Electrophilic Aromatic Substitution

Benzene appears to be a remarkably stable (36 kcal/mole more) and unreactive compared to alkenes, such as cyclohexene or ethylene, or even alkanes, such as cyclohexane or ethane.



When ethylene or cyclohexene is allowed to react with bromine (an addition reaction), a dibrominated product is formed. However, when benzene is allowed to react with bromine in the absence of catalyst, nothing occurs. It is much less reactive.

In the case of alkanes such as ethane or cyclohexane, light (hv) or heat are required for the bromination to occur (this is a substitution). For benzene, there is still no reaction under these conditions.

However, this is not to say that benzene is completely unreactive. With a Lewis acid catalyst, benzene can be made to react.



This is an <u>Electrophilic Aromatic Substitution</u>. Electrophiles seek electrons (e⁻) or negative charge Nucleophiles seek positive charge or donate electrons

In electrophilic aromatic substitution, an electrophile (E^+) is substituted for a hydrogen on the aromatic ring.

Aromatic compounds are very stable and unreactive. In this type of reaction, the electrophile must be especially reactive (electron deficient). *The General Mechanism:*



The pi system of the benzene ring acts as the nucleophile.

The cation formed in the reaction is resonance stabilized (conjugated with the two double bonds). However, it is not aromatic.

Note that the positive charge is ortho and para to the electrophile.

Once the aromatic stabilization is lost, it is easily regained (remember that by staying aromatic, the compound becomes more stable). Hence the last step (loss of proton) is fast to regenerate the aromatic system.

Electrophilic Aromatic Halogenation



Where X = halogen (Cl, Br, and I) M = metal Fe, B, or Al

In this reaction, MX_3 (FeBr₃, AlCl₃, BBr₃) is a Lewis Acid catalyst (a Lewis Acid is a substance that can accept a pair of electrons). MX_3 has an empty orbital to accept a pair of electrons. Chlorine or bromine alone are not strong enough electrophiles to react with the weakly nucleophilic benzene by themselves. The catalyst converts the halogen into a stronger electrophile, which can then react with benzene.

Mechanism:



In halogenation, the Lewis Acid catalyst is regenerated at the end of the reaction.

Sulfonation



In this reaction, SO₃ is the electrophile.



This reaction of SO_3 is followed by loss of proton from the conjugated cation intermediate (similar to the one we saw in halogenation).

Nitration



Mechanism:



In strong acid (H_2SO_4), nitric acid is protonated to give $H_2NO_3^+$. Loss of water generates the nitronium ion that acts as an electrophile.

Friedel-Crafts Alkylation



Friedel-Crafts Acylation



Where R = alkyl (methyl, ethyl, *t*-butyl, etc.) Y = halogen (Cl, Br, and I), or RC(O)OR (an anhydride functionality)





acetophenone



acylium ion

This reaction proceeds through a resonance stabilized acylium ion



Another example:



Electrophilic Aromatic Substitution for Substituted Benzenes

Substituents already present on the benzene ring determine: The <u>position</u> of the reaction. The <u>reactivity</u> of the system.

Resonance and Inductive Effects

A substituent can **donate** or **withdraw** electrons from the aromatic ring in 2 ways: Inductive effects Resonance effects.

Inductive effects are due to the intrinsic electronegativity of the atoms and to bond polarity in functional groups. These effects operate by donating or withdrawing electrons through the sigma (σ) bonds. An **electron donating group** will direct to the **ortho/para** position while an **electron withdrawing group** will direct to the **meta** position. This effect is considered **weak** compared to resonance effects.

Resonance effects operate though conjugation by donating or withdrawing electrons through pi (π) bonds. An **electron donating group** will direct to the **ortho/para** position while an **electron withdrawing group** will direct to the **meta** position. This effect is considered **strong** compared to inductive effects.

Example:



Alkyl groups direct ortho and para

How to determine position and reactivity



Aromatic compound with a heteroatom attached (has lone pair of electrons) is considered a resonance donating system and will direct the reaction to the *ortho* or *para* positions because they have higher electron density as seen through the resonance structures



Aromatic compounds with a conjugated double bond conjugated to the aromatic ring are generally resonance withdrawing (especially if Z is electronegative) and will direct aromatic substitution to the *meta* position, where there is no partial positive charge.





Examples:























