

Synthesis, Characterization and Physico-chemical Properties of Novel Mixed Ligand Platinum(II) Complexes with Nitrogen and Sulfur Atoms

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Abstract: - Recently, a keen interest of researchers has been caused by the purposeful construction of compounds based on multinuclear complexes of transition metals as a new range of molecular biologically active substances. The analysis according to known datum of investigation of mixed ligand complexes (MLC) of the transition d-metals indicates that their constitutions and structures depend on condition of synthesis, nature of donor atoms and initial compounds of d-metals. In presented paper the results of physico-chemical investigation of synthesized individual and mixed ligand platinum(II) complexes with ethylene-aminoacetic and mercaptoacetic acids were given. The technique of synthesis of individual and mixed ligand platinum(II) complexes with ethylene-diaminoacetic and mercaptoacetic acids has been developed. The structures, thermoprecipitation processes and physico-chemical properties of the mentioned compounds have been studied by elemental analysis, IR-spectroscopy, thermography and conductometric method. When the obtained complex compounds interact with test-microorganisms they indicate antimicrobial activity.

Key-Words: - Synthesis, Mixed ligand, Platinum(II) complexes, Nitrogen and Sulfur Atoms, Complex formation, Physico-chemical properties, Antimicrobial activity.

1 Introduction

Coordination chemistry of transition metals with stable nitro-sulfide radicals and mixed ligand complexes (MLC) belongs to one of the most actively developing areas of modern inorganic chemistry. The number of such multinuclear complexes is constantly growing, and new features in the chemical behavior and physical properties of these compounds are found. Recently, a keen interest of researchers has been caused by the purposeful construction of compounds based on multinuclear complexes of transition metals as a new range of molecular biologically active substances. The analysis according to known datum of investigation of MLC of the transition elements (d-metals) indicates that their constitutions and structures depend on condition of synthesis, nature of donor atoms and initial compounds of d-metals. Recently among MLC of d-metals the reagents based on MLC of platinum(II) become promising. Interest to investigation of MLC of Pt(II) is related to their possession of biological activity [1, 2]. MLC platinum (II) with different sulfur and nitrogen ligands have been investigated insufficiently [3, 4].

For example, MLC platinum(II) with mercaptoacetate HSCH_2COOH was learned in [5],

where synthesized complexes hold ethylene-diamine (or pyridine) as second component and have dimer fragments through triol bridges. However, individual and MLC Pt(II) with ethylene-diaminoacetic acid (EDDA) has not been studied yet, whereas complexes of mercaptoacetic acid of mononuclear type have not been obtained.

Due to unusual combinations of properties inherent in the nature of molecular compounds with mixed ligand complexes, they can find prospects for practical use in various fields. However, despite the progress in the chemical construction of MLC of active molecules, the question of their directed formation is far from complete solution. The development of principles for their production, as well as understanding of their inherent biological-structural correlations, is a fundamental problem. Among multinuclear transition metal complexes, complex compounds containing nitrogen and sulfur-containing mixed ligand components as a ligand are few.

In presented paper the results of physico-chemical investigation of synthesized individual and mixed ligand Pt(II) complexes with ethylene-aminoacetic and mercaptoacetic acids were given.

2 Experimental Part

Mercaptoacetic acid HSCH_2COOH of "Serva" company and ethylene-diaminoacetic acid $\text{HOOCH}_2\text{CN}-\text{CH}_2\text{CH}_2-\text{NCH}_2\text{COOH}$ of "Rolan" company have been taken without additional purification. Disodium salt of EDDA has been obtained by neutralization of carboxyl group with NaOH by sequentially concentrating, evaporating and solidifying by ethanol. IR-spectra of the synthesized complex compounds as suspension in vaseline and fluoridated oils and as tablet with KBr have been drawn by spectrometers "Thermo scientific, Nicolet IS.10" and "Bruker IFS-113V" (the spectral range is 200-500 and 400-4000 cm^{-1} respectively). The interpretation of the IR-spectra has been accomplished by known method considering reference data [6-8].

The average molar electroconductivity of prepared aqueous and aqueous-alcohol solutions of the synthesized complexes has been measured by conductometric method with conductometer KEL-1142 at 25°C. Thermal resistances of the complexes were studied by "STA 449 F3 Yupiter" derivatograph of "NETZSCH" company at 20-800°C temperature limit and at 10 degree/min heating rate. Chemical analysis of the compounds has been carried out according to known techniques [9-11].

2.1 Synthesis Procedure

Synthesis of $[\text{Pt}(\text{EDDA})(\text{NH}_3)_2]\text{Cl}_2$. 0.4733g (0.4171mol) of the complex $[\text{Pt}(\text{NH}_3)_4]\text{Cl}_2$ was dissolved in 25ml of distilled water, filtered and heated up to 50°C. 0.2712g (1.5580 mol) of EDDA with 10% excess of ligand was added into hot solution mixing continuously. pH of reaction mixture reached 6 by adding 15%-HCl solution. Then reaction mixture evaporated up to small bulk at 70°C. Precipitation is filtered and washed with cold (iced) water, then with ethanol and sulfuric ester. Afterwards precipitation was dried on air and in vacuum-desiccator over solid CaCl_2 up to constant mass. The obtained compound dissolves in hot water and ethyl alcohol. Yield is 0.5531g (82% weight).

The found mass %: Pt – 40.66; N – 11.52; Cl – 14.70; C – 15.03; H – 13.51. For $\text{C}_6\text{H}_{18}\text{O}_4\text{N}_4\text{PtCl}_2$. The calculated mass %: Pt – 40.98; N – 11.76; Cl – 14.89; C – 15.13; H – 13.44.

Synthesis of $[\text{Pt}(\text{SCH}_2\text{COOH})_2(\text{NH}_3)_2]$. 0.3641g (1.0901mol) of $[\text{Pt}(\text{NH}_3)_4]\text{Cl}_2$ complex was dissolved in 20 ml distilled water, then filtered and

heated up to 45-50°C. 0.2007 g (2.1786 mol) ligand – mercaptoacetic acid HSCH_2COOH was added into prepared hot $[\text{Pt}(\text{NH}_3)_4]\text{Cl}_2$ solution with stirring. Reaction mixture was heated up to 60°C with stirring, then evaporated in water bath up to small bulk. With cooling for 2 days, yellow precipitation fell from the reaction mixture. After complete precipitation, it was washed with cold (iced) water, then with ethanol and sulfuric ester. Later, precipitation was dried on air, then in vacuum-desiccator over solid CaCl_2 up to constant mass. The obtained compound dissolves in water and in ethyl alcohol. Yield per % weight is 0.3425g (76.4% weight).

The found mass %: Pt – 47.59; N – 6.94; S – 15.71; C – 11.77; H – 3.03. For $\text{C}_4\text{H}_{12}\text{N}_2\text{S}_2\text{O}_4\text{Pt}$. The calculated mass%: Pt – 47.43; N – 6.80; S – 15.59; C – 11.68; H – 2.91.

Synthesis of $[\text{Pt}(\text{EDDA})(\text{SCH}_2\text{COOH})_2]$. 0.3477g (0.6283 mol) of $[\text{Pt}(\text{EDDA})(\text{NH}_3)_2]\text{Cl}_2$ was dissolved in 20 ml of distilled water and filtered. 0.1345g (1.4606 mol) of ligand mercaptoacetic acid - HSCH_2COOH was added into this solution with stirring. Reaction mixture was evaporated in water bath at 60°C up to small bulk. With cooling small light-yellow crystalline precipitation fell off the reaction mixture. The obtained precipitation was dried on air and in vacuum-desiccator over solid CaCl_2 up to constant mass. The obtained compound dissolves in hot water and ethyl alcohol. Yield per % weight is 0.1261g (80.7% weight).

The found mass %: Pt – 35.43; S – 11.70; N – 5.17; C – 21.86; H – 3.38. For $\text{C}_{10}\text{H}_{18}\text{N}_2\text{S}_2\text{O}_8\text{Pt}$. The calculated mass%: Pt – 35.25; S – 11.58; N – 5.06; C – 21.70; H – 3.25.

$[\text{Pt}(\text{OOCH}_2\text{CN}(\text{CH}_2)_2\text{NCH}_2\text{COO}^-)]$ synthesis. This complex compound has been obtained by two ways. 0.3726g (1.1156 mol) of $[\text{Pt}(\text{NH}_3)_4]\text{Cl}_2$ complex was dissolved in 20 ml distilled water, filtered and heated up to 50°C. Then 0.2438g (1.2827 mol) of 15%-excess of disodium salt of ethylene-diaminoacetic ligand that was dissolved in 10 ml of distilled water was added into this hot solution with stirring. pH of the reaction mixture reached 8.5 alkalizing with NaOH base, the mixture was evaporated in water bath up to small bulk. With cooling flaky white-iridescent precipitation fell down. After this procedure precipitation was dried on air, following in vacuum-desiccator over solid CaCl_2 up to stable mass. The obtained compound dissolves in hot water. Yield is 0.2977g (72.3% weight).

The found mass %: Pt – 52.9; N – 7.71; C – 19.66; H – 2.91. For $C_6H_{10}N_2O_4Pt$. The calculated mass %: Pt – 52.84; N – 7.58; C – 19.52; H – 2.70.

3 Results and Discussion

Below we consider the results of the analysis of competing methods that are used to synthesize compounds with MLC. Mixed ligand complexes are kinetically stable both in solution and in the solid state, which makes them convenient objects in a synthetic sense. The high symmetry of molecules with respect to donor fragments is favorable for the implementation of the bridge function and, therefore, for the construction of multidimensional structures.

The comparison of IR-spectrum of the neutral ligands and synthesized complexes - *cis*-[Pt(EDDA)(NH₃)₂]Cl₂ (I), *trans*-[Pt(SCH₂COOH)₂(NH₃)₂] (II), *cis*-[Pt(EDDA)(SCH₂COOH)] (III) and [PtEDDA] (IV) allows to determine uniquely the structure and the coordination way of their ligands. In the IR-spectrum of the used ligands the observed asymmetric intensive bands of adsorption whose frequencies (ν , cm⁻¹) are 1686 и 1690 cm⁻¹ have been related to neutral carboxyl group of EDDA and HSCH₂COOH ligands, respectively.

In the IR-spectrum of the disodium salt of the ligand – EDDA that contains diacetic anions one intensive asymmetrical adsorption band with 1582 cm⁻¹ frequency was observed. In the IR-spectrum of *cis*-[Pt(EDDA)(NH₃)₂]Cl₂ complex at 1690 cm⁻¹ observed adsorption band does not change during transferring from neutral acid to the complex. It indicates that the chelating of the ligand does not carry out in the complex (I) through oxygen atom of the carboxyl groups. In the IR-spectrum of the complex (I) observed within 3300-3280 cm⁻¹ frequency wide and accurate band was related to coordinated NH-group. The adsorption bands within 3400-3350 cm⁻¹ frequency are specific to free NH-groups of the ligand. The observed adsorption bands in the IR-spectrum of the complex (I) are different for coordinated ammonia ($\nu_{Pt-N} = 446.5$ cm⁻¹; $\nu_{N-H} = 1580$ and $\rho = 948$ cm⁻¹) and for NH-group of the ligand ($\nu_{Pt-N} = 350.4$ cm⁻¹; $\nu_{N-H} = 1562$ cm⁻¹). It signals non-equivalency of the coordinated atoms of nitrogen in the complex. *Cis*-position of the complex (I) is proven according to expression of Pt-N bond in the complex (I) by two adsorption bands

and according to its dependency on known rule of fluctuating selection [11]. Significant change of frequencies of valent fluctuations ν_{NH} arises analogously in consequence of forming of hydrogen bonds in the complex (I).

In the IR-spectrum of HSCH₂COOH ligand there is adsorption band of fluctuation 2561 cm⁻¹ specific for SH-groups. This adsorption band is absent in the IR-spectra of *trans*-[Pt(SCH₂COOH)₂(NH₃)₂] (II) and *cis*-[Pt(EDDA)(SCH₂COOH)₂] (III) which indicates formation of deprotonated SH-groups as a result of coordination of the ligand with metal through sulfur atom. Adsorption bands that belong to Pt-S bond showed up in the IR-spectra of complexes (II) and (III) within low frequency range. There is one adsorption band at 368 cm⁻¹ for *trans*-complex II and there are two ones at 360 and 372 cm⁻¹ for *cis*-complex (III).

The existence of just one adsorption band belonging to Pt-S bond in the IR-spectrum of complex (II) attests to *trans*-position, but existence of two bands indicates *cis*-position of ligands in the complex. Furthermore, one accurate adsorption band at 510 cm⁻¹ in the IR-spectrum of complex (II) was attributed to Pt-N bond by us [12]. The asymmetrical IR-bands – 1694 and 1689 cm⁻¹ of carboxyl groups participating in the ligands, respectively in the complexes (II) and (III) prove latter.

The ligand – EDDA is coordinated bidentately *cis*-position through two nitrogen atoms forming one metal chelate ring. The existence of two accurate IR-bands in 453 and 470 cm⁻¹ ($\delta_{N-H} = 1567$ cm⁻¹) frequencies is confirmed in the complex (III). In other words, in that case imperative *cis*-coordination of mercaptoacetic acid arises. When the complex (I) is treated in an alkaline medium the carboxyl group of the ligand – EDDA is deprotonated. Two molecules of ammonia are substituted and tetradentate coordination of the ligand in the complex (IV) develops in the coordination sphere of the complex forming three penta-membered metal chelate cycles.

We attributed observed adsorption bands 510 and 496 cm⁻¹ $\delta_{N-H} = 586$ cm⁻¹ located in *cis*-position to each other in the IR-spectrum of the complex (IV) to the valence bond ν_{Pt-N} . For valence fluctuation within 1592 and 1580 cm⁻¹ range asymmetric adsorption bands that belong to acetic anions were observed. When the complex (IV) is treated with concentrated hydrochloric acid, it is obvious that penta-membered metal chelate cycle is opened, chlorine atoms get into the coordination sphere and the [Pt(EDDA)Cl₂]-composited complex is formed.

An elemental analysis of the $[\text{Pt}(\text{EDDA})\text{Cl}_2]$ complex goes with following constitution.

The found mass %: Pt – 44.25; Cl – 16.19; N – 6.41; C – 16.51; H – 2.83. For $[\text{Pt}(\text{EDDA})\text{Cl}_2]$. The calculated mass %: Pt – 44.13; Cl – 16.03; N – 6.33; C – 16.30; H – 2.71.

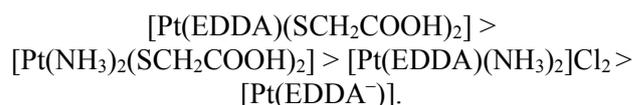
The IR-spectrum of the $[\text{Pt}(\text{EDDA})\text{Cl}_2]$ complex within $1500\text{--}4000\text{ cm}^{-1}$ is analogous with spectrum of the complex (I). In the low-frequency range of IR-spectrum the observed adsorption bands 346 and 351 cm^{-1} were attributed to $\nu_{\text{Pt-Cl}}$ valence bond. In the $[\text{Pt}(\text{EDDA})\text{Cl}_2]$ complex ethylene-diaminoacetate and chlorine atoms were coordinated in the cis-position relative to each other.

Thermogravimetric studies of the obtained complexes I-IV showed that their thermal decomposition occurs differently depending on their constitutions and structures. The complexes I, III and IV are stable up to 276.240 and 258°C , respectively. A rupture of the ligands in the complexes II and IV that were accurately fixed on the thermograms occurs in two stages. The complex II is stable until 315°C which is proved by accurate area of TG curve, then the complex decomposes that is accompanied by occurrence of two exothermic effects at 355 and 410°C . The decomposition process of the complex II finishes at 475°C . The decomposition of the complex IV begins at 258°C and occurs at different rates within $258\text{--}485^\circ\text{C}$. Some exothermic effects were marked on the DTA curve at 320 , 430 and 450°C . Maybe the last exo-effect is related to partial formation of platinum oxide.

Determination of average molar electro-conductivity (μ) of $1 \times 10^{-3}\text{M}$ of aqueous solution of the synthesized complexes demonstrate their electrolyte feature. Namely, for example, when the reaction is carried out with initial reagents with regard to $\text{M:L}=1:2$ ratio, electrolyte like 1:2 is formed during synthesis of mixed $[\text{Pt}(\text{EDDA})(\text{SCH}_2\text{COOH})_2]$ -composed complex.

The technique taken from [13-15] reference has been applied for determination of antimicrobial activity of the synthesized complexes of platinum(II). The relative antimicrobial activities of the complexes (I-IV) were evaluated by value of the minimum bactericidal concentration (MBC) in the proper microbial load. The investigation of the biological activity of the synthesized complexes indicates that they are biologically active. Microbes taken from various systematic groups were used as test-microorganisms: staphylococcus, diphtheria, grass bacillus, anthrax, and coliforms.

The results of the experiments showed that there is function between activities of compounds and their constitutions, concentrations, contact time, and also kind of bacteria. The consequence of some complexes per antimicrobial activity with their lability range has been determined arraying of obtained results indescending order per growth of microbes. It was found that the sequence of the range of Pt(II) complexes with mixed ligands per antimicrobial activity correlates according to following lability range:



As seen from installed range the most selective, antimicrobial active is cis- $[\text{Pt}(\text{EDDA})(\text{SCH}_2\text{COOH})_2]$ complex (III). After that complex (III) can be tested, for example, in infected wound as model, then in the content of multicomponent antimicrobial drugs (jellies, ointments and polymer films) for treatment of experimental infected wound. The physico-chemical parameters of the synthesized complexes were shown in the Table 1 and 2.

Table 1. The decomposition temperature and molar electro-conductivity of synthesized mixed Pt(II) complexes (No 1-4)

Synthesized complexes of Pt(II)	Decomposition temperature, $^\circ\text{C}$	Molar electro-conductivity, $\text{Sm} \cdot \text{cm}^2 \cdot \text{mol}^{-1}$
1	275	221
2	315	28
3	240	47
4	258	42



Table 2. The solubility and relative antimicrobial activity of synthesized Pt(II) complexes (No 1-4)

Synthesized complexes of Pt(II)	Solubility, g/10 ml H ₂ O	Relative antimicrobial activity of synthesized Pt(II) complexes
1	0.76	Gold staphylococcus (strong)
2	0.89	Coliform (medium)
3	0.82	Candida (medium)
4	0.66	Serratia (medium)

Finally, we note the following. To obtain efficient exchange-coupled mixed-ligand complexes of platinum (II), it is necessary to implement the direct coordination of the nitro-sulfide group with a metal ion. However, the mixed ligand complexes are weak donors and by their nature are organic compounds, hence dissolve well in non-polar solvents. Salts of metals, on the contrary, dissolve well in polar media and coordinate primarily high-polar molecules. For this reason, the metal must be introduced into interaction with the mixed ligand complexes in the form of a specially created transition matrix, which: firstly, ensures the solubility of the metal-containing component in non-polar organic media, secondly, increases its acceptor capacity to the extent that the metal ion could coordinate the nitro-sulfide group. At the early stage, it is necessary to introduce coordinated ligands, easily substitutable with nitro-sulfide, into the multinuclear metal-containing matrix. Such stringent requirements for a metal-containing matrix lead to the fact that the range of such matrices is rather limited. Example of the effective ligand in the construction of such multinuclear compounds is trimethyl acetate anion, since its branched group ensures the solubility of compounds in low-polar organic media, and tendency to realize bridge function of the carboxylate fragment contributes to the formation of multinuclear complexes. If these multinuclear complexes are present on the

periphery of weakly bound ligands, such as acetone, it becomes possible to substitute them with radical molecules, which can lead to the formation of bioactive compounds.

4 Conclusion

Hence, the synthesizing technique of individual and mixed ligand complexes of platinum(II) with ethylene-diamino-diacetic and mercaptoacetic acids has been worked on. Their structures, process of thermal decomposition, physico-chemical and antimicrobial properties have been studied. The obtained individual and mixed ligand platinum(II) complexes with ethylene-diamino-diacetic and mercaptoacetic acids are bi and tetradentately coordinated depending on condition of synthesis of EDDA. But in the complex with mercaptoacetic acid the latter is coordinated just monodentately through sulfur atom of deprotonated sulfhydryl group of the ligand. All complexes (I-IV) are decomposed without melting and final product of thermolysis is metallic platinum.

In the future, the solution of the next problem is envisaged. When designing complex compounds, containing nitrogen- and sulfur-containing groups as a ligand, it is extremely important to obtain them in the form of single crystals, since only the presence of structural information makes it possible to process a biochemical experiment based on the choice of the model of the active structure of the complex. In addition, without knowledge of the structure of such complex compounds, it is impossible to carry out sound quantum-chemical calculations aimed at clarifying the mechanisms of exchange interactions.

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