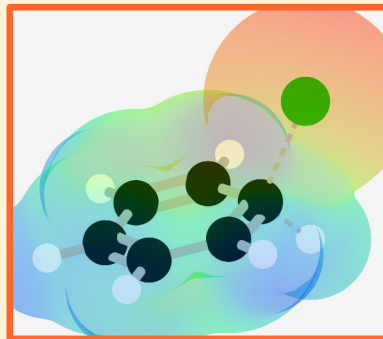


HIGHLIGHTS

- General mechanism (not showing the different activation methods).
- Bromination (& chlorination).
- Nitration (& reduction of the nitro group to an amine).
- Sulfonation (is a reversible reaction).
- Friedel-Crafts alkylation (is of limited value due to over addition and rearrangements).
- Friedel-Crafts acylation (solves the problems of the Friedel-Crafts alkylation).



Electrophilic aromatic substitution is a general reaction that exchanges a hydrogen atom on an aromatic (benzene) ring with an electrophile. The most common examples are halogenation, nitration, sulfonation and the Friedel-Crafts reactions.

The reaction involves activation of the electrophile to create a powerful electrophile (often a cation). This is necessary as aromatic rings are unusually stable due to delocalization of their π electrons. This is the only step that differs for all the reactions shown here. The next step is addition of the electrophile to the ring. This is hard as it breaks the aromaticity. The resulting cationic intermediate is resonance stabilized but is not aromatic. Finally, proton transfer or deprotonation regenerates the aromatic ring and gives the product. This step is easy as the molecule regains the stability of aromaticity. Almost any basic molecule can achieve it.

CHEMISTRY CLASSICS

π NUCLEOPHILES PART 4

ELECTROPHILIC AROMATIC SUBSTITUTION



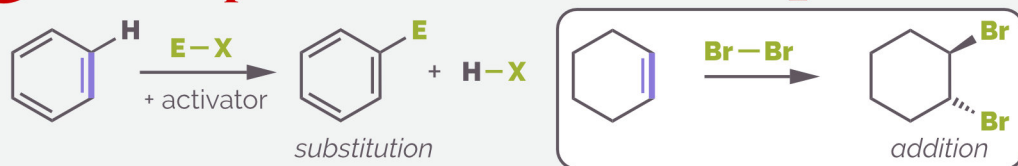
© gjr for makingmolecules.com
This handout is shared under a
Creative Commons Attribution-
NonCommercial-ShareAlike
BY-NC-ND-SA 4.0 licence.



Page 47

Electrophilic Aromatic Substitution

1. Electrophilic aromatic substitution $S_{E}Ar$ reaction



- Aromatic rings undergo **substitution** while alkenes participate in addition reactions
- Difference due to **stability of aromatic rings** caused by delocalization of electrons

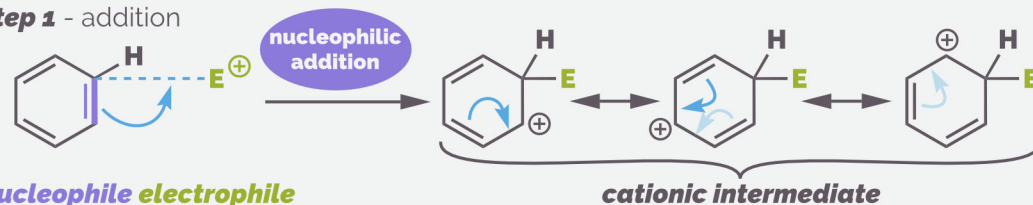
2. General mechanism of $S_{E}Ar$ reaction

step 0 - electrophile activated by Lewis acid or dehydration



- The main difference between all $S_{E}Ar$ reactions is **activation** of the **electrophile**

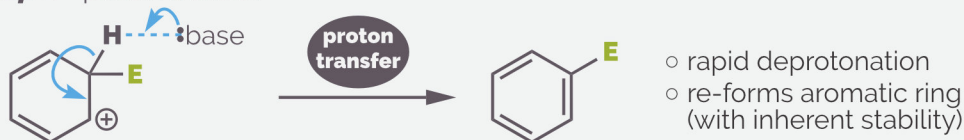
step 1 - addition



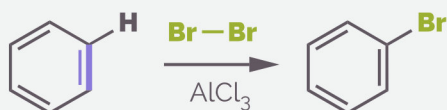
nucleophile electrophile

1. Electron rich **aromatic ring** is the **nucleophile**;
2. Attacks **activated electrophile**;
3. **Breaks** the aromaticity (disfavored);
4. Electrons of **carbocation intermediate** are delocalized but not aromatic.

step 2 - proton transfer

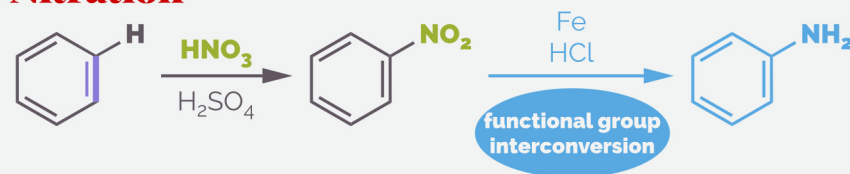


3. Bromination



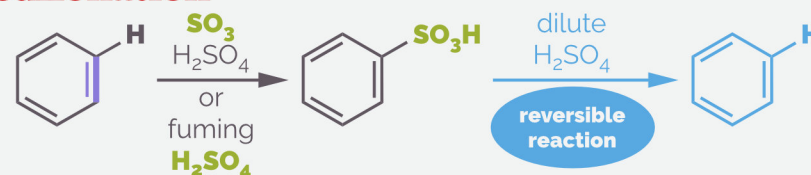
- activation involves Lewis acid activation of halogen
- works for chlorination as well

4. Nitration



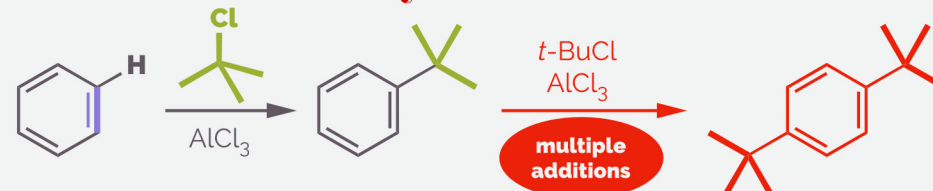
- Activation involves the dehydration of nitric acid
- Nitro group readily converted to amine by reduction with various metals in acid

5. Sulfonation



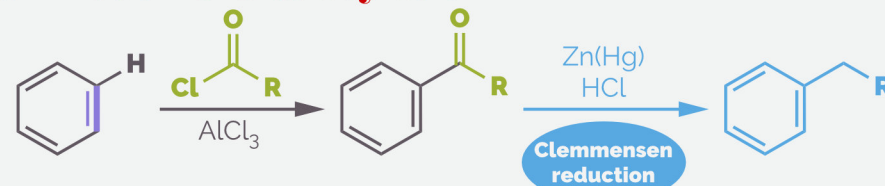
- Sulfur trioxide may not need activation
- Reaction reversible and used as a blocking group

6. Friedel-Crafts alkylation



- Activation of alkyl halide must form stabilized cation or rearrangements an issue
- Activates ring making multiple additions a problem

6. Friedel-Crafts acylation



- Alkyl halide activated with Lewis acid
- Must form stabilised carbocation or rearrangements an issue
- Activates ring making multiple additions a problem