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Ministry of Health of the Russian Federation

Department of Chemistry and Physics

EDUCATIONAL-METHODICAL HANDBOOK

"CHEMISTRY"

FOR IMPLEMENTATION OF LABORATORY WORKS AND EXTERNAL AUDITORIAL

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Part 2

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Content

TOPIC: BASIC CONCEPTS IN BIOORGANIC CHEMISTRY. ISOMERISM OF ORGANIC COMPOUNDS

The purpose of the lesson: to consider the basic concepts of bioorganic chemistry, based on theoretical aspects and the formulation of organic chemistry.

The purpose of the work of students in class

The student should know:

a) The main provisions of the theory of the structure of organic compounds Butlerova.

b) Classification of organic compounds.

The student should be able to:

a) Formulate the basic rules of the IUPAC substitution nomenclature.

b) Use the rules of the substitution nomenclature in the names of organic compounds that are the objects of study of bioorganic chemistry.

c) Classify organic compounds taking into account the structure of the chain and the functional groups present in the molecule.

Questions for testing the basic (subject) level:

1. What kind of chemistry is called organic and why?

2. What is the nomenclature and its types?

3. The main classes of organic compounds.

4. Homological series, the principle of combining substances in the homology series.

5. Atomic orbitals and their hybridization.

6. Covalent and hydrogen bonds in organic compounds.

Theoretical part

The scientific classification and nomenclature of organic compounds are based on the principles of the theory of the chemical structure of organic compounds. Butlerova:

1. Atoms in molecules are connected to each other in a certain sequence according to their valencies. The sequence of interatomic bonds in a molecule is called its chemical structure and is reflected by a single structural formula (the formula of the structure).

2. Chemical structure can be established by chemical methods. (At present, modern physical methods are also used).

3. The properties of substances depend on their chemical structure.

4. By the properties of a given substance, one can determine the structure of its molecule, and according to the structure of a molecule, it is possible to foresee properties.

5. Atoms and groups of atoms in a molecule have mutual influence on each other.

The Butlerov theory was the scientific foundation of organic chemistry and contributed to its rapid development. Based on the theory, A.M. Butlerov explained the phenomenon of isomerism, predicted the existence of different isomers, and for the first time received some of them.

All organic compounds are divided into the following main series:

Acyclic - they are also called aliphatic, or fatty compounds. These compounds have an open chain of carbon atoms.

These include:

1. The limiting (saturated)

2. Unsaturated (unsaturated)

Cyclic - connections with a ring of atoms closed in a ring. These include:

1. Carbocyclic (isocyclic) - compounds, in the ring system of which only carbon atoms enter:

a) alicyclic (limiting and unsaturated);

b) Aromatic.

2. **Heterocyclic** - compounds whose ring system, in addition to the carbon atom, includes atoms of other elements - heteroatoms (oxygen, nitrogen, sulfur, etc.).

The simplest organic compounds are ***hydrocarbons***, compounds containing only carbon and hydrogen. All other organic compounds-for example, those containing O, N, and the halogen atoms-are classified as being ***derived from hydrocarbons***. At first glance, you might think that the hydrocarbons represent a very limited set of molecules; however, several hundred thousand molecules exist that contain only hydrogen and carbon atoms.

*Hydrocarbons* can be separated into three main groups:

1. **Saturated** hydrocarbons are hydrocarbons that contain only single bonds between the carbon atoms. Saturated hydrocarbon molecules can be cyclic or acyclic. A cyclic hydrocarbon is one in which a chain of carbon atoms has formed a ring.

An acyclic hydrocarbon is one that does not contain a ring of carbon atoms.

2. **Unsaturated** hydrocarbons are hydrocarbons that contain double or triple bonds between carbon atoms.

3. **Aromatic** hydrocarbons are hydrocarbons that contain benzene rings or similar features.

The saturated and unsaturated hydrocarbons are often referred to as the aliphatic Hydrocarbons:
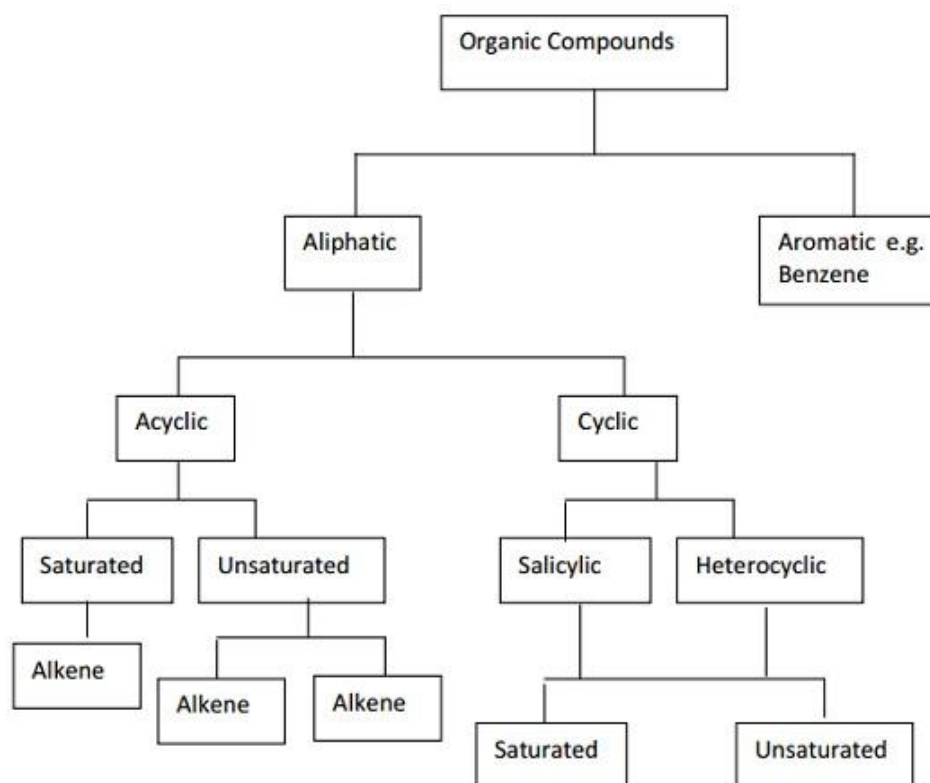
At present **three types of nomenclature** are used for the name of organic compounds: a trivial, rational and systematic nomenclature - the nomenclature IUPAC (IUPAC) - International Union of Pure and Applied Chemistry (International Union of Pure and Applied Chemistry).

The **trivial** (historical) nomenclature is the first nomenclature that emerged at the beginning of the development of organic chemistry, when there was no classification and theory of the structure of organic compounds. Organic compounds were given random names by source of production (oxalic acid, malic acid, vanillin), color or odor (aromatic compounds), less often by chemical properties (paraffins). Many such names are often used so far. For example: urea, toluene, xylene, indigo, acetic acid, butyric acid, valeric acid, glycol, alanine and many others.

Rational nomenclature - for this nomenclature, the name of an organic compound is usually called the simplest (most often the first) term of a given homologous series. All other compounds are considered as derivatives of this compound, formed by the replacement of hydrogen atoms with hydrocarbon or other radicals (for example: trimethylacetic aldehyde, methylamine, chloroacetic acid, methyl alcohol). At present, such a nomenclature is used only in those cases when it gives a particularly clear idea of the connection.

The **systematic nomenclature** - the nomenclature of IUPAC - is an international unified chemical nomenclature. The systematic nomenclature is based on the modern theory of the structure and classification of organic compounds and tries to solve the main problem of the nomenclature: the name of each organic compound must contain the correct names of the functions (substituents) and the basic skeleton of the hydrocarbon and should be such that the name can be used to write the only correct structural formula.

In the substitution nomenclature, one hydrocarbon fragment serves as the basis for the name, while others are considered as hydrogen substituents (for example, (C6H5) 3CH-triphenylmethane).

**How to name organic compounds using the IUPAC rules**

In order to name organic compounds you must first memorize a few basic names. These names are listed within the discussion of naming alkanes. In general, the base part of the name reflects the **number** of carbons in what you have assigned to be the **parent chain**. The **suffix** of the name reflects the type(s) of functional group(s) present on (or within) the parent chain. Other groups which are attached to the parent chain are called **substituents**.

- Alkanes - saturated hydrocarbons
  The names of the straight chain saturated hydrocarbons for up to a 12 carbon chain are shown below. The names of the substituents formed by the removal of one hydrogen from the end of the chain is obtained by changing the suffix -**ane** to -**yl**.

Number of Carbons	Name
1	**meth**ane
2	**eth**ane
3	**prop**ane
4	**but**ane
5	**pent**ane
6	**hex**ane
7	**hept**ane
8	**oct**ane
9	**non**ane
10	**dec**ane
11	**undec**ane
12	**dodec**ane

- There are a few common branched substituents which you should memorize. These are shown below.

isopropyl   sec-butyl   tert-butyl   isobutyl
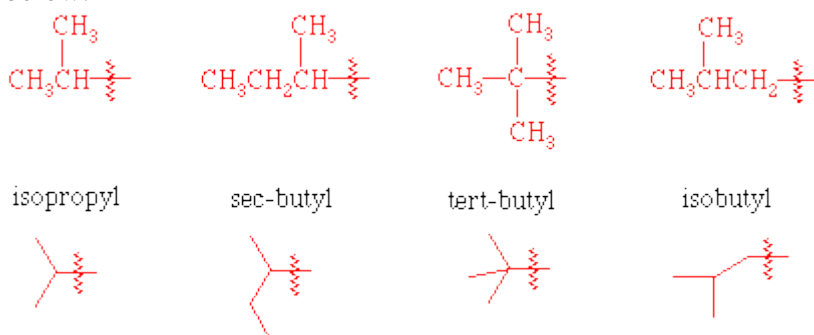
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- Here is a simple list of rules to follow. Some examples are given at the end of the list.
1. Identify the longest carbon chain. This chain is called the parent chain.
2. Identify all of the substituents (groups appending from the parent chain).
3. Number the carbons of the parent chain from the end that gives the substituents the lowest numbers. When compairing a series of numbers, the series that is the "lowest" is the one which contains the lowest number at the occasion of the first difference. If two or more side chains are in equivalent positions, assign the lowest number to the one which will come first in the name.

4. If the same substituent occurs more than once, the location of each point on which the substituent occurs is given. In addition, the number of times the substituent group occurs is indicated by a prefix (di, tri, tetra, etc.).
5. If there are two or more different substituents they are listed in alphabetical order using the base name (ignore the prefixes). The only prefix which **is** used when putting the substituents in alphabetical order is **iso** as in isopropyl or isobutyl. The prefixes sec- and tert- are not used in determining alphabetical order except when compared with each other.
6. If chains of equal length are competing for selection as the parent chain, then the choice goes in series to:
   a) the chain which has the greatest number of side chains.
   b) the chain whose substituents have the lowest- numbers.
   c) the chain having the greatest number of carbon atoms in the smaller side chain.
   d) the chain having the least branched side chains.
7. A cyclic (ring) hydrocarbon is designated by the prefix **cyclo-**which appears directly in front of the base name.

In summary, the name of the compound is written out with the substituents in alphabetical order followed by the base name (derived from the number of carbons in the parent chain). Commas are used between numbers and dashes are used between letters and numbers. There are **no** spaces in the name.
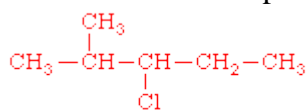
Here are some
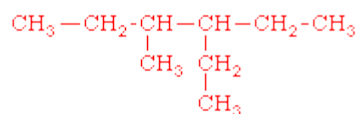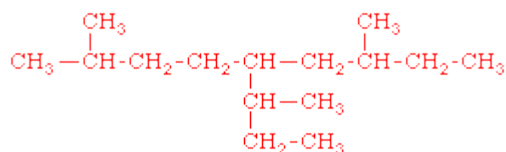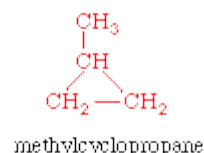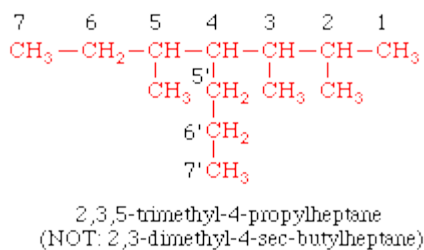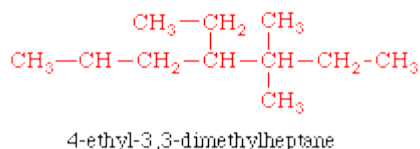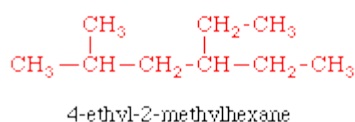
examples:

- Alkyl halides
  The halogen is treated as a substituent on an alkane chain. The halo- substituent is considered of equal rank with an alkyl substituent in the numbering of the parent chain. The halogens are represented as follows:
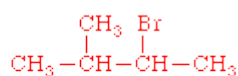
| F | fluoro- |
| Cl | chloro- |

Br	bromo-
I	iodo-

- Here are some examples:

3-chloro-2-methylpentane

2-bromo-3-methylbutane

-

- Alkenes and Alkynes - unsaturated hydrocarbons
  Double bonds in hydrocarbons are indicated by replacing the suffix **-ane** with **-ene**. If there is more than one double bond, the suffix is expanded to include a prefix that indicates the number of double bonds present (**-adiene**, **-atriene**, etc.). Triple bonds are named in a similar way using the suffix **-yne**. The position of the multiple bond(s) within the parent chain is(are) indicated by placing the number(s) of the first carbon of the multiple bond(s) directly in front of the base name.
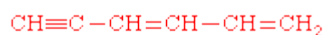
  Here is an important list of rules to follow:

1. The parent chain is numbered so that the multiple bonds have the lowest numbers (double and triple bonds have priority over alkyl and halo substituents).
2. When both double and triple bonds are present, numbers as low as possible are given to double and triple bonds even though this may at times give "-yne" a lower number than "-ene". When there is a choice in numbering, the double bonds are given the lowest numbers.
3. When both double and triple bonds are present, the -en suffix follows the parent chain directly and the -yne suffix follows the -en suffix (notice that the e is left off, -en instead of -ene). The location of the double bond(s) is(are) indicated before the parent name as before, and the location of the triple bond(s) is(are) indicated between the -en and -yne suffixes. See below for examples.
4. For a branched unsaturated acyclic hydrocarbon, the parent chain is the longest carbon chain that contains the **maximum number of double and triple bonds**. If there are two or more chains competing for selection as the parent chain (chain with the most multiple bonds), the choice goes to (1) the chain with the greatest number of carbon atoms, (2) the # of carbon atoms being equal, the chain containing the maximum number of double bonds.
5. If there is a choice in numbering not previously covered, the parent chain is numbered to give the substituents the **lowest** number at the **first point of difference**.

Here are some examples:

$CH_3-CH=CH-CH_2-CH=CH_2$

1,4-hexadiene

$CH\equiv C-CH=CH-CH=CH_2$

1,3-hexadien-5-yne

$CH_3-CH=CH-C\equiv CH$

3-penten-1-yne

$CH_3-\overset{\overset{\textstyle CH_3}{|}}{\underset{\underset{\textstyle CH_3}{|}}{C}}-CH_2-CH_2-CH=CH_2$

5,5-dimethyl-1-hexene

$\underset{6}{CH}\equiv \underset{5}{C}-\overset{\overset{\textstyle CH_2-CH_3}{|}}{\underset{4}{C}}=\overset{\overset{\textstyle \overset{\textstyle CH_2}{|}}{}}{\underset{3}{C}}-\underset{2}{CH}=\underset{1}{CH_2}$
(with $CH_2-CH_2-CH_3$ below position 3)

3,4-dipropyl-1,3-hexadien-5-yne

1,4,4-trimethylcyclobutene
(NOT: 2,3,3-trimethylcyclobutene)

- Alcohols
  Alcohols are named by replacing the suffix **-ane** with **-anol**. If there is more than one hydroxyl group (-OH), the suffix is expanded to include a prefix that indicates the number of hydroxyl groups present (**-anediol**, **-anetriol**, etc.). The position of the hydroxyl group(s) on the parent chain is(are) indicated by placing the number(s) corresponding to the location(s) on the parent chain directly in front of the base name (same as alkenes).

  Here is an important list of rules to follow:

1. The hydroxyl group takes precedence over alkyl groups and halogen substituents, as well as double bonds, in the numbering of the parent chain.
2. When both double bonds and hydroxyl groups are present, the -en suffix follows the parent chain directly and the -ol suffix follows the -en suffix (notice that the e is left off, -en instead of -ene). The location of the double bond(s) is(are) indicated before the parent name as before, and the location of the hydroxyl group(s) is(are) indicated between the -en and -ol suffixes. See below for examples. Again, the hydroxyl gets priority in the numbering of the parent chain.
3. If there is a choice in numbering not previously covered, the parent chain is numbered to give the substituents the **lowest** number at the **first point of difference**.
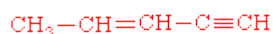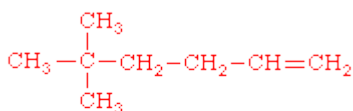
  Here are some examples:

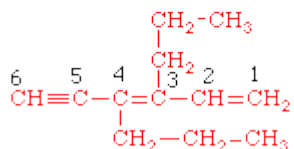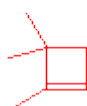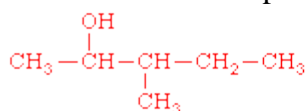$CH_3-\overset{\overset{\textstyle OH}{|}}{CH}-\overset{\overset{\textstyle \;}{}}{\underset{\underset{\textstyle CH_3}{|}}{CH}}-CH_2-CH_3$

3-methyl-2-pentanol

$CH_3-\overset{\overset{\textstyle OH}{|}}{CH}-\overset{\overset{\textstyle OH}{|}}{CH}-CH_3$

2,3-butanediol

2-cyclopenten-1-ol

- Ethers

  You are only expected to know how to name ethers by their commmon names. The two alkyl groups attached to the oxygen are put in alphabetical order with spaces between the names and they are followed by the word ether. The prefix di- is used if both alkyl groups are the same.

  Here are some examples:

  $CH_3-CH_2-O-CH_2-CH_3$ $CH_3-O-CH_2-CH_3$

         diethyl ether   ethyl methyl ether

- Aldehydes

  Aldehydes are named by replacing the suffix **-ane** with **-anal**. If there is more than one -CHO group, the suffix is expanded to include a prefix that indicates the number of -CHO groups present (**-anedial** - there should not be more than 2 of these groups on the parent chain as they must occur at the ends). It is not necessary to indicate the position of the -CHO group because this group will be at the end of the parent chain and its carbon is automatically assigned as C-1.

  Here is an important list of rules to follow:

1. The carbonyl group takes precedence over alkyl groups and halogen substituents, as well as double bonds, in the numbering of the parent chain.
2. When both double bonds and carbonyl groups are present, the -en suffix follows the parent chain directly and the -al suffix follows the -en suffix (notice that the e is left off, **-en** instead of -ene). The location of the double bond(s) is(are) indicated before the parent name as before, and the -al suffix follows the -en suffix directly. Remember it is not necessary to specify the location of the carbonyl group because it will automatically be carbon #1. See below for examples. Again, the carbonyl gets priority in the numbering of the parent chain.
3. There are a couple of common names which are acceptable as IUPAC names. They are shown in the examples at the end of this list but at this point these names will not be accepted by the computer. Eventually they will be accepted.
4. If there is a choice in numbering not previously covered, the parent chain is numbered to give the substituents the **lowest** number at the **first point of difference**.

  Here are some examples:

  propanal

  3-methylbutanal

  3-methyl-3-butenal

  methanal
  (common name: formaldehyde)

  ethanal
  (common name: acetaldehyde)

  Benzaldehyde

- Ketones

  Ketones are named by replacing the suffix **-ane** with **-anone**. If there is more than one carbonyl group (C=O), the suffix is expanded to include a prefix that indicates the number of carbonyl groups present (**-anedione**, **-anetrione**, etc.). The position of the carbonyl group(s) on the parent chain is(are) indicated by placing the number(s) corresponding to the location(s) on the parent chain directly in front of the base name (same as alkenes).
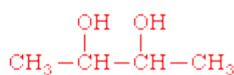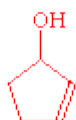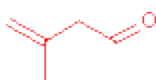
  Here is an important list of rules to follow:

1. The carbonyl group takes precedence over alkyl groups and halogen substituents, as well as double bonds, in the numbering of the parent chain.
2. When both double bonds and carbonyl groups are present, the -en suffix follows the parent chain directly and the -one suffix follows the -en suffix (notice that the e is left off, **-en** instead of -ene). The location of the double bond(s) is(are) indicated before the parent name as before, and the location of the carbonyl group(s) is(are) indicated between the -en and -one suffixes. See below for examples. Again, the carbonyl gets priority in the numbering of the parent chain.
3. If there is a choice in numbering not previously covered, the parent chain is numbered to give the substituents the **lowest** number at the **first point of difference**.

   Here are some examples:

propanone
(common name: acetone)

2-butanone

3-methyl-3-buten-2-one

2,4-pentanedione
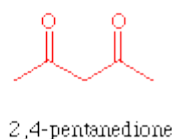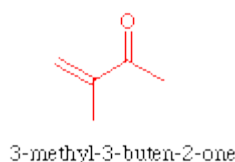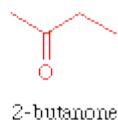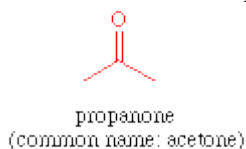
- Carboxylic Acids

  Carboxylic acids are named by counting the number of carbons in the longest continuous chain including the carboxyl group and by replacing the suffix **-ane** of the corresponding alkane with **-anoic acid**. If there are two -COOH groups, the suffix is expanded to include a prefix that indicates the number of -COOH groups present (**-anedioic acid** - there should not be more than 2 of these groups on the parent chain as they must occur at the ends). It is not necessary to indicate the position of the -COOH group because this group will be at the end of the parent chain and its carbon is automatically assigned as C-1.

  Here is an important list of rules to follow:

1. The carboxyl group takes precedence over alkyl groups and halogen substituents, as well as double bonds, in the numbering of the parent chain.
2. If the carboxyl group is attached to a ring the parent ring is named and the suffix -carboxylic acid is added.
3. When both double bonds and carboxyl groups are present, the -en suffix follows the parent chain directly and the -oic acid suffix follows the -en suffix (notice that the e is left off, **-en** instead of -ene). The location of the double bond(s) is(are) indicated before the parent name as before, and the -oic acid suffix follows the -en suffix directly. Remember it is not necessary to specify the

location of the carboxyl group because it will automatically be carbon #1. See below for examples. Again, the carboxyl gets priority in the numbering of the parent chain.

4. There are several common names which are acceptable as IUPAC names. They are shown in the examples at the end of this list **but** at this point these names will **not** be accepted by the computer. Eventually they will be accepted.

5. If there is a choice in numbering not previously covered, the parent chain is numbered to give the substituents the **lowest** number at the **first point of difference**.

Here are some examples:

methanoic acid
(common name: formic acid)

ethanoic acid
(common name: acetic acid)

3-methylpentanoic acid

benzoic acid

salicylic acid
(common name)

ethanedioic acid
(common name: oxalic acid)

3-butenoic acid
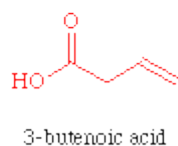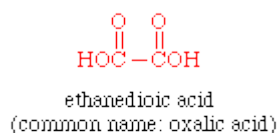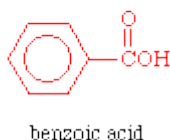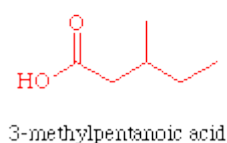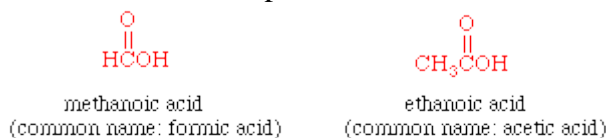
- Esters
  Systematic names of esters are based on the name of the corresponding carboxylic acid. Remember esters look like this:

acyl group   alkyl group
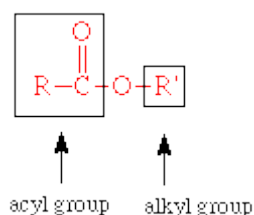
The alkyl group is named like a substituent using the **-yl** ending. This is followed by a space. The acyl portion of the name (what is left over) is named by replacing the **-ic acid** suffix of the corresponding carboxylic acid with **-ate**.

Here are some examples:

$$CH_3CH_2\overset{\overset{\displaystyle O}{\|}}{C}OCH_3$$
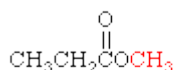
methyl propanoate

$$\bigcirc - \overset{\overset{\displaystyle O}{\|}}{C}OCH_2CH_3$$

ethyl benzoate

$$CH_3\overset{\overset{\displaystyle O}{\|}}{C}OC(CH_3)_3$$
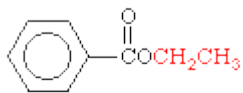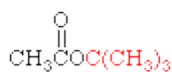
tert-butyl acetate

- Amines
  You are only expected to know how to name amines by their common names . They are named like ethers, the alkyl (R) groups attached to the nitrogen are put in alphabetical order with no spaces between the names and these are followed by the word amine. The prefixes di- and tri- are used if two or three of the alkyl groups are the same.
  NOTE: Some books put spaces between the parts of the name, but we will not. Follow the examples.

  Here are some examples:

  $$NH(CH_3)_2$$

  dimethylamine

  $$CH_3CH_2\overset{\displaystyle NH}{\underset{\displaystyle CH_3}{|}}$$
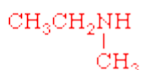
  ethylmethylamine

- Summary of functional groups

Functional group	Prefix	Suffix
carboxylic acids	none	-oic acid
aldehydes	none	-al
ketones	none	-one
alchols	hydroxy-	-ol
amines	amino-	-amine
ethers	alkoxy-	-ether
fluorine	fluoro-	none
chlorine	chloro-	none
bromine	bromo-	none
iodine	iodo-	none

STRUCTURAL ISOMERISM

cules that have the same molecular formula, but have a different arrangement of the atoms
cludes any different arrangements which are simply due to the molecule rotating as a whole,

particular bonds.

For example, both of the following are the same molecule. They are ***not isomers.*** Both are butane.
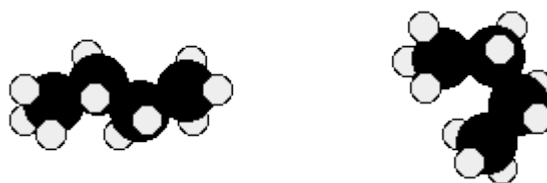
There are also endless other possible ways that this molecule could twist itself. There is completely free rotation around all the carbon-carbon single bonds.

If you had a model of a molecule in front of you, you would have to take it to pieces and rebuild it if you wanted to make an isomer of that molecule. If you can make an apparently different molecule just by rotating single bonds, it's not different - it's still the same molecule.

What are structural isomers?

In structural isomerism, the atoms are arranged in a completely different order. This is easier to see with specific examples.

What follows looks at some of the ways that structural isomers can arise. The names of the various forms of structural isomerism probably don't matter all that much, but you must be aware of the different possibilities when you come to draw isomers.

Types of structural isomerism

Chain isomerism

These isomers arise because of the possibility of branching in carbon chains. For example, there are two isomers of butane, C_4H_{10}. In one of them, the carbon atoms lie in a "straight chain" whereas in the other the chain is branched.

$$CH_3-CH_2-CH_2-CH_3$$

$$\begin{array}{c} CH_3 \\ | \\ CH_3-CH-CH_3 \end{array}$$
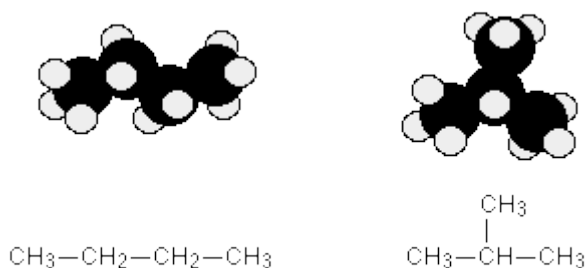
Be careful not to draw "false" isomers which are just twisted versions of the original molecule. For example, this structure is just the straight chain version of butane rotated about the central carbon-carbon bond.

$$\begin{array}{c} CH_3-CH_2 \\ | \\ CH_3-CH_2 \end{array}$$
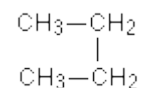
You could easily see this with a model. This is the example we've already used at the top of this

page.
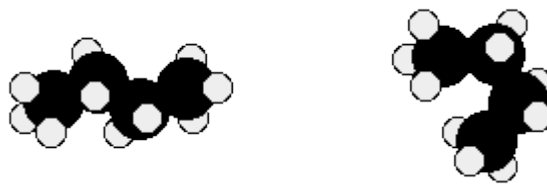
Pentane, C_5H_{12}, has three chain isomers. If you think you can find any others, they are simply twisted versions of the ones below. If in doubt make some models.

$$CH_3-CH_2-CH_2-CH_2-CH_3$$

$$CH_3-CH_2-\overset{\overset{\displaystyle CH_3}{|}}{CH}-CH_3$$

$$CH_3-\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}-CH_3$$
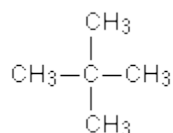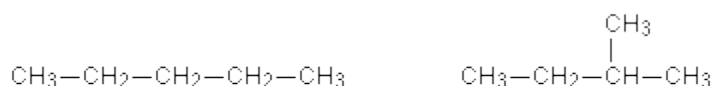
Position isomerism

In position isomerism, the basic carbon skeleton remains unchanged, but important groups are moved around on that skeleton.

For example, there are two structural isomers with the molecular formula C_3H_7Br. In one of them the bromine atom is on the end of the chain, whereas in the other it's attached in the middle.

$$CH_3-CH_2-CH_2-Br \qquad CH_3-\overset{\overset{\displaystyle }{}}{CH}-CH_3$$
$$\underset{\displaystyle Br}{|}$$

1-bromopropane   2-bromopropane
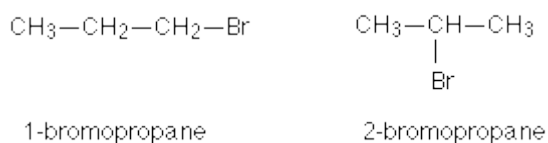
If you made a model, there is no way that you could twist one molecule to turn it into the other one. You would have to break the bromine off the end and re-attach it in the middle. At the same time, you would have to move a hydrogen from the middle to the end.

Another similar example occurs in alcohols such as C_4H_9OH

$$CH_3-CH_2-CH_2-CH_2-OH \qquad CH_3-CH_2-\overset{\overset{\displaystyle }{}}{CH}-CH_3$$
$$\underset{\displaystyle OH}{|}$$

butan-1-ol   butan-2-ol
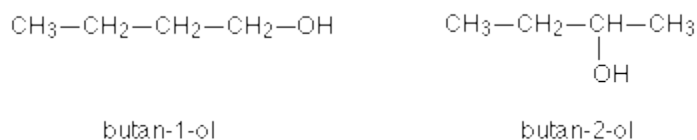
These are the only two possibilities provided you keep to a four carbon chain, but there is no reason why you should do that. You can easily have a mixture of chain isomerism and position isomerism - you aren't restricted to one or the other.

So two other isomers of butanol are:
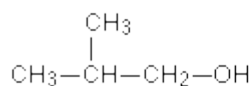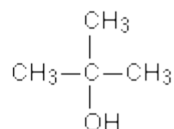
2-methylpropan-1-ol   2-methylpropan-2-ol

You can also get position isomers on benzene rings. Consider the molecular formula C_7H_7Cl. There are four different isomers you could make depending on the position of the chlorine atom. In one case it is attached to the side-group carbon atom, and then there are three other possible positions it could have around the ring - next to the CH_3 group, next-but-one to the CH_3group, or opposite the CH_3 group.
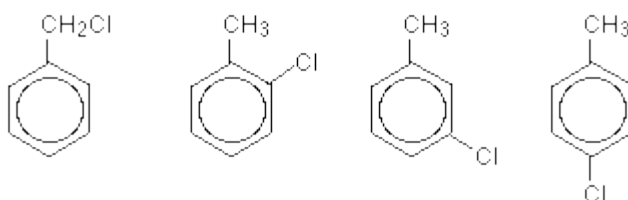
Functional group isomerism

In this variety of structural isomerism, the isomers contain different functional groups - that is, they belong to different families of compounds (different homologous series).

For example, a molecular formula C_3H_6O could be either propanal (an aldehyde) or propanone (a ketone).
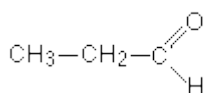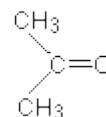
propanal   propanone

There are other possibilities as well for this same molecular formula - for example, you could have a carbon-carbon double bond (an alkene) and an -OH group (an alcohol) in the same molecule.

$$CH_2=CH-CH_2-OH$$
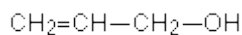
Another common example is illustrated by the molecular formula $C_3H_6O_2$. Amongst the several structural isomers of this are propanoic acid (a carboxylic acid) and methyl ethanoate (an ester).
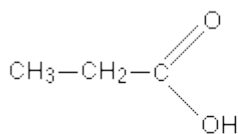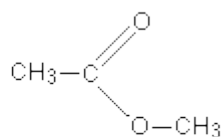
propanoic acid   methyl ethanoate

STEREOISOMERISM - GEOMETRIC ISOMERISM

Geometric isomerism (also known as cis-trans isomerism or E-Z isomerism) is a form of stereoisomerism. This page explains what stereoisomers are and how you recognise the possibility of geometric isomers in a molecule.

Further down the page, you will find a link to a second page which describes the E-Z notation for naming geometric isomers. You shouldn't move on to that page (even if the E-Z notation is what your syllabus is asking for) until you are really confident about how geometric isomers arise and how they are named on the cis-trans system.

The E-Z system is better for naming more complicated structures but is more difficult to understand than cis-trans. The cis-trans system of naming is still widely used - especially for the sort of simple molecules you will meet at this level. That means that irrespective of what your syllabus might say, you will have to be familiar with both systems. Get the easier one sorted out before you go on to the more sophisticated one!

What is stereoisomerism?

What are isomers?

Isomers are molecules that have the same molecular formula, but have a different arrangement of the atoms in space. That excludes any different arrangements which are simply due to the molecule rotating as a whole, or rotating about particular bonds.

Where the atoms making up the various isomers are joined up in a different order, this is known as structural isomerism. Structural isomerism is not a form of stereoisomerism, and is dealt with on a separate page.

What are stereoisomers?

In stereoisomerism, the atoms making up the isomers are joined up in the same order, but still manage to have a different spatial arrangement. Geometric isomerism is one form of stereoisomerism.

Geometric (cis / trans) isomerism

How geometric isomers arise

These isomers occur where you have restricted rotation somewhere in a molecule. At an introductory level in organic chemistry, examples usually just involve the carbon-carbon double bond - and that's what this page will concentrate on.

Think about what happens in molecules where there is *unrestricted* rotation about carbon bonds - in other words where the carbon-carbon bonds are all single. The next diagram shows two

possible configurations of 1,2-dichloroethane.

free rotation about this single bond
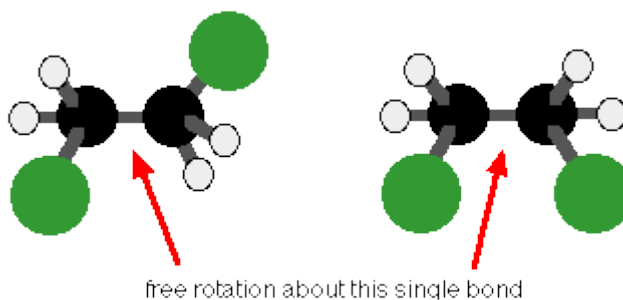
These two models represent exactly the same molecule. You can get from one to the other just by twisting around the carbon-carbon single bond. These molecules are ***not isomers***.

If you draw a structural formula instead of using models, you have to bear in mind the possibility of this free rotation about single bonds. You must accept that these two structures represent the same molecule:
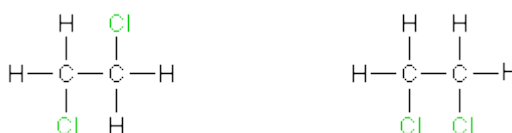
But what happens if you have a carbon-carbon double bond - as in 1,2-dichloroeth<u>ene</u>?

no rotation about this double bond
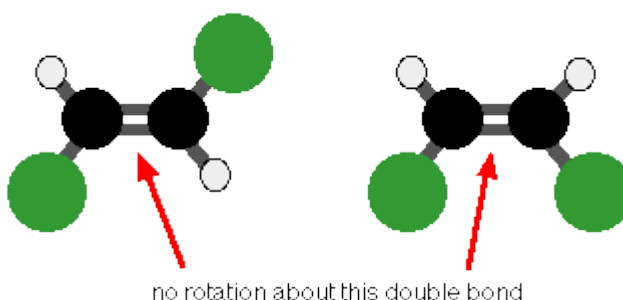
These two molecules aren't the same. The carbon-carbon double bond won't rotate and so you would have to take the models to pieces in order to convert one structure into the other one. That is a simple test for isomers. If you have to take a model to pieces to convert it into another one, then you've got isomers. If you merely have to twist it a bit, then you haven't!

Drawing structural formulae for the last pair of models gives two possible isomers.

In one, the two chlorine atoms are locked on opposite sides of the double bond. This is known as the ***trans*** isomer. (*trans* : from latin meaning "across" - as in transatlantic).

In the other, the two chlorine atoms are locked on the same side of the double bond. This is know as the ***cis*** isomer. (*cis* : from latin meaning "on this side")
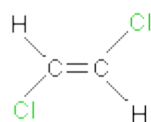
trans-1,2-dichloroethene   *cis*-1,2-dichloroethene
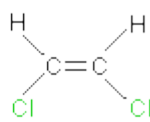
The most likely example of geometric isomerism you will meet at an introductory level is but-2-ene. In one case, the CH_3 groups are on opposite sides of the double bond, and in the other case they are on the same side.
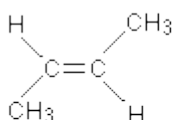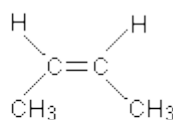
trans-but-2-ene   *cis*-but-2-ene

The importance of drawing geometric isomers properly

It's very easy to miss geometric isomers in exams if you take short-cuts in drawing the structural formulae. For example, it is very tempting to draw but-2-ene as

$$CH_3CH=CHCH_3$$
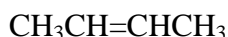
If you write it like this, you will almost certainly miss the fact that there are geometric isomers. If there is even the slightest hint in a question that isomers might be involved, *always* draw compounds containing carbon-carbon double bonds showing the correct bond angles (120°) around the carbon atoms at the ends of the bond. In other words, use the format shown in the last diagrams above.

How to recognise the possibility of geometric isomerism

You obviously need to have restricted rotation somewhere in the molecule. Compounds containing a carbon-carbon double bond have this restricted rotation. (Other sorts of compounds may have restricted rotation as well, but we are concentrating on the case you are most likely to meet when you first come across geometric isomers.) If you have a carbon-carbon double bond, you need to think carefully about the possibility of geometric isomers.

What needs to be attached to the carbon-carbon double bond?

Think about this case:
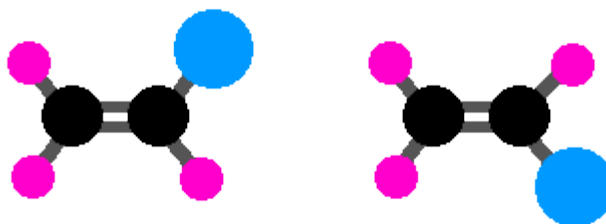
Although we've swapped the right-hand groups around, these are still the same molecule. To get from one to the other, all you would have to do is to turn the whole model over.

You **won't** have geometric isomers if there are two groups the same on one end of the bond - in this case, the two pink groups on the left-hand end.

So . . . there must be two different groups on the left-hand carbon and two different groups on the right-hand one. The cases we've been exploring earlier are like this:
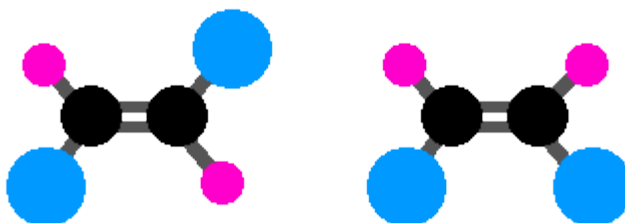
But you could make things even more different and still have geometric isomers:
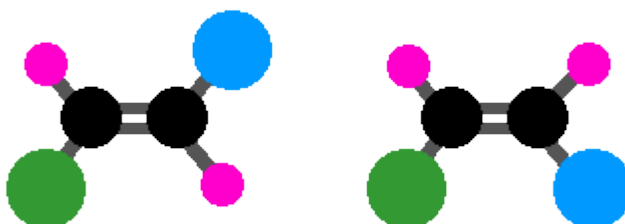
Here, the blue and green groups are either on the same side of the bond or the opposite side.

Or you could go the whole hog and make everything different. You still get geometric isomers, but by now the words *cis* and *trans* are meaningless. This is where the more sophisticated E-Z notation comes in.
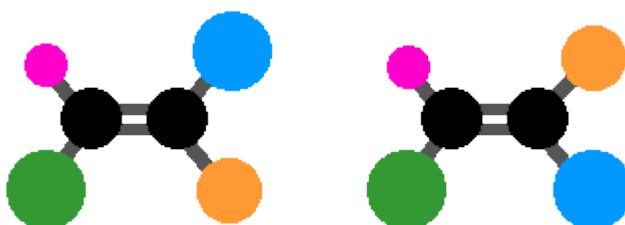
Summary

To get geometric isomers you must have:

restricted rotation (often involving a carbon-carbon double bond for introductory purposes);
two different groups on the left-hand end of the bond and two different groups on the right-hand

end. It doesn't matter whether the left-hand groups are the same as the right-hand ones or not.

The effect of geometric isomerism on physical properties

The table shows the melting point and boiling point of the cis and trans isomers of 1,2-dichloroethene.

isomer	melting point (°C)	boiling point (°C)
cis	-80	60
trans	-50	48

In each case, the higher melting or boiling point is shown in red.

You will notice that:

the trans isomer has the higher melting point;
the cis isomer has the higher boiling point.

This is common. You can see the same effect with the cis and trans isomers of but-2-ene:

isomer	melting point (°C)	boiling point (°C)
cis-but-2-ene	-139	4
trans-but-2-ene	-106	1

Why is the boiling point of the cis isomers higher?

There must be stronger intermolecular forces between the molecules of the cis isomers than between trans isomers.

Taking *1,2-dichloroethene* as an example:

Both of the isomers have exactly the same atoms joined up in exactly the same order. That means that the van der Waals dispersion forces between the molecules will be identical in both cases.

The difference between the two is that the cis isomer is a polar molecule whereas the trans isomer is non-polar.

Both molecules contain polar chlorine-carbon bonds, but in the cis isomer they are both on the same side of the molecule. That means that one side of the molecule will have a slight negative

charge while the other is slightly positive. The molecule is therefore polar.
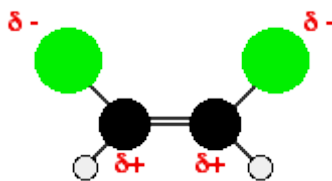
Because of this, there will be dipole-dipole interactions as well as dispersion forces - needing extra energy to break. That will raise the boiling point.

A similar thing happens where there are CH_3 groups attached to the carbon-carbon double bond, as in *cis-but-2-ene*.

Alkyl groups like methyl groups tend to "push" electrons away from themselves. You again get a polar molecule, although with a reversed polarity from the first example.
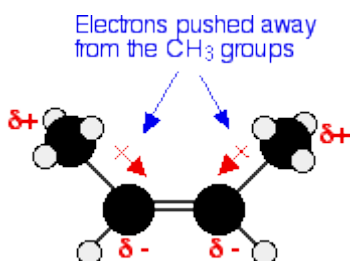
By contrast, although there will still be polar bonds in the trans isomers, overall the molecules are non-polar.
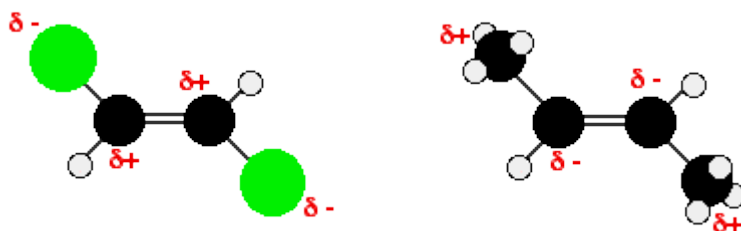
The slight charge on the top of the molecule (as drawn) is exactly balanced by an equivalent charge on the bottom. The slight charge on the left of the molecule is exactly balanced by the same charge on the right.

This lack of overall polarity means that the only intermolecular attractions these molecules experience are van der Waals dispersion forces. Less energy is needed to separate them, and so their boiling points are lower.

Why is the melting point of the cis isomers lower?

You might have thought that the same argument would lead to a higher *melting point* for cis isomers as well, but there is another important factor operating.

In order for the intermolecular forces to work well, the molecules must be able to pack together

efficiently in the solid.

Trans isomers pack better than cis isomers. The "U" shape of the cis isomer doesn't pack as well as the straighter shape of the trans isomer.

The poorer packing in the cis isomers means that the intermolecular forces aren't as effective as they should be and so less energy is needed to melt the molecule - a lower melting point.

Tasks for independent work

Control questions:

1. Basic theses of the theory of the structure of organic compounds Butlerova. Isomerism as a specific phenomenon of organic chemistry.

2. Classification features of organic compounds: the structure of the carbon skeleton and the nature of the functional group. Functional group. Structural formula. Structural isomers.

3. Basic rules for the preparation of names for the nomenclature of IUPAC for organic compounds; substitutive and radical-functional nomenclature.

4. Ancestral structure, substitutes, characteristic groups. Show on specific examples.

5. The main classes of biologically important organic compounds: alcohols, phenols, thiols, amines, ethers, sulfides, aldehydes, ketones, carboxylic acids. Organic radicals.

6. What is isomerism and what kinds of it are known to you?

7. What electronic effects do you know of the substitutes?

8. The main methods of the YUPAK nomenclature of compounds.

9. Atomic orbitals and their hybridization.

10. Structural and spatial isomerism.

11. Configuration and conformation.

Do the exercises:

1. To name the connections according to the IUPAC substitution nomenclature:
a) $HOOCCH_2-CH_2COOH$
b) $H_2N-CH_2CH_2CH_2-COOH$
c) $HSCH_2CH(NH_2)COOH$

2. Name for the IUPAC substitution nomenclature:
a) $HOOC-CHO$
b) $CH_3-CH(CH_3)CH_2CH(NH_2)COOH$
c) $CH_3-CHCH_2CH(NH_2)COH$

3. Write the structure of compounds using structural formulas:
a) 2-Bromo-1,1,1-trifluoro-2-chloroethane
b) propanetriol-1,2,3, 2-oxopentanedioic acid
c) propanone
d) ethanedial
e) trans-butenedioic acid.

4. Draw the structural formulas of the following compounds:
a) 2-methyl-3-chlorohept-5-en-1-ol
b) 2-Cyclopentylhex-5-yn-1-ol
c) 1- (3-methyl-5-ethylcycloheptyl) cyclohexane-1,4-diol

d) 4-amino-2- (2-chloro-propyl) cyclohexane
e) (2-methyl-3-ethylpentyl) benzene

5. For the following connections:
a) depict the structural formula, indicating in it all covalent and donor-acceptor bonds
b) depict the electronic structures (Lewis)
c) indicate the formal charge on each of the non-hydrogen atoms:

CH_2N_2 (diazomethane), $C_2H_5NO_2$ (nitroethane), CH_3CN (acetonitrile).

6. Write the structural formulas of all isomers of the formulas:
a) C_2H_4O
b) C_3H_5OH
c) C_3H_9N
e) C_3H_4O

7. Write the structural formulas of all isomers with the gross formula $C_2H_6O_2$. Determine for each of them the connection class and the type of isomerism.

8. Draw Newman's projections for ethane, propane and butane in the obscured and inhibited conformations. For which compound is the inhibited conformation least stable?

9. Draw the structures of the following compounds:
a) methylbutane　　　　　　b) cyclohexane　　　　　　c) but-1-ene

d) 3-ethyl,2-methylhex-1-ene　　　e) 3-chlorobut-1-ene

f) 1,1-dichloropropane　　　g) 2,2,4-trimethylheptane　　h) pent-2-ene

10. Name the connections for the IUPAC substitution nomenclature:
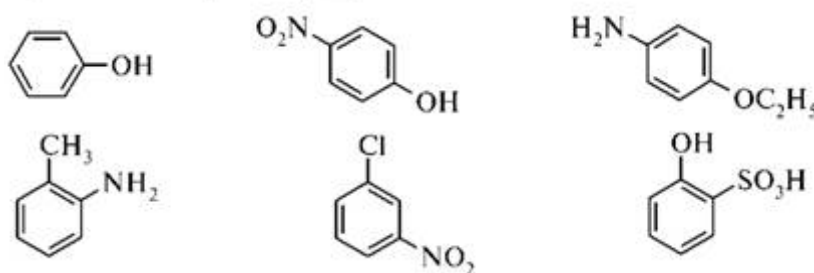
11. Name the connections by the substitution nomenclature:
a) $CH_3 – C(O) – CH_3$
б) $HS – CH_2 – CH(NH_2) – COOH$
в) $HOOC – CH_2 - CH_2 C(O) – COOH$
г) $CH_2(OH) – CH(OH) - CH_2(OH)$
specify the functional groups.

12. Write the structural formula for the compounds: propenal, p-aminobenzenesulfonic acid, oxobutanedioic acid, diethylamine.

Name the connection for the IUPAC nomenclature. Specify a functional group.

13. The rowan fruit contains a significant amount of malic acid, which is 2-hydroxybutanedioic acid. Write down its structural formula.

14. ε-Aminocaproic acid, depressing fibrinolysis and used as a blood thinning agent, has the structure:

H_2N - CH_2 - CH_2 - CH_2 - CH_2 - CH_2 - $COOH$
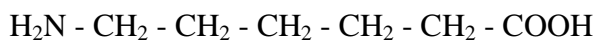
Name this connection. Specify the functional groups.

15. Trichlorethylene - a means for inhalation anesthesia - is called 1,1,2 - trichloroethene. Write down its structural formula. To what class of compounds does it belong?

16. Glutamic acid, which is a part of proteins, has the structure:

$HOOC$-CH_2-CH_2-CH (NH_2) -$COOH$. Name this connection.
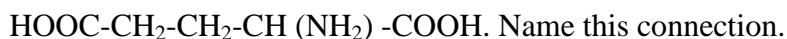
17. Name the following alkyl radicals:

1) CH_3- 2) CH_3-CH_2- 3) $CH_3-CH_2-CH_2-$

4) $CH_3-CH_2-CH_2-CH_2-$ 5) $CH_3-CH-CH_2-CH_3$
                                             |

                                               CH_3

6) $CH_3-CH-CH_2-$ 7) CH_3-C-CH_3 8) $CH_3-CH-CH_3$
        | | |
        CH_3
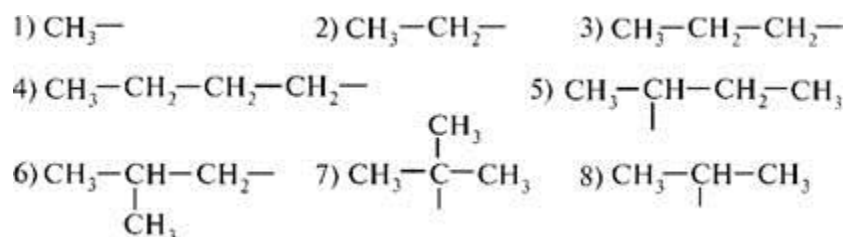
18. Write the structural formulas for the following compounds:

a) 2,2,4-trimethylpentane d) 2-methyl-3-chloro-3-ethylhexane

b) 2-chloropropene d) 2-methylbutene-2

c) 3-bromohexane f) aniline.

19. Write the structural formulas for the following compounds:

a) nitrobenzene d) 2-methylbutadiene-1,3

b) 2-chloropropanoic acid e) 3-Oxobutanoic acid.

c) benzoic acid e) cyclobutane.

20. Write the structural formulas for the following compounds:

a) o-methylaniline d) propanediol-1,2

b) 2-methyl-5-ethylheptin-3-d) propanethiol-1

c) methyldiisopropylmethane f) propanone

21. Name the connections for the IUPAC substitution nomenclature:

a)
$$H_3C-CH-C\underset{OH}{\overset{O}{\diagup}} \qquad H_3C-\underset{CH_3}{\overset{CH_3}{\underset{|}{\overset{|}{C}}}}-CH_3 \qquad H_3C-\underset{Cl}{\overset{|}{CH}}-CH_2-OH$$

b)
$$H_3C-C\equiv C-\underset{|}{\overset{|}{CH}}-\underset{CH_3}{\overset{|}{CH}}-CH_3 \qquad H_3C-\underset{Br}{\overset{Br}{\underset{|}{\overset{|}{C}}}}-C\underset{OH}{\overset{O}{\diagup}}$$

$$H_3C-CH=CH-COOH \qquad H_2N-CH_2-CH_2-COOH$$

c)

$$H_3C-CH-COOH \\ \underset{OH}{\overset{|}{}}$$
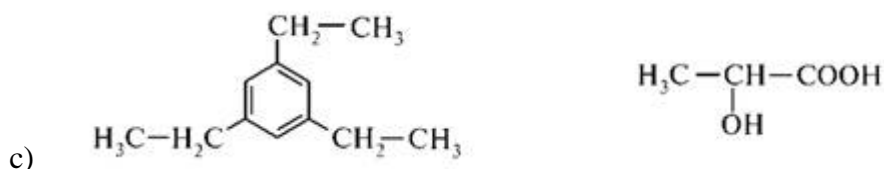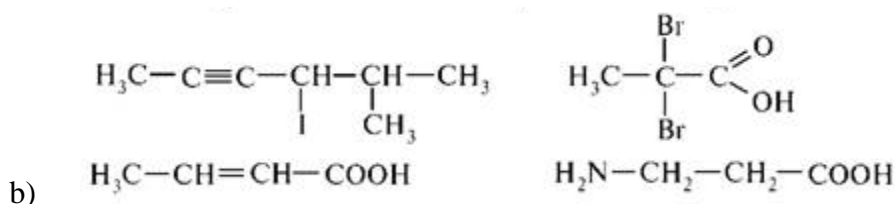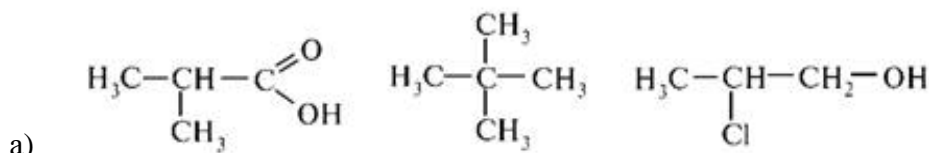
22. A covalent bond is formed. . .

a) a pair of electrons provided by an atom

b) due to the socialization of a pair of electrons when overlapping atomic orbitals of two (or more) atoms

c) due to the electrostatic attraction between the charged particles with the completed outer electron shells

23. What is the connection called the σ-bond?

a) the covalent bond formed in the lateral overlapping of the atomic p-orbitals of the bound atoms

b) the covalent bond formed when the atomic orbitals overlap along the internuclear axis

c) ionic bond formed during axial overlapping of atomic orbitals of bound atoms

d) the ionic bond formed in the lateral overlap of the atomic orbitals of the bound atoms

24. A π-connection is called. . .

a) a covalent bond formed upon axial overlapping of any atomic orbitals of the bound atoms

b) the covalent bond formed when the atomic p-orbitals overlap along the internuclear axis

c) a covalent bond formed in the lateral overlapping of atomic p-orbitals of bound atoms

d) the ionic bond formed in the lateral overlap of the atomic orbitals of the bound atoms

25. Hybridization of atomic orbitals is. . .

a) the interaction of atomic orbitals of different atoms with the formation of hybrid orbitals

b) interaction of different atomic types that are similar in energy but similar in energy to a given atom with the formation of hybrid orbitals of the same shape and energy

c) interaction of identical atomic energy orbitals of the same type, but different in energy, with the formation of hybrid orbitals of the same shape and energy

Test tasks:
1. Correspondence of hydrocarbon and type of hybridization of atomic orbitals carbon in the molecule:
1) ethane   a) sp
2) ethylene   b) sp^2
3) acetylene   c) sp^3
                         d) sp^2d
Answer: 1 ..., 2 ..., 3 ...

2. Compounds that are among themselves isomers:
a) hexane
b) 2,3-dimethylpentane
c) 2,3-Dimethylbutane
d) 2,2-dimethylpropane

3. The general formula of the homologous series of compound
$CH3-CH = CH-CH = CH2$ ...
a) C_nH_{2n-2}
b) $C_nH_{2n + 2}$
c) C_nH_{2n}

d) C_nH_{2n-6}

4. Compounds for which geometric isomers are possible:
a) 1,2 dichlorobutane
b) 3-hexene
c) ethynyl chloride
d) 1,2-Dimethylcyclobutane

5. Correspondence of formulas and names of compounds:
1) C_6H_6 a) styrene
2) $C_6H_5CH_3$ b) xylene
3) $CH_3C_6H_4CH_3$ c) toluene
                  d) benzene
Answer: 1 ..., 2 ..., 3 ....

6. Substances, isomeric butylene ...
a) butane
b) Butyne
c) cyclobutane
d) butadiene-1,2

7. Name of the compound $HC \equiv C\text{-}\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}\text{-}CH = CH_2$ according to the systematic nomenclature ...

a) 3,3-dimethylpentene-1-yn-4
b) 3,3-Dimethyl-pentyn-1-en-4
c) 3-methyl-3-ethynyl-butene-2
d) 3-Vinyl-3-methylbutyn-1

8. The name of the acid, which is the homologue of acetic acid:
a) ant
b) benzoic acid
c) oleic
d) oxalic

9. Names of pentanone-2 isomers according to the rational nomenclature:
a) diethyl ketone
b) methyl ethyl ketone
c) methylbutyl ketone
d) ethyl acetic aldehyde

10. Compounds whose molecules include a carbonyl group:
a) aldehydes
b) phenols
c) ethers
d) ketones

Timing of a 3-hour lesson:
1. Organizational moment - 2 minutes.
2. The survey - 40 min.

3. Explanation of the work - 25 min.
4. Performance and execution of work - 30 min.
5. Presentation of the new material - 45 min.
6. Verification of work and assignment to the house - 3 min.

TOPIC: ACIDITY AND BASICITY OF ORGANIC COMPOUNDS

The purpose of the lesson is to form a knowledge of the acidity and basicity of biologically active compounds. On the basis of theoretical knowledge, to develop skills and abilities to predict the reactivity of biological compounds, to solve situational problems.

The purpose of the activities of students in class
The student **should know**:
a) Determination of acid and base according to the theory of Bronsted and Lewis.
b) Factors affecting acidity and basicity of compounds.
c) Quantitative characteristics of the strength of acids and bases.

The student **should be able to**:
a) Predict acidic and basic properties of compounds.
b) Compare the acidic and basic properties of organic molecules.
c) Predict the possibility of reactions between molecules exhibiting acid-base properties.

Questions for testing the baseline level:
1. What is electronegativity of elements?
2. Formulate the main provisions of Butlerov's theory.
3. Theories of acids and bases of Bronsted and Lowry, Lewis.
4. Electron-donor and electron-withdrawing substituents.
5. What is a radical, a substitute, a characteristic group?
6. How are organic compounds classified depending on the functional groups that make up the molecules of substances?
7. The main classifications of organic compounds.
8. What is isomerism and what kinds of it are known to you?
9. What electronic effects do you know of the substitutes?
10. The main methods of the YUPAK nomenclature of compounds.

Theoretical part

Important aspects of the reactivity of organic compounds are their acidic and basic properties. These properties often cause the existence of most organic biomolecules in the conditions of the organism in the ionic state.

The most common concept of acidity and basicity of organic compounds is the **Bronsted-Lowry theory**. When an acid in solution reacts with a base, what is actually functioning as the acid is the hydroxonium ion. For example, a proton is transferred from a hydroxonium ion to a hydroxide ion to make water.

$$H_3O^+_{(aq)} + OH^-_{(aq)} \longrightarrow 2H_2O_{(l)}$$
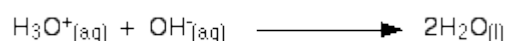
e electrons, but leaving out the inner ones:

This proton is transferred . . .   . . . to this lone pair.
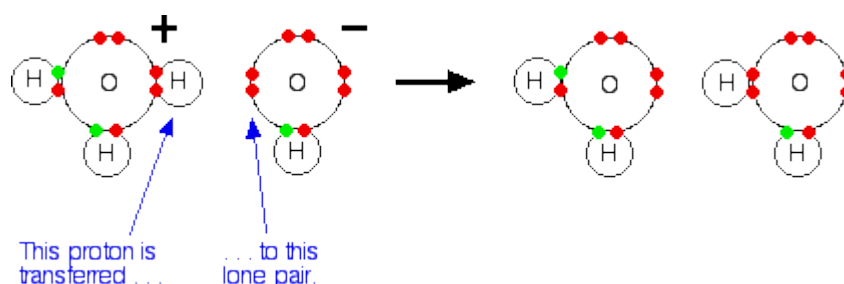
It is important to realise that whenever you talk about hydrogen ions in solution, $H^+_{(aq)}$, what you are actually talking about are hydroxonium ions.

The hydrogen chloride / ammonia problem

This is no longer a problem using the Bronsted-Lowry theory. Whether you are talking about the reaction in solution or in the gas state, ammonia is a base because it accepts a proton (a hydrogen ion). The hydrogen becomes attached to the lone pair on the nitrogen of the ammonia via a co-ordinate bond.

Incoming hydrogen ion attaches to this lone pair . . .

. . . and forms an ammonium ion.
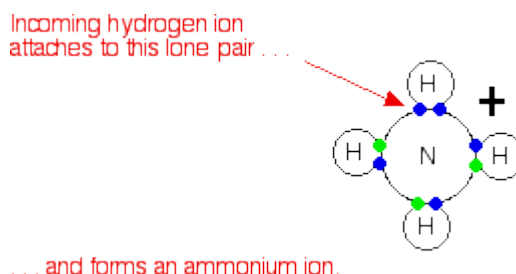
If it is in solution, the ammonia accepts a proton from a hydroxonium ion:

$$NH_{3(aq)} + H_3O^+_{(aq)} \longrightarrow NH_4^+_{(aq)} + H_2O_{(l)}$$
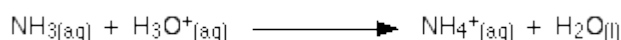
If the reaction is happening in the gas state, the ammonia accepts a proton directly from the hydrogen chloride:

$$NH_{3(g)} + HCl_{(g)} \longrightarrow NH_4^+_{(s)} + Cl^-_{(s)}$$
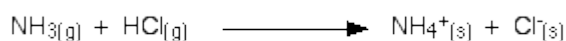
Either way, the ammonia acts as a base by accepting a hydrogen ion from an acid.

Conjugate pairs

When hydrogen chloride dissolves in water, almost 100% of it reacts with the water to produce hydroxonium ions and chloride ions. Hydrogen chloride is a strong acid, and we tend to write this as a one-way reaction:

$$H_2O + HCl \longrightarrow H_3O^+ + Cl^-$$

In fact, the reaction between HCl and water is reversible, but only to a very minor extent. In order to generalise, consider an acid HA, and think of the reaction as being reversible.

$$HA + H_2O \rightleftharpoons H_3O^+ + A^-$$

Thinking about the *forward reaction:*

- The HA is an acid because it is donating a proton (hydrogen ion) to the water.
- The water is a base because it is accepting a proton from the HA.

But there is also a *back reaction* between the hydroxonium ion and the A⁻ ion:

- The H_3O^+ is an acid because it is donating a proton (hydrogen ion) to the A⁻ ion.
- The A⁻ ion is a base because it is accepting a proton from the H_3O^+.

The reversible reaction contains *two* acids and *two* bases. We think of them in pairs, called ***conjugate pairs***.
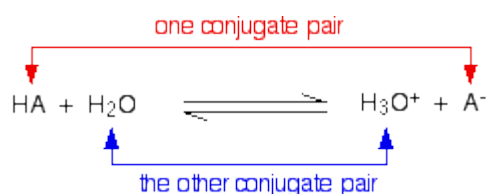
When the acid, HA, loses a proton it forms a base, A⁻. When the base, A⁻, accepts a proton back again, it obviously refoms the acid, HA. These two are a conjugate pair.

Members of a conjugate pair differ from each other by the presence or absence of the transferable hydrogen ion.

If you are thinking about HA as the acid, then A⁻ is its conjugate base.

If you are thinking about A⁻ as the base, then HA is its conjugate acid.

The water and the hydroxonium ion are also a conjugate pair. Thinking of the water as a base, the hydroxonium ion is its conjugate acid because it has the extra hydrogen ion which it can give away again.

Thinking about the hydroxonium ion as an acid, then water is its conjugate base. The water can accept a hydrogen ion back again to reform the hydroxonium ion.

A second example of conjugate pairs

This is the reaction between ammonia and water that we looked at earlier:
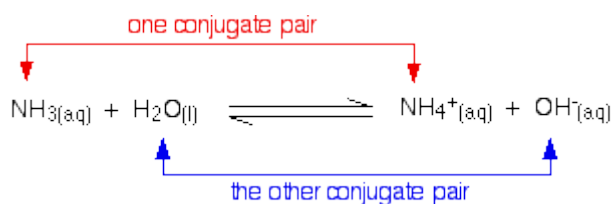
Think first about the forward reaction. Ammonia is a base because it is accepting hydrogen ions from the water. The ammonium ion is its conjugate acid - it can release that hydrogen ion again to reform the ammonia.

The water is acting as an acid, and its conjugate base is the hydroxide ion. The hydroxide ion can accept a hydrogen ion to reform the water.

Looking at it from the other side, the ammonium ion is an acid, and ammonia is its conjugate base. The hydroxide ion is a base and water is its conjugate acid.

Amphoteric substances

You may possibly have noticed (although probably not!) that in one of the last two examples, water was acting as a base, whereas in the other one it was acting as an acid.

A substance which can act as either an acid or a base is described as being ***amphoteric***.
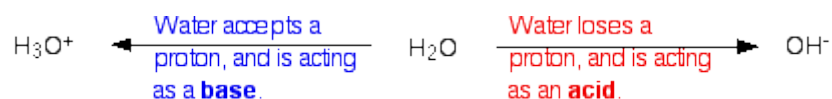
Note: You might also come across the term ***amphiprotic*** in this context. The two words are related and easily confused.

An *amphiprotic* substance is one which can both donate hydrogen ions (protons) and also accept them. Water is a good example of such a compound. The water acts as both an acid (donating hydrogen ions) and as a base (by accepting them). The "protic"

part of the word refers to the hydrogen ions (protons) either being donated or accepted. Other examples of amphiprotic compounds are amino acids, and ions like HSO_4^- (which can lose a hydrogen ion to form sulphate ions or accept one to form sulphuric acid).

But as well as being amphiprotic, these compounds are also *amphoteric*. Amphoteric means that they have reactions as both acids and bases. So what is the difference between the two terms?

All amphiprotic substances are also amphoteric - but the reverse isn't true. There are amphoteric substances which don't either donate or accept hydrogen ions when they act as acids or bases. There is a whole new definition of acid-base behaviour that you are just about to meet (the Lewis theory) which doesn't necessarily involve hydrogen ions at all.

A Lewis acid is an electron pair acceptor; a Lewis base is an electron pair donor (see below).

Some metal oxides (like aluminium oxide) are amphoteric - they react both as acids and bases. For example, they react as bases because the oxide ions accept hydrogen ions to make water. That's not a problem as far as the definition of amphiprotic is concerned - but the reaction as an acid is. The aluminium oxide doesn't contain any hydrogen ions to donate! But aluminium oxide reacts with bases like sodium hydroxide solution to form complex aluminate ions.

You can think of lone pairs on hydroxide ions as forming dative covalent (coordinate) bonds with empty orbitals in the aluminium ions. The aluminium ions are accepting lone pairs (acting as a Lewis acid). So aluminium oxide can act as both an acid and a base - and so is amphoteric. But it *isn't* amphiprotic because *both* of the acid reaction and the base reaction don't involve hydrogen ions.

I have gone through 40-odd years of teaching (in the lab, and via books and the internet) without once using the term amphiprotic! I simply don't see the point of it. The term amphoteric takes in all the cases of substances functioning as both acids and bases without exception. The term amphiprotic can only be used where both of these functions involve transference of hydrogen ions - in other words, it can only be used if you are limited to talking about the Bronsted-Lowry theory. Personally, I would stick to the older, more useful, term "amphoteric" unless your syllabus demands that you use the word "amphiprotic".

The Lewis Theory of acids and bases

This theory extends well beyond the things you normally think of as acids and bases.

The theory

- An acid is an electron pair acceptor.
- A base is an electron pair donor.

The relationship between the Lewis theory and the Bronsted-Lowry theory

Lewis bases

It is easiest to see the relationship by looking at exactly what Bronsted-Lowry bases do when they accept hydrogen ions. Three Bronsted-Lowry bases we've looked at are hydroxide ions, ammonia and water, and they are typical of all the rest.

A hydroxide ion picks up a
hydrogen ion by attaching it to one
of the lone pairs on the oxygen.
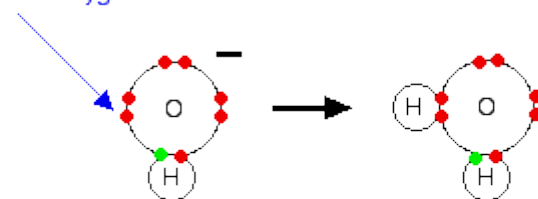
Ammonia picks up a hydrogen ion
by attaching it to the lone pair on
the nitrogen.
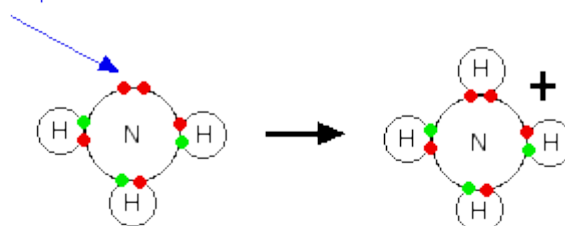
Water picks up a hydrogen ion by
attaching it to one of the lone pairs
on the oxygen.
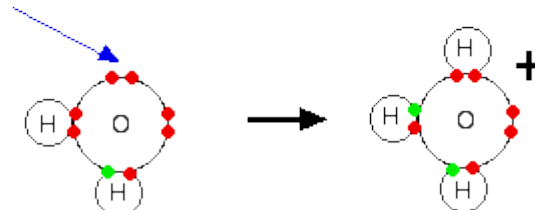
The Bronsted-Lowry theory says that they are acting as bases because they are combining with hydrogen ions. The reason they are combining with hydrogen ions is that they have lone pairs of electrons - which is what the Lewis theory says. The two are entirely consistent.

So how does this extend the concept of a base? At the moment it doesn't - it just looks at it from a different angle.

But what about other similar reactions of ammonia or water, for example? On the Lewis theory, *any* reaction in which the ammonia or water used their lone pairs of electrons to form a co-ordinate bond would be counted as them acting as a base.

Here is a reaction which you will find talked about on the page dealing with co-ordinate bonding. Ammonia reacts with BF_3 by using its lone pair to form a co-ordinate bond with the empty orbital on the boron.
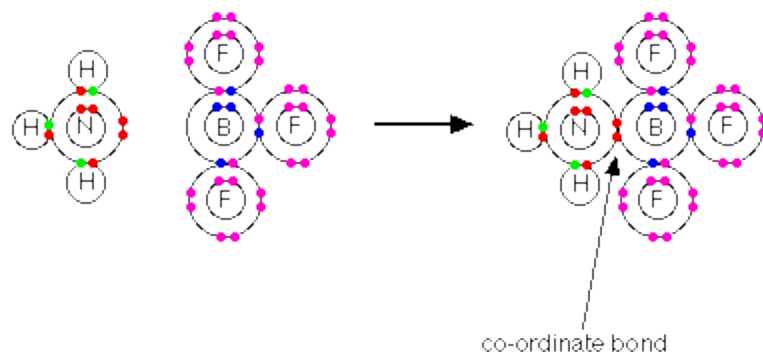
co-ordinate bond

As far as the ammonia is concerned, it is behaving exactly the same as when it reacts with a hydrogen ion - it is using its lone pair to form a co-ordinate bond. If you are going to describe

it as a base in one case, it makes sense to describe it as one in the other case as well.

Lewis acids

Lewis acids are electron pair acceptors. In the above example, the BF_3 is acting as the Lewis acid by accepting the nitrogen's lone pair. On the Bronsted-Lowry theory, the BF_3 has nothing remotely acidic about it.

This is an extension of the term *acid* well beyond any common use.

What about more obviously acid-base reactions - like, for example, the reaction between ammonia and hydrogen chloride gas?

$$NH_{3(g)} + HCl_{(g)} \longrightarrow NH_4^+{}_{(s)} + Cl^-{}_{(s)}$$

What *exactly* is accepting the lone pair of electrons on the nitrogen. Textbooks often write this as if the ammonia is donating its lone pair to a hydrogen ion - a simple proton with no electrons around it.

That is misleading! You don't usually get free hydrogen ions in chemical systems. They are so reactive that they are always attached to something else. There aren't any uncombined hydrogen ions in HCl.

There isn't an empty orbital anywhere on the HCl which can accept a pair of electrons. Why, then, is the HCl a Lewis acid?

Chlorine is more electronegative than hydrogen, and that means that the hydrogen chloride will be a polar molecule. The electrons in the hydrogen-chlorine bond will be attracted towards the chlorine end, leaving the hydrogen slightly positive and the chlorine slightly negative.

The lone pair on the nitrogen of an ammonia molecule is attracted to the slightly positive hydrogen atom in the HCl. As it approaches it, the electrons in the hydrogen-chlorine bond are repelled still further towards the chlorine.

Eventually, a co-ordinate bond is formed between the nitrogen and the hydrogen, and the chlorine breaks away as a chloride ion.

This is best shown using the "curly arrow" notation commonly used in organic reaction mechanisms.
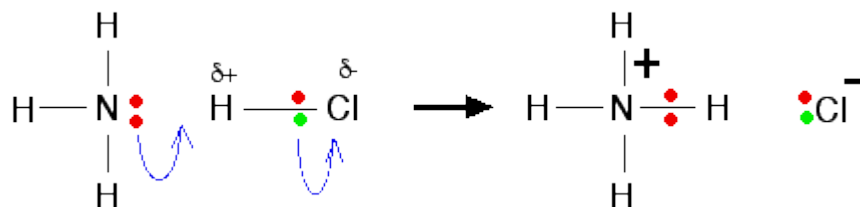
The whole HCl molecule is acting as a Lewis acid. It is accepting a pair of electrons from the ammonia, and in the process it breaks up. *Lewis acids don't necessarily have to have an existing empty orbital.*

A final comment on Lewis acids and bases

- A Lewis acid is an electron pair acceptor.

- A Lewis base is an electron pair donor.

Electronegativity matters when the acidity of compounds having the same radicals and elements of the acid center relating to the same period of the periodic system of DI Mendeleyev is compared (that is, when practically no the polarizability changes):

C–H acid	N–H acid	O–H acid	S–H acid	O–H acids	
$C_2H_5CH_2$–H propane	C_2H_5NH–H ethylamine	C_2H_5O–H ethanol	C_2H_5S–H ethanethiol	C_6H_5O–H phenol	CH_3COO–H acetic acid
$pK_a = 50$	$pK_a = 30$	$pK_a = 16$	$pK_a = 10,6$	$pK_a = 10$	$pK_a = 4,8$

The more electronegative is the element in the acid center, the more it is able to carry a negative charge, and the more stable the anion formed, and accordingly the stronger the acid.

- from the *polarizability* of the heteroatom. The greater the polarizability of the heteroatom, the stronger the corresponding acid. For example: R-SH and R-OH. Thiols are stronger acids than alcohols, since the S atom is more polarized than the O atom.

The polarizability of an atom characterizes the measure of the displacement (dispersal) of valence electrons under the action of an external electric field. The more electrons in an atom and the further they are from the nucleus, the greater is its polarizability. Within the group of Mendeleev's table of elements, the stability of anions increases with the increase in the atomic number of the element, as the volume of electronic orbitals increases, and a better opportunity exists for delocalization of the negative charge. Therefore, SH acids are stronger acids than OH acids.

Thiols, like stronger acids, in contrast to alcohols, react not only with alkali metals, but also with alkalis, as well as oxides and salts of heavy metals (mercury, lead, arsenic, chromium, bismuth, etc.):

$$R — SH + NaOH \rightarrow R — S — Na + H_2O$$

меркаптид Na

$$2R — SH + HgCl_2 \rightarrow \begin{matrix} R — S \\ R — S \end{matrix} \Big> Hg + 2\,HCl$$

меркаптид ртути
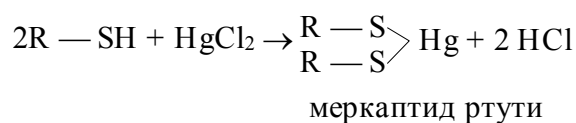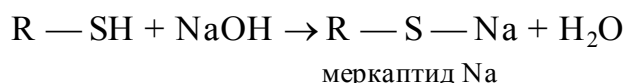
Mercaptides of mercury and silver are insoluble in water, so this reaction underlies amperometric determination of thiols in biological fluids.

So, with the same radicals, the acidity decreases in the series:

$$SH > OH > NH > CH.$$
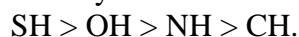
- on the nature of the substituent R (its length, the presence of a conjugated system, the delocalization of the electron density). For example: CH_3-OH, CH_3-CH_2-OH, CH_3-CH_2-CH_2-OH. Acidity is less, as the length of the radical increases.

At the same acid center, the strength of alcohols, phenols and carboxylic acids is not the same. Phenols are stronger acids than alcohols due to the p, s-conjugation (+ M) of the (-OH) group. The O-H bond is more polarized in phenols. Phenols can interact even with salts. Carboxylic acids in comparison with alcohols containing the same R are stronger acids, since the O-H bond is significantly polarized due to the M-effect of the group> C = O. In addition, the

carboxylate anion is more stable than the alcohol anion due to p, s-conjugation in the carboxyl group.

When speaking of an atom's ability to polarize a bond, we often use the **term inductive effect**. An inductive effect is simply the shifting of electrons in a σ bond in response to the electronegativity of nearby atoms. Metals, such as lithium and magnesium, inductively donate electrons, whereas reactive non-metals, such as oxygen and nitrogen, inductively withdraw electrons. Inductive effects play a major role in understanding chemical reactivity, and we'll use them many times throughout this text to explain a variety of chemical phenomena. When speaking of an atom's ability to polarize a bond, we often use the term inductive effect.

Polar Covalent Bonds: Dipole Moments

Just as individual bonds are often polar, molecules as a whole are often polar also. Molecular polarity results from the vector summation of all individual bond polarities and lone-pair contributions in the molecule. As a practical matter, strongly polar substances are often soluble in polar solvents like water, whereas nonpolar substances are insoluble in water. Net molecular polarity is measured by a quantity called the dipole moment and can be thought of in the following way: assume that there is a center of mass of all positive charges (nuclei) in a molecule and a center of mass of all negative charges (electrons). If these two centers don't coincide, then the molecule has a net polarity.

The **dipole moment**, μ (Greek mu), is defined as the magnitude of the charge Q at either end of the molecular dipole times the distance r between the charges, Q x r. Dipole moments are expressed in debyes (D), where 1 D 3.336 = 10^{-30} coulomb meter (C · m) in SI units.

Dipole Moments of Some Compounds

Compound	Dipole moment (D)	Compound	Dipole moment (D)
NaCl	9.00	NH_3	1.47
CH_2O	2.33	CH_3NH_2	1.31
CH_3Cl	1.87	CO_2	0
H_2O	1.85	CH_4	0
CH_3OH	1.70	CH_3CH_3	0
CH_3CO_2H	1.70	Benzene	0
CH_3SH	1.52		

Formal Charges

Closely related to the ideas of bond polarity and dipole moment is the concept of assigning formal charges to specific atoms within a molecule, particularly atoms that have an apparently "abnormal" number of bonds. Look at dimethyl sulfoxide (CH_3SOCH_3), for instance, a solvent commonly used for preserving biological cell lines at low temperatures. The sulfur atom in dimethyl sulfoxide has three bonds rather than the usual two and has a formal positive charge. The oxygen atom, by contrast, has one bond rather than the usual two and has a formal negative charge. Note that an electrostatic potential map of dimethyl sulfoxide shows the oxygen as negative (red) and the sulfur as relatively positive (blue), just as the formal charges suggest.

Formal negative charge on oxygen

Formal positive charge on sulfur

Dimethyl sulfoxide
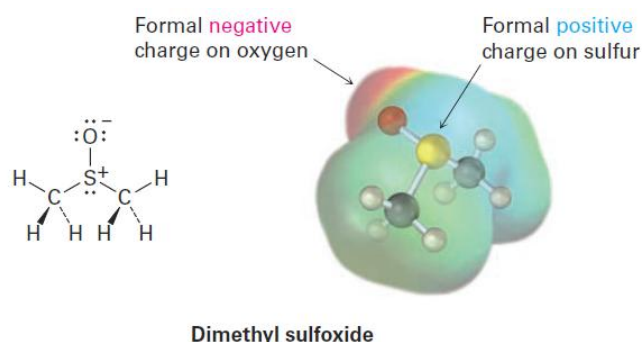
Formal charges, as the name suggests, are a formalism and don't imply the presence of actual ionic charges in a molecule. Instead, they're a device for electron "bookkeeping" and can be thought of in the following way: a typical covalent bond is formed when each atom donates one electron. Although the bonding electrons are shared by both atoms, each atom can still be considered to own one electron for bookkeeping purposes. In methane, for instance, the carbon atom owns one electron in each of the four C–H bonds, for a total of four. Because a neutral, isolated carbon atom has four valence electrons, and because the carbon atom in methane still owns four, the methane carbon atom is neutral and has no formal charge.

Resonance

Most substances can be represented by the Kekul line-bond structures we've been using up to this point, but an interesting problem sometimes arises. Look at the acetate ion, for instance. When we draw a line-bond structure for acetate, we need to show a double bond to one oxygen and a single bond to the other. But which oxygen is which? Should we draw a double bond to the "top" oxygen and a single bond to the "bottom" oxygen or vice versa?
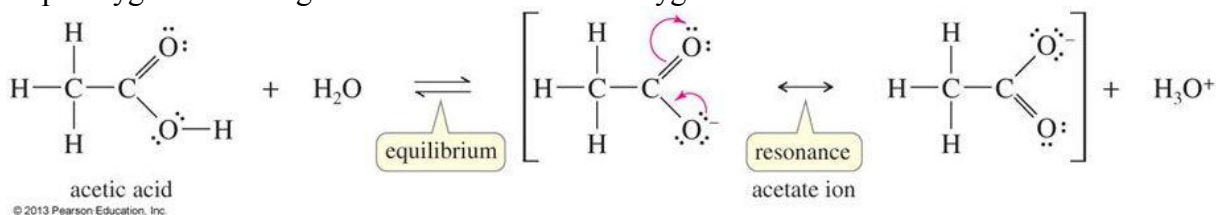
Although the two oxygen atoms in the acetate ion appear different in line-bond structures, they are in fact equivalent. Both carbon–oxygen bonds, for example, are 127 pm in length, midway between the length of a typical C–O single bond (135 pm) and a typical C=O double bond (120 pm). In other words, neither of the two structures for acetate is correct by itself.

The two individual line-bond structures for acetate are called resonance forms, and their special resonance relationship is indicated by the double-headed arrow between them. The only difference between resonance forms is the placement of the π and nonbonding valence electrons. The atoms themselves occupy exactly the same place in both resonance forms, the connections between atoms are the same, and the three-dimensional shapes of the resonance forms are the same.

A good way to think about resonance forms is to realize that a substance like the acetate ion is no different from any other. Acetate doesn't jump back and forth between two resonance forms, spending part of the time looking like one and part of the time looking like the other. Rather, acetate has a single unchanging structure that we say is a **resonance hybrid** of the two individual forms and has characteristics of both. The only "problem" with acetate is that we can't draw it accurately using a familiar line-bond structure—line-bond structures just don't work well for resonance hybrids. The difficulty, however, lies with the representation of acetate on paper, not with acetate itself.

Predicting Acid–Base Reactions from pKa Values

Compilations of pKa values like those in Table

Functional group	Example	pKa	conj. base
Alkane	CH_4	~50	$:CH_3^{\ominus}$
Amine	$:NH_3$	~35	$:NH_2^{\ominus}$
Alkyne	$R{-}{\equiv}{-}H$	25	$R{-}C{\equiv}C:^{\ominus}$
Water	HO–H	16	$:OH^{\ominus}$
Protonated amines	$NH_4^{\oplus} Cl^{\ominus}$	10	$:NH_3$
Carboxylic acids	H_3C O OH	5	H_3C O $O:^{\ominus}$
Hydrochloric acid	HCl	–8	$:Cl:^{\ominus}$

Weaker acid → Stronger acid (down the pKa column)
Stronger base → Weaker base (up the conj. base column)

useful for predicting whether a given acid–base reaction will take place because H$^+$ will always go from the stronger acid to the stronger base. That is, an acid will donate a proton to the conjugate base of a weaker acid, and the conjugate base of a weaker acid will remove the proton from a stronger acid. For example, since water (pKa = 15.74) is a weaker acid than acetic acid (pKa 4.76), hydroxide ion holds a proton more tightly than acetate ion does. Hydroxide ion will therefore react with acetic acid, CH_3CO_2H, to yield acetate ion and H_2O.

$$CH_3CO_2H_{(aq)} + H_2O_{(l)} \rightleftharpoons CH_3CO_2^-{}_{(aq)} + H_3O^+{}_{(aq)}$$

Acid · Base · Conjugate base · Conjugate acid
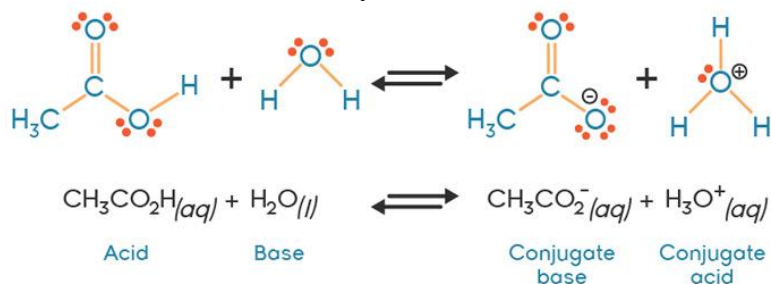
Another way to predict acid–base reactivity is to remember that the product conjugate acid in an acid–base reaction must be weaker and less reactive than the starting acid and that the product conjugate base must be weaker and less reactive than the starting base. In the reaction of acetic acid with hydroxide ion, for example, the product conjugate acid (H_2O) is weaker than the starting acid ($CH3CO2H$) and the product conjugate base (CH_3CO_2H) is weaker than the starting base (OH^-).

•The stronger the acid the weaker the conjugate base.
•The stronger the base the weaker the conjugate acid.

$$CH_3COOH + H_2O \rightleftharpoons CH_3COO^- + H_3O^+$$

weak acid · weak base · Left side favored · strong base · strong acid
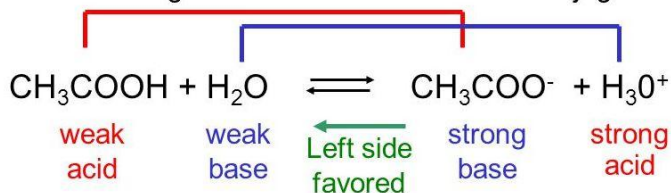
Organic Acids and Organic Bases

Almost all biological reactions involve organic acids and organic bases. Although it's too early to go into the details of these processes now, you might keep the following generalities in mind as your study progresses.

Organic Acids

Organic acids are characterized by the presence of a positively polarized hydrogen atom (blue in electrostatic potential maps) and are of two main kinds: those acids such as methanol and acetic acid that contain a hydrogen atom bonded to an electronegative oxygen atom (O–H) and those such as acetone and acetyl CoA that contain a hydrogen atom bonded to a carbon atom next to a C=O double bond (O=C–C–H).

Methanol ($pK_a = 15.54$) Acetic acid ($pK_a = 4.76$) Acetone ($pK_a = 19.3$)
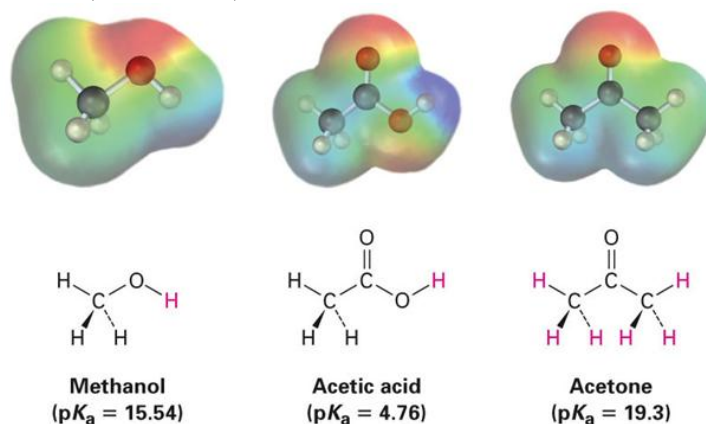
Methanol contains an O–H bond and is a weak acid, while acetic acid also contains an O–H bond and is a somewhat stronger acid. In both cases, acidity is due to the fact that the conjugate base resulting from loss of H+ is stabilized by having its negative charge on a strongly electronegative oxygen atom. In addition, the conjugate base of acetic acid is stabilized by resonance.

Compounds called carboxylic acids, which contain the –CO2H grouping, occur abundantly in all living organisms and are involved in almost all metabolic pathways. Acetic acid, pyruvic acid, and citric acid are examples. You might note that at the typical pH of 7.3 found within cells, carboxylic acids are usually dissociated and exist as their carboxylate anions, $-CO_2$.

Organic Bases

Organic bases are characterized by the presence of an atom (reddish in electrostatic potential maps) with a lone pair of electrons that can bond to H+. Nitrogen-containing compounds such as methylamine are the most common organic bases and are involved in almost all metabolic pathways, but oxygen-containing compounds can also act as bases when reacting with a sufficiently strong acid.

Note that some oxygen-containing compounds can act both as acids and as bases depending on the circumstances, just as water can. Methanol and acetone, for instance, act as acids when they donate a proton but as bases when their oxygen atom accepts a proton.

Methylamine Methanol Acetone

Laboratory work № 8
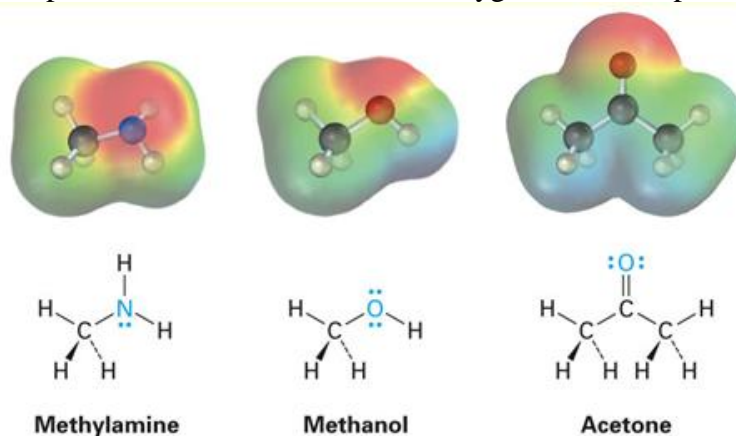
Reagents and equipment:
1. Distilled water.
2. Ethanol, ethylene glycol.
3. Metallic sodium.
4. Aqueous solutions: 2% copper (II) sulfate, 10% sodium hydroxide, 10% HCl.
5. 1% alcohol solution of phenolphthalein.
6. Phenol.
7. Aniline, diethylamine.
8. A saturated solution of picric acid.
9. A tripod with test tubes, test tubes with a gas outlet tube.
10. The alcohol lamp.

Experiment 1. Preparation of sodium ethoxide and its hydrolysis

In a dry test tube, place 3 drops of ethanol and add a piece of metallic sodium, previously squeezed from kerosene on the filtered paper, as large as the rice seed. Collect the evolved hydrogen by covering the tube with a stopper. Then remove the plug and hold the test tube with a hole in the flame of the burner. A mixture of hydrogen and air burns with a characteristic "barking" sound. A white precipitate of sodium ethoxide is dissolved in 2-4 drops of ethanol and add 1 drop of 1% alcohol solution of phenolphthalein. Then add 1-2 drops of water to the test tube. Explain the appearance of crimson color.

Conclusion:

Experiment 2. Preparation of copper (II) ethylene glycolate

In a test tube, add 2 drops of a 2% solution of copper (II) sulphate and 2 drops of 10% sodium hydroxide solution. Add 1 drop of ethylene glycol to the pellet and shake the tube. Copper glycolate is formed, a solution of which has a blue color. This reaction is used to detect organic compounds containing a diol fragment (two hydroxyl groups at neighboring carbon atoms).

Conclusion:

Experiment 3. Formation of sodium phenolate and its decomposition by acid

In a test tube with 3 drops of water, place a few crystals of phenol and shake. To the resulting turbid emulsion add a 10% solution of sodium hydroxide drop by drop, to a clear solution. Acidify this solution with a few drops of 10% hydrochloric acid solution.

Conclusion:

Experiment 4.. Basicity of aliphatic and aromatic amines

a) Add 2 drops of water to two test tubes. Then place 1 drop of aniline in the 1st tube, and in the 2nd - 1 drop of diethylamine and shake. Compare the solubility of these amines in water. Determine the pH of the solutions of aniline and diethylamine.

b) To aniline emulsion in water, add 1 drop of 10% hydrochloric acid solution. A clear solution forms. To a solution of diethylamine, add 3 drops of a saturated solution of picric acid. And stir. Place the tube in a glass with cold water. After a while the precipitate of picrate of diethylamine precipitates.

Conclusion:

Tasks for independent work

Control questions:

1. Write the equation for the reaction for the preparation of sodium phenolate. Why does phenol, in contrast to alcohols, react with alkalis?

2. What is the reason for the more acidic character of phenolic hydroxyl compared to alcohol?

3. Why is the turbidity of the solution observed when adding HCl to a solution of sodium phenolate? Why is sodium phenolate not decomposed by water?

4. Write a scheme for the interaction of ethylene glycol with copper (II) hydroxide to form a chelate complex of copper glycolate.

5. Which structural fragment contains organic compounds that dissolve copper (II) hydroxide?

6. Write a diagram of the interaction of diethylamine with picric acid (2,4,6-trinitrophenol).

7. Compare the acidity of ethylene glycol and ethanol. What reactions can confirm the difference in their acidity?

8. How are the acids divided according to the nature of the element bound to the proton?

9. What is Ka, pKa? What is the relationship between their magnitude and the strength of the acid?

10. Determine the acid and base according to the Bronsted theory.

11. What factors determine the strength of acids? List them.

12. How does acidity depend on the nature of the atom in the acid center? How does it change in groups, in periods? Why?

13. Describe the effect of donor and acceptor substituents on the strength of acids and bases.

14. How does the acidity depend on the nature of the solvent?

15. What are p- and p-bases? Give examples.

16. What quantity is the quantitative characteristic of the strength of the bases? The physical meaning of pK.

17. Determination of acids and bases according to the theory of Lewis.

18. The essence of the principle of hard and soft acids and bases. Describe hard and soft acids and bases. Acidity of body fluid systems.

19. Write the equation for the reactions of obtaining sodium ethoxide and its hydrolysis.

20. What property of alcohols is manifested in the reaction with metallic sodium?

21. Is it possible to detect the acid properties of a standard using color indicators?

22. Why do alcohols react with sodium more slowly than water?

23. Why does water decompose sodium ethoxide?

24. Compare the basicity of diethylamine and aniline.

25. Why is a clear solution formed when aniline is added to the emulsion of hydrochloric acid? Write the reaction equation.

Do the exercises:

1. Define the concepts of "acid" and "basis" according to the theory of Bronsted-Lowry. Give examples where the compound, depending on the conditions, exhibits acidic or basic properties.

2. Arrange these compounds in order of decreasing acidity, indicating the acid centers:

a) Ethanol, ethane, ethanamine

b) phenol, *p*-nitrophenol, *p*-aminophenol

c) methanol, methanthiol.

Answer explain.

3. Which alcohol from each pair of compounds will show stronger acid properties:
1) CH_3—CH_2—CH_2—CH_2—OH и CH_3—CH_2—CH_2—OH
2) CH_3— CH_2— OH и HO— CH_2— CH_2— OH?

4. In the reactions listed, indicate the conjugate acid-base pairs:

1) $CH_3-C\underset{OH}{\overset{O}{\big\langle}} + H\ddot{O}H \rightleftharpoons CH_3-C\underset{O^-}{\overset{O}{\big\langle}} + H_3O^+$

2) $C_6H_5NH_2 + HCl \rightleftharpoons C_6H_5\overset{+}{N}H_3 + Cl^-$
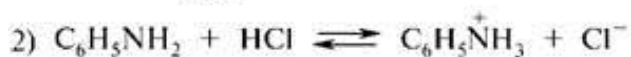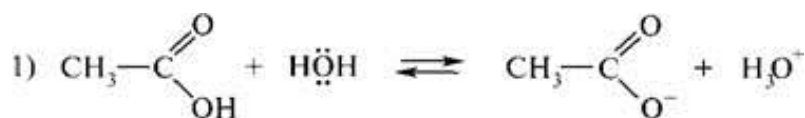
Write formulas for calculating the strength of acids and bases.

5. Determine the acid and base centers in the following compounds:
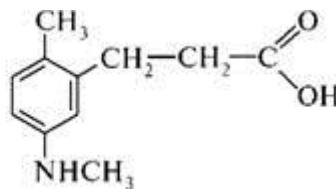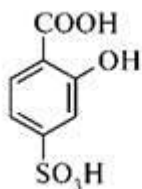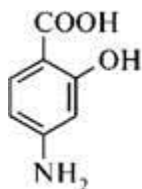
6. Indicate the acid centers in the molecules of the given compounds and arrange them in descending order of acidity:
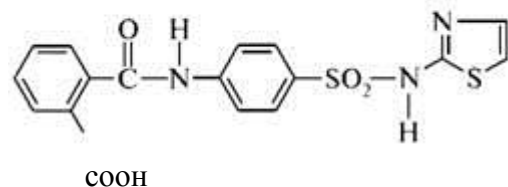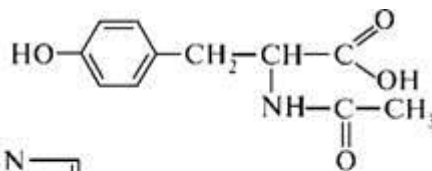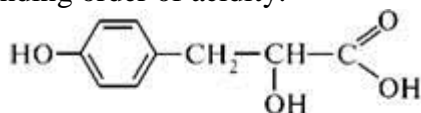
7. Compare the main properties of the following compounds:

a) diethyl ether, diethyl sulfide, diethylamine

b) aniline, acetyl anilide, cyclohexylamine.

Answer explain.

8. Indicate the main centers in the molecules of the given compounds and arrange them in descending order of basicity
:
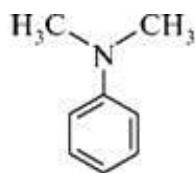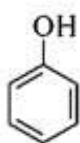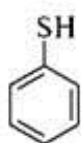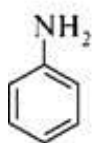
9. Arrange these compounds in order of decreasing acidity, explaining the answer by the distribution of electron density in molecules:
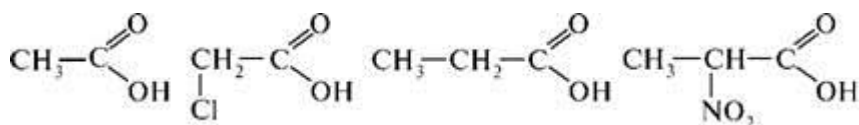
10. Compare the basicity of the following compounds: 2-aminoethanol and ethylamine, aniline. For a stronger base, write a salt formation reaction.

11. Indicate the centers of basicity in the molecule of Novocain - an ester of p-aminobenzoic acid and diethylaminoethanol, which is used in surgical practice for local anesthesia. Write a reaction for the formation of a salt of novocaine with hydrochloric acid.

12. Compare the acid properties of alcohols and thiols. Explain the differences from the positions of the electronic structure of atoms forming an acid center. Provide a scheme of reactions that prove the acid properties of these compounds.

13. Is it possible to form hydrogen bonds in alcohols. Answer to clarify. Does the formation of hydrogen bonds affect the properties of compounds?

14. For the treatment of acute and chronic poisoning BAL (British antilyuizit) and succimer are used. Give the names of these compounds according to the systematic nomenclature.
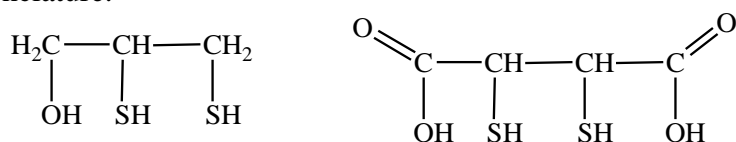
Establish acidity centers in the molecules of these compounds, which of them predominantly determine the acidity of each compound.

15.
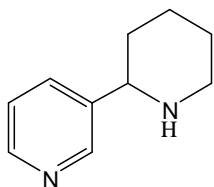
The molecule of the anabasin alkaloid contains two nitrogen atoms. Select the most basic center in the molecule of the compound and give the structure of its anabasine salt with hydrochloric acid.

Test tasks:
1. A number of compounds whose acidity increases:
a) glycerin; phenol; water
b) ethanol; water; phenol
c) phenol; ethylene glycol; methanol
d) ethanol, methanol, phenol

2. Alcohol interacting with a freshly precipitated solution of copper (II) hydroxide:
a) CH_3OH
b) $C_6H_{11}OH$
c) $CH_2(OH)–CH(OH)–CH_2OH$
d) $CH_2(OH)–CH_2–CH_2–CH_3$

3. A compound that reacts chemically with sodium hydroxide:
a) C_6H_5OH
b) CH_3CH_2OH

c) $C_6H_{13}OH$

d) $C_6H_5–CH_2OH$

4. Solubility of alcohols in water series $C_3H_7OH{\rightarrow}C_4H_9OH{\rightarrow}C_5H_{11}OH$ …

a) decreases

b) does not change

c) decreases, and then increases

d) increases

5. Reagent, which forms a violet staining of the solution in the interaction with phenol:

a) bromine water

b) sodium hydroxide

c) copper (II) hydroxide

d) ferric chloride (III)

6. The sequence of compounds in order of increasing their acid properties:

a) glycerin

b) hexanol

c) ethanol

d) phenol

7. Conformity of compounds and solutions of reagents for their qualitative determination:

1) phenol	a) iron (III) chloride
2) ethylene glycol	b) copper (II) hydroxide
3) acetylene	c) sodium hydroxide
	e) Chloride diammine silver

Answer: 1- ..., 2- ..., 3- ....

8. In the substance CH_3-CH_2-OH, the bond between carbon and oxygen atoms:

a) covalent nonpolar

b) covalent polar

c) ionic

d) hydrogen

9. Arrange the substances in order of increasing acidity:

a) H-OH

b) C_2H_5OH

c) CH_3COOH

d) C_6H_5OH

10. Polyatomic are called alcohols, in the molecule of which

a) many oxygen atoms

b) many carbon atoms

c) two or more hydroxyl groups

d) two or more carboxyl groups

Timing of a 3-hour lesson:

1. Organizational moment - 2 minutes.

2. The survey - 40 min.

3. Explanation of the work - 25 min.

4. Performance and execution of work - 30 min.

5. Presentation of the new material - 45 min.

6. Verification of work and assignment to the house - 3 min.

Literature:

TOPIC: POLY- AND HETERO-FUNCTIONAL COMPOUNDS

The purpose of the lesson is to generate knowledge about the spatial structure and specific chemical properties of aliphatic hetero-functional compounds as a basis for the subsequent study and understanding of their metabolic transformations in the body. On the basis of theoretical knowledge, develop skills in solving problems of optical isomerism of molecules and its medical and biological applications, in predicting stereoisomers and their reactivity, in identifying various functional groups.

The purpose of the activities of students in class
The student should know:
a) Classification of heterofunctional compounds.
b) Structure and properties of biologically important classes of poly- and hetero-functional compounds.
c) Specific reactions of poly- and hetero-functional compounds.
d) Heterofunctional benzene derivatives used as medicaments.

The student **should be able to**:
a) Prove the amphoteric properties of α-amino acids.
b) Confirm by the reaction equations the presence of two carboxyl and two alcohol groups in tartaric acid.
c) Write a diagram of the ketone decomposition of acetoacetic ether.

Questions for testing the baseline level:
1. Acidity and basicity of organic molecules.
2. How are the acids divided according to the nature of the element bound to the proton?
3. Define acid and base according to the Bronsted theory.
4. Describe the effect of donor and acceptor substituents on the strength of acid and bases.
5. What is the quantitative characteristic of the strength of the bases? The physical meaning of pK.
6. Determination of acids and bases according to Lewis theory.
7. Pearson's theory. The essence of the hard and soft acids and bases principle. Describe hard and soft acids and bases. Acidity of body fluid systems.
8. Types of organic acids (OH-, SH-, NH- and CH-acids).
9. Types of organic bases. p-base and p-base. Give examples.
10. Factors determining acidity and basicity: electronegativity and polarizability of the atom of the acid and base centers, delocalization of the charge through a system of conjugated bonds, electronic effects of substituents, solvation effect.

Theoretical part

Metabolism (/məˈtæbəlɪzəm/, from Greek: μεταβολή metabolē, "change") is the set of life-sustaining chemical transformations within the cells of organisms. The three main purposes of metabolism are the conversion of food/fuel to energy to run cellular processes, the conversion of food/fuel to building blocks for proteins, lipids, nucleic acids, and some carbohydrates, and the elimination of nitrogenous wastes. These enzyme-catalyzed reactions allow organisms to grow and reproduce, maintain their structures, and respond to their environments. The word metabolism can also refer to the sum of all chemical reactions that occur in living organisms, including digestion and the transport of substances into and between different cells, in which case the set of reactions within the cells is called intermediary *metabolism* or *intermediate metabolism* (*Wiki*).

The vast majority of substances involved in metabolism belongs to poly- or heterofunctional compounds.

Functional groups most common in compounds involved in vital processes:

FUNCTIONAL GROUPS IN ORGANIC CHEMISTRY

FUNCTIONAL GROUPS ARE GROUPS OF ATOMS IN ORGANIC MOLECULES THAT ARE RESPONSIBLE FOR THE CHARACTERISTIC CHEMICAL REACTIONS OF THOSE MOLECULES. IN THE GENERAL FORMULAE SHOWN BELOW FOR EACH FUNCTIONAL GROUP, 'R' REPRESENTS THE REST OF THE MOLECULE, AND 'X' REPRESENTS ANY HALOGEN ATOM.

● HYDROCARBONS ● SIMPLE OXYGEN HETEROATOMICS ● HALOGEN HETEROATOMICS ● CARBONYL COMPOUNDS ● NITROGEN-BASED ● SULFUR-BASED ● AROMATIC

ALKANE — Naming: -ane — e.g. ethane
ALKENE — Naming: -ene — e.g. ethene
ALKYNE — Naming: -yne — e.g. ethyne
ALCOHOL — Naming: -ol — e.g. ethanol
ETHER — Naming: -oxy -ane — e.g. methoxyethane
EPOXIDE — Naming: -ene oxide — e.g. ethene oxide
HALOALKANE — Naming: halo- — e.g. chloroethane

ALDEHYDE — Naming: -al — e.g. ethanal
KETONE — Naming: -one — e.g. propanone
CARBOXYLIC ACID — Naming: -oic acid — e.g. ethanoic acid
ACID ANHYDRIDE — Naming: -oic anhydride — e.g. ethanoic anhydride
ESTER — Naming: -yl -oate — e.g. ethyl ethanoate
AMIDE — Naming: -amide — e.g. ethanamide
ACYL HALIDE — Naming: -oyl halide — e.g. ethanoyl chloride

AMINE — Naming: -amine — e.g. ethanamine
NITRILE — Naming: -nitrile — e.g. ethanenitrile
IMINE — Naming: -imine — e.g. ethanimine
ISOCYANATE — Naming: -yl isocyanate — e.g. ethyl isocyanate
AZO COMPOUND — Naming: azo- — e.g. azoethane
THIOL — Naming: -thiol — e.g. methanethiol
ARENE — Naming: -yl benzene — e.g. ethyl benzene

Chemists observed early in the study of organic compoundsthat certain groups of atoms and associated bonds, known as *__functional groups,__* confer specific reactivity patterns on the molecules of which they are a part. Although the properties of each of the several million organic molecules whose structure is known are unique in some way, all molecules that contain the same functional group have a similar pattern of reactivity at the functional group site. Thus, functional groups are a key organizing feature of organic chemistry. By focusing on the functional groups present in a *__molecule__* (most molecules have more than one functional group), several of the reactions that the molecule will undergo can be predicted and understood.

Because carbon-to-carbon and carbon-to-hydrogen bonds are extremely strong and the *__charge__* of the electrons in these covalent bonds is spread more or less evenly over the bonded atoms, hydrocarbons that contain only single bonds of these two types are not very *__reactive__*. The reactivity of a molecule increases if it contains one or more weak bonds or bonds that have an unequal distribution of electrons between the two atoms. If the two electrons of a *__covalent bond__* are, for one reason or another, drawn more closely to one of the bonded atoms, that *__atom__* will develop a partial negative charge and the atom to which it is bonded will develop a partial positive charge. A covalent bond in which the electron pair linking the atoms is shared unequally is known as a *__polar bond__*. Polar bonds, and any other bonds that have unique electronic properties, confer the potential for *__chemical reaction__* on the molecule in which they are present. This is because, for every reaction, one or more bonds of a molecule must be broken and new bonds formed. The presence of a partial negative charge (a region of high electron density) will draw to itself other atoms or groups of atoms that are deficient in electron density. This initiates the process of bond breaking that is a prerequisite for a chemical reaction. For these reasons, molecules with regions of increased or decreased electron density are especially important for chemical change.

There are two major bonding features that generate the reactive sites of functional groups. The first, already mentioned, is the presence of multiple bonds. Both double and triple bonds have regions of high electron density lying outside the atom-to-atom bond axis. Double and triple bonds are known as functional groups, a term that is used to identify atoms or groups of atoms within a molecule that are sites of comparatively high reactivity. A second type of reactive site results when an atom other than carbon or hydrogen (termed a ***heteroatom***) is bonded to carbon. All heteroatoms have a greater or lesser attraction for electrons than does carbon. Thus, each bond between a carbon and a heteroatom is polar, and the degree of polarity depends on the difference between the electron-attracting properties of the two atoms. The most important atomic groupings that contain such reactive polar bonds are also able to generate functional groups.

To emphasize the generality of reactions between molecules that contain the same functional group, chemists often represent the less reactive portions of a molecule by the symbol R. Thus, all molecules that contain a double bond, however complicated, can be represented by the general formula for an *alkene*—i.e.,

$$\begin{array}{c} R \\ R \end{array} \!\! \Big\rangle C = C \Big\langle \!\! \begin{array}{c} R \\ R \end{array}$$
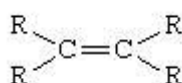
This type of formula suggests that the molecule will undergo those reactions that are common to double bonds and that the reaction will occur at the double bond. The rest of the molecule, represented by the four R groups, will remain unchanged by the reaction occurring at the functional group site.

Molecules with more than one functional group, called ***polyfunctional***, may have more complicated properties that result from the identity—and interconnectedness—of the multiple functional groups. Many natural products contain several functional groups located at specific sites within a large, complicated, three-dimensional structure.

A brief overview of the principal functional groups is presented here.

A significant importance in living systems belongs to ***heterofunctional compounds*** that involve different functional groups in the same molecule.

Some types of combining functional groups in heterofunctional compounds

Heterofunctional classes	Functional groups		Representatives formula	trivial name
Amino alcohols	NH_2	OH	$H_2NCH_2CH_2OH$	Colamine
Hydroxy carbonyl compounds	OH	$\rangle C=O$	$HOCH_2CHCH=O$ $\quad\quad\quad OH$	Glyceraldehyde
Hydroxy carboxylic acids	OH	COOH	$HOCH_2COOH$	Glycolic acid
Amino acids	NH_2	COOH	H_2NCH_2COOH	Glycine
Oxo acids	=O	COOH	$CH_3\underset{O}{\overset{\|}{C}}COOH$	Pyruvic acid

Among hetero-functional compounds in natural objects, aminoalcohols, amino acids, hydroxycarbonyl compounds, and also hydroxy and oxo acids are most common.

In the aromatic series, the basis of important natural biologically active compounds and synthetic drugs is p-aminophenol, and p-aminobenzoic, salicylic and sulfanilic acids (respectively):
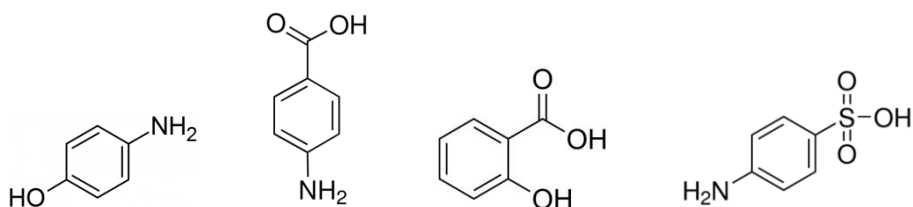
The systematic names of hetero-functional compounds are constructed according to the general rules of the substitution nomenclature. However, trivial names are preferred for a number of widely used acids. Their Latin names serve as the basis for the names of anions and derivatives of acids, which often do not coincide with Russian trivial names.

The chemical properties of poly- and hetero-functional compounds are largely determined by the properties of the corresponding monofunctional derivatives. Therefore, there is a certain similarity in the behavior of both classes of compounds: poly- and hetero-functional compounds exhibit the properties inherent in monofunctional compounds, i.e. the ability to react in each functional group.

However, the simultaneous presence of several functional groups in the molecule leads to the appearance of certain differences in the properties of mono-, poly- and hetero-functional compounds. First, in poly- and hetero-functional compounds, there may be an increase or, conversely, a weakening of some properties characteristic of monofunctional compounds. Secondly, specific chemical properties may appear in poly- and hetero-functional compounds, which are most important for ensuring the biological functions performed by these substances.

Acidity. *Accumulation of acid groups in the organic compound increases the acid properties of the compounds. Compare:*

$CH_3 - CH_2 - OH$ $\qquad\qquad\qquad$ $HO-CH_2 - CH_2 - OH$
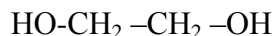
Ethanol $\qquad\qquad\qquad\qquad\qquad$ Ethylene glycol

Ethylene glycol exhibits stronger acid properties than ethanol, which is due to the -I effect of the group CH_2OH

Basicity. *Accumulation of the basic amino groups in the molecule increases the basic properties of the compounds.*
Let's compare:

$$CH_3 - C \overset{O}{\underset{NH_2}{\diagup}}$$
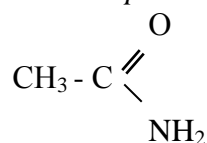
acetamide, shows a neutral character and does not react with dilute mineral acids.

A urea (2-NH_2 group) forms with them fairly stable salts:

$$H_2N-C-NH_2 \xrightarrow{HCl, H2O} \left[\overset{+}{H_2N}-\underset{OH}{\overset{|}{C}}-NH_2\ Cl \right]^-$$
$$\underset{O}{\overset{\|}{}}$$

Urea $\qquad\qquad\qquad\qquad\qquad$ Hydrochloride
$\qquad\qquad\qquad\qquad\qquad\qquad\qquad$ urea
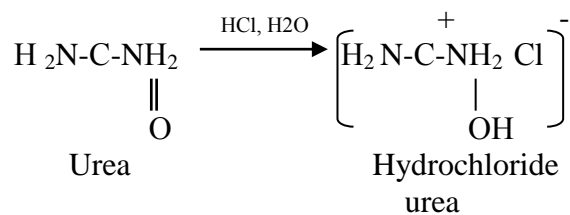
Amphotericity. *Heterofunctional compounds containing simultaneously acidic and basic functional groups exhibit amphoteric properties.*

For example: amphotericity of α-amino acids is due to the presence of functional groups of acid (COOH) and basic (NH₂) in the molecule. Therefore, they form salts with both alkalis and acids.

Reactivity and specific properties of biologically important heterofunctional compounds. Aminoalcohols

Amino-alcohols are those compounds containing simultaneously both amino and hydroxy groups in the molecule.

These two functional groups are fragilely held by one carbon atom, resulting in the elimination of ammonia or water. The simplest representative of amino alcohols is 2-aminoethanol, a compound in which both groups are located at adjacent carbon atoms. 2-Aminoethanol (trivial name of colamino) is a structural component of complex lipids - phosphatidylethanolamines.

With strong acids, 2-aminoethanol forms stable salts:

α-Aminoalcohols are able to form colored intracomplex compounds with copper hydroxide.
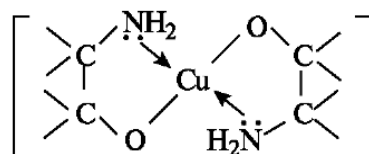
The quaternary ammonium base - hydroxide (2-hydroxyethyl) trimethylammonium [HOCH₂CH₂N $^+$ (CH₃)₃]OH⁻ - is of great importance as a vitamin-like substance regulating fat metabolism. Its cation is called choline.

An important role in the body belongs to amino alcohols, containing as a structural fragment the residue of pyrocatechol. They have a common name for catecholamines. This group includes representatives of biogenic amines formed in the body. To catecholamines belong dopamine, norepinephrine and adrenaline, performing, like acetylcholine, the role of neurotransmitters. Adrenaline is involved in the regulation of cardiac activity, with physiological stress it is released into the blood ("a hormone of fear").
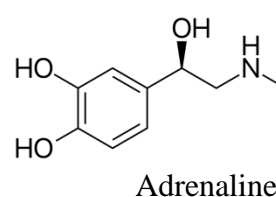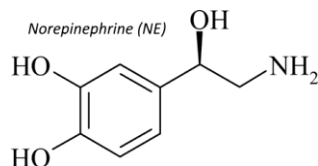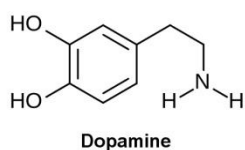
Hydroxycarbonyl compounds

Hydroxycarbonyl refers to compounds containing simultaneously hydroxyl and aldehyde (or ketone) groups in the molecule.

In accordance with this, hydroxyaldehydes and hydroxy ketones are distinguished.

The most famous representatives of these classes of compounds are glycerol aldehyde and dihydroxyacetone, which play a large role in biochemical processes in the form of phosphates.

Hydroxy- and amino acids

Hydroxy acids are compounds containing both hydroxyl and carboxyl groups in the molecule. Amino acids contain an amino group and a carboxyl group in the molecule.

In the aliphatic series, the α-, β-, γ-, etc. hydroxy- and amino acids are distinguished according to the mutual arrangement of the functional groups. The letter of the Greek alphabet is indicated by the position of the other functional group relative to the carboxyl group, while the reading is taken from the carbon atom closest to the carboxyl group, that is, from the C-2 atom. Note that in the substitution nomenclature for substituted carboxylic acids, the α-, β-, γ-, and so on are not used.

Acid-base properties

In heterofunctional compounds, depending on the nature of the functional groups and their location in the molecule, it is possible to enhance or, on the contrary, attenuate certain properties characteristic of monofunctional compounds. For example, the acidity of hydroxy acids is higher than that of unsubstituted acids. Amino acids, which contain both acidic and basic functional groups, exhibit amphoteric properties, that is, the ability to interact with both acids and bases. In neutral aqueous solutions or the crystalline state, amino acids exist predominantly in the form of internal salts (dipolar ions), as shown by the example of γ-aminobutyric acid.
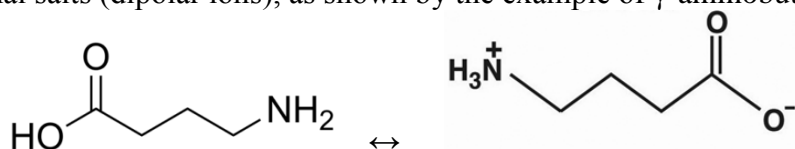
Polybasic hydroxy acids

Apple, citric, isocitric acids, as well as oxaloacetic and previously considered succinic and fumaric acids are participants in a cycle of tricarboxylic acids, also called the citric acid cycle, or the Krebs cycle. This is a universal stage of oxidative catabolism of carbohydrates and other compounds in the presence of oxygen.

The transformations of these acids occurring in the organism are, by their chemical nature, oxidation or reduction reactions. For each of these acids, the reactions are catalyzed by specific enzymes using coenzymes. For oxidation-reduction processes, the most characteristic is the participation of coenzymes of nicotinamide nature, the structure and properties of which are discussed in detail below. In the following, only their abbreviated names NAD^+ and NADH are used. It should be taken into account that with the participation of NAD + oxidative processes are carried out, and with the participation of NADH - the reducing processes.

Apple acid in significant quantities is found in immature apples, mountain ash, fruit juices. In the body l-malic acid is formed by hydration of fumaric acid.

trans-butenedioic acid
(fumaric acid)

?-hydroxybutanedioic acid
(L-malic acid)
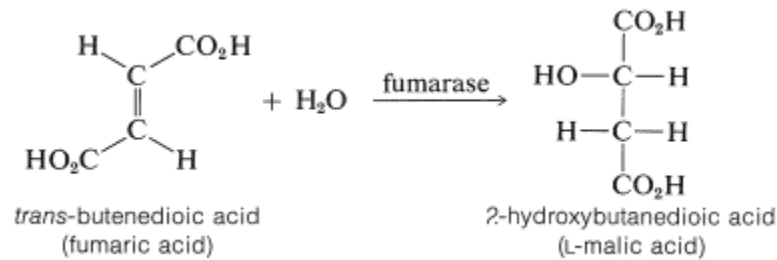
Citric acid is found in citrus fruits (lemons, oranges), grapes, gooseberries, and also in tobacco leaves.

The biosynthesis of citric acid occurs as an aldol condensation from oxaloacetic acid and acetylcoenzyme A.
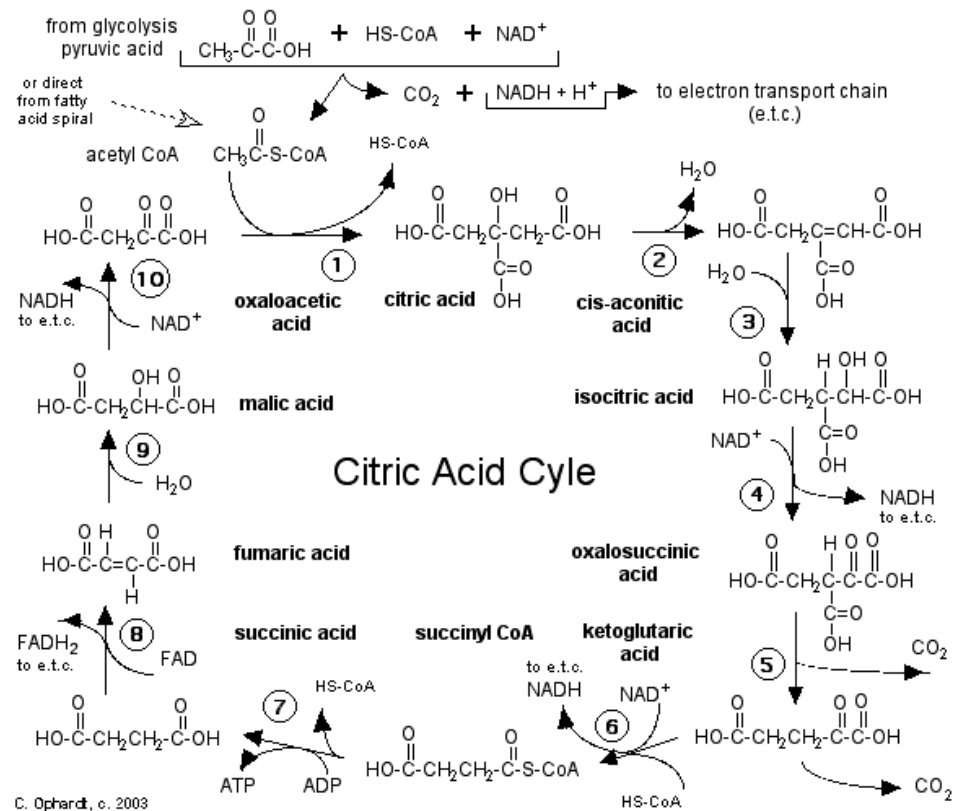
Tartaric acids are representatives of dihydroxydicarboxylic acids, contain two asymmetric carbon atoms and therefore should exist as four stereoisomers, but in fact three stereoisomers are known.

Oxoacids

Oxoacids are compounds containing carboxylic and aldehyde (or ketone) groups simultaneously in the molecule.

In accordance with this, aldehyde acids and ketonic acids are distinguished.

The simplest aldehyde acid is glyoxalic (glyoxylic) acid, which usually exists as a hydrate (HO) 2CHCOOH. It is found in unripe fruits, but as it ripens, its quantity decreases.

An important role in biochemical processes is played by ketonic acids - pyruvic, acetoacetic and oxaloacetic.

Pyruvic acid is one of the intermediate products of lactic acid and alcohol fermentation of carbohydrates. The pyruvic acid due to its name is due to the fact that it was first isolated during pyrolysis of grape acid.

Pyruvic acid is decarboxylated by heating with dilute and decarbonylated (cleaves CO) - with concentrated sulfuric acid.
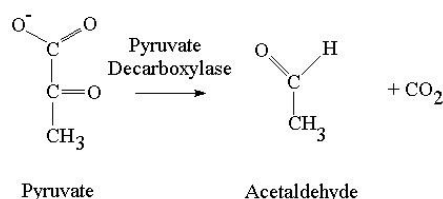
In the enzymatic decarboxylation of pyruvic acid, acetaldehyde associated with coenzyme ("active acetaldehyde") is obtained. It can be oxidized in the presence of coenzyme A to acetylcoenzyme A.
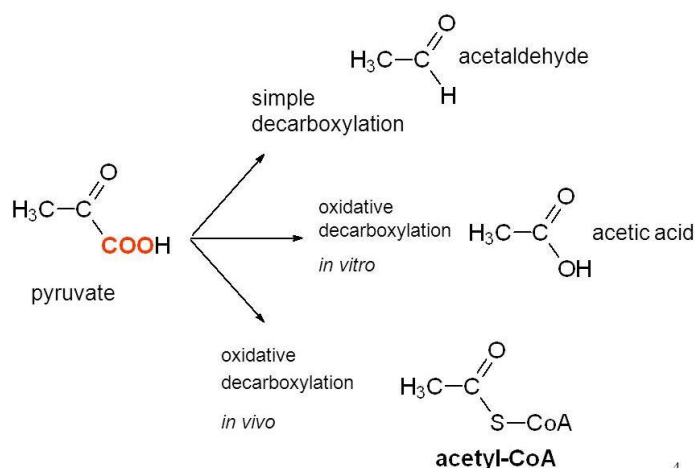
Oxaloacetic acid is simultaneously α- and β-oxo acid. It is formed during the oxidation of malic acid (*see above*).

Further, oxaloacetic acid upon condensation with acetylcoenzyme A is converted to citric acid.

Acetoacetic acid is a representative of β-oxo acids. In the free state, it represents a syrupy liquid that slowly releases carbon dioxide.

Heterofunctional benzene derivatives as medicaments

The inextricable relationship of chemistry and medicine is clearly manifested in the field of the creation and use of medicines. Back in the XVI century. the founder of jatrochemistry Paracelsus argued that "the real goal of chemistry is not in the manufacture of gold, but in the

preparation of medicines." Since ancient times, biologically active organic compounds have been selected empirically, and the appearance of a number of drugs has often been due to the case. At present, all synthesized compounds must undergo biological activity tests (biological screening). This is important for revealing the general patterns of the relationship between the structure of compounds and their biological activity. The "structure-property" problem serves as the foundation for the purposeful creation of effective medicines.

In recent decades, many new medicines have appeared. However, some groups of previously known drugs retain a great importance, in particular with the benzene nucleus as a structural basis.

Benzene itself can cause acute and chronic poisoning. It has an irritating effect on the skin, its vapor in a high concentration causes excitation, a breathing disorder.

Monofunctional benzene derivatives in most cases also have pronounced toxic properties. Phenol, aniline, halogen derivatives of the aromatic series are the starting or intermediate products of the large-tonnage chemical industry. In this regard, it is necessary to take into account their toxic effect.

Benzoic acid. It is used in the form of sodium salt as an expectorant. In its free form, benzoic acid is found in some resins and balms, as well as in cranberries and cranberries, but more often is contained in a bound form, for example as an N-benzoyl derivative of aminoacetic acid, called hippuric acid. This acid is formed in the liver from benzoic and aminoacetic (glycine) acids and is excreted in the urine. In clinical practice, the amount of hippuric acid in the urine of patients (after taking sodium benzoate) is judged on the effectiveness of the detoxifying function of the liver.
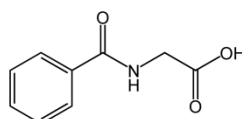
hippuric acid

p-**Aminophenol and its derivatives**. As a heterovenous compound, p-aminophenol can form derivatives for each functional group individually and simultaneously in two functional groups. P-aminophenol itself is toxic; interest for medicine is its derivative - acetaminophen, which has analgesic (analgesic) and antipyretic effect.
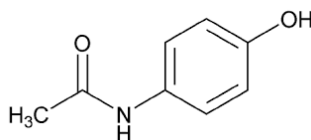
p-Aminobenzoic acid (PABA) and its derivatives. Esters of aromatic amino acids are capable, to varying degrees, of causing local anesthesia. This property is particularly noticeable in para-derivatives. In medicine, anesthesin (PABA ethyl ester) and Novocain (PABA 2-diethylaminoethyl ester) are used. Novocain is used as a salt (hydrochloride), which is associated with the need to increase its solubility in water.
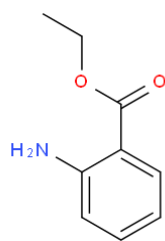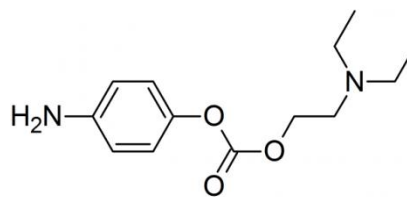
Anesthesin   Novocain

Salicylic acid and its **derivatives**. Salicylic acid belongs to the group of phenolic acids. As a compound with the ortho-disposition of the functional groups, it decarboxylates upon heating to form phenol.

Salicylic acid is moderately soluble in water, gives an intense staining with ferric chloride, on which the qualitative detection of the phenolic hydroxyl group is based. Salicylic acid exhibits antirheumatic, antipyretic and antifungal action, but as a strong acid (pKa 3.0) it irritates the gastrointestinal tract and is therefore only applied externally. Inside apply its derivatives - salts or ethers.

Salicylic acid is able to form derivatives for each functional group. Practical value have sodium salicylate, esters on the carboxyl group - methyl salicylate, phenyl salicylate (salol), and also on the hydroxyl group - acetylsalicylic acid (aspirin).
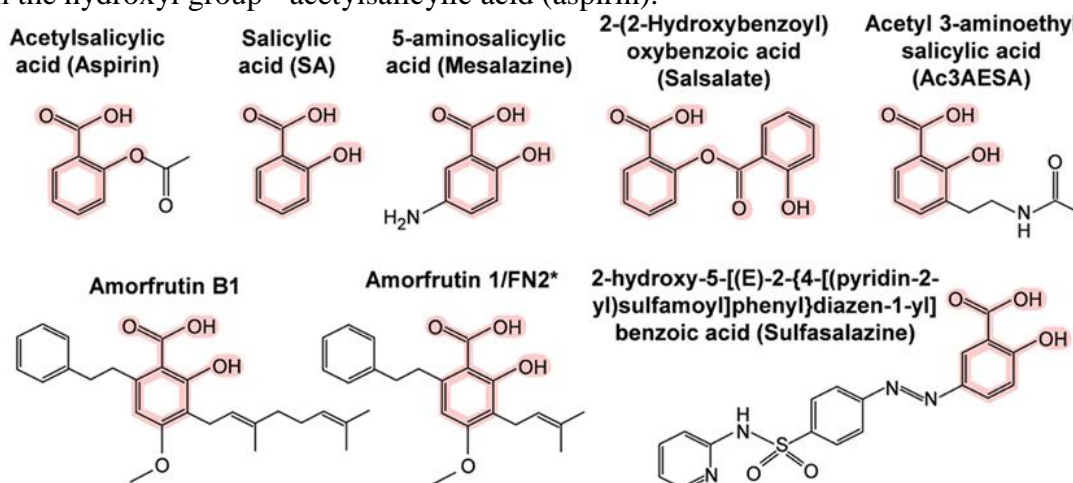
Salicylic acid was first obtained by oxidation of salicylic aldehyde contained in a plant of Tavolga (genus Spireae). Hence its original name - spiro acid, which is associated with the name aspirin (the initial letter "a" denotes acetyl). Acetylsalicylic acid is not found in nature.

Polyfunctional compounds

Polyfunctional refers to compounds in whose molecules there are several identical functional groups.

Among the polyfunctional compounds involved in vital processes, compounds with hydroxyl and carboxyl functional groups are most widely represented. Of particular interest are β-dicarbonyl compounds. Compounds with several amino groups are less common.

Polyhydric alcohols and phenols

Diatomic alcohols, i.e. alcohols containing two hydroxyl groups, are collectively referred to as diols, or glycols, and triatomic alcohols are called triols. Representatives of such alcohols are ethylene glycol and glycerol, respectively. The general name for polyhydric alcohols is polyols.

The composition of many natural compounds includes in the form of fragments diatomic phenols - catechol, resorcin, hydroquinone.

Ethanol Ethylene glycol Glycerin

catechol resorcinol hydroquinone
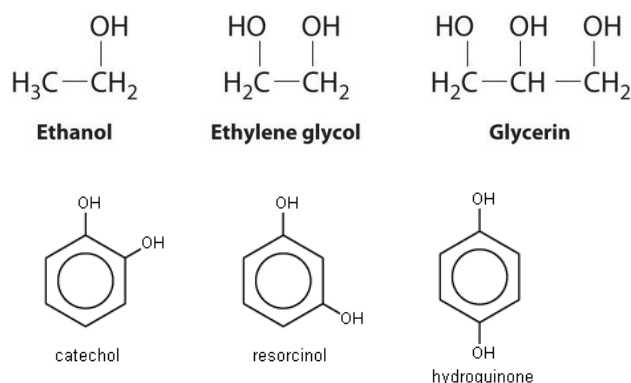
Ethylene glycol (ethanediol-1,2) is a highly toxic liquid (melting point -16 ° C, bp 197 ° C), used in the technique for the preparation of antifreeze liquids with a low freezing point.

Glycerin (propanetriol-1,2,3) - a nontoxic viscous liquid of sweet taste (melting point 17 ° C, bp 290 ° C), is part of most lipids. It is used as a component of ointments to soften the skin.

Pyrocatechin (o-dihydroxybenzene), also called catechol, is a structural fragment of many biologically active substances, in particular catecholamines. Monomethyl ester pyrocatechol - guaiacol - is used as a component in the composition of medicines for catarrh of the upper respiratory tract.

Resorcinol (m-dihydroxybenzene) is used as an antiseptic and disinfectant for skin diseases.

Hydroquinone (p-dihydroxybenzene), which has a reducing ability, is a structural fragment of a number of compounds. In the organism, the reducing ability of the substituted hydroquinone fragment makes it a participant in the important process of electron transport from the oxidized substrate to oxygen.

Alcohols of higher atomicity include pentites and hexitols, i.e., respectively, five- and six-atom alcohols with an open chain. The accumulation of hydroxyl groups in the molecule leads to the appearance of a sweet taste. Representatives of pentites and hexitols - xylitol and sorbitol - are sugar substitutes for diabetics.

Polyhydric cyclic alcohol myoinosit refers to vitamin-like compounds (vitamins of group B) and is a structural component of complex lipids - phosphatidylinositols. In plants, phytic acid, which is myo-inositol hexaphosphate, is widely distributed. Calcium or a mixed calcium-magnesium salt of phytic acid, called phytin, improves the state of the nervous system in diseases associated with a lack of phosphorus in the body.

Dicarboxylic acids

Carboxylic acids, containing in their composition one carboxyl group, are called mono-basic, two-dibasic, etc. They are all crystalline substances.

The systematic names of dicarboxylic acids are constructed according to the general rules of the substitution nomenclature. However, for most of them trivial names are preferred. Their Latin names serve as the basis for the names of anions and derivatives of acids, which often do not coincide with Russian trivial names.

Oxalic acid is the simplest dibasic acid. Some of its salts, for example calcium oxalate, are difficult to dissolve and often form stones in the kidney and bladder (oxalate stones).

Succinic acid in a noticeable amount was found in amber, from which it was called acid itself and its derivatives succinates (from Latin succinium - amber).

Maleic and fumaric acids are representatives of unsaturated dicarboxylic acids with one double bond. Fumaric acid is involved in metabolic processes occurring in the body.

Maleic acid   Fumaric acid
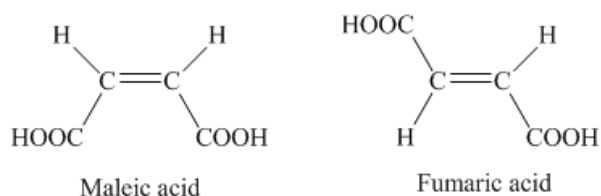
Diamines

Most known are tetramethylenediamine, or putrescin $H_2N(CH_2)_4NH_2$, and pentamethylenediamine, or cadaverine $H_2N(CH_2)_5NH_2$. They have long been considered cadaveric poisons, that is, substances formed during the decarboxylation of diamino acids and causing the poisonousness of rotting proteins. At present, it has been clarified that other substances impart toxic properties to proteins during decay.

Reactivity and specific reactions of polyhydric alcohols and phenols

Polyfunctional compounds can exhibit the properties inherent in monofunctional compounds, i.e. the ability to react in each functional group, so there is some similarity in the behavior of monofunctional and polyfunctional compounds. However, the simultaneous presence of several functional groups causes a specific reactivity, as shown in the example of the reactions given below.

Acidic properties. Polyhydric alcohols are more acidic than monatomic alcohols, which is a consequence of the «-I» effect of one hydroxyl group relative to another and more complete delocalization of the negative charge in the conjugate base. Thus, ethylene glycol exhibits stronger acid properties than ethanol.

Chelating. Polyhydric alcohols containing hydroxyl groups at neighboring carbon atoms, when reacted with heavy metal hydroxides, for example, copper (11) hydroxide in an alkaline

medium, form intracomplex, so-called chelate compounds. Such compounds are usually highly soluble in water and intensely colored, so the reaction is used as a qualitative one. In the interaction of ethylene glycol or glycerin with copper hydroxide (11), an intensely blue staining results from the formation of copper (11) glycollate or copper (11) glycerate.
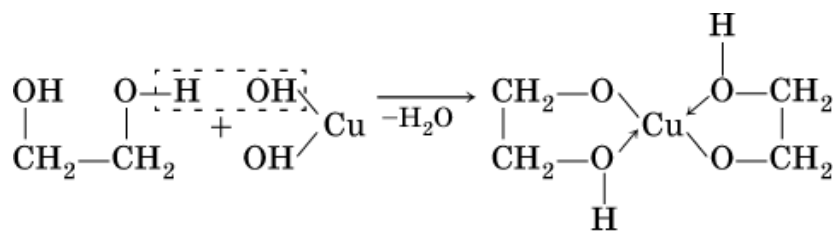
Blue color
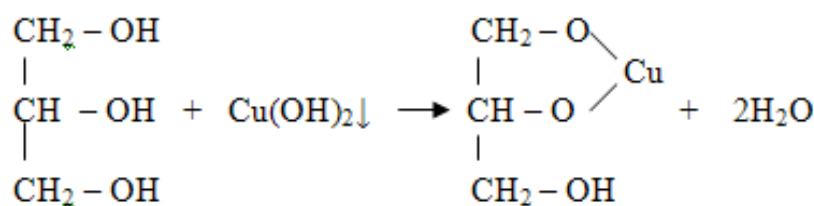
Dark blue color

This qualitative reaction is characteristic for open-chain polyols and certain cyclic alcohols in which the hydroxyl groups are sufficiently close together.

Dehydration. Heating of ethylene glycol with sulfuric acid leads to the intermolecular cleavage of two water molecules and the formation of dioxane.
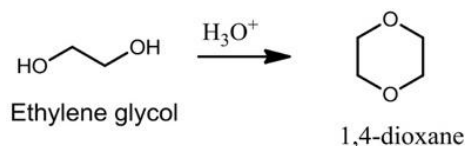
Dioxane (bp 101 $^{\circ}$C) is known as a good solvent, mixed with water and hydrocarbons, very toxic.

Chlorinated dibenzo derivatives of dioxane have an even higher toxicity. Notorious fame is 2,3,7,8-tetrachlorodibenzo-n-dioxin (or just dioxin), causing extremely low concentrations of severe diseases of the immune and hematopoietic systems. The entry of dioxin into the soil, which occurs with the use of some herbicides (where it is contained as a minor impurity), poses a serious environmental problem.

Formation of esters. Some esters of glycerin with inorganic acids, in particular nitric and phosphoric, are important. Trinitrate glycerin, or nitroglycerin, is formed by the action of nitric acid on glycerol in the presence of sulfuric acid.
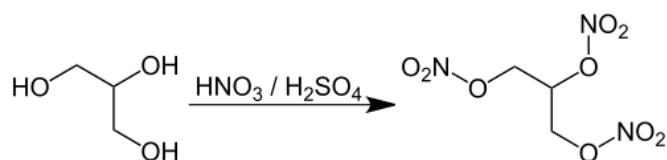
Trinitrate glycerin - an explosive. In low concentrations (as a 1% solution in ethanol) it is used as a vasodilator.

As a result of the action of phosphoric acid on glycerol, a mixture of α-glycerophosphate and β-glycerophosphate is formed. Glycerophosphates are used as fortifying agents. They are the structural elements of phospholipids.

Oxidation-reduction reactions. Reactions of this type are characteristic of diatomic phenols with ortho- and para positions of hydroxyl groups in the benzene ring. Among the products of oxidation of such diatomic phenols, quinones are of particular interest.

hydroquinone   *para*-benzoquinone
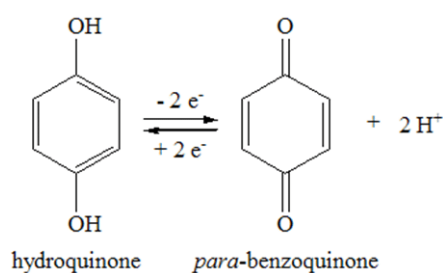
Quinones contain a peculiar system of conjugated bonds, called a quinoid grouping, which includes two double bonds in a ring and double bonds of two carbonyl groups.

Acidic properties. With the accumulation of acidic groups, the acidic properties of the compounds increase. The acidity of dicarboxylic acids is greater than that of monocarboxylic acids. Thus, oxalic acid (pKa 1.23) is much stronger than acetic acid (pKa 4.76), which is due to the -I-effect of the COOH group, and due to this more complete delocalization of the negative charge in the conjugate base.
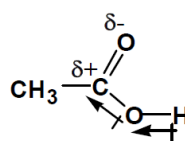
The influence of the substituent is most clearly manifested when it is close to the acid center.

The Inductive Effect in Aliphatic Carboxylic Acids

- Electron-withdrawing groups stabilize a conjugate base, making a carboxylic acid more acidic.
- Electron-donating groups destabilize the conjugate base, making a carboxylic acid less acidic.
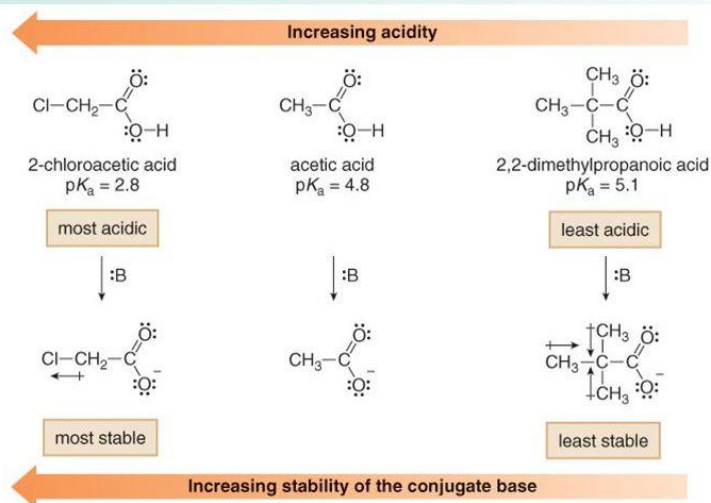
Decarboxylation. When heated with sulfuric acid, oxalic acid is decarboxylated, and the formed formic acid decomposes further.
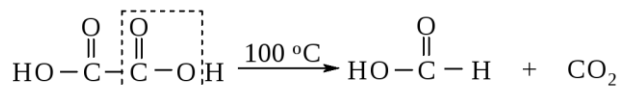
Malonic acid is readily decarboxylated when heated above 100 ° C.
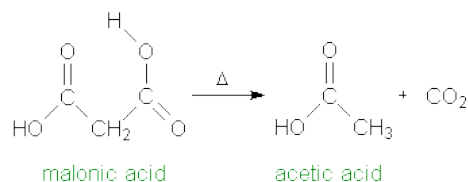
Keto-enol tautomerism

Tautomerism (dynamic isomerism) is a mobile equilibrium between mutually transforming structural isomers.
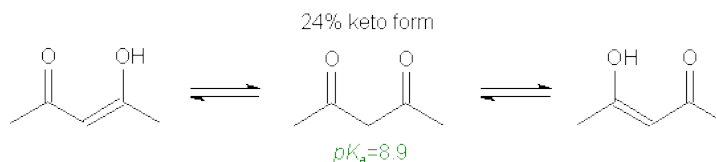
Tautomers exist together in the same sample of matter and constantly pass into each other. The most common is prototropic tautomerism, which consists in the interconversion of tautomers with proton transfer. Acetoacetic ether has a keto-enol tautomerism, one of the types of prototropic tautomerism. In an equilibrium mixture at a temperature of 250 ° C, 92.5% of the ketone and 7.5% enol forms are contained.

Tautomeric forms of acetoacetic ether

During the transition of the ketone form to the enol hydrogen atom from C-2 (α-carbon atom, CH-acid center) moves to the oxygen atom of the ketone group (the main center). The mobility of this hydrogen atom is explained by the fact that the a-carbon atom is connected with two electron-withdrawing groups-carbonyl and ester. Due to the strong -I effect of each of these groups, a CH-acid center appears in the a-carbon atom. Enol forms of carbonyl compounds are unstable. However, in some cases, enol forms can be quite stable, for example, the enol form of acetoacetic ether is stabilized by the formation of a conjugated system and an intramolecular hydrogen bond.

Most reactions of acetoacetic ether proceed with the participation of the enol form. Acetoacetic ether in the enol form gives a color with iron (III) chloride; the unsaturation of the enol form is proved by the decolorization of bromine water.

Tautomerism of β-dicarbonyl compounds

The specific proton mobility of the hydrogen atom at the α-carbon atom in the carbonyl compounds (weak CH-acid center) manifests itself in their ability to condensation reactions. If the mobility of such a hydrogen atom increases so much that it can split off in the form of a proton, it will lead to the formation of a mesomeric ion (I), the negative charge of which is dispersed between carbon and oxygen atoms. The reverse addition of a proton to this ion in accordance with its boundary structures can lead either to the initial carbonyl compound or to the enol.

Accordingly, the carbonyl compound can exist in equilibrium with the isomer-enol form. This kind of isomerism is called tautomerism, and isomers, which are in a state of mobile equilibrium, are tautomers.

Tautomerism is an equilibrium dynamic isomerism. Its essence lies in the mutual transformation of isomers with the transfer of some mobile group and the corresponding redistribution of the electron density.

In the case under consideration, proton transfer takes place between the ketone and enol forms, so this equilibrium is called prototropic tautomerism, in particular, keto-enol tautomerism.

In monocarbonyl compounds (aldehydes, ketones, esters), the equilibrium is almost completely displaced toward the ketone form. For example, the enol form in acetone is only 0.0002%. In the presence of a second electron-withdrawing group, the content of the enol form increases for the α-carbon atom (for example, the second carbonyl group). Thus, in the 1,3-dicarbonyl compound acetylacetone (pentanedione-2,4) the enol form predominates.

The enol form of acetylacetone is additionally stabilized by the conjugated second p-bond and the intramolecular hydrogen bond.

Many reactions involving the formation and transformation of carbonyl compounds, as will be shown later, proceed through intermediate enol forms or derivatives of these forms.

Laboratory work № 9

Reagents and equipment:

1. Distilled water.

2. Concentrated and 10% solutions of sulfuric acid.

3. Aqueous solutions: 15% tartaric acid, 5% potassium hydroxide, 2% copper (II) sulfate, 10% sodium hydroxide, barium hydroxide and iodine in potassium iodide.

4. Citric acid, acetoacetic ether.

5. A tripod with test tubes, test tubes with a gas outlet tube.

6. The alcohol lamp.

Experiment 1. Proof of the presence of two carboxyl groups in tartaric acid

Put 1 drop of 15% solution of tartaric acid into the tube, 2 drops of 5% potassium hydroxide solution and shake. Gradually begins to stand out a white crystalline precipitate of a slightly soluble in water acidic potassium salt of tartaric acid (potassium hydrotartrate). If the precipitate does not drop out, cool the tube under a stream of water and rub the inner wall of the tube with a glass rod. Add 4-5 drops of potassium hydroxide solution to the test tube. The crystalline precipitate gradually dissolves, since a middle potassium salt of tartaric acid (potassium tartrate) is readily soluble in water. Solution the potassium tartrate retain until the next experiment.

Conclusion:

Experiment 2. Proof of the presence of hydroxyl groups in tartaric acid

Place 2 drops of 2% copper (II) sulfate solution in two test tubes; and 10% sodium hydroxide solution. A blue precipitate of copper (II) hydroxide precipitates. In 1-st tube add a solution of potassium tartrate, obtained in the previous experiment. The precipitate of copper (II) hydroxide dissolves to form a blue solution. Liquids in both test tubes heat to boiling. In the 1st

test tube the color of the liquid does not change to the second blue precipitate of copper (II) hydroxide is converted to copper (II) oxide of black color. The resulting blue solution is called Fehling's reagent and is used to detect glucose in the urine.

Conclusion:

Experiment 3. Decomposition of citric acid

In a dry tube equipped with a gas outlet tube, place a spatula of citric acid and 10 drops of concentrated sulfuric acid, heat. The end of the gas outlet tube is lowered into a 1-tube with 5 drops of a solution of barium hydroxide. After the solution has become cloudy, transfer the gas outlet tube into a 2-tube containing 2 drops of iodine solution in potassium iodide, previously discolored by the addition of a few drops of 10% sodium hydroxide solution. In the 2nd test tube, a pale yellow precipitate appears.

Citric acid, being an α-hydroxy acid, decomposes with sulfuric acid to form acetone, carbon dioxide and formic acid.

acetone dicarboxylic acid
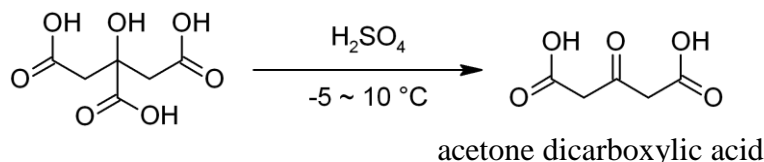
Conclusion:

Experiment 4. Ketone cleavage of acetoacetic ether

Place 5 drops of acetoacetic ether and 5 drops of 10% sulfuric acid solution into a test tube with a gas outlet tube. Heat the end of the gas outlet tube into the 1st tube with 5 drops of barium hydroxide solution, after the solution has become turbid, transfer the gas outlet tube into a 2-tube containing 2 drops of iodine solution in potassium iodide, previously discolored by adding a few drops of a 10% solution sodium hydroxide. In the 2nd test tube, a pale yellow precipitate appears.

Conclusion:

Tasks for independent work

Control questions:

1. Stereoisomerism. Optical isomerism of molecules and its medico-biological significance. Elements of symmetry of molecules.

2. Asymmetric carbon atom (center of chirality).

3. Optical activity. Enantiomeria. Diastereometry.

4. The racemates. The resolution of racemates.

5. Relationship between the spatial structure of compounds and their biological activity.

6. General characteristics of the reactivity of heterofunctional compounds. Acid-base properties.

7. Heterofunctional substituent as a factor influencing the chemical properties of the reaction center. Specific reactions of heterofunctional compounds.

8. Biologically important classes of hetero-functional compounds and their properties. Unsaturated carboxylic acids. Oxyacids (hydroxy acids). Amino acids. Oxoacids. Write a diagram of the interaction of acetoacetic ether with dilute sulfuric acid.

9. What cleavage products of acetoacetic ether are found in the 1st and 2nd test tubes? Write diagrams of the corresponding reactions for detecting the cleavage products.

10. Write the diagrams of the formation of hydrotartrate and potassium tartrate.

11. What is the formation of two salts of tartaric acid?

12. Write a scheme for the interaction of copper (II) hydroxide with potassium tartrate. What structural element is the reaction?

13. What is the product of decomposition of citric acid found in the 1st test tube? Write a reaction scheme.

Do the exercises:

1. Give formulas and systematic names for the simplest hydroxy and amino acids.

2. Bring the reaction of glycolic acid with alcohol and ammonia.

3. Give an acylation reaction of glycolic acid.

4. Give the reaction of dehydration of malic acid, leading to the formation of fumaric acid in the body.

5. Provide the reaction of tartaric acid with copper hydroxide.

6. Get diethyl malic acid

7. Write a reaction for the dehydration of malic acid (cleavage of H2O).

8. Give the alkylation reaction of ethanolamine, leading to the formation of choline.

9. Give the keto-enol tautomerism of acetylcoenzyme A.

10. Write the formulas for D- and L-lactic acid.

Test tasks:
1. Select representatives (2) of multifunctional connections:
a) ethanediol
b) lactic acid
c) glycerin
d) butanoic acid
e) ethanol

2. Which of the compounds forms acidic and middle salts:
a) methanal
b) ethanol
c) succinic acid
d) propanoic acid
e) lactic acid

3. Name the compound: $HOOC-CH_2-CH_2-CH_2-COOH$
a) glycerin
b) pentanoic acid
c) glutaric acid
d) ethanediol
e) succinic acid

4. Indicate the functional groups of amino alcohols:
a) -OH;   -COOH
b) -OH;   - NH_2
c) -C = O;   -COOH

5. What groups in the molecule are responsible for the amphoteric properties of the compound?
a) -OH and -NH_2
b) -OH and -COOH
c) -NH_2 and -COOH
d) -C = O and -COOH

6. Which of the statements does not correspond to the molecule of paracetamol
a) contains an amino group
b) contains only the same functional groups
c) all carbon atoms are in the second valence state
d) contains a phenolic moiety

1. Indicate the formula of oxaloacetic acid.

a) $H_3C-\underset{\underset{O}{\|}}{C}-O-CH_2-C\overset{O}{\underset{OH}{<}}$

b) $H_3C-\underset{\underset{NH_2}{|}}{CH}-CH_2-C\overset{O}{\underset{OH}{<}}$

в) $HOOC-\underset{\underset{O}{\|}}{C}-CH_2-COOH$

г) $\underset{OH}{\overset{O}{\|}}C-C\overset{O}{\underset{OH}{<}}$
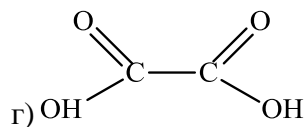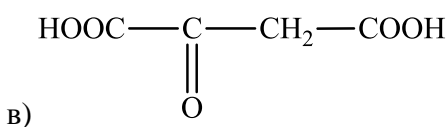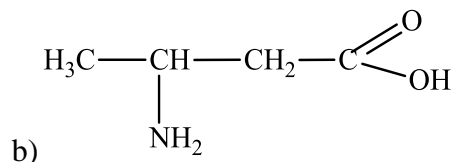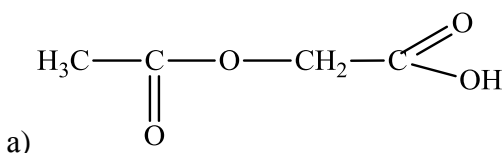
1. Indicate which compound is related to ketoacids

a) HOOC—CO—CO—OH (structure: O=C(OH)—C(=O)—OH, oxalic acid-like)

b) H_3C—C(=O)—COOH

c) H_3C—CH(OH)—COOH

d) H_3C—C(=O)—CH_2—COOH
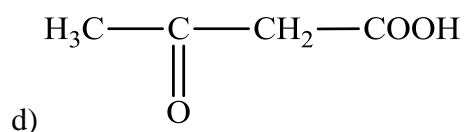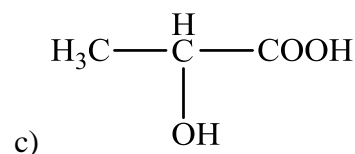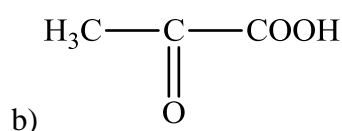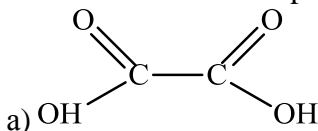
1. 1. Indicate the formula of acetoacetic (3-oxobutanoic acid).

a) HOOC—C(=O)—CH_2—COOH

b) H_3C—C(=O)—COOH

c) H_3C—C(=O)—CH_2—COOH

d) HO—C(=O)—C(=O)—OH
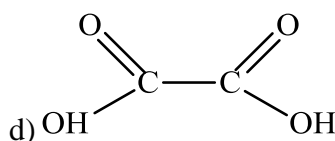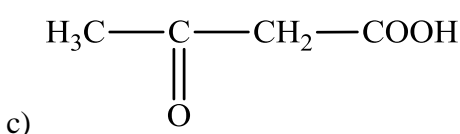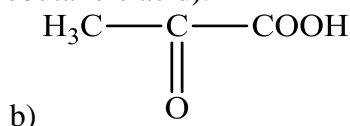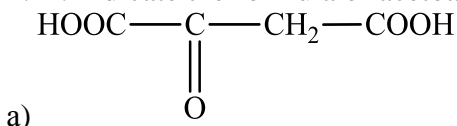
10. Indicate the enol form of pyruvic (2-oxopropanoic) acid

a) H_3C—C(=O)—C(=O)—OH

b) H_2C=C(OH)—C(=O)—OH

c) H_3C—C(OH)=CH—C(=O)—OH

d) H_3C—C(=O)—CH_2—C(=O)—OH
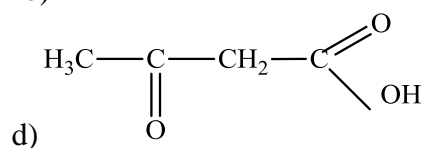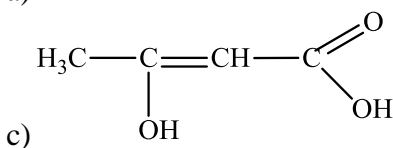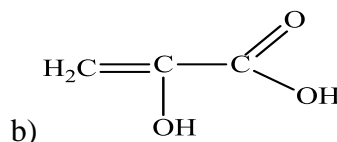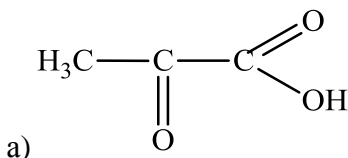
11. Choose from the proposed formulas serine (2-amino-3-hydroxypropanoic acid).

a) H_2N—CH(—CH_2—COOH)—COOH

b) H_2N—CH(—CH_3)—C(=O)—OH

c) H_2N—CH_2—C(=O)—OH

d) H_2N—CH(—CH_2—OH)—C(=O)—OH
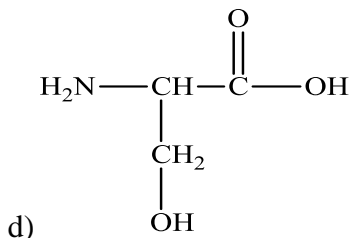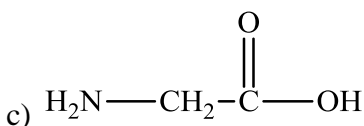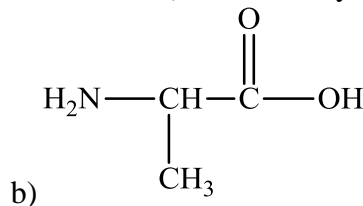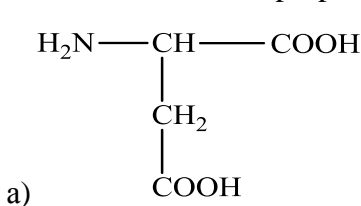
12. With the intramolecular dehydration of which compound, lactones are obtained:
a) α-hydroxypropanoic acid
b) γ-aminobutyric acid
c) γ-aminopropanoic acid
d) γ-hydroxybutyric acid

13. Which compound is related to hydroxy acids?

a) milk
b) Butter
c) pyruvic
d) glutaric

14. To dicarboxylic hydroxy acids refers to
a) malic acid
b) tartaric acid
c) fumaric acid
d) maleic acid

15. Which pairs of compounds are enantiomers?
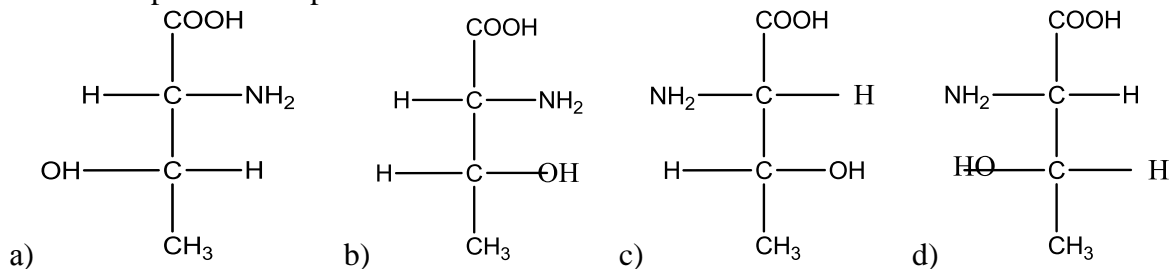
a)
$$\begin{array}{c} COOH \\ | \\ H-C-NH_2 \\ | \\ OH-C-H \\ | \\ CH_3 \end{array}$$

b)
$$\begin{array}{c} COOH \\ | \\ H-C-NH_2 \\ | \\ H-C-OH \\ | \\ CH_3 \end{array}$$

c)
$$\begin{array}{c} COOH \\ | \\ NH_2-C-H \\ | \\ H-C-OH \\ | \\ CH_3 \end{array}$$

d)
$$\begin{array}{c} COOH \\ | \\ NH_2-C-H \\ | \\ HO-C-H \\ | \\ CH_3 \end{array}$$

Timing of a 3-hour lesson:

1. Organizational moment - 2 minutes.
2. The survey - 40 min.
3. Explanation of the work - 25 min.
4. Performance and execution of work - 30 min.
5. Presentation of the new material - 45 min.
6. Verification of work and assignment to the house - 3 min.

Literature:

TOPIC: BIOLOGICALLY ACTIVE HETEROCYCLIC COMPOUNDS

The purpose of the lesson is to form a knowledge of the structure and features of the chemical behavior of heterocyclic compounds that have biological activity.

The purpose of the activities of students in class

The student should know:

a) Definition and classification of heterocyclic compounds.

b) Structure and properties of five-membered heterocycles with two or more heteroatoms.

c) Structure and properties of pyridine and its derivatives.

d) Structure and properties of six- and seven-membered heterocycles with two or more heteroatoms.

e) Bicyclic heterocycles.

The student **should be able to**:

a) Determine whether the compound belongs to a particular type of heterocycle.

b) Carry out qualitative reactions to the antipyrine and amidopyrine.

c) Conduct a qualitative reaction (murexide test) on substances containing a purine base.

Questions for testing the baseline level:

1. Poly- and hetero-functional compounds.

2. Classification and the simplest representatives of poly- and hetero-functional compounds.

3. General characteristics of the reactivity of heterofunctional compounds. Acid-base properties.

4. Heterofunctional substituent as a factor influencing the chemical properties of the reaction center.

5. Specific reactions of heterofunctional compounds.

6. Biologically important classes of hetero-functional compounds and their properties. Unsaturated carboxylic acids.

7. Oxyacids (hydroxy acids) and oxo acids.

8. Amino acids and amino alcohols. Polyhydric alcohols.

9. Conjugation and aromaticity.

10. Electronic structure of pyridine and pyrrole nitrogen atoms. Heterofunctional derivatives of benzene.

11. Tautomerism. Lactim-lactam tautomerism.

Theoretical part

Heterocyclic compound, also called heterocycle, any of a major class of organic chemical compounds characterized by the fact that some or all of the atoms in their molecules are joined in rings containing at least one atom of an element other than carbon (C). The cyclic part (from Greek kyklos, meaning "*circle*") of heterocyclic indicates that at least one ring structure is present in such a compound, while the prefix hetero- (from Greek *heteros*, meaning "*other*" or "*different*") refers to the noncarbon atoms, or heteroatoms, in the ring. In their general structure, heterocyclic compounds resemble cyclic organic compounds that incorporate only carbon atoms in the rings-for example, cyclopropane (with a three-carbon-atom ring) or benzene (with a six-

carbon-atom ring)-but the presence of the heteroatoms gives heterocyclic compounds physical and chemical properties that are often quite distinct from those of their all-carbon-ring analogs.

Heterocyclic compounds include many of the biochemical material essential to life. For example, nucleic acids, the chemical substances that carry the genetic information controlling inheritance, consist of long chains of heterocyclic units held together by other types of materials. Many naturally occurring pigments, vitamins, and antibiotics are heterocyclic compounds, as are most hallucinogens. Modern society is dependent on synthetic heterocycles for use as drugs, pesticides, dyes, and plastics.

The most common heterocycles are those having five- or six-membered rings and containing heteroatoms of **nitrogen** (N), **oxygen** (O), or **sulfur** (S). The best known of the simple heterocyclic compounds are pyridine, pyrrole, furan, and thiophene. A molecule of pyridine contains a ring of six atoms-five carbon atoms and one nitrogen atom. Pyrrole, furan, and thiophene molecules each contain five-membered rings, composed of four atoms of carbon and one atom of nitrogen, oxygen, or sulfur, respectively.

Pyridine and **pyrrole** are both nitrogen heterocycles-their molecules contain nitrogen atoms along with carbon atoms in the rings. The molecules of many biological materials consist in part of pyridine and pyrrole rings, and such materials yield small amounts of pyridine and pyrrole upon strong heating. In fact, both of these substances were discovered in the 1850s in an oily mixture formed by strong heating of bones. Today, pyridine and pyrrole are prepared by synthetic reactions.Their chief commercial interest lies in their conversion to other substances, chiefly dyestuffs and drugs. Pyridine is used also as a solvent, a waterproofing agent, a rubber additive, an alcohol denaturant, and a dyeing adjunct.

Furan is an oxygen-containing heterocycle employed primarily for conversion to other substances (including pyrrole). Furfural, a close chemical relative of furan, is obtained from oat hulls and corncobs and is used in the production of intermediates for nylon. Thiophene, a sulfur heterocycle, resembles benzene in its chemical and physical properties. It is a frequent contaminant of the benzene obtained from natural sources and was first discovered during the purification of benzene. Like the other compounds, it is used primarily for conversion to other substances. Furan and thiophene were both discovered in the latter part of the 19th century.

In general, the physical and chemical properties of heterocyclic compounds are best understood by comparing them with ordinary organic compounds that do not contain heteroatoms.

It is known that the bonds of the nitrogen atom with carbon atoms are characteristic for the class of amines. By entering into a cyclic structure, these groups exhibit both certain properties of the amines and specific specific properties due to the cyclic structure.

For heterocyclic compounds, the use of different nomenclatures is allowed. Trivial names are widely used. The numbering in the cycle starts from the heteroatom (the seniority of the heteroatoms is determined by the order O, S, N):
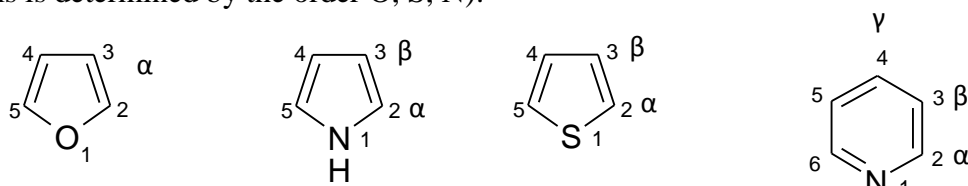
Compounds classified as heterocyclic probably constitute the largest and most varied family of organic compounds. After all, every carbocyclic compound, regardless of structure and functionality, may in principle be converted into a collection of heterocyclic analogs by replacing one or more of the ring carbon atoms with a different element. Even if we restrict our consideration to oxygen, nitrogen and sulfur (the most common heterocyclic elements), the permutations and combinations of such a replacement are numerous.

Nomenclature

Devising a systematic nomenclature system for heterocyclic compounds presented a formidable challenge, which has not been uniformly concluded. Many heterocycles, especially amines, were identified early on, and received trivial names which are still preferred. Some monocyclic compounds of this kind are shown in the following chart, with the common (trivial) name in bold and a systematic name based on the Hantzsch-Widman system given beneath it in blue. The rules for using this system will be given later. For most students, learning these common names will provide an adequate nomenclature background.
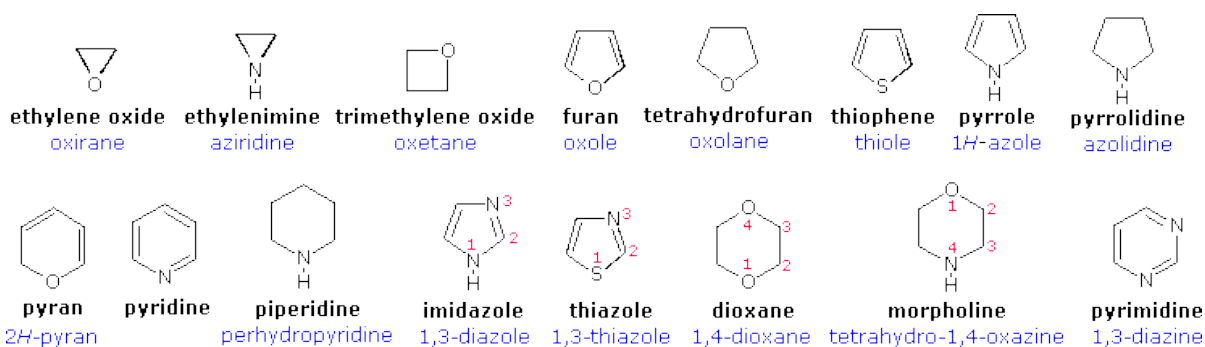
An easy to remember, but limited, nomenclature system makes use of an elemental prefix for the heteroatom followed by the appropriate carbocyclic name. A short list of some common prefixes is given in the following table, priority order increasing from right to left. Examples of this nomenclature are: ethylene oxide = oxacyclopropane, furan = oxacyclopenta-2,4-diene, pyridine = azabenzene, and morpholine = 1-oxa-4-azacyclohexane.

Element	oxygen	sulfur	selenium	nitrogen	phosphorous	silicon	boron
Valence	II	II	II	III	III	IV	III
Prefix	Oxa	Thia	Selena	Aza	Phospha	Sila	Bora

The **Hantzsch-Widman** system provides a more systematic method of naming heterocyclic compounds that is not dependent on prior carbocyclic names. It makes use of the same hetero atom prefix defined above (dropping the final "a"), followed by a suffix designating ring size and saturation. As outlined in the following table, each suffix consists of a ring size root (blue) and an ending intended to designate the degree of unsaturation in the ring. In this respect, it is important to recognize that the saturated suffix applies only to **completely saturated ring systems**, and the unsaturated suffix applies to rings incorporating **the maximum number of non-cumulated double bonds**. Systems having a lesser degree of unsaturation require an appropriate prefix, such as "dihydro"or "tetrahydro".

Ring Size	3	4	5	6	7	8	9	10

Suffix								
Unsaturated	**ir**ene	**et**e	**ol**e	**in**e	**ep**ine	**oc**ine	**on**ine	**ec**ine
Saturated	**ir**ane	**et**ane	**ol**ane	**in**ane	**ep**ane	**oc**ane	**on**ane	**ec**ane

Despite the general systematic structure of the Hantzsch-Widman system, several exceptions and modifications have been incorporated to accommodate conflicts with prior usage. Some examples are:

• The terminal "e" in the suffix is optional though recommended.
• Saturated 3, 4 & 5-membered nitrogen heterocycles should use respectively the traditional "iridine", "etidine" & "olidine" suffix.
• Unsaturated nitrogen 3-membered heterocycles may use the traditional "irine" suffix.
• Consistent use of "etine" and "oline" as a suffix for 4 & 5-membered unsaturated heterocycles is prevented by their former use for similar sized nitrogen heterocycles.
• Established use of oxine, azine and silane for other compounds or functions prohibits their use for pyran, pyridine and silacyclohexane respectively.

Examples of these nomenclature rules are written in blue, both in the previous diagram and that shown below. Note that when a maximally unsaturated ring includes a saturated atom, its location may be designated by a "#*H* " prefix to avoid ambiguity, as in pyran and pyrrole above and several examples below. When numbering a ring with more than one heteroatom, the highest priority atom is #1 and continues in the direction that gives the next priority atom the lowest number.
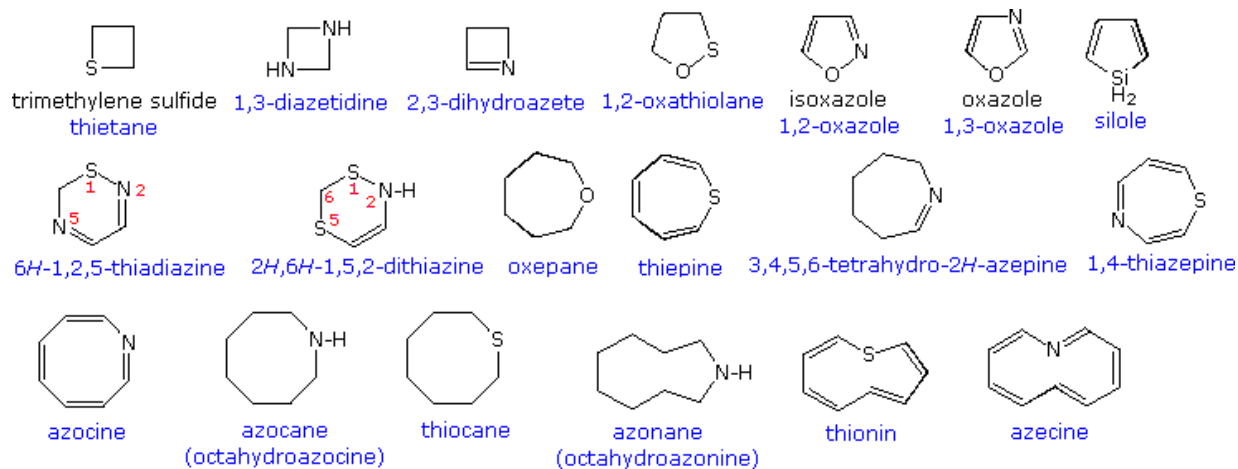
All the previous examples have been monocyclic compounds. Polycyclic compounds incorporating one or more heterocyclic rings are well known. A few of these are shown in the following diagram. As before, common names are in black and systematic names in blue. The two quinolines illustrate another nuance of heterocyclic nomenclature. Thus, the location of a fused ring may be indicated by a lowercase letter which designates the edge of the heterocyclic ring involved in the fusion, as shown by the pyridine ring in the green shaded box.

indole
2,3-benzopyrrole

isoindole

indolizine

quinoline
1-azanaphthalene
benzo[b]pyridine

isoquinoline
2-azanaphthalene
benzo[c]pyridine

purine

carbazole
dibenzopyrrole

dibenzofuran

2*H*-chromene

xanthene
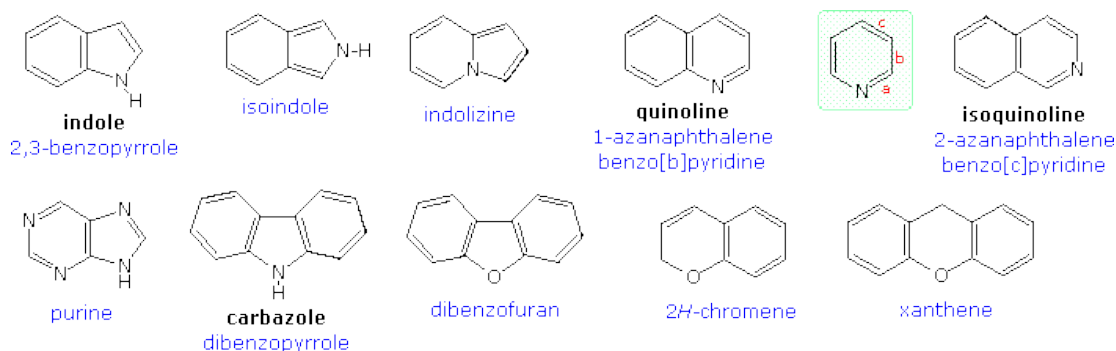
Heterocyclic rings are found in many naturally occurring compounds. Most notably, they compose the core structures of mono and polysaccharides, and the four DNA bases that establish the genetic code. By clicking on the above diagram some other examples of heterocyclic natural products will be displayed.

Pyridine

Pyridine is a colourless hygroscopic liquid with a characteristic odour. It is a basic heterocyclic compound containing one nitrogen atom and five carbon atoms in its molecules and is used as a solvent and in preparing other organic chemicals. A flammable, colorless or yellowish liquid base that results from the dry distillation of organic matter containing nitrogen, has a penetrating odor, and is used in analytical chemistry and in the manufacture of various drugs and vitamins.

Pyridine(CAS.NO:110-86-1) is a basic heterocyclic organic compound with the chemical formula C_5H_5N. It is structurally related to benzene, with one methine group (=CH-) replaced by a nitrogen atom. The pyridine ring occurs in many important compounds, including azines and the vitamins niacin and pyridoxal.

Pyridine is miscible with water and virtually all organic solvents. It is weakly basic, and with hydrochloric acid it forms a crystalline hydrochloride salt that melts at 145–147 °C. Most chemical properties of pyridine are typical of a heteroaromatic compound. In organic reactions, pyridine behaves both as a tertiary amine, undergoing protonation, alkylation, acylation, and N-oxidation at the nitrogen atom, and as an aromatic compound, undergoing nucleophilic substitutions.

Because of the electronegative nitrogen in the pyridine ring, the molecule is relatively electron deficient. It, therefore, enters less readily electrophilic aromatic substitution reactions, which are characteristic of benzene derivatives. However, unlike benzene and its derivatives, pyridine is more prone to nucleophilic substitution and metalation of the ring by strong organometallic bases. The reactivity of pyridine can be distinguished for three chemical groups. With electrophiles, electrophilic substitution takes place where pyridine expresses aromatic properties. With nucleophiles, pyridine reacts via its 2nd and 4th carbon atoms and thus behaves similar to imines and carbonyls. The reaction with many Lewis acids results in the addition to the nitrogen atom of pyridine, which is similar to the reactivity of tertiary amines. The ability of

pyridine and its derivatives to oxidize, forming amine oxides (N-oxides), is also a feature of tertiary amines.

The nitrogen center of pyridine features a basic lone pair of electrons. Because this lone pair is not part of the aromatic ring, pyridine is a base, having chemical properties similar to those of tertiary amines. The pKa of the conjugate acid is 5.25. Pyridine is protonated by reaction with acids and forms a positively charged aromatic polyatomic ion called pyridinium. The bond lengths and bond angles in pyridine and pyridinium are almost identical. The pyridinium cation is isoelectronic with benzene. Pyridinium p-toluenesulfonate (PPTS) is an illustrative pyridinium salt; it is produced by treating pyridine with p-toluenesulfonic acid.

Pyridine can act as Lewis base, donating its pair of electron to a Lewis acid as in the sulfur trioxide pyridine complex.

Pyridine itself is a relatively weak ligand in forming complexes with transition metal ions. For example, it forms a 1:1 complexes with nickel(II), Ni^{2+}, and copper(II), Cu^{2+}, with $logK_1$ values of ca. 1.9 and 2.6, respectively. The infrared spectra of pyridine complexes have been discussed in detail. Picolinic acid, which is a substituted derivative of pyridine, forms strong complexes due to the chelate effect; 2,2′-bipyridine and 1,10-phenanthroline, which can also be viewed as substituted derivatives of pyridine, also form strong complexes, such as in Ferroin, which can be used as an redox indicator in the quantitative analysis of iron.

Acid-base properties of heterocyclic compounds

The most important biologically important are the nitrogen-containing five-and six-membered heterocycles of both natural and synthetic origin.

They are components of a number of important biologically active compounds - some natural amino acids (histidine, tryptophan, proline, hydroxyproline), biogenic amines (histamine, serotonin), vitamins, nitrogen bases of pyrimidine and purine series, nucleotides, nucleic acids, hemoglobin, chlorophyll, alkaloids and a number of drugs.

The acid-base properties of these heterocycles depend on the electronic structure of the nitrogen atom, the nature of the distribution of the electron density in the heterocycle (the presence or absence of an aromatic conjugate system involving electrons of nitrogen atoms), the ability to ionize and solvate.

Acidity of five-membered heterocycles with nitrogen heteroatoms. These include pyrrole, imidazole and pyrrolidine (*see above*).

Pyrrolidine is a product of the complete hydrogenation of pyrrole. All these compounds belong to NH-acids. To compare the acidity of these compounds, it is necessary to compare the stability of the conjugate bases (anions) formed by them.

pyrrole

imidazole

pyrrolidine
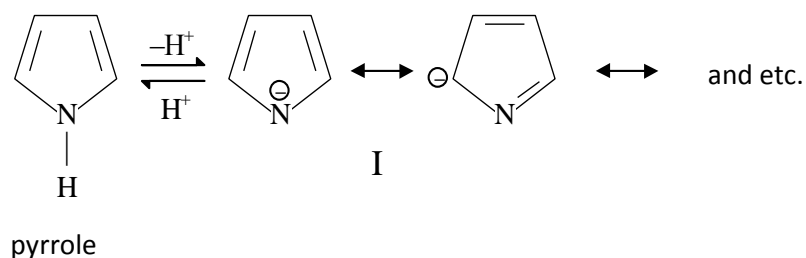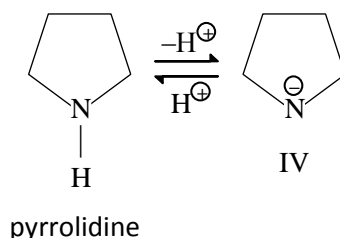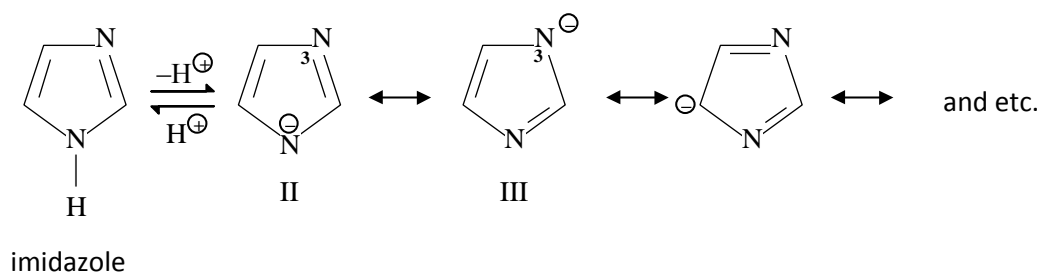
The anion formed after the proton is split off from imidazole is stabilized

by delocalizing the charge throughout the molecule, thanks to the coupling system, but mainly on the N3 atom, as shown by the resonant (limiting) structures (II) and (III). The contribution of other resonant structures with charges on carbon atoms is less significant, since it is more beneficial for a more electronegative nitrogen atom to retain a charge (a pair of electrons). The electron density is divided, as it were, between both nitrogen atoms.

In the anion (I), formed from pyrrole, there are fewer possibilities for delocalization of the charge, and therefore, based on the lower stability of the anion (I), it can be concluded that pyrrole is a weaker acid than imidazole.

NH-acids are, as a rule, very weak acids. So the acidity constant (pKa) for imidazole is ~ 14, and for pyrrole ~ 16.5, i.e. imidazole has slightly more acidic properties than methanol, and pyrrole is even weaker than methanol as acid.

Therefore, both these heterocycles form salts only when they interact with alkaline

metals or very strong bases - with alkali metal hydroxides at high temperature, for example:

potassium pyrroleate
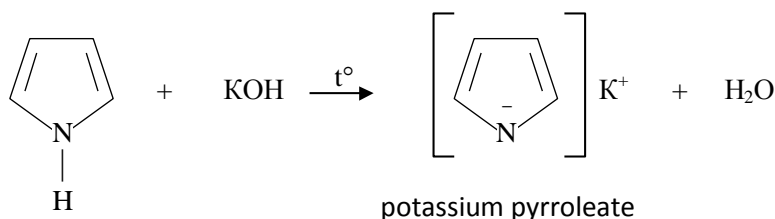
Of the compounds under discussion, pyrrolidine has the lowest acidity, since the anion (IV) is the least stable in comparison with the anions mentioned above. This is due to the extremely low degree of delocalization of the charge on the aliphatic (saturated, sp3-hybridization) part of the anion.

Basicity of nitrogen-containing five-membered heterocycles. The basis of heterocyclic nitrogen-containing compounds is due to the presence of an unshared pair of electrons on a nitrogen atom capable of taking a proton.

The pyrrolidine, a saturated heterocycle that is not an aromatic compound,

in principle, is a secondary aliphatic amine. Due to the presence of an unshared pair of electrons on the sp^3-hybrid orbitals of the nitrogen atom, it easily attaches a proton, exhibiting greater intrinsicity than pyrrole and imidazole, in which the nitrogen atoms are in the sp^2-hybrid

state. In addition, the solvation effect has a significant effect on the stability of the pyrrolidinium cation in aqueous solution:
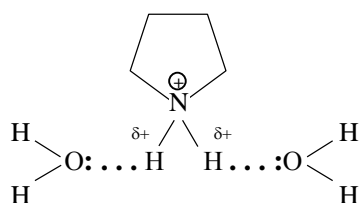
In the imidazole, only the pyridine (N_3) nitrogen atom is capable of protonation, since it contains an unshared pair of electrons on the sp^2-hybrid orbitals that do not participate in the formation of the aromatic sextet. The imidazolium ion formed upon interaction with acids retains aromatic properties:

imidazole hydrochloride
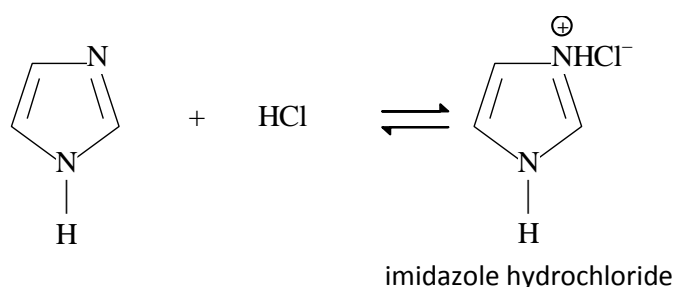
Due to the fact that imidazole displays amphoteric properties (according to NH-acid, according to N_3-base), its molecules can interact with each other due to intermolecular hydrogen bonds, forming associates.

N – H- acid centers

N: - base centers
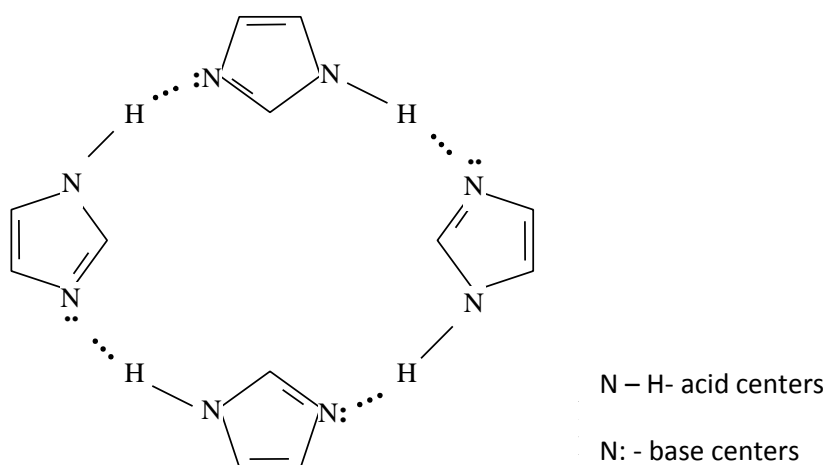
In pyrrole, the unshared pair of electrons of the nitrogen atom located on the p-orbitals is delocalized, that is, it participates in the formation of an aromatic conjugated system, and therefore protonation of the nitrogen atom in pyrrole is difficult. Pyrrole is a very weak base (pK_{BH}^+- 3.8), weaker even than alcohols. At the same time, in the molecule of pyrrole due to conjugation, the electron density at carbon atoms (especially in the α-positions) is increased, which makes them susceptible to proton attack:
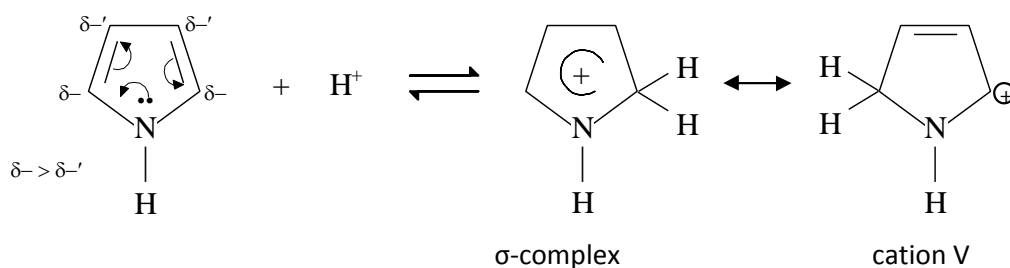
One of the limiting structures of the formed σ-complex, for example, the cation (V), attacking the second molecule of pyrrole as an electrophile, leads to the formation of a new cation (VI), and finally a pyrrole resin is obtained, which has no practical application:
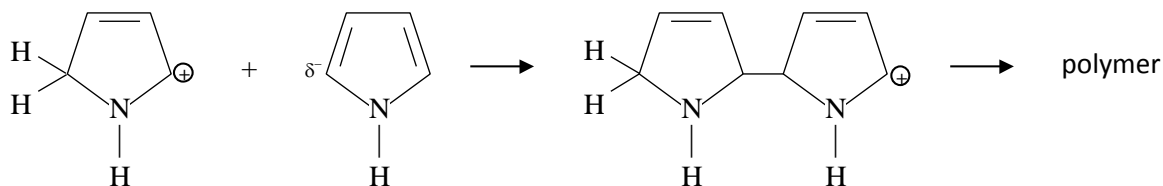
Thus, pyrrole in the presence of strong acids loses aromaticity and enters the addition (polymerization) reactions. This property of pyrrole is called acidophobia; it is even more pronounced in furan, but not inherent in thiophene.

Summarizing the foregoing, it is obvious that the acid properties of the compounds under consideration decrease in the series: imidazole> pyrrole> pyrrolidine, and the main ones increase in the series: pyrrol <imidazole <pyrrolidine. Imidazole and pyrrole form salts with strong bases, and pyrrolidine and imidazole with acids. Imidazole is thus an amphoteric compound.

Basicity of six-membered heterocyclic compounds with one and two heteroatoms. These include pyridine, piperidine (the product of complete hydrogenation of pyridine) and pyrimidine (see above):

In aromatic heterocycles (pyridine and pyrimidine), nitrogen atoms are located in the sp^2-hybridized state (an unshared pair of electrons is located on the sp^2-hybrid orbital and does not participate in conjugation), and in piperidine - in sp3-hybridized state, as in the case of pyrrolidine. As a consequence, a more pronounced basicity is manifested in the compound with sp3-hybridized nitrogen atom compared to with sp^2-hybridized, i.e. piperidine is a stronger base than pyridine.

In the aqueous medium, the basicity is mainly determined by the solvation effect of the protonated heterocycles. From the comparison of the solvation of pyridinium (I) and piperidinium (II) cations, it is obvious that the first of them is hydrated to a lesser degree (by one water molecule) than the second (by two water molecules):
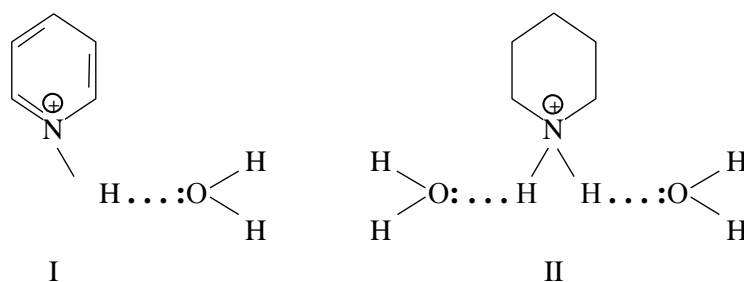
The basicity constants determined in water confirm the much greater basicity of piperidine (pK_{BH}^+ 11.12) compared with pyridine (pK_{BH}^+ 5.17). By the expression of the basic properties, piperidine differs little from the secondary aliphatic amine-diethylamine having pK_{BH}^+ 11.09.

Pyridine, although a relatively weak base, but with strong mineral acids, forms salts:

pyridinium chloride
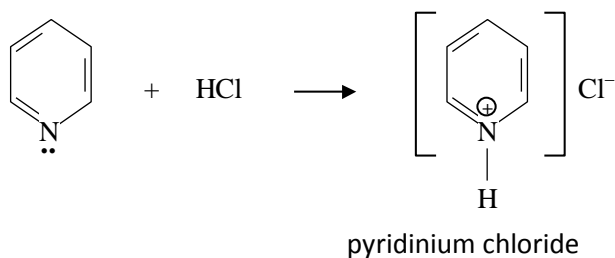
Pyrimidine - a six-membered heterocycle with two nitrogen heteroatoms, is an even weaker base than pyridine. This is due to the mutual retraction of the electron density by nitrogen atoms, which are more electronegative than carbon atoms.
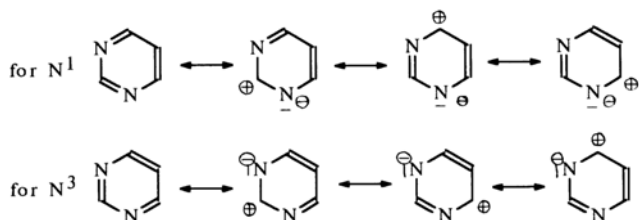
The protonation of pyrimidine can be carried out only by very strong acids, with the salt being formed with only one nitrogen atom:

пиримидиний гидросульфат
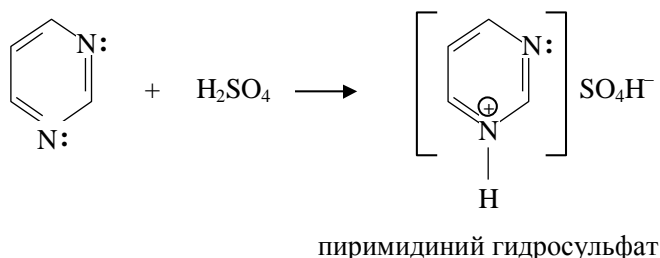
Consequently, the basic properties of six-membered nitrogen-containing heterocycles decrease in the series: piperidine> pyridine> pyrimidine.

Laboratory work № 10

Reagents and equipment:

1. Distilled water.

2. Concentrated solution of nitric acid.

3. Aqueous solutions: 1% ferric chloride, 5% sodium nitrite, 10% sodium hydroxide, 10% ammonia, 10% sulfuric acid.

4. Uric acid.

5. Antipyrine and amidopyrine; pyridine.

6. Red litmus or versatile paper.

7. A rack with test tubes, test tubes with a gas outlet tube.

8. The alcohol lamp.

Experiment 1. Reaction of antipyrine and amidopyrine with ferric chloride (III)

In the tube, place a few crystals of antipyrine, add 2 drops of water and a drop of 1% ferric chloride solution (III). An intensive and persistent orange-red coloration appears, which does not disappear when standing. For comparison, place several crystals of amidopyrine in another tube, add 2 drops of water and 1 drop of 1% ferric chloride solution (III). Appears violet coloration, rapidly disappearing. Add at once 3 more drops of ferric chloride (III). The color appears again, remains somewhat longer, but gradually fades.

The staining of the antipyrine with iron (III) chloride is due to the formation of a complex compound of ferropyrin, amidopyrine, by the formation of oxidation products.

The reaction with iron (III) chloride is qualitative, which makes it possible to distinguish between amidopyrine and antipyrine.

Conclusion:

Experiment 2. Reaction of antipyrine and amidopyrine with nitrous acid

In the tube place several crystals of antipyrine, add 2 drops of water, 1 drop of 10% solution of sulfuric acid and 1 drop of 5% sodium nitrite solution. Appears emerald green coloration, gradually disappearing, especially with excess sodium nitrite. For comparison, place several crystals of amidopyrine in another tube. Add 2 drops of water, 1 drop of 10% sulfuric acid solution and 1 drop of 5% sodium nitrite solution. There is unstable purple staining. If the staining disappears too quickly, add a little more amidopyrine. Amidopyrine forms colored oxidation products.

Similar to the reactions with iron (III) chloride, the reaction with nitrous acid is used in pharmaceutical practice to recognize the antipyrine and amidopyrine and distinguish them from each other.

Conclusion:

Experiment 3. The solubility of pyridine in water and its basic nature

Put 1 drop of pyridine into the test tube. Pay attention to its characteristic smell (smell of denatured alcohol). Add 1 drop of water, immediately a clear solution is obtained. Add 4 more drops of water. Pyridine is highly soluble in water and mixes with it in all respects.

Using a forceps, take a narrow strip of red litmus paper (on a common table) and moisten it with a solution of pyridine, for which tilt the tube with the solution. You can see only a slight blueing of the red litmus paper, more precisely - the transition from red to violet, indicating a weakly basic nature of pyridine.

Conclusion:

Experiment 4. The solubility of uric acid and its sodium salt in water

Place a small amount (at the tip of the spatula) of uric acid in a test tube. Add drop by drop of water, each time shaking the test tube. Note the poor solubility of uric acid in water. In cold water, uric acid is almost insoluble: 1 part of it dissolves in 39,000 parts of water.

After adding 8 drops of water, the dissolution is still not noticeable. It is, however, only 1 drop of 10% sodium hydroxide solution to be added, as the cloudy solution is immediately brightened by the formation of a relatively readily soluble disubstituted sodium salt. Keep the resulting solution for later experience.

Conclusion:

Experiment 5. Discovery of uric acid (murexide assay)

Place a drop of a solution of the sodium salt of uric acid on the slide using a pipette (see experiment 4). Add 1 drop of concentrated nitric acid (on a common table) and gently evaporate, holding the glass above the flame of the burner at some distance (about 10 cm). Once the solution has evaporated and a slight reddening of the spot begins at the site of the former drop, stop heating. When the glass has cooled, place 1 drop of 10% ammonia solution on the side of the stain. At the place of contact, a strip of purple-violet color (murexide probe) is observed.

When oxidized with nitric acid, uric acid, like other purine bases (for example, caffeine), forms alloxanthin. When the alloxanthine formed is moistened with ammonia, the ammonium salt is obtained which is very unstable in the free form of purple acid, murexide. Murexide test is used in the analysis of urinary stones. This sample is also used when opening caffeine, theobromine and other purine bases.

Conclusion:

Tasks for independent work

Control questions:

1. Biologically important heterocyclic systems. Five-membered heterocycles with one heteroatom. Pyrrole, furan, thiophene. The concept of the structure of tetrapyrene compounds (porphin, gemm). Linear tetrapyrene compounds.

2. Indole (benzopyrrole). Structure, properties. Biologically active derivatives of indole.

3. Five-membered heterocycles with two or more heteroatoms. Imidazole, properties; medico-biological significance of the derivatives.

4. Pyrazole, oxazole, thiazole. Structure, properties, biological functions of derivatives. Pyrazolone-3 is the structural basis of non-narcotic analgesics (analgin).

5. Six-membered heterocycles with one heteroatom. Pyridine, nicotinic acid and nicotinamide. Isonicotinic (γ-pyridinecarboxylic acid), medico-biological functions of derivatives.

6. Six-membered heterocycles with one heteroatom: pyrimidine, pyrazine. Hydroxy- and amino-derivatives of pyrimidine are components of nucleic acids. Barbituric acid and its derivatives.

7. Bicyclic heterocycles. Purin. Hydroxy- and aminopurines. Uric acid. Lactim-lactam tautomerism. Adenine; medico-biological significance of derivatives, tautomeric forms.

8. The concept of alkaloids. Hygrene, nicotine. Derivatives of tropane are atropine and cocaine. Methylated xanthines - caffeine, theophylline, theobromine.

9. What are the causes of the appearance of the color of the antipyrine and amidopyrine with iron (III) chloride. What practical value is the reaction of antipyrine and amidopyrine with iron (III) chloride.

10. Write a diagram of the interaction of the antipyrine with nitrous acid. By what mechanism is the reaction of antipyrine with nitrous acid? Where is the reaction of antipyrine and amidopyrine with nitrous acid used?

Do the exercises:
1. Arrange these compounds in a row to increase their basicity:
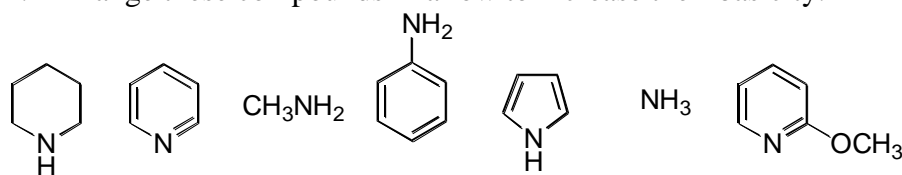
2. 2. Acridine is more basic than pyridine, and benzo [h] quinoline is vice versa. Than this can be explained?

Акридин   Пиридин   Бензо[h]хинолин

pK$_a$ 5.60   pK$_a$ 5.23   pK$_a$ 4.25   (H$_2$O)
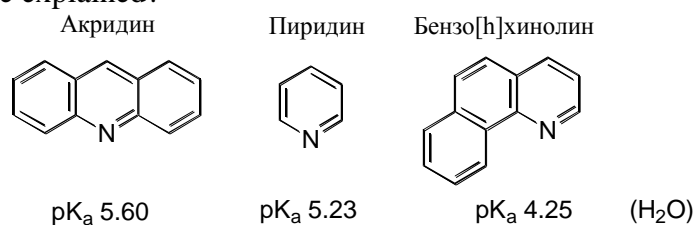
3. γ- Piron exhibits stronger basic properties than acetone or divinyl ether. Why? Which of the oxygen atoms in the γ-pyron molecule is more basic?

   γ-Пирон
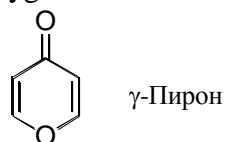
4. Explain the change in the basic properties in the next series of connections:

pK$_a$ (H$_2$O)   5.17   5.68   5.97   6.02
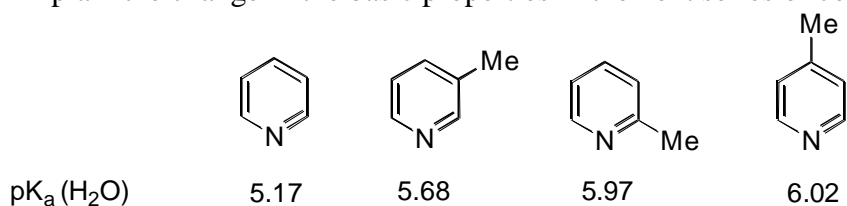
5. Arrange the following connections in order of increasing basicity:

а)

б)
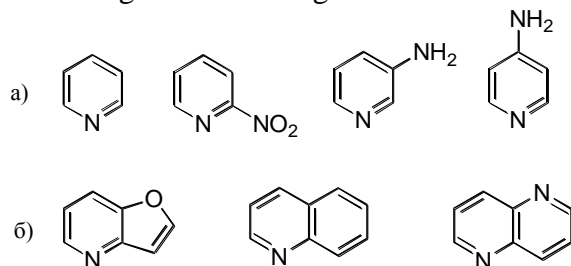
6. Arrange the joints in order of increasing NH-acidity:

а)

б)

в)
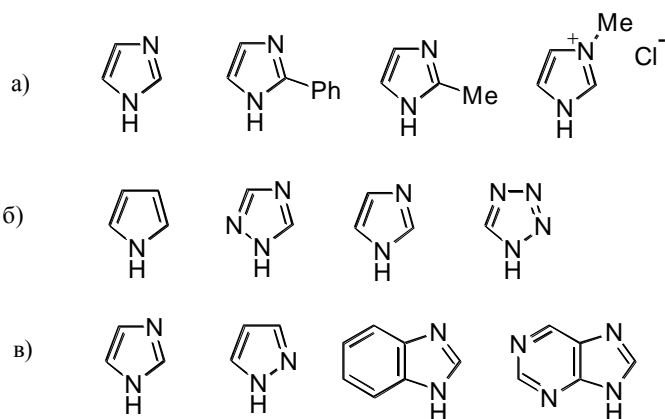
7. Which of these heterocycles belong to the π-excess? π-scarce? π-amphoteric? Why
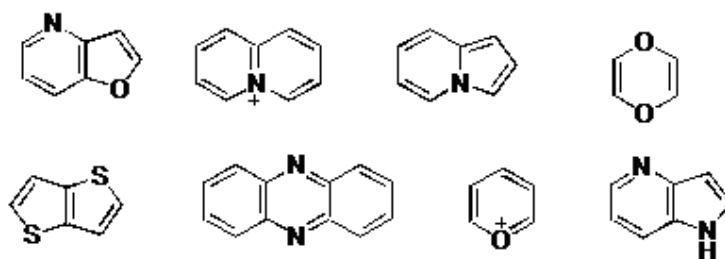
8. Why does pyridine show a basic character? Write a diagram of the interaction of pyridine with water.

9. Write tautomeric forms of uric acid. Write a diagram of the interaction of uric acid with sodium hydroxide.

10. Explain the causes of staining in the murexide sample. What is the use in medicine of a murexide test?

Test tasks:
1. Which heterocycles are aromatic?

I   II   III   IV
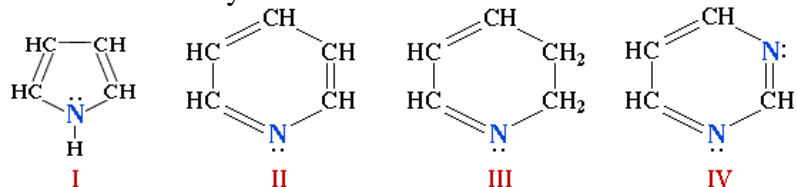
2. Which formula corresponds to pyrimidine?

а)   б)   в)   г)
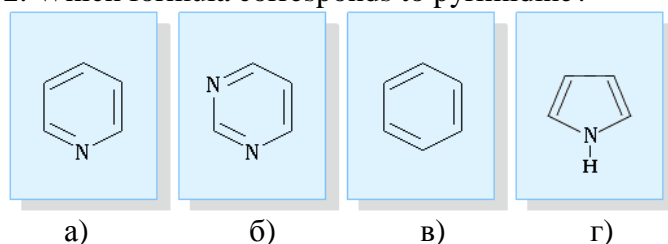
3. Specify the correct order of increasing the properties of the base for the following nitrogen-containing compounds:

a) pyrrole <pyridine <dimethylamine <ammonia

b) ammonia <pyrrole <pyridine <dimethylamine

c) dimethylamine <ammonia <pyridine <pyrrole

d) pyrrole <pyridine <ammonia <dimethylamine

4. In what order is the ease of electrophilic substitution reactions increasing for the following compounds?

a) pyridine <benzene <pyrrole

b) pyrrole <benzene <pyridine

c) benzene <pyridine <pyrrole

d) benzene <pyrrole <pyridine

5. Among the heterocycles represented, the base properties are:

а)   б)

в)   г)
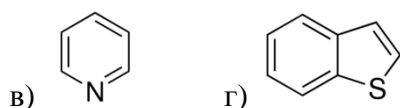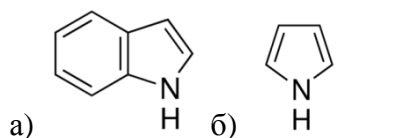
6. The unpaired electron pair of the heteroatom does not participate in conjugation with the p-electrons of the carbon atoms of the ring in the molecule …

а)   б)   в)   г)
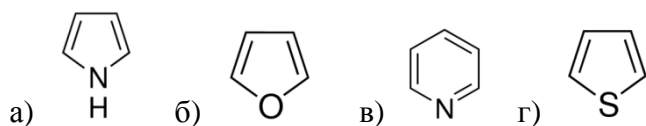
7. The composition of nucleic acids includes heterocyclic bases, which are ...

a) derivatives of thiophene

b) pyrrole derivatives

c) derivatives of purine

d) derivatives of furan

8. Nicotinic acid is a derivative of:

a) pyridine

b) indole

c) imidazole

 d) pyrimidine

e) pyrazole

1. Piperidine is a derivative:

a) pyridine

b) pyrrole

c) pyrimidine

d) pyrazine

e) pyridazine

2. Diazines include:

a) pyridine

b) piperidine

c) pyrimidine

d) pyrrole

e) pyrroline

3. Six-membered heterocyclic compounds include:

a) pyrazole

b) pyran

c) pyrrole

d) pyrroline

e) Thiazole.

4. The six-membered heterocyclic compounds include:

a) thiazole

b) thiophene

c) imidazole

d) pyridine

e) pyrrole

5. For qualitative determination of the antipyrine, use:

a) sodium nitrite

b) bromine water

c) potassium permanganate

d) sodium hydroxide

e) sulfuric acid

6. Dibasol is a derivative:

a) benzopyrrole

b) furan

c) benzimidazole

d) indole

e) pyrazole

7. Pyridine has the following properties:

a) the main

b) Acidic

c) amphoteric

d) oxidative

e) Rehabilitation

8. Five-membered heterocyclic compounds with one heteroatom include:

a) xanthine

b) pyrimidine

c) furan

d) quinoline

e) pyridine

9. Five-membered heterocyclic compounds include:

a) Purine

b) imidazole

c) pyridine

d) quinoline

e) Thiazole

10. Condensed heterocycles include:

a) Purine

b) Thymine

c) piperidine

d) imidazole

e) pyrrolidine

11. The pyrazolone-3 derivatives are:

a) porphin

b) analgin

c) pyridine

d) furacilin

e) pyrrole

12. Vitamin B1 (thiamine) contains the nucleus:

a) pyridine

b) piperidine

c) purine

d) pyrimidine

e) pyran

Timing of a 3-hour lesson:

1. Organizational moment - 2 minutes.

2. The survey - 40 min.

3. Explanation of the work - 25 min.

4. Performance and execution of work - 30 min.

5. Presentation of the new material - 45 min.

6. Verification of work and assignment to the house - 3 min.

Literature:

TOPIC: α-AMINO ACIDS

The purpose of the lesson: to generate knowledge about the structure and properties of the most important α-amino acids, as a chemical basis for further study of dynamic biochemistry in part of amino acids; to reveal the influence of the nature of the substituent and the spatial structure of the molecules on the reactivity.

The purpose of the activities of students in class

The student should know:

a) Classification of α-amino acids.

b) In what form do α-amino acids exist in different media.

c) Chemical properties of amino acids.

The student **should be able to**:

a) Give names to amino acids and their derivatives.

b) Qualitatively determine the amino acids in the mixture with other substances.

c) Write reactions of interaction of amino acids with acylating and alkylating reagents, with formaldehyde, nitrous acid, ninhydrin.

Questions for testing the baseline level:

1. Biologically important heterocyclic systems. Five-membered heterocycles with one heteroatom. Pyrrole, furan, thiophene. The concept of the structure of tetrapyrene compounds (porphin, gemm). Linear tetrapyrene compounds.

2. Indole (benzopyrrole). Structure, properties. Biologically active derivatives of indole.

3. Five-membered heterocycles with two or more heteroatoms. Imidazole, properties; medico-biological significance of the derivatives.

4. Pyrazole, oxazole, thiazole. Structure, properties, biological functions of derivatives. Pyrazolone-3 is the structural basis of non-narcotic analgesics (analgin).

5. Six-membered heterocycles with one heteroatom. Pyridine, nicotinic acid and nicotinamide. Isonicotinic (γ-pyridinecarboxylic acid), medico-biological functions of derivatives.

6. Six-membered heterocycles with one heteroatom: pyrimidine, pyrazine. Hydroxy- and amino-derivatives of pyrimidine are components of nucleic acids. Barbituric acid and its derivatives.

7. Bicyclic heterocycles. Purin. Hydroxy- and aminopurines. Uric acid. Lactim-lactam tautomerism. Adenine; medico-biological significance of derivatives, tautomeric forms.

8. The concept of alkaloids. Hygrene, nicotine. Derivatives of tropane are atropine and cocaine. Methylated xanthines - caffeine, theophylline, theobromine.

9. Chemical properties of the amino group. Basicity and nucleophilicity of the amino group.

10. Oxidation of thiols and reduction of disulfides.

Theoretical part

Amino acids are organic compounds which contain both an amino group and a <u>carboxyl group</u>.

$$-NH_2 \qquad \overset{\overset{\textstyle O}{\|}}{-C}-O-H$$

amino group   carboxyl group
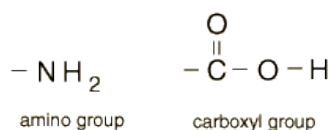
Amino acids have the general form:

$$H_2N-\overset{\overset{\textstyle COOH}{|}}{\underset{\underset{\textstyle R}{|}}{C}}-H$$

R-group
<u>Hydrocarbon</u>
<u>Neutral</u>
<u>Acid or base</u>

$$H_2N-\overset{\overset{\textstyle COOH}{|}}{\underset{\underset{\textstyle H}{|}}{C}}-H$$

Glycine (gly)
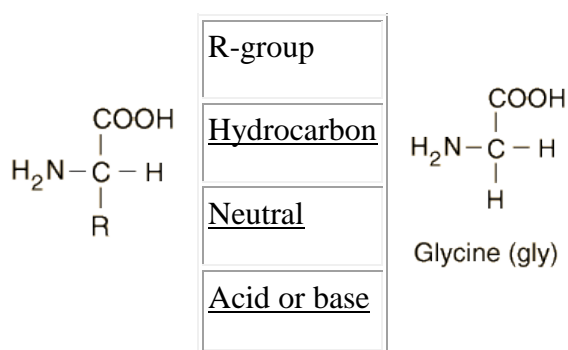
where the COOH is understood to be the carboxyl group shown above. There are 20 amino acids which make up the proteins, distinguished by the R-group. The simplest of the amino acids, glycine, has just H as an R-group.

Amino acids are the structural elements from which proteins are built. When amino acids bond to each other, it is done in the form of an amide , making a connection which is called a peptide linkage. This can be illustrated with the two simplest amino acids, glycine and alanine.

In this way, amino acids are organic compounds made of *carbon*, *hydrogen*, *oxygen*, *nitrogen*, and (in some cases) sulfur bonded in characteristic formations. Strings of amino acids make up proteins, of which there are countless varieties. Of the 20 amino acids required for manufacturing the proteins the human body needs, the body itself produces only 12, meaning that we have to meet our requirements for the other eight through nutrition. This is just one example of the importance of amino acids in the functioning of life. Another cautionary illustration of amino acids' power is the gamut of diseases (most notably, sickle cell anemia) that impair or claim the lives of those whose amino acids are out of sequence or malfunctioning. Once used in dating objects from the distant past, amino acids have existed on Earth for at least three billion years—long before the appearance of the first true organisms.

HOW IT WORKS

A "MAP" OF AMINO ACIDS

Amino acids are organic compounds, meaning that they contain carbon and hydrogen bonded to each other. In addition to those two elements, they include nitrogen, oxygen, and, in a few cases, sulfur. The basic structure of an amino-acid molecule consists of a carbon atom bonded to an amino group ($-NH_2$), a carboxyl group ($-COOH$), a hydrogen atom, and a fourth group that differs from one amino acid to another and often is referred to as the-R group or the side chain. The-R group, which can vary widely, is responsible for the differences in chemical properties.

This explanation sounds a bit technical and requires a background in chemistry that is beyond the scope of this essay, but let us simplify it somewhat. Imagine that the amino-acid molecule is like the face of a compass, with a carbon atom at the center. Raying out from the center, in the four directions of the compass, are lines representing chemical bonds to other atoms or groups of atoms. These directions are based on models that typically are used to represent amino-acid molecules, though north, south, east, and west, as used in the following illustration, are simply terms to make the molecule easier to visualize.

To the south of the carbon atom (C) is a hydrogen atom (H), which, like all the other atoms or groups, is joined to the carbon center by a chemical bond. To the north of the carbon center is what is known as an amino group ($-NH_2$). The hyphen at the beginning indicates that such a group does not usually stand alone but normally is attached to some other atom or group. To the east is a carboxyl group, represented as-COOH. In the amino group, two hydrogen atoms are bonded to each other and then to nitrogen, whereas the carboxyl group has two separate oxygen atoms strung between a carbon atom and a hydrogen atom. Hence, they are not represented as O_2.

Finally, off to the west is the R-group, which can vary widely. It is as though the other portions of the amino acid together formed a standard suffix in the English language, such as -tion. To the front of that suffix can be attached all sorts of terms drawn from root words, such as educate or satisfy or revolt-hence, education, satisfaction, and revolution. The variation in the terms attached to the front end is extremely broad, yet the tail end, -tion, is a single formation. Likewise the carbon, hydrogen, amino group, and carboxyl group in an amino acid are more or less constant.

A FEW ADDITIONAL POINTS.

The name amino acid, in fact, comes from the amino group and the acid group, which are the most chemically reactive parts of the molecule. Each of the common amino acids has, in addition to its chemical name, a more familiar name and a three-letter abbreviation that frequently is used to identify it. In the present context, we are not concerned with these abbreviations. Amino-acid molecules, which contain an amino group and a carboxyl group, do not behave like typical molecules. Instead of melting at temperatures hotter than 392°F (200°C), they simply decompose. They are quite soluble, or capable of being dissolved, in water but are insoluble in nonpolar solvents (oil-and all oil-based products), such as benzene or ether.

RIGHT-HAND AND LEFT-HAND VERSIONS.

All of the amino acids in the human body, except glycine, are either right-hand or left-hand versions of the same molecule, meaning that in some amino acids the positions of the carboxyl group and the R-group are switched. Interestingly, nearly all of the amino acids occurring in nature are the left-hand versions of the molecules, or the L-forms. (There-fore, the model we have described is actually the left-hand model, though the distinctions between "right" and "left"-which involve the direction in which light is polarized-are too complex to discuss here.)

Right-hand versions (D-forms) are not found in the proteins of higher organisms, but they are present in some lower forms of life, such as in the cell walls of bacteria. They also are found in some antibiotics, among them, streptomycin, actinomycin, bacitracin, and tetracycline. These

antibiotics, several of which are well known to the public at large, can kill bacterial cells by interfering with the formation of proteins necessary for maintaining life and for reproducing.

AMINO ACIDS AND PROTEINS

A chemical reaction that is characteristic of amino acids involves the formation of a bond, called a peptide linkage, between the carboxyl group of one amino acid and the amino group of a second amino acid. Very long chains of amino acids can bond together in this way to form proteins, which are the basic building blocks of all living things. The specific properties of each kind of protein are largely dependent on the kind and sequence of the amino acids in it. Other aspects of the chemical behavior of protein molecules are due to interactions between the amino and the carboxyl groups or between the various R-groups along the long chains of amino acids in the molecule.

NUMBERS AND COMBINATIONS.

Amino acids function as monomers, or individual units, that join together to form large, chainlike molecules called polymers, which may contain as few as two or as many as 3,000 amino-acid units. Groups of only two amino acids are called dipeptides, whereas three amino acids bonded together are called tripeptides. If there are more than 10 in a chain, they are termed polypeptides, and if there are 50 or more, these are known as proteins.

All the millions of different proteins in living things are formed by the bonding of only 20 amino acids to make up long polymer chains. Like the 26 letters of the alphabet that join together to form different words, depending on which letters are used and in which sequence, the 20 amino acids can join together in different combinations and series to form proteins. But whereas words usually have only about 10 or fewer letters, proteins typically are made from as few as 50 to as many as 3,000 amino acids. Because each amino acid can be used many times along the chain and because there are no restrictions on the length of the chain, the number of possible combinations for the formation of proteins is truly enormous. There are about two quadrillion different proteins that can exist if each of the 20 amino acids present in humans is used only once. Just as not all sequences of letters make sense, however, not all sequences of amino acids produce functioning proteins. Some other sequences can function and yet cause undesirable effects, as we shall see.

REAL-LIFE APPLICATIONS

DNA (deoxyribonucleic acid), a molecule in all cells that contains genetic codes for inheritance, creates encoded instructions for the synthesis of amino acids. In 1986, American medical scientist Thaddeus R. Dryja (1940-) used amino-acid sequences to identify and isolate the gene for a type of cancer known as retinoblastoma, a fact that illustrates the importance of amino acids in the body.

Amino acids are also present in hormones, chemicals that are essential to life. Among these hormones is insulin, which regulates sugar levels in the blood and without which a person would die. Another is adrenaline, which controls blood pressure and gives animals a sudden jolt of energy needed in a high-stress situation—running from a predator in the grasslands or (to a use a human example) facing a mugger in an alley or a bully on a playground. Biochemical studies of amino-acid sequences in hormones have made it possible for scientists to isolate and produce artificially these and other hormones, including the human growth hormone.

AMINO ACIDS AND NUTRITION

Just as proteins form when amino acids bond together in long chains, they can be broken down by a reaction called hydrolysis, the reverse of the formation of the peptide bond. That is exactly what happens in the process of digestion, when special digestive enzymes in the stomach enable the breaking down of the peptide linkage. (Enzymes are a type of protein—see Enzymes.) The amino acids, separated once again, are released into the small intestine, from whence they pass into the bloodstream and are carried throughout the organism. Each individual cell of the organism then can use these amino acids to assemble the new and different proteins required for its specific functions. Life thus is an ongoing cycle in which proteins are broken into individual amino-acid units, and new proteins are built up from these amino acids.

ESSENTIAL AMINO ACIDS.

Out of the many thousands of possible amino acids, humans require only 20 different kinds. Two others appear in the bodies of some animal species, and approximately 100 others can be found in plants. Considering the vast numbers of amino acids and possible combinations that exist in nature, the number of amino acids essential to life is extremely small. Yet of the 20 amino acids required by humans for making protein, only 12 can be produced within the body, whereas the other eight-isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine-must be obtained from the diet. (In addition, adults are capable of synthesizing arginine and histidine, but these amino acids are believed to be essential to growing children, meaning that children cannot produce them on their own.)

A complete protein is one that contains all of the essential amino acids in quantities sufficient for growth and repair of body tissue. Most proteins from animal sources, gelatin being the only exception, contain all the essential amino acids and are therefore considered complete proteins. On the other hand, many plant proteins do not contain all of the essential amino acids. For example, lysine is absent from corn, rice, and wheat, whereas corn also lacks tryptophan and rice lacks threonine. Soybeans are lacking in methionine. Vegans, or vegetarians who consume no animal proteins in their diets (i.e., no eggs, dairy products, or the like) are at risk of malnutrition, because they may fail to assimilate one or more essential amino acid.

Многообразные пептиды и белки состоят из остатков α-аминокислот. Общее число встречающихся в природе аминокислот достигает 300, однако некоторые из них обнаружены лишь в определенном сообществе или даже в одном организме. Среди них выделяется группа из 20 наиболее важных α-аминокислот.

RULES FOR THE NOMENCLATURE OF THE NATURAL AMINO ACIDS AND RELATED SUBSTANCES

The following rules are designed to eliminate the current confusion in the nomenclature of the a-amino acids that arise from the hydrolysis of proteins, and of the compounds and derivatives of these acids.

Rule 1. The configurational relationship of the asymmetric a-carbon atom of an amino acid capable of optical isomerism should be indicated by a symbol prefixed to the name; however, if a specific statement or the context makes it clear which isomer is under consideration, the symbol may be omitted.

Rule 2. Distinction between the stereoisomers of the amino acids is made by a prefixed small capital letter D or L to denote the configurational family to which the a-ca&on atom belongs. The D and L are to be pronounced dee and ell, respectively, not dextro and levo. An

additional symbol to denote the direction of the rotation (i.e., a plus or a minus sign enclosed in parentheses) is not necessary.

Rule 3. Where confusion is possible between the use of the capital letter prefix for the configuration of the a-carbon atom in amino acid nomenclature and for that of the highest numbered asymmetric carbon atom in carbohydrate nomenclature, a subscript is added to the capital letter prefix. Where the prefix is used in the amino acid sense, the subscript s is added; where the prefix is used in the carbohydrate sense, the subscript g is added. These subscripts (lower-case roman letters) refer, respectively, to serine, the fundamental substance to which amino acids that bear structural resemblance to the carbohydrates can be formally related, and to glyceric aldehyde, the fundamental substance to which the configuration of the carbohydrates is formally related.

Rule 4. If the configurational relationship of the a-carbon atom has not been definitely established, the actual direction of the rotation ina specified solvent, preferably of the free amino acid in water, is designated by the prefixes dextro or levo in lower-case italic letters or, alternatively, by a plus or a minus sign enclosed in parentheses.

Rule 5. The prefix meso- or its abbreviation ms- in lower-case italic letters is used to denote the isomers of amino acids and derivatives of these that are optically inactive because of internal compensation.

Rule 6. Where the amino acid has two centers of asymmetry so constituted t,hat int,ernal compensation is impossible, the form which has the Lconfiguration at the a-carbon atom is designat,ed the L-amino acid and the form that has the opposite configuration at both asymmetric carbon atoms is designated the n-amino acid.

Rule 7. Salts and derivatives of amino acids including peptides are designated with the use of a small capital letier to denote the configurational family of the cr-carbon atom or atoms, this letter being placed immediately before the name of the parent acid or its radical. The customary rules of nomenclature are otherwise observed.

Table of basic amino acids
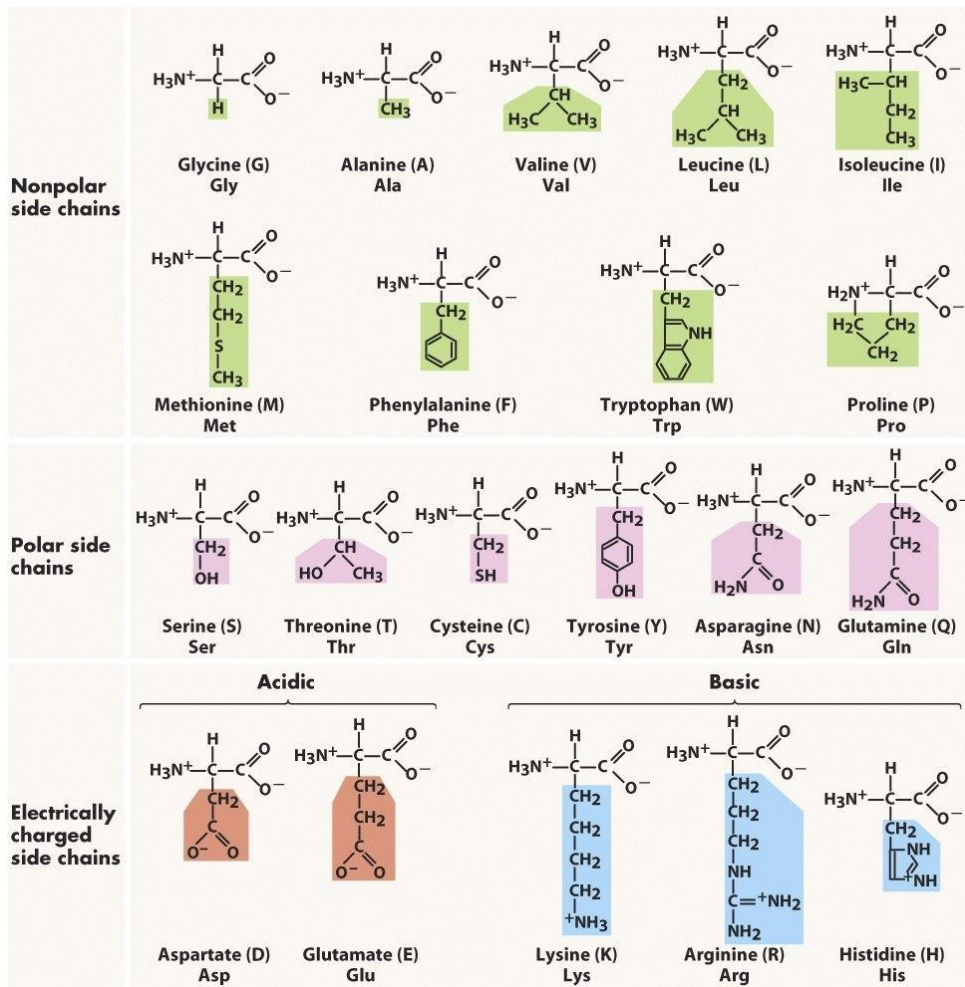
Optical isomerism of α-amino acid
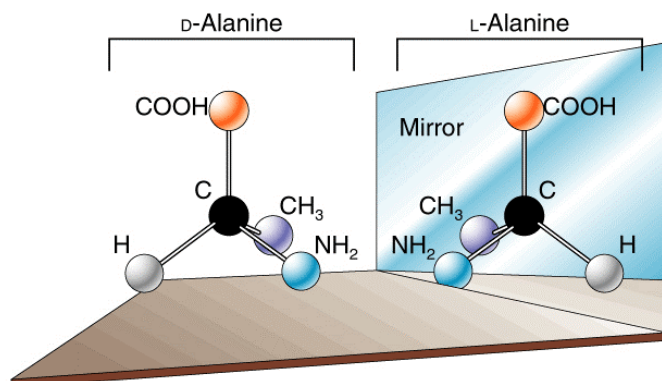
Physio Chemical Properties of Amino acids:

1. Solubility:
Most of the amino acids are usually soluble in water, and insoluble in organic solvents.
2. Melting Point:
Amino acids are generally melt at higher temperature of ten above 2000C.
3. Taste:
Amino acids may be sweet (Gly, Ala & Val), tasteless (Leu) or Bitter (Arg & Ile).

4. Optical Properties:

All amino acids possess optical isomers due to the presence of asymmetric α-carbon atoms.

5. Zwitter ion and Isoelectric point:

The name zwitter is derived from the German word which means "hybrid". Zwitter ion (or) dipolar ion is a hybrid molecule containing positive & negatively ionic groups. Basically the proton shifts from carboxyl group to amino group of the self molecule at normal pH cellular levels.

6. Titration Curve of Glycince:

Glycine is optically inactive, simplest amino acid because which have no asymmetric carbon atom. Acid-Base titration involves the gradual addition (or) removal of protons. It has three different stages when the Glycine undergoes acid-base titration.

Chemical Properties of Amino acids:

Chemical reactions of amino acids due to carboxyl and amino groups:

II.   I) Due to Carboxyl group:

a) Decarboxylation:

The amino acids will undergo alpha decarboxylation to form the corresponding "amines". Thus important amines are produced from amino acids.

- Histidine   → Histamine + CO_2
- Tyrosine   →Tyramine + CO_2
- Tryptophan   →Tryptamine + CO_2
- Lysine   →Cadaverine + CO_2
- Glutamic acid   → Gamma Amino Butyric Acid (GABA) + CO_2

b) Reaction with Alkalies (Salt formation):

The carboxyl group of amino acids can release a H+ ion with the formation of Carboxylate (COO–) ions. These may be neutralized by cations like Na+ and Ca+2 to form Salts. Thus amino acids react with alkalies to form "Salts".

$$R—CH—COO\,\boxed{H\ +\ HO}\,Na \longrightarrow R—CH—COO·Na\ +\ H_2O$$
$$\qquad\ \ |\qquad\qquad\qquad\qquad\qquad\qquad\quad |$$
$$\qquad NH_2 \qquad\qquad\qquad\qquad\qquad\qquad NH_2$$

c) Reaction with Alcohols (Esterification) :

When the amino acids is reacted with alcohol to form, "Ester". The esters are volatile in contrast to the form amino acids.

$$R—CH—COO\,\boxed{H\ +\ HO}—C_2H_5 \xrightarrow{\text{Acid catalyst}} R—CH—COO—C_2H_5\ +\ H_2O$$
$$\qquad\ \ |\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad |$$
$$\qquad NH_2 \qquad\qquad\qquad\qquad\qquad\qquad\quad NH_2$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\text{Ethyl ester}$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\text{of amino acid}$$
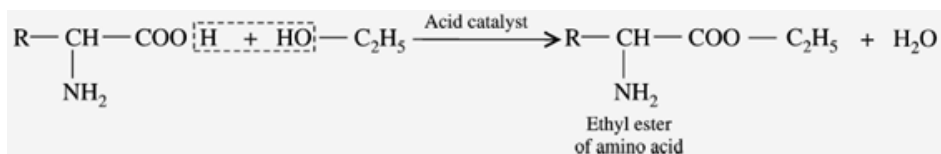
d) Reaction with Amines:

Amino acid reacts with Amines to form "Amides".

$$R—CH—CO\,\boxed{OH\ +\ H}\,HN—R' \longrightarrow R—CH—CO—NH—R' + H_2O$$
$$\qquad\ \ |\qquad\qquad\qquad\qquad\qquad\qquad\qquad\ \ |$$
$$\qquad NH_2 \qquad\qquad\qquad\qquad\qquad\qquad\quad NH_2$$
$$\text{Amino acid}\qquad\qquad\text{Amine}\qquad\qquad\qquad\text{Amide}\qquad\qquad\text{Water}$$
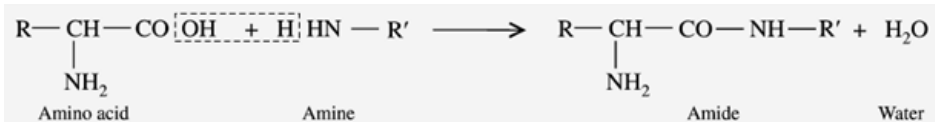
II) Due to Amino group:

a) *Reaction with Mineral acids* (Salt formation)

When the amino acids are treated with mineral acids (like HCl), it forms "Acid Salts".

b) *Reaction with Formaldehyde*:

When the amino acid reacts with two molecules of Formaldehyde it forms "N-dimethylol derivative" (Hydroxy-methyl derivative). This reaction is done in two steps. These derivatives are insoluble in water and resistant to attack by microorganisms.
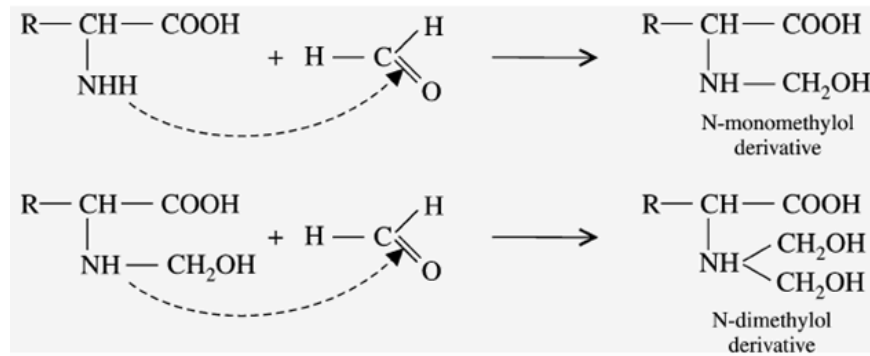
c) *Reaction with Benzaldehyde*:

When the amino acid reacts with Benzaldehyde, it gives "Schiff's base".
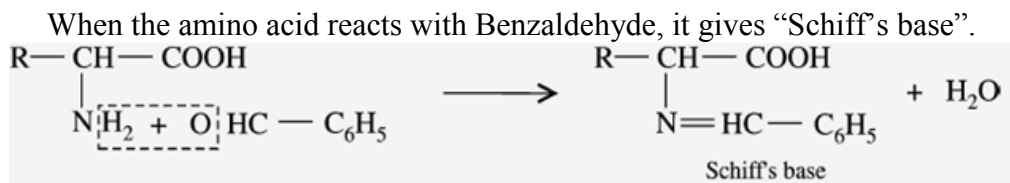
d) *Reaction with Nitrous acid* (Van slyke reaction):

When the amino acids react with Nitrous acid (HNO2) to liberate N2 gas and to produce the corresponding "α-hydroxyl acid". The imino acids Proline and Hydroxyproline do not respond to this reaction.
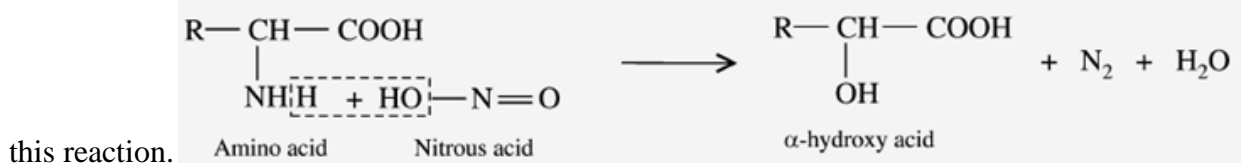
e) *Reaction with Sanger's reagent*:

"1-flouro-2,4-dinitrobenzene" is called Sanger's reagent (FDNB). In mildly alkaline solution, sanger's reagent reacts with α-amino acid to produce Yellow colored derivative, DNB-amino acid.
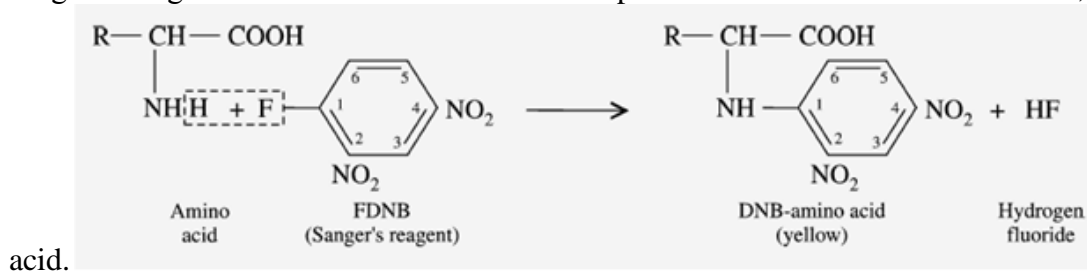
f) *Reaction with DANSYl Chloride*:

DANSYl chloride means "Dimethyl Amino Naptha Sulphonyl Chloride". When the amino acid reacts with DANSYl chloride reagent, it gives a "Flourescent DANSYl derivative".
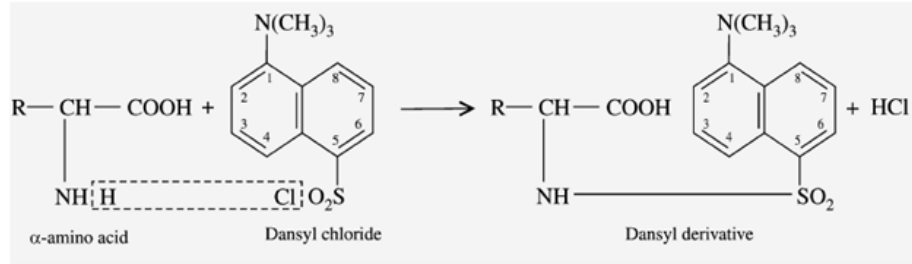
g) *Reaction with acylating agents* (Acylation):

When the amino acids react with "Acid chloride" and acid anhydride (Pthalic anhydride) in alkaline medium it gives "pthaloyl amino acid".
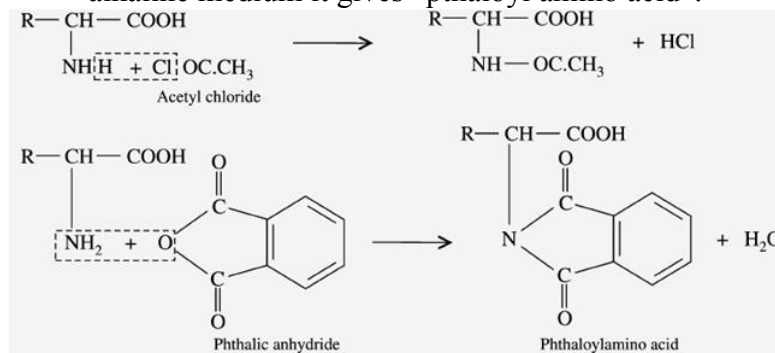
c) Due to amino & carboxyl group:

II. *Ninhydrin reaction*:

Step 1:

Ninhydrin (=indane 1,2,3-trione hydrate) is a powerful oxidizing agent and causes oxidative decarboxylation of α-amino acids producing CO2, NH3 and an aldehyde with one less carbon atom than the parent amino acid.
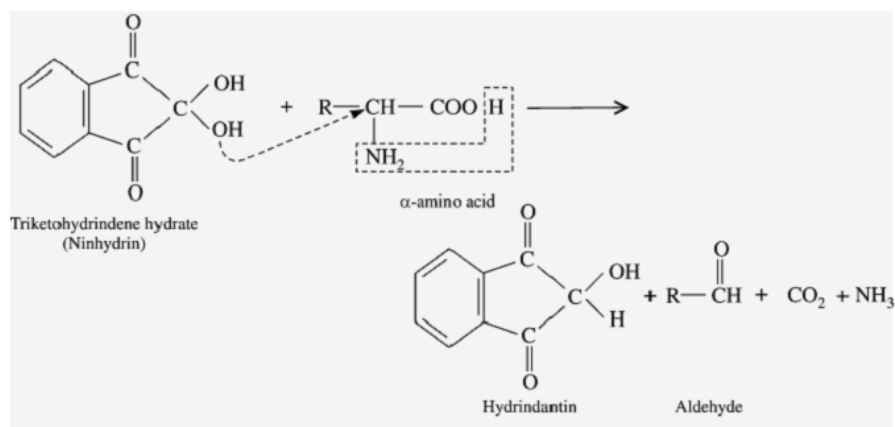
Step 2:

The reduced ninhydrin then reacts with the liberated NH3 and a mole of ninhydrin, forming Blue-colored Rhumann's complex.

Ninhydrin · Ammonia · Hydrindantin

Diketohydrindylidene-diketohydrindamine
(Ruheman's purple)
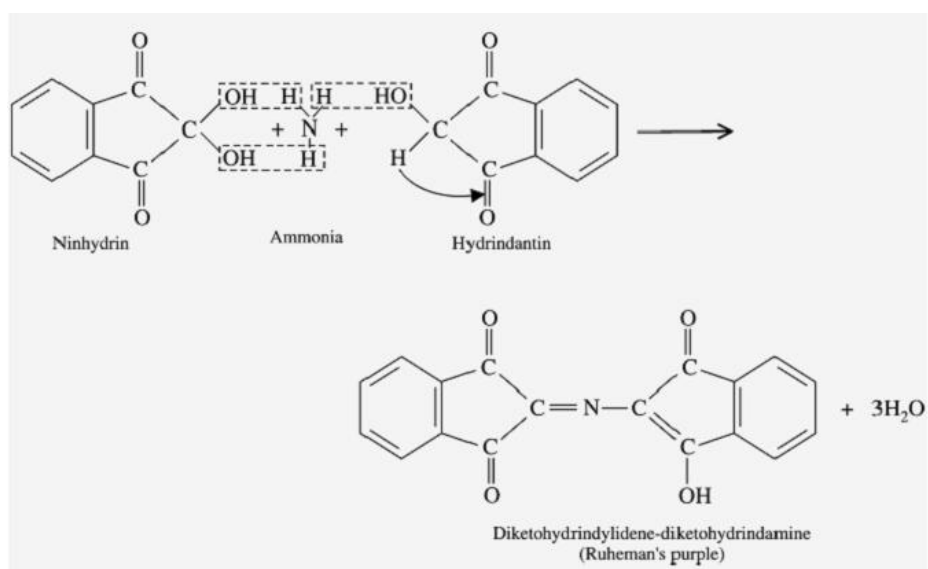
This reaction is very sensitive reaction and it is used for amino acid and imino acid identification.

When Amino acids (or) Imino acid reacts with Ninhydrin molecule it gives Color. When it gives Purple color (Rhumann's Complex) –the Unknown sample is Amino acids (Which have primary amine –NH2) or it is gives Yellow color – the Unknown sample is Imino acid (-NH-).

II.   *Reaction with Edmann's degradation*:

Edmann's reagent is "phenylisothiocyanate". When amino acids react with Edmann's reagent it gives "phenyl thiohydantoic acid" finally it turns into cyclized form "Phenyl thiohydantoin" (Edmann's derivative).
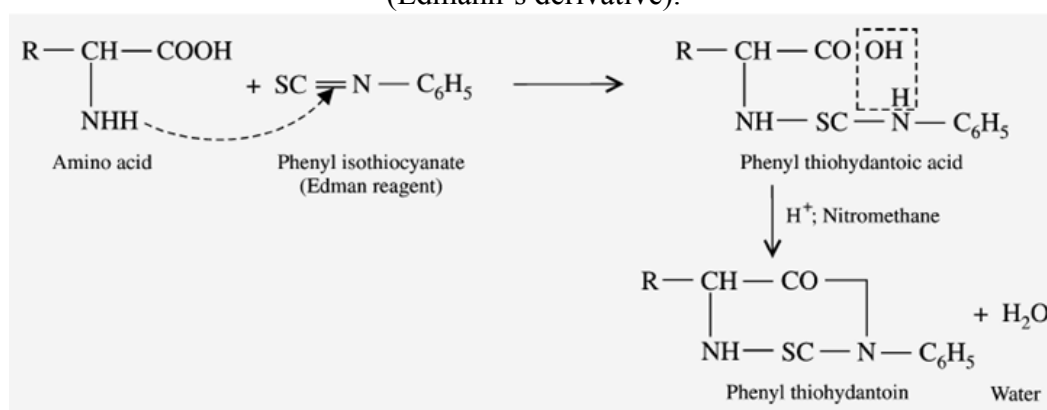
II.   **Synthesis of α-Amino Acids**
     1)   Amination of alpha-bromocarboxylic acids, illustrated by the following equation, provides a straightforward method for preparing alpha-aminocarboxylic acids. The bromoacids, in turn, are conveniently prepared from carboxylic acids by reaction with Br_2 + PCl_3. Although this direct approach gave mediocre results when used to prepare simple amines from alkyl halides, it is more effective for making amino acids, thanks to the reduced nucleophilicity of the nitrogen atom in the product. Nevertheless, more complex procedures that give good yields of pure compounds are often chosen for amino acid synthesis.

$$R-\underset{Br}{\underset{|}{CH}}-CO_2H \ + \ 2\ NH_3 \xrightarrow{S_N2} R-\underset{\overset{\oplus}{N}H_3}{\underset{|}{CH}}-CO_2^{\ominus} \ + \ NH_4Br$$
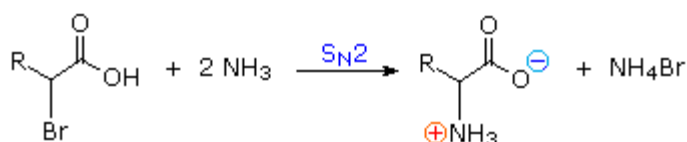
2) By modifying the nitrogen as a phthalimide salt, the propensity of amines to undergo multiple substitutions is removed, and a single clean substitution reaction of 1º- and many 2º-alkylhalides takes place. This procedure, known as the Gabriel synthesis, can be used to advantage in aminating bromomalonic esters, as shown in the upper equation of the following scheme. Since the phthalimide substituted malonic ester has an <u>acidic hydrogen</u> (colored orange), activated by the two ester groups, this intermediate may be converted to an <u>ambident anion</u> and alkylated. Finally, base catalyzed hydrolysis of the phthalimide moiety and the esters, followed by acidification and thermal decarboxylation, produces an amino acid and phthalic acid (not shown).
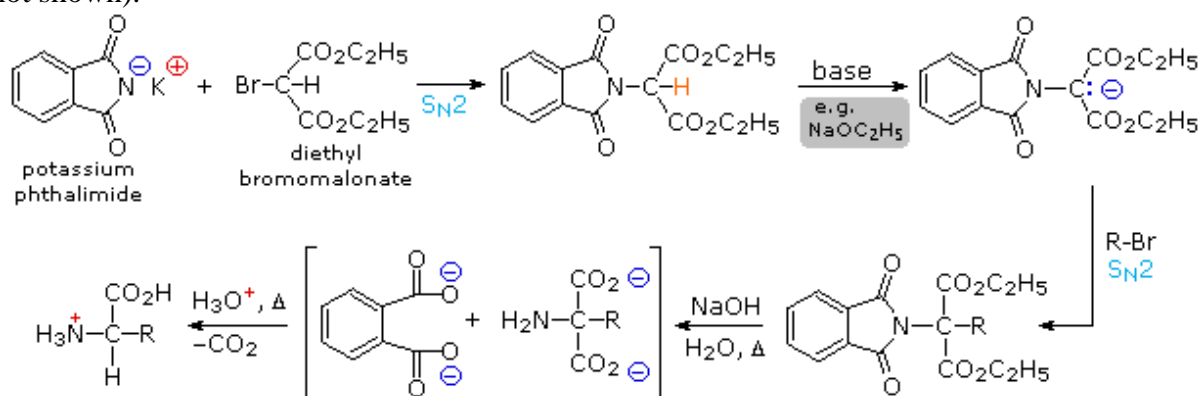
3) An elegant procedure, known as the **Strecker synthesis**, assembles an alpha-amino acid from ammonia (the amine precursor), cyanide (the carboxyl precursor), and an aldehyde. This reaction (shown below) is essentially an imino analog of <u>cyanohydrin formation</u>. The alpha-amino nitrile formed in this way can then be hydrolyzed to an amino acid by either acid or base catalysis.
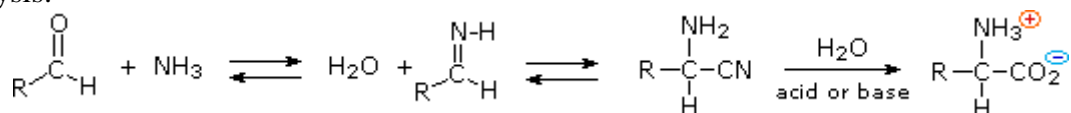
4) Resolution The three synthetic procedures described above, and many others that can be conceived, give racemic amino acid products. If pure **L** or **D** enantiomers are desired, it is necessary to <u>resolve</u> these racemic mixtures. A common method of resolving racemates is by diastereomeric salt formation with a pure chiral acid or base. This is illustrated for a generic amino acid in the following diagram. Be careful to distinguish charge symbols, shown in colored circles, from optical rotation signs, shown in parenthesis.

In the initial display, the carboxylic acid function contributes to diastereomeric salt formation. The racemic amino acid is first converted to a benzamide derivative to remove the basic character of the amino group. Next, an ammonium salt is formed by combining the carboxylic acid with an optically pure amine, such as brucine (a relative of strychnine). The structure of this amine is not shown, because it is not a critical factor in the logical progression of steps. Since the amino acid moiety is racemic and the base is a single enantiomer (levorotatory in this example), an equimolar mixture of diastereomeric salts is formed (drawn in the green shaded box). Diastereomers may be separated by crystallization, chromatography or other physical manipulation, and in this way one of the isomers may be isolated for further treatment, in this illustration it is the (+):(-) diastereomer. Finally the salt is broken by acid treatment, giving the resolved (+)-amino acid derivative together with the recovered resolving agent (the optically active amine). Of course, the same procedure could be used to obtain the (-)-enantiomer of the amino acid.
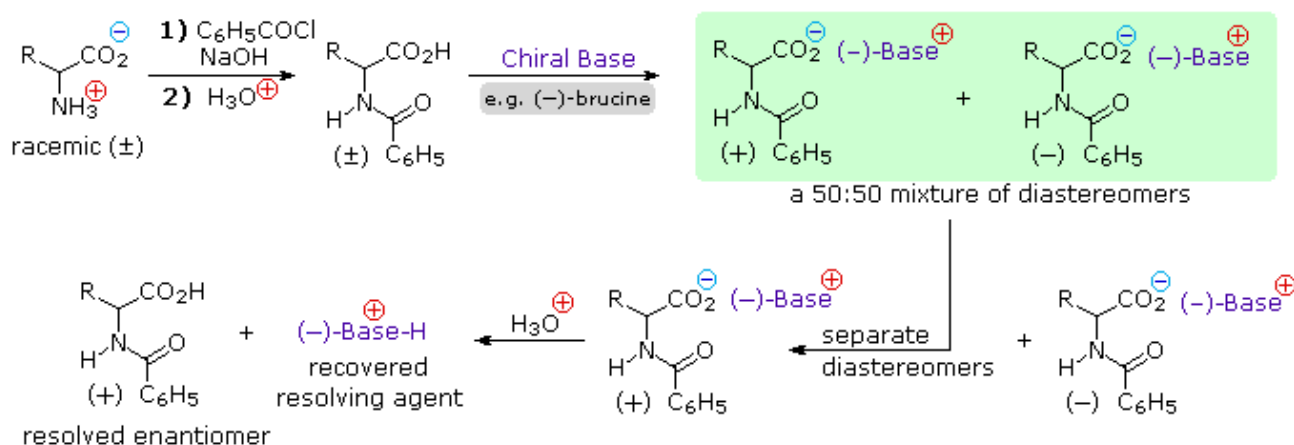
Since amino acids are <u>amphoteric</u>, resolution could also be achieved by using the basic character of the amine function. For this approach we would need an enantiomerically pure chiral acid such as tartaric acid to use as the resolving agent. By clicking on the above diagram, this alternative resolution strategy will be illustrated. Note that the carboxylic acid function is first esterified, so that it will not compete with the resolving acid.

Resolution of aminoacid derivatives may also be achieved by enzymatic discrimination in the hydrolysis of amides. For example, an aminoacylase enzyme from pig kidneys cleaves an amide derivative of a natural L-amino acid much faster than it does the D-enantiomer. If the racemic mixture of amides shown in the green shaded box above is treated with this enzyme, the L-enantiomer (whatever its rotation) will be rapidly converted to its free zwitterionic form, whereas the D-enantiomer will remain largely unchanged. Here, the diastereomeric species are transition states rather than isolable intermediates. This separation of enantiomers, based on very different rates of reaction, is called **kinetic resolution**.

Laboratory work № 11

Reagents and equipment:

1. Distilled water.

2. Concentrated solution of acetic acid.

3. Aqueous solutions: 1% glycine, 1% α-alanine, 0.1% ninhydrin, 5% sodium nitrite, 0.1% hydrochloric acid and 0.1% sodium hydroxide.

4. Solid copper carbonate (II).

5. Formalin.

6. A solution of methyl red.

7. Congo Indicator.

8. A tripod with test tubes, test tubes with a gas outlet tube.

9. The alcohol lamp.

Experiment 1. Reaction of glycine with ninhydrin

In a test tube, place 4 drops of 1% glycine solution and 2 drops of a 0.1% solution of ninhydrin. The contents of the tube gently heat until a blue-red color appears.

Conclusion:

Experiment 2. Reaction of glycine with formaldehyde

Place 5 drops of 1% glycine solution and 1 drop of methyl red indicator into the tube. The solution is dyed yellow (neutral medium). Add an equal volume of formalin to the resulting mixture. Note the appearance of the red color (acidic medium). This reaction, called "titration" is used to quantify carboxyl groups in α-amino acids.

Conclusion:

Experiment 3. Reaction of glycium with nitrous acid

Put 5 drops of 1% glycine solution into the tube and equal volume of 5% solution of sodium nitrite. Add concentrated acetic acid and shake the mixture gently. Gas evolution is observed. The reaction is used to quantify amino groups in amino acids.

Conclusion:

Experiment 4. Formation of a complex salt of glycine copper

Place 1 ml of a 1% glycine solution in a test tube. Add dry copper carbonate (II) on the tip of the spatula and heat the mixture. The solution is dyed blue.

Conclusion:

Experiment 5. Amphoteric properties of α-alanine

a) Place 5 drops of 1% α-alanine solution in a tube and add dropwise 0.1% hydrochloric acid solution, colored by the Congo indicator in blue, until the pink-red color appears.

b) Place 5 drops of 1% α-alanine solution in a test tube and add a 0.1% sodium hydroxide solution colored by phenolphthalein dropwise until the color disappears.

Conclusion:

Tasks for independent work

Control questions:

1. What substances are amino acids and why is it that α-amino acids have an important biological significance?

2. Classification of α-amino acids and their nomenclature. Isomerism of amino acids.

3. Properties of α-amino acids. Why are α-amino acids capable of interacting with acids and alkalis?

4. Methods of obtaining amino acids.

5. Write an equation for the reaction of the reaction of glycine with ninhydrino. What external characteristics is characterized by the reaction of a-amino acids with ninhydride? What practical application does this reaction have? What are the causes of the discoloration of the indicator?

6. Write a diagram of the interaction of glycine with nitrous acid. Name the compounds formed. What practical application has the reaction of amino acids with nitrous acid (Van Slyck method)?

7. Write an equation for the reaction of the reaction of glycine with formaldehyde. What practical application has the reaction of α-amino acids with formaldehyde (the method of Sørensen)?

8. Write a scheme for the interaction of glycine with copper (II) carbonate. What color is characteristic for solutions of complex copper salts? What type of complexation has here?

9. Write an equation for the reaction of the reaction of α-alanine with sodium hydroxide. Why does the color of the indicator change during the reaction?

10. Write the equation for the reaction of the reaction of α-alanine with hydrochloric acid. Why does the color of the indicator change during the reaction?

Do the exercises:

1. There are four test tubes in which 4 compounds are filled: water, tyrosine, arginine, glycine. How can you define each connection? Write the corresponding reaction equations.

2. Write the equations for the reactions of alanine with:
a) ethyl alcohol
b) hydrochloric acid
c) ninhydrin
d) Carbobenzoxochloride

3. Write the equations of tyrosine reactions with:
a) nitric acid
b) 2,4-dinitrofluorobenzene
c) nitrous acid
d) sodium hydroxide

4. Write the equations of serine reactions by:
a) NH_2 group
b) for the COOH group

5. What is the basis for the optical activity of natural α -amino acids? Do all protein amino acids exhibit optical properties?

6. Write the D- and L-forms of the amino acids. In what optically active form are they contained in natural proteins?

7. Which α-amino acids isolated from proteins have 2 asymmetric carbon atoms? Write down their structural formulas.

8. What kind of universal reactions are characteristic for protein amino acids? Write the equations of the corresponding reactions.

9. What kind of reaction is specific for:
a) aromatic amino acids
b) cysteine
c) tyrosine
d) tryptophan
e) arginine
f) histidine?
Write the equations of the corresponding reactions.

10. Write down the formulas for natural amino acids that have in a neutral environment:
a) a positive charge
b) negative charge

11. Prove that protein amino acids are amphoteric compounds.

12. Write a scheme of dissociation of the amino acid in the acidic, alkaline and neutral pH range. Indicate the charge of the amino acid.

13. In which pH range is acidic, neutral or basic, there will be an isoelectric point:
a) monoaminodicarboxylic acids
b) monoaminomonocarboxylic acids
c) diaminomonocarboxylic acids?
Explain why and give examples.

14. Write the formulas of methionine and histidine in the form of bipolar ions. How these amino acids will be charged in excess:
a) acids
b) alkali?

Test tasks:
1. Which of the above formulas of organic substances refer to amino acids?

$$\text{a } H_2N-\overset{\overset{O}{\|}}{C}-NH_2 \quad \text{b } H_3C-\underset{\underset{NH_2}{|}}{CH}-\overset{\overset{O}{\|}}{C}-OH \quad \text{c } H_3C-\overset{\overset{O}{\|}}{C}-NH_2$$

$$\text{d } \underset{\underset{NH_2}{|}}{CH_2}-\overset{\overset{O}{\|}}{C}-OH \qquad \text{e } H-\overset{\overset{O}{\|}}{C}-NH_2$$
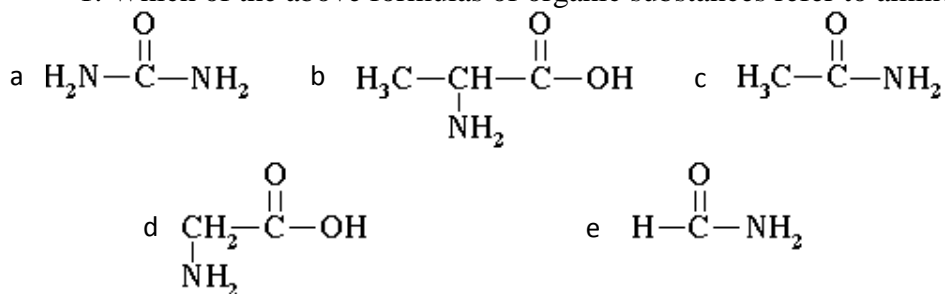
1) a, c
2) a, e
3) b, d
4) c, e

2. Indicate the isomers of aminobutyric acid.

$$\text{a } NH_2-\underset{\underset{CH_3}{|}}{CH}-\overset{\overset{O}{\|}}{C}-OH \quad \text{b } CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{NH_2}{|}}{C}}-\overset{\overset{O}{\|}}{C}-OH \quad \text{c } CH_3-\underset{\underset{NH_2}{|}}{CH}-CH_2-\overset{\overset{O}{\|}}{C}-OH$$

$$\text{d } \underset{\underset{NH_2}{|}}{\overset{\overset{CH_3}{|}}{CH}}-CH_2-CH_2-\overset{\overset{O}{\|}}{C}-OH \quad \text{e } CH_2-\underset{\underset{NH_2\ CH_3}{|\ \ |}}{\overset{\overset{CH_3\ O}{|\ \ \|}}{C}}-C-OH \quad \text{f } H_2N-CH_2-CH_2-\overset{\overset{O}{\|}}{C}-OH$$
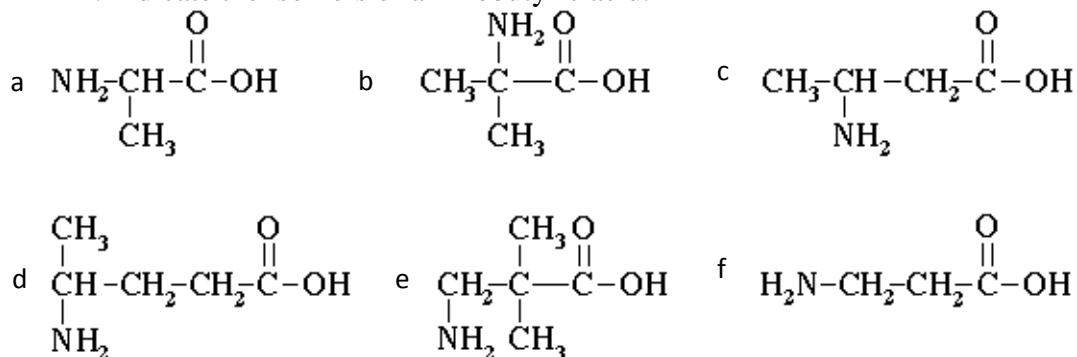
1) a, d
2) b, c
3) d, e
4) e, f

3. In the scheme of transformations

$$CH_3-\overset{\overset{\textstyle O}{\|}}{C}-H \xrightarrow{\ X\ } CH_3COOH \xrightarrow{\ Y\ } \underset{\underset{\textstyle Cl}{|}}{CH_2}-COOH \xrightarrow{\ NH_3\ } Z$$
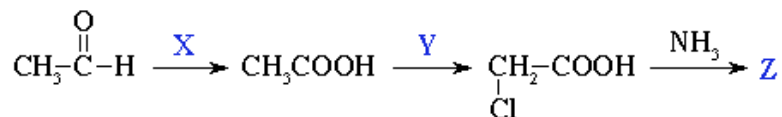
substances X, Y and Z can be:
   a) X - [O]; Y is Cl2; Z-aminoethanoic acid
   b) X is H_2; Y is Cl_2; Z-aminoethanoic acid
   c) X - [O]; Y = HCl; Z-amide of acetic acid
   d) X is H2; Y = HCl; Z-amide of acetic acid

   4. The ester is formed by the reaction of aminoacetic acid. . .
   a) with sodium hydroxide
   b) with a solution of sulfuric acid
   c) with aminoacetic acid
   d) with ethanol

   5. As a result of the intermolecular cyclization reaction of α-amino acids,
   a) lactams
   b) lactones
   c) cyclic anhydrides
   d) lactides
   e) diketopiperazines

   6. During the decarboxylation reactions of amino acids, the following are formed:
   a) hydroxy acids
   b) unsaturated carboxylic acids
   c) oxo acids
   d) biogenic amines

   7. When intermolecular dehydration of α-amino acids is formed:
   a) lactams
   b) lactims
   c) diketopiperazines
   d) lactides

   8. Is it possible to distinguish glycine from proline by:
   a) ninhydrin reaction
   b) Van Slyck reaction?

TOPIC PART TWO: PEPTIDES. PROTEINS

The purpose of the lesson is to develop knowledge about the structure and chemical basis of the structural organization of oligopeptides, polypeptides and protein molecules for further study of the biological functions of various proteins at the molecular level.

The purpose of the activities of students in class
The student should know:
a) The spatial structure of polypeptides and proteins.
b) Characteristic properties and signs of the secondary, tertiary and quaternary structure.
c) Qualitative reactions to proteins.
d) Signs of globular and fibrillar proteins.

The student **should be able to**:
a) Describe the structure of the peptide group.
b) Write the chemistry of determining the amino acid sequence in proteins (the Edman method, the DNP method, the dansyl method).

Questions for testing the baseline level:
1. What substances are called amino acids and why is it that α-amino acids have an important biological significance?
2. Classification of α-amino acids and their nomenclature.
3. Isomerism of amino acids.
4. Physical and chemical properties of amino acids.
5. Acid-base properties of amino acids.
6. Biologically important chemical reactions of α-amino acids.
7. Methods of obtaining amino acids.

Theoretical part

Proteins
Proteins are large biomolecules, or macromolecules, consisting of one or more long chains of amino acid residues. Proteins perform a vast array of functions within organisms, including catalysing metabolic reactions, DNA replication, responding to stimuli, and transporting molecules from one location to another. Proteins differ from one another primarily in their sequence of amino acids, which is dictated by the nucleotide sequence of their genes, and which usually results in protein folding into a specific three-dimensional structure that determines its activity (*Wiki*).

Proteins are compounds found in all living cells, in animals and plants. They play a variety of important roles and are essential to maintain the structure and function of all lifeforms. The word 'protein' is derived from the Greek word protos, meaning "primary" or "first". Proteins are vital for the growth and repair, and their functions are endless. Each and every property that characterizes a living organism is affected by proteins, whether it is a bacteria or a human body.

Proteins perform many functions which are essential for life. The building blocks of proteins are the twenty naturally occurring amino acids. The chemical and physical structure of amino acids and proteins, describe the topology proteins and discuss an important enzyme and penicillin amidase. These amino acids are liberated when proteins are hydrolyzed. Proteins are the polymers of -amino acids.

$$\text{Proteins} \xrightarrow{\text{hydrolysis}} \text{Peptides} \xrightarrow{\text{hydrolysis}} \text{Amino acids}$$

All proteins contain the elements carbon, hydrogen, oxygen, nitrogen and sulfur some of these may also contain phosphorus, iodine, and traces of metals like ion, copper, zinc and manganese.

The name protein is derived from the Greek word proteins meaning of prime importance. As enzymes, they catalyze biochemical reactions, as hormones they regulate metabolic processes and as antibodies they protect the body against toxic substances.

Composition of Proteins

1.   Proteins are made of long chains of amino acids.
2.   Proteins are composed of carbon, hydrogen, oxygen and nitrogen arranged as the strands of amino acids.
3.   The digestive system breaks down protein containing food into individual amino acids.
4.   The body then resembles the amino acids in different orders to make new proteins, which can be used for growth, repairing tissues, hormones and as enzymes.
5.   As proteins are made of amino acids joined together by peptide bonds amino acids can be called the basic molecules of life.

A strand of amino acids that makes up a protein may contain 20 different kinds of amino acids. Amino acids are the building blocks of proteins. Each has an amine group at one end and an acid group at the other and a distinctive side chain. The backbone is the same for all amino acids. The side chain differs from one amino acid to the next while the nitrogen is in the amine group.
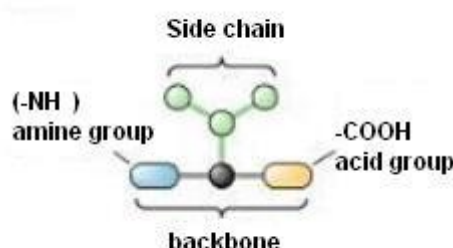
Protein Structure

Increasingly, drug developers are looking to large molecules and particularly proteins as a therapeutic option. Formulation of a protein drug product can be quite a challenge, but without a good understanding of the nature of protein structure and the conformational characteristics of the specific protein being formulated, the results can be ruinous. This technical brief aims to give the reader a quick overview of protein structure. It will also cover briefly how protein structure can be affected during formulation and some of the analytical methods which can be used both to determine the structure and analyze the stability of the protein.

The term *structure* when used in relation to proteins, takes on a much more complex meaning than it does for small molecules. Proteins are macromolecules and have four different levels of structure – primary, secondary, tertiary and quaternary.

Primary Structure

There are 20 different standard L-α-amino acids used by cells for protein construction (*see above*). Amino acids, as their name indicates, contain both a basic amino group and an acidic carboxyl group. This difunctionality allows the individual amino acids to join together in long chains by forming *peptide bonds:* amide bonds between the $-NH_2$ of one amino acid and the -COOH of another. Sequences with fewer than 50 amino acids are generally referred to

as *peptides*, while the terms *protein* or *polypeptide*are used for longer sequences. A protein can be made up of one or more polypeptide molecules. The end of the peptide or protein sequence with a free carboxyl group is called the *carboxy-terminus* or *C-terminus*. The terms *amino-terminus* or *N-terminus* describe the end of the sequence with a free α-amino group.

The amino acids differ in structure by the substituent on their side chains. These side chains confer different chemical, physical and structural properties to the final peptide or protein. The structures of the 20 amino acids commonly found in proteins are shown in Figure 1. Each amino acid has both a one-letter and three-letter abbreviation. These abbreviations are commonly used to simplify the written sequence of a peptide or protein.

Depending on the side-chain substituent, an amino acid can be classified as being acidic, basic or neutral. Although 20 amino acids are required for synthesis of various proteins found in humans, we can synthesize only 10. The remaining 10 are called essential amino acids and must be obtained in the diet.

The amino acid sequence of a protein is encoded in DNA. Proteins are synthesized by a series of steps called transcription (the use of a DNA strand to make a complimentary messenger RNA strand - mRNA) and translation (the mRNA sequence is used as a template to guide the synthesis of the chain of amino acids which make up the protein). Often, post-translational modifications, such as glycosylation or phosphorylation, occur which are necessary for the biological function of the protein. While the amino acid sequence makes up the***primary structure*** of the protein, the chemical/biological properties of the protein are very much dependent on the three-dimensional or tertiary structure.

Secondary Structure

Stretches or strands of proteins or peptides have distinct characteristic local structural conformations or **secondary structure**, dependent on hydrogen bonding. The two main types of secondary structure are the α-helix and the ß-sheet.

The *α-helix* is a right-handed coiled strand. The side-chain substituents of the amino acid groups in an α-helix extend to the outside. Hydrogen bonds form between the oxygen of the C=O of each peptide bond in the strand and the hydrogen of the N-H group of the peptide bond four amino acids below it in the helix. The hydrogen bonds make this structure especially stable. The side-chain substituents of the amino acids fit in beside the N-H groups.

The hydrogen bonding in a *ß-sheet* is between strands (inter-strand) rather than within strands (intra-strand). The sheet conformation consists of pairs of strands lying side-by-side. The carbonyl oxygens in one strand hydrogen bond with the amino hydrogens of the adjacent strand. The two strands can be either parallel or anti-parallel depending on whether the strand directions (N-terminus to C-terminus) are the same or opposite. The anti-parallel ß-sheet is more stable due to the more well-aligned hydrogen bonds.

Tertiary Structure

The overall three-dimensional shape of an entire protein molecule is the **tertiary structure**. The protein molecule will bend and twist in such a way as to achieve maximum stability or lowest energy state. Although the three-dimensional shape of a protein may seem irregular and random, it is fashioned by many stabilizing forces due to bonding interactions between the side-chain groups of the amino acids.

Under physiologic conditions, the hydrophobic side-chains of neutral, non-polar amino acids such as phenylalanine or isoleucine tend to be buried on the interior of the protein molecule thereby shielding them from the aqueous medium. The alkyl groups of alanine, valine, leucine and isoleucine often form hydrophobic interactions between one-another, while aromatic groups such as those of phenylalanine and tryosine often stack together. Acidic or basic amino acid side-chains will generally be exposed on the surface of the protein as they are hydrophilic.

The formation of disulfide bridges by oxidation of the sulfhydryl groups on cysteine is an important aspect of the stabilization of protein tertiary structure, allowing different parts of the protein chain to be held together covalently. Additionally, hydrogen bonds may form between different side-chain groups. As with *disulfide bridges*, these hydrogen bonds can bring together

two parts of a chain that are some distance away in terms of sequence. *Salt bridges*, ionic interactions between positively and negatively charged sites on amino acid side chains, also help to stabilize the tertiary structure of a protein.

LEVELS OF PROTEIN STRUCTURE

Primary Structure

Secondary Structure

β-Sheet

α-Helix

Tertiary Structure

Quaternary Structure

Particle Sciences
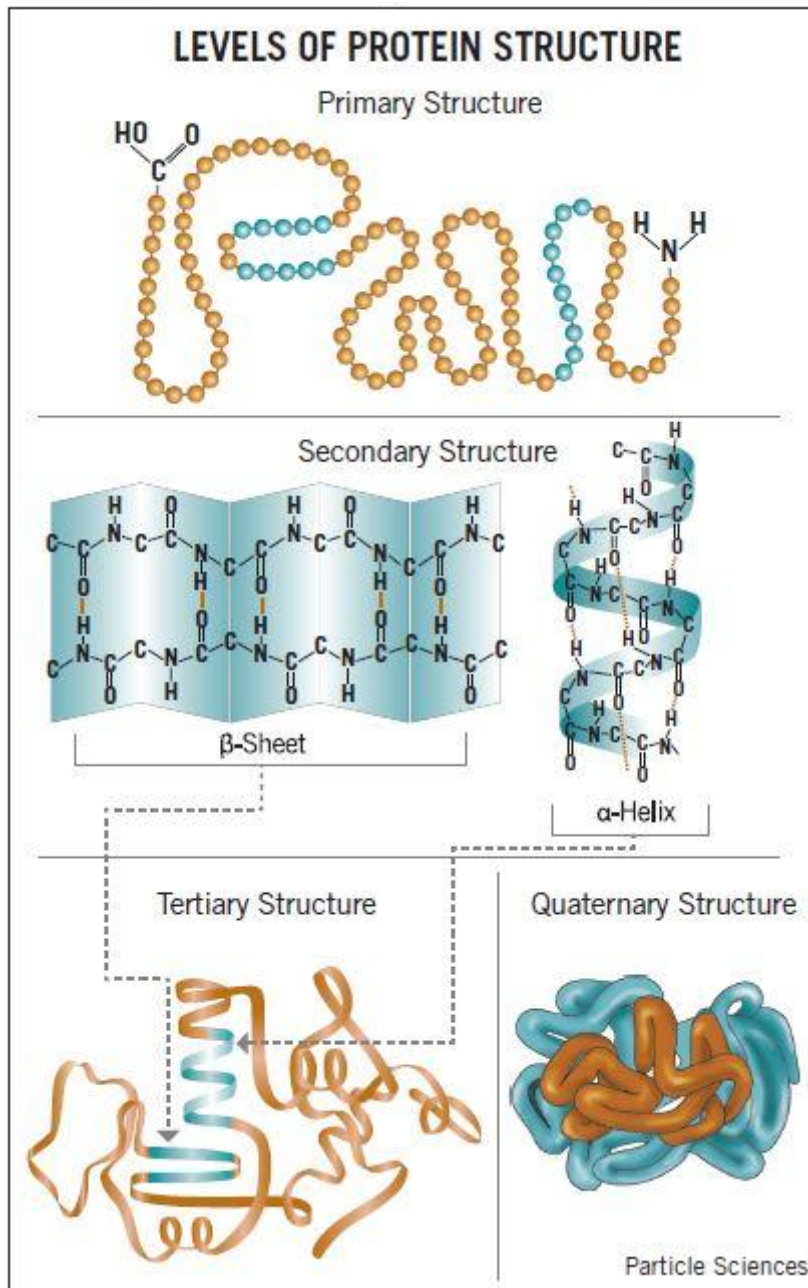
Quaternary Structure

Many proteins are made up of multiple polypeptide chains, often referred to as *protein subunits*. These subunits may be the same (as in a homodimer) or different (as in a heterodimer).

The *quaternary structure* refers to how these protein subunits interact with each other and arrange themselves to form a larger aggregate protein complex. The final shape of the protein complex is once again stabilized by various interactions, including hydrogen-bonding, disulfide-bridges and salt bridges. The four levels of protein structure are shown in Figure 2.

Protein Stability

Due to the nature of the weak interactions controlling the three-dimensional structure, proteins are very sensitive molecules. The term native state is used to describe the protein in its most stable natural conformation in situ. This native state can be disrupted by a number of external stress factors including temperature, pH, removal of water, presence of hydrophobic surfaces, presence of metal ions and high shear. The loss of secondary, tertiary or quaternary structure due to exposure to a stress factor is called denaturation. Denaturation results in unfolding of the protein into a random or misfolded shape.

A denatured protein can have quite a different activity profile than the protein in its native form, usually losing biological function. In addition to becoming denatured, proteins can also form aggregates under certain stress conditions. Aggregates are often produced during the manufacturing process and are typically undesirable, largely due to the possibility of them causing adverse immune responses when administered.

In addition to these physical forms of protein degradation, it is also important to be aware of the possible pathways of protein chemical degradation. These include oxidation, deamidation, peptide-bond hydrolysis, disulfide-bond reshuffling and cross-linking. The methods used in the processing and the formulation of proteins, including any lyophilization step, must be carefully

examined to prevent degradation and to increase the stability of the protein biopharmaceutical both in storage and during drug delivery.

Protein Structure Analysis

The complexities of protein structure make the elucidation of a complete protein structure extremely difficult even with the most advanced analytical equipment. An amino acid analyzer can be used to determine which amino acids are present and the molar ratios of each. The sequence of the protein can then be analyzed by means of peptide mapping and the use of Edman degradation or mass spectroscopy. This process is routine for peptides and small proteins, but becomes more complex for large multimeric proteins.

Peptide mapping generally entails treatment of the protein with different protease enzymes in order to chop up the sequence into smaller peptides at specific cleavage sites. Two commonly used enzymes are trypsin and chymotrypsin. Mass spectroscopy has become an invaluable tool for the analysis of enzyme digested proteins, by means of peptide fingerprinting methods and database searching. Edman degradation involves the cleavage, separation and identification of one amino acid at a time from a short peptide, starting from the N-terminus.

One method used to characterize the secondary structure of a protein is circular dichroism spectroscopy (CD). The different types of secondary structure, α-helix, ß-sheet and random coil, all have characteristic circular dichroism spectra in the far-uv region of the spectrum (190-250 nm). These spectra can be used to approximate the fraction of the entire protein made up of each type of structure.

A more complete, high-resolution analysis of the three-dimensional structure of a protein is carried out using X-ray crystallography or nuclear magnetic resonance (NMR) analysis. To determine the three-dimensional structure of a protein by X-ray diffraction, a large, well-ordered single crystal is required. X-ray diffraction allows measurement of the short distances between atoms and yields a three-dimensional electron density map, which can be used to build a model of the protein structure.

The use of NMR to determine the three-dimensional structure of a protein has some advantages over X-ray diffraction in that it can be carried out in solution and thus the protein is free of the constraints of the crystal lattice. The two-dimensional NMR techniques generally used are NOESY, which measures the distances between atoms through space, and COESY, which measures distances through bonds.

Properties of Proteins

A protein is a biological macro molecule composed of one or more chain of amino acids linked by peptide bonds. In general, we speak of protein when the string contains more than 50 amino acids. For smaller sizes, we speak of peptide and polypeptide, but more often they are simply "small protein".

The Dutch chemist Gerhard Mulder (1802-1880) discovered proteins. The word protein comes from the Greek **"protos"** which means first, essential. This probably refers to the fact that proteins are essential to life and they often constitute the majority share (60%) of the dry weight of cells. Another theory that would make reference protein as the adjective protean, with the Greek God Proteus who could change shape at will. The proteins indeed adopt many forms and provide multiple functions. But, this was not discovered until much later, during the twentieth century.

Solubility in Water
1. The relationship of proteins with water is complex. The secondary structure of proteins depends largely on the interaction of peptide bonds with water through hydrogen bonds.
2. Hydrogen bonds are also formed between protein (alpha and beta structures) and water. The protein-rich static ball are more soluble than the helical structures.

3. At the tertiary structure, water causes the orientation of the chains and hydrophilic radicals to the outside of the molecule, while the hydrophobic chains and radicals tend to react with each other within the molecule (cf. hydrophobic effect).
4. The solubility of proteins in an aqueous solution containing salts depends on two opposing effects on the one hand related to electrostatic interactions ("salting in") and other hydrophobic interactions (salting out).

Denaturation

A protein is denatured when its specific three-dimensional conformation is changed by breaking some bonds without breaking its primary structure. It may be, for example, the disruption of helix areas. The denaturation may be reversible or irreversible. It causes a total or partial loss of biological activity. This is an important property of protein.

There are a number of Denaturing agents as follows.

1. **Physical agents:** Heat, radiation, pH
2. **Chemical agents:** Urea solution which forms new hydrogen bonds in the protein, organic solvents, detergents.

Laboratory work № 12

Reagents and equipment:
1. A tripod with test tubes.
2. Distilled water.
3. Egg white.
4. Aqueous solutions: 10% sodium hydroxide, copper (II) sulfate, 10% lead acetate (II).
5. Concentrated solution of nitric acid.
6. The alcohol lamp.

Experience 1. Biuret reaction to a peptide bond
Place 5-6 drops of the egg white solution in a tube, add an equal volume of 10% sodium hydroxide solution, and add 1 to 2 drops of copper (II) sulfate solution along the wall. The appearance of a violet color is observed.

Conclusion:

Experiment 2. Xantoprotein reaction of proteins
Place 10 drops of egg white solution and 2 drops of concentrated nitric acid into the tube. Carefully heat the contents of the tube, shaking all the time. The solution and the precipitate are colored yellow. After cooling the tube, carefully add 1-3 drops of 10% sodium hydroxide solution until a bright orange color appears.

Conclusion:

Experiment 3. Reaction to the presence of sulfur-containing α-amino acids
Put 10 drops of egg white solution into the tube and double the volume of 10% sodium hydroxide solution. Mix the contents of the tube, heat to boiling (1-2 min.), Add 5 drops of 10%

lead acetate (II) to the resulting alkaline solution and boil again. Note the appearance of a gray-black precipitate.

Conclusion:

Tasks for independent work

Control questions:

1. Primary structure of peptides and proteins. Composition and amino acid sequence. Enzymatic hydrolysis of proteins.

2. Chemical methods for determining the primary structure of peptides and proteins: the dinitrophenylation method, the Edman method, the dansyl method.

3. Structure and synthesis of peptides. Method for protecting the amino group, activation of the carboxyl group
- Dipeptides.
- Tripeptides.
- Peptide antibiotics.
- Peptide hormones.
- Peptide toxins.
- Neuropeptides.

4. Spatial structure of polypeptides and proteins:
- Structure of the peptide group.
- Secondary structure of polypeptides and proteins: α-helix, β-fold structure, collagen spiral.
- Tertiary structure of proteins; electrostatic and hydrophobic interactions in the structure, hydrogen and disulfide bonds; active center ("gap") in the tertiary structure of lysozyme.
Quaternary structure of the protein.
- Denaturation and renaturation of native conformation.

5. Write a diagram of biuret formation. What are the external signs of a positive biuret reaction?

6. Do all proteins give a biuret reaction? The presence of a structural fragment in a molecule is necessary for a positive biuret reaction? Can this reaction be considered positive?

7. What α-amino acids in the protein can be opened with the xantoprotein reaction? On the example of the corresponding amino acid, write its reaction with nitric acid. Is this reaction qualitative for protein?

8. Write a general scheme for the reaction of the protein with lead (II) acetate. What α-amino acids in a protein can be discovered by this qualitative reaction?

Do the exercises:

1. Write the structural formulas of protein amino acids and characterize them according to the biological and chemical classification.

2. Give examples of rare α-amino acids, sometimes found in proteins.

3. Which protein amino acids are derived: a) aromatic acids, b) heterocyclic acids?

4. Write formulas of natural amino acids, amides of which play a major role in the biochemistry of living organisms. Give the formulas of these amides and characterize their biological role.

5. Which protein amino acids in the solution give an acid reaction:
a) monoaminomonocarboxylic
b) mono-aminodicarboxylic
c) diaminomonocarboxylic acids?

6. Make up the formula of the dipeptide, consisting of amino acid residues - alanine and leucine (2-amino-4-methylpentanoic acid).

7. Write a scheme for the reaction of the tripeptide-alanyl-leucylglycine hydrolysis.

8. Write the equations for the reactions of glutathione with: a) ninhydrin; b) copper hydroxide in an alkaline medium.

9. Make up the formula of the dipeptide, consisting of the residues of aminoacetic acid (glycine) and 2-amino-3-hydroxypropanoic acid (serine).

10. Write a scheme for the reaction of the hydrolysis of tripeptide - glycylserylalanine (alanine -2-aminopropanoic acid).

Test tasks:
1. The coiling of a spiral into a tangle-"globule" characterizes:
a) the primary structure of the protein
b) secondary structure of the protein
c) tertiary structure of the protein
d) quaternary structure of the protein

2. When burning proteins, there is a smell:
a) rotten eggs
b) ammonia
c) burnt feathers (horns)
d) burnt rubber

3. The appearance of a yellow color when the protein solution interacts with concentrated nitric acid indicates the presence in the protein of amino acid residues containing:
a) -SH
b) hydroxyl group
c) benzene ring
d) an aldehyde group

4. Proteins that protect against bacteria entering the cell:
a) hemoglobin
b) antibodies
c) Enzymes
d) antitoxins

5. Proteins can be found:
a) xantoprotein reaction d) with potassium permanganate
b) the effect of the indicator e) with the help of a biuret reaction

c) by the appearance of an odor when burning e) by the reaction of a "silver mirror"

6. What statements about proteins are correct?
a) the proteins are hydrolyzed to amines
b) Peptide bonds are present in the macromolecule of the protein
c) during the hydrolysis of proteins amino acids are formed
d) hydrogen bonds are present in the macromolecule of proteins
e) with nitric acid, the proteins give a black color
e) the main function of proteins in the body - energy

7. The spatial configuration of a protein molecule resembling a spiral (secondary structure of the protein) is formed due to numerous:
a) disulfide bonds
b) peptide bonds
c) hydrogen bonds
d) ester bridges

8. The process of irreversible clotting of proteins is called:
a) Denaturation
b) polymerization
c) polycondensation
d) hybridization

9. Structural feature of molecules of amino acids, distinguishing them from each other:
a) the radical
b) amino group
c) carboxyl group
d) nitro group

10. In the primary structure of protein molecules, the amino acid residues are linked together by the following chemical bond:
a) disulphide
b) Peptide
c) hydrogen
d) ionic

11. The synthesis of proteins occurs in the cell organelles, called:
a) chloroplasts
b) ribosomes
c) mitochondria
d) Golgi apparatus

12. The first protein, which managed to decipher the primary structure (in 1954), was:
a) casein
b) insulin
c) gliadin
d) keratin

13. When concentrated nitric acid acts on proteins (xantoprotein reaction), the following appears:
a) yellow color
b) red-violet coloring

c) black precipitate
d) a blue precipitate

14. Renaturation is a process:
a) a violation of the natural structure of the protein
b) restoration of the natural structure of the protein
15. Choose a protein that performs a predominantly structural function
a) collagen
b) catalase
c) actin
d) gamma globulin

Timing of a 3-hour lesson:
1. Organizational moment - 2 minutes.
2. The survey - 40 min.
3. Explanation of the work - 25 min.
4. Performance and execution of work - 30 min.
5. Presentation of the new material - 45 min.
6. Verification of work and assignment to the house - 3 min.

Literature:

The purpose of the lesson is to form the knowledge of the structure and chemical properties of nucleic acids and their monomeric units - nucleotides, the chemical basis for assimilating various levels of structural organization of nucleic acid macromolecules and the action of nucleotide coenzymes.

The purpose of the activities of students in class
The student should know:
a) Structure and chemical properties of nucleic acids.
b) Structure and properties of nucleotides as a basis for assimilation of various levels of structural organization of macromolecules of nucleic acids.
c) Effect of nucleotide coenzymes.

The student **should be able to**:
a) Write tautomeric transformations of nucleic bases.
b) To depict the structure of nucleosides.
c) Write structural formulas for nucleotides.
d) Write the structure of the three-nucleotide segments of the DNA chain.
e) Write schemes of reversible oxidation-reduction reactions involving coenzyme NAD +.

Questions for testing the baseline level:
1. Primary structure of peptides and proteins. Composition and amino acid sequence. Enzymatic hydrolysis of proteins.
2. Chemical methods for determining the primary structure of peptides and proteins: the dinitrophenylation method, the Edman method, the dansyl method.
3. Structure and synthesis of peptides. Method for protecting the amino group, activation of the carboxyl group
   - Dipeptides.
   - Tripeptides.
   - Peptide antibiotics.
   - Peptide hormones.
   - Peptide toxins.
   - Neuropeptides.
4. Spatial structure of polypeptides and proteins:
   - Structure of the peptide group.

5. Spatial structure of polypeptides and proteins:
   - Secondary structure of polypeptides and proteins: α-helix, β-fold structure, collagen spiral.
   The spatial structure of polypeptides and proteins:
   - Tertiary structure of proteins; electrostatic and hydrophobic interactions in the structure, hydrogen and disulfide bonds; active center ("gap") in the tertiary structure of lysozyme.
   The spatial structure of polypeptides and proteins:
   Quaternary structure of the protein.
   Denaturation and renaturation of native conformation.
9. Do all proteins give a biuret reaction? The presence of a structural fragment in a molecule is necessary for a positive biuret reaction? Can this reaction be considered positive?
10. What α-amino acids in the protein can be opened with the xantoprotein reaction? On the example of the corresponding amino acid, write its reaction with nitric acid. Is this reaction qualitative for protein?

<center>**Theoretical part**</center>

Nucleic acid, naturally occurring chemical compound that is capable of being broken down to yield phosphoric acid, sugars, and a mixture of organic bases (purines and pyrimidines). Nucleic acids are the main information-carrying molecules of the cell, and, by directing the process of protein synthesis, they determine the inherited characteristics of every living thing. The two main classes of nucleic acids are *deoxyribonucleic acid* (DNA) and *ribonucleic acid* (RNA).

From the time of discovery of nucleic acids by Fredrick Miescher in 1870, they were long regarded as something of a curiosity until the structures of the monomer units, the nucleotides, was established in 1909 and that of RNA was proposed by Levene and Tipson in 1935. Nucleic acids are basically of two types- DNA and RNA, which are polymers of nucleotide chains. Each nucleotide comprises of three parts, firstly - a sugar moiety which is a pentose (five-membered-ring) joined to a second part-phosphate groups.

Structure and Roles of DNA and RNA in cells

DNA is the genetic material found in living organisms, all the way from single-celled bacteria to multicellular mammals like you and me. Some viruses use RNA, not DNA, as their genetic material, but aren't technically considered to be alive (since they cannot reproduce without help from a host).

DNA in cells

In eukaryotes, such as plants and animals, DNA is found in the **nucleus**, a specialized, membrane-bound vault in the cell, as well as in certain other types of organelles (such as mitochondria and the chloroplasts of plants). In prokaryotes, such as bacteria, the DNA is not enclosed in a membranous envelope, although it's located in a specialized cell region called the **nucleoid**.

In eukaryotes, DNA is typically broken up into a number of very long, linear pieces called **chromosomes**, while in prokaryotes such as bacteria, chromosomes are much smaller and often circular (ring-shaped). A chromosome may contain tens of thousands of **genes**, each providing instructions on how to make a particular product needed by the cell.

From DNA to RNA to proteins

Many genes encode protein products, meaning that they specify the sequence of amino acids used to build a particular protein. Before this information can be used for protein synthesis, however, an RNA copy (transcript) of the gene must first be made. This type of RNA is called a **messenger RNA** (**mRNA**), as it serves as a messenger between DNA and the ribosomes, molecular machines that read mRNA sequences and use them to build proteins. This progression from DNA to RNA to protein is called the "central dogma" of molecular biology.

Importantly, not all genes encode protein products. For instance, some genes specify **ribosomal RNAs** (**rRNAs**), which serve as structural components of ribosomes, or **transfer RNAs** (**tRNAs**), cloverleaf-shaped RNA molecules that bring amino acids to the ribosome for protein synthesis. Still other RNA molecules, such as tiny **microRNAs** (**miRNAs**), act as regulators of other genes, and new types of non-protein-coding RNAs are being discovered all the time.

Nucleotides

DNA and RNA are polymers (in the case of DNA, often very long polymers), and are made up of monomers known as **nucleotides**. When these monomers combine, the resulting chain is called a **polynucleotide** (*poly-* = "many").

Each nucleotide is made up of three parts: a nitrogen-containing ring structure called a nitrogenous base, a five-carbon sugar, and at least one phosphate group. The sugar molecule has a central position in the nucleotide, with the base attached to one of its carbons and the phosphate group (or groups) attached to another. Let's look at each part of a nucleotide in turn.
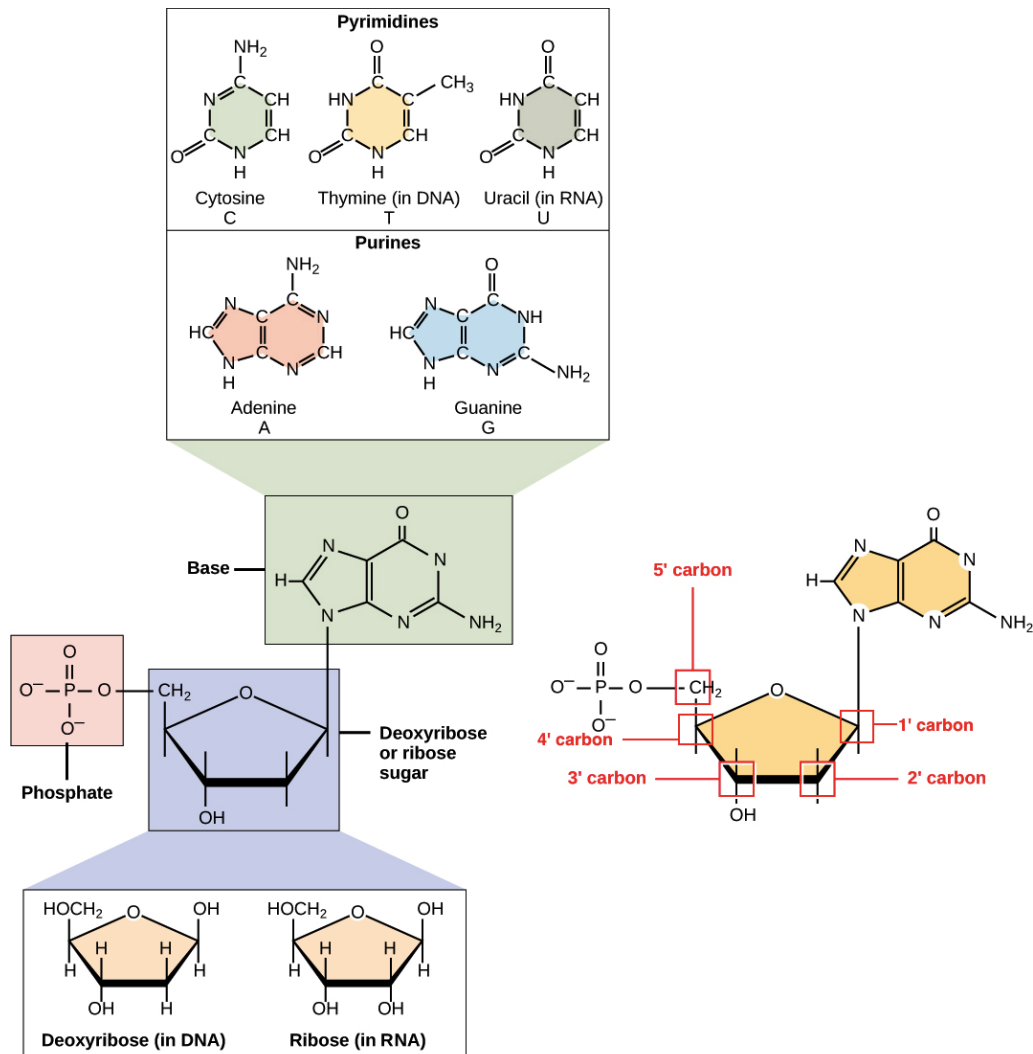
Image of the components of DNA and RNA, including the sugar (deoxyribose or ribose), phosphate group, and nitrogenous base. Bases include the pyrimidine bases (cytosine, thymine in DNA, and uracil in RNA, one ring) and the purine bases (adenine and guanine, two rings). The phosphate group is attached to the 5' carbon. The 2' carbon bears a hydroxyl group in ribose, but no hydroxyl (just hydrogen) in deoxyribose.

Nitrogenous bases

The nitrogenous bases of nucleotides are organic (carbon-based) molecules made up of nitrogen-containing ring structures.

Each nucleotide in DNA contains one of four possible nitrogenous bases: adenine (A), guanine (G) cytosine (C), and thymine (T). Adenine and guanine are **purines**, meaning that their structures contain two fused carbon-nitrogen rings. Cytosine and thymine, in contrast, are **pyrimidines** and have a single carbon-nitrogen ring. RNA nucleotides may also bear adenine, guanine and cytosine bases, but instead of thymine they have another pyrimidine base called uracil (U). As shown in the figure above, each base has a unique structure, with its own set of functional groups attached to the ring structure.

In molecular biology shorthand, the nitrogenous bases are often just referred to by their one-letter symbols, A, T, G, C, and U. DNA contains A, T, G, and C, while RNA contains A, U, G, and C (that is, U is swapped in for T).

Sugars

In addition to having slightly different sets of bases, DNA and RNA nucleotides also have slightly different sugars. The five-carbon sugar in DNA is called **deoxyribose**, while in RNA, the sugar is **ribose**. These two are very similar in structure, with just one difference: the second carbon of ribose bears a hydroxyl group, while the equivalent carbon of deoxyribose has a hydrogen instead. The carbon atoms of a nucleotide's sugar molecule are numbered as 1′, 2′, 3′,

4′, and 5′ (1′ is read as "one prime"), as shown in the figure above. In a nucleotide, the sugar occupies a central position, with the base attached to its 1′ carbon and the phosphate group (or groups) attached to its 5′ carbon.

Phosphate

Nucleotides may have a single phosphate group, or a chain of up to three phosphate groups, attached to the 5' carbon of the sugar. Some chemistry sources use the term "nucleotide" only for the single-phosphate case, but in molecular biology, the broader definition is generally accepted^11start superscript, 1, end superscript

In a cell, a nucleotide about to be added to the end of a polynucleotide chain will bear a series of three phosphate groups. When the nucleotide joins the growing DNA or RNA chain, it loses two phosphate groups. So, in a chain of DNA or RNA, each nucleotide has just one phosphate group.

Polynucleotide chains

A consequence of the structure of nucleotides is that a polynucleotide chain has **directionality** – that is, it has two ends that are different from each other. At the **5' end**, or beginning, of the chain, the 5' phosphate group of the first nucleotide in the chain sticks out. At the other end, called the **3' end**, the 3' hydroxyl of the last nucleotide added to the chain is exposed. DNA sequences are usually written in the 5' to 3' direction, meaning that the nucleotide at the 5' end comes first and the nucleotide at the 3' end comes last.

As new nucleotides are added to a strand of DNA or RNA, the strand grows at its 3' end, with the 5′ phosphate of an incoming nucleotide attaching to the hydroxyl group at the 3' end of the chain. This makes a chain with each sugar joined to its neighbors by a set of bonds called a **phosphodiester linkage**.

Properties of DNA

Deoxyribonucleic acid, or DNA, chains are typically found in a **double helix**, a structure in which two matching (complementary) chains are stuck together, as shown in the diagram at left. The sugars and phosphates lie on the outside of the helix, forming the backbone of the DNA; this portion of the molecule is sometimes called the **sugar-phosphate** backbone. The nitrogenous bases extend into the interior, like the steps of a staircase, in pairs; the bases of a pair are bound to each other by hydrogen bonds.
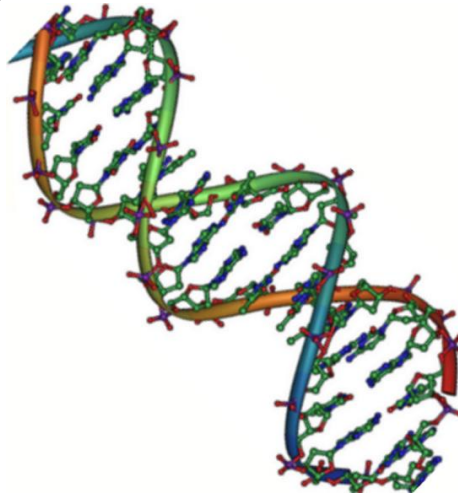
Structural model of a DNA double helix.

The two strands of the helix run in opposite directions, meaning that the 5′ end of one strand is paired up with the 3′ end of its matching strand. (This is referred to as **antiparallel** orientation and is important for the copying of DNA.)

So, can any two bases decide to get together and form a pair in the double helix? The answer is a definite no. Because of the sizes and functional groups of the bases, base pairing is highly specific: A can only pair with T, and G can only pair with C, as shown below. This means that the two strands of a DNA double helix have a very predictable relationship to each other.

For instance, if you know that the sequence of one strand is 5'-AATTGGCC-3', the complementary strand must have the sequence 3'-TTAACCGG-5'. This allows each base to match up with its partner:

5'-AATTGGCC-3' 3'-TTAACCGG-5'

These two strands are complementary, with each base in one sticking to its partner on the other. The A-T pairs are connected by two hydrogen bonds, while the G-C pairs are connected by three hydrogen bonds.

When two DNA sequences match in this way, such that they can stick to each other in an antiparallel fashion and form a helix, they are said to be **complementary**.
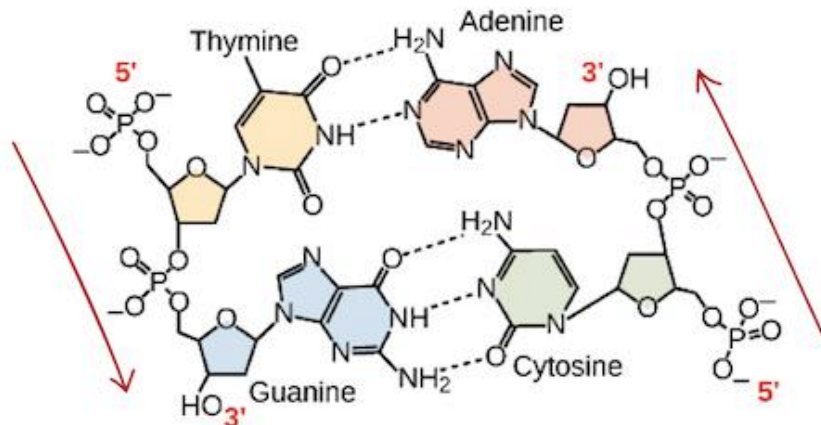
Hydrogen bonding between complementary bases holds DNA strands together in a double helix of antiparallel strands. Thymine forms two hydrogen bonds with adenine, and guanine forms three hydrogen bonds with cytosine.

Properties of RNA

Ribonucleic acid (RNA), unlike DNA, is usually single-stranded. A nucleotide in an RNA chain will contain ribose (the five-carbon sugar), one of the four nitrogenous bases (A, U, G, or C), and a phosphate group. Here, we'll take a look at four major types of RNA: messenger RNA (mRNA), ribosomal RNA (rRNA), transfer RNA (tRNA), and regulatory RNAs.

Tasks for independent work

Control questions:

1. What acids are called nucleic acids?

2. Composition and structure of the nucleotide.

3. How are nucleosides formed?

4. Structure of nucleic acids.

5. Features of nucleotides.

6. Write lactim-lactam tautomeric transformations of the following pyridine and purine nucleic bases: uracil, thymine, guanine, cytosine.

7. Write the complementary interaction of uracil, thymine, guanine, cytosine with the appropriate base.

8. Write the structure of N-glycosides: adenosine, uridine, deoxycytidine

9. Write the structural formulas of nucleotides: 5'-uridilovogo-to-you, thymidyl c-ti, cytidine monophosphate. Specify the N-glycoside and ester bonds.

10. Write the structure of the tri-nucleotide segments of the DNA chain, if it is known that in the complementary chain they correspond to the sequence of ATG and ACG.

Test tasks:

1. Nucleotide that is not part of RNA:

a) CMF

b) UMF

c) AMF

d) GMF

e) TMF

2. A nucleotide that is not part of the DNA:

a) dCMF

b) UMF

c) d AMF

d) dGMP

e) TMF

3. In nucleic acids, the phosphodiester bond is formed between the atoms of the pentose residue:

a) $1^1 - 2^1$
b) $1^1 - 3^1$
c) $1^1 - 5^1$
d) $2^1 - 5^1$
e) $3^1 - 5^1$

4. A compound formed from a nitrogenous base and ribofuranose:
a) ribonucleoside
b) deoxyribonucleoside
c) Ribonucleotide
d) deoxyribonucleotide
e) nucleotide

5. A compound formed from uracil and ribofuranose:
a) adenosine
b) thymidine
c) cytidine
d) uridine
e) guanosine

6. A compound formed from cytosine and ribofuranose:
a) adenosine
b) thymidine

c) cytidine
d) uridine
e) guanosine

7. A compound formed from guanine and ribofuranose:
a) adenosine
b) thymidine
c) cytidine
d) uridine
e) guanosine

8. The DNA molecule is:
a) deoxyribonucleic acid
b) dinucleic acids
c) d-nucleic acids
d) 2-nucleic acids
e) nucleic acids

9. Nucleoside can be obtained from the nucleotide by cleavage:
a) hydrochloric acid
b) phosphoric acid
c) acetic acid
d) oxalic acid
e) Ethyl alcohol

10. RNA monomer.
a) adenosine monophosphate
b) nucleoside diphosphates
c) nucleic bases
d) nicotinic acid
e) thymidine monophosphate

11. Monomer DNA:
a) nucleosides
b) nucleoside diphosphates
c) nucleic bases
d) deoxyguanosine monophosphate
e) Purine

12. It has anhydride bond:
a) nucleoside polyphosphates
b) nucleosides
c) adenosine triphosphoric acid
d) nucleoside cyclophosphates
e) thymidylic acid

Timing of a 3-hour lesson:
1. Organizational moment - 2 minutes.
2. The survey - 40 min.
3. Explanation of the work - 25 min.
4. Performance and execution of work - 30 min.
5. Presentation of the new material - 45 min.

6. Verification of work and assignment to the house - 3 min.

Literature:

The purpose of the lesson: to generate knowledge about the structure and properties of the most important carbohydrates. To study their classification, properties and structure. Form the knowledge of the stereochemical structure, tautomeric forms and the most important properties of monosaccharides as a basis for understanding their metabolic transformations in the body, as well as for studying the structural organization of disaccharides, polysaccharides, the relationship of their structure with biological functions.

The purpose of the activities of students in class
The student should know:
a) Enantiomers. σ-Diastereomers.
b) Relative configuration. D- and L-Stereochemical series.
c) Monosaccharides. Structure and stereoisomerism. Chemical properties of monosaccharides.
d) Polysaccharides. The most important representatives of polysaccharides, their chemical properties.

The student **should be able to**:
a) Use knowledge to explain the biological functions of carbohydrates.
b) Confirm the chemistry of biological processes with reaction equations.
c) Write diagrams of conformational transformations and explain types of isomerism.

Questions for testing the baseline level:
1. Biologically important heterocyclic systems. Five-membered heterocycles with one heteroatom. Pyrrole, furan, thiophene. The concept of the structure of tetrapyrene compounds (porphin, gemm). Linear tetrapyrene compounds.
2. Indole (benzopyrrole). Structure, properties. Biologically active derivatives of indole.
3. Five-membered heterocycles with two or more heteroatoms. Imidazole, properties; medico-biological significance of the derivatives.
4. Pyrazole, oxazole, thiazole. Structure, properties, biological functions of derivatives. Pyrazolone-3 is the structural basis of non-narcotic analgesics (analgin).
5. Six-membered heterocycles with one heteroatom. Pyridine, nicotinic acid and nicotinamide. Isonicotinic (γ-pyridinecarboxylic acid), medico-biological functions of derivatives.
6. Six-membered heterocycles with one heteroatom: pyrimidine, pyrazine. Hydroxy- and amino-derivatives of pyrimidine are components of nucleic acids. Barbituric acid and its derivatives.
7. Bicyclic heterocycles. Purin. Hydroxy- and aminopurines. Uric acid. Lactim-lactam tautomerism. Adenine; medico-biological significance of derivatives, tautomeric forms.
8. The concept of alkaloids. Hygrene, nicotine. Derivatives of tropane are atropine and cocaine. Methylated xanthines - caffeine, theophylline, theobromine.
9. Chemical properties of the amino group. Basicity and nucleophilicity of the amino group.
10. Oxidation of thiols and reduction of disulfides.

Theoretical part

A carbohydrate (/kɑːrboʊˈhaɪdreɪt/) is a biomolecule consisting of carbon (C), hydrogen (H) and oxygen (O) atoms, usually with a hydrogen–oxygen atom ratio of 2:1 (as in water); in other words, with the empirical formula $C_m(H_2O)_n$ (where m may be different from n). This formula holds true for monosaccharides. Some exceptions exist; for example, deoxyribose, a

sugar component of DNA, has the empirical formula $C_5H_{10}O_4$. The carbohydrates are technically hydrates of carbon; structurally it is more accurate to view them as aldoses and ketoses .

The term is most common in biochemistry, where it is a synonym of 'saccharide', a group that includes sugars, starch, and cellulose. The saccharides are divided into four chemical groups: monosaccharides, disaccharides, oligosaccharides, and polysaccharides. Monosaccharides and disaccharides, the smallest (lower molecular weight) carbohydrates, are commonly referred to as sugars. The word saccharide comes from the Greek word σάκχαρον (sákkharon), meaning "sugar". While the scientific nomenclature of carbohydrates is complex, the names of the monosaccharides and disaccharides very often end in the suffix -ose, as in the monosaccharides fructose (fruit sugar) and glucose (starch sugar) and the disaccharides sucrose (cane or beet sugar) and lactose (milk sugar).

Carbohydrates perform numerous roles in living organisms. Polysaccharides serve for the storage of energy (e.g. starch and glycogen) and as structural components (e.g. cellulose in plants and chitin in arthropods). The 5-carbon monosaccharide ribose is an important component of coenzymes (e.g. ATP, FAD and NAD) and the backbone of the genetic molecule known as RNA. The related deoxyribose is a component of DNA. Saccharides and their derivatives include many other important biomolecules that play key roles in the immune system, fertilization, preventing pathogenesis, blood clotting, and development.

Starch and sugars are the most important carbohydrates in human diet. They are found in a wide variety of natural and processed foods. Starch is a polysaccharide. It is abundant in cereals (wheat, maize, rice), potatoes, and processed food based on cereal flour, such as bread, pizza or pasta. Sugars appear in human diet mainly as table sugar (sucrose, extracted from sugarcane or sugar beets)), lactose (abundant in milk), glucose and fructose, both of which occur naturally in honey, many fruits, and some vegetables. Table sugar, milk, or honey are often added to drinks and many prepared foods such as jam, biscuits and cakes.

Cellulose, a polysaccharide found in the cell walls of all plants, is one of the main components of insoluble dietary fiber. Although it is not digestible, insoluble dietary fiber helps to maintain a healthy digestive system by easing defecation. Other polysaccharides contained in dietary fiber include resistant starch and inulin, which feed some bacteria in the microbiota of the large intestine, and are metabolized by these bacteria to yield short-chain fatty acids (*Wiki*).

Carbohydrates. Classification, isomerism, properties

Carbohydrates can be classified according to size (i.e., the number of sugar units per molecule). The term "saccharide" (derived from Latin for sugar) is the chemical name for a sugar unit. A monosaccharide is composed of one simple sugar unit. A disaccharide is composed of two simple sugar units. Oligosaccharides contain from 2 up to 10 sugar units. A polysaccharide is composed of over 10 sugar units.
Mild acid hydrolysis will convert both disaccharides and polysaccharides to monosaccharides.
A monosaccharide (simple sugar) can not be converted to smaller sugar units by hydrolysis in dilute acid.
Monosaccharides are the simplest carbohydrates (simple sugars) which are not cleaved by hydrolysis to smaller carbohydrates. They are characterized by the general formula $(CH_2O)_n$, where n is any integer from 3 - 7 (3 to 7 carbons in length).
Monosaccharides are name based on either functional group or number of carbon atoms. A monosaccharide with a ketone group is referred to as a ketose. A monosaccharide
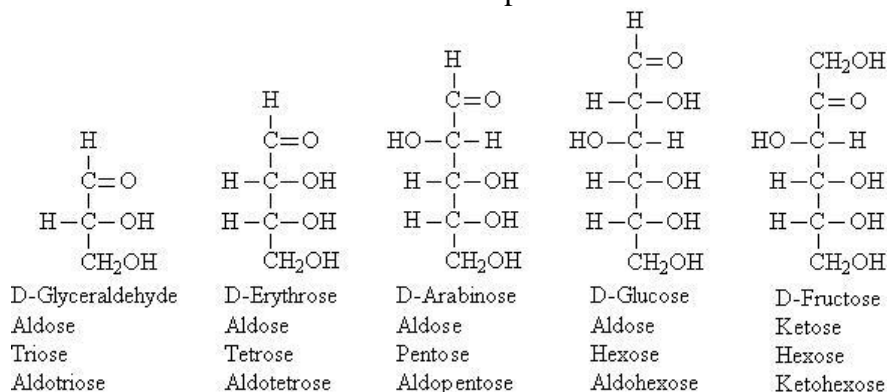
with an aldehyde group is referred to as an aldose. A 3 carbon sugar is a triose, a 4 carbon sugar is a tetrose, and so on. Combining these designates such sugars as an aldotetrose or a ketopentose. For example, an aldotetrose is a four-carbon sugar that contains an aldehyde functional group.

The following table indicates the designation of a monosaccharide based on the number of carbon atoms in the molecule and functional group.

# of carbon atoms	Aldose	Ketose
3	aldotriose	ketotriose
4	aldotetrose	ketotetrose
5	aldopentose	ketopentose
6	aldohexose	ketohexose

In addition to these names each of the simple sugars has a common name. Glyceraldehyde is an aldotriose. Glucose is an aldohexose. Fructose is a ketohexose. Galactose is an aldohexose. Ribose is an aldopentose

D-Glyceraldehyde	D-Erythrose	D-Arabinose	D-Glucose	D-Fructose
Aldose	Aldose	Aldose	Aldose	Ketose
Triose	Tetrose	Pentose	Hexose	Hexose
Aldotriose	Aldotetrose	Aldopentose	Aldohexose	Ketohexose

Stereoisomerism

Isomers are compounds with identical molecular formulas. Isomers can be categorized into the two different groups of constitutional isomers or stereoisomers.

Constitutional isomers have the same molecular formula but a different molecular framework (different bonding constitution). Because constitutional isomers have different bonding constitutions, they are different molecules. This means that constitutional isomers have different physical and chemical properties. Ethanol CH_3CH_2OH and dimethyl ether CH_3OCH_3 are constitutional isomers. Both have the same molecular formula (C_2H_6O) but differ in how the atoms are connected.

Stereoisomers are molecules containing the same atoms bonded identically but the bonded atoms are oriented differently in space. That is to say, they have identical bonding constitutions but differ in how the atoms are oriented in the space around the atoms to which they are bonded.

Stereoisomers can be further separated into the two categories of diastereomers and enantiomers. One type of diastereomers (or geometric stereoisomers) differ by "cis" and "trans" orientations.

Enantiomers are a class of stereoisomers related like an object and its mirror image. Enantiomers differ in their "handedness" as the left hand and right hand are related. Enantiomers are a pair of mirror image molecules that can not be superimposed on each other. Superimposed suggests that two mirror image molecules can be mentally merged into one object as they are brought together.

There are two prominent "handed" biologically important molecules. The D- sugars and L-amino acids. The designations of D- and L- refer to how the pair of enantiomers differ in their bonding configurations. In biochemistry, D is a symbol used as a prefix to indicate the spatial configuration of certain organic compounds with asymmetric carbon atoms. It is used if an organic compound has a configuration about an asymmetric carbon atom (chiral center) analogous to that of D-glyceraldehyde (the arbitrarily chosen standard), in which the hydroxy (OH) functional group is on the right side of the asymmetric carbon atom.

The term "chirality" refers to the "handedness" of a molecule. Chiral molecules have a chiral center and these pair of molecules can not be superimposed. A chiral center is an atom with four different substituents. A carbon atom that has four different groups bonded to it is called asymmetric carbon or a chiral carbon. On the other hand, (humor!) achiral molecules (molecules "without handedness") can be superimposed.

Enantiomers are identical in most physical and chemical properties such as: melting point, boiling point, density, and chemical reactions typical for the functional groups present in the molecule.

However, there are two physical properties which permit discernment of chirality: 1. Chiral molecules differ in their interaction with plane polarized light. (Chiral molecules are sometimes called optical isomers.) A polarimeter is an instrument that allows plane polarized light to pass through aqueous solution of the molecule. The (+) isomer rotates plane polarized light clockwise. The (-) isomer rotates plane polarized light counterclockwise. Achiral molecules do not rotate polarized light in either direction. Racemic mixtures contain equal mix of (+) and (-) isomers. Racemic mixtures show NO rotation of polarized light.

2. Chiral also molecules differ in their interaction with other chiral compounds. Chiral molecules specifically recognize other chiral molecules. For example, L-amino acid protein enzyme (chiral molecule)

How many stereoisomers can a molecule have? The number of possible stereoisomers depends upon the number of chiral centers in the molecule. Van't Hoffs rule states: number of stereoisomers = 2^n , where n = number of chiral centers. For example, a molecule with 2 chiral centers can have 4 stereoisomers.

Fischer projections are a standard method for depicting the three-dimensional arrangement of atoms on a page.
1. Tetrahedral carbon atoms are represented by two crossed lines.
2. The horizontal lines represent bonds coming out of the page.
3. The vertical lines represent bonds going into the page.
4. Carbonyl carbon is place at or near the top in Fischer projections.
5. Fischer projections can be rotated 180° without changing their meaning, but not by 90° or 270°.
6. Carbohydrates with more than one stereogenic center are shown by stacking the centers on top of one another, with the carbonyl carbon again placed at or near the top. D-sugars have the stereogenic carbon farthest from the carbonyl with the hydroxyl group written on the right of the molecule.

H
|
C=O
|
H—C—OH
|
CH₂OH

(structures omitted — Fischer projections)

D-Glyceraldehyde   D-Erythrose   D-Arabinose   D-Glucose   D-Fructose

D-Glyceraldehyde   D-Erythrose   D-Arabinose   D-Glucose   D-Fructose
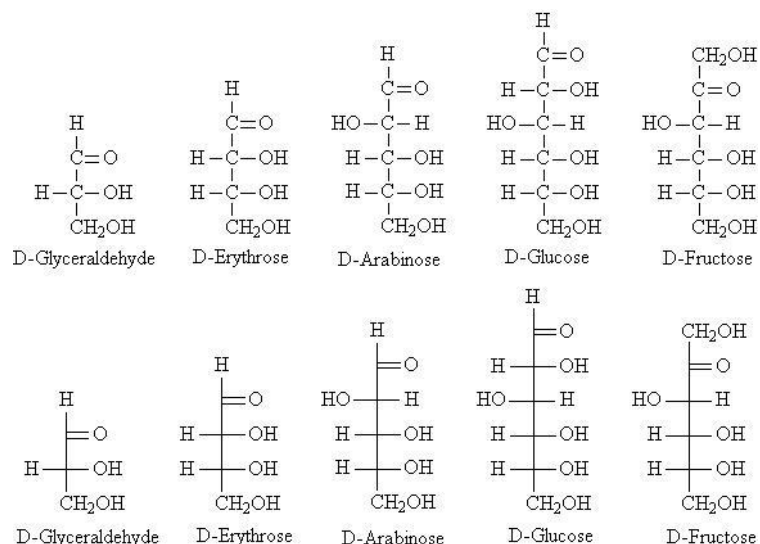
Important Monosaccharides

D-Glyceraldehyde an aldotriose is the simplest carbohydrate. It has one stereogenic center. It is a sweet colorless crystalline solid, $C_3H_6O_3$, that is an intermediate compound in carbohydrate metabolism. D-glyceraldehyde is the arbitrarily chosen standard for the assignment of the D configuration. In a D sugar, the hydroxy functional group is on the right side of the asymmetric carbon atom. D-glyceraldehyde (D for dextrorotatory) rotates light to the right.

H
|
C=O
|
H—C—OH
|
CH₂OH

D-Glyceraldehyde
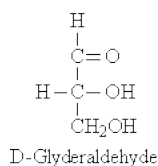
D-Glucose is an aldohexose with four stereogenic centers stacked on top of one another. It is also referred to as dextrose, grape sugar, or blood sugar. It has the empirical formula $C_6H_{12}O_6$. This carbohydrate occurs in the sap of most plants and in the juice of grapes and other fruits. Glucose can be obtained by hydrolysis of a variety of carbohydrates, e.g., milk and cane sugars, maltose, cellulose, or glycogen, but it is usually manufactured by hydrolysis of cornstarch with steam and dilute acid; the corn syrup thus obtained contains also some dextrins and maltose. Glucose tastes only about three-fourths as sweet as table sugar (sucrose). The presence of glucose can be detected by use of Fehling's solution; various modifications of this test are used to detect glucose in urine, which may be a symptom of diabetes.

H
|
C=O
|
H—C—OH
|
CH₂OH

D-Glyceraldehyde
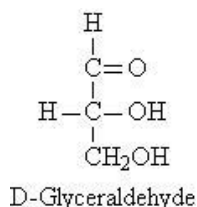
In actuality the open-chain form of glucose is present in very small concentrations in aqueous solutions or in living cells. It exists predominantly in either of the two cyclic forms of α-D-glucose or β-D-glucose. The hydroxyl group at C-5 reacts with the carbonyl group at C-1 to produce either of the two cyclic forms via the formation of a cyclic intramolecular hemiacetal.

Recall that hemiacetals are formed when the oxygen of a hydroxy group bonds with the carbonyl carbon of either an aldehyde or ketone.

These cyclic forms are enantiomeric pairs due to the fact that a new chiral carbon is created at C-1 in the cyclization process.
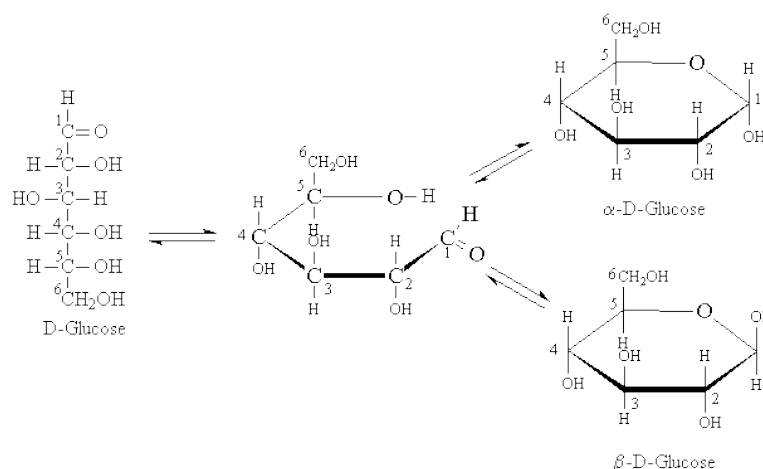
Cyclic hemiacetals are formed if both the hydroxyl and the carbonyl group are in the same molecule by an intramolecular nucleophilic addition. Five and six-membered cyclic hemiacetals are particularly stable and many carbohydrates therefore exist in equilibrium between open-chain and cyclic forms.

Pyranose is the six-membered cyclic hemiacetal formed from aldohexoses. (The name comes *from* the six-membered cyclic ether pyran.) Furanose is the five-membered cyclic hemiacetal formed by the ketohexose fructose. (The name comes comes from the five-membered cyclic ether furan.)

Pyranose and *furanose* rings can be represented by Haworth projections. Haworth projections are planar representations of the furanose and pyranose forms of carbohydrates. These type projections allow the cis-trans relationships among hydroxyl groups to be seen. In which the hemiacetal ring is drawn as if it were flat and is viewed edge-on with the oxygen atom at the upper right.

The relationship between a Fischer projection and a Haworth projection is that the group on the right in a Fischer projection is down in the Haworth projection. The group on the left in a Fischer projection is up in a Haworth projection. For D-sugars, the terminal -CH$_2$OH group is always up in Haworth projections, whereas for L-sugars the terminal -CH$_2$OH group is down.

Glucose exists in aqueous solution primarily as the six-membered pyranose form resulting from intramolecular nucleophilic addition of the -OH group at C5 to the C1 carbonyl group.

D-Fructose (levulose or fruit sugar) is the sweetest of all sugars. It is found in honey, corn syrup, and in the fruit and other parts of plants. It is much sweeter than sucrose (cane sugar). It is a ketohexose. Glucose and fructose are formed in equal amounts when sucrose is hydrolyzed by the enzyme invertase or by heating with dilute acid; the resulting equimolar mixture of fructose and glucose, called invert sugar, is the major component of honey. Fructose is a reducing sugar.

Fructose exists to the extent of about 80% in the pyranose form and about 20% as the five-membered furanose form resulting from addition of the -OH group at C5 to the C2 carbonyl group.

α-D-Fructose

β-D-Fructose

D-Fructose

D-Fructose
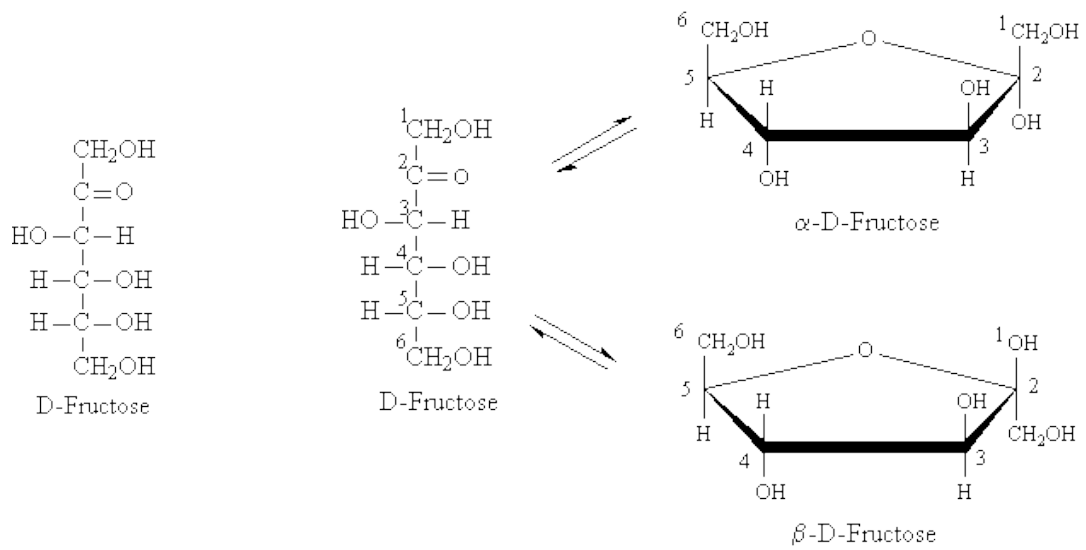
D-Galactose is found in the biological system as a component of the disaccharide lactose, or milk sugar.

α-D-Galactose

β-D-Galactose

D-Galactose
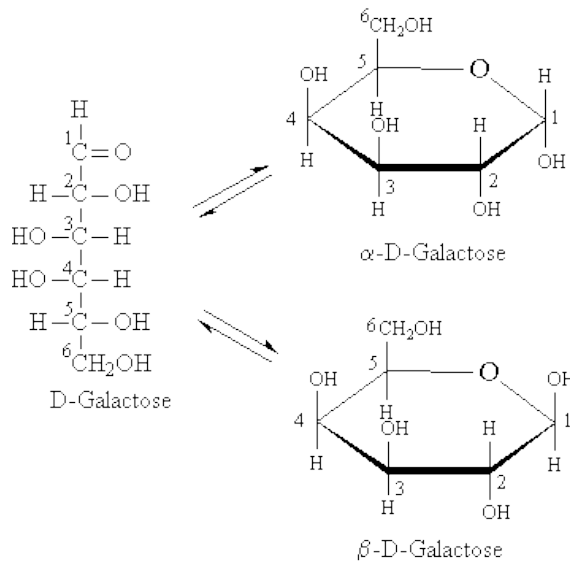
Ribose is a pentose sugar occurring as a component of riboflavin, nucleotides, and nucleic acids.

α-D-Ribose
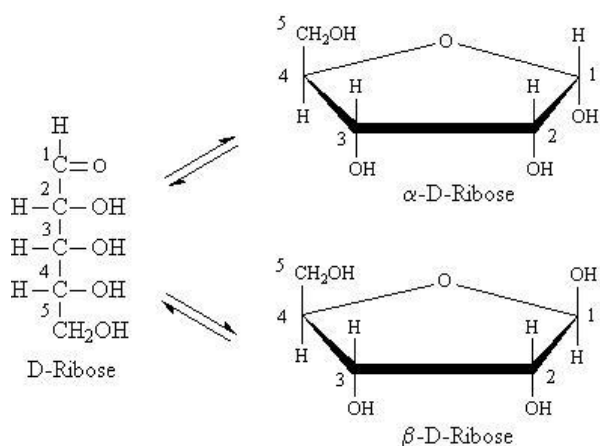
D-Ribose

β-D-Ribose

DNA, the molecule that carries the genetic information of the cell, contains 2-deoxyribose. The hydroxy group has been replaced by a hydrogen at carbon number 2, hence the designation of "2-deoxy."

β-D-2-Deoxyribose
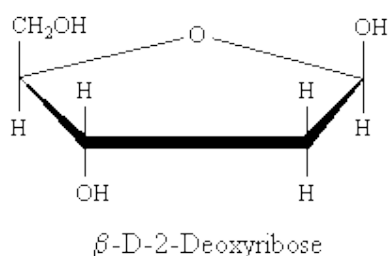
Reducing sugars

Early biochemists devised analytical methods for the detection and quantification of sugars. Some of these tests (e.g., Benedict's Test or Fehling's reagent) were based on the aldehyde or ketone groups in the sugar structures. Sometimes the test gave a color change as a metal ion was reduced to the metal itself or to an ion of lower oxidation state. In other words, the reagent oxidized the sugar while the sugar reduced the oxidation state of the ions.

A **reducing sugar** is any sugar which reacts in basic Cu^{2+} solution to yield Cu_2O precipitate (Benedict's Test). That is, they are sugars that contain aldehyde groups that can be oxidized to carboxylic acids. All monosaccharides are reducing sugars. All the common disaccharides, except sucrose, are reducing sugars. Lactose, maltose, cellobiose are reducing sugars. Sucrose is not a reducing sugar. Polysaccharides are not reducing sugars. A sugar must exist as the linear form in solution to be a reducing sugar.

Disaccharides

Oligosaccharides are formed by joining two to ten monosaccharides.

Aldehydes react with alcohols to form hemiacetals. The hemiacetal can react further to yield an acetal.
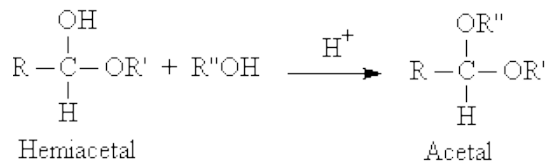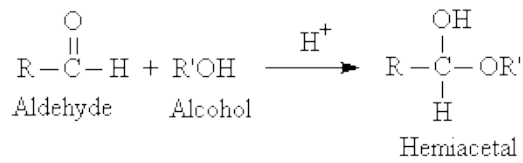
Sugars undergo the same type of reaction to yield a glycoside.

Disaccharides are the most common oligosaccharide. These sugars are produced when two monosaccharides are linked by an "oxygen bridge" called an O-glycosidic bond.

Maltose is formed from two α-D-glucose molecules. It is a disaccharide linked by an α (1→4) glyclosidic bond. The # 1 carbon of one molecule is bonded to the #4 carbon of the other molecule. Maltose is a reducing sugar.
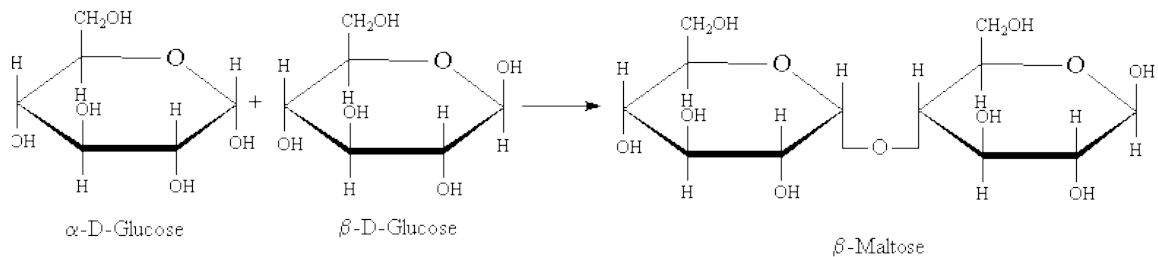
Lactose is formed from one galactose and one glucose molecule. It is a disaccharide linked by an β (1→4) glycosidic bond.
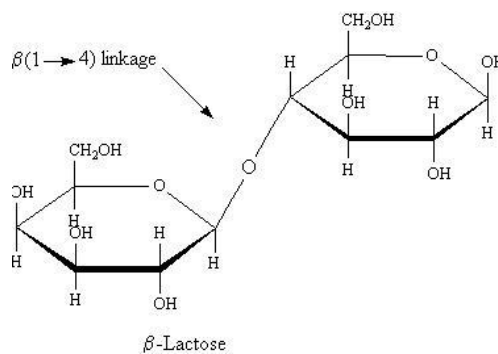
Sucrose is formed from one glucose and one fructose molecule. It is a disaccharide linked by an α,β (1→ 2) glycosidic bond.

Sucrose
β-D-Fructofuranosyl-α-D-glucopyranoside
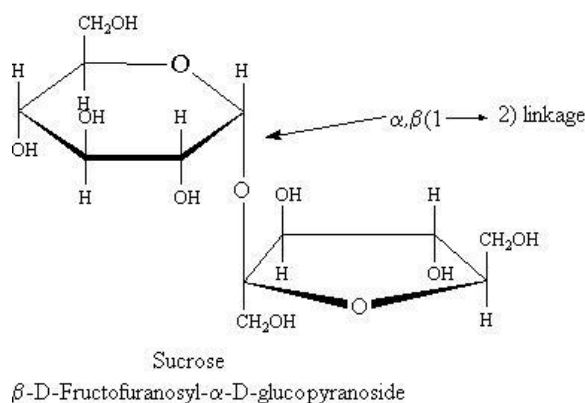
Polysaccharides are extended polymers of monosaccharide units joined by O-glycosidic linkages.

Some roles of polysaccharides:

1. Energy storage.
2. Insoluble polysaccharides can serve as structural and protective elements in cell walls of bacteria and plants and in connective tissue and cell coats of animals.
3. Polysaccharides can lubricate skeletal joints and provide adhesion between cells.
4. Complex sugar chains attached to lipids and proteins can act as signals that determine the intracellular location or the metabolic fate of these glycoconjugates.

Starch is a heterogeneous material composed other the glucose polymer amylose and amylopectin. Upper MW limit about 500,000. 20% of plant starch. Up to 80% in plants such as corn. Helical coil secondary structure. Less soluble since hydrogen bonds are intramolecular.

Amylose

The inner portion of a starch granule, consisting of relatively soluble polysaccharides having an unbranched, linear, or spiral structure.

Amylopectin

The outer portion of a starch granule consisting of insoluble, highly branched polysaccharides of high molecular weight. Upper MW limit about 1 million. 80% of plant starch. Branched, extended structure better for storage/retrieval.

Glycogen is a polysaccharide that is the main form of carbohydrate storage in animals and occurs primarily in the liver and muscle tissue. It is readily converted to glucose as needed by the body to satisfy its energy needs. Also called animal starch. Branched, extended structure better for storage/retrieval.

Cellulose is the most abundant polysaccharide, indeed the most abundant organic molecule in the world. Plant structural sugar. Straight fiber-like secondary structure. Each residue is turned 180 degrees relative to the preceding residue.

Laboratory work № 13

Reagents and equipment:
1. Distilled water.
2. Concentrated solution of hydrochloric acid.

3. Aqueous solutions: 0.5% D-glucose, 0.5% fructose, 1% sucrose, 1% lactose, 10% sodium hydroxide, 2% copper sulfate (II), 5% silver nitrate, 10% ammonia, 0 , 5% starch paste and heavily diluted iodine, 10% sulfuric acid, dilute I2 solution in KI, hydrolyzate solution.

4. Resorcinol is dry.

5. A tripod with test tubes, test tubes with a gas outlet tube.

6. The alcohol lamp.

Experiment 1. Proof of the presence of hydroxyl groups in D-glucose

Place 1 drop of 0.5% D-glucose solution and 6 drops of 10% sodium hydroxide NaOH into the tube. To the resulting mixture add 1 drop of 2% solution of copper (II) sulfate CuSO4. The resulting precipitate of copper (II) hydroxide Cu (OH) 2 dissolves rapidly and a clear blue solution is obtained. Keep the resulting solution for the next experiment.

Conclusion:

Experiment 2. Reduction of copper (II) hydroxide by glucose in alkaline medium (Trommer test)

To the blue solution obtained in the previous experiment, add a few drops of water to the height of the liquid layer in a test tube of 18-20 mm. Heat it over the burner flame, holding the tube obliquely so that only the upper part of the solution is heated, and the lower one remains for monitoring (without heating). Heat only until the boiling point, but do not boil. When heated, the color of the top of the solution changes from blue to yellow-red. This reaction is called a Trommer probe and is used to open glucose in the urine.

Conclusion:

Experiment 3. Recovery of ammonia solution of silver hydroxide by glucose

Put 1 drop of 5% silver nitrate AgNO3 into the tube, add drops of 10% sodium hydroxide NaOH and 3-4 drops of 10% aqueous ammonia solution until the precipitate formed silver hydroxide. The resulting transparent ammoniacal silver hydroxide solution is a glucose oxidizing reagent (Tollens reagent).

Add to the resulting reagent 1 drop of 0.5% glucose solution and lightly heat the tube above the flame of the burner until the solution starts to ripen. Further, the reaction proceeds without heating and metallic silver falls out either as a black precipitate or precipitates on the test tube walls in the form of a brilliant mirror coating (hence the name "silver mirror" reaction).

Conclusion:

Experiment 4. Selivanov reaction to fructose

Put a grain of dry resorcinol into the tube and 2 drops of concentrated hydrochloric acid (on a common table). Add 2 drops of a 0.5% solution of fructose and heat to the beginning of the boil. Gradually the liquid acquires a red color.

The reaction is due to the formation of a non-stable compound - hydroxymethylfurfural. Under the action of concentrated hydrochloric acid, hydroxymethylfurfurol condenses with resorcinol, giving a colored compound.

Conclusion:

Experiment 5. Absence of a reducing ability in sucrose

Place 1 drop of 1% sucrose solution and 6 drops of 10% NaOH solution into a test tube. Add 5-6 drops of water for dilution (the height of the liquid layer is 18-20 mm). Add 1 drop of 2% CuSO4. A clear blue solution of the complex copper (II) salt with sucrose is formed. Carefully heat the tube above the burner flame so that only the upper part of the solution is heated, and the lower one remains without heating (for monitoring). Heat only to boil, but do not boil. The color of the solution does not change. Recall that with D-glucose under similar conditions (see experiment 1), the color of the upper part of the solution changed to yellow-red.

Conclusion:

Experience 6. The restoring ability of lactose

Place 1 drop of 1% lactose solution and 4 drops of 10% NaOH solution into a test tube. Add 1 drop of 2% $CuSO_4$. The resulting blue residue of Cu $(OH)_2$ dissolves when the tube is shaken to form a blue solution of the complex copper (II) salt with lactose. Add a few drops of water for dilution to a liquid layer height of 18-20 mm. Carefully heat the tube above the burner

flame so that only the upper part of the solution is heated, and the lower one remains without heating (for monitoring). Heat only to boil, but do not boil. When heated, the color of the top of the solution changes to yellow-red. Recall that a similar result is observed with D-glucose (see experiment 1) (Trommer's test is positive), whereas in the experiment with sucrose (see experiment 5) under the same conditions the color of the upper part of the solution does not change.

Conclusion:

Experience 7. Qualitative reaction to starch

Place 5 drops of 0.5% starch paste solution and 1 drop of strongly diluted iodine into the tube. The solution is dyed blue. Heat the solution, it discolores; when cooling, the color is restored.

Conclusion:

Experiment 8. Acidic hydrolysis of starch

In a test tube, place 1 drop of 0.5% paste. Add 2 drops of 10% H_2SO_4 solution and place the tube in a boiling water bath. The muddy paste solution becomes transparent after 20 minutes. Using a pipette, apply 1 drop of hydrolyzate to the slide and add 1 drop of diluted I_2 solution to

KI (to make this solution 1 drop of I2 solution in KI, place in a separate tube and top up with water to make a light yellow solution). If the sample does not give a positive iodine starch reaction (blue staining), add 8 drops of 10% NaOH to the tube to create an alkaline medium. Then add 1 drop of 2% $CuSO_4$. Will the Trommer test be positive?

Conclusion:

Tasks for independent work

Control questions:
1. Monosaccharides. Structure and stereoisomerism.
2. The phenomenon of mutarotation. Projection formulas of Fisher, Hevors formula (on the example of glucose and fructose).
3. Chemical properties of monosaccharides: a) complexation reactions; b) electrophilic-nucleophilic properties (alkylation, acylation reactions); c) oxidation-reduction properties - epimerization reactions, oxidation and reduction reactions of monosaccharides.
4. Disaccharides. Their structure, α- and β-glycosidic bonds.
5. Restoring disaccharides. The way in which they form a glycosidic bond. Lactose and maltose, their biological significance.
6. Non-reducing disaccharides, the principle of the formation of a glycosidic bond in them. Sucrose.
7. Biological fragments of natural glycosides on the example of geniciobiosis. Aminoglycosides (or carbohydrate antibiotics) - on the example of streptomycin.
8. Polysaccharides, the structure of starch, glycogen, dextrans, cellulose.
9. Heteropolysaccharides and mixed biopolymers: chondroitin sulfates, hyaluronic acid, proteoglycans, peptidoglycans, glycoproteins.
10. Indicate the types of bonds between the monosaccharide units of this polysaccharide.

Do the exercises:
1. Write a scheme for the reactions of hydrolysis of sucrose, maltose, lactose. Give the full name to these disaccharides.
2. Explain why maltose and lactose have restorative properties.
3. What polysaccharides are called homopolysaccharides? From which monosaccharide units are built macromolecules of amylose, amylopectin, cellulose, glycogen, dextran? Specify the types of connection between D-glucopyranose residues in them.
4. How is the conformational structure of the chain connected with the spatial structure? Show me the example of amylose and cellulose.
5. Write the reaction of hydrolysis of maltose, which is a structural unit of starch. In what environment does this reaction occur? Which monosaccharide is obtained as a result of complete hydrolysis of starch?
6. What changes in the secondary structure of polysaccharide chains of starch indicate the absence of blue staining with iodine?

7. Explain why a positive Trommer test indicates complete hydrolysis of the starch?

8. Write the structure of sucrose (with the help of Heus's formulas). What is the configuration of the anomeric carbon atoms in the residues of D-fructose and D-glucose that make up the sucrose molecule?

9. Why is sucrose incapable of cycloxo-tautomerism?

10. Explain the reason for the lack of reducing properties in sucrose?

Test tasks:

1. Glucose in the industry receive ...
a) synthesis from formaldehyde
b) cracking of oil products
c) hydrolysis of starch
d) synthesis from carbon dioxide and water

2. Among the listed disaccharides, non-reducing ones are:
a) sucrose
b) maltose
c) cellobiose
d) lactose

3. Macromolecules of starch and cellulose are formed from individual glucose molecules by the reaction:
a) esterification
b) polycondensation
c) polymerization
d) oxidation

4. Cellulose forms esters, interacting with ... (2 correct answers)
a) nitric acid
b) hydrochloric acid
c) acetic anhydride
d) oxygen

3. What substances are natural polymers (2 correct answers)?
a) starch
b) lactose
c) cellulose
d) fructose

4. Starch from cellulose can be distinguished ...
a) by reaction with copper (II) hydroxide
b) reaction with iodine
c) reaction by etirification
d) hydrolysis followed by the reaction of the "silver mirror"

7. Monosaccharides include:
a) maltose
b) fructose
c) lactose
d) heparin
e) glycogen.

8. Glucose is:
a) ketohexose
b) ketopentose
c) aldohexose
d) aldopentose
e) disaccharide.

9. The composition of sucrose includes residues:
a) two glucose molecules
     b) two molecules of fructose
c) glucose and fructose
d) galactose and glucose.

10. A physiologically important homopolysaccharide is:
a) hyaluronic acid
b) chondroitin sulfate
c) glycogen
d) cellulose.

Timing of a 3-hour lesson:
1. Organizational moment - 2 minutes.
2. The survey - 40 min.
3. Explanation of the work - 25 min.
4. Performance and execution of work - 30 min.
5. Presentation of the new material - 45 min.
6. Verification of work and assignment to the house - 3 min.

Literature:

TOPIC: LIPIDES

The purpose of the lesson is to form a knowledge of the structure and chemical properties of lipids, their classification and chemical properties.

The purpose of the activities of students in class
The student should know:
a) What are the lipids and the features of their structure.
b) Classification of lipids.
c) Structural components of lipids.
d) Simple and complex lipids.
e) General reactions to terpenes and steroids.

The student **should be able to**:
a) Write the equation of dehydration of terpinhydrate, leading to a mixture of terpineols, α and β.
b) Prove the unlimited terpenes, their easy oxidizability. Write down the equations of the reactions of these properties.
c) Write the equation for the bromocamphor reduction reaction to borneol.
d) From the series of proposed substances, select the smell of camphor and bromcampor by smell and determine where the substance is.
e) From a series of proposed substances, choose turpentine and open it.
e) Detect alpha-ketol and keto groups in corticosteroids.

Questions for testing the baseline level:
1. What acids are called nucleic acids?
2. Composition and structure of the nucleotide.
3. How are nucleosides formed?
4. Structure of nucleic acids.
5. Features of nucleotides.
6. Write lactim-lactam tautomeric transformations of the following pyridine and purine nucleic bases: uracil, thymine, guanine, cytosine.
7. Write the complementary interaction of uracil, thymine, guanine, cytosine with the appropriate base.
8. Write the structure of N-glycosides: adenosine, uridine, deoxycytidine
9. Write the structural formulas of nucleotides: 5'-uridilovogo-to-you, thymidyl c-ti, cytidine monophosphate. Specify the N-glycoside and ester bonds.
10. Write the structure of the tri-nucleotide segments of the DNA chain, if it is known that in the complementary chain they correspond to the sequence of ATG and ACG.
eleven.

Theoretical part

1. Definition of Lipids:
Lipids are a heterogeneous group of organic compounds that are important constituents of plant and animal tissues. They are arbitrarily classed together according to their solubility in organic solvent such as benzene, ether, chloroform, carbon terachloride (the so-called fat solvents) and their insolubility in water. Their solubility properties are a function of their alkane-like structures.
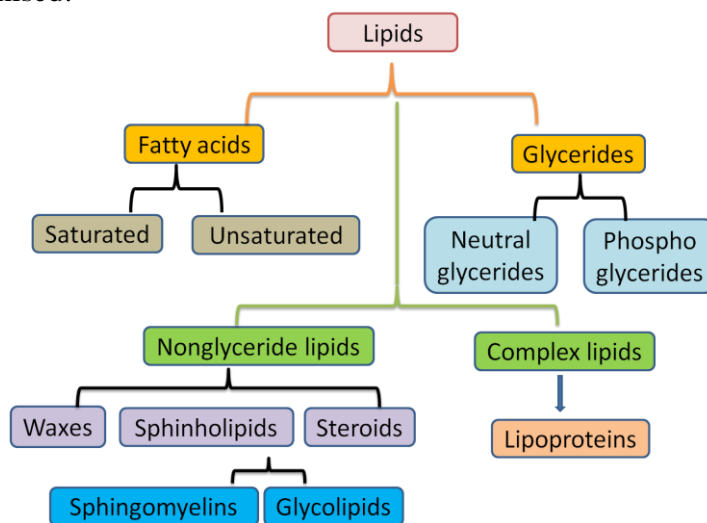
Edible lipids constitute approximately 25-28% of the diet and they serve as a starting material for the production of many important commodities such as soap products. The role of lipids in the diet has received a great deal of attention because of the apparent connection

between saturated fats and blood cholesterol with arterial disease. Lipids are the most important energy storage compounds in the animal kingdom.

In contrast, plants store most of their energy in the form of carbohydrates, primarily as starch. In addition, lipids provide insulation for the vital organs, protecting them from mecha¬nical shock and maintaining optimum body temperature. Lipids are integral components of cell membrane structure and, as such, are associated with transportation across cellular membranes.

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2. Classification of Lipids:

Unlike polysaccharides and proteins, lipids are not polymers-they lack a repea¬ting momomeric unit. However, like carbohydrates, they can be classified according to their hydrolysis products and according to similarities in their molecular structures. Three major subclasses are recognised:

1. Simple lipids:
(a) Fats and oils which yield fatty acids and glycerol upon hydrolysis.

(b) Waxes, which yield fatty acids and long-chain alcohols upon hydrolysis.

2. Compound lipids:
(a) Phospholipids, which yield fatty acids, glycerol, phosphoric acid and a nitrogen-containing alcohol upon hydrolysis.

(b) Glycolipids, which yield fatty acids, sphingosine or glycerol, and a carbo¬hydrate upon hydrolysis.

(c) Sphingolipids, which yield fatty acids, sphingosine, phosphoric acid, and an alcohol component upon hydrolysis.

3. Steroids:
Compounds containing a phenanthrene structure that are quite different from lipids made up of fatty acids.

Simple lipids:

Fats and oils are the most abundant lipids found in nature. Both types of com¬pounds are called triacylglycerols because they are esters composed of three fatty acids joined to glycerol, a trihydroxy alcohol:
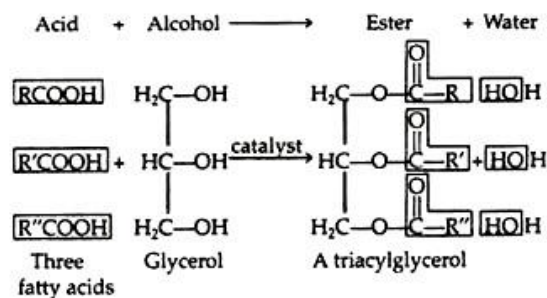
Further classification of triacylglycerols is made on the basis of their physical states at room temperature. It is customary to call a lipid a fat if it is solid at 25°C, and an oil if it is a liquid at the same temperature. (These differences in melting points reflect diffe¬rences in the degree of unsaturation of the constituent fatty acids.) Furthermore, lipids obtained from animal sources are usually solids whereas oils are generally of plant origin. Therefore, we commonly speak of animal fats and vegetable oils.

3. Physical Properties of Lipids:

As previously mentioned, lipids may be either liquids or non-crystalline solids at room temperature. Contrary to popular belief, pure fats and oils are colourless, odorless, and tasteless. The characteristic colours, odours, and flavours associated with lipids are imparted to them by foreign substances that have been absorbed by the lipid and are soluble in them.

For example, the yellow colour of butter is due to the presence of the pigment carotene; the taste of butter is a result of two compounds, diacetyl ($CH_3COCOCH_3$), and 3-hydroxy-2-butanone ($CH_3COCHOHCH_3$), that are produced by bacteria in the ripening of the cream. Fats and oils are lighter than water, having densities of about 0.8 gm/cm3. They are poor conductors of heat and electricity and, therefore, serve as excellent insulators for the body.

4. Chemical Properties of Lipids:

a. Saponification:

Triacylglycerols may be hydrolysed by several procedures, the most common of which utilizes alkali or enzymes called lipases. Alkaline hydrolysis is termed saponification because one of the products of the hydrolysis is a soap, generally sodium or potassium salts of fatty acids.

This hydrolysis reaction also provides a useful analytical method for the determination of a constant, the saponification number, which is characteristic of the simple lipids. The saponification number of a lipid is defined as the number of milligrams of potassium hydroxide required to saponify 1 gm. of a fat or an oil. It gives an indication of the average molar mass of the lipid.
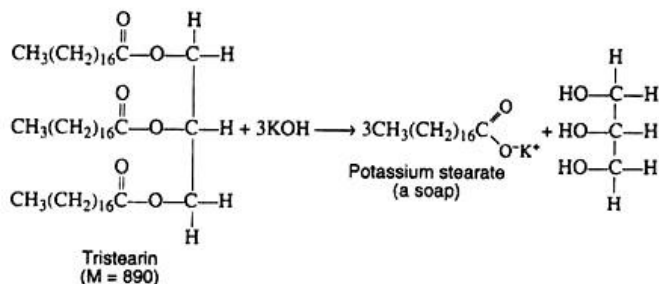
$$\text{Saponification no.} = \left(\frac{3 \text{ moles KOH}}{\text{mole lipid}}\right)\left(\frac{(56 \text{ g mole}^{-1} \text{ KOH})(1000 \text{ mg g}^{-1})}{\text{g mole}^{-1} \text{ lipid}}\right)$$

$$\text{Saponification no. of tristearin} = \frac{168,000 \text{ mg KOH per mole lipid}}{890 \text{ g lipid per mole lipid}} = 189 \text{ mg KOH per g lipid}$$

A lipid that contains long-chain fatty acids will have fewer molecules of acid per unit mass than one containing the short- chain fatty acids. Consequently, a lipid with preponderance of long-chain fatty acids will have a low saponification number in comparison to a lipid containing short-chain fatty acids.

In other words, a small saponification number for a fat or an oil indicates a high molar mass. The point is clarified by the method of determination of the saponification number of tristearin. Experimentally, a weighed sample of fat (tristearin) is saponified with a standard

solution of alcoholic potassium hydroxide. Following saponification the excess alkali is determined by titration with standard acid.

b. Halogenation:

Unsaturated fatty acids, whether they are free or combined as esters in fats and oils, react with halogens by addition at the double bond(s). The reaction (halogenation) results in the decolourisation of the halogen solution.
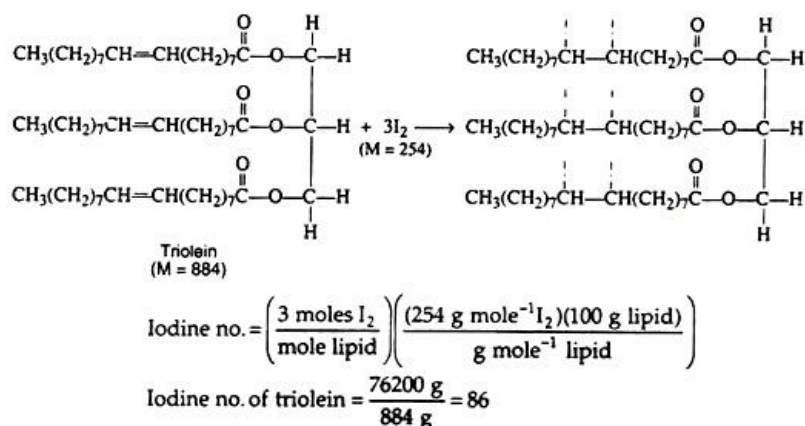
Since the degree of absorption by a fat or oil is proportional to the number of double bonds in the fatty acid moieties, the amount of halogen absorbed by a lipid can be used as an index of the degree of unsaturation.

The index value is called the iodine number and is defined as the number of grams of iodine (or iodine equivalent) that will add to 100 grams of fat or oil. This value is influenced by a number of factors. Such as percentage of unsaturated fatty acid in the triacylglycerol molecule and the degree of unsaturation of each fatty acid.

As a general rule, a high iodine number indicates a high degree of unsaturation. Natural fats that have a preponderance of saturated fatty acids have iodine numbers of about 10-50; those that contain an abundance of polyunsaturated fatty acids have iodine numbers of 120-150.

One example is the determination of the iodine number of triolein. The equation indicates the addition of molecular iodine. In actual practice, however, the reagents used are the inter-halogens iodine mono-chloride (IC1), or iodine mono-bromide (IBr), both of which are more reactive than iodine alone.

A weighed sample of lipid is treated with an excess of the iodine reagent. After the reaction is completed, the unused iodine is determined by titration with a standard solution of sodium thiosulfate.

$$\text{Iodine no.} = \left(\frac{3 \text{ moles } I_2}{\text{mole lipid}}\right)\left(\frac{(254 \text{ g mole}^{-1} I_2)(100 \text{ g lipid})}{\text{g mole}^{-1} \text{ lipid}}\right)$$

$$\text{Iodine no. of triolein} = \frac{76200 \text{ g}}{884 \text{ g}} = 86$$

c. Hydrogenation:

A large-scale commercial industry has been developed for the purpose of transforming vegetable oils into solid fats. The process of converting oils to fats by means of hydrogenation is sometimes referred to as hardening. One method consists of bubbling hydrogen gas under pressure (25 lb/in2) into a tank of hot oil (200°C) containing a finely dispersed nickel catalyst. An example is the conversion of triolein to tristearin is given in the figure.
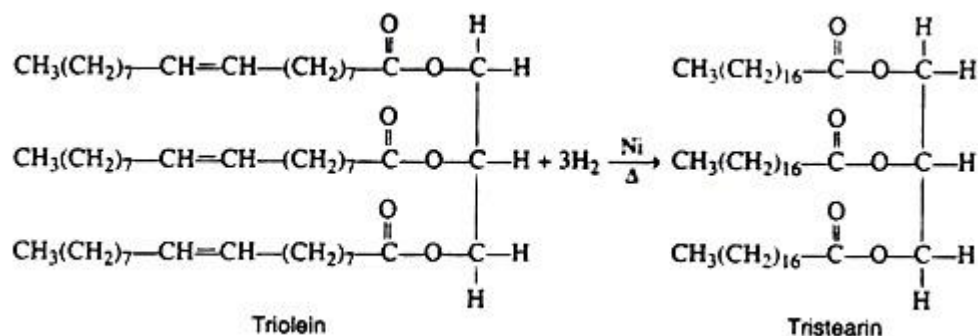
The equation represents the complete saturation of an unsaturated lipid. In the actual hardening process, the extent of hydrogenation is controlled so as to maintain a certain number of unsaturated linkages. If all the bonds become hydrogenated, the product becomes hard and brittle like tallow.

$$CH_3(CH_2)_{16}\overset{O}{\underset{}{C}}-O-\overset{H}{\underset{}{C}}-H$$
$$CH_3(CH_2)_{16}\overset{O}{\underset{}{C}}-O-\overset{}{\underset{}{C}}-H + 6H_2 \xrightarrow{Catalyst} 3CH_3(CH_2)_{16}CH_2OH + \begin{matrix} H \\ HO-C-H \\ HO-C-H \\ HO-C-H \\ H \end{matrix}$$
$$CH_3(CH_2)_{16}\overset{O}{\underset{}{C}}-O-\overset{}{\underset{H}{C}}-H$$

Tristearin   n-Octadecanol   Glycerol
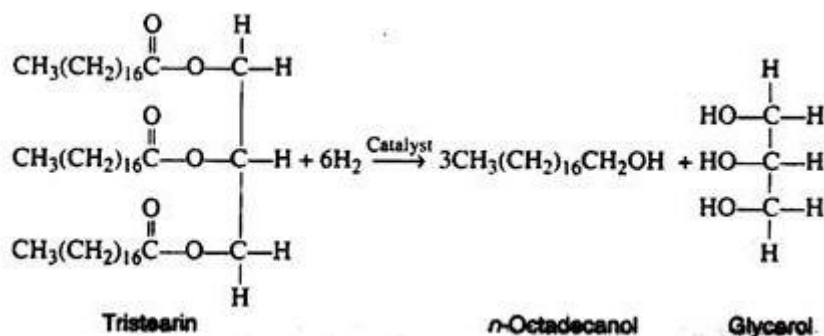
If reaction conditions are properly controlled, it is possible to prepare a fat with a desirable physical consistency (soft and pliable). In this manner, inexpensive and abundant vegetable oils (cottonseed, corn, and soybean) are converted into oleomargarine and cooking fats. The peanut oil in peanut butter has been partially hydrogenated to prevent the oil from sepa¬rating out.

Today, because of the possible connection between saturated fats and arterial disease, many people are cooking with the vegetable oils (especially safflower seed oil) rather than with the hydrogenated products. If the hydrogenation of an oil is allowed to continue for a long period of time, glycerol and long-chain alcohols are formed e.g., tristearin to glycerol. These long chain alcohols are employed in the manufacture of synthetic detergents.

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5. Special Features of Lipids:

a. Rancidity:

The term rancid is applied to any fat or oil that develops a disagreeable odour. Two principal chemical reactions are responsible for causing rancidity-hydrolysis and oxidation.

Butter is particularly susceptible to hydrolytic rancidity because it contains many of the lower molar mass acids (butyric, caproic) all of which have offensive odours. Under moist and warm conditions, hydrolysis of the ester linkages occurs, liberating the volatile acids. Microorganisms present in the air furnish the enzymes (lipases) that catalyse the process. Rancidity can easily be prevented by storing butter covered in a refrigerator.

Oxidative rancidity occurs in triacylglycerols containing unsaturated fatty acids. The reaction is quite complex, but it is believed that the first step involves the formation of a free radical, followed by production of hydro peroxides. Further reactions occur in which bonds are cleaved and the short-chain; offensive-smelling carboxylic acids are liberated.

Rancidity is a major concern of the food industry, and chemists involved in this area are continually seeking new and better substances to act as antioxidants. Such compounds are added in very small amounts (0.01-0.001%) to suppress rancidity.

They have a greater affinity for oxygen than the lipid to which they are added and thus func¬tion by preferentially depleting the supply of adsorbed oxygen. Two naturally – occurring antioxidants are vitamin E and ascorbic acid (vitamin C).

b. Drying Oils:

A drying oil is any substance that causes a paint or varnish to develop a hard, protective coating. It is the susceptibility of highly unsaturated oils to react with oxygen that accounts for their usefulness in the paint industry. Linseed oil is especially reactive and is most commonly used. The term drying may be a misnomer because it implies that the protec¬tive coating is formed by the evaporation of the solvent.

Instead, the drying process involves an oxidation followed by a polymerization reaction that results in the formation of a vast interlocking network of triacylglycerols joined by peroxide

bridges. These oxidation-polymerisation reactions are catalyzed by metal ions (lead, manganese, cobalt), and salts of these metals are included in paint to hasten the drying process.

Oil paints are suspension of very finely divided pigments in linseed oil. Olicloths is made by the application of several coasts of linseed oil on woven fabric. Linoleum is a mixture of linseed oil, ground cork, and resin that has been pressed together and "dried".
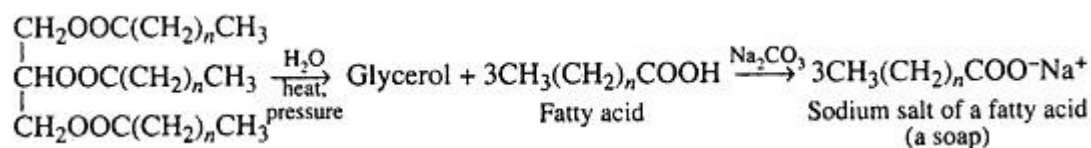
Waxes:

A wax is an ester of a long-chain alcohol (usually mono-hydroxy) and a fatty acid. The acids and alcohols normally found in waxes have chains of the order of 12-34 carbon atoms in length. Waxes are easily melted solids that are widely distributed in nature and are found in both plant and animal matters. They are not as easily hydrolysed as the triacylglycerols and therefore are useful as protective coatings.

Plant waxes are found on the surfaces of leaves and stems and serve to protect the plant from dehydration and from invasion by harmful organisms. Carnauba wax, largely myricylcerotate, $C_{25}H_{51}COOC_{30}H_{61}$, is obtained from the leaves of certain Brazilian palm trees and is used as a floor and automobile wax and as a coating on carbon paper.

Animal waxes also serve as protective coatings. They are found on the surface of feathers, skin and hair, and help to keep these surfaces soft and pliable. Beeswax, which is mostly myricyl palmitate, $C_{15}H_{31}COOC_{30}H_{61}$, is secreted by the wax glands of the bee. Spermaceti wax, mainly cetyl palmitate, $C_{15}H_{31}COOC_{16}H_{33}$, is found in the head cavi¬ties and the blubber of the sperm whale.

Spermaceti crystallizes in heavy white flakes when whale oil is exposed to air and chilled. It is used primarily in ointments, in cosmetics, and in the manufacture of candies. Lanolin, obtained from wool, is a mixture of fatty acid esters of the steriods lanosteriol and agnosterol. It finds widespread medical applications as a base for creams, ointments, and salves.

$$CH_2OOC(CH_2)_nCH_3$$
$$CHOOC(CH_2)_nCH_3 \xrightarrow[\text{heat, pressure}]{H_2O} \text{Glycerol} + 3CH_3(CH_2)_nCOOH \xrightarrow{Na_2CO_3} 3CH_3(CH_2)_nCOO^-Na^+$$
$$CH_2OOC(CH_2)_nCH_3$$

Fatty acid   Sodium salt of a fatty acid (a soap)

Compound Lipids:

a. Phospholipids:

The phospholipids, also called phos¬phatides, are compound lipids that are derivatives of glycerol phosphate:

Glycerol phosphate
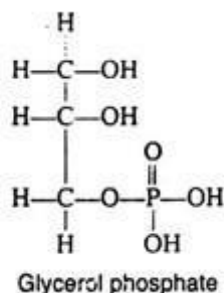
Phospholipids are found in all living organisms. Regardless of their source, they have quite consistent structures. Phospholipids are particularly abundant in liver, brain and spinal tissue and are found in the outer membranes of most cells. They appear to be essential components of cell structure since the amount of phospholipids present in animal tissues remains relatively constant, even during starvation when the cell's supply of simple lipids is depleted.

Phospholipids are large molecules con¬taining both a polar and a nonpolar component. They are the most polar of all the lipids. It is believed that their primary function is to act as an emulsifying agent at cell membrane surfaces, where water-insoluble lipids and water-soluble materials (such as proteins) must be capable of intimate association.

It is thought that phospholipids take part in fat metabolism by promoting the transportation of lipids in the blood stream, primarily in an aqueous medium. Phospho¬lipids

also play important roles in the electron transport system in secretory processes, and in the transport of ions across cell membranes. There is increased speculation regarding their functions in brain and ner¬vous tissue, but till now their exact purpose is not known.

Two commonly found phospholipids (lecithin and cephalins) are described here:

1. Lecithin:

Lecithin is probably the most common of the phospholipids. It contains the important quaternary ammonium salt choline. $HOCH_2CH_2N+(CH_3)_3$, joined to a phosphoric acid residue by means of an ester linkage. The nitrogen in choline carries a positive charge and the phosphate a negative charge so that in solution at most pH values, lecithin exists as an internal salt or zwitterion.

The structure and hydrolysis products of lecithin are:

Lecithin
(Phosphatidyl choline)
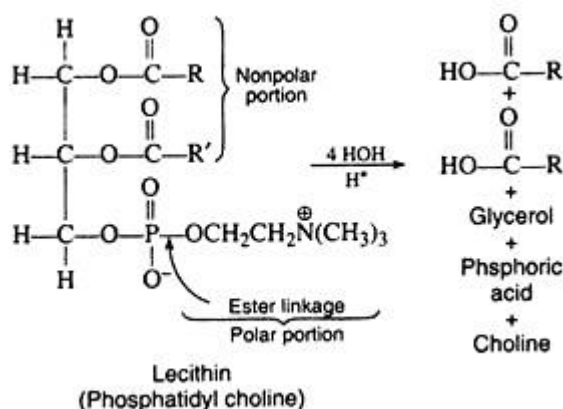
Pure lecithin is a waxy white solid that quickly darkens when exposed to air. In contrast to fats and oils, it is colloidally dispersed in water and is insoluble in acetone. It is, therefore, possible to separate licithin from an ether extract by the addition of acetone. Lecithin is especially abundant in egg yolk and soybeans. When obtained from the latter source it is used as an emulsifying agent in the dairy and confectionery industries.
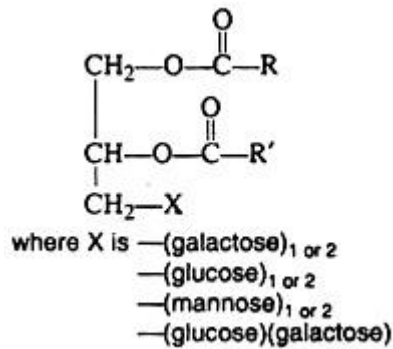
2. Cephalins:

The chief difference between the cephalins and lecithins lies in the nitrogenous base component that is linked to the phosphate moiety. In the cephalins, the choline is replaced by ethanolamine, $HOCH_2CH_2NH_2$, or by the amino acid serine, $HOCH_2CH(NH_2)COOH$. The term cephalin is derived from its chief occurrence in the body, namely the head and spinal tissue (Greek, kephalikos, head). It is thought that cephalins play an important role in the process of blood clotting:

Phosphatidylethanolamine   Phosphatidylserine

Cephalins
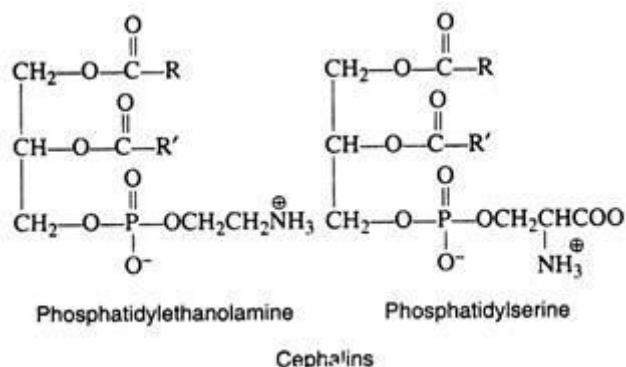
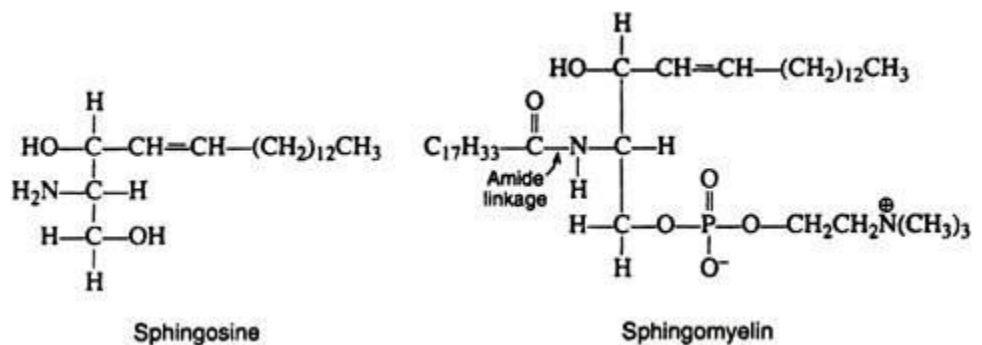### b. Glycolipids:

Several groups of compounds are found containing both lipid and carbohydrate moieties. Those that are water soluble are termed liposaccharides and are thought of as derived carbohydrates. Those that retain solubility in nonpolar organic solvents are classed as glycolipids. One group of glycolipids contains fatty acids, glycerol, and various carbohydrates.

$$CH_2-O-\overset{\overset{\textstyle O}{\|}}{C}-R$$
$$CH-O-\overset{\overset{\textstyle O}{\|}}{C}-R'$$
$$CH_2-X$$

where X is —(galactose)$_{1\ or\ 2}$
—(glucose)$_{1\ or\ 2}$
—(mannose)$_{1\ or\ 2}$
—(glucose)(galactose)

Another group, the cerebrosides, are sphingosine derivatives and, thus, may be classified either as glycolipids or sphingolipids. Cerebrosides occur primarily in the brain (7% of the solid matter) and in the myelin sheath of nerves. It has been suggested that they function in the transmission of nerve impulses across synapses.

They are also believed to be present at receptor sites for acetylcholine and other neurotransmitters. The fatty acids found in cerebrosides are unusual in that they contain 24 carbon atoms. Cerebrosides most often contain D-galactose attached by an acetal linkage at carbon-1 of sphingosine. Unlike most lipids, they are insoluble in ether but may be extracted into warm alcohol or pyridine.

Sphingosine

Sphingomyelin

Two severe lipid storage diseases are caused by errors in the metabolism of the glycolipids. In Gaucher's disease, the glycolipids contain glocose instead of galactose. These abnormal glycolipids accumulate in the brain, spleen and kidney cells. An infant with Tay-Sachs disease lacks an enzyme that breaks down glycolipids, so they accumulate in the tissue of the brain and the eyes.

A cerebroside
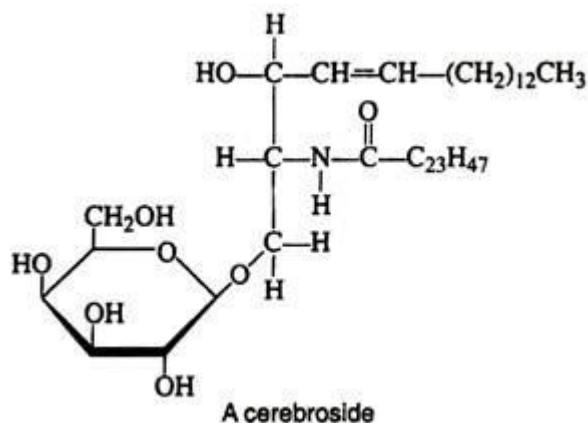
c. Sphingolipids:

Sphingolipids occur in the membranes of both plants and animals, with only a minor amount found in depot fat. They- contain the long-chain unsaturated amino alcohol sphingsine

instead of glycerol. Also present are fatty acids, phosphate, and an alcohol component. The most abundant sphingolipid is sphingomyelin, which contains choline as the alcohol group.

Niemann-Pick disease is another lipid storage disease in which sphingo myelins build up in the brain, liver, and spleen, resul¬ting in mental retardation and early death.

_____

6. Functions of Lipids:

It is established that lipids play extremely important roles in the normal functions of a cell. Not only do lipids serve as highly reduced storage forms of energy, but they also play an intimate role in the structure of cell membrane and organellar membranes. Lipids are not transported in the free form in circulating blood plasma, but move as chylomicrons.

Chylomicrons are very low density lipoproteins, which can be absorbed from the intestinal lumen easily. Lipids also move through the circulation as free fatty acid-albumin complexes.

Testosterone

Progesterone

Estradiol

Estrone

Estrogens
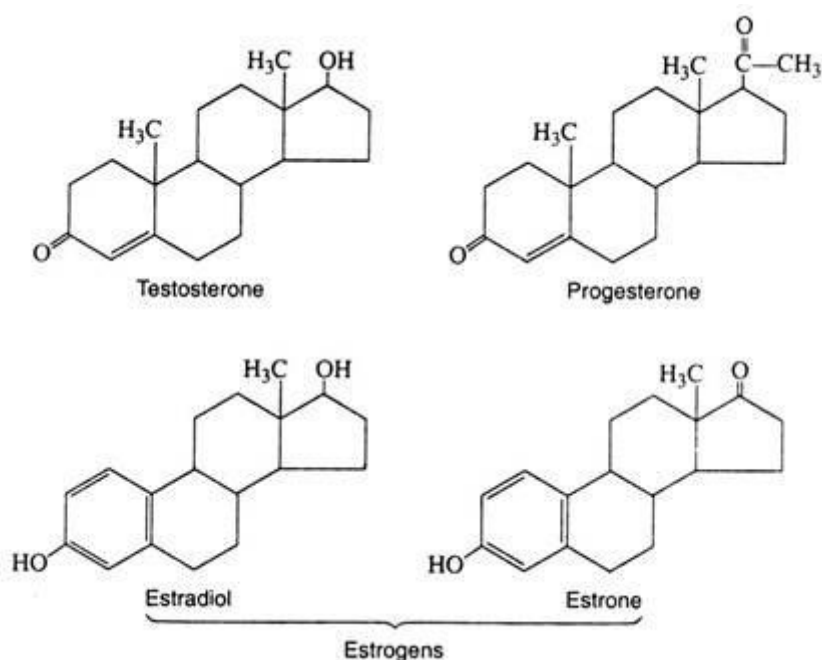
Lipids also participate in metabolic activities directly or indirectly. These can be described as follows:

1. Lipids are major sources of energy in animals and high lipid-containing seeds.

2. Activators of enzymes:

There are many enzymes, which require lipid micelles for maximum activation, e.g., three microsomal enzymes, namely, glucose-6-phosphatase, stearyl CoA desaturase and ω-mono oxygenase, and β-hydroxy butyric dehydrogenase (a mitochondrial enzyme), require phosphatidyl choline micelles for activation.

3. Components of electron transport chain (ETC):

The ETC in the inner membranes of mitochondria is buried in a phospholipid substrate.

4. Acts as substrate:

α-Acyl-β-oleyl phosphatidyl choline specifically serves as the acceptor of a CH3 group from S- adenosyl methionine, which adds across the double bond of β-oleyl moiety to form the cyclopropane function of lactobacillic acid.

5. Lipids as glycosyl carrier:

The isoprenoid compound, undecaprenyl phos¬phate, acts as a lipophilic carrier of a glycosyl moiety in the synthesis of bacterial cell wall lipopolysaccharides and peptidoglycans.

Laboratory work № 14

Reagents and equipment:

1. Distilled water.
2. Concentrated sulfuric acid solution.
3. Aqueous solutions: 0.1N KMnO$_4$, 30% sodium hydroxide, bromine water, 0.5N KI, terpinhydrate, 0.5% starch paste, 5% chloramine.
4. Turpentine, chloroform, bromocamphor.
5. A tripod with test tubes, test tubes with a gas outlet tube.
6. Measuring and dropping pipettes.

Experience 1. Proof of terpenicity

To 1 drop of turpentine add 2 drops of bromine water, shake. Observe the notes in the notebook.
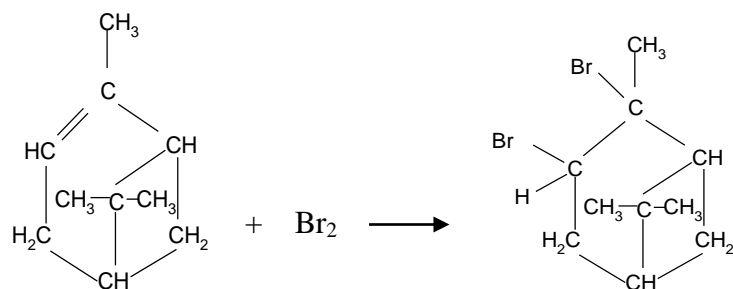
Conclusion:

Experience 2. Easy oxidation of terpenes

Oxidability of terpenes is the second qualitative reaction to the limitlessness. To 1 drop of 0.1N. KMnO4 in 5 water drops add 1 drop of turpentine, shake. Observe observations and conclusions in a notebook.
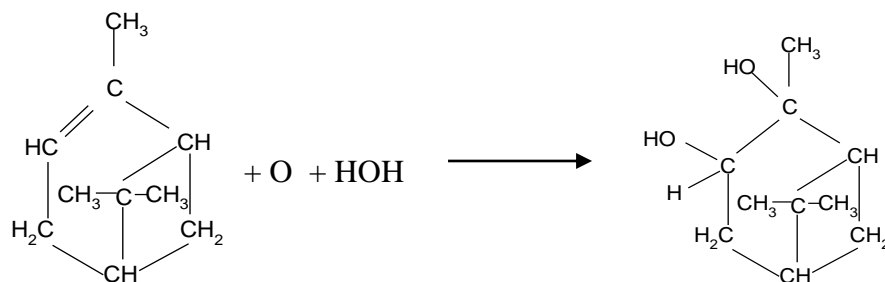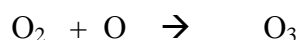

Conclusion:

Experience 3. Activation of oxygen by terpenes

To 1 drop of 0.5% starch paste solution, add 1 drop of 0.5 N KI and 1 drop of turpentine, shake - a dark violet color appears, gradually turning into blue, indicating the release of free iodine due to the oxidation of potassium iodide.

Terpenes readily oxidize O_2 of air at the site of the double bond, forming peroxides, which readily decompose, activating oxygen giving ozone:

$$O_2 \ + \ O \ \rightarrow \ \ O_3$$

Active oxygen is qualitatively determined by the isolation of iodine upon addition of KI.

Conclusion:

Experiment 4. Dehydration of terpinhydrate 1.8 monohydrate monohydrate, which is an alcohol and can dehydrate with the formation of an unsaturated compound - terpene with a pleasant odor, the unlimitability of which is easy to establish: place 2 spatulas of terpinhydrate in a test tube, add 2 ml of water and heat to boiling. Cool the solution and add a few drops of conc. sulfuric acid. Read the smell of the product and the cloudiness of the solution. This reaction is used in pharmacolysis as a reaction confirming the authenticity of terpinhydrate.

Conclusion:

Experience 5. Study of qualitative reactions to bromampamor
Qualitative reactions to bromocamphor are based on the splitting off of the bromine atom and transferring it either to a volatile copper compound (Belshtein test) or to free bromine. The latter reaction is carried out in the presence of a strong oxidizing agent - chloramine in a hydrochloric acid medium: dissolve 2 spatulas of bromocamphor in 2 ml of ethanol. Prove the presence of bromine breakdown Belshtein. Add 1 ml of 30% NaOH solution and 1 spatula of zinc dust to the obtained alcohol solution. Boil the mixture for 3-4 minutes, cool, filter off zinc residues, neutralize the filtrate with hydrochloric acid until slightly acidic reaction (pH = 5), then add 1 ml of 5% chloramine solution and 1 ml of chloroform, mix well. In what color was the chloroform layer painted? This reaction is recommended for the qualitative determination of bromocamphor.

Conclusion:

Experience 6. Studying the properties of corticosteroids

The corticosteroid hormones of the adrenal cortex always contain a keto group at position 3, a free or esterified group - COCH2OH - at position 17 and one or two double bonds in ring "A" of the sterane nucleus. This determines the generality of their chemical properties.

a) Detection of the keto group: add 0.5 ml of phenylhydrazine sulfate solution to 0.5 ml of an alcohol solution of any corticosteroid and heat on a water bath for 7-10 minutes. As a result of the condensation reaction, a yellow product must be formed.

Conclusion:

b) Detection of the alpha-ketol group -COCH2OH: add 0.5 ml of Feling's reagent to 0.5 ml of alcohol solution of prednisone or prednisolone and heat in a water bath. As a result of oxidation of the alpha-ketol group to the carboxyl group, a red precipitate of copper (I) oxide is released.

Conclusion:

c) Detection of double bonds: add 0.5 ml of an alcohol solution of bromine (light yellow color) to 0.5 ml of an alcohol solution of any corticosteroid, mix well. Explain why the color of bromine disappears.

These reactions you will use when analyzing the derivatives of corticosteroids.

Conclusion:

Experience 7. General reaction to steroids (Lieberman-Burkhard reaction)

Place several steroid crystals on the slide, add 3 drops of acetic anhydride and 2 drops of concentrated H_2SO_4, mix with a glass rod. After 1-2 minutes, yellow color should appear.

Attention! Preparations of steroids give with concentrated sulfuric acid colors of different colors - this property is used in the pharmanalysis.

Tasks for independent work

Control questions:

1. What compounds are related to lipids? How are they classified?

2. Simple and complex lipids.

3. Define the concepts of "terpenes" and "steroids". What ties and what distinguishes these compounds.

4. Common reactions to terpenes.

5. Indicate asymmetric carbon atoms in the formulas of limonene, pinene, camphor.

6. What compounds are formed from pinene when standing under the action of O2 air and how to detect them?

7. How camphor reacts with a) hydroxylamine; b) sodium bisulfite; c) phenylhydrazine; d) semicarbazide.

8. What compounds are called steroids?

9. Features of corticosteroids. Detection of keto group, keto-alcohol group and double bonds in them. Which of the reactions to corticosteroids are characteristic of other steroids?

10. The general reaction to steroids is the Lieberman-Burkhard reaction.

Test tasks:

1. Lipids dissolve in all substances listed below except:
a) ether
b) water
c) benzene
d) chloroform

2. Structurally, all lipids are:
a) with ethers
b) higher alcohols
c) esters
d) polycyclic alcohols

3. Structural lipids include all of the following:
a) phospholipids
b) glycolipids
c) triglycerides
d) sterols

4. The composition of triglycerides includes all of the elements listed below except:
a) H b) O c) S d) C

5. The main lipids of membranes are:
a) triglycerides
b) glycolipids
c) Waxes
d) phospholipids

6. Esters of higher fatty acids and polycyclic alcohols are called:
a) Waxes
b) sterols
c) sterols

7. The most common saturated higher fatty acids, which are part of lipids:
a) palmitic
b) acetic acid
c) stearic acid
d) ant

8. How many isoprene fragments contain diterpenes:
a) 2 b) 3 c) 4 d) 6

9. Camphor refers to
a) to monoterpenes
b) diterpenes
c) sesquiterpenes
d) triterpenes

10. Provitamin A of vitamin A is:
a) γ - carotene b) β - carotene c) α - carotene

11. How many isoprene fragments contain triterpenes:
a) 2 b) 3 c) 4 d) 6

12. The main component of turpentine is:
a) limonene b) terpinene
c) α-pinene d) camphene

13. Acyclic terpenes include:
a) geraniol b) citronellol
c) Nerol d) Citronellal
e) limonene e) terpinenes

14. Monocyclic monoterpenes include:
a) geraniol b) citronellol
c) pinene d) citronellal
e) limonene e) terpinenes

15. Bicyclic monoterpenes include:
a) geraniol b) citronellol
c) pineny d) camphor
e) limonene e) terpinenes

16. The following applies to sesquiterpenes:
a) kicking
b) Camphor
c) limonene
d) farnesol

17. Diterpenes include:

a) phytol
b) Camphor
d) cis- and tansretinal
e) farnesol

18. Triterpenes include:
a) phytol
b) Camphor
c) squalane
d) borneol

19. The structural features of cardiac glycids include:
a) the aromatic nature of ring A
b) the presence of phenolic OH at the C-3 atom
c) the presence of an unsaturated lactone ring in position 17 of the gonan system;
d) the β-hydroxyl group at the C11 atom
e) the presence of a branched C8-C10 alkyl radical at position C17

20. How many isoprene fragments contain sesquiterpenes:
a) 2 b) 3 c) 4 d) 5 e) 6

Timing of a 3-hour lesson:
1. Organizational moment - 2 minutes.
2. The survey - 40 min.
3. Explanation of the work - 25 min.
4. Performance and execution of work - 30 min.
5. Presentation of the new material - 45 min.
6. Verification of work and assignment to the house - 3 min.