

Synthesis, Crystal Structures and Characterization of a New Antitumor Cu(II) Complex with N-sulfonamide Ligand

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A new Cu(II) complex with N-sulfonamide ligand, [Cu(N-(5-(4-methylphenyl)-[1,3,4]-thiadiazole-2-yl)-toluenesulfonamidate)₄](CH₃)₂NH₂⁺)₂ (complex) has been synthesized and characterized. The X-ray crystal structure of the complex has been determined. The Cu(II) ion is four-coordinated, forming a CuN₄ chromophore. The ligand acts as monodentate, coordinating the metal ion through a single N_{thiadiazole} atom. The complex has a square planar geometry. The characterization of the complex has been studied by FT-IR, electronic, EPR spectroscopic and magnetic methods.

Keywords: copper complex, N-substituted sulphonamides, crystal structure, ERP spectrum

Metal ions are important for the course of the vital functions of the living organisms where they occur under the form of complex or chelate combinations, as well as for the methods of analysis and control of the medical substances by forming complexes [1-5].

The stability of the complex combinations depends on: the nature of the metal ion generating the complex, the nature of the ligand, the relative affinity of the donor atoms for the acceptor atoms and ions and the affinity for electrons of the central metal atom and with the basic character of the ligand. The participation of some given functional groups within a metal bond depends on its level of competition with the existing neighbouring functional groups, as well as on the competition of the protons and of the metal ions with the potential donor atoms [3].

The synthesis of Cu(II) complexes with N-sulfonamides ligands greatly increased in the past twenty years due to the diversity of biological activity of the resulting compounds: antimicrobial, anti-inflammatory, SOD mimetic, nuclease and antitumor activity. Studies have shown that Cu(II) complexes with different types of ligands can be used as potential *chemical nucleases* [6-8].

In this context, we have described the nuclease activity of several copper-sulfonamide complexes [9-12]. In the present paper we report the synthesis and the physico-chemical characterization of a new Cu(II) complex with N-substituted heterocyclic sulfonamide: HL=N-(5-(4-methylphenyl)-[1, 3, 4]-thiadiazole-2-yl)-toluenesulfonamide. Its structure was determined by X-ray diffraction. Their IR, EPR, electronic spectra and its magnetic susceptibility were investigated and discussed, along with the structural and spectral comparisons with those of the analogous complexes. Antitumor activity of this complex will be the subject of a future article.

Experimental part

Materials and physical measurements

Copper sulfate pentahydrate, copper acetate monohydrate, N,N'-dimethylamine and methanol were purchased from commercial sources and used as received.

Elemental analyses (C, N, H, S) were performed with Vario EL analyser. IR spectra were recorded with a Jasco FT/IR-4100 spectrophotometer using diffuse reflectance

of incident radiation focused on a sample, in the 4000-400 cm⁻¹ range. All melting points were determined in open capillaries with an Electrothermal IA 9100 apparatus and were uncorrected. Diffuse reflectance spectra were carried out on a Jasco V-550 spectrophotometer. Magnetic susceptibilities were measured at room temperature with the Faraday MSB-MKI balance. Hg[Co(NCS)₄] was used as susceptibility standard. Electronic paramagnetic resonance (EPR) spectra were performed at room temperature with a Bruker ELEXSYS spectrometer operating at the X-band frequency.

The synthesis, structure and properties of the ligand HL have been reported [13].

Synthesis of the complex [Cu(N-(5-(4-methylphenyl)-[1,3,4]-thiadiazole-2-yl)-toluenesulfonamidate)₄](CH₃)₂NH₂⁺)₂ complex

Cu(CH₃COO)₂ · H₂O (0.20g, 1 mmol) was added under continuous stirring to a solution of (0.690g, 2 mmols) HL ligand dissolved in a mixture of 50 mL methanol and 10 mL N, N'-dimethylamine. The resulting green solution was stirred for two hours and was then left to stand at room temperature. After one month by the slow evaporation of the solvent, brown crystals suitable for X-ray diffraction were obtained.

Data for compound (yield 65%).

Anal. Calcd. mass fractions of elements, w/ %, for C₂₈H₂₈CuN₁₄S₈O₈ (Mr = 1533.33) are: C 53.21, H 4.69, N 12.78, S 16.69; found: C 53.09; H 4.25; N 11.84; S 17.02. IR (KBr) ν_{max}/cm⁻¹: 1442 (thiadiazole); 1278(S=O), 1140 (S=O), 917 (S-N). UV/Vis (solid) λ_{max}/nm: 300 (π→π*), 396 (LMCT), 510 (d-d). ε=70 cm⁻¹M⁻¹) (Yield ca. 58%).

X-ray crystallography

A brown crystal of the complex was mounted on a glass fiber and used for data collection. Crystal data were collected at 293(2) K using a dual microsource SuperNova Diffractometer and Cu K_α radiation (λ = 1.54184 Å).

Using Olex 2 [14], the structure was solved with the Superflip [15] structure solution program using Charge Flipping and refined with the ShelXL [16] refinement package using Least Squares minimisation. A summary

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of the crystal data, experimental details and refinement results is listed in table 1.

Results and discussions

Crystal structures of $[\text{Cu}(\text{L})_4][(\text{CH}_3)_2\text{NH}_2^+]_2$ complex

Relevant bond distances and angles for the complex are collected in table 2.

The molecular structure and crystallographic numbering scheme for the complex are illustrated in figure 1.

The crystal structure of the complex contains a CuN_4 entity in a square planar geometry. In this complex, the Cu(II) ion is coordinated by four molecules of ligand. Each ligand acting as monodentate and coordinates the metal ion through one N_{thiadiazole} atom of the thiadiazole rings. The Cu1-N_{thiadiazole} distances (1.988(2) - 2.002(2) Å) are similar to those reported for other complexes with ligands containing a thiadiazole ring [17, 18]. The coordination bond angles ranging from 89.10(9)° [N22-Cu1-N33] to 90.89(9)° [N22-Cu1-N33], confirm the regular square-planar

geometry of the complex. The distortion of the square-planar geometry (commonly known as tetrahedrality) can be determined from the angle subtended by two planes, each encompassing the copper and two adjacent atoms. The dihedral angle between the planes N22Cu1N33 and N22Cu1N33 (the tetrahedrality) equal to 0° confirms that the five atoms (Cu1 and the four N_{thiadiazole} atoms) are in the same plane so the regular square-planar geometry of the CuN_4 chromophore. For the complex, the crystalline packing of the symmetrical unit also includes a $(\text{CH}_3)_2\text{NH}_2^+$ molecules from the reaction medium, that does not coordinate the Cu(II) ion.

The complex also presents the C-H... π interactions, involving the H4 and H7 atoms which points towards the center of the methylphenyl ring in the same complex molecule. Intramolecular C-H... π interactions contribute to the stabilization of the $[\text{Cu}(\text{L})_4][(\text{CH}_3)_2\text{NH}_2^+]_2$ complex (fig. 2).

Also, the complex is stabilised by intermolecular strong and weak hydrogen interactions [19], implicating hydrogen atoms from the N, N'- dimethylamine, N_{dimethylamine} and N_{sulfonamido} or O_{sulfonamido} atoms. The geometric

Table 1
CRYSTAL DATA AND REFINEMENT FOR $[\text{Cu}(\text{L})_4][(\text{CH}_3)_2\text{NH}_2^+]_2$ COMPLEX

Complex	
Empirical formula	C ₆₈ H ₇₂ Cu N ₁₄ O ₈ S ₈
Formula weight	1533.43
Temperature	293(2) K
Wavelength	1.54184 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 11.5783(6) Å α = 78.441(4)° b = 12.6625(6) Å β = 81.530(4)° c = 13.0863(4) Å γ = 76.040(4)°
Volume	1814.25(16) Å ³
Z	2
Calculated density	1.403 g/cm ³
Absorption coefficient	3.100 mm ⁻¹
F(000)	799
Crystal size	0.15 x 0.19 x 0.25 mm
θ range for data collection	4.58 to 71.84°
Limiting indices	-14 ≤ h ≤ 14, -15 ≤ k ≤ 15, -16 ≤ l ≤ 16
Reflections collected/unique	6899 / 5472 [R(int) = 0.0382]
Completeness to θ = 27.48	99.54 %
Data/restraints/parameters	6899 / 4 / 484
Goodness-of-fit on F ²	1.030
Final R indices [I > 2σ(I)]	R1 = 0.0583, wR2 = 0.1201
R indices (all data)	R1 = 0.0449, wR2 = 0.1342

Table 2
SELECTED BOND DISTANCES (Å) AND ANGLES (°) FOR THE COMPLEX

Complex	
<i>Bond distances</i>	
Cu1-N22	1.998 (2)
Cu1-N33	2.002 (2)
<i>Bond angles</i>	
N22-Cu1-N22	179.998 (1)
N22-Cu1-N33	89.11 (9)
N22-Cu1-N33	89.10 (9)
N22-Cu1-N33	90.89 (9)
N22-Cu1-N33	90.89 (9)
N33-Cu1-N33	179.997 (2)

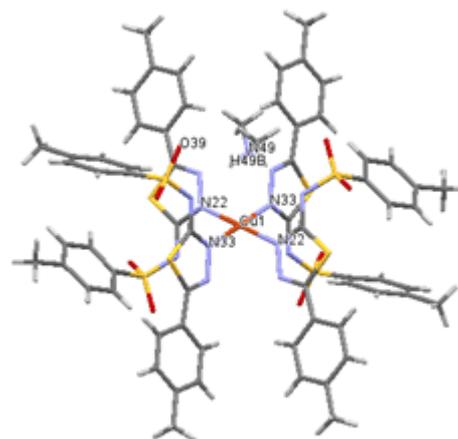


Fig. 1. Molecular structure of the complex $[\text{Cu}(\text{L})_4][(\text{CH}_3)_2\text{NH}_2^+]_2$

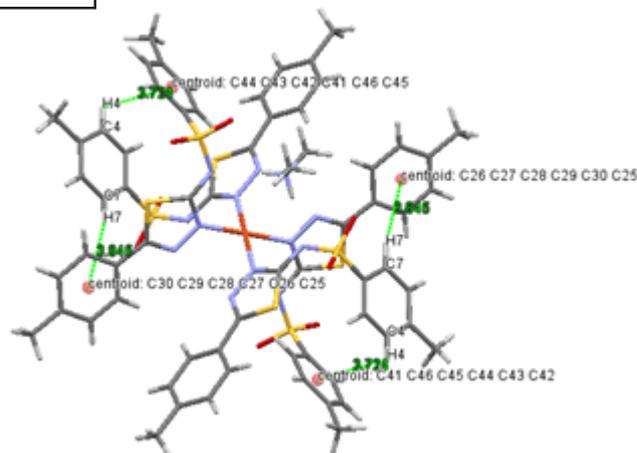


Fig. 2. Crystal packing of the complex $[\text{Cu}(\text{L})_4][(\text{CH}_3)_2\text{NH}_2^+]_2$ showing the C-H... π interactions

D-H...A	d(D-H) (Å)	d(H...A) (Å)	d(D...A) (Å)	<(DHA) (°)
N49-H49A ...N11 (strong)	0.900	2.003	2.897	172.38
N49-H49B....N36(strong)	0.900	2.084	2.981	173.73
N49-H49B...O39(weak)	0.990	2.426	3.000	121.89

Table 3
HYDROGEN INTERACTIONS FOR
THE COMPLEX

parameters defining the hydrogen interactions are collected in table 3.

In the complex, the sulfonamide ligand (HL) acting as monodentate through a nitrogen atom of the thiadiazole heterocycle. The sulfonamide molecules of this type can behave as bidentate ligands as well through the N atom from the thiadiazole moiety and through one of the O atoms and even through the N_{sulfonamido} atom from the sulfonamido moiety [20].

The presence of aromatic rings like methylphenyl in the structure of the sulfonamides is probably the main variable determining their capacity to destroy DNA. Their complexes have a higher capacity to destroy DNA than the non-coordinated sulfonamide ligand. These plane aromatic rings allow the complex molecule to come closer to DNA through intercalation between neighboring base pairs of the DNA chains, and then link with them through π -stacking bonds [12].

Spectroscopic and magnetic properties

The IR spectrum of the complex present a similar pattern with the other Cu(II) complexes with N-substituted sulfonamide. The most remarkable difference occurs in the band corresponding to the stretching vibration of the thiadiazole ring, which is shifted from 1542 cm⁻¹ (HL) in the free ligand to 1442 cm⁻¹ (1) in the complex. The characteristic band corresponding to the ν (S-N) appears at 917 cm⁻¹ shifted to higher frequencies with respect to those of the uncoordinated ligands (906 cm⁻¹(HL)). These modifications in the thiadiazole heterocycle and in the sulfonamide group are attributed to the involvement to the N_{thiadiazole} atom in coordination of Cu(II) and to the deprotonation of the sulfonamido moiety for the both complexes [21]. Bands due to the antisymmetric and symmetric vibration modes of the S=O bond appear at 1278 and 1140 cm⁻¹, ca. 20 cm⁻¹ lower than those corresponding to the free ligand; [22, 23] such a decrease can be related to the electron transfer from the deprotonated, negatively charged N atom to the sulfonyl oxygen atoms, which results in partial single-bond character for the S-O bonds [24]. Such electron transfer increases the bond order of the S-N moiety, thus accounting for the 25 cm⁻¹ shift towards higher wave numbers of the band due to the stretching mode of this bond. The lack of bands close to 3200 cm⁻¹, which were originally present in the spectra of the free ligands confirm deprotonation of the N-H bonds. This deprotonation of N_{sulfonamido} atom determines a weak conjugation effect among the three N, S, O atoms of the moiety. In general, the patterns of the IR spectrum are similar to those observed for other cooper N-sulfonamide derivatives [23, 25].

The solid electronic spectrum of the complex display a band near 400 nm (396 nm) assigned to a LMCT transition. The complex exhibits a d-d band at 510 nm. This pattern, characteristic for square-planar geometry, agrees well with the crystallographic data [26].

The polycrystalline X-band EPR spectrum of the complex is axial. The EPR parameters, obtained by simulation [27] are $g_{||} = 2.23$, $g_{\perp} = 2.024$ and $A_{||} = 185 \times 10^4$ cm⁻¹ (fig. 3).

According to the Bertini classification, the value of $A_{||}$ can be correlated with the geometry of the complex [28]. Thus, values between 160 and 200 $\times 10^4$ cm⁻¹ correspond to a square-planar geometry. As $g_{||} > g_{\perp}$ in the complexes, the unpaired electron must be in the $d_{x^2-y^2}$ (or d_{xy}) orbital [29]. The room temperature magnetic moment of the complex ($\mu_{\text{eff}} = 1.73$ MB) is consistent with the presence of a single unpaired electron.

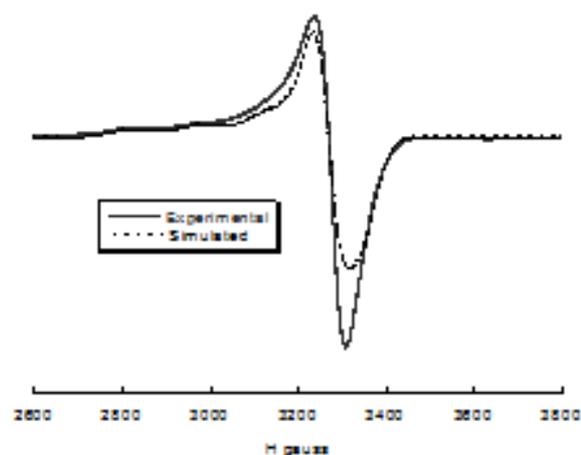


Fig. 3. X-band polycrystalline powder EPR spectrum of the complex

Conclusions

A new Cu (II) complex with N-sulfonamide ligand, Cu(N-(5-(4-methylphenyl)-[1,3,4]-thiadiazole-2-yl)-toluene-sulfonamide)₄((CH₃)₂NH₂⁺)₂ was synthesized and characterized. The crystalline structure of the complex was attributed using X-ray diffraction and was confirmed by the data obtained from elemental analysis, spectral (IR, UV-Vis, EPR) and magnetic determinations.

Crystallographic data without structure factors for the structure reported in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publications no. CCDC-1519070. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk; www.ccdc.cam.ac.uk/data/request/cif).

Acknowledgement: Adriana Hangan is thankful for the financial support offered by research grant Resurse Umane PNII -PD 474/2010.

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Manuscript received: 28.08.2017