Reactions of Anhydrides

- **Hydrolysis**
  - In hydrolysis, an anhydride is cleaved to give two molecules of carboxylic acid:

![Chemical structure of hydrolysis reaction]

- **Esterification (Alcoholysis)**
  - Anhydrides react with alcohols to give one molecule of ester and one molecule of carboxylic acid—a useful method for the preparation of esters.
Example of Esterification

- Preparation of aspirin:

\[
\text{salicylic acid } \quad \text{ + } \quad \text{acetic anhydride}
\]

Reactions of Anhydrides

- Reaction with Ammonia and Amines – Formation of Amides
  - Anhydrides react with ammonia, as well as 1° or 2° amines, to form amides.
  - Note that two moles of amine are required (one forms the amide, the other acts as a base).
Example of Amide Formation

- Preparation of acetamide

\[
\text{acetic anhydride} + 2 \text{NH}_3 \rightarrow \text{acetamide} + \text{ammonium acetate}
\]

Preparation of Acid Chlorides

- Reaction of carboxylic acids with thionyl chloride:

\[
\text{benzoic acid} + \text{SOCl}_2 \xrightarrow{\text{reflux}} \text{benzoyl chloride} + \text{SO}_2 + \text{HCl}
\]

benzoic acid

thionyl chloride

benzoyl chloride

sulfur dioxide

hydrogen chloride

HCl
Reactions of Acid Chlorides

➢ Hydrolysis
  • Acid chlorides are cleaved by water to give a carboxylic acid and HCl:

\[
\text{C-Cl} + \text{H}_2\text{O} \rightarrow \text{C-OH} + \text{HCl}
\]

Reactions of Acid Chlorides

➢ Formation of esters
  • Added amine base will precipitate HCl:

\[
\begin{align*}
\text{C-Cl} + \text{CH}_3\text{OH} & \xrightarrow{\text{Et}_3\text{N}} \text{C-OCH}_3 + \text{Et}_3\text{N}\cdot\text{HCl} \\
\end{align*}
\]
Reactions of Acid Chlorides

➢ Formation of amides:

\[
\begin{align*}
\text{CH}_3\text{C} & \text{Cl} + \text{HN(CH}_2\text{CH}_3) & \text{Et}_2\text{O} \\
\text{m-toluoyl chloride} & \text{diethylamine} & \text{Et}_2\text{O}
\end{align*}
\]

Reactions of Amides

➢ Hydrolysis
  • Amides are relatively unreactive.
  • They can be hydrolyzed with refluxing concentrated aqueous acid (e.g., HCl) or aqueous base (NaOH or KOH).
Amide Hydrolysis in Acid

$H_2C(NCH_3)_2 + H_2O + HCl \xrightarrow{\Delta} \text{N,N-dimethylformamide}$

$HCOOH + \text{CH}_3\text{N}(CH_3)_2 \text{Cl}^\ominus \text{formic acid} \text{dimethylammonium chloride}$

Base-Promoted Amide Hydrolysis

$\text{Benzamide} + H_2O + KOH \xrightarrow{\Delta} \text{Potassium benzoate} + NH_3$

$\text{potassium benzoate}$
Some Important Amides

- Penicillin V

- Lysergic acid diethyl amide (LSD)