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Coordination Sites in Nucleotides: X-Ray Crystal Structure of the Ternary Complex Copper(II)–Uridine 5′-Monophosphate–2,2′-Dipyridylamine

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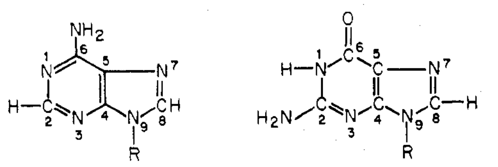
The preparation and molecular structure of the dimeric species $[Cu(5'\text{-}UMP)(dpa)(H_2O)]_2 \cdot 5H_2O$ are reported where 5′-UMP represents uridine 5′-monophosphate and dpa represents 2,2′-dipyridylamine. The most interesting feature is that the nucleotide coordinates to the metal ion through the phosphate group only, while the uracil base is far removed from the Cu^{2+} coordination sphere. This is the first crystallographic evidence that a nucleotide complex can exist without direct metal–base bonding, and also the first crystal structure determination of a metal–UMP complex. The coordination sphere of the Cu^{2+} ions is square pyramidal, with the following ligands: two oxygen atoms from different phosphate groups, two nitrogen atoms of the dipyridylamine ligand, and one water molecule in an axial position. The copper ions are bridged by two phosphate groups, an arrangement which gives rise to an eight-membered ring. The two sugar rings have very unusual puckering modes, namely C(2′)-exo and O(1′)-endo, respectively. The two subunits within a dimer differ also in their torsion angles around the glycosidic C(1′)–N(1) bond: one has an anti conformation while the other one shows an unusual syn conformation. The uracil bases as well as the dipyridylamines take part in intermolecular stacking interactions in the crystal. Other intermolecular forces are hydrogen bridges between most of the polar groups. The coordination behavior of UMP in this structure is compared to the coordination of other nucleotides in metal ion complexes, and the possible influence of the second ligand (dipyridylamine) within the ternary complex is discussed. Crystallographic details for $[Cu(UMP)(dpa)(H_2O)]_2 \cdot 5H_2O$: space group $P2_1$ (No. 4), $a = 7.739$ (3), $b = 18.248$ (6), $c = 17.473$ (7) Å, $\beta = 90.04$ (2)°, $V = 2467.6$ Å^3, $Z = 2$. The final agreement factors for data with $I > 3\sigma$ are $R_F = 0.086$ and $R_{wF} = 0.089$ for 2692 reflections.

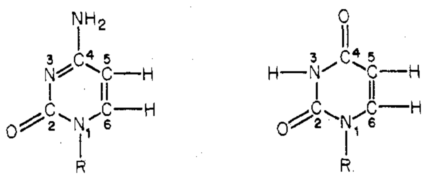
Introduction

The interaction of metal ions with nucleotides has attracted a lot of interest during the last few years, either with respect to the action of metalloenzymes that use a nucleotide as a coenzyme[1] or in relation with the action of Pt(II) complexes as anticancer drugs.[2] As the different nucleotides have many different potential binding sites to metal ions, their coordination behavior is not easily predictable and is often controversial in the literature. Besides the atoms of the nucleoside bases (especially N(1) and N(7) of the purines, N(3) of the pyrimidines, and the oxygen atom of the carbonyl group), there is also the phosphate group as a possible binding site.[3,4] Even the hydroxyl groups of the ribose have been shown to coordinate to metal atoms.[5] There has arisen in the last few years especially a discrepancy between the structures that were determined by x-ray crystallography[3] and the interpretations of the results of metal ion nucleotide investigations in solution.[4] This is particularly true for complexes with purine nucleotides, where the crystallographic results often show the purine to be coordinated through the N(7) position to the metal ion, supported by hydrogen-bonding interactions from coordinated water molecules to the phosphate group of the nucleotide and the functional group in the 6 position of the base.[6] Solution studies, in contrast, show direct phosphate–metal coordination together with N(7)–metal coordination at the pH values around 7,[7] with the phosphate coordination being the dominant influence.[4] Additionally, it was shown that in solution the coordination behavior of a nucleotide can change in going from a binary to a ternary complex,[8] in which one additional ligand like 2,2′-bipyridine (bpy)[9] is introduced. In such a ternary complex, the solution structure of the predominant species can be described in the following way: the metal ion is coordinated by the phosphate group of the nucleotide and the nitrogen atoms of the bipyridyl ligand, while the base of the nucleotide does not interact with the metal but instead forms a stacking adduct with the aromatic rings of bipyridyl.[8b] This led us to investigate by x-ray methods the structure of a ternary nucleotide complex, in this case copper(II)–uridine 5′-monophosphate–2,2′-dipyridylamine.[10]


adenine, R = H
adenosine, R = ribose

guanine, R = H
guanosine, R = ribose

purines


cytosine, R = H
cytidine, R = ribose

uracil, R = H
uridine, R = ribose

pyrimidines

Table I. Crystal Data for $[Cu(5'\text{-}UMP)(dpa)(H_2O)]_2 \cdot 5H_2O$

Space Group: $P2_1$ (Monoclinic)

$a = 7.739$ (3) Å
$b = 18.248$ (6) Å
$c = 17.473$ (7) Å
$\beta = 90.04$ (2)°
$V = 2467.6$ Å^3
$Z = 2$
μ(Mo Kα) = 10.6 cm^{-1}

Mol wt 1239.5
$\rho_{calcd} = 1.67$ g/cm^3
$\rho_{measd} = 1.65$ g/cm^3 by flotation in ethanol/bromoform
$R_F = 0.086$
$R_{wF} = 0.089$ for 2692 reflections with $I > 3\sigma(I)$

Experimental Section

The crystal used for the structure determination was prepared by vapor diffusing[11a] an aqueous solution of Cu^{2+} ($Cu(NO_3)_2 \cdot 3H_2O$, Mallinckrodt), disodium uridine 5′-monophosphate ($Na_2(5'\text{-}UMP) \cdot 6H_2O$, Sigma), and 2,2′-dipyridylamine (dpa, Aldrich), each at 5×10^{-3} M, against *tert*-butyl alcohol. The pH of the aqueous solution had been adjusted earlier with NaOH to a value of 7. Small green plates formed after about 5 weeks. The crystals were filtered and washed with cold water.

X-Ray Diffraction Data. A thin plate with dimensions 0.33 × 0.80 × 0.025 mm was mounted along its long axis (b^*) on a glass fiber. Preliminary precession photographs were consistent with a space group of either $P2_1$ or $P2_1/m$, but since we have an optically active ribose in our compound we could exclude the latter space group, which contains a mirror plane. The unit-cell parameters and other crystallographic details are given in Table I. Data were collected in the *hkl*, $hk\bar{l}$ quadrant on a Nonius CAD-3 diffractometer with Zr-filtered Mo Kα radiation by the $\theta/2\theta$ scan technique up to a 2θ limit of 45°.

0020-1669/78/1317-0027$01.00/0

Table II

Final Atomic Parameters for $[Cu(5'\text{-}UMP)(dpa)(H_2O)]_2 \cdot 5H_2O$

Atom	x	y	z	B^a	Atom	x	y	z	B^a
Cu(1)	0.4353 (3)	0.2293 (1)	−0.0550 (1)	*b*	Cu(2)	0.0911 (3)	0	0.0179 (1)	*b*
P(1)	0.4286 (6)	0.0932 (2)	0.0625 (2)	*b*	P(2)	0.1171 (6)	0.1346 (3)	−0.0971 (3)	*b*
C(12)	0.523 (3)	0.293 (1)	0.353 (1)	3.9 (4)	C(22)	−0.278 (3)	0.295 (1)	−0.447 (1)	4.3 (5)
C(14)	0.799 (3)	0.354 (1)	0.344 (1)	4.3 (5)	C(24)	−0.088 (3)	0.399 (1)	−0.462 (1)	4.9 (5)
C(15)	0.887 (3)	0.288 (1)	0.367 (1)	3.9 (4)	C(25)	0.073 (3)	0.356 (1)	−0.448 (1)	4.6 (5)
C(16)	0.793 (2)	0.228 (1)	0.378 (1)	3.5 (4)	C(26)	0.038 (3)	0.283 (1)	−0.431 (1)	3.9 (4)
C(11′)	0.531 (2)	0.155 (1)	0.383 (1)	3.1 (4)	C(21′)	−0.149 (2)	0.179 (1)	−0.398 (1)	3.3 (4)
C(12′)	0.343 (2)	0.152 (1)	0.404 (1)	2.9 (4)	C(22′)	−0.055 (2)	0.118 (1)	−0.442 (1)	3.3 (4)
C(13′)	0.246 (2)	0.144 (1)	0.327 (1)	3.0 (4)	C(23′)	−0.016 (2)	0.064 (1)	−0.376 (1)	2.9 (3)
C(14′)	0.374 (2)	0.110 (1)	0.273 (1)	3.4 (4)	C(24′)	−0.071 (2)	0.105 (1)	−0.305 (1)	2.6 (3)
C(15′)	0.378 (2)	0.145 (1)	0.197 (1)	3.3 (4)	C(25′)	0.076 (2)	0.102 (1)	−0.241 (1)	2.9 (4)
C(112)	0.534 (2)	0.371 (1)	0.015 (1)	2.3 (3)	C(212)	−0.065 (2)	−0.139 (1)	−0.031 (1)	2.1 (3)
C(113)	0.587 (3)	0.417 (1)	0.073 (1)	3.1 (4)	C(213)	−0.136 (2)	−0.187 (1)	−0.086 (1)	3.7 (4)
C(114)	0.674 (3)	0.386 (1)	0.135 (1)	3.9 (4)	C(214)	−0.197 (3)	−0.161 (1)	−0.156 (1)	4.1 (4)
C(115)	0.705 (2)	0.313 (1)	0.136 (1)	3.8 (4)	C(215)	−0.199 (3)	−0.087 (1)	−0.165 (1)	3.6 (4)
C(116)	0.645 (2)	0.271 (1)	0.075 (1)	3.2 (4)	C(216)	−0.126 (2)	−0.041 (1)	−0.110 (1)	3.2 (4)
C(122)	0.434 (2)	0.378 (1)	−0.120 (1)	3.0 (4)	C(222)	0.030 (2)	−0.137 (1)	0.103 (1)	2.6 (3)
C(123)	0.408 (2)	0.432 (1)	−0.178 (1)	3.3 (4)	C(223)	0.043 (2)	−0.183 (1)	0.167 (1)	3.8 (4)
C(124)	0.402 (3)	0.407 (1)	−0.253 (1)	4.1 (5)	C(224)	0.074 (3)	−0.150 (1)	0.237 (1)	4.8 (5)
C(125)	0.422 (3)	0.335 (1)	−0.269 (1)	4.3 (5)	C(225)	0.089 (3)	−0.075 (1)	0.242 (1)	3.3 (4)
C(126)	0.452 (2)	0.286 (1)	−0.211 (1)	3.3 (4)	C(226)	0.076 (2)	−0.035 (1)	0.178 (1)	2.6 (3)
N(11)	0.612 (2)	0.229 (1)	0.376 (1)	3.2 (3)	N(21)	−0.131 (2)	0.254 (1)	−0.430 (1)	3.6 (3)
N(13)	0.625 (2)	0.351 (1)	0.342 (1)	4.0 (4)	N(23)	−0.240 (2)	0.369 (1)	−0.459 (1)	4.2 (4)
N(111)	0.550 (2)	0.297 (1)	0.014 (1)	2.4 (3)	N(211)	−0.056 (2)	−0.068 (1)	−0.045 (1)	2.1 (3)
N(121)	0.444 (2)	0.306 (1)	−0.137 (1)	2.4 (3)	N(221)	0.048 (2)	−0.064 (1)	0.107 (1)	3.2 (3)
N(131)	0.450 (2)	0.404 (1)	−0.045 (1)	2.7 (3)	N(231)	−0.006 (2)	−0.170 (1)	0.032 (1)	3.1 (8)
O(1)	0.375 (2)	0.166 (1)	0.028 (1)	2.7 (2)	O(4)	0.286 (1)	0.174 (1)	−0.122 (1)	2.8 (2)
O(2)	0.286 (2)	0.040 (1)	0.074 (1)	3.0 (3)	O(5)	0.152 (1)	0.058 (1)	−0.072 (1)	2.8 (2)
O(3)	0.589 (2)	0.060 (1)	0.024 (1)	2.9 (2)	O(6)	0.004 (1)	0.178 (1)	−0.043 (1)	2.1 (2)
O(11)	0.661 (2)	0.155 (1)	−0.088 (1)	3.7 (3)	O(21)	−0.091 (2)	0.089 (1)	0.071 (1)	3.2 (3)
O(12)	0.368 (2)	0.292 (1)	0.342 (1)	5.6 (4)	O(22)	−0.416 (2)	0.272 (1)	−0.448 (1)	4.4 (3)
O(14)	0.876 (2)	0.415 (1)	0.329 (1)	5.3 (4)	O(24)	−0.068 (2)	0.469 (1)	−0.466 (1)	6.2 (4)
O(11′)	0.547 (2)	0.119 (1)	0.308 (1)	3.3 (3)	O(21′)	−0.085 (2)	0.181 (1)	−0.325 (1)	3.7 (3)
O(12′)	0.326 (2)	0.085 (1)	0.448 (1)	4.8 (3)	O(22′)	−0.168 (2)	0.090 (1)	−0.499 (1)	4.9 (3)
O(13′)	0.098 (2)	0.097 (1)	0.338 (1)	4.2 (3)	O(23′)	−0.124 (2)	0.000 (1)	−0.382 (1)	4.5 (3)
O(15′)	0.494 (2)	0.110 (1)	0.148 (1)	3.0 (3)	O(25′)	0.007 (1)	0.131 (1)	−0.175 (1)	2.9 (2)
O(301)	0.527 (3)	−0.037 (1)	0.487 (1)	7.5 (5)	O(304)	0.520 (3)	0.077 (1)	−0.206 (1)	8.2 (5)
O(302)	−0.461 (2)	−0.011 (1)	−0.331 (1)	6.8 (4)	O(305)	−0.642 (3)	0.160 (1)	−0.393 (1)	8.5 (7)
O(303)	−0.130 (2)	0.136 (1)	0.224 (1)	5.4 (4)					

Anisotropic Thermal Parameters[c]

Atom	$10^4\beta_{11}$	$10^4\beta_{22}$	$10^4\beta_{33}$	$10^4\beta_{12}$	$10^4\beta_{13}$	$10^4\beta_{23}$
Cu(1)	97 (4)	8 (1)	18 (1)	7 (3)	−8 (3)	−3 (1)
P(1)	87 (9)	12 (1)	16 (2)	7 (6)	−6 (6)	−1 (2)
Cu(2)	93 (4)	9 (1)	18 (1)	−13 (3)	−7 (3)	3 (1)
P(2)	114 (9)	14 (2)	19 (2)	10 (6)	1 (6)	1 (3)

[a] Isotropic temperature factor, in units of Å². [b] Anisotropic parameters listed at bottom of table. [c] The form of the thermal ellipsoids is $\exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + \beta_{12}hk + \beta_{13}hl + \beta_{23}kl)]$.

The diffraction pattern was in general quite weak and did not extend much beyond $2\theta = 40°$. A scan speed of 10°/min was used,[11b] with the scan defined as $\Delta\theta = (1.2 + 0.1 \tan \theta)°$. Each reflection was scanned between 2 and 8 times, depending upon its intensity. Background counts were taken at the beginning and at the end of each scan. Zirconium foil attenuators were automatically inserted to prevent the count rate from exceeding 2500 counts/s.[11b] As a check on the stability of the diffractometer and the crystal, the (4,0,0), (0,$\bar{6}$,0), and (0,0,$\bar{10}$) reflections were measured at 60-reflection intervals. An abrupt steplike drop in intensity during data collection, observed in all three check reflections in the same way, could be attributed to an instability in the diffractometer. An empirical correction for that intensity loss of about 15% was applied to the affected data. Subsequent data processing reduced the 4394-reflection data set into 2692 independent reflections with $I > 3\sigma_I$.[11c] The standard deviation of each intensity reading, F_o^2, was estimated using the expression $\sigma(F_o^2) = ((\text{peak} + \text{background counts}) + (0.04)^2(\text{net intensity})^2)^{1/2}$. Values of F_o^2 were corrected for Lorentz and polarization effects. An empirical absorption correction curve[11d] was applied, based on the observation that the intensity of an axial reflection (at $\chi = 90°$) showed a variation of about 15% with spindle angle ϕ.

Solution and Refinement of the Structure. The structure was solved with conventional heavy-atom methods: the coordinates of two copper atoms and one phosphorus atom were obtained from a Patterson synthesis, and the other nonhydrogen atoms were located from a series of difference Fourier maps.[12] Since in space group $P2_1$ the origin along y is not fixed, we set the y coordinate for one copper atom to zero and all the other y coordinates were defined relative to this position. The correct optical form could easily be identified because of the known absolute configuration of D-ribose. Subsequent cycles of least-squares refinement, with anisotropic thermal parameters for the Cu and P atoms and isotropic thermal parameters for the C, O, and N atoms, resulted in the successful convergence of all atomic parameters (a total of 329 variables). In the least-squares procedure, the parameters of the dimeric molecule were split into two equal sets and refined in two different matrices. The electron density of one oxygen atom of a water of crystallization was lower than for the others, and its occupancy factor refined to 0.78. Calculated hydrogen positions (for the carbon-bonded hydrogens and the N(3) hydrogen) were included but not refined in the last cycle of refinement with a temperature factor of 5.0 Å². The final agreement factors[13] are $R_F = 0.086$ and $R_{wF} = 0.089$ for data with $I > 3\sigma_I$ (2692 reflections).

Results and Discussion

Description of the Molecular Structure. Figure 1 shows one unit of the dimeric molecule with the numbering system that

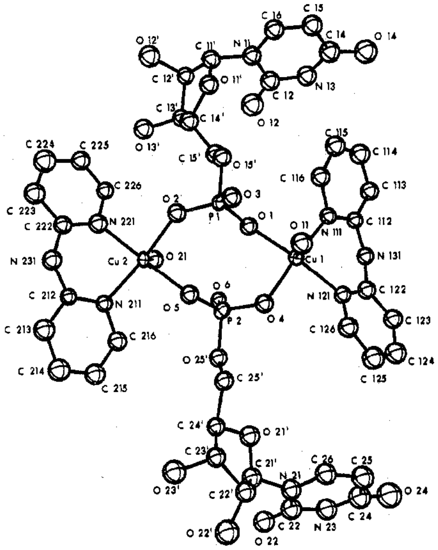


Figure 1. ORTEP plot of the $[Cu(5'\text{-}UMP)(dpa)(H_2O)]_2$ molecule. Note that the two halves of the molecule appear rather similar even though they are not crystallographically related. The numbering scheme used for the nucleotide units is equivalent in the last digit to standard nucleotide notation. For example, N(13) and N(23) both refer to the N(3) atom of uracil, while C(11′) and C(21′) correspond to the C(1′) atom of ribose. The atoms in all molecular plots in this paper are shown as 50% probability ellipsoids.

is used throughout this paper.[14] The positional and thermal parameters with their estimated standard deviations are given in Table II. Bond distances and angles are listed in Tables III and IV. A table of observed and calculated structure factors is available (supplementary material). Despite the fact that there is no crystallographic symmetry between the two units within a dimer, there are a lot of similarities between them: both copper ions have a square-pyramidal coordination sphere built up by the two nitrogen atoms of dpa, two oxygen atoms from phosphate groups, and a water molecule in the axial position. The ribose groups point away from the center of the molecule and bring the uracil bases to positions far removed from the copper atoms. Unlike the crystal structures of all other metal ion nucleotide complexes,[6,15–17] there is no interaction at all between the copper ions and the bases of the nucleotide, uracil, in this molecule. Besides the similarity between the two subunits in this dimer, there is a difference mainly in the sugar geometry and in the sugar–base linkage. We will discuss the individual components of the complex separately.

Uracil Bases. The two uracil bases do not differ much in their geometry from what is found in various uracil derivatives, where the base is not coordinated to a metal ion.[18] The bases are reasonably flat, as can be seen from the results in Table V. It is noteworthy that C(1′), the ribose carbon atom attached to N(1), is bent out of the plane toward the sugar residue. It was actually observed earlier, in structures of uncomplexed nucleosides and nucleotides, that the largest deviations from the ring plane usually occur with exocyclic substituent atoms.[19,21]

Ribose Groups. The two ribose rings in this structure show very unusual geometries, conformations only rarely observed in nucleoside or nucleotide structures.[19,20] The angles that characterize the puckering of the ribose rings and the geometry of the sugar relative to the base and the phosphate group are given in Table VI. Ribose C(21′)–C(25′) shows an O(1′)-endo[21] puckering conformation (Figure 2a). To our knowledge, such a conformation for a nucleotide or nucleoside was reported only once before: namely, in the x-ray structure of dihydrothymidine.[22] The rotation around the glycosyl linkage for this nucleotide base is anti,[23] which is expected for pyrimidine nucleotides.[25] While the conformation around the

Table III. Bond Distances in $[Cu(5'\text{-}UMP)(dpa)(H_2O)]_2{\cdot}5H_2O$

Bond	Å	Bond	Å
Cu(1)–O(1)	1.92 (1)	Cu(2)–O(2)	1.94 (1)
Cu(1)–O(4)	1.93 (1)	Cu(2)–O(5)	1.95 (1)
Cu(1)–O(11)	2.29 (1)	Cu(2)–O(21)	2.35 (1)
Cu(1)–N(111)	1.95 (1)	Cu(2)–N(211)	2.01 (1)
Cu(1)–N(121)	2.00 (1)	Cu(2)–N(221)	1.98 (1)
P(1)–O(1)	1.51 (1)	P(2)–O(4)	1.55 (1)
P(1)–O(2)	1.49 (1)	P(2)–O(5)	1.50 (1)
P(1)–O(3)	1.54 (1)	P(2)–O(6)	1.52 (1)
P(1)–O(15′)	1.61 (1)	P(2)–O(25′)	1.61 (1)
C(11′)–C(12′)	1.50 (3)	C(21′)–C(22′)	1.53 (3)
C(12′)–C(13′)	1.55 (2)	C(22′)–C(23′)	1.54 (2)
C(13′)–C(14′)	1.50 (3)	C(23′)–C(24′)	1.51 (2)
C(14′)–C(15′)	1.48 (3)	C(24′)–C(25′)	1.60 (2)
C(11′)–O(11′)	1.45 (2)	C(21′)–O(21′)	1.38 (2)
C(14′)–O(11′)	1.49 (2)	C(24′)–O(21′)	1.43 (2)
C(12′)–O(12′)	1.46 (2)	C(22′)–O(22′)	1.43 (2)
C(13′)–O(13′)	1.44 (2)	C(23′)–O(23′)	1.43 (2)
C(15′)–O(15′)	1.40 (2)	C(25′)–O(25′)	1.38 (2)
C(11′)–N(11)	1.50 (2)	C(21′)–N(21)	1.49 (3)
N(11)–C(12)	1.41 (3)	N(21)–C(22)	1.39 (3)
C(12)–O(12)	1.21 (3)	C(22)–O(22)	1.15 (3)
C(12)–N(13)	1.34 (3)	C(22)–N(23)	1.38 (3)
N(13)–C(14)	1.35 (3)	N(23)–C(24)	1.30 (3)
C(14)–O(14)	1.30 (3)	C(24)–O(24)	1.28 (3)
C(14)–C(15)	1.43 (3)	C(24)–C(25)	1.50 (3)
C(15)–C(16)	1.32 (3)	C(25)–C(26)	1.38 (3)
C(16)–N(11)	1.40 (2)	C(26)–N(21)	1.41 (3)
N(111)–C(112)	1.36 (2)	N(211)–C(212)	1.32 (2)
C(112)–C(113)	1.37 (2)	C(212)–C(213)	1.42 (2)
C(113)–C(114)	1.38 (3)	C(213)–C(214)	1.39 (3)
C(114)–C(115)	1.37 (3)	C(214)–C(215)	1.37 (3)
C(115)–C(116)	1.38 (3)	C(215)–C(216)	1.39 (3)
C(116)–N(111)	1.38 (2)	C(216)–N(211)	1.36 (2)
C(112)–N(131)	1.36 (2)	C(212)–N(231)	1.32 (2)
N(121)–C(122)	1.35 (2)	N(221)–C(222)	1.35 (2)
C(122)–C(123)	1.41 (3)	C(222)–C(223)	1.40 (3)
C(123)–C(124)	1.39 (3)	C(223)–C(224)	1.37 (3)
C(124)–C(125)	1.35 (3)	C(224)–C(225)	1.39 (3)
C(125)–C(126)	1.36 (3)	C(225)–C(226)	1.33 (2)
C(126)–N(121)	1.34 (2)	C(226)–N(221)	1.37 (2)
C(122)–N(131)	1.40 (2)	C(222)–N(231)	1.40 (2)

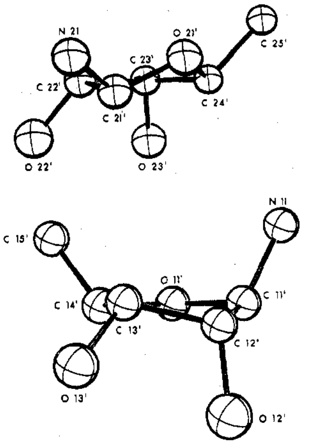


Figure 2. (a, top) Sugar conformation of ribose C(21′)–C(25′), looking parallel to the plane formed by the atoms C(22′), C(23′), and C(24′). The O(1′)-endo puckering shown here is also evident from the torsion angles τ_0–τ_4 and the best plane calculation given in Table VI. O(21′) is displaced from the plane of the other four atoms of the ring by 0.54 Å toward the same side of C(25′), while the other atoms deviate only by about 0.04 Å from the plane. (b, bottom) Sugar conformation of ribose C(11′)–C(15′), looking parallel to the plane formed by the atoms C(11′), O(11′), and C(14′). This plot shows unambiguously the C(2′)-exo conformation of this ring, as C(12′) is removed by 0.38 Å out of the plane of the other atoms towards the other side of C(15′) (Table VI).

Table IV. Bond Angles in [Cu(5′-UMP)(dpa)(H_2O)]$_2$·5H_2O

Bond	Angle, deg	Bond	Angle, deg
N(111)-Cu(1)-N(121)	88.9 (6)	N(211)-Cu(2)-N(221)	89.7 (5)
N(111)-Cu(1)-O(1)	91.6 (5)	N(221)-Cu(2)-O(2)	87.4 (6)
N(111)-Cu(1)-O(4)	169.5 (6)	N(211)-Cu(2)-O(5)	174.8 (6)
N(111)-Cu(1)-O(11)	100.9 (5)	N(211)-Cu(2)-O(21)	89.7 (5)
N(121)-Cu(1)-O(1)	166.6 (5)	N(221)-Cu(2)-O(2)	161.3 (5)
N(121)-Cu(1)-O(4)	87.4 (5)	N(221)-Cu(2)-O(5)	91.8 (5)
N(121)-Cu(1)-O(11)	102.0 (5)	N(221)-Cu(2)-O(21)	107.9 (5)
O(1)-Cu(1)-O(4)	89.8 (5)	O(2)-Cu(2)-O(5)	90.9 (5)
O(1)-Cu(1)-O(11)	91.0 (5)	O(2)-Cu(2)-O(21)	90.3 (5)
O(4)-Cu(1)-O(11)	89.6 (5)	O(5)-Cu(2)-O(21)	95.2 (5)
Cu(1)-O(1)-P(1)	139.8 (7)	Cu(2)-O(5)-P(2)	134.2 (7)
Cu(1)-O(4)-P(2)	125.1 (6)	Cu(2)-O(2)-P(1)	139.1 (8)
O(1)-P(1)-O(2)	114.9 (7)	O(4)-P(2)-O(5)	111.4 (7)
O(1)-P(1)-O(3)	113.2 (7)	O(4)-P(2)-O(6)	114.5 (7)
O(1)-P(1)-O(15′)	107.1 (7)	O(4)-P(2)-O(25′)	103.0 (6)
O(2)-P(1)-O(3)	113.7 (7)	O(5)-P(2)-O(6)	114.7 (6)
O(2)-P(1)-O(15′)	103.3 (7)	O(5)-P(2)-O(25′)	107.9 (7)
O(3)-P(1)-O(15′)	103.2 (7)	O(6)-P(2)-O(25′)	104.2 (6)
P(1)-O(15′)-C(15′)	117 (1)	P(2)-O(25′)-C(25′)	121 (1)
C(11′)-C(12′)-C(13′)	105 (1)	C(21′)-C(22′)-C(23′)	101 (1)
C(11′)-C(12′)-O(12′)	104 (1)	C(21′)-C(22′)-O(22′)	108 (1)
O(12′)-C(12′)-C(13′)	109 (1)	O(22′)-C(22′)-C(23′)	114 (1)
C(12′)-C(13′)-O(13′)	109 (1)	C(22′)-C(23′)-O(23′)	111 (1)
C(12′)-C(13′)-C(14′)	105 (1)	C(22′)-C(23′)-O(23′)	104 (1)
O(13′)-C(13′)-C(14′)	111 (1)	O(23′)-C(23′)-C(24′)	107 (1)
C(13′)-C(14′)-C(15′)	113 (2)	C(23′)-C(24′)-C(25′)	111 (1)
C(13′)-C(14′)-O(11′)	107 (1)	C(23′)-C(24′)-O(21′)	108 (1)
C(14′)-C(15′)-O(15′)	111 (2)	C(24′)-C(25′)-O(25′)	107 (1)
C(15′)-C(14′)-O(11′)	107 (1)	C(25′)-C(24′)-O(21′)	105 (1)
C(14′)-O(11′)-C(11′)	110 (1)	C(24′)-O(21′)-C(21′)	103 (1)
O(11′)-C(11′)-C(12′)	107 (1)	O(21′)-C(21′)-C(22′)	108 (1)
O(11′)-C(11′)-N(11)	107 (1)	O(21′)-C(21′)-N(21)	107 (1)
C(12′)-C(11′)-N(11)	117 (1)	C(22′)-C(21′)-N(21)	116 (1)
C(12)-N(11)-C(16)	120 (2)	C(22)-N(21)-C(26)	123 (2)
C(11′)-N(11)-C(12)	124 (1)	C(21′)-N(21)-C(22)	120 (2)
C(11′)-N(11)-C(16)	114 (2)	C(21′)-N(21)-C(26)	116 (1)
N(11)-C(12)-O(12)	121 (2)	N(21)-C(22)-O(22)	124 (2)
N(11)-C(12)-N(13)	114 (2)	N(21)-C(22)-N(23)	113 (2)
O(12)-C(12)-N(13)	124 (2)	O(22)-C(22)-N(23)	123 (2)
C(12)-N(13)-C(14)	127 (2)	C(22)-N(23)-C(24)	128 (2)
N(13)-C(14)-O(14)	119 (2)	N(23)-C(24)-O(24)	123 (2)
N(13)-C(14)-C(15)	117 (2)	N(23)-C(24)-C(25)	121 (2)
O(14)-C(14)-C(15)	124 (2)	O(24)-C(24)-C(25)	115 (2)
C(14)-C(15)-C(16)	118 (2)	C(24)-C(25)-C(26)	112 (2)
C(15)-C(16)-N(11)	123 (2)	C(25)-C(26)-N(21)	123 (2)
Cu(1)-N(111)-C(112)	126 (1)	Cu(2)-N(211)-C(212)	122 (1)
Cu(1)-N(111)-C(116)	120 (1)	Cu(2)-N(211)-C(216)	117 (1)
C(116)-N(111)-C(112)	113 (1)	C(216)-N(211)-C(212)	120 (1)
N(111)-C(112)-C(113)	125 (2)	N(211)-C(212)-C(213)	120 (1)
N(111)-C(112)-N(131)	118 (1)	N(211)-C(212)-N(231)	124 (1)
N(131)-C(112)-C(113)	117 (1)	N(231)-C(212)-C(213)	116 (2)
C(112)-C(113)-C(114)	119 (2)	C(212)-C(213)-C(214)	121 (2)
C(113)-C(114)-C(115)	119 (2)	C(213)-C(214)-C(215)	115 (2)
C(114)-C(115)-C(116)	118 (2)	C(214)-C(215)-C(216)	122 (2)
C(115)-C(116)-N(111)	125 (2)	C(215)-C(216)-N(211)	121 (2)
Cu(1)-N(121)-C(122)	122 (1)	Cu(2)-N(221)-C(222)	124 (1)
Cu(1)-N(121)-C(126)	120 (1)	Cu(2)-N(221)-C(226)	117 (1)
C(126)-N(121)-C(122)	118 (1)	C(226)-N(221)-C(222)	117 (1)
N(121)-C(122)-C(123)	122 (2)	N(221)-C(222)-C(223)	123 (2)
N(121)-C(122)-N(131)	121 (1)	N(221)-C(222)-N(231)	119 (2)
N(131)-C(122)-C(123)	117 (2)	N(231)-C(222)-C(223)	118 (2)
C(122)-C(123)-C(124)	117 (2)	C(222)-C(223)-C(224)	118 (2)
C(123)-C(124)-C(125)	121 (2)	C(223)-C(224)-C(225)	120 (2)
C(124)-C(125)-C(126)	119 (2)	C(224)-C(225)-C(226)	119 (2)
C(125)-C(126)-N(121)	123 (2)	C(225)-C(226)-N(221)	123 (2)
C(112)-N(131)-C(122)	128 (1)	C(212)-N(231)-C(222)	129 (1)

exocyclic C(5′)–O(5′) bond is gauche,trans for both ribose groups, the puckering of the ring and the conformation about the glycosidic C(1′)–N(1) bond are different.

The ribose characterized by C(11′)–C(15′) shows again a rather unusual puckering mode, namely C(2′)-exo (Figure 2b). This can be seen again from the best plane calculation and the torsion angles τ_0–τ_4 in Table VI. This conformation was already shown to occur in the ribose group of vitamin B_{12}.[26] Sundaralingam found the same C(2′)-exo configuration in the structure of α-pseudouridine and noted that this conformation, while rarely observed in β-nucleosides, is actually quite common in the α-nucleosides.[27] The conformation of the angle between the sugar plane and the uracil plane is syn, again an exceptional case for a pyrimidine nucleotide,[25] but one which is consistent with the other nucleotides that show a C(2′)-exo sugar puckering.[26,27]

Table V. Displacement (in Å)[a] of the Atoms of the Uracil and Dipyridylamine Planes

Planes 1 and 2: Least-Squares Planes of the Uracil Groups

Plane 1: direction cosines (−0.0886, +0.2641, +0.9605)		Plane 2: direction cosines (−0.0782, −0.1717, −0.9821)	
N(11)	0.04	N(21)	−0.05
C(12)	0.03	C(22)	0.01
O(12)	−0.06	O(22)	0.01
N(13)	0.05	N(23)	0.01
C(14)	−0.01	C(24)	0.07
O(14)	−0.02	O(24)	−0.08
C(15)	0.00	C(25)	0.06
C(16)	−0.04	C(26)	−0.03
C(11′)	−0.14[b]	C(21′)	−0.38[b]

Planes 3 and 4: Least-Squares Planes of the Pyridine Rings around Cu(1)

Plane 3: direction cosines (+0.8648, +0.1311, −0.4853)		Plane 4: direction cosines (+0.9901, +0.1263, −0.0623)	
N(111)	−0.04	N(121)	−0.05
C(112)	0.03	C(122)	0.02
C(113)	−0.03	C(123)	0.01
C(114)	−0.01	C(124)	−0.01
C(115)	0.00	C(125)	−0.01
C(116)	0.02	C(126)	0.04
N(131)	0.05[b]	N(131)	0.12[b]
Cu(1)	−0.38[b]	Cu(1)	−0.38[b]

Planes 5 and 6: Least-Squares Planes of the Pyridine Rings around Cu(2)

Plane 5: direction cosines (+0.9858, −0.0842, −0.1457)		Plane 6: direction cosines (+0.8983, −0.0894, −0.4307)	
N(211)	0.03	N(221)	0.01
C(212)	−0.02	C(222)	0.00
C(213)	−0.02	C(223)	0.00
C(214)	0.04	C(224)	0.01
C(215)	−0.03	C(225)	−0.01
C(216)	−0.01	C(226)	0.00
N(231)	−0.03[b]	N(231)	−0.05[b]
Cu(2)	0.47[b]	Cu(2)	0.46[b]

[a] Standard deviations of the positions of the C, N, and O atoms are estimated to be around 0.01 Å. [b] Atoms which were included in the plane calculation with zero weight.

2,2′-Dipyridylamine Ligands. All four pyridine rings of the 2,2′-dipyridylamines are essentially planar (Table V), and their bond distances and angles are in the expected range (Tables III and IV). The metal ion is removed by 0.38–0.47 Å out of the plane of the pyridine rings, which is surprising since one would have thought that maximum metal–ligand overlap would be achieved if the metal were coplanar with the pyridine rings. The two rings within each ligand are tilted relative to each other, forming angles of 25° (dpa around Cu(1)) and 17° (dpa around Cu(2)) between the two normals of the planes. This can be expected for a six-membered chelate ring in which the bridging atom between the two pyridine rings is an sp^3-hybridized nitrogen atom. But the tilt angle is much larger than that found in the binary Cu–dpa complex, $Cu(dpa)_2(ClO_4)_2$, where it was only 9°.[28] However, the tilt angles in our structure are not unreasonably high, as compared with the 38.2° found in a palladium complex of dpa.[29]

The Copper Coordination Sphere. The two Cu^{2+} ions have almost identical square-pyramidal coordination spheres in our structure (Figure 3). The axial ligand (a water molecule) is further away from the metal ion than the four equatorial ligands (two nitrogen atoms from dpa and two phosphate oxygens). While the average $Cu–O(H_2O)$ distance is 2.32 (1) Å, the average bond lengths of the metal to the equatorial ligands are Cu–N = 1.99 (1) Å and Cu–O = 1.93 (1) Å, respectively. The Cu atom is slightly removed (by 0.2 Å) from the equatorial plane toward the axial ligand. Such a geometry is expected in a square-pyramidal Cu^{2+} complex.[30]

Table VI. Torsion Angles[a] and Best Plane Calculations for the Ribose Groups[b]

Torsion Angles (deg)

	Ribose group C(11′)–C(15′)	Ribose group C(21′)–C(25′)
τ_0	13	−42
τ_1	−23	31
τ_2	24	−7
τ_3	−16	−17
τ_4	2	36
ψ_{OO}	64	72
ψ_{OC}	−178	−172
χ_{CN}	89 (syn)	−113 (anti)
ϕ	135	178
$\psi = \psi_{OC}$	−178	−172
ψ'	107	111

Least-Squares Planes: Displacement (in Å) of Atoms in Ribose Ring

Direction cosines (−0.1131, −0.8852, +0.4513)		Direction cosines (−0.8852, −0.4569, −0.0870)	
C(11′)	0.01	C(21′)	0.03
C(12′)	0.38[c]	C(22′)	−0.04
C(13′)	−0.01	C(23′)	0.04
C(14′)	0.01	C(24′)	−0.03
O(11′)	−0.01	O(21′)	−0.54[c]
C(15′)	−1.16[c]	C(25′)	−1.11[c]

[a] Symbols used in this paper are taken from ref 21. [b] Standard deviations of angles and atomic positions in this table are estimated to be around 1° and 0.01 Å, respectively. [c] Atoms which were included in the plane calculation with zero weight.

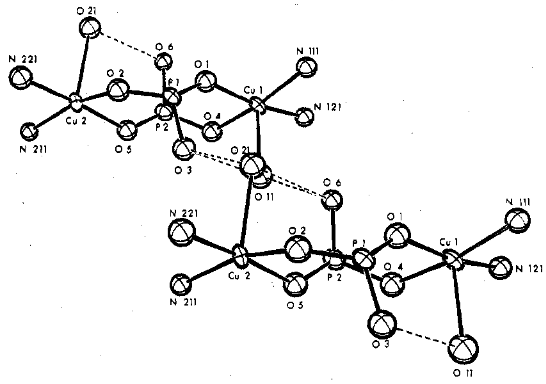


Figure 3. Coordination sphere of the Cu ions and the core of the dimeric unit. Note presence of eight-membered $(Cu–O–P–O)_2$ puckered rings and network of intramolecular and intermolecular hydrogen bonds (dotted lines) connecting the phosphate groups to the coordinated water molecules.

The two Cu^{2+} ions of one dimeric unit are held together by two bridging phosphate groups. Besides the direct coordination of O(1) and O(4) to Cu(1) (and O(2) and O(5) to Cu(2)), there are also a number of hydrogen bridging interactions that connect the copper/phosphate units of neighboring molecules, as will be described later. The copper, oxygen, and phosphate atoms in the core of the molecule form an eight-membered puckered ring, as shown in Figure 3.

Hydrogen Bonds and Intermolecular Forces. In the structure found for this complex there is an extensive net of H bonds between the many possible donor and acceptor sites. Actually all hydroxyl and carbonyl oxygens, as well as all the nitrogen atoms, are involved. All H bonds are listed in Table VII with their bond lengths. As the H positions were not located, we assumed distances between N and O atoms of less than 3.0 Å as possible H-bonded distances and also checked the resulting angles.[31] Only two of all the H bonds were found to be intramolecular, namely between O(11) and O(3) and

Table VII. Intramolecular and Intermolecular Hydrogen Bond Lengths (Å)

(A) Intramolecular Hydrogen Bonds			
O(11)-O(3)	2.67 (2)	O(21)-O(6)	2.67 (2)
(B) Intermolecular Hydrogen Bonds			
O(11)-O(6)	2.81 (2)	O(21)-O(3)	2.66 (2)
O(11)-O(304)	2.72 (2)	O(21)-O(303)	2.82 (2)
O(3)-N(131)	2.89 (2)	O(6)-N(231)	2.78 (2)
O(13′)-O(303)	2.76 (2)	O(23′)-O(302)	2.77 (2)
O(22′)-O(24)	2.94 (2)	O(23′)-O(14)	2.63 (2)
O(12′)-O(24)	2.93 (2)	O(11′)-O(303)	2.92 (2)
O(12′)-O(301)	2.80 (2)	O(4)-O(304)	2.92 (2)
N(13)-O(302)	2.82 (3)	N(23)-O(301)	2.85 (3)
O(22)-O(305)	2.85 (3)	O(302)-O(304)	2.72 (3)

between O(21) and O(6). All the others are intermolecular bonds that contribute to the stability of the crystal structure. This actually leads to some sort of a hydrogen-bonded "polymer", where the phosphate oxygen of one dimer is H bonded to the Cu-coordinated water of the next dimer unit, and so on. N(131) and N(231), which are, as expected,[32] not involved in metal coordination, form H bonds to the phosphate oxygen atoms O(3) and O(6) of neighboring molecules.

Other H bonds lie between hydroxyl groups and carbonyl groups, such as O(23′)-O(14), O(22′)-O(24), and O(12′)-O(24). All the other H bonds involve water molecules of crystallization. All of these except H_2O (305) form more than one H bond to other atoms. That might be one reason why H_2O (305) is present in the crystal to only about 75%. The H bond which may be present between H_2O (303) and O(11′) could represent one of the rare cases where the ring oxygen of a ribose acts as an acceptor of a H bond.[33]

Base-Stacking Interactions. The other intermolecular forces of interest are base-stacking interactions between the aromatic rings. There are essentially two different stacking interactions found in this structure, as can be seen in Figure 4. The first one is between two dipyridylamines of adjacent molecules, where the two rings are located pairwise above each other and are approximately parallel. There is a slight deviation from an exactly parallel condition, with the tilt angle between the normals of the planes of the stacked rings being 5.3 and 4.0°, respectively, while the average distance between the rings is 3.67 and 3.35 Å.

The other interaction between aromatic systems in this crystal structure is found between the uracils of two adjacent molecules (Figure 4). A view perpendicular to the planes of the bases is shown in Figure 5. The average distance between the two rings is 3.37 Å, and the tilt angle between the normals of the planes is 0.9°; i.e., the two planes are essentially coplanar. As can be seen from Figure 5, the two uracils are not at all eclipsed. In contrast, there is only a small overlapping region found, but this result confirms the finding of the literature[34] that electronegative atoms form close contact with adjacent aromatic systems. In our case we find this contact between the carbonyl function of one base and the ring of the other base. This is actually quite similar to the pattern found for the stacking between two thymidines in the structure of 1-methylthymidine/9-methyladenine.[35a] It has been noticed that the most common type of stacking is that "involving partially overlapping bases, with the carbon–heteroatom bonds of one base interacting with the polarizable ring of an adjacent base".[35b]

The tendency of the uracil bases to stack that way, (i.e., with the carbonyl functions in the 2 position pointing in the same general direction) must be quite large, as this stacking mode is probably the reason for the less favorable syn conformation of the sugar linkage in the nucleotide with the C(2′)-exo puckering mode. The two uracil bases can only lie one above the other with the 2-carbonyl groups pointing to the same side if their torsion angles around C(1′)–N(1) differ by about 180°, which means that the nucleotides have to have opposite syn/anti conformations.

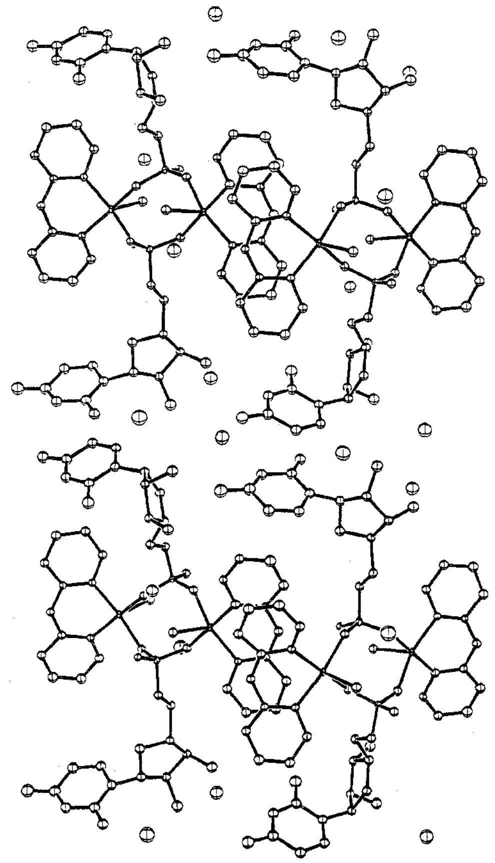


Figure 4. A plot of four dimeric units showing the stacking of the uracil bases and of the pyridine rings of the dipyridylamine ligands. Unconnected atoms are the oxygens of the water molecules of crystallization.

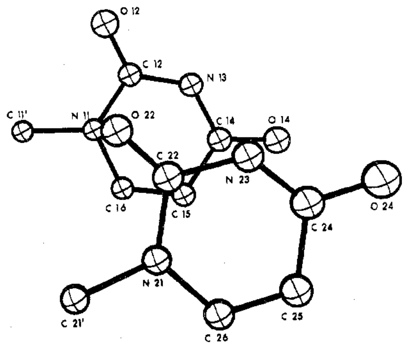


Figure 5. Intermolecular stacking of two uracil groups looking perpendicular to the planes of the bases. The interaction between the carbonyl group C(22)–O(22) and the aromatic ring of the other uracil appears clearly in this picture.

Coordination Tendency of 5′-UMP. As this is the first crystal structure of a transition metal ion complex with 5′-UMP, there are no prior reports with which we can compare our results. However, there are two complexes of uracil and dihydrouracil known in which Hg^{2+} coordinates to both bases through O(4).[36]

Purine nucleotides coordinate in two different ways: either through direct N(7) coordination plus hydrogen-bonded phosphate coordination to give a sort of loose macrochelate[6] or in a polymeric fashion, in which the nucleotide is covalently attached through both N(7) and phosphate to two or more different metals.[15] Nucleotide complexes with pyrimidines are much less common, and the only complexes that are known up to now are those that contain cytosine monophosphate (CMP). With Co^{2+} and Cd^{2+} CMP forms a polymeric net, where each nucleotide coordinates to different metal ions through the phosphate group and N(3) of the cytosine base.[16a] There is also an additional weak interaction of O(2) observed in an investigation of a Cd–CMP complex.[16c] In a recent paper by Aoki[16b] it was shown that CMP coordinates to Mn^{2+} through the phosphate group and O(2) of the base and not, as expected, N(3).

N(3), the common binding site in cytosine and its derivatives,[3] is not available for coordination in uracil under usual pH conditions, as it is still protonated and has a p*K* value of higher than 9.2.[37,38] However, there are still the two carbonyl oxygens, O(2) and O(4), in the uracil base that could complex.[36]

Solution Studies. Solution studies of the binary Cu–UMP system under comparable conditions show a variety of possible interactions between the metal ion and the uracil base: Berger and Eichhorn[40] concluded from their ^1H NMR line-broadening experiments at pH 7.5 that there is some weak interaction of Cu^{2+} with the base, most probably at O(4). From ^{31}P NMR studies at pH 7.0, Kotowycz[41] found evidence for phosphate coordination, and from ^{13}C NMR experiments he was able to show that Cu^{2+} has an influence on the C(5), C(4), and C(2) signals, a hint for metal–base interaction at N(3) or O(4).[41] Early potentiometric and spectrophotometric measurements did not lead to the detection of any metal ion–base interaction.[42] However, studies done with 5′-UTP, whose uracil group should behave very similarly to metals as that of 5′-UMP, showed a lowering of the p*K* value for N(3) by 1.7 log units to a pK of 7.8 in the presence of Cu^{2+}, indicating that there is some metal–base interaction.[39] But in the case of the ternary complex Cu(bpy)(UTP), the p*K* of the deprotonation at N(3) was only lowered by 0.5 log unit.[39] This shows that in solution the metal ion–nucleic acid base interaction is smaller in such a ternary complex than in a binary complex.[38,39]

Conclusion

In view of the blocking of the N(3) position by a H atom, it does not seem that surprising that the uracil base in our complex does not interact with the metal ion. We can probably rationalize our findings by looking closer at the results of solution studies on ternary complexes. It was found that, in ternary systems containing Cu^{2+} and either AMP, ATP,[8b,43] ITP,[43,44] or GTP[44] and an aromatic heterocyclic amine like bpy[8b,43,44] or tryptophan,[45] the main species present in solution has a structure in which the base of the nucleotide no longer coordinates to the metal ion but forms a stacking adduct with the second ligand within the ternary complex. As dpa, the amine ligand in our complex, shows a similar coordination behavior[46] with respect to the formation of ternary complexes[47] as bpy, the structure found for Cu(UMP)(dpa) seems to be reasonable. We also find the phosphate group and the amine ligand in the Cu^{2+} coordination sphere, but instead of an intramolecular stacking adduct we have intermolecular stacking interactions. In a crystal, where intermolecular forces are collectively much stronger than in dilute solution, it is reasonable to find an intermolecular stacking of the two aromatic systems. It will be interesting to see in future x-ray studies of ternary complexes with other nucleotides if the same coordination pattern is found as in this complex. It would be especially interesting to show by x-ray crystallography how a ligand with several binding sites like a nucleotide can change its coordination behavior in going from a binary to a ternary complex.[48]

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Registry No. $[Cu(5'\text{-}UMP)(dpa)(H_2O)]_2 \cdot 5H_2O$, 64520-38-3.

Supplementary Material Available: A listing of the observed and calculated structure factors of $[Cu(5'\text{-}UMP)(dpa)(H_2O)]_2 \cdot 5H_2O$ (18 pages). Ordering information is given on any current masthead page.

References and Notes

(1) A. S. Mildvan and C. H. Grisham, *Struct. Bonding (Berlin)*, **20**, 1 (1974).
(2) T. A. Connors and J. J. Roberts, Ed., "Platinum Coordination Complexes in Cancer Chemotherapy", Springer-Verlag, Heidelberg, 1974.
(3) D. J. Hodgson, *Prog. Inorg. Chem.*, in press.
(4) (a) A. T. Tu and M. T. Heller in "Metal Ions in Biological Systems", H. Sigel, Ed., Vol. 1, Marcel Dekker, New York, N.Y., 1974, pp 1–49; (b) G. L. Eichhorn in "Inorganic Biochemistry", Vol. 2, G. L. Eichhorn, Ed., Elsevier, Amsterdam, 1973, p 1191.
(5) (a) D. M. L. Goodgame, I. Jeeves, C. D. Reynolds, and A. C. Skapski, *Nucleic Acids Res.*, **2**, 1375 (1975); (b) J. F. Conn, J. J. Kim, F. L. Suddath, P. Blattmann, and A. Rich, *J. Am. Chem. Soc.*, **96**, 7152 (1974).
(6) (a) K. Aoki, *Bull. Chem. Soc. Jpn.*, **48**, 1260 (1975); (b) P. deMeester, D. M. L. Goodgame, T. J. Jones, and A. C. Skapski, *C. R. Hebd. Seances Acad. Sci., Ser. C*, **279**, 667 (1974); (c) G. R. Clark and J. D. Orbell, *J. Chem. Soc., Chem. Commun.*, 139 (1974); (d) P. deMeester, D. M. L. Goodgame, A. C. Skapski, and B. T. Smith, *Biochim. Biophys. Acta*, **340**, 113 (1974); (e) P. deMeester, D. M. L. Goodgame, T. J. Jones, and A. C. Skapski, *Biochem. J.*, **139**, 791 (1974); (f) K. Aoki, *Acta Crystallogr., Sect. B*, **32**, 1454 (1976); (g) A. D. Collins, P. deMeester, D. M. L. Goodgame, and A. C. Skapski, *Biochim. Biophys. Acta*, **402**, 1 (1975).
(7) G. P. P. Kuntz and G. Kotowycz, *Biochemistry*, **14**, 4144 (1975), and literature cited therein.
(8) (a) H. Sigel, *Angew. Chem., Int. Ed. Engl.*, **14**, 394 (1975); *Angew. Chem.*, **87**, 391 (1975); (b) C. F. Naumann and H. Sigel, *J. Am. Chem. Soc.*, **96**, 2750 (1974).
(9) Abbreviations used in this paper are: bpy for 2,2′-bipyridyl; dpa for 2,2′-dipyridylamine; AMP, CMP, and UMP for the 5′-monophosphates of adenosine, cytidine, and uridine; ATP, ITP, GTP, and UTP for the 5′-triphosphates of adenosine, inosine, guanosine, and uridine, respectively.
(10) A preliminary account of this work has appeared: B. E. Fischer and R. Bau, *J. Chem. Soc., Chem. Commun.*, 272 (1977).
(11) (a) G. H. Stout and L. H. Jensen, "X-Ray Structure Determination: A Practical Guide", Macmillan, New York, N.Y., 1968, p 65. (b) On the Nonius CAD-3 diffractometer, the scan speed (10°/min) and maximum counting rate (2500 counts/s) are preset by the manufacturer and are not subject to variation by the user. (c) Of the 4394 reflections measured, 1120 were duplicate (i.e., reflections measured more than once), and 582 were weak ($I < 3\sigma$). The remaining 2692 reflections were retained for the subsequent structure analysis. (d) T. C. Furnas, "Single Crystal Orienter Manual", General Electric Co., Milwaukee, Wis., 1966.
(12) The major computations in this work were performed on the USC IBM 370/158 computer using CRYM, an amalgamated set of crystallographic programs developed by Dr. R. E. Marsh and his research group at the California Institute of Technology.
(13) $R_F = \sum ||F_o| - |F_c|| / \sum |F_o|$; $R_{wF} = (\sum w ||F_o| - |F_c||^2 / \sum w F_o^2)^{1/2}$.
(14) The numbering system of the nucleotide units given in the text and the figures is identical in the last digit to standard notation. For example, atoms N(13) and N(23) both correspond to the N(3) atom of uracil, while atoms C(11′) and C(21′) refer to the C(1′) atom of ribose.
(15) (a) K. Aoki, G. R. Clark, and J. D. Orbell, *Biochim. Biophys. Acta*, **425**, 369 (1976); (b) P. deMeester, D. M. L. Goodgame, T. J. Jones, and A. C. Skapski, *ibid.*, **353**, 392 (1974); (c) D. M. L. Goodgame, I. Jeeves, C. D. Reynolds, and A. C. Skapski, *Nucleic Acids Res.*, **2**, 1375 (1975).
(16) (a) G. R. Clark and J. D. Orbell, *J. Chem. Soc., Chem. Commun.*, 697 (1975); (b) K. Aoki, *ibid.*, 748 (1976); (c) R. Bau, R. W. Gellert, and J. Shiba, Abstracts of the 7th International Conference on Organometallic Chemistry, Venice, Italy, 1975, p 238.
(17) D. M. L. Goodgame, I. Jeeves, F. L. Phillips, and A. C. Skapski, *Biochim. Biophys. Acta*, **378**, 153 (1975).
(18) D. Voet and A. Rich, *Progr. Nucleic Acid Res. Mol. Biol.*, **10**, 183 (1970).
(19) M. Sundaralingam, *Biopolymers*, **7**, 821 (1969).
(20) G. A. Jeffrey and M. Sundaralingam, *Adv. Carbohydr. Chem. Biochem.*, **30**, 445 (1974); **31**, 347 (1975).
(21) The conformational terms were adapted from: W. Saenger, *Angew. Chem., Int. Ed., Engl.*, **12**, 591 (1973); *Angew. Chem.*, **85**, 680 (1973). The O(1′)-endo conformation corresponds to $^{\circ}E$ in ref 20; cf. C. Altona and M. Sundaralingam, *J. Am. Chem. Soc.*, **94**, 8205 (1972).
(22) J. Konnert, I. L. Karle, and J. Karle, *Acta Crystallogr., Sect. B*, **26**, 770 (1970).
(23) $\chi_{CN} = 247°$ in the definition of Saenger[21] corresponds to $\phi_{CN} = 67°$ in the definition of Donohue and Trueblood.[24]
(24) J. Donohue and K. N. Trueblood, *J. Mol. Biol.*, **2**, 363 (1960).
(25) P.O.P.Ts'o, Ed., "Basic Principles in Nucleic Acid Chemistry", Vol. 1, Academic Press, New York and London, 1974, p 483.
(26) D. C. Hodgkin, J. Lindsay, R. A. Sparks, K. N. Trueblood, and J. G. White, *Proc. R. Soc. London, Ser. A*, **266**, 494 (1962); C. Brink-Shoemaker, D. W. J. Cruickshank, D. C. Hodgkin, M. J. Kamper, and D. Pilling, *ibid.*, **278**, 1 (1964).
(27) D. C. Rohrer and M. Sundaralingam, *J. Am. Chem. Soc.*, **92**, 4950 (1970).

(28) J. E. Johnson, T. A. Beinecke, and R. A. Jacobson, *J. Chem. Soc. A*, 1371 (1971).

(29) H. C. Freeman and M. R. Snow, *Acta Crystallogr.*, **18**, 843 (1965).

(30) E. Sinn, *Inorg. Chem.*, **15**, 2698 (1976).

(31) Reference 11a, p 303.

(32) G. Anderegg, *Helv. Chim. Acta*, **54**, 509 (1971).

(33) D. C. Rohrer and M. Sundaralingam, *J. Am. Chem. Soc.*, **92**, 4956 (1970).

(34) C. E. Bugg, J. M. Thomas, M. Sundaralingam, and S. T. Rao, *Biopolymers*, **10**, 175 (1970).

(35) (a) K. Hoogsteen, *Acta Crystallogr.*, **16**, 907 (1963), cf. ref. 34. (b) C. E. Bugg, in "The Jerusalem Symposia of Quantum Chemistry and Biochemistry", Vol. IV, E. D. Bergmann and B. Pullman, Ed., The Israel Academy of Sciences and Humanities, Jerusalem, 1972, p 192.

(36) J. A. Carrabine and M. Sundaralingam, *Biochemistry*, **10**, 292 (1971).

(37) A. M. Fiskin and M. Beer, *Biochemistry*, **4**, 1289 (1965).

(38) H. Sigel, *J. Am. Chem. Soc.*, **97**, 3209 (1975).

(39) H. Sigel, *Eur. J. Biochem.*, **3**, 530 (1968).

(40) N. A. Berger and G. L. Eichhorn, *Biochemistry*, **10**, 1857 (1971).

(41) G. Kotowycz, *Can. J. Chem.*, **52**, 924 (1974).

(42) A. T. Tu and C. G. Friederich, *Biochemistry*, **7**, 4367 (1968).

(43) Ch. F. Naumann, B. Prijs, and H. Sigel, *Eur. J. Biochem.*, **41**, 209 (1974).

(44) H. Sigel, Ch. F. Naumann, and B. Prijs, *Eur. J. Biochem.*, **46**, 589 (1974).

(45) Ch. F. Naumann and H. Sigel, *FEBS Lett.*, **47**, 122 (1974); *J. Am. Chem. Soc.*, **98**, 730 (1976).

(46) B. E. Fischer, Ph. D. Thesis, University of Basel, Switzerland, 1975.

(47) H. Sigel in "Metal Ions in Biological Systems", Vol. 2, H. Sigel, Ed., Marcel Dekker, New York, N.Y., 1974, p 63.

(48) After this article was submitted, two related papers have appeared in the literature. One paper describes the crystal structure of the polymeric $[Co_2(H_2O)_4(5'\text{-UMP})_2]_n$, which also shows the "phosphate only" type of coordination for 5′-UMP [B. A. Cartwright, D. M. L. Goodgame, I. Jeeves, and A. C. Skapski, *Biochim. Biophys. Acta*, **477**, 195 (1977)]. In contrast, the crystal structure of the ternary complex $[Cu(5'\text{-IMP})(bpy)(H_2O)_2]\cdot NO_3\cdot H_2O$ [K. Aoki, *J. Chem. Soc., Chem. Commun.*, 600 (1977)] shows nucleotide–metal binding through the base (in this case, hypoxanthine) and not through the phosphate group.

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Molecular Structure and Magnetic Properties of *trans*-Bis(L-methioninato)copper(II), $Cu(C_5H_{10}NO_2S)_2$

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The crystal and molecular structure of bis(L-methioninato)copper(II), Cu(L-Met)$_2$, $Cu(C_5H_{10}NO_2S)_2$, has been determined from single-crystal three-dimensional x-ray data collected by counter methods. The compound crystallizes as elongated blue six-sided plates in the space group $P2_1$(C_2^2, No. 4) with $Z = 2$, $a = 9.487$ (5) Å, $b = 5.061$ (3) Å, $c = 15.563$ (8) Å, $\beta = 92.46$ (3)°, $d_{\text{calcd}} = 1.601$ g/cm^3, and $d_{\text{obsd}} = 1.60(1)$g/cm^3. Least-squares refinement of 1191 reflections having $F^2 \geq 3\sigma(F^2)$ gave a conventional R factor of 0.046. There are no discrete molecules in the crystal; it consists of isolated sheets of Cu(II) ions with tetragonal N_2O_4 ligand sets formed by trans coordination of two L-methionine molecules. Additional interactions with carboxylate ions from neighboring methionine molecules lead to two apical Cu–O bonds and link the Cu(II) ions to form a carboxylate-bridged sheet structure. The structure of Cu(L-Met)$_2$ is compared with that reported by others for racemic Cu(D,L-Met)$_2$. Infrared spectra and magnetic properties of both complexes are presented and discussed. Effective magnetic moments of the racemic complex fell in the range 1.85–1.90 μ_B at temperatures between 270 and 6.2 K and followed Curie law behavior. Similarly, effective magnetic moments of Cu(L-Met)$_2$ fell in the range 1.76–1.87 μ_B at temperatures between 270 and ~13.5 K; below 13.5 K, the magnetic moment steadily decreased to 1.65 μ_B at 4.2 K. ESR spectra of both polycrystalline complexes were measured at Q- and X-band frequencies over wide temperature ranges. Crystallographic similarities between the free methionine ligands and their complexes with Cu(II), Zn(II), and Cd(II) are presented and discussed.

Introduction

Our interest in the Cu(II) complexes of sulfur-containing ligands[2] and in the magnetic properties of carboxylate-bridged Cu(II) lattice structures[3] led us to investigate the Cu(II) complexes of D,L- and L-methionine. Other workers have shown that the CuN_2O_4 ligand set in the D,L complex consists of trans equatorial N_2O_2 bonding along with two apical bonds to carboxylate oxygen atoms of neighboring ligands.[4] Well-separated planar arrays of these bridged Cu(II) ions form the overall crystal structure. We are unaware of prior characterizations of bis(L-methioninato)copper(II), Cu(L-Met)$_2$. Our analysis of the infrared spectrum of this complex, using known spectral/structural guidelines,[5] indicated that the ligand might be bound to Cu(II) in the less common cis fashion. Further, the mode of ligand bonding could not be determined unambigously by preliminary ESR studies at X-band; although the expected axial spectra were observed for Cu(D,L-Met)$_2$, isotropic spectra were obtained with Cu(L-Met)$_2$. To determine the coordination geometry unambiguously, the crystal structure of Cu(L-Met)$_2$ has been determined and is reported here.

In the present work, both complexes are further characterized by ESR and infrared spectral measurements and by magnetic susceptibility studies over the 270–4.2 K temperature range. Lastly, a strong similarity between the crystal structures of certain free amino acids (such as L-methionine) and their complexes with divalent metal ions such as Cu(II), Zn(II), and Cd(II) is noted.

Experimental Section

Preparation of Complexes. The Cu(II) complex of either D,L- or L-methionine was prepared readily by the urea hydrolysis technique. In a typical experiment, a solution of 0.43 g of $CuCl_2\cdot 2H_2O$ (2.5 mmol), 0.75 g of D,L- or L-methionine (5.0 mmol), and 0.15 g of urea (2.5 mmol) in 25 mL of hot water was filtered through a Millipore membrane (0.22-μm pore size) and maintained at 80 °C for 48 h. The complexes crystallized as six-sided blue plates which were separated from the hot solution by filtration, washed with H_2O, and air-dried. Typical yields were ~70%. Anal. Calcd for Cu(Met)$_2$, $C_{10}H_{20}N_2O_4S_2Cu$: C, 33.37; N, 7.78; H, 5.60. Found for Cu(L-Met)$_2$: C, 32.43; N, 7.53; H, 5.96. Found for Cu(D,L-Met)$_2$: C, 33.30; N, 7.68; H, 5.59.

To facilitate ESR studies, Cu(II) was doped at the ~1 wt % level into Zn(Met)$_2$ lattices. Aqueous solutions containing 0.75 g (2.5 mmol) of either D,L- or L-methionine, 0.337 g (2.47 mmol) of $ZnCl_2$, and 0.004 g (0.02 mmol) of $CuCl_2.2H_2O$ were neutralized to pH ~7.5 with dilute aqueous NaOH, filtered while hot, and concentrated by evaporation at room temperature. The concentrated filtrates deposited pale blue crystalline products which were collected by filtration, washed with water, and dried in vacuo over P_2O_5.

Anal. Calcd for 1% Cu(Met)$_2$ in Zn(Met)$_2$, $C_{10}H_{20}N_2O_4S_2Zn$ (1% Cu): C, 33.20; N, 7.74; H, 5.57; Zn 17.89; Cu, 0.20. Found for 1% Cu/Zn(L-Met)$_2$: C, 33.16; N, 7.74; H, 5.39; Zn, 17.85; Cu, 0.32.