

Structural Properties of a Nearly Stoichiometric Diammineplatinum(II) Complex with Inosine 5'-Monophosphate

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Abstract: A nonstoichiometric compound, $[\text{Na}_2(5'\text{-IMPH})_2 \cdot 16\text{H}_2\text{O}]_{0.14}[\text{Na}_2((\text{NH}_3)_2\text{Pt}(5'\text{-IMP})_2) \cdot 15\text{-}16\text{H}_2\text{O}]_{0.86}$, has been prepared and investigated by single-crystal X-ray methods (5'-IMP = the dianion of inosine 5'-monophosphate). The compound is isomorphous with the monosodium salt of 5'-IMP and several $\text{Pt}^{\text{II}}\text{-}5'\text{-IMP}$ complexes previously reported to be nonstoichiometric. The coordination geometry about the $\text{Pt}(\text{II})$ is essentially square planar with the N(7) atom of the hypoxanthine base and the ammonia ligand and their twofold related symmetry mates occupying the four coordination sites. Analysis of the structural parameters in these complexes [N(7) to N(7) distance, dihedral angle between hypoxanthine bases] and a detailed study of the crystal packing of the title compound further verify our earlier proposal that the nonstoichiometry of the $\text{Pt}(\text{II})$ compounds may result from a competition between the crystal packing forces operative in the sodium salts of 5'-IMP and the coordination-induced distortions in this basic 5'-IMP structural motif. The present study also adds further support to our earlier suggestion that the crystal structure analysis of $\text{Na}_2[(\text{NH}_3)_2\text{Pt}(5'\text{-IMP})_2] \cdot 15\text{-}16\text{H}_2\text{O}$, reported by others previously, was probably performed on a stoichiometric compound.

Introduction

Both carcinogens and cancer drugs are widely believed to produce their effects via interaction with nucleic acids.¹⁻³ Many of the most effective agents are bifunctional and thus can interact with two nucleophilic sites on a nucleic acid.^{2,3} The most nucleophilic sites are the N(7) sites on guanosine moieties.³ The extremely promising drug *cis*- $\text{Pt} \equiv \text{cis}-[(\text{NH}_3)_2\text{Pt}^{\text{II}}\text{Cl}_2]$ is also believed to interact with nucleic acids⁴ and to have its highest affinity for guanosine bases.³ Thus, it would be desirable to obtain structural information on complexes containing the *cis*- $(\text{NH}_3)_2\text{Pt}^{\text{II}}$ moiety and one or more nucleotides. This goal has been hampered by difficulty normally encountered in crystallizing transition-metal nucleotide species as nonpolymeric complexes.

Inosine has a coordination chemistry very similar to guanosine and inosine 5'-monophosphate (5'-IMP) complexes are more readily crystallized than guanosine 5'-monophosphate (5'-GMP) complexes.

A crystalline complex has been prepared from the reaction of *cis*- $(\text{NH}_3)_2\text{Pt}^{\text{II}}(\text{H}_2\text{O})_2]^{2+}$ with 5'-IMP.² In this complex, N(7), the likely and available binding site in nucleic acids, of two 5'-IMP moieties is bound to Pt. There appeared to be three particularly fascinating aspects of this complex. First, the complex could serve as a model for the intrastrand cross-linking^{3,4} by a metal to two adjacent nucleotide subunits in a polynucleotide chain. Second, the reported nonstoichiometry of the complex (only about 56% of the available Pt sites are reported to be occupied²) suggests a competition between the covalent binding forces in the platinum complex and the crystal packing forces operative in the sodium salts of 5'-IMP.^{5,6} Finally, there are major differences between the molecular topology assumed by the $[(\text{NH}_3)_2\text{Pt}(5'\text{-IMP})_2]^{2-}$ complex anion and those displayed by the $[(\text{en})\text{Pt}(\text{guanosine})_2]^{2+}$ (where en = ethylenediamine) and the $[(\text{NH}_3)_2\text{Pt}(\text{guanosine})_2]^{2+}$ complex cations.^{7,8}

More recently, Bau⁹ has studied the reaction of $(\text{en})\text{Pt}^{\text{II}}$ with $\text{Na}_2(5'\text{-IMP})$. The resulting complex is nonstoichiometric (about 38% Pt occupancy) and structurally very similar to the diammine complex.² The addition of the structural information on the $(\text{en})\text{Pt}^{\text{II}}$ complex appeared to strengthen the supposition that the reaction of (ammine) Pt^{II} reagents with 5'-IMP leads to nonstoichiometric compounds.

A more complete grasp of the structural chemistry of these systems was provided by the study of the reaction of $(\text{dien})\text{Cu}^{\text{II}}$, where dien = diethylenetriamine, with $\text{Na}_2(5'\text{-IMP})$.¹⁰ The complex formed was stoichiometric, but disordered. An evaluation of the structural parameters in the monosodium,⁵ the $(\text{NH}_3)_2\text{Pt}^{\text{II}}$,² the $(\text{en})\text{Pt}^{\text{II}}$,⁹ and $(\text{dien})\text{Cu}^{\text{II}}$ ¹⁰ compounds of 5'-IMP allowed a reasonable systematization of the published results. However, the $(\text{NH}_3)_2\text{Pt}^{\text{II}}$ parameters did not follow the projected trends as well as could be expected and we therefore prepared a crystalline complex from the reaction of $(\text{tn})\text{Pt}^{\text{II}}$, where tn = trimethylenediamine, with 5'-IMP.

A structural analysis of the nonstoichiometric (Pt occupancy 76-80%) complex of 5'-IMP with $(\text{tn})\text{Pt}^{\text{II}}$ ¹¹ provided a vital link in the rationalization of the structural parameters in these compounds. The only reasonable way of rationalizing the now relatively large set of structural parameters was to assume that the structural data reported for the nonstoichiometric $(\text{NH}_3)_2\text{Pt}^{\text{II}}$ complex of Skapski and Goodgame² were actually those of a *stoichiometric* complex.

In an attempt to verify this rather surprising result of our analysis, we have prepared a diammine complex of 5'-IMP following the literature procedure² and report here on a structural study of a second complex. The data reported here are for a nonstoichiometric complex (about 86% Pt occupancy) and the structural parameters reinforce our conclusion that the parameters in the original diammine complex² are those of a stoichiometric complex.

At this juncture, it is not clear as to the reasons why compounds of different stoichiometries are obtained with the same $\text{Pt}(\text{II})$ moiety. It seems possible that, within any given batch of crystals, a variation exists in the Pt content and that the usual batch elemental analysis is misleading. We are presently investigating the factors which influence the Pt content.

Experimental Section

The diammineplatinum(II) complex was prepared in a manner analogous to that in the literature.² Since evidently different preparations lead to different stoichiometries, we describe our conditions here as follows. *cis*- $\text{Pt}(\text{NH}_3)_2\text{Cl}_2$ (0.93 g) was suspended in a solution of AgNO_3 (0.654 g) in water (40 mL). The mixture was warmed to 60 °C and maintained at this temperature with stirring for 15 min. The AgCl was removed while hot and then a solution of $\text{Na}_2\text{IMP} \cdot 3\text{H}_2\text{O}$ dissolved in the minimum volume of water was added to the still warm

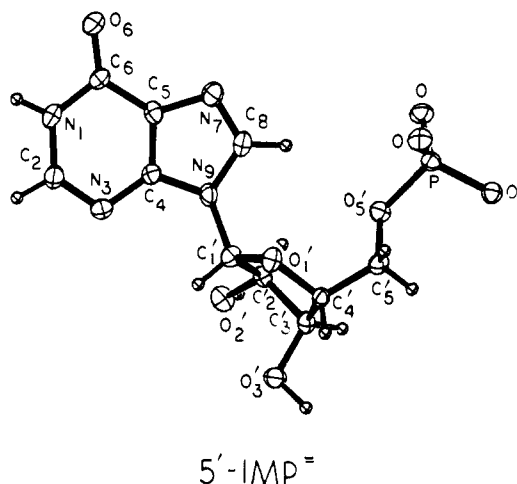


Figure 1. Stereochemistry and atomic numbering in the 5'-IMP dianion.

solution. This solution was filtered (pH 6.9) and set aside for slow evaporation at ambient temperature. After 7 days, elongated prisms were collected, washed with a small volume of ice-cold water, and air dried.

Preliminary oscillation and Weissenberg photographs showed that the crystals had cell data consistent with those reported earlier.² A well-formed crystal with the following faces and mean dimensions was chosen for a complete diffractometer study: (001)-(00 $\bar{1}$) 0.10 mm, (010)-(0 $\bar{1}$ 0) 0.10 mm, (T00)-(100) 0.40 mm. Unit-cell dimensions and their associated standard deviations were derived from a least-squares fit to the setting angles of 15 three-dimensional reflections measured on a Syntex P-1 automated diffractometer. Standard crystallographic data are as follows: $a = 8.767$ (3) Å, $b = 22.935$ (6) Å, $c = 22.410$ (6) Å, $V = 4506.0$ Å³, crystal system orthorhombic, space group $C222_1$, $Z = 4$, $d_{\text{measd}} = 1.815$ (6) g cm⁻³. Only the c axis differs significantly from the cell constants reported in ref 1 ($c = 22.436$ Å).

The 7574 reflections in the $hkl-h\bar{k}\bar{l}$ quadrant (including standards and systematic absences) to $2\theta = 60^\circ$ were surveyed on the diffractometer, employing graphite-monochromatized Mo $K\alpha$ radiation. The intensity measurements were made in the θ - 2θ scan mode; individual scan speeds, 2-24° min⁻¹, were determined by a rapid scan at the calculated Bragg peak. Three standards were monitored after every 100 reflections and their intensities showed no systematic variation over the course of the experiment. The 7574 measured intensities were symmetry averaged and reduced to a set of 3660 independent values; of these, 3313 had $I_{\text{av}} > 0.5\sigma(I)_{\text{av}}$ and were used for the structural refinement. Observational variances were based on the following

equation: $\sigma^2(I) = S + (B_1 + B_2)(T_S/2T_B)^2 + (pI)^2$, where S , B_1 , and B_2 are the scan and extremum background counts, T_S and T_B are the scan and individual background counting times ($T_B = T_S/4$), and p was taken to be 0.04 and represents the expected error proportional to the diffracted intensity.¹² The intensities and their standard deviations were corrected for Lorentz and polarization effects and the effects of absorption ($\mu = 35$ cm⁻¹; maximum and minimum transmission factors, on I , of 0.73 and 0.63, respectively). The squared structure factors were placed on an approximate absolute scale by the method of Wilson.¹³

A structure factor-Fourier calculation based on the atomic positional parameters for the 5'-IMP ligand and the Pt atom in the isomorphous In complex¹¹ gave an R value ($\sum ||F_o| - |F_c|| / \sum |F_o|$) of 0.21 based on the 1334 reflections with $\sin(\theta)/\lambda$ less than 0.5. The calculated Fourier map allowed the positioning of the ammonia ligand, the Na^+ ion, and three waters of crystallization. A second structure factor-Fourier calculation revealed four additional waters of crystallization in general positions and one water lying on a special site (on the 2_a axis with multiplicity 0.5). Thus, at this stage, we had located all of the nonhydrogen atoms of the complex and deduced the location of 7.5 water molecules per asymmetric unit.

Refinement of this model, based on the full data set and anisotropic thermal parameters for all atoms except two waters of crystallization and minimizing the quantity $\sum w(|F_o| - |F_c|)^2$ where $w = 4F_o^2 / \sigma(F_o^2)$, reduced the R value to 0.09. A difference-Fourier synthesis allowed the positioning of all of the hydrogen atoms associated with the 5'-IMP ligand and those associated with four of the water molecules. The hydrogen atoms on the ammonia ligand gave evidence of free rotation about the Pt-N vector, and we also could not locate the hydrogen atoms associated with four of the waters of solvation.

Continued refinement, now allowing the occupancy of the Pt atom to vary, reduced the R value rather dramatically to about 0.06. The thermal parameters of the Pt atom decreased slightly (~5%). The resulting occupancy of the Pt was 86.4%. The ammonia ligand was constrained to assume the same occupancy factor as the Pt atom. A second difference-Fourier map was now computed. Except for a peak at 0.85 e/Å³ near the Pt atom, the map was essentially featureless with maximum + and - peaks of 0.8 and 0.4 e/Å³, respectively. The reduction in the Pt occupancy requires charge compensation to yield a neutral formulation for the crystal. We do not find, as was deduced in the In complex,¹¹ evidence for a second Na^+ site. We assume (see below) that the 5'-IMP ligand is protonated in about 14% of the unit cells to provide charge neutrality. The measured density seems to suggest that there should be one more water of hydration. Our analysis does not allow us to definitely locate this water molecule.

In the final cycle of refinement, there were some shift/errors slightly larger than 1 [for the ammonia nitrogen atom N(10) and four of the oxygen atoms of the solvent waters [W(1,5,6,10)]]. Some of these parameters were oscillatory, and we decided to terminate the refinement. The final R , weighted R [$(\sum w(|F_o| - |F_c|)^2 / \sum w|F_o|^2)^{1/2}$], and goodness of fit [$(\sum w(|F_o| - |F_c|)^2 / (\text{NO} - \text{NV}))^{1/2}$],^{1,2} where NO

Table I. Final Nonhydrogen Atom Positional Parameters^a

atom	x	y	z	atom	x	y	z
Pt ^c	1/2	15025 (2) ^b	1/4	C(4)	2384 (8)	3033 (3)	2490 (6)
Na	1438 (6)	4617 (2)	652 (2)	C(5)	3267 (9)	2627 (3)	2797 (3)
P	1114 (2)	1239 (1)	204 (1)	C(6)	3838 (9)	2764 (4)	3370 (3)
O(1')	-160 (8)	2669 (2)	1343 (2)	C(8)	2558 (11)	2228 (3)	1963 (4)
O(2')	2791 (7)	3685 (3)	997 (3)	C(1')	1038 (9)	3056 (3)	1499 (3)
O(3')	-61 (10)	3773 (2)	568 (2)	C(2')	1922 (10)	3169 (3)	932 (3)
O(5')	1033 (7)	1909 (2)	421 (3)	C(3')	572 (9)	3207 (4)	488 (4)
O(6)	4558 (7)	2447 (3)	3717 (3)	C(4')	-480 (8)	2746 (3)	715 (3)
O(7)	484 (6)	1213 (2)	-426 (2)	C(5')	-470 (9)	2160 (4)	405 (4)
O(8)	2795 (6)	1095 (2)	235 (3)	W(1)	787 (13)	1/2	1/2
O(9)	167 (10)	894 (2)	629 (2)	W(2)	2782 (9)	592 (3)	4613 (4)
N(1)	3484 (8)	3346 (3)	3529 (3)	W(3)	5046 (14)	1264 (3)	1032 (3)
N(3)	2030 (8)	3595 (3)	2676 (3)	W(4)	439 (30)	1308 (7)	3220 (5)
N(7)	3363 (8)	2130 (2)	2447 (5)	W(5)	4087 (24)	4817 (3)	3981 (5)
N(9)	1937 (8)	2773 (3)	1976 (3)	W(6)	1601 (41)	4672 (6)	1916 (10)
N(10) ^c	3322 (13)	892 (3)	2505 (9)	W(7)	4189 (27)	4757 (10)	2079 (10)
C(2)	2624 (10)	3713 (4)	3196 (4)	W(10)	4163 (23)	62 (9)	1405 (9)

^a Parameters $\times 10^5$ for the Pt atom; parameters $\times 10^4$ for the remaining atoms. ^b Values in parentheses here and in succeeding tables are estimated standard deviations in the least significant figure. ^c The occupancy of Pt is 0.432; the occupancy of N(10) is 0.860.

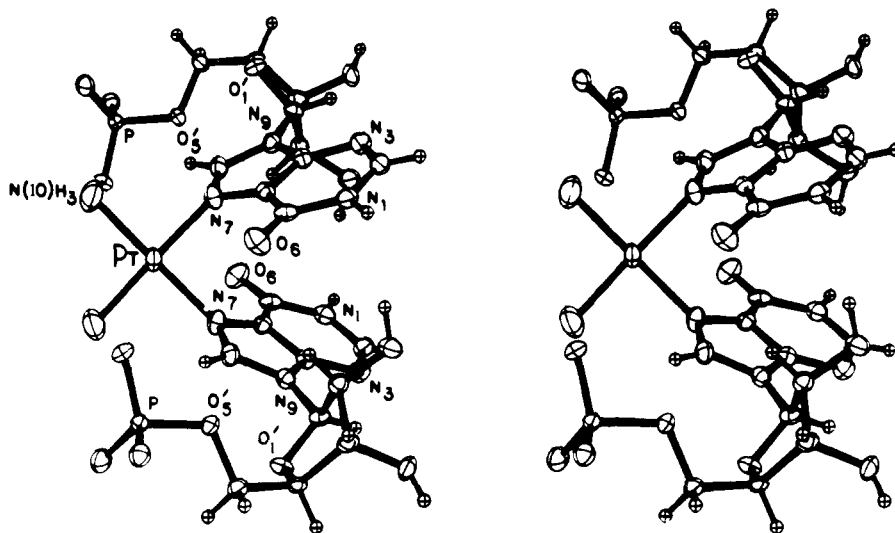


Figure 2. A stereoview of the molecular conformation of the *cis*-[(NH₃)₂Pt(5'-IMP)₂]²⁻ complex anion.

= 3313 parameters and NV = 290 variables] were 0.061, 0.056, and 1.7, respectively.

Neutral scattering factors for the hydrogen¹⁴ and nonhydrogen¹⁵ atoms were taken from recent sources. Anomalous dispersion corrections ($\Delta f'$ and $\Delta f''$) were applied to the scattering factors for all of the nonhydrogen atoms.¹⁶ In all of the calculations, we have assumed that the absolute configuration of the crystal was such that the sugar moiety had the absolute configuration D.

Final nonhydrogen atoms positional parameters are given in Table I. The anisotropic thermal parameters for the nonhydrogen atoms, complete hydrogen atom parameters, and a list of calculated and observed structure factor amplitudes are available.¹⁷ The crystallographic calculations were performed with a standard set of programs.¹⁸

Discussion

Description of the Molecular Structure of the *cis*-[(NH₃)₂Pt(5'-IMP)₂]²⁻ Dianion. The molecular conformation of the *cis*-[(NH₃)₂Pt(5'-IMP)₂]²⁻ complex anion is presented in the stereoview of Figure 2. The Pt atom occupies a special position on the crystallographic twofold axis along the *b* axis of the crystal. The primary coordination about the Pt atom is approximately square planar (Table II and Figure 2), although there is a measurable distortion toward a tetrahedral environment (Table III). The Pt-N(7) distance at 2.036 (8) Å is typical of those found in other Pt-purine complexes¹⁹ and the Pt-N(10) (ammine) bond at 2.032 (13) Å is also typical. The Pt atom is markedly out of the plane of the hypoxanthine base (0.659 (8) Å) as was found in Skapski's diamine complex (0.59 Å).²

The structure presented here, like the other nonstoichiometric Pt(II) complexes with 5'-IMP^{9,11} and the earlier report on this system,² bears a strong resemblance to the structures of the monosodium⁵ and the disodium⁶ salts of 5'-IMP. In fact, we believe that the most correct formulation of the crystal is as follows: [Na₂(5'-IMP)₂·16H₂O]_{0.14}[Na₂((NH₃)₂Pt(5'-IMP)₂)·15-16H₂O]_{0.86}, where 5'-IMP^H = the protonated monoanion of 5'-IMP. In the structure of the monosodium salt of 5'-IMP, a water molecule lies on the crystallographic twofold axis along *b* and links, via hydrogen bonds of the type OH₂···N(7), two symmetry-related 5'-IMP anions. In our data crystal, we find that 86% of the time this water molecule is replaced by the diammineplatinum(II) moiety, which then links the two symmetry-related 5'-IMP anions via *cis* Pt-N(7) coordination bonds (Figure 2). In the Pt occupied unit cells, there are adjustments in the positioning of the 5'-IMP ligands in response to the formation of the Pt-N(7) bonds (Figure 3).

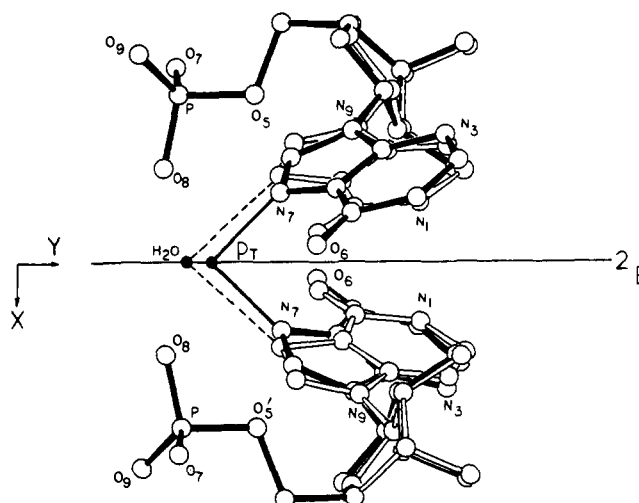


Figure 3. A comparison between the positioning of the 5'-IMP ligands in the monosodium salt of 5'-IMP, unshaded bonds, and the nonstoichiometric diammineplatinum(II) complex of 5'-IMP.

An interesting aspect of the rearrangement of the 5'-IMP ligands is that most of the adjustment takes place in the hypoxanthine ring of the 5'-IMP, with the phosphate and ribose moieties remaining relatively fixed when compared to the positions of these fragments in the monosodium salt (Figure 3). The hypoxanthine ring is rotated approximately along the N(9)-C(6) vector such that the N(7) atoms lie closer to the twofold axis than in the monosodium salt (Figure 3). The relative rigidity of the phosphate and sugar moieties is a direct result of the Na⁺ counterion and its interactions, as will be discussed below.

Our formulation here differs from that we propose for the nonstoichiometric complex¹¹ ([Na₄(5'-IMP)₂·15H₂O]_{0.2}[Na₂(Pt(5'-IMP)₂(trimethylenediamine))·13.5H₂O]_{0.8}), where we believe that the charge balance required by the less than full occupancy of the Pt(II) sites is attained by additional Na⁺ sites. Here, we propose, owing to the absence in the X-ray analysis of any other possible Na⁺ site, that the 5'-IMP ligand is protonated in 15% of the unit cells. In fact, two of the P-O oxygen bonds not involved in the phosphoester linkage are measurably longer [P-O(7) and P-O(8) = 1.518 (6) and 1.512 (6) Å vs. P-O(9) = 1.491 (7) Å] than the third. Sundaralingam⁵ has proposed that it is the phosphate oxygen atom O(8) (we have retained wherever possible the nomenclature and

Table II. Final Nonhydrogen Atom Interatomic Distances (Å) and Angles (deg)

A. Primary Coordination Sphere about the Platinum Atom			
Bond Lengths			
Pt-N(7)	2.036 (8)	Pt-N(10)	2.032 (13)
Bond Angles			
N(7)-Pt-N(10)	88.7 (4)	N(7)-Pt-N(7) ^a	90.0 (4)
N(7)-Pt-N(10) ^a	176.0 (4)	N(10)-Pt-N(10) ^a	92.9 (5)
B. Inosine 5'-Phosphate Ligand			
Bond Lengths			
P-O(5')	1.615 (6)	N(3)-C(2)	1.306 (11)
P-O(7)	1.518 (6)	N(3)-C(4)	1.390 (11)
P-O(8)	1.512 (6)	N(7)-C(5)	1.385 (11)
P-O(9)	1.491 (7)	N(7)-C(8)	1.313 (12)
O(5')-C(5')	1.437 (10)	N(9)-C(1')	1.478 (10)
O(1')-C(1')	1.419 (10)	N(9)-C(4)	1.354 (11)
O(1')-C(4')	1.447 (9)	N(9)-C(8)	1.364 (11)
O(2')-C(2')	1.415 (10)	C(1')-C(2')	1.511 (11)
O(3')-C(3')	1.422 (10)	C(2')-C(3')	1.549 (11)
O(6)-C(6)	1.237 (10)	C(3')-C(4')	1.493 (11)
N(1)-C(2)	1.354 (11)	C(4')-C(5')	1.515 (11)
N(1)-C(6)	1.415 (11)	C(4)-C(5)	1.393 (12)
		C(5)-C(6)	1.415 (11)
Bond Angles			
O(5')-P-O(7)	107.5 (3)	O(2')-C(2')-C(1')	109.5 (6)
O(5')-P-O(8)	103.7 (3)	O(2')-C(2')-C(3')	115.5 (6)
O(5')-P-O(9)	106.8 (3)	C(1')-C(2')-C(3')	99.1 (6)
O(7)-P-O(8)	112.9 (3)	O(3')-C(3')-C(2')	105.6 (6)
O(7)-P-O(9)	111.8 (3)	O(3')-C(3')-C(4')	111.2 (7)
O(8)-P-O(9)	113.5 (4)	C(2')-C(3')-C(4')	102.3 (6)
P-O(5')-C(5')	114.4 (5)	O(1')-C(4')-C(3')	107.4 (6)
C(1')-O(1')-C(4')	107.8 (6)	O(1')-C(4')-C(5')	109.6 (6)
C(2)-N(1)-C(6)	124.8 (7)	C(3')-C(4')-C(5')	118.0 (6)
C(2)-N(3)-C(4)	111.7 (7)	O(5')-C(5')-C(4')	110.4 (6)
C(5)-N(7)-C(8)	107.1 (8)	N(1)-C(2)-N(3)	125.9 (8)
Pt-N(7)-C(5)	126.3 (6)	N(3)-C(4)-N(9)	126.7 (8)
Pt-N(7)-C(8)	123.2 (7)	N(3)-C(4)-C(5)	126.7 (6)
C(1')-N(9)-C(4)	125.2 (7)	N(9)-C(4)-C(5)	106.6 (7)
C(1')-N(9)-C(8)	126.8 (7)	N(7)-C(5)-C(4)	107.8 (7)
C(4)-N(9)-C(8)	107.8 (7)	N(7)-C(5)-C(6)	132.4 (8)
O(1')-C(1')-N(9)	107.4 (6)	C(4)-C(5)-C(6)	112.0 (7)
O(1')-C(1')-C(2')	106.3 (6)	O(6)-C(6)-N(1)	120.6 (8)
N(9)-C(1')-C(2')	114.3 (6)	O(6)-C(6)-C(5)	128.3 (8)
N(7)-C(8)-N(9)	110.7 (8)	N(1)-C(6)-C(5)	111.1 (7)
C. Coordination about the Sodium Atom			
Bond Lengths			
Na-O(2')	2.564 (8)	Na-W(2) ^d	2.474 (9)
Na-O(3')	2.347 (8)	Na-W(6)	2.839 (23)
Na-W(1) ^b	2.591 (10)	Na-W(10) ^c	2.805 (21)
Na-W(2) ^c	2.413 (9)		
Bond Angles			
O(2')-Na-O(3')	66.2 (4)	W(1) ^b -Na-W(2) ^c	76.1 (4)
O(2')-Na-W(1) ^b	143.2 (4)	W(1) ^b -Na-W(2) ^d	75.1 (4)
O(2')-Na-W(2) ^c	135.7 (4)	W(1) ^b -Na-W(6)	125.8 (7)
O(2')-Na-W(2) ^d	89.7 (4)	W(1) ^b -Na-W(10) ^e	71.4 (6)
O(2')-Na-W(6)	73.3 (7)	W(2) ^c -Na-W(2) ^d	82.5 (4)
O(2')-Na-W(10) ^e	116.8 (6)	W(2) ^c -Na-W(6)	10.0 (7)
O(3')-Na-W(1) ^b	79.2 (4)	W(2) ^c -Na-W(10) ^e	90.7 (6)
O(3')-Na-W(2) ^c	154.6 (4)	W(2) ^d -Na-W(6)	159.0 (7)
O(3')-Na-W(2) ^d	85.4 (4)	W(2) ^d -Na-W(10) ^e	146.5 (6)
O(3')-Na-W(6)	98.3 (7)	W(6)-Na-W(10) ^e	54.4 (8)
O(3')-Na-W(10) ^e	87.2 (6)		

^a $1 - x, y, 1/2 - z$. ^b $-x, 1 - y, -1/2 + z$. ^c $1/2 - x, 1/2 + y, 1/2 - z$. ^d $1/2 - x, 1/2 - y, -1/2 + z$. ^e $1/2 + x, 1/2 + y, z$.

numbering in the X-ray analysis of the monosodium salt⁵) which is protonated in the monosodium salt. Thus, the proposition that the data crystal is a mixture of the structure of the monosodium salt and the diammineplatinum(II) complex is consistent if not directly proven by our data and analysis.

Table III. Least-Squares Planes and the Deviations of Individual Atoms from These Planes^a

A. Equatorial Plane about the Pt Atom (0.0365X - 0.0Y - 0.9993Z = -5.4388 Å)			
Pt	-0.000	N(10)	-0.065
N(7)	0.066	N(10) ^b	0.065
N(7) ^b	-0.066		
B. 5'-IMP Ligand Planes			
1. Nine-Atom Framework (0.8262X + 0.3480Y - 0.4430Z = 1.6790 Å)			
N(1)	0.012	N(7)	0.028
C(2)	0.012	C(8)	0.003
N(3)	0.004	N(9)	-0.024
C(4)	-0.003	O(6)	-0.115*
C(5)	0.007	C(1')	0.024*
C(6)	-0.039	Pt	0.659*
2. Imidazole Ring (0.8156X + 0.3608Y - 0.4524Z = 1.6822 Å)			
C(4)	0.008	C(8)	0.001
C(5)	-0.008	N(9)	-0.006
N(7)	0.004		
3. Pyrimidine Ring (0.8308X + 0.3395Y - 0.4410Z = 1.6416 Å)			
N(1)	0.014	C(4)	-0.004
C(2)	0.003	C(5)	0.020
N(3)	-0.008	C(6)	-0.024
C. Best Mean Plane of the Ribose Moiety (0.6744X - 0.7025Y - 0.2272Z = -5.0754 Å)			
C(1')	0.002	C(4')	0.003
O(1')	-0.003	C(2')	0.631*
C(3')	-0.002	C(5')	1.111*

^a In each of the equations of the planes, X, Y, and Z are coordinates (Å) referred to the orthogonal axes a, b, and c. Atoms indicated by an asterisk were given zero weight in calculating the planes; other atoms were equally weighted. ^b Transformed by $-x, -y, 1/2 - z$.

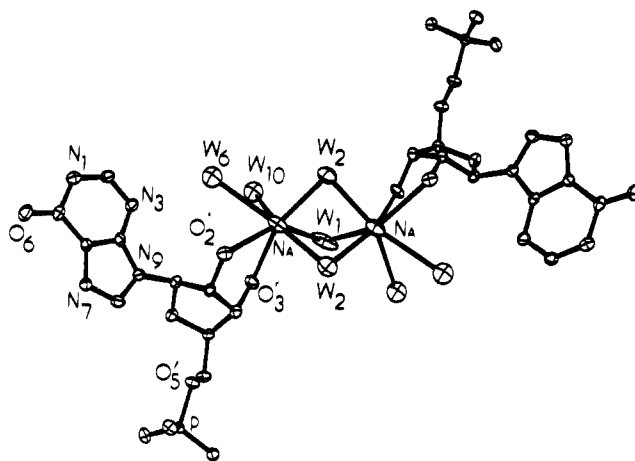


Figure 4. The Na⁺ ion coordination polyhedra. Note in particular the coupling of the sodium coordination shells and the strong binding of the hydroxyl oxygen atoms of the sugar moiety to the Na⁺ ion.

Given the nonstoichiometry of the crystal, all of the parameters we report here concerning the 5'-IMP ligand are a weighted average of those in the monosodium salt (14%) and the diammineplatinum(II) complex (86%). We have previously argued¹¹ that the important structural parameters in the nonstoichiometric (en)Pt^{II}⁹ and (tn)Pt^{II}¹¹ complexes fall approximately on the simple straight line drawn between the parameters in the monosodium salt and those reported for the supposed nonstoichiometric (NH₃)₂Pt^{II} compound.² The analysis¹¹ predicts for an 86% Pt complex that the observed N(7)···N(7) distance and purine-purine dihedral angle between twofold related 5'-IMP ligands should be 2.88 Å and 41°, respectively. Our experimentally measured values are 2.88 (1) Å and 40.7 (6)°. Relevant parameters for the monosodium

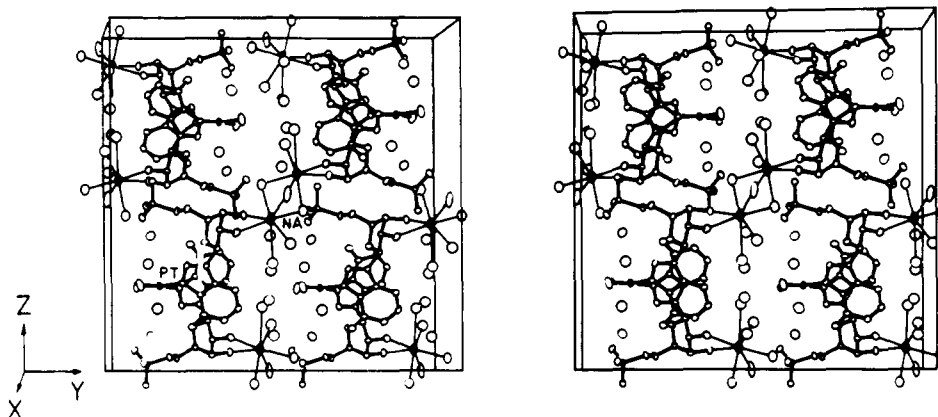


Figure 5. A stereoview of the crystal packing along the *a* axis. The Pt and Na⁺ sites have been shaded for emphasis.

Table IV. A Comparison of the Structural Parameters in the Monosodium Salt and Several Pt(II) Complexes of 5'-IMP

compd	M-N(7), Å	N(7)...N(7), Å	dihedral angle, deg	% Pt	ref
Na[5'-IMPH]		3.48 (2)	22	0	5
[(en)Pt(5'-IMP) ₂] ²⁻	2.07 (2)	3.26	31	38	9
[(tn)Pt(5'-IMP) ₂] ²⁻	2.08 (1)	2.96 (2)	38 (1)	~76	11
[(NH ₃) ₂ Pt(5'-IMP) ₂] ²⁻	2.036 (8)	2.88 (1)	40.7 (5)	~86	this work
[(NH ₃) ₂ Pt(5'-IMP) ₂] ²⁻	2.02	2.83	43	100 ^a	2

^a Originally reported to be ~56% (ref 2).

salt and the other Pt complexes are presented in Table IV. The excellent agreement between the values predicted by our simple analysis of these systems and those we have obtained experimentally allow two important points: (1) our very simple and straightforward analysis is probably correct, and (2) the parameters in the diammineplatinum(II) complex of Skapski and Goodgame² very probably correspond to a *stoichiometric* complex as we have suggested elsewhere.¹¹

Other conformational parameters of some importance are the nearly planar purine ring (presumably dominated by the Pt site) and the common C(2') endo pucker and anti orientation of the ribosyl moiety. The C(8)-N(9)-C(1')-O(1') torsion angle changes from 41° in the monosodium salt to 53° in this (diammine)platinum complex of IMP. The conformation about the C(4')-C(5') bond is *gauche-gauche*.

Sodium Coordination and Solvent Structure. We believe that a fundamentally important aspect in this and other structures in this series is the presence of the Na⁺ counterion and its interactions in the crystal, particularly with the 5'-IMP ligand. Individually, the Na⁺ ions are seven coordinate (Table II and Figure 4). Five of the Na⁺ coordination bonds are strong with Na⁺-O distance lying between 2.3 and 2.6 Å, and two weaker interactions have bond lengths of about 2.8 Å. In addition, the sodium sites are triply coupled about the twofold crystallographic axis parallel to the *a* axis via three Na⁺-H₂O-Na⁺ bond systems (Figure 4). The three bridging water molecules are the two symmetry-related W(2) sites and the W(1) which lies on the twofold axis parallel to *a*. This coupling of the Na⁺ coordination polyhedra plays an essential role in the crystal packing (Figures 4 and 5). In particular, the ribose hydroxyl oxygen atoms O(2') and O(3') are strongly bonded to the Na⁺ ion; very likely this strong coupling of the ribose group to the Na⁺ ion prevents this portion of the molecule from responding to the effects of the formation of the Pt-N(7) linkages (see above).

The phosphate group is also tightly bound owing to a variety of intermolecular hydrogen bonds (Table V). In addition to coordination to the Na⁺ ion, each of the two ribose hydroxyl oxygens donates a hydrogen bond to a phosphate oxygen on two symmetry-related molecules. Two other hydrogen bonds

Table V. Probable Hydrogen-Bonding Scheme

A. Probable Hydrogen Bonds					
D	H	A	D...A, Å	H...A, Å	∠D-H...A, deg
N(1)	H(1)	O(7) ^a	2.71 (1)	1.76	176
O(2')	H(O2')	O(7) ^b	2.70 (1)	1.75	154
O(3')	H(O3')	O(8) ^c	2.62 (1)	1.88	152
W(2)	H(W21)	O(9) ^d	2.73 (1)	1.82	151
W(3)	H(W31)	O(8) ^e	2.69 (1)	1.74	162
W(3)	H(W32)	O(6) ^f	2.79 (1)	1.77	161
W(5)	H(W51)	O(7) ^a	2.74 (1)	1.77	156
W(5)	H(W52)	O(9) ^g	2.70 (1)	1.81	149
W(4)	H(W41)	O(9) ^d	2.80 (1)	1.69	168
B. Possible Hydrogen Bonds					
D	A	D...A			
W(1)	O(8) ^a	2.85 (1)			
W(1)	O(8) ^g	2.85 (1)			
W(2)	W(3) ^f	2.84 (2)			
W(6)	N(3) ^e	2.91 (1)			
W(6)	W(10) ^h	2.59 (3)			

^a $1/2 - x, 1/2 - y, 1/2 + z$. ^b $1/2 + x, 1/2 - y, -z$. ^c $-1/2 + x, 1/2 - y, -z$. ^d $-x, y, 1/2 - z$. ^e x, y, z . ^f $1 - x, y, 1/2 - z$. ^g $1/2 - x, 1/2 + y, 1/2 - z$. ^h $-1/2 + x, 1/2 + y, z$.

of the type Na⁺-O...O (phosphate) involving water molecules W(1) and W(2) were also observed. These hydrogen-bond interactions, along with the influence of the Na⁺ coordination, firmly fix that portion of the 5'-IMP molecule other than the hypoxanthine ring. Two more noteworthy hydrogen bonds are N(1)-H...O(7) and W(6)-H...N(3). The first one represents a base-phosphate interaction whereas the latter is of the type Na-water...base.

In summary, as we have postulated previously,^{10,11} there appears to be an interesting and fundamentally important interplay between the effects of the Pt coordination and crystal packing forces in the nonstoichiometric Pt(II) complexes of 5'-IMP. In fact, the diammine complex studied by Skapski and Goodgame,² which we postulate is stoichiometric, has molecular parameters strikingly different than those for the bis-

(guanosine) complexes of Bau⁷ and Cramer,⁸ suggesting again that the influence of the crystal packing forces prevails *even* at stoichiometry.

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Supplementary Material Available: Listing of hydrogen atom parameters and structural factor amplitudes (23 pages). Ordering information is given on any current masthead page.

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Structural Factors in the Facile Carbomagnesiation of Isolated Carbon-Carbon Double Bonds¹

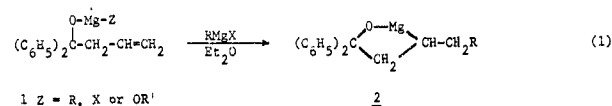
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Abstract: The structural features in the carbinol and the Grignard reagent, the role of alternative coordination sites on the olefin, the effect of varying the donor solvent, and the role of transition metal catalysts were investigated for the carbomagnesiation of a series of 1,1-diphenyl-*n*-alken-1-ols, where *n* = 0, 1, 2, and 4. Allyl-, benzyl- and *tert*-butylmagnesium bromides in ethyl ether and diallylmagnesium in benzene were shown to add to such carbinols to yield either the corresponding carbinol or olefin in which the R group of the magnesium reagent was attached principally to the ω carbon or the original carbinol. In some reactions, and especially with 1-methoxy-1,1-diphenyl-3-butene, positional isomers of the resulting olefin indicated the occurrence of concurrent carbinol-ion rearrangements. The carbometalation is markedly promoted by transition metal catalysis, especially that by nickel. Strong donor solvents, such as tetrahydrofuran and amine coordination sites on the olefin substrate, caused a pronounced retardation of the carbomagnesiation. In light of these observations and other studies of the stereochemical course of reaction, a mechanism for the uncatalyzed carbomagnesiation is proposed involving the intramolecular rearrangement of an alkenoxy(alkyl)magnesium (**27**). In such a complex the incompletely coordinated magnesium is envisaged as initiating an electrophilic attack on the proximate olefinic π bond. Infrared and NMR spectroscopic studies of alkenols are drawn upon to support these views. The fostering action of nickel salts on such carbometalations is ascribed to the reactivity of π -allylnickel intermediates.

The tendency to add to, or to effect substitution at, a wide variety of functional groups has permitted Grignard reagents to exert a pervasive influence on organic synthesis. However, although diverse polar, unsaturated bonds, such as carbonyl, azomethine, cyano, and thiocarbonyl groups, do add such reagents readily, olefinic and acetylenic linkages have generally been found to be unreactive.³ The one established exception has been an olefinic group, either conjugated with a carbonyl or similar group, or forming the exocyclic ethylenic unit of a fulvene,⁴ where, by using copper catalysis⁵ or by resorting to more reactive Grignard reagents (allylic or *tert*-alkyl), smooth addition can be achieved. However, in 1965 we observed another structural feature that facilitated the addition of Grignard reagents to carbon-carbon unsaturation, namely the presence of a neighboring hydroxyl group.⁶ Thus, alkenols in the form of their magnesium salts were found to undergo ready addition of the carbon-magnesium bond to their olefinic

linkage (carbomagnesiation) in refluxing ether, when allylic or *tert*-alkyl Grignard reagents were employed⁷ (eq 1).



This anchimeric assistance for carbomagnesiation has aroused considerable interest as to its scope and its mechanistic path. Subsequent studies in our laboratory and elsewhere have shown that this reaction can be realized with alkenols,⁶⁻⁸ alkenols,^{7,8} alkenyldialkylamines,⁹ alkenylalkyl ethers,⁷ and vinylic pyridines.¹⁰ Similar, anchimerically assisted additions of organolithium^{9,11} and -zinc¹² reagents have also been uncovered. These developments seem also to have prompted a renewed study of the carbomagnesiation of simple olefins under forcing conditions. By use of pressures of 30-70 atm and