We rationalize these observations in the following way: The rate of thioether inversion will be enhanced by stabilization of the intermediate, and this will be favored by a greater charge density on the metal atom to which the thioether is coordinated. In early discussion of this problem, Haake and Turley[51] had proposed a lone pair displacement mechanism for inversion at platinum in a square-planar complex. More recently, Abel and co-workers[52] have provided a more satisfactory approach in which they apply classical treatments of pyramidal inversion[53,54] to inversion at sulfur. The inversion process is assumed to proceed through an intermediate involving a planar, three-coordinate sulfur atom with sp^2 hybridization and a lone pair of electrons accommodated in a p orbital perpendicular to the bonding plane. This model leads to the conclusion that the barrier to inversion should be *raised* by the presence of more electronegative substituents X in $X\text{-}SR_2$ but *lowered* by an increased degree of π overlap between X and S in the transition state. Thus, in both ways the more strongly electron-withdrawing groups trans to coordinated sulfur would be expected to raise the barrier to inversion. (Variations between ligands are, however, still small in comparison with the large reduction in $\Delta G^{\ddagger}$ occurring when a sulfur-containing ligand is coordinated to a metal atom.) Our results therefore suggest that the fluorinated alkoxy group is *more strongly electron withdrawing* than Cl^-.

The concept of a more strongly electron-withdrawing group implies a higher degree of *ionic* character to the bond, which seems at first sight to be incompatible with an observation of greater trans influence. However, we suggest that it would be an oversimplification to infer from the higher trans-influence of alkoxide over chloride a greater degree of covalency in the Pt–O over the Pt–Cl bond. Rather, it is due to an inductive electron-withdrawing effect by the ligand, which robs the trans ligand of electron density from its σ orbital and thus leads to smaller values of the coupling constants. Concentration on the covalent interactions of ligands in discussions of the trans influence has perhaps been overemphasized, and we would suggest that other factors are involved. This is particularly the case when the ligands in question bond to the metal through atoms of significantly different character. First-row donors, such as oxygen and nitrogen, are hard to compare with second-row and later elements (P, S, Cl^-, Br^-, I^-) that possess π-acceptor character.

In virtually all bonding situations, bond effects are dependent on both the electronegativities of the linked atoms ("ionic character") and effective orbital overlap between them ("covalent character"). Within the series of ligands bonding through oxygen, the increasing trans influence parallels the increasing basicity of the ligand and the associated increase in the covalent character of the metal–ligand bond. Overlap is more significant than electronegativity change in this group. Similarly, within the halide series, the order of increasing trans influence runs $Cl^- < Br^- < I^-$; this is the converse of the increase in electronegativity but corresponds to the increase in the covalent character of the metal–halide bond. In contrast, the greater trans influence of $-C(CF_3)_2O^-$, OH^-, and N_3^- relative to Cl^- may then be attributed to their greater electronegativity, leading to the withdrawal of electron density from the metal σ orbitals.

The generalized order of trans influence usually presented[28] is therefore a composite of these two effects, and hence it is not surprising that many small inversions of the sequence are observed when different metal complexes are used to establish a comparative trans influence.

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X-ray Structure of a Ternary Metal Complex: Copper(II)–Inosine 5′-Monophosphate–Imidazole. Metal Binding to the N(7) Atom of the Nucleotide in a Mixed-Ligand System Containing an Aromatic Amine

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A ternary metal–nucleotide complex, $Na_2[Cu(5'\text{-}IMP)_2(im)_{0.8}(H_2O)_{1.2}(H_2O)_2]\cdot 12.4H_2O$, has been prepared and its structure analyzed by X-ray diffraction (5′-IMP = inosine 5′-monophosphate; im = imidazole). The complex crystallizes in space group $C222_1$ with $a = 8.733$ (4) Å, $b = 23.213$ (5) Å, $c = 21.489$ (6) Å, and $Z = 4$. The structure was solved by the heavy-atom method and refined by full-matrix least-squares technique on the basis of 2008 observed reflections to a final R value of 0.087. Symmetry-related 5′-IMP anions coordinate in cis geometry through the N(7) atoms of the bases. The other cis positions of the coordination plane are statistically occupied by nitrogen atoms of disordered im groups and water oxygens with occupancies 0.4 and 0.6, respectively. Water oxygens in axial positions complete the octahedral coordination of Cu(II). The complex is isostructural with *cis*-$[Pt(5'\text{-}IMP)_2(NH_3)_2]^{2-}$, a model proposed for Pt(II) binding to DNA. The base binding observed in the present case is different from the typical "phosphate only" binding shown from earlier studies on metal–nucleotide complexes containing various other π-aromatic amines.

Introduction

During the past few years interaction of metal ions with nucleic acid constituents has been a field of active research.[1] This activity is motivated, in large part, by the well-recognized role of metal ions in the biochemistry of nucleic acids[2] and by the speculation that the antineoplastic agents, notably *cis*-$[Pt(NH_3)_2Cl_2]$, exhibit their activity by binding to DNA.[3] Metal–nucleotide complexes containing heteroaromatic N bases are of special interest since

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0020-1669/85/1324-1065$01.50/0

Table I. Crystal Data

mol formula	$Cu(C_{10}N_4O_8PH_{11})_2(C_3N_2H_4)_{0.8}Na_2\cdot 15.6H_2O$
space group	$C222_1$
cryst size, mm	0.15 × 0.375 × 0.65
a, Å	8.733 (4)
b, Å	23.213 (5)
c, Å	21.489 (6)
V, Å^3	4356.6
Z	4
mol wt	1136.7
D_{calcd}, g cm^{-3}	1.73
D_{measd}, g cm^{-3}	1.72
radiation (λ, Å)	Mo Kα (0.7107)
μ(Mo Kα), cm^{-1}	6.64
temp, °C	23
2θ upper limit, deg	50
no. of reflcns measd	2297
no. of reflcns used ($I \geqslant 3\sigma(I)$)	2008
R^a	0.087
$R_w{}^b$	0.098

[a] $R = \Sigma(|F_o| - |F_c|)/\Sigma|F_o|$. [b] $R_w = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{1/2}$

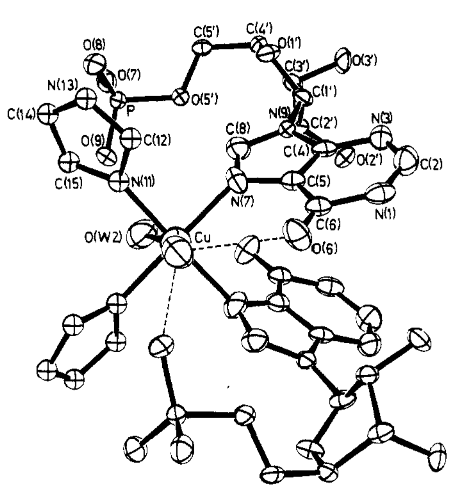

Figure 1. Structure of the (5′-IMP)$_2$Cu^{II} complex ion with imidazole coordination (~40% imidazole occupancy). Broken lines indicate hydrogen bonds.

these complexes can be considered as models for the substrate–metal ion–aromatic amine centers found in proteins.[4] Solution studies[4,5] on such ternary complexes have shown that, in the presence of the π-aromatic amine, the metal–nucleotide interaction takes place at the phosphate group and not at the base. Crystallographic studies on metal–nucleotide complexes containing diverse π-aromatic amines like bpy,[6] dpa, and *o*-phen have provided direct evidence for the existence of such a binding mode of nucleotides in the solid state.[7-11]

The im group, which is an important and versatile binding site for metal ions in many biological systems,[12-15] is expected to exert a similar influence on the coordination behavior of nucleotides.[13,14,16] However, no X-ray crystallographic studies have been carried out so far on a metal–nucleotide complex with im. We have now isolated a Cu(II)–5′-IMP complex containing the im group, and in this paper we report its X-ray structure, wherein the metal ion binds to the N(7) atoms of the nucleotides.

Experimental Section

Synthesis. The complex $[Cu(im)_3(H_2O)](NO_3)_2$ was prepared by mixing copper nitrate (BDH) and im (BDH) in a 1:3 ratio in aqueous solution at laboratory temperature. Slow evaporation of the resultant solution yielded violet crystals. The nucleotide complex was then prepared by mixing solutions of Na$_2$-5′-IMP (Sigma) and $[Cu(im)_3(H_2O)](NO_3)_2$, both at 5×10^{-3} M, and adjusting to pH 6.8. Vapor diffusion of the reaction mixture against *tert*-butyl alcohol yielded greenish blue platelike crystals after about 2 weeks. Anal.[17] Calcd for $C_{22.4}H_{56.4}CuN_{9.6}Na_2O_{31.6}P_2$: C, 23.65; H, 4.96; N, 11.82. Found: C, 24.89; H, 5.33; N, 11.5.

Collection and Reduction of the X-ray Intensity Data. Crystal data are given in Table I. Unit cell dimensions and their associated standard deviations were derived from a least-squares fit to the setting angles for 20 carefully selected and centered reflections on a CAD-4 diffractometer. The intensities of 2297 reflections were collected up to θ = 25° on the diffractometer employing graphite-monochromated Mo Kα radiation. Data were collected in the ω/2θ mode with a scan speed of 1°/min. Intensities of two control reflections measured after every 3000 s showed no significant variations during the course of the experiment. The data were corrected for Lorentz and polarization effects but not for absorption.

Solution and Refinement of the Structure. The positional parameters of the Cu atom were deduced from a three-dimensional Patterson synthesis. A subsequent difference Fourier synthesis revealed the positions of all the non-hydrogen atoms except the atoms of the im group and lattice water molecules. Several cycles of isotropic refinement reduced the conventional R value to 0.15. Successive difference Fourier maps yielded positions of three oxygens of lattice waters in general positions and one water oxygen lying on a twofold axis parallel to a. The atoms of the im moiety could still not be clearly located, suggesting that they are disordered. Two further cycles of refinement based on anisotropic thermal parameters for all the atoms gave an R value of 0.12. A difference Fourier map at this stage revealed positions corresponding to atoms of im and also peaks at O(W3) and O(W4). The electron density for these atoms was approximately 50% of that observed for corresponding atoms of the nucleotide group. Further, the atoms at O(W3) and O(W4), while being close to the im group (O(W3)···C(12) = 1.41 Å; O(W3)···N(13) = 1.49 Å; O(W4)···C(14) = 2.04 Å; O(W4)···C(15) = 1.38 Å), could not be explained on the basis of alternative positions of disordered im atoms. This observation suggested the nonstoichiometry of the structure with respect to im content. The following structural model was developed to account for these features: When O(W1) coordinates to Cu(II), the lattice waters O(W3) and O(W4) link the coordinated water through a hydrogen bond of the type O(W4)···O(W1)···O(W3). In the absence of these three water molecules, the im nitrogen at nearly the same position as O(W1) coordinates to Cu(II). The contribution from O(W1), O(W3), O(W4), and the atoms of the im group were included in further cycles of refinement with partial occupancies of 0.5 each. Inspection of bond lengths and bond angles in the im molecule showed considerable distortions from expected geometry. A difference Fourier computed with the removal of the im group resulted in its reappearance at the same position. It was noticed that the map also contained some peaks higher than the mean noise level in the vicinity of disordered atoms of im group. Attempts to identify atoms of the im molecule in alternative positions were unsuccessful, as they made no chemical sense. Therefore, the im moiety was refined as a rigid group[18]

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(6) Abbreviations: bpy = 2,2′-bipyridyl; dpa = 2,2′-bipyridylamine; *o*-phen = 1,10-phenanthroline; im = imidazole; 5′-AMP, 5′-IMP, 5′-UMP, and 5′-CMP = the 5′-monophosphates of adenosine, inosine, uridine, and cytidine, respectively; 3′-GMP = guanosine 3′-monophosphate; 5′-ATP = adenosine 5′-triphosphate; 5′-IMPH = inosine 5′-monophosphate (protonated form); en = ethylenediamine; dien = diethylenetriamine; tn = trimethylenediamine.

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(17) The discrepancy in the values for carbon is probably due to the nonstoichiometry of the complex. It is possible that within any given batch of crystals a variation exists in the im content and the usual batch elemental analysis is an average value. The stoichiometry is assigned on the basis of structural analysis on a single crystal, and this formula is used to calculate the chemical content.

Table II. Final Fractional Parameters ($\times 10^4$) for Non-Hydrogen Atoms with Their Esd's in Parentheses

atom	*x*	*y*	*z*
Cu	0	1538 (1)	2500
P	3922 (2)	1212 (1)	4681 (1)
Na	3612 (6)	4572 (2)	4368 (2)
O(5′)	4023 (6)	1891 (2)	4514 (2)
O(7)	4508 (7)	1160 (2)	5346 (3)
O(8)	4949 (7)	901 (2)	4232 (2)
O(9)	2240 (6)	1073 (2)	4609 (3)
N(1)	1453 (7)	3398 (3)	1430 (3)
C(2)	2306 (12)	3744 (3)	1781 (4)
N(3)	2896 (9)	3629 (3)	2329 (3)
C(4)	2582 (8)	3082 (3)	2492 (4)
C(5)	1721 (8)	2678 (3)	2178 (3)
C(6)	1114 (9)	2837 (3)	1590 (4)
O(6)	428 (8)	2523 (3)	1206 (3)
N(7)	1685 (9)	2177 (3)	2519 (4)
C(8)	2544 (9)	2268 (3)	3009 (4)
N(9)	3094 (7)	2804 (3)	3014 (3)
C(1′)	4014 (8)	3092 (3)	3510 (3)
C(2′)	3156 (8)	3165 (3)	4121 (3)
O(2′)	2260 (6)	3670 (2)	4075 (3)
C(3′)	4464 (8)	3182 (3)	4582 (4)
O(3′)	5140 (8)	3747 (2)	4534 (3)
C(4′)	5548 (9)	2747 (3)	4310 (3)
O(1′)	5259 (6)	2716 (2)	3651 (2)
C(5′)	5491 (9)	2142 (3)	4592 (4)
O(W1)[a]	1627 (13)	959 (4)	2447 (5)
O(W2)	33 (9)	1359 (3)	3741 (4)
O(W3)[a]	4099 (26)	1344 (9)	1910 (9)
O(W4)[a]	2388 (36)	315 (12)	3440 (13)
O(W5)	2068 (8)	578 (3)	486 (4)
O(W6)	4107 (13)	5000	0
O(W7)	4 (41)	4777 (3)	1053 (6)
O(W8)	−1086 (29)	−327 (6)	3250 (8)
O(W9)[b]	5505 (57)	4977 (26)	3781 (27)
O(W10)[b]	5801 (59)	−399 (22)	2922 (26)
N(11)[c]	1627 (13)	959 (4)	2447 (5)
C(12)[c]	2686 (13)	1055 (4)	1988 (5)
N(13)[c]	3965 (13)	738 (4)	2124 (5)
C(14)[c]	3697 (13)	445 (4)	2666 (5)
C(15)[c]	2252 (13)	581 (4)	2866 (5)

[a] Occupancy 0.6. [b] Disordered water molecule. O(W10) has occupancy 0.5. [c] Atoms of the imidazole group with occupancy 0.4. The imidazole moiety is refined as a rigid group.

with isotropic thermal parameters. Refinement of the population parameters of im atoms and the water molecules suggested that they were present with occupancies approximately 0.4 and 0.6, respectively. Two more lattice waters were identified in a subsequent Fourier map,[19] one of them, viz. O(W10), being disordered over two positions related by a twofold axis and separated by 2.3 Å. Refinement of this model with occupancy 0.5 for O(W10) reduced *R* to 0.089. The hydrogen atoms of the 5′-IMP ligand were placed in calculated positions with the temperature factors (*B* values) 1.5 $Å^2$ greater than those of the atoms to which they are attached. Finally, two cycles of refinement were performed, holding the hydrogen atom parameters fixed. This led to convergence with final *R* and R_w values of 0.087 and 0.098, respectively. The weighting scheme employed was $w = 0.27/(\sigma_F^2 + 0.046|F|^2)$. A final difference Fourier showed no significant residual peaks with the exception of peaks near the disordered atoms of the order of 0.2 e/$Å^3$ and a peak at 1.2 e/$Å^3$ near the Cu site.

Neutral scattering factor curves for copper and sodium were taken from ref 20. The scattering factors as available in SHELX-76 were used for all other atoms. Anomalous dispersion corrections were applied to the scattering factors of all non-hydrogen atoms.[21] Final atomic positional parameters for the non-hydrogen atoms are given in Table II.[22]

Table III. Bond Lengths (Å) Involving Non-Hydrogen Atoms with Esd's in Parentheses

Cu-N(7)	2.089 (7)	Cu-N(11)	1.961 (10)
Cu-O(W1)	1.961 (10)	Cu-O(W2)	2.700 (8)
N(1)-C(2)	1.330 (11)	C(2)-N(3)	1.312 (11)
N(3)-C(4)	1.346 (10)	C(4)-C(5)	1.378 (10)
C(5)-C(6)	1.419 (11)	C(6)-O(6)	1.252 (10)
C(6)-N(1)	1.381 (11)	C(5)-N(7)	1.375 (10)
N(7)-C(8)	1.311 (11)	C(8)-N(9)	1.334 (10)
N(9)-C(4)	1.369 (10)	N(9)-C(1′)	1.494 (10)
C(1′)-C(2′)	1.520 (10)	C(2′)-C(3′)	1.512 (10)
C(2′)-O(2′)	1.412 (9)	C(3′)-C(4′)	1.502 (10)
C(3′)-O(3′)	1.442 (9)	C(4′)-O(1′)	1.441 (9)
O(1′)-C(1′)	1.427 (9)	C(4′)-C(5′)	1.531 (11)
C(5′)-O(5′)	1.418 (9)	P-O(5′)	1.611 (5)
P-O(7)	1.522 (6)	P-O(8)	1.508 (6)
P-O(9)	1.514 (6)	N(11)-C(12)	1.370 (16)
C(12)-N(13)	1.370 (15)	N(13)-C(14)	1.370 (16)
C(14)-C(15)	1.370 (16)	C(15)-N(11)	1.370 (15)

Table IV. Bond Angles (deg) Involving Non-Hydrogen Atoms with Esd's in Parentheses

N(7)-Cu-N(7′)	89.6 (3)	N(7)-Cu-O(W1)	88.7 (3)
N(7)-Cu-O(W2)	94.7 (3)	N(7)-Cu-O(W1′)	175.2 (3)
N(7)-Cu-O(W2′)	97.8 (3)	O(W1)-Cu-O(W2)	86.8 (4)
O(W1)-Cu-O(W1′)	93.4 (4)	O(W1)-Cu-O(W2′)	81.1 (4)
O(W2)-Cu-O(W2′)	162.3 (3)	Cu-N(7)-C(5)	127.3 (6)
Cu-N(7)-C(8)	122.2 (6)	N(1)-C(2)-N(3)	127.4 (8)
C(2)-N(3)-C(4)	110.1 (7)	N(3)-C(4)-C(5)	128.8 (7)
C(4)-C(5)-C(6)	117.6 (7)	C(5)-C(6)-N(1)	112.7 (7)
C(6)-N(1)-C(2)	123.3 (7)	C(5)-C(6)-O(6)	127.9 (7)
N(1)-C(6)-O(6)	119.2 (7)	C(4)-C(5)-N(7)	109.1 (7)
C(6)-C(5)-N(7)	133.2 (7)	C(5)-N(7)-C(8)	106.2 (6)
N(7)-C(8)-N(9)	111.2 (7)	C(8)-N(9)-C(4)	108.4 (6)
N(9)-C(4)-C(5)	105.0 (6)	N(9)-C(4)-N(3)	126.3 (7)
C(8)-N(9)-C(1′)	128.0 (6)	C(4)-N(9)-C(1′)	123.4 (6)
O(1′)-C(1′)-C(2′)	105.1 (6)	C(1′)-C(2′)-C(3′)	101.3 (6)
C(2′)-C(3′)-C(4′)	101.8 (6)	C(3′)-C(4′)-O(1′)	107.7 (6)
C(4′)-O(1′)-C(1′)	108.2 (5)	N(9)-C(1′)-O(1′)	106.7 (6)
N(9)-C(1′)-C(2′)	113.7 (6)	C(2′)-C(3′)-O(3′)	106.7 (6)
O(3′)-C(3′)-C(4′)	109.0 (6)	O(2′)-C(2′)-C(1′)	107.8 (6)
O(2′)-C(2′)-C(3′)	116.3 (6)	C(3′)-C(4′)-C(5′)	116.3 (6)
C(5′)-C(4′)-O(1′)	109.7 (6)	C(4′)-C(5′)-O(5′)	111.0 (6)
C(5′)-O(5′)-P	115.0 (5)	O(5′)-P-O(7)	105.9 (3)
O(5′)-P-O(8)	107.2 (3)	O(5′)-P-O(9)	104.0 (3)
O(7)-P-O(8)	111.1 (3)	O(7)-P-O(9)	113.9 (3)
O(8)-P-O(9)	113.9 (3)		

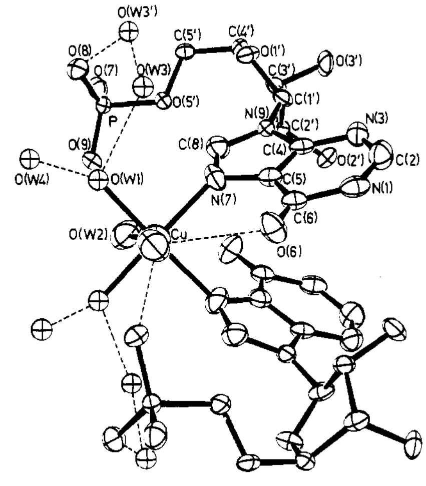

Figure 2. Structure of the $(5'\text{-IMP})_2Cu^{II}$ complex ion with water coordination (~60% water occupancy). Broken lines indicate hydrogen bonds.

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(18) A regular pentagon with bond distances of 1.37 Å and bond angles of 108° was fitted to the atoms N(11), C(12), N(13), C(14), and C(15) and refined as a rigid group with N(11) as a pivot atom. The parameters refined were the positional parameters of the pivot atom, three orientation angles, and individual isotropic thermal parameters. The program used was SHELX-76.

(19) The positions of all the water molecules, except O(W4), in the present case correspond closely to those present in the structure, $[Pt(5'\text{-IMP})_2(NH_3)_2]^{2-}$.

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Table V. Comparison of the Structural Parameters of the Sodium Salt and Metal Complexes of 5′-IMP

complex	interligand N(7)···N(7) dist, Å	dihedral angle between purine planes, deg	% metal	ref
Na[5′-IMPH]	3.48	22.0	0	27
$[Pt(5'\text{-IMP})_2(en)]^{2-}$	3.26	31.0	ca. 38	23
$[Pt(5'\text{-IMP})_2(tn)]^{2-}$	2.93	38.2	ca. 74	25
$[Pt(5'\text{-IMP})_2(NH_3)_2]^{2-}$	2.88	40.7	ca. 86	26
$[Pt(5'\text{-IMP})_2(NH_3)_2]^{2-}$	2.83	43.0	100[a]	24
$[Co(5'\text{-IMP})_2(H_2O)_4]^{-}$	2.89	39.9	100	32
$[Cu(5'\text{-IMP})_2(dien)]^{2-}$	3.23	30.4	100	29
$[Cu(5'\text{-IMP})_2(im)_{0.8}(H_2O)_{1.2}(H_2O)_2]^{2-}$	2.97	35.5	100	present work

[a] Originally reported to be 56%.

Results and Discussion

Description of the Molecular Structure. In the crystal structure the Cu(II) ion lies on a twofold axis along *b* and has an octahedral coordination. The symmetry-related 5′-IMP anions coordinate to the metal ion in cis position through the N(7) atoms of the bases, the Cu–N(7) distance being 2.089 (7) Å. The other cis positions of the coordination plane are statistically occupied by nitrogen atoms of disordered im groups (Figure 1) and water oxygens (Figure 2) with occupancies 0.4 and 0.6, respectively. The Cu–N_{im}/Cu–O(W1) bond lengths (1.961 (10) Å) are shorter than the Cu–N(7) distances. The remaining axial coordination sites are occupied by water oxygens (O(W2)) at longer distances (2.700 (8) Å). The axially coordinated water O(W2) forms two hydrogen bonds with O(6) of the base and O(9) of the phosphate belonging to the same molecule (Figures 1 and 2). The hydrogen-bonding scheme that links the ligand water O(W1) with phosphate oxygen O(8) (through O(W3) and its symmetry equivalent O(W3′)) and with O(W4) (Figure 2) is observed only in the absence of the im group.

The structure of $Na_2[Cu(5'\text{-IMP})_2(im)_{0.8}(H_2O)_{1.2}(H_2O)_2]\cdot 12.4H_2O$, like the Pt(II) complexes with 5′-IMP,[23–26] bears a strong resemblance to the structures of sodium salts of 5′-IMP.[27,28] In the structure of Na-5′-IMPH[27] a water molecule lies on a crystallographic twofold axis and links two symmetry-related 5′-IMP anions via hydrogen bonds of the type $OH_2\cdots N(7)$. In the Pt(II) complexes, the metal ion links the two symmetry-related 5′-IMP ligands through *cis*-Pt–N(7) coordination bonds. An important and interesting aspect of these complexes is that most of them are nonstoichiometric with respect to the metal content. Although the present structure is very similar to the Pt(II) complexes, it is nonstoichiometric only with respect to imidazole occupancy. The possibility of this structure also having fractional occupancy of the metal ion was considered. However, results from an occupancy refinement of copper seem to rule out this possibility. The only other Cu(II) complex where such a cis binding of nucleotides has been observed is $Na_2[Cu(5'\text{-IMP})_2(dien)]\cdot 10H_2O$.[29] In this case, the complex is stoichiometric, but the copper positions were found to be disordered between two positions related by a twofold axis. Thus, the Cu(II) ion alternatively forms a strong equatorial bond to N(7) of one 5′-IMP ligand and a weaker axial interaction with N(7) of the related ligand and vice versa.

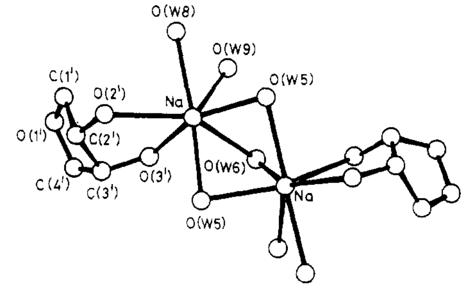

Figure 3. Coordination around the sodium ion, showing water bridges between the two sodium ions related by twofold symmetry. Note the five-membered chelate involving the sodium ion and sugar atoms.

Molecular Conformation and Dimensions. In the structure, the Cu(II) ion is significantly out of the plane of the purine ring (0.75 Å). Thus, although the angle N(7)–Cu–N(7) is 89.6°, the dihedral angle between the two bases is only 36.8°. This value is close to that observed for the Pt(II) complexes of 5′-IMP. (Table V). The corresponding angle in the sodium salt of 5′-IMPH is 22°. The interligand N(7)···N(7) distance in the present molecule is 2.9 Å. The ribose moiety displays the C(2′) endo[30] puckering mode. The orientation of the sugar with respect to the purine framework is anti ($\chi_{CN} = 51.2°$). The conformation about the C(4′)–C(5′) bond is gauche–gauche. These conformational parameters are similar to those observed for other metal complexes where the nucleotides are in cis position.

In view of the fact that the esd's in bond lengths and bond angles of the 5′-IMP ligand are comparatively large, a detailed discussion of these parameters is unwarranted. However, they agree well, within the limits of experimental error, with the reported values for other complexes in this series. The purine plane is approximately planar, with the exocyclic atoms O(6) and C(1′) deviated by 0.14 and 0.03 Å, respectively, out of the plane. The imidazole and pyrimidine rings of the purine framework are inclined to each other by 2.6° about the C(4)–C(5) bond.

Sodium Coordination. The present structure, like most of the other structures in this series, has sodium as a counterion. The complex $[Pt(Me\text{-}5'\text{-GMP})_2(tn)]$[31] and (en)$Co^{III}$[32] complexes of oxopurine nucleotides, however, do not have such a counterion. The sodium ion is seven-coordinate. Two of the coordination sites are occupied by the ribosyl hydroxyl atoms O(2′) and O(3′). The atoms O(2′), C(2′), C(3′), O(3′), and Na^+ ion constitute a five-membered chelate. The remaining five sites of the sodium coordination are occupied by water molecules. The nearest sodium ion is related by a twofold axis and separated by a distance of 3.37 Å. These two sodium ions share three water oxygens. Among these, the water O(W6) lies on the crystallographic axis along *a*, and the other two are symmetry-related O(W5) sites (Figure 3).

Stacking Interactions and Hydrogen Bonds. In the absence of intercomplex base–base interactions, the structure is dominated by intracomplex interactions between twofold symmetry-related nucleotides. The notable interaction is between O(6) and C(8) of the twofold-related ligand (C(8)···O(6) = 3.15 Å). This type of interaction is typical of $(nucleotide)_2Pt^{II}$ complexes. Apart from this contact, there are significant intracomplex sugar-base interactions involving the sugar oxygen atom O(1′) (O(1′)···C(5) = 3.18 Å, O(1′)···C(4) = 3.21 Å, O(1′)···C(6) = 3.22 Å, O-

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(22) All computations were carried out on a DEC-10 computer. The structure was solved and refined with: Sheldrick, G. M. "SHELX-76"; Cambridge University: Cambridge, England, 1976. Diagrams were prepared with: Johnson, C. K. "ORTEPII", Report ORNL-5138; Oak Ridge National Laboratory; Oak Ridge, TN, 1976. Calculations other than those specifically noted were performed with locally written programs.

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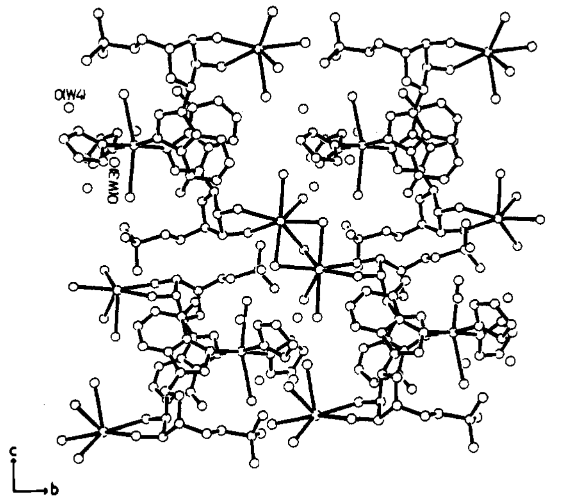

Figure 4. Packing of the molecules in the unit cell viewed down *a*. Water molecules O(W1) (not marked in the Figure), O(W3), and O(W4) have occupancy ~0.6, and atoms of imidazole group have occupancy ~0.4.

(1′)···N(1) = 3.28 Å, O(1′)···C(2) = 3.33 Å, O(1′)···N(3) = 3.39 Å). It can be seen from the above values that the sugar oxygen O(1′) interacts approximately equally with the pyrimidine atoms. Similar sugar–base interactions were also observed in the structure of Na-5′-IMPH.

The packing of molecules is shown in Figure 4. The phosphate group is rigidly held through a network of intermolecular hydrogen bonds. In addition to coordination to the sodium ion, the two hydroxyl oxygens of the ribose form hydrogen bonds with the oxygens of symmetry-related phosphate groups. The N(1) atom donates its proton to the phosphate oxygen O(7), which is of significance since it represents a base–phosphate interaction.

General Conclusions

As mentioned earlier, the cis geometry of the nucleotides around the Cu(II) ion in the present structure is similar to that observed for the (nucleotide)$_2$Pt^{II} complexes. Most of these Pt(II)–5′-IMP complexes are nonstoichiometric. Kistenmacher and co-workers[25] have shown that these nonstoichiometric complexes are made up of two types of unit cells, one of which can be associated with the sodium salt of 5′-IMP and the other with Pt(II) complexes of 5′-IMP. The occupancy of the (amine)Pt^{II} moiety in the series of complexes [Pt(5′-IMP)$_2$(amine)]$^{2-}$ ranges from 38% to 100% (Table V). It is clear from the table that a higher occupancy of (amine)Pt^{II} group results in the decrease of the N(7)···N(7) distance and the increase in the dihedral angle between the purine bases of the symmetry-related 5′-IMP nucleotides. As pointed out by Chiang et al.[29] earlier, the comparative parameters shown in Table V suggest that there exists a strong competition between the crystal-packing forces operative in the sodium salts of 5′-IMP and the distortion of the structure owing to the simultaneous binding of two bases by the metal moiety. In the [Cu(5′-IMP)$_2$(dien)]$^{2-}$ complex, due to the presence of the bulkier dien ligand, the metal ion forms a weaker bond with one of the nucleotides (vide supra) and consequently effects minimal distortion. On the other hand, with im in the cis position in the present case, the Cu(II) ion is able to link the two nucleotides by strong bonds and bring about greater distortion in the basic structure, comparable to that shown by Pt(II) complexes. The structural similarities displayed by the sodium salts, the Pt(II) complexes, and the Cu(II) complexes are highly significant in terms of the possible effect on a polynucleotide structure owing to intrastrand cross-linking by a metal complex.

Another interesting feature of the structure is that the cis binding of nucleotides through N(7) atoms to Cu(II) has the effect of labilizing the Cu–N$_{im}$ bonds. We have observed the complete removal of the ethylenediamine molecules from the metal site on similar binding of nucleotides.[32] This suggests that the coordinated bases of oxopurine nucleotides have a very strong trans-directing influence, so that even thermodynamically and kinetically inert amino groups can be labilized.[33]

The present crystallographic study on a ternary metal–nucleotide complex containing an aromatic ligand was mainly prompted by the solution studies of Sigel and co-workers.[4,5] In such a ternary system they have shown that the metal ion–aromatic amine moiety prefers to bind to the phosphate oxygen donors rather than to the nitrogen donors of the nucleotides. X-ray structural studies on Cu(II) and Cd(II) ternary complexes composed of a nucleotide monophosphate and a π-aromatic base like bpy, dpa, and *o*-phen have confirmed this mode of binding in most cases: i.e., [Cu(5′-AMPH)(bpy)(H$_2$O)]$_2$$^{2+}$,[7] [Cu(3′-GMP)(*o*-phen)(H$_2$O)]$_2$,[8] [Cu(5′-IMP)(dpa)(H$_2$O)]$_2$,[9] [Cu(5′-CMP)(dpa)(H$_2$O)]$_2$,[10] [Cu(5′-UMP)(dpa)(H$_2$O)]$_2$,[11] and [Cd(5′-UMP)(dpa)(H$_2$O)].[10] All the Cu(II) complexes have a dimeric structure, with the aromatic amines coordinating through their nitrogen donors and the nucleotide bridging the two Cu(II) centers through the phosphate oxygens. The nucleotide base does not bind to the metal ion, contrary to what is observed in binary complees of the type [M(nucleotide)(H$_2$O)$_5$].[1d–f] Though the Cd(II) complex is polymeric, the metal coordinates only to phosphate oxygens. The complex [Cu(5′-IMPH)(bpy)(H$_2$O)$_2$](NO$_3$)[34] in which the binding is through the N(7) atom of the base is the only exception. The metal–purine binding in this case, as pointed out by Bau and co-workers,[9] is most likely a consequence of protonation of the phosphate group, making it less attractive as a ligand to the metal ion. Metal–phosphate binding mode is also shown in the two ternary metal complexes with 5-ATP, viz. [Cu(5′-ATP)(*o*-phen)]$_2$·7H$_2$O[35] and [Zn(5′-ATP)(bpy)]·4H$_2$O.[36] It was concluded, therefore, that the "phosphate only" binding mode is typical for ternary complexes containing π-aromatic amines. Sigel and co-workers have suggested that the aromatic amine due to its π-accepting properties imparts discriminating properties to the metal ion.[5a,14,16]

On the basis of the results obtained from solution studies, it was concluded that the im moiety would also impart similar discriminating properties to metal ions.[13,14,16] Accordingly, the (im)Cu^{II} or the (im)$_2$Cu^{II} moiety would bind to the oxygen atoms of the phosphate rather than to the nitrogen atoms of the base. The present study, however, shows that the (im)$_2$Cu^{II} moiety binds to the N(7) atoms of the base but not to the phosphate oxygens. Thus, the structures in the solid state and solution are obviously different. As has been pointed out earlier, the 5′-IMP anions in ternary complexes containing ammonia, en, dien, and tn prefer to stack in the manner observed in the present structure. However, such stacked interactions do not exist in the complex [Cu(5′-IMP)(dpa)(H$_2$O)]$_2$,[33] which contains the heteroaromatic N base dpa instead of im in the present case. The differences in the mode of binding of the 5′-IMP ligand in Cu(II) complexes containing dpa and im may be due to the less pronounced π-accepting property of im as compared to that of dpa. The present work emphasizes the need for more crystallographic studies on ternary metal–nucleotide complexes containing the im moiety.

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Registry No. [Cu(im)$_3$(H$_2$O)](NO$_3$)$_2$, 94957-33-2.

Supplementary Material Available: Tables of temperature factors, bond parameters of sodium coordination polyhedra, least-squares planes, parameters of possible hydrogen bonds, and observed and calculated structure factors (18 pages). Ordering information is given on any current masthead page.

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(33) In this connection attention is drawn to a proposal made by Barton and Lippard to explain the possible modes of Pt(II) binding to DNA. On the basis of the reactivities of oligomeric platinum base complexes, they suggest the possible labilization of ammonia molecules from the platinum coordination plane when *cis*-(diamine)Pt^{II} moiety binds to the bases in DNA. The reactive sites thus created on the Pt(II) center could then be occupied by ligating groups in the complementary strand of the duplex, resulting in a stable strongly bound complex with intra- and interstrand cross-links: Barton, J. K.; Lippard, S. J. "Nucleic Acid-Metal Ion Interactions"; Wiley: New York, 1980; Chapter 2.

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