The triclinic cell parameters [a = 6.737 (1), b = 1.803 (7), c = 10.444 (1) Å, α = 94.767 (8), β = 108.30 (1), γ = 97.43 (1) °, V = 512.4 (2) Å^3 (Nethaji *et al.*, 1992)] could not be transformed to our primitive monoclinic cell using standard cell-reduction programs. The data were corrected for Lorentz and polarization effects. The structures were solved by direct methods using *SHELXS*86 (Sheldrick, 1985) and refined by full-matrix least squares (*SHELX*76; Sheldrick, 1976) with anisotropic displacement parameters for all non-H atoms.

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Lists of structure factors, anisotropic displacement parameters and H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71807 (15 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: HL1043]

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2′,3′-Didehydro-2′,3′-dideoxy-5-hydroxymethyluridine

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Abstract

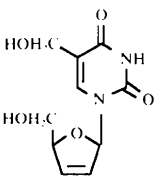
The furanose ring in $C_{10}H_{12}N_2O_5$ adopts the O(4′)-*endo* envelope conformation (^0E) and the glycosidic torsion angle C(2)—N(1)—C(1′)—O(4′), χ, is 245.2 (3)°. The pseudorotational parameters are P = 102.7° and τ_m = 5.2°. The CH_2OH group on C(5′) has the t conformation [γ = 179.2 (2)°].

Comment

A number of 2′,3′-dideoxyribonucleosides and 2′,3′-didehydro-2′,3′-dideoxyribonucleosides are potent inhibitors of the human immunodeficiency virus (HIV), the etiological agent of acquired immunodeficiency syndrome (AIDS). 3′-Azido-3′-deoxythymidine (AZT) is used extensively for the treatment of AIDS and AIDS-Related Complex (Broder, Mitsuya, Yarchoan & Pavlakis, 1990; De Clercq, 1991; Yarchoan, Pluda, Perno, Mitsuya & Broder, 1991). 2′,3′-Didehydro-2′,3′-dideoxythymidine (D4T) has been reported to have a comparable potency to AZT against HIV (Baba *et al.*, 1987; Lin, Schinazi & Prusoff, 1987; Mansuri *et al.*, 1989).

5-Hydroxymethyl-2′-deoxyuridine (HMdUrd) is a novel antimetabolite with broad-spectrum antiviral activity (Gupta *et al.*, 1992; Shiau, Shinazi, Chen & Prusoff, 1988) and low systemic toxicity (Meldrum, Gupta, Lowes & Paterson, 1985). HMdUrd-5′-monophosphate is a good inhibitor of thymidylate synthase (Kempf, Barfknecht, Shaffer, Osaki &

Mertes, 1976), and HMdUrd-5′-triphosphate is a moderate inhibitor of HIV-1 reverse transcriptase (Tao, Johansson, Stening, Oberg & Datema, 1989). 2′,3′-Didehydro-2′,3′-dideoxy-5-hydroxymethyluridine (D4HMUrd), which has the structural features of both D4T and HMdUrd was synthesized as a potential anti-HIV agent. This investigation is part of a series of conformational studies in progress to determine the effect of changes in structure on antiviral activity (Gupta *et al.*, 1987; Jia, Tourigny, Stuart, Delbaere & Gupta, 1990*ab*; Gupta *et al.*, 1992).



D4HMUrd

Owing to the fact that puckering reduces the steric interactions between adjacent substituents, five-membered furanose rings are generally non-planar. Consequently, C(2′)-*endo* and C(3′)-*endo* puckering modes are preferred, as the non-bonding interactions between furanose-ring substituents are at a minimum (Saenger, 1984). In D4HMUrd the steric contacts are reduced because substituents at C(2′) and C(3′) are H atoms which are in the plane of the ring. The furanose ring adopts the O(4′)-*endo* envelope conformation (^0E), and the displacement of O(4′) from the mean plane through C(1′)—C(2′), C(3′) and C(4′) is 0.071 (4) Å. A pseudo-rotational analysis of the furanose-ring torsion angles in terms of the two degrees of freedom for ring puckering (Altona & Sundaralingam, 1972) gives a phase angle $P = 102.7°$ and a puckering amplitude $\tau_m = 5.2°$, which indicates a high degree of planarity. The flattening of the furanose ring has also been reported for other modified nucleosides (Birnbaum, Giziewicz, Lin & Prusoff, 1989; Harte, Starrett, Martin & Mansuri, 1991). The glycosidic torsion angle C(2)—N(1)—C(1′)—O(4′), χ, has a value of 245.2 (3)°, which is within the usual range for pyrimidine nucleosides that have the *anti* conformation. The 5′-CH_2OH side chain exhibits the *t* conformation. The distance between the N(1) base and the C(5′) exocyclic substituent is 4.13 (3) Å, which is in agreement with the value expected for their equatorial orientation (Saenger, 1984). The pyrimidine ring is not completely planar; the atoms with the largest deviations from the mean plane are C(4) [$\Delta = 0.026$ (4) Å] and C(5) [$\Delta = 0.022$ (4) Å].

The crystal structure is stabilized by two intermolecular hydrogen bonds per unit cell. The first is N(3)—H(3)···O(4)($-\frac{1}{2}+x$, $\frac{3}{2}-y$, $1-z$). The distances N(3)···O(4) and H(3)···O(4) are 2.85 (3) and 1.89 Å, respectively, and the angle N(3)—H(3)···O(4) is 169.5°. The second is O(5,2)—H(5,2)···O(5′)($1-x$, $\frac{1}{2}+y$, $\frac{3}{2}-z$) with distances O(5,2)···O(5′) 2.69 (2), H(5,2)···O(5′) 1.76 Å and angle O(5,2)—H(5,2)···O(5′) of 173.5°. The presence of an intramolecular hydrogen bond [C(6)—H(6)···O(4′)] has been reported for 5-hydroxymethyl-2′-deoxyuridine (Birnbaum, Deslauriers, Lin, Shiau & Prusoff, 1980). In D4HMUrd the corresponding distances are C(6)···O(4′) 2.94 (3) and H(6)···O(4′) 2.76 Å, which are not considered to be significantly different from the sum of the van der Waals radii of the contributing atoms.

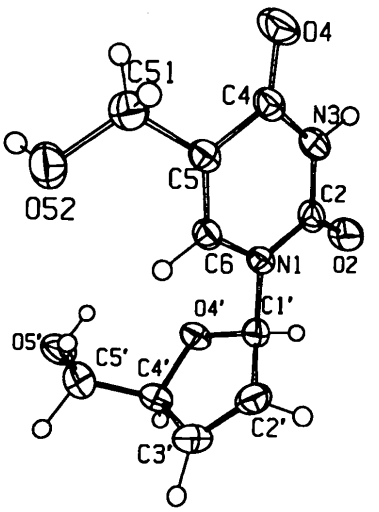


Fig. 1. Perspective *ORTEP*II view (Johnson, 1976) of the title compound with atomic numbering.

Experimental

The title compound (Kumar, Shi, Stuart, Qualtiere & Gupta, 1994) was crystallized from methanol–diethyl ether as colourless plates.

Crystal data

$C_{10}H_{12}N_2O_5$	Cu $K\alpha$ radiation
$M_r = 240.14$	$\lambda = 1.5418$ Å
Orthorhombic	Cell parameters from 25 reflections
$P2_12_12_1$	$\theta = 19$–$45°$
$a = 5.0862$ (5) Å	$\mu = 0.99$ mm^{-1}
$b = 8.0018$ (8) Å	$T = 287$ K
$c = 26.067$ (3) Å	Plates
$V = 1060.9$ (2) Å^3	0.40 × 0.25 × 0.025 mm
$Z = 4$	Colourless
$D_x = 1.504$ Mg m^{-3}	

Data collection

CAD-4 diffractometer	$\theta_{max} = 75°$
$\omega/2\theta$ scans	$h = -2 \rightarrow 6$
Absorption correction: none	$k = -6 \rightarrow 10$
	$l = -17 \rightarrow 32$

1676 measured reflections
1315 independent reflections
1315 observed reflections
R_{int} = 0.024

3 standard reflections
frequency: 83.33 min
intensity variation: 1%

Refinement

Refinement on F
R = 0.040
wR = 0.039
S = 3.489
1315 reflections
156 parameters
H-atom parameters not refined
$w = 1/\sigma^2(F)$
$(\Delta/\sigma)_{max}$ = 0.196

$\Delta\rho_{max}$ = 0.382 e Å^{-3}
$\Delta\rho_{min}$ = −0.249 e Å^{-3}
Extinction correction: Larson (1970)
Extinction coefficient: 0.230
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

were applied. X-ray diffraction data were processed (including Bayesian treatment) and the structure was solved, by direct methods, using *Xtal*3.0 (Hall & Stewart, 1990). All calculations were performed on a VAX 3100 computer at the University of Saskatchewan.

This research was funded by grants from the Medical Research Council of Canada to SVG and LTJD.

Lists of structure factors, anisotropic displacement parameters and H-atom coordinates have been deposited with the IUCr (Reference: CD1065). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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

$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
N(1)	0.5950 (5)	0.3238 (3)	0.58047 (7)	0.0276 (6)
C(2)	0.5367 (6)	0.4167 (3)	0.53694 (9)	0.0335 (8)
O(2)	0.3651 (5)	0.3799 (3)	0.50687 (8)	0.0497 (8)
N(3)	0.6912 (6)	0.5586 (3)	0.53098 (8)	0.0350 (7)
C(4)	0.8879 (6)	0.6133 (3)	0.56303 (9)	0.0302 (8)
O(4)	1.0192 (5)	0.7377 (2)	0.55241 (7)	0.0435 (7)
C(5)	0.9230 (6)	0.5165 (3)	0.60933 (9)	0.0261 (7)
C(51)	1.1202 (6)	0.5760 (3)	0.6480 (1)	0.0326 (8)
O(52)	1.0800 (5)	0.5053 (2)	0.69723 (7)	0.0376 (6)
C(6)	0.7819 (6)	0.3767 (3)	0.61521 (9)	0.0267 (7)
C(1′)	0.4474 (6)	0.1692 (3)	0.59051 (9)	0.0326 (8)
C(2′)	0.6212 (7)	0.0217 (3)	0.6010 (1)	0.0400 (1)
C(3′)	0.5632 (7)	−0.0415 (3)	0.6462 (1)	0.0382 (9)
C(4′)	0.3510 (6)	0.0564 (3)	0.6715 (1)	0.0332 (8)
O(4′)	0.2965 (4)	0.1900 (2)	0.63625 (7)	0.0339 (6)
C(5′)	0.4206 (7)	0.1268 (4)	0.7231 (1)	0.0420 (9)
O(5′)	0.2099 (5)	0.2169 (3)	0.74569 (7)	0.0493 (8)

Table 2. *Selected geometric parameters* (Å, °)

N(1)—C(2)	1.388 (3)	C(5)—C(6)	1.338 (4)
N(1)—C(6)	1.379 (3)	C(51)—O(52)	1.417 (3)
N(1)—C(1′)	1.471 (4)	C(1′)—C(2′)	1.500 (4)
C(2)—O(2)	1.209 (4)	C(1′)—O(4′)	1.428 (3)
C(2)—N(3)	1.390 (4)	C(2′)—C(3′)	1.316 (4)
N(3)—C(4)	1.375 (4)	C(3′)—C(4′)	1.488 (4)
C(4)—O(4)	1.230 (3)	C(4′)—O(4′)	1.437 (3)
C(4)—C(5)	1.446 (3)	C(4′)—C(5′)	1.499 (4)
C(5)—C(51)	1.500 (4)	C(5′)—O(5′)	1.420 (4)
C(6)—N(1)—C(2)	121.3 (2)	N(1)—C(2)—O(2)	123.6 (3)
C(6)—N(1)—C(1′)	119.5 (2)	N(3)—C(2)—O(2)	122.3 (2)
C(2)—N(1)—C(1′)	119.1 (2)	O(52)—C(51)—C(5)	112.7 (2)
C(4)—N(3)—C(2)	127.1 (2)	N(1)—C(1′)—O(4′)	109.0 (2)
C(4)—C(5)—C(6)	118.5 (2)	N(1)—C(1′)—C(2′)	113.2 (3)
C(4)—C(5)—C(51)	118.3 (2)	O(4′)—C(1′)—C(2′)	104.8 (2)
C(6)—C(5)—C(51)	123.2 (2)	C(1′)—C(2′)—C(3′)	109.5 (3)
C(1′)—O(4′)—C(4′)	110.1 (2)	C(4′)—C(5′)—O(5′)	112.6 (3)
N(3)—C(4)—C(5)	115.3 (2)	O(4′)—C(4′)—C(5′)	109.8 (2)
N(3)—C(4)—O(4)	121.1 (2)	O(4′)—C(4′)—C(3′)	104.4 (2)
C(5)—C(4)—O(4)	123.7 (3)	C(5′)—C(4′)—C(3′)	115.0 (3)
N(1)—C(6)—C(5)	123.4 (2)	C(2′)—C(3′)—C(4′)	110.9 (3)
N(1)—C(2)—N(3)	114.1 (2)		

All non-H atoms were found on an E map and refined anisotropically. All H-atom positional parameters were calculated but not refined. Dispersion and extinction corrections

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Thiamin Acetate, $C_{12}H_{17}N_4OS^+.C_2H_3O_2^-$

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Abstract

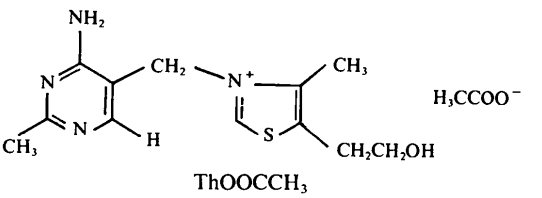
In thiamin acetate crystals, the thiamin cation {3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-5-(2-hydroxyethyl)-4-methylthiazolium} adopts the usual *F* conformation, with torsion angles C5′—C3,5′—N3—C2 and N3—C3,5′—C5′—C4′ (between the pyridinyl and thiazolium moieties) of 5.6 (7) and −83.5 (6)°, respectively. Hydrogen bonds involving the O5γ—H hydroxyl and N4α′—H_2 amine groups and the N1′ and N3′ pyrimidine atoms interconnect the thiamin cations. The acetate anions are hydrogen bonded to the N4α′—H_2 group and probably also to the C2—H group of the thiazole ring.

Comment

Thiamin (vitamin B_1, Th^+) is an essential dietary component for man and other animals. Its pyrophosphoric acid ester is a coenzyme for several enzyme systems catalysing the decarboxylation of α-keto acids and the transfer of acyl or aldehyde groups (Krampitz, 1969).

Structural studies of Th^+ derivatives in the solid state began in 1962, when the crystal structure of thiamin chloride hydrochloride monohydrate ($ThCl.HCl.H_2O$) was reported (Kraut & Reed, 1962). Since then, several thiamin derivatives have been studied by X-ray diffraction, including both saline compounds containing Th^+ or HTh^{2+} cations and true complexes where a metallic centre is directly bonded to thiamin, usually, though not always, through a pyrimidine N atom (Hu, 1991; Aoki, Yamazaki & Adeyemo, 1991; Jin, Liu, Wei & Wang, 1990; Louloudi, Hadjiliadis, Feng, Sukumar & Bau, 1990).

In this paper we report the crystal structure of thiamin acetate, $ThOOCCH_3$. As far as we know, only one other thiamin salt with an organic anion (thiamin picrolonate; Shin, Pletcher, Blank & Sax, 1977) has been characterized structurally.



$ThOOCCH_3$

Fig. 1 shows an *ORTEP* (Johnson, 1971, and supplementary instructions) diagram of the compound. In general, the values for the pyrimidine and thiazolium rings are in good agreement with those found in other unsubstituted N1′-deprotonated thiamin derivatives (Pletcher, Sax, Sengupta, Chu & Yoo, 1972; Shin, Pletcher, Blank & Sax, 1977), especially with those of thiamin picrolonate dihydrate. Differences from this compound [other than that concerning the C4—C5 distance, which seems likely to have been misprinted in the paper by Shin, Pletcher, Blank & Sax (1977)] arise in the N3′—C4′ and C4′—N4α′ distances (respectively shorter and longer in the acetate) and the angles between the pyrimidine ring and its 4′- and 5′-substitutents (C4′—C5′—C3,5′, C6′—C5′—C3,5′, N3′—C4′—N4α′ and C5′—C4′—N4α′). These differences may be due to the difference between the hydrogen-bond patterns observed in the two compounds (see below). In $ThOOCCH_3$, the thiazolium

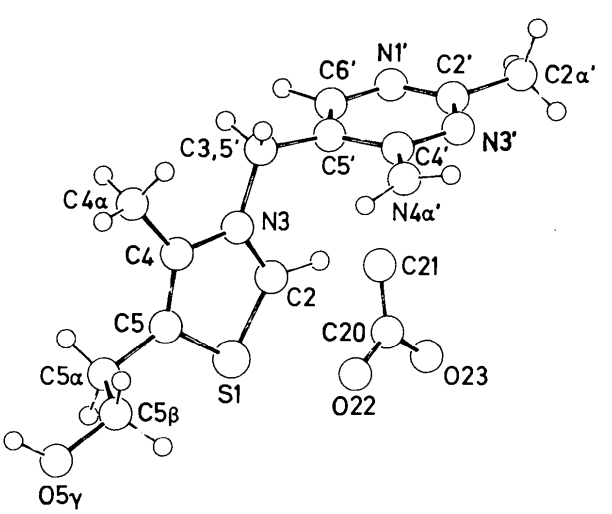


Fig. 1. *ORTEP*II (Johnson, 1971, and supplementary instructions) drawing of the compound.