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Intercalative Stacking Interactions and Interligand Hydrogen Bonding in Metal Purine Complexes. Crystal and Molecular Structure of (*N*-Salicylidene-*N*'-methylethylenediamine)(theophyllinato)copper(II) Monohydrate

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(*N*-Salicylidene-*N*'-methylethylenediamine)(theophyllinato)copper(II), Cu($O_3N_6C_{17}H_{20}$), crystallizes as the monohydrate in the orthorhombic system, space group $P2_12_12_1$, with a = 23.080 (16), b = 10.480 (6), c = 7.627 (1) Å; V = 1844.8 Å^3; Z = 4; d_{measd} = 1.56 (1), d_{calcd} = 1.58 g cm^{-3}. Intensities for 2694 independent reflections were collected by counter methods and used in the structural solution and refinement. The final R, weighted R and goodness-of-fit values are 0.038, 0.037, and 1.9, respectively. The primary coordination sphere about the copper is approximately square planar with the tridentate Schiff base ligand and N(7) of the theophylline monoanion occupying the four coordination positions. The complex exhibits an interligand hydrogen bond between the secondary amine terminus of the Schiff base chelate and the carbonyl group at C(6) of the theophylline moiety. The crystal structure also contains helical arrays of self-stacked complexes about the twofold screw axis in the c direction. The relationship between the stacking interactions and intercalation of metal-containing biological probes is discussed.

Introduction

The present understanding of interligand interactions (i.e., interactions between two or more ligands in the primary coordination sphere of a metal) is at best qualitative. It is often impossible to "factor out" the steric (nonbonding and bonding) and electronic contributions which affect the affinity of a series of ligands for a given metal center. The affinities of ligands with essentially constant steric requirements but varying electronic properties (e.g., 3- or 4-substituted pyridines) can be ascertained and made to vary smoothly in the expected direction.[1] Steric changes often lead to rather abrupt (discontinuous) changes in the affinity of ligands for a given metal.[2]

Interplay between steric and electronic contributions is known to be of importance in many biological systems. For example, the selectivity of enzymatic systems and the strong preference of a metal ion for one or, at most, a few sites on a protein may result from the existence of both electronically and sterically favored regions on the protein or enzyme. The preference for a particular substrate relies in a large measure on the steric properties at the active site.

Furthermore, it is now clear that the affinity of metal ions for the base binding sites in nucleic acids [primarily the nitrogen atoms on the constituent nucleoside (guanosine, adenosine, cytidine, or thymidine) residues] cannot solely be a function of the nucleophilicity of the coordination site.[3] The selectivity of metal-containing or metal-mediated systems for these bases must arise then from factors other than the electronic properties of the donor sites in these bases.

As part of a program designed to elucidate the nature of interligand interactions in general, but more specifically interactions which involve the nucleic acid purine or pyrimidine bases or their nucleosides, we have prepared several complexes containing the ligand theophylline, 1,3-dimethyl-2,6-dioxopurine, in a formally monoanionic form.[4,5] This substituted purine can be considered as a model for the nucleoside guanosine.[4,5] When a metal coordinates through N(7), the steric and hydrogen bonding potential near the metal-binding site of theophylline and guanosine are very similar.[4,5] Complexes of guanosine itself are difficult to isolate; this is in part due to the poor solubility of the nucleoside.

Previous detailed studies of complexes of the theophylline anion involved octahedral coordination.[4,5] We are interested in studying complexes of lower coordination number, in particular "square-planar" complexes of copper(II), for several reasons. These include (1) the apparent affinity of copper(II) for guanosine–cytidine-rich regions of nucleic acids,[3] (2) the possibility that an interaction could take place between the exocyclic oxygen at C(6) of the pyrimidine ring and the metal center (a subject of some controversy with both theoretical and experimental considerations suggesting that such a "chelate" type of interaction is implausible),[6] (3) the fact that copper(II) has been widely used to explore and has played an important role in determining the favored binding sites on the nucleic acid bases,[3] and (4) the possibility that interligand interactions might lead to a solution to the specific problem of the heavy-metal labeling of nucleic acids and might in general provide successful probes for nucleic acid structure.[5]

As part of this effort, we have synthesized several chelate complexes of copper(II) with the nucleic acid constituents. In this report, we describe the preparation and the crystal and molecular structure of a copper(II)–theophylline complex containing the tridentate Schiff base *N*-salicylidene-*N*'-methylethylenediamine.

Experimental Section

Preparation of (*N*-salicylidene-*N*'-methylethylenediamine)(theophyllinato)copper(II). The complex (chloro)(*N*-salicylidene-*N*'-methylethylenediamine)copper(II) was prepared by the method of Sacconi and Bertini.[7] A solution of the aquated cation was obtained by the addition of $AgNO_3$ (0.31 g, 2 mmol) to an aqueous solution (25 ml) of the chloro complex (0.5 g, 2 mmol). The solution was filtered to remove the precipitated AgCl, and diethylamine (0.2 ml, 2 mmol) and theophylline (0.33 g, 2 mmol) were added to the filtrate. The mixture was then heated for about $^1/_2$ hr on a steam bath in order to dissolve the theophylline completely. The microcrystalline product which formed upon cooling was collected and washed with ether (yield about 90%). The ir spectrum of this material contained bands attributable to theophylline, in particular 1690, 1265, and 1230 cm^{-1}.

Violet-red crystals of the theophylline complex were obtained by slow evaporation of an acetone solution. The magnetic moment in solution (CH_2Cl_2) was determined from the chemical shift difference between the methylene chloride signal in the sample tube and that in a concentric capillary by applying Evans' method.[8] The measured value of 1.8 BM is typical of tridentate Schiff base complexes of copper(II).[9]

Collection and Reduction of the X-Ray Intensity Data. The violet-red (*N*-salicylidene-*N*'-methylethylenediamine)(theophyllinato)copper(II) complex crystallizes as elongated orthorhombic prisms with [001] as the prism axis. Preliminary diffraction photographs showed the crystal system to be orthorhombic with systematic absences ($h00$, $h = 2n + 1$; $0k0$, $k = 2n + 1$; $00l$, $l = 2n + 1$) consistent with the space group $P2_12_12_1$. Unit cell dimensions and their associated standard deviations were derived on the basis of a least-squares fit to the 2θ, ω, and χ settings for 13 carefully centered reflections. The crystal density was measured by neutral buoyancy methods and indicated one formula unit plus one water molecule per asymmetric volume. Complete crystal data are given in Table I.

A total of 11,265 reflection (the $+h$ hemisphere to 2θ = 57°) were measured on a Syntex $P\bar{1}$ computer-controlled diffractometer; molybdenum graphite-monochromatized radiation was employed. The

Table I. Crystal Data for (*N*-Salicylidene-*N*′-methylethylenediamine)(theophyllinato)copper(II) Monohydrate

$a = 23.080\ (16)$ Å
$b = 10.480\ (6)$ Å
$c = 7.627\ (1)$ Å
$V = 1844.8$ Å^3
Space group $P2_12_12_1$
$Z = 4$
$Cu(O_3N_6C_{17}H_{20})\cdot H_2O$
Mol wt 437.9
$d_{\text{measd}} = 1.56\ (1)$ g cm^{-3}
$d_{\text{calcd}} = 1.58$ g cm^{-3}
$\mu = 12.6$ cm^{-1}

crystal used in data collection was an orthorhombic prism with dimensions 0.30 × 0.16 × 0.15 mm^3 (the long axis aligned approximately along ϕ). Intensity data were collected by the θ–2θ scan technique; individual scan speeds were determined by a rapid scan at the calculated Bragg peak, and the rate of scanning varied from 2.0 to 24.0° min^{-1}. Three standards were monitored after every 100 reflections, and their intensities showed no unusual variation over the course of the experiment. The 11,265 measured intensities, which included standards and systematic absences, were then combined to yield a set of 2694 independent values. All reflections were assigned observational variances based on the equation $\sigma^2(I) = S + (B_1 + B_2)(T_S/2T_B)^2 + (pI)^2$, where S, B_1, and B_2 are the scan and background extremum counts, T_S and T_B are the scan and individual background counting times ($T_B = 1/4T_S$ for all reflections), and $p = 0.04$ and represents the expected error proportional to the diffracted intensity.[10] Intensities and their standard deviations were corrected for Lorentz and polarization effects; the amplitudes of reflections with negative intensities were set equal to zero. No correction for absorption was deemed necessary ($\mu = 12.6$ cm^{-1}); the maximum error introduced by the neglect of absorption effects was estimated to be about 3% in I. The squared structure factors were placed on an approximate absolute scale by the method of Wilson.[11]

Solution and Refinement of the Structure. The position of the copper atom was determined from an unsharpened, three-dimensional Patterson map. Two cycles of structure factor–Fourier calculations led to the positioning of the 27 other heavy atoms in the asymmetric unit (including all the heavy atoms, $R = \sum||F_o| - |F_c||/\sum|F_o| = 0.26$). Six cycles of isotropic least-squares refinement, minimizing $\sum w(|F_o| - |F_c|)^2$ where $w = 4F_o^2/\sigma^2(F_o^2)$, reduced the R value to 0.118. A difference Fourier map was computed, and the 22 independent hydrogen atoms were located. Four further cycles of refinement, including in the list of variables anisotropic thermal parameters for all the heavy atoms, led to a final R value of 0.038. The final weighted R value $[R_w = (\sum w(F_o - F_c)^2/\sum wF_o^2)^{1/2}]$ and goodness of fit $[(\sum w(F_o - F_c)^2/(NO - NV))^{1/2}]$, where NO = 2694 observations and NV = 253 parameters, were 0.037 and 1.9, respectively. Neutral scattering factor curves for all nonhydrogen atoms were taken from the compilation of Hanson, Herman, Lea, and Skillman;[12] the scattering curve for H was that of Stewart, Davidson, and Simpson.[13] The real part of the scattering curve for Cu was corrected for anomalous dispersion effects.[14] Final heavy-atom parameters are collected in Table II; hydrogen atom parameters are given in Table III. A complete list of calculated and observed structure factor amplitudes is available.[15]

The structure factor and Fourier calculations were done using the X-Ray 67 series of programs;[16] the least-squares refinements were performed with an extensively modified version of ORFLS;[17] best planes were computed with the program of Pippy and Ahmed;[18] the illustrations were prepared with the aid of the computer program ORTEP.[19] All other calculations were performed with locally written programs.

Discussion

A perspective view of the (*N*-salicylidene-*N*′-methylethylenediamine)(theophyllinato)copper(II) complex is shown in Figure 1. The copper is approximately square planar with the tridentate Schiff base ligand and N(7) of the theophylline moiety occupying the four coordination sites. The N(7) position of purines is accessible for coordination in nucleosides and nucleotides;[3] we therefore expect that the mode of binding shown in Figure 1 is possible in such systems. Furthermore, since theophylline has a carbonyl group at C(6), as does guanosine, we anticipate that interactions involving this exocyclic function may be extrapolated to N(7)-bonded guanosine systems.

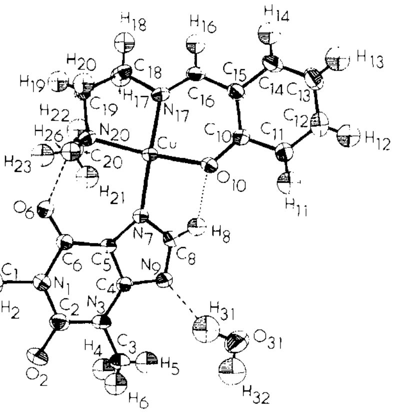

Figure 1. A perspective view of the (*N*-salicylidene-*N*′-methylethylenediamine)(theophyllinato)copper(II) complex. The water of crystallization is also shown. Hydrogen bonds are indicated by dashed lines, and the C–H· · ·O interaction is shown by the dotted line (see text). The thermal ellipsoids are drawn at the 50% probability level.

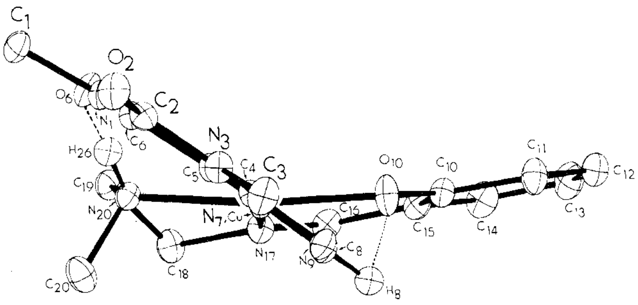

Figure 2. A view of the complex down the N(7)–Cu bond. Note in particular the disposition of the theophylline plane relative to the tridentate Schiff base and the interligand interactions.

We have noted elsewhere[4,5] that the carbonyl group at C(6) in theophylline has a distinct tendency to form interligand hydrogen bonds with chelate ligands containing hydrogen-bond donor groups. Such an interligand hydrogen bond also exists in this Schiff base complex and is indicated by the dashed line in Figure 1. Figure 2 is an illustration of the molecular conformation of the complex as viewed down the N(7)–Cu bond. As can be readily seen, the plane of the theophylline ligand is oriented such that the carbonyl oxygen O(6) comes into a hydrogen-bond contact with the secondary amine hydrogen atom H(26) at the *N*-methylethylenediamine terminus of the tridentate Schiff base ligand. The specifics of this interligand hydrogen bond are as follows: N(20)···O(6), 2.839(4) Å; H(26)···O(6), 2.05 Å; N(20)–H(26)···O(6) angle, 150°. These values are typical of those we have found in other interligand hydrogen-bond systems involving coordinated theophylline and polyamine ligands,[4,5] and the H···O distance is indicative of a relatively strong hydrogen bond (<2.2 Å).[20] It should also be noted that in the observed orientation of the theophylline ligand there is a short contact (Figure 2) between the hydrogen atom off C(8) of the imidazole ring of theophylline and O(10), the exocyclic oxygen atom of the salicylidene portion of the tridentate Schiff base (H(8)···O(10) = 2.50 Å, C(8)–H(8)···O(10) = 103°). We have observed similar interactions involving C(8)–H(8) in several purine complexes.[5,21,22]

A point of some interest in this complex is the possible involvement of the pyrimidine exocyclic oxygen O(6) in a five-membered chelate structure when a metal atom is coordinated at N(7) of the imidazole ring. The absence of chelate formation in a copper complex of 9-methylhypoxanthine led Sletten[6] originally to propose that such chelation was implausible based on geometric considerations (in essence, it was

Table II. Final Heavy-Atom Parameters ($\times 10^4$)[a]

Atom	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
Cu	1866 (0.1)	74 (0.3)	1043 (0.5)	7 (0.05)	48 (0.3)	151 (0.6)	0 (0.1)	−4 (0.2)	−6 (0.5)
O(2)	4585 (1)	−3152 (2)	2128 (4)	11 (0.4)	83 (2)	225 (6)	10 (0.7)	−7 (1)	−1 (3)
O(6)	2603 (1)	−2922 (2)	2454 (3)	11 (0.4)	62 (2)	202 (5)	−1 (0.7)	2 (1)	27 (3)
O(10)	2005 (1)	1811 (2)	1629 (4)	9 (0.4)	52 (2)	276 (6)	3 (0.7)	−10 (1)	−28 (3)
O(31)	4445 (1)	2663 (3)	649 (4)	20 (0.5)	104 (3)	337 (8)	−9 (1)	−15 (2)	52 (5)
N(1)	3593 (1)	−3022 (2)	2212 (4)	11 (0.5)	49 (2)	149 (5)	3 (0.8)	−5 (1)	3 (3)
N(3)	4164 (1)	−1333 (2)	1125 (4)	8 (0.4)	65 (2)	162 (5)	1 (0.7)	5 (1)	−3 (4)
N(7)	2716 (1)	−191 (2)	873 (3)	9 (0.4)	46 (2)	159 (5)	0 (0.7)	−6 (1)	−4 (3)
N(9)	3619 (1)	521 (2)	125 (4)	9 (0.4)	58 (2)	156 (6)	−2 (0.8)	2 (1)	16 (3)
N(17)	1042 (1)	387 (2)	710 (4)	8 (0.4)	67 (2)	140 (5)	−3 (0.8)	−5 (1)	−1 (3)
N(20)	1646 (1)	−1777 (2)	725 (3)	10 (0.4)	54 (2)	136 (5)	−3 (0.8)	−4 (1)	2 (3)
C(1)	3573 (2)	−4352 (3)	2841 (5)	21 (0.8)	52 (3)	180 (8)	5 (1)	−5 (2)	16 (4)
C(2)	4141 (1)	−2532 (3)	1836 (4)	11 (0.5)	67 (3)	136 (6)	3 (1)	−5 (2)	−13 (4)
C(3)	4723 (1)	−799 (3)	617 (5)	9 (0.5)	83 (3)	244 (9)	3 (1)	9 (2)	2 (5)
C(4)	3659 (1)	−655 (3)	836 (4)	9 (0.5)	53 (2)	115 (6)	1 (1)	−2 (1)	−12 (3)
C(5)	3121 (1)	−1133 (2)	1305 (4)	8 (0.4)	49 (2)	125 (6)	0 (1)	1 (2)	−7 (3)
C(6)	3058 (1)	−2377 (3)	2019 (4)	10 (0.5)	51 (2)	118 (5)	2 (1)	−3 (1)	−6 (3)
C(8)	3045 (1)	734 (3)	168 (4)	11 (0.6)	51 (2)	148 (6)	1 (1)	−1 (2)	8 (3)
C(10)	1628 (1)	2709 (3)	1958 (4)	11 (0.5)	55 (3)	142 (6)	1 (1)	−5 (2)	4 (4)
C(11)	1828 (1)	3917 (3)	2570 (5)	14 (0.6)	59 (3)	221 (8)	0 (1)	−14 (2)	−8 (4)
C(12)	1456 (2)	4877 (3)	3000 (5)	23 (0.8)	54 (3)	182 (7)	2 (1)	−1 (2)	−1 (5)
C(13)	860 (2)	4721 (3)	2803 (6)	18 (0.7)	64 (3)	227 (8)	11 (1)	16 (2)	−1 (4)
C(14)	650 (1)	3600 (3)	2166 (5)	12 (0.6)	78 (3)	212 (8)	10 (1)	10 (2)	5 (5)
C(15)	1021 (1)	2570 (3)	1738 (4)	11 (0.5)	58 (3)	134 (6)	6 (1)	2 (2)	11 (4)
C(16)	769 (1)	1412 (3)	1086 (5)	8 (0.5)	69 (3)	154 (6)	2 (1)	2 (2)	16 (4)
C(18)	735 (1)	−755 (3)	103 (5)	9 (0.5)	74 (3)	173 (7)	−5 (1)	−3 (2)	−14 (4)
C(19)	1012 (1)	−1882 (3)	1005 (5)	11 (0.5)	68 (3)	143 (6)	−6 (1)	3 (2)	−5 (4)
C(20)	1819 (1)	−2297 (3)	−990 (5)	16 (0.6)	95 (3)	189 (7)	−5 (1)	10 (2)	−44 (5)

[a] Estimated standard deviations are enclosed in parentheses. The form of the anisotropic ellipsoid is $\exp[-(B_{11}h^2 + B_{22}k^2 + B_{33}l^2 + 2B_{12}hk + 2B_{13}hl + B_{23}kl)]$.

Table III. Hydrogen Atom Positional ($\times 10^3$) and Isotropic Thermal Parameters

Atom	x	y	z	B,[a] Å^2
H(1)	385	−500	207	4.0
H(2)	362	−450	403	4.0
H(3)	319	−480	233	4.0
H(4)	488	−131	−31	4.0
H(5)	475	0	30	4.0
H(6)	498	−90	162	4.0
H(8)	288	150	−27	3.0
H(11)	223	405	268	4.0
H(12)	160	566	343	4.0
H(13)	60	538	314	4.5
H(14)	24	350	199	4.0
H(16)	36	141	91	3.0
H(17)	77	−83	−113	3.5
H(18)	34	−70	40	3.5
H(19)	87	−265	53	3.5
H(20)	93	−185	223	3.5
H(21)	219	−185	−143	4.5
H(22)	152	−215	−184	4.5
H(23)	189	−320	−95	4.5
H(26)	184	−224	149	3.0
H(31)	427	175	80	6.0
H(32)	481	250	150	6.0

[a] The hydrogen atom isotropic temperature parameters were set about equal to those of the atoms to which they are attached; see Figure 1.

argued that the necessary distortions in the M–N(7)–C(5,8) angles in order to accomplish chelation would result in a large decrease in the overlap of the metal and N(7) orbitals). However, the recent structure of bis(6-mercapto-9-benzylpurine)palladium(II) has revealed a five-membered chelate involving N(7) and S(6).[23] This result may be a consequence of the greater versatility of sulfur in comparison to oxygen in forming bonds to metals. Such versatility would allow a strong metal–sulfur bond and a favorable metal–nitrogen(7) bond.

Our observation that the exocyclic oxygen at C(6) forms the interligand hydrogen bond in preference to any chelate formation may then be related to the following considerations. (1) In the tridentate Schiff base complex of copper(II) only one site for complexation is available in the primary coordination sphere; therefore, chelation by the theophylline moiety would necessitate displacement of either the secondary amine nitrogen N(20) or the salicylidene oxygen O(10). Neither of these possibilities seems likely. (2) A second possibility, however, exists: that of a secondary interaction between the exocyclic oxygen O(6) and the copper via the open axial positions of the square-planar system. We and others have observed such interactions in square-planar copper(II) complexes of cytosine and cytidine.[24-26] The absence of such an interaction in the present complex suggests that the interligand hydrogen bond is formed in preference to the axial interaction. It is interesting that a very similar situation exists in the 9-methylhypoxanthine complex of Sletten[6] where the pyrimidine oxygen O(6) forms an interligand hydrogen bond with a coordinated water molecule.

We believe, then, that in 6-oxopurines interligand hydrogen bonding will play a significant role in the molecular conformation of their transition metal complexes when hydrogen-bond donor groups are available on chelated or unidentate ligands. It is further anticipated that such interligand interactions may ultimately provide a means of selectively causing metal complexes to react with one of the four common nucleosides.[5]

As we have noted above, copper(II) has a known preference for the extension of its coordination sphere from simple square planar to penta- or hexacoordination (the so-called (4 + 1) and (4 + 2) coordination geometries).[27] Furthermore, we noted that this extension of the primary coordination sphere about the metal center does not involve the 6-oxo group on the theophylline. The Schiff base complex does, however, qualitatively extend its coordination sphere and in a rather unusual way. Helical arrays of complexes about the twofold screw axes parallel to c are formed in the crystal. Two features of these stacks are of particular interest. (1) As can be seen in Figure 3, the imidazole rings of two symmetry-related complexes occupy approximate axial positions of the square-planar copper(II) system. Consideration of the distances from the copper to the atoms of the imidazole ring (see

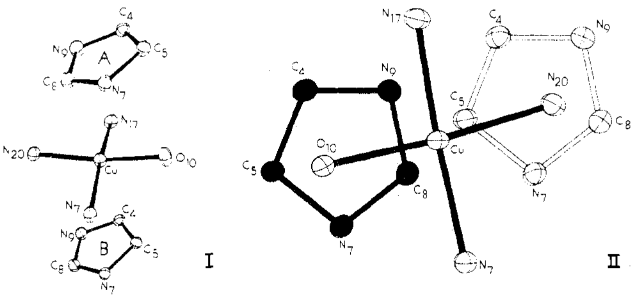

Figure 3. Two views of the primary and secondary coordination sphere about the Cu atom: I, a perspective view; II, a projection normal to the plane of the imidazole rings. The copper to imidazole ring atom distances (Å) are as follows: for ring A, N(7), 3.810; N(9), 3.367; C(4), 3.899; C(5), 4.164; C(8), 3.265; for ring B, N(7), 4.061; N(9), 4.692; C(4), 4.197; C(5), 3.780; C(8), 4.565.

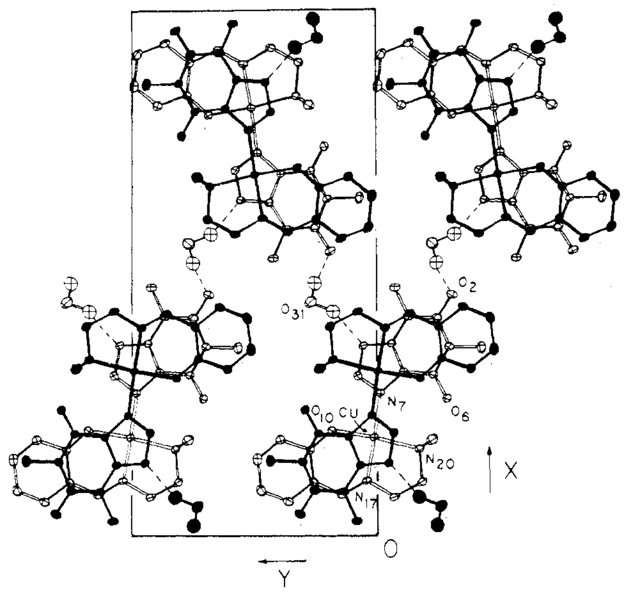

Figure 4. A view down the *c* axis of the crystal packing. Hydrogen bonds are indicated by dashed lines. The shaded molecules lie above the unshaded molecules.

Figure 3) suggests very weak bonding (a recent structure[28] with an equatorial Cu–C bond, 1.995 (4) Å, would seem to indicate that an upper limit for a meaningful[27] axial Cu–C bond would be on the order of 2.9 Å; the shortest Cu–C-(imidazole) distance exceeds this value by some 0.4 Å). There may, however, be some further contribution to the strength of the axial interactions owing to the overlap of the Cu–N(20) and Cu–O(10) heterobonds with the imidazole rings. (2) As shown in Figure 4, there is yet another type of interaction found in these stacks of complexes; namely, the significant overlap of the salicylidene rings with the pyrimidine portion of the theophylline moiety. The mean separation between two theophylline planes is 6.92 Å with the asymmetrically intercalated salicylidene rings having mean distances of 3.29 and 3.62 Å to the facially stacked theophylline moieties (Figure 4). These parameters are in accord with expectations based on other crystallographic data.[29]

Such stacking interactions are known to play a significant role in the crystal and solution chemistry of purines, pyrimidines, nucleosides, nucleotides, and nucleic acids.[29,30] Furthermore, it has been shown that many drug–nucleic acid interactions involve intercalative binding (e.g., drugs with extensive π systems such as the aminoacridenes,[31] actinomycin,[32] daunomycin,[33] chloroquine,[34] and ethidium bromide[35]). The presence of the intercalative interactions in the present structure is of significant importance in this respect.

Table IV. Heavy-Atom Interatomic Distances (Å) and Angles (deg)[a]

(a) Primary Coordination Sphere about the Copper Atom

Bond Lengths

Cu–N(7)	1.986	Cu–N(20)	2.020
Cu–N(17)	1.947	Cu–O(10)	1.902

Bond Angles

N(7)–Cu–N(17)	168.6	N(17)–Cu–N(20)	84.3
N(7)–Cu–N(20)	96.1	N(17)–Cu–O(10)	92.0
N(7)–Cu–O(10)	89.0	N(20)–Cu–O(10)	171.9

(b) *N*-Salicylidene-*N*′-methylethylenediamine Chelate

Bond Lengths

O(10)–C(10)	1.306	C(15)–C(10)	1.418
C(10)–C(11)	1.426	C(15)–C(16)	1.435
C(11)–C(12)	1.363	C(16)–N(17)	1.278
C(12)–C(13)	1.393	N(17)–C(18)	1.466
C(13)–C(14)	1.361	C(18)–C(19)	1.509
C(14)–C(15)	1.416	C(19)–N(20)	1.483
		N(20)–C(20)	1.472

Bond Angles

Cu–O(10)–C(10)	128.5	C(14)–C(15)–C(16)	118.7
O(10)–C(10)–C(11)	119.1	C(15)–C(16)–N(17)	126.1
O(10)–C(10)–C(15)	124.1	C(16)–N(17)–C(18)	121.2
C(11)–C(10)–C(15)	116.7	Cu–N(17)–C(16)	126.4
C(10)–C(11)–C(12)	122.0	Cu–N(17)–C(18)	112.1
C(11)–C(12)–C(13)	120.6	N(17)–C(18)–C(19)	106.9
C(12)–C(13)–C(14)	119.4	C(18)–C(19)–N(20)	107.1
C(13)–C(14)–C(15)	121.7	Cu–N(20)–C(19)	107.6
C(10)–C(15)–C(14)	119.4	Cu–N(20)–C(20)	113.2
C(10)–C(15)–C(16)	121.9	C(19)–N(20)–C(20)	111.6

(c) Theophylline Anion

Bond Lengths

N(1)–C(1)	1.475	N(7)–C(5)	1.399
N(1)–C(2)	1.395	N(7)–C(8)	1.344
N(1)–C(6)	1.415	N(9)–C(4)	1.350
N(3)–C(2)	1.370	N(9)–C(8)	1.344
N(3)–C(3)	1.459	C(2)–O(2)	1.234
N(3)–C(4)	1.383	C(4)–C(5)	1.386
C(5)–C(6)	1.420	C(6)–O(6)	1.241

Bond Angles

C(1)–N(1)–C(2)	116.3	N(3)–C(2)–O(2)	121.5
C(1)–N(1)–C(6)	117.2	N(1)–C(2)–N(3)	117.0
C(2)–N(1)–C(6)	126.4	N(3)–C(4)–N(9)	126.2
C(2)–N(3)–C(3)	119.4	N(3)–C(4)–C(5)	121.9
C(2)–N(3)–C(4)	120.1	N(9)–C(4)–C(5)	111.9
C(3)–N(3)–C(4)	120.4	N(7)–C(5)–C(4)	106.4
Cu–N(7)–C(5)	138.0	N(7)–C(5)–C(6)	132.0
Cu–N(7)–C(8)	118.9	C(4)–C(5)–C(6)	121.5
C(5)–N(7)–C(8)	103.0	N(1)–C(6)–O(6)	119.4
C(4)–N(9)–C(8)	102.1	N(1)–C(6)–C(5)	112.9
N(1)–C(2)–O(2)	121.4	C(5)–C(6)–O(6)	127.7
		N(7)–C(8)–N(9)	116.6

[a] Bond length esd's: Cu–N(O), 0.001 Å; C–C, 0.004 Å; C–N, 0.004 Å; C–O, 0.004 Å. Bond angle esd's: N–Cu–N(O), 0.06°; C–C–N(O), 0.3°; N–C–N, 0.3°.

Our results qualitatively suggest that the intercalative interactions involving metal complexes with extensive π systems may exist in a substantially similar manner. Furthermore, it has recently been shown that metal-containing biological probes such as β-hydroxyethanethiolo(2,2′,2″-terpyridine)platinum(II)[36] may be involved in intercalative interactions with sites on calf thymus DNA by competitive inhibition of the binding of ethidium bromide.

Bond Distances and Angles. The bond lengths and angles in the primary coordination sphere about the copper atom are collected in Table IV. The Cu–N(7) bond length, 1.986 (1) Å, is shorter than in the closely related complex (dichloro)-bis(9-methyl-6-oxopurine)(diaquo)copper(II) (2.055 (1) Å)[6] but very similar to the observed value of 1.995 (2) Å in (tetraaquo)(9-methyladenine)copper(II) sulfate.[37]

The Cu–N(17) (1.947 (1) Å) and Cu–O(10) (1.902 (1) Å)

Table V. Least-Squares Planes and the Deviations (Å) of Individual Atoms from These Planes[a]

(a) Primary Coordination Plane Including Copper Atom
$(0.0539X + 0.1667Y - 0.9845Z = -0.5064\ \text{Å})$

Cu	−0.032	N(7)	0.156
O(10)	−0.151	N(17)	0.170
		N(20)	−0.144

(b) Salicylidene Ring
$(0.0746X + 0.3409Y - 0.9371Z = -0.1505\ \text{Å})$

C(10)	−0.001	C(14)	0.001
C(11)	0.028	C(15)	0.002
C(12)	−0.001	C(16)	−0.011
C(13)	−0.018	O(10)	−0.022
N(17)	−0.039*	C(18)	−0.066*

(c) Nine-Atom Framework of Coordinated Theophylline Anion
$(-0.0863X - 0.3940Y - 0.9150Z = -1.0445\ \text{Å})$

N(1)	0.033	C(5)	−0.020
C(2)	−0.016	C(6)	0.008
N(3)	−0.020	N(7)	−0.027
C(4)	0.003	C(8)	0.018
O(2)	−0.052*	N(9)	0.021
O(6)	0.020*	C(1)	0.147*
		C(3)	0.003*

(d) Imidazole Ring of Coordinated Theophylline Anion
$(-0.1002X - 0.4094Y - 0.9068Z = -1.1425\ \text{Å})$

N(7)	−0.007	C(4)	−0.001
N(9)	−0.004	C(5)	0.004
		C(8)	0.007

(e) Pyrimidine Ring of Coordinated Theophylline Anion
$(-0.0810X - 0.3842Y - 0.9197Z = -1.0268\ \text{Å})$

N(1)	0.020	C(4)	0.020
N(3)	−0.004	C(5)	−0.016
C(2)	−0.016	C(6)	−0.004

[a] In each of the equations of the planes, X, Y, and Z are coordinates (Å) referred to the orthogonal axes a, b, and c. Atoms designated by an asterisk were given zero weight in calculating the planes; other atoms were weighted equally.

bond lengths are consistent with those reported for other tridentate Schiff base–copper(II) complexes,[38] but high standard deviations for the latter complexes preclude any systematic comparison. The Cu–N(17) and Cu–O(10) distances can, however, be compared to those found in bidentate Schiff base complexes of Cu(II) (Lingafelter and Braun:[39] Cu–N = 1.970 Å, Cu–O = 1.902 Å) and tetradentate copper(II) Schiff base complexes (Calligaris, Nardin, and Randaccio:[40] Cu–N = 1.928 Å, Cu–O = 1.903 Å). This comparison reveals that the Cu–O(10) distance is relatively constant in going from bidentate to tetradentate chelation, while the Cu–N(17) bond length systematically contracts by about 0.02 Å for each increase in ligating position.

While the copper atom is essentially in the "plane" of its four ligated atoms (Table V(a)), the best-plane calculation indicates that there is a substantial tetrahedral component to the basic square-planar geometry (coordinated atom deviations of about ±0.15 Å). The tetrahedral distortion of the coordination sphere about the copper may result from the difference in the sizes of the chelate rings—a six-membered ring from the salicylidene portion and a five-membered chelate from the *N*-methylethylenediamine portion—and the concurrent steric requirements of each.

While there have been extensive studies on the structural parameters in bidentate[39] and tetradentate[40] Schiff base complexes, we know of only a few structural reports on other tridentate complexes[38] (there has, however, been somewhat more work done on the synthesis and solution properties of tridentate Schiff base complexes).[9] Our parameters, Table IV, are in quite good agreement with the average values found in the bidentate complexes[39] (maximum difference 0.025 Å, average difference 0.010 Å) and the tetradentate complexes[40] (maximum difference 0.032 Å and average difference 0.011 Å). Some of these deviations may be related to the differences in the number of coordination sites in the Schiff base ligand as noted above. As expected, the salicylidene ring is reasonably planar (Table V(b)).

The parameters in the *N*-methylethylenediamine portion of the tridentate ligand are in good agreement with other structure determinations.[4,5,43]

The bond lengths and angles in the coordinated theophylline anion (Table IV) are in excellent agreement with those in the well-determined structure of *trans*-(theophyllinato)(chloro)bis(ethylenediamine)cobalt(III) chloride.[4] The only significantly different bond length is one of the exocyclic bonds, N(1)–C(1): 1.475 (4) Å in this study and 1.455 (4) Å in the trans theophylline complex (the average bond length difference is 0.007 Å and well within our expectations based on the estimated standard deviations in each structure). The bond angles are also in excellent agreement: maximum difference 1.0° (N(3)–C(2)–O(2)), with an average difference of 0.4°.

As we have noted previously and above,[4,5] there is considerable variability in the exocyclic bond angles at N(7) in response to interligand hydrogen bonding or chelation. This structure again shows this feature (Cu–N(7)–C(5) = 138.0 (4)° and Cu–N(7)–C(8) = 118.9 (4)°) as one might expect from the presence of the interligand hydrogen bond.

The nine-atom framework of the theophylline moiety is significantly nonplanar (Table V); the imidazole ring is, however, quite planar, while the pyrimidine ring retains a significant degree of nonplanarity owing to the presence of the exocyclic methyl and oxo groups. As is typical of purines,[41,42] both coordinated and uncoordinated, there is a significant fold about the C(4)–C(5) bond—dihedral angle of 2.0 (3)°. The degree of folding is similar to that observed in the *cis*-[5] and *trans*-bis(ethylenediamine)cobalt(III)[4] complexes of theophylline, 2.4 (6) and 2.3 (3)°, respectively, and in other systems.[41,42]

Crystal Packing. The crystal packing as viewed down the short c axis is illustrated in Figure 4. The packing is dominated by two principal features. (1) The layering of the complexes is approximately parallel to (001). These intrasheet complexes are linked together via hydrogen bonds involving the water of crystallization: O(31)–H(31)···N(9) [x, y, z] and O(31)–H(32)···O(2) [$2_1(b)$, $1 - x$, $1/2 + y$, $1/2 - z$] (Figure 4, Table VI). Including the interligand hydrogen bond and the C–H···O interaction described above, all potential hydrogen bond donors

Table VI. Distances and Angles in the Interactions of the Type D–H···A

D	H	A	D–H, Å	D···A, Å	H···A, Å	D–H···A, deg
			Hydrogen Bonds			
N(20)	H(26)	O(6)[a]	0.87	2.839	2.05	150[d]
O(31)	H(31)	N(9)[a]	1.05	2.972	2.04	147
O(31)	H(32)	O(2)[b]	1.07	2.936	1.88	168
			Others			
C(8)	H(8)	O(10)[a]	0.95	2.877	2.50	103
C(8)	H(8)	O(6)[c]	0.95	3.432	2.54	155
C(20)	H(21)	O(10)[c]	1.04	3.305	2.37	149

[a] x, y, z. [b] $1 - x, {}^1/_2 + y, {}^1/_2 - z$. [c] ${}^1/_2 - x, -y, -{}^1/_2 + z$. [d] The interligand hydrogen bond.

and acceptors are utilized in the structure. (2) The columnar stacking of twofold screw-related complexes is along the *c* axis. The stacking in these columns has been discussed in detail above.

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Supplementary Material Available. A listing of structure factor amplitudes will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for $4.50 for photocopy or $2.50 for microfiche, referring to code number AIC408446.

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Structural Studies of the Intercalation Complexes $TiS_2 \cdot NH_3$ and $TaS_2 \cdot NH_3$

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Crystal structures of the intercalation complexes $TiS_2 \cdot NH_3$ and $TaS_2 \cdot NH_3$ from X-ray powder intensity data are reported. In $TiS_2 \cdot NH_3$, nitrogen is on the midplane between layers in a trigonal-prismatic sulfur environment. The nitrogen cannot be located in $TaS_2 \cdot NH_3$. $TiS_2 \cdot NH_3$ is rhombohedral with three layers per (hexagonal) unit cell; $TaS_2 \cdot NH_3$ is hexagonal with two layers per unit cell. The respective lattice constants are $a = 3.427$ (2) and $c = 26.55$ (2) Å and $a = 3.320$ (5) and $c = 18.16$ (2) Å. Twinning or stacking faults were found to be important.

Introduction

In 1969 Ruthardt and Weiss[1] reported intercalation complexes between TiS_2 and both aliphatic amides and aqueous hydrazine. Gamble and coworkers[2] subsequently showed that the intercalation reaction is quite general. A large class of these compounds is formed between layered disulfides and diselenides of 4B and 5B transition metal and molecular Lewis bases, both organic and inorganic. These new complexes are interesting because of their remarkably anisotropic electron-transport properties[3] and the unusual superconducting properties of the niobium and tantalum dichalcogenide compounds.[4] These electronic properties can be changed systematically by modifying of the electronic and geometrical characteristics of the molecular intercalate. Therefore, the nature of the interaction or chemical bond between intercalate and chalcogenide layer is important. Progress has been