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SPECTRAL INVESTIGATIONS AND DFT STUDY OF MIXED THEOPHYLLINE-N,N-CHELATING LIGAND COPPER(II) COMPLEXES

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ABSTRACT. Three new mixed-ligand theophylline (th) complexes, $[Cu(th)_2(dmen)(H_2O)]\cdot H_2O\cdot$(1), $[Cu(th)_2(tmeda)(H_2O)]\cdot 0.5H_2O$ (2) and $[Cu(th)_2(dpen)(H_2O)]\cdot 5H_2O$ (3), were synthesized and investigated by means of infrared and ESR spectroscopic methods. As co-ligands the following ethylenediamine derivatives were used: N,N-dimethyl-ethylenediamine (dmen), N,N,N',N'-tetramethyl-ethylenediamine (tmeda) and *meso*-1,2-diphenyl-ethylenediamine (dpen). Structural parameters of the complexes were investigated by using the unrestricted Becke three-parameter hybrid exchange functional, combined with the Lee–Yang–Parr correlation functional (B3LYP) and LANL2DZ basis set for geometry optimizations. Complexes 1-3 adopt square pyramidal geometries.

Keywords: *copper(II) complexes, electron paramagnetic resonance, meso-1,2-diphenyl-ethylenediamine, N, N-dimethyl-ethylenediamine, N, N, N', N'-tetramethyl-ethylenediamine, theophylline, DFT*

INTRODUCTION

Derivatives of xanthine group nucleobases, like theophylline, have been known for a long time, and commonly used for their biologic effects. Their coordination compounds may serve as model compounds for the interaction of metal ions with molecules of biologic interest.

Theophylline (Scheme 1), *i.e.,* 1,3-dimethyl-2,6-dioxo-purine, in neutral or basic media acts as monodentate ligand and coordinates through the N7 atom which is the preferred binding site in 6-oxopurines [1–3]. The deprotonated theophylline may act as bidentate ligand forming N7/O6 chelates [4].

In our previous works, we reported some new mixed-ligand complexes containing theophyllinato anions and bidentate N,O-donor and N,N-donor ligands [5-7].

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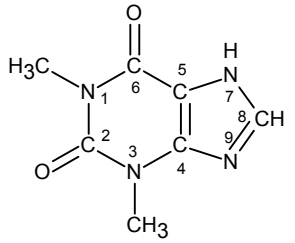
Here we report the synthesis and spectroscopic investigations of three new mixed-ligand copper(II)-theophylline complexes containing N,N-donor chelating co-ligands. The geometry of complexes was optimized at B3LYP/LANL2DZ level of theory.



Scheme 1

RESULTS AND DISCUSSION

The complexes $[Cu(th)_2(dmen)(H_2O)]\cdot H_2O$ (**1**), $[Cu(th)_2(tmeda)(H_2O)]\cdot 0.5H_2O$ (**2**) and $[Cu(th)_2(dpen)(H_2O)]\cdot 5H_2O$ (**3**) were synthesised from theophylline and appropriate N,N-chelating diamine copper(II) complexes in basic media according to published methods [5, 7]. Compounds **1**–**3** were isolated in good yield as microcrystalline solids and were characterized by elemental analyses, IR and ESR spectroscopy.

The infrared spectra of all copper(II) complexes show the two strong bands of theophylline assigned to the stretching vibration of carbonyl groups shifted towards lower wavenumbers, due to the deprotonation of theophylline and participation of C(6)=O and C(2)=O groups in intra- or intermolecular hydrogen bond formation. The C=N vibrations of the theophylline are shifted to lower wave numbers in complexes suggesting that the ligand coordinates through one of the imidazole nitrogen atoms, acting as monodentate ligand.

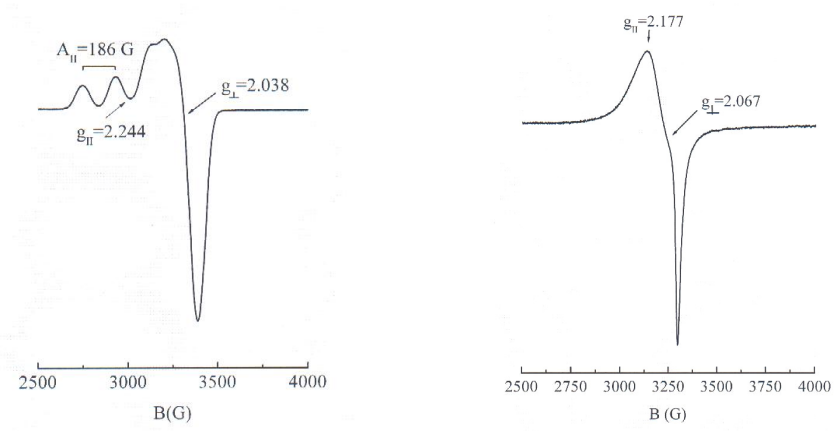
In all spectra of complexes the symmetric and antisymmetric stretching vibrations of coordinated NH_2 groups can be assigned in the 3285–3154 cm^{-1} region. There are significant changes in the bands assigned to N–H vibrations due to deprotonation of theophylline at N(7) site and coordination of the diamine type ligands The diamines are coordinated as bidentate ligands through the nitrogen atoms.

The ν_{CH} vibrations of ligands appear at 2851–2954 cm^{-1} and 3027–3066 cm^{-1} for aliphatic CH_2 and aromatic CH, respectively.

The presence of strong broad bands in FTIR spectra of the complexes at 3500–3200 cm^{-1} may be assigned to various types of hydrogen bonds [5].

Complexes **1** - **3** are monomeric. The room temperature ESR powder spectrum of $[Cu(th)_2(tmeda)(H_2O)]\cdot 0.5H_2O$ (**2**) (Fig. 1a) exhibits four

hyperfine lines in the $g_{\parallel}$ region and a strong absorption signal in the $g_{\perp}$ region. The shape of the spectrum and the values of ESR parameters ($g_{\parallel}$ = 2.244 and $g_{\perp}$ = 2.038, $A_{\parallel}$ = 186 G) correspond to a square pyramidal symmetry suggesting a CuN_4O environment for copper ion. The powder ESR spectrum of $[Cu(th)_2(dpen)(H_2O)]\cdot 5H_2O$ (**3**) at room temperature indicates a square-pyramidal symmetry. The axial components of the g tensor ($g_{\parallel}$=2.177, $g_{\perp}$ = 2.067) are typically for a CuN_4O chromophore around the metal ion. For complexes **1-3** no hyperfine splitting was observed because of the interaction of paramagnetic electron with the nitrogen nuclei.



a b

Figure 1. Powder ESR spectra of **2** (a) and **3** (b).

Computational details

Geometry optimizations were performed by using the density functional theory (DFT), and the unrestricted Becke three-parameter hybrid exchange functional, combined with the Lee–Yang–Parr correlation functional (B3LYP) and LANL2DZ basis sets. The *Gaussian09* electronic structure program package was used for calculations [8].

Optimized geometries

The molecular structures of the complexes **1**–**3** were optimized in the gaseous phase. The optimized structures are displayed in Figure 2.

Three possible binding modes were modelled: without bonding of the water molecule, with one coordinated water molecule and with two coordinated water molecules. The results showed that the pyramidal structure presents higher stabilization energy than the octahedral and (strongly distorted)

tetrahedral by 10–20 kcal/mol. The optimized structure of complexes **1-3** presents square pyramidal geometry around the pentacoordinated Cu(II), the base of distorted pyramid consisting of four N atoms of the diamine ligand and the N7 atom of each of the two theophyllinate moieties. One of the water molecules is positioned on the coordination axis, in axial position. The second water molecule in complexes **1-2** and the remaining 5 molecules in the case of complex **3** are relatively far from the central Cu(II) atom; consequently, it can be considered as being located outside the coordination sphere of Cu(II).

The main geometric parameters of complexes **1-3**, optimized at B3LYP/LANL2DZ level of theory, are listed in Table 1. Theoretical calculations revealed that the majority of optimized bond lengths are slightly longer than the experimental values of pentacoordinated copper(II) ion with same donor atoms. This can be a consequence of having performed the theoretical calculations for isolated molecules in gaseous phase, while the experimental results obtained for complexes were recorded for the compounds in solid state. Thus for complex **1** the Cu-N distances for coordinated diamine are slight longer than Cu-N distances (2.121, and 1.192 Å) found in ($[Cu^{II}$(dmen)(1,2-dtsq)$]_n$ (1,2-dtsq = 1,2-dithiosquarate), where the copper(II) ions bind to 1,2-dtsq oxygen atoms with relatively strong axial bonds [9].

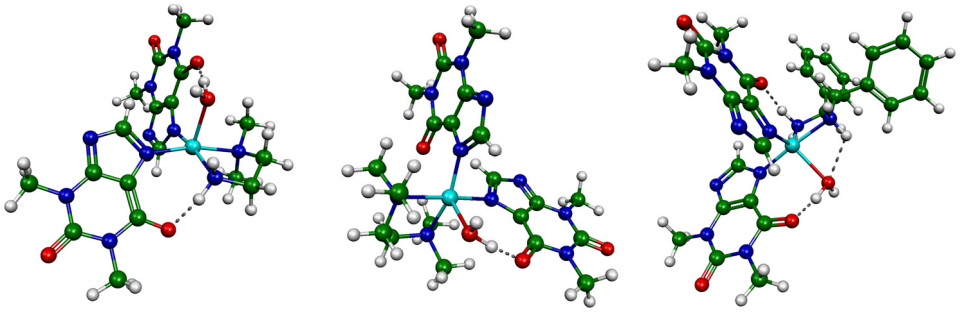
In complex **2** the calculated Cu–N distances for the diamine are longer than in $[Cu(NCS)_2(C_6H_{16}N_2)(H_2O)]$ (2.042 and 2.026 Å), and the Cu–O_w distance is shorter than Cu–O_w distance (2.342 Å) found in $[Cu(NCS)_2(C_6H_{16}N_2)(H_2O)]$, where the copper(II) has also a square pyramidal coordination [10].

In complex **3** the calculated Cu–N distances for the chelating diamine are longer than in diaqua(1R,2R)-N,N'-bis(4-methylbenzyl)-1,2-diphenyl-ethane-1,2-diamine)-copper(II)diperchlorate dihydrate (1.987 and 2.033 Å), where the copper(II) displays square planar coordination [11].

The theophyllinato moieties coordinating by N7 present Cu–N calculated distance in the range 2.061–2.181 Å, longer than those found in diaqua-bis(theophyllinato)–bis(benzylamine)copper(II) (2.029 Å) centrosymmetrical complex whose structure has previously been determined [12].

According to the calculated values, only one of the water molecules considered for optimization is located inside the coordination sphere. Therefore, the Cu(II) atom is pentacoordinated, all Cu(II) complexes exhibit a distorted pyramidal geometry.

The Cu–O distances with all co-ligands and water follow the same behaviour. They do never differ by more than 0.031 Å. The differences between Cu–N bond lengths for N7 bonded theophylline are nearly 0.063 Å (see Table 1).



1 **2** 3

Figure 2. B3LYP/LANL2DZ optimized structures of the copper(II) complexes **1**-**3**. (Color code: C – grey, N – blue, O – red, H – white, Cu – cyan)

The results show that in the most stable structures the C=O, OH and NH groups form intramolecular H-bonds of the type: C=O···H–N–H and C=O···H-O-H in **1**, C=O···H–O–H in **2**, and C=O···H–O–H, H–O–H···H–N–H, and C=O···H–N–H in **3** (Figure 2). These H-bonds have important role in the stabilization of molecules.

Table 1. Calculated structural parameters.

	1	**2**	**3**
Distances (Å)			
Cu–N_7	2.033	2.009	1.992
Cu–N_7'	2.023	2.055	2.015
Cu–N	2.161	2.157	2.056
Cu–N'	2.061	2.186	2.108
Cu–O_w	2.239	2.248	2.270
Angles (°)			
N–Cu–N'	82.93	83.92	81.63
N_7–Cu–N'	90.33	91.38	96.50
N_7–Cu–N_7'	91.41	91.85	94.07
N_7'–Cu–N	92.66	91.47	90.90
N_7–Cu–O_w	98.36	68.86	94.96

N_7 and N_7' represent the N7 donor atom of the theophylline ligands, N and N' the N donor atoms of the diamine ligand.

Vibrational analysis

The vibrational modes are analyzed by means of the atom movements, calculated in Cartesian coordinates and by visual inspection of the animated vibrations with Gabedit program [13]. Several selected calculated harmonic

frequencies are listed in Table 2, in comparison with the experimental data. The calculated values of the predicted harmonic vibrational frequencies are relatively close to the frequencies found in the experimental FTIR spectrum of the complex.

Table 2. Comparison of the observed and calculated vibrational spectra.

Assignment	Exp. IR 1 (KBr)	Calcd. 1	Exp. IR 2 (KBr)	Calcd. 2	Exp. IR 3 (KBr)	Calcd. 3
O−H str.	3435	3787	3567 3517	3785	3462	3778
N−H str.	3285 3154	3557 3097	–	–	3245 3161	3567 3328
C−H str.	2948 2924 2882 2851	3162 3079 3069 3025	2963 2929	3144 3079 3040 3023	2948 2918 2851	3220 3160 3076
C=O str.	1686 1642	1666 1625	1690 1636	1667 1631	1690 1641	1666 1623

CONCLUSIONS

In summary, we have synthesized and characterized three new mixed-ligand theophyllinato-N,N-donor coordination compounds. A combination of spectroscopic methods and density functional calculations has been used to describe the structure of complexes. For the Cu(II)theophylline complexes with diamine ligands the local symmetry around the Cu(II) ion is strongly influenced by the nature of amines. IR investigations suggest monodentate coordination of the theophylline, respectively the bidentate coordination of the diamine ligands to central copper ion with N atoms. According to the ESR data, all complexes contain the $\{CuN_4O\}$ chromophore, with square pyramidal coordination geometries around the central copper(II) ion. The theophylline coordinates *via* the N7 nitrogen.

Theoretical investigations at B3LYP/LANL2DZ level of the theory revealed that the utilized technique is efficient in optimizing structural geometries of systems based on organic molecules and copper(II) ions.

EXPERIMENTAL SECTION

All reagents and solvents were commercially available and were used without further purification.

Synthesis of (N,N-dimethyl-ethylenediamine)(aqua)-bis(theophylli nato)-copper(II) monohydrate, $[Cu(th)_2(dmen)(H_2O)]\cdot H_2O$ (**1**): To a suspension of

theophylline (0.4 g, 2.02 mmol) in water (15 cm^3), N,N-dimethyl-ethylenediamine (0.5 cm^3) was added. The resulted clear solution was mixed with a second solution of $Cu(NO_3)_2 \cdot 2H_2O$ (0.2195 g, 1 mmol) in an N,N-dimethyl-ethylenediamine–water mixture (1:5). The reaction mixture was heated at 50°C for 60 min. under stirring and stored at room temperature over night. The resulted blue polycrystalline powder was collected by filtration, washed with aqueous N,N-dimethyl-ethylenediamine (5%) and dried. M.W.: 545.78. Yield: 81%. Elemental analysis: found (calc.) for $C_{18}H_{30}N_{10}O_6Cu$: C 39.58 (39.56), H 5.54 (5.45), N 25,66 (25.41).

(N,N,N',N'-tetramethyl-ethylenediamine)(aqua)-bis(theophyllinato) - copper(II) monohydrate, $[Cu(th)_2(tmeda)(H_2O)] \cdot 0.5H_2O$ (**2**) was obtained similarly from N,N,N,N-tetramethyl-ethylenediamine. M.W.: 556.08. Yield: 62%.

Aqua-(meso-1,2-diphenyl-ethylenediamine)-bis(theophyllinato)-copper(II) pentahydrate (**3**), $[Cu(th)_2(dpen)(H_2O)] \cdot 5H_2O$ was obtained with the same procedure, by heating at reflux for 3 hours, from (meso-1,2-diphenyl-ethylenediamine). Violet crystals were collected. M.W.: 742.25. Yield: 41%. Elemental analysis: found (calc.) for $C_{28}H_{42}N_{10}O_{10}Cu$: C 45.33 (45.31), H 5.18 (5.70), N 18.63 (18.87).

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