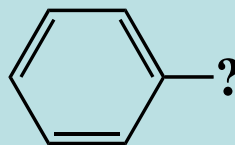


Chapter 15

Reactions of Aromatic Compounds

Benzenoid hydrocarbons are often called **arenes**. The symbol used to represent the **aryl group**



is **Ar**, so arene compounds are **ArH**
and substituted arenes are **ArX**.

Ar-
Aryl group

ArH
Generic arene

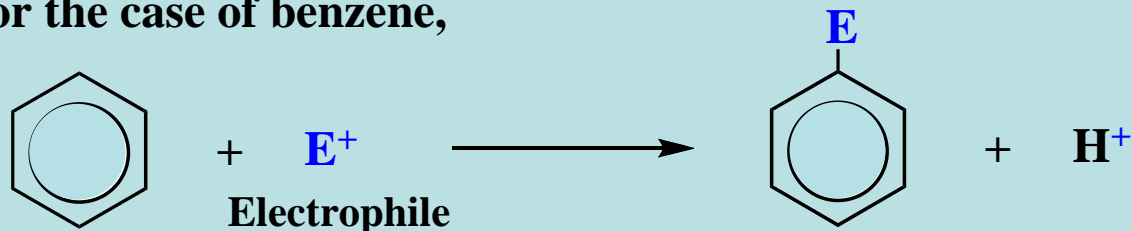
ArX
Substituted arene

Electrophilic Aromatic Substitution

This most characteristic reaction of arenes may be used to introduce a variety of substituents into the structure:

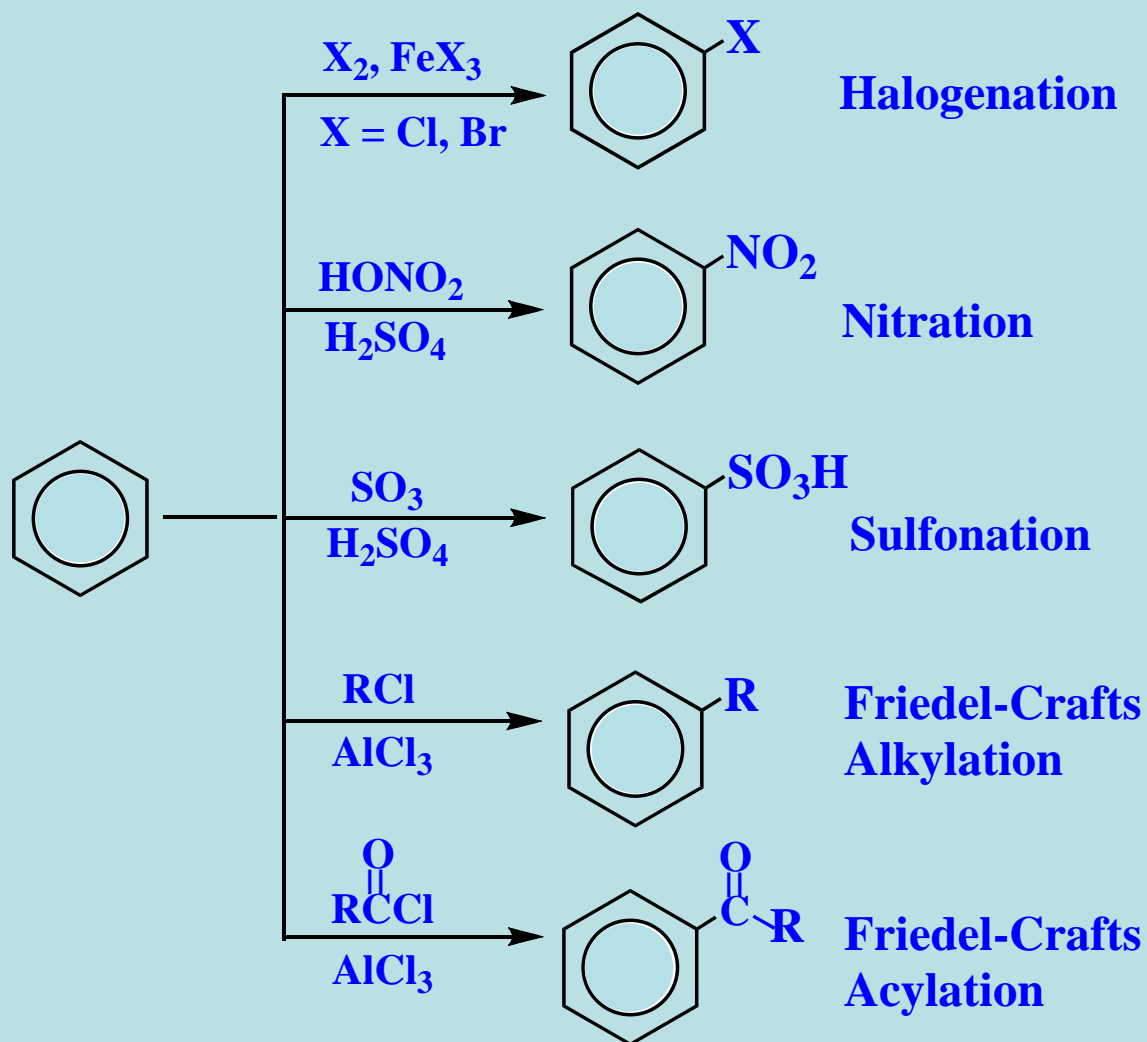


For the case of benzene,



Note: In these reactions, an electrophile **substitutes** for an H on the aromatic ring. This substitution contrasts with the **addition** of an electrophile to an alkene. In addition to an alkene, the **weaker π -bond is replaced by stronger σ -bonds, but this does not occur with an arene because the large stabilizing resonance energy of the aromatic ring would be lost.**

Examples of Electrophilic Aromatic Substitution Reactions

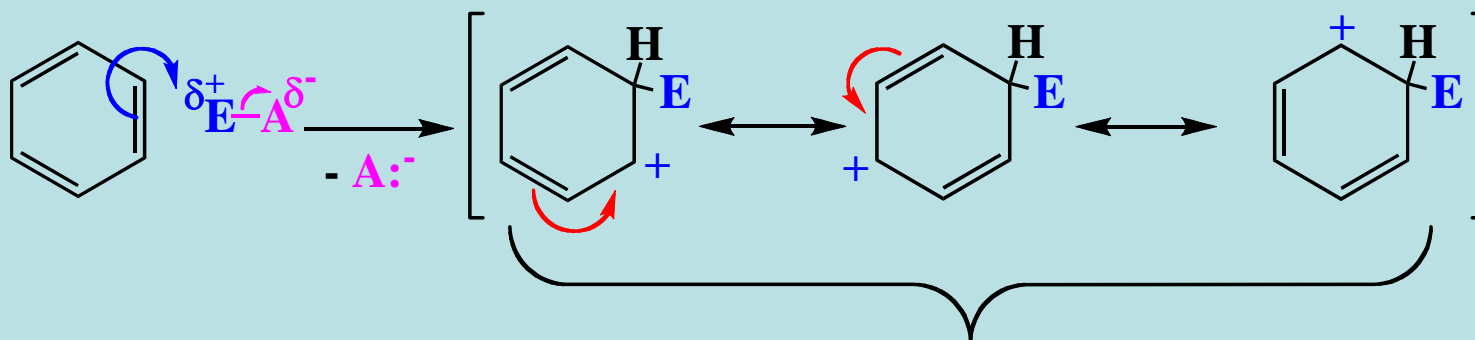


These reactions are commonly used synthetic procedures for modifying arenes. They proceed by a general mechanism initiated by addition of an electrophile E^+ to the aromatic π -system, forming a nonaromatic carbocation intermediate called an arenium ion.

Description of Mechanism Using Resonance Structures

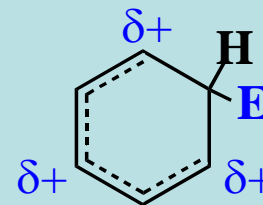
Step 1: Attack by the Electrophile

Two π -electrons form a σ -bond to the incoming electrophile yielding a delocalized carbocation intermediate called an **arenium ion**.

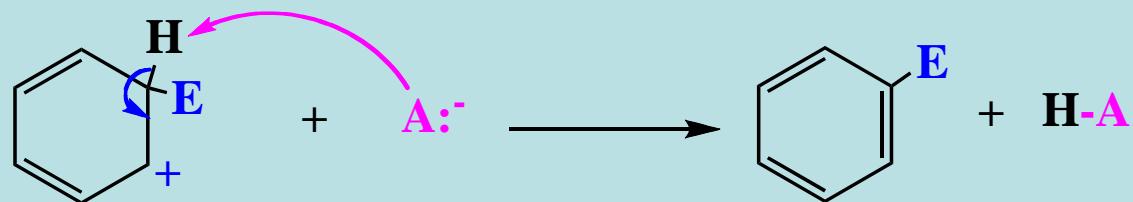


These resonance structures show the distribution of positive charge in the **arenium ion**.

The arenium ion is non-aromatic, but it is reasonably stable because of charge dispersal over the carbons *ortho* and *para* to the site of attachment of the electrophile.

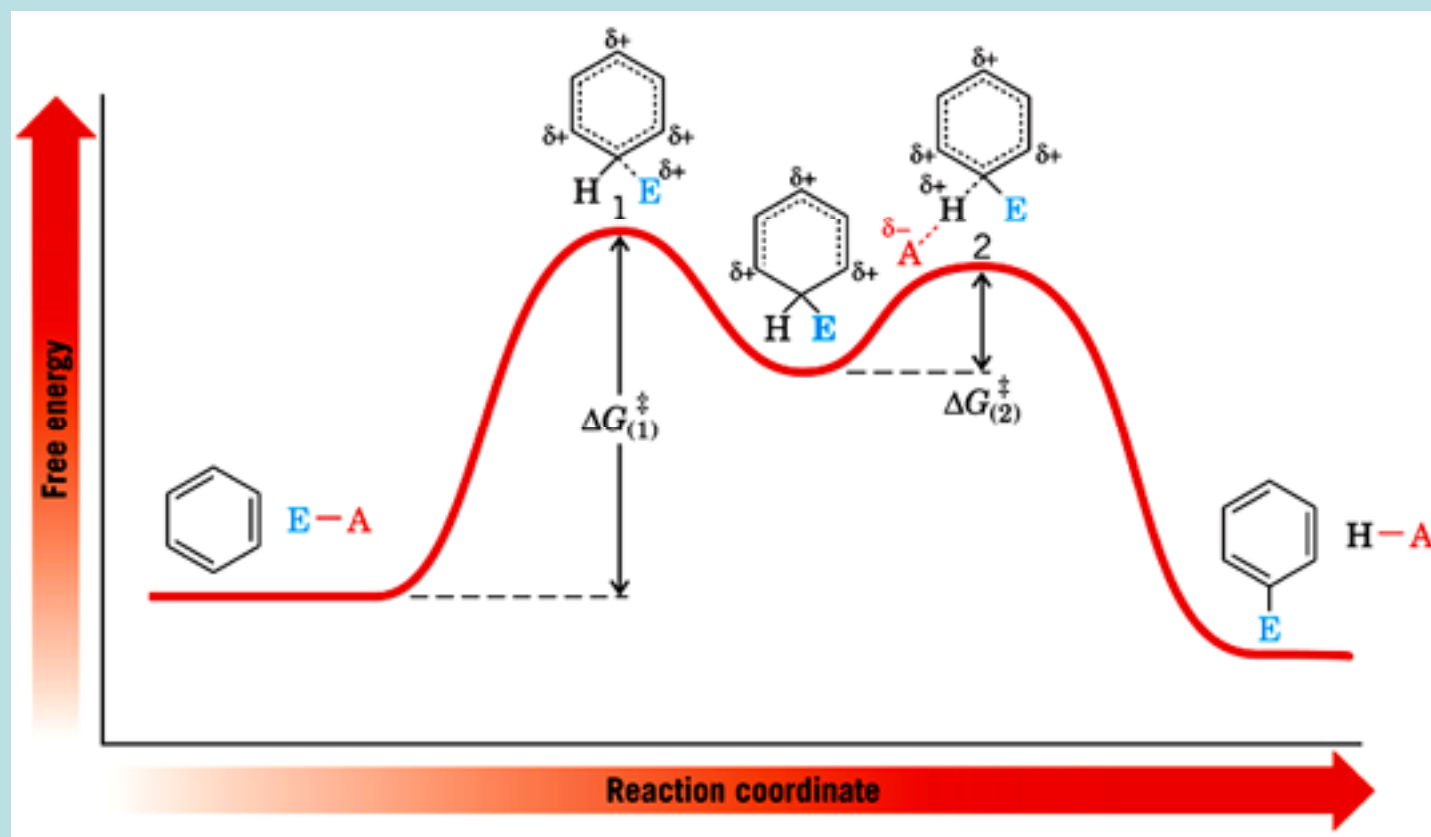


*Step 2: Deprotonation of the Arenium Ion
and Re-aromatization*



The Lewis base that attacks and removes the proton may, as shown, be the conjugate base of the electrophile or some other Lewis base that may be present.

Free-Energy Diagram for an Electrophilic Aromatic Substitution Reaction

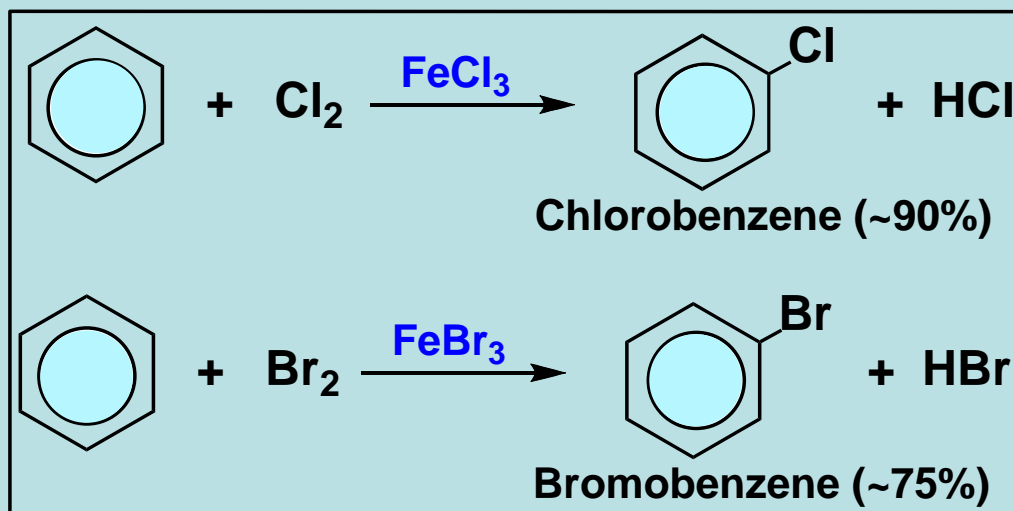


The much larger energy of activation requirement for Step 1 makes it the slow, **rate-determining step**.

Halogenation of Benzene

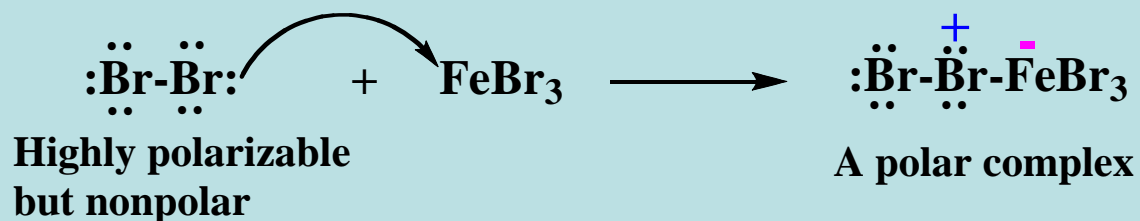
Halogenation of benzene and other arenes is one of the most common ways to **functionalize** aromatics. The reaction of benzene with Cl_2 or Br_2 requires catalysis by a **Lewis acid**. (Benzene, in contrast to alkenes, will not decolorize a solution of Br_2 in CCl_4 .)

Commonly employed Lewis acids are the iron halides, preformed or generated in situ:

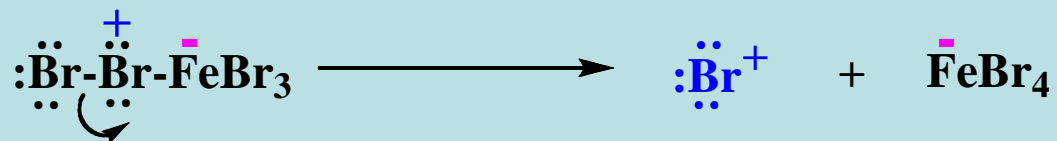


Role of the Catalyst

The Lewis acid complexes with and **polarizes** the X_2 producing a **more reactive electrophile** capable of disrupting the rather stable aromatic π -system in benzene and other arenes.

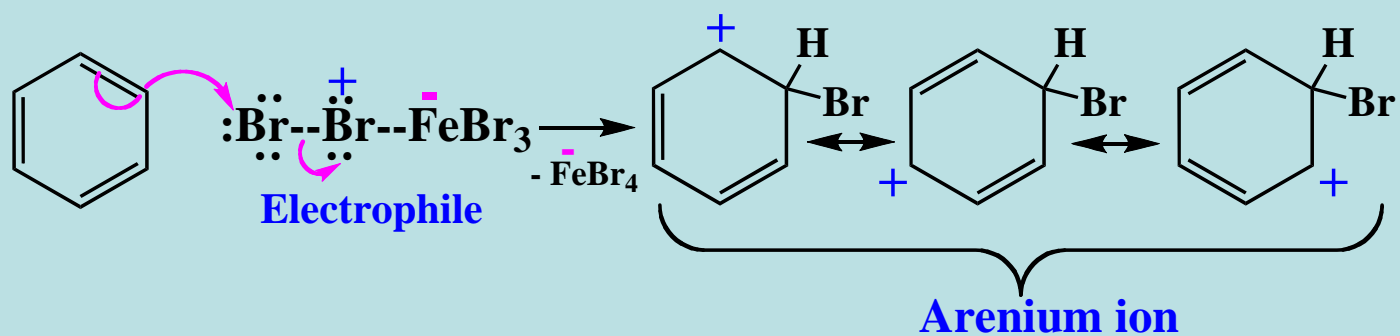


The complex transfers a positive bromide ion to the π -system of the arene. The effective electrophile in the bromination reaction is sometimes written as Br^+ , formed as shown below, but direct involvement of the complex is more likely.

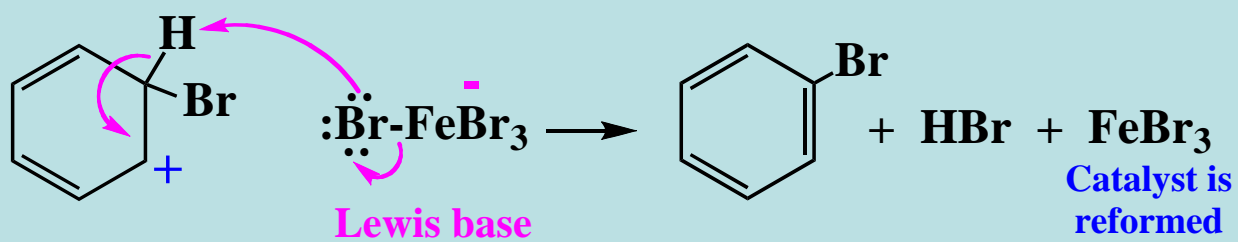


Mechanism:

Step 1: Electrophilic Attack



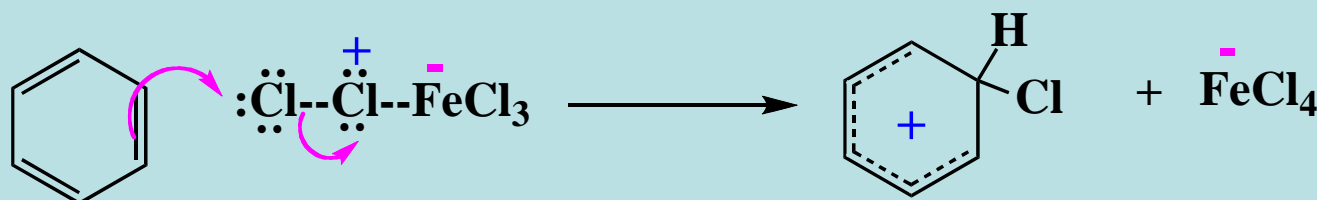
Step 2: Deprotonation and Re-aromatization



Chlorination of Benzene

Chlorination of benzene proceeds by a mechanism parallel with that for bromination, a complex of FeCl_3 and Cl_2 providing the **effective electrophile** $[\text{Cl}^+]$.

Step 1: Electrophilic Attack



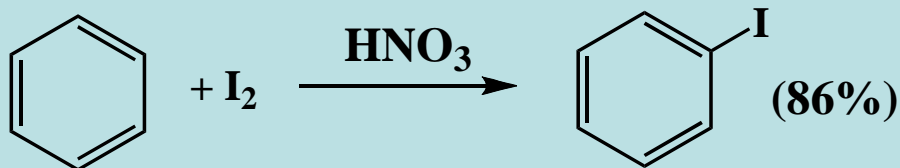
Fluorination of Benzene

Direct reaction of F_2 with benzene is very exothermic and proceeds explosively. Special procedures are required to carry out this reaction safely .

Fluorobenzene and other monofluoroarenes may be synthesized indirectly by way of aryl diazonium ions, which will be considered later.

Iodination of Benzene

Direct iodination of benzene with I_2 is a very slow reaction because of the unfavorable bond energy changes, but it can be achieved in the presence of an oxidizing agent.



Alternatively, iodobenzene and other iodoarenes may be prepared indirectly by way of aryl diazonium ions.

Reactivity in the Halogenation of Benzene

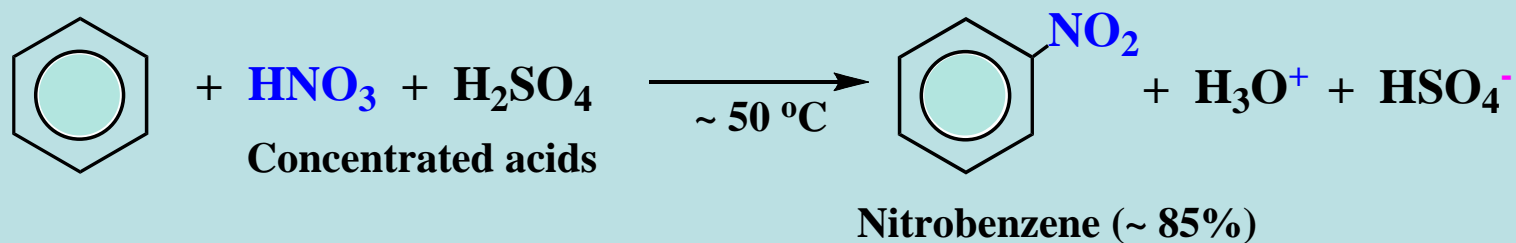
Fluorination > Chlorination > Bromination > Iodination

Explosively reactive

Very slow

Nitration of Benzene

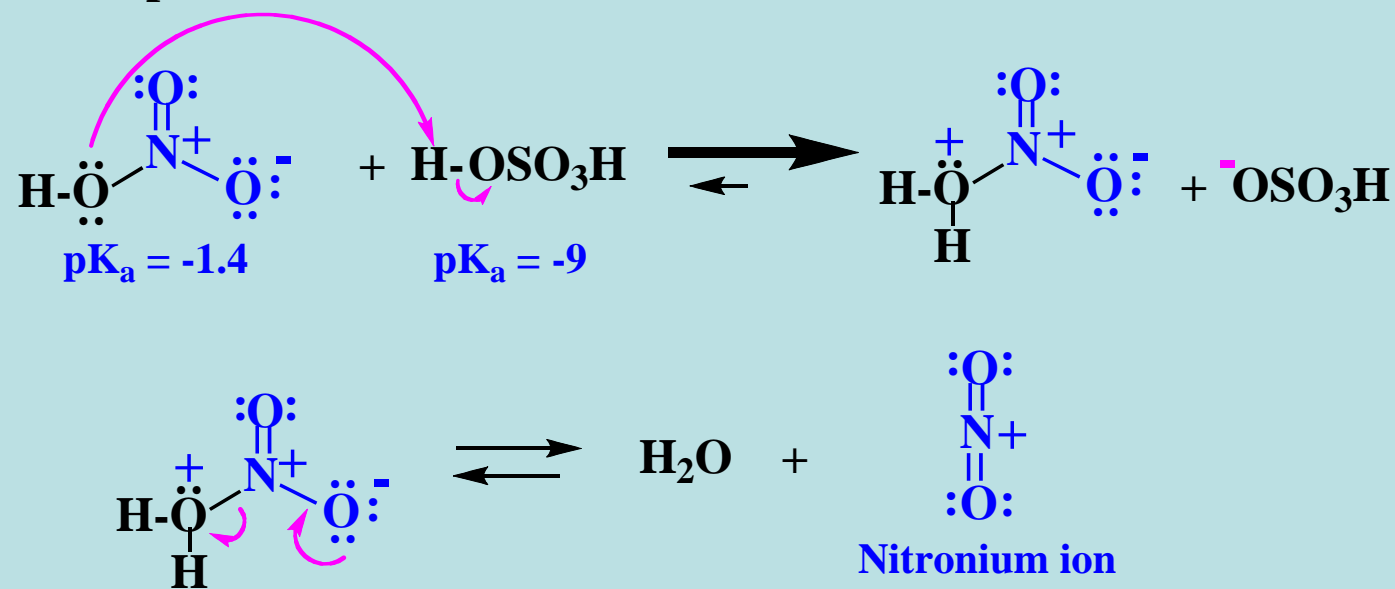
Benzene reacts only slowly with hot concentrated nitric acid to give nitrobenzene. The reaction is much faster in a mixture of concentrated nitric acid ($\text{pK}_a = -1.4$) and concentrated sulfuric acid, a much stronger acid ($\text{pK}_a = -9$).



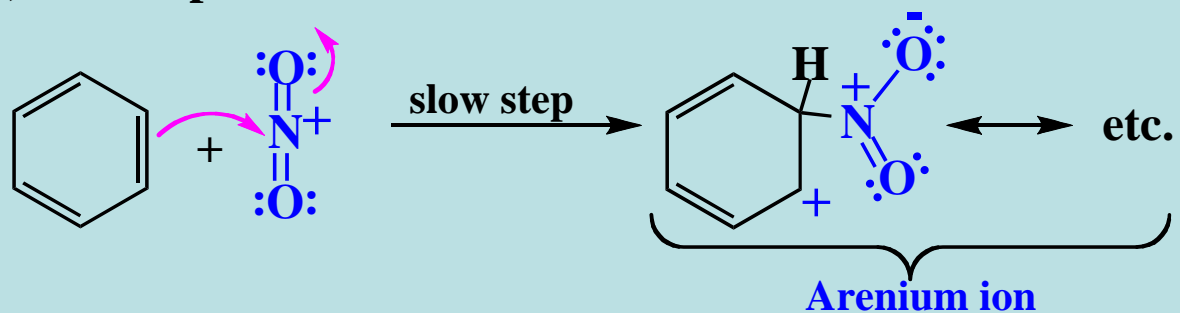
Mechanism of Nitration

(1) Generation of the Electrophile

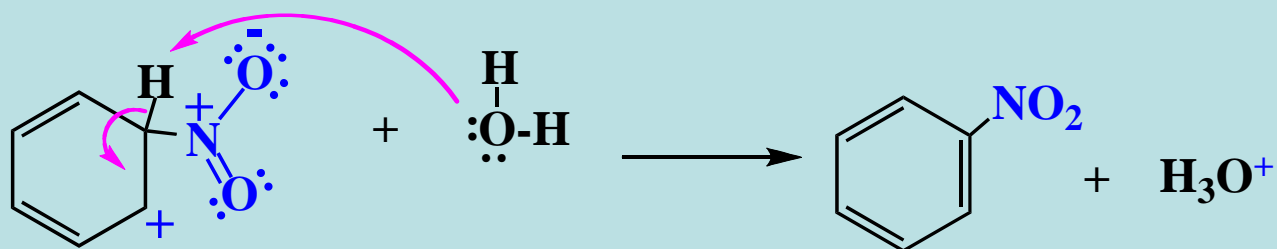
Nitric acid undergoes reversible dehydration in the presence of concentrated sulfuric acid producing the **nitronium ion**, a strong electrophile.



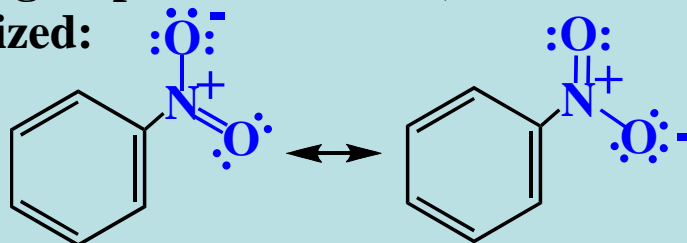
(2) Electrophilic Attack



(3) Deprotonation and Re-aromatization

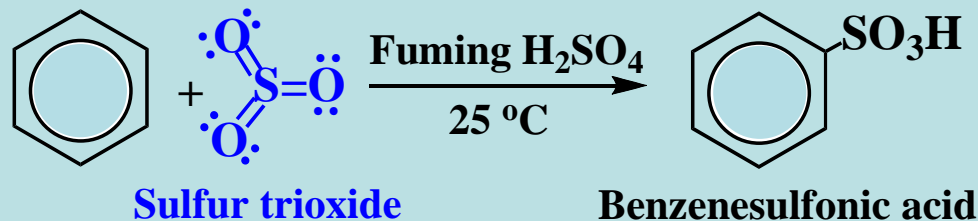


Remember, the nitro group is zwitterionic, and resonance stabilized:



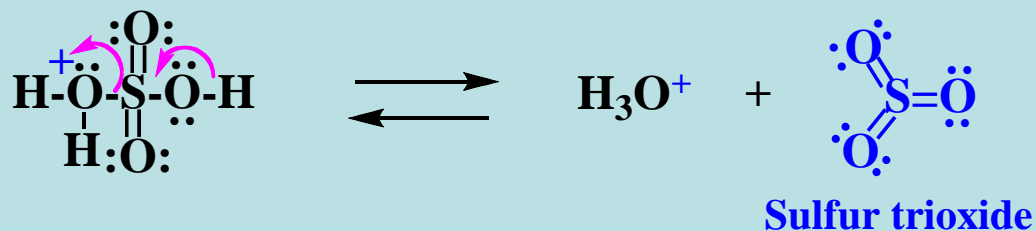
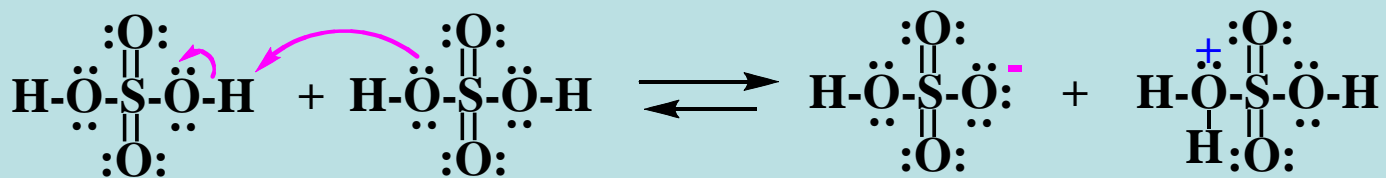
Sulfonation of Benzene

Benzene reacts with **fuming sulfuric acid** (concentrated sulfuric acid plus added SO_3 , the actual electrophile) to give benzenesulfonic acid.

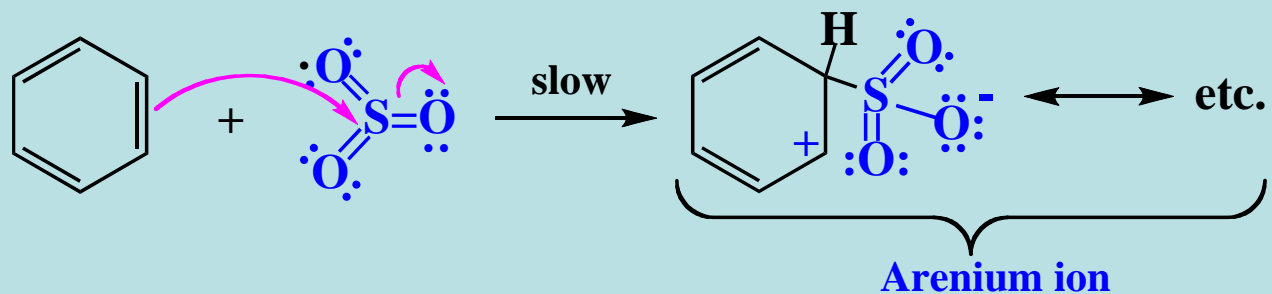


In concentrated sulfuric acid alone, an equilibrium-limited supply of SO_3 effects slow sulfonation.

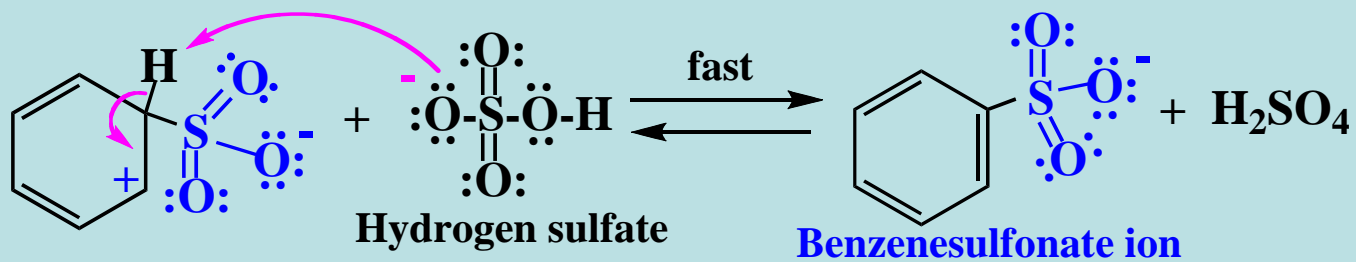
(1) Generation of the Electrophile



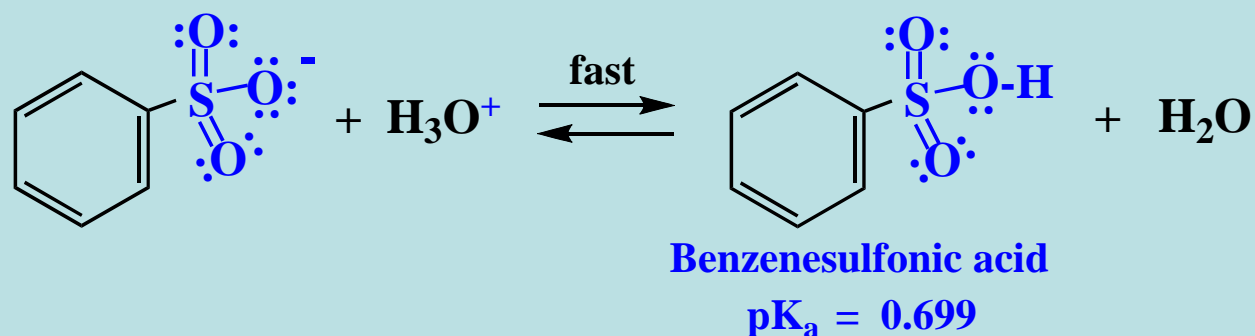
(2) Electrophilic Attack



(3) Deprotonation and Re-aromatization

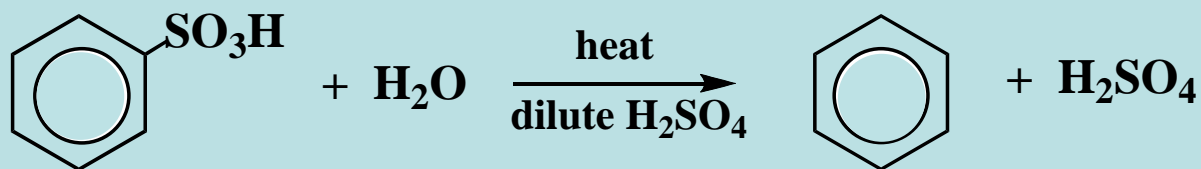


(4) Acid-Base Equilibrium



Synthetic Applications

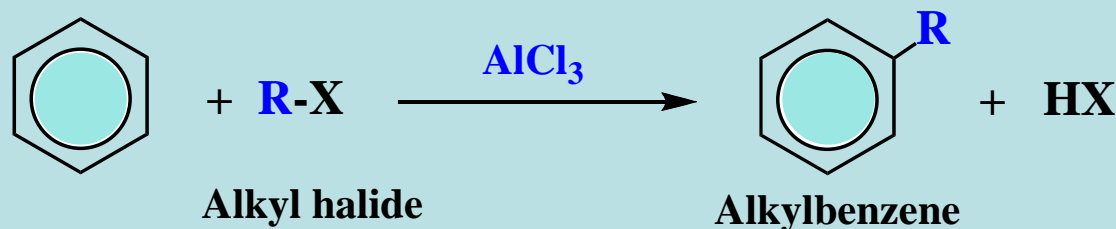
Although introduction of a sulfonic acid group is generally of more limited interest than other electrophilic substitution reactions, the **reversibility** of sulfonation leads to its use in synthetic strategy. Heating arylsulfonic acids in dilute sulfuric acid removes the sulfonic acid function.



Friedel-Crafts Alkylation

Discovered in 1877 by French chemist Charles Friedel and his American collaborator James Crafts, this **alkylation reaction** (one introducing an alkyl group) and the related **acylation reaction** (one introducing an acyl group) are among the most useful synthetic reactions.

Alkylation of an Arene

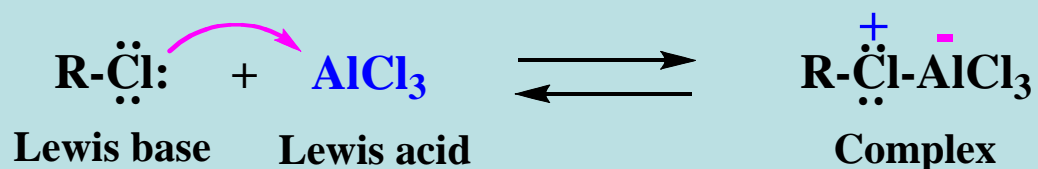


This reaction requires a **Lewis acid catalyst**, typically aluminum chloride, AlCl_3 . Many variations of the Friedel-Crafts alkylation reaction have been developed. All proceed by similar mechanisms.

A Mechanism for the Alkylation Reaction

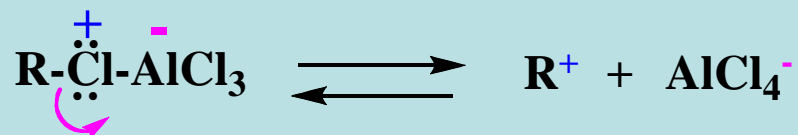
The Lewis acid catalysts generally required in Friedel-Crafts reactions promote formation of strong **electrophiles**.

(1) Generation of the Electrophile

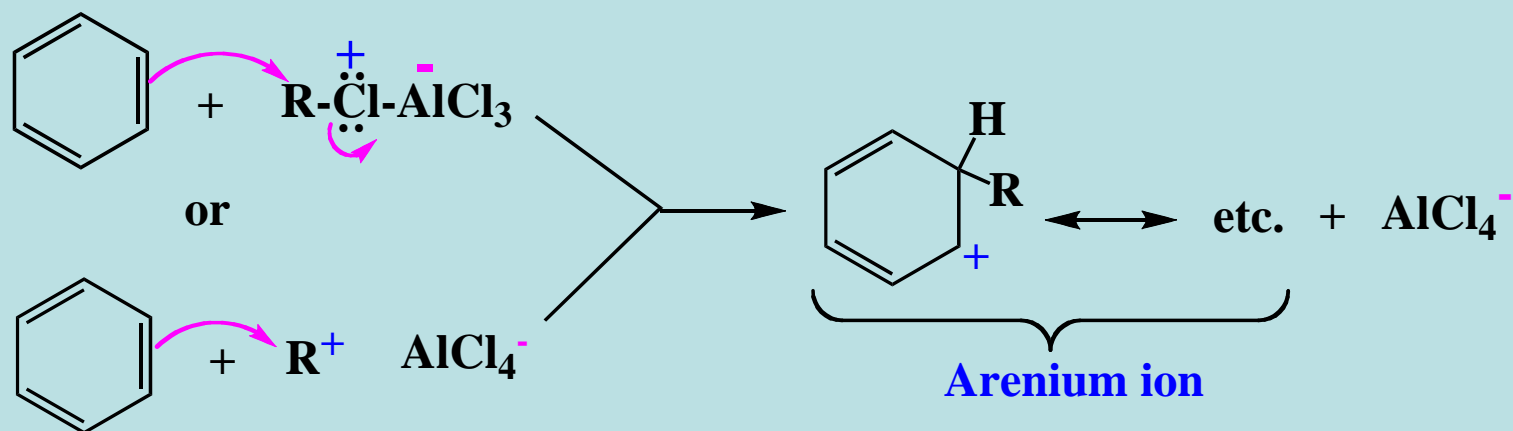


With 1° halides, the complex itself, acting as an R⁺ transfer agent, reacts with the arene.

With 2° and 3° alkyl halides, dissociation to **carbocation intermediates** seems to occur, and the resulting R⁺ species react with the arene.



(2) Electrophilic Attack

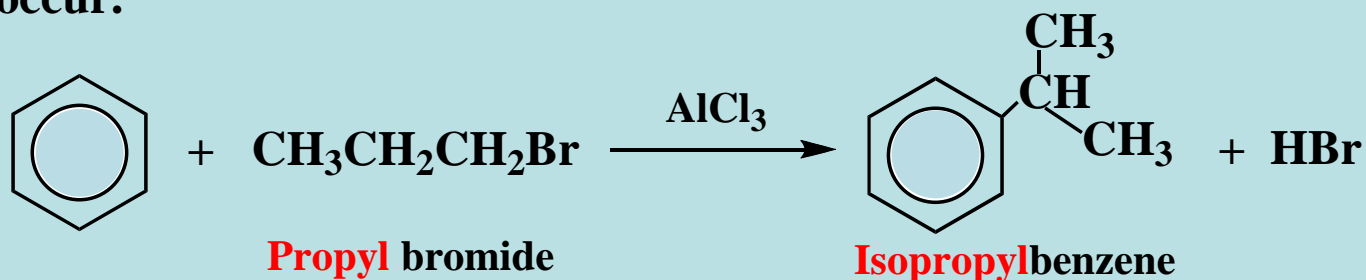


(3) Deprotonation and Re-aromatization

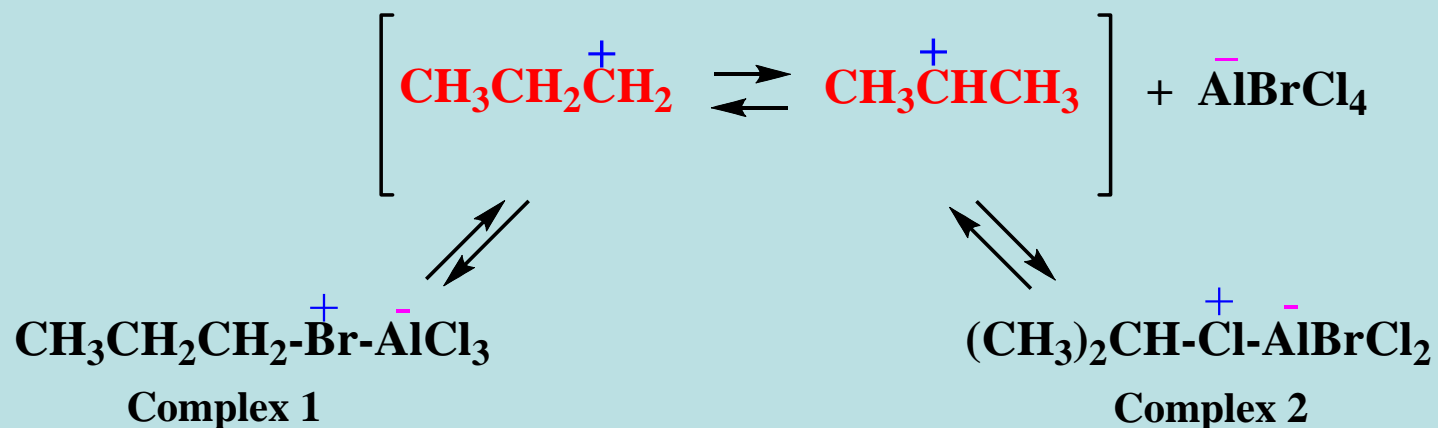


Evidence for Carbocation Intermediates

Skeletal rearrangement is observed in Friedel-Crafts alkylation reactions when concurrent change to a more stable carbocation can occur.



It is believed rearrangement occurs during reversible dissociation to a short-lived carbocation:

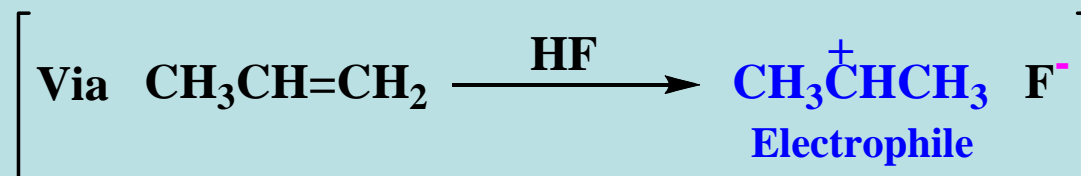
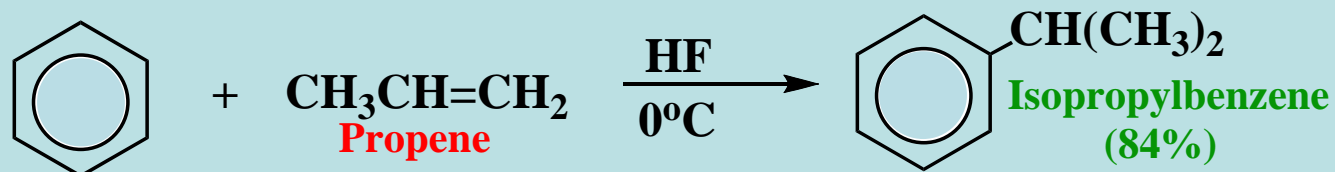


Other Alkylation Methods

Any reaction that produces carbocations (or carbocation-like intermediates) may be used to alkylate benzene and other arenes.

Examples

1) **Alkenes** alkylate arenes in the presence of strong acids:



2) **Alcohols** alkylate arenes in the presence of strong acids:

