






Chapter 12: Lipids

Lipids: Intro

Triglycerides
Phospholipids
Steroids
Saponification
Metabolism of fats

| Key | |
|---|----------|
|  | hydrogen |
|  | carbon |
|  | oxygen |
|  | nitrogen |
|  | sodium |

Lipids:

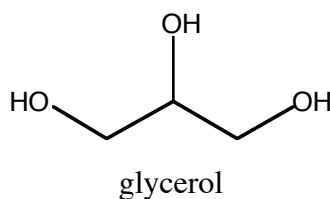
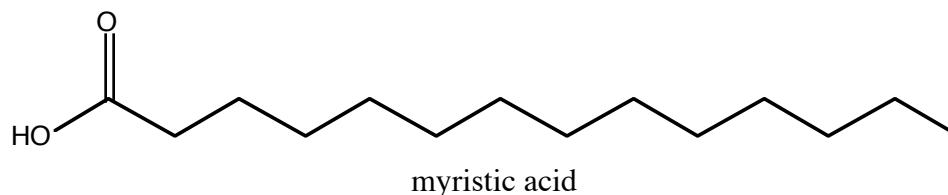
The term lipid is somewhat poorly defined: it is generally applied to oily or greasy biochemical substances which are not soluble in water. While proteins and sugars are distinctive because of similarities in chemical structure, the chemistry of lipids is varied, and so their physical properties (insolubility in water, oily consistency, etc.) loosely define this family of compounds. We will examine a few members of this very diverse collection molecules.

Triglycerides

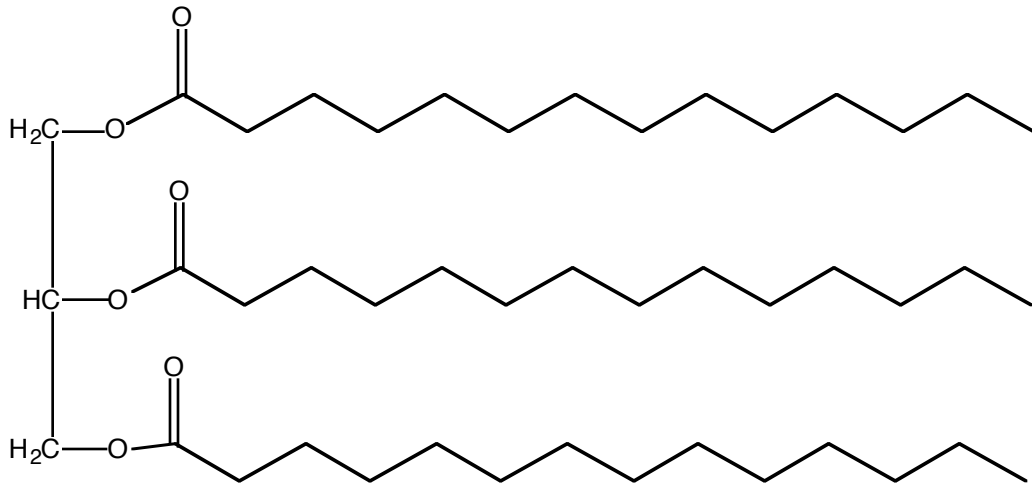
By far the most common lipid found in the human body is the triglyceride. Triglycerides are esters which form from the reaction of long-chain fatty acids and the glycerol molecule according to the scheme we learned earlier when we studied alcohols:



Shown below is the myristic acid molecule and the glycerol molecule, as well as the triglyceride formed from them, trimyristin. This is the major triglyceride in cows milk.

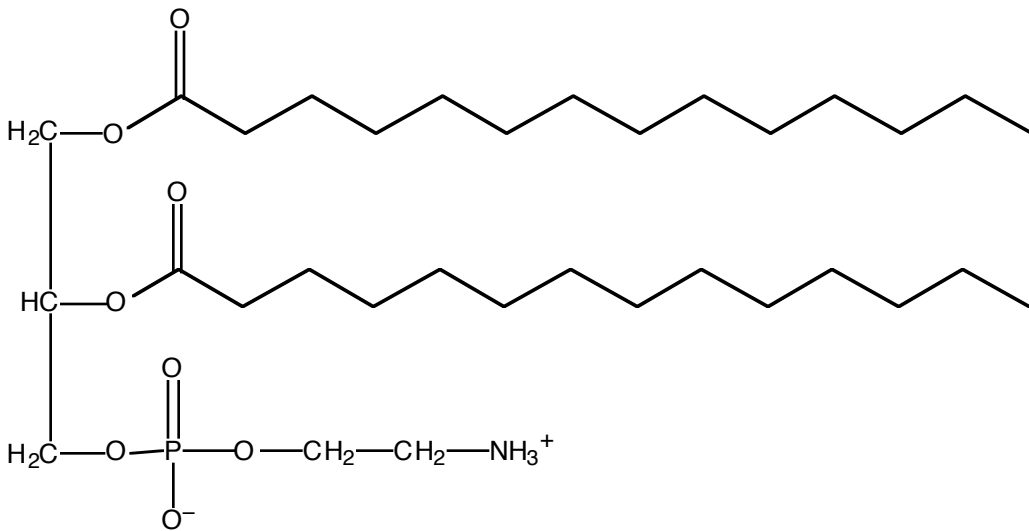


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trimyristin

A second class of lipids is called phospholipids. These compounds again use glycerol as a backbone, but contain only 2 conventional esters, which, like triglycerides utilize fatty acids. The third carbon, however, forms what is known as a phosphate ester, usually with a nitrogenous base. An example of a phospholipid is a class of compounds, known as cephalins. These are characterized by the ethanolamine groups attached to the phosphate group as shown below:



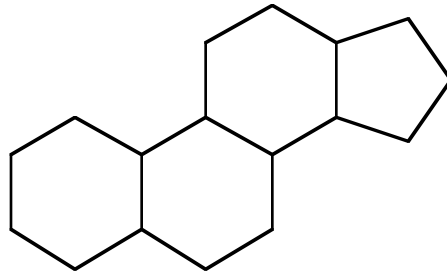
A Cephalin Molecule (Phosphatidyl Ethanolamine)

Cephalins are found in nervous tissue and are also essential to the clotting of blood. We have arbitrarily depicted a cephalin based on myristic acid.

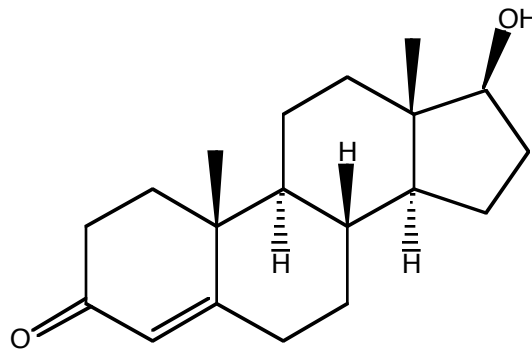
Steroids

Steroids are molecules which contain the steroid nucleus, a characteristic arrangement of rings as shown below:

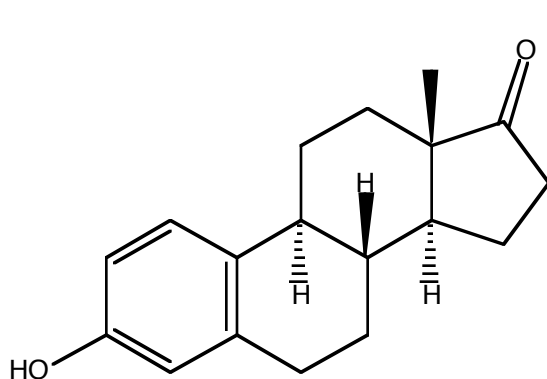
12 Lipids-4



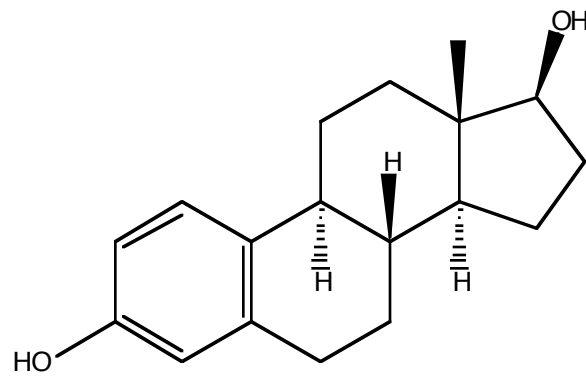
Steroids are utilized in a variety of roles in the body. Steroids are precursors of Vitamin D, hormones, bile salts, and structural elements in cell membranes. A few famous steroids are shown below.



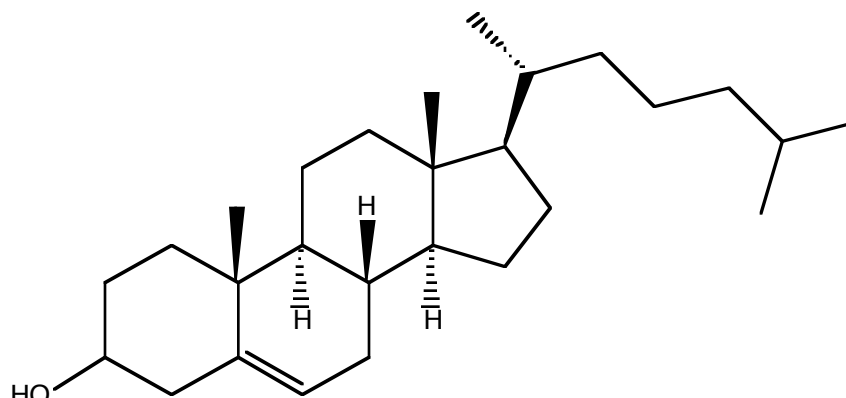
testosterone



estrone



estradiol



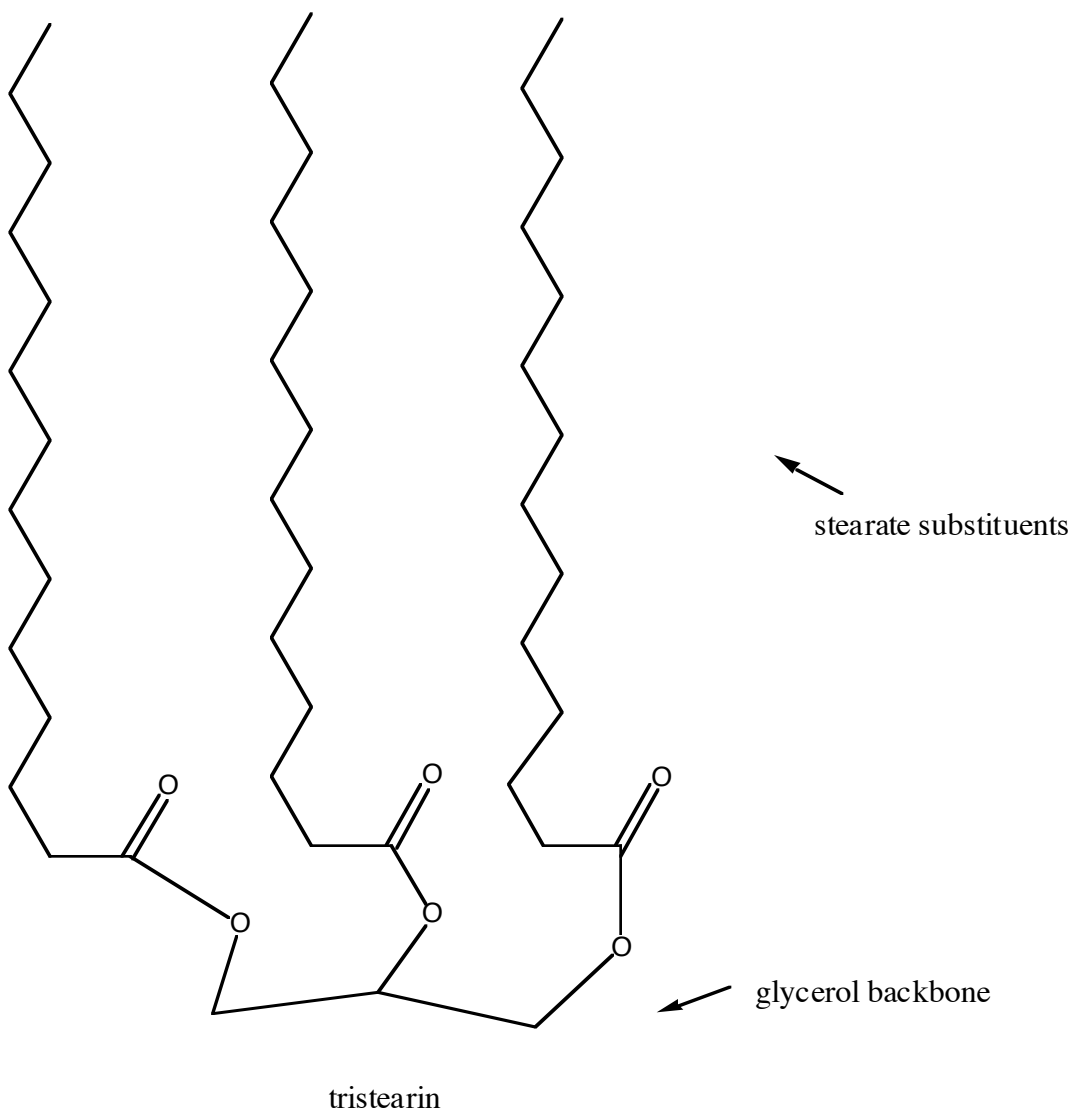
cholesterol

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Both estrone and estradiol are members of a class of compound named estrogens (usually classified as female sex hormones). Note the structural similarity between testosterone and estradiol. In fact, in females, estradiol is synthesized from testosterone.

Saponification: The Strange Story of Buster the Wonder Horse

Buster was truly a wonder horse: he could add, subtract, multiply and do differential calculus simply by tapping his hoof on the ground. He loved to eat alfalfa and do math in the meadow which his owners bought for him in gratitude for all the cash his performances pulled in. Buster used some of the glucose directly to power his massive hooves around the meadow and to fuel his impressive brain. But, like all sedentary and neurotic modern day horses, Buster started to put on weight as he approached middle age (in horse years). In fact, he was storing glucose as fat using the chemical reaction known as the **3 carbon squish**. He built up long chain carboxylic acids, also known as fatty acids, such as stearic acid--18 carbons long. He then added them to a glycerol molecule (three acids for each glycerol) to form a **triglyceride** known as **tristearin**, which he stored on his flanks as adipose tissue. Here's a sketch of a tristearin molecule:



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From time to time he tried to diet, eating only a small serving of oatmeal 3 times a day, and he lost a little weight. While he was doing so, his body utilized the stored fat via a reaction known as the **two carbon chop**.

But all good things must come to an end, and, one fine spring day, Buster solved his last addition problem, opened the daily paper for the last time, and began to solve his daily sudoku puzzle, swallowed his last mouthful of alfalfa, and breathed his last breath. His owners, not known for their sentimentality, sold his body to a rendering plant, where the collagen in Buster's great hooves was converted into glue, the meat on his bones to dog food, and his copious supply of horse fat into soap.

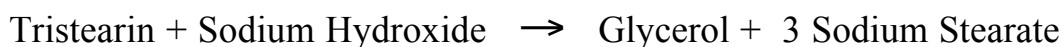
It is this last process which interests us here, because it utilizes a very famous reaction which reverses the esterification reaction that we have already studied. It is known as the **saponification of an ester**. In the presence of base, an ester is converted back into the alcohol and the acid from which it was ironically created. Actually, the acid itself is not produced, but rather the salt of the acid. The general scheme for a saponification reaction is as follows:



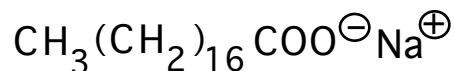
As noted above, the ester used in forming fatty tissue is known as a triglyceride, formed from an alcohol (glycerol, which has 3 alcoholic groups) and three molecules of fatty acid. The saponification of a triglyceride, then, is described by the following reaction:



In Buster's case, his triglyceride of choice was tristearin, whose parents were glycerol and 3 molecules of stearic acid. Saponification of this ester proceeded according to:

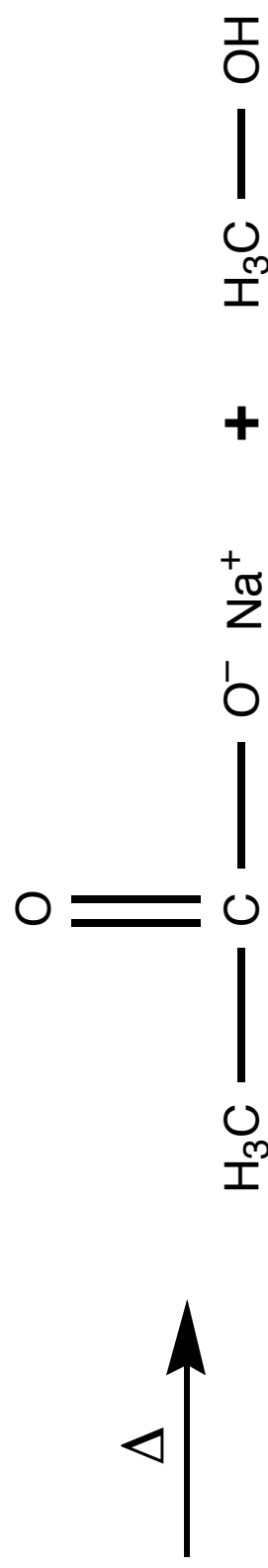
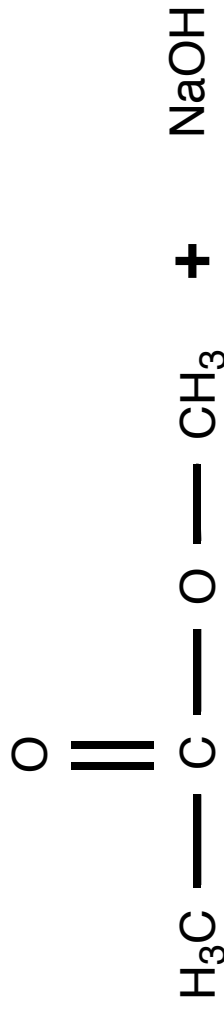
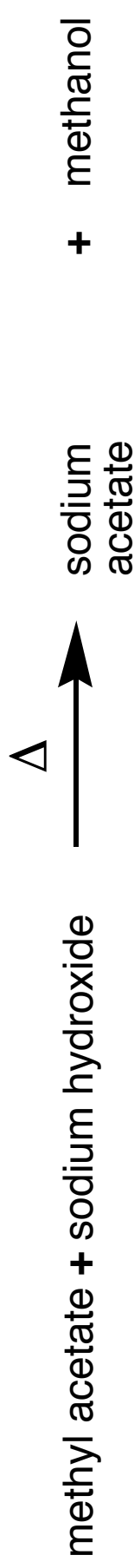


The saponification of a simple ester is shown in great detail in the figures on the next two pages. We note in passing that, due to the basic nature of the reaction medium, the sodium salt of the acid (as opposed to the acid itself) is formed in saponification reactions. Thus, in the saponification of tristearin, our product is sodium stearate:

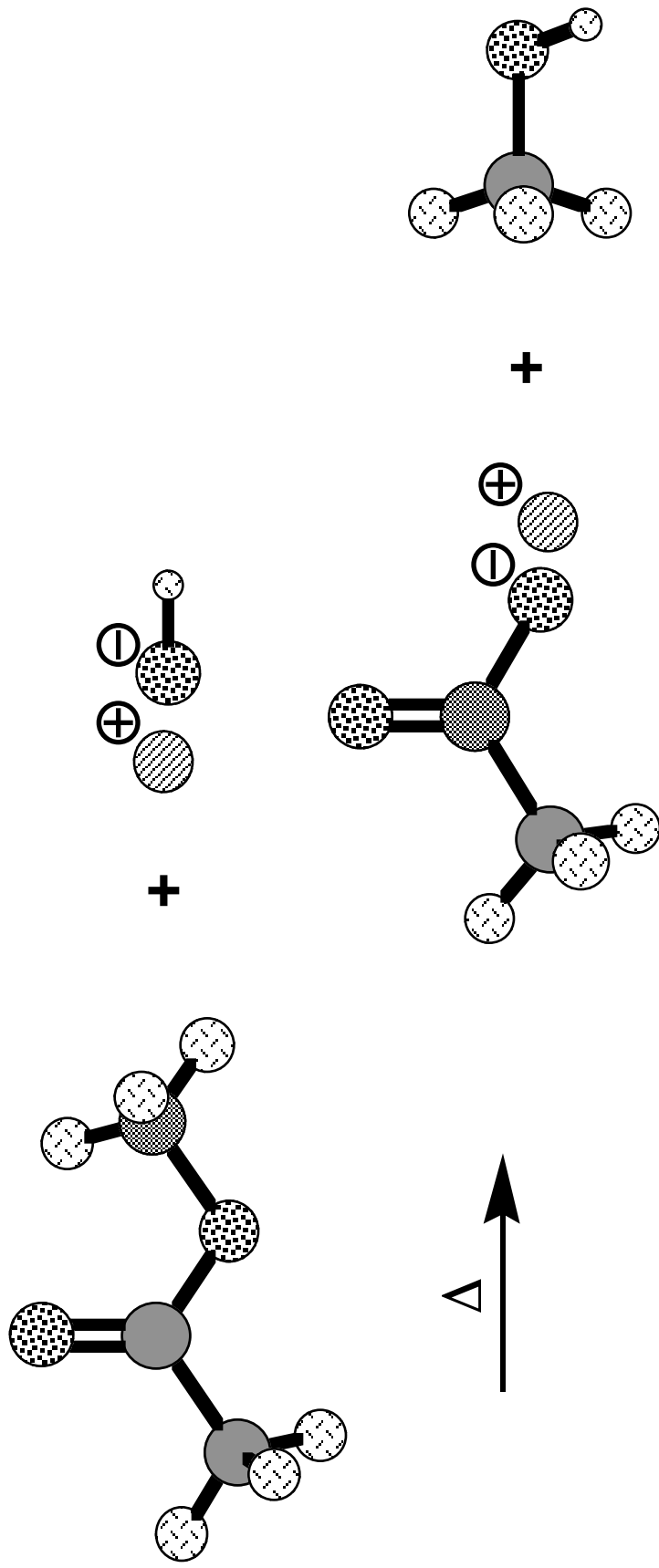
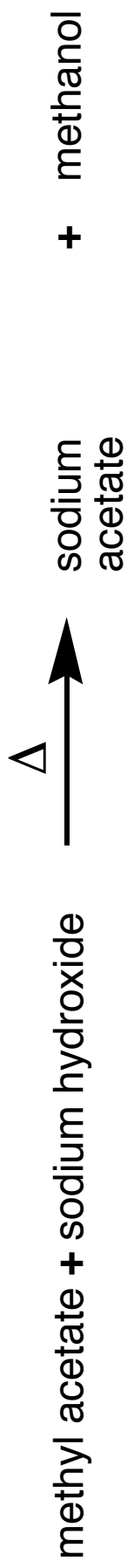


But Buster's story does not end here. The products of his saponification were mixed with some perfumes and colorings and formed into bars of soap: the glycerol provided softness, smoothness, and lather, and the sodium stearate provided the cleaning power. Some of the soap made it onto the shelves of the Wilson's Farms store at the corner of Prospect and COnnecticut Streets in Buffalo, New York, where it was purchased one night by a student in the luxurious

Hydrolysis of Esters



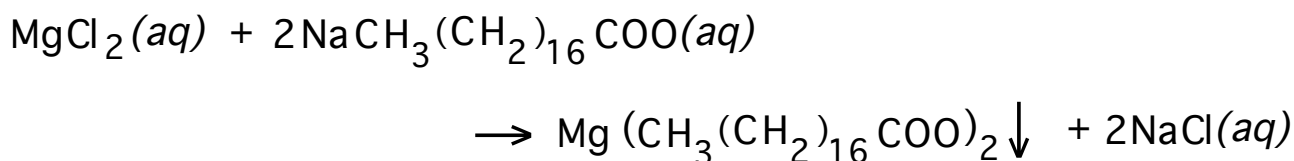
Hydrolysis of Esters



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new dorms at D'Youville College. Later that night, he decided to take a shower, and break in his new bar of soap.

The municipal water supply in buffalo is noted for its "hardness", which simply means that it contains relatively high concentrations of ionic compounds of elements like calcium, magnesium and zinc. These can and do react with stearate salts in soap according to the following scheme:



As the equation shows, the magnesium stearate, insoluble in water, deposits as a precipitate. Magnesium stearate, calcium stearate, zinc stearate, and several other stearate based ionic compounds form precipitates when you rinse the soap off your body in a shower. These precipitates are the major ingredient in the disagreeable deposit which we know as soap scum.

The sun shines and warms the earth. It also powers the formation of glucose in alfalfa and oats. Buster the horse eats the oats and performs wonders. He also puts on weight, and so, when he dies, though his achievements may die with him, his body fat lives on, rendered (via **saponification**) to form glycerine and the sodium salt of stearic acid, This is turned into soap, and each time we shower, we wash a little bit of buster down the drain. But a little bit of him stays with us in the form of the soap scum that clings to our shower walls and our tubs. Sic transit Buster.

Two Carbons at a Time

Every naturally occurring fatty acid has an even number of carbon atoms in it. In **Lipogenesis** (the synthesis of fatty acids in the human body), long chained fatty acids are built up, 2 carbon atoms at a time. In β -oxidation, the catabolic pathway for fatty acids in the human body, the acids are chopped up, two carbons at a time, and energy stored in the fatty acid is subsequently recovered.

We refer to the synthetic route for the production of fatty acid as the two carbon squish, since we squish carbon atoms onto the fatty acid chain 2 at a time.

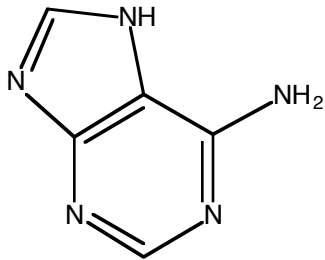
We refer to the pathway for oxidation of fatty acids as the 2 carbon chop, since the fatty acid chain is shortened and oxidized two carbons at a time.

The chop and the squish both depend on a molecule known as acetyl coenzyme A. This molecule consists of an acetyl (2 carbon) group, bonded to a sulfur atom in coenzyme A. By

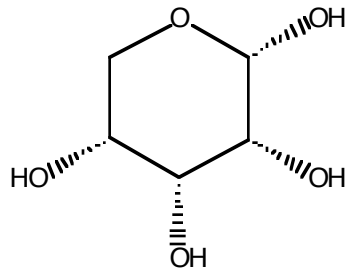
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itself, coenzyme A is often referred to as CoA or SCoA, and acetyl Coenzyme A is often referred to as acetylCoA or acetylSCoA. This molecule is central to virtually all metabolism, and fossil records indicate that its emergence occurred prior to the development of eukaryotic cells. It's been with us a long time.

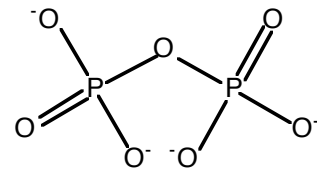
What is it? Well, these are the components of coenzyme A (except for an extra phosphate stuck to a ribose):



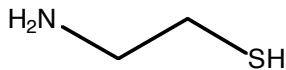
adenine
pantathionate



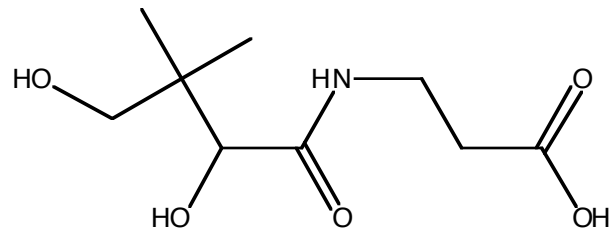
ribose



diphosphate



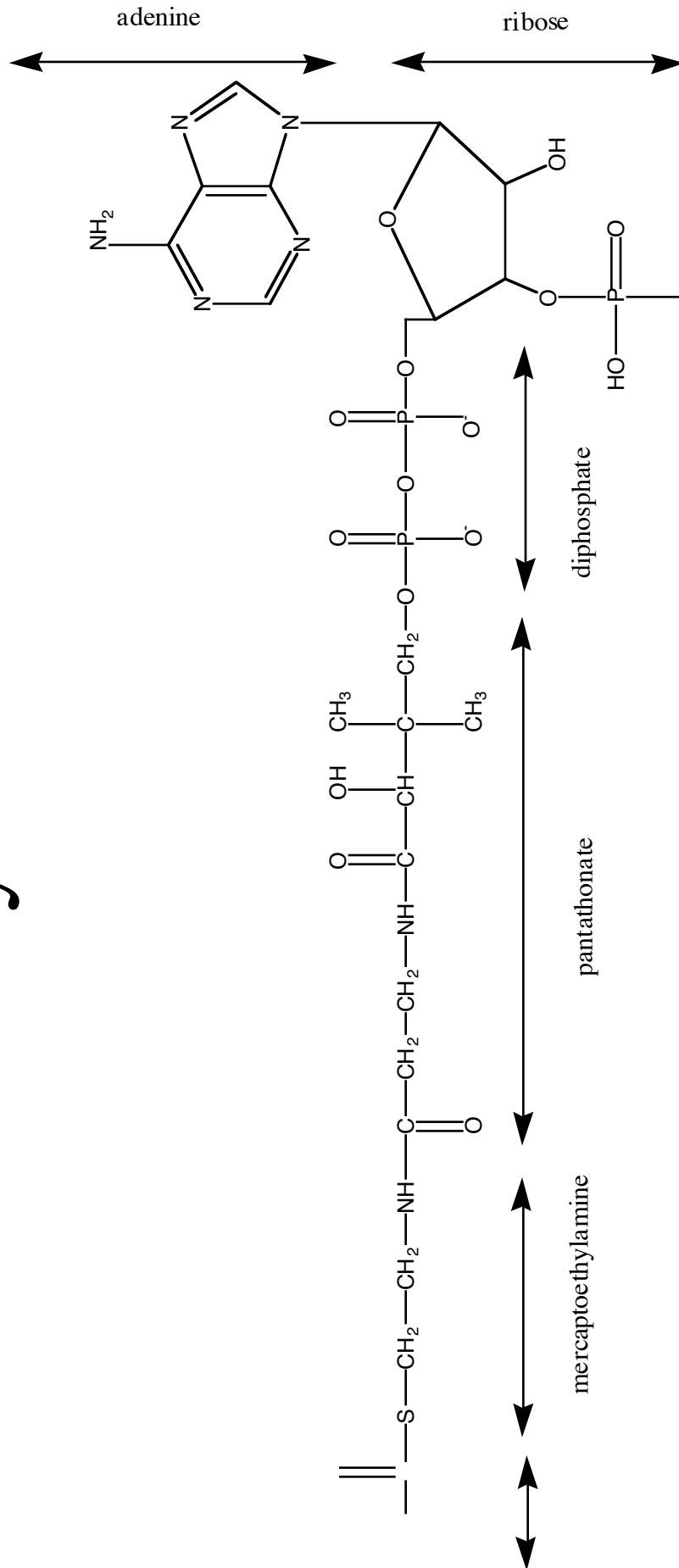
mercaptoethylamine



pantothenic acid

acetyl-CoA

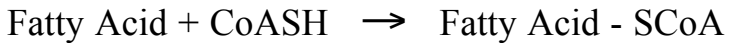
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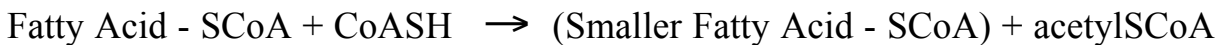
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So what does all this have to do with the metabolism of fats (specifically fatty acids). Simply this: coenzyme A pulls off two carbons from a fatty acid, transports these to the mitochondria, where they are utilized by the Krebs Cycle (soon to be explained) in producing energy (among other things).

Basically what happens is this:



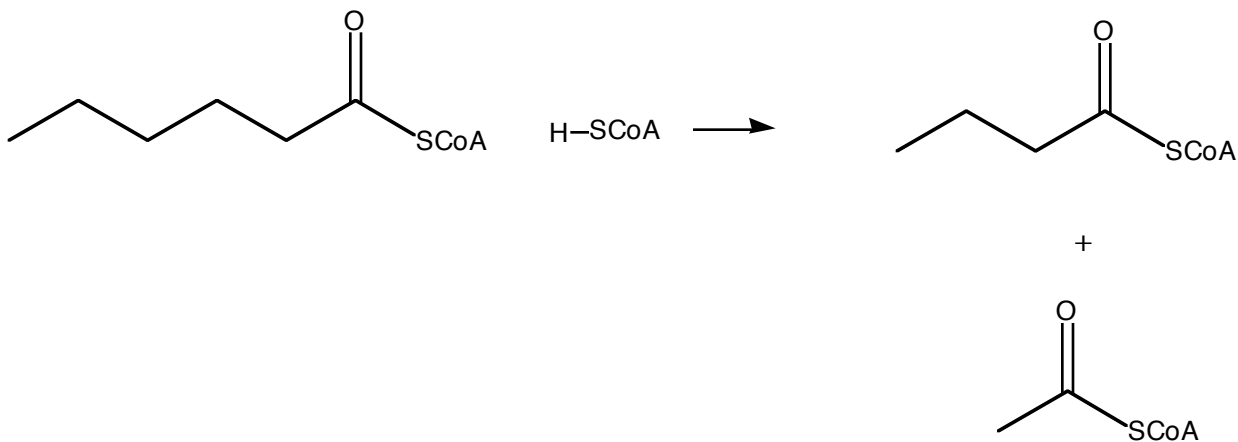
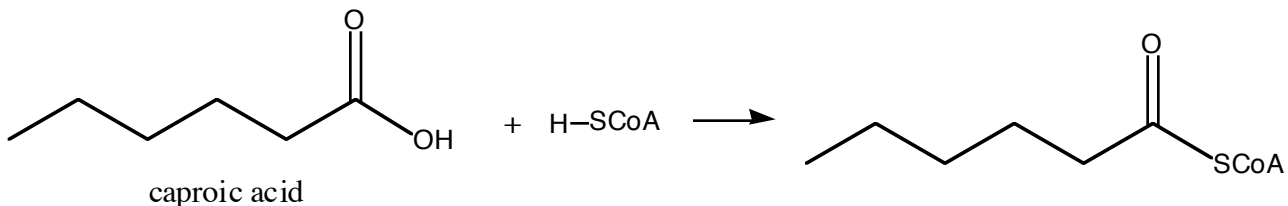
followed by:



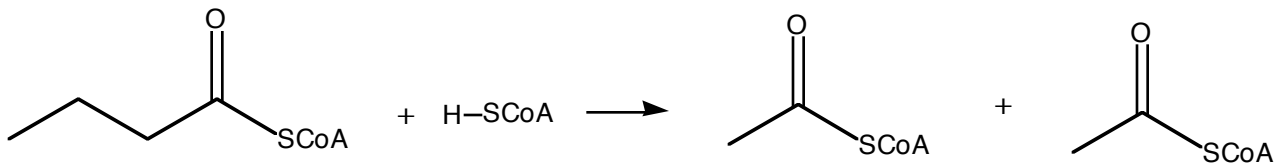
and:



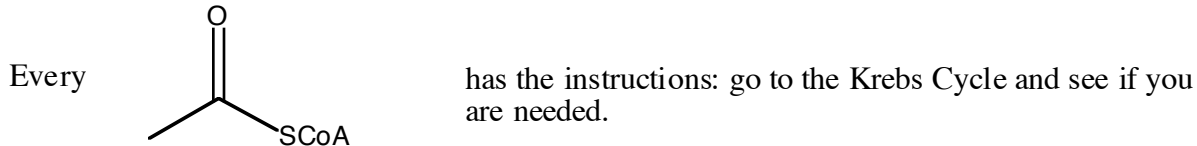
and on and on until all the carbons are used up. The catabolism of a small carboxylic acid (caproic acid) is a three step process, detailed below:



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Remember :the goal of all this is to make lots and lots of acetyl coenzyme A subunits.



What about **lipogenesis**. This process uses a new molecule called acyl carrier protein which attaches and builds up the fatty acid using molecules of acetylSCoA in a chemical sequence quite different from the one we just saw, using different enzymes and different intermediate compounds from those we used in β -oxidation (2 carbon chop).

There is one exception of course---acetylSCoA is crucial for each process.

The acyl carrier protein molecule, by the way, requires another vitamin, biotin. So we need (at least) two kinds of vitamins for proper fat metabolism: Pantothenic acid (B5) for both β -oxidation and lipogenesis, and biotin (a B vitamin without a number) is necessary for the manufacture and storage of fat in adipose tissue.