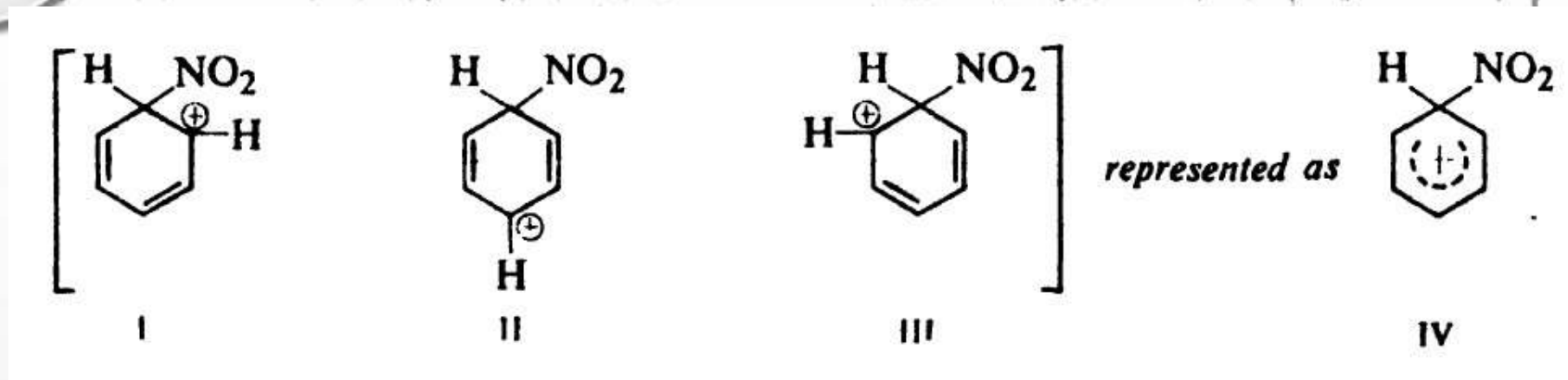
The combination of nitric acid and sulfuric acid produces  $\text{NO}_2^+$  (nitronium ion) ➤

The reaction with benzene produces nitrobenzene ➤

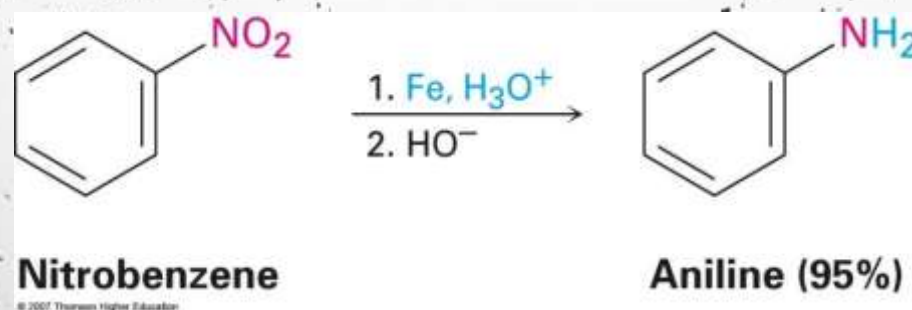


We ? ion carboniumthisof structuretheis whatJust ➤  
— find that we can represent

It by three structures (I, II, and III) that differ from each ➤  
positiveand bondsdoubleof positionin onlyother  
charge.

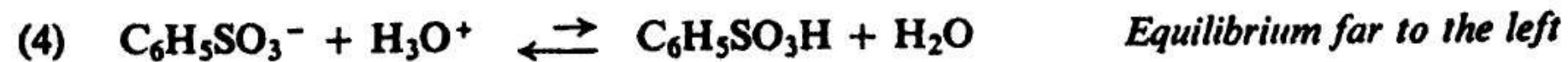
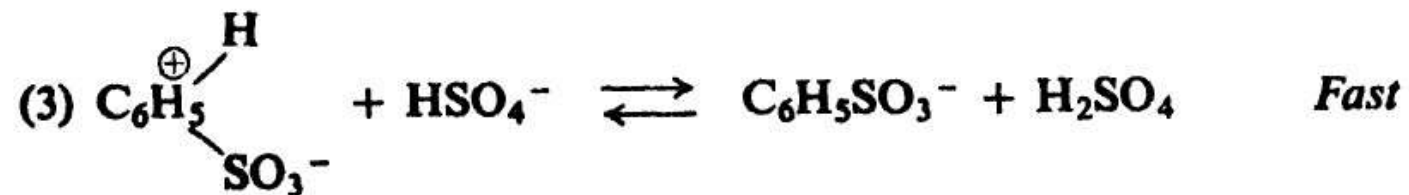
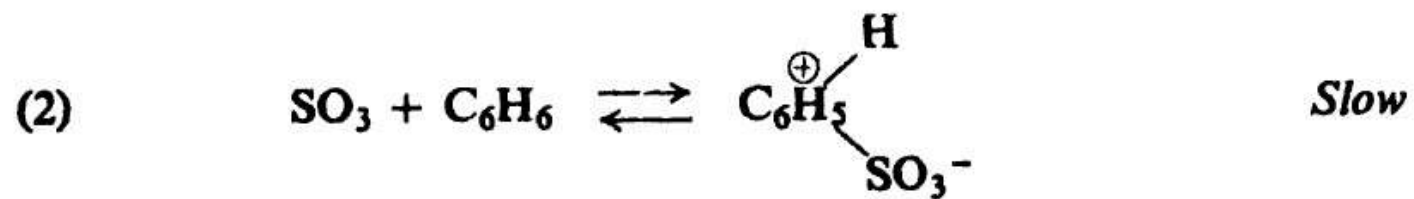
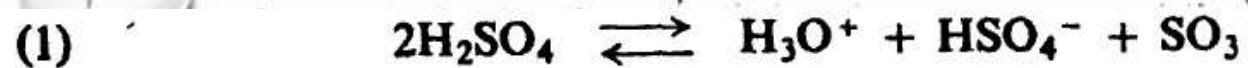


The Nitro group can be reduced to an Amino group if needed ➤



## Mechanism of sulfonation

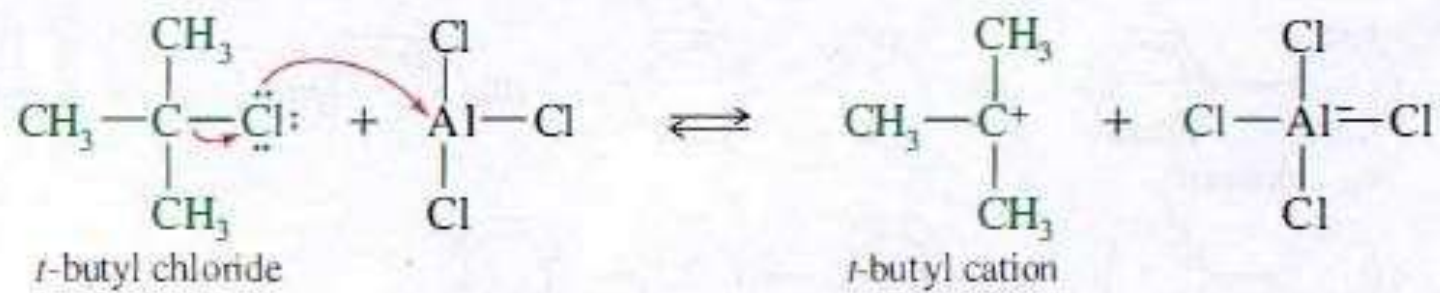
- Substitution of H by  $\text{SO}_3$  (sulfonation) ➤
- $\text{SO}_3$  and acid sulfuric mixture with Reaction ➤
- ("Fuming  $\text{H}_2\text{SO}_4$ )
- conjugate or trioxide sulfur species Reactive ➤
- acid



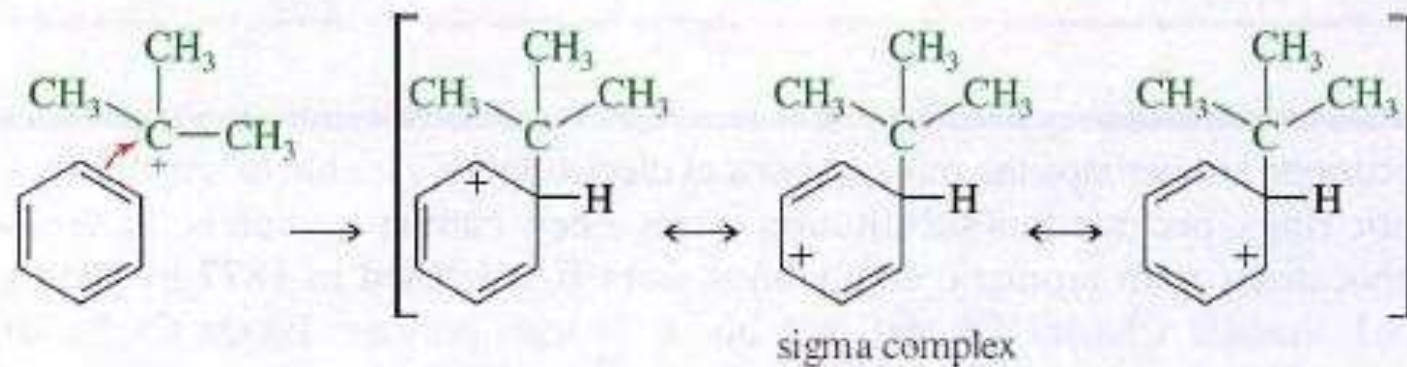
## Mechanism of Friedel-Crafts alkylation

- Friedel-Crafts alkylation is an electrophilic aromatic substitution in which a carbocation acts as the electrophile which an alkyl

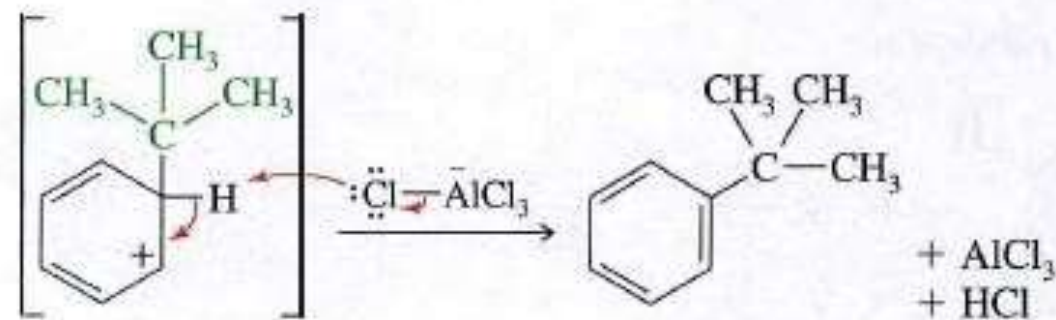
**Step 1:** Formation of a carbocation.



**Step 2:** Electrophilic attack forms a sigma complex.

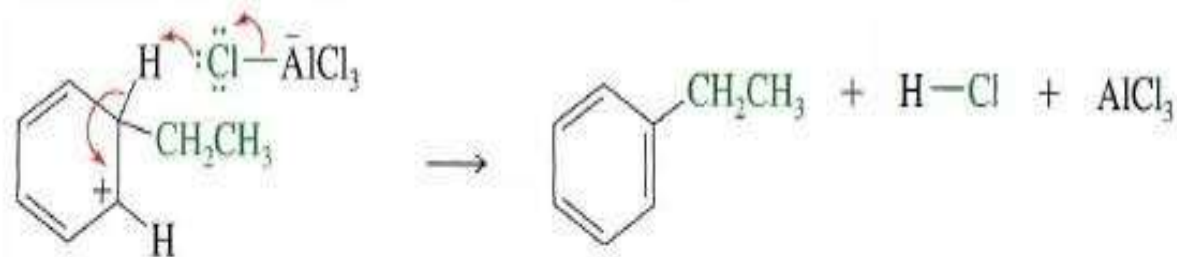
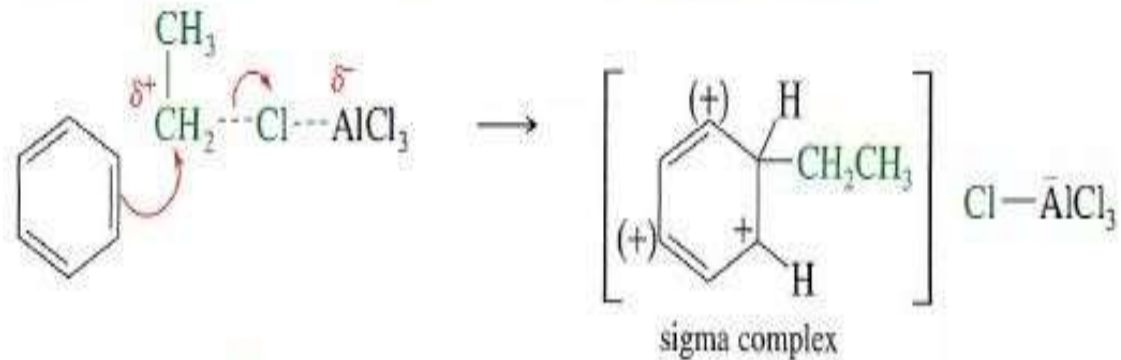
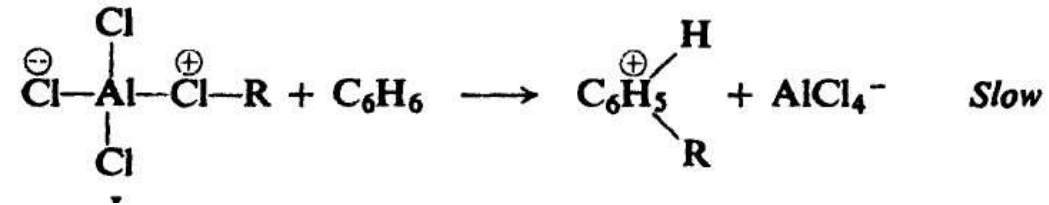


**Step 3:** Loss of a proton regenerates the aromatic ring and gives the alkylated product.





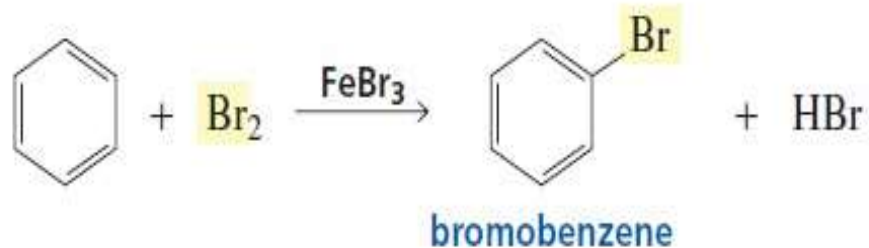
In certain cases, there is no free carbonium ion involved. Instead, the alkyl group is transferred -without a pair of electrons- directly to the aromatic ring from the polar complex, I, between  $\text{AlCl}_3$  and the alkyl halide:



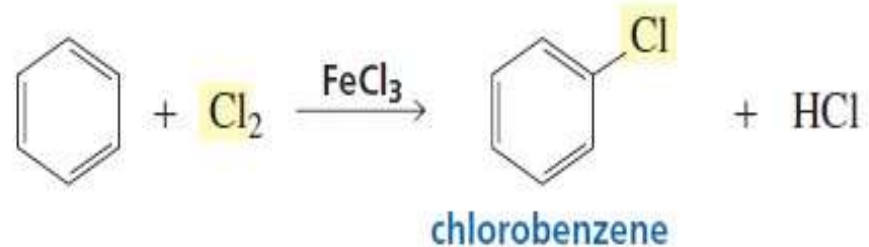
# Mechanism of halogenation

a requires benzene of chlorination or bromination The  
as ferric bromide or ferric chloride Lewis acid such

bromination

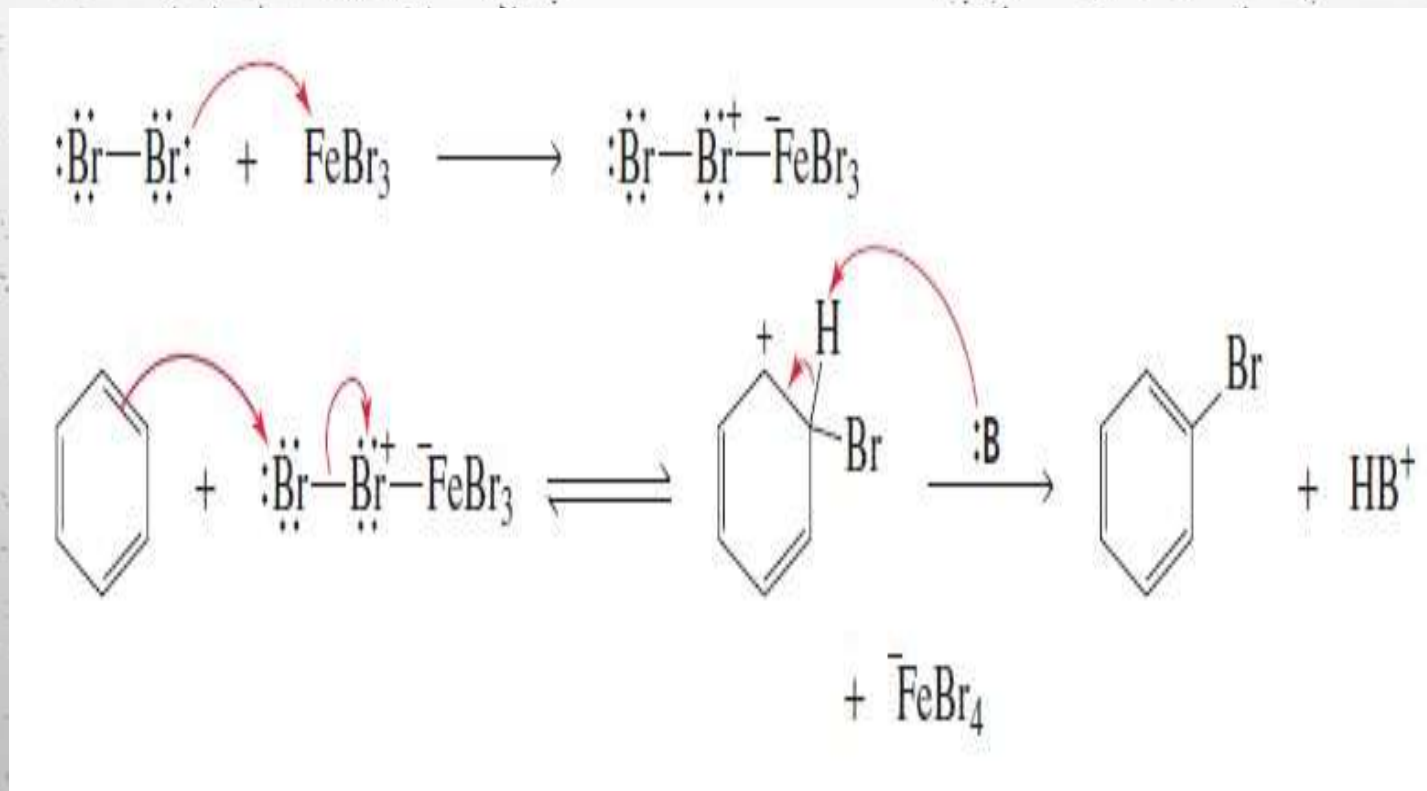


chlorination



In the first step of the bromination reaction, bromine  
donates a lone pair to the Lewis acid. This weakens the Br-  
Br bond, thereby providing the electrophile necessary for  
electrophilic aromatic substitution

reaction the from base a reaction, the of step last the in ➤  
 mixture  
 Removes a proton from the carbocation intermediate. ➤  
 The  
 is catalyst the that show equation following ➤  
 regenerated:

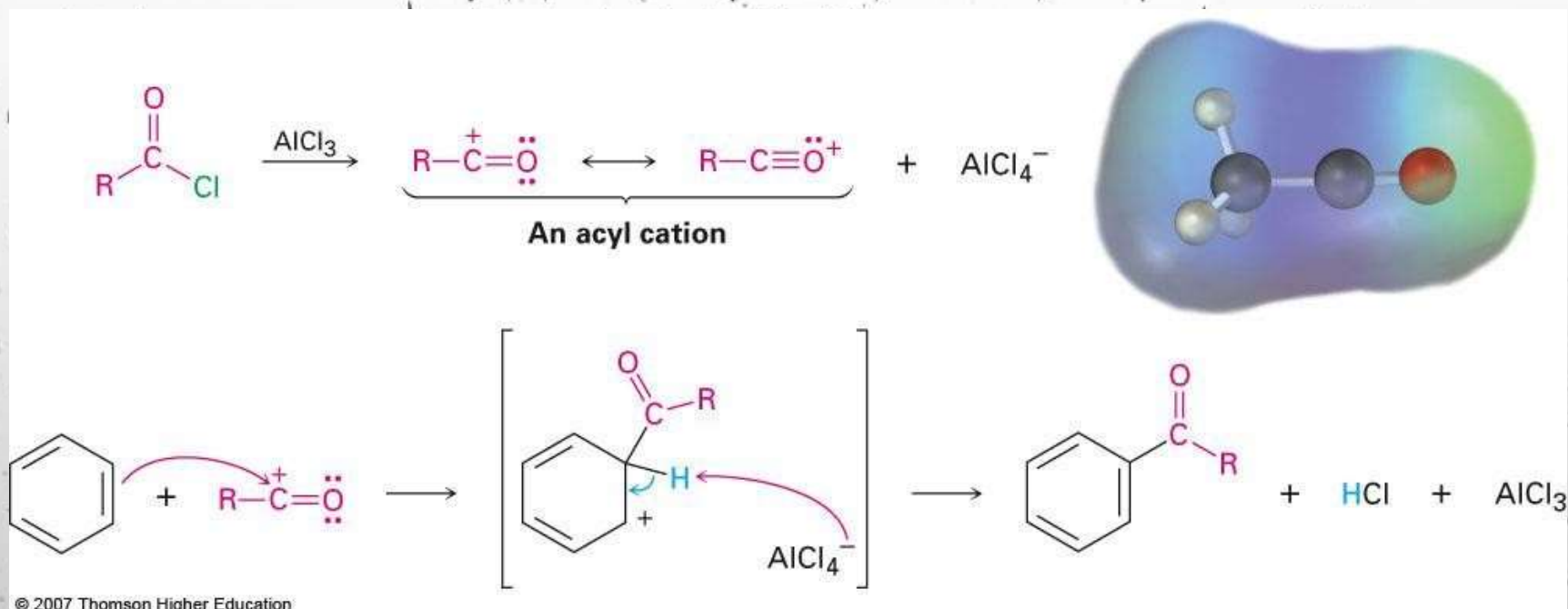


# MECHANISM OF FRIEDEL-CRAFTS ACYLATION

Similar to alkylation ➤

Reactive electrophile: resonance-stabilized acyl cation ➤

An acyl cation does not rearrange ➤



Can reduce carbonyl to get alkyl product ➤

