

## The Crystal and Molecular Structure of Thiamine Bromide Hydrobromide Hemihydrate

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(Received 3 May 1976; accepted 22 June 1976)

The crystal structure of protonated thiamine bromide hemihydrate,  $C_{12}H_{19}N_4O_{1.5}SBr_2$ , has been determined in order to compare its structural features with those of protonated thiamine chloride monohydrate and protonated thiamine iodide. The unit-cell parameters are:  $a = 30.598$  (5),  $b = 6.355$  (1),  $c = 24.292$  (3) Å,  $\beta = 134.12^\circ$ ; space group  $C2/c$ ;  $Z = 8$ . A total of 1033 reflections with  $F_o^2 < 2\sigma(F_o^2)$ ,  $2\theta < 40^\circ$  were collected on a four-circle diffractometer with Mo  $K\alpha$  radiation by the  $\theta$ - $2\theta$  scan technique. The structure was solved by the heavy-atom method. The Br, S and water O atoms were given anisotropic thermal parameters in the refinement. The positions of the H atoms were calculated. Full-matrix least-squares refinement yielded a conventional  $R$  of 0.059. The conformation of the thiamine cation is the one usually found for unsubstituted thiamine derivatives. The thiamine cations, bromide anions and water molecules are linked together in a three-dimensional network by a system of hydrogen bonds and  $S \cdots Br$  dipolar contacts. The relative molecular packing of the chloride, bromide and iodide salts of protonated thiamine is discussed.

### Introduction

In the course of our research on thiamine structures (Lee & Richardson, 1976; Richardson, Franklin & Thompson, 1975), we prepared thiamine bromide hydrobromide hemihydrate,  $HThiBr_2 \cdot \frac{1}{2}H_2O$ , where  $HThi^{2+}$  is  $(C_{12}H_{18}N_4OS)^{2+}$ . This material is not isomorphous with the anhydrous hydroiodide (Lee & Richardson, 1976) nor the monohydrated hydrochloride (Kraut & Reed, 1962). In view of recent interest in the conformation of the thiamine cation (Jordan, 1974, 1976; Sax, Pulsinelli & Pletcher, 1974), we decided to determine the structure of the hydrobromide and investigate the thiamine conformation in this salt.

### Experimental

Crystals of  $HThiBr_2 \cdot \frac{1}{2}H_2O$  were prepared by mixing equivalent amounts of aqueous  $HThiCl_2 \cdot H_2O$  and NaBr, and allowing the resulting solution to evaporate. Thin, colorless, needle-like plates were deposited. One crystal,  $0.02 \times 0.6 \times 0.05$  mm, was mounted on a glass fiber with epoxy cement, with the needle axis approximately parallel to the fiber axis. The crystal dimensions are parallel to **a**, **b** and **c** respectively.

The crystal was aligned about **b\*** on a Picker four-

circle diffractometer. Cell dimensions were determined from scans of the axial and  $h0l$  reflections out to  $2\theta = 40^\circ$  with Mo  $K\alpha$  radiation at a take-off angle of  $1.5^\circ$  ( $\lambda = 0.70926$  for Mo  $K\alpha_1$ ,  $0.7107$  Å for Mo  $K\alpha$ ):  $a = 30.598$  (5),  $b = 6.355$  (1),  $c = 24.292$  (3) Å,  $\beta = 134.12^\circ$ ;  $d_{obs.} = 1.67$ ,  $d_{calc.} = 1.70$  g cm<sup>-3</sup> for eight units of  $C_{12}H_{19}N_4O_{1.5}SBr_2$ ; systematic absences  $hkl$  ( $h + k$  odd) and  $h0l$  ( $l$  odd); space group  $C2/c$  or  $Cc$ . The choice of  $C2/c$  was supported by the successful refinement of the structure in this group.

Previously described procedures were used for the data collection and reduction to the structure factors (Richardson, 1974). Of the 1774 reflections with  $2\theta < 40^\circ$  in the independent quadrant, 1033 had  $F_o^2 > 2\sigma(F_o^2)$  and were classified as observed. A standard reflection was measured approximately every 2 h, and showed no significant variation with time. No absorption correction was made ( $\mu$  for Mo  $K\alpha$  radiation =  $51.7$  cm<sup>-1</sup>).

Scattering factors for neutral Br, S, O, N, C and H atoms were taken from *International Tables for X-ray Crystallography* (1968), as was the correction for the anomalous scattering of Br. Major computer programs employed included Zalkin's *FORDAP*, Busing & Levy's *ORFLS*, and Busing, Martin & Levy's *ORFFE*. In the full-matrix least-squares refinements, the function minimized was  $\Sigma w\Delta^2$ , where  $w = 1/\sigma^2(F)$  and  $\Delta = \|F_o\| - \|F_c\|$ . Unweighted and weighted residuals,  $R_1$  and  $R_2$  respectively, were calculated after each refinement:  $R_1 = \Sigma\Delta/\Sigma|F_o|$ ,  $R_2 = [\Sigma w\Delta^2/\Sigma wF_o^2]^{1/2}$ .

The structure was solved by the usual heavy-atom

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methods. After location and refinement of the two Br atoms and the 18 atoms of the thiamine cation, an electron density difference map revealed the water molecule on a crystallographic twofold axis. A refinement with anisotropic thermal parameters for the Br and S atoms, and isotropic thermal parameters for the remaining atoms, gave  $R_1 = 0.066$ ,  $R_2 = 0.078$ . The positions of the geometrically fixed H atoms were calculated and included as fixed contributions in the final cycles of refinement; the water molecule was also treated anisotropically at this point, as it had a large isotropic thermal parameter ( $\sim 10 \text{ \AA}^2$ ). In the last cycle 101 parameters were refined. The final  $R_1$  and  $R_2$  values were 0.059 and 0.068 respectively. A value of 1.3 was obtained for the function  $[\sum w\Delta^2/(NO - NV)]^{1/2}$ , where  $NO$  and  $NV$  are the numbers of observations and variable parameters. The average parameter shift was 0.4 e.s.d. on the final cycle.\*

An electron density difference map revealed several peaks and a hole  $\sim 1 \text{ e \AA}^{-3}$  deep in the vicinity of the water molecule, perhaps indicating disorder or partial occupation of the site. Peaks of  $\sim 0.5 \text{ e \AA}^{-3}$  were observed in the vicinity of the methyl groups and the amino group (for which the H positions were not calculated) but no sets of peaks having the correct spatial relationship for a methyl group (for example), could be discerned. Aside from these peaks, no other significant peaks or holes were observed on the map.

The final coordinates and thermal parameters are given in Tables 1–3.

### Discussion

A projection of the structure of a thiamine cation onto the (010) plane is shown in Fig. 1. The bond distances and angles are listed in Tables 4 and 5. These are similar to corresponding values in other thiamine structures (Kraut & Reed, 1962; Lee & Richardson, 1976;

\* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32029 (8 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Richardson, Franklin & Thompson, 1975). The thiazolium and pyrimidine rings are planar with the atoms in a given ring generally deviating less than 0.01 Å from the best plane through that ring.

The conformation of the thiamine cation can be described in terms of torsion angles  $\varphi_T$ , C(8)–C(7)–N(1)–C(6), and  $\varphi_P$ , N(1)–C(7)–C(8)–C(9), as first proposed by Pletcher & Sax (1972). In the present structure these angles are 2 (2) and 77 (3)° respectively. This conformation is the one normally observed for thiamine derivatives which are unsubstituted at C(6); in particular, it is the same as that for thiamine hydrochloride ( $\varphi_T = 9.0$ ,  $\varphi_P = 76.1^\circ$ ) and thiamine hydroiodide ( $\varphi_T = -5.9$ ,  $\varphi_P = 81.0^\circ$ ).

Distances for hydrogen bonds and other short contacts are shown in Fig. 1, and relevant angles are listed in Table 6. The amino group N(2) is hydrogen bonded to two bromide ions. The protonation site is presumably N(4) as the N(4)  $\cdots$  O(1)<sup>st</sup> distance of 2.71

Table 1. Positional and isotropic thermal parameters for the nonhydrogen atoms in  $\text{HThiBr}_2 \cdot \frac{1}{2}\text{H}_2\text{O}$

The standard deviation in the last significant figure is given in parentheses.

	$10^4 x$	$10^3 y$	$10^4 z$	$B (\text{Å}^2)$
Br(1)	1053.5 (9)	173.6 (3)	4168 (1)	*
Br(2)	1848.8 (7)	9.7 (3)	2332 (1)	*
S	2758 (2)	494.4 (8)	617 (2)	*
O(1)	4184 (4)	266 (2)	2896 (6)	3.5 (2)
C(1)	4223 (7)	337 (3)	2373 (9)	4.4 (4)
C(2)	3752 (7)	221 (3)	1593 (9)	3.6 (4)
C(3)	3106 (6)	273 (2)	1194 (8)	2.5 (3)
C(4)	2744 (6)	173 (3)	1227 (8)	2.2 (3)
C(5)	2884 (7)	-22 (3)	1680 (9)	3.9 (4)
N(1)	2195 (5)	276 (2)	802 (6)	2.0 (3)
C(6)	2142 (6)	446 (2)	457 (8)	2.5 (3)
C(7)	1721 (6)	200 (2)	781 (8)	2.5 (3)
C(8)	1183 (6)	344 (2)	346 (8)	2.2 (3)
C(9)	1174 (6)	537 (2)	632 (8)	2.2 (3)
N(2)	1675 (5)	606 (2)	1353 (7)	3.3 (3)
N(3)	682 (5)	660 (2)	230 (7)	2.7 (3)
C(10)	188 (6)	600 (3)	-480 (8)	2.4 (3)
C(11)	-356 (8)	743 (3)	-972 (10)	4.3 (4)
N(4)	166 (5)	420 (2)	-774 (7)	3.0 (3)
C(12)	659 (6)	293 (3)	-369 (8)	2.7 (3)
O(2)	0	590 (5)	-2500	*

\* Atom defined anisotropically (Table 2).

Table 2. Anisotropic thermal parameters for selected atoms in  $\text{HThiBr} \cdot \frac{1}{2}\text{H}_2\text{O}$

The expression for the anisotropic temperature factor is  $T_i = \exp(-\beta_{11}h^2 - \beta_{22}k^2 - \beta_{33}l^2 - \beta_{12}hk - \beta_{13}hl - \beta_{23}kl)$ . The standard deviation in the last significant figure is given in parentheses.

	$\beta_{11}$	$\beta_{22}$	$\beta_{33}$	$\beta_{12}$	$\beta_{13}$	$\beta_{23}$
Br(1)	0.00272 (5)	0.0267 (7)	0.00392 (8)	-0.0024 (2)	0.00258 (6)	-0.0029 (2)
Br(2)	0.00195 (4)	0.0267 (6)	0.00286 (7)	-0.0002 (2)	0.00157 (5)	-0.0007 (2)
S	0.0014 (1)	0.020 (1)	0.0023 (2)	0.0012 (4)	0.0014 (1)	0.0017 (5)
O(2)	0.0045 (8)	0.05 (1)	0.012 (2)	0.0	-0.0015 (9)	0.0

Å is normal for a N—H...O hydrogen bond. Protonation at N(4) has been observed in all other thiamine structures in which hydrogen-atom positions have been accurately determined (see, for example, Kraut & Reed, 1962; Richardson *et al.*, 1975). The O(1) hydroxy group of the thiazolium side chain is probably hydrogen bonded to Br(2)<sup>viii</sup>, which would account for the O(1)...Br(2)<sup>viii</sup> distance of 3.20 Å. Two C—H groups, C(12)—H(C12) and C(6)—H(C6), are sufficiently close to Br(1) anions to be regarded as

hydrogen bonded to them. Such C—H hydrogen bonding is a common feature in thiamine structures, particularly in the case of C(6) (Pletcher & Sax, 1972; Kraut & Reed, 1962; Richardson *et al.*, 1975).

The O(2) water molecule is located in a large cavity in the thiamine structure, as can be clearly seen in Fig. 2. This may account for the large thermal parameter and possible disorder observed for O(2). The O(2) molecule is weakly hydrogen bonded to two Br(1) anions.

Other significant short contacts worthy of mention are those made to the thiazolium S and N(1) atoms. The Br(1)<sup>viii</sup> ion is 3.49 Å from S, in almost the same plane as the thiazolium ring. This distance is 0.3 Å

Table 3. *Calculated positions of the hydrogen atoms*

	10 <sup>3</sup> x	10 <sup>3</sup> y	10 <sup>3</sup> z
H(C1A)	465	314	260
H(C1B)	414	493	228
H(C2A)	382	62	169
H(C2B)	382	258	125
H(C6)	176	539	12
H(C7A)	192	184	133
H(C7B)	158	54	54
H(N4)	-22	378	-131
H(C12)	63	155	-62

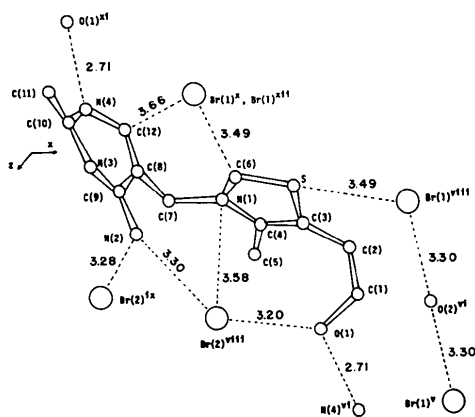


Fig. 1. The thiamine cation in HThiBr<sub>2</sub>·½H<sub>2</sub>O. Important short contacts are shown. See caption to Fig. 2 for the symmetry code.

Table 4. *Bond distances in HThiBr<sub>2</sub>·½H<sub>2</sub>O*

O(1)—C(1)	1.43 (3) Å	C(7)—C(8)	1.50 (2) Å
C(1)—C(2)	1.55 (2)	C(8)—C(9)	1.42 (3)
C(2)—C(3)	1.51 (3)	C(9)—N(2)	1.37 (2)
C(3)—S	1.73 (2)	C(9)—N(3)	1.33 (2)
S—C(6)	1.67 (2)	N(3)—C(10)	1.33 (2)
C(6)—N(1)	1.31 (2)	C(10)—C(11)	1.50 (2)
N(1)—C(4)	1.38 (2)	C(10)—N(4)	1.33 (2)
C(4)—C(5)	1.51 (3)	N(4)—C(12)	1.35 (2)
C(4)—C(3)	1.33 (3)	C(12)—C(8)	1.35 (2)
N(1)—C(7)	1.50 (3)		

Table 5. *Bond angles in HThiBr<sub>2</sub>·½H<sub>2</sub>O*

O(1)—C(1)—C(2)	111 (2)°	N(1)—C(7)—C(8)	113 (1)°
C(1)—C(2)—C(3)	112 (2)	C(7)—C(8)—C(12)	120 (2)
C(2)—C(3)—S	119 (2)	C(7)—C(8)—C(9)	125 (1)
C(2)—C(3)—C(4)	129 (1)	C(12)—C(8)—C(9)	115 (1)
C(4)—C(3)—S	112 (1)	C(8)—C(9)—N(2)	121 (1)
C(3)—S—C(6)	90 (1)	C(8)—C(9)—N(3)	123 (1)
S—C(6)—N(1)	113 (1)	N(2)—C(9)—N(3)	116 (2)
C(6)—N(1)—C(7)	124 (1)	C(9)—N(3)—C(10)	118 (2)
C(6)—N(1)—C(4)	115 (2)	N(3)—C(10)—N(4)	122 (1)
C(7)—N(1)—C(4)	121 (1)	N(3)—C(10)—C(11)	119 (2)
N(1)—C(4)—C(5)	121 (2)	N(4)—C(10)—C(11)	119 (1)
N(1)—C(4)—C(3)	111 (1)	C(10)—N(4)—C(12)	121 (1)
C(5)—C(4)—C(3)	128 (1)	N(4)—C(12)—C(8)	121 (2)

Table 6. *Some important angles (°) for hydrogen bonding and other contacts*

See caption to Fig. 2 for the symmetry code.

N(4)—H(N4)...O(1) <sup>xi</sup>	163	Br(2) <sup>viii</sup> ...N(1)—C(7)	95
C(12)—H(C12)...Br(1) <sup>x</sup>	156	O(2) <sup>ii</sup> ...Br(1)...S <sup>xiii</sup>	111
C(6)—H(C6)...Br(1) <sup>xiii</sup>	157	O(2) <sup>ii</sup> ...Br(1)...H(C6) <sup>ii</sup>	106
Br(1) <sup>viii</sup> ...O(2) <sup>vi</sup> ...Br(1) <sup>v</sup>	126	O(2) <sup>ii</sup> ...Br(1)...H(C12) <sup>xiv</sup>	113
Br(2) <sup>ix</sup> ...N(2)...Br(2) <sup>viii</sup>	91	S <sup>xiii</sup> ...Br(1)...H(C6) <sup>ii</sup>	88
C(9)—N(2)...Br(2) <sup>ix</sup>	131	S <sup>xiii</sup> ...Br(1)...H(C12) <sup>xiv</sup>	108
C(9)—N(2)...Br(2) <sup>viii</sup>	138	H(C6) <sup>ii</sup> ...Br(1)...H(C12) <sup>xiv</sup>	127
N(4) <sup>vi</sup> ...O(1)...Br(2) <sup>viii</sup>	124	O(1) <sup>xiii</sup> ...Br(2)...N(2) <sup>xiii</sup>	141
N(4) <sup>vi</sup> ...O(1)—C(1)	119	O(1) <sup>xiii</sup> ...Br(2)...N(2) <sup>xv</sup>	82
Br(2) <sup>viii</sup> ...O(1)—C(1)	113	O(1) <sup>xiii</sup> ...Br(2)...N(1) <sup>xiii</sup>	82
C(6)—S...Br(1) <sup>viii</sup>	171	N(2) <sup>xiii</sup> ...Br(2)...N(2) <sup>xv</sup>	106
C(3)—S...Br(1) <sup>viii</sup>	99	N(2) <sup>xiii</sup> ...Br(2)...N(1) <sup>xiii</sup>	59
Br(2) <sup>viii</sup> ...N(1)—C(4)	76	N(2) <sup>xv</sup> ...Br(2)...N(1) <sup>xiii</sup>	100
Br(2) <sup>viii</sup> ...N(1)—C(6)	96		

shorter than the van der Waals S...Br distance, and represents a dipolar contact between the bromide ion and the S atom, which carries a partial positive charge. [Jordan (1974, 1976) discusses the crystallographic and quantum-mechanical evidence for charge distribution in the thiazolium ring.] Sitting almost directly over the N(1) atom, which may also carry a partial positive charge (Jordan, 1974), is a Br(2)<sup>viii</sup> ion at the van der Waals distance. The empty  $p_z$  orbital on N(1) is thus in a position for charge-transfer interaction with Br(2) as well as being correctly oriented for participation in the  $\pi$  system of the thiazolium ring.

The hydrogen bonds and dipolar contacts described above define a distorted tetrahedron about each of the Br atoms (Table 6), suggesting that the interactions involve the four  $sp^3$  lone pairs on the bromide ion. However, in view of the fact that each bromide ion has several other neighbors at distances not much greater than the van der Waals separation (*i.e.*  $\lesssim 3.75$  Å); the description of the bromide surroundings as tetrahedral is oversimplified.

The molecular packing (Fig. 2) can be simply described. Molecules i and viii are related to each other by a screw axis parallel to [010], as are iii and vi. These screw-related molecules are linked in infinite spiral chains in the  $y$  direction by a system of hydrogen bonds involving the amino groups and the Br(2) anions. In turn, each screw-related pair in the chain is linked to a centrosymmetrically equivalent pair by N(4)—H(N4)...O(1) hydrogen bonds to form corrugated sheets parallel to [101]. Finally, a three-dimensional network is completed by interactions of the type S...Br(1)...H<sub>2</sub>O...Br(1)...S which link adjacent sheets together. This interaction, which has been omitted from Fig. 2 for the sake of clarity, may be seen in Fig. 1. The weak interactions involving C(12)—H(C12)...Br(1), C(6)—H(C6)...Br(1), and N(1)...Br(2) provide additional linkages between the sheets and further stabilize the structure.

### Comparison of the packing in thiamine hydrochloride, hydrobromide and hydroiodide

Although a wide range of conformations appear to be accessible to a free thiamine cation (Jordan, 1974), only two have been observed in the crystalline state: one in which  $\varphi_T = 5 \pm 10$ ,  $\varphi_P = 85 \pm 10^\circ$ , and one in which  $\varphi_T = 105 \pm 5$ ,  $\varphi_P = 140 \pm 5^\circ$ . These have been designated the F and S conformations by Blank, Rodrigues, Pletcher & Sax (1976). The F configuration observed in the present structure is by far the more common. This could be due to one or more of the following reasons. First, the F conformation could in fact be the more stable (Blank *et al.*, 1976). Second, the F conformation might be one which allows the better packing of thiamine cations. Third, hydrogen bonding and other short contacts might stabilize certain conformations relative to others. A comparison of the structures of thiamine hydrohalides shows that the second hypothesis can be rejected, and sheds some light on the third.

The structures of HThiCl<sub>2</sub>·H<sub>2</sub>O, HThiBr<sub>2</sub>·½H<sub>2</sub>O and HThiI<sub>2</sub> are shown in Fig. 3 in projection onto the N(1)—C(7)—C(8) plane of cation i. Data for the hydrochloride and hydroiodide were taken from Kraut & Reed (1962) and Lee & Richardson (1976) respectively. The lengths of the hydrogen bonds and dipolar contacts to the thiazolium N and S atoms have been included in each structure.

Gross differences in the packing of thiamine cations are immediately obvious. The F thiamine conformation, which is observed in all these structures, thus appears not to be a result of some especially stable arrangement of thiamine cations in this conformation.

An analysis of the immediate surroundings of the thiamine cation in each structure is more revealing. There are several common features in the three structures as well as certain differences. Many of the differences have to do with the varying placement of the

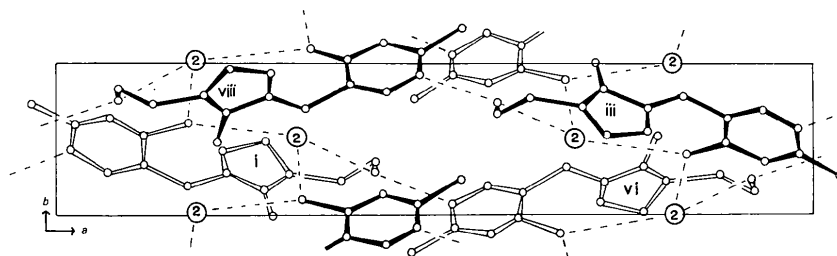


Fig. 2. Packing diagram for thiamine hydrobromide hemihydrate. The view is approximately perpendicular to the hydrogen-bonded sheets of thiamine cations. The large numbered circles represent Br(2) anions, which lie close to the plane of the paper. Hydrogen bonds involving N(4)...O(1), O(1)...Br(2), and N(2)...Br(2) are indicated by the dashed lines. Symmetry code, superscript: none or (i)  $x, y, z$ ; (ii)  $x, 1 - y, \frac{1}{2} + z$ ; (iii)  $1 - x, 1 - y, 1 - z$ ; (iv)  $1 - x, y, \frac{1}{2} - z$ ; (v)  $\frac{1}{2} + x, \frac{1}{2} + y, z$ ; (vi)  $\frac{1}{2} + x, \frac{1}{2} - y, \frac{1}{2} + z$ ; (vii)  $\frac{1}{2} - x, \frac{1}{2} - y, 1 - z$ ; (viii)  $\frac{1}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z$ ; (ix)  $x, 1 + y, z$ ; (x)  $x, -y, z - \frac{1}{2}$ ; (xi)  $x - \frac{1}{2}, \frac{1}{2} - y, z - \frac{1}{2}$ ; (xii)  $x, 1 - y, z - \frac{1}{2}$ ; (xiii)  $\frac{1}{2} - x, y - \frac{1}{2}, \frac{1}{2} - z$ ; (xiv)  $x, -y, \frac{1}{2} + z$ ; (xv)  $x, -1 + y, \frac{1}{2} - z$ .

$\beta$ -hydroxyethyl side chain. For example, in the hydrobromide and hydroiodide, but not in the hydrochloride, the  $-\text{OH}$  group on this side-chain is a hydrogen-bond acceptor for the protonated pyrimidine  $\text{N}(4)-\text{H}(\text{N}4)$  group, and a hydrogen-bond donor to the halide ion.

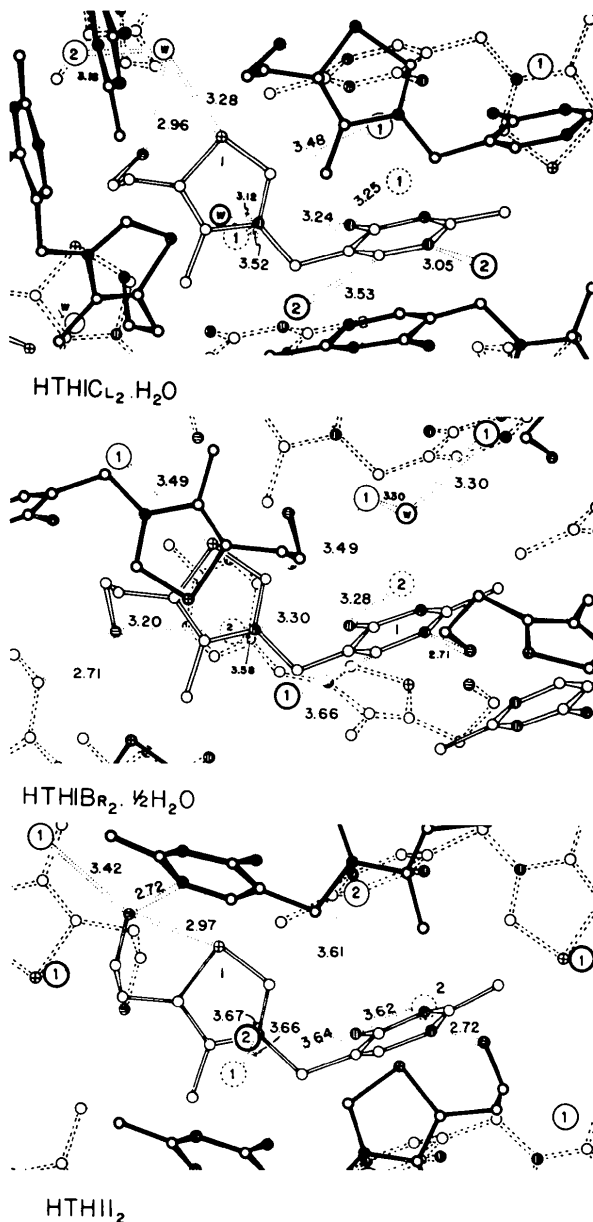


Fig. 3. The structures of thiamine hydrohalides projected onto the  $\text{N}(1)-\text{C}(7)-\text{C}(8)$  plane of cation  $i$ . The large numbered circles are halide ions; the circles containing the letter  $W$  represent water molecules. The small circles with crosses represent  $S$  atoms, vertically hatched circles are  $N$  atoms, horizontally hatched circles are  $O$  atoms, and plain circles are  $C$  atoms.

Also, the  $S$  atom makes short contacts to different atoms in the three structures: to a water molecule in the hydrochloride, to a bromide ion in the hydrobromide, and to the  $\beta$ -hydroxyethyl  $\text{OH}$  group in the hydroiodide.

The similarities in each of the structures are as follows. First, the amino group on the pyrimidine ring is a hydrogen-bond donor to two halide ions. Also, one of these halide ions lies below the plane of the thiazolium ring in a position suitable for weak dipolar contact to  $\text{N}(1)$ , an atom which may carry a partial positive charge. Lastly, the  $\text{C}(6)-\text{H}(\text{C}6)$  group on the thiazolium ring is involved in a weak hydrogen bond to the halide.

The double interaction of the halide ion with the amino group and with the thiazolium  $N$  atom might be thought to stabilize the  $F$  conformation of thiamine; however, this feature does not persist in other thiamine structures in which thiamine is in the  $F$  conformation. For example, in thiamine pyrophosphate hydrochloride (Pletcher & Sax, 1972), the amino group forms  $\text{N}-\text{H} \cdots \text{Cl}$  hydrogen bonds, but the closest  $\text{Cl}^-$  approach to the thiazolium  $N$  atom is 3.92 Å, considerably longer than the van der Waals distance.

The failure to find some specific structural feature common to all thiamine structures probably means that the  $F$  conformation of thiamine is indeed the more stable, as has been proposed by Blank *et al.* (1976).

We thank Mr Kenneth Franklin and Mrs Teresa Figg Franklin for their assistance during the data collection. This work has been funded by a grant from the National Research Council of Canada.

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