# The *X*-Ray Structure of the $[Cu(5'\text{-GMP})_2(en)(H_2O)_2]^{2-}$ Complex Ion (5'-GMP = guanosine 5'-monophosphate; en = ethylenediamine). Its Close Resemblance with Platinum Co-ordination in *cis*-Diamineplatinum(II)–Nucleotide Complexes

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The crystal structure of $Ca[Cu(5'\text{-GMP})_2(en)(H_2O)_2] \cdot 8H_2O$ (5'-GMP = guanosine 5'-monophosphate; en = ethylenediamine) shows the copper atom to be coplanar with the two nitrogen atoms of ethylenediamine and the N(7) atoms of two 5'-GMP moieties in the *cis* configuration.

Although *cis*-$[Pt(NH_3)_2Cl_2]$ is now in clinical use against several kinds of tumours, the mechanism of its action is not fully understood.[1] Most of the available evidence shows the DNA of tumour cells to be the molecular target of *cis*-$[Pt(NH_3)_2Cl_2]$,[2] with the platinum atom binding the N(7) atoms of two adjacent guanine bases in the same strand.[3] The

**Table 1.** Structural parameters in some *cis*-diamineplatinum(II)–nucleotide complexes and in $[Cu(5'\text{-GMP})_2(en)(H_2O)_2]^{2-}$

| Complex | M–N(7)/Å | N(7)···N(7)/Å | Dihedral angle (°) between purine planes | Reference |
|---|---|---|---|---|
| $[Pt(5'\text{-IMP})_2(NH_3)_2]^{2-}$ [a] | 2.02 | 2.83 | 43 | 5 |
| $[Pt(5'\text{-IMP})_2(tn)^2]^{-}$ [b] | 2.08(1) | 2.96 | 38 | 6 |
| $[Pt(Me5'\text{-GMP})_2(tn)]^{2-}$ [c] | [d] | 2.86 | 39.6 | 7 |
| $[Cu(5'\text{-GMP})_2(en)(H_2O)_2]^{2-}$ | 2.04(2)av. | 2.83 | 42.5 | [e] |

[a] 5'-IMP = Inosine 5'-monophosphate. [b] tn = Trimethylenediamine. [c] Me5'-GMP = Methyl ester of guanosine 5'-monophosphate. [d] Not reported. [e] This work.

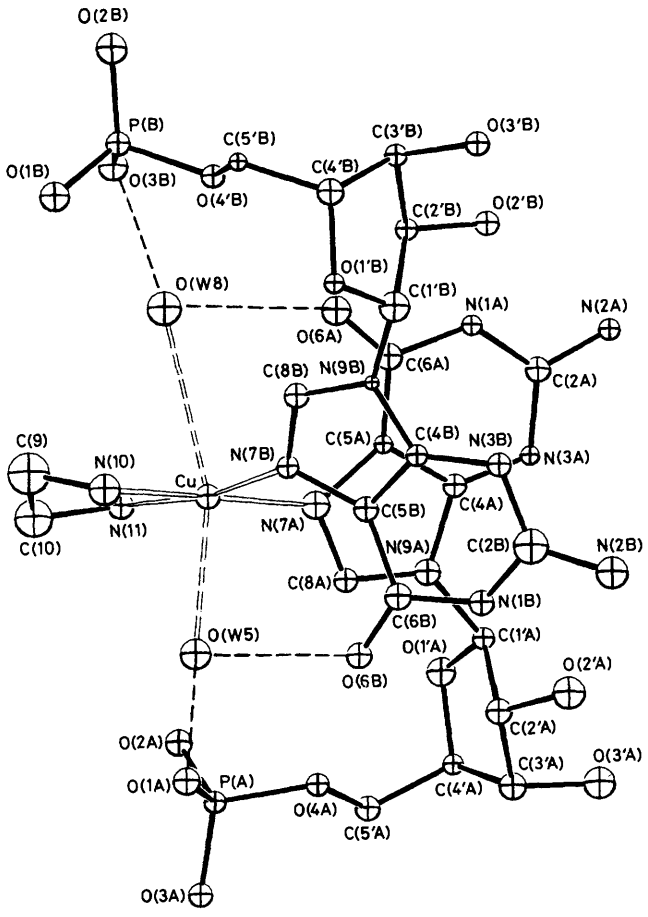


**Figure 1.** ORTEP drawing of the $[Cu(5'\text{-GMP})_2(en)(H_2O)_2^2]^-$ complex ion. Single broken lines indicate hydrogen bonds. Bond lengths and angles around copper: Cu–N(7A) 2.06(2), Cu–N(7B) 2.02(2), Cu–N(10) 1.98(2), Cu–N(11) 2.06(2), Cu–O(W8) 3.02(2), and Cu–O(W5) 2.50(2) Å; N(10)–Cu–N(11) 84.9(7), N(7A)–Cu–N(7B) 87.7(7), N(10)–Cu–N(7B) 95.2(7), N(11)–Cu–N(7A) 92.3(8), and O(W8)–Cu–O(W5) 161.6(7)°.

distortion induced in the DNA structure could lead, upon replication, to serious damage in the daughter strand and to cell death. Crystallographic investigations on *cis*-diamineplatinum(II) complexes with purine nucleosides and nucleotides are in agreement with this hypothesis and show the platinum atom to have a square-planar co-ordination from the two nitrogen atoms of the amine and two N(7) atoms of the purine base.[4]

As a part of our studies on the stereochemistry of metal ion complexes with nucleosides and nucleotides, we have prepared the compound $Ca[Cu(5'\text{-GMP})_2(en)(H_2O)_2]\cdot 8H_2O$ by mixing in aqueous solution stoicheiometric amounts of $[Cu(en)(H_2O)_2]SO_4$, the sodium salt of 5'-GMP, and $CaCl_2$ (5'-GMP = guanosine 5'-monophosphate; en = ethylenediamine). On cooling the slightly warm solution (pH *ca.* 7) small light blue plates separated overnight.

*Crystal data* for $Ca[Cu(5'\text{-GMP})_2(en)(H_2O)_2]\cdot 8H_2O$: monoclinic, space group $P2_1$, $a = 10.997(2)$, $b = 21.693(4)$, $c = 8.872(2)$ Å, $\beta = 94.69(1)°$, $U = 2109.4$ Å$^3$, $Z = 2$. Intensity data were collected on a Phillips PW 1100 diffractometer with Mo-$K_\alpha$ radiation for $2\theta \leq 50°$. The structure was solved by the heavy atom technique and refined by isotropic least-squares cycles to $R$ and $R_w$ factors of 0.074 and 0.064 respectively, over 1266 reflections with $I \geq 2.5\sigma(I)$.†

The molecular structure of the $[Cu(5'\text{-GMP})_2(en)(H_2O)_2]^{2-}$ complex ion is shown in Figure 1. The copper atom is co-ordinated by the two nitrogen atoms of ethylenediamine and the two N(7) atoms of the 5'-GMP moieties, at the corners of a slightly distorted square. The deviations from the best least-squares plane through the five atoms are: −0.074, −0.081, +0.086, −0.089, and +0.084 Å respectively for Cu, N(7A), N(7B), N(10), and N(11). Two further water molecules at 2.50(1) and 3.02(1) Å complete an elongated octahedral geometry around the copper atom. The calcium ions are co-ordinated by four water molecules, two ribose hydroxy oxygen atoms, and one phosphate oxygen atom at distances in the range 2.34—2.49 Å.

Both ribosyl moieties have the common C(2')-*endo* puckered conformation and their orientation with respect to purine is *anti*. The conformation about the C(4')–C(5') bond is *gauche–gauche*. 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 (Figure 1). No intra- or inter-molecular purine–purine stacking is observed.

In connection with the possible distortions induced on a polynucleotide structure by intrastand cross linking, Table 1 shows some significant structural parameters for the present compound and for some *cis*-diamineplatinum(II)–nucleotide complexes. To our knowledge this is the first non-platinum metal complex of this kind where the central metal ion shows a co-ordination essentially identical to the analogous platinum complex. $[Cu(5'\text{-IMP})_2(dien)]^{2-}$ (dien = diethylenetriamine) reported by Marzilli *et al.*[8] shows the copper atom bound to two *cis* 5'-IMP moieties, which are however in axial and equatorial positions, with two different Cu–N(7) bond lengths. From a stereochemical point of view, copper appears a potential candidate for platinum substitution in antitumour active metal complexes.

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† The atomic co-ordinates for this work 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.