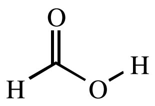
Chapter 15 – Carboxylic Acids and Esters

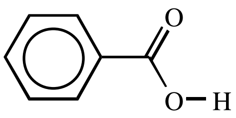
15.1 Occurrence, Names, and Physical Properties of Carboxylic Acids

Almost all naturally occurring acids are carboxylic acids (-CO_2H). They are weak acids (Chapter 8, p. 223). The other type of acid your book mentions, sulfonic acids (RSO_3H), are generally strong acids and don't occur naturally. Their salts (sulfonates, $RSO_3^-Na^+$) are commonly used in detergents, dyes, and pharmaceuticals. We won't consider sulfonic acids further.

Carboxylic acid groups are always terminal groups with a carbonyl carbon also bound to a hydroxy group. Your book lists some common carboxylic acids on p. 453. These and some others include:



formic acid



benzoic acid

$CH_3(CH_2)_{16}CO_2H$

stearic acid

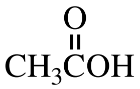
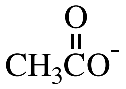
Formic acid is the principal ingredient and stinging agent of most ant bites. Benzoic acid is found in many plants: for example, the Voodoo lily uses it to attract insects needed for pollination. Stearic acid is found in beef tallow (fat) and (after reaction with NaOH) is one of the active components in old lye soap as well as modern soaps (sodium tallowate appears on the ingredient labels of soaps, it is a mixture of several similar sodium salts of carboxylic acids, one of which is sodium stearate).

Dicarboxylic acids have 2 -CO_2H groups and tricarboxylic acids have 3 -CO_2H groups (citric acid has 3 -CO_2H groups). You might at first guess that dicarboxylic acids would yield more acidic solutions than comparable monocarboxylic acids, but there usually isn't much difference between them. For example 0.1 M $CH_3CH_2CH_2CO_2H$ has pH of 2.91, while

$HO_2CCH_2CH_2CO_2H$ has the very similar pH of 2.60. The one case where having multiple $-CO_2H$ groups is important is when they are close together. Thus 0.1 *M* $HO_2CCH_2CO_2H$ (one fewer $-CH_2-$ group) has a pH of 1.93 and 0.1 *M* HO_2CCO_2H (two fewer $-CH_2-$ groups) has a pH of 1.13. Even so, the difference in pH is less than 1 unit (roughly a factor of 3.5 times more acidic).

Carboxylic acids follow similar solubility trends to alcohols. That is, the small acids (1 – 4 carbons) are completely soluble in water, then as the chains get longer solubility decreases (see Table 15.1, p. 454 of textbook). Except for formic acid, acid strength (i.e. K_a, p. 264 of textbook) doesn't depend on the length of the carbon chain attached to the carboxylic acid group. Formic acid is different because it has a hydrogen bound to the acid group. Carboxylic acids also hydrogen bond with each other, as well as water. The result is higher boiling and melting points than might be expected solely on the basis of their size. In basic solutions, these species exist as carboxylate anions (RCO_2^-).

To name carboxylic acids, find the longest carbon chain. Use the suffix "oic acid" in place of the final "e." For the ions, "oic acid" becomes "oate ion." For common names, "ic acid" and "ate ion" are used. Thus for ethane:

 $CH_3\overset{\overset{O}{\|}}{C}OH$	 $CH_3\overset{\overset{O}{\|}}{C}O^-$
ethanoic acid	ethanoate ion
acetic acid	acetate ion

In general, the IUPAC name is used. The exceptions are for acids whose common names are widely used.

15.2 Acidity of Carboxylic Acids

Since all carboxylic acids are weak acids, all exist in an equilibrium in water. The generic equilibrium equation is:

$$RCO_2H_{(aq)} + H_2O_{(\ell)} \rightleftharpoons RCO_2^-{}_{(aq)} + H_3O^+{}_{(aq)} \qquad K_a = \frac{[RCO_2^-][H^+]}{[RCO_2H]} \approx 10^{-5}$$

where $[H_3O^+] \equiv [H^+]$. (Recall that the water does not change concentration and therefore is incorporated into the K_a constant.) Most simple carboxylic acids have acid dissociation constants equal to about 10^{-5}. Such a small K_a means that very little of the acid is ionized in water. Nonetheless, carboxylic acids are much stronger acids than phenols (typical $K_a = 10^{-10}$).

Carboxylic acids react with bases, but only strong bases completely remove the proton (hydrogen ion) from the acid group. The resulting carboxylate ion is then a weak base. When a strong acid is added to a solution containing carboxylate ions, the acid protonates it, regenerating the parent carboxylic acid.

$$RCO_2H + OH^- \rightarrow RCO_2^- + H_2O$$

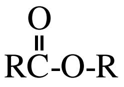
$$RCO_2^- + H_3O^+ \rightarrow RCO_2H + H_2O$$

As we saw earlier, small carboxylic acids are quite water soluble. However, these acids don't normally reside in our bodies (except sometimes as food, e.g. acetic acid (vinegar)). The carboxylic acids that are found in human tissue are typically fatty acids. These are acids with long carbon chains that cause them to have very low solubility. When a proton is removed from a fatty acid, the resulting carboxylate ion will always have a significantly higher solubility (even if in absolute terms the solubility is still low).

Finally, carboxylic acids are very stable to air oxidation. Further oxidation beyond the carboxylic acid results in the break-up of the molecule to carbon dioxide (CO_2) and water. This kind of oxidation occurs only under the harshest conditions (e.g. burning).

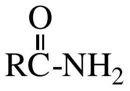
15.3 Conversion of Carboxylic Acids to Esters

Several chemicals of great synthetic utility are derived from carboxylic acids. Three are also of significant biological significance. Four molecules derived from carboxylic acids and another that is related to one of the carboxylic acid derivatives:



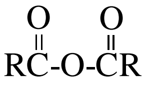
$$\mathrm{R\overset{\overset{O}{\|}}{C}\text{-}O\text{-}R}$$

ester



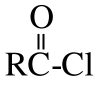
$$\mathrm{R\overset{\overset{O}{\|}}{C}\text{-}NH_2}$$

amide



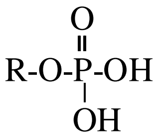
$$\mathrm{R\overset{\overset{O}{\|}}{C}\text{-}O\text{-}\overset{\overset{O}{\|}}{C}R}$$

anhydride



$$\mathrm{R\overset{\overset{O}{\|}}{C}\text{-}Cl}$$

acid chloride

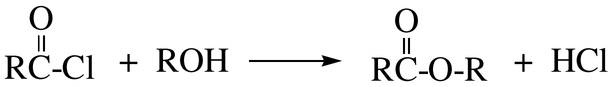


$$\mathrm{R\text{-}O\text{-}\underset{\underset{OH}{|}}{\overset{\overset{O}{\|}}{P}}\text{-}OH}$$

phosphate ester

Each of these compounds can be made from carboxylic acids and each can converted back to a carboxylic acid by hydrolysis. The high reactivity of anhydrides and acid chlorides causes them never to be found free in nature. Note the phosphate ester is somewhat different than the molecule your book draws (top figures on p. 460). The book has an unnecessary carbonyl group between R and the phosphate group. While phosphate esters (or phosphoesters) are extremely important biologically, there are none that you would probably familiar with from everyday experience. We'll discuss the first two carboxylic acid derivatives here, esters and phosphate esters later in this chapter and amides in Chapter 16.

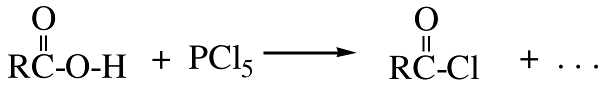
Of these derivatives, the acid chlorides are by far the most reactive. They react with almost any molecule with a polar –OH bond. This includes water and alcohols. For example:



$$\mathrm{R\overset{\overset{O}{\|}}{C}\text{-}Cl} + \mathrm{ROH} \longrightarrow \mathrm{R\overset{\overset{O}{\|}}{C}\text{-}O\text{-}R} + \mathrm{HCl}$$

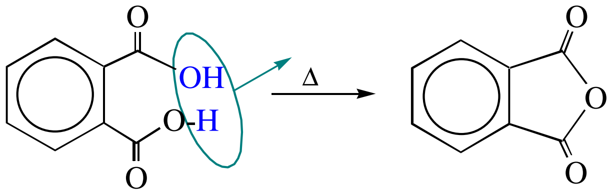
where R = H or an organic group. Here we see an acyl group ($\mathrm{R\overset{\overset{O}{\|}}{C}\text{-}}$) transferred to the alcohol.

This provides a simple way to make esters. (Acid chlorides are almost always made from carboxylic acids, so there is normally no reason to do the reaction with water.) Acid chlorides are frequently made by adding a chlorinating agent (e.g. $SOCl_2$) to a carboxylic acid.

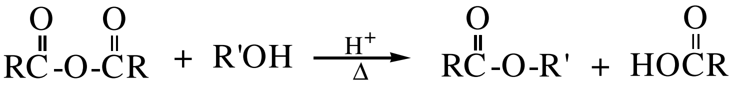


$$R\overset{\overset{O}{\|}}{C}\text{-O-H} + PCl_5 \longrightarrow R\overset{\overset{O}{\|}}{C}\text{-Cl} + \cdots$$

Anhydrides also serve as acyl transfer agents, but they are less reactive. This has tradeoffs. Anhydrides are easier to handle, but more forceful conditions are required for their reaction making them less accessible. As the name suggests removing water from a carboxylic acid can make an anhydride. This direct method only works for compounds that will yield cyclic anhydrides. An example of which is shown below. We won’t worry about other reactions that produce anhydrides.

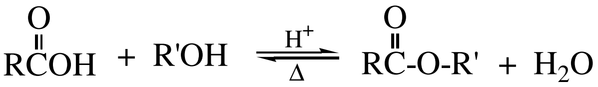


Reacting an anhydride with an alcohol is similar to running this reaction in reverse. Unlike the reaction of an acid chloride with an alcohol, this reaction requires heat and an acid catalyst.



$$R\overset{\overset{O}{\|}}{C}\text{-O-}\overset{\overset{O}{\|}}{C}R + R'OH \xrightarrow[\Delta]{H^+} R\overset{\overset{O}{\|}}{C}\text{-O-R}' + HO\overset{\overset{O}{\|}}{C}R$$

Esters can also be made directly through the reaction of carboxylic acids and alcohols.

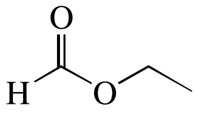
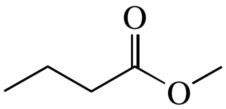
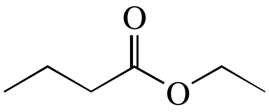
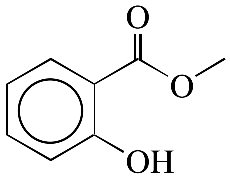


$$R\overset{\overset{O}{\|}}{C}OH + R'OH \underset{\Delta}{\overset{H^+}{\rightleftharpoons}} R\overset{\overset{O}{\|}}{C}\text{-O-R}' + H_2O$$

A drawback to this reaction is that it is an equilibrium, rather than a reaction that yields complete conversion. To overcome this a very large excess of the acid or alcohol is usually employed to drive the equilibrium to the right. These reactions are typically conducted when the water can be easily removed during the reaction. A second problem that limits the usefulness of this reaction is that the presence of the acid can lead to dehydration of the alcohol (see Chap. 12).

15.4 Occurrence, Names, and Physical Properties of Esters

Esters are common in biological systems and are frequently present in the foods we eat. Esters are generally pleasant smelling substances. The examples of esters shown below bear this out.

			
ethyl methanoate	methyl butanoate	ethyl butanoate	methyl salicylate
ethyl formate	methyl butyrate	ethyl butyrate	
rum	apples	pineapples	oil of wintergreen

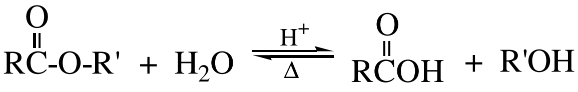
For the first three esters, notice how similar they are, yet how different are the flavors they generate. You should realize that the flavors of these and most other things depend on a blend of chemicals. Those shown here are the principal flavorants in the respective food item. This explains why many items that are "flavored" (e.g. banana flavored) don't quite taste like the real thing. Many people think that "all natural" flavorings are better than synthetic ones because they are purer and not made from chemicals. Ironically, the opposite is true. All nature flavorings sometimes taste better because they are less pure. It's the impurities that give the "natural" flavoring its expected taste. Oil of wintergreen is an example of a flavorant that actually is essentially the only flavoring agent in the plant. Thus, in this case, it is quite difficult to differentiate the natural from the synthetic.

The names given these esters are both systematic, although the first one is the preferred IUPAC name. In each case for RCO_2R', R' is named as a simple substituent (e.g. methyl, ethyl, etc.). In the IUPAC system, R is named by counting the carbon chain (including the carbonyl carbon), selecting the appropriate alkane name, and replacing the "–e" with "–oate." In the old system, one counts the carbon chain and selects the acid name with the same carbon chain. The "–ic acid" is replaced by "–ate." The latter naming system is still used with some frequency.

Esters are generally weakly polar. As always, polarity decreases as molecular size increases. This results in slightly elevated boiling points as compared to comparably sized molecules. Your book uses methyl acetate (bp = 57 ºC) as an example. 2-Methylbutane has nearly the same molecular size, shape, and weight and boils at 28 ºC. In contrast, butanoic acid (which is a better comparison than the book's acetic acid) boils at 164 ºC. The difference is that butanoic acid can hydrogen bond with itself and other molecules, while esters can hydrogen bond to molecules possessing –OH bonds, they cannot do so with themselves.

15.5 Some Reactions of Esters

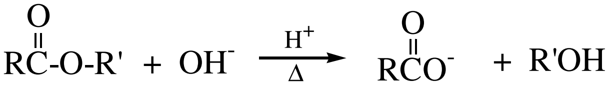
Esters are comparatively stable molecules and usually react slowly unless harsh conditions or catalysts (e.g. enzymes) are present. For example, they can react with water (essentially



$$R\overset{\overset{O}{\|}}{C}\text{-O-R'} + H_2O \underset{\Delta}{\overset{H^+}{\rightleftharpoons}} R\overset{\overset{O}{\|}}{C}OH + R'OH$$

formation reactions run backwards) or with external base, OH^-. If one goes back to the equilbrium at the bottom of p. 5 of the notes and, instead of using excess alcohol, one uses excess water, the equilibrium shifts to form a carboxylic acid and alcohol.

The reaction between added base and an ester is called <u>saponification</u>. This is the process by which soap was made years ago. Lye (a sodium hydroxide solution made from extracting wood ashes with water) was mixed with animal fat (which contains ester groups). The resulting material was soap which is principally the sodium salt of the resulting carboxylic acids and glycerin.

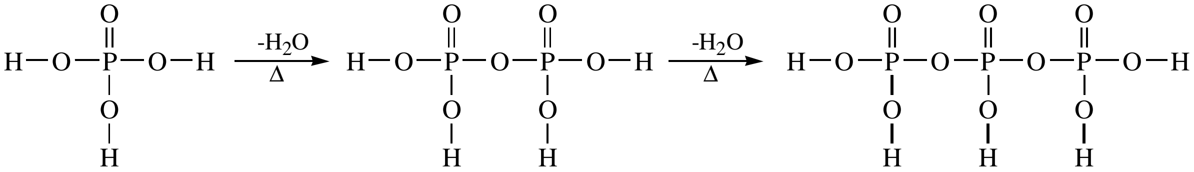


$$R\overset{\overset{\displaystyle O}{\|}}{C}\text{-O-R}' + OH^- \xrightarrow[\Delta]{H^+} R\overset{\overset{\displaystyle O}{\|}}{C}O^- + R'OH$$

Modern soaps use very similar ingredients but, because of purity and additives, they are much less harsh to the skin. Two asides: (i) The Celtic word *saipo* is the origin of the words *soap* and *saponification*. (ii) Soap has been known since at least 2800 BC (Sumeria), stone tablets indicate that it was used initially for cleaning wool and was only later (*ca.* 1500 BC) used for personal cleaning. Your book shows the mechanism for this reaction nicely on p. 469. It also discusses how soap works on p. 556 (Chapter 19).

15.6 Organophosphate Esters and Anhydrides

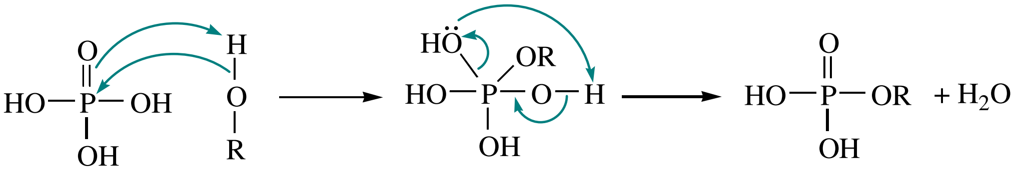
Phosphoric acid and its esterified derivatives are some of the more common molecules found in the body. The phosphate groups improve solubility and are a way for the body to store or release energy. As you know, phosphoric acid has the formula H_3PO_4. It forms anhydrides just like carboxylic acids do, with the one exception that because they have three –OH groups, poly(anhydrides) are possible.



While a weak acid, the middle molecule (pyrophosphoric acid, do you see the origin of the name?) is somewhat more acidic than phosphoric acid itself (K_{a1} is about 7 times larger). This difference is small enough not to have a major effect.

We will now discuss phosphoric acid, but the same discussion applies equally to pyrophosphoric acid and the tri-acid as well as their various esters. At very low pH (relative to K_{a1}) only the fully protonated form (H_3PO_4) exists in solution, while at very high pH (relative to K_{a3}) only the fully deprotonated form (PO_4^{3-}) exists in solution. In between the high and low pH limits, either two or three species will be present in significant amounts and an equilibrium involving them will exist. The position of the equilibrium (and hence their concentrations) changes as the pH changes.

Just like carboxylic acids may be esterified (converted into esters), so can phosphoric acids. The esterification process is essentially the same as the dehydration described above, with the exception that, again, there are multiple sites for an ester linkage in each of the phosphoric acids shown above. On p. 472 the book shows the esterification of pyrophosphate ester trianion. The esterification of simple phosphoric acid is similar and is shown below.



Your book chooses to discuss the ester it does because of its central importance to all biology. The diphosphate and triphosphate linkages shown at the beginning of this section are how energy is moved about in a cell. Energy is stored in adenosine triphosphate (ATP) and released when one phosphate linkage is hydrolyzed to yield adenosine diphosphate (ADP). These molecules are esters of a particular nucleoside. Nucleosides are molecules made up of a sugar molecule (in this case β-D-ribose) and a nucleic acid (one of the acids in DNA/RNA, in this case adenine). The energy release is about 7 Calories (28 kJ) per mole of ATP/ADP. This energy is energy within a cell. Fat is long-term storage.

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