The *cis*-Binding of Inosine 5′-Monophosphate and Guanosine 5′-Monophosphate to Cobalt(III) in 1:1 Metal-nucleotide Complexes; *X*-Ray Crystal Structures of Ternary Complexes with Ethylenediamine

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X-Ray structural studies on the ternary complexes $[Co(en)_2(OH_2)_2][Co(5'\text{-IMP})_2(OH_2)_4]Cl_2\cdot 4H_2O$ (**1**) and $[Co(en)_2(OH_2)_2][Co(5'\text{-GMP})_2(OH_2)_4]Cl_2\cdot 4H_2O$ (**2**) (en = ethylenediamine; 5′-IMP = inosine 5′-monophosphate; 5′-GMP = guanosine 5′-monophosphate) show that they are isomorphous and that cobalt binds to two symmetry-related nucleotide moieties in the *cis*-position through the N(7) atoms on the bases; this mode of binding is observed for the first time in a 1:1 metal–nucleotide complex.

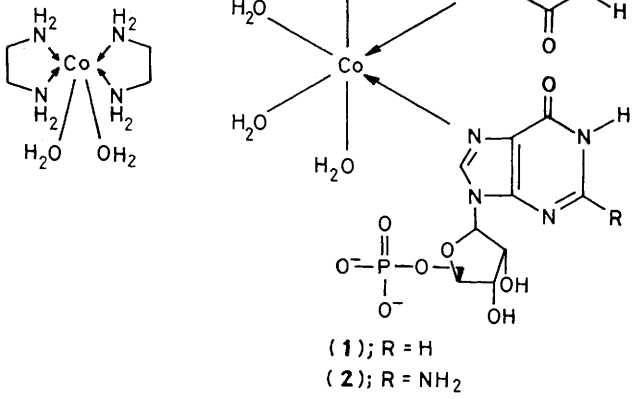
In recent years research activity on the interaction of metal ions with nucleic acid constituents has intensified following Rosenberg's[1] observation that certain Pt^{II} compounds are anti-tumour agents. One of the proposed explanations for the activity of these drugs is the formation of an intrastrand linkage in DNA between two guanosine bases bound through N(7) atoms to a single Pt^{II} centre. Intrastrand cross-linking models[2] involving Pt^{II} and guanosine, inosine 5′-monophosphate (5′-IMP), and the phosphate methyl ester of guanosine 5′-monophosphate (Me-5′-GMP) are known. We report the preparation and structural studies of the ternary complexes (**1**) and (**2**) where two 6-oxopurine nucleotides co-ordinate to the Co^{III} centre in the *cis*-position through the N(7) atoms of the bases, as in the case of the 1:2 Pt^{II} complexes mentioned.

The complexes were prepared by mixing aqueous solutions of $[Co(en)(H_2O)_3Cl]SO_4$ (en = ethylenediamine) and the disodium salt of the nucleotides (5′-IMP or 5′-GMP) in equimolar ratio; the resultant solutions were allowed to evaporate at room temperature. Yellow needle-shaped crystals appeared after about one week.

Crystal data: orthorhombic, space group $C222_1$; (**1**): a = 8.725(1), b = 25.891(5), c = 21.212(5) Å, Z = 8; (**2**): a = 8.733(2), b = 26.169(4), c = 21.288(4) Å, Z = 8. Intensity data were collected on a CAD-4 diffractometer with Mo-K_α radiation for $2\theta \leq 45°$. The structures were solved by the heavy-atom method and refined to present R values of 0.093 and 0.10 for 1725 and 1702 reflections for (**1**) and (**2**), respectively, with anisotropic temperature factors.†

The molecular structure of the $[Co(5'\text{-IMP})(en)(H_2O)_3]^+$ complex ion is shown in Figure 1. Contrary to expectation the chelate ligand and nucleotide are not co-ordinated to the same metal ion. The metal ions lie on two independent 2-fold axes. The metal ion on 2a is octahedrally co-ordinated by two en molecules and two water molecules; the other on 2b also has an octahedral co-ordination with two N(7) atoms of symmetry-related 6-oxopurine nucleotides in the *cis*-position and four water molecules. The ribosyl moiety has the C(2′)-*endo* pucker structure and its orientation with respect to the purine framework is *anti*. The conformation about the C(4′)–C(5′) bond is *gauche–gauche*. The charge-neutralising chloride ion and the carbon atoms of the en molecule are disordered. The structure of (**2**) is similar except for the additional NH_2 group at the C(2) position.

The structures of compounds (**1**) and (**2**), like the Pt^{II} complexes with 6-oxopurine nucleotides, are based on those of the



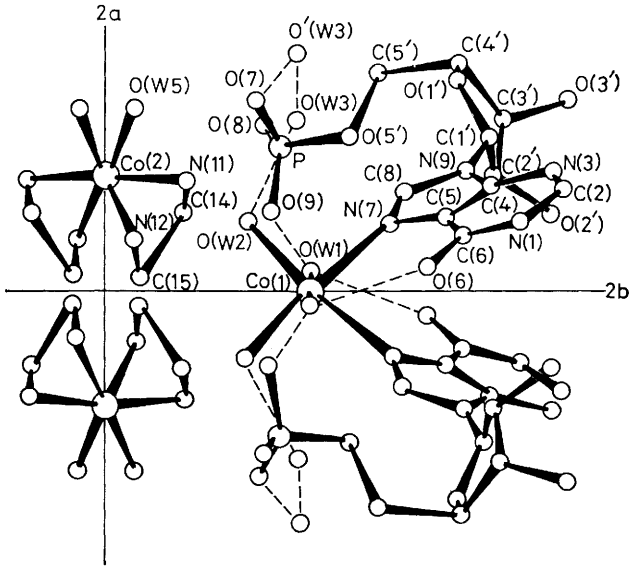


Figure 1. Structure of $[Co(5'\text{-IMP})(en)(H_2O)_3]^+$. Broken lines indicate hydrogen bonds. Co-ordinating distances: Co(1)–N(7) 2.18(1), Co(1)–O(W1) 2.10(1), Co(1)–O(W2) 2.08(1), Co(2)–N(11) 2.00(2), Co(2)–N(12) 2.03(3), and Co(2)–O(W5) 1.94(2) Å. Disorder of the en molecule is not illustrated.

† 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.

Table 1. Structural parameters in (nucleotide)Co^{III} and some bis(nucleotide)Pt^{II} complexes.

Complex	Interligand N(7) · · · · N(7) distance (Å)	Dihedral angle (°) between purine planes	Metal (%)	Reference
Na_2[5′-GMP]	3.18	2.3	0	4
Na[5′-IMPH][a]	3.48	22	0	3
$[Pt(5'\text{-IMP})_2(tn)]^{2-}$	2.93	38.2	*ca.* 74	2 (Table 1)
$[Co(5'\text{-GMP})(en)(H_2O)_3]^{+}$	2.92	41.5	100	Present work
$[Co(5'\text{-IMP})(en)(H_2O)_3]^{+}$	2.89	39.9	100	Present work
$[Pt(Me\text{-}5'\text{-GMP})_2(tn)]$	2.86	39.6	100	2
$[Pt(5'\text{-IMP})_2(NH_3)_2]^{2-}$	2.88	40.7	*ca.* 86	2 (Table 1)

[a] Disodium salt of 5′-IMP is isomorphous with the monosodium salt, Na[5′-IMPH]. tn = trimethylenediamine.

sodium salts[3,4] of the respective nucleotides. Co^{III} links the two nucleotides through *cis*-co-ordination bonds by replacing water in the sodium salt of 5′-IMP or the sodium ion in the sodium salt of 5′-GMP. The metal ion is markedly out of the plane of the purine base (0.65 Å); thus, although the angle N(7)–Co–N(7) is 82°, the dihedral angle between the two bases is only 39.9° [values for (**1**)].

Most of the Pt^{II}–5′-IMP complexes mentioned are non-stoicheiometric. Chiang *et al*[5] have rationalized these unusual stoicheiometries in terms of the crystal packing forces which are operative in the sodium salt of 5′-IMP compared with the co-ordinating tendency of the Pt^{II} fragment. The comparative structural parameters given in Table 1 suggest that Co^{III} co-ordination-induced distortion in the structures of sodium salts of 6-oxopurine nucleotides is comparable to that shown by Pt^{II} complexes.

Our preliminary studies on the structure of the $[Ni(5'\text{-GMP})(en)(H_2O)_3]\cdot 5H_2O$ complex indicate that it is isomorphous with the Co^{III} complexes discussed. The structural similarities displayed by the sodium salts, Pt^{II} complexes, (en)Co^{III} complexes, and the (en)Ni^{II} complex of 6-oxopurine nucleotides are highly significant in terms of the possible effect on polynucleotide structure due to intrastrand cross-linkage by a metal complex.

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