Benzene and Aromatic Compounds

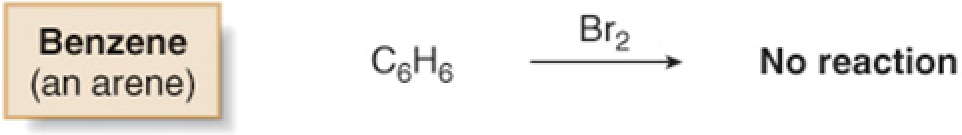
Chapter 15

Organic Chemistry, *8th Edition*

John McMurry

Background

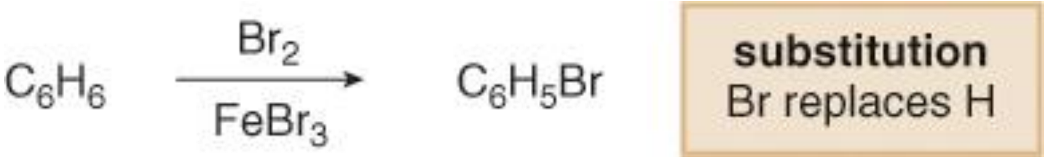
- Benzene (C_6H_6) is the simplest aromatic hydrocarbon (or arene).
- Four degrees of unsaturation.
- It is planar.
- All C—C bond lengths are equal.
- Whereas unsaturated hydrocarbons such as alkenes, alkynes and dienes readily undergo addition reactions, benzene does not.



Benzene
(an arene)

$$C_6H_6 \xrightarrow{Br_2} \text{No reaction}$$

- Benzene reacts with bromine only in the presence of $FeBr_3$ (a Lewis acid), and the reaction is a substitution, not an addition.

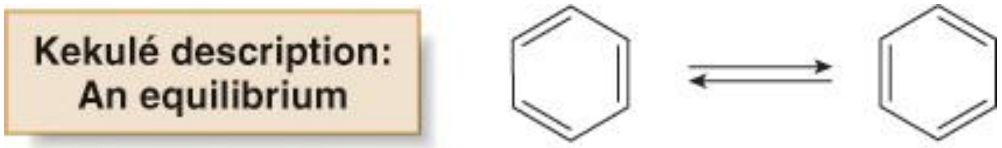


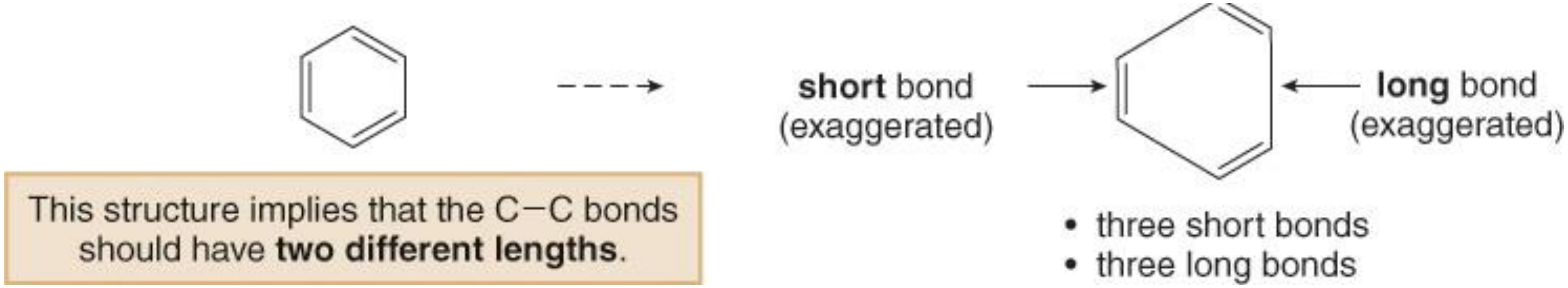
$$C_6H_6 \xrightarrow[FeBr_3]{Br_2} C_6H_5Br$$

substitution
Br replaces H

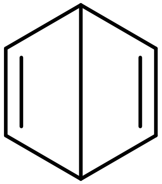
Background

- August Kekulé (1865) proposed that benzene was a rapidly equilibrating mixture of two compounds, each containing a six-membered ring with three alternating π bonds.





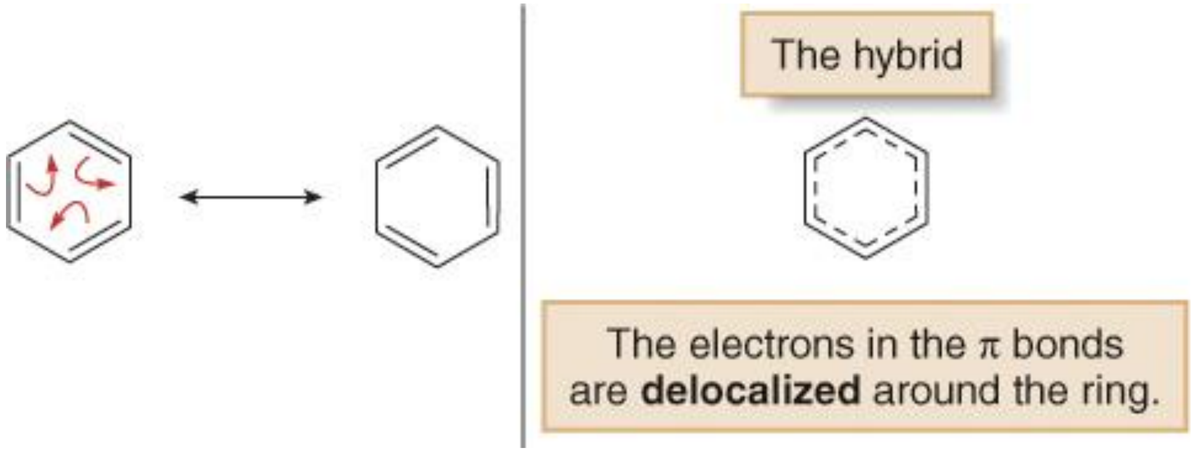
- All C—C bond lengths are equal!



James Dewar (1967) : the Dewar benzene was prepared in 1962 but it is not stable and it converts to benzene

The Structure of Benzene: Resonance

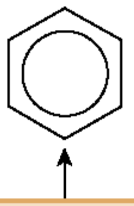
- The true structure of benzene is a resonance hybrid of the two Lewis structures.



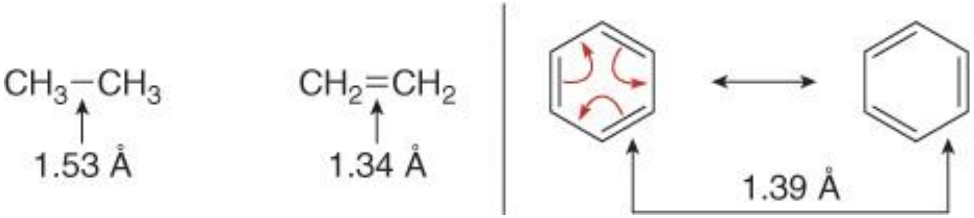
The hybrid

The electrons in the π bonds are **delocalized** around the ring.

Some texts draw benzene as a hexagon with an inner circle:

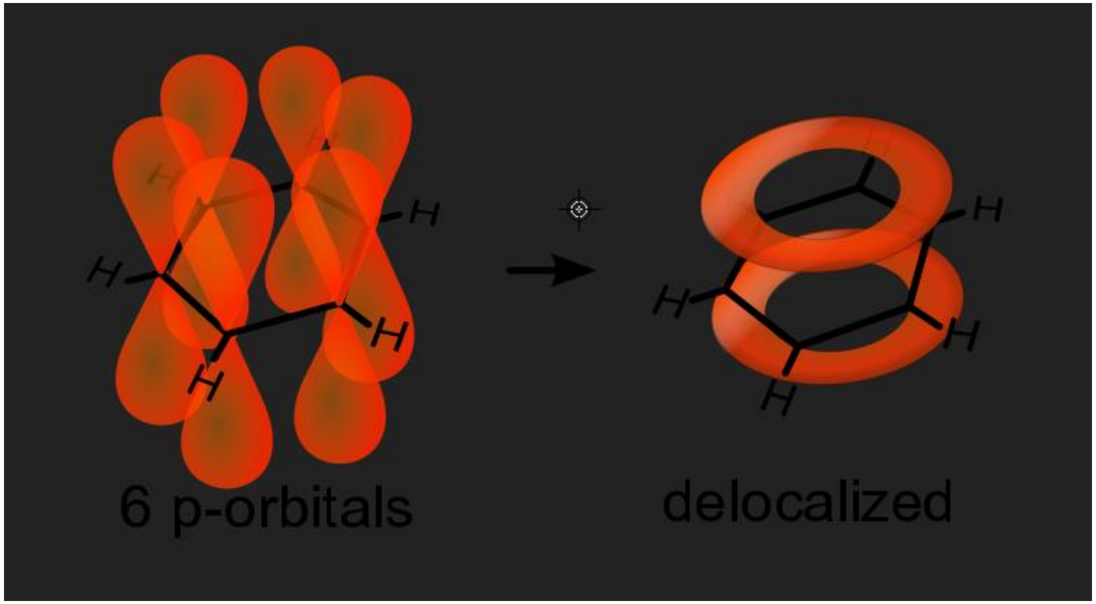


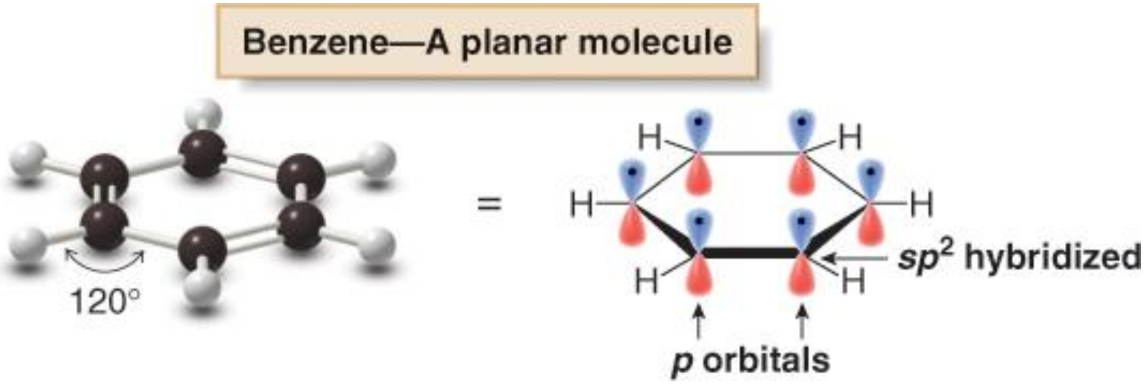
The circle represents the **six π electrons,** distributed over the six atoms of the ring.



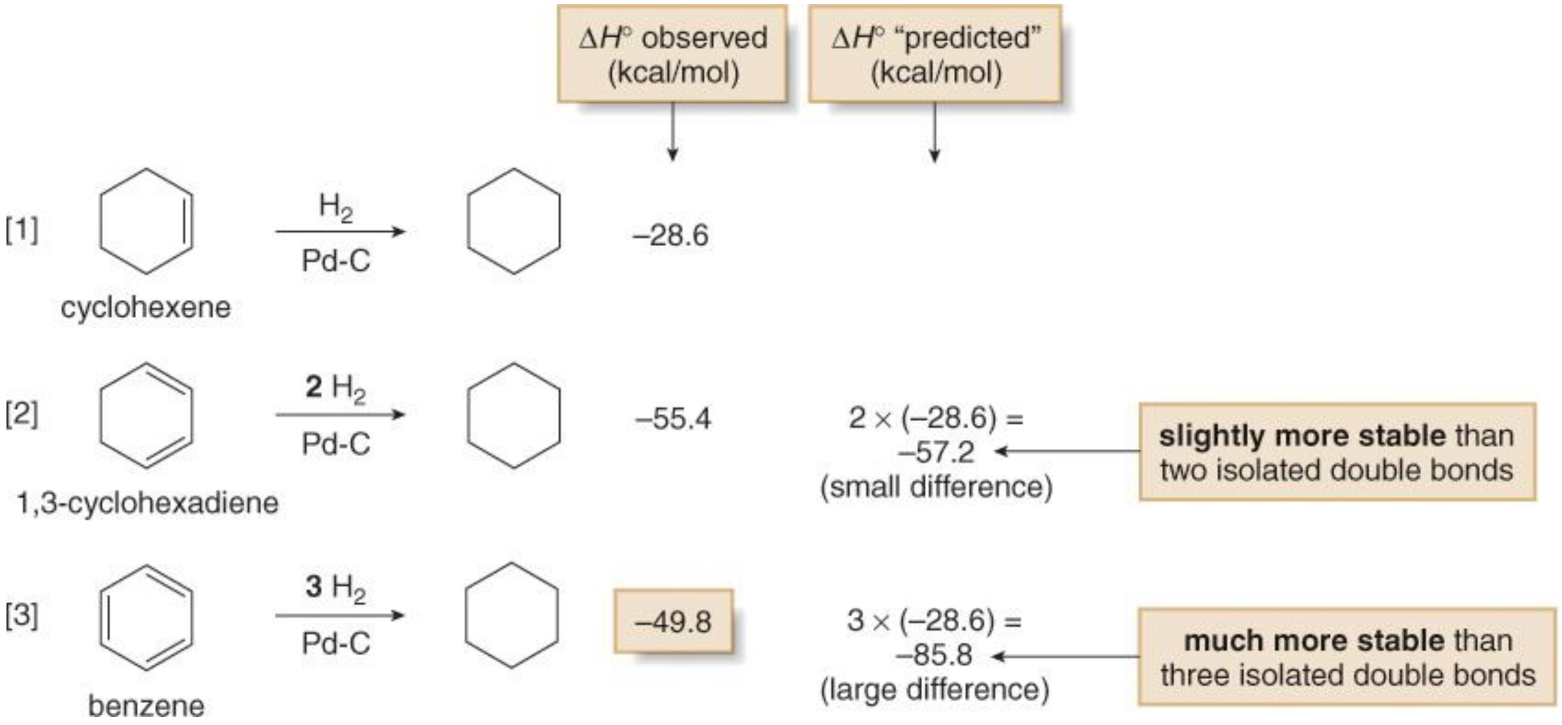
The C–C bonds in benzene are equal and intermediate in length.

The Structure of Benzene: MO

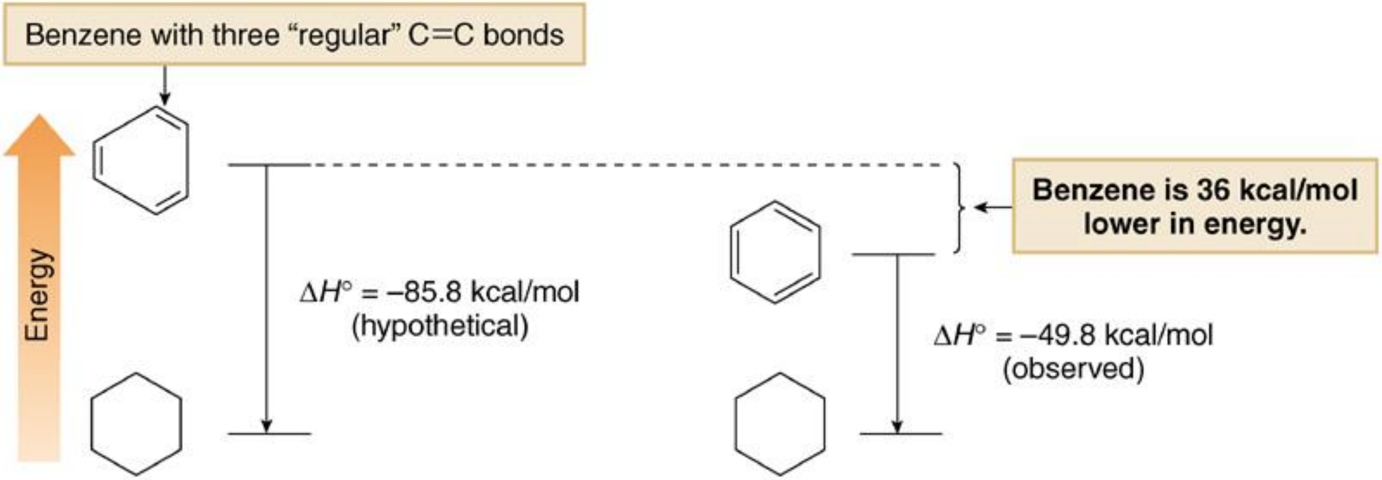




Aromaticity – Resonance Energy



	Reactant	Reagents	ΔH° observed (kcal/mol)	ΔH° "predicted" (kcal/mol)	
[1]	cyclohexene	H_2, Pd-C	–28.6		
[2]	1,3-cyclohexadiene	**2** H_2, Pd-C	–55.4	2 × (–28.6) = –57.2 (small difference)	**slightly more stable** than two isolated double bonds
[3]	benzene	**3** H_2, Pd-C	–49.8	3 × (–28.6) = –85.8 (large difference)	**much more stable** than three isolated double bonds



Benzene with three "regular" C=C bonds

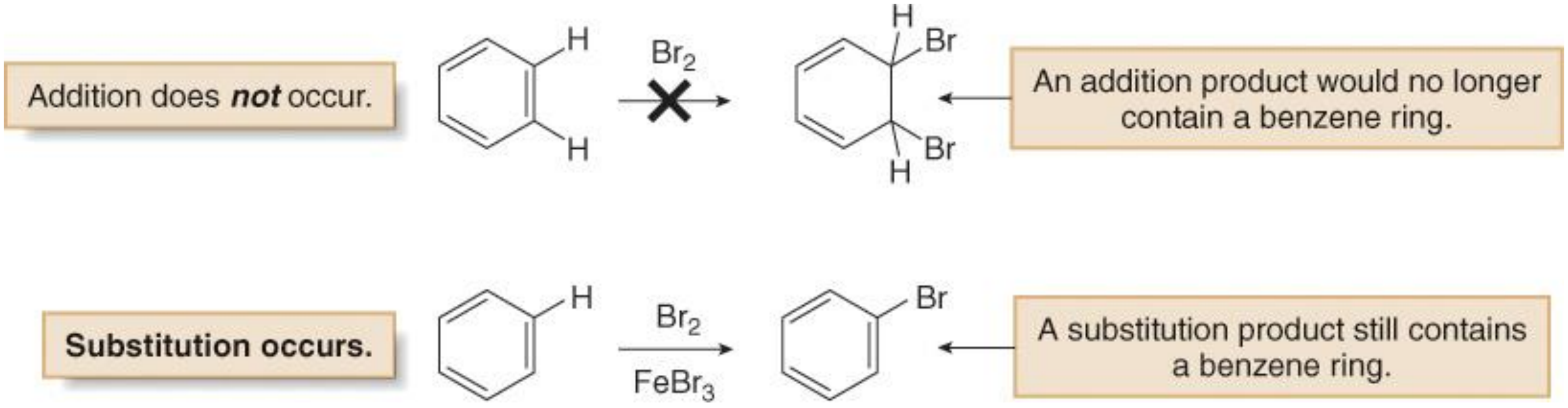
ΔH° = –85.8 kcal/mol
(hypothetical)

ΔH° = –49.8 kcal/mol
(observed)

Benzene is 36 kcal/mol lower in energy.

Stability of Benzene - Aromaticity

- Benzene does not undergo addition reactions typical of other highly unsaturated compounds, including conjugated dienes.



Addition does *not* occur.

An addition product would no longer contain a benzene ring.

Substitution occurs.

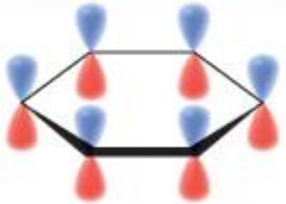
A substitution product still contains a benzene ring.

The Criteria for Aromaticity

Four structural criteria must be satisfied for a compound to be aromatic.

[1] A molecule must be cyclic.

Cyclic compound

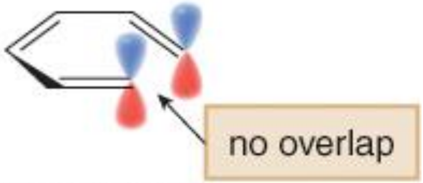


benzene

Every *p* orbital overlaps with two neighboring *p* orbitals.

aromatic

Acyclic compound



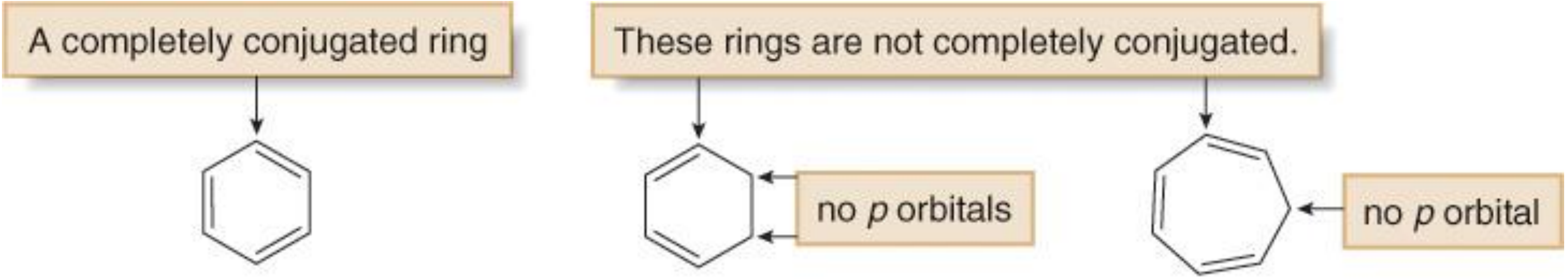
1,3,5-hexatriene

There can be no overlap between the *p* orbitals on the two terminal C's.

not aromatic

The Criteria for Aromaticity

[2] A molecule must be completely conjugated (all atoms sp^2).



A completely conjugated ring

These rings are not completely conjugated.

no *p* orbitals

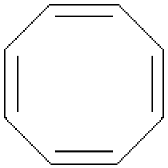
no *p* orbital

benzene
a *p* orbital on **every** C
aromatic

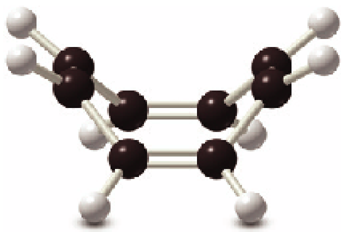
1,3-cyclohexadiene
not aromatic

1,3,5-cycloheptatriene
not aromatic

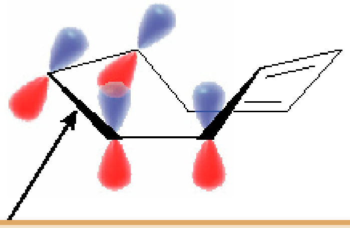
[3] A molecule must be planar.



cyclooctatetraene
not aromatic



a tub-shaped,
eight-membered ring



Adjacent *p* orbitals cannot overlap.
Electrons cannot delocalize.

The Criteria for Aromaticity—Hückel's Rule

[4] A molecule must satisfy Hückel's rule.

- An aromatic compound must contain $4n + 2$ π electrons ($n = 0, 1, 2$, and so forth).
- Cyclic, planar, and completely conjugated compounds that contain $4n$ π electrons are especially unstable, and are said to be *antiaromatic.*

Benzene
An aromatic compound

$4n + 2 = 4(1) + 2 =$
6 π electrons
aromatic

Cyclobutadiene
An antiaromatic compound

$4n = 4(1) =$
4 π electrons
antiaromatic

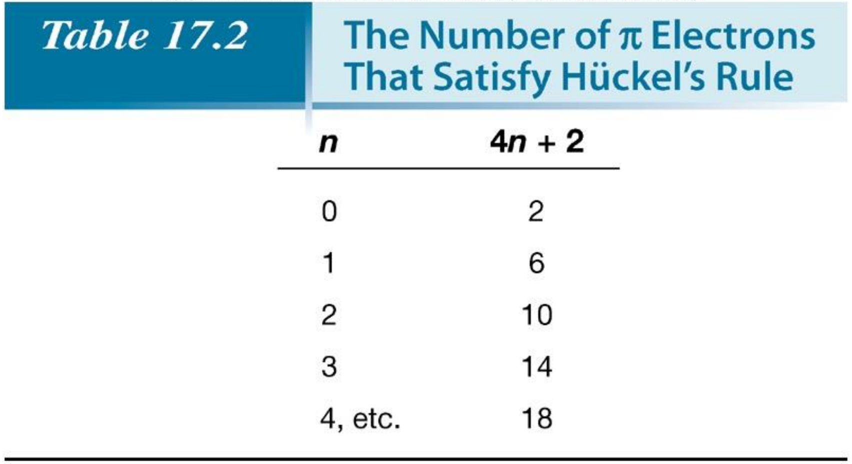
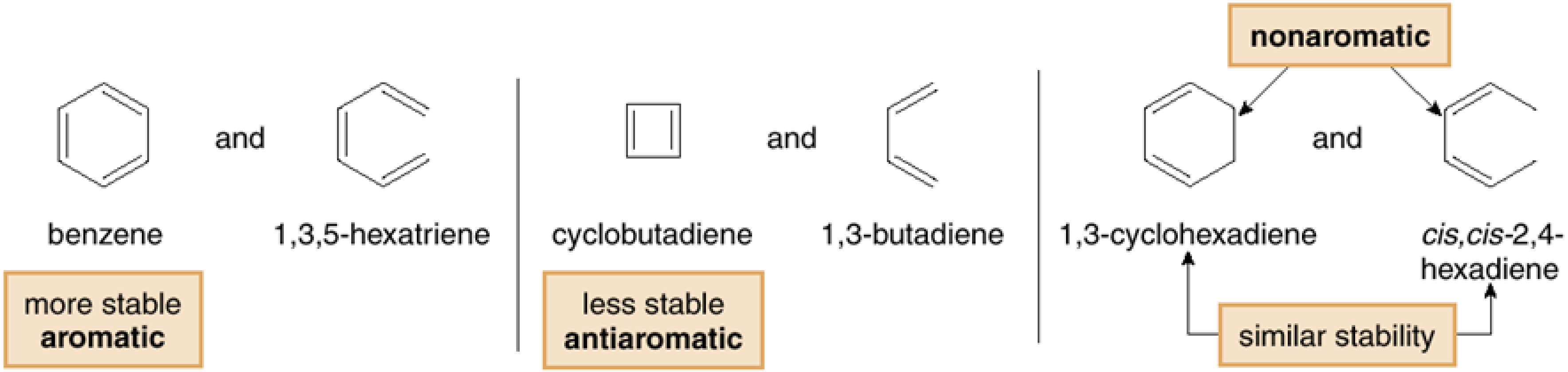


Table 17.2 The Number of π Electrons That Satisfy Hückel's Rule

n	$4n + 2$
0	2
1	6
2	10
3	14
4, etc.	18

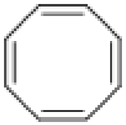
The Criteria for Aromaticity—Hückel's Rule

1. Aromatic—A cyclic, planar, completely conjugated compound with 4*n* + 2 π electrons.
2. Antiaromatic—A cyclic, planar, completely conjugated compound with 4*n* π electrons.
3. Not aromatic (nonaromatic)—A compound that lacks one (or more) of the following requirements for aromaticity: being cyclic, planar, and completely conjugated.



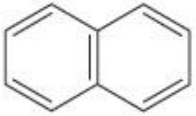
Examples of Aromatic Rings

Cyclooctatetraene
8 π electrons

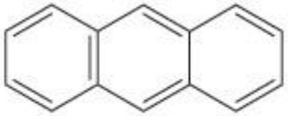


planar
antiaromatic

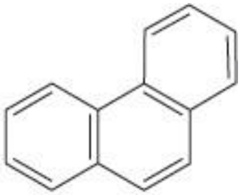
puckered
nonaromatic



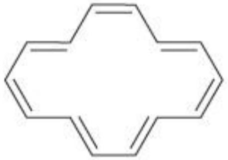
naphthalene
10 π electrons



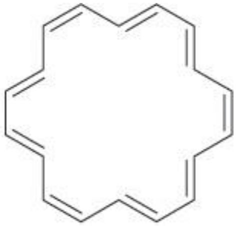
anthracene
14 π electrons



phenanthrene
14 π electrons

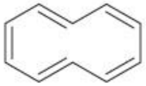


[14]-annulene
$4n + 2 = 4(3) + 2 =$
14 π electrons
aromatic



[18]-annulene
$4n + 2 = 4(4) + 2 =$
18 π electrons
aromatic

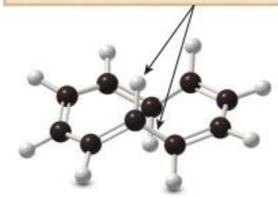
[10]-Annulene fits Hückel's rule,
but it's **not planar**.



[10]-annulene
10 π electrons
not aromatic

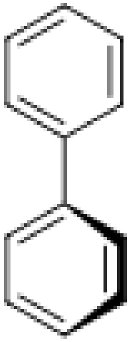
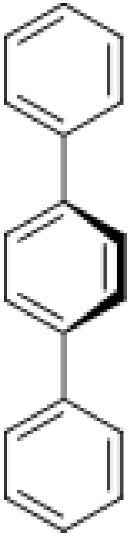
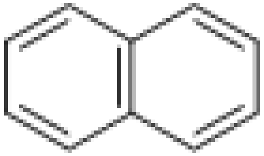
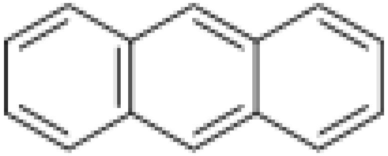
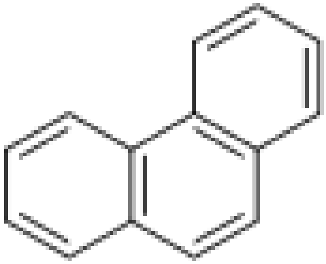
=

The molecule puckers to keep
these H's further away from each other.



3-D representation

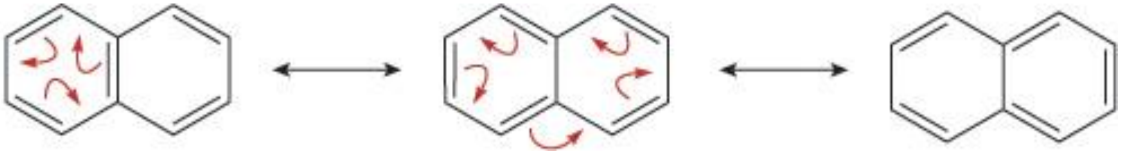
Polycyclic Aromatic Hydrocarbons

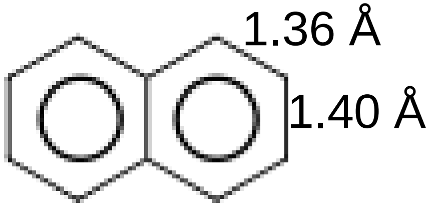






biphenyl   terphenyl   naphthalene   anthracene   phenanthrene

No interactions between rings   61 kcal/mol   84 kcal/mol   92 kcal/mol

Three resonance structures for naphthalene



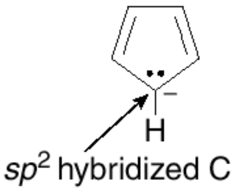


Other Aromatic Compounds

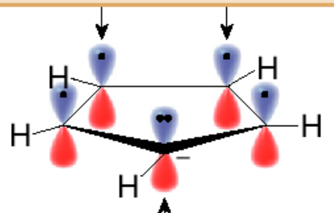
cyclopentadiene
not aromatic
$pK_a = 15$

cyclopentadienyl anion
aromatic
a stabilized conjugate base

The cyclopentadienyl anion

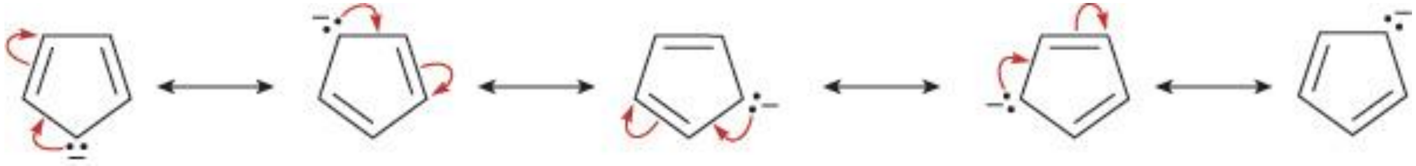


The ring is completely conjugated with **6 π electrons**.

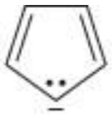


The lone pair resides in a *p* orbital.

- The cyclopentadienyl anion is aromatic because it is cyclic, planar, completely conjugated, and has six π electrons.

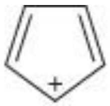


Other Aromatic Compounds



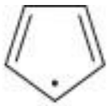
cyclopentadienyl anion
- **6** π electrons
- contains $4n + 2$ π electrons

aromatic



cyclopentadienyl cation
- **4** π electrons
- contains $4n$ π electrons

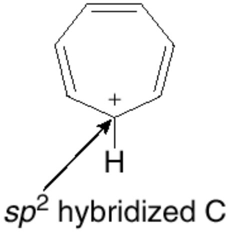
antiaromatic



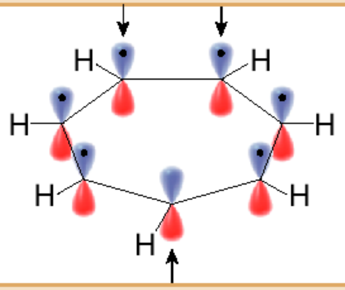
cyclopentadienyl radical
- **5** π electrons
- does not contain either $4n$ or $4n + 2$ π electrons

nonaromatic

The tropylium cation



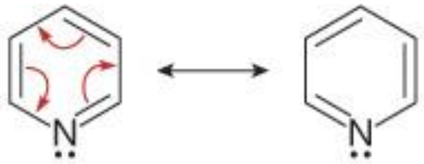
The ring is completely conjugated with **6 π electrons**.



One *p* orbital is vacant.

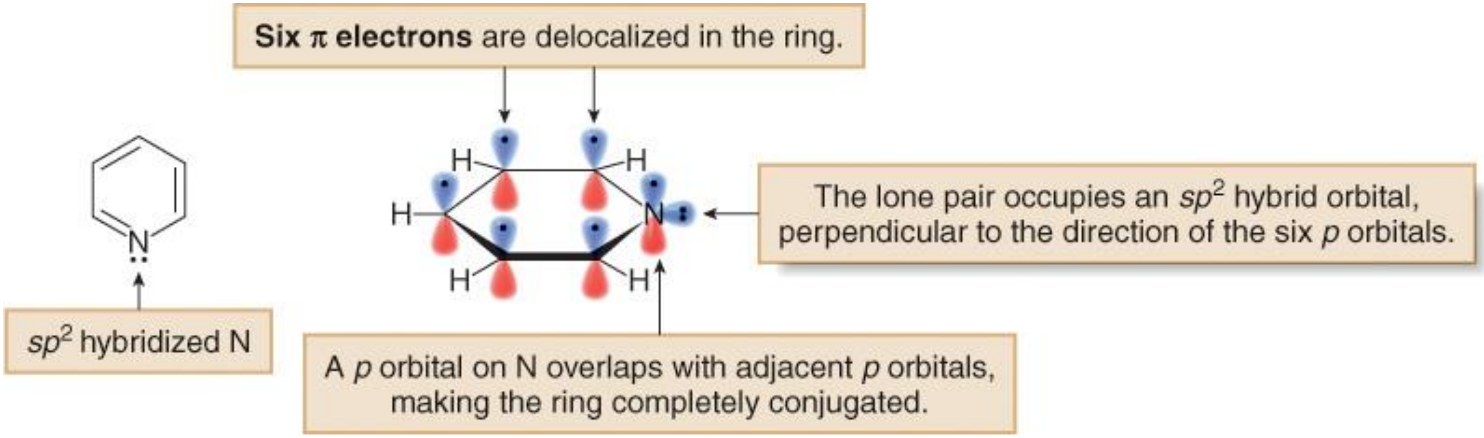
- The tropylium cation is aromatic because it is cyclic, planar, completely conjugated, and has six π electrons delocalized over the seven atoms of the ring.

Aromatic Heterocycles



two resonance structures for pyridine

6 π electrons



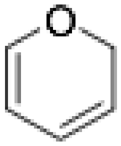
Six π electrons are delocalized in the ring.

The lone pair occupies an *sp*^{2} hybrid orbital, perpendicular to the direction of the six *p* orbitals.

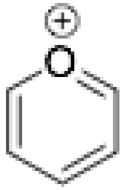
sp^2 hybridized N

A *p* orbital on N overlaps with adjacent *p* orbitals, making the ring completely conjugated.

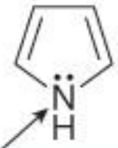
2H-pyran
4 π electrons
nonaromatic



2H-pyrilium ion
6 π electrons
aromatic

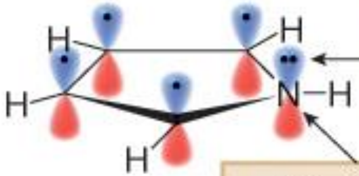


Aromatic Heterocycles



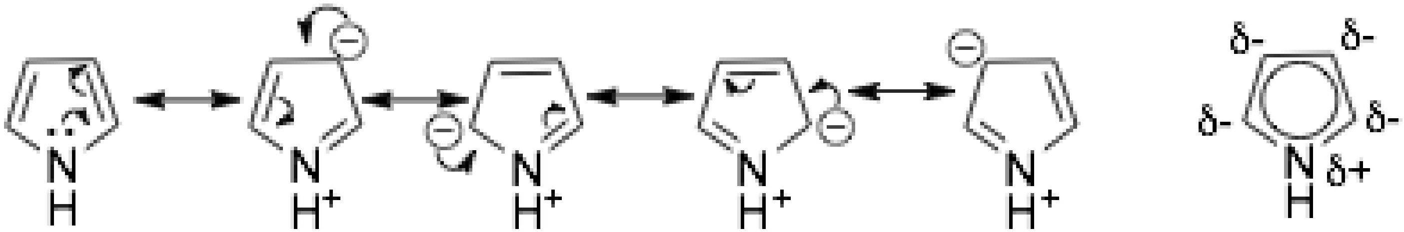
sp^2 hybridized N

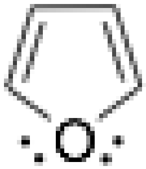
The ring is completely conjugated with **6 π electrons**.



The lone pair resides in a *p* orbital.

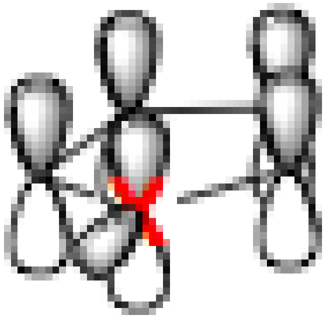
sp^2 hybridized N





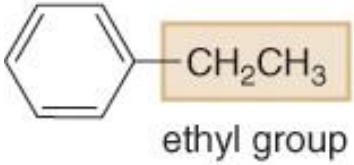
furan

thiophen

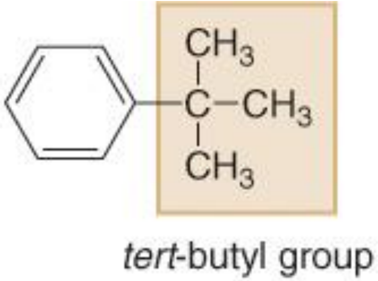


Nomenclature: 1 Substituent

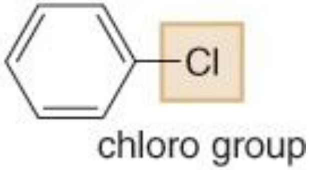
Systematic:



ethylbenzene

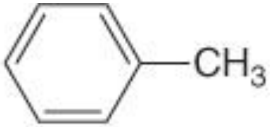


tert-butylbenzene

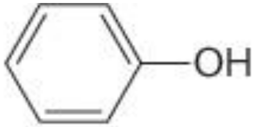


chlorobenzene

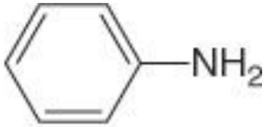
Common:



toluene
(methylbenzene)



phenol
(hydroxybenzene)



aniline
(aminobenzene)

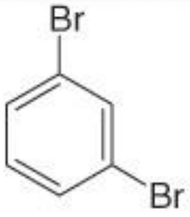
Nomenclature: 2 Substituents

Identical:

1,2-disubstituted benzene
ortho isomer

1,2-dibromobenzene
o-dibromobenzene

1,3-disubstituted benzene
meta isomer



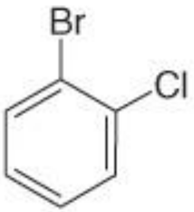
1,3-dibromobenzene
m-dibromobenzene

1,4-disubstituted benzene
para isomer

1,4-dibromobenzene
p-dibromobenzene

Different:

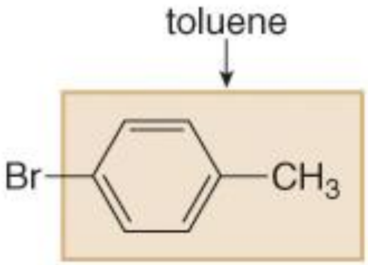
Alphabetize two different substituent names:



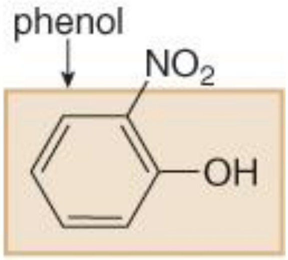
***o*-bromochloro-benzene**

***m*-fluoronitro-benzene**

Use a common root name:



p*-bromo**toluene*

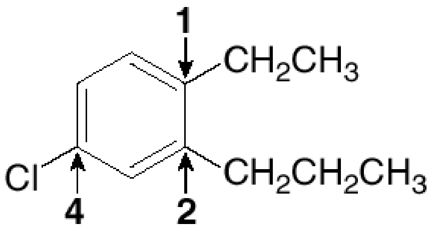


o*-nitro**phenol*

Nomenclature: 3 or More Substituents

Examples of naming polysubstituted benzenes

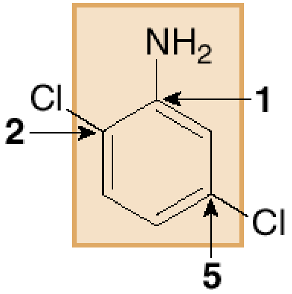
[1]



- Assign the lowest set of numbers.
- Alphabetize the names of all the substituents.

4-chloro-1-ethyl-2-propylbenzene

[2]

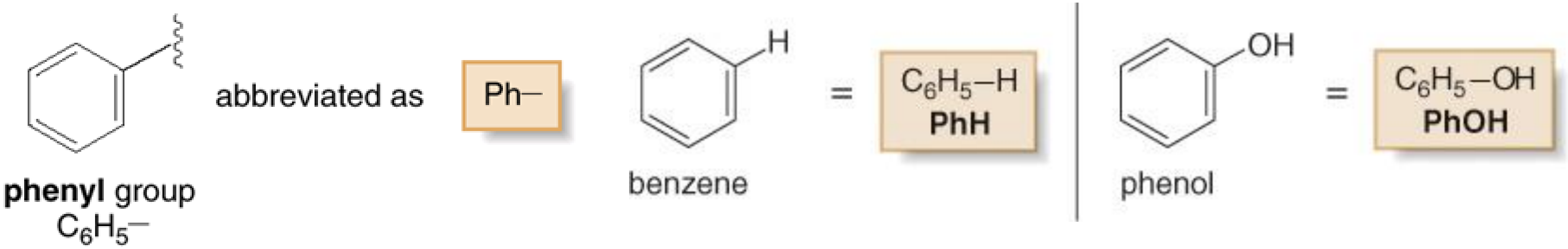


- Name the molecule as a derivative of the common root **aniline.**
- Designate the position of the NH_2 group as “1,” and then assign the lowest possible set of numbers to the other substituents.

2,5-dichloroaniline

Nomenclature

- A benzene substituent is called a phenyl group, and it can be abbreviated in a structure as “Ph-”.

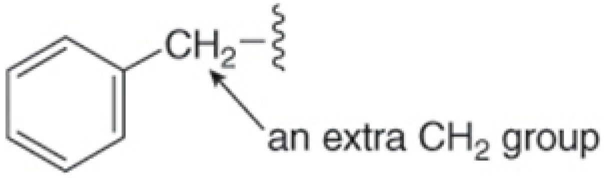


phenyl group
C_6H_5-

benzene = C_6H_5-H
PhH

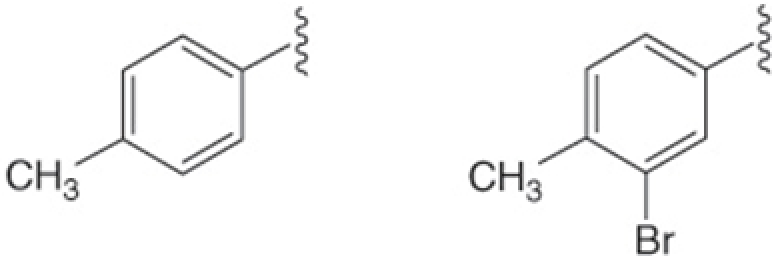
phenol = C_6H_5-OH
PhOH

- The benzyl group:



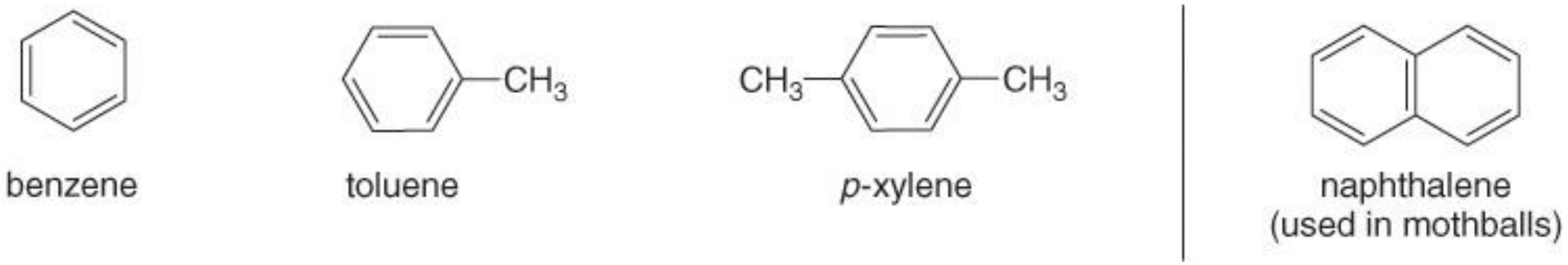
benzyl group
$C_6H_5CH_2-$

- Aryl groups:



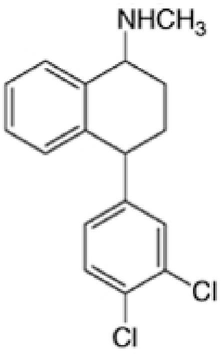
Interesting Aromatic Compounds

- Benzene and toluene, are obtained from petroleum refining and are useful starting materials for synthetic polymers.
- Compounds containing two or more benzene rings that share carbon—carbon bonds are called polycyclic aromatic hydrocarbons (PAHs). Naphthalene, the simplest PAH, is the active ingredient in mothballs.

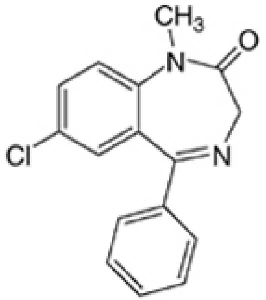


The components of the gasoline additive BTX

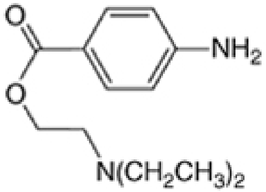
Interesting Aromatic Compounds



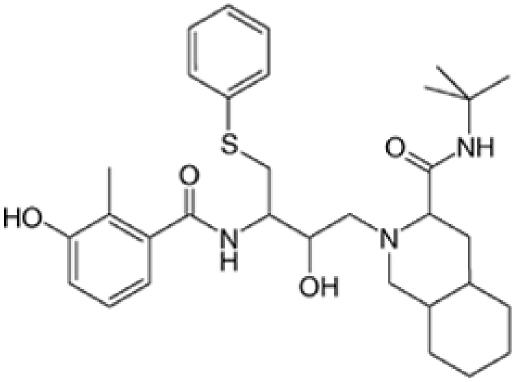
- Trade name: **Zoloft**
- Generic name: **sertraline**
- Use: a psychotherapeutic drug for depression and panic disorders



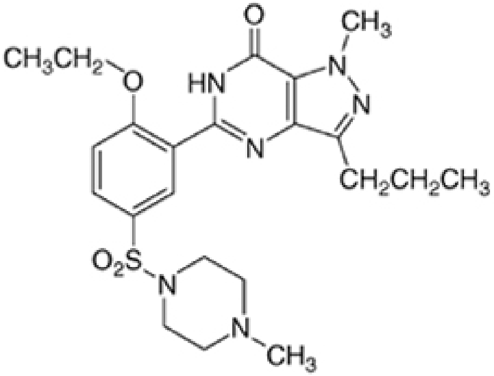
- Trade name: **Valium**
- Generic name: **diazepam**
- Use: a sedative



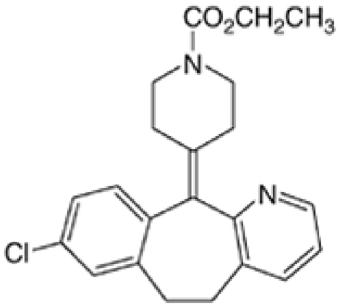
- Trade name: **Novocain**
- Generic name: **procaine**
- Use: a local anesthetic



- Trade name: **Viracept**
- Generic name: **nelfinavir**
- Use: an antiviral drug used to treat HIV



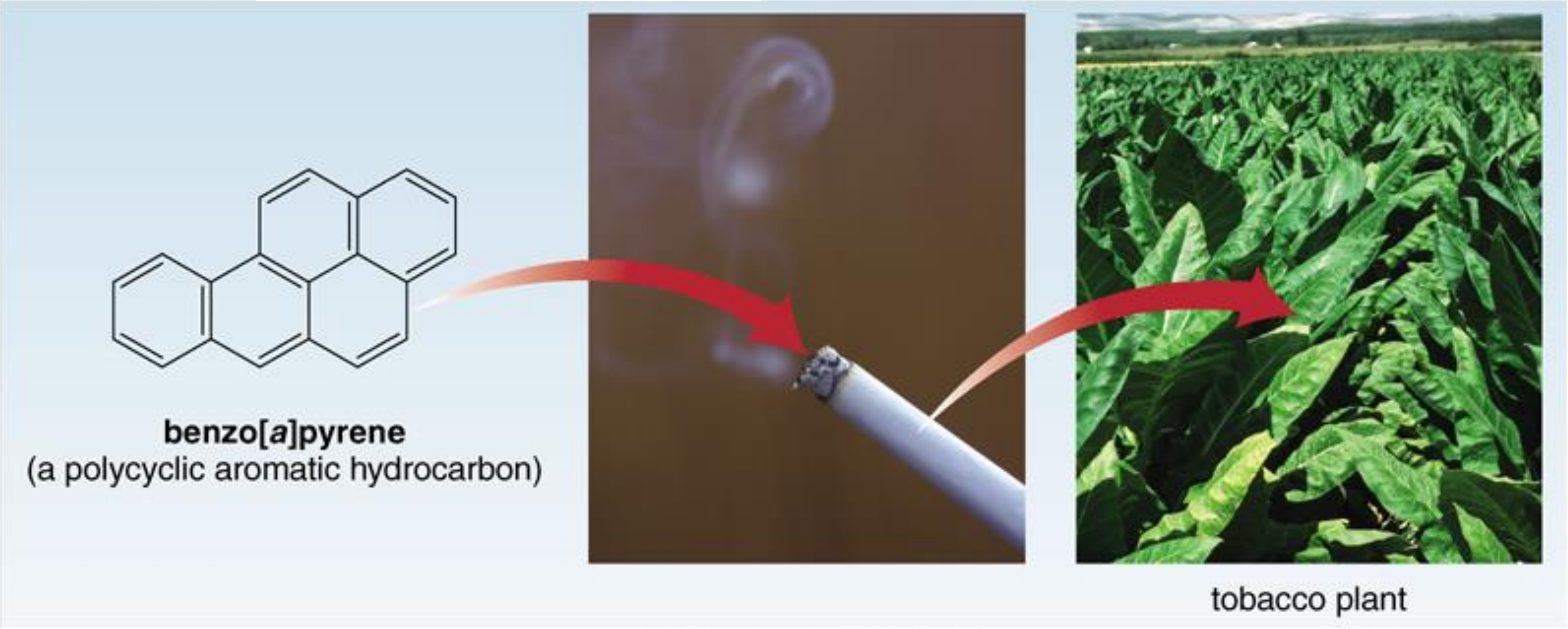
- Trade name: **Viagra**
- Generic name: **sildenafil**
- Use: a drug used to treat erectile dysfunction



- Trade name: **Claritin**
- Generic name: **loratadine**
- Use: an antihistamine for seasonal allergies

Interesting Aromatic Compounds

- Benzo[*a*]pyrene, produced by the incomplete oxidation of organic compounds in tobacco, is found in cigarette smoke.



benzo[*a*]pyrene
(a polycyclic aromatic hydrocarbon)

tobacco plant

© David Young-Wolff/PhotoEdit

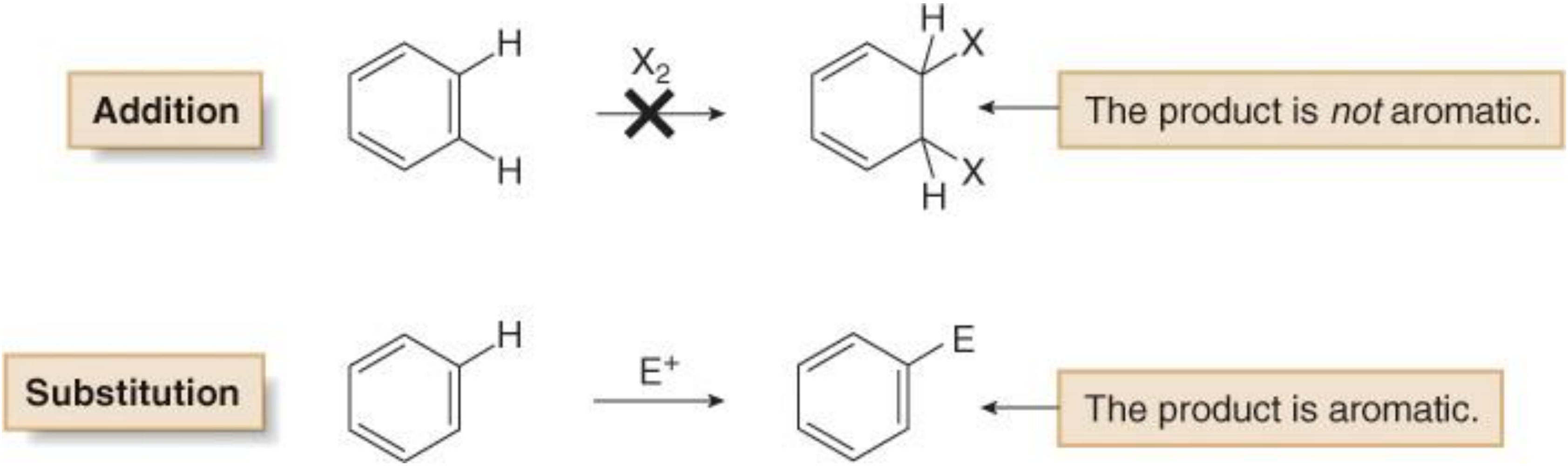
© Corbis

- When ingested or inhaled, benzo[a]pyrene and other similar PAHs are oxidized to carcinogenic products.

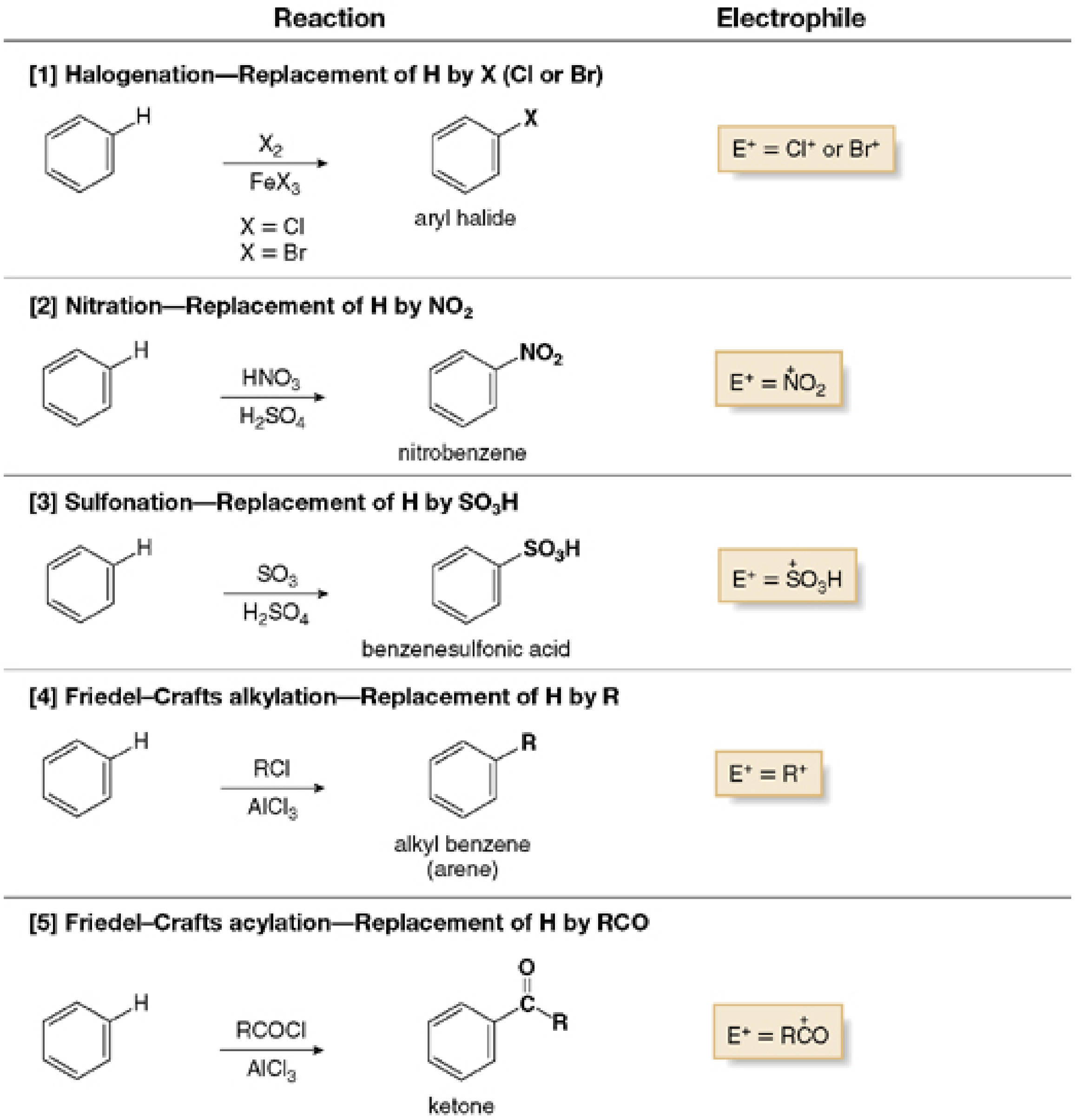
Electrophilic Aromatic Substitution

Chapter 16
Organic Chemistry, *8th Edition*
John McMurry

Introduction

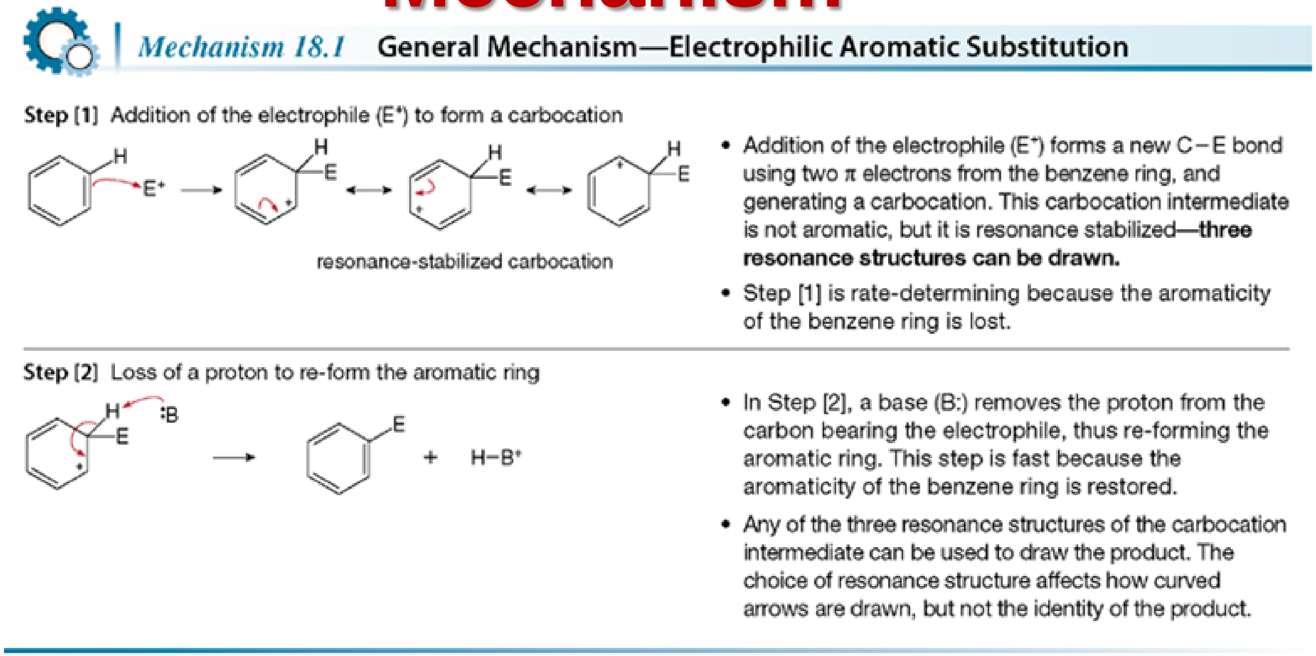


Introduction



Reaction	Electrophile
[1] Halogenation—Replacement of H by X (Cl or Br)	
$\xrightarrow[FeX_3]{X_2}$ aryl halide X = Cl X = Br	$E^+ = Cl^+$ or Br^+
[2] Nitration—Replacement of H by NO_2	
$\xrightarrow[H_2SO_4]{HNO_3}$ nitrobenzene	$E^+ = \overset{+}{N}O_2$
[3] Sulfonation—Replacement of H by SO_3H	
$\xrightarrow[H_2SO_4]{SO_3}$ benzenesulfonic acid	$E^+ = \overset{+}{S}O_3H$
[4] Friedel–Crafts alkylation—Replacement of H by R	
$\xrightarrow[AlCl_3]{RCl}$ alkyl benzene (arene)	$E^+ = R^+$
[5] Friedel–Crafts acylation—Replacement of H by RCO	
$\xrightarrow[AlCl_3]{RCOCl}$ ketone	$E^+ = R\overset{+}{C}O$

Mechanism



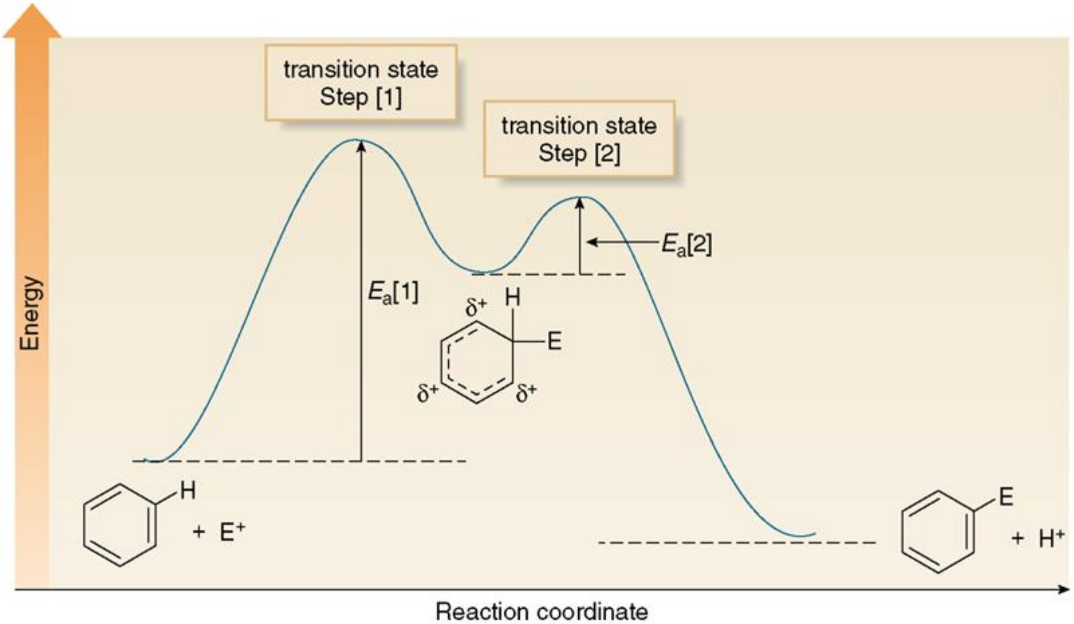
Mechanism 18.1 **General Mechanism—Electrophilic Aromatic Substitution**

Step [1] Addition of the electrophile (E^+) to form a carbocation

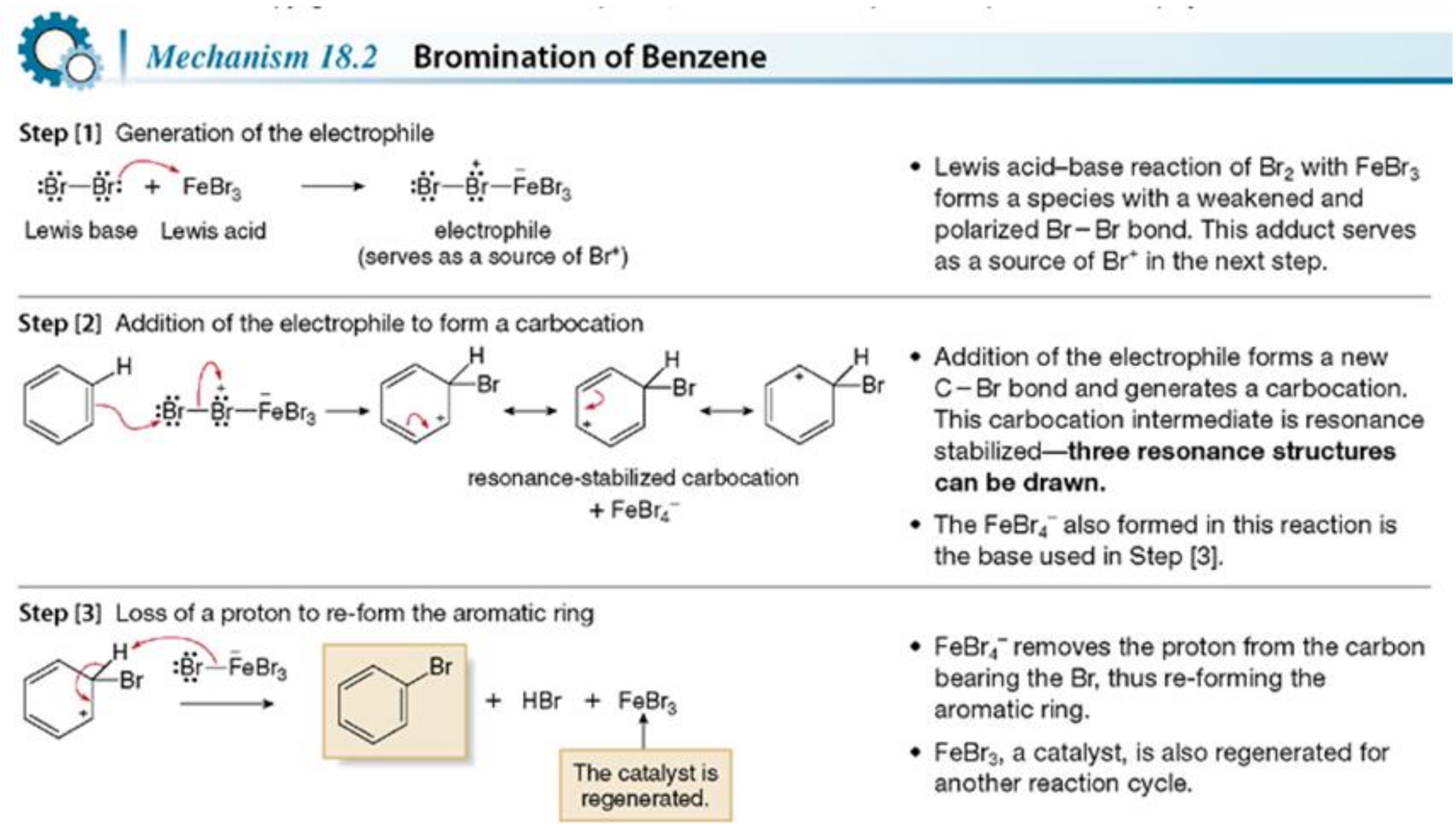
- Addition of the electrophile (E^+) forms a new C–E bond using two π electrons from the benzene ring, and generating a carbocation. This carbocation intermediate is not aromatic, but it is resonance stabilized—**three resonance structures can be drawn.**
- Step [1] is rate-determining because the aromaticity of the benzene ring is lost.

Step [2] Loss of a proton to re-form the aromatic ring

- In Step [2], a base (B:) removes the proton from the carbon bearing the electrophile, thus re-forming the aromatic ring. This step is fast because the aromaticity of the benzene ring is restored.
- Any of the three resonance structures of the carbocation intermediate can be used to draw the product. The choice of resonance structure affects how curved arrows are drawn, but not the identity of the product.



Halogenation



Mechanism 18.2 Bromination of Benzene

Step [1] Generation of the electrophile

Lewis base Lewis acid

electrophile (serves as a source of Br^+)

- Lewis acid–base reaction of Br_2 with $FeBr_3$ forms a species with a weakened and polarized Br–Br bond. This adduct serves as a source of Br^+ in the next step.

Step [2] Addition of the electrophile to form a carbocation

resonance-stabilized carbocation + $FeBr_4^-$

- Addition of the electrophile forms a new C–Br bond and generates a carbocation. This carbocation intermediate is resonance stabilized—**three resonance structures can be drawn.**
- The $FeBr_4^-$ also formed in this reaction is the base used in Step [3].

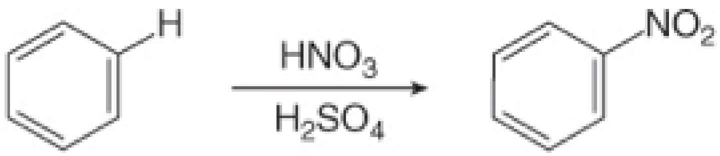
Step [3] Loss of a proton to re-form the aromatic ring

+ HBr + $FeBr_3$

The catalyst is regenerated.

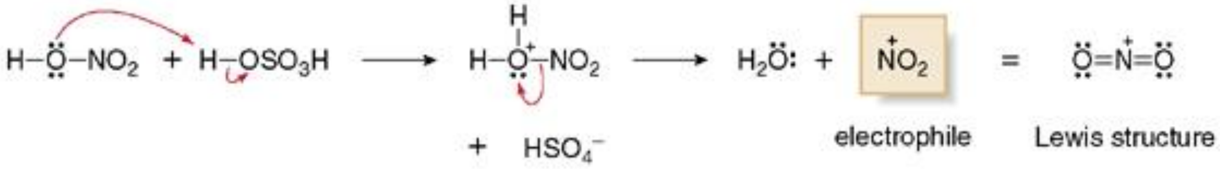
- $FeBr_4^-$ removes the proton from the carbon bearing the Br, thus re-forming the aromatic ring.
- $FeBr_3$, a catalyst, is also regenerated for another reaction cycle.

Nitration



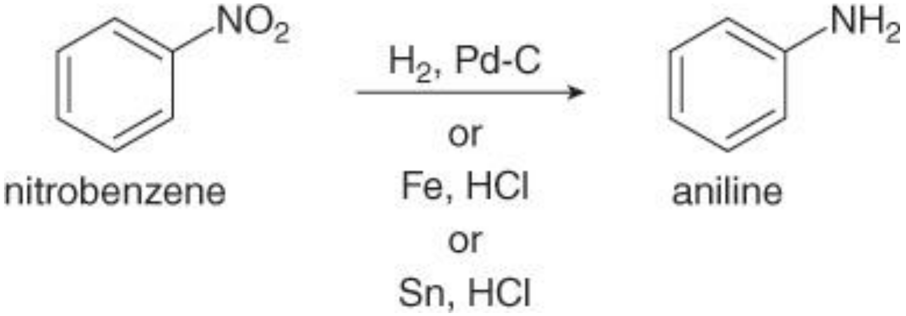
nitrobenzene

Mechanism 18.3 Formation of the Nitronium Ion ($^+NO_2$) for Nitration



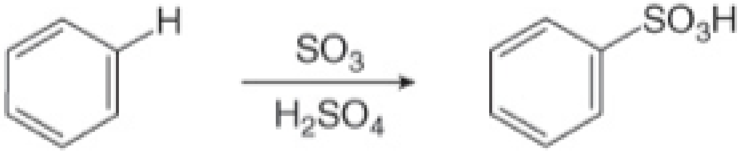
Nitro Group Reduction

Aromatic nitro groups (NO_2) can readily be reduced to amino groups (NH_2) under a variety of conditions.



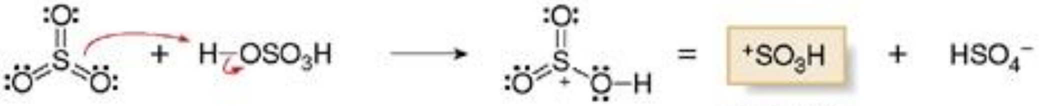
Sulfonation

Sulfonation



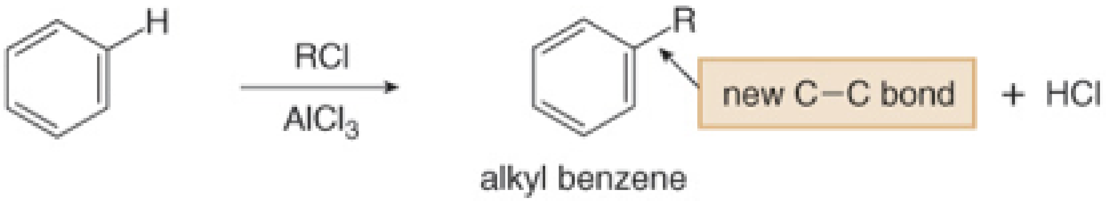
benzenesulfonic acid

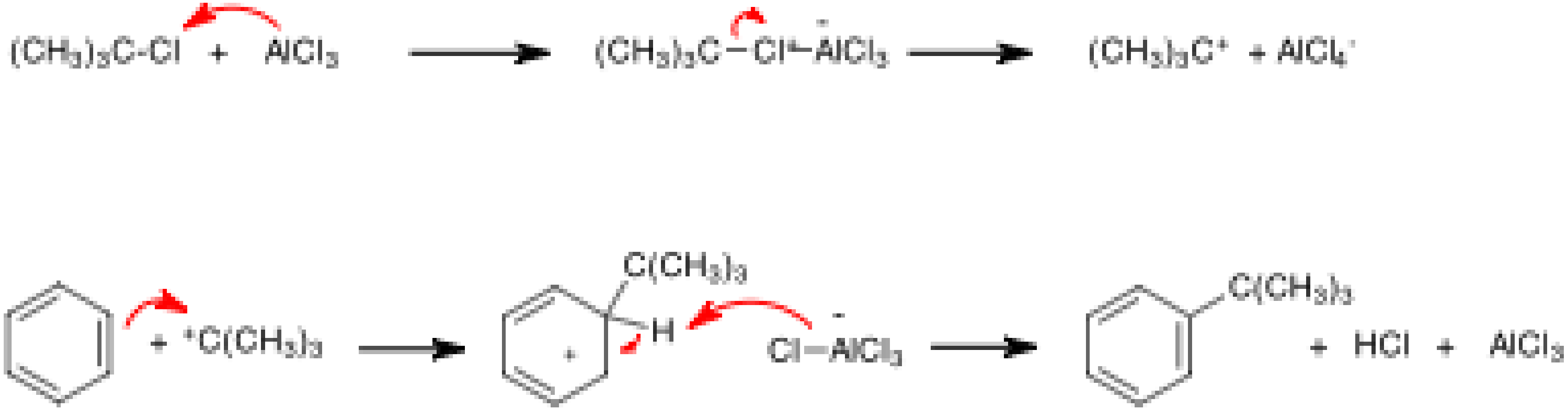
Mechanism 18.4 Formation of the Electrophile $^+SO_3H$ for Sulfonation



electrophile

Friedel-Crafts Alkylation

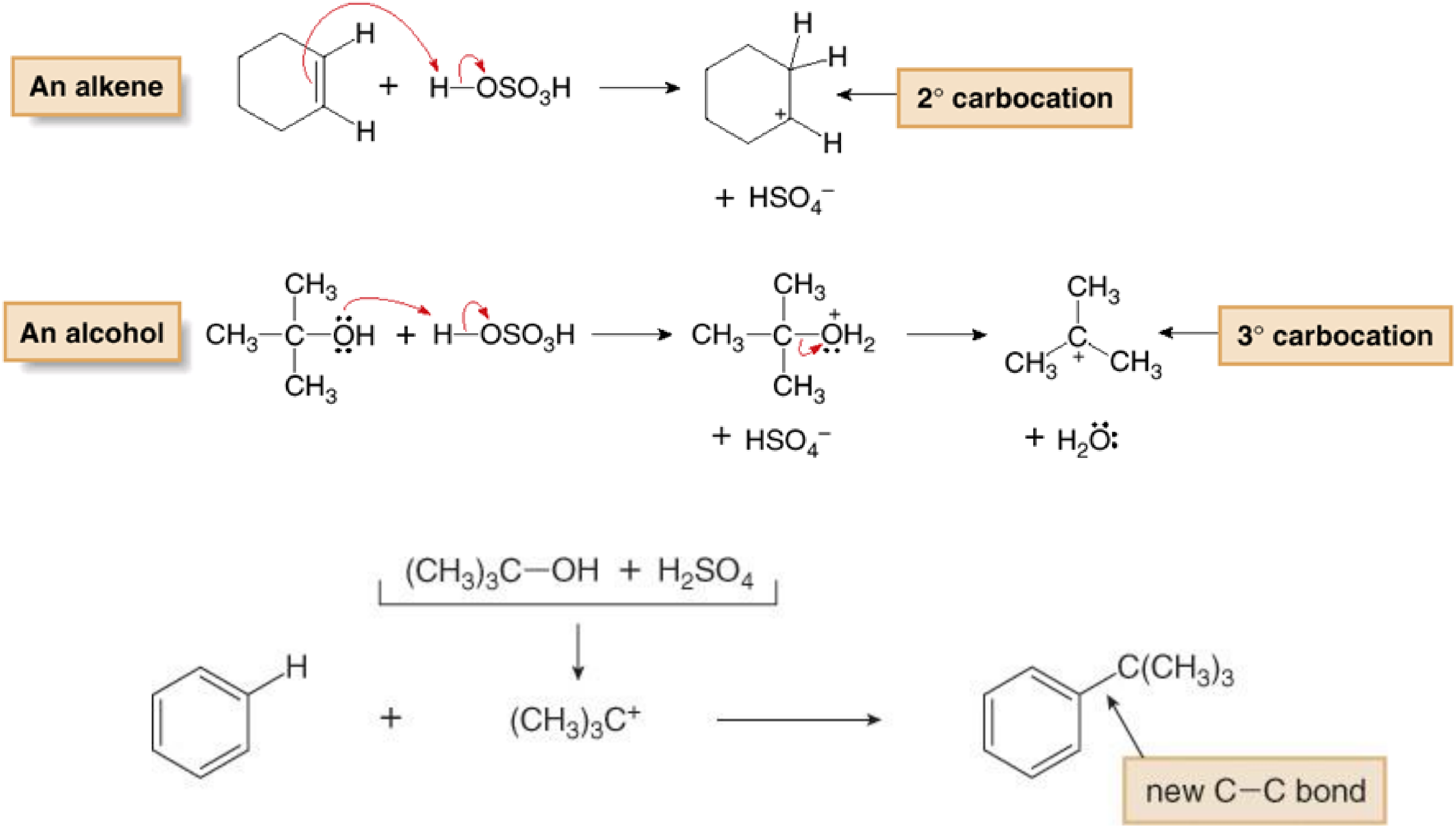




Best with 2ry and 3ry halides

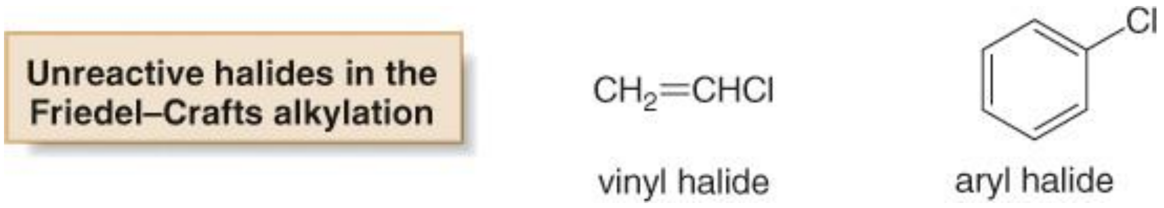
Friedel-Crafts Alkylation

Other functional groups that form carbocations can also be used as starting materials.



Limitations

[1] Vinyl halides and aryl halides do not react in Friedel-Crafts alkylation.

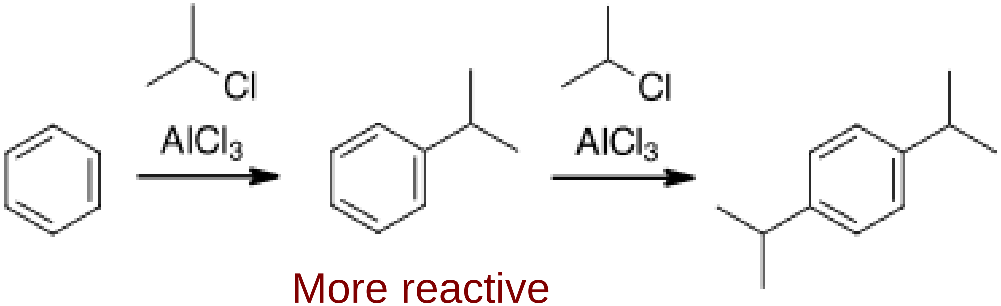

Unreactive halides in the Friedel–Crafts alkylation

$CH_2{=}CHCl$

vinyl halide

aryl halide

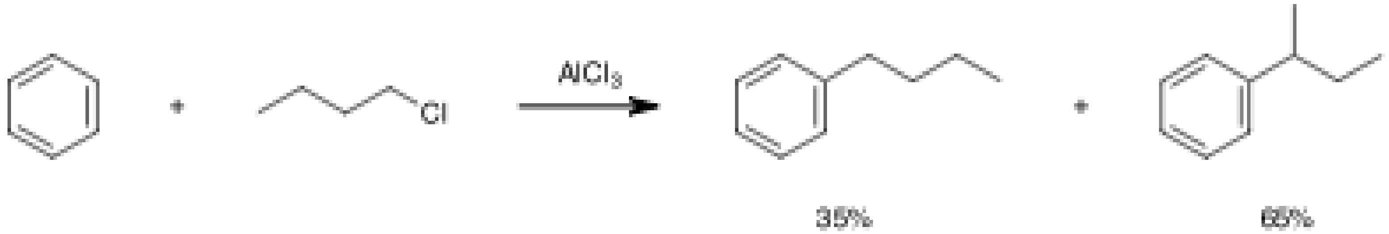
[2] Disubstituted products are obtained in F.-C. alkylations, but not in acylations.

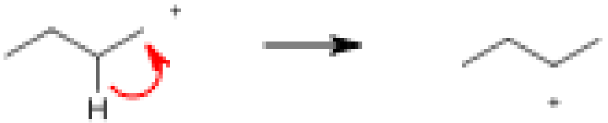


More reactive
than benzene

Limitations

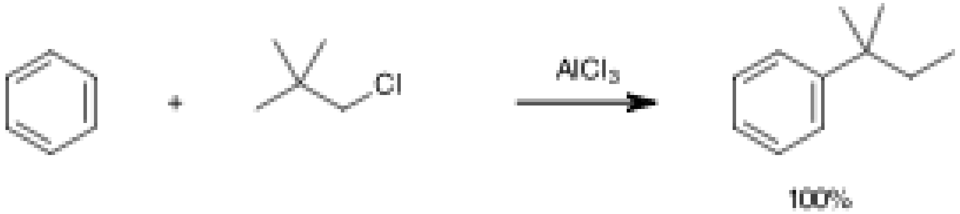
[3] Rearrangements can occur.

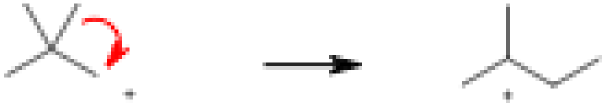




1ry
less stable

2ry
more stable



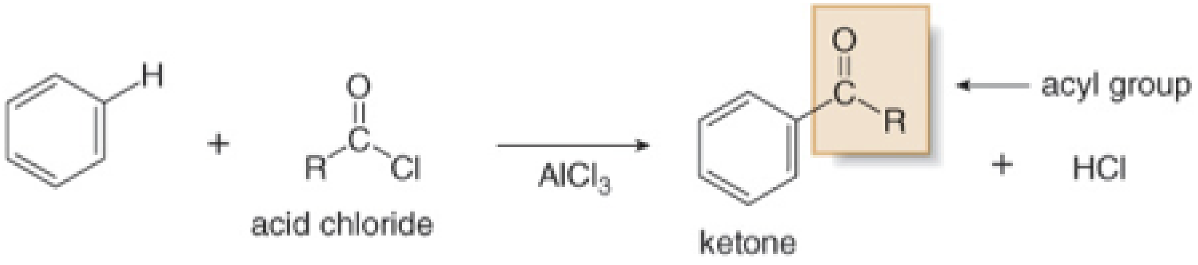


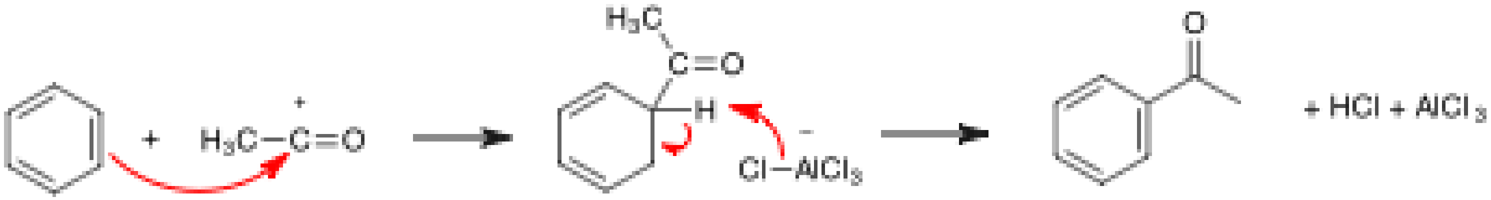
1ry
less stable

3ry
more stable

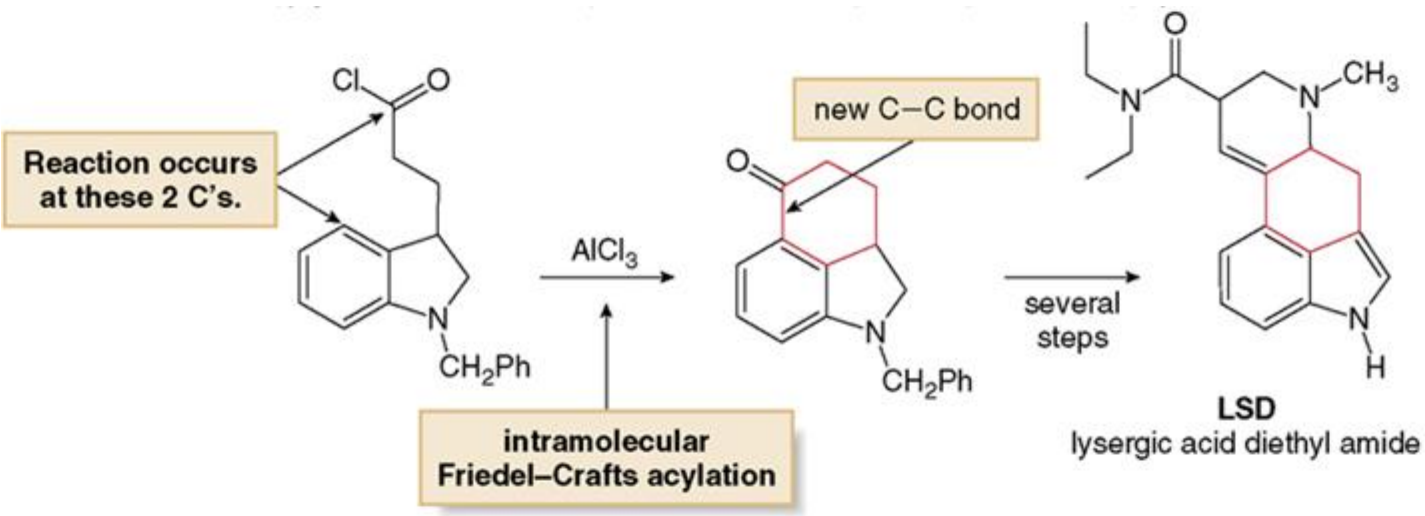
Friedel-Crafts Acylation

**Friedel–Crafts acylation—
General reaction**

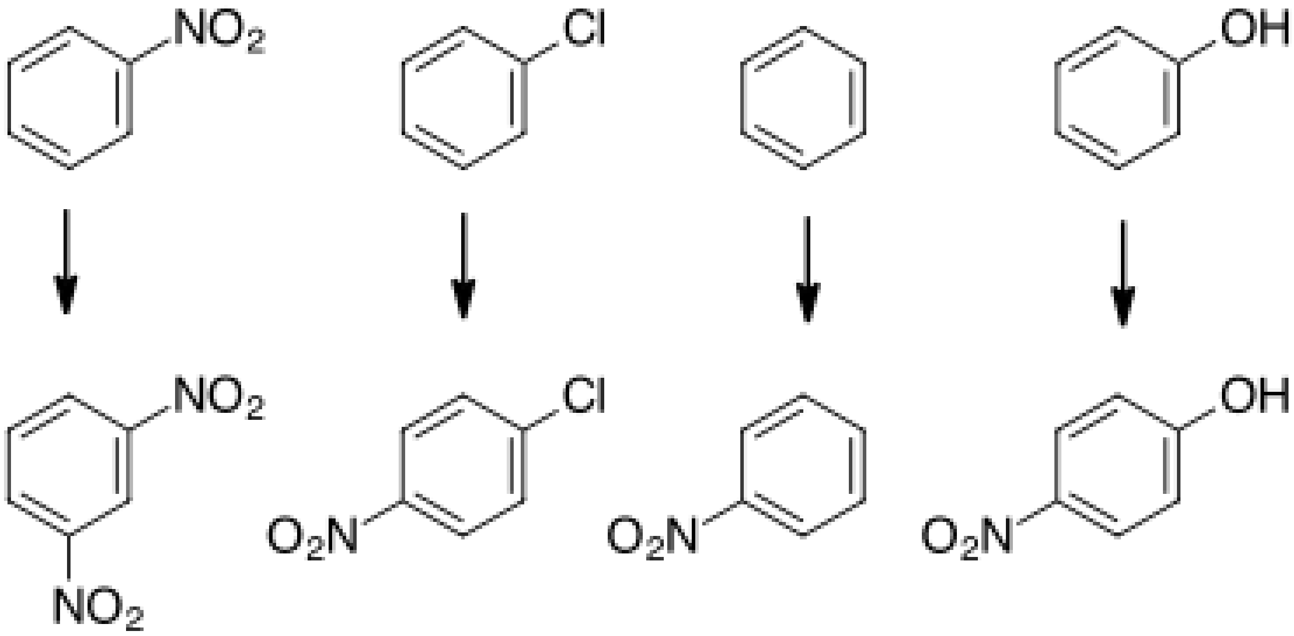




intramolecular Friedel-Crafts reactions.



Nitration of Substituted Benzenes

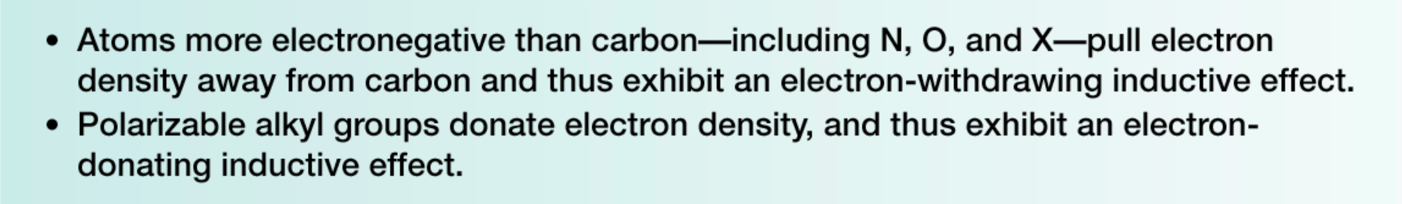


Relative rates	6×10^{-8}	0.033	1	1000

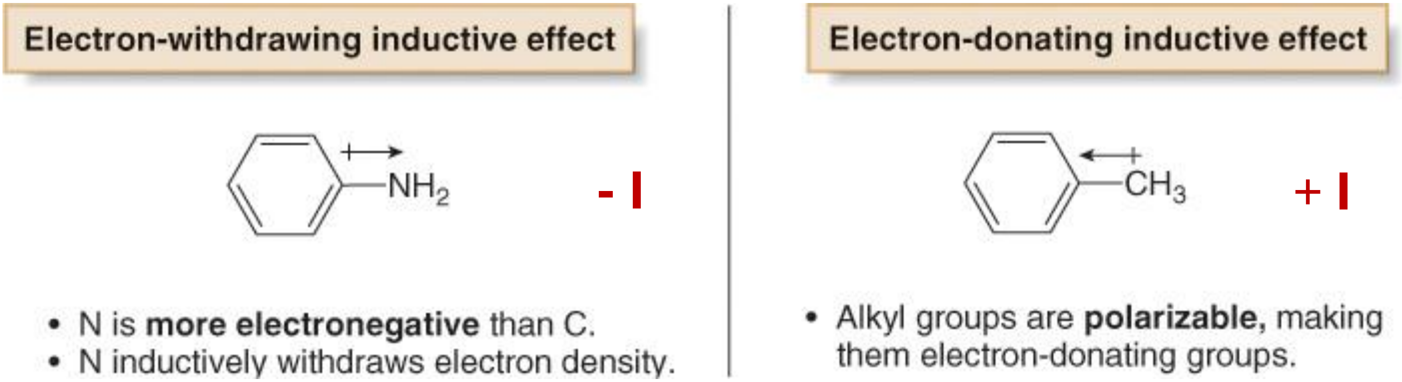
Substituents modify the electron density in the benzene ring, and this affects the course of electrophilic aromatic substitution.

Substituted Benzenes

Inductive effects (through σ bonds):



- Atoms more electronegative than carbon—including N, O, and X—pull electron density away from carbon and thus exhibit an electron-withdrawing inductive effect.
- Polarizable alkyl groups donate electron density, and thus exhibit an electron-donating inductive effect.



Electron-withdrawing inductive effect

- N is **more electronegative** than C.
- N inductively withdraws electron density.

Electron-donating inductive effect

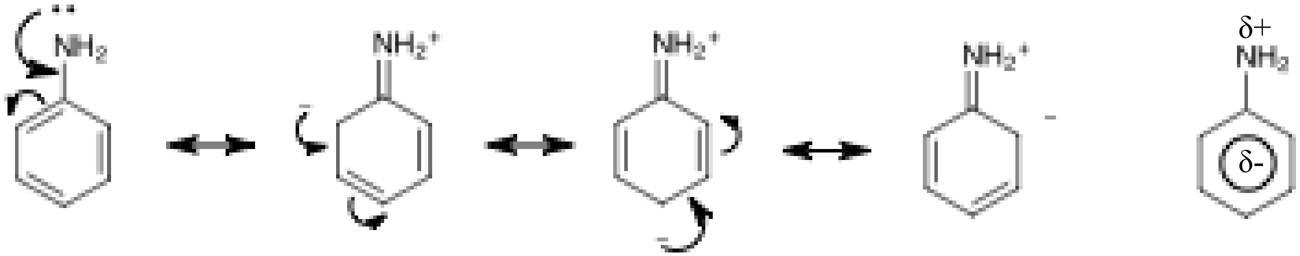
- Alkyl groups are **polarizable,** making them electron-donating groups.

- I	$-NH_3^+$ $-CF_3$	$-NH_2$, -NHR $-NR_2$	-OH -OR	-F -Cl -Br -I	-CHO -COR -COOH -COOR	-CN	SO_3H SO_2R	$-NO_2$
+ I	$-CH_3$ -Alkyl $-SiR_3$							

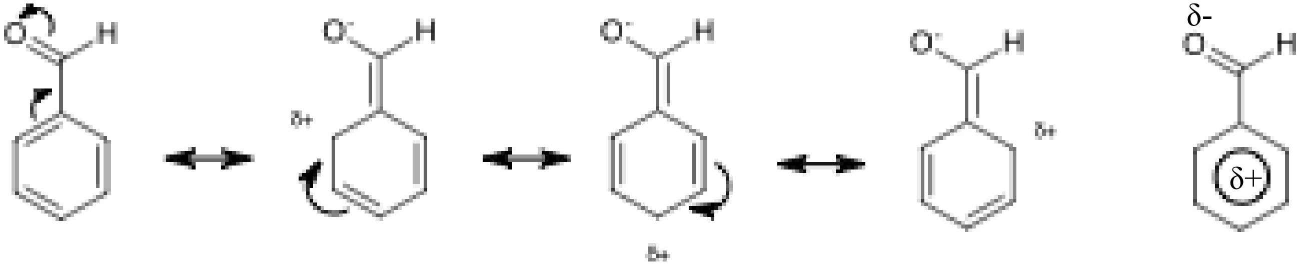
Substituted Benzenes

Resonance effects (through π bonds) are only observed with substituents containing lone pairs or π bonds.

- Substituents containing lone pairs are electron donating **(+ R)**



- Substituents –Y=Z (C_6H_5-Y=Z), where Z is more electronegative than Y are electron accepting **(- R)**

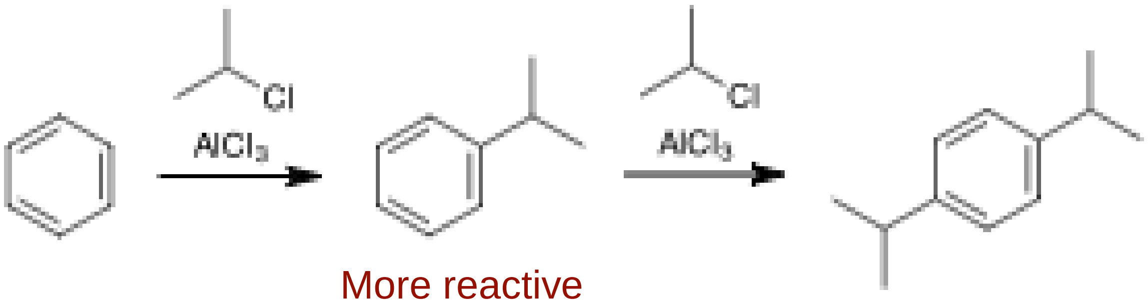


Substituted Benzenes: Activation

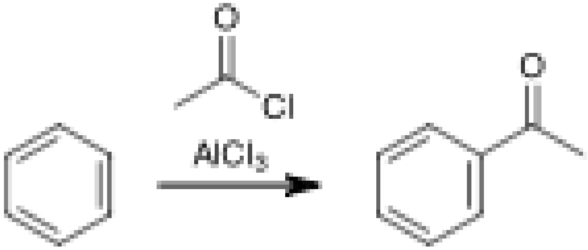
		+ *R*		- *R*			
		+*R* > -*I*	-*I* >+*R*				
- *I*	$-NR_3+$ CF_3	$-NH_2$, $-OH$ $-NHR$ $-OR$ $-NR_2$	-F -Cl -Br -I	-CHO -COR -COOH -COOR	CN	SO_3H SO_2R	$-NO_2$
+ *I*	$-CH_3$ -Alkyl $-SiR_3$						

- Substituents that increase the electron density on the ring activate the ring towards electrophiles. Substituents that decrease the electron density on the ring deactivate the ring towards electrophiles.
- To predict whether a substituted benzene is more or less electron rich than benzene itself, we must consider the net balance of both the inductive and resonance effects.

Substituted Benzenes: Activation



More reactive
than benzene



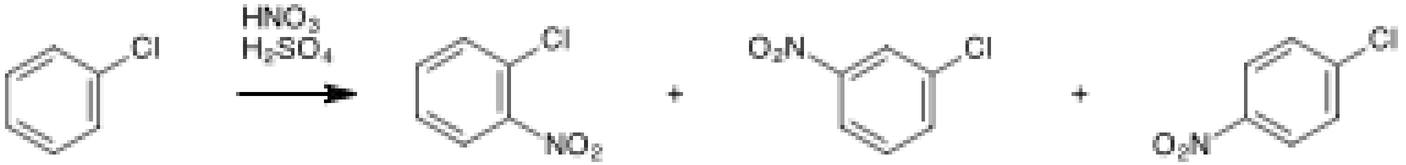
Less reactive
than benzene

Substituted Benzenes: Orientation

+R > -I (-OR, -NR2): activating, o- p- directing

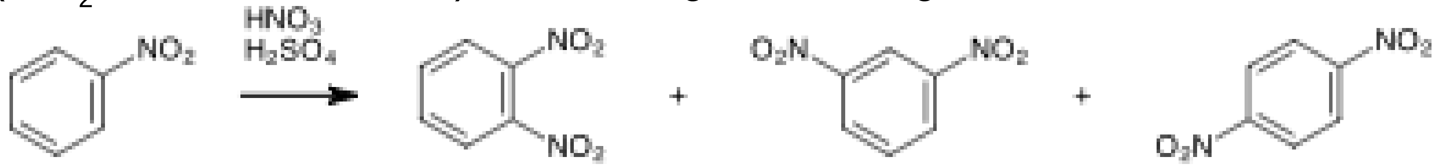
30% traces 70%

-I > +R (-F, -Cl, -Br, -I): deactivating, o- p- directing



35% traces 65%

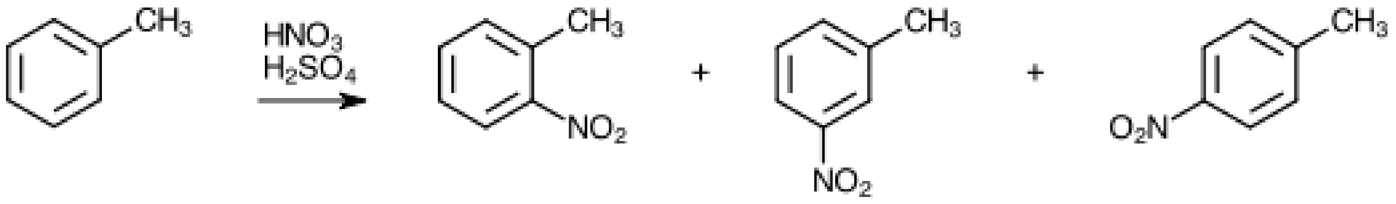
-I, -R (-NO_2, -SO3H, -CN, -COR): deactivating, m- directing.



5% 90% 5%

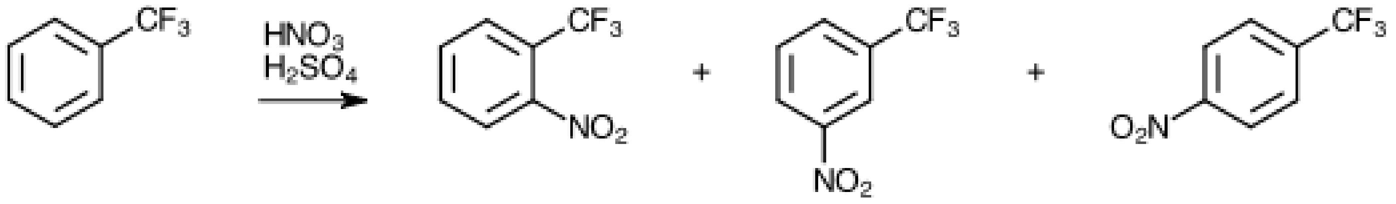
Substituted Benzenes: Orientation

+ I: activating, -o -p directing (same as + R)



58%　　5%　　37%

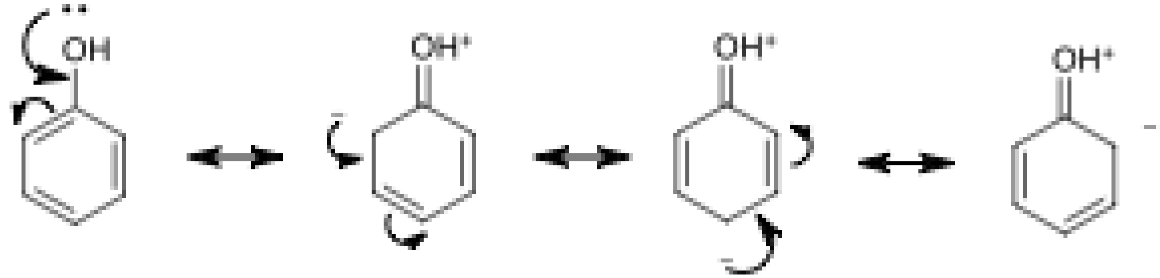
- I: deactivating, -m directing (same as - R)

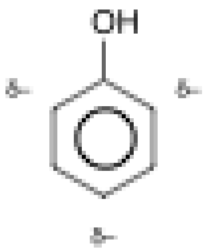


6%　　91%　　3%

Substituted Benzenes: Orientation

The new group is located either ortho, meta, or para to the existing substituent. The resonance effect of the first substituent determines the position of the second incoming substituent

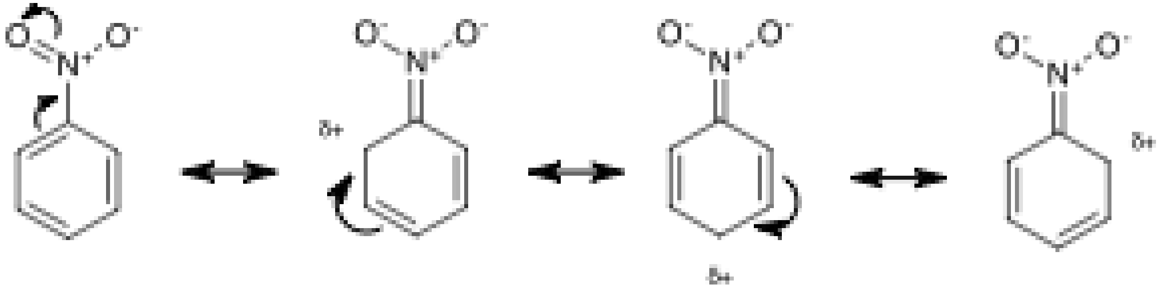


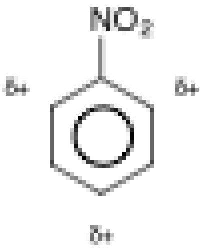


+R

orto

para

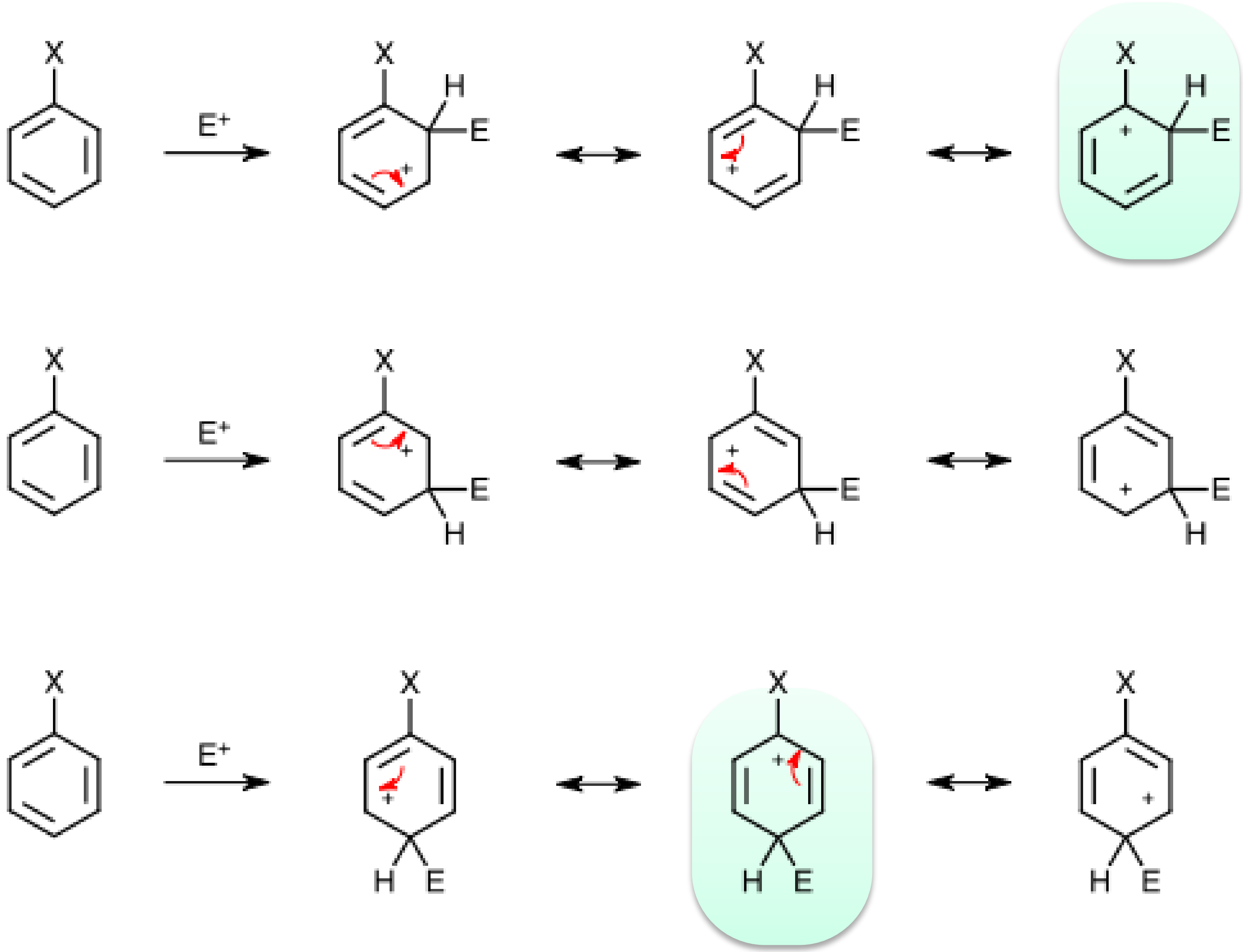




-R

meta

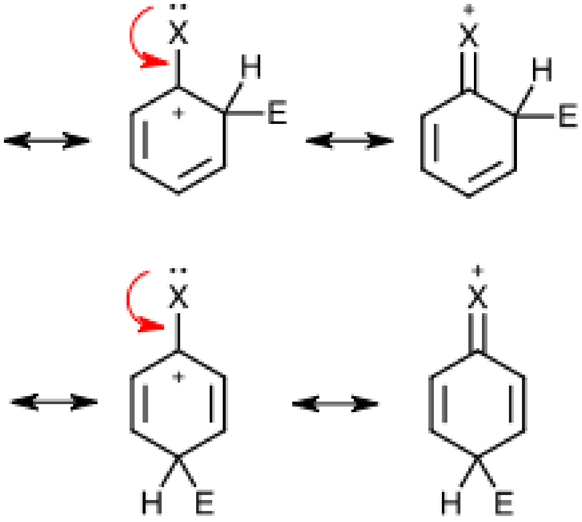
Substituted Benzenes: Orientation



Substituted Benzenes: Orientation

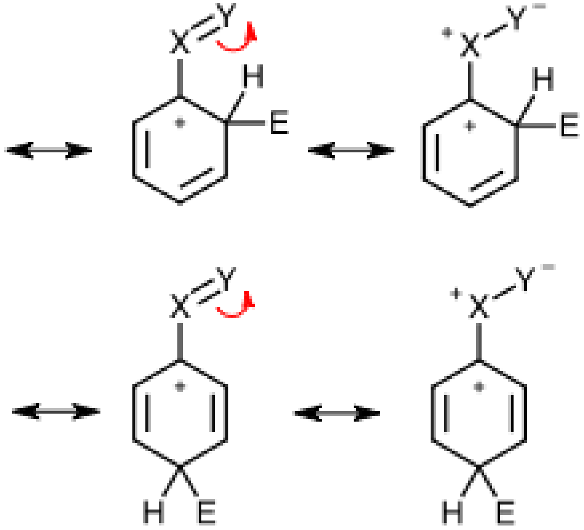
+ R

-o, -p intermediates are resonance stabilised



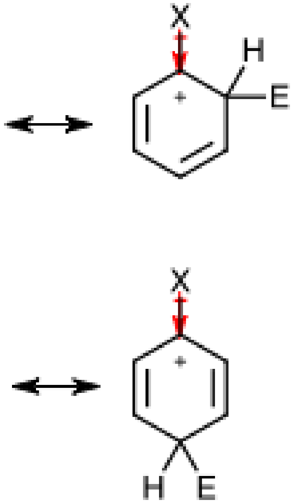
- R

-o, -p intermediates are resonance destabilised



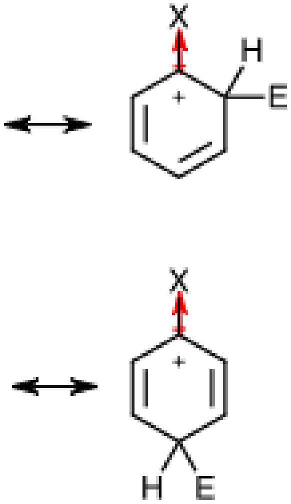
+ I

-o, -p intermediates are inductively stabilised

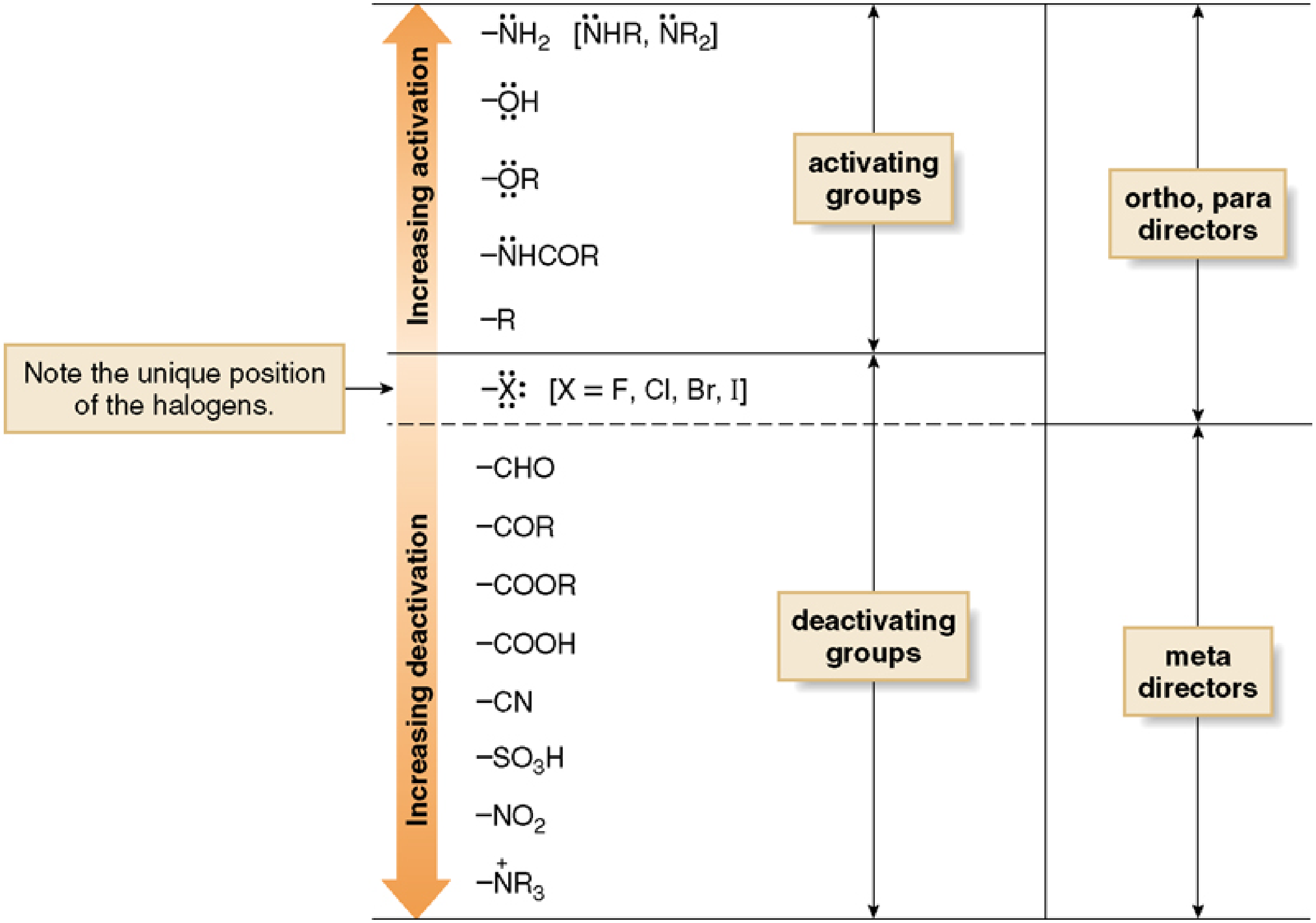


- I

-o, -p intermediates are inductively destabilised



Substituent Effects. Summary



Increasing activation

$-\ddot{N}H_2$ $[\ddot{N}HR, \ddot{N}R_2]$

$-\underset{..}{\ddot{O}}H$

$-\underset{..}{\ddot{O}}R$

$-\ddot{N}HCOR$

$-R$

$-\underset{..}{\ddot{X}}:$ [X = F, Cl, Br, I]

$-CHO$

$-COR$

$-COOR$

$-COOH$

$-CN$

$-SO_3H$

$-NO_2$

$-\overset{+}{N}R_3$

Increasing deactivation

activating groups

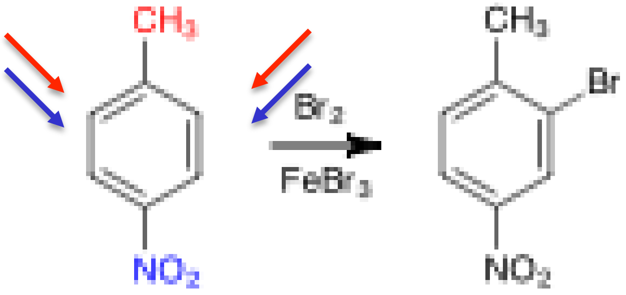
deactivating groups

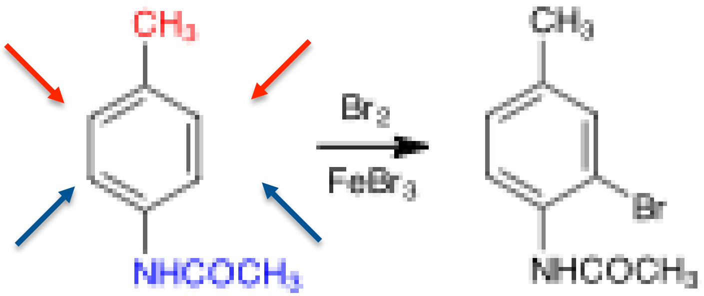
ortho, para directors

meta directors

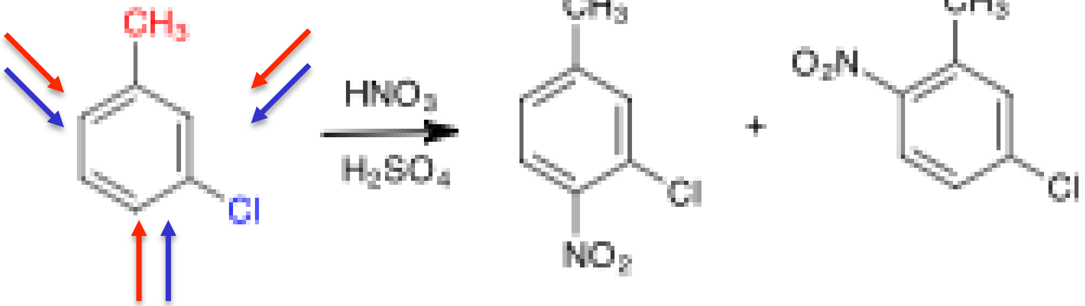
Note the unique position of the halogens.

Disubstituted Benzenes

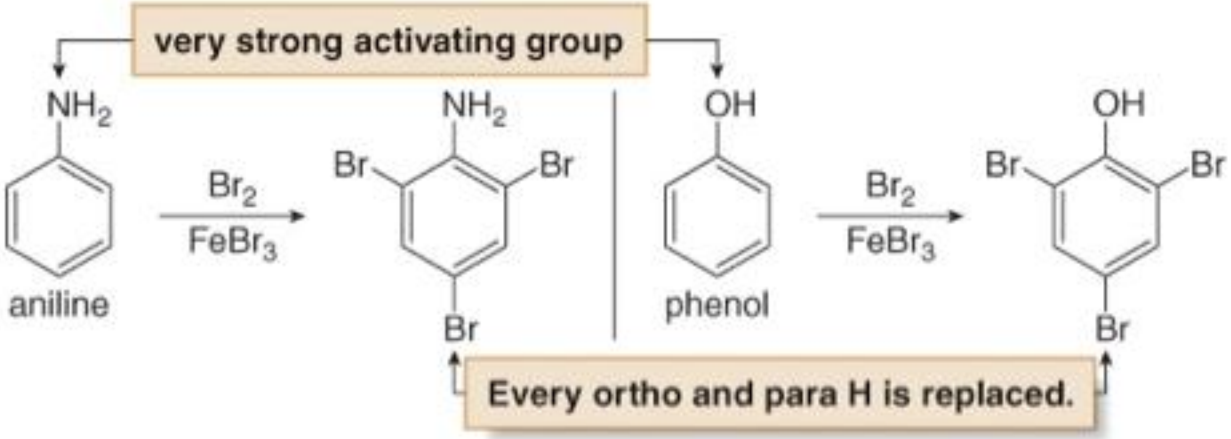




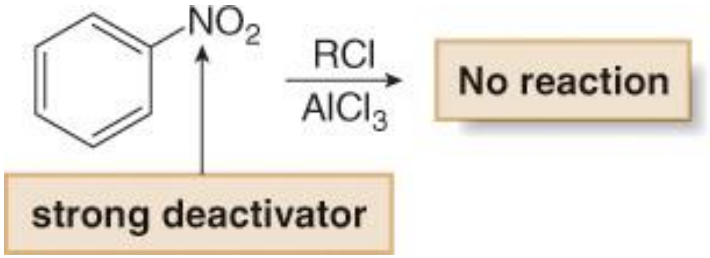
sterically hindered



Further Examples

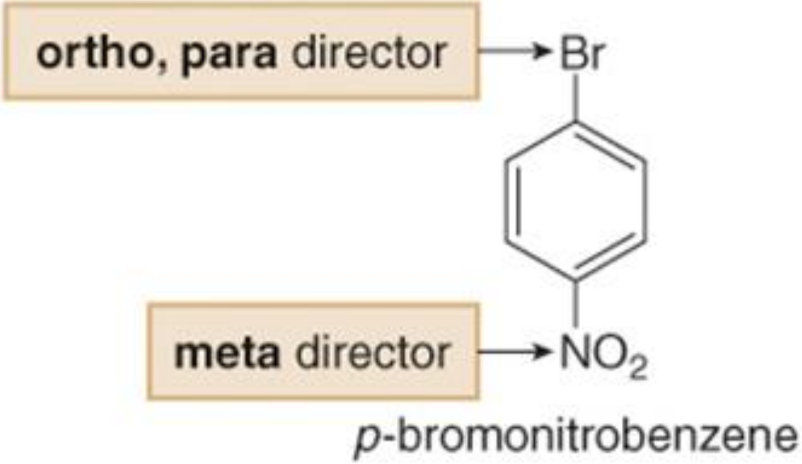

very strong activating group

Every ortho and para H is replaced.


No reaction

strong deactivator

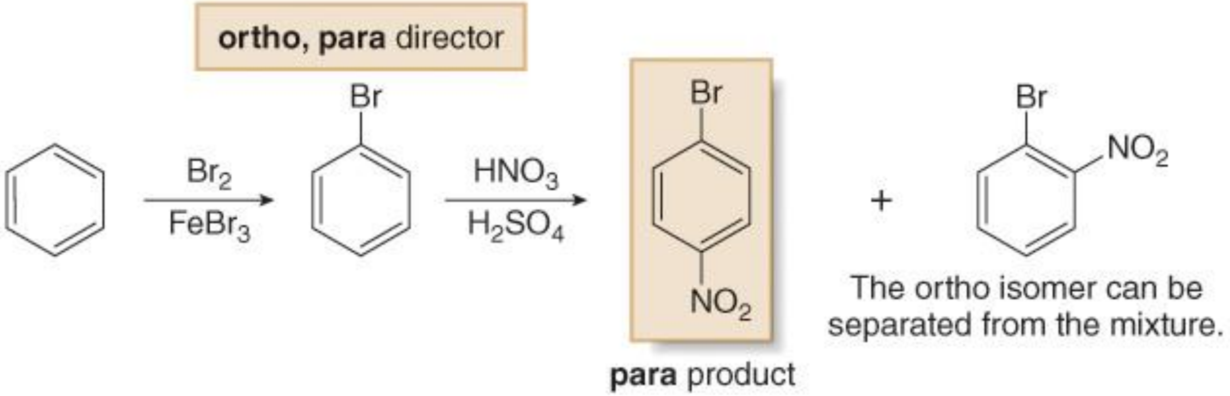
Synthesis of Polysubstituted Benzenes



p-bromonitrobenzene

Synthesis of Polysubstituted Benzenes

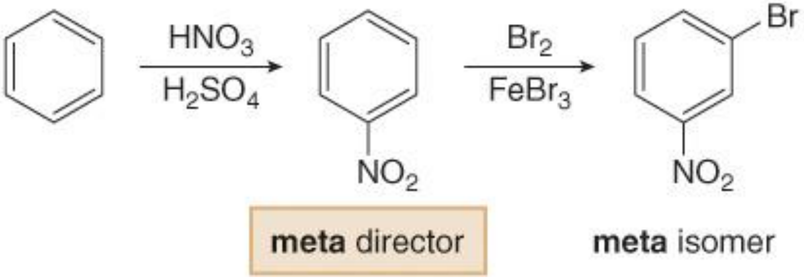
Pathway [1]: Bromination before nitration



The ortho isomer can be separated from the mixture.

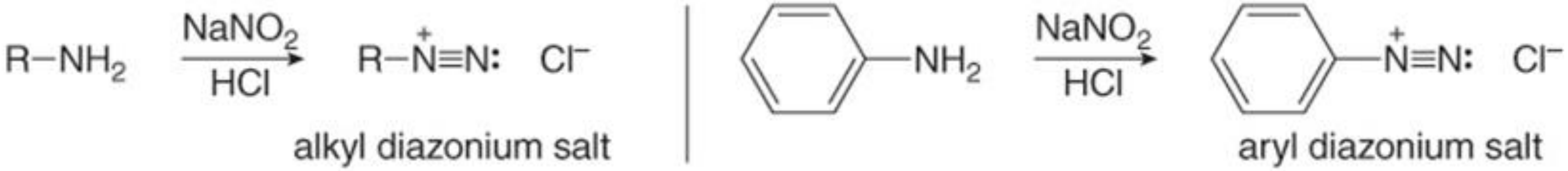
This pathway gives the desired product.

Pathway [2]: Nitration before bromination



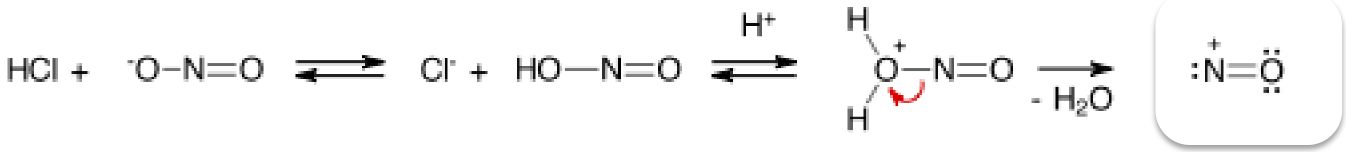
This pathway does NOT form the desired product.

Reaction of Amines with Nitrous Acid



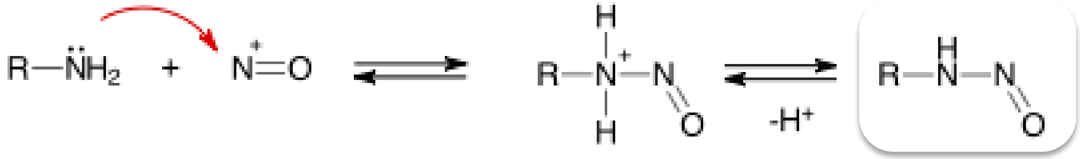
Reaction of Amines with Nitrous Acid

1. generation of the electrophile



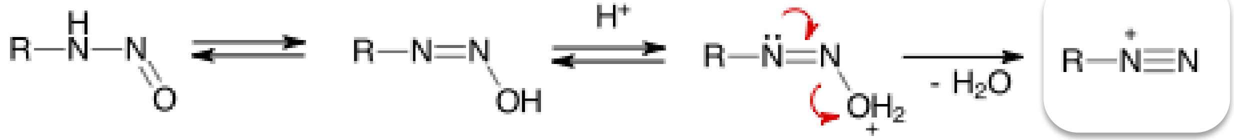
nitrosonium ion

2. nitrosation



N-nitrosamine

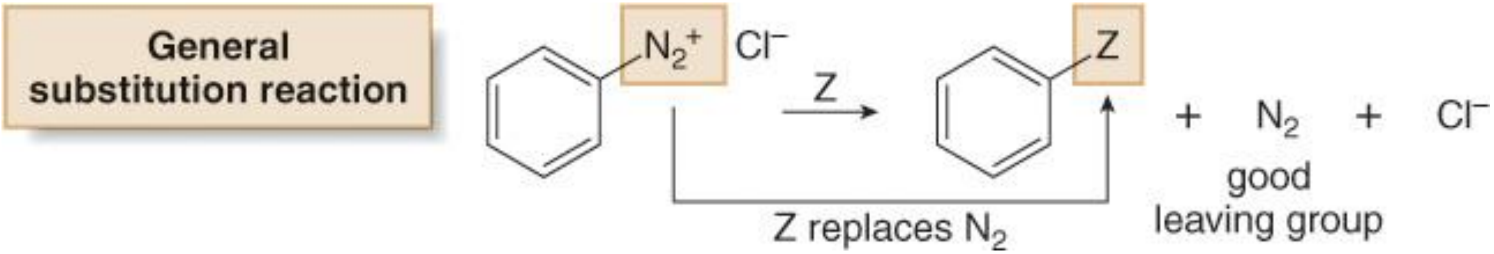
3. acid-catalysed elimination



diazonium ion

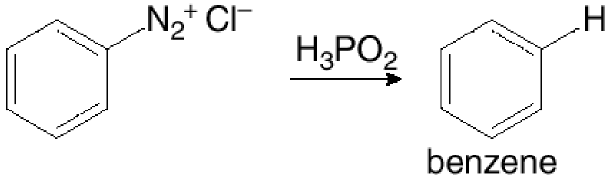
Substitution Reactions of Aryl Diazonium Salts

- Aryl diazonium salts react with a variety of reagents to form products in which a nucleophile Z replaces N_2, a very good leaving group.
- The mechanism of these reactions varies with the identity of Z.



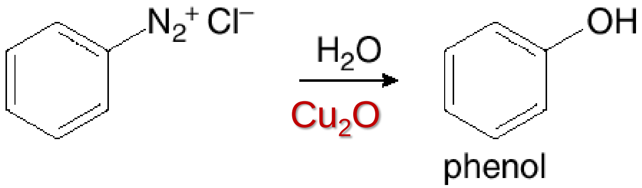
Substitution Reactions of Aryl Diazonium

Substitution by H—Synthesis of benzene



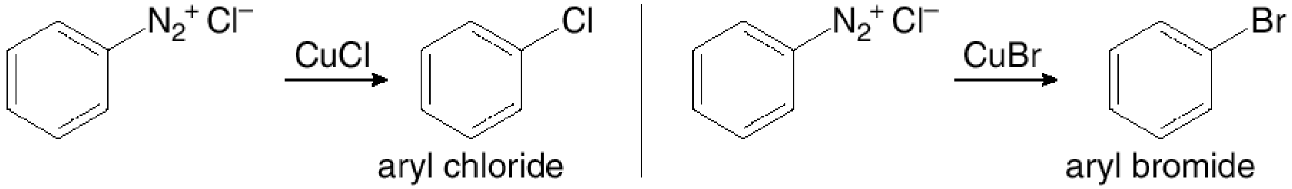
A diazonium salt reacts with hypophosphorus acid to form benzene. This reaction is useful in synthesizing compounds that have substitution patterns that are not available by other means.

Substitution by OH—Synthesis of phenols



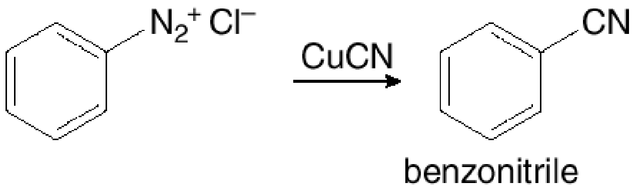
Substitution Reactions of Aryl Diazonium

Substitution by Cl or Br—Synthesis of aryl chlorides and bromides



This is called the Sandmeyer reaction. It provides an alternative to direct chlorination and bromination of the aromatic ring using Cl_2 or Br_2 and a Lewis acid catalyst.

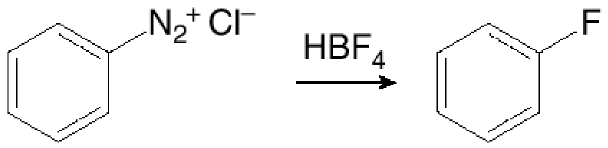
Substitution by CN—Synthesis of benzonitriles



Since the cyano group can be converted into a variety of other functional groups, this reaction provides easy access to a wide variety of benzene derivatives.

Substitution Reactions of Aryl Diazonium Salts

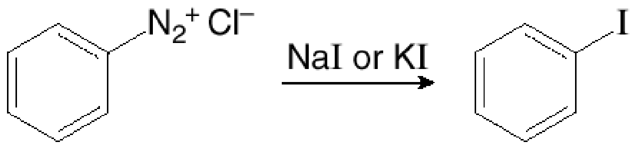
Substitution by F—Synthesis of aryl fluorides



aryl fluoride

This is a useful reaction because aryl fluorides cannot be produced by direct fluorination with F_2 and a Lewis acid catalyst.

Substitution by I—Synthesis of aryl iodides

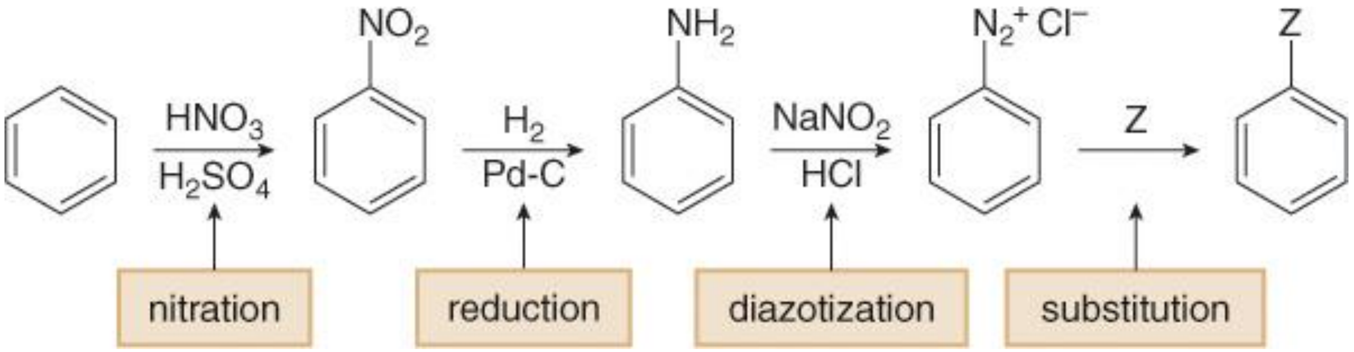


aryl iodide

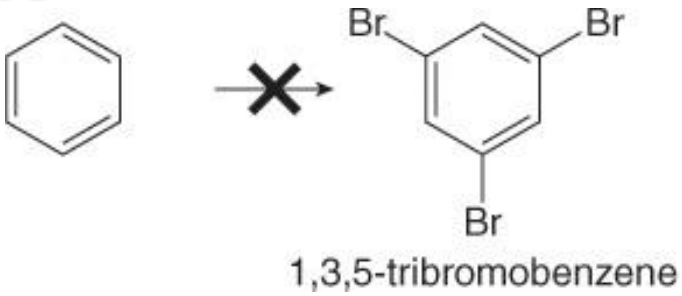
This is a useful reaction because aryl iodides cannot be produced by direct iodination with I_2 and a Lewis acid catalyst.

Substitution Reactions of Aryl Diazonium Salts

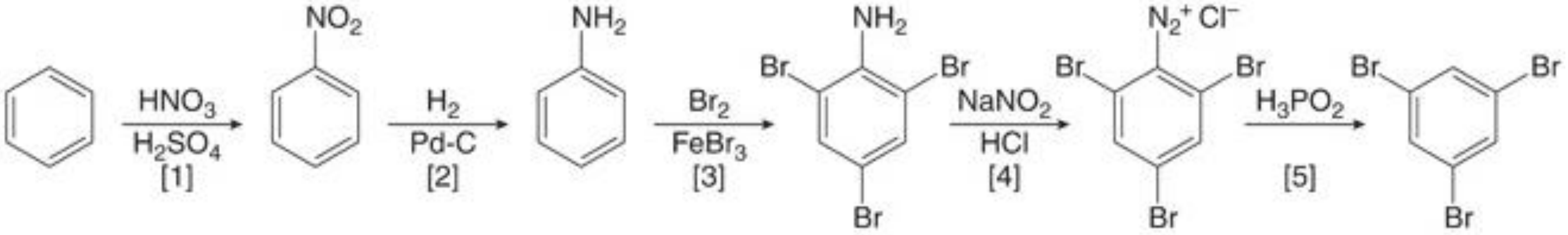
Diazonium salts provide easy access to many different benzene derivatives. Keep in mind the following four-step sequence, because it will be used to synthesize many substituted benzenes.



Substitution Reactions of Aryl Diazonium Salts



The Br atoms are ortho, para directors located meta to each other.

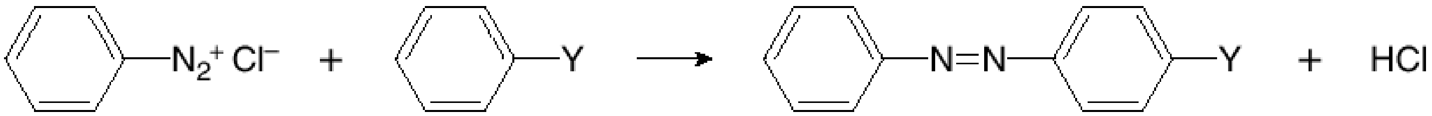


- Nitration followed by reduction forms aniline ($C_6H_5NH_2$) from benzene (Steps [1] and [2]).
- Bromination of aniline yields the tribromo derivative in Step [3].
- The NH$_2$ group is removed by a two-step process: diazotization with NaNO$_2$ and HCl (Step [4]), followed by substitution of the diazonium ion by H with H$_3$PO$_2$.

Coupling Reactions of Aryl Diazonium Salts

- When a diazonium salt is treated with an aromatic compound activated by a strong electron-donor group, a substitution reaction takes place giving an azo compound.

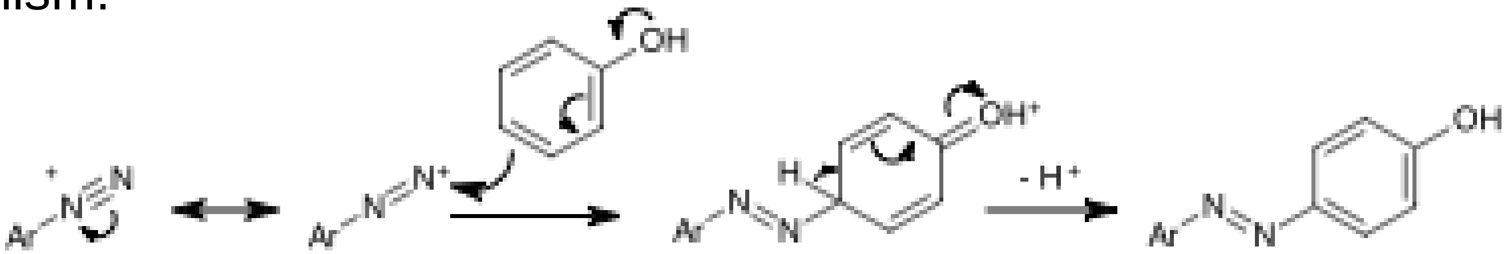
Azo coupling



Y = NH_2, NHR, NR_2, OH
(a strong electron-
donor group)

azo compound

Mechanism:

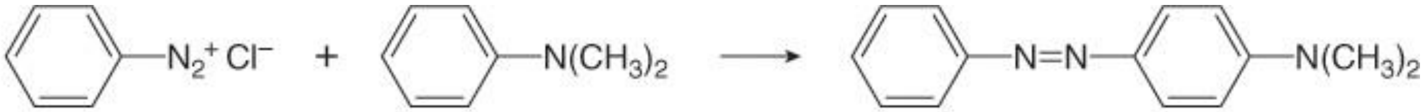


The para position is preferred for steric reasons

Azo Dyes

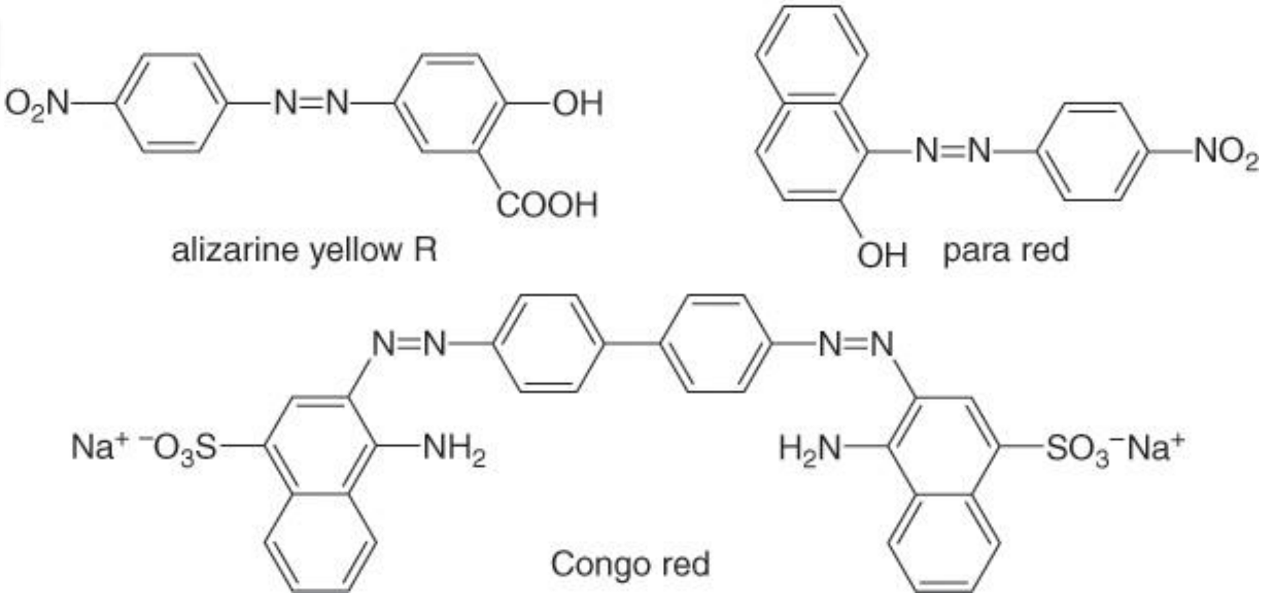
- Azo compounds are highly conjugated, rendering them colored. Many of these compounds are synthetic dyes. Butter yellow was once used to color margarine.

Example



a yellow azo dye
“butter yellow”

Three azo dyes

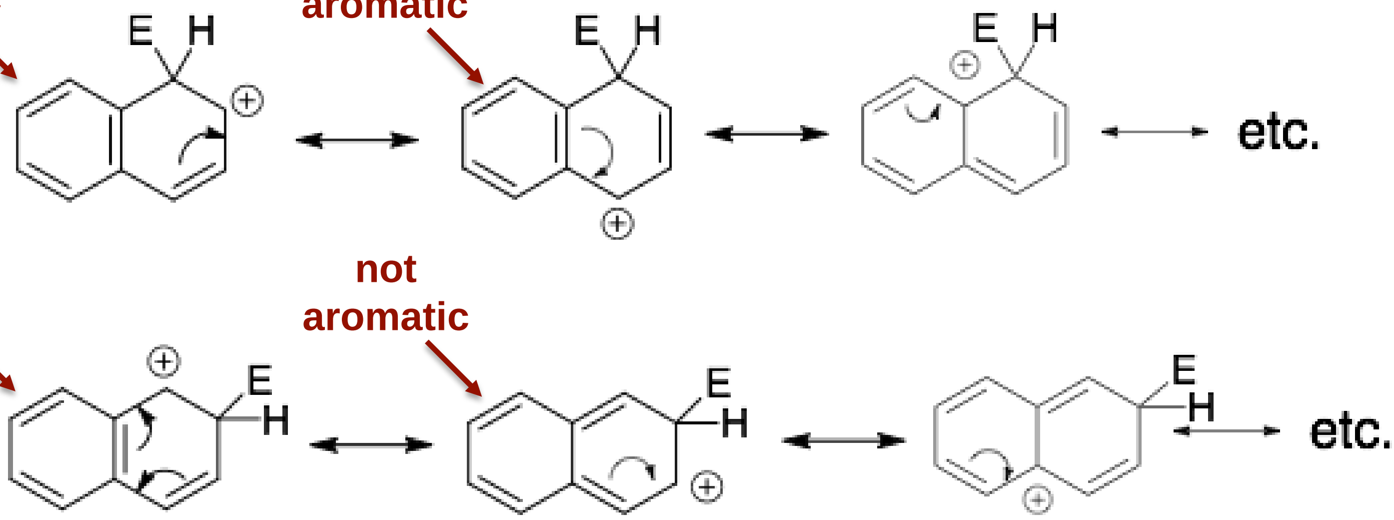


alizarine yellow R

para red

Congo red

S_EAr in Polyciclic Aromatic Compounds



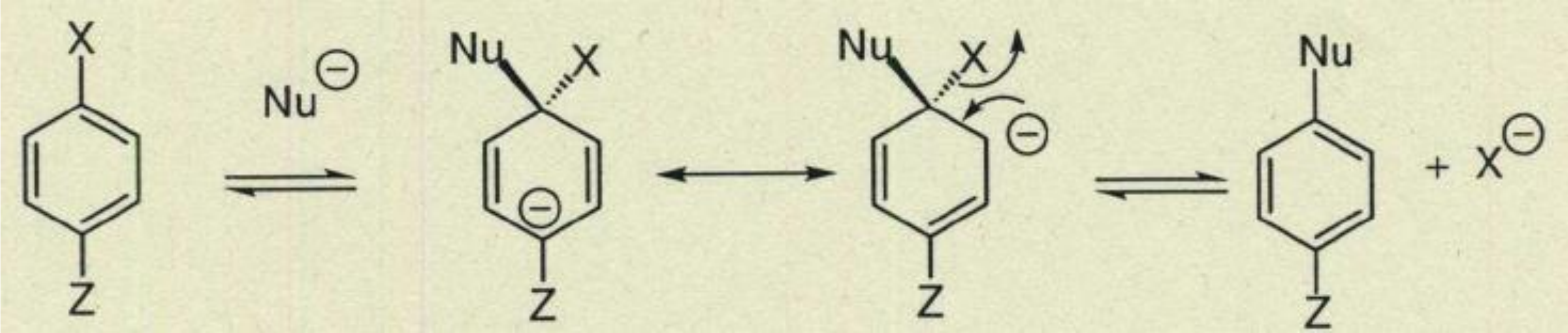
aromatic

aromatic

aromatic

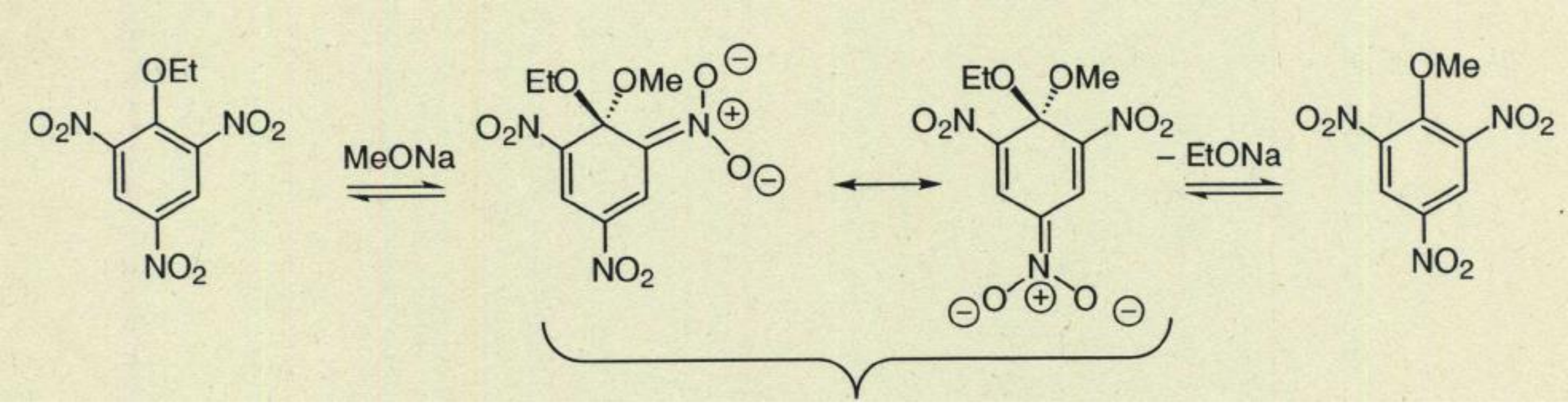
not aromatic

Nucleophilic Aromatic Substitutions, S_NAr



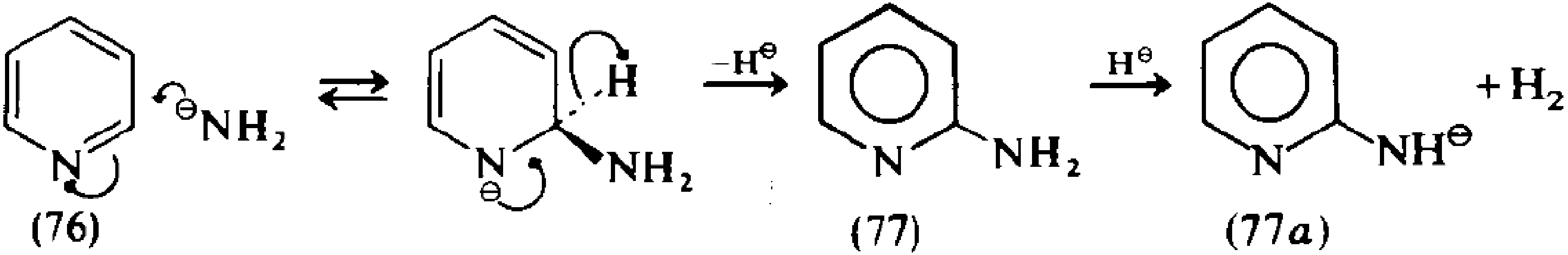
Z = Electron Accepting Substituent (sigma or π: NO_2, CN, N_2^+, SO_2R)
X = Leaving Group

Example

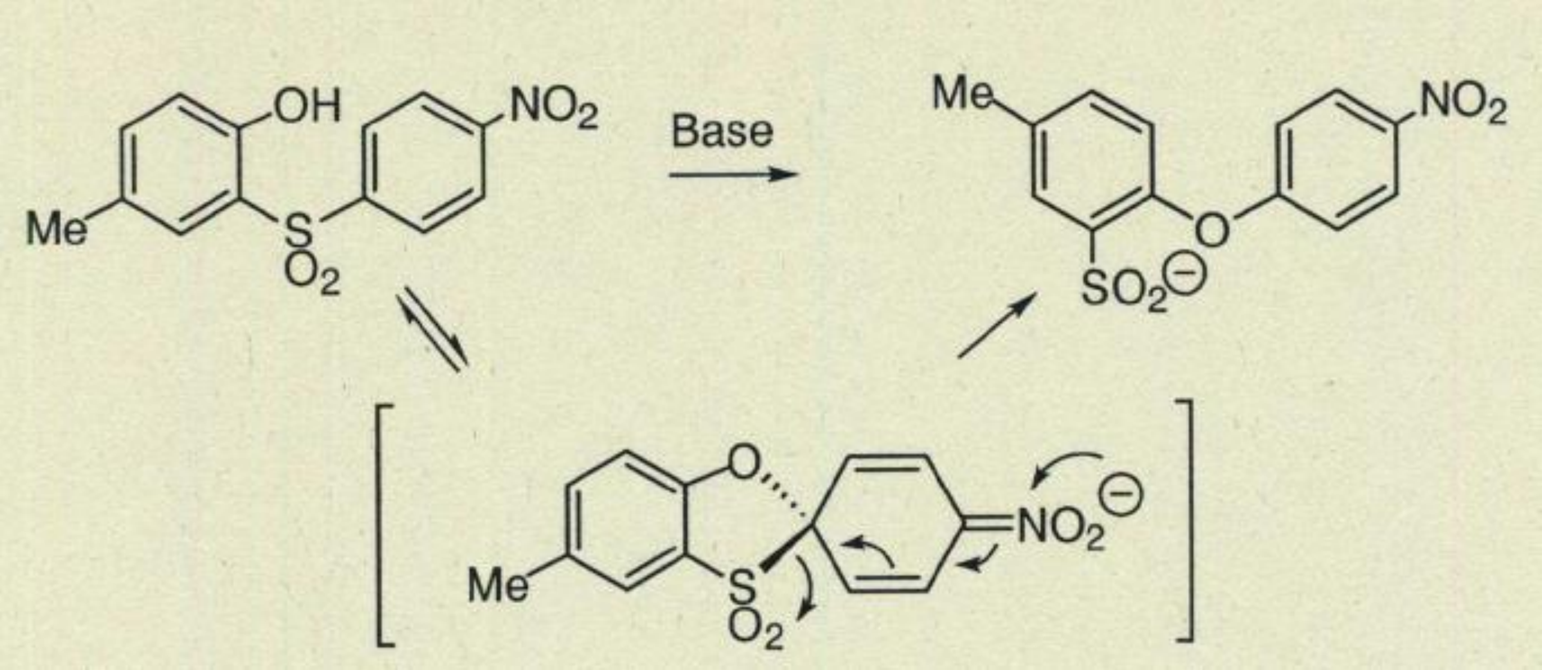


Examples of S$_N$Ar

1)

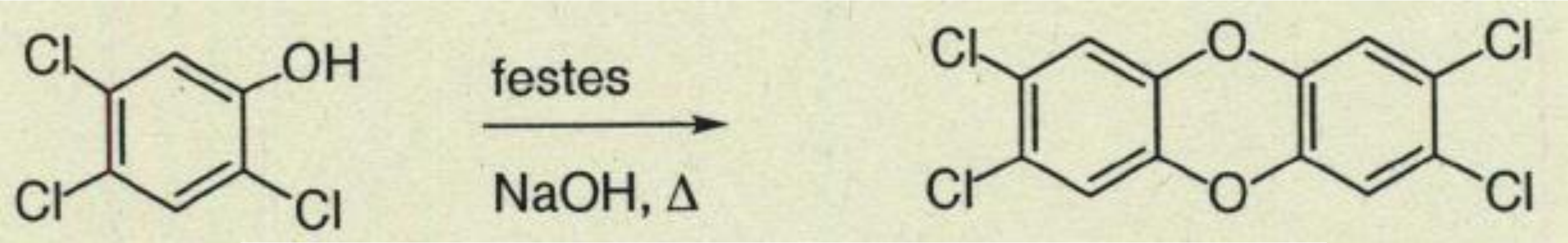


2)

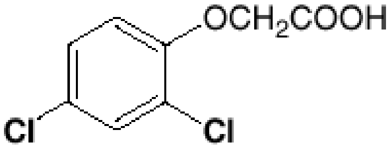


Examples of S_NAr

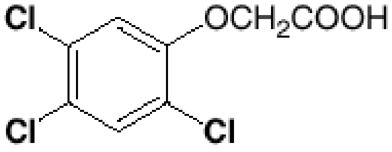
3)



Herbicides were used extensively during the Vietnam War to defoliate dense jungle areas. The concentration of certain herbicide by-products in the soil remains high today.

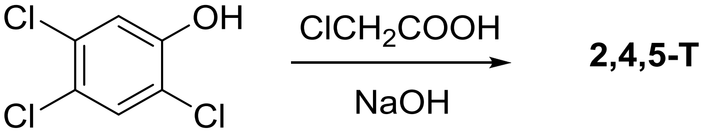


2,4-D
2,4-dichlorophenoxy-
acetic acid
herbicide

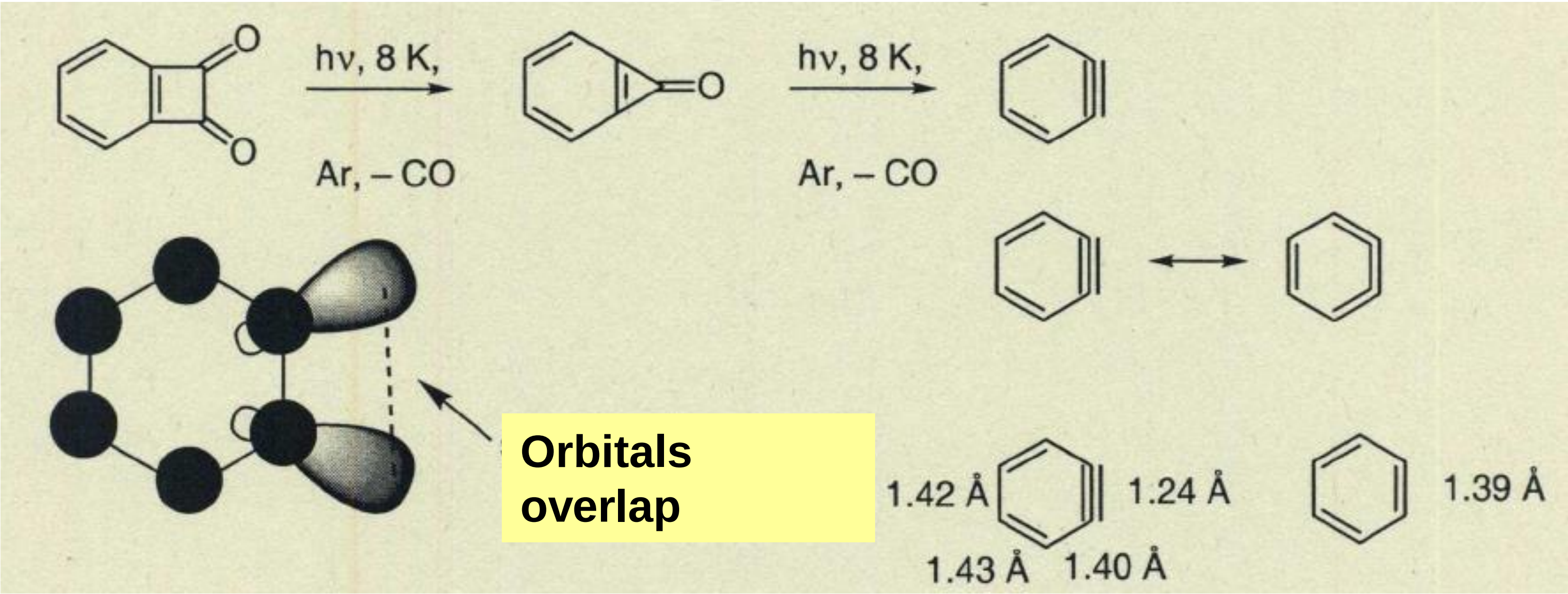


2,4,5-T
2,4,5-trichlorophenoxy-
acetic acid
herbicide

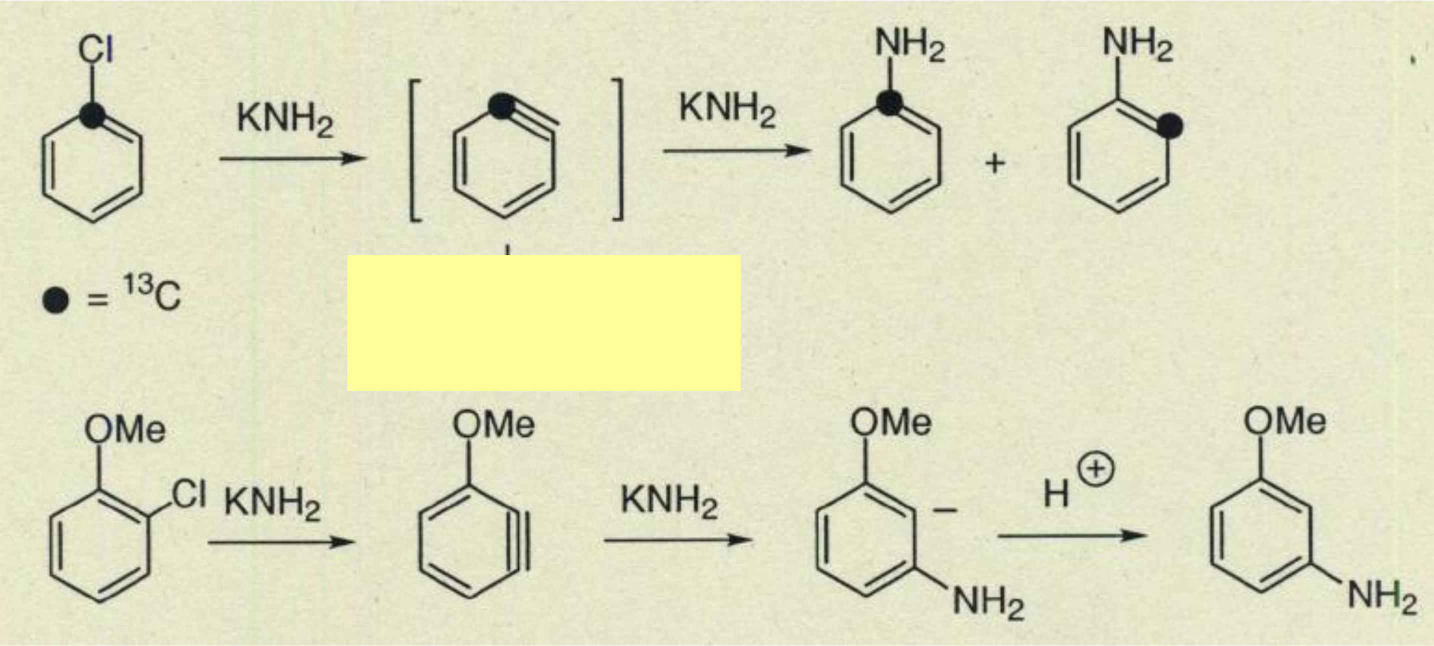
the active components in **Agent Orange**,
a defoliant used in the Vietnam War



Benzyne

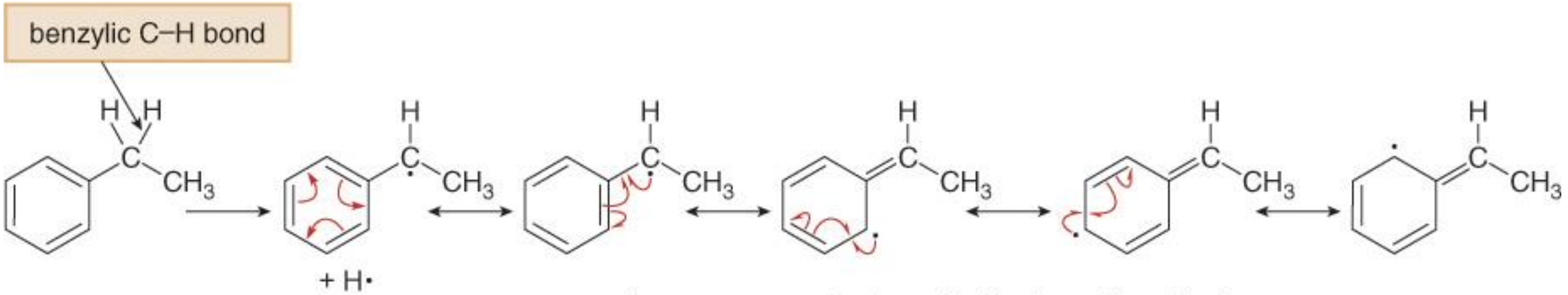


Orbitals overlap

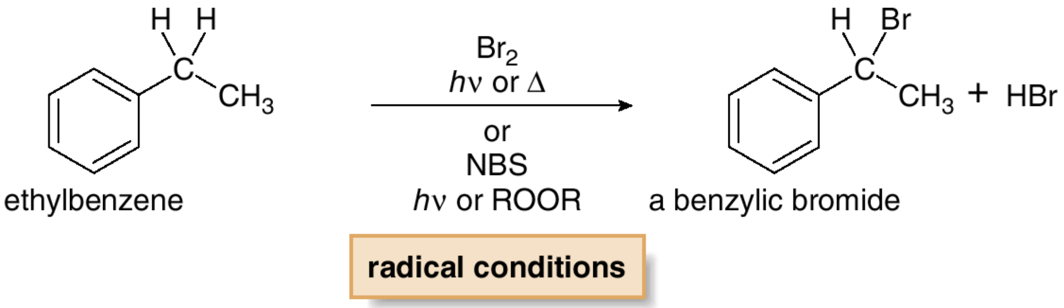


Side Chain Reactivity: Radical Halogenation

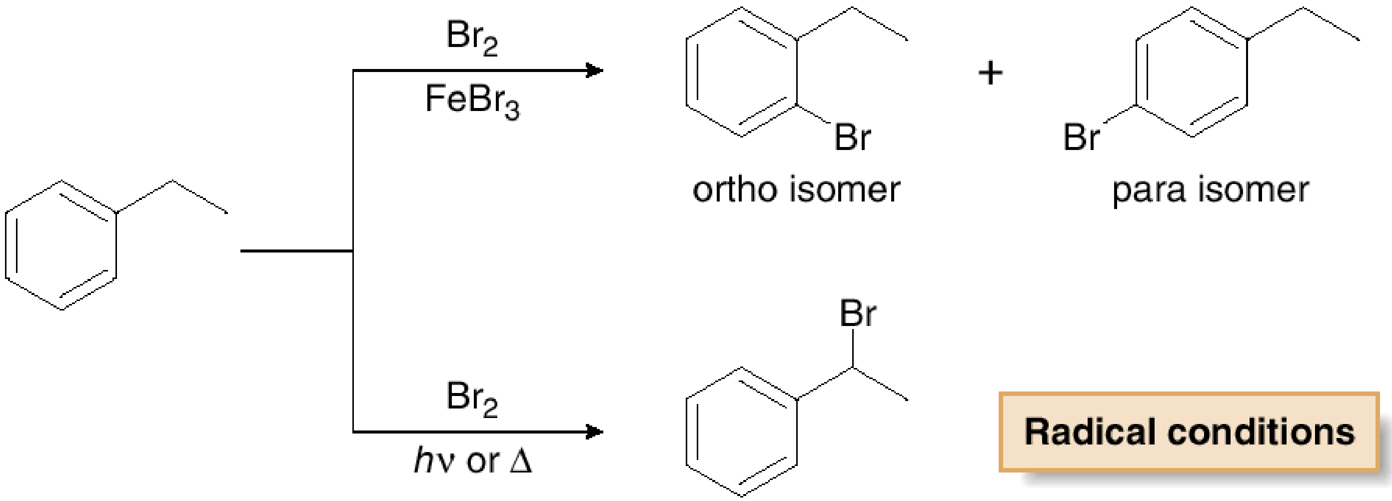
Benzylic C—H bonds are weaker than most other *sp*^{3} hybridized C—H bonds, because homolysis forms a resonance-stabilized benzylic radical.



five resonance structures for the benzylic radical



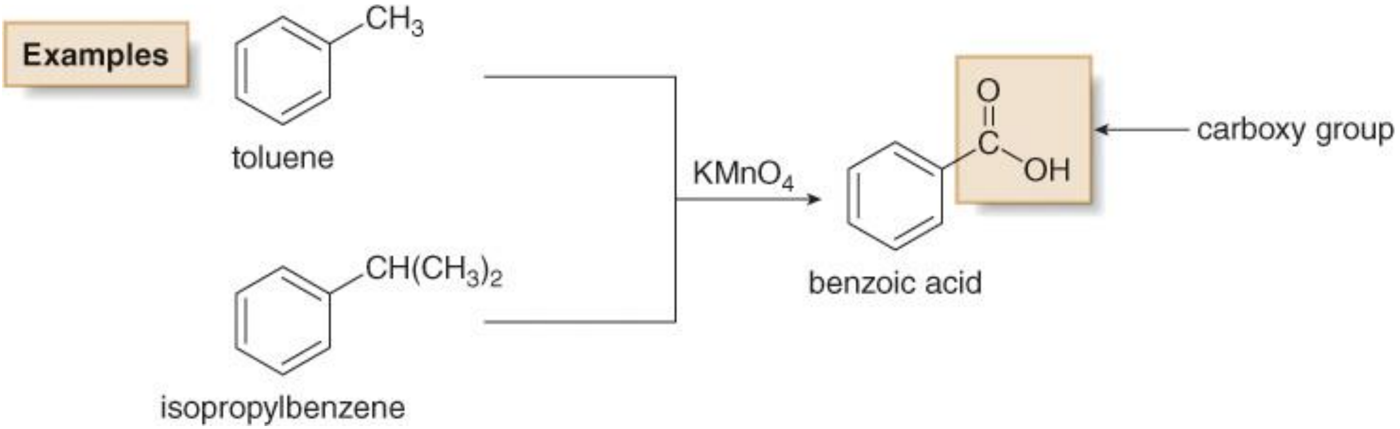
Side Chain Reactivity

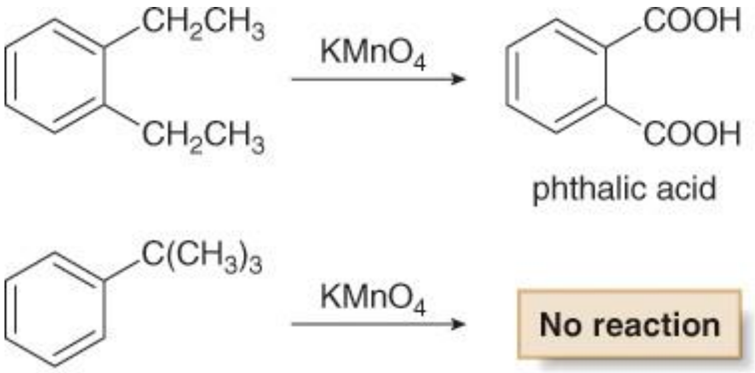


Ionic conditions

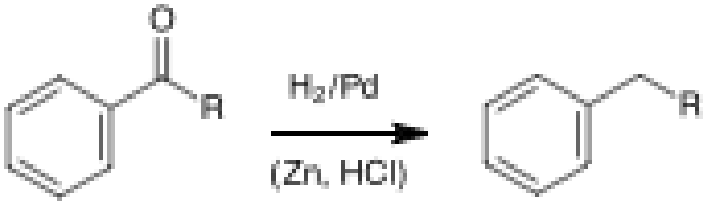
Radical conditions

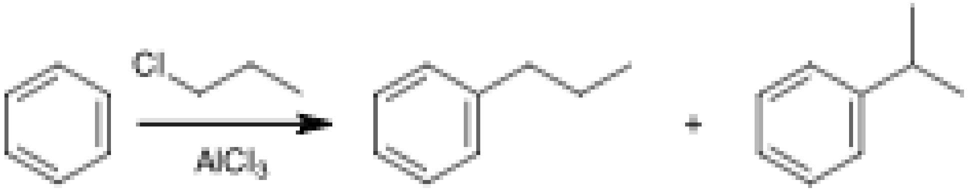
Side Chain Reactivity: Oxidation





Side Chain Reactivity: Reduction





(+ disubstituted products)