Carboxylic Acid Nomenclature

Acids are named by replacing the "e" with "oic" and then adding the word "acid". There are many common names for carboxylic acids that are in use. Several examples are shown below.

- Formic Acid
- Methanoic Acid
- Acetic Acid
- Ethanoic Acid
- Adipic Acid
- Hexanedioic Acid
- Benzoic Acid
- Benzene Carboxylic Acid
- Cyclopentane Carboxylic Acid
- Oxalic Acid
- Malonic Acid
- Succinic Acid
- Fumaric Acid
- Maleic Acid
- Phthalic Acid

Naming other acid derivatives: Pages 907-910; Problem 20.12 on Page 9.10—DO ON YOUR OWN

Carboxylic Acid Properties

Carboxylic acids form hydrogen bonds. As their name implies, carboxylic acids are considerably more acidic than alcohols due to the resonance stabilization of the carboxylate. Carboxylate salts of 6 carbons or less are typically quite water soluble.

Acidity: Pages 902-904; Problem 20.9 on Page 904

Electron withdrawing and donating groups will influence the acidity of carboxylic acids just like we saw previously with alcohols. The typical pKa range for a carboxylic acid is 4-5.

\[
\begin{align*}
pK_a & \quad 4.75 \\
& \quad 2.59 \\
& \quad 0.23 \\
& \quad 4.19 \\
& \quad 3.41 \\
& \quad 4.46 
\end{align*}
\]
Preparation of Carboxylic Acids
Acids can be made by several types of oxidation reactions, hydrolysis of nitriles, or by the addition of Grignard reagents to carbon dioxide.

![Chemical reactions and structures](image)

1. KMnO₄, NaOH, H₂O, heat
2. H₃O⁺

Tollen’s Test for aldehydes

![Chemical reactions and structures](image)

Hydrolysis of a nitrile—covered later in this chapter. Pages 936-937.

Reactions of Carboxylic Acids:

![Chemical reactions and structures](image)

Remember NaBH₄ only reduces aldehydes and ketones.

BH₃ is selective for carboxylic acids:

Carboxylic Acid Derivatives
Much of the chemistry of carboxylic acids occur with and to form derivatives. From the most reactive to the least reactive: acid halides, anhydrides, esters, and amides represent the most common carboxylic acid derivatives.

![Chemical structures](image)
Acetonitrile: although they don’t have a carbonyl, the nitrile carbon has the same oxidation state as a carboxylic acid and is often referred to as a derivative. They are named after the parent acid.

Nucleophilic Acyl Substitution

Nearly all the chemistry of carboxylic acid derivatives involves the addition of a nucleophile to the carbonyl carbon followed by loss of a leaving group to affect a nucleophilic substitution on the acyl carbon. This is a two step process. Often the leaving group is very electronegative and the nucleophile is weak (neutral). An example is the formation of an ester from an acid chloride. These reactions form HCl and a base is used to neutralize the acid by deprotonating the intermediate.

It is generally easy to go from a more reactive carboxylic acid derivative to a less reactive one. It is very difficult to go the other direction.
**Reaction Types**

The nucleophilic acyl substitution with weak nucleophiles can be classified into various reaction types depending on what kind of nucleophile is adding.

\[
\begin{align*}
R^+Z^- + H^-Nuc & \rightarrow R^-Z^- + H^+Z^- & \text{General NAS Reaction} \\
R^+Z^- + H^-OH & \rightarrow R^-OH + H^+Z^- & \text{Hydrolysis} \\
R^+Z^- + H^-OR' & \rightarrow R^-OR' + H^+Z^- & \text{Alcoholysis} \\
R^+Z^- + H^-NH_3 & \rightarrow R^-NH_2 + H^+Z^- & \text{Aminolysis}
\end{align*}
\]

**Reactions of Acid Chlorides**

The most reactive and versatile derivative, acid chlorides can be used to make any derivative.

![Formation of Acid Chloride: MECHANISM 20.2 Page 918 — Write this out.](image)

\[
\begin{align*}
R^-Cl + NaO^-CH_3 & \rightarrow R^-O^-CH_3 + NaCl
\end{align*}
\]
Mechanism for Nucleophilic Acyl Substitution with acid chlorides: MECHANISM 20.3  Page 918—Write this out.

This mechanism is generic for all nucleophilic acyl substitutions of acid chlorides.

Practice Problem

Other reactions of acid chlorides:
Reactions of Anhydrides: Pages 922-925

Anhydrides will react very similar to acid chlorides. They are limited only by the lack of different anhydrides that are readily prepared. If you want anhydrides other than acetic or cyclic anhydrides you must make them from acid chlorides. Thus, it is easier to just use the acid chloride itself to make esters and amides.

Preparation of Acid Anhydrides

1. $\text{RCOCl} + \text{NaOCH}_3 \rightarrow \text{RCOCH}_3 + \text{NaCl}$
2. $\text{RCOCl} + \text{HOCH}_3 \rightarrow \text{RCOCH}_3 + \text{pyridine-HCl}$
3. $\text{HOCH}_2\text{COCH}_2\text{OH} \rightarrow \text{HOOC} + \text{H}_2\text{O}$
Reactions of Anhydrides

Hydrolysis:
\[
\text{Anhydride} + \text{H}_2\text{O} \xrightarrow{\text{heat}} \text{Acid} + \text{Base}
\]

Alcoholysis:
\[
\text{Anhydride} + \text{R-OH} \xrightarrow{\text{base}} \text{Acyl} + \text{R-OH}
\]

Aminolysis:
\[
\text{Anhydride} + \text{RNH}_2 \xrightarrow{\text{base}} \text{Acyl} + \text{RNH}_2
\]

Mechanism for Nucleophilic Acyl Substitution with Acid Anhydrides:

\[
\text{Anhydride} + \text{R-OH} \xrightarrow{\text{base}} \text{Acyl-R} + \text{HOAc}
\]

This mechanism is generic for all nucleophilic acyl substitutions of acid anhydrides

Reduction of anhydride:
\[
\text{Anhydride} \xrightarrow{1. \text{LiAlH(Ot-Bu)}_3} \text{Alcohol} \xrightarrow{2. \text{H}_3\text{O}^+} \text{Acid}
\]
Preparation of Esters
The preparation of esters from acids is limited. The deprotonated acid will react with methyl or primary alkyl halides via an $S_N2$ reaction. With a large excess of alcohol and an acid catalyst, a Fischer Ester synthesis can be undertaken. This is limited to cheap readily available alcohols like methanol and ethanol. Other esters are more easily prepared from the acid chloride.

![Mechanism for Fischer Esterification: Mechanism 20.6 on Page 925. Draw this out.](image)

![Mechanism for Acid Catalyzed Hydrolysis: Mechanism 20.8 on Page 928.](image)

You can think of $A^-$ as similar to $B$: You could use water as the general base as well because it's really $H_2O^+$ in solution.
Saponification: Mechanism 20.7 on Page 927. Write out this mechanism.

Lactones (cyclic esters)

Other reactions of esters:

Grignard reagents do double additions to esters and acid chlorides. Review from CH. 12 and also Mechanism 20.10 on page 931.
Preparation of Amides

It is very difficult to prepare amides directly from carboxylic acids. This is because the acid and the amine will simply do an acid-base reaction to make an ammonium cation and a carboxylate anion. The most convenient way to make amides is by reacting an acid chloride with ammonia, a primary or a secondary amine.

\[
\text{RCl} + \text{NH}_3 \rightarrow \text{RNH}_2 + \text{HCl}
\]

Page 931-932. Amides from acid chlorides and amines is quite fast.
Amides can also be prepared by the reaction of anhydrides or esters with ammonia, primary or secondary amines. Write out the following mechanisms.

\[
\begin{align*}
\text{H}_3\text{C} \equiv \text{O} + \text{H}_3\text{C} \equiv \text{NCH}_3 & \quad \rightarrow \quad \text{H}_3\text{C} \equiv \text{NCH}_3 + \text{H}_3\text{C} \equiv \text{O} \\
\text{OCH}_3 + \text{H}_3\text{C} \equiv \text{NCH}_3 & \quad \rightarrow \quad \text{OCH}_3 + \text{CH}_3\text{OH}
\end{align*}
\]

There are better ways to directly convert a carboxylic acid into an amide.

Need a special reagent that makes the -OH a good leaving group (coupling reagent): \textit{Dicyclohexylcarbodiimide (DCC)}

Mechanism for DCC mediated amide formation: This is a long mechanism and you are NOT responsible for it as it is not in your book. Just know the transformation. But if you like a challenge look the mechanism up and try it!
Mechanism for Acid Catalyzed Hydrolysis of an Amide: Mechanism 20.10 on Page 933.


Dehydration of amides:

Reactions of nitriles: Hydrolysis, Reduction and Nucleophilic additions.

\[
\begin{align*}
R-CN & \xrightarrow{H_3O^+} R-COOH \\
\text{hydrolysis also works under basic (\text{OH}) conditions} \\
\end{align*}
\]

\[
\begin{align*}
R-CN & \xrightarrow{1. \text{R-MgBr}, 2. H_3O^+} R-CO \text{R} \\
\text{Very similar to Grignard reaction below but add H}^- \text{ instead of R}. \\
\end{align*}
\]

\[
\begin{align*}
R-CN & \xrightarrow{1. \text{LiAlH}_4, 2. H_3O^+} R-\text{NH}_2 \\
\text{New Reaction: See middle of Page 937} \\
\end{align*}
\]

Acidic Hydrolysis of a Nitrile

Mechanism 20.14 on Page 936.
Basic Hydrolysis of a Nitrile

Mechanism 20.15 on page 937.

Retrosynthesis problems:

any 2 carbon or less starting material
N+ any 2 carbon or less starting material

NH₂

MeBr (1 eq)

LiAlH₄

C₂N

NaCN

Br₂, light

Cl

O

O

HO

MgBr

15

Br