

Host–guest-like thiamine–anion complexation in thiaminium bis(tetrafluoroborate)

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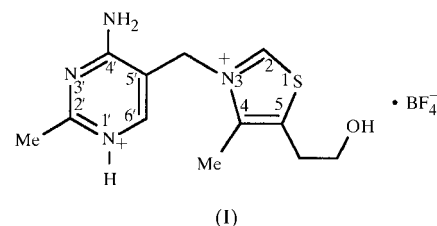
In the title compound, 3-[(4-amino-2-methyl-5-pyrimidin-1-yl)methyl]-5-(2-hydroxyethyl)-4-methylthiazolium(2+) bis-(tetrafluoroborate), $C_{12}H_{18}N_4OS^{2+} \cdot 2BF_4^-$, the divalent thiamine cation (in the *F* conformation) is associated with BF_4^- anions *via* two characteristic bridging interactions between the thiazolium and pyrimidinium rings, *i.e.* $C-H \cdots BF_4^- \cdots$ pyrimidinium and $N-H \cdots BF_4^- \cdots$ thiazolium interactions. Thiamine molecules are linked by $N-H \cdots O$ hydrogen bonds to form a helical chain structure.

Comment

Thiamine pyrophosphate is a coenzyme for a number of metabolic enzymes (Krampitz, 1969). Studies of the thiamine–anion system as a model for coenzyme–substrate interactions are of interest because in the reactions catalyzed by thiamine, a substrate anion such as pyruvate directly interacts with thiamine at the C2 site (Breslow, 1958).

Thiamine exists either as a monovalent cation with a quaternary N atom on the thiazolium moiety or as a divalent cation (H-thiamine) with an additional H atom at N1' of the pyrimidine ring. It has been observed (Aoki *et al.*, 1991) that in thiamine–anion complexes, the anions are associated with thiamine through two types of characteristic bridging interactions, forming host–guest-like anion complexation. Moreover, thiamine molecules themselves form various hydrogen-bonded structures and, together with anions in some cases, build up distinct higher-order supramolecular structures (Aoki *et al.*, 1993, 1999). There are two types of hydrogen-bonded chain structures depending on whether N1' of the pyrimidine moiety is protonated. One type of chain structure incorporates an $O53-H \cdots N1'$ hydrogen bond, such as in N1'-unprotonated thiamine(ClO_4) $\cdot H_2O$ (Kozioł *et al.*, 1987), thiamine(BF_4) $\cdot H_2O$ (Aoki *et al.*, 1990) and thiamine(PF_6) $\cdot H_2O$ (Aoki *et al.*, 1988). Another type has an $N1'-H \cdots O53$

hydrogen bond, as in N1'-protonated H-thiamine(ClO_4) $_2$ (Aoki *et al.*, 1988). These observations led us to further examine (i) the host–guest-like thiamine–anion complexation in H-thiamine(BF_4) $_2$, (I), and (ii) whether a chain structure similar to that in H-thiamine(ClO_4) $_2$ occurs in (I).



The structure of (I) contains a divalent thiamine cation with N1' protonated and two disordered BF_4^- ions (denoted *A* and *B*), as shown in Fig. 1. The molecular dimensions of thiamine in (I) are in agreement with the known N1'-protonated thiamine (Cramer *et al.*, 1981). The protonation at N1' influences the $C2'-N1'-C6'$ bond angle and the opposite $C4'-N4'$ bond length. These values are 119.9 (4) $^\circ$ and 1.318 (5) Å in (I), while they are 115.0 (3) $^\circ$ and 1.337 (4) Å in thiamine- $(BF_4) \cdot H_2O$, which has an N1'-unprotonated pyrimidine ring. The C5-hydroxyethyl side chain folds back towards the thiazolium ring, with torsion angles (Pletcher *et al.*, 1977) $\varphi_{5\alpha}$ ($S1-C5-C51-C52$) = -67.5 (7) $^\circ$ and $\varphi_{5\beta}$ ($C5-C51-C52-O53$) = 64.4 (7) $^\circ$. This conformation results in a close contact between O53 and the electropositive S1 atom (Jordan, 1974), with $O53 \cdots S1 = 3.029$ (3) Å, which is a common structural feature of thiamine compounds.

The thiamine molecule adopts the usual *F* conformation in terms of the torsion angles (Pletcher *et al.*, 1977); φ_T ($C5'-C35'-N3-C2$) = 11.4 (7) $^\circ$, and φ_P ($N3-C35'-C5'-C4'$) = -82.8 (5) $^\circ$. Aoki *et al.* (1993) have noted that when thiamine is in the *F* form there are two well defined 'anion holes' between

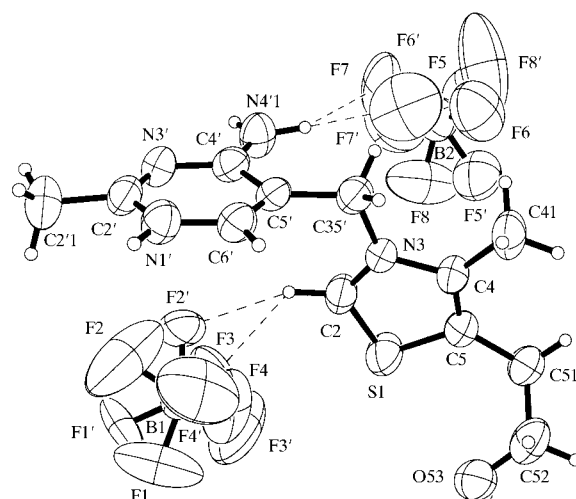


Figure 1
H-thiamine(BF_4) $_2$ drawn with 50% probability displacement ellipsoids. Note that the BF_4^- anions are associated to thiamine at the two 'anion holes' through two types of bridging interactions, *i.e.* $C2-H \cdots BF_4^- \cdots$ pyrimidinium and $N4'-H \cdots BF_4^- \cdots$ thiazolium. Broken lines denote hydrogen bonds.

the thiazolium and pyrimidine rings. The area denoted 'anion hole I' is occupied by an anion which bridges the two rings through a C2—H···anion···pyrimidine-ring interaction, and 'anion hole II' is occupied by an anion which bridges the two rings through an N4'1—H···anion···thiazolium-ring interaction. In (I), the *A* anion accepts a hydrogen bond from C2 (C2—H···F3 or C2—H···F2', see Table 3) and makes a close stacking interaction with the pyrimidinium ring (Table 2), thus being located in 'anion hole I'. The *B* anion lies in 'anion hole II' to form an N4'1—H···F7 or N4'1—H···F6' hydrogen bond (Table 3) and a close contact with the thiazolium ring (Table 2). These two types of thiamine–anion complexation also exist in thiamine(BF₄)·H₂O, in which 'anion hole II' is occupied by a water molecule (Aoki *et al.*, 1990). The anion complexation at 'anion hole I' occurs only for the *F* conformation but not for the other two energetically favourable conformations, *S* ($\varphi_T = \pm 100^\circ$, $\varphi_P = \pm 150^\circ$) and *V* ($\varphi_T = \pm 90^\circ$, $\varphi_P = \mp 90^\circ$), and so is peculiar to the *F* form. On the other hand, the anion complexation at 'anion hole II' is also possible for a thiamine molecule in the *S* form, but it requires large anions, such as CdCl₄²⁻ (Richardson *et al.*, 1975) and HgCl₄²⁻ (Hadjiiladis *et al.*, 1983), rather than small anions like ClO₄⁻ or BF₄⁻. In the *V* form, none of these 'anion holes' are available. It therefore appears that thiamine–anion complexation plays an important role in determining molecular conformations and *vice versa*.

As expected, a helical chain structure in the 'head-to-tail' fashion is formed along the twofold screw axis in the *b* direction through N1'—H···O53 hydrogen bonds, where O53 acts as an acceptor, between the pyrimidinium 'head' of a thiamine molecule and the hydroxyethyl 'tail' of the other one (Fig. 2). The repeat period of the helical chain is the length of the *b* axis (7.565 Å). The *A* anion is located inside the spiral and is attached to the chain through the C2—H···BF₄⁻···pyrimidinium interaction mentioned above. The *B* anion lies outside the spiral and interacts with the chain through the N4'1—H···BF₄⁻···thiazolium contact and, at the same time, links two neighbouring chains through N4'1—H···BF₄⁻···H—O53 hydrogen bonds. This chain structure is similar to that in H-thiamine(ClO₄)₂ but different from that in thiamine(ClO₄)·H₂O and thiamine(BF₄)·H₂O, where the

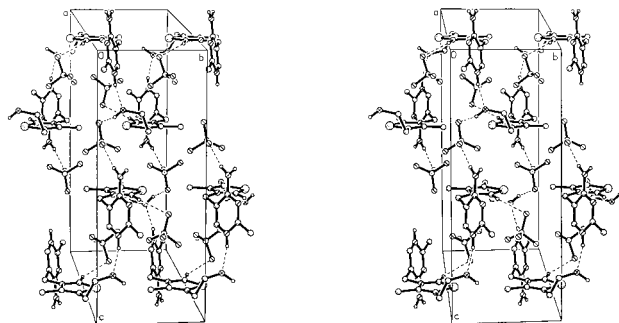


Figure 2
A stereoview of the crystal packing, showing the formation of the helical molecular chain in the *b* direction. Only those H atoms involved in hydrogen bonds are shown. The minor disordered positions of the BF₄⁻ anions have been omitted for clarity. Broken lines denote hydrogen bonds.

molecular chain is constructed through O53—H···N1' hydrogen bonds, with longer repeat periods of 11.234 and 11.134 Å, respectively.

It is of interest to note the molecular self-association in thiamine–anion systems. For example, a polymeric chain structure with each anion molecule held between hydrogen-bonded thiamine–thiamine dimers is commonly formed for [PtCl₄]²⁻ (Cramer *et al.*, 1988), [PtCl₆]²⁻ (Aoki *et al.*, 1993) and [Pt(NO₂)₄]²⁻ (Hu *et al.*, 2001) anions, while the linear SCN⁻ anion facilitates the formation of a triple helical structure (Hu & Zhang, 1993) in which each helical chain consists of alternate thiamine and anion molecules. Therefore, the higher-order structures in thiamine–anion systems depend not only on the nature of thiamine itself but also on that of the anions.

Experimental

Crystals of (I) were obtained at room temperature by the slow evaporation of an aqueous solution (pH = 2) of thiamine chloride hydrochloride (69.2 mg, 0.2 mmol) and NaBF₄ (43.9 mg, 0.4 mmol).

Crystal data

C₁₂H₁₈N₄OS²⁺·2BF₄⁻
M_r = 439.98
 Monoclinic, *P*2₁/*n*
a = 13.8490 (10) Å
b = 7.5650 (10) Å
c = 18.554 (5) Å
 β = 101.900 (10)^o
V = 1902.1 (6) Å³
Z = 4

D_x = 1.536 Mg m⁻³
 Mo *K*α radiation
 Cell parameters from 20 reflections
 θ = 6.5–11.2^o
 μ = 0.26 mm⁻¹
T = 293 (2) K
 Tabular, colourless
 0.45 × 0.40 × 0.12 mm

Table 1

Selected geometric parameters (Å, °).

S1—C2	1.673 (4)	N1'—C2'	1.347 (5)
S1—C5	1.715 (4)	N1'—C6'	1.350 (5)
C2—N3	1.308 (5)	C2'—N3'	1.309 (5)
N3—C4	1.403 (5)	N3'—C4'	1.361 (5)
N3—C35'	1.484 (5)	C4'—N4'1	1.318 (5)
C4—C5	1.342 (5)	C4'—C5'	1.427 (5)
C35'—C5'	1.496 (5)	C5'—C6'	1.332 (6)
C2—S1—C5	91.5 (2)	C2'—N1'—C6'	119.9 (4)
N3—C2—S1	112.5 (3)	N3'—C2'—N1'	122.4 (4)
C2—N3—C4	113.5 (4)	C2'—N3'—C4'	118.2 (4)
C2—N3—C35'	123.8 (3)	N3'—C4'—C5'	121.5 (4)
C4—N3—C35'	122.7 (4)	C6'—C5'—C4'	116.1 (4)
C5—C4—N3	111.9 (4)	C6'—C5'—C35'	120.7 (4)
C4—C5—S1	110.6 (3)	C4'—C5'—C35'	123.2 (4)
N3—C35'—C5'	113.0 (4)	C5'—C6'—N1'	121.8 (4)

Table 2

Contact distances (Å).

N1'···F2'	3.188 (11)	C2'···F2	3.117 (17)
C2'···F2'	3.031 (11)	C4···F6	3.377 (7)
N3'···F2'	3.106 (9)	N3···F8	3.183 (7)
N1'···F4'	3.179 (19)	C4···F8	3.247 (7)
C6'···F4'	3.178 (17)	C4···F5'	3.226 (18)
N1'···F2	3.217 (17)	N3···F6'	3.21 (2)

Table 3
Hydrogen-bonding geometry (Å, °).

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
C2—H2...F3	1.01 (4)	2.29 (4)	3.035 (8)	130 (3)
C2—H2...F2'	1.01 (4)	2.20 (4)	3.154 (11)	156 (3)
N4'1—H41D...F2 ⁱ	0.79 (4)	2.09 (5)	2.875 (8)	169 (4)
N4'1—H41D...F3 ⁱ	0.79 (4)	2.41 (4)	3.132 (12)	153 (4)
N4'1—H41E...F7	0.96 (5)	1.94 (5)	2.859 (7)	158 (4)
N4'1—H41E...F6'	0.96 (5)	2.02 (5)	2.96 (3)	165 (4)
N1'—H1'...O53 ⁱⁱ	0.86 (4)	1.92 (4)	2.763 (6)	166 (4)
O53—H53...F5 ⁱⁱⁱ	0.93 (3)	1.97 (4)	2.855 (8)	157 (5)
O53—H53...F5 ⁱⁱⁱ	0.93 (3)	2.09 (5)	2.886 (16)	143 (5)

Symmetry codes: (i) $1 - x, 2 - y, -z$; (ii) $\frac{3}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z$; (iii) $2 - x, 2 - y, -z$.

Data collection

Siemens P4 diffractometer	$h = -1 \rightarrow 16$
ω scans	$k = -1 \rightarrow 8$
4564 measured reflections	$l = -22 \rightarrow 21$
3348 independent reflections	3 standard reflections
1501 reflections with $I > 2\sigma(I)$	every 100 reflections
$R_{\text{int}} = 0.022$	intensity decay: none
$\theta_{\text{max}} = 25.0^\circ$	

Refinement

Refinement on F^2	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.055$	$w = 1/[\sigma^2(F_o^2) + (0.04P)^2]$
$wR(F^2) = 0.124$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 0.99$	$(\Delta/\sigma)_{\text{max}} = -0.011$
3348 reflections	$\Delta\rho_{\text{max}} = 0.24 \text{ e } \text{Å}^{-3}$
377 parameters	$\Delta\rho_{\text{min}} = -0.19 \text{ e } \text{Å}^{-3}$

Each of the two BF_4^- ions is disordered over two positions around the common B atom. The occupancy factors were refined to give values of 0.538 and 0.462 for the *A* anion, and 0.752 and 0.248 for the *B* anion. All H atoms were located from difference Fourier maps and refined isotropically, except for those of the methyl groups, which were added at ideal positions.

Data collection: *XSCANS* (Siemens, 1994); cell refinement: *XSCANS*; data reduction: *SHELXTL* (Siemens, 1994); program(s) used to solve structure: *SHELXTL*; program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: DA1186). Services for accessing these data are described at the back of the journal.

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