Chapter 12
Reactions of Arenes:
Electrophilic Aromatic Substitution

\[
\text{H} + \overset{\delta^+}{E} \overset{\delta^-}{Y} \rightarrow \text{H} + \overset{E}{Y}
\]
12.1
Representative Electrophilic Aromatic Substitution Reactions of Benzene
Electrophilic aromatic substitutions include:

- Nitration
- Sulfonation
- Halogenation
- Friedel-Crafts Alkylation
- Friedel-Crafts Acylation
Table 12.1: Nitration of Benzene

Nitrobenzene (95%)
Table 12.1: Sulfonation of Benzene

\[
\text{Benzenesulfonic acid (100%)}
\]
Table 12.1: Halogenation of Benzene

\[
\begin{align*}
\text{Benzene} + \text{Br}_2 & \xrightarrow{\text{FeBr}_3} \text{Bromobenzene} + \text{HBr} \\
\end{align*}
\]

Bromobenzene (65-75%)
Table 12.1: Friedel-Crafts Alkylation of Benzene

\[
\text{Table 12.1: Friedel-Crafts Alkylation of Benzene}
\]

\[
\text{H} + (\text{CH}_3)_3\text{C} + \text{AlCl}_3 \rightarrow \text{C}((\text{CH}_3)_3) + \text{HCl}
\]

\textit{tert-Butylbenzene (60%)}

\[
\text{H} + (\text{CH}_3)_3\text{C} + \text{AlCl}_3 \rightarrow \text{C}((\text{CH}_3)_3) + \text{HCl}
\]
Table 12.1: Friedel-Crafts Acylation of Benzene

1-Phenyl-1-propanone (88%)
12.2
Mechanistic Principles
of
Electrophilic Aromatic Substitution
Step 1: attack of electrophile on $\pi$-electron system of aromatic ring

highly endothermic

carbocation is allylic, but not aromatic
Step 2: *loss of a proton from the carbocation intermediate*

This step is highly exothermic.

It restores aromaticity of the ring.
Based on this general mechanism:

what remains is to identify the electrophile in nitration, sulfonation, halogenation, Friedel-Crafts alkylation, and Friedel-Crafts acylation to establish the mechanism of specific electrophilic aromatic substitutions
12.3
Nitration of Benzene
Nitration of Benzene

Electrophile is nitronium ion

\[
\text{H} + \text{HONO}_2 + \text{H}_2\text{SO}_4 \rightarrow \text{NO}_2 + \text{H}_2\text{O}
\]
Step 1: attack of nitronium cation on π-electron system of aromatic ring
Step 2: loss of a proton from the carbocation intermediate
Where does nitronium ion come from?

\[
\begin{align*}
\text{H}_2\text{SO}_4 &
\quad \rightarrow
\quad \begin{array}{c}
\overset{\text{+}}{\text{O}} = \overset{\text{+}}{\text{N}} = \overset{\text{+}}{\text{O}} \\
\overset{\text{O}}{\text{H}}
\end{array}
\quad +
\quad \overset{\text{+}}{\text{O}} = \overset{\text{+}}{\text{N}} = \overset{\text{+}}{\text{O}}
\end{align*}
\]

\[\text{H}_2\text{SO}_4 \quad \leftrightarrow \quad \overset{\text{O}}{\text{N}} = \overset{\text{O}}{\text{H}}\]
12.4
Sulfonation of Benzene
Several electrophiles present:
a major one is sulfur trioxide
Step 1: attack of sulfur trioxide on $\pi$-electron system of aromatic ring
Step 2: loss of a proton from the carbocation intermediate
Step 3: protonation of benzenesulfonate ion
12.5
Halogenation of Benzene
Halogenation of Benzene

Electrophile is a Lewis acid-Lewis base complex between FeBr$_3$ and Br$_2$.
The $\text{Br}_2$-$\text{FeBr}_3$ complex is more electrophilic than $\text{Br}_2$ alone.
Step 1: attack of $\text{Br}_2$-$\text{FeBr}_3$ complex on $\pi$-electron system of aromatic ring
Step 2: loss of a proton from the carbocation intermediate
12.6 Friedel-Crafts Alkylation of Benzene
**Friedel-Crafts Alkylation of Benzene**

Electrophile is tert-butyl cation

\[
\text{Catalyst: AlCl}_3
\]

\[
\text{Benzene} + (\text{CH}_3)_3\text{CCl} \xrightarrow{\text{AlCl}_3} \text{Benzene-C(CH}_3)_3 \xrightarrow{} + \text{HCl}
\]

Electrophile is tert-butyl cation
acts as a Lewis acid to promote ionization of the alkyl halide

\[
(CH_3)_3C\text{:+Cl} + AlCl_3 \rightleftharpoons (CH_3)_3C\text{:+Cl\text{--;AlCl}_3}
\]
Role of AlCl$_3$

acts as a Lewis acid to promote ionization of the alkyl halide

$$(\text{CH}_3)_3\text{C} \equiv \text{Cl} \quad + \quad \text{AlCl}_3 \quad \leftrightarrow \quad (\text{CH}_3)_3\text{C} \equiv \overline{\text{Cl}} \equiv \overline{\text{AlCl}_3}$$

$$(\text{CH}_3)_3\text{C} \quad + \quad \overline{\text{Cl}} \equiv \overline{\text{AlCl}_3}$$
Step 1: attack of tert-butyl cation on π-electron system of aromatic ring
Step 2: loss of a proton from the carbocation intermediate
Rearrangements in Friedel-Crafts Alkylation

Carbocations are intermediates. Therefore, rearrangements can occur

\[ \text{Isobutyl chloride} \rightarrow \text{tert-Butylbenzene (66\%)} \]
Isobutyl chloride is the alkyl halide. But *tert*-butyl cation is the electrophile.

\[
\text{Ph} + (\text{CH}_3)_2\text{CHCH}_2\text{Cl} \xrightarrow{\text{AlCl}_3} \text{PhC(\text{CH}_3)_3}
\]

Isobutyl chloride  *tert*-Butylbenzene (66%)
Rearrangements in Friedel-Crafts Alkylation

H₃C-C-CH₂Cl-AlCl₃

H₃C-C-CH₂ + :Cl-AlCl₃

H₃C-C-CH₂ + :Cl-AlCl₃
Reactions Related to Friedel-Crafts Alkylation

Cyclohexene is protonated by sulfuric acid, giving cyclohexyl cation which attacks the benzene ring.

Cyclohexylbenzene (65-68%)
12.7
Friedel-Crafts Acylation of Benzene
Friedel-Crafts Acylation of Benzene

Electrophile is an acyl cation

\[
\text{CH}_3\text{CH}_2\text{C}≡\text{O}^+ : \quad \leftrightarrow \quad \text{CH}_3\text{CH}_2\text{C}≡\text{O}^+ :
\]
Step 1: attack of the acyl cation on π-electron system of aromatic ring
Step 2: loss of a proton from the carbocation intermediate
Acid Anhydrides

can be used instead of acyl chlorides

\[
\text{PhH} + \text{CH}_3\text{COCOCH}_3 \xrightarrow{\text{AlCl}_3} \text{PhCOCH}_3
\]

Acetophenone (76-83%)

\[
+ \text{CH}_3\text{COOH}
\]
12.8

Acylation-Reduction
Reduction of aldehyde and ketone carbonyl groups using Zn(Hg) and HCl is called the Clemmensen reduction.

\[
\text{Acylation-Reduction}
\]

permits primary alkyl groups to be attached to an aromatic ring

\[
\begin{align*}
\text{ benzene + } & \text{RCOCI} \quad \text{AlCl}_3 \\
\text{H} \quad & \quad \text{O} \\
\rightarrow & \quad \text{O} \\
\text{C} \quad & \quad \text{CR} \\
\text{Zn(Hg), HCl} \\
\text{CH}_2\text{R}
\end{align*}
\]

Reduction of aldehyde and ketone carbonyl groups using Zn(Hg) and HCl is called the *Clemmensen reduction*. 
Reduction of aldehyde and ketone carbonyl groups by heating with $\text{H}_2\text{NNH}_2$ and KOH is called the Wolff-Kishner reduction.

Acylation-Reduction

permits primary alkyl groups to be attached to an aromatic ring.

Reduction of aldehyde and ketone carbonyl groups by heating with $\text{H}_2\text{NNH}_2$ and KOH is called the \textit{Wolff-Kishner reduction}. 
Example: Prepare isobutylbenzene

No! Friedel-Crafts alkylation of benzene using isobutyl chloride fails because of rearrangement.
Recall

**Chemical Reaction**

\[ \text{Isobutyl chloride} + (\text{CH}_3)_2\text{CHCH}_2\text{Cl} \xrightarrow{\text{AlCl}_3} \text{tert-Butylbenzene} \]

(66%)
Use Acylation-Reduction Instead

\[
\text{苯} + (\text{CH}_3)_2\text{CHCCl} \rightarrow \text{CH}_2\text{CH(CH}_3\text{)}_3
\]

\[
\text{AlCl}_3 \quad \text{Zn(Hg)} \quad \text{HCl}
\]