Chapter 14: Functional Derivatives of Carboxylic Acids

Carboxylic acid

Acid halide

Carboxylic acid

Acid anhydride

A

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14.1 Nomenclature of Carboxylic Acid Derivatives

a) Acid Halides

Acid halides are named by changing the suffix -ic acid in the name of the parent carboxylic acid to -yl halide.

Acetyl chloride: Benzoyl chloride:

b) Acid Anhydrides

- Symmetrical anhydrides are named by changing the suffix *acid* in the name of the parent carboxylic acid to *anhydride*.
- Mixed anhydrides are named bu identifying the two parent carboxylic acids from both acyl groups and
 placing those names in alphabetical order before without the acid part of the name before the word
 anhydride.

Acetic anhydride: Acetic benzoic anhydride:

c) Esters

• The alkyl or aryl group attached to the -O- is named first followed by the name the carboxylic acid in which -ic acid has been replaced with -ate.

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d) Amides

- Amides are named by dropping the suffix -oic acid from the IUPAC name for the parent acid (or -ic acid from common names) and adding amide.
- If the nitrogen atom of an amide is bonded to an alkyl or aryl group, the group is named and its location on the nitrogen is indicated by *N*-.

Acetamide

N-Methylacetamide

N,N-Dimethylformamide

14.2 Characteristic Reactions of Carboxylic Acid Derivatives

Aldehydes and Ketones: Nucleophilic Acyl Addition Reactions (Ch 12)

$$Nu: + \underset{R}{\overset{R}{\longrightarrow}} C = O \longrightarrow \left[\begin{array}{c} Nu \longrightarrow {\overset{\bigcirc}{\longrightarrow}} \\ Nu \longrightarrow {\overset{\bigcirc}{\longrightarrow}} \\ R \end{array} \right] \xrightarrow{H^{\overset{\bigcirc}{\longrightarrow}}} Nu \longrightarrow {\overset{\bigcirc}{\longrightarrow}} R$$

Carboxylic Acid Derivatives: Nucleophilic Acyl Substitution Reactions

Nu:
$$+ \underset{LG}{\overset{R}{\bigvee}} = 0 \longrightarrow \begin{bmatrix} Nu & O^{\odot} \\ Nu & LG \end{bmatrix} \xrightarrow{\overset{C}{\bigvee}} \underset{Nu}{\overset{R}{\bigvee}} = 0$$

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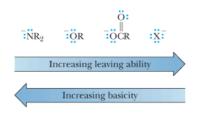
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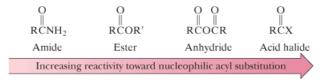
Reactivity of Carboxylic Acid Derivatives in the Nucleophilic Acyl Substitution Reaction

$$Nu: + \underset{LG}{\overset{R}{\overset{}}} C = O \longrightarrow \left[\begin{array}{c} O \\ Nu \longrightarrow \underset{LG}{\overset{}} R \\ \end{array} \right] \xrightarrow{\overset{\Phi}{\overset{}}} \underset{Nu}{\overset{R}{\overset{}}} C = O$$

Leaving Groups



Best Leaving Group = highest reactivity toward substitution



14.3 Hydrolysis of Carboxylic Acid Derivatives to Carboxylic Acids

Reaction of carboxylic acid derivatives with water: Hydrolysis.

a) Hydrolysis of Acyl Halides

b) Hydrolysis of Acid Anhydrides

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c) Hydrolysis of Esters to Acids

Under acidic conditions:

$$\begin{array}{c} O \\ \hline \\ O \\ \hline \\ \end{array} \begin{array}{c} H_2O \\ \hline \\ H^{\dagger} \end{array}$$

Under basic conditions (Saponification):

d) Hydrolysis of Amides

$$\begin{array}{c}
O \\
NH_2
\end{array}$$

$$\begin{array}{c}
H_3O^+ \text{ or } OH^-, H_2O \\
\text{heat}
\end{array}$$

Very slow, requires prolonged heating under strongly acidic or basic conditions.

14.4 Reactions of Carboxylic Acid Derivatives with Alcohols

Ester formation.

a) Acyl Halides to Esters

Role of pyridine:

b) Acid Anhydrides to Esters

Aspirin

Anhydrides are less efficient because only half of of the anhydride is used, the other half is wasted

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c) Esters to Esters (Transesterification)

d) Amides to Esters?

Amides cannot be converted directly to esters since they are less reactive.

14.5 Reactions of Carboxylic Acid Derivatives with Amines

Amide formation with ammonia, 1°, or 2° amine.

a) Acyl Halide to Amide

b) Acid Anhydrides to Amides

acetaminophen

Anhydrides are less efficient than acid chlorides because half of the anhydride is "wasted".

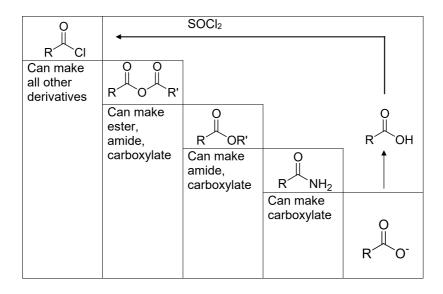
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c) Esters to Amides

14.6 Interconversion of Carboxylic Acid Derivatives (Summary)



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14.7 Reaction of Esters with Grignard Reagents

Esters are first reduced to ketones which will react then to 3° alcohols.

Grignard adds twice to the carbonyl carbon: because ketones are more reactive (mere electrophilic), it is **impossible to isolate** the ketone intermediate.

14.8 Reduction of Carboxylic Acid Derivatives

a) Acid Chlorides to 1° Alcohols

b) Esters to 1° Alcohols

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b) Amides to Amines

$$\begin{array}{c}
O \\
N \\
H
\end{array}$$

$$\begin{array}{c}
1. \text{ LiAlH}_4, \text{ ether} \\
\hline
2. \text{ H}_2\text{O}
\end{array}$$

$$\begin{array}{c}
O \\
N \\
\hline
1. \text{ LiAlH}_4, \text{ ether} \\
\hline
2. \text{ H}_2O
\end{array}$$

Review

Provide conditions for these transformations. More than one step may be required

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Provide conditions for these transformations. More than one step may be required.