X-Ray Crystal Structures of the Ternary Complexes $[Cd(5'\text{-}UMP)(dpa)(H_2O)_2]_n$ (5′-UMP=uridine 5′-phosphate, dpa=2,2′-dipyridylamine): Metal Ion Bridged Stacking between Nucleotide Bases and Aromatic Amine Rings, and $[Cu(5'\text{-}CMP)(dpa)(H_2O)]_2$ (5′-CMP=cytidine 5′-phosphate): Phosphate Only Metal Bonding

By KATSUYUKI AOKI

(*The Institute of Physical and Chemical Research, Wako-shi, Saitama* 351, *Japan*)

Summary *X*-Ray crystal structure analyses of the ternary complexes $[Cd(5'\text{-}UMP)(dpa)(H_2O)_2]\cdot 5H_2O$ (5′-UMP = uridine 5′-phosphate and dpa = 2,2′-dipyridylamine) and $[Cu(5'\text{-}CMP)(dpa)(H_2O)]_2\cdot 5H_2O$ (5′-CMP = cytidine 5′-phosphate) have shown that the former is polymeric with a stacked structure between the uracil base and the dpa ligand *via* a metal–phosphate bridge, and the latter is dimeric with an unstacked structure involving metal bonding to the phosphate group only and not to the cystosine base of the nucleotide.

THE current interest in ternary metal ion–nucleotide complexes containing aromatic heterocyclic amines such as 2,2′-bipyridyl (bpy) can be attributed to the fact that these complexes can be regarded as simple models for the naturally occurring substrate–metal ion–aromatic amino acid centres found in proteins.[1] In such a ternary complex system, a metal ion is assumed to bridge the aromatic amine and the phosphate group of the nucleotide, thus stabilizing an intramolecular stacking interaction between the aromatic rings of the two constituents.[1] We have previously reported[2] on the existence of such a complex in the crystal structure of $[Cu(5'\text{-}AMPH)(bpy)(H_2O)]_2.(NO_3)_2.6H_2O$ [5′-AMPH = adenosine 5′-phosphate (protonated form)].

We report here the *X*-ray crystal structure of the ternary complexes $[Cd(5'\text{-}UMP)(dpa)(H_2O)_2]_n$ (5′-UMP = uridine 5′-phosphate and dpa = 2,2′-dipyridylamine), which provide additional evidence for such a metal ion bridged adduct having a stacked structure in ternary complex systems other than the AMP–bpy–Cu^{II} system, and of $[Cu(5'\text{-}CMP)(dpa)(H_2O)]_2$ (5′-CMP = cytidine 5′-phosphate), which is the first example of a metal–CMP complex in which only the phosphate group, but not the cytosine base, is involved in the metal co-ordination sphere. The structural change from an unstacked opened form found in the CMP complex to a stacked folded form in the UMP complex is discussed in terms of the conformational change of the phosphate backbone.

The UMP–dpa–Cd complex (colourless needles) was prepared from $Na_2(5'\text{-}UMP)$ (10^{-4} M), $Cd(NO_3)_2.4H_2O$ (3×10^{-4} M), and dpa (3×10^{-4} M) at pH *ca.* 7. *Crystal data*: $[Cd(5'\text{-}UMP)(dpa)(H_2O)_2]\cdot 5H_2O$, monoclinic, space group $P2_1$, a = 17·625(6), b = 6·812(4), c = 12·156(4) Å, β = 104·69(3)°, Z = 2, U = 1411·7 Å^3, D_m = 1·72, D_c =

1·722 g cm^{-3}. The current R is 0·043 for 2504 reflections [$2\theta \leqslant 50°$, $F_0 > 3\sigma(F_0)$; Rigaku diffractometer; Mo-K_α radiation].†

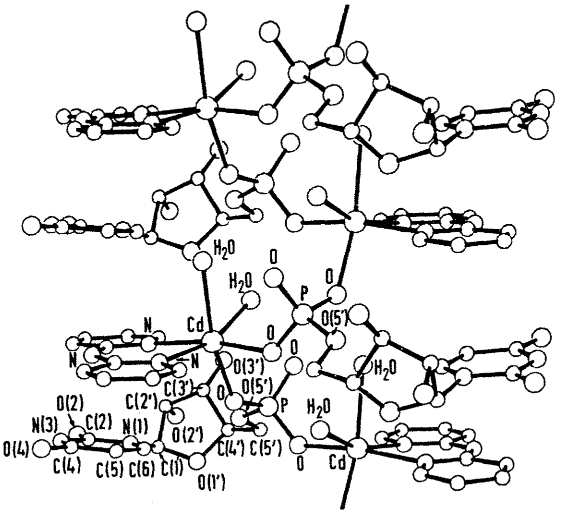
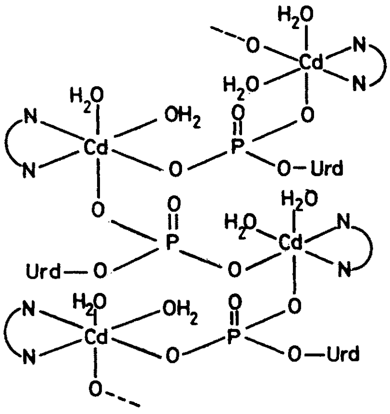


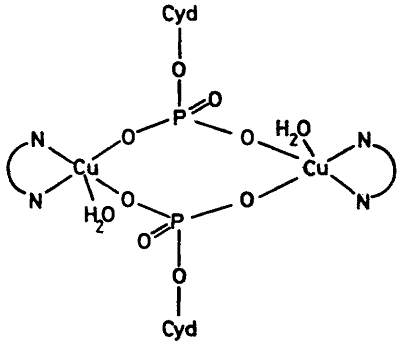
FIGURE 1. A segment of the polymeric [Cd(5'-UMP)(dpa)-$(H_2O)_2]_n$ structure, showing the stacking arrangement between the uracil bases and the dpa rings *via* direct or indirect metal ion bridges.

The complex forms a polymeric structure of composition $[Cd(5'\text{-}UMP)(dpa)(H_2O)_2]_n$ as shown in Figure 1 and the schematic representation in structure (**1**), where the Cd atom is bound, in a slightly distorted octahedral arrangement, to two phosphate oxygens of different nucleotide molecules [Cd–O$_{av}$ 2·253 Å], to two nitrogens of a bidentate dpa ligand [Cd–N$_{av}$ 2·331 Å], and to two water molecules [Cd–OH$_2$ 2·290 and 2·537 Å]. In turn, each phosphate group links two Cd atoms, thereby producing an infinite $[\text{–Cd–O–P–O–Cd–O–P–O–}]_n$ spiral from which uracil bases and dpa ligands project outwards and stack on each other.

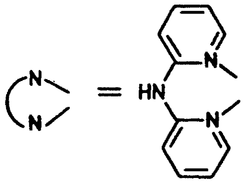
A feature of particular interest is the presence of the metal ion bridged stacking between the nucleotide bases and aromatic amine rings; the uracil base is stacked *via* a metal–phosphate bridge on one of the pyridyl rings of a dpa ligand (3·4 Å spacing), which in turn is also stacked, with no direct metal ion bridge, on an adjacent uracil base (3·3 Å spacing). The stacking is then of the –D–U–D–U– type (D = dpa, U = uracil base). The crystal structure is further stabilized by another type of –D–D– self stacking (3·4 Å spacing). However, there is no inter-base hydrogen bonding or uracil–uracil base stacking. The UMP molecule adopts the energetically preferred conformation: the *anti*^{3} base with $\chi_{CN}{}^3 = -165·2°$, C(3')-*endo*^{3} sugar pucker, and *gauche–gauche*^{3} conformation about the C(4')–C(5') bond.



(1)



(2)



The CMP–dpa–Cu complex (small green plates) was prepared from $Na_2(5'\text{-}CMP)$ (3×10^{-4} M), $Cu(NO_3)_2·2H_2O$ (9×10^{-4} M), and dpa (9×10^{-4} M) at pH *ca.* 4. *Crystal data*: $[Cu(5'\text{-}CMP)(dpa)(H_2O)]_2·5H_2O$, monoclinic, space group $P2_1$, a = 7·724(3), b = 18·221(6), c = 18·563(6) Å, β = 99·00(2)°, Z = 2, U = 2580·4 Å^3, D_m = 1·61, D_c = 1·593 g cm^{-3}. The current R is 0·103 for 1865 reflections [$2\theta \leqslant 40°$, $F_0 > 3\sigma(F_0)$; Rigaku diffractometer; Mo-K_α radiation].†

Figure 2 shows the dimeric molecular structure of the complex [see also schematic representation in structure (**2**)], where each Cu atom is in a distorted square-pyramidal environment, with the basal plane defined by the two phosphate oxygens of the different nucleotide molecules [Cu(1)–O$_{av}$ 1·97 Å and Cu(2)–O$_{av}$ 1·94 Å], and by a bidentate dpa ligand [Cu(1)–N$_{av}$ 1·97 Å and Cu(2)–N$_{av}$ 2·03 Å], and with the apical position occupied by a water molecule [Cu(1)–OH$_2$ 2·31 Å and Cu(2)–OH$_2$ 2·37 Å]. The two Cu atoms and the two phosphate groups then form an eight-membered puckered ring, which is stabilized by two

---

† The atomic co-ordinates for these structures 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 fhe full literature citation for this communication.

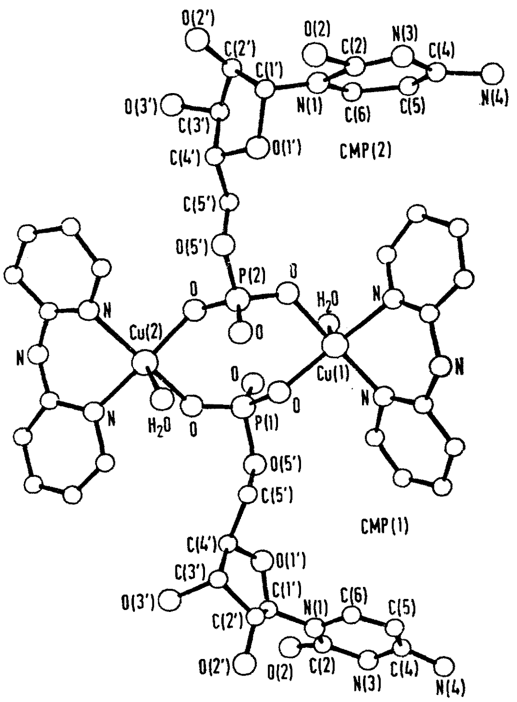
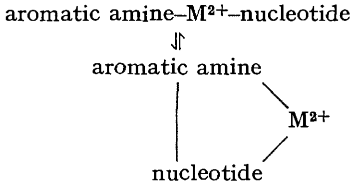


FIGURE 2. The molecular structure of the dimeric $[Cu(5'\text{-}CMP)(dpa)(H_2O)]_2$.

hydrogen bonds between the apical water molecules and the phosphate oxygens. The crystal lattice is significantly stabilized by predominant intermolecular self stacking between cytosine bases (3·8 Å spacing) and between dpa ligands (3·3, 3·4, 3·7, and 4·0 Å spacings) instead of intra- or inter-molecular base–dpa stacking. There is one inter-base hydrogen bond between the exocyclic groups N(4) and O(2) (3·02 Å). The two CMP molecules show a common *anti* conformation with $\chi_{CN} = -98°$ [CMP(1)] and $-125°$ [CMP(2)]. However, the two ribose rings exhibit the very rare C(1′)-*exo*[3] [CMP(1)] and C(4′)-*endo* [CMP(2)] pucker, and the conformation about the C(4′)–C(5′) bond is also rare: *gauche–trans*[3] in both nucleotides.

In the UMP–dpa–Cd complex the UMP nucleotide actually co-ordinates to a metal ion through the phosphate group only. However, this provides only partial evidence for the 'phosphate only' metal binding mode[4,5] that is believed to be typical for such ternary complexes, since the uracil base is a poor ligand owing primarily to the presence of a proton at the N(3) site at pH <*ca.* 9, as pointed out by Bau *et al.*[4,5] In contrast, the CMP–dpa–Cu complex provides convincing proof for this binding rule, because in all the six reported CMP–metal binary complexes,[6] the cytosine base unit is involved in the metal co-ordination. This 'phosphate only' binding, therefore, has now been substantiated for the four common nucleotides 5′-CMP, 5′-UMP,[4] 5′-AMP,[2] and 3′-GMP[5] (3′-GMP = guanosine 3′-phosphate), but not for inosine 5′-phosphate (5′-IMP).[7]‡

Molecular structures of ternary complexes adopting the 'phosphate only' metal bonding mode can be divided into two types, a stacked folded form found in the UMP–dpa–Cd and AMP–bpy–Cu[2] complexes, and an unstacked opened form in the CMP–dpa–Cu, UMP–dpa–Cu,[4] and GMP–phen–Cu[5] (phen = 1,10-phenanthroline) complexes. The type of complex formed is primarily governed by the conformation about the C(4′)–C(5′) bond of the phosphate group, *i.e.*, *gauche–gauche* and *gauche–trans* (or *trans–gauche*) conformations are responsible for folded and opened forms, respectively. This observation rationalizes the intramolecular equilibrium (1) which has been observed between an opened and a stacked form in solution.[1]


(1)

$$\begin{array}{c}\text{aromatic amine–M}^{2+}\text{–nucleotide}\\ \rightleftharpoons \\ \text{aromatic amine} \\ | \quad \diagdown \\ | \qquad \text{M}^{2+} \\ | \quad \diagup \\ \text{nucleotide}\end{array} \qquad (1)$$

(*Received, 28th March* 1979; *Com.* 321.)

---

‡ *Added in proof:* Recently this binding rule has also been confirmed for (5′-IMP) in another ternary complex, $[Cu(5'\text{-}IMP)(dpc)(H_2O)]_2\cdot 4H_2O$, R. W. Gellert, B. E. Fischer, and R. Bau, submitted for publication.

[1] C. F. Naumann and H. Sigel, *J. Amer. Chem. Soc.*, 1974, **96**, 2750.

[2] K. Aoki, *J. Amer. Chem. Soc.*, 1978, **100**, 7106.

[3] For a definition of these conformational terms, see W. Saenger, *Angew. Chem.*, 1973, **85**, 680.

[4] B. E. Fischer and R. Bau, *J.C.S. Chem. Comm.*, 1977, 272; *Inorg. Chem.*, 1978, **17**, 27.

[5] C.-Y. Wei, B. E. Fischer, and R. Bau, *J.C.S. Chem. Comm.*, 1978, 1053.

[6] R. W. Gellert and R. Bau, in 'Metal Ions in Biological Systems,' Vol. 8, ed. H. Sigel, Marcel Dekker, New York, in the press.

[7] K. Aoki, *J.C.S. Chem. Comm.*, 1977, 600.