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New Cu(II) and Co(II) octaazamacrocyclic complexes with 2-amino-3-phenylpropanoic acid

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Abstract: New cationic Cu(II) and Co(II) complexes with *N*,*N*',*N*",*N*"'-tetrakis(2-pyridylmethyl)-1,4,8,11-tetraazacyclotetradecane (tpmc) and the anion of 2-amino-3-phenylpropanoic acid (*S*-phenylalanine) were prepared. The complexes were analyzed and characterized by elemental analysis, conductometric, polarimetric, magnetic and cyclic voltammetric measurements, as well as by spectroscopic data (UV/Vis, IR). Both complexes are binuclear with the general formula $[M_2(S\text{-Phe})tpmc](ClO_4)_3 \cdot nH_2O$; *S*-PheH = *S*-phenylalanine, M(II) = Cu, n = 7; Co, n = 0. Based on previously reported data for some familiar complexes and the present results, pentacoordinated geometry was proposed. Both of the central metal ions are coordinated with two pyridyl and two cyclam nitrogens and bridged with $–N–(CH_2)_3–N–$ portions of the cyclam ring and oxygen atoms of the *S*-phenylalaninate ion. Antimicrobial screening of the complexes, solvent, starting salts and ligands alone was performed against fungi, mould and some bacteria. In certain cases, enhanced activity of Co(II) complex towards bacteria compared with the relevant free ligands and starting salts was detected.

Keywords: Cu(II) and Co(II) complexes; pendant octaazamacrocycle; *S*-phenylalanine.

INTRODUCTION

Metal aminocarboxylate complexes have been the subject of extensive research for many years. They are used to study phenomenon of the structure, stability, magnetic properties and non-covalent interactions important in chemical reactions, molecular recognition and regulation of biochemical processes, for a better understanding of enzyme–metal ion–substrate complexes, which play an

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important role in metalloenzyme-catalysed biochemical reactions.[1–13] The antimicrobial activity of such types of complexes was also the subject of some investigations.[11,13] Mixed-ligand mononuclear complexes of Cu(II) and Co(II)/(III) with *S*-/*R*-phenylalanine and *N*-donor ligands: 2,2'-bipyridyl, 1,10-phenantroline, imidazole, *N*,*N*'-diethylethylenediamine-*N*,*N*'-di-α-butyrato dianion, 3,3',4,5,5'--pentamethyl-4'-ethyl-2,2'-dipyrrolyl-methene were prepared and described.[6–10] The aminocarboxylato ligands in these complexes are bidentate chelates connected to the metal ions *via* the carboxylate oxygen and the amino group, *N*,*O* mode. In Co(III) complexes with *N*,*N*-bis(carboxymethyl)-*S*-phenylalanine including as the secondary ligand aliphatic or aromatic aminocarboxylates *S*-/*R*-phenylalanine/*S*-tryptophan, NH–π interaction was observed as an important factor for molecular recognition and stabilisation of their crystal molecular structures.[7] In the same paper, this interaction was also studied in solution for Co(III) ternary complexes with *N*,*N*-bis(carboxymethyl)-*S*-phenylalanine or nitrilotriacetic acid including one of the following amino acids / derivatives: glycine, *S*-proline/phenylglycine/alanine/leucine/4-methylphenylalanine/tyrosine or *S*,*R*-chlorophenyl--alanine. Bis(aminocarboxylato) square-planar Cu(II) complexes of *N*,*O*-bonded *S*-methionine/phenylalanine/tryptophan were isolated and investigated by thermal and spectroscopic (UV/Vis, IR, EPR) methods.[10] In the complexes of transition metal ions with *N*-substituted *S*-phenylalanine the COO^- group is coordinated to Co(II) and Cd(II) as bidentate *O*,*O*'- (thus forming chelate rings) or to Zn(II) as *O*-monodentate.[11]The formation of pentanuclear Cu(II) complexes with *S*-phenylalanine/tryptophanhydroxamic acid was also studied in solution and the structure was predicted using a combined potentiometric, spectrophotometric, CD and ESI–MS study and X-ray data of similar species of β-alaninehydroxamic acid.[12] Mononuclear complexes of divalent Co, Cu, Ni and Zn with amino acid-derived compounds were also described.[13]

On the other hand, polyazamacrocyclic ligands and their metal complexes are an attractive field of investigation due to their numerous unusual structural, spectral, redox and biological properties and possible applications as catalysts, new magnetic materials, ion selective potentiometric sensors, antimicrobial or agents for nucleic acid cleavage.[14–23]

In previous papers, a series of binuclear Co(II) complexes with pendant arm octaazamacrocycle *N*,*N*',*N*'',*N*'''-tetrakis(2-pyridylmethyl)-1,4,8,11-tetraazacyclotetradecane (tpmc) and an additional aliphatic α-/β-aminocarboxylate having linear or branched chain (glycine, *S*-alanine, *S*-aminobutyric/α-aminoisobutyric/β-aminobutyric/β-aminoisobutyric acid, *S*-norvaline/*S*-valine), or *N*-methyl glycine derivatives (*N*-methyl/*N*,*N*-dimethylglycine), were described. The general formula was $[Co_2(A)tpmc]B_3$; A^- = anion of the corresponding amino acid/ /derivative, B = ClO_4^-/BF_4^-. It is supposed that the A ligands are coordinated with Co(II) *via* the COO^- group in bridged[17–19] or a combined chelate-bridged

mode,[19] whereas the $–NH_2$ group remains uncoordinated. Metal centres are also bridged with $N–(CH_2)_3–N$ fragments of the cyclam ring.

The aim of the present study was the preparation, characterization and antimicrobial testing of Co(II)/Cu(II) tpmc complexes with *S*-phenylalanine, as a representative of aromatic amino acids and the comparison of the results with data for the related described complexes containing aliphatic amino acids or aliphatic/aromatic carboxylates.[16–22]

EXPERIMENTAL

Metal–organic perchlorate salts must be handled with caution! Since they contain both oxidizing and reducing groups and metal ions are sometimes effective catalysts, serious explosions are possible! Use only the absolute minimum of material required and never heat more than a few crystals!

Preparation

$Cu(ClO_4)_2·6H_2O$,[24] $Co(ClO_4)_2·6H_2O$,[25] tpmc[26] and $[Cu_2tpmc](ClO_4)_4$[27] were prepared and purified by the procedures described elsewhere. All other chemicals, as *p.a.* commercial products, were used as received.

*$[Cu_2$(S-Phe)tpmc$](ClO_4)_3·7H_2O$ (**1**)*

$[Cu_2tpmc](ClO_4)_4$ (50 mg; 0.046 mmol) was dissolved in 5 mL of 4:1 mixture CH_3CN–$–H_2O$ (v/v). To this solution, *S*-phenylalanine (15 mg; 0.091 mmol) dissolved in 4 mL of 1:1 mixture $CH_3CN–H_2O$, (v/v) previously neutralized with NaOH (0.1 mol L^{-1}) to pH ≈ 7.0 (controlled with pH strips 6.4–8.0) was slowly added. The colour gradually changed from blue–violet to blue. The reaction mixture was refluxed and stirred at ≈ 80 °C for the following 3 h, then concentrated to 1/3 of its initial volume on a water bath. It was allowed to cool to room temperature, covered with parafilm and left in a refrigerator undisturbed to crystallize slowly. The blue precipitate was vacuum-filtered, washed with small portions of cold CH_3CN and deionised water and air-dried. The product was then powered and recrystallized from deionised water. The blue microcrystalline product was removed by suction, washed with small portions of deionised water and left in a desiccator over silica gel. The product was stable to open air. Decomposition occurred at ≈190 °C (checked with a hot plate equipped with a microscope). Yield: 70 %.

*$[Co_2$(S-Phe)tpmc$](ClO_4)_3$ (**2**)*

$Co(ClO_4)_2·6H_2O$ (260 mg, 0.709 mmol) and tpmc (200 mg, 0.355 mmol) were dissolved in a minimum volume of CH_3CN. The mixture was warmed on a water bath to 80 °C and stirred. An aqueous solution of *S*-phenylalanine (72 mg; 0.355 mmol) previously neutralized with NaOH (0.1 mol L^{-1}) to pH ≈ 7.0 (controlled with pH strips 6.4–8.0) was gradually added dropwise to the first solution. The reaction mixture was refluxed with stirring for 2.5 h (at 80 °C). The obtained brownish–purple solution was evaporated on a water bath to 1/2 of its initial volume. It was left in a refrigerator well closed overnight, whereby a dark purple precipitate contaminated with a small amount of violet side-product $[Co_2(OH)tpmc](ClO_4)_3$ appeared. The precipitate was removed by suction, dried, recrystallized from CH_3CN and washed properly with small portions of cold CH_3OH. This procedure was repeated until a pure purple microcrystalline compound was obtained, which was dried and stored in a dessicator over silica gel. The compound was stable in the solid state to open air at room temperature and on

heating to 200 °C, but on prolonged standing of its solution, dark brown $Co(OH)_3$ formed. Yield: 63 %.

Analytical methods and applied instruments

Elemental analyses were performed by standard methods in the Centre for Instrumental Analyses, ICTM, Belgrade. The Cu content in complex **1** was determined by atomic absorption spectrophotometry using a Perkin-Elmer AAS-5100/PC instrument. The electronic absorption spectra of the complexes in CH_3CN/DMF solutions (1.0×10^{-3} mol L^{-1}) were recorded on a GBC UV/Vis Cintra 20 spectrophotometer. The reflectance spectrum of complex **2** was recorded on a CARY 17D spectrophotometer using MgO as the standard. The position of the broad maxima were corrected using the Kubelka–Munks function.[28] Magnetic susceptibility measurements were realised at room temperature (20±2 °C) using an MSB-MKI balance calibrated with $Hg[Co(SCN)_4]$ (Sherwood Scientific Ltd., England). The data were corrected for diamagnetic susceptibilities using Pascal constants.[29] The IR spectra were run on a Nicolet 6700 FTIR spectrometer (ATR technique) in the range 400–4000 cm^{-1}. Molar electrical conductivities in CH_3CN/DMF (1.0×10^{-3} mol L^{-1}) were measured at room temperature on a Hanna instruments HI 8820N conductometer. The optical rotation for the complexes and *S*-phenylalanine alone were measured at 589 nm at ambient temperature (20±2 °C) using a tube of 1 dm on a Rudolf Research Analytical Autopol IV automatic polarimeter (c = 2.2×10^{-4} for complex **1**, 2.4×10^{-4} for **2** and 2.4×10^{-3} mol L^{-1} for *S*-phenylalanine). Electrochemical measurements on complex **1** were performed using electronic equipment Metrohm 797 VC Computrace in a standard three-electrode cell: a Pt disc as the working electrode, standard Ag/AgCl as the reference electrode and Pt as the auxiliary one. Measurements were performed in 10 mL of CH_3CN. The concentration of complex **1** was 1.0×10^{-4} mol L^{-1}. Cyclic voltammetry (CV) was performed with sweep rates of 50, 100 and 200 mV s^{-1} in the potential range from –1 to 1 V *vs.* Ag/AgCl. Electrochemical measurements on complex **2** were also performed in a standard three-electrode cell but with a glassy carbon (GC) as the working electrode, saturated calomel (SCE) as a reference and Pt as the auxiliary electrode. The measurements were realised in 100 mL of a mixture of CH_3CN: aqueous NaOH (1.0 mol L^{-1}) solution (3:7, v/v). CV was performed by changing the potential in the range from –0.5 to 0.4 V *vs.* SCE at a sweep rate of 100 mV s^{-1}. The change in the potential was achieved using a sweep generator, EDT Research, the impulses of which were brought to a potentiostat, Bruker Potentio-Galvanostat EI30. An *XY* plotter, Hewlett Packard 7015 X–Y, was used. All measurements were performed at room temperature (20±2 °C). Oxygen was removed from the system by continuous bubbling with oxygen-free N_2.

For the preliminary antimicrobial test, the agar well diffusion method was applied.[30] The screening was performed against the following 6 cultures of microorganisms: the Gram-(+) bacteria *Micrococcus lysodeikticus* ATCC 4698 and *Staphylococcus aureus* ATCC 25923, the Gram-(+) bacterium forming spores, *Bacillus subtilis* ATCC 6633, the Gram-(–) bacterium *Escherichia coli* ATCC 25922, the fungi *Candida albicans* ATCC 24433 and the mould *Aspergillus niger* ATCC 12066. Nutrition (cultivation) medium was Mueller–Hinton agar for the bacteria and Sabouraud dextrose agar for the fungi. The incubation temperature was 37 °C for the bacteria and 28 °C for the fungi. The solvents: CH_3CN, DMSO and CH_3OH, ligands *S*-PheH in CH_3OH and a suspension of tpmc in CH_3CN, aqueous solutions of $Co(ClO_4)_2\cdot6H_2O$ and $Cu(ClO_4)_2\cdot6H_2O$ and the complexes **1** and **2** in DMSO (1.0 mg mL^{-1}) were tested separately. In the holes of agar plates (Ø 0.8 cm), 100 µL of each compound solution were applied. Neither of the complexes showed antifungal activity. The antibacterial activities of complexes **1** and **2** were quantified by the dilution method in agar (the minimum inhibition con-

centration was determined, *MIC*).[31,32] The initial concentration of the complexes was 8 mg mL^{-1} in DMSO. This solution was doubly diluted to give concentrations in the range 8–0.125 mg mL^{-1}. 0.5 mL of the solution of the tested substances was mixed with 9.5 mL of melted and cooled nutrition agar. The bacteria were seeded on the surface of the agar plate. After incubation for 24 h, the *MIC* values were determined as the lowest concentration of the complex preventing visible growth of the bacteria.

ACD/ChemSketch (Freeware version) was employed for drawing Figs. 1 and 4 and prediction of the relative M···M distances within the complexes described in this paper.

RESULTS AND DISCUSSION

New cationic binuclear Cu(II) and Co(II) complexes with pendant arm octa-azamacrocyclic ligand tpmc and *S*-phenylalanine, representing an aromatic aminocarboxylate ligand, were successfully isolated. The Cu(II) complex was prepared by the expansion of the coordination sphere of $[Cu_2tpmc](ClO_4)_4$ with the anion of *S*-phenylalanine in the molar ratio of reactants ≈1:2. The yield of the target complex was thus approximately two times higher than in the case of the direct synthesis starting from the reactants. The Co(II) complex was prepared by direct synthesis using the reactants $Co(ClO_4)_2 \cdot 6H_2O$, tpmc and neutralized *S*--phenylalanine in the molar ratio ≈2:1:1. In both syntheses, *S*-phenylalanine was neutralized to pH ≈ 7.0 to enhance its donor ability and to suppress the formation of violet $[Co_2(OH)tpmc](ClO_4)_3$ during the synthesis of the Co(II)complex, which was always present as a side-product, even in pure aqueous solution.

Complex **1** (t = 20±2 °C) was well soluble in CH_3CN, H_2O, CH_3OH and DMSO but insoluble in C_2H_5OH. Complex **2** (t = 20±2 °C) was well soluble in CH_3CN, DMSO and DMF and sparingly in H_2O and CH_3OH.

The analytical results obtained for the prepared complexes were as follows.

*Complex **1***. Anal. Calcd. for $Cu_2C_{43}H_{68}N_9O_{21}Cl_3$ (FW 1280.58): C, 40.33; H, 5.35; N, 9.84; Cu, 9.91 %. Found: C, 40.34; H, 4.97; N, 9.72; Cu, 9.52 %.

*Complex **2***. Anal. Calcd. for $Co_2C_{43}H_{56}N_9O_{15}Cl_3$ (FW 1145.27): C, 45.10; H, 4.75; N, 11.01 %. Found: C, 44.92; H, 4.92, N, 10.68 %.

The values of molar electrical conductivities measured in CH_3CN and DMF for both complexes are given in Table I. In CH_3CN, for both complexes, they were between those found for 1:3 (literature range 340–420 S cm^2 mol^{-1}) and for 1:4 (500 S cm^2 mol^{-1}) type of electrolytes. In DMF, the value was slightly higher for complex **1**, while complex **2** in DMF corresponded to a 1:3 type (literature range 200–240 S cm^2 mol^{-1}) (Table I).[33]

Considering the results of elemental analyses and conductivity measurements, the general formulas of the complexes were proposed as $[M_2(S$--Phe)tpmc$](ClO_4)_3 \cdot nH_2O$, *S*-PheH = *S*-phenylalanine, M(II) = Cu, n = 7; Co, n = 0.

The electronic absorption spectrum of the blue Cu(II) complex **1** recorded in CH_3CN has a broad absorption maximum in the visible region corresponding to d–d transitions. The position and intensity of the maximum was similar to those

found for congeneric described binuclear Cu(II)tpmc complexes containing benzoate/hydrogenphthalate instead of *S*-phenylalanine ligand.[20] X-Ray structure analyses[16] of these complexes confirmed a coordination number 5 and the chromophore CuN_4O, which are also supposed for complex **1**. In addition, in UV part of the spectra, very intensive dented bands at 220–305 nm (ε from 4700 to 13596 L mol^{-1} cm^{-1}) could be ascribed to charge transfer (CT) transitions. In DMF, the position of the absorption maximum was similar but more intense; CT dented bands were found at 275–318 nm (ε from 4748 to 5769 L mol^{-1} cm^{-1}).

TABLE I. Electronic spectral data for complexes **1** and **2** in CH_3CN[a]/DMF[b], reflectance spectrum[c], molar conductivities (Λ_M) and magnetic moments (μ_{eff}) at room temperature compared with some relevant published analogues

Complex[d]	λ_{max} / nm (ε / L mol^{-1} cm^{-1})	ΛM S cm^2 mol^{-1}	μeff μ_B per M(II)
$[Cu_2tpmc](ClO_4)_4$[27]	680 (340)[a] 594[c]	510[a]	1.90
$[Cu_2(S\text{-Phe})tpmc](ClO_4)_3\cdot 7H_2O$	650 (235)[a] 648(381)[b]	445[a] 276[b]	2.05
$[Co_2(OH)tpmc](ClO_4)_3\ H_2O$[35]	489 (60), 574 (80)[a]	–	–
$[Co_2(S\text{-Ala})tpmc](ClO_4)_3\cdot H_2O$[17]	459 (60), 512 (75), *sh* 551(58)[a]; 452, 508, *sh* 560[c]	–	4.62
$[Co_2(S\text{-Phe})tpmc](ClO_4)_3$	460 (66), 512(85), *sh* 555(61)[a]; 471 (67), 510 (77), *sh* 559(59)[b]; 425, 482, 538[c]	476[a] 219[b]	4.21

[a]in CH_3CN; [b]in DMF, [c]reflectance spectrum; [d]tpmc = *N*,*N*',*N*'',*N*'''-tetrakis(2-pyridylmethyl)-1,4,8,11-tetraazacyclotetradecane; *S*-PheH = *S*-phenylalanine; *S*-AlaH = *S*-alanine; sh-shoulder

The magnetic moment of 2.05 μ_B per Cu(II) at room temperature (Table I) was in the range 1.75–2.20 μ_B found previously for similar five-coordinated Cu(II) complexes with one unpaired electron and in which there is no significant magnetic interaction.[20–22,34]

In binuclear complexes, the phenylalaninate-bridged ligand has, theoretically, the possibility for coordination in several modes represented in Fig. 1.[34]

In the electronic absorption spectrum of complex **2** recorded in CH_3CN/ /DMF (Table I), two maxima and one shoulder corresponding to d–d transitions for high-spin Co(II) complexes were observed. From Table I is obvious that maxima positions and the ε values for complex **2** are comparable with the given data for $[Co_2(S\text{-ala})tpmc](ClO_4)_3\cdot H_2O$[17] in CH_3CN, which contains the aliphatic *S*--alanine, suggesting the same CoN_4O chromophore but differ from those for $[Co_2(OH)tpmc](ClO_4)_3$.[35] The coordination number 5, as the most probable due to the lower symmetry than for coordination number 6, found in congeneric complexes is assumed.[36] However, there is a bathochromic shift of all maxima in the spectra of complex **2** in solution (recorded both in CH_3CN and DMF) compared

with the reflectance spectrum of the complex, which was not the case for the *S*--alaninate analogue. This fact implies some changes in the geometry, conformation or coordination sphere upon dissolution of the complex containing *S*-phenylalanine. The reason might be the introduction of the more bulky phenyl group in the aminocarboxylato ligand.

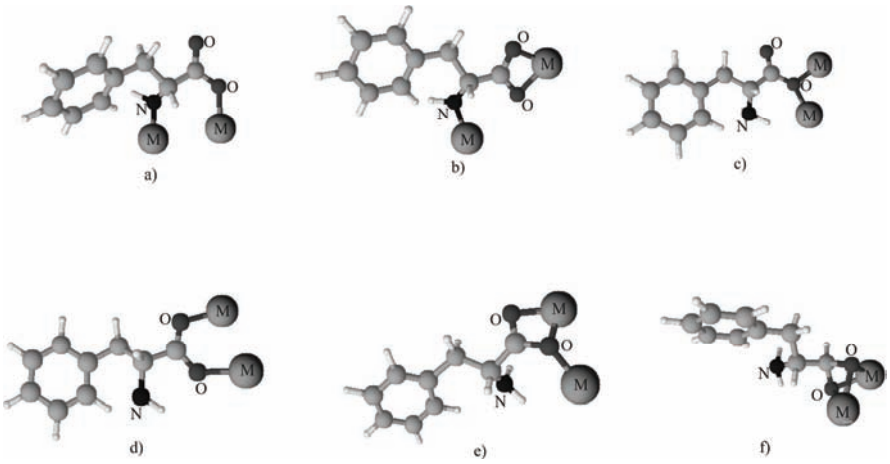

Fig. 1. Some of the theoretically possible coordination modes of the phenylalaninate ligand in binuclear bridged complexes: a) *N*,*O*-; b) combined chelate-bridged, *O*,*O*',*N*-; c) monoatomic *O*,*O*-; d) *O*,*O*'-; e) combined chelate-bridged *O*,*O*,*O*'-; f) combined chelate-bridged *O*,*O*,*O*',*O*'-.

The UV part of the spectrum of complex **2** in CH_3CN contains several unresolved maxima in the range 250–290 nm, with ε around 4350 L mol^{-1} cm^{-1}, belonging to CT transitions. In the spectrum recorded in DMF, there is sharp maximum at 276 nm (ε = 4730 L mol^{-1} cm^{-1}), originating also from CT. The magnetic moment at room temperature for the complex **2** (Table I) of 4.21 μ_B falls in the range 3.96–4.75 μ_B/Co(II) found for high-spin analogous complexes with 3 unpaired electrons.[18,29]

In IR spectra of the complexes, the following bands (in cm^{-1}) were present: a medium broad band with maxima ≈3573 of ν(O–H) from the crystal bonded molecules of H_2O overlapping the valence vibrations of $–NH_2$ in the spectrum of **1** and a doublet at 3313 and 3279 from ν(NH_2) in the spectrum of **2**; a strong sharp band ≈1610 in both complexes, originating from skeletal valence vibrations of the pyridine ring from tpmc included in coordination, which was found at 1588 in the spectrum of free tpmc, a strong band of ν(ClO_4^-) which was not included in the coordination at 1101 for **1**, *i.e.*, 1065 for **2**, as well as a medium sharp band from δ(ClO_4^-) at 624 for **1,** *i.e.*, at 619 for **2**. Finally, weak bands at 473 corresponding to ν(M–N) for **1** and 463 for **2** and at 407 are ascribed to ν(M–O).[37]

The bands of the asymmetrical and symmetrical vibrations of the –COO⁻ group, $\nu_{as}(OCO^-)$ and $\nu_s(OCO^-)$ and the values $\Delta\nu = \nu_{as} - \nu_s$ for the free ligand and both complexes, together with the corresponding values for the analogous Co(II) *S*-alaninate complex are given in Table II. The shift of ν_{as} and ν_s in the spectra of complexes **1** and **2** was evidence for the participation of the carboxylic group in the coordination. The electronic absorption spectral data (Figs. 1a and 1b) excluded *N*,*O*-chelate coordination of the *S*-phenylalaninate anion. Furthermore, the electronic spectra for the Co(II) tpmc *S*-alaninate and *S*-phenylalaninate complexes and the increasing of their $\Delta\nu$ values compared with those found for the uncoordinated ligands were similar, suggesting the same coordination mode. This together with the absence of a band over 1650 cm^{-1} indicated the participation of both O atoms in the coordination, *i.e.*, the *O*,*O*'-bridged coordination mode, hence the mode in Fig. 1c could be excluded.

TABLE II. IR spectral data values (cm^{-1}) of ν(OCO) for the free aminocarboxylate, complexes **1** and **2** and the Co(II)tpmc *S*-alaninate analogue[17]

Compound[a]	$\nu_{as}(OCO^-)$	$\nu_s(OCO^-)$	$\Delta\nu$
S-PheH	1562	1408	154
$[Cu_2(S\text{-Phe})tpmc](ClO_4)_3\cdot 7H_2O$ (**1**)	1573	1398	175
$[Co_2(S\text{-Phe})tpmc](ClO_4)_3$ (**2**)	1578	1357	221
S-AlaH	1594	1413	181
$[Co_2(S\text{-Ala})tpmc](ClO_4)_3\cdot H_2O$[17]	1575	1350	225

[a]Abbreviations as in Table I

The $\Delta\nu$ value for both complexes was higher than that for uncoordinated *S*--phenylalanine (154 cm^{-1}). For the complex **1**, it was 175 and for **2,** 221 cm^{-1}, meaning a stronger bond in the latter case. Moreover, the $\Delta\nu$ value of the Co(II) complex was comparable with that found for the analogous *S*-alaninate Co(II) complex, 225cm^{-1},[17] suggesting almost the same strength of the Co–O bonds.

For complex **1**, $[M]_{589}$ is –1408.64°, and for complex **2,** +498.59°, which is significantly higher than the value for the corresponding *S*-alaninato Co(II) complex of +168°,[17] while for the *S*-phenylalanine alone $[M]_{589}$ is –20.63° at room temperature. The origin of the optical rotation in the *S*-alaninate complex was ascribed to the "vicinal effect" alone.[17] The value of the molar optical rotation is most probably increased in complex **2** due to the conformational and configurational contribution to the overall activity, as well as due to the greater asymmetry in the complex ion. As for the complex **1**, representing the first Cu(II)tpmc complex with an optically active aminocarboxylate, there is no comparable published data for familiar complexes, although its value of $[M]_{589}$ is also rather high.

The electrochemical behaviour of the synthesized complexes was studied by cyclic voltammetry. First the voltammograms of the starting complex $[Cu_2tpmc](ClO_4)_4$, tpmc and the aminocarboxylate salt were recorded in CH_3CN.

Measurements were performed in the range of –1.0 to +1.0 V at scan speeds of 50, 100 and 200 mV s^{-1}. A representative CV of complex **1** at 200 mV s^{-1} is shown in Fig. 2. The same correlation was observed using a lower rate of potential change but with increasing rate, the cyclic voltammogram was broader, showing that the adsorption of the complex on the working electrode was a relatively slow process. The absence of peaks on both voltammograms suggests the electrochemical stability of the complex under the investigated conditions. The electrochemical behaviour of similar dicarboxylato Cu(II)tpmc complexes was previously studied using lower rates, when it was observed that with decreasing the rate of potential change on the electrodes and by holding the potential, some peaks appeared or became more intensive.[21]

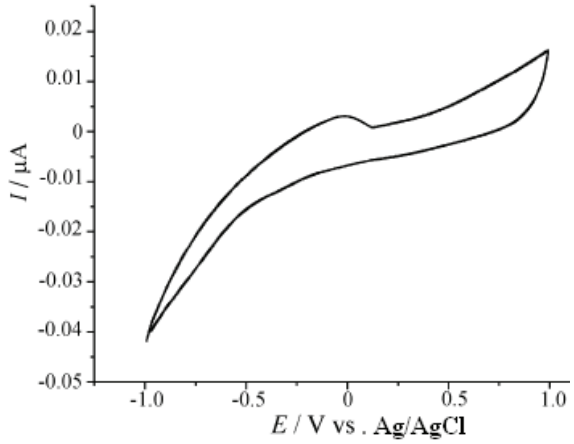

Fig. 2. Cyclic voltammogram of the complex: $[Cu_2(S\text{-Phe})tpmc](ClO_4)_3 \cdot 7H_2O$ in CH_3CN (scan rate: of 200 mV s^{-1}).

The state of the working electrode in the second experiment was first determined by potentiodynamic measurement in the basic electrolyte in the absence of complex **2**. Then complex **2** was added, for which the cyclic voltammogram is presented in Fig. 3. As the obtained curves are identical, it was concluded that the Co(II) complex is electrochemically stable in this electrolyte in the potential range –0.5 to +0.4 V *vs.* SCE and that there is no "charge transfer". On expanding the potential range towards more negative potential than –0.6 V *vs.* SCE, there were no essential changes, except the start of H_2 evolution. On expanding the potential range towards more positive potential than +0.65 V *vs.* SCE, the complex was completely decomposed and peaks due to the oxidative decomposition of its products appeared.

A computer program was applied for the optimization of the possible geometries and coordination modes of aminocarboxylato ligands. Thereby it was seen that in the Cu(II)tpmc complex with *S*-phenylalanine with bridged *O*,*O*'-coordination, the approximate Cu···Cu distance was larger (≈5.1 Å) than in the case of the analogous *μ-O*,*O*'-benzoato complex (≈4.5 Å), for which such a coordi-

nation was confirmed by X-ray analysis. This is quite understandable due to the steric hindrance of the more bulky benzyl than phenyl group and introduction of amino group in the first complex. Unfortunately, for the corresponding Co(II)tpmc complex, no comparable X-ray analyses data exist for analogous complexes. However, by using the same program, the Co···Co distance in this complex was estimated to be ≈5.0 and ≈4.8 Å in the related complex with *S*-alanine.

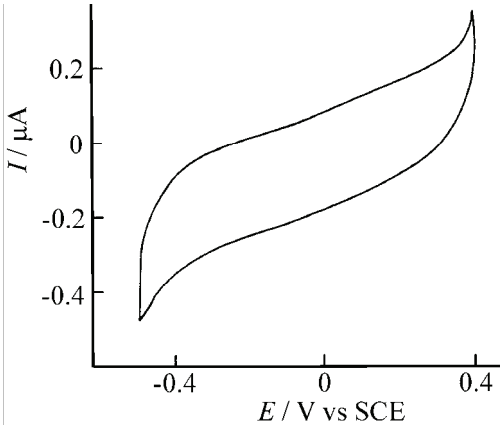

Fig. 3. Cyclic voltammogram of the complex $[Co_2(S\text{-Phe})tpmc](ClO_4)_3$ (scan rate: 100 mV s^{-1}).

Based on all the above reported results, the asymmetrical *μ-O,O'* manner of coordination is proposed as the most probable, with one oxygen in the base of a square-pyramidal geometry and the other in the axial position of a trigonal-bipyramid (Fig. 4).

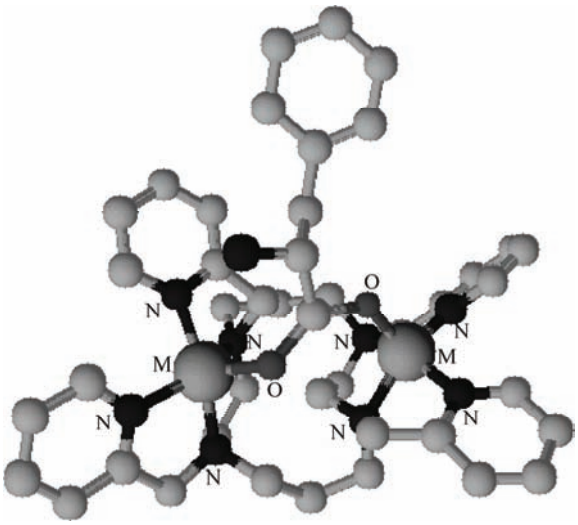

Fig. 4. Proposed geometry of the complex cation $[M_2(S\text{-Phe})tpmc]^{3+}$, M(II) = Co/Cu within complexes **1** and **2**.

The antimicrobial study showed that the solvents, ligands, simple salts and complex **1** were inactive up to 400 μg mL^{-1} against all the studied microorganisms. Both complexes were inactive against the tested fungi and mould. Complex **2** had moderate activity towards some of the studied bacteria (Table III). The Co(II) complex was more active than the analogous Cu(II) complex, suggesting that it is kinetically less stable under the investigated conditions.

TABLE III. Minimum inhibitory concentration (*MIC*), in μg mL^{-1}, of the complexes **1** and **2**

Complex	Solvent	M.L.[a]	S.A.[a]	E.C.[a]	B.S.[a]
$[Cu_2(S\text{-Phe})tpmc](ClO_4)_3 \cdot 7H_2O$	DMSO	>400	>400	>400	>400
$[Co_2(S\text{-Phe})tpmc](ClO_4)_3$		50	100	200	>400

[a]M.L, *M. lysodeikticus* ATCC 4698; S.A, *S. aureus* ATCC 25923; E.C, *E. coli* ATCC 25922; B.S, *B. subtilis* ATCC 6633

CONCLUSIONS

In this paper, the first Cu(II)tpmc complex with an aminocarboxylate ligand and the first Co(II)tpmc complex with an aromatic aminocarboxylate were described. Their composition was consistent with binuclear 3+ cationic complexes. The molar ratio of tpmc and *S*-phenylalanine anion was 1:1. Based on spectral analyses, conductometric and magnetic measurements, cyclic voltammetry and previously published congeneric complexes, pentacoordinated geometry with an *exo* coordination mode of the octaazamacrocyclic ligand in the boat conformation, with a *μ-O,O'*-bonded *S*-phenylalaninato ion is proposed. The cobalt(II) complex showed moderate antibacterial activity against some strains. The complexes were compared mutually and with some related already published complexes.

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И З В О Д

НОВИ Cu(II) И Co(II) ОКТААЗАМАКРОЦИКЛИЧНИ КОМПЛЕКСИ СА 2-АМИНО-3-ФЕНИЛ-ПРОПАНСКОМ КИСЕЛИНОМ

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Добијена су два нова комплекса Cu(II) и Co(II) са *N,N',N'',N'''*-тетракис(2-пиридилметил)-1,4,8,11-циклотетрадеканом (tpmc-ом) и анјоном 2-амино-3-фенил-пропанске киселине (*S*-фенилаланина). Они су анализирани и окарактерисани: елементалном анализом, кондуктометријским, полариметријским, магнетним и циклично-волтаметријским мерењима, као и

спектроскопским подацима (UV/Vis, IR). Оба комплекса су динуклеарна опште формуле $[M_2(S\text{-Phe})tpmc](ClO_4)_3{\cdot}nH_2O$; *S*-PheH = *S*-фенилаланин, M(II) = Cu, $n = 7$; Co, $n = 0$. На основу раније добијених података за сродне комплексе и нових резултата претпостављена је пентакоординациона геометрија. Оба централна метална јона су координована за по два пиридил и два цикламова азота и премошћена $–N–(CH_2)_3–N–$ фрагментима цикламовог прстена и кисеониковим атомима *S*-фенилаланинато јона. Антимикробни тест комплекса, растварача, полазних соли и самих лиганада је извршен на гљивице, плесни и бактерије. У извесним случајевима нађена је повећана активност комплекса Co(II) према појединим бактеријама у односу на одговарајуће слободне лиганде и полазне соли.

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