16.S: CHEMISTRY OF BENZENE - ELECTROPHILIC AROMATIC SUBSTITUTION (SUMMARY)

CONCEPTS & VOCABULARY

16.0 Introduction

- Aromatic compounds don't typically undergo addition reactions.
- Aromatic compounds typically undergo substitution reactions.

16.1 Electrophilic Aromatic Substitution Reactions: Bromination

- Aromatic molecules only react with strong electrophiles.
- The first step in many electrophilic aromatic substitution mechanisms is activation or formation of the electrophile.
- The electrophilic aromatic substitution mechanism occurs in two steps. The first is addition of the electrophile to the ring and the second is elimination of a hydrogen from the ring to re-form the pi bond and restore aromaticity.
- In bromination of an aromatic ring, molecular bromine (Br_2) is reacted with iron tribromide ($FeBr_3$) to form the strongly electrophilic bromine cation and $FeBr_4$. Following this, the aromatic ring is reacted with the bromine cation and adds to the ring to form a benzenonium cation. This molecule then reacts with one of the bromine atoms from $FeBr_4$ to lose a hydrogen forming the product and HBr as well as reforming the iron tribromide.

16.2 Other Aromatic Substitutions

- Aluminum bromide ($AlBr_3$) can be used in place of $FeBr_3$ to create the bromine cation. Also the chlorides of alumnium and iron can also be used to create a chlorine cation which will also undergo electrophilic aromatic substitution.
- Reacting nitric acid and sulfuric acid forms nitronium (NO_2^+), which will react with aromatics for form nitro compounds.
- Sulfonation of aromatics can be accomplished by reacting with sulfur trioxide and sulfuric acid to yield sulfonic acids.

16.3 Alkylation and Acylation of Aromatic Rings - The Friedel-Crafts Reaction

- Friedel-Crafts reactions incorporate activation of alkyl and acyl halides by reacting them with a Lewis Acid catalyst, $AlCl_3$.
- Friedel-Crafts alkylations allow for adding alkyl chains to aromatic rings.
- After activation with aluminum chloride, alkyl carbocations can undergo rearrangement if it leads to a more stable intermediate.
- Friedel-Crafts acylations add alkyl ketones to aromatic rings.

16.4 Substituent Effects in Substituted Aromatic Rings

- Aromatic inductive effects are caused by differences in electronegativity between atoms bonded to the ring and the ring carbons.
- Most common heteroatoms (N, O, halogens) donate electron density toward the ring inductively.
- Aromatic resonance effects are caused by conjugation of substituents with the pi bonds of the ring.
- Substituents that increase the electron density of the ring activate the ring (make more reactive) toward electrophilic substitution.
- Substituents that decrease the electron density of the ring deactivate the ring (make less reactive) toward electrophilic substitution.

16.4b An Explanation of Substituent Effects

- Steric effects can increase para substitution as ortho/para directors become larger.
- Activating groups are ortho/para (o, p) directors.
- Deactivating groups are meta directors.
- Alkyl groups inductively donate electron density to the ring making them o, p directors.
- Groups with an O or N attached to the aromatic ring are activators and o, p directors due to resonance.
- Groups with a pi bond attached to the aromatic ring are deactivators and m directors due to resonance.
- Halogens are o, p directors, but are deactivators.

16.5 Trisubstituted Benzenes: Additivity of Effects

- When there is more than one group attached to an aromatic ring, these groups may reinforce directing effects (cooperative) or have opposing directing effects (non-cooperative).

16.6 Nucleophilic Aromatic Substitution

- Highly activated aromatic rings can react with strong nucleophiles through a substitution mechanism.
- The mechanism typically begins with addition of a nucleophile followed by elimination of a leaving group.

16.7 Benzyne

- Under highly reactive conditions, a mechanism that begins with elimination for form a benzyne molecule intermediate followed by addition of a nucleophile resulting in nucleophilic aromatic substitution.

16.8 Oxidation of Aromatic Compounds

- Alkyl side-chains can be oxidized to benzoic acid (or a benzoic acid derivative if there are other groups present on the ring) by potassium permanganate ($KMnO_4$) as long as the benzylic carbon has at least one hydrogen attached.
- Radical halogenation will occur at the benzylic carbon, due to stabilization of radical intermediates.

16.9 Reduction of Aromatic Compounds

- Catalytic hydrogenation (H_2 and a catalyst) can be used to reduce many aromatic side-chains.
- Nitro groups can be selectively reduced to amines with $SnCl_2$ and HCl or with Fe and HCl.
- Carbonyls adjacent to the ring can be reduced by either Clemmensen reduction (Zn(Hg) and HCl.
- Birch reductions can reduce aromatic rings.

16.10 Synthesis of Polysubstituted Benzenes

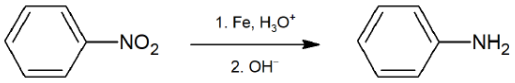
- Multistep synthesis requires a combination of forward (from the starting material) and backward (from the target compound) thinking.

SKILLS TO MASTER

- Skill 16.1 Write detailed electrophilic aromatic substitution mechanisms (halogentation, nitration, sulfonation, Friedel-Crafts alkyation and acylation).
- Skill 16.2 Write detailed mechanisms for formation of reactive electrophiles.
- Skill 16.3 Predict and explain rearrangements that can occur during Friedel-Crafts alkylation.
- Skill 16.4 Explain activation and deactivation of aromatic rings toward electrophilic aromatic substitution.
- Skill 16.5 Explain ortho, para vs. meta directing during electrophilic aromatic substitution reactions.
- Skill 16.6 Combine activation and deactivation and directing effects to predict products of reactions of substituted aromatic molecules.
- Skill 16.7 Write detailed nucleophilic aromatic substitution mechanisms through addition-elimination.
- Skill 16.8 Write detailed nucleophilic aromatic substitution mechanisms through benzyne elimination-addition.
- Skill 16.9 Draw products of oxidation of aromatic molecules.
- Skill 16.10 Draw products of reduction of aromatic side-chains.
- Skill 16.11 Draw mechanisms for reduction of aromatic rings.
- Skill 16.12 Solve multistep synthesis problems incorporating directing effects and side-chain reactions.

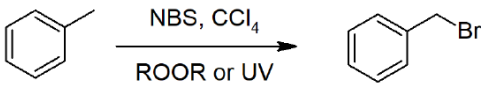
SUMMARY OF REACTIONS

Reduction of Nitro Group



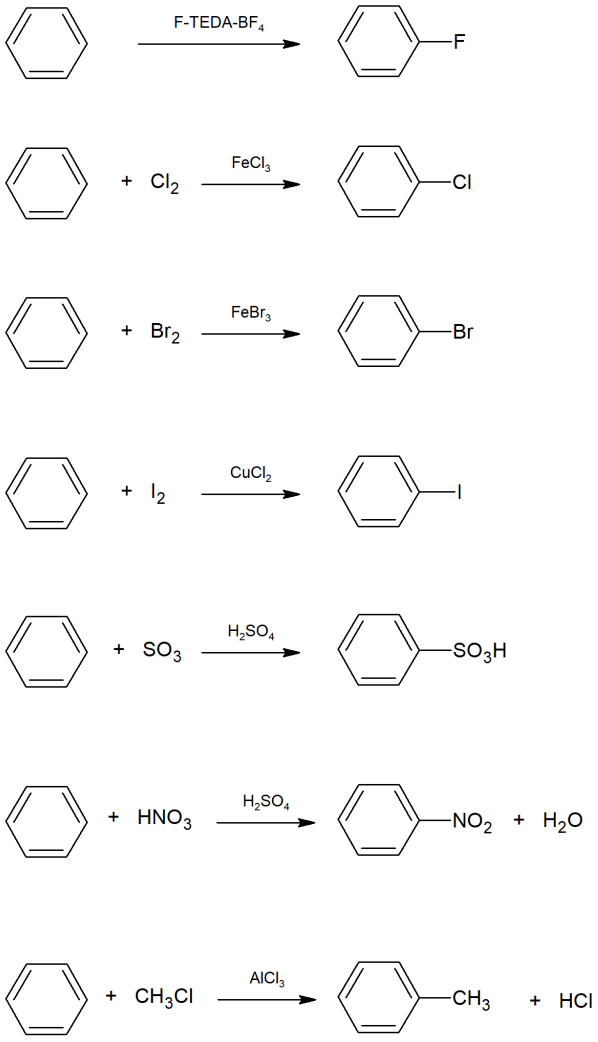
Oxidation of Alkylbenzene

Benzylic Bromination of Alkylbenzene



Reduction of Aromatic Compounds

Electrophilic Aromatic Substitution



Nucleophilic Aromatic Substitution