Reactions of Aromatic Compounds
2 - Di and Polysubstitution

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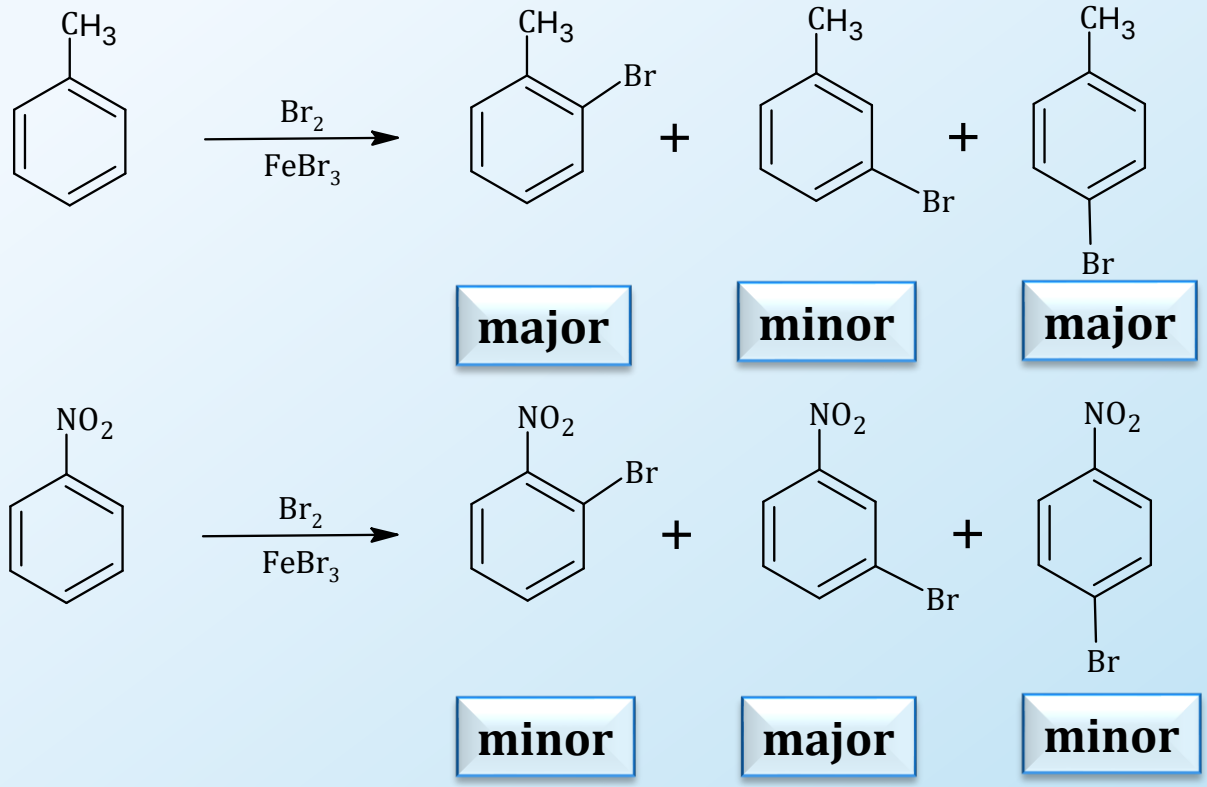
Effect of the Substituent

Consider the following two reactions. The proportion of the major product indicates the group already present on the benzene ring has some effect on the reactivity of the benzene.



Disubstitution - Effect of Substituents

The nature of groups **already on** an aromatic ring affect both the reactivity and orientation of subsequent substitution. Some groups "activate" the benzene ring, making it more nucleophilic while some "deactivate" the ring making it a weaker nucleophile. In both cases further substitution occurs, but where, depends on the activator or deactivator on the benzene ring.

Activating Groups	Deactivating groups
• Make benzene more electron rich; • Making benzene more nucleophilic; • Reaction is faster.	• Make benzene less electron rich; • Making benzene less nucleophilic; • Reaction is slower.
• Ortho para directors.	• Meta directors.
• Electron donating groups already present on the benzene ring.	• Electron withdrawing groups already present on the benzene ring.

Ortho-Para and Meta Directors

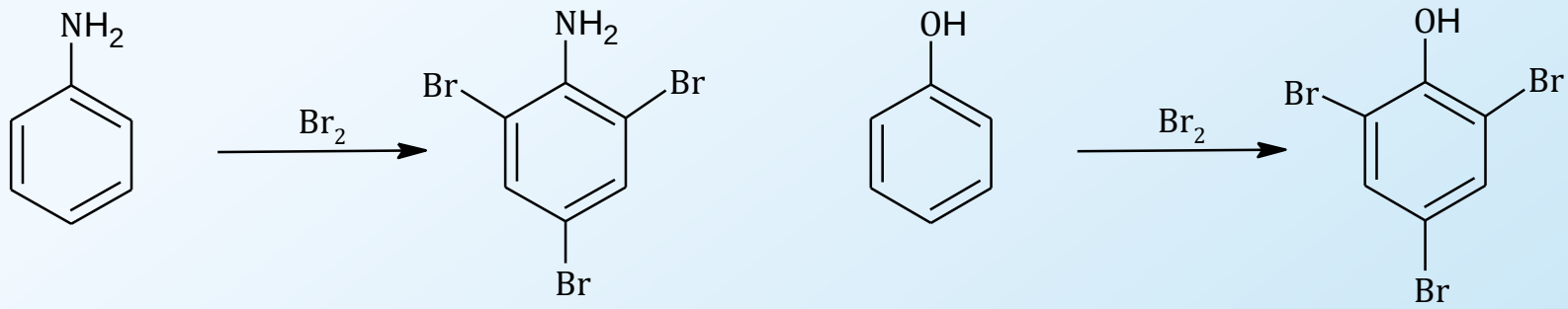
Reactivity: The Effect of Electron-Releasing and Electron-Withdrawing Groups.

- Electron-releasing groups activate the ring for further reaction.
- Electron-withdrawing groups deactivate the ring for further reaction.

Ortho – Para directors Activators	Meta Directors Deactivators
Strongly Activating **$-NH_2$, -NHR, $-NR_2$** **-OH, $-O^-$**	**Strongly Deactivating** **$-NO_2$, $-NR_3^+$, $-CF_3$, $-CCl_3$**
Moderately Activating **$-NHCOCH_3$, -NHCOR** **$-OCH_3$, -OR**	**Moderately Deactivating** **-CN, $-SO_3H$, -COOH, -COOR** **-CHO, -COR**
Weakly Activating **$-CH_3$ and –R groups, -Ph**	
Weakly Deactivating **-F, -Cl, -Br, -I**	

Highly Activating Groups

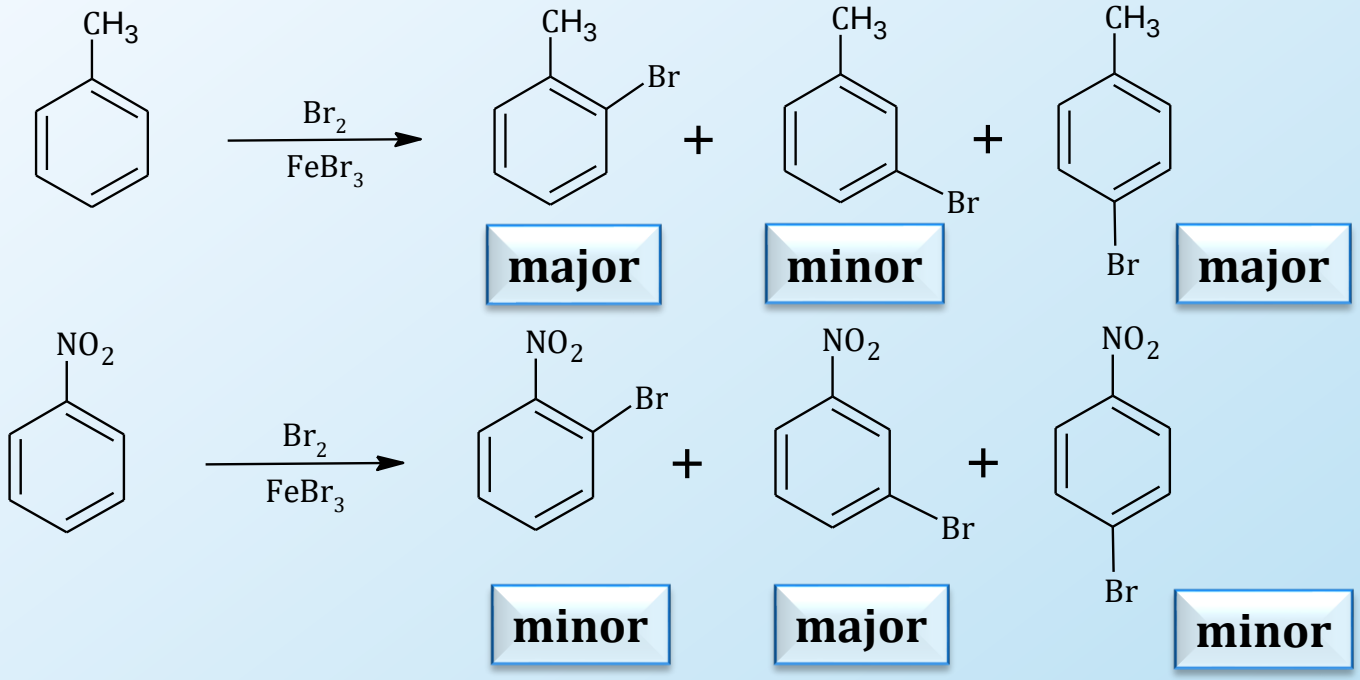
Amino and hydroxyl groups are highly activating groups. These groups are so activating that catalysts are often not necessary during some reactions.



Reason for Orientation

When the electrophile attacks the ortho, meta or para position, there are resonance structures formed from the resulting carbocation (of the benzene ring). The group already present on the benzene ring will contribute to the resonance structures formed during the second substitution. Some resonance structures contribute more to the stability of the intermediate than others which leads to the major product being meta or ortho/para.

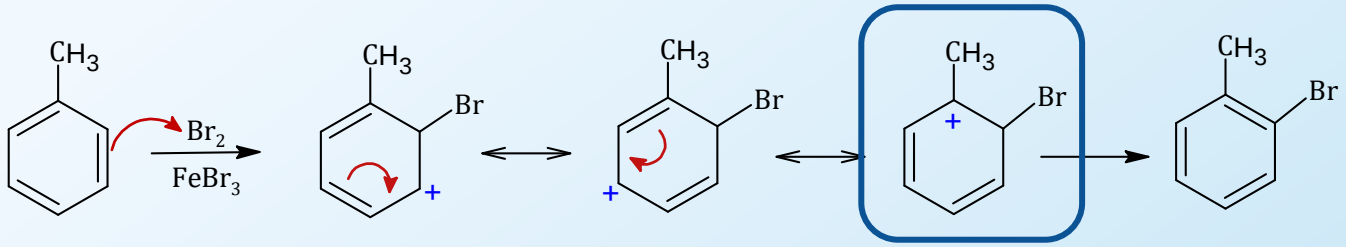
The next few slides show these resonance structures.



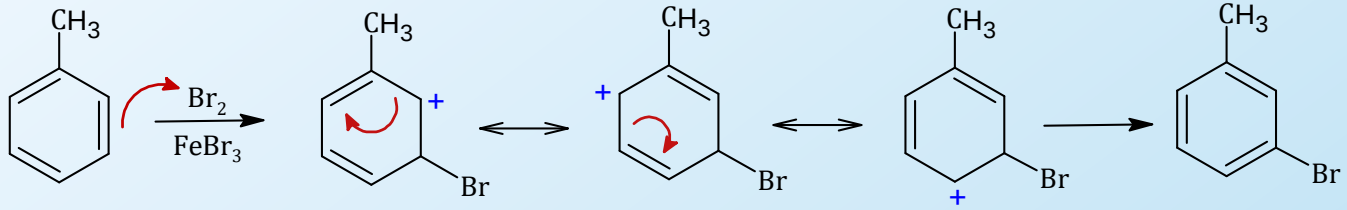
Orientation Effect – Activating Group

A methyl (CH_3) group directs electrophilic attack ortho and para, because the electron-donating inductive effect of CH_3 stabilizes the carbocation intermediate as boxed shown below.

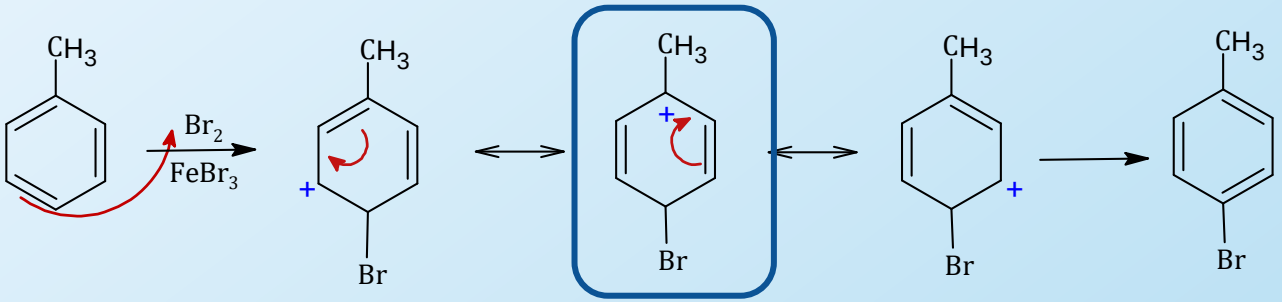
Ortho attack



Meta attack



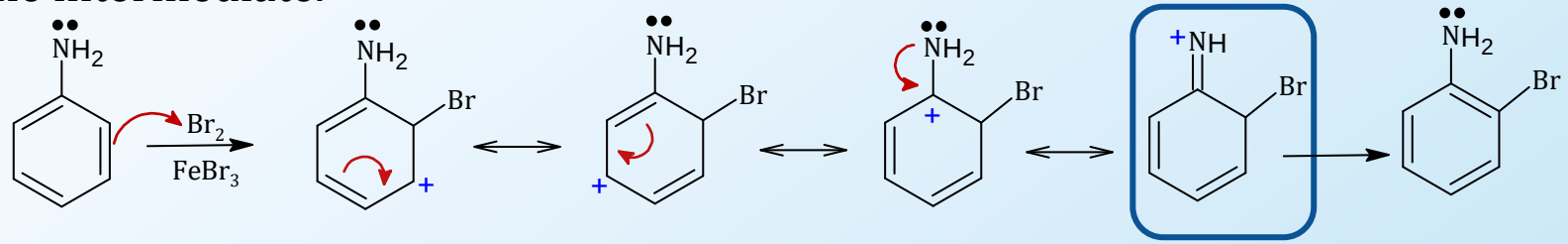
Para attack



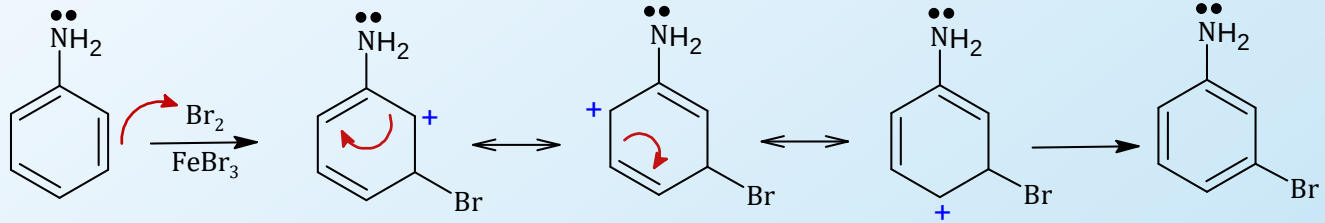
Orientation Effect – Activating Group, Contd..

The NH_2 group directs electrophilic attack ortho and para, because the carbocation intermediate has additional resonance stabilization from the lone pair of electrons on NH_2 group. The more the resonance structures the more stable the intermediate.

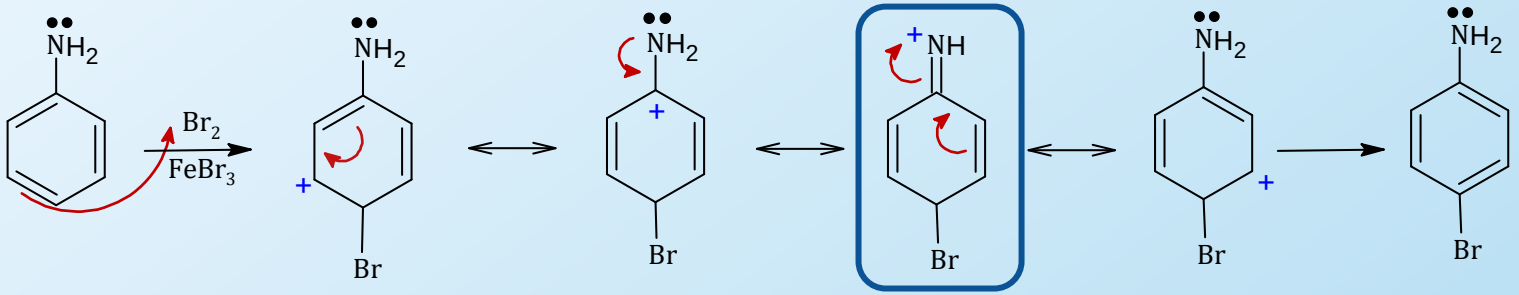
Ortho attack



Meta attack



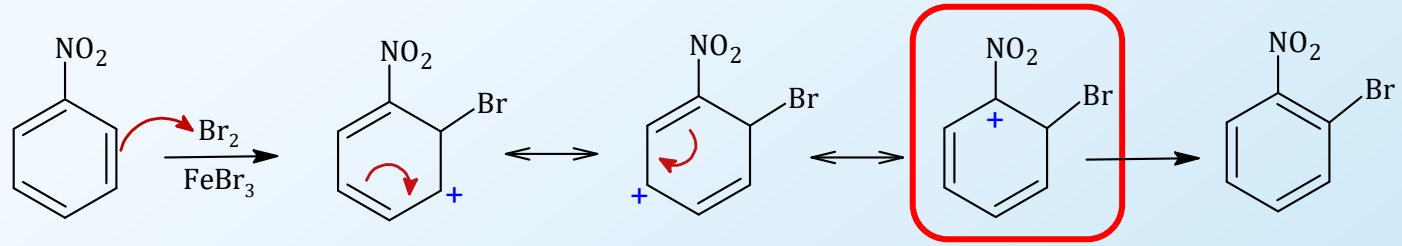
Para attack



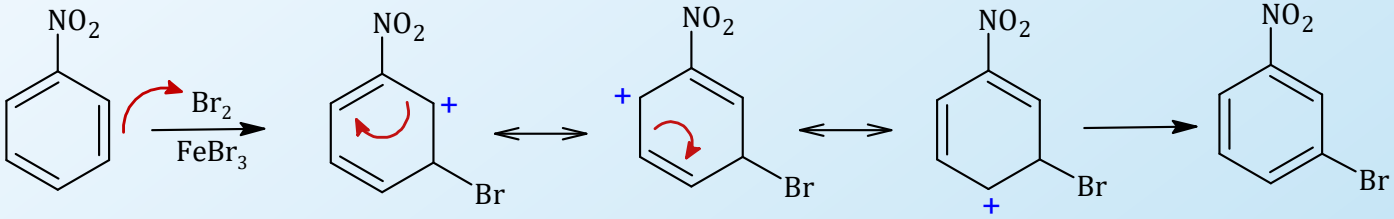
Orientation Effect – Deactivating Group

With the NO_2 group (and all meta directors), meta attack occurs because attack at the ortho and para position gives a destabilized carbocation intermediate.

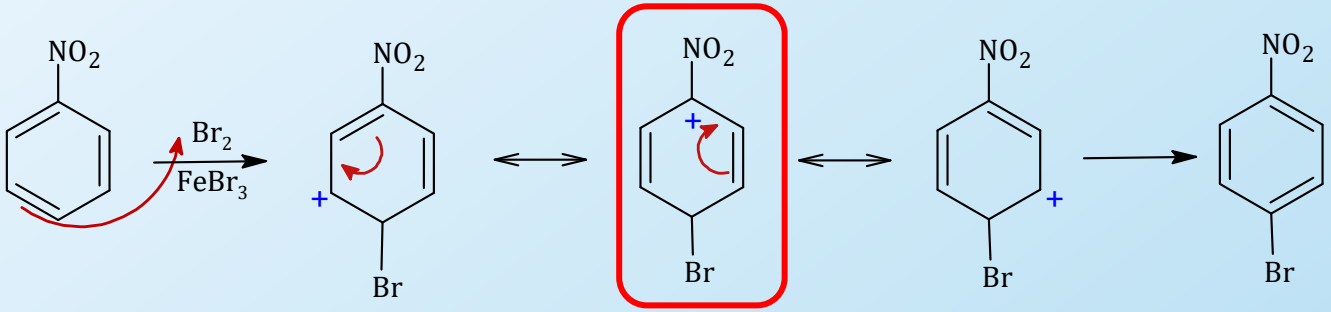
Ortho attack



Meta attack

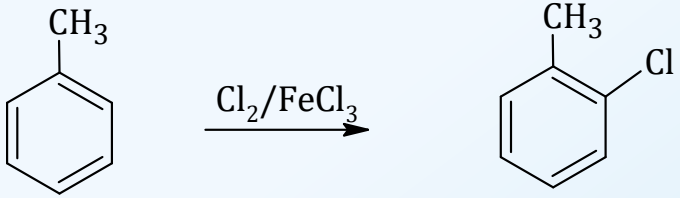


Para attack

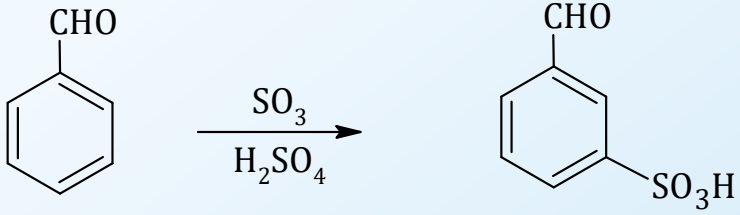


Worked Examples: Disubstitutions

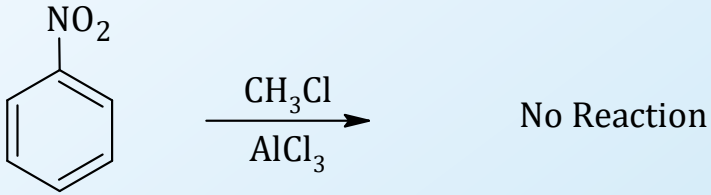
Complete the following reactions with the appropriate major products.



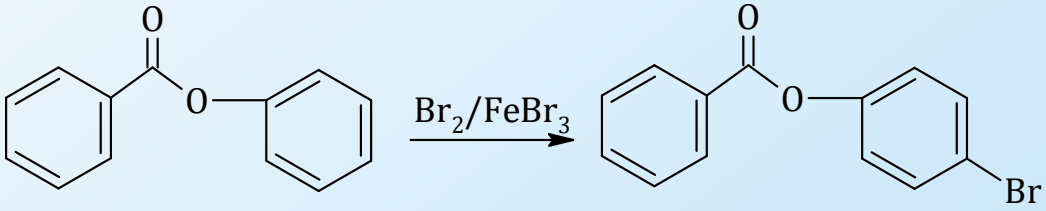
Ortho and para (not drawn) because alkyl groups are op director.



Meta because CHO is electron withdrawing, thus m director.



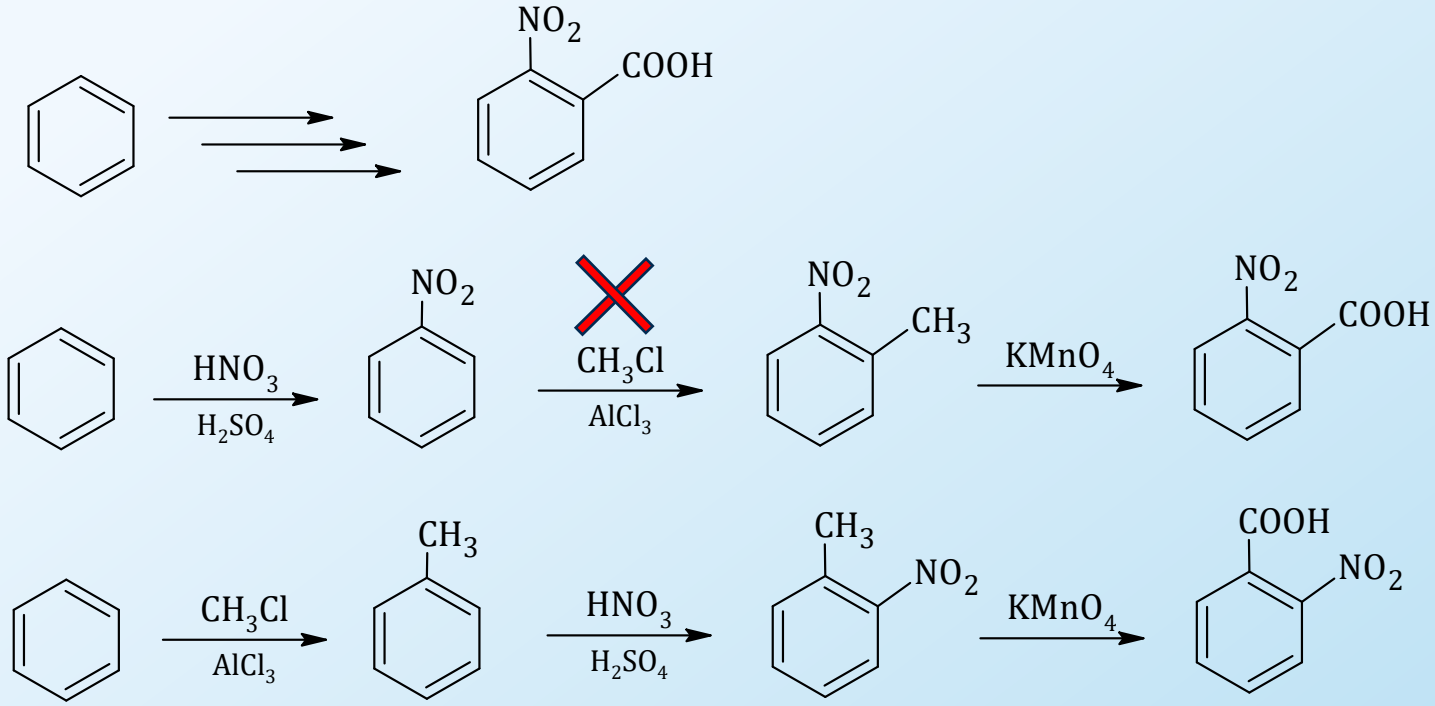
Nitro groups are electron withdrawing and FC reactions do not occur in those cases.



In the two benzenes, the right one has O, an electron donator, directly attached to benzene hence it is the activated one. Para subs more than ortho because of steric hinderance.

Synthetic Applications

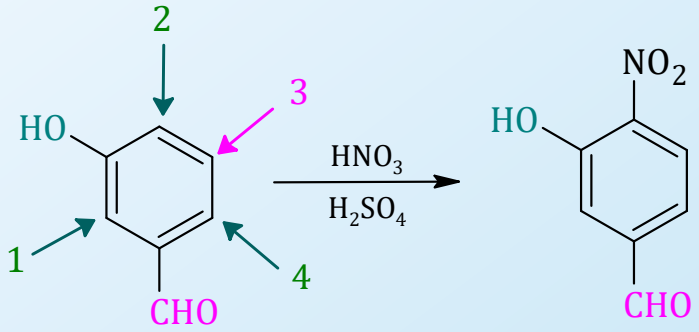
When designing a synthesis of substituted benzenes, the order in which the substituents are introduced is crucial. Example: in synthesizing ortho-nitrobenzoic acid from benzene, nitration of benzene first will deactivate the benzene ring and ortho substitution will not occur. Hence Friedel Craft alkylation has to be done first, then the nitro group can be added to the ortho position.



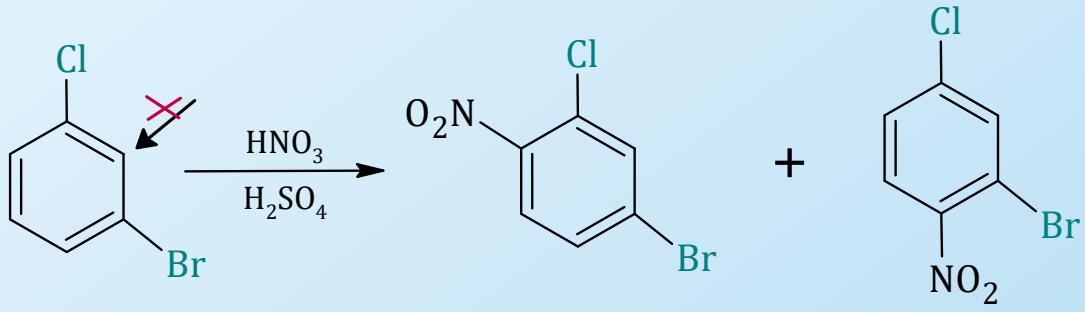
Trisubstitution on Benzene Ring

When two substituents are present on the ring initially, the more powerful activating group will determine the orientation of subsequent substitution.

- Ortho-para directors determine orientation over meta directors. See the green arrows below – those indicate the activated positions and pink is the deactivated one. The more powerful activating group decides the major product.
- Note that position 1 is sterically hindered even though activated.

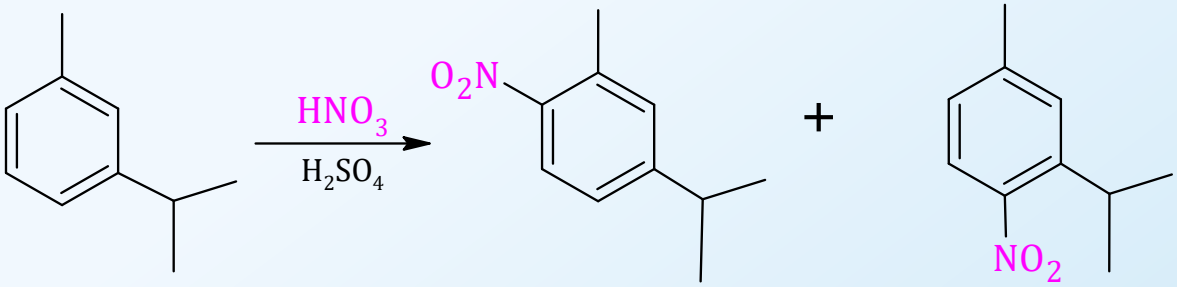


- Substitution does not occur between meta substituents due to steric hindrance

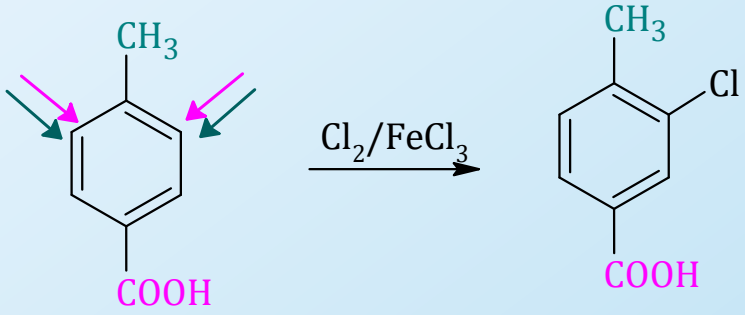


Trisubstitution on Benzene contd…

- If both groups are the same directors; then follow the steric hinderance rule.



- The best kind of synthesis when the two groups can give only one product due to activating and deactivating natures of groups.



Key Concepts

- Activating and deactivating groups
- Resonance stabilization of intermediate
- Trisubstitutions