4.7 HYDROLYSIS OF ESTERS

Hydrolysis of esters is just the reverse of esterification:

\[
\text{CH}_3\text{COCH}_3 + \text{H-O-H} \xrightarrow{\text{H}^+} \text{CH}_3\text{COOH} + \text{HOCH}_3
\]

It may be easier to see how the ester is split in two by placing the H-O-H molecule strategically under the ester functional group, as shown.

a) \[
\text{CH}_3\text{C}^\text{O-OCH}_3 \xrightarrow{\text{H}^+} \text{H-C-C}^\text{O-H} + \text{HOCH}_3
\]

b) \[
\text{COCOCH}_3 \xrightarrow{\text{H}^+} \text{C-C-O-H} + \text{H-O-CH}_3
\]

c) \[
\text{H-C-O-C-C-H} \xrightarrow{\text{H}^+} \text{C-C-O-H} + \text{H-C-C-=O-H}
\]

Try showing the hydrolysis for the following:

\[
\text{CH}_3\text{C}^\text{O-OCH}_3 + \text{H-O-H} \xrightarrow{\text{H}^+} \]

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Hydrolysis of esters is an **exergonic reaction**. However in the absence of a catalyst the activation energy barrier is often high enough to prevent hydrolysis from occurring at a significant rate.

There are in fact a lot of stable ester compounds in biological organisms that do not hydrolyze at an appreciable rate unless a specific **esterase** enzyme is available to lower that activation energy barrier. Fats (triglycerides) contain 3...
ester groups, but in the absence of esterase enzymes they hydrolyze only very slowly at typical biological temperatures and pH and can be stored in your body for long periods of time.

\[
\begin{align*}
\text{H}_2\text{C} & \text{-O-} \text{C-} (\text{CH}_2)_{16} \text{CH}_3 & (\text{C}_{16}) \\
\text{H} & \text{-O-} \text{C-} (\text{CH}_2)_{14} \text{CH}_3 & (\text{C}_{16}) \\
\text{H}_2\text{C} & \text{-O-} \text{C-} (\text{CH}_2)_{16} \text{CH}_3 & (\text{C}_{16})
\end{align*}
\]

**Acetylcholine** (structure shown below) is a neurotransmitter released at the **neuromuscular junction** and elsewhere. Acetylcholine is released from the ends of neurons at muscle. The acetylcholine binds to receptors in the membrane of the muscle cells and stimulates contraction of the muscle. It contains 2 functional groups. Name them.

\[
\text{Acetylcholine}
\]

\[
\text{CH}_3 \text{CH}_3 \text{CH}_3 + \text{N-CH}_2\text{CH}_2\text{O-} \text{C-} \text{CH}_3
\]

Wikipedia:”neuromuscular junction”

It is important that this activity not continue indefinitely and so an enzyme **acetylcholinesterase** is present which catalyzes the hydrolysis of the acetylcholine ester bond.
The separate product molecules no longer bind to the acetylcholine receptor site. Thus hydrolysis terminates the activity of the acetylcholine.

or written another way

\[
\begin{align*}
\text{Acetylcholine} & \quad \text{Acetylcholinesterase} \\
\text{CH}_3\text{NCH}_2\text{CH}_2\text{OCCH}_3 + \text{H}_2\text{O} & \quad \rightarrow \\
\text{CH}_3\text{NCH}_2\text{CH}_2\text{OH} + \text{HOCCCH}_3 \\
\end{align*}
\]

Succinyl choline (sometimes abbreviated sux) is an IV neuromuscular **blocker**
sometimes used to relax the muscles during surgery. Succinyl choline (or molecules like it) can be used to relax the tracheal muscles when inserting a plastic tube into the trachea to ensure an adequate air supply (**intubation**). This may be done either to allow mechanical respiration during surgery or to overcome airway obstructions due to trauma or other causes.
Succinylcholine binds the same receptors as acetylcholine, but after initial muscle contraction it causes relaxation. Among other adverse effects, patients tend to feel post-operative muscle pain from the initial extensive muscle contraction. It is hydrolyzed by an enzyme in the blood stream called pseudocholinesterase. Draw the structure of the products formed from the hydrolysis of succinyl choline.

\[
\begin{align*}
\text{CH}_3 & \quad \text{O} & \quad \text{O} & \quad \text{CH}_3 \\
\text{CH}_3\text{NCH}_2\text{CH}_2\text{OCH}_2\text{COCH}_2\text{CH}_2\text{NCH}_3 & & \text{CH}_3 \\
\text{Cl}^- & \quad \text{CH}_3 & & \text{Cl}^- & \quad \text{CH}_3
\end{align*}
\]

+ 2 H₂O →

Lactones (ester rings) can be hydrolyzed in similar fashion

\[
\begin{align*}
\text{GHB lactone} & & \text{GHB} \\
\text{OH} & & \text{OH} \\
+ \text{H-O-H} & - \text{H}^+ & \rightarrow
\end{align*}
\]

Try showing the hydrolysis product of the following:

\[
\begin{align*}
\text{+ H}_2\text{O} & - \text{H}^+
\end{align*}
\]
Can you predict why the original molecule in the third hydrolysis might not be too stable?

**Esters have fruity smells.**

Esters are responsible for many of the fruity smells and flavors found in fruits. Ethyl butanoate is a major component of peach flavor. Pentyl propanoate is a major component of apricot flavor. Methyl and ethyl acetate are found in pineapple along with other esters. Draw their structures.

Most fruit smells and flavors actually result from a combination of several different esters. When fruits start to spoil the esters are often hydrolyzed into alcohols and carboxylic acids. The carboxylic acids are responsible for the sharp unpleasant flavor associated with spoiled fruit.

\[
\text{fruity} \quad \rightleftharpoons \quad \text{sharp}
\]

Write the chemical equation for the hydrolysis of

a) methyl acetate (found in pineapples)
b) ethyl butanoate (in peaches)