

## Week 6

# Electrophilic Aromatic Substitution

## 6.1 Electrophilic Aromatic Substitution 1

2/15:

- Discusses the aromaticity of fluorescein as an example to review from last class.
- Reactions of aromatic compounds are divided into two classes: Electrophilic and nucleophilic aromatic substitutions.
- Example:
  - $\text{C}_6\text{H}_6 \xrightarrow{\text{H}_3\text{O}^+} \text{C}_6\text{H}_6$  means no reaction?
  - $\text{C}_6\text{H}_6 \xrightarrow{\text{D}_3\text{O}^+} \text{C}_6\text{D}_6$ ; thus, a substitution is occurring.
- Mechanism:

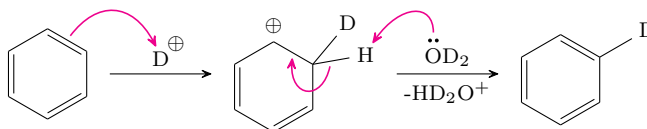


Figure 6.1: Electrophilic aromatic substitution mechanism.

- To begin, one of the  $\pi$ -bonds of benzene attacks  $\text{D}^+$ . This causes the loss of aromaticity, but the carbocation is highly resonance delocalized.
  - Although we *could* make an alcohol at this point, this would lead to the loss of aromaticity in the product, so we won't do that.
  - Instead, we do an  $\text{E}_1$ -type reaction.
  - The first step is the RDS.
  - The intermediate in this mechanism is called the **arenium ion**, the **Wheland intermediate**, or the **sigma complex**.
  - Note that the electrophile used in this reaction has to be a very special, very reactive, very strong electrophile in order to make up the energy gap.
- We know that the sigma complex exists because we can trap the intermediate.
  - Whether or not we see the product react again depends on whether the product or starting material is more nucleophilic.
  - Adding an EDG to the benzene makes the reaction proceed faster.

- A good EDG will stabilize the arenium ion, lowering the activation barrier of the first step (the RDS).
- Halogenation.
- General form.
 
$$\text{PhH} + \text{Br}_2 \xrightarrow{\text{cat. FeBr}_3} \text{PhBr} + \text{HBr}$$
  - $\text{Br}_2$  is too unreactive to have chemistry with benzene on its own.
  - In particular, when we say that  $\text{Br}_2$  is too unreactive, we mean that there is not enough  $\text{Br}^+$  character, i.e., it is not a good enough electrophile.
  - To overcome the problem, we add  $\text{Br}_2$  to  $\text{FeBr}_3$ , a good Lewis acid with an open valence site. It follows that  $\text{Br}-\text{Br}^+-\text{Fe}^-\text{Br}_3$  is a super awesome electrophile!
- Mechanism.

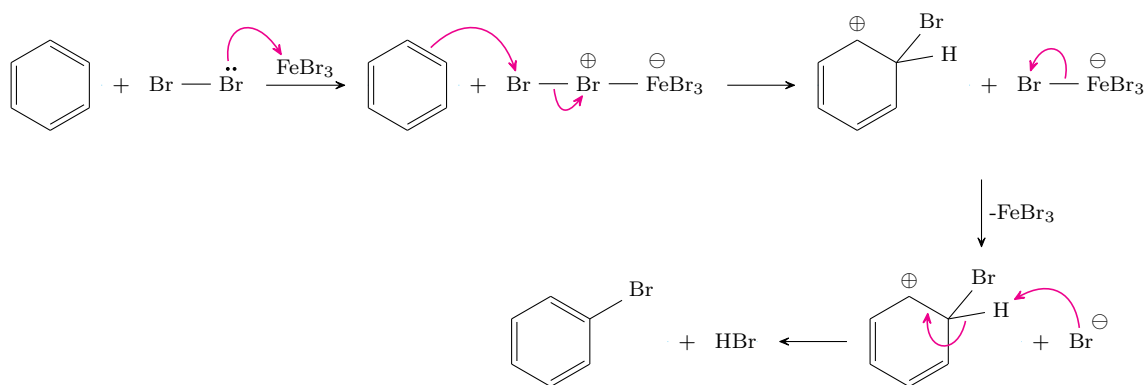
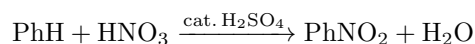
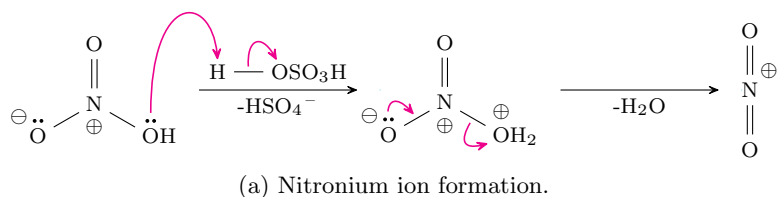


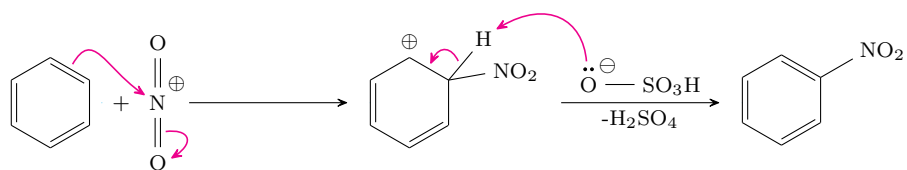
Figure 6.2: EAS halogenation mechanism.

- For chlorination, we use catalytic  $\text{AlCl}_3$ .
- For iodination, we use catalytic  $\text{CuI}_2$ .
- Nitration.
- General form.



- We start with nitric acid, but as before, the nitrogen is not electrophilic enough.
- Thus, we add catalytic sulfuric acid. Since  $\text{H}_2\text{SO}_4$  is stronger than  $\text{HNO}_3$ , it protonates nitric acid to  $\text{H}_2\text{NO}_3^+$ , which quickly splits into  $\text{H}_2\text{O} + \text{NO}_2^+$ , where  $\text{NO}_2^+$  is the nitronium ion (a super electrophile!).
- Mechanism.





(b) Nitration of benzene.

Figure 6.3: EAS nitration mechanism.