Models for the Interaction of Zn^{2+} with DNA. The Synthesis and X-ray Structural Characterization of Two Octahedral Zn Complexes with Monomethyl Phosphate Esters of 6-Oxopurine 5'-Monophosphate Nucleotides

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Abstract: Two closely related compounds, *cis*-$[Zn(H_2O)_4(Me\text{-}5'\text{-}IMP)_2]$ and *cis*-$[Zn(H_2O)_4(Me\text{-}5'\text{-}GMP)_2]$, have been prepared and investigated by single-crystal X-ray methods (Me-5'-IMP and Me-5'-GMP are the monoanionic ligands inosine 5'-monophosphate and guanosine 5'-monophosphate both with the phosphate group methylated). The Me-5'-IMP complex crystallizes in the orthorhombic system, space group $P2_12_12_1$, with a = 12.304 (4) Å, b = 14.045 (6) Å, c = 20.997 (9) Å, V = 3628.8 Å^3, and Z = 4. The Me-5'-GMP complex crystallizes in the monoclinic system, space group $C2$, with a = 28.631 (6) Å, b = 12.235 (2) Å, c = 12.350 (2) Å, β = 113.22 (1)°, V = 3975.8 Å^3, Z = 4. The structures were solved by standard heavy-atom Patterson and Fourier techniques and were then refined by full-matrix least-squares analysis using 3162 observed reflections and varying 353 parameters to an R value of 0.0665 for the Me-5'-IMP complex and using 3148 observed reflections and varying 417 parameters to an R value of 0.0606 for the Me-5'-GMP complex. The coordination geometry about the Zn is a distorted octahedron with the two bases in a cis arrangement and water occupying the four remaining coordination sites. The orientation of the bases in these two crystal structures and in the crystal structure of the square-planar complex [Pt(tn)(Me-5'-GMP)$_2$] is similar. In particular, the base–base dihedral angle is small (32.9–39.6°), consistent with an intramolecular base–base interaction. Despite the similarities in molecular geometry, these three structures exhibit very different intermolecular stacking. Both Me-5'-GMP structures have extensive purine base overlap with N7 of one base stacking over N9 of the other base (overlap of five-membered rings) and also with overlap of the six-membered pyrimidine rings. The intermolecular stacking distance for the ZnMe(GMP) structure is 3.24 Å. In the Me-5'-IMP structure, the bases do not overlap. These structures are discussed in terms of a new model for metal-facilitated rewinding of DNA. In this model, the Zn binds to two adjacent G's in one strand of a double helix, and Watson–Crick base pairing is not disrupted.

Zinc holds a special position in the chemistry and biochemistry of nucleic acids. Unlike some other metal ions. Zn^{2+} can facilitate the total rewinding of DNA when DNA is melted in the presence of Zn^{2+} ions in the ratio Zn/P of 4:1.[1,2] Other metal ions are either ineffective or less effective in this regard and require the addition of salt or chelating agents to rewind the helix. The ability of Zn^{2+} to facilitate rewinding has been attributed to the balanced affinity of this cation for N in the heterocyclic nucleic acid bases and for O in the phosphodiester group.[2] Thus. at elevated temperatures, it is proposed that Zn^{2+} holds the bases in register by binding between strands, whereas on cooling, the Zn^{2+} migrates to the phosphate groups and stabilizes the helix.[1,2] A detailed understanding of the bases involved and the specific metal-binding sites on these bases is not available. Zinc is the most effective metal in inducing base stacking in AMP derivatives.[3]

In addition to structural effects, Zn^{2+} often promotes reactions involving either degradation or synthesis of nucleic acids. For example, Zn^{2+} is very effective in promoting polyribonucleotide degradation.[4] but. along with other metal species, it is not effective at degrading DNA.[5] Zinc is a useful catalyst in template-directed oligonucleotide synthesis.[6]

Since Zn^{2+} influences both structures and reactions of nucleic acids, it is not surprising that Zn is found in many enzymes which have such a role in nucleic acid biochemistry. For example, the type II restriction enzyme, Eco RI, recently was shown to contain one Zn per monomeric enzyme.[7] Furthermore, this Zn is essential. Many nucleic acid polymerases contain Zn.[8] Additionally, a nucleic acid regulatory protein, Factor A, also contains Zn.[9] Finally, some enzymes, such as SI nuclease, require Zn as a cofactor.[10,11]

Evidence generally points to the involvement of the Zn at the interface between the protein and nucleic acid. For example, metal chelators, such as EDTA, inhibit specific binding between Factor A and 5S RNA in the 7S particle containing these polymers.[9]

Despite the importance of Zn in so many chemical and biochemical processes involving nucleic acids, there have been relatively few studies involving isolated and structurally characterized Zn complexes with nucleic acid components, particularly nucleotides.[12-14] Indeed, with one exception,[15] structurally characterized metal (exclusive of alkali and alkaline earth) complexes of mononucleotides have involved phosphate monoesters which carry two negative charges per phosphate group in the normal protonation state. Consequently, the role of the phosphate groups, either through direct metal binding or through electrostatic interaction with the metal, is probably overemphasized in comparison to the nucleotide monomer unit in nucleic acids where the phosphodiester group carries only one negative charge.

In order to obtain more realistic models of metal binding to nucleic acids, we are studying metal complexes with nucleotides

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further esterified at the phosphate group. The phosphodiester grouping is similar in charge and geometry to this group in nucleic acids. In this report, we describe the structures of two closely related Zn complexes with mononucleotides esterified at the phosphate group. The compounds are unusual for Zn species with nucleic acid components in that they have octahedral stereochemistry. These complexes may have broader relevance than nucleic acid chemistry in that the coordination environment bears some resemblance to that proposed for the Zn center in glyoxalase I.[16]

Experimental Section

Methylation of the phosphate group in the nucleotides inosine 5′-monophosphate (IMP) and guanosine 5′-monophosphate (GMP) utilized the procedure of Khorana[17] with modifications. Dicyclohexylcarbodiimide (Sigma), DCC, 1.6 g, was added, with stirring, to a suspension of nucleotide monophosphate free acid (500 mg, Sigma) in methanol (250 mL, previously dried over molecular sieves (Fischer, grade 514) in a 500-mL round-bottom flask. The reaction flask was sealed and left at room temperature. The reaction was followed by TLC using a propanol/water/ammonium hydroxide 7:2:1 solvent system (solvent A of ref 17). After 24–48 h, no starting material was detected. The methanol was then evaporated under vacuum to ~5 mL, and water (100 mL) was added to precipitate DCC and its byproducts. The solution was filtered and the filtrate extracted 3 times with petroleum ether (boiling range 35–58 °C). The aqueous solution was evaporated under vacuum to ~50 mL and passed through the zinc form of a Dowex-50 ion-exchange column (1.5 cm × 30 cm). (The column was prepared by passing a 1 N zinc acetate solution through Bio Rad AG50W-X8 resin until zinc was detected in the eluent by colorimetric methods[18] and then by washing with three bed volumes of water.) The effluent fractions containing the product were identified by UV absorbance after spotting on a silica gel plate treated with a fluorescent indicator (254-nm phosphor, Analtech). The fractions were pooled and reduced in volume to 4 mL, and acetone (200 mL) was added to precipitate the product, which was then collected and dried at room temperature under vacuum (typical yield, 55%). For analysis, the complexes were crystallized by vapor diffusion of acetone into an aqueous solution containing 20 mg of product and 1 mL of water. Anal. Calcd for $Zn(C_{11}H_{14}N_4O_8P)_2 \cdot 8H_2O$: C, 28.35; H, 4.75; N, 12.03. Found: C, 28.59; H, 4.75; N, 11.83. ^1H NMR (TSP):[19] δ 8.431 (s, H8), 8.231 (s, H2), 6.157 (d, H1′), 3.537 (d, CH_3). ^{31}P NMR (TMP):[19] δ −1.47. Anal. Calcd for $Zn(C_{11}H_{15}N_5O_8P)_2 \cdot 14H_2O$: C, 24.70; H, 5.42; N, 13.09. Found: C, 24.38; H, 4.70; N, 13.36. ^1H NMR (TSP): δ 8.081 (s, H8), 5.948 (d, H1′), 3.528 (d, CH_3). ^{31}P NMR (TMP): δ −1.54. Crystals of the Me(IMP) analogue obtained from this preparative study were used for the X-ray study. Crystals of the Me(GMP) analogue for the X-ray study were grown from H_2O. Note that the crystals were somewhat unstable, and this may account for the difference in H_2O content.[20]

^1H and ^{31}P NMR spectral measurements were made on a Nicolet 360 NB (360 MHz, ^1H) and IBM WP-200SY spectrometers (81.01 MHz, ^{31}P).

Diffraction data were collected on an automated Syntex $P2_1$ diffractometer located at Georgia Tech utilizing graphite-monochromatized Mo Kα radiation (λ = 0.71069 Å) in the θ–2θ scan mode, with the take-off angle set to 6.75° and 2θ range of 4–50°, variable scan rate 2.02–23.9°/min, and a scan width of 2°. Stationary background counts were measured at the beginning (bgd1) and at the end (bgd2) of each scan with a total background-to-scan time ratio, TR, of 1. Intensities were calculated from the total scan count (CT) and background counts by the relationship I = CT − (TR)(bgd1 + bgd2). The intensities were assigned standard deviations according to the formula $\sigma^2(I)$ = CT + $(TR)^2$(bgd1 + bgd2). Lorentz and polarization corrections were made. There were no significant variations in the three standard reflections. The structure was solved by standard heavy-atom Patterson and Fourier techniques and refined by full-matrix least-squares analysis. An overall scale factor was varied and the x, y, and z coordinates of all non-hydrogen atoms were refined. For the Me(IMP) analogue the Zn, P, and O atoms were refined anisotropically and the remaining atoms were refined isotropically, and for the Me(GMP) analogue all atoms except H were refined anisotropically. Computations were performed by using the SHELXTL system version 3, a minicomputer version of the SHELX program system, on a Data General Eclipse S/140 computer located at Emory. Crystal data and experimental details are outlined in Table I.

Table I. Crystal Data and Experimental Details of the X-ray Diffraction Study

	$[Zn(H_2O)_4(Me\text{-}5'\text{-}IMP)_2]\cdot 2(H_2O)$	$[Zn(H_2O)_4(Me\text{-}5'\text{-}GMP)_2]\cdot 6(H_2O)$[20]
a, Å	12.305 (4)	28.631 (6)
b, Å	14.045 (6)	12.235 (2)
c, Å	20.997 (9)	12.350 (2)
α, deg	90.0	90.0
β, deg	90.0	113.22 (1)
γ, deg	90.0	90.0
V, Å^3	3628.8 (2.6)	3975.8 (1.3)
Z	4	4
MW	895.95	998.06
d_{calcd}, g·cm^{-3}	1.64	1.67
d_{exptl}, g·cm^{-3}	1.64	1.67
space group	$P2_12_12_1$	$C2$
crystal size, mm^3	0.92 × 0.15 × 0.37	0.30 × 0.37 × 0.07
μ, cm^{-1}	8.51	8.05
F(000)	1624	2000
std reflcns	3 out of 100 data	3 out of 100 data
tot unique data	3455	3535
tot obsd data[a]	3162	3148
no. of parameters varied	353	417
weighting scheme	$1/(\sigma^2(F) + 0.00482\,F^2)$	$1/(\sigma^2(F) + 0.00464\,F^2)$
R[b]	0.0665	0.0606
Rw[c]	0.0731	0.0644

[a] $F > 3\sigma_F$. [b] $R = \sum(|F_{obsd} - F_{calcd}|)/\sum F_o$. [c] $Rw = \sum(|F_{obsd} - F_{calcd}|\text{-}wt^{1/2})/[\sum((F_{obsd})(wt)^{1/2})]$.

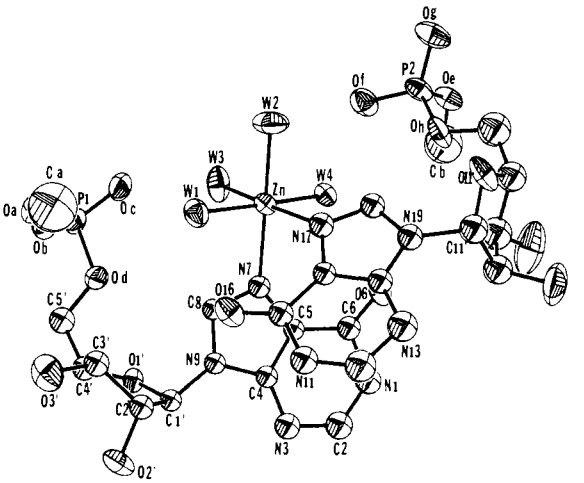

Figure 1. Stereochemistry and atomic numbering in the ZnMe(IMP) complex. Note that all atoms are not labeled but the numbering of the unlabeled atoms follows directly from the numbered atoms.

Results and Discussion

Preparation of the Methyl Nucleotide Complexes. The large scale preparation of the methyl nucleotides and their conversion to metal salts by the cation-exchange method described above has proved to be a general procedure not only for the nucleotides reported here but also for nucleotides containing cytosine, uracil, thymine, and adenine. The method also gives methylated deoxynucleotides in good yields. Preliminary studies indicate that the method can be applied to ethyl derivatives and to other metals (K, Cd, Ba, and Rb). To date, Zn complexes appear to be most readily isolated and crystallized. This finding is in contrast to the relative paucity of isolated and crystallized Zn compounds of nucleic acid components.

Structures of the Zn Complexes. The final non-hydrogen positional parameters for *cis*-$[Zn(H_2O)_4(Me\text{-}5'\text{-}IMP)_2]$ and *cis*-$[Zn(H_2O)_4(Me\text{-}5'\text{-}GMP)_2]$ (hereafter referred to as ZnMe(IMP) and ZnMe(GMP)) are given in Tables II and III, respectively. The molecular conformations of the complexes are

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(19) TSP = (tetramethylsilyl)propionic acid; TMP = trimethyl phosphate.
(20) Three of the waters in the ZnMe(GMP) crystal were quite disordered and would not refine well.

Table II. Final Non-Hydrogen Atom Positional Parameters for ZnMe(IMP)[a]

atom	x/a	y/b	z/c
Zn	−781 (1)	5323 (1)	4205 (1)
P1	616 (2)	7575 (2)	2404 (1)
P2	−4584 (2)	4566 (2)	5188 (1)
Oa	1166 (6)	6900 (5)	1890 (3)
Ob	578 (5)	8537 (6)	2094 (3)
Oc	−410 (5)	7188 (7)	2661 (3)
Od	1472 (5)	7586 (4)	2978 (3)
Oe	−5267 (5)	5155 (4)	5681 (3)
Of	−4043 (5)	5201 (5)	4717 (3)
Og	−5331 (5)	3813 (4)	4943 (4)
Oh	−3610 (5)	4115 (5)	5582 (3)
W1[b]	394 (5)	4985 (4)	3504 (3)
W2	−1858 (5)	4404 (5)	3727 (3)
W3	−1291 (5)	6497 (4)	3681 (3)
W4	−1966 (4)	5736 (4)	4865 (2)
N1	1065 (6)	6009 (5)	6398 (3)
N3	2491 (5)	6785 (5)	5840 (3)
N7	437 (5)	6163 (4)	4687 (3)
N9	2071 (5)	6870 (4)	4709 (3)
N11	2538 (5)	3639 (5)	5189 (3)
N13	1345 (6)	2863 (5)	5894 (3)
N17	−315 (5)	4114 (5)	4771 (3)
N19	−546 (5)	3213 (4)	5625 (3)
Ca	1406 (11)	5930 (9)	2067 (7)
Cb	−4776 (9)	5931 (8)	6010 (5)
C2	2029 (7)	6483 (6)	6373 (4)
C4	1854 (6)	6613 (5)	5324 (3)
C5	848 (6)	6176 (5)	5309 (5)
C6	358 (6)	5826 (5)	5870 (4)
C8	1207 (5)	6588 (5)	4351 (3)
C1′	3107 (6)	7250 (5)	4467 (3)
C2′	2819 (6)	6504 (5)	4119 (4)
C3′	3462 (7)	6628 (6)	3431 (4)
C4′	3277 (7)	7707 (5)	3394 (4)
C5′	2497 (7)	8027 (6)	2887 (4)
C12	2342 (8)	3074 (6)	5686 (4)
C14	551 (6)	3281 (5)	5533 (4)
C15	695 (6)	3844 (5)	5008 (3)
C16	1779 (6)	4046 (5)	4792 (4)
C18	−1024 (6)	3722 (5)	5161 (4)
C11′	−1117 (7)	2723 (7)	6167 (4)
C12′	−1075 (7)	3358 (7)	6761 (4)
C13′	−2128 (9)	3905 (8)	6699 (5)
C14′	−2893 (8)	3133 (7)	6430 (5)
C15′	3872 (10)	3441 (9)	6067 (6)
O6	−510 (4)	5432 (4)	5963 (3)
O16	2059 (4)	4514 (4)	4325 (3)
O1′	2865 (4)	7953 (3)	4012 (2)
O11′	−2204 (5)	2603 (4)	5994 (3)
O2′	4933 (4)	6769 (4)	4205 (3)
O3′	4240 (6)	6318 (5)	2972 (3)
O12′	−1081 (7)	2763 (7)	7317 (4)
O13′	−2565 (9)	4325 (7)	7264 (4)
W5	4054 (6)	9053 (6)	1424 (4)
W6	5652 (14)	9399 (12)	2326 (8)
W7	4793 (14)	9584 (13)	2515 (8)
W8	6840 (22)	9292 (19)	1966 (13)

[a] Parameters ×10[4]. [b] W = water oxygen.

Table III. Final Non-Hydrogen Atom Positional Parameters for ZnMe(GMP)[a]

atom	x/a	y/b	z/c
Zn	8782 (1)	6162[b]	6500 (1)
P1	8071 (1)	4627 (2)	−353 (2)
P2	9011 (1)	9905 (2)	4970 (2)
Oa	8535 (3)	4126 (6)	684 (5)
Ob	8219 (2)	5649 (5)	−784 (5)
Oc	7946 (3)	3775 (5)	8597 (5)
Od	7660 (3)	4685 (6)	84 (5)
Oe	8837 (3)	9287 (5)	5783 (6)
Of	9136 (2)	8982 (5)	4211 (5)
Og	9436 (3)	10677 (5)	5483 (6)
Oh	8570 (3)	10586 (6)	4055 (6)
W1	9176 (2)	5083 (5)	7911 (5)
W2	8330 (3)	6602 (6)	7400 (5)
W3	9271 (3)	7512 (6)	7369 (7)
W4	8359 (2)	7308 (5)	5251 (5)
N1	7857 (3)	4267 (6)	2450 (6)
N2	7442 (3)	2749 (7)	1416 (7)
N3	7643 (3)	2803 (6)	3437 (5)
N7	8265 (3)	4875 (6)	5612 (6)
N9	7936 (3)	3193 (6)	5534 (5)
N11	9344 (3)	2872 (6)	4915 (7)
N12	9481 (5)	2152 (7)	3361 (10)
N13	9466 (3)	4035 (6)	3507 (6)
N17	9254 (3)	5758 (5)	5592 (7)
N19	9414 (3)	5934 (5)	3984 (6)
Ca	8995 (5)	3839 (11)	10558 (11)
Cb	8078 (5)	10093 (11)	3371 (11)
C2	7648 (3)	3258 (7)	2470 (7)
C4	7879 (3)	3437 (7)	4386 (7)
C5	8082 (3)	4468 (7)	4456 (7)
C6	8079 (3)	4948 (7)	3411 (7)
C8	8158 (3)	4078 (7)	6209 (7)
C1′	7820 (3)	2137 (7)	5944 (7)
C2′	8296 (3)	1481 (7)	6664 (7)
C3′	8393 (3)	1824 (8)	7918 (8)
C4′	7857 (3)	1948 (7)	7853 (7)
C5′	7774 (4)	2705 (8)	8747 (8)
C12	9430 (4)	3062 (9)	3906 (8)
C14	9395 (3)	4844 (7)	4183 (7)
C15	9298 (3)	4734 (7)	5163 (7)
C16	9302 (3)	3667 (7)	5641 (8)
C18	9314 (3)	6448 (7)	4827 (7)
C11′	9475 (3)	6447 (7)	2962 (7)
C12′	8980 (3)	6574 (7)	1899 (7)
C13′	8810 (3)	7699 (7)	2030 (7)
C14′	9315 (3)	8292 (7)	2581 (8)
C15′	9338 (3)	9286 (8)	3366 (8)
O6	8243 (2)	5847 (5)	3267 (5)
O16	9254 (3)	3415 (6)	6572 (6)
O1′	7571 (2)	2345 (5)	6699 (5)
O11′	9677 (2)	7493 (5)	3296 (5)
O2′	8159 (3)	337 (5)	6517 (7)
O3′	8678 (3)	1044 (7)	8803 (7)
O12′	9085 (3)	6505 (5)	877 (5)
O13′	8468 (3)	8156 (6)	1003 (6)
W5	8781 (5)	8673 (10)	9031 (10)
W6	5126 (5)	1641 (66)	9583 (17)
W7	6659 (5)	5379 (11)	9176 (10)

[a] Parameters ×10[4]. [b] Fixed position.

shown in Figures 1 and 2, respectively. Tables with complete bond lengths, bond angles, and least-squares planes as well as F_{obsd} and F_{calcd} are contained in the supplementary material.

Metal Environment. Except for the substituent on the C2 position, the two zinc complexes are essentially isostructural and have a pseudooctahedral metal environment with two 6-oxopurine bases coordinated through N7 in cis coordination sites. Water molecules occupy the four remaining coordination sites in these neutral complexes. The phosphodiester groups form an intramolecular hydrogen bond to some of the coordinated water ligands and are not directly coordinated to zinc (vide infra). These two complexes are the first examples of octahedral binding in zinc complexes of nucleic acid constituents. All other reported zinc complexes of this type have approximately tetrahedral coordination.[14,21] The Zn–N7 bond length values for these octahedral complexes, 2.149 (10) and 2.158 (10) Å for ZnMe(IMP) and of 2.143 (10) and 2.127 (12) Å for ZnMe(GMP), can be compared with the average Zn–N7 distance of 2.031 (8) Å computed for a number of tetrahedral complexes.[14] A similar slight increase in bond length has also been observed in copper–purine complexes where the average M–N7 bond is 2.016 (3) Å for octahedral and

(21) In $ZnCl_2$–(1-methylcytosine)$_2$, the Zn is bound to two Cl and to two N3 of 1-methylcytosine in a pseudotetrahedral arrangement (see ref 12); In Zn^{II}–H_2(ATP)–2,2′-bipyridyl dimer, the zinc is bound to two oxygen atoms from different γ-phosphate groups, one oxygen from the β-phosphate group, and the two nitrogen atoms of the bipyridyl ligand. The sixth position is completed by a weakly bound α-phosphate oxygen so that the zinc atoms are in a distorted octahedral environment. However, this compound is not a model for nucleic acid binding (see ref 13).

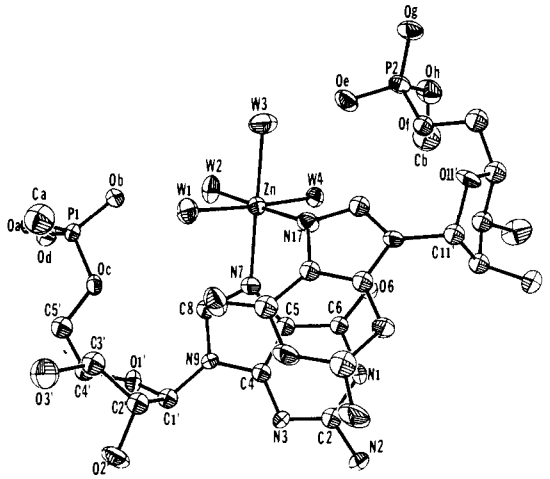

Figure 2. Sterochemistry and atomic numbering in the ZnMe(GMP) complex. See caption of Figure 1.

Table IV. Selected Bond Lengths, Å

	ZnMe(IMP)	ZnMe(GMP)
Zn–W1	2.118 (15)	2.122 (10)
Zn–W2	2.105 (16)	2.082 (11)
Zn–W3	2.080 (15)	2.158 (11)
Zn–W4	2.093 (15)	2.083 (9)
Zn–N7	2.158 (16)	2.143 (10)
Zn–N17	2.149 (16)	2.127 (12)
C4–C5	1.383 (14)	1.377 (13)
C5–N7	1.402 (13)	1.404 (12)
N7–C8	1.324 (13)	1.330 (13)
C8–N9	1.360 (13)	1.361 (11)
N9–C4	1.367 (13)	1.393 (12)
N9–C1′	1.473 (14)	1.473 (13)
C1′–C2′	1.548 (15)	1.529 (13)
C2′–C3′	1.519 (15)	1.521 (14)
C3′–C4′	1.534 (15)	1.511 (15)
C4′–C5′	1.503 (15)	1.530 (15)
C4′–O1′	1.435 (13)	1.420 (10)
O1′–C1′	1.406 (13)	1.402 (14)

1.986 (1) Å for tetrahedral coordination.[14] The longer M–N7 bond in octahedral complexes may be due to the more crowded coordination environment. Selected bond lengths and bond angles are given in Tables IV and V. respectively.

Base Geometry and Conformation. Both cis and trans isomers of $Pt(NH_3)_2Cl_2$ are mutagenic. but only the cis isomer has significant antitumor activity.[22] This structure activity relationship may be due in part to the conformational changes in DNA induced by metal binding to bases in the same DNA strand. Consequently, the relative base conformation in metal bis(nucleic acid component) complexes is of great interest, particularly for the base–base and base–metal interactions.[22] The base–base dihedral angles of ZnMe(IMP) and ZnMe(GMP), 36.8° and 32.9°, respectively, are well within the range of 30–40° found for $(IMP)_2$ and $(GMP)_2$ metal complexes (Table VI).[15,23-29] The base–metal dihedral

Table V. Selected Bond Angles, deg

	ZnMe(IMP)	ZnMe(GMP)
W1–Zn–N7	88.5 (4)	90.0 (3)
W2–Zn–N7	174.7 (5)	90.8 (4)
W3–Zn–N7	91.3 (5)	177.2 (4)
W4–Zn–N7	91.3 (4)	91.9 (3)
N7–Zn–N17	89.3 (5)	90.8 (4)
W1–Zn–N17	91.4 (4)	92.7 (3)
W2–Zn–N17	87.0 (5)	178.3 (3)
W3–Zn–N17	177.6 (5)	91.0 (4)
W4–Zn–N17	92.2 (4)	94.0 (3)
Zn–N7–C8	119.7 (6)	121.2 (6)
Zn–N7–C5	134.0 (6)	133.4 (7)
C5–N7–C8	103.4 (7)	103.2 (7)
N7–C8–N9	113.4 (7)	113.4 (8)
C8–N9–C4	107.1 (7)	107.0 (7)
C15–N17–C18	104.8 (7)	104.3 (8)
N17–C18–N19	112.6 (8)	112.4 (8)
C18–N19–C14	107.1 (7)	106.5 (8)
N9–C1′–O1′	107.8 (7)	108.2 (7)
N9–C1′–C2′	114.1 (7)	113.0 (8)
O1′–C1′–C2′	105.9 (7)	106.2 (7)
C1′–C2′–C3′	102.0 (7)	102.1 (8)
C2′–C3′–C4′	101.8 (7)	101.5 (7)
C3′–C4′–O1′	104.2 (7)	105.0 (8)
C4′–O1′–C1′	111.7 (6)	111.2 (7)

angles of the two structures reported here and the only other reported structurally characterized methyl 5′-nucleotide complex, $[Pt(tn)(Me\text{-}5'\text{-}GMP)_2]$[15] (PtMe(GMP), tn = 1,3-diaminopropane), are in the narrow range of 52–55°, whereas the other metal–bisnucleotide complexes in Table VI have the base–metal dihedral angle in the range 62–67°. The one exception is $[Cu(dien)(5'\text{-}IMP)_2]^{2-}$ (dien = diethylenetriamine) with a relatively small angle of 46.4°.

Values for the bond lengths and bond angles of the heterocyclic purine bases (see supplementary material) correlate well with values obtained for the uncomplexed nucleotide and nucleoside analogues.[30-32] The metal coordination does not usually affect the geometry of the ligand system.[14] Deviations from the best least-squares plane for the nine-atom base framework of the IMP analogue is greater than for the GMP analogue (see supplementary material), a situation also found for the inosine dihydrate and guanosine dihydrate structures.[31] As with most purine bases, the nine-atom framework is measurably nonplanar. The dihedral angles between the imidazole rings and the pyrimidine rings are 1.7° and 0.7° for the two bases of ZnMe(IMP) and 1.8° for both bases of ZnMe(GMP). Also, the Zn atom is greatly displaced from the purine planes with displacement values of 0.50 and 0.66 Å for ZnMe(IMP) and 0.44 and 0.95 Å for ZnMe(GMP) (see supplementary material).

Conformational Analysis of the Sugar Moiety. Metal–nucleotide solid-state sugar conformations fall into two major categories, C3′ endo. anti, gauche$^+$ and C2′ endo, anti, gauche$^+$ with the base orientation about the glycosyl bond in the anti range ($0 \le \chi \le 90°$) and the conformation about the exocyclic C4′–C5′ bond in the gauche$^+$ domain ($45° \le \psi \le 60°$).[14] Conformations for the complexes reported here are C3′ endo, anti, gauche$^+$, as also found in PtMe(GMP).[15]

The conformation of the sugar ring in nucleotides and nucleosides can be examined by using a concept of pseudorotation, which utilizes a quantitative description of puckering and conformation in terms of the maximum torsion angle (τ_m) and the "phase angle" of pseudorotation (P), which is a function of the interrelationship between the five torsion angles (τ_0–τ_4) in the

(22) Kistenmacher, T. J.; Orbell, J. D.; Marzilli, L. G. "Platinum, Gold, and Other Metal Chemotherapeutic Agents"; Lippard, S. J., Ed.; American Chemical Society: Washington, DC, 1983; ACS Symp. Ser. No. 209, pp 191–207. The base–base dihedral angle is the angle formed by the intersection of the planes that pass through the two bases. Similarly, the base–metal dihedral angle is the angle formed by the intersection of the plane that passes through the base and the plane that passes through the plane about the metal which includes the metal, the base ligand atoms, and the other ligand atoms in the plane.

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Table VI. Summary of Important Parameters of Several $(IMP)_2$ and $(GMP)_2$ Metal Complexes

compound	angle between planes, deg B/B	B/M	M–N(7), Å	N(7)···M···N(7), deg	N(7)··· N(7), Å	interligand O(6)···C(8), Å	space group	ref
cis-$[Pt(NH_3)_2(5'\text{-}IMP)_2]^{2-}$	40.7	61.8	2.036 (8)	90.0	2.88 (1)	2.99	$C222_1$	23
$[Pt(tn)(5'\text{-}IMP)_2]^{2-}$	38.2[a] (40.9)	63.9	2.08 (1)	90.2	2.96 (2)	3.02	$C222_1$	23, 24
$[Pt(en)(5'\text{-}IMP)_2]^{2-}$	31		2.07 (2)		3.26		$C222_1$	23, 25, 26
$[Cu(dien)(5'\text{-}IMP)_2]^{2-}$	30.4 (3)	46.4	1.917 (5) eq	78.6 (2)	3.228 (7)	3.142	$P2_12_12$	27
			3.003 (5) ax					
$[Co(H_2O)_4(5'\text{-}IMP)_2]^{1-}$	39.6	66.4	2.183	82.5	2.879	3.177	$C222_1$	28
$[Co(H_2O)_4(5'\text{-}GMP)_2]^{1-}$	41.5[a] (39.9)	67.3	2.173	84.4	2.918	3.208	$C222_1$	28
$[Cd_2(H_2O)_6(5'\text{-}(IMP)^{2-})(5'\text{-}IMP^{1-})_2]$[b]	31.4		2.42	79.1			$C2$	29
			2.40					
			2.27					
$[Pt(tn)(Me\text{-}5'\text{-}GMP)_2]$	39.6	53.0	2.021	90.1	2.862	2.957	$P4_322$	15, 24
cis-$[Zn(H_2O)_4(Me\text{-}5'\text{-}IMP)_2]$	36.8	55.5	2.149 (10)	89.3	3.028	3.099	$C2_12_12_1$	this work
		52.4	2.159 (16)			3.00		
cis-$[Zn(H_2O)_4(Me\text{-}5'\text{-}GMP)_2]$	32.9	51.7	2.143 (10)	89.5	3.044	3.069	$C2$	this work
		52.9	2.127 (12)			3.012		

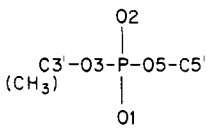
[a] Our values in parentheses calculated from the coordinates differed from those reported in the reference by more than 1°. [b] Polymeric compound.

Table VII. P and τ_m of Related Nucleoside, Nucleotide, and Dinucleotide Complexes

complex	P, deg	τ_m, deg	ref
ZnMe(IMP)	11.8	37.2	this work
	17.0	39.0	
ZnMe(GMP)	12.9	36.5	this work
	9.1	34.7	
PtMe(GMP)	13.6	37.8	15
Ni(IMP)	9.7	36.4	35
NaGpC[a]			
G	7.4	37.6	26
C	16.6	41.5	
GMP	4.7	35.7	32
Na(IMP)	167.3	40.0	30
$[Pt(tn)_2(IMP)_2]^{2-}$	160.8	42.0	24
$[Pt(NH_3)_2(IMP)_2]^{2-}$	161.6	40.2	23
$[Cu(dien)(IMP)_2]^{2-}$	167.8	33.8	27
$[Co(en)(IMP)_2]^{1-}$	169.3	33.9	28
$[Co(en)(GMP)_2]^{1-}$	170.9	35.9	28

[a] GpC = Guanylyl-3′,5′-cytidine.

Table VIII. Angles about the Phosphodiester Group of Various Types of Complexes



compound	phosphate angles O2–P–O1	O3–P–O5	ref
ZnMe(IMP)	117.6	107.6	this work
	118.1	105.7	
ZnMe(GMP)	118.2	105.3	this work
	118.4	104.9	
$Pt(tn)(Me\text{-}5'\text{-}GMP)_2$	119.1	105.1	15
$(NH_4)(GpC)$[a]	118.8	104.7	36
Na(GpC)	120.6	104.3	26
$Ca(GpC)_2$	119.0	102.0	37
$Pt(NH_3)_2(IMP)_2$	112.9[b]	106.0[c]	23

[a] See Table VII. [b] The average value of various combinations of O1, O2, and O3. [c] The average values of various combinations of O5 with O1, O2, and O3.

nonplanar five-membered ring.[33] The phase angle, P, and the maximum pucker, τ_m, are calculated with eq 1 and 2.[33]

$$\tan P = \frac{(\tau_4 + \tau_1) - (\tau_3 + \tau_0)}{2\tau_2(\sin 36 + \sin 72)} \quad (1)$$

$$\tau_2 = \tau_m \cos P \quad (2)$$

All the possible conformations are grouped into two categories, type N ($P = 0 \pm 90°$) or 3′ endo and type S ($P = 180 \pm 90°$) or 2′ endo. A majority of the ribose and deoxyribose P values fall in the ranges 0–36° and 144–180°.[33] In general, for transition-metal complexes with one bound nucleotide, the sugar has a C3′ endo, anti, gauche$^+$ conformation (type N). For example, in the case of octahedral cobalt and nickel 5′-purine nucleotide complexes, the metal coordination sphere contains the purine N7 and five water molecules. Some of the water molecules hydrogen bond to the phosphate oxygens and others are hydrogen bonded to the C6 amino or C6 oxo group.[34] The metal–$(IMP)_2$ structures are all C2 endo, anti, gauche$^+$ (type S) (Table VII)[15,23–24,26–28,30,32,35] while the three bis(methyl nucleotide) complexes are all type N.

Phosphate Groups. The phosphate groups of ZnMe(GMP) and ZnMe(IMP) form intramolecular hydrogen bonds to some of the coordinated waters. Specifically, for ZnMe(GMP), hydrogen bonds (distances in parentheses) are formed between Ob of P1 and two waters, W1 (2.74 Å) and W2 (2.65 Å), and between Oe of P2 and two waters, W3 (2.86 Å) and W4 (2.73 Å). For ZnMe(IMP), hydrogen bonds formed between Oc of P1 and W1 (2.68 Å) and between Of of P2 and W2 (2.59 Å). The related compound PtMe(GMP) has an analogous phosphate conformation with the phosphate group hydrogen-bonded to two uncoordinated water molecules which are located in positions close to that expected for an axially distorted octahedral environment about the platinum.

The angles about the phosphate group for the three methyl nucleotide complexes correlates well with the analogous angles about the phosphate group in GpC salts (Table VIII).[15,23,26,36,37] The nonalkylated O2–P–O1 angle is ~118°, and the O3–P–O5 angle involving the phosphodiester linkage is ~104°. The bond angles about the phosphate group of the nucleotide–metal complex, *cis*-$[Pt(NH_3)_2(IMP)_2]^{2-}$, correlate well with what could be the phosphodiester linkage. but the possible O2–P–O1 angles for the nonalkylated oxygens are smaller (~112°) than for the dinucleotide monophosphate or for the complexes studied here (Table VIII). The phosphate group bond lengths are typical of those found for the NaGpC.[26] The bond lengths involving the nonesterified oxygens have an average length of 1.49 (2) and 1.48 (2) Å for ZnMe(IMP) and ZnMe(GMP), respectively. compared with an average of 1.47 (7) Å for NaGpC. The phosphate bond lengths involving the esterified oxygens have average values of 1.58 (2) and 1.57 (2) Å for ZnMe(IMP) and ZnMe(GMP), respectively. compared with 1.60 (7) Å for NaGpC. In contrast, the bond lengths from P to esterified O and nonesterified O

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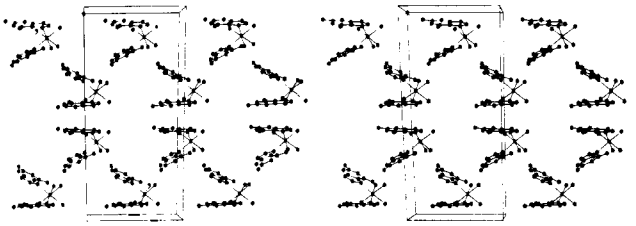

Figure 3. Stereoview of the crystal packing along the *c* axis of ZnMe(GMP). The sugar and phosphate groups as well as the solvent waters have been deleted for clarity.

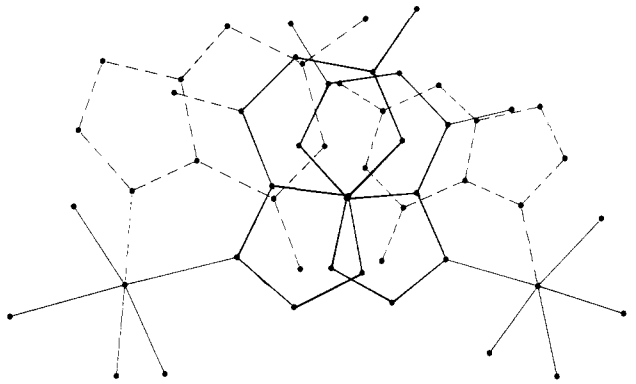

Figure 4. Perspective view of the $A_1 \cdots A_2$ (3.24Å) stacking arrangement in ZnMe(GMP).

average 1.62 (6) Å° and 1.51 (11) Å, respectively, for *cis*-$[Pt(NH_3)_2(IMP)_2]^{2-}$.[23]

Base Stacking. As mentioned above, ZnMe(IMP), ZnMe(GMP), and PtMe(GMP) have very similar molecular structures. All three have a relatively short intramolecular interbase O6···C8 distance (Table VI). The bases stack intramolecularly with the pyrimidine ring of one base overlapping with the pyrimidine ring of the other base. However, despite similarities in the molecular geometries of these three related compounds, the extent and nature of the intermolecular interactions are quite different.

In all three compounds, the relative orientation of the bases with respect to the N7–M–N7 plane is the so-called "head-to-tail" (htt) configuration. For example, the 6-oxo groups are on opposite sides of the plane. A so-called "head-to-head" (hth) configuration has the 6-oxo groups on the same side of this plane. However, this terminology is only sufficient for dealing with intramolecular interactions where the coordination of the endocyclic N to the metal limits the orientation of the bases. We introduce a terminology which defines the region of the bases across from the sugar (N7, C5, C6, and N1) as the "top" and the half of the base closest to the sugar (C2, N3, C4, and N9) as the "bottom". Furthermore, we specify which rings on the base overlap. Thus, the structure discussed above could be called htt, 6 over 6, ttt (top-to-top). However, the ttt designation is superfluous. No single simple designation will eliminate the need for a more complete discription of the structure, but we will use the ttt and ttb (top-to-bottom) description here to facilitate the discussion of the intermolecular stacking.

The two nucleotides in the ZnMe(GMP) molecule do not have identical environments or orientations with respect to the ligating atoms. For convenience, we call one nucleotide A and the other nucleotide B. In the crystal, there is extensive intermolecular stacking between A bases with considerable overlap. The bases are essentially coplanar with the angle between the two stacking bases at 2.4°. The complexes stack in pairs (Figure 3). We call the A nucleotide of the two complexes A_1 and A_2, respectively (Figure 4). The A_1 pyrimidine ring stacks over the A_2 pyrimidine ring (and the A_1 imidazole ring stacks over the A_2 imidazole ring) in a "top-to-bottom" (ttb) arrangement such that if the bases were completely overlapping, N9 of one base would stack above N7 of the other base (this stacking can be abbreviated as 6 to 6, 5 to 5, ttb) (Figure 4). The intermolecular base stacking interplanar separation is 3.24 Å,[38] a value close to the average for DNA, 3.4 Å.[39]

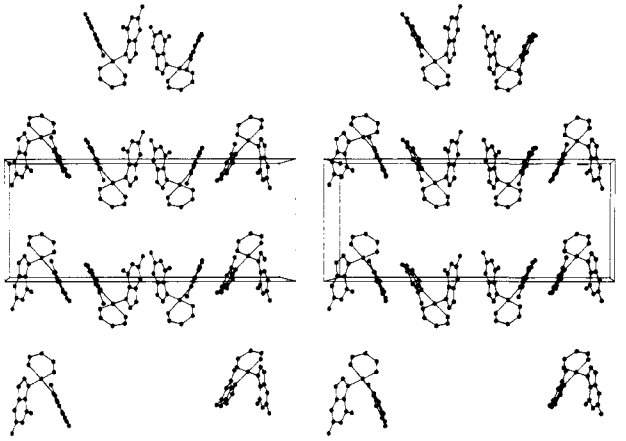

Figure 5. Stereoview of the crystal packing along the *a* axis of PtMe(GMP). The sugar and phosphate groups as well as the solvent waters have been deleted for clarity.

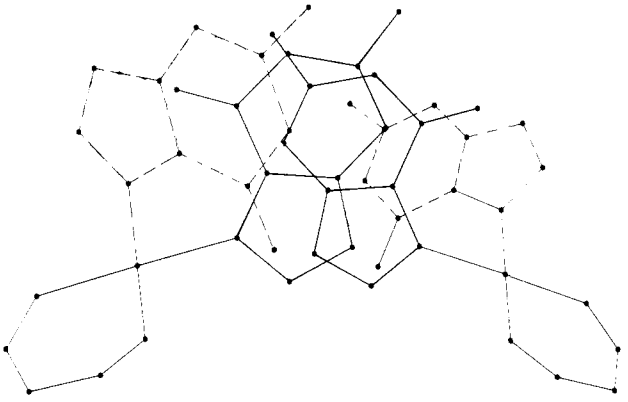

Figure 6. Perspective view of the stacking arrangement in PtMe(GMP) (3.39 Å).

In PtMe(GMP), the orientation of the two nucleotides in each molecule is identical. Both bases in each complex stack with a base of an adjacent complex (Figure 5). The bases are almost coplanar with the angle between the two stacking bases at 7.4°. The intermolecular base stacking interplanar separation is 3.39 Å.[38] The base stacking is 6 to 6. 5 to 5, ttb, as described above (Figure 6). This stacking leads to a helical arrangement with four molecules per helical turn (Figure 5).[15]

A helical arrangement of intermolecularly stacked Pt complexes has been observed for $[Pt(en)(Guo)_2]^{2+}$ [40] and *cis*-$[Pt(NH_3)_2(Guo)_2]^{2+}$ (Guo = guanosine, en = ethylenediamine).[25] However, the stacking interactions are different. In both of these closely related structures, the nucleoside engages in stacking interactions with adjacent complexes. The bases stack ttt with the imidazole ring over the pyrimidine ring and the pyrimidine ring over the imdazole ring (5 to 6, 6 to 5, ttt) as is found in the crystal structures of inosine dihydrate and guanosine dihydrate.[31] The intermolecular base stacking distances are 3.34 and 3.37 Å for alternating stacking pairs in the $[Pt(NH_3)_2(Guo)_2]^{2+}$ structure and 3.31 Å for all the stacking pairs in the $[Pt(en)(Guo)_2]^{2+}$ structure.

The ZnMe(IMP) intermolecular interactions are quite different from those of the two Me(GMP) complexes. The Me(IMP)

(38) The intermolecular base stacking separation was determined by calculating the best least-squares plane of one base and taking the average of the distances of the atoms in the other stacking base to the calculated plane.

(39) Arnott, S.; Smith, P. J. C.; Chandrasekaran, R. "Handbook *Biochemistry* and *Molecular* Biology", 3rd ed.; Fasman, G. D., Ed.; CRC: Cleveland, OH 1975; Vol. 2, Sect. B, p 411.

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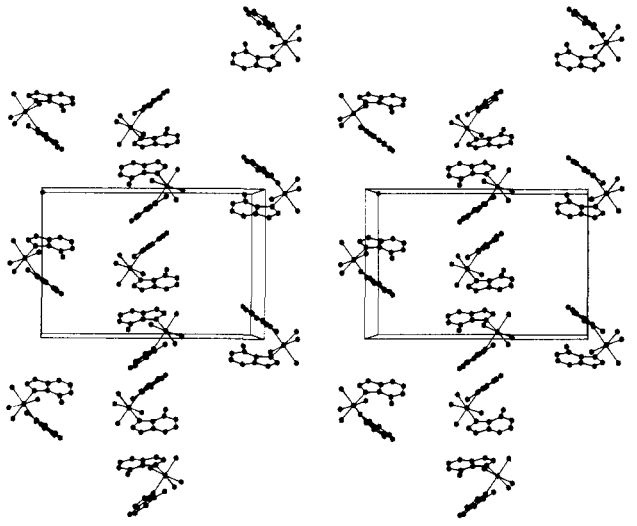

Figure 7. View of the crystal packing along the *a* axis of ZnMe(IMP). The sugar and phosphate groups as well as the solvent waters have been deleted for clarity.

Table IX. Comparison of the Intramolecular Dihedral Angle and the Intermolecular Interbase Separation

	intramolecular dihedral angle, deg	intermolecular interbase separation, Å	ref
PtMe(GMP)	39.6	3.30	15
ZnMe(GMP)	32.9	3.248	this work
$[Pt(NH_3)_2(Guo)_2]^{2+}$	74	3.34	40
		3.37	
$[Pt(en)(Guo)_2]^{2+}$	71	3.31	25

complex appears, see Figure 7, to be stacking intermolecularly, but close examination reveals that the ajdacent base is laterally displaced and there is no base overlap.

In general, extensive overlap in base stacking is unusual.[41] Usually a polar substituent of one base is positioned over the ring of a neighboring base, giving only partial overlap of the bases. Sundaralingam et al.[41] found unusually extensive overlap in the stacked bases in guanosine dihydrate and inosine dihydrate crystals.[31] The two platinum–guanosine structures mentioned above, as well as the crystal structure[42] of a polymeric copper–5′-GMP complex, $[Cu_3(H_2O)_8(5'\text{-}GMP)_3]$, have base stacking with extensive overlap of the imidazole ring over the pyrimidine ring and the pyrimidine ring over the imidazole ring (ttt). The ZnMe(GMP) and the PtMe(GMP) crystal structures are the first examples we know of in which there is 6 to 6, 5 to 5, ttb stacking.[43] Also, these are the only examples of top-to-bottom intermolecular stacking in 6-oxopurine nucleotide complexes. Furthermore, the overlap is extensive.

For metal complexes, extensive intramolecular interactions were originally thought to preclude intermolecular stacking.[15] However, a small base–base dihedral angle (which is related to intramolecular stacking) does not preclude intermolecular stacking; this can be seen from a comparison of intramolecular dihedral angles and interbase separations of the Me(GMP) complexes with those for the platinum–guanosine complexes with their relatively large dihedral angles (Table IX, also see ref 40).

Hydrogen Bonding. Both ZnMe(IMP) and ZnMe(GMP) have extensive hydrogen-bonding interactions with waters of crystallization. Although the ZnMe(IMP) complex molecules are relatively well separated, some intercomplex interactions occur. The coordinated water molecules hydrogen bond to phosphate groups of adjacent complexes (e.g., W2–Ob, 2.63 Å). Also the O3′ and N1 atoms hydrogen bond to uncoordinated waters (e.g., W7–O13′ and W6–N11 are 2.89 and 2.78 Å, respectively). The ZnMe(GMP) has a closer packing environment and consequently has many more hydrogen-bonding interactions. The phosphate oxygens hydrogen bond to N1 (e.g., Og–N11, 2.76 Å) and to water coordinated to Zn (e.g., Ob–W2, 2.65 Å) of adjacent complexes as well as to uncoordinated waters (e.g., W7–Od, 2.75 Å). The sugar oxygen O2′ also hydrogen bonds to the phosphate oxygen (e.g., O12′–Ob, 2.73 Å) of adjacent complexes. The PtMe(GMP) crystal has fewer uncoordinated water molecules. The primary hydrogen bonding interactions involve the phosphate oxygens hydrogen bonding to N2 and O2′ of adjacent molecules as well as to the water molecules occupying the pseudoaxial coordination sites.

A New Model for Metal-Facilitated Rewinding of DNA. Good evidence exists that GG sequences in DNA are most important in Cu- and Pt-promoted rewinding of DNA.[44-46] Here, Pt will designate antitumor Pt compounds with available cis coordination positions. In any reasonable rewinding model, the metal must be bound to two bases. The molecules reported here are the first examples of Zn bonded to two nucleic acid bases in a nucleotide complex, and, in addition, one complex is a model for Zn binding to a GG sequence.

In the most widely accepted models for rewinding, the metal participates in an interstrand cross-link.[1,2,47,48] For such cross-linking to occur, the hydrogen bonds between the affected bases must be broken. For GC base pairs, N3 of C participates in Watson–Crick base pairing but is the only reasonable strong metal binding site on C. In addition, the hydrogen-bonding pyrimidine ring of G must move away from the vicinity of C since the metal would bind to N7 of G and a conformational change would be necessary for an N3–M–N7 interaction, as proposed in one model.[48] Some metal ions, such as Ag or Hg, which can bind to N1 of G and N3 of T are not required to undergo these changes and bind to DNA in an entirely different way.[47] For rewinding to occur, the interstrand cross-linking process must be reversed and the metal must move out of the cross-link. This movement is *not* possible for Pt since it is inertly attached. Another problem with the cross-link model involves labile metal species. Currently, there is no evidence that there is any preferred assocation of A with T or G with C in metal complexes with both ligands present. Also, there is no apparent reason to expect such an association. Therefore, it is difficult to rationalize why, in denatured DNA, there is not more slippage.

We propose an alternative model which does not suffer from these problems and which is able to account for numerous observations with several different metal species. In this model, the metal binds to the N7 of two adjacent G's is the same strand *without* disruption of the base pairing. In fact, the H bonding may be strengthened since the NH_2 and NH groups of G should be a better H bond donor as the result of placing an electrophile at N7; however, O6 of G would be a weaker acceptor. This bonding would require some change in local helical twist, base stacking, etc., which could extend several base pairs on either side of the metalated $(GC)_2$.

Consider the following observations which are consistent with and support this model:

First, of the metal species known to be superior at facilitating DNA renaturation—Cu, Zn, Cd, and Pt—only Cd has not yet

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been shown to follow the patterns indicated in Table VI. For Cu, Zn, and Pt, the metal-bound bases appear to participate in stacking interactions in the solid. This stacking is consistent with the enhanced CD in both Pt(DNA) adducts[49-53] and Pt–nucleotide adducts[54] such as those in Table VI. The DNA CD effect increases with GC content[51,52] and is most prominent at low levels of added Pt. $<\sim 0.1$ Pt/P.[51,52]

Second, as yet unpublished studies from this laboratory demonstrate that GN1HC hydrogen bonds remain largely intact on reaction with Pt compounds with DNA.[55] A recent study on oligonucleotides reaches the same conclusion.[56]

Third, approximately the same level of Pt to (DNA)P of ~ 0.05 is responsible both for effective renaturation of DNA[46] and dramatic changes in the overall DNA structure.[51] Observations relating to DNA structural changes include T_m (melting temperatures),[57,58] shortening as measured by EM[57] and viscosity changes.[46] This level of Pt corresponds closely to the GG sequence content. Furthermore, numerous studies have shown that Pt prefers to bind to G[46] and that GG intrastrand cross-links are formed preferentially.[59,60] The binding of Pt is at N7 such as in PtMe(GMP).[15]

Fourth, while Pt facilitates rewinding it also lowers T_m. This effect can be understood if the helix adjacent to the Pt-binding site is distorted such as to weaken the duplex in this area. Numerous lines of evidence point to such small areas of instability; see, for example, ref 46. For Cu^{2+}. the melting appears to be due to AT regions.[44,45] This weakening accounts for the disruption of H-bonding in Pt–oligonucleotide adducts[60] for short oligonucleotides but not in DNA[55] or in larger oligonucleotides.[56] Changes in the ^{31}P NMR spectrum of nucleosomes.[61] DNA.[61,62] and oligonucleotides[62,63] suggest that structural changes may occur in oligonucleotides similar to those which occur in DNA and in nucleosomes. The magnitude of the changes in the ^{31}P NMR spectrum (~ 1 ppm) is consistent with a syn conformation of one base, in keeping with the "head-to-tail" models studied here and previously.[15] However, other explanations for this shift are possible.

Fifth, for labile metal species (Cd, Cu, and Zn), the metal would be bound to a thermodynamically favorable site. The problem of lability as described above for the interstrand cross-linking model is thus avoided.

Finally, Zn^{2+} appears to favor GC-rich regions of DNA and to protect these regions from protonation.[64,65] These observations are consistent with the model proposed here.

Conclusion

Metals bind at numerous sites on DNA, and, for species such as Zn, undoubtedly the nature of the interaction with the bases, whatever it might be, would alone not be sufficient to permit renaturation if additional Zn ions were not neutralizing the charge on the DNA strands. The DNA molecule is complex, and many physical techniques provide average parameters for the entire molecule. The proposal we have put forth may be viewed as an alternative to be considered in the design of future experiments. The model stems from our consideration of the molecules described in this study. These molecules are not the best small molecule analogues for our proposed model since the bases are in the htt arrangement, although one interpretation of the ^{31}P NMR data discussed above would be that of G base has been converted to the syn conformation. However, Lippert and Lock have now found several examples of hth Pt complexes which also participate in intermolecular stacking interactions.[66] Certainly, we eagerly await X-ray results on metal–oligonucleotide complexes.[67]

Finally, glyoxalase I has been shown by EXAFS to contain two imidazole N's and four to five additional light atom donors (N or O).[16] The compounds reported here would be useful compounds to study with EXAFS since they are closer models for the Zn site in glyoxalase than the complexes utilized in the original study.

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Registry No. IMP, 131-99-7; GMP, 85-32-5; *cis*-$[Zn(H_2O)_4(Me\text{-}5'\text{-}IMP)_2]$, 94024-67-6; *cis*-$[Zn(H_2O)_4(Me\text{-}5'\text{-}GMP)_2]$, 94041-97-1; $[Zn(H_2O)_4(Me\text{-}5'\text{-}IMP)_2]\cdot 2H_2O$, 94024-68-7; $[Zn(H_2O)_4(Me\text{-}5'\text{-}GMP)_2]\cdot 6H_2O$, 94041-98-2.

Supplementary Material Available: Least-squares planes and the deviations of individual atoms from these planes, bond lengths, bond angles, anisotropic temperature factors, hydrogen coordinates and temperature factors and tables of observed and calculated structure factors (52 pages). Ordering information is given on any current masthead page.

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