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Interactions of metal ions with the intermediate of thiamine catalysis Crystal structures of Cd(II), Hg(II) and Pt(II) complexes of 2-(α-hydroxybenzyl)thiamine

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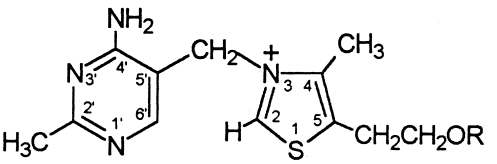
Abstract

Five complexes of formulae $Cd(HBT)X_3 \cdot H_2O$, $Hg_2X_5(HBT)$ (X=Cl, Br), and $Pt(HBT)(NO_2)_3$ were prepared by reacting CdX_2, HgX_2 and $K_2Pt(NO_2)_4$ with 2-(α-hydroxybenzyl)thiamine (HBT), an active intermediate of thiamine catalysis, and their crystal structures were determined by X-ray diffraction. The metal ion binds to the N(1′) site of the pyrimidine ring in each case, despite the different shapes and sizes of metal coordination units; a tetrahedral unit in the cadmium complexes, a double-metal unit consisting of two tetrahedral Hg(II) ions in the mercury complexes and a square-planar unit in the platinum complex. The HBT ligands in these complexes adopt the S conformation, as usually observed in C(2)-substituted derivatives of thiamine, with average torsion angles φ_T being ±99° and φ_P being ±175°. A 'two-point' anion-bridge between the amino group of the pyrimidine ring and the cationic thiazolium ring of the same molecule is found in all the structures, being of the form N(4′α)–H . . . X_1–M–X_2 . . . thiazolium-ring (M=metal ion), which is one of the factors that affect the S conformation. Stacking interactions between the pyrimidine and phenyl rings play an important role in the molecular conformation and crystal packing. The intramolecular close contact between the oxygen of the C(2)-substituent and the sulfur of the thiazolium ring is also a common feature to these complexes, which gives the mechanistic implications.

Keywords: C(2)-substituted derivative of thiamine; Complex; Crystal structure

1. Introduction

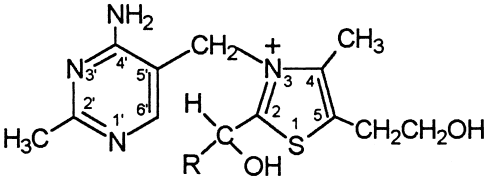
Thiamine (vitamin B_1) has a physiological function in the form of its pyrophosphate (TPP) (I), which acts as a coenzyme for a number of enzymes involved in catalyzing the decarboxylation of α-keto acids or the transfer of aldehyde or acyl groups [1]. According to Breslow [2,3], the catalytic function depends on the dissociation of a proton from the C(2) position of the thiazolium ring, leading to the formation of a carbanion of TPP that could be added to the carbonyl group of the substrate such as pyruvate. Upon decarboxylation, the so-called 'active aldehyde' intermediate (II) is formed, which reacts subsequently with an acceptor to give the product.



R = H thiamine

$H_2P_2O_6^-$ thiamine pyrophosphate

I



R = Ph 2-(α-hydroxybenzyl)thiamine

II

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It is well known that a divalent metal ion Mg(II) is required as a cofactor for thiamine catalysis [4,5]. Other divalent metal ions such as Mn(II), Co(II), Zn(II) and Cd(II) also show activity but with less efficiency [6,7]. Attempts to establish the role of the metal ion led to a large body of crystal structures of thiamine–metal compounds [8]. These compounds exist in two forms: ionic salts with a metal-containing anion [9–16] and metal complexes where direct metal bonding to thiamine is observed [17–30]. The latter shows metal ion bonding to N(1′) of the pyrimidine ring in the major cases [17–25,27–29] and to the hydroxyethyl oxygen of thiamine [26–29] or the pyrophosphate group of TPP [30] in the minor cases. In spite of the importance of C(2)-substituted derivatives as intermediates in thiamine reactions, research on the metal complexes with such derivatives is relatively rare. Hadjiliadis et al. [31,32] recently reported crystal structures of Hg(II) complexes of 2-(α-hydroxybenzyl)thiamine (HBT) [31] and 2-(α-hydroxybenzyl)thiamine monophosphate (HBTMP) [32], both of which show metal bonding to the N(1′) site.

In order to ascertain the general aspect of the interactions between metal ions and the thiamine intermediates, we tried to prepare the metal complexes with HBT in aqueous and methanolic aqueous solutions. We report here five crystal structures, of which $Cd(HBT)Cl_3\cdot H_2O$ (**1**) and $Cd(HBT)Br_3\cdot H_2O$ (**2**) are isomorphous to the reported HBT–Hg(II) complex, $Hg_2Cl_5(HBT)$ (**3**) and $Hg_2Br_5(HBT)$ (**4**) are the first example showing a double-metal unit bonding to the pyrimidine N(1′), and $Pt(HBT)(NO_2)_3$ (**5**) provides evidence that a metal ion not belonging to group IIB binds to HBT through N(1′) and is therefore the first of its type.

2. Experimental

2.1. Preparation of the complexes

2-(α-Hydroxybenzyl)thiamine chloride hydrochloride (HBTCl·HCl) was synthesized by using the method described in the literature [33]. The resulting light-yellow product was recrystallized from water by the addition of acetone.

$Cd(HBT)Cl_3\cdot H_2O$ (**1**), $Hg_2Cl_5(HBT)$ (**3**) and $Hg_2Br_5(HBT)$ (**4**) were prepared by reacting equimolar (0.1 mmol) amounts of HBTCl·HCl and metal halide, $CdCl_2$ for **1**, $HgCl_2$ for **3** and $HgBr_2$ for **4**, respectively,

Table 1
Crystal data and details of data collection and structure refinement for the five complexes

Complex	**1**	**2**	**3**	**4**	**5**
Formula	$C_{19}H_{25}CdCl_3N_4O_3S$	$C_{19}H_{25}Br_3CdN_4O_3S$	$C_{19}H_{23}Cl_5Hg_2N_4O_2S$	$C_{19}H_{23}Br_5Hg_2N_4O_2S$	$C_{19}H_{23}N_7O_8PtS$
Formula weight	608.26	741.61	949.92	1172.18	704.59
Space group	$P2_1/n$	$P2_1/n$	$P\bar{1}$	$P\bar{1}$	$P2_1/n$
a (Å)	9.6077(8)	9.762(1)	10.068(1)	10.260(1)	8.116(2)
b (Å)	7.677(3)	7.740(2)	17.286(2)	17.531(4)	16.207(3)
c (Å)	31.554(2)	31.952(5)	7.646(1)	7.730(2)	19.337(4)
α (°)			91.99(1)	91.52(2)	
β (°)	90.170(7)	90.39(1)	94.79(1)	94.70(1)	96.18(3)
γ (°)			83.16(1)	83.40(1)	
V (Å^3)	2327.5(9)	2414.2(8)	1316.2(3)	1376.3(5)	2528.7(9)
Z	4	4	2	2	4
D_{calc} (g cm^{-3})	1.736	2.040	2.397	2.829	1.851
Crystal size (mm)	0.1×0.2×0.6	0.1×0.2×0.25	0.15×0.25×0.3	0.02×0.15×0.18	0.16×0.18×0.32
μ(Mo Kα) (cm^{-1})	13.1	59.8	122.6	185.0	56.9
Scan technique	ω	ω	$\omega-2\theta$	$\omega-2\theta$	ω
2θ Range (°)	5–55	5–55	5–55	5–55	3–45
Reflections measured	6191	6432	6496	5843	4645
Reflections used (M)	4196	5542	4075	2632	3312
Observed reflections	4196	2986	4075	2632	1696
with $F_o > n\sigma(F_o)$	3	4	3	3	4
Variables (N)	281	284	308	299	351
Weighting scheme[a] (w)	1	$[\sigma^2(F_o^2)+(0.17P)^2+1.88P]^{-1}$	1	$1/\sigma^2(F_o)$	$[\sigma^2(F_o^2)+(0.1P)^2]^{-1}$
R[b]	0.035	0.075	0.044	0.058	0.054
Rw[c]	0.036	0.217	0.043	0.045	0.122
S[d]	1.72	0.99	2.62	3.19	0.84
Max. shift/error	0.008	0.026	0.099	0.031	0.229
Max. and min. residual (e Å^{-3})	0.47, −0.73	1.98, −2.32	1.21, −1.79	2.07, −1.70	1.04, −0.52

[a] $P=(F_o^2+2F_c^2)/3$ for **2** and **5**.
[b] $R=\Sigma\,\|\|F_o|-|F_c\|/\Sigma\,|F_o|$ using observed reflections with $F_o>n\sigma(F_o)$.
[c] $Rw=[\Sigma\,w(|F_o|-|F_c|)^2/\Sigma\,w|F_o|^2]^{1/2}$ for **1**, **3** and **4** and $Rw=[\Sigma\,w(F_o^2-F_c^2)^2/\Sigma\,w(F_o^2)^2]^{1/2}$ for **2** and **5**.
[d] $S=[\Sigma\,w(|F_o|-|F_c|)^2/(M-N)]^{1/2}$ for **1**, **3** and **4** and $S=[\Sigma\,w(F_o^2-F_c^2)^2/(M-N)]^{1/2}$ for **2** and **5**.

each dissolved in a mixed solution of water and methanol (v/v 1:1) and adjusting the pH value to 5 by using 0.1 N KOH solution. Colourless crystals formed after a few days.

The colourless crystals of $Cd(HBT)Br_3 \cdot H_2O$ (**2**) were obtained by employing a similar method to the above but using HBTCl·HCl (0.1 mmol), $Cd(CH_3CO_2)$ (0.1 mmol) and NaBr (0.4 mmol) as starting materials.

$Pt(HBT)(NO_2)_3$ (**5**) was prepared by reacting HBTCl·HCl (0.1 mmol) with $Ag(NO_3)$ (0.2 mmol) in water. Then the AgCl formed was filtered off and to the filtrate was added an aqueous solution of $K_2Pt(NO_2)_4$ (0.1 mmol). Light-yellow crystals were obtained from the resulting solution after 2 weeks.

2.2. X-ray structure determination

A crystal for each compound was mounted on a glass fiber for X-ray measurement. Reflection data were collected on a Rigaku AFC7R diffractometer for **1**, **2**, **3** and **4**, and on a Siemens R3m/E diffractometer for **5** with graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å) at 293 K. The details of crystal data, data collection and structure refinement are summarized in Table 1. Intensity data were corrected for absorption effects. The programs used for structure calculations are UNICSIII [34] for **1**, **3** and **4**, SHELXL [35] for **2** and **5**. All structures were solved by heavy-atom methods and refined by block-diagonal least-squares on F for **1**, **3** and **4** and full-matrix least-squares on F^2 for **2** and **5**. The Hg(2) atom in **3** and the four oxygen atoms of the NO_2^- groups in **5** are disordered, each in two possible positions. The occupancy factors were estimated according to their electron densities. The phenyl group in **5** was refined as a regular hexagon. The non-hydrogen atoms were refined anisotropically. All hydrogen atoms were calculated at their ideal positions except for **1**, in which all hydrogen atoms were located on difference Fourier maps. Hydrogen atoms were fixed in the final refinements for all the structures. The final positional parameters and anisotropic displacement parameters are given in Supplementary data.

3. Results

Bond lengths and angles of the metal coordination units for the five complexes are listed in Table 2. The molecular dimensions of HBT ligands (given in Supplementary data) agree well among these complexes. Compared with the N(1′)-protonated HBT [36], a major difference is in the C(2′)–N(1′)–C(6′) bond angles and the C(4′)–N(4′α) bond lengths (average 116° for the bond angles and 1.33 Å for the bond lengths for the five complexes). The protonation at N(1′) has more effect on increasing the bond angle (121.1°) and decreasing the bond length (1.310 Å) than does the metallation.

Table 2
Bond lengths (Å) and angles (°) for the metal coordination units[a]

	1	**2**
Cd–N(1′)	2.251(3)	2.257(9)
Cd–X(1)	2.506(1)	2.579(2)
Cd–X(2)	2.416(1)	2.533(2)
Cd–X(3)	2.472(1)	2.582(2)
N(1′)–Cd–X(1)	100.34(9)	100.7(2)
N(1′)–Cd–X(2)	115.61(8)	113.6(2)
N(1′)–Cd–X(3)	122.58(8)	123.2(2)
X(1)–Cd–X(2)	107.94(4)	109.51(6)
X(1)–Cd–X(3)	101.36(4)	101.46(6)
X(2)–Cd–X(3)	106.87(4)	106.87(6)
	3[b]	**4**
Hg(1)–N(1′)	2.250(6)	2.289(12)
Hg(1)–X(1)	2.572(3)	2.653(3)
Hg(1)–X(2)	2.544(3)	2.651(3)
Hg(1)–X(3)	2.360(4)	2.480(3)
Hg(2)–X(1)	2.882(3)	2.984(3)
Hg(2)–X(2)	2.931(3)	2.962(3)
Hg(2)–X(4)	2.321(3)	2.433(2)
Hg(2)–X(5)	2.286(3)	2.422(3)
Hg(2)′–Cl(1)	2.512(8)	
Hg(2)′–Cl(2)	2.444(9)	
Hg(2)′–Cl(4)	2.422(6)	
Hg(2)′–Cl(5)	2.612(8)	
N(1′)–Hg(1)–X(1)	108.7(2)	108.6(4)
N(1′)–Hg(1)–X(2)	97.2(2)	97.6(4)
N(1′)–Hg(1)–X(3)	126.6(2)	120.8(4)
X(1)–Hg(1)–X(2)	97.1(1)	99.3(1)
X(1)–Hg(1)–X(3)	105.4(1)	109.7(1)
X(2)–Hg(1)–X(3)	117.9(1)	118.2(1)
X(1)–Hg(2)–X(2)	82.5(1)	85.7(1)
X(1)–Hg(2)–X(4)	99.7(1)	100.6(1)
X(1)–Hg(2)–X(5)	105.5(1)	105.9(1)
X(2)–Hg(2)–X(4)	93.8(1)	95.8(1)
X(2)–Hg(2)–X(5)	102.4(1)	105.1(1)
X(4)–Hg(2)–X(5)	151.5(1)	147.1(1)
Cl(1)–Hg(2)′–Cl(2)	101.4(3)	
Cl(1)–Hg(2)′–Cl(4)	108.0(2)	
Cl(1)–Hg(2)′–Cl(5)	107.4(3)	
Cl(2)–Hg(2)′–Cl(4)	104.8(3)	
Cl(2)–Hg(2)′–Cl(5)	107.8(2)	
Cl(4)–Hg(2)′–Cl(5)	124.9(3)	
	5	
Pt–N(1′)	2.02(1)	
Pt–N(11)	1.965(8)	
Pt–N(12)	1.971(8)	
Pt–N(13)	1.96(2)	
N(1′)–Pt–N(11)	89.7(7)	
N(1′)–Pt–N(12)	93.9(7)	
N(1′)–Pt–N(13)	176.1(7)	
N(11)–Pt–N(12)	176.3(8)	
N(11)–Pt–N(13)	87.4(8)	
N(12)–Pt–N(13)	89.0(8)	

[a] X = Cl for **1** and **3** and Br for **2** and **4**.
[b] The occupancy factors are 0.90 for Hg(2) and 0.10 for Hg(2)′ in **3**.

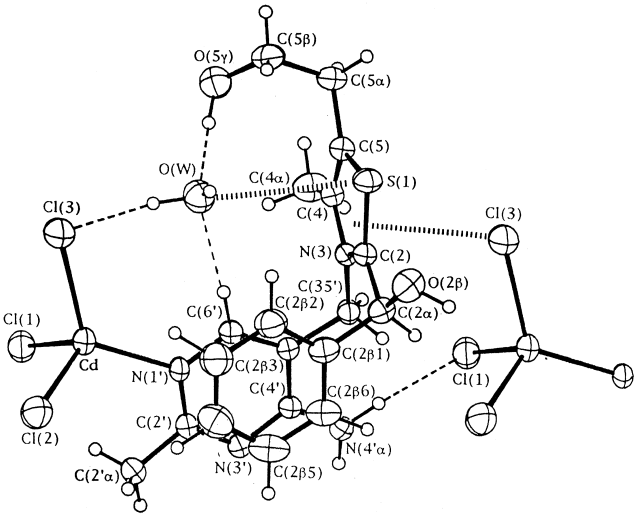

Fig. 1. Molecular structure of **1**, showing that a Cd(II)-coordination unit translated one unit along *a* axis forms the 'two-point' bridge, N(4′α)–H . . . Cl(1)–Cd–Cl(3) . . . thiazolium-ring and that a water molecule is held by the complex molecule through three hydrogen bonds and an O(W) . . . thiazolium-ring close contact. Broken lines denote hydrogen bonds and grating lines denote close contacts.

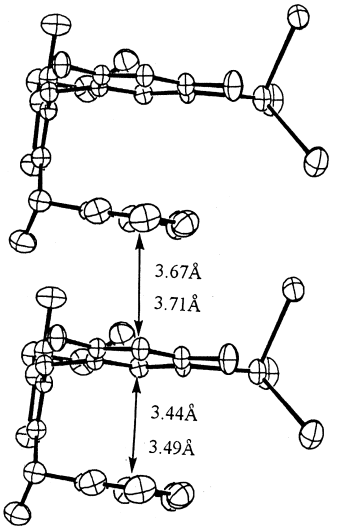

Fig. 2. Intra- and intermolecular ring stacking between the pyrimidine and phenyl rings with average contact distances for **1** (top number) and **2** (bottom number).

3.1. Cadmium complexes Cd(HBT)$Cl_3 \cdot H_2O$ (1) and Cd(HBT)$Br_3 \cdot H_2O$ (2)

The structure of **1** is shown in Fig. 1; that of **2** is similar and not shown. Although HBT coordinates to a tetrahedral $[CdX_3]^{-1}$ unit through N(1′), some structural features similar to the uncomplexed HBT are observed. The ligand adopts the S conformation in terms of the torsion angles defined by Pletcher et al. [36]: φ_T = C(5′)–C(35′)–N(3)–C(2) and φ_P = N(3)–C(35′)–C(5′)–C(4′) are 97.4(4) and −173.5(3)° for **1** and −97.5(2) and 173.3(9)° for **2**, respectively. This conformation is characterized by H(6′) directing over the thiazolium ring. The C(2) substituent is oriented in such a way that the phenyl ring is parallel to the pyrimidine ring forming a close intramolecular stacking. The average separation between the two aromatic rings is 3.44 Å in **1** and 3.49 Å in **2**. The complex molecules are further involved in intermolecular stacking between the pyrimidine and phenyl rings along the **b** direction with an average contact distance of 3.67 Å in **1** and 3.71 Å in **2** (Fig. 2). Another significant intramolecular close contact [37] exists between O(2β) of the substituent and the electropositive S(1) of the thiazolium ring (Table 3).

As seen previously in the thiamine compounds in which the molecules assume the S conformation, there is a 'two-point' anion-bridge [23] between the pyrimidine and thiazolium rings in **1** and **2**, that is, a halide atom X(1) forms a hydrogen bond with N(4′α) and another halide

Table 3
Hydrogen bonds and short contacts in **1** and **2**[a,b]

Donor-H	Acceptor	D . . . A (Å)		H . . . A (Å)		D–H . . . A (°)	
Hydrogen bonds		**1**	**2**	**1**	**2**	**1**	**2**
N(4′α)–H(4′1)	N(3′)[i]	3.136(4)	3.15(1)	2.23	2.29	171	176
N(4′α)–H(4′2)	X(1)[ii]	3.362(3)	3.490(9)	2.47	2.72	154	151
O(2β)–H(2β)	X(1)[iii]	3.046(3)	3.126(9)	2.06	2.31	173	171
O(5γ)–H(5γ)	O(W)	2.706(4)	2.71(1)	1.75	1.91	179	162
C(6′)–H(6′)	O(W)	3.439(5)	3.50(1)	2.44	2.58	176	171
O(W)–H(W1)	X(3)	3.104(3)	3.24(1)	2.11		170	
O(W)–H(W2)	O(5γ)[iv]	2.769(5)	2.73(1)	1.86		168	
Close contacts (Å)		**1**	**2**			**1**	**2**
S(1)	O(2β)	2.782(3)	2.78(1)	O(W)	C(5)	3.327(5)	3.28(1)
C(2)	X(3)[ii]	3.527(4)	3.63(1)	C(5′)	C(2β1)	3.444(5)	3.48(2)
N(3)	X(3)[ii]	3.449(3)	3.560(8)	C(5′)	C(2β6)	3.382(6)	3.43(2)
O(W)	C(4)	3.371(5)	3.33(1)	C(6′)	C(2β1)	3.452(5)	3.51(2)

[a] Symmetry code: for **1**, (none) *x*, *y*, *z*; (i) 2−*x*, 1−*y*, −*z*; (ii) 1+*x*, *y*, *z*; (iii) 1+*x*, *y*−1, *z*; (iv) 1.5−*x*, *y*−0.5, 0.5−*z*; for **2**, (none) *x*, *y*, *z*; (i) −*x*, 1−*y*, −*z*; (ii) *x*−1, *y*, *z*; (iii) *x*−1, *y*−1, *z*; (iv) 0.5−*x*, *y*−0.5, 0.5−*z*.

[b] X = Cl for **1** and Br for **2**.

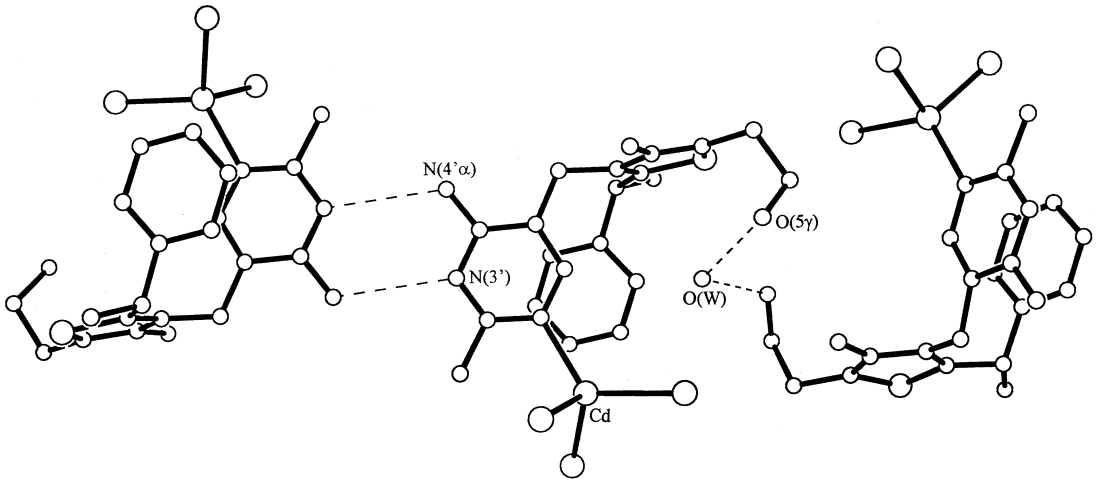

Fig. 3. Polymeric chain structure in **1**. Note that the dimers are formed through N(4′α)–H . . . N(3′) hydrogen bonds, which are further connected by hydrogen bonds into a chain. Broken lines denote hydrogen bonds.

X(3) of the same metal coordination unit stacks on the thiazolium ring, as shown in Table 3. Interestingly, we note that the complex molecule captures a water molecule through three hydrogen bonds, O(5γ)–H . . . O(W), C(6′)–H . . . O(W) and Cl(3) . . . H–O(W), and an O(W) . . . thiazolium-ring close contact. These interactions, together with those mentioned above stabilize the molecular conformation.

Crystal packing is dominated by three kinds of interactions, the 'two-point' bridge in the **a** direction, the aromatic ring stacking along the **b** direction and a pair of interbase hydrogen bonds, N(4′α)–H . . . N(3′), in the **c** direction creating a dimer across an inversion centre. The dimers are linked with the intervention of a water molecule into a chain (Fig. 3).

*3.2. Mercury complexes Hg_2Cl_5(HBT) (**3**) and Hg_2Br_5(HBT) (**4**)*

Compound **3** is isostructural with **4** except that Hg(2) in **3** is disordered at two sites. Fig. 4 shows the molecular structure of **4**. The metal coordination unit consists of two distorted tetrahedra sharing two vertexes. Despite the bulky double-metal unit $[Hg_2X_5]^{-1}$, the HBT ligand remains to coordinate to the metal ion through N(1′) of the pyrimidine ring. There is a close contact between Hg(2) and O(5γ) of a neighbouring molecule, 2.988(8) Å in **3** and 3.10(1) Å in **4** (Table 4). This distance is longer than the normal bond length of Hg–O(5γ) [2.60(2) Å] in the Hg–thiamine complex [26] but shorter than the sum of van der Waals radii (3.25 Å) estimated by using van der Waals radii of 1.73 Å for mercury, suggested by Canty and Deacon [38], and 1.52 Å for oxygen [39]. Accordingly, the O(5γ) atom can be considered to be a weak secondary coordination, which makes the Hg(2) distorted from a tetrahedron to a triangular bipyramid. The feasibility of this weak bonding is supported by the tetrahedral O(5γ) with two lone pairs, one aligned with Hg(2) and the other with the proton of O(2β). If the Hg(2) . . . O(5γ) interaction is considered, we can describe the complex as a cyclic dimer $[Hg_2X_5(HBT)]_2$ with two HBT ligands bridged by two $[Hg_2X_5]^{-1}$ units across a centre of symmetry, very similar to the situations of $[Mn(thiamine)Cl_2(H_2O)]_2^{2+}$ [28] and $[Cd(thiamine)Cl_3]_2$ [29] complexes.

The following structural features are found in **3** and **4**. (i) The ligand assumes the S conformation with the torsion angles: $\varphi_T = 96.5(9)°$ in **3** and 99(2)° in **4**; $\varphi_P = -171.7(7)°$ in **3** and −176(2)° in **4**. (ii) The C(2α)–O(2β) bond points to the direction of the C(2)–S(1) bond resulting in a close contact between O(2β) and S(1). (iii) The 'two-point'

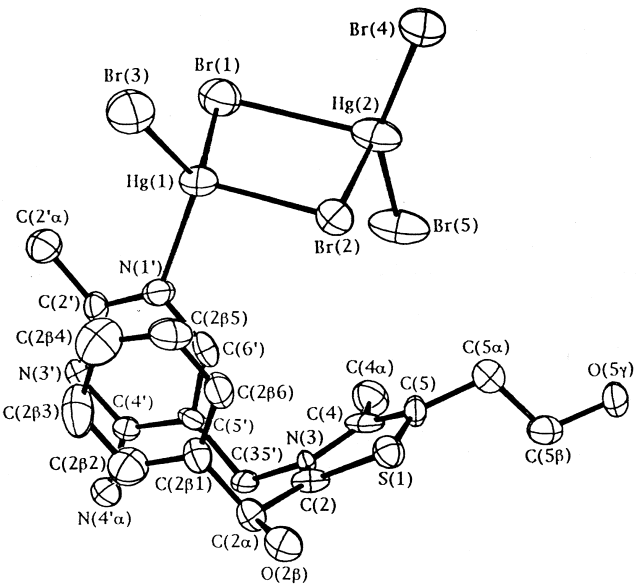

Fig. 4. Molecular structure of **4**, showing a double-metal unit binding to the N(1′) site.

Table 4
Hydrogen bonds and short contacts in **3** and **4**[a,b]

Donor-H	Acceptor	D . . . A (Å)		H . . . A (Å)		D–H . . . A (°)	
Hydrogen bonds		**3**	**4**	**3**	**4**	**3**	**4**
N(4′α)–H(4′1)	N(3′)^{i}	3.12(1)	3.09(2)	2.15	2.12	177	180
N(4′α)–H(4′2)	X(1)^{ii}	3.546(8)	3.74(2)	2.61	2.80	165	163
O(2β)–H(2β)	O(5γ)^{iii}	2.87(1)	2.89(2)	1.92	1.92	163	172
O(5γ)–H(5γ)	X(2)^{iv}	3.325(7)	3.46(1)	2.41	2.50	157	161
Close contacts (Å)		**3**	**4**			**3**	**4**
S(1)	O(2β)	2.919(7)	2.89(1)	C(2β5)	C(2′)^{v}	3.47(1)	3.48(3)
N(3)	X(4)^{ii}	3.379(7)	3.48(1)	S(1)	X(5)^{v}	3.419(4)	3.487(5)
C(4)	X(4)^{ii}	3.299(9)	3.37(2)	Hg(2)	O(5γ)^{vi}	2.988(8)	3.10(1)
C(2β2)	C(5′)	3.42(1)	3.40(3)	Hg(2)′	O(5γ)^{vi}	3.37(1)	

[a] Symmetry code: (none) *x, y, z*; (i) $1-x, 1-y, -z$; (ii) $x-1, y, z$; (iii) $1-x, -y, 1-z$; (iv) $2-x, -y, 1-z$; (v) $x, y, 1+z$; (vi) $2-x, -y, -z$.
[b] X=Cl for **3** and Br for **4**.

bridge is of the form N(4′α)–H . . . X(1)–Hg(2)–X(4) . . . thiazolium-ring. (iv) The stacking interactions between the pyrimidine and phenyl rings run along the **c** direction, with average intramolecular separations 3.51 Å in **3** and 3.55 Å in **4** and intermolecular separations 3.56 Å in **3** and 3.60 Å in **4**.

The dimers are formed through N(4′α)–H . . . N(3′) hydrogen bonds and they are further associated into a chain extending along the **b** direction. This occurs through a pair of hydrogen bonds between O(2β) and O(5γ) atoms.

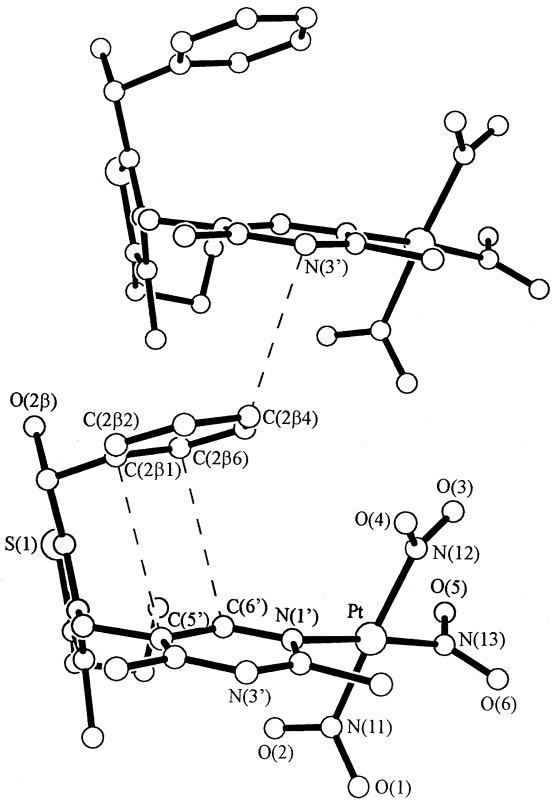

Fig. 5. Molecular structure of **5** and partial ring stacking interactions. The minor positions of disordered NO_2^- groups are not shown for clarity. Broken lines denote the closest contacts.

*3.3. Platinum complex Pt(HBT)(NO$_2$)$_3$ (**5**)*

As is shown in Fig. 5, the Pt(II) ion is coordinated by an N(1′) atom of the pyrimidine ring and three N atoms of the NO_2^- groups in a square-planar geometry. The coordination plane is approximately perpendicular to the pyrimidine ring with a dihedral angle of 72.2(5)°. The Pt–N(1′) distance, 2.02(1) Å, is very close to that in Pt(thiamine)$Cl_3 \cdot H_2O$, 2.01(2)Å [21], and slightly shorter than that in *trans*-[Pt(dmso)(thiamine)Cl_2][Ph_4B], 2.06(1) Å [24]. The torsion angles φ_T and φ_P are −106(2) and −179(2)°, corresponding to the S conformation. The 'two-point' bridge is found here again. As is given in Table 5, the pyrimidine and thiazolium moieties are bridged by the Pt(II) coordination unit from a neighbouring molecule through an N(4′α)–H . . . O(5) [and O(6)] bifurcated hydrogen bond and an O(3) . . . thiazolium-ring close contact. It can be seen from Fig. 5 that unlike the above structures, the pyrimidine and phenyl rings are not fully but partially stacked on each other, either intra- or intermolecularly. Table 5 shows that the closest intramolecular contacts are C(5′) . . . C(2β1) and C(6′) . . . C(2β6) [both 3.50(2) Å], and the closest intermolecular contact is C(2β4) . . . N(3′) $(x+1, y, z)$, 3.50(3) Å. This partial stacking interaction is probably due to the obstruction of the metal coordination plane perpendicular to the pyrimidine ring.

The crystal packing mode is similar to that in **1** or **3**. The difference is only in that the thiamine dimers created by interbase hydrogen bonds are connected in a tail-to-tail fashion through hydrogen bonds of O(5γ) . . . O(5γ) $(2-x, -y, 1-z)$ across an inversion centre. This hydrogen bond may be formed with a disordered hydrogen atom attached to O(5γ).

4. Discussion

There are many common structural features among the five complexes though they are in three kinds of crystalline forms. The present work indicates that the N(1′) site is

Table 5
Hydrogen bonds and short contacts in **5**[a]

Donor-H		Acceptor	D . . . A (Å)	H . . . A (Å)	D–H . . . A (°)
Hydrogen bonds					
N(4′α)–H(4′1)		N(3′)[i]	3.08(2)	2.23	175
N(4′α)–H(4′2)[b]		O(5)[ii]	3.50(2)	2.65	168
		O(6)[ii]	2.98(2)	2.28	139
O(5γ)		O(5γ)[iii]	2.96(6)		
Close contacts (Å)					
S(1)	O(2β)	2.75(2)	C(5′)	C(2β1)	3.50(2)
C(2)	O(3)[ii]	3.11(3)	C(6′)	C(2β6)	3.50(2)
N(3)	O(3)[ii]	3.09(4)	C(2β4)	N(3′)[iv]	3.50(3)

[a] Symmetry code: (none) *x*, *y*, *z*; (i) $1-x$, $1-y$, $1-z$; (ii) $x-0.5$, $0.5-y$, $z-0.5$; (iii) $2-x$, $-y$, $1-z$; (iv) $x+1$, *y*, *z*.
[b] Bifurcated hydrogen bond.

favoured by metal bonding in the case of HBT. This may be rationalizable from an electronic effect, namely the high basicity of this site. The Cd–N(1′) bond length of 2.251(3) Å in **1** is comparable with that in Cd(thiamine)$Cl_3 \cdot 0.6H_2O$, 2.239(2) Å [17]. This bond length increases with the decrease of electronegativity of anionic ligands, indicated by the values in **2** and **4** containing Br^- ligands being larger than those in **1** and **3** containing Cl^- ligands, while the C(2′)–N(1′)–C(6′) bond angle increases with increasing electronegativity. Somewhat surprisingly, the crystal structures of metal complexes of C(2)-substituted derivatives reported so far, including this work, are exclusively those of HBT and HBTMP. Attempts to prepare metal complexes of other C(2)-adducts only led to the salt-type compounds in our laboratory. A distinct structural aspect of HBT different from other C(2)-adducts is aromatic ring stacking between the pyrimidine and phenyl rings. Thus, the structure of the HBT complex could be stabilized by such a stacking interaction. The intramolecular stacking distances are in the order of free HBT (3.41 Å)<**1** (3.44 Å)<**2** (3.49 Å)<**3** (3.51 Å)<**4** (3.55 Å), indicative of an influence of the shape and size of the metal coordination unit on the aromatic stacking.

Pletcher et al. [36] defined the conformations of thiamine and its derivatives in three forms: F ($\varphi_T \approx 0$, $\varphi_P \approx \pm 90°$), S ($\varphi_T \approx \pm 100$, $\varphi_P \approx \pm 150°$) and V ($\varphi_T \approx \pm 90$, $\varphi_P \approx \mp 90°$). The crystal structure data show that the F conformation is common to C(2) free thiamine and the S conformation is characteristic of C(2)-substituted derivatives. The factors affecting the conformation of thiamine have been an interesting point. Shin et al. [40,41] argued that the conformation of thiamine is largely influenced by intramolecular properties. It is obvious that the conformation of HBT depends on the intrinsic property of the molecule since all the HBT compounds are in the S-form in spite of different space groups and metal coordination units. This intrinsic property may arise from the tendency to form the O(2β) . . . S(1) close contact and ring stacking interaction. In view of that these two interactions are observed in all of the HBT compounds, it seems possible that both of these factors are important in stabilizing the molecular conformation. On the other hand, Aoki et al. [22,23] proposed that the S conformation is associated with the 'two-point' bridge as described above while the F conformation is accompanied by a 'one-point' bridge like N(4′α)–H . . . X . . . thiazolium-ring. Not only the 'two-point' bridge exists in the HBT–metal complexes but also it was found in the metal complexes and metal–anion salts of C(2) free thiamine in the S-form (see Table 8 in Ref. [23]). This implies that the crystal packing force also imposes an effect on the conformation. Moreover, we noticed that the V conformation has never been reported for the crystal structure of thiamine or TPP but it was recently found in the crystal structures of thiamine-dependent enzymes [42–44], indicating that the V conformation may result from an environment influence imposed by the enzymes. Therefore, the conformation favoured by thiamine should be a combined result of intra- and intermolecular forces.

Besides the aromatic ring stacking, an important structural feature common to the HBT compounds is the close contact of O(2β) . . . S(1). This interaction not only affects the molecular conformation but has mechanistic implications. The possible functions are, for example, (i) to provide a specific electrostatic substrate–coenzyme recognition, (ii) to stabilize the C(2) substituent in the position of catalytic reaction, and/or (iii) to facilitate the deprotonation from O(2β), which is required by the mechanism of Breslow [2,3].

It is of interest to note that all the HBT–metal complexes manifest a very similar packing mode. The molecular packing is controlled by three factors. (i) A polymeric chain structure is formed with hydrogen-bonded [N(4′α)–H . . . N(3′)] dimers connected by hydrogen bonds involving the water molecule and the O(5γ) atom in **1** and **2**, a pair of O(2β)–H . . . O(5γ) hydrogen bonds in **3** and **4** and hydrogen bonds between the symmetry-related O(5γ) atoms in **5**. (ii) The molecular chains are associated with each other by the 'two-point' bridge interactions. (iii) Interestingly, all the HBT compounds including free HBT show one of the axes having a similar length, that is the *b* axis for **1** and **2**, *c* axis for **3** and **4**, *a* axis for **5** (which is

slightly longer because of the partial stacking) and *b* axis for the free HBT. This axis is the direction of aromatic ring stacking.

Supplementary data

Supplementary data are available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK on request, quoting the deposition numbers CCDC118802–CCDC118806.

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References

[1] L.O. Krampitz, Annu. Rev. Biochem. 38 (1969) 213.
[2] R. Breslow, J. Am. Chem. Soc. 80 (1958) 3719.
[3] R. Breslow, E. McNelis, J. Am. Chem. Soc. 81 (1959) 3080.
[4] A. Schellenberger, Angew. Chem., Int. Ed. Engl. 6 (1967) 1024.
[5] M.C. Scrutton, Inorg. Biochem. 1 (1973) 381.
[6] D.E. Green, D. Herbert, V. Subrahmanyan, J. Biol. Chem. 138 (1941) 327.
[7] A.A. Gallo, I.L. Hansen, H.Z. Sable, T.J. Swift, J. Biol. Chem. 247 (1972) 5913.
[8] M. Louloudi, N. Hadjiliadis, Coord. Chem. Rev. 135–136 (1994) 429.
[9] D.A. Clemente, G. Bandoli, F. Benetollo, A. Marzotto, J. Cryst. Mol. Struct. 4 (1974) 1.
[10] M.R. Caira, G.V. Fazakerley, P.W. Linder, L.R. Nassimbeni, Acta Crystallogr., Sect. B 30 (1974) 1660.
[11] M.F. Richardson, K. Franklin, D.M. Thompson, J. Am. Chem. Soc. 97 (1975) 3204.
[12] G. Blank, M. Rodrigues, J. Pletcher, M. Sax, Acta Crystallogr., Sect. B 32 (1976) 2970.
[13] C.L. MacLaurin, M.F. Richardson, Acta Crystallogr., Sect. C 39 (1983) 854.
[14] N. Hadjiliadis, A. Yannopoulos, R. Bau, Inorg. Chim. Acta 69 (1983) 109.
[15] K. Aoki, T. Tokuno, K. Takagi, Y. Hirose, I.-H. Suh, A. Adeyemo, G.N. Williams, Inorg. Chim. Acta 210 (1993) 17.
[16] J.S. Casas, A. Castineiras, M.D. Couce, G. Martinez, J. Sordo, J.M. Varela, J. Organomet. Chem. 517 (1996) 165.
[17] R.E. Cramer, R.B. Maynard, J.A. Ibers, J. Am. Chem. Soc. 103 (1981) 76.
[18] R.E. Cramer, R.B. Maynard, R.S. Evangelista, J. Am. Chem. Soc. 106 (1984) 111.
[19] K. Aoki, H. Yamazaki, J. Am. Chem. Soc. 107 (1985) 6242.
[20] A. Bencini, E. Borghi, Inorg. Chim. Acta 135 (1987) 85.
[21] R.E. Cramer, R.E. Kirkup, M.J.J. Carrie, Inorg. Chem. 27 (1988) 123.
[22] E. Archibong, A. Adeyemo, K. Aoki, H. Yamazaki, Inorg. Chim. Acta 156 (1989) 77.
[23] K. Aoki, N.-H. Hu, H. Yamazaki, A. Adeyemo, Inorg. Chim. Acta 175 (1990) 247.
[24] R.E. Cramer, M.J.J. Carrie, Inorg. Chem. 32 (1993) 3509.
[25] J.S. Casas, A. Castineiras, M.D. Couce, A. Sanchez, J. Sordo, J.M. Varela, Polyhedron 14 (1995) 1825.
[26] Z.-S. Jin, P.-J. Liu, G.-C. Wei, W.-Y. Wang, Chin. Sci. Bull. 35 (1990) 383.
[27] K. Aoki, H. Yamazaki, A. Adeyemo, Inorg. Chim. Acta 180 (1991) 117.
[28] N.-H. Hu, Inorg. Chim. Acta 186 (1991) 209.
[29] J.S. Casas, E.E. Castellano, M.D. Couce, A. Sanchez, J. Sordo, J.M. Varela, J. Zukerman-Schpector, Inorg. Chem. 34 (1995) 2430.
[30] K. Aoki, H. Yamazaki, J. Am. Chem. Soc. 102 (1980) 6878.
[31] M. Louloudi, N. Hadjiliadis, J.-A. Feng, S. Sukumar, R. Bau, J. Am. Chem. Soc. 112 (1990) 7233.
[32] K. Dodi, I.P. Gerothanassis, N. Hadjiliadis, A. Schreiber, R. Bau, I.S. Butler, P.J. Barrie, Inorg. Chem. 35 (1996) 6513.
[33] J.J. Mieyal, G. Bantle, R.G. Votaw, I.A. Rosner, H.Z. Sable, J. Biol. Chem. 246 (1971) 5213.
[34] T. Sakurai, K. Kobayashi, Rikagaku Kenkyusho Hokoku 55 (1979) 69.
[35] G.M. Sheldrick, SHELXL-97, University of Gottingen, Germany, 1997.
[36] J. Pletcher, M. Sax, G. Blank, M. Wood, J. Am. Chem. Soc. 99 (1977) 1396.
[37] M. Sax, P. Pulsinelli, J. Pletcher, J. Am. Chem. Soc. 96 (1974) 155.
[38] A.J. Canty, G.B. Deacon, Inorg. Chim. Acta 45 (1980) L225.
[39] A. Bondi, J. Phys. Chem. 68 (1964) 441.
[40] W. Shin, J. Pletcher, G. Blank, M. Sax, J. Am. Chem. Soc. 99 (1977) 3491.
[41] W. Shin, D.-G. Oh, C.-H. Chae, T.-S. Yoon, J. Am. Chem. Soc. 115 (1993) 12238.
[42] Y. Lindqvist, G. Schneider, U. Ermler, M. Sundstrom, EMBO J. 11 (1992) 2373.
[43] Y.A. Muller, G.E. Schulz, Science 259 (1993) 965.
[44] F. Dyda, W. Furey, S. Swaminathan, M. Sax, B. Farrenkopf, F. Jordan, Biochemistry 32 (1993) 6165.