Interaction of Metal Ions with 6-Oxopurine Nucleotides. Part 1. *X*-Ray Structures of Ternary Cobalt(III) Complexes with Inosine 5′-Monophosphate or Guanosine 5′-Monophosphate†

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The crystal structures of two ternary metal nucleotide complexes of cobalt, $[Co(en)_2(H_2O)_2][Co(5'\text{-IMP})_2(H_2O)_4]Cl_2\cdot4H_2O$ (**1**) and $[Co(en)_2(H_2O)_2][Co(5'\text{-GMP})_2(H_2O)_4]Cl_2\cdot4H_2O$ (**2**), have been analysed by *X*-ray diffraction (en = ethylenediamine, 5′-IMP = inosine 5′-monophosphate, and 5′-GMP = guanosine 5′-monophosphate). Both complexes crystallize in the orthorhombic space group $C222_1$ with a = 8.725(1), b = 25.891(5), c = 21.212(5)Å, Z = 4 for (**1**) and a = 8.733(2), b = 26.169(4), c = 21.288(4)Å, Z = 4 for (**2**). The structure of (**1**) was solved by the heavy-atom method, while that of (**2**) was deduced from (**1**). The structures were refined to R values of 0.09 and 0.10 for 1 546 and 1 572 reflections for (**1**) and (**2**) respectively. The two structures are isomorphous. A novel feature is that the chelate ligand en and the nucleotide are not co-ordinated to the same metal ion. One of the metal ions lying on the two-fold a axis is octahedrally co-ordinated by two chelating en molecules and two water oxygens, while the other on the two-fold b axis is octahedrally co-ordinated by two N(7) atoms of symmetry-related nucleotides in a *cis* position and four water oxygens. The conformations of the nucleotides are C(2′)-*endo*, *anti*, and *gauche–gauche*. In both (**1**) and (**2**) the charge-neutralising chloride ions are disordered in the vacant space between the molecules. These structures bear similarities to the mode of nucleotide co-ordination to Pt^{II} complexes of 6-oxopurine nucleotides, which are the proposed models for intrastrand cross-linking in DNA by a metal complex.

There has been a burgeoning interest in the interaction of metal ions with nucleic acid constituents during the past few years,[1,2] mainly due to the following reasons: (*i*) metal ions play an important role in the biochemistry of nucleic acids, (*ii*) certain platinum complexes, notably *cis*-$[Pt(NH_3)_2Cl_2]$, are used as effective antitumour drugs which are widely believed to produce their effects *via* interaction with nucleic acids, and (*iii*) a diversity of metal ions and metal compounds has been employed to probe into the function of nucleic acids and as aids in the separation, purification, and structural investigations of these biomolecules.

Many metal complexes with nucleic acid constituents have been investigated by *X*-ray diffraction.[3–5] Studies on binary complexes of metal ions such as Co^{II}, Ni^{II}, Mn^{II}, or Fe^{II} with 6-oxopurine nucleotides in particular, have shown that the nucleotides co-ordinate through the N(7) atom of the base to give the structural type $[Mn^{II}(\text{nucleotide})(H_2O)_5]$.[4] In recent years we have been particularly interested in the co-ordination behaviour of 6-oxopurine nucleotides in ternary complexes.[6,7] Marzilli and Kistenmacher[8] have shown that the interligand interactions between ternary ligands such as ethylenediamine, and nucleic acid derivatives in the primary co-ordination sphere are important in influencing the stereoselectivity of the binding of metal complexes to nucleic acid derivatives. So far only Pt^{II}[9–11] and Cu^{II}[12,13] ternary nucleotide complexes containing such chelate ligands have been structurally characterized. In this paper, we report the preparation and *X*-ray structures of Co^{III} complexes with inosine 5′-monophosphate (5′-IMP) or guanosine 5′-monophosphate (5′-GMP) and containing ethylenediamine (en) as a ternary ligand. A preliminary account of this work has appeared.[14]

Experimental

Preparation of the Complexes.—The complex $[Co(en)(H_2O)_3Cl]SO_4$ was prepared by the procedure reported for the synthesis of *cis*-$[Co(en)_2(H_2O)Cl]SO_4$,[15] except that an equimolar ratio of the cobalt salt, $CoCl_2$, and en was employed. The resulting yellow crystals were washed with ice-cold water, ethanol, and diethyl ether.

The ternary nucleotide complexes were prepared by mixing aqueous solutions of $[Co(en)(H_2O)_3Cl]SO_4$ and the disodium salt of the nucleotide (5′-IMP or 5′-GMP) in an equimolar ratio. The resultant solutions were allowed to evaporate at room temperature. Yellow needle-shaped crystals appeared after *ca.* 1 week.

Collection and Reduction of X-*Ray Intensity Data.*—Unit-cell dimensions and their associated standard deviations, for both $[Co(en)_2(H_2O)_2][Co(5'\text{-IMP})_2(H_2O)_4]Cl_2\cdot4H_2O$ (**1**) and $[Co(en)_2(H_2O)_2][Co(5'\text{-GMP})_2(H_2O)_4]Cl_2\cdot4H_2O$ (**2**), were derived from a least-squares fit to the setting angles of 20 carefully selected and centred reflections on a Nonius CAD-4 automated diffractometer. Intensity data were collected in the ω–2θ scan mode with a constant scan speed of 1° min^{-1} and scan width $\Delta\theta = (0.75 + 0.45 \tan\theta)$. The intensities of two standard reflections were monitored every 3 000 s and showed no systematic variations over the duration of the experiment. The intensities were corrected for Lorentz and polarization effects, but not for absorption. Crystal data are given in Table 1.

Structure Solution and Refinement.—The structure of (**1**) was established by the heavy-atom method. In the Patterson map, the two metal ions were located on special positions, *i.e.* the two non-equivalent two-fold axes along a and b. A weighted difference Fourier map with these two metal positions revealed all the non-hydrogen atoms except the carbon atoms of the en molecule and the chloride ion. In the subsequent Fourier map, the carbon atoms of the en molecule were identified. However,

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† *Supplementary data available:* see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1988, Issue 1, pp. xvii—xx.

Abbreviations used are those recommended by the IUPAC–IUB commission on Biochemical Nomenclature, *Eur. J. Biochem.*, 1970, **15**, 203.

Table 1. Crystal data for $[Co(en)_2(H_2O)_2][Co(5'\text{-}IMP)_2(H_2O)_4]Cl_2\cdot 4H_2O$ (**1**) and $[Co(en)_2(H_2O)_2][Co(5'\text{-}GMP)_2(H_2O)_4]Cl_2\cdot 4H_2O$ (**2**)

Compound	(**1**)	(**2**)
Formula	$C_{24}H_{58}Cl_2Co_2N_{12}O_{26}P_2$	$C_{24}H_{60}Cl_2Co_2N_{14}O_{26}P_2$
M	590.35	605.35
Crystal system	Orthorhombic	Orthorhombic
Space group	$C222_1$	$C222_1$
a/Å	8.725(1)	8.733(2)
b/Å	25.891(5)	26.169(4)
c/Å	21.212(5)	21.288(4)
U/Å^3	4 791.8	4 865.0
Z	4	4
D_c/g cm^{-3}	1.63	1.65
D_m/g cm^{-3}	1.64	1.66
F(000)	2 448	2 512
Crystal dimensions/mm	0.18 × 0.23 × 0.50	0.10 × 0.25 × 0.60
λ(Mo-K_α)/Å	0.7107	0.7107
μ(Mo-K_α)/cm^{-1}	9.12	9.00
2θ upper limit (°)	45	45
No. of reflections measured	2 431	2 485
No. of reflections used [$I \geqslant 3\sigma(I)$]	1 546	1 572
$R\ [=\Sigma\lvert F_o - \lvert F_c\rvert\rvert/\Sigma F_o]$	0.09	0.10
$R'\ \{=[\Sigma w(F_o - \lvert F_c\rvert)^2/\Sigma w F_o^2]^{\frac{1}{2}}\}$	0.12	0.14

Table 2. Final fractional co-ordinates (× 10^4) with e.s.d.s in parentheses for the non-hydrogen atoms of (**1**)

Atom	*x*	*y*	*z*
Co(1)	0	1 719(1)	2 500
Co(2)	−2 870(6)	0	5 000
P	−3 598(4)	1 439(1)	470(2)
O(5′)	−3 777(10)	2 063(3)	549(4)
O(7)	−4 637(11)	1 189(4)	953(4)
O(8)	−4 110(12)	1 301(4)	−200(4)
O(9)	−1 949(12)	1 358(4)	593(4)
N(1)	−1 716(14)	3 421(4)	3 627(5)
C(2)	−2 476(20)	3 761(6)	3 270(7)
N(3)	−2 984(14)	3 671(4)	2 692(5)
C(4)	−2 585(14)	3 166(4)	2 505(7)
C(5)	−1 783(17)	2 826(5)	2 826(6)
C(6)	−1 328(16)	2 944(5)	3 479(6)
O(6)	−663(13)	2 646(4)	3 851(4)
N(7)	−1 668(13)	2 360(4)	2 483(6)
C(8)	−2 403(19)	2 455(5)	1 947(7)
N(9)	−2 955(15)	2 945(5)	1 953(5)
C(1′)	−3 799(16)	3 180(5)	1 401(6)
C(2′)	−2 879(16)	3 185(5)	815(6)
O(2′)	−1 885(11)	3 641(4)	778(5)
C(3′)	−4 125(16)	3 205(6)	316(6)
O(3′)	−4 682(12)	3 691(3)	226(4)
C(4′)	−5 308(16)	2 849(5)	622(6)
O(1′)	−5 099(13)	2 890(4)	1 292(4)
C(5′)	−5 246(17)	2 273(5)	418(7)
N(11)	−2 791(23)	669(6)	4 546(8)
N(12)	−1 275(42)	−267(8)	4 370(11)
C(14)	−2 024(35)	646(11)	3 934(11)
C(15)	−395	280	4 132
O(W1)	36(16)	1 692(4)	1 509(4)
O(W2)	−1 759(19)	1 171(5)	2 489(8)
O(W3)	−4 261(29)	1 584(12)	3 002(11)
O(W4)	−7 383(79)	404(16)	5 430(22)
O(W5)	−4 496(27)	271(7)	5 546(11)

Table 3. Final positional parameters (× 10^4) with e.s.d.s in parentheses for the non-hydrogen atoms of (**2**)

Atom	*x*	*y*	*z*
Co(1)	0	1 712(1)	2 500
Co(2)	−2 886(8)	0	5 000
P	−3 562(5)	1 446(2)	456(2)
O(5′)	−3 747(14)	2 058(4)	531(5)
O(7)	−4 631(15)	1 197(4)	925(5)
O(8)	−4 092(14)	1 304(4)	−209(5)
O(9)	−1 906(14)	1 358(4)	585(5)
N(1)	−1 778(18)	3 375(6)	3 632(6)
C(2)	−2 538(25)	3 710(8)	3 270(8)
N(2)	−2 878(26)	4 176(7)	3 530(8)
N(3)	−2 966(16)	3 641(6)	2 684(6)
C(4)	−2 590(20)	3 148(5)	2 507(9)
C(5)	−1 768(21)	2 787(7)	2 835(7)
C(6)	−1 398(21)	2 928(7)	3 469(7)
O(6)	−743(16)	2 614(5)	3 857(5)
N(7)	−1 641(16)	2 339(4)	2 476(7)
C(8)	−2 339(22)	2 436(6)	1 942(8)
N(9)	−2 929(19)	2 931(6)	1 932(6)
C(1′)	−3 771(22)	3 165(6)	1 407(7)
C(2′)	−2 818(21)	3 183(6)	804(7)
O(2′)	−1 855(14)	3 637(4)	782(6)
C(3′)	−4 080(20)	3 182(6)	308(7)
O(3′)	−4 617(15)	3 675(4)	217(5)
C(4′)	−5 263(22)	2 842(6)	616(7)
O(1′)	−5 044(17)	2 877(4)	1 277(4)
C(5′)	−5 204(23)	2 276(6)	414(8)
N(11)	−2 813(28)	673(8)	4 530(10)
N(12)	−1 280(39)	−293(10)	4 416(11)
C(14)	−2 104(43)	676(17)	3 988(14)
C(15)	−172	242	3 911
O(W1)	86(18)	1 679(4)	1 513(5)
O(W2)	−1 778(20)	1 176(5)	2 512(8)
O(W3)	−4 292(31)	1 537(14)	3 004(11)
O(W4)	−3 073(56)	475(8)	1 584(15)
O(W5)	−4 616(35)	258(7)	5 516(9)

bond distances in the en group, particularly those associated with one of the carbon atoms, C(15), were unsatisfactory. On refinement it was observed that C(15) showed a very high thermal parameter (*B ca.* 20 Å^2), and tended to move away from the earlier position, resulting in less satisfactory bond parameters for the group. Attempts to find alternative positions were unsuccessful. Therefore, the position of this disordered atom as initially located in the Fourier map was fixed in further cycles of refinement. The charge-neutralising chloride ion was also disordered. Although a few peaks were identified for Cl^- in the vacant space between the molecules, refinement of these positions with partial occupancies was not satisfactory and therefore its contribution was ignored. The hydrogen atoms of the nucleotide molecule, except those bonded to O(2′) and O(3′), were fixed on the basis of geometrical considerations as they could not be located in the difference map. The contribution from these hydrogen atoms, with $B_{iso}(H) = B_{iso}(C,N) + 1.5$, was included in the subsequent cycles of refinement, but were not refined.

The structure of (**2**) was deduced from that of the isomorphous compound (**1**). Five cycles of isotropic least-squares refinement using the atomic parameters of (**1**), except those of the carbon atoms of en, the oxygen atoms of the lattice water molecules, and the disordered chloride ion, as starting parameters reduced the *R* value to 0.20. A difference Fourier synthesis at this stage revealed the positions of the remaining non-hydrogen atoms. As in the case of (**1**) the carbon atoms of the en groups were found to be disordered, the disorder of C(15) being particularly severe. Therefore the position of C(15) was fixed as in the case of (**1**). The chloride ions were found to be randomly disordered in this structure also. As before, hydrogen atoms were fixed on the basis of geometrical considerations and both their positional and thermal parameters were not refined.

Scattering factors were taken from International Tables.[16] Both structures were refined by the block-diagonal least-squares method using a program due to Shiono.[17] The weighting scheme employed was of the form $w = 1/\sigma^2(F_o)$. Computations were carried out on a DEC 1090 computer. Anomalous dispersion corrections were applied to the scattering factors of all non-hydrogen atoms. Diagrams were drawn using the program ORTEP-II.[18]

Atomic co-ordinates are given in Table 2 for (**1**) and Table 3 for (**2**). Additional material available from the Cambridge Crystallographic Data Centre comprises thermal parameters.

Results and Discussion

The molecular structure of $[Co(en)_2(H_2O)_2][Co(5'\text{-}IMP)_2(H_2O)_4]Cl_2{\cdot}4H_2O$ (**1**) together with the atomic numbering scheme is shown in Figure 1. Interatomic distances and angles are listed in Tables 4 and 5.

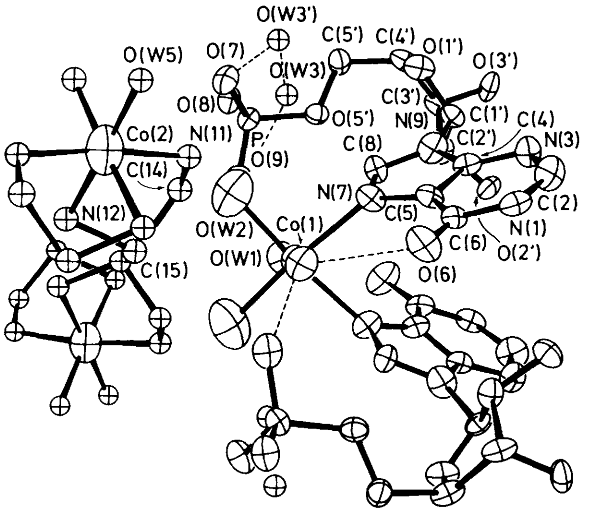

Figure 1. Structure of $[Co(en)_2(H_2O)_2]^{3+}[Co(5'\text{-}IMP)_2(H_2O)_4]^-$ in (**1**). Broken lines indicate hydrogen bonds. The structure of $[Co(en)_2(H_2O)_2]^{3+}[Co(5'\text{-}GMP)_2(H_2O)_4]^-$ in (**2**) is similar except for the additional NH_2 group at the C(2) position

Table 4. Bond lengths (Å) involving the non-hydrogen atoms, with e.s.d.s in parentheses

	(**1**)	(**2**)		(**1**)	(**2**)
Co(1)–N(7)	2.21(1)	2.18(1)	Co(1)–O(W1)	2.10(1)	2.10(1)
Co(1)–O(W2)	2.09(1)	2.09(2)	Co(2)–N(11)	1.98(2)	2.03(2)
Co(2)–N(12)	2.05(3)	2.02(3)	Co(2)–O(W5)	1.94(2)	1.99(3)
N(1)–C(2)	1.34(2)	1.34(2)	C(2)–N(2)		1.37(3)
C(2)–N(3)	1.32(2)	1.32(2)	N(3)–C(4)	1.41(2)	1.38(2)
C(4)–C(5)	1.31(2)	1.38(2)	C(5)–C(6)	1.47(2)	1.44(2)
C(6)–O(6)	1.25(2)	1.30(2)	C(6)–N(1)	1.32(2)	1.26(2)
C(5)–N(7)	1.41(2)	1.41(2)	N(7)–C(8)	1.33(2)	1.31(2)
C(8)–N(9)	1.36(2)	1.40(2)	N(9)–C(4)	1.34(2)	1.38(2)
N(9)–C(1′)	1.51(2)	1.47(2)	C(1′)–C(2′)	1.48(2)	1.53(2)
C(2′)–C(3′)	1.52(2)	1.53(2)	C(2′)–O(2′)	1.47(2)	1.46(2)
C(3′)–C(4′)	1.53(2)	1.51(2)	C(3′)–O(3′)	1.36(2)	1.39(2)
C(4′)–O(1′)	1.44(2)	1.42(2)	O(1′)–C(1′)	1.38(2)	1.37(2)
C(4′)–C(5′)	1.55(2)	1.54(2)	C(5′)–O(5′)	1.42(2)	1.42(2)
P–O(5′)	1.63(1)	1.62(1)	P–O(7)	1.51(1)	1.51(1)
P–O(8)	1.53(1)	1.53(1)	P–O(9)	1.48(1)	1.49(1)
N(11)–C(14)	1.46(3)	1.31(4)	N(12)–C(15)	1.69	2.01
C(14)–C(15)	1.76	2.04			

The structures of (**1**) and (**2**) are essentially isomorphous except for the substituent on C(2), and are also isostructural with bis(6-oxopurine nucleotide) Pt^{II} complexes.[9–11,19,20] A novel and unexpected feature of the structures is that the ternary ligand en and the nucleotide moieties are not co-ordinated to the same metal ion. The symmetry-related nucleotides [5′-IMP in (**1**) and 5′-GMP in (**2**)] co-ordinate in *cis* positions through the N(7) atoms of the bases to the metal ion Co(1), lying on a crystallographic two-fold axis parallel to *b*. The Co–N(7) distances are 2.21(1) and 2.18(1) Å for (**1**) and (**2**) respectively. These values are significantly longer than the M–N(7) distances (2.02—2.08 Å) observed for the analogous Pt^{II} complexes.[9–11,19,20] However, they are close to the Co–N(7) bond length of 2.16 Å reported for a binary Co(5′-IMP) complex.[21] The remaining octahedral co-ordination sites of Co(1) are occupied by water molecules, at an average distance of 2.10 Å in both compounds. The metal ion Co(2) lies on a second crystallographic two-fold axis parallel to *a*. The six co-ordination sites of Co(2) are occupied by four nitrogen atoms of two bidentate en molecules $[Co\text{–}N(en)_{av} = 2.02$ in (**1**) and 2.03 Å in (**2**)] and two water oxygen atoms [Co–O(W) = 1.94 in (**1**) and 1.99 Å in (**2**)]. As found in Pt^{II} complexes, the metal ion Co(1) is significantly out of the plane of the purine rings, deviations being 0.68 and 0.67 Å in (**1**) and (**2**) respectively. Therefore, even though the N(7)–Co–N(7′) angles are 82.6(4)° in (**1**) and 82.3(5)° in (**2**), the dihedral angle between the two purine bases is only 39.7 in (**1**) and 40.6° in (**2**). Although the deviations of the metal ions from the plane of the purine bases in bis(nucleotide) Pt^{II} complexes are of the same order, the N(7)–M–N(7′) angles are close to 90° (90—92°).[9–11,19,20] Interestingly, the dihedral angle between the purine planes both in the present complexes and Pt^{II} complexes, where the metal occupancy is close to 100%, compare very well (Table 6). Therefore the conformation of the *cis*-bound nucleotides has a certain amount of rigidity which cannot be drastically changed by the nature of the metal ion. The near orthogonality in the bond angle at Pt^{II} is apparently due to the shorter M–N(7) bonds compared to the present case. Another relevant parameter in these type of structures is the N(7)$\cdots$N(7′) distance which is 2.91 in (**1**) and 2.87 Å in (**2**).

The structures of compounds (**1**) and (**2**), like the Pt^{II} complexes of 6-oxopurine nucleotides, bear a strong resemblance to those of the sodium salts of 5′-IMP[22] and 5′-GMP.[23] In the structure of Na(5′-IMPH)[22] a water molecule lies on a crystallographic two-fold axis and links two symmetry-related 5′-IMPH anions *via* hydrogen bonds of the type $OH_2\cdots N(7)$, while in the case of $Na_2(5'\text{-}GMP)$,[23] a sodium ion lies on a pseudo-two-fold symmetry axis and binds the two 5′-GMP moieties through $Na^+\cdots N(7)$ interactions. In (**1**) and (**2**), the metal ion replaces the water molecule or Na^+ and links the nucleotides through *cis*-M–N(7) co-ordination bonds.

Although both *cis* and *trans* isomers of $[Pt(NH_3)_2Cl_2]$ are mutagenic, only the *cis* isomer has shown significant antitumour activity.[24] One of the explanations proposed for the binding of the *cis* isomer to DNA is the formation of an intrastrand linkage in DNA between two guanosine bases bound through N(7) atoms to a single platinum centre. In this context, the structural parameters, in particular the dihedral angles between the bases, in bis(nucleotide) metal complexes are of great significance. The comparative structural parameters for some of the complexes are given in Table 6.

The conformation about the glycosidic bond is *anti*.[25] The torsion angle C(4)–N(9)–C(1′)–O(1′) is 119 and 121° in (**1**) and (**2**) respectively. The nucleotides in both compounds have a *gauche–gauche* conformation about the C(4′)–C(5′) bond. The ribosyl moiety displays the C(2′)-*endo* puckering mode. These conformations are commonly observed in other metal complexes having similar nucleotide geometry.[9,10,19,20] It may

Table 5. Bond angles (°) involving the non-hydrogen atoms, with e.s.d.s in parentheses

	(1)	(2)		(1)	(2)
N(7)–Co(1)–O(W1)	91.1(4)	97.7(5)	N(7)–Co(1)–O(W2)	91.5(5)	90.9(6)
N(7)–Co(1)–N(7′)	82.6(4)	82.3(5)	N(7)–Co(1)–O(W1′)	91.8(4)	91.7(5)
N(7)–Co(1)–O(W2′)	174.0(5)	172.9(6)	O(W1)–Co(1)–O(W2)	88.7(5)	90.7(6)
O(W1)–Co(1)–O(W1′)	176.2(4)	175.4(6)	O(W1)–Co(1)–O(W2′)	88.7(5)	86.3(6)
O(W2)–Co(1)–O(W2′)	94.5(6)	95.9(6)	N(11)–Co(2)–N(12)	87.4(9)	90.3(10)
N(11)–Co(2)–O(W5)	91.3(8)	90.1(9)	N(11)–Co(2)–N(11′)	176.0(7)	176.4(9)
N(11)–Co(2)–N(12′)	89.9(9)	87.2(10)	N(11)–Co(2)–O(W5′)	91.6(8)	92.6(9)
N(12)–Co(2)–O(W5)	175.7(10)	174.3(11)	N(12)–Co(2)–N(12′)	94.5(11)	92.3(11)
N(12)–Co(2)–O(W5′)	89.6(10)	93.4(11)	O(W5)–Co(2)–O(W5′)	86.3(9)	80.9(9)
Co(1)–N(7)–C(5)	132.9(9)	131.9(11)	Co(1)–N(7)–C(8)	118.2(9)	118.1(13)
N(1)–C(2)–N(2)		117.2(17)	N(1)–C(2)–N(3)	125.1(14)	126.5(17)
N(2)–C(2)–N(3)		116.3(17)	C(2)–N(3)–C(4)	109.9(12)	108.6(15)
N(3)–C(4)–C(5)	127.3(12)	128.7(16)	C(4)–C(5)–C(6)	119.4(12)	114.7(15)
C(5)–C(6)–N(1)	110.4(11)	115.9(15)	C(6)–N(1)–C(2)	127.5(12)	125.3(16)
C(5)–C(6)–O(6)	126.4(12)	122.3(15)	N(1)–C(6)–O(6)	123.2(12)	121.8(16)
C(4)–C(5)–N(7)	110.1(12)	107.8(15)	C(6)–C(5)–N(7)	129.9(12)	135.0(15)
C(5)–N(7)–C(8)	104.4(11)	105.8(14)	N(7)–C(8)–N(9)	109.7(12)	111.3(15)
C(8)–N(9)–C(4)	108.7(11)	106.8(14)	N(9)–C(4)–C(5)	107.1(12)	106.2(15)
N(9)–C(4)–N(3)	125.5(12)	125.0(15)	C(8)–N(9)–C(1′)	122.8(11)	125.6(14)
C(4)–N(9)–C(1′)	128.5(11)	127.6(14)	O(1′)–C(1′)–C(2′)	108.0(11)	106.8(14)
C(1′)–C(2′)–C(3′)	101.4(11)	100.8(13)	C(2′)–C(3′)–C(4′)	99.5(11)	101.2(13)
C(3′)–C(4′)–O(1′)	106.9(11)	107.4(13)	C(4′)–O(1′)–C(1′)	108.1(9)	110.1(13)
N(9)–C(1′)–O(1′)	108.2(10)	109.2(14)	N(9)–C(1′)–C(2′)	112.9(11)	112.3(14)
C(2′)–C(3′)–O(3′)	112.7(11)	109.8(13)	O(3′)–C(3′)–C(4′)	112.0(11)	112.1(13)
O(2′)–C(2′)–C(1′)	111.9(11)	111.5(13)	O(2′)–C(2′)–C(3′)	110.9(11)	113.4(13)
C(3′)–C(4′)–C(5′)	115.9(11)	114.9(14)	C(5′)–C(4′)–O(1′)	109.9(11)	109.4(13)
C(4′)–C(5′)–O(5′)	110.2(11)	111.6(14)	C(5′)–O(5′)–P	116.5(8)	118.1(10)
O(5′)–P–O(7)	107.2(5)	107.5(6)	O(5′)–P–O(8)	107.4(5)	107.5(6)
O(5′)–P–O(9)	102.5(5)	103.4(6)	O(7)–P–O(8)	110.7(5)	108.6(7)
O(7)–P–O(9)	113.8(6)	114.3(7)	O(8)–P–O(9)	114.5(6)	115.1(7)
Co(2)–N(11)–C(14)	114.3(15)	117.0(22)	N(11)–C(14)–C(15)	100.4	117.3
C(14)–C(15)–N(12)	99.0	87.0	C(15)–N(12)–Co(2)	102.7	113.3

Table 6. A comparison of the structural parameters in the sodium salts and metal complexes of 6-oxopurine nucleotides

Compound	Interligand N(7) ··· N(7′)/Å	Dihedral angle (°) between purine planes	N(7)–M–N(7′)/°	Ref.
Na_2(5′-GMP)	3.18	2.3		23
Na(5′-IMPH)	3.48	22.0		22
$[Pt(5'\text{-}IMP)_2(pd)]^{2-}$	2.93	38.2	90.2	10
$[Pt(Me\text{-}5'\text{-}GMP)_2(pd)]$	2.86	39.6	90.1	11
$[Pt(5'\text{-}IMP)_2(NH_3)_2]^{2-a}$	2.88	40.7	90.0	20
$[Pt(5'\text{-}IMP)_2(en)]^{2-}$	3.26	31.0		9
$[Pt(5'\text{-}IMP)_2(NH_3)_2]^{2-b}$	2.83	43.0	89.0	19
$[Cu(5'\text{-}GMP)_2(en)(H_2O)_2]^{2-}$	2.83	42.5	87.7	13
$[Cu(5'\text{-}GMP)_2(im)_{0.8}(H_2O)_{1.2}(H_2O)_2]^{2-c}$	2.97	35.5	89.6	6
$[Cu(5'\text{-}IMP)_2(dien)]^{2-}$	3.23	30.4	78.6	12
$[Co(5'\text{-}IMP)_2(H_2O)_4]^-$	2.91	39.7	82.6	This work
$[Co(5'\text{-}GMP)_2(H_2O)_4]^-$	2.87	40.6	82.3	This work

[a] 86% Pt. [b] 100% Pt. [c] im = Imidazole.

be noted that in the case of binary complexes of the type $[M^{II}(nucleotide)(H_2O)_5]$, the conformations about N(9)–C(1′) and C(4′)–C(5′) are the same as above, but the sugar puckering is C(3′)-*endo*.

The bond lengths and angles in the nucleotides are in overall agreement with those found in Pt^{II} complexes. As mentioned earlier, the en molecules around Co(2) are disordered. The disorder is mainly associated with the carbon atom C(15). The two bonds associated with this atom are significantly longer than normal. The purine base is approximately planar. In both (**1**) and (**2**), C(5) shows a deviation from the mean plane through the nine-atom framework on the same side as Co(1) [0.06 in (**1**) and 0.05 Å in (**2**)]. The atom O(6) is out of the plane by 0.09 Å in both cases in a direction opposite to that of C(5). The N(2) atom, in the case of (**2**) is off the plane by 0.05 Å on the same side as O(6). The imidazole and pyrimidine rings of the purine bases make an angle of 3.1° in both complexes about the C(4)–C(5) bond.

In the absence of intercomplex base–base interactions, the structure is dominated by intracomplex interactions between two-fold symmetry related nucleotides. The interactions involve O(1′) of the sugar and the pyrimidine ring of the symmetry-related nucleotide. The significant interactions for (**1**) are O(1′) ··· N(1) 3.11, O(1′) ··· C(6) 3.16 and O(1′) ··· C(2) 3.33 Å; the corresponding interactions in (**2**) are 3.07, 3.16, and 3.18 Å respectively. Such sugar–base interactions were also observed in the structure of Na(5′-IMPH).[22] Apart from these, intracomplex base–base interactions are also observed, particu-

Table 7. Possible hydrogen bonds

Donor(D)	Acceptor(A)	Distance (D) ··· (A)/Å (1)	Distance (D) ··· (A)/Å (2)	Angle subtended at the donor atom (°)	(1)	(2)
N(1)	O(8^{VI})	2.69	2.72	C(2)–N(1) ··· O(8^{VI})	119	117
				C(6)–N(1) ··· O(8^{VI})	114	117
O(2′)	O(8^{IV})	2.72	2.71	C(2′)–O(2′) ··· O(8^{IV})	127	125
O(3′)	O(9^{V})	2.64	2.63	C(3′)–O(3′) ··· O(9^{V})	108	108
O(W1)	O(6^{II})	2.64	2.63	Co(1)–O(W1) ··· O(6^{II})	105	106
O(W1)	O(9^{I})	2.74	2.76	Co(1)–O(W1) ··· O(9^{I})	135	135
O(W2)	O($W3^{I}$)	2.66	2.61	Co(1)–O(W2) ··· O($W3^{I}$)	109	113
O(W3)	O($W3^{III}$)	2.49	2.48	O(W2) ··· O(W3) ··· O($W3^{III}$)	94	94
O($W3^{III}$)	O(7^{I})	2.62	2.62	O(W3) ··· O($W3^{III}$) ··· O(7^{I})	122	125
O(W5)	O($W4^{I}$)	2.56		Co(2) ··· O(W5) ··· O($W4^{I}$)	135	
N(11)	O(7^{III})	2.82	2.79	Co(2)–N(11) ··· O(7^{III})	125	125
N(12)	O(3^{VII})	2.95	2.92	Co(2)–N(12) ··· O(3^{VII})	108	112
O(W4)	O(7^{I})		2.72			

Symmetry codes: I, x, y, z; II, $-x, y, \frac{1}{2} - z$; III, $-1 - x, y, \frac{1}{2} - z$; IV, $\frac{1}{2} + x, \frac{1}{2} - y, -z$; V, $-\frac{1}{2} + x, \frac{1}{2} - y, \bar{z}$; VI; $-\frac{1}{2} - x, \frac{1}{2} - y, \frac{1}{2} + z$; VII, $-\frac{1}{2} - x, -\frac{1}{2} + y, \frac{1}{2} - z$.

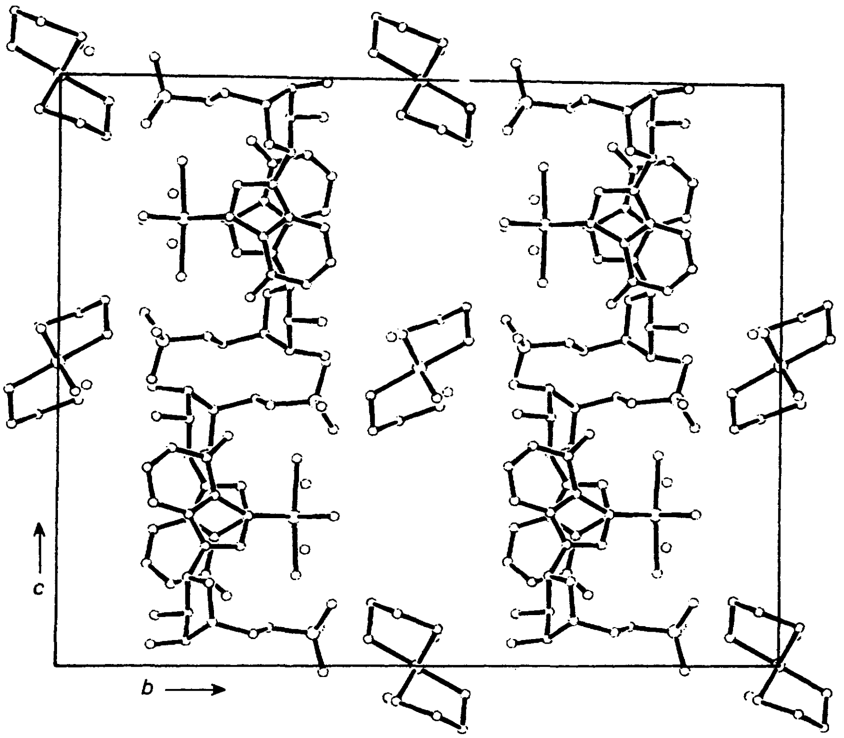

Figure 2. Packing of molecules of (**1**) viewed down *a*

larly between O(6) and C(8) of the symmetry-related nucleotides. The O(6) ··· C(8) distance is 3.20 in (**1**) and 3.22 Å in (**2**). Similar interactions are also observed in the bis(nucleotide) Pt^{II} complexes; for example, a very short O(6) ··· C(8) contact (2.96 Å) has been reported for the complex [Pt(Me-5′-GMP)$_2$(pd)] (pd = propane-1,3-diamine, Me-5′-GMP = phosphate methyl esters of 5′-GMP).[11]

The possible hydrogen bonds are given in Table 7. The ligand water, O(W1), donates both hydrogens to form intracomplex hydrogen bonds of the type O(9) ··· O(W1) ··· O(6). The lattice water, O(W3), links the co-ordinated water, O(W2), and phosphate oxygen, O(7), through hydrogen bonds. These hydrogen bonds are shown in Figure 1. In both (**1**) and (**2**), the 2′-hydroxyl oxygen, O(2′), donates its proton to the phosphate oxygen, O(9). The other significant hydrogen bond is N(1)–H ··· O(8), as it represents the sugar–base interaction. The N(11) atom of en donates a proton to the phosphate oxygen, O(7), and N(12) donates to the 3′-hydroxyl oxygen.

The crystal packing (Figure 2) is similar in both structures. The [Co(nucleotide)$_2$(H$_2$O)$_4$]$^-$ anions lie in rows parallel to the *c* axis of the crystal. The sugar–phosphate hydrogen bonds link the neighbouring nucleotides within the row. The Co(2) ions carrying en lie in rows between rows of [Co(nucleotide)$_2$(H$_2$O)$_4$]$^-$. Lattice waters and disordered chloride ions occupy the vacant channels parallel to *a* between [Co(en)$_2$(H$_2$O)$_2$]$^{3+}$ cations. The packing of molecules in the present structures is similar to that observed for bis(nucleotide) Pt^{II} complexes[20] except for the nature of the cations. In the latter, hydrated Na^+ ions sit between the complexed nucleotide anions, while in the present structures $[Co(en)_2(H_2O)_2]^{3+}$ moieties occupy the space between the rows of metal–nucleotide anions.

Conclusions

One of the important aspects of the chemistry of metal interactions with nucleic acids is the selectivity shown by inorganic species in their co-ordination behaviour. Marzilli and Kistenmacher[8] have suggested that the exocyclic groups of purine and pyrimidine rings are a key to selectivity. These exocyclic groups can function in such a way as either to hinder co-ordination through steric factors or alternatively stabilize co-ordination by participating in favourable hydrogen bonding interactions with the other ligands in the primary co-ordination sphere of the metal. Although the objective of this study was to understand more about the principles governing such interactions, this objective has not been fully realized due to the fact that the ternary ligand en and the nucleotide are not co-ordinated to the same metal ion. Nevertheless, the role of the chelating ligand en in metal–nucleotide complexation is clearly seen. In contrast to the present ternary structures, in the case of binary structures, in the absence of en, the 6-oxopurine nucleotides co-ordinate through the N(7) atom of the base and the octahedral co-ordination of the metal ion is completed by water oxygens.

An important feature of the structures is the ligand separation between two metal centres on nucleotide co-ordination, which is observed here for the first time. A possible mechanism for such a reaction may be postulated as follows. In the first instance, the *cis* geometry of the nucleotides around the metal ion through N(7) co-ordination is determined by the Co^{III}(en) moiety. As suggested by Barton and Lippard,[26] the co-ordinated bases of 6-oxopurine nucleotides have a very strong *trans* directing influence, so that subsequently, the en molecule is completely labilized from the metal centre. The reaction may be depicted as shown by equations (1) and (2), where NMP = 5′-IMP or 5′-GMP. However, in the case of Pt^{II}(amine) complexes,[9–11,19,20]

$$[Co(en)(H_2O)_4]^{3+} + 2\ 5'\text{-NMP} \longrightarrow [Co(en)(5'\text{-NMP})_2(H_2O)_2]^- + 2H_2O \quad (1)$$

$$[Co(en)(5'\text{-NMP})_2(H_2O)_2]^- + [Co(en)(H_2O)_4]^{3+} \longrightarrow [Co(en)_2(H_2O)_2]^{3+}[Co(5'\text{-NMP})_2(H_2O)_4]^- \quad (2)$$

Cu^{II}(en) complex,[13] or a Cu^{II}(dien) complex (dien = diethylenetriamine)[12] the reaction does not proceed to step (2).

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