

# **ELECTROPHILIC AROMATIC SUBSTITUTION**

**By Doctoral Students**

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- **Background**
- **General Mechanism**
- **EAS**

- Halogenation
- Nitration
- Sulfonation
- Friedel Crafts-acylation
- Friedel Crafts-alkylation

- **Directing groups**

- Ortho, Para, Meta directing groups



## Background

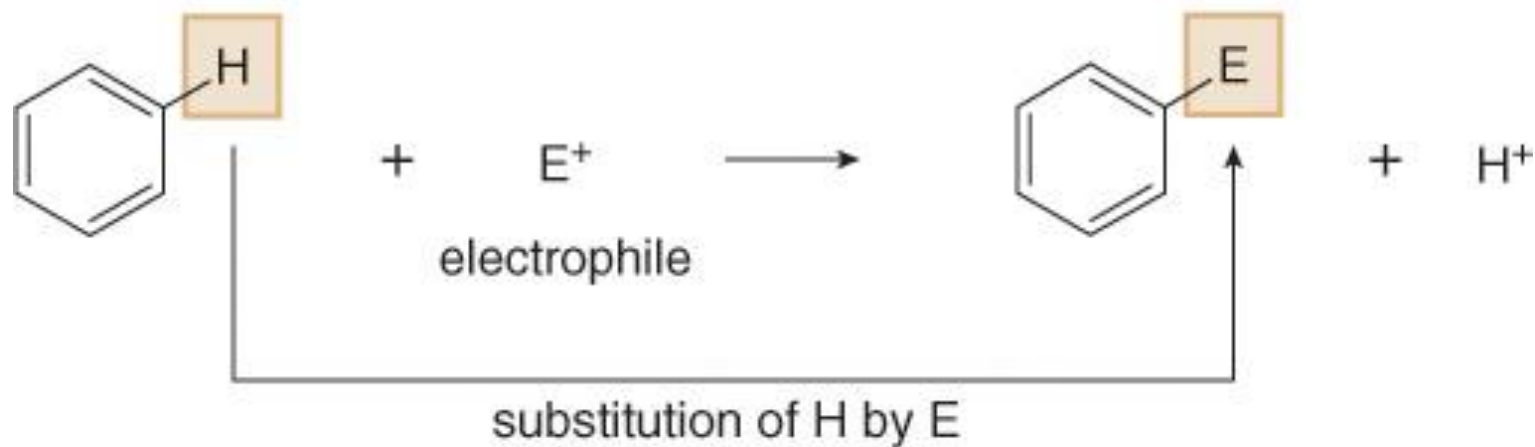


- **EAS**
- **E**lectrophilic **A**romatic **S**ubstitution
  - Electrophilic : Electron loving ( +,  $\delta+$ )
  - Aromatic : ( Cyclic , planar, conjugated, following Hackle's rule)  $\longrightarrow$  Benzene
  - Substitution : Replacement of a proton with E group.

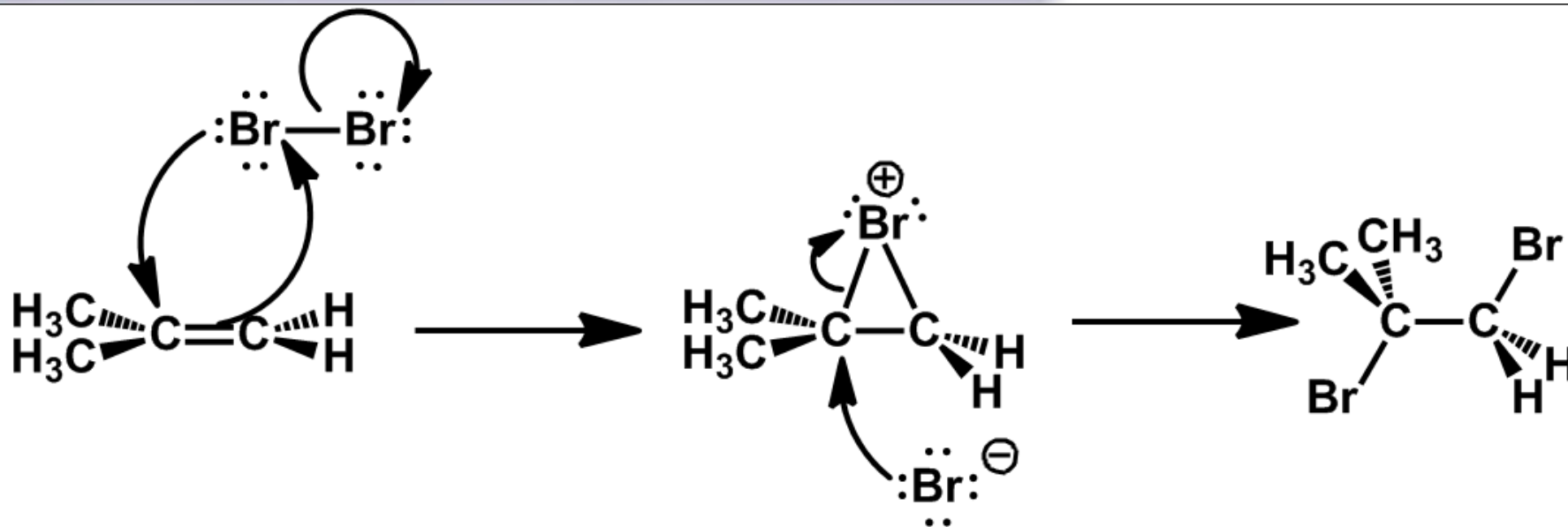
# General reaction



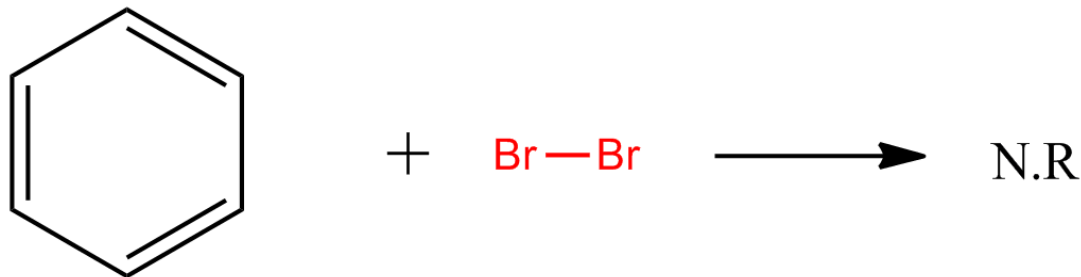
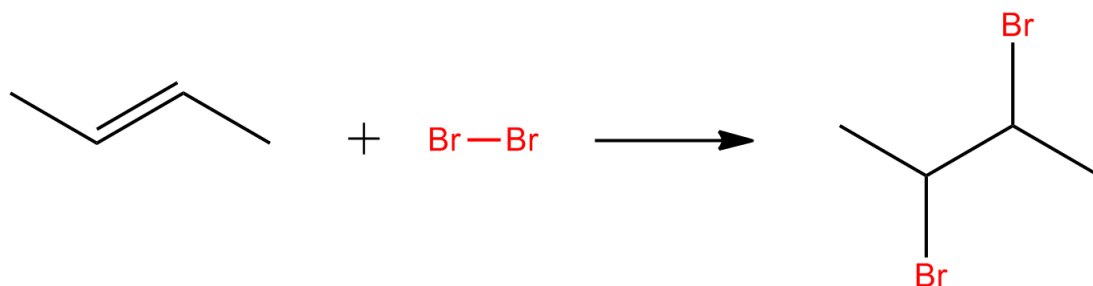
## Electrophilic aromatic substitution—General reaction



## Why Substitution Not addition?



## Why Substitution Not addition?



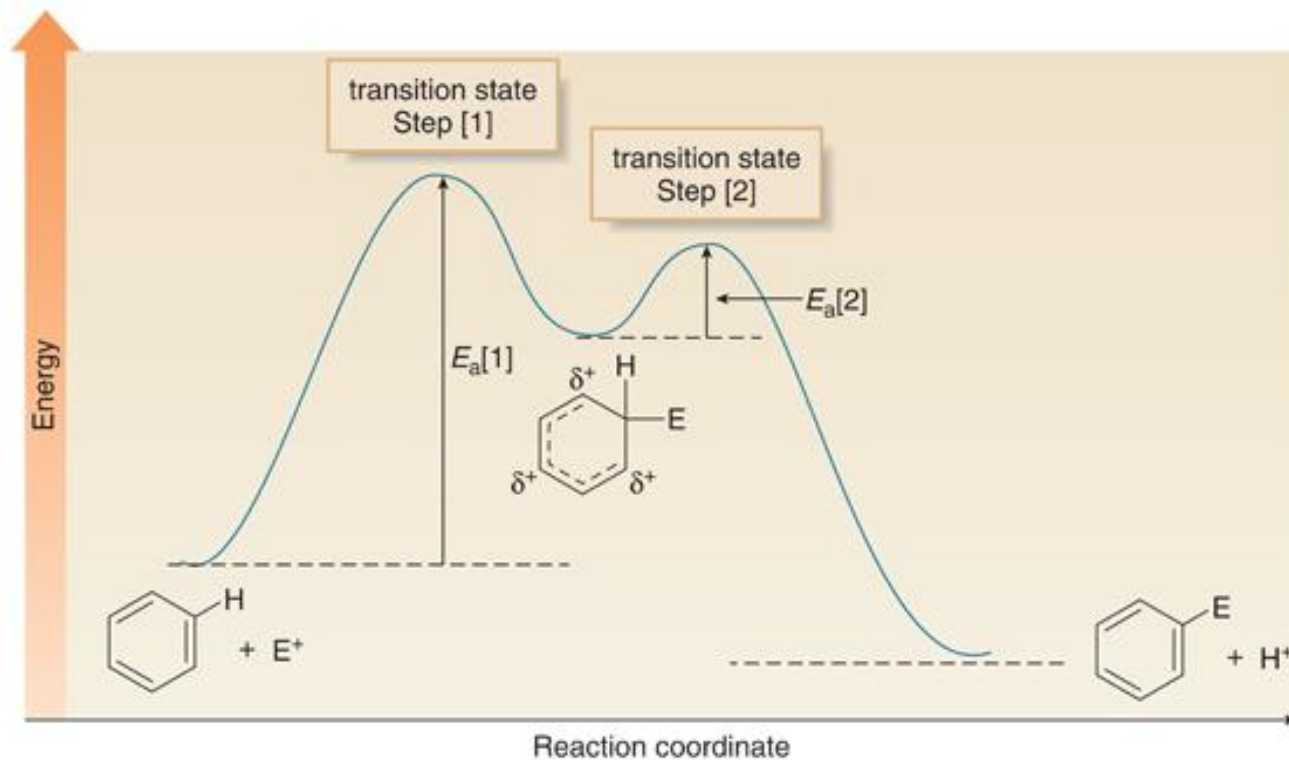
The Pi Bonds are far more stable in Benzene than in alkene ( **Resonance effect** )





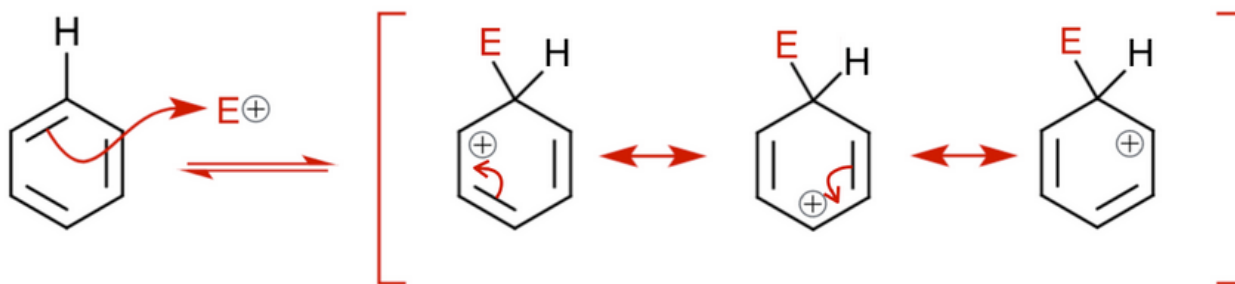
**Figure 18.2** Energy diagram for electrophilic aromatic substitution:  $\text{PhH} + \text{E}^+ \rightarrow \text{PhE} + \text{H}^+$

- The mechanism has two steps so there are two energy barriers.
- Step [1] is rate-determining; its transition state is at higher energy.

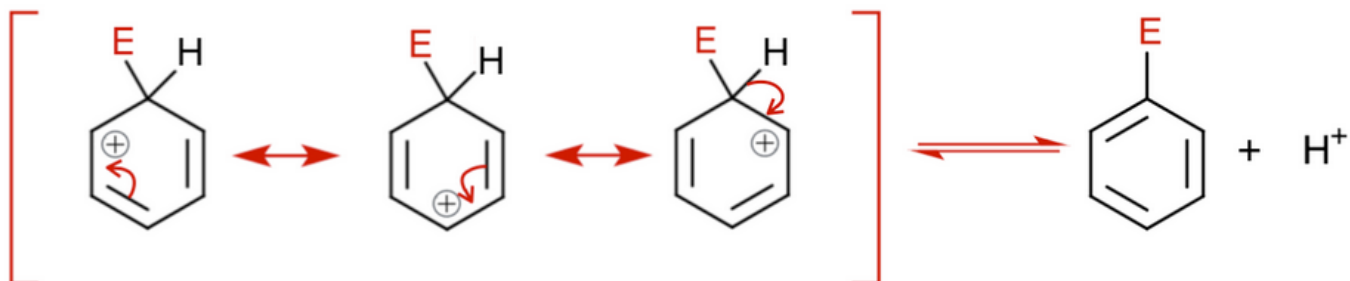


# General Mechanism

## Step 1: Electrophilic Attack



## Step 2: Proton Loss



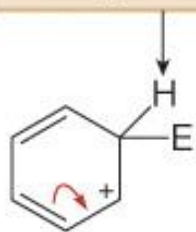


# General Mechanism

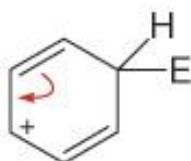


- ◆ Always draw in the H atom on the carbon bonded to E. This serves as a reminder that it is the only  $sp^3$  hybridized carbon in the carbocation intermediate.
- ◆ Notice that the positive charge in a given resonance structure is always located ortho or para to the new C–E bond. In the hybrid, therefore, the charge is delocalized over three atoms of the ring.

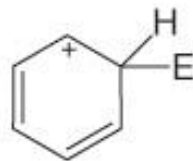
Always draw in the H atom at the site of electrophilic attack.



(+) ortho to E

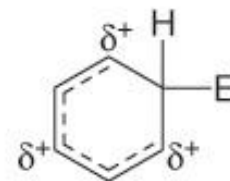


(+) para to E



(+) ortho to E

The hybrid

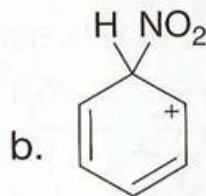
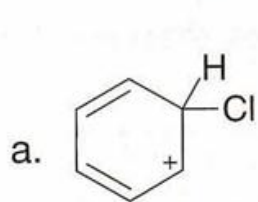


# Homework

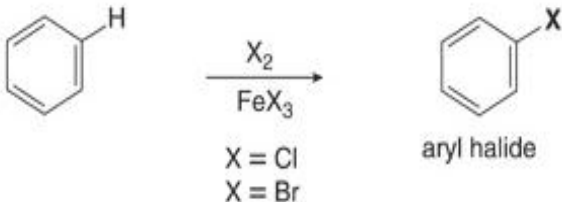
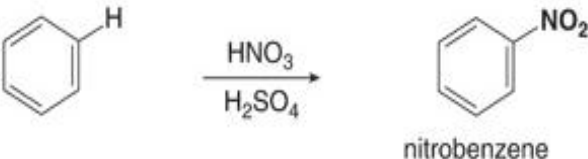
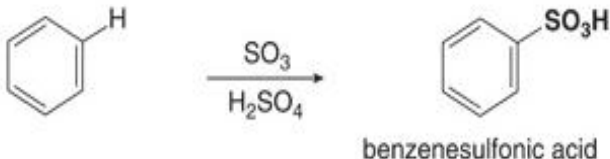
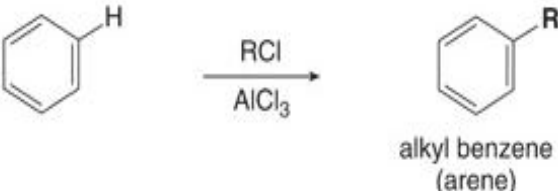
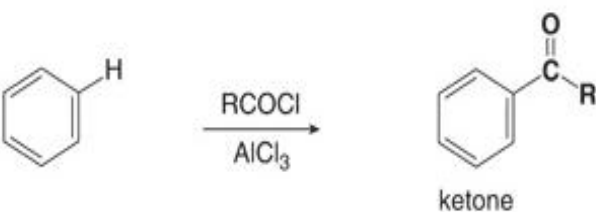


Why is benzene less reactive towards electrophiles than an alkene, even though it has more  $\pi$  electrons than an alkene (six versus two)?

Draw two more resonance structures for each cation.



**Figure 18.1** Five examples of electrophilic aromatic substitution

Reaction	Electrophile
<p><b>[1] Halogenation—Replacement of H by X (Cl or Br)</b></p>  <p style="text-align: center;">X = Cl X = Br</p> <p style="text-align: center;">aryl halide</p>	$E^+ = \text{Cl}^+ \text{ or } \text{Br}^+$
<p><b>[2] Nitration—Replacement of H by NO<sub>2</sub></b></p>  <p style="text-align: center;">nitrobenzene</p>	$E^+ = \text{NO}_2^+$
<p><b>[3] Sulfonation—Replacement of H by SO<sub>3</sub>H</b></p>  <p style="text-align: center;">benzenesulfonic acid</p>	$E^+ = \text{SO}_3\text{H}^+$
<p><b>[4] Friedel–Crafts alkylation—Replacement of H by R</b></p>  <p style="text-align: center;">alkyl benzene (arene)</p>	$E^+ = \text{R}^+$
<p><b>[5] Friedel–Crafts acylation—Replacement of H by RCO</b></p>  <p style="text-align: center;">ketone</p>	$E^+ = \text{RCO}^+$

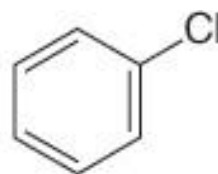
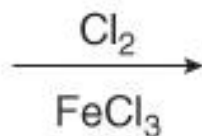
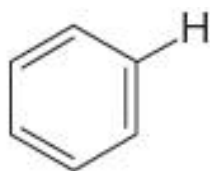
Friedel–Crafts alkylation and acylation, named for Charles Friedel and James Crafts who discovered the reactions in the nineteenth century, form new carbon–carbon bonds.

# Halogenation



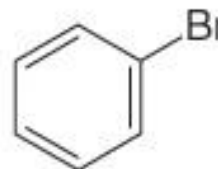
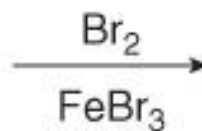
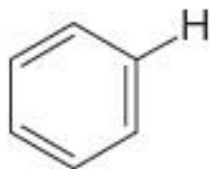
- ❖ In halogenation, benzene reacts with  $\text{Cl}_2$  or  $\text{Br}_2$  in the presence of a Lewis acid catalyst, such as  $\text{FeCl}_3$  or  $\text{FeBr}_3$ , to give the aryl halides chlorobenzene or bromobenzene respectively.
- ❖ Analogous reactions with  $\text{I}_2$  and  $\text{F}_2$  are not synthetically useful because  $\text{I}_2$  is too unreactive and  $\text{F}_2$  reacts too violently.

## Chlorination



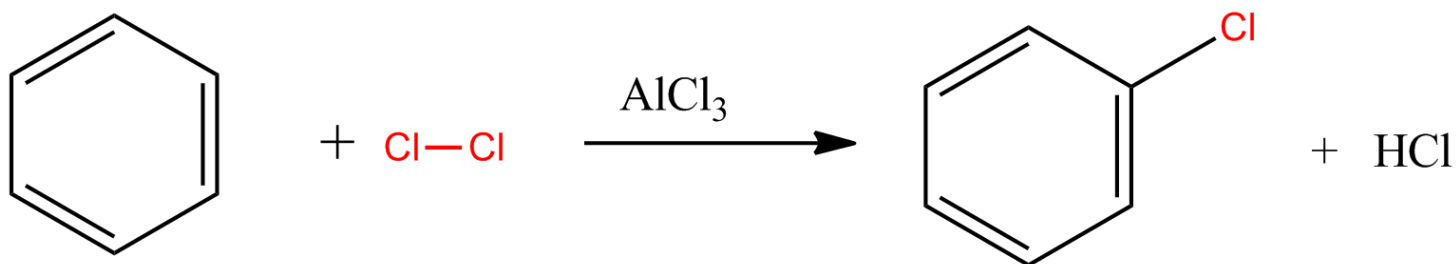
chlorobenzene

## Bromination



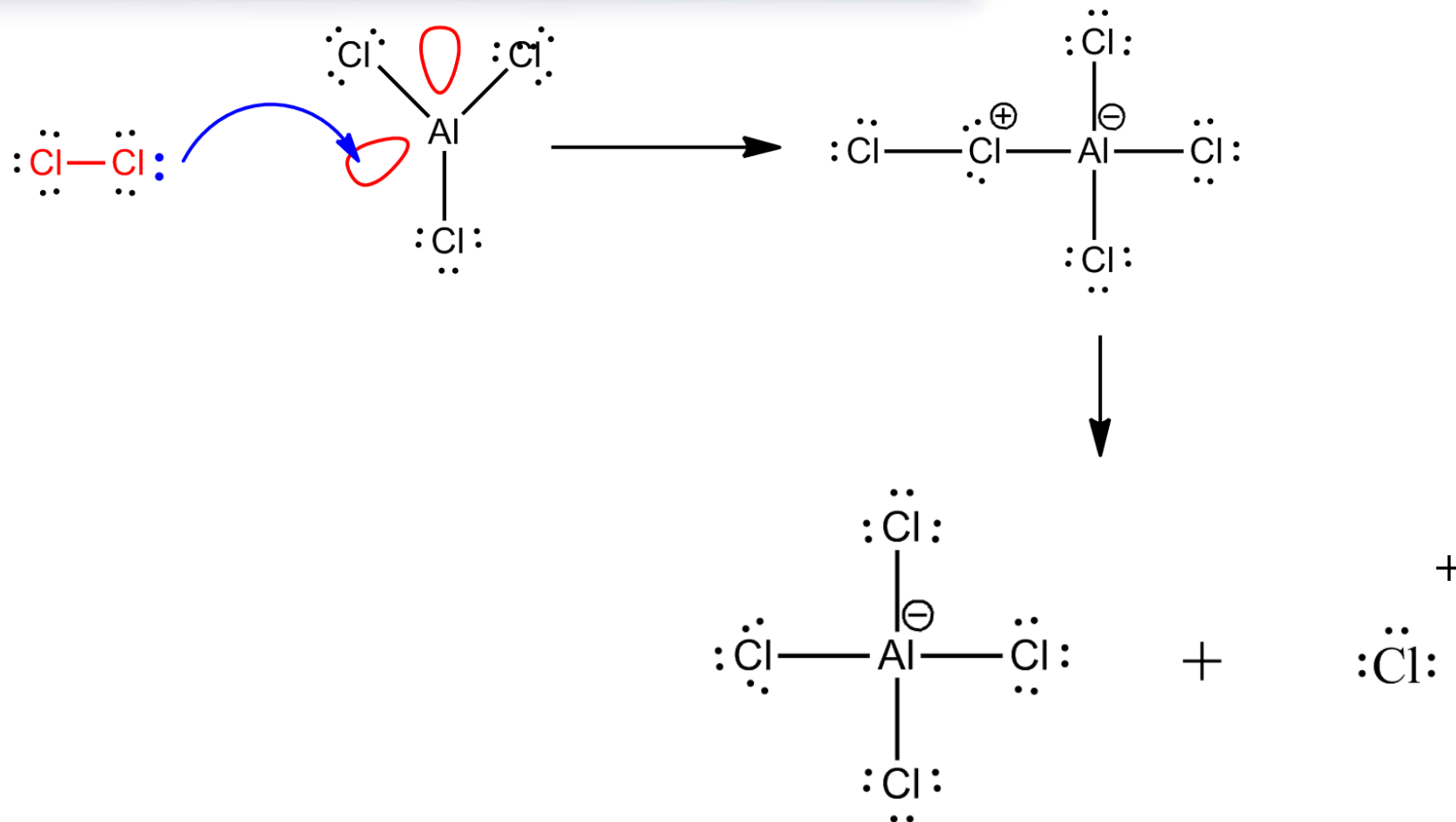
bromobenzene

# Halogenation Mechanism



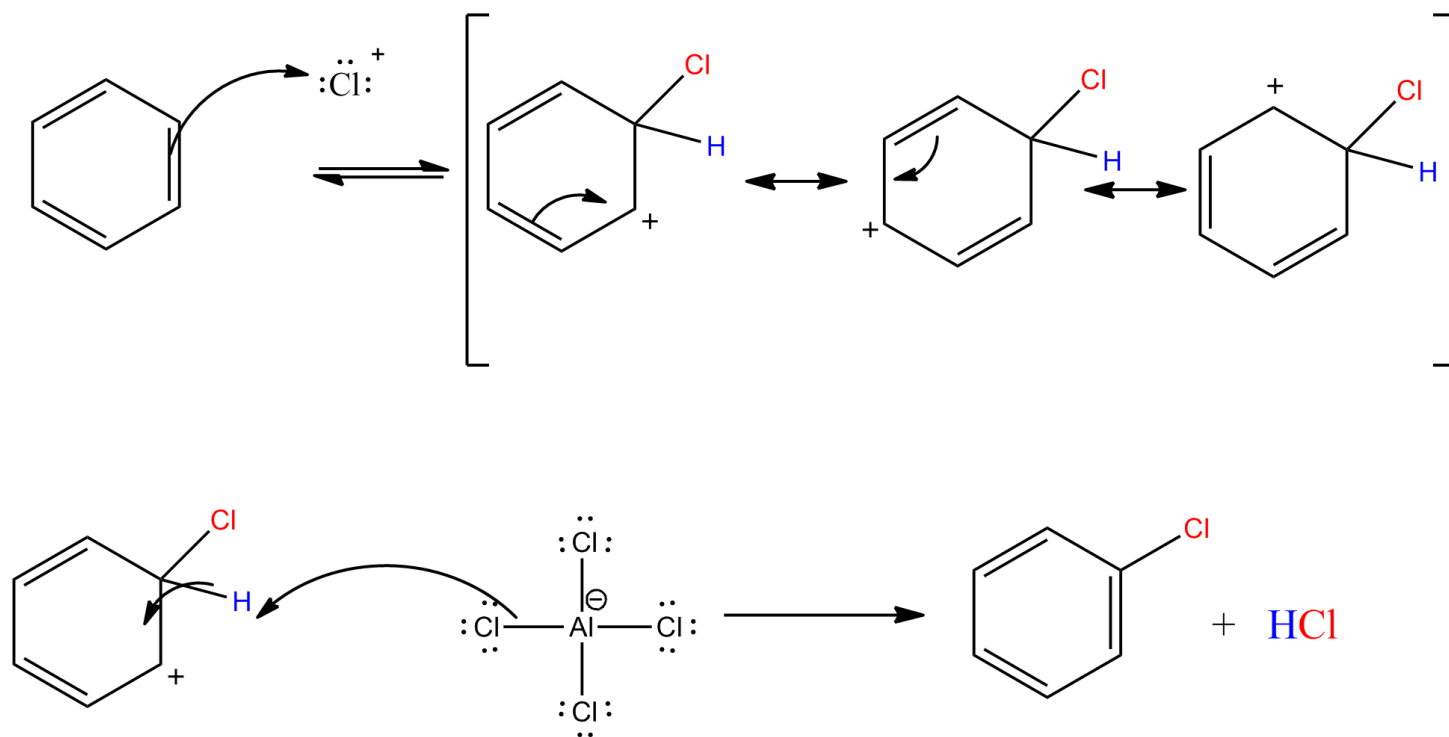


# Halogenation Mechanism





# Halogenation Mechanism



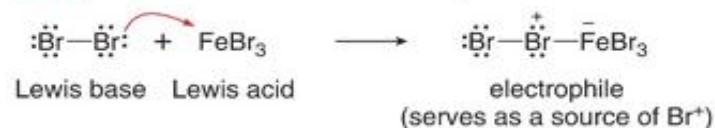
# Halogenation Mechanism



## MECHANISM 18.2

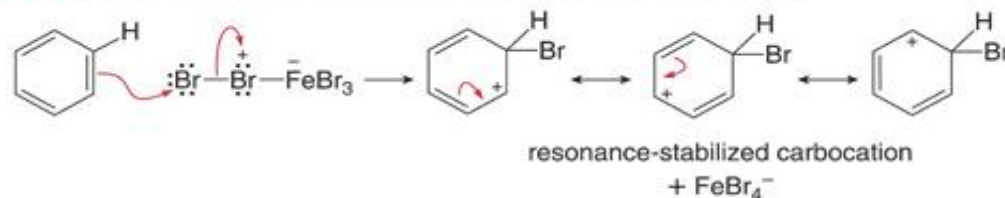
### Bromination of Benzene

#### Step [1] Generation of the electrophile



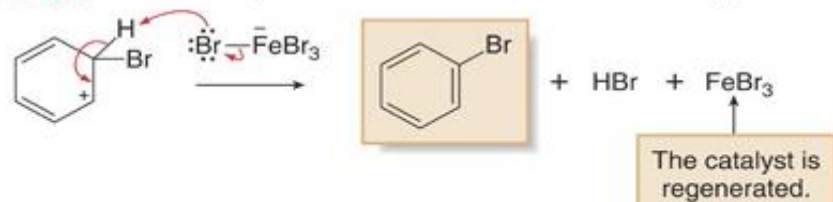
- ◆ Lewis acid–base reaction of  $\text{Br}_2$  with  $\text{FeBr}_3$  forms a species with a weakened and polarized  $\text{Br}-\text{Br}$  bond. This adduct serves as a source of  $\text{Br}^+$  in the next step.

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



- ◆ Addition of the electrophile forms a new  $\text{C}-\text{Br}$  bond and generates a carbocation. This carbocation intermediate is resonance stabilized—**three resonance structures can be drawn**.
- ◆ The  $\text{FeBr}_4^-$  also formed in this reaction is the base used in Step [3].

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



- ◆  $\text{FeBr}_4^-$  removes the proton from the carbon bearing the  $\text{Br}$ , thus re-forming the aromatic ring.
- ◆  $\text{FeBr}_3$ , a catalyst, is also regenerated for another reaction cycle.

# Homework

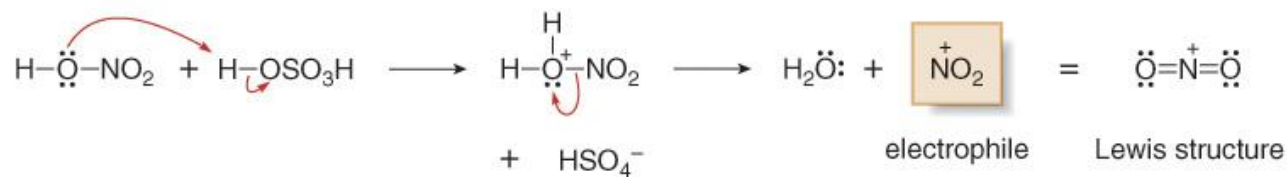


- 4 Draw a detailed mechanism for the chlorination of benzene using  $\text{Cl}_2$  and  $\text{FeCl}_3$ .

# Nitration and Sulfonation



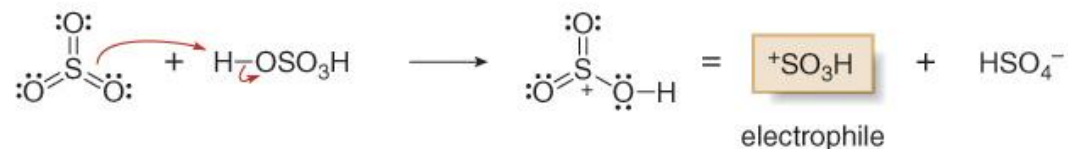
## Formation of the Nitronium Ion ( ${}^+\text{NO}_2$ ) for Nitration

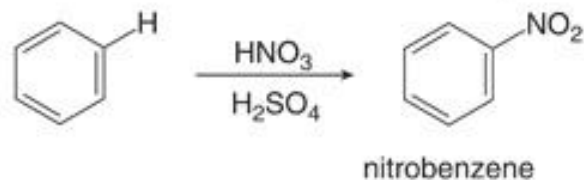


In **sulfonation**, protonation of sulfur trioxide,  $\text{SO}_3$ , forms a positively charged sulfur species ( ${}^+\text{SO}_3\text{H}$ ) that acts as an electrophile.



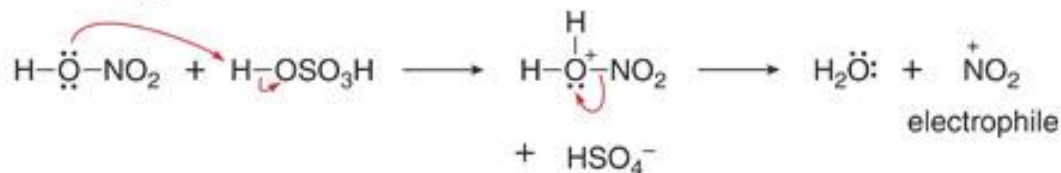
## Formation of the Electrophile ${}^+\text{SO}_3\text{H}$ for Sulfonation



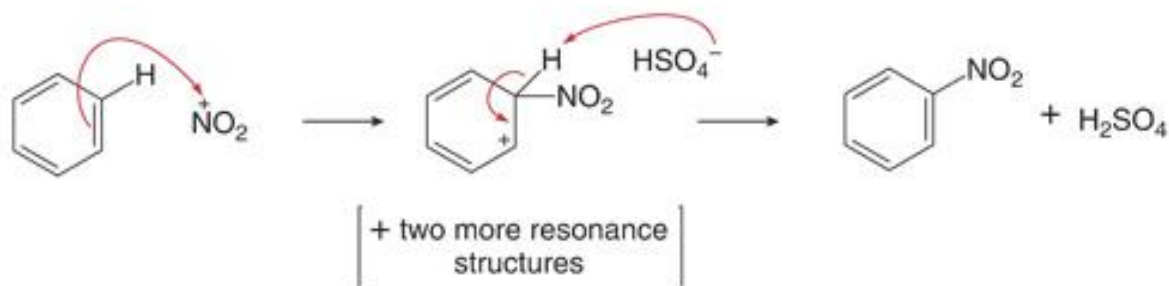
**SAMPLE PROBLEM 18.1** Draw a stepwise mechanism for the nitration of a benzene ring.**SOLUTION**

We must first generate the electrophile and then write the two-step mechanism for electrophilic aromatic substitution using it.

Generation of the electrophile  $^+\text{NO}_2$ :



Two-step mechanism for substitution:



Any species with a lone pair of electrons can be used to remove the proton in the last step. In this case, the mechanism is drawn with  $\text{HSO}_4^-$ , formed when  $^+\text{NO}_2$  is generated as the electrophile.

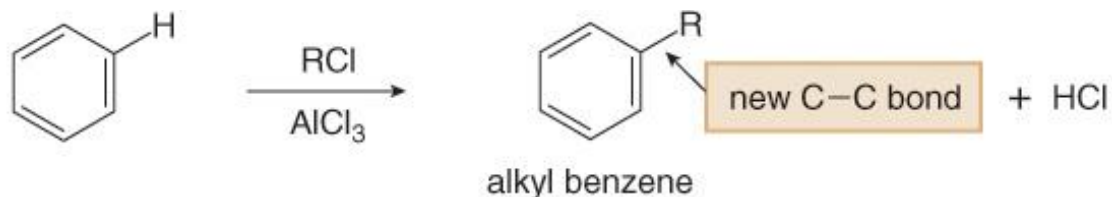
**PROBLEM 18.5** Draw a stepwise mechanism for the sulfonation of benzene with  $\text{SO}_3$  and  $\text{H}_2\text{SO}_4$ .



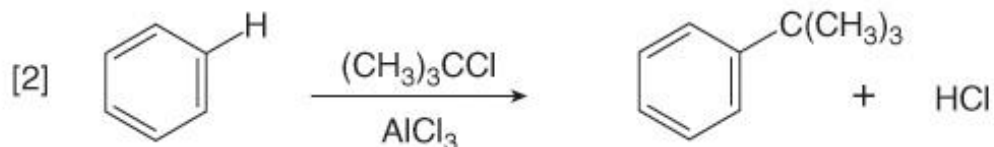
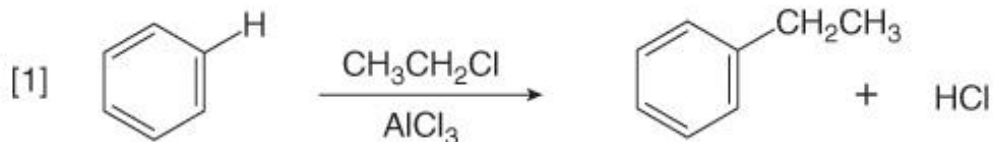
# Friedel Crafts-alkylation

- In Friedel-Crafts alkylation, treatment of benzene with an alkyl halide and a Lewis acid ( $\text{AlCl}_3$ ) forms an alkyl benzene.

## Friedel-Crafts alkylation— General reaction



## Examples

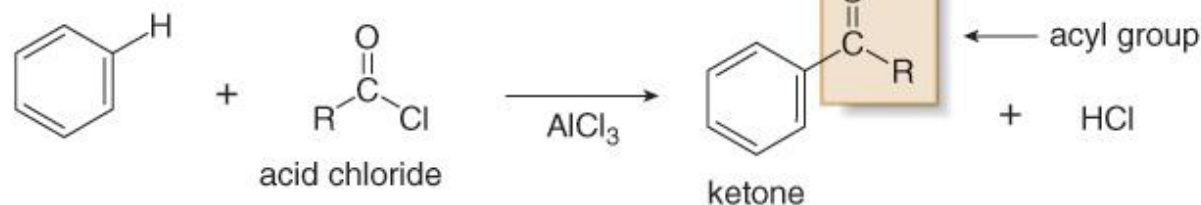




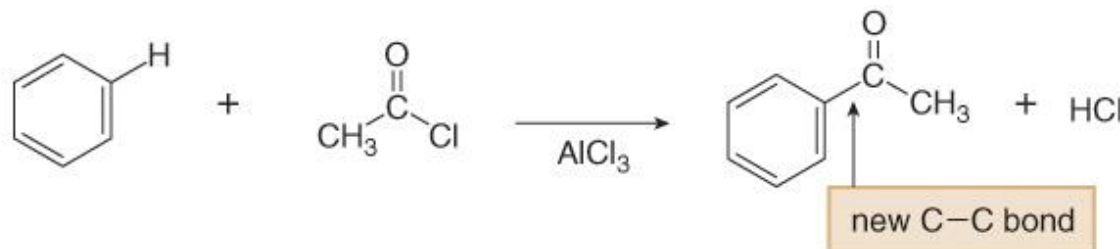
# Friedel Crafts-acylation

- ❖ In Friedel-Crafts acylation, a benzene ring is treated with an acid chloride ( $\text{RCOCl}$ ) and  $\text{AlCl}_3$  to form a ketone.
- ❖ Because the new group bonded to the benzene ring is called an acyl group, the transfer of an acyl group from one atom to another is an acylation.

## Friedel-Crafts acylation— General reaction



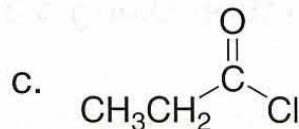
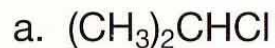
## Example



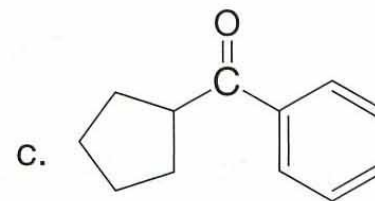
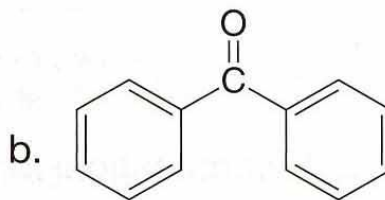
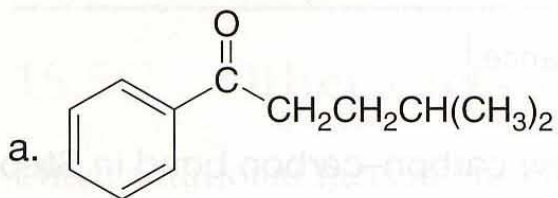
# Homework



- 6 What product is formed when benzene is treated with each organic halide in the presence of  $\text{AlCl}_3$ ?



- 7 What acid chloride would be needed to prepare each of the following ketones from benzene using a Friedel–Crafts acylation?

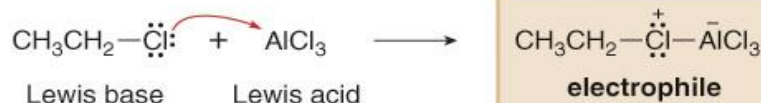


# Mechanism



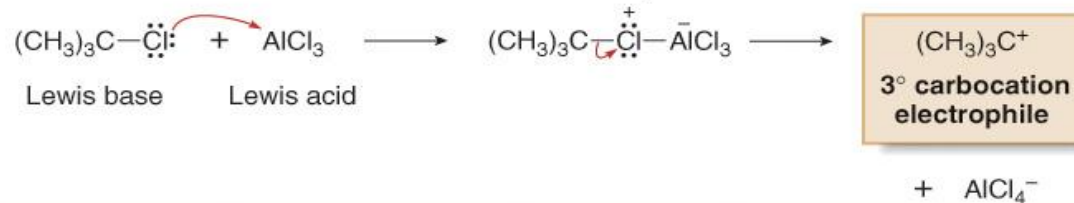
## Formation of the Electrophile in Friedel–Crafts Alkylation—Two Possibilities

For  $\text{CH}_3\text{Cl}$  and  $1^\circ \text{RCl}$ :



Lewis acid–base complex

For  $2^\circ$  and  $3^\circ \text{RCl}$ :



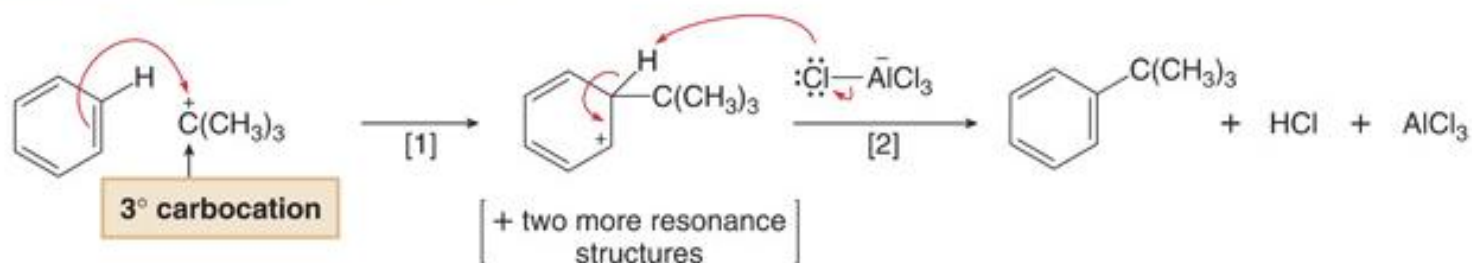
- ◆ For  $\text{CH}_3\text{Cl}$  and  $1^\circ \text{RCl}$ , the Lewis acid–base complex itself serves as the electrophile for electrophilic aromatic substitution.
- ◆ With  $2^\circ$  and  $3^\circ \text{RCl}$ , the Lewis acid–base complex reacts further to give a  $2^\circ$  or  $3^\circ$  carbocation, which serves as electrophile. Carbocation formation occurs only with  $2^\circ$  and  $3^\circ$  alkyl chlorides, because they afford more stable carbocations.

# Mechanism



## MECHANISM 18.3

### Friedel-Crafts Alkylation Using a 3° Carbocation



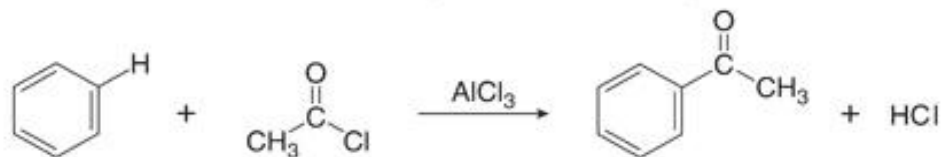
- ◆ Addition of the electrophile (a 3° carbocation) forms a new carbon-carbon bond in Step [1].
- ◆  $\text{AlCl}_4^-$  removes a proton on the carbon bearing the new substituent, thus re-forming the aromatic ring in Step [2].



# Mechanism

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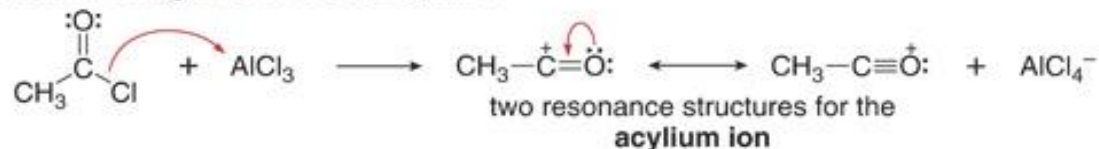
**SAMPLE PROBLEM 18.2** Draw a stepwise mechanism for the following Friedel–Crafts acylation.



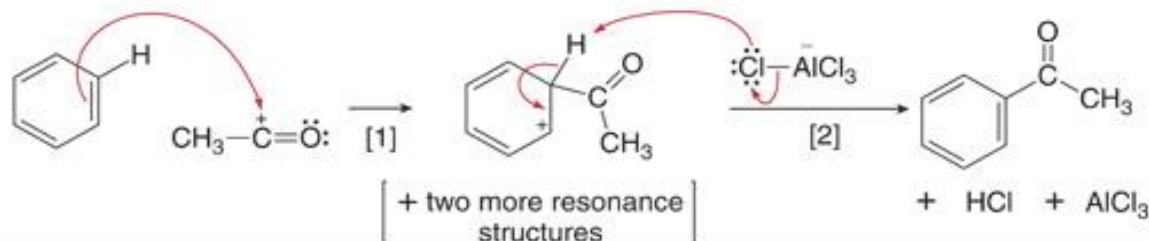
## SOLUTION

We must first generate the acylium ion, and then write the two-step mechanism for electrophilic aromatic substitution using it for the electrophile.

Generation of the electrophile ( $\text{CH}_3\text{CO}^+$ ):



Two-step mechanism for substitution:

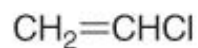


**PROBLEM 18.8** Draw a stepwise mechanism for the Friedel–Crafts alkylation of benzene with  $\text{CH}_3\text{CH}_2\text{Cl}$  and  $\text{AlCl}_3$ .

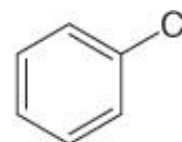
## Limitation in Friedel Crafts-alkylation

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

Unreactive halides in the  
Friedel–Crafts alkylation

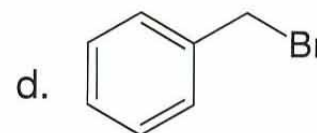
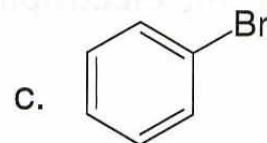
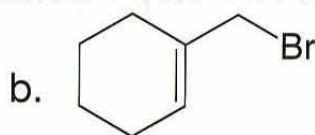
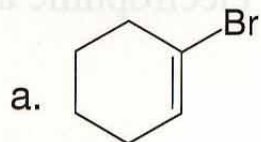


vinyl halide



aryl halide

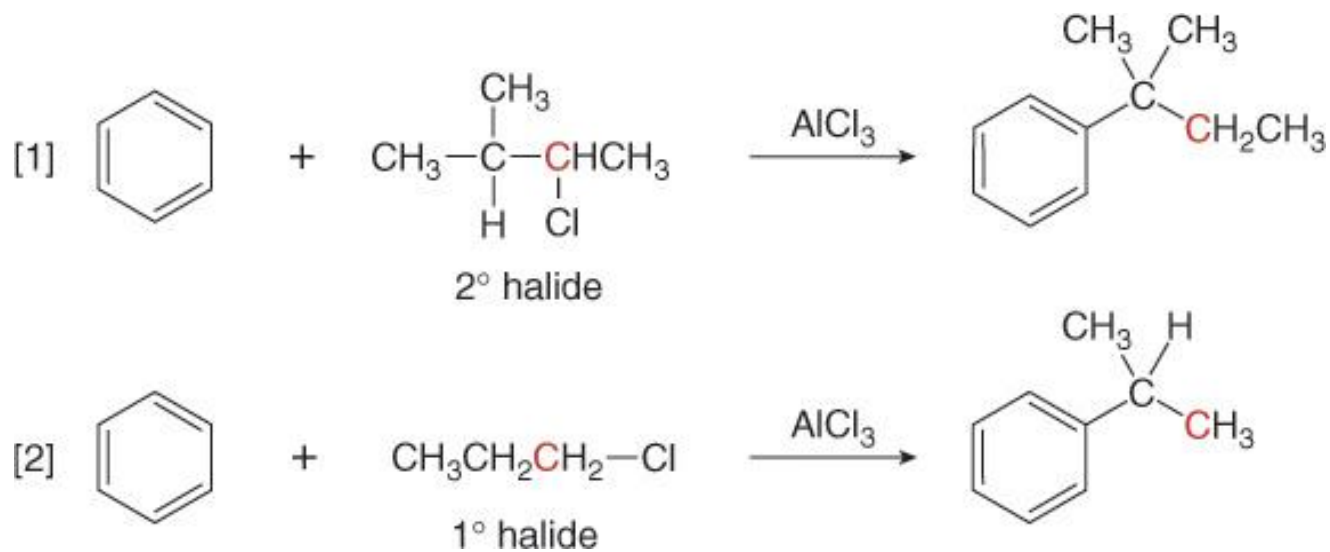
3.9 Which halides are unreactive in a Friedel–Crafts alkylation reaction?





## Limitation in Friedel Crafts-alkylation

[2] Rearrangements can occur.

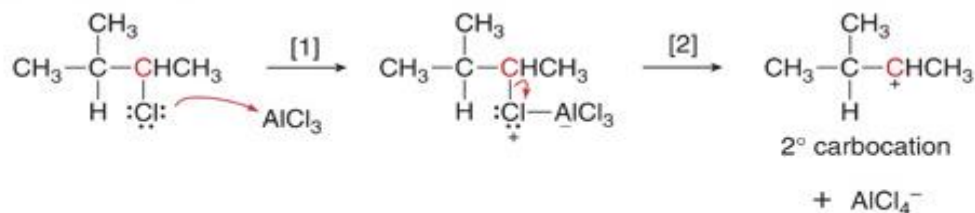




## MECHANISM 18.4

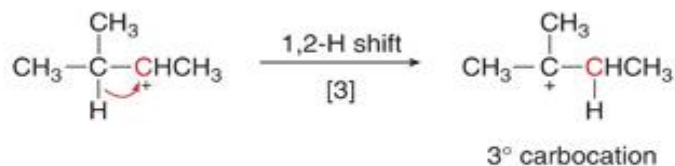
### Friedel-Crafts Alkylation Involving Carbocation Rearrangement

#### Steps [1] and [2] Formation of a 2° carbocation



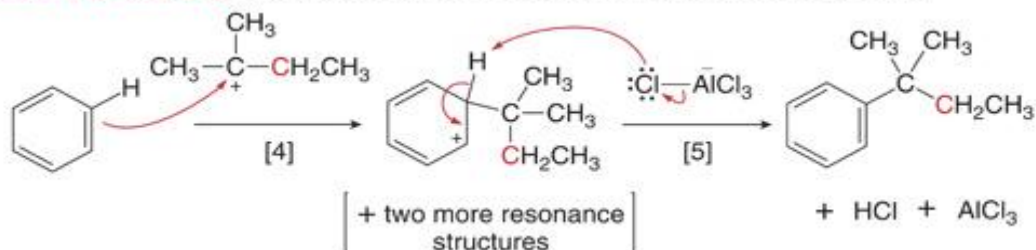
- Reaction of the alkyl chloride with  $\text{AlCl}_3$  forms a complex that decomposes in Step [2] to form a **2° carbocation**.

#### Step [3] Carbocation rearrangement



- 1,2-Hydride shift** converts the less stable 2° carbocation to a more stable 3° carbocation.

#### Steps [4] and [5] Addition of the carbocation and loss of a proton

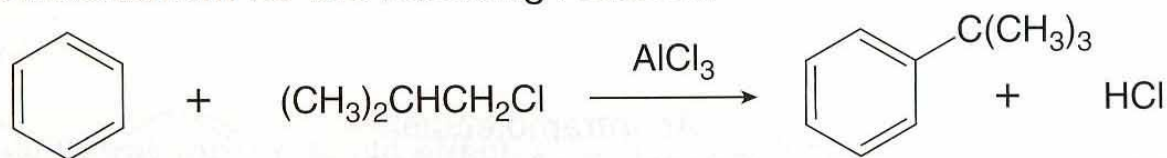


- Friedel-Crafts alkylation occurs by the usual two-step process: **addition of the carbocation** followed by **loss of a proton** to form the alkylated product.

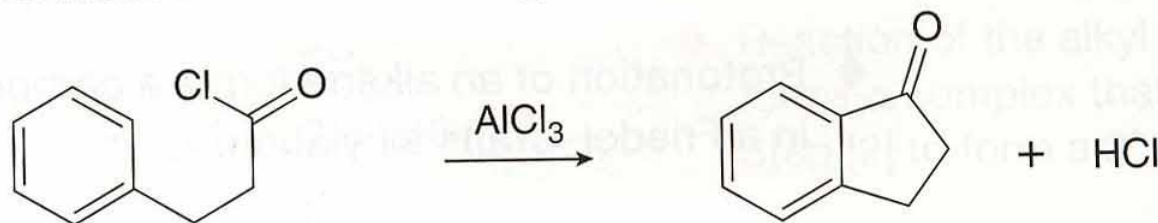
# Homework



- 10 Draw a stepwise mechanism for the following reaction.

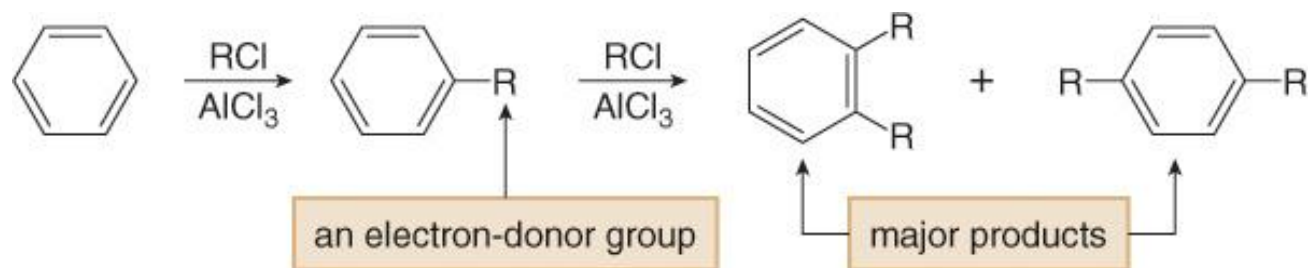


- 12 Draw a stepwise mechanism for the following intramolecular reaction.



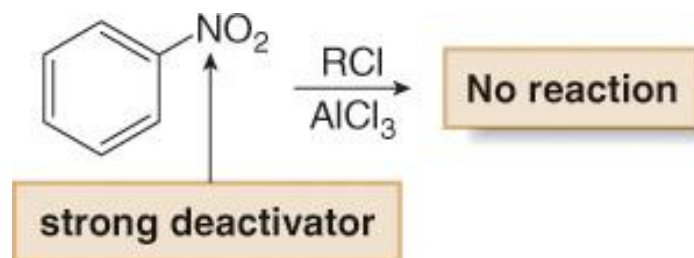
## Limitation in Friedel Crafts-alkylation

•Treatment of benzene with an alkyl halide and  $\text{AlCl}_3$  places an electron-donor R group on the ring. Since R groups activate the ring, the alkylated product ( $\text{C}_6\text{H}_5\text{R}$ ) is now more reactive than benzene itself towards further substitution, and it reacts again with  $\text{RCl}$  to give products of polyalkylation.



## Limitation in Friedel Crafts-alkylation

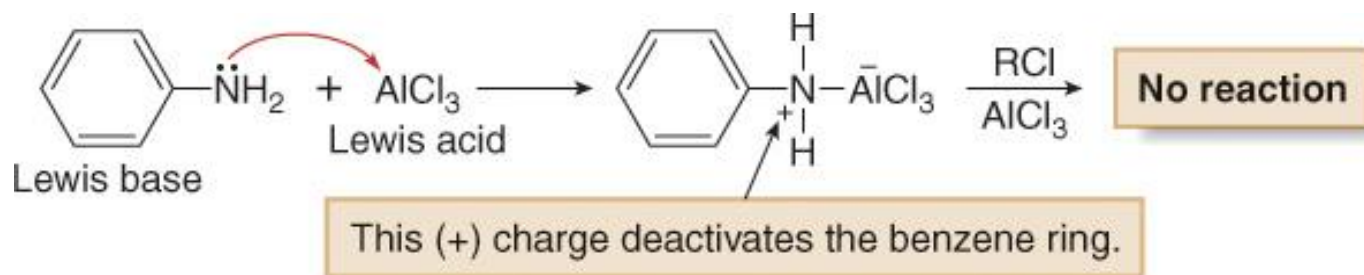
- A benzene ring deactivated by strong electron-withdrawing groups (i.e. any of the meta directors) is not electron rich enough to undergo Friedel-Crafts reactions.





## Limitation in Friedel Crafts-alkylation

•Friedel–Crafts reactions also do not occur with  $\text{NH}_2$  groups because the complex that forms between the  $\text{NH}_2$  group and the  $\text{AlCl}_3$  catalyst deactivates the ring towards Friedel–Crafts reactions.

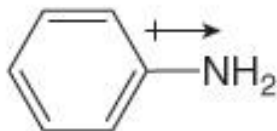




## Substituted Benzene (Directing Groups)

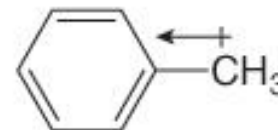
- ◆ Donation of electron density to the ring makes benzene more electron rich.
  - ◆ Withdrawal of electron density from the ring makes benzene less electron rich.
- 
- ◆ Atoms more electronegative than carbon—including N, O, and X—pull electron density away from carbon and thus exhibit an electron-withdrawing 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



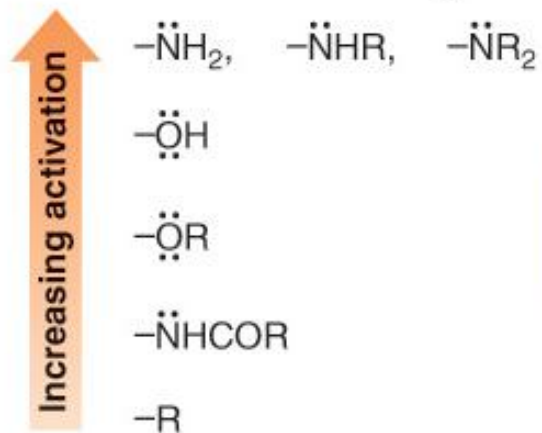
- Alkyl groups are **polarizable**, making them electron-donating groups.

# Directing Groups



## [1] ortho, para directors and activators

- ◆ Substituents that *activate* a benzene ring and direct substitution ortho and para.



General structure

$-\text{R}$  or  $-\text{Z:}$

# Directing Groups



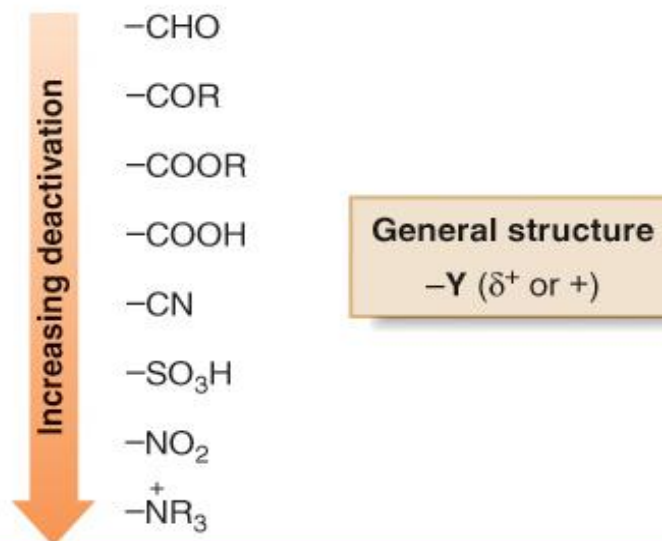
## [2] ortho, para deactivators

- ◆ Substituents that *deactivate* a benzene ring and direct substitution ortho and para.



## [3] meta directors

- ◆ Substituents that direct substitution meta.
- ◆ All meta directors *deactivate* the ring.

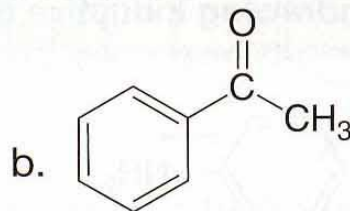
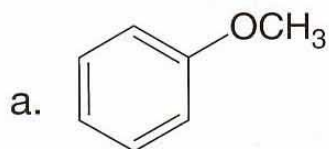


# Homework



**3.13** Which substituents have an electron-withdrawing and which have an electron-donating inductive effect: (a)  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2-$ ; (b)  $\text{Br}-$ ; (c)  $\text{CH}_3\text{CH}_2\text{O}-$ ?

**.14** Draw all resonance structures for each compound and use the resonance structures to determine if the substituent has an electron-donating or electron-withdrawing resonance effect.

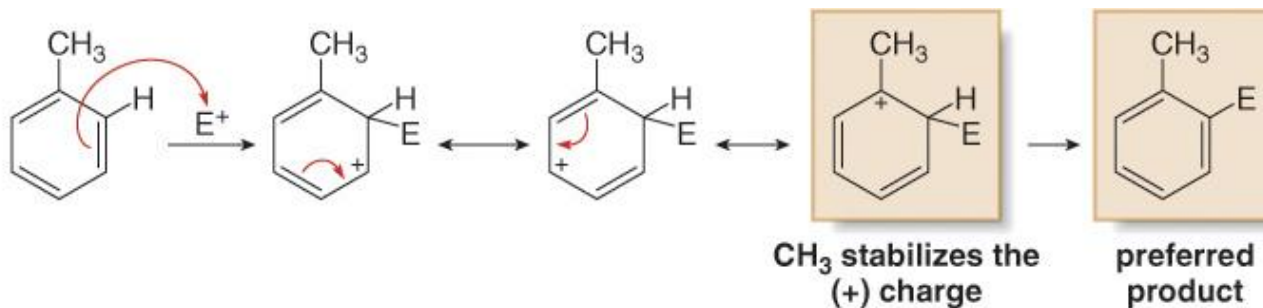




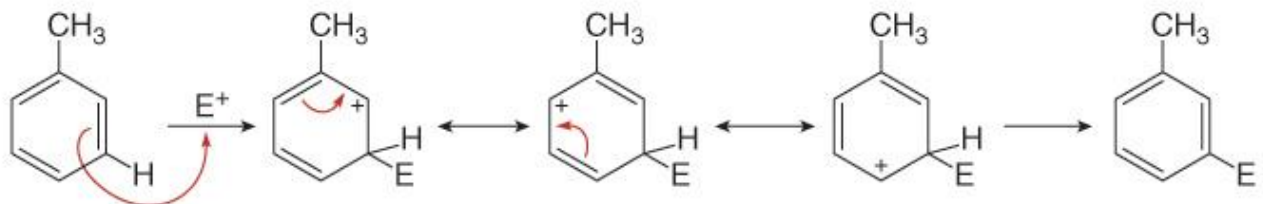
# Directing Groups



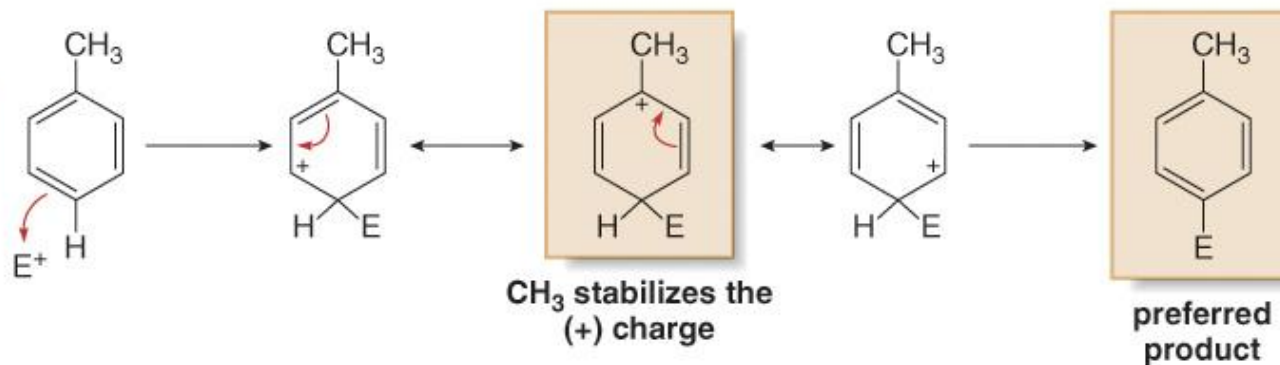
ortho  
attack



meta  
attack

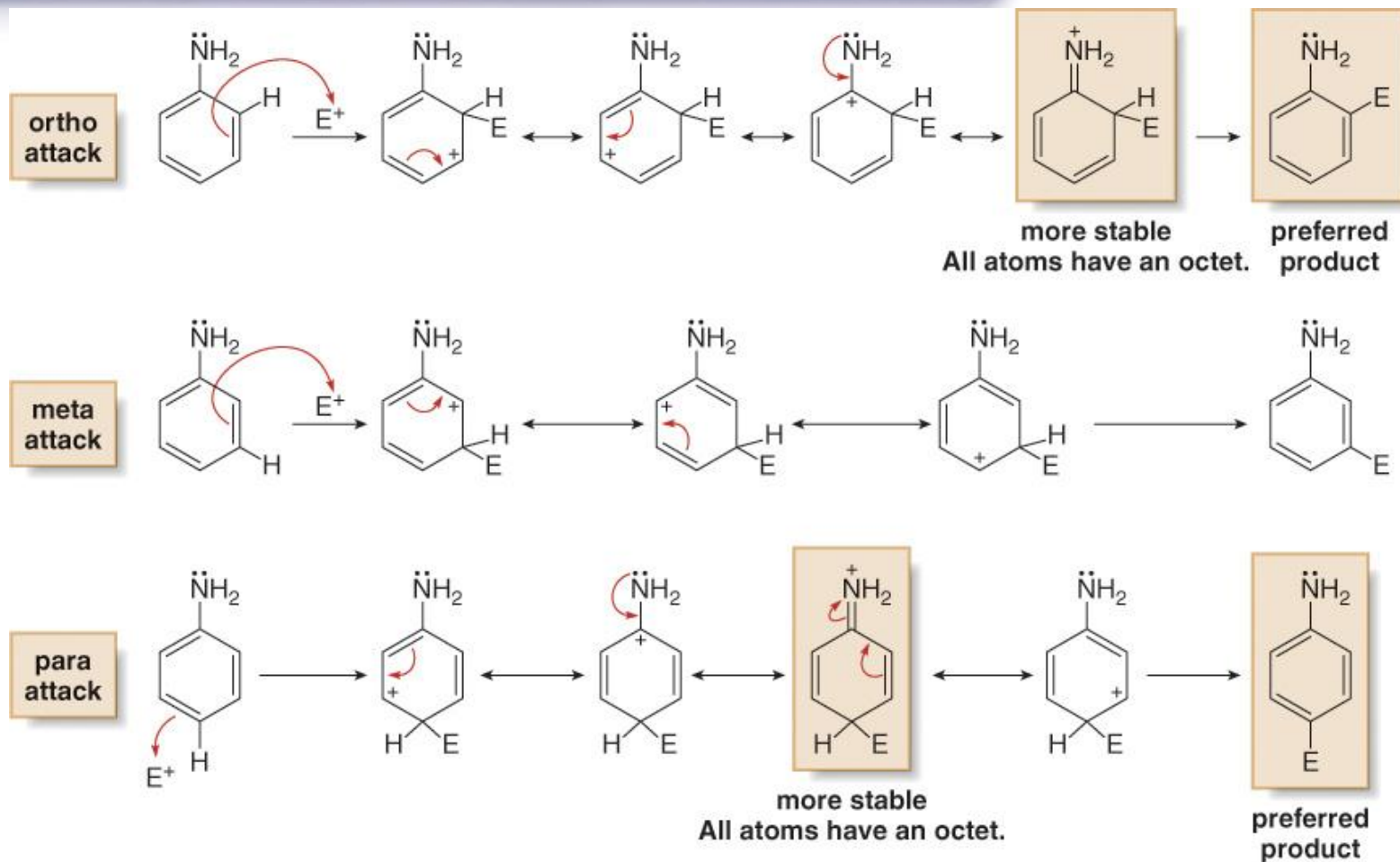


para  
attack

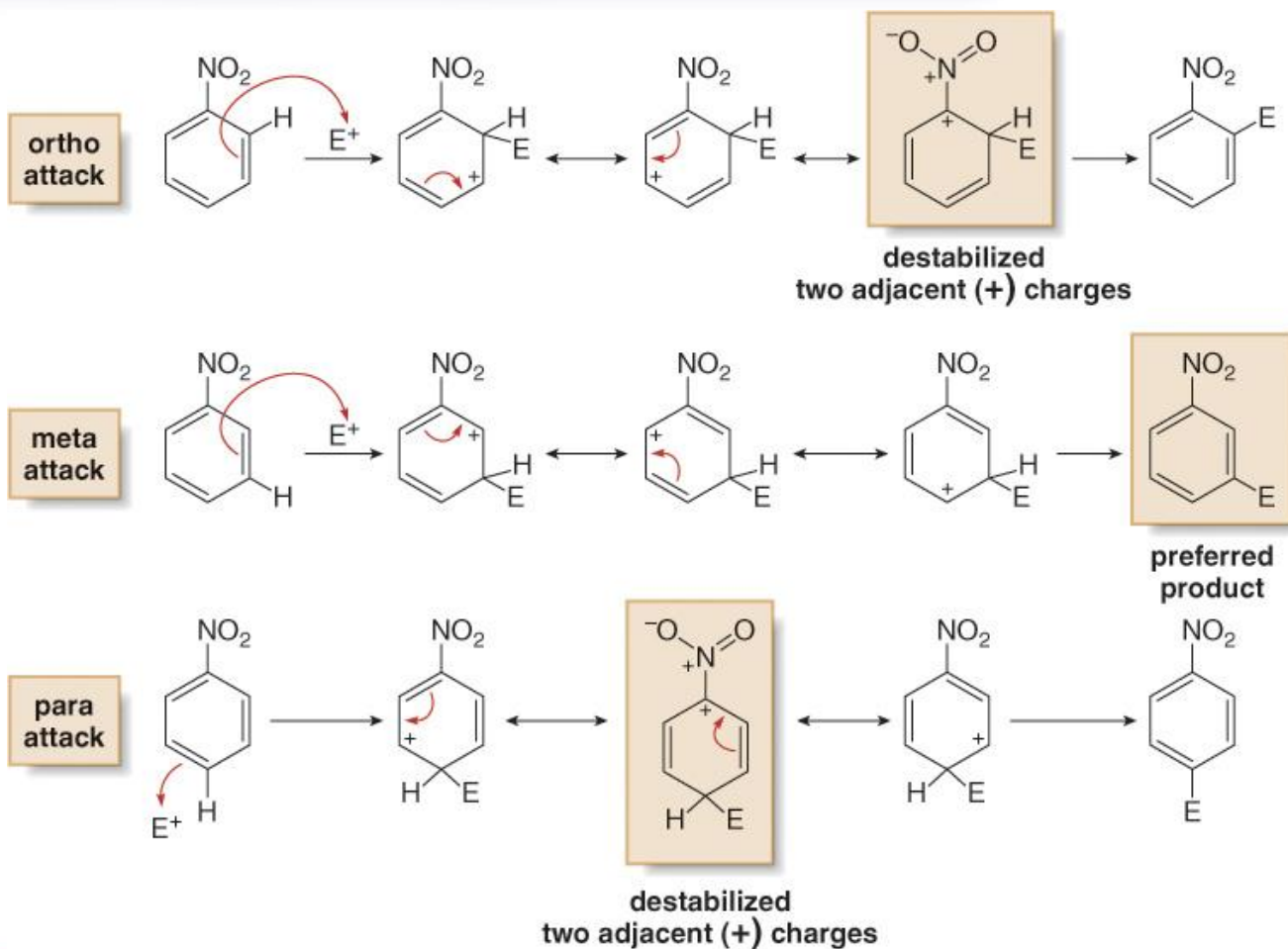




# Directing Groups



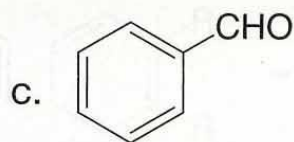
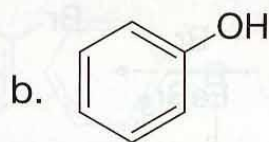
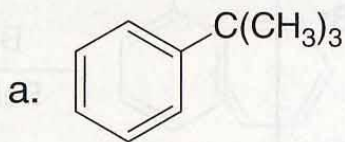
# Directing Groups



# Directing Groups



- 20** Draw all resonance structures for the carbocation formed by ortho attack of the electrophile  $^+\text{NO}_2$  on each starting material. Label any resonance structures that are especially stable or unstable.



- 21** Use the procedure illustrated in Sections 18.9A–C to show why chlorine is an ortho, para director.

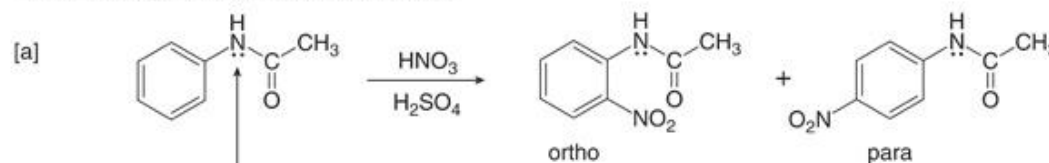
**SAMPLE PROBLEM 18.4**

Draw the products of each reaction and state whether each reaction is faster or slower than a similar reaction with benzene.

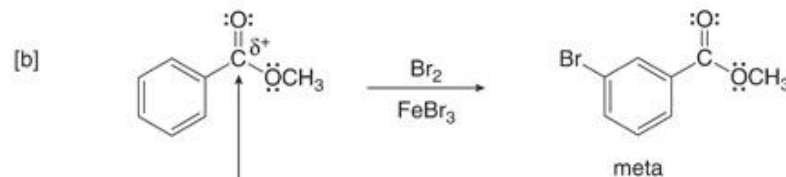
**SOLUTION**

To draw the products:

- Draw the Lewis structure for the substituent to see if it has a lone pair or partial positive charge on the atom bonded to the benzene ring.
- Classify the substituent—ortho, para activating, ortho, para deactivating, or meta deactivating—and draw the products.



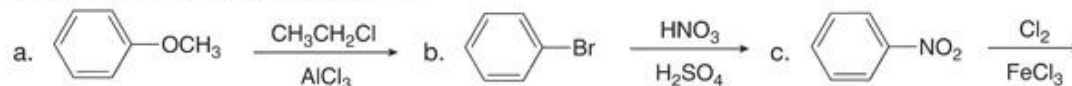
The lone pair on N makes this group an **ortho, para activator**.  
This compound reacts faster than benzene.



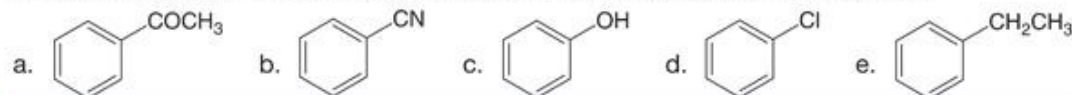
The  $\delta^+$  on this C makes the group a **meta deactivator**.  
This compound reacts more slowly than benzene.

**PROBLEM 18.16**

Draw the products of each reaction.

**PROBLEM 18.17**

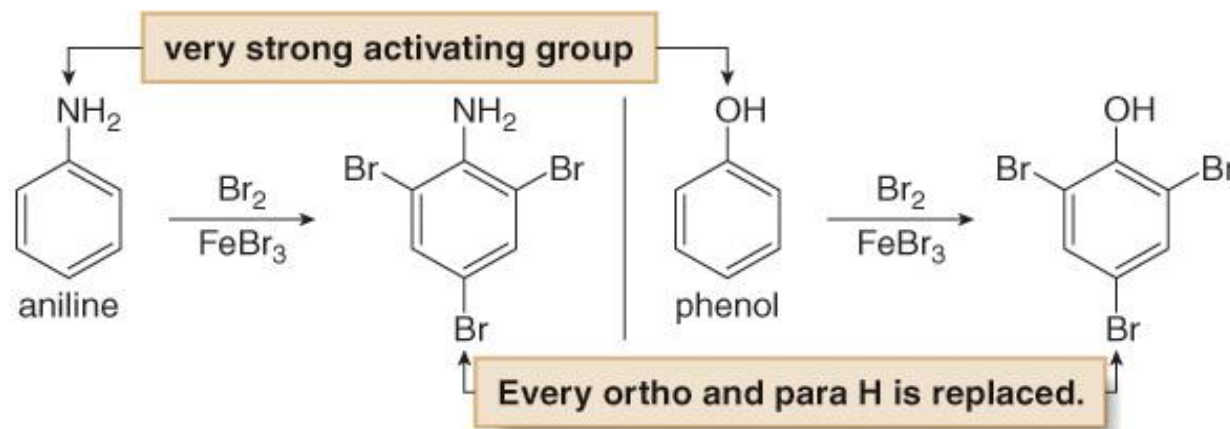
Draw the products formed when each compound is treated with  $\text{HNO}_3$  and  $\text{H}_2\text{SO}_4$ . State whether the reaction occurs faster or slower than a similar reaction with benzene.



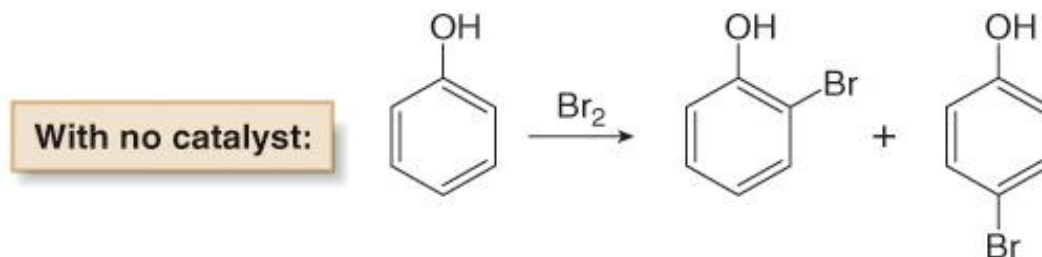


# Limitations in EAS

- ❖ Benzene rings activated by strong electron-donating groups—OH, NH<sub>2</sub>, and their derivatives (OR, NHR, and NR<sub>2</sub>)—undergo polyhalogenation when treated with X<sub>2</sub> and FeX<sub>3</sub>.



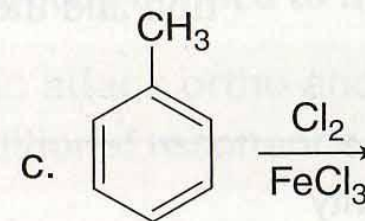
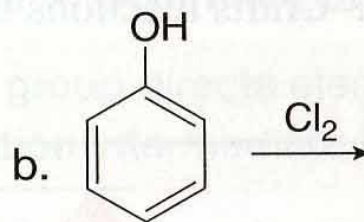
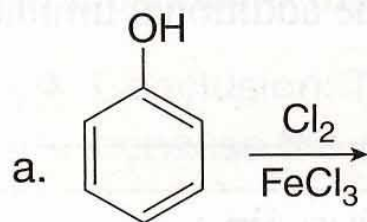
**Monosubstitution** of H by Br occurs with Br<sub>2</sub> *alone* without added catalyst to form a mixture of ortho and para products.



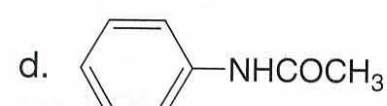
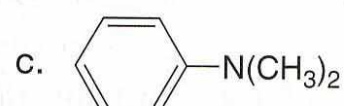


# Homework

**.22** Draw the products of each reaction.

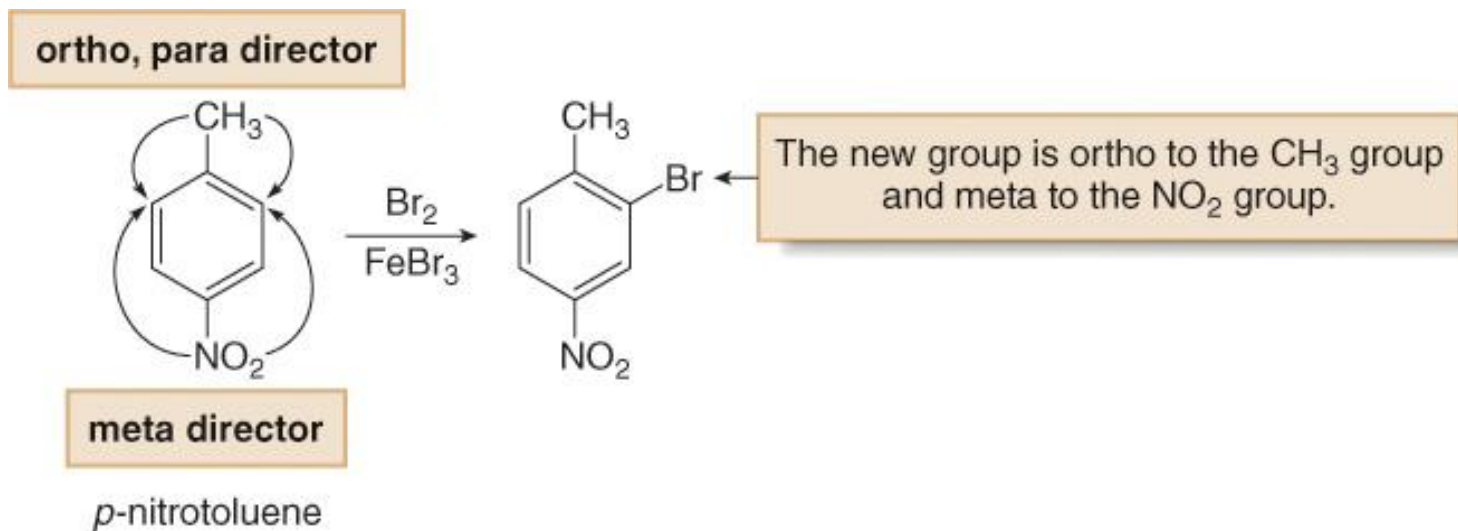


**.23** Which of the following compounds undergo Friedel–Crafts alkylation with  $\text{CH}_3\text{Cl}$  and  $\text{AlCl}_3$ ? Draw the products formed when a reaction occurs.



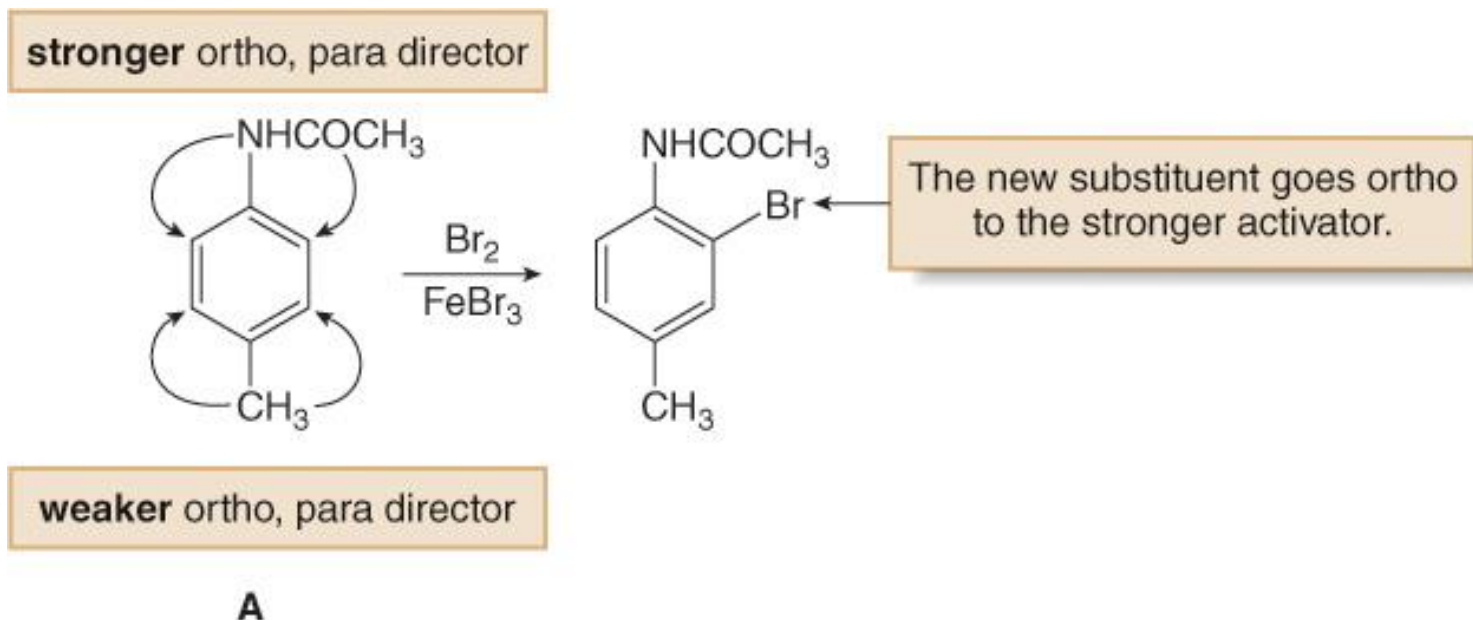
# Disubstituted Benzene

- ❖ When the directing effects of two groups reinforce, the new substituent is located on the position directed by both groups.



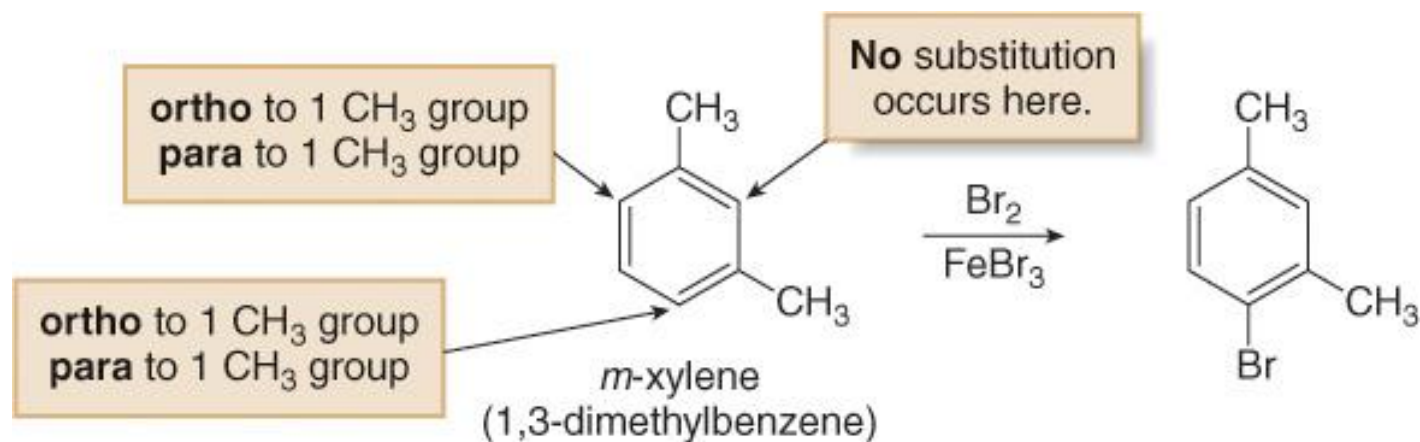
# Disubstituted Benzene

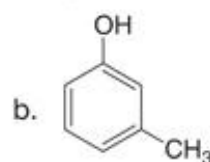
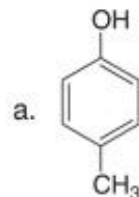
- ❖ If the directing effects of two groups oppose each other, the more powerful activator “wins out”.



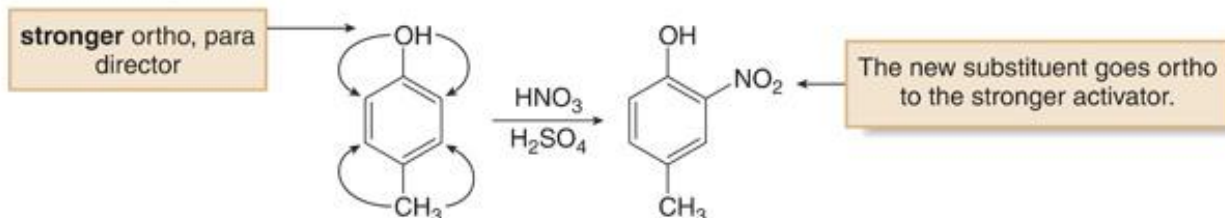
# Disubstituted Benzene

- ❖ No substitution occurs between two meta substituents because of crowding.

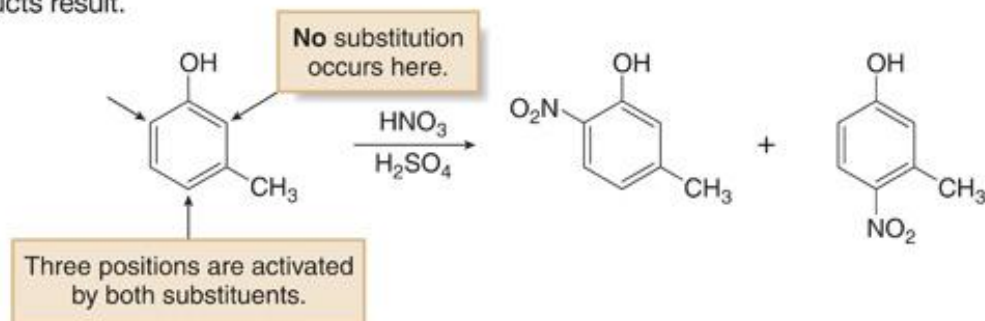
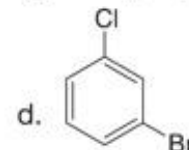
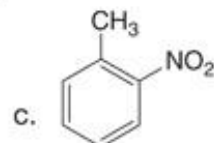
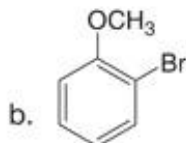
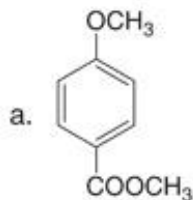


**SAMPLE PROBLEM 18.5** Draw the products formed from nitration of each compound.**SOLUTION**

[a] Both the OH and CH<sub>3</sub> groups are ortho, para directors. Because the OH group is a stronger activator, substitution occurs ortho to it.

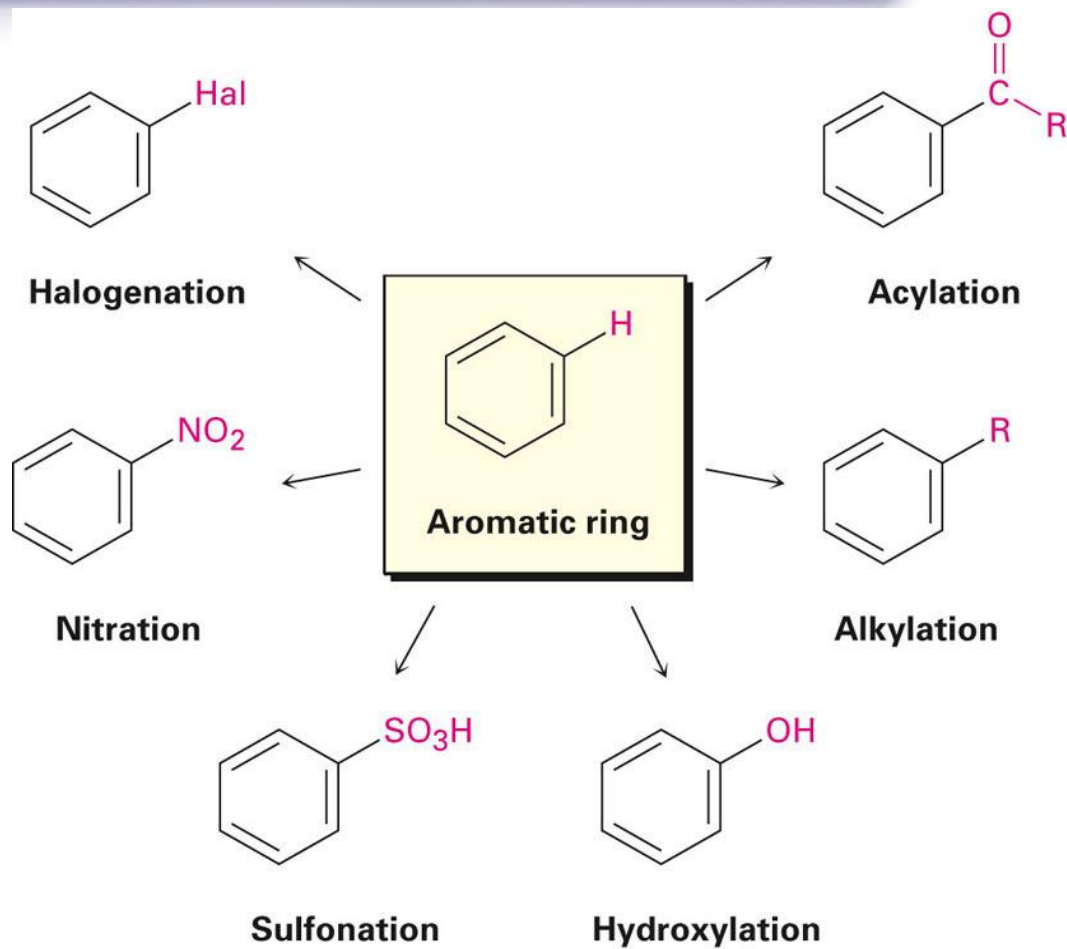


[b] Both the OH and CH<sub>3</sub> groups are ortho, para directors whose directing effects reinforce each other in this case. No substitution occurs between the two meta substituents, however, so two products result.

**PROBLEM 18.24** Draw the products formed when each compound is treated with HNO<sub>3</sub> and H<sub>2</sub>SO<sub>4</sub>.



# Summary



## References



- McMurry's Organic Chemistry , 7<sup>th</sup> Edition.
- Graham Solomons and Craig Fryhle Organic Chemistry , 11<sup>th</sup> edition.
- مدخل الى ميكانيكا التفاعلات العضوية ، د.الصادق عبدالله عبيد د.علي مجيد.
- Janice Gorzyski Smith Organic Chemistry , First Edition, University of Hawaii .

**Thank You !**

