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Synthesis and Study of Copper(II) Complexes with Aspartic Acid, Serine, and Valine

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Abstract — Binary and ternary copper(II) complexes with aspartic acid (H_2Asp), serine (HSer), and valine (HVal) were prepared by electrochemical and chemical procedures. The purity of the compounds was confirmed by elemental and thermogravimetric analyses. According to the IR spectra, all the complexes contain a five-membered chelate ring in which the Cu(II) atom is bonded with the oxygen atom of the carboxy group and nitrogen atom of the amino group. This is also confirmed by the ESR spectra.

Complexation of natural amino acids as components of proteins is of undoubted interest [1]. It is particularly urgent to study mixed-ligand complexes, since real biological systems simultaneously contain several substances capable of complexation with a metal ion. For example, it is known [2] that mixed-ligand complexes involving two amino acids play an important role in metal transport.

Copper is an essential trace element in a human body [3]; the majority of Cu(II) ions in blood plasma are in the form of mixed complexes with amino acids, peptides, and other biomolecules [4]. A series of mixed-ligand Cu(II) complexes with amino acids in solution were studied by polarography [5], UV spectroscopy [6], circular dichroism spectroscopy [7], ESR [8], potentiometry [6, 9–11], and voltammetry [12]; their stability constants were determined, and their structure in solution was discussed.

Examination of properties of solid mixed-ligand complexes can reveal relationships between the bioactivity of a compound and its composition and structure. Despite numerous papers concerning complexation of Cu(II) ions with amino acids, the structure and properties of solid binary and ternary compounds are studied insufficiently. This may be caused, in particular, by the fact that it is difficult to prepare and isolate these compounds pure. Previously [13, 14] we suggested a procedure for anodic synthesis of binary compounds of *d* elements with various organic ligands, showing advantages as compared to common chemical synthesis of these compounds. We determined the range of potential difference between the electrodes of the electrochemical cell, at which the compounds could be prepared in high yields (90–95%) without side anodic processes.

The goal of this study was to examine the possibility of electrochemical synthesis of mixed-ligand complexes in various media, to compare the results with those yielded by chemical synthesis, and to determine the physicochemical properties of the complexes.

We found that pure organic solvents (acetonitrile, ethanol, dioxane, dimethylformamide, dimethyl sulfoxide) are unsuitable for electrochemical synthesis, because amino acids are poorly soluble in them.

Evaluation of the solubility of 1 : 1 amino acid mixtures (H_2Asp–HVal, H_2Asp–HSer) in aqueous-organic solvents showed that acceptable solubility (~0.05 M) is provided by water–ethanol (60–90% alcohol) and water–dioxane (80–90% dioxane) mixtures. When amino acids are taken in a 1 : 1 ratio, the relative content of the CuLL′ species in the near-electrode space is several times higher than that of the binary complexes because of the higher stability of the mixed-ligand complexes ($\Delta \log K$ ~1 [5, 8–11]); therefore, the mixed complexes should precipitate first.

Because of the low electrical conductivity of the nonaqueous systems, we added a supporting electrolyte (lithium perchlorate). The resulting solutions tended to supersaturation, which complicated isolation of the synthesis products.

With pure water as solvent, the reaction can be performed without supporting electrolyte, since the electrical conductivity of the solution is provided by ligand dissociation. In this case, the reaction system is the simplest and contains no foreign ions which might compete in the complexation. The schemes of the electrode processes in synthesis of binary and mixed-ligand complexes are similar.

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Table 1. Color and composition of electrochemically synthesized compounds, according to elemental and titrimetric analysis

Comp. no.	Color	Found, %				Formula	Calculated, %			
		C	H	Cu	N		C	H	Cu	N
I	Blue	22.15	5.45	14.67	6.46	$C_8H_{24}CuN_2O_{14}$	22.05	5.55	14.58	6.43
II	Blue-violet	34.29	7.33	18.07	8.04	$C_{10}H_{26}CuN_2O_7$	34.33	7.49	18.16	8.01
III	Bog green	23.45	5.34	20.72	8.98	$C_6H_{16}CuN_2O_8$	23.42	5.24	20.65	9.10
IV	Dark blue	32.87	5.42	19.36	8.42	$C_9H_{18}CuN_2O_7$	32.78	5.50	19.27	8.49
V	Dark green	23.74	5.21	17.89	7.89	$C_7H_{18}CuN_2O_{10}$	23.77	5.13	17.96	7.92

At anode:

$$Cu + 2HL - 2e \longrightarrow CuL_2 + 2H^+,$$
$$(Cu + HL + HL' - 2e \longrightarrow CuLL' + 2H^+),$$

At cathode:

$$2HL + 2e \longrightarrow H_2 + 2L^-.$$

As the complex migrates toward the cathodic space, the contribution of side reactions increases, so that the yield of the complex decreases to 80–85%.

At cathode:

$$CuL_2 + 2H^+ + 2e \longrightarrow Cu + 2HL,$$
$$(CuLL' + 2H^+ + 2e \longrightarrow Cu + HL + HL').$$

According to the analytical data (Table 1), the compounds prepared have the compositions $Cu(HAsp)_2 \cdot 6H_2O$ (**I**), $CuVal_2 \cdot 3H_2O$ (**II**), $CuSer_2 \cdot 2H_2O$ (**III**), $Cu(HAsp)Val \cdot H_2O$ (**IV**), and $Cu(HAsp)Ser \cdot 3H_2O$ (**V**). The purity of the compounds was confirmed by elemental and thermogravimetric analyses and by IR spectroscopy.

Comparative analysis of the complexes prepared chemically and electrochemically revealed only insignificant differences in their compositions. According to the elemental and thermogravimetric analyses, the complexes prepared by electrochemical synthesis contain smaller amount of water; the IR spectra of related complexes prepared chemically and electrochemically contain the same set of absorption bands.

According to thermogravimetric data, molecules of water of crystallization and coordinated water are removed from the compounds at low temperatures (up to 220°C, Table 2). The process is accompanied in all cases by a weak endothermic effect in the DTA curve. Heating to 300–350°C results in decomposition of the amino acid groups in the binary and ternary complexes, with intense weight loss observed in the TG curves. Further slight oscillation of the sample weight (within 3–5%) may be due to formation of nonstoichiometric copper oxides. The processes occur in the range 400–1000°C.

The IR spectra of all the complexes (Table 3) contain an absorption band at about 3400 cm^{-1}, belonging to the OH stretching vibrations and suggesting the presence of water molecules. In the IR spectra of the complexes, the antisymmetric stretching vibration frequency of the carboxy group (1635–1618 cm^{-1} for pure amino acids) decreases by 20–30 cm^{-1}, which is indicative of carboxylate coordination with the metal ion [15].

In the IR spectra of the serine complexes, the antisymmetric stretching vibrations of the carboxy group and bending vibrations of the amino group give a broad band at 1627–1600 cm^{-1}.

The spectra of aspartic acid and its complexes contain a band (shoulder) at 1690 cm^{-1} belonging to the stretching vibrations of the un-ionized carboxy group. This fact indicates that one of the carboxy groups is not involved in the coordination.

The stretching vibrations of the protonated amino group (antisymmetric at 1560–1597 cm^{-1} and symmetric at 1502–1506 cm^{-1}) [15] in the spectra of the complexes are lacking, but the NH_2 bending band is observed at 1627 cm^{-1}, suggesting the coordination of the amino group with the Cu(II) ion. This is also indicated by the presence of the Cu–N vibration bands in the spectra of all the complexes at 570–589 cm^{-1} [16] and of two absorption bands in the ranges 3153–3290 and 3310–3315 cm^{-1}, corresponding to the NH_2 stretching vibrations [17].

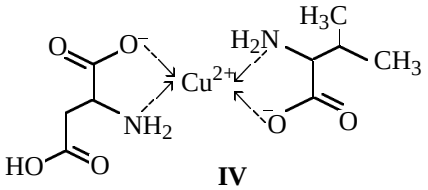
The above data show that all the complexes contain a five-membered chelate ring, with the copper ion bonded to the oxygen atom of the carboxy group and nitrogen atom of the amino group.

The ESR spectra of the mixed-ligand complexes, recorded at room temperature from the powders, suggest the axial symmetry of the nearest surrounding of

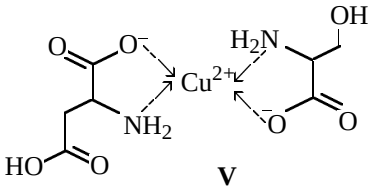
Table 2. Thermogravimetric data for the compounds prepared electrochemically

Comp. no.	Temperature range, °C	Weight loss, mg (%)	Assignment
I	80–220	10 (24.17)	$-H_2O$
	220–420	24 (58.01)	$-C_8H_{24}O_{14}N_2$
	420–1000	7.37 (17.82)	Formation of CuO + Cu_2O
II	40–190	6 (16.98)	$-H_2O$
	190–550	22 (62.27)	$-C_{10}H_{26}O_7N_2$
	550–1000	7.33 (20.75)	Formation of CuO + Cu_2O
III	60–170	6 (12.91)	$-H_2O$
	170–400	30 (64.53)	$-C_6H_{16}O_8N_2$
	400–1000	10.49 (22.56)	Formation of CuO + Cu_2O
IV	40–220	3 (7.19)	$-H_2O$
	220–420	30 (71.98)	$-C_9H_{18}O_7N_2$
	420–1000	8 (19.19)	Formation of CuO + Cu_2O
V	60–190	6 (16.80)	$-H_2O$
	190–420	24 (67.23)	$-C_7H_{18}O_{10}N_2$
	420–1000	5.7 (15.97)	Formation of CuO + Cu_2O

the metal ion; the spin Hamiltonian parameters (for **IV**: $g_\perp$ 2.085, $g_\parallel$ 2.240; for **V**: $g_\perp$ 2.091, $g_\parallel$ 2.235) correspond to the planar structure of the coordination core with the *trans* arrangement of the carboxy and amino groups [18, 19].



IV



V

Formation of the *trans* isomers under the synthesis conditions may be due to the higher stability of this structure in complexes with glycine derivatives, which was proved by quantum-chemical calculations [20].

Thus, we demonstrated the feasibility of the anodic synthesis of mixed-ligand copper(II) complexes with two different amino acids; it is preferable to perform the synthesis in water.

EXPERIMENTAL

The IR spectra in the range 350–4000 cm^{-1} were recorded on an Infralyum FT-02 spectrometer (mulls in mineral oil). The ESR spectra were taken on a Radiopan SE/X-2543 spectrometer. The magnetic field was determined with a built-in JTM-6 NMR magnetometer. The frequency was determined accurately using diphenylpicrylhydrazyl as reference.

The TG curves (20–1000°C) were taken on an

Table 3. Assignment of bands in the IR spectra of amino acids and their complexes

Compound	IR spectrum, cm^{-1}
H_2Asp	3138 m [$\nu_{as}(^+NH_3)$], 1690 m [ν(COOH)], 1618 s [$\delta_{as}(COO^-)$], 1560 s [$\delta_{as}(^+NH_3)$], 1502 s [$\delta_s(^+NH_3)$], 1419 m [$\nu_s(COO^-)$]
H_2Ser	~3400 br [ν(OH)], 3120 m [$\nu_{as}(^+NH_3)$], 1635 s [$\nu_{as}(COO^-)$], 1574 s [$\delta_{as}(^+NH_3)$], 1506 s [$\delta_s(^+NH_3)$], 1432 s [$\nu_s(COO^-)$]
HVal	3129 m [$\nu_{as}(^+NH_3)$], 1621 s ν_{as}[(COO^-)], 1597 s [$\delta_{as}(^+NH_3)$], 1505 s [$\delta_s(^+NH_3)$], 1416 m [$\nu_s(COO^-)$]
I	~3400 br [ν(OH)], 3268 s [$\nu_{as}(NH_2)$], 3157 s [$\nu_s(NH_2)$], 1627 s [$\delta(NH_2)$], 1593 s [$\nu_{as}(COO^-)$], 1408 m [$\nu_s(COO^-)$], 582 m [νMN)]
II	~3420 br [ν(OH)], 3244 m [$\nu_{as}(NH_2)$], 3290 sh [$\nu_s(NH_2)$], 1570 m [$\delta(NH_2)$], 1617 s [$\nu_{as}(COO^-)$], 1392 sh [$\nu_s(COO^-)$], 582 m [ν(MN)]
III	~3400 br [ν(OH)], 3315 m [$\nu_{as}(NH_2)$], 3237 m [$\nu_s(NH_2)$], 1623 s [$\delta(NH_2)$], 1623 s [$\nu_{as}(COO^-)$], 1396 m [$\nu_s(COO^-)$], 589 m [ν(MN)]
IV	~3400 br [ν(OH)], 3265 s [$\nu_{as}(NH_2)$], 3153 s [$\nu_s(NH_2)$], 1627 br [$\delta(NH_2)$], 1586 s [$\nu_{as}(COO^-)$], 1398 sh [$\nu_s(COO^-)$], 573 m [ν(MN)]
V	~3400 br [ν(OH)], 3310 s [$\nu_{as}(NH_2)$], 3234 s [$\nu_s(NH_2)$], ~1600 br [$\delta(NH_2)$], ~1600 br [$\nu_{as}(COO^-)$], 1402 m [$\nu_s(COO^-)$], 570 m [ν(MN)]

MOM derivatograph (Hungary) using platinum crucibles, a Pt/Pt–Rh thermocouple, and aluminum oxide as reference. The sample weight was 50 mg, and heating rate, 10 deg min^{-1}.

For the electrochemical synthesis, we used asymmetric current with rectangular pulses, according to [21]; the process was performed in a glass three-electrode cell [22] with the working and auxiliary electrodes made from copper. The glass separator retained in the cathodic space the finely dispersed copper powder formed by cathodic reduction. The cell was temperature-controlled by passing water (25°C) through the jacket. The potential was maintained constant in the range 0.5–1.5 V with a 0.001 V accuracy using a PI-50.1.1 potentiostat controlled with a PR-8 programmer. Anodic decarboxylation of the ligand, in contrast to hydroxy acid systems [14], is observed only at a very large potential difference between the electrodes (~50 V). The current efficiency was determined with a copper coulometer or by measuring the current in the circuit and the electrolysis time.

The chemical synthesis of mixed-ligand complexes was performed by dissolving freshly prepared copper hydroxide in aqueous solutions of the ligands at the reactant molar ratio of 1 : 1 : 1 [11]. Copper hydroxide was added with heating on a water bath to a solution of a mixture of amino acids. After the precipitate ceased to dissolve, the solution was filtered, concentrated, and left to crystallize for a day. The crystalline precipitate was filtered off, dried in a desiccator over P_2O_5, and analyzed. Isolation of the complexes was complicated by formation of viscous solutions in the course of evaporation.

The copper content in the compounds was determined by complexometric titration with murexide [23], and the contents of C, H, and N, by elemental volumetric analysis.

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