STUDIA UNIVERSITATIS BABEŞ-BOLYAI, CHEMIA, LV, 1, 2010

CU(II) COMPLEXES WITH N-SUBSTITUTED SULFONAMIDES

ADRIANA HANGAN[a], JOAQUIN BORRAS[b], LUMINITA OPREAN[a]

ABSTRACT. The paper reports the synthesis, physical and chemical characterization of two complexes with Cu(II) and N-substituted sulfonamide as ligands:
[Cu(*N*-(5-ethyl-1,3,4-thiadiazol-2-yl)-4-methylbenzene-sulfonamidate)$_2$(ethylenediamine)] (**1**) and [Cu(*N*-[5-(ethylsulfanyl)-1,3,4-thiadiazol-2-yl]benzenesulfonamidate)$_2$(H_2O)$_3$] (**2**). The structures of complexes were confirmed by elemental analysis, IR, UV-Vis spectroscopy, magnetic measurements and electronic paramagnetic resonance (EPR) spectra. Correlations of the results obtained from physico-chemical investigations afford the assignment of the most probable structural formulae for the metal complexes. The ligands act as monodentate, coordinating the metal ion geometry through a single $N_{thiadiazole}$ atom. The complex **1** present a square-planar and the complex 2 present a slightly distorted square pyramidal geometry.

Keywords: *copper(II) complexes, sulfonamides N-substituted*

INTRODUCTION

The study of N-substituted heterocyclic sulfonamide ligands shown their ability to coordinate biologically important metallic ions. The pharmacological activity and the chelating properties of sulfonamides allow the synthesis of metallic complexes with various therapeutic activities, which serve as models for metalloenzymes. Studies have shown that copper(II) complexes with N-substituted sulfonamides as ligands can be used as potential “chemical nucleases”. The aromatic rings in the structure of these ligands can be intercalated between the bases of the DNA chain. The cleavage of the DNA chain is a result of the complex interaction with the DNA bases and the formation of ROS (due to the presence of Cu(II)) [1-5].

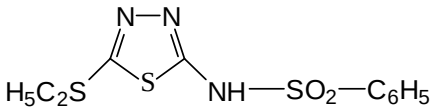
Taking into consideration these aspects, in this paper we report the synthesis and characterization of two Cu(II) complexes with *N*-(5-ethyl-1,3,4-thiadiazol-2-yl)-4-methylbenzenesulfonamide (HL1) and *N*-[5-(ethylsulfanyl) -1,3,4-thiadiazol-2-yl]benzenesulfonamide (HL2). The ethylenediamine molecule as bidentate ligand and the water molecule as monodentate ligand also participate to the coordination of Cu(II) in the complex 1 respectively complex 2.

[a] *Universitatea de Medicina si Framacie, Facultatea de Farmacie, Str. Ion Creanga Nr. 12, RO- Cluj-Napoca, Romania, acomsa6@yahoo.com*
[b] *Universidad de Valencia, Facultad de Farmacia, 46100 Burjassot, Valencia, Spain*

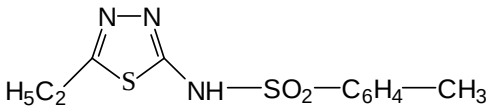
RESULTS AND DISCUSSION

The synthesized ligands (scheme 1) previously reported [2,6] can coordinate various metallic ions through N, S, O atoms present in their molecule. Thus, they can behave like monodentate, bidentate or polydentate ligands. In most cases, the coordination can take place at the two nitrogen atoms of the thiadiazole moiety $\mathbf{N_{thiadiazole}}$, the nitrogen atom of the sulfonamide $\mathbf{N_{sulfonamide}}$, protonated or deprotonated, and even at the sulfur $\mathbf{S_{sulfonamide}}$ or oxygen $\mathbf{O_{sulfonamide}}$ atom from the same sulfonamide moiety. In the majority of the syntheses of metallic complexes, the nitrogen atom of the sulfonamide moiety becomes deprotonated. Through its negative charge it thus contributes to the compensation of the positive charges of the metallic ions which generate the complexes [7,8].

The elemental analyses show that the complexes are type $[Cu(L1)_2(ethylenediamine)]$ (complex **1**) and $[Cu(L2)_2(H_2O)_3]$ (complex **2**). The compounds are microcrystalline powders, insoluble in methanol, ethanol, acetone, chloroform and soluble in dimethylformamide and in dimethylsulfoxide. The complexes are stable at room temperature and light.



N-(5-ethyl-1,3,4-thiadiazol-2-yl)-4-methylbenzenesulfonamide (**HL1**)



N-[5-(ethylsulfanyl)-1,3,4-thiadiazol-2-yl]benzenesulfonamide(**HL2**)

Scheme 1

Spectroscopic and magnetic properties

The IR spectra of both complexes present a similar pattern. The most remarkable difference occurs in the band corresponding to the stretching vibration of the thiadiazole ring, which is shifted from 1530 cm^{-1} (HL1) and 1566 cm^{-1} (HL2) in the free ligands to 1482 cm^{-1} (complex **1**) and 1486 cm^{-1} (complex **2**) in the complexes. The characteristic band corresponding to the v(S–N) appears at 930 cm^{-1} (complex **1**) and 938 cm^{-1} (complex **2**) shifted towards higher frequencies with respect to those of the uncoordinated ligands. These modifications in the thiadiazole heterocycle and in the sulfonamide

group correspond to the involvement to the $N_{thiadiazole}$ atom in coodination of Cu(II) and to the deprotonation of the sulfonamido moiety [9,10]. This deprotonation will also lead to an electron delocalization involving the atoms of the sulfonamide moiety and the atoms from the thiadiazole ring [11]. There are also modifications of the values of the symmetrical and asymmetrical valence vibrations [$v_s(SO_2)$ and $v_{as}(SO_2)$] for the S=O bond of the sulfonamide moiety, as they too shift to lower frequencies in the complex's IR spectrum (1123 and 1297 cm^{-1} (complex **1**) respectively 1142 and 1300 cm^{-1} (complex **2**)). The IR spectrum of the complex **1** shows an overlap of some other bands on the bands corresponding to the ligands, which makes them difficult to assign. Thus, the characteristic bands of the -NH_2 group of ethylenediamine (2900 cm^{-1}, 1600 cm^{-1} and 1460 cm^{-1}) cannot be distinguished from the sulfonamide ligand bands [12,13].

UV-Vis, EPR and magnetic properties

The solid electronic spectrum of both complexes displays a band near 400 nm (395 nm for complex **1** and 402 nm for complex **2**) assigned to a LMCT transition. The complex 1 exhibits a d-d band at 606 nm and the complex 2 show a d-d band at 669 nm. This band (for complex 2) is in the 600-850 nm range stated by literature for Cu(II) with square pyramidal geometry, showing a CuN_2O_3 chromophore [14,15].

The presence of ethylenediamine in the complexe 1 leads to a stronger separation between the e_g-t_{2g} orbitals of the Cu(II) ion, leading to a shift towards lower wave-lenghts for the electron transitions of the metallic ion [14]. This pattern is characteristic for distorted square-planar cooper (II) complexes [16].

The polycrystalline X-band EPR spectra of the both complexes are axial. The EPR parameters, obtained by simulation [17] are $g_{\|}$ = 2.135, $g_{\perp}$ = 2.075 and $A_{\|}$= 180 x 10^{-4} cm^{-1} for complex **1** (figure 1) and $g_{\|}$ = 2.22, $g_{\perp}$ = 2.09 and $A_{\|}$= 150 x 10^{-4} cm^{-1} (figure 2) for complex **2.** According to the Bertini classification, the values of $A_{\|}$ for complex 1 and complex 2 can be correlated with the structure of the complex [18]. Thus, values between 160 and 200 x 10^{-4} cm^{-1} correspond to a square-planar geometry. The value of $A_{\|}$ for complex **1** can be correlated with the geometry of the complex [18]. Values between 130 and 160 cm^{-1} correspond to a square pyramidal or distorted trigonal bipyramidal geometry. As $g_{\|} > g_{\perp}$ in the complexes, the unpaired electron must be in the $d_{x^2-y^2}$ (or d_{xy}) orbital [19].

The room temperature magnetic moments of complexe 1 (μeff = 1.72 MB) and for complex 2 (μeff = 1.83 MB) are consistent with the presence of a single unpaired electron.

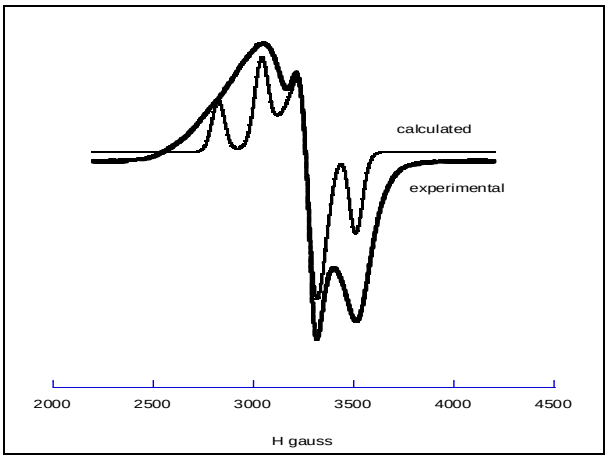


Figure 1. X Band EPR of the compound **1**

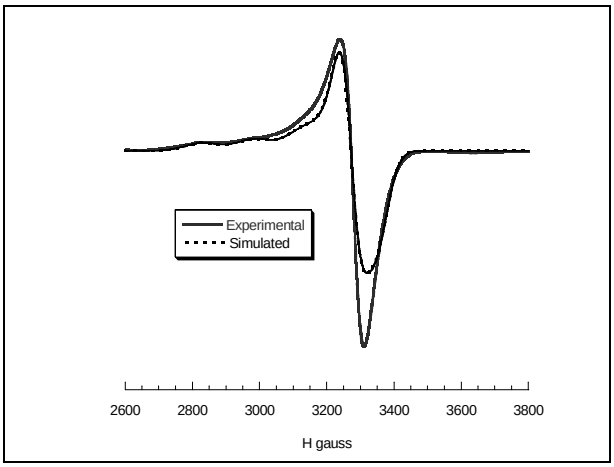
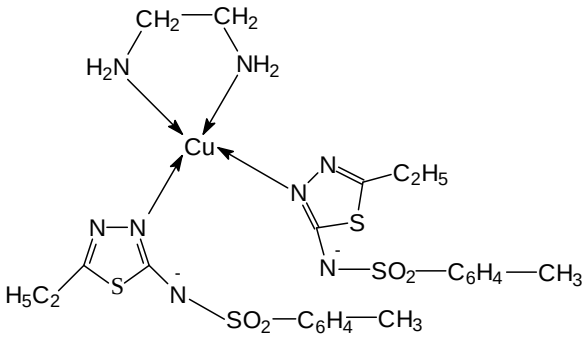


Figure 2. X Band EPR of the compound **2**

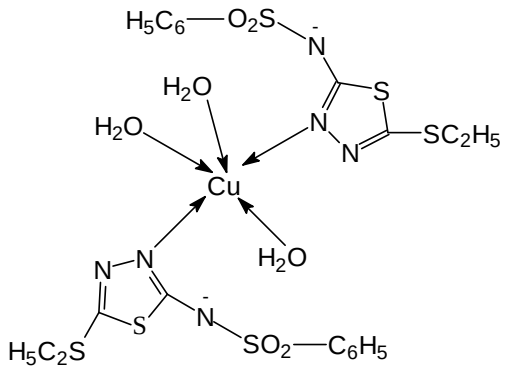
CONCLUSIONS

Two complexes of Cu(II) with sulfonamides N-substituted were synthesized: $[Cu(L1)_2$(ethylenediamine)] (complex **1**) and $[Cu(L2)_2(H_2O)_3]$ (complex **2**). The results offered by distinct methods for structural characterization of the complexes (i.e. elemental analysis, spectral (IR, UV-Vis, EPR) and magnetic determinations) together with the crystallographic data available for other mononuclear copper (II) complexes containing the same N-substituted sulfonamide ligands (HL1 and HL2) [2,6] allowed us to propose the structural formulae shown in figure 3. The capacity of DNA cleavage by

copper-sulfonamides complexes is of considerable interest because of their potential use as ”chemical nucleases” and thus, as chemotherapeutic and antiviral agents.



Complex 1 – $[Cu(L1)_2(ethylenediamine)]$



Complex 2 – $[Cu(L2)_2(H_2O)_3]$

Figure 3. The proposed structure of two complexes C1 and C2

EXPERIMENTAL SECTION

Materials and physical measurements

Copper chloride dihydrate, copper acetate monohydrate and ethylenediamine were purchased from commercial sources. All reagents used were of analytical grade. The two ligands (HL1 and HL2) used for the synthesis of the complexes were synthesized by our group.

Elemental analysis (C, N, H, S) were performed on a Perkin-Elmer device, using the combustion technique. IR spectra were recorded with a Perkin–Elmer FT-IR 1730 spectrophotometer using powder samples in KBr disks, in the 4000-400 cm^{-1} range. Fast ion bombardment (FAB) mass spectra were obtained on a VG Autospec spectrometer in m-nitrobenzene as a solvent. Diffuse reflectance spectra (nujol mulls) were carried out on a Shimadzu UV-2101 PC 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.

Synthesis of the ligands
N-(5-ethyl-1,3,4-thiadiazol-2-yl)-4-methylbenzenesulfonamide (**HL1**) and
N-[5-(ethylsulfanyl)-1,3,4-thiadiazol-2-yl]benzenesulfonamide (**HL2**)

The two ligands were obtained and characterized as previously reported by our group [2,19].

Synthesis of the complexes
[Cu(N-(5-ethyl-1,3,4-thiadiazol-2-yl)-4-methylbenzenesulfonamidate)$_2$(ethylenediamine)] ***(1)***

1 mmol of the ligand (HL1) is dissolved in 40 ml of methanol. To this solution is added 1 mmol of $CuCl_2 \cdot 2H_2O$ and the mixture is stirred until the cooper salt is completely dissolved, forming a green solution. 0.5 mmol of ethylenediamine are added dropwise. The solution turns to blue, forming a violet precipitate (Cu(II)-ethylenediamine complex). The mixture is stirred at room temperature for three hours. The precipitate is then filtered. The filtrate is kept at room temperature in a crystallizer. After four weeks by the slow evaporation of the solvent a blue crystalline powder was obtained. This powder was than filtrated and further crystallized using methanol.
Data for complex **1** (yield 68%).
$C_{24}H_{32}CuN_8S_4O_4$ (688): C 42.03 (calc. 41.86); H 4.58 (4.65); N 16.45 (14.27); S 18.93 (18.60)%. IR (KBr) (ν_{max} (cm^{-1})): 1482 (thiadiazole); 1297, 1123 $\nu(SO_2)$; 930 ν(S–N). Solid UV/Vis (λ_{max}) (nm): 395 (LMCT), 606 (d-d).

*[Cu(N-[5-(ethylsulfanyl)-1,3,4-thiadiazol-2-yl]benzenesulfonamidate)$_2$(H_2O)$_3$] **(2)***

1 mmol of HL2 ligand is dissolved in a mixture of 40 ml methanol. Separately, a solution of 0.5 mmol $Cu(CH_3COO)_2$ H_2O and 5 ml of water was prepared. The copper solution is added to the ligand solution under continuous stirring. The resulting mixture is stirred at room temperature for two hours. The resulting light green solution is kept in a crystallizer at room temperature. After a few days, the complex was obtained as a green crystalline powder. This powder was then filtrated and further crystallized using methanol.

Data for complex **2** (yield 65%).
$C_{20}H_{26}CuN_6S_6O_7$ (718): C 33.18 (calc. 33.42); H 3.54 (3.62); N 11.38 (11.69); S 27.03 (26.74)%. IR (KBr) (ν_{max} (cm^{-1})): 1486 (thiadiazole); 1300, 1142 $\nu(SO_2)$; 938 ν(S–N). Solid UV/Vis ($\lambda_{max)}$ (nm): 402(LMCT), 669 (d-d).

ACKNOWLEDGEMENT

The authors are thankful for the financial support offered by research grants CNCSIS 1467 and PN II 61-003.

REFERENCES

1. B. Marcias, I. Garcia, M.J. Villa, M. Gonzalez-Alvarez, J. Borras, A. Castineiras, *Journal of Inorganic Chem*istry, **2003**, *96,* 367.
2. A. Hangan, J. Borras, M. Liu-Gonzalez, L. Oprean, *Z. Anorg. Allg. Chem*., **2007**, *633*, 1837.
3. M. Gonzalez-Alvarez, G. Alzuet, J. Borras et al., *Journal of Biological Inorganic Chemistry*, **2008**, *13*, 1249.
4. A.M. Thomas, M. Nethaji, S. Mahadevan et al., *Journal of Inorgani Biochem*istry, **2004**, *98*, 1087.
5. J. L. Garcia-Gimenez, G. Alzuet, M. Gonzalez-Alvarez, M. Liu-Gonzalez, A. Castineiras, J. Borras, *Journal of Inorganic Biochem*istry, **2009**, *103*, 243.
6. A. Hangan, J. Borras, M. Liu-Gonzalez, L. Oprean, *Revista de Chimie*, **2009**, *60*, 755.
7. M. Gonzalez-Alvarez, G. Alzuet, J. Borras, M. Pitie, B. Meunier, *Journal of Biological Inorganic Chemistry*, **2003**, *8*, 644.
8. B. Marcias, M.V. Villa, B. Gomez, J. Borras, G. Alzuet, M. Gonzalez-Alvarez, A. Castineiras, *Journal of Bioinorganic Chemistry*, **2007**, *101*, 441.
9. M. Gonzalez-Alvarez, G. Alzuet, J. Borras, L. Castillo de Agudo, S. Garcia-Granada, J.M. Montejo-Bernardo, *Journal of Inorganic Biochemistry*, **2004**, *98*, 189.
10. J. Casanova, G. Alzuet, S. Ferrer, J. Latorre, J.A. Ramirez, J. Borras*, Inorganica Chimica Acta*, **2000**, *304*, 170.
11. C.A. Otter, S.M. Couchman, J.C. Jeffery, K.L.V. Mann, E. Psillakis, M.D. Ward, *Inorganica Chimica Acta*, **1998**, *278*, 178.
12. M.J. Begley, P. Hubberstey, J. Stroud, *Polyhedron*, **1997**, *16*, 805.
13. G. Alzuet, S. Ferrer, J. Borras, R. Martinez-Manez, *Polyhedron*, **2000**, *19*, 725.
14. A.B.P Lever, “Inorganic Electronic Spectroscopy”, Elsevier, New York, **1984**, 356.
15. I. Beloso, J. Borras, J. Castro, J. A. Garcia-Vazquez, P. Perez-Lourido, J. Romero, A. Sousa, *European Journal of Inorganic Chemistry*, **2004**, *3*, 635.

16. B.J. Hathaway, “Comprehensive Coordination Chemistry”, Pergamon Press, Inc, New -York, **1987**, chapter 9.
17. WINEPR-Simfonia 1.25. (1994-1996) Bruker Analytik GmbH: Kalsruhe.
18. I. Bertini, R. Drago, “ESR and NMR of Paramagnetic Species in Biological and Related System”, Springer, Boston, **1980**.
19. E. Colacio, J.P. Costes, R. Kivekas, J.P. Laurant, J. Ruiz, M. Sundberg, *Journal of Inorganic Chemistry*, **1991**, *30*, 1475.