Organic Chemistry Review
for
Medical Biochemistry

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The Relationship of Organic Chemistry to Biochemistry

You should review the following classes of compounds, their nomenclature and reactions. This course will be MUCH easier (and much more intellectually satisfying) if you do. Luckily, only a small fraction of the organic chemistry that you learned as undergrads is required to get going in biochemistry.

A. Alkanes: Saturated Hydrocarbons
   1. Nomenclature

Table 1: Molecular and Condensed Structural Formulas, and Boiling and Melting Points, for the First Ten Normal Alkanes

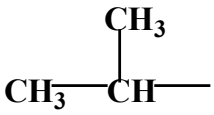
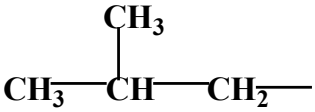
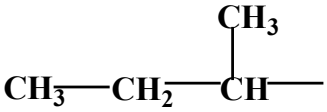
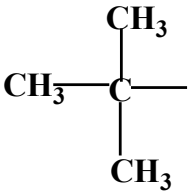
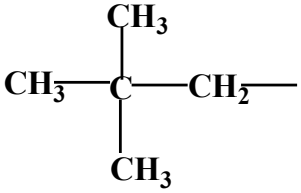
Molecular Formulas[a]	Condensed Structural Formula	Name	Boiling Point (^oC)	Melting Point (^oC)
CH_4	CH_4	Methane	-164	-182
C_2H_6	CH_3CH_3	Ethane	-89	-183
C_3H_8	$CH_3CH_2CH_3$	Propane	-42	-190
C_4H_{10}	$CH_3CH_2CH_2CH_3$	Butane	0	-138
C_5H_{12}	$CH_3CH_2CH_2CH_2CH_3$	Pentane	36	-130
C_6H_{14}	$CH_3CH_2CH_2CH_2CH_2CH_3$	Hexane	69	-95
C_7H_{16}	$CH_3CH_2CH_2CH_2CH_2CH_2CH_3$	Heptane	98	-91
C_8H_{18}	$CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_3$	Octane	126	-57
C_9H_{20}	$CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$	Nonane	151	-51
$C_{10}H_{22}$	$CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$	Decane	174	-30

[a] the general formula for all alkanes, normal or branched, is C_nH_{2n+2},where n=the number of carbons

Alkyl groups

methyl	CH_3-
ethyl	CH_3CH_2-
propyl	$CH_3CH_2CH_2$-
butyl	$CH_3CH_2CH_2CH_2$-

Table 2: The Most Important Branched Alkyl Groups

Name	Structure	Type of Group
Isopropyl		**Secondary**
Isobutyl		**Primary**
***Sec*-Butyl**		**Secondary**
***Tert*-Butyl**		**Tertiary**
Neopentyl		**Primary**

2. Physical properties. Alkanes and alkyl groups are nonpolar and therefore hydrophobic; they are insoluble in water and are responsible for hydrophobic interactions. Hydrocarbons and water are immiscible, i.e., "oil and water don't mix." (Motor oil is pure hydrocarbon; cooking oil is triglyceride, which is mostly hydrocarbon.)

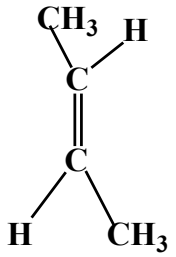
   The density of hydrocarbons is considerably less than 1.0 (a typical value is 0.7), which is why oil floats on water.

3. Chemical reactions. In the lab, alkanes are relatively unreactive in the sense that the structures cannot be modified in a controlled way. They can however be burned with oxygen at high temperature to form carbon dioxide and water, a reaction called **combustion**. Example: $CH_4 + 2O_2 \rightarrow CO_2 + 2H_2O$. This reaction, which is vital to technology and to life, releases a lot of energy. Alkanes are said to be **saturated** because they have the maximum number of C-H bonds per carbon atom. These energy-rich bonds enable alkanes to react with more oxygen (gram for gram) than any other class of organic molecule. Alkanes are the most "energy-dense" organic fuels in that more energy is released per gram than with other organic compounds.

   Cells also combust the hydrocarbon portions of food molecules, but in a highly controlled way and at body temperature.

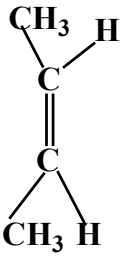
B. Alkenes.

1. Structural characteristics. Alkenes are hydrocarbons with a double bond. Example: ethylene, $CH_2{=}CH_2$. The double bond is planar and rigid. When other substituents are attached to it, the relative position of the substituent is designated as **cis** (same side) or **trans** (opposite side).



Trans-2-Butene

b.p. +1°



cis-2-Butene

b.p. +4°

Geometric isomers

2. Nomenclature. The standard nomenclature is to add an -ene ending to the root name of the parent compound, as in ethylene, $CH_2{=}CH_2$. This system is usually not used for biochemistry. Instead, we speak in terms of an unsaturated group in a molecule when there is a double bond. Fatty acids that contain a single double bond are called mononsaturated ("monos"); those with more than one are polyunsaturated ("polys").

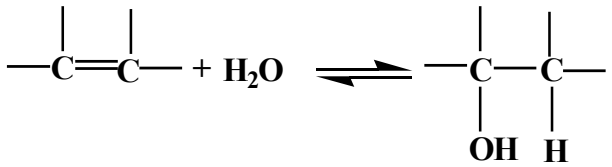
3. Physical properties. Alkenes are nonpolar, hydrophobic. Fatty acids with double bonds are essentially as hydrophobic as saturated fatty acids.

4. Reactions of biochemical importance

a. Hydrogenation (reduction) to alkanes. $>C{=}C< + 2\,[H] \longrightarrow >CH{-}CH<$

The brackets signify the addition of two hydrogen atoms without specifying the nature of the reductant, i.e., the hydrogen source. In the lab, hydrogen gas can be used. Cells use other reductants.

b. Hydration to alcohols.



C. Aromatics

1. Structural characteristics. These are cyclic compounds with two or more double bonds that have much greater chemical stability than the C=C bonds of aliphatic alkenes. Benzene is the prototype, shown below. It is a resonance hybrid of two structures, with six electrons shared by all six-carbon atoms.

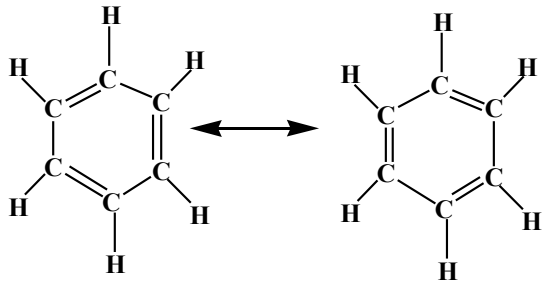


Figure 1: We start the three ordinary covalent bonds for each carbon (structure A) and put in the extra six electrons as three double bonds. Because there are two ways to do this, we get two structures.

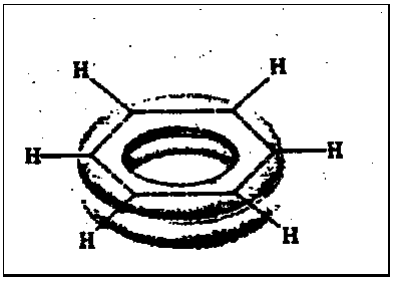
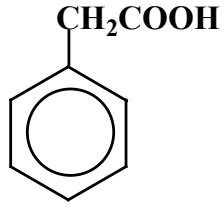
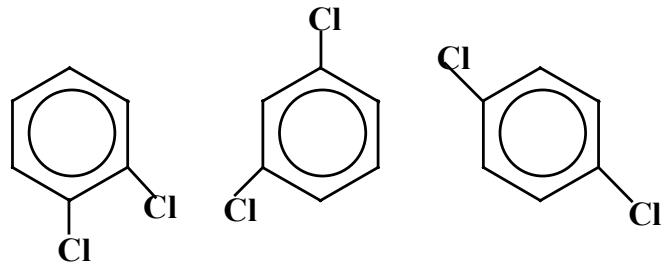


Figure 2: Benzene. The two donut-shaped clouds hold a total of six electrons.

2. Nomenclature. The benzene ring as a substituent is called the **phenyl** group. For example, benzene attached to acetic acid becomes phenylacetic acid:



The relationships of substituents on the ring itself are either **ortho, meta,** or **para,** as shown below.



1,2 (ortho) ***1,3 (meta)*** ***1,4 (para)***

3. Physical properties. Similar to alkenes.

4. Reactions of biochemical significance. Many important biomolecules are aromatic. The reactions they undergo in the cell do not have clear counterparts in organic chemistry. The cell has come up with novel ways to handle these unreactive molecules.

D. Alcohols.

1. Structural characteristics. These have the hydroxyl (-OH) functional group. The best known example is ethyl alcohol, or ethanol, CH_3CH_2-OH.

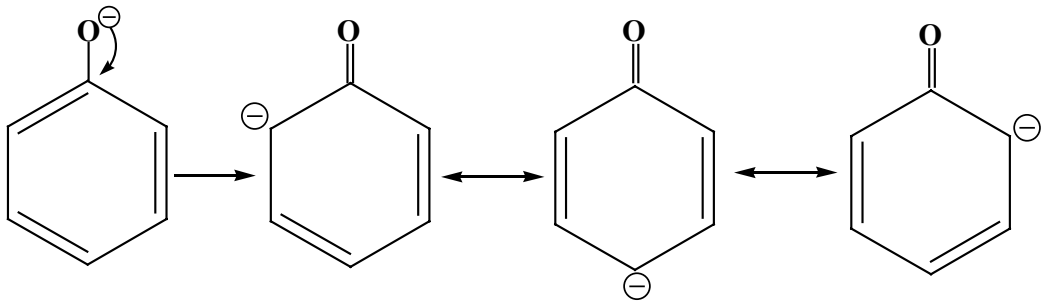
2. Nomenclature. The -ol suffix is attached to the name of the appropriate alkyl group. Aside from ethanol and methanol, pure alcohols of low molecular weight are rare in human biochemistry. However, the hydroxyl group is found everywhere, such as in carbohydrates and in compounds with other functional groups. The naming of compounds with more than one functional group will be discussed in a later section. Benzene with a single -OH attached to the ring is **phenol.**

3. Physical Properties. The hydroxyl group is hydrophilic and much more soluble in water than in a hydrocarbon solvent (by a factor of about 5000). The first few members of the homologous series, up to butanol, are therefore more soluble in water than in hydrocarbon solvents. The longer alcohols, such as octanol, are only sparingly soluble in water. Octanol and water form a commonly used two-phase system.

Aliphatic alcohols are extremely weak acids, not significantly dissociated at physiological pH. In strong alkali they can be made to dissociate to **alkoxide anions**.

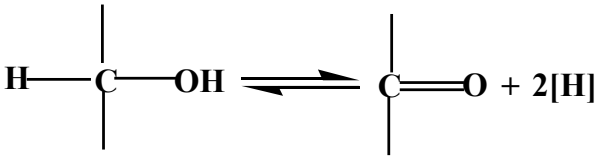
$$ROH \longrightarrow RO^- + H^+$$

Aromatic alcohols such as phenol are significantly acidic because the **phenolate anion** can be stabilized by resonance.

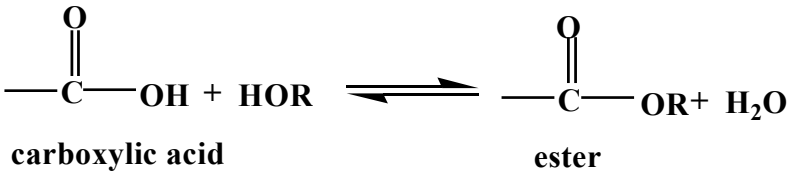


4. <u>Reactions of biochemical importance</u>.

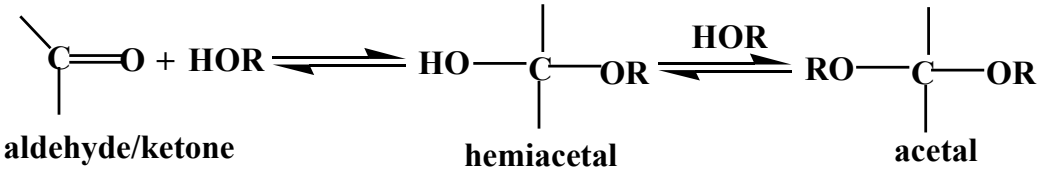
a. Oxidation to aldehydes and ketones, usually via dehydrogenation.



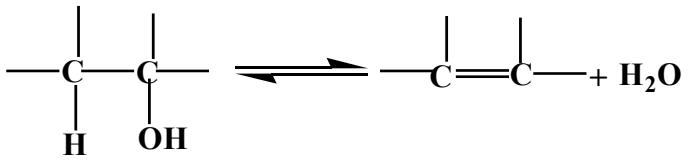
b. Formation of esters and phosphoesters.



c. Formation of hemiacetals and acetals.



d. Dehydration to alkenes.



E. Amines

1. Structural characteristics. These molecules contain the amino group. The first member of the series is ammonia.

NH_3	Ammonia
$R—NH_2$	**Primary amines** have one hydrogen replaced by R (*two* H's remain)
$R—NH—R'$	**Secondary amines** have two hydrogens replaced by R (*one* H remains)
$R—N(R'')—R'$	**Tertiary amines** have all three hydrogens replaced by R (*no* H remains)

The R groups in secondary and tertiary amines may be the same or different.

Note that the use of primary, secondary, and tertiary for amines is not quite the same as for alcohols. For alcohols we look at how many R groups are on a *carbon*; for amines we look at how many are on the *nitrogen*.

2. Nomenclature. Combine the alkyl prefix with the suffix "amine." For example, CH_3NH_2 is methylamine.

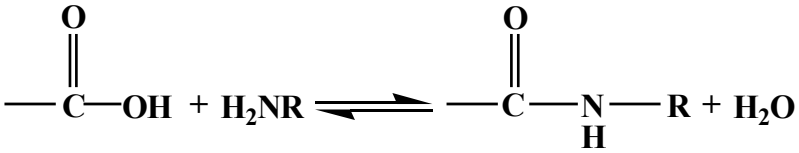
3. Physical properties. The amino group is hydrophilic, with a polarity similar to the hydroxyl group. It is about 2000 times more soluble in water than in a hydrocarbon solvent. Therefore, the first few members of the amine homologous series are water-soluble. Importantly, amines are **bases** that exist at physiological pH mainly in the protonated form:

$$RNH_3^+ \rightleftharpoons RNH_2 + H^+$$

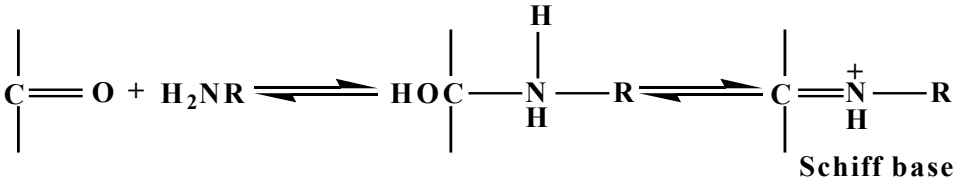
The protonated forms are called **ammonium ions**. Acid-base equilibria and pH will be discussed in detail in a subsequent lecture. The ammonium ions are essentially insoluble in organic solvents.

4. Reactions of biochemical importance.

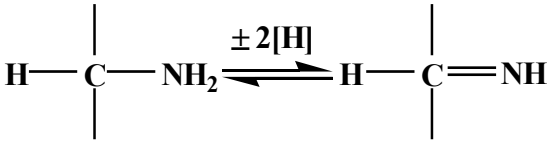
a. Formation of amides



b. Formation of Schiff bases by condensation with aldehydes or ketones



c. Formation of Schiff bases by dehydrogenation.

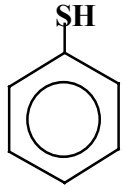


F. Thiols/mercaptans

1. Structural characteristics. These compounds contain sulfur as RSH or RSR´.

2. Nomenclature. The –SH group is called the thio- or the mercapto- group. Examples:

CH_3CH_2-SH **ethylmercaptan**

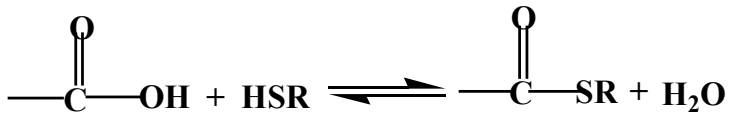


thiophenol

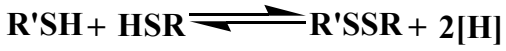
3. Physical characteristics. The -SH group is not clearly polar or nonpolar, but somewhere in between.

4. Reactions of biochemical importance.

   a. Formation of thioesters



   b. Oxidation to disulfides via dehydrogenation



G. Aldehydes and ketones

1. Structural characteristics**.** Both aldehydes and ketones have a **carbonyl** group, >C=O, composed of a **carbonyl oxygen** atom. Aldehydes have one –H attached to the **carbonyl carbon**, whereas ketones have two alkyl groups. Examples:

aldehyde **ketone**

2. Nomenclature. The common names of aldehydes are derived from the names of the corresponding carboxylic acids by replacing -ic acid by -aldehyde. Examples: formaldehyde, acetaldehyde. The simplest aliphatic ketone is acetone. All members of the ketone family are named from the two groups attached to the carbonyl, followed by ketone. Example: methyl ethyl ketone. In IUPAC nomenclature, adehydes are named after the parent compound by attaching an -al suffix, whereas ketones are named by attaching a -one suffix. The >C=O group in ketones is often referred to as the **keto** group.

3. The >C=O group is polar, and is more soluble in water than in organic solvents. The first four members of the homologous series are water-soluble.

4. Reactions of biochemical importance.

   a. Reduction to alcohols. This is the reverse of the dehydrogenation reaction described above in the alcohol section.

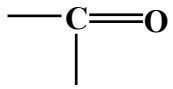
   b. Formation of hemiacetals and hemiketals. This was described above in the section on alcohols.

   c. Formation of Schiff bases with amines. This was described in the section on amines.

d. Aldol condensation/cleavage. This is one of several reactions involved in the making and breaking of carbon-carbon bonds, and will be discussed later (page 18).

H. Carboxylic Acids.

1. Structural characteristics. This class of compounds has the **carboxyl** group,



which is easier to write as $^{\Pi}$COOH.

2. Nomenclature. See chart below. Once the alkyl chain gets beyond the length of about 8, the carboxylic acids are referred to as **fatty acids**. The carbon atoms in the chain are numbered from the carboxyl end. There is also a Greek lettering system to indicate the relation of carbon atoms to the COOH end:

Table 3: Alkyl Carboxylic Acids

Components	Trivial Name	Systematic Name
1	Formic	
2:0	Acetic	
3:0	Propionic	
4:0	Butyric	
5:0	Valeric	Pentanoic
6:0	Caproic	Hexanoic
8:0	Caprylic	Octanoic
10:0	Capric	Decanoic
12:0	Lauric	Dodecanoic
14:0	Myristic	Tetradecanoic
16:0	Palmitic	Hexadecanoic
16:1(9)	Palmitoleic	*cis*-9-hexadecenoic
18:0	Stearic	Octadecenoic
18:1(9)	Oleic	*cis*-9-octadecenoic
18:1(11)	Vaccenic	*cis*-11-octadecenoic
18:2(9,12)	Linoleic	*All cis*-9,12-octadecenoic
18:3(9,12,15)	Linolenic	*All cis*-9,12,15-octadecatrienoic
20:4(5,8,11,14)	Arachidonic	All cis-5,8,11,14-eicosatetraenoic
24:0	Lignoceric	Tetracosanoic

$$\overset{\omega}{-CH_3}-\ CH_2-\ CH_2-\ \overset{\delta}{CH_2}-\ \overset{\gamma}{CH_2}-\ \overset{\beta}{CH_2}-\overset{\alpha}{CH_2}-COOH$$

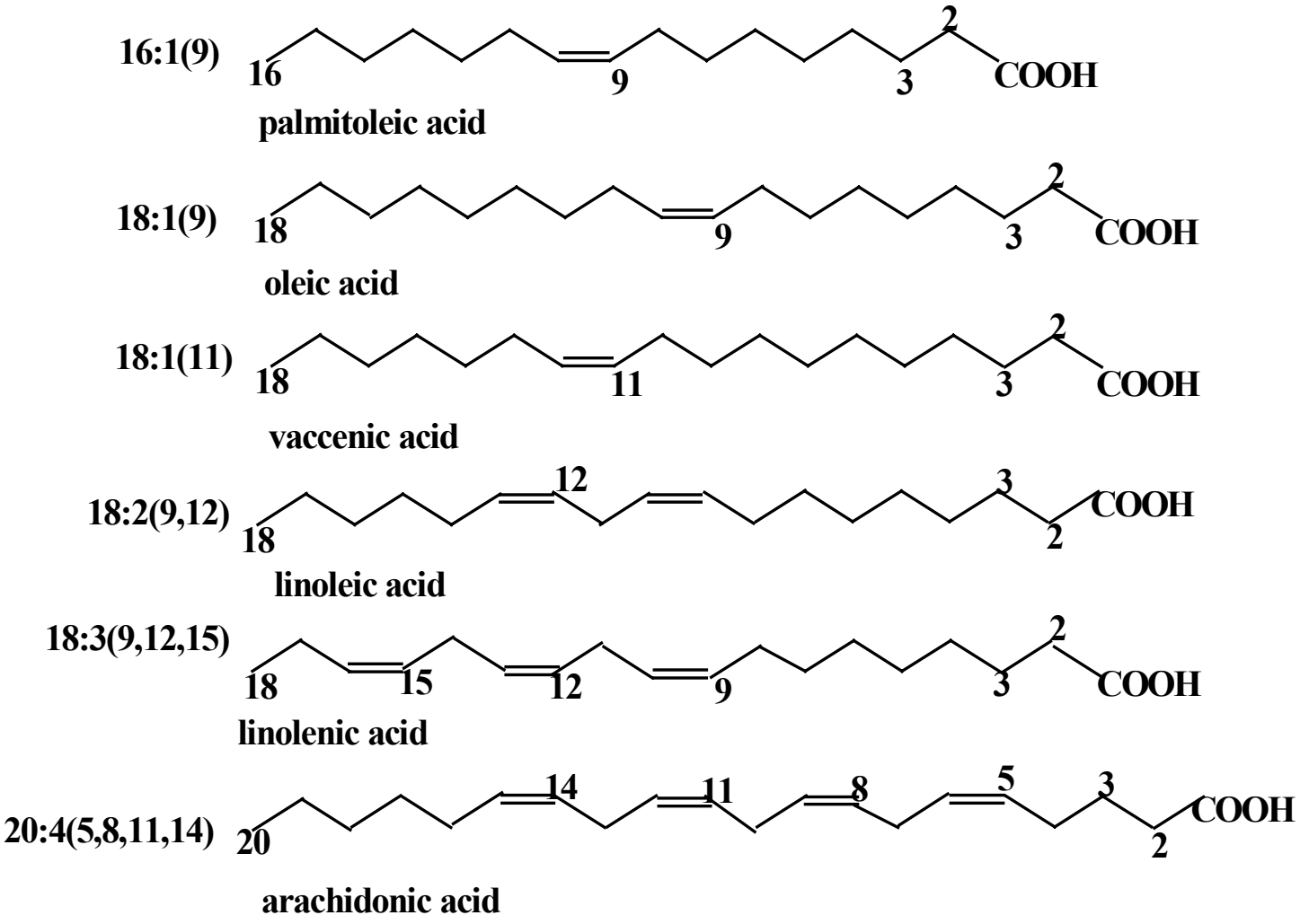
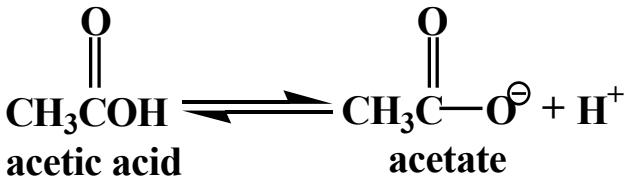


Figure 3: Some common unsaturated fatty acids. The configuration is *cis* around each double bond, and multiple double bonds are spaced at three-carbon intervals.

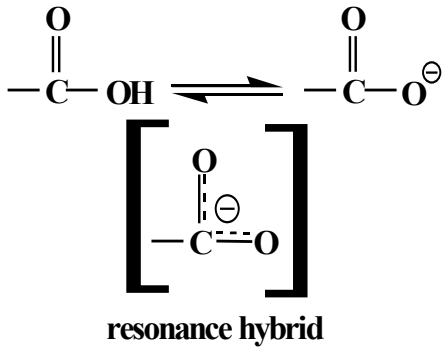
See next section for nomenclature of carboxylic acid salts.

3. Physical properties. The COOH group is hydrophilic, making the first few members of the homologous series water-soluble.

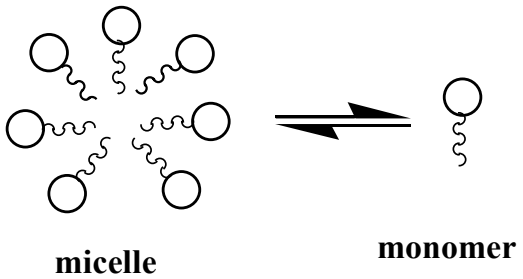
Carboxylic acids are weak acids, dissociating in water to form a **carboxylate anion**. The salt of the acid is named by replacing the –ic acid with –ate. Example: acetic acid/acetate.



The dissociation of the —OH group in —COOH is more favorable than the dissociation of —OH in an alcohol because the carboxylate anion is stabilized by resonance:

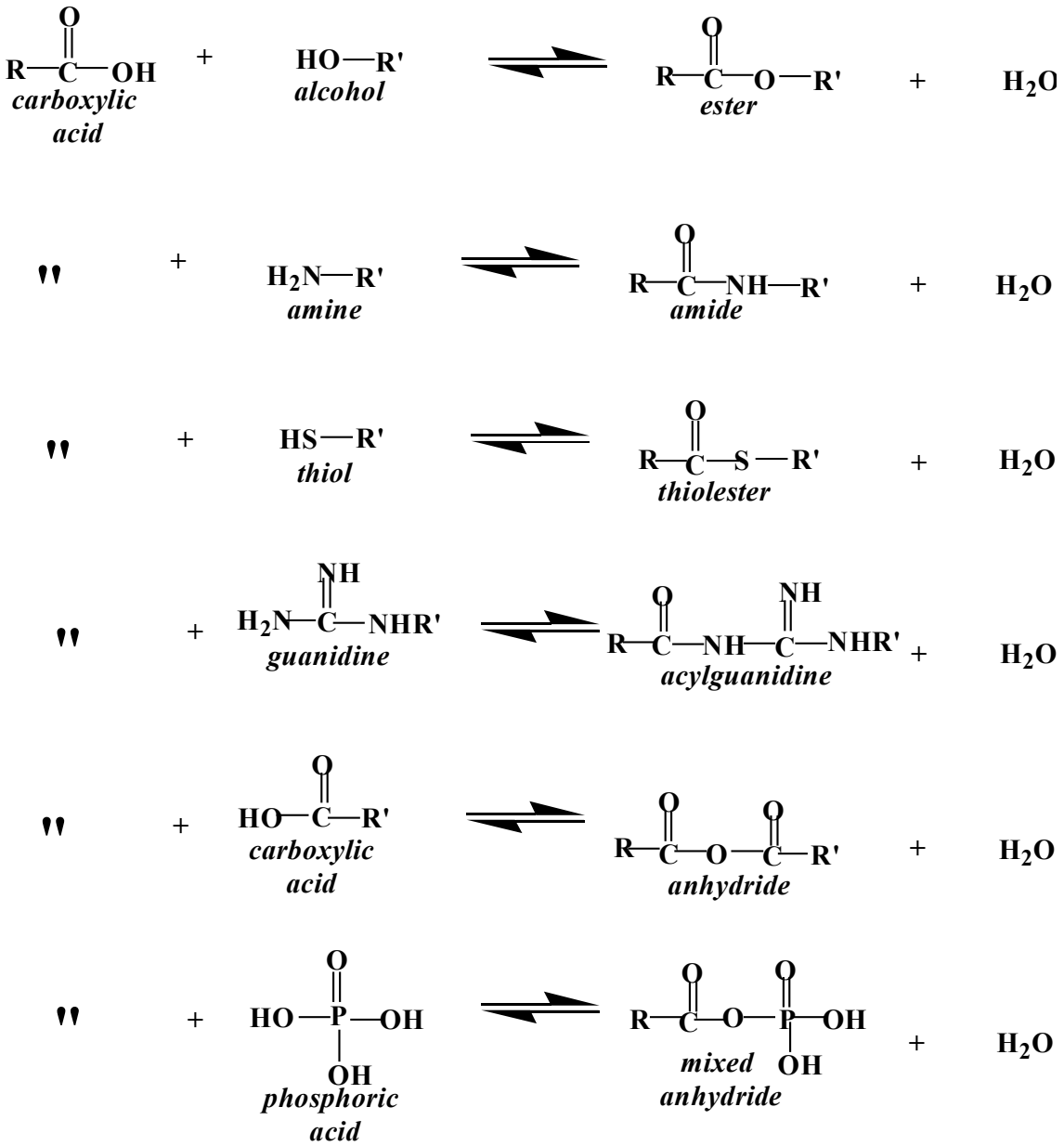


The carboxylate anion is extremely hydrophilic, and essentially insoluble in organic solvents. The anionic forms of fatty acids are strongly amphipathic, and form **detergent micelles** in water.

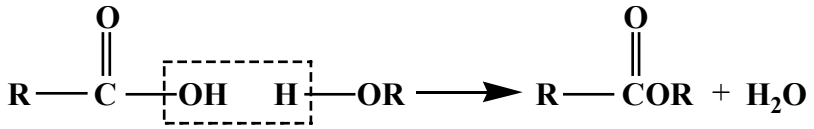


4. Reactions of biochemical significance. The most important is the formation of **carboxylic acid derivatives**, which include esters, amides, thiolesters, and anhydrides.

Derivatives formed from carboxylic acids.



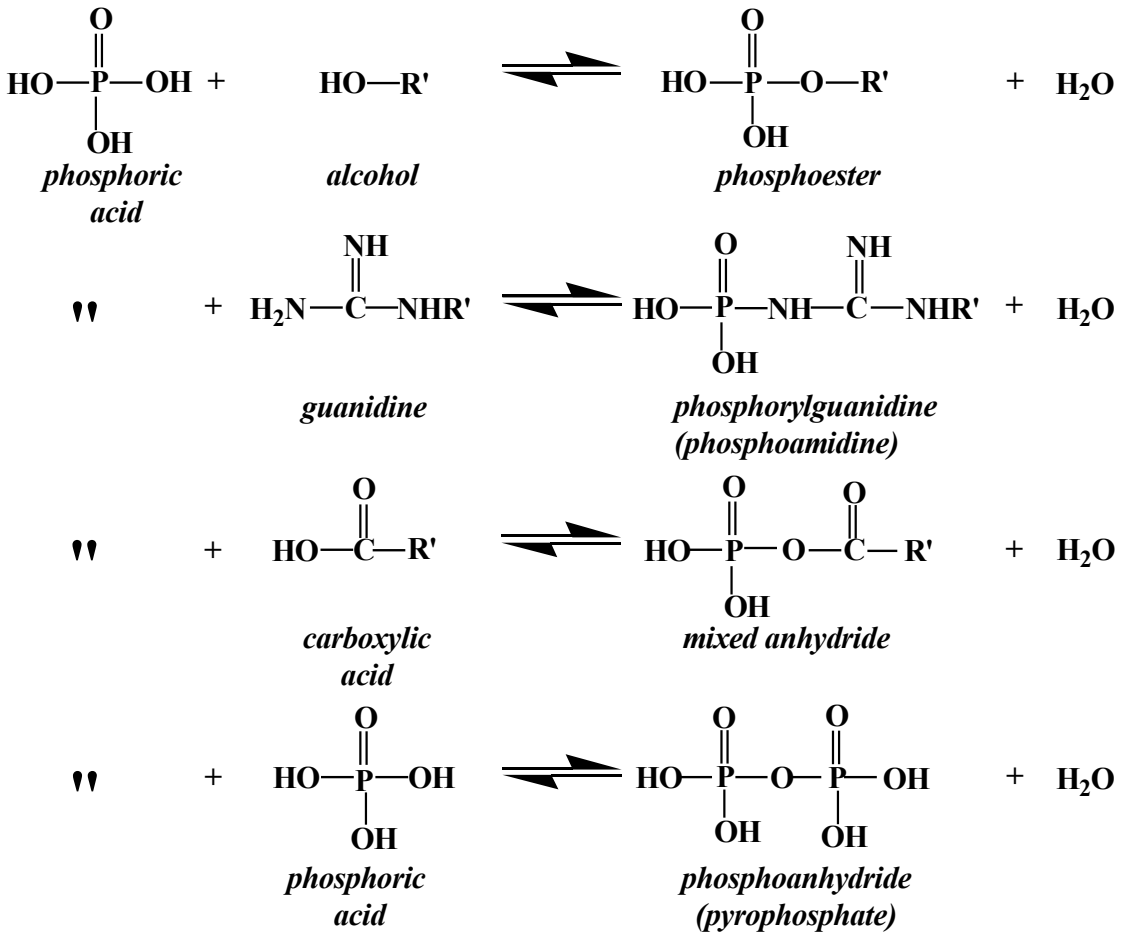
Formation of these derivations occurs by elimination of water from the reactants and is most easily visualized via "lasso" chemistry. Example:



I. Phosphoric acid and its derivatives. This exceedingly important class of compounds will be

discussed in detail later in the course. Much of the chemistry of phosphate is qualitatively similar to that of carboxylic acids.

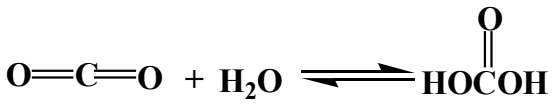
Derivatives formed from phosphoric acid.



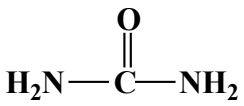
The derivatives are hydrophilic although their relative solubility in various solvents differs.

J. Carbon dioxide, carbonic acid and derivatives.

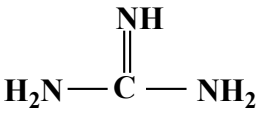
1. Structural characteristics. The structure of carbon dioxide is O=C=O, usually written as CO_2. Addition of water, H-OH, to CO_2 produces carbonic acid, H_2CO_3.



2. Derivatives of carbonic acid.



urea



guanidine

3. Physical properties. Carbon dioxide is a gas, but with significant solubility in water and organic solvents. This will be discussed in the section on acid base chemistry and blood gases. All the derivatives of carbonic acid are hydrophilic.

K. Compounds with more than one functional group.

1. Dicarboxylic acids.

HOOC——COOH
Oxalic acid
Ethanedioic acid

$HOOCCH_2COOH$
Malonic acid
Propanedioic acid

$HOOCCH_2CH_2COOH$
Succinic acid
Butanedioic acid

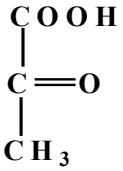
$HOOCCH_2CH_2CH_2COOH$
Glutaric acid
Pentanedioic acid

$HOOCCH_2CH_2CH_2CH_2COOH$
Adipic acid
Hexanedioic acid

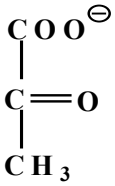
2. Keto acids.

a. ∀-keto acids.

In these the keto group is adjacent to the carboxylic group. The most common in biochemistry is pyruvic acid and its salt, pyruvate:

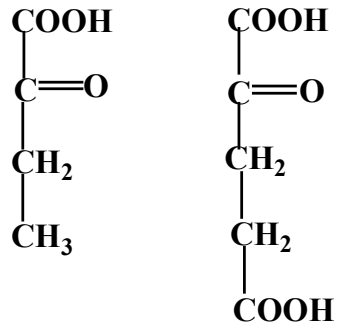


Pyruvic acid



Pyruvate

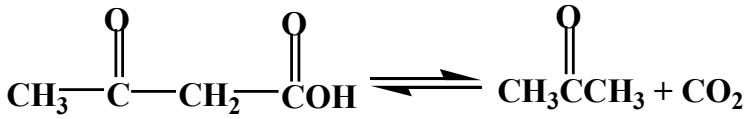
The systematic name is ∀-keto followed by the name of the parent acid. This system is used for all keto acids other than pyruvate, e.g.,



α-ketobutyrate **α-ketoglutarate**

b. ∃-keto acids

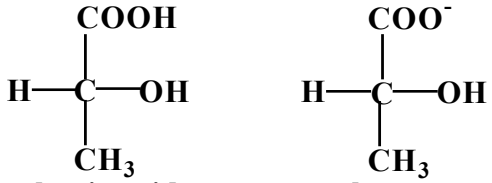
In these the keto group is two carbons removed from the carboxyl group. ∃-keto acids readily undergo decarboxylation:



3. Hydroxy acids.

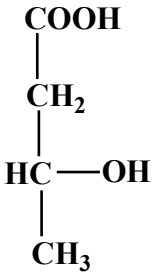
a. ∀-hydroxy acids.

A hydroxy group is alpha to the carboxyl. The most common one in biochemistry is lactic acid and its salt, lactate. Other ∀-hydroxy acids are either named after the parent acid or given common names of their own.



lactic acid **lactate**

b. ∃-hydroxy acid.

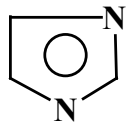


β-hydroxybutyric acid

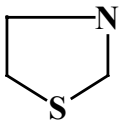
4. Polyfunctional compounds containing two or more hydroxyls are usually classified as carbohydrates and will be considered separately.

L. Heterocyclic compounds.

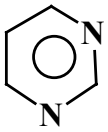
1. Structural characteristics. A heterocyclic compound is one that contains a ring with more than one kind of atom. Some of those encountered in biochemistry are shown below.



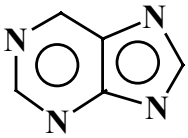
imidazole



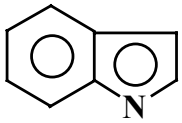
thiazole



pyrimidine



purine

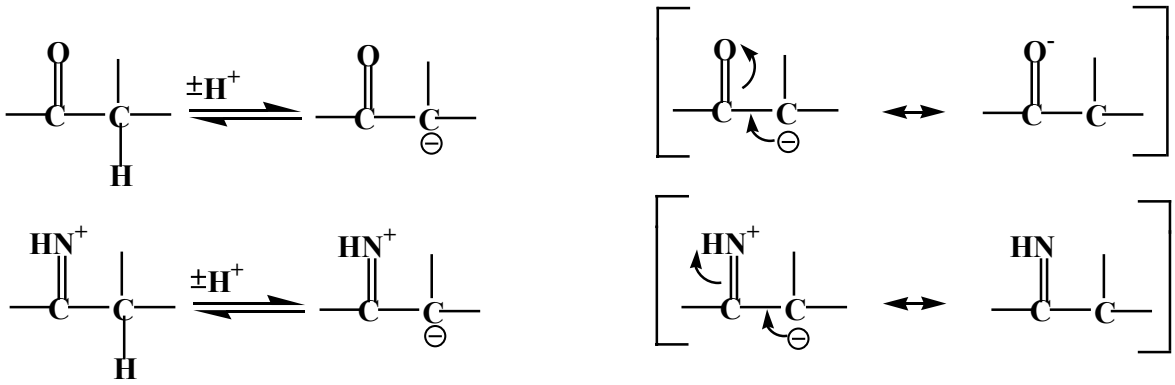


indole

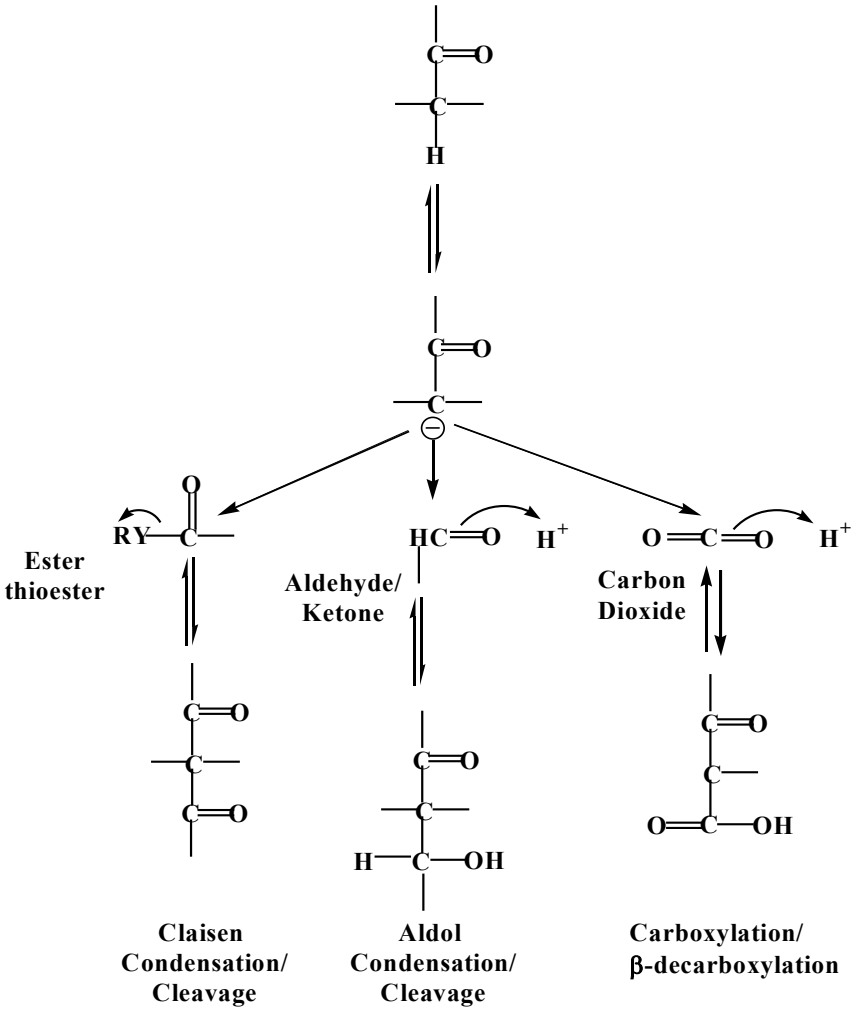
M. Making and breaking carbon-carbon bonds.

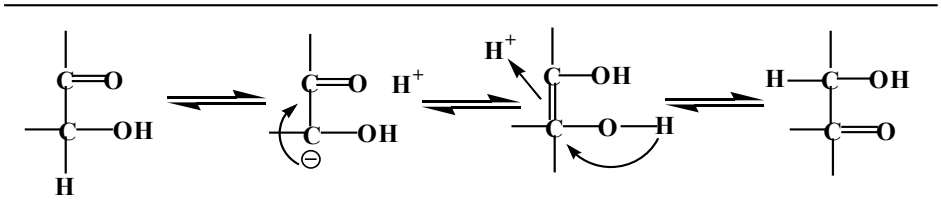
1. Almost always requires the formation of a resonance-stabilized carbanion as an attacking group, or as a leaving group.

2. Structural requirement for resonance stabilized carbanion. The anion forms on a carbon adjacent to a C=O or C=N group.



3. Some reactions.





ISOMERIZATION