Ministry of Health of the Republic of Belarus Educational institution "Gomel State Medical University"

Department of General and Bioorganic Chemistry

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METHODOLOGICAL MANUAL

for conducting the laboratory class with the first-year students of the Faculty of International Students studying in the specialty 7-07-0911-01 "Medical business" (FIS) English-speaking students in the discipline "Medical chemistry"

Topic 13: Coordination compounds

Time: 2 hours

THE TRAINING AND EDUCATIONAL GOALS, MOTIVATION TO STUDY THE TOPIC

The purpose of the class:

To teach students to make formulas of complex compounds and equations of complex formation reactions. This knowledge is necessary for future doctors to understand the structure and role of natural complexes (chelates) in the vital activity of living organisms. To familiarize students with the methodology of qualitative analysis of metal cations in aqueous solutions and biological fluids using complexometry.

The tasks of the class:

As a result of the class, the student *must know:*

1) the essence of Werner's coordination theory;

2) classification and nomenclature of complex compounds;

3) the concept of stability of complex compounds;

4) structure of molecules of intracomplex compounds.

The student *must be able to:*

1) write down the equations of complexation reactions in molecular and molecularionic forms;

2) classify complex compounds and name them according to IUPAC rules;

3) describe the mechanism of formation of bonds in complex compounds;

4) discuss metal-ligands equilibria in water solutions and stability of coordination compounds.

Motivation to study the topic:

Complex compounds play an important role in biology and medicine. For example, most of the metals that make up the living tissues of the body are in the form of strong complex compounds called chelates. Many medicines also have a chelated structure.

The use of complex compounds is the basis of complexometry, which is widely used in the practice of biomedical, sanitary-hygienic and pharmaceutical analysis.

Some complex compounds are used as preserving agents for storing blood, while others are used as medicines for removing toxic metal ions from the body, including radioactive isotopes.

NECESSARY EQUIPMENT

1. Methodological manual for students on the topic "Coordination compounds".

2. Reference materials of physico-chemical constants for the 1st year education international students.

3. Chemical reagents and equipment necessary for laboratory work.

CONTROL QUESTIONS ON THE TOPIC OF THE CLASS

1. Structure of complex compounds: Werner's theory. The basic terms and definitions.

2. Classification and nomenclature of complex compounds. Structure of molecules of intracomplex compounds.

3. Equilibria in solutions of the complex compounds. The complexing ability of ions of s-, p- and d-elements. Methods of obtaining complex compounds.

4. Biological role of coordination compounds.

COURSE OF THE CLASS

The theoretical part

1. STRUCTURE OF COMPLEX COMPOUNDS: WERNER'S THEORY. THE BASIC TERMS AND DEFINITIONS

Complex compounds are compounds containing complex ions in crystal lattices that can independently exist in solutions or melts.

Complex (coordination) compounds are compounds in which the covalence number of the central atom is greater than its ordinary covalence number.

For example:



Covalence number of Si is 4, it is not a coordination compound.

 $\begin{bmatrix} \mathbf{F} \\ \mathbf{F} \\ \mathbf{Si} \\ \mathbf{F} \\ \mathbf{F} \\ \mathbf{F} \end{bmatrix}^{2-}$

Covalence number of Si is 6, it is a coordination compound.

Alfred Werner in 1898 proposed theory to explain the formation and structure of coordination compounds.

According to Werner's theory, coordination compounds consist of:

- a central atom (ion), known as a complexing agent;
- ligands (ions or polar molecules);
- ions of outer sphere (counter ions).

Some of the complex compounds don't contain ions of outer sphere.



Figure 1 – Structure of complex compounds

Central atoms (complexing agents) are usually metals, and seldom nonmetals (for example, B, P, and Si). They are characterized by their:

a) oxidation numbers,

b) coordination numbers.

A coordination number is a number of covalent bonds which a central atom forms with its ligands. The most typical coordination numbers correspond to definite oxidation numbers (charges) of the central ion:

Oxidation number	Coordination number
+ 1	2
+ 2	4, 6
+ 3	4,6
+ 4	6, 8

Ligands are ions or polar molecules that surround the metals in coordination ions. They contain one or several donor atoms bond directly to the metal ions. Ligands are classified according to their **denticity** – the number of donor atoms in a single ligand that bind to a central atom in a coordination compound:

• *unidentate ligands* form one covalent bond with a complexing agent. They are:

a) anions: Cl⁻; Br⁻; I⁻; F⁻; CN⁻; SCN⁻; NO₂⁻; H⁻; OH⁻;

b) molecules: H₂O; NH₃; CO; NO;

c) cations: $NH_2NH_3^+$.

• *bidentate ligands* form two covalent bonds with the complexing agents. They are:

a) anions of diprotic acids: SO_4^{2-} ; SO_3^{2-} ; CO_3^{2-} ; $C_2O_4^{2-}$;

b) molecules: NH₂-CH₂-CH₂-NH₂ (ethylenediamine); NH₂-CH₂-COOH (glycine).

• *polydentate ligands* can form three, four, five and six covalent bonds with the complexing agents [1-3].

For example, the chelating agent ethylenediaminetetraacetic acid (EDTA) is able to form stable complex compounds and has denticity four or six (EDTA binds to metals via 4 oxygen and 2 nitrogen atoms):

$$\begin{array}{c} \text{HOOCH}_2\text{C} \\ \text{N} - \text{CH}_2 - \text{CH}_2 - \text{N} \\ \text{HOOCH}_2\text{C} \\ \end{array} \\ \begin{array}{c} \text{CH}_2\text{COOH} \\ \text{CH}_2\text{COOH} \end{array}$$

EDTA is produced as several salts, in particular disodium EDTA (Trylone B); the number of donor atoms is 6:

$$\begin{array}{c} \text{HOOCH}_2\text{C} & \text{CH}_2\text{COONa} \\ \text{N} - \text{CH}_2 - \text{CH}_2 - \overset{\frown}{\text{N}} \\ \text{NaOOCH}_2\text{C} & \text{CH}_2\text{COOH} \end{array}$$

2. CLASSIFICATION AND NOMENCLATURE OF COMPLEX COMPOUNDS. STRUCTURE OF MOLECULES OF INTRACOMPLEX COMPOUNDS.

Classification of complex compounds

1. According to the nature of their ligands:

a) complexes with monodentate ligands:

• aqua complexes: [Cu(H₂O)₄]SO₄;

• ammine complexes: [Ni(NH₃)₄]Cl₂;

hydroxo complexes: K₂[Zn(OH)₄];

- acido complexes: K₄[Fe(CN)₆];
- carbonyls: [Fe(CO)₅];
- complexes with mixed ligands: Na[Al(OH)₄(H₂O)₂];

b) complexes with bi- and polydentate ligands.

Among them the chelate complexes are most important. They contain bi- and polydentate ligands forming cycles. Bidentate and polydentate ligands are called chelating agents because of their ability to hold the metal atom like a claw (from the Greek *chele*, means "claw"). For example, a copper (II) complex with ethylenediamine:

$$\begin{array}{c} CH_2 - H_2N \\ | \\ CH_2 - H_2N \end{array} \begin{array}{c} Cu \\ NH_2 - CH_2 \\ NH_2 - CH_2 \end{array}$$

Intracomplex compounds are chelate complexes in which molecules the central atom is a part of a cycle and forms covalent bonds in two different ways.

For example, the complex of Fe (III) with oxalic acid contains three iron-oxygen bonds formed by the donor-acceptor mechanism and three iron-oxygen bonds formed the coupling mechanism:

$$HO - C = O$$

$$Fe$$

$$O - C = O$$

$$Fe$$

$$O = C - OH$$

$$O$$

$$HO$$

$$C - C$$

$$HO$$

$$O$$

2. According to the charge of inner sphere:

- a) cationic: [Cr(NH₃)₃(H₂O)₃]³⁺Cl₃;
- b) anionic: $K_4 [Fe(CN)_6]^{4-}$;
- c) neutral: $[Pt(NH_3)_2Cl_2]^0$.

Nomenclature of coordination compounds

The rules for naming of complex compounds are the following:

1) the cation is named before the anion;

2) within a complex ion the ligands are named first, in alphabetical order, and the metal ion is named last;

3) the names of

• *anionic ligands* end with the letter o:

Cl ⁻ – chloro;	$CN^{-} - cyano;$	OH ⁻ – hydroxo;
Br [−] – brom <mark>o</mark> ;	SCN ⁻ – thiocyanato;	H ⁻ – hydrido;
I [−] −iodo;	NO_2^- – nitro;	SO_4^{2-} – sulfato;
F−− fluoro;	NO_3^- – nitrato;	$C_2O_4^{2-}$ – oxalato.

• neutral ligands: NH₃ – ammine, H₂O – aqua, CO – carbonyl, NO – nitrosyl;

• cationic ligand hydrazinium: NH₂N⁺H₃

5) the oxidation number of the metal is written Roman numeral in brackets (II, IV) following the name of the metal;

6) if the complex is an anionic type, its name ends with suffix -ate.

Metal	In cationic complexes	In anionic complexes
Al	aluminum	aluminate
Cr	chromium	chromate
Co	cobalt	cobaltate
Cu	copper	cuprate
Au	gold	aurate
Fe	iron	ferrate
Ag	silver	argentate
Sn	tin	stannate
Pb	lead	plumbate
W	tungsten	tungstate
Ni	nickel	nickelate
Hg	mercury	mercurate

Table 1 – Naming of metals

For example,

complex compound of cationic type:

[Cu⁺²(NH₃)₄]SO₄ tetraamminecopper (II) sulfate

complex compound of anionic type:

 $Na_3[Cr^{+3}(OH)_6]$ sodium hexahydroxochrom<u>ate</u> (III)

3. EQUILIBRIA IN SOLUTIONS OF THE COMPLEX COMPOUNDS. THE COMPLEXING ABILITY OF IONS OF s-, p- AND d-ELEMENTS. METHODS OF OBTAINING COMPLEX COMPOUNDS

According to their ability to dissociate in aqueous solutions, complex compounds are divided into two categories:

a) electrolytes: $K_4[Fe(CN)_6]$; $H_2[PtCl_4]$; $[Ag(NH_3)_2]OH$

b) non-electrolytes do not contain counter ions: [Pt(NH₃)₂Cl₂]

In aqueous solutions coordination compounds, which are electrolytes, break down into ions. Dissociation of complex compounds involves two steps:

• *primary dissociation* which proceeds irreversibly as ionization of strong electrolytes:

$$K_4[Fe(CN)_6] \rightarrow 4K^+ + [Fe(CN)_6]^{4-1}$$

• *secondary dissociation* which proceeds reversibly as ionization of weak electrolytes:

 $[Fe(CN)_6]^{4-} \rightleftharpoons Fe^{2+} + 6CN^{-}$

The equilibrium constant, which describes metal-ligands equilibrium, is denoted as *instability constant* (K_{ins}):

$$K_{ins} = \frac{[Fe^{2+}] \times [CN^{-}]^{6}}{[[Fe(CN)_{6}]^{4-}]}$$

The lower K_{ins} value, the greater stability of coordination compound.

Stability of complex compounds can be characterized by a formation constant (K_f):

$$K_{f} = \frac{1}{K_{ins}}$$

Stability of coordination compounds depends upon their structure:

a) the smaller ionic radius and the greater electric charge of a complexing agent, the greater attraction of ligands towards it; d-block metals are the best complexing agents;

b) the greater a number of donor atoms in a ligand the greater stability of coordination compounds.

Especially stable chelates. This phenomenon is known as the *chelate effect*. The chelate effect consists in the high stability of chelate complexes in comparison with their non-chelate analogues [1-3].

Examples of complex formation reactions:

a) $HgI_2 + 2KI \rightarrow K_2[HgI_4]$ (potassium tetraiodomercurate (II))

b) $AlCl_3 + 6NaOH \rightarrow 3NaCl + Na_3[Al(OH)_6]$ (sodium hexahydroxoaluminate)

c) $AgCl + 2NH_3 \rightarrow [Ag(NH_3)_2]Cl$ (diamminesilver (I) chloride)

Examples of destruction of complex compounds:

a) $[Ag (NH_3)_2]^+ + 2CN^- \rightarrow [Ag(CN)_2]^- + 2NH_3^0$ more stable complex, $K_{ins}[Ag(CN)_2]^- < K_{ins}[Ag(NH_3)_2]^+$ b) $AgNO_3 + NaCl \rightarrow AgCl\downarrow + NaNO_3$; $AgCl + 2NH_3 \rightarrow [Ag(NH_3)_2]Cl$ $[Ag(NH_3)_2]Cl + 2HNO_3 \rightarrow AgCl\downarrow + 2NH_4NO_3$ $K_{sp}(AgCl) = 1.78 \times 10^{-10} < K_{ins}[Ag(NH_3)_2]^+ = 5.75 \times 10^{-8}$

$$\begin{split} [Ag(NH_3)_2]Cl + KI & \longrightarrow AgI \downarrow + KCl + 2NH_3 \\ K_{sp}(AgI) = 8.3 \times 10^{-17} < K_{ins}[Ag(NH_3)_2]^+ = 5.75 \times 10^{-8} \end{split}$$

4. BIOLOGICAL ROLE OF COORDINATION COMPOUNDS

In a human body all metals (except Na and K) are bounded into stable complexes with bioligands: amino acids, proteins, vitamins, hormones and other organic compounds. Most important are metal complexes with proteins. They are hemoglobin, chlorophyll and numerous metal enzymes.

Hemoglobin is the protein molecule in red blood cells that carries oxygen from the lungs to the body's tissues and returns carbon dioxide from the tissues back to the lungs.

Hemoglobin is a globular protein belonging to the group of hemeproteins. Hemoglobin can be divided into two parts; a protein part and a heme group. One molecule of hemoglobin is made up of four polypeptide chains; two alpha chains and two beta chains.



Figure 2 – Structure of hemoglobin, heme group

In vivo, complexes of metal cations and bioligands are continuously formed and destroyed. Exchange with the environment maintains a constant concentration of metals and ligands, thus providing **metal-ligand homeostasis**.

The disturbance of metal-ligand homeostasis in vivo results in different diseases.

For example, iron deficiency is responsible for anemia, and its excess results in siderosis. Sources of iron are meat, liver.

Calcium deficiency is responsible for osteoporosis, its excess results in cataracts and atherosclerosis. Sources of calcium are milk, cheese, cottage cheese.

Modern medicine widely applies complex compounds to correct metal-ligands homeostasis in a body and thus treat different diseases.

• The cis-isomer of [Pt (NH₃)₂Cl₂] has been used to control tumors and cancers.

• Some complexes of gold, for example $Na_3[Au(S_2O_3)_2]$, are used to treat tuberculosis and rheumatoid arthritis.

• The chelate complex of calcium with EDTA ligands, named tetacine, is applied to treat heavy metals poisoning:



• Chelating agents such as EDTA and its sodium salt are also applied to bind and remove toxic metals from a human body. A small amount of EDTA prevents lead cations from acting as catalysts for the oxidation of fats and oils. Chelating agents are applied to dissolve kidneys stones. Calcium oxalate ($Ca_2C_2O_4$) which is a component of kidneys stones is readily dissolved in EDTA and its sodium salt Na_2H_2Y according to the equation:

 $Ca_2C_2O_4 + Na_2H_2Y \rightleftharpoons [CaY]^{2^-} + Na_2C_2O_4 + 2H^+$ [3]

The practical part

Safety instructions before laboratory work.

LABORATORY WORK *Preparing of cationic complexes*

Test 1. Preparing of Cu (II) ammine complex

Treat 2-3 drops of copper (II) sulfate solution with some drops of sodium hydroxide solution and mark the color of copper (II) hydroxide precipitate. Dissolve a prepared precipitate in 1-2 ml of 25 % ammonia solution. Mark a color of a prepared solution. Give a systematic name to the prepared complex compound. Write the chemical equations of fulfilled reactions:

 $CuSO_4 + NaOH \rightarrow Cu(OH)_2 + 4NH_3 \rightarrow$

Test 2. Preparing of Ni (II) ammine complex

Treat 2-3 drops of nickel (II) sulfate solution with some drops of sodium hydroxide solution and mark the color of nickel (II) hydroxide precipitate. Dissolve a prepared precipitate in 1-2 ml of 25 % ammonia solution. Mark a color of a prepared solution. Give a systematic name to the prepared complex compound. Write the chemical equations of fulfilled reactions:

 $NiSO_4 + NaOH \rightarrow Ni(OH)_2 + 6NH_3 \rightarrow Ni(OH)_2 + Ni$

Preparing of anionic complexes

Test 3. Preparing of Bi (III) acido complex

Pour 3-4 drops of bismuth (III) nitrate solution into a test tube and add some drops of potassium iodide up to the formation of dark bismuth (III) iodide precipitate. Dissolve the obtained precipitate in 1-2 ml of potassium iodide solution. What is the color of a prepared solution? Give a systematic name to the prepared complex compound. Write the chemical equations of fulfilled reactions:

Bi $(NO_3)_3 + KI \rightarrow$ BiI₃ + KI \rightarrow

Test 4. Preparing of hydroxo complex

Pour 3-4 drops of chromium salt solution into test tube and treat it with 2-3 drops of sodium hydroxide solution up to the formation of precipitate. Mark the color of prepared precipitate and dissolve it in the excess of alkali solution. Mark the color of prepared solution and give systematic name for the hydroxo complex. Write the equations of the reactions:

$$CrCl_3 + NaOH \rightarrow Cr(OH)_3 + 3NaOH \rightarrow Cr(OH)_3 + 3Na$$

Preparing of chelate coordination compound

Add 3 drops of iron (III) chloride solution to two test tubes. Leave one as a control, and add 3 drops of an alkali solution to the other. Add 12-15 drops of 1 M oxalic acid solution to the resulting

precipitate until it is completely dissolved. Add 1 drop of 0.01 M of NH₄CNS solution to both test tubes, which forms a red-blood colored solution of iron (III) rhodanide (thiocyanate) Fe(CNS) salt with Fe^{3+} ions. In which of the test tubes is coloring observed? Write the equations of the reactions:

$$FeCl_{3} + 3NaOH \rightarrow Fe(OH)_{3} \downarrow + 3NaCl$$

red-brown ppt
$$HO - C = O \qquad O - C = O$$
$$HO - C = O \qquad Fe \qquad O - C = O$$
$$O = C - O \qquad O = C - OH$$
$$O = C - OH$$
$$O = C - OH$$
$$HO = C - O \qquad HO = C - OH$$
$$O = C - OH$$
$$HO = C - O \qquad HO = C - OH$$
$$HO = C - OH$$
$$HO = C - OH$$

*Test reaction for Fe*³⁺: FeCl₃ + 3NH₄SCN \leftrightarrow Fe(SCN)₃ + 3NH₄Cl red blood sln

Make a conclusion about stability of chelate complex compounds.

Control over the assimilation of the topic

It is conducted in the form of written independent work of students.

QUESTIONS FOR SELF-CONTROL OF KNOWLEDGE

1. Structure of complex compounds: Werner's theory. Define the following terms: coordination compounds, complexing agent, ligands, coordination number. What is deference between unidentate, bidentate and polydentate ligands.

2. Classification and nomenclature of complex compounds. Structure of molecules of intracomplex compounds. Give examples of chelate complexes.

3. Equilibria in solutions of the complex compounds. Instability and stability constants. The complexing ability of ions of s-, p- and d-elements.

4. Methods of obtaining complex compounds.

5. Biological role of coordination compounds. The use of complex compounds in medicine.

Exercises for the self – control

1. Calculate the electric charges of the following complex ions:

 $[Ni^{+2}(CN)_4]; [Cr^{+3}(NH_3)_6]; [Zn(OH)_4]; [Pt^{+4}(NH_3)_4Cl_2]; [Cr^{+3}(CN)_4Br_2].$

Make up the formulas of complex compounds by adding ions of the outer sphere. Give systematic names for the obtained compounds.

2. Determine oxidation and coordination numbers of central atoms in the following coordination compounds:

 $\label{eq:K2} \begin{array}{lll} K_2[PtBr_4]; & Na_4[Fe(CN)_6]; & [Pb(NH_3)_6]SO_4; & [Cu(H_2O)_4]SO_4; & [Cr(NH_3)_5Cl]Cl_2; \\ K[Co(H_2O)_2(NO_2)_4]. \end{array}$

Give their systematic names.

3. Write formulas for the following complex compounds:

a) tetraamminedicyanoplatinum (IV) bromide;

b) ammonium diaquatetranitrocobaltate (III);

c) potassium bromopentanitroplatinate (IV);

d) tetraamineaquadichlorocobalt (III) chloride;

e) sodium hexacyanochromate (III);

f) diamminetetrachloroplatinum (IV);

g) potassium octacyanomolybdate (IV);

h) sodium tetrahydroxoplumbate (II);

i) ammonium tetrafluoroargentate (I);

j potassium tetracyanoaurate (III).

4. Write equations for primary and secondary ionization of the following coordination compounds:

a) $Na_3[FeF_4Cl_2];$

c) $[Al(H_2O)_6]_2(SO_4)_3;$

b) [CoCl(NH₃)₄H₂O]Cl₂;

d) $K_3[Cu(CN)_4]$.

Write expressions for K_{ins} of their complex ions. Name the complex compounds.

QUESTIONS FOR INDEPENDENT WORK OF STUDENTS (IWS)

1. Bioligands.

2. Factors affecting the stability of complex compounds.

LIST OF SOURCES USED

1. Medical chemistry : textbook for students of higher education establishments – med. univ., inst. and acad. / V.O. Kalibabchuk, V.I. Halynska, L.I. Hryshchenko et al. ; ed. by V.O. Kalibabchuk. – 6th ed., corr. – Kyiv : AUS Medicine Publishing, 2018. – P. 16-23.

2. Основы химии для иностранных студентов = Essential chemistry for foreign students : учебно-методическое пособие / С. В. Ткачёв [и др.]. – 5-е изд. – Минск : БГМУ, 2018. – С. 106-112. – Режим доступа: <u>http://rep.bsmu.by:8080/han-dle/BSMU/21054.</u>

3. Общая химия : учеб. пособие для студентов лечебного факультета, обучающихся на английском языке. В двух частях. Часть 2. = General Chemistry : Educational guidance for students medical department in English medium. In two parts. Part 2. – В. А. Филиппова, А. В. Лысенкова, Л. В. Чернышева. – Гомель : УО «Гомельский государственный медицинский университет», 2013. – 180 с. – URI: http://elib.gsmu.by/handle/GomSMU/10939.