

COMPLEX COMBINATIONS OF Cu(II) WITH MIXED LIGANDS

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abstract: This paper describes the synthesis and characterization of several Cu(II) complexes using 2,2'-bipyridin as a primary ligand and L-tyrosine, L-tryptophan and L-histidine as secondary ligands. Complex combinations were characterized through EPR spectra, IR-spectroscopy, electronic spectra, thermogravimetry analysis and elemental analysis. Analyzing the results we were able to determine the geometry of complex combinations that were obtained.

Introduction

Complex combinations of metal ions with amino acids are important because of their biological applications. In 1965 Szazuchin O. and his team studied the synthesis of complex combinations of Zn(II) and Ni(II) with amino acids: D-penicillamine and L-cysteine. These complex combinations have biological and therapeutic activities [1a].

Protein phosphorylation is recognized as an important step in information transfer and control of various biological processes such as enzyme activity [1b,2a]. X-ray structural studies have revealed that Serine phosphorylation of the active and less active forms of an allosteric enzyme muscle phosphorylase induces a conformational transition due to electrostatic or hydrogen bonds involving the phosphate moiety and histidine and arginine residues [2b,3]. A classical example of electrostatic interactions that play a vital role in enzyme activity is that revealed for a zinc enzyme carboxypeptidase A. In its complex with a substrate, glycyl-L-tyrosine, it fixes the substrate by electrostatic interactions between the carboxylate group of the substrate and the arginine guanidinium group of the enzyme [4]. Ternary Cu(II) complexes containing aromatic heterocycles such as phen and aromatic amino acids such as phenylalanine (Phe) and L-tyrosine (Tyr) have been shown to be stabilized by calculating the ring stacking equilibrium constant for a hypothetical equilibrium involving ternary species with and without stacking interactions [5]. X-ray crystal structure analysis of Cu(histamine)(L-Tyr) [6], Cu(phen)(L-Trp) [7], (Trp=tryptophan), Cu(bpy)(L-Trp) (bpy = 2,2'-bipyridine), [Cu(bpy)(L-Tyr)ClO₄].2H₂O [8] etc. revealed that the intramolecular stacking exists in the complex in the solid state.

This paper describes the synthesis and characterization of several Cu(II) complexes using 2,2'-bipyridin as a primary ligand and L-tyrosine, L-tryptophan and L-histidine as secondary ligands. We used this type of ligands to prove, by spectral measurements, that

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only complexes with a certain geometry can show π - π stacking intramolecular interactions. Characterization of the new prepared complexes was made by EPR spectra, IR-spectroscopy, electronic spectra, thermogravimetry analysis and elemental analysis.

Experimental

Reagents

The required chemicals were purchased from Merck and Chimopar Bucharest and all manipulations were performed using materials as received.

Physical measurements

The content of metallic ions was determined by atomic absorption spectroscopy with AAS 1N spectrometer Carl Zeiss Jena ; C, H, and N were analyzed with a Carlo Erba elemental analyzer. Elemental analyses were performed after drying the complexes at

60°C. Electronic spectra were recorded by the diffuse-reflectance technique, using MgO as diluting matrix, on a JASCO V-550 spectrophotometer. IR spectra were recorded with a BioRad FTS 135 spectrophotometer in the 4000-400 cm^{-1} region using KBr pellets. All the complexes were studied by thermogravimetry (TG) in static air atmosphere, with a sample heating rate of 10 °C/min. using DuPont 2000 ATG thermo balance. EPR spectra were obtained with an ART-6, model IFA-Bucharest, X-band spectrometer (9.01 GHz) on line with a PC equipped with a 100KHz field modulation unit, on polycrystalline powders and solutions at room temperature and 77K.

Synthesis of complexes

Synthesis of [Cu(bpy)(L-Tyr)NO₃].3H₂O(**1**)

Cu(NO₃)₂.3H₂O (1,21g, 5 mmol) and bpy (0,78g, 5mmol) were dissolved in 0,2 M HCl (25ml) by heating, and after cooling a solution of L-Tyr (0,91g, 5mmol) in 1 M NaOH (10 ml) was added. The mixture was concentrated in vacuo and kept at room temperature. The blue crystals which separated were collected and recrystallised from water. Anal. Calc. for C₁₉H₂₄N₄O₉Cu: C, 44,18; H, 4,65; N, 10,85; Cu, 12,40. Found: C, 44,87; H, 4,08; N, 10,15; Cu, 12,20%.

Synthesis of [Cu(bpy)(L-Trp)NO₃].H₂O(**2**) and [Cu(bpy)(L-histidine)NO₃].2H₂O(**3**)

These complexes were prepared by the method described above but using 1,02g

L-Trp (5 mmol) and 0,78g histidine (5mmol). The light-blue crystals which separated were collected and recrystallised from water. Anal. Calc. for [Cu(bpy)(L-Trp)NO₃].H₂O, C₂₁H₂₁N₅O₆Cu: C, 50,09; H, 4,17; N, 13,91; Cu, 12,72. Found: C, 50,83; H, 3,74; N, 13,78; Cu, 12,47%, and calc. for [Cu(bpy)(histidine)NO₃].2H₂O, C₁₅H₁₉N₇O₇Cu: C, 40,67; H, 4,23; N, 17,29; Cu, 13,55. Found: C, 40,89; H, 3,86; N, 16,93; Cu, 13,32%.

Results and Discussion

These complexes have a low solubility in chloroform, acetone, ethanol and water but they are insoluble in dimethylformamide (DMF).

The IR spectral data

In IR spectra of newly prepared complexes there are 3 bands assigned to NO_3^- ion bound to Cu(II) center: 1451 – 1456 cm^{-1} (ν_1), 1378-1393 cm^{-1} (ν_2), 1016-1040 cm^{-1} (ν_3) ranges. The splitting of the bands situated at higher wave numbers (ν_1 - ν_2) is about 60 – 70 cm^{-1} indicating the coordinate of nitrate ion in a monodentate fashion [9].

Also, the ν_{COO^-} bands shifts towards lower wave numbers while the ν_{COO^-} frequencies shift towards higher wave numbers compare to the positions of these bands in the IR spectrum of free aminoacid.

The $\delta_{\text{NH}(1)}$ and $\delta_{\text{NH}(2)}$ frequencies shift towards higher wave numbers in the IR spectra of the complexes together with the vanishing of the ν_{NH} frequencies. This behavior suggests the coordination of the aminoacid through $-\text{NH}_2$ and $-\text{COO}^-$ group in a bidentate fashion

Table 1. IR Spectral Data for the Ligands and their Complexes (cm^{-1}).

Compound	$\nu_{\text{COO}(s)}$	$\nu_{\text{COO}(as)}$	ν_{NH}	$\delta_{\text{NH}(1)}$	$\delta_{\text{NH}(2)}$	$\nu_{\text{C-N-C}}$	$\nu_{\text{C::N}}$	ν_{NO_3}
L- Tyrosine	1415	1583	3121	1662	1535	-	-	-
2,2'- bipyridina	-	-	-	-	-	-	1572	-
[Cu(bpy)(L-Tyr)NO ₃].3H ₂ O	1380	1621	-	1705	1578	-	1528	1456 1393 1040
L-Tryptophan	1393	1608	3103	1645	1520	1108	-	-
[Cu(bpy)(L-Trp)NO ₃].H ₂ O	1344	1630	-	1683	1568	1104	1530	1451 1382 1020
L-histidine	1387	1610	3112	1638	1517	1115	1580	-
[Cu(bpy)(histidin)NO ₃].2H ₂ O	1339	1652	-	1672	1560	1110	1580	1453 1541 1378 1534 1024

The $\nu_{\text{C::N}}$ frequency of 2,2'-bipyridine ligand shifts with 30 – 40 cm^{-1} towards lower wave numbers in the IR spectra of complexes compare to the IR spectrum of free ligand, thus indicating the coordination to Cu(II) through the two sp^2 hybridized nitrogen atoms. In the IR spectra of Cu(II) complexes with L-histidine as a secondary ligand there is an additional $\nu_{\text{C::N}}$ frequency in the 1531-1535 cm^{-1} range. This behavior indicates the coordination of L-histidine ligand through the sp^2 hybridized nitrogen atom.

The electronic absorption data

The electronic spectroscopy data for the complexes in solid state are presented in table 2.

The UV-VIS spectra of [Cu(bpy)(L-Tyr)NO₃].3H₂O and [Cu(bpy)(L-Trp)NO₃].H₂O complexes show two distinct bands at 11435 cm^{-1} and 14980 cm^{-1} for the former one and at 11790 cm^{-1} and 15120 cm^{-1} for the later complex. The position of these two bands is a strong indication of a square-pyramidal geometry [10].

Table 2. Electronic Spectral Data for Complexes in Solid State (cm⁻¹).

Compounds	Assignment d-d (cm ⁻¹)			Geometry
	$z^2 \rightarrow x^2 - y^2$	$xy \rightarrow x^2 - y^2$	$xz, yz \rightarrow x^2 - y^2$	
[Cu(bpy)(L-Tyr)NO ₃].3H ₂ O	11435	-	14980	Square-pyramidal
[Cu(bpy)(L-Trp)NO ₃].H ₂ O	11790	-	15120	Square-pyramidal
[Cu(bpy)(histidin)NO ₃].2H ₂ O	13125	16300	17230	Octahedral

The UV-VIS spectrum of [Cu(bpy)(L-histidine)NO₃].2H₂O complex shows two absorption bands at 16300 cm⁻¹ and 17230 cm⁻¹ and a third weak absorption band at 13215 cm⁻¹, suggesting a distorted octahedral geometry.

The coordination of sp² hybridized heterocyclic nitrogen atom of histidine in the axial position (for Cu(II) complexes with histidine) increases the splitting between d_{z²} and d_{x²-y²} orbitals as well as between d_{xz}, d_{yz} and d_{x²-y²} orbitals [11].

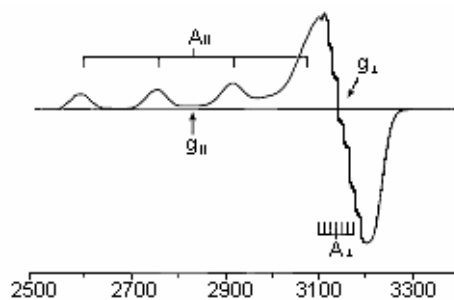
EPR spectra

EPR spectra in X-band for Cu(II) complexes **1**, **2**, **3** were recorded using ethanolic solutions at 77K.

Table3. EPR parameters of the complexes

Compounds	g_{\perp}	g_{\parallel}	A_{\parallel}	A_{\perp}
[Cu(bpy)(L-Tyr)NO ₃].3H ₂ O	2,03	2,18	152	13,8
[Cu(bpy)(L-Trp)NO ₃].H ₂ O	2,02	2,20	150	14,5
[Cu(bpy)(histidin)NO ₃].2H ₂ O	2,09	2,29	185	17

The frozen ethanolic solution spectra of [Cu(bpy)(L-Tyr)NO₃].3H₂O and [Cu(bpy)(L-Trp)NO₃].H₂O are identical, Fig 1, with g_{\perp} =2,03, g_{\parallel} =2,18 and A_{\parallel} =152 Gauss, respective g_{\perp} =2,02, g_{\parallel} =2,20 and A_{\parallel} =150 Gauss. The seven lines of hypersuperfine structure of EPR spectra indicates the presence of 3 nitrogen atoms around the Cu(II) ion [11]. The frozen ethanolic solution spectra of [Cu(bpy)(L-histidine)NO₃].2H₂O indicates that there are 4 nitrogen atoms around Cu(II) ion [11]. The splitting parameters g_{\perp} and g_{\parallel} values depend on the ground level occupied by the paramagnetic electron of Cu(II). Thus, if the ground state of Cu(II) is B_{1g}(d_{x²-y²) then the two parameters are related by the following relationship: $g_{\parallel} > g_{\perp} > 2,002$ and the complex shows an axial distortion [12].}

**Fig. 1.** Frozen solution EPR-spectra of [Cu(bpy)(L-Tyr)NO₃].3H₂O recorded at 77 K in ethanol.

Thermal Decomposition

The complexes of this study were investigated by thermogravimetry (TG). Experimental data for thermo gravimetric analysis are presented in table 4. The TG and DTG indicate a loss of weight from 90° –110°C corresponding to 3 molecules of water per mol of complex combination (1), one molecule of water per mol of complex combination (2), and 2 molecules of water per mol of complex combination (3).

Table 4. Experimental data for thermo gravimetric analysis

Compounds	Temperature range (°C)	Eliminated fragment	Weight lose	
			exp. %	calc. %
[Cu(bpy)(L-Tyr)NO ₃].3H ₂ O	90-110	3H ₂ O	10,08	10,46
	365-560	bpy ; Ph-OH	47,86	48,25
	650-670	-C ₃ NO ₂ H ₅	16,33	16,86
	785	CuO (residue)	15,89	15,50
[Cu(bpy)(L-Trp)NO ₃].H ₂ O	93-108	H ₂ O	3,20	3,57
	340-580	bpy ; heterocycle	53,28	54,07
	610-635	-C ₃ NO ₂ H ₅	16,76	17,29
	775	CuO (residue)	16,31	15,90
[Cu(bpy)(histidin)NO ₃].2H ₂ O	98-109	2H ₂ O	7,25	7,62
	275-380	bpy	33,69	33,05
	490-680	heterocycle; -C ₃ NO ₂ H ₅	31,97	32,62
	745	CuO (residue)	16,27	16,94

The TG and DTG curves for (1) and (2) complex combinations are similar with the exception of the temperature of lost of weight, Fig. 2(a). Thus, the second step has two consecutive effects which indicates the loss of one molecule of *bpy* and the heterocyclic fragment of aminoacid molecule while the third step corresponds to the loss of -C₃NO₂H₅ fragment of the aminoacid molecule.

For complexe (3), Fig. 2(b), the second step of decomposition corresponds to the loss of the primary ligand, *bpy*, in the 200 – 380°C range which is much smaller than the corresponding temperature range of complexes (1) and (2). The third step of decomposition cumulates two consecutive effects that correspond to the loss of secondary ligand. For all complexes the last decomposition step corresponds to the loss of NO₃⁻ group in the 675-785°C range.

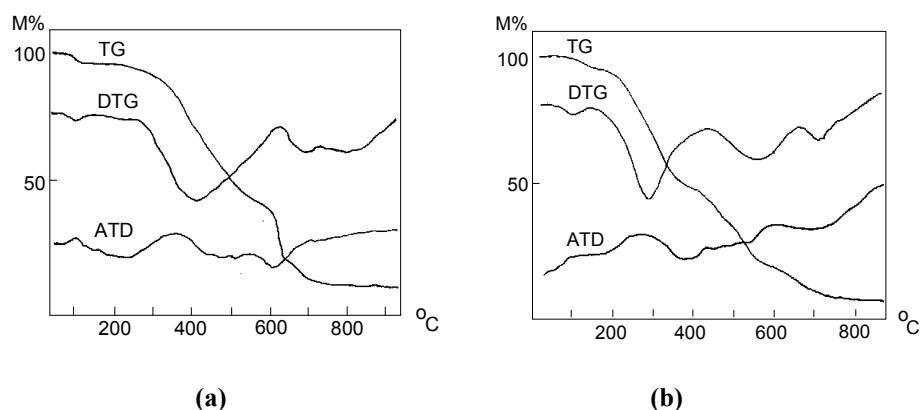
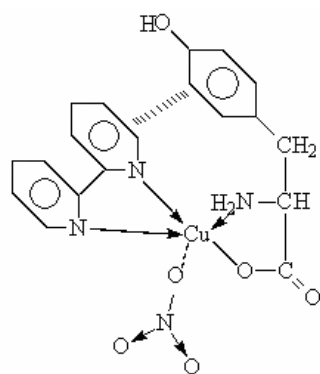
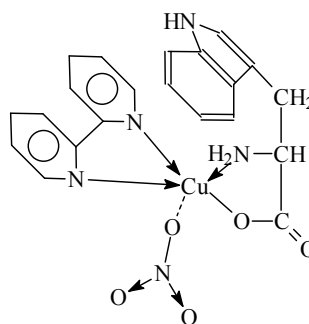


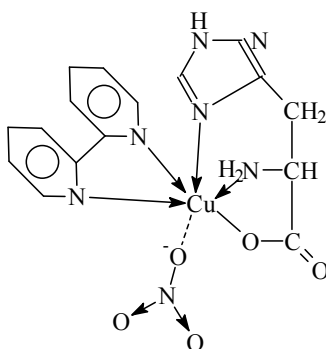
Fig. 2. TG, DTG and ATD curves for (a) -[Cu(bpy)(L-Trp)NO₃].H₂O ; (b) -[Cu(bpy)(L-histidine)NO₃].2H₂O

The values of temperature that characterizes the weight loss indicate that the stability of complexes decreases following the sequence: **(1)** \cong **(2)** > **(3)**. The final residue, for all complexes, was analyzed by IR spectroscopy and was identified as CuO, and %M corresponds to the calculated one.

The physico-chemical data led to the conclusion that the $[\text{Cu}(\text{bpy})(\text{L-Tyr})\text{NO}_3] \cdot 3\text{H}_2\text{O}$ and $[\text{Cu}(\text{bpy})(\text{L-Trp})\text{NO}_3] \cdot \text{H}_2\text{O}$ complexes have a square-pyramidal geometry similar to that of $[\text{Cu}(\text{bpy})(\text{L-Tyr})\text{ClO}_4] \cdot 2\text{H}_2\text{O}$ [8] complex which suggests that the NO_3^- ion has no influence upon coordination geometry. The solid-state structure of $[\text{Cu}(\text{bpy})(\text{L-Tyr})\text{ClO}_4] \cdot 2\text{H}_2\text{O}$ [8] complex shows π - π intermolecular stacking (3,02Å). For both prepared complexes the geometry is identical and the metallic center is surrounded by similar ligands which might suggest that the π - π stacking interactions are favored.

**(1)****(2)**

The UV-VIS spectra of complex **(3)** containing histidine as a secondary ligand show medium intensity absorption bands specific to an octahedral geometry. The coordination of sp^2 hybridized nitrogen atom of amino acid heterocycle in the axial position of Cu(II) complexes with histidine leads to the conclusion that these complexes have an axial distortion [11].

**(3)**

For complex (3) the intermolecular π - π stacking interactions may lack due to the formation of a co-ordinative bond between Cu(II) ion and sp^2 hybridized nitrogen atom of aminoacid heterocycle.

The presence of intermolecular interactions can give rise to an increase of thermal stability of the complex [8]. Thus, the decomposition temperatures of $[\text{Cu}(\text{bpy})(\text{L-Tyr})\text{NO}_3] \cdot 3\text{H}_2\text{O}$ and $[\text{Cu}(\text{bpy})(\text{L-Trp})\text{NO}_3] \cdot \text{H}_2\text{O}$ complexes confirm a greater stability than the prepared complexes with an octahedral distorted geometry.

As a conclusion one might say that the presence of π - π stacking interactions is possible unless a co-ordinative bond is formed between Cu(II) ion and sp^2 hybridized nitrogen atom of the aminoacid heterocycle.

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