

Organic Chemistry Review

This document reviews the functional groups and reactions of organic chemistry that are important to biochemistry. Organic chemistry is the study of the covalent chemical compounds that contain primarily Carbon and Hydrogen. Organic molecules can also contain small amounts of the nonmetallic elements Fluorine, Chlorine, Bromine, Iodine, Oxygen, Nitrogen, and/or Sulfur. Within the realm of organic chemistry there are more than 6,000,000 known compounds and new compounds are being discovered or synthesized at a rate of over 100,000 per year.

Why are there so many different organic compounds?

1. Carbon is one of the few elements that can form numerous stable covalent bonds with itself, with other carbon atoms.
2. Carbon must form four covalent bonds to satisfy the octet rule. These bonds can be any combination of single bonds, double bonds, or triple bonds so that the octet rule is satisfied.
3. Carbon can form stable covalent bonds with other non-metals, such as the halogens, hydrogen, oxygen, nitrogen, and sulfur.
4. The covalent bonds with the other non-metals can be single, double, or triple bonds, provided the other element can share sufficient electrons to form these bonds and at the same time satisfy the octet rule.

The carbon atoms within an organic molecule are classified by the number of other carbon atoms it is bonded to. A primary (1°) carbon atom is bonded to only one other carbon atom; a secondary (2°) carbon atom is bonded to two other carbons; a tertiary (3°) carbon is bonded to three other carbons; and a quaternary (4°) carbon has all four of its bonds to other carbon atoms.

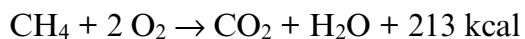
The Hydrocarbons

This major class of molecules is composed of only carbon and hydrogen. The hydrocarbons are nonpolar molecules, there is very little difference between the electronegativity of carbon and hydrogen. Since they are nonpolar they are water insoluble. Water is a very polar molecule – “like dissolves like”. Within the Hydrocarbon class of compounds there are two subclasses, the Aliphatic Hydrocarbons and the Aromatic Hydrocarbons. Aliphatic Hydrocarbons are divided into three groups, two of which are important to biochemistry; the Alkanes and Alkenes.

The Alkanes

The Alkanes are saturated hydrocarbons. They contain only carbon and hydrogen and all of the covalent bonds between the atoms are single bonds. In Alkanes, all non carbon-carbon bonds are carbon-hydrogen bonds, the molecule is saturated with, contains the maximum possible amount of hydrogen atoms. IUPAC nomenclature of the alkanes is based on the names of the straight chain (normal) molecules. All alkanes end in “ane”. Side chains (branches, R groups) off the parent carbon chain are named as alkyl groups (methyl, ethyl, isopropyl, etc.) and their location on the parent molecule is indicated by the lowest combination of numbers.

Alkanes undergo two typical chemical reactions, only one of which is important to biochemistry - Combustion. Combustion is the complete oxidation of organic molecules yielding CO_2 , H_2O , and energy. An example of combustion is:



All organic molecules can undergo combustion reactions.

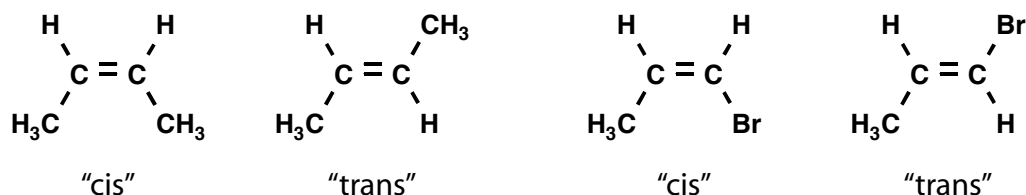
The Alkenes

The Alkenes are unsaturated hydrocarbons. They contain carbon and hydrogen and one or more carbon-carbon double bonds (less than a saturating amount of hydrogen). IUPAC nomenclature for the alkenes is similar to that of the alkanes except the names of the alkenes all end in "ene" and the position of the carbon-carbon double bond is given the lowest possible number. Since carbon-carbon double bonds are not free to rotate, the alkenes exhibit a form of Stereoisomerism called Geometric Isomerism or Cis-Trans Isomerism. Cis-Trans Isomers contain the same alkyl side chains (functional groups), but their arrangement around the carbon-carbon double bond, their geometry, is different.

General Examples:

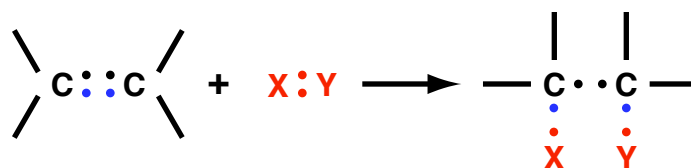


Specific Examples:

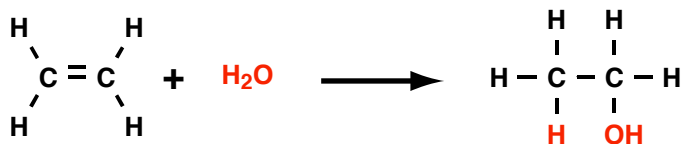
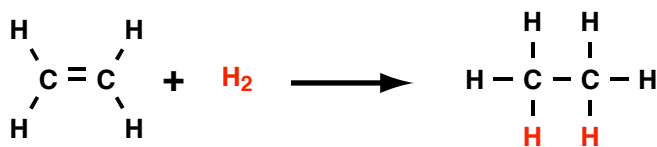


Alkenes undergo Addition Reactions. Molecules of the type XY add across the double bond. X adds to one of the carbons of the double bond, Y goes to the other, and the double bond is reduced to a single bond. The molecule XY can be H₂, Cl₂, Br₂, HCl, HBr, or H₂O.

General Reaction:



Specific Examples:

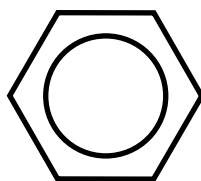


Adding H₂ across a double bond is called hydrogenation; adding Cl₂ or Br₂ across the double bond is termed halogenation; adding HCl or HBr is called hydrohalogenation; and adding H₂O across a double bond is termed hydration. Hydrogenation and hydration of carbon-carbon double bonds occurs in biological systems.

Alkenes also undergo addition reactions between themselves. In the presence of an appropriate catalyst alkenes will add to themselves resulting in the formation of addition polymers. Polyethylene, polypropylene, polyvinyl-chloride (PVC), and Teflon are all examples of alkene addition polymers.

The Aromatic Hydrocarbons

Aromatic Hydrocarbons are based upon the molecule Benzene.



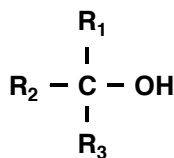
Aromatic molecules contain 6 or more delocalized π (Pi) electrons that are shared equally by all member atoms of the ring. This delocalization of electrons over the entire ring results in a very stable molecule. Aromatic hydrocarbons do not undergo addition reactions because this type of reaction would destroy the stable configuration of π electrons. Rather they take part in Substitution Reactions, where one or more of the hydrogens on the ring is replaced by a different element or functional group.

The Oxygen Containing Organic Compounds

The Alcohols

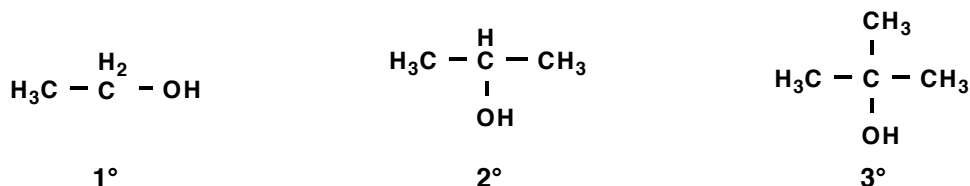
The alcohols contain one or more Hydroxyl groups; -OH

General Structure:



where R_1 , R_2 , and R_3 can be hydrogen or an alkyl group. Alcohol nomenclature is based upon the nomenclature of the alkanes, with two changes/additions. The “e” of the name of the parent alkane is dropped and “ol” is added in its place (ethane → ethanol) and the hydroxyl functional group is given the lowest possible number (or set of numbers).

Alcohols are polar molecules because oxygen is much more electronegative than carbon or hydrogen. In an alcohol, the oxygen has a partial negative charge (δ^-); the carbon and hydrogen of the alcohol group have a partial positive charge (δ^+). Since alcohols are polar the smaller alcohols (6 or fewer carbons) are water soluble.



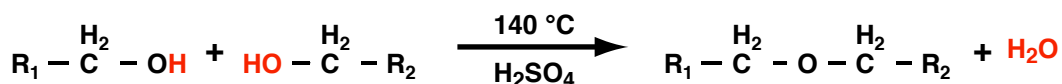
If the hydroxyl group of an alcohol is attached to a carbon atom that is bonded to zero or one other carbon atom the resulting molecule is termed a primary (1°) alcohol (see above). If the hydroxyl group is bonded to a carbon that is covalently linked to two other carbon atoms it is a secondary (2°) alcohol. A tertiary (3°) alcohol has the hydroxyl group attached to a carbon that is covalently bonded to three other carbons. The chemistry of 1° , 2° , and 3° alcohols varies.

Alcohols undergo two types of reactions important to biochemistry. Alcohol molecules undergo Dehydration Reactions and the hydroxyl group of an alcohol can be Oxidized.

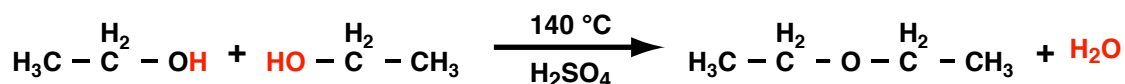
Dehydration Reactions

In a Dehydration Reaction a molecule of water is removed from the reacting species. Depending upon the reaction conditions, alcohols are dehydrated either by an Intermolecular or an Intramolecular reaction mechanism. In the laboratory, *in vitro*, both reactions require an acid catalyst and high temperatures. Intermolecular dehydration reactions occur at a lower temperature and the water molecule is removed from between two reacting alcohol molecules. The product of an intermolecular alcohol dehydration reaction is an Ether

General Reaction:



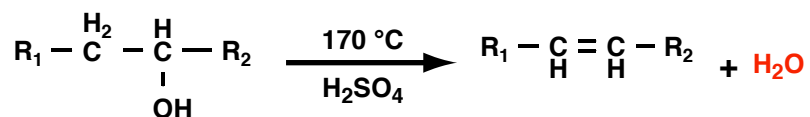
Specific Example:



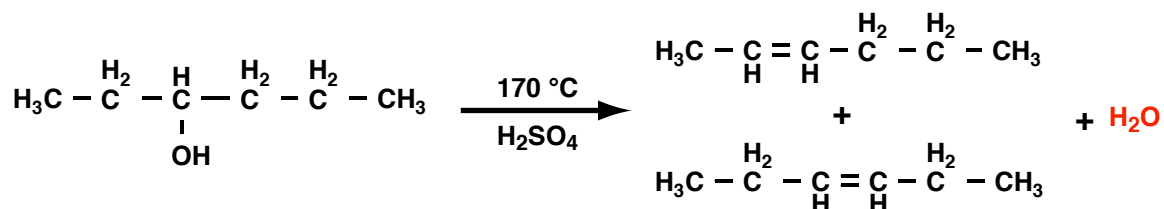
Intramolecular dehydration reactions require a higher temperature to proceed and the water molecule

is removed from within a single alcohol molecule. The product of an intramolecular alcohol dehydration reaction is an Alkene.

General Reaction:



Specific Example:

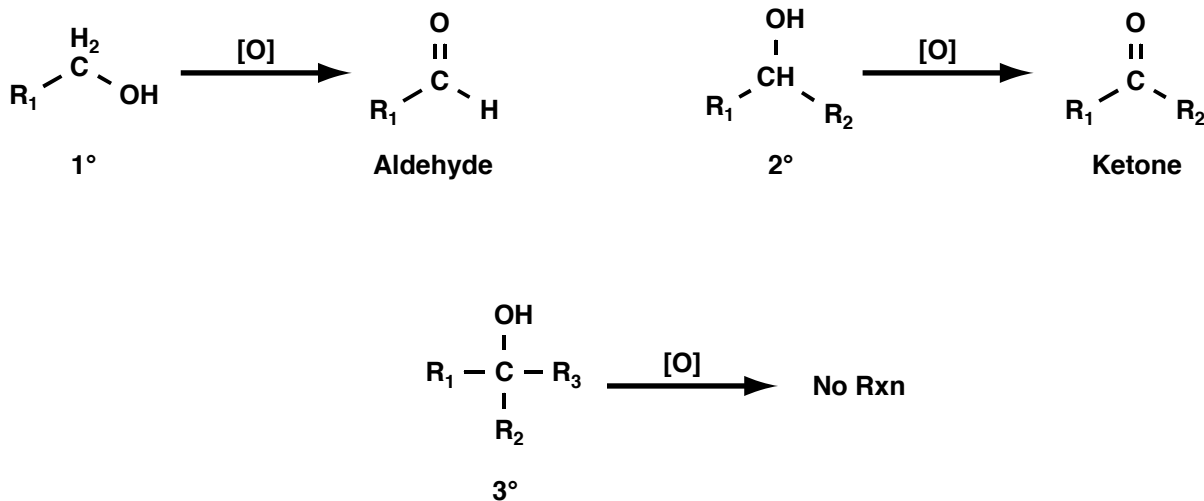


Biological systems are capable of dehydrating alcohols to form ethers or alkenes. However, cells must and do employ significantly milder conditions.

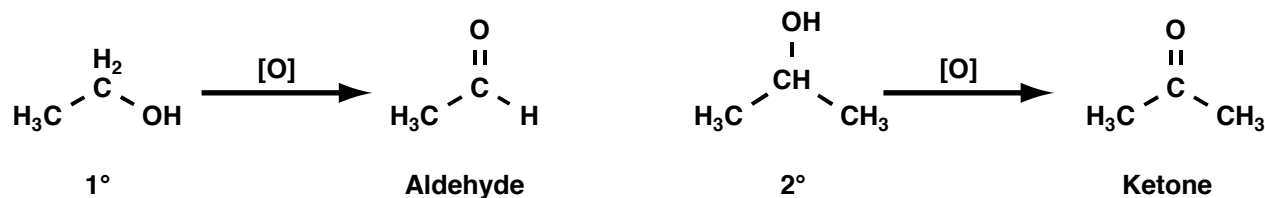
Oxidation Reaction

When an alcohol undergoes oxidation, the hydroxyl group is oxidized to a carbonyl group, C=O. During an oxidation reaction, electrons are lost from the reacting species. In organic chemistry and biochemistry the loss of electrons is usually accompanied by a loss of hydrogen atoms or a gain of oxygen atoms. The oxidation of an alcohol results in the loss of two hydrogen atoms, one from the hydroxyl group and the second from the carbon atom carrying the hydroxyl group. The product of the reaction depends upon the type of alcohol oxidized. Primary alcohols yield Aldehydes; secondary alcohols produce Ketones; tertiary alcohols cannot be oxidized without breaking carbon-carbon bonds.

General Reaction:

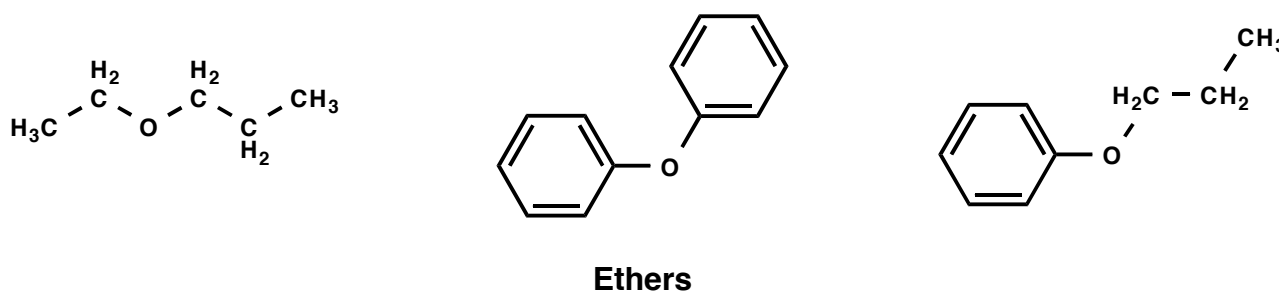


Specific Examples:



The Ethers

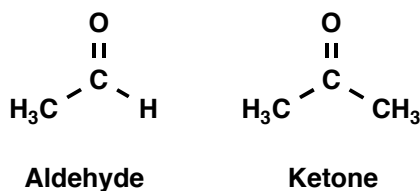
Ethers all contain the ether functional group, C–O–C, two organic groups (two alkyl, two aromatic, or one of each) bonded to an oxygen atom.



They are formed by the intermolecular dehydration of alcohols. Ethers are polar molecules, oxygen is more electronegative than carbon. Ethers are less polar than alcohols and therefore they are less water soluble than alcohols. Ethers are formed in biological systems and once formed they are relatively inert.

The Aldehydes and Ketones

The aldehydes and ketones are treated together because they both contain the carbonyl functional group, C=O, and therefore their chemistries are similar. An aldehyde contains the carbonyl group as the terminal carbon, carbon 1, whereas, ketones have the carbonyl group on an interior carbon (not carbon 1).



Aldehydes are named by dropping the “e” from the name of the parent alkane and adding “al” in its place (ethane → ethanal). The carbon atom carrying the carbonyl group is always carbon 1 of the aldehyde and the other functional groups on the molecule are numbered from this starting point. Ketones are named by dropping the “e” from the name of the parent alkane and adding “one” in its place (propane → propanone). The carbon atom carrying the carbonyl group in the ketone is given the lowest possible number and the other functional groups are numbered accordingly, i.e., given the

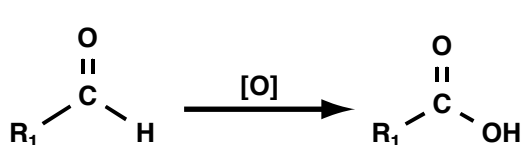
lowest possible set of numbers. The carbonyl group takes precedence over the other functional groups discussed so far.

Aldehydes and Ketones are polar molecules, oxygen is more electronegative than carbon. Aldehydes and Ketones are less polar than alcohols, but more polar than ethers. Their solubility in water is less than that of alcohols, but greater than that of ethers.

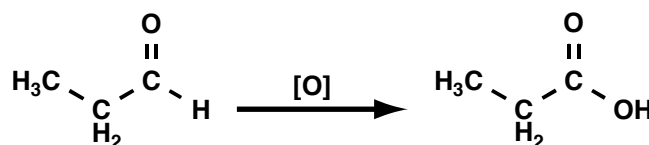
The chemistry of aldehydes and ketones is possibly the most complex in the realm of organic chemistry. Aldehydes can be oxidized. Aldehydes and ketones can be reduced, they can react with alcohols, and they can react with each other.

Oxidation Reaction

When aldehydes are oxidized the carbonyl group is converted to a Carboxylic Acid group, $-\text{COOH}$. This oxidation is accompanied by the addition of an oxygen ($-\text{OH}$) to the carbonyl carbon. Aldehydes are easily oxidized. Metal ions such as Ag^+ and Cu^{2+} at room temperature can act as oxidizing agents. When silver ion is the oxidizing agent, it is reduced to metallic silver forming a silver mirror on the reaction vessel. Oxidation of aldehydes by Ag^+ is the Tollen's Test or Tollen's Reaction. When Cu^{2+} is the oxidizing agent, it is reduced to Cu_2O , a brick red water insoluble compound (precipitate). The oxidation of aldehydes by Cu^{2+} is the Benedict's Test. These two reactions are used as simple tests for aldehydes.



General Rxn

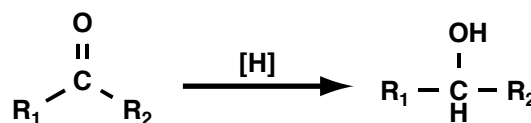
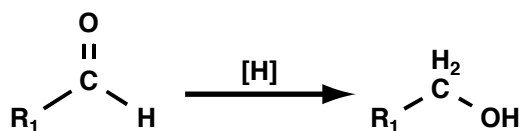


Specific Example

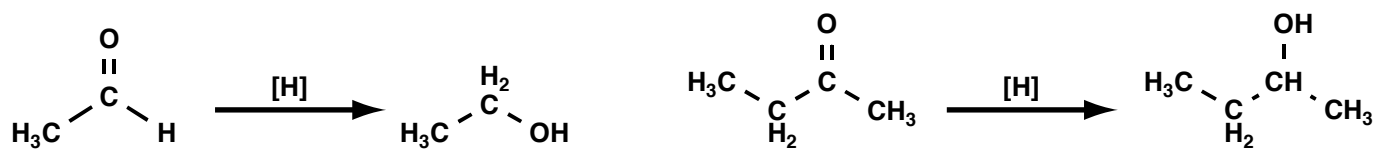
Reduction Reaction

When aldehydes and ketones are reduced the corresponding alcohols are produced. During a reduction reaction electrons are gained by the reacting species. In organic chemistry and biochemistry the gain of electrons is often accompanied by the gain of hydrogen or the loss of oxygen. In the reduction of aldehydes and ketones, the carbonyl oxygen and the carbonyl carbon each gain a hydrogen. The reduction of an aldehyde produces a 1° alcohol; the reduction of a ketone produces a 2° alcohol.

General Reaction:

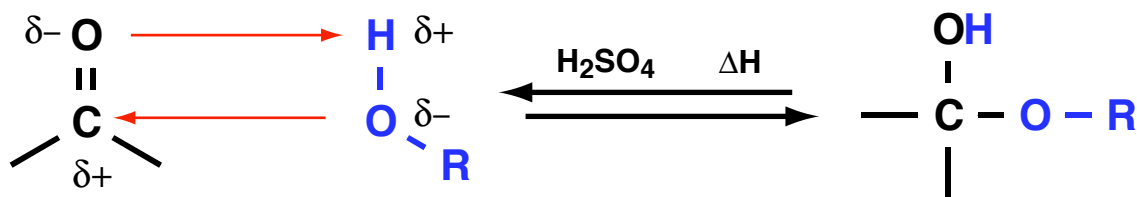


Specific Examples:

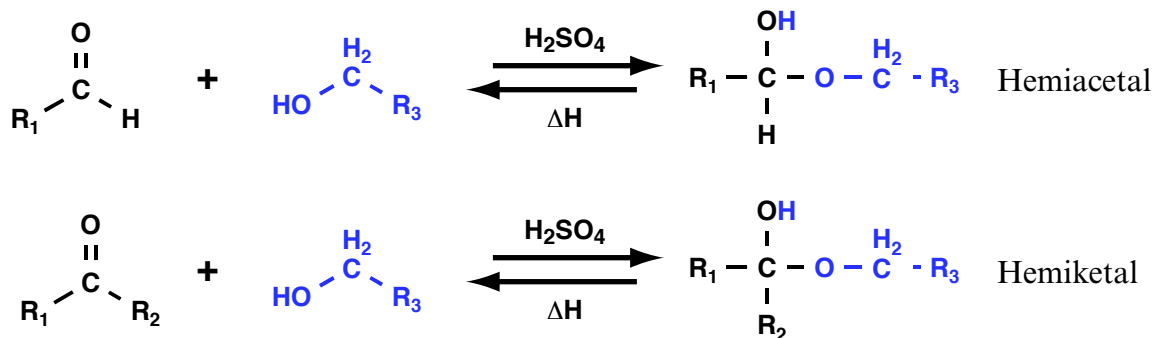


Reaction with Alcohols (An Addition Reaction)

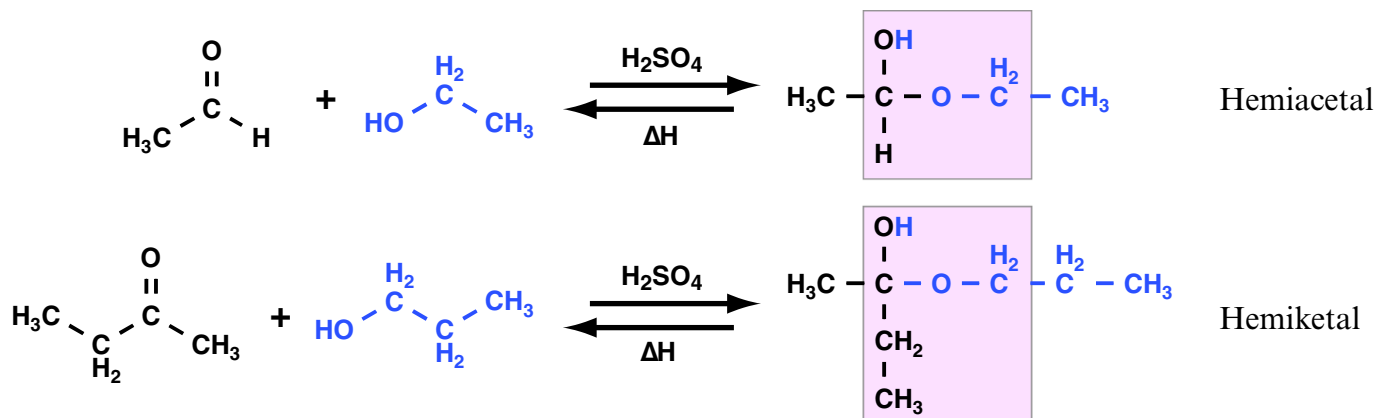
Aldehydes and ketones undergo Addition Reactions. Alcohols react with aldehydes and ketones by an addition reaction. The products of the addition reaction between equal molar amounts of aldehydes and alcohols are Hemiacetals, whereas, the product formed from equal molar amounts of ketones and alcohols are known as Hemiketals. Mechanistically, in the presence of an acid catalyst and a small amount of heat, the partially negatively charged hydroxyl oxygen of the alcohol attacks the partially positively charged carbonyl carbon of the aldehyde or ketone and the partially negatively charged carbonyl oxygen attacks the partially positively charged hydroxyl hydrogen. The alcohol is added across the carbon-oxygen double bond of the carbonyl group.



General Reaction:

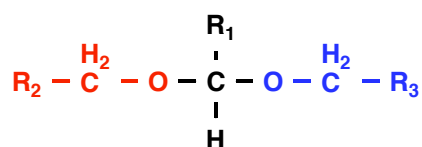


Specific Examples:



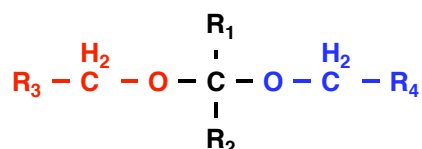
Hemiacetals are recognized by finding an ether linkage (C-O-C) where one of the carbons of the ether linkage also carries a -OH and a -H. The hemiketal is an ether linkage where one of the carbons involved in the ether linkage also carries a -OH and an organic (-R) group {see above}.

Hemiacetals and hemiketals are very reactive compounds. Only a very few hemiacetals and/or hemiketals can be isolated in pure form. Usually they rapidly revert to the starting materials (re) establishing an equilibrium. The hydroxyl (-OH) group that is part of the hemiacetal or hemiketal functional group is a very reactive chemical group. It is much more reactive than the hydroxyl groups of simple alcohols. The hydroxyl group of hemiacetals and hemiketals will rapidly react with another alcohol molecule or with any excess alcohol molecules to form Acetals and Ketals, respectively. This reaction between hemiacetals or hemiketals and alcohols is a dehydration reaction. An acetal functional group has the following appearance:



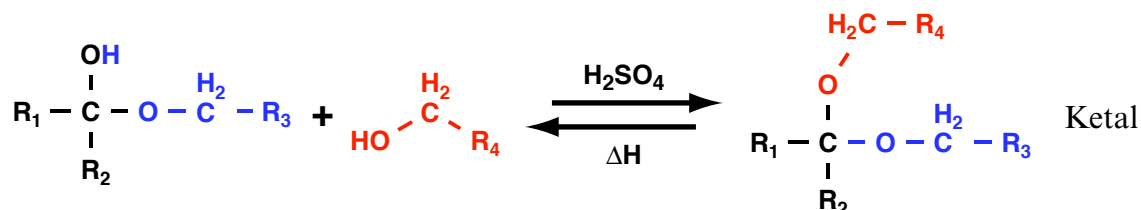
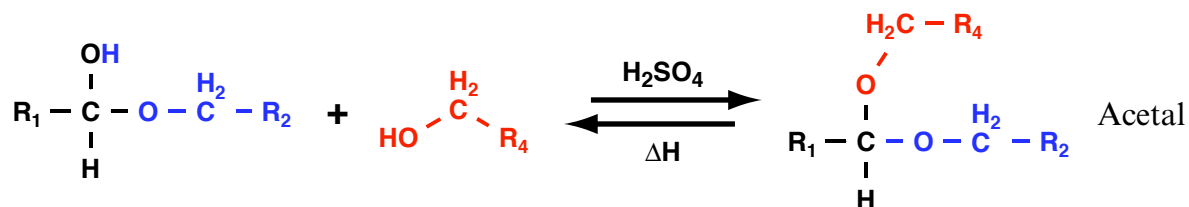
It is a diether (C-O-C-O-C) with a organic (-R) group and an -H attached to the middle carbon of the diether. The R group on the middle carbon is the carbon chain of the original aldehyde.

A ketal functional group has the following appearance:

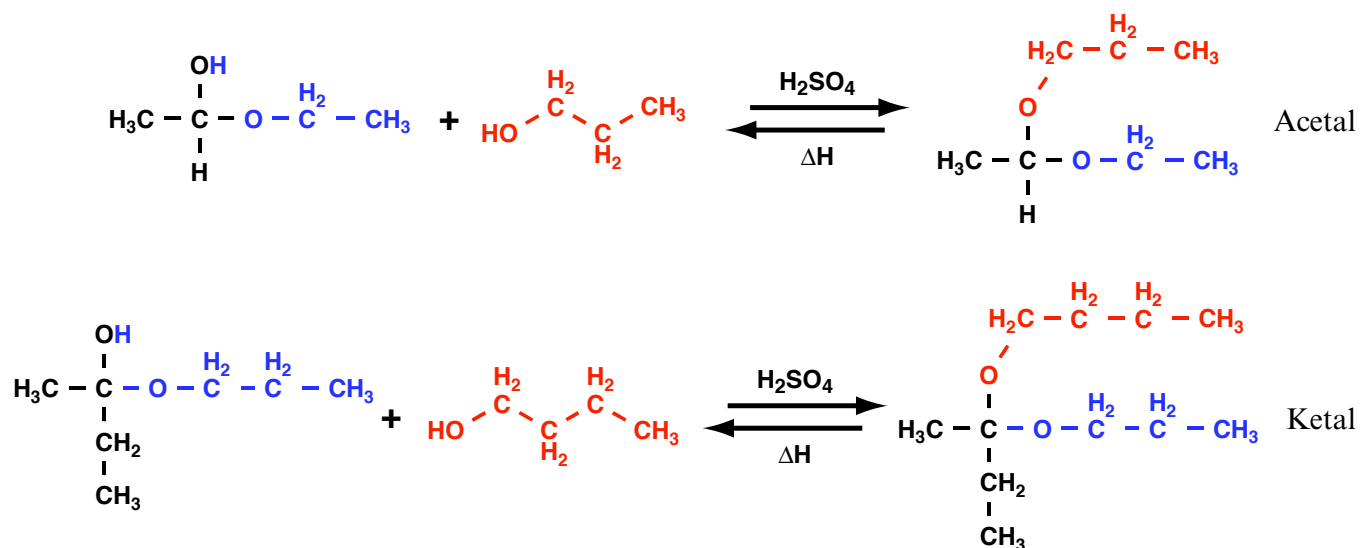


It is a diether (C-O-C-O-C) with two organic (-R) groups attached to the middle carbon of the diether. The R groups bonded to the middle carbon are the carbon chains of the original ketone.

General Reaction:



Specific Examples:



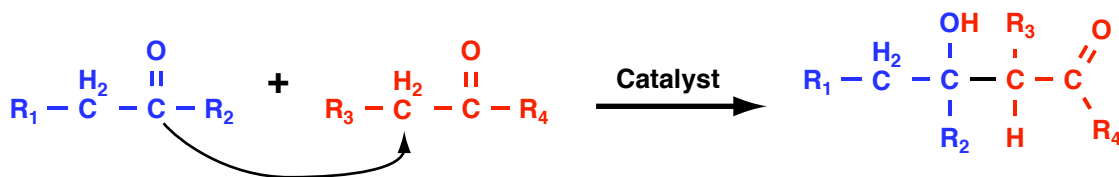
Acetal and ketals can be synthesized in two steps as outlined above (aldehyde or ketone + alcohol → hemiacetal or hemiketal + alcohol → acetals or ketals), or they can be formed in a single step (aldehyde or ketone + >2× molar excess alcohol → acetal or ketal).

Acetals and ketals are more stable than hemiacetals and hemiketals, many can be isolated in pure form. However, in the presence of an acid or other suitable catalyst and H₂O they are rapidly broken down into the starting materials; an aldehyde or a ketone and two alcohols.

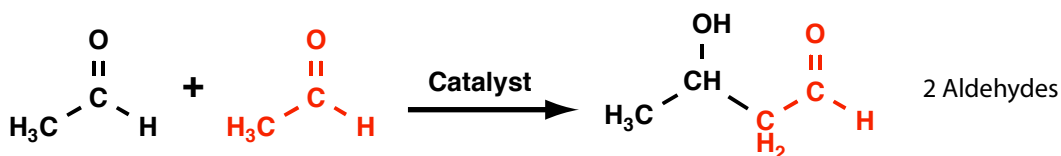
Reaction with Other Aldehydes or Ketones (an Addition Reaction / The Aldol Condensation)

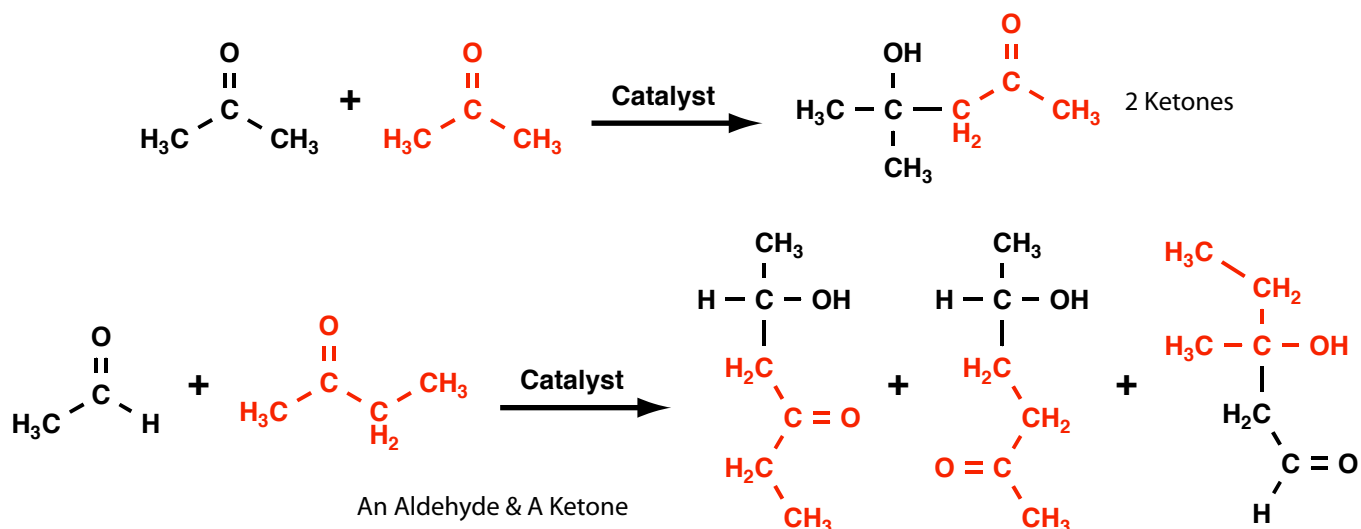
When aldehydes and/or ketones react with each other the carbon adjacent to the carbonyl carbon on one molecule attacks the carbonyl carbon of the second. This reaction forms new carbon-carbon bonds. The reaction is called an Aldol Condensation.

General Reaction:



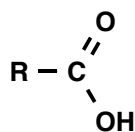
Specific Examples:





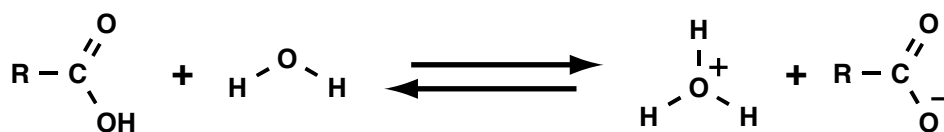
Carboxylic Acids

Carboxylic acids contain one or more Carboxyl functional groups; $-\text{COOH}$. Their general structure is:



Carboxylic acids are very polar molecules, oxygen is more electronegative than carbon and there are two oxygen atoms attached to a single carbon atom. Carboxylic acids are considerably more polar and more water soluble than alcohols.

Carboxylic acids are weak acids. The simple alkyl carboxylic acids have pK_a 's in the range of 3 to 9. When dissolved in water carboxylic acids establish equilibria with their corresponding Carboxylate Anions.



When naming a carboxylic acid, the "e" from the name of the parent alkane is dropped and the ending "oic acid" is added (propane \rightarrow propanoic acid). The name of the corresponding carboxylate anion is formed by dropping the "ic acid" ending and adding "ate" in its place (propanoic acid \rightarrow propanoate). The carboxylic acid group is always carbon 1 in the numbering scheme, it takes precedence over all other organic functional groups because it is the most oxidized.

Carboxylic acids undergo Neutralization reactions, Reduction reactions, and Dehydration reactions.

The Neutralization Reaction

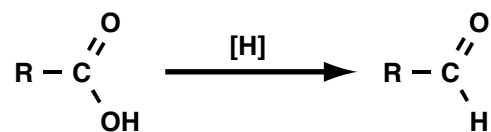
Carboxylic acids are neutralized by bases forming Carboxylate Salts. These salts are true ionic

compounds and therefore are very polar and very water soluble.

The Reduction Reaction

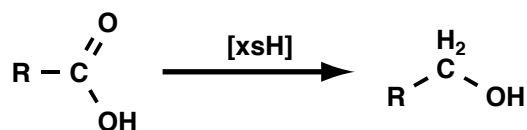
When carboxylic acids undergo reduction with an equal molar amount of reducing agent the product is the corresponding aldehyde.

General Reaction



When an excess of reducing agent is employed in the reaction, the carboxylic acid is reduced all the way back to the corresponding 1° alcohol.

General Reaction



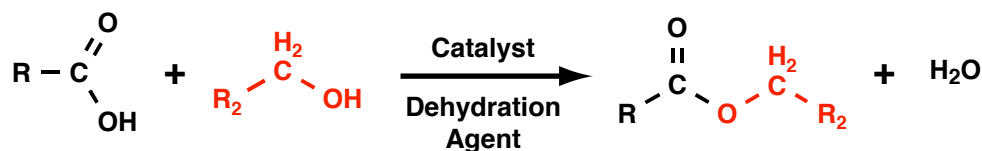
The Dehydration Reactions

Carboxylic acids react with alcohols, ammonia, and oxygen containing acids (oxiacids; e.g., sulfuric acid or phosphoric acid) via dehydration reactions.

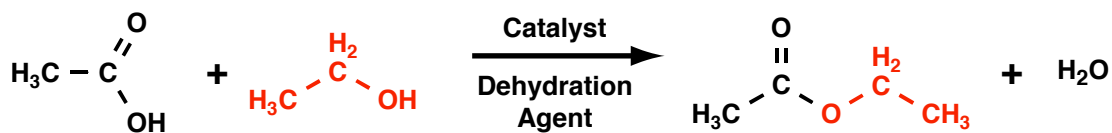
with Alcohols

When carboxylic acids react with alcohols the product is an Ester

General Reaction:



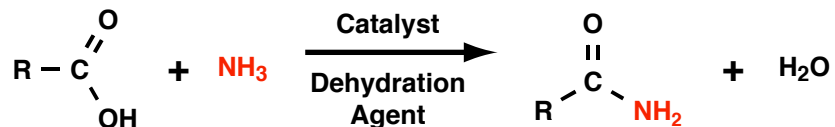
Specific Example:



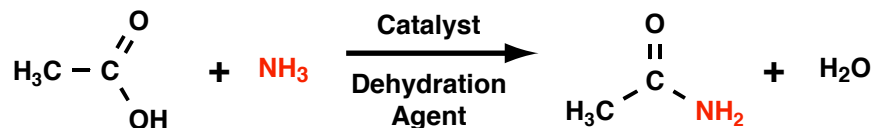
with Ammonia

When carboxylic acids react with ammonia the product is an Amide

General Reaction:

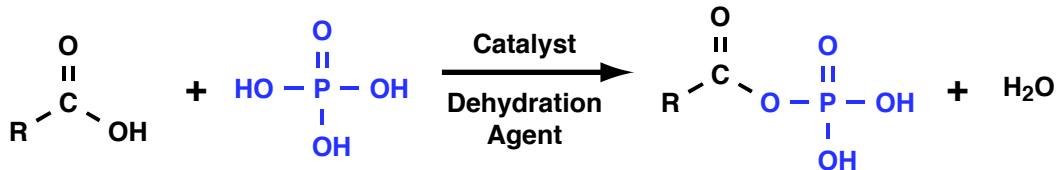
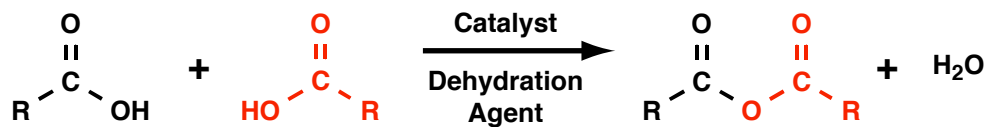


Specific Example:



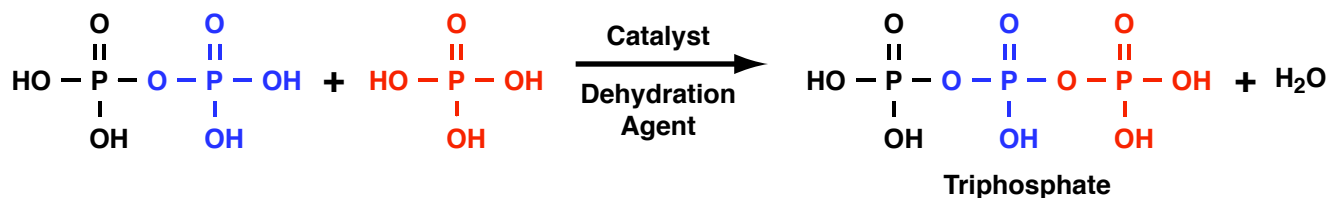
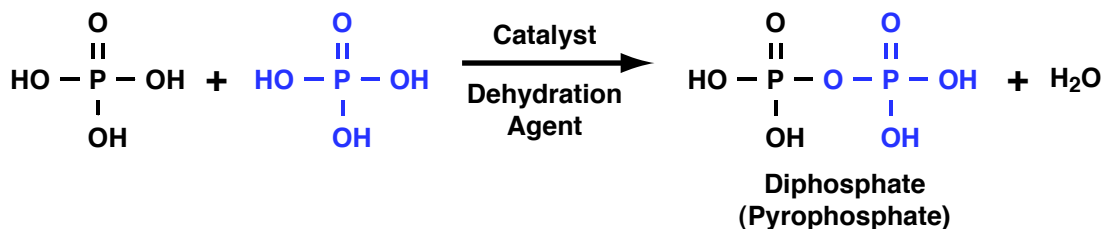
with Oxiacids

When carboxylic acids react with other oxygen containing acids the product is an Acid Anhydride. If the dehydration reaction is between two organic acids (two carboxylic acids) the product is an Organic Acid Anhydride or a Carboxylic Acid Anhydride. If the reaction is between an organic acid and an inorganic oxiacid the product is a Mixed Acid Anhydride.



Oxygen containing mineral acids, especially phosphoric and sulfuric acids, undergo similar dehydration reactions to produce phosphoric acid anhydrides and sulfuric acid anhydrides.

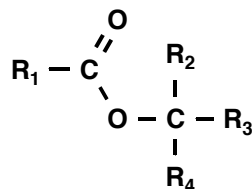
General Reaction:



Acid anhydrides are unstable high energy compounds. When water is added back to an acid anhydride the corresponding acids are formed and a large quantity of energy (heat) is liberated.

The Esters

Esters are formed by the dehydration reaction between carboxylic acids and alcohols. All esters have the following general structure:

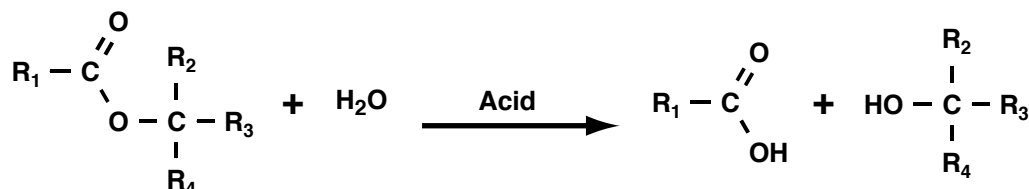


R₁, R₂, R₃, & R₄ can be hydrogens, alkyl groups, and/or aromatic groups. Esters are named by naming the carbon chain of the reactant alcohol, followed by the name of the carboxylate anion involved in the reaction.

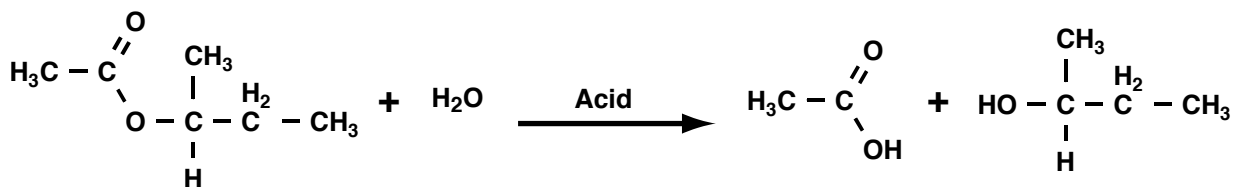
Esters, like the carboxylic acids and alcohols used for their synthesis, are polar molecules. They are more polar than alcohols but less polar than carboxylic acids.

Esters undergo Hydrolysis Reactions catalyzed by either strong acids or strong bases. When an ester is hydrolyzed in the presence of a strong acid the product is the corresponding carboxylic acid and alcohol.

General Reaction:

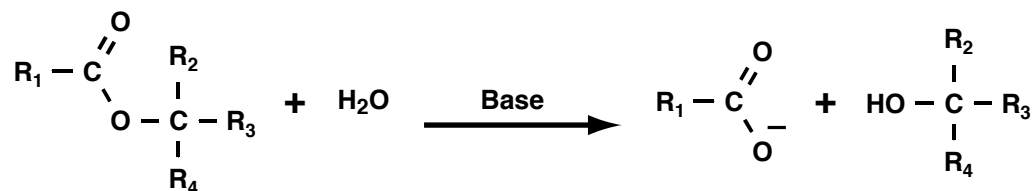


Specific Example:

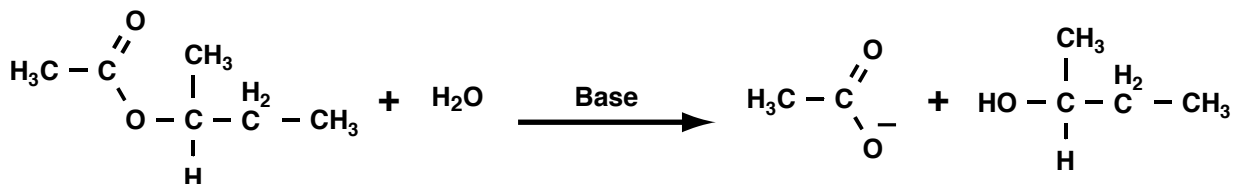


When an ester is hydrolyzed in the presence of a strong base the product is the corresponding salt of the carboxylate anion and an alcohol. During base catalyzed hydrolysis of an ester, as fast as the carboxylic acid forms it is neutralized by the base present in the reaction mixture to form the salt; acid + base → salt. The base catalyzed hydrolysis of an ester is called Saponification (Soap Forming). Salts of long chain (> 8 C) carboxylic acids (carboxylate anions) are soaps.

General Reaction:



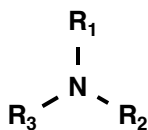
Specific Example:



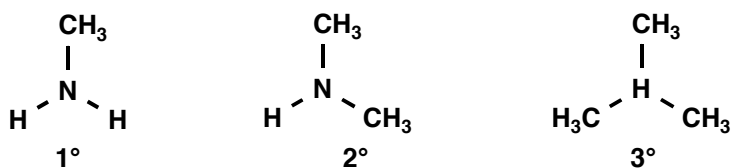
The Nitrogen Containing Organic Compounds

The Amines

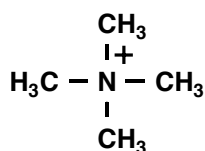
Amines can be considered as organic derivatives of ammonia. They all have the following general structure:



Specific Examples:



Amines are classified as primary, secondary, or tertiary according to how many organic substituents are bonded to the nitrogen atom. A primary amine has one organic group bonded to the nitrogen, a secondary amine has two organic groups, and a tertiary has three. When a fourth organic group bonds to the nitrogen through the unshared pair of electrons on the nitrogen, the compound is a Quaternary Ammonium Ion, which has a positive charge and forms ionic compounds with anions.

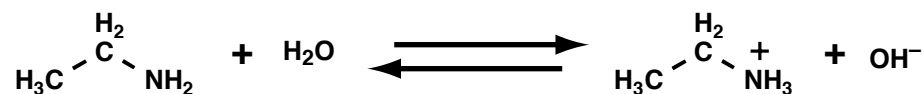


Amines are polar molecules because nitrogen is much more electronegative than carbon or hydrogen.

In an amine, the nitrogen has a partial negative charge (δ^-); the carbon and/or hydrogen have a partial positive charge (δ^+). Since they are polar molecules they are water soluble. Nitrogen is less electronegative than oxygen therefore amines are less polar than the oxygen containing organic molecules.

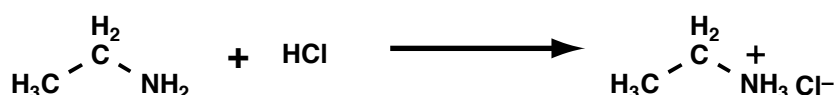
Amines are weak bases, they will accept a proton (H^+) from water or acids when dissolved in water.

Specific Example:



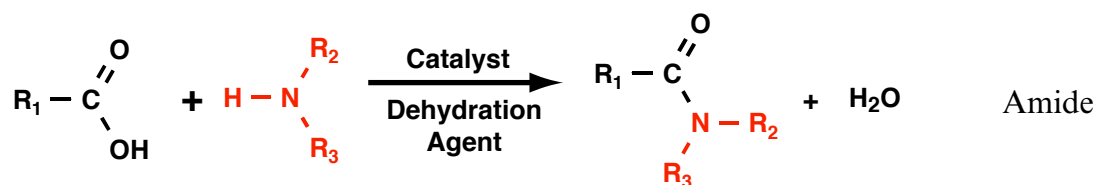
When an amine accepts a proton from water the product is an Ammonium Cation. The pK_a 's of amines range from 7 to 12.

Since amines are weak bases, they undergo neutralization reactions with acids to form Alkyl Ammonium Salts. These salts are true ionic compounds and therefore are very polar and very water soluble.

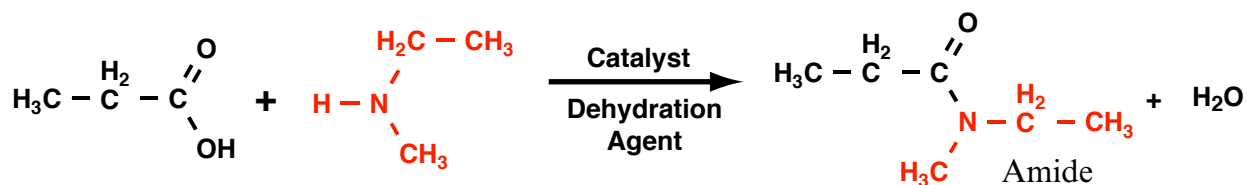


Primary and secondary amines undergo Dehydration Reactions with carboxylic acids. This reaction is identical to the reaction of ammonia with carboxylic acids. The product of the reaction is an Amide.

General Reaction:

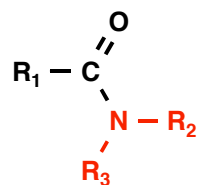


Specific Example:



The Amides

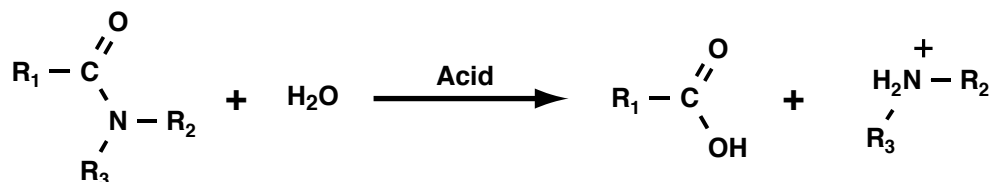
Amides are formed by the dehydration reaction between carboxylic acids and amines. The amide functional group is as follows:



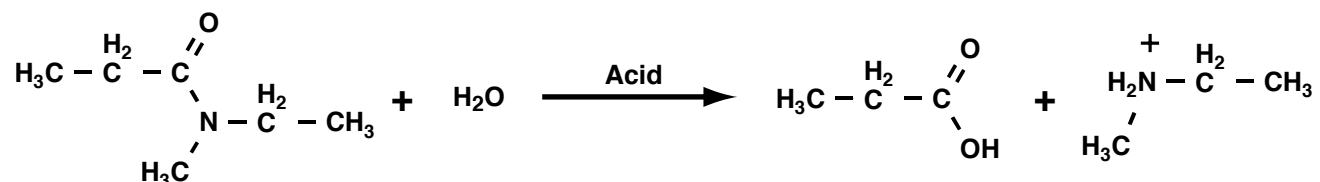
Amides are polar compounds since nitrogen and oxygen are more electronegative than carbon and hydrogen. Amides are very water soluble.

Amides undergo Hydrolysis Reactions. The hydrolysis reaction can be catalyzed by strong acids or strong bases. When the hydrolysis reaction is catalyzed by a strong acid the product is the corresponding carboxylic acid and alkyl ammonium salt. During the reaction water is added across the amide bond to break the bond. As fast as the amine forms it is neutralized by the acid present in the reaction mixture to form the salt. The anion of the salt is the anion of the acid used for hydrolysis.

General Reaction:

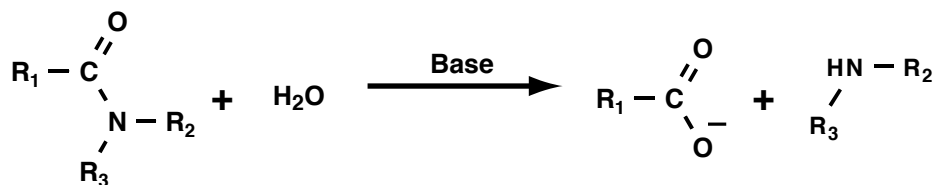


Specific Example:



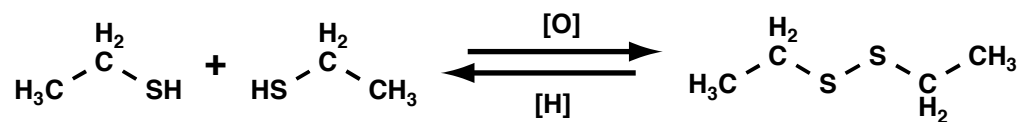
When the hydrolysis reaction is catalyzed by a strong base the product is the corresponding carboxylate salt and the amine. During the reaction water is added across the amide bond to break the bond. As fast as the carboxylic acid forms it is neutralized by the base present in the reaction mixture to form the salt. The cation of the salt is the cation of the base used for the reaction.

General Reaction:



Specific Example:

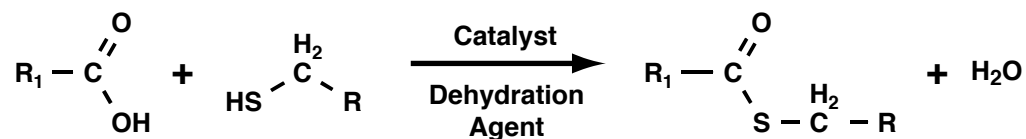
Specific Example:



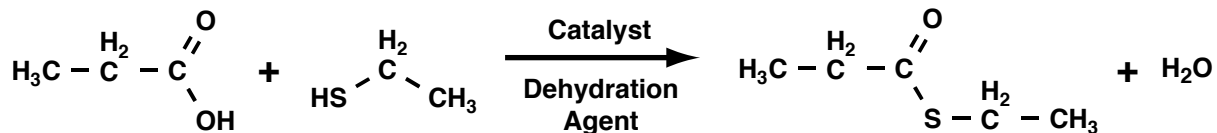
Thioester Formation

Thiols react with carboxylic acids to form Thioesters via a dehydration reaction.

General Reaction:



Specific Example:

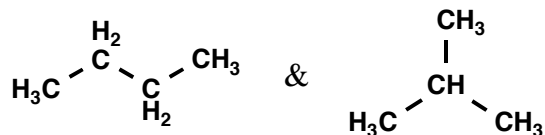


Thioesters are high energy compounds. When these compounds are hydrolyzed, when water is added back across the thioester bond, the corresponding carboxylic acid and thiol are formed and a large amount of energy (heat) is liberated.

Stereoisomerism and Molecular Symmetry

Symmetry is defined as a correspondence in size, shape, and relative position of parts that are on opposite sides of a dividing line or plane.

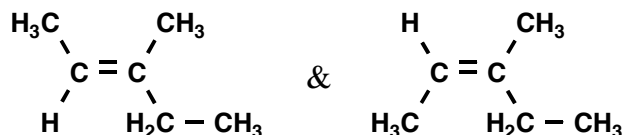
Several types of isomers are encountered in organic chemistry. The first type is the constitutional or structural isomer. Constitutional isomers have identical empirical formulas but different structures. The atoms making up the molecule are arranged as different side chains or into different functional groups. For example:



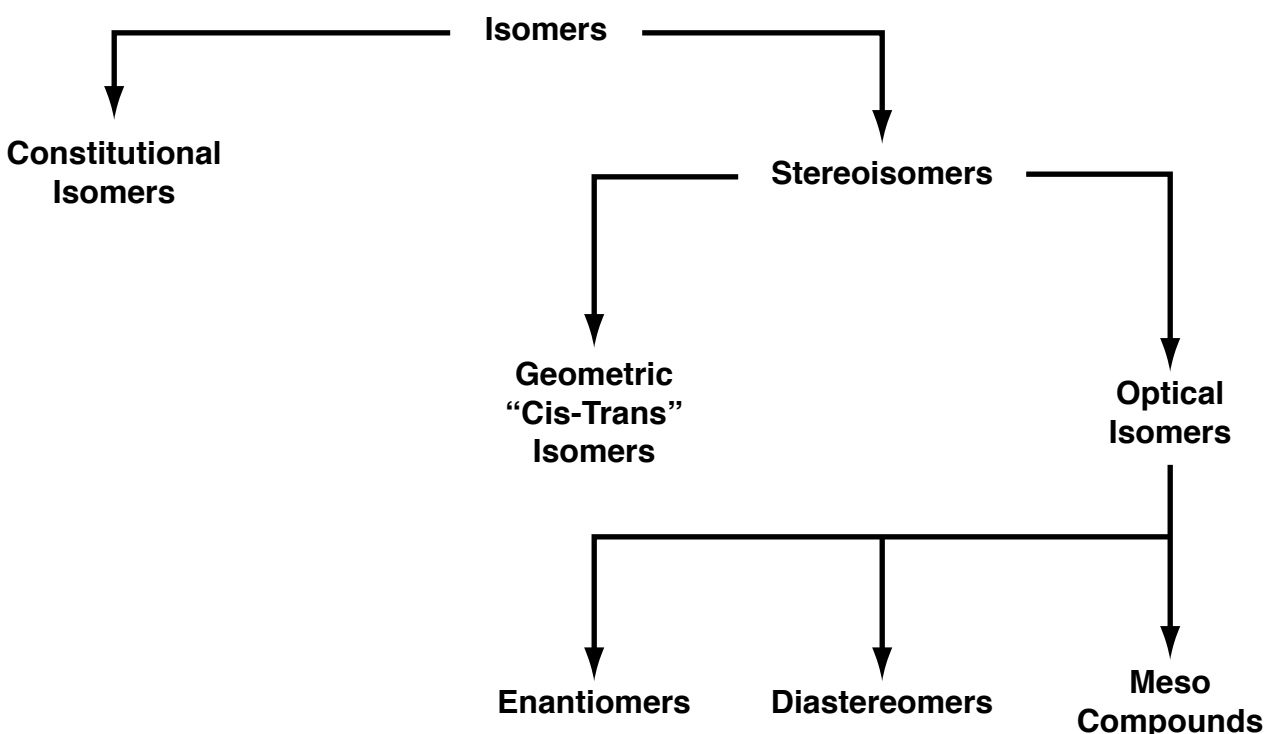
are constitutional isomers, as are:



The second major type of isomer are the stereoisomers. These molecules have the same empirical formula and the same functional groups but the groups are arranged differently in space. One subset of the stereoisomers are the geometric or “cis-trans” isomers. In the geometric isomers the different groups are arranged differently around a carbon-carbon double bond. An example of a “cis-trans” isomer pair is:

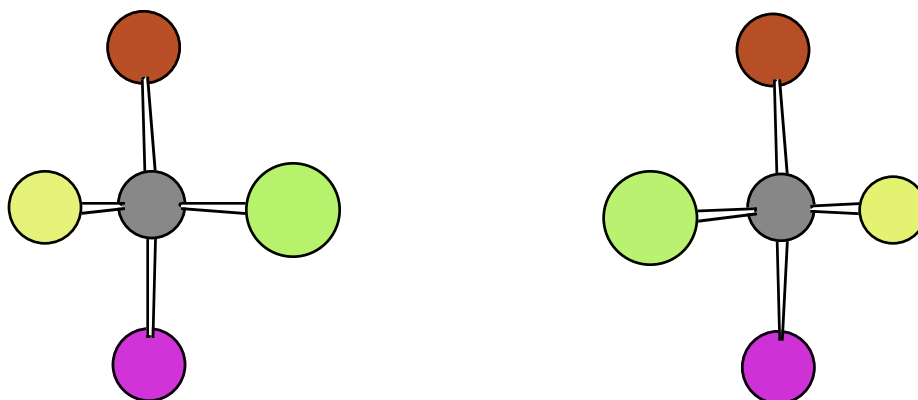


The second subset of the stereoisomers are the optical isomers. This subset of the stereoisomers shares a common physical property, they all rotate plane polarized light. Hence the name - optical isomers. There are several different groups in the optical isomer subset. The largest subset of the optical isomers is the Enantiomers. Optical isomers also include the Diastereomers and Meso compounds.



Before enantiomers are discussed at a chemical level an easily visualized example will be explored. Look at your right hand. It has a central region, the palm, and attached to this central region are 5 different groups, the five fingers. Your right hand is asymmetric, since the groups (fingers) on opposite sides of a line dividing your hand in half are different. Now look at your left hand. It also has a central region with five different groups attached. The five fingers on your right hand are for the most part identical to the five fingers on your left hand. However, the fingers are arranged such that your two hands are different. If you were to hold your right hand up to mirror the reflection would look exactly like your left hand. Similarly, the mirror image of your left hand looks like your right hand. Your two hands are mirror images of each other. Furthermore, your two hands are non-superimposable. You cannot lay one hand on top of the other and have your fingers line up with each other. Your hands are asymmetric, non-superimposable, mirror images of each other.

Now look at these two molecules (models).



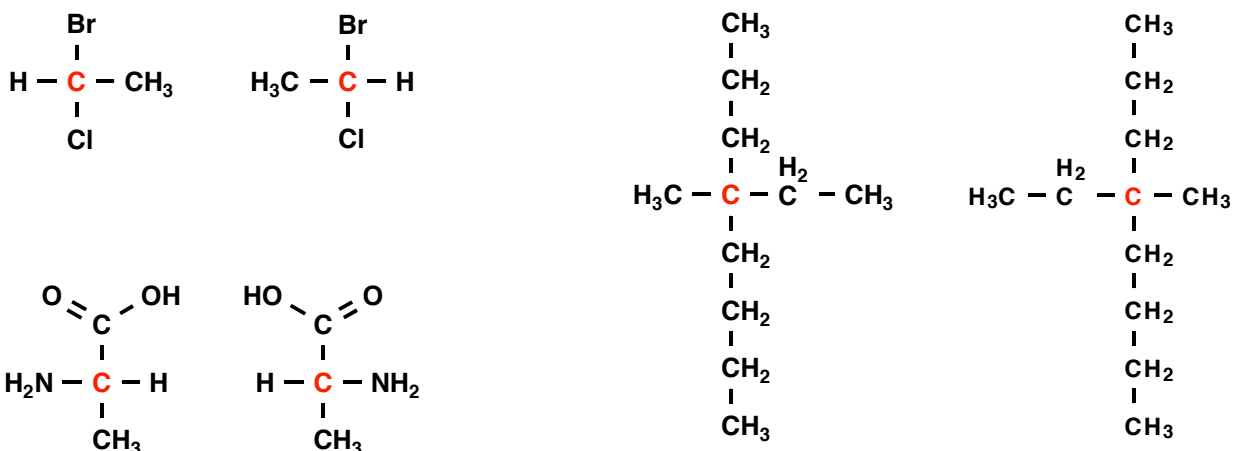
The first molecule has a central carbon atom with four different groups attached to it. The second molecule also has a central carbon atom with the same four groups attached, but the four groups are attached to the central atom in a different arrangement. The configuration of groups around the central atom is different. These molecules are Stereoisomers. They have the same empirical formula and the same functional groups, but the groups are arranged in space differently. The groups are arranged such that the resulting molecules are non-superimposable mirror images of each other. In addition, these molecules are asymmetric since the groups on either side of any line that divides the molecules in half are different. A pair of stereoisomers that are asymmetric, non-superimposable mirror images of each other are Enantiomers. These two molecules are enantiomers of each other or an Enantiomer Pair. Since enantiomers are non-superimposable mirror images they always exist in pairs.

The central carbon atom, the atom to which the four different groups are attached, is called a Chiral Carbon Atom, or an Asymmetric Carbon Atom, or a Tetrahedral Stereocenter. Molecules that contain a chiral carbon atom are called Chiral Molecules, Asymmetric Molecules, or Optical Isomers.

Two terms need to be defined.

1. Configuration The configuration of a molecule is the absolute arrangement of atoms, groups of atoms, or functional groups around a central atom. A molecule has one and only one configuration. The configuration of a molecule can be changed only by breaking chemical bonds, moving atoms, groups of atoms, or functional groups around the central atom, and reforming chemical bonds. **When the mirror image of a molecule with one chiral carbon atom is drawn, the configuration of atoms around the chiral carbon is changed, the opposite configuration is depicted.**
2. Conformation. The conformation of a molecule is the stable arrangement of atoms brought about by rotation around single bonds. A molecule can have millions different stable conformations, each different from the other by a small amount of rotation around a single chemical bond.

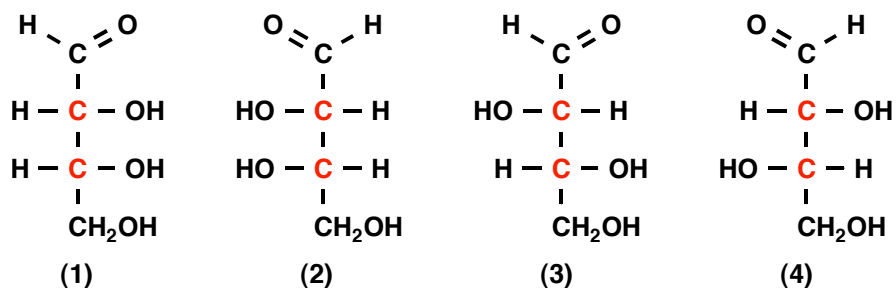
Given below are several examples of chiral molecules:



All of these molecules are chiral molecules. They contain a chiral carbon atom (shown in red). Each of these molecules exists as a pair of non-superimposable mirror images, as a pair of enantiomers.

The molecules depicted above are drawn as Fischer Projections. When a molecule is drawn in this way, by convention, the two vertical bonds attached to the chiral carbon are thought of as projecting behind the plane of the paper and the two horizontal bonds are thought of as projecting in front of the plane of the paper. Remember, a carbon atom with four attached groups has a tetrahedral shape and a Fischer Projection reflects the tetrahedral shape with two bonds behind the paper and two bonds in front.

The molecule (1) depicted below is a chiral molecule, but it is different from those depicted above in that it contains two chiral carbon atoms (in red).



Since it is a chiral molecule, a non-superimposable, mirror image of it exists. This isomer, this enantiomer, is depicted above (2). By definition chiral carbon atoms have two unique configurations and these two different configurations are depicted in the mirror images, as a pair of enantiomers (see the definition of configuration above). If a molecule has more than one chiral carbon, a new stereoisomer can be created by changing the configuration around only one of the chiral carbon atoms. When the configuration around carbon 2 of molecule (1) is changed, stereoisomer (3) is formed. Since (3) is a chiral molecule, a non-superimposable, mirror image of it exists. This enantiomer, is depicted above (4).

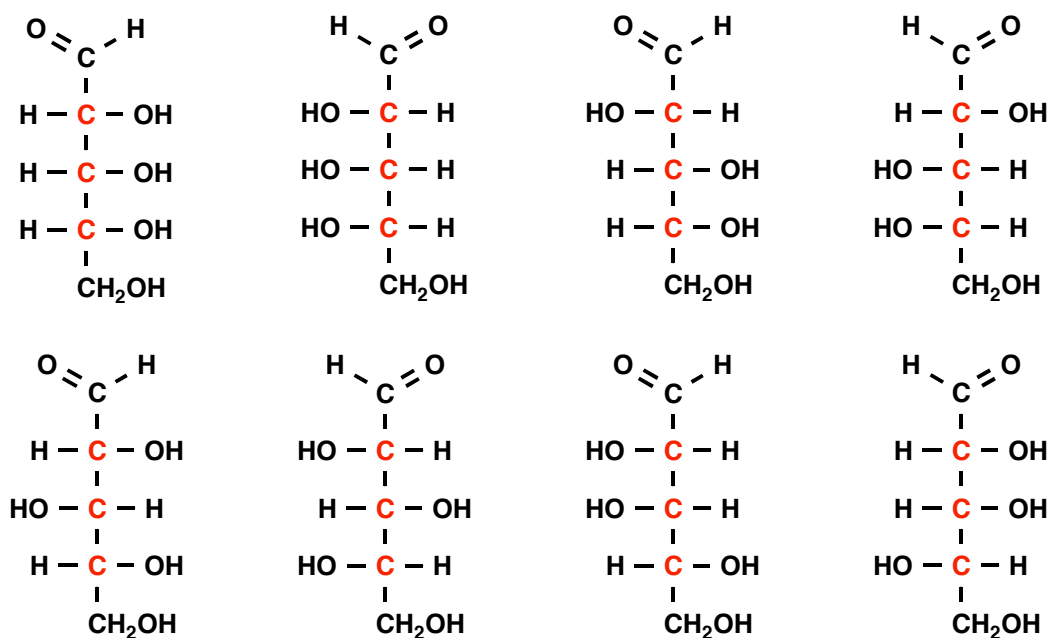
The above example demonstrates that when more than one chiral carbon is present in a molecule more than one pair of enantiomers, more than two stereoisomers, can exist. Jacobus van't Hoff studied stereoisomers and postulated the existence of numerous stereoisomers for molecules with more than one chiral carbon. **van't Hoff's rule** allows one to calculate the maximum number of possible

stereoisomers. The maximum number of possible stereoisomers is 2^n , where n is the number of chiral carbon atoms. A molecule with 2 chiral carbons can exist as 2^2 or 4 stereoisomers. The maximum number of enantiomer pairs is given by $2^2/2$.

Compare molecule (1) depicted above with (3). They are clearly not identical molecules, the configuration of groups around carbon 2 is different. They are isomers of each other since they have the same empirical formula $C_4H_8O_4$. They contain more than one chiral carbon atom, but they are not mirror images of each other, they are not enantiomers. These two molecules belong to the group of optical isomers called Diastereomers. For two molecules to be diastereomers they must meet four criteria:

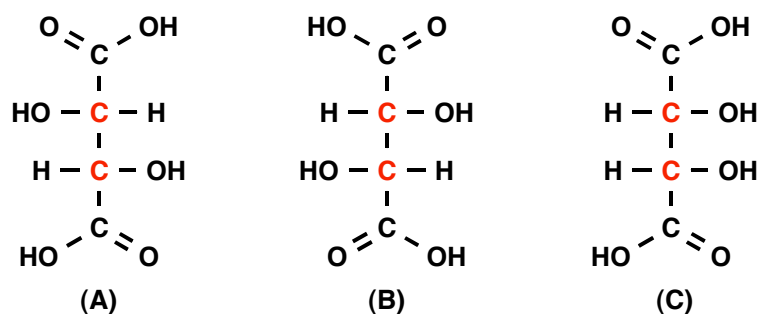
1. They must be isomers.
2. They must contain more than one chiral carbon atom.
3. The configuration around one or more of the chiral carbons in the molecules must be different.
4. They are not enantiomers.

A molecule with three chiral carbon atoms can exist as 2^3 or 8 possible stereoisomers. There are four pairs of enantiomers. A molecule with 3 chiral carbons with all its stereoisomers is depicted below.



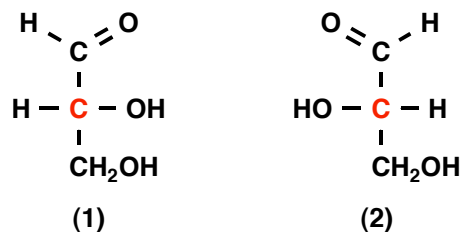
The molecules that are not enantiomers of each other are related to each other as diastereomers.

The molecules depicted below; (A), (B), & (C); each contains two chiral carbon atoms, carbons two and three. From van't Hoff's rule one would expect a total four stereoisomers. Molecule (B) is the mirror image, the enantiomer, of molecule (A). The third molecule (C) is a stereoisomer of the other two, but its mirror image is superimposable. If the mirror image of (C) is drawn and rotated 180° within the plane of the paper, what results is a molecule that can be superimposed upon (C). The mirror image can be superimposed upon (C) because this isomer contains an internal plane of symmetry. This plane of symmetry passes midway between carbon 2 and carbon 3. When this plane is drawn, you can easily see that the top half of the molecule is identical to the bottom half.



Stereoisomers that contain more than one chiral carbon atom and an internal plane of symmetry are called Meso compounds. Isomer (C) is a meso compound (isomer) of (A) and (B). Using van't Hoff's rule the maximum number of stereoisomers can be calculated. However, there are molecules, like those depicted above, that have fewer than the maximum number of stereoisomers. The various stereoisomers have to be drawn out to determine if one of the possible forms has an internal plane of symmetry, if one of the isomers is a meso compound and therefore does not have a mirror image.

Lets look at a pair of simple enantiomers.



The IUPAC name of these molecules are 2,3-dihydroxypropanal. In biochemistry they are called [glyceraldehyde](#). If enantiomers exist in pairs, there must be a way of designating the two different isomers, the two different enantiomers, the two different configurations from each other. How are the two enantiomeric forms designated? The ultimate method is X-ray crystallography. This experimental technique can determine the precise atomic configuration of any molecule that can be crystallized. However, this technique is not usually needed, a simpler method exists. First, draw the structures of the two enantiomers so that the most oxidized functional group is at the top of the Fischer projections. Second, travel around the chiral carbon from the most oxidized group to the least oxidized group (H). If the direction traveled from most oxidized to least oxidized is Clockwise, or to the Right, the molecule is designated as the D form. D stands for Dextro (Right). If the direction traveled was Counterclockwise, or to the Left, the molecule is designated L for Levo (Left). Molecule (1) is [D-glyceraldehyde](#), molecule (2) is [L-glyceraldehyde](#).

[Note to students currently taking or have taken an in-depth Organic Chemistry course (e.g., Chem 023 & Chem 024): The D and L terminology is the old method (1906) of designating the stereochemical configuration of chiral carbon atoms and/or chiral molecules. It is still used extensively in biochemistry. The current system in organic chemistry for designating the configuration of chiral carbon atoms is the R, S system (R = Rectus {Right}; S = Sinister {Left}). With a few exceptions the old D designation corresponds to the current R and the old L corresponds to the current S.]

Do a pair of enantiomers have different chemical or physical properties?

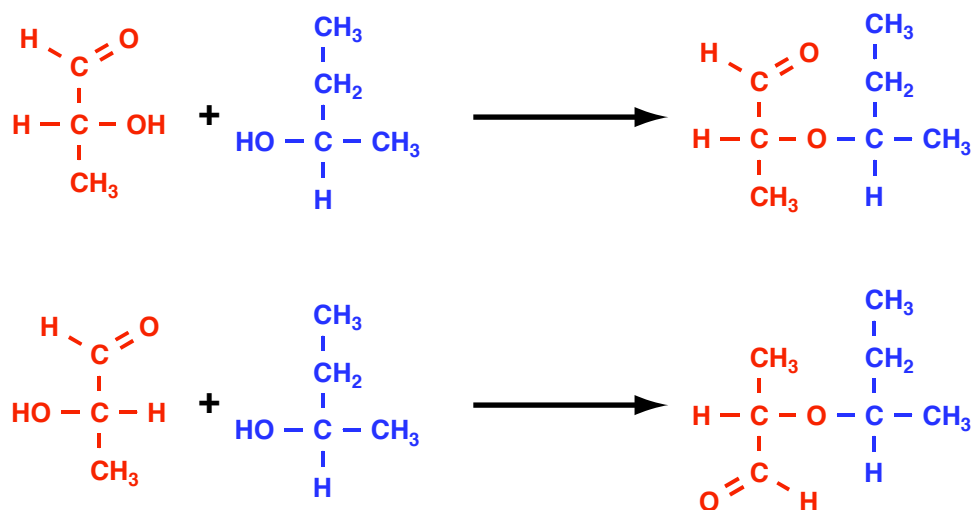
If a pair of enantiomers have different physical and chemical properties what are they?

With one exception the molecules that comprise a pair of enantiomers have identical physical properties. They have the identical melting points, boiling points, density, color, etc. They do vary in one physical property; how they Rotate Plane Polarized Light.

Light, when it leaves its source, radiates in all possible planes. A plane polarizer is a piece of plastic or glass that has specific organic molecules, imbedded in it or coated on top, that prevents the passage of light in all planes except one. Light emerging from a plane polarizer is Plane Polarized Light. When plane polarized light passes through a glass tube containing one enantiomer of a pair, the plane of the light is rotated by a fixed constant amount, a fixed number of degrees to the left or right. The other enantiomer of the pair rotates plane polarized light the exact same amount, the same number of degrees, but in the opposite direction. For example if one enantiomer rotates plane polarized light 27° to the left, the other enantiomer will rotate the plane polarized light 27° to the right. The molecules are called Optical Isomers because they rotate plane polarized light in opposite directions.

Don't confuse the D or L designation with the direction that a pure enantiomer rotates plane polarized light. D or L designate the absolute configuration of groups around the asymmetric carbon atom. D enantiomers can rotate light to the right or to the left and L enantiomers can rotate light to the left or to the right. For example D-glucose will rotate a beam of plane polarized light to the right and, as expected, L-glucose rotates the beam of plane polarized light the same number of degrees to the left. Conversely, D-fructose will rotate plane polarized light to the left and L-fructose will rotate the light the same number of degrees to the right.

The chemical properties of a pair of enantiomers are, under most circumstances, identical. However, there is one difference. Chiral compounds react with other chiral compounds at different rates. When a pair of enantiomers react with an achiral molecule, a molecule that does not contain a chiral carbon, the reactions occur at identical rates. However, when a pair of enantiomers reacts with a chiral molecule, the reaction occurs at different rates. The reactions depicted below will occur at unique and different rates. Reaction (1) occurs at a rate of X moles of product formed per minute. Reaction (2) will occur at a rate that is different from the rate of reaction (1). The rate of reaction (2) can be faster or slower than the rate of reaction (1), but it will never be equal. The difference in rates can not be predicted, but a pair of enantiomers will always react with a chiral molecule at two different rates.



We are chiral beings, the demonstration with left and right hands illustrates this point. The fact that we are chiral beings composed of chiral molecules (as we will see shortly) and the fact that chiral molecules react with other chiral molecules at different rates explains why in nature only one of two enantiomers are utilized by living creatures. One stereoisomer of a pair of enantiomers will have biological activity, the other enantiomer will be useless or toxic.