



CHEMISTRY 2500

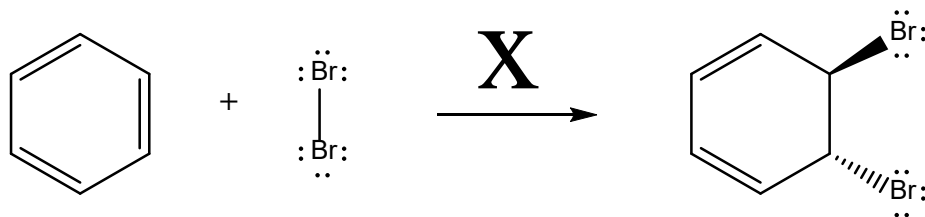
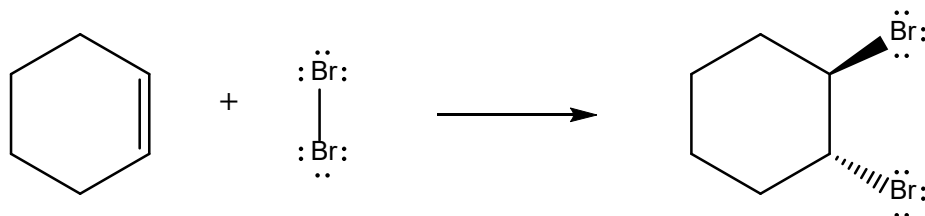
Topic #10: Synthesis Using Aromatic Materials

Spring 2020

Dr. Susan Findlay

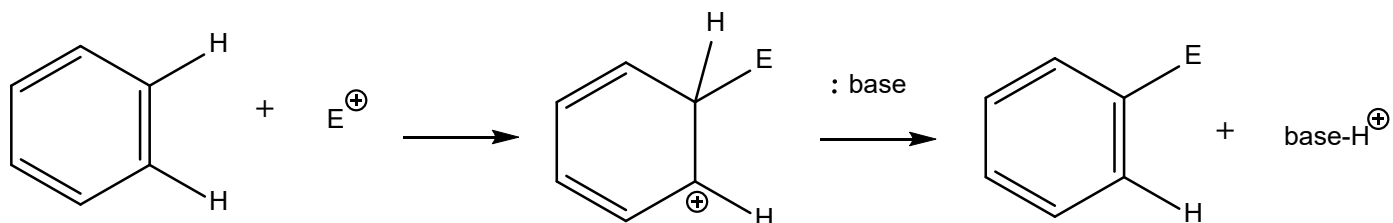
Electrophilic Aromatic Substitution

- Benzene has an electron-rich π system and can therefore act as a nucleophile; however, it is not thermodynamically favourable to lose the stability conferred by aromaticity. As such, benzene will not undergo the same electrophilic addition reactions as nonaromatic alkenes and alkynes:



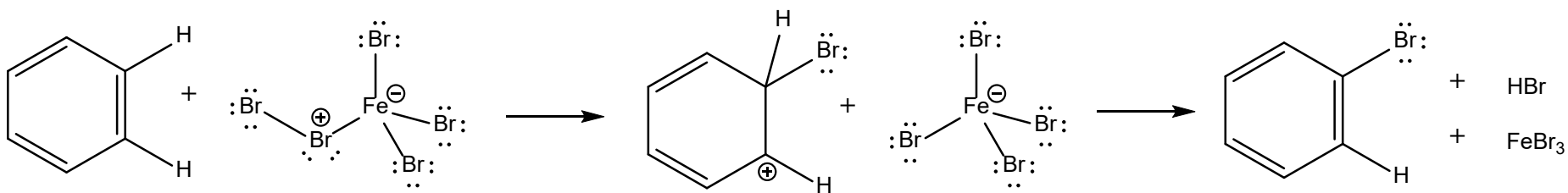
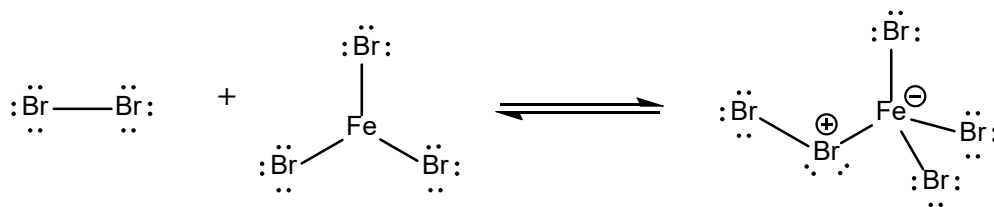
Electrophilic Aromatic Substitution

- Instead, aromatic compounds undergo addition-elimination reactions ("electrophilic aromatic substitution") in which an electrophile is added then H^+ is eliminated. The net effect is substitution of a hydrogen atom with the electrophilic group:



Electrophilic Aromatic Substitution

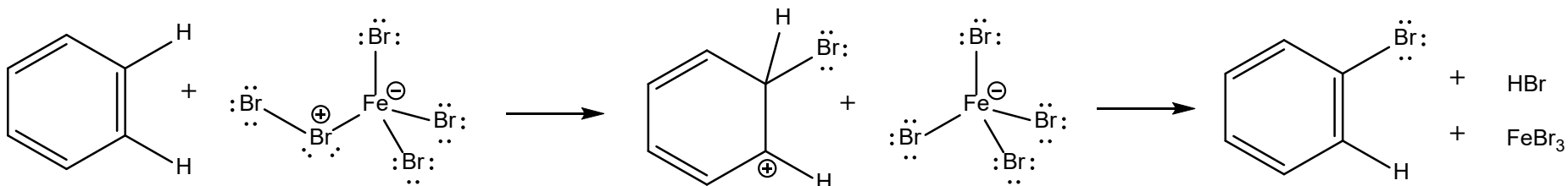
- To make an electrophile that functions as if it were "Br⁺", for example, add Br₂ to a strong Lewis acid such as FeBr₃ or AlBr₃:



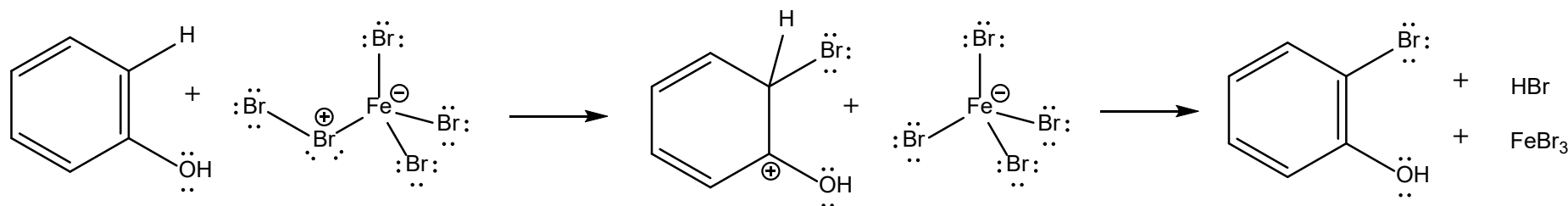
- Similarly, a "Cl⁺" analogue can be generated by reacting Cl₂ with FeCl₃ or AlCl₃.

Electrophilic Aromatic Substitution

- Looking at the mechanism on the previous page, it is obvious that the rate limiting step will be the first step. Any substituents that stabilize the carbocation intermediate will therefore make the reaction proceed more quickly. Compare:



VS.



- The hydroxy group is considered to be an **activating group** because it increases the rate of electrophilic aromatic substitution.
- All electron donating groups (even alkyl groups which are only electron donating by induction) are activating groups.



Electrophilic Aromatic Substitution

- Activating groups are **ortho/para directors**, introducing the electrophile 1,2- or 1,4- to the activating group. Why are these two products so heavily favoured over the meta (1,3-) product?



Electrophilic Aromatic Substitution

- Electrons withdrawing groups are **deactivating groups** by making the π system less nucleophilic.
- The nitro group is electron-withdrawing by resonance, and nitrobenzene reacts with electrophiles much more slowly than benzene does. It is a **meta director**, giving primarily the 1,3-product. Why?

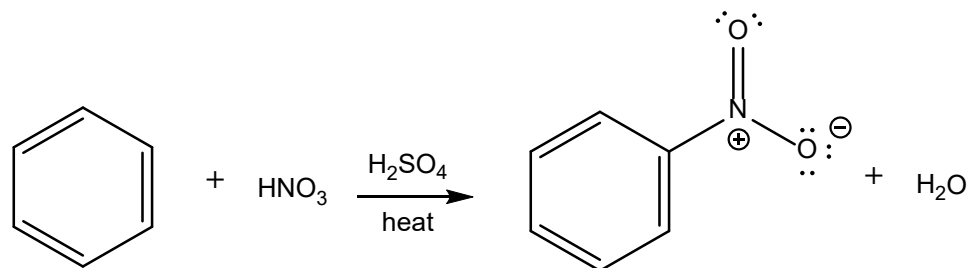
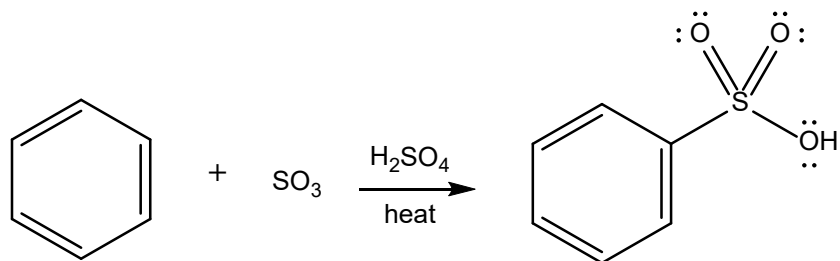
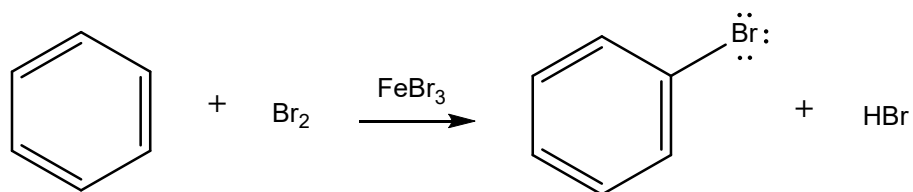


Electrophilic Aromatic Substitution

- Halobenzenes (e.g. chlorobenzene) undergo electrophilic aromatic substitution more slowly than benzene BUT give primarily the ortho and para products. Explain this apparent contradiction.

Electrophilic Aromatic Substitution

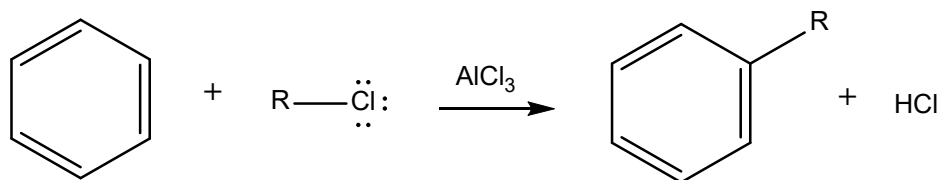
- Halogenation (Cl or Br – not I!) is not the only electrophilic aromatic substitution reaction. It is also possible to introduce nitro groups and sulfonic acid groups:



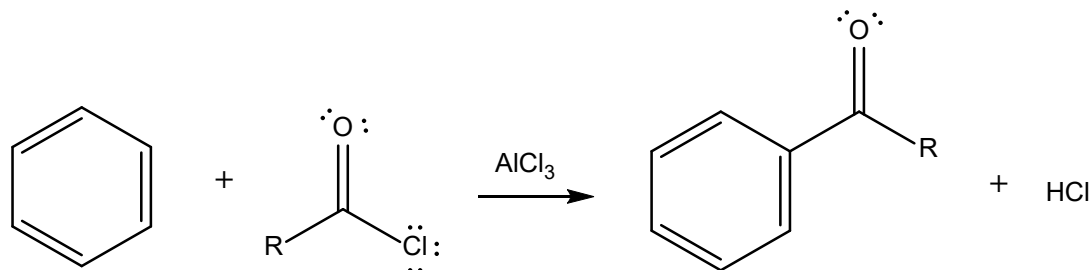
*Nitro groups can be reduced to -NH_2 by hydrogenation (H_2 and Pd/C)

Electrophilic Aromatic Substitution

- It is also possible to introduce alkyl groups and acyl groups to a benzene ring using a type of electrophilic aromatic substitution called the **Friedel-Crafts** reaction.
- Friedel-Crafts Alkylation:

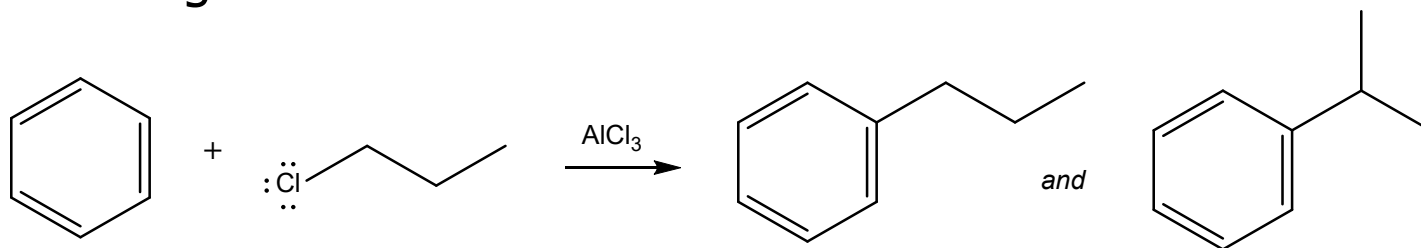


- Friedel-Crafts Acylation (R ≠ H, Cl, NH₂ or OH):



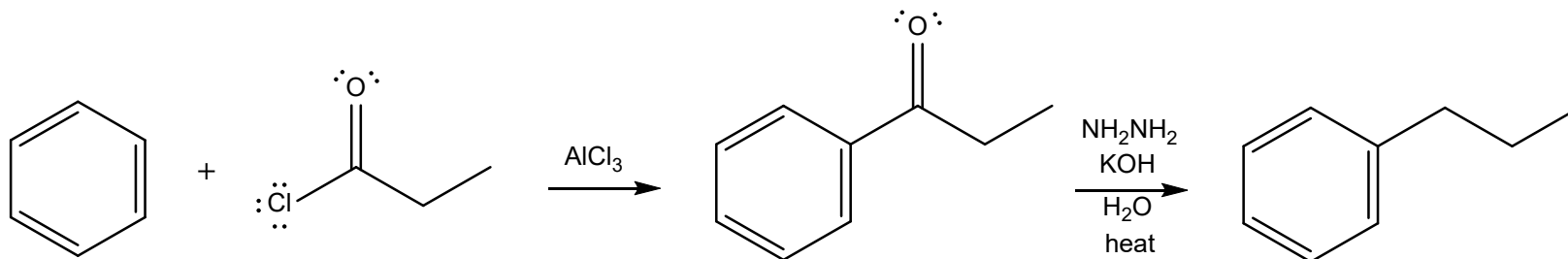
Electrophilic Aromatic Substitution

- Both reactions proceed according to the standard electrophilic aromatic substitution mechanism; however, in the alkylation reaction, the electrophile can undergo carbocation rearrangements:



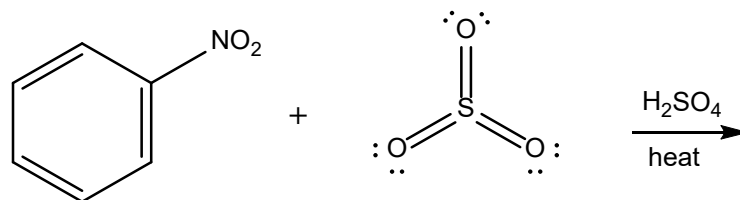
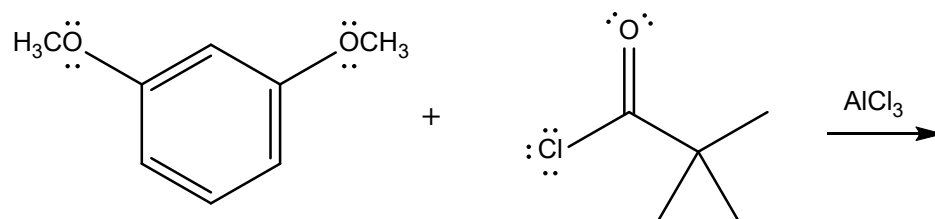
Electrophilic Aromatic Substitution

- This problem can be circumvented by doing the corresponding acylation reaction then reducing the ketone to CH_2 (using, for example, the Wolff-Kischner reaction which you'll learn about in CHEM 2600):

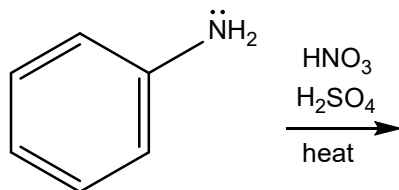
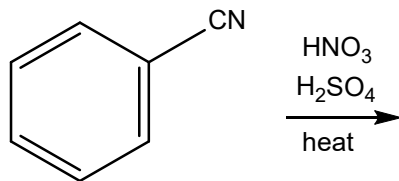


Electrophilic Aromatic Substitution

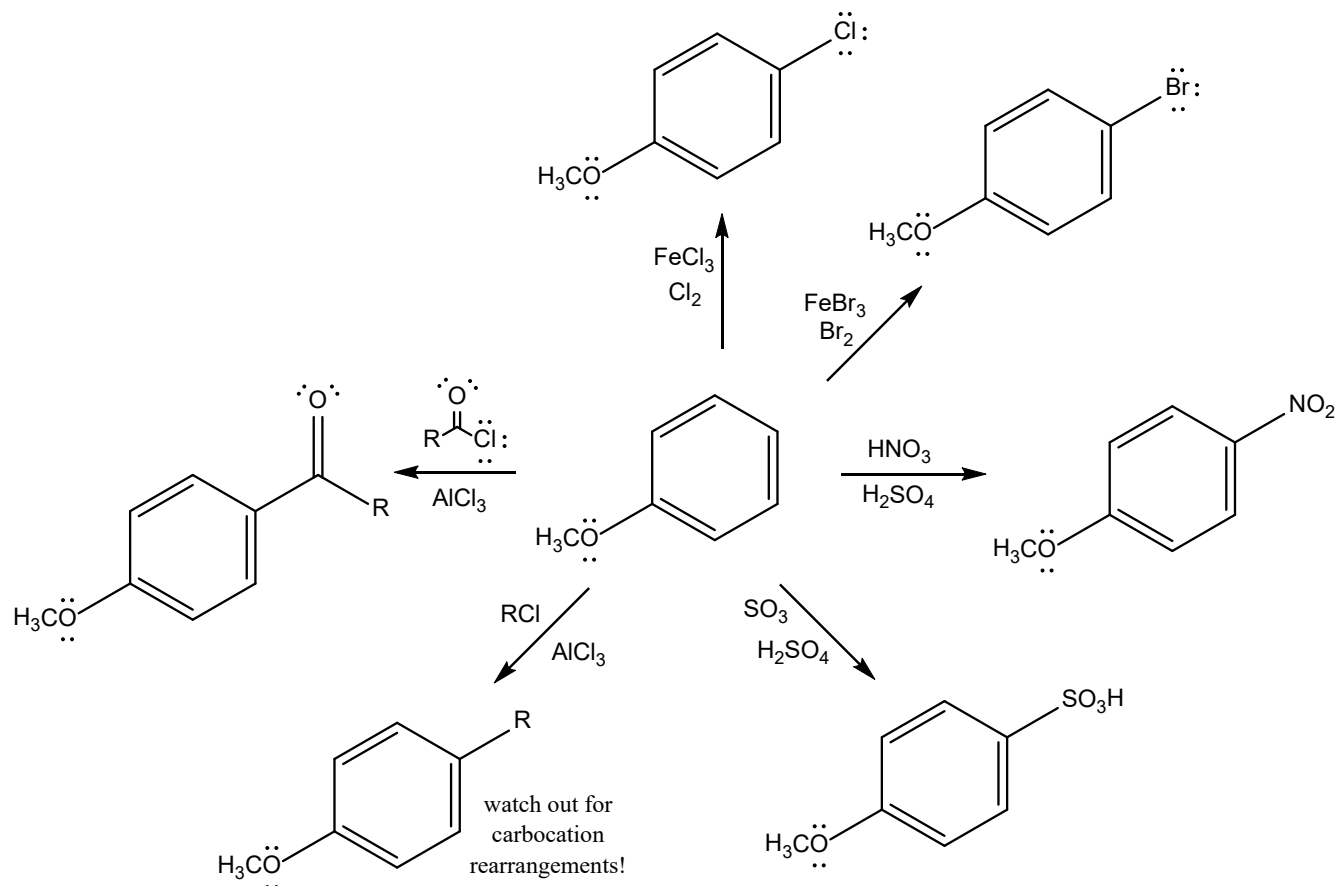
- What are the major organic products for the following reactions?



Electrophilic Aromatic Substitution

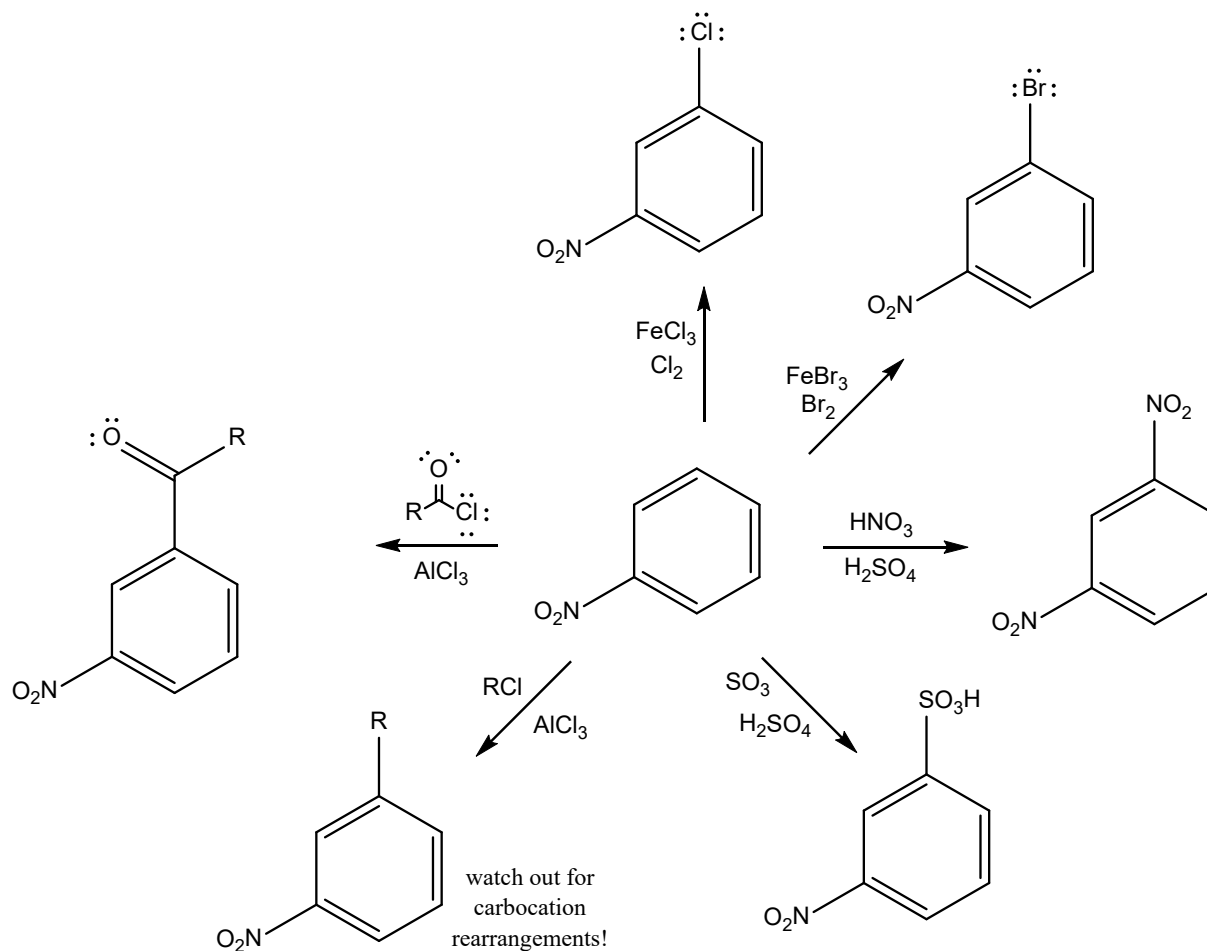


Electrophilic Aromatic Substitution (Summary)



These reactions are faster than they would be with benzene as the starting material. The electron-donating methoxy group activates the aromatic ring (makes it more nucleophilic than benzene).

Electrophilic Aromatic Substitution (Summary)



These reactions are slower than they would be with benzene as the starting material. The electron-withdrawing nitro group deactivates the aromatic ring (makes it less nucleophilic than benzene).