

Crystallographic Studies on Metal–Nucleotide Base Complexes. V.* Tetraaquo-bis-(9-methyladenine)copper(II) Dichloride Dihydrate

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$[(C_6H_7N_5)_2Cu \cdot 4H_2O]Cl_2 \cdot 2H_2O$ crystallizes from water in space group $C2/m$ or $C2$ with $a=15.482$, $b=6.894$, $c=11.269$ Å, $\beta=114.42^\circ$. The structure determination is based on 1239 reflexions collected on a diffractometer with Mo $K\alpha$ radiation. The structure was refined satisfactorily by full-matrix least-squares calculations both in $C2$ and $C2/m$. Final R is 0.031 in $C2/m$. In the centrosymmetric space group the complex unit contains both a twofold axis and a mirror plane. The copper ion is coordinated in a (2+4) inverted Jahn–Teller distorted octahedral configuration. The adenine base is coordinated through N(7) with a short axial bond, Cu–N(7)=2.008 Å. In the equatorial plane four water molecules are bonded, Cu–O=2.162 Å. The chloride ion is not coordinated to copper, but is hydrogen bonded to the purine base at C(2) and C(8). The amino group forms bifurcated hydrogen bonds to two of the water molecules in the coordination sphere. Pairs of centrosymmetrically related adenine ligands are hydrogen bonded through N(1) and the amino group.

Introduction

Interaction between metal ions and nucleic acids has been extensively studied by spectroscopic methods (Eichhorn, 1973). Several mechanisms have been proposed to explain the lowering of the melting temperature of DNA by certain transition metal ions. However, the influence of anions on these systems may also be of importance (Chang & Marzilli, 1974). The importance of anion–purine base interaction in biopolymers is inferred by the variation in melting temperature of DNA by varying salt concentration (Homaguchi & Geiduschek, 1962). In a previous paper the crystal structure of a copper–9-methyladenine sulphato complex has been described (Sletten, 1974). To investigate the influence of different anions on the coordination geometry, the corresponding chloride has now been studied.

Experimental

The compound was synthesized by dissolving 9-methyladenine in 0.1 *N* HCl and adding 0.1 *M* $CuCl_2$ solution. The pH was adjusted to be slightly acid by addition of 0.1 *N* NaOH (Weiss & Venner, 1966). The mixture was filtered and after a few days green spherulites appeared. They were washed in water and methanol and redissolved in water. This procedure was repeated several times before suitable crystals were obtained.

Weissenberg films indicated three possible space groups; $C2$, Cm , and $C2/m$. Cell dimensions were obtained from 2θ settings of 12 reflexions measured on a Siemens diffractometer. The crystal used for data collection was mounted along **b** and had dimensions $0.50 \times 0.48 \times 0.06$ mm. The experimental procedure is

described elsewhere (Sletten, 1974). Within the sphere of reflexion limited at $\sin \theta/\lambda=0.64$, 1264 unique reflexions were recorded. Of these, 25 were less than the threshold value of $2\sigma_c$, where σ_c is the estimated error due to counting statistics. The data were corrected for Lorentz and polarization effects. Absorption correction was carried out with a modified Busing & Levy (1957) procedure.

Crystal data

$[(C_6H_7N_5)_2Cu \cdot 4H_2O]Cl_2 \cdot 2H_2O$, F.W. = 540.8, $a=15.482$ (7), $b=6.894$ (10), $c=11.269$ (5) Å, $\beta=114.42$ (3)°, $V=1095.6$ Å³, $D_m=1.68$, $D_x=1.68$ g cm⁻³, $Z=2$, $\lambda(Mo K\alpha)=0.71069$ Å, $\mu=13.2$ cm⁻¹.

Structure determination

Tentatively space group $C2/m$ was adopted and the structure was solved by the heavy-atom method. The refinement by full-matrix least-squares calculations converged at $R=0.031$ ($R=\sum||F_o|-|F_c||/\sum|F_o|$). All non-hydrogen atoms were refined with anisotropic temperature factors and the hydrogen atoms were refined isotropically.

Both $C2/m$ and Cm require a crystallographic mirror plane through the adenine ligands. However, the presence of such a mirror plane does not comply with previous structure determinations of purine molecules. Often the purine ring is found to be non-planar with a bend around C(4)–C(5) (Sletten & Jensen, 1969). Furthermore, U_{22} for atoms located on the mirror plane was found to be much larger than U_{11} and U_{33} , indicating deviation from planarity. Refinement in $C2$ was carried out and converged satisfactorily at a final R of 0.029 despite considerable pseudosymmetry. Comparing the two R values according to Hamilton's R test, $C2$ is more probable than $C2/m$ at the 0.5%

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significance level. However, the deviations from planarity observed in C2 are hardly significant (Table 1). Moreover U_{22} is not improved by changing from $C2/m$ to C2. None of the differences found between bond lengths and angles in the two refinements is more than 2σ . Thus, for convenience $C2/m$ was chosen rather than C2; the refinements, however, are inconclusive in resolving the space-group ambiguity. A similar case has been reported for adenine dihydrochloride where $Pnma$ was chosen rather than $Pn2_1a$ (Kistenmacher & Shigematsu, 1974).

The observed and calculated structure factors are listed in Table 2. The scattering curves used for Cu, O, N, C are those given in *International Tables for X-ray Crystallography* (1962) and for H that published by Stewart, Davidson & Simpson (1965). Atomic parameters in $C2/m$ are listed in Table 3. All calculations were carried out on a UNIVAC 1110 computer. The main programs used originate from the Weizmann Institute of Science, Rehovoth, Israel, and have been modified by Dr D. Rabinovich, cand. real. K. Åse and cand. real. L. Milje. *ORTEP* was used for making the stereo drawings (Johnson, 1970).

Table 1. *The deviations from planarity in space group C2, compared to the thermal parameters U_{22} in C2 and $C2/m$*

	C2 Y (Å)	C2 U_{22} (Å ²)	$C2/m$ U_{22} (Å ²)
C(2)	-0.0040 (27)	0.102 (3)	0.103 (3)
C(4)	-0.0003 (15)	0.045 (1)	0.043 (1)
C(5)	0.0055 (16)	0.038 (1)	0.038 (1)
C(6)	0.0028 (20)	0.044 (1)	0.042 (1)
C(8)	0.0044 (18)	0.041 (2)	0.041 (1)
C(9)	0.0087 (31)	0.082 (3)	0.092 (3)
N(1)	0.0036 (17)	0.083 (2)	0.081 (2)
N(3)	0.0072 (22)	0.077 (2)	0.079 (2)
N(6)	0.0088 (19)	0.070 (2)	0.074 (2)
N(7)	0.0015 (14)	0.041 (1)	0.041 (1)
N(9)	-0.0004 (19)	0.047 (1)	0.047 (1)
Cu	0.0000	0.0374 (2)	0.0372 (3)

Table 3. *The final atomic parameters*

(a) Non-hydrogen atoms (coordinates $\times 10^5$ and temperature parameters $\times 10^4$). Standard deviations are in parentheses. Anisotropic temperature factor = $\exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{23}klb^*c^* + 2U_{13}hla^*c^*)]$.

	X/a	Y/b	Z/c	U_{11}	U_{22}	U_{33}	U_{12}	U_{23}	U_{13}
Cu	0	0	0	199 (2)	372 (3)	134 (2)	0	0	52 (2)
Cl	27943 (5)	0	90136 (6)	379 (4)	660 (5)	256 (3)	0	0	114 (3)
C(2)	21069 (20)	0	56000 (25)	292 (13)	1027 (26)	140 (10)	0	0	67 (11)
C(4)	22941 (16)	0	37630 (21)	222 (10)	432 (13)	187 (10)	0	0	80 (9)
C(5)	13214 (16)	0	30144 (20)	213 (10)	382 (12)	152 (10)	0	0	81 (9)
C(6)	07236 (17)	0	36878 (22)	233 (11)	419 (13)	207 (11)	0	0	114 (9)
C(8)	20179 (16)	0	17024 (21)	240 (11)	413 (13)	185 (10)	0	0	114 (9)
C(9)	37378 (20)	0	32531 (34)	199 (12)	923 (27)	377 (15)	0	0	131 (11)
N(1)	11587 (16)	0	50058 (20)	284 (11)	810 (17)	169 (10)	0	0	114 (8)
N(3)	27371 (14)	0	50799 (19)	207 (10)	790 (17)	162 (9)	0	0	36 (8)
N(6)	-02137 (15)	0	31619 (21)	225 (10)	741 (17)	179 (10)	0	0	93 (9)
N(7)	11589 (13)	0	16936 (17)	206 (9)	407 (11)	158 (8)	0	0	84 (7)
N(9)	27192 (14)	0	29121 (19)	185 (9)	471 (12)	229 (9)	0	0	97 (8)
O(2)	06131 (11)	22274 (23)	92374 (13)	397 (8)	492 (9)	308 (7)	17 (7)	-5 (6)	41 (6)
O(3)	42885 (15)	0	77251 (23)	255 (10)	653 (14)	365 (12)	0	0	35 (9)

Table 2. *Observed and calculated structure factors ($\times 10$)*

For reflexions with observed intensity less than the threshold value of $2\sigma_e$, the F_o 's are marked with - signs.

h	k	l	F_o	F_c
0	0	0	1000	1000
0	0	1	1000	1000
0	0	2	1000	1000
0	0	3	1000	1000
0	0	4	1000	1000
0	0	5	1000	1000
0	0	6	1000	1000
0	0	7	1000	1000
0	0	8	1000	1000
0	0	9	1000	1000
0	0	10	1000	1000
0	0	11	1000	1000
0	0	12	1000	1000
0	0	13	1000	1000
0	0	14	1000	1000
0	0	15	1000	1000
0	0	16	1000	1000
0	0	17	1000	1000
0	0	18	1000	1000
0	0	19	1000	1000
0	0	20	1000	1000
0	0	21	1000	1000
0	0	22	1000	1000
0	0	23	1000	1000
0	0	24	1000	1000
0	0	25	1000	1000
0	0	26	1000	1000
0	0	27	1000	1000
0	0	28	1000	1000
0	0	29	1000	1000
0	0	30	1000	1000
0	0	31	1000	1000
0	0	32	1000	1000
0	0	33	1000	1000
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0	0	35	1000	1000
0	0	36	1000	1000
0	0	37	1000	1000
0	0	38	1000	1000
0	0	39	1000	1000
0	0	40	1000	1000
0	0	41	1000	1000
0	0	42	1000	1000
0	0	43	1000	1000
0	0	44	1000	1000
0	0	45	1000	1000
0	0	46	1000	1000
0	0	47	1000	1000
0	0	48	1000	1000
0	0	49	1000	1000
0	0	50	1000	1000
0	0	51	1000	1000
0	0	52	1000	1000
0	0	53	1000	1000
0	0	54	1000	1000
0	0	55	1000	1000
0	0	56	1000	1000
0	0	57	1000	1000
0	0	58	1000	1000
0	0	59	1000	1000
0	0	60	1000	1000
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0	0	62	1000	1000
0	0	63	1000	1000
0	0	64	1000	1000
0	0	65	1000	1000
0	0	66	1000	1000
0	0	67	1000	1000
0	0	68	1000	1000
0	0	69	1000	1000
0	0	70	1000	1000
0	0	71	1000	1000
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0	0	73	1000	1000
0	0	74	1000	1000
0	0	75	1000	1000
0	0	76	1000	1000
0	0	77	1000	1000
0	0	78	1000	1000
0	0	79	1000	1000
0	0	80	1000	1000
0	0	81	1000	1000
0	0	82	1000	1000
0	0	83	1000	1000
0	0	84	1000	1000
0	0	85	1000	1000
0	0	86	1000	1000
0	0	87	1000	1000
0	0	88	1000	1000
0	0	89	1000	1000
0	0	90	1000	1000
0	0	91	1000	1000
0	0	92	1000	1000
0	0	93	1000	1000
0	0	94	1000	1000
0	0	95	1000	1000
0	0	96	1000	1000
0	0	97	1000	1000
0	0	98	1000	1000
0	0	99	1000	1000
0	0	100	1000	1000

Results and discussion

The complex unit

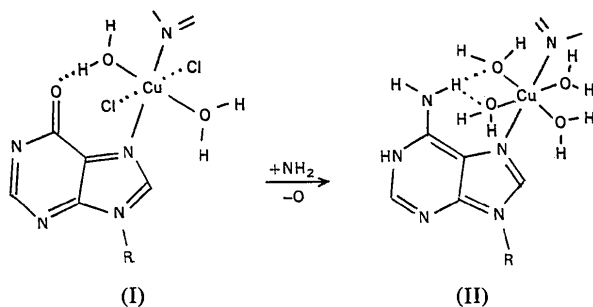
In Fig. 1 the molecular dimensions of the complex are shown. The copper ion has an unusual coordination

Table 3 (cont.)

(b) Hydrogen atoms (parameters $\times 10^3$). Isotropic temperature factor = $\exp[-8\pi^2 U \sin^2 \theta/\lambda^2]$.

	X/a	Y/b	Z/c	U
H(2)	239 (2)	0	656 (3)	51 (9)
H(8)	222 (2)	0	101 (3)	24 (6)
H(61)	-048 (2)	0	381 (3)	42 (8)
H(62)	-052 (2)	0	239 (3)	27 (7)
H(91)	402 (3)	106 (6)	371 (3)	127 (14)
H(92)	383 (4)	0	258 (5)	114 (20)
H(21)	112 (2)	287 (4)	968 (2)	71 (9)
H(22)	19 (2)	295 (4)	871 (3)	71 (9)
H(31)	397 (4)	0	693 (5)	120 (21)
H(32)	390 (3)	0	796 (4)	65 (14)

geometry with two short axial Cu-N bonds and four long equatorial Cu-O bonds. Cu(II) complexes showing inverted Jahn-Teller distortion are expected to be less stable than those with traditional (4+2) coordination. The ligands are all formally neutral, the chloride ion does not enter the coordination sphere. Cu-N(7) is slightly longer than in the corresponding sulphato complex [Cu-N(7)=1.995 Å], but significantly shorter than in the chloro complex of hypoxanthine [Cu-N(7)=2.055 Å] (Sletten, 1974; Sletten & Thorstensen, 1974). In the latter the chloride ion is weakly coordinated to copper (Cu-Cl=2.787 Å).



There is a dramatic change in coordination in going from hypoxanthine (I) to adenine (II). The chloride ions are expelled by water molecules and the Cu-O bond lengths in the equatorial plane are increased by 0.2 Å. The arrangement enables the water molecules to engage in hydrogen bonding to the amino group through a bifurcated hydrogen atom. The distance N(6)-H(62)···O(2)=2.945 (3) Å is of normal length with an angle of 132° at H(62). The indirect chelation

involving a hydrogen bond between the C(6) substituent and the coordination sphere is a persistent feature in all copper-purine complexes where N(9) is blocked. In the sulphato complex of adenine the SO_4^{2-} ion is coordinated to copper and hydrogen bonded to N(6).

The high crystallographic symmetry imposed on the complex is favourable for lowering the crystal packing energy. However, the inverted Jahn-Teller distortion is not necessarily a result of steric or crystal packing re-

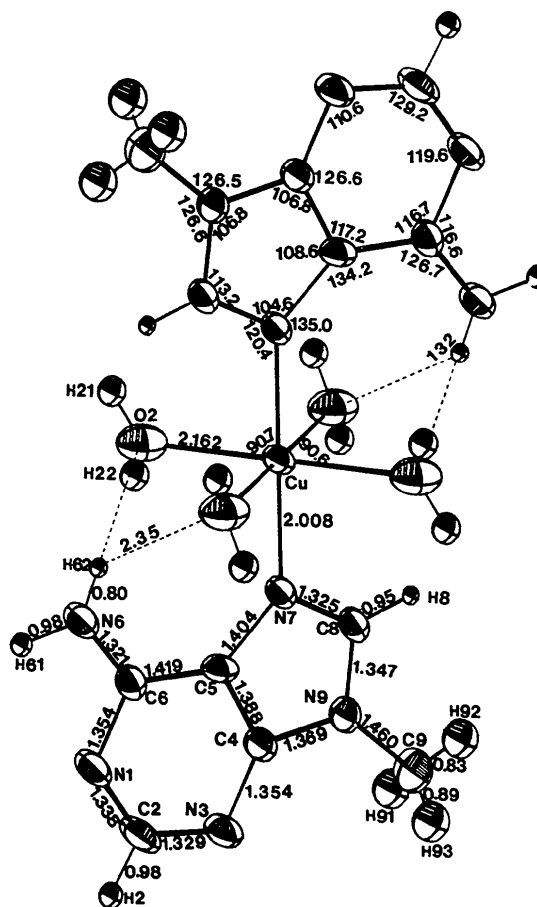


Fig. 1. Interatomic distances and angles in the $[\text{Cu}(\text{Ade})_2 \cdot (\text{H}_2\text{O})_4]^{2+}$ complex. The σ 's in bond lengths are: Cu-O(N) 0.002 Å, C-C(N) 0.003-0.004 Å, H-C(N) (O) 0.03-0.07 Å. The σ 's for angles involving only non-hydrogen atoms are in the range 0.1-0.2°, and for those involving hydrogens 1-5°.

Table 4. Hydrogen-bond distances and angles

	Position of acceptor atom	Distances (Å)		Angle (°)
		D···A	H···A	D-H···A
N(6)-H(61)···N(1)	$\bar{x}, y, 1-z$	2.984 (4)	2.01 (4)	174 (2)
N(6)-H(62)···O(2)	$\bar{x}, y, 1-z$	2.945 (3)	2.35 (3)	132 (1)
O(2)-H(21)···Cl	$\frac{1}{2}-x, \frac{1}{2}+y, 2-z$	3.099 (2)	2.26 (3)	166 (3)
O(2)-H(22)···O(3)	$\frac{1}{2}-x, \frac{1}{2}+y, z$	2.806 (2)	1.97 (3)	170 (2)
O(3)-H(31)···N(3)	x, y, z	2.956 (3)	2.16 (5)	161 (5)
O(3)-H(32)···Cl	x, y, z	3.199 (3)	2.46 (6)	173 (3)
C(2)-H(2)···Cl	x, y, z	3.543 (3)	2.57 (4)	169 (3)
C(8)-H(8)···Cl	$x, y, z-1$	3.694 (3)	2.74 (3)	180 (2)

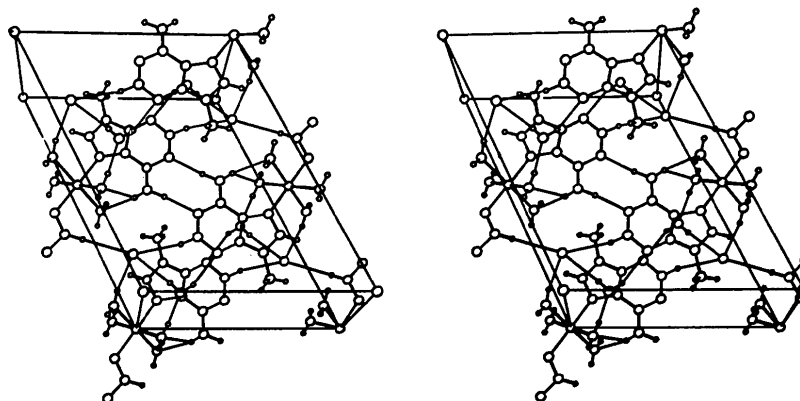


Fig. 2. Stereoscopic drawing of the crystal packing viewed approximately along **b**, with **c** parallel to the interocular line. The drawing was made by ORTEP (Johnson, 1970).

quirements. With a Cu–O distance of 2.0 Å rather than 2.16 Å the hydrogen bonds involving the amino group would have a more favourable geometry. The spectroscopic properties of the complex in solution will be investigated.

The dimensions of the adenine ligand are shown in Fig. 1. A comparison with the geometry of the corresponding ligand in the sulphato complex shows close agreement. However, in the present compound, the bonds adjacent to the coordination site are both slightly longer than in the sulphato complex. This is contrary to what one would expect by comparing the Cu–N(7) lengths in the two complexes.

Hydrogen bonding and crystal packing

The molecular packing is shown in a stereo drawing viewed approximately along **b** (Fig. 2), and intermolecular dimensions are given in Table 4. Coplanar adenine ligands related by a centre of symmetry are hydrogen bonded in a DNA-like pattern through N(1) and the amino group; N(6)–H(61)···N(1) = 2.984 Å with hydrogen-bond angle 174°. The corresponding values for the sulphato complex are 2.986 Å and 179°.

The non-coordinated water molecule forms a coplanar hydrogen-bond bridge between N(3) and the chloride ion. There are also strong indications that the coplanar C(2)–H(2)···Cl···H(8)–C(8) arrangement is part of the hydrogen-bonding scheme. The distances Cl···H(2) of 2.57 Å and Cl···H(8) of 2.74 Å are clearly less than the van der Waals contact. The angles at H(2) and H(8) are 169 (2)° and 180 (2)°, respectively.

The molecular layers are linked along **b** through hydrogen bonds from the chloride ion and the non-coordinated water molecule to water molecules in the coordination sphere. The hydrogen-atom surroundings of the chloride ion may be described as a distorted trigonal bipyramid. The chloride–purine interaction found in the present compound is consistent with that observed for the chloride–guanosine system (Chang & Marzilli, 1974).

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