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A Novel Type of Bidentate Purine–Metal Bonding. *Catena*-tetraaquo-μ-purine-copper(II) Sulphate Dihydrate

PER IVAR VESTUES and EINAR SLETTEN

Department of Chemistry, University of Bergen, 5014 Bergen-U, Norway

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[$Cu(C_5H_4N_4)(H_2O)_4]SO_4 \cdot 2H_2O$, orthorhombic, space group Pbca, a = *11.912(5)* Å, b = *17.828(2)* Å, c = *12.673(2)* Å, Z = *8. The data were collected on a CAD-4 diffractometer using an on-line PDP 11/55 computer for structure analysis. The structure was refined to R = 0.119. The Cu ion is octahedrally surrounded, binding equatorially to N(7) and N(9) in two symmetry related purine rings, thus producing a polymeric chain. The other positions are occupied by water molecules. The Cu–N(9) distance (2.036 Å) is in the range expected for a dative bond while the Cu–N(7) distance (1.903 Å) is close to the value expected for a covalent bond. The purine ligand is neutral being protonated at N(1). The sulphate group is disordered and there is a large degree of pseudo-symmetry in the structure.*

Introduction

Since the first paper on crystallographic structure determination of metal complexes of nucleic acid constituents appeared, a large amount of structural data has been presented. Various substituted purines have been used, and the work has been concentrated on bases with the N(9)-position blocked, to obtain more realistic models of nucleic acid monomers. So far no X-ray structure determination of a metal complex of purine with no exocyclic groups has been published. However, a few reports exist where metal complexes of unsubstituted purine have been characterized by means of other methods. In the most recent work, it is proposed that metals are attached to the purine at N(3) and N(9) forming di- or oligomeric structures [1].

The present paper presents the crystal structure of a copper–purine 1:1 complex.

Experimental

The compound was prepared from commercially available starting materials used without further purification. It was synthesized using a procedure described by Weiss and Venner [2]. To get suitable crystals for X-ray study the compound was recrystallized from a hot 1:1 ethanol–water mixture. Blue crystalline plates appeared upon cooling.

Crystallography

A crystal of $[Cu(C_5H_4N_4)(H_2O)_4]SO_4 \cdot 2H_2O$ (dimensions approximately 0.36 × 0.08 × 0.04 mm) was mounted along *a*. The cell parameters were determined at room temperature from 25 centered general reflexions on an Enraf Nonius CAD-4 diffractometer: $a = 11.912(5)$ Å, $b = 17.828(2)$ Å, $c = 12.673(2)$ Å, $V = 2691.6$ Å^3, *Pbca*, $Z = 8$, $M = 387.8$, $\mu = 18.95$ cm^{-1}, $d_{calc} = 1.92$ g cm^{-3}, $d_{obs} = 2.02$ g cm^{-3} (flotation in $CHBr_3/C_4H_8Br_2$), MoK$_\alpha$, $\lambda = 0.71069$ Å, graphite monochromator. An analysis of the intensity peak profile indicated that the ω-scan technique should be used. The scan rate was determined by a fast prescan (10° min^{-1}). Reflexions having $\sigma(I)/I \geqslant 0.5$ were considered unobserved and were not remeasured. The relative standard deviation, $\sigma(I)/I$, required for the final data was set equal to 0.03 provided that the maximum time spent on any one reflexion was less than 90 sec. Backgrounds were measured by extending the scan 25% on either side of the peak. A total of 2358 unique reflexions were recorded in the range $1° \leqslant \theta \leqslant 27°$. Of these, 1503 had $I > \sigma_c$ where σ_c is the estimated error due to counting statistics. The relatively large number of unobserved reflexions is mainly due to the small size of the crystal and the presence of pseudosymmetry.

A second data set was collected on the same crystal using $\theta/2\theta$ scans. At a later stage a third set was collected using a larger crystal. However, refinements based on these data gave essentially the same results as the first one.

The structure was solved by the Patterson method and refined by full-matrix least-squares calculation on a UNIVAC 1110 computer. The copper atom was found lying on a screw-axis. A Fourier synthesis based on the phases determined by the heavy atom revealed the position of the purine base, the coordinated water molecules and the sulphate group. A

TABLE I. The Final Atomic Parameters.

(a) Non-hydrogen atoms. (Temperature parameters × 100). 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_{13}	U_{23}
Cu	0.11988(12)	0.25067(9)	−0.00166(13)	2.20(8)	2.54(8)	2.84(8)	−0.07(6)	−0.17(6)	0.34(6)
S	0.3719(3)	0.1298(2)	0.2637(3)	3.8(2)	3.6(2)	3.6(2)	−0.2(2)	1.0(2)	−0.6(2)
O(1)	0.1086(8)	0.3475(5)	−0.0829(8)	4.0(5)	3.3(5)	4.3(5)	−0.4(4)	−1.8(5)	0.7(5)
O(2)	0.1971(9)	0.1953(6)	−0.1648(10)	4.3(6)	4.8(6)	6.8(8)	−0.8(5)	−0.4(6)	0.7(6)
O(3)	0.1424(12)	0.1527(6)	0.0749(9)	9.1(9)	3.8(6)	5.7(7)	−1.7(6)	−2.3(7)	1.6(5)
O(4)	0.0481(10)	0.3019(6)	0.1624(9)	6.4(7)	4.8(6)	4.4(6)	−1.6(5)	0.0(5)	0.4(5)
O(5)	0.3763(11)	0.2114(6)	0.2738(10)	6.6(8)	3.9(6)	7.6(9)	−0.3(6)	0.4(7)	−1.2(6)
O(9)	0.4907(20)	0.4624(10)	0.3920(15)	18.3(21)	9.3(13)	9.7(13)	5.7(14)	3.4(14)	2.3(11)
O(10)	0.2716(19)	0.4505(10)	0.3865(16)	15.3(19)	9.9(13)	11.5(15)	−3.8(13)	−3.8(14)	−0.6(12)
N(1)	0.4337(11)	0.4671(7)	0.1343(10)	5.0(8)	3.8(7)	4.4(7)	−0.6(6)	−2.0(6)	0.6(6)
N(3)	0.2556(11)	0.4097(6)	0.1027(10)	5.0(7)	3.0(6)	4.5(7)	−0.2(5)	−1.0(6)	−1.5(5)
N(7)	0.4720(9)	0.2816(5)	0.0360(7)	4.2(6)	1.8(5)	1.6(5)	−0.1(4)	0.2(4)	−0.3(4)
N(9)	0.2794(9)	0.2814(6)	0.0363(9)	2.9(6)	3.0(6)	4.2(6)	0.7(5)	0.0(5)	−0.2(5)
C(2)	0.3179(14)	0.4696(9)	0.1355(15)	4.0(8)	4.5(9)	6.5(11)	−0.4(7)	0.4(8)	−1.8(8)
C(4)	0.3154(11)	0.3496(7)	0.0712(10)	2.9(7)	3.3(7)	3.0(7)	1.3(5)	0.8(5)	0.6(5)
C(5)	0.4350(11)	0.3493(7)	0.0751(10)	2.9(6)	3.2(7)	2.6(6)	1.1(5)	0.6(5)	−0.1(5)
C(6)	0.4931(11)	0.4112(8)	0.1109(12)	2.2(6)	4.3(8)	4.3(8)	0.0(6)	−0.5(6)	0.8(7)
C(8)	0.3710(11)	0.2432(7)	0.0139(11)	3.6(7)	1.4(8)	4.0(7)	−1.1(5)	0.8(6)	0.0(5)

(b) Disordered oxygen atoms (occupancy 0.5). Isotropic temperature factor = $\exp[-8\pi^2 U \sin^2\theta/\lambda^2]$

	X/a	Y/b	Z/c	$U \times 100$
O(6)	0.4226(19)	0.0989(12)	0.1576(17)	3.8(5)
O(61)	0.3630(22)	0.1118(13)	0.1604(19)	5.1(6)
O(7)	0.4314(18)	0.0931(12)	0.3409(17)	4.4(5)
O(71)	0.4965(22)	0.1114(14)	0.2880(20)	6.0(6)
O(8)	0.2504(20)	0.1109(12)	0.2583(19)	5.2(5)
O(81)	0.3058(31)	0.0878(20)	0.3464(29)	10.0(11)

(c) Hydrogen atoms as determined from Fourier difference map

	X/a	Y/b	Z/c
H(1)	0.50	0.50	0.15
H(2)	0.26	0.50	0.15
H(6)	0.55	0.41	0.08
H(8)	0.37	0.19	0.01
H(11)	0.06	0.41	−0.09
H(12)	0.08	0.37	−0.06
H(21)	0.26	0.24	−0.17
H(22)	0.23	0.15	−0.14
H(31)	0.05	0.13	0.08
H(32)	0.21	0.10	0.11
H(41)	0.01	0.35	0.15
H(42)	−0.01	0.26	0.19

succeeding Fourier synthesis based on the phases of the atoms already determined revealed two oxygen atoms from crystal water. Furthermore, three additional peaks were located in the vicinity of the sulphate group, indicating disorder. This was later confirmed by refinement on partial occupancy of three oxygen atoms of the SO_4^{2-} group. The occupancies did not deviate significantly from 0.5 and were kept fixed at this value in the succeeding refinements. The hydrogen atoms on the purine ring and on the coordinated water molecules were located in a Fourier difference map. These atoms were included in the calculations, but not refined.

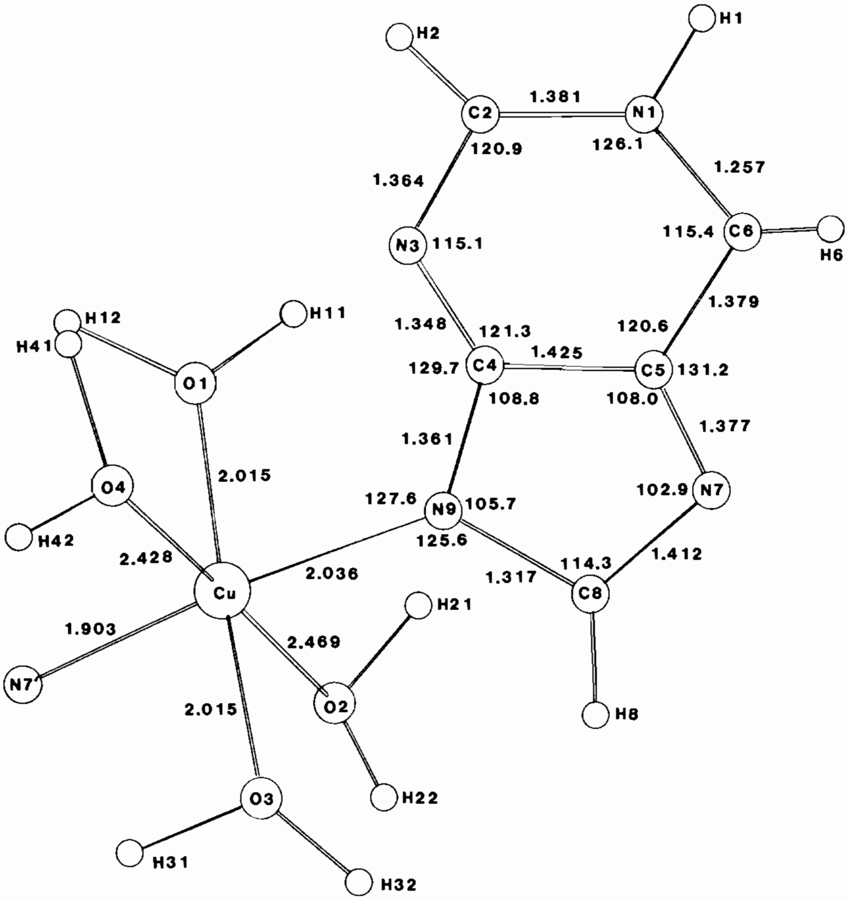


Fig. 1. Interatomic distances and angles in the complex unit. The σ's in bond lengths are: Cu–N 0.017 Å, Cu–O 0.020–0.028 Å, C–C(N) 0.020–0.025 Å. The σ's in angles at C(N) are 0.8–1.5°.

All non-hydrogen atoms with multiplicity one, except those from crystal water were refined anisotropically, the remaining atoms isotropically. The final refinement gave an $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ of 0.119 and R_w of 0.099.

The standard deviation of an observation of unit weight was 2.58. In the refinement the reflexions were given weight $w = 1/\sigma_F^2$, where σ_F is based on counting statistics only.

Table I contains the positional and thermal parameters from the last cycle of refinement along with the standard deviations as estimated from the inverse matrix.

The relatively high R-value is caused by several factors, the most important being the large degree of pseudosymmetry and the disordered sulphate group. Also the thermal parameters as listed in Table I, show some anomalies which may be due to the same factors.

All calculations were carried out on a UNIVAC 1110 computer using the X-RAY 76 programs [3] and ORTEP [4].

TABLE II. Bond Angles in the Coordination Sphere of Copper (σ = 0.5°).

O(1)–Cu–O(2)	86.4	O(2)–Cu–N(9)	87.5
O(1)–Cu–O(3)	175.7	O(3)–Cu–O(4)	87.7
O(1)–Cu–O(4)	95.2	O(3)–Cu–N(7)'	88.3
O(1)–Cu–N(7)'	94.6	O(3)–Cu–N(9)	89.7
O(1)–Cu–N(9)	87.2	O(4)–Cu–N(7)'	89.1
O(2)–Cu–O(3)	90.4	O(4)–Cu–N(9)	91.3
O(2)–Cu–O(4)	177.9	N(7)'–Cu–N(9)	178.0
O(2)–Cu–N(7)'	91.8		

Results and Discussion

The molecular dimensions of the complex are shown in Fig. 1 and Table II. The complex units are bridged by purines through N(7) and N(9) forming a polymeric chain. The coordination around copper is (4 + 2), two of the equatorial positions being occupied by N(7) and N(9) and the four remaining positions in the coordination sphere being occupied by water molecules. The purine ligand is a N(1)–H tautomer as opposed to the free base where the proton is found to reside on N(7) [5].

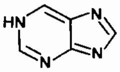
Recently the IR spectra of a series of metal chloride complexes of purines have been published [1]. The authors propose a scheme where the purine ligand exists as a N(7)–H tautomer, assigning an absorption band to the ν_{NH} vibrational mode of the imidazole part of the ring. Two structural models consistent with this assignment were proposed involving either a double bridged N(3), N(9) dimer or a N(3), N(9) bridged oligomer. Neither of these models are in accordance with the present structure. The replacement of chloride by sulphate is not expected to influence the choice of metal binding sites.

The IR spectra of this type of compounds are rather complicated and assignments may be ambiguous. It is also known that an IR spectrum of the dried, amorphous compound may have little relevance to the structure in the freshly prepared, hydrated compound [6].

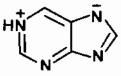
Neutral C(6)-substituted purines, *e.g.* adenine and hypoxanthine are found to form N(3), N(9) bridged tetramers [7, 8]. Thus far, this is the first metal complex of neutral purines which is found to involve N(7), N(9) bridging. However, one example of a N(7), N(9) bonded methylmercury complex of deprotonated adenine is known [9]. This type of bonding is fairly common in simple imidazole metal complexes.

The metal-binding properties of the coordination sites N(7) and N(9) are expected to be almost identical. However, the Cu–N(7) distance (1.903(16) Å) is found to be approximately 8σ shorter than the Cu–N(9) distance (2.036(16) Å). Since essentially the same results are obtained using three different data sets the difference is indeed significant. One way to explain the apparent inconsistency is to invoke some kind of disorder. Because of near axial symmetry of the purine ligand around the C(8)–H direction the positions of the N(7) and N(9) atoms may be interchanged. Disorder of this type with almost complete overlap of double positions is difficult to resolve by least-squares refinement. The presence of double positions will usually be reflected in the thermal parameters and in the residual difference map. In the present structure there are some anomalies in the thermal parameters, however the final difference map does not indicate disorder in the purine moiety. Furthermore, in the crystal packing arrangement the hydrogen bond between the ligand and the sulphate, N(1)–H···SO_4^{2-} = 2.77 Å, is only compatible with a single ligand position. A reorientation so as to interchange N(7) and N(9) will cause a rupture of this hydrogen bond with no suitable acceptor group in the new position.

Neutral imidazole and purine ligands form dative metal bonds to Cu^{2+} in the range 2.00–2.05 Å while the imidazolate ion forms covalent Cu–N bonds in the range 1.91–1.99 Å. In a $[Cu(Im^-)(Im)Cl]$ complex the neutral imidazole ligand is coordinated at Cu–N = 2.058(4) Å while the bridging imidazolate ion coordinates at 1.963(5) Å [10]. In $[Cu(Im)_4$-(Methoxyacetate)$_2]$ the imidazole ligands are two non-equivalent pairs [11]. One pair, Cu–N 1.913 Å, appears to be bonded to copper with the displacement of protons and the other pair, Cu–N 2.045 Å, without proton displacement. Apparently in the present structure, the imidazole part of purine at N(9) acts as a neutral ligand and at N(7) functions as a negatively charged ligand. The molecular dimensions of the purine ligand (Fig. 1) are shown to have rather high standard deviations preventing a detailed comparison with the uncomplexed molecule. However, the bond lengths in the imidazole part of the ligand are consistent with the idea of a 'negative' N(7) side and a 'neutral' N(9) side. In addition to the normal Kekule-type structure which can be written for the N(1)–H tautomer (I) one may also include a polarized form (II) to account for the observed dimensions:

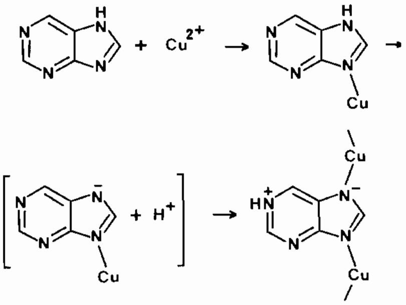


I



II

The following mechanism may be suggested for the reaction between copper and purine based on the result of the structure determination:



Assuming that the N(7)–H tautomer found in the solid state is predominant in solution, the first step involves the formation of a dative bond between copper and N(9). The metal bonding increases the acidity of the imidazole proton which is labilized leaving a partial negative charge on N(7). The proton is in a consecutive step attached to N(1) – the most basic nitrogen in the pyrimidine ring. Normally a tautomeric shift is followed by redistribution of charge. In the present case, the different bonding modes of copper seem to prevent an equalization of charge between N(7) and N(9). In solution one may envisage the following equilibrium:

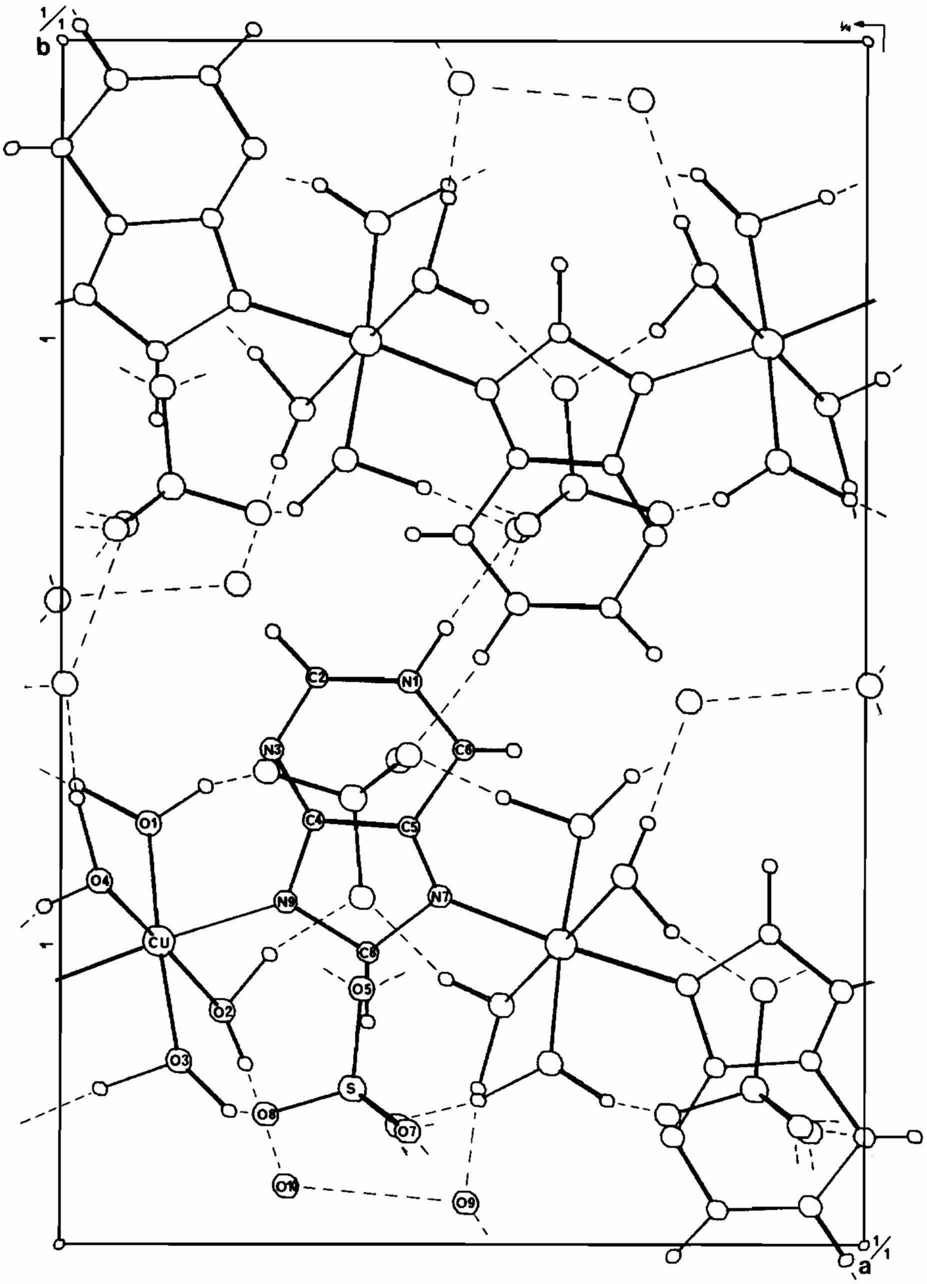


Fig. 2. The *c*-projection of the unit cell.

$N(7){-}Cu\cdots N(9) \rightleftharpoons N(7)\cdots Cu{-}N(9)$

One may obtain one of the species in crystalline form under certain experimental conditions, depending mainly on a favourable crystal packing arrangement.

In the coordination sphere the plane of the purine ligand is positioned so as to intersect the angle between the equatorial and the axial water ligand, the purine plane making a dihedral angle of 50° with the equatorial plane. Since there is no hydrogen bond between purine and the coordinating water molecules the ligands are arranged in such a way as to produce a minimum of steric interaction. A small but significant dissymmetry in the exocyclic coordination angles at N(7) is observed (∠Cu–N(7)–C(5) = 130.0° and ∠Cu–N(7)–C(8) = 126.6°) though far less pronounced than in complexes of C(6)-substituted purines where the average difference is about 15°.

The sulphate group is disordered and occupies two alternate positions. The S–O(5) bond is stationary an the disorder is produced by a 30–50° rotation about this bond. Refinement on partial occupancy

TABLE III. Hydrogen Bond Distances and Angles. σ(D•••A) = 0.03 A, σ(°) = 5°.

Bond	Position of acceptor atom			Distances (Å)		Angle (°)
				D•••A	H•••A	D–H•••A
O(1)–H(11)•••O(8)	x,	½ – y,	–½ + z	2.73	2.2	98
O(1)–H(11)•••O(81)	x,	½ – y,	–½ + z	2.76	1.9	119
O(1)–H(12)•••O(6)	–½ + x,	½ – y,	–z	2.59	2.5	112
O(2)–H(21)•••O(5)	x,	½ – y,	–½ + z	2.81	1.8	155
O(2)–H(22)•••O(10)	x,	½ – y,	–½ + z	2.82	1.9	167
O(3)–H(31)•••O(7)	–½ + x,	y,	½ – z	2.93	1.8	150
O(3)–H(31)•••O(71)	–½ + x,	y,	½ – z	2.56	1.8	116
O(3)–H(32)•••O(8)	x,	y,	z	2.75	2.0	114
O(3)–H(32)•••O(61)	x,	y,	z	2.93	1.9	128
O(4)–H(41)•••O(9)	–½ + x,	y,	½ – z	3.02	2.1	150
O(4)–H(42)•••O(5)	–½ + x,	y,	½ – z	2.73	1.8	158
O(9)–H••••••O(6)	1 – x,	½ + y,	½ – z	2.71		
O(10)–H••••••O(9)	x,	y,	z	2.61		
N(1)–H(1)••••O(7)	1 – x,	½ + y,	½ – z	2.77	1.9	151
N(1)–H(1)••••O(71)	1 – x,	½ + y,	½ – z	2.87	2.1	130

gave equal weight to both sites. In both positions the sulphate group serves as hydrogen bond acceptor (Table III). The sulphate group is situated on the top of the imidazole part of the purine ring thus effectively preventing any stacking interaction. The molecular packing is shown in Fig. 2. The polymeric copper–purine–copper chain runs along the *a*-axis. These chains are cross linked in the *b*-direction *via* hydrogen bonds involving the sulphate group.

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