The $[Pt^{IV}Cl_6]^{2-}$/thiamine system. Crystal structures of (H-thiamine)$[PtCl_6] \cdot H_2O$ and (H-thiamine)$_2[PtCl_6]Cl_2 \cdot 2H_2O$: host–guest-like anion coordination

Katsuyuki Aoki*, Tsutomu Tokuno, Koji Takagi and Yuji Hirose

Department of Materials Science, Toyohashi University of Technology, Tempaku-cho, Toyohashi 441 (Japan)

Il-Hwan Suh

Department of Physics, Chungnam National University, Daejeon 307-764 (South Korea)

Adegboye O. Adeyemo* and George N. Williams

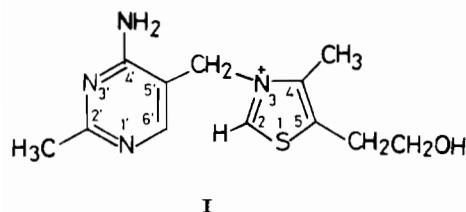*Department of Chemistry, Savannah State College, Savannah, GA 31404 (USA)*

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Abstract

The reaction of $PtCl_4$ with (H-thiamine)Cl_2 and (H-thiamine)$(ClO_4)_2$ in water produced a 1:1 salt (H-thiamine)$[PtCl_6] \cdot H_2O$ (**1**) and a 2:1 double salt (H-thiamine)$_2[PtCl_6]Cl_2 \cdot 2H_2O$ (**2**), respectively, whose crystal structures have been determined by X-ray diffraction. In both compounds, the Pt(IV) atom does not directly bind to thiamine but is linked as an octahedral $[PtCl_6]^{2-}$ anion to a cationic thiamine; a $[PtCl_6]^{2-}$ ion bridges between the thiazolium and the pyrimidinium moieties of the same thiamine molecule, through (i) a hydrogen bonding between the C(2)H of the thiazolium ring and the Cl^- of the $[PtCl_6]^{2-}$ ion and (ii) an electrostatic interaction between the pyrimidinium ring plane and the same Cl^-. There is another type of anion bridge between the pyrimidinium and the thiazolium rings of the same thiamine molecule, through (i) a hydrogen bonding between the amino N(4'α)H of the pyrimidinium ring and the Cl^- of the other $[PtCl_6]^{2-}$ ion in **1** or the free Cl^- ion in **2** and (ii) an electrostatic contact between the thiazolium plane and the same Cl^-. Biological relevance of this host–guest-like anion coordination is mentioned in brief as a possible model for the substrate fixation to coenzyme and/or the coenzyme fixation to apoenzyme. Results are also compared with those of the $[Pt^{II}Cl_4]^{2-}$/thiamine system (R.E. Cramer, R.E. Kirkup and M.J.J. Carrie, *Inorg. Chem., 27* (1988) 123).

Introduction

Thiamine (**I**; vitamin B$_1$) is a cofactor, as its pyrophosphate ester, for a number of metabolic enzymes catalyzing the decarboxylation of α-keto acids and the transfer of aldehyde or acyl groups [1]. These thiamine enzymes further require a divalent metal ion, Mg^{2+}, for their functions [2]. Other divalent metal ions such as Mn^{2+}, Co^{2+}, Zn^{2+} or Cd^{2+} also activate pyruvate carboxylase with somewhat reduced activities [3]. Mg^{2+} ion is believed to be involved in the formation of the

enzyme–coenzyme complex through the metal bonding either to the base moiety of thiamine, possibly at N(1′) [4] or to the pyrophosphate group [5]. Metal bonding to the N(1′) site or to the pyrophosphate group has, indeed, been exemplified in the crystal structures; the former includes Cd^{2+} [6a, f], Cu^+ [6b, c], Zn^{2+} [6d–f], Co^{2+} [6e, g], Pt^{2+} [6h], Hg^{2+} [6i], Rh^{2+} [6j] and Mn^{2+} [6k], and the latter includes Cu^{2+} [7]. [Cd(thiamine)(SCN)$_3$] [6f] and [Mn(thiamine)Cl$_2$(H$_2$O)$_2$]$_2$[thiamine]$_2$Cl$_4 \cdot 2H_2O$ [6k] are unique in that the metal binds to the hydroxyethyl O(5γ) of thiamine. A total of eight crystal structures of salt-type, i.e. no direct metal bonding to thiamine, has also been reported; these include as counter ions $[MCl_4]^{2-}$ ($M = Cu^{2+}$ [8a], Cd^{2+} [8b], Co^{2+} [8c], Hg^{2+} [8d] and Pt^{2+} [6h]), $[UO_2Cl_4]^{2-}$ [8e] and $[Mg(H_2O)_6]^{2+}$ [8f].

In continuation of our X-ray investigations on thiamine–metal ion interactions [6c, e, f, j, 7] we report here the synthesis and crystal structures of two compounds derived from the reaction of $PtCl_4$ with thiamine (the $[Pt^{IV}Cl_6]^{2-}$/thiamine system), a 1:1 salt (H-thi-

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*Authors to whom correspondence should be addressed.

amine)[PtCl$_6$]·H$_2$O (**1**) and a 2:1 double salt (H-thi-amine)$_2$[PtCl$_6$]Cl$_2$·2H$_2$O (**2**). No direct Pt(IV)–thiamine bonding exists but, instead, stereospecific interactions between a thiamine as a host and a metal anion as a guest occur; this host–guest-like anion coordination is mentioned as a model for the coenzyme fixation to apoenzyme and/or the substrate fixation to coenzyme. Results are compared with those of the [Pt^{II}Cl$_4$]$^{2-}$/thiamine system reported by Cramer et al. [6h].

Experimental

Preparation of (H-thiamine)[PtCl$_6$]·H$_2$O (1) and (H-thiamine)$_2$[PtCl$_6$]Cl$_2$·2H$_2$O (2)

PtCl$_4$ (34 mg, 0.1 mmol) dissolved in 10 ml of hot (80 °C) water and (H-thiamine)Cl$_2$ (34 mg, 0.1 mmol) for **1** or (H-thiamine)(ClO$_4$)$_2$ (47 mg, 0.1 mmol) for **2** in 10 ml of water were mixed to give a light yellow solution (pH about 3). Yellowish orange crystals formed after 1 day by allowing the solution to stand at room temperature. Yields were 68% (**1**) and 66% (**2**). *Anal.* Calc. for C$_{12}$H$_{20}$Cl$_6$N$_4$O$_2$PtS (**1**): C, 20.08; H, 2.91; N, 8.09. Found: C, 20.27; H, 2.85; N, 8.06%. Calc. for

C$_{24}$H$_{40}$Cl$_8$N$_8$O$_4$PtS$_2$ (**2**): C, 27.52; H, 3.85; N, 10.70. Found: C, 28.02; H, 3.89; N, 10.81%.

X-ray structure determination

Details of crystal data and data collection along with refinement are summarized in Table 1. No absorption corrections were made for **1** and **2** since variations in intensity of axial reflections ($\chi \sim 90°$ with the spindle angle ϕ) were within 5% from the mean for **1** and 4% for **2**. The structures were solved by heavy-atom methods and refined by block-diagonal least-squares methods. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were located from difference Fourier maps except for those of the methyl groups, for which idealized positions were calculated, and those of each water in **1** and **2**. These H atoms were included in the final cycles of the refinement but fixed ($B = 6$ Å^2). The final R and R_w values were 0.046 and 0.057 for **1**, respectively, and 0.044 and 0.059 for **2**. The final positional parameters of non-hydrogen atoms for **1** and **2** are listed in Tables 2 and 3, respectively. See also 'Supplementary material'.

Neutral atomic scattering factors and anomalous dispersion corrections for Pt, Cl, and S were taken from

TABLE 1. Crystal and refinement data

Compound	1	2
Formula	C$_{12}$H$_{20}$Cl$_6$N$_4$O$_2$PtS	C$_{24}$H$_{40}$Cl$_8$N$_8$O$_4$PtS$_2$
M_r	692.19	1047.48
Space group	$P\bar{1}$	$P\bar{1}$
a (Å)	11.141(3)	10.635(1)
b (Å)	11.231(1)	11.150(1)
c (Å)	8.878(1)	8.468(3)
α (°)	105.35(1)	91.12(2)
β (°)	92.34(1)	94.93(2)
γ (°)	89.86(1)	106.14(1)
V (Å^3)	1070.3(3)	960.0(4)
Z	2	1
$F(000)$	664	518
D_{calc} (g cm^{-3})	2.148	1.812
Crystal size (mm)	0.21×0.22×0.27	0.19×0.21×0.25
μ(Mo Kα) (cm^{-1})	74.89	44.00
Transmission factors [a]	0.95–1.05	0.96–1.04
Diffractometer	Enraf-Nonius CAD4	Enraf-Nonius CAD4
Radiation	Mo Kα (0.71073 Å)	Mo Kα (0.71073 Å)
Scan type	ω–2θ	ω–2θ
2θ Range (°)	3.0–50.0	3.0–50.0
T (°C)	23	23
Reflections measured	3961	3569
Unique reflections used, m ($F_o > 3\sigma(F_o)$)	3044	3353
Variables, n	238	214
Weighting scheme, w	$\sigma(F_o)^{-2}$	$\sigma(F_o)^{-2}$
R [b]	0.046	0.044
R_w [c]	0.057	0.059
S [d]	2.6	1.9
$(\Delta\rho)_{max}$ (e/Å^3)	1.8	1.1

[a]Normalized to an average of unity. [b]$R = \Sigma|F_o - |F_c||/\Sigma F_o$. [c]$R_w = [\Sigma w(F_o - |F_c|)^2/\Sigma wF_o^2]^{1/2}$. [d]$S = [\Sigma w(F_o - |F_c|)^2/(m-n)]^{1/2}$.

TABLE 2. Atomic coordinates of (H-thiamine)[PtCl$_6$]·H$_2$O (1)

Atom	x	y	z
Pt(1)	0.0	0.0	0.0
Pt(2)	0.5	0.5	0.5
Cl(1)	0.0122(3)	−0.0937(4)	0.2047(4)
Cl(2)	0.1826(3)	0.0988(4)	0.0875(4)
Cl(3)	−0.1011(4)	0.1659(4)	0.1536(4)
Cl(4)	0.4759(3)	0.3525(3)	0.6355(4)
Cl(5)	0.6337(3)	0.6115(3)	0.6949(4)
Cl(6)	0.3421(3)	0.6123(3)	0.6302(4)
N(1′)	0.2450(10)	−0.2236(10)	0.3573(13)
C(2′)	0.3114(12)	−0.2096(12)	0.2373(16)
N(3′)	0.3716(10)	−0.1095(10)	0.2431(12)
C(4′)	0.3657(11)	−0.0138(11)	0.3689(14)
C(5′)	0.2957(11)	−0.0201(11)	0.5004(14)
C(6′)	0.2394(12)	−0.1305(12)	0.4858(14)
C(2′α)	0.3105(15)	−0.3169(14)	0.0966(17)
N(4′α)	0.4273(10)	0.0863(10)	0.3657(14)
C(3,5′)	0.2869(11)	0.0850(12)	0.6418(15)
S(1)	0.0631(3)	0.2995(3)	0.4852(4)
C(2)	0.1431(11)	0.1730(12)	0.4800(15)
N(3)	0.2079(9)	0.1862(9)	0.6144(11)
C(4)	0.1952(11)	0.2970(11)	0.7239(14)
C(5)	0.1174(10)	0.3710(11)	0.6717(13)
C(4α)	0.2604(12)	0.3247(12)	0.8818(15)
C(5α)	0.0778(12)	0.5004(12)	0.7462(15)
C(5β)	−0.0536(13)	0.5063(13)	0.7954(17)
O(5γ)	−0.1293(8)	0.4516(9)	0.6630(11)
O(W)	0.5826(16)	0.0920(22)	0.1253(20)

TABLE 3. Atomic coordinates of (H-thiamine)$_2$[PtCl$_6$]Cl$_2$·2H$_2$O (2)

Atom	x	y	z
Pt	0.0	0.0	1.0
Cl(1)	0.0439(2)	0.0049(2)	0.7359(3)
Cl(2)	−0.0270(3)	0.1988(2)	0.9851(3)
Cl(3)	0.2228(2)	0.0854(3)	1.0761(3)
Cl(4)	0.5552(2)	0.3592(3)	0.3859(3)
N(1′)	0.1538(7)	0.3546(8)	0.6781(9)
C(2′)	0.1240(9)	0.4361(9)	0.7741(11)
N(3′)	0.0107(7)	0.4639(7)	0.7584(9)
C(4′)	−0.0807(8)	0.4020(8)	0.6386(10)
C(5′)	−0.0542(8)	0.3142(8)	0.5318(10)
C(6′)	0.0668(9)	0.2937(9)	0.5548(11)
C(2′α)	0.2225(11)	0.5000(11)	0.9097(13)
N(4′α)	−0.1931(8)	0.4326(8)	0.6285(10)
C(3,5′)	−0.1480(9)	0.2523(8)	0.3930(10)
S(1)	−0.3309(2)	−0.0739(2)	0.5512(3)
C(2)	−0.2249(8)	0.0685(9)	0.5572(10)
N(3)	−0.2383(6)	0.1296(7)	0.4277(8)
C(4)	−0.3383(8)	0.0620(8)	0.3166(9)
C(5)	−0.3989(8)	−0.0519(8)	0.3649(10)
C(4α)	−0.3662(10)	0.1165(9)	0.1606(10)
C(5α)	−0.5094(9)	−0.1538(9)	0.2835(11)
C(5β)	−0.4645(10)	−0.2570(10)	0.2024(12)
O(5γ)	−0.3946(7)	−0.3137(7)	0.3163(9)
O(W)	0.2608(8)	0.3533(8)	0.2637(11)

the International Tables for X-ray Crystallography [9]. All calculations were performed with the UNICSIII program system [10] on a Data General 20 K computer at Toyohashi University of Technology.

Results

Bond lengths and angles of the thiaminium cation are listed in Table 4 (for those of the [PtCl$_6$]$^{2-}$ anion

TABLE 4. Bond lengths (Å) and angles (°) of the thiaminium cation

	1	2
N(1′)–C(2′)	1.36(2)	1.328(14)
C(2′)–N(3′)	1.30(2)	1.321(13)
N(3′)–C(4′)	1.33(1)	1.371(10)
C(4′)–C(5′)	1.45(2)	1.420(13)
C(5′)–C(6′)	1.36(2)	1.367(14)
C(6′)–N(1′)	1.33(2)	1.366(11)
C(2′)–C(2′α)	1.49(2)	1.507(13)
C(4′)–N(4′α)	1.33(2)	1.327(13)
C(5′)–C(3,5′)	1.48(2)	1.496(11)
C(3,5′)–N(3)	1.50(2)	1.488(10)
S(1)–C(2)	1.67(1)	1.670(8)
C(2)–N(3)	1.34(2)	1.320(11)
N(3)–C(4)	1.37(1)	1.393(9)
C(4)–C(5)	1.35(2)	1.343(12)
C(5)–S(1)	1.72(1)	1.729(9)
C(4)–C(4α)	1.51(2)	1.505(13)
C(5)–C(5α)	1.50(2)	1.496(11)
C(5α)–C(5β)	1.54(2)	1.535(16)
C(5β)–O(5γ)	1.42(2)	1.431(14)
N(1′)–C(2′)–N(3′)	123(1)	123.4(9)
C(2′)–N(3′)–C(4′)	119(1)	117.4(8)
N(3′)–C(4′)–C(5′)	121(1)	121.8(8)
C(4′)–C(5′)–C(6′)	115(1)	116.8(8)
C(5′)–C(6′)–N(1′)	122(1)	119.7(9)
C(6′)–N(1′)–C(2′)	119(1)	121.0(8)
N(1′)–C(2′)–C(2′α)	116(1)	119.1(9)
N(3′)–C(2′)–C(2′α)	121(1)	117.5(9)
N(3′)–C(4′)–N(4′α)	116(1)	115.1(8)
C(5′)–C(4′)–N(4′α)	122(1)	123.2(8)
C(4′)–C(5′)–C(3,5′)	123(1)	123.0(8)
C(6′)–C(5′)–C(3,5′)	122(1)	120.1(8)
C(5′)–C(3,5′)–N(3)	113(1)	113.7(7)
C(3,5′)–N(3)–C(2)	122(1)	124.4(7)
C(3,5′)–N(3)–C(4)	123(1)	122.0(7)
S(1)–C(2)–N(3)	110.5(9)	112.8(7)
C(2)–N(3)–C(4)	115(1)	113.3(7)
N(3)–C(4)–C(5)	111(1)	112.4(8)
C(4)–C(5)–S(1)	110.6(9)	110.3(7)
C(5)–S(1)–C(2)	92.1(6)	91.1(4)
N(3)–C(4)–C(4α)	122(1)	120.5(7)
C(5)–C(4)–C(4α)	127(1)	127.0(8)
C(4)–C(5)–C(5α)	131(1)	130.1(8)
S(1)–C(5)–C(5α)	118.4(9)	119.6(7)
C(5)–C(5α)–C(5β)	113(1)	113.7(8)
C(5α)–C(5β)–O(5γ)	109(1)	110.2(8)

and those involving hydrogen atoms see 'Supplementary material').

Structure of (H-thiamine)[PtCl$_6$]·H$_2$O (1)

Figure 1 shows a perspective view of the compound, which consists of a divalent thiaminium cation with the N(1') site protonated, two crystallographically independent [PtCl$_6$]$^{2-}$ anions, each of which locates on a center of symmetry, and a water molecule. The thiamine molecule is in the usually observed F conformation with the torsion angles $\phi_T = $ C(5')–C(3,5')–N(3)–C(2) = 7.1 and $\phi_P = $ N(3)–C(3,5')–C(5')–C(4') = 74.3° (these conformational terms were defined by Pletcher, and co-workers [11]); the dihedral angle between the pyrimidinium and the thiazolium rings is 102.4(4)° (see 'Supplementary material'). The hydroxyethyl side chain is folded back towards the thiazolium ring to make a close contact between the electronegative O(5γ) and the electropositive [11, 12] S(1) atom; O(5γ)...S(1) = 2.973(10) Å and the torsion angles $\phi_{5\alpha}$ [11] = S(1)–C(5)–C(5α)–C(5β) = 72.9 and $\phi_{5\beta}$ [11] = C(5)–C(5α)–C(5β)–O(5γ) = −57.0°. The acidic [13] C(2)-hydrogen takes part in the hydrogen-bonding interaction with the [Pt(1)Cl$_6$]$^{2-}$ anion, which is located over the pyrimidinium ring of the same thiamine molecule: C(2)...Cl(1) = 3.60(1), H...Cl(1) = 2.59 Å and C(2)–H...Cl(1) = 153°; Cl(1)...N(1') = 3.38(1) Å. The [Pt(2)Cl$_6$]$^{2-}$ anion also makes close contacts with the pyrimidinium and the thiazolium moieties of t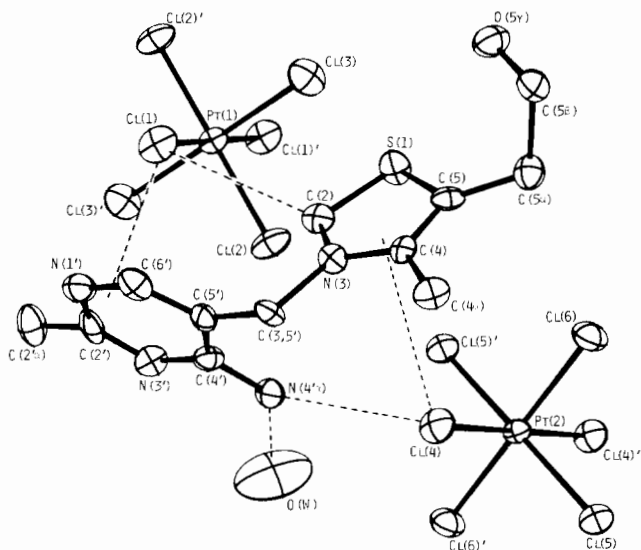he same thiamine molecule through an N(4'α)–H...Cl$^-$ hydrogen bond and a Cl$^-$...thiazolium ring electrostatic interaction: N(4'α)...Cl(4) = 3.33(1), H...Cl(4) = 2.42 Å and N(4'α)–H...Cl(4) = 143°; Cl(4)...C(4) = 3.35(1) Å.

Crystal packing is mainly determined by hydrogen bonding and electrostatic interactions (Fig. 2 and Table 5). Two thiamine molecules assemble in a 'head-to-tail' fashion to form a self-dimer (across a center of symmetry at (0,0,$\frac{1}{2}$)) through a pair of hydrogen bonds between the pyrimidinium 'head' N(1')–H and the hydroxyethyl 'tail' O(5γ). To this quarternary cationic thiaminium–thiaminium dimer, a [PtCl$_6$]$^{2-}$ anion molecule (which rides on an inversion center at (0,0,0)) attaches through three points, each involving the Cl(1) atom, that is, a C(2)–H...Cl(1) hydrogen bond and a Cl(1)...pyrimidinium interaction, mentioned above, and an electrostatic contact between the Cl(1) and the thiazolium ring of the pairing molecule: Cl(1)...N(3) = 3.30(1) Å (Fig. 3). Furthermore, the repetition of this structural unit along the c axis produces a one-dimensional molecular column (Fig. 3). These columns occupy four corners of the unit cell and are connected to each other via water or metal anion bridges. The [Pt(2)Cl$_6$]$^{2-}$ anion, which locates at the body center ($\frac{1}{2}, \frac{1}{2}, \frac{1}{2}$), accepts three hydrogens from N(4'α), O(W) and O(5γ), thereby connecting neighbouring columns.

Structure of (H-thiamine)$_2$[PtCl$_6$]Cl$_2$·2H$_2$O (2)

A perspective view of the compound is drawn in Fig. 4. The compound is comprised of a thiaminium cation, a PtCl$_6^{2-}$ anion, which locates on an inversion center, a Cl$^-$ anion and a water. The thiamine molecule is protonated at N(1') and adopts the F conformation with the folded hydroxyethyl side chain; $\phi_T = -11.4$ and $\phi_P = -93.0°$, the dihedral angle between the pyrimidinium and the thiazolium rings = 80.2(3)° (see 'Supplementary material'), O(5γ)...S(1) = 3.180(8) Å, $\phi_{5\alpha} = -80.6$ and $\phi_{5\beta} = 59.3°$. In a similar manner as 1, the [PtCl$_6$]$^{2-}$ ion bridges between the thiazolium and the pyrimidinium moieties of the same thiamine molecule through a C(2)–H...Cl$^-$ hydrogen bond and a Cl$^-$...pyrimidinium-ring electrostatic contact: C(2)...Cl(1) = 3.375(10), H...Cl(1) = 2.82 Å and C(2)–H...Cl(1) = 112°; Cl(1)...C(6') = 3.551(10) Å. The free chloride ion Cl(4) forms another bridge between the pyrimidinium and the thiazolium moieties of the same thiamine molecule through an N(4'α)–H...Cl$^-$ hydrogen bond and a Cl$^-$...thiazolium ring electrostatic interaction: N(4'α)...Cl(4) = 3.135(8), H...Cl(4) = 2.28 Å and N(4'α)–H...Cl(4) = 149°; Cl(4)...N(3) = 3.812(9) Å.

As shown in Fig. 5 and Table 6, the crystal packing is similar to that in 1 (this can best be seen when the b axis in Fig. 5 is superposed on the $-a$ axis in Fig. 2). A 'head-to-tail' hydrogen bonded [thiaminium–thiaminium]$^{4+}$ dimer forms and incorporates a

Fig. 1. Molecular structure of (H-thiamine)[PtCl$_6$]·H$_2$O (1) showing a C(2)–H...Cl(1)...pyrimidine-ring interaction (broken lines) and an N(4'α)–H...Cl(4)...thiazolium-ring interaction (broken lines). The chloro ligands, Cl(n) and Cl(n)', are related by an inversion center. Thermal ellipsoids are at the 50% probability level.
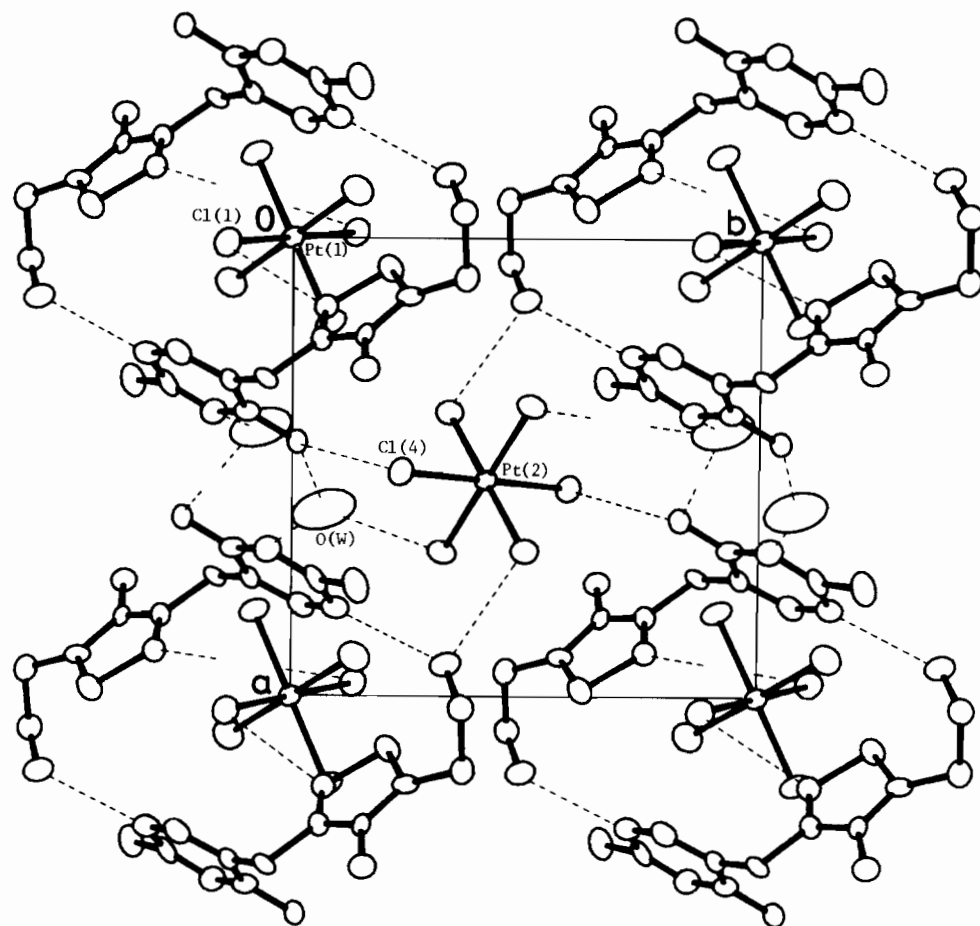
Fig. 2. Perspective view showing the crystal packing of **1**. Note the formation of a hydrogen-bonded thiaminium–thiaminium dimer across an inversion center and the $[PtCl_6]^{2-}$ incorporation into the dimer (see also Fig. 3). Broken lines denote hydrogen bonds.

TABLE 5. Hydrogen bonds and other short contacts for **1**[a]

Hydrogen bonds Donor(D)–H	Acceptor (A)	D–H (Å)	D...A (Å)	H...A (Å)	D–H...A (°)
N(1')–H	O(5γ)[i]	1.17	2.83(2)	1.75	151
N(4'α)–H1	O(W)	1.00	2.82(2)	1.84	166
N(4'α)–H2	Cl(4)	1.07	3.329(11)	2.42	143
C(2)–H	Cl(1)	1.09	3.595(12)	2.59	153
O(5γ)–H	Cl(5)[ii]	0.94	3.170(10)	2.23	178
O(W)–H1[b]	N(3')[iii]		3.39(2)		
O(W)–H2[b]	Cl(6)[iv]		3.53(2)		

Other short contacts (<3.6 Å for those involving Cl and S atoms and <3.5 Å for those involving other non-H atoms)

A	B	A...B (Å)	A	B	A...B (Å)
C(4')	N(4'α)[v]	3.48(2) stack[c]	Cl(1)	C(6')	3.582(14) stack
C(5')	N(4'α)[v]	3.41(2) stack	Cl(1)	N(3)[i]	3.299(11) stack
C(3,5')	O(W)[v]	3.50(3)	Cl(1)	C(4)[i]	3.445(14) stack
S(1)	O(5γ)	2.973(10)	Cl(4)	N(3)	3.498(11) stack
S(1)	Cl(3)	3.391(5)	Cl(4)	C(4)	3.354(14) stack
C(2)	Cl(2)	3.407(13)	Cl(4)	C(4α)	3.382(14) stack
C(5α)	Cl(6)	3.502(15)	Cl(6)	N(1')[vi]	3.547(13) stack
Cl(1)	N(1')	3.381(12) stack	O(W)	O(W)[iii]	3.14(3)

[a]Symmetry code: (none) x, y, z; (i) −x, −y, 1−z; (ii) x−1, y, z; (iii) 1−x, −y, −z; (iv) 1−x, 1−y, 1−z; (v) 1−x, −y, 1−z; (vi) x, 1+y, z. [b]This hydrogen atom was not located. [c]'stack' means stacking interaction.
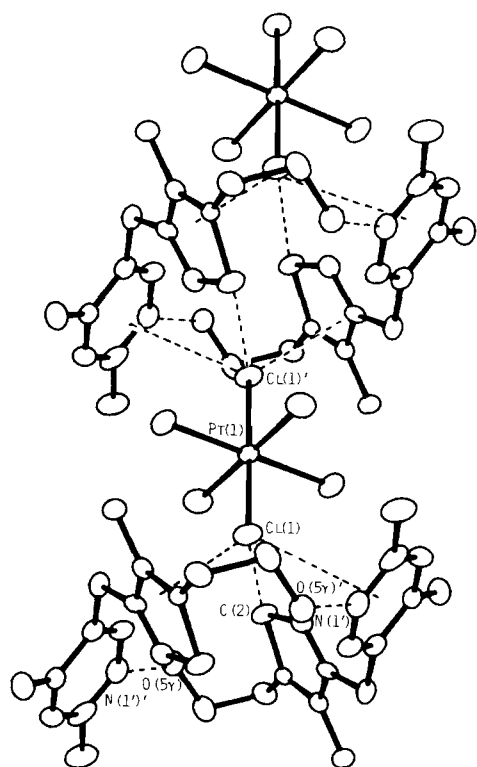
Fig. 4. Molecular structure of (H-thiamine)$_2$[PtCl$_6$]Cl$_2 \cdot$2H$_2$O (2) showing a C(2)–H...Cl(1)...pyrimidine-ring interaction (broken lines) and an N(4'α)–H...Cl(4)...thiazolium-ring interaction (broken line). The chloro ligands, Cl(n) and Cl(n)', are related by an inversion center. Thermal ellipsoids are at the 50% probability level.

Fig. 3. Inclusion of a [PtCl$_6$]$^{2-}$ ion into two 'head-to-tail' hydrogen-bonded (broken lines) thiaminium–thiaminium dimers in 1 and 2. The anion is held to the dimers through a C(2)–H...Cl(1)...pyrimidine-ring bridge (broken lines) to one thiamine and through a Cl(1)...thiazolium-ring contact (a broken line) of the pairing thiamine.

[PtCl$_6$]$^{2-}$ anion, resulting in the formation of a molecular column which runs along the c axis and locates at each corner of the unit cell. A minor difference in the crystal packings between 1 and 2 is the pyrimidinium–pyrimidinium ring-ring stacking across a center of symmetry with the average spacing of 3.38 Å and the closest contact of 3.47(1) Å between C(4') and C(4') in 2, instead of the water-bridged base–base hydrogen bonds in 1.

Discussion

Comparison of the [PtCl$_6$]$^{2-}$/thiamine and [PtCl$_4$]$^{2-}$/thiamine [6h] systems

Cramer *et al.* have reported [6h] the synthesis and crystal structures of three compounds resulting from the reaction of (H-thiamine)Cl$_2$ with K$_2$PtCl$_4$ (the [PtCl$_4$]$^{2-}$/thiamine system): an ionic 1:1 salt (H-thiamine)[PtCl$_4$], an ionic 2:1 double salt (H-thiamine)$_2$[PtCl$_4$]Cl$_2 \cdot$2H$_2$O and the 1:1 complex [Pt(thiamine)Cl$_3$] $\cdot$ H$_2$O, where there is no metal bonding to thiamine in the former two but direct metal bonding through N(1') in the latter. Interestingly, the present
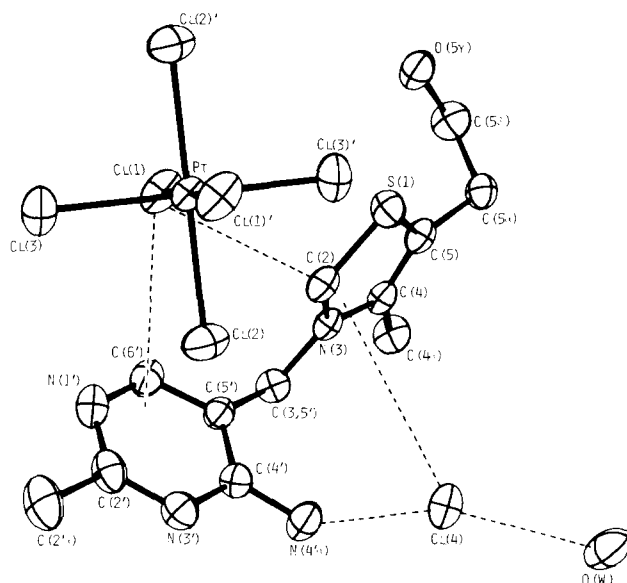
[PtCl$_6$]$^{2-}$/thiamine system also gives two salts with the corresponding salt composition, i.e. a 1:1 salt (H-thiamine)[PtCl$_6$]$\cdot$H$_2$O (1) and a 2:1 double salt (H-thiamine)$_2$[PtCl$_6$]Cl$_2 \cdot$2H$_2$O (2). Furthermore, despite the different oxidation states of the metals, Pt(II) versus Pt(IV), and the different geometries of the metal anions, square-planar [PtCl$_4$]$^{2-}$ versus octahedral [PtCl$_6$]$^{2-}$, there are interesting common structural features among these four salts. (i) The metal anion interacts with thiamine in two ways, one being a C(2)–H...Cl$^-$...pyrimidinium-ring interaction (for (H-thiamine)[PtCl$_4$] [6h] C(2)...Cl(2) = 3.59(2) and Cl(2)...C(6') = 3.40(2) Å and for (H-thiamine)$_2$[PtCl$_4$]Cl$_2$ [6h] C(2)...Cl(2) = 3.877(6) and Cl(2)...C(2') = 3.274(6) Å) and the other being a N(4'α)–H...Cl$^-$...thiazolium-ring one (for H-thiamine)[PtCl$_4$] [6h] N(4'α)...Cl(4) = 3.18(2) and Cl(4)...N(3) = 3.79(1) Å and for (H-thiamine)$_2$[PtCl$_4$]Cl$_2$ [6h] N(4'α)...Cl(3) = 3.173(5) and Cl(3)...N(3) = 3.479(5) Å). (ii) A 'head-to-tail' hydrogen-bonded thiaminium–thiaminium dimer forms, as major cases through a pair of direct N(1')–H...O(5γ) hydrogen bonds or as a minor case for (H-thiamine)$_2$[PtCl$_4$]Cl$_2$ [6h] through water-bridged hydrogen bonds N(1')–H...O(W)–H...O(5γ). (iii) A [PtCl$_4$]$^{2-}$ or a [PtCl$_6$]$^{2-}$ ion is held into two cationic thiaminium dimers, one above and one below, through a C(2)–H...Cl$^-$...pyrimidinium-ring interaction as noted in (i) plus an electrostatic contact between the Cl$^-$ and the thiazolium ring of the pairing thiamine of the
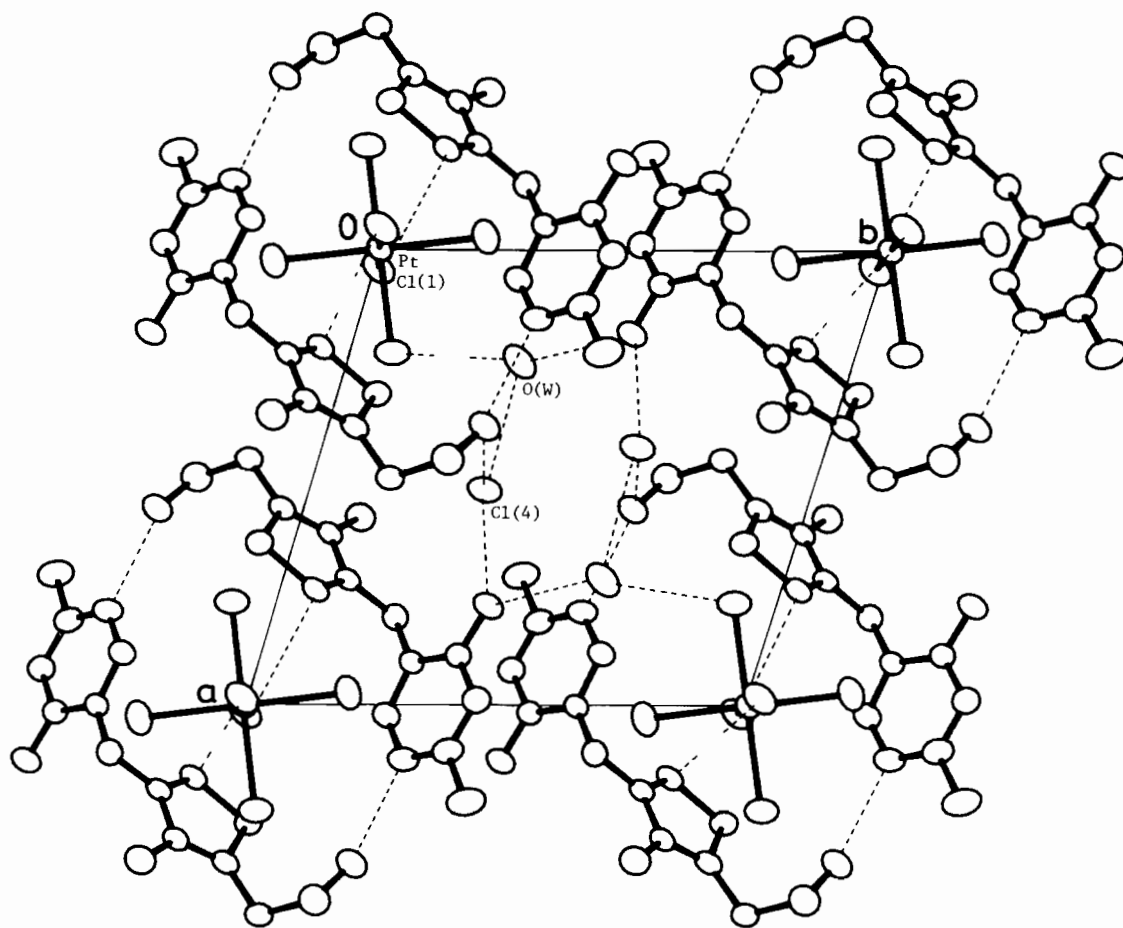
Fig. 5. Perspective view showing the crystal packing of **2**. Note the formation of a hydrogen-bonded thiaminium–thiaminium dimer across an inversion center and the $[PtCl_6]^{2-}$ incorporation into the dimer. Broken lines denote hydrogen bonds.

dimer, forming a distinctly well-defined higher-order structure (as shown in Fig. 3), a so-called supramolecule [14]. In particular, the structural feature (iii), that is, the formation of the supramolecule, is characteristic of both the $[PtCl_4]^{2-}$/thiamine and the $[PtCl_6]^{2-}$/thiamine systems. An effort is now directed towards obtaining a complex which involves the metal–N(1') bonding for the $[PtCl_6]^{2-}$/thiamine system.

Thiamine as a naturally occurring cationic host and two 'anion holes'

As observed not only in this work but also in a variety of anion salts of thiamine (see below), thiamine acts as a naturally occurring monovalent cationic host because of the quarternary nitrogen N(3) of the thiazolium moiety or as a divalent one with the additional protonation at the N(1') of the pyrimidine ring, thus interacting with an anion(s) to form a host–guest-like complex. We notice here that there are *two* well-defined 'anion holes' around a thiamine molecule: one 'anion hole' ('anion hole I') is occupied by an anion molecule which bridges between the pyrimidine and thiazolium

moieties through a C(2)–H...anion...pyrimidine inter-action and the other 'anion hole' ('anion hole II') is occupied by an anion which bridges between the two rings through an N(4'α)–H...anion...thiazolium bridge. It is well documented, theoretically [12] and experimentally [15], that thiamine adopts three energetically favorable conformations, i.e., F-form ($\phi_T = 0$ and $\phi_P = \pm 90°$ defined by Pletcher *et al.* [11b]), S-form ($\phi_T = \pm 100$ and $\phi_P = \pm 150°$) or V-form ($\phi_T = \pm 90$ and $\phi_P = \pm 90°$). The 'anion hole I' exists only when thiamine adopts the F conformation, while the 'anion hole II' occurs for thiamine with either the F- or S-forms but this is not available for thiamine with the V-form because a hydrogen of the N(4'α) group comes too near the C(2) of the thiazolium ring for any anion to form such an anion-bridging between the two ring moieties. Thus these 'anion holes' appear to be important as a factor affecting the conformation of thiamine, since the conformation of thiamine is of critical importance for its catalytic functions [4, 16]. It should be noted here that the 'anion holes I and II' exhibit rather broad anion specificity since a variety of anions with different sizes

TABLE 6. Hydrogen bonds and other short contacts for **2**[a]

Hydrogen bonds

Donor(D)–H	Acceptor (A)	D–H (Å)	D...A (Å)	H...A (Å)	D–H...A (°)
N(1')–H	O(5γ)[i]	0.94	2.719(11)	1.79	167
N(4'α)–H1	O(W)[ii]	0.91	2.835(14)	1.98	157
N(4'α)–H2	Cl(4)[iii]	0.95	3.135(8)	2.28	149
C(2)–H	Cl(1)	1.08	3.375(10)	2.82	112
O(5γ)–H	Cl(4)[i]	1.04	3.138(8)	2.19	150
O(W)–H1[b]	Cl(3)[iv]		3.262(9)		
O(W)–H2[b]	Cl(4)		3.194(9)		

Other short contacts (<3.6 Å for those involving S and Cl atoms and <3.5 Å for those involving other non-H atoms)

A	B	A...B (Å)	A	B	A...B (Å)
C(6')	O(W)	3.309(13)	Cl(1)	C(2)[i]	3.487(10) stack
C(2'α)	O(W)[v]	3.49(2)	Cl(1)	N(3)[i]	3.252(8) stack
N(3')	C(5')[ii]	3.488(12) stack[c]	Cl(1)	C(4)[i]	3.476(10) stack
N(3')	C(3,5')[ii]	3.420(11) stack	Cl(1)	C(3,5')[i]	3.535(10) stack
C(4')	C(4')[ii]	3.470(12) stack	Cl(2)	N(1')	3.556(8) stack
C(4')	C(5')[ii]	3.487(12) stack	Cl(2)	C(2')	3.330(9) stack
C(6')	N(4'α)[ii]	3.433(12) stack	Cl(2)	N(3')	3.504(8) stack
S(1)	O(5γ)	3.180(8)	Cl(3)	S(1)[vi]	3.283(3) stack
S(1)	Cl(4)[i]	3.486(3)	Cl(3)	C(2)[vi]	3.579(9) stack
Cl(1)	C(6')	3.551(10) stack			

[a]Symmetry code: (none) *x, y, z*; (i) −*x*, −*y*, 1−*z*; (ii) −*x*, 1−*y*, 1−*z*; (iii) *x*−1, *y*, *z*; (iv) *x, y, z*−1; (v) *x, y*, 1+*z*; (vi) −*x*, −*y*, 2−*z*. [b]This hydrogen atom was not located. [c]'stack' means stacking interaction.

and shapes occupy these positions. These anions or anionic groups which occupy the 'anion hole(s) I and/or II' for thiamine with the *F*-form include, for example, Cl⁻ [6k, 13, 17a, b], Br⁻ [17c], I⁻ [17d], phosphate [6j, 17e], NO_3^- [7, 17f–h], picrolonate [17i], sulfonate [17j], PF_6^- [17k], ClO_4^- [17k], NCS⁻ [17l], BF_4^- [17l], $[CuCl_4]^{2-}$ [8a], N(1')-bonded-$[CuCl_2]^-$ [6b] or −$[CuBr_2]^-$ [6c], or N(1')-bonded-$[Zn(NCS)_3]^-$ [6f] or −$[Cd(NCS)_3]^-$ [6f], and those which occupy the 'anion hole II' for thiamine with the *S*-form include $[CdCl_4]^{2-}$ [8b], $[CoCl_4]^{2-}$ [8c] or N(1')-bonded-$[CdCl_3]^-$ [6a] or −$[ZnCl_3]^-$ [6d].

Biological implications of the two 'anion holes': coenzyme fixation to apoenzyme and/or substrate fixation to coenzyme

We here consider possible biological functions of these 'anion holes' in the reaction processes of thiamine pyrophosphate-dependent enzymes. Hawkins *et al.* have identified a common sequence motif in thiamine pyrophosphate-binding enzymes, which has been postulated to form the cofactor binding site of these enzymes [18]: approximately 30 amino acid residues in length beginning with the highly conserved sequence –glycine–aspartate–glycine– and concluding with the highly conserved sequence –asparagine–asparagine–. The importance of the conserved aspartate in this –GDG– sequence has been demonstrated for pyruvate decarboxylase from *Zymomonas mobilis* [19]: substitution of

asparagine, threonine or glycine for aspartate-440 completely abolishes enzyme activity. It is therefore apparent that the carboxylate group of aspartate-440 directly takes part in coenzyme- and/or substrate-binding and/or catalytic reactions. Assuming that thiamine adopts the most frequently observed *F* conformation in the active site of the enzyme, we can expect that the carboxylate group of aspartate-440 occupies the 'anion hole I' or the 'anion hole II'. Furthermore, considering that pyruvate, a substrate anion, should be near the catalytic site C(2) [20] of the thiazolium ring, we present here two possible models for coenzyme/apoenzyme and/or substrate/coenzyme interactions: (i) the aspartate-440 carboxylate anion of the apoenzyme occupies the 'anion hole I' and/or the substrate pyruvate anion takes the 'anion hole II' or (ii) its reverse. It should be noted here that, because of the broad anion specificity of these anion holes, more precise recognition mechanism may be needed: this is especially true for the substrate recognition and this may be done by the apoenzyme before the substrate reaches the 'anion hole I' or 'II' of thiamine fixed in the apoenzyme.

Supplementary material

Tables of hydrogen atomic parameters (Table D1), anisotropic thermal parameters (Tables D2 and D3), bond lengths and angles of the $[PtCl_6]^{2-}$ anion (Table

D4) and those involving hydrogen atoms (Table D5), least-squares planes of the thiaminium molecule (Table D6), and observed and calculated structure factors (Tables D7 and D8) are available from K.A.

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