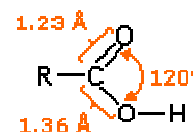1. **Nomenclature of Carboxylic Acids**
2. **Preparation of Carboxylic Acids**
3. **Reactivity**
4. **Soaps and Detergents**
5. **Fats and Oils**

TEST – Carboxylic acides, esters and fats.
- Give the names
- Carboxylic acides Reactions
- Esterification and hydrolysis
- Saponification

Carboxylic Acids

The carboxyl functional group that characterizes the carboxylic acids is unusual in that it is composed of two functional groups described earlier in this text. As may be seen in the formula on the right, the carboxyl group is made up of a hydroxyl group bonded to a carbonyl group. It is often written in condensed form as $-CO_2H$ or $-COOH$. Other combinations of functional groups were described previously, and significant changes in chemical behavior as a result of group interactions were described (e.g. phenol & aniline). In this case, the change in chemical and physical properties resulting from the interaction of the hydroxyl and carbonyl group are so profound that the combination is customarily treated as a distinct and different functional group.
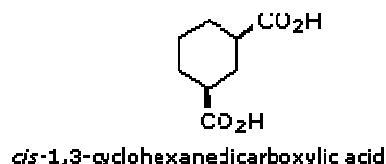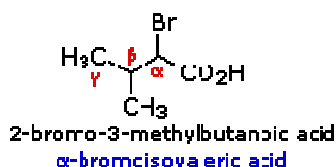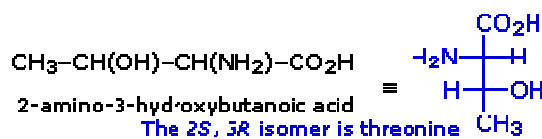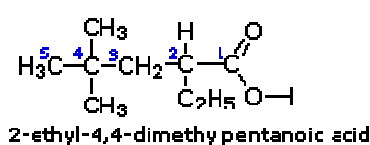
1. Nomenclature of Carboxylic Acids
As with aldehydes, the carboxyl group must be located at the end of a carbon chain. In the IUPAC system of nomenclature the carboxyl carbon is designated #1, and other substituents are located and named accordingly. The characteristic IUPAC suffix for a carboxyl group is "**oic acid**", and care must be taken not to confuse this systematic nomenclature with the similar common system. These two nomenclatures are illustrated in the following table, along with their melting and boiling points.

Formula	Common Name	Source	IUPAC Name	Melting Point	Boiling Point
HCO_2H	formic acid	ants (L. formica)	methanoic acid	8.4 ℃	101 ℃
CH_3CO_2H	acetic acid	vinegar (L. acetum)	ethanoic acid	16.6 ℃	118 ℃
$CH_3CH_2CO_2H$	propionic acid	milk (Gk. protus prion)	propanoic acid	-20.8 ℃	141 ℃
$CH_3(CH_2)_2CO_2H$	butyric acid	butter (L. butyrum)	butanoic acid	-5.5 ℃	164 ℃
$CH_3(CH_2)_3CO_2H$	valeric acid	valerian root	pentanoic acid	-34.5 ℃	186 ℃
$CH_3(CH_2)_4CO_2H$	caproic acid	goats (L. caper)	hexanoic acid	-4.0 ℃	205 ℃
$CH_3(CH_2)_5CO_2H$	enanthic acid	vines (Gk. oenanthe)	heptanoic acid	-7.5 ℃	223 ℃
$CH_3(CH_2)_6CO_2H$	caprylic acid	goats (L. caper)	octanoic acid	16.3 ℃	239 ℃
$CH_3(CH_2)_7CO_2H$	pelargonic acid	pelargonium (an herb)	nonanoic acid	12.0 ℃	253 ℃
$CH_3(CH_2)_8CO_2H$	capric acid	goats (L. caper)	decanoic acid	31.0 ℃	219 ℃

Substituted carboxylic acids are named either by the IUPAC system or by common names. If you are uncertain about the IUPAC rules for nomenclature you should review them now. Some common names, the amino acid threonine for example, do not have any systematic origin and must simply be memorized. In other cases, common names make use of the Greek letter notation for carbon atoms near the carboxyl group. Some examples of both nomenclatures are provided below.


2-ethyl-4,4-dimethylpentanoic acid

CH₃–CH(OH)–CH(NH₂)–CO₂H
2-amino-3-hydroxybutanoic acid
The 2S, 3R isomer is threonine

2-bromo-3-methylbutanoic acid
α-bromoisovaleric acid

cis-1,3-cyclohexanedicarboxylic acid

Simple dicarboxylic acids having the general formula $HO_2C–(CH_2)_n–CO_2H$ (where n = 0 to 5) are known by the common names: Oxalic (n=0), Malonic (n=1), Succinic (n=2), Glutaric (n=3), Adipic (n=4) and Pimelic (n=5) Acids. Common names, such as these can be troublesome to remember, so mnemonic aids, which take the form of a catchy phrase, have been devised. For this group of compounds one such phrase is:
"**O**h **M**y **S**uch **G**ood **A**pple **P**ie".

2. Carboxylic Acid Natural Products

Carboxylic acids are widespread in nature, often combined with other functional groups. Simple alkyl carboxylic acids, composed of four to ten carbon atoms, are liquids or low melting solids having very unpleasant odors. The **fatty acids** are important components of the biomolecules known as **lipids**, especially fats and oils. As shown in the following table, these long-chain carboxylic acids are usually referred to by their common names, which in most cases reflect their sources. A mnemonic phrase for the C_{10} to C_{20} natural fatty acids capric, lauric, myristic, palmitic, stearic and arachidic is: "**C**urly,**L**arry & **M**oe **P**erform **S**illy **A**ntics" (note that the names of the three stooges are in alphabetical order). Interestingly, the molecules of most natural fatty acids have an even number of carbon atoms. Analogous compounds composed of odd numbers of carbon atoms are perfectly stable and have been made synthetically. Since nature makes these long-chain acids by linking together acetate units, it is not surprising that the carbon atoms composing the natural products are multiples of two. The double bonds in the unsaturated compounds listed on the right are all cis (or Z).

FATTY ACIDS

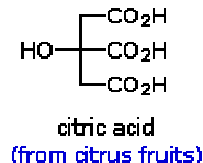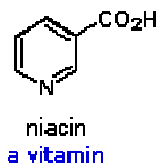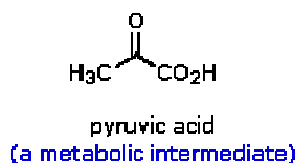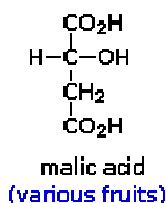| Saturated			Unsaturated		
Formula	Common Name	Melting Point	Formula	Common Name	Melting Point
$CH_3(CH_2)_{10}CO_2H$	lauric acid	45 °C	$CH_3(CH_2)_5CH=CH(CH_2)_7CO_2H$	palmitoleic acid	0 °C
$CH_3(CH_2)_{12}CO_2H$	myristic acid	55 °C	$CH_3(CH_2)_7CH=CH(CH_2)_7CO_2H$	oleic acid	13 °C
$CH_3(CH_2)_{14}CO_2H$	palmitic acid	63 °C	$CH_3(CH_2)_4CH=CHCH_2CH=CH(CH_2)_7CO_2H$	linoleic acid	-5 °C
$CH_3(CH_2)_{16}CO_2H$	stearic acid	69 °C	$CH_3CH_2CH=CHCH_2CH=CHCH_2CH=CH(CH_2)_7CO_2H$	linolenic acid	-11 °C
$CH_3(CH_2)_{18}CO_2H$	arachidic acid	76 °C	$CH_3(CH_2)_4(CH=CHCH_2)_4(CH_2)_2CO_2H$	arachidonic acid	-49 °C
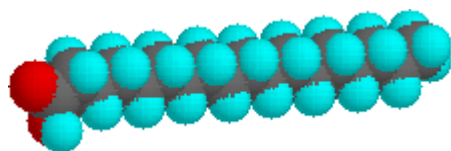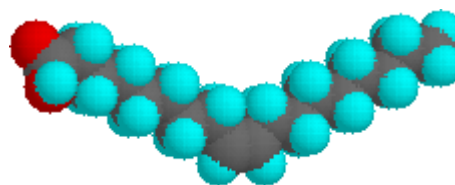
stearic acid   **oleic acid**

The following formulas are examples of other naturally occurring carboxylic acids. The molecular structures range from simple to complex, often incorporate a variety of other functional groups, and many are chiral.

malic acid
(various fruits)

pyruvic acid
(a metabolic intermediate)

niacin
a vitamin

citric acid
(from citrus fruits)

biotin
(a cell growth factor)

abietic acid
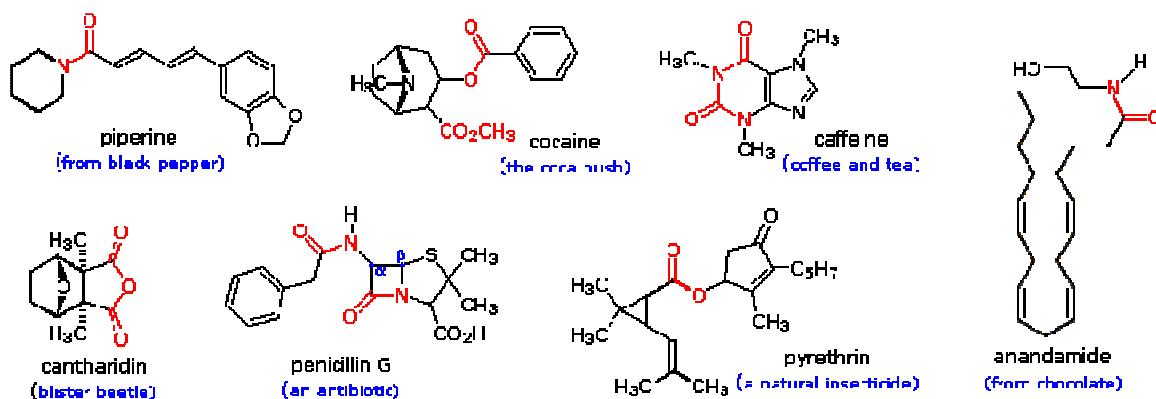(pine resin)

cholic acid
(from bile)
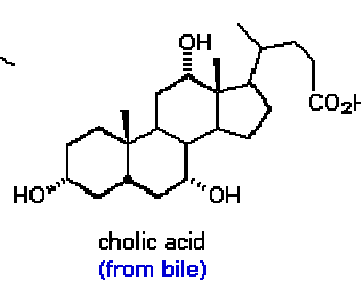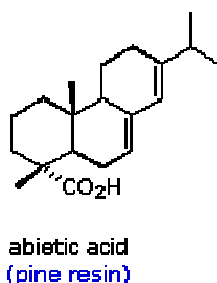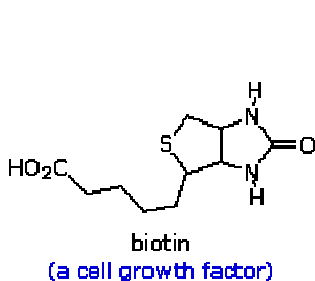
3. Related Carbonyl Derivatives

Other functional group combinations with the carbonyl group can be prepared from carboxylic acids, and are usually treated as related derivatives. Five common classes of these **carboxylic acid derivatives** are listed in the following table. Although nitriles do not have a carbonyl group, they are included here because the functional carbon atoms all have the same oxidation state. The top row (yellow shaded) shows the general formula for each class, and the bottom row (light blue) gives a specific example of each. As in the case of amines, amides are classified as 1°, 2° or 3°, depending on the number of alkyl groups bonded to the nitrogen.

acyl halide	anhydride	ester	amide	nitrile
R—C(=O)X X = F, Cl, Br or I	R—C(=O)—O—C(=O)—R	R—C(=O)O-R''	R—C(=O)NR'$_2$ R' = H or alkyl	R—C$\equiv$N
C_2H_5—C(=O)Cl propanoyl chloride	H_3C—C(=O)—O—C(=O)—CH_3 acetic anhydride	H_3C—C(=O)O-C_2H_5 ethyl acetate	H—C(=O)NH$_2$ formamide	H_3C—C$\equiv$N acetonitrile

Functional groups of this kind are found in many kinds of natural products. Some examples are shown below with the functional group colored red. Most of the functions are amides or esters, cantharidin being a rare example of a natural anhydride. Cyclic esters are called **lactones**, and cyclic amides are referred to as **lactams**. Penicillin G has two amide functions, one of which is a β-lactam. The Greek letter locates the nitrogen relative to the carbonyl group of the amide.

piperine
(from black pepper)

cocaine
(the coca bush)

caffeine
(coffee and tea)

anandamide
(from chocolate)

cantharidin
(blister beetle)

penicillin G
(an antibiotic)

pyrethrin
(a natural insecticide)

Preparation of Carboxylic Acids

The carbon atom of a carboxyl group has a high oxidation state. It is not surprising, therefore, that many of the chemical reactions used for their preparation are oxidations. Such reactions have been discussed in previous sections of this text, and the following diagram summarizes most of these. To review the previous discussion of any of these reaction classes simply click on the number (**1** to **4**) or descriptive heading for the group.

1. Oxidation of Arene Side-Chains

H_3C ... C_2H_5 $\xrightarrow[H_2O,\ heat]{KMnO_4}$ HO_2C ... CO_2H

$CH_2CH_2CH_3$ CO_2H
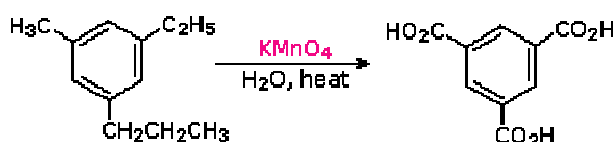
2. Oxidation of 1°-Alcohols

$\xrightarrow[(H_2CrO_4)]{Jones'\ Reagent}$
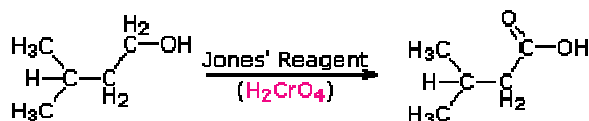
3. Oxidation of Aldehydes

$\xrightarrow[(Ag^+\ in\ NH_4OH)]{Tollens'\ Reagent}$

4. Oxidative Cleavage of Alkenes and Alkynes

or $R-C\equiv C-R$ $\xrightarrow[H_2O,\ heat]{KMnO_4}$ $2\ R-C$
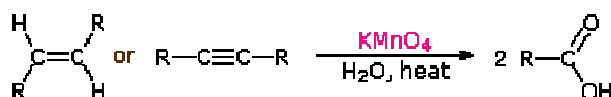
Two other useful procedures for preparing carboxylic acids involve hydrolysis of nitriles and carboxylation of organometallic intermediates. As shown in the following diagram, both methods begin with an organic halogen compound and the carboxyl group eventually replaces the halogen. Both methods require two steps, but are complementary in that the nitrile intermediate in the first procedure is generated by a S_N2 reaction, in which cyanide anion is a nucleophilic precursor of the carboxyl group. The hydrolysis may be either acid or base-catalyzed, but the latter give a carboxylate salt as the initial product. In the second procedure the electrophilic halide is first transformed into a strongly nucleophilic metal derivative, and this adds to carbon dioxide (an electrophile). The initial product is a salt of the carboxylic acid, which must then be released by treatment with strong aqueous acid.

Hydrolysis of Nitriles

$$R-CH_2-Br \xrightarrow[S_N2]{NaCN} R-CH_2-C\equiv N \xrightarrow[heat]{H_2O + H_3O^-} R-CH_2-C\underset{OH}{\overset{O}{\diagup}} + NH_4^-$$
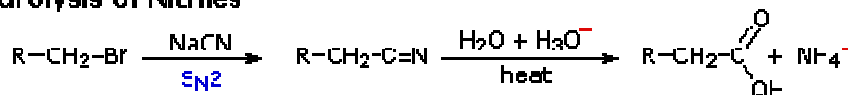
Carboxylation of Organometallic Reagents

$$R-Br \xrightarrow[ether]{Mg} R-Mg-Br \xrightarrow[2) H_3O^+]{1) CO_2} R-C\underset{OH}{\overset{O}{\diagup}} - Mg(OH)Br$$
$$(or\ R-Cl\ or\ R-I)\qquad (Grignard\ reagent)$$

$$\text{(phenyl lithium)} \xrightarrow[2) H_3O^+]{1) CO_2} \ \text{benzoic acid} + LiBr$$
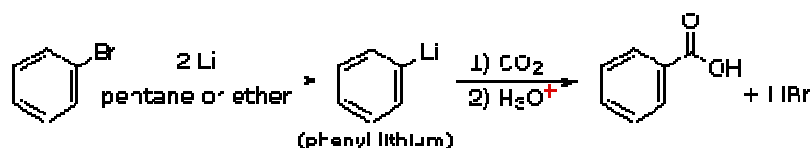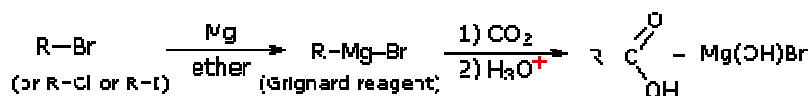
Reactions of Carboxylic Acids

1. Salt Formation

Because of their enhanced acidity, carboxylic acids react with bases to form ionic salts, as shown in the following equations. In the case of alkali metal hydroxides and simple amines (or ammonia) the resulting salts have pronounced ionic character and are usually soluble in water. Heavy metals such as silver, mercury and lead form salts having more covalent character (3rd example), and the water solubility is reduced, especially for acids composed of four or more carbon atoms.

$$RCO_2H + NaHCO_3 \longrightarrow RCO_2^{(-)} Na^{(+)} + CO_2 + H_2O$$
$$RCO_2H + (CH_3)_3N \longrightarrow RCO_2^{(-)} (CH_3)_3NH^{(+)}$$
$$RCO_2H + AgOH \longrightarrow RCO_2^{\delta(-)} Ag^{\delta(+)} + H_2O$$

Carboxylic acids and salts having alkyl chains longer than six carbons exhibit unusual behavior in water due to the presence of both hydrophilic (CO_2) and hydrophobic (alkyl) regions in the same molecule. Such molecules are termed **amphiphilic** (Gk. amphi = both) or **amphipathic**. Depending on the nature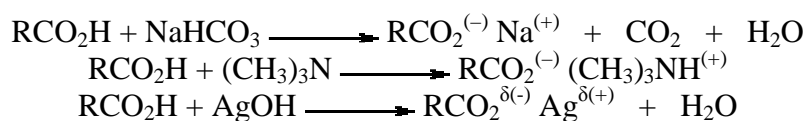 of the hydrophilic portion these compounds may form monolayers on the water surface or sphere-like clusters, called micelles, in solution.

2. Substitution of the Hydroxyl Hydrogen

This reaction class could be termed **electrophilic substitution at oxygen**, and is defined as follows (E is an electrophile). Some examples of this substitution are provided in equations (1) through (4).

$$RCO_2-H + E^{(+)} \longrightarrow RCO_2-E + H^{(+)}$$

If E is a strong electrophile, as in the first equation, it will attack the nucleophilic oxygen of the carboxylic acid directly, giving a positively charged intermediate which then loses a proton. If E is a weak electrophile, such as an alkyl halide, it is necessary to convert the carboxylic acid to the more nucleophilic carboxylate anion to facilitate the substitution. This is the procedure used in reactions 2 and 3. Equation 4 illustrates the use of the reagent diazomethane (CH_2N_2) for the preparation of methyl esters. This toxic and explosive gas is always used as an ether solution (bright yellow in color). The reaction is easily followed by the evolution of nitrogen gas and the disappearance of the reagent's color. This reaction is believed to proceed by the rapid bonding of a strong electrophile to a carboxylate anion.

1. (CH3)2C=CH2 / H2SO4 catalyst

2. H3C—C(CH3)2—C(=O)OH → NaOH → H3C—C(CH3)2—C(=O)O⁻ Na⁺ → CH3-I, SN2 → H3C—C(CH3)2—C(=O)O-CH3

3. (benzoic acid) → AgOH → (benzoate) $\delta-$ O Ag $\delta+$ → allyl bromide, SN2 → (allyl benzoate) + AgBr

4. (cyclohexene carboxylic acid) → CH2N2 / ether → (methyl ester) + N2

diazomethane, CH2N2 has the structure: H2C=N⁺=N⁻
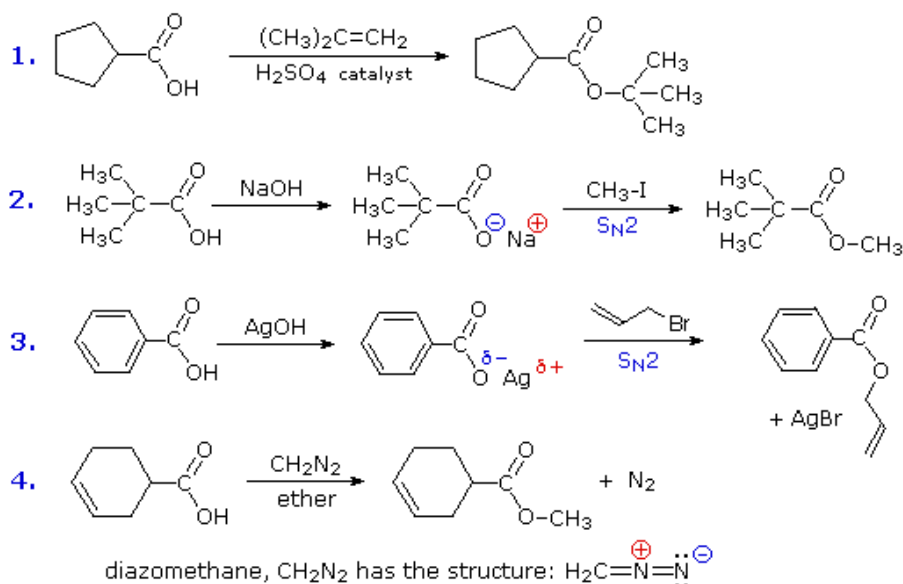
3. Substitution of the Hydroxyl Group

Reactions in which the hydroxyl group of a carboxylic acid is replaced by another nucleophilic group are important for preparing functional derivatives of carboxylic acids. The alcohols provide a useful reference chemistry against which this class of transformations may be evaluated. In general, the hydroxyl group proved to be a poor leaving group, and virtually all alcohol reactions in which it was lost involved a prior conversion of –OH to a better leaving group. This has proven to be true for the carboxylic acids as well. Four examples of these hydroxyl substitution reactions are presented by the following equations. In each example, the new bond to the carbonyl group is colored magenta and the nucleophilic atom that has replaced the hydroxyl oxygen is colored green. The hyd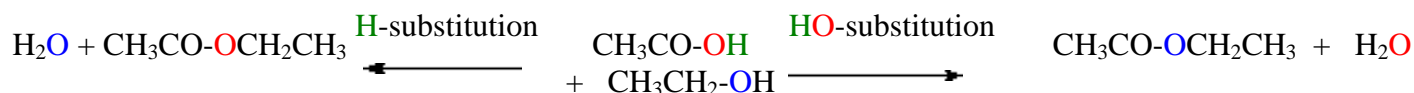roxyl moiety is often lost as water, but in reaction #1 the hydrogen is lost as HCl and the oxygen as SO_2. This reaction parallels a similar transformation of alcohols to alkyl chlorides, although itsmechanism is different. Other reagents that produce a similar conversion to acyl halides are PCl_5 and $SOBr_2$. The amide and anhydride formations shown in equations #2 & 3 require strong heating, and milder procedures that accomplish these transformations will be described in the next chapter.

1. O_2N–(C6H4)–C(=O)OH → SOCl2 / heat → O_2N–(C6H4)–C(=O)Cl + HCl + SO_2

2. H–C(=O)OH + (phenyl)N(CH3)H → toluene, 110° C → H–C(=O)–N(CH3)(phenyl) + H_2O

3. 6 F_3C–C(=O)OH + P_2O_5 → heat → 3 F_3C–C(=O)–O–C(=O)–CF_3 + 2 H_3PO_4

4. H_3C–C(=O)OH + C_2H_5OH ⇌ H_2SO_4 → H_3C–C(=O)–O–C_2H_5 + H_2O
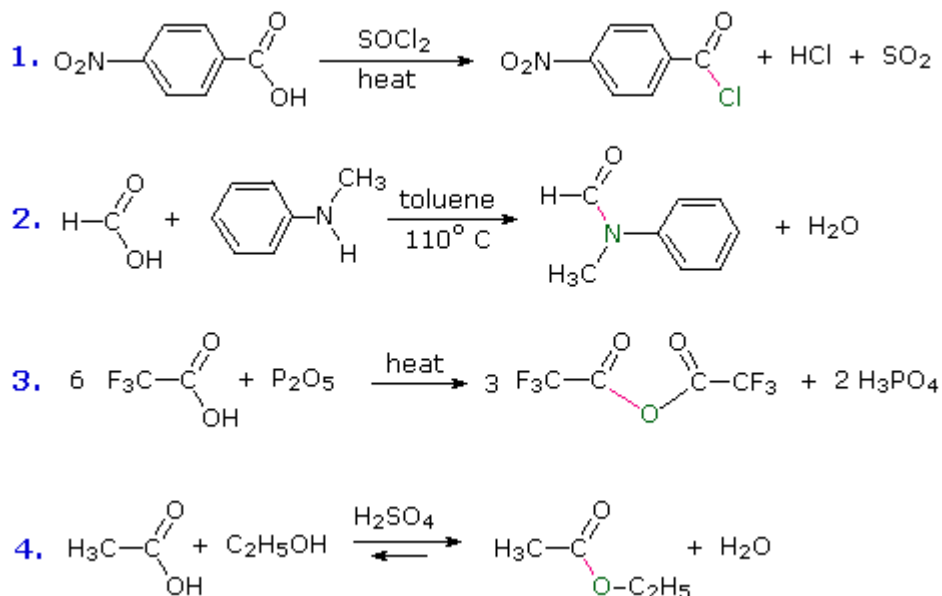
Reaction #4 is called **esterification**, since it is commonly used to convert carboxylic acids to their ester derivatives. Esters may be prepared in many different ways; indeed, equations #1 and #4 in the previous diagram illustrate the formation of tert-butyl and methyl esters respectively. The acid-catalyzed formation of ethyl acetate from acetic acid and ethanol shown here is reversible, with an equilibrium constant near 2. The reaction can be forced to completion by removing the water as it is formed. This type of esterification is often referred to as **Fischer esterification**. As expected, the reverse reaction, **acid-catalyzed ester hydrolysis**, can be carried out by adding excess water.

A thoughtful examination of this reaction (#4) leads one to question why it is classified as a hydroxyl substitution rather than a hydrogen substitution. The following equations, in which the hydroxyl oxygen atom of the carboxylic acid is colored red and that of the alcohol is colored blue, illustrate this distinction (note that the starting compounds are in the center).
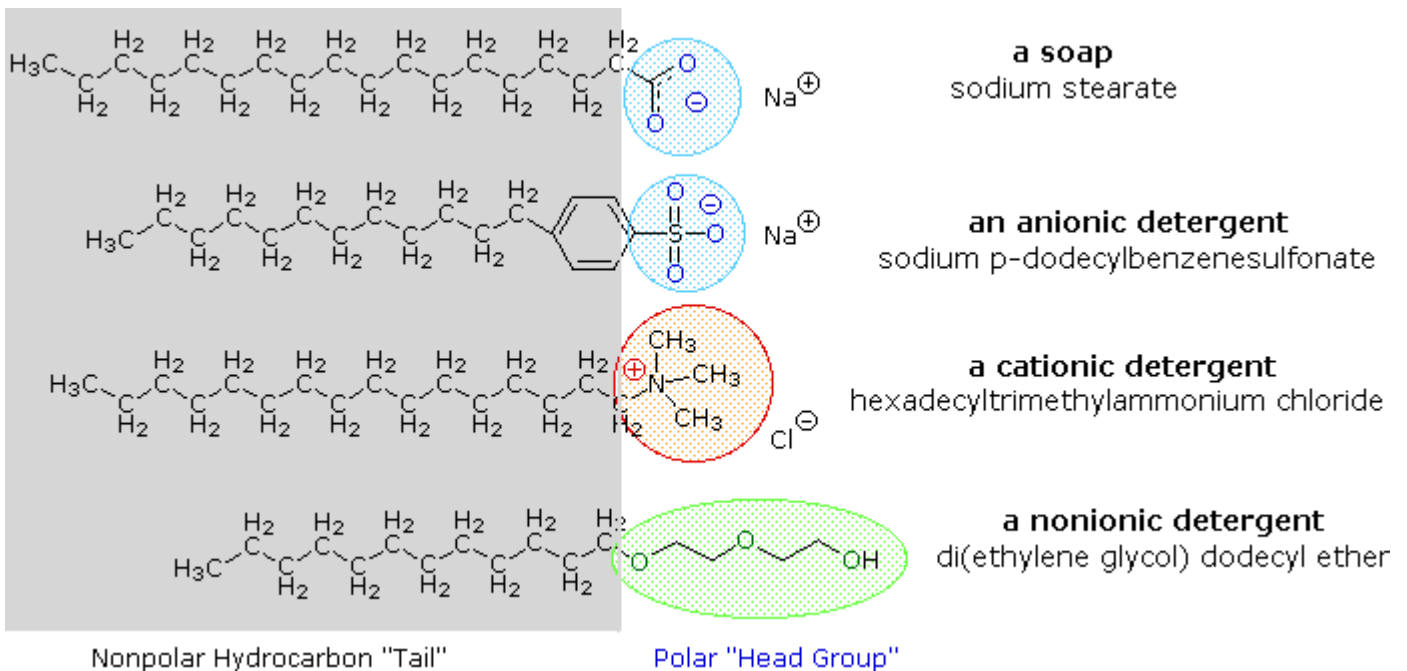
$$H_2O + CH_3CO\text{-}OCH_2CH_3 \quad \xleftarrow{\text{H-substitution}} \quad \begin{matrix} CH_3CO\text{-}OH \\ + \ CH_3CH_2\text{-}OH \end{matrix} \quad \xrightarrow{\text{HO-substitution}} \quad CH_3CO\text{-}OCH_2CH_3 \ + \ H_2O$$

In order to classify this reaction correctly and establish a plausible mechanism, the oxygen atom of the alcohol was isotopically labeled as ^{18}O (colored blue in our equation). Since this oxygen is found in the ester product and not the water, the hydroxyl group of the acid must have been replaced in the substitution. A mechanism for this general esterification reaction will be displayed on clicking the "Esterification Mechanism" button; also, once the mechanism diagram is displayed, a reaction coordinate for it can be seen by clicking the head of the green "energy diagram" arrow. Addition-elimination mechanisms of this kind proceed by way of tetrahedral intermediates (such as A and B in the mechanism diagram) and are common in acyl substitution reactions. Acid catalysis is necessary to increase the electrophilic character of the carboxyl carbon atom, so it will bond more rapidly to the nucleophilic oxygen of the alcohol. Base catalysis is not useful because base converts the acid to its carboxylate anion conjugate base, a species in which the electrophilic character of the carbon is reduced. Since a tetrahedral intermediate occupies more space than a planar carbonyl group, we would expect the rate of this reaction to be retarded when bulky reactants are used. To test this prediction the esterification of acetic acid was compared with that of 2,2-dimethylpropanoic acid, $(CH_3)_3CO_2H$. Here the relatively small methyl group of acetic acid is replaced by a larger tert-butyl group, and the bulkier acid reacted fifty times slower than acetic acid. Increasing the bulk of the alcohol reactant results in a similar rate reduction.
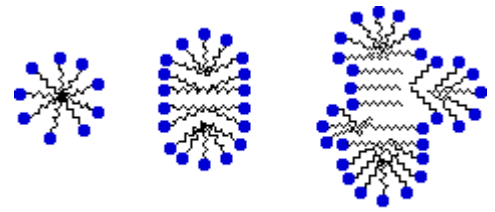
Soaps and Detergents

Carboxylic acids and salts having alkyl chains longer than eight carbons exhibit unusual behavior in water due to the presence of both hydrophilic (CO_2) and hydrophobic (alkyl) regions in the same molecule. Such molecules are termed **amphiphilic** (Gk. amphi = both) or **amphipathic**. Fatty acids made up of ten or more carbon atoms are nearly insoluble in water, and because of their lower density, float on the surface when mixed with water. Unlike paraffin or other alkanes, which tend to puddle on the waters surface, these fatty acids spread evenly over an extended water surface, eventually forming a monomolecular layer in which the polar carboxyl groups are hydrogen bonded at the water interface, and the hydrocarbon chains are aligned together away from the water. This behavior is illustrated in the diagram on the right. Substances that accumulate at water surfaces and change the surface properties are called **surfactants**.
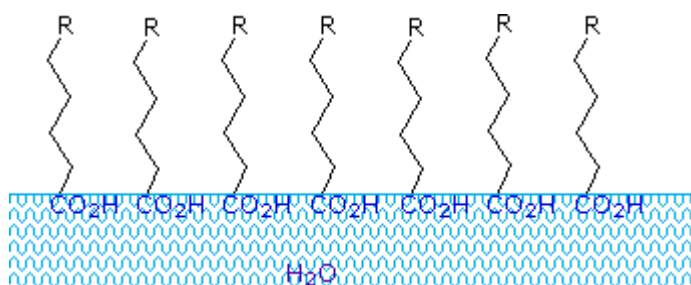
Alkali metal salts of fatty acids are more soluble in water than the acids themselves, and the amphiphilic character of these substances also make them strong surfactants. The most common examples of such compounds are soaps and detergents, four of which are shown below. Note that each of these molecules has a nonpolar hydrocarbon chain, the "tail", and a polar (often ionic) "head group". The use of such compounds as cleaning agents is facilitated by their surfactant character, which lowers the surface tension of water, allowing it to penetrate and wet a variety of materials.

	a soap
	sodium stearate
	an anionic detergent
	sodium p-dodecylbenzenesulfonate
	a cationic detergent
	hexadecyltrimethylammonium chloride
	a nonionic detergent
	di(ethylene glycol) dodecyl ether

Nonpolar Hydrocarbon "Tail"   Polar "Head Group"

Very small amounts of these surfactants dissolve in water to give a random dispersion of solute molecules. However, when the concentration is increased an interesting change occurs. The surfactant molecules reversibly assemble into polymolecular aggregates called **micelles**. By gathering the hydrophobic chains together in the center of the micelle, disruption of the hydrogen bonded structure of liquid water is minimized, and the polar head groups extend into the surrounding water where they participate in

micelle assemblies of amphiphiles

hydrogen bonding. These micelles are often spherical in shape, but may also assume cylindrical and branched forms, as illustrated on the right. Here the polar head group is designated by a blue circle, and the nonpolar tail is a zig-zag black line.
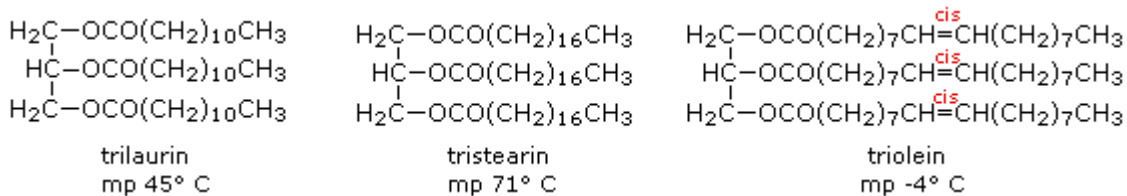
Fats and Oils

The triesters of fatty acids with glycerol (1,2,3-trihydroxypropane) compose the class of lipids known as fats and oils. These **triglycerides** (or triacylglycerols) are found in both plants and animals, and compose one of the major food groups of our diet. Triglycerides that are solid or semisolid at room temperature are classified as fats, and occur predominantly in animals. Those triglycerides that are liquid are called oils and originate chiefly in plants, although triglycerides from fish are also largely oils. Some examples of the composition of triglycerides from various sources are given in the following table.

Source	Saturated Acids (%)					Unsaturated Acids (%)		
	C_{10} & less	C_{12} lauric	C_{14} myristic	C_{16} palmitic	C_{18} stearic	C_{18} oleic	C_{18} linoleic	C_{18} unsaturated
Animal Fats								
butter	15	2	11	30	9	27	4	1
lard	-	-	1	27	15	48	6	2
human fat	-	1	3	25	8	46	10	3
herring oil	-	-	7	12	1	2	20	52
Plant Oils								
coconut	-	50	18	8	2	6	1	-
corn	-	-	1	10	3	50	34	-
olive	-	-	-	7	2	85	5	-
palm	-	-	2	41	5	43	7	-
peanut	-	-	-	8	3	56	26	7
safflower	-	-	-	3	3	19	76	-

As might be expected from the properties of the fatty acids, fats have a predominance of saturated fatty acids, and oils are composed largely of unsaturated acids. Thus, the melting points of triglycerides reflect their composition, as shown by the following examples. Natural mixed triglycerides have somewhat lower melting points, the melting point of lard being near 30 ° C, whereas olive oil melts near -6 ° C. Since fats are valued over oils by some Northern European and North American populations, vegetable oils are extensively converted to solid triglycerides (e.g. Crisco) by partial hydrogenation of their unsaturated components. Some of the remaining double bonds are isomerized (to trans) in this operation. These saturated and trans-fatty acid glycerides in the diet have been linked to long-term health issues such as atherosclerosis.

$$H_2C-OCO(CH_2)_{10}CH_3$$
$$HC-OCO(CH_2)_{10}CH_3$$
$$H_2C-OCO(CH_2)_{10}CH_3$$

trilaurin
mp 45° C

$$H_2C-OCO(CH_2)_{16}CH_3$$
$$HC-OCO(CH_2)_{16}CH_3$$
$$H_2C-OCO(CH_2)_{16}CH_3$$

tristearin
mp 71° C

$$H_2C-OCO(CH_2)_7CH\overset{cis}{=}CH(CH_2)_7CH_3$$
$$HC-OCO(CH_2)_7CH\overset{cis}{=}CH(CH_2)_7CH_3$$
$$H_2C-OCO(CH_2)_7CH\overset{cis}{=}CH(CH_2)_7CH_3$$

triolein
mp -4° C

Triglycerides having three identical acyl chains, such as tristearin and triolein (above), are called "simple", while those composed of different acyl chains are called "mixed". If the acyl chains at the end hydroxyl groups (1 & 3) of glycerol are different, the center carbon becomes a chiral center and enantiomeric configurations must be recognized.

The hydrogenation of vegetable oils to produce semisolid products has had unintended consequences. Although the hydrogenation imparts desirable features such as spreadability, texture, "mouth feel," and increased shelf life to naturally liquid vegetable oils, it introduces some serious health problems. These occur when the cis-double bonds in the fatty acid chains are not completely saturated in the hydrogenation process. The catalysts used to effect the addition of hydrogen isomerize the remaining double bonds to their trans configuration. These unnatural **trans-fats** appear to to be associated with increased heart disease, cancer, diabetes and obesity, as well as immune response and reproductive problems.