Enraf–Nonius (1990). *MolEN*. An interactive structure solution procedure. Enraf–Nonius, Delft, The Netherlands.
Farrar, D. H. & Ferguson, G. (1982). *J. Crystallogr. Spectrosc. Res.* **12**, 465–471.
Harada, M., Kai, Y., Yasuoka, N. & Kasai, N. (1976). *Bull. Chem. Soc. Jpn*, **49**, 3472–3477.
Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Schagen, J. D., Staver, L., van Meurs, F. & Williams, G. (1989). CAD-4 Version 5.0. Enraf–Nonius, Delft, The Netherlands.

Acta Cryst. (1993). C**49**, 1178–1180

Interactions of Thiamine with Anions. Structure of Thiamine Dithiocyanate†

NING-HAI HU*

Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun 130022, People's Republic of China

SUI-LI ZHANG

Jilin Institute of Biology, Changchun 130012, People's Republic of China

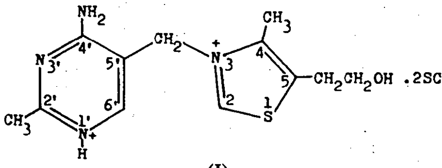
(*Received* 13 *May* 1992; *accepted* 30 *November* 1992)

Abstract

The crystal structure analysis of {3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-5-(2-hydroxyethyl)-4-methylthiazol}ium dithiocyanate reveals that there are two types of anion bridges between the two aromatic rings of the same thiamine which adopts the usual *F* conformation, one of which involves a contact between H(C2) on the thiazolium ring and the hydroxy O atom from a neighbouring molecule. The crystal packing shows a novel triple helical structure formed by strongly hydrogen-bonded thiamine–SCN$^-$ molecular chains.

Comment

Thiamine, as its pyrophosphate ester, is a coenzyme in a number of important metabolic processes such as the decarboxylation of α-keto acids. The reactions proceed through C(2)-substituted thiamines, which are intermediates in the reaction pathway (Breslow, 1958). It has been suggested that thiamine–anion salts can serve as model compounds for thiamine–substrate interactions based on the fact that the thiamine molecule fixes an anionic group near the active C(2)-position through both hydrogen bonding and electrostatic interactions (Aoki, Yamazaki, Waragai & Itokawa, 1988). In order to further examine such interactions we have determined the structure of thiamine dithiocyanate (I).



(I)

The crystal cleaves easily along {001} planes. In the structure, the thiamine cation adopts the usual *F* conformation in terms of the torsion angles (Pletcher, Sax, Blank & Wood, 1977): φ_T = C(5′)—C(35′)—N(3)—C(2) = 0.4 (6)° and φ_P = N(3)—C(35′)—C(5′)—C(4′) = 81.2 (5)°; the dihedral angle between the pyrimidine and thiazolium rings is 78.1 (2)°. The C(5) hydroxyethyl side chain folds back towards the thiazolium moiety to make a close contact of 2.868 (4) Å between O(53) and S(1). These structural features are similar to those found in thiamine.SCN and its monohydrate (Aoki, Hu, Yamazaki & Adeyemo, 1990), in which the thiamines are in free-base form. The molecular dimensions of the thiamine are in good agreement with those of thiamine containing a protonated pyrimidine ring (Shin & Lah, 1987; Aoki *et al.*, 1988). Compared with the free-base form, the protonation of N(1′) in this structure causes the C(6′)—N(1′)—C(2′) bond angle and the N(1′)—C(2′) bond length to increase and the C(2′)—N(3′) and C(4′)—N(41′) bond lengths to decrease.

Two types of anion bridges between the two aromatic rings of the same thiamine have been suggested to be factors affecting the *F* conformation of thiamine and provide a model for thiamine–substrate interactions (Aoki, Yamazaki & Adeyemo, 1991). In the present structure the thiocyanate anion, S(12)—C(12)—N(12), bridges the two aromatic rings through an N(41′)—H···N(12) hydrogen bond and an SCN$^-$···thiazolium-ring electrostatic interaction (Fig. 1) [closest contact N(12)···N(3) = 3.066 (6) Å]. An O(53) atom from a neighbouring thiamine ($\frac{1}{2}+x$, $\frac{1}{2}-y$, $-z$) seems to act as another bridge. The O(53) atom is involved in a stacking interaction with the pyrimidine ring by locating over the ring plane [closest contact O(53)···N(1′) = 3.079 (6) Å and perpendicular distance O(53)···pyrimidine ring = 2.955 (3) Å] and an O···H—C interaction with the acidic H atom at C(2) [O(53)···C(2) = 3.676 (6), O(53)···H(C2) = 2.66 Å; sum of van der Waals radii

---

† 4-Amino-5-[(5-hydroxyethyl-4-methylthiazol-3-ylio)methyl]-2-methyl-1-pyrimidinium dithiocyanate.

0108-2701/93/061178-03$06.00

for O···H = 2.72 Å (Bondi, 1964); O(53)···H—C(2) = 158°]. The thiamine molecule in the *F* conformation as a host holds a guest hydroxyl group near to the C(2) site in a pincer-like encirclement through electrostatic interactions. This is the first observation in thiamine structures of this type of thiamine interaction with a hydroxyl group.

The crystal packing is in an interesting mode. As is shown in Fig. 2, a thiamine cation is connected with an N(11)—C(11)—S(11) anion by an N(1′)—H···N(11) hydrogen bond, and this anion further with another thiamine by an S(11)···H—O(53) hydrogen bond (Table 2) to form a helical molecular chain along the **a** direction. The distance at which the helical chain takes one turn, the pitch length, is three times the length of the *a* axis. By translation symmetry, there are three such chains twisted around each other, thus creating a triple helical structure. The electrostatic interactions between the SCN$^-$ anion and adjacent thiazolium rings, and between the O(53) atom and the pyrimidine ring, as mentioned above, hold the triple helix together. Moreover, one triple helix is linked to the other in the **b** direction by hydrogen bonds involving S(12)—C(12)—N(12) anions and the amino groups of thiamines (Table 2), but in the **c** direction only by van der Waals contacts. This explains the cleavability of the crystal perpendicular to the **c** direction.

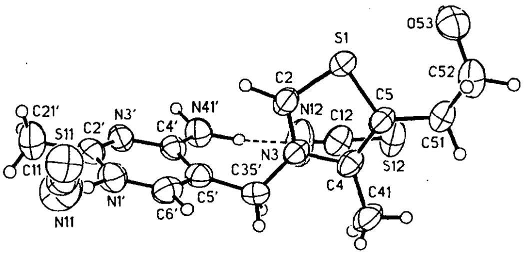


Fig. 1. Molecular structure of thiamine dithiocyanate. Dashed lines represent hydrogen bonds.

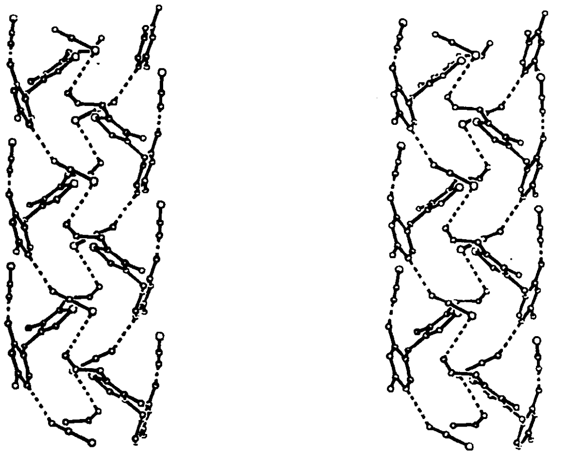


Fig. 2. A stereoscopic view of the triple helical structure viewed down the *c* axis. Dashed lines represent hydrogen bonds.

Experimental

Crystal data

$C_{12}H_{18}N_4OS^{2+}.2SCN^-$
M_r = 382.52
Orthorhombic
Pbca
a = 8.029 (1) Å
b = 23.091 (5) Å
c = 20.110 (5) Å
V = 3728 (1) Å^3
Z = 8
D_x = 1.363 Mg m^{-3}
D_m = 1.361 Mg m^{-3}
Density measured by flotation in cyclohexane and chloroform

Mo *Kα* radiation
λ = 0.71069 Å
Cell parameters from 22 reflections
θ = 3.8–9.7°
μ = 0.40 mm^{-1}
T = 295 K
Tabular
0.58 × 0.42 × 0.20 mm
Colourless
Crystal source: from aqueous solution of thiamine.Cl.HCl and KSCN

Data collection

Nicolet *R3m/E* diffractometer
ω scans
Absorption correction: empirical
T_{min} = 0.89, T_{max} = 0.95
2992 measured reflections
2925 independent reflections
1963 observed reflections
[$F_o > 3\sigma(F_o)$]

R_{int} = 0.007
θ_{max} = 24°
$h = 0 \rightarrow 9$
$k = 0 \rightarrow 26$
$l = 0 \rightarrow 22$
2 standard reflections monitored every 98 reflections
intensity variation: < 2.5%

Refinement

Refinement on F
Final R = 0.052
wR = 0.047
S = 1.91
1963 reflections
217 parameters
Unit weights applied

$(\Delta/\sigma)_{max}$ = 0.01
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.31 e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic thermal parameters* (Å^2)

U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
N(1′)	0.7985 (4)	0.0979 (2)	0.1052 (2)	0.054 (1)
C(2′)	0.7009 (6)	0.0729 (2)	0.1520 (2)	0.052 (2)
N(3′)	0.5504 (4)	0.0552 (2)	0.1390 (2)	0.050 (1)
C(4′)	0.4886 (5)	0.0630 (2)	0.0767 (2)	0.044 (1)
C(5′)	0.5880 (6)	0.0875 (2)	0.0253 (2)	0.046 (2)
C(6′)	0.7437 (6)	0.1042 (2)	0.0423 (2)	0.053 (2)
C(21′)	0.7732 (7)	0.0660 (2)	0.2195 (3)	0.073 (2)
N(41′)	0.3335 (4)	0.0455 (2)	0.0667 (2)	0.055 (1)
C(35′)	0.5338 (6)	0.0898 (2)	−0.0458 (2)	0.053 (2)
S(1)	0.2359 (2)	0.2247 (1)	−0.0546 (1)	0.059 (1)
C(2)	0.3664 (6)	0.1770 (2)	−0.0195 (2)	0.050 (2)
N(3)	0.4194 (4)	0.1379 (1)	−0.0622 (2)	0.044 (1)
C(4)	0.3585 (6)	0.1451 (2)	−0.1263 (2)	0.045 (1)
C(5)	0.2559 (6)	0.1910 (2)	−0.1311 (2)	0.047 (1)

C(41)	0.4084 (7)	0.1043 (2)	−0.1802 (2)	0.064 (2)
C(51)	0.1639 (7)	0.2116 (2)	−0.1918 (2)	0.060 (2)
C(52)	0.1524 (7)	0.2768 (2)	−0.1977 (2)	0.069 (2)
O(53)	0.0652 (4)	0.3017 (1)	−0.1433 (2)	0.069 (1)
S(11)	1.2310 (2)	0.2715 (1)	0.1148 (1)	0.073 (1)
C(11)	1.1388 (6)	0.2079 (2)	0.1220 (2)	0.066 (2)
N(11)	1.0801 (6)	0.1638 (2)	0.1270 (2)	0.092 (2)
S(12)	−0.0936 (2)	0.0538 (1)	−0.1516 (1)	0.082 (1)
C(12)	0.0439 (6)	0.0505 (2)	−0.0918 (2)	0.059 (2)
N(12)	0.1406 (6)	0.0477 (2)	−0.0512 (2)	0.101 (2)

Table 2. *Bond lengths* (Å), *bond angles* (°) *and hydrogen-bond geometry* (Å, °)

N(1′)—C(2′)	1.354 (6)	N(3)—C(4)	1.388 (5)
C(2′)—N(3′)	1.303 (6)	C(4)—C(5)	1.345 (6)
N(3′)—C(4′)	1.361 (5)	C(5)—S(1)	1.731 (4)
C(4′)—C(5′)	1.423 (6)	C(4)—C(41)	1.493 (6)
C(5′)—C(6′)	1.351 (7)	C(5)—C(51)	1.505 (6)
C(6′)—N(1′)	1.347 (6)	C(51)—C(52)	1.513 (7)
C(2′)—C(21′)	1.485 (7)	C(52)—O(53)	1.420 (6)
C(4′)—N(41′)	1.325 (6)	S(11)—C(11)	1.651 (6)
C(5′)—C(35′)	1.496 (6)	C(11)—N(11)	1.128 (7)
C(35′)—N(3)	1.479 (6)	S(12)—C(12)	1.635 (5)
S(1)—C(2)	1.675 (5)	C(12)—N(12)	1.127 (7)
C(2)—N(3)	1.316 (5)		
N(1′)—C(2′)—N(3′)	122.1 (4)	C(35′)—N(3)—C(4)	121.0 (3)
C(2′)—N(3′)—C(4′)	118.7 (4)	S(1)—C(2)—N(3)	112.2 (3)
N(3′)—C(4′)—C(5′)	121.2 (4)	C(2)—N(3)—C(4)	114.1 (3)
C(4′)—C(5′)—C(6′)	116.6 (4)	N(3)—C(4)—C(5)	112.1 (3)
C(5′)—C(6′)—N(1′)	120.6 (4)	C(4)—C(5)—S(1)	110.3 (3)
C(6′)—N(1′)—C(2′)	120.7 (4)	C(5)—S(1)—C(2)	91.2 (2)
N(1′)—C(2′)—C(21′)	117.2 (4)	N(3)—C(4)—C(41)	120.3 (4)
N(3′)—C(2′)—C(21′)	120.7 (4)	C(5)—C(4)—C(41)	127.5 (4)
N(3′)—C(4′)—N(41′)	116.2 (4)	S(1)—C(5)—C(51)	122.2 (3)
C(5′)—C(4′)—N(41′)	122.6 (4)	C(4)—C(5)—C(51)	127.5 (4)
C(4′)—C(5′)—C(35′)	123.0 (4)	C(5)—C(51)—C(52)	114.1 (4)
C(6′)—C(5′)—C(35′)	120.0 (4)	C(51)—C(52)—O(53)	111.8 (4)
C(5′)—C(35′)—N(3)	114.8 (3)	S(11)—C(11)—N(11)	178.1 (5)
C(35′)—N(3)—C(2)	124.8 (3)	S(12)—C(12)—N(12)	178.7 (5)

D—H···*A*	*D*···*A*	H···*A*	*D*—H···*A*
N(1′)—H···N(11)	2.760 (6)	1.72	162
O(53)—H···S(11$^{\rm i}$)	3.223 (4)	2.23	166
N(41′)—H1···N(12)	2.834 (6)	1.76	165
N(41′)—H2···S(12$^{\rm ii}$)	3.447 (4)	2.62	134

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

The structure was solved by direct methods and refined by block-diagonal least squares on *F* with anisotropic thermal parameters for non-H atoms. All H atoms were located on a difference map and fixed with isotropic thermal parameters ($U = 0.06$ Å^2) in the final cycles of the refinement. All calculations were performed using the *SHELXTL* program system (Sheldrick, 1983).

Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and intermolecular contacts have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55896 (24 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: OH1007]

References

Aoki, K., Hu, N.-H., Yamazaki, H. & Adeyemo, A. (1990). *Acta Cryst.* C**46**, 1483–1487.

Aoki, K., Yamazaki, H. & Adeyemo, A. (1991). *Inorg. Chim. Acta*, **180**, 117–124.

Aoki, K., Yamazaki, H., Waragai, K. & Itokawa, H. (1988). *Acta Cryst.* C**44**, 1949–1955.

Bondi, A. (1964). *J. Phys. Chem.* **68**, 441–451.

Breslow, R. (1958). *J. Am. Chem. Soc.* **80**, 3719–3726.

Pletcher, J., Sax, M., Blank, G. & Wood, M. (1977). *J. Am. Chem. Soc.* **99**, 1396–1403.

Sheldrick, G. M. (1983). *SHELXTL Users Manual.* Revision 4. Nicolet XRD Corporation, Madison, Wisconsin, USA.

Shin, W. & Lah, M. S. (1987). *Acta Cryst.* C**43**, 125–129.

Acta Cryst. (1993). C**49**, 1180–1182

Non-Steroidal Anti-inflammatory Drugs. II. Structure of (*E*)-2,6-Di-*tert*-butyl-4-[2-(4-fluorophenyl)ethenyl]phenol

K. Ravikumar

Laboratory of Crystallography, Indian Institute of Chemical Technology, Hyderabad - 500 007, India

(*Received* 9 *September* 1992; *accepted* 10 *December* 1992)

Abstract

The central ethylenic double bond, C(7)=C(8) [1.296 (9) Å], is shorter than a normal C=C double bond. The two substituted phenyl rings are twisted by 15.5 (9) and 17.6 (9)°, respectively, out of the plane of the double bond. The dihedral angle between the mean planes of the two phenyl rings is 33.1 (1)°.

Comment

2,6-Di-*tert*-butylphenol derivatives appear to be a new class of non-steroidal anti-inflammatory drugs with antioxidant properties (Ikuta, Shirota, Kobayashi, Yamagishi, Yamada, Yamatsu & Katayama, 1987). The title compound has anti-inflammatory activity and is one of a series of related compounds prepared by Lazer, Wong, Possanza, Graham & Farina (1989). Their biological activity and molecular structure are being studied.

The bond length C(1)—F [1.367 (6) Å] is in good agreement with those in other fluorine-substituted phenyl rings (Taga, Yamamoto & Osaki, 1985; Kemmish & Hamor, 1990). However, the bond angle C(2)—C(1)—C(6) [122.3 (4)°] is significantly greater than 120°. This can be attributed to the strong σ-electron withdrawing properties of F, in agreement with the observation of Domenicano & Murray-Rust (1979). This enlargement of the angle is accompanied by shortening of the C—C bonds C(1)—C(2) [1.353 (8) Å] and C(1)—C(6) [1.361 (9) Å], compared to the central C—C bonds C(2)—C(3) [1.375 (7) Å] and C(6)—C(5) [1.398 (7) Å] of this ring (Colapietro,

0108-2701/93/061180-03$06.00