Interactions of Metal Ions with Nucleotides. Metal Bonding to N(7) in the Ternary Copper(II)–Inosine 5′-Phosphate Complex [Cu(5′-IMP)-(2,2′-bipyridyl)(H_2O)$_2$]·NO_3·H_2O: *X*-Ray Crystal Structure Analysis, and Metal Bonding to Both N(7) and Phosphate in the Binary Complex [Cu(5′-IMP)]·H_2O: *X*-Ray Characterization

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Summary *X*-Ray crystal structure analysis of the ternary complex [Cu(inosine 5′-phosphate)(2,2′-bipyridyl)(H_2O)$_2$]·NO_3·H_2O and single-crystal *X*-ray characterization of the binary complex [Cu(inosine 5′-phosphate)]·H_2O show the former to be monomeric with the square-pyramidal copper ion directly bonded to N(7) of the base, to the bidentate bipyridyl ligand, and to two water molecules, and the latter to be isostructural with the previously

reported zinc analogue, forming a two-dimensional polymer with the tetrahedral copper ion directly bonded to N(7) and to three phosphate oxygen atoms.

NUMEROUS investigations have demonstrated that metal ions could mediate in various reactions of nucleic acid in many biological processes,[1] but the detailed roles of metal ions are not known. To obtain fundamental knowledge on interactions of metal ions with components of nucleic acids, we have undertaken a systematic crystallographic study on nucleotide–metal ion interactions in binary complex systems.[2] We have now extended these studies to simple ternary complex systems to investigate substrate–metal ion–enzyme complex models. We report here the crystal structure of the ternary complex $[Cu(5'\text{-}IMP)(bipy)(H_2O)_2]\cdot NO_3\cdot H_2O$ (bipy = 2,2′-bipyridyl; 5′-IMP = inosine 5′-phosphate), and *X*-ray evidence that the binary complex $[Cu(5'\text{-}IMP)]\cdot H_2O$ is isostructural with the zinc analogue.[3] We also report the effect of the second ligand, bipy, on the metal co-ordination ability and the stereochemistry of the complexes formed.

The ternary complex (deep blue plates) was prepared from $Na_2(5'\text{-}IMP)$, $Cu(NO_3)_2$, and bipy in an equimolar ratio at pH 6. *Crystal data:* $[Cu(5'\text{-}IMP)(bipy)(H_2O)_2]\cdot NO_3\cdot H_2O$, orthorhombic, space group $P2_12_12_1$, $a = 16{\cdot}197(6)$, $b = 23{\cdot}580(7)$, $c = 6{\cdot}974(3)$ Å, $Z = 4$, $D_m = 1{\cdot}69(1)$, $D_c = 1{\cdot}703$ g cm^{-3}. Intensity data were collected on a Rigaku automated diffractometer with Cu-K_α radiation up to 2θ limits of 135°. The structure was solved by heavy atom methods and refined to a final R value of 0·058 for 2252 reflections with $F_0 > 3\sigma(F_0)$.†

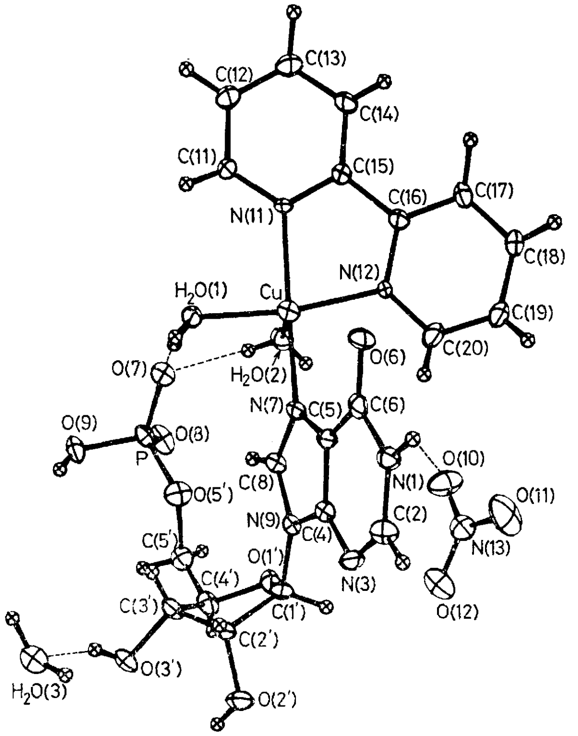

FIGURE 1. The molecular structure of $[Cu(5'\text{-}IMP)(bipy)(H_2O)_2]\cdot NO_3\cdot H_2O$. Broken lines represent the hydrogen bonds.

The structure of the ternary complex is shown in Figure 1. The complex is composed of the monomeric $[Cu(5'\text{-}IMP)(bipy)(H_2O)_2]^+$ cation and the nitrate anion; the phosphate group is present as a monovalent anion. The copper ion is in a square-pyramidal environment with N(7) of the hypoxanthine base [Cu–N(7) 1·993(6) Å], the bidentate bipy ligand [Cu–N 2·008(6) and 2·003(6) Å], and a water molecule [Cu–OH_2 1·987(6) Å] in the equatorial positions and another water molecule [Cu–OH_2 2·287(6) Å] in the axial position. The dihedral angle between the plane of the hypoxanthine ring and the plane through the four atoms bonded to the copper atom in the equatorial positions is 60·8°. The copper atom is displaced by 0·142 Å out of the equatorial plane towards the axial water ligand. The base displays the *anti*[4] conformation, with $\chi_{CN}{}^4 = -158{\cdot}2°$. The ribose ring has the C(3′)-*endo*[4] conformation. The conformation about the C(4′)–C(5′) bond is *gauche–gauche*.[4] The metal ion is not directly bonded to the phosphate oxygen atoms, but is connected to them *via* two water ligands, as is found for monomeric metal–purine nucleotide complexes.[5] Two intramolecular hydrogen bonds from these two water ligands to the same phosphate oxygen atom [$H_2O \cdots$ O(phosphate) 2·772(9) and 2·701(9) Å] stabilize the molecular structure. Though an intramolecular hydrogen bond between the substituent at C(6) of the purine base and a water ligand is commonly observed in water ligand-containing metal–purine base[6,7] and metal–purine nucleotide[5,8] complexes, this complex involves an intermolecular hydrogen bond between O(6) and the axial water ligand of the adjacent molecule [O(6) $\cdots OH_2$ 2·746(9) Å] instead of the above intramolecular one hydrogen bond. The crystal packing is dominated by intercomplex hydrogen bonding and the stacking arrangement of bipy ligands (3·55 Å spacing). There is neither interbase hydrogen bonding nor base stacking.

Nucleotide–anion interaction is also important in connection with the denaturation power of anions on nucleic acids.[7] The nitrate anion interacts with the hypoxanthine base through one hydrogen bond [N(1) $\cdots$ O(nitrate) 2·790(12) Å]. This hydrogen bond donor property of N(1) should be common for interaction between inosine bases and anions such as NO_3^-, ClO_4^- and SO_4^{2-}.

The binary complex (light blue needles) was prepared from $Na_2(5'\text{-}IMP)$ and $Cu(NO_3)_2$ in an equimolar ratio at pH 4. *Crystal data* (Weissenberg and precession photographs): $[Cu(5'\text{-}IMP)]\cdot H_2O$, orthorhombic, space group $P2_12_12_1$, $a = 17{\cdot}46(2)$, $b = 15{\cdot}94(2)$, $c = 5{\cdot}08(1)$ Å, $Z = 4$, $D_m = 2{\cdot}03(1)$, $D_c = 2{\cdot}009$ g cm^{-3}. These cell parameters are very similar to those reported for the $[Zn(5'\text{-}IMP)]\cdot H_2O$ complex (space group $P2_12_12_1$, $a = 16{\cdot}486$, $b = 15{\cdot}759$, $c = 5{\cdot}580$ Å).[3] In addition, comparison of the distribution of reflection intensities in corresponding Weissenberg photographs indicates that these structures are essentially isomorphous.

Thus we suggest that the binary copper complex is a two-dimensional polymer with the copper ion tetrahedrally co-ordinated to N(7) of the hypoxanthine base and three phosphate oxygen atoms of the three different phosphate groups as schematically shown in Figure 2.

This polymeric structure is particularly noteworthy in connection with nucleotide transport across membranes by

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† The atomic co-ordinates for this structure are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

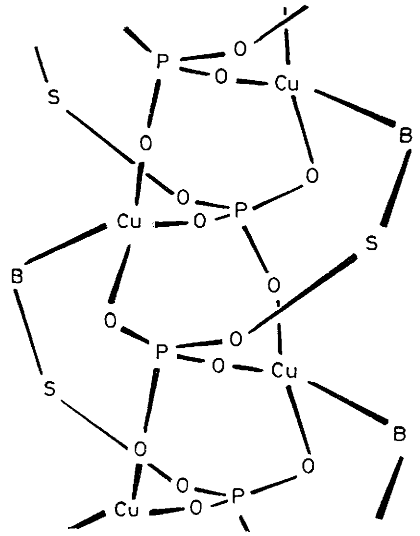

FIGURE 2. A schematic drawing of a segment of the polymeric chain structure of $[Cu(5'\text{-}IMP)]_n$. The sugar and base groups are denoted as S and B respectively.

metal ions;[9] *i.e.*, if the degree of polymerization is appropriate, this structure is favourable for nucleotide diffusion by metal–phosphate bonding, thus decreasing the charge on the nucleotide, and also by increasing the permeability of the lipid bilayer.

It is interesting to consider the effect of the second ligand, bipy, on the metal co-ordination ability and on the stereochemistry of the ternary and binary complexes. N(7) is the preferable binding site for both complexes, as has been observed for many hypoxanthine or guanine base-containing metal complexes, but the binary complexes involve metal–phosphate bonding and form polymeric structures; in contrast the ternary complexes do not involve metal–phosphate bonding and form monomeric structures. This indicates that Fischer and Bau's statement[10] that "the 'phosphate-only' type of co-ordination is typical for mixed-ligand complexes containing an aromatic heterocyclic amine like bipyridyl" is not correct.

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