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Synthesis and crystal structure of the μ_2-{tris[bis(diphenylphosphine)methane]}-μ_3-3-methyl-8-ethylxanthine-*N,O,O*]-μ_3-chloro-triangle-tricopper(I)-water complex exhibiting a novel oxopurine coordination mode

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Abstract

The synthesis and crystal structure of the trinuclear compound $[Cu_3(L)(Cl)(dppm)_3]\cdot H_2O$, where L is the doubly deprotonated form of 3-methyl-8-ethylxanthine and dppm is (diphenylphosphine)methane, are reported. The compound crystallizes in the monoclinic system, space group $P2_1/m$, with cell constants $a=13.411(3)$, $b=21.944(4)$, $c=13.870(8)$ Å, $\beta=114.82(3)°$ and $Z=2$. The structure was solved and refined to $R=0.082$ ($R_w=0.064$). The structure consists of a triangle of copper atoms held together by an apical μ_3-bridging chloride, one μ_3-oxopurine and three μ_2-bis(diphenylphosphine)methane ligands. The main feature of the complex is the novel μ_2-O(2) bridging coordination mode of the oxopurine derivative.

Keywords: Crystal structures; Copper complexes; Purine complexes; Trinuclear complexes

1. Introduction

It is well known that some metal–diphosphine and metal–purine complexes exhibit good antitumour activities [1,2]. Accordingly, interest in the preparation and properties of metal–phosphine–purine complexes arises from the use of these as model compounds for the metal–DNA interaction as well as the possible existence of a synergic effect in their biological activity. Thus considerable effort to understand this chemistry has been made in recent years, mainly in the field of gold(I) complexes [1,3,4]. In view of this, as a continuation of our studies on metal complexes of purine bases [1–7], we wish to report here a novel μ_3-(N,O,O) chelation mode of 3-methyl-8-ethylxanthine in the $[Cu_3(L)(Cl)(dppm)_3]\cdot H_2O$ complex, where L is the doubly deprotonated form of 3-methyl-8-ethylxanthine and dppm is bis(diphenylphosphine)methane.

2. Experimental

2.1. Synthesis

On reacting CuCl with dppm in dichloromethane by the procedure reported earlier [8], a product with the empirical formula Cu(Cl)(dppm) was obtained. The $[Cu_3(L)(Cl)(dppm)_3]\cdot H_2O$ complex was prepared by refluxing for 1 h, in a 1:1 ratio, 3-methyl-8-ethylxanthine, previously deprotonated with KOH in water, and Cu(Cl)(dppm) in an ethanol/water mixture (20:1) under N_2 atmosphere. From the resulting clear, colourless solution, by slow evaporation at room temperature, air-stable white crystals were obtained. *Anal.* Calc. for $C_{83}H_{79}N_4O_3P_6ClCu_3$: C, 62.67; H, 5.01; N, 3.52; Cu, 11.88. Found: C, 61.9; H, 4.9; N, 3.4; Cu, 12.2%.

2.2. Physical measurements

Microanalyses of C, H and N, copper determination and IR spectra were obtained as described previously [7].

2.3. Crystal data

$C_{83}H_{79}N_4O_3P_6ClCu_3$, monoclinic, $a=13.411(3)$, $b=21.944(4)$, $c=13.870(8)$ Å, $\beta=114.82(3)°$, $V=3705(1)$ Å^3, space group $P2_1/m$, $D_{calc}=1.425$ g cm^{-3}, $Z=2$, $F(000)=1640.0$ and μ(Mo Kα)$=1.07$ mm^{-1}.

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2.4. X-ray data collection and structure determination

Single-crystal data collection was performed on a Siemens R3m/V diffractometer at 293 K using graphite monochromatized Mo Kα ($\lambda = 0.71069$ Å) radiation. A prismatic white crystal with dimensions $0.19 \times 0.17 \times 0.15$ mm was used.

It should be noted that several crystals were tested, but all of them displayed only moderate diffraction power. Numerous attempts were also made to obtain better crystals using gel and salting-out methods, but there was no improvement in the crystal quality.

The unit cell parameters were calculated by least-squares refinement of 25 well-centred reflections in the range $5 < 2\theta < 25$. The data were collected in ω–2θ scan mode ($3 < 2\theta < 50$). The intensities of three standard reflections, checked after every 120 min, showed only statistical variation. A total of 5916 reflections was collected, with 1193 considered as observed ($I > 4\sigma(I_o)$). The data were corrected for Lorentz and polarization effects. In keeping with the very poor crystal quality and very poor statistics of the small reflections, the main interest was focused on the coordination mode of the ligands and the most general features of the structure. Refinements and geometrical parameters of the compound obtained in both $P2_1$ and $P2_1/m$ space groups suggested the choice of the latter.

The structure was solved by the Patterson method and refined by Fourier synthesis using the SHELXTL PLUS program [9]. From this procedure, all nonhydrogen atoms were located. In the final cycles the chloro, copper and phosphorus atoms were refined anisotropically, the remaining nonhydrogen atoms were refined isotropically, and the H atoms were ignored. Appropriate positional and vibrational constraints were applied to atoms occupying special positions. Because of the poor quality of the data the following constrictions were applied: First, all phenyl rings were refined as a rigid group having a common isotropic temperature factor. Second, because the bond lengths and angles involving C(5), N(7), C(10) and C(11) were abnormal, these atoms were placed at their calculated positions by comparison with the reported crystal data for purine compounds, and then the purine was refined as a rigid group. Finally, all the atoms lying on the symmetry plane, except the Cu(2) and Cl(1) atoms, exhibited very high temperature factors; they were refined with a common isotropic temperature factor. The atomic scattering and dispersion factors used were those included in the program package.

The function minimized was $\Sigma w(\Delta F)^2$ ($1/w = \sigma^2(F_o)$), resulting in a final $R = \Sigma|F_o - F_c|/\Sigma|F_o|$ value of 0.082 and an $R_w = [\Sigma w(|F_o| - |F_c|)^2/w\Sigma|F_o|^2]^{1/2}$ value of 0.064. The maximum and minimum peaks in the difference Fourier map were 1.93 and -0.83 e Å^{-3}, respectively. Atomic coordinates derived from the final cycle of refinement with their standard deviations are given in Table 1. See also Section 4.

3. Results and discussion

The structure consists of neutral, discrete trinuclear [Cu_3(L)(Cl)(dppm)$_3$] molecules and lattice water. Within the Cu_3 core, the metal rings are situated at the corners of a triangle, held together by an apical μ_3-bridging chlorine atom, three μ_2-bis(diphenylphosphine)methane ligands and one μ_3-oxopurine ligand. A perspective view of the whole molecule and the coordinated purine ligand is shown in Fig. 1, together

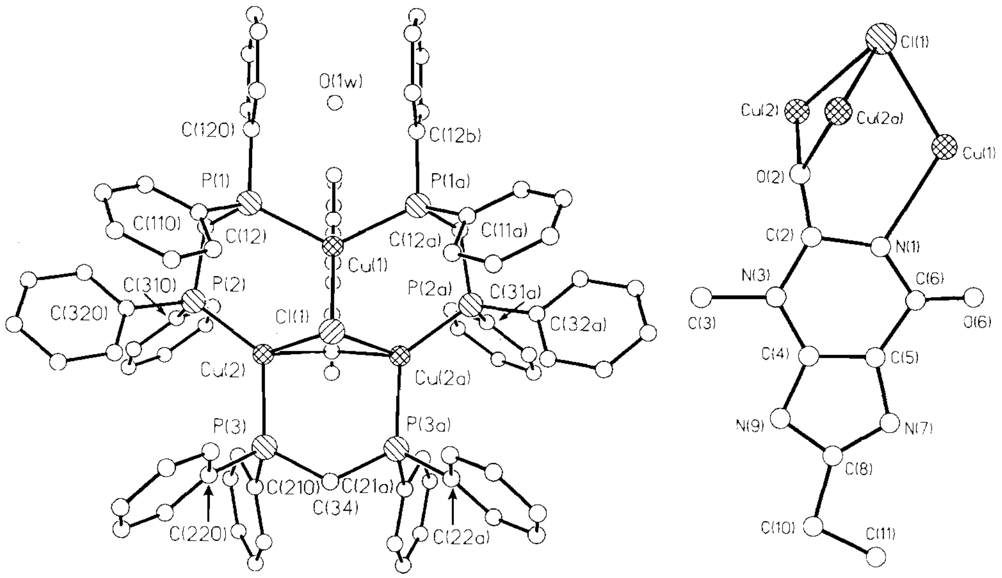

Fig. 1. The molecular structure of [Cu_3(L)(Cl)(dppm)$_3$]·H_2O with the atomic numbering scheme.

Table 1
Atomic coordinates ($\times 10^4$) and U (Å^2)

Atom	x/a	y/b	z/c	U
Cu(1)	0(6)	2500	1596(6)	63(6)
Cu(2)	2216(4)	1745(2)	2730(3)	42(3)
P(1)	−849(9)	1581(4)	1198(8)	49(7)
P(2)	1333(9)	952(4)	1696(8)	33(7)
P(3)	3892(7)	1782(5)	4131(7)	35(7)
Cl(1)	1319(11)	2500	3488(12)	74(11)
C(12)	−97(24)	1082(13)	624(23)	23(11)
C(34)	4280(46)	2500	4988(48)	137(5)
N(1)	840(42)	2500	400(36)	165(6)
O(2)	2343(35)	2500	1891(35)	178(7)
O(1W)	−2111(32)	2500	−3143(30)	178(7)
C(111)	−452(15)	1274(7)	3313(26)	35(6)
C(112)	−488	885	4094	35(6)
C(113)	−1011	321	3811	35(6)
C(114)	−1498	146	2746	35(6)
C(115)	−1462	534	1965	35(6)
C(110)	−939	1098	2248	35(6)
C(121)	−3125(31)	1674(9)	396(14)	67(6)
C(122)	−4193	1677	−402	67(6)
C(123)	−4372	1609	−1462	67(6)
C(124)	−3482	1537	−1724	67(6)
C(125)	−2413	1534	−926	67(6)
C(120)	−2235	1603	134	67(6)
C(211)	4795(13)	1444(8)	2845(21)	25(5)
C(212)	5610	1325	2494	25(5)
C(213)	6711	1425	3168	25(5)
C(214)	6999	1645	4194	25(5)
C(215)	6184	1764	4546	25(5)
C(210)	5083	1663	3871	25(5)
C(221)	4825(16)	750(14)	5538(19)	27(5)
C(222)	4819	334	6296	27(5)
C(223)	4034	384	6707	27(5)
C(224)	3256	851	6360	27(5)
C(225)	3262	1267	5602	27(5)
C(220)	4046	1217	5191	27(5)
C(311)	2066(16)	1090(8)	130(24)	47(6)
C(312)	2750	976	−378	47(6)
C(313)	3452	473	−84	47(6)
C(314)	3469	84	719	47(6)
C(315)	2784	198	1227	47(6)
C(310)	2083	701	933	47(6)
C(321)	646(16)	−230(15)	1769(11)	39(6)
C(322)	681	−794	2248	39(6)
C(323)	1337	−871	3330	39(6)
C(324)	1957	−385	3933	39(6)
C(325)	1922	178	3455	39(6)
C(320)	1267	256	2373	39(6)
C(2)	2013	2500	893	137(5)
N(3)	2464	2500	168	165(6)
C(4)	1790	2500	−900	137(5)
C(5)	664	2500	−1275	137(5)
C(6)	118	2500	−603	137(5)
N(7)	256	2500	−2371	165(6)
C(8)	1158	2500	−2561	137(5)
N(9)	2115	2500	−1700	165(6)
O(6)	−877	2500	−863	178(7)
C(3)	3657	2500	531	137(5)
C(11)	170	2500	−4394	137(5)
C(10)	1322	2500	−3542	137(5)

[a] Equivalent isotropic U defined as $U=(1/3)\sum_i\sum_j(a_i^* a_j^*)(a_i \cdot a_j)$.

with the atomic numbering scheme. Selected bond distances and angles are listed in Table 2.

The complex has C_s symmetry, with the Cu(1), Cl(1) and C(34) atoms, the water and the purine molecules located on the mirror plane of symmetry. This results in the formation of an isosceles triangle of Cu(I) atoms, with Cu(1)···Cu(2) = 3.181 Å and Cu(2)···Cu(2a) = 3.312 Å. Within this triangle each copper atom displays a distorted tetrahedral arrangement. Inspection of the structure reveals a μ_3-(N(1),O(2),O(2)) coordination mode of the doubly deprotonated xanthine derivative, through the exocyclic O(2) atom to Cu(2) and Cu(2a) with bond distances of 2.072(33) Å and through the N(1) atom to Cu(1) with a bond distance of 2.364(63) Å.

The genuine participation of carbonyl groups in metal–purine complexes has often been postulated as a critical step in the mechanism for the antitumour activity of *cis*-diammineplatinum(II) complexes [10,11], but was not fully established until 1986, when two titanocene–oxopurine complexes were reported [12,13]. Afterwards, another example of N(7)/O(6) chelation mode was described for a trimethylplatinum–theophylline hexamer [14]. In addition, two copper(II) complexes having an unbalanced N(7)/O(6) oxopurine chelation mode have been reported [15,16], the Cu(II)–O(6) bond distance being greater than 2.8 Å. It should be noted that none of these complexes contain hydrogen bonds involving the O(6) atom, which, as was stated earlier [15], is one of the factors preventing O(6) coordination to the metal ion.

Although one example of N(1)/O(2) chelation mode in purine complexes exists [11], the main feature of our complex is the μ_2-O(2) bridging coordination mode, which, to the best of our knowledge, is the first example reported so far. In addition to this new coordination mode, the Cu_3 cluster presents a μ_3-Cl occupying the fourth coordination position of the Cu(I) ions. This μ_3-halogen–copper coordination mode is not new, but its documentation for non-cubane-like compounds has been rather meagre [17,18].

It should be noted that the doubly deprotonated N,O,O coordination of the ligand to the metal centres is clearly supported by IR spectroscopy (see Fig. 2).

Table 2
Selected bond lengths (Å) and angles (°)

Cu(1)–P(1)	2.267(10)	Cu(2)–P(2)	2.251(10)
Cu(1)–Cl(1)	2.474(14)	Cu(2)–P(3)	2.273(9)
Cu(1)–N(1)	2.364(63)	Cu(2)–Cl(1)	2.521(15)
Cu(2)–O(2)	2.072(33)		
P(1)–Cu(1)–Cl(1)	108.7(4)	P(2)–Cu(2)–Cl(1)	124.0(5)
P(1)–Cu(1)–N(1)	99.7(6)	P(3)–Cu(2)–Cl(1)	95.4(4)
Cl(1)–Cu(1)–N(1)	113.9(11)	P(2)–Cu(2)–O(2)	113.9(10)
P(1)–Cu(1)–P(1a)	125.6(6)	P(3)–Cu(2)–O(2)	99.6(11)
P(2)–Cu(2)–P(3)	129.7(4)	Cl(1)–Cu(2)–O(2)	82.9(13)

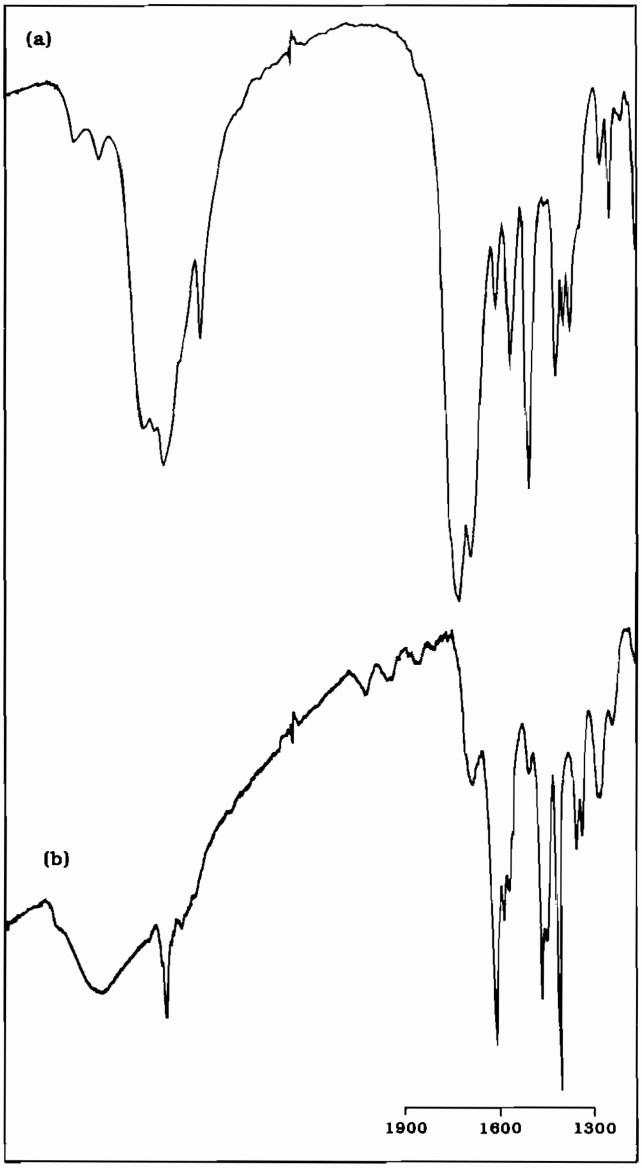

Fig. 2. IR spectra of (a) 3-methyl-8-ethylxanthine and (b) $[Cu_3(L)(Cl)(dppm)_3] \cdot H_2O$.

When the IR spectra of the free ligand and the complex (in the 4000–1600 cm^{-1} range) are compared, one can observe in the spectrum of the latter the lack of the corresponding ν(N–H) and ν(C(2)=O) bands, which appear in the spectrum of the former at 3200–2900 and 1712 cm^{-1}, respectively. Furthermore, the ν(C(6)=O) band is slightly shifted to lower frequencies (ca. 40 cm^{-1}), which can be justified on the basis of both the presence of a hydrogen bond and the deprotonation of N(7) [6,13].

On the other hand, the charge balance indicates that the L ligand acts in a doubly deprotonated fashion by deprotonation of N(1) and N(7) atoms. From an analysis of the resonant canonical forms, we can expect that the negative charge on N(7) would be spread over the N(7), N(9) and O(6) atoms. This situation, in which the negative charge lies on atoms different from those participating in the coordination, is not new in purine complexes [19,20]. Nevertheless, this electronic distribution could suggest a favourable electronic disposition of the O(6) atom compared with the O(2) atom with respect to coordination to a soft polarizable metal fragment [13,21]. Thus, we feel that the fact that coordination is through N(1)/O(2), instead of N(1)/O(6), can be explained mainly on the basis of the formation of a hydrogen bond between the O(6) atom and the water molecule (O(6)···O(1w)=2.889 Å), which, as was mentioned above, seems to be one of the factors preventing the O(6) coordination.

Nevertheless, more examples of this kind of complex are needed before some insight into the electronic and steric factors governing this chelation mode of binding can been derived; we are currently working on such studies.

4. Supplementary material

The coordinates, bond lengths and angles, anisotropic thermal parameters and observed and calculated structure factors are available from the authors on request.

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