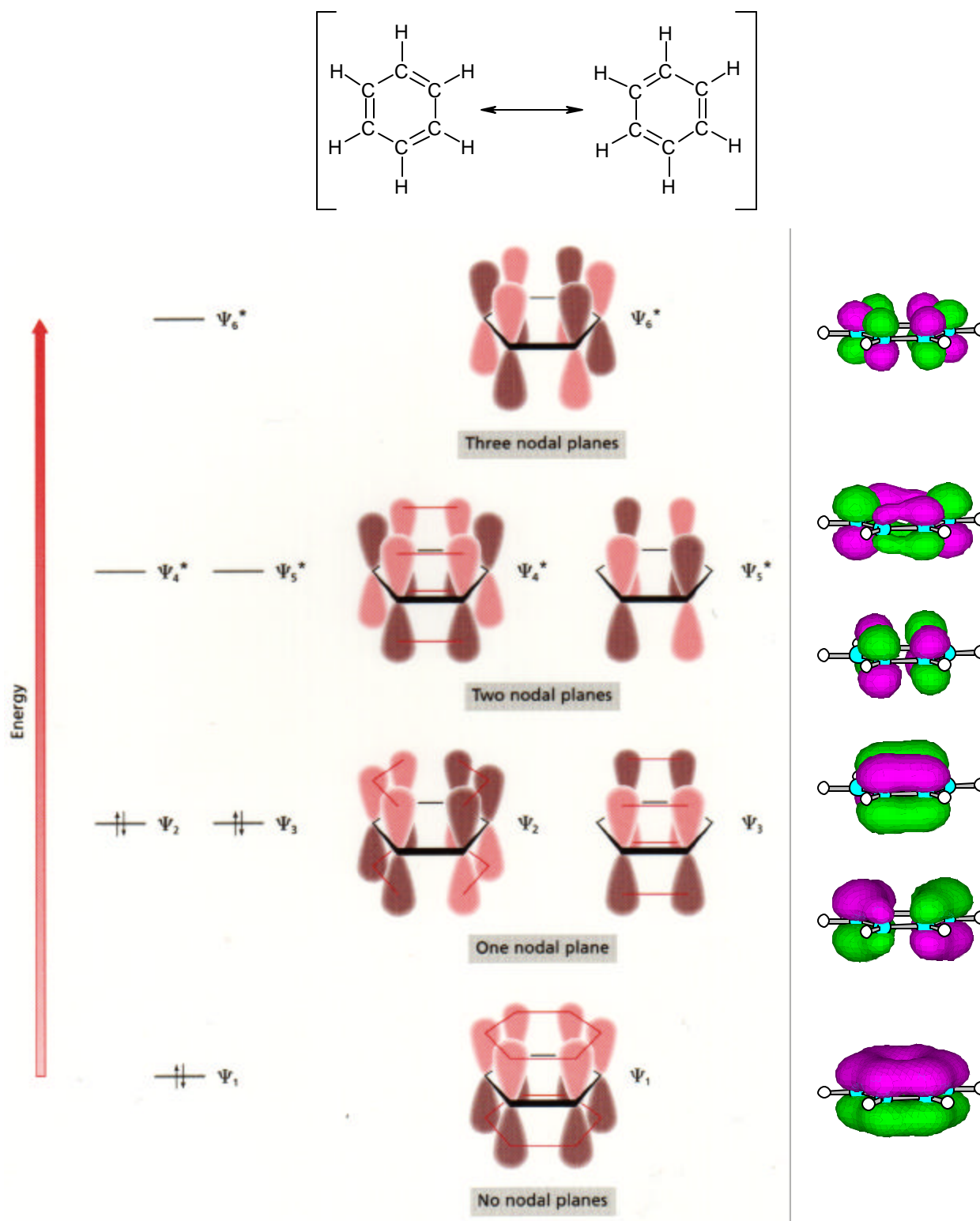


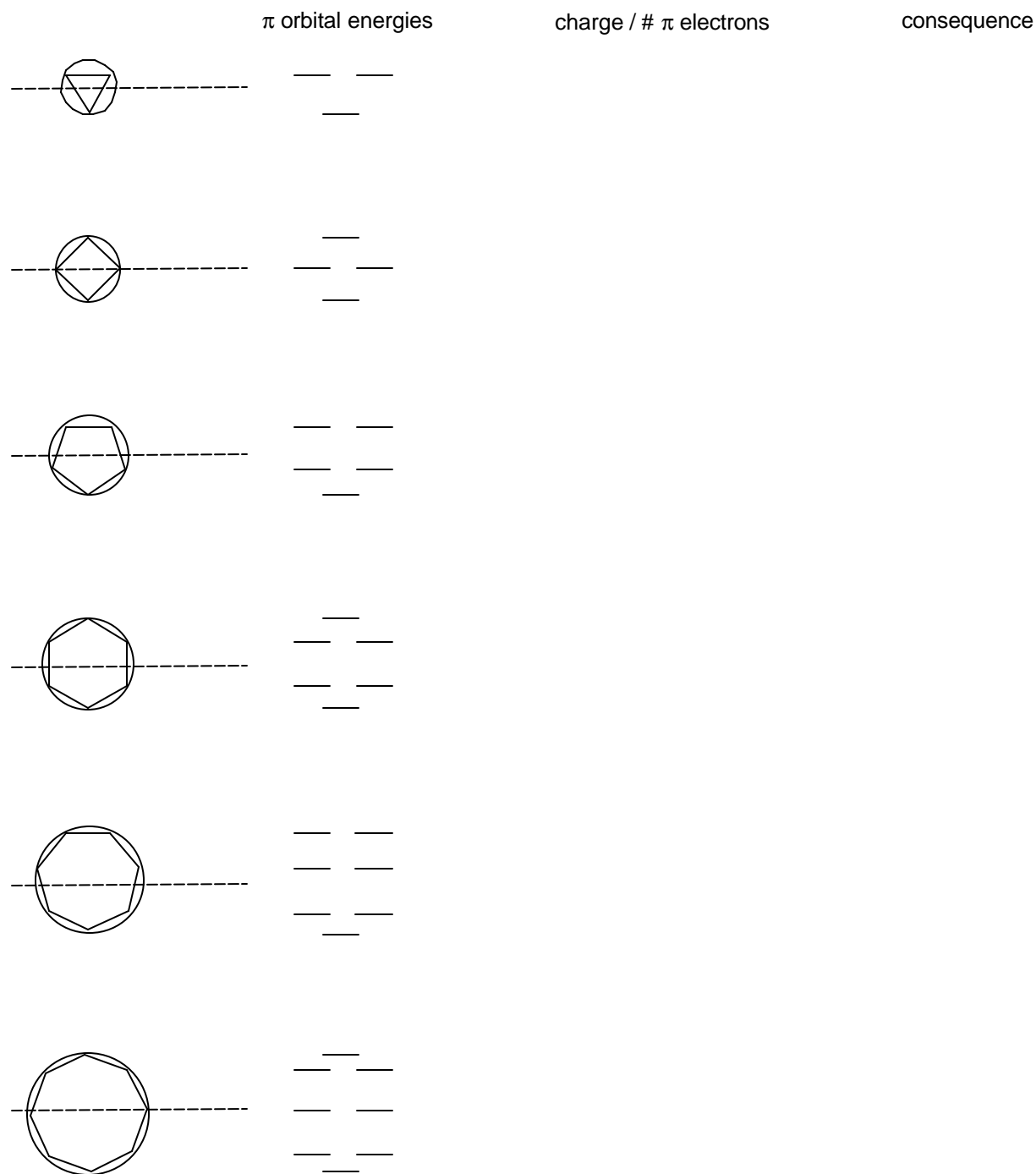
Electrophilic Aromatic Substitution Reactions

Benzene (discovered 1825 by a (Physical!) chemist, Michael Faraday) is special!

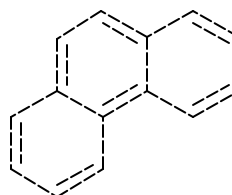
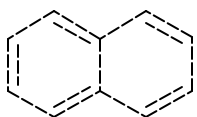


- Hückel Rule: *any* aromatic molecule is planar with $4N + 2 \pi$ electrons

- Graph theory can be used to rationalize aromaticity of monocyclic hydrocarbons

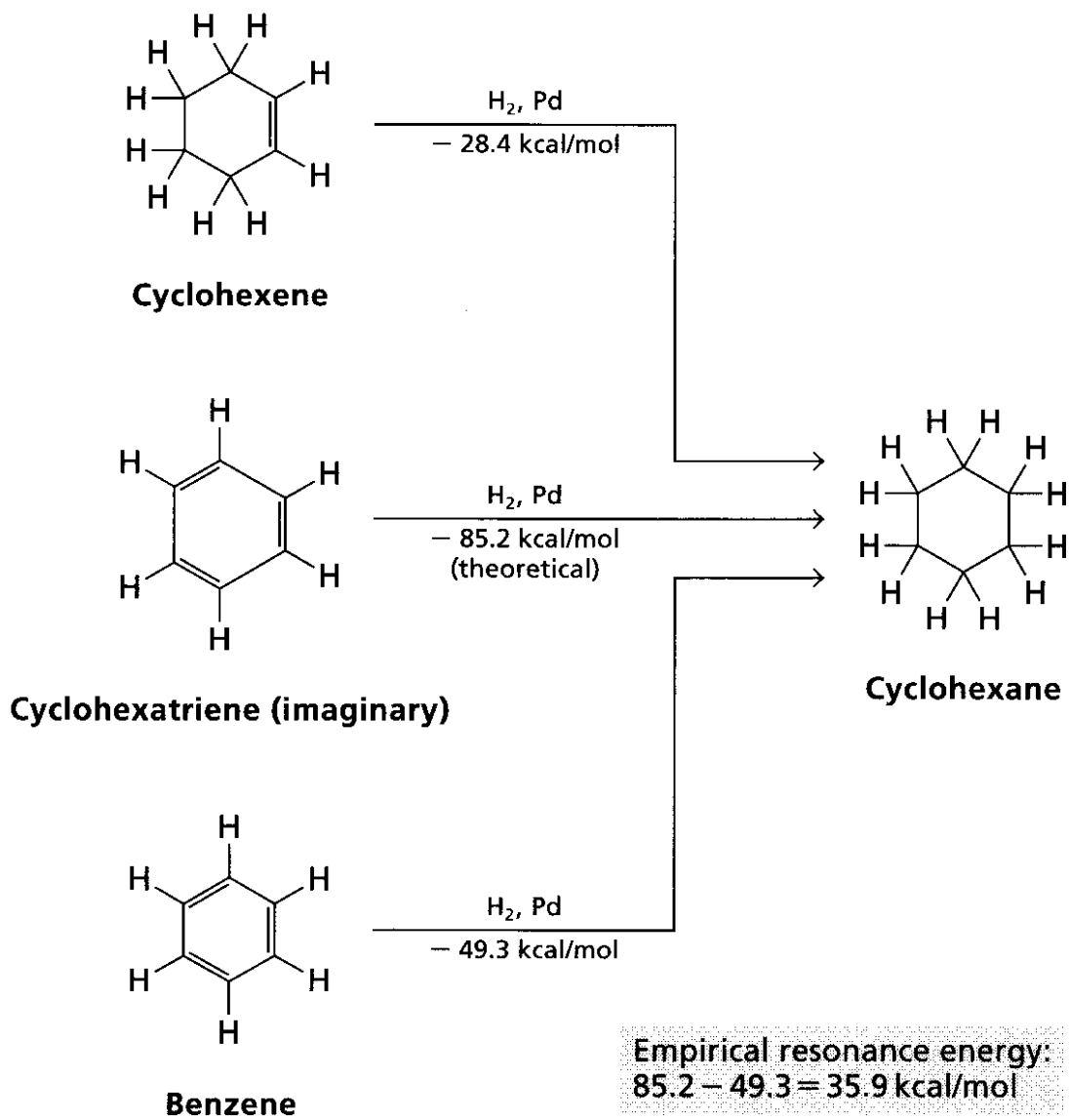


- The $4N + 2$ rule also applies to **polycyclic** aromatic systems also (but no easy graph theory)

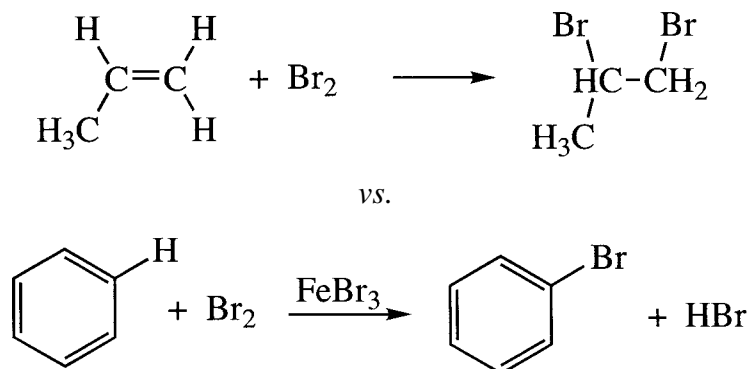


“Aromaticity” assessed using empirical resonance energy

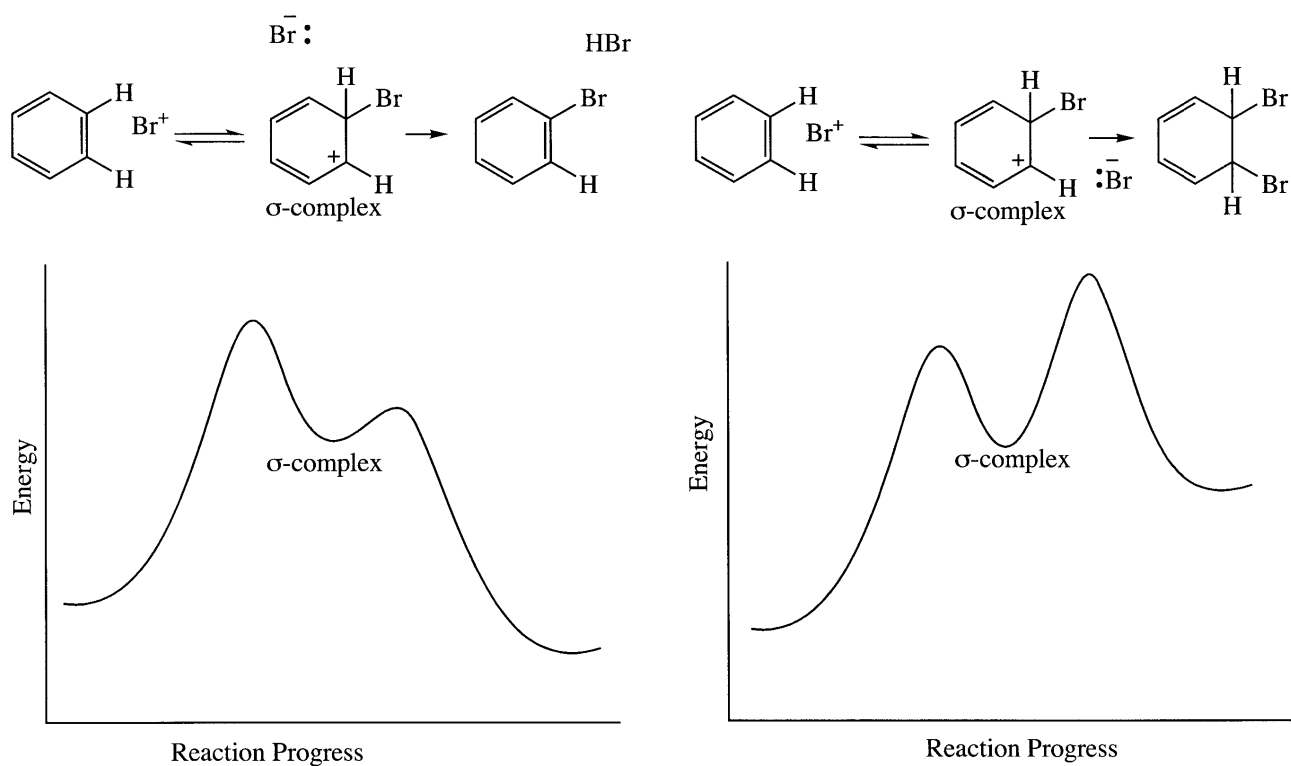
- Benzene is more thermodynamically stable than predicted from the degree of unsaturation



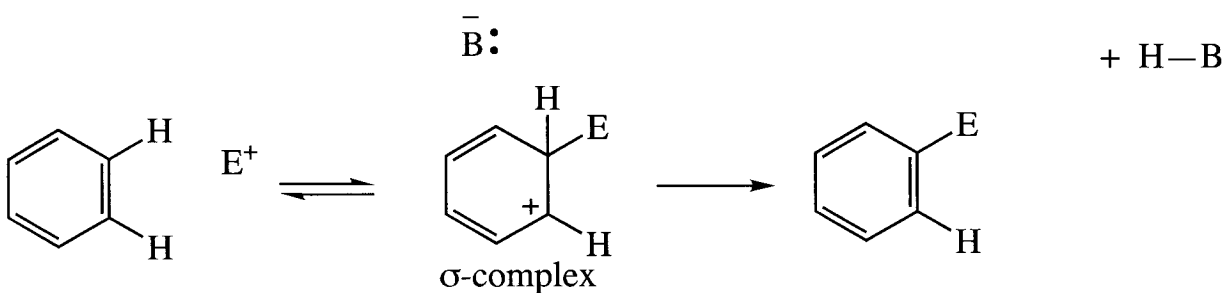
- Benzene undergoes electrophilic substitution rather than electrophilic addition



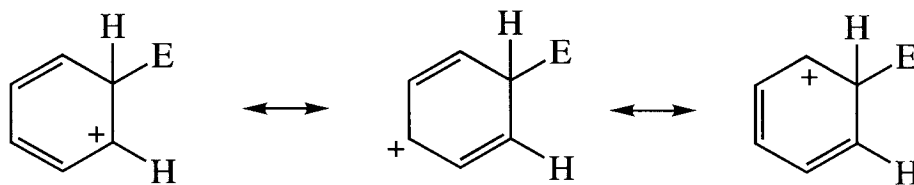
- Resonance energy is thought to drive the choice of substitution over addition



- The general mechanism of **all** electrophilic substitution reactions is given by:

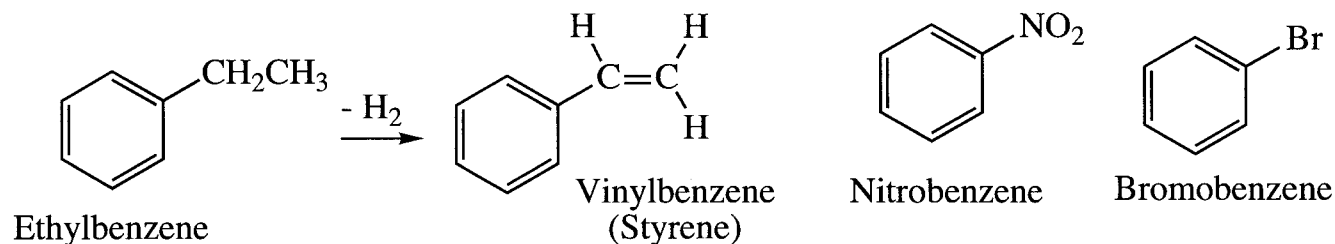


- The σ -complex is a very important intermediate; stabilized by delocalization of the positive charge.

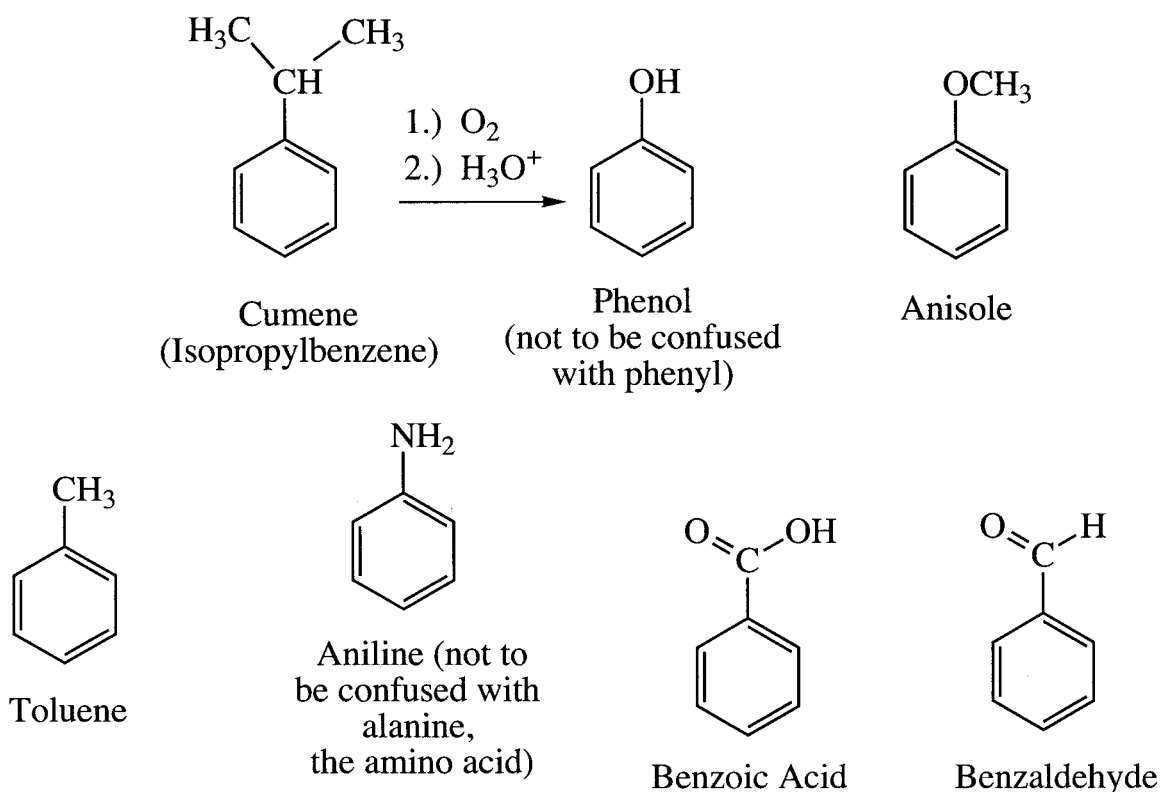


Nomenclature of Aromatic compounds: some examples

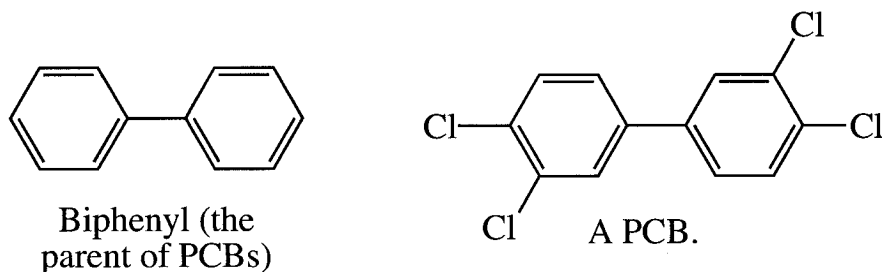
- Some benzene derivatives are simply named by the substituent followed by "benzene"



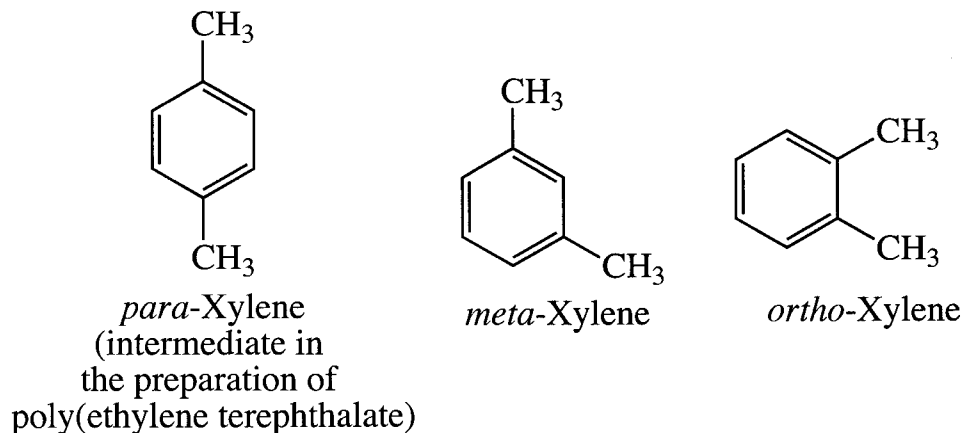
- Many older benzene derivatives have well-entrenched historical names that are now officially accepted as valid "root" name for further substitution



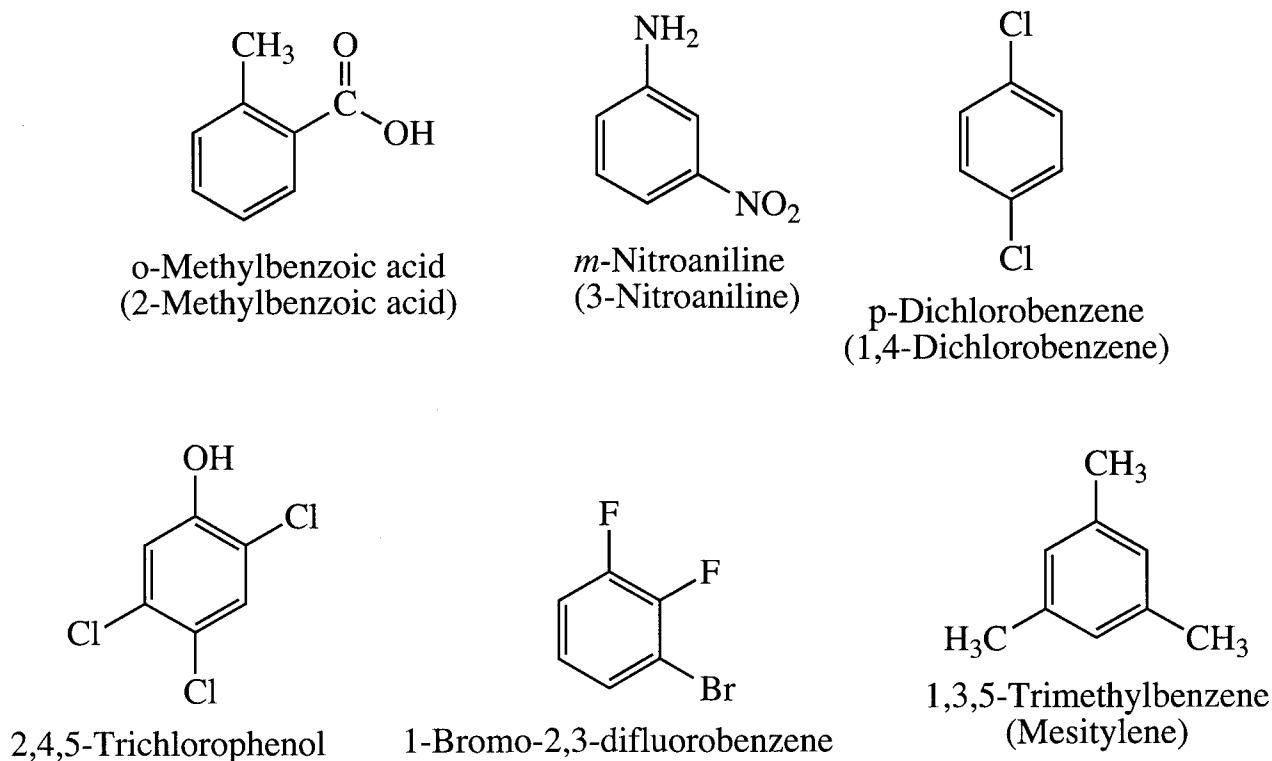
- Polycyclic aromatic compounds also have many "trivial" names that have stuck



In disubstituted benzenes, the relative positions of the two substituents must be specified. There are two ways in which this is done. IUPAC uses a numbering system. A trivial method also persists.



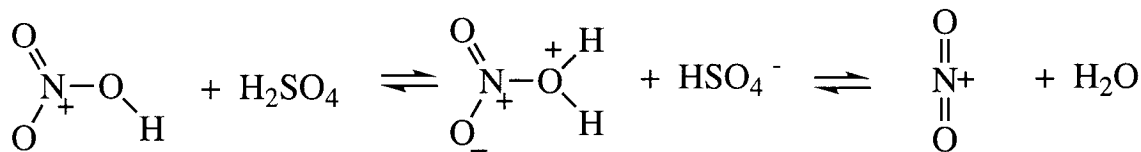
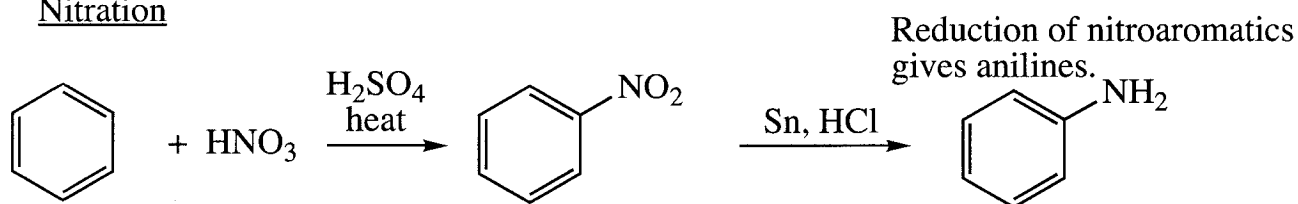
Polysubstituted Benzenes are named as derivatives of the parent benzene (if applicable). Substituent positions are numbered from the dominant functional group, or follow rules akin to those for numbering alkanes.



Specific Examples of Electrophilic Aromatic Substitution: Generation of Electrophiles

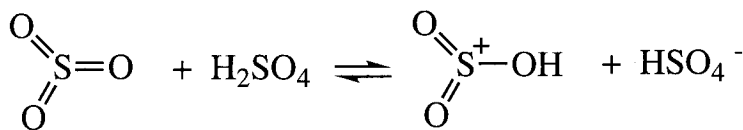
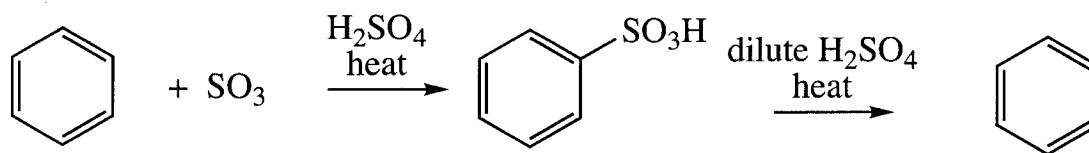
Key to most EAS reactions is the generation of the electrophiles under specific conditions

Nitration

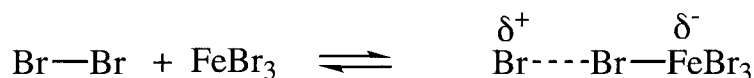
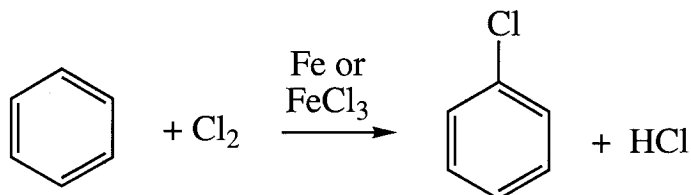
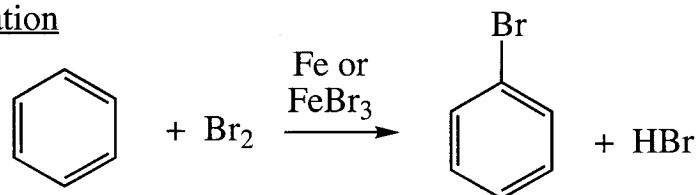


In the case of nitration, E^+ is NO_2^+ .

Sulfonation

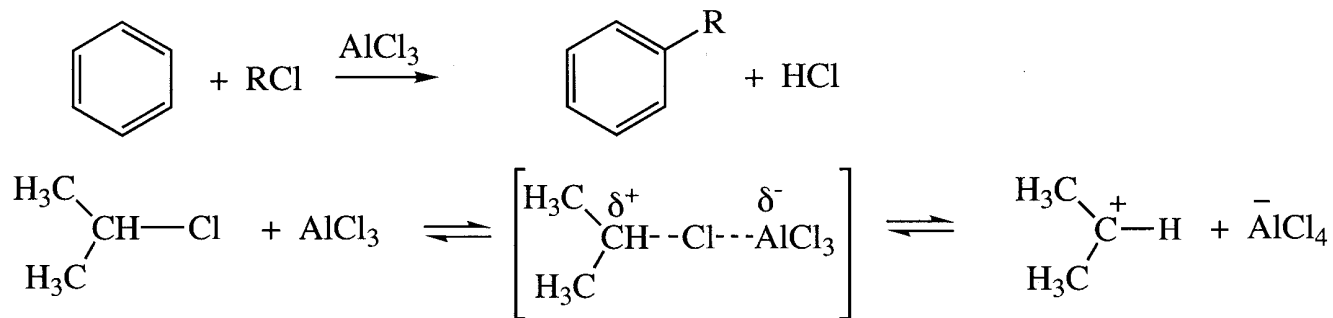


Halogenation

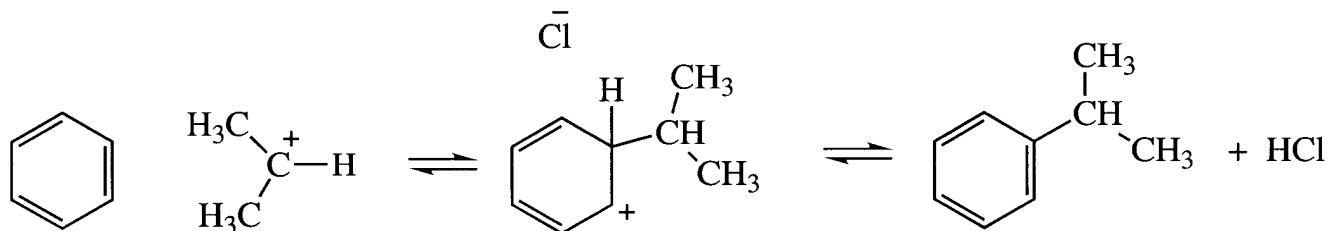


Alkylation: the Friedel-Crafts Reaction

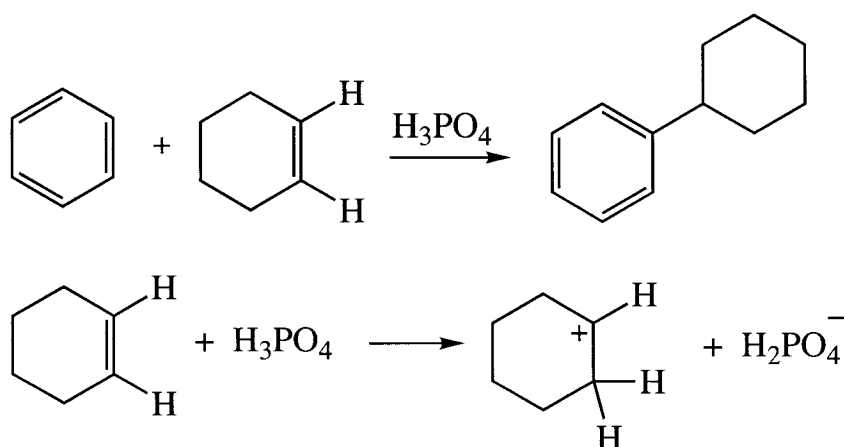
- Lewis Acid activation is the original F-C condition



- Mechanism: the “normal” EAS process

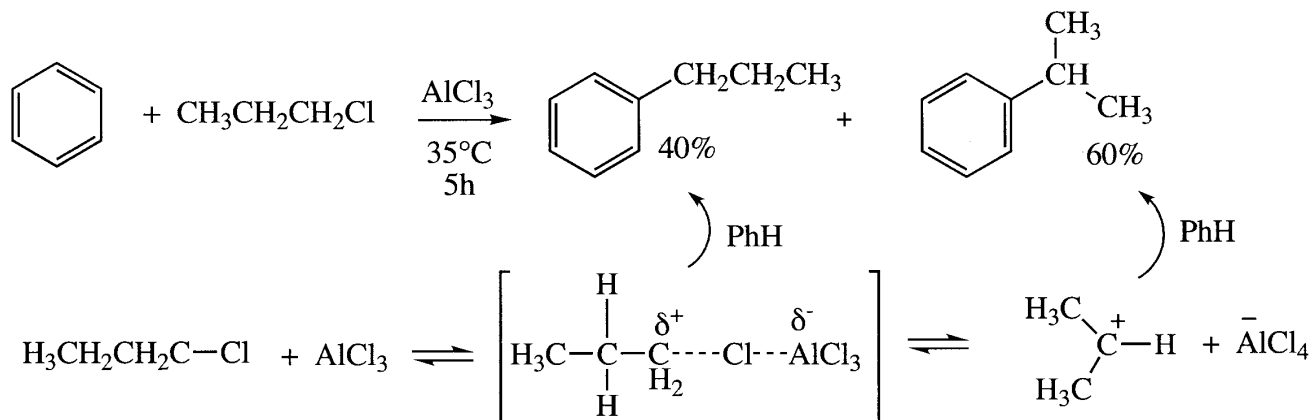


- Brønsted Acid Activation is also possible, and usually grouped with FC

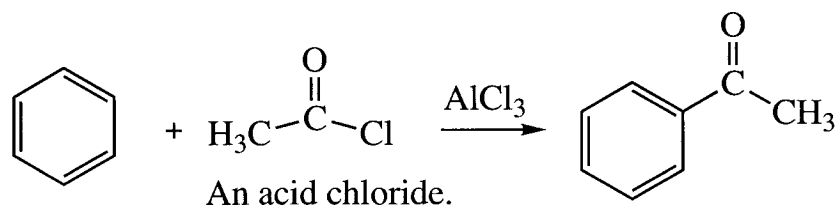


- Caution: carbocation rearrangement may occur during the Friedel-Crafts Alkylation!

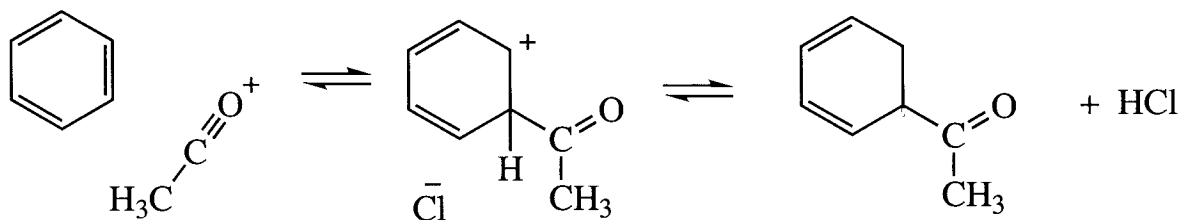
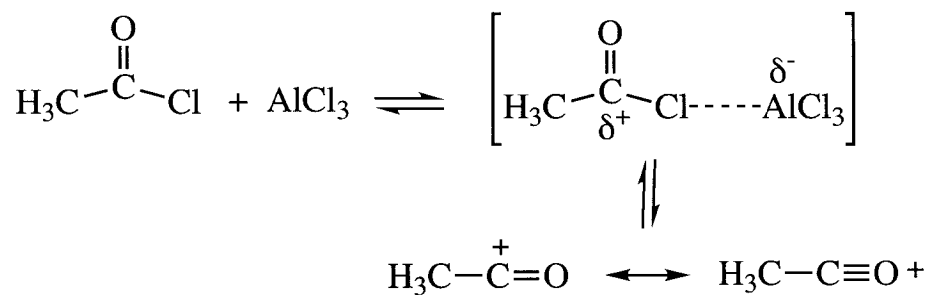
Rearrangement is always a concern when carbocations are involved and alkyl or hydride shift is possible.



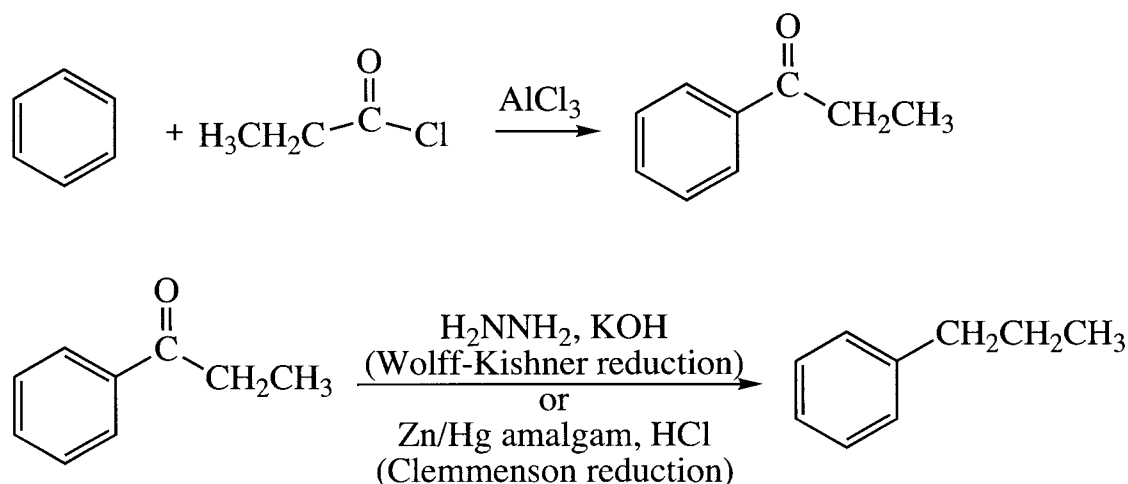
Acylation: another EAS reaction enabled by Friedel-Crafts conditions.



- Mechanism



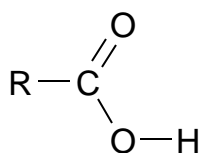
- Friedel-Crafts acylation can be used to circumvent the problem of carbocation rearrangement



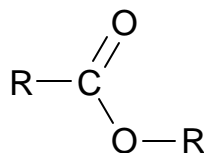
What is an “acid chloride”? A primer on the carboxylic acid family

- The following are all members of the “family” related to the carboxylic acids
- You need to know all of them to excel in organic chemistry

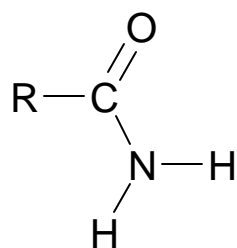
The “parent” carboxylic acid



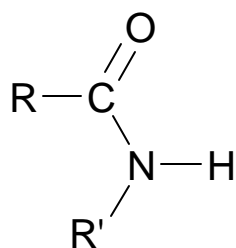
The ester



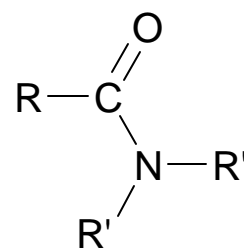
The amides



1° amide

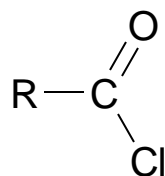


2° amide

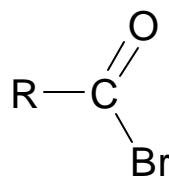


3° amide

The acid halides

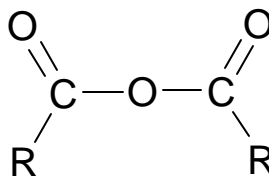


acid chloride



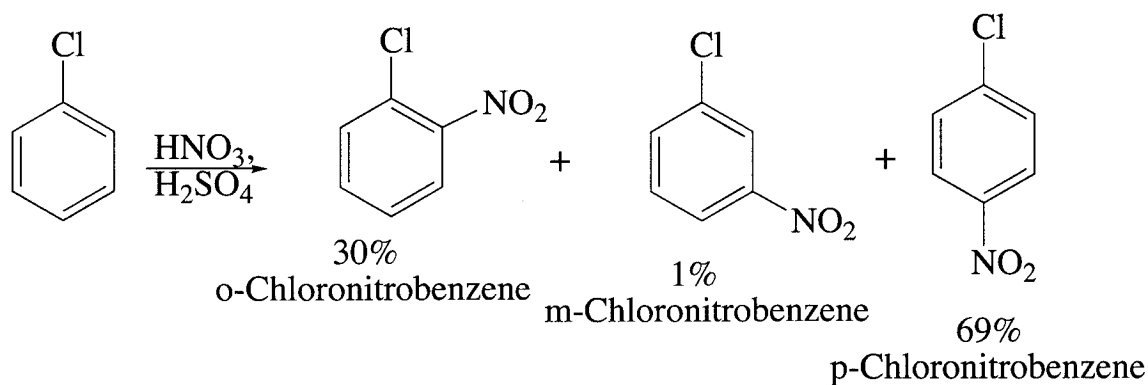
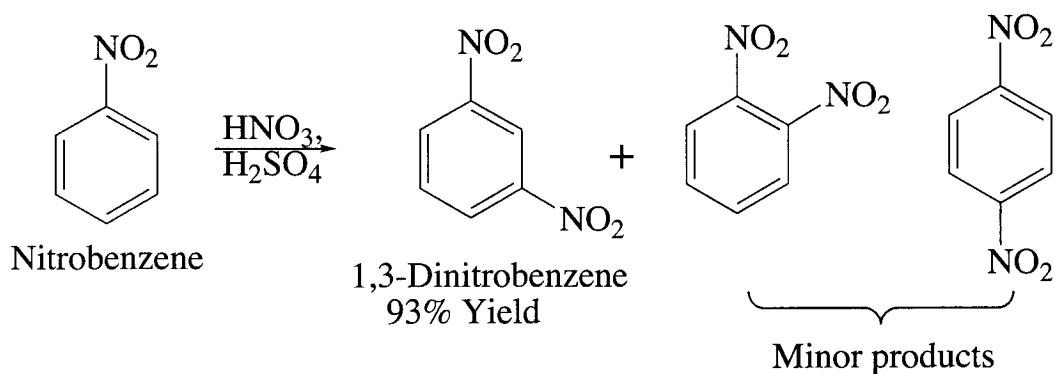
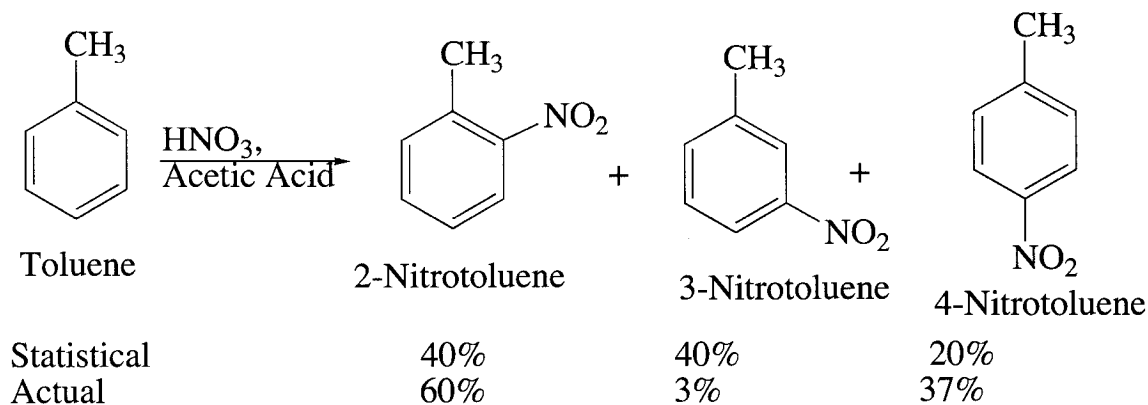
acid bromide

The anhydrides

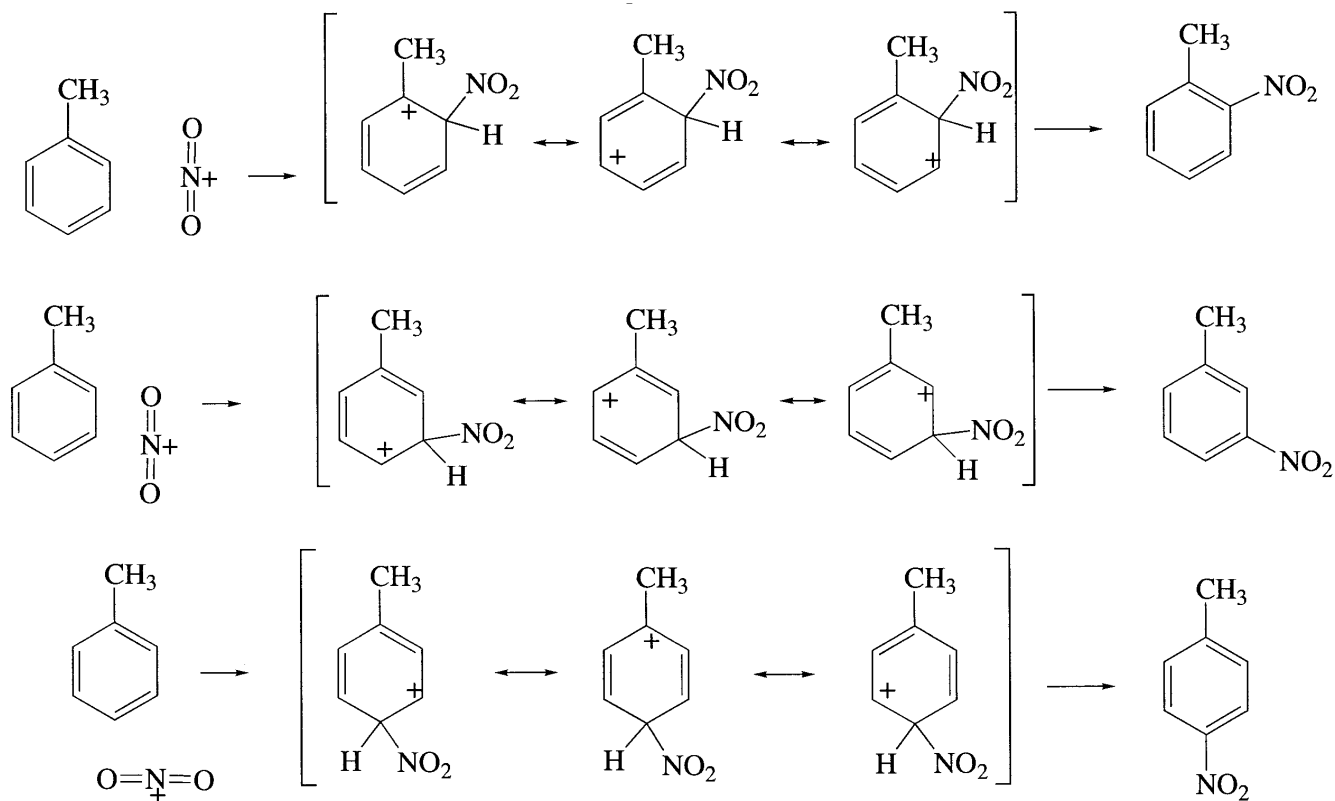


Electrophilic Aromatic Substitution on Substituted Benzenes

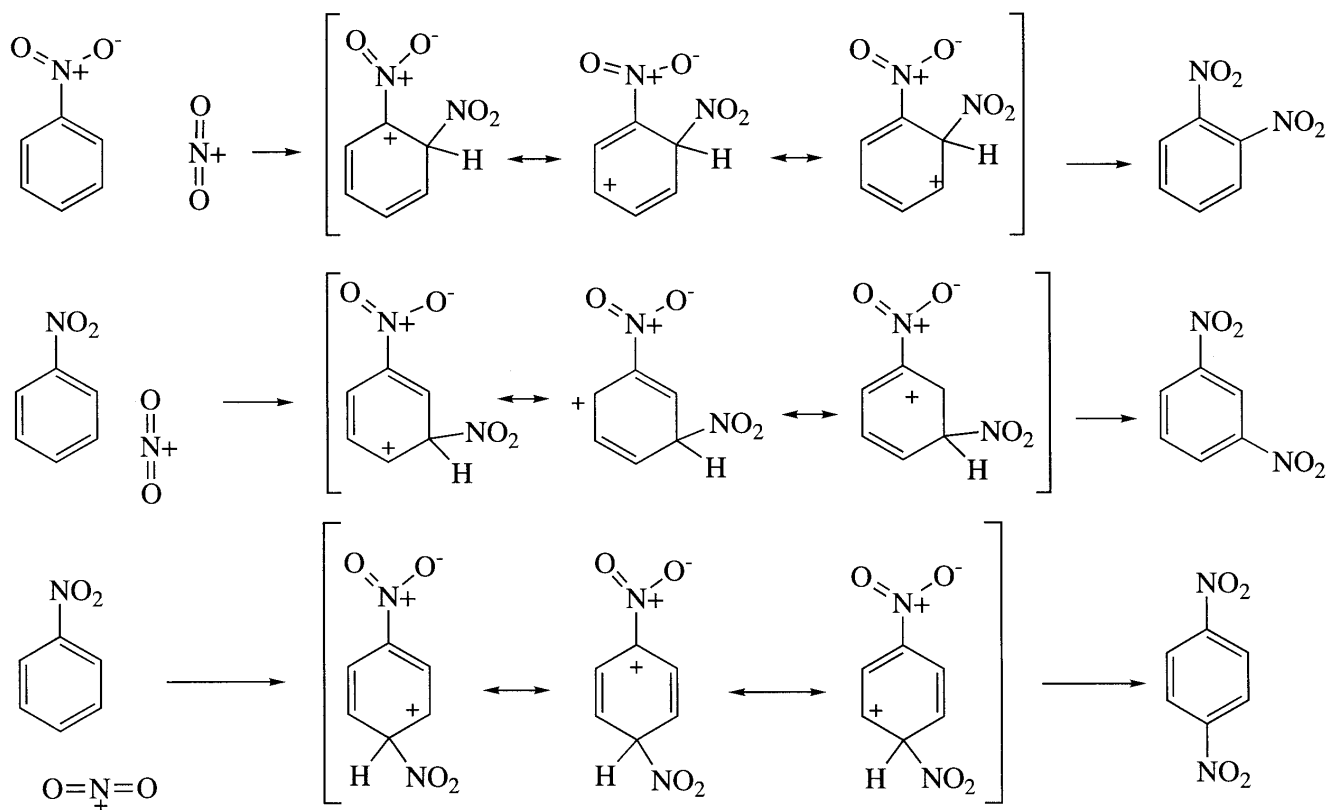
- In practice, some unusual results are encountered. Consider the following:



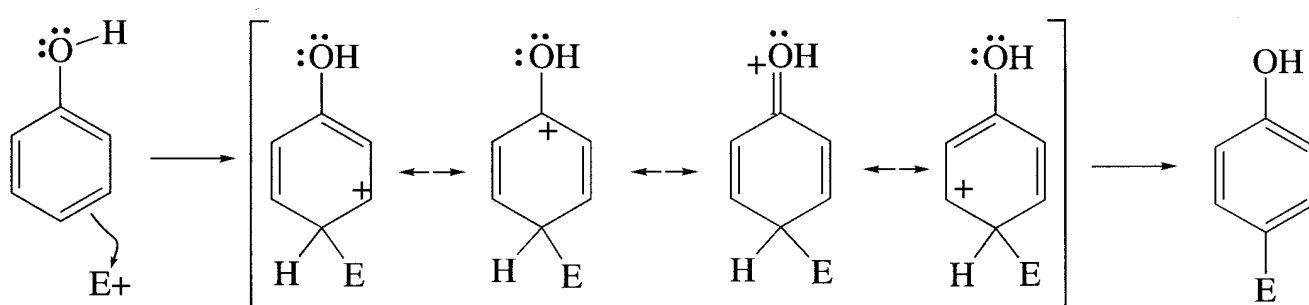
- We consider two cases to explain these observations: #1 direction *via* activation



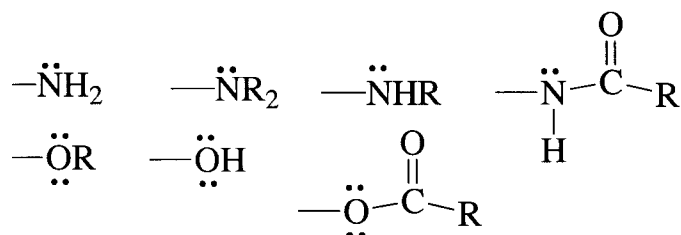
- #2 direction *via* deactivation



- Substituents with adjacent lone pairs are a special case



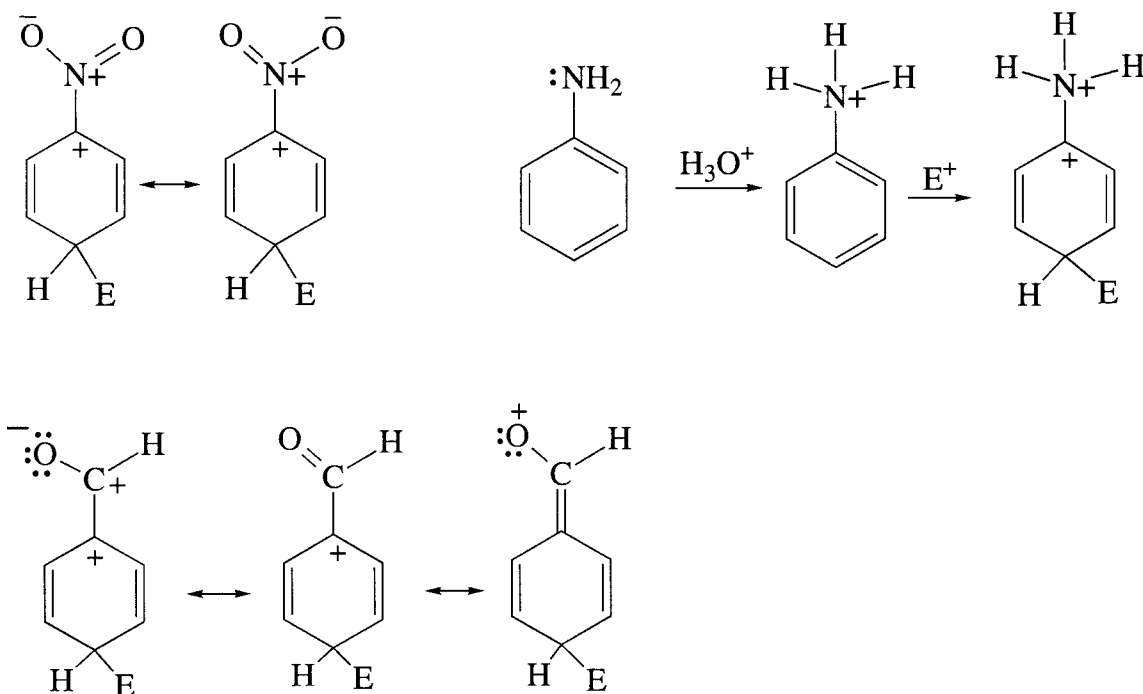
Groups that count as *o,p* directors and are activating are:



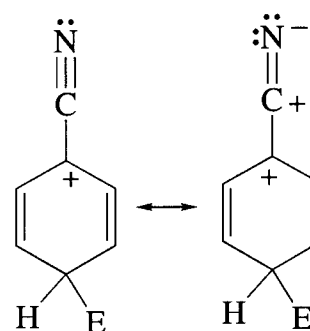
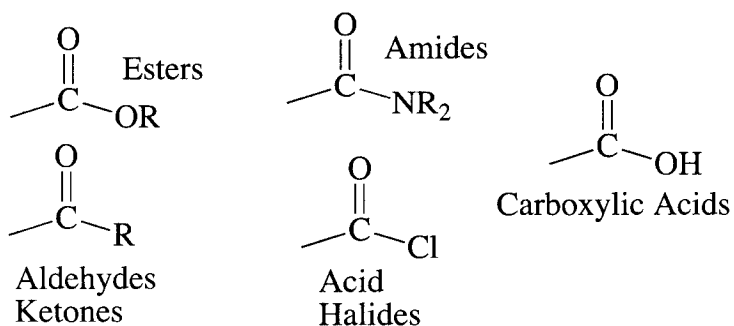
Groups that count as *o,p*-directors, but are *deactivating* are:



- Meta* directing groups include the following:



All of the following are meta-directors:

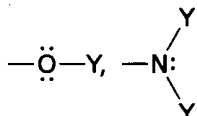
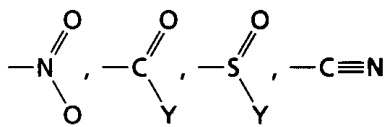


For similar reasons, nitrile substituents are also meta-directors.

A Summary of Directing Effects for Electrophilic Aromatic Substitution

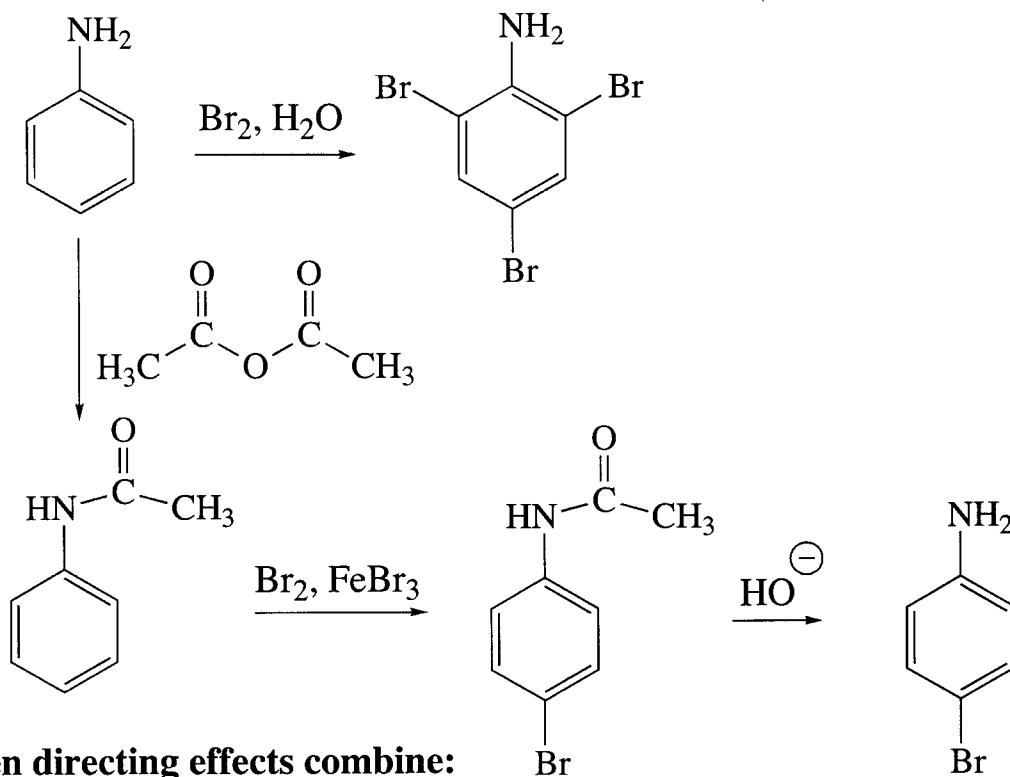
Table 12.1

The reactivity of  toward electrophilic substitution.

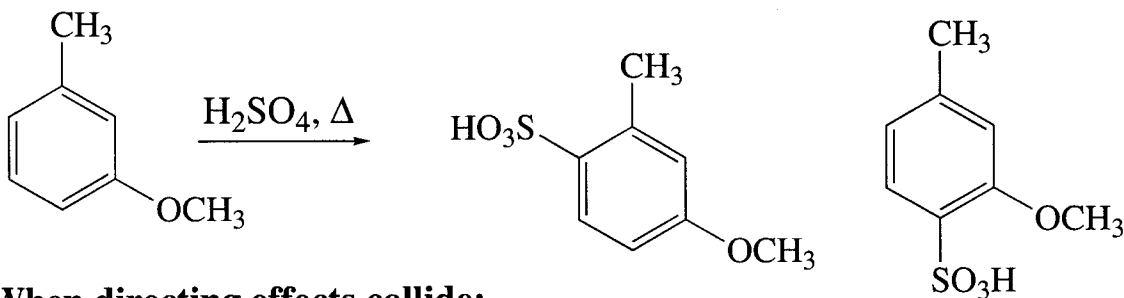
X	<i>Rate of reaction vs. benzene</i>	<i>Position of substitution</i>	<i>Electronic factors</i>
—alkyl	Faster	<i>ortho, para</i>	Inductive > resonance
 $Y = H, \text{ alkyl, aryl, acyl}$	Faster	<i>ortho, para</i>	Resonance > inductive Stabilization of charged intermediates
— \ddot{X} : $X = Cl, Br, I$	Slower	<i>ortho, para</i>	Inductive > resonance
 $Y = H, OH, \text{ alkyl, aryl, alkoxy}$	Slower	<i>meta</i>	Resonance = inductive Deactivation of <i>ortho</i> and <i>para</i> positions
— NR_3^+	Slower	<i>meta</i>	Inductive > resonance

- Some additional considerations

Aniline tends to over-react



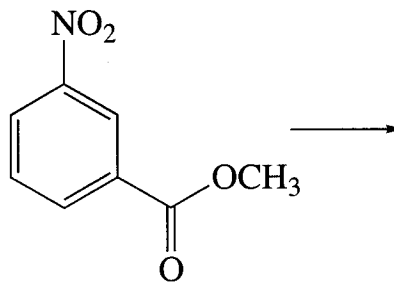
When directing effects combine:



When directing effects collide:



When deactivating effects combine:

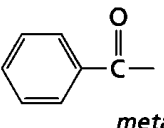
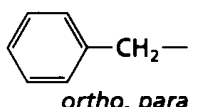
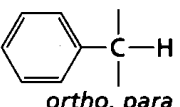
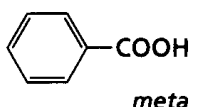
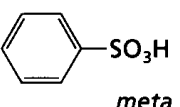
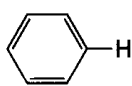
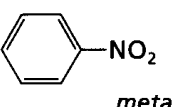
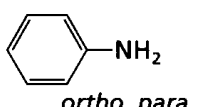
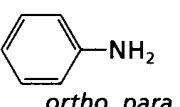
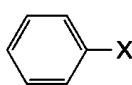


Important non-EAS Reactions that are Utilized in Conjunction with EAS reactions

- Include the protection/deprotection sequence for anilines
- Include the reversibility of sulfonation (also a protecting/deprotecting sequence)
- Alkyl groups on aromatic rings are more susceptible to oxidation to carboxylic acids
- Aniline is synthesized *via* reduction of nitro groups (no other method!)
- Aniline can itself easily be replaced by other groups

Table 12.2

Equivalent functional groups in substituted benzene derivatives, including those with different directing influences in electrophilic substitution reactions.

<i>This functionality:</i>	<i>Is equivalent to:</i>	<i>Reaction type</i>
 <i>meta</i>	 <i>ortho, para</i>	Reduction (Clemmensen, Wolff-Kishner, Raney Ni, H ₂ and Pd/C)
 <i>ortho, para</i>	 <i>meta</i>	Oxidation with permanganate or dichromate
 <i>meta</i>		Acid hydrolysis (aqueous H ₂ SO ₄)
 <i>meta</i>	 <i>ortho, para</i>	Reduction (SnCl ₂ /HCl; H ₂ /Pd)
 <i>ortho, para</i>		X = H, F, Cl, Br, I, CN, NO ₂ via diazonium salt (Chapter 23)

Propose syntheses for:

