Metal ion interactions with vitamin B_1. Crystal structures of $Zn(thiamine)(SCN)_3$ having a metal–base bond and $Cd(thiamine)(SCN)_3$ having a metal–hydroxyethyl bond

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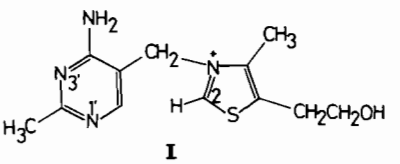
Abstract

The crystal structures of $Zn(thiamine)(SCN)_3$ (**1**) and $Cd(thiamine)(SCN)_3$ (**2**) have been determined by X-ray diffraction methods. The zinc complex **1** forms a discrete structure in which the tetrahedral Zn(II) ion is bonded by the pyrimidine ring nitrogen N(1′) and three thiocyanato ligands through nitrogen atoms. The cadmium complex **2** forms a polymeric structure with the octahedral Cd(II) ion bonded by the lateral hydroxyethyl oxygen O (5γ) of thiamine and five thiocyanato ligands, one terminal and the others bridging ones. Each thiamine ligand in **1** and **2** adopts the usually observed *F* conformation. A thiocyanato ligand bridges between the thiazolium and the pyrimidine rings of the same thiamine molecule through a C(2)–H...SCN^- hydrogen bond and an SCN^-...pyrimidine ring electrostatic contact; this is a factor that affects the *F* conformation of thiamine. This anion-bridge is also emphasized as a substrate fixation model. Crystal data: $C_{15}H_{17}N_4OS_4Zn$ (**1**), monoclinic, space group $P2_1/a$, $a = 17.764(5)$, $b = 12.484(2)$, $c = 12.104(2)$ Å, $\beta = 125.46(2)°$, $V = 2186.4(9)$ Å^3, $Z = 4$, and $R = 0.043$ for 2076 observed reflections ($F_o > 3\sigma(F_o)$); $C_{15}H_{17}CdN_7OS_4$ (**2**), triclinic, space group $P\bar{1}$, $a = 8.118(4)$, $b = 10.076(4)$, $c = 14.174(5)$ Å, $\alpha = 94.32(3)$, $\beta = 85.88(3)$, $\gamma = 111.49(4)°$, $V = 1075(2)$ Å^3, $Z = 2$, and $R = 0.072$ for 3940 reflections ($F_o > 3\sigma(F_o)$).

Introduction

Much interest has been focussed on metal ion interactions with thiamine (**I**; vitamin B_1) because thiamine-dependent enzymes require a divalent metal ion, Mg^2, for their functions [1], thus leading to a growing body of crystal structures of metal compounds of thiamine [2–4]. However, among eighteen crystal structures so far reported, half [2] are salt type, i.e., no direct metal bonding to thiamine. It is only recently that the metal–thiamine bonding through the ring nitrogen N(1′) was first reported for $Cd(thiamine)Cl_3$ by Cramer *et al.* [3a], thereafter followed by additional nine crystal structures, Cu^+ [3b, c], Zn^{2+} [3d, f], Co^{2+} [3e, f], Pt^{2+} [2g], Hg^{2+} [3g], and Rh^{2+} [3h] complexes, all of which except a rhodium complex [3h] are polyhalogenometal compounds. The Cu^{2+}–thiamine pyrophosphate complex [4] is unique in that the metal binds to the pyrophosphate group but not N(1′).



I

We report here two crystal structures of thiocyanatometal complexes of thiamine: $Zn(thiamine)(SCN)_3$ (**1**) provides an additional example involving the metal bonding to the pyrimidine N(1′), while $Cd(thiamine)(SCN)_3$ (**2**) is the first example showing the metal bonding to the hydroxyethyl terminal oxygen O(5γ). Zn^{2+} and Cd^{2+} ions belong to those ions which activate pyruvate carboxylase with somewhat reduced activities [5]. Factors

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that affect the thiamine conformation are considered in terms of thiamine–anion interactions.

Experimental

Preparations

The zinc and the cadmium compounds were obtained by reacting thiaminium·$(SCN)_2$ with $Zn(OAc)_2 \cdot 2H_2O$ or $Cd(OAc)_2 \cdot 2H_2O$ in water (2:1 molar ratio).

Data collection and processing

Details of crystal data and data collection together with refinement data are summarized in Table 1. Intensities were corrected for Lorentz and polarization effects but not for absorption since the variations in F_o of axial reflections, at $\chi \sim 90°$ with the spindle angle ϕ were within 3% from the mean for **1** and within 5% for **2**.

Solution and refinement of the structures

Both structures were solved by heavy-atom methods and refined by block-diagonal least-squares methods, minimizing the function $\Sigma w(F_o - |F_c|)^2$. Thermal parameters of all non-hydrogen atoms were refined anisotropically. All hydrogen atoms except one attached to O(5γ) in **2** were located from difference Fourier maps and their positional and isotropic thermal parameters were refined for **1** while those in **2** were included in the structure factor calculations of the final cycles of refinements but fixed ($B = 5$ Å^2). The final atomic parameters are listed in Tables 2 and 3 for **1** and **2**, respectively.

Neutral atomic scattering factors were used with Zn, Cd, and S corrected for anomalous dispersion [6]. All calculations were performed with the UNICSIII program system [7] on a FACOM 780 computer.

TABLE 1. Summary of crystal data, data collection and structure refinement

Compound	Zn(thiamine)$(SCN)_3$ (**1**)	Cd(thiamine)$(SCN)_3$ (**2**)
Formula	$C_{15}H_{17}N_7OS_4Zn$	$C_{15}H_{17}CdN_7OS_4$
M	504.98	552.01
Crystal system	monoclinic	triclinic
Space group	$P2_1/a$	$P\bar{1}$
a (Å)	17.764(5)	8.118(4)
b (Å)	12.484(2)	10.076(4)
c (Å)	12.104(2)	14.174(5)
α (°)		94.32(3)
β (°)	125.46(2)	85.88(3)
γ (°)		111.49(4)
V (Å^3)	2186.4(9)	1075(2)
Z	4	2
D_{calc} (g cm^{-3})	1.53	1.71
$F(000)$	1032	552
Crystal size (mm)	$0.14 \times 0.20 \times 0.22$	$0.25 \times 0.45 \times 0.45$
Crystal color	colorless	colorless
Diffractometer	Rigaku AFC	Nonius CAD4
μ (Mo Kα) (cm^{-1})	15.37	14.06
Transmission factors[a]	0.97–1.03	0.95–1.04
T (K)	293	293
Reflections measured	$\pm h, +k, +l$	$+h, \pm k, \pm l$
Scan type	ω–2θ	ω–2θ
2θ Range (°)	3.0–45.0	3.0–55.0
Scan speed (° min^{-1})	4.0	variable (1.27–4.12)
Scan range (°)	$1.2 + 0.5 \tan \theta$	$1.0 + 0.35 \tan \theta$
No. reflections measured	3016	4085
No. observed unique reflections (m) [$F_o > 3\sigma(F_o)$]	2076	3940
Variables (n)	312	253
Weighting scheme (w)	$\sigma(F_o)^{-2}$	1.0 for $F_o \leqslant 50.0$
$\sqrt{w}$		$50.0/F_o$ for $F_o > 50.0$
R[b]	0.043	0.072
R_w[c]	0.026	0.087
S[d]	1.55	2.20
$\Delta\rho_{max}$ (e Å^{-3})	0.43	0.72

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

TABLE 2. Atomic parameters ($\times 10^5$ for Zn and $\times 10^4$ for others) for Zn(thiamine)$(SCN)_3$ (**1**)

	x	y	z	B_{eq} (Å^2)[a]
Zn	19996(4)	16435(5)	38830(6)	3.3
N(1′)	958(2)	2552(3)	3612(3)	2.7
C(2′)	1070(3)	3230(4)	4572(4)	3.0
N(3′)	437(2)	3921(3)	4393(3)	3.0
C(4′)	−369(3)	3993(4)	3143(5)	3.2
C(5′)	−521(3)	3341(4)	2076(4)	2.8
C(6′)	157(3)	2640(4)	2362(4)	3.0
C(2′α)	1980(3)	3238(4)	5941(4)	4.2
N(4′α)	−978(3)	4698(3)	3023(4)	4.3
C(3,5′)	−1337(3)	3496(4)	622(4)	3.3
S(1)	−3308(1)	1859(1)	405(1)	4.1
C(2)	−2237(3)	2307(4)	1089(4)	3.3
N(3)	−2204(2)	2982(3)	276(3)	2.4
C(4)	−3051(3)	3141(4)	−968(4)	2.7
C(5)	−3735(3)	2576(4)	−1063(4)	3.1
C(4α)	−3129(3)	3911(4)	−1982(5)	4.1
C(5α)	−4740(3)	2548(5)	−2194(5)	4.8
C(5β)	−5324(3)	3047(5)	−1771(6)	7.3
O(5γ)	−5234(2)	2353(4)	−749(4)	9.4
S(11)	3944(1)	−39(1)	8054(2)	5.7
C(11)	3168(3)	404(4)	6557(5)	4.3
N(11)	2608(3)	730(3)	5483(4)	5.1
S(21)	4348(1)	3830(1)	4409(1)	5.3
C(21)	3543(3)	3116(4)	4287(4)	3.7
N(21)	2954(3)	2608(4)	4156(4)	4.8
S(31)	1686(1)	−443(1)	481(1)	4.8
C(31)	1590(3)	277(4)	1509(4)	3.1
N(31)	1538(3)	788(3)	2248(4)	4.4

[a] $B_{eq} = \frac{4}{3}\Sigma\Sigma\beta_{ij}\mathbf{a}_i \cdot \mathbf{a}_j$.

TABLE 3. Atomic parameters ($\times 10^5$ for Cd and $\times 10^4$ for others) for Cd(thiamine)$(SCN)_3$ (**2**)

	x	y	z	B_{eq} (Å^2)[a]
Cd	1284(8)	26733(6)	10867(4)	2.9
N(1′)	7480(10)	8563(8)	6602(5)	3.6
C(2′)	7025(11)	9704(9)	6612(6)	3.4
N(3′)	7024(10)	10417(8)	5854(5)	3.8
C(4′)	7444(11)	9876(10)	5011(6)	3.7
C(5′)	7876(11)	8667(10)	4923(6)	3.5
C(6′)	7877(12)	8049(10)	5739(6)	3.7
C(2′α)	6519(15)	10233(11)	7565(7)	4.7
N(4′α)	7499(14)	10593(10)	4243(7)	5.6
C(3,5′)	8423(12)	8070(11)	4004(6)	4.3
S(1)	3853(3)	5912(3)	2884(2)	4.1
C(2)	5213(12)	6983(11)	3673(6)	3.9
N(3)	6901(9)	7219(7)	3431(5)	3.0
C(4)	7140(10)	6499(8)	2589(5)	2.7
C(5)	5615(11)	5754(9)	2189(5)	3.0
C(4α)	8974(11)	6633(10)	2228(6)	3.8
C(5α)	5298(12)	4821(10)	1298(6)	3.6
C(5β)	4407(12)	3265(10)	1494(7)	4.1
O(5γ)	2658(8)	3007(6)	1925(4)	3.3
S(11)	−2690(6)	3924(4)	4162(2)	7.8
C(11)	−1677(14)	3524(10)	3213(6)	4.1
N(11)	−1002(13)	3236(10)	2536(6)	5.1
S(21)	−1639(4)	22(2)	1712(2)	4.3
C(21)	−1575(11)	−1043(9)	781(6)	3.0
N(21)	−1542(11)	−1793(9)	143(5)	4.0
S(31)	−2533(3)	2250(2)	−49(2)	3.8
C(31)	−1880(10)	3842(9)	−462(5)	2.8
N(31)	−1453(10)	4966(8)	−758(5)	3.8

[a] $B_{eq} = \frac{4}{3}\Sigma\Sigma\beta_{ij}\mathbf{a}_i \cdot \mathbf{a}_j$.

Results

Selected interatomic distances and angles are listed in Table 4.

Zinc(II) complex 1

Figure 1 shows the molecular structure of the complex. The complex forms a discrete Zn(thiamine)$(SCN)_3$ structure in which the tetrahedral Zn(II) ion is coordinated to a thiamine molecule through the pyrimidine ring nitrogen N(1′) and three thiocyanato ligands through nitrogen atoms. The thiamine ligand is in the usual *F* conformation [8] with torsion angles ϕ_T [8] = C(5′)–C(3,5′)–N(3)–C(2) = −10.2(7)° and ϕ_P [8] = N(3)–C(3,5′)–C(5′)–C(4′) = −82.8(6)°; the dihedral angle between the pyrimidine and the thiazolium rings is 96.0(1)°. The C(5)–hydroxyethyl side chain is folded back towards the thiazolium ring with a short contact of 2.915(4) Å between the O(5γ) and S(1) atoms (sum of van der Waals radii for S…O = 3.32 Å [9]: $\phi_{5\alpha}$ [8] = S(1)–C(5)–C(5α)–C(5β) = 64.7(6)° and $\phi_{5\beta}$ [8] = C(5)–C(5α)–C(5β)–O(5γ) = −66.6(6)°.

The crystal packing is mainly dominated by hydrogen-bonding and electrostatic interactions (Fig. 2 and Table 5). All the three hydrogen atoms attached to the amino N(4′α) and hydroxy O(5γ) groups of thiamine participate in hydrogen-bonding. The N(4′α) donates a proton to the pyrimidine ring nitrogen N(3′) of a neighboring molecule related by a center of symmetry, thus forming a pyrimidine dimer, and another proton to the thiocyanato sulfur S(31) belonging to another neighboring molecule. This thiocyanato group further locates over and in parallel to the thiazolium ring with the closest contact of 3.537(5) Å between the S(31) and C(4) atoms, thus bridging between the pyrimidine and thiazolium moieties of the same thiamine molecule, as shown also in Fig. 1. The O(5γ) forms a hydrogen bond with the thiocyanato S(11) acceptor of a neighboring molecule translated along the *a* axis. The acidic C(2)–hydrogen takes part in hydrogen-bonding with

TABLE 4. Selected interatomic distances (Å) and angles (°)

Zn(thiamine)$(SCN)_3$ (1)		Cd(thiamine)$(SCN)_3$ (2)	
(a) Metal coordination sphere			
Zn–N(1′)	2.027(4)	Cd–O(5γ)	2.351(6)
Zn–N(11)	1.946(4)	Cd–N(11)	2.307(9)
Zn–N(21)	1.946(5)	Cd–(21)′	2.316(8)
Zn–N(31)	1.961(4)	Cd–N(31)	2.291(8)
		Cd–S(21)	2.711(2)
		Cd–S(31)″	2.676(3)
(b) Thiamine ligand			
N(1′)–C(2′)	1.356(7)		1.33(1)
C(2′)–N(3′)	1.331(7)		1.34(1)
N(3′)–C(4′)	1.355(4)		1.35(1)
C(4′)–C(5′)	1.414(8)		1.38(2)
C(5′)–C(6′)	1.361(7)		1.36(1)
C(6′)–N(1′)	1.352(4)		1.36(1)
C(2′)–C(2′α)	1.501(5)		1.50(1)
C(4′)–N(4′α)	1.336(7)		1.34(1)
C(5′)–C(3,5′)	1.509(5)		1.50(1)
C(3,5′)–N(3)	1.487(7)		1.48(1)
S(1)–C(2)	1.670(5)		1.660(9)
C(2)–N(3)	1.322(7)		1.33(1)
N(3)–C(4)	1.393(4)		1.39(1)
C(4)–C(5)	1.351(8)		1.33(1)
C(5)–S(1)	1.723(5)		1.727(9)
C(4)–C(4α)	1.501(8)		1.50(1)
C(5)–C(5α)	1.492(5)		1.49(1)
C(5α)–C(5β)	1.531(10)		1.50(1)
C(5β)–O(5γ)	1.442(9)		1.44(1)
N(1′)–C(2′)–N(3′)	125.2(3)		125.4(8)
C(2′)–N(3′)–C(4′)	118.1(4)		116.2(9)
N(3′)–C(4′)–C(5′)	120.0(5)		122.7(9)
C(4′)–C(5′)–C(6′)	117.8(3)		116.2(8)
C(5′)–C(6′)–N(1′)	122.6(5)		123.1(10)
C(6′)–N(1′)–C(2′)	116.3(4)		116.3(8)
N(1′)–C(2′)–C(2′α)	118.6(4)		116.0(9)
N(3′)–C(2′)–C(2′α)	116.3(4)		118.6(10)
N(3′)–C(4′)–N(4′α)	115.5(5)		117.3(10)
C(5′)–C(4′)–N(4′α)	124.5(3)		119.9(9)
C(4′)–C(5′)–C(3,5′)	122.5(4)		124.2(9)
C(6′)–C(5′)–C(3,5′)	119.3(5)		119.5(10)
C(5′)–C(3,5′)–N(3)	114.2(5)		112.9(8)
C(3,5′)–N(3)–C(2)	123.4(3)		125.5(7)
C(3,5′)–N(3)–C(4)	122.4(4)		121.0(7)
S(1)–C(2)–N(3)	111.9(3)		112.4(7)
C(2)–N(3)–C(4)	114.2(4)		113.4(7)
N(3)–C(4)–C(5)	111.8(4)		112.4(7)
C(4)–C(5)–S(1)	110.3(3)		110.5(6)
C(5)–S(1)–C(2)	91.8(3)		91.3(4)
N(3)–C(4)–C(4α)	120.3(4)		119.9(7)
C(5)–C(4)–C(4α)	127.7(3)		127.7(8)
C(4)–C(5)–C(5α)	129.0(5)		129.1(8)
S(1)–C(5)–C(5α)	120.7(5)		120.4(6)
C(5)–C(5α)–C(5β)	111.5(5)		112.1(7)
C(5α)–C(5β)–O(5γ)	106.4(5)		109.8(9)

the neighboring thiocyanato sulfur S(21), which in turn parallelly rides on the pyrimidine ring of the same thiamine with the average separation of 3.71 Å between them (also shown in Fig. 2). There are two additional electrostatic interactions between

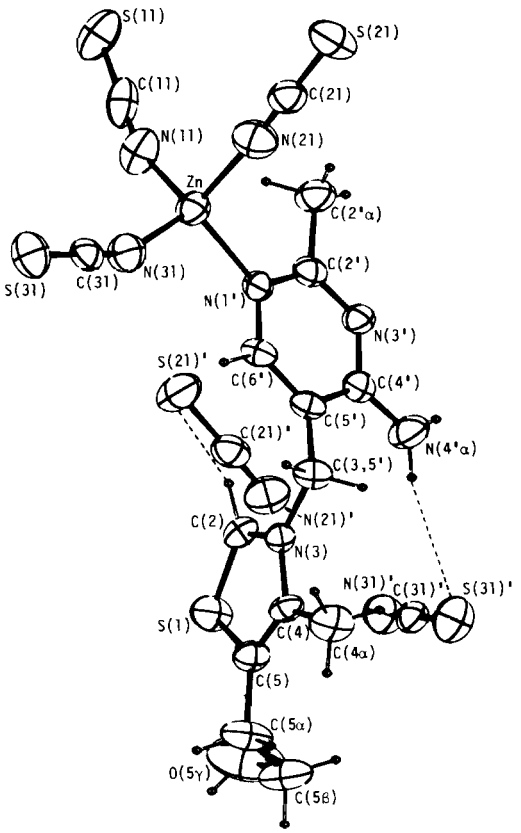

Fig. 1. Molecular structure of Zn(thiamine)$(SCN)_3$ (1) showing the metal bonding to the pyrimidine N(1′) and an N(4′α)–H...S(31)′–C(31)′–N(31)′...thiazolium ring interaction and a C(2)–H...S(21)′–C(21)′–N(21)′... pyrimidine ring interaction. Broken lines denote hydrogen bonds.

SCN^- groups and thiamine rings (not shown in Fig. 2): a parallel S(11)–C(11)–N(11)...pyrimidine contact and an S(31)...thiazolium contact (Table 5).

Cadmium(II) complex 2

As Fig. 3 shows, the complex forms a polymeric $[Cd(thiamine)(SCN)_3]_n$ structure in which the cadmium atom is octahedrally coordinated to a thiamine molecule through the O(5γ) hydroxyethyl group and to five thiocyanato ligands through three nitrogens and two sulfurs. One thiocyanato S(11)–C(11)–N(11) behaves as a terminal ligand, while the other two act as bridging ligands; S(21)–C(21)–N(21) bridges between Cd and Cd′ atoms across a center of symmetry and S(31)–C(31)–N(31) between Cd and Cd″ atoms across another center of symmetry, each to form an eight-membered ring which is nearly planar and roughly perpendicular to one another, thus producing a one-dimensionally polymeric structure. The thiamine ligand adopts the *F* conformation with $\phi_T = 0(1)°$ and $\phi_P = -80(1)°$ and with the dihedral

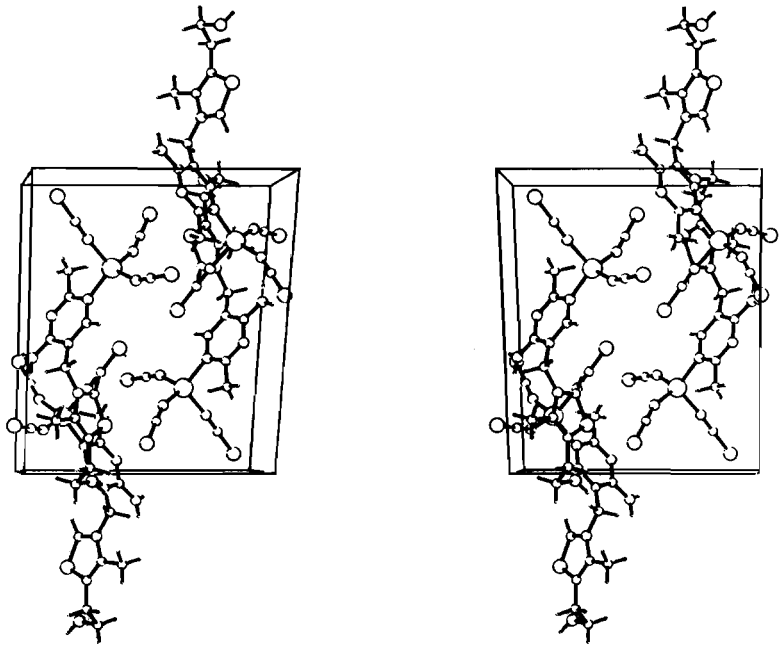

Fig. 2. A stereoscopic view showing the crystal packing of **1**, viewed down the *c* axis with the *b* axis being horizontal and the *a* axis vertical. Hydrogen bonds are omitted.

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

Hydrogen bonds				
Donor (D)–H	Acceptor (A)	D–H (Å)	D...A (Å)	H...A (Å)
N(4′α)–H1	N(3′^{i})	0.89(5)	3.192(6)	2.31(5)
N(4′α)–H2	S(31^{ii})	0.90(3)	3.569(4)	2.72(4)
C(2)–H	S(21^{ii})	1.04(3)	3.600(4)	2.60(4)
O(5γ)–H	S(11^{iii})	0.87(7)	3.270(5)	2.49(8)

Other short contacts between non-H atoms (less than 3.7 Å for those with S atoms and less than 3.4 Å for others)

A	B	A...B (Å)	A	B	A...B (Å)
C(3,5′)	O(5γ^{iv})	3.389(8)	S(21)	S(21^{vii})	3.479(2)
S(1)	O(5γ)	2.915(4)	C(21)	C(2^{iv})	3.310(7)
S(11)	S(1^{v})	3.516(3)	S(31)	C(4^{iv})	3.537(5)
S(11)	N(1′^{vi})	3.680(5)	S(31)	C(2^{viii})	3.486(6)
S(11)	C(5′^{vi})	3.533(6)	S(31)	N(3^{viii})	3.566(4)
S(11)	C(6′^{vi})	3.483(6)			

[a]Symmetry operations: (none) x, y, z; (i) $-x, 1-y, 1-z$; (ii) $-\frac{1}{2}+x, \frac{1}{2}-y, z$; (iii) $-1+x, y, -1+z$; (iv) $\frac{1}{2}+x, \frac{1}{2}-y, z$; (v) $\frac{1}{2}+x, \frac{1}{2}-y, 1+z$; (vi) $\frac{1}{2}-x, -\frac{1}{2}+y, 1-z$; (vii) $1-x, 1-y, 1-z$; (viii) $-x, -y, -z$.

angle between the pyrimidine and thiazolium rings of 100.7(3)°. The conformation of the C(5)–hydroxyethyl group is similar to that of **1**: $\phi_{5\alpha} = -67.2(6)°$ and $\phi_{5\beta} = 64.0(1)°$ and O(5γ)...S(1) = 2.977(6) Å. Two types of thiocyanate-bridges between the pyrimidine and thiazolium rings of the same thiamine molecule occur here again: an N(4′α)–H...S(21)–C(21)–N(21)...thiazolium bridge with the closest contact of 3.610(9) Å between the S(21) and C(4) atoms and a C(2)–H...S(11)–C(11)–N(11)...pyrimidine bridge with the average separation of 3.88 Å between the SCN^- and the pyrimidine ring.

The crystal lattice is built up by interlinking $[Cd(thiamine)(SCN)_3]_n$ molecular chains running in zigzag along the *b* axis through hydrogen-bonding and electrostatic interactions (Fig. 4 and Table 6). These involve thiocyanate-bridges mentioned above and further two hydrogen bonds between the amino N(4′α) and the thiocyanato S(11) and between the hydroxyethyl O(5γ) and the pyrimidine N(1′) and a parallel electrostatic contact between the thiazolium ring and the S(11)–C(11)–N(11).

Discussion

Comparison for the four thiamine–metal structures, Zn(thiamine)Cl_3 [3d], Cd(thiamine)Cl_3 [3a], Zn(thiamine)$(SCN)_3$ (1) and Cd(thiamine)$(SCN)_3$ (2)

Structural parameters of the four thiamine complexes with zinc(II) and cadmium(II) ions are compiled in Table 7. Of special interest is that the

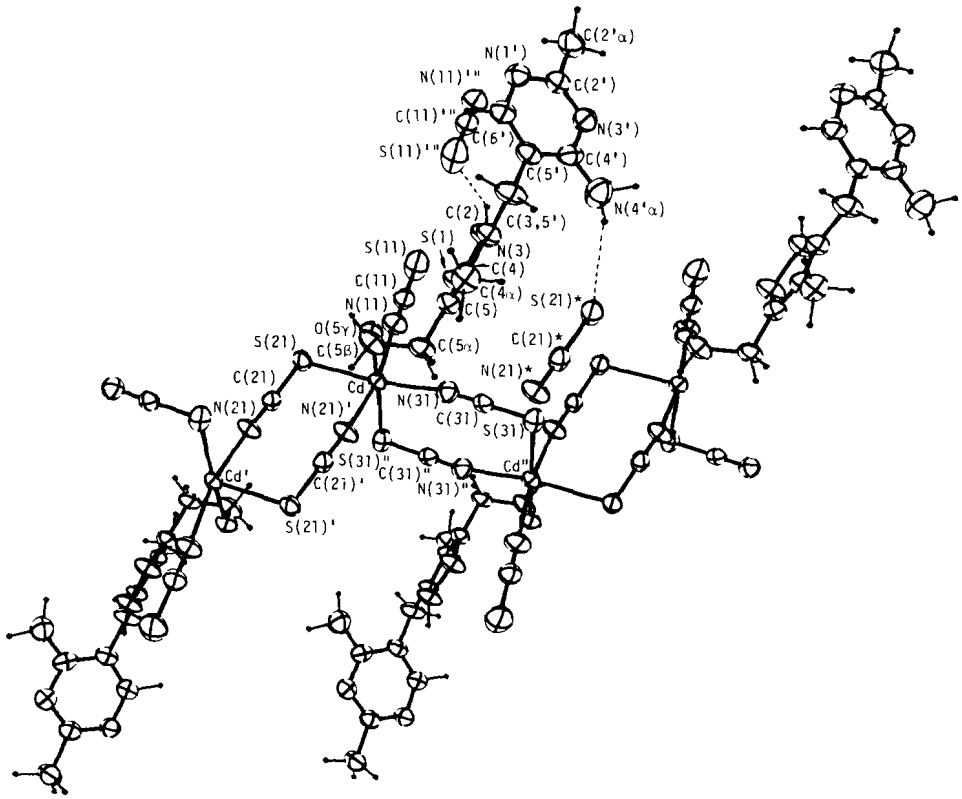

Fig. 3. Segment of the polymeric structure of $[Cd(thiamine)(SCN)_3]_n$ (2), showing the metal bonding to the hydroxyethyl O(5γ), an N(4'α)–H...S(21)*–C(21)*–N(21)*...thiazolium ring interaction and a C(2)–H...S(11)'''–C(11)'''–N(11)'''...pyrimidine ring interaction. Broken lines denote hydrogen bonds.

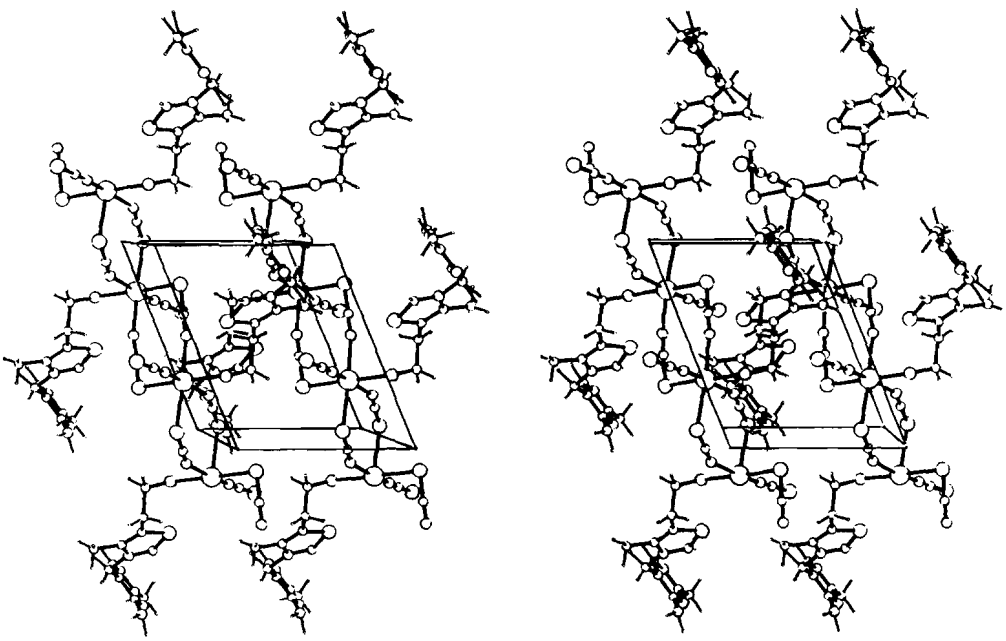

Fig. 4. A stereoscopic view showing the crystal packing of 2, viewed down the *c* axis with the *a* axis horizontal and the *b* axis vertical. Hydrogen bonds are omitted.

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

Hydrogen bonds				
Donor (D)–H	Acceptor (A)	D–H (Å)	D...A (Å)	H...A (Å)
N(4′α)–H1	S(21^{i})	1.11	3.649(10)	2.63
N(4′α)–H2	S(11^{i})	1.10	3.43(1)	2.39
C(2)–H	S(11^{ii})	1.00	3.548(9)	2.65
O(5γ)–H[b]	N(1′^{iii})		2.685(10)	

Other short contacts between non-H atoms (less than 3.7 Å for those with S atoms and less than 3.4 Å for others)

A	B	A...B (Å)	A	B	A...B (Å)
N(1′)	C(5β^{iii})	3.33(1)	C(21)	N(21^{vi})	3.33(1)
S(1)	O(5γ)	2.977(6)	N(21)	C(5β^{vi})	3.27(1)
S(11)	N(3^{iv})	3.686(9)	S(31)	C(5β^{iv})	3.57(1)
S(11)	C(4^{iv})	3.593(10)	C(31)	C(31^{vii})	3.37(1)
C(11)	N(4′α^{v})	3.22(1)	C(31)	N(31^{vii})	3.12(1)
C(11)	C(4α^{iv})	3.37(2)	N(31)	S(1^{vii})	3.583(8)
S(21)	N(3^{v})	3.672(7)	N(31)	C(5α^{vii})	3.35(1)
S(21)	C(4^{v})	3.610(9)	N(31)	N(31^{vii})	3.28(1)
C(21)	C(4α^{v})	3.39(1)			

[a]Symmetry operations: (none) x, y, z; (i) $1+x, 1+y, z$; (ii) $-x, 1-y, 1-z$; (iii) $1-x, 1-y, 1-z$; (iv) $-1+x, y, z$; (v) $-1+x, -1+y, z$; (vi) $-x, -y, -z$; (vii) $-x, 1-y, -z$. [b]This H atom was not located.

introduction of SCN^- in place of Cl^- as an anion ligand does not affect the metal binding site of thiamine for Zn^{2+} ion, but does have an effect for the Cd^{2+} ion, that is, the metal ligation site is N(1′) in both the Zn^{2+} compounds while it changes from N(1′) to O(5γ) in the Cd^{2+} compounds. Though an exact factor(s) responsible for such an alteration for Cd^{2+} is not clear, the electronic effects of anion ligands on the electronic structure of the metal ion may be one of most important factors affecting the metal binding site. Thus for Zn(thiamine)Cl_3 [3d] and Cd(thiamine)Cl_3 [3a], both involving the metal–N(1′) bond, electronic effects of $3Cl^-$ ions on Zn(II) and Cd(II) ions may be equal, while for Zn(thiamine)$(SCN)_3$ having the metal–N(1′) bond and Cd(thiamine)$(SCN)_3$ containing the metal–O(5γ) bond, electronic effects of anion ligands may be different because the Zn(II) atom is bonded by three SCN^- ligands through three nitrogens while the Cd(II) atom is bonded by five SCN^- ligands through three nitrogens and two sulfurs. The coordination geometry, tetrahedral or octahedral, is unlikely to be such an alteration factor, since the metal–N(1′) bonding has indeed been observed in an octahedral rhodium(II) complex [3h]. It is also evident from Table 7 that the conformation of thiamine, *F* or *S*, does not affect the metal–N(1′) bonding, and vice versa.

TABLE 7. Relevant structural parameters for Zn(thiamine)Cl_3, Cd(thiamine)Cl_3, Zn(thiamine)$(SCN)_3$, and Cd(thiamine)$(SCN)_3$

	Zn(thiamine)Cl_3	Cd(thiamine)Cl_3	Zn(thiamine)$(SCN)_3$	Cd(thiamine)$(SCN)_3$
Metal binding site of thiamine	N(1′)	N(1′)	N(1′)	O(5γ)
Metal binding sites of anion ligands	$3Cl^-$	$3Cl^-$	3N of $3SCN^-$	3N and 2S of $5SCN^-$
Coordination geometry	tetrahedral	tetrahedral	tetrahedral	octahedral
Conformation of thiamine	*S*	*S*	*F*	*F*
C(4′)–N(4′α) bond length (Å)	1.336(6)	1.346(3)	1.336(7)	1.34(1)
O(5γ)...S(1) contact (Å)	2.878(4)	2.879(3)	2.915(4)	2.977(6)
N(4′α)–H...X1–M–X2...thiazolium or N(4′α)–H...X...thiazolium interactions				
N(4′α)...X1 or X distance (Å)	3.474(3) [X1 = Cl11]	3.395(2) [X1 = Cl2]	3.569(4) [X = S(31)′]	3.649(10) [X = S(21)*]
H...X1 or X distance (Å)	"	"	2.72(4)	2.63
X2 or X...thiazolium contact[b] (Å)	3.42 [X2 = Cl12]	3.39 [X2 = Cl3]	3.52 [X = S(31)′]	3.48 [X = S(21)*]
C(2)–H...X...pyrimidine interactions				
C(2)...X distance (Å)			3.600(4) [X = S(21)′]	3.548(9) [X = S(11)**]
H...X distance (Å)			2.60(4)	2.65
X...pyrimidine contact[b] (Å)			3.71	3.88
Reference	3d	3a	this work	this work

[a]Atomic parameters for the hydrogen atom not reported. [b]Perpendicular distance to the ring plane.

Table 7 also indicates that the effect of the N(1)-coordination on the C(4′)–N(4′α) bond length [3a] is minor: the values of the C(4′)–N(4′α) bond length (1.336(6)–1.346(3) Å) in N(1′)-metallated thiamines are comparable to that (1.34(1) Å) of a free thiamine in the present Cd(II) complex. This is in sharp contrast to the prominent effect of the N(1′)-protonation, i.e., the decrease of the bond length [3a]. Another characteristic feature common to the four thiamine structures is an intramolecular O(5γ)...S(1) interaction, which is little affected by the metal bonding to the O(5γ) atom in **2**, suggesting that such an electrostatic interaction is of considerable significance.

Factors affecting the conformation of thiamine

We reemphasize here the factors determining the thiamine conformation, on which we argued for polyhalogenometal–thiamine compounds [3c]. As Table 7 shows, the *S* conformation is associated with a 'two-point' anion (X)-bridge between the amino N(4′α) group and the cationic thiazolium ring such as N(4′α)–H...X1–M–X2...thiazolium, while the *F* conformation accompanies a 'one-point' anion-bridge like N(4′α)–H...X...thiazolium. Another factor is more definitive in the sense that it affects the *F* form but not the *S* form, that is, another anion-bridge between the acidic thiazolium C(2)–H and the pyrimidine ring like C(2)–H...X...pyrimidine.

Conclusions

The zinc complex **1** is, to our knowledge, the eleventh example that involves the metal–N(1′) bond, while the cadmium complex **2** is the first that contains the metal–O(5γ) bond. The metal bonding to the base N(1′), the most basic site [10] in thiamine, is usual, while the metal bonding to the O(5γ) may exceptionally occur only when peculiar combinations of metal ions and anion ligands are achieved, for example, for the present cadmium ion–ambident thiocyanato ligand system; indeed, Cd^{2+} ion does bind to the N(1′) for the halide ligand system [4a]. The ability of Zn^{2+} and Cd^{2+} to bind to N(1′), a site suggested to be bound by Mg^{2+} in enzyme systems [11], may explain, at least partially, an observation [5] that both metal ions can replace Mg^{2+} as activators in thiamine-dependent enzyme reactions.

We reemphasize here that an anion-bridge between C(2)–H and the pyrimidine ring is a factor affecting the *F* conformation of thiamine. In addition, this anion-bridge could serve as a model for the substrate (e.g., pyruvate anion) fixation near to the catalytic C(2) site and also suggests a role for the most stable *F* conformation as an anchor for the substrate, possibly through an electrostatic interaction.

Supplementary material

Tables of atomic parameters of hydrogen atoms, anisotropic thermal parameters, complete bond lengths and angles, least-squares planes, and structure factors are available from the authors on request.

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