Aromatic Hydrocarbon

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Aromaticity & AROMATIC COMPOUND

- Aromaticity is a property describing the way in which a conjugated ring of unsaturated bonds, lone pairs, or empty orbitals exhibits a stabilization stronger than would be expected by the stabilization of conjugation alone.

- Aromaticity can also be considered a manifestation of cyclic delocalization and of resonance.

- Aromatic compounds, also known as arenes or aromatics, are chemical compounds that contain conjugated planar ring systems with delocalised pi electron clouds instead of discrete alternating single and double bonds. Typical aromatic compounds are benzene and toluene. They should satisfy Hückel's rule.

Huckle Rule:

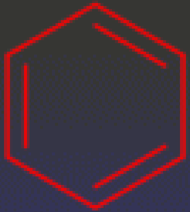
A cyclic ring molecule follows Hückel's rule when the number of its π-electrons equals $4n+2$ where n is zero or any positive integer,

Criteria for simple aromatics are:

1.follow Huckel's rule, having $4n+2$ electrons in the delocalized p-orbital cloud;

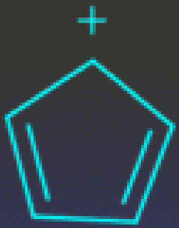
2.be able to be planar and are cyclic;

3.every atom in the circle is able to participate in delocalizing the electrons by having a p-orbital or an unshared pair of electrons.



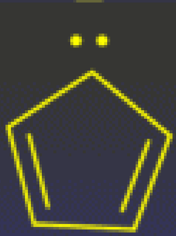
6 π electrons

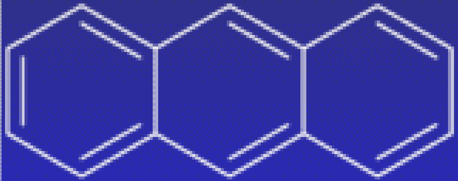
Aromatic



4 π electrons

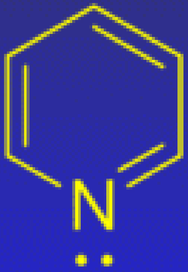
Not Aromatic





14 π electrons

Aromatic

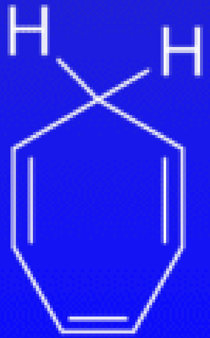


6 π electrons

Aromatic

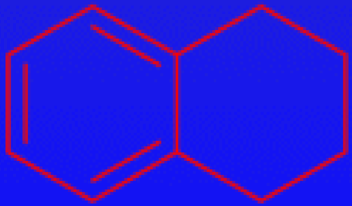
6 π electrons

Aromatic



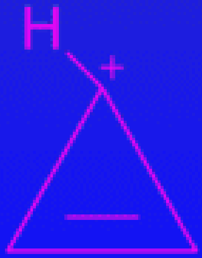
6 π electrons

Not Aromatic



6 π electrons

Not Aromatic



2 π electrons

Aromatic

Anti- and Nonaromatic

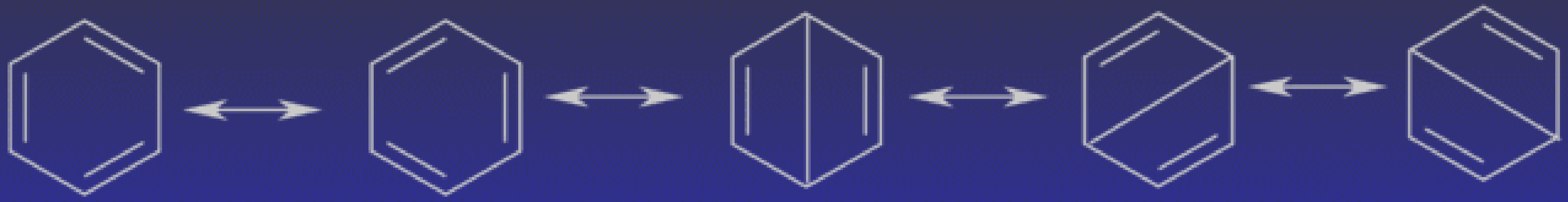
Non aromatic compounds, are not aromatic due to reasons such as lack of planarity or disruption of delocalization. They may contain 4n or 4n+2 π electrons.

Antiaromatic compounds are planar, cyclic, conjugated systems with an even number of pairs of electrons. Such compounds satisfy the first three criteria for aromaticity. i.e. they are planar, cyclic with an uninterrupted ring of p orbital bearing atoms. But they have an even number of pairs of π electrons (4n, n = 1, 2, 3 etc). Antiaromatic compound is less stable compared to an analogous cyclic compound with localized electrons (in 4n+2 systems delocalization increases the stability where as in 4n systems, delocalization decreases stability)

4 electrons (even number of pairs; 4n, n = 1)
Cyclic, planar, uninterrupted ring of p orbital bearing atoms (conjugation)
Antiaromatic

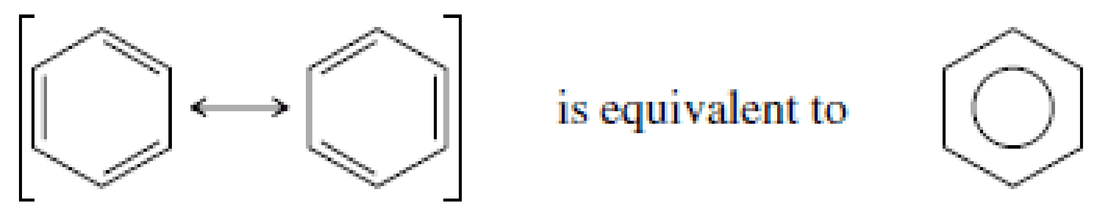
Cyclopropenyl anion
4 electron (even number of pairs; 4n, n = 1):
Theoretically antiaromatic; not stable

Benzene



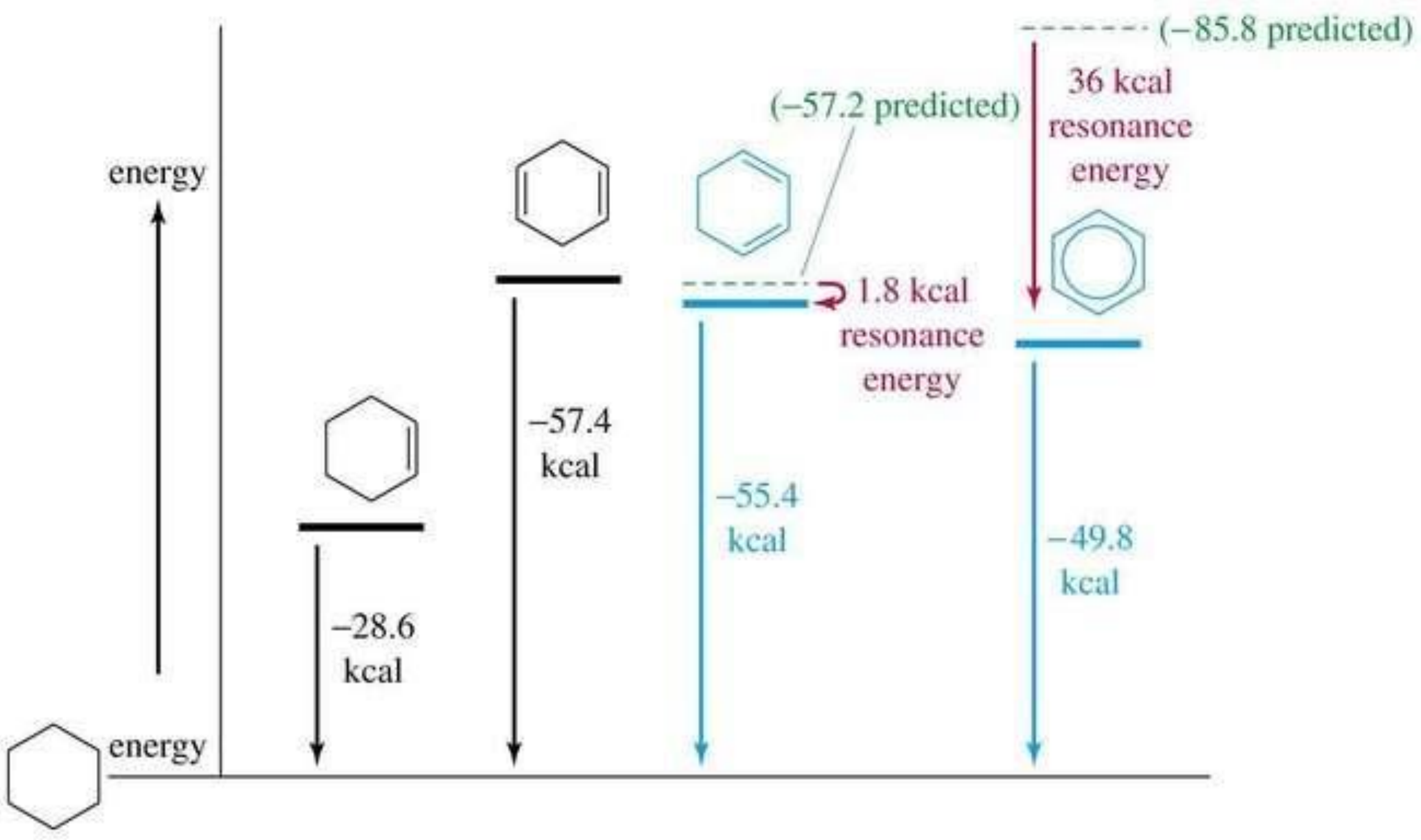
Kekule Benzene (80%)

Dewar Benzene (20%)

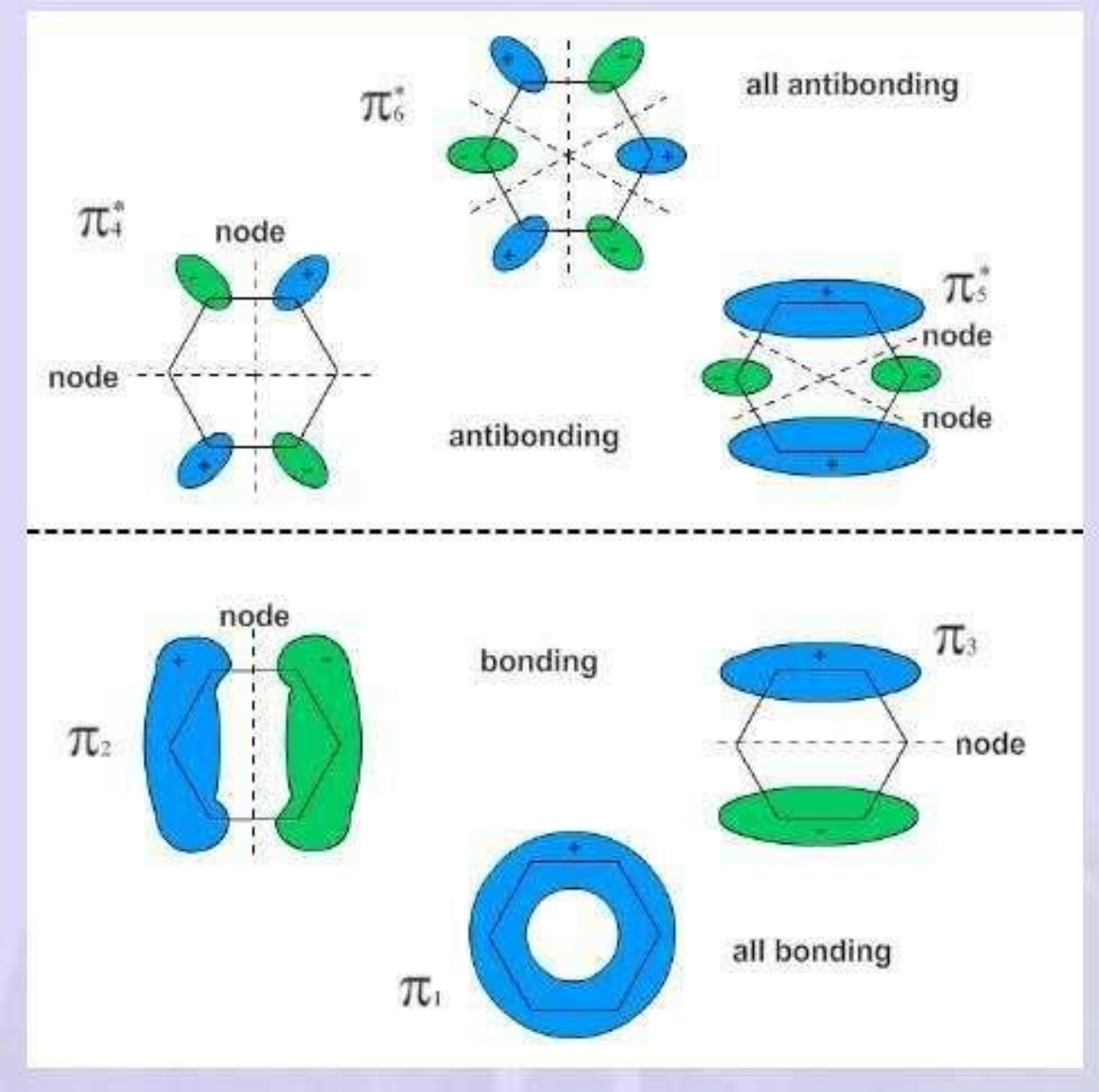


is equivalent to

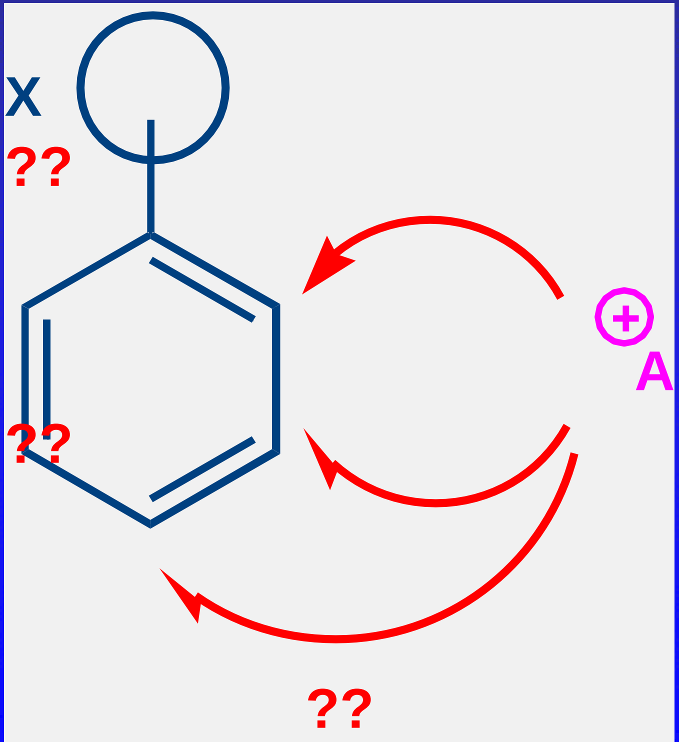
Unusual Stability of Benzene



MO’s for Benzene

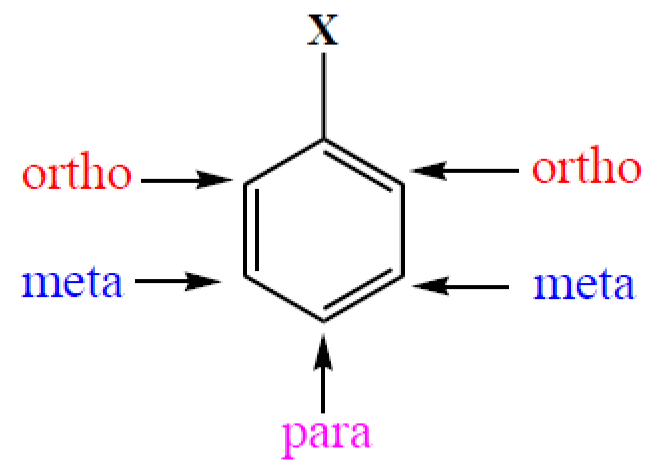


- What happens when there is a substituent already present?
- Where does the second substitution go?
- Is the attack by the second electrophile directed, or is its approach strictly random?



... or does it matter?

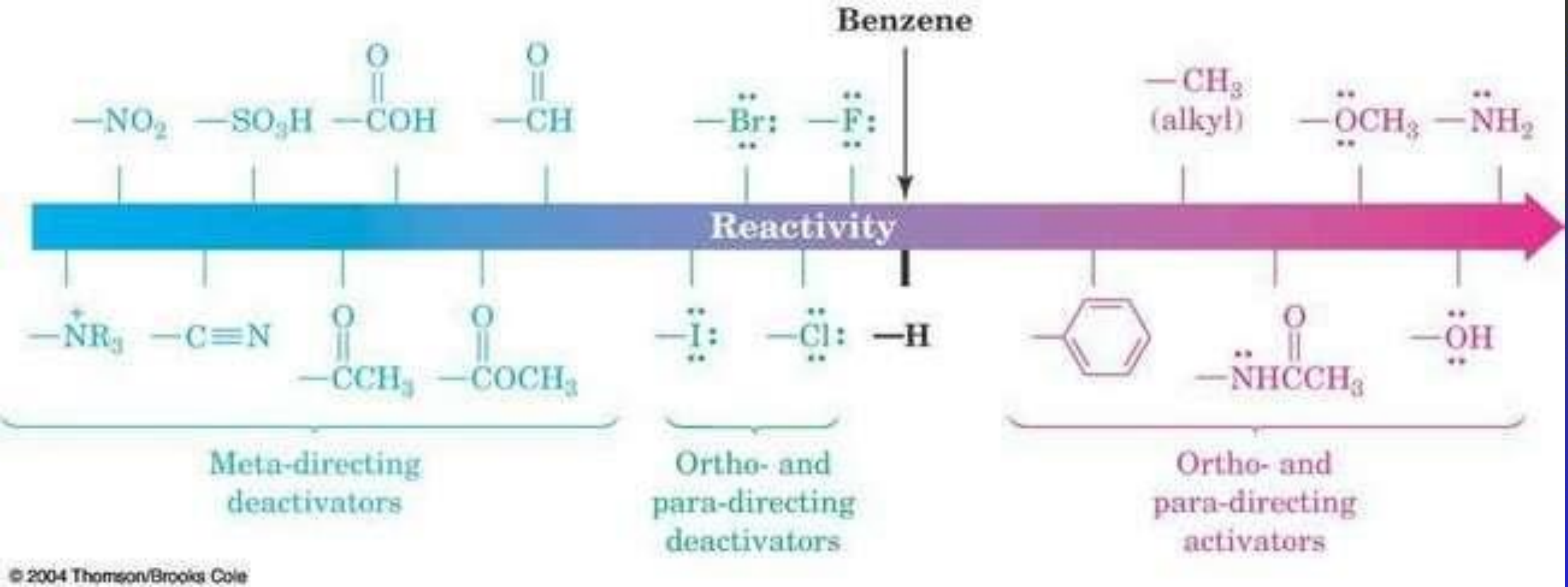
Substituent Effects in Aromatic Rings



★ Substituents can cause a compound to be (much) more or (much) less reactive than benzene

★ Substituents affect the orientation of the reaction – the positional relationship is controlled

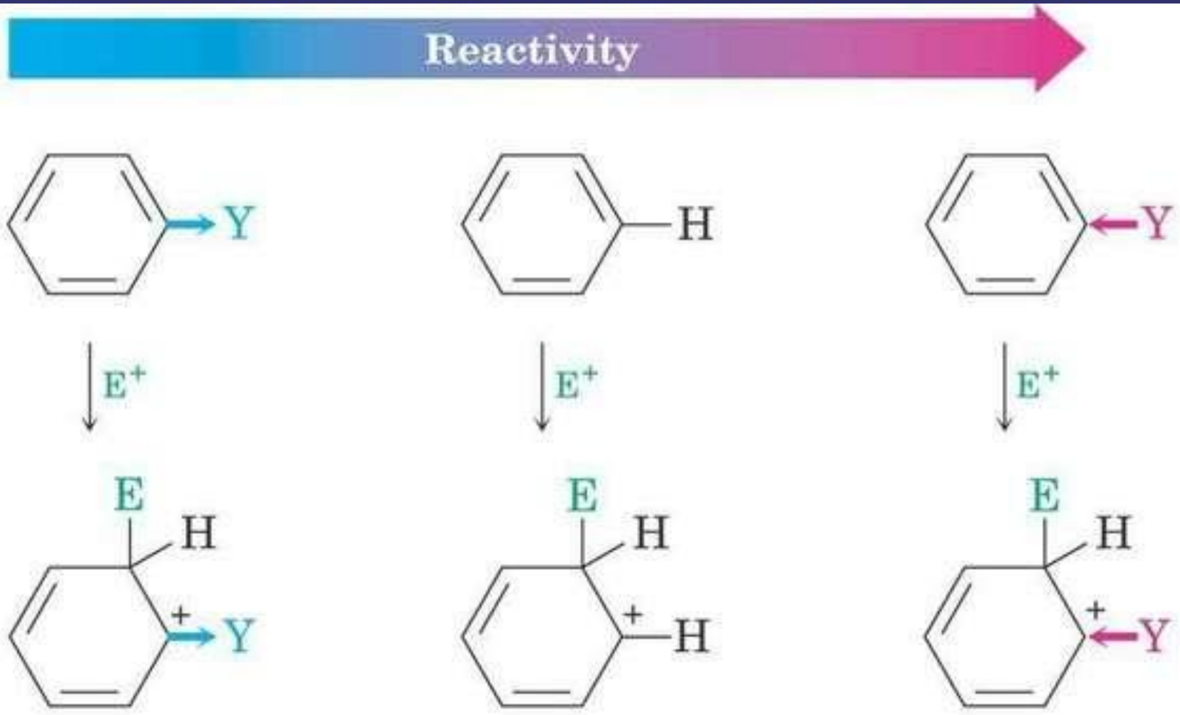
– ortho- and para-directing activators, ortho- and para-directing deactivators, and meta-directing deactivators



Origins of Substituent Effects

- An interplay of *inductive effects* and *resonance effects*
- Inductive effect - withdrawal or donation of electrons through a σ bond
- Resonance effect - withdrawal or donation of electrons through a π bond due to the overlap of a *p* orbital on the substituent with a *p* orbital on the aromatic ring

- ★ **Activating groups donate electrons to the ring, stabilizing the Wheland intermediate (carbocation)**
- ★ **Deactivating groups withdraw electrons from the ring, destabilizing the Wheland intermediate**

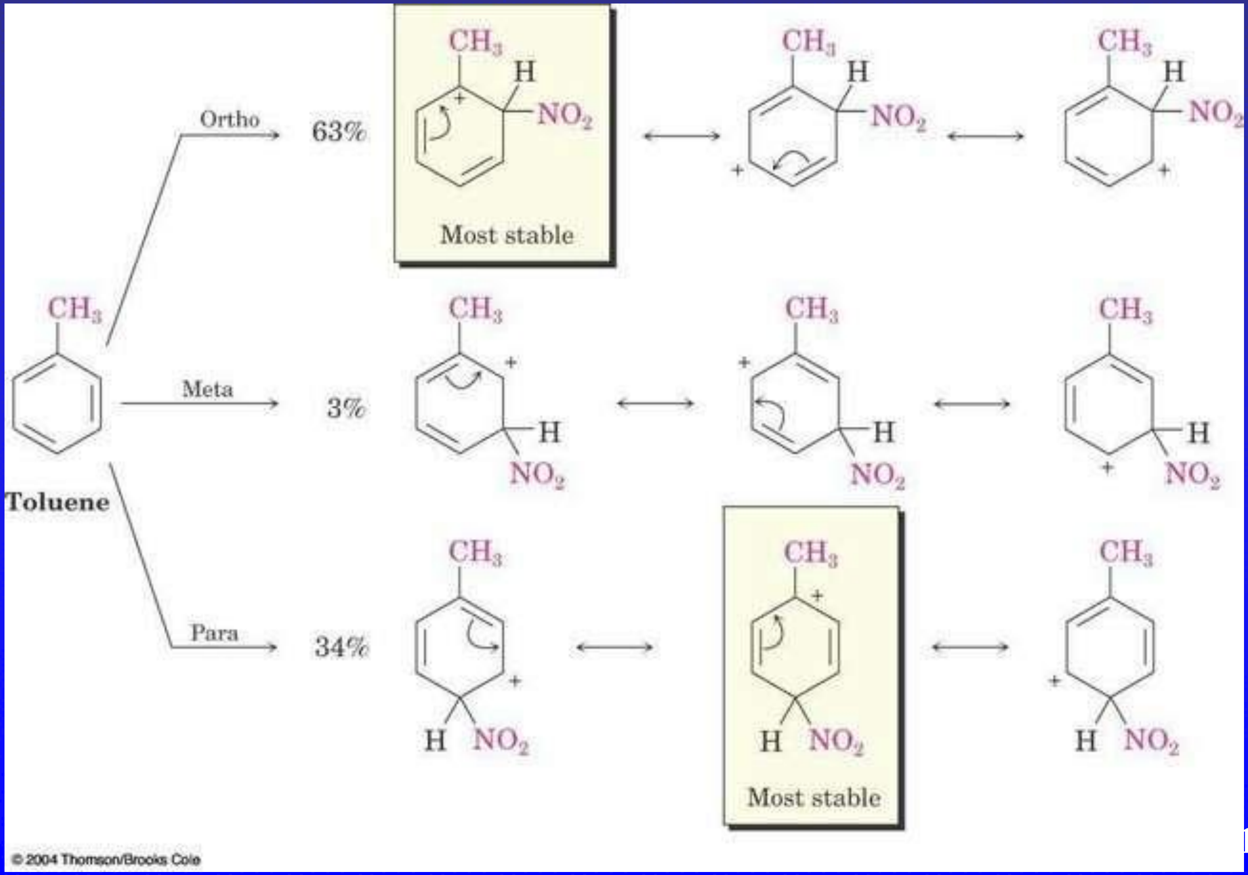


Y withdraws electrons; carbocation intermediate is less stable, and ring is less reactive.

Y donates electrons; carbocation intermediate is more stable, and ring is more reactive.

Ortho- and Para-Directing Activators: Alkyl Groups

- Alkyl groups activate: direct further substitution to positions ortho and para to themselves
- Alkyl group is most effective in the ortho and para positions



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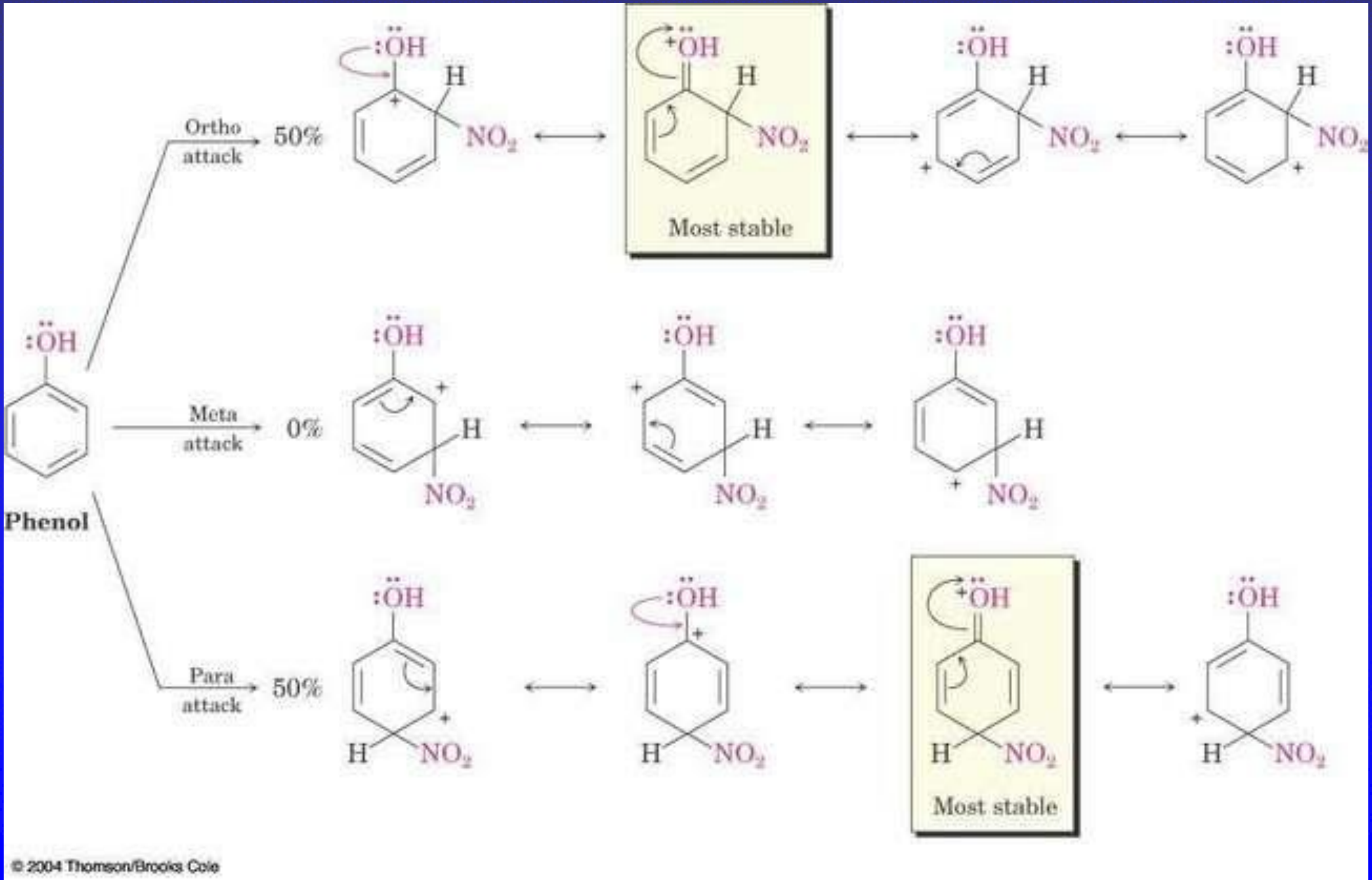
Ortho- and Para-Directing Activators: OH and NH$_2$

- ★ Alkoxyl, and amino groups have a strong, electron-donating resonance effect
- ★ Most pronounced at the ortho and para positions



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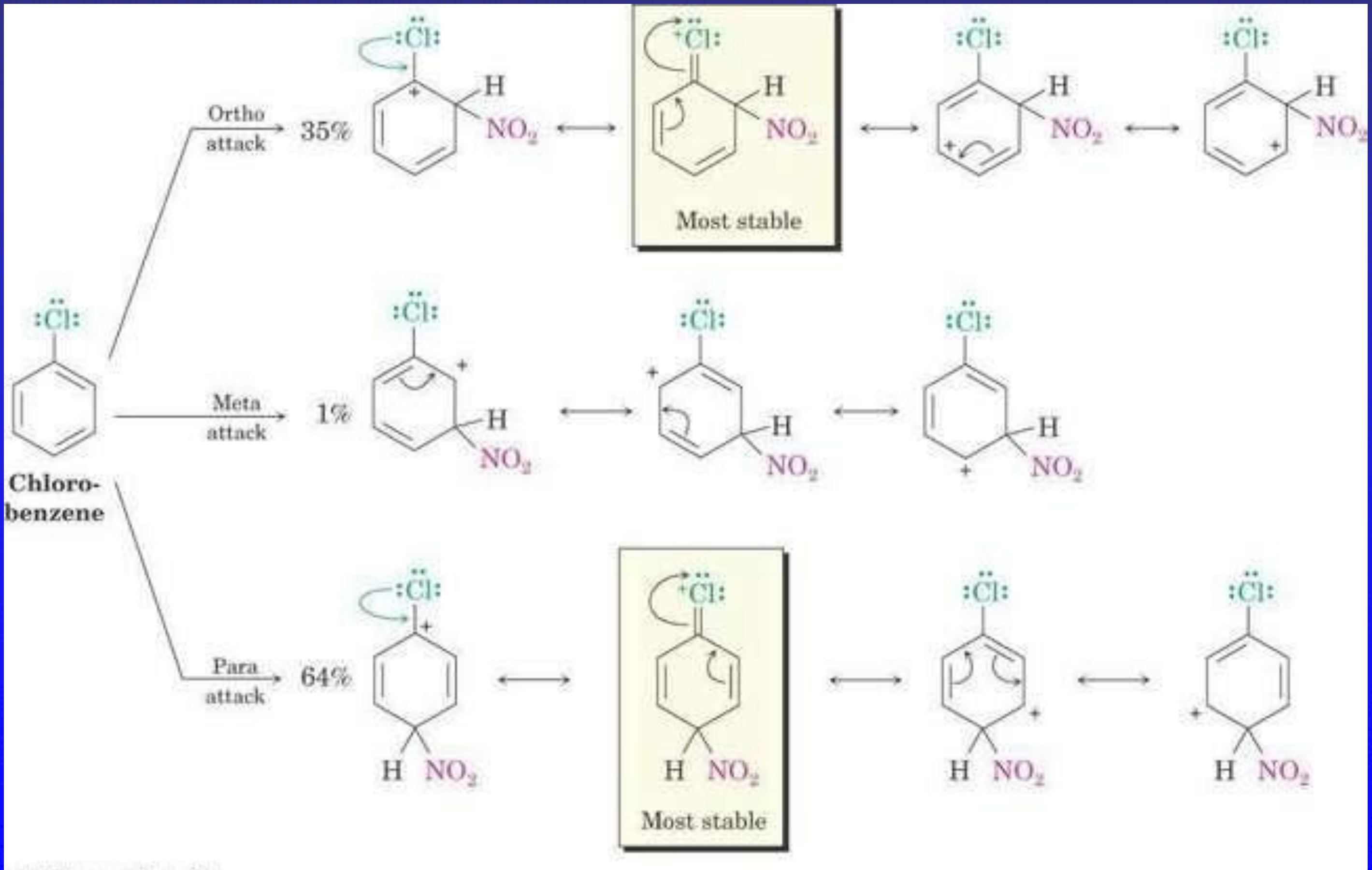
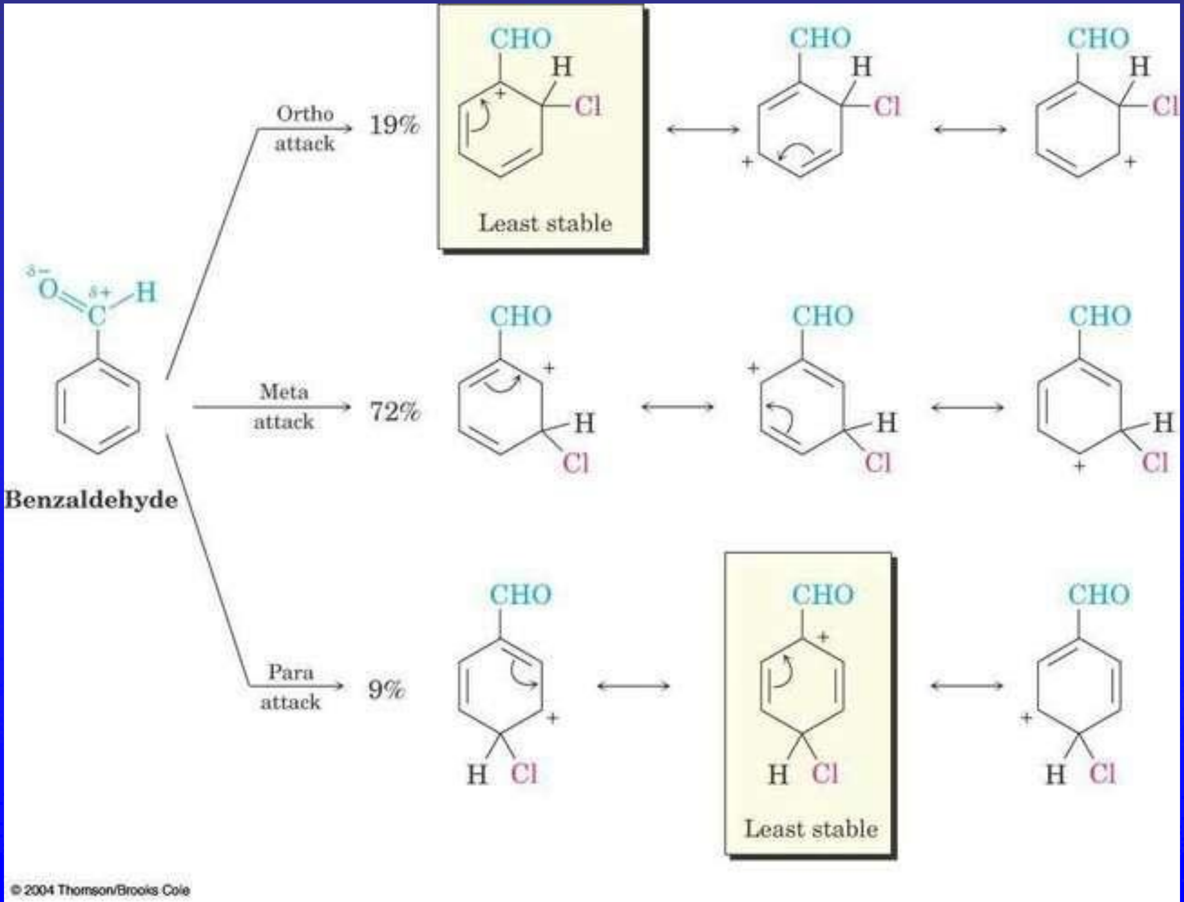
Ortho- and Para-Directing Deactivators: Halogens

- **Electron-withdrawing inductive effect outweighs weaker electron-donating resonance effect**
  - **Resonance effect is only at the ortho and para positions, stabilizing carbocation intermediate**

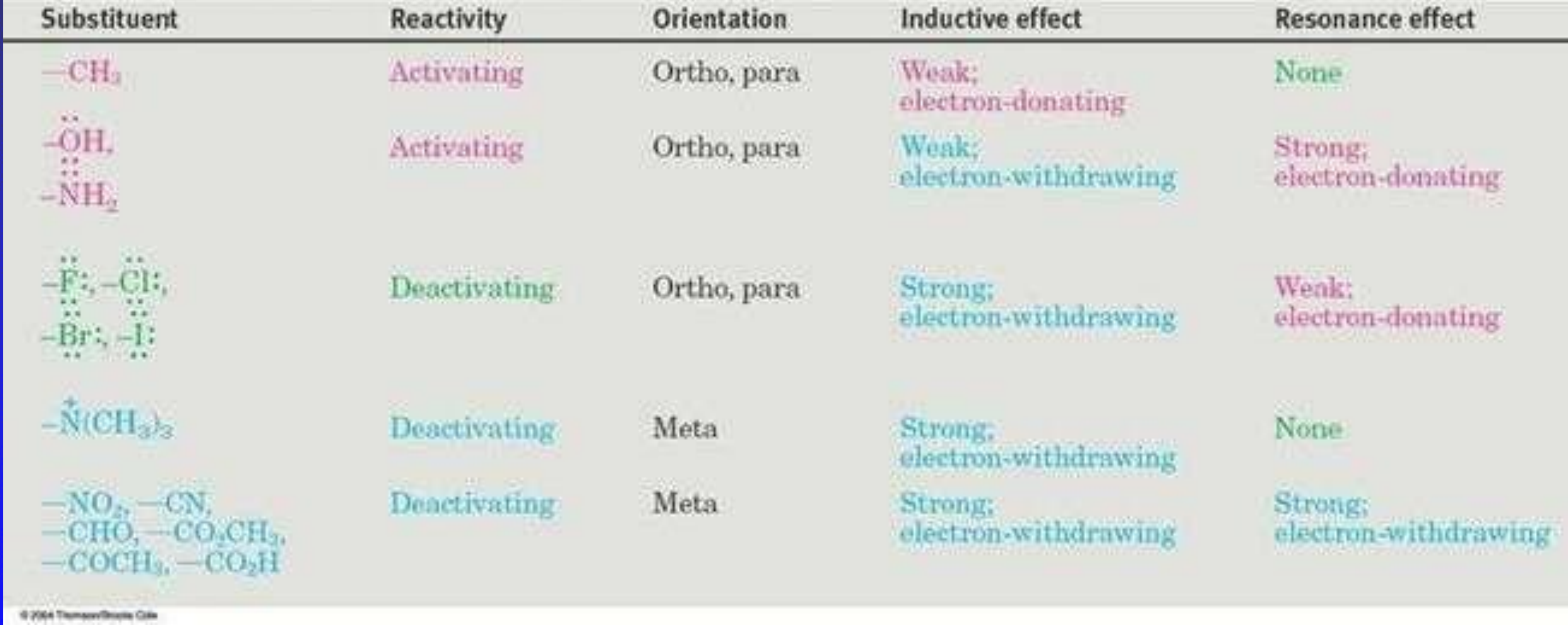


Meta-Directing Deactivators

- Inductive and resonance effects reinforce each other
- Ortho and para intermediates destabilized by deactivation from carbocation intermediate
- Resonance cannot produce stabilization



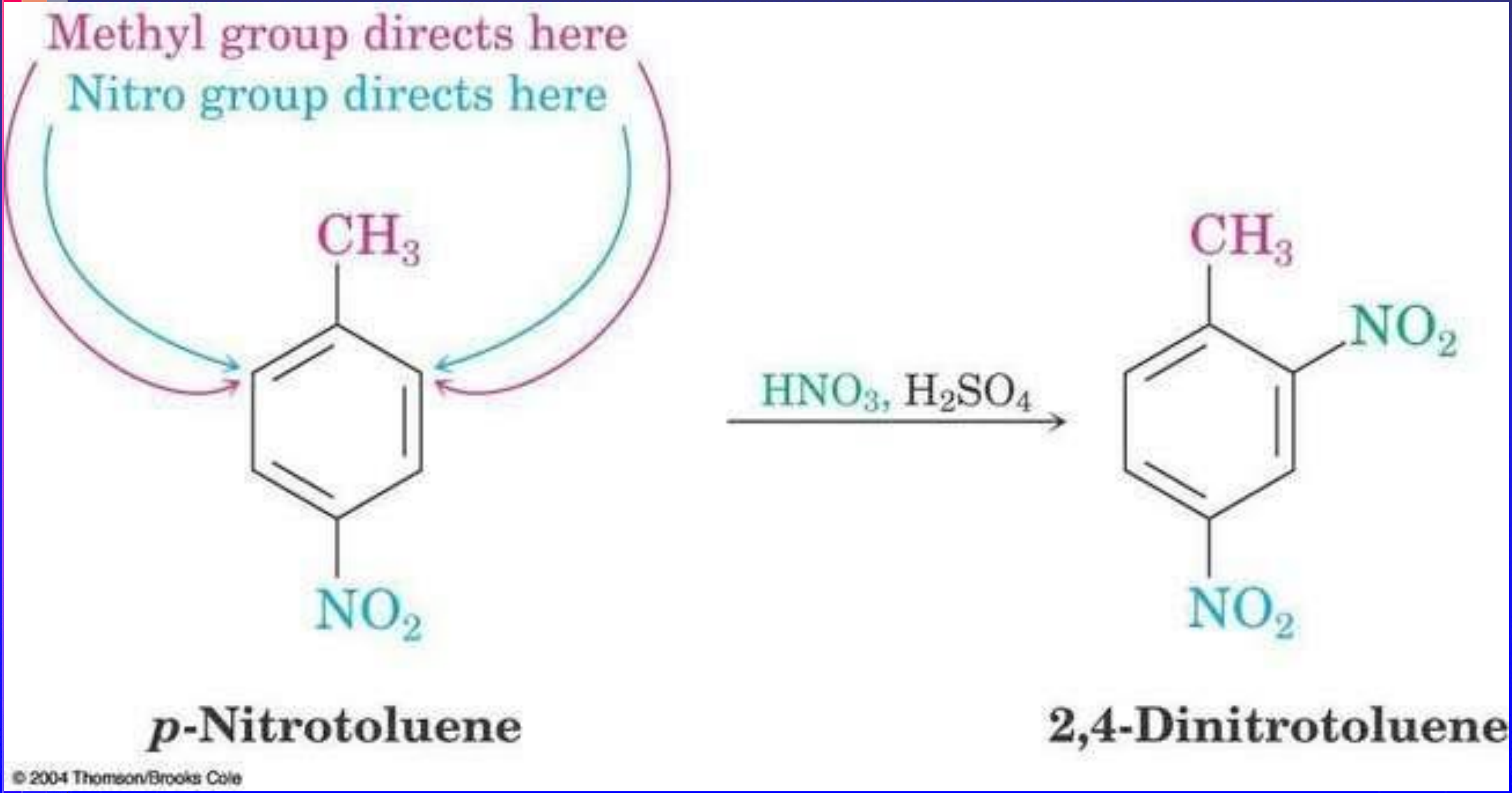
Summary Table: Effect of Substituents in Aromatic Substitution



Substituent	Reactivity	Orientation	Inductive effect	Resonance effect
$-\mathrm{CH}_3$	Activating	Ortho, para	Weak; electron-donating	None
$-\ddot{\mathrm{O}}\mathrm{H}$, $-\ddot{\mathrm{N}}\mathrm{H}_2$	Activating	Ortho, para	Weak; electron-withdrawing	Strong; electron-donating
$-\ddot{\mathrm{F}}:$, $-\ddot{\mathrm{Cl}}:$, $-\ddot{\mathrm{Br}}:$, $-\ddot{\mathrm{I}}:$	Deactivating	Ortho, para	Strong; electron-withdrawing	Weak; electron-donating
$-\overset{+}{\mathrm{N}}(\mathrm{CH}_3)_3$	Deactivating	Meta	Strong; electron-withdrawing	None
$-\mathrm{NO}_2$, $-\mathrm{CN}$, $-\mathrm{CHO}$, $-\mathrm{CO_2CH_3}$, $-\mathrm{COCH_3}$, $-\mathrm{CO_2H}$	Deactivating	Meta	Strong; electron-withdrawing	Strong; electron-withdrawing

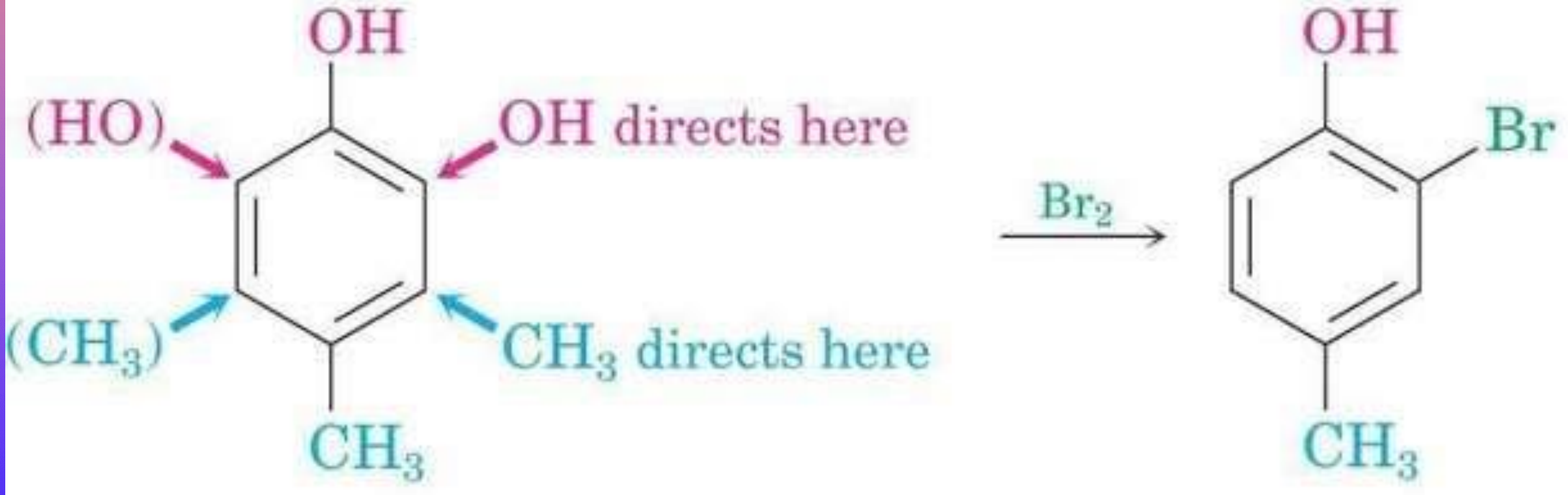
Trisubstituted Benzenes: Additivity of Effects

- **If the directing effects of the two groups are the same, the result is additive**



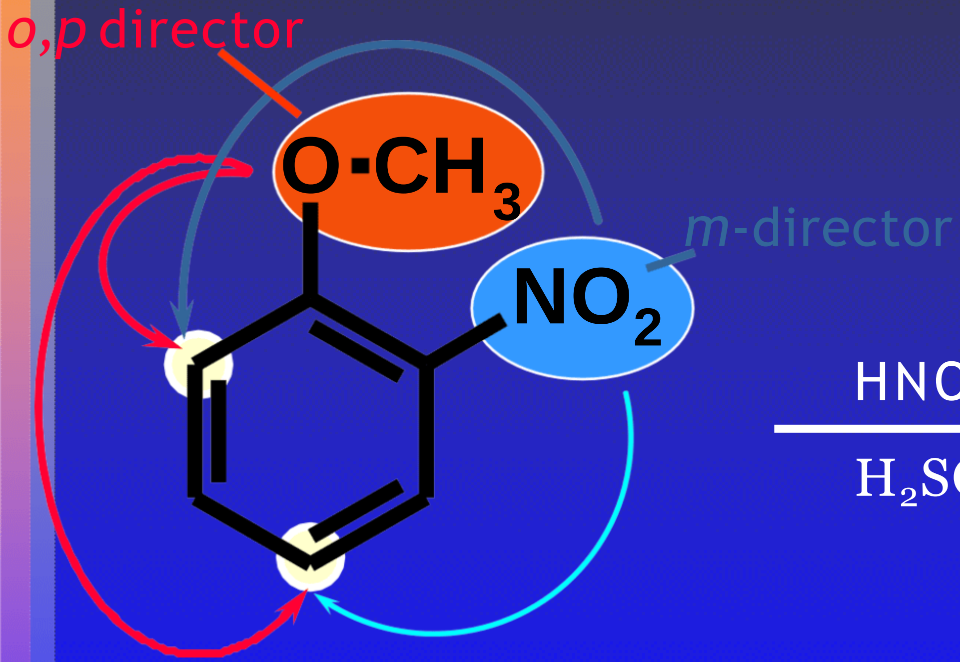
Substituents with Opposite Effects

- If the directing effects of two groups oppose each other, the more powerful activating group decides the principal outcome
- Often gives mixtures of products



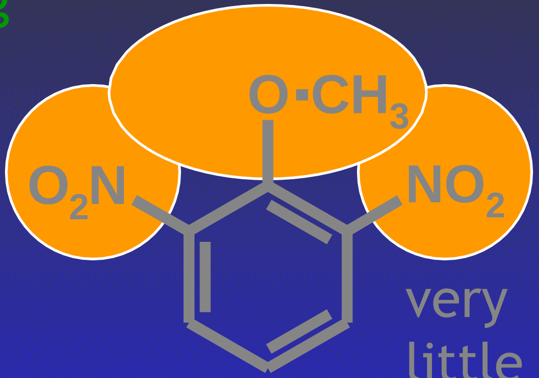
p-Methylphenol
(*p*-Cresol)

2-Bromo-4-methylphenol
(major product)



$\xrightarrow[H_2SO_4]{HNO_3}$

steric crowding



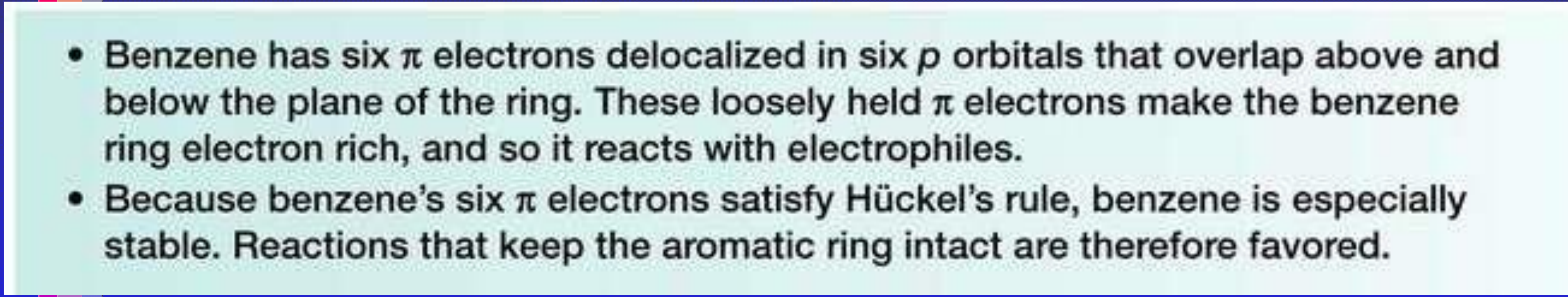
very little formed

major product

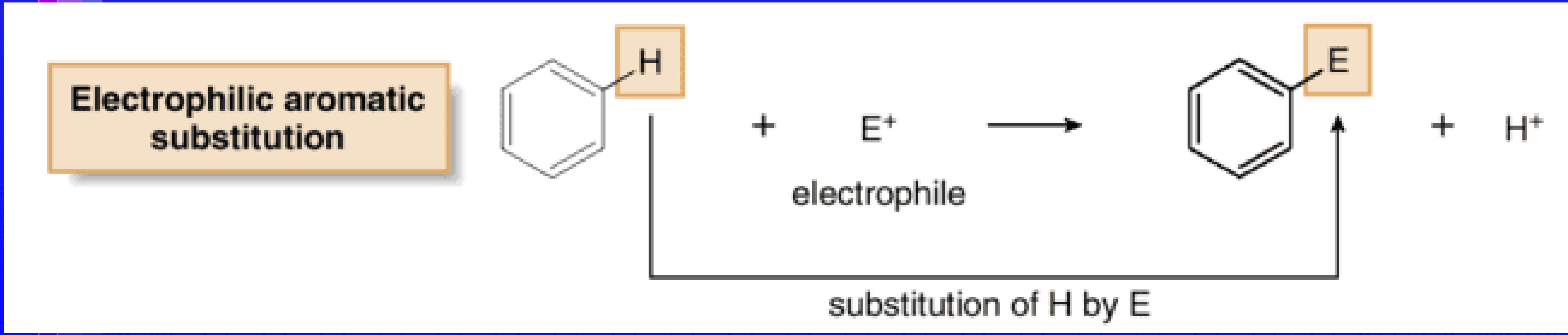
When groups direct to the same positions it is easy to predict the product.

Electrophilic Aromatic Substitution

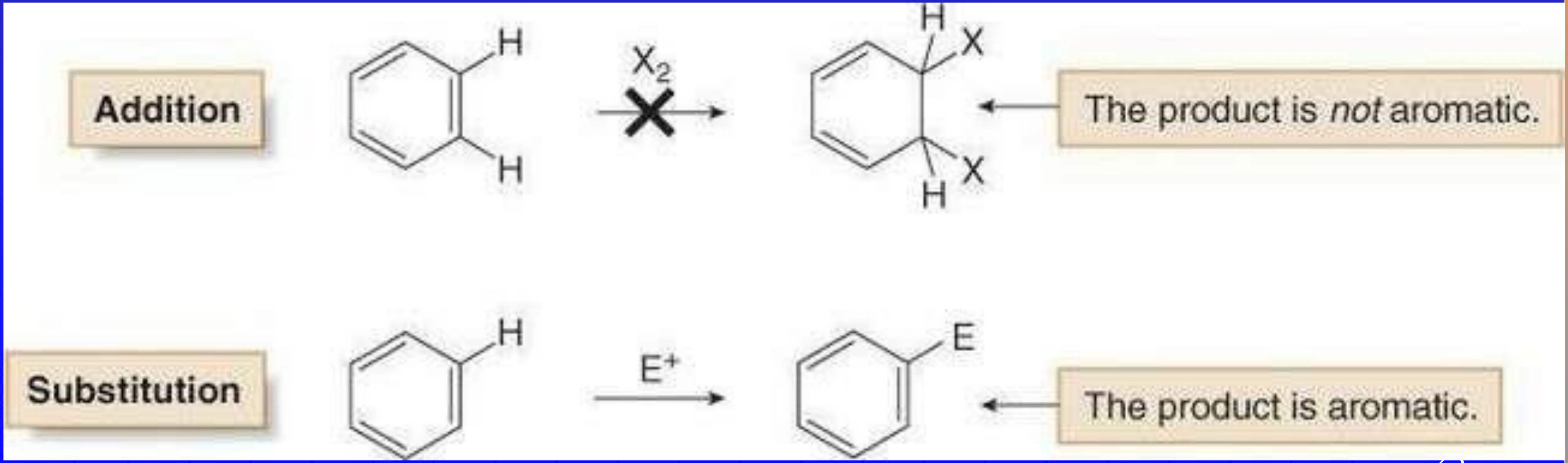
- The characteristic reaction of benzene is **electrophilic aromatic substitution**—a hydrogen atom is replaced by an electrophile.



- Benzene has six π electrons delocalized in six *p* orbitals that overlap above and below the plane of the ring. These loosely held π electrons make the benzene ring electron rich, and so it reacts with electrophiles.
- Because benzene's six π electrons satisfy Hückel's rule, benzene is especially stable. Reactions that keep the aromatic ring intact are therefore favored.

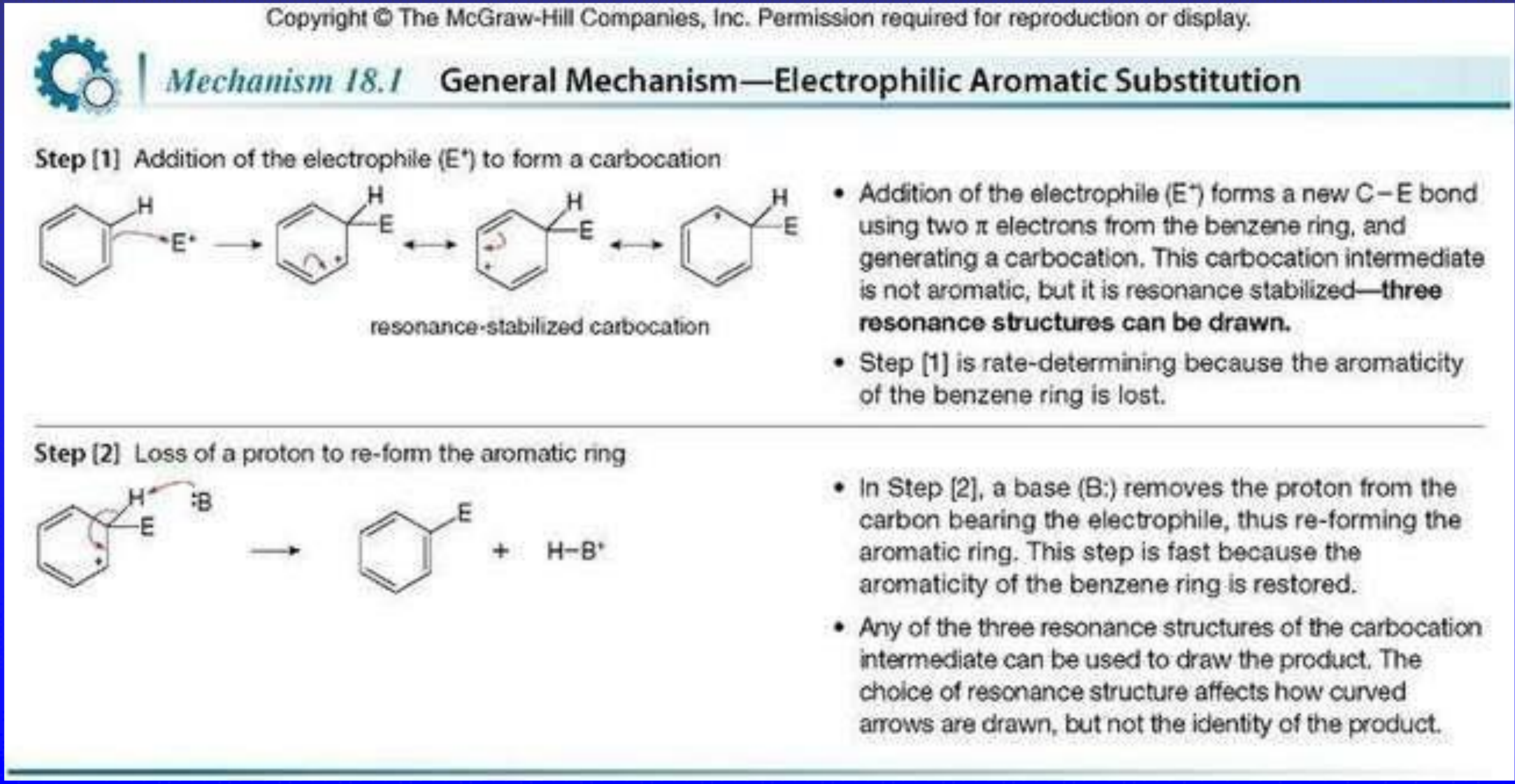


- Benzene does not undergo addition reactions like other unsaturated hydrocarbons, because addition would yield a product that is not aromatic.
- Substitution of a hydrogen keeps the aromatic ring intact.
- There are five main examples of electrophilic aromatic substitution.



GENERAL MECHANISM OF ELECTROPHILIC AROMATIC SUBSTITUTION

- Regardless of the electrophile used, all electrophilic aromatic substitution reactions occur by the same two-step mechanism—addition of the electrophile E+ to form a resonance-stabilized carbocation, followed by deprotonation with base, as shown below:



Mechanism 18.1 General Mechanism—Electrophilic Aromatic Substitution

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

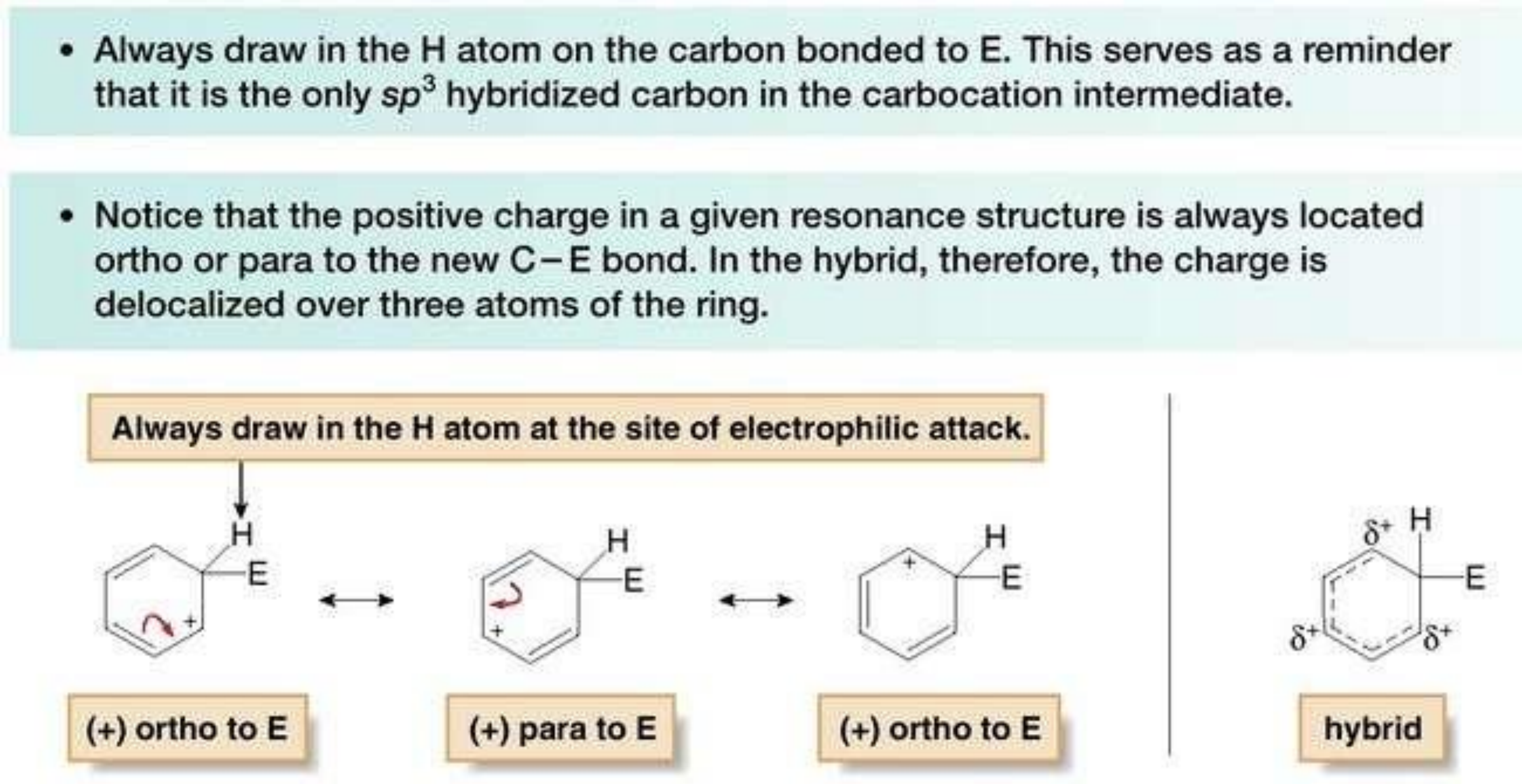
resonance-stabilized carbocation

- 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.

- **The first step in electrophilic aromatic substitution forms a carbocation, for which three resonance structures can be drawn. To help keep track of the location of the positive charge:**



- Always draw in the H atom on the carbon bonded to E. This serves as a reminder that it is the only sp^3 hybridized carbon in the carbocation intermediate.

- Notice that the positive charge in a given resonance structure is always located ortho or para to the new C–E bond. In the hybrid, therefore, the charge is delocalized over three atoms of the ring.

Always draw in the H atom at the site of electrophilic attack.

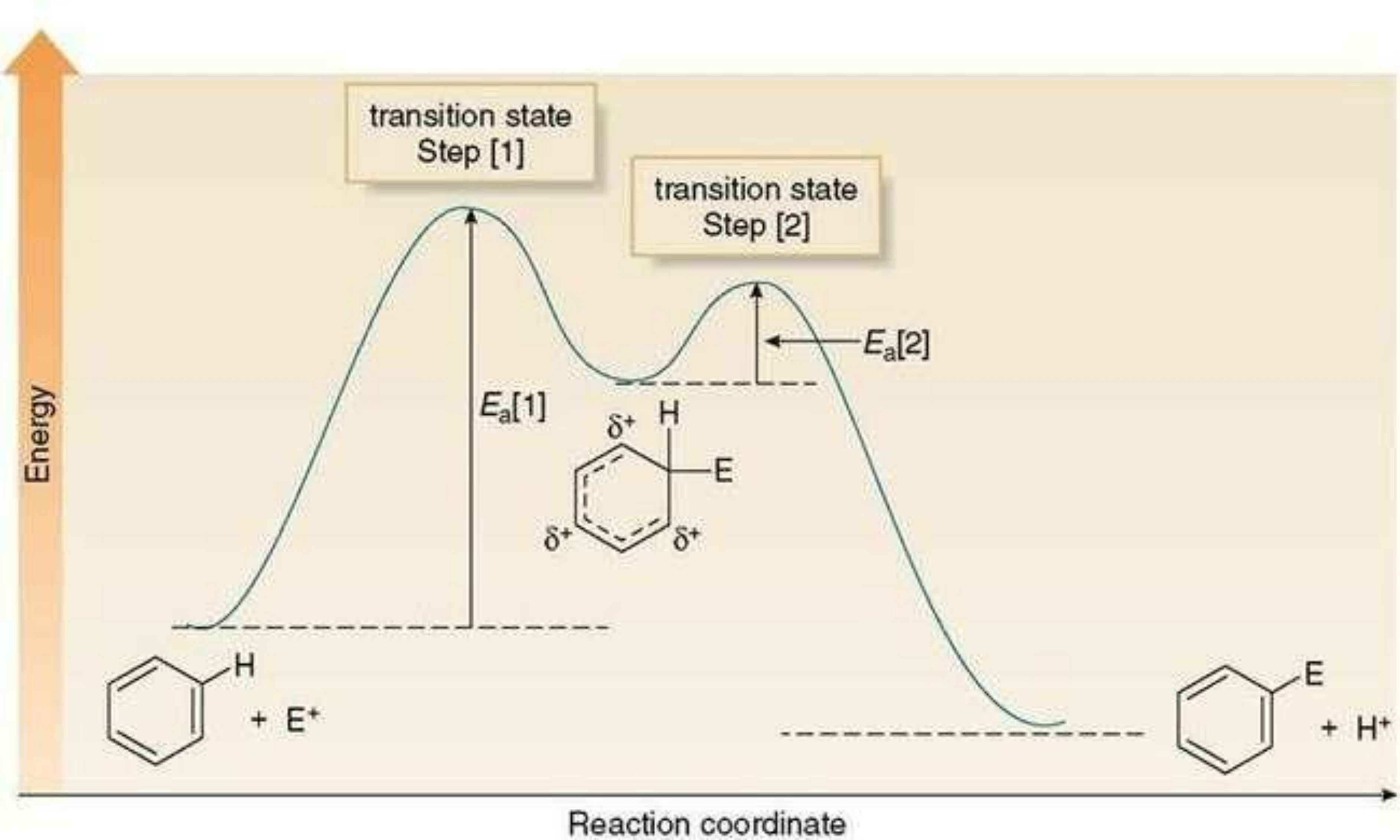
(+) ortho to E

(+) para to E

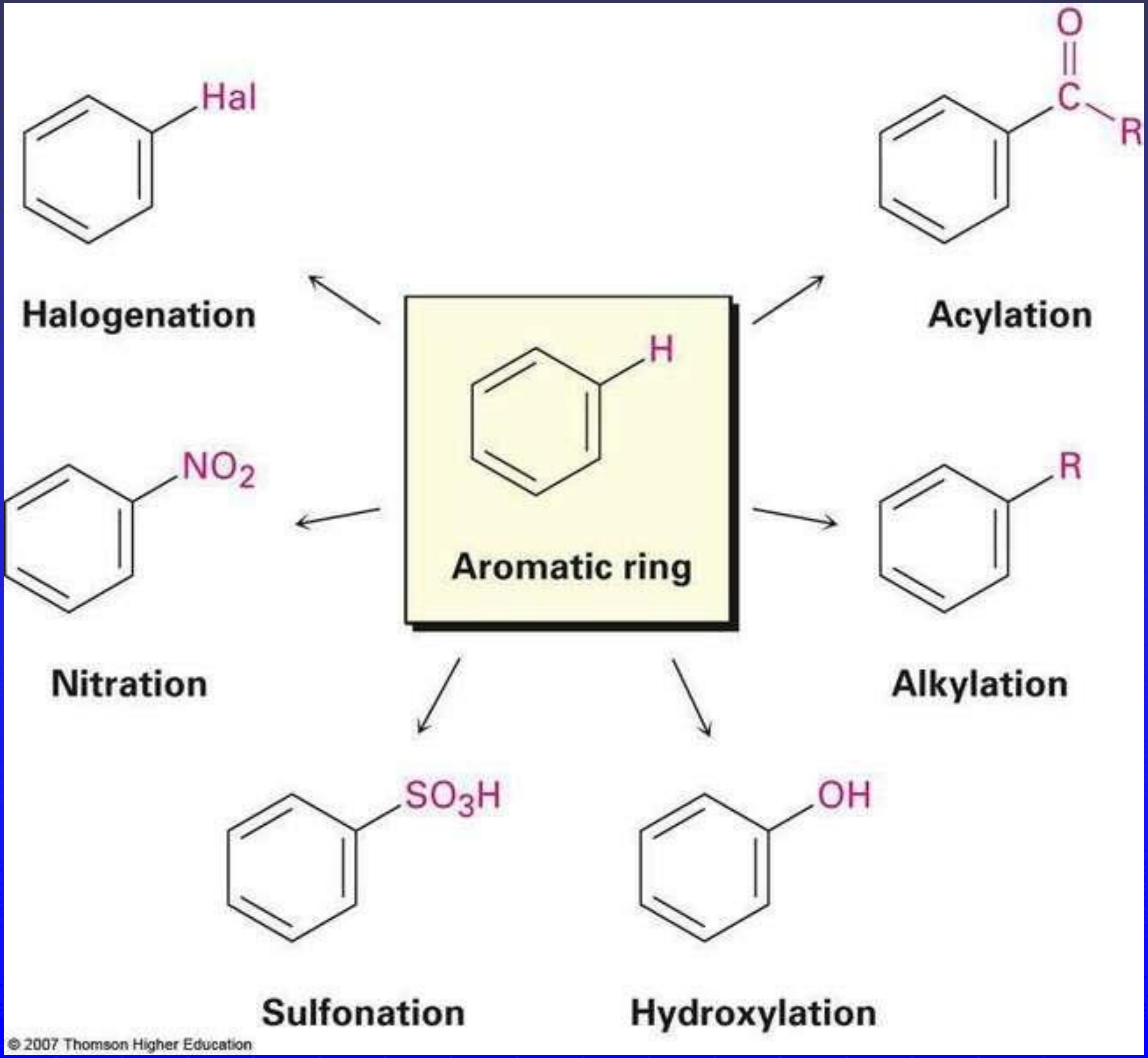
(+) ortho to E

hybrid

Energy Profile diagram for electrophilic aromatic substitution



Electrophilic Aromatic Substitution



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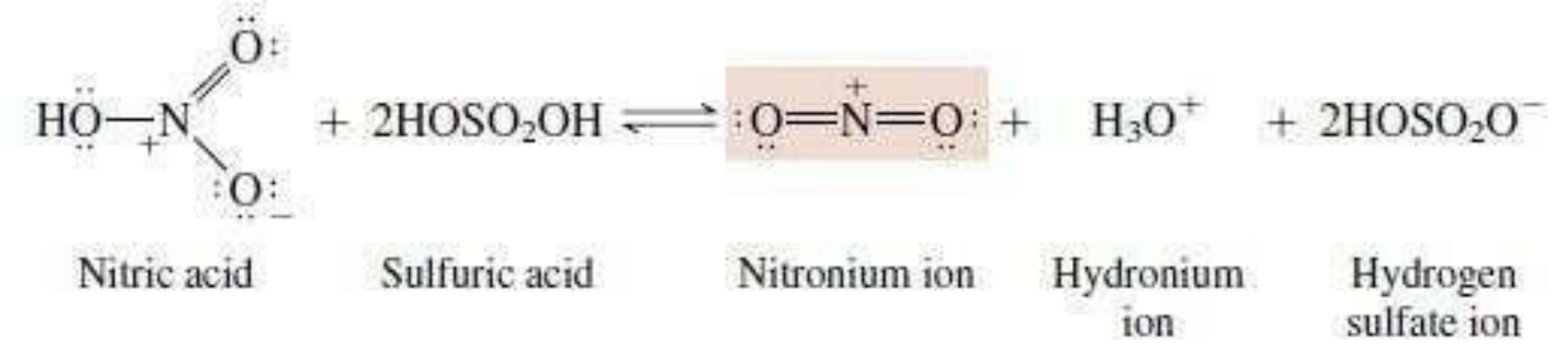
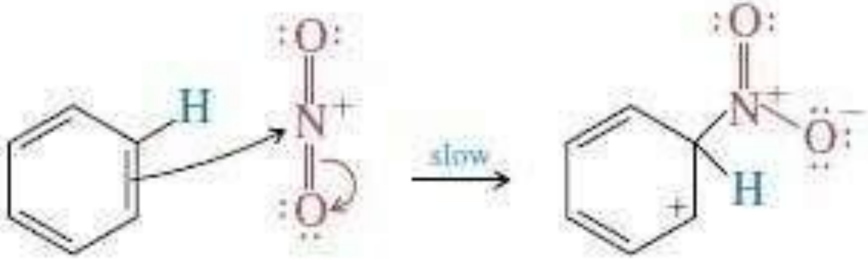
NITRATION

The electrophile (E) that reacts with benzene is *nitronium ion* . The concentration of nitronium ion in nitric acid alone is too low to nitrate benzene at a convenient rate, but can be increased by adding sulfuric acid.



Electrophile is the nitronium ion (NO_2^+)

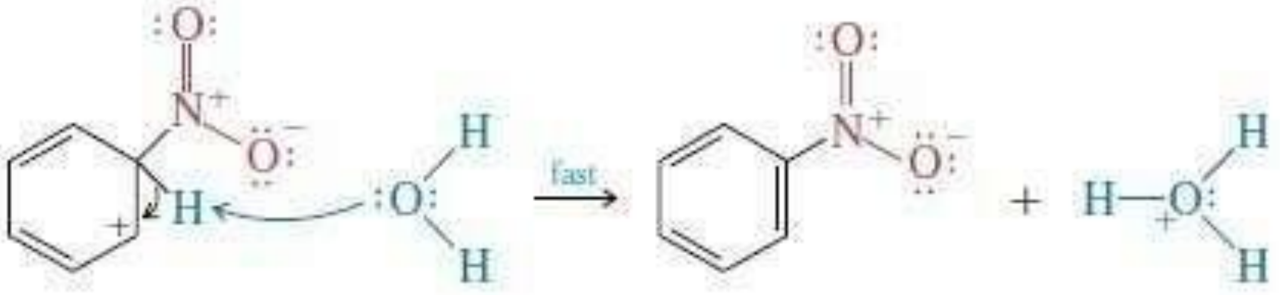
Step 1: Attack of nitronium cation on the π system of the aromatic ring



Benzene and nitronium ion

Cyclohexadienyl cation intermediate

Step 2: Loss of a proton from the cyclohexadienyl cation



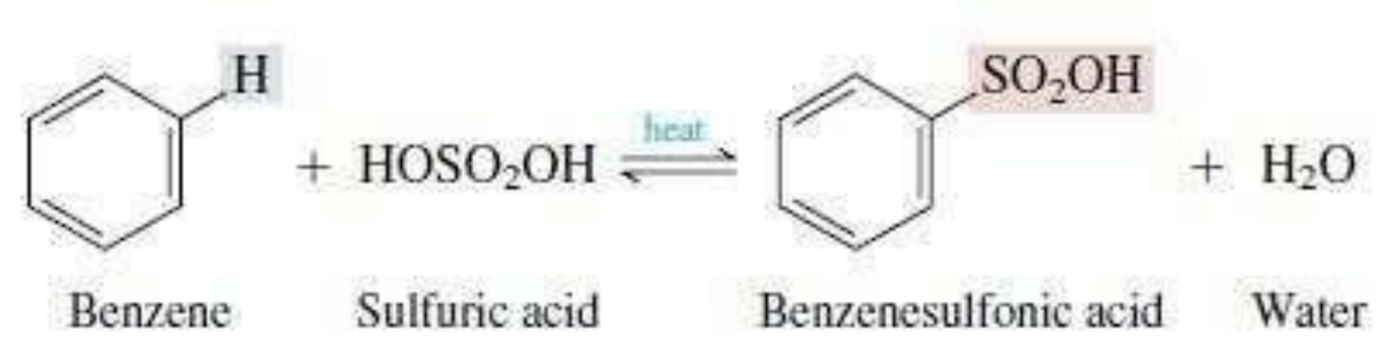
Cyclohexadienyl cation intermediate

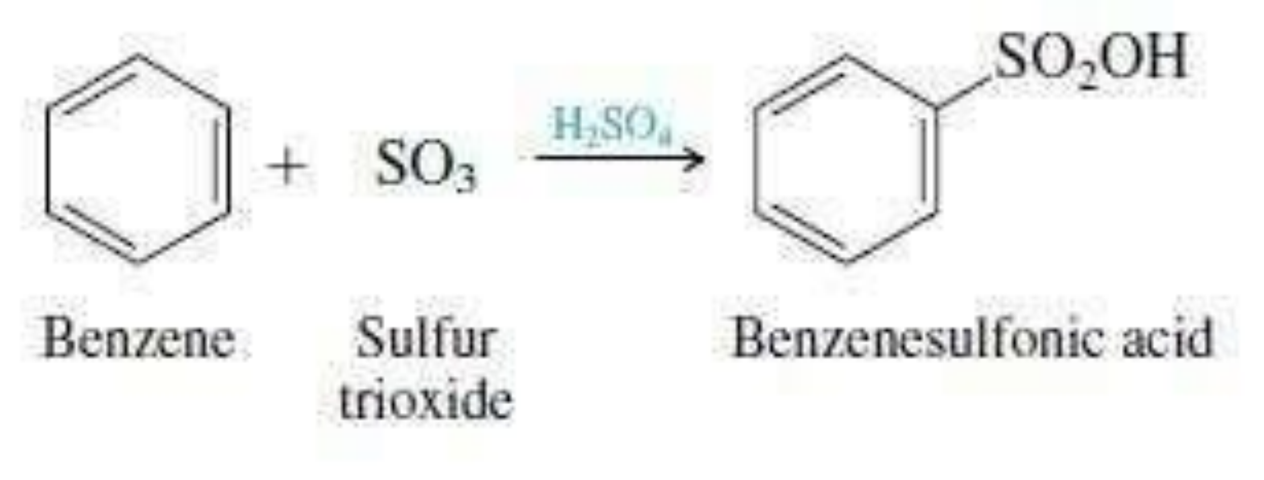
Water

Nitrobenzene

Hydronium ion

Sulfonation

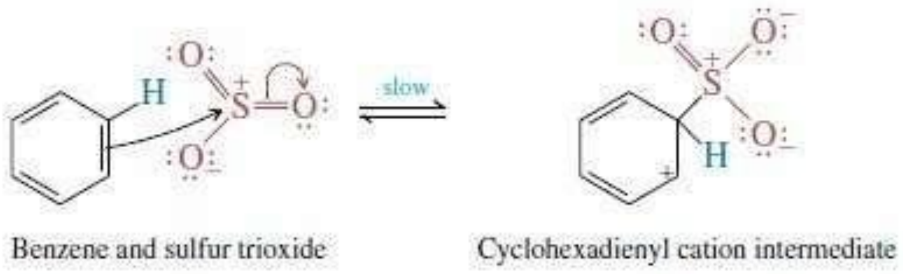




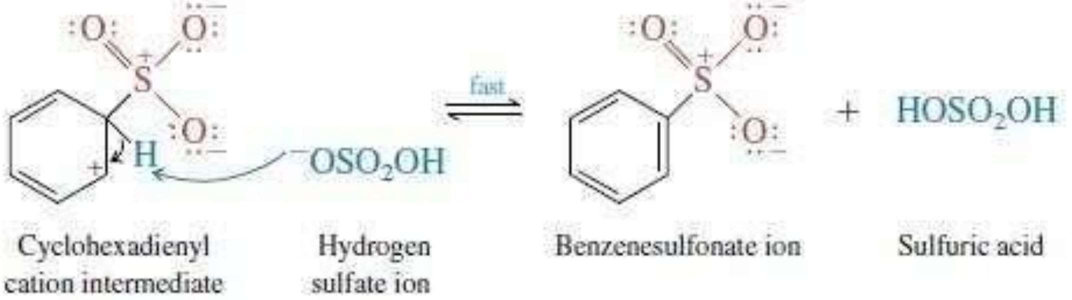
Fuming sulfuric acid – combination of SO_3 and H_2SO_4

Electrophile is HSO_3^+ or SO_3

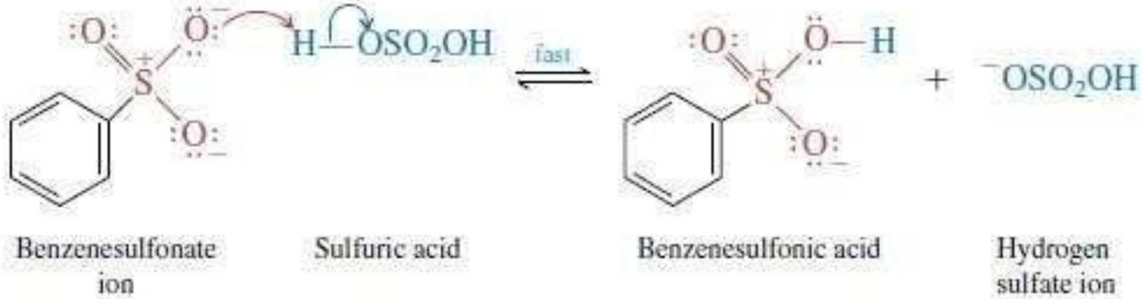
Step 1: Sulfur trioxide attacks benzene in the rate-determining step



Step 2: A proton is lost from the sp^3 hybridized carbon of the intermediate to restore the aromaticity of the ring. The species shown that abstracts the proton is a hydrogen sulfate ion formed by ionization of sulfuric acid.

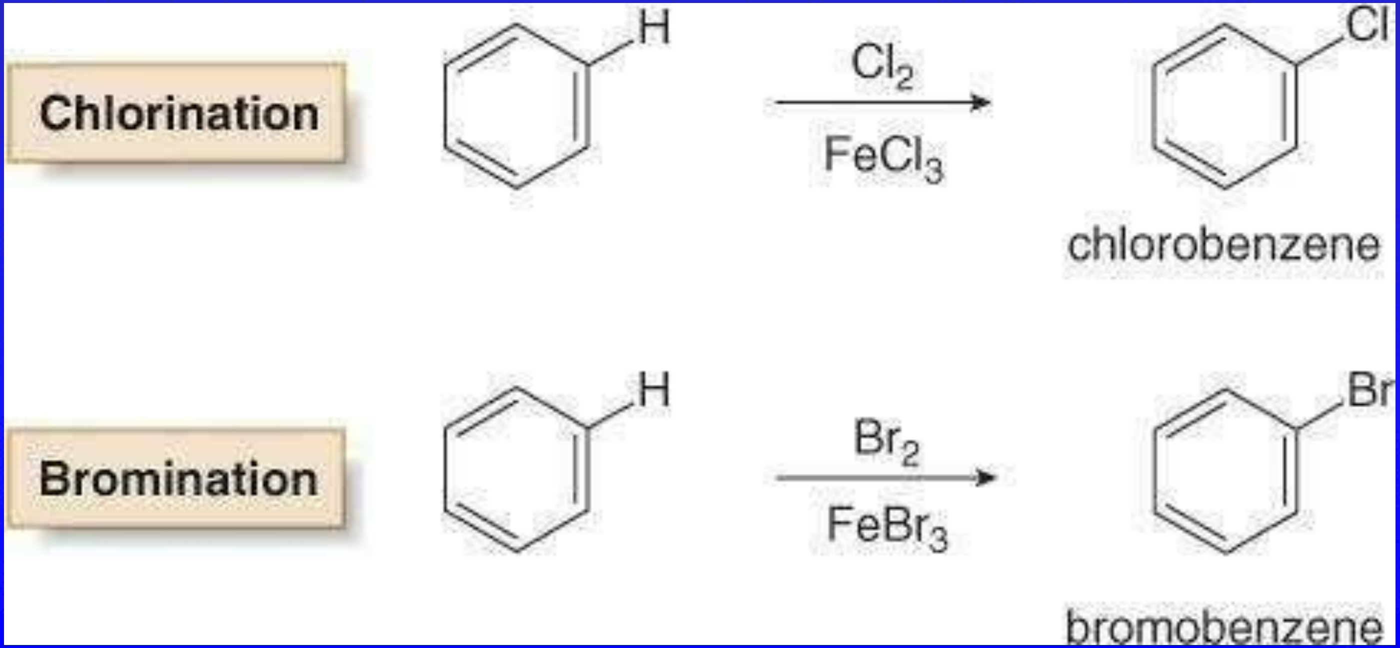


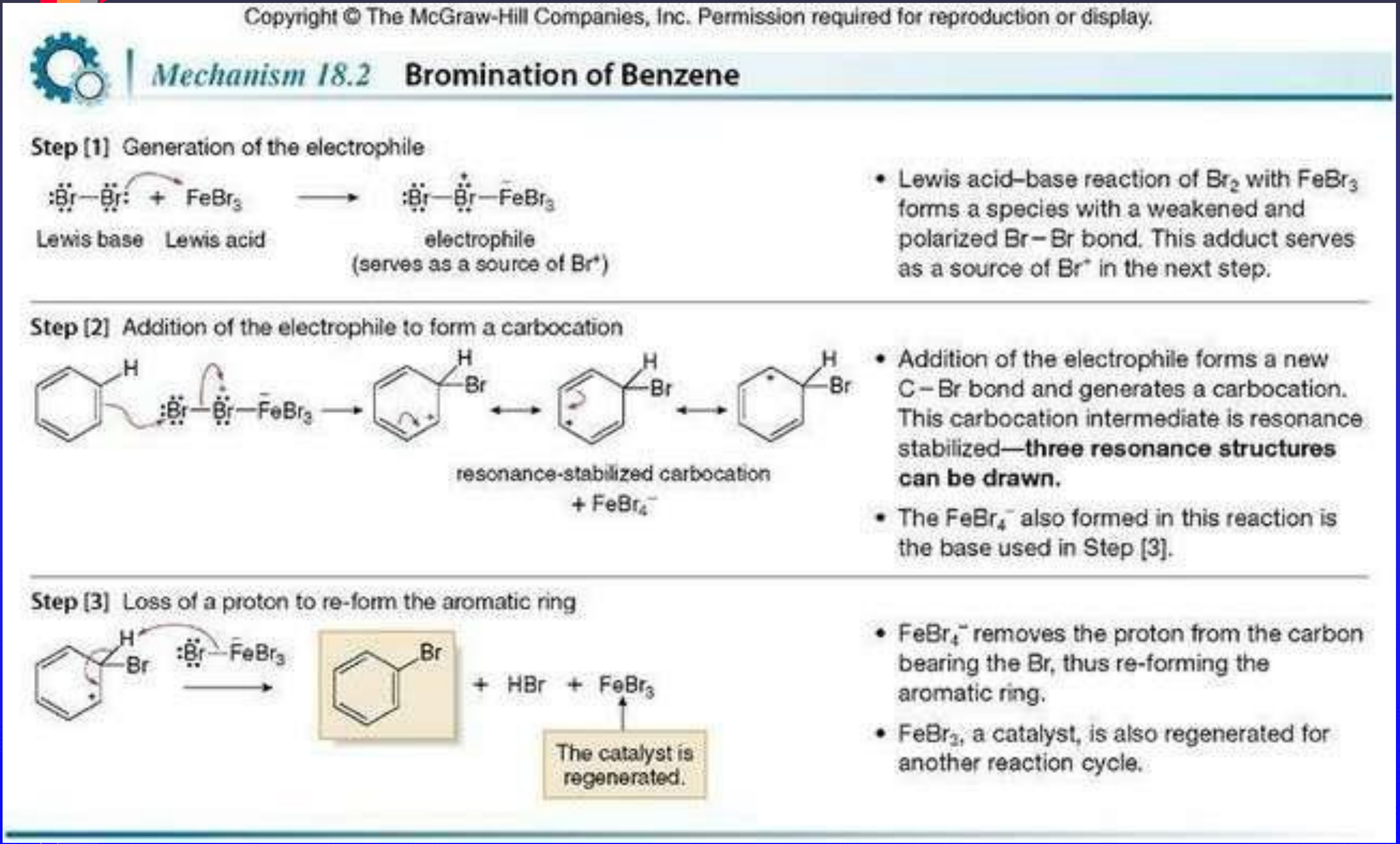
Step 3: A rapid proton transfer from the oxygen of sulfuric acid to the oxygen of benzenesulfonate completes the process.



Halogenation

- In **halogenation**, benzene reacts with Cl_2 or Br_2 in the presence of a Lewis acid catalyst, such as **$FeCl_3$** or **$FeBr_3$**, to give the aryl halides chlorobenzene or bromobenzene respectively.
- Analogous reactions with I_2 and F_2 are not synthetically useful because I_2 is too unreactive and F_2 reacts too violently.





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

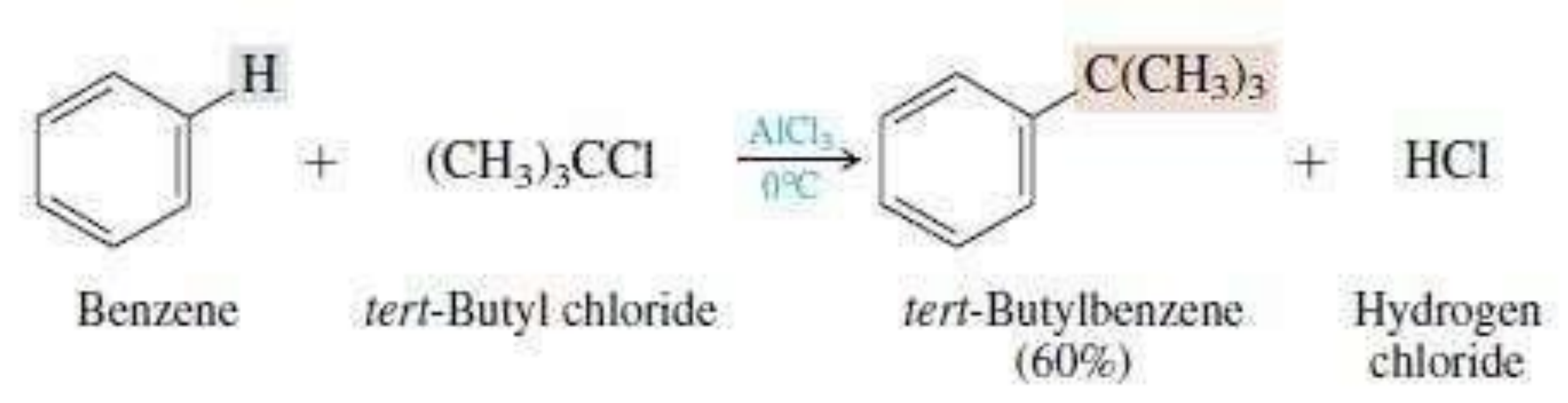
$+ HBr + FeBr_3$

The catalyst is regenerated.

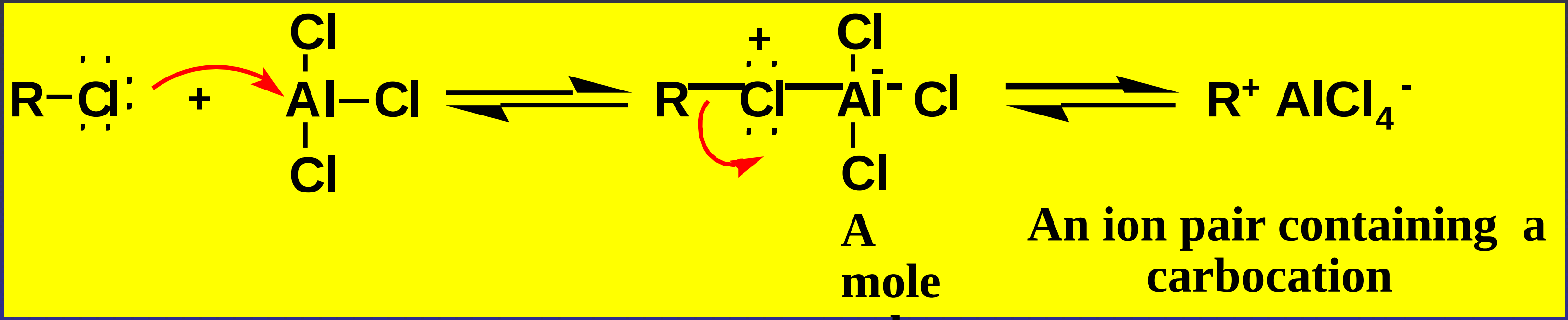
- $FeBr_4^-$ removes the proton from the carbon bearing the Br, thus re-forming the aromatic ring.
- $FeBr_3$, a catalyst, is also regenerated for another reaction cycle.

Friedel-Crafts Alkylation

- **Friedel-Crafts alkylation forms a new C-C bond between an aromatic ring and an alkyl group.**



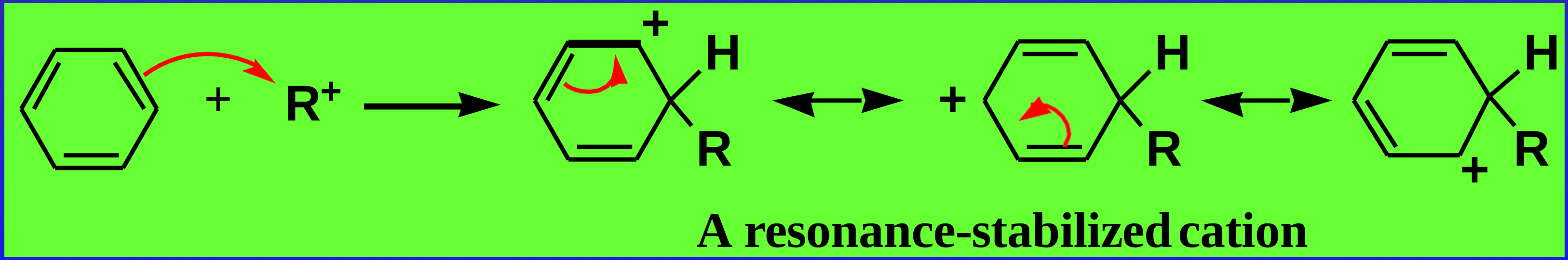
Step 1: Formation of an alkyl cation as an ion pair.



A molecular complex

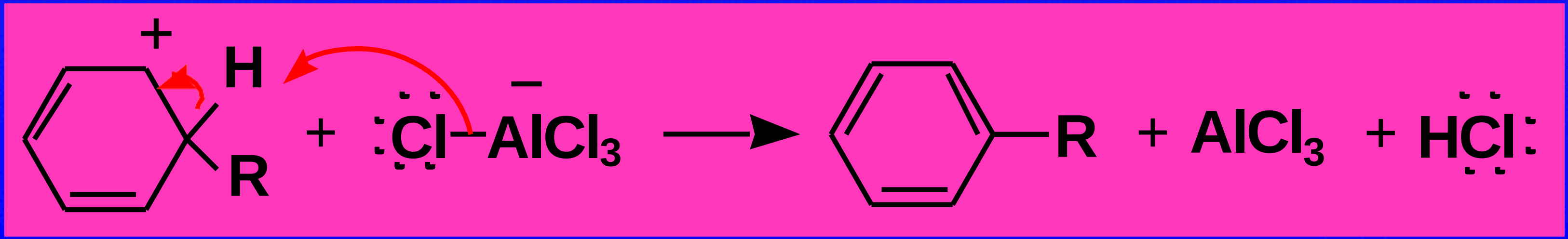
An ion pair containing a carbocation

Step 2: Attack of the alkyl cation.



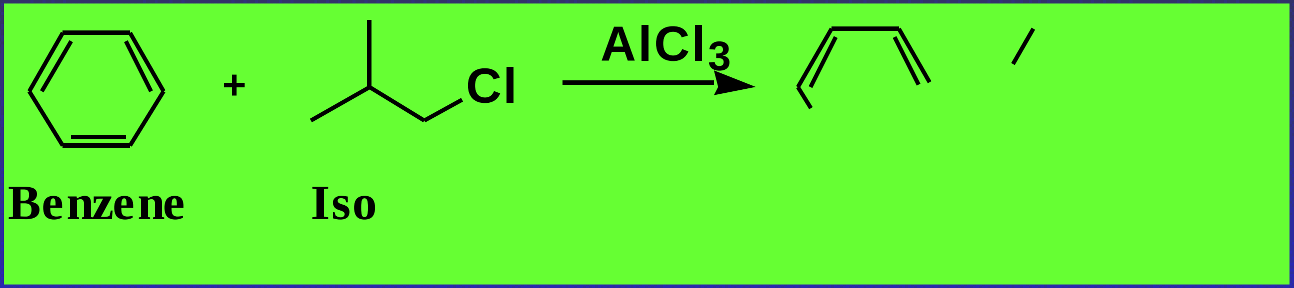
A resonance-stabilized cation

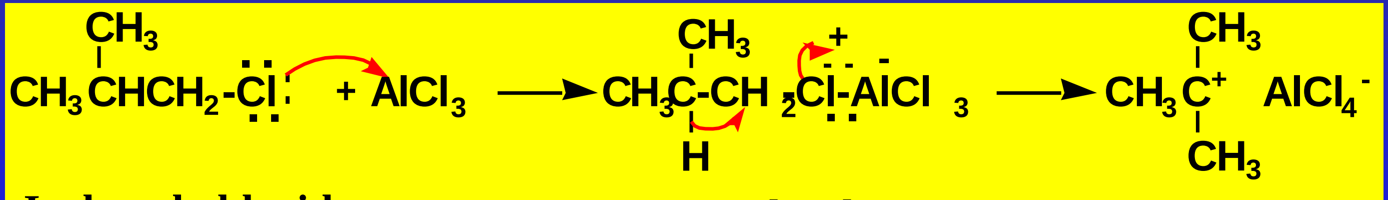
Step 3: Proton transfer regenerates the aromatic ring.



★There are four major limitations on Friedel-Crafts alkylations:

1. Carbocation rearrangements are common





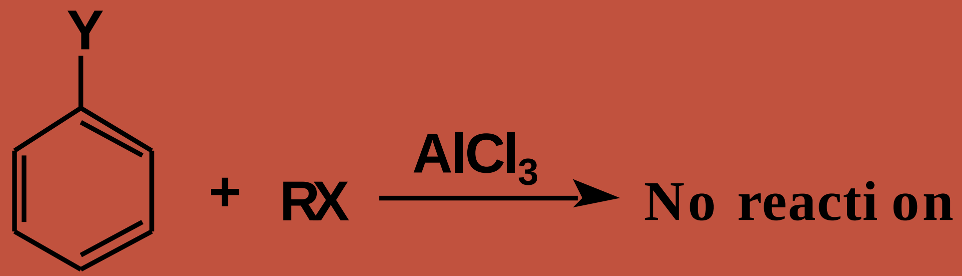
$$CH_3\overset{CH_3}{CH}CH_2\text{-}\ddot{\underset{\cdot\cdot}{Cl}}: + AlCl_3 \longrightarrow CH_3\overset{CH_3}{\underset{H}{C}}\text{-}CH_2\overset{+}{\ddot{Cl}}\text{-}\overset{-}{Al}Cl_3 \longrightarrow CH_3\overset{CH_3}{\underset{CH_3}{C^+}}\;AlCl_4^-$$

Isobutyl chloride

a molecular complex

an ion pair

2. F-C alkylation fails on benzene rings bearing one or more of these strongly electron-withdrawing groups.



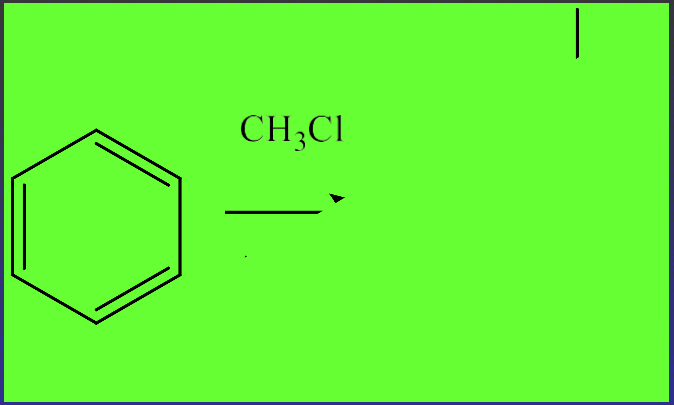
When Y Equals Any of These Groups, the Benzene Ring Does Not Undergo Friedel-Crafts Alkylation

$-\overset{O}{\overset{\|}{C}}H$ $-\overset{O}{\overset{\|}{C}}R$ $-\overset{O}{\overset{\|}{C}}OH$ $-\overset{O}{\overset{\|}{C}}OR$ $-\overset{O}{\overset{\|}{C}}NH_2$

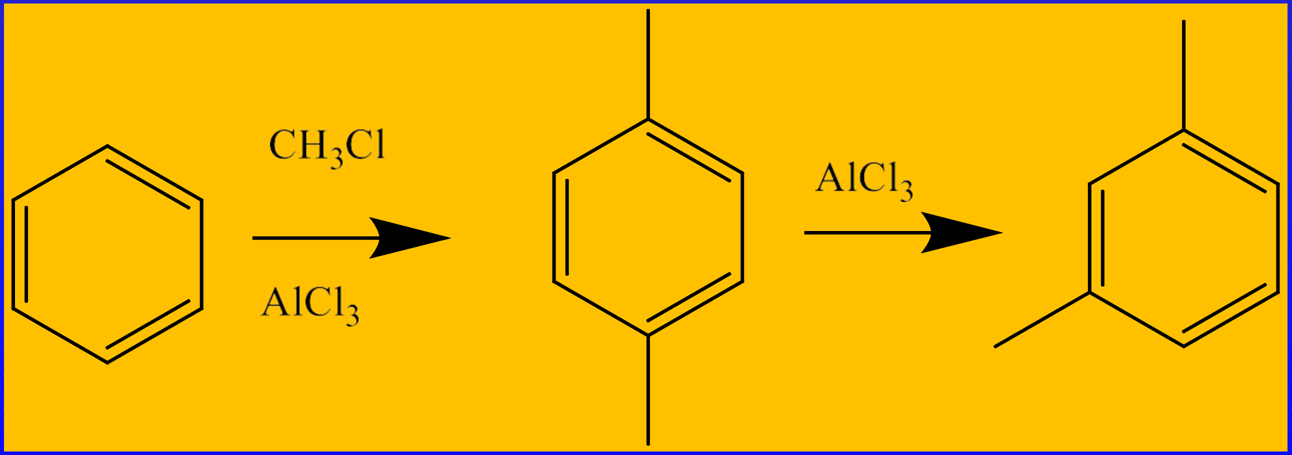
$-SO_3H$ $-C{\equiv}N$ $-NO_2$ $-NR_3^+$

$-CF_3$ $-CCl_3$

3. F-C multiple alkylation can occur more rapidly than monoalkylation. The first alkyl group activates the ring to the second substitution.

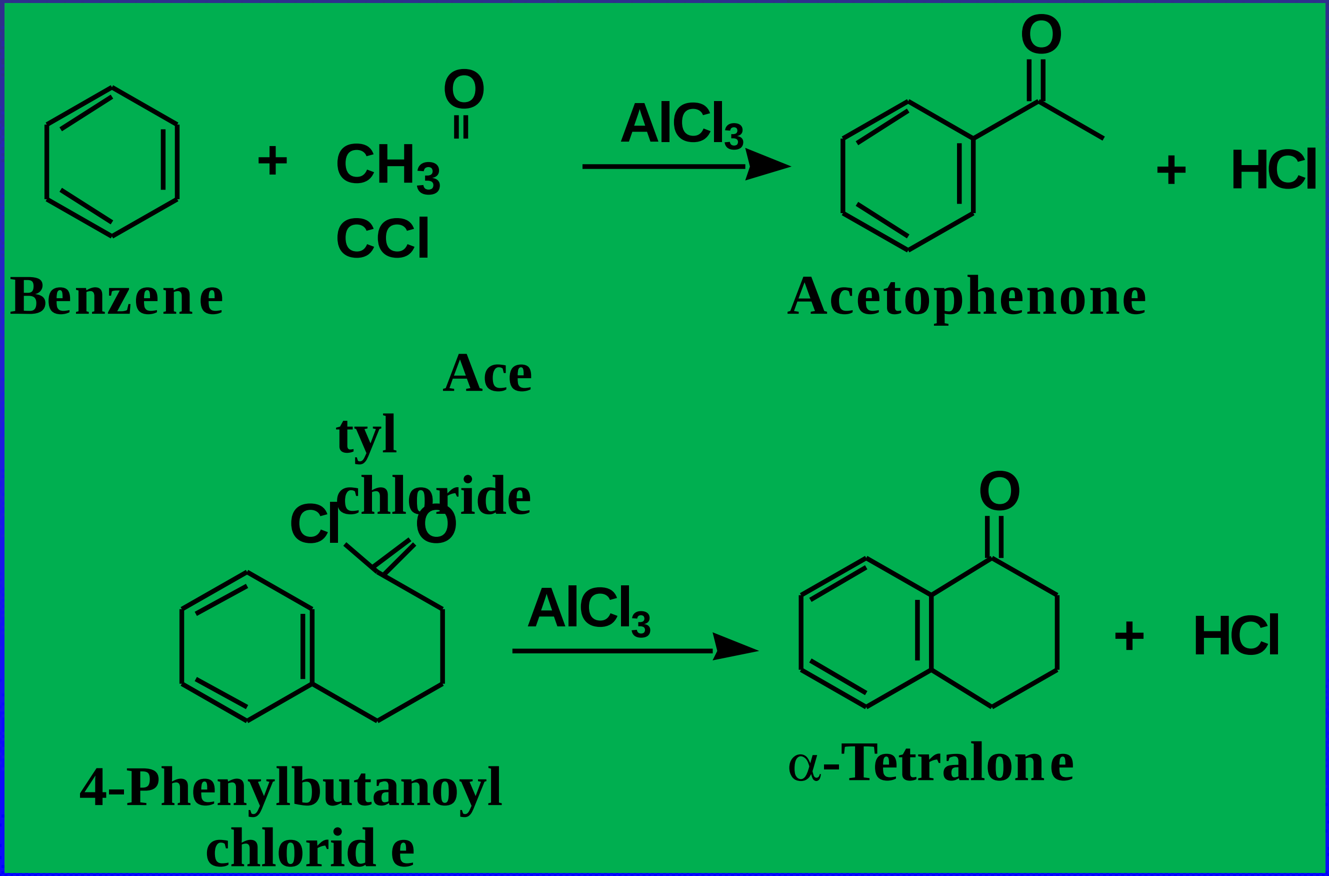


4. The steps in the Friedel Crafts Alkylation are reversible and rearrangments may occur.

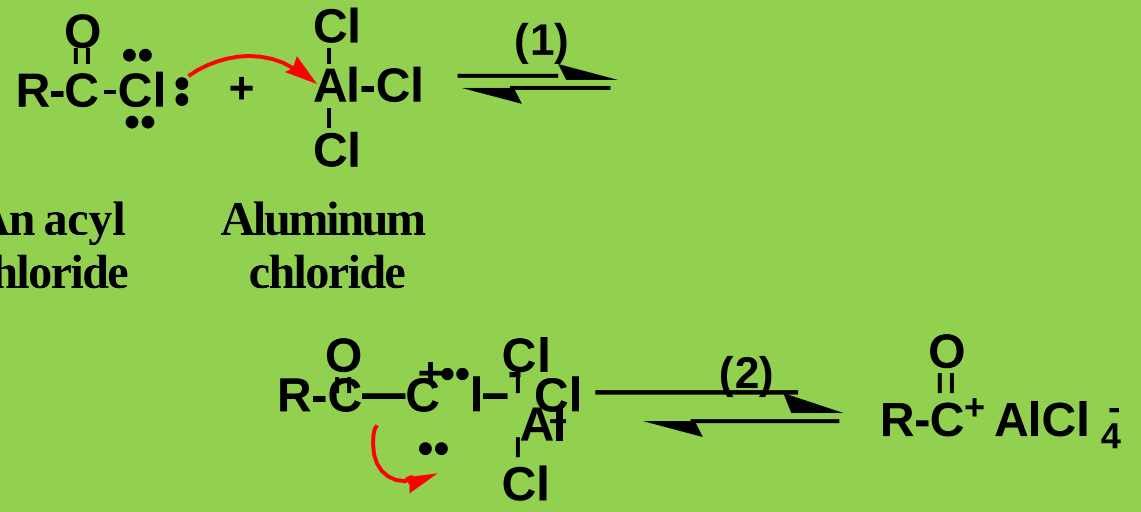


Friedel-Crafts Acylation

- **Friedel-Crafts acylation forms a new C-C bond between a benzene ring and an acyl group.**



⋆The electrophile is an acylium ion.



$$R-\overset{O}{\overset{\|}{C}}-\ddot{\underset{..}{Cl}}: + \underset{Cl}{\overset{Cl}{Al}}-Cl \overset{(1)}{\rightleftharpoons}$$

An acyl chloride

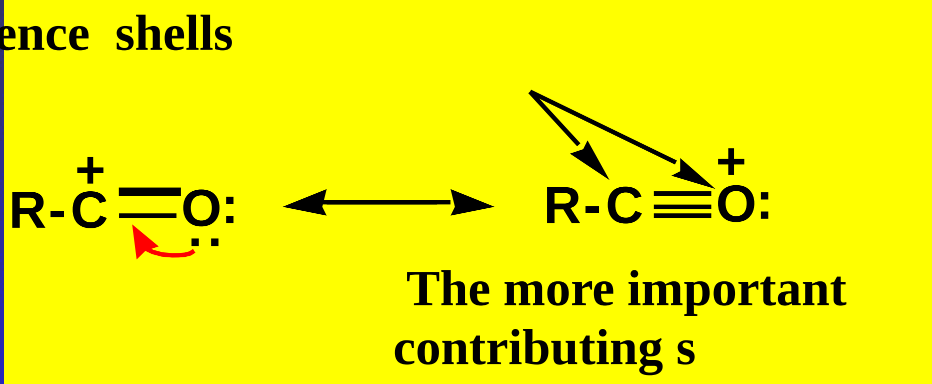
Aluminum chloride

$$R-\overset{O}{\overset{\|}{C}}-\overset{+}{\ddot{Cl}}-\underset{Cl}{\overset{Cl}{\overset{-}{Al}}}-Cl \overset{(2)}{\rightleftharpoons} R-\overset{O}{\overset{\|}{C^{+}}}\ AlCl_4^-$$

A molecular complex with a positive charge charge on

An ion pair containing an acylium ion

– An acylium ion is represented as a resonance hybrid of two major contributing structures.



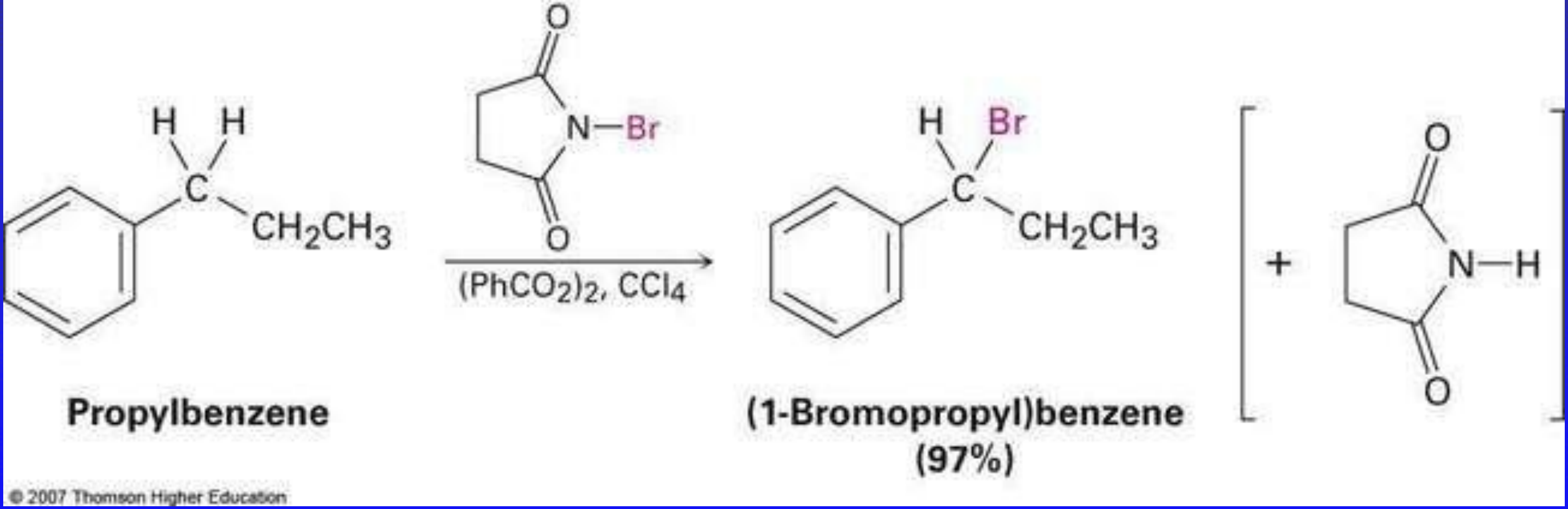
complete valence shells

The more important contributing s tructure

- Friedel-Crafts acylations are free of major limitation of Friedel-Crafts alkylations; acylium ions do not rearrange, do not polyacylate (why?), do not rearrange.

Side chain halogenation

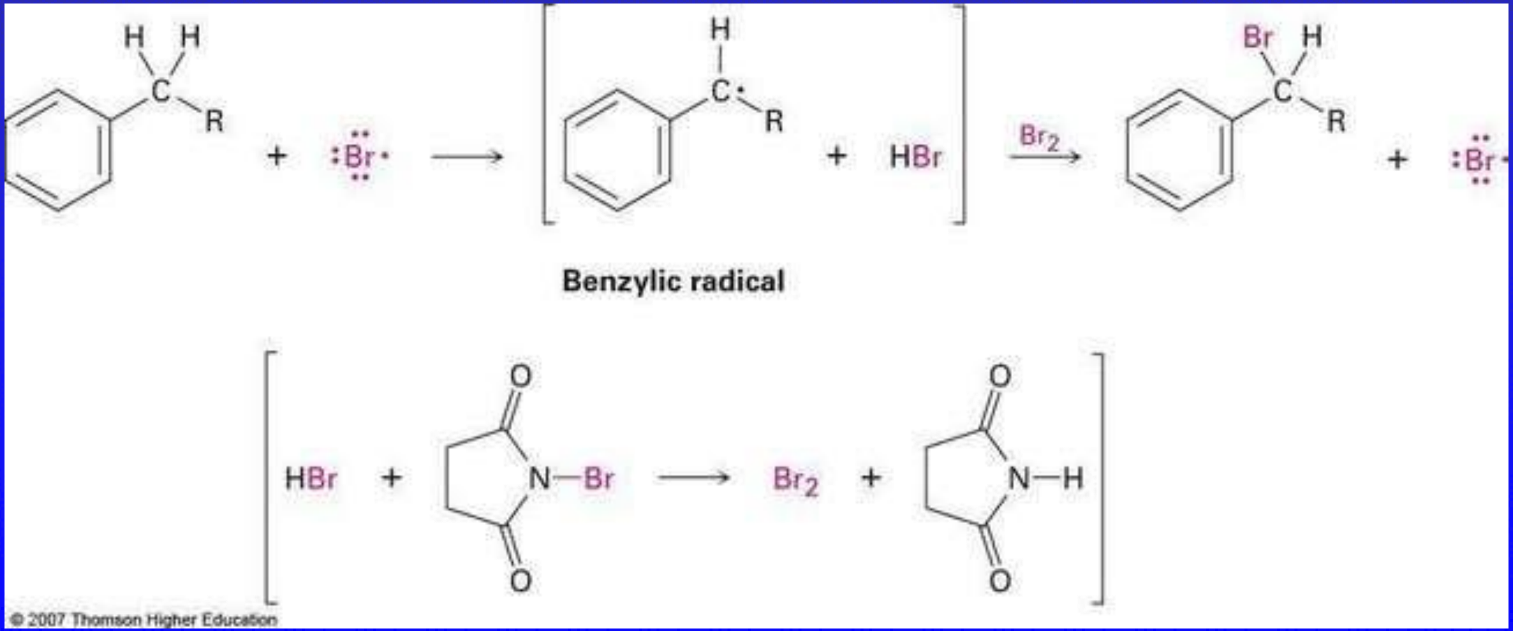
Reaction of an alkylbenzene with *N*-bromo-succinimide (NBS) and benzoyl peroxide (radical initiator) introduces Br into the side chain.



Propylbenzene

(1-Bromopropyl)benzene
(97%)

- Abstraction of a benzylic hydrogen atom generates an intermediate benzylic radical
- Reacts with Br_2 to yield product
- Br· radical cycles back into reaction to carry chain



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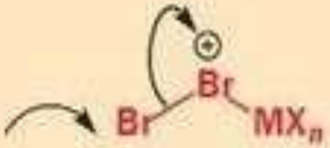
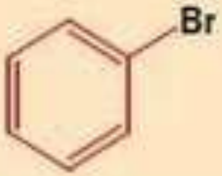
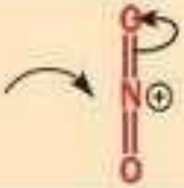
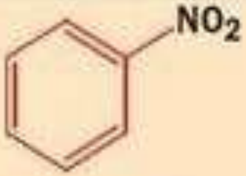
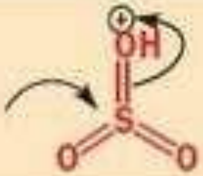
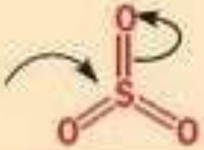
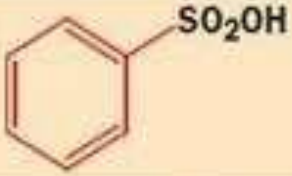
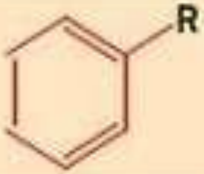
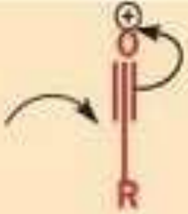
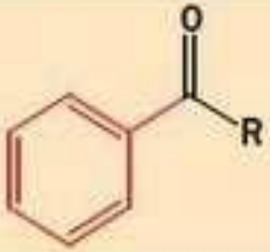
Summary of the main electrophilic substitutions on benzene

Reaction	Reagents	Electrophile	Products
bromination	Br_2 and Lewis acid, e.g. $AlCl_3$, $FeBr_3$, Fe powder		
nitration	$HNO_3 + H_2SO_4$		
sulfonation	concentrated H_2SO_4 or $H_2SO_4 + SO_3$ (oleum)	 or 	
Friedel–Crafts alkylation	RX + Lewis acid usually $AlCl_3$		
Friedel–Crafts acylation	RCOCl + Lewis acid usually $AlCl_3$		

Organic compounds containing nitrogen

$R-NO_2$

Nitro alkan

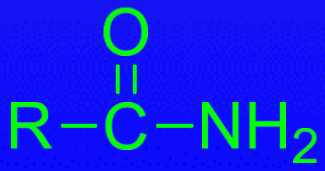
$R-ONO$

$R-CN$

Alkyl Cyanide

$R-NC$

Alkyl isocyanide



$$R-\overset{\overset{\displaystyle O}{\|}}{C}-NH_2$$

Amide

Preparation of nitro compounds

1. Vapour phase nitration of alkanes

Hydrocarbons on heating with fuming nitric acid at 693-793 K are converted into nitroalkanes.

$$\underset{}{CH_3{-}CH_3} + \underset{\text{(Fuming)}}{HNO_3} \xrightarrow{\Delta} \underset{\text{(low yield)}}{CH_3{-}CH_2{-}NO_2} + H_2O$$

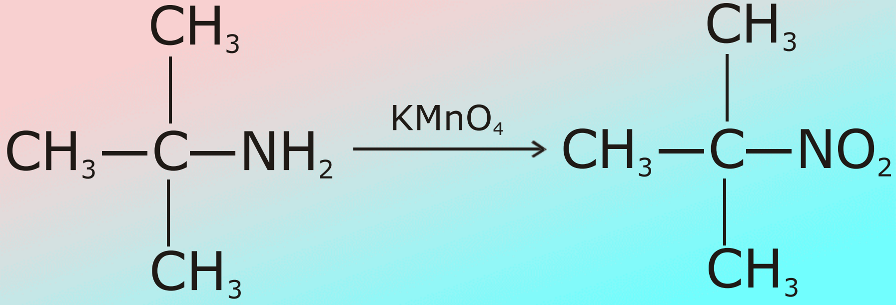
2.Treatment of alkyl halides with alcoholic $AgNO_3$

Iodoalkanes on treatment with alcoholic $AgNO_2$ are converted into nitroalkanes besides alkylnitriles.

$$CH_3{-}CH_2{-}I + AgNO_2 \longrightarrow \underset{\text{nitroethane}}{CH_3{-}CH_2{-}NO_2} + \underset{\text{ethyl nitrile}}{C_2H_5{-}O{-}N{-}O}$$

3. Oxidation of t-alkyl amines with $KMnO_4$

The amine must be primary and —NH_2 group should be attached to a tertiary carbon.



$$CH_3-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}-NH_2 \xrightarrow{KMnO_4} CH_3-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}-NO_2$$

4. Nitration of Aromatic nitro compounds

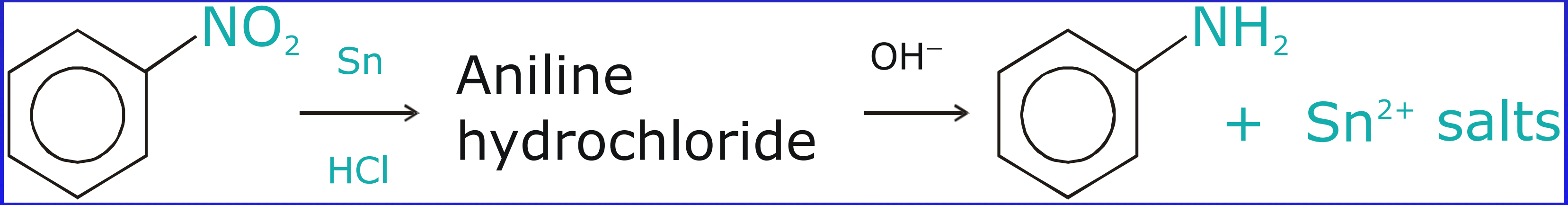
Nitration is performed with a mixture of concentrated nitric and sulphuric acid (source of nitronium ion).

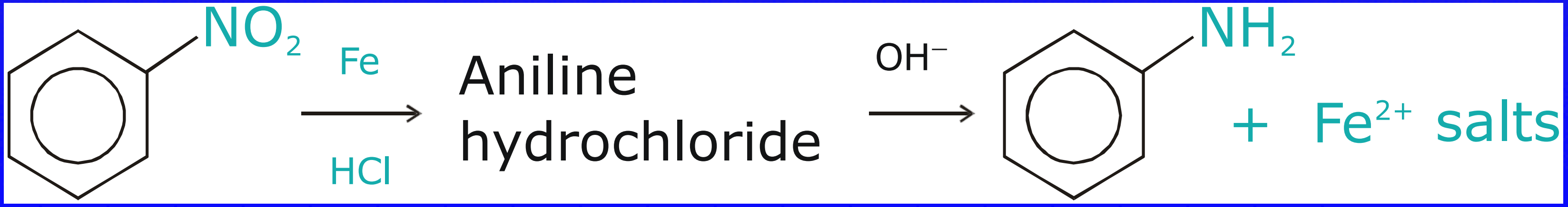
Reactions of nitro compounds

Reduction

1. Reduction in acidic medium

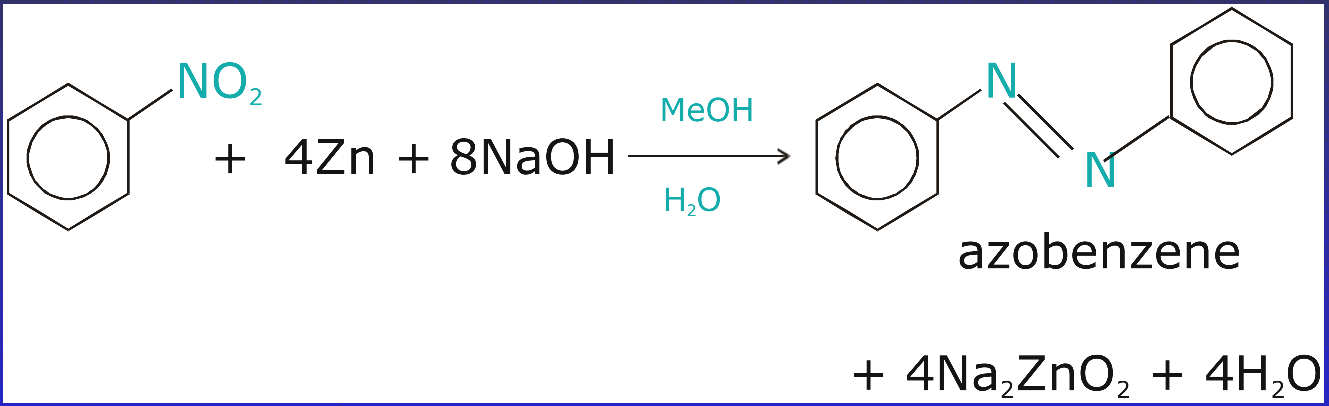
By metal in acidic solutions: Metals(Fe, Sn and Zn) and HCl are used for reducing a nitro group to an amino group.

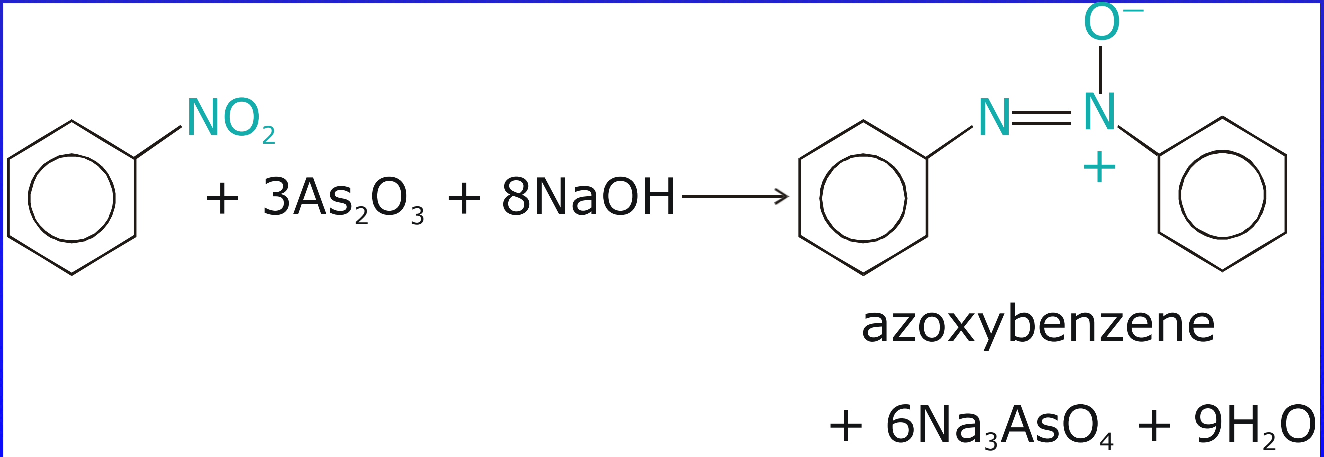




2.Reduction in basic medium

Forms different products depending on reducing reagent.



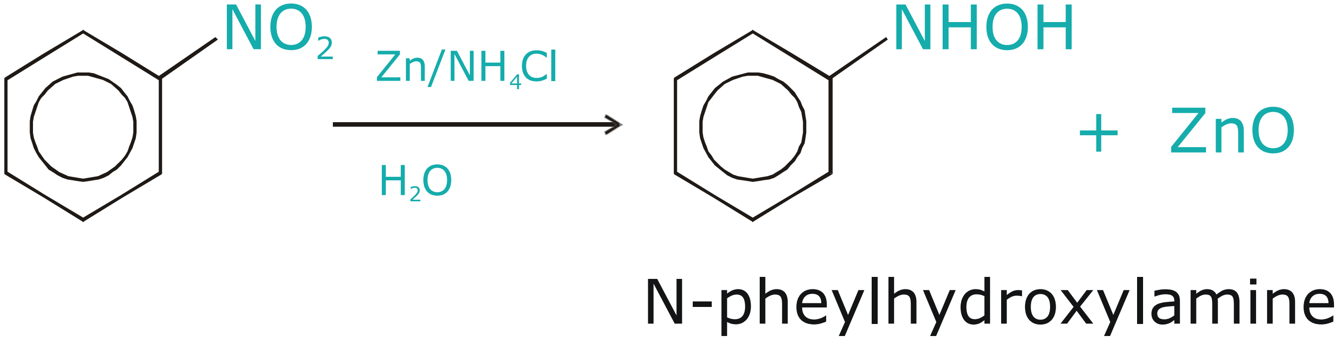


3.Reduction in neutral medium

Reduction in neutral medium: Zinc dust and ammonium chloride convert nitro benzene to corresponding hydroxylamine.

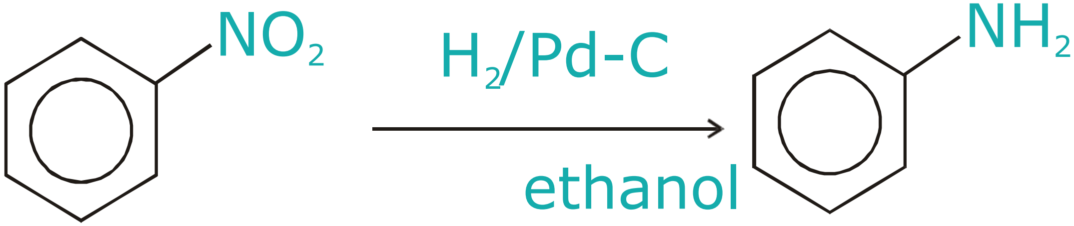
$$CH_3NO_2 + 4[H] \xrightarrow[\Delta]{Zn/NH_4Cl} CH_3-NHOH + H_2O$$

N-methyl hydroxyl amine



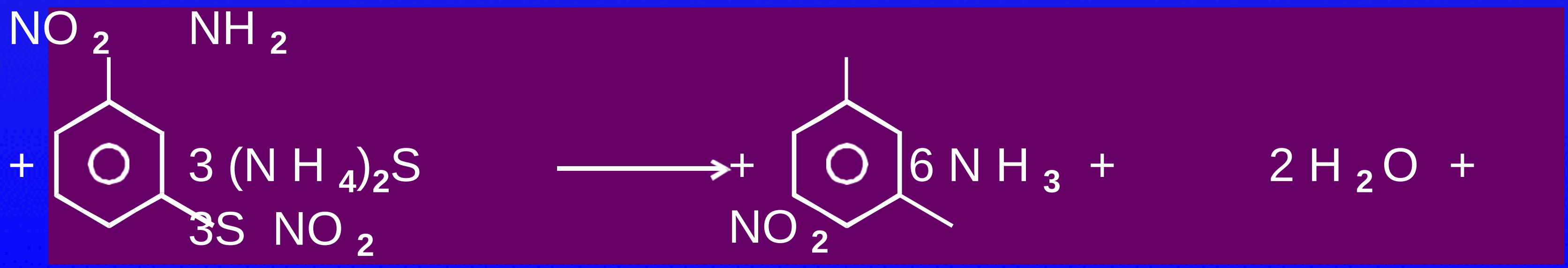
4.Catalytic reduction:

Easily reduced by catalytic hydrogenation using Pd/C catalyst in ethanol.



5.Selective reduction

One nitro group can be reduced without affecting the second group on benzene ring using ammonium sulphide orsodium polysulphide.



6.Reduction with $LiAlH_4$

Aliphatic nitro-compounds are reduced to primary amines with $LiAlH_4$.

$$CH_3NO_2 \;\downarrow\;\downarrow LiA\downarrow lH_4\downarrow \xrightarrow{ether} CH_3NH_2$$

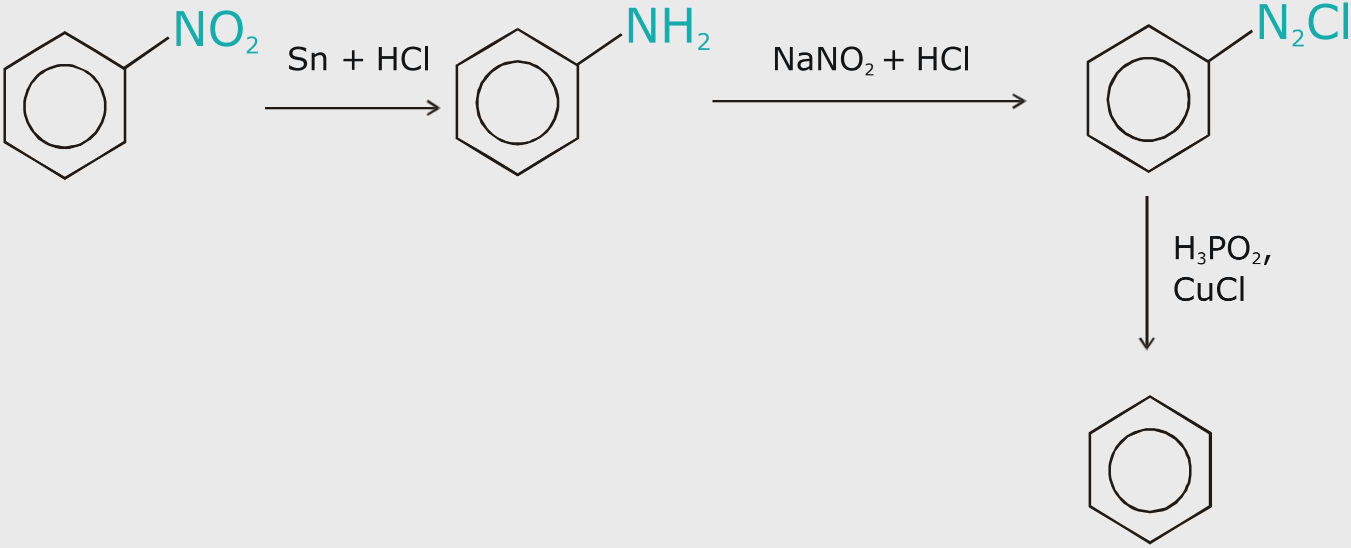
Aromatic nitro-comopunds on reduction with $LiAlH_4$ give azo compounds.

$$2\,C_6H_5NO_2 \;\downarrow\downarrow LiA\downarrow lH_4\downarrow\rightarrow C_6H_5 — N{=\!=}N — C_6H_5$$

Azo benzene

Removal of nitro group

Nitro group can be removed from aromatic ring via reduction to amine followed by deoxidization with HNO_2 and then reductive removal of the diazonium group using sodium borohydride or hypo phosphorus acid/Cu^+ mixture.



Hydrolysis of aliphatic nitro compounds

Primary nitro-compounds are hydrolysed by boiling HCl or by 85% H_2SO_4 to a carboxylic acid and hydroxylamine.

$$RCH_2NO_2 + H_2O + HCl \downarrow\downarrow^{\Delta} \rightarrow RCOOH + NH_2OHHCl$$

1° Nitro alkane

Carboxylic acid

Hydroxylamin e hydrochloride

Secondary nitro-compounds are hydrolysed by boiling hydrochloric acid to ketones and nitrous oxide.

$$2R_2CHNO_2 \downarrow\downarrow^{Boi}\downarrow^{ling}\downarrow^{H}\downarrow^{Cl}\downarrow\rightarrow 2R_2CO + N_2O + H_2O$$

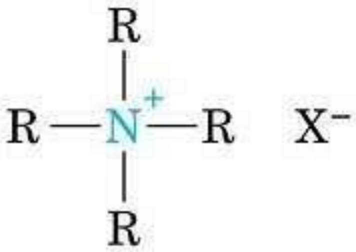
ketone Nitrous oxide

Tertiary nitro-compounds are generally unaffected by HCl.

Amines

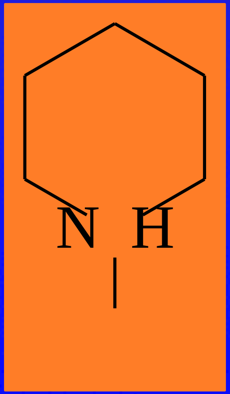
Primary (1°): one C-N bond, 2 N-H bonds. Secondary (2°): two C-N bonds, 1 N-H bond. Tertiary (3°): three C-N bonds, no N-H bond.

Quaternary (4°): four C-N bonds, nitrogen has a + formal charge.



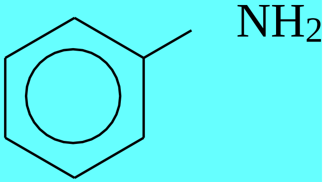
$$R-\overset{\overset{\displaystyle R}{|}}{\underset{\underset{\displaystyle R}{|}}{N^{+}}}-R \quad X^{-}$$

A quaternary ammonium salt

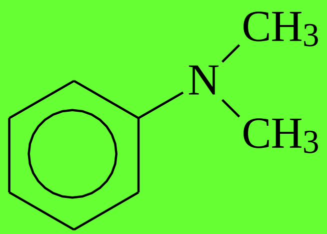


Aromatic Amines

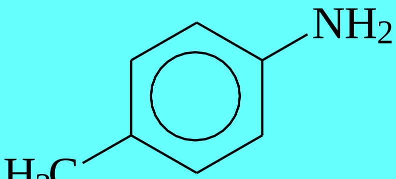
Amino group is bonded to a benzene ring. Parent compound is called aniline.



aniline



N,*N*-dimethylaniline

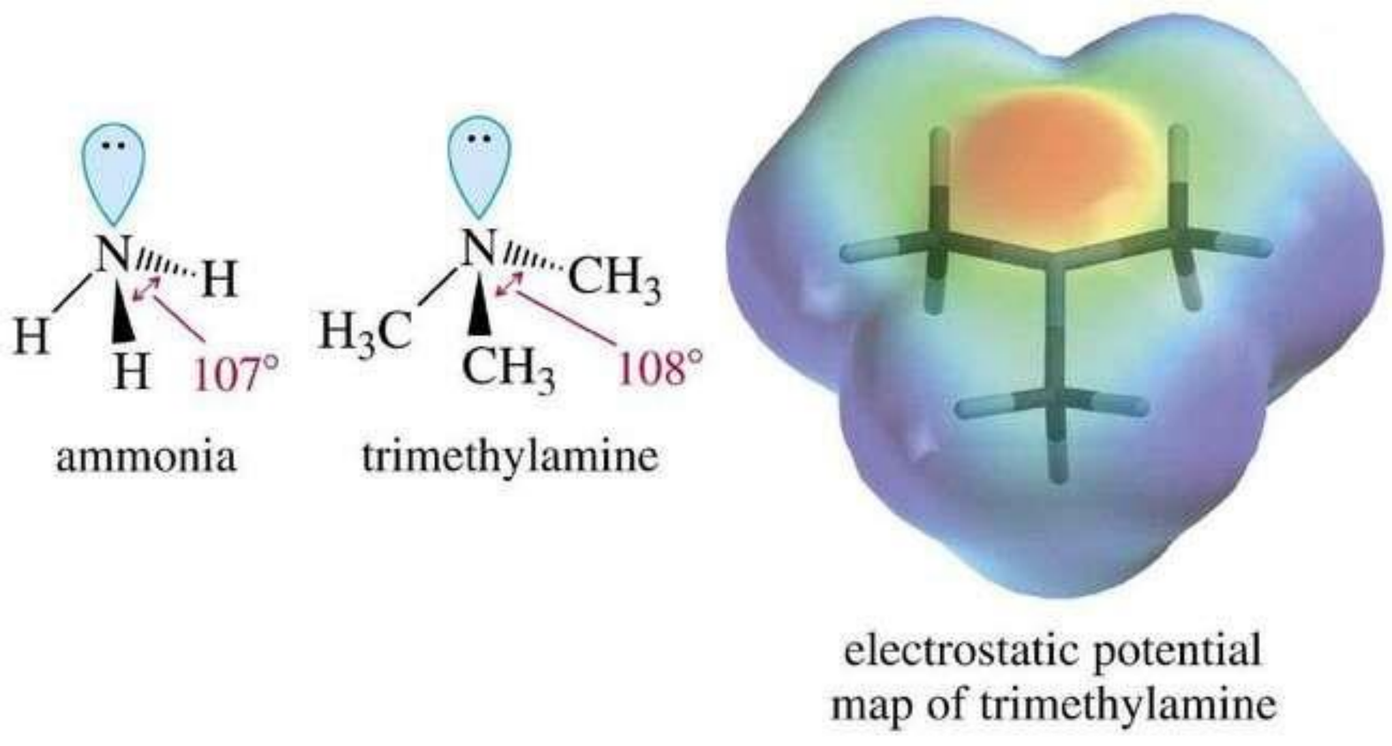


4-methylaniline
or *p*-toluidine

Structure of Amines

Bonding to N is similar to that in ammonia N is sp^3-hybridized

C–N–C bond angles are close to 109° tetrahedral value



ammonia

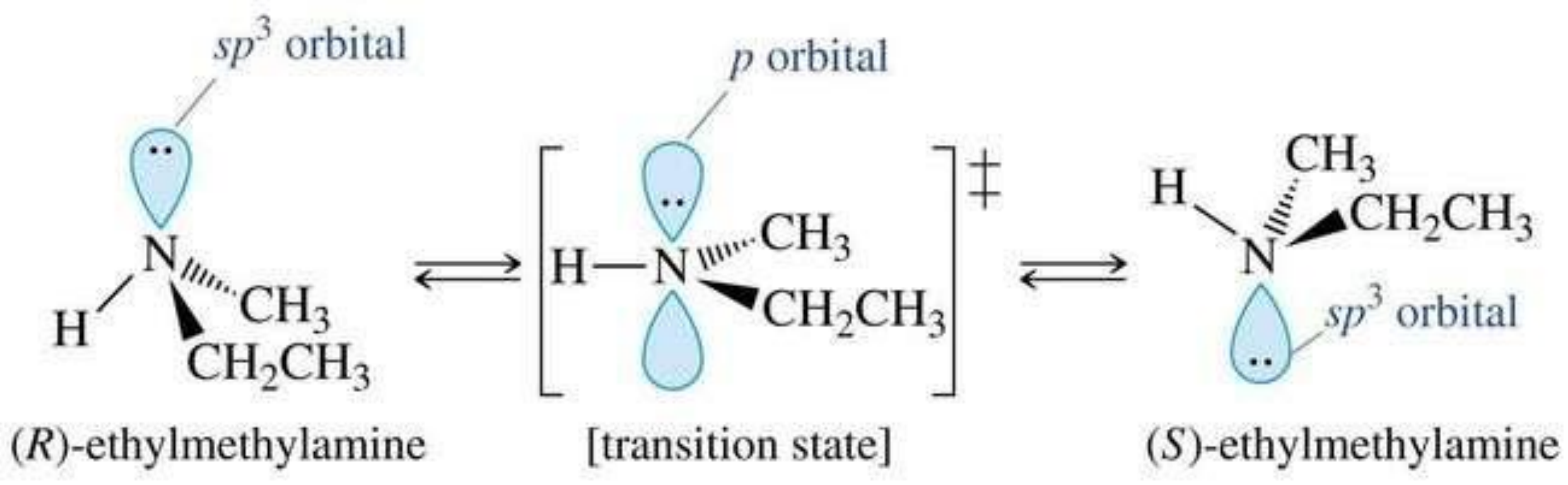
trimethylamine

electrostatic potential map of trimethylamine

Chirality of Amines

An amine with three different substituents on nitrogen is chiral (in principle but not in practice): the lone pair of electrons is the fourth substituent

Most amines that have 3 different substituents on N are not resolved because the molecules interconvert by pyramidal inversion



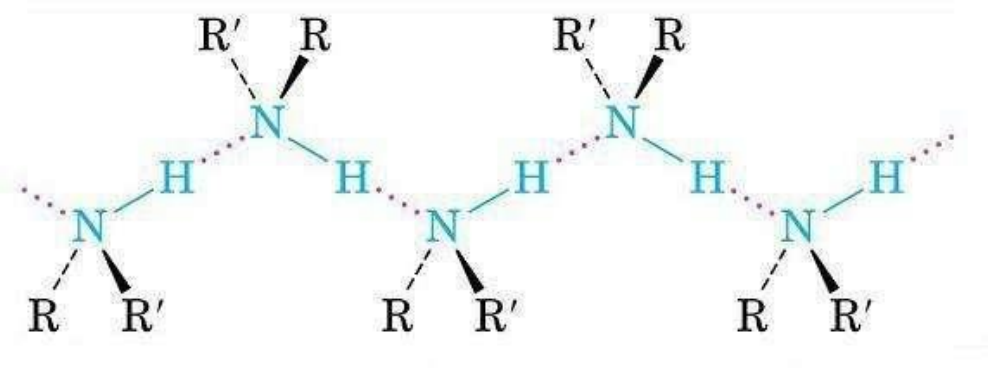
(R)-ethylmethylamine

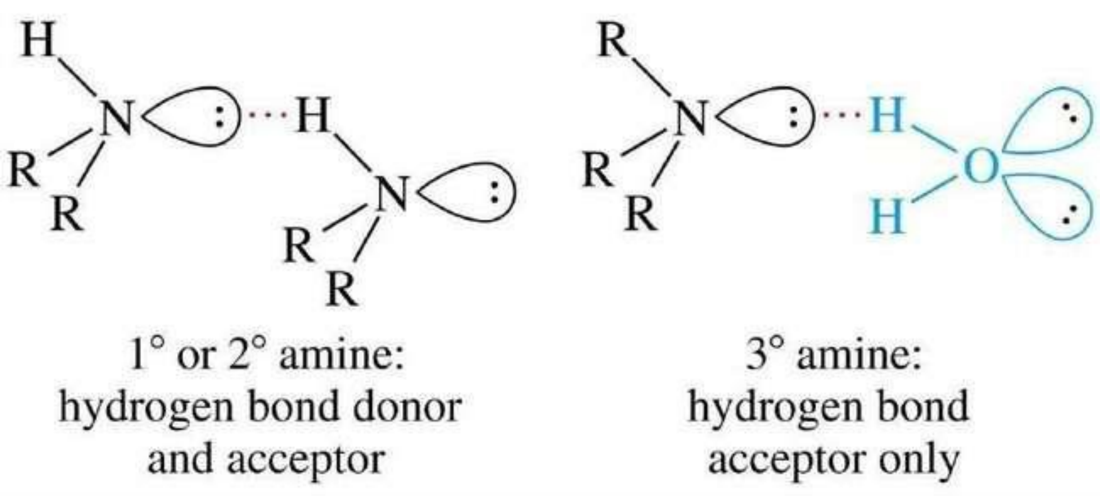
[transition state]

(S)-ethylmethylamine

Amines Form H-Bonds

- Amines with fewer than five carbons are water-soluble
- Primary and secondary amines form hydrogen bonds, increasing their boiling points





1° or 2° amine:
hydrogen bond donor
and acceptor

3° amine:
hydrogen bond
acceptor only

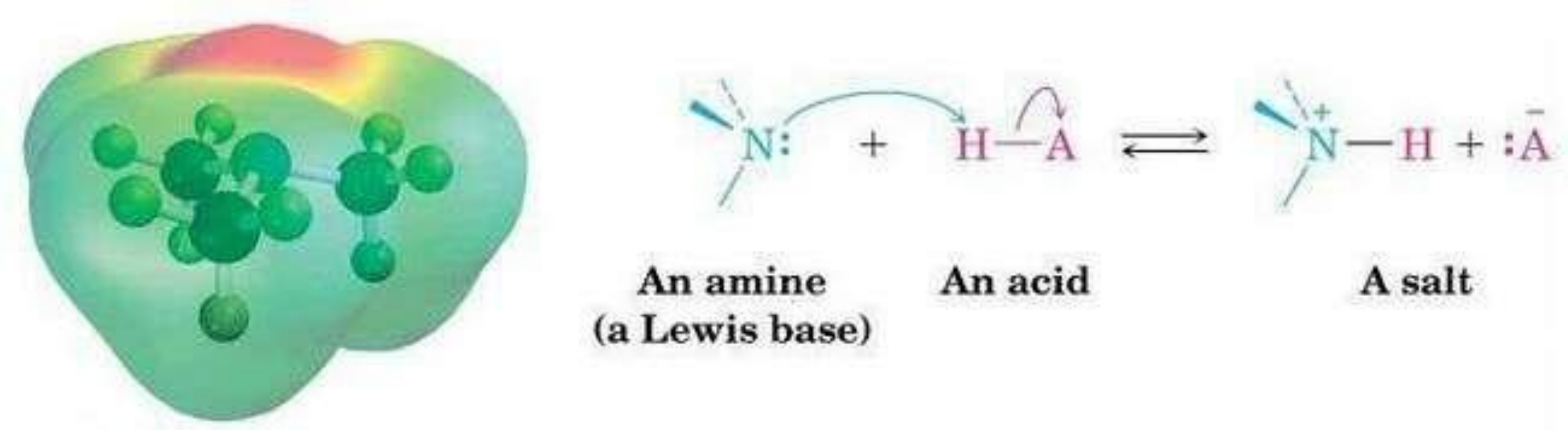
Basicity of Amines

Lone pair of electrons on nitrogen can accept a proton from an acid.

Aqueous solutions are basic.

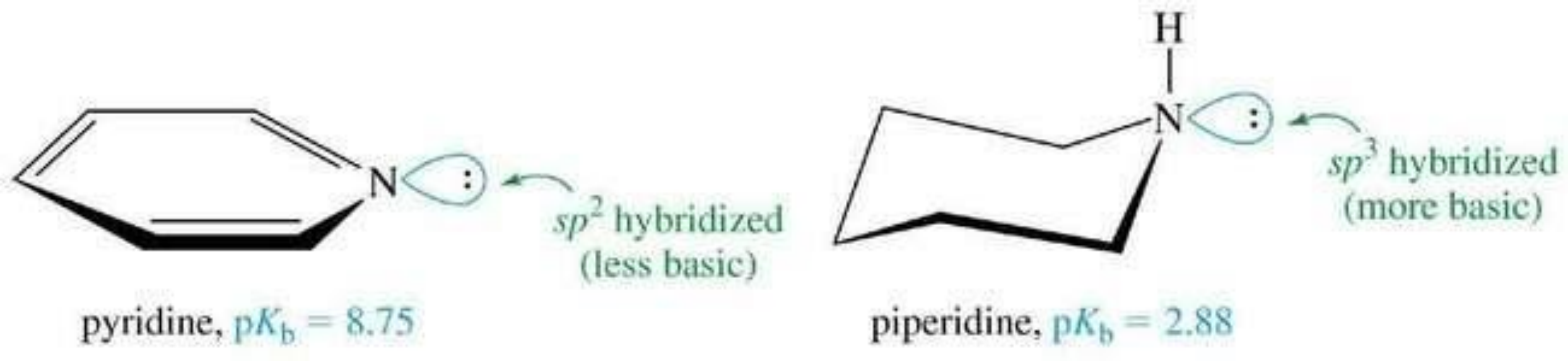
Ammonia pK_b = 4.74

Alkyl amines are usually stronger bases than ammonia. Increasing the number of alkyl groups decreases solvation of ion, but increases the availability of lone pair on nitrogen atom.

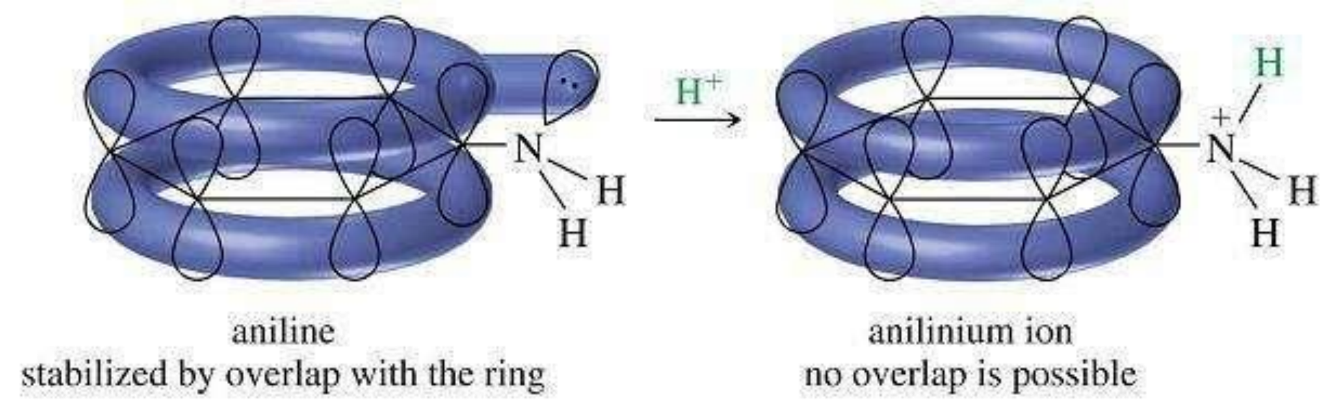


Effects on basicity

Hybridization Effects: Electrons are held more tightly in orbitals with more *s* character, so those compounds are weaker bases.

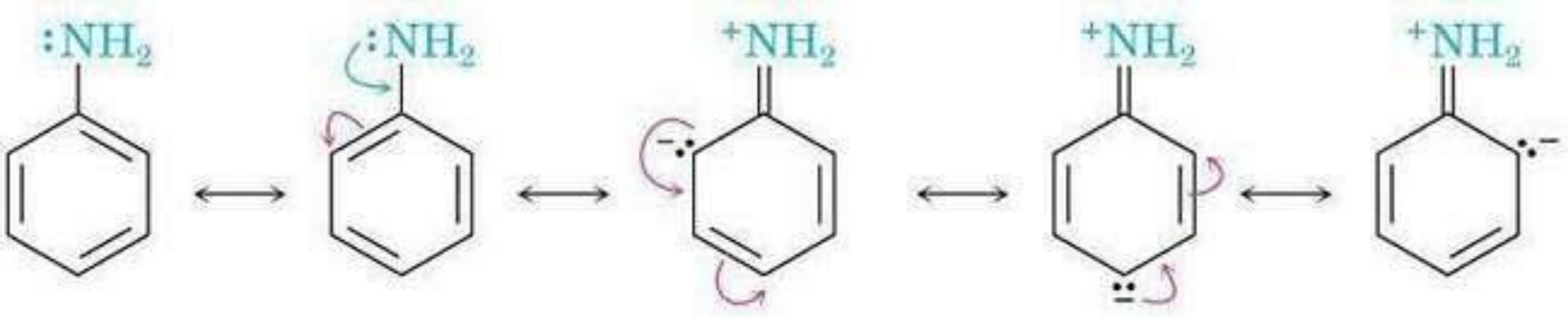


Resonance: Any delocalization of the electron pair weakens the base.



Basicity of Substituted Arylamines

TheN lone-pair electrons in arylamines are delocalized by interaction with the aromatic ring π electron system and

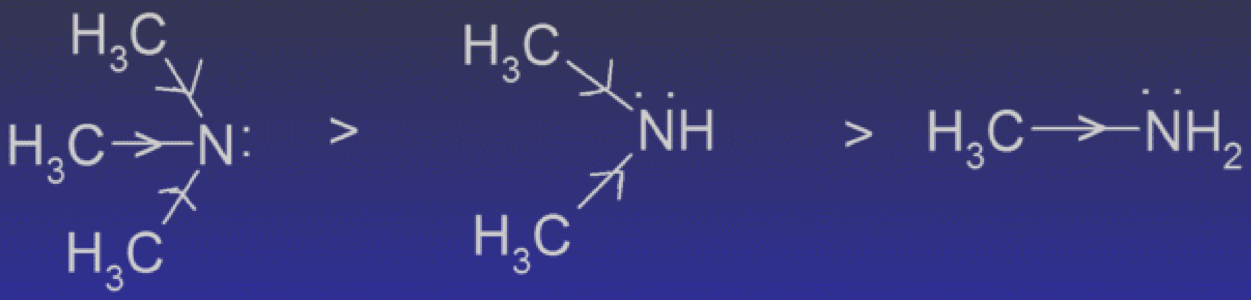


Can be more basic or less basic than aniline.

Electron-donating substituents (such as ↓CH_3, ↓NH_2, ↓OCH_3) increase the basicity of the corresponding arylamine.

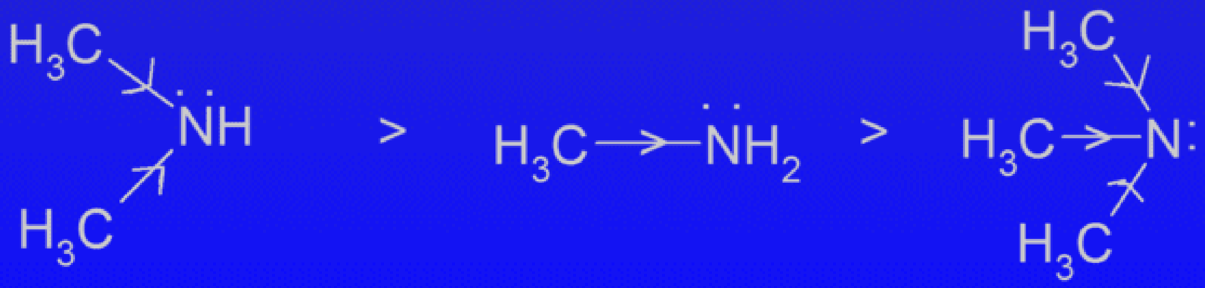
Electron-withdrawing substituents (such as ↓Cl, ↓NO_2, ↓CN) decrease arylamine basicity.

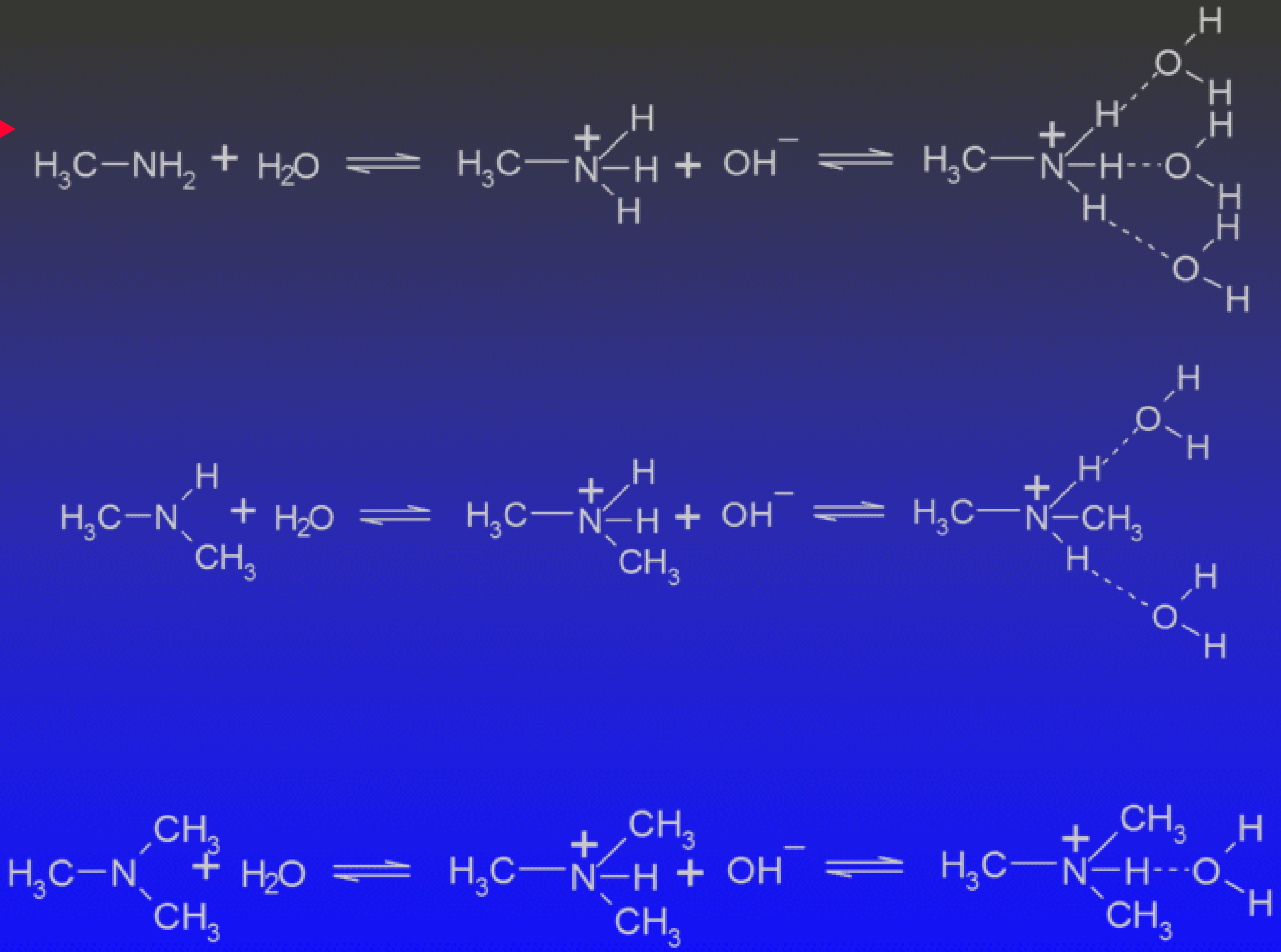
Basic Strength of Amines:



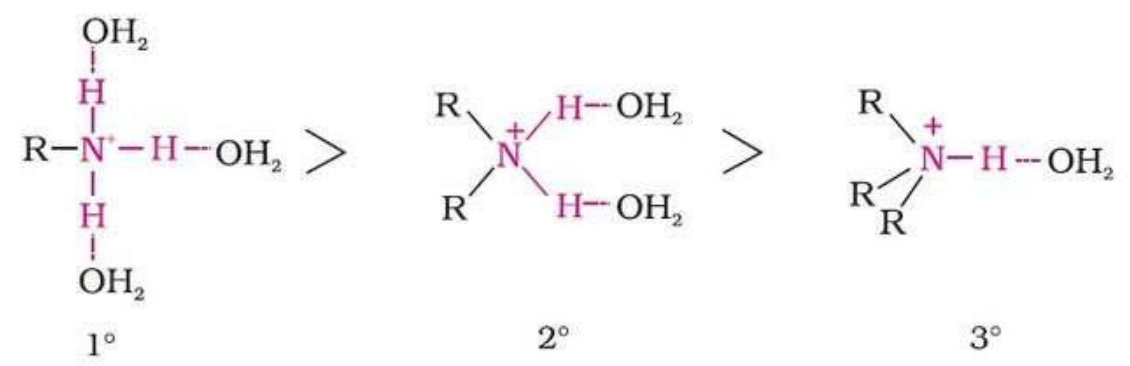
Due to the presence of more +I groups electron density on nitrogen atom increases as a result tertiary amine is more basic than primary amine.

In aqueous solution:

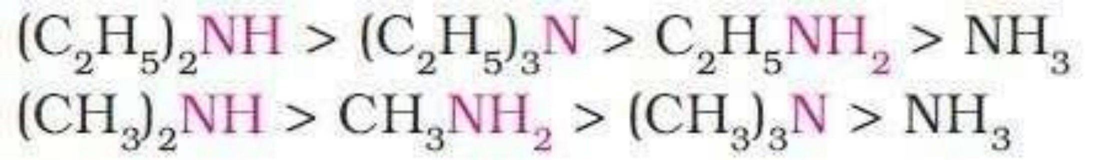




Decreasing order of extent of H-bonding in water and order of stability of ions by solvation.



Greater is the stability of the substituted ammonium cation, stronger should be the corresponding amine as a base. Thus, the order of basicity of aliphatic amines should be: primary > secondary > tertiary, which is opposite to the inductive effect based order. when the alkyl group is small, like –CH3 group, there is no steric hindrance to H-bonding. In case the alkyl group is bigger than CH3 group, there will be steric hinderance to H-bonding. Therefore, the change of nature of the alkyl group, e.g., from –CH3 to –C2H5 results in change of the order of basic strength. Thus, there is a subtle interplay of the inductive effect, solvation effect and steric hinderance of the alkyl group which decides the basic strength of alkyl amines in the aqueous state. The order of basic strength in case of methyl substituted amines and ethyl substituted amines in aqueous solution is as follows:

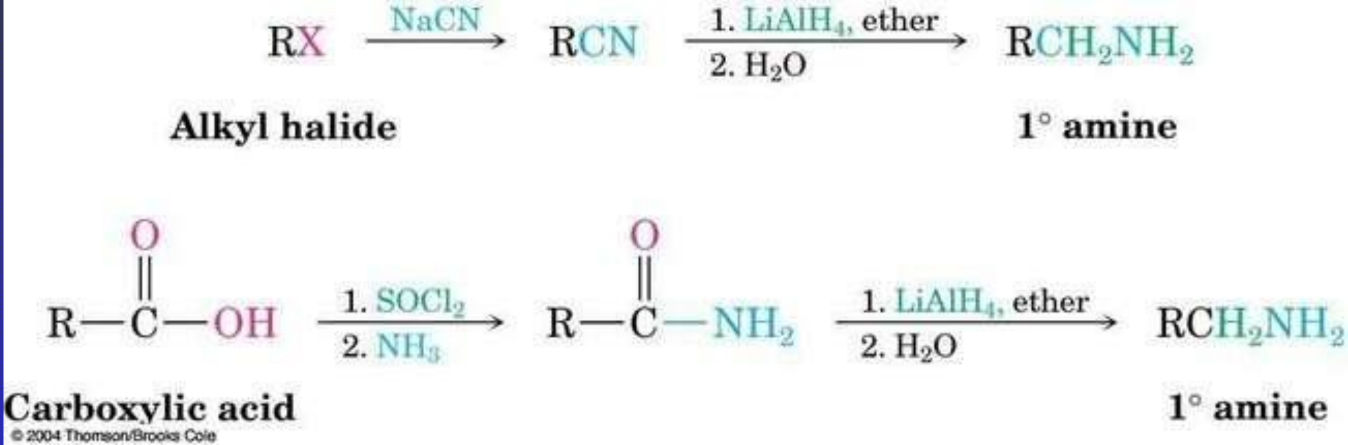


$(C_2H_5)_2NH > (C_2H_5)_3N > C_2H_5NH_2 > NH_3$

$(CH_3)_2NH > CH_3NH_2 > (CH_3)_3N > NH_3$

Synthesis of Amines

Reduction of nitriles and amides.

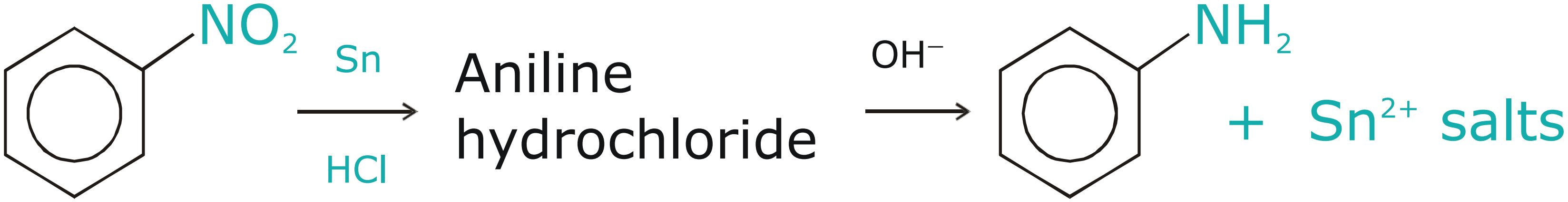


$$RX \xrightarrow{NaCN} RCN \xrightarrow[2.\ H_2O]{1.\ LiAlH_4,\ ether} RCH_2NH_2$$

$$R-\overset{O}{\overset{\|}{C}}-OH \xrightarrow[2.\ NH_3]{1.\ SOCl_2} R-\overset{O}{\overset{\|}{C}}-NH_2 \xrightarrow[2.\ H_2O]{1.\ LiAlH_4,\ ether} RCH_2NH_2$$

Reduction in acidic medium

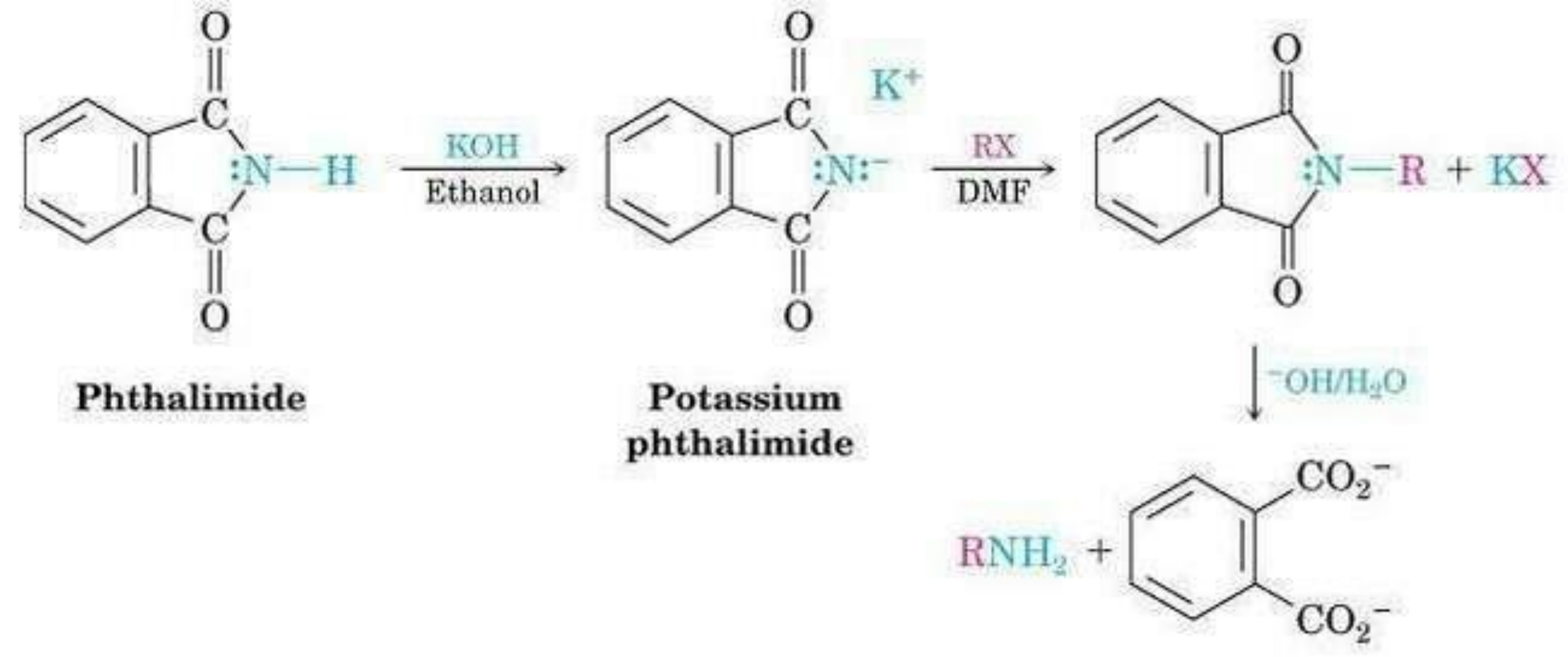
By metal in acidic solutions: Metals(Fe, Sn and Zn) and HCl are used for reducing a nitro group to an amino group.



Gabriel Synthesis of Primary Amines

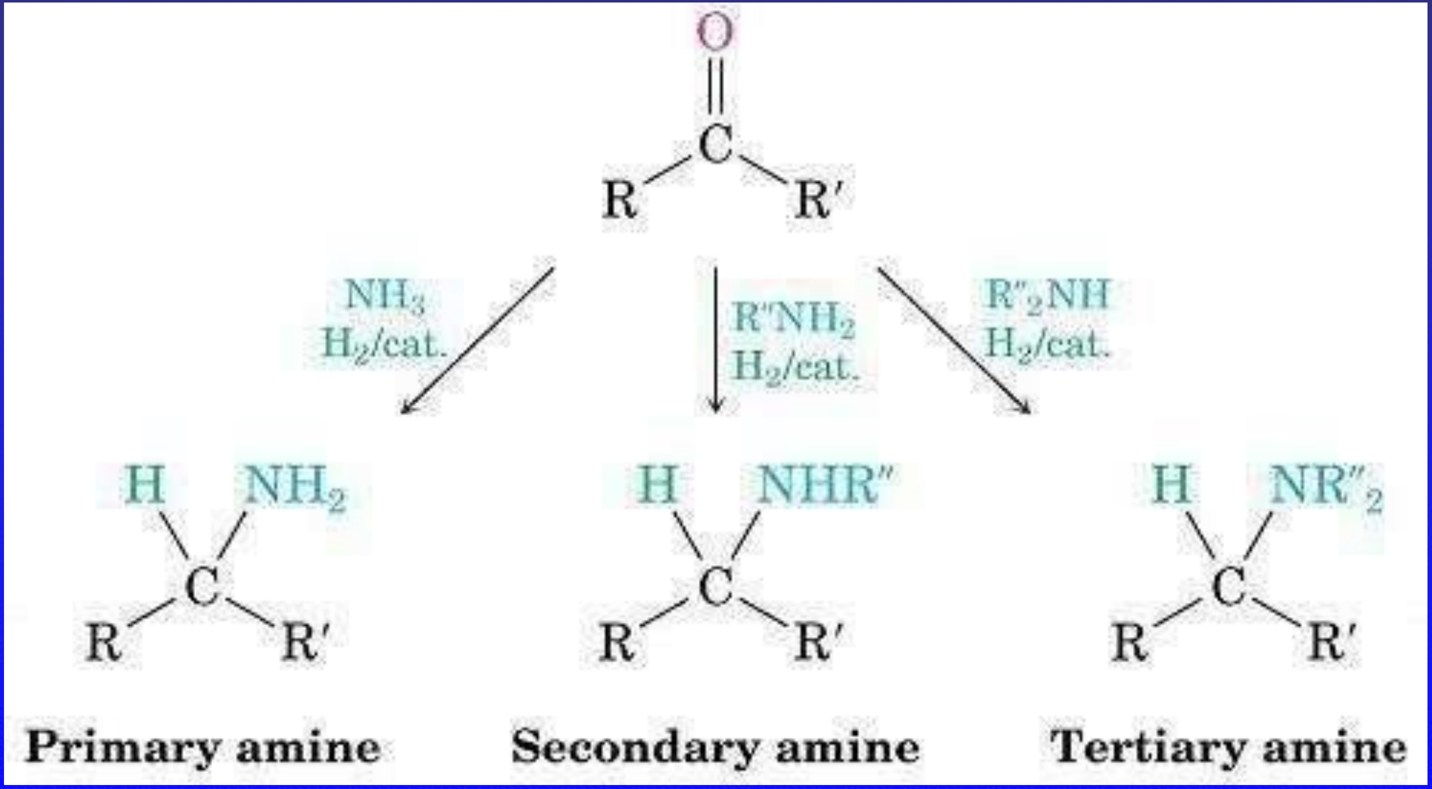
A phthalimide alkylation for preparing a primary amine from an alkyl halide

The N-H in imides (↓CONHCO↓) can be removed by KOH followed by alkylation and hydrolysis



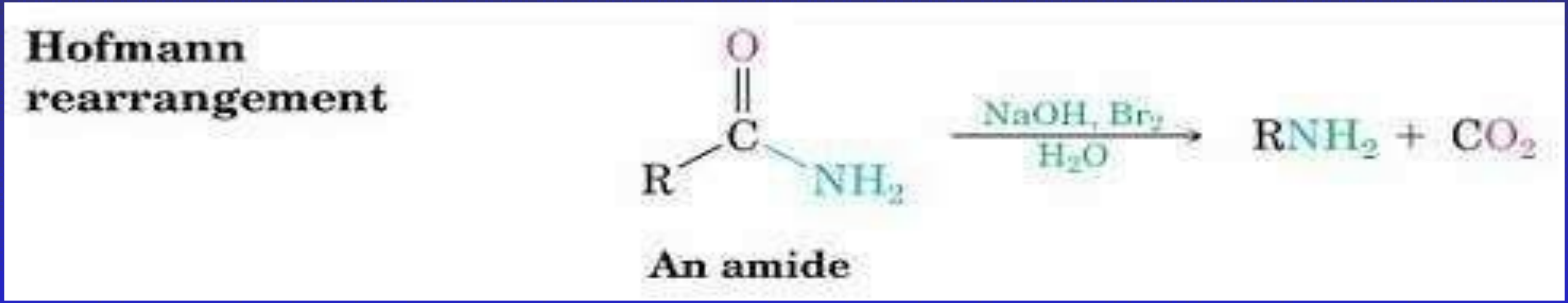
Reductive Amination of Aldehydes and Ketones

Treatment of an aldehyde or ketone with ammonia or an amine in the presence of a reducing agent



Hofmann and Curtius Rearrangements

Hofmann rearrangement: $RCONH_2$ reacts with Br_2 and base. Gives high yields of arylamines and alkylamines.



Heating an acyl azide prepared from substitution an acid chloride.

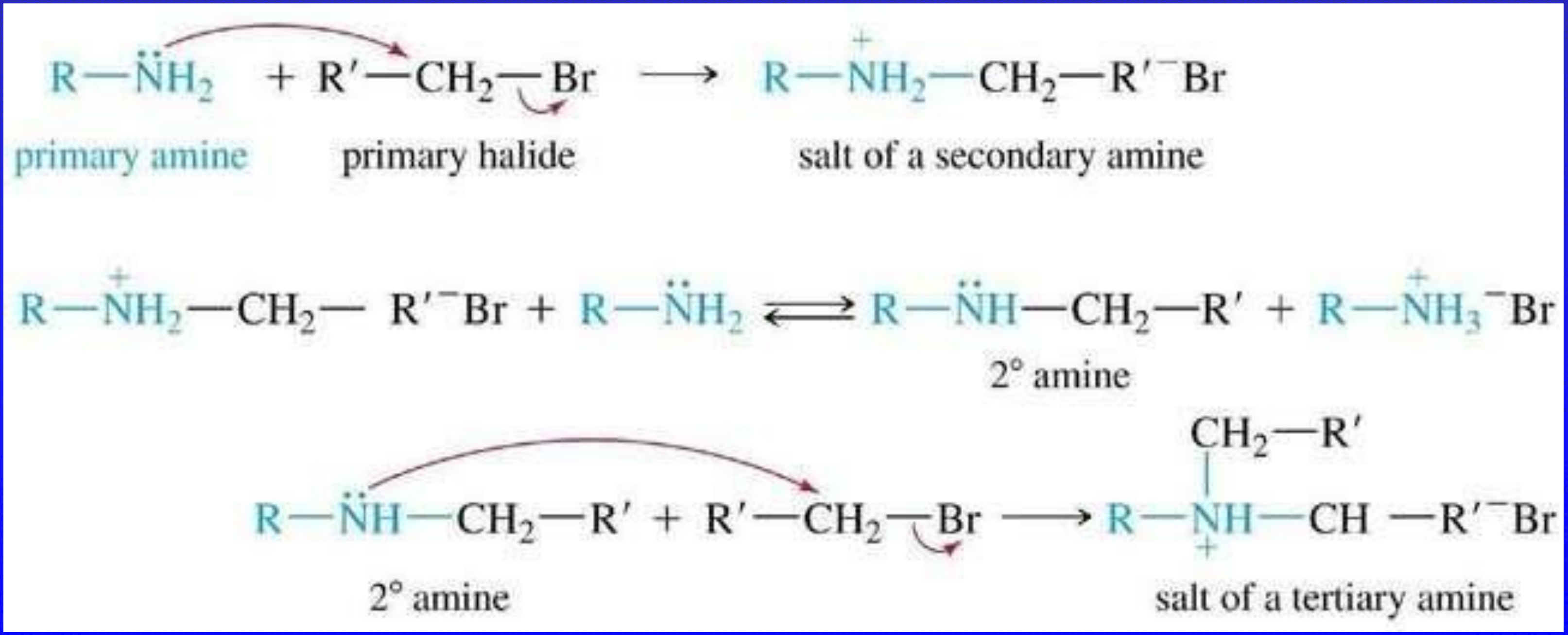
Migration of ↓R from C=O to the neighboring nitrogen with simultaneous loss of a leaving group.

Reaction of Amines

Alkylation of Amines

Amines react with 1° alkyl halides via the S_N2 mechanism.

Mixtures of the mono-, di-, and tri-alkylated products are obtained.

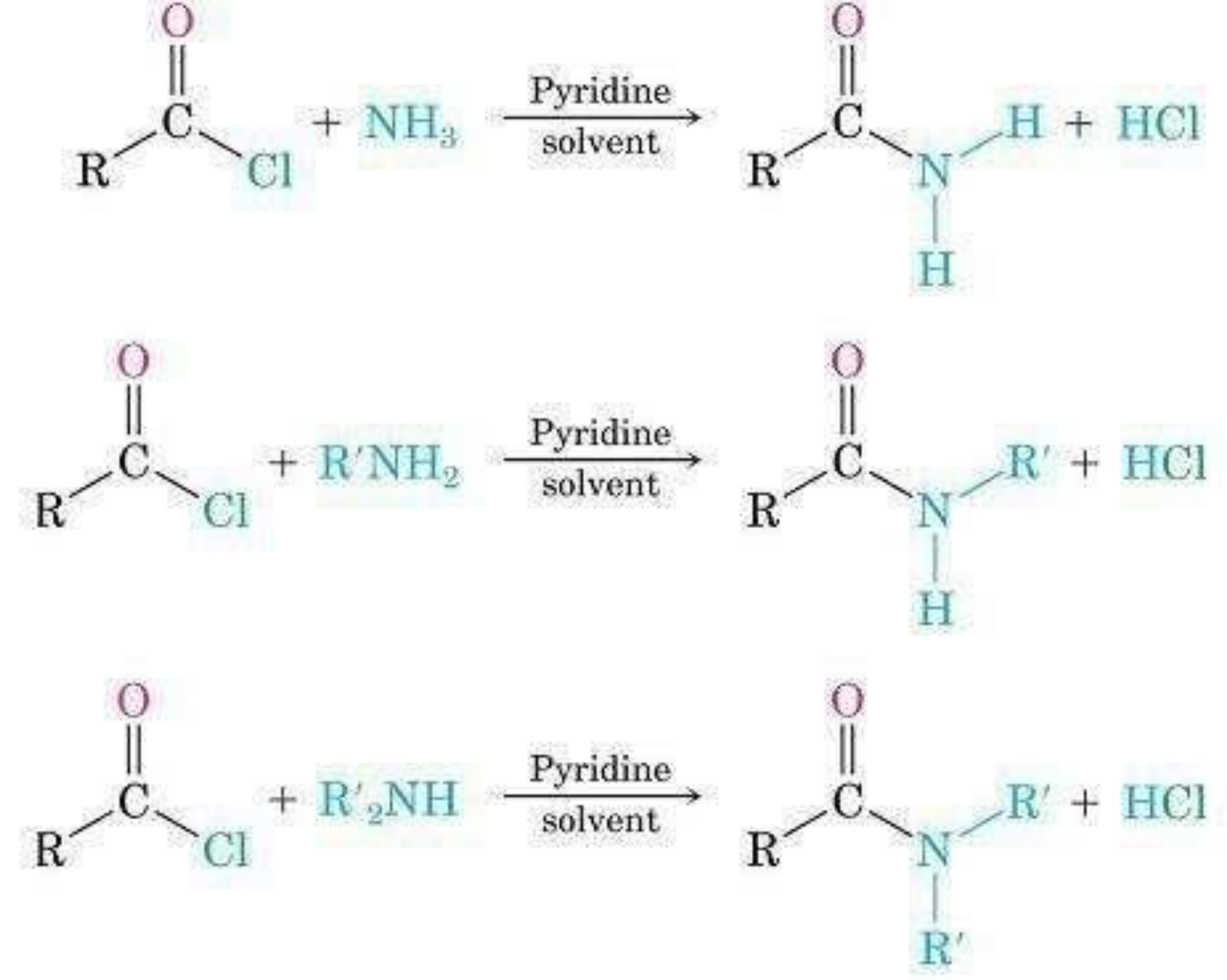


$$R-\ddot{N}H_2 + R'-CH_2-Br \longrightarrow R-\overset{+}{N}H_2-CH_2-R'\ {}^{-}Br$$

$$R-\overset{+}{N}H_2-CH_2-R'\ {}^{-}Br + R-\ddot{N}H_2 \rightleftarrows R-\ddot{N}H-CH_2-R' + R-\overset{+}{N}H_3\ {}^{-}Br$$

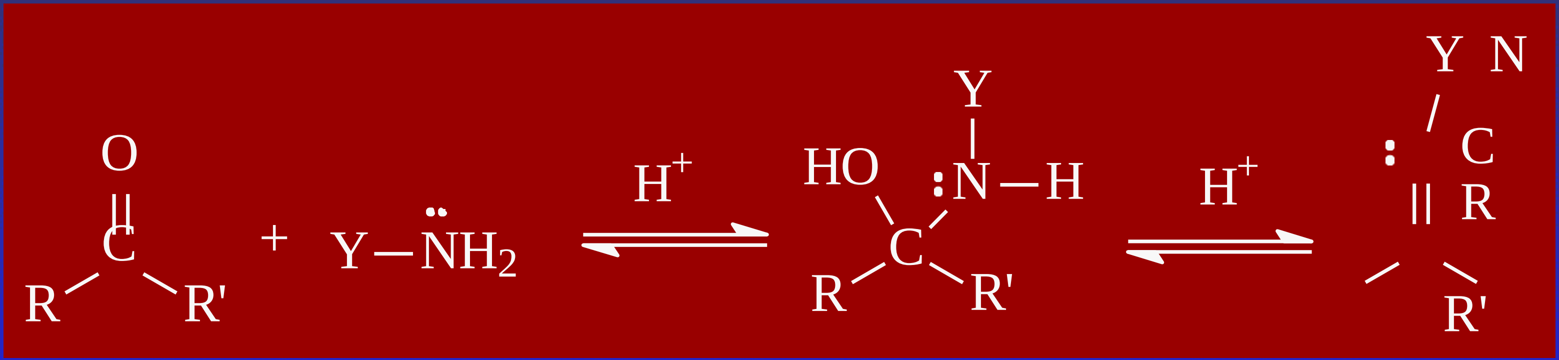
$$R-\ddot{N}H-CH_2-R' + R'-CH_2-Br \longrightarrow R-\underset{+}{\overset{\overset{CH_2-R'}{|}}{N}}H-CH-R'\ {}^{-}Br$$

Acylation of Amines by Acid



Reactions with C=O

Ammonia and primary amines react with carbonyls to give an imine (Schiff base).

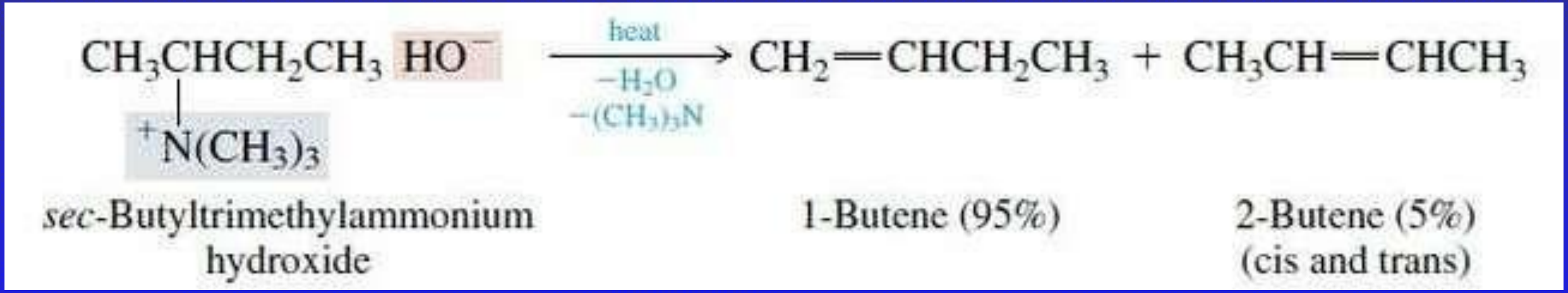


Y = H or alkyl gives an imine
Y = OH gives an oxime
Y = NHR gives a hydrazone

Hofmann Elimination

When quaternary ammonium hydroxides are heated, they undergo elimination to form an alkene and an amine. This reaction is known as the **Hofmann elimination.**

Elimination in alkyltrimethylammonium hydroxides proceeds in the direction that gives the *less* substituted alkene.



$$CH_3\underset{\underset{{}^+N(CH_3)_3}{|}}{C}HCH_2CH_3\ HO^- \xrightarrow[-H_2O \atop -(CH_3)_3N]{\text{heat}} CH_2{=}CHCH_2CH_3 + CH_3CH{=}CHCH_3$$

sec-Butyltrimethylammonium hydroxide

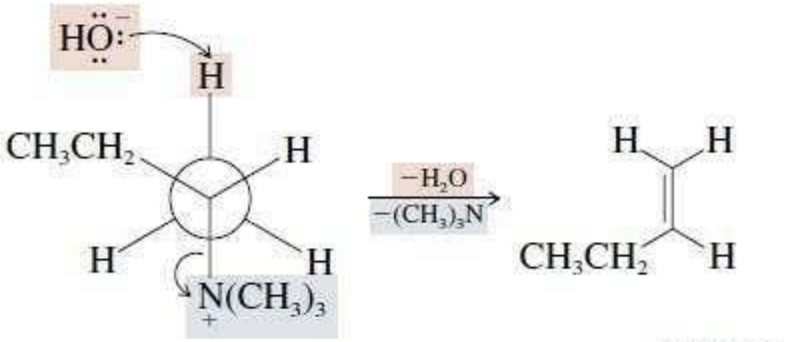
1-Butene (95%)

2-Butene (5%) (cis and trans)

Hofmann elimination is opposite to that predicted by the Zaitsev rule. Elimination reactions of alkyltrimethylammonium hydroxides are said to obey the **Hofmann rule;** they yield the less substituted alkene.

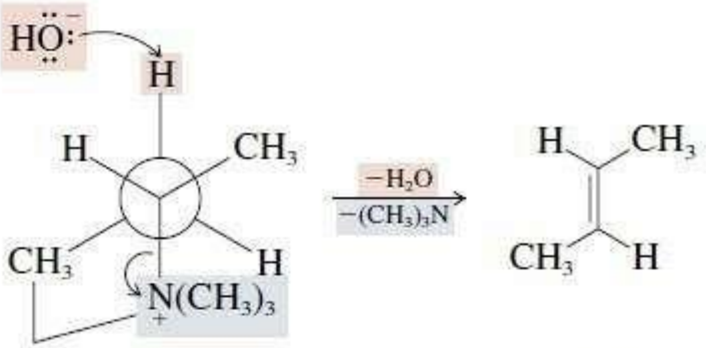
E2 transition state requires an anti relationship between the proton that is removed and the trimethylammonio group. The least sterically hindered hydrogen is removed by the base in Hofmann elimination Reactions.

(*a*) *Less crowded:* Conformation leading to 1-butene by anti elimination:



1-Butene
(major product)

(*b*) *More crowded:* Conformation leading to *trans*-2-butene by anti elimination:



These two groups
crowd each other

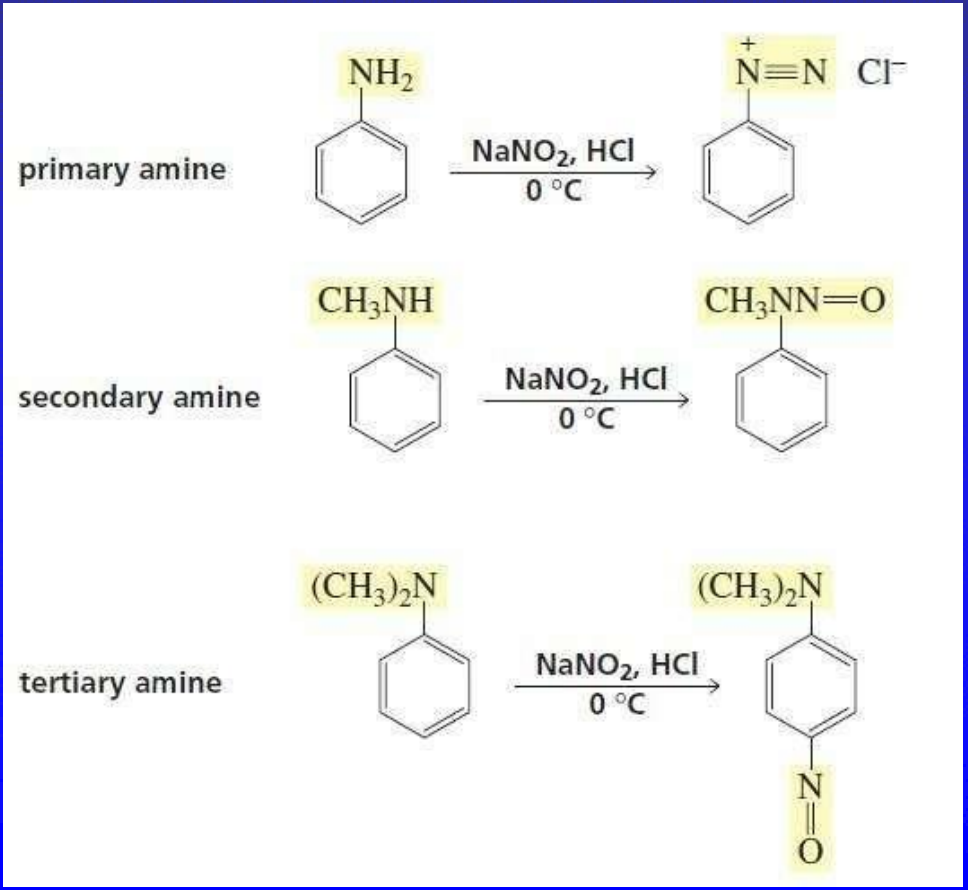
trans-2-Butene
(minor product)

Reactions of amines with nitrous acid

1° Amines form diazonium salts, R-N$^+$≡N. Alkyldiazonium salts are unstable, but arenediazonium salts are widely used for synthesis.

2° Amines form *N*-nitrosoamines, $R_2N-N=O$, found to cause cancer in laboratory animals.

3° Amines electrophilic aromatic substitution by nitrosyl cation takes place with *N*,*N*-dialkylarylamines.



Distinction between primary, secondary and tertiary amines

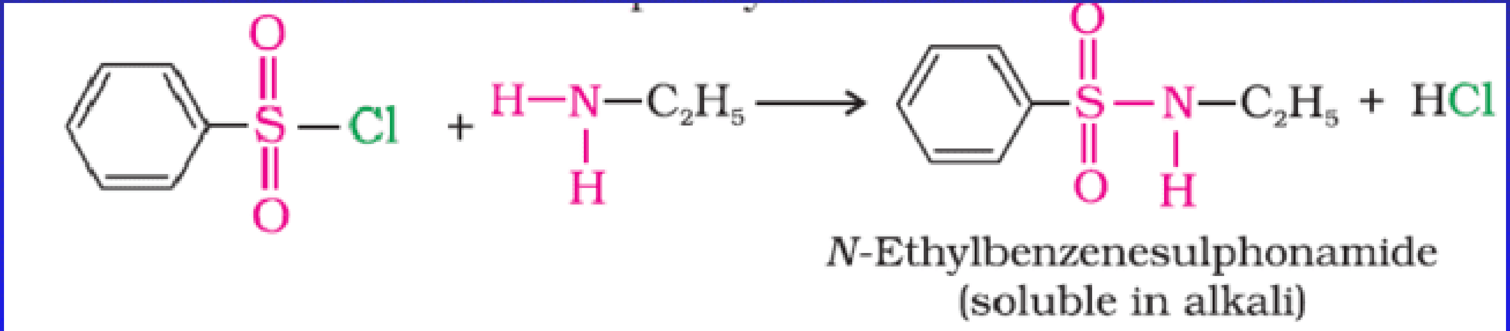
Carbyl amine test: primary amine is warmed with chloroform and alcoholic potash, an alkyl isocyanide(carbyl amine is formed which gives a offensive smell. Secondary and tertiary amine don’t give this reaction.

$$\mathrm{R-NH_2 + CHCl_3 + 3KOH(alc.)} \downarrow\downarrow^{\Delta}\rightarrow \mathrm{R-N}\overset{\rightarrow}{=} + \mathrm{3KCl + 3H_2O}$$

Hinsberg’s reagent

Benzenesulphonyl chloride which is also known as Hinsberg’s reagent, reacts with primary and secondary amines to form sulphonamides.

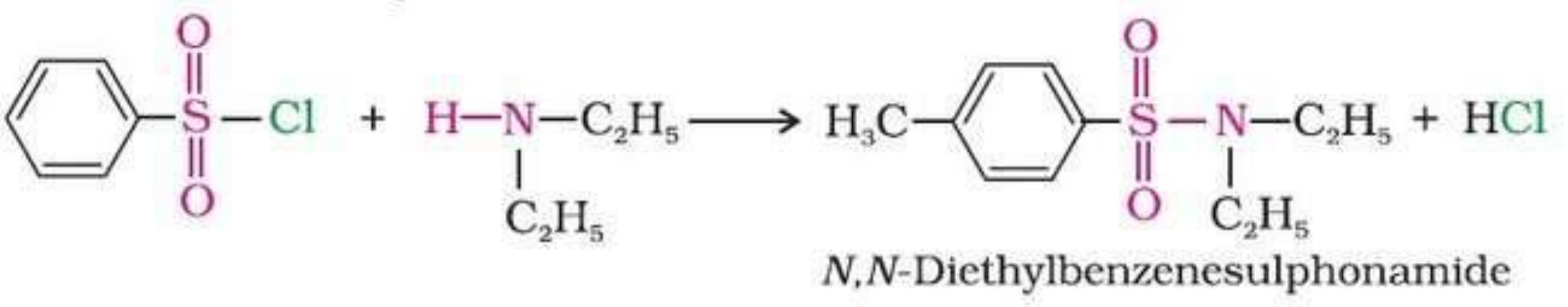
(a) The reaction of benzenesulphonyl chloride with primary amine yields N-ethylbenzenesulphonyl amide.



N-Ethylbenzenesulphonamide
(soluble in alkali)

The hydrogen attached to nitrogen in sulphonamide is strongly acidic due to the presence of strong electron withdrawing sulphonyl group. Hence, it is soluble in alkali.

(b) In the reaction with secondary amine, N,N diethylbenzene sulphonamide is formed.



N,N-Diethylbenzenesulphonamide

Since N, N-diethylbenzene sulphonamide does not contain any hydrogen atom attached to nitrogen atom, it is not acidic and hence insoluble in alkali.

(c) Tertiary amines do not react with benzenesulphonyl chloride. This property of amines reacting with benzenesulphonyl chloride in a different manner is used for the distinction of primary, secondary and tertiary amines and also for the separation of a mixture of amines.