

CH 318 N

LECTURE 22

Textbook Assignment: Chapter 22

Homework (for credit): POW 11 posted

Today's Topics: Benzene & Its Reactions

Notice & Announcements:

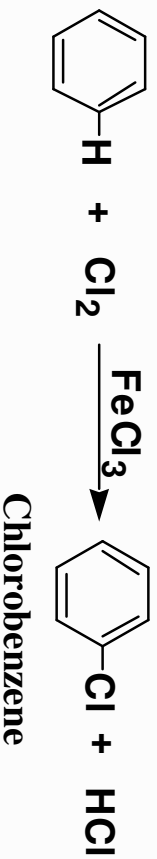
ORGANIC LECTURE SERIES

Reactions of Benzene & Its Derivatives

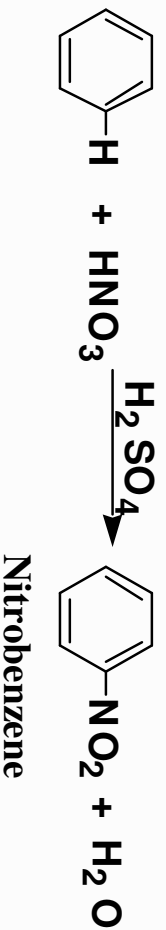
Reactions of Benzene

The most characteristic reaction of aromatic compounds is substitution at a ring carbon:

Halogenation:



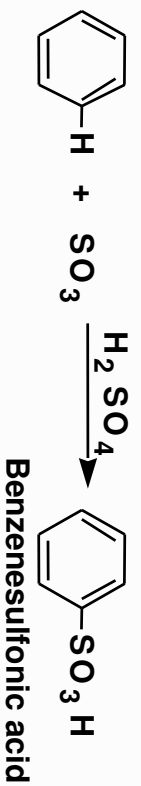
Nitration:



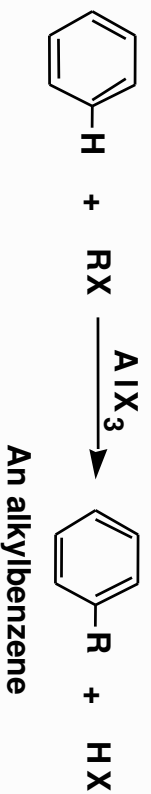
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Reactions of Benzene

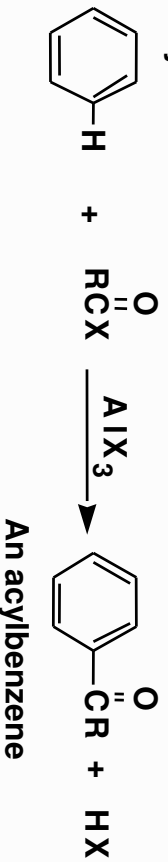
Sulfonation:



Alkylation:



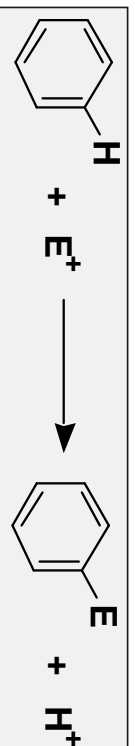
Acylation:



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Electrophilic Aromatic Substitution

- Electrophilic aromatic substitution: a reaction in which a hydrogen atom of an aromatic ring is replaced by an electrophile

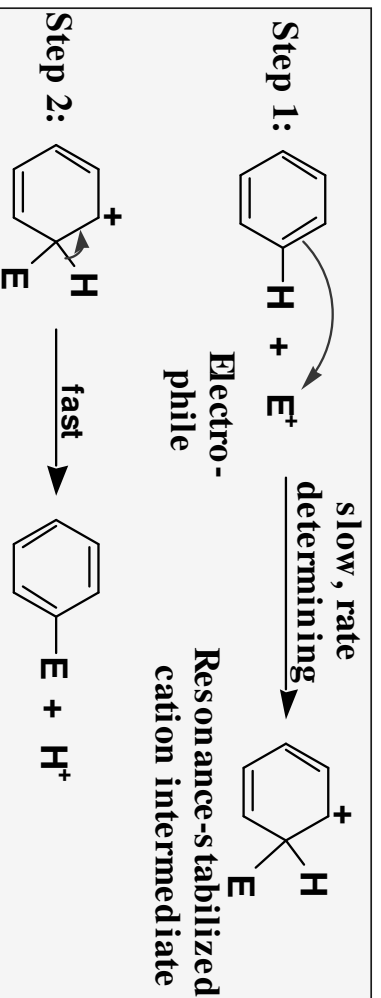


- In this section:
 - several common types of electrophiles
 - how each is generated
 - the mechanism by which each replaces hydrogen

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EAS: General Mechanism

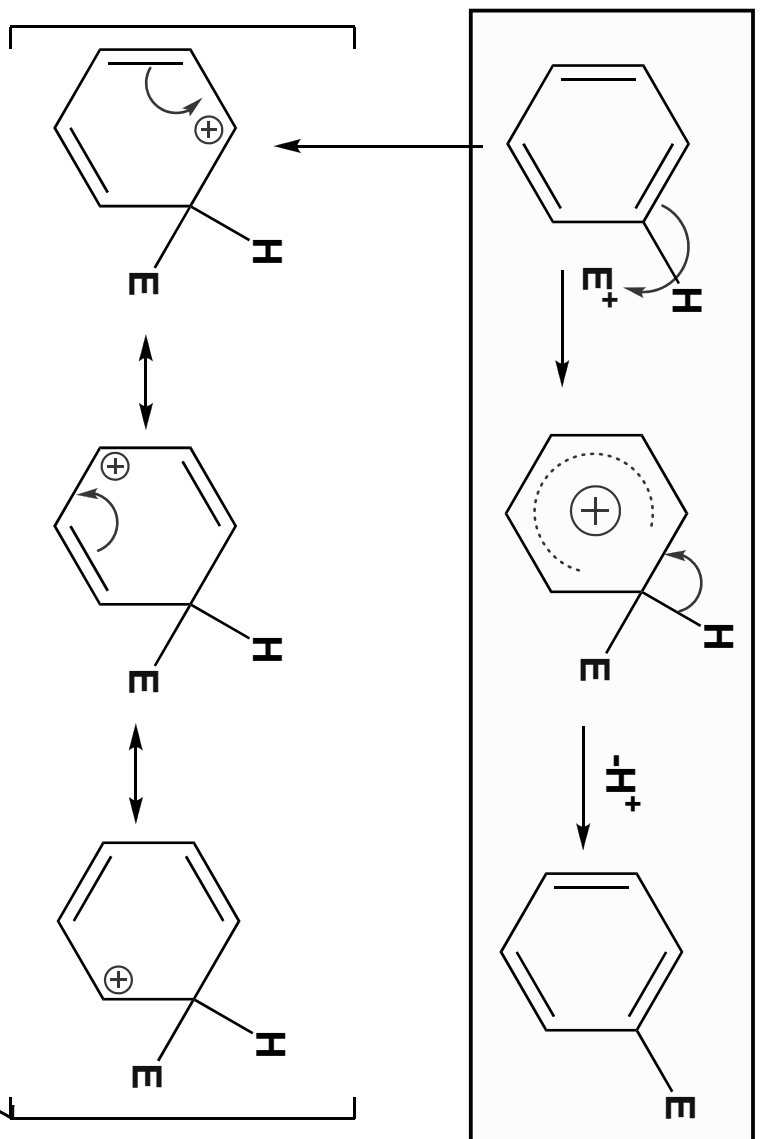
- A general mechanism



- Key question: What is the electrophile and how is it generated?

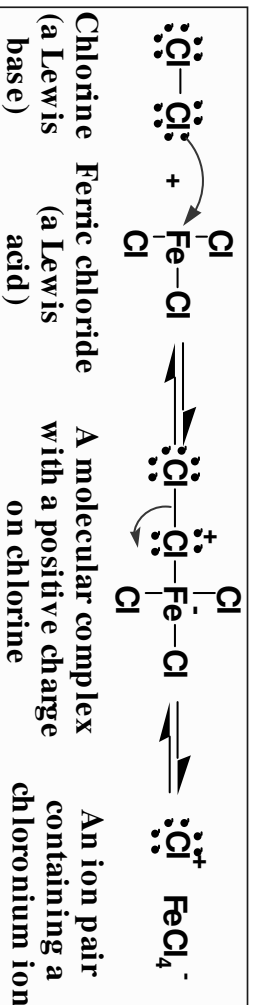
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Electrophilic Aromatic Substitution (EAS)

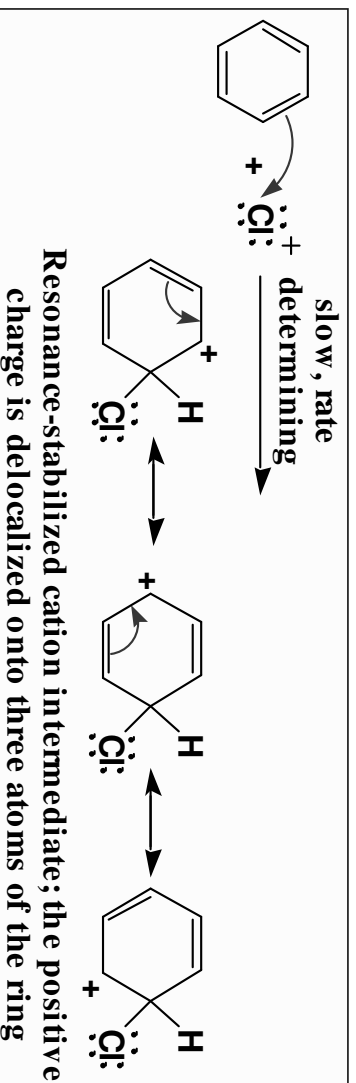


Chlorination

Step 1 : formation of a chloronium ion

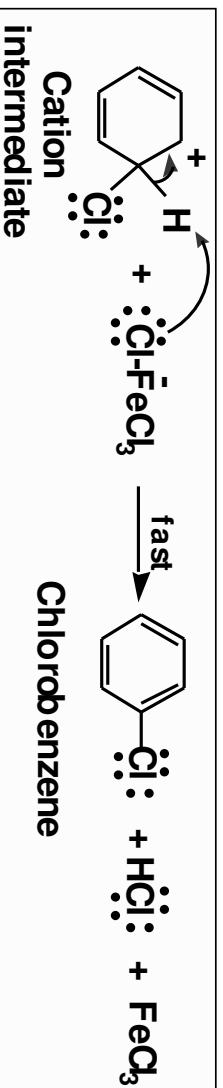


Step 2: attack of the chloronium ion on the ring



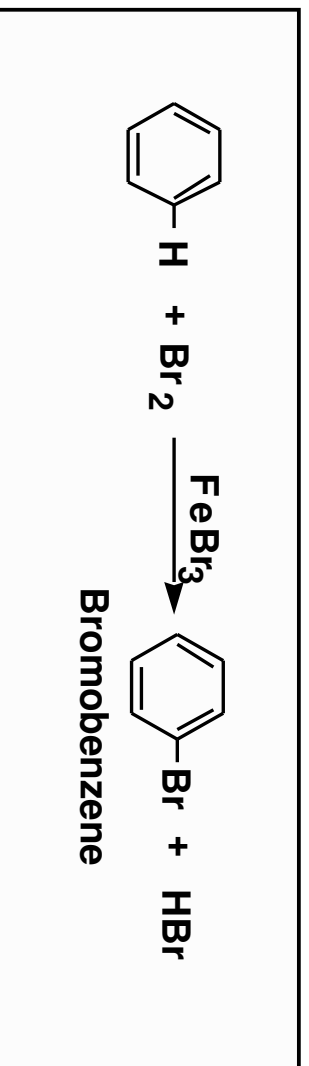
Chlorination

Step 3: proton transfer regenerates the aromatic character of the ring



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Bromination

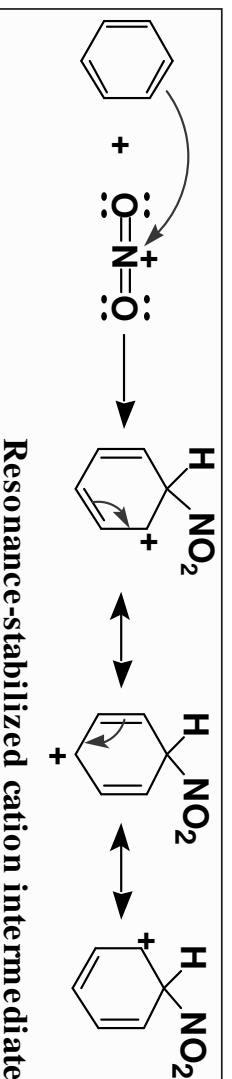


This is the general method for
Substitution of halogen onto a benzene ring
 (CANNOT be halogenated by Free Radical Mechanism)

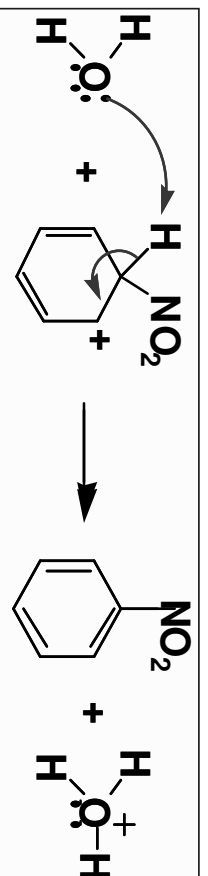
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Nitration

Step 1 : attack of the nitronium ion (an electrophile) on the aromatic ring (a nucleophile)



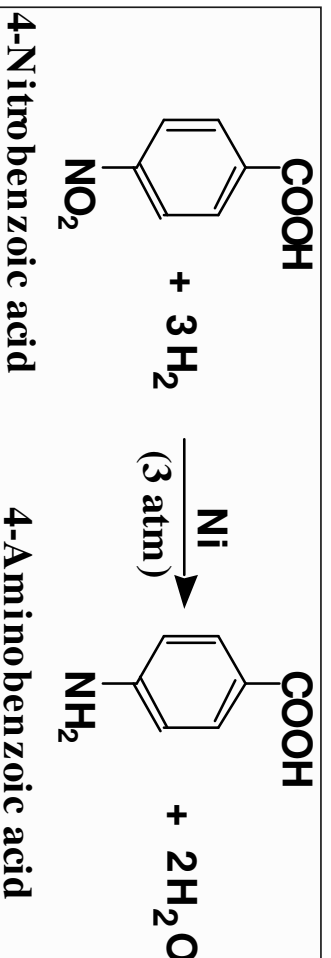
Step 2: proton transfer regenerates the aromatic ring



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Nitration

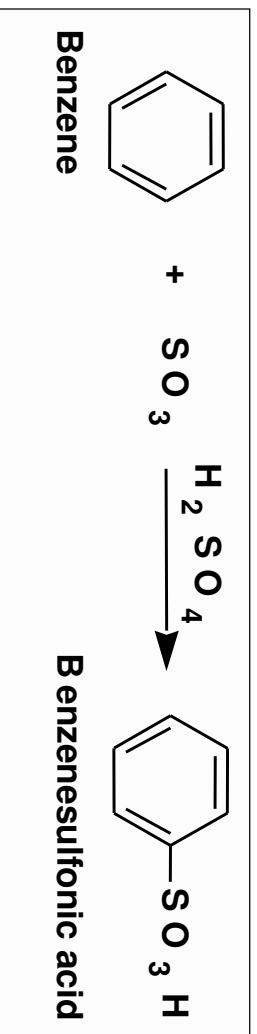
- A particular value of nitration is that the nitro group can be reduced to a 1° amino group



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Sulfonation

- Carried out using concentrated sulfuric acid containing dissolved sulfur trioxide

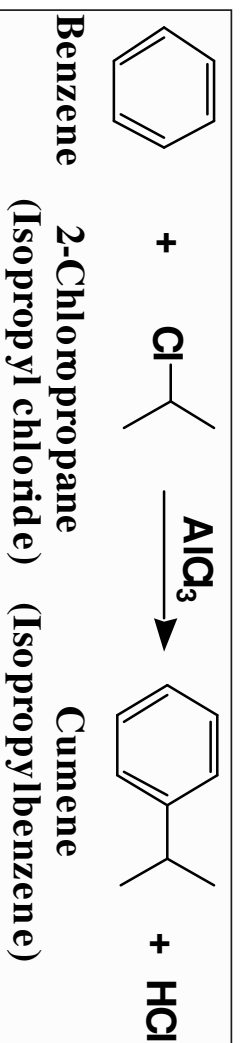


(SO_3 in H_2SO_4 is sometimes called “fuming” sulfuric acid.)

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Friedel-Crafts Alkylation

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

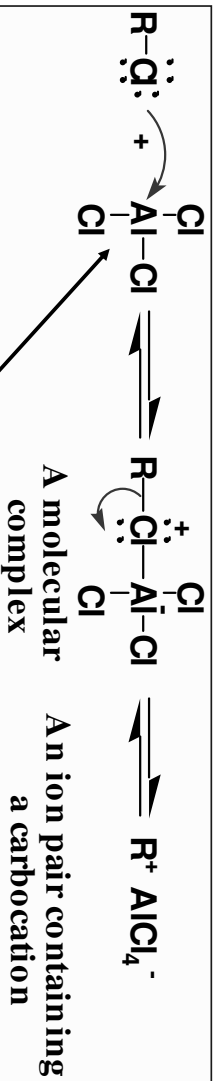


The electrophilic partner is a carbocation;
it will arrange to the most stable ion: allylic > 3° > 2° > 1°

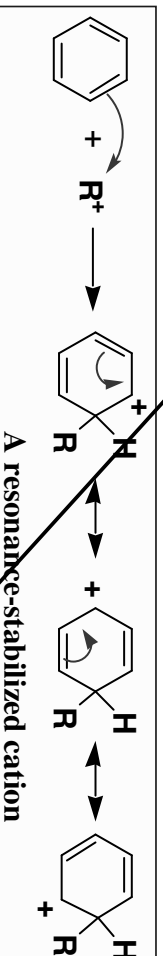
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Friedel-Crafts Alkylation

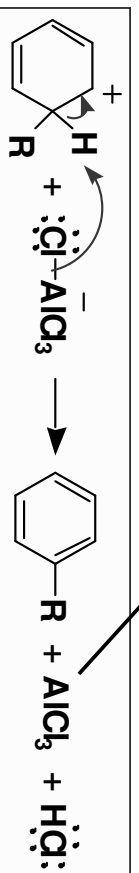
Step 1 : formation of an alkyl cation as an ion pair



Step 2: attack of the alkyl cation on the aromatic ring



Step 3: proton transfer regenerates the aromatic ring



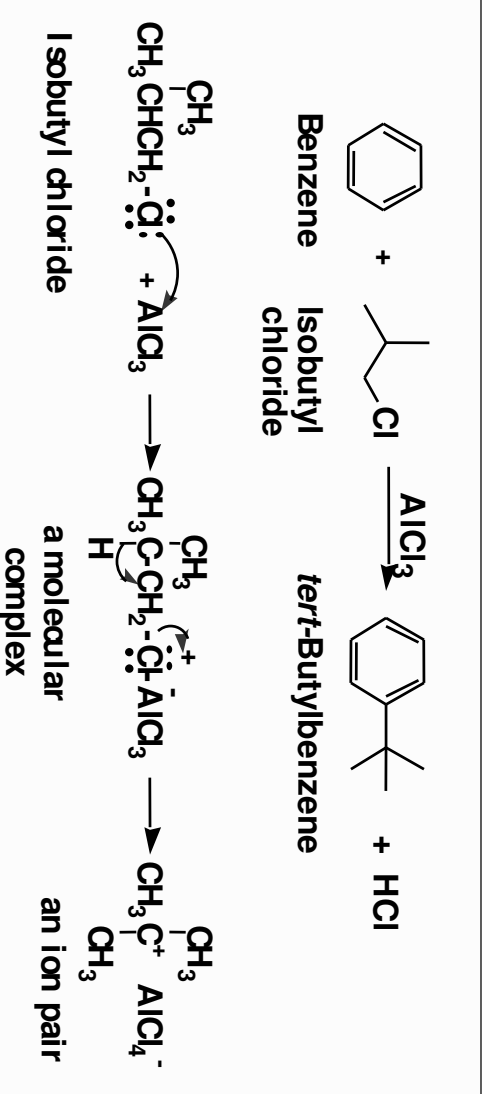
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Friedel-Crafts Alkylation

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There are two major limitations on Friedel-Crafts alkylations:

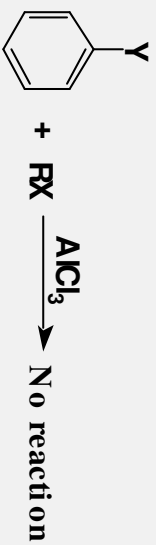
1. carbocation rearrangements are common:



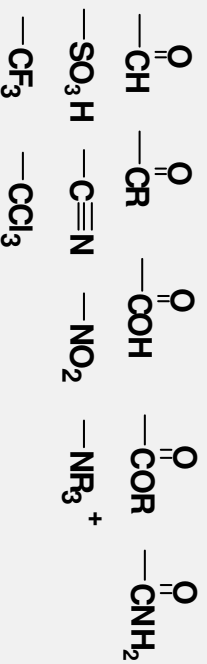
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Friedel-Crafts Alkylation

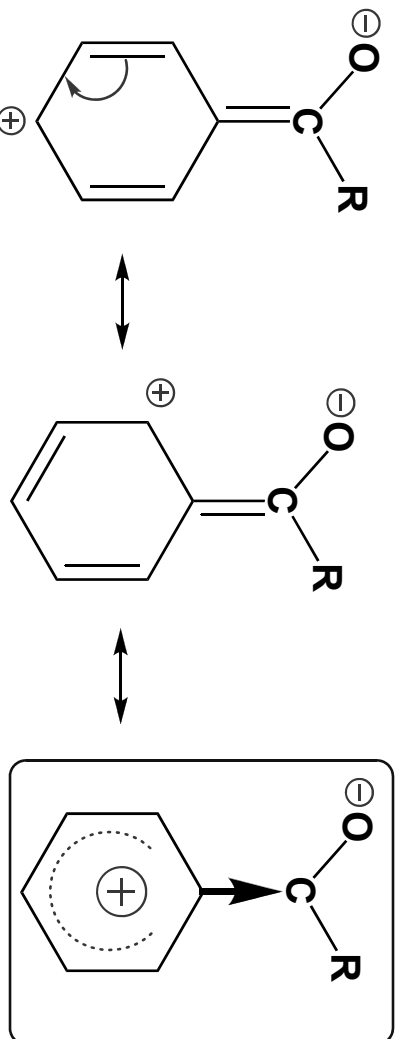
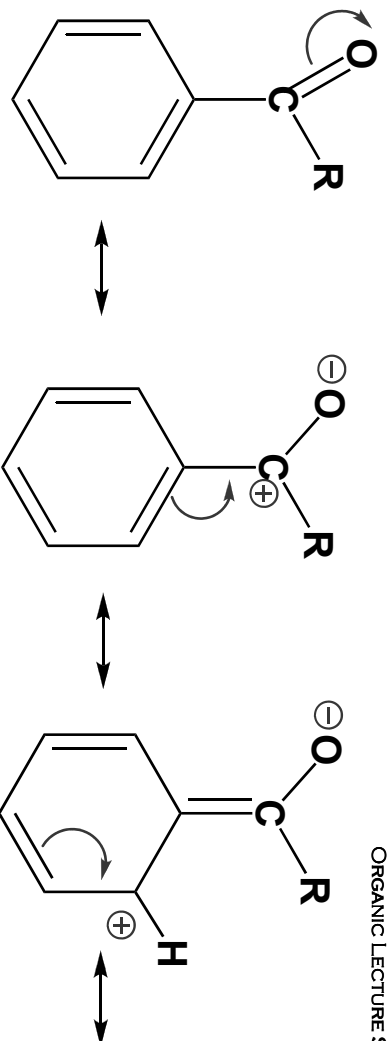
2. F-C alkylation fails on benzene rings bearing one or more of these strongly **electron-withdrawing groups**



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

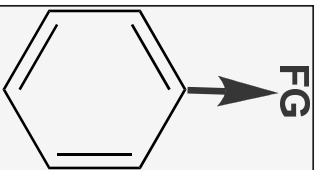


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The “De-activation” of Aromatic Systems



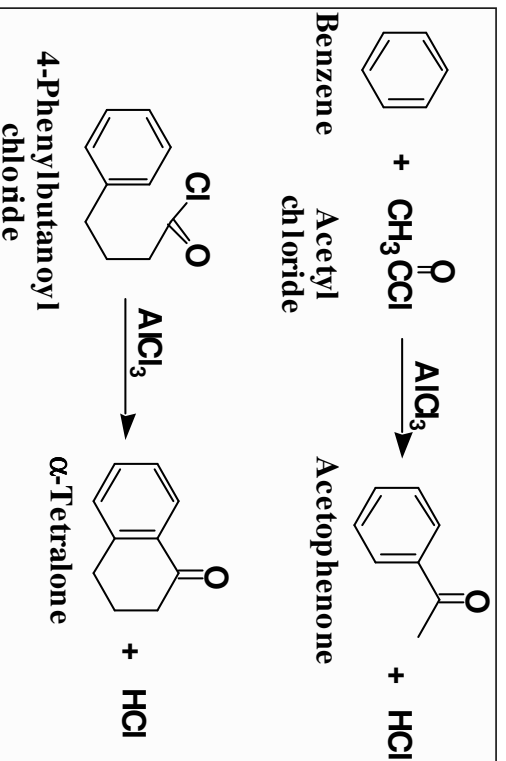
If the FG is an e⁻ withdrawing substituent, then the ring system becomes more electron poor and is said to be “deactivated” towards electrophilic aromatic substitution. EAS occurs at a slower rate.

Note: deactivation refers to the **rate** of EAS

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Friedel-Crafts Acylation

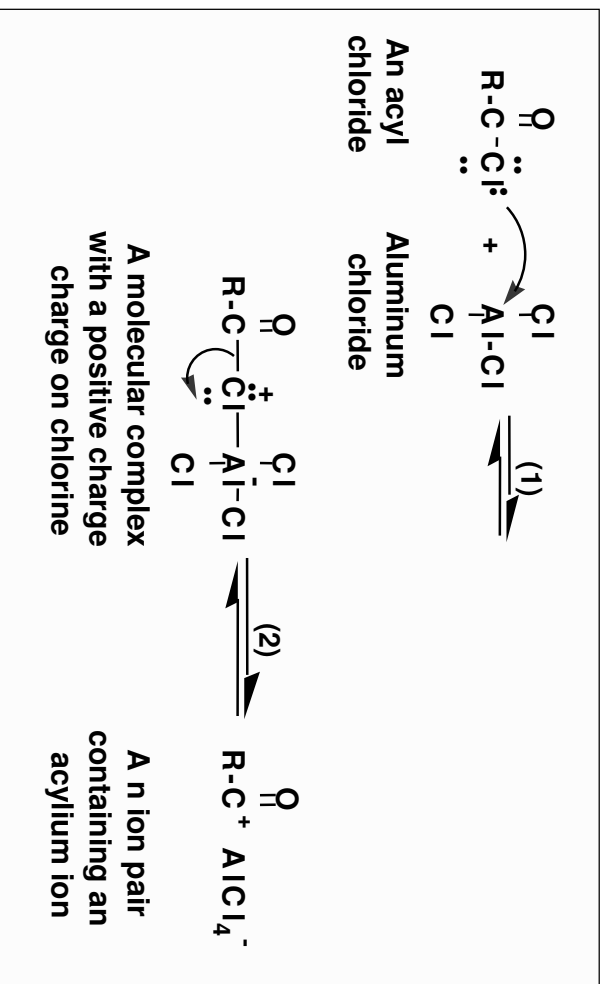
- Friedel-Crafts **acylation** forms a new C-C bond between a benzene ring and an acyl group:



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Friedel-Crafts Acylation

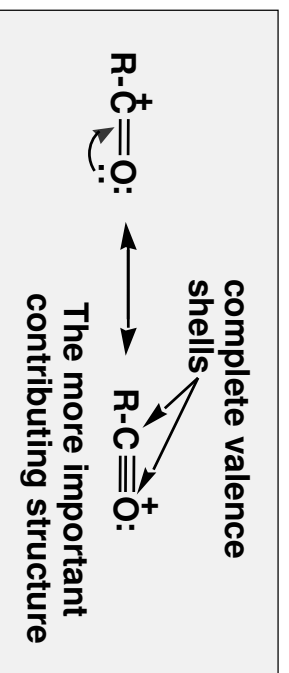
- The electrophile is an **acylium ion**



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Friedel-Crafts Acylation

- an acylium ion is a resonance hybrid of two major contributing structures

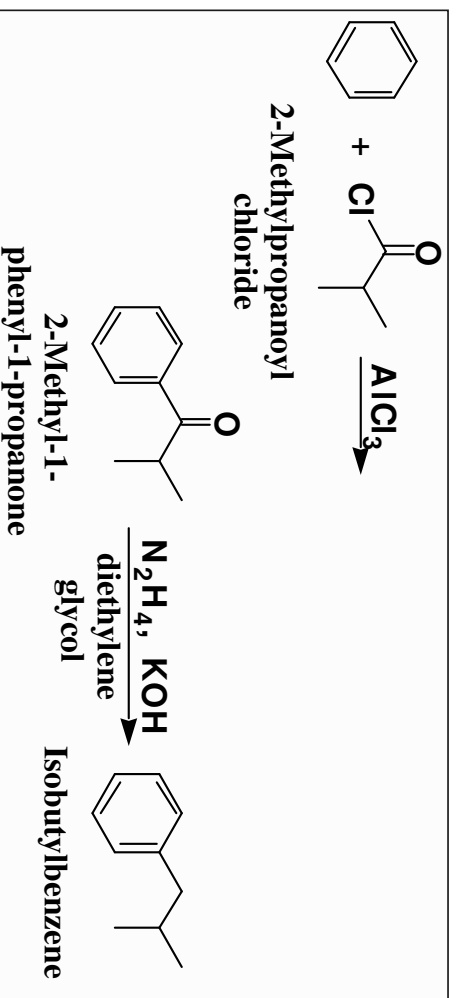


- F-C acylations are free of a major limitation of F-C alkylations; **acylium ions do not rearrange.**

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Friedel-Crafts Acylation

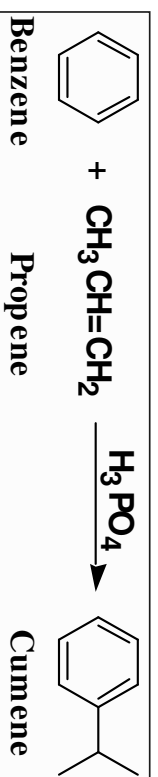
A special value of F-C acylations is preparation of **unrearranged** alkylbenzenes:



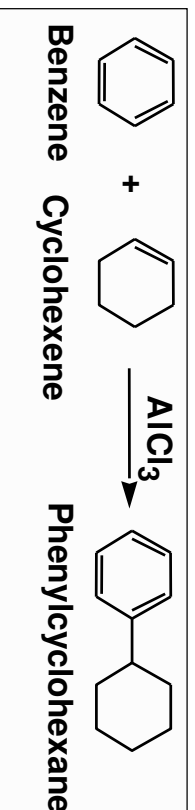
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Other Aromatic Alkylations

- Carbocations are also generated by:
 - treatment of an alkene with a proton acid, most commonly H_2SO_4 , H_3PO_4 , or HF/BF_3



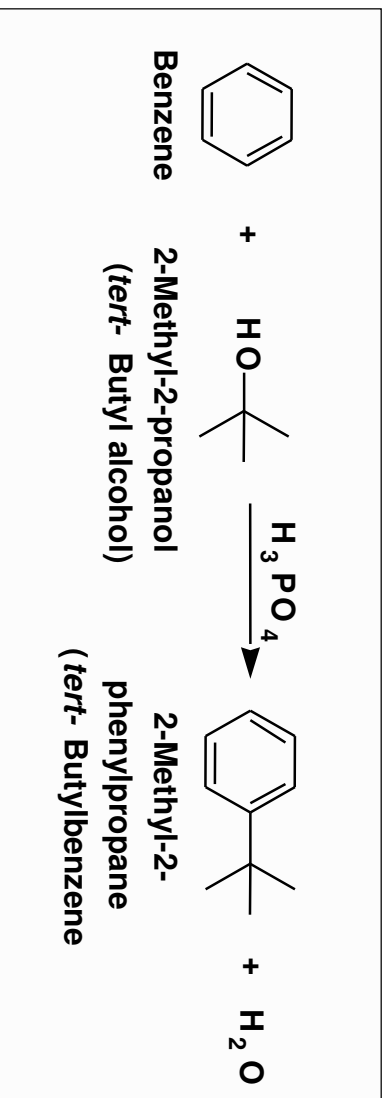
- by treating an alkene with a Lewis acid



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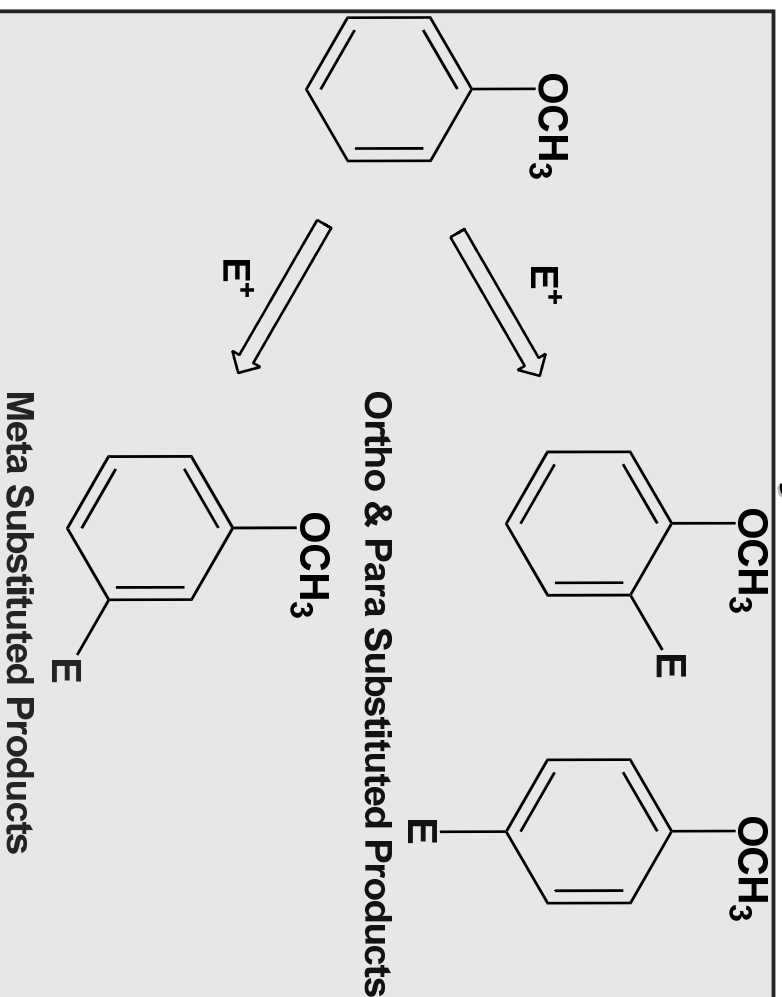
Other Aromatic Alkylations

– and by treating an alcohol with H_2SO_4 or H_3PO_4



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Di- and Polysubstitution



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Di- and Polysubstitution

Orientation on nitration of monosubstituted benzenes:

Substituent	ortho +				
	ortho	meta	para	meta	
—OCH ₃	44	-	55	99	trace
—CH ₃	58	4	38	96	4
—Cl	70	-	30	100	trace
—Br	37	1	62	99	1
—COOH	18	80	2	20	80
—CN	19	80	1	20	80
—NO ₂	6.4	93.2	0.3	6.7	93.2

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Di- and Polysubstitution

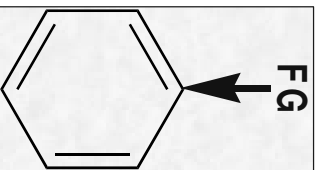
- Orientation:
 - certain substituents direct preferentially to ortho & para positions; others to meta positions
 - substituents are classified as either **ortho-para directing** or **meta directing** toward further substitution

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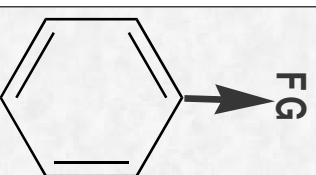
Di- and Polysubstitution

- **Rate**
 - certain substituents cause the rate of a second substitution to be greater than that for benzene itself; others cause the rate to be lower
 - substituents are classified as **activating** or **deactivating** toward further substitution

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If the FG is an e⁻ donating substituent, then the ring system becomes more electron rich and is said to be "activated" towards electrophilic aromatic substitution. EAS is at a faster rate.

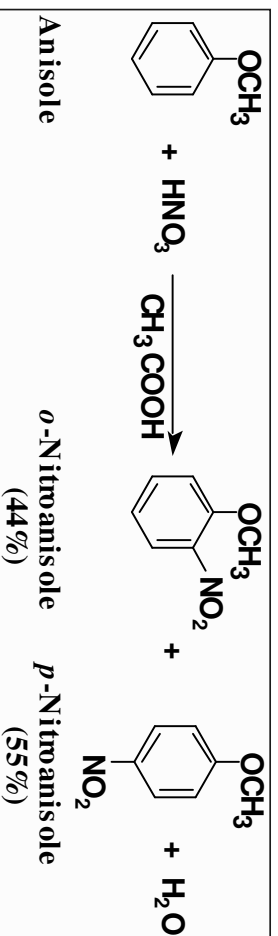


If the FG is an e⁻ withdrawing substituent, then the ring system becomes more electron poor and is said to be "deactivated" towards electrophilic aromatic substitution. EAS occurs at a slower rate.

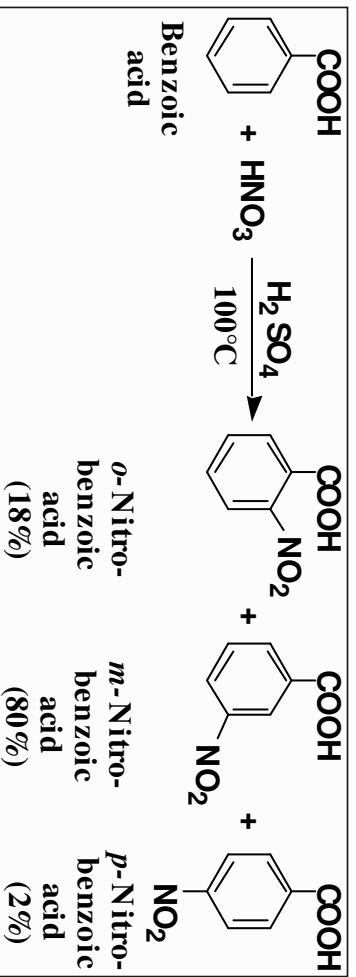
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Di- and Polysubstitution

— **OCH₃** is ortho-para directing:

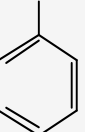


— **CO₂H** is meta directing



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Di- and Polysubstitution

Ortho-para Directing	
Strongly activating	$\text{—}\ddot{\text{N}}\text{H}_2$ $\text{—}\ddot{\text{N}}\text{HR}$ $\text{—}\ddot{\text{N}}\text{R}_2$ $\text{—}\ddot{\text{O}}\text{H}$ $\text{—}\ddot{\text{O}}\text{R}$
Moderately activating	$\text{—}\ddot{\text{N}}\text{HCO}$ $\text{—}\ddot{\text{N}}\text{HCOAr}$ $\text{—}\ddot{\text{O}}\text{CR}$ $\text{—}\ddot{\text{O}}\text{CAR}$
Weakly activating	—R 
Weakly deactivating	$\text{—}\ddot{\text{F}}:$ $\text{—}\ddot{\text{Cl}}:$ $\text{—}\ddot{\text{Br}}:$ $\text{—}\ddot{\text{I}}:$
Meta Directing	
Moderately deactivating	$\text{—}\overset{\text{O}}{\parallel}\text{CH}$ $\text{—}\overset{\text{O}}{\parallel}\text{CR}$ $\text{—}\overset{\text{O}}{\parallel}\text{COH}$ $\text{—}\overset{\text{O}}{\parallel}\text{COR}$
Strongly deactivating	$\text{—}\overset{\text{O}}{\parallel}\text{CNH}_2$ $\text{—SO}_3\text{H}$ $\text{—C}\equiv\text{N}$ —NO_2 —NH_3^+ —CF_3 —CCl_3

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Di- and Polysubstitution

- **Generalizations:**

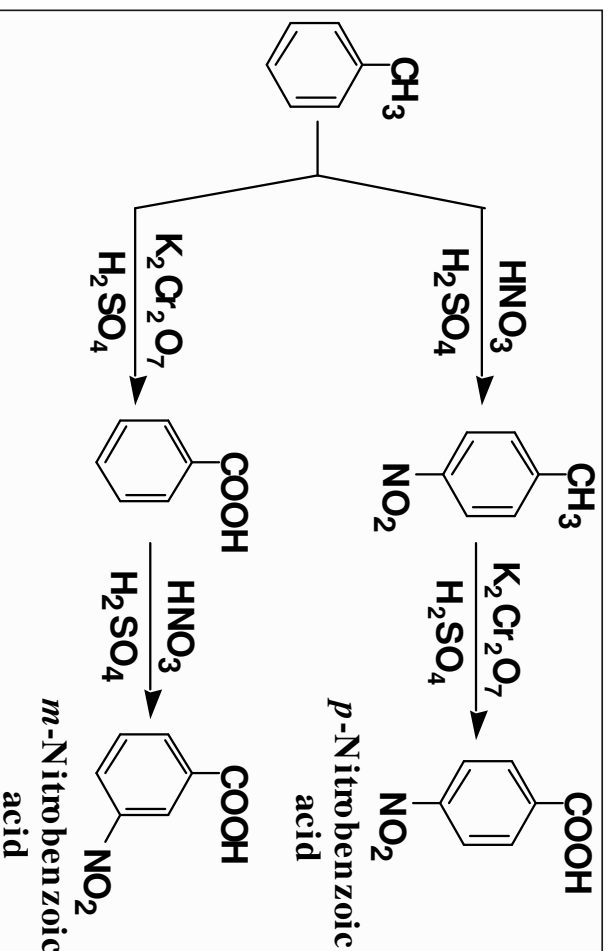
- alkyl, phenyl, and all other substituents in which the atom bonded to the ring has an unshared pair of electrons are ortho-para directing; all other substituents are meta directing
- all ortho-para directing groups except the halogens are activating toward further substitution; the halogens are weakly deactivating

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Di- and Polysubstitution

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the order of steps is important:



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Theory of Directing Effects

- The rate of EAS is limited by the slowest step in the reaction
- For almost every EAS, the **rate-determining step is attack of E⁺** on the aromatic ring to give a resonance-stabilized cation intermediate
- The **more stable this cation intermediate, the faster the rate-determining step** and the faster the overall reaction

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Theory of Directing Effects

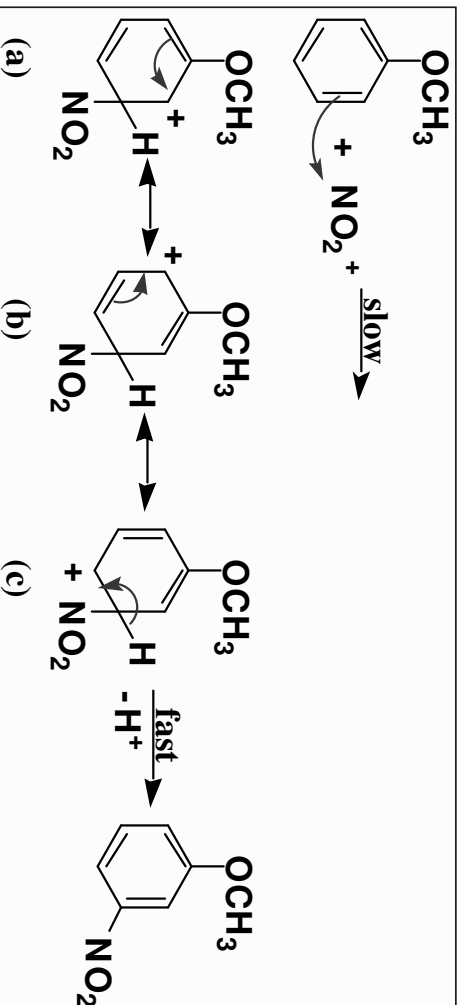
- For ortho-para directors, ortho-para attack forms a more stable cation than meta attack
 - ortho-para products are formed faster than meta products
- For meta directors, meta attack forms a more stable cation than ortho-para attack
 - meta products are formed faster than ortho-para products

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Theory of Directing Effects

Nitration of anisole

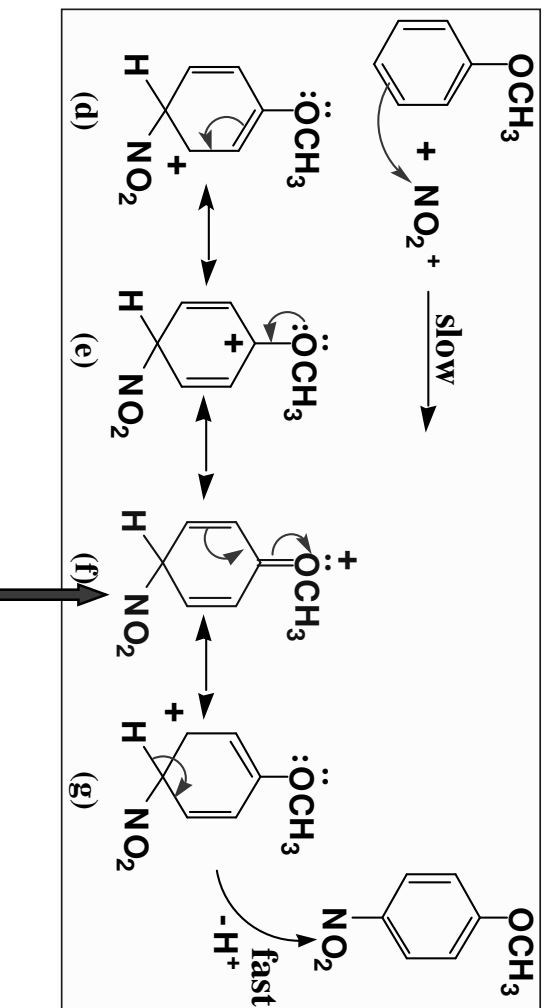
-OCH₃; examine the meta attack:



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Nitration of anisole

-OCH₃; examine the ortho-para attack:



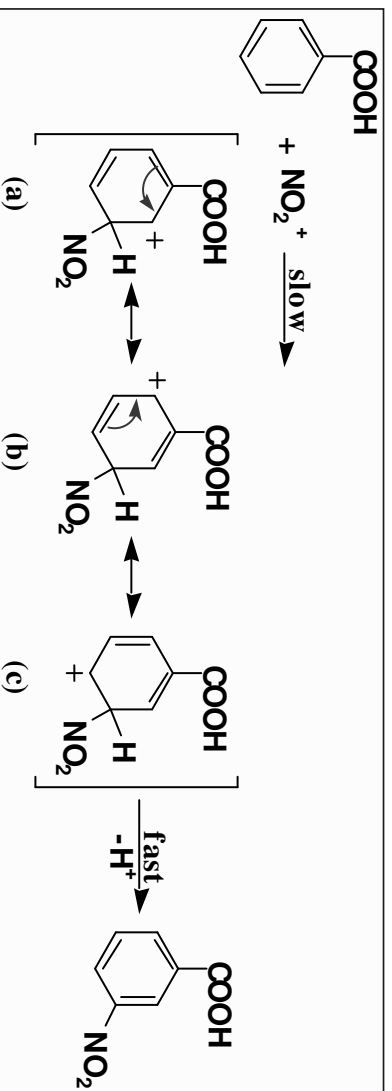
This resonance structure accounts for the selectivity

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Theory of Directing Effects

Nitration of benzoic acid

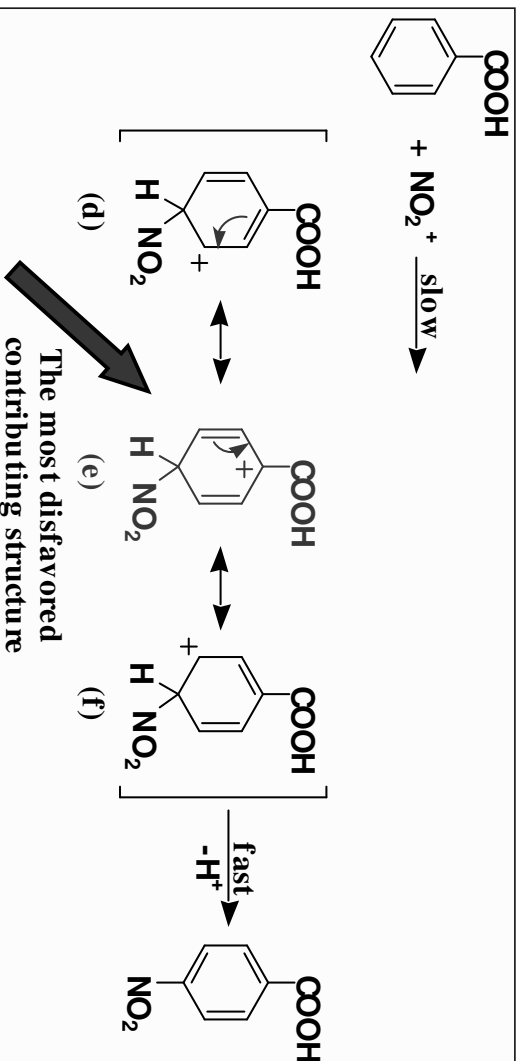
-NO₂; examine the meta attack:



4.1

Nitration of benzoic acid

-NO₂: assume ortho-para attack:



This resonance structure accounts for the selectivity

4.2

Activating-Deactivating

- Any resonance effect, such as that of -NH₂, -OH, and -OR, that delocalizes the positive charge on the cation intermediate lowers the activation energy for its formation, and has an **activating** effect toward further EAS
- Any resonance effect, such as that of -NO₂, -CN, -CO, and -SO₃H, that decreases electron density on the ring **deactivates** the ring toward further EAS

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Activating-Deactivating

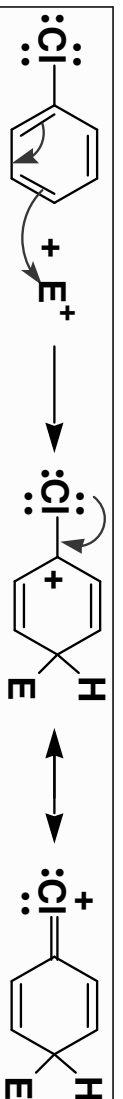
- Any inductive effect, such as that of -CH₃ or other alkyl group, that releases electron density toward the ring **activates** the ring toward further EAS
- Any inductive effect, such as that of halogen, -NR₃⁺, -CCl₃, or -CF₃, that decreases electron density on the ring **deactivates** the ring toward further EAS

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Activating-Deactivating

➤ for the **halogens**, the inductive and resonance effects run counter to each other, but the former is somewhat stronger

➤ **the net effect is that halogens are deactivating but ortho-para directing**

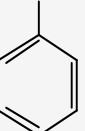


Inductive effect is slightly dominant

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Di- and Polysubstitution

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Ortho-para Directing	
Strongly activating	$\text{--}\ddot{\text{N}}\text{H}_2$ $\text{--}\ddot{\text{N}}\text{HR}$ $\text{--}\ddot{\text{N}}\text{R}_2$ $\text{--}\ddot{\text{O}}\text{H}$ $\text{--}\ddot{\text{O}}\text{R}$
Moderately activating	$\text{--}\ddot{\text{N}}\text{HCO}$ $\text{--}\ddot{\text{N}}\text{HCOAr}$ $\text{--}\ddot{\text{O}}\text{CO}$ $\text{--}\ddot{\text{O}}\text{COAr}$
Weakly activating	--R 
Weakly deactivating	$\text{--}\ddot{\text{F}}\text{:}$ $\text{--}\ddot{\text{Cl}}\text{:}$ $\text{--}\ddot{\text{Br}}\text{:}$ $\text{--}\ddot{\text{I}}\text{:}$
Meta Directing	
Moderately deactivating	$\text{--}\overset{\text{O}}{\parallel}\text{CH}$ $\text{--}\overset{\text{O}}{\parallel}\text{CR}$ $\text{--}\overset{\text{O}}{\parallel}\text{COH}$ $\text{--}\overset{\text{O}}{\parallel}\text{COR}$
Strongly deactivating	--NO_2 $\text{--SO}_3\text{H}$ --NH_3^+ $\text{--C}\equiv\text{N}$ --CF_3 --CCl_3

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