

Міністерство освіти і науки України ДЕРЖАВНИЙ БІОТЕХНОЛОГІЧНИЙ УНІВЕРСИТЕТ Факультет ветеринарної медицини Кафедра фізіології та біохімії тварин

# В. О. Приходченко, Н. І. Гладка, О. М. Денисова

# NITROGEN-CONTAINING COMPOUNDS

# НІТРОГЕНОВМІСНІ СПОЛУКИ

Навчально-методичний посібник

Харків 2023

## Міністерство освіти і науки України ДЕРЖАВНИЙ БІОТЕХНОЛОГІЧНИЙ УНІВЕРСИТЕТ Факультет ветеринарної медицини Кафедра фізіології та біохімії тварин

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для здобувачів другого (магістерського) рівня вищої освіти денної форми навчання зі спеціальності 211 Ветеринарна медицина

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Навчальний посібник призначений для аудиторної роботи іноземних студентів, які навчаються англійською мовою за спеціальністю "Ветеринарна медицина". У посібнику викладено основні питання хімії, зокрема біоорганічної. Значну увагу приділено хімічній структурі, номенклатурі, фізичним та хімічним властивостям амідів, амінів та різних груп амінокислот, які зустрічаються в природі та є структурними компонентами живих організмів.

# УДК 54(07)

## Відповідальний за випуск О. М. Денисова, канд. біол. наук.

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# **BRIEF CONTENTS**

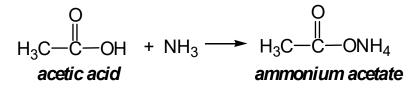
Nitrogen-Containing Compounds	5
1. Amides	5
2. Amines	8
3. Amino Acids	166
Recommended books	31

# 1. Amides

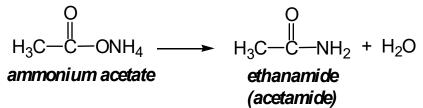
Many organic compounds contain nitrogen. The *amines and amides* are the two major classes of *nitrogencontaining compounds*. Amines isolated from plants form a group of compounds called *alkaloids*. Thousands of alkaloids have been isolated. Many of these compounds exhibit physiological activity. Examples of common alkaloid compounds include *quinine*, used in the treatment of malaria; *strychnine*, a poison; *morphine*, a narcotic; and *caffeine*, a stimulant. Many other drugs are also nitrogen-containing compounds. Amides are nitrogen derivatives of carboxylic acids. These compounds are found as polymers, both commercially, as in nylon, and biologically, as in proteins.

### **Amides: Nomenclature and Physical Properties**

Carboxylic acids react with ammonia to form ammonium salts:



When heated, ammonium salts of carboxylic acids lose a molecule of water and are converted to *amides*:



In amides, the carbon atom of a carbonyl group is bonded directly to a nitrogen atom of a  $-NH_2$ , -NH-R, or  $-N < R_2^R$  group. The amide structure occurs in numerous substances, including proteins and some synthetic polymers, such as nylon.

Following are the rules for forming both the IUPAC and the common names for amides:

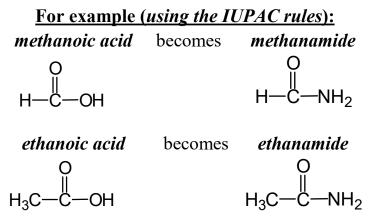
#### **IUPAC Rules for Naming Amides**

**Step 1.** To establish the parent name, identify the longest continuous carbon chain that includes the amide group.

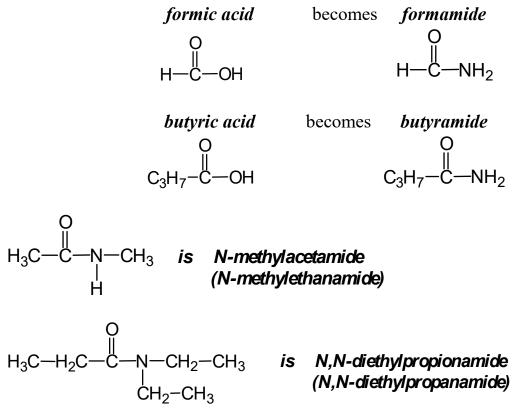
**Step 2.** Drop the *-oic acid* ending from the name of the carboxylic acid containing the same-length carbon chain as the amide.

Step 3. Add the suffix *–amide*.

**Step 4.** When the nitrogen atom of the amide is bonded to an alkyl or other group, the group is named as a prefix to the amide name proceded by the letter *N*, such as *N*-methyl.



In a like manner, the common names for amides are formed from the **<u>common</u> <u>names</u>** of the corresponding carboxylic acids, by dropping the *-ic* or *-oic acid* ending and adding the suffix *-amide*. Thus,



## **Chemical Properties of Amides**

Hydrolysis is one of the more important reactions of amides. This type of

reaction is analogous to the hydrolysis of carboxylic acid esters. The amide is cleaved into two parts, the carboxylic acid portion and the nitrogen-containing portion. As in ester hydrolysis, this reaction requires the presence of a strong acid or a strong base for it to occur in the laboratory. Amide hydrolysis is accomplished in living systems during the degradation of proteins by enzymatic reactions under much milder conditions. *Hydrolysis of an unsubstituted amide in an acid solution produces a carboxylic acid and an ammonium salt:* 

$$C_{3}H_{7}-C-NH_{2} + H_{2}O + HCI \xrightarrow{t^{\circ}} C_{3}H_{7}-C-OH + NH_{4}CI$$
  
butyramide butyric acid

Basic hydrolysis results in the production of ammonia and the salt of a carboxylic acid:

$$\begin{array}{c} O & O \\ \parallel \\ C_{3}H_{7}-C-NH_{2} + NaOH \xrightarrow{t^{\circ}} C_{3}H_{7}-C-ONa + NH_{3} \\ \textbf{butyramide} & \textbf{sodium butyrate} \end{array}$$

After a meal, proteins are digested by successive amide hydrolysis. This process starts in the stomach, where proteins are made smaller and some amino acids are released. Because the stomach contains HCl, the amino acids are liberated as carboxylic acids and amine salts. For example, an amide bond between two amino acids is hydrolyzed as follows:

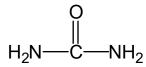
 $\begin{array}{c} R & O & R & O \\ - + & | & | & | \\ CI H_3N-CH-C-NH-CH-C-OH + H_2O + HCI \longrightarrow 2 CI H_3N-CH-C-OH \\ (where R can be various groups of atoms) \end{array}$ 

Protein digestion is completed in the small intestine, and the amino acids are absorbed into the bloodstream. Because the small intestine is not acidic, amino acids take the form of carboxylates and amine salts. For example, an amide bond between two amino acids is hydrolyzed as follows:

$$\begin{array}{c} R & O & R & O \\ + & \parallel & \parallel & \parallel \\ H_3N-CH-C-NH-CH-C-OH + H_2O \longrightarrow 2 H_3N-CH-C-O \\ (where R can be various groups of atoms) \end{array}$$

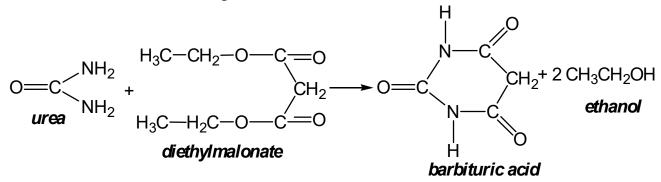
#### Urea

The body disposes of nitrogen by the formation of a diamide known as **urea**:



Urea is a white solid that melts at 133°C. It is soluble in water and therefore is excreted from the body in the urine. The normal adult excretes about 30 g of urea daily.

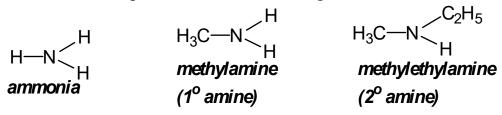
Urea is a common commercial product as well. It is widely used in fertilizers to add nitrogen to the soil or as a starting material in the production of plastics and barbiturates. Here's an example:

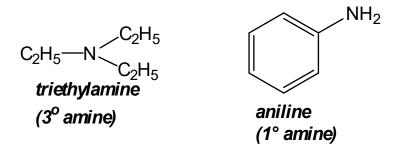


The various barbiturate drugs have certain organic groups substituted for the hydrogen atoms on the CH<sub>2</sub>. When two ethyl groups replace these hydrogen atoms, the compound is known as *barbital*, which is a controlled substance (depressant) and a hypnotic. The unsubstituted barbituric acid has no hypnotic properties. There are many barbiturate drugs.

# 2. Amines

<u>Nomenclature and Physical Properties.</u> An amine is a substituted ammonia molecule with basic properties and has the general formula RNH<sub>2</sub>, R<sub>2</sub>NH, or R<sub>3</sub>N, where R is an alkyl or an aryl group. Amines are classified as primary (1°), secondary (2°), or tertiary (3°), depending on the number of hydrocarbon groups attached to the nitrogen atom. Some examples include the following:





## **Naming Amines**

The IUPAC System *names simple aliphatic amines* by using the name of the alkane (omitting the final *-e*) and adding the ending *-amine*. The NH<sub>2</sub> and side chains are located by number on the parent carbon chain, as shown here:

		2-propanamine
ethanamine	1-propanamine	NH2
$CH_3CH_2NH_2$	$CH_3CH_2CH_2NH_2$	$H_3C$ — $CH$ — $CH_3$

Secondary and tertiary amines are named as N-substituted primary amines by using the longest continuous carbon chain as the parent name. A capital N in the name indicates the alkyl groups attached to the nitrogen atom. Here are some examples:

$$H_{3}C - NH - CH_{2} - CH_{2} - CH_{3} \qquad N-methyl-1-propanamine$$

$$H_{3}C - N - CH_{2} - CH_{2} - CH_{2} - CH_{3} \qquad N-ethyl-N-methyl-1-butanamine$$

$$CH_{3} - CH_{2} - CH_{2} - CH_{2} - CH_{2} - CH_{3} \qquad N-ethyl-N-methyl-1-butanamine$$

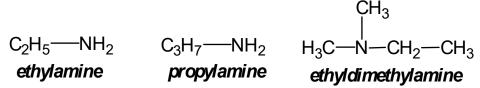
$$H_{3}C - N - CH_{2} - CH_{2} - CH_{2} - CH_{3} - CH_{3}$$

In naming *diamines*, the final *-e* of the alkane name is not omitted, as is shown here:

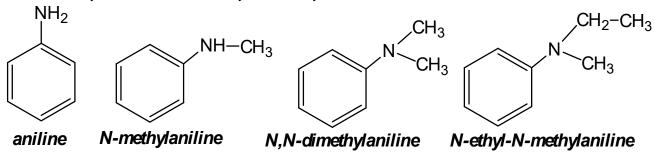
$$H_2N$$
— $CH_2$ — $CH_2$ — $CH_2$ — $NH_2$  *1,3-propanediamine*

$$H_2N-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-NH_2$$
 1,6-hexanediamine

Simple amines are most often referred to by their common names. The names for aliphatic amines are formed by naming the alkyl group or groups attached to the nitrogen atom, followed by the ending *-amine*. Thus, CH<sub>3</sub>NH<sub>2</sub> is *methylamine*, (CH<sub>3</sub>)<sub>2</sub>NH is *dimethylamine*, and (CH<sub>3</sub>)<sub>3</sub>N is *trimethylamine*. Other examples are as follows:

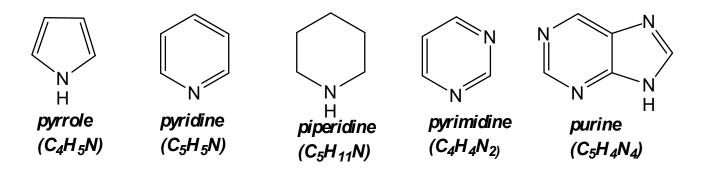


The most important *aromatic amine is aniline* ( $C_6H_5NH_2$ ). Derivatives are named as substituted anilines. To identify substituted aniline in which the substituent group is attached to the nitrogen atom, an *N*- is placed before the group name to indicate that the substituent is bonded to the nitrogen atom, not to a carbon atom in the ring. For example, the following compounds are called *aniline*, *N*-*methylaniline*, *N*,*N*-*dimethylaniline*, and *N*-*ethyl*-*N*-*methylaniline*:



Physiologically, aniline is a toxic substance. It is easily absorbed through the skin and affects both the blood and the nervous system. Aniline reduces the oxygencarrying capacity of the blood by converting hemoglobin to methemoglobin. Methemoglobin is the oxidized form of hemoglobin in which the iron has gone from a + 2 to a + 3 oxidation state.

Ring compounds in which the atoms in the ring are not all alike are known as **heterocyclic compounds**. The most common heteroatoms are oxygen, nitrogen, and sulfur. A number of the nitrogen-containing heterocyclic compounds are present in naturally occurring biological substances such as DNA, which controls heredity. The structural formulas of several nitrogen-containing heterocyclics are as follows:



Amines are capable of hydrogen bonding with water. As a result, the aliphatic amines with up to six carbons are quite soluble in water. Methylamine and ethylamine are flammable gases with a strong ammoniacal odor. Trimethylamine has a "fishy" odor. Higher-molar-mass amines have obnoxious odors. The foul odors arising from dead fish and decaying flesh are due to amines released by bacterial decomposition.

Two of these compounds are diamines, 1,4-butanediamine and 1,5pentanediamine.

Each compound contains two amino groups:

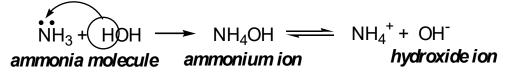
$$H_2N - CH_2 - CH_2 - CH_2 - CH_2 - OH_2 -$$

Simple aromatic amines are all liquids or solids. They are colorless or almost colorless when freshly prepared but become dark brown or red when exposed to air and light.

## **Chemical Properties of Amines**

### 1. Alkaline Properties of Amines

In many respects, amines resemble ammonia in their reactions. Thus, amines are bases and, like ammonia, produce OH ions in water:

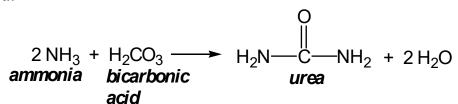


Methylamine and aniline react in the same manner:

$$\begin{array}{rcl} H_{3}C & \longrightarrow & \left[H_{3}C & \longrightarrow & \left[H_{3}C & \longrightarrow & \left[H_{3}C & \longrightarrow & \left[H_{3}C & \longrightarrow & H_{3}\right]^{+} + & OH^{-} \\ \hline methylamine & & methylammonium & hydroxide \\ ion & & ion \end{array}\right]$$

Like ammonia, amines are weak bases. Methylamine is a slightly stronger base than ammonia, and aniline is considerably weaker than ammonia. The pH values for 0.1 *M* solutions are methylamine, 11.8; ammonia, 11.1; and aniline, 8.8.

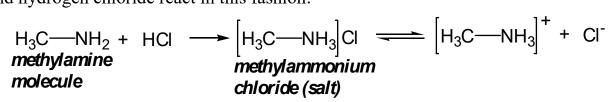
Amines are much more basic than amides, and our bodies recognize this difference. The liver converts ammonia, which is basic and toxic, into the safer diamide, urea:



Urea does not react with water to form the hydroxide ion. Thus, we normally excrete nitrogen without making the blood or urine too basic. In contrast, blood ammonia levels increase during liver cirrhosis, and the increased blood pH that results can be life threatening.

#### 2. Salt Formation

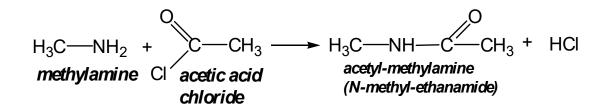
An amine reacts with a strong acid to form a salt; for example, methylamine and hydrogen chloride react in this fashion:



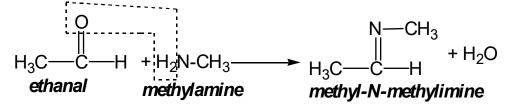
Many amines or amino compounds are more stable in the form of the hydrochloride salt. When the free amine is wanted, the HCl is neutralized to liberate the free amine.

#### 3. Formation of Amides

Primary and secondary amines react with acid chlorides to form substituted amides, as shown here:



4. Amines will react with aldehydes and ketones to form compounds containing the nitrogen analog of a carbonyl group. These compounds are *called imines*.



### 5. Testing for the various types of amines

The reaction between amines and nitrous acid was used in the past as a very neat way of distinguishing between primary, secondary and tertiary amines.

However, the product with a secondary amine is a powerful carcinogen, and so this reaction is no longer carried out at this level.

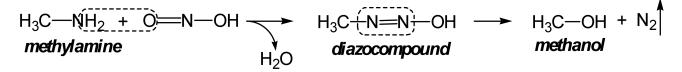
Nitrous acid, HNO<sub>2</sub>, (sometimes written as HO–N=O to show its structure) is unstable and is always prepared *in situ*.

It is usually made by react a solution containing sodium or potassium nitrite (sodium or potassium nitrate (III)) with hydrochloric acid. Nitrous acid is a weak acid and so you get the reaction:

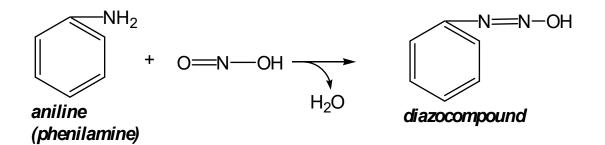
$$HCl + KNO_2 \rightarrow KCl + HNO_2$$

#### a). Primary amines and nitrous acid

Amongst the products you get an alcohol where the  $-NH_2$  group has been replaced by OH. The nitrogen is given off in quantities exactly as suggested by the equation. By measuring the amount of nitrogen produced, you could use this reaction to work out the amount of amine present in the solution.



b). Aromatic primary amines and nitrous acid



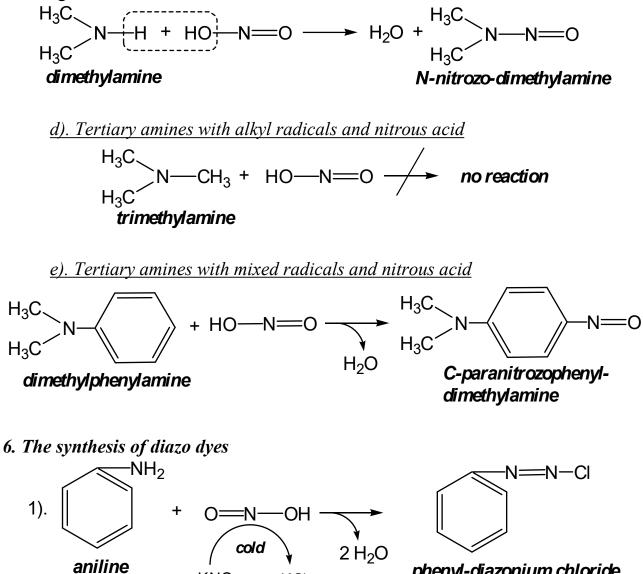
#### c). Secondary amines and nitrous acid

+ KNO<sub>2</sub>

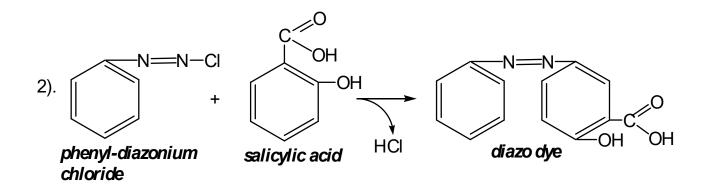
+ 2 HCI

KCI

You get yellow oil called a *nitrosamine*. These compounds are powerful carcinogens – avoid them!



phenyl-diazonium chloride



-N = N - chromophore group (adds color)

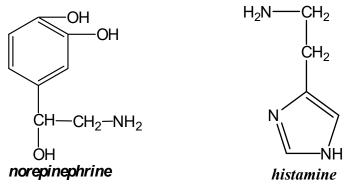
- OH and (or) -COOH auxochromic groups (fixes the dye to the painting object)

## Sources and Uses of Selected Amines

Nitrogen compounds are found throughout the plant and animal kingdoms. Amines, substituted amines, and amides occur in every living cell. Many of these compounds have important physiological effects. Several examples of well-known nitrogen compounds follow.

**Biogenic amines** are derived from amino acids and act as neurotransmitters and hormones in animals. The neurotransmitters are intimately involved in the brain chemistry of feelings and perception. For example, GABA (gamma-aminobutyric acid, NH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>COOH), slows nerve action and can bring relaxation, while *norepinephrine* affects our focus and concentration.

Norepinephrine is also classified as a catecholamine. Biogenic amines that act as hormones include the "fight-or-flight" hormone epinephrine (also a catecholamine) as well as histamine, an important component in allergic reactions.



As these examples illustrate, biogenic amines are central to coordinating many of our body's processes.

## **Learning Check**

1. Write formulas for N-methylbutanamide.

2. Name the following compound and identify this compound as 1°, 2°, or 3° amine:

 $H_3C - CH_2 - CH_2 - NH_2$ 

3. Give the structural formula for the organic product of the following reaction and name the reaction products:

 $H_3C - C - NH_2 + NaOH -$ 

4. Write the formula and name for the product when ethylamine reacts with butyric acid.

5. Write the formula and name for the product when ethylmethylamine reacts with propionic acid.

6. Give the structural formula for the organic product of the following reaction and name the reaction products:

$$C_4H_9 - C - NH_2 + HOH + HCI$$

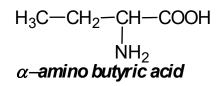
7. Write the formula and name for the product when pentylamine reacts with methanol.

8. Write the formula and name for the product when ethylamine reacts with nitrous acid.

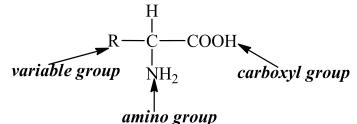
9. Write the formula and name for the product when butylmethylamine reacts with nitrous acid.

# 3. Amino Acids

Each amino acid has at least two functional groups: an amino group (–NH<sub>2</sub>) and a carboxyl group (–COOH). The amino acids found in proteins are called **alpha** ( $\alpha$ ) **amino acids** because the amino group is attached to the first or ( $\alpha$ ) carbon atom adjacent to the carboxyl group. The beta ( $\beta$ ) position is the next adjacent carbon, the gamma ( $\gamma$ ) position the next, and so on. The following formula represents an  $\alpha$ -amino acid:



Amino acids as a whole are represented by this general formula:



The portion of the molecule designated R is commonly referred to as the amino acid side chain. It is not restricted to alkyl groups and may contain (a) open-chain, cyclic, or aromatic hydrocarbon groups; (b) additional amino or carboxyl groups; (c) hydroxyl groups; or (d) sulfur-containing groups.

Amino acids are divided into four groups based on the characteristics of the amino acid side chains. This classification has been chosen to emphasize the importance of the side chains in protein structure.

**1.** *Nonpolar amino acids*: The side chain for each of these amino acids is either aliphatic or aromatic in nature and is hydrophobic. These amino acids don't interact with water well and are commonly found buried in the middle of a protein structure.

**2.** *Polar, uncharged amino acids*: The side chains of these amino acids contain polar bonds from functional groups such as alcohols or amides. These groups are attracted to water and are, thus, hydrophilic. The exterior surface of water-soluble proteins is coated with these amino acids.

**3.** *Acidic amino acids*: Each of these amino acids has a side chain that contains a carboxylic acid. So the side chain can donate a hydrogen ion and is classified as an acid. Under common physiological conditions (pH=7), these side chains lose their hydrogen ions and form carboxylate anions. Acidic amino acids are also known as "negatively charged" amino acids because of this trait.

**4.** *Basic amino acids*: The side chain of each of these amino acids contains nitrogen that can act as a base. These side chains can accept a hydrogen ion under common physiological conditions (pH=7) and become cations. Thus, basic amino acids are also known as "positively charged" amino acids.

The names, formulas, and abbreviations of the common amino acids are given in Table 1. Two of these (aspartic acid and glutamic acid) are classified as acidic, three (lysine, arginine, and histidine) are basic, and the remainder as neutral amino acids.

delus.			Table 1.			
Name	Three-letter	<b>One-letter</b>	Formula			
	abbreviation	abbreviation				
Nonpolar						
Alanine	Ala	A	H <sub>3</sub> C—CH—COOH   NH <sub>2</sub>			
Isoleucine	Ile	Ι	$H_3C$ — $CH_2$ — $CH$ — $CH$ — $COOH$ $\begin{vmatrix} & \\ & \\ & \\ & \\ & \\ & CH_3 & NH_2 \end{vmatrix}$			
Leucine	Leu	L	$H_{3}C$ $CH$ $CH_{2}$ $CH$ $CH_{2}$ $CH$ $COOH$ $H_{3}C$ $H_{2}$			
Methionine	Met	М	$\begin{array}{c c} H_2C &CH_2CHCOOH \\   &   \\ S &CH_3 & NH_2 \end{array}$			
Phenylalanine	Phe	F				
Proline	Pro	Р	N COOH H			
Tryptophan	Try	W	CH <sub>2</sub> —CH-COOH NH <sub>2</sub>			
Valine	Val	V	$H_3C$ $H_3C$ $H_3C$ $H_2$ $H_3C$ $H_2$			
		Polar, Uncha	0			
Asparagine	Asp	N	$ \begin{array}{c} H_2N \longrightarrow CH_2 \longrightarrow C$			
Cysteine	Cys	С	$\begin{array}{c} CH_2 & -CH & -COOH \\   &   \\ SH & NH_2 \end{array}$			
Glutamine	Gln	Q	$H_2N$ — $CH_2$ — $CH_2$ — $CH$ — $COOH$ I $NH_2$			
Glycine	Gly	G	HCHCOOH   NH <sub>2</sub>			

Serine	Ser	S	НОСН <sub>2</sub> СНСООН	
	501	5	 NH <sub>2</sub>	
Threonine	Thr	Т	H <sub>3</sub> CCHCHCOOH     OH NH <sub>2</sub>	
Tyrosine	Tyr	Y		
Acidic				
Aspartic acid	Asp	D	HOOC-CH2-CH-COOH	
	-		I NH <sub>2</sub>	
Glutamic acid	Glu	Е	HOOC—CH <sub>2</sub> —CH <sub>2</sub> —CH—COOH	
			NH <sub>2</sub>	
Basic				
Arginine	Arg	R	$\begin{array}{ c c c c c } HN & HN & H_2C & H_2C & H_2C & HC & COOH \\ H_2N & & & & & \\ H_2N & & \\ $	
Histidine	His	Н	HN NH <sub>2</sub>	
Lysine	Lys	K	$\begin{array}{c c} H_2C - $	

Perhaps the most important role played by amino acids is as the building blocks for proteins. However, selected amino acids also have physiological importance on their own. Many neurotransmitters are amino acids or their derivatives. For example, glycine and glutamic acids function as chemical messengers between nerve cells in some organisms.

## **Essential Amino Acids**

During digestion, protein is broken down into its constituent amino acids, which supply much of the body's need for amino acids. Ten of the amino acids are **essential amino acids** because they are essential to the normal functioning of the human body. Since the body is not capable of synthesizing them, they must be supplied in our diets if we are to enjoy normal health. Some animals require other amino acids in addition to those listed for humans.

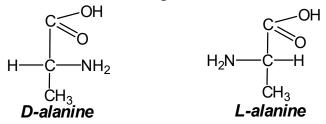
## **Essential Amino Acids for Humans**

Arginine Histidine Isoleucine Leucine Lysine Methionine Phenylalanine Threonine Tryptophan Valine

On a nutritional basis, proteins are classified as *complete* or *incomplete*. A complete protein supplies all the essential amino acids; an incomplete protein is deficient in one or more essential amino acids. Many proteins, especially those from vegetable sources, are incomplete. For example, protein from corn (maize) is deficient in lysine. Lysine, methionine, and tryptophan are now used to enrich human food and livestock feed as a way to extend the world's limited supply of high-quality food protein.

#### **D-Amino Acids and L-Amino Acids**

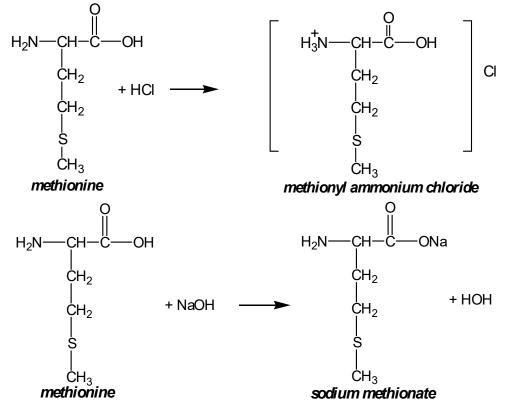
All amino acids, except glycine, have at least one asymmetric carbon atom. For example, two stereoisomers of alanine are possible:



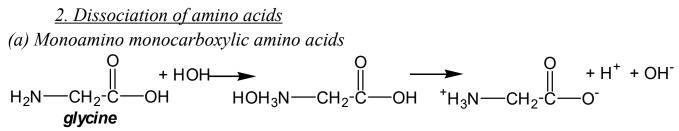
Fischer projection formulas illustrate the D and L configurations of amino acids in the same way they illustrate the configurations of D- and L-glyceraldehyde. The –COOH group is written at the top of the projection formula, and the D configuration is indicated by writing the alpha –NH<sub>2</sub> to the right of carbon 2. The L configuration is indicated by writing the alpha –NH<sub>2</sub> to the left of carbon 2. Although some **D- amino acids** occur in nature, only **L-amino acids** occur in proteins.

### I. Amphoterism

<u>1. Amino acids are *amphoteric* (or *amphiprotic*); that is, they can react either as an acid or as a base. For example, with a strong base such as sodium hydroxide, alanine reacts as an acid:</u>

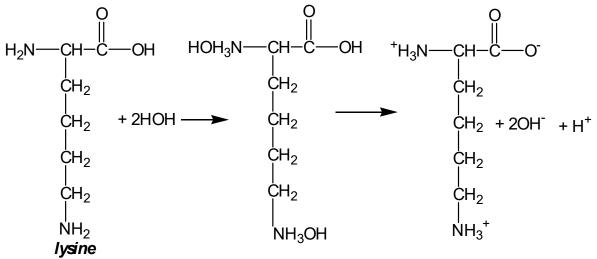


Amino acids are classified as basic, neutral, or acidic, depending on whether the ratio of  $-NH_2$  to -COOH groups in the molecules is greater than 1:1, equal to 1:1, or less than 1:1, respectively. Furthermore, this ratio differs from 1:1 only if the amino acid side chain (R–) contains an additional amino or carboxyl group. For example, if the side chain contains a carboxyl group, the amino acid is considered acidic. Thus, the R– group determines whether an amino acid is classified as basic, neutral, or acidic.



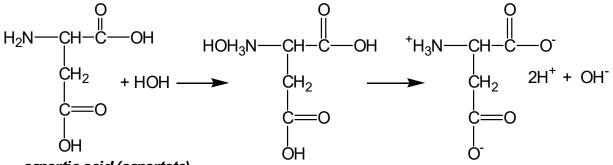
Proteins, in which this type of acids predominate, are called neutral, the pH of the solutions is  $\approx 7$ .

(b) Diamino monocarboxylic amino acids



Proteins, in which this type of acid predominates, are called alkaline, the medium is alkaline, pH>7.

(c) Monoamino dicarboxylic amino acids

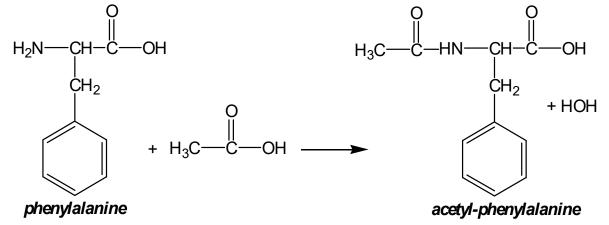


## aspartic acid (aspartate)

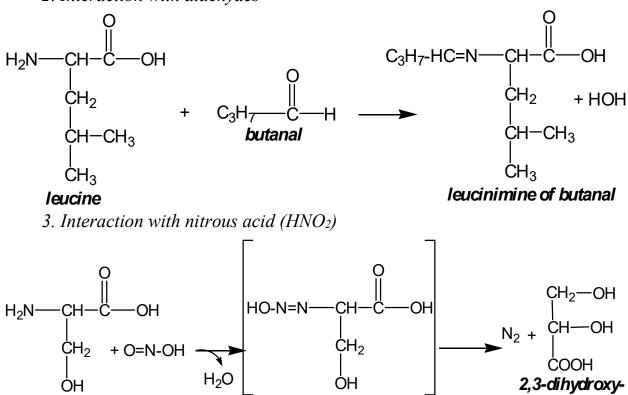
Proteins, which mainly contain dicarboxylic acids, are called acidic, the medium is acidic, pH < 7.

## II. Properties of amino acids as amines

1. Interaction with carboxylic acids (acylation reaction)



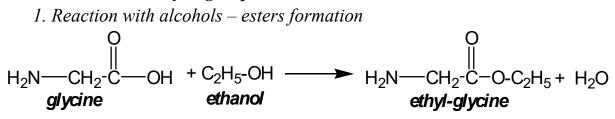
2. Interaction with aldehydes



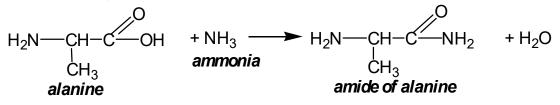
 $\alpha$ -Amino acids react with nitric (III) acid (nitrous acid) at room temperature to produce hydroxy acids and nitrogen gas. The amount in moles of amino groups in a sample can be measured by collecting and measuring the volume of nitrogen gas released.

#### III. Reactions on carboxylic group:

serine



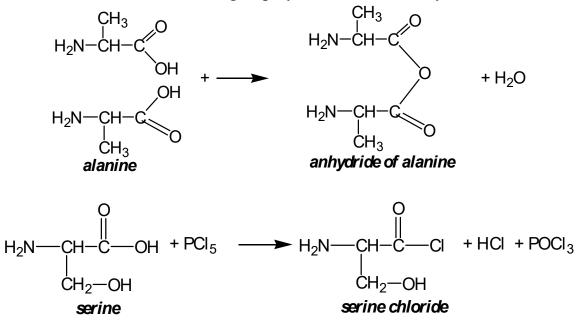
2. Reaction with ammonia – amides formation. The amides of aspartic and glutamic acids, asparagine and glutamine, play an important role in the transport of ammonia in the body.



23

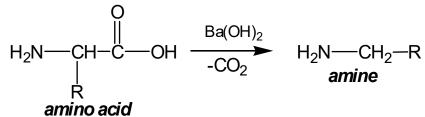
propanoic acid

*3. Formation of halogenanhydrides and anhydrides* (like carbonyl acids). Before this reaction blocked aminogroup by formation of N-acylderivatives.

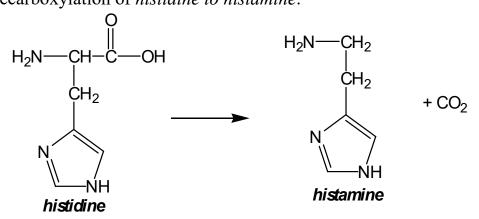


### **IV. Decarboxylation**

Amino acids may be decarboxylated by heat, acids, bases or specific enzymes to the primary amines:

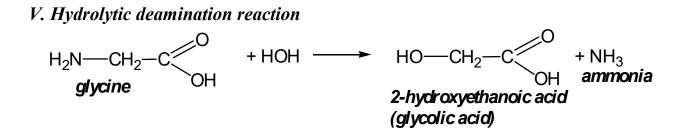


Some of the decarboxylation reactions are of great importance in the body, for example, decarboxylation of *histidine to histamine*:



In the presence of foreign protein introduced into the body, very large quantities of histamine are produced in the body and allergic reactions become

evident. In extreme cases shock may result. The physiological effects of histamine may be neutralized or minimized by the use of chemical compounds known as antihistamines.



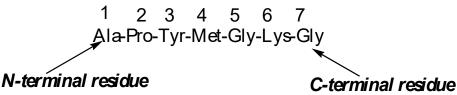
## VI. Peptide formation

Two amino acids can react in a similar way – the carboxyl group of one amino acid reacts with the amino group of the other amino acid.

In amino acid chemistry, amide bonds that link amino acids together are given the specific name of peptide bond. A **peptide bond** is a bond between the carboxyl group of one amino acid and the amino group of another amino acid. Under proper conditions, many amino acids can bond together to give chains of amino acids containing numerous peptide bonds.

If three amino acid residues are included in a molecule, it is a tripeptide; if four, a tetrapeptide; if five, a pentapeptide; and so on. Peptides containing up to about 40–50 amino acid units in a chain are called **polypeptides**. The units making up the peptide are amino acids, minus the elements of water, and are referred to as *amino acid residues* or, simply, residues. Still longer chains of amino acids are known as proteins.

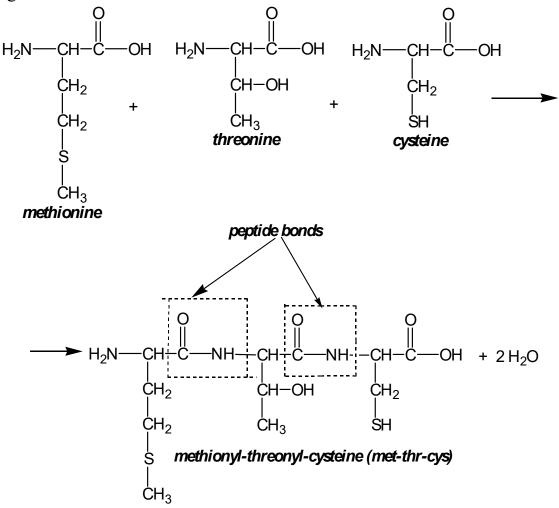
In linear peptides, one end of the chain has a free amino group and the other end a free carboxyl group. The amino-group end is called the *N-terminal residue* and the other end the *C-terminal residue*:



The sequence of amino acids in a chain is numbered starting with the Nterminal residue, which is written on the left. The C-terminal residue is written on the right.

Peptides are named as acyl derivatives of the C-terminal amino acid, with the C-terminal unit keeping its complete name. The *-ine* ending of all but the C-terminal

amino acid is changed to -yl, and these are listed in the order in which they appear, starting with the N-terminal amino acid:



If three different amino acids react – for example, glycine, alanine, and threonine – six tripeptides, in which each amino acid appears only once, are possible:

Gly-Ala-Thr	Ala-Thr-Gly	Thr-Ala-Gly
Gly-Thr-Ala	Ala-Gly-Thr	Thr-Gly-Ala

It is clearly evident that a particular sequence of amino acid residues is essential for proper polypeptide function. This sequence aligns the side-chain characteristics (large or small; polar or nonpolar; acidic, basic, or neutral) in the proper positions for a specific polypeptide function.

## **Types of peptides**

1. Dipeptides: compound formed when two amino acids linked by 1 peptide bond.

Examples: Carnosine ( $\beta$ -alanyl-L-histidine), Anserine ( $\beta$ -alanyl-N-methylhistidine), Aspartame (Asparaginyl-phenylalanine).

2. Tripeptides: compound formed when three amino acids linked by 2 peptide bond.

Examples: Glutathione (Glutamyl-cystinyl-glycine), Ophthalmic acid (L-γ-Glutamyl-α-L-amino butyryl-glycine).

**3. Oligopeptides:** compound formed when more than 2 and less than 20 amino acids are linked by peptide bonds.

Examples: Tetrapeptide; Tulfsin (thrionyl-lysyl-prolyl-arginine), Endomorphin-1 (Tyrosyl-prolyl-tryptophyl-phenylalanine), Amanitin (Decapeptide), Netropsin.

**4. Polypeptides:** compound formed when more than 20 amino acids are linked by peptide bond.

Examples: Insulin, Growth hormone

# **Functions of peptides**

> Precursor of protein: Peptides are precursor of protein.

➤ As alkaloids: Peptides are also the constituents of alkaloids (Alkaloids are group of secondary metabolites such as Nicotin, Caffeine, Terpentine, Ergotamine etc).

➤ As Antimicrobial agent: Peptides possess antibacterial properties. Secondary metabolites of bacteria and fungi have antimicrobial activity. Eg. Penicillin G (valine- cystein-phenylacetic acid)

≻ As Hormones: Peptides acts as hormones eg. Insulin, Somatostatin, vasopressin etc

## > Peptides also act as growth factors.

≻ As anti-oxidant: Peptide functions as anti-oxidant. They scavenge free radicals. Eg. Carnosine

> Clinical diagnosis: hyper secretion of peptide in urine is indicator for mental state of disturbance like depression, schizophrenia etc.

➤ As structural component: peptides form long chains creating structural protein which provides support to body. Eg. Keratin, collagen

# Learning Check

- 1. Write formulas for
- (a) N-ethylbutanamide
- (b) N-methyl-2-methylpropanamide
- (c) *N*,*N*-diethylhexanamide

2. Give the products of the acidic and basic hydrolysis of

(a)  

$$H_3C - CH_2 - C + HOH + HOH + H^+$$
  
 $H_3C - CH_2 - C + NaOH + NAO$ 

3. Name the following compounds and identify these compounds as  $1^\circ$ ,  $2^\circ$ , or  $3^\circ$  amines:

(a)H<sub>3</sub>C—CH<sub>2</sub>—CH<sub>2</sub>—NH<sub>2</sub>

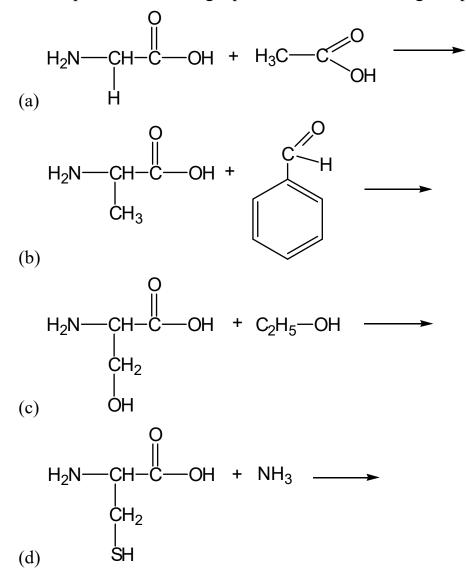
$$\begin{array}{c} H_{3}C \longrightarrow CH_{2} \longrightarrow CH_{2} \longrightarrow CH_{3} \\ (b) & CH_{3} \\ & \downarrow \\ CH_{3} \\ HC \longrightarrow NH_{2} \\ (c) & CH_{3} \end{array}$$

(d)H<sub>3</sub>C-CH<sub>2</sub>-NH-CH<sub>2</sub>-CH<sub>3</sub>

4. Write the formula and name for the product when ethylamine reacts with

- (a) propionic acid
- (b) ethanol
- (c) nitrite acid (nitrous acid HO–N=O)
- 5. Write the reaction between
- (a) Leucine and hydrogen chloride (HCl)
- (b) Leucine and sodium hydroxide (NaOH)

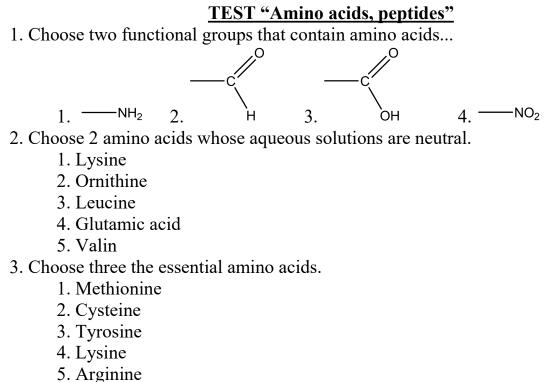
6. Complete the following equations and name the organic products:



7. Write the reaction decarboxylation of lysine.

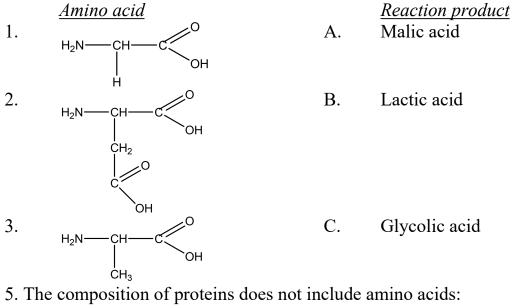
8. Show the reaction between arginine and alanine to yield the dipeptide Arg-Ala.

9. Show the reaction between threonine and glycine to yield the dipeptide Gly-Thr.



6. Glycine

4. Match the compounds resulting from the hydrolytic deamination reaction of the following amino acids.



- 1. Valin
- 2. γ-Aminobutyric acid
- 3. Arginine
- 4. β-Alanine
- 5. Glycine

6. Choose 2 amino acids whose aqueous solutions are alkaline.

1. Lysine

- 2. Ornithine
- 3. Leucine
- 4. Glutamic acid
- 5. Valin

7. Choose three the non-essential amino acids.

- 1. Methionine
- 2. Alanine
- 3. Asparagine
- 4. Lysine
- 5. Glutamic acid
- 6. Glycine

8. The structure of the amino acids consists of four main elements:

- 1. Carbon
- 2. Hydrogen
- 3. Sodium
- 4. Oxygen
- 5. Calcium
- 6. Nitrogen

# **RECOMMENDED BOOKS**

# **Basic:**

1. Organic Chemistry (third edition): student study guide and solutions manual / David Klein, 2016.

2. Chemistry (third edition): introducing inorganic, organic and physical chemistry / A. Burrows, J. Holman, A Parsons, G. Pilling, G. Price – Oxford, 2017.

3. General, Organic and Biological Chemistry (seventh edition) / H. Stephan Stoker – Boston, 2014.

# Additional:

4. Organic Chemistry byT. W. Graham Solomons, Craig B. Fryhle, Scott A. Snyder. – January 20, 2016.

5. Textbook of Organic Chemistry Paperback by V K Ahluwalia, Rakesh K Parashar – 1 January 2012.

6. Organic Chemistry (second edition) / Jonathan Clayden, Nick Greeves, Stuart Warren. – Oxford, 2012.

Навчальне видання

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## NITROGEN-CONTAINING COMPOUNDS

## НІТРОГЕНОВМІСНІ СПОЛУКИ

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