Note added in proof:– We have recently learned that the distribution $\exp(\kappa \cos \alpha)$, which is fundamental to the phase probability distributions above, was first derived by von Mises (1918) from the principle of maximum likelihood of Gauss. Its relation to the Gaussian distribution has prompted statisticians to refer to it as the circular normal distribution. A review of the properties and applications of it and other circular distributions has been written by Batschelet (1965).

We are grateful to Eduardo Padlan for the use of his data from *Glycera* hemoglobin, to Michael Rossmann and David Blow for their helpful comments on the manuscript and to Warner Love for his encouragement and support. We also acknowledge the support of the U.S. Public Health Service through predoctoral fellowship GM-15907 (EEL) and GM30009 (WAH) and grant AM02528 and thank the Johns Hopkins Faculty of Arts and Sciences for computing funds.

References

BATSCHELET, E. (1965). *Statistical Methods for the Analysis of Problems in Animal Orientation and Certain Biological Rhythms*. Amer. Inst. of Biol. Sci. Monograph Washington, D.C.
BLOW, D. M. & CRICK, F. H. C. (1959). *Acta Cryst.* **12**, 794.
COCHRAN, W. (1955). *Acta Cryst.* **8**, 473.
COULTER, C. L. (1965). *J. Mol. Biol.* **12**, 292.
CULLIS, A. F., MUIRHEAD, H., PERUTZ, H. F., ROSSMANN, M. G. & NORTH, A. C. T. (1961). *Proc. Roy. Soc.* A**265**, 15.
DICKERSON, R. E., KENDREW, J. C. & STRANDBERG, B. E. (1961). *Acta Cryst.* **14**, 1188.
GREEN, D. W., INGRAM, V. M. & PERUTZ, M. F. (1954). *Proc. Roy. Soc.* A**225**, 287.
KARLE, J. (1966). *Acta Cryst.* **21**, 273.
KARLE, J. & HAUPTMAN, H. (1956). *Acta Cryst.* **9**, 635.
KARLE, J. & KARLE, I. L. (1966). *Acta Cryst.* **21**, 849.
LIPSCOMB, W. N., COPPOLA, J. C., HARTSUCK, J. A., LUDWIG, M. L., MUIRHEAD, H., SEARL, J. & STEITZ, T. A. (1966). *J. Mol. Biol.* **19**, 423.
MAIN, P. & ROSSMANN, M. G. (1966). *Acta Cryst.* **21**, 67.
MATTHEWS, B. W. (1966). *Acta Cryst.* **20**, 82.
MISES, R. VON (1918). *Physical. Z.* **19**, 490.
MUIRHEAD, H., COX, J. M., MAZZARELLA, L. & PERUTZ, M. F. (1967). *J. Mol. Biol.* **28**, 117.
NORTH, A. C. T. (1965). *Acta Cryst.* **18**, 212.
PADLAN, E. A. & LOVE, W. E. (1968). *Nature, Lond.* **220**, 376.
ROSSMANN, M. G. & BLOW, D. M. (1961). *Acta Cryst.* **14**, 641.
ROSSMANN, M. G. & BLOW, D. M. (1963). *Acta Cryst.* **16**, 39.
ROSSMANN, M. G. & BLOW, D. M. (1964). *Acta Cryst.* **17**, 1474.
SIM, G. A. (1959). *Acta Cryst.* **12**, 813.
WATSON, G. N. (1952). *A Treatise on the Theory of Bessel Functions*, Chap. 2 & 3. Cambridge Univ. Press.
WHITTAKER, E. T. & WATSON, G. N. (1952). *A Course of Modern Analysis*, Chap. 2–4. Cambridge Univ. Press.

Acta Cryst. (1970). B**26**, 143

The Crystal Structure of *N*-Benzyl-4-methylthiazolium Bromide

BY L. POWER,* J. PLETCHER AND M. SAX

The Biocrystallography Laboratory, Veterans Administration Hospital, Pittsburgh, Pa. 15240, *U.S.A.*

and The Crystallography Laboratory, University of Pittsburgh, Pittsburgh, Pa. 15213, *U.S.A.*

(*Received* 27 *February* 1969)

The crystal structure of *N*-benzyl-4-methylthiazolium bromide, $C_{11}NSH_{12}Br$, was determined from three-dimensional X-ray diffraction data. The crystals are monoclinic and the space group is $P2_1/c$ with four molecules per unit cell. The axial dimensions are $a=9{\cdot}162\pm0{\cdot}003$, $b=11{\cdot}770\pm0{\cdot}004$ and $c=11{\cdot}070\pm0{\cdot}004$ Å, $\beta=81{\cdot}93\pm0{\cdot}04°$. The structure was solved by the heavy-atom method and refined by means of full-matrix least squares. The final R value was 0·056 on 1991 reflections which included 221 unobserved. The bond lengths in the thiazolium ring are compared with those in thiamine and thiamine pyrophosphate. The conformation of the rings in this molecule differs substantially from that observed for the other two molecules. A weak CH···Br bifurcated hydrogen bond occurs in the structure. Another interaction is observed between the sulfur atom and the bromide ion as the Br···S interatomic distances average 0·3 Å less than the sum of their van der Waals radii.

Introduction

Breslow & McNelis (1958) have pointed out that in a number of biochemical reactions involving thiamine pyrophosphate (TPP) as coenzyme the thiazolium zwitterion is the site of primary reaction. It was shown that the attachment of an aromatic ring on the *N*-methylene group of a thiazolium ring facilitates the formation of the catalytic zwitterion due to the inductive effect of the aromatic ring. The *N*-benzyl thiazolium salt and TPP are both effective catalysts to these

* Permanent address: The University of Townsville, Pimlico, Townsville, Queensland, Australia.

reactions in enzyme-free model systems. The present study of the crystal structure of *N*-benzyl-4-methylthiazolium bromide (BTB) was undertaken in order to examine bond lengths of the thiazolium portion and the conformation of the rings.

Crystal data

$C_{11}NSH_{12}Br$, M.W. = 270·20, monoclinic, $a = 9{\cdot}162 \pm 0{\cdot}003$, $b = 11{\cdot}770 \pm 0{\cdot}004$, $c = 11{\cdot}070 \pm 0{\cdot}004$ Å and $\beta = 81{\cdot}93 \pm 0{\cdot}04°$; $V = 1181{\cdot}92$ Å^3, $Z = 4$, $D_o = 1{\cdot}52$ g.cm^{-3}, $D_c = 1{\cdot}518$ g.cm^{-3}. $F(000) = 548$. Space group $P2_1/c$ (No. 14). μ for Cu $K\alpha$ radiation = 64·8 cm^{-1}.

Experimental

Crystals of BTB were kindly supplied by Dr R. Breslow of Columbia University. They were recrystallized from methanol by slow dropwise addition of ether. The crystals are white and grow as diamond shaped plates normal to [001] with the *b* axis along the longer of the two diagonals of the diamond. The specimen used measured 0·11 × 0·43 × 0·38 mm. The cell constants and relative intensities were measured with a Picker automatic diffractometer equipped with a scintillation counter, using Cu $K\alpha$ radiation. The intensities were corrected for Lorentz and polarization factors and absorption. A total of 1991 reflections were collected of which 221 were unobserved. All reflections for which $I \leq 3\sigma(I)$ were treated as unobserved, where $\sigma(I) = [S + 4(B_1 + B_2)]^{1/2}$, S is the total number of counts accumulated during a 2θ scan over a 2° range at 2° min^{-1}, B_1 is the total number of counts in 15 sec at the initial setting and B_2 is the total number of counts in 15 sec at the terminal setting.

The bromine atom was located from a three-dimensional unsharpened Patterson map and the remaining non-hydrogen atoms from two cycles of structure factor calculations and Fourier syntheses. At this stage the R value ($R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$) was 27·2 per cent. Scattering factors used for bromine, sulfur, nitrogen and carbon atoms were those of Cromer & Waber (1965). The atomic scattering factor for the hydrogen atoms was that of Stewart, Davidson & Simpson (1965). Anomalous dispersion corrections were made for bromine and sulphur using values listed in *International Tables for X-ray Crystallography* (1962).

Least-squares refinement

The structure factor least-squares program *ORFLS* (Busing, Martin & Levy, 1962) modified by Shiono (1965) for the IBM 7090 computer was used. Initially unit weight was assigned to each reflection and isotropic temperature factors applied for two cycles which reduced R to 15·6%. A further cycle of least-squares using anisotropic temperature factors and unit weight produced an R of 9·7%. At this stage of the refinement a Fourier difference synthesis allowed the location of all hydrogen atoms. A least-squares cycle based on all atoms, giving the hydrogen atoms the anisotropic temperature factors of the atoms to which they were bonded, reduced R to 8·3% (the hydrogen positional parameters were refined but their thermal parameters were held constant). Application of the absorption correction and a change to a weighting scheme based on the σ of the individual reflections reduced R to 5·6% on all reflections and 5·2% on the observed. In the final weighting scheme $W = 1/\sigma^2$ where $\sigma = \sigma_{exp} + 0{\cdot}05F$. In this expression σ_{exp} is the experimental σ based on counting statistics. This weighting scheme was used because it was found empirically to produce a constant $W\Delta^2$ as a function of $|F|$.

The final atomic parameters and their standard deviations are given in Table 1 and the vibration parameters and their standard deviations are given in Table 2. The observed structure amplitudes and those calculated with the parameters of Tables 1 and 2 are given in Table 3.

Table 1. *Fractional coordinates and e.s.d.'s*

	x	*y*	*z*
Br	0·03627 (5)	0·18114 (4)	0·02096 (4)
S	0·95437 (9)	0·10229 (9)	0·3256 (1)
N	0·1995 (3)	0·4272 (3)	0·1748 (2)
C(13)	0·3376 (6)	0·0919 (4)	0·4624 (4)
C(4)	0·2327 (4)	0·4692 (3)	0·0560 (3)
C(5)	0·8426 (5)	0·0645 (3)	0·4564 (3)
C(2)	0·1036 (4)	0·4888 (3)	0·2450 (3)
C(6)	0·2640 (5)	0·3219 (3)	0·2181 (4)
C(9)	0·5967 (7)	0·4249 (7)	0·3534 (6)
C(8)	0·4529 (6)	0·4181 (5)	0·3249 (4)
C(7)	0·4192 (5)	0·3371 (3)	0·2439 (4)
C(12)	0·5277 (6)	0·2643 (5)	0·1884 (5)
C(11)	0·6701 (7)	0·2755 (8)	0·2183 (7)
C(10)	0·7034 (6)	0·3495 (7)	0·2991 (8)
H(131)	0·315 (6)	0·178 (4)	0·455 (4)
H(132)	0·342 (5)	0·055 (4)	0·375 (4)
H(133)	0·434 (6)	0·101 (4)	0·488 (4)
H(5)	0·854 (5)	0·406 (3)	0·033 (4)
H(2)	0·073 (5)	0·482 (3)	0·311 (4)
H(61)	0·201 (5)	0·284 (3)	0·283 (4)
H(62)	0·258 (5)	0·266 (3)	0·162 (4)
H(9)	0·623 (7)	0·464 (6)	0·415 (6)
H(8)	0·380 (6)	0·464 (5)	0·352 (4)
H(12)	0·463 (6)	0·171 (4)	0·128 (5)
H(11)	0·750 (6)	0·213 (6)	0·177 (6)
H(10)	0·804 (6)	0·356 (5)	0·336 (6)

Discussion

The molecular geometry is summarized in Figs. 1, 2 and 3 and in Tables 4 and 5. In Tables 4 and 5 are shown for comparison the bond lengths and angles of the corresponding portions of the thiamine pyrophosphate hydrochloride molecule (Pletcher & Sax, 1969) and of thiamine chloride hydrochloride (Kraut & Reed, 1962). These data exhibit an overall good agreement between similar bonds in BTB and the other two compounds. The bonds in the thiazolium ring of BTB agree to better than 2σ, except for N–C(2) and C(4)–C(5), which are both shorter by 3 to 4σ. Although

Breslow & McNelis (1958) have stated that the increase in catalytic activity from BTB to thiamine is partly due to the greater inductive effect of the pyrimidine ring with respect to the benzene ring, it is uncertain whether or not the observed bond shortening is a consequence of this chemical effect since the deviations are of borderline significance.

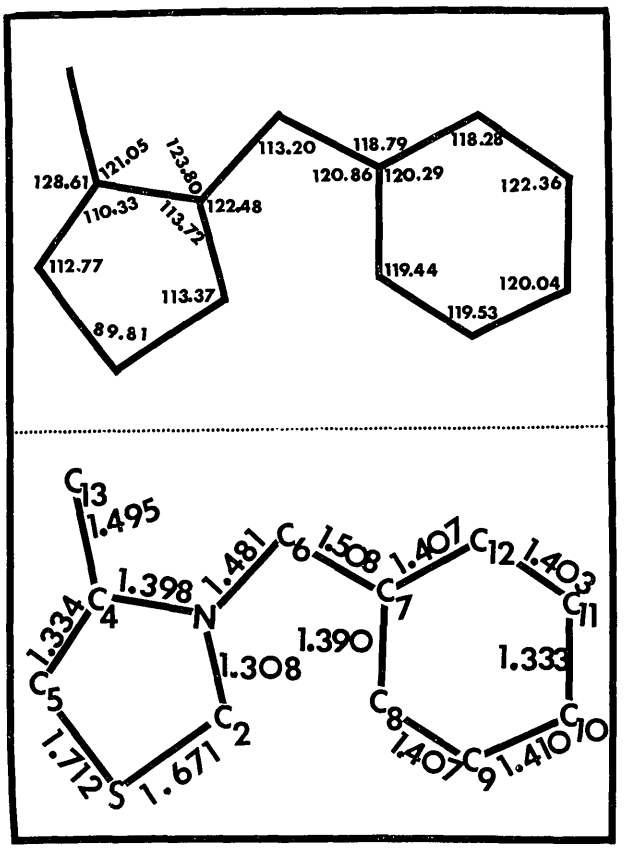


Fig. 1. Bond distances and valency angles in *N*-benzyl-4-methylthiazolium bromide.

In Table 4 are shown the bond lengths of the benzene ring prior to and after absorption correction during the refinement. A marked shift in length of 0·07 Å occurred for the bond C(10)–C(11) as compared with average shifts of 0·024 Å for the other bonds of the benzene ring and of 0·018 Å for all other bonds of the whole molecule. A rigid-body analysis using a program written by Schomaker & Trueblood (1968) and modified by Shiono (1968) for the IBM 1130 computer produced the bond lengths as listed in Table 4, which show the C(10)–C(11) bond length of 1·333 Å. No definite explanation could be found to account for this abnormally short bond. It is possible that a systematic error was introduced with the application of the absorption correction (correction factor applied to the F's varied from 1·37 to 2·07 with the average correction amounting to 1·50) since the second largest change following the absorption correction is observed for the parallel bond between C(7) and C(8). However, the bond distances following the absorption correction agree much better in general with the other two structures. It is also possible that the rigid-body analysis does not provide an appropriate description of the vibrational parameters of the benzene ring.

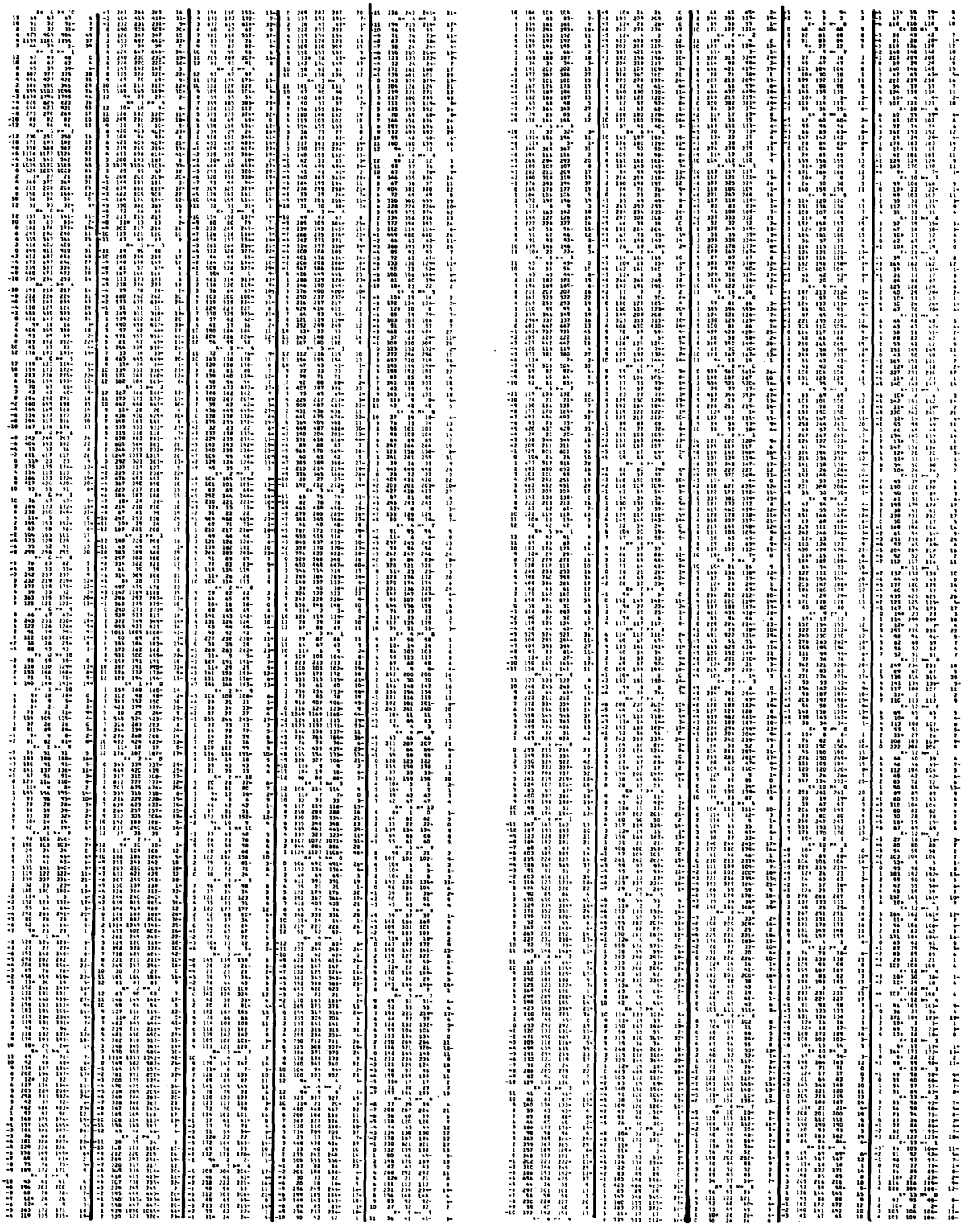
The equations of the planes of the thiazolium and benzene rings are given in Table 6 along with distances from the planes. Both rings are quite planar and in the case of the thiazolium ring, the methyl and methylene substituents deviate only slightly from the plane. The dihedral angle between the benzene and thiazolium rings is 75·7°. Although this value compares favorably with that found in thiamine (76°, Kraut & Reed, 1962) and thiamine pyrophosphate (83·3°, Pletcher & Sax, 1969), the conformation of the rings in BTB does differ substantially. If the coplanar conformation of the two rings (as in thiochrome) is taken as a reference, then the conformation in BTB is described by a clockwise rotation about the C(6)–N bond of 103·4° and a counterclockwise rotation about the C(6)–C(7) bond of 55·3°. The magnitudes of the corresponding angles in thiamine are 9·4 and 73·5° and in thiamine pyrophosphate 3·6 and 93·2° (Pletcher & Sax, 1969). Since BTB does

Table 2. *Atomic vibration parameters*

	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Br	0·01655 (9)	0·00786 (5)	0·00649 (6)	−0·00085 (3)	0·00036 (5)	0·00003 (2)
S	0·0136 (1)	0·00809 (9)	0·00774 (9)	−0·00148 (8)	−0·00167 (9)	0·00015 (6)
N	0·0103 (3)	0·0068 (2)	0·0061 (2)	−0·0006 (2)	−0·0006 (2)	0·0007 (1)
C(13)	0·0173 (6)	0·0091 (4)	0·0068 (3)	0·0003 (4)	0·0014 (3)	0·0002 (3)
C(4)	0·0117 (4)	0·0073 (3)	0·0059 (3)	−0·0010 (3)	−0·0010 (2)	−0·0001 (2)
C(5)	0·0160 (5)	0·0081 (3)	0·0062 (3)	0·0009 (3)	0·0016 (3)	0·0006 (2)
C(2)	0·0100 (4)	0·0078 (3)	0·0062 (3)	0·0001 (2)	−0·0003 (3)	0·0001 (2)
C(6)	0·0132 (5)	0·0064 (3)	0·0080 (3)	0·0001 (3)	−0·0007 (3)	0·0002 (2)
C(9)	0·0194 (9)	0·0206 (9)	0·0135 (6)	−0·0032 (7)	−0·0073 (6)	0·0028 (6)
C(8)	0·0135 (6)	0·0144 (5)	0·0109 (5)	0·0007 (4)	−0·0030 (4)	−0·0000 (4)
C(7)	0·0122 (5)	0·0089 (3)	0·0076 (3)	0·0009 (3)	0·0001 (3)	0·0021 (2)
C(12)	0·0152 (6)	0·0120 (5)	0·0125 (5)	0·0043 (4)	0·0015 (4)	0·0023 (4)
C(11)	0·0132 (7)	0·0209 (9)	0·0165 (7)	0·0059 (7)	0·0012 (6)	0·0073 (7)
C(10)	0·0109 (6)	0·0210 (8)	0·0195 (9)	−0·0007 (6)	−0·0034 (6)	0·0101 (7)

Table 3. *Observed and calculated structure factors*

The columns within each group, in order from left to right, are the running index l, $10F_o$, $10F_c$, $10A_c$ and $10B_c$. The unobserved reflections, which were assigned zero weight in the least squares refinement, are marked *.



not possess any substituents on the benzene ring, a greater freedom of rotation is permitted than is possible with the amino pyrimidine ring of thiamine.

As seen in Fig. 2, there are distances between the sulfur and bromine atoms of 3·476 (2) and 3·491 (2) Å which are shorter than the sum of the van der Waals radii, 3·80 Å (Pauling, 1960). It would appear that in this compound there are weak interactions between the atoms of the sulfur–bromine chains, similar to those observed by Sax, Pletcher & Pulsinelli (1969) in the related compound 2-(α-hydroxyethyl)-3,4-dimethylthiazolium bromide.

A hydrogen bond between bromine and C(2) seems a likely possibility in view of the polarity of the C(2)–H(2) bond. Assuming that the hydrogen bond radius of CH is 1·64 Å (Pletcher & Sax, 1969) and that the acceptor radius of bromide ion is 1·98 Å (Wallwork, 1962), the expectation value for a C(2)···Br^- hydrogen

Table 4. *Bond lengths* (Å)

	BTB	TPP*	Thiamine†	BTB prior to absorption correction	Benzene ring after rigid-body analysis
S——C(2)	1·671 (4)	1·673 (3)	1·667 (6)	1·689	
S——C(5)	1·712 (5)	1·715 (3)	1·718 (6)	1·732	
C(4)—C(5)	1·334 (6)	1·354 (4)	1·349 (7)	1·316	
N——C(4)	1·398 (5)	1·391 (4)	1·401 (7)	1·416	
N——C(2)	1·308 (5)	1·324 (4)	1·332 (7)	1·329	
N——C(6)	1·481 (5)	1·498 (4)	1·476 (7)	1·484	
C(6)—C(7)	1·499 (6)	1·500 (4)	1·496 (8)	1·486	1·508
C(13)–C(4)	1·495 (6)	1·495 (5)	1·479 (8)	1·514	
C(7)—C(8)	1·374 (7)			1·417	1·390
C(8)—C(9)	1·400 (10)			1·395	1·407
C(9)—C(10)	1·392 (11)			1·384	1·410
C(10)–C(11)	1·318 (11)			1·388	1·333
C(11)–C(12)	1·396 (10)			1·369	1·403
C(12)–C(7)	1·390 (7)			1·361	1·407
C(5)—H(5)	0·93				
C(2)—H(2)	0·74				
C(6)—H(61)	0·90				
C(6)—H(62)	0·96				
C(8)—H(8)	0·88				
C(9)—H(9)	0·88				
C(10)–H(10)	1·06				
C(11)–H(11)	1·08				
C(12)–H(12)	1·44				
C(13)–H(131)	1·04				
C(13)–H(132)	1·05				
C(13)–H(133)	0·97				

* Pletcher & Sax (1969).
† Kraut & Reed (1962).

Table 5. *Bond angles*

	BTB	TPP*	Thiamine†
C(5)—S——C(2)	89·8 (2)°	91·3 (2)°	91·8 (3)°
C(4)—C(5)—S	112·8 (3)	111·0 (2)	110·7 (4)
N——C(4)—C(5)	110·3 (3)	111·6 (3)	111·9 (4)
C(4)—N——C(6)	123·8 (4)	121·9 (2)	121·8 (4)
C(2)—N——C(6)	122·5 (3)	124·3 (2)	124·9 (4)
C(2)—N——C(4)	113·7 (3)	113·8 (2)	113·3 (4)
S——C(2)—N	113·4 (3)	112·4 (2)	112·3 (4)
N——C(6)—C(7)	113·2 (3)	111·3 (2)	113·5 (4)
N——C(4)—C(13)	121·1 (4)	120·4 (3)	120·2 (4)
C(5)—C(4)—C(13)	128·6 (4)	128·0 (3)	127·9 (5)
C(6)—C(7)—C(12)	118·8 (4)		
C(6)—C(7)—C(8)	120·9 (4)		
C(11)–C(12)–C(7)	118·3 (5)		
C(7)—C(8)—C(9)	119·4 (5)		
C(8)—C(9)—C(10)	119·5 (7)		
C(10)–C(11)–C(12)	122·4 (7)		
C(9)—C(10)–C(11)	120·0 (7)		
C(12)–C(7)—C(8)	120·3 (5)		

* Pletcher & Sax (1969).
† Kraut & Reed (1962).

Table 6. *Equations to the ring planes relative to the crystallographic axes*

(*a*) The thiazolium ring

$$0{\cdot}79232X+0{\cdot}54122Y+0{\cdot}38991Z=4{\cdot}9232\,.$$

Atoms included	Atoms not included	Distances from plane
S		−0·00225 Å
N		0·00085
C(4)		−0·00297
C(5)		0·00328
C(2)		0·00111
	C(13)	−0·03506
	C(6)	−0·01431

(*b*) The benzene ring

$$-0{\cdot}12960X-0{\cdot}65441Y+0{\cdot}71942Z=-1{\cdot}16233$$

C(7)	0·01073 Å
C(8)	−0·00849
C(9)	−0·00491
C(10)	0·01684
C(11)	−0·01481
C(12)	0·00064

bond is 3·62 Å. C(2) is engaged in two contacts of this type with bromide ions. One of these distances is 3·542 Å to a bromide ion whose coordinates are related to those in Table 2 by a screw axis. The other is 3·631 Å to the *c*-glide related bromide ion. In the first case the C(2)H(2)···Br angle is 124°, and the H(2)···Br distance is 3·06 Å. In the second case the respective values are 143° and 3·00 Å. The favorable orientation of the C(2)–H(2) bond for the formation of a bifurcated hydrogen bond together with the observed C(2)···Br distances makes it reasonable to classify this interaction as a weak hydrogen bond.

This research is supported by the U.S. Public Health Service, National Institutes of Health, through Grant No. HE-09068.

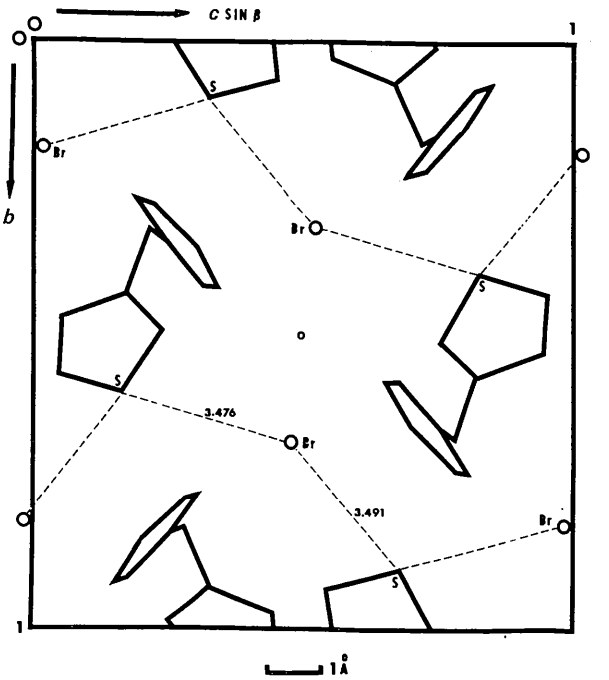


Fig. 2. The (100) projection showing the bromine–sulfur interactions and the relative orientation of the benzene and thiazolium rings.

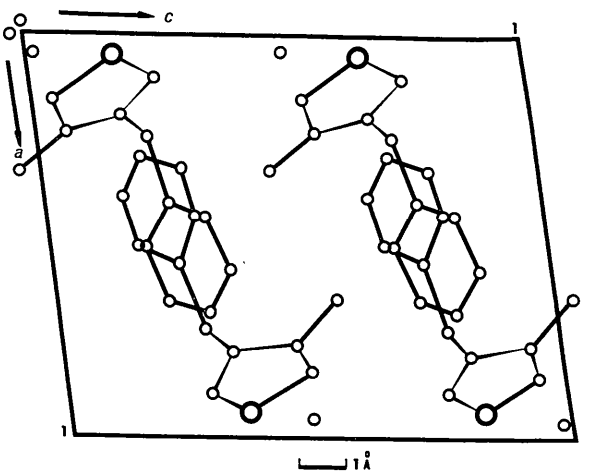


Fig. 3. The (010) projection.

References

BRESLOW, R. & MCNELIS, E. (1958). *J. Amer. Chem. Soc.* **81**, 3080.

BUSING, W. R., MARTIN, K. O. & LEVY, H. A. (1962). *ORFLS, A Fortran Crystallographic Least Squares Program*. Oak Ridge National Laboratory, Report ORNL-TM-305, Oak Ridge, Tennessee.

CROMER, D. T. & WABER, J. T. (1965). *Acta Cryst.* **18**, 104.

International Tables for X-ray Crystallography (1962). Vol. III. Birmingham: Kynoch Press.

KRAUT, J. & REED, H. J. (1962). *Acta Cryst.* **15**, 747.

PAULING, L. (1960). *The Nature of the Chemical Bond*, 3rd ed. Ithaca: Cornell Univ. Press.

PLETCHER, J. & SAX, M. (1969). To be published.

SAX, M., PLETCHER, J. & PULSINELLI, P. (1969). To be published.

SCHOMAKER, V. & TRUEBLOOD, K. (1968). *Acta Cryst.* B**24**, 63.

SHIONO, R. (1965). A modification of *ORFLS* for the Crystallography Laboratory, University of Pittsburgh.

SHIONO, R. (1968). Technical Report, Crystallography Laboratory, University of Pittsburgh.

STEWART, R. F., DAVIDSON, R. E. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175.

WALLWORK, S. C. (1962). *Acta Cryst.* **15**, 758.