

Table 3. Bond lengths (Å) and bond angles (°) of non-hydrogen atoms with *e.s.d.*'s in parentheses

C(1)–C(2)	1.508 (6)	C(1)–N(1)	1.530 (5)
C(1)–C(3)	1.498 (6)	N(1)–N(2)	1.446 (4)
C(1)–C(4)	1.521 (6)		
C(3)–C(1)–C(2)	112.5 (4)	N(1)–C(1)–C(3)	108.5 (4)
C(4)–C(1)–C(2)	112.0 (4)	N(1)–C(1)–C(4)	104.2 (3)
C(4)–C(1)–C(3)	111.4 (4)	N(2)–N(1)–C(1)	119.2 (3)
N(1)–C(1)–C(2)	107.8 (3)		

contribute significant stabilizing force in holding the molecule in a stable crystalline state.

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Structure of Thiamine Picrate

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Abstract. $C_{12}H_{17}N_4OS^+ \cdot C_6H_2N_3O_7^-$, $M_r = 493.455$, triclinic, $P\bar{1}$, $a = 10.464$ (1), $b = 12.951$ (1), $c = 8.6615$ (8) Å, $\alpha = 107.368$ (8), $\beta = 104.627$ (8), $\gamma = 70.544$ (9)°, $V = 1040.9$ (2) Å³, $Z = 2$, $D_x = 1.574$ g cm⁻³, $\lambda(\text{Mo } K\alpha) = 0.71073$ Å, $\mu = 2.09$ cm⁻¹, $F(000) = 512$, $T = 293$ K, $R = 0.047$ for 2595 observed reflections. The thiamine molecule adopts the *S* conformation. There are three kinds of ring-stacking interactions: pyrimidine–phenyl, thiazolium–thiazolium and phenyl–phenyl.

Introduction. Thiamine (vitamin B₁), as its pyrophosphate ester, is a cofactor for a number of metabolic enzymes catalyzing the decarboxylation of α -keto acids and the transfer of aldehyde or acyl groups (Krampitz, 1969). Structural investigations of molecular interactions between thiamine and an anion molecule containing both a carboxyl (or its analogue) group(s) and a ring moiety(ies) are of interest to examine the ring–ring stacking and/or thiamine–carboxyl interaction modes; a carboxyl group functions as a model for the carboxyl group of a substrate that should be

fixed close by the C(2) catalytic site and a ring moiety is a model for the indole π system of the tryptophan residue of the apoenzyme at the active center (Heinrich, Moack & Wiss, 1971; Kochetov & Usmanov, 1970; Kochetov, Usmanov & Mevkh, 1973). We report here the crystal structure of the thiamine picrate, where the picrate anion bears carboxyl-like nitro groups and a phenyl ring; there is a partial overlap between the phenyl ring of picric acid and the neutral pyrimidine moiety of the thiamine molecule which adopts the *S* conformation but no interaction between the nitro group and the thiazolium moiety.

Experimental. The complex was prepared by mixing thiamine nitrate (32.7 mg, 0.1 mmol) dissolved in 10 mL of water and sodium picrate (26.9 mg, 0.1 mmol) in 10 mL water and allowing the solution to stand at room temperature. Yellow rod-like crystals formed after a few months. Crystal 0.51 × 0.42 × 0.40 mm, Rigaku diffractometer, graphite-monochromated Mo $K\alpha$ radiation; cell parameters by a least-squares fitting of diffractometer setting angles for 19 reflections ($20 < 2\theta < 30^\circ$); reflection data $2\theta_{\max} = 55^\circ$ ($h = -12$ to 12, $k = 0$ to 16, $l = -10$ to 10),

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Table 1. Fractional atomic coordinates ($\times 10^4$) and equivalent isotropic temperature factors with e.s.d.'s in parentheses

$$B_{eq} = \frac{1}{3} \sum_i \sum_j \beta_{ij} a_i a_j$$

	x	y	z	$B_{eq}(\text{\AA}^2)$
S(1)	-254 (1)	1053 (1)	3296 (1)	2.52 (4)
C(2)	1176 (3)	140 (3)	4020 (4)	2.1 (1)
N(3)	1286 (3)	-908 (2)	3164 (3)	1.9 (1)
C(4)	201 (3)	-1029 (3)	1859 (4)	2.0 (1)
C(4 α)	182 (4)	-2158 (3)	782 (5)	3.4 (1)
C(5)	-740 (3)	-29 (3)	1777 (4)	2.2 (1)
C(5 α)	-2121 (4)	190 (3)	678 (4)	2.7 (1)
C(5 β)	-3303 (4)	513 (3)	1625 (5)	2.8 (1)
O(5 γ)	-3060 (3)	-230 (2)	2632 (3)	3.8 (1)
C(3,5')	2476 (3)	-1855 (3)	3604 (4)	2.2 (1)
N(1')	5210 (3)	-1633 (2)	1737 (4)	2.6 (1)
C(2')	5562 (3)	-2681 (3)	799 (4)	2.4 (1)
C(2' α)	6636 (4)	-2935 (4)	-216 (6)	4.3 (2)
N(3')	5045 (3)	-3508 (2)	697 (4)	2.5 (1)
C(4')	4047 (3)	-3288 (3)	1577 (4)	2.2 (1)
N(4' α)	3587 (3)	-4166 (2)	1454 (4)	3.6 (1)
C(5')	3559 (3)	-2193 (3)	2549 (4)	2.0 (1)
C(6')	4215 (3)	-1423 (3)	2593 (4)	2.3 (1)
O(1P)	1113 (3)	2478 (2)	5815 (3)	3.6 (1)
O(2P)	-1119 (3)	4063 (3)	6923 (4)	4.7 (1)
O(3P)	-693 (5)	5531 (4)	8514 (7)	11.9 (3)
O(4P)	3929 (4)	6070 (3)	6021 (5)	6.9 (2)
O(5P)	2562 (3)	7023 (2)	7771 (4)	4.6 (1)
O(6P)	4403 (3)	2027 (3)	3979 (4)	5.8 (1)
O(7P)	2431 (4)	1722 (3)	3127 (5)	7.3 (2)
N(1P)	-385 (3)	4687 (3)	7473 (4)	3.8 (1)
N(2P)	3042 (3)	6159 (3)	6776 (5)	3.8 (1)
N(3P)	3190 (4)	2265 (3)	4050 (4)	3.5 (1)
C(1P)	1458 (4)	3318 (3)	5912 (4)	2.3 (1)
C(2P)	860 (3)	4449 (3)	6831 (4)	2.3 (1)
C(3P)	1398 (4)	5331 (3)	7132 (4)	2.7 (1)
C(4P)	2526 (4)	5196 (3)	6481 (4)	2.6 (1)
C(5P)	3110 (4)	4181 (3)	5472 (5)	2.7 (1)
C(6P)	2584 (4)	3303 (3)	5182 (4)	2.4 (1)

ω - 2θ scan, scan speed 2° min^{-1} in 2θ , ω -scan width $(1.2 + 0.5 \tan \theta)^\circ$, background measured for 5 s on either side of the peak; intensity checks for three standard reflections showed little ($-1.7 \rightarrow +0.8\%$) variation, 3720 independent reflections, 2595 (69.8%) observed with $F_o > 3\sigma(F_o)$ and used in refinement; Lp corrections, no absorption or extinction correction. Structure solved with *MULTAN78* (Main, Hull, Lesinger, Germain, Declercq & Woolfson, 1978) and refined with block-diagonal least squares on F with anisotropic thermal parameters, H atoms located on a difference Fourier map and refined isotropically. $\sum w(F_o - |F_c|)^2$ minimized, $R = 0.047$, $wR = 0.046$, $S = 0.90$ where $w = 1$ for all data, $(\Delta/\sigma)_{\text{max}} = 0.347$ [H2(C2' α)], max. and min. heights in final difference map 0.39 and -0.35 e \AA^{-3} , respectively. Final atomic coordinates with their e.s.d.'s are listed in Table 1.* Atomic scattering factors from *International Tables for X-ray Crystallography* (1974). All calculations performed with *UNICSIII* program (Sakurai & Kobayashi, 1979) on a FACOM 380 computer.

* Lists of structure factors, anisotropic thermal parameters, refined H-atom positions, bond distances and angles involving the H atoms, least-squares planes, and close contacts have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44625 (19 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Discussion. Figs. 1 and 2 show the molecular structure with the numbering scheme of the thiamine picrate and the crystal packing, respectively. Bond distances and angles and hydrogen bonds are listed in Table 2.

The molecular dimensions of the thiamine cation are in good agreement with those of thiamine, which contains a neutral pyrimidine ring (Cramer, Maynard & Ibers, 1981). The thiamine molecule takes the *S* conformation with torsion angles of $\varphi_T = \text{C}(2)-\text{N}(3)-\text{C}(3,5')-\text{C}(5') = -99.3 (4)$ and $\varphi_P = \text{N}(3)-\text{C}(3,5')-\text{C}(5')-\text{C}(4') = -122.9 (4)^\circ$. The pyrimidine and the thiazolium ring planes make a dihedral angle of $74.0 (1)^\circ$. The C(5) hydroxyethyl side chain is folded back towards the thiazolium moiety from the opposite

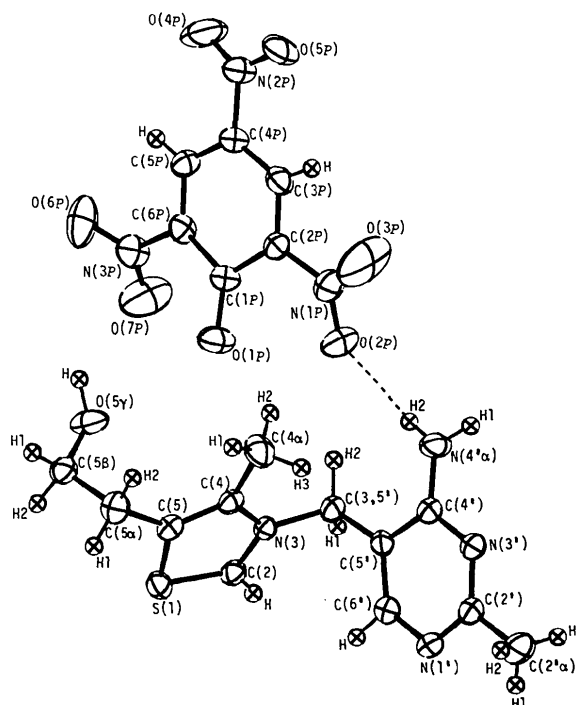


Fig. 1. Molecular structure with the numbering scheme. Thermal ellipsoids are drawn at a 50% probability level for non-H atoms. A broken line denotes a hydrogen bond.

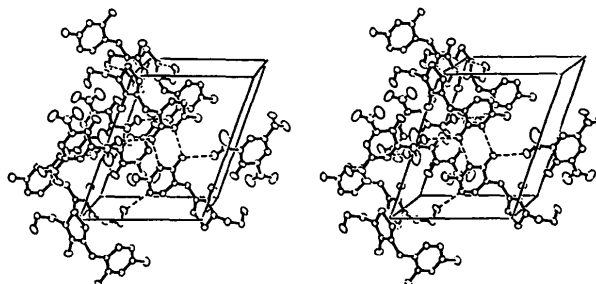


Fig. 2. Stereoview of the crystal packing viewed down the c axis, with the a axis horizontal, and the b axis vertical. Broken lines denote hydrogen bonds.

Table 2. *Interatomic distances (Å) and angles (°) with e.s.d.'s in parentheses*

Thiamine molecule			
S(1)–C(2)	1.680 (3)	C(3,5')–C(5')	1.505 (5)
S(1)–C(5)	1.729 (3)	N(1')–C(2')	1.341 (4)
C(2)–N(3)	1.320 (4)	C(2')–N(3')	1.324 (6)
N(3)–C(4)	1.399 (4)	N(3')–C(4')	1.351 (5)
C(4)–C(5)	1.350 (4)	C(4')–C(5')	1.415 (4)
C(4)–C(4a)	1.485 (5)	C(5')–C(6')	1.374 (6)
C(5)–C(5a)	1.506 (4)	C(6')–N(1')	1.338 (5)
C(5a)–C(5β)	1.530 (6)	C(2')–C(2'a)	1.492 (7)
C(5β)–O(5γ)	1.405 (6)	C(4')–N(4'a)	1.343 (6)
N(3)–C(3,5')	1.491 (4)		
C(2)–S(1)–C(5)	91.0 (2)	N(3)–C(3,5')–C(5')	112.2 (3)
S(1)–C(2)–N(3)	112.4 (2)	C(3,5')–C(5')–C(4')	125.0 (4)
C(2)–N(3)–C(4)	114.2 (2)	C(3,5')–C(5')–C(6')	119.2 (3)
N(3)–C(4)–C(5)	111.4 (3)	N(1')–C(2')–N(3')	125.9 (4)
C(4)–C(5)–S(1)	111.0 (2)	C(2')–N(3')–C(4')	118.2 (3)
N(3)–C(4)–C(4a)	120.4 (3)	N(3')–C(4')–C(5')	120.3 (4)
C(5)–C(4)–C(4a)	128.2 (3)	C(4')–C(5')–C(6')	115.7 (3)
S(1)–C(5)–C(5a)	120.6 (2)	C(5')–C(6')–N(1')	124.5 (3)
C(4)–C(5)–C(5a)	128.1 (3)	C(6')–N(1')–C(2')	115.3 (4)
C(5)–C(5a)–C(5β)	119.9 (3)	N(1')–C(2')–C(2'a)	116.8 (4)
C(5a)–C(5β)–O(5γ)	111.2 (3)	N(3')–C(2')–C(2'a)	117.3 (3)
C(2)–N(3)–C(3,5')	121.2 (2)	N(3')–C(4')–N(4'a)	115.4 (3)
C(4)–N(3)–C(3,5')	124.6 (2)	C(5')–C(4')–N(4'a)	124.3 (4)
Picrate molecule			
C(1P)–C(2P)	1.455 (4)	N(1P)–O(2P)	1.212 (5)
C(2P)–C(3P)	1.365 (6)	N(1P)–O(3P)	1.198 (6)
C(3P)–C(4P)	1.372 (6)	C(4P)–N(2P)	1.450 (6)
C(4P)–C(5P)	1.384 (4)	N(2P)–O(4P)	1.221 (7)
C(5P)–C(6P)	1.355 (6)	N(2P)–O(5P)	1.231 (4)
C(6P)–C(1P)	1.463 (6)	C(6P)–N(3P)	1.459 (4)
C(1P)–O(1P)	1.229 (5)	N(3P)–O(6P)	1.216 (5)
C(2P)–N(1P)	1.448 (6)	N(3P)–O(7P)	1.216 (5)
C(1P)–C(2P)–C(3P)	123.9 (4)	C(3P)–C(4P)–N(2P)	118.9 (3)
C(2P)–C(3P)–C(4P)	120.2 (3)	C(5P)–C(4P)–N(2P)	120.2 (4)
C(3P)–C(4P)–C(5P)	120.8 (4)	C(4P)–N(2P)–O(4P)	118.2 (3)
C(4P)–C(5P)–C(6P)	119.0 (4)	C(4P)–N(2P)–O(5P)	118.3 (4)
C(5P)–C(6P)–C(1P)	125.1 (3)	C(1P)–C(6P)–N(3P)	117.8 (3)
C(6P)–C(1P)–C(2P)	110.5 (3)	C(5P)–C(6P)–N(3P)	117.1 (4)
C(2P)–C(1P)–O(1P)	125.2 (4)	C(6P)–N(3P)–O(6P)	118.8 (3)
C(6P)–C(1P)–O(1P)	124.3 (3)	C(6P)–N(3P)–O(7P)	118.2 (4)
C(1P)–C(2P)–N(1P)	119.7 (4)	O(2P)–N(1P)–O(3P)	121.1 (5)
C(3P)–C(2P)–N(1P)	116.5 (3)	O(4P)–N(2P)–O(5P)	123.6 (4)
C(2P)–N(1P)–O(2P)	120.4 (3)	O(6P)–N(3P)–O(7P)	122.7 (3)
C(2P)–N(1P)–O(3P)	118.5 (4)		
Hydrogen bonds			
N(4'a)···N(3'')	3.118 (4)	O(5γ)···N(1''')	2.797 (5)
N(4'a)···O(2P'')	3.186 (6)	C(2)···O(5γ'')	3.061 (4)

Symmetry code: (none) x, y, z ; (i) $1-x, -1-y, -z$; (ii) $-x, -y, 1-z$; (iii) $-1+x, y, z$.

side to the pyrimidine ring with torsion angles of $\varphi_{5\alpha} = S(1)–C(5)–C(5\alpha)–C(5\beta) = -66.9 (4)$ and $\varphi_{5\beta} = C(5)–C(5\alpha)–C(5\beta)–O(5\gamma) = -47.5 (4)^\circ$.

There are three types of interactions between the thiamine cation and the picrate molecules: a hydrogen bond between the thiamine amino N(4'a) and the picric acid nitro O(2P), electrostatic interactions between the positively charged thiazolium S(1) and two oxygens of the two different picrate molecules which are stacked on each other (see below), one being the carbonyl O(1P) and the other the nitro O(5P), and pyrimidine–phenyl ring–ring stacking. The average spacing and the tilt angle between the pyrimidine and the phenyl planes are 3.61 Å and 5.2 (1)°, respectively, with the closest contact of 3.515 (5) Å between C(4') and C(5P).

Thiamine molecules dimerize by themselves in two different ways, one through a pair of N(4'a)···N(3')

interbase hydrogen bonds and the other through a pair of CH···O hydrogen bonds between the thiazolium C(2) and the hydroxyethyl O(5γ), each pair being related by a center of symmetry. A pair of C(2)–H···O(5γ) hydrogen bonds form a large molecular cage composed of (–thiazolium ring–hydroxyethyl side chain–)₂, where partial ring stacking occurs between the two thiazolium rings with an average spacing of 3.42 Å. There is no pyrimidine–pyrimidine ring stacking.

Partial ring stacking also occurs in a pair of the rings of picric acid related by a center of symmetry with average spacing 3.63 Å, thus forming the stacking sequence of pyrimidine–phenyl–phenyl–pyrimidine.

It appears that the thiamine conformation does not affect the pyrimidine–aromatic ring stacking or *vice versa*; the picrolonate salt (Shin, Pletcher, Blank & Sax, 1977) and thiamine indole-3-propionate (Ishida, Matsui, Inoue, Hirano, Yamashita, Sugiyama, Sugiura & Tomita, 1985), where each thiamine assumes the *F* conformation, also involve pyrimidine–aromatic ring stacking interactions. On the contrary, the thiamine conformation seems to affect thiamine interactions with the carboxyl-like functional group or *vice versa*; a nitro group of picrolonate (Shin *et al.*, 1977) or a sulfonyl group of naphthalene 1,5-disulfonate (Shin & Lah, 1987) is located near to the thiazolium ring to form a C(2)H···O hydrogen bond and is further capped probably by the electrostatic interactions with the pyrimidine ring adopting the *F* conformation, whereas the present picrate salt in which the thiamine molecule adopts the *S* conformation does not exhibit such a nitro–thiazolium interaction.

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