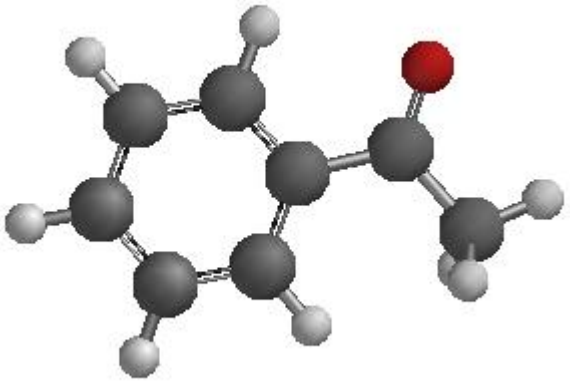
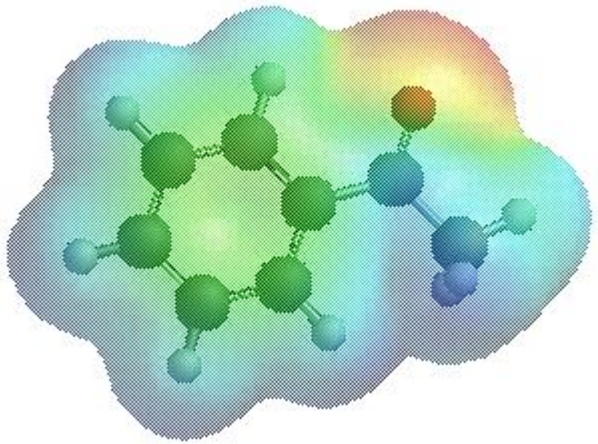
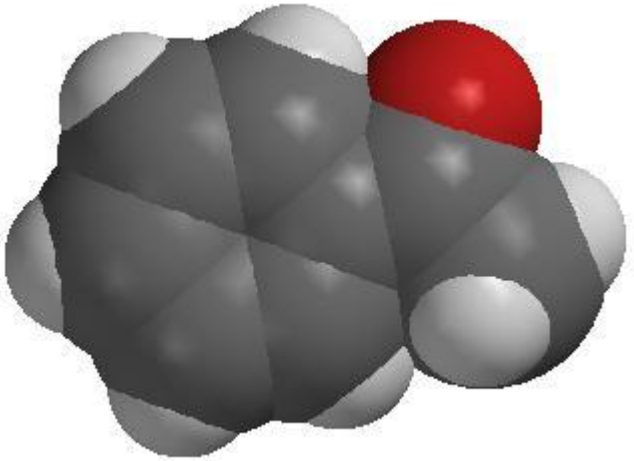




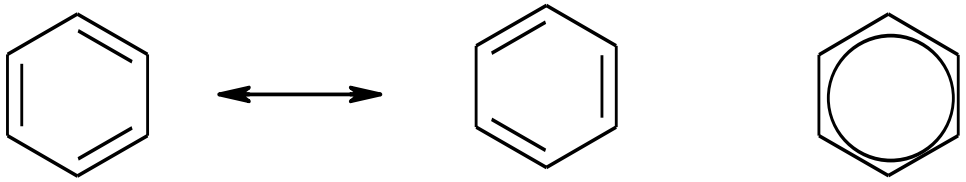
Chapter 4: Aromatic Compounds



General Properties

Benzene:

- formula: C_6H_6
- IHD: 4 (highly unsaturated)
- chemical reactivity: substitution, but only 1 product ∴ all H atoms must be equivalent
- structure: cyclic, planar, sp^2 hybridized
  - Benzene is cyclic, is planar,
  - has an interrupted cloud of π electrons,
  - and has three pairs of electrons in the π cloud.



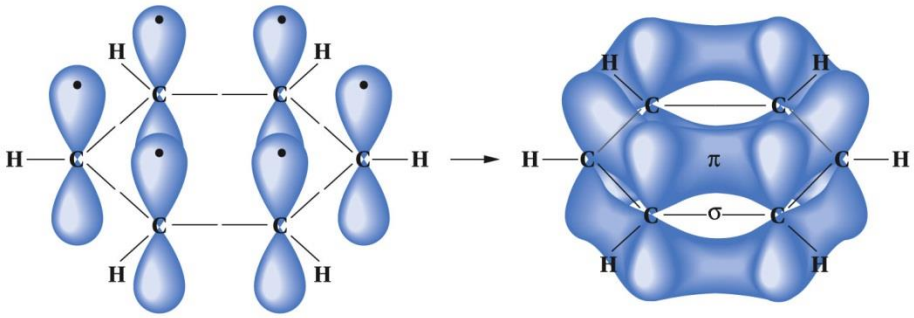
Kekule structure

Robinson structure

General Properties

Benzene:

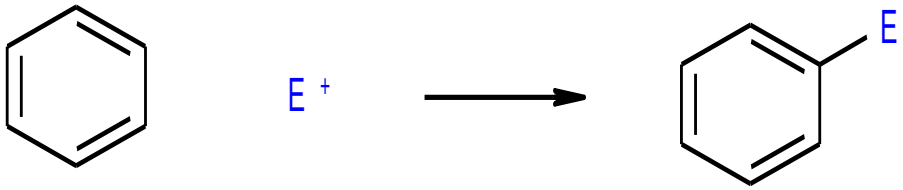
- C-C bond length: 1.39 Å
  - Intermediate to C-C (1.54 Å) and C=C (1.34 Å)
  - All C-C bond lengths are the same ➔ resonance!

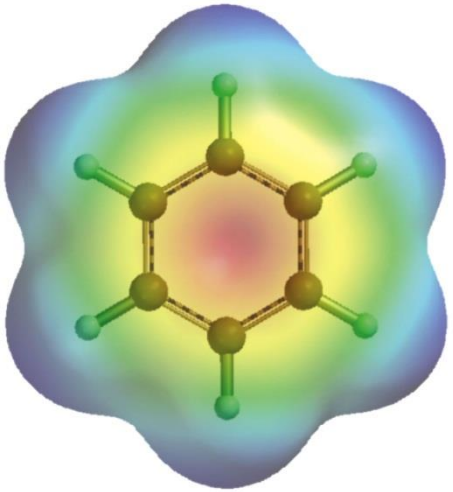


General Properties

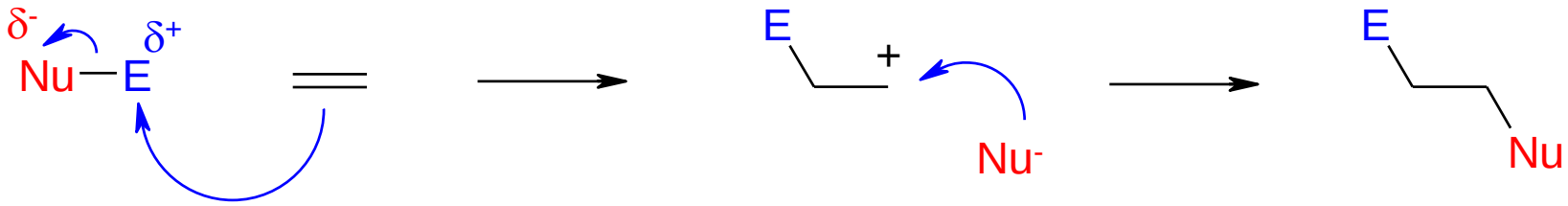
Benzene:

Chemical reactivity: electrophilic substitution





as opposed to electrophilic addition



General Properties

Why the difference between benzene and an alkene?

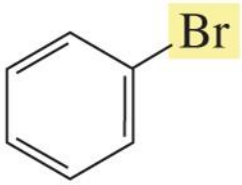
Aromaticity: the extra stability associated with aromatic compounds.

Aromatic compounds are:

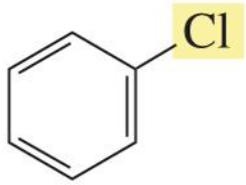
- Cyclic
- planar
- fully conjugated
- contain $4n + 2$ π electrons (n=1,2,3…) (Huckel's rule: equivalent to an odd number of π electrons pairs in the ring system).

Naming Monosubstituted Benzenes

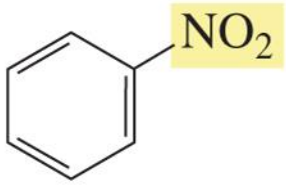
Some monosubstituted benzenes are named
by adding the name of the substituent to "benzene."



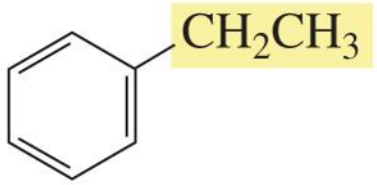
bromobenzene



chlorobenzene



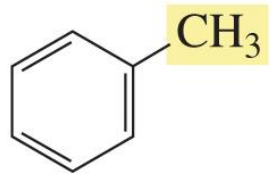
nitrobenzene



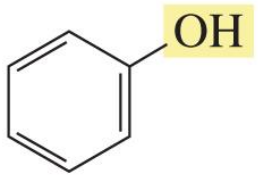
ethylbenzene

Naming Monosubstituted Benzenes

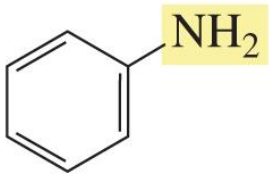
Some monosubstituted benzenes have names that incorporate the substituent.



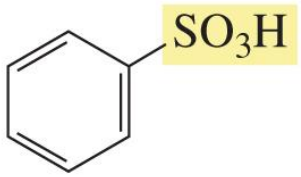
toluene



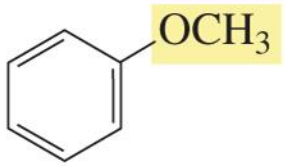
phenol



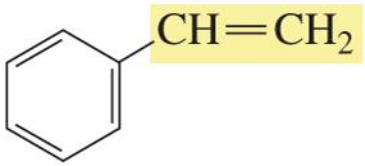
aniline



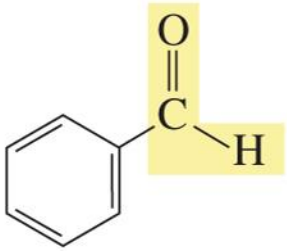
benzenesulfonic acid



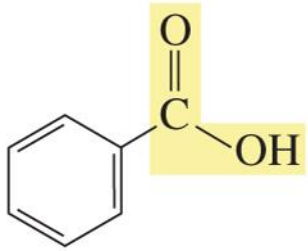
anisole



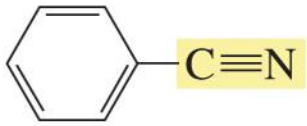
styrene



benzaldehyde

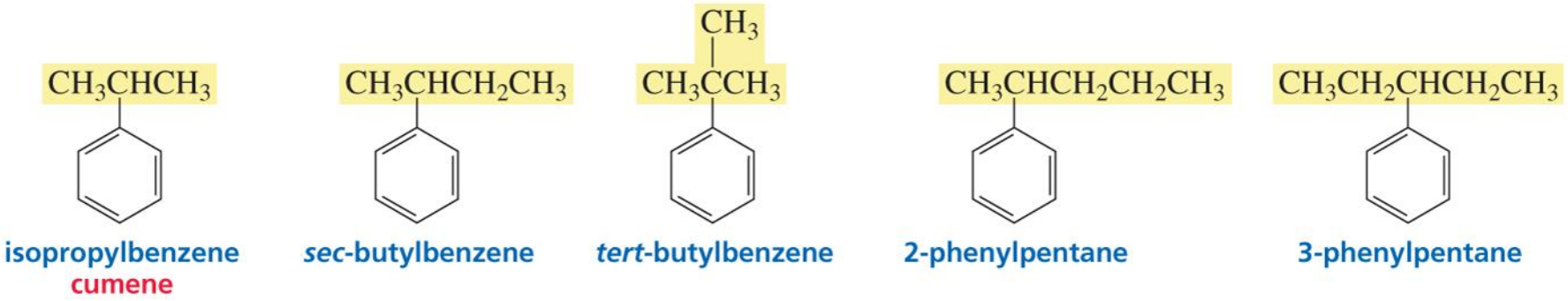


benzoic acid



benzonitrile

Alkyl-Substituted Benzenes

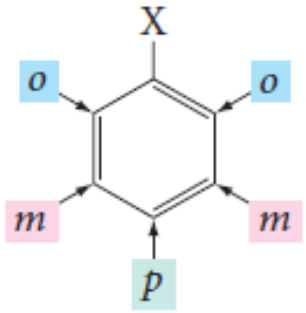


Name as an alkyl-substituted benzene
when the alkyl group has a name.

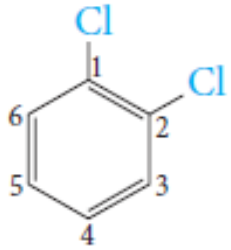
Otherwise, name as a phenyl-substituted alkane.

Toluene (methyl substituent on benzene) is an exception.

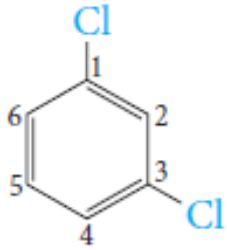
When two substituents are present, three isomeric structures are possible.



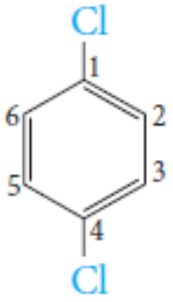
Specific examples are



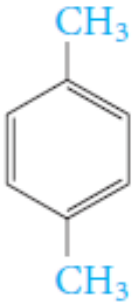
ortho-dichloro-benzene



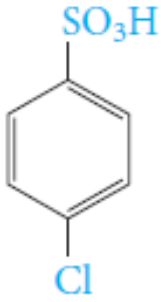
meta-dichloro-benzene



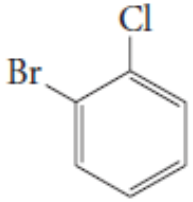
para-dichloro-benzene



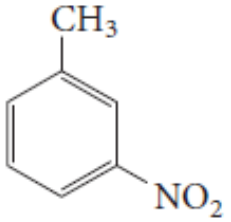
para-xylene**



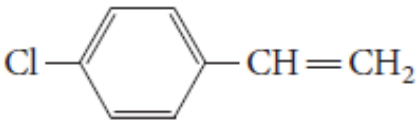
para-chlorobenzene-sulfonic acid



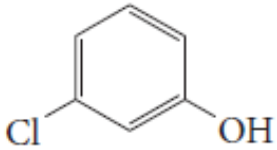
o-bromochlorobenzene
(note alphabetical order)



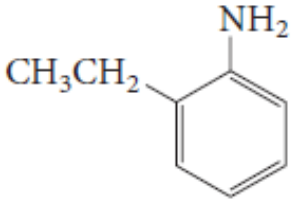
m-nitrotoluene



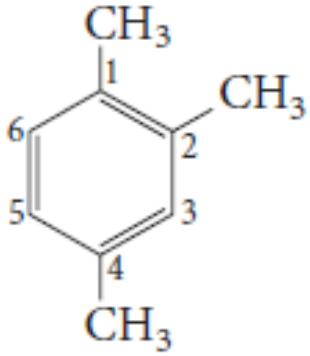
p-chlorostyrene



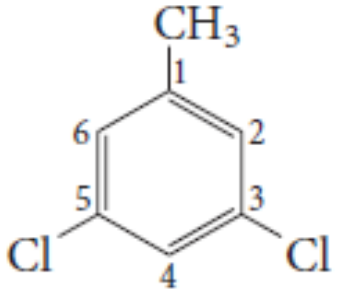
m-chlorophenol



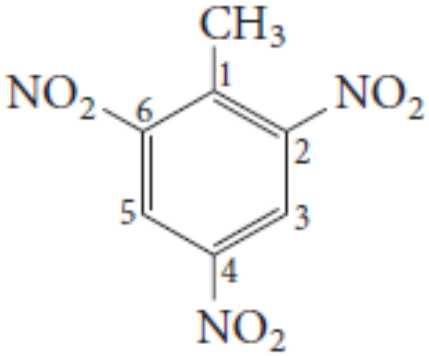
o-ethylaniline



1,2,4-tri-
methylbenzene

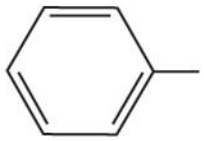


3,5-dichlorotoluene

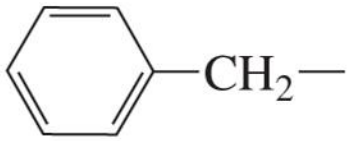


2,4,6-trinitrotoluene
(TNT)

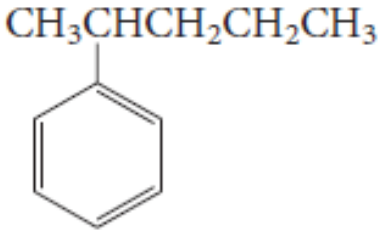
Phenyl and Benzyl Substituents



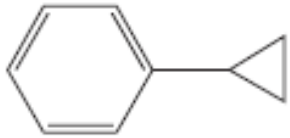
phenyl group



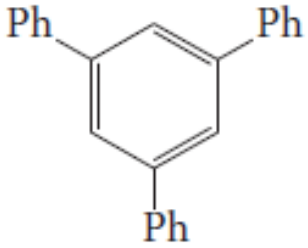
benzyl group



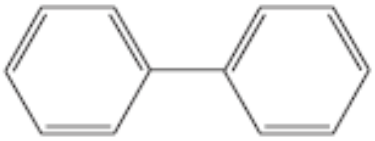
2-phenylpentane
(or 2-pentylbenzene)



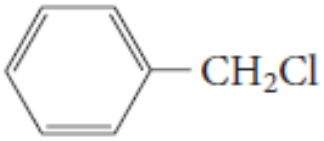
phenylcyclopropane
(or cyclopropylbenzene)



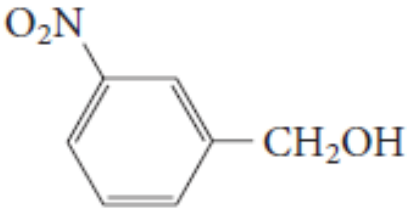
1,3,5-triphenylbenzene



biphenyl



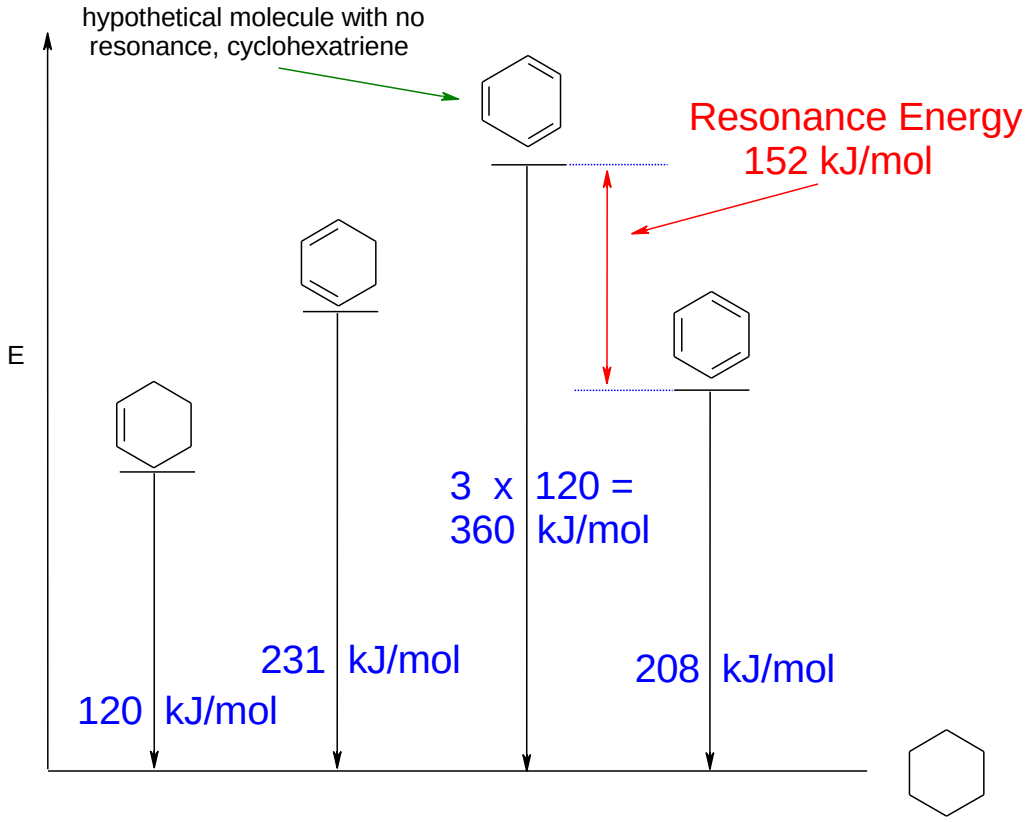
benzyl chloride



m-nitrobenzyl alcohol

Resonance Energy

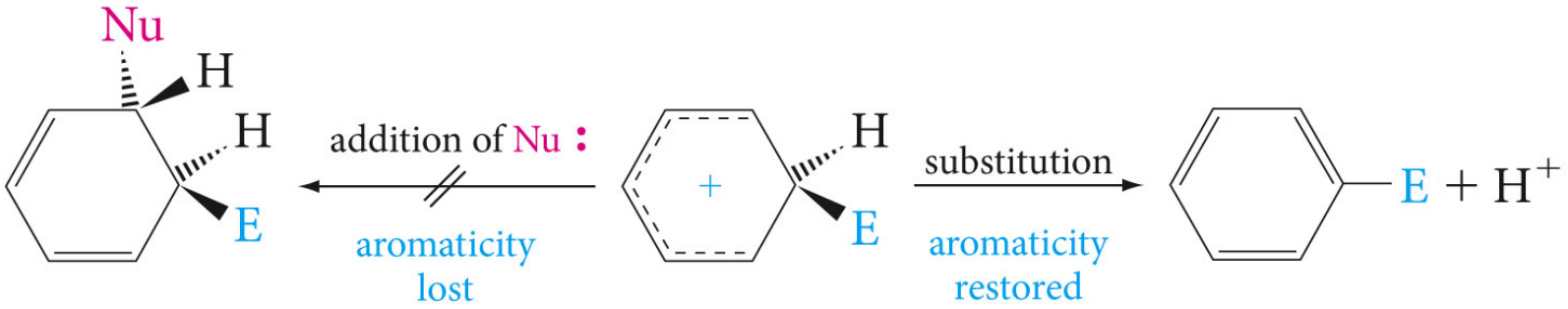
The resonance energy is a measure of the extra stability of the cyclic conjugated system compared to the corresponding number of isolated double bonds, i.e.



Resonance Energy

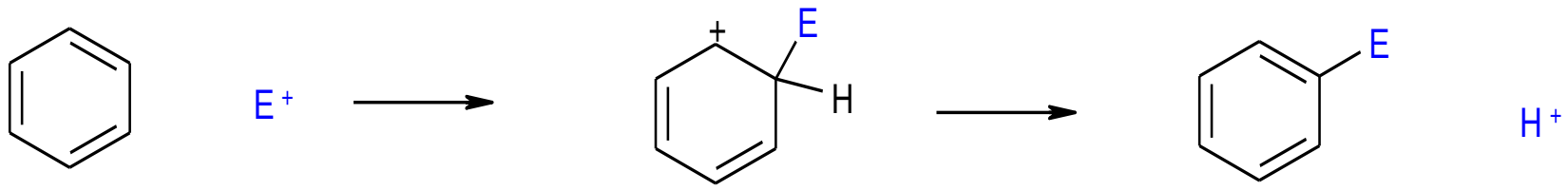
The large resonance stabilization energy seen in aromatic compounds results in two effects on their chemical reactivity:

1) Since the resonance stabilization energy is lost when an electrophile adds to the ring you need to use much stronger electrophiles than for alkenes/alkynes, generally this means using a catalyst.
2) The resonance energy can be regained if the intermediate carbocation loses a H^+, this results in a substitution rather than the addition seen in alkenes/alkynes. The H^+ is lost to a base, even weak ones suffice here.

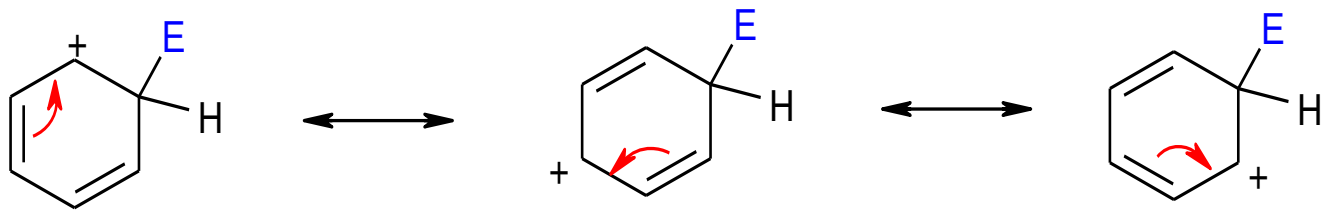


Mechanism of Electrophilic Aromatic Substitution (EArS)

In general all EArS reactions proceed by the same mechanism:



benzenonium ion
(a carbocation)

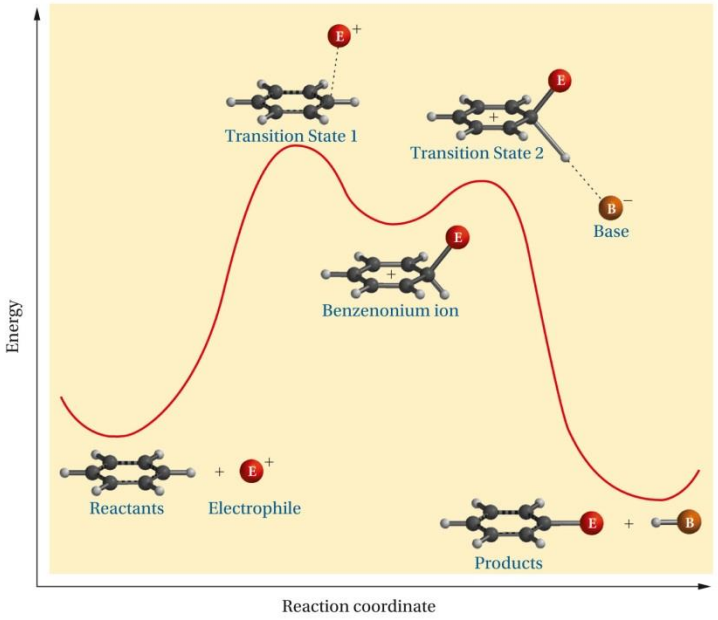


ortho para ortho

Benzenonium resonance structures

Mechanism of Electrophilic Aromatic Substitution (EArS)

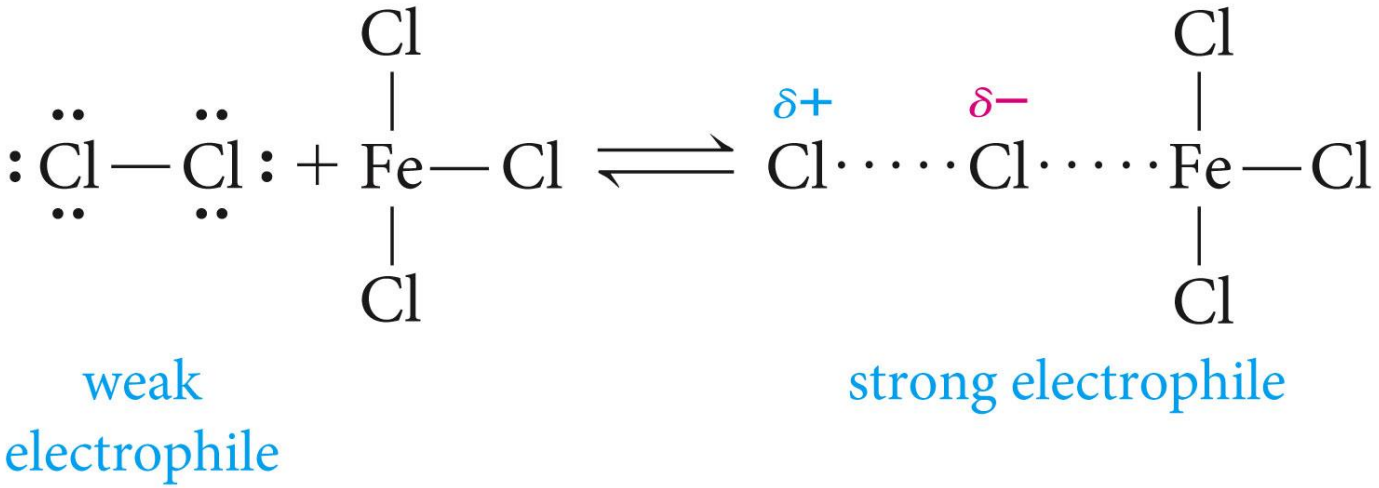
As with allenes and alkynes, the carbocation generated by the addition of the electrophilic is a stable intermediate, i.e.



The formation of the carbocation is the rate determining step as it takes energy to break the aromaticity.

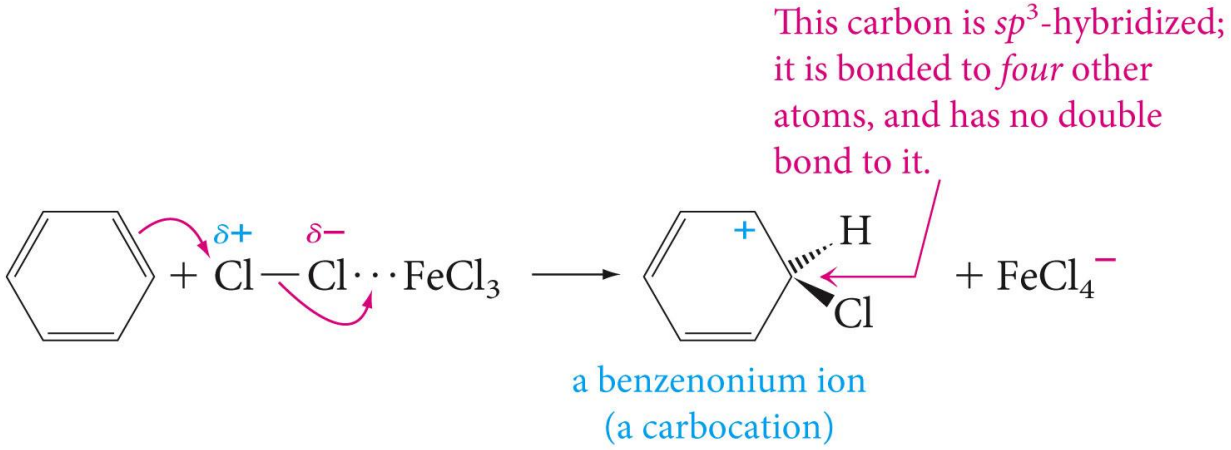
EArS - Halogenation

- Cl_2 and Br_2 are weak electrophiles on their own so need to be "activated" by using a Lewis acid catalyst.
- Commonly the corresponding iron trihalide is used, $FeCl_3$ or $FeBr_3$

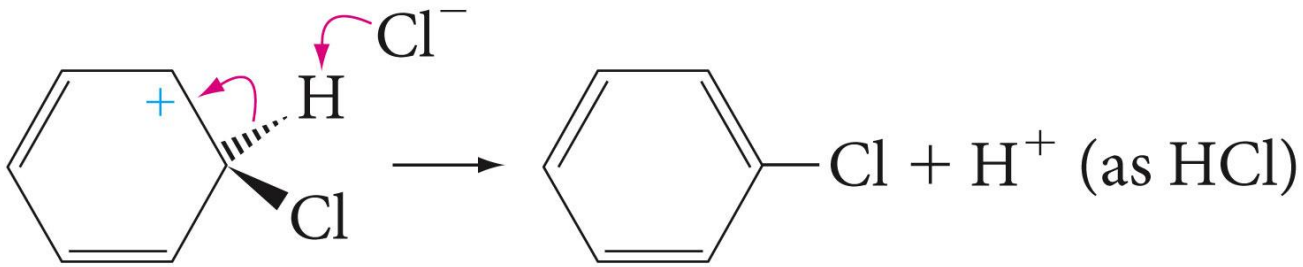


EArS - Halogenation

The rate determining step is:

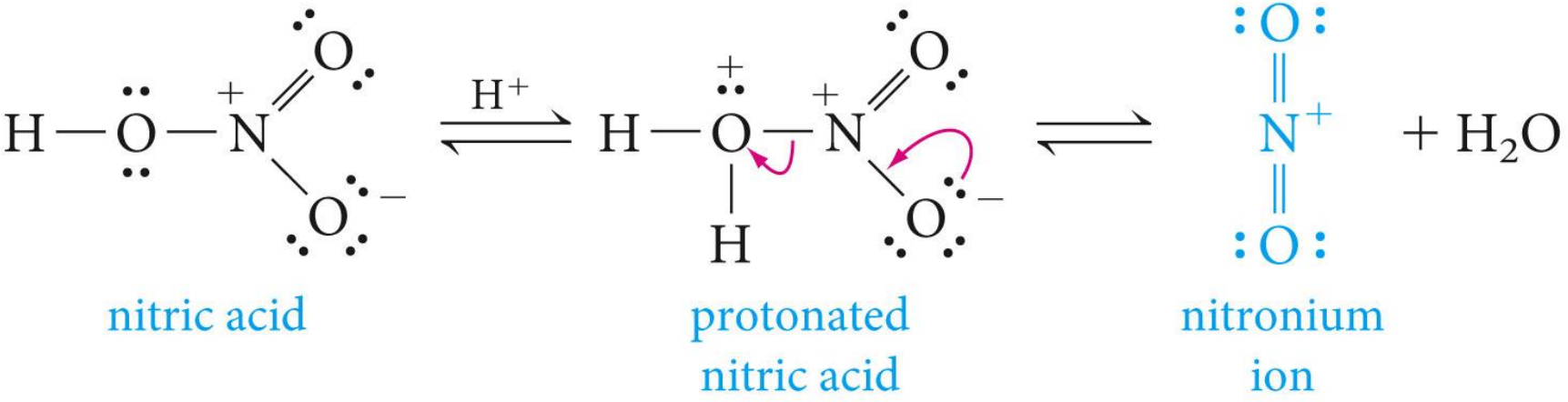


The base in this case is the chloride ion:



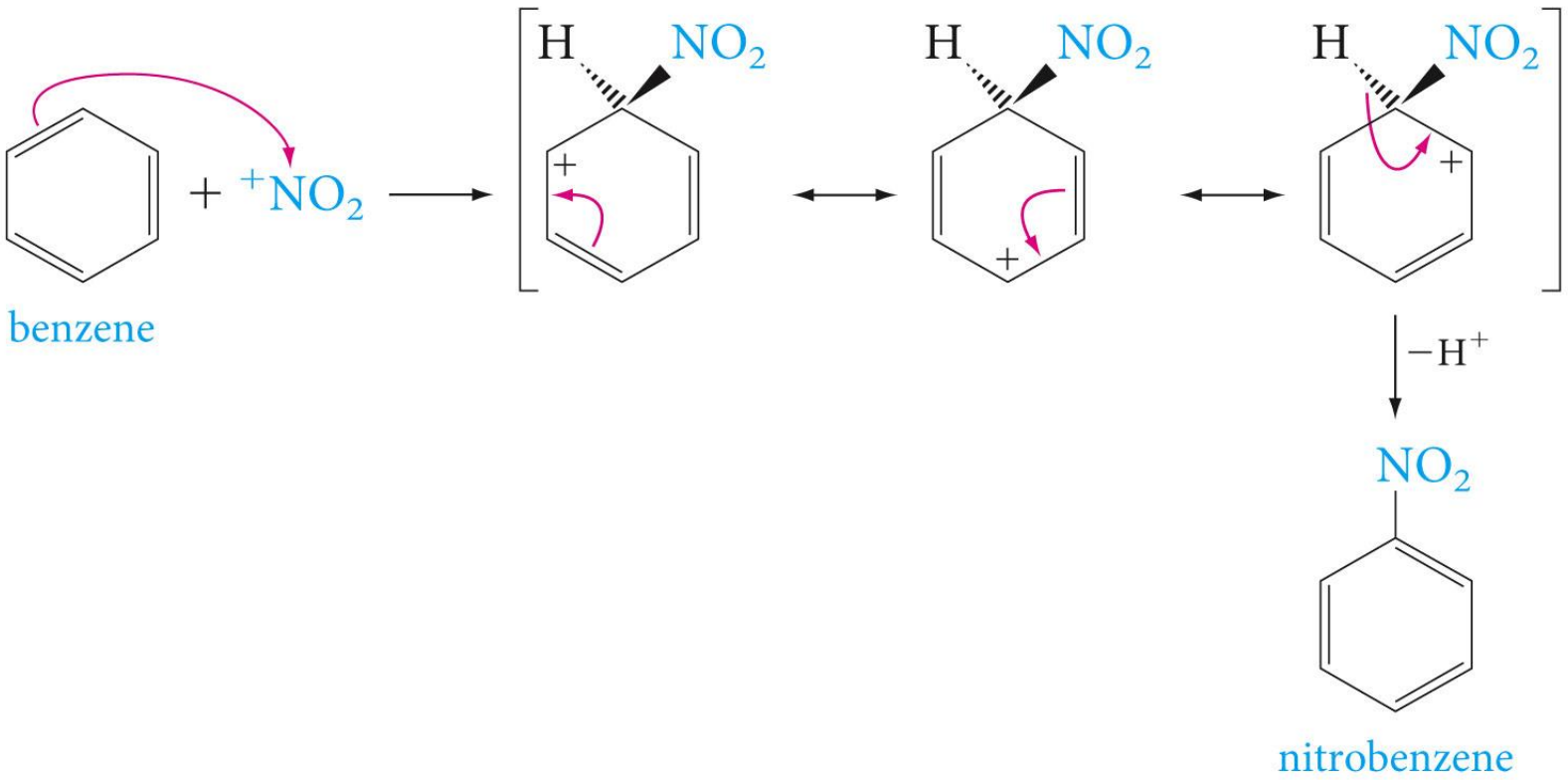
EArS - Nitration

In the case of nitration, sulfuric acid is used to generate a more reactivity electrophile, a nitronium ion.



EArS - Nitration

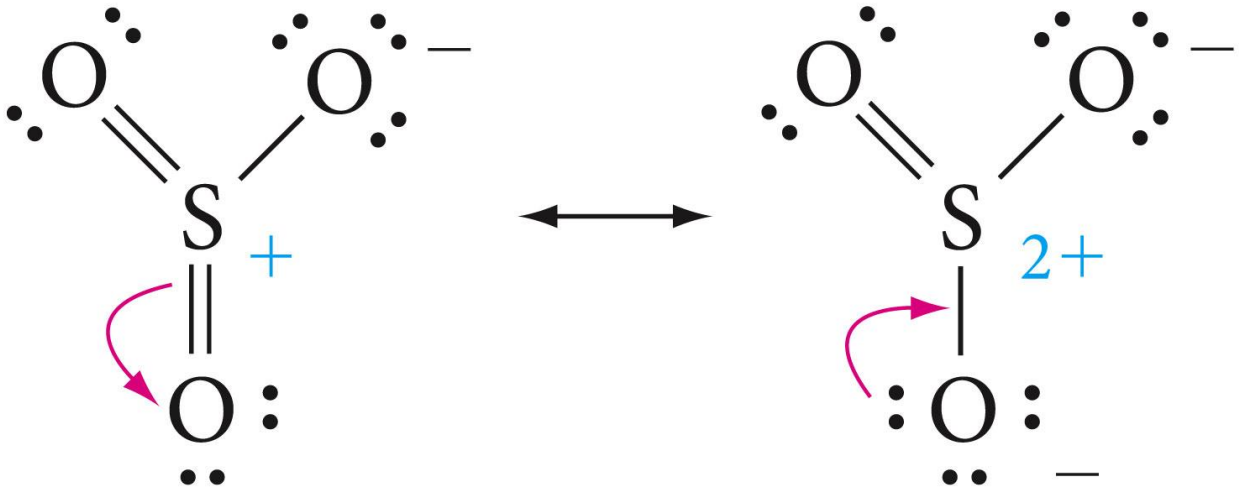
The product of the reaction is nitrobenzene, i.e.



EArS - Sulfonation

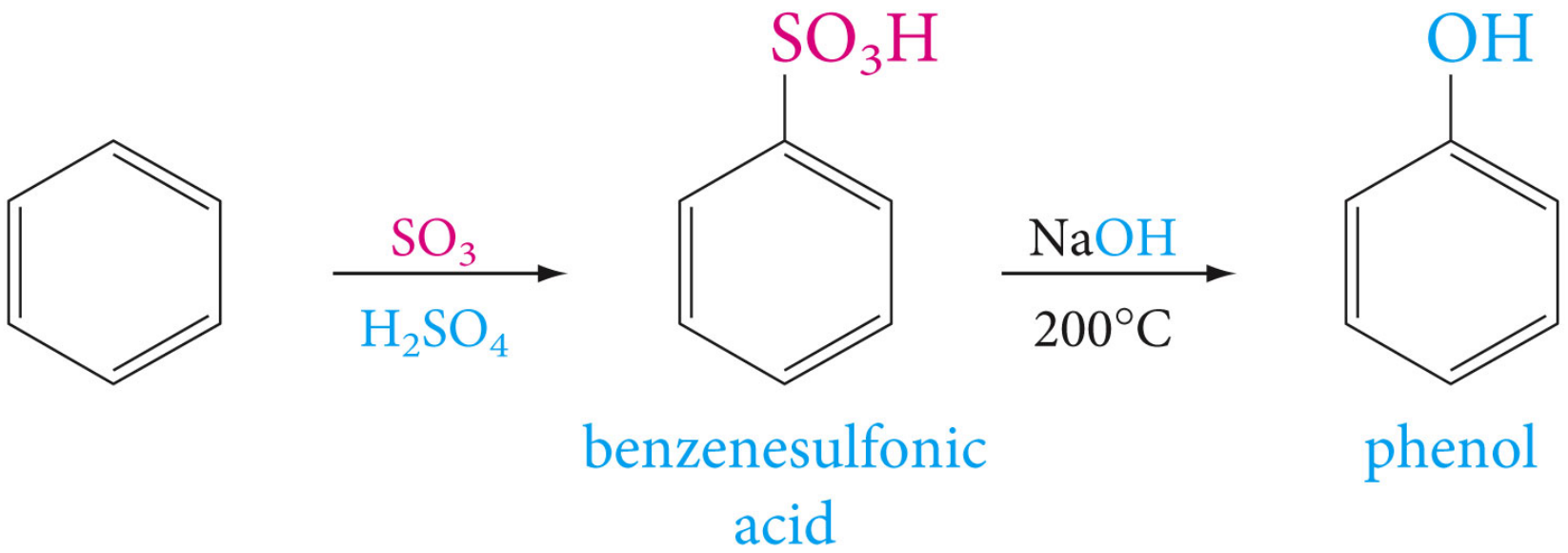
Sulfonation will generate a benzenesulfonic acid.

The electrophile used is sulfur trioxide, which is a strong electrophile, i.e.



EArS - Sulfonation

While benzenesulfonic acids are useful in their own right, they are also convenient as they can be modified to a phenol easily, i.e.



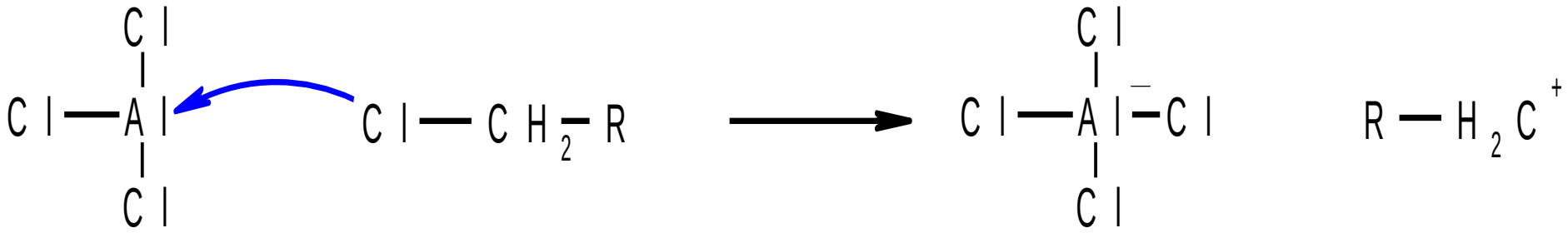
EArS - Alkylation

Alkylation will add an alkane group to benzene. In this case we need a carbocation as the electrophile. There are two ways to do this:

1) Friedel-Crafts alkylation
2) Alkylation using an alkene and acid

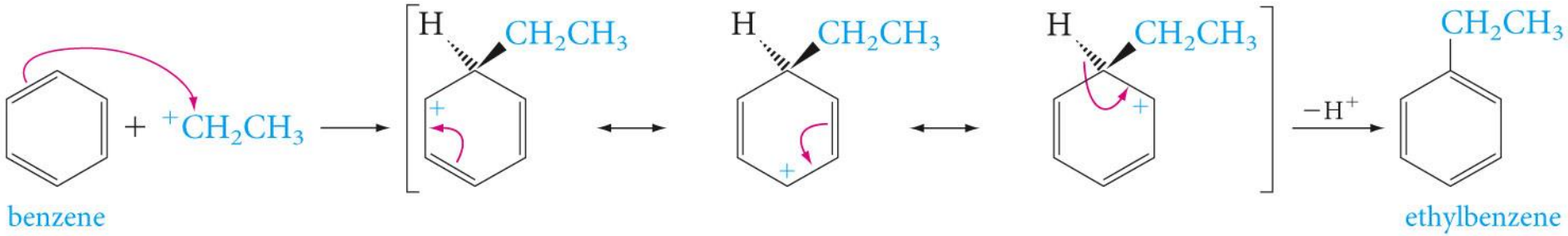
Friedel-Crafts Alkylation

This process uses an alkyl halide (Cl or Br usually) and a Lewis acid catalyst similar to a halogenation reaction. In this case we use the corresponding aluminum trihalide as the Lewis acid catalyst.



Friedel-Crafts Alkylation

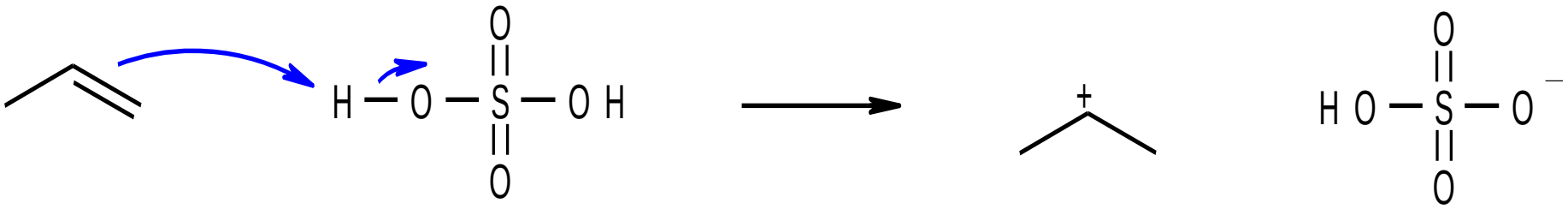
The product is an alkylbenzene, i.e.



Note: there are limitations to Friedel-Crafts reactions, they can not be done on a nitrobenzene or benzenesulfonic acid as these group complex with the aluminum chloride catalyst deactivation it.

Alkylation from Alkenes

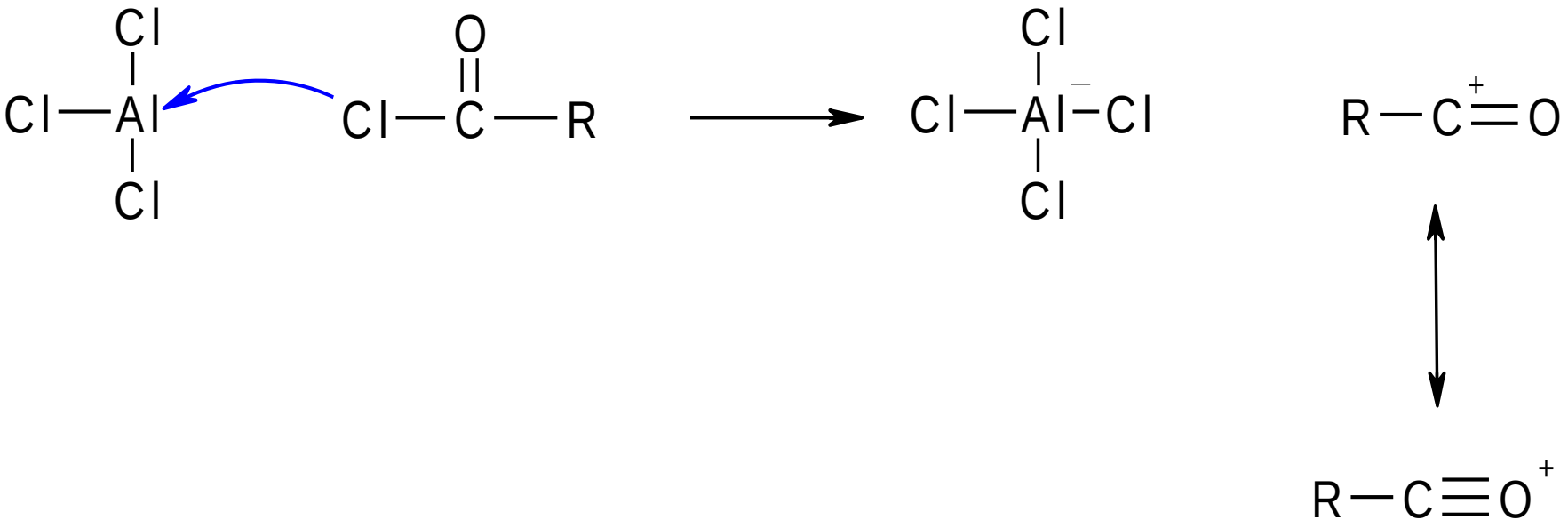
Alkylation can also be achieved by using an alkene and an acid (sulfuric as the conjugate base is a poor nucleophile), i.e.



Note: this will generate the Markovnikov carbocation!

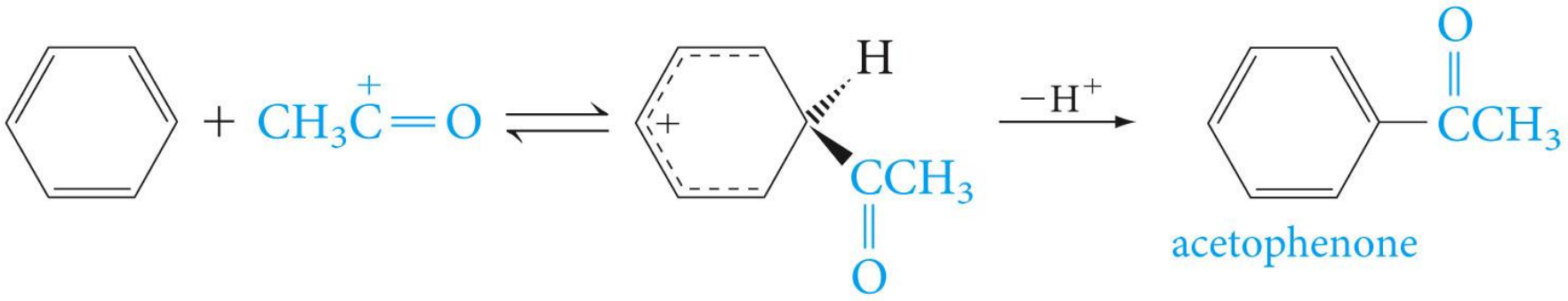
Friedel-Crafts Acylation

This process is identical to an alkylation except we use an acyl chloride, i.e.



Friedel-Crafts Acylation

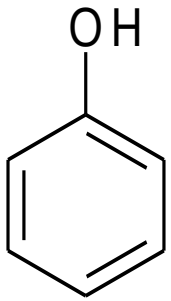
The product is a phenyl ketone, i.e.



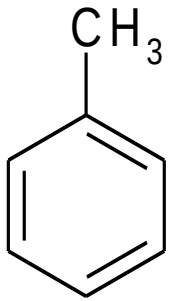
Note: the same limitations for nitro and sulfonic acid groups apply.

Reaction Rates

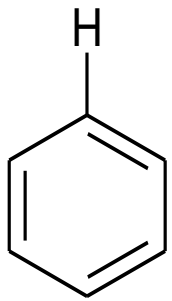
Experimentally you can observe the following relative rates of reaction:



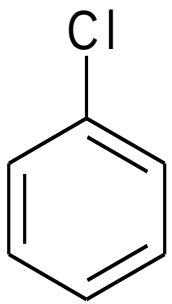
phenol
1000



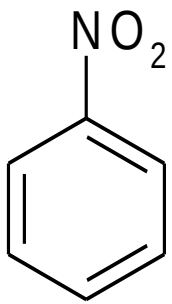
toluene
24.5



benzene
1



chlorobenzene
0.033

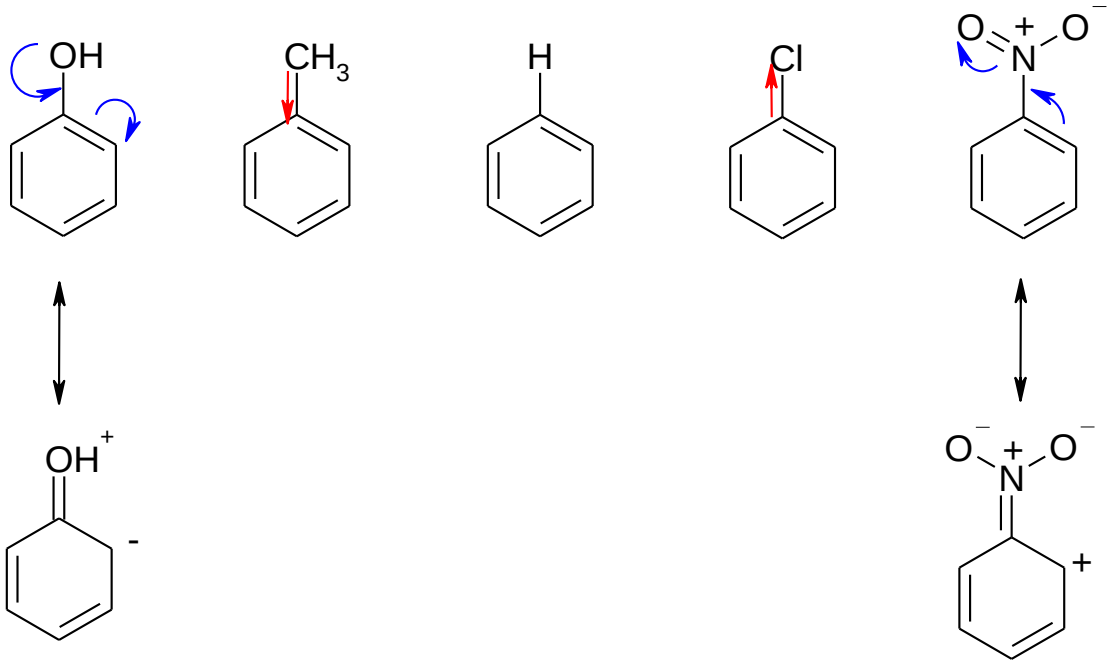


nitrobenzene
0.0000001

What is causing these differences?

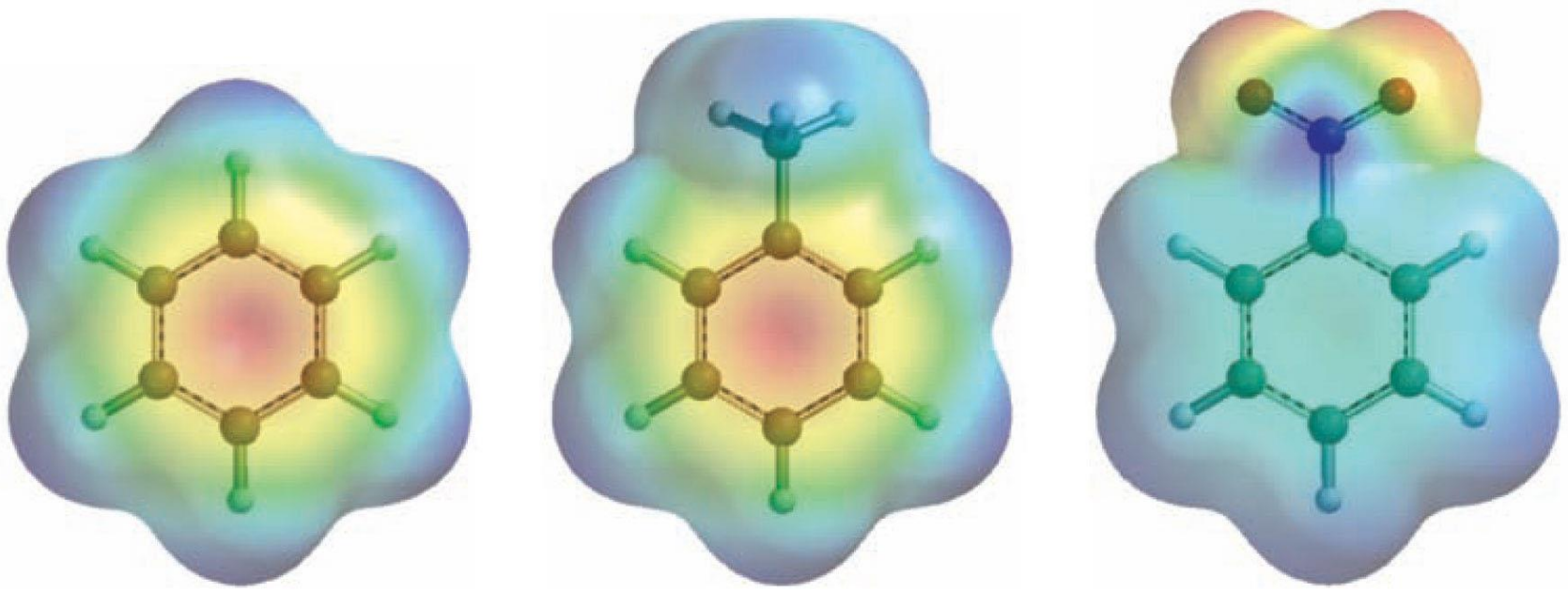
Reaction Rates

The reaction depends on the attack of an electrophile on the benzene ring, this means the charge density in the ring will be very important. Groups that increase the charge density will speed up the reaction while those that decrease charge density slow it down.



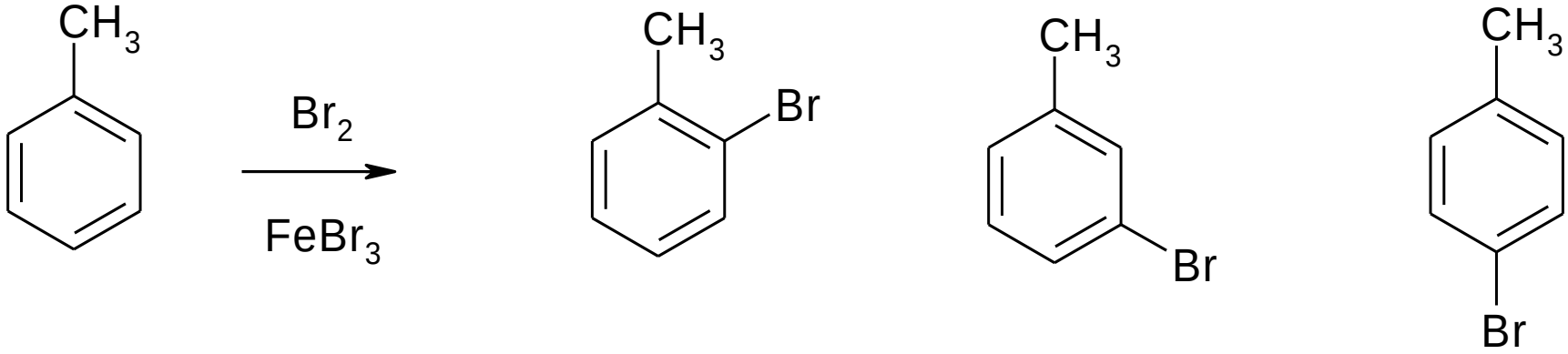
Reaction Rates

This can also be seen in the electron density of these molecules, i.e.

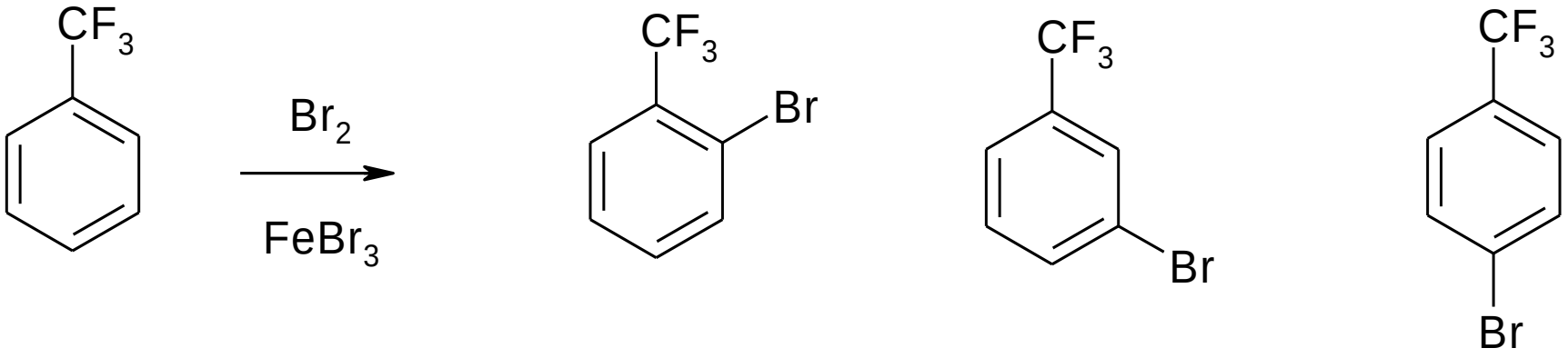


Directing Effects

A second experimental observation is:



per cent yield 63% 3% 34%



per cent yield 6% 91% 3%

Directing Effects

The directing effects are caused by the same processes that control the rate of the reaction. The table right groups substituents as o,p-directing or m-directing.

These are relative to an H atom.

Electron donating groups (EDG) activate the ring and are o,p-directing.

Electron withdrawing groups (EWG) deactivate the ring and are m-directing.

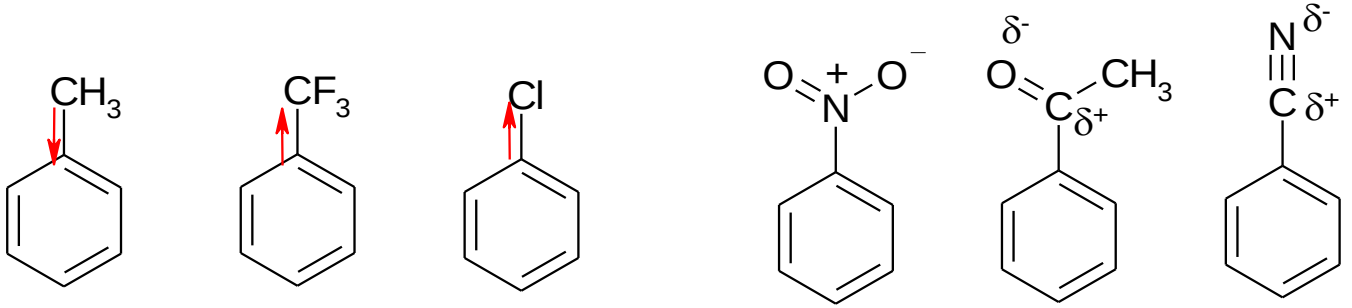
Why?

	Substituent group	Name of group	
Ortho,Para-Directing	$-\ddot{N}H_2$, $-\ddot{N}HR$, $-\ddot{N}R_2$	amino	Activating
	$-\ddot{O}H$, $-\ddot{O}CH_3$, $-\ddot{O}R$	hydroxy, alkoxy	
	$-\ddot{N}HC(=O)-R$	acylamino	
	$-CH_3$, $-CH_2CH_3$, $-R$	alkyl	
	$-\ddot{F}:$, $-\ddot{Cl}:$, $-\ddot{Br}:$, $-\ddot{I}:$	halo	Deactivating
Meta-Directing	$-C(=O)-R$ $-C(=O)-\ddot{O}H$	acyl, carboxy	
	$-C(=O)-\ddot{N}H_2$ $-C(=O)-\ddot{O}R$	carboxamido, carboalkoxy	
	$-S(=O)(=O)-\ddot{O}H$	sulfonic acid	
	$-C\equiv N:$	cyano	
	$-N^{+}(=O:)-\ddot{O}:^{-}$	nitro	

Directing Effects

Two effects can account for these observations:

1) *Inductive effects*: this is the donation or withdrawal of electron density through the bond due to the EN of the atom.
   - Alkyl groups are weakly EDG so activating
   - Halides are more EN so weakly EWG and deactivating, but o,p-directing because of the lone pair electrons
   - Any group where the atom attached to the ring has a formal or partial positive charge and no lone pair electrons, this includes nitro, cyano, carbonyl and alkyl halides.

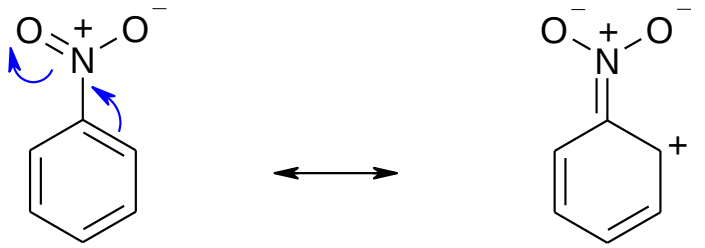


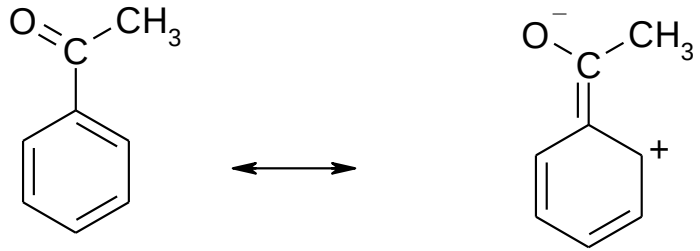
Directing Effects

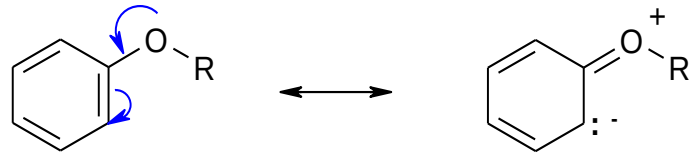
2) *Resonance effects*: this is the donation or withdrawal of electrons in the π system by resonance.
   - Any group where the atom attached to the ring has a lone pair of electrons such as N and O. These are activating.
   - Halides are more EN so weakly EWG and deactivating, but o,p-directing because of the lone pair electrons
   - Any group where the atom attached to the ring has a formal or partial positive charge and no lone pair electrons but attached to a more EN atom by multiple bonds, this includes nitro, cyano, sulfonyl and carbonyl groups.

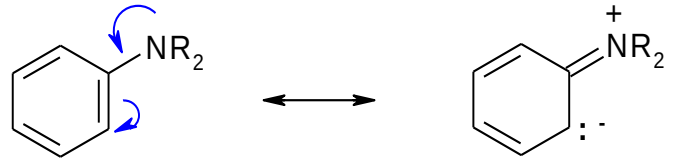
Directing Effects

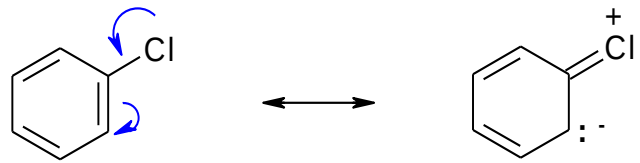
Examples of resonance effects:











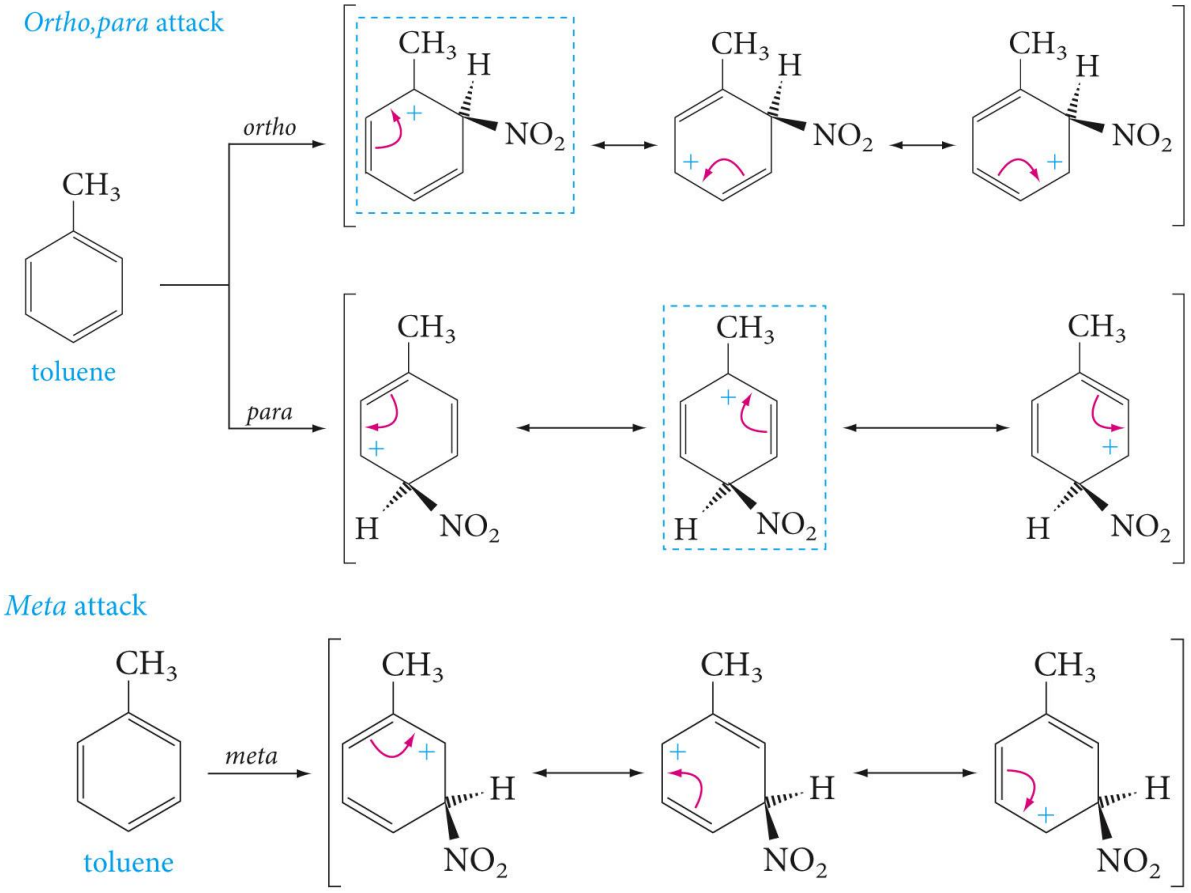
Electron withdrawal:

Electron donation:

Directing Effects

So how does this effect a reaction?

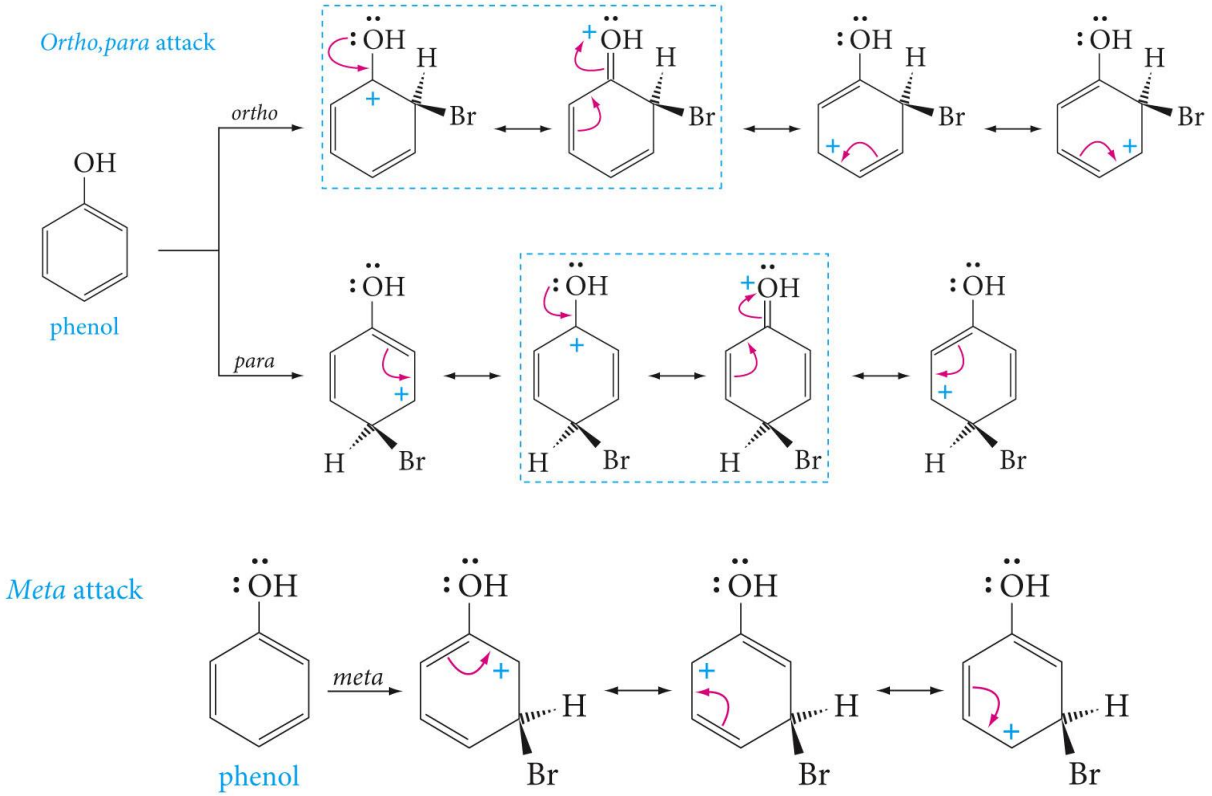
Activating o,p-directing group, i.e. CH_3



Directing Effects

So how does this effect a reaction?

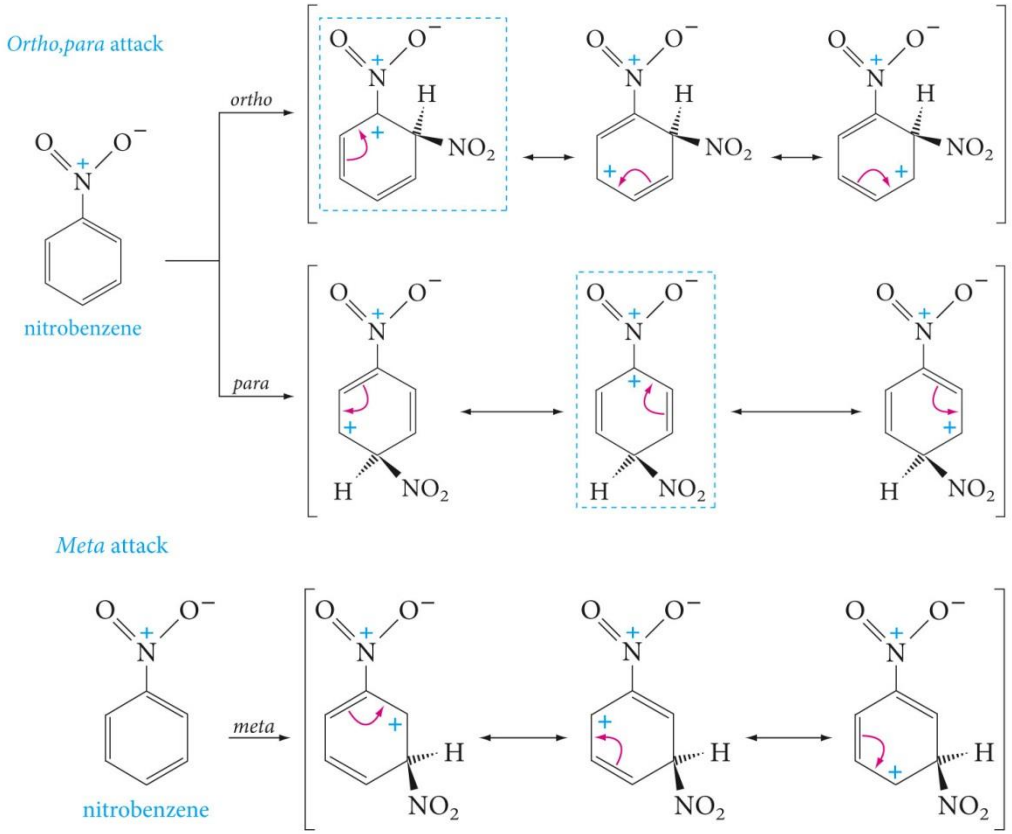
Activating o,p-directing group, i.e. OH



Directing Effects

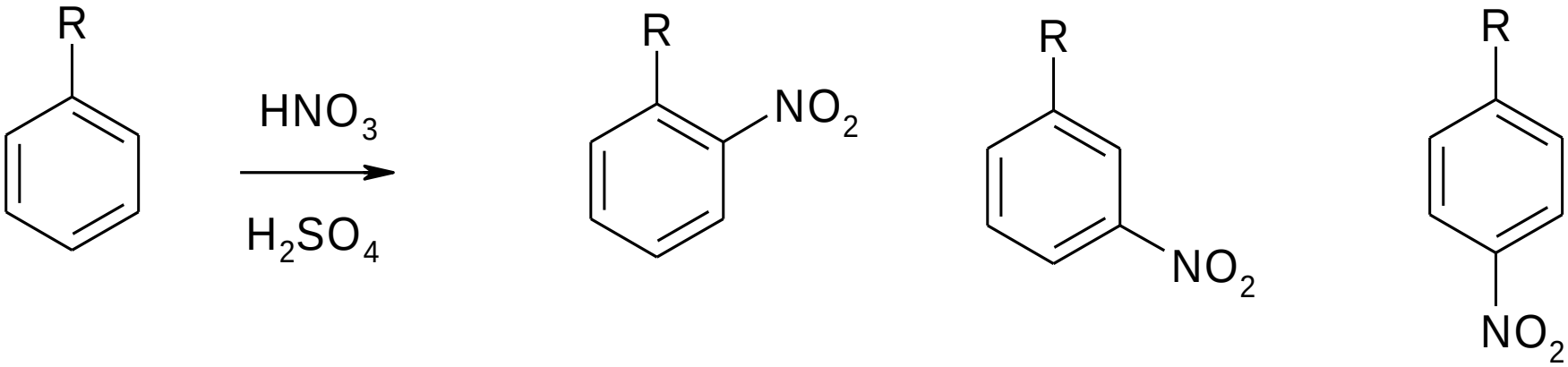
So how does this effect a reaction?

Deactivating m-directing group, i.e. NO_2



Directing Effects

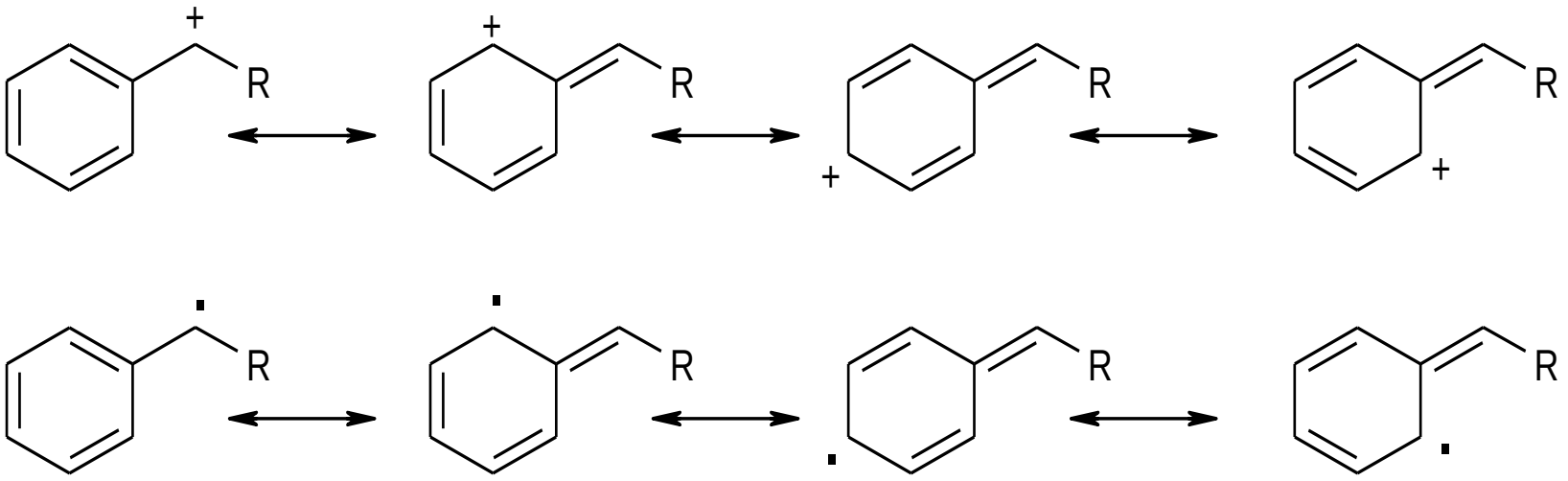
Besides electronic effects the size of the substituent can effect the location of a subsequent reaction. These are ***steric effects***, i.e.



per cent yield for -R	% ortho	% meta	%para
$-CH_3$	58	4	37
$-CH_2CH_3$	49	6	49
$-CH(CH_3)_2$	30	8	62
$-C(CH_3)_3$	16	11	73

Benzylic Reactions

The benzylic position has an enhanced reactivity similar to an allylic position, i.e.

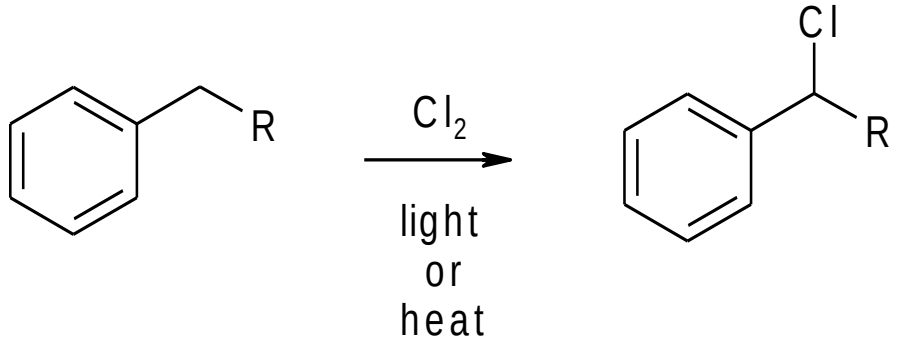


As a result both benzylic cations and radicals form easily.

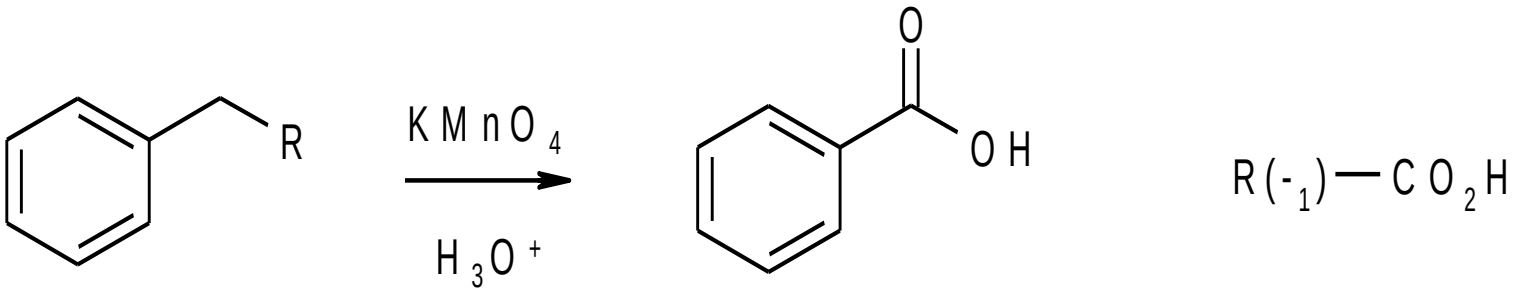
Benzylic Reactions

Common reactions for benzylic sites:

Radical halogenation:

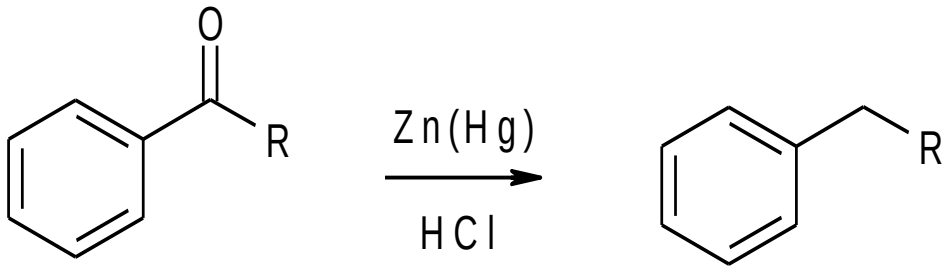


Oxidation:

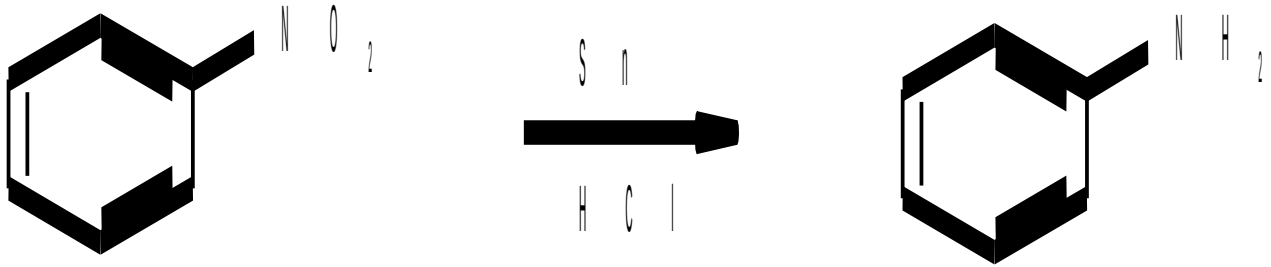


Other Functional Group Modifications

Reduction of carbonyls

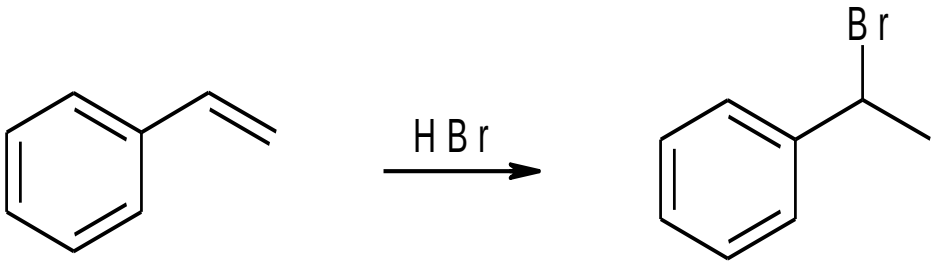


Reduction of nitro to amines

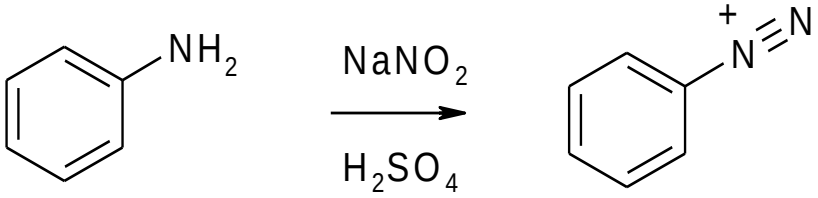


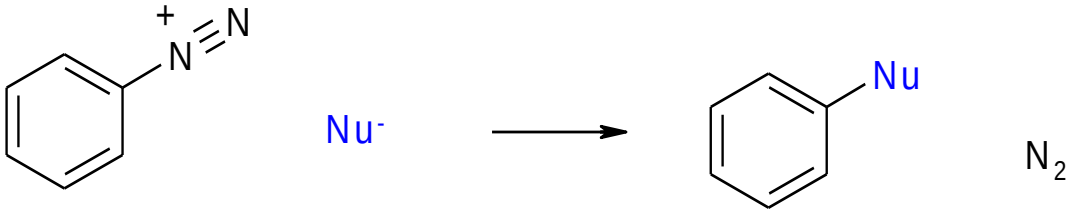
Other Functional Group Modifications

Addition to alkenes (Markovnikov addition product)



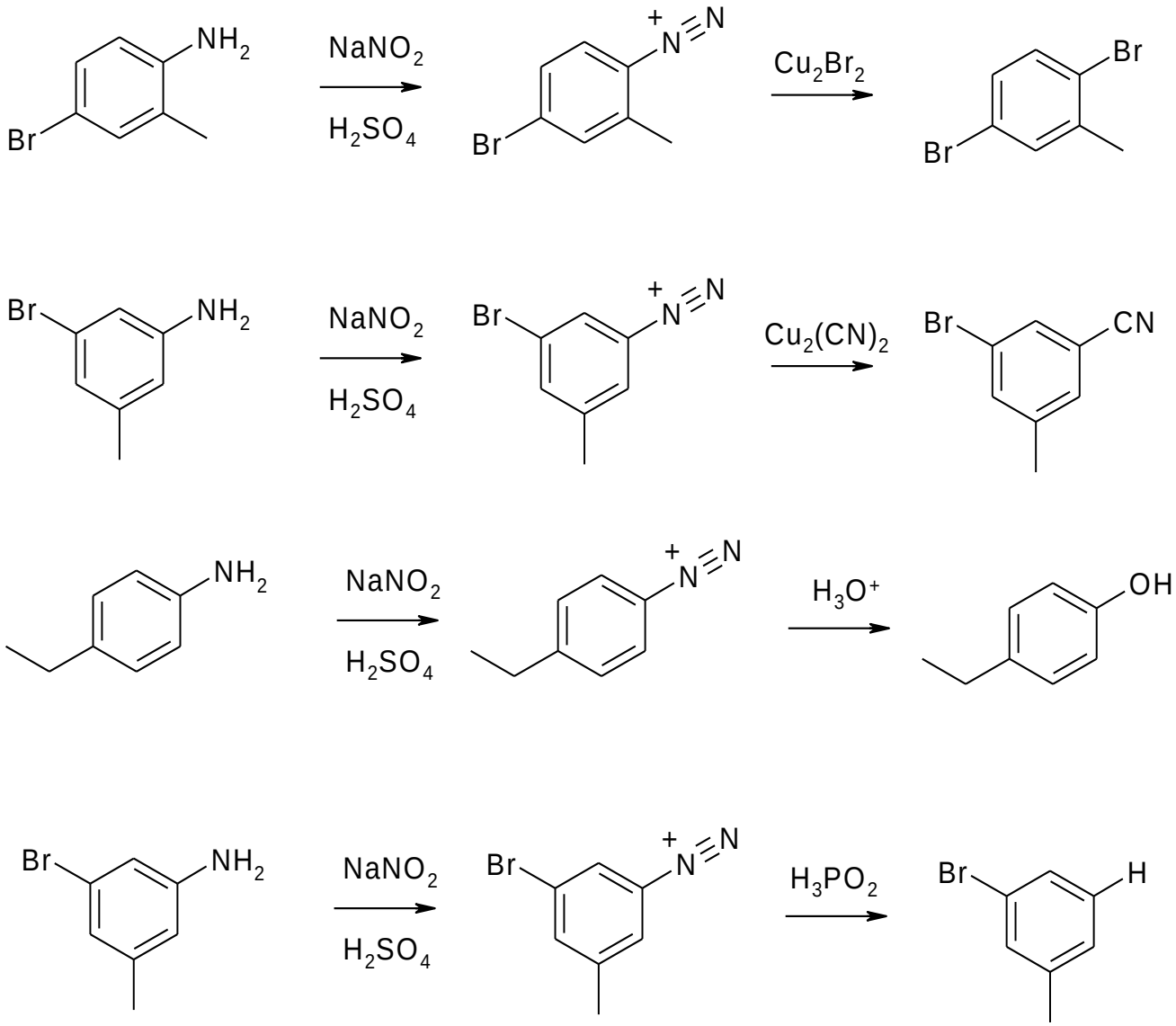
Diazonium salts allows for a Nucleophilic attack!





Examples of Using Diazonium Salts

Controlled synthesis!



Synthesis of Aromatic Compounds

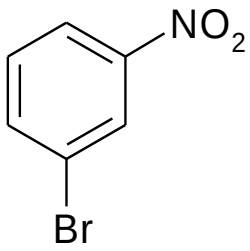
You know what you want to make so the idea is to work backwards from the product, using well know reactions, to the starting material.

This process is known as *Retrosynthesis*.

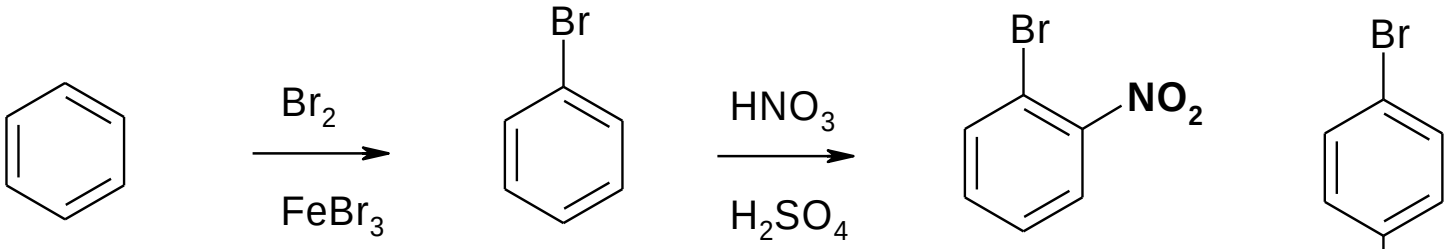
This means you need to how the reactions and their directing effects, i.e.

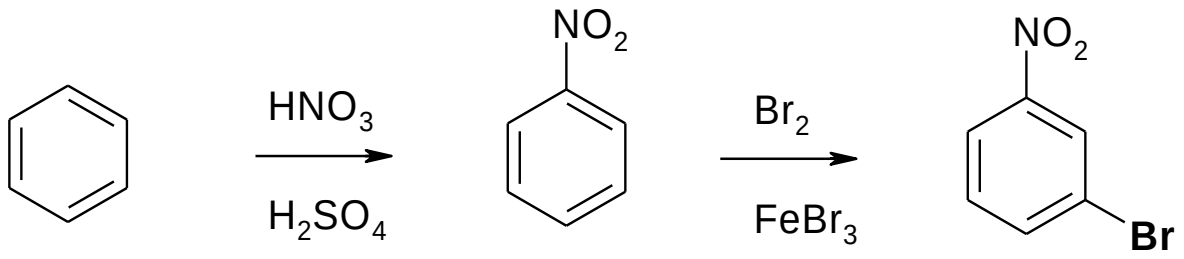
Synthesis of Aromatic Compounds

"Direct" introduction of groups:



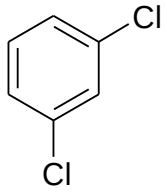
desired product



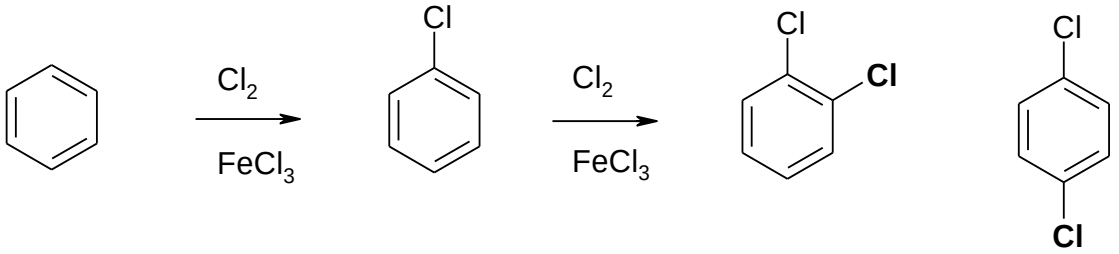


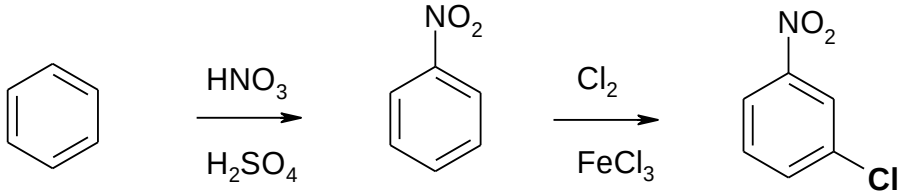
Synthesis of Aromatic Compounds

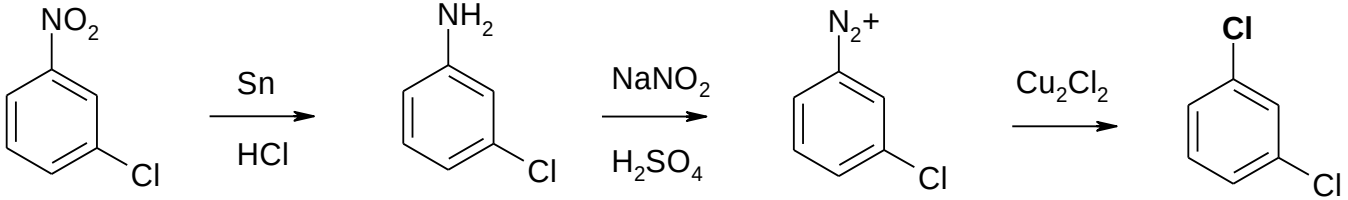
"Indirect" introduction of groups:



desired product

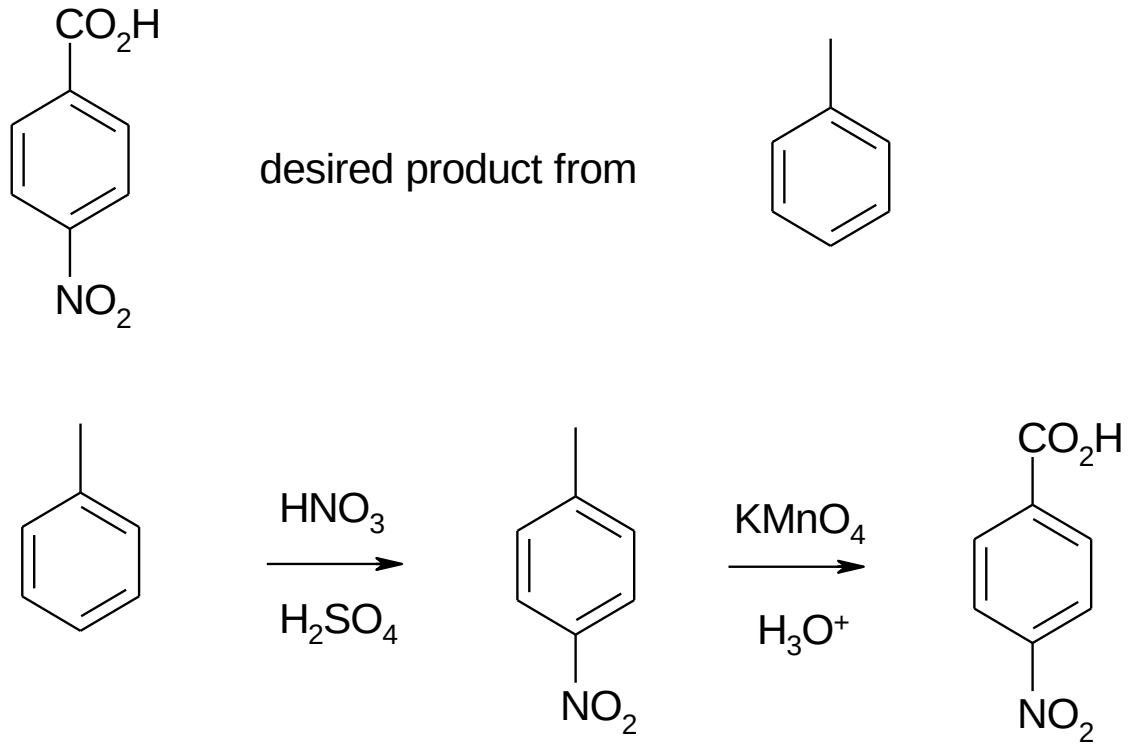






Synthesis of Aromatic Compounds

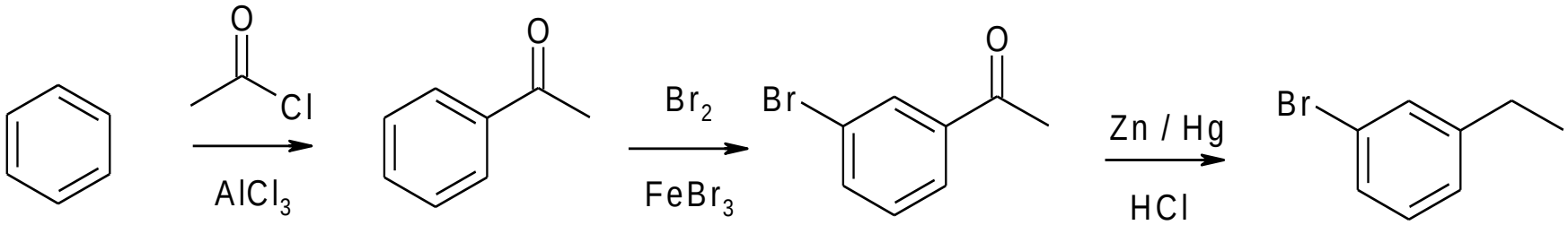
Unusual substitution patterns:



Synthesis of Aromatic Compounds

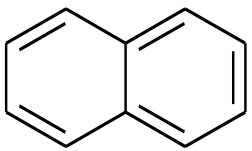
Unusual substitution patterns:

desired product from

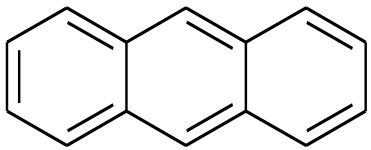


Polycyclic Aromatic Hydrocarbons

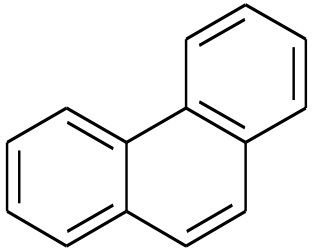
A number of polycyclic (multiple fused rings) hydrocarbons exist. They still obey Huckel's rule, alternating single & double bonds etc. They also exhibit a reduced reactivity to addition / substitutions and react by EArS.



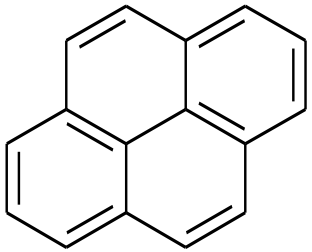
naphthalene



anthracene



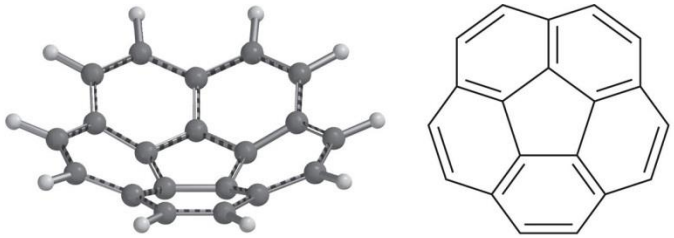
phenanthrene



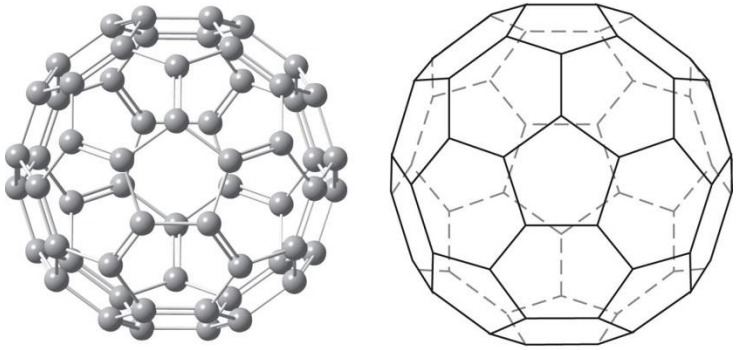
pyrene

Polycyclic Aromatic Hydrocarbons

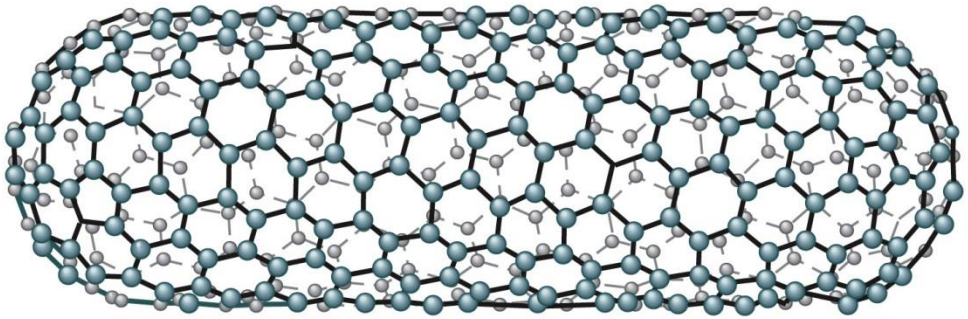
Two other cases of polycyclic hydrocarbons exist, fullerenes and carbon nanotubes. These compounds have interesting properties of electrical conductance and very high strength.



corannulene



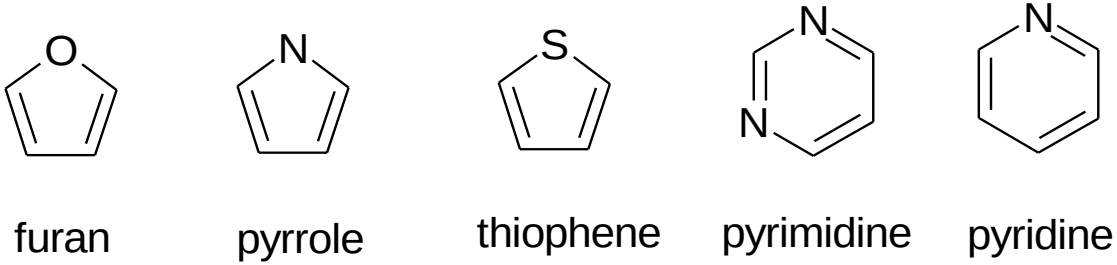
C_{60} (the pi bonds are not shown)



Carbon nanotube[1]

Heterocyclic Aromatic Compounds

Aromatic compounds with a non-carbon (hetero) atom in the ring are possible. In many cases that atom provides a lone pair of electrons as part of the 4n + 2 π electrons in the system. Examples include:



Heterocyclic Aromatic Compounds

- The heteroatom has significant effects on the chemical reactivity.
- They are commonly used as polar aprotic (no acidic H atom) solvents.
- They are very common in biology.
- For more information see Chapter 13.