Chapter 16: Carboxylic Acids, Esters, and Other Acid Derivatives

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An organic compound with carboxyl functional group
Carboxyl group: A carbonyl group (C=O) with a hydroxyl group (—OH) bonded to the carbonyl carbon atom
A general structural representation for a carboxyl group is shown below

![Carboxylic Acid](image)
**Carboxylic Acid Derivative**

An organic compound synthesized from or converted into a carboxylic acid.

Four important carboxylic acid derivatives:

- Esters
- Acid chlorides
- Acid anhydrides
- Amides

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**Common names of carboxylic acids**

Common names are usually derived from some Latin or Greek word that is related to a source for the acid.

Name of a monocarboxylic acid is formed by taking the Latin or Greek root name for the specific number of carbon atoms and appending the suffix “-ic” acid.

- The positions of substituents are denoted by Greek alphabet rather than numbers with reference to the carbonyl carbon (C₁), e.g., C₂ is alpha (α), C₃ is beta (β), C₄ is gamma (γ), and C₅ is delta (δ).

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**IUPAC Rules for Naming Monocarboxylic Acids**

- **Rule 1**: Select the longest carbon chain that includes the carbon atom of the carboxyl group as the parent chain.
- **Rule 2**: Name the parent chain by changing the “-e” ending of the corresponding alkane to “-oic” acid.
- **Rule 3**: Number the parent chain by assigning the #1 to the carboxyl carbon atom.
- **Rule 4**: Determine the identity and location of any substituents in the usual manner, and append this information to the front of the parent chain name.
First Six Unbranched Monocarboxylic Acids

<table>
<thead>
<tr>
<th>Length of Carbon Chain</th>
<th>Structural Formula</th>
<th>Latin or Greek Root</th>
<th>Common Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>C₁ monoacid</td>
<td>H—COOH</td>
<td>form-</td>
<td>formic acid</td>
</tr>
<tr>
<td>C₂ monoacid</td>
<td>CH—COOH</td>
<td>acet-</td>
<td>acetic acid</td>
</tr>
<tr>
<td>C₃ monoacid</td>
<td>CH₂—CH—COOH</td>
<td>propion-</td>
<td>propionic acid</td>
</tr>
<tr>
<td>C₄ monoacid</td>
<td>CH₃(CH₂)₂—COOH</td>
<td>butyry-</td>
<td>butyric acid</td>
</tr>
<tr>
<td>C₅ monoacid</td>
<td>CH₃(CH₂)₃—COOH</td>
<td>valer-</td>
<td>valeric acid</td>
</tr>
<tr>
<td>C₆ monoacid</td>
<td>CH₃(CH₂)₄—COOH</td>
<td>capro-</td>
<td>caproic acid</td>
</tr>
</tbody>
</table>

*The mnemonic “Frogs are polite, being very courteous” is helpful in remembering, in order, the first letters of the common names of these six simple saturated monocarboxylic acids.

Carboxylic Acids

<table>
<thead>
<tr>
<th>Carboxylic acids</th>
<th>Formula</th>
<th>found in</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formic acid (methanoic acid)</td>
<td>HCOOH</td>
<td>蚁酸</td>
</tr>
<tr>
<td>Acetic acid (ethanoic acid)</td>
<td>CH₃COOH</td>
<td>醋酸</td>
</tr>
<tr>
<td>Propionic acid (propionic acid)</td>
<td>CH₃(CH₂)₂COOH</td>
<td>Swiss cheese</td>
</tr>
<tr>
<td>Butyric acid (butyric acid)</td>
<td>CH₃(CH₂)₃COOH</td>
<td>硬脂酸</td>
</tr>
<tr>
<td>Valeric acid (pentanoic acid)</td>
<td>CH₃(CH₂)₄COOH</td>
<td>玛瑙树脂</td>
</tr>
<tr>
<td>Caproic acid (hexanoic acid)</td>
<td>CH₃(CH₂)₅COOH</td>
<td>山羊脂肪</td>
</tr>
<tr>
<td>Caprylic acid (heptanoic acid)</td>
<td>CH₃(CH₂)₆COOH</td>
<td>山羊脂肪</td>
</tr>
<tr>
<td>Capric acid (octanoic acid)</td>
<td>CH₃(CH₂)₇COOH</td>
<td>山羊脂肪</td>
</tr>
<tr>
<td>Palmitic acid (nonanoic acid)</td>
<td>CH₃(CH₂)₈COOH</td>
<td>山羊脂肪</td>
</tr>
<tr>
<td>Steric acid (octadecanoic acid)</td>
<td>CH₃(CH₂)₁₈COOH</td>
<td>棕榈油</td>
</tr>
</tbody>
</table>

Dicarboxylic and Saturated Acids

**Dicarboxylic Acids:** Carboxylic acid that contains two carboxyl groups.

**Saturated acids:** Named by appending the suffix “-dioic” acid to the corresponding alkane name.

Aromatic Carboxylic Acids

The simplest aromatic carboxylic acid is called benzoic acid.

Other simple aromatic acids are named as derivatives of benzoic acid.
First Six Unbranched Dicarboxylic Acids

<table>
<thead>
<tr>
<th>Length of Carbon Chain</th>
<th>Structural Formula</th>
<th>Latin or Greek Root</th>
<th>Common Name*</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_2 diacid</td>
<td>HOOC—COOH</td>
<td>oxal-</td>
<td>oxalic acid</td>
</tr>
<tr>
<td>C_3 diacid</td>
<td>HOOC—CH_2—COOH</td>
<td>malon-</td>
<td>malonic acid</td>
</tr>
<tr>
<td>C_4 diacid</td>
<td>HOOC—(CH_2)_2—COOH</td>
<td>succin-</td>
<td>succinic acid</td>
</tr>
<tr>
<td>C_5 diacid</td>
<td>HOOC—(CH_2)_3—COOH</td>
<td>glutar-</td>
<td>glutaric acid</td>
</tr>
<tr>
<td>C_6 diacid</td>
<td>HOOC—(CH_2)_4—COOH</td>
<td>adip-</td>
<td>adipic acid</td>
</tr>
<tr>
<td>C_7 diacid</td>
<td>HOOC—(CH_2)_5—COOH</td>
<td>pimel-</td>
<td>pimelic acid</td>
</tr>
</tbody>
</table>

*The mnemonic “Oh-oh, each good apple pie” is helpful in remembering, in order, the first letters of the common names of these six simple dicarboxylic acids.

Common Acids

**Acetic Acid: CH_3COOH**
- Vinegar is 4%-8% (v/v) acetic acid solution
- Colorless liquid with sharp odor

**Oxalic acid: HOOC-COOH - found in spinach and cabbage**
- Harmful at high concentrations
- Used to remove rust, bleach straw, and leather and ink stains

Polyfunctional Carboxylic Acids (PCA)

PCAs contain at least one or more functional groups other than carboxyl group

PCAs are commonly found in living organisms and play an important role in human body
- Occur in many fruits
- Used in over the counter skin care products and prescription drugs

Common types of PCAs:
- Unsaturated acids
- Hydroxy acids
- Keto acids

Unsaturated Acids

Contain at least one carbon-carbon double bond (C=C):

Two types of monounsaturated carboxylic acids:
- Trans - unsaturated carboxylic acids
- Cis – unsaturated carboxylic acids

Examples:
- Propenoic acid (acrylic acid) used in the manufacture of polymeric materials.
- Futenedioic acid - has two forms
  - Fumaric acid: trans-form
  - Maleic acid: cis-form
Hydroxy Acids

Contain at least one hydroxyl group and are naturally present in many foods

Examples:
- Glycolic acid: present in juice from sugar cane and sugar beets
- Lactic acid: Present in sour milk, sauerkraut, and dill pickles
- Malic acid and tartaric acid occur naturally in fruits

Keto Acids

Contain a carbonyl (C=O) group within a carbon chain.

Example:
- Pyruvic acid - simplest keto acid with odor resembling that of vinegar (acetic acid) and it is also a metabolic acid

Reactions of β-keto acids.

β-keto acids are readily decarboxylated.

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 \quad \text{CH-COOH} & \quad \text{CH}_3 \quad \text{CH}_2 + \text{CO}_2
\end{align*}
\]

Metabolic acids

Metabolic acids: Polyfunctional acids formed as intermediates of metabolic reactions in the human body.

There are eight such acids that will appear repeatedly in the biochemistry chapters

Metabolic acids are derived from:
- Propionic acid, (C₃ mono acid): lactic, glyceric, and pyruvic acids
- Succinic acid (C₄ diacid): fumaric, oxaloacetic, and malic acids
- Glutaric acid (C₅ diacid): α-ketoglutaric and citric acids
At Room Temperature and Pressure

Straight chain carboxylic acids with 1-9 carbon atoms are liquids and strong odors.
Straight chain carboxylic acids with >10 C atoms are waxy solids with no odor.
Aromatic and dicarboxylic acids: Odorless solids

Melting and Boiling Points

Most polar organic compounds because of the presence of polar C=O and polar -OH groups
Form H-bonding due to strong polar groups
Therefore have highest melting and boiling points compared to those of other types of compounds.

Boiling Points

Hydrogen Bonding in Carboxylic Acids

A given carboxylic acid molecule form two hydrogen bonds to another carboxylic acid molecule, producing a “dimer”, a complex with a mass twice that of a single molecule.
Physical properties of carboxylic acids
Carboxyl groups exhibit very strong hydrogen bonding.

Acidity

\[ R-C-OH \rightleftharpoons R-C-O^- + H^+ \]
Carboxylic acid
Carboxylate ion
Hydrogen ion

\[ R-C-OH + NaOH \rightarrow R-C-O^-Na^+ + H_2O \]
Carboxylic acid
Strong base
Carboxylic acid salt
Water

Oxidation of Alcohols to Carboxylic Acids
- Non-aromatic carboxylic acids: Oxidation of primary alcohols or aldehydes, using an oxidizing agent such as K$_2$Cr$_2$O$_7$
- Aromatic carboxylic acids: Oxidation of a carbon side chain (alkyl group) on a benzene derivative
- Examples:

\[
\text{Ethanol} \xrightarrow{[O]} \text{Acetaldehyde} \xrightarrow{[O]} \text{Acetic acid}
\]

\[
\text{[Aromatic derivative]} \xrightarrow{K_2Cr_2O_7, H_2SO_4} \text{Carboxylic acid} + \text{CO}_2 + 3\text{H}_2\text{O}
\]

Oxidation of primary alcohols

\[
\text{Oxidation of a primary alcohol:} \quad \text{[O]} \quad \text{[O]} \quad \text{Carboxylic acid}
\]

1° Alcohol
An aldehyde
Oxidation of secondary and tertiary alcohols

Oxidation of a secondary alcohol:

\[
\text{Oxidation of a secondary alcohol:} \quad \overset{\text{OH}}{\text{R}^1\text{C}-\text{R}^2} + (\overset{\text{O}}{\text{O}}) \quad \text{H} \quad \overset{\text{R}^1\text{C}-\text{R}^2}{\text{OH}} \quad \text{A ketone}
\]

Oxidation of a tertiary alcohol:

\[
\text{Oxidation of a tertiary alcohol:} \quad \overset{\text{OH}}{\text{R}^1\text{C}-\text{R}^2} + (\overset{\text{O}}{\text{O}}) \quad 2^\text{'} \text{ Alcohol} \quad \text{No reaction} \quad 3^\text{'} \text{ Alcohol}
\]

Acidity Carboxylic Acids

Carboxylic acids are weak acids.
In water they dissociate to release protons (H\(^+\)) and form carboxylate ion (RCOO\(^-\)). Equilibrium reactions and equilibrium lies towards the left indicating that small amount of acid is ionized.

Monocarboxylic acids release one H\(^+\) to form carboxylate ion with one negative charge.
Dicarboxylic acids release two H\(^+\) ions to form carboxylate ion with two negative charges and so on.

Reactions of Carboxylic acids with bases

Carboxylic acids react with bases to form salt and water.

\[
\text{R-COOH} + \text{NaOH} \rightarrow \text{R-COONa} + \text{H}_2\text{O}
\]

Naming carboxylic acid salts:

- Positive ion name (Na\(^+\), K\(^+\) etc) followed by anion (RCOO\(^-\)) name (drop "-ic acid" and replace with "-ate")
- Names of anion and cation are written as separate words.
- Example 1: CH\(_3\)COO\(^-\)Na\(^+\) -- Sodium acetate
- Example 2: C\(_6\)H\(_5\)COO\(^-\)K\(^+\) -- Potassium benzoate

Carboxylic acid salts are more soluble in water than their parent acids.
- Example: Benzoic acid = 3.4 g/L; sodium benzoate = 550g/L.

Oxidation of Aldehydes

Tollen’s and Benedict’s

\[
\text{Oxidation of alkyl side chain substituted on a benzene ring}
\]

\[
\text{Ar} \cdot \text{CH}_2\cdot \text{CH}_2 \rightarrow \text{Ar} \cdot \text{COOH}
\]

\[
\text{Ar} \cdot \text{CH}_2\cdot \text{CH}_2 \rightarrow \text{Ar} \cdot \text{COOH}
\]

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Uses of Carboxylic Acid Salts

Good antimicrobial and antifungal agents

Benzoate salts: Effective (0.1%, m/m) against yeast and mold in beverages, jams and jellies, etc.

Sodium sorbate: Inhibits mold and yeast in dairy products, dried fruits, some meat and fish products

Propionate: Used in preservation of baked goods

Benzoate and sorbate can't be used in yeast leavened baked goods as they inhibit mold and yeast

Esters: Carboxylic Acid Derivatives

An ester is a carboxylic acid derivative in which the —OH portion of the carboxyl group has been replaced with an —OR group

The simplest ester, which has two carbon atoms, has a hydrogen atom attached to the ester functional group

There are two three-carbon esters

The simplest aromatic ester is derived from benzoic acid

Esterification Reaction

Esters are produced by an esterification reaction

Esterification reaction: Reaction of a carboxylic acid with an alcohol (or phenol) to produce an ester

Esterification reaction require a strong acid catalyst such as H_2SO_4

Preparation of esters. Esterification

acid + alcohol -----> ester + H_2O
Cyclic Esters (Lactones)

Hydroxy acids contain both a hydroxyl and a carboxyl group and such compounds have the capacity to undergo intermolecular esterification to form cyclic esters.

Takes place in situations where a five- or six-membered ring can be formed.

Cyclic esters are called lactones.

Naming Esters

The name for the alcohol part of the ester appears first and is followed by a separate word giving the name for the acid part of the ester.

The name for the alcohol part of the ester is simply the name of the R group (alkyl, cycloalkyl, or aryl) present in the —OR portion of the ester.

The name for the acid part of the ester is obtained by dropping the “-ic” acid ending for the acid’s name and adding the suffix “-ate.”

IUPAC names for lactones are generated by replacing the “-ic” ending of the parent hydroxycarboxylic acid name with “-olide” and identifying the hydroxyl-bearing carbon by number.

Alkyl(R’) alkan(R)oate (a two-part name)

R’ = Alkyl (R’) group is attached to the O

methylmethanolate

isopropylbenzoate

ethylbutanolate
Flavor/Fragrance Agents

Esters are largely responsible for the flavor and fragrance of fruits and flowers.
Generally the natural flavor or odor is due to a mixture of esters with one dominant ester.
The structures of esters in natural flavors are closely related to one another.
Example, the apple and pineapple flavoring agents differ by one carbon atom (methyl versus ethyl).

Pheromones and Medications

A number of pheromones (sex hormones) contain ester functional group.
For example: Isoamyl acetate is an alarm pheromone in honey bee and methyl p-hydroxybenzoate is a sexual attractant for canine species.
Several medicines including aspirin, benzocain (a local anesthetic) and oil of wintergreen (a counterirretant) are esters.

Isomers of Carboxylic Acids

Functional Group Isomers: Carboxylic acids and esters with the same number of carbon atoms and the same degree of saturation.
Skeletal Isomers: Both carboxylic acid and esters exhibit skeletal isomers.
Positional Isomers: Esters exhibit positional isomerism, i.e., the functional group can change its position.

Physical Properties of Esters

No hydrogen atom attached to oxygen atoms, therefore they don’t form H-bonding among other molecules of itself.
Therefore have lower BP than those of alcohols and acids.
Lower molecular weight esters are soluble in water because they can from H-bonding with water molecules.
Esters with 5 or more carbon atoms are sparingly soluble in water.
Esters have pleasant odor.
Ester–Water Hydrogen Bonding

Low-molecular-mass esters are soluble in water because of ester–water hydrogen bonding.

Ester Hydrolysis

Ester Hydrolysis: breaking the carbon–oxygen single (C-O) bond that holds the “alcohol part” and the “acid part” in an ester

Results in the formation of an alcohol and a carboxylic acid (reverse of esterification process)

Ester hydrolysis needs a strong catalyst such as an acid, a base or an enzyme

Saponification: hydrolysis of an organic compound, under basic conditions, in which a carboxylic acid salt is one of the products

Hydrolysis of esters.

\[
\text{CH}_3\text{CH}_2\text{O}^+ + \text{H}_2\text{O}^+ \xrightarrow{\text{heat}} \text{CH}_3\text{CH}_2\text{OH} + \text{CH}_3\text{CO}^+
\]

• Hydrolysis of acid chlorides

• Hydrolysis of acid anhydrides

Fatty acids and Glycerides

Fatty Acids

Glycerides
Hydrolysis of Glycerides: Saponification

\[
\begin{align*}
\text{CH}_2\text{O} & \xrightarrow{\text{M}^+ \text{OH}^- \text{H}_2\text{O}} \text{CH}_2\text{OH} \\
\text{CH} & \xrightarrow{\text{H}_2\text{O} \text{H}_3\text{O}^+} \text{CH}_2\text{OH} + \text{Soap} \\
\text{CH}_3\text{O} & \xrightarrow{\text{M}^+ \text{OH}^- \text{H}_2\text{O}} \text{CH}_2\text{OH} \\
\text{Fat or oil} & = \text{Na}^+ \text{ or } \text{K}^+ \\
\text{(triglyceride)} & \\
\end{align*}
\]

Metal alkanoate (-oate suffix for anion)

E.g. sodium salt of proponic acid is named as sodium proponate

Nomenclature of Carboxylate salts

Metal alkanoate (-oate suffix for anion)

E.g. sodium salt of proponic acid is named as sodium proponate

Thioesters

Thioester: A sulfur-containing analog of an ester in which an —SR group has replaced the —OR group.

The most important naturally occurring thioester is acetyl coenzyme A.

Acetyl coenzyme: plays a central role in the metabolic cycles of the body to obtain energy to “run itself”

Polyesters

Polymers are formed by reacting difunctional monomers

Examples: dicarboxylic acids and dialcohols are used for the formation of polyesters

Two important polymers:

- Poly(ethylene terephthalate) (PET)
- Lactomer
Poly(ethylene terephthalate)**

Poly(ethylene terephthalate) (PET): Prepared by reacting terephthalic acid (a diacid) and ethylene glycol (a dialcohol)
Used for making textiles and other plastic applications

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**Biodgradable Polymers**

Lactomer: Used in surgical staples because of its biodgradable nature
It simply dissolves after several weeks and the by-products formed are lactic acid and glycolic acid both of which are part of human body

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**Acid Anhydrides**

Acid Anhydrides: A carboxylic acid derivative in which the “-OH” portion of the carboxyl group has been replaced with a “acyl” group.
Two types of acid anhydrides:
- Symmetrical acid anhydrides
- Mixed anhydrides

General reaction

\[ R\text{-CO} - \text{OH} + \text{HO}-R' \rightarrow R\text{-CO}-R' + \text{H}_2\text{O} \]

---

**Nomenclature of Acid Anhydrides**

Alkanoic anhydride (-oic anhydride suffix)

E.g. anhydride of proponoic acid is named as proponoic anhydride
Acid Chloride

Acid Chloride: A carboxylic acid derivative in which the “-OH” portion of the carboxyl group has been replaced with a “-Cl” atom.

Naming Acid Chlorides

- Replace the “-ic acid” ending of the common name of the parent carboxylic acid with “-yl chloride.”
- Replace the “-oic acid” ending of the IUPAC name of the parent carboxylic acid with “-oyl chloride.”

Nomenclature of Acid Halides

Alkanoyl halide (-oyl halide suffix)
or use common acyl name from acid
E.g. chloride of proponoic acid is named as proponoyl chloride

Preparation of Acid Chlorides

Preparation of acid chlorides: Parent carboxylic acid is reacted with one of several inorganic chlorides (PCl₃, PCl₅, or SOCl₂).

Uses: Useful starting materials for the synthesis of other carboxylic acid derivatives such as esters and amides.

General Example:

Acyl Transfer Reactions

Acyl group: The portion of a carboxylic acid that remains after the —OH group is removed from the carboxyl carbon atom.

Carboxylic acids, acid chlorides as well as acid anhydrides contain acyl groups

Compounds with acyl groups when reacted with an alcohol or phenol result in the formation of an ester
Inorganic Acids Esters: phosphate esters

Inorganic acids such as sulfuric, phosphoric, and nitric acids react with alcohols to form esters (similar to carboxylic acids).

The most important biochemical inorganic esters are phosphate esters.

Phosphoric Acid Anhydrides

Three biologically important phosphoric acids are phosphoric acid, diphosphoric acid, and triphosphoric acid.

Examples of such esters in the human body include adenosine diphosphate (ADP), and adenosine triphosphate (ATP).

Nitroglycerin

An inorganic tri-nitrate ester of glycerol (trinitro glycerine)

Used for making explosives

Used to treat heart related diseases, e.g., chest pain