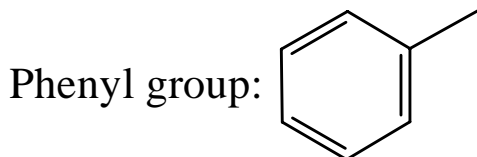


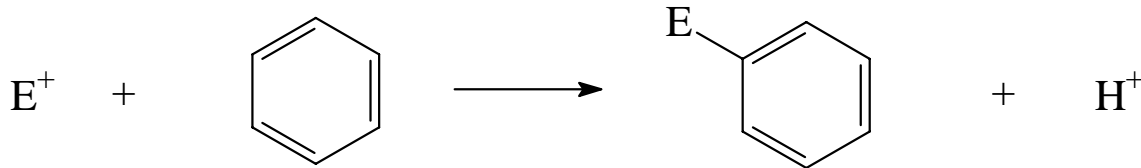
Electrophilic Aromatic Substitution



Shorthand for phenyl: Ph-, C₆H₅-, φ-.

An aryl group is an aromatic group: phenyl, substituted phenyl, or other aromatic group. Shorthand: Ar-

Generalized electrophilic aromatic substitution:

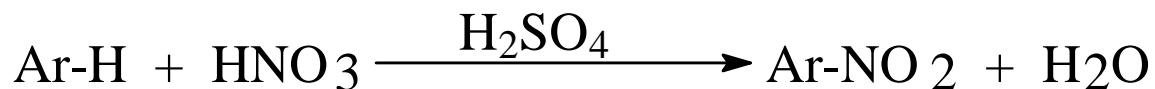


Electrophile-
Lewis acid:
may be \oplus
or neutral.

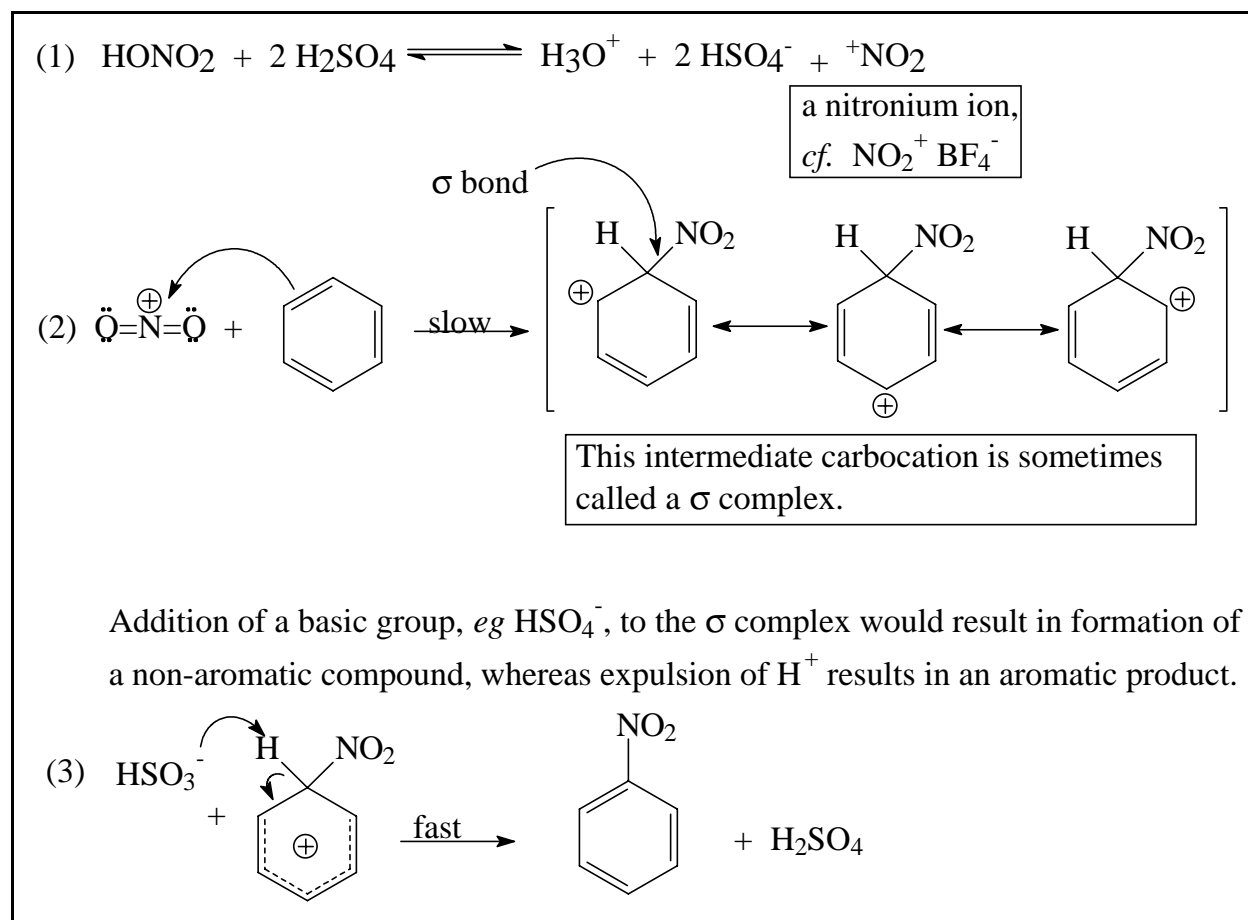
Nucleophile-
Lewis base.
Shorthand:
Ar-H

Product: neutral if
electrophile is \oplus ;
 \ominus if electrophile
is neutral.
Shorthand: Ar-E

1. Nitration —

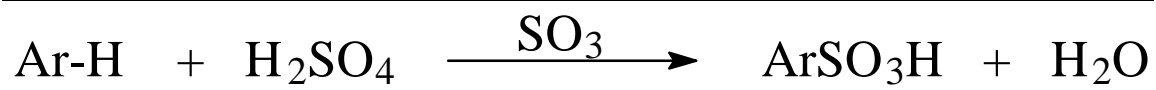


Mechanism

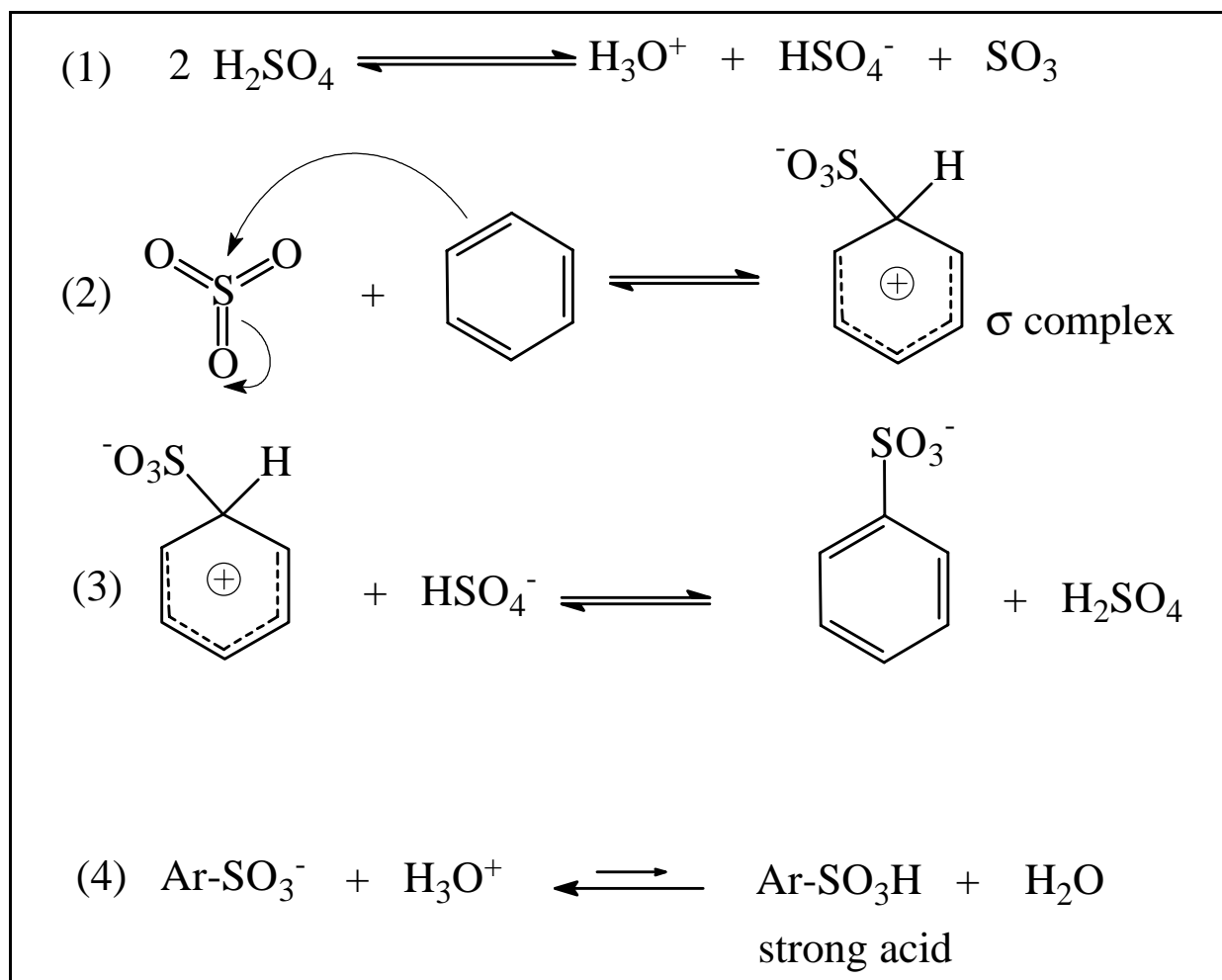


Since the nitro group can often be reduced to the amine group (tin or iron and HCl are frequently used to effect this reduction), $\text{ArNO}_2 \longrightarrow \text{Ar-NH}_2$, nitration is often used to ultimately make an aryl amine.

2. Sulfonation —

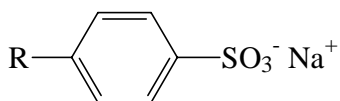


Mechanism



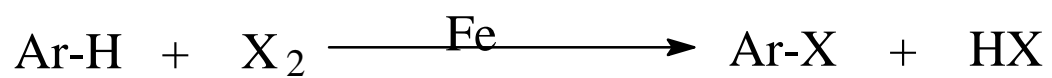
Note the following —

- ☞ Sulfonic acids (eg, ArSO_3H), derivatives of sulfuric acid, are strong acids and are highly ionized in water.
- ☞ Each step in the sulfonation mechanism is an equilibrium; therefore, the entire reaction is an equilibrium. Thus, Ar-H can be sulfonated using fuming sulfuric acid, $\text{H}_2\text{SO}_4 \cdot \text{SO}_3$, and $\text{Ar-SO}_3\text{H}$ can be desulfonated (to Ar-H) by boiling it in a dilute solution of sulfuric acid.
- ☞ Sulfonation of an aromatic ring can provide a route to a *phenol*, Ar-OH . If a sulfonic acid is *fused* with solid KOH , the $-\text{SO}_3\text{H}$ group is replaced by $-\text{OH}$. [Owing to the vigorous reaction conditions, there are limitations with regard to which substituents may be present on the ring.]
- ☞ Sulfonation of an aromatic ring provides a highly polar site capable of hydrogen bonding; this gives rise to water solubility. Dyes are sometimes made water soluble in this way.
- ☞ Some synthetic detergents have the structure

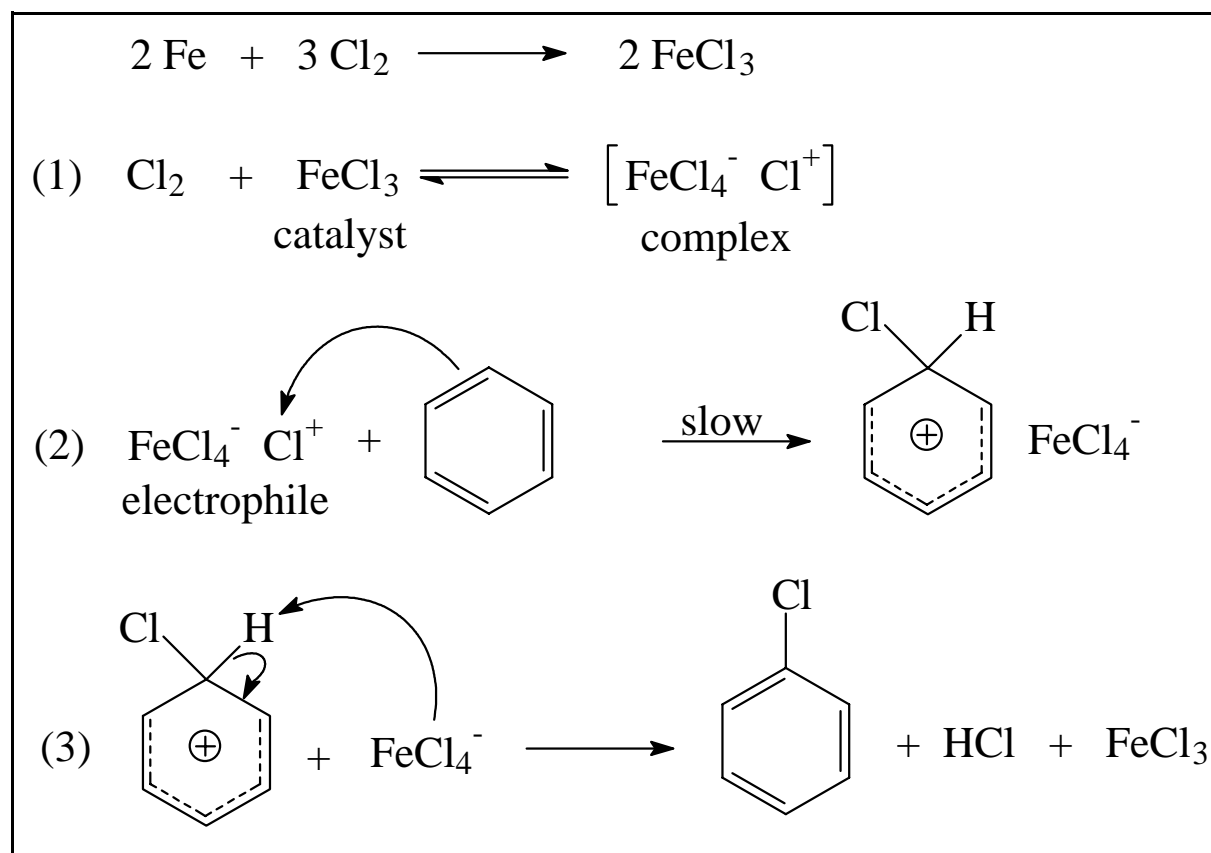


, where R is a long-chain alkyl group. The ionic "head" is *hydrophilic* and the long "tail" is *hydrophobic*. This combination enables this material to disperse oily material in water.

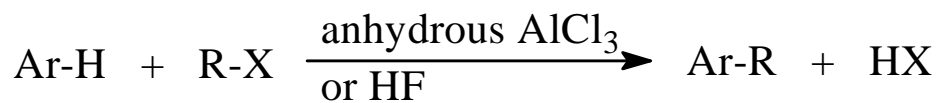
3. Halogenation —



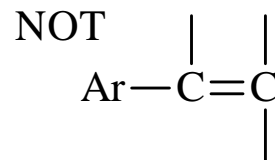
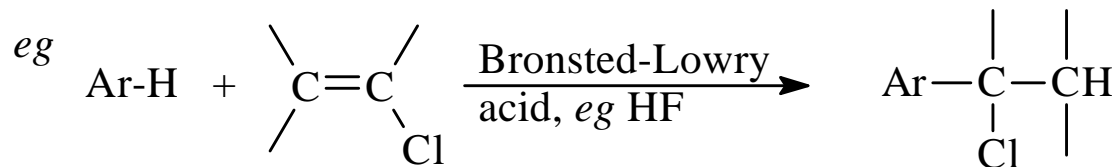
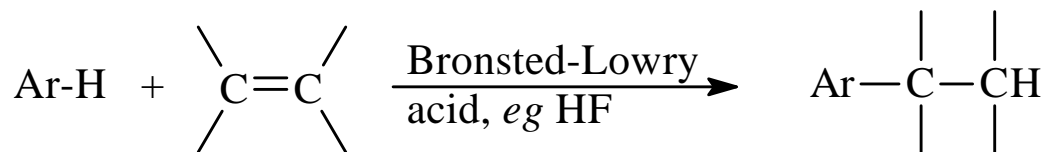
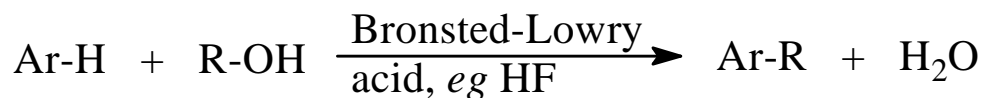
Mechanism



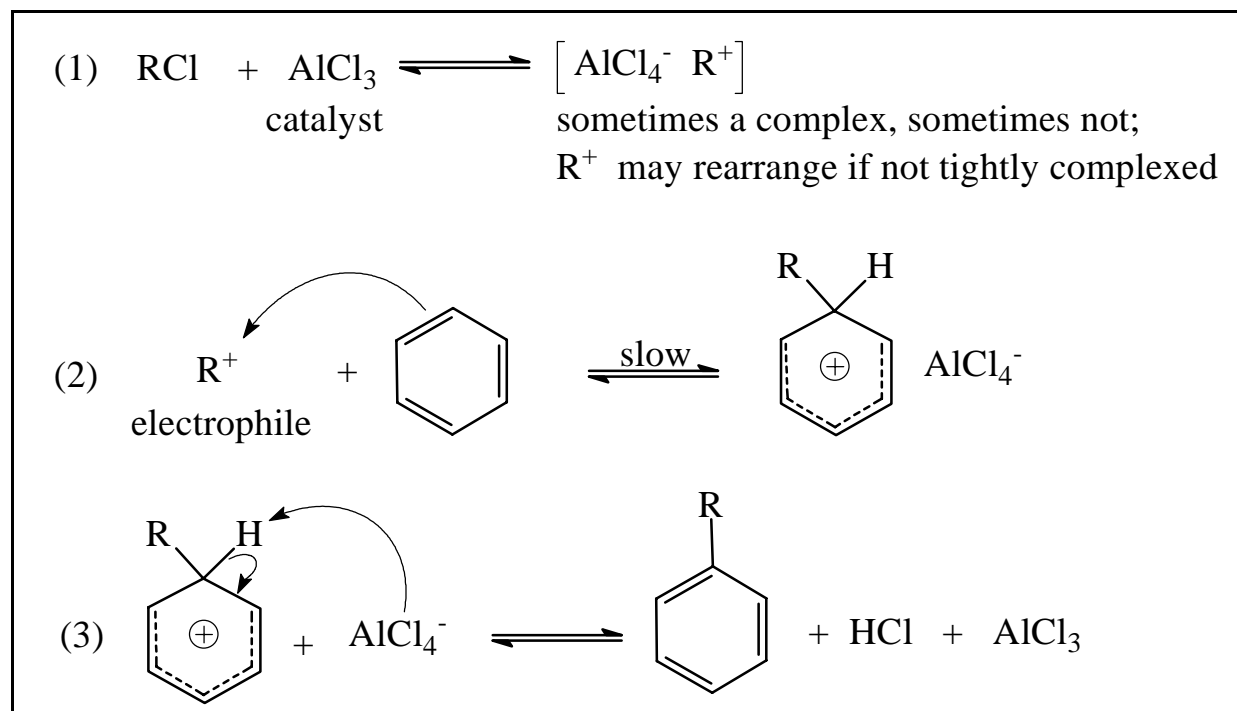
4. Friedel-Crafts Alkylation —



X = halogen, R = alkyl, NOT vinyl, NOT aryl



Mechanism

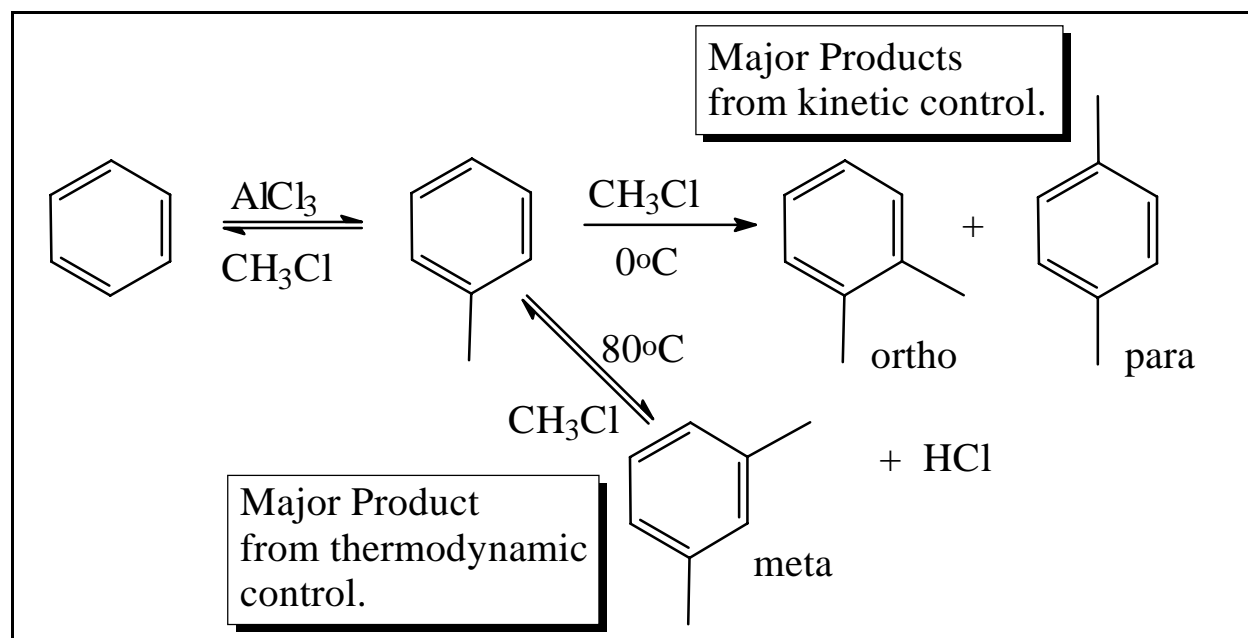


Since a carbocation can be the electrophile in this mechanism, a variety of carbocation *precursors* could be used: alkenes, for example. Since aryl and vinyl carbocations are unstable, Ar-X and vinyl-X cannot be used as precursors for these species.

Limitations on Friedel-Crafts Alkylation —

- ☞ The alkyl group may rearrange.
- ☞ Any group which *deactivates* an aromatic ring more than the halogens (*vide infra*) cannot be present on the ring prior to F-C alkylation, nor can $-\text{NH}_2$, $-\text{NHR}$, or $-\text{NR}_2$.
- ☞ Alkyl groups *activate* aromatic rings toward electrophilic substitution; therefore, polyalkylation is a problem.

Another case of Rate vs Equilibrium Control —



Limitations —

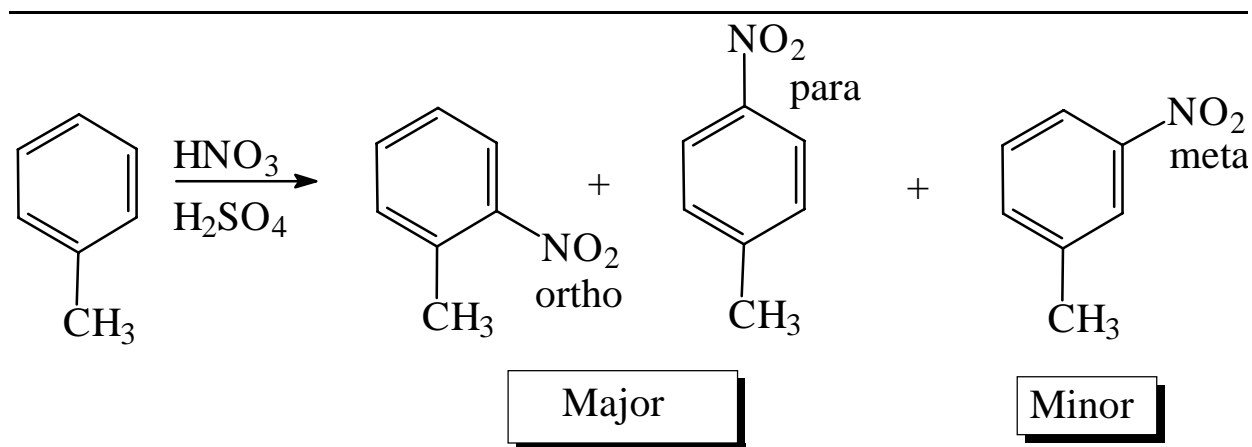
☞ Any group which *deactivates* an aromatic ring more than the halogens (*vide infra*) cannot be present on the ring prior to F-C acylation, nor can -NH_2 , -NHR , or -NR_2 .

However, the acylium ion does *not* rearrange and polyacylation is not a problem because the acyl group *deactivates* the ring toward further electrophilic substitution.

Effect of Substituents Already on the Ring

Reactivity: Activating or Deactivating —

If we allow toluene and benzene to react with mixtures of nitric and sulfuric acids under the same conditions and the toluene reacts 25 times faster than the benzene, we say it is 25 times more reactive. We would also say that the methyl group *activates* the aromatic ring toward nitration. Since the other electrophilic aromatic substitutions have mechanisms similar to nitration, we might expect the methyl group to activate the aromatic ring toward these reactions; usually, it does.



If we nitrate toluene, we find that the major products are *p*-nitrotoluene and *o*-nitrotoluene; only a small amount of *m*-nitrotoluene is formed.

We say the methyl group is an *ortho*, *para* director for electrophilic substitutions.

The table below shows the effect of some common aromatic ring substituents on electrophilic substitution —

Activating; Ortho, Para Directing

Strongly activating: $-\text{NH}_2$, $-\text{NHR}$, $-\text{NR}_2$, $-\text{OH}$.

Moderately activating: $-\text{OR}$, $-\text{NH-CO-R}$.

Weakly activating: $-\text{C}_6\text{H}_5$, $-\text{R}$.

Deactivating; Meta Directing

$-\text{NO}_2$, $-\text{N}^+\text{R}_3$, $-\text{C}\equiv\text{N}$, $-\text{COOH}$, $-\text{SO}_3\text{H}$, $-\text{CHO}$, $-\text{CRO}$.

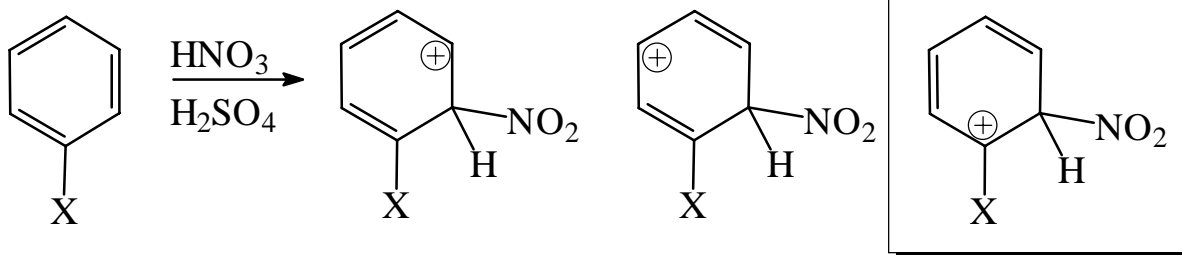
Deactivating; Ortho, Para Directing

Weakly deactivating: $-\text{F}$, $-\text{Cl}$, $-\text{Br}$, $-\text{I}$.

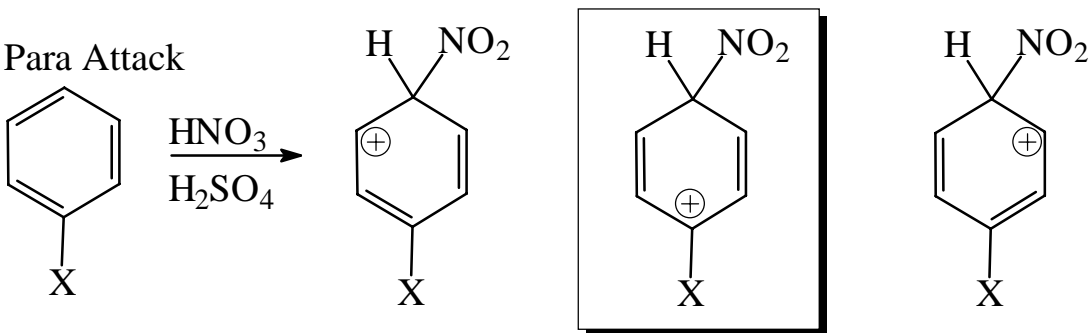
Except for the halogens, activating groups activate all positions of the ring, but have greater effect on *o* & *p*; deactivating groups deactivate all positions of the ring, but have greater effect on *o* & *p*.

The rate of formation of *o*, *m* or *p* isomers depends on the rate of formation of the precursor carbocations (σ complexes).

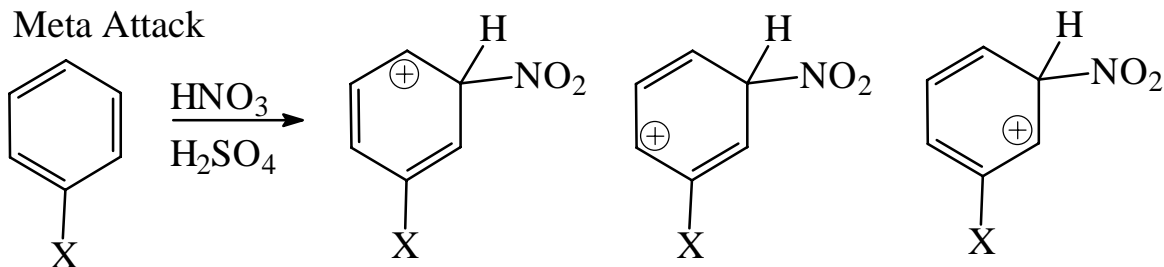
Ortho Attack



Para Attack



Meta Attack



Boxed resonance structures make an especially large contribution if X is electron *releasing*; they make an especially small contribution if X is electron *withdrawing*.

Note: *ortho* and *para* attack form carbocations with one boxed structure; the carbocation resulting from *meta* attack has no boxed structures.

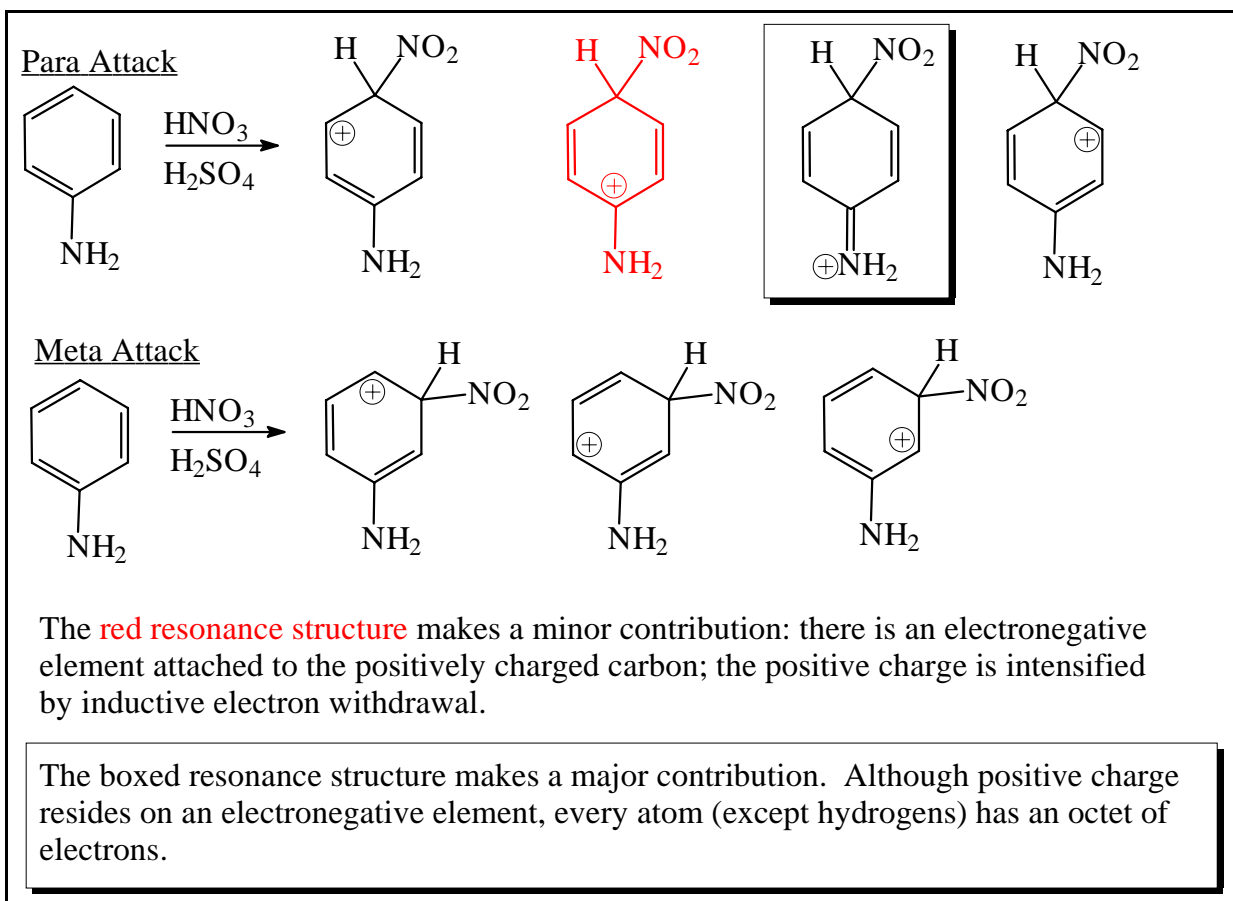
OK. Electron withdrawing groups on the ring destabilize the transition state leading to the σ -complex, and electron donating ones stabilize the transition state, so reaction occurs faster with electron donating groups. And the effect is greatest at the ortho and para positions so an electron withdrawing group is meta directing because it deactivates the o and p positions.

BUT, two questions.

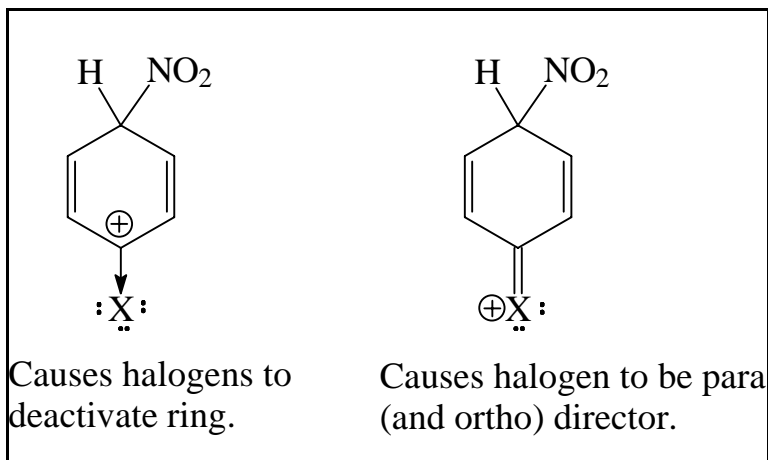
- 1) Why are some groups which appear to be electron withdrawing, $-\text{NO}_2$ for example, deactivating and meta directing as expected, while others, $-\text{NH}_2$ for example, are activating and o, p directing?*
- 2) Why are the halogens deactivating and o, p directing?*

OK.

- Note that all the groups which would seem to be deactivating meta directors and turn out to be activating o, p directors, $-\text{OH}$ and $-\text{NH}_2$, for example, carry at least one pair of unshared electrons. These unshared electrons are delocalized into the ring as the σ -complex intermediate forms if attack is at the ortho or para position.

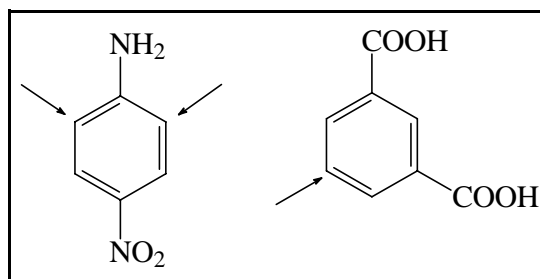


- 2) When halogen is the ring substituent it seems that its ability to donate electrons *via* resonance determines the preferred orientation of attack by the electrophile, while reactivity is controlled by its inductive electron withdrawing effect.



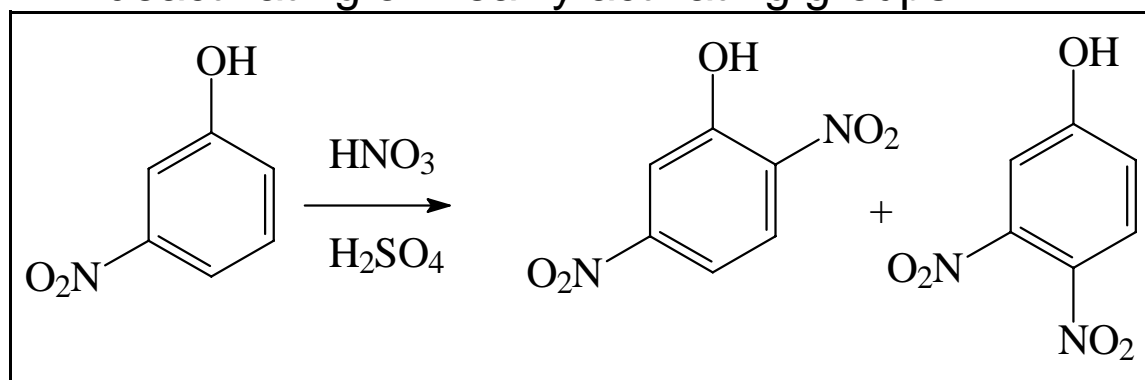
Position of Electrophilic Attack for Disubstituted Benzenes

- 1) Where two groups reinforce each other, the outcome is obvious.



In cases of opposing effects prediction is more difficult and mixtures may result.

- 2) Strongly activating groups usually win out over deactivating or weakly activating groups.



- 3) There is usually little substitution between two groups which are meta to each other.

