and fumaric acids have been used in the current studies.

The question of why the enzyme chooses to use a cluster instead of a simple metal ion coordinated to the protein needs to be addressed. A tempting explanation for the need of the cluster lies in its redox characteristic and the possibility of controlling the enzyme through the oxidation states of the cluster and their properties. The Beinert et al. studies show that oxidation of the $[Fe_4S_4]^{2+}$ cluster in the presence of substrate leads to a $[Fe_3S_4]$ cluster and inactivation of the enzyme. However, this cluster can be reduced again with reincorporation of the Fe^{2+} ion and reactivation of the enzyme. In this way, the enzyme might be turned on and off. The use of the redox property to induce a conformational change in the enzyme and thereby trigger the hydration has also been proposed.[44]

Finally, regardless of whether the chemistry described mimics the biology or not in the final analysis, it is clearly an effective way to hydrate alkene centers of this type, and the $[(tn)_2Co(OH)(OH_2)]^{2+}$ ion used could be an effective reagent for this purpose. There are indications that the metal ion exerts substantial constraints on the organic chemistry other than those effects attributed to propinquity and a substitute for a proton. Such effects are probably more common than we have realized and act in both inhibitory and enhancement roles. They clearly need further investigation.

Acknowledgment. We are grateful to Dr. Karl Hagen for stimulating discussions and for the suggestion concerning the use of a displaced thiol, to the Microanalytical Unit of the Australian National University, and the NMR Service at the Research School of Chemistry, Australian National University.

Note Added in Proof. Sir John Cornforth has suggested an alternative explanation for the rate-determining protonation in the cyclization of the maleato and fumarato esters—namely, that general acid catalyzed rearrangement of the enol to the ester would be an equally good if not better description of the process rather than protonation of a "carbanion". The delocalization of the carbanion is alluded to in the discussion but the consequences are not spelled out. A common intermediate for the maleato and fumarato cyclizations could arise and the difference in the rate of cyclization would then come largely from the equilibrium constant for the formation of the enol intermediate from the two isomers.

(44) Ramsay, R. R.; Dreyer, J.-L.; Schloss, J. V.; Jackson, R. H.; Coles, C. J.; Beinert, H.; Cleland, W. W.; Singer, T. P. *Biochemistry* **1981**, *20*, 7476-7482.

Registry No. *cis*-$[Co(en)_2(methylmaleato)_2]ClO_4$, 97430-94-9; *cis*-$[Co(en)_2(ethylfumarato)(Me_2SO)](ClO_4)_2$, 97430-96-1; *trans*-$[Co(en)_2(ethylfumarato)_2]ClO_4$, 97430-98-3; *trans*-$[Co(tn)_2(ethylfumarato)_2]ClO_4$, 97431-00-0; *cis*-$[Co(en)_2(tert\text{-}butylmaleato)_2]ClO_4$, 97431-02-2; $[Co(en)_2(methylmalato)](ClO_4)_2$, 97431-04-4; $[Co(en)_2(methylmalato)]Br_2$, 97431-05-5; $[Co(en)_2(methylmalato)]Br_2 \cdot 2H_2O$, 97431-06-6; *cis*-$[Co(tn)_2(OH)(OH_2)](ClO_4)_2$, 14099-49-1; *cis*-$[Co(en)_2(Me_2SO)_2](ClO_4)_3$, 14781-36-3; *cis*-$[Co(en)_2(OH)(OH_2)](ClO_4)_2$, 14099-49-1; *trans*-$[Co(tn)_2(OH)(OH_2)](ClO_4)_2$, 61634-20-6; sodium methyl maleate, 27750-22-7; sodium *tert*-butyl maleate, 97431-07-7; sodium ethyl fumarate, 55141-86-1; maleic anhydride, 108-31-6; ethylfumaric acid, 2459-05-4; sodium 3-chloropropenoate, 16987-03-4; sodium 2-chloropropenoate, 16987-02-3; sodium propenoate, 137-40-6; aconitase, 9024-25-3.

Supplementary Material Available: Listing of crystal data, Table I, data collection details, Table II, starting phases generated by MULTAN, Table III, details of the course of refinement, Table IV, least-squares planes, Table VII, intermolecular contacts, Table VIII, perspective view of the unit cell, Figure 5, the derivation of the rate law for the intramolecular cyclization of *cis*-$[Co(en)_2(OH_2)(methylmaleato)]^{2+}$, details of the treatment of the kinetic data, and rate constants for the intramolecular hydration of the $[(en)_2Co(OH_2)(methylmaleato)]^{2+}$ ion, Table IX, thermal parameters, Table XIII, calculated hydrogen atom coordinates, Table XIV, and a listing of structure factor amplitudes, Table XV (28 pages). Ordering information is given on any current masthead page.

X-ray Studies on Metal Ion Interactions with Vitamins. 1. Crystal and Molecular Structure of the Tetrakis(μ-acetato)bis(thiamin monophosphate)dirhodium(II) Sesquihydrate Complex: Thiamin Base–Metal Bonding

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Abstract: The crystal and molecular structure of $[Rh_2(acetato)_4(thiamin\ monophosphate)_2] \cdot 1.5H_2O$ has been determined by X-ray diffraction methods. The thiamin monophosphate ligand, a phosphate ester of vitamin B_1, coordinates to the two axial positions of the dirhodium–tetraacetate cage through the pyrimidine ring nitrogen N(1′). Electronic rather than steric considerations, i.e., a high basicity of N(1′), rationalize the metal bonding at this site. The thiamin moiety of the molecule assumes the frequently observed F conformation with $\phi_T = -3°$ and $\phi_P = -81°$. The C(5) ethyl ester phosphate side chain of the molecule is folded back over the thiazolium ring on the same side as the pyrimidine amino N(4′α). The thiamin monophosphate molecule forms a dimeric structure across a crystallographic center of inversion through the three types of interactions between the thiamin moiety and the phosphate group of its pairing molecule; the phosphate anion interacts bifunctionally with the thiazolium ring via a hydrogen bonding with the acidic C(2)H and an electrostatic interaction with the positively charged S(1) atom, and it further contacts, possibly electrostatically, with the pyrimidine ring. Biological implications of this observation and a possible role of the metal ion in the enzymic processes are briefly discussed in connection with the substrate fixation mechanism. The present structure is only the third X-ray example showing the metal bonding to the thiamin base. Crystallographic details for $[Rh_2(C_2H_3O_2)_4(C_{16}H_{23}N_4O_8PS)_2] \cdot 1.5H_2O$: space group $P\bar{1}$, $a = 14.974$ (9) Å, $b = 10.119$ (4) Å, $c = 8.281$ (3) Å, $\alpha = 96.97$ (3)°, $\beta = 74.38$ (4)°, $\gamma = 99.68$ (4)°, $V = 1187$ (1) Å^3, $Z = 1$. The final discrepancy factors R_F and R_{wF} are 0.058 and 0.067, respectively, for 2448 reflections with $F_o > 3\sigma(F_o)$.

Vitamins are well-known as essential nutrients for animal organisms and play a key role in biology.[1] The physiological role of vitamins is now well established, at least for water-soluble ones, as cofactors for a variety of enzymes. These vitamin-dependent

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enzymes often contain tightly bound metal atoms at the active sites or require metal ions as additional cofactors for their functions. These involve thiamin enzymes,[2] biotin enzymes,[2] flavin enzymes,[3] and pyridine nucleotide enzymes.[2] Despite the importance of metal ions in these enzyme systems, however, the role of metal ions is not well understood, and, in particular, the nature of interactions between vitamins and such metal ions is not clear. We have undertaken X-ray studies on vitamin–metal ion complexes in order to elucidate stereochemical aspects of their interactions, which may provide a basis for the understanding of the role of metal ions in the enzymic processes.

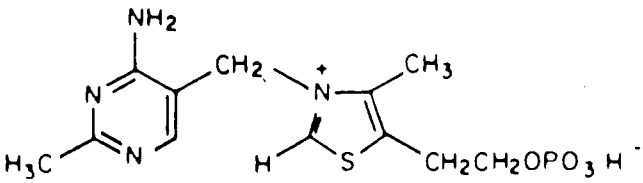
Thiamin (vitamin B_1), as its pyrophosphate ester, is a cofactor for a number of metabolic enzymes catalyzing the decarboxylation of α-keto acids and the transfer of aldehyde or acyl groups.[4] It is now well established that the substrate reacts with the coenzyme thiamin pyrophosphate at the C(2) site of the thiazolium moiety to form a reaction intermediate hydroxyethyl thiamin pyrophosphate.[5] These thiamin enzymes also require divalent metal ions such as Mg(II) or Mn(II) ions for their functions.[2] The metal ion is suggested to be involved in the formation of the enzyme–coenzyme complex.[6,7] Although it is generally believed[8] that the metal ion binds primarily through the pyrophosphate moiety of the coenzyme, there also exist an enzyme study[7] and some NMR data of model reactions in solution suggesting the metal bonding to the thiamin moiety directly[7,9] or indirectly,[8b,c] i.e., via a water ligand through the N(1′) or directly to the N(3′)[10] of the pyrimidine base. To the best of our knowledge, there have been reported eight crystal structures[11-13] of thiamin or its pyrophosphate involving metal ions, the majority of which are salt type, i.e., no direct bonding between them; only the $[Cd(thiamin)Cl_3]$[12a] and $[Cu(thiamin)Cl_2]$[12b] show the metal bonding to the N(1′) and the [Cu(thiamin pyrophosphate)(1,10-phenanthroline)(H_2O)][13] solely to the pyrophosphate moiety.

Earlier,[14] we suggested the rhodium(II) coordination to the thiamin at the N(1′) site in the isolated tetrakis(μ-acetato)dirhodium(II)–thiamin complexes on the basis of the X-ray structure of the thiamin model compound and because of the poor crystallinity of these thiamin complexes. We have now succeeded in the isolation and the structure determination of the analogous rhodium(II) complex of thiamin monophosphate (TMP, **1**), $[Rh_2(AcO)_4(TMP)_2]\cdot 1.5H_2O$ and have unambiguously confirmed this prediction. The metal coordination to the N(1′) site among a variety of possible metal binding sites for thiamin monophosphate ligand is rationalizable from electronic rather than steric considerations. The biological significance of the interaction mode between the anion and the thiamin moiety and the possible role of the metal ion in enzymic processes are emphasized in connection with the substrate fixation mechanism. This is only the third crystallographic investigation of a metal–thiamin derivative complex in which the metal ion is attached to the thiamin base and the first metal complex for thiamin monophosphate. It is also the first structural study of an octahedral thiamin complex.

Table I. Crystal Data and Experimental Details

compd	Rh(acetato)$_2$(thiamin monophosphate)·0.75H_2O
formula	$C_{16}H_{24.5}N_4O_{8.75}PRhS$
fw	578.83
a, Å	14.974 (9)
b, Å	10.119 (4)
c, Å	8.281 (3)
α, deg	96.97 (3)
β, deg	74.38 (4)
γ, deg	99.68 (4)
V, Å^3	1187.3 (1.0)
Z	2
space group	$P\bar{1}$
density, g cm^{-3}	1.619 (calcd); 1.68 (1)[a] (exptl)
cryst shape and dimens	plate with {100}, 0.02 mm; {010}, 0.17 mm; {001}, 0.27 mm
radiatn	Mo Kα (λ = 0.71073 Å) from graphite monochromator
temp, °C	23
μ, cm^{-1}	9.07
transmissn factors	0.96–1.04[b]
receiving aperature	3 × 3 mm, 21 cm from crystal
takeoff angle, deg	5.0
scan speed, deg	2.0 in 2θ/min
scan range, deg	1.3 + 0.5 tan θ
bkgd counting, s	10 at the lower and upper limits of each scan
diffractometer	Rigaku
2θ limits, deg	3.0–50.0
scan mode	ω scan for 2$\theta \leq 30°$ ω–2θ scan for 2$\theta > 30.0°$
unique data measd	4136
unique data used ($F_o > 3\sigma(F_o)$)	2448
final no. of variables	349
error in observation of unit weight	2.39 electrons
R	0.058
R_{wF}	0.067

[a] Measured by flotation in an ethyl iodide/chloroform mixture. [b] Normalized to an average of unity.



Experimental Section

Preparation of [Rh(AcO)$_2$(TMP)]·2H_2O. $[Rh_2(AcO)_4]\cdot 2MeOH$[15] (51 mg, 10^{-1} mmol) dissolved in 15 mL of hot (80 °C) water and 76 mg (2 × 10^{-1} mmol) of thiamin monophosphate chloride (Sigma) in 5 mL of water were mixed to give a green solution (pH about 4). Subsequent adjustment of pH to about 6 with 2 drops of dilute NaOH solution was accompanied by color change to blue-violet.[16] Reddish violet plates formed after 1 day by allowing the solution to stand at room temperature. They were filtered off, washed with a little water, and air-dried (yield

(1) Wagner, A. F.; Folkers, K. "Vitamins and Coeznymes"; Wiley: New York, 1964.
(2) Scrutton, M. C. *Inorg. Biochem.* **1973**, *1*, 381–437.
(3) Hemmerich, P.; Lauterwein, J. *Inorg. Biochem.* **1973**, *2*, 1168–1190.
(4) Krampitz, L. O. *Annu. Rev. Biochem.* **1969**, *38*, 213–240.
(5) Breslow, R. *J. Am. Chem. Soc.* **1958**, *80*, 3719–3726.
(6) Green, D. E.; Herbert, D.; Subrahmanyan, V. *J. Biol. Chem.* **1941**, *138*, 327–339.
(7) Schellenberger, A. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 1024–1035.
(8) (a) Wittorf, J. H.; Gubler, C. J. *Eur. J. Biochem.* **1970**, *14*, 53–60. (b) White, W. D.; Drago, R. S. *Inorg. Chem.* **1971**, *10*, 2727–2735. (c) Gallo, A. A.; Hansen, I. L.; Sable, H. Z.; Swift, T. J. *J. Biol. Chem.* **1972**, *247*, 5913–5920. (d) Grande, H. J.; Houghton, R. L.; Veeger, C. *Eur. J. Biochem.* **1973**, *37*, 563–569. (e) Katz, H. B.; Kustin, K. *Biochim. Biophys. Acta* **1973**, *313*, 235–248. (f) Kluger, R.; Smyth, T. *Can. J. Biochem.* **1978**, *56*, 999–1001.
(9) Hadjiliadis, N.; Markopoulos, J.; Pneumatikakis, G.; Katakis, D.; Theophanides, T. *Inorg. Chim. Acta* **1977**, *25*, 21–31.
(10) (a) Gary, J.; Adeyemo, A. *Inorg. Chim. Acta* **1981**, *55*, 93–98. (b) Adeyemo, A. O. *Ibid.* **1981**, *55*, 177–178.
(11) (a) Clemente, D. A.; Bandoli, G.; Benetollo, F.; Marzotto, A. *J. Cryst. Mol. Struct.* **1974**, *4*, 1–14. (b) Caira, M. R.; Fazakerley, G. V.; Linder, P. W.; Nassimbeni, L. R. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1974**, *B30*, 1660–1666. (c) Richardson, M. F.; Franklin, K.; Thompson, D. M. *J. Am. Chem. Soc.* **1975**, *97*, 3204–3209. (d) Blank, G.; Rodrigues, M.; Pletcher, J.; Sax, M. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1976**, *B32*, 2970–2975. (e) MacLaurin, C. L.; Richardson, M. F. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1983**, *C39*, 854–856.
(12) (a) Cramer, R. E.; Maynard, R. B.; Ibers, J. A. *J. Am. Chem. Soc.* **1981**, *103*, 76–81. (b) Cramer, R. E.; Maynard, R. B.; Evangelista, R. S. *Ibid.* **1984**, *106*, 111–116.
(13) Aoki, K.; Yamazaki, H. *J. Am. Chem. Soc.* **1980**, *102*, 6878–6880.
(14) Aoki, K.; Yamazaki, H. *J. Am. Chem. Soc.* **1984**, *106*, 3691–3692.
(15) Legzdins, P.; Mitchell, R. W.; Rempel, G. L.; Ruddick, J. D.; Wilkinson, G. *J. Chem. Soc. A* **1970**, 3322–3326.
(16) This color change suggests the rhodium bonding to the nitrogen atom(s), most probably N(1′), because it is well-known[17] that the visible spectra of dirhodium tetraacetate adducts are very sensitive to the donor atom and pK_a of the N(1′) is approximately 5.[8c]
(17) Kitchens, J.; Bear, J. L. *J. Inorg. Nucl. Chem.* **1969**, *31*, 2415–2421.

Table II. Final Heavy-Atom Parameters for $[Rh_2(acetato)_4(thiamin\ monophosphate)_2]\cdot 1.5H_2O$[a]

atom	x	y	z	B_{eq} or B, Å^2
Rh	−767 (1)	300 (1)	646 (1)	2.74 (0.04)
O(11)	−317 (5)	971 (8)	2733 (8)	3.5 (0.2)
O(12)	1120 (5)	396 (8)	1556 (8)	3.6 (0.2)
O(13)	−295 (5)	2170 (7)	−231 (9)	3.4 (0.2)
O(14)	1153 (5)	1585 (7)	−1475 (9)	3.5 (0.2)
C(11)	500 (8)	879 (11)	2758 (12)	3.5 (0.3)
C(12)	790 (9)	1418 (14)	4380 (15)	5.0 (0.4)
C(13)	555 (9)	2426 (13)	−1094 (15)	4.6 (0.4)
C(14)	900 (10)	3809 (13)	−1725 (20)	6.1 (0.5)
N(1′)	−2165 (5)	952 (9)	2136 (10)	3.0 (0.2)
C(2′)	−3028 (6)	215 (10)	2402 (12)	2.6 (0.3)
N(3′)	−3758 (6)	438 (8)	3674 (10)	2.8 (0.2)
C(4′)	−3660 (7)	1518 (10)	4786 (11)	2.4 (0.3)
C(5′)	−2804 (7)	2384 (10)	4574 (12)	2.6 (0.3)
C(6′)	−2087 (7)	2034 (10)	3244 (12)	2.8 (0.3)
C(2′α)	−3175 (8)	−956 (11)	1145 (14)	3.8 (0.3)
N(4′α)	−4416 (6)	1702 (9)	6041 (10)	3.4 (0.3)
C(3,5′)	−2634 (7)	3579 (10)	5750 (12)	3.0 (0.3)
S(1)	−3731 (2)	6302 (3)	4174 (4)	3.6 (0.1)
C(2)	−3407 (7)	4784 (10)	4220 (12)	3.0 (0.3)
N(3)	−3013 (5)	4776 (8)	5445 (10)	2.7 (0.2)
C(4)	−2939 (7)	5996 (10)	6452 (12)	2.8 (0.3)
C(5)	−3312 (7)	6935 (11)	5921 (13)	3.1 (0.3)
C(4α)	−2555 (8)	6092 (11)	7975 (14)	3.9 (0.4)
C(5α)	−3394 (8)	8343 (11)	6618 (14)	3.7 (0.3)
C(5β)	−4392 (8)	8507 (12)	7624 (15)	3.9 (0.4)
O(5γ)	−4635 (5)	7717 (8)	9046 (9)	3.8 (0.2)
P(5δ)	−5545 (2)	6632 (3)	9422 (4)	3.4 (0.1)
O(5δ1)	−5308 (5)	5381 (7)	8119 (9)	3.8 (0.2)
O(5δ2)	−5614 (5)	6273 (7)	11193 (8)	3.5 (0.2)
O(5δ3)	−6349 (6)	7124 (8)	9051 (11)	4.8 (0.3)
O(W1)	−178 (1)	344 (2)	−90 (2)	5.5 (0.4)
O(W2)	−249 (3)	154 (4)	−175 (5)	6.2 (0.9)

[a] Positional parameters are multiplied by 10^4 and equivalent temperature factors are of the form $B_{eq} = {}^4/_3\sum\sum\beta_{ij}a_ia_j$ for the heavy atoms except for the water molecules O(W1) and O(W2) for which positional parameters are multiplied by 10^3 and isotropic temperature factors are of the form $T = \exp[-B(\sin\theta/\lambda)^2]$.

67%). Anal. Calcd for $RhC_{16}H_{23}N_4O_8PS$: C, 31.96; H, 4.53; N, 9.32. Found: C, 31.26; H, 4.36; N, 9.23.

Collection and Reduction of the X-ray Intensity Data. Oscillation and Weissenberg photographs indicated that the crystal was the triclinic system with the space group $P1$ or $P\bar{1}$. Cell constants were determined from 15 high-order reflections ($17° < 2\theta$ (Mo Kα) $< 26°$) on a Rigaku automated diffractometer. Details of the crystal parameters along with data collection are summarized in Table I.

The crystal was mounted such that the c axis was nearly parallel to the ϕ axis of the diffractometer. Throughout the data collection the intensities of the three standard reflections were measured every 100 reflections as a check of the stability of the crystal and the instrument; a maximum variation in intensity of <2% was noted, and no decay correction was applied to the data. The diffraction pattern was in general weak and did not extend beyond $2\theta = 40°$, mostly due to the small crystal size and the disordering of the crystallization water molecules. Of a total of 4136 independent intensities measured in the range $2\theta \leq 50°$, 2448 reflections for which $F_o > 3\sigma(F_o)$ were used in the solution and refinement of the structure. Intensities[18] were corrected for Lorentz and polarization effects. The anisotropy of absorption was checked for the axial 002 reflection (near $\chi = 90°$) in 10° sets of ϕ; the crystal showed a variation of less than 3.8% from the mean, and no correction was made for absorption.

Solution and Refinement of the Structure. The structure was solved by Patterson and Fourier methods and refined by the block-diagonal least-squares method.[19] The space group $P\bar{1}$ was confirmed by successful refinement of the structure. The function $\sum w(F_o - |F_c|)^2$ was minimized with the weighting factor w equal to $1/\sigma(F_o)^2$. A total of 29 atoms out of the 31 non-hydrogen atoms were assigned anisotropic thermal parameters, and the two crystallization water molecules, which were disordered,[20] were assigned isotropic ones. At this stage, the discrepancy factors R_F[21] and R_{wF} were 0.063 and 0.071, respectively. A subsequent difference Fourier map revealed 14 out of the 23 hydrogen atoms, which were added in the final refinement with isotropic thermal parameters. The final R_F and R_{wF} and the standard deviation of one observation of unit weight[21] were 0.058, 0.067, and 2.4, respectively, for 2448 reflections (m) and 349 variables (n), from which $m/n = 7.0$. No unusual trend was observed in an analysis of $\sum w(F_o - |F_c|)^2$ as a function of either $(\sin\theta)/\lambda$ or F_o. A final difference Fourier map showed no other features with an absolute value of greater than 0.7 e Å^{-3} near the rhodium position.

Neutral atomic scattering factors[22] were used with Rh, S, and P corrected for anomalous dispersion.[22] The final atomic parameters for the non-hydrogen atoms with the equivalent isotropic temperature factors are listed in Table II. The anisotropic temperature factors for the non-hydrogen atoms and the atomic parameters for the hydrogen atoms are available in Tables D1[23] and D2,[23] respectively. Bond distances and angles involving the hydrogen atoms are given in Table D3.[23] A list of final calculated and observed structure amplitudes is collected in Table D4.[23]

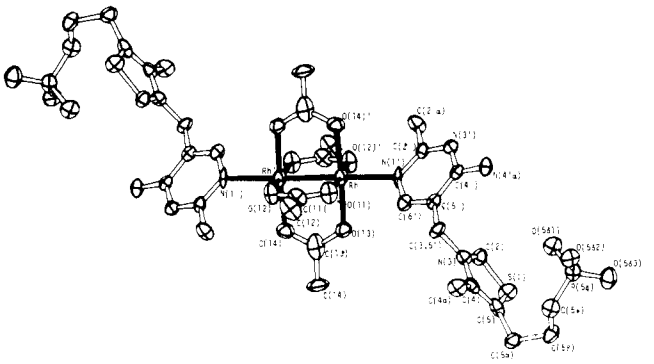


Figure 1. Molecular structure of the tetrakis(μ-acetato)bis(thiamin monophosphate)dirhodium(II) unit along with the numbering scheme showing the metal bonding to the thiamin base through the pyrimidine N(1′) site and the folded structure of the thiamin monophosphate molecule.

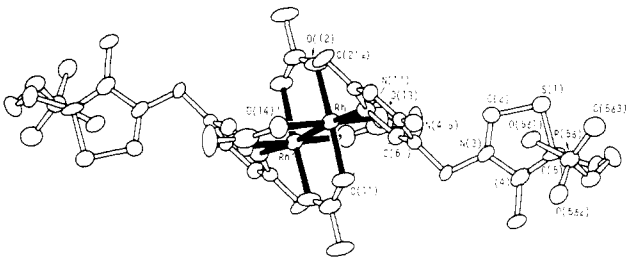


Figure 2. Perspective view showing the disposition of the pyrimidine ring and the folded conformation of the C(5) ethyl ester phosphate side chain. Broken lines denote C(6′)H···O(11) interligand hydrogen bonds.

Results and Discussion

Description of the Crystal and Molecular Structure of the Tetrakis(μ-acetato)bis(thiamin monophosphate)dirhodium(II) Sesquihydrate Complex. The crystal structure of the complex is composed of the discrete $[Rh_2(AcO)_4(TMP)_2]$ and 1.5 crystallization water molecules in the cell. Figure 1 shows the molecular

(18) For each reflection, the intensity, I, and its standard deviation, $\sigma(I)$, were calculated from the equations $I = I_P - (T_P/T_B)(B_1 + B_2)/2$ and $\sigma(I) = Q[I_P + (T_P/T_B)^2(B_1 + B_2)/4]^{1/2}$, where I_P is the total integrated count, T_P is the counting time for the scan, T_B is the counting time for each background, B_1 and B_2 are the background counts on each side of the scan, and Q is the reliability factor and was set euqal to 1.0 in this case.

(19) Computations were carried out with the UNICS III program system: Sakurai, T.; Kobayashi, K. *Rikagaku Kenkyusho Hokoku* **1979**, *55*, 69–77.

(20) Occupancy factors for O(W1) and O(W2) were estimated to be 0.5 and 0.25, respectively, on the basis of the values of their temperature factors; a separation of 2.17 (4) Å between the water molecules is prohibitively short, thus each of the water positions may be half-occupied at most. A discrepancy of the water contents between the crystal examined and the freshly prepared crystals (microanalysis and density measurement showed two water molecules per rhodium (ρ_{calcd} = 1.682 g cm^{-3})) indicates a loss of water molecules under X-rays.

(21) $R_F = \sum||F_o| - |F_c||/\sum F_o$, $R_{wF} = (\sum w|F_o - |F_c||^2/\sum wF_o^2)^{1/2}$, and the standard deviation of an observation of unit weight = $[\sum w|F_o - |F_c||^2/(m - n)]^{1/2}$.

(22) "International Tables for X-ray Crystallography"; Kynoch Press: Birmingham, England, 1974; Vol. IV.

(23) Supplementary material.

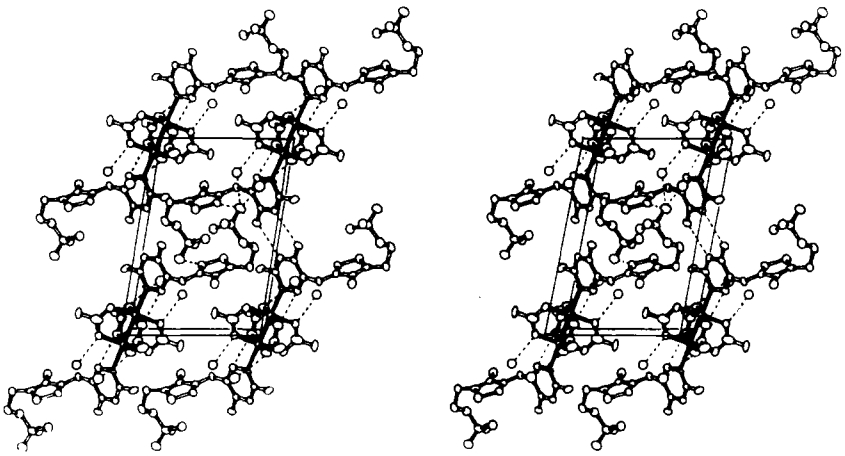


Figure 3. Stereoview of the crystal packing along the *c* axis. The *b* axis is horizontal. Broken lines indicate hydrogen bonds.

struture of the $[Rh_2(AcO)_4(TMP)_2]$ unit, which involves a crystallographic center of inversion at the midpoint of the Rh–Rh bond. The thiamin monophosphate ligand, a neutral zwitterion with the quaternary nitrogen N(3) cation and the singly ionized phosphate group,[24] coordinates to the two axial positions of the dirhodium–tetraacetate cage through the pyrimidine base nitrogen N(1′), as expected by an earlier X-ray investigation[14] of the model compound $[Rh_2(AcO)_4(AAMP)]$ (AAMP = 4-amino-5-(aminomethyl)-2-methylpyrimidine). The dimensions of the dirhodium–tetraacetate core have normal values[25] (Table III): Rh–Rh′ = 2.405 (1) Å, Rh–O(acetate) = 2.04 $(1)_{av}$ Å, ∠Rh′–Rh–O = 88.1 $(3)_{av}$°, and ∠Rh–O–C = 119.2 $(8)_{av}$°. The Rh atom lies 0.069 (4) Å out of the equatorial acetate oxygen atom plane toward the axial N(1′). The Rh–N(1′) distance is 2.284 (8) Å and the Rh′–Rh–N(1′) linkage is rather bent with an angle about Rh of 173.5 (2)°. To avoid unfavorable steric interactions, the base ring system is positioned nearly symmetrically between the rhodium acetate planes: C(2′α)···O(12)′ = 3.29 (1) Å, C(2′α)···O(14)′ = 3.28 (1) Å, C(6′)···O(11) = 2.93 (1) Å, and C(6′)···O(13) = 3.26 (1) Å. More strictly described, however, the base plane is declined about the Rh–N(1′) vector toward the O(11) and O(14)′ atom side (Figure 2): the Rh atom deviates from the base plane by 0.71 (2) Å on the same side as the O(11) atom; the internal rotation angles C(6′)–N(1′)–Rh–O(11) = 32.2 (7)° and C(6′)–N(1′)–Rh–O(13) = −56.7 (7)°. This is probably due to the formation, albeit weak, of a C(6′)–H···O(11) hydrogen bonding: H(C6′)···O(11) = 2.5 (1) Å (sum of van der Waals radii[26] = 2.70 Å for the distance *r*(H···O)), ∠C(6′)–H···O(11) = 101 (6)°, and ∠C(11)–O(11)···H = 142 (2)°, while H(C6′)···O(13) = 2.82 (9) Å, ∠C(6′)–H···O(13) = 110 (6)°, and ∠C(13)–O(13)···H = 156.8 (8)°.

The bond distances and angles of the thiamin monophosphate molecule are mostly as expected[27] (Table III). The pyrimidine and the thiazolium rings are reasonably planar (Table IV), with maximum deviations of 0.021 (8) Å for the pyrimidine ring and 0.006 (8) Å for the thiazolium ring. In addition, the substituent atoms attached to the two rings are nearly coplanar with the rings. The two ring planes make a dihedral angle of 99.1 (3)°. The thiamin moiety exhibits the characteristic F conformation,[28,29] which is usually observed for thiamins with no substituent at C(2),[30] with respect to the C(3,5′) methylene bridge atom: ϕ_T[28]

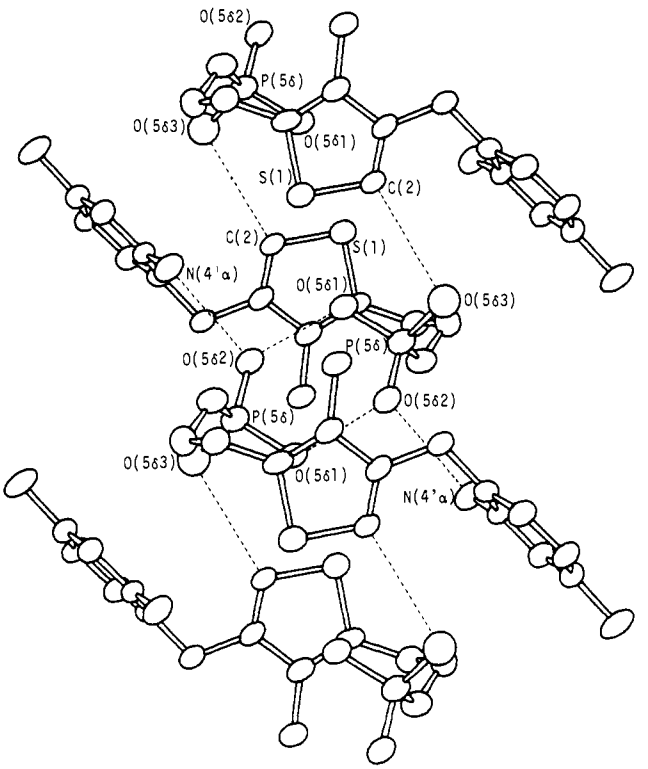


Figure 4. Perspective view showing the dimer formation of the thiamin monophosphate molecules and its array in the crystal, where a dimeric structure is formed through interactions between the thiazolium and the phosphate group of its pairing molecule across a crystallographic center of symmetry: a C(2)H···O(5δ3) hydrogen bonding and a S(1)···O(5δ1) electrostatic interaction. This dimer unit is connected with itself by two O(5δ1)H···O(5δ2) hydrogen bonds formed between the phosphate groups across another center of symmetry. Note that the pyrimidine moiety caps on the phosphate oxygen O(5δ3) of its pairing molecule. Broken lines show hydrogen bonds.

= C(5′)–C(3,5′)–N(3)–C(2) = −3 (1)° and ϕ_P = N(3)–C(3,5′)–C(5′)–C(4′) = −81 (1)°. The C(5) ethyl ester phosphate side chain is folded back toward the thiazolium moiety with a partial overlapping between them and is syn-related[11d] with the pyrimidine amino substituent N(4′α), i.e., on the same side of the thiazolium ring (Figure 2): $\phi_{5\alpha}$[28] = S(1)–C(5)–C(5α)–C(5β) = 76 (1)°, $\phi_{5\beta}$ = C(5)–C(5α)–C(5β)–O(5γ) = 63 (1)°, $\phi_{5\gamma}$ = C(5α)–C(5β)–O(5γ)–P(5δ) = −125.8 (8)°; a closest contact of O(5δ1)···C(5) = 3.30 (1) Å. Thus the conformation of the thiamin monophosphate molecule is very similar to that observed in the (thiamin monophosphate)·(phosphate)·trihydrate structure,[31]

(24) The protonation occurs at the O(5δ1) oxygen, as judged by locating the hydrogen atom in the difference Fourier map and by the P(5δ)–O(5δ1) bond length of 1.583 (8) Å. This is further supported by the hydrogen bonding system.

(25) Some average dimensions of the Rh_2(carboxylato)$_4L_2$ (L = nitrogen donor ligand) framework are compared in Table D5.[23]

(26) Taylor, R.; Kennard, O. *J. Am. Chem. Soc.* **1982**, *104*, 5063–5070.

(27) Bond distances and angles for the metal-complexed, neutral, and protonized thiamins are compared in Table D6.[23]

(28) For a definition of these conformational terms, see: Pletcher, J.; Sax, M.; Blank, G.; Wood, M. *J. Am. Chem. Soc.* **1977**, *99*, 1396–1403.

(29) Conformational parameters are compared for various thiamins in Table D7.[23]

(30) Shin, W.; Pletcher, J.; Blank, G.; Sax, M. *J. Am. Chem. Soc.* **1977**, *99*, 3491–3499.

Table III. Heavy-Atom Bond Lengths (Å) and Angles (Deg) in $[Rh_2(acetato)_4(thiamin\ monophosphate)_2]\cdot 1.5H_2O$

(a) Coordination Sphere			
Bond Lengths			
Rh–Rh′	2.405 (1)	Rh–N(1′)	2.284 (8)
Rh–O(11)	2.024 (7)	Rh–O(12)′	2.045 (7)
Rh–O(13)	2.053 (7)	Rh–O(14)′	2.043 (7)
Bond Angles			
Rh′–Rh–N(1′)	173.5 (2)	Rh′–Rh–O(11)	87.8 (2)
Rh′–Rh–O(12)′	87.9 (2)	Rh′–Rh–O(13)	88.5 (2)
Rh′–Rh–O(14)′	88.0 (2)	N(1′)–Rh–O(11)	85.7 (3)
N(1′)–Rh–O(12)′	98.6 (3)	N(1′)–Rh–O(13)	91.5 (3)
N(1′)–Rh–O(14)′	92.0 (3)	O(11)–Rh–O(12)′	175.6 (3)
O(11)–Rh–O(13)	89.0 (3)	O(11)–Rh–O(14)′	90.2 (3)
O(12)′–Rh–O(13)	88.2 (3)	O(12)′–Rh–O(14)′	90.3 (3)
O(13)–Rh–O(14)′	176.4 (3)		
(b) Acetate Ligands			
Bond Lengths			
C(11)–O(11)	1.25 (1)	C(13)–O(13)	1.28 (1)
C(11)–O(12)	1.28 (1)	C(13)–O(14)	1.29 (2)
C(11)–C(12)	1.53 (2)	C(13)–O(14)	1.51 (2)
Bond Angles			
Rh–O(11)–C(11)	119.9 (6)	Rh–O(13)–C(13)	119.0 (8)
Rh–O(12)′–C(11)′	118.1 (7)	Rh–O(14)′–C(13)′	119.7 (7)
O(11)–C(11)–O(12)	126 (1)	O(13)–C(13)–O(14)	125 (1)
O(11)–C(11)–C(12)	116.8 (9)	O(13)–C(13)–C(14)	119 (1)
O(12)–C(11)–C(12)	117 (1)	O(14)–C(13)–C(14)	117 (1)
(c) Thiamin Monophosphate Ligand			
Bond Lengths			
N(1′)–C(2′)	1.36 (1)	C(2′)–N(3′)	1.33 (1)
N(3′)–C(4′)	1.36 (1)	C(4′)–C(5′)	1.41 (1)
C(5′)–C(6′)	1.37 (1)	C(6′)–N(1′)	1.35 (1)
C(2′)–C(2′α)	1.51 (1)	C(4′)–N(4′α)	1.34 (1)
C(5′)–C(3,5′)	1.49 (1)	C(3,5′)–N(3)	1.50 (1)
S(1)–C(2)	1.70 (1)	C(2)–N(3)	1.31 (1)
N(3)–C(4)	1.41 (1)	C(4)–C(5)	1.35 (2)
C(5)–S(1)	1.74 (1)	C(4)–C(4α)	1.51 (2)
C(5)–C(5α)	1.48 (2)	C(5α)–C(5β)	1.53 (2)
C(5β)–O(5γ)	1.44 (1)	O(5γ)–P(5δ)	1.584 (7)
P(5δ)–O(5δ1)	1.583 (8)	P(5δ)–O(5δ2)	1.526 (8)
P(5δ)–O(5δ3)	1.492 (10)		
Bond Angles			
Rh–N(1′)–C(2′)	128.0 (7)	Rh–N(1′)–C(6′)	114.2 (6)
N(1′)–C(2′)–N(3′)	125.6 (9)	C(2′)–N(3′)–C(4′)	118.5 (8)
N(3′)–C(4′)–C(5′)	120.2 (8)	C(4′)–C(5′)–C(6′)	116.3 (8)
C(5′)–C(6′)–N(1′)	124.3 (8)	C(6′)–N(1′)–C(2′)	115.0 (7)
N(1′)–C(2′)–C(2′α)	117.4 (8)	N(3′)–C(2′)–C(2′α)	117.1 (8)
N(3′)–C(4′)–N(4′α)	116.2 (8)	C(5′)–C(4′)–N(4′α)	123.5 (8)
C(4′)–C(5′)–C(3,5′)	123.6 (8)	C(6′)–C(5′)–C(3,5′)	119.9 (8)
C(5′)–C(3,5′)–N(3)	112.9 (9)	C(3,5′)–N(3)–C(2)	123.1 (8)
C(3,5′)–N(3)–C(4)	121.4 (9)	S(1)–C(2)–N(3)	111.7 (7)
C(2)–N(3)–C(4)	115.5 (9)	N(3)–C(4)–C(5)	110.8 (9)
C(4)–C(5)–S(1)	111.0 (8)	C(5)–S(1)–C(2)	91.0 (6)
N(3)–C(4)–C(4α)	120.7 (9)	C(5)–C(4)–C(4α)	128.4 (9)
C(4)–C(5)–C(5α)	129.0 (10)	S(1)–C(5)–C(5α)	120.0 (9)
C(5)–C(5α)–C(5β)	112.0 (9)	C(5α)–C(5β)–O(5γ)	108.7 (10)
C(5β)–O(5γ)–P(5δ)	122.3 (7)	O(5γ)–P(5δ)–O(5δ1)	105.6 (4)
O(5γ)–P(5δ)–O(5δ2)	103.3 (4)	O(5γ)–P(5δ)–O(5δ3)	110.8 (5)
O(5δ1)–P(5δ)–O(5δ2)	109.6 (4)	O(5δ1)–P(5δ)–O(5δ3)	106.6 (5)
O(5δ2)–P(5δ)–O(5δ3)	120.1 (4)		

which is a sole X-ray example of a thiamin monophosphate, where $\phi_T = -7°$, $\phi_P = -85°$, $\phi_{5\alpha} = 76°$, $\phi_{5\beta} = 66°$, and $\phi_{5\gamma} = -129°$ and a dihedral angle between the two planes = 90°. The ethyl ester monophosphate conformation in the current structure also resembles the folded form in thiamin pyrophosphate hydrochloride[32] but differs from the extended form in thiamin pyrophosphate neutral zwitterions[33,34] and its copper adduct.[13] This is consistent with the conformational variability of the C(5) side chain as a function of its environment, as pointed out by Pletcher and Sax.[33]

The crystal packing is mainly dominated by an extensive hydrogen-bonding system (Figure 3 and Table V). The TMP molecule interacts with itself in an interesting manner. First, it forms a dimeric structure across a crystallographic center of inversion (Figures 3 and 4), where the thiazolium moiety of a molecule is connected with the phosphate group of its partner molecule by both a C(2)–H hydrogen bonding[35] and an electrostatic interaction[36] between the electropositive S(1) atom and the electronegative phosphate oxygen O(5δ1): C(2)···O(5δ3) = 3.20 (1) Å, H(C2)···O(5δ3) = 2.31 (7) Å, ∠C(2)–H···O(5δ3) = 160 (6)°, ∠P(5δ)–O(5δ3)···H = 105 (2)°; S(1)···O(5δ1) = 2.905 (8) Å (sum of van der Waals radii[26] = 3.30 Å for r(S···O)). The thiazolium and the O(5δ1)–P(5δ)–O(5δ3) planes make a dihedral angle of 153.4 (4)°. Hence a cage with the composition of [thiazolium ethyl phosphate]$_2$ is formed, where the two parallel thiazolium rings are separated with a mean spacing of 3.9 Å but are not overlapped. In this dimeric molecular unit, the pyrimidine ring is oriented such that it caps on the phosphate group of its pairing molecule with a closest contact of 3.44 (1) Å between the C(2′) and O(5δ3) atoms. Second, in the lattice, this dimer unit is further connected with itself in an *ab* plane by the formation of two interbase hydrogen bonds between the N(4′α)H and N(3′) across a center of symmetry (Figure 3): N(4′α)···N(3′) = 3.26 (1) Å, H···N(3′) = 2.25 (8) Å, ∠N(4′α)–H···N(3′) = 175 (8)°. Third, the dimer unit is additionally linked in an *ac* plane through the formation of two interphosphate hydrogen bonds, which are very short, across another center of symmetry (Figure 4): O(5δ1)···O(5δ2) = 2.54 (1) Å, H(O5δ1)···O(5δ2) = 1.7 (1) Å, ∠O(5δ1)–H···O(5δ2) = 169 (9)°. This phosphate–phosphate connection is further stabilized by both an additional hydrogen bond between the phosphate O(5δ2) and the pyrimidine N(4′α)H and an electrostatic interaction[37] between the same O(5δ2) atom and the cationic quaternary nitrogen N(3) (Figure 4): N(4′α)···O(5δ2) = 2.89 (1) Å, H···O(5δ2) = 2.02 (9) Å, ∠N(4′α)–H···O(5δ2) = 168 (8)°; O(5δ2)···N(3) = 3.163 (9) Å. There is no pyrimidine base–base stacking. It is of interest to note here that this crystal packing feature, in addition to the molecule conformation noted above, is remarkably similar to that in (TMP)·(H_2PO_4)·3H_2O (compare Figure 5 in ref 31).

Crystallization water molecules, which are disordered,[20] stabilize the crystal lattice by forming hydrogen-bonding bridges between the phosphate oxygen O(5δ3) and acetate oxygens O(13) and O(14) (Figure 3): O(5δ3)···O(W1)···O(13) = 2.80 (2) and 2.95 (2) Å; O(5δ3)···O(W2)···O(12) = 2.79 (4) and 3.11 (5) Å. Additionally, O(W1) locates nearly over the pyrimidine ring and O(W2) intercalates between the pyrimidine substituents[39] (Figure 5).

Factors Affecting Tetrakis(μ-acetato)dirhodium(II) Binding for Thiamin Monophosphate. The most interesting structural feature of the complex is the metal bonding to the thiamin base nitrogen N(1′). Metal bonding to the N(1′) among the five possible metal ligand sites for thiamin monophosphate may be rationalizable from electronic considerations of these sites. The absence of the metal

(31) Karle, I. L.; Britts, K. *Acta Crystallogr.* **1966**, *20*, 118–124.
(32) Pletcher, J.; Sax, M. *Science (Washington D.C.)* **1966**, *154*, 1331–1333; *J. Am. Chem. Soc.* **1972**, *94*, 3998–4005.
(33) Pletcher, J.; Wood, M.; Blank, G.; Shin, W.; Sax, M. *Acta Crystallogr., Sect. B.: Struct. Crystallogr. Cryst. Chem.* **1977**, *B33*, 3349–3359.
(34) Pletcher, J.; Blank, G.; Wood, M.; Sax, M. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1979**, *B35*, 1633–1637.
(35) The corresponding C–H hydrogen bonding has been observed in many other thiamin structures.[11c]
(36) This type of interaction between the thiazolium sulfur and electronegative atoms has been observed in many other thiamin structures.[12b]
(37) The corresponding short contact between the thiazolium nitrogen and electronegative atoms such as chloride,[11c,e,38a] bromide,[38b] or oxygen[13] has been found in some other thiamin structures.
(38) (a) Lee, W. E.; Richardson, M. F. *Can. J. Chem.* **1976**, *54*, 3001–3006. (b) Thompson, D. M.; Richardson, M. F. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1977**, *B33*, 324–328.
(39) The formation of sandwiches and half sandwiches of water molecules between nucleic acid bases has been reported: Parthasarathy, R.; Srikrishnan, T.; Ginell, S. L. In "Biomolecular Stereodynamics"; Sarma, R. H., Ed.; Adenine: New York, 1983; Vol. 1, pp 261–267.

Table IV. Least-Squares Planes and the Deviation (Å) of Individual Atoms from These Planes[a]

(a) Equatorial Plane Including the Acetate Oxygens ($-0.878X + 0.356Y + 0.159Z = 1.133$)					
O(11)	−0.007 (4)	O(12)′	−0.007 (4)	O(13)	0.007 (4)
O(14)′	0.006 (4)	Rh*	0.069 (4)		
(b) Six Atom Plane of the Pyrimidine Ring ($-0.552X + 0.692Y - 0.744Z = 1.153$)					
N(1′)	−0.013 (6)	C(2′)	0.021 (8)	N(3′)	−0.004 (5)
C(4′)	−0.013 (7)	C(5′)	0.016 (7)	C(6′)	−0.002 (8)
C(2′α)*	0.10 (2)	N(4′α)*	−0.03 (1)	C(3,5′)*	−0.01 (2)
H1(N4′α)*	−0.04 (9)	H2(N4′α)*	−0.08 (10)	H(C6′)*	0.02 (10)
Rh*	−0.71 (2)	O(11)*	−1.89 (2)	O(12)′*	0.45 (2)
O(13)*	0.75 (2)	O(14)′*	−2.22 (2)	O(W2)*	3.06 (4)
(c) Five Atom Plane of the Thiazolium Ring ($-0.718X - 0.219Y + 0.414Z = 4.045$)					
S(1)	−0.0004 (6)	C(2)	0.003 (8)	N(3)	0.000 (5)
C(4)	−0.004 (7)	C(5)	0.006 (8)	C(3,5′)*	−0.04 (2)
C(4α)*	0.08 (2)	C(5α)*	0.02 (2)	H(C2)*	−0.01 (7)
P(5δ)*[b]	0.20 (2)	O(5δ1)*[b]	0.62 (2)	O(5δ3)*[b]	−0.43 (2)
(d) Three Atom Plane Through the Phosphate P(5δ), O(5δ1), and O(5δ3) Atoms[b] ($0.387X + 0.588Y - 0.563Z = -0.845$)					
P(5δ)[b]	0.0	O(5δ1)[b]	0.0	O(5δ3)[b]	0.0
S(1)*	0.49 (3))	C(2)*	−0.25 (3)		
(e) Dihedral Angles (Deg) Between the Planes					
(b)/(c)	99.1 (3)	(b)/(d)	56.3 (4)	(c)/(d)	153.4 (4)

[a] In each of the equations of the planes, X, Y, and Z are triclinic coordinates measured in Å units along the crystallographic a, b, and c axes, respectively. Atoms designated by an asterisk (*) were given zero weight in calculating the planes. [b] These atoms are symmetry-related by $-x - 1$, $1 - y$, $1 - z$, relative to the reference molecule at x, y, z.

Table V. Possible Hydrogen-Bonding Scheme and Other Short Contacts

Hydrogen Bonding

A	B	C	d_{AC}, Å	d_{BC}, Å	∠ABC, deg	symmetry for C
N(4′α)	H1(N4′α)	N(3′)	3.16 (1)	2.25 (8)	175 (8)	$-1 - x, -y, 1 - z$
N(4′α)	H2(N4′α)	O(5δ2)	2.89 (1)	2.02 (9)	168 (8)	$-1 - x, 1 - y, 2 - z$
C(6′)	H(C6′)	O(11)	2.93 (1)	2.53 (11)	101 (6)	x, y, z
C(2)	H(C2)	O(5δ3)	3.20 (1)	2.31 (7)	160 (6)	$-1 - x, 1 - y, 1 - z$
O(5δ1)	H(O5δ1)	O(5δ2)	2.54 (1)	1.66 (11)	169 (9)	$-1 - x, 1 - y, 2 - z$
O(W1)[a]		O(13)	2.95 (2)			x, y, z
O(W1)[a]		O(5δ3)	2.80 (2)			$-1 - x, 1 - y, 1 - z$
O(W2)[a]		O(12)	3.11 (5)			$-x, -y, -z$
O(W2)[a]		O(5δ3)	2.79 (4)			$-1 - x, 1 - y, 1 - z$

Other Interaction

A	C	d_{AC}, Å	symmetry for C
C(6′)	O(13)	3.36 (1)	x, y, z
C(2′α)	O(12)	3.29 (1)	$-x, -y, -z$
C(2′α)	O(14)	3.28 (1)	$-x, -y, -z$
C(2′α)	O(5γ)	3.18 (1)	$x, y, 1 + z$
C(3,5′)	O(W1)	3.38 (2)	$x, y, 1 + z$
C(3,5′)	O(W2)	3.17 (5)	$x, y, 1 + z$
C(3,5′)	O(5δ2)	3.13 (1)	$-1 - x, 1 - y, 2 - z$
S(1)	O(5δ1)	2.905 (8)	$-1 - x, 1 - y, 1 - z$
C(2)	O(5δ1)	3.05 (1)	$-1 - x, 1 - y, 1 - z$
N(3)	O(5δ2)	3.163 (9)	$-1 - x, 1 - y, 2 - z$
C(4)	O(5δ2)	3.30 (1)	$-1 - x, 1 - y, 2 - z$
C(5)	O(5δ1)	3.30 (1)	x, y, z

[a] Hydrogen atoms of these water molecules were not located.

bonding to the thiazolium S(1) atom is possibly simply due to its electropositive nature,[12b] and no interaction with the phosphate oxygens, which are known as "hard base", is probably attributed to a "soft acid" character of the dirhodium(II) tetraacetate nucleus.[40] The lacking of the metal attachment to the amino substituent N(4′α) is also usual because this amino group is highly conjugated with the pyrimidine ring and therefore has considerable double-bond character with a concomitant lowered basicity.[41] In an earlier report,[14] we suggested tht the failure of the metal bonding to the ring nitrogen N(3′), which is flanked by the methyl and amino substituents, may be due to the steric constraint imposed by the octahedral environment about the Rh atom. Most recently, however, we have obtained X-ray evidence against this argument: in the crystal structure of $[Rh_2(AcO)_4(ADMP)_2]$,[44] which involves an analogous ligand 2-amino-4,6-dimethylpyrimidine (ADMP), the dirhodium–tetraacetate nucleus is occupied at the two axial positions actually by the pyrimidine ring nitrogen, which is interposed by the two substituents, and the amino group forms a bifurcated interligand hydrogen bond with two acetate oxygens. Thus it appears more plausible that the absence of the metal bonding to the N(3′) is not due to the steric

(40) Cotton, F. A.; Felthouse, T. R. *Inorg. Chem.* **1980**, *19*, 323–328.
(41) Sundaralingam, M. *Biopolymers* **1969**, *7*, 821–860; in fact, there has been no X-ray example showing metal bonding to this group (in cytosine, adenine, and guanine) in nucleic acid constituent–metal complexes,[42] though the deprotonated amino group becomes a good ligand, as substantiated in some X-ray structures.[43]
(42) Gellert, R. W.; Bau, R. *Met. Ions Biol. Syst.* **1979**, *8*, 1–56.
(43) (a) Prizant, L.; Oliver, M. J.; Rivest, R.; Beauchamp, A. L. *J. Am. Chem. Soc.* **1979**, *101*, 2765–2767. (b) Prizant, L.; Rivest, R.; Beauchamp, A. L. *Can. J. Chem.* **1981**, *59*, 2290–2297. (c) Graves, B. J.; Hodgson, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 5608–5612. (d) Faggiani, R.; Lippert, B.; Lock, C. J. L.; Speranzini, R. A. *Ibid.* **1981**, *103*, 1111–1120.

(44) $[Rh_2(AcO)_4]$ reacts with 2-amino-4,6-dimethylpyrimidine (ADMP) to give the triclinic $[Rh_2(AcO)_4(ADMP)_2]$ and the monoclinic $[Rh_2(AcO)_4(ADMP)_2]\cdot 2H_2O$ crystalline forms; the structural feature of the $[Rh_2(AcO)_4(ADMP)_2]$ unit is essentially equivalent for the both forms. The molecular structure of the monoclinic form is shown in Figure D1.[23] Structural details will appear elsewhere.

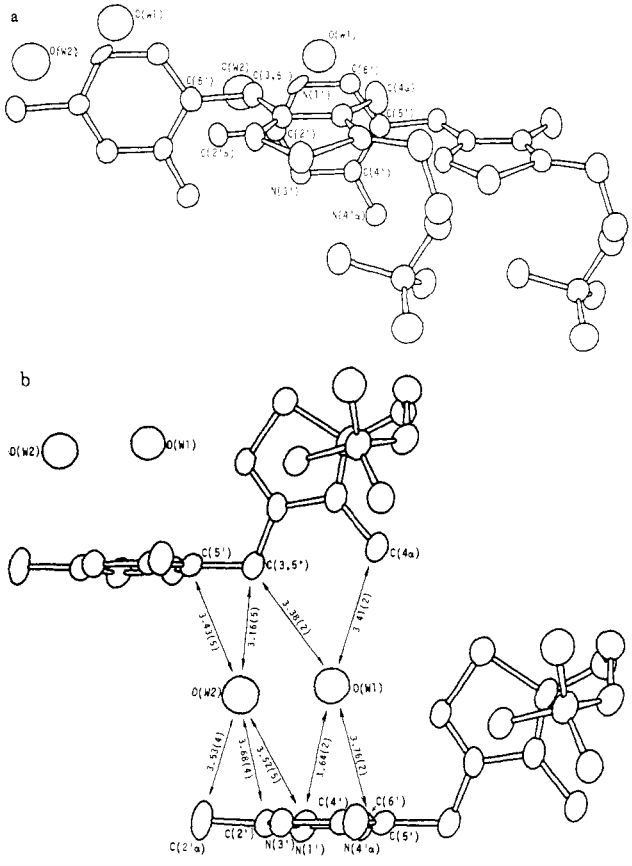


Figure 5. Perspective view showing the disposition of the water molecules (a) and the edge view (b); the numbers indicate interatomic distances (Å).

effect but due to the electronic effect, namely, low basicity[45] of N(3'). On the contrary, the N(1') coordination is reasonable from its high basicity[45] and from no steric hindrance between ligands. In addition, the metal bonding to the N(1') but not to the N(3') site in the Cd(thiamin)Cl_3[12a] and Cu(thiamin)Cl_2[12b] structures, which have less hindered tetrahedral and trigonal-planar coordination arrangements, respectively, supports this prediction.

Metal bonding nature argued here may be also true for the Mg^{2+} ion, which is an actual metal ion as an additional cofactor in the enzyme system, except for the possibility of the metal bonding to the phosphate group because of a "hard" character of Mg^{2+}. Similarly, we can expect an analogous coordination stereochemistry for an *octahedrally* hydrated $[Mg(H_2O)_6]^{2+}$ ion in solution. But in this case, we can not expect the formation of interligand hydrogen bond(s), as observed in the present $[Rh_2(AcO)_4]$ system between the C(6')H and an acetate oxygen. Rather, water ligand may impose a steric hindrance as a result of interligand interactions with the C(6')H and/or C(2'α)H_3 of the N(1')-bound thiamin base. This steric constraint, however, may loosen by a longer ligation bond of Mg^{2+}; the Mg^{2+}–N axial bond distance has been observed to vary from 2.297 (8) to 2.419 (4) Å in the octahedral magnesium tetraphenylporphyrin complexes.[46]

Comparison of the Three Metal–Thiamin Complexes $Rh_2(AcO)_4(TMP)_2$, Cd(thiamin)Cl_3,[12a] and Cu(thiamin)Cl_2.[12b] Characteristic structural features common to these three structures are as follows. First, metal atoms are coordinated to the thiamin base through the N(1') site. This is rationalized from a high basicity of N(1'), as noted above. Second, as Cramer et al. have clearly demonstrated,[12a] effects of the metal coordination to the pyrimidine base on the geometry of the thiamin ligand are minor except those on the C(4')–N(4'α) bond length and the C(2')–N(1')–C(6') bond angle: though a limited accuracy of this analysis precludes a detailed comparison, the C(4')–N(4'α) bond length of 1.336 (11) Å in the present structure is essentially identical with 1.334 (5) Å[12a] observed in the N(1')-deprotonated free base, 1.339 (3) Å in the Cu–thiamin complex,[12b] and 1.346 (3) Å in the Cd–thiamin complex,[12a] but is 0.02 Å longer than that[12a] of the protonated thiamin. The observation of the same trend, that is, the increase of the C(4')–N(4'α) bond, in contrast to the protonated thiamin, despite the different electronic states of the coordination units, i.e., formally neutral $[Rh_2(AcO)_4]$ and ionic $[CdCl_3]^-$ or $[CuCl_2]^-$, is interesting in the connection with the prediction[12b] by Cramer et al. that electronic nature of the bonding unit may reflect the resonance structures of the pyrimidine base associated with the C(4')–N(4'α) bond strength. In this regard, it is of special interest to see, in the future, effects of the cationic $[Mg(H_2O)_6]^{2+}$ coordination on the C(4')–N(4'α) bond because Cramer et al. have suggested[12a,b] that the protonation or metal coordination at the N(1') site affects the strength of the basicity of the amino N(4'α) atom and consequently its reactivity as a hydrogen bond donor[47] or as a base[7] in the reaction of thiamin with the substrate. Effect of the metal coordination on the internal bond angle at the coordination site is also in sharp contrast with that of protonation: the C(2')–N(1')–C(6') bond angle of 115.0 (7)° in the present complex is practically equivalent with 115.3 (5)°[12a] in the free base, 115.6 (2)° in the Cu–thiamin complex, and 116.5 (2)° in the Cd–thiamin complex but is significantly smaller than 121.0 (8)°[12a] of the protonated form. However, this is a rather common structural aspect, often observed also in the metal–nucleic acid derivative structures.[48]

Major differences include the following: first, F conformation of the thiamin ligand in the present and the Cu–thiamin structures and S conformation in the Cd–thiamin structure, thus metal coordination to the pyrimidine base does not affect on the thiamin conformation; second, the pyrimidine base stacking in the Cd- and the Cu–thiamin structures and no base stacking in the present structure, hence the promotion of the base stacking by metal coordination is not always the case;[12b] third, instead, stacking-type contacts between the pyrimidine base and the negatively charged phosphate oxygen and water molecules in the present structure and none for the Cd- and the Cu–thiamin structures, showing the positively charged nature of the pyrimidine base in the present structure, since water molecule is known[39] to stack or intercalate between nucleic acid bases if the bases are electron-deficient.

Possible Roles of the Metal Ion. Anion interactions with the thiamin moiety observed here suggest some implications concerning the nature of metal ion- and substrate–thiamin interactions. In the present structure, the phosphate anion attaches to the thiazolium ring bifunctionally, namely a hydrogen bonding with the C(2)H and an electrostatic interaction with the S(1), and it further interacts, possibly electrostatically, with the pyrimidine base that adopts F conformation. Thus, if we assume that the coenzyme thiamin pyrophosphate holds the most stable F conformation when it reacts with the substrate pyruvate anion,[49] we can expect the fixation of the pyruvate in the vicinity of the reaction site C(2) in a similar manner, where the metal ion could function as an electron sink, thus polarizing the electron density of the ligand toward the metal ion; such induced electron deficiency of the pyrimidine base may be favorable for interactions with the substrate anion.

Another role of the metal ion is to fix the coenzyme in the catalytic center of the enzyme through the formation of a metal ion bridge between the pyrimidine base and the enzyme, as suggested in a model[7] by Schellenberger. Such a substrate fixation may be more efficient for a closer adjustment of the coenzyme to fit the stereochemistry required for the reaction at the catalytic center than via a metal ion bridge through the phosphate group,

(45) Mizukami, S.; Hirai, E. *J. Org. Chem.* **1966**, *31*, 1199–1202.
(46) McKee, V.; Ong, C. C.; Rodley, G. A. *Inorg. Chem.* **1984**, *23*, 4242–4248.
(47) Gallo, A. A.; Mieyal, J. J.; Sable, H. Z. *Bioorg. Chem.* **1978**, *4*, 147–177.
(48) Hodgson, D. J. *Prog. Inorg. Chem.* **1977**, *23*, 211–254.
(49) Ionization constant (pK_a) of pyruvic acid is 2.5 (Heilbron, I. M.; Bunbury, H. Y. "Dictionary of Organic Compounds"; Oxford University Press: New York, 1944; Vol. III, p 564).

because the pyrophosphate ethyl ester side chain is extremely flexible.

Significance

The present structure is only the third X-ray example showing the metal coordination to the thiamin base and the first of a thiamin monophosphate complexed with a metal atom. This is of particular importance because in five[11] of the seven[11,12] X-ray-characterized thiamin–metal ion complexes there is no direct bond formed between a metal ion and thiamin, though there is some NMR evidence[7,9,10] for metal ion binding to the thiamin base in solution. Metal coordination at the N(1′) site is consistent with Schellenberger's suggestion[7] from enzyme studies. Electronic rather than steric factors are responsible for the metal attachment to the N(1′) but not to the N(3′) sites.

Widespread occurrence of the stable F conformation of the thiamin molecule in a variety of the thiamin crystal structures, frequent observation of the participation of the thiazolium C(2)H in the formation of the hydrogen bonding with anions, and the participation of the thiazolium S(1) in the electrostatic interaction with anions suggest that pyruvate anion could be incorporated into the vicinity of the catalytic C(2) site in the enzyme system in a manner similar to the phosphate anion–thiamin moiety interactions observed in the present structure. We are aware that this substrate fixation model is highly speculative. Particularly, this model has a disadvantage from a "least motion" concept which had been applied by Pletcher and Sax[50] to the addition mechanism of the thiazolium ylide to pyruvate, because in our model the carbonyl carbon atom of pyruvate, a site to be attacked, is rather far from the reaction center C(2) atom. Clearly, more crystallographic studies are necessary to understand the nature of the metal coordination, particularly the electronic effects on the thiamin base, in connection with a possible role of the metal ion in the enzymic processes on complexation with the pyrimidine base to induce an electron deficiency of the base, which is advantageous for the fixation of the substrate anion.

Supplementary Material Available: Listings of anisotropic temperature factors, hydrogen atom parameters, bond lengths and angles involving hydrogen atoms, observed and calculated structure amplitudes, selected structural parameters for the $Rh_2(O_2CR)_4L_2$ framework, bond lengths and angles in the various thiamin structures, torsion angles in the various thiamin structures, and the molecular structure of $[Rh_2(AcO)_4(ADMP)_2]$ (19 pages). Ordering information is given on any current masthead page.

(50) Turano, A.; Furey, W.; Pletcher, J.; Sax, M.; Pike, D.; Kluger, R. *J. Am. Chem. Soc.* **1982**, *104*, 3089–3095.

A ^{31}P Magic Angle Spinning NMR Study of the Cation Distribution in $Zn_{3-x}Mg_x(PO_4)_2$

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Abstract: Phosphates of the solid solution $Zn_{3-x}Mg_x(PO_4)_2$ with x = 0, 0.5, 1.0, 1.2, 1.25, 1.5, 1.75, 1.9, 2.0, 2.1, 2.2, 2.5, and 3.0 have been investigated by using ^{31}P magic angle spinning NMR. All samples with $x > 0$ have the γ-$Zn_3(PO_4)_2$ structure which contains one phosphorus site and two cation sites, one octahedral and one five-coordinated. Single ^{31}P resonances are observed at 3.9 ppm for x = 0.5 and at 0.1 ppm for x = 3.0 ($Mg_3(PO_4)_2$); for compositions in the range $1 < x < 3$, four resonances, with varying intensity ratios, are observed at 3.9, 3.1, 0.9, and 0.1 ppm, apparently resulting from the presence of four distinct phosphorus environments. These four environments can be rationalized in terms of the structure, and by equating the proportion of each type of environment to the intensity of the corresponding ^{31}P resonance, the distribution of the cations over the two different sites can be calculated at each composition. The results suggest that magic angle spinning NMR will become a powerful tool for studying cation distributions in disordered systems.

Recent applications of magic angle spinning NMR (MASNMR) to the study of minerals and other inorganic solids have shown that chemical shift values are sensitive to a variety of structural factors.[2] In aluminosilicates, for example, ^{27}Al spectra can readily distinguish between Al in tetrahedral and octahedral sites[3] and even between Al in crystallographically distinct tetrahedral sites, while ^{29}Si spectra clearly reveal differences between crystallographically equivalent silicon atoms that have slightly different, local environments.[4] Studies of inorganic phosphates using ^{31}P MASNMR have shown that the isotropic and anisotropic chemical shifts are influenced by the degree of condensation of the PO_4 tetrahedra.[5,6] In a systematic study of a large number of ortho- and pyrophosphates, we have found that the ^{31}P chemical shift spans a wide range of values, making it, in some cases, extraordinarily sensitive to subtle differences in the structure. In this paper, we show that ^{31}P MASNMR can

Table I.

	bond distances, Å		
	$Mg_3(PO_4)_2$[13]	γ-$Zn_3(PO_4)_2$[12]	$Zn_2Mg(PO_4)_2$[14]
	P–O		
P–O_1	1.54	1.57	1.52
P–O_2	1.51	1.58	1.59
P–O_3	1.53	1.54	1.54
P–O_4	1.53	1.58	1.50
	M_1–O		
M–O_1	2.14	2.31	2.34
M–O_2	1.97	2.02	1.89
M–O_3	2.06	2.02	2.02
M–O_4	2.01	2.16	2.00
M–O_4·	1.96	1.98	2.00
	M_2–O		
M–O_1 (×2)	2.03	1.95	2.03
M–O_2 (×2)	2.18	2.16	2.19
M–O_3 (×2)	2.15	2.21	2.22

(1) (a) Chemical Crystallography Laboratory. (b) Inorganic Chemistry Laboratory.
(2) Magi, M.; Lippmaa, E.; Samoson, A.; Englehardt, G.; Grimmer, A.-R. *J. Phys. Chem.* **1984**, *88*, 1518.
(3) Klinowski, J.; Thomas, J. M.; Fyfe, C. A.; Gobbi, G. C. *Nature (London)* **1982**, *296*, 533.
(4) Lippmaa, E.; Magi, M.; Samoson, A.; Engelhardt, G.; Grimmer, A.-R. *J. Am. Chem. Soc.* **1980**, *102*, 4889.
(5) Grimmer, A.-R.; Haubenreisser, U. *Chem. Phys. Lett.* **1983**, *99*, 487.
(6) Duncan, T. M.; Douglass, D. C. *Chem. Phys.* **1984**, *87*, 339.

0002-7863/85/1507-6249$01.50/0