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X-Ray Structural Studies of Metal–Nucleoside and Metal–Nucleoside Monophosphate Complexes: New Perspectives

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The X-ray structures of metal–nucleoside and metal–nucleoside monophosphate complexes published from 1980 to the end of 1991 are examined and classified. The first 3d trans bis divalent metal ion–nucleoside complex and the first thymidine complexes with Au and Hg are discussed. The structures for purine nucleotides are classified as $[M(NMP)(H_2O)_5]$; cis-$[M(NMP)_2]$; ternary M(NMP)(L), where L is a pyridine such as dpa, phen, or bpy, of three subtypes: (a) no direct M–NMP bonding and intramolecular stacking between the nucleotide and the base, (b) with a M–O(phosphate) bond and (c) with a M–N(7) of the purine base bond; and polymeric. The more relevant metal–pyrimidine nucleotide structures are also discussed.

Key Words: *metal ion, nucleoside, nucleotide, X-ray structure*

INTRODUCTION

The study of the interaction of metal ions with nucleosides and nucleotides (Fig. 1) is increasing in interest owing to the importance

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of these compounds in biology and toxicology. The anti-tumor activity of some platinum complexes, the presence of metal ions in the replication and transcription of DNA, the catalytic activity of RNA and the role of divalent cation–nucleotide complexes in the catalytic center of some enzymes, as for instance phosphorylase b, are the major topics that indicate the interest in metal–nucleoside complexes.[1-5]

Despite the interest and the many efforts of different laboratories during the last thirty years the X-ray structures of metal–nucleoside complexes reported in the literature are limited. For example, no X-ray structure of Fe(III) or Cr(III) with nucleosides or nucleotides is known. Very good reviews have been published, although mostly covering work through 1980[6-14]; platinum nucleobase chemistry has been reviewed recently,[15] and a general two-volume handbook of nucleobase complexes has appeared.[16] A recent article in this journal dealt with ternary nucleotide complexes.[17]

In the last decade, new structures of metal–nucleoside complexes have been studied, and novel modes of binding illustrated. In this paper, the general trends of crystalline metal–nucleoside complexes are summarized,[18-97] and the relevant new structures that have appeared from 1980 until the end of 1991 are described.

PURINE NUCLEOSIDE AND NUCLEOSIDE MONOPHOSPHATE DERIVATIVES

Structures of purine nucleosides and nucleoside monophosphates published from 1980 to the end of 1991 are summarized in Table I. These data are complementary to those previously published.[6,13]

Purine Nucleoside Complexes

The structures of some new complexes of Hg, Pd, Pt, Au and Zn[26,27,32,55,56,76] have been studied (Table I). Nucleoside complexes with 3d metals both in divalent[77] and trivalent[18] oxidation states were reported in the seventies in structural studies by Marzilli and Kistenmacher. The Cu(II) cytidine complex was the first nucleoside complex crystallized and structurally characterized with bind-

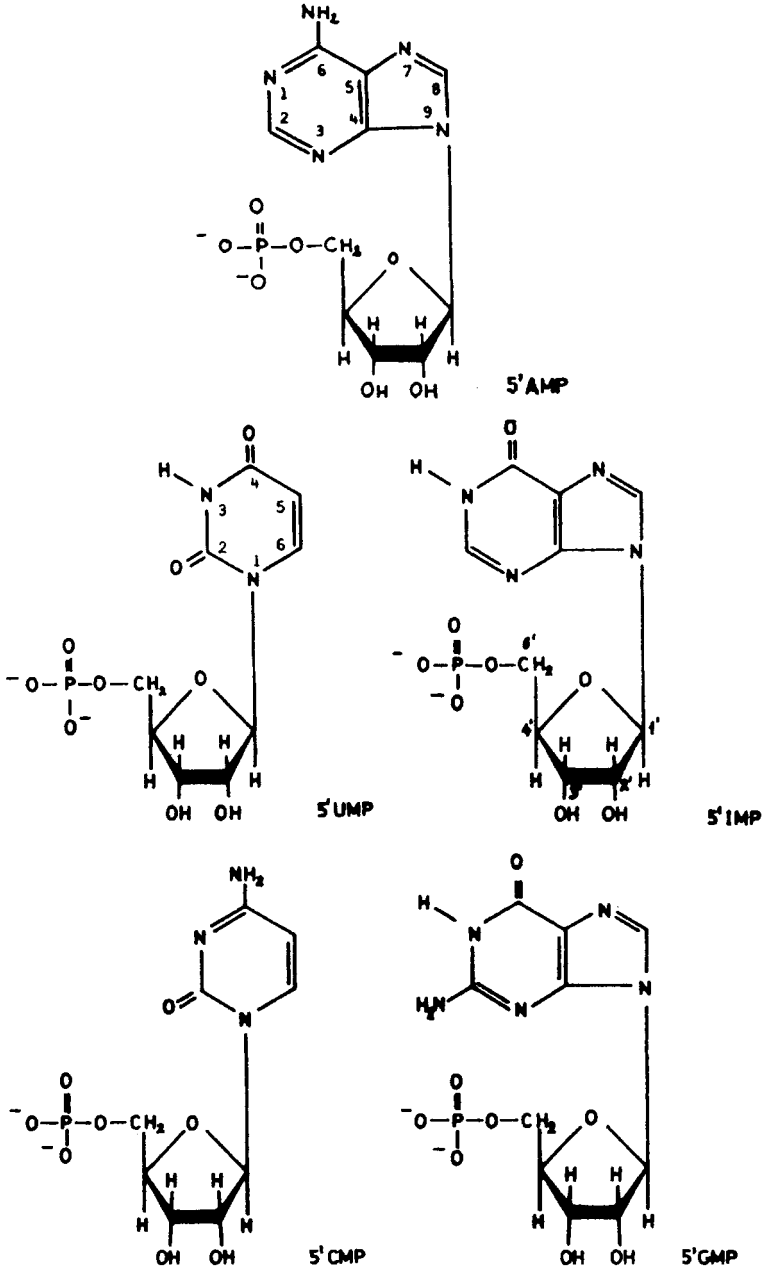

FIGURE 1 Formulae and atom labeling for the common nucleotides.

TABLE I

X-ray structural data of metal–purine nucleoside and purine nucleotide complexes

Compound	Geom. Around the Metal	Coordination Site	d M–L (pm)	Sugar Pucker	Glycosidic Bond	Refs.
$[Cu(5'\text{-AMPH})(phen)\cdot(H_2O)]_2(NO_3)_2\cdot 8H_2O$		O(phosphate) stacking				22
$[Pt(bpy)(en)]^{2+}(5'\text{-AMP})^{2-}$	sq. pl.	none (stacking)		C(2')-endo	anti	25
$[Pd(dien)(guo)](ClO_4)_2$	sq. pl.	N(7)	201.9	C(2')-endo	anti	26
$[Pt((guo)_2(R,S\text{-dach})]^{2+}$						27
$Hg(guo)Br_2$	dist. sq.	N(7)	215.	C(2')-endo	anti	32
$[Fe(5'\text{-GMP})(H_2O)_5]\cdot 3H_2O$	oct.	N(7)	219.1	C(3')-endo	anti	34
$[Co(en)_2(H_2O)_2]$ $[Co(5'\text{-GMP})_2(H_2O)_4]Cl_2\cdot 4H_2O$	cis oct.	N(7)	218.1	C(2')-endo	anti	37
$[Ni(c3',5'\text{-GMP})(H_2O)_5]\cdot(c3',5'\text{-GMP})\cdot 5H_2O$	oct.	N(7)			syn	39
$[Ni(5'\text{-GMPH})_2(en)(H_2O)_2](en)\cdot 6.5H_2O$	cis oct.	N(7)	Ni(A): 214.6–215.1 Ni(B): 212.8–218.2	C(3')-endo	anti	40,41
$[Ni(en)_{1.3}(H_2O)_{1.4}(H_2O)_2]$	cis oct.	N(7)	212	C(2')-endo	anti	42
$[Ni(5\text{-dGMP})_2(en)_{0.7}(H_2O)_{0.6}\cdot(H_2O)_2]\cdot 7H_2O$						
$[Ni(en)_2(H_2O)_2]$ $[Ni(5'\text{-GMP})_2(H_2O)_4]\cdot 6H_2O$	cis oct.	N(7)	213	C(2')-endo	anti	42

$[(Cu_3(3'\text{-GMP})_2(3'\text{-GMPH})_2 \cdot (H_2O)_5] \cdot 7H_2O$	sq. pyr.	Cu(1):N(7) and O(phosphate)	Cu(1): 199.8 192–197		syn (A) anti (B)	46
		Cu(2):O(phosphate)	Cu(2): 201–255			
$[Cu(2'\text{-GMPH})_2(H_2O)_3] \cdot 5H_2O$	oct.	N(7)	201.2–205.2	C(2')-endo C(2')-endo	syn	47
		O(5')	138	C(3')-exo		
$[Cu(phen)_2(H_2O)](3',5'\text{-cGMP})_2 \cdot 9H_2O$		no direct bonding stacking			syn	48
$Ca[Cu(5'\text{-GMP})_2(en)(H_2O)_2] \cdot 8H_2O$	cis oct.	N(7)	206–202	C(2')-endo	anti	50
$[Cu(5'\text{-GMP})(dpa)(H_2O)]_2 \cdot 3H_2O$						22
$[Zn(Me\text{-}5'\text{-GMP})_2(H_2O)_4]$	cis oct.	N(7)	214.3–212.7	C(3')-endo C(2')-endo	anti	51
$[Pt(Me\text{-}5'\text{-GMP})_2(tn)]$.	cis sq. pl.	N(7)	286		anti	53
$[(MeHg)_2(\mu\text{-ino})]ClO_4$	linear	Hg(1)–N(1) Hg(2)–N(7)	211 206	–	–	55
$(ino^+)(AuBr_4)^- \cdot 2H_2O$	sq. pl.	no direct bond		C(2')-exo	anti	56
$[Mn(5'\text{-IMP})(H_2O)_5] \cdot 2H_2O$	oct.	N(7)	231.8–233.6	C(3')-endo C(3')-endo C(2')-endo	anti anti anti	34
$[Fe(5'\text{-IMP})(H_2O)_5] \cdot 2H_2O$	oct.	N(7)	(1) 225.6 (2) 230.8 (3) 224.3	C(3')-endo C(3')-endo C(2')-endo	anti anti anti	57,58
$[Co(5'\text{-dIMP})(H_2O)_5] \cdot 2H_2O$	oct.	N(7)	214.5	C(3')-endo	anti	60
$[Co(en)_2(H_2O)_2][Co(5'\text{-IMP})_2(H_2O)_4].Cl_2 \cdot 4H_2O$	cis oct.	N(7)	221	C(2')-endo	anti	37
$[Ni(5'\text{-IMPH})_2(en)(H_2O)_2] \cdot 13H_2O$	cis oct.	N(7)	212.9	C(3')-endo	anti	41

TABLE I (*Continued*)

Compound	Geom. Around the Metal	Coordination Site	d M–L (pm)	Sugar Pucker	Glycosidic Bond	Refs.
$[Cu(3',5'\text{-cIMP})(phen)(H_2O)_2]\cdot[NO_3]\cdot 2H_2O$	sq. pyr.	N(7)	199.5	–	syn	48
$Ca[Cu(5'\text{-IMP})_2(H_2O)_4]\cdot 6.7H_2O$	cis oct.	N(7)	204	C(2')-endo	anti	50
$[Cu(bim)(H_2O)_5]^{2+}[5'\text{-IMP}]^{2-}\cdot 3H_2O$	oct	no direct bond stacking		C(3')-endo	anti	63,64
$[Cu(5'\text{-IMP})(dpa)(H_2O)]_2$	sq. pyr.	O(phosphate)	192	C(3')-endo O(4')-endo C(3')-endo	anti	65,66
$Na_2[Cu(5'\text{-IMP})_2(im)_{0.8}\cdot(H_2O)_{3.2}]\cdot 12.4H_2O$	cis oct.	N(7)	208.9	–	–	68
$[Zn(Me\text{-}5'\text{-IMP})_2(H_2O)_4]$	cis oct.	N(7)	214.9 215.9	C(3')-endo C(2')-endo	anti	51
$[Zn(xao)_2(H_2O)_4]\cdot 2H_2O$	trans oct.	N(7)	216.6	(a) C(2')-endo (b) C(3')-exo	anti anti	76

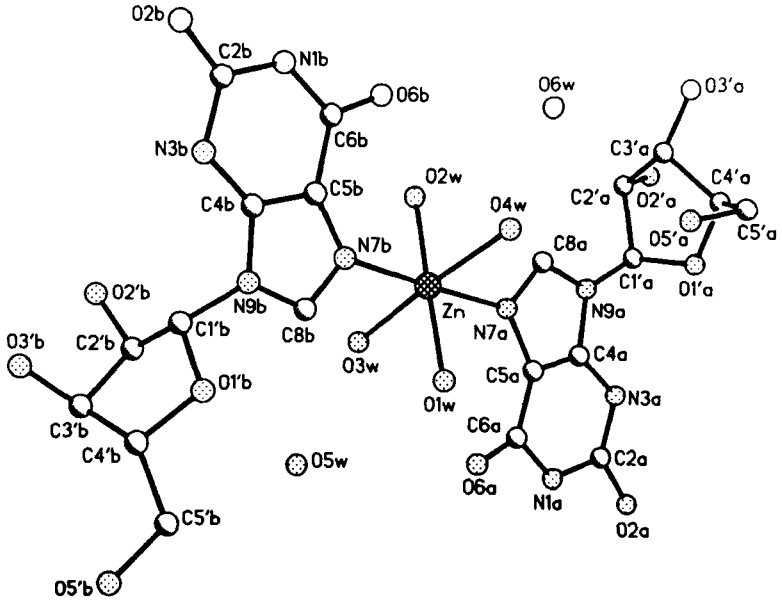

FIGURE 2 View of the $[Zn(xao)_2(H_2O)_4]$ structure (Ref. 76).

ing relevant to metal–DNA interactions. More recently, the complex $[Zn(xao)_2(H_2O)_4]\cdot 2H_2O$ was reported to be the first divalent 3d metal purine nucleoside complex with a known crystalline structure,[76] where the xao* ligands occupy trans octahedral coordination positions (Fig. 2). This conformation differs from the usual cis square arrangement of other bis nucleoside complexes, e.g., $Pt(guo)_2$ complexes,[28,29] and also from the usual cis octahedral $M(NMP)_2$ for 3d metal purine nucleotide complexes (Table II).

Complexes of Purine Nucleotides of the Type $[M(NMP)(H_2O)_5]\cdot nH_2O$

To the previously known structures[20,33,35,36,38,52,59] of 1:1 M–NMP complexes, some new complexes[34,57,58] of this type (Fig. 3) with M–N(7) bond and hydrogen bonding between phosphate and a coordinated water molecule and with C(3′)-endo and anti-

*See list of abbreviations at end of article.

TABLE II

Summary of important parameters of several cis-$M(NMP)_2$ purine neucleotide compounds (Adapted from Ref. 51)

Compound	Dihedral Angle Between Purine Bases (deg)	N(7)–M–N(7) Angle (deg)	d N(7)–N(7) in pm	Ref.
Na_2[5′-GMP]	2.3		318	100
$[Co(5'\text{-GMP})_2(H_2O)_4]^-$	40.6	82.3	287	37
$[Ni(5'\text{-GMPH})_2(en)(H_2O)_2]$	30.9 (A) and 21.7 (B)	88.5 (A) and 85.6 (B)	299	40,41
$[Ni(en)_{1.3}(H_2O)_{1.4}(H_2O)_2]$	44.4	84.3	285	42
$[Ni(5\text{-dGMP})_2(en)_{0.7}(H_2O)_{0.6}(H_2O)_2]\cdot 7H_2O$				
$[Ni(5'\text{-GMP})_2(H_2O)_4]^{2-}$	41.0	86.1	292	42
$[Cu(5'\text{-GMP})_2(en)(H_2O)]^{2-}$	42.5	87.7	283	50
$[Zn(Me\text{-}5'\text{-GMP})_2(H_2O)_4]$	32.9	89.5	304.4	51
$[Pt(Me\text{-}5'\text{-GMP})_2(tn)]$	39.6	90.1	286.2	53
Na(5′-IMPH)	22.0	–	348	101
$[Co(5'\text{-IMP})_2(H_2O)_4]^-$	39.7	82.6	291	37
$[Ni(5'\text{-IMPH})_2(en)(H_2O)_2]$	26.1	89.0	298.3	41
$[Cu(5'\text{-IMP})_2(H_2O)_4]$	–	87.8	–	50
$[Cu(5'\text{-IMP})_2(im)_{0.8}(H_2O)_{3.2})]^{2-}$	35.5	89,6	297	68
$[Cu(5'\text{-IMP})_2(dien)]^{2-}$	30.4	78.6	322.8	69
$[Zu(Me\text{-}5'\text{-IMP})_2(H_2O)_4]$	36.8	89.3	302.8	51
$[Pt(5'\text{-IMP})_2(NH_3)_2]^{2-}$	43	89.0	283	72
$[Pt(5'\text{-IMP})_2(NH_3)_2]^{2-}$	40.7	90.0	288	73
$[Pt(5'\text{-IMP})_2(en)]^{2-}$	31	–	326	74
$[Pt(5'\text{-IMP})_2(tn)]^{2-}$	38.2(40.9)	90.2	296	75

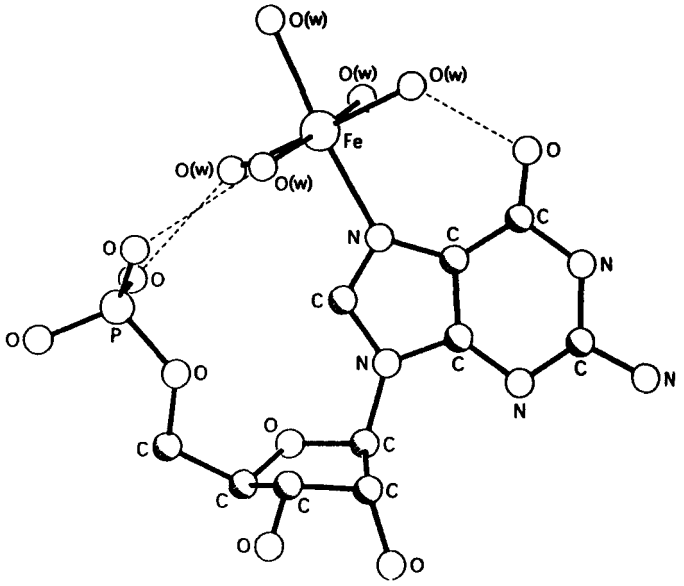

FIGURE 3 Molecule structure of $[Fe(5'\text{-GMP})(H_2O)_5]\cdot H_2O$. Dashed lines indicate intramolecular hydrogen bonds (Ref. 34).

conformation[99] have been obtained by Goodgame. With Ni(II)–cGMP, Co(II)–dGMP[39,60] and Co(II)-(sugar-broken) IMP, with a sugar oxidized ribose,[98] similar structures have been obtained. The first Fe(II)–5'GMP and 5'-IMP complexes have been obtained. The complexes $[Fe(5'\text{-IMP})(H_2O)_5]\cdot 2H_2O$[57,58] and $[Mn(5'\text{-IMP})(H_2O)_5\cdot 2H_2O$[34] crystallize with a unit cell in which there are three independent molecules, two of which have the ribose ring C(3')-endo and one C(2')-endo. Goodgame supports the suggestion that at least in some of the $[M(NMP)(H_2O)_5]$ systems there may be little energy difference between the two conformations and both may coexist in solution; the C(3')-endo normal conformation in these complexes may derive from the crystallization conditions, especially the temperature employed.[34]

Complexes of Purine Nucleotides of the Type cis $M(NMP)_2$

One major novel type of X-ray structure published in the last decade is represented by 3d metal ion cis $M(NMP)_2$ complexes.

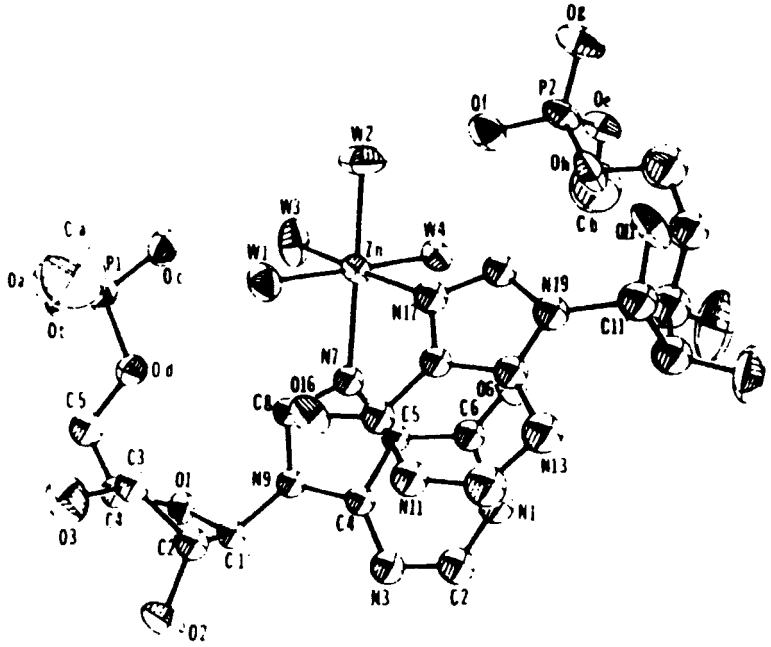

FIGURE 4 Stereochemistry in the $Zn(Me\text{-}5'\text{-}IMP)_2$ complex (Ref. 51).

In these complexes, the cation has a distorted octahedral coordination and is bound to two N(7) of each nucleotide, and the phosphate group is interacting through a hydrogen bond with one water molecule of the first coordination sphere of the metal ion (Fig. 4). Previously only Pt(II)[72–75] and Cu[69] complexes and a polymeric Cd(II) one[71] were known; several data of these complexes are summarized in Table II. These structures are relevant to understanding the coordination of divalent metals with DNA and RNA.

Structures of these nucleotide complexes are known for 5′-GMP and 5′-IMP and for octahedral Co(III), Ni(II), Cu(II), Zn(II) and square planar Pt(II) complexes. The glycosidic bond is normally anti but the sugar pucker can be either C(2′)-endo[37,42,50] or C(3′)-endo[40,41] and, for the Zn–(Me-5′-GMP) complex, C(3′)-endo and C(2′)-endo for each nucleoside molecule.[51]

Some of these complexes for Ni(II) and Cu(II) show coordination properties essentially identical to the analogous platinum complexes[41,42,50] with NH_3 or ethylendiamine ligands in the equa-

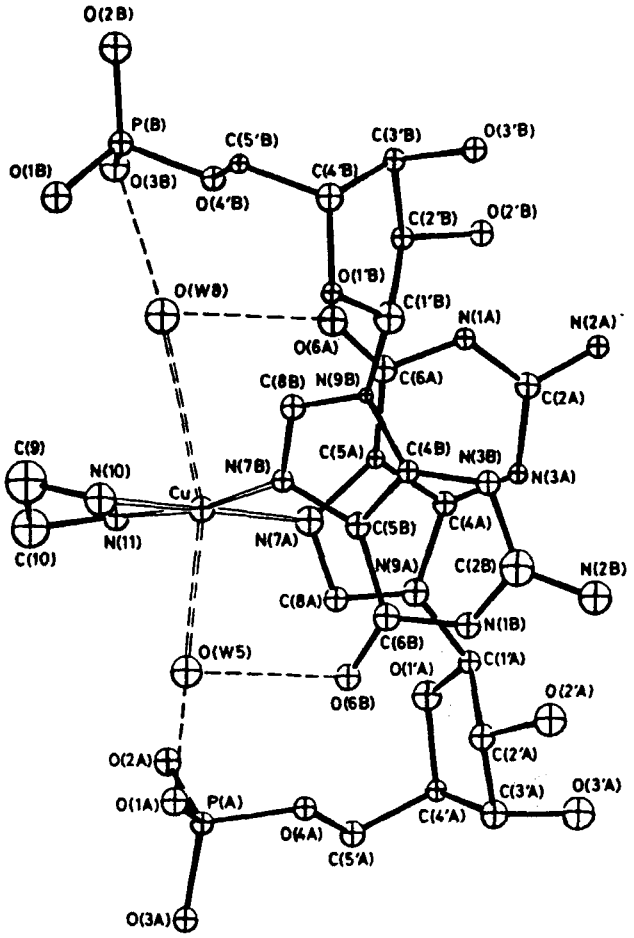

FIGURE 5 Drawing of the $[Cu(5'\text{-}GMP)_2(en)(H_2O)_2]^{2-}$ complex. Single broken lines indicate hydrogen bonds (Ref. 50).

torial plane where the N(7) of purines are bound (Fig. 5). From a stereochemical point of view only, copper and nickel appear as potential candidates for platinum substitution in antitumor active metal complexes.[50]

The dihedral angle between the purine bases (Table II) is normally between 26.1[41] and 44.4°.[42] These values are well within the range 30–40° for $Pt(NMP)_2$ purine monophosphate com-

plexes.[53,72–75] The exception to the rule is the $Ni(GMPH)_2$ B molecule with a dihedral angle of only 21.7°.[41]

Some of these structures present intramolecular base stacking.[41,51,53] Since it is known that the stacking between mononucleotides follows the order 5′-AMP > 5′-GMP > 5′-IMP > 5′-CMP > 5′-UMP,[102] the known X-ray structure, which indicates for GMP derivatives a stacking between the purine bases in cis coordination, is in agreement. No structure of this type is yet known for 5′-AMP derivatives, but the complex $[Ni(5'\text{-}AMP)_2]^{2-}$ was described in solution,[103] and the enthalpies of formation measured by calorimetric methods at 25°C; a difference between the enthalpies of formation between [Ni(5′-AMP)] and $[Ni(5'\text{-}AMP)_2]^{2-}$ of −11.6 kJ/mol can be assigned tentatively to the stacking enthalpy between the adenine rings in cis positions.[104]

In the formation and isolation of some of these complexes,[37,41,50] the replacement of coordinated ethylenediamine molecules by two water molecules has been attributed to the strong trans effect of N(7)-bonded purine.[37] One ethylenediamine displaced is retained in the crystalline structure for the $Ni(5'GMPH)_2$ complex (Fig. 6),[41] where intermolecular stacking can also be observed.

Ternary Complexes M(NMP)(L), Where L Is a Heterocyclic Ligand

Although ternary compounds are very important to understand the active center of enzymes or the interactions of metals complexes with nucleic acids, no X-ray structure of a ternary M–amino acid or peptide–purine nucleoside or nucleotide compound is known. It was mentioned above that the first relevant nucleoside complex[77] of a divalent metal (Cu(II)) contained cyd, a pyrimidine nucleoside. In the previous section, ternary complexes with ligands as NH_3 or ethylendiamine were discussed. However, ternary compounds with ligands such as dpa, terpy, bim, bpy or phen are also known.

These structures present three structural types:

(a) Ternary complexes M(NMP)(L) where there is stacking between the purine base and L, but no direct bonding between the metal ion and the nucleotide. The first structure of this type was

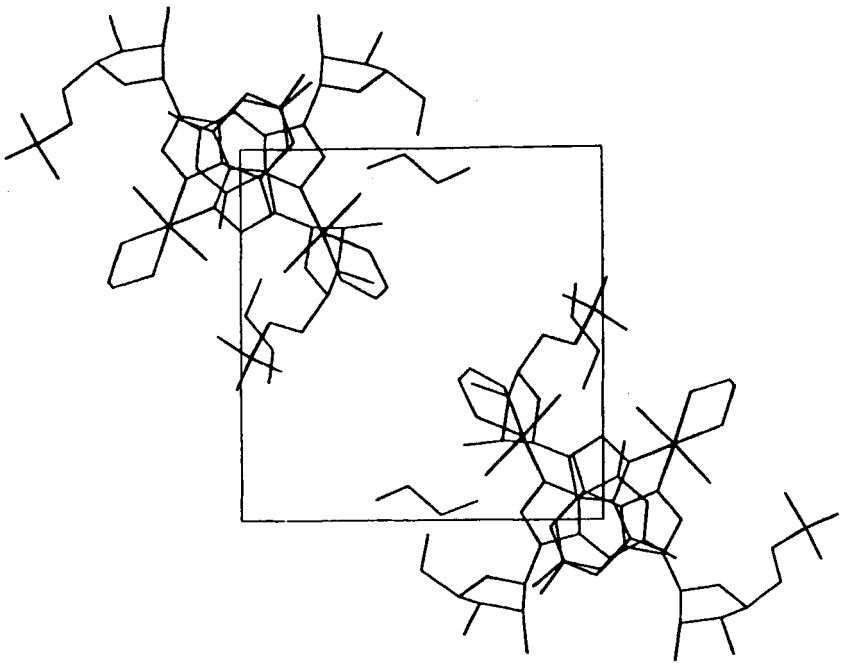

FIGURE 6 Cell projection of $[Ni(5'\text{-}GMPH)_2(en)(H_2O)_2](en)\cdot 6.5H_2O$ parallel to b (Ref. 41).

$[Pt(terpy)Cl]_2(5'\text{-}AMP)_2\cdot 4.5H_2O$ published by Lippard.[24] Now three other compounds are known: $[Pt(bpy)(en)]^{2+}$–$[5'\text{-}AMP]^{2-}$[25] (Fig. 7), $[Cu(phen)_2(H_2O)][3',5'c\text{-}GMP]_2\cdot 9H_2O$[48] and $[Cu(bim)(H_2O)_5)]^{2+}[5'\text{-}IMP]^{2-}\cdot 3H_2O$.[63,64] Figure 7 shows the structure described by Yamauchi[25]; the distance between the bases is 350 pm, the average value for all these compounds. These compounds are very important to understand the interaction of intercalating compounds with nucleic acids.[1,9,105,106] These structural studies also agree with the solution studies with ligands such as tryptophan, leucine or histidine and nucleotides; such studies indicate that an increase in formation constants is due to hydrophobic or solvophobic interactions.[107–109] Recently, Yamauchi has measured the enthalpy for the stacking between $[Pt(bpy)(en)]^{2+}$ and 5'-AMP, obtaining a value of -25.6 kJ/mol[110] by calorimetric methods.

(b) Ternary complexes M(NMP)(L) where there is a direct bond

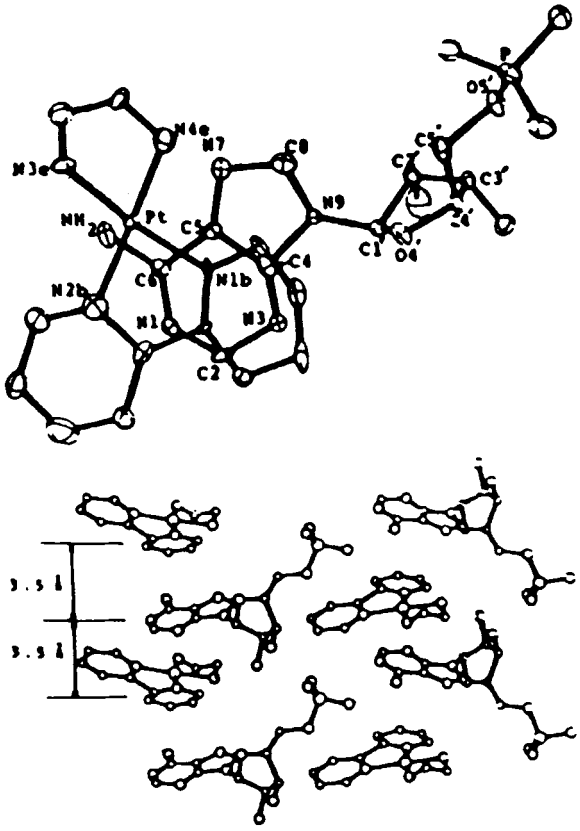

FIGURE 7 View of $[Pt(bpy)(en)]^{2+}$–[5′-AMP]$^{2+}$ (Ref. 25).

M–O(phosphate) to the nucleotide. Some new complexes of this type have been structurally characterized. In addition to the previously known $[Cu(5'\text{-AMPH})(bpy)(H_2O)]_2^{2+}$ with intramolecular stacking between the adenine ring and bipyridine (d = 340 pm),[21] $[Cu(5'\text{-IMP})(dpa)(H_2O)_2]_2 \cdot 4H_2O$[67] and $[Cu(3'\text{-GMP})(phen)(H_2O)_2] \cdot 7H_2O$[49] without intramolecular stacking, other ternary structures have been studied. The complexes $[Cu(5'\text{-AMP})(phen)(H_2O)]_2^{2+}$,[22] $[Cu(5'\text{-GMP})(dpa)(H_2O)]_2 \cdot 3H_2O$,[22] and $[Cu(5'\text{-IMP})(dpa)(H_2O)]_2$[65,66] present a dimeric $(Cu-O-P-O)_2$ unit without intramolecular stacking in the 5′-GMP and 5′-IMP derivatives and with intramolecular stacking in the 5′-AMP derivative. Figure

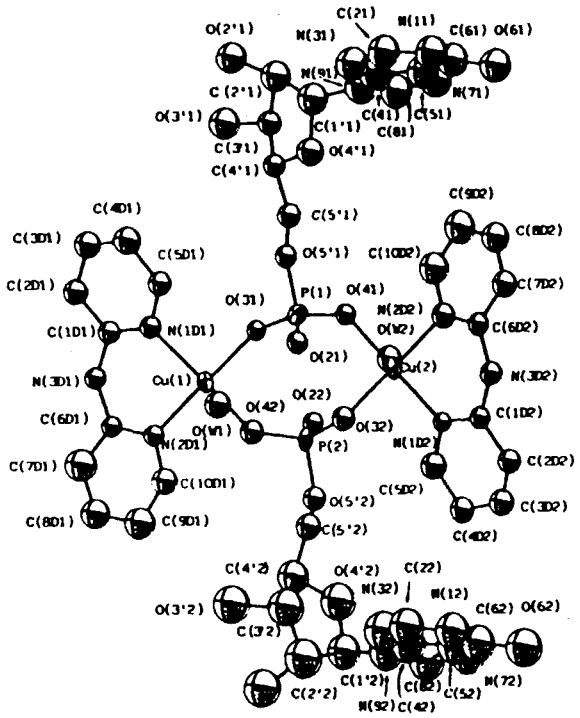

FIGURE 8 Drawing of the $[Cu(5'\text{-IMP})(dpa)(H_2O)]_2$ molecule (Ref. 65 and 66).

8 shows the structure of $[Cu(5'\text{-IMP})(dpa)(H_2O)]_2$, in which intermolecular stacking is important in the packing of this crystal.

This structure type also occurs with pyrimidine nucleotides. The presence of intramolecular stacking in the case of the 5′-AMP derivatives can be explained by thermodynamic factors owing to the greater importance of stacking for adenine nucleoside compared to the other purine nucleosides.[102]

(c) Ternary M(NMP)(L) complexes where the metal is bound to the N(7) of the purine ring. This structure type is present for the complexes $[Cu(5'\text{-IMPH})(bpy)(H_2O)_2](NO_3).H_2O$[61] and [Cu(3′,5′-cIMP)(phen)$(H_2O)_2$](NO_3).[48] In Fig. 9 the Cu–N(7) bond and the lack of Cu–phosphate interaction can be observed.

The reasons for preferences between (a), (b) or (c) structures

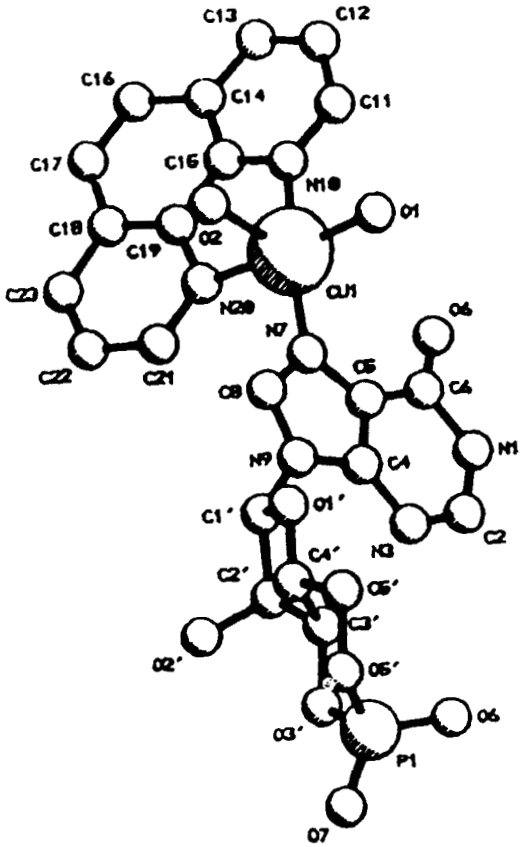

FIGURE 9 Molecular structure of $[Cu(3',5'\text{-IMP})(bpy)(H_2O)_2]^+$ (Ref. 48).

are not easy to explain; normally the metal is Cu(II) and the ligands are very similar. However, it can be inferred as a rule that in these ternary complexes with pyridine ligands, metallic bonding with O(phosphate) prevents direct bonding with the base, especially with 5'-AMP derivatives where the stacking energies are important[102]; when the stacking interaction is not so important the N(7) is preferred for metal coordination (for 5'-IMP or 3',5'-cIMP derivatives with phen or bpy). Also the pH and temperature conditions can play an important role. (Note that is the complex $[Cu(5'\text{-IMPH})(bpy)(H_2O)_2](NO_3).H_2O$ the nucleotide is protonated with

TABLE III

X-ray structural data for metal–pyramidine nucleoside and pyrimidine nucleoside monophosphate complexes

Compound	Geom. Around the Metal	Coordination Site	d M–L (pm)	Sugar Pucker	Glycosidic Bond	Refs.
$Zn(Me\text{-}5'\text{-}CMP)_2 \cdot 9H_2O$	dist. tet (head to tail polymeric	N(3) O(phosphate)	200.3 198.3 dZn-O(2) = 270	C(3')-endo	anti	84
$Zn(Me\text{-}2'\text{-}dCMP)_2 \cdot 11H_2O$	dist. tet	N(3) O(phosphate)	200 195 dZn-O(2) = 272	disordered	–	84
$[Cd(5'\text{-}dCMP)(H_2O)_2]$, (orthorhombic)	oct.	N(3) O(2) O(phosphate)	229 264 222	C(2')-endo	anti	89
$[Cd(5'\text{-}dCMP)(H_2O)_2] \cdot 3H_2O$ (monoclinic)	dist. pent. bipyr.	N(3) O(2) O(phosphate)	235 av. 273 av. 227–289	C(3')-endo and C(3')-endo, C(4')-exo	anti	89
$[Cu(5'dUMP)(dpa)(H_2O)]_2 \cdot 5H_2O$	–	O(phosphate)	–	–	–	22
$[Cd(5'\text{-}UMP)(H_2O)_2] \cdot 2H_2O$	oct.	O(phosphate)	234,226 231,226	C(3')-endo C(2')-exo	anti	95
$[Cd_2(5'\text{-}dUMP)_2(H_2O)_6]$	oct.	O(phosphate)	221,229, 229,232, 220,214	C(1')-endo C(4')-exo	anti	95
$[Au(PMe_3)(AZT^-)]$	linear	N(3)	206.9	A: C(2')-endo/ C(3')-exo B: C(3')-exo/ C(4')-endo	anti	96
$[CH_3Hg(thd^-)]$	linear	N(3)	A: 207 B: 210 C: 210	C(3')-exo C(3')-exo C(3')-exo	anti	97

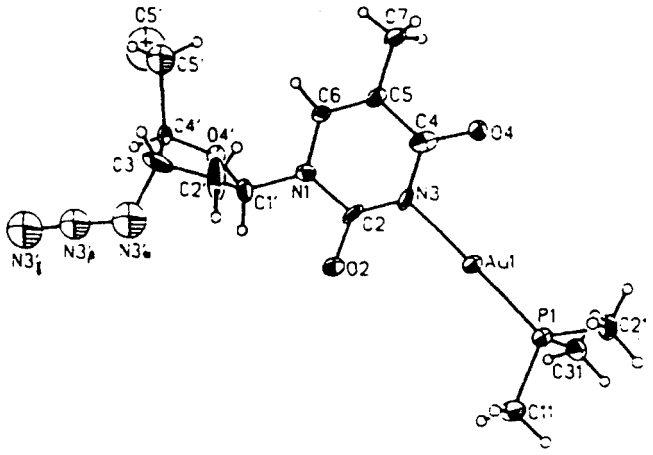

FIGURE 10 Structure of the ([PMe_3)Au(AZT$^-$)] complex (Ref. 96).

a direct M–N(7) bond but not in [Cu(5′-IMP)(dpa)(H_2O)]$_2$ with a M–O(phosphate)bond.)

Other Metal–Purine Nucleotide Structures

Other different types of structures have been described, especially for polymeric structures. A relevant Cu(II)–O(5′) of the ribose ring interaction is described[47] for the [Cu(2′-GMPH)$_2$(H_2O)]·5H_2O polymeric structure. The polymeric Cd–5′-IMP complex[71] also presents these rare metal–ribose interactions in its polymeric structure.

PYRIMIDINE NUCLEOSIDE AND NUCLEOSIDE MONOPHOSPHATE DERIVATIVES

The number of X-ray structure of metal pyrimidine nucleoside[77–80,95,96] and monophosphate nucleotide complexes[22,74,81–85,94] is limited. Table III shows data for the several structures described from 1980; this table is complementary with those previously published.[6,13]

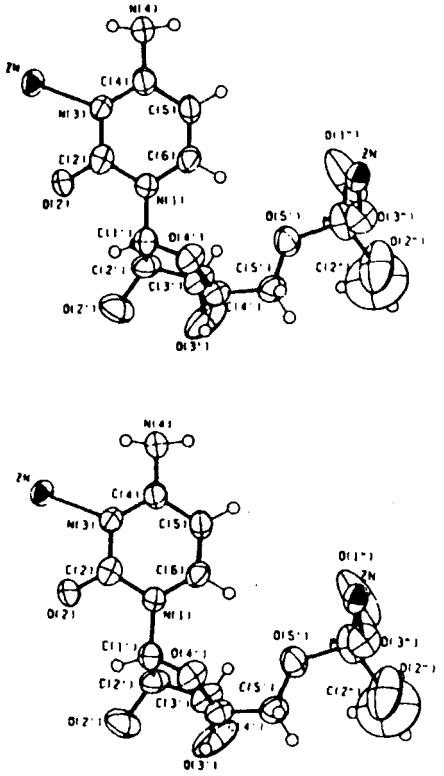

FIGURE 11 View of the $Zn(Me\text{-}5'\text{-}CMP)_2.9H_2O$ complex (Ref. 84).

Pyrimidine Nucleoside Metal Complexes

The complex $[Cu(cyd)(glygly)]\cdot 2H_2O$ is the unique example of metal–peptide–nucleoside or nucleotide compound until now,[77,78] and it is relevant for understanding peptide–metal–nucleic acid interactions. Two more cyd complexes bound by N(3) were described later but before 1980.[79,80] These have Pt(II) as the central metal.

Recently the crystalline structures of $[(PMe_3)Au(AZT^-)]$[96] and $[CH_3Hg(thd^-)]$[97] where the metal shows linear coordination and is bound to the N(3) of a deprotonated thymine (Fig. 10) have been published. The interest in finding good anti-AIDS drugs will increase the number of studies with thymidine and thymidine derivatives like AZT with metals.[96]

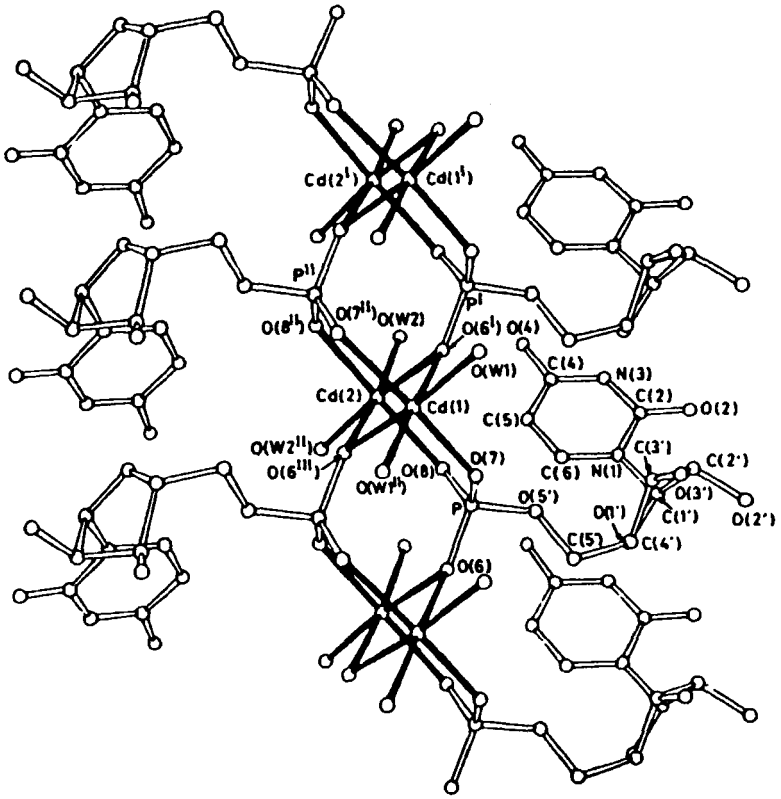

FIGURE 12 The polymeric structure of $[Cd(5'\text{-UMP})(H_2O)_2].2H_2O$ (Ref. 95).

Pyrimidine Nucleotide Metal Complexes

In addition to the previously known crystalline structures[74,81–83,85–88,90–94] some new crystalline structure are known for Zn(II), Cd(II) and Cu(II) pyrimidine nucleotide complexes,[84,89,22,95] but still now the number is not very high. These structures are normally polymeric.

The metal bonds to two O(phosphate)and the N(3) of the pyrimidine base in the Zn–(Me-5'-CMP) and Zn–(Me-5'-dCMP) complexes[84] where a Zn(II)–O(2) intramolecular interaction also exists. Such interactions present values from 208 pm for Mn(II)[81]

to 299 pm for Pt(II),[74,91] and about 270–272 pm for these Zn(II) complexes (Fig. 11).

The structures of two Cd(II) complexes with (5′-UMP) and (5′-dUMP) are linearly polymeric (Fig. 12), with Cd(II) interacting only with the phosphate group. These structures show some similarities with the $[Co_2(5'\text{-UMP})_2(H_2O)_4]_n$ structure described by Goodgame *et al.*[92]

Some ternary complexes with dpa and 5′-UMP or 5′-dUMP are known.[22,93,94] The structures are dimeric and are similar to the type *b* ternary purine nucleotide complexes with a $(Cu-O-P-O-)_2$ bridge described in Fig. 8.

CONCLUSIONS

Nucleoside and nucleotide complexes exhibit diverse structures. This diversity has, to some extent, precluded a full understanding of factors influencing the structural types formed. However, a number of features have been identified, including stacking interactions, which explain some of these features. Additional structural types are needed to gain a full understanding of such interactions. Mixed-ligand complexes are of interest because they reveal interligand interactions which form the basis of molecular recognition.[111] There is a paucity of mixed-ligand complexes, especially with amino acid and peptide ligands. Crystallization of nucleoside and nucleotide complexes continues to be a challenge.[112] However, in some cases the crystalline architecture can be exploited to prepare mixed-metal complexes.[112] More recently, several laboratories, such as those of Sigel,[107] Rizzarelli,[109] and Yamauchi[110] are providing valuable data to aid in uncovering the factors that influence the solution structures.

ABBREVIATIONS

For the nucleotides and nucleosides: ado: adenosine; 5′-AMP: adenosine 5′-monophosphate; 5′-AMPH: protonated adenosine 5′-monophosphate; 3′-AMP: adenosine 3′-monophosphate; 2′-AMP: adenosine 2′-monophosphate; 5′-dAMP: deoxyadenosine

5′-monophosphate; AZT: 3′-azido-3′-dThd; AZT^-: deprotonated AZT; guo: guanosine; 5′-GMP: guanosine 5′-monophosphate; Me-5′-GMP: guanosine 5′-monophosphate methyl ester; ino: inosine; 5′-IMP: inosine 5′-monophosphate; xao: xanthosine; cyd: cytidine; 5′-CMP: cytidine 5′-monophosphate; 5′-UMP: uridine 5′-monophosphate; thd: thymidine; thd^-: deprotonated thymidine; NMP: nucleoside monophosphate in general.

For other ligands: en: ethylenediamine; dien: diethylenetriamine; tn: triethylenediamine; dpa: 2,2′ dipyridylamine; im: imidazole; bim: benzimidazole; phen: 1,10 phenanthroline; bpy: 2,2′-bipyridine; terpy: terpyridine; R,S-dach: 1R,2S diaminocyclohexane.

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