

Chapter 9 Lecture Notes: Carboxylic Acids, Amines, and Amides

Educational Goals

1. Given the structure of a **carboxylic acid**, **carboxylate ion**, **ester**, **amide**, or **amine molecule**, be able to give the systematic names and vice versa.
2. Know and understand the intermolecular forces that attract carboxylic acid, amine, or amide molecules to one another, and how these forces affect boiling points and melting points.
3. Identify **amines** as primary (1°), secondary (2°), or tertiary (3°). Compare and contrast **amines** and **quaternary ammonium ions**.
4. Predict the products for the reactions of carboxylic acids with water, alcohols, amines, ammonia, or with strong bases.
5. Predict the products for the reactions of amines with water or with strong acids.
6. Predict the products for the acid-catalyzed **hydrolysis of an amide**.
7. Identify **chiral carbon** atoms in structural formulas. Given the number of chiral carbons in a molecule, determine the number of **stereoisomers**.
8. Define the term **enantiomer**. Compare and contrast **enantiomers** and **diastereomers**.

Organic compounds are categorized into various _____ by the presence of distinct **functional groups**.

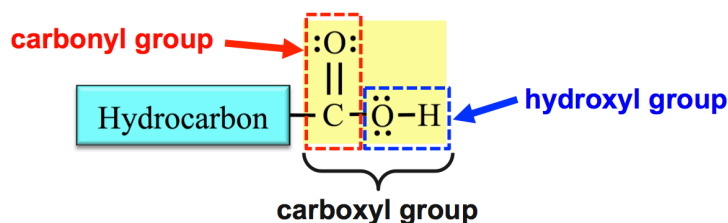
A **functional group** is an _____, _____ *of atoms*, or _____ that gives a compound a particular set of physical and chemical properties.

Carboxylic Acids

The Structure of Carboxylic Acids

Carboxylic acids contain a _____ **functional group** attached to a hydrocarbon (alkyl group) part.

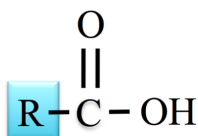
Carboxyl groups contain both a _____ **group**, which is a carbon double bonded to an oxygen ($C=O$), and a _____ **group** ($-OH$) that are connected to each other and the hydrocarbon part as shown below.



The **carboxyl group** is sometimes drawn as “COOH” or “CO₂H” in condensed structures:



Chemists use the letter “**R**” in the general structures to represent either a hydrocarbon/alkyl group part *or* any other organic group of atoms.

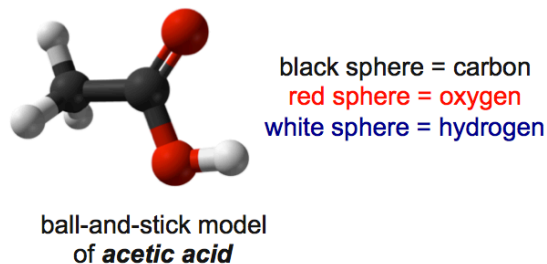
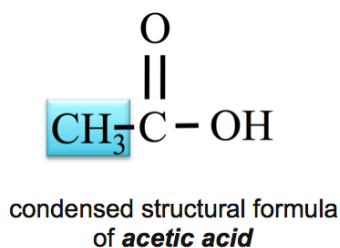


general form of a carboxylic acid molecule

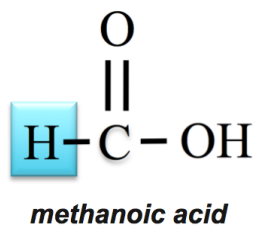
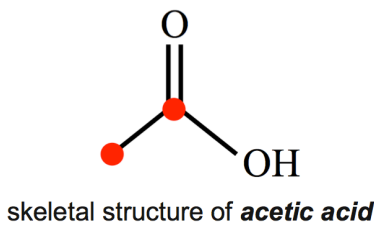
A specific example of a carboxylic acid is **acetic acid**.

- White vinegar is a mixture composed of 95% water and 5% acetic acid.

The hydrocarbon part (**R**) in acetic acid is a methyl group (**CH₃**).



The skeletal structure of **acetic acid** is shown below. I have added dots to indicate the carbon atom positions.



Although **methanoic acid**, contains a hydrogen (**H**) bonded to the carbonyl group instead of an alkyl group (**R**) it is still classified as carboxylic acid.

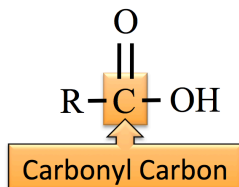
Methanoic acid is the molecule that is responsible for the stinging sensation caused by some ant bites.

Naming Carboxylic Acids

We will use the IUPAC system for naming carboxylic acid molecules. The systematic naming of carboxylic acids is based on the hydrocarbon naming method.

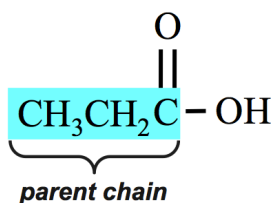
Step 1: Find and name the **parent chain**.

The parent chain of a carboxylic acid is the longest continuous chain of carbon atoms that _____ the **carbonyl carbon**. The **carbonyl carbon** is the carbon in the carbonyl group (**C=O**).



Count the number of carbon atoms in the parent chain (*include the carbonyl carbon*). Starting with the alkane name that corresponds to the number of carbon atoms in the parent chain, replace the “e” at the end of the alkane name with “**oic acid**.”

Example: the parent chain of a carboxylic acid that contains *three* carbons is called **propanoic acid**.



propane \longrightarrow propanoic acid

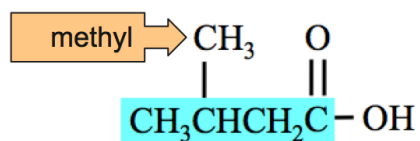
If there are *no substituents on the parent chain*, the naming is complete. In this case the name of the molecule (above) would be **propanoic acid**.

If there are substituents on the parent chain, you will need to continue with the steps that follow.

Step 2: Name any alkyl group **substituents**.

Alkyl groups are named in the same way as we did for hydrocarbons.

Example:

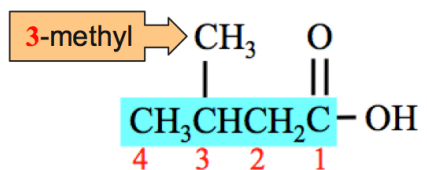


Step 3: Determine the *point of attachment* of alkyl group(s) to the parent chain.

In order to assign "position numbers" to the substituents, the carbons *in the parent chain* are numbered.

_____ *numbering at the* _____ *carbon.*

Example: the carbons in the parent chain of the molecule shown below are assigned position numbers:

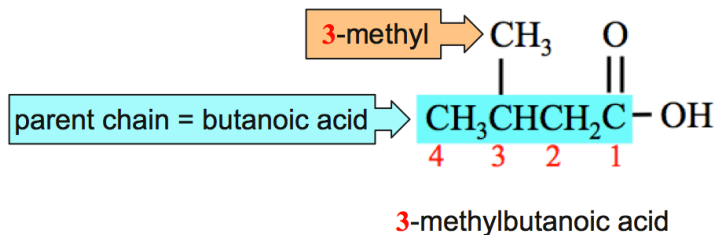


Step 4: Construct the name of the carboxylic acid by placing the alkyl groups in alphabetical order and specifying their position numbers, followed by the name of the parent chain.

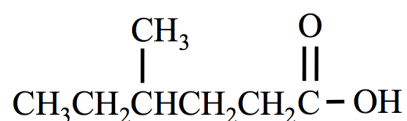
Use a *dash* between position *numbers* and *letters*.

Add the labels di, tri, or tetra in front of the alkyl group name **if** two, three, or four (respectively) *identical* substituents are present.

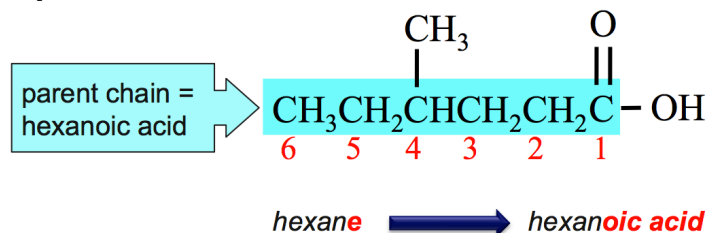
Example:



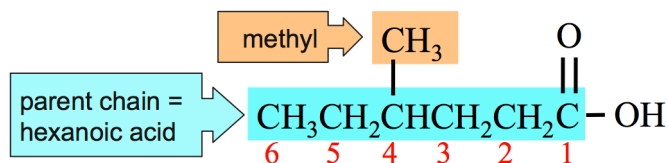
Naming Carboxylic Acids Example: Name the molecule that is shown below.



Step 1: Find and name the **parent chain**.

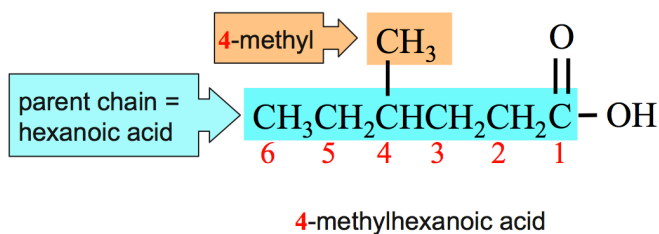


Step 2: Name any alkyl group substituents.

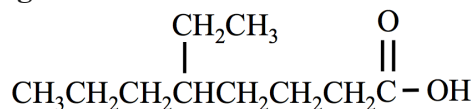


Step 3: Determine the *point of attachment* of alkyl group(s) to the parent chain.

Step 4: Construct the name of the carboxylic acid by placing the alkyl groups in alphabetical order and specifying their position numbers, followed by the name of the parent chain.

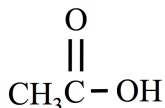


Understanding Check: Name the molecule that is shown below.



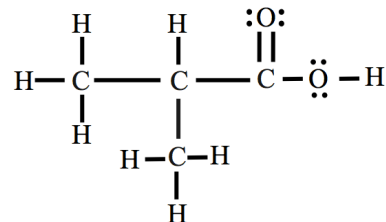
Understanding Check

The *common name* of the molecule shown below is acetic acid. What is the IUPAC systematic name for acetic acid?

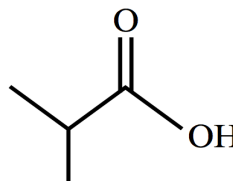
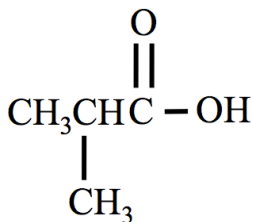


Let's do a problem in which we are given the name of a carboxylic acid and wish to draw its structural formula.

Example: Draw the *line bond structure* of 2-methylpropanoic acid.



For comparison, the *condensed and skeletal structure* of 2-methylpropanoic acid are shown below.



Understanding Check

Draw the line bond, condensed, and skeletal structural formulas of *decanoic acid*.

Hydroxyl, Fluorine, Chlorine, and Bromine Substituents

So far, you have only seen alkyl group substituents. It is not uncommon to see carboxylic acids that contain other *atoms* or *groups of atoms* that are named as substituents.

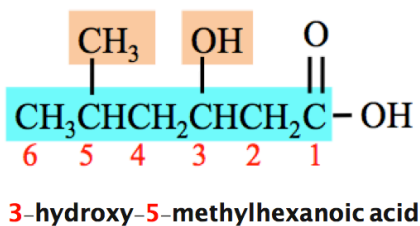
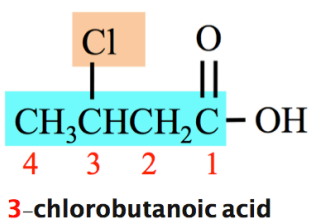
A hydroxyl group (-OH), fluorine atom, chlorine atom, or bromine atom that is bonded to *the parent chain* of a carboxylic acid is named as a substituent.

The table below list the names used for these substituents.

Names of Non Alkyl Substituents	
Substituent	Name
OH	hydroxy
F	fluoro
Cl	chloro
Br	bromo

Use position numbers and alphabetize these substituents, along with any alkyl group substituents, when naming carboxylic acids.

Examples:



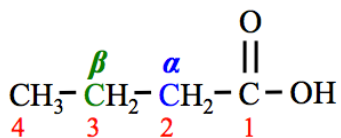
Alpha (α) and Beta (β) Carbons

Two of the carbon positions in the parent chain of carboxylic acids are designated as “ α ” or “ β .”

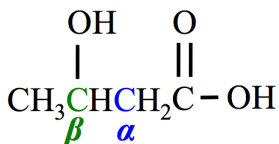
- The α and β designations are not part of the IUPAC naming system, however they are commonly used.

The carbons that are designated as carbon number **2** and **3** in the IUPAC system are often referred to as the α carbon and β carbon, respectively.

Example: The α carbon and β carbon are labeled in the structure of *butanoic acid* shown below.



Example: The IUPAC systematic name of the molecule shown below is **3-hydroxybutanoic acid**. It is named β -hydroxybutanoic acid when using the α/β designation.



Understanding Check

Lactic acid is another name for α -hydroxypropanoic acid.

- Draw the condensed structure of **lactic acid**.

- What is the IUPAC systematic name for lactic acid?

Water Solubility of Carboxylic Acids

The water solubility of an organic compound depends on the compound's ability to interact with water. All carboxylic acid molecules have a significantly strong attraction to water through hydrogen bonding and dipole-dipole interactions.

Small carboxylic acid molecules have significant water solubility.

As the _____ region (hydrocarbon part) of carboxylic acids gets larger, their water solubility _____; this is true not only for carboxylic acids, but for all organic molecules.

Water Solubility of Carboxylic Acids

Molecule Name	Condensed Structure	Water Solubility (g/100 mL)
methanoic acid	HCOOH	miscible*
ethanoic acid	CH ₃ COOH	miscible
propanoic acid	CH ₃ CH ₂ COOH	miscible
butanoic acid	CH ₃ CH ₂ CH ₂ COOH	miscible
pentanoic acid	CH ₃ CH ₂ CH ₂ CH ₂ COOH	3.7
hexanoic acid	CH ₃ CH ₂ CH ₂ CH ₂ CH ₂ COOH	1.0

*miscible indicates that the substance will mix/dissolve at any carboxylic acid to water ratio.

Names, Structural Formulas, and Natural Sources of Various Carboxylic Acids

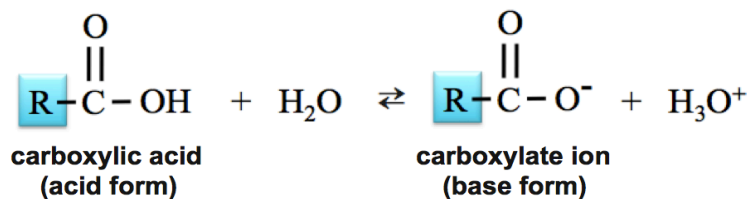
Number of Carbons	IUPAC Name	Common Name	Condensed Structure	Source(s)
1	methanoic acid	formic acid	HCOOH	insect stings
2	ethanoic acid	acetic acid	CH ₃ COOH	bacterial fermentation
3	propanoic acid	propionic acid	CH ₃ CH ₂ COOH	bacterial production
4	butanoic acid	butyric acid	CH ₃ (CH ₂) ₂ COOH	butter
5	pentanoic acid	valeric acid	CH ₃ (CH ₂) ₃ COOH	valerian (an herb)
6	hexanoic acid	caproic acid	CH ₃ (CH ₂) ₄ COOH	goat fat
7	heptanoic acid	enanthic acid	CH ₃ (CH ₂) ₅ COOH	rancid oils
8	octanoic acid	caprylic acid	CH ₃ (CH ₂) ₆ COOH	coconuts and breast milk
9	nonanoic acid	pelargonic acid	CH ₃ (CH ₂) ₇ COOH	pelargonium (a genus of flowering plants)
10	decanoic acid	capric acid	CH ₃ (CH ₂) ₈ COOH	coconuts and palm kernel oil
12	dodecanoic acid	lauric acid	CH ₃ (CH ₂) ₁₀ COOH	coconut oil
16	hexadecanoic acid	palmitic acid	CH ₃ (CH ₂) ₁₄ COOH	palm oil
18	octadecanoic acid	stearic acid	CH ₃ (CH ₂) ₁₆ COOH	chocolate
20	icosanoic acid	arachidic acid	CH ₃ (CH ₂) ₁₈ COOH	peanut oil

Chemical Reactions of Carboxylic Acids

1) Reaction of Carboxylic Acids with Water

Carboxylic acids have the word “_____” in their names because they readily donate an H⁺ in acid-base reactions.

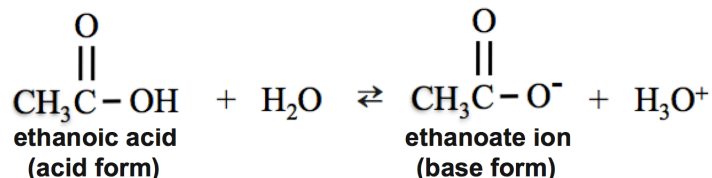
When placed in water, a carboxylic acid molecule acts as an acid and water acts as a base. An H⁺ from the hydroxyl group (OH) of the carboxylic acid is donated to H₂O.



The **base form** of a carboxylic acid is called a _____.

- A carboxylate ion has a charge of (1-) because of the _____ **charge** on the single-bonded oxygen. Recall that an oxygen atom with just one single bond has a (1-) formal charge.

A specific example of the reaction of a carboxylic acid and water is the reaction ethanoic acid and water.



The **base form** of ethanoic acid is named **ethanoate ion**.

Carboxylate ions are named by replacing the “-____” suffix of their *acid form* name with “-____.”

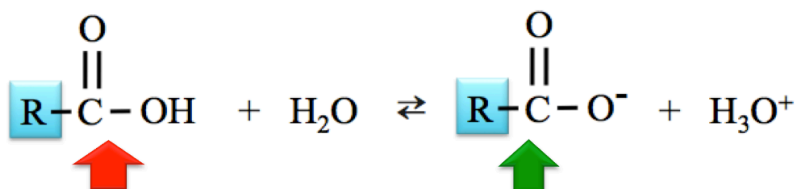
Examples:

ethanoic acid → ethanoate ion

acetic acid → acetate ion

3-methylpentanoic acid → 3-methylpentanoate ion

When a carboxylic acid is placed in water, a reaction occurs between the acid and the water, and an equilibrium is established.



There is some of the *acid form* present and some of the *base form* present at equilibrium.

Carboxylic acids are considered to be “*weak acids*” because their K_a values are much less than 1.

Acid Name	Acid Formula	K_a	$\text{p}K_a$ $\text{p}K_a = -\log(K_a)$
Acetic acid	CH_3COOH	$1.8 \times 10^{-5} \text{ M}$	4.74
2-hydroxypropanoic acid (lactic acid)	$\text{CH}_3\text{CH}_2(\text{OH})\text{COOH}$	$1.4 \times 10^{-4} \text{ M}$	3.86
propanoic acid	$\text{CH}_3\text{CH}_2\text{COOH}$	$1.3 \times 10^{-5} \text{ M}$	4.88

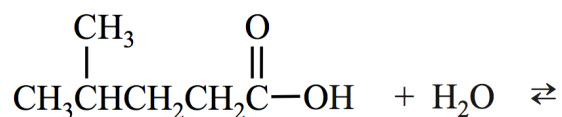
When carboxylic acid/carboxylate ion conjugate pairs are in a solution, even if the solution contains other dissolved species, the relative amounts of the *acid form* and *base form* can be predicted by the Henderson-Hasselbalch Equation.

- The implications of the Henderson-Hasselbalch Equation are shown in the table below.

Solution Condition	Relative Amounts of Acid and Base Forms
$\text{pH} < \text{p}K_a$	$[\text{HA}] > [\text{A}^-]$
$\text{pH} > \text{p}K_a$	$[\text{A}^-] > [\text{HA}]$
$\text{pH} = \text{p}K_a$	$[\text{HA}] = [\text{A}^-]$

Understanding Check

Add the products for the following reaction:



Understanding Check

Draw the **condensed structure of the base form** (carboxylate ion) for each of the following carboxylic acids **and** write the name of each carboxylate ion.

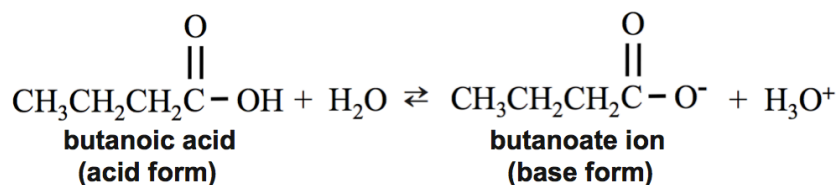
a. octanoic acid

b. 3-methylbutanoic acid

c. 5-methylhexanoic acid

Understanding Check

When a carboxylic acid is placed in water, it reacts with water and an equilibrium is established. For example, butanoic acid reacts with water as shown here:

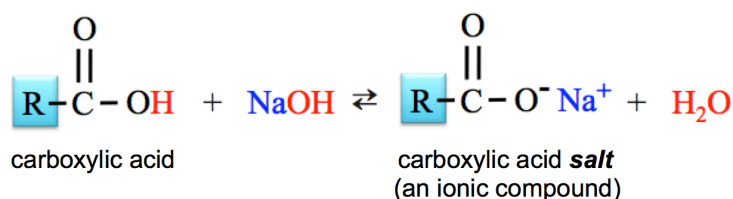


In many biochemical applications, it is of interest to understand whether the **acid form** or the **base form** of a species is predominant. We use the implications of the Henderson-Hasselbalch Equation to predict the predominant species at any particular pH.

The pK_a of butanoic acid is about 4.8. Is the **acid form** or **base form** of butanoic acid predominant at physiological pH (~7.4)?

2) Neutralization: Reaction of a Carboxylic Acid and a Hydroxide Ion

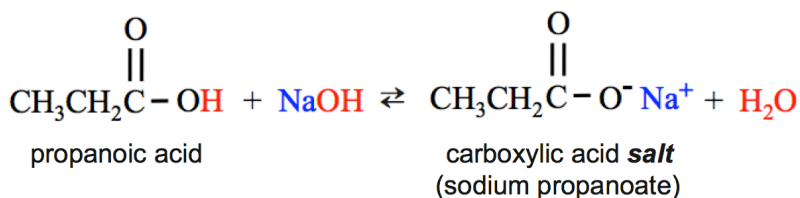
In a **neutralization reaction**, a carboxylic acid will react with a **hydroxide-containing base** compound to produce **H₂O** and a **carboxylic acid salt**.



This is the same neutralization reaction that you learned in a previous chapter; the **H⁺** from the acid bonds to the **OH⁻** to produce **H₂O**.

The _____ **ion** and the _____ **from the base** make an **ionic compound** called a **carboxylic acid** _____.

A specific example of the **neutralization** of a carboxylic acid is the reaction of propanoic acid and sodium hydroxide:



Water Solubility of Carboxylate Ions

A **carboxylic acid salt** formed from a carboxylate anion and a Na^+ or K^+ cation is water **soluble** if its “R” group contains less than twelve carbon atoms.

If its “R” group contains twelve or more carbons, then it is _____.

- The attraction of water to the _____ of the carboxylate ion makes the salts more water soluble than their carboxylic acid conjugates.

A carboxylic acid salt formed from a *carboxylate anion* and a Ca^{2+} or Mg^{2+} cation is water **insoluble**.

It is the Ca^{2+} and Mg^{2+} ions that are responsible for the build up of **soap scum** in bathtubs and showers.

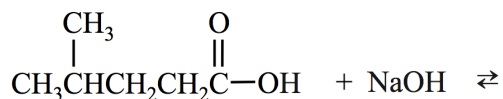
Water with significant amounts of Ca^{2+} and/or Mg^{2+} ions is called **hard water**.

The long-chain carboxylate ions in soap combine with Ca^{2+} or Mg^{2+} to form *insoluble solids* (precipitates) called **soap scum**.

In order to prevent the formation of soap scum and other Ca^{2+} and Mg^{2+} precipitates, Ca^{2+} and Mg^{2+} can be removed from water, in a device called a **water softener** before the water is distributed throughout a home’s plumbing system. Water softeners operate by exchanging Na^+ ions for Ca^{2+} and Mg^{2+} ions.

The Water Solubility of Carboxylic Acids and the Carboxylate Ions of Their Na^+ or K^+ Salts	
$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{OH} \end{array}$ <p>Acid Form</p>	$\begin{array}{c} \text{O} \\ \\ \text{R}-\text{C}-\text{O}^- \end{array}$ <p>Base Form</p>
<p>When R gets to five carbons, the water solubility decreases dramatically.</p>	<p>If $\text{R} < 12$: water soluble</p> <p>If $\text{R} \geq 12$: amphipathic (forms monolayers or micelles)</p>

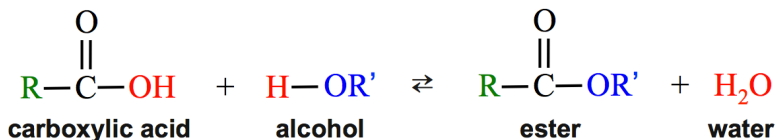
Understanding Check: Add the products for the following neutralization reaction.



3) Esterification: The Reaction of a Carboxylic Acid and an Alcohol

In an **esterification reaction**, a carboxylic acid reacts with an alcohol to produce an _____ and water.

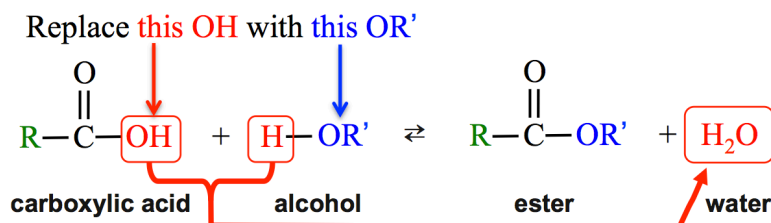
The general form for the esterification reaction is:



In order to keep track of them in the general reaction, we use “R” for the hydrocarbon part of the carboxylic acid, and “R’ ” for the hydrocarbon part of the alcohol.

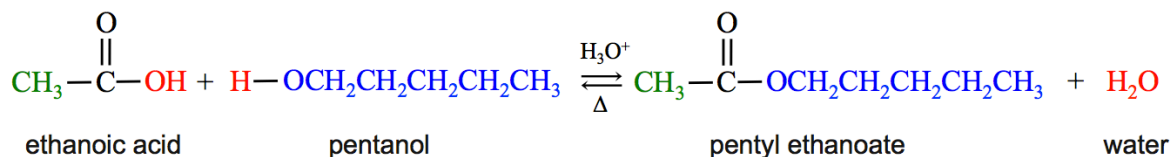
- R and R’ may, or may not, be identical.

An ester is produced when the **OH** from the carboxylic acid is replaced with the **OR’** from the alcohol. The **OH** from the carboxylic acid combines with the **H** from the alcohol to produce **H₂O**.



Esterification reactions can be done in the lab by heating a carboxylic acid and alcohol mixture in the presence of a strong acid catalyst.

A specific example of an esterification reaction is the reaction of ethanoic acid and pentanol (an alcohol):



The *ester formed in the reaction above*, pentyl ethanoate, has the distinct aroma of bananas.

Many esters have pleasant aromas and flavors, and occur naturally in foods. Esters are often added to foods as artificial flavors. They are also used in perfumes.

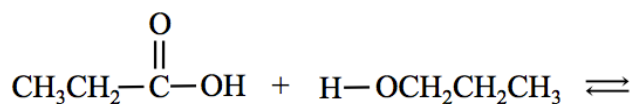
The Greek delta symbol (Δ) is written below the arrows in the chemical equation when heat is used to increase the rate of a reaction, as shown in the equation above.

Likewise, when catalysts, such as H_3O^+ , are used, the formula or name of the catalyst is written above the arrows.

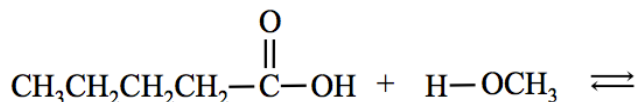
Understanding Check

Add the products for the following esterification reactions:

a.

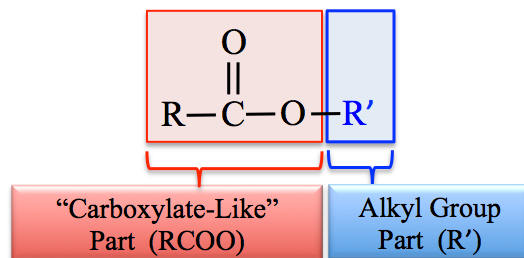


b.

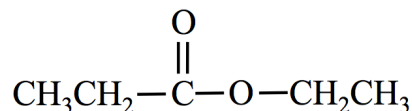


Naming Esters

The IUPAC method for naming esters involves naming the **R'** alkyl group part first, followed by the “*carboxylate-like*” part.



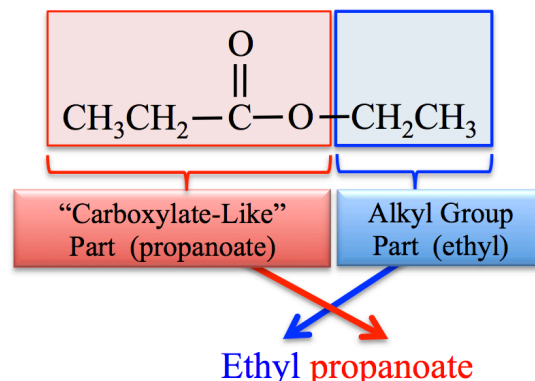
Example: Name the ester shown below:



SOLUTION:

- 1) Identify the alkyl group (**R'**) part and the carboxylate-like part.
- 2) The ester is named by writing the alkyl group (**R'**) part name first, then a space, followed by the name that the “carboxylate-like” part would have *if it were an actual carboxylate ion*.

In this example, the “carboxylate-like” part contains three carbons, therefore its name would be *propanoate* if it were an actual carboxylate ion. The alkyl group (**R'**) is an **ethyl** group. The name of this ester is **ethyl propanoate**.



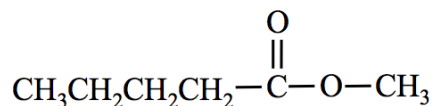
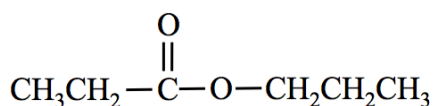
Many naturally-occurring esters contain alkyl groups composed of more than four carbons. In chapter 4, you learned the names of alkyl groups with four or fewer carbons (i.e. methyl, ethyl, propyl, butyl).

The table below lists the names and structures of nonbranched alkyl groups composed of 5-10 carbons.

Names and Structures of Some Alkyl Groups		
Number of Carbons	Alkyl Group Name	Condensed Structure
5	pentyl	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₃
6	hexyl	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₃
7	heptyl	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₃
8	octyl	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₃
9	nonyl	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₃
10	decyl	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₃

Understanding Check

Write the name of each of the esters shown below:

**Understanding Check**

Draw the condensed structure of **octyl butanoate**.

4) Decarboxylation of Carboxylic Acids

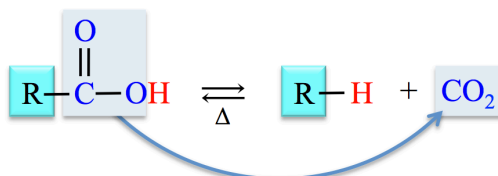
Carboxylic acids undergo a decomposition reaction called _____.

This reaction is very important in the citric acid cycle and other biological processes.

- The carbon dioxide that we exhale is produced by decarboxylation reactions in two of the reactions of the citric acid cycle.

In decarboxylation reactions, a _____ **group** (COOH) is _____ and **replaced by a hydrogen atom**.

The general form for the decarboxylation reaction is:

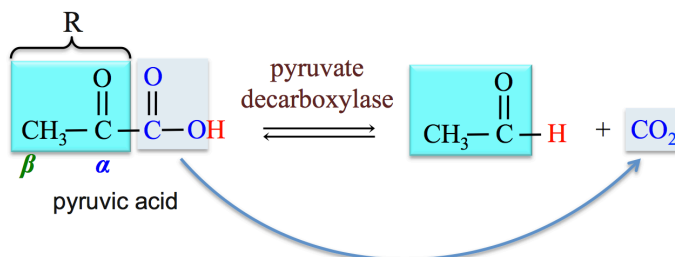


Decarboxylation reactions require heat and/or a catalyst.

The enzymes in biological systems that catalyze decarboxylation reactions are called **decarboxylases**.

Carboxylic acids with an **R** group composed of an alkyl group **only** do not readily undergo decarboxylation reactions. However, when the alpha (α) or beta carbon (β) of the **R** group is double bonded to an oxygen, then decarboxylation reactions readily occur.

- Example:** the decarboxylation of pyruvic acid (an important reaction in yeast):



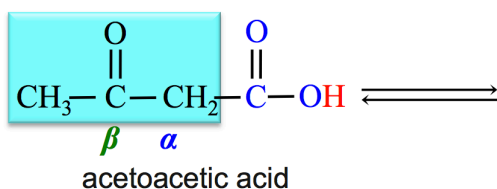
Note that we have expanded our definition of the “**R**” group to be **any organic group** that is unchanged in a reaction. The carbonyl group at pyruvate’s α -carbon is unchanged in this decarboxylation reaction.

Decarboxylation is not only an important reaction in yeast, it also take place in cellular respiration in other animals.

Understanding Check

The production of molecules called **ketone bodies** occurs in humans when large amounts of stored fat are used to produce energy. This can occur during dieting, starvation conditions, or other conditions in a process called **ketosis**. The production of ketone bodies is useful since cells in the brain **cannot** get energy from molecules other than sugars or ketone bodies. When **acetoacetic acid** (one of the three ketone body molecules) is produced in ketosis, it is subsequently converted to another ketone body molecule in a **decarboxylation reaction**.

Predict (draw) the products of this decarboxylation reaction of acetoacetic acid (shown below).



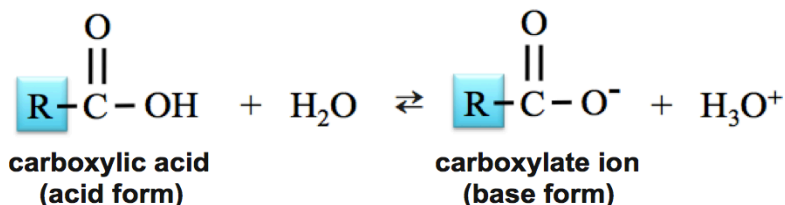
NOTE: The **carbonyl** (C=O) **group** at the β -carbon of **acetoacetic acid** is not affected by the reaction; it is considered to be part of the **R** group.

- The **carboxyl group** (COOH) is removed and replaced with a hydrogen.

Summary of the Reactions of Carboxylic Acids

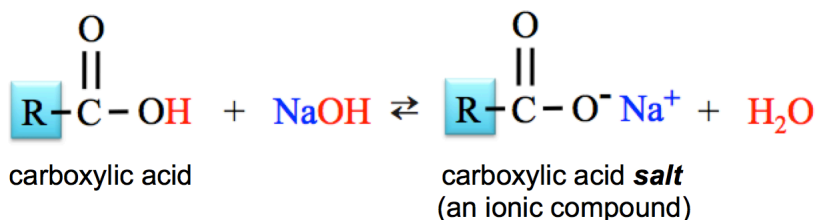
1) Reaction of Carboxylic Acids with Water

When placed in water, a carboxylic acid molecule acts as an acid and water acts as a base. An H^+ from the hydroxyl group (OH) of the carboxylic acid is donated to H_2O .



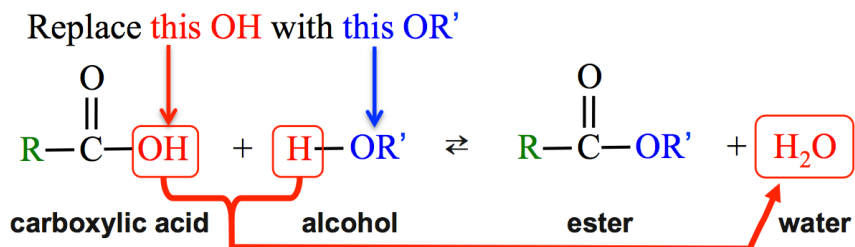
2) Neutralization: Reaction of a Carboxylic Acid and a Hydroxide Ion

In a **neutralization** reaction, a carboxylic acid will react with a *hydroxide-containing base* compound to produce H_2O and a *carboxylic acid salt*.



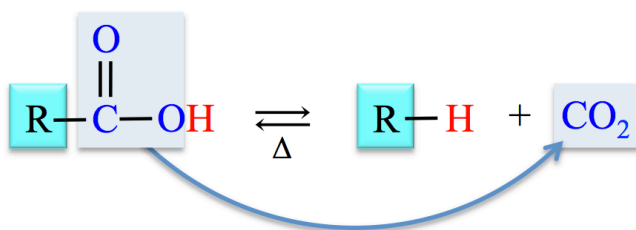
3) Esterification: The Reaction of a Carboxylic Acid and an Alcohol

In an *esterification reaction*, a carboxylic acid reacts with an alcohol to produce an *ester* and water.



4) Decarboxylation of Carboxylic Acids

In decarboxylation reactions, a *carboxyl group* (COOH) is *removed* and *replaced by a hydrogen atom*.



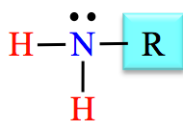
Amines

The Structure of Amines

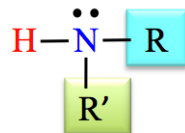
Amines contain a _____ **atom** with *one* lone pair and *three* single bonds to **R** groups or hydrogens.

Amines are classified as primary (1°), secondary (2°), or tertiary (3°) based on the number of **R** groups that they contain.

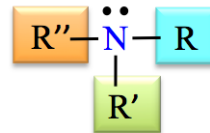
The general forms of the three categories of amines are:



primary (1°) amine



secondary (2°) amine

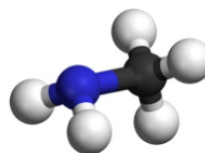
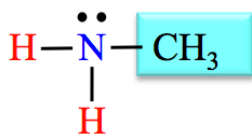


tertiary (3°) amine



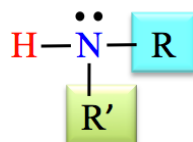
In _____ (1°) **amines**, a nitrogen is bonded to _____ **R** group and _____ hydrogen atoms.

An example of a **primary amine** is methanamine. The structural formula and ball-and-stick model for methanamine are shown below (blue sphere = nitrogen, black sphere = carbon, and white sphere = hydrogen).



methanamine

In _____ (2°) **amines**, a nitrogen is bonded to _____ **R** groups and _____ hydrogen atom.

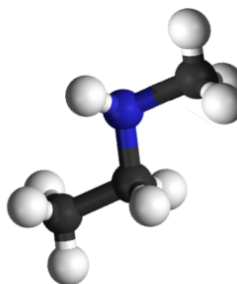
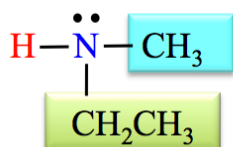


secondary (2°) amine



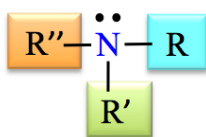
One **R** group is written as **R**, and the other as **R'**, to indicate that *they are not necessarily the same alkyl group*.

An example of a **secondary amine** is *N*-methylethanamine:



N-methylethanamine

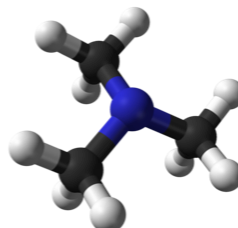
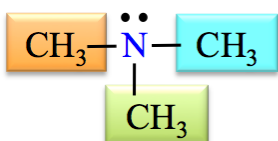
In **tertiary (3°) amines**, a nitrogen is bonded to **three R** groups.



tertiary (3°) amine



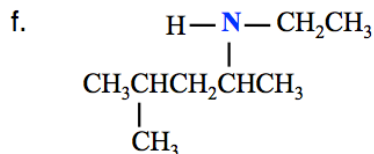
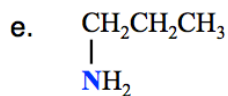
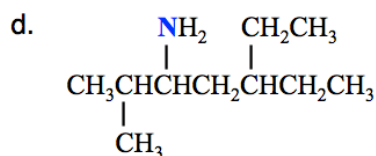
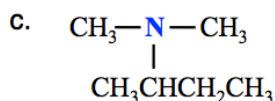
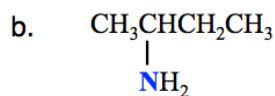
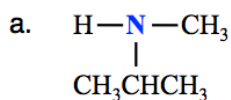
An example of a **tertiary amine** is *N,N*-dimethylmethanamine:



N,N-dimethylmethanamine

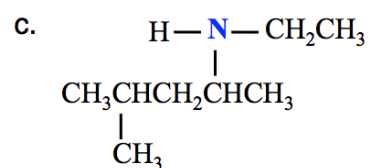
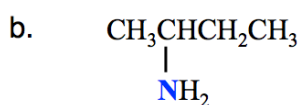
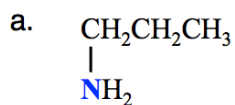
Understanding Check

Identify each of the amines shown below as either primary (1°), secondary (2°), or tertiary (3°).



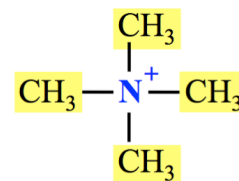
Understanding Check

Draw the **skeletal structure** of each of the **amines** shown below:



A **quaternary ammonium ion** is formed when *an* _____ hydrogen *or* alkyl group (**R**) is added to an amine.

The **nitrogen** in a quaternary ammonium ion *does not have a lone pair* and, therefore has a _____ of **1+**.



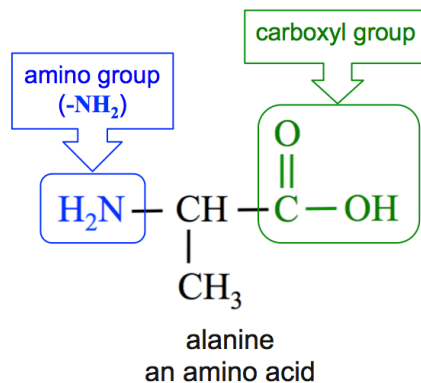
tetramethylammonium ion

An example of a **quaternary ammonium ion** is the tetramethylammonium ion, which occurs naturally in some animals.

Some molecules contain **more than one** type of functional group.

For example, molecules called **amino acids** contain both an **amino group** ($-\text{NH}_2$) *and* a carboxyl group ($-\text{COOH}$).

An example of an **amino acid** is alanine:



Amino acids are the precursors to **proteins**.

Naming Amines

The *systematic method* that we will use for naming amines is based on the hydrocarbon naming method.

Step 1. Find and name the *parent chain*.

The *parent chain* is the longest, continuous chain of carbon atoms that **contains the point of attachment to the nitrogen**.

- Starting with the alkane name that corresponds to the number of carbon atoms in the **parent chain**, replace the “e” at the end of the alkane name with “**amine**.”

Example: if the parent chain of an amine contains two carbons, it would be called *ethanamine*.

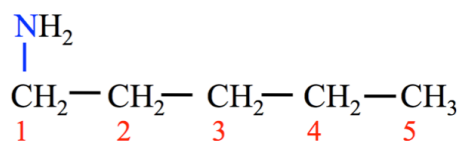


For amines with **more than two carbons**, the position of the *point of attachment to the nitrogen* must be indicated by adding a number **before the parent chain name**, as described below.

Assign *position numbers* to the carbons in the parent chain. Position number **1** is assigned to the carbon at the *end of the parent chain* that is **nearest to the point of attachment to the** _____.

If the nitrogen is bonded to carbon number **1** of the parent chain, then “**1-**” is used as a prefix to the parent chain name.

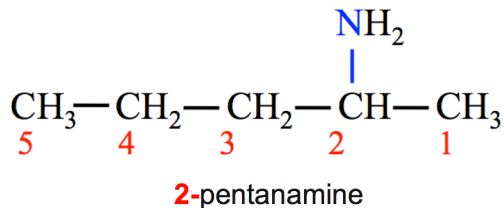
- For example, in the molecule below, the parent chain is called **1-pentanamine**.



1-pentanamine

If the nitrogen is bonded to carbon number 2 of the parent chain, then “2-” is used as a prefix to the parent chain name.

- For example, in the molecule below, the parent chain is called 2-pentanamine.



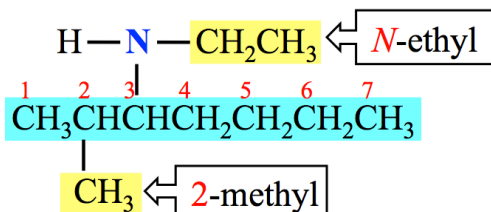
This is analogous to the numbers that you used as prefixes for the parent chain names of alkenes to indicate the position of the double bond.

Step 2. Name any alkyl group substituents.

Alkyl group substituents that are attached to the parent chain are named in the same way as you did for alkanes.

For secondary and tertiary amines, the *nonparent chain R* group(s) attached to the nitrogen are named as substituents.

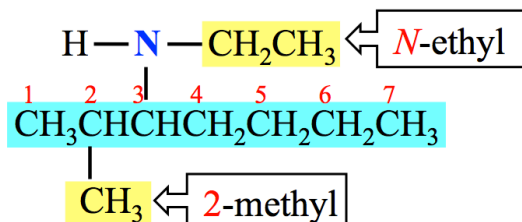
- “N-” is written in front of the **R** group substituent name, instead of a position *number*, in order to indicate that the **R** group is *attached to the* _____.
- For example, the amine shown below has a *methyl* substituent attached to the *parent chain* and an *ethyl* substituent attached to the **nitrogen**.



Step 3. Construct the name of the amine by placing the alkyl groups in alphabetical order and specifying their position, followed by the name of the parent chain.

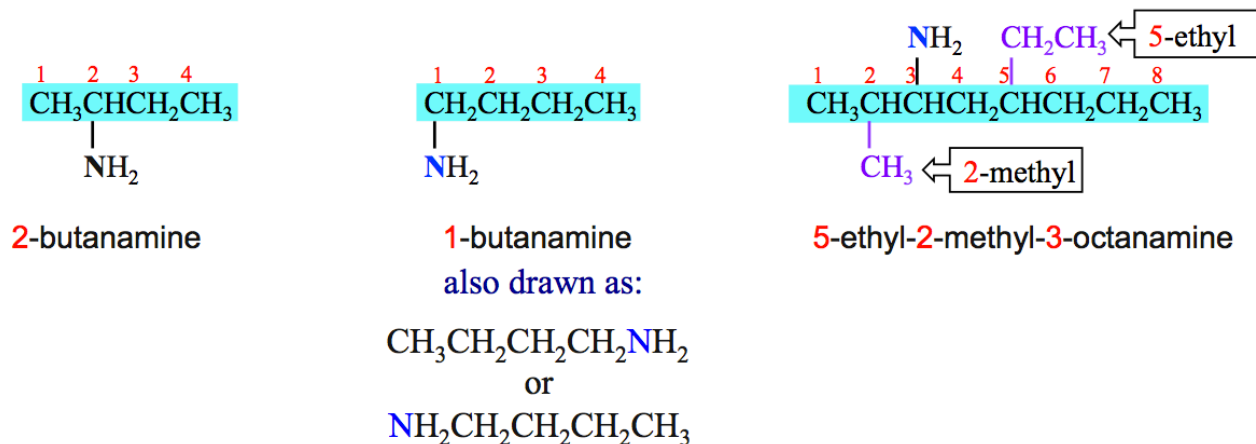
- This is done the same way as you did for hydrocarbons and carboxylic acids.
- Remember to use a dash between position numbers (or “N”) and letters.

The name of the amine shown below is: *N-ethyl-2-methyl-3-heptanamine*.

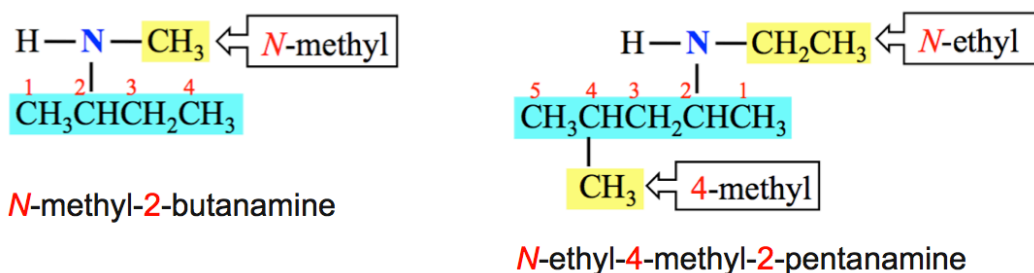


Other Examples:

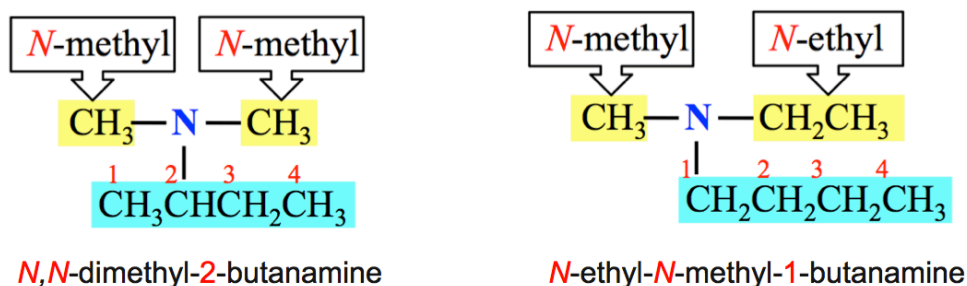
Names and Structures of Primary (1°) Amines



Names and Structures of Secondary (2°) Amines



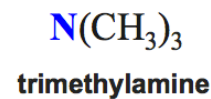
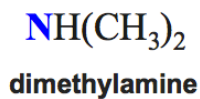
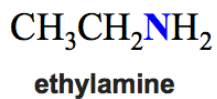
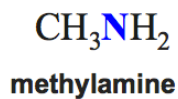
Names and Structures of Tertiary (3°) Amines



Common Names for Amines

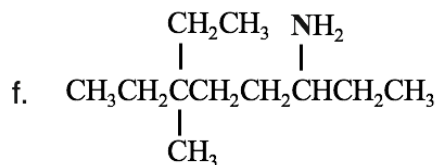
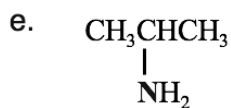
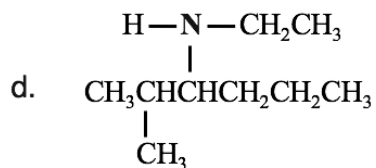
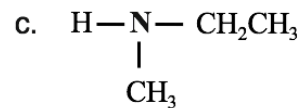
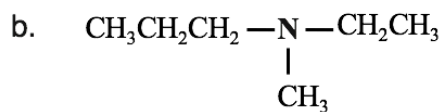
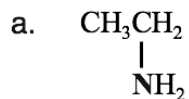
Simple amines, those with a relatively few number of carbon atoms, are often identified by **common names** by placing “amine” after the names of the alkyl group(s) that are attached to the nitrogen.

Examples:



Understanding Check

Write the **systematic names** for each of the amines shown below:



Understanding Check

Draw the condensed **and** skeletal structure of each of the amines listed below.

2-methyl-3-hexanamine

N-methyl-2-propanamine

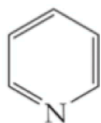
N,N-diethylethanamine

Heterocyclic Compounds

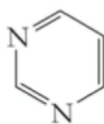
You have seen cyclic compounds such as cyclohexane and cyclopentane. The rings of the cyclic compounds that you have seen so far have contained *only carbon atoms*.

Cyclic compounds that contain atoms _____ carbon are known as **heterocyclic compounds**.

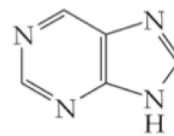
Examples of heterocyclic compounds are:



pyridine



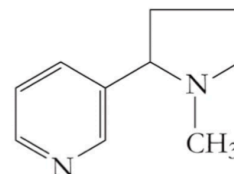
pyrimidine



purine

Heterocyclic, **nitrogen-containing** rings are very common in plants and animals.

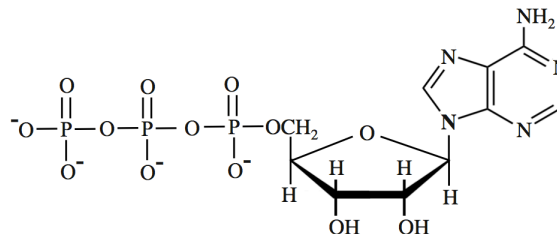
- **Example:** Nicotine is a naturally occurring, nitrogen-containing heterocyclic molecule from the tobacco plant.



nicotine

Adenosine triphosphate (ATP), used by nature in both plants and animals, is an important compound for energy storage.

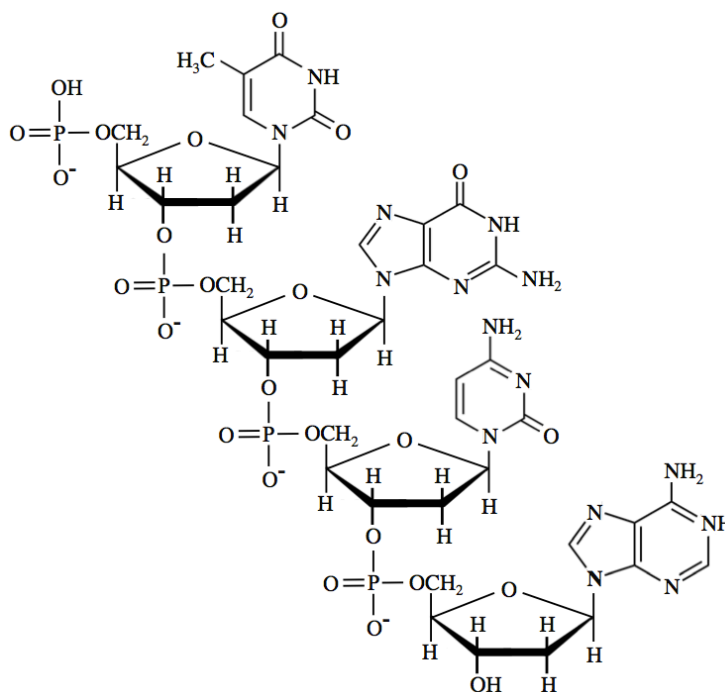
ATP has **nitrogen-containing** heterocyclic rings **and** an **oxygen-containing** heterocyclic ring.



adenosine triphosphate (ATP)

DNA and RNA have both **nitrogen-containing** and **oxygen-containing** heterocyclic ring structures.

A structural formula for a *small portion* of DNA is shown here.



Properties of Amines

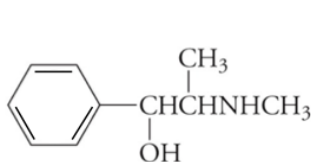
Many amines have the foul odor of decomposing fish.

Amines frequently occur in plants and animals.

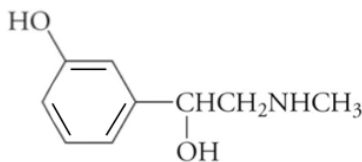
_____ amines can irritate skin, eyes, and mucous membrane and are toxic when ingested.

Many synthetic and naturally occurring amines are _____ active.

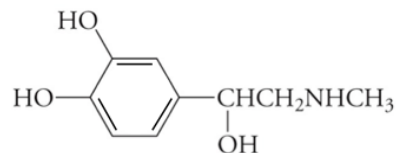
- Examples of physiologically active amines:



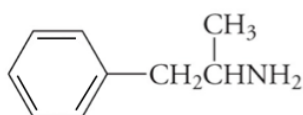
pseudoephedrine



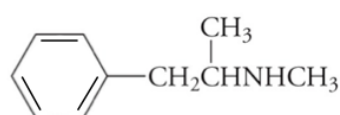
phenylephrine



epinephrine



amphetamine



methamphetamine

Pseudoephedrine and **phenylephrine** cause vasoconstriction and are used as a nasal decongestant.

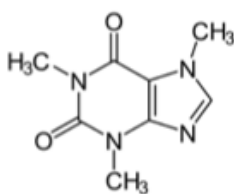
Epinephrine (also called *adrenaline*) is a naturally occurring hormone and neurotransmitter that is associated with the stimulation of the fight-or-flight response.

Amphetamine and **methamphetamine** are strong stimulators of the central nervous system.

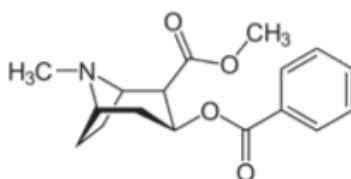
- **Amphetamine** is used as a treatment for attention deficit hyperactivity disorder (ADHD), obesity, and narcolepsy.
- **Methamphetamine** has widespread use as an illegal “recreational” psychostimulant and was the focus of the popular TV drama “Breaking Bad.” Methamphetamine is rarely prescribed as a therapeutic drug because of its many undesirable side effects.

The term “_____” is used for physiologically active amines that occur in nature (i.e. bacteria, fungi, plants, and animals).

- Some examples of *alkaloids* are shown below.



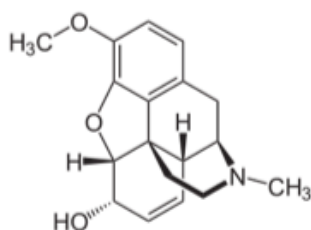
caffeine



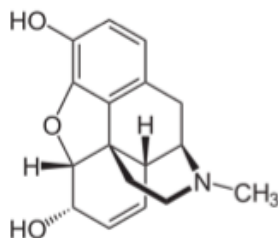
cocaine

Caffeine is a stimulant that is produced in high concentration by coffee plants and is also found in seeds, leaves, nuts, and berries of other plants. It serves as a natural insecticide.

Cocaine is a very strong, central nervous system stimulant that is produced in the leaves of the coca plant.



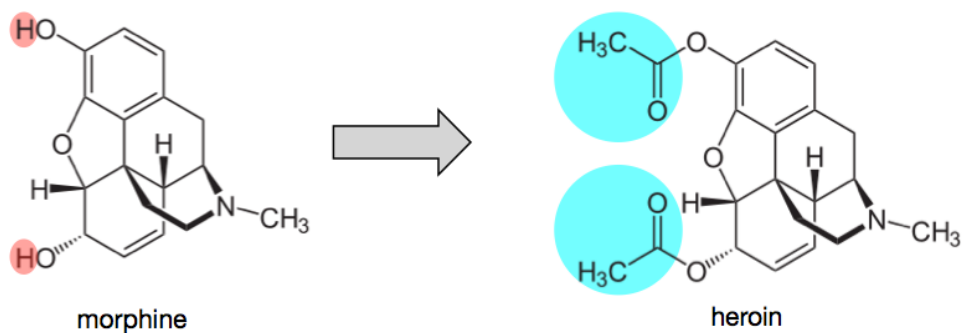
codeine



morphine

Codeine and **morphine** are the two most abundant psychoactive components of opium, the dried extract of opium poppy seeds. **Codeine** is used as a pain reliever and to treat coughs. **Morphine** is used to treat severe pain. It is highly addictive.

Heroin is produced *from morphine* by a chemical reaction that replaces the hydrogens of the hydroxyl (-OH) groups with *acetyl groups* (CH₃C=O, highlighted in blue).



Water Solubility of Amines

All *amine* molecules have the ability to interact with water through hydrogen bonding and dipole-dipole interactions.

Small amines have significant water solubility.

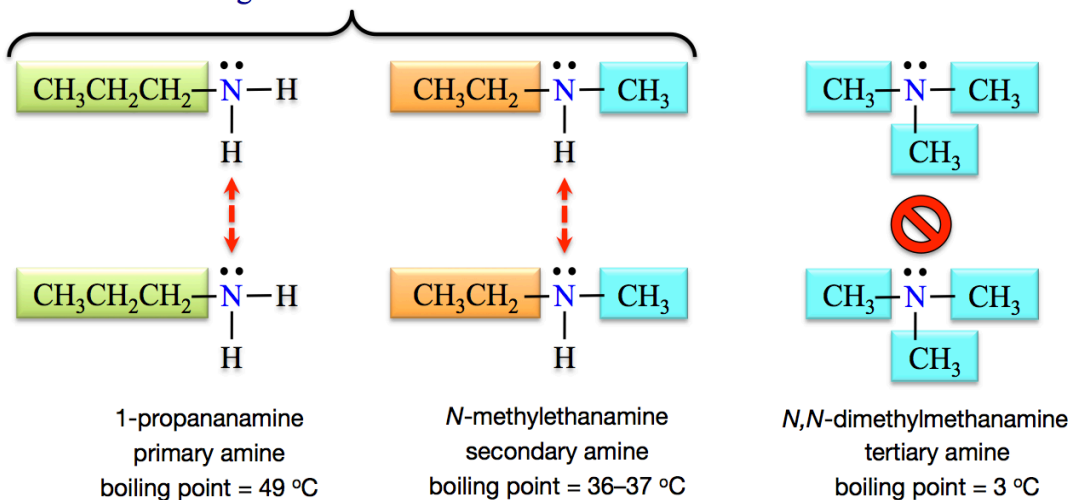
As the *hydrocarbon parts* of amines get *larger*, their water solubility *decreases*; as is the case for all organic molecules.

Boiling and Melting Points of Amines

Amines are polar and can interact with each other through dipole-dipole forces, therefore they have higher boiling and melting points than hydrocarbon molecules of similar size.

Tertiary amines do not have N-H bonds, and are therefore _____ of hydrogen bonding with each other.

Only the 1° and 2° Amines Exhibit Hydrogen Bonding Between their Molecules.



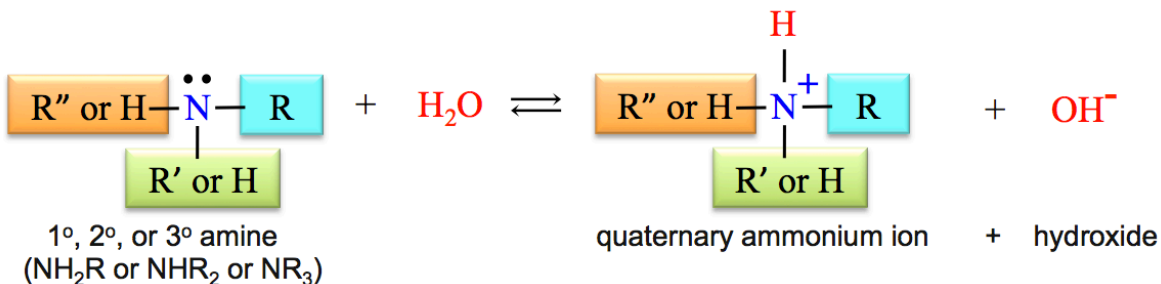
For this reason, primary and secondary amines have higher boiling points than tertiary amines of similar size.

Chemical Reactions of Amines

1) Reactions of Amines with Water

An amine acts as a _____ when it reacts with *water* to produce a *quaternary ammonium ion* and a *hydroxide ion*.

- The general form of the reaction of an amine with water is shown below.



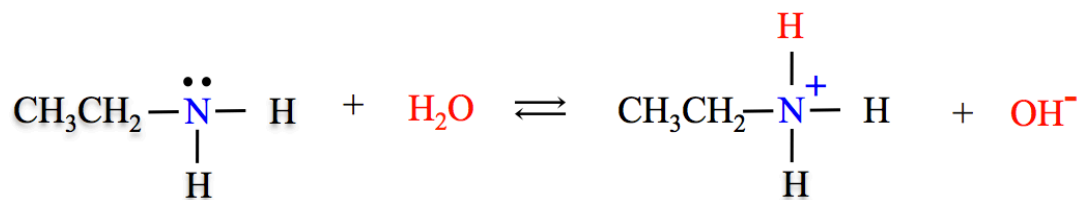
The lone pair on the amine **nitrogen** forms a bond to the **H⁺** from water.

When amines are put into *pure water*, the pH is _____ since hydroxide ions are produced in this reaction.

The *amine* and the *quaternary ammonium ion* are a _____ *pair*.

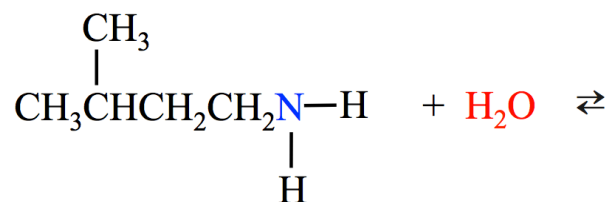
- The *amine* is the *base form* and the *quaternary ammonium ion* is the *acid form*.
- When an amine/quaternary ammonium ion conjugate pair is in a mixture that contains other dissolved species, the relative amounts of the *acid form* and *base form* can be predicted by the Henderson-Hasselbalch Relationship.

A specific example of the reaction of an amine with water is the reaction of ethanamine with water:



Understanding Check

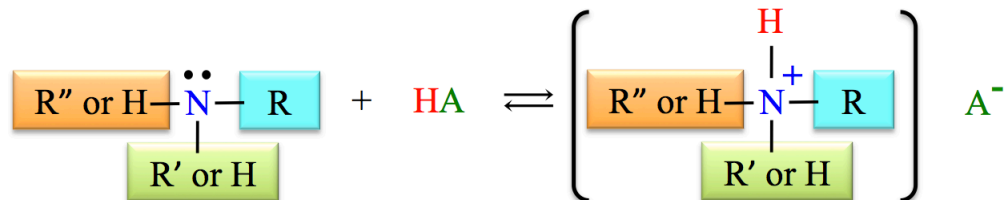
Add the products for the following reaction:



2) Reaction of Amines with Acids

An amine will react with an *acid* to produce a *quaternary ammonium compound* in a _____ *reaction*.

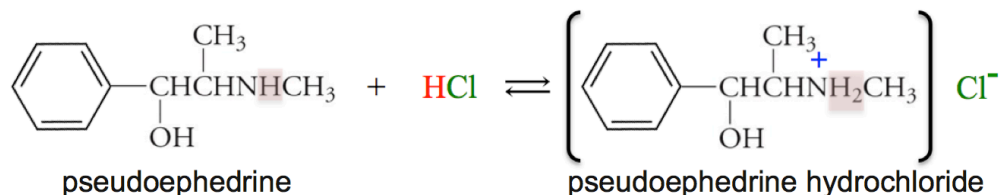
- The general form of the equation for the reaction of an amine with an acid is shown below:



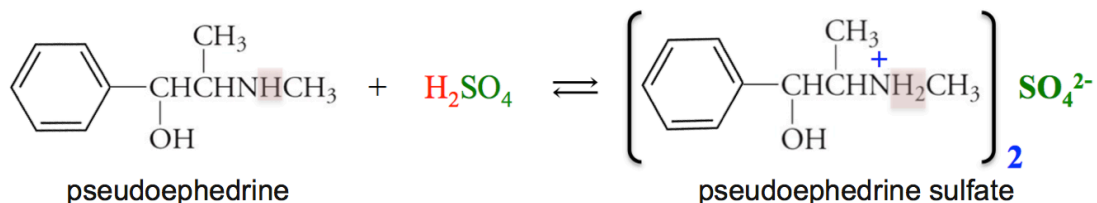
The lone pair on the amine **nitrogen** forms a bond to the **H⁺** from the acid.

Amines that are used as medications, both legal and illegal, are often administered as quaternary ammonium ions in order to increase their water-solubility.

- For example, pseudoephedrine hydrochloride, used in the decongestant sold as *Allegra D* by Bayer Healthcare, and as *Benadryl* by Johnson and Johnson, can be prepared by the reaction of pseudoephedrine and HCl.

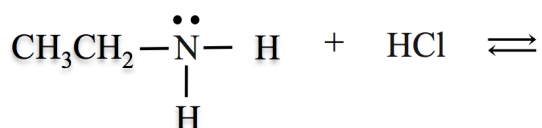


- Pseudoephedrine sulfate, used in *Claritin D*, can be prepared by the reaction of pseudoephedrine and sulfuric acid (H₂SO₄).



Understanding Check

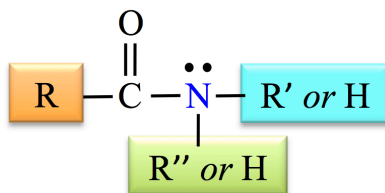
Add the product for the following reaction:



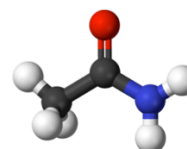
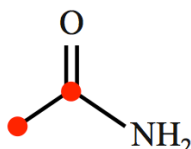
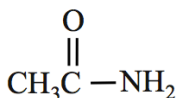
Amides

The Structure of Amides

Amides contain both a **carbonyl group** (C=O), **and** a nitrogen (N), with the nitrogen bonded to the **carbonyl carbon**. The general form of an amide is shown below.



A specific example of an amide is *ethanamide*. The condensed structural formula, skeletal formula, and a ball-and-stick model for *ethanamide* are shown below.



black sphere = carbon, red sphere = oxygen, blue sphere = nitrogen, and white sphere = hydrogen

The amide bonding pattern occurs in nature in the structure of proteins.

Naming Amides

We will use the IUPAC system for naming amide molecules. The systematic method for naming amides is based on the hydrocarbon naming method.

Step 1: Find and name the parent chain.

The parent chain of an amide is the longest continuous chain of carbon atoms that includes the _____ **carbon** - just as we did with *carboxylic acids*.

Starting with the alkane name that corresponds to the number of carbon atoms in the parent chain, replace the “e” at the end of the alkane name with “**amide**.”

- For example, if the parent chain of an amide contains *three* carbons, it is called *propanamide*.



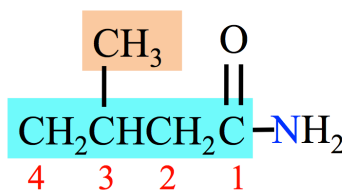
Step 2: Name any alkyl group substituents.

Alkyl groups are named in the same way as was done for hydrocarbons.

Step 3: Determine the *point of attachment* of any alkyl groups.

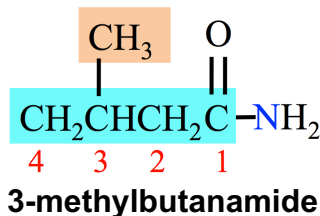
Substituents are assigned positions based on their point of attachment to the parent chain or to the nitrogen. Begin numbering the parent chain at the *carbonyl carbon*.

- For example, the amide shown below has a “**3-methyl**” substituent.

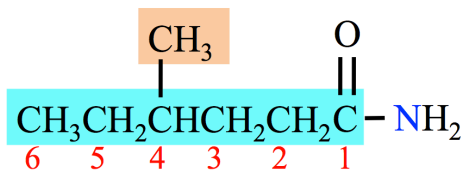


Step 4: Construct the name of the amide by placing the alkyl groups in alphabetical order and specifying their positions, followed by the name of the parent chain.

- Use a *dash* between positions and *letters*.
- Add the labels di, tri, or tetra in front of the alkyl group name **if** two, three, or four (respectively) identical substituents are present.



Example: Name the amide shown below.



Step 1: Find and name the parent chain. **hexanamide**

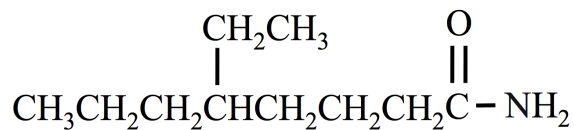
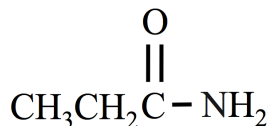
Step 2: Name any alkyl group substituents. **methyl**

Step 3: Determine the *point of attachment* of any alkyl groups. **4-methyl**

Step 4: Construct the name of the amide by placing the alkyl groups in alphabetical order and specifying their positions, followed by the name of the parent chain.

4-methylhexanamide

Understanding Check: Name the molecules that are shown below.



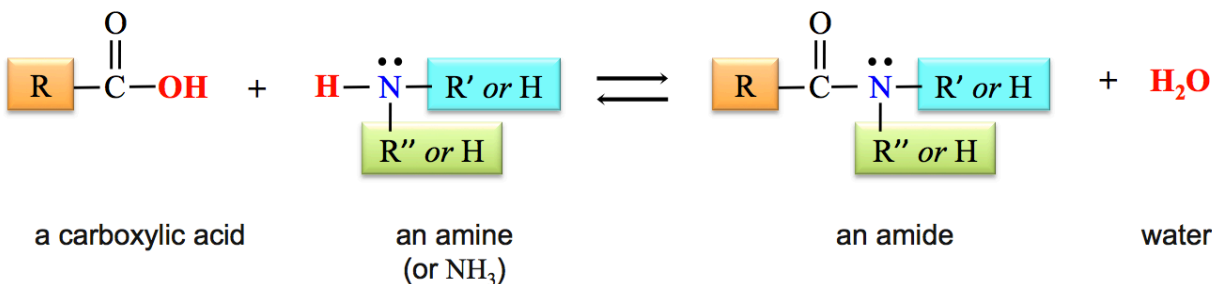
Understanding Check:

Draw the *line bond*, *condensed*, and the *skeletal* structural formula of **pentanamide**.

Formation of Amides: The Reaction of Carboxylic Acids with Amines

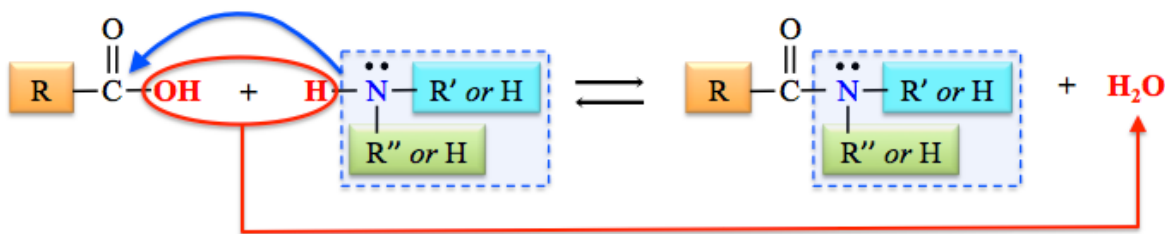
An **amide** is produced when a _____ reacts with an _____ or **ammonia** (NH₃).

The general form of this reaction is shown below.



An easy way to predict and draw the products of this reaction is to:

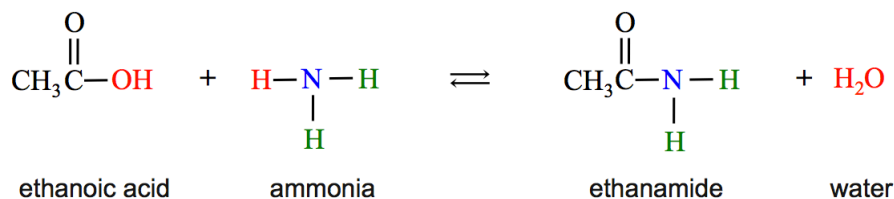
- 1) Draw the structures of the carboxylic acid and the amine (or ammonia) with the (OH) from the carboxylic acid and an H from the amine (or ammonia) **adjacent** to each other.
- 2) Remove the (OH) from the carboxylic acid and an H from the amine (or ammonia), and then combine the H and OH to make H₂O.
- 3) Bond the **nitrogen** and its remaining groups to the **carbonyl carbon** of the carboxylic acid.



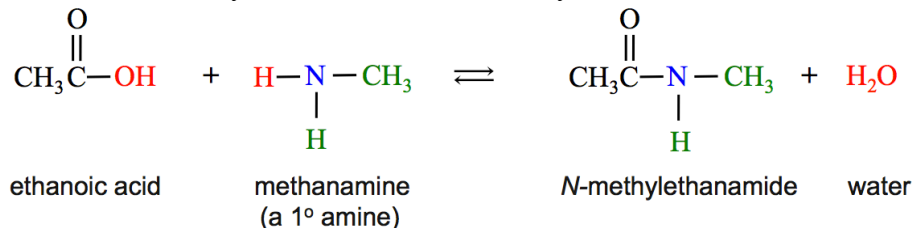
An amide can form when a carboxylic acid reacts with ammonia, with a primary, or with a secondary amine.

• Examples:

- a) Formation of an amide by the reaction of a carboxylic acid and *ammonia*.

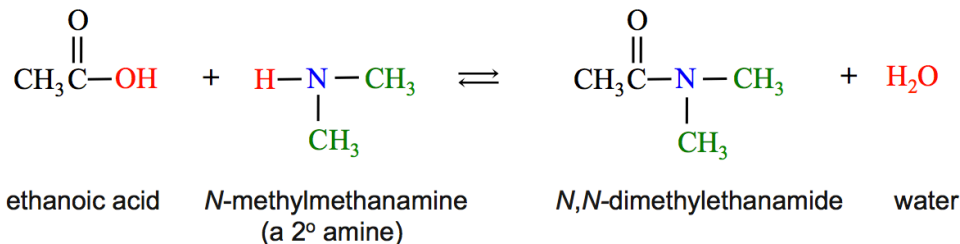


- b) Formation of an amide by the reaction of a carboxylic acid and a 1° amine.



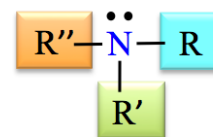
The “N-methyl” in “N-methylethanamide” indicates that there is a *methyl* substituent bonded to the nitrogen.

c) Formation of an amide by the reaction of a carboxylic acid and a 2° amine.



The “*N,N*-dimethyl” in “*N,N*-dimethylethanamide” indicates that there are two *methyl* substituents bonded to the nitrogen.

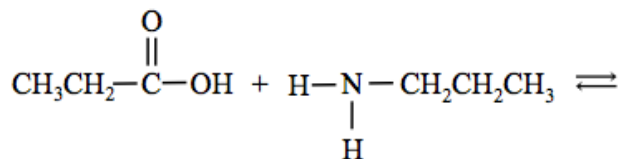
Amides are not formed from 3° amines because 3° amines do not have a _____ attached to the nitrogen.



tertiary (3°) amine
NR₃

Understanding Check:

Add the products for the following reaction *and name* the *amide* that is produced:

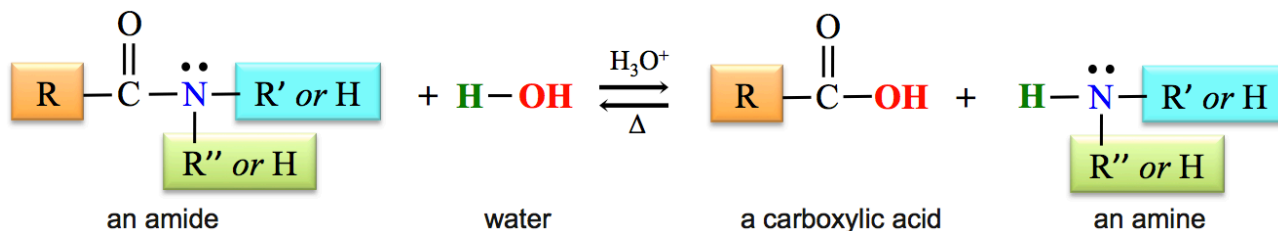


Naming Hint: There will be a substituent attached to the nitrogen (not the parent chain). You will use “*N*-” in the name to indicate that a substituent is bonded to the nitrogen.

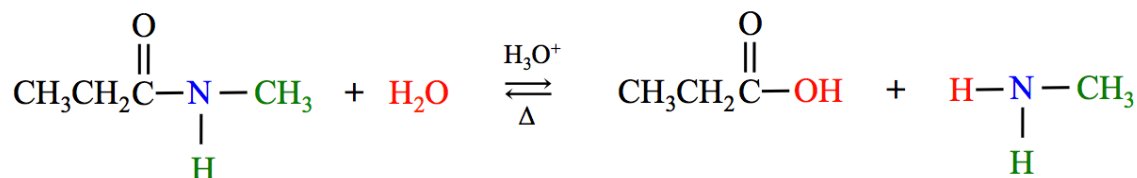
Hydrolysis of Amides

The _____ of the *amide formation* reaction is the **hydrolysis of amides**.

With heat and an acid catalyst, an amide can be hydrolyzed to produce a **carboxylic acid** and an **amine** (or ammonia).

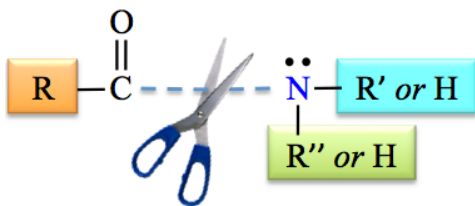


A specific example of this reaction is the hydrolysis of *N*-methylpropanamide.

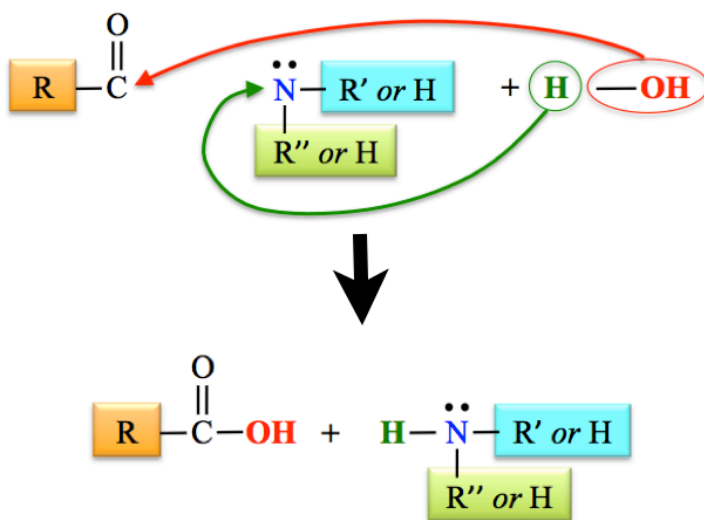


Beginning with the structure of **any** amide and water, an *easy way to predict and draw the products* of this reaction is to:

- 1) Break the bond between the **carbonyl group** and the **nitrogen**.

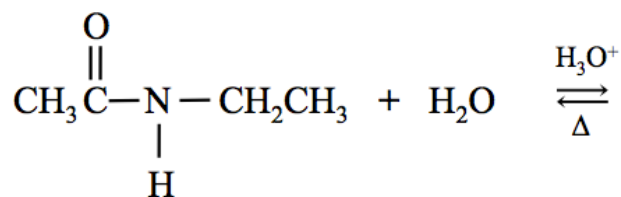


- 2) Bond the **OH** from water to the **carbonyl carbon**, and bond the **H** from **water** to the **nitrogen**.



Understanding Check:

Add the products for the following amide hydrolysis reaction *and* name **both** of the products:



Enantiomers and Diastereomers

Stereoisomers are molecules that have the *same* molecular formula, have the *same* atomic connections, but have *different* three-dimensional arrangements of the atoms.

We have seen some examples of stereoisomers in the past (chapter 4) - **geometric isomers**.

When *stereoisomers* exist because of **limited bond rotation**, they are called **geometric isomers**.

You saw that geometric isomers could occur for certain cycloalkanes and alkenes.

- We designated the geometric isomers as either *cis* or *trans*.

Another type of stereoisomers occurs when _____ **groups are bonded to the** _____ **atom**.

- In these cases, there are two distinct, three-dimensional arrangements of the atoms.

For our purposes, we will be concerned with the pairs of stereoisomers that result whenever four different groups are bonded to the same **carbon atom**.

A carbon atom that carries **four different groups** is called a “_____.”

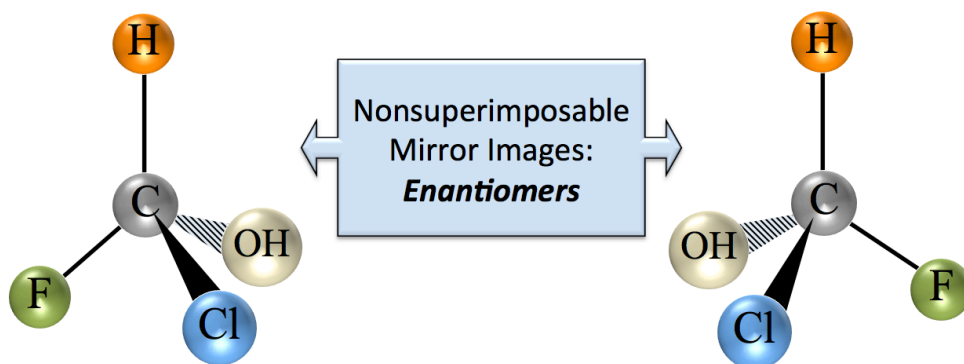
The two distinct, three-dimensional arrangements of the atoms around the chiral carbon are **mirror images** of each other.

When four different groups are arranged in the tetrahedral geometry (we called it AB₄), the mirror images are _____ identical.

- Another way to describe nonidentical mirror images is with the term “*nonsuperimposable mirror images*.”

Stereoisomers such as these, which are nonsuperimposable mirror images of each another, are called _____.

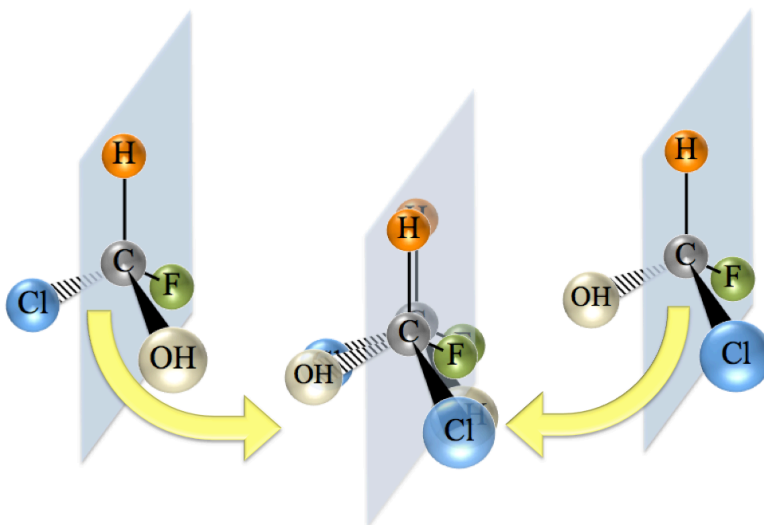
An example of a pair of stereoisomers (*an enantiomer pair*) that results from the presence of a **chiral carbon** is shown below.



Recall that in *wedge and dash* illustrations of three-dimensional objects, **solid wedges** indicate bonds that would be coming **out and above** the page (toward the viewer). **Dashed shapes** indicate bonds that would be coming **out and behind** the page (away from the viewer). Regular lines (neither wedge nor dash) indicate bonds that would exist **on the plane** of the page.

The image shown here may help you to visualize and understand that the two molecules shown in the previous slide are not identical.

I have graphically depicted the failed attempt to superimpose the pair of enantiomers.



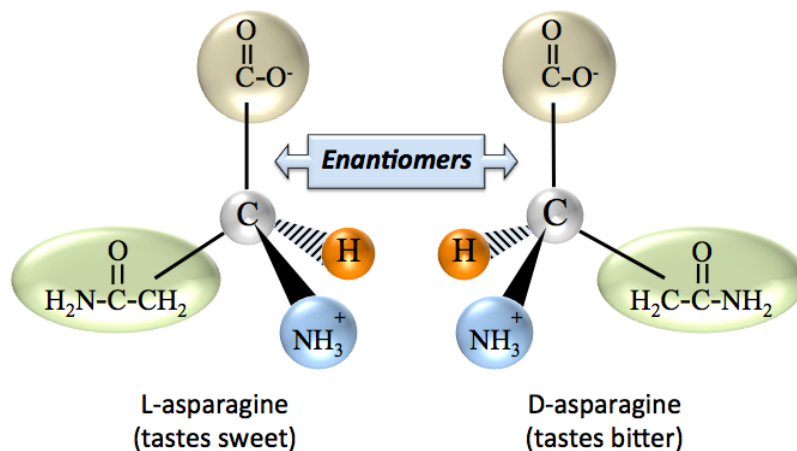
Pairs of enantiomers have very _____ *physical properties*.

- For this reason, they are very difficult to separate (purify) from each other. For example, their boiling points are so similar that separation by distillation is not possible.

They do _____ in a couple of important ways.

- Since enantiomers' arrangements of electrons are mirror images of each other, they interact with light in different ways. It is for this reason that enantiomers are sometimes called "optical isomers."
- Another important difference in enantiomers is the way they behave in *biological systems*.
- Since enantiomers do not have identical three-dimensional shapes, they do not behave identically when interacting with biomolecules such as enzymes or the receptors that are responsible for taste.

- **Example:** One of the enantiomers of asparagine (L-asparagine) has a sweet taste. The other enantiomer (D-asparagine) has a bitter taste.



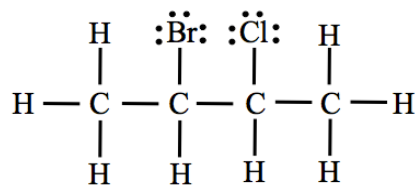
Many enzymes are "**stereospecific**." This means that they will catalyze a reaction for only *one* particular enantiomeric reactant and/or will catalyze the formation of only one enantiomeric product.

For example, when the antibiotic that we call penicillin is made by enzymatic reactions by mold, only one of the enantiomers (penicillin) is produced.

Plants produce only one enantiomer of the glucose molecule (D-glucose). It is therefore understandable that all organisms - with only one known exception of particular bacterium - will only metabolize the D-glucose enantiomer.

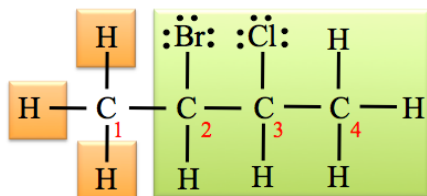
Let's do an example problem in order to help you identify **chiral carbons**.

Example: The line bond structure of 2-bromo-3-chlorobutane is shown below. How many **chiral carbons** are in this molecule?

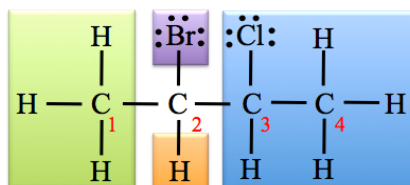


Solution: Consider each carbon individually. A carbon is **chiral** if it is bonded to *four different groups*.

Carbon number 1 is **not** chiral. It is bonded to four groups, however, the four groups are not all *different* from each other. I have highlighted the four groups that are bonded to carbon number 1 in the structure shown below. Three of the groups are hydrogens.

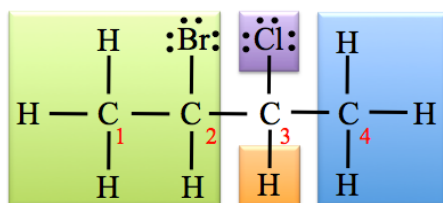


Carbon number 2 is chiral; it is bonded to *four different groups*

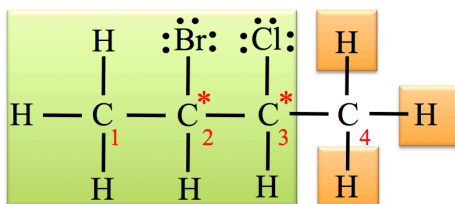


IMPORTANT: A mistake that chemistry students sometimes make is to consider only the four *atoms* to which a carbon is bonded. If you were to do that with this molecule, you might think that **carbon number 2** is *not* chiral since it is bonded to *two other carbons* (carbon number 1 and 3). Be careful; you must consider the entire *group of atoms to which a carbon is bonded in order to determine if that carbon is chiral*. It is for this reason that I highlighted the *entire groups* that are bonded to carbon number 2 in the structure shown above.

Carbon number 3 is chiral; it is bonded to *four different groups*.



Carbon number 4 is not chiral. Three of the groups are the same - three hydrogens.



There are two **chiral carbons** in 2-bromo-3-chlorobutane - carbons number **2** and **3**.

Diastereomers

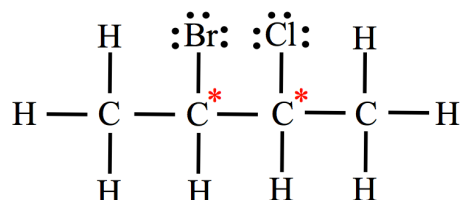
When _____ *than one chiral carbon* is present in a molecule, then more than one pair of enantiomers will exist.

The *number of stereoisomers* that can exist depends on the *number of _____ carbons*.

If we let “**n**” represent *the number of chiral carbons* in a molecule, then the maximum number of stereoisomers is calculated as follows:

$$\text{Maximum Number of Stereoisomers} = 2^n$$

Example: In our previous example problem, we determined that 2-bromo-3-chlorobutane contained *two chiral carbons*.



Therefore the *maximum number of stereoisomers* that 2-bromo-3-chlorobutane has is:

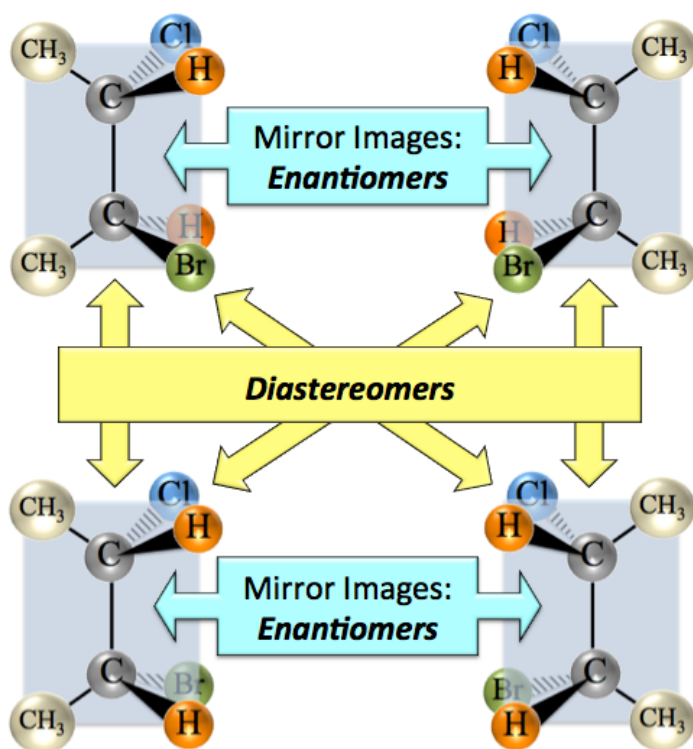
$$\text{Maximum Number of Stereoisomers} = 2^n = 2^2 = 4$$

The **four** stereoisomers of 2-bromo-3-chlorobutane, *two pairs* of mirror images, are shown on the right.

You learned about the relationship between nonsuperimposable mirror image molecules, called *enantiomers*.

Nonsuperimposable molecules *that are not mirror images of each other*, but are in the group of 2^n stereoisomers, are called _____.

- The *enantiomer* relationships are indicated with blue arrows.
- The *diastereomer* relationships are indicated with yellow arrows.



It may be helpful for you to compare and contrast *enantiomers* and *diastereomers* by using a “family relationship” analogy of *siblings* (for enantiomers) and *cousins* (for diastereomers).

You will see more enantiomers, diastereomers, and geometric isomers in the biochemistry chapters of this course.

Understanding Check:

What is the *maximum number of stereoisomers* that can exist for each of the molecules shown below?

