# Metal–Nucleotide Interactions: Crystal Structures† of $Ca[Cu(5'\text{-}GMP)_2(en)(H_2O)_2]\cdot 8H_2O$ (5′-GMP = Guanosine 5′-Monophosphate, en = Ethylenediamine) and $Ca[Cu(5'\text{-}IMP)_2(H_2O)_4]\cdot 6.7H_2O$ (5′-IMP = Inosine 5′-Monophosphate)‡

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The compounds $Ca[Cu(5'\text{-}GMP)_2(en)(H_2O)_2]\cdot 8H_2O$ (**1**) and $Ca[Cu(5'\text{-}IMP)_2(H_2O)_4]\cdot 6.7H_2O$ (**2**) have been prepared and their structures determined (5′-GMP = guanosine 5′-monophosphate, en = ethylenediamine, and 5′-IMP = inosine 5′-monophosphate). Crystals of (**1**) are monoclinic space group $P2_1$, with $a$ = 10.997(2), $b$ = 21.693(4), $c$ = 8.872(2) Å, β = 94.69(1)°, and $Z$ = 2. Crystals of (**2**) are orthorhombic, space group $C222_1$, with $a$ = 8.757(2), $b$ = 23.229(5), $c$ = 21.212(5) Å, and $Z$ = 4. Both structures were solved by the heavy-atom technique and refined by full-matrix least-squares calculations to $R$ = 0.074 and $R'$ = 0.064 for 1 266 reflections for (**1**) and to $R$ = 0.094 and $R'$ = 0.093 for 1 275 reflections for (**2**). In both structures the copper ion shows an elongated octahedral co-ordination with the two nucleotide moieties in *cis* positions bound through the N(7) purine atoms. In (**2**) the ethylenediamine ligand has been replaced by two water molecules. Both crystal structures are essentially based on those of the sodium salts of the respective nucleotides.

In the last few years metal–nucleotide interactions have been actively investigated in view of their importance in many biochemical processes. One of the most interesting aspects of these investigations is their connection with the anti-tumour properties of some platinum(II) complexes. It has been shown in fact that the DNA of tumour cells is the molecular target of these compounds and particularly of *cis*-$[Pt(NH_3)_2Cl_2]$.[1]

Most of the available evidence points towards the formation of an intrastrand linkage of the platinum atom with the N(7) atoms of the two adjacent guanine bases.[2] The distortion induced in the DNA structure could lead, upon replication, to serious damage in the daughter strand and to cell death.

Structures of *cis*-diammine platinum(II) complexes with nucleosides and nucleotides show invariably the platinum atom to be square planar, co-ordinated by two N(7) atoms of the purine bases in *cis* positions and the two ammine nitrogen atoms.[3]

In an attempt to find stereochemically valid metal substitutes for the platinum atom, we have recently prepared the compound $Ca[Cu(5'\text{-}GMP)_2(en)(H_2O)_2]\cdot 8H_2O$ (5′-GMP = guanosine 5′-monophosphate, en = ethylenediamine) and reported its structure.[4] In the complex anion $[Cu(5'\text{-}GMP)_2(en)(H_2O)_2]^{2-}$ the copper atom shows a square-planar environment of the two nitrogen atoms of ethylenediamine and the N(7) atoms of the two 5′-GMP moieties in the *cis* configuration. Two further water molecules complete an elongated octahedral geometry quite common for the copper atom. The ability of copper(II) to form four coplanar bonds to nitrogen atoms with two purines in a *cis* position linked through the N(7) atoms is also demonstrated by the crystal structure of $Na_2[Cu(5'\text{-}IMP)_2(im)_{0.8}(H_2O)_{1.2}]\cdot 12.4H_2O$ (5′-IMP = inosine 5′-monophosphate, im = imidazole).[5]

These results prompted us to investigate a series of compounds obtained by the reaction of $[Cu(en)(H_2O)_2]SO_4$ and several nucleotides. We report here the detailed structural analysis of $Ca[Cu(5'\text{-}GMP)_2(en)(H_2O)_2]\cdot 8H_2O$ and of the reaction product between $[Cu(en)(H_2O)_2]SO_4$ and 5′-IMP.

**Table 1.** Crystal data

| Complex | $Ca[Cu(5'\text{-}GMP)_2(en)(H_2O)_2]\cdot 8H_2O$ | $Ca[Cu(5'\text{-}IMP)_2(H_2O)_4]\cdot 6.7H_2O$ |
|---|---|---|
| Formula | $C_{22}H_{36}CaCuN_{12}O_{18}P_2\cdot 8H_2O$ | $C_{20}H_{30}CaCuN_8O_{20}P_2\cdot 6.7H_2O$ |
| $M$ | 1 066.3 | 986.9 |
| Space group | $P2_1$ | $C222_1$ |
| $a$/Å | 10.997(2) | 8.757(2) |
| $b$/Å | 21.693(4) | 23.229(5) |
| $c$/Å | 8.872(2) | 21.212(5) |
| β/° | 94.69(1) | |
| $U$/Å$^3$ | 2 109.4 | 4 314.9 |
| $Z$ | 2 | 4 |
| $D_c$/g cm$^{-3}$ | 1.68 | 1.52 |
| λ(Mo-$K_\alpha$)/Å | 0.7107; graphite monochromator | 0.7107; graphite monochromator |
| Crystal dimensions/mm | 0.038 × 0.125 × 0.200 | 0.100 × 0.250 × 0.425 |
| μ(Mo-$K_\alpha$)/cm$^{-1}$ | 6.40 | 6.36 |
| Scan type | θ—2θ | θ—2θ |
| Scan width/° | 1.0 + 0.30 tan(θ) | 0.8 |
| Scan speed/° s$^{-1}$ | 0.05 | 0.05 |
| 2θ range/° | $4 \leqslant 2\theta \leqslant 50$ | $4 \leqslant 2\theta \leqslant 50$ |
| Reflections used | 1 266 [$I \geqslant 2.5\sigma(I)$] | 1 275 [$I \geqslant 3\sigma(I)$] |
| No. of parameters | 256 | 157 |
| $R^a$ | 0.074 | 0.094 |
| $R'^b$ | 0.064 | 0.093 |

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

## Experimental

*Preparations.*—Both $Ca[Cu(5'\text{-}GMP)_2(en)(H_2O)_2]\cdot 8H_2O$ (**1**) and $Ca[Cu(5'\text{-}IMP)_2(H_2O)_4]\cdot 6.7H_2O$ (**2**) were prepared by mixing in aqueous solution stoicheiometric amounts of $[Cu(en)(H_2O)_2]SO_4$ and the sodium salt of 5′-GMP (or 5′-IMP) in the presence of calcium ions (pH *ca.* 7). On cooling the slightly

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† *Supplementary data available:* see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1987, Issue 1, pp. xvii—xix.

‡ The abbreviations used are those recommended by the IUPAC–IUB Commission on Biochemical Nomenclature, *Eur. J. Biochem.*, 1970, **15**, pp. 203—208.

**Table 2.** Positional parameters (× $10^4$) with estimated standard deviations in parentheses for Ca[Cu(5′-GMP)$_2$(en)(H$_2$O)$_2$]·8H$_2$O and Ca[Cu(5′-IMP)$_2$(H$_2$O)$_4$]·6.7H$_2$O

(*a*) Ca[Cu(5′-GMP)$_2$(en)(H$_2$O)$_2$]·8H$_2$O

| Atom | *X*/*a* | *Y*/*b* | *Z*/*c* | Atom | *X*/*a* | *Y*/*b* | *Z*/*c* |
|---|---|---|---|---|---|---|---|
| Cu | 2 003(3) | 8 150 | 2 754(4) | O(6b) | −153(14) | 6 939(7) | 1 926(19) |
| N(1a) | −1 689(16) | 9 411(9) | 3 836(21) | N(7b) | 571(16) | 8 265(10) | 972(20) |
| C(2a) | −2 558(22) | 9 121(12) | 4 588(29) | C(8b) | 563(22) | 8 738(12) | 160(30) |
| N(2a) | −3 569(17) | 9 407(9) | 4 727(21) | N(9b) | −553(16) | 8 785(8) | −616(20) |
| N(3a) | −2 394(16) | 8 528(9) | 5 170(21) | C(1′b) | −955(25) | 9 286(13) | −1 558(32) |
| C(4a) | −1 340(21) | 8 307(11) | 4 940(27) | C(2′b) | −1 081(21) | 9 891(11) | −697(28) |
| C(5a) | −390(21) | 8 576(11) | 4 140(26) | C(3′b) | −1 045(19) | 10 365(11) | −2 031(25) |
| C(6a) | −533(24) | 9 179(12) | 3 527(30) | C(4′b) | −177(22) | 10 054(11) | −3 022(31) |
| O(6a) | 163(15) | 9 485(8) | 2 897(20) | C(5′b) | 1 121(18) | 10 288(11) | −2 961(25) |
| N(7a) | 574(17) | 8 141(12) | 4 126(22) | O(1′b) | −183(13) | 9 405(7) | −2 672(17) |
| C(8a) | 215(22) | 7 632(12) | 4 814(28) | O(2′b) | −2 169(14) | 9 960(7) | 50(18) |
| N(9a) | −910(18) | 7 705(9) | 5 297(23) | O(3′b) | −2 243(13) | 10 402(7) | −2 752(18) |
| C(1′a) | −1 641(21) | 7 258(11) | 6 116(28) | P(b) | 2 940(6) | 10 540(3) | −920(8) |
| C(2′a) | −1 906(23) | 6 676(11) | 5 142(29) | O(1b) | 3 799(15) | 10 117(8) | −1 752(19) |
| C(3′a) | −2 005(22) | 6 201(13) | 6 433(29) | O(2b) | 2 971(15) | 11 196(8) | −1 471(20) |
| C(4′a) | −1 076(20) | 6 429(11) | 7 737(26) | O(3b) | 3 129(15) | 10 458(8) | 787(19) |
| C(5′a) | 143(20) | 6 130(12) | 7 850(28) | O(5′b) | 1 580(13) | 10 267(7) | −1 336(17) |
| O(1′a) | −947(15) | 7 088(8) | 7 456(20) | N(10) | 3 374(16) | 8 148(12) | 1 433(22) |
| O(2′a) | −2 962(16) | 6 756(9) | 4 185(21) | N(11) | 3 350(15) | 8 181(11) | 4 505(20) |
| O(3′a) | −3 201(16) | 6 233(9) | 6 865(20) | C(9) | 4 510(27) | 8 321(16) | 2 439(36) |
| P(a) | 2 217(6) | 6 132(3) | 6 600(8) | C(10) | 4 542(25) | 8 067(16) | 3 834(33) |
| O(1a) | 2 511(14) | 6 204(8) | 4 997(19) | Ca | −4 084(5) | 10 244(3) | −1 470(6) |
| O(2a) | 2 790(14) | 6 616(8) | 7 642(18) | O(w1) | −4 649(17) | 10 817(9) | −3 844(23) |
| O(3a) | 2 487(13) | 5 493(8) | 7 254(17) | O(w2) | −3 607(16) | 11 295(9) | −531(22) |
| O(5′a) | 761(13) | 6 240(7) | 6 517(18) | O(w3) | −4 200(14) | 9 108(8) | −1 843(19) |
| N(1b) | −1 973(18) | 7 248(9) | 760(23) | O(w4) | −441(15) | 10 103(8) | 1 124(21) |
| C(2b) | −2 739(28) | 7 604(15) | −153(36) | O(w5) | 2 196(15) | 7 003(7) | 2 572(20) |
| N(2b) | −3 899(20) | 7 389(10) | −444(26) | O(w6) | 3 357(18) | 8 837(10) | −1 430(25) |
| N(3b) | −2 344(16) | 8 170(11) | −682(20) | O(w7) | 1 948(19) | 7 771(8) | −2 105(24) |
| C(4b) | −1 152(20) | 8 273(12) | −214(26) | O(w8) | 2 569(16) | 9 508(8) | 2 606(21) |
| C(5b) | −355(23) | 7 943(11) | 805(29) | O(w9) | −3 735(17) | 4 470(9) | 4 548(22) |
| C(6b) | −764(23) | 7 328(12) | 1 217(31) | O(w10) | 4 825(18) | 7 160(9) | −3 452(24) |

(*b*) Ca[Cu(5′-IMP)$_2$(H$_2$O)$_4$]·6.7H$_2$O

| Atom | *X*/*a* | *Y*/*b* | *Z*/*c* | Atom | *X*/*a* | *Y*/*b* | *Z*/*c* |
|---|---|---|---|---|---|---|---|
| Cu | 0 | 1 582(2) | 2 500 | C(5′) | 5 461(22) | 2 184(8) | 4 577(9) |
| N(1) | 1 449(17) | 3 448(7) | 1 432(7) | O(5′) | 3 996(13) | 1 914(4) | 4 520(5) |
| C(2) | 2 373(24) | 3 814(9) | 1 768(9) | O(1) | 4 823(16) | 945(5) | 4 167(6) |
| N(3) | 2 953(18) | 3 656(6) | 2 317(7) | O(2) | 4 494(13) | 1 142(5) | 5 311(6) |
| C(4) | 2 562(21) | 3 105(7) | 2 478(10) | O(3) | 2 174(15) | 1 121(5) | 4 584(6) |
| C(5) | 1 675(19) | 2 717(7) | 2 178(8) | P | 3 853(6) | 1 242(2) | 4 647(2) |
| C(6) | 1 076(21) | 2 898(8) | 1 573(8) | Ca$^{a}$ | 3 522(10) | 4 671(4) | 4 517(4) |
| O(6) | 341(16) | 2 585(5) | 1 213(6) | O(w1) | 1 633(18) | 995(6) | 2 497(10) |
| N(7) | 1 622(16) | 2 214(6) | 2 519(8) | O(w2) | −8(19) | 1 447(6) | 3 681(6) |
| C(8) | 2 495(22) | 2 295(8) | 3 014(9) | O(w3)$^{b}$ | 4 226(24) | 1 440(10) | 1 897(10) |
| N(9) | 3 087(17) | 2 822(6) | 3 014(7) | O(w4) | 2 916(22) | 4 251(8) | 5 632(8) |
| O(1′) | 5 247(13) | 2 749(5) | 3 665(5) | O(w5)$^{a}$ | 792(40) | 4 791(14) | 4 379(16) |
| O(2′) | 2 272(15) | 3 693(5) | 4 113(6) | O(w6)$^{a}$ | 3 856(42) | 4 685(15) | 3 356(16) |
| O(3′) | 5 089(15) | 3 778(5) | 4 556(5) | O(w7)$^{a}$ | 3 949(40) | 4 982(15) | 459(16) |
| C(1′) | 4 001(20) | 3 122(7) | 3 527(8) | O(w8)$^{b}$ | −5 600(39) | 202(14) | 6 067(17) |
| C(2′) | 3 127(21) | 3 195(7) | 4 136(8) | O(w9)$^{b}$ | 3 162(45) | 5 235(17) | 1 428(18) |
| C(3′) | 4 481(19) | 3 210(7) | 4 598(9) | O(w10)$^{b}$ | 5 764(45) | 1 011(19) | 2 956(19) |
| C(4′) | 5 530(20) | 2 753(8) | 4 324(8) | | | | |

$^{a}$ Site occupation factor 0.5. $^{b}$ Variable site occupation factor (see text).

warm solution (*ca.* 40 °C) small light blue plates separated overnight in both cases.

[Cu(en)(H$_2$O)$_2$]SO$_4$ was prepared according to Baldwin.[6]

*Crystal-structure Determinations.*—Crystal data and data collection procedures are summarized in Table 1. Cell constants were determined by least-squares fitting of 25 accurately centred reflections. Intensity data, collected on a Philips PW 1100 automatic diffractometer at room temperature, were corrected for Lorentz, polarization, and absorption effects[7] [maximum and minimum transmission factors; 0.92, 0.77(1) and 0.90, 0.80(**2**)]. The intensities of three standard reflections were monitored periodically for stability control during data collection.

Both structures were solved by the heavy-atom method, using Patterson and electron density syntheses. In the polar space groups $P2_1$ and $C222_1$ the choice between the two possible enantiomeric structures was made on the basis of the known absolute configuration of D-ribose. The structures were refined by the full-matrix least-squares technique. The function minimized was $\Sigma w(|F_o| - |F_c|)^2$ with weights $w = a/[\sigma^2(F) + bF^2]$, where $a$ and $b$ are adjustable parameters. Isotropic thermal parameters were used for all atoms except for the copper co-ordination sphere in the 5′-IMP complex (**2**) which was refined

**Table 3.** Selected bond lengths (Å) and angles (°) with estimated standard deviations in parentheses

(*a*) $Ca[Cu(5'\text{-}GMP)_2(en)(H_2O)_2]\cdot 8H_2O$

| | | | |
|---|---|---|---|
| Cu–N(7a) | 2.06(2) | Cu–N(7b) | 2.02(2) |
| Cu–N(10) | 1.98(2) | Cu–N(11) | 2.06(2) |
| Cu–O(w5) | 2.50(1) | Cu–O(w8) | 3.02(2) |
| Na(7a)–Cu–N(7b) | 87.8(7) | N(7a)–Cu–O(w5) | 95.9(8) |
| N(7a)–Cu–N(11) | 95.2(7) | N(7a)–Cu–O(w8) | 101.7(8) |
| N(7b)–Cu–N(10) | 92.3(8) | N(7b)–Cu–O(w5) | 97.3(8) |
| N(7b)–Cu–O(w8) | 88.6(8) | N(10)–Cu–N(11) | 84.9(7) |
| N(10)–Cu–O(w5) | 83.5(8) | N(10)–Cu–O(w8) | 78.9(8) |
| N(11)–Cu–O(w5) | 91.2(7) | N(11)–Cu–O(w8) | 82.2(7) |
| N(7a)–Cu–N(10) | 179.4(10) | N(7b)–Cu–N(11) | 170.6(9) |
| O(w5)–Cu–O(w8) | 161.6(9) | | |

(*b*) $Ca[Cu(5'\text{-}IMP)_2(H_2O)_4]\cdot 6.7H_2O$

| | | | |
|---|---|---|---|
| Cu–N(7) | 2.04(1) | Cu–O(w1) | 1.97(1) |
| Cu–O(w2) | 2.52(1) | | |
| N(7)–Cu–O(w1) | 89.6(6) | N(7)–Cu–O(w2) | 94.1(6) |
| O(w1)–Cu–O(w2) | 85.4(7) | N(7)–Cu–N(7′)* | 88.1(6) |
| O(w1)–Cu–O(w1′)* | 92.7(7) | O(w2)–Cu–N(7′)* | 96.1(6) |
| O(w2)–Cu–O(w1′)* | 84.8(7) | O(w2)–Cu–O(w2′)* | 165.7(7) |
| N(7)–Cu–O(w1′)* | 177.3(6) | | |

* The atoms N(7′), O(w1′), and O(w2′) are symmetry related respectively to N(7), O(w1), and O(w2) by the two-fold axis through the Cu atom.

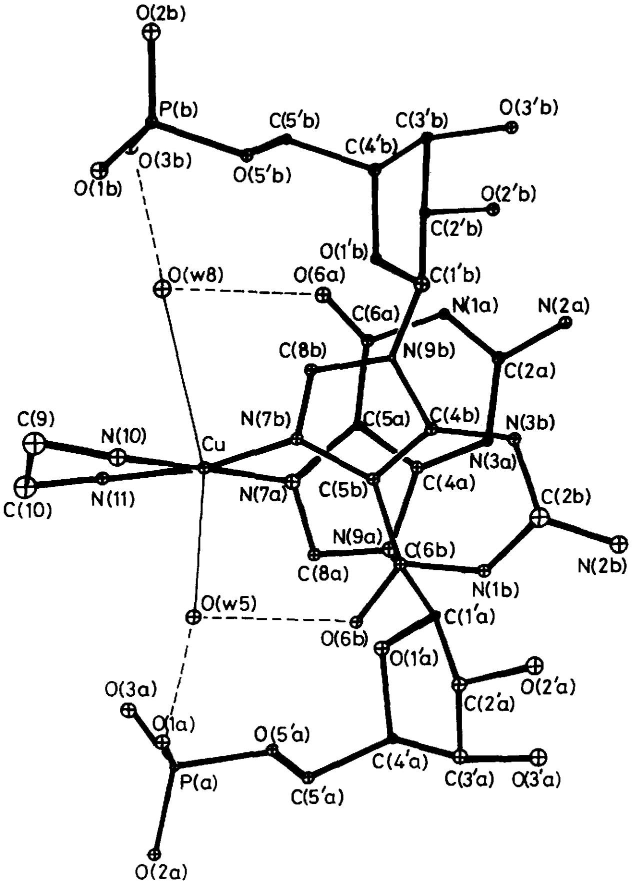

**Figure 1.** ORTEP drawing of $Ca[Cu(5'\text{-}GMP)_2(en)(H_2O)_2]\cdot 8H_2O$ (**1**). Thermal ellipsoids for non-hydrogen atoms at 30% probability

anisotropically. Hydrogen atoms were included in calculated positions. Population parameters of four disordered lattice water molecules in the 5′-IMP complex (**2**) were allowed to refine yielding a total occupancy factor of 1.7.

All calculations were performed with the SHELX 76 set of programs[7] which use the analytical approximation for the atomic scattering factors and anomalous dispersion corrections for all atoms from International Tables.[8] The molecular plots were produced by ORTEP.[9]

Table 2 shows the final atomic co-ordinates with estimated standard deviations obtained from the least-squares inverse matrix.

## Results and Discussion

*Structure of* $Ca[Cu(5'\text{-}GMP)_2(en)(H_2O)_2]\cdot 8H_2O$ (**1**).—The crystal structure of $Ca[Cu(5'\text{-}GMP)_2(en)(H_2O)_2]\cdot 8H_2O$ consists of $[Cu(5'\text{-}GMP)_2(en)(H_2O)_2]^{2-}$ anions and $Ca^{2+}$ cations. In the complex anion, the copper atom is co-ordinated by the two nitrogen atoms of ethylenediamine and the two N(7) atoms of the 5′-GMP moieties thus forming an almost regular square. Two water molecules at 2.50(1) and 3.02(2) Å complete an elongated octahedral geometry around the copper atom (Figure 1). Deviations from the best least-squares plane though N(7a), N(7b), N(10), N(11) are −0.074, −0.081, 0.086, −0.089, and 0.085 Å respectively for Cu, N(7a), N(7b), N(10), and N(11). Bond lengths and angles around the copper atom are reported in Table 3. The calcium ions are co-ordinated by four water molecules, two ribose hydroxyl-oxygen atoms, and one phosphate oxygen with distances in the range 2.34(2)—2.49(2) Å.

Both ribosyl rings show the common C(2′) *endo*-puckering and their orientation with respect to purine is *anti* [$\chi_{CN}(a)^3 = -121.02°$ and $\chi_{CN}(b) = -128.18°$. Notations a and b refer to labelling in Figure 1]. The conformation about the C(4′)–C(5′) bond is *gauche–gauche* [$\tau(a)^3 = 62.02°$ and $\tau(b) = 54.35°$].

Extensive intra- and inter-molecular hydrogen bonding is observed. Two strong intramolecular hydrogen bonds are formed by each water molecule co-ordinated to the copper ion, with the purine O(6) and with one phosphate oxygen atom [O(w5)···O(6b) = 2.60, O(w5)···O(1a) = 2.76, O(w8)···O(6a) = 2.68, and O(w8)···O(3b) = 2.72 Å]. These bonds give an essential contribution to the stability of the back-folded configuration of the nucleotide. No intra- or inter-molecular purine–purine stacking is observed.

*Structure of* $Ca[Cu(5'\text{-}IMP)_2(H_2O)_4]\cdot 6.7H_2O$ (**2**).—The crystal structure of $Ca[Cu(5'\text{-}IMP)_2(H_2O)_4]\cdot 6.7H_2O$ consists of $[Cu(5'\text{-}IMP)_2(H_2O)_4]^{2-}$ anions and disordered $Ca^{2+}$ cations (the calcium ions occupy two sites related by the two-fold axis). The copper atom lies on the two-fold axis along *b* and is square-planar co-ordinated by the two symmetry related N(7) atoms of the 5′-IMP moieties and two water molecules which have replaced the ethylenediamine of the starting reagent. The 5′-IMP anions bind the copper atom in *cis* positions. Two further symmetry related water molecules at 2.52(1) Å complete a distorted octahedron (Figure 2). Deviations from the least-squares plane through N(7), O(w1) and their symmetry related atoms are 0.024 and −0.023 Å respectively. Bond lengths and angles around the copper atom are reported in Table 3.

The ribose ring shows the C(2′) *endo*-puckering and its orientation with respect to the purine is *anti* ($\chi_{CN} = -133.97°$). The conformation about the C(4′)–C(5′) bond is *gauche–gauche* ($\tau = 60.00°$).

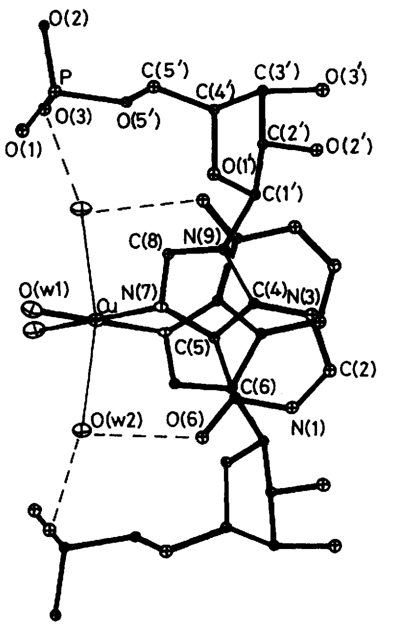

**Figure 2.** ORTEP drawing of $Ca[Cu(5'\text{-}IMP)_2(H_2O)_4]\cdot6.7H_2O$ (**2**). Thermal ellipsoids for non-hydrogen atoms are shown at 30% probability

The co-ordination polyhedron around the disordered calcium ion is constituted by five disordered water molecules and the two hydroxyl-oxygen atoms of the ribose group at distances in the range 2.33(3)—2.66(2) Å. The hydrogen-bonding network is quite similar to that observed in the 5'-GMP complex (**1**) [O(w2) $\cdots$ O(6) = 2.67, O(w2) $\cdots$ O(3) = 2.81 Å].

*Comparison with Analogous Platinum Complexes.*—The crystal structures of both compounds, like all the 1:2 ternary metal complexes of 6-oxopurine nucleotides and an aliphatic amine or imidazole,[5,10–13] are essentially based on those of the sodium salts of the respective nucleotides,[14,15] as first pointed out by Marzilli and co-workers.[10a] In these structures a water molecule links two nucleotides through hydrogen bonds $H_2O(1) \cdots N(7)$. The nucleotide moieties fold back forming two intramolecular hydrogen bonds $O(6) \cdots H_2O(2)$ and O(phosphate) $\cdots$ $H_2O(2)$, where $H_2O(2)$ is a water molecule hydrogen-bonded to $H_2O(1)$. In the metal complexes the platinum(II) or copper(II) ions bind two nucleotides *via cis*-M–N(7) co-ordination. The conformation of the nucleotide moieties is approximately the same and the two intramolecular hydrogen bonds O(6) $\cdots$ $H_2O$ and O(phosphate) $\cdots$ $H_2O$ are formed with a water molecule loosely bound to the metal in an octahedral position.

These structures have contributed to elucidating the mechanism of platinum binding to adjacent guanine bases in the same strand of DNA.[2] In fact the dihedral angle between the purine planes varies between 22° in Na[5'-IMPH][14] and 43° in $[Pt(5'\text{-}IMP)_2(NH_3)_2]^{2-}$.[10] The distortion induced in the DNA structure, upon binding of the platinum atom, would inhibit DNA replication and be responsible for the selective cytotoxicity of *cis*-$[Pt(NH_3)_2Cl_2]$.

The similarity of these structures, no matter which is the purine *cis*-binding moiety, whether a water molecule or platinum(II), a copper(II) or cobalt(III) ion, shows that the metal co-ordination does not affect the stereochemistry of these complexes. Furthermore the two purine bases are always oriented head-to-tail, with a rigorous or approximate $C_2$ molecular symmetry, but this arrangement seems rather unlikely in native DNA.[16] The crystal structure of *cis*-$[Pt(NH_3)_2\{d(pGpG)\}]$ [d(pGpG) = di(guanosine-5')diphosphate] shows, in all four independent molecules, the purine bases in the head-to-head orientations, with the two O(6) oxygen atoms on the same side of the platinum co-ordination plane.[17] The angles between the co-ordinated purine bases range from 76 to 87°. Analogous values of this angle have been found in other examples of head-to-head arrangements in platinum–bis(guanine) complexes.[10a] This obviously would lead to a much greater distortion of the DNA conformation than expected on the basis of the mononucleotide complex structure.

An interesting aspect of the structure of (**2**) is the replacement of the ethylenediamine molecule in the metal environment by two water molecules. This has been already observed by other authors and attributed to the strong *trans* effect of the N(7) bonded purines.[13] It has been pointed out that this effect might have interesting implications for the mode of binding of *cis*-$[Pt(NH_3)_2Cl_2]$ to DNA, although the kinetic lability of copper(II) and platinum(II) complexes is quite different. In fact platinum, after binding two bases of the same strand, could bind two additional ligands in the complementary strand, forming a firmly bound complex with intra- and inter-strand cross-links.[18] There is considerable evidence that *cis*-$[Pt(NH_3)_2Cl_2]$ forms interstrand cross-links although this may not be the critical lesion responsible for the cytotoxicity of the drug.[19]

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