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Structure of Thiamine Nitrate, $C_{12}H_{17}N_4OS^+.NO_3^-$

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Abstract. $M_r = 327{\cdot}36$, monoclinic, $P2_1/c$, $a = 6{\cdot}554$ (1), $b = 12{\cdot}275$ (2), $c = 18{\cdot}544$ (2) Å, $\beta = 97{\cdot}61$ (1)°, $V = 1478{\cdot}7$ (3) Å^3, $Z = 4$, $D_m = 1{\cdot}462$ (1), $D_x = 1{\cdot}470$ Mg m^{-3}, Cu $K\alpha$, $\lambda = 1{\cdot}5418$ Å, $\mu = 21{\cdot}51$ mm^{-1}, $F(000) = 688$, $T = 293$ K, final $R = 0{\cdot}056$ for 2515 independent reflections. The molecule has a neutral pyrimidine ring and maintains the characteristic *F* conformation frequently observed in other thiamine compounds with a neutral or cationic pyrimidine ring. This indicates the inherent stability of this *F* form for thiamine free of substituents on the thiazolium C(2) atom.

Introduction. Thiamine pyrophosphate is a coenzyme for a number of different enzyme systems which catalyse the transfer of aldehyde or acyl groups and the decarboxylation of α-keto acids (Krampitz, 1969). Since a detailed structural study can be useful in obtaining a more complete understanding of the chemical properties of thiamine compounds, we have undertaken X-ray structural studies on a series of related compounds (Inoue, Hirano, Sugiyama, Ishida & Nakagaki, 1982; Ishida, Matsui, Inoue, Hirano, Yamashita & Sugiyama, 1983). As part of this program we here report the crystal structure of thiamine nitrate.

Experimental. Crystallized from aqueous solution (0·2 mol dm^{-3}) as platelets, 0·4 × 0·4 × 0·3 mm; Rigaku automated four-circle diffractometer, graphite-monochromated Cu $K\alpha$ radiation; lattice parameters determined by least-squares fit to 2θ and -2θ values of 20 independent reflections ($50° < |2\theta| < 60°$); D_m by flotation in CCl_4/C_6H_6 mixture; intensity data up to $2\theta = 130°$ collected, ω–2θ scan, scan speed 4° (2θ) min^{-1}, scan width (2θ) (1·1 + 0·15 tanθ)°, background 5 s (both sides of each peak) at 40 kV and 150 mA; h 0–7, k 0–14, l −21–21; 2515 [2366 with $I > 3\sigma(I)$] independent reflections measured; four reference reflections monitored at 100 reflection intervals showed no crystal deterioration; Lorentz and polarization corrections applied, absorption ignored; structure solved by direct methods with *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), refined by least squares with anisotropic thermal parameters for all non-H atoms; H atoms located from difference Fourier map, included in refinement with isotropic thermal parameters; final $R = 0{\cdot}056$, $R_w = 0{\cdot}062$; $\sum w(|F_o| - |F_c|)^2$ minimized, $w = 0{\cdot}612$ for $F_o = 0{\cdot}0$, $w = 1{\cdot}0$ for $0{\cdot}0 < F_o \leq 13{\cdot}0$, $w = 1{\cdot}0/[1{\cdot}0 + 0{\cdot}196(F_o - 13{\cdot}0)]$ for $F_o > 13{\cdot}0$; final difference map devoid of significant features (−0·3–0·2 e Å^{-3}), all shifts in the parameters $< \frac{1}{3}\sigma$ in final cycle; atomic scattering factors and anomalous-dispersion corrections from *International Tables for X-ray Crystallography* (1974); all numerical calculations made on an ACOS-900 computer at the Computation Center of Osaka University using the *Universal Crystallographic Computing System* (1979).*

Discussion. Final atomic parameters of non-H atoms are listed in Table 1, bond distances and angles in Table 2. Fig. 1 shows a perspective view of the molecule with the atomic numbering scheme. The molecular dimensions of the thiamine molecule, for which the pyrimidine N(1′) atom is deprotonated, are comparable to those observed in thiamine chloride monohydrate (Pletcher, Sax, Sengupta, Chu & Yoo, 1972) and thiamine picrolonate dihydrate (Shin, Pletcher, Blank & Sax, 1977), both of which also exist as the unprotonated base. The bond lengths involving H atoms range from 0·81 (5) [O(5γ)–H(5γ)] to 1·17 (4) Å [C(5β)–H(5β*b*)], and the angles involving H atoms appear to be normal [97 (3)–127 (2)°]. Both of the aromatic rings in this molecule are virtually planar with small deviations from strict planarity: the shift from the plane ranges from −0·01 (0) [C(5′)] to 0·008 (4) Å [C(4′)] for the pyrimidine ring and from −0·006 (4) [C(4)] to 0·009 (5) Å [C(5)] for the thiazolium ring. The dihedral angle between these two planes is 84·6 (2)°. The conformation of the thiamine molecule could be satisfactorily classified in terms of the two torsion angles about the bonds from the methylene carbon C(35′) to the respective rings: φ_T

* Lists of structure factors, anisotropic thermal parameters for non-H atoms, and coordinates and isotropic thermal parameters for H atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39006 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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[C(5′)–C(35′)–N(3)–C(2)] and φ_P [N(3)–C(35′)–C(5′)–C(4′)] (Pletcher & Sax, 1972). Basically, three kinds of conformers have been observed in the thiamine molecule (Shin, Pletcher, Blank & Sax, 1977): $F(\varphi_T \simeq 0°,\ \varphi_P \simeq \pm 90°)$, $S(\varphi_T \simeq \pm 100°,\ \varphi_P \simeq \pm 150°)$ and $V(\varphi_T \simeq \pm 90°,\ \varphi_P \simeq \mp 90°)$ forms. Among them, the F conformation has been most frequently found in thiamine derivatives when the thiazolium C(2) atom is free of substituents. The present conformation [$\varphi_T = 5{\cdot}9\ (5)°$, $\varphi_P = 83{\cdot}1\ (4)°$] also belongs to this form, providing additional support for the observation that the F conformation is the predominant form of the free thiamine molecule. The conformation of the 5-(β-hydroxyethyl) side chain is describable by the two torsion angles $\varphi_{5\alpha}$ [S(1)–C(5)–C(5α)–C(5β)] and $\varphi_{5\beta}$ [C(5)–C(5α)–C(5β)–O(5γ)]. Although the $\varphi_{5\alpha}$ value, −92·8 (4)°, in this molecule belongs to the range commonly observed in a majority of thiamine derivatives (±60 to ±90°) (Shin, Pletcher, Blank & Sax, 1977), the value for $\varphi_{5\beta}$, 175·7 (3)°, is quite different from the most frequently observed range (within 10° from ±60°) (Shin, Pletcher, Blank & Sax, 1977). In the conformational comparison with thiamine chloride monohydrate ($\varphi_T = 2{\cdot}6$, $\varphi_P = 76{\cdot}8$, $\varphi_{5\alpha} = 66{\cdot}8$ and $\varphi_{5\beta} = -64{\cdot}6°$), for example, the essential difference exists in the $\varphi_{5\beta}$. This disposition appears to be due to the packing specificity required for the O(5γ)-participating hydrogen bond (described below).

Table 1. *Atomic coordinates for non-H atoms* (×10⁴) *with e.s.d.'s in parentheses*

	x	y	z	B_{eq}(Å²)*
Thiamine				
S(1)	2263 (1)	814 (1)	8423 (1)	3·1
C(2)	2106 (5)	1334 (3)	7579 (2)	2·7
N(3)	635 (4)	2050 (2)	7448 (1)	2·3
C(4)	−473 (5)	2234 (3)	8029 (2)	2·5
C(4α)	−2174 (6)	3043 (3)	7960 (2)	3·9
C(5)	247 (5)	1624 (3)	8612 (2)	2·9
C(5α)	−392 (6)	1628 (3)	9364 (2)	3·2
C(5β)	−2096 (6)	824 (4)	9462 (2)	3·8
O(5γ)	−2457 (4)	844 (3)	10206 (2)	4·6
C(35′)	201 (6)	2664 (3)	6744 (2)	2·6
N(1′)	4313 (4)	2592 (2)	5509 (2)	2·7
C(2′)	3645 (5)	1722 (3)	5113 (2)	2·6
C(2′α)	4787 (6)	1426 (3)	4488 (2)	3·8
N(3′)	2040 (4)	1101 (2)	5204 (1)	2·4
C(4′)	940 (5)	1364 (3)	5747 (2)	2·4
N(4′α)	−663 (5)	734 (3)	5824 (2)	3·8
C(5′)	1494 (5)	2282 (3)	6187 (2)	2·3
C(6′)	3197 (5)	2845 (3)	6045 (2)	2·6
Nitrate				
N(1)	6674 (5)	76 (3)	7270 (2)	3·0
O(2)	8294 (5)	−387 (3)	7200 (2)	7·1
O(3)	5663 (5)	−197 (3)	7749 (2)	5·6
O(4)	6117 (5)	856 (2)	6854 (2)	4·4

* The B values are the equivalent isotropic temperature factors calculated from $B_{eq} = \frac{4}{3}(B_{11}a^2 + B_{22}b^2 + B_{33}c^2 + acB_{13}\cos\beta)$.

Table 2. *Bond lengths* (Å) *and angles* (°) *between non-H atoms*

Thiamine			
S(1)–C(2)	1·680 (4)	S(1)–C(5)	1·726 (4)
C(2)–N(3)	1·304 (5)	N(3)–C(4)	1·395 (4)
N(3)–C(35′)	1·500 (5)	C(4)–C(4α)	1·486 (6)
C(4)–C(5)	1·350 (5)	C(5)–C(5α)	1·508 (5)
C(5α)–C(5α)	1·519 (6)	C(5β)–O(5γ)	1·430 (5)
C(35′)–C(5′)	1·496 (5)	N(1′)–C(2′)	1·337 (5)
N(1′)–C(6′)	1·347 (5)	C(2′)–C(2′α)	1·504 (6)
C(2′)–N(3′)	1·328 (5)	N(3′)–C(4′)	1·352 (4)
C(4′)–N(4′α)	1·327 (5)	C(4′)–C(5′)	1·410 (5)
C(5′)–C(6′)	1·368 (5)		
C(2)–S(1)–C(5)	91·0 (2)	S(1)–C(2)–N(3)	112·5 (3)
C(2)–N(3)–C(4)	114·4 (3)	C(2)–N(3)–C(35′)	123·5 (3)
C(4)–N(3)–C(35′)	122·1 (3)	N(3)–C(4)–C(4α)	120·2 (3)
N(3)–C(4)–C(5)	111·6 (3)	C(4α)–C(4)–C(5)	128·2 (3)
S(1)–C(5)–C(4)	110·6 (3)	S(1)–C(5)–C(5α)	120·3 (3)
C(4)–C(5)–C(5α)	129·0 (3)	C(5)–C(5α)–C(5β)	114·0 (3)
C(5α)–C(5β)–O(5γ)	108·8 (3)	N(3)–C(35′)–C(5′)	112·6 (3)
C(2′)–N(1′)–C(6′)	114·8 (3)	N(1′)–C(2′)–C(2′α)	117·1 (3)
N(1′)–C(2′)–N(3′)	126·6 (3)	C(2′α)–C(2′)–N(3′)	116·3 (3)
C(2′)–N(3′)–C(4′)	117·9 (3)	N(3′)–C(4′)–N(4′α)	116·7 (3)
N(3′)–C(4′)–C(5′)	120·0 (3)	N(4′α)–C(4′)–C(5′)	123·4 (3)
C(35′)–C(5′)–C(4′)	121·6 (3)	C(35′)–C(5′)–C(6′)	121·7 (3)
C(4′)–C(5′)–C(6′)	116·6 (3)	N(1′)–C(6′)–C(5′)	124·2 (3)
Nitrate			
N(1)–O(2)	1·226 (5)	N(1)–O(3)	1·223 (5)
N(1)–O(4)	1·254 (4)		
O(2)–N(1)–O(3)	120·6 (4)	O(2)–N(1)–O(4)	118·4 (3)
O(3)–N(1)–O(4)	120·9 (3)		

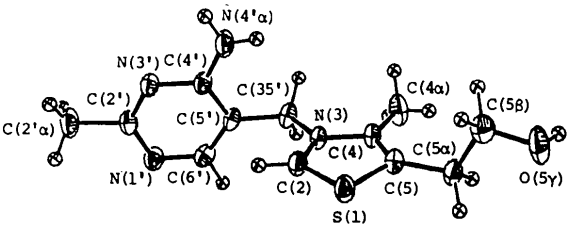

Fig. 1. Perspective view of thiamine cation, along with the atomic numbering used.

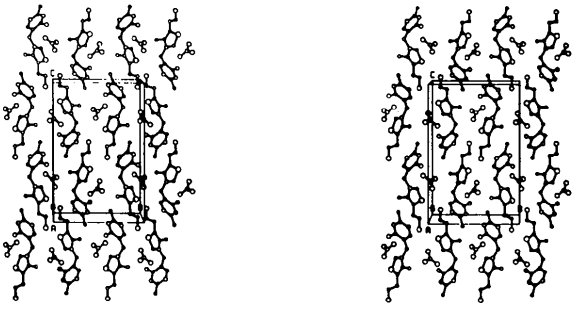

Fig. 2. A stereoscopic view of the structure, viewed along the a axis.

Fig. 2 shows the stereoscopic drawing of the crystal packing. The hydrogen bonds and short contacts formed are listed in Table 3. The O(5γ) atom of thiamine is hydrogen bonded to the N(1′) atom of a neighboring pyrimidine ring translated by a c-glide symmetry, consequently forming an infinite chain along **c**. The nitrate ions existing between these chains are connected with the neighboring thiamine molecules by O(4)···N(4′) and O(4)···C(2) hydrogen bonds. Although the latter distance is relatively long, it appears to be reasonable, judging from the C–H···O direction,

Table 3. *Intermolecular hydrogen bonds and other significant short contacts* (Å)

Hydrogen bonds

D (at *x,y,z*)	*A*	Symmetry	*D*···*A*	H···*A*	∠*D*–H···*A* (°)
C(2)	O(4)*N**	*x, y, z*	3·161 (5)	2·29 (4)	147 (3)
O(5γ)	N(1′)	$-1+x, \frac{1}{2}-y, \frac{1}{2}+z$	2·966 (4)	2·16 (5)	178 (5)
N(4′α)	N(3′)	$-x, -y, 1-z$	3·011 (4)	2·13 (4)	173 (4)
N(4′α)	O(4)*N**	$-1+x, y, z$	3·033 (4)	2·23 (5)	168 (5)

Short contacts (*A* at *x,y,z*)

A	*B*	Symmetry	
S(1)	O(5γ)	$-x, -y, 2-z$	3·246 (3)
S(1)	O(3)*N*	*x, y, z*	2·967 (4)
C(2)	O(2)*N*	$-1+x, y, z$	3·276 (6)
C(2)	C(4′)	*x, y, z*	3·382 (5)
C(2)	O(3)*N*	*x, y, z*	2·978 (5)
C(4)	O(4)*N*	$-1+x, y, z$	3·363 (5)
C(4)	O(2)*N*	$1-x, \frac{1}{2}+y, \frac{3}{2}-z$	3·302 (5)
C(4α)	O(3)*N*	$-x, \frac{1}{2}+y, \frac{3}{2}-z$	3·291 (5)
C(4α)	O(2)*N*	$1-x, \frac{1}{2}+y, \frac{3}{2}-z$	3·235 (6)
C(5α)	C(2′)	$x, \frac{1}{2}-y, \frac{1}{2}+z$	3·473 (5)
C(5α)	N(3′)	$x, \frac{1}{2}-y, \frac{1}{2}+z$	3·475 (5)
C(35′)	O(2)*N*	$1-x, \frac{1}{2}+y, \frac{3}{2}-z$	3·165 (6)
C(4′)	N(3)	*x, y, z*	3·296 (4)
N(4′α)	O(2)*N*	$-1+x, y, z$	3·056 (5)
C(5′)	C(2)	*x, y, z*	2·811 (5)
C(6′)	O(4)*N*	*x, y, z*	3·333 (5)
C(6′)	O(3)*N*	$1-x, \frac{1}{2}+y, \frac{3}{2}-z$	3·300 (5)

* The suffix *N* indicates the nitrate ion.

to consider it to be a hydrogen bond, and a corresponding hydrogen bond has been observed in many other thiamine structures (Richardson, Franklin & Thompson, 1975). Furthermore, the nitrate ions participate in the relatively strong short contacts (less than 3·1 Å) of O(3)···S(1), O(3)···C(2) and O(2)···N(4′α) atomic pairs. These interactions, in addition to an N(4′α)···N(3′) hydrogen bond, contribute to the stabilization of the molecular packing in the *a* and *b* directions.

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Structure of 9-Ethyl-7-methylguaninium Iodide Dimethyl Sulfoxide Solvate, $C_8H_{12}N_5O^+.I^-.C_2H_6OS$

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Abstract. $M_r = 399{\cdot}25$, monoclinic, $P2_1/c$, $a = 10{\cdot}266$ (2), $b = 6{\cdot}976$ (1), $c = 22{\cdot}059$ (4) Å, $\beta = 97{\cdot}66$ (1)°, $V = 1565{\cdot}8$ (4) Å^3, $Z = 4$, $D_m = 1{\cdot}734$ (5), $D_x = 1{\cdot}693$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, μ(Cu $K\alpha$) = 17·65 mm^{-1}, $F(000) = 796$, $T = 293$ K. Final $R = 0{\cdot}085$ for 2659 independent reflections. The molecular dimensions, especially in the imidazole moiety, are significantly different from those of neutral guanine. The crystal structure consists of extensive overlapping of the centrosymmetrically related guaninium rings.

Introduction. 7-Methylguaninium is a biologically important nucleic acid base forming the 'cap' structure of most eukaryotic mRNA's (Shatkin, 1976). The presence of this base, in the form of m^{7}GpppN(m), has been shown to be necessary for the efficient binding of mRNA to ribosome and the translation of the mRNA to proteins (Tamura, Imae & Strominger, 1976; Spratt & Strominger, 1976; Weber, Hickey, Nuss & Baglioni, 1977). On the other hand, the main site of DNA attacked by the mutagenic alkylating agents is the N(7) atom of guanine base (Brookes & Lawley, 1964). Elucidation of the structural properties of N(7)-alkylated guanine and comparison with the neutral molecule may be useful in gaining a more complete understanding of the above-mentioned biological phenomena. We have therefore determined the crystal structure of 9-ethyl-7-methylguaninium (MEG) iodide.

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