



CHEMISTRY 2600

Topic #9: Benzene and Its Reactions

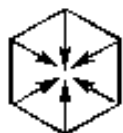
Fall 2018

Dr. Susan Findlay

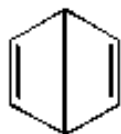
The Structure of Benzene

- Benzene was originally isolated from coal tar and found to:
 - Have a molecular formula of C_6H_6 (DU = 4)
 - Undergo substitution reactions but not addition reactions
 - Form three different dibromides ($C_6H_4Br_2$)

- In the 1800s, several possible structures were proposed:



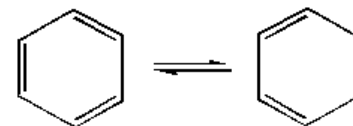
Klaus



Dewar benzene



Now known as
Prismane.

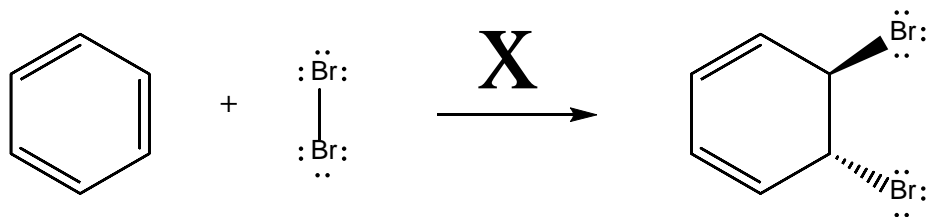
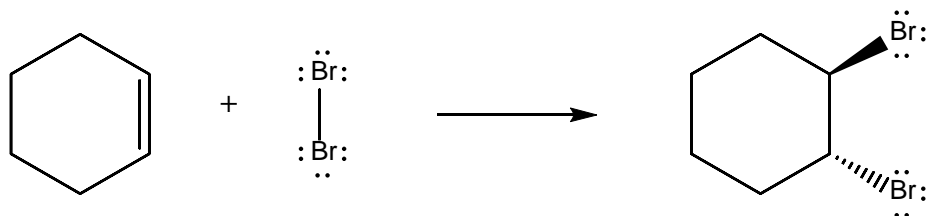


The Kekulé
structure - 1865

- The Kekulé structure was the closest; however, he thought that the molecule switched rapidly from one cyclohexatriene to the other. We now know that that's not how resonance works and that, actually, the π electrons are delocalized and all six C-C bonds have the same bond order ($1\frac{1}{2}$) and length (140 pm). We also know that benzene is unusually stable due to its **aromaticity** (see CHEM 2500 notes).

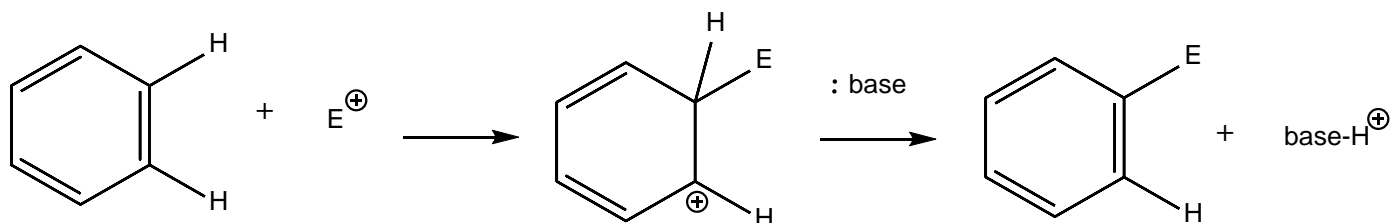
Electrophilic Aromatic Substitution

- 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:



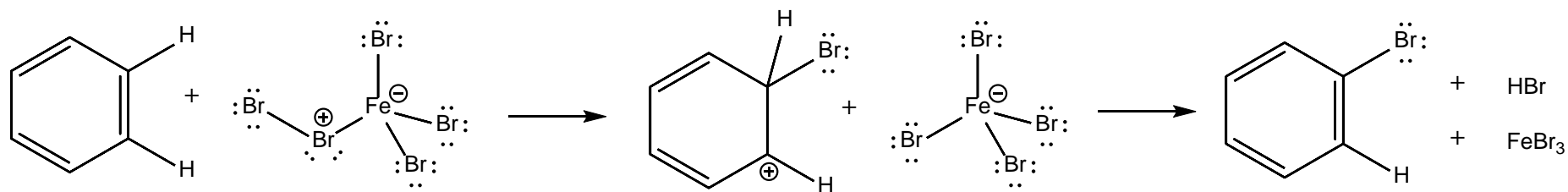
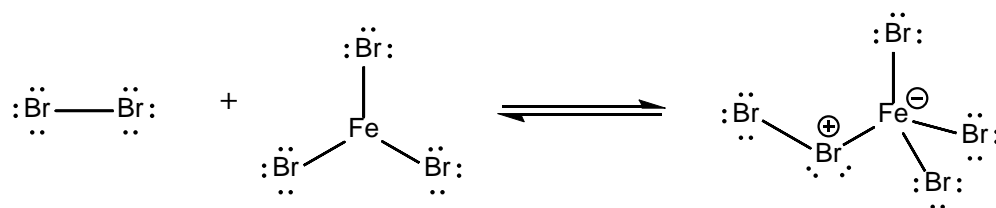
Electrophilic Aromatic Substitution

- 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

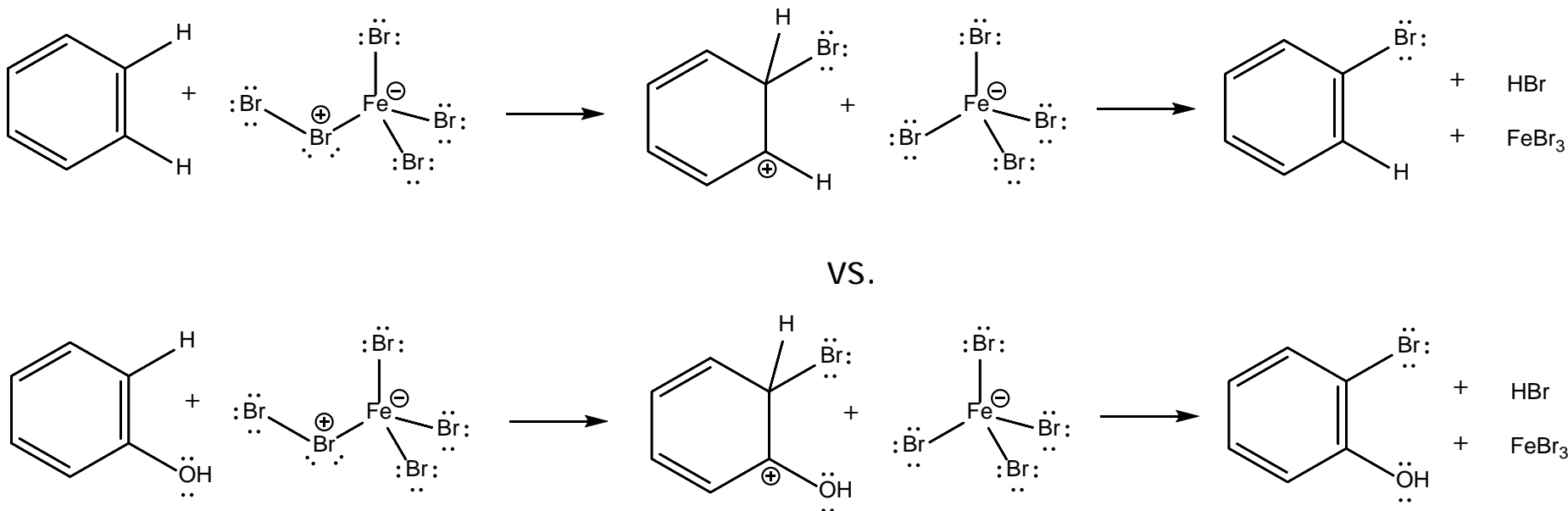
- To make an electrophile that functions as if it were "Br⁺", for example, add Br₂ to a strong Lewis acid such as FeBr₃ or AlBr₃:



- 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:



- 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?

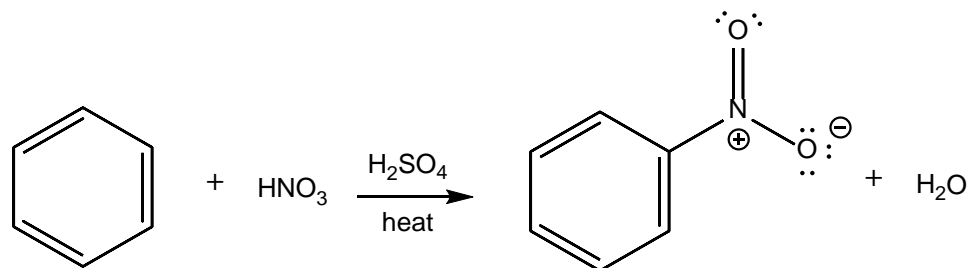
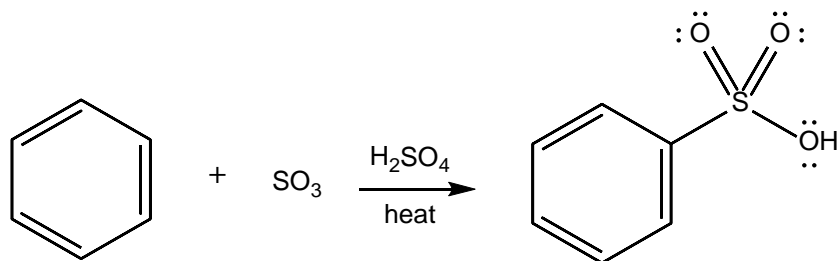
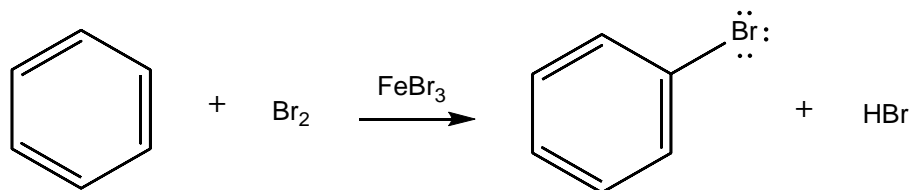


Electrophilic Aromatic Substitution

- 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

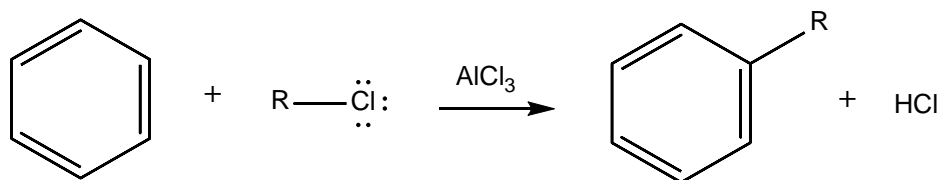
- Halogenation (Cl or Br – not I!) is not the only electrophilic aromatic substitution reaction. It is also possible to introduce nitro groups and sulfonic acid groups:



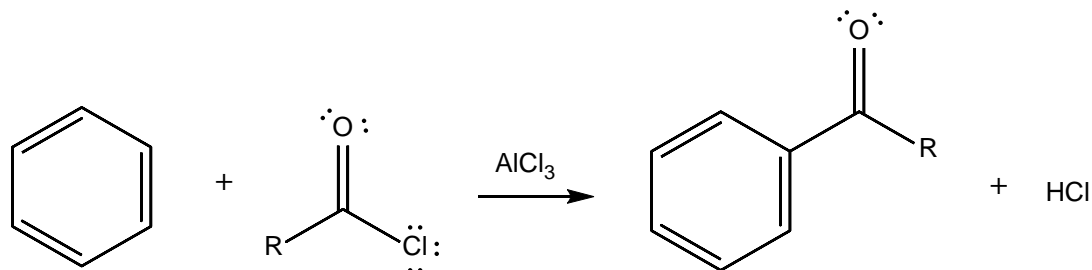
*Nitro groups can be reduced to -NH_2 by hydrogenation (H_2 and Pd/C)

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:

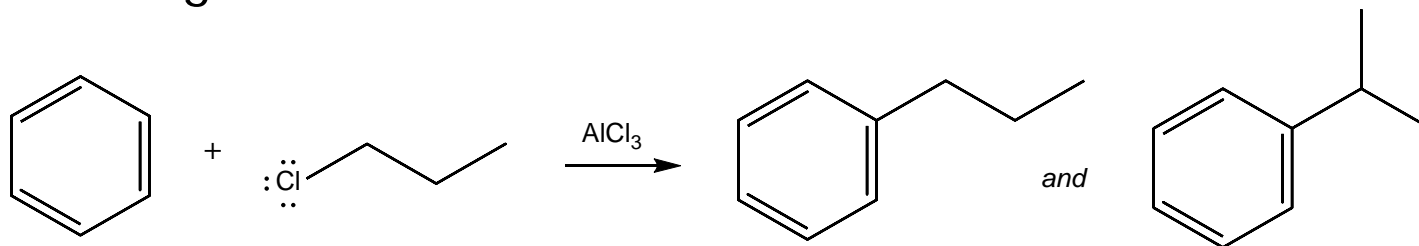


- Friedel-Crafts Acylation (R ≠ H, Cl, NH₂ or OH):



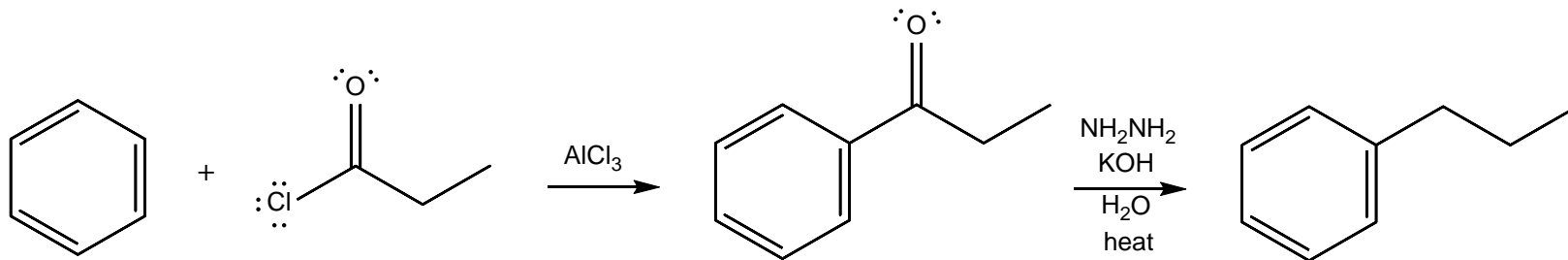
Electrophilic Aromatic Substitution

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



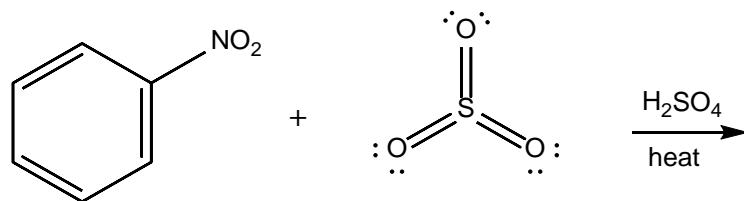
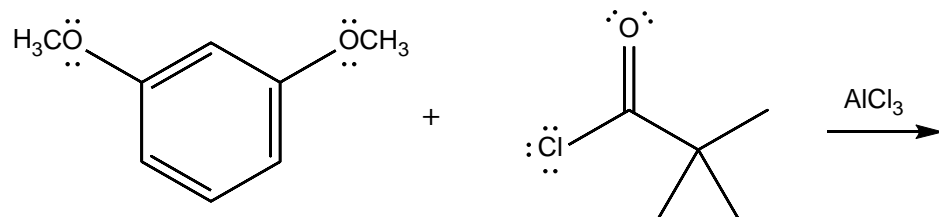
Electrophilic Aromatic Substitution

- This problem can be circumvented by doing the corresponding acylation reaction then reducing the ketone to CH_2 (using, for example, a Wolff-Kishner reduction):

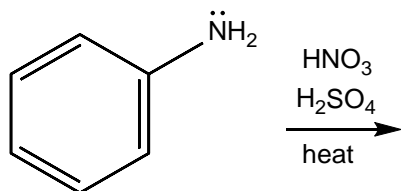
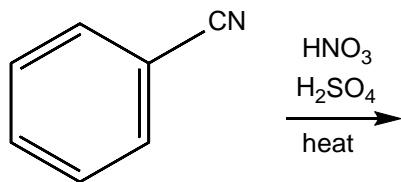


Electrophilic Aromatic Substitution

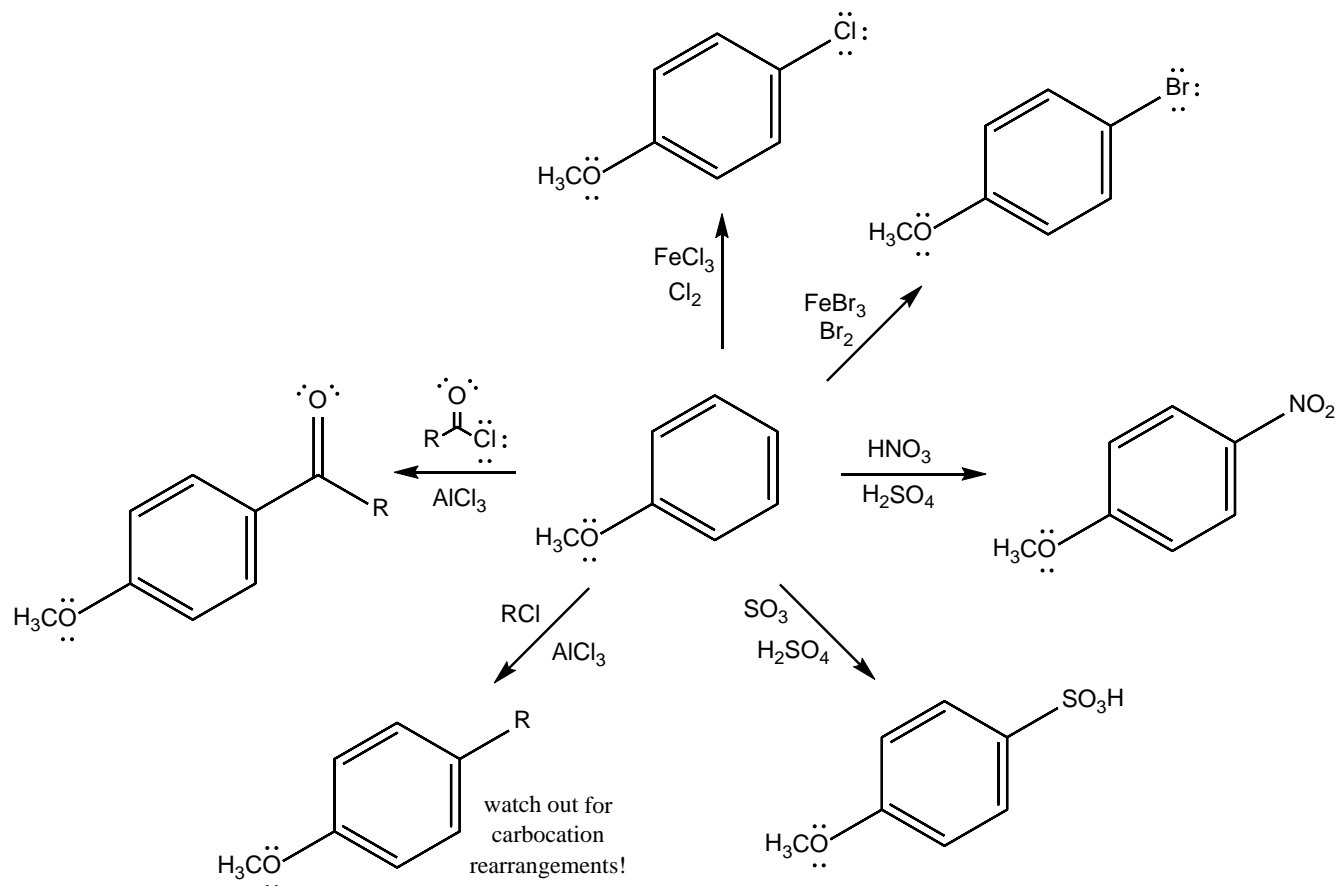
- What are the major organic products for the following reactions?



Electrophilic Aromatic Substitution

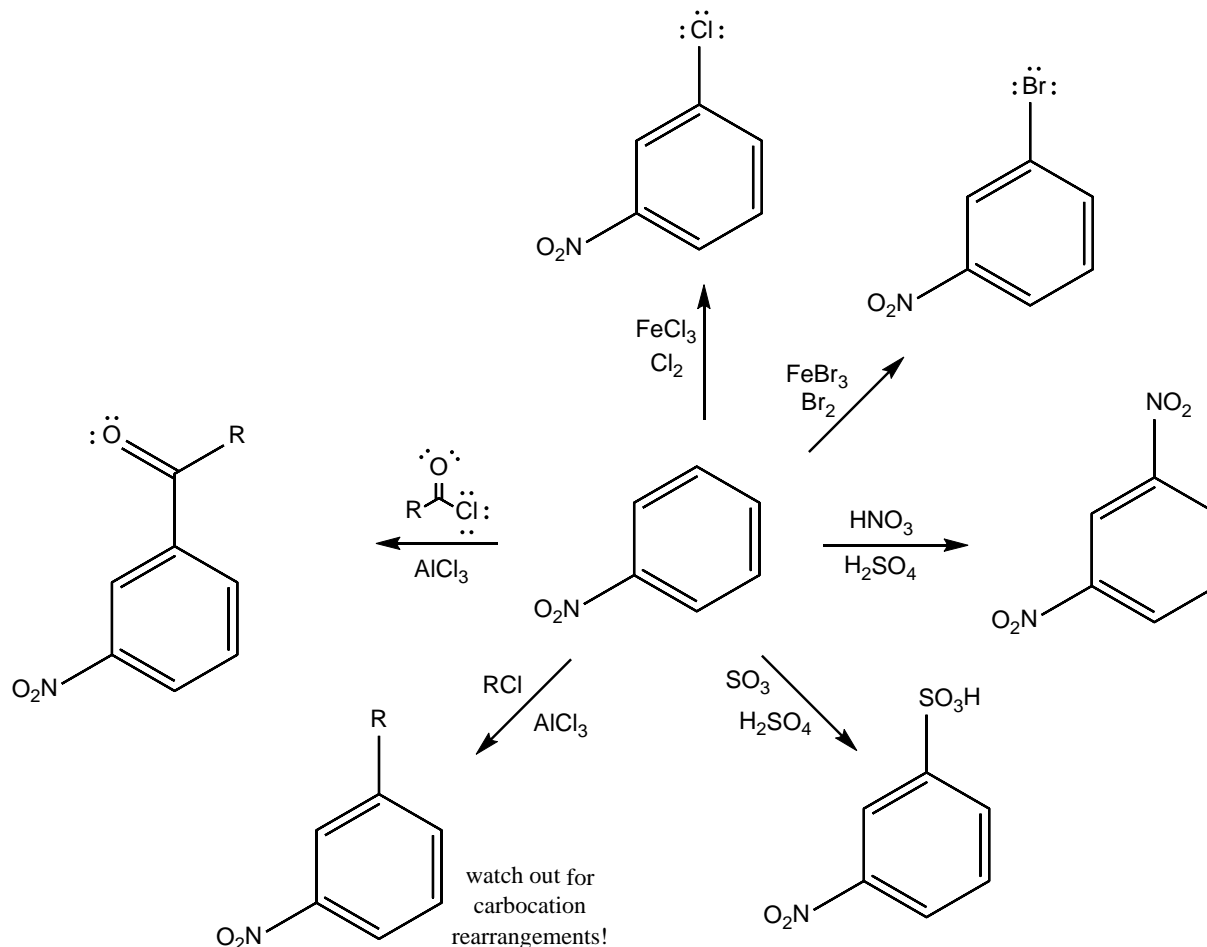


Electrophilic Aromatic Substitution (Summary)



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).

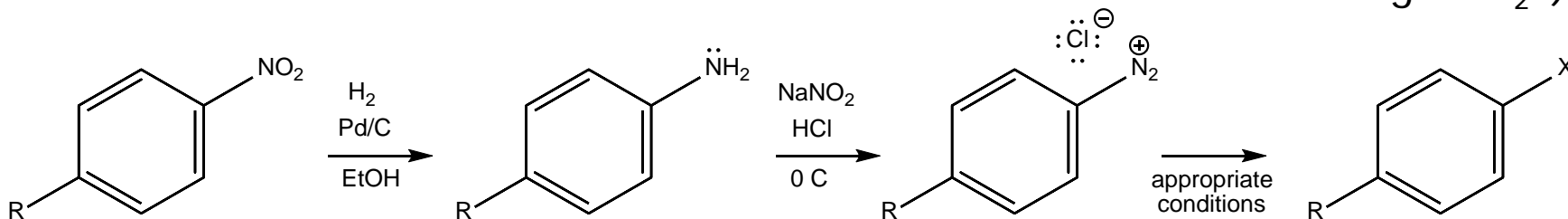
Electrophilic Aromatic Substitution (Summary)



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).

Diazonium Salts to Functionalize Benzene

- While we don't often wish to prepare a nitro compound (unless our goal is to design explosives), the nitro group can be converted to a wide variety of different substituents via a three-step process:
 - First, the nitro group is reduced to an amino group by hydrogenation
 - Second, the amino group is converted to a diazonium salt ($\text{Ar-N}_2^+\text{X}^-$)
 - Third, the diazonium salt is converted into the substituent
 - CuCl/KCl gives Ar-Cl ,
 - CuBr/KBr gives Ar-Br
 - CuCN/KCN gives Ar-CN
 - KI gives Ar-I
 - H_3PO_2 gives Ar-H
 - HBF_4/heat gives Ar-F
 - $\text{H}_2\text{O}/\text{heat}$ gives Ar-OH
(use H_2SO_4 instead of HCl when making Ar-N_2^+)



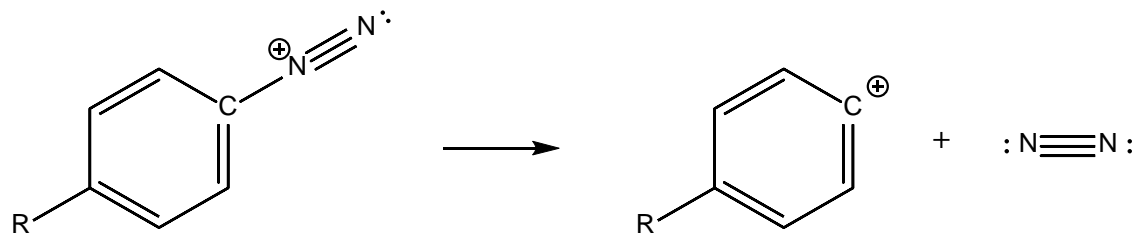


Diazonium Salts to Functionalize Benzene

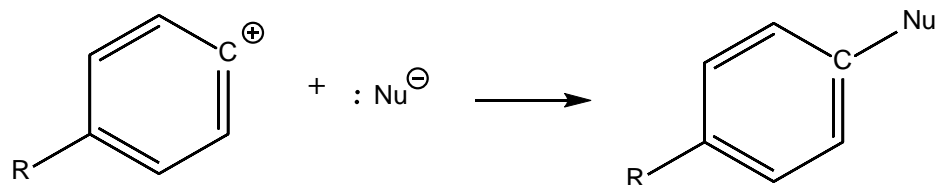
- How does the diazonium salt form?
 - First, the NaNO_2 deprotonates the acid, giving HNO_2 .
 - Second, more acid reacts with the HNO_2 giving NO^+ and water.
 - Finally, the aniline reacts with NO^+ to give the diazonium salt and water:

Diazonium Salts to Functionalize Benzene

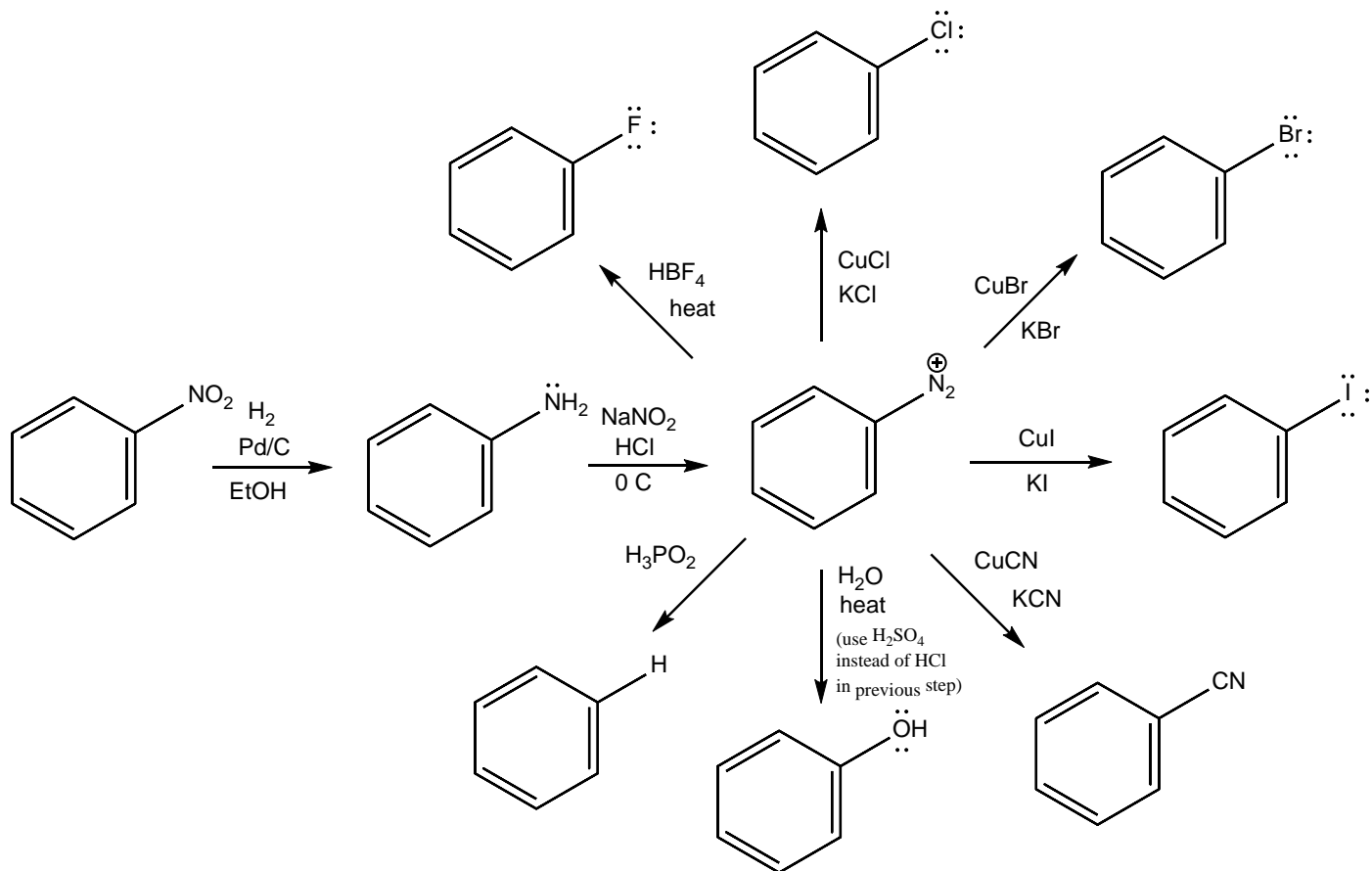
- N_2 is an **excellent** leaving group (one of the best there is), so it's not difficult to imagine it leaving, leaving behind a phenyl cation:



- This is a gross oversimplification of the real mechanism (which likely proceeds via radical intermediates), but allows us to rationalize how a diazonium salt can be converted into an aryl halide, cyanide or phenol:



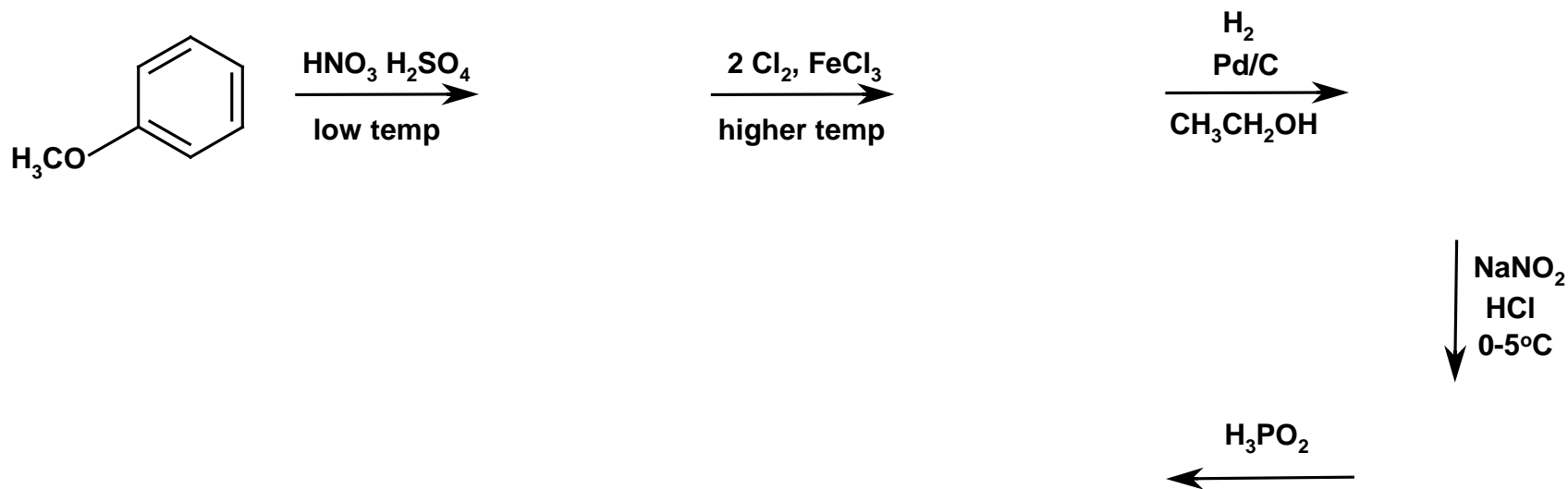
Diazonium Salts to Functionalize Benzene



*Be careful handling diazonium salts. They tend to be explosive!
If you want to store a diazonium salt, it has to be at low temperature and the counterion has to be large (BF_4^- or PF_6^-)* 21

Diazonium Salts to Functionalize Benzene

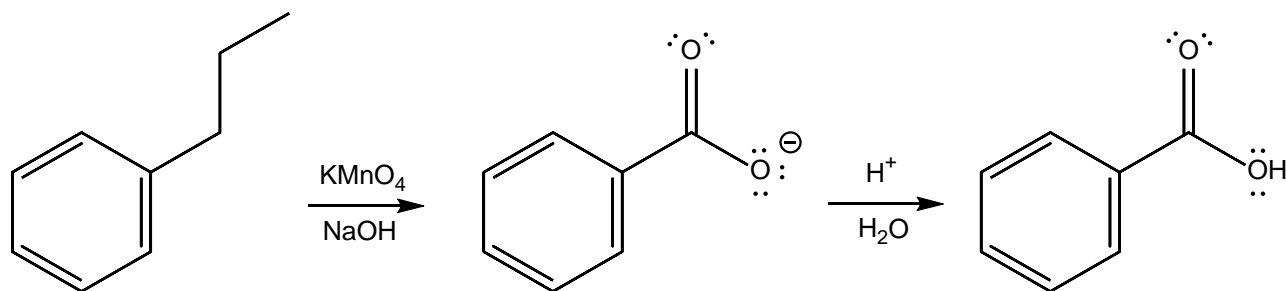
- Why would you want to introduce a nitro group just to take it off again? ($\text{ArH} \rightarrow \text{ArNO}_2 \rightarrow \text{ArNH}_2 \rightarrow \text{ArN}_2^+ \rightarrow \text{ArH}$)
- Sometimes, NO_2 is useful as a "blocking" group. Consider the following sequence of reactions:



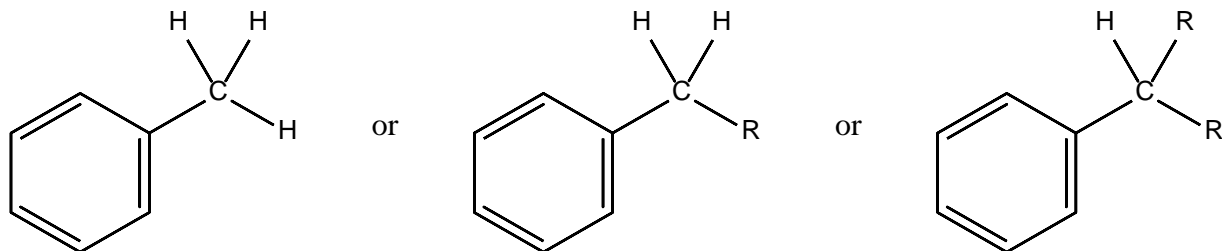
This is the only way to prevent Cl from adding para to $-\text{OCH}_3$. 22

Reactions of Benzene (Oxidation)

- Recall that when we discussed oxidizing agents, you were warned that potassium permanganate (KMnO_4) had to be used cold and with care. At room temperature, KMnO_4 can oxidize an alkyl chain right off a benzene ring!



- This reaction works on any alkyl chain which has a benzylic hydrogen atom:



Reactions of Benzene (Oxidation)

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

