Crystal Structure and Spectroscopic Behaviour of a Binuclear Copper(II) Complex of Mefenamic Acid and Dimethylsulfoxide

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Copper(II), Mefenamic Acid, Crystal Structure, Spectral Data

The crystal structure of the binuclear Cu(II) complex [Cu(mef)\textsubscript{2}(DMSO)]\textsubscript{2} (mef = deprotonated N-2,3-dimethylphenyl-anthranilic acid; DMSO = dimethylsulfoxide) has been determined by single-crystal X-ray diffractometry. It crystallizes in the triclinic space group \textit{P\textbar{I}} with \(Z = 1\). IR and electronic spectra of the compound are also discussed briefly.

\textbf{Introduction}

Some derivatives of anthranilic and phenylanthranilic acids are biologically active materials. One of them, N-2,3-dimethylphenylanthranilic acid (mefenamic acid, mefH) is a well known nonsteroidal antiinflammatory drug [1]. The activity of this type of drugs is often enhanced if they are used in form of their Cu(II) complexes [2-4]. Therefore, and as part of our current studies devoted to the characterization of copper complexes with pharmacological activity [5-10], we have initiated work on compounds containing derivatives of phenylanthranilic acid as ligands.

In this paper, we present our results on the structural and spectroscopic characteristics of one of these complexes, the dimeric [Cu(mef)\textsubscript{2}(DMSO)]\textsubscript{2}, containing mefenamate as a ligand.

\textbf{Experimental}

\textbf{Synthesis of the complex}

1.20 g (5 mmol) of mefenamic acid (Sigma) was dissolved in 280 ml of distilled water at room temperature and with continuous stirring, and immediately neutralized by dropwise addition of a 0.1 N solution of NaOH. To this solution, 0.60 g (2.5 mmol) of CuSO\textsubscript{4}·5H\textsubscript{2}O (Fluka), dissolved in 60 ml of water, was added dropwise under continuous stirring. The brown suspension which rapidly appears, was separated by centrifugation at 15,000 r.p.m., washed with water and again centrifugated several times. A suspension of this product in dimethylsulfoxide (DMSO) generates a green, apparently amorphous, material. Its recrystallization from diethyl ether produced a number of well formed crystalline platelets.

\textbf{Determination of the crystal structure}

The thin crystal plates turned out to diffract poorly. Only about 40% of the reflection intensities collected up to 0.84 Å resolution, were above two standard deviations of measurement errors. The axial DMSO ligand exhibits positional disorder and is distributed in two crystal sites, one of them with an occupancy close to 0.75. Several hydrogen atoms were located at approximate positions in a difference Fourier map. However, all hydrogens, except the ones belonging to the disordered DMSO ligand, were positioned stereochemically and included in the refinement riding on the atom to which they are bonded with a common isotropic thermal parameter (which converged to \(U = 0.086(9)\) Å\(^2\)). During the refinement, the CH \(_2\) hydrogen atoms were allowed to rotate as a rigid group around the corresponding C-C bond as to maximize the sum of the electron density at the three calculated hydrogen positions.

\textbf{Crystal data}

\([C\textsubscript{32}H\textsubscript{32}O\textsubscript{10}N\textsubscript{2}SCu\textsubscript{2}] \_2; M = 1243.94, \text{ triclinic, space group } P\textbar{I} (\text{Nr. } 2), a = 11.166(4), b = 11.362(3), c = 13.927(4) \text{ Å}, \alpha = 71.25(2), \beta = 71.25(2), \gamma = 64.29(2)\)\(^\circ\),

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Fig. 1. ORTEP plot of \([\text{Cu(mef)}_2\text{DMSO}]_2\). Only one of the two lattice positions occupied by the disordered DMSO ligand is shown. Dashed lines indicate hydrogen bonds.

\[ V = 1500.0(8) \, \text{Å}^3, \quad Z = 1, \quad D_c = 1.377 \, \text{g-cm}^{-3}, \quad \mu(\text{Mo-K} \alpha) = 0.840 \, \text{mm}^{-1}. \]

Unit cell parameters were obtained by least-squares refinement of \([\sin \theta/\lambda]^2\) values for 19 reflections in the 12.66 < 2\(\theta\) < 32.24° range.

Data processing and structure solution

A green rhombic single crystal plate with approximate dimensions 0.24 \times 0.20 \times 0.06 mm was used. Intensity data were collected at 293(2) K on an Enraf-Nonius CAD-4 diffractometer, using monochromated Mo-K\(\alpha\) radiation (0.71073 Å) with a scan mode \(\omega - 2\theta\). 3861 independent reflections were collected in the range 1.55 < 2\(\theta\) < 24.97°, and 1596 independent reflections with I > 2\(\sigma(I)\) were used for further computations. Intensity data were corrected for Lorentz, polarization and absorption effects [11]. The structure was solved by Patterson and Fourier methods and the final molecular model obtained by anisotropic full-matrix least-squares refinement of non-hydrogen atoms (Programs used were SDP [12], SHELX-76 [13], SHELX-86 [14], SHELX-93 [15] and ORTEP [16]). Final agreement indices were \(R_1 = 0.080\) and \(wR_2 = 0.168\).

Tables containing final atomic positional and thermal parameters, anisotropic displacement parameters and hydrogen atom positions are available from the authors on request and were also deposited at the Fachinformationszentrum Karlsruhe GmbH, D-76344 Eggenstein-Leopoldshafen (FRG), on quoting the depository number CSD 59456, the names of the authors and the journal citation.

Spectroscopic measurements

The IR spectrum of the compound was obtained with a Bruker IFS 66 FTIR instrument using the KBr pellet technique. The electronic spectra were recorded on a Spectronic-3000 spectrophotometer, using 10 mm quartz cells. Measurements in the 400 - 800 nm range were performed in diethyl ether solutions whereas those in the spectral range between 400 and 250 nm were recorded in DMSO solutions.

Results and Discussion

Crystal structure

An ORTEP [16] plot of the structure, showing the labeling of the non-hydrogen atoms and their
Table I. Selected bond distances (Å) and angles (°) in [Cu(mef)₂DMSO]₂.

<table>
<thead>
<tr>
<th>Bond/Angle</th>
<th>Value</th>
<th>References</th>
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<td>Cu-O(12)</td>
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<td></td>
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<tr>
<td>Cu-O(22)</td>
<td>1.954(7)</td>
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<td>Cu-O(11)</td>
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<td>Cu-O(21)</td>
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<td>Cu-O(1)</td>
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<tr>
<td>Cu-Cu'</td>
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<td>S(1)</td>
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<tr>
<td>S'-O(1)</td>
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<tr>
<td>S-C(1)</td>
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<td>S-C(2)</td>
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<td>S''-C(1)</td>
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<tr>
<td>O(11)-C(11)</td>
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<tr>
<td>O(12)-C(11)</td>
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<td>N(11)-C(18)</td>
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<td>C(11)-O(12)</td>
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<td>C(112)-C(114)</td>
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<td>N(21)-C(28)</td>
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</table>

A similar arrangement has been recently established in the binuclear Cu(II) complex with Suprofen (another interesting antiinflammatory drug [22]) and acetonitrile of composition [Cu(Sup)₂CH₃CN]₂ [9].

As expected, the phenyl and anthranilic rings are planar to within experimental accuracy; they subtend dihedral angles of 50.5(5)° (ligand 1) and 68.7(3)° (ligand 2). The carboxylic carbon atoms depart from the corresponding anthranilic plane by 0.12(1) Å for ligand 1 and 0.04(1) Å for ligand 2. The methyl carbon atoms are coplanar with the corresponding phenyl rings. The amide nitrogen atoms are coplanar with the corresponding phenyl and anthranilic rings which are linked by them.

The dinuclear Cu(II) complex is further stabilized by a pair of bent N-H···O intradimer H-bonds, with N(11)···O(11) and N(21)···O(22') distances of 2.68(1) and 2.71(1) Å, respectively, and N(11)-H(11)···O(11) and N(21)-H(21)···O(22') angles of 137(1) and 123(1)°, respectively.

Infrared spectrum

The infrared spectrum of the complex shows a very well defined pattern, clearly consistent with the described structural characteristics and useful for the identification of the complex. In the higher frequency range the N-H stretching vibration appears as a medium intensity band located at 3323 cm⁻¹ whereas CH₃-stretching bands are found at 3098, 3010, 2916 and 2860 cm⁻¹ [23, 24]. Other characteristic mefenamate vibrations are the strong 1624 and 1392 cm⁻¹ bands, assignable to ν(CH₃), and ν(COO⁻) and ν₃(COO⁻), respectively [9, 23, 24] and the strong ring modes at 1585 and 1467 cm⁻¹. This last band overlaps probably with a CH₃ deformational mode, whereas one N-H deformation appears at 1510 cm⁻¹.

The typical ν(S=O) mode of DMSO is found as a medium intensity band at 953 cm⁻¹. In the free ligand this band is located at 1055 cm⁻¹ [25] and its displacement to lower frequency is typical for oxygen coordination [26].

Other IR-bands are found at 1286 (s), 1157 (m), 1033 (m), and 830 (s) cm⁻¹.

Electronic spectrum

In binuclear copper(II) complexes, such as the present one, three electronic transitions are usually...
found in the UV-Vis spectrum (bands I, II and III). The usually broad band I has been assigned to the \(xz, yz \rightarrow x^2 - y^2\) d-d transitions in the Cu(II) centers [27]. A shoulder in the low energy side of this band, assigned to the \(z^2 \rightarrow x^2 \rightarrow y^2\) transition, can often be observed [9]. The origin of band II is not totally clear, but its presence indicates a dinuclear structure [9, 27], whereas band III originates from a carboxyl-Cu(II) charge transfer transition [28].

In the present case band I is seen as a very broad feature centered at ca. 680 nm whereas band II is found at 350 nm. A third band located at 285 nm may be tentatively assigned to band III.

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