

Preparation and properties of Cu(II) complexes with *N,N',N'',N'''*-tetrakis(2-pyridylmethyl)-1,4,8,11-tetraazacyclotetradecane (tpmc) and pseudohalides (NCO[−] or NCSe[−]). Part II

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(Received 11 June, revised 2 September 2003)

Abstract: Two new Cu(II) complexes with *N,N',N'',N'''*-tetrakis(2-pyridylmethyl)-1,4,8,11-tetraazacyclotetradecane (tpmc) and pseudohalides (NCO[−] or NCSe[−]) were isolated. Elemental analyses (C, H, N, Cu) corresponded to the formulas: [Cu₂(NCO)tpmc](ClO₄)₃ · 2CH₃CN and [Cu₂(NCSe)₂tpmc](ClO₄)₂ · 2H₂O · C₂H₅OH. The coordination mode of tpmc and these ambidentate pseudohalides, geometries, spectral characteristics (VIS, IR) and other properties were compared with those of the previously described [Cu₂(NCS)₂tpmc](ClO₄)₂. Antimicrobial activity towards selected bacteria and yeast was tested and found for the NCSe but not the NCO complex.

Keywords: copper(II) complexes, octaazamacrocyclic, isocyanato ligand, isoselenocyanato ligand, antimicrobial activity.

INTRODUCTION

Natural metalloproteins containing Cu(I)/(II) and Fe(II) (respiratory pigments: hemocyanin, hemoglobin, hemerythrin *etc.*) are necessary for animals, due to their ability to bind, transport and release O₂.¹ Copper containing proteins in plants and animal organisms play an important role in metabolic processes, such as oxygen and electron transfer, hydroxylation and oxidative catalysis.² For this reason, the preparation and investigation of Cu(II) complexes capable of mimicking some of the principal functions of the mentioned metalloproteins is of interest. A number of various metal complexes with saturated polyazamacrocyclic ligands having pendant arms have recently been reviewed.³ Among them are those with the octaazamacrocyclic ligand *N,N',N'',N'''*-tetrakis(2-pyridylmethyl)-1,4,8,11-tetraazacyclotetradecane (tpmc), both with or without other ligand(s).^{4–7} Due to the flexibility of tpmc which bears four 2-pyridylmethyl groups, the size, nature, and number of the additional ligands, the geometry around the

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central ion, as well as its radius can be varied. Interestingly, the structure of free tpmc was only recently solved by X-ray analysis,⁸ although it was prepared 17 years ago, and a great number of its metal complexes have been examined by crystallography. Some Co (II) and Cu (II) complexes with tpmc showed microbiological activity.^{4,6,7}

In previous studies, six binuclear tpmc Cu(II) or Co(II) complexes with one or two pseudohalides (N_3^- , NCO^- , NCS^- or NCSe^-) were prepared and characterized.^{5,6} Some of them were biologically active with respect to particular representatives of microorganisms.

Continuing this research, two new cationic Cu(II)-tpmc complexes with NCO^- or NCSe^- were isolated and characterized. The corresponding di-thiocyanato complex⁵ was tested against some microorganisms, together with the mentioned complexes, the starting $[\text{Cu}_2(\text{tpmc})](\text{ClO}_4)_4$ and simple pseudohalide salts.

EXPERIMENTAL

Preparation

CAUTION: Perchlorate salts of metal complexes with organic ligand are potentially explosive and should be prepared and handled with extreme caution! Always prepare a small amount of the sample, do not shake it vigorously, and do not heat it in the solid state above 105 °C!

KSeCN , $[\text{Cu}_2\text{tpmc}](\text{ClO}_4)_4$ and $[\text{Cu}_2(\text{NCS})_2\text{tpmc}](\text{ClO}_4)_2$, were prepared according to known procedures.^{4a,5,9} The other chemicals were commercial products.

$[\text{Cu}_2(\text{NCO})\text{tpmc}](\text{ClO}_4)_3 \cdot 2\text{CH}_3\text{CN}$ (**1**) and $[\text{Cu}_2(\text{NCSe})_2\text{tpmc}](\text{ClO}_4)_2 \cdot 2\text{H}_2\text{O} \cdot 2\text{C}_2\text{H}_5\text{OH}$ (**2**)

A solution of $[\text{Cu}_2\text{tpmc}](\text{ClO}_4)_4$ (272 mg; 0.250 mmol) in 30 cm³ of CH_3CN was heated in a nitrogen atmosphere at 60 °C for 30 min. Then a solution of NaNCO (41 mg; 0.625 mmol) or KSeCN (90 mg; 0.625 mmol) in 2 cm³ of water was added dropwise during 20 min under continuous stirring and heating at the same temperature. The colour of the reaction mixture turned from blue-violet to turquoise for complex **1** or green for complex **2**. The solution was concentrated by heating at 70 °C until the commencement of crystallization, covered with parafilm and left at room temperature for 24 h. The turquoise (*i.e.*, dark green) crystals were separated by suction, washed with cold acetonitrile several times, dried in an Abder-Halden apparatus with ethanol for 2 h, and stored in a vacuum desiccator. Yield of **1**: 114 mg (41 %). Anal. Found: Cu, 10.62; C, 41.79; H, 4.58; N, 13.63 %. Calcd. for $\text{C}_{39}\text{H}_{50}\text{N}_{11}\text{O}_{13}\text{Cl}_3\text{Cu}_2$ ($MW = 1114.31$): Cu, 11.40; C, 42.03; H, 4.52; N, 13.82 %. Yield of **2**: 251 mg (85 %). Anal. Found: Cu, 10.16; C, 38.73; H, 4.62; N, 12.32 %. Calcd. for $\text{C}_{38}\text{H}_{54}\text{N}_{10}\text{O}_{11}\text{Cl}_2\text{Se}_2\text{Cu}_2$ ($MW = 1182.80$): Cu, 10.74; C, 38.59; H, 4.60; N, 11.84 %.

Analytical methods

Elemental analysis (C, H, N) was carried out by standard micro methods in the Center for Instrumental Analysis, Faculty of Chemistry, University of Belgrade. The copper content was determined by atomic absorption spectrophotometry using a Perkin-Elmer 703 instrument with a HGA 300 graphite furnace. The electronic absorption spectra were recorded on a GBC UV-VIS 911A spectrophotometer. A Perkin-Elmer FTIR 31725X spectrometer was used for recording the IR spectra (KBr disc). The magnetic susceptibilities were measured at room temperature with a MSB-MKI balance (Sherwood Scientific Ltd., Cambridge, England). $\text{HgCo}(\text{SCN})_4$ was the calibration standard. Diamagnetic corrections were performed with Pascal constants.¹⁰

RESULTS AND DISCUSSION

Copper(II)-tpmc complexes with isocyanato (**1**) or two isoselenocyanato (**2**) anionic ligands were obtained by enlargement of the $[\text{Cu}_2\text{tpmc}](\text{ClO}_4)_4$ coordination sphere with the corresponding pseudohalide anion(s). The mole ratio of $[\text{Cu}_2\text{tpmc}](\text{ClO}_4)_4$ and pseudohalide was 1:3 in both cases. The formula for the complex cation **1**, based on elemental analyses, corresponds to $[\text{Cu}_2(\text{NCO})\text{tpmc}]^{3+}$, and for the complex cation **2**, as in

the case of the isothiocyanato analogue (complex cation **3**),⁵ $[\text{Cu}_2(\text{NCSe})_2\text{tpmc}]^{2+}$. Complexes **1** and **3** are air-stable, while complex **2** during prolonged exposition to the atmosphere might slowly decompose (a small amount of red elementary Se appeared).

The room temperature values of $\mu_{\text{eff}}/\text{Cu}$ atom for complexes **1** and **2** of 1.95 and 1.75 B.M., respectively, are consistent with the Cu(II) state (1 unpaired electron).¹¹ For complex **1**, this value is in the range found for simple paramagnetics. However, the μ_{eff} for complex **2** is close to the spin-only value (1.73 B.M.) and could indicate some magnetic interaction between the metal centers. For previously described Cu(II)-tpmc complexes with pseudohalides, the $\mu_{\text{eff}}/\text{Cu}$ values were: bi-NCS⁻ (complex **3**), 1.78; 1,1- μ -N₃⁻, 1.76 and for bi-N₃⁻ 1.93 B.M. Among the studied binuclear Cu(II)-tpmc complexes, only the μ -OH⁻ complex has a weak antiferromagnetic interaction, which was obvious at lower temperatures.^{4a}

TABLE I. Electronic absorption spectral data

Complex	$\lambda_{\text{max}}/\text{nm}$ ($\epsilon/\text{dm}^3\text{mol}^{-1}\text{cm}^{-1}$)			
	Acetone		Aqueous solution	
1	–	723 (410)	–	669 (299)
2	455 (1341)	684 (420)	450 (1017)	698 (295)
3	412 (1920)	695 (303)	–	673 (273) ⁵
$[\text{Cu}_2(\text{N}_3)_2\text{tpmc}](\text{ClO}_4)_2$ ⁵	–	–	–	664 (195) ⁵

The electronic absorption spectral data of **1–3** in acetone and water are given in Table I. The absorption maxima are in the range of 660–700 nm found for d-d transitions in familiar binuclear pentacoordinated Cu (II) complexes^{4a,4i,5} (Table I). A 9 nm shift of the absorption maximum in the spectrum of the NCSe-complex (**2**) recorded in acetone towards higher wavelengths compared with the NCS-complex (**3**) was found. This is in accordance with the fact that NCSe⁻ is very close, but slightly higher than NCS⁻ in the spectrochemical series. However, in the spectra recorded in aqueous solution of the same complexes, a shift of 15 nm in the opposite direction was found. This indicates an influence of the solvent on the composition of the complex, dissociation and/or hydrolysis (especially in aqueous solution). One of the possible explanations could be the effect of solvent molecules on electron density transformations caused by the breaking and forming of new intra- and intermolecular bonds. The corresponding values of the molar absorptive coefficients (ϵ) are higher for the NCSe- than for the NCS-complex in both solvents due to the lower symmetry and greater distortion from regular geometry in the former case. The more intensive bands found in the range 412–450 nm are ascribed to charge transfer (CT).

In the IR spectra, the expected characteristic bands belonging to: the skeletal vibrations of the pyridine ring at about 1608 cm^{-1} (sharp, strong) and $\nu(\text{ClO}_4)$ at about 1096 cm^{-1} (strong, broad) were found. The assignment of the sharp, medium band at 624 cm^{-1} is not unambiguous as the $\delta(\text{ClO}_4)+\delta(\text{NCO})$ ¹² and $\nu(\text{CSe})$ ¹³ vibrations are expected at the same position.

TABLE II. Positions of selected IR bands in the spectra of the complexes

Complex.	Assignment	NCY (bound <i>via</i> N)/cm ⁻¹	YCN (bound <i>via</i> Y)/cm ⁻¹	Found/cm ⁻¹
1	v(CN)	2150–2100 ¹⁴	2240–2280 ¹²	2218
	v(CO)	1300–1340 ¹⁴	1060–1300 ¹²	1297
	δ(NCO)	610–660 ¹²	590–630 ¹²	624 [#]
2	v(CN)	< 2080 ¹³	> 2080 ¹³	2066
	v(CSe)	620–700 ¹³	500–550 ¹³	625 [#]
	δ(NCSe)	> 400 ¹³	< 400 ¹³	471
3	v(CN)	2040–2080 ¹⁵	2080–2130 ¹⁵	2070 ⁵
	v(CS)	780–860 ¹³	690–720 ¹³	762 ⁵
	δ(NCS)	≈480 ¹³	420 ¹³	480 ⁵

[#] Overlapping region with δ(ClO₄)

By comparing the wave numbers of the v(CN), v(CY) and δ(NCY) bands (Y = O for complex **1**, Se for complex **2** and S for complex **3**) with the literature data (Table II), it is supposed that the N atom from pseudohalides is the ligator in all complexes.

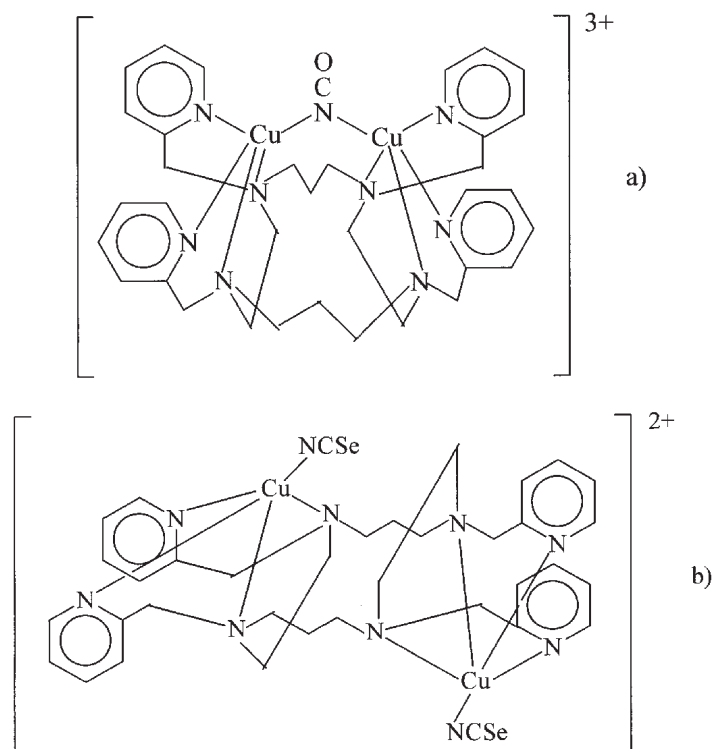


Fig. 1. Schematic presentations of the proposed geometries for the complex cations $[\text{Cu}_2(\text{NCO})\text{tpmc}]^{3+}$ (a) and $[\text{Cu}_2(\text{NCSe})_2\text{tpmc}]^{2+}$ (b).

Although the bands for $\nu(\text{CN})$ and $\nu(\text{CO})$ in the spectrum of complex **1** are practically between the regions expected for coordination *via* N and O atom (Table I), and the band for $\delta(\text{NCO})$ partially overlaps with the $\delta(\text{ClO}_4)$ band, coordination through the N atom is more probable. Namely, the Cu(II) ion is an intermediate hard-soft acid (Pearson's acid-base theory).¹⁶ The O atom as donor, being smaller and more electronegative than N, would make the NCO^- anion too hard for such an intermediate acid. On the other hand, N as ligator gives the NCO^- anion softness. In the case of complex **2**, the proposed mode of coordination *via* the N atom is supported by the IR data (Table II). Coordination *via* the voluminous Se atom is unfavoured, as in that case the SeCN^- anion would be a soft base as with the NCS^- anion (N-donor is a hard donor and S-donor a soft one).¹⁶ In addition, it was found that for the first row of transition metals, coordination with NCO^- or NCSe^- ligands *via* N is preferred in most of the cases.¹³

TABLE III. The results of the microbiological activity tests

Culture of microorganisms	Complex 2
<i>Escherichia coli</i>	+
<i>Staphylococcus aureus</i>	-
<i>Bacillus thuringiensis</i>	-
<i>Pseudomonas aeruginosa</i>	+
<i>Candida albicans</i>	-

+ = appearance of activity with an inhibition zone diameter to 5 cm; - = activity was not detected

On the basis of all data, it is proposed that in the first complex two coppers are bridged through the common N from NCO^- (1,1- μ -N),¹⁷ and the tpmc assumes a *boat* conformation (Fig. 1a). However, in the second complex, two NCSe^- ligands (more voluminous than in the case of NCS^-), are in the *trans* position and the tpmc is in a *chair* conformation (Fig. 1b). The proposed geometries were similar to those of the analogous Co(II) complexes⁶ and $[\text{Cu}_2(\text{NCS})_2\text{tpmc}](\text{ClO}_4)_2$ (complex **3**).⁵ They are presented in Fig. 1. As for the azido Cu(II)-tpmc complexes, it is worth mentioning that both monoazido (1,1- μ -N) and *trans*-diazido (singly coordinated to each Cu ion) binuclear complexes were isolated. In both cases an end-on way of pseudohalide ion coordination was proposed.⁵

Study of biological activity

The complexes were tested against selected bacteria and unicellular yeast by monitoring the suppression of growth, using the disc diffusion technique.¹⁸ The crystals (5 mg) of complexes were directly applied onto Mueller Hinton agar. The results are listed in Table III. Complexes **1** and **3** were inactive against the tested microorganisms. Only complex **2** showed some activity towards some of the selected microorganisms. The activity was enhanced in comparison with the free components of the complex: $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ and KSeCN (tpmc was found to be completely inactive). The

reason for this could be its greater hydrolysisability and lowest stability. In addition, it is necessary to break two coordination bonds to release NCO^- from the complex cation **1**. However, the breaking of only one coordination bond releases NCS^- or NCSe^- from complexes **2** and **3**. Another reason is the larger steric hindrance caused with the bigger Se than with either the O or S atom, as well as the presence of a small amount of elementary Se due to complex decomposition.

Acknowledgment: This work was partially supported by the Ministry of Science and Technology of the Republic of Serbia (Project No. 1318) to which authors' thanks are due. We are also grateful to M. Šumar, M. Sc., for assistance in the practical work and to D. Mitić, M. Sc. for the microbiological screening.

ИЗВОД

ДОБИЈАЊЕ И ОСОБИНЕ Cu(II) КОМПЛЕКСА СА N,N',N'',N''' -ТЕТРАКИС(2-ПИРИДИЛМЕТИЛ)-1,4,8,11-ТЕТРААЗАЦИКЛОТЕТРАДЕКАНОМ (трмс) И ПСЕУДОХАЛОГЕНИДИМА (NCO^- ИЛИ NCSe^-). II ДЕО

ГОДАНА ВУЧКОВИЋ^а, ЗОРАН МИОДРАГОВИЋ^а И СЛАЂАНА ТАНАСКОВИЋ^б

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Добијена су два нова Cu(II) комплекса са N,N',N'',N''' -тетракис(2-пиридилметил)-1,4,8,11-тетраазацикотетрадеканом (трмс) и псеудохалогенидима (NCO^- или NCSe^-). Елементарна анализа (C, H, N, Cu) одговарала је формулама: $[\text{Cu}_2(\text{NCO})\text{трмс}](\text{ClO}_4)_3 \cdot 2\text{CH}_3\text{CN}$ и $[\text{Cu}_2(\text{NCSe})_2\text{трмс}](\text{ClO}_4)_2 \cdot 2\text{H}_2\text{O} \cdot \text{C}_2\text{H}_5\text{OH}$. Начин координације трмс-а и ових амбидентатних псеудохалогенида, геометријски распоред, спектралне карактеристике (VIS, IR) и др. су упоређене са раније описаним $[\text{Cu}_2(\text{NCS})_2\text{трмс}](\text{ClO}_4)_2$. Антимикробна активност према неким бактеријама и гљивицама је тестирана и нађена само у случају NCSe комплекса.

(Примљено 11. јуна, ревидирано 2. септембра 2003)

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