

Structure, spectral and magnetic behaviours of tetrakis(flufenamato)(caffeine)(aqua)di copper(II)—first example of two non-equivalent ligands at the apex

M. Melník,^a M. Koman,^{a*} and T. Glowiak^b

^a Department of Inorganic Chemistry, Slovak Technical University, 812 37 Bratislava, Slovak Republic

^b Institute of Chemistry, University of Wroclaw, F. Joliot-Curie 14, 50-383 Wroclaw, Poland

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Abstract—The crystal and molecular structure of the tetrakis(flufenamato)(caffeine)(aqua)dicopper(II) $Cu_2(fluf)_4(caf)(H_2O)$, was determined by direct methods and Fourier techniques. The two copper(II) atoms are bridged by four carboxylate group, with the apical ligand of a water molecule around Cu(1), and a caffeine molecule around Cu(2). The spectral and magnetic properties are also discussed. © 1998 Elsevier Science Ltd. All rights reserved

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Dimeric copper(II) acetate-type complexes constitute a class of compounds with a long history. The earliest reference to copper acetate is from the year 1597 [1]. In these complexes two copper(II) atoms are bridged by four carboxylate groups in a syn-syn arrangement [2]. The apical positions are usually occupied either by oxygen or nitrogen containing ligands. Each copper displays a distorted square pyramidal geometry. The dimeric complex usually show marked antiferromagnetism [3–5].

Fenamates (mefanamic, niflumic and flufenamic acids) constitute an important group of analgetics which are believed to act through inhibition of prostaglandin biosystems, like other anti-inflammatory analgeties [6]. It is known that some drugs act via chelation [7] or via the inhibition of metalloenzymes [8], but little is known about the modification of activity of most drugs when their ligating potential is utilized. The interaction of the copper(II) atom which plays a vital role in a number of quite different biological processes, with therapeutically administered drugs is a subject of considerable interest.

On the basis of spectral and magnetic properties of copper(II) flufenamate monohydrate a dimeric structure was proposed [9] similar to that of copper(II) acetate monohydrate [10].

In order to better understand some aspects of metal ion-drug interactions, we have studied here the complexation of flufenamic acid [flu, or N-(α,α,α -trifluoro*m*-tolyl)anthranilic acid] in the presence of caffeine (caf). The derivative Cu₂(fluf)₄(caf)(H₂O) was prepared, studied by spectral and magnetic methods and also characterized by X-ray crystallography.

EXPERIMENTAL

Preparation

 $Cu(fluf)_2H_2O$ was prepared as described by Melnik et al. [9]. The green $Cu_2(fluf)_4(caf)(H_2O)$ was prepared by treating caffeine with $Cu(fluf)_2H_2O$ in an equimolar ratio in hot methanol. The resulting solution was fil-

^{*} Author to whom correspondence should be addressed.

tered and the filtrate left to stand at room temperature, allowing fine green crystals to precipitate out. These were filtered off, washed with cold methanol and dried at room temperature. Calc. : for $Cu_2(fluf)_4(caf)(H_2O)$: Cu, 7.59%; C, 51.71%; N, 10.05%; H, 3.62%. Found : Cu, 7.82%; C, 51.4%; N, 8.95%; H, 3.21%.

Spectral studies

Electronic spectrum in the region 10–28 kK was measured with a Perkin–Elmer 450 spectrophotometer. IR spectrum in region 400–3600 cm⁻¹ was measured with an IR 10 spectrometer. In both cases, Nujol suspension techniques were used. The EPR spectrum of powdered sample was obtained using a Varian E4 spectrometer at room temperature.

Magnetic susceptibility measurements

Magnetic susceptibility of polycrystaline sample was measured by Faraday method over the temperature range of 77–300 K using a sensitive Cahn RG-HV electrobalance. Hg[Co(NCS)₄] was used as calibrant [11], the value of 16.44 10⁻⁶ cm³ g⁻¹ was taken as its magnetic susceptibility [12]. Magnetism of sample was found to be field-independent. The effective magnetic moments were calculated from the equation $\mu_{\text{eff}} = 2.83 (X_{\text{M}} \cdot \text{T})^{1/2}$.

Crystallography

Data collection and cell refinement was carried out using Kuma (1991) KM4 diffractometer software [13]. Intensity data were corrected to Lorenz and polarization factors. The structure was solved by the heavy atom method with SHELX86 [14], and subsequent Fourier synthesis using SHELXL93 [15]. Anisotropic thermal parameters were refined for all nonhydrogen atoms. Geometrical analyses was performed using SHELXL93 [15]. The structures were drawn using ORTEP [15]. The final parameters after refinement are summarized in Table 1. Select bond distances and angles are in Table 2.

Supplementary material including non-hydrogen and hydrogen atomic coordinates ($\times 10^4$), anisotropic displacement parameters for nonhydrogen atoms [Å² × 10³] have been deposited at the Cambridge Crystallographic Data Centre. Observed and calculated structural factors are available on request from the correspondence author.

RESULTS AND DISCUSSION

The IR spectrum of the complex is very complex. The spectrum of $Cu_2(fluf)_4(caf)(H_2O)$ shows an absorption band at 3250 cm⁻¹. This frequency corresponds to the antisymmetric and symmetric OH

Table 1. Crystal data and structure refinement for $[Cu_2(fluf)_4(caf)(H_2O)]$

Identification code	jon2
Formula	$C_{32,50}H_{23}CuF_6N_4O_6$
FW	743.09
Temperature (K)	293(2)
Wavelength (Å)	0.71069
Crystal system	Monoclinic
Space group	P21/m
<i>a</i> (Å)	11.777(2)
b (Å)	23.156(5)
c (Å)	12.502(3)
α (°)	90
β (°)	95.67(3)
γ()	90
$V(Å^3)$	3392.7(12)
Ζ	4
$D_{\text{calc}} (\text{mg m}^3)$	1.455
Absorption coefficient (mm ⁻¹)	0.725
<i>F</i> (000)	1508
Crystal size (mm)	$0.40 \times 0.31 \times 0.27$
θ range (°)	2.27-25.05
Index ranges	0/h/14, 0/k/27,
	-14/l/14
Reflections collected	6459
Independent reflections	$6159 (R_{int} = 0.0439)$
Absorption correction	No
Refinement method	Full-matrix least-
	squares on F^2
Data/restraints/parameters	6159/0/472
Goodness-of-fit on F^2	1.001
Final R indices $[I > 2\sigma(I)]$	$R_1 = 0.0489,$
	$wR_2 = 0.1322$
R indices (all data)	$R_1 = 0.1381,$
	$wR_2 = 0.1745$
Largest diff. peak and hole ($eÅ^{-3}$)	0.747 and -0.814

stretch and confirms presence of water in the compound. The carboxylate stretching frequencies $v_{as}(COO^-)$ at 1625 cm⁻¹ and $v_s(COO^-)$ at 1390 cm⁻¹ are characteristic of copper(II) carboxylate compounds [17]. The stretching vibration of the C=N of heterocyclic ring appears at around 1590 cm⁻¹ and on complexation a shift to higher frequencies is observed [18,19]. In the present complex this shift to about 1605 cm⁻¹ may suggest bond formation by the metal atom to the nitrogen atom of caffeine, thereby increasing the dipolar contribution of C=N⁺ in the heterocyclic ring.

The electronic spectrum of the complex shows band at $14.2 \times 1000 \text{ cm}^{-1}$ (band I) which was identified as *d-d* transition of the copper(II), and a shoulder at $27 \times 1000 \text{ cm}^{-1}$ (band II). The shoulder (band II) is characteristic of the bridging system with antiferromagnetic interaction [20].

The EPR spectrum obtained for the powdered sample of $Cu_2(fluf)_4(caf)(H_2O)$ at room temperature contained the typical absorption bands of an axially

$\begin{array}{cccccccc} O(22)-C(21) & 1.262(5) \\ N(11)-C(18) & 1.395(6) \\ N(21)-C(28) & 1.397(6) \\ N(31)-C(28) & 1.397(6) \\ O(11)-Cu(1)-O(11)\#1 & 87.8(2) \\ O(11)\#1-Cu(1)-O(21) & 168.92(12) \\ O(11)\#1-Cu(1)-O(1) & 97.93(13) \\ O(21)\#1-Cu(1)-O(1) & 93.11(14) \\ O(11)\#1-Cu(1)-Cu(2) & 83.94(9) \\ \end{array}$	$\begin{array}{ccc} Cu(2) & -O(12)\#1 & 1.9\\ Cu(2) & -O(22)\#1 & 1.9\\ O(11) & -C(11) & 1.2\\ O(21) & -C(21) & 1.2 \end{array}$	328(12) 58(3) 59(5) 67(5) 70(5)
$\begin{array}{llllllllllllllllllllllllllllllllllll$	N(11)—C(13) 1.3	81(6)
$\begin{array}{cccc} N(21) & -C(28) & 1.397(6) \\ N(31) & -C(31) & 1.360(7) \\ \hline O(11) & -Cu(1) & -O(11)\#1 & 87.8(2) \\ O(11) \#1 & -Cu(1) & -O(21) & 168.92(12) \\ O(11) & -Cu(1) & -O(1) & 97.93(13) \\ O(21)\#1 & -Cu(1) & -O(1) & 93.11(14) \\ O(11)\#1 & -Cu(1) & -Cu(2) & 83.94(9) \\ \hline \end{array}$	N(21)C(23) 1.3	71(7)
N(31)—C(31) $1.360(7)$ O(11)—Cu(1)—O(11)#1 $87.8(2)$ O(11)#1—Cu(1)—O(21) $168.92(12)$ O(11)—Cu(1)—O(1) $97.93(13)$ O(21)#1—Cu(1)—O(1) $93.11(14)$ O(11)#1—Cu(1)—Cu(2) $83.94(9)$	N(31)C(38) 1.3	21(8)
O(11)— $Cu(1)$ — $O(11)$ #187.8(2) $O(11)$ #1— $Cu(1)$ — $O(21)$ 168.92(12) $O(11)$ — $Cu(1)$ — $O(1)$ 97.93(13) $O(21)$ #1— $Cu(1)$ — $O(1)$ 93.11(14) $O(11)$ #1— $Cu(1)$ — $Cu(2)$ 83.94(9)		
$\begin{array}{llllllllllllllllllllllllllllllllllll$	$\begin{array}{c} O(11) &Cu(1) &O(21) \\ O(21) &Cu(1) &O(21)\#1 \\ O(21) &Cu(1) &O(1) \\ O(11) &Cu(1) &Cu(2) \\ O(21) &Cu(1) &Cu(2) \\ O(12) &Cu(2) &O(22) \\ O(12) &Cu(2) &O(22)\#1 \\ O(12) &Cu(2) &O(22)\#1 \\ O(12) &Cu(2) &O(22)\#1 \\ O(12) &Cu(2) &O(22)\#1 \\ O(12) &Cu(2) &O(21)\#1 \\ O(22) &Cu(2) &O(21)\#1 \\ O(22) &Cu(2) &Cu(1) \\ O(22) &Cu(2) &Cu(1) \\ O(21) &O(21) &Cu(1) \\ C(21) &O(21) &Cu(2) \\ \end{array}$	$\begin{array}{c} 90.00(13)\\ 90.1(2)\\ 93.11(14)\\ 83.94(9)\\ 85.03(9)\\ 177.39(14)\\ 90.6(2)\\ 90.7(2)\\ 102.91(13)\\ 90.1(2)\\ 83.89(9)\\ 83.04(9)\\ 123.5(3)\\ 123.1(3)\\ 110.1(4) \end{array}$

Table 2. Selected bond lengths [Å] and angles [°] for $[Cu_2(fluf)_4(caf)(H_2O)]$

Symmetry transformations used to generate equivalent atoms: #1x, -y + 1/2, z

symmetric binuclear species [21]. The spectral feature of the powder at room temperature shows absorptions at low and high fields (Hz₁ and Hz₂, respectively), with an asymmetrical absorption near 4500 G (H_T2). One absorption is missing because |D| > h.v at the X-band frequency used. The spectrum can be interpreted using a spin Hamiltonian for axial symmetry

$$H = g_{11}\beta H_z S_z + g_{\perp} (H_X S_X + H_Y S_Y) + D(S_Z^2 + 2/3)$$

where S = 1 for the thermally accessible triple state and the other symbols have their usual meaning. The value obtained for the spin Hamiltonian parameters are: $g_{\perp} = 2.065$; $g_{\Pi} = 2.356$; $\langle g \rangle = 2.169$ and $|D| = 0.326 \text{ cm}^{-1}$. The |D| value of 0.326 cm⁻¹ is large compared to the magnetic quantities (approximately 3.00 G), but is smaller compared to vibrational frequencies. The values are comparable to those found in binuclear copper(II) carboxylates [17].

The molar susceptibilities corrected for diamagnetism and magnetic moments for $Cu_2(fluf)_4$ (caf)(H₂O) are reported at various temperature in Table 3 and graph μ_{eff} (B.M.) against T on Fig. 1.

The temperature susceptibility data can be described by the equation

Table 3. Magnetic data for $Cu_2(fluf)_4(caf)(H_2O)$ (-dia-magnetic corr. $\times 10^6 = 347$)

T(K)	$X'_{\rm M} imes 10^6$	$\mu_{\rm eff}({ m B.M.})$
93	500	0.60
113	566	0.72
133	642	0.82
153	760	0.95
173	850	1.09
193	895	1.17
213	900	1.24
231	913	1.31
253	945	1.38
273	976	1.46
293	932	1.48

$$X'_{\rm M} = \frac{g^2 N \beta^2}{3k {\rm T}} \frac{1}{1 + 1/3 \exp^{-2J/k {\rm T}}} + N_z$$

where -2J is exchange coupling constant, and other



Fig. 1. Temperature dependence of the effective magnetic moment (μ_{eff}) for $Cu_2(fluf)_4(caf)(H_2O)$.

symbols have the usual meaning. The spectroscopic splitting factor g_{av} was obtained from the EPR spectrum and used as constants in the least-square fitting process. The least-squares fitting was performed using

a Fortran V program on an Univac 1108 computer. The energy separation (-2J) between the triplet and singlet states of 275(10) cm⁻¹ which was obtained is similar to those of related copper(II) carboxylates [5,17].

Crystal structure of $Cu_2(fluf)_4(caf)(H_2O)$ with labeling of atoms is shown in Fig. 2. The compound exists as a dimer consisting of two non-equivalent distorted square-based pyramidal copper(II) polyhedra, joined by four carboxilic groups of flufenamato ions formed a square-based around each copper(II) atom. While the apex around Cu(1) is occupied by a water molecule at a distance of 2.141(5) Å, around Cu(2) by a caffeine at a distance of 2.239(5) Å. To our knowledge, this is the first example in this series of dimer copper(II) carboxylates, which the apex position are occupied by two different donor ligands. The Cu—Cu distance is 2.633(1) Å. The displacement of the copper(II) atoms from the basal plane toward the apical ligands also differ, Cu(1) by 0.189 Å and Cu(2) by 0.223 Å.

This molecule follows the trends already noted for this type of dimer. The Cu—Cu separation (2.633(1) Å) as well as Cu—L bond distances are similar to those observed in other Cu(II) carboxylates [2,22].

The bio-test of the compound is in progress and will be published elsewhere.



Fig. 2. The molecular structure of $Cu_2(fluf)_4(caf)(H_2O)$.

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