

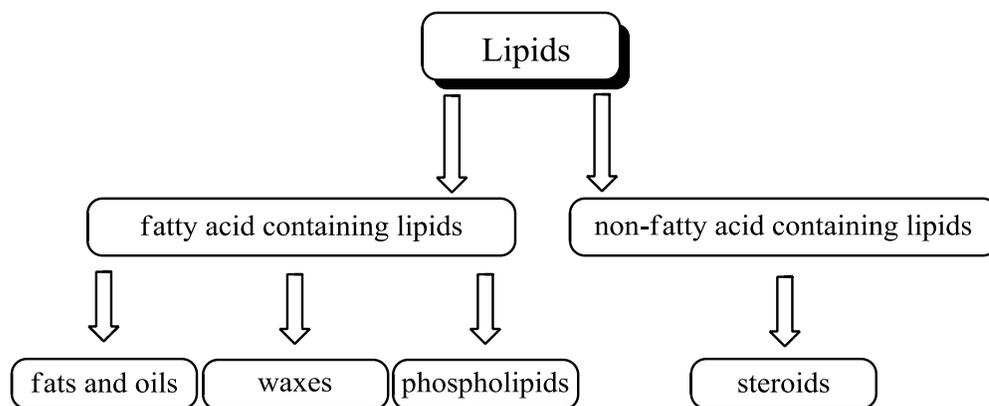
UNIT (11) MOLECULES OF LIFE: LIPIDS AND PROTEINS

11.1 | Types of Lipids

Lipids are also biochemical compounds that contain carbon, hydrogen, and oxygen. But lipids, unlike carbohydrates, share no common structural features. The definition of a lipid is more functional or operational.

Lipids are biomolecules that are *insoluble in water* but *soluble in organic solvents*.

We will classify lipids into two major categories: fatty-acid containing lipids and non-fatty acid containing lipids.



11.2 | Fatty Acids

The fundamental building blocks of many lipids are long-chain carboxylic acids called **fatty acids**. Fatty acids always contain an *even* number of carbon atoms and typically range between 10 and 20. This is a direct result of the biosynthetic pathways used to produce fatty acids.

The fatty acids can be saturated, monounsaturated, or polyunsaturated.

A *saturated fatty acid* contains only carbon-carbon single bonds in the hydrocarbon chain.

A *monounsaturated fatty acid* contains one C = C double bond in the hydrocarbon chain.

A *polyunsaturated fatty acid* contains two or more C = C double bonds in the hydrocarbon chain.

Table 11.1 lists the names and structures of common fatty acids often found in lipid structures.

Fatty acid general structure $R\text{---COOH}$

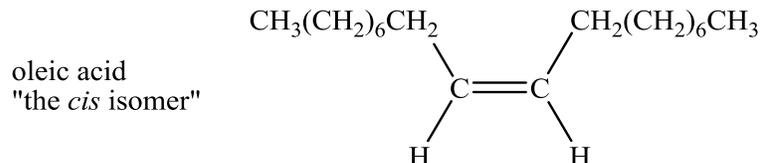
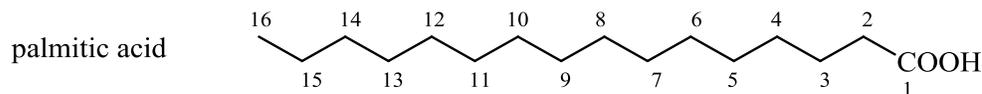


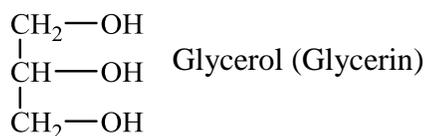
Table 11.1 Common Saturated and Unsaturated Fatty Acids

Number of carbon atoms	Number of double bonds	Name	Formula	Source
12(12:0)	0	Lauric acid	$\text{CH}_3(\text{CH}_2)_{10}\text{CO}_2\text{H}$	coconut
14(14:0)	0	Myristic acid	$\text{CH}_3(\text{CH}_2)_{12}\text{CO}_2\text{H}$	nutmeg
16(16:0)	0	Palmitic acid	$\text{CH}_3(\text{CH}_2)_{14}\text{CO}_2\text{H}$	palm
16(16:1)	1	Palmitoleic acid	$\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{CH}(\text{CH}_2)_7\text{CO}_2\text{H}$	macadamia nuts
18(18:0)	0	Stearic acid	$\text{CH}_3(\text{CH}_2)_{16}\text{CO}_2\text{H}$	lard
18(18:1)	1	Oleic acid	$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{CO}_2\text{H}$	olives
18(18:2)	2	Linoleic acid	$\text{CH}_3(\text{CH}_2)_4(\text{CH}=\text{CHCH}_2)_2(\text{CH}_2)_6\text{CO}_2\text{H}$	safflower
18(18:3)	3	Linolenic acid	$\text{CH}_3\text{CH}_2(\text{CH}=\text{CHCH}_2)_3(\text{CH}_2)_6\text{CO}_2\text{H}$	flax

11.3 | The Structure of Fats and Oils

Animal **fats** and vegetable **oils** are lipid esters known as *triglycerides*. Recall from *unit 9* that esters are made up of an acid part and an alcohol part.

The acid part of the lipid esters are fatty acids and the alcohol is glycerol.



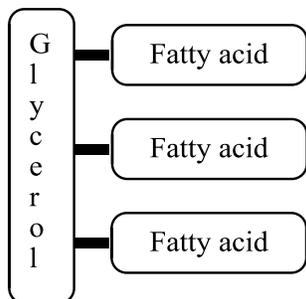
Glycerol (older name glycerin) is a small chain alcohol containing three carbons with a hydroxyl (-OH) group bound at each carbon. A single molecule of glycerol can react with up to three fatty acid molecules, one at each OH group.

A **monoglyceride** contains one fatty acid attached to glycerol, a **diglyceride** contains two fatty acids and a **triglyceride** contains three fatty acids.

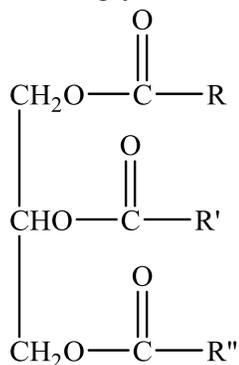
Most naturally occurring triglycerides contain three different fatty acids and are called mixed triglycerides. Although the fatty acid chain length can vary in mixed triglycerides, they tend to be all saturated or unsaturated. Triglycerides containing saturated fatty acid chains and unsaturated chains on the same molecule are rare.

The type of fatty acid present in a triglyceride influences its physical appearance. **Fats** are triglycerides containing saturated fatty acids and are *solids* at room temperature, i.e.: lard, while **oils** contain unsaturated fatty acids and are *liquids* at room temperature. This is a direct result of the packing ability of the triglycerides. Saturated chains can pack close together because there are no carbon-carbon double bonds to disrupt the linear nature of the chains. The result is a solid. In contrast, unsaturated chains are “kinked” by a *cis*-conformation of the carbon-carbon double bond. This prevents unsaturated chains from packing closely together. The result is a liquid.

Unsaturated fats can also have a *trans*-configuration. Most people generally recognize unsaturated fats as a healthy alternative to saturated fats. However, *trans*-fats are not required by the body and do not promote good health because they have a packing ability comparable to saturated fats. But technically they are unsaturated and therefore can easily mislead consumers seeking unsaturated fats in their daily diet. This is the reason most food producers must now specify the content of *trans*-fat in their products.



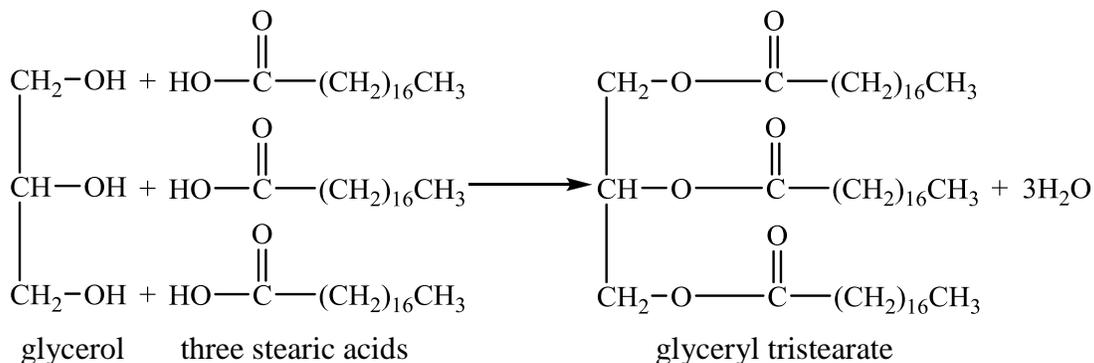
A generalized formula of a triglyceride can be shown as:



Worked Example 11-1

Write an equation for the esterification of glycerol with three molecules of stearic acid.

Solution



11.4 | Chemical Properties of Fats and Oils

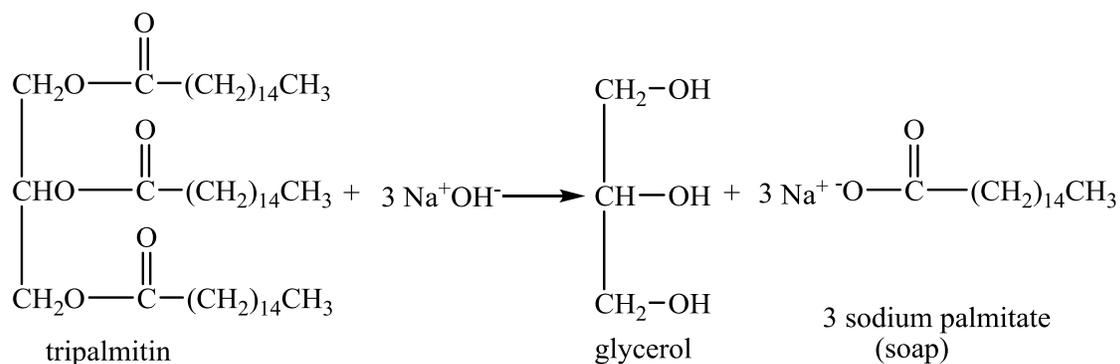
The chemical reactions of fats and oils are the same as those discussed for esters (*unit 9, hydrolysis of esters*) and alkenes (*unit 7, hydrogenation of alkenes*).

1. Saponification (soap making)

Triglycerides (fats or oils) can be hydrolyzed (broken down) to produce glycerol and three fatty acids. When a strong base is used (i.e.: NaOH), glycerol and the sodium salts of the fatty acids are produced. The sodium salts of fatty acids are called **soaps**.



For example, the saponification of glyceryl tripalmitate (tripalmitin, from palm oil) produces sodium palmitate (a soap) according to the following reaction:



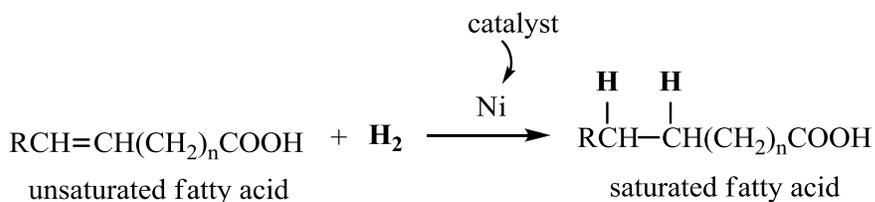
Practice 11-1

A particular glyceride contains myristic acid, palmitoleic acid, and stearic acid. How many moles of NaOH are needed to saponify 3 moles of this triglyceride? Write the complete balance equation.

Answer

2. Hydrogenation

Recall from *unit 7* that double bonds in alkenes can be reduced to single bonds by reacting the alkenes with hydrogen (H_2) in the presence of a catalyst. Carbon-carbon double bonds in unsaturated fatty acids of triglycerides can undergo the same reaction.



In a commercial application called “partial hydrogenation”, vegetable oil is treated with hydrogen, but the reaction is stopped before all of the double bonds have been removed. Complete hydrogenation would produce a very brittle product; whereas “partial hydrogenation” changes the oil to a soft semi-solid fat.

Practice 11-2

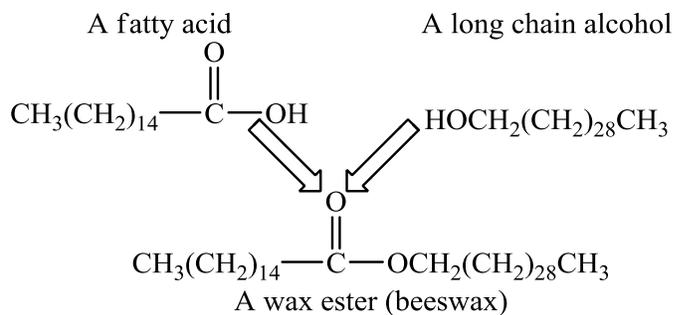
A particular glyceride contains palmitic acid, linoleic acid, and linolenic acid. How many moles of H_2 are needed to completely saturate 1 mol of this triglyceride?

Answer

11.5 | Waxes

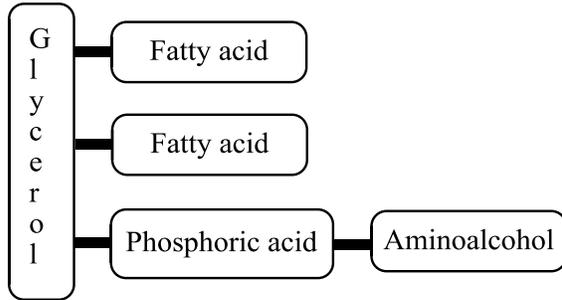
Waxes are simple lipids that, like oils and fats, are also esters of fatty acids. However, the alcohol portion of a wax is derived from long-chain alcohols (12-32 carbons) rather than glycerol. Compare the wax structure below with that of a triglyceride. Note the presence of long hydrocarbon chains on each side of the ester functional group in waxes.

Wax: Fatty acid — Long-chain alcohol



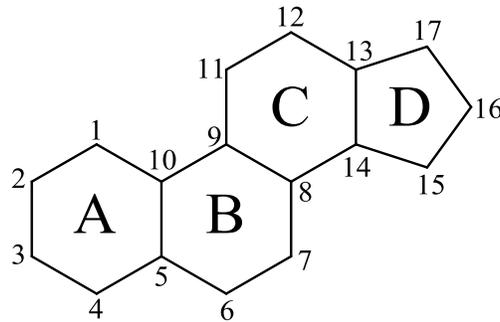
11.6 | Phosphoglycerides

Phosphoglycerides are a family of lipids that are similar to glycerides except that one –OH group of glycerol is replaced by the ester of phosphoric acid and an aminoalcohol.



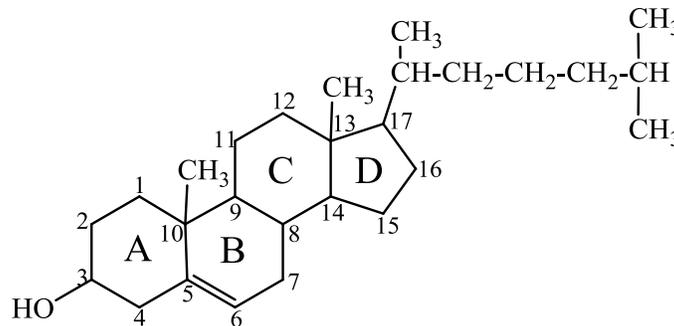
11.7 | Steroids

Structurally, steroids are easily recognized because they all contain a characteristic four-fused ring system; three cyclohexane rings and one cyclopentane ring. Each carbon of a steroid molecule is *numbered* and each ring carries a *letter* designation.



Steroid ring system

The most abundant steroid found in the human body, and the most important, is **cholesterol**.



The *-ol* ending in *cholesterol* indicates an alcohol functional group, this is located on carbon 3.

Notice the following:

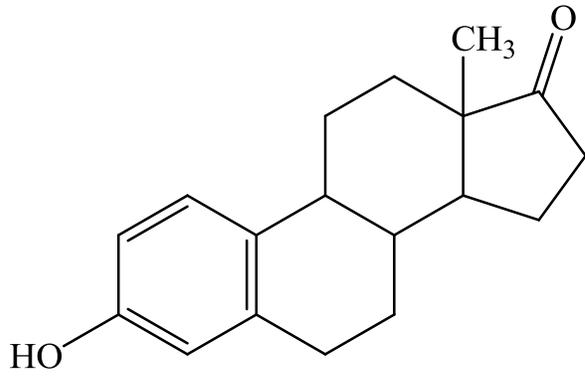
- A hydroxyl ($-OH$) group on carbon 3.
- A methyl ($-CH_3$) group on carbon 10.
- A methyl ($-CH_3$) group on carbon 13.
- A double bond between carbons 5 and 6.
- A carbon chain at carbon 17.

In humans, most steroids function as **hormones**, powerful chemical messengers that transport signals from one cell to another. There are two main classes of steroid hormones: the *sex hormones* and the *adrenocortical hormones*.

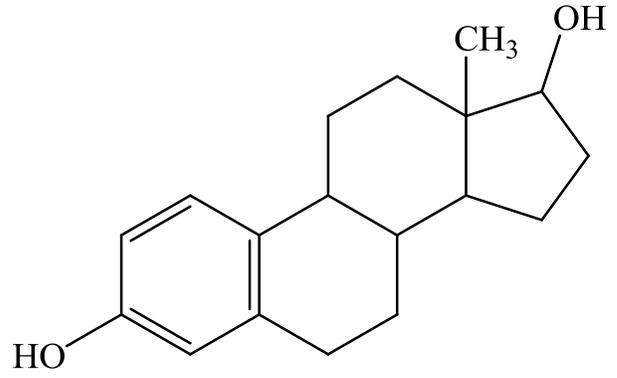
Sex hormones control reproduction and secondary sex characteristics and adrenocortical hormones regulate numerous biochemical processes.

Sex Hormones

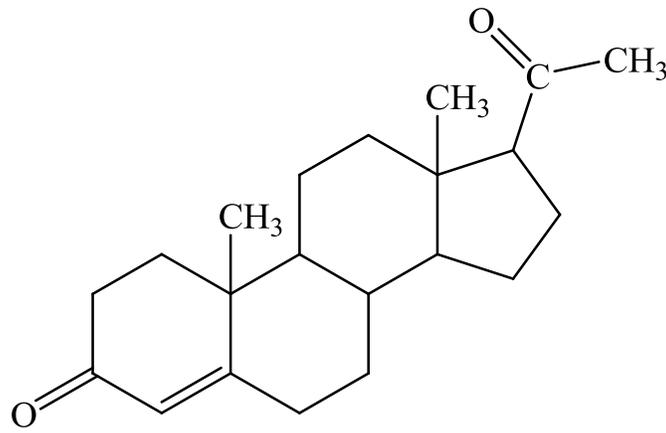
Major groups	Biological effects	Most important
Estrogens	Female sex hormones	Estrone and Estradiol
Progestins	Pregnancy hormones	Progesterone
Androgens	Male sex hormones	Testosterone and Androsterone



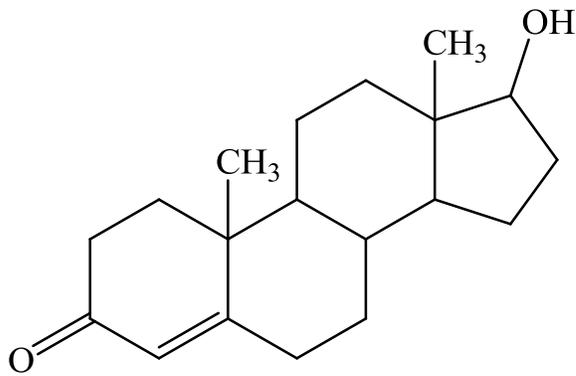
estrone



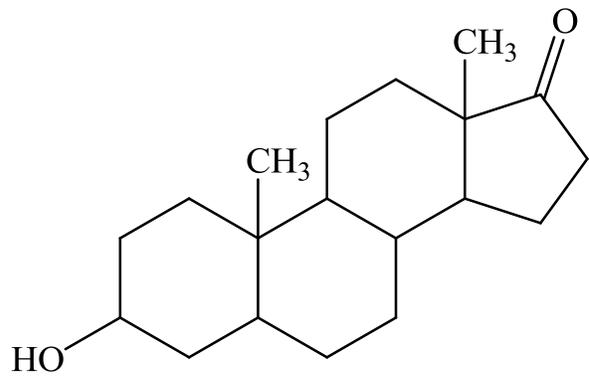
estradiol



progesterone



testosterone



androsterone

PROTEINS

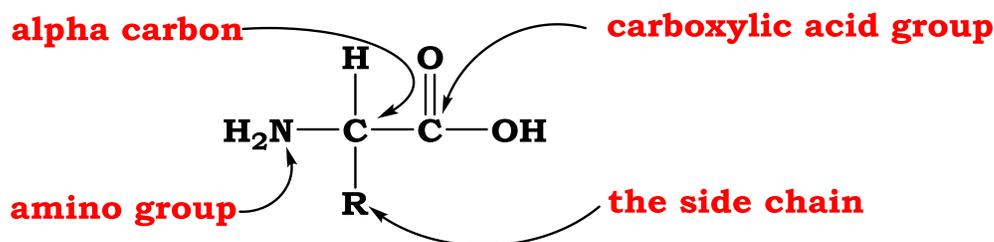
The word "protein" is derived from the Greek word *proteios*, meaning "first", an indication of the importance of these substances. Proteins play an important role in a variety of biological systems, i.e.: oxygen transport, components of skin and hair, muscle movement, as biological catalysts (enzymes), regulate metabolic processes (hormones), and the list goes on and on and on.

Proteins are large complex polymers of amino acids, the monomeric unit of proteins. Amino acids are connected by an amide linkage called a peptide bond. Our study of proteins begins with a survey of amino acids commonly found in proteins.

11.8 | The Amino Acids

Amino acids are organic molecules that contain an amino group and a carboxyl group. The amino acids in proteins are called alpha (α)-amino acids because the amino group is attached to the α -carbon. A carbon connected to any carboxylic acid carbon is termed an α -carbon.

Amino acids are generally represented using the following formula:



All amino acids (except proline) contain $-H$, $-NH_2$, and $-COOH$ bound to the α -carbon. They are differentiated by the side chains (called R-groups) also bound to the α -carbon.

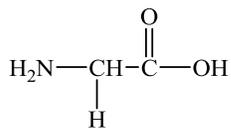
11.9 | Classification of Amino Acids

The difference between amino acids depends on their side-chain R groups because this is the only point of difference (all amino acids contain a carboxyl group, an amino group, and an H). The most important characteristic of R groups is polarity. As a result, amino acids are classified into four groups: nonpolar, polar acidic, polar basic, and polar-neutral amino acids.

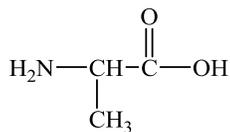
Amino acids are known by common names and each is abbreviated using a three-letter code.

The 20 amino acids commonly used to make proteins are listed in the following table.

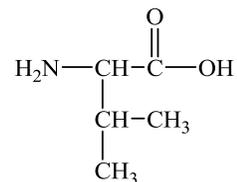
Nonpolar Amino Acids



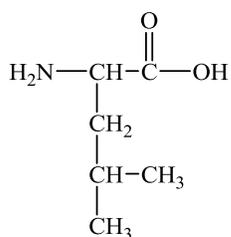
Glycine (Gly)



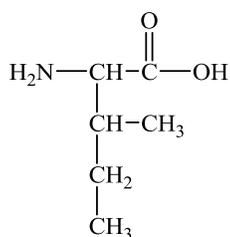
Alanine (Ala)



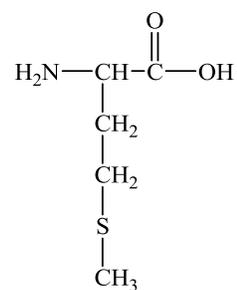
Valine (Val)



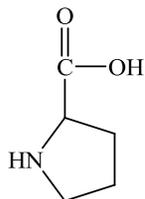
Leucine (Leu)



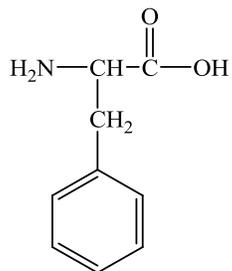
Isoleucine (Ile)



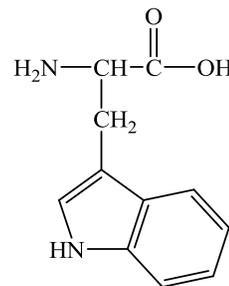
Methionine (Met)



Proline (Pro)

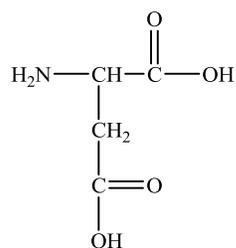


Phenylalanine (Phe)

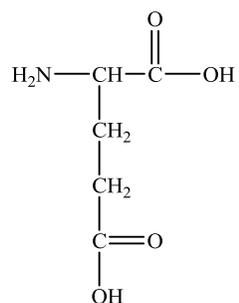


Tryptophan (Trp)

Polar-Acidic Amino Acids

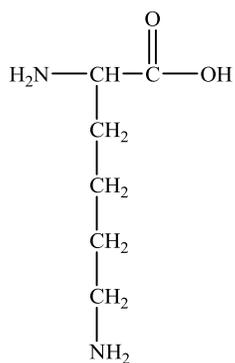


Aspartic acid (Asp)

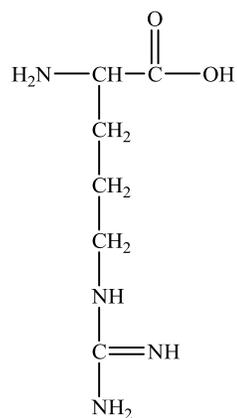


Glutamic acid (Glu)

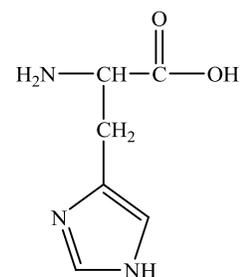
Polar-Basic Amino Acids



Lysine (Lys)

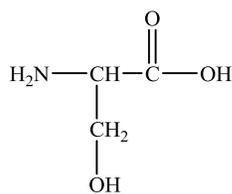


Arginine (Arg)

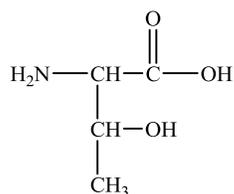


Histidine (His)

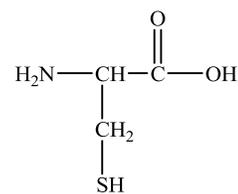
Polar-Neutral Amino Acids



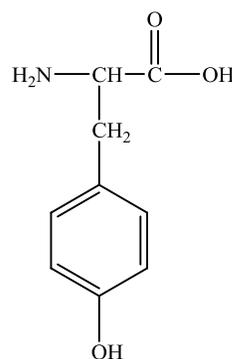
Serine (Ser)



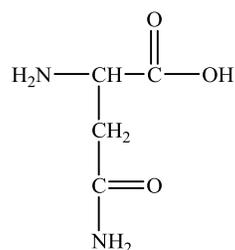
Threonine (Thr)



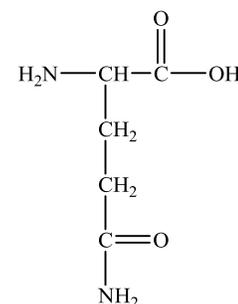
Cysteine (Cys)



Tyrosine (Tyr)



Asparagine (Asn)



Glutamine (Gln)

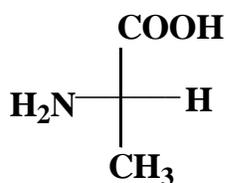
11.10 | Amino Acid Stereoisomers

All α -amino acids, except glycine, are **chiral** because the α -carbon is bound to *four different* groups. Glycine is exempt because it has two hydrogen atoms attached to the α -carbon (recall chiral carbons must have four different groups attached).

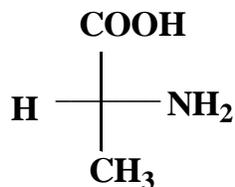
As chiral molecules, amino acids can exist as D or L isomers (recall *unit 10*).

When writing Fischer projections for amino acids, the $-\text{COOH}$ group is always written at the top and the R group at the bottom. If the NH_2 is on the **L**eft we have the L- isomer, if it is on the **R**ight, we have the D- isomer. In biological systems, only "L" isomers are found in proteins.

An example: L-Alanine, and D-Alanine



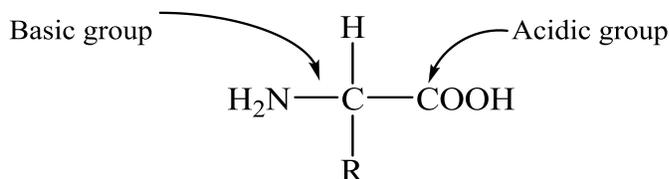
L-Alanine



D-Alanine

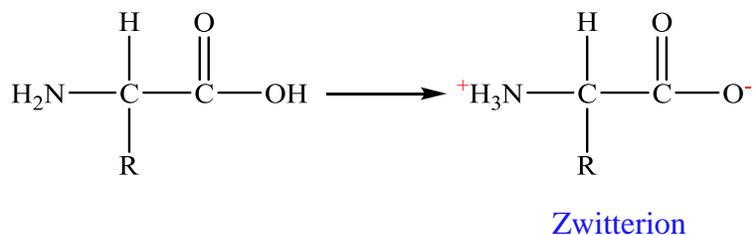
11.11 | Amino Acids as Acids and Bases

Amino acids contain an acidic group (-COOH) and a basic group (NH₂).



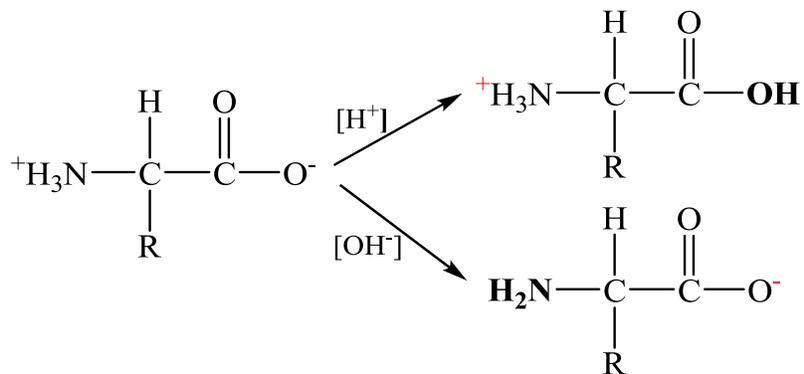
The carboxylic acid (COOH) has a tendency to donate H⁺ and the amine group (NH₂) has a tendency to accept H⁺.

The product of this “internal” acid-base reaction is a dipolar ion (two poles) called a *zwitterion* (from the German meaning “double ion”). When the carboxylic acid donates H⁺ it becomes carboxylate (COO⁻). Therefore, the name indicates whether H⁺ is present (carboxylic **acid**) or absent (carboxylate). For example; glutamic **acid** (H⁺ present on carboxylic acid) and glutamate (H⁺ absent).



Zwitterions are simultaneously electrically charged and electrically neutral. They contain positive and negative charges that cancel resulting in a net charge of zero. Zwitterions are the neutral form of the amino acid despite the presence of “ion” in the name.

Zwitterions gain H⁺ in acidic solutions and lose H⁺ in basic solutions.



At a certain pH the positive and negative charges of an amino acid are equal resulting in an overall net charge of zero. This pH is called the **isoelectric point** (pI), where only the neutral form of the amino acid (zwitterion) exists at the pI.

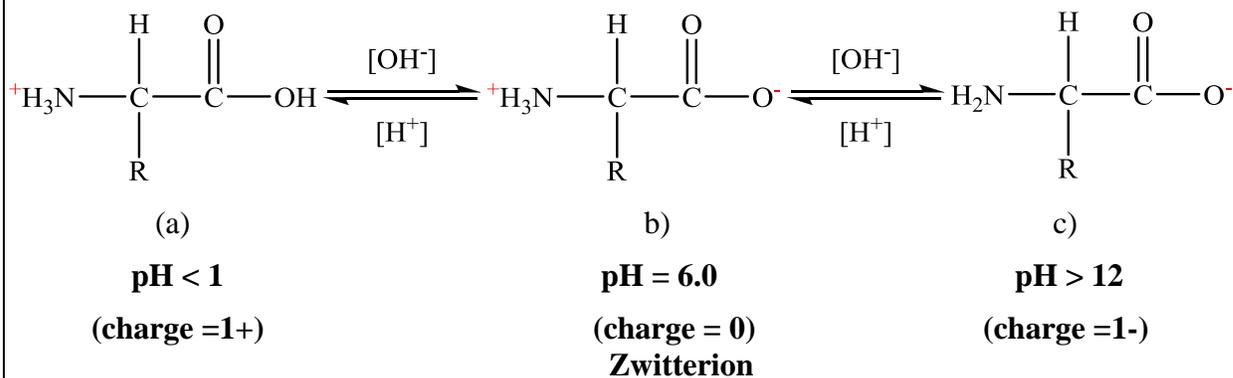
Worked Example 11-2

The pI value for an amino acid is 6.0. Draw the general form of the amino acid that predominates in solution at each of the following pH values:

- a) pH < 1 b) pH = 6.0 c) pH > 12

Solution

At low pH (pH < 1) both amino and carboxyl groups are protonated giving an overall charge of 1+. At high pH (pH > 12) both groups have lost their protons giving an overall charge of 1-. Zwitterion present at pH = pI.



Practice 11-3

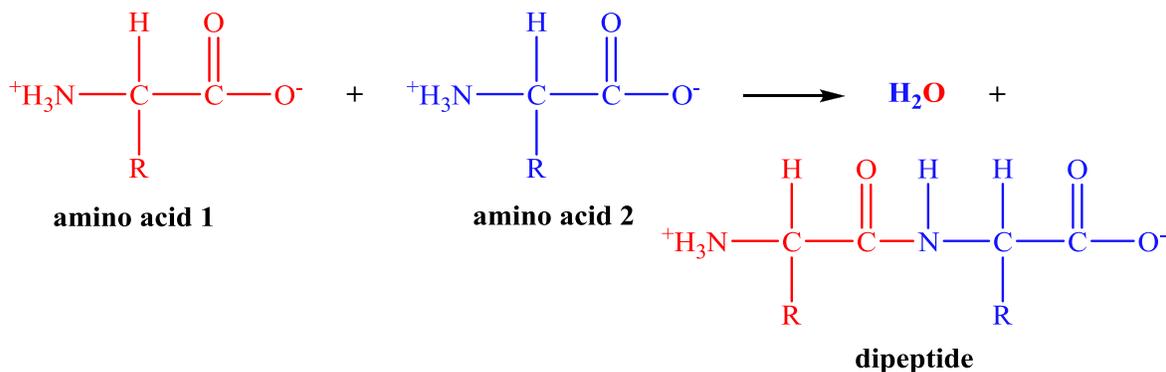
Draw the structure of alanine in:

- a) Strongly acidic solution
b) Strongly basic solution

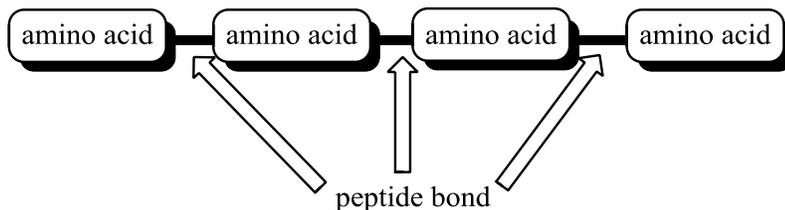
Answer

11.12 | The Peptide Bond

Individual amino acids in a protein molecule are linked by **peptide bonds**. A **peptide bond** forms when a carboxylic acid from one amino acid reacts with the amino group of another amino acid. Peptide bond is the name that biochemists give to the amide bond.



If three amino acid residues are present in a molecule, it is a tripeptide; if four, a tetrapeptide; and so on. It is worth noting that once amino acids are connected, we no longer call them “amino acids”, instead, we refer to the bonded units as “residues.”



All peptide chains will have an amino group at one end (a free, unbound $-\text{NH}_3^+$) and a carboxylate at the other (a free $-\text{COO}^-$). By convention, we draw peptides and proteins with the **N-terminal** (unreacted or free amino group) on the left end of the peptide chain and the **C-terminal** (the carboxylate group) on the right end of the polypeptide.

Peptides are named by listing the amino acid residues in order from the N- to C-terminal. For example, a dipeptide could be written as (Ala-Gly), a tripeptide as (Thr-Gly-Ala), and a pentapeptide as (Lys-His-Ala-Thr-Gly).

Worked Example 11-3

Explain why the notation Gly-Ala and Ala-Gly represent two different molecules.

Solution

Gly is the N-terminal end of Gly-Ala and Ala is the N-terminal end of Ala-Gly.

Practice 11-4

Write the structure of tripeptide Gly-Val-Ser.

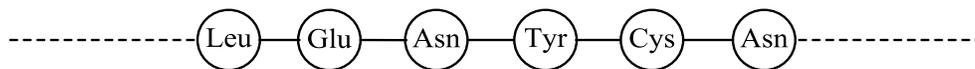
Answer

11.13 | Protein Structure

In general, proteins are defined as polypeptide chains having 50 or more amino acids. Protein structure is described using four levels of organization: primary, secondary, tertiary, and quaternary structure.

The Primary Structure of Proteins

The **primary structure** of a protein is simply the sequence of amino acids that makes up the peptide chain. We show a segment of a protein that contains leucine, glutamine, asparagine, tyrosine, cysteine, and asparagines as:



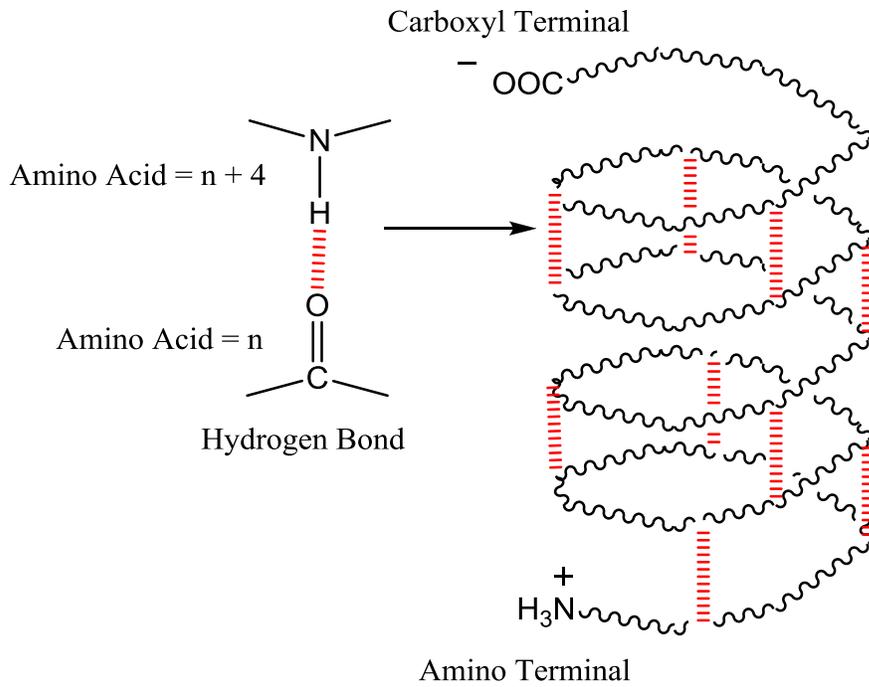
The Secondary Structure of Proteins

Proteins fold or align in a consistent manner which generates specific repeating patterns. These patterns are referred to as **secondary structures**.

There are two common types of protein secondary structures: the **alpha helix** (α -helix) and the **beta pleated sheet** (β -pleated sheet).

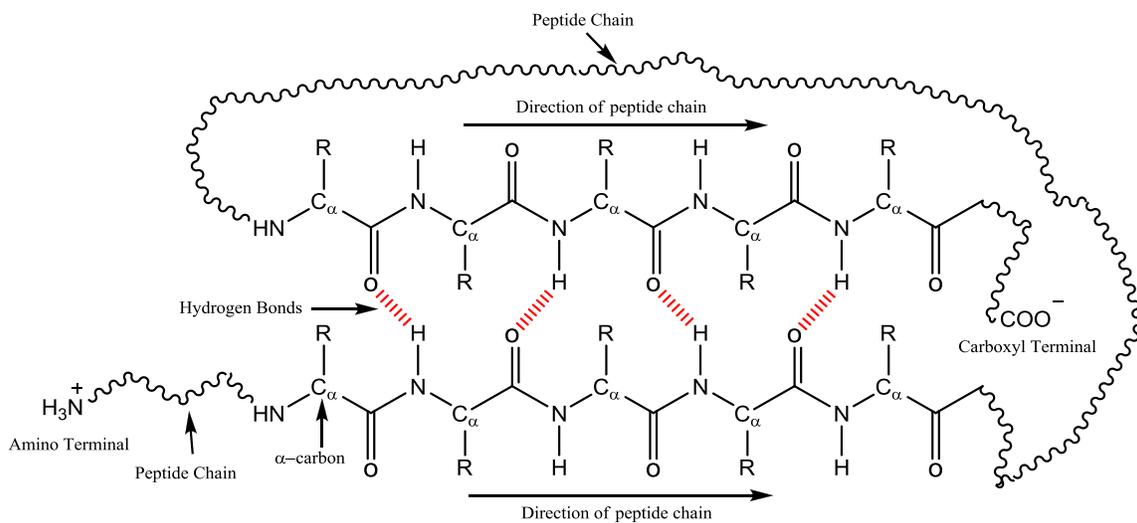
Hydrogen bonding is responsible for the secondary structure of proteins.

α -helix: An α -helix is basically a spring-like structure stabilized by hydrogen bonds formed between a carbonyl oxygen and an amino hydrogen separated by 4 amino acid residues. This bonding holds the polypeptide chain in the helical shape

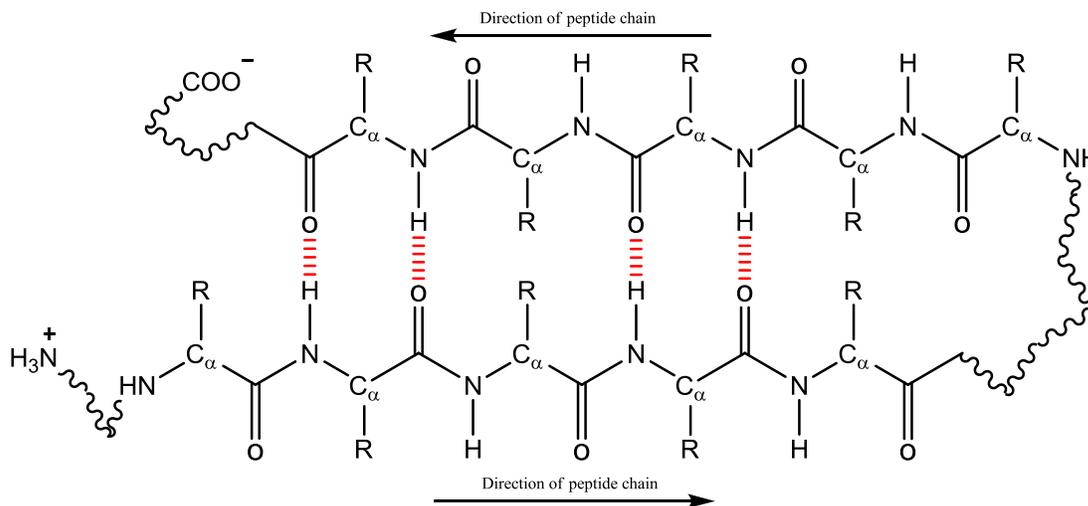


β -pleated sheet: A less common type of secondary structure is called a β -pleated sheet. β -pleated sheets form when portions of the polypeptide chain align side by side in a sheet-like array held together by hydrogen bonds. The hydrogen bonds are again formed between carbonyl oxygens and amino hydrogens, but unlike α -helices, the residues may be separated by great distances on the polypeptide chain. The direction of the polypeptide chain is always determined from the amino terminal and follows the repeating pattern of $N-C_{\alpha}-C_{(carbonyl)}-N-C_{\alpha}-C_{(carbonyl)}-N-C_{\alpha}-C_{(carbonyl)}$. The sheets may be parallel or antiparallel depending on the direction of the chains involved.

A parallel β -pleated sheet. Note the chains involved run in the same direction.



An antiparallel β -pleated sheet.



The Tertiary Structure of Proteins

The overall three-dimensional shape that results from attractive forces between amino acid *side chains* is referred to as a tertiary structure of proteins. Tertiary structures are the first form of functional proteins and are formed by interacting secondary structures.

The Quaternary Structure of Proteins

The highest level of protein organization is called the quaternary structure. It is formed by interacting tertiary structures and it represents some of the most complex proteins known. Quaternary structures are typically composed of two or more protein subunits (tertiary structures). Non-protein components may also be present. Hemoglobin is a tetramer (four subunits) containing two copies of one polypeptide and two copies of another: two identical chains of 141 amino acid residues each (alpha) and two identical chains of 146 residues each (beta).

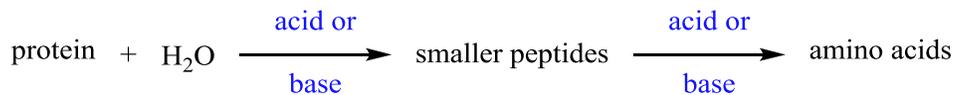
11.14 | Denaturation of Proteins

Denaturation is the partial or complete disorganization of a protein's characteristic three-dimensional shape as a result of disruption of its secondary, tertiary, and quaternary structural interactions. Denaturation renders the protein nonfunctional and can be caused by a variety of factors, i.e.; heat, acids, bases, organic compounds, heavy metal ion, and mechanical agitation.

11.15 | Protein Hydrolysis

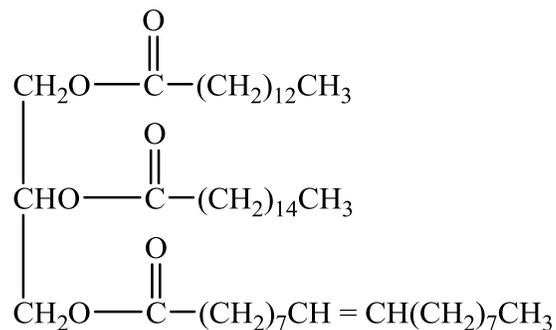
Our body's digestive system must break down proteins into amino acid units for them to be absorbed from the intestine into the blood. Once absorbed, amino acids can be used to synthesize the human proteins.

The process of protein digestion involves hydrolysis reactions that are catalyzed by enzymes.



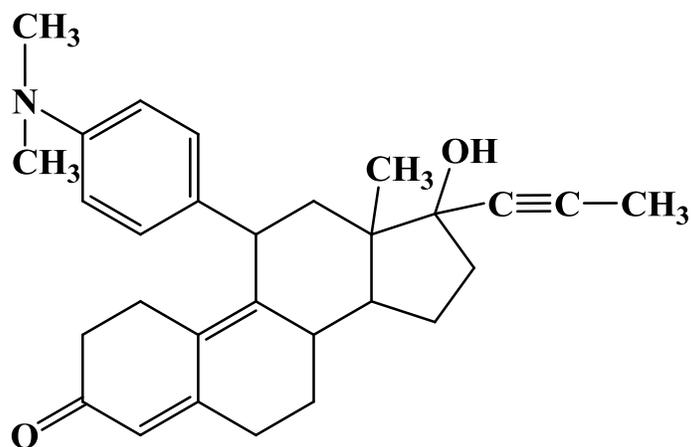
Homework Problems

- 11.1 What are the products when the following triglyceride undergoes saponification with NaOH?



- 11.2 Write an equation for the full hydrogenation of a triglyceride containing glycerol, oleic acid, linoleic acid, and palmitic acid. How many moles of H_2 are required to completely hydrogenate one mole of this triglyceride?

- 11.3 A drug called RU486 has the following structure:



RU486

- How is the structure of RU486 similar to that of progesterone?
- How do the two structures differ?

- 11.4 Use the three-letter abbreviation to name the amino acid(s) having
- An alcohol functional group
 - An acidic side group
 - An α -amino group in a ring
 - A benzene ring
- 11.5 The pI value for amino acid cysteine is 5.1. Draw the structure of cysteine that predominates in solution at each of the following pH values:
- pH < 1
 - pH = 5.1
 - pH > 12
- 11.6 There are a total of six different amino acid sequences for a tripeptide containing one molecule each of alanine, leucine, and glutamic acid. Using three-letter abbreviations for the amino acids, draw the six possible sequences of amino acids.
- 11.7 Suppose a sample of protein is denatured and another sample of the same protein is completely hydrolyzed. Compare the final products of these processes.