

Chemistry 204: Carboxylic Acids and their Derivatives

Carboxylic Acids

Introduction. Nomenclature. Properties. Acid-Base Chemistry

general structure:

Spectroscopy of Carboxylic Acids:

Nomenclature.

To name carboxylic acids:

- change the -e ending of alkane to -oic acid
- carboxylic carbon is always carbon #1

When the -OH group is (theoretically) removed from the carboxylic acid, acyl groups are obtained:

Structure of Carboxylic Acids: Hydrogen Bonding

- carboxylic acids exist mostly as dimers:

Because of this association and the strongly polar nature of the carboxyl group, carboxylic acids have boiling points considerably higher than other compounds of similar weight

Acidity of Carboxylic Acids

In carboxylate anions, resonance stabilization is important and can be used to assist to rationalization of the appreciable acidity of carboxylic acids.

Compare the acidity of carboxylic acids with that of alcohols:

Thus, carboxylic acids exhibit appreciable acidity and react with relatively weak bases to form salts. The fact that these salts are soluble in water provides a convenient method for the separation of carboxylic acids from water-insoluble nonacidic (organic) compounds.

Substituent Effects on Acidity of Carboxylic Acids

In general, electron-withdrawing groups near the COOH group stabilize the carboxylate anion and therefore *increase* the acidity of the acid. Electron-donating groups have the opposite effect.

Preparation of Carboxylic Acids

- (C203) Oxidation of 1° Alcohols

- Hydrolysis of Nitriles (section Ch 18.4E)

mechanism of acid hydrolysis:

mechanism of base hydrolysis:

- Carboxylation of R-MgX or R-Li with CO₂

Note: three complementary methods of increasing a carbon chain by one carbon:

Reactions of Carboxylic Acids

- (C203) Reduction using lithium aluminum hydride (LiAlH_4)

- Formation of Acid Chlorides From Carboxylic Acids Using thionyl chloride (SOCl_2)

mechanism:

- Acid-catalyzed Formation of Esters Using Alcohols (Fischer esterification)

-important method for converting carboxylic acids into esters

mechanism:

examples:

Functional Derivatives of Carboxylic Acids

Functional derivatives of carboxylic acids are those compounds that are transformed into carboxylic acids by hydrolysis.

Resonance in functional derivatives of carboxylic acids:

Reactivity Considerations

The typical reaction of carboxylic acids and their functional derivatives is **nucleophilic acyl substitution**. This process proceeds by a **tetrahedral intermediate**.

General mechanisms:

a) direct attack by a nucleophile

b) acid catalyzed nucleophilic acyl substitution

The rate of nucleophilic acyl substitution depends primarily on two factors:

a) electronics: the more polarized the carbonyl group, the faster the reaction

b) steric factors: in general, other factors being equal, more sterically hindered carbonyl groups are attacked less readily than less hindered carbonyl groups

Specific Reactions:

We will use the summary, and look at selected mechanisms and some additional reactions of acyl derivatives of carboxylic acids.

- 1) base and acid-catalyzed hydrolysis of nitriles
- 2) formation of acid chlorides from carboxylic acids
- 3) acid-catalyzed esterification of carboxylic acids (Fischer esterification)
 - these have been discussed previously
- 4) hydrolysis of esters to carboxylic acids

mechanism (acid catalysis)

A related reaction is acid-catalyzed *transesterification* of one ester to another:

mechanism:

back to the reaction of esters to acids (hydrolysis)

alternate mechanism 1 (t-butyl, benzyl esters; acid catalysis)

Hydrolysis of esters in aqueous base is called *saponification*. This hydrolysis process is non-reversible, and uses a stoichiometric amount of base

5) hydrolysis of acid chlorides (or acid anhydrides) to carboxylic acids.

Similarly, acid chlorides (or anhydrides) can be converted to esters using alcohols.

6) hydrolysis of amides to carboxylic acids

acid-catalyzed:

base-promoted:

7) formation of amides

a) direct conversion of carboxylic acids into amides

This is a *very poor* method, and is almost never used. Similarly, the reaction between esters and amines is a poor method, and is almost never used.

Two better methods:

b) reaction of amines with acid chlorides (or anhydrides)

c) reaction of amines with carboxylic acids activated by DCC (**d**icyclohexylcarbodiimide) (27E)

This highly effective reaction is mild. It is used regularly for the formation of peptide amide bonds in amino acid and protein synthesis.

mechanism:

strategic peptide coupling of α -amino acids:

Summary of interconversion of functional derivatives:

Other Reactions of Functional Derivatives

(some we have seen before in C203)

Reduction with Lithium Aluminum Hydride

a) carboxylic acids

b) acid chlorides

c) esters

Esters can also be reduced to alcohols using diisobutylaluminum hydride (DIBAL-H).

If the reduction is performed at low temperature ($-78\text{ }^{\circ}\text{C}$), then aldehydes can be isolated directly.

d) amides

The product of reduction of amides with LiAlH_4 is usually an amine rather than an alcohol.

mechanisms:

e) nitriles

Nitriles may be reduced to 1° amines with LiAlH_4 or to aldehydes with DIBAL-H.

Reactions of Organometallic Reagents (Grignard or Organolithium Reagents)

a) esters (C203)

- react to form 3° alcohols (if ester is formate, 2° alcohols)

b) nitriles

Nitriles react with these reagents to form ketones.