Chapter 18: Carboxylic Acids

18.1: Carboxylic Acid Nomenclature (please read)
suffix: -oic acid

18.2: Structure and Bonding (please read)

18.3: Physical Properties. The carboxylic acid functional group contains both a hydrogen bond donor (\(-\text{OH}\)) and a hydrogen bond acceptor (\(\text{C}=\text{O}\)).

Carboxylic acids exist as hydrogen bonded dimers.

\[ \text{H}_3\text{C} \quad \text{O} \quad \text{H} \quad \text{H}_3\text{C} \quad \text{O} \quad \text{H} \]

acetic acid
**18.4: Acidity of Carboxylic Acids.** The pKₐ of carboxylic acids typically ~ 5. They are significantly more acidic than water or alcohols.

Bronsted Acidity (Ch. 1.13): Carboxylic acids transfer a proton to water to give H₃O⁺ and carboxylate anions, RCO₂⁻

\[
\begin{align*}
&\text{RCO}_2\text{OH} + \text{H}_2\text{O} \rightleftharpoons \text{RCO}_2^- + \text{H}_3\text{O}^+ \\
&K_a = \frac{[\text{RCO}_2^-][\text{H}_3\text{O}^+]}{[\text{RCO}_2\text{H}]} \quad \text{pK}_a = -\log K_a
\end{align*}
\]

- typically ~ 10⁻⁵ for carboxylic acid
- typically ~ 5 for carboxylic acid

<table>
<thead>
<tr>
<th>CH₃CH₃</th>
<th>CH₃CH₂OH</th>
<th>PhOH</th>
<th>CH₃CO₂H</th>
<th>HCl</th>
</tr>
</thead>
<tbody>
<tr>
<td>pKₐ</td>
<td>~50-60</td>
<td>16</td>
<td>10</td>
<td>4.7</td>
</tr>
</tbody>
</table>

Increasing acidity

The greater acidity of carboxylic acids is attributed to greater stabilization of carboxylate ion by:

a. Inductive effect of the C=O group

b. Resonance stabilization of the carboxylate ion

4 π-electrons delocalized over three p-orbitals

C-O bond length of a carboxylate are the same
Bronsted Acid: proton donor ($H^+$)
weak acids (and bases) do not fully dissociate

$$H-A + H_2O \rightleftharpoons H_3O^+ + A^-$$

$$K_a = \frac{[H_3O^+] [A^-]}{[H-A]}$$  acid dissociation constant

$$pK_a = -\log K_a$$
$$pH = -\log [H_3O^+]$$

Henderson-Hasselbalch Equation: Relates $pK_a$ with pH

$$pH = pK_a + \log \frac{[A^-]}{[H-A]}$$

when $[A^-] = [H-A]$, the pH = $pK_a$

$$pH - pK_a = \log \frac{[A^-]}{[H-A]}$$

$$\frac{[A^-]}{[H-A]} = 10^{(pH-pK_a)}$$

18.5: Substituents and Acid Strength. The $pK_a$ of a carboxylic acid can be influenced by substituents on the $\alpha$-carbon, largely through inductive effects. Electron-withdrawing groups increase the acidity (lower $pK_a$) and electron-donating groups decrease the acidity (higher $pK_a$). (see table 18.2, p. 743)

<table>
<thead>
<tr>
<th></th>
<th>$pK_a$</th>
<th>$pK_a$</th>
<th>$pK_a$</th>
<th>$pK_a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{H}_2\text{COOH}$</td>
<td>4.7</td>
<td>2.9</td>
<td>1.3</td>
<td>0.9</td>
</tr>
<tr>
<td>$\text{H}_2\text{ClCOOH}$</td>
<td>4.9</td>
<td>5.1</td>
<td>4.8</td>
<td>4.9</td>
</tr>
<tr>
<td>$\text{H}_2\text{CH}_2\text{CH}_2\text{COOH}$</td>
<td>4.9</td>
<td>5.1</td>
<td>4.8</td>
<td>4.9</td>
</tr>
</tbody>
</table>

Inductive effects work through $\sigma$-bonds, and the effect falls off dramatically with distance

<table>
<thead>
<tr>
<th></th>
<th>$pK_a$</th>
<th>$pK_a$</th>
<th>$pK_a$</th>
<th>$pK_a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{H}<em>2\text{O}</em>{\text{OH}}$</td>
<td>4.9</td>
<td>4.5</td>
<td>4.1</td>
<td>2.8</td>
</tr>
</tbody>
</table>
18.6: **Ionization of Substituted Benzoic Acids.** The charge of the carboxylate ion cannot be delocalize into the aromatic ring. Electron-donating groups decrease the acidity. Electron-withdrawing groups increase the acidity. (Table 18.3, p. 745)

![Structural formulas]

<table>
<thead>
<tr>
<th>R</th>
<th>$pK_a$ (stronger acid)</th>
<th>$pK_a$ (stronger base)</th>
<th>$pK_a$ (weaker base)</th>
<th>$pK_a$ (weaker acid)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-CH₃</td>
<td>3.9</td>
<td>4.3</td>
<td>4.4</td>
<td></td>
</tr>
<tr>
<td>-F</td>
<td>3.3</td>
<td>3.9</td>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>-Cl</td>
<td>2.9</td>
<td>3.8</td>
<td>4.0</td>
<td></td>
</tr>
<tr>
<td>-Br</td>
<td>2.8</td>
<td>3.8</td>
<td>4.0</td>
<td></td>
</tr>
<tr>
<td>-OCH₃</td>
<td>4.1</td>
<td>4.1</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>-NO₂</td>
<td>2.2</td>
<td>3.5</td>
<td>3.4</td>
<td></td>
</tr>
</tbody>
</table>

18.7: **Salts of Carboxylic Acids.** Carboxylic acids react with base to give carboxylate salts.

![Balanced chemical equation]

$\text{RCOOH} + \text{NaOH} \rightarrow \text{RCOO}^- + \text{H}_2\text{O} + \text{Na}^+$

$pK_a$ values:

<table>
<thead>
<tr>
<th>$pK_a$ (stronger acid)</th>
<th>$pK_a$ (stronger base)</th>
<th>$pK_a$ (weaker base)</th>
<th>$pK_a$ (weaker acid)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>15.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Detergents and Micelles:** substances with polar (*hydrophilic*) head groups and *hydrophobic* tail groups form aggregates in water with the carboxylate groups on the outside and nonpolar tails on the inside.
18.8: Dicarboxylic Acids. one carboxyl group acts as an electron-withdrawing group toward the other and lowers its pKa; the effect decreases with increasing separation

\[
\begin{align*}
\text{O} & \quad \text{HO-} \quad \text{C} \quad \text{O} \\
\text{O} & \quad \text{O} \quad \text{H}_2\text{O} \quad + \quad \text{H}_2\text{O} \quad \text{pK}_{a1} \quad + \quad \text{H}_2\text{O} \quad \text{pK}_{a2}
\end{align*}
\]

Oxalic acid (n= 0)  \( pK_{a1} = 1.2 \)  \( pK_{a2} = 4.2 \)
Malonic acid (n= 1)  2.8  5.7
Succinic acid (n=2)  4.2  5.6
Glutaric acid (n=3)  4.3  5.7
Adipic acid (n=4)  4.4  5.4
Pimelic acid (n=5)  4.7  5.6

18.9: Carbonic Acid (please read)

\[
\begin{align*}
\text{O} & \quad \text{HO-} \quad \text{C} \quad \text{O} \\
\text{O} & \quad \text{O} \quad \text{H}_2\text{O} \quad + \quad \text{H}_2\text{O} \quad \text{pK}_{a1} \quad + \quad \text{H}_2\text{O} \quad \text{pK}_{a2}
\end{align*}
\]

~ 6.4  ~ 10.2

18.10: Sources of Carboxylic Acids. Summary of reaction from previous chapters that yield carboxylic acids (Table 18.4, p. 791)

a. Side-chain oxidation of alkylbenzene to give benzoic acid derivatives (Ch. 11.12): reagent: \( K_2\text{Cr}_2\text{O}_7, \text{H}_3\text{O}^+ \)-or- \( \text{KMnO}_4 \)

b. Oxidation of primary alcohols (Ch. 15.9)
reagent: \( K_2\text{Cr}_2\text{O}_7, \text{H}_3\text{O}^+ \)

c. Oxidation of aldehydes (Ch. 17.14)
reagent: \( K_2\text{Cr}_2\text{O}_7, \text{H}_3\text{O}^+ \)
18.11: Synthesis of Carboxylic Acids by the Carboxylation of Grignard Reagents. Grignard reagents react with CO₂ to afford carboxylic acids. An additional carbon (the CO₂H group, which is derived from CO₂) is added to the Grignard reagent.

Grignard reagents are strong bases and strong nucleophiles. As such, they are incompatible with acidic (alcohols, thiols, amines, carboxylic acid, amides,) or electrophilic (aldehydes, ketones, esters, nitrile, halides) groups.

18.12: Synthesis of Carboxylic Acids by the Preparation and Hydrolysis of Nitriles. Cyanide ion is an excellent nucleophile and will react with 1° and 2° alkyl halides and tosylates to give nitriles. This reaction adds one carbon. The nitrile can be hydrolyzed to a carboxylic acid.

Cyanohydrins (Ch. 17.7) are hydrolyzed to α-hydroxy-carboxylic acids.
(Table 18.5, p. 753)

a. Conversion to acid chlorides (Ch. 12.7). Reagent: SOCl₂

\[
R\text{-CO}_2\text{H} \xrightarrow{\text{SOCl}_2, \Delta} R\text{-C}\text{Cl} + \text{SO}_2 + \text{HCl}
\]

b. Reduction to a 1° alcohol (Ch. 15.3). Reagent: LiAlH₄
Carboxylic acids are reduced to 1° alcohols by LAH, but not by NaBH₄.

\[
\begin{align*}
R\text{-CO}_2\text{H} & \xrightarrow{\text{a. LiAlH}_4, \text{THF}} R\text{CH}_2\text{OH} \\
R\text{-CO}_2\text{H} & \xrightarrow{\text{b. H}_2\text{O}^+} R\text{CH}_2\text{OH}
\end{align*}
\]

c. Acid-catalyzed esterification (Ch. 15.8)
Reagent: alcohol (R’ OH), H⁺ (-H₂O)

\[
R\text{-CO}_2\text{H} \xrightarrow{\text{ROH, H}^⁺ (-\text{H}_2\text{O})} R\text{-C}\text{OR}’
\]

18.14: Mechanism of Acid-Catalyzed Esterification.
Fischer Esterification (p. 754-755)

\[
R\text{-CO}_2\text{H} \xrightarrow{\text{ROH, H}^⁺} R\text{-C}\text{OR}’ + \text{H}_2\text{O}
\]
18.15: Intramolecular Ester Formation: Lactones. Lactones are cyclic esters derived from the intramolecular esterification of hydroxy-carboxylic acids. 4-Hydroxy and 5-hydroxy acids cyclize readily to form 5- and 6-membered ring ($\gamma$ and $\delta$) lactones.

\[
\begin{align*}
\text{HO-CH}_2\text{-CH}_2\text{-CH}_2\text{-C-} & \text{OH} \quad \rightarrow \quad \text{O} \\ \gamma\text{-butyrolactone} & \text{+ H}_2\text{O}
\end{align*}
\]

\[
\begin{align*}
\text{HO-CH}_2\text{-CH}_2\text{-CH}_2\text{CH}_2\text{-C-} & \text{OH} \quad \rightarrow \quad \text{O} \\ \delta\text{-valerolactone} & \text{+ H}_2\text{O}
\end{align*}
\]

18.16: Decarboxylation of Malonic Acid and Related Compounds. Carboxylic acids with a carbonyl or nitrile group at the $\beta$-position will decarboxylate (lose CO$_2$) upon heating.

Decarboxylation initially leads to an enol of the $\beta$-carbonyl group. This is a key step in the acetoacetic ester synthesis and malonic acid synthesis (Ch. 20.6).
18.17: Spectroscopic Analysis of Carboxylic Acids
Infrared Spectroscopy
Carboxylic acids:
- Very broad O-H absorption between 2500 - 3300 cm\(^{-1}\)
  broader than that of an alcohol
- Strong C=O absorption bond between 1700 - 1730 cm\(^{-1}\)

\[\text{OH} \quad \text{O} \quad \text{O-H} \quad \text{C=O} \quad \text{C-H}\]

\[\text{OH} \quad \text{O} \quad \text{No} \quad \text{C=O} \quad \text{C-H}\]

\[\text{C=O}\quad (180 \text{ ppm})\]

\[\delta \approx 12\]

\[\text{D}_2\text{O}\]

\[^1H\text{ NMR:}\] The -CO\(_2\text{H}\) proton is a broad singlet near \(\delta \approx 12\). When \(\text{D}_2\text{O}\) is added to the sample the -CO\(_2\text{H}\) proton is replaced by D causing the resonance to disappear (same for alcohols). The -CO\(_2\text{H}\) proton is often not observed.

\[^{13}\text{C NMR:}\] The chemical shift of the carbonyl carbon in the \(^{13}\text{C}\) spectrum is in the range of \(~165 – 185\). This range is distinct from the aldehyde and ketone range \(~190 – 220\)
problem 18.33b

Chapter 19: Carboxylic Acid Derivatives: Nucleophilic Acyl Substitution

19.1: Nomenclature of Carboxylic Acid Derivatives
(please read)