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Short communication

Characterization of a Cu(II) complex of sulfadimethoxine

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Abstract

The molecular structure of $[Cu(sulfadimet)_2]\cdot SO(CH_3)_2$ (sulfadimet=sulfadimethoxine=4-*p*-aminobenzenesulfonamido-2,6-dimethoxypyrimidine) was determined by single crystal X-ray diffractometry. It crystallizes in the monoclinic space group $P2_1/c$ with $Z=4$. The Cu(II) cation is in a distorted CuN_5 square pyramidal coordination, involving four sulfadimethoxine molecules, one of them acting as a bidentate ligand. The infrared spectrum is briefly discussed on the basis of the structural peculiarities of the complex.

Keywords: Copper(II) complex; Sulfadimethoxine; Crystal structure; IR spectrum

A number of sulfonamides, such as sulfanilamide, sulfapyridine, sulfathiazole and sulfadiazine were the first effective chemotherapeutic agents employed systematically for the prevention and cure of bacterial infections in humans [1,2].

After the introduction of penicillin and other antibiotics the popularity and applications of sulfonamides decreased rapidly. However, they are still considered as useful in certain therapeutic fields, especially in the case of ophthalmic infections as well as infections in the urinary and gastrointestinal tract [1].

On the other hand, the complex formation between metal ions and sulfadrugs, pointing to the combined antibacterial activity of sulfonamides and the antimicrobial activity of heavy metals constitute an important field of research. Notwithstanding, the literature on the chemistry of these types of sulfonamide derivatives, and especially their structural characteristics, is rather incomplete and often controversial [1].

Copper (II) complexes of different sulfonamides have been prepared and investigated in recent years [3–8]. In this context, and also as a continuation of our own studies on copper complexes with pharmacological activity [9–18], we obtained single crystals of the respective sulfadimethoxine complex and determined its structural characteristics and vibrational-spectroscopic behavior.

The complex was obtained by interaction of the ligand with a Cu(II) solution, as follows: sulfadimethoxine, Sigma (3.10 g, 0.01 mol) was suspended in 100 ml of distilled water and dissolved by dropwise addition of 1 M NaOH (final pH 9–10). The obtained solution was filtered off and 1.25 g (0.005 M) of $CuSO_4\cdot 5H_2O$ (Sigma) dissolved in 50 ml of water was added dropwise under continuous stirring; after this, the agitation was continued for a further half an hour. The precipitated product, in the form of a green-yellowish powder, was separated by filtration and washed several times with distilled water. Finally, it was dried in air in the absence of light. The yield of various preparations was around 40%. The composition of the complex was confirmed by chemical analysis. Analysis calcd. for $[Cu(sulfadimet)_2]\cdot H_2O$: $C_{24}H_{28}N_8O_9S_2Cu$: C 41.13, H 3.71, N 15.99, S 9.14 Cu 9.07; found C 40.94, H 4.05, N 15.86, S 9.25, Cu 9.20%.

The complex is insoluble in water and in most of the common solvents, and very soluble only in dimethylsulfoxide (DMSO) and *N,N′*-dimethylformamide (DMF).

After several attempts, using the two last mentioned solvents for the recrystallization of the complex powder, it was possible to obtain a small number of very little single

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crystals adequate for a X-ray structural analysis, from DMSO. As shown by the results of this analysis, one solvent molecule replaced the crystallization water of the original product. Besides, a comparison of the IR spectra of both complexes clearly confirms the same metal-to-ligand arrangement and overall structural characteristics independently of the presence of H_2O or DMSO in the lattice.

FTIR spectra, in the range between 4000 and 200 cm^{-1}, were measured as KBr pellets on a Bomem MB 102 instrument.

Crystallographic studies were performed at 293 (2) K, on a green rhombic crystalline plate of approximate dimensions $0.08\times0.06\times0.04$ mm, using graphite monochromated MoKα radiation ($\lambda=0.71073$ Å), with a Kappa CCD diffractometer.

The structure was solved by direct and Fourier methods and the final molecular model obtained by anisotropic full-matrix least-squares refinement of the nonhydrogen atoms. Intensity data were corrected for Lorentz, polarization and absorption [19].

The H-atoms were located in a Fourier difference map. However, all but the amine hydrogen atoms (refined isotropically), were positioned stereochemically and refined with the riding model. The methyl hydrogen atoms were treated in the refinement as rigid bodies and allowed to rotate along the corresponding C–C bond such as to maximize the sum of the observed electron density at the three calculated H-positions. As expected, all methyl groups converged to staggered positions.

Programs used were DENZO and SCALEPACK for data reduction and correction [20] and SHELXS-97 [21] and SHELXL-97 [22] for structure solution and refinement, respectively.

Crystal data, collection procedures and refinement results are summarized in Table 1. Fig. 1 shows a stereoscopic view of the Cu(II) environment. For clarity, the used atomic numbering scheme is presented in Fig. 2 as an ORTEP [23] drawing of a part of the structure. Selected bond distances and angles around the metal center are given in Table 2.

The Cu(II) cation is five-fold coordinated to the N-atoms of four sulfadimethoxine ligands, conforming a distorted square-pyramidal environment. The cations forms four short Cu–N bonds at the pyramidal basis, two of them with a sulfadimethoxine ligand acting as a bidentate ligand through a pyrimidine nitrogen atom [Cu–N(23) = 2.048(2) Å] and the amide N-atom [Cu–N(22) = 2.047(2) Å]. A third bond occurs along the lone electron pair of the N-atom of the terminal amino group belonging to a symmetry related ligand [Cu–N(21″) = 2.054(3) Å], while the fourth short bond involves the pyrimidine nitrogen atom of a different ligand [Cu–N(13) = 1.980(3) Å]. A weaker Cu–N bond occurs at the pyramid apex, through the lone electron pair of the terminal amino group of another symmetry related ligand [Cu–N(11′) = 2.369(3) Å].

These peculiar metal-to-ligand interactions generate a polymeric structure involving all the mentioned coordination positions of sulfadimethoxine in bonding to different cations, with the same arrangement around of each of them. Charge neutrality in each of the $[Cu(sulfadimet)_2]\cdot$DMSO complex moieties is achieved by deprotonation of the amide group of both sulfadimethoxine ligands.

Tables containing complete information on atomic coordinates and equivalent isotropic parameters, bond distances, angles and anisotropic displacement parameters are available from the authors upon request and have been

Table 1
Crystal data, intensity collection parameters and refinement results for $[Cu(sulfadimet)_2]\cdot$DMSO

Empirical formula	$C_{26}H_{32}N_8O_9S_3Cu$
Formula weight (g mol^{-1})	760.32
Crystal system/space group	Monoclinic/$P2_1/c$
a (Å)	13.0524(2)
b (Å)	13.6038(3)
c (Å)	19.0358(3)
β (°)	103.558(1)
Z	4
D_x (calc.) (mg m^{-3})	1.537
$F(000)$	1572
θ range for data collection (°)	1.60–25.00
Index ranges	$-15\le h\le 14,\ -16\le k\le 16,\ -22\le l\le 22$
Reflections collected	72 268
Independent reflections	5799 [$R_{int}=0.0998$)
Observed reflections [$I>2\sigma(I)$]	4646
Data/restraints/parameters	5799/0/436
Goodness-of-fit on F^2	1.002
Final R indices [$I>2\sigma(I)$]	$R_1=0.0414,\ wR_2=0.1062$
Final R indices (all data)	$R_1=0.0589,\ wR_2=0.1172$
Largest diff. peak and hole (e $Å^{-3}$)	0.397 and −0.059

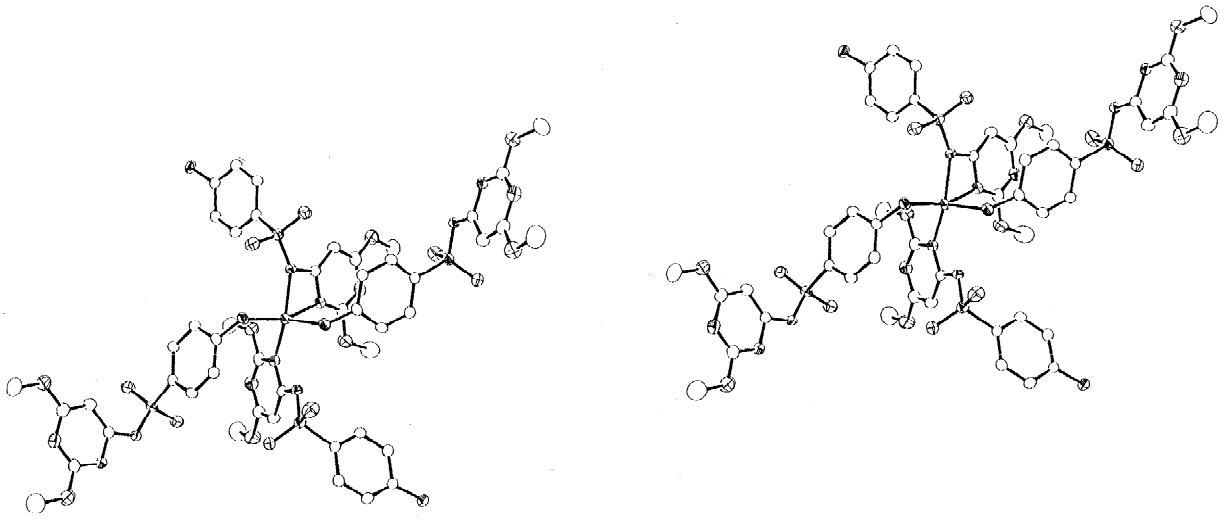

Fig. 1. Plot of [Cu(sulfadimet)$_2$].DMSO showing a stereoscopic view of the copper(II) environment and atoms displacement ellipsoids at 30% probability level. For clarity, the DMSO solvent molecule and the H atoms are not included in the drawing. Carbon atoms are shown with a simple boundary ellipse, oxygen atoms with boundary and principal ellipses and nitrogen atoms with boundary and principal ellipses and octant shading.

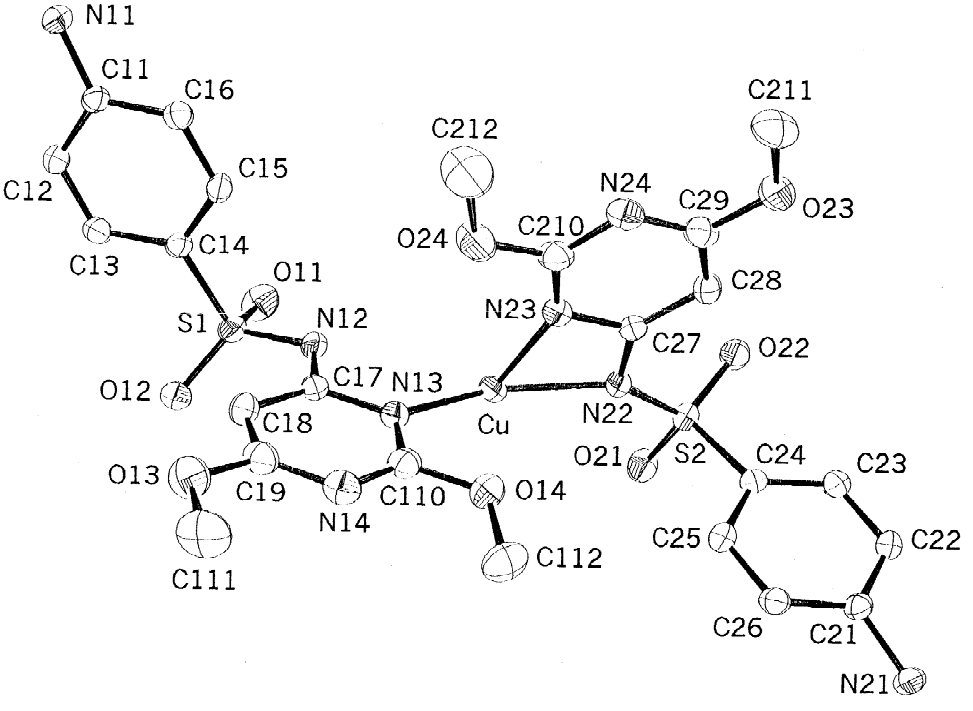

Fig. 2. Plot of the Cu(II) bonding to two of the four ligand molecules in [Cu(sulfadimet)$_2$]·DMSO, showing the non-H atom numbering scheme.

Table 2
Bond distances (Å) and angles (°) around Cu(II) in [Cu(sulfadimet)$_2$]·DMSO[a]

Cu(1)–N(13)	1.980(2)	Cu(1)–N(23)	2.048(2)
Cu(1)–N(22)	2.047(2)	Cu(1)–N(21)#1	2.054(3)
Cu(1)–N(11)#2	2.369(3)		
N(13)–Cu(1)–N(23)	97.26(10)	N(13)–Cu(1)–N(22)	148.90(10)
N(23)–Cu(1)–N(22)	64.68(9)	N(13)–Cu(1)–N(21) #1	96.52(10)
N(23)–Cu(1)–N(21)#1	159.60(11)	N(22)–Cu(1)–N(21)#1	96.16(10)
N(13)–Cu(1)–N(11)#2	114.25(11)	N(23)–Cu(1)–N(11)#2	94.51(10)
N(22)–Cu(1)–N(11)#2	93.16(10)	N(21)#1–Cu1–N(11)#2	93.46(11)

[a] Symmetry transformations used to generate equivalent atoms: #1: $-x+1,\ y-1/2,\ -z+1/2$; #2: $-x+2,\ y+1/2,\ -z+1/2$.

deposited at the Cambridge Crystallographic Data Centre, reference number CCDC200183.

The positions of some of the most characteristic vibrations of the free sulfadimethoxine ligand and the $[Cu(sulfadimet)_2]\cdot H_2O$ complex are compared in Table 3. The proposed assignment is based on some general references [24,25] as well as on data of related complexes [3–8]. Some brief comments on these assignments are made as follows:

- The antisymmetric stretching mode of the NH_2–amino groups is broadened and slightly displaced to lower wavenumbers after coordination, whereas the corresponding symmetric mode appears with a doublet structure and also displaced to lower energies. The broadening and the doublet structure are surely a consequence of the two different Cu–NH_2 bond lengths present in the structure.
- The characteristic $\delta(NH_2)$ scissors mode is also broadened and presents a weak unfolding (shoulder at 1550 cm^{-1}) after complex formation.
- The ν(NH) amido stretching of the nondeprotonated amido groups remains at the same energy after complexation.
- Most of the phenyl and pyrimidine modes are scarcely affected by coordination. Notwithstanding, the 1430 cm^{-1} band of the free ligand appears with a doublet structure in the complex, probably originated in the participation of one of the ring N-atoms in bonding.
- The stretching modes of the SO_2 groups lie in the ranges which are characteristic for these vibrations and they remain practically unaffected by coordination, in agreement with the fact that they are not involved in metal-to-ligand bonds. The $\nu_{as}(SO_2)$ mode is, apparently, partially coupled with the C–N stretching of the amino group, a fact which explains the doublet structure in this region after coordination, as a consequence of the involvement of the amino groups in metal bonding.
- The small shift of the ν(S–N) vibration after coordination can be explained by the deprotonation of some of the NH groups and the concomitant reinforcement of the involved S–N distances.

Table 3
Characteristic IR bands (cm^{-1}) of the spectra of sulfadimethoxine and the $[Cu(sulfadimet)_2]\cdot H_2O$ complex

Sulfadimethoxine	$[Cu(sulfadimet)_2]\cdot H_2O$	Assignment
3482 m	3467 m, br	$\nu_{as}(NH_2)$
3376 s	3370 s, 3307 m	$\nu_s(NH_2)$
3233 m	3230 m	ν(NH) amido
2855 m	2863 m	ν_s(CH) O–CH_3
1600 vs	1600 vs, 1550 sh	$\delta(NH_2)$
1550 vs	1550 vs	ν-phenyl ring
1430 vs	1466 vs, 1428 vs	ν-pyrimidine ring
1354 vs	1377 vs, 1360s	$\nu_{as}(SO_2)+\nu$(CN) amino
1202 vs	1204 vs	ρ(O–CH_3)
1140 vs	1142 vs	$\nu_s(SO_2)$
1087 s	1085 s	δ(CH) phenyl
879 vs	885 vs	ν(S–N)
809 s	806 s	δ(CH) phenyl

Abbreviations: vs, very strong; s, strong; m, medium; br, broad; sh, shoulder.

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