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# The $PtCl_4^{2-}$/Thiamin System. Structures of a Complex, Pt(thiamin)$Cl_3$·$H_2O$, and Two Salts, (Hthiamin)($PtCl_4$) and (Hthiamin)$_2$($PtCl_4$)$Cl_2$·$2H_2O$

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The interaction of thiamin with $PtCl_4^{2-}$ in aqueous solution leads to an ionic 1:1 salt (Hthiamin)($PtCl_4$), an ionic 2:1 double salt (Hthiamin)$_2$($PtCl_4$)$Cl_2$·$2H_2O$ and the 1:1 complex Pt(thiamin)$Cl_3$·$H_2O$, whose crystal structures are reported here. Examination of the thiamin conformation in several polychlorometal anion containing structures suggests that bridging interactions of these anions between the thiazolium and pyrimidine rings of thiamin constitute a determining factor of the conformation of the thiamin moiety. The reaction of Pt(thiamin)$Cl_3$·$H_2O$ with DMSO was studied, and the reaction pathway is discussed in light of $^{195}$Pt and $^1$H NMR results and conductivity measurements. Crystallographic data for (Hthiamin)$PtCl_4$: space group $P\bar{1}$, $a$ = 9.806 (3) Å, $b$ = 11.769 (9) Å, $c$ = 8.350 (5) Å, $\alpha$ = 103.00 (5)°, $\beta$ = 95.00 (5)°, $\gamma$ = 82.36 (4)°, $V$ = 928.2 (8) Å$^3$, $Z$ = 2; final discrepancy factors are $R_1$ = 0.070 and $R_2$ = 0.104 for 4438 reflections with $F > 3\sigma(F)$. Crystallographic data for (Hthiamin)$_2$($PtCl_4$)$Cl_2$·$2H_2O$: space group $P\bar{1}$, $a$ = 11.449 (7) Å, $b$ = 12.214 (6) Å, $c$ = 6.932 (4) Å, $\alpha$ = 103.10 (4)°, $\beta$ = 102.86 (5)°, $\gamma$ = 73.78 (4)°, $V$ = 893.3 (8) Å$^3$, $Z$ = 1; final discrepancy factors are $R_1$ = 0.049 and $R_2$ = 0.047 for 4455 reflections with $F > 3\sigma(F)$. Crystallographic data for Pt(thiamin)$Cl_3$·$H_2O$: space group $P\bar{1}$, $a$ = 9.714 (6) Å, $b$ = 15.081 (6) Å, $c$ = 6.927 (3) Å, $\alpha$ = 93.86 (3)°, $\beta$ = 109.78 (4)°, $\gamma$ = 98.43 (4)°, $V$ = 937.2 (8) Å$^3$, $Z$ = 2; final discrepancy factors are $R_1$ = 0.0623 and $R_2$ = 0.0623 for 2348 reflections with $F > 3\sigma(F)$.

## Introduction

The pyrophosphate ester of thiamin (Vitamin $B_1$) is the active cofactor in several metabolic enzymes catalizing the decarboxylation of α-keto acids and the transfer of aldehyde or acyl groups.[1,2] All of these enzymes also require a divalent metal ion cofactor, $Mg^{2+}$. In the course of understanding the mechanism of these enzymes, the possibility of metal ion binding to thiamin has been suggested by Schellenberger. So far, three crystal structures have been reported in which a metal ion is bound to thiamin.[3-5]

Theophanides has reported[6] the synthesis, and proposed structures, for two compounds resulting from the reaction of (Hthiamin)$Cl_2$ with $K_2PtCl_4$ in aqueous solution: a salt of formula (thiamin)$_2$($PtCl_4$) and a zwitterionic complex Pt(thiamin)$Cl_3$, where the metal is bound through N(1′). In our hands[7] the procedure reported[6] to produce (thiamin)$_2$($PtCl_4$) instead always produced Pt(thiamin)$Cl_3$. Here we report a synthetic procedure for both (Hthiamin)($PtCl_4$) and Pt(thiamin)$Cl_3$, a study of these materials in DMSO solution and the crystal structures of (I) an ionic 1:1 salt (Hthiamin)($PtCl_4$), (II) an ionic 2:1 double salt (Hthiamin)$_2$($PtCl_4$)$Cl_2$·$2H_2O$, and (III) the 1:1 complex Pt(thiamin)$Cl_3$·$H_2O$.

## Experimental Section

**Synthesis of Pt(thiamin)$Cl_3$·$H_2O$.** The reaction was carried out in aqueous solution at pH 3–4, with an excess of thiamin to increase the yield. Twenty milliliters of an aqueous solution 0.06 M in $K_2PtCl_4$ was mixed with 20 mL of a solution 0.12 M in (Hthiamin)$Cl_2$ at room temperature. A yellow precipitate appeared within minutes. The mixture was stirred for 24 h and the precipitate collected by filtration through a glass frit, washed with 3 × 5-mL portions of 95% ethanol followed by 3 × 5-mL portions of anhydrous diethyl ether. Anal. Calcd for $C_{12}H_{19}N_4O_2SPtCl_3$: C, 24.63; H, 3.25; N, 9.65; Pt, 33.37; Cl, 18.19. Found:[8] C, 25.17; H, 3.19; N, 9.73; Pt, 32.99; Cl, 18.17. The degree of hydration was established from the X-ray analysis.

**Table I.** $^1$H NMR Spectral Data and Peak Assignments in DMSO-$d_6$ (δ(TMS) = 0.0 ppm)

| peak assignt[a] | chem shift[c] (Hthiamin)-$Cl_2$ | (thiamin)-$NO_3$ | Pt(thiamin)-$Cl_3$ | (Hthiamin)-($PtCl_4$) |
|---|---|---|---|---|
| H(2)[b] | 9.98 (s, 1 H) | 9.48 (s, 1 H) | 9.63 (s, 1 H) | 9.92 (s, 1 H) |
| H(21′) | 2.54 (s, 3 H) | 2.38 (s, 3 H) | 3.04 (s, 3 H) | 2.57 (s, 3 H) |
| H(35′) | 5.63 (s, 2 H) | 5.35 (s, 2 H) | 5.45 (s, 2 H) | 5.68 (s, 2 H) |
| H(41) | 2.57 (s, 3 H) | 2.50 (s, 3 H) | 2.49 (s, 3 H) | 2.59 (s, 3 H) |
| H(41′)[b] | 9.23 (s, 2 H) | 7.15 (s, 2 H) | 7.80 (s, 2 H) | 9.20 (s, 1 H) |
| | | | | 8.94 (s, 1 H) |
| H(51) | 3.07 (t, 2 H) | 3.07 (t, 2 H) | 3.07 (t, 2 H) | 3.07 (t, 2 H) |
| H(52) | 3.65 (t, 2 H) | 3.67 (q, 2 H) | 3.65 (t, 2 H) | 3.67 (t, 2 H) |
| H(53)[b] | | 5.24 (t, 1 H) | 5.25 (s, 1 H) | |
| H(6′) | 8.37 (s, 1 H) | 8.08 (s, 1 H) | 8.46 (s, 1 H) | 8.57 (s, 1 H) |

[a] The protons are numbered according to the numbering scheme of the non-hydrogen atoms to which they are bound. [b] These protons undergo exchange with $D_2O$. [c] s = singlet, t = triplet, and q = quartet.

The compound is insoluble in numerous organic solvents or solvent pairs. It dissolved well only in DMSO. However, within 15 min significant decomposition is evident by $^1$H NMR spectroscopy (vide infra).

**Synthesis of (Hthiamin)($PtCl_4$).** Ten milliliters of an aqueous solution 0.2 M in $K_2PtCl_4$ was mixed with 10 mL of a solution 0.2 M in (Hthiamin)$Cl_2$. A salmon precipitate appeared immediately. After the solution was stirred for 24 h at room temperature, the precipitate was collected and washed as previously described (vide supra). Anal. Calcd for $C_{12}H_{18}N_4OSPtCl_4$: C, 23.87; H, 2.98; N, 9.28; Pt, 32.35; Cl, 23.51. Found:[8] C, 23.94;, H, 3.06; N, 9.30; Pt, 31.59; Cl, 21.57.

**$^1$H NMR Studies.** Spectra of (Hthiamin)$Cl_2$, thiamin nitrate and (Hthiamin)($PtCl_4$) in DMSO were determined. The corresponding chemical shifts as well as the chemical shifts of a freshly prepared solution of Pt(thiamin)$Cl_3$ in DMSO are reported in Table I. No $^{195}$Pt–$^1$H coupling between the metal ion and the H(6′) has been detected.

A $^1$H NMR spectrum acquired on a fresh DMSO solution of (Hthiamin)($PtCl_4$) displays only the signals typical of protonated thiamin (Table I). Over a period of 15 min, signals due to (Hthiamin)($PtCl_4$) diminish and those due to Pt(thiamin)$Cl_3$ appear and grow.

A typical $^1$H NMR spectrum in DMSO of a freshly prepared sample of Pt(thiamin)$Cl_3$ shows not only peaks for the complex but also traces of another component (Figure 1a). After only 15 min, the peaks of the minor component become half as large as those for Pt(thiamin)$Cl_3$ and additional minor peaks appear (Figure 1b). With time, the spectrum becomes even more complicated. The first two sets of peaks disappear slowly, and eventually, after a week, the presence of free thiazole [δ 8.79 (H(2)), 2.30 (H(41))][9,10] among a complex mixture of several components is detected.

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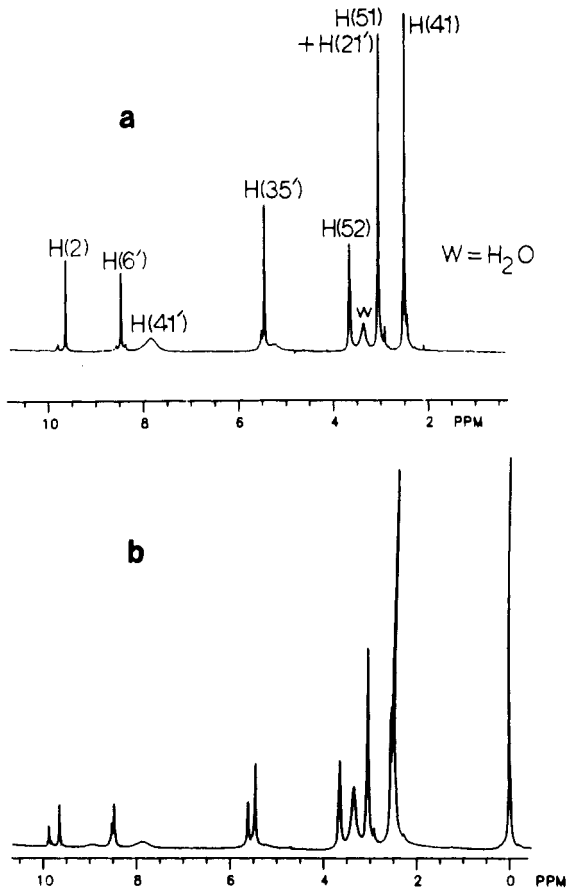


**Figure 1.** (a) $^1H$ NMR spectrum of a freshly prepared sample of Pt(thiamin)$Cl_3$ in DMSO. (b) $^1H$ NMR spectrum of sample 15 min after preparation.

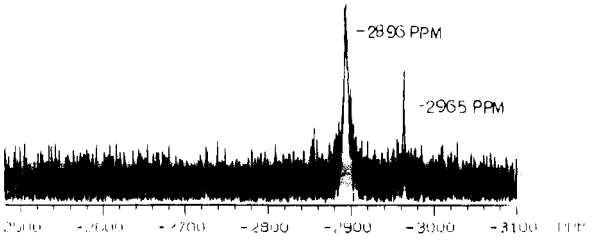


**Figure 2.** $^{195}Pt$ NMR spectrum of a sample of Pt(thiamin)$Cl_3$ in DMSO 60 min after preparation.

**$^{195}Pt$ NMR Studies.** $^{195}Pt$ NMR shifts were referenced to the $^{195}Pt$ resonance of $H_2PtCl_6$. In the $^{195}Pt$ NMR spectrum of a freshly prepared solution of Pt(thiamin)$Cl_3$ only one resonance at $\delta = -2896$ is observed. After 60 min, the spectrum (Figure 2) shows two peaks, one at $\delta = -2896$ and another sharp resonance at $\delta = -2965$. After 3 h, the peak at $\delta = -2896$ has practically broadened into the base line, while the peak at $\delta = -2965$ has increased in intensity.

A comparison of the $^{195}Pt$ shifts with that of KPt(DMSO)$Cl_3$ was helpful in identifying the species in solution. A $^{195}Pt$ spectrum of KPt(DMSO)$Cl_3$[11] in DMSO showed one sharp resonance at $\delta = -2964$. The spectrum after $^1/_2$ h showed an additional sharp resonance at $\delta = -3455$. These resonances are in close agreement with those reported by Goggin[12] for $(Pt(DMSO)Cl_3)^-$ and $Pt(DMSO)_2Cl_2$, respectively. In the presence of thiamin nitrate, the $^{195}Pt$ NMR spectrum of KPt(DMSO)$Cl_3$ showed a small peak at $\delta = -2965$ and a more intense one at $\delta = -3393$.

**Conductivity Measurements.** Conductance measurements at room temperature (25 °C) were carried out for four thiamin salts, as well as Pt(thiamin)$Cl_3$ and are reported in Table II. A fresh DMSO solution of Pt(thiamin)$Cl_3$ yields a nearly zero value, indicating the compound to be a nonconductor. However, conductance increases as a function of time and levels off after several hours, at a value consistent with a 1:1 electrolyte, in agreement with data reported by Theophanides.[6]

**Table II.** Equivalent Conductance of Thiamin Compounds in DMSO

| compd | $\Lambda_{equiv}$, $cm^2\ \Omega^{-1}$ $equiv^{-1}$ | compd | $\Lambda_{equiv}$, $cm^2\ \Omega^{-1}$ $equiv^{-1}$ |
|---|---|---|---|
| (thiamin)($Ph_4B$) | 26.4 | (thiamin)($NO_3$) | 38.1 |
| Pt(thiamin)$Cl_3$ | | (Hthiamin)($PtCl_4$) | 51.7 |
| after 3 min | 3.4 | (Hthiamin)$Cl_2$ | 53.3 |
| after 180 min | 32.1 | | |

## X-Ray Crystallographic Studies

**Preparation of the Crystals.** Because of the rapid decomposition when III is dissolved in DMSO, no recrystallization was possible in this solvent. Numerous attempts, using various techniques, to grow single crystals from the direct reaction of $(PtCl_4)^{2-}$ and (Hthiamin)$Cl_2$ led to microcrystalline powders. A few clusters of very thin, bladelike crystals of Pt(thiamin)$Cl_3 \cdot H_2O$ were finally obtained from a mixture of 7 mL of 0.05 M (Hthiamin)$Cl_2$ and 1 mL of $K_2PtCl_4$, also 0.05 M, when the mixture was allowed to stand overnight at room temperature. These tiny crystals grew upon further addition of 1 to 2 drops per day of the $K_2PtCl_4$ solution. After a week, a few crystals suitably large for X-ray crystallography resulted.

Diffraction quality crystals of I and II were obtained by slow evaporation of the aqueous filtrate from the synthesis of Pt(thiamin)$Cl_3$.

**X-ray Data Collection and Reduction.** An orange, chunky crystal of (Hthiamin)($PtCl_4$) (I), a yellow platelike crystal of $(Hthiamin)_2(PtCl_4)Cl_2 \cdot 2H_2O$ (II), and a yellow bladelike crystal of Pt(thiamin)$Cl_3 \cdot H_2O$ (III), with a hairy belly, were chosen for this study. Each crystal was glued on a glass fiber with its longest edge parallel to the fiber, by using epoxy cement. The cell parameters and their standard deviations were determined by a least-squares fit of the angular coordinates of 15 unique reflections with $2\theta$ values from 41 to 55° for I, from 3.5 to 19° for II, and from 18 to 35° for III. Partial rotation axial photographs and output from the diffractometer autoindexing routine for each crystal showed no symmetry, indicating the crystal systems to be triclinic. The centrosymmetric space group $P\bar{1}$ was assumed for each crystal and was confirmed by satisfactory refinement of the structures to low error indices. Data collection and processing were carried out by using standard procedures in our laboratory.[13] A summary of the crystal data, as well as data collection and refinement parameters for each crystal, is given in Table III.

Data were corrected for decay based on the intensity of three standard reflections measured every 50 reflections for I and II and every 100 reflections for III. For I, variations of up to 20% in the intensities of the check reflections required recentering of the crystal periodically during data collection. Intensities for check reflections of II and III varied at most 10% and 13%, respectively. Only intensities for which $I > 3\sigma(I)$ were used in the solution and refinement of each structure. Data were corrected for Lorentz and polarization effects. An absorption correction was applied on the data set of each crystal, based on a definition of the crystal shape[14] for I and II and based on $\psi$ scans[15] for III.

**Solution and Refinement of the Structures.** The structure of each crystal was solved by employing heavy-atom methods.

For I, two positions for the platinum ions, located at the inversion centers 0, 0, 0 and $^1/_2$, $^1/_2$, $^1/_2$, were deduced from a three-dimensional Patterson map. Subsequent difference Fourier maps revealed the positions of all remaining non-hydrogen atoms. An absorption correction applied to the data set with a 4 × 4 × 4 grid, followed by anisotropic refinement, led to $R_1 = 0.071$ and $R_2 = 0.105$. A close examination of the electron density maps revealed considerable electron density around the Pt and Cl positions. A survey of reflections whose weighted-residual-square values were unusually large (>300) pinpointed 41 reflections whose intensity peak profiles were skewed to either side of the peak center, possibly due to crystal movement. Removal of these 41 reflections from the original data set followed by one cycle of refinement resulted in a lowering of the error indices and a significant decrease in spurious electron density. Having traced the problem to these reflections, we proceeded with the structure refinement using the original data set. The

(11) KPt(DMSO)$Cl_3$ was prepared according to the method described by: Kukushkin, Yu. N.; Vyaz'menskii, Yu. E.; Zorina, L. T. *Russ. J. Inorg. Chem.* (*Engl. Transl.*) **1968**, 1573–1576.

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**Table III.** Summary of Crystal Parameters and Data Collection for I–III

| | (Hthiamin)($PtCl_4$) | (Hthiamin)$_2$($PtCl_4$)$Cl_2$·$2H_2O$ | Pt(thiamin)$Cl_3$·$H_2O$ |
|---|---|---|---|
| formula | $C_{12}H_{18}N_4OSPtCl_4$ | $C_{24}H_{40}N_8S_2O_4PtCl_6$ | $Cl_2H_{19}N_4O_2SPtCl_3$ |
| fw | 603.26 | 976.48 | 584.5 |
| $a$, Å | 9.806 (3) | 11.449 (7) | 9.714 (6) |
| $b$, Å | 11.769 (9) | 12.214 (6) | 15.081 (6) |
| $c$, Å | 8.350 (5) | 6.932 (4) | 6.927 (3) |
| $\alpha$, deg | 103.00 (5) | 103.10 (4) | 93.86 (3) |
| $\beta$, deg | 95.79 (4) | 102.86 (5) | 109.78 (4) |
| $\gamma$, deg | 82.36 (4) | 73.78 (4) | 98.43 (4) |
| $V$, Å$^3$ | 928.2 (8) | 893.3 (8) | 937.2 (8) |
| $Z$ | 2 | 1 | 2 |
| $d$, g/cm$^3$ | 2.16 (calcd, 25 °C) | 1.81 (calcd, 25 °C)<br>1.80 (2) (exptl, 25 °C) | 2.07 (calcd) |
| space group | $P\bar{1}$ | $P\bar{1}$ | $P\bar{1}$ |
| cryst dimens, mm | 0.17 × 0.12 × 0.30 | 0.14 × 0.025 × 0.16 | 0.03 × 0.25 × 0.8 |
| radiation, Å | Mo K$\alpha$ | Mo K$\alpha$ | Mo K$\alpha$ |
| $\mu$, cm$^{-1}$ | 86.3 | 47.3 | 52.55 |
| transmissn coeff | 0.38–0.54 | 0.56–0.88 | 0.60–1.00 |
| $2\theta$ limits, deg | 3.0–65.0 | 3.0–60.0 | 3.0–50.0 |
| $p$ | 0.02 | 0.02 | 0.02 |
| final no. of variables | 217 | 208 | 220 |
| no. of unique data measd | 6684 | 6516 | 3456 |
| no. of unique data used ($I > 3\sigma(I)$) | 4438 | 4455 | 2348 |
| $R_1$ | 0.070 | 0.049 | 0.0623 |
| $R_2$ | 0.104 | 0.047 | 0.0623 |
| overdetermination ratio | 20.3 | 21.4 | 10.7 |

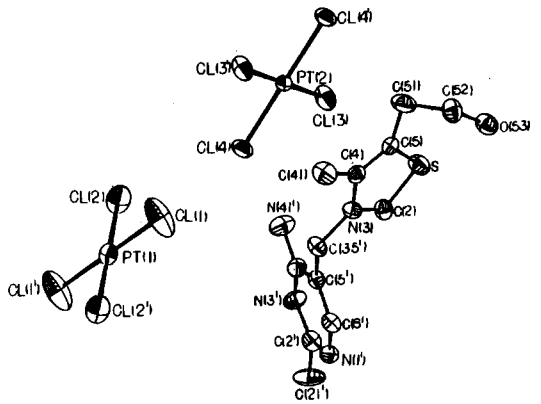


**Figure 3.** Perspective view of (Hthiamin)$PtCl_4$ showing the atomic numbering scheme used. 50% thermal ellipsoids are shown. The chloro ligands, Cl($n$) and Cl($n'$), are related by an inversion center.

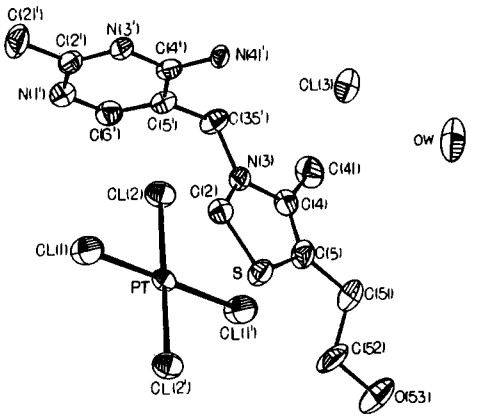


**Figure 4.** Persepctive view of the double salt (Hthiamin)$_2$($PtCl_4$)$Cl_2$·$2H_2O$ using 50% thermal ellipsoids. Chloro ligands Cl(1) and Cl(1′) are related by a center of inversion.

final $R$ values are $R_1 = 0.070$ and $R_2 = 0.104$, and in the last cycle of refinement, all the 217 variables had shifted by less than 0.33 esds. The final difference Fourier map with an esd of 0.46 e/Å$^3$ still showed significant density about 0.8 Å from the Pt positions.

The structure solution and refinement of crystals of II and III proceeded similarly to that of I. Location of the Pt position via a Patterson map was followed by location of all remaining non-hydrogen atoms in the ensuing Fourier maps.

**Table IV.** Positional Parameters for (Hthiamin)($PtCl_4$)

| | $x$ | $y$ | $z$ |
|---|---|---|---|
| Pt(1) | 0.0 | 0.0 | 0.0 |
| Pt(2) | 0.5 | 0.5 | 0.5 |
| Cl(1) | 0.1513 (8) | 0.1155 (7) | 0.1617 (7) |
| Cl(2) | −0.0025 (6) | 0.1058 (5) | −0.1998 (7) |
| Cl(3) | 0.6172 (5) | 0.4271 (4) | 0.2650 (5) |
| Cl(4) | 0.3965 (5) | 0.3303 (4) | 0.4514 (5) |
| S | 0.9387 (5) | 0.2874 (4) | 0.4401 (5) |
| N(1′) | 0.731 (1) | −0.204 (1) | 0.302 (2) |
| C(6′) | 0.734 (2) | −0.107 (1) | 0.427 (2) |
| C(2′) | 0.665 (2) | −0.193 (1) | 0.158 (2) |
| C(21′) | 0.664 (2) | −0.303 (1) | 0.022 |
| N(3′) | 0.596 (2) | −0.094 (1) | 0.129 (2) |
| C(4′) | 0.597 (2) | 0.003 (1) | 0.250 (2) |
| N(41′) | 0.533 (2) | 0.103 (1) | 0.214 (2) |
| C(5′) | 0.671 (2) | −0.002 (1) | 0.409 (2) |
| C(35′) | 0.669 (2) | 0.102 (1) | 0.552 (2) |
| N(3) | 0.760 (1) | 0.190 (1) | 0.533 (1) |
| C(2) | 0.848 (3) | 0.173 (1) | 0.417 (2) |
| C(4) | 0.766 (2) | 0.296 (1) | 0.651 (2) |
| C(41) | 0.678 (2) | 0.321 (2) | 0.796 (2) |
| C(5) | 0.855 (2) | 0.361 (1) | 0.613 (2) |
| C(51) | 0.884 (2) | 0.480 (1) | 0.705 (2) |
| C(52) | 1.039 (2) | 0.475 (2) | 0.794 (2) |
| O(53) | 1.141 (1) | 0.424 (1) | 0.678 (1) |

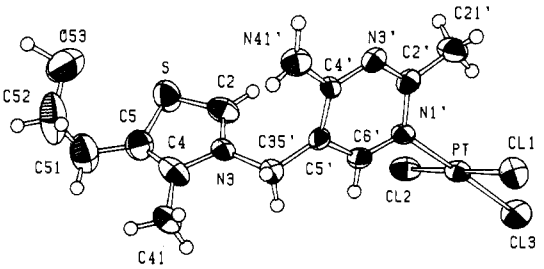


**Figure 5.** Perspective view and numbering scheme of the complex Pt(thiamin)$Cl_3$ using 50% thermal ellipsoids.

For II, application of an absorption correction by using a 4 × 4 × 4 grid followed by anisotropic refinement resulted in final $R$ indices of $R_1 = 0.049$ and $R_2 = 0.047$. After the last cycle of refinement, shifts of all 208 parameters were less than one-tenth of their corresponding esds, the biggest remaining peak being equivalent to 0.21 e/Å$^3$.

In III, the absorption correction was made using $\psi$ scans of four reflections with $2\theta$ values ranging from 19.84 to 35.26°. All hydrogens but H(41′), H(53), and the H's of the solvent were assigned fixed pos-

**Table V.** Positional Parameters for $(Hthiamin)_2(PtCl_4)Cl_2 \cdot 2H_2O$

| | x | y | z |
|---|---|---|---|
| Pt | 0.0 | 0.0 | 0.0 |
| Cl(1) | −0.1446 (2) | 0.0528 (1) | 0.2045 (3) |
| Cl(2) | −0.0785 (1) | 0.1717 (1) | −0.1209 (2) |
| Cl(3) | 0.3343 (1) | 0.3781 (2) | 0.6179 (2) |
| S | 0.2567 (1) | 0.0084 (1) | 0.4853 (2) |
| N(1′) | −0.2465 (5) | 0.3529 (3) | 0.5282 (7) |
| C(6′) | −0.1578 (6) | 0.3194 (5) | 0.4106 (8) |
| C(2′) | −0.2247 (5) | 0.4132 (5) | 0.7142 (5) |
| C(21′) | −0.3283 (6) | 0.4497 (6) | 0.835 (1) |
| N(3′) | −0.1184 (4) | 0.4396 (4) | 0.7942 (7) |
| C(4′) | −0.0247 (5) | 0.4020 (4) | 0.6882 (8) |
| N(41′) | 0.0819 (5) | 0.4271 (4) | 0.7763 (7) |
| C(5′) | −0.0442 (5) | 0.3415 (4) | 0.4855 (7) |
| C(35′) | 0.0511 (6) | 0.3078 (5) | 0.3521 (8) |
| N(3) | 0.1413 (4) | 0.1954 (4) | 0.3748 (6) |
| C(2) | 0.1411 (5) | 0.1281 (4) | 0.5010 (8) |
| C(4) | 0.2331 (5) | 0.1519 (5) | 0.2561 (8) |
| C(41) | 0.2400 (6) | 0.2161 (6) | 0.1020 (9) |
| C(5) | 0.3053 (6) | 0.0493 (5) | 0.2992 (9) |
| C(51) | 0.4133 (6) | −0.0281 (6) | 0.200 (1) |
| C(52) | 0.4138 (7) | −0.1534 (1) | 0.175 (1) |
| O(53) | 0.5121 (5) | −0.2238 (4) | 0.0694 (7) |
| O(W) | 0.5458 (4) | 0.2800 (5) | 0.3536 (7) |

**Table VI.** Positional Parameters for $Pt(thiamin)Cl_3 \cdot H_2O$

| | x | y | z |
|---|---|---|---|
| Pt | 0.1379 (1) | 0.1689 (1) | 0.2699 (1) |
| Cl(1) | 0.3724 (5) | 0.2560 (4) | 0.3567 (8) |
| Cl(2) | −0.0880 (6) | 0.0782 (4) | 0.1889 (8) |
| Cl(3) | 0.0359 (6) | 0.2721 (4) | 0.0654 (9) |
| C(35′) | 0.319 (2) | −0.150 (1) | 0.332 (3) |
| N(1′) | 0.230 (2) | 0.077 (1) | 0.443 (2) |
| C(2′) | 0.292 (2) | 0.090 (1) | 0.658 (3) |
| C(21′) | 0.268 (2) | 0.169 (2) | 0.769 (3) |
| N(3′) | 0.376 (2) | 0.034 (1) | 0.760 (2) |
| C(4′) | 0.389 (2) | −0.040 (1) | 0.665 (2) |
| N(41′) | 0.479 (2) | −0.092 (1) | 0.780 (3) |
| C(5′) | 0.312 (2) | −0.066 (1) | 0.450 (3) |
| C(6′) | 0.239 (2) | −0.001 (1) | 0.354 (3) |
| S | 0.0989 (8) | −0.3379 (4) | 0.533 (1) |
| C(2) | 0.168 (2) | −0.235 (2) | 0.504 (3) |
| N(3) | 0.244 (2) | −0.235 (1) | 0.381 (2) |
| C(4) | 0.254 (2) | −0.321 (2) | 0.302 (3) |
| C(41) | 0.334 (2) | −0.330 (2) | 0.156 (3) |
| C(5) | 0.180 (3) | −0.384 (2) | 0.372 (4) |
| C(51) | 0.168 (3) | −0.483 (2) | 0.334 (5) |
| C(52) | 0.269 (4) | −0.521 (2) | 0.500 (6) |
| O(53) | 0.249 (5) | −0.498 (2) | 0.691 (4) |
| O(W) | 0.332 (5) | 0.400 (3) | −0.007 (5) |

itions idealized to $d_{C-H}$ = 0.95 Å and $d_{N-H}$ = 0.95 Å and were refined isotropically. On the basis of 220 variables and 2346 observations, refinement of this model converged to values of $R_1$ and $R_2$ of 0.062. After the last cycle of refinement, the 220 parameters shifted by less than 0.6 esds. The two biggest remaining peaks are equivalent to about 2.0 e/Å$^3$ and are located in the vicinity of the Pt atoms.

The final positional parameters of I, II, and III are listed in Tables IV–VI along with the standard deviations. Hydrogen positional parameters of III and thermal parameters of I, II, and III are listed in Tables XIII–XVI (supplementary material). Figures 3–5 display ORTEP drawings of I, II, and III, respectively, and their labeling scheme.

## Description of the Structures

**Structure of the Salts.** The centrosymmetric triclinic unit cell of $(Hthiamin)PtCl_4$ contains two thiamin cations related by an inversion center and two independent tetrachloroplatinate anions, each of which resides on a center of symmetry. In contrast, II is a double salt, whose asymmetric unit consists of a thiamin cation, a chloride anion, a water molecule and half of a tetrachloroplatinate anion, which is located at a center of symmetry. In both compounds, the cation is protonated thiamin, which carries a +2 charge. In the unit cell of I, the four negative charges that are required for electroneutrality are provided by the two $(PtCl_4)^{2-}$ ions. In the unit cell of II, the four negative charges are provided by one $(PtCl_4)^{2-}$ ion and two $Cl^-$ ions.

**Table VII.** Bond Lengths (Å)

| | I | II | III |
|---|---|---|---|
| Pt–Cl(1) | 2.276 (7) | 2.280 (2) | 2.316 (5) |
| Pt–Cl(2) | 2.292 (6) | 2.231 (6) | 2.277 (6) |
| Pt–Cl(3) | 2.312 (4) | | 2.282 (6) |
| Pt–N(1′) | | | 2.01 (2) |
| Pt–Cl(4) | 2.297 (4) | | |
| N(1′)–C(6′) | 1.36 (2) | 1.359 (7) | 1.32 (3) |
| N(1′)–C(2′) | 1.34 (2) | 1.341 (7) | 1.39 (2) |
| C(2′)–N(3′) | 1.32 (2) | 1.314 (7) | 1.33 (2) |
| C(2′)–C(21′) | 1.52 (2) | 1.511 (9) | 1.46 (3) |
| N(3′)–C(4′) | 1.35 (2) | 1.352 (7) | 1.31 (2) |
| C(4′)–N(41′) | 1.34 (2) | 1.321 (7) | 1.34 (2) |
| C(4′)–C(5′) | 1.45 (2) | 1.432 (7) | 1.42 (2) |
| C(5′)–C(6′) | 1.34 (2) | 1.366 (8) | 1.37 (3) |
| C(5′)–C(35′) | 1.50 (2) | 1.498 (8) | 1.49 (3) |
| C(35′)–N(3) | 1.50 (2) | 1.487 (7) | 1.49 (2) |
| N(3)–C(2) | 1.33 (2) | 1.331 (7) | 1.30 (3) |
| N(3)–C(4) | 1.41 (2) | 1.392 (7) | 1.40 (3) |
| C(2)–S | 1.68 (2) | 1.678 (6) | 1.65 (2) |
| C(5)–S | 1.73 (2) | 1.729 (6) | 1.74 (3) |
| C(4)–C(5) | 1.34 (2) | 1.352 (8) | 1.33 (3) |
| C(5)–C(51) | 1.49 (2) | 1.526 (9) | 1.47 (4) |
| C(4)–C(41) | 1.51 (2) | 1.490 (8) | 1.48 (3) |
| C(51)–C(52) | 1.62 (3) | 1.50 (1) | 1.45 (5) |
| C(52)–O(53) | 1.44 (2) | 1.444 (9) | 1.43 (5) |

As in other structures containing protonated thiamin,[16-20] the cation is protonated at the N(1′) position. Although the hydrogen atoms in the molecule were not located, the site of protonation was deduced from the angle C(6′)–N(1′)–C(2′)[4] and from the hydrogen-bonding scheme about the N(1′) atom. Bond lengths within the cation for I and II (Table VII) are indistinguishable from one another and from previously reported thiamin structures in the F conformation.[4,17] There are also no significant differences in the bond angle measurements for the two compounds.

Calculations of least-square planes for both the pyrimidine and the thiazolium rings in I and II (Tables XVII and XVIII, supplementary material) show that the rings are strictly planar. The orientation of these planes about the methylene bridge for both structures is that of the F conformer. The angles $\Phi_T$ and $\Phi_P$[17] for I are +9.0 and +76.7°, respectively, the absolute values of which are identical with those noted for $(Hthiamin)Cl_2$.[16] In II, these are +0.3 and +85.8°, respectively. The values for two bond angles, C(2)–N(3)–C(35′) and C(4)–N(3)–C(35′), which are good indicators of molecular conformation, are those expected for the F form, and are statistically different from thiamin structures in the S conformation.[4,5]

The torsion angles $\Phi_{5\alpha}$ and $\Phi_{5\beta}$, which describe the conformation of the hydroxyethyl side chain,[21] are quite different in the two compounds. In I, $\Phi_{5\alpha}$ = −67.6° and $\Phi_{5\beta}$ = −56.3°, while in II, these are +36.4 and +176.4°, respectively. This variance results from the S–O(53) intramolecular contact, which is observed in I but is absent in II. The $\Phi_{5\alpha}$ angle observed for I is typical of those structures where the hydroxyethyl side chain rotates toward the thiazolium ring to allow this electrostatic interaction. The S–O(53) distance of 3.02 (1) Å in I is much shorter than the van der Waals distance between these two atoms and falls within the reported range 2.88–3.06 Å for this interaction.[4,22]

Hydrogen bonds and electrostatic contacts are the predominant intermolecular interactions in the crystal structures of both I and II. These contacts (Tables VIII and IX) are representative of those observed in thiamin and thiamin-related compounds. The

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**Table VIII.** Possible Hydrogen-Bonding Interactions, A–H--B, and Other Short Contacts in (Hthiamin)$PtCl_4$

| A | B | equiv posn of B | A--B, Å |
|---|---|---|---|
| | | Hydrogen Bonds | |
| N(1′) | Cl(2) | $1-x, -y, -z$ | 3.29 (1) |
| N(1′) | Cl(4) | $1-x, -y, 1-z$ | 3.23 (1) |
| N(1′) | O(53) | $2-x, -y, 1-z$ | 2.76 (2) |
| N(41′) | Cl(4) | $x, y, z$ | 3.18 (2) |
| N(41′) | N(3′) | $1-x, -y, -z$ | 2.99 (2) |
| O(53) | Cl(3) | $2-x, 1-y, 1-z$ | 3.07 (1) |
| Cl(4) | O(53) | $-1+x, y, z$ | 3.22 (1) |
| | | Electrostatic Contacts | |
| S | O(53) | $x, y, z$ | 3.02 (1) |
| S | Cl(1) | $1+x, y, z$ | 3.404 (8) |
| C(2) | Cl(2) | $1+x, y, 1+z$ | 3.59 (2) |
| C(2) | Cl(2) | $1-x, -y, -z$ | 3.59 (2) |
| N(3) | Cl(2) | $1+x, y, 1+z$ | 3.28 (2) |
| C(4) | Cl(2) | $1+x, y, 1+z$ | 3.33 (2) |
| C(2′) | Cl(2) | $1-x, -y, -z$ | 3.56 (2) |
| C(6′) | Cl(1) | $1-x, -y, 1-z$ | 3.53 (2) |
| C(6′) | Cl(2) | $1-x, -y, -z$ | 3.40 (2) |
| C(6′) | Cl(4) | $1-x, -y, 1-z$ | 3.46 (2) |
| O(53) | C(2) | $2-x, -y, 1-z$ | 3.56 (2) |
| N(3′) | Cl(1) | $1-x, -y, -z$ | 3.59 (2) |

**Table IX.** Possible Hydrogen-Bonding Interactions, A–H--B, and Other Short Contacts in (Hthiamin)$_2(PtCl_4)Cl_2 \cdot 2H_2O$

| A | B | equiv posn of B | A--B, Å |
|---|---|---|---|
| | | Hydrogen Bonds | |
| N(1′) | O(W) | $1-x, y, z$ | 2.706 (7) |
| N(41′) | N(3′) | $-x, 1-y, 2-z$ | 3.053 (7) |
| N(41′) | Cl(3) | $x, y, z$ | 3.173 (5) |
| C(2) | Cl(1) | $-x, -y, 1-z$ | 3.318 (6) |
| Cl(3) | O(W) | $x, y, z$ | 3.165 (5) |
| O(W) | O(53) | $-x+1, -y, -z$ | 2.826 (5) |
| N(1′) | Cl(3) | $-x, 1-y, 1-z$ | 3.470 (4) |
| | | Electrostatic Contacts | |
| N(3) | Cl(3) | $x, y, z$ | 3.479 (5) |
| C(4) | Cl(3) | $x, y, z$ | 3.553 (6) |
| C(2′) | Cl(2) | $x, y, 1+z$ | 3.274 (6) |
| N(3′) | Cl(2) | $x, y, 1+z$ | 3.343 (5) |
| C(6′) | Cl(1) | $x, y, z$ | 3.222 (6) |
| C(35′) | Cl(2) | $x, y, z$ | 3.529 (6) |
| C(35′) | Cl(3) | $x, y, z$ | 3.581 (6) |
| S | Cl(1) | $-x, -y, 1-z$ | 3.053 (5) |
| O(53) | Cl(3) | $1-x, -y, 1-z$ | 3.106 (5) |

hydrogen bond between the C(2) proton and a chloro ligand observed in II is consistent with the acidic nature of this proton[16]. Other hydrogen-bond donors include the N(1′) atom, the exocyclic nitrogen N(41′), and the hydroxy oxygen atom O(53). Typical bases involved in these contacts are the chloro ligands bound to the Pt(II) ion, the N(3′) atom of the pyrimidine group, the oxygen atom of a water molecule, and a chloride counterion.

The most frequently observed electrostatic contacts in thiamin structures occur between the positively charged atoms of the thiazolium ring and electronegative atoms or ions. These interactions are observed in both compounds, together with similar dipolar attractions between chloride ions and the pyrimidine moiety, which acquires positive charge via coordination of a proton to N(1′).

The coordination about the Pt(II) ion in both crystal structures is strictly planar since the Pt position is at an inversion center. The square planar geometry is also confirmed by bond angle measurements (Table X). There are no significant differences in the metrical parameters in the anion in this structure compared to previous reports of $(PtCl_4)^{2-}$-containing structures.[22-24]

**Structure of the Complex.** The crystal structure of Pt(thiamin)$Cl_3 \cdot H_2O$ consists of two complexes and two water molecules per centrosymmetric triclinic unit cell. Interactions between complexes consist of base stacking of pyrimidine rings, electrostatic interactions and hydrogen bonds. All other contacts are van der Waals contacts, and none is shorter than 3.70 Å.

The pyrimidine rings stack in a head-to-tail fashion across an inversion center with a mean separation of 3.45 (5) Å. Pyrimidine stacking was previously observed in the structure of the two other monomeric complexes;[4,5] however, the stacking arrangement here is different and results in an unusual network of hydrogen bonds and dipolar interactions between molecules within stacked pairs and between molecules of adjacent stacked pairs (Table XI).

Within a pair, the exocyclic N(41′) of one molecule stacks over C(6′) of a second pyrimidine ring and also hydrogen bonds to Cl(1) of the second molecule (Figure 6). This causes the pyrimidine to be overlapped by C(35′), C(4′), C(5′), and N(41′) of the other molecule (Figure 7, supplementary material). Atoms C(2′), N(3′), and C(4′) of each of this pair of stacked molecules are approached on the outer side by a Cl(2) atom of one of the molecules of the next stacked pair along the stacking direction (Figure 6). Fur-

**Table X.** Bond Angles (deg)

| | I | II | III |
|---|---|---|---|
| Cl(1)–Pt–Cl(2) | 89.7 (2) | 90.59 (6) | 177.6 (2) |
| Cl(1)–Pt–Cl(3) | | | 90.4 (2) |
| Cl(2)–Pt–Cl(3) | | | 91.9 (2) |
| Cl(3)–Pt–Cl(4) | 89.6 (1) | | |
| Cl(1)–Pt–N(1′) | | | 89.2 (5) |
| Cl(2)–Pt–N(1′) | | | 88.5 (5) |
| Cl(3)–Pt–N(1′) | | | 178.2 (5) |
| Pt–N(1′)–C(2′) | | | 124 (1) |
| Pt–N(1′)–C(6′) | | | 120 (1) |
| C(2′)–N(1′)–C(6′) | 118 (1) | 119.9 (5) | 115 (2) |
| N(3′)–C(2′)–N(1′) | 122 (1) | 123.0 (5) | 121 (2) |
| N(3′)–C(2′)–C(21′) | 119 (2) | 119.8 (5) | 120 (2) |
| N(1′)–C(2′)–C(21′) | 117 (2) | 117.1 (5) | 119 (2) |
| C(2′)–N(3′)–C(4′) | 118 (1) | 119.3 (4) | 121 (2) |
| N(41′)–C(4′)–N(3′) | 116 (2) | 117.5 (5) | 117 (2) |
| N(41′)–C(4′)–C(5′) | 123 (1) | 122.4 (5) | 121 (2) |
| N(3′)–C(4′)–C(5′) | 120 (1) | 120.2 (5) | 121 (2) |
| C(6′)–C(5′)–C(4′) | 117 (1) | 117.3 (5) | 113 (2) |
| C(6′)–C(5′)–C(35′) | 120 (1) | 119.5 (5) | 122 (2) |
| C(4′)–C(5′)–C(35′) | 123 (1) | 123.0 (5) | 125 (2) |
| N(1′)–C(6′)–C(5′) | 122 (1) | 120.1 (5) | 127 (2) |
| N(3)–C(35′)–C(5′) | 112 (1) | 114.1 (4) | 114 (2) |
| C(2)–N(3)–C(4) | 114 (1) | 114.9 (4) | 114 (2) |
| C(2)–N(3)–C(35′) | 125 (1) | 124.9 (4) | 124 (2) |
| C(4)–N(3)–C(35′) | 120 (1) | 120.2 (4) | 122 (2) |
| N(3)–C(2)–S | 112 (1) | 111.4 (4) | 113 (2) |
| C(2)–S–C(5) | 91.4 (8) | 91.6 (3) | 90 (1) |
| C(4)–C(5)–C(51) | 126 (2) | 127.7 (5) | 128 (2) |
| C(4)–C(5)–S | 111 (1) | 110.9 (4) | 111 (2) |
| C(51)–C(5)–S | 122 (1) | 121.4 (4) | 120 (2) |
| C(5)–C(4)–N(3) | 111 (1) | 111.2 (5) | 104 (2) |
| C(5)–C(4)–C(41) | 129 (1) | 128.4 (5) | 129 (2) |
| N(3)–C(4)–C(41) | 120 (1) | 120.3 (5) | 120 (2) |
| C(5)–C(51)–C(52) | 110 (1) | 110.8 (6) | 114 (3) |
| C(51)–C(52)–O(53) | 112 (1) | 109.5 (6) | 111 (3) |

**Table XI.** Possible Hydrgen-Bonding Interactions, A–H--B, and Other Short Contacts in Pt(thiamin)$Cl_3 \cdot H_2O$

| A | B | equiv posn of B | A--B, Å |
|---|---|---|---|
| | | Hydrogen Bonds | |
| Cl(1) | O(W) | $x, y, z$ | 3.40 (4) |
| Cl(3) | O(W) | $x, y, z$ | 3.43 (6) |
| C(2) | Cl(2) | $-x, -y, 1-z$ | 3.43 (2) |
| N(41′) | Cl(1) | $1-x, -y, 1-z$ | 3.28 (2) |
| N(3′) | C(35′) | $1-x, -y, 1-z$ | 3.49 (2) |
| O(W) | O(53) | $x, 1+y, -1+z$ | 2.65 (5) |
| N(3′) | N(41′) | $1-x, -y, 2-z$ | 3.02 (2) |
| | | Electrostatic Contacts | |
| Cl(3) | N(3) | $-x, -y, -z$ | 3.30 (1) |
| Cl(3) | C(4) | $-x, -y, -z$ | 3.31 (2) |
| S | O(53) | $x, y, z$ | 3.07 (4) |
| Cl(2) | C(2′) | $-x, -y, 1-z$ | 3.43 (2) |
| Cl(2) | N(3′) | $-x, -y, 1-z$ | 3.19 (2) |
| Cl(2) | C(4′) | $-x, -y, 1-z$ | 3.39 (2) |

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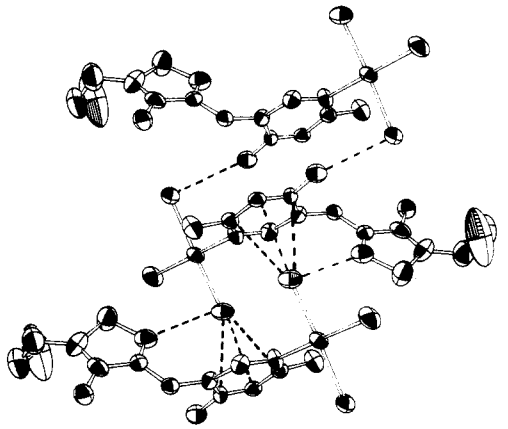

**Figure 6.** Perspective view of Pt(thiamin)$Cl_3$ showing close contacts (broken lines) between 3 molecules at $x, y, z$; $1-x, -y, 1-z$; and $-x, -y, 1-z$ belonging to two adjacent pairs.

thermore, centrosymmetrically related pyrimidines belonging to adjacent stacks are connected by two interbase hydrogen bonds between N(41′) and N(3′) (Figure 8, supplementary material).

A major factor to account for this unusual arrangement in the base stacking is probably the geometry of the metal ion coordination sphere. In Cu(thiamin)$Cl_2$ and Cd(thiamin)$Cl_3$, the trigonal and tetrahedral geometries respectively place the bulky chloro ligands away from the pyrimidine ring, leaving an open space above the ring so that another pyrimidine may stack over it. In the case of Pt(thiamin)$Cl_3$, the 70° dihedral angle between the coordination plane and the pyrimidine plane places the chloro ligands Cl(1) and Cl(2) near the pyrimidine plane, above and below it. In Cu(thiamin)$Cl_2$, C(4′) of one ring stacks directly above C(2′) of another ring in a head-to-tail fashion. Such an overlap of the two pyrimidine rings in Pt(thiamin)$Cl_3 \cdot H_2O$ would result in steric repulsions between N(41′) and the cis chloro ligands. As a result, C(4′) of one ring stacks over N(3′) of the other ring. In Cu(thiamin)$Cl_2$, the base-stacking interaction is strong enough to force rotation about the Cu–N(1′) bond so that the coordination plane and the pyrimidine become coplanar. A similar rotation in Pt(thiamin)$Cl_3$ is resisted due to a severe steric interaction that would result between a cis chloro ligand and the C(21′) methyl group in such a coplanar arrangement.

In addition to these base-stacking interactions, there are also dipolar interactions between atoms of the positively charged thiazolium ring, C(2), N(3), and C(4), and two of the coordinated chloro ligands Cl(2) and Cl(3) (Table XI), similar to those observed in the two salts reported here.

There is a strong O(53)–O(W) hydrogen bond but none between O(53) and any coordinated Cl, in contrast to what is observed in the two other monomeric complexes.[4,5] A hydrogen bond exists between Cl(2) and the acidic group C(2)–H of a neighboring molecule. The distance, 3.43 (2) Å, is comparable with those found for the similar interaction in Cd(thiamin)$Cl_3$ and Cu(thiamin)$Cl_2$.[4,5]

The coordination sphere of Pt is square planar as shown by least-square plane calculation (Table XIX, supplementary material). The metal ion is bonded to the N(1′) of the pyrimidine ring of thiamin. This is the fourth X-ray structure reporting this type of complexation.[3-5] Relevant bond distances and bond angles are given in Table VII and X. The Pt–N(1′) distance, 2.01 (2) Å, is similar to the Pt–N bond distance in the square-planar Pt complex of caffeine 2.021 (5) Å.[25] The Pt–Cl distance to the trans chloro ligand Cl(3), 2.282 (6) Å, is indistinguishable from one of the cis distances Pt–Cl(2), 2.277 (6) Å. The other cis Pt–Cl(1) bond is slightly longer, 2.316 (5) Å. One may explain this distortion by noting that Cl(1) experiences the strongest hydrogen bonding in the molecule through its interaction with N(41′) and $H_2O$ (Table XI).

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**Table XII.** Cl–Cl Nonbonding Distances in the Polychlorometal Anions of Thiamin Compounds

| compd | dist, Å | conformation | ref |
|---|---|---|---|
| (Hthiamin)$PtCl_4$ | 3.243 (6) | F | *a* |
| (Hthiamin)$_2(PtCl_4)Cl_2$ | 3.262 | F | *a* |
| Pt(thiamin)$Cl_3$ | 3.27 | F | *a* |
| (Hthiamin)$CuCl_4$ | 3.42 (4) | F | 19 |
| Zn(thiamin)$Cl_3$ | 3.7 (5) | S | 29 |
| Cu(thiamin)$Cl_2$ | 3.867 | F | 5 |
| (Hthiamin)$CdCl_4$ | 4.00 (5) | S | 18 |
| Cd(thiamin)$Cl_3$ | 4.0 (1) | S | 4 |

[a] This work.

Calculations of least-square planes for the thiazolium and the pyrimidine rings show them to be planar (Table XIX, supplementary material). An interesting feature of the pyrimidine ring is its positive nature previously observed only in the dimeric rhodium structure.[3] The electron deficiency of the pyrimidine is shown by the strong electrostatic contacts between the C(2′), N(3′), C(4′), and C(6′) positions of one molecule and Cl(2) and N(41′) of neighboring molecules. The interaction between Cl(2) and N(41′) and N(3′), in particular, suggests that N(3′) carries significant positive charge.

The torsion angles[17] $\Phi_P$ and $\Phi_T$ in Pt(thiamin)$Cl_3 \cdot H_2O$ are $\Phi_T = -5.3°$ and $\Phi_P = +70.0°$, corresponding to the F form of thiamin, which has been observed in most of the reported thiamin structures. The torsion angles that describe the conformation of the hydroxyethyl side chain[21] are $\Phi_{5\alpha} = 78°$ and $\Phi_{5\beta} = 56°$. The resulting short O(53)–S contact, 3.07 (4) Å, falls at the long end of the range of distances reported for other thiamin derivatives with the same structural feature,[4,21] 2.88–3.06 Å. It is longer than those for Cu(thiamin)$Cl_2$ and Cd(thiamin)$Cl_3$ in which this distance is 2.913 (3) and 2.879 (3) Å, respectively. Since metal complexes exhibit both the shortest, 2.879 (3) Å for Cd(thiamin)$Cl_3$, and longest distance, 3.07 (4) Å for III, it appears that metal coordination has little influence on this interaction, in contrast to our preliminary suggestion.[5]

The limited accuracy of the C(4′)–N(41′) distance, 1.34 (2) Å, excludes any detailed comparison with the similar distances obtained for the other complexes.

## Discussion

**Effects of Polychlorometal Anions on Thiamin Conformation.** Since the conformation of thiamin, defined by the angles[17] $\Phi_T$ and $\Phi_P$, may affect the catalytic function of the thiamin pyrophosphate cofactor,[26] it is essential to determine the importance of intramolecular and intermolecular forces in causing one conformation to be preferred over another. Jordan has published calculations which show that thiamin chloride, an F conformer, and hydroxyethylthiamin, an S conformer, both lie in low-energy regions of Lennard–Jones potential maps and show practically no difference in potential energy.[28] This small energy difference likewise implies that the factors which determine thiamin conformation can be very subtle forces. The numerous crystallographic studies on thiamin and thiamin-related compounds provide a rich resource for studying the three known conformations, V, F, and S, in the solid state.[17,27]

We synthesized and determined the structure of the tetraphenylborate salt of thiamin[7] with the goal of incorporating a bulky but nonhydrogen-bonding anion in the structure to minimize intermolecular forces. The crystallographic study of the tetraphenylborate salt where only three hydrogen bonds exist is the first thiamin structure where neither hydrogen bonding, base stacking, nor electrostatic contacts between the thiazolium ring and electronegative entities form an extensive network of interactions. It is significant because it strongly suggests that the F conformation is preferred by the isolated thiamin cation.

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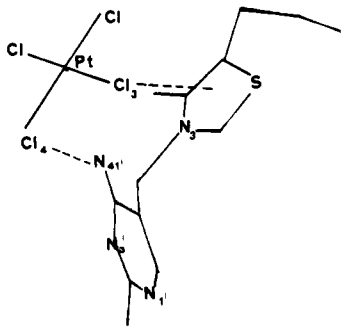


**Figure 9.** Sketch showing a $PtCl_4^{2-}$ ion bridging the pyrimidine N(41′) substituent and the thiazolium ring.

Examination of the structures of thiamin salts of polychlorometal ions listed in Table XII reveal a common structural feature noticed by Sax.[30] In most of these compounds, the polychlorometallo moiety, $(M^{n+}Cl_x)^{x-n}$, is simultaneously involved in hydrogen bonding with the N(41′) amino group of the pyrimidine and electrostatic contacts with the thiazolium ring. In (Hthiamin)$CuCl_4$, the amino group forms hydrogen bonds of 3.33 and 3.44 Å with Cl(1) and Cl(2), respectively. At the same time Cl(2) forms electrostatic contacts with the thiazolium ring atoms that average to 3.6 (2) Å. Long-range contacts between the other chloro ligand Cl(3) and the thiazolium ring average to 3.74 (4) Å.[19] Similarly, in (Hthiamin)$CdCl_4$, a hydrogen bond of 3.306 (3) Å exists between the amino functionality and a chloro ligand, Cl(4). Another chloro ligand, Cl(2), bridges to the thiazolium ring by forming nonbonding contacts averaging 3.6 (2) Å.[18] From an inspection of the (Hthiamin)$PtCl_4$ and (Hthiamin)$_2(PtCl_4)Cl_2 \cdot 2H_2O$ crystal structures, we recognize similar interactions. In (Hthiamin)$PtCl_4$, one chloro ligand is involved in a strong hydrogen bond to N(41′), 3.18 (2) Å, and simultaneously forms long dipole contacts with the thiazolium ring averaging to 3.8 (1) Å. Similar, tough stronger interactions occur in (Hthiamin)$_2(PtCl_4)Cl_2 \cdot 2H_2O$ where Cl(3) forms a hydrogen bond with N(41′), 3.173 (5) Å, and at the same time forms short dipolar contacts with N(3) and C(4) of the thiazolium ring (Table IX).

In the metal ion complexes of thiamin, this bridging interaction also exists. In Cu(thiamin)$Cl_2$, an F conformer, the Cl(1) ligand of the $(CuCl_2)^-$ moiety forms a hydrogen bond of 3.25 (2) Å with N(41′) and, at the same time, forms dipolar contacts with the thiazolium atoms that average to 3.6 (2) Å. The shortest contact between the other chloro ligand, Cl(2), and these atoms is 3.581 (2) Å. An analogous situation exists in Cd(thiamin)$Cl_3$, an S conformer. In this structure, Cl(2) hydrogen bonds to N(41′) of thiamin. Again, in a bridging fashion, the other chloro ligands, Cl(1) and Cl(3), participate in electrostatic interactions with the thiazolium ring atoms, which result in nonbonding distances that average to 3.6 (2) Å. In Pt(thiamin)$Cl_3 \cdot H_2O$, two chloro ligands of the $PtCl_3^-$ moiety bridge the two rings through dipolar contacts. Cl(3) interacts with the thiazolium atoms and Cl(2) interacts with C(2) of the thiazolium and at the same time with three atoms of the pyrimidine ring. Finally, in Zn(thiamin)$Cl_3$, the only other unsubstituted thiamin complex that crystallizes in the S form,[29] this bridging pattern is also evident. One chloro ligand, Cl(1), is a hydrogen bond acceptor for the amino nitrogen, while another, Cl(3), interacts with the thiazolium ring via nonbonding distances of 3.6 (1) Å.

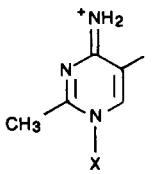
It is apparent from these crystallographic results that the polychlorometal anion in these structures can function as a bridge between the pyrimidine amino group and the thiazolium ring as illustrated by the structure of (Hthiamin)$PtCl_4$ (Figure 9). Two stabilizing forces in the crystal structure—that of hydrogen bonding to N(41′) and electrostatic attractions to the thiazolium ring—are therefore provided by the chloro ligands bound to the metal ion.

The observation that the Cd(II)- and Zn(II)-containing thiamin compounds crystallize in the unusual S conformation can be rationalized by examining the Cl–Cl nonbonding distances in each of the polychlorometal anions of the compounds studied[30] (Table XII). For compounds in which the F conformer is found, this distance averages to 3.4 (3) Å. In contrast, in the compounds where the S conformer is found, the average Cl–Cl distance is 3.9 (2) Å. This difference suggests that, in the presence of anions such as $(CdCl_4)^{2-}$, $(CdCl_3)^-$, and $(ZnCl_3)$-, the thiamin molecule reorients the pyrimidine and thiazolium rings in order to accommodate the bulkier metallate anion and still maintain the stabilizing crystal forces. In so doing, the conformation is shifted from the F form to the S form, which causes the nonbonding distance between the active centers N(41′) and C(2) to markedly increase from 3.6 (1) to 5.356 (9) Å. Thus the F form is favored by smaller metal anions with shorter Cl–Cl distances, and the S form is stabilized when these distances are larger.

These crystallographic results should not be interpreted to mean that other low-energy conformers of thiamin are not present in solution. Neither do these results identify the conformation of the thiamin pyrophosphate cofactor when bound to the native enzyme. However, induction of a particular thiamin conformation due to interaction with differently spaced chloro ligands of polychlorometal ions, suggests a mechanism whereby the enzyme could specify a particular thiamin conformation. Pairs of negatively charged moieties, i.e., carboxylate anions separated by the necessary distance and present near the enzymatic active site, could form similar interactions with thiamin, thereby orienting the cofactor in the conformation best suited for catalysis.

**Pt(thiamin)$Cl_3$ in DMSO Solution.** $^1H$ NMR spectra of Cd(thiamin)$Cl_3$ and Cu(thiamin)$Cl_2$ show resonances indistinguishable from those of thiamin nitrate, suggesting that, in solution, these complexes largely dissociate to form free, unprotonated thiamin.[7] Similar studies on Pt(thiamin)$Cl_3$ show that it is possible to characterize a nondissociated complex of the nonlabile Pt(II) ion. $^1H$ NMR data for Pt(thiamin)$Cl_3$ presented in Table I are clearly different from those acquired for the unprotonated ligand. Most of the resonances for Pt(thiamin)$Cl_3$ are shifted downfield compared to those for unprotonated thiamin and occur midway between those of protonated and unprotonated thiamin. However, the two protons, H(6′) and H(21′), that shift the most. 0.4 and 0.6 ppm, respectively, are downfield of those for protonated thiamin. The H(21′) peak is well resolved from the H(41) thiazolium methyl resonance, in contrast to the uncomplexed forms of thiamin where these are only 0.1 ppm apart. These findings are consistent with Pt(II) coordination to the N(1′) pyrimidine atom since, upon coordination, the protons closest to the coordination site are expected to experience the largest changes in chemical shifts, which are usually downfield.

There is also a downfield shift of 0.7 ppm for the H(41′) resonance. This shift is also in the same direction as that observed upon thiamin protonation (Table I), but is smaller. This finding suggests that metallation induces a similar electronic effect on the pyrimidine ring as protonation and makes the fractional contribution of the resonance form



where X = H or a metal ion, more important to the overall electronic structure. This would also enable the $NH_2$ amino group to participate in better hydrogen bonding with the $Me_2SO$ solvent, resulting in the downfield shift of these protons.

Both the C(35′) bridge and C(2) of the thiazolium ring show significant downfield shifts of about 0.25 and 0.15 ppm, respectively. The other thiazolium ring protons show no shift in their $^1H$ NMR resonance, precluding possible metal–thiazolium interaction.

A $^{195}Pt$ NMR spectrum of a freshly prepared solution of III shows one broad resonance at $\delta = -2896$. The broadness of the

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(30) Sax, M., private communication.

peak arises from the bonding of Pt(II) to a quadrupole nucleus, nitrogen.[31,32] The resonance observed here is comparable to that observed for Pt(4-EtPy)$Cl_3$ ($\delta$ = -2772 in $CH_2Cl_2$).[33]

None of the $^1H$ NMR shifts observed here agree with those reported by Theophanides[6] for Pt(thiamin)$Cl_3$. The chemical shifts cited by these authors for H(6') and H(41') are shifted from those we have observed by 0.2 ppm upfield and 0.6 ppm downfield, respectively. All other thiamin resonances differ by less than 0.1 ppm. However, none are identical. It is possible that the NMR spectrum reported by Theophanides was not acquired on a freshly prepared sample and is, therefore, that of a reaction product of Pt(thiamin)$Cl_3$ and the solvent. Our $^1H$ NMR results also differ from those reported by Adeyemo[34] for this complex. In fact, Adeyemo's results are more consistent with those we observe for the first main decomposition product resulting from the reaction of Pt(thiamin)$Cl_3$ with DMSO (see Figure 1b).

The spectrum shown in Figure 1b is that of Pt(thiamin)$Cl_3$ after it was allowed to stand in DMSO for 15 min. It shows the proton resonances of the complex and another component in solution, indicative of a possible reaction between the complex and DMSO. The nature of this reaction was elucidated with the acquisition of $^{195}Pt$ and $^1H$ NMR data along with conductance measurements.

Conductance results in DMSO which show that Pt(thiamin)$Cl_3$ is a nonconductor are indicative of a nondissociated complex. With time the conductance increases and after several hours, a comparison to other thiamin salts (Table II) shows that a 1:1 electrolyte is present in solution. Two possible reactions, a and b, will produce compounds that are consistent with these conductance findings.

$$\text{Pt(thiamin)Cl}_3 + \text{DMSO} \rightarrow \text{(Pt(thiamin)(DMSO)Cl}_2)^+ + \text{Cl}^- \quad \text{(a)}$$

$$\text{Pt(thiamin)Cl}_3 + \text{DMSO} \rightarrow \text{(thiamin)}^+ + \text{(Pt(DMSO)Cl}_3)^- \quad \text{(b)}$$

On the basis only of conductivity data, Theophanides[6] postulated the reaction a takes place. However, our $^{195}Pt$ NMR data provide strong evidence that reaction b, where thiamin has been displaced by DMSO, has occurred. Figure 2 shows two $^{195}Pt$ resonances observed for a DMSO solution of Pt(thiamin)$Cl_3$ 1 h after mixing: one at $\delta$ = -2896, attributed to Pt(thiamin)$Cl_3$ and another at $\delta$ = -2965. This latter resonance, identical with the $^{195}Pt$ signal we have observed for K[Pt(DMSO)$Cl_3$],[12] confirms the presence of the complex anion (Pt(DMSO)$Cl_3$)$^-$ in solution. We do not detect the presence of Pt(DMSO)$_2Cl_2$ $\delta$ ($^{195}Pt$) = -3455)[12] in solutions of Pt(thiamin)$Cl_3$.

Due to the large trans effect of DMSO and its negative charge, (Pt(DMSO)$Cl_3$)$^-$ is very reactive toward the positively charged thiamin molecule. The course of this subsequent reaction is currently under study.

**Registry No.** I, 111290-95-0; II, 111290-96-1; III, 111290-97-2; $K_2PtCl_4$, 10025-99-7; Pt(DMSO)$Cl_3^-$, 31203-96-0; (Hthiamin)$Cl_2$, 67-03-8; (thiamin)$NO_3$, 532-43-4; $^{195}Pt$, 14191-88-9.

**Supplementary Material Available:** Listings of hydrogen atom parameters for Pt(thiamin)$Cl_3 \cdot H_2O$ (Table XIII) and anisotropic temperature factors (Tables XIV-XVI) and best weighted least-squares planes (Tables XVII-XIX) for (Hthiamin)$PtCl_4$, (Hthiamin)$_2(PtCl_4)Cl_2 \cdot 2H_2O$, and Pt(thiamin)$Cl_3 \cdot H_2O$ and two ORTEP diagrams of stacking and interbase interactions in Pt(thiamin)$Cl_3 \cdot H_2O$ (Figures 7 and 8) (9 pages); listings of observed and calculated structure factor amplitudes for all three compounds (48 pages). Ordering information is given on any current masthead page.

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# S,O- versus S,N-Chelation in the Reactions of the *cis*-Diamminediaquaplatinum(II) Cation with Methionine and *S*-Methylcysteine[1]

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The reactions of *cis*-Pt$(NH_3)_2(H_2O)_2^{2+}$ with *S*-methyl-L-cysteine (mecysH) and L-methionine (metH) have been followed by $^1H$, $^{13}C$, $^{15}N$, and $^{195}Pt$ NMR (the last two with ammine ligands substituted with $^{15}N$). With a small excess of platinum, and with pH maintained near 5, the chelate products Pt$(NH_3)_2$(mecys-*S*,*N*)$^+$ and Pt$(NH_3)_2$(met-*S*,*N*)$^+$ are formed. In each case, the different configurations about sulfur give two slowly interconverting diastereomers. In strongly acidic solution (pH $\leq$0.5), the initial product in the reaction with mecysH is Pt$(NH_3)_2$(mecysH-*S*,*O*)$^{2+}$ (two diastereomers), which slowly converts to the S,N-chelate. A similar reaction sequence occurs with methionine, but *cis*-Pt$(NH_3)_2$(metH-*S*)$_2^{2+}$ is also formed, in competition with Pt$(NH_3)_2$(metH-*S*,*O*)$^{2+}$. All of these complexes slowly lose ammonia on standing.

## Introduction

The best characterized complexes of platinum and palladium with the sulfur-containing amino acid methionine and its analogues are the dichloro complexes M(LH)$Cl_2$. X-ray crystal structure determinations have been carried out, inter alia, for the complexes with M = Pt, LH = L-methionine (metH),[2] *S*-ethyl-L-cysteine[3] and M = Pd, LH = *S*-methyl-L-cysteine (mecysH).[4] In each of these, there is a S,N-chelate ring. In the unit cell, there is one molecule of each of the two diastereomers arising from the different configurations of the S-alkyl group and the nonbonding electron pair on sulfur. After some initial confusion,[5,6] the $^1H$ NMR spectra of M(mecys)$Cl_2^-$ (M = Pd, Pt) have been interpreted as showing unequivocally that S,N-chelate rings are present

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