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Interaction between Transition Metals and Nucleic Acids. Part IV. Synthesis and Molecular Structure of Cu(UraN-Medpt-H), the Copper(II) Complex of a Pentamine Ligand Derived from Uracil

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Abstract

The title compound Cu(UraN-Medpt-H), crystallizes in the triclinic space group $P\bar{1}$ with two formula units in a cell of dimensions $a = 11.296(4)$, $b = 11.469(4)$, $c = 13.589(5)$ Å, $\alpha = 71.83(6)$, $\beta = 113.77(7)$ and $\gamma = 113.38(7)°$. The structure was solved by the heavy-atom method and refined by least-squares calculations to $R = 0.083$ for 1475 counter data. The geometry around the copper atom shows a slightly distorted trigonal bipyramid. The uracil, H_3BO_3 and H_2O molecules are involved in a crowded network of H-bonds.

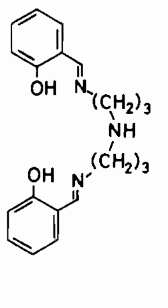
Introduction

In order to obtain bifunctional molecules which might be able, like the antibiotic bleomycin [1], to complex a transition metal cation and also to bind to deoxyribonucleic acids, we have previously prepared several Schiff bases by condensation of 5-formyluracil with various di-, tri- or tetra-amines [2, 3]. Unfortunately, these compounds were not stable enough in aqueous solutions to allow tests of biological activity to be carried out. For this reason, we have converted these Schiff bases to the corresponding amines by reduction of the imine functions and studied their complexing ability toward copper(II). We have obtained crystals for one of the complexes and in this paper we report the detailed results of its X-ray analysis.

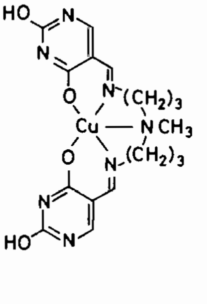
Experimental

Synthesis of Cu(UraN-Medpt-H)

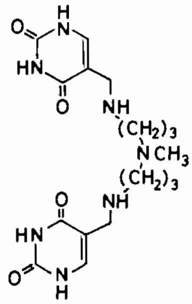
0.5 mmol of Schiff base is partially dissolved in 10 ml of ethanol 95 and heated at 50 °C. 100 mg of $NaBH_4$ in 2 ml of EtOH 95 are added while heating is maintained [2]. The reduction of the imine functions is followed by UV spectroscopy: the absorption band at 315 nm disappears and is replaced by a band at 270 nm. The reaction is complete after 15 min. After cooling, the salts are filtered off and the filtrate is evaporated to dryness; methanol is added and then removed under vacuum to eliminate most of the borate salts. The amine is dissolved in 1 ml of water, and 9 ml of ethanol 95. 0.5 mmol of $Cu(OAc)_2\cdot H_2O$ in the minimum of water are added. An intense blue color appears immediately. After slow evaporation, blue crystals are obtained.



Saldpt



Cu UraN-Medpt



UraN-Medpt-H

X-ray Structure

Crystals were obtained by slow saturation of an ethanolic solution. A crystal of dimensions 0.1 × 0.1 × 0.3 mm, sealed in a Lindemann capillary with a drop of mother liquor, was used for data collection and determination of the unit cell on a Philips PW 1100 diffractometer using graphite monochromated Cu Kα radiation ($\lambda = 1.5418$ Å).

Crystal data

Molecular formula $C_{17}H_{27}N_7O_4{}^{2-}Cu^{2+}\cdot 2(BO_3H_3)\cdot 2H_2O\cdot 0.5C_2H_5OH$, $M = 639$ triclinic system, space

0020-1693/86/$3.50

group $P\bar{1}$, $a = 11.296(4)$, $b = 11.469(4)$, $c = 13.589(5)$ Å, $\alpha = 71.83(6)$, $\beta = 113.77(7)$, $\gamma = 113.38(7)°$.

Parameters values were obtained by the least-squares refinement of 36 well-centered reflections. The data were collected using the θ 2θ scan technique with a speed of 0.05° s^{-1} and a scan width of 1.7° + 0.2° tan θ. The three standards reflections monitored every two hours showed an overall decrease of 10% and a correction was made for crystal deterioration. From 3808 independent intensities, 1475 with $I > 3\sigma(I)$ were considered as observed.

From the Patterson function, the Cu atom was located: then Fourier synthesis gave the position of all the atoms of the molecule. After refinement of the parameters, a difference Fourier map was calculated which clearly indicated the presence of solvent molecules. This appeared to be a planar complex of two molecules, each having four atoms and two isolated peaks probably linked together by H-bonds. It seemed most likely that the two intriguing solvate molecules were H_3BO_3 (or $H_2BO_3^-$) acids, and that the isolated peaks were water molecules. An empirical absorption correction [4] was applied reducing the R factor from 0.15 to 0.13. The structure was then refined anisotropically. On a difference Fourier map, an ethanol solvent molecule which displayed high thermal motion was located. It was introduced in the refinement as a rigid group with an occupation factor of 0.5. The H atoms linked to the C atoms were introduced in theoretical positions ($d_{C-H} = 1.08$ Å) with a temperature factor equal to that of the bonded atom. On a subsequent difference Fourier map, H atoms were clearly visible on the nitrogen atoms N(1), N(1′), N(8) and N(8′). It was not possible to locate those of the solvent molecules. The final R factors were 0.083 and $R_w = 0.085$. The weighting scheme was $w^{-1} = (\sigma^2(F) + 0.014\ F^2)^{-1}$ where $\sigma(F)$ was based on counting statistics. The minimized function was $\Sigma w(|F_o| - |F_c|)^2$.

All calculations were made on a Mini 6/43 Bull computer. The main program used was SHELX 76 [5] with coefficients for analytical approximation to the scattering factors and anomalous dispersion corrections from International Tables [6]. Bond lengths and angles are reported in Table I.*

Discussion

Synthesis of the Complex

As models of transferrin iron(III) complexes with polyamines derived from Saldpt-type ligands were

TABLE I. Bond Lengths (Å) and Bond Angles (°), with the e.s.d.s in Parentheses

Cu–O4	2.22(1)
Cu–N8	2.01(1)
Cu–N12	2.07(1)
Cu–O4′	2.00(1)
Cu–N8′	1.99(1)
N1–C2	1.37(2)
N1–C6	1.38(2)
C2–O2	1.26(2)
C2–N3	1.29(2)
N3–C4	1.38(2)
C4–O4	1.29(2)
C4–C5	1.42(2)
C5–C6	1.33(2)
C5–C7	1.51(2)
C7–N8	1.49(2)
N8–C9	1.52(2)
C9–C10	1.53(3)
C10–C11	1.44(3)
C11–N12	1.51(2)
N12–C13	1.46(3)
N12–C11′	1.48(2)
N1′–C2′	1.36(2)
N1′–C6′	1.34(2)
C2′–O2′	1.28(2)
C2′–N3′	1.34(2)
N3′–C4′	1.34(2)
C4′–O4′	1.34(2)
C4′–C5′	1.44(2)
C5′–C6′	1.31(2)
C5′–C7′	1.48(3)
C7′–N8′	1.45(2)
N8′–C9′	1.46(2)
C9′–C10′	1.52(3)
C10′–C11′	1.61(3)
O1A–B1	1.37(2)
O2A–B1	1.36(3)
B1–O3A	1.36(3)
O1B–B2	1.36(3)
O2B–B2	1.39(3)
B2–O3B	1.38(3)
OH–CH2	1.38(4)
CH2–CH3	1.46(4)
O4–Cu–N8	92(1)
O4–Cu–N12	101(1)
O4–Cu–O4′	110(1)
O4–Cu–N8′	83(1)
N8–Cu–N12	99(1)
N8–Cu–O4′	81(1)
N8–Cu–N8′	169(1)
N12–Cu–O4′	150(1)
N12–Cu–N8′	92(1)
O4′–Cu–N8′	92(1)
C2–N1–C6	120(1)
N1–C2–O2	117(1)
N1–C2–N3	122(1)
O2–C2–N3	122(1)
C2–N3–C4	121(1)

(continued on facing page)

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*Final atomic coordinates with estimated standard deviations and structural factors are available as supplementary material from author C.R.

TABLE I. *(continued)*

N3–C4–O4	119(1)
N3–C4–C5	120(1)
O4–C4–C5	121(1)
Cu–O4–C4	119(1)
C4–C5–C6	118(1)
C4–C5–C7	119(1)
C6–C5–C7	123(1)
N1–C6–C5	120(1)
C5–C7–N8	112(1)
Cu–N8–C7	111(1)
Cu–N8–C9	123(1)
C7–N8–C9	111(1)
N8–C9–C10	111(2)
C9–C10–C11	117(2)
C10–C11–N12	117(2)
Cu–N12–C11	115(1)
Cu–N12–C13	114(1)
Cu–N12–C11′	110(1)
C11–N12–C13	105(1)
C11–N12–C11′	104(1)
C13–N12–C11′	109(1)
C2′–N1′–C6′	122(1)
N1′–C2′–O2′	118(1)
N1′–C2′–N3′	121(1)
O2′–C2′–N3′	121(1)
C2′–N3′–C4′	117(1)
N3′–C4′–O4′	116(1)
N3′–C4′–C5′	124(1)
O4′–C4′–C5′	121(1)
Cu–O4′–C4′	125(1)
C4′–C5′–C6′	116(2)
C4′–C5′–C7′	117(1)
C6′–C5′–C7′	127(2)
N1′–C6′–C5′	121(2)
C5′–C7′–N8′	114(1)
Cu–N8′–C7′	111(1)
Cu–N8′–C9′	117(1)
C7′–N8′–C9′	108(1)
N8′–C9′–C10′	110(2)
C9′–C10′–C11′	114(2)
N12–C11′–C10′	113(2)
O1A–B1–O2A	121(2)
O1A–B1–O3A	119(2)
O2A–B1–O3A	119(2)
O1B–B2–O2B	123(2)
O1B–B2–O3B	121(2)
O2B–B2–O3B	116(2)
OH–CH2–CH3	112(2)

previously synthesized and characterised [7, 8]. Recently Gampp *et al.* have studied the stability and structure of Cu(II) complexes with linear pentadentate ligands by EPR [9], potentiometry and spectroscopy [10] but to our knowledge, no copper(II) complex of this type has been isolated.

The synthesis of the ligand has been previously described [2]. Various attempts to prepare the copper complexes from the amine hydrochlorides in the presence of a base were unsuccessful. The synthesis could be achieved by reduction of the imine functions by NaBH$_4$, the free amine being isolated and used without further purification for the synthesis of the complex. Cu(UraN-Medpt-H) was isolated as crystals whose elemental analysis showed the presence of some boron.**

Structure of Cu(UraN-Medpt-H)

The structure of the complex is illustrated on Fig. 1. The Cu atom is pentacoordinated to N(8), N(8′), N(12), O(4) and O(4′) atoms. The geometry around the Cu atom is that of a distorted trigonal bipyramid with its main axis along the Cu–N(8) and Cu–N(8′) bonds, the Cu atom lying in the plane of three atoms: O(4), O(4′) and N(12). This geometry is commonly observed in the molecular structures of Schiff base Cu(II) complexes Cu(UraN-Medpt) [3], Cu(DiMeBardpt) [11] and Cu(mbpN) [12], and also in the structures of Co(II) [13, 14] and Ni(II) complexes [15]. Pertinent distances and angles, illustrating the metal environment, are compared in Table II. However, the overall geometry of the complex differs significantly from those observed previously [3, 11]. In the present structure, the two uracil planes are approximately parallel (dihedral angle: 13°), while they are roof-shaped in Cu(UraN-Medpt) and Cu(DiMeBardpt), with dihedral angles between the two uracil moieties which are 85° and 72°, respectively. It is obvious that because of the sp^2 hybridization of N(8) and N(8′), the planes cannot be coplanar in Cu(UraN-Medpt) and Cu(DiMeBardpt), whereas

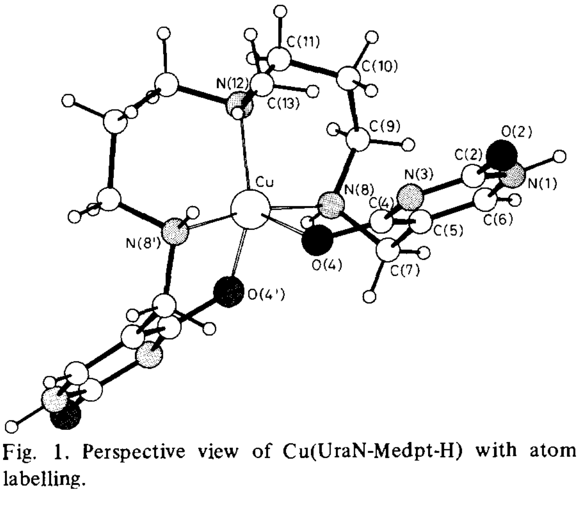

Fig. 1. Perspective view of Cu(UraN-Medpt-H) with atom labelling.

**The synthesis of the corresponding copper(II) complexes with the other previously described polyamines [2] was carried out. They were isolated as amorphous powder but could not be characterised because they did not show reproducible elemental analysis due to contamination with borate salts. For all of them, the values of the half-wave potential were at *ca.* −1.2 V (*vs.* SCE) on a rotating platinum electrode.

TABLE II. Geometry of Selected Pentadentate Ligands of Cu(II), Co(II) and Ni(II): Average Bond Lengths (Å) and Angles (°) in: (a) Cu(UraN-Medpt) [3]; (b) Cu(DiMeBardpt) [11]; (c) Cu(UraN-Medpt-H) (this study); (d) Cu(mbpN) [12]; (e) Co(Saldpt) [13], (f) Co(Saldpt) [14]; (g) Ni(Saldpt) [15]

	(a) Cu	(b) Cu	(c) Cu	(d) Cu	(e) Co	(f) Co	(g) Ni
M–N(12)	2.151	2.072	2.373	2.071	2.136	2.170	2.060
M–N(8)	1.938	1.932	1.966	2.000	2.061	2.066	2.028
M–O(4)	2.089	2.070	1,937	2.110	1.945	1.961	1.984
N(8)–M–N(8′)	179	177	175	169	180	177	177
O(4)–M–O(4′)	101	103	152	110	128	127	146
O(4)–M–N(12)	130	109	106	101	115	116	111
O(4′)–M–N(12)	130	147	101	150	116	117	102
N(8)–M–N(12)	90	86	89	99	90	89	91
N(8)–M–O(4)	92	90	90	92	89	89	91
N(8)–M–O(4′)	88	86	93	81	90	93	93
N(8′)–M–N(12)	90	95	86	92	90	88	90
N(8′)–M–O(4)	88	93	90	83	91	90	87
N(8′)–M–O(4′)	92	91	89	92	90	90	88

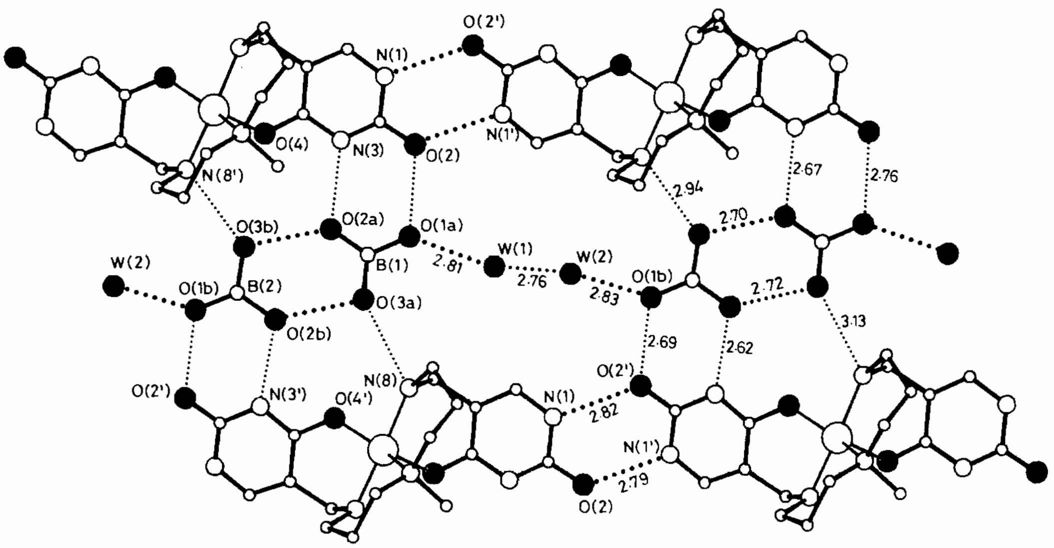

Fig. 2. The hydrogen bond network.

the sp^3 hybridization at N(8) and N(8′) in Cu(UraN-Medpt-H) allows more flexibility around the copper ion and leads to a geometry where the two planes are parallel.

Only a small number of reflections could be observed due to the difficulties encountered in obtaining good data from the crystal in mother liquor. Also, the presence of crystallization solvent and the probable disorder of the ethanol molecule did not allow an accurate refinement of the structure to be made. Because of the presence of the two molecules of H_3BO_3, it is difficult to conclude whether the complex is neutral, as observed in the case of Cu(UraN-Medpt) [3] and Cu(DiMeBardpt) [11], or diprotonated and thus associated with two $H_2BO_3^-$ anions. On the difference Fourier maps, H atoms were positioned on N(1) and N(1′), but none were found on N(3) and N(3′). Unfortunately the H atoms of the H_3BO_3 molecules were not visible. Moreover, the analysis of the H-bond network does not remove the ambiguity.

The H_3BO_3 molecules play an important role in the crystallization of the complex by building up a crowded network of H-bonds. In Fig. 2, the molecules involved in the hydrogen bonding scheme are represented. Each uracil ring is linked to a similar ring on a vicinal molecule by two bonds: N(1)–H····· O(2′) (2.82 Å) and O(2)·····H–N(1′) (2.79 Å). Thus, the Cu(UraN-Medpt-H) molecules form infinite chains elongated along the *a* + *c* directions. These chains are linked via parallel chains of H_3BO_3 and water molecules. The two molecules of orthoboric acid form a planar hydrogen-bonded dimer which links two uracil moieties, each of them belonging to two neighbouring uracil chains. The link is assured by strong H-bonds: N(3)•••O(2a) (2.67 Å), O(2)••• O(1a) (2.76 Å), N(3′)•••O(2b) (2.62 Å) and O(2′)••• O(1b) (2.69 Å). Two H-bonds join N(8)–H to O(3a) (3.13 Å) and N(8′)–H to O(3b) (2.94 Å).

The two water molecules bridge two orthoboric dimers through H-bonds: O(1a)•••W(1) (2.81 Å), W(1)•••W(2) (2.76 Å) and W(2)•••O(1b) (2.83 Å). An infinite chain of $H_3BO_3-H_2O$ is thus built up which runs parallel to the uracil chains. The ethanol molecule which lies in a hole of the crystal between two chains of complexes is hydrogen-bonded to W(2) (2.82 Å). All the atoms involved on this H-bond network are approximately in the same plane (mean deviation: 0.5 Å, largest deviations N(8) (1.2 Å), N(8′) (0.8 Å) and W(1) (0.9 Å). Figure 3 illustrates how complexes are stacked, but there is no superposition of the uracil groups.

The orthoboric acid, which is historically known as the first hydrogen-bound crystal structure to be examined by X-ray diffraction [16, 17], forms an extensive sheet of H bonds. In the present structure, the mean B–O interatomic distance is 1.367 Å (with e.s.d. 0.012 from distribution) which coincides with the B–O bond distance observed in the precise neutron diffraction study of the orthoboric acid D_3BO_3 [18]: 1.367 Å (0.015 from distribution). The H-bond distances in the dimer of H_3BO_3 (present structure) are: O(2a)•••O(3b): 2.70 Å and O(2b)••• O(3a): 2.72 Å (2.713 Å in D_3BO_3).

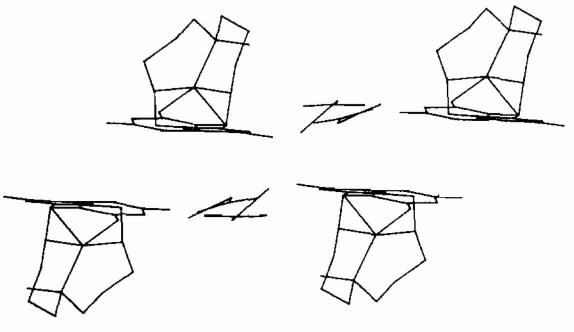

Fig. 3. Stacking of the molecule. A view in the plane of the uracil group.

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