

The X-ray structure determination was undertaken to probe the molecule for evidence of an interaction through the carbon σ bonds that allows a significant degree of cooperativity between the two 'isolated' π -electronic systems, the strained double bond and the pentafulvene moiety. The carbon σ bonds C7—C8 and C10—C11 are 1.532 (1) Å; these bond lengths are not significantly shorter than normal sp^3 — sp^3 bond lengths (March, 1985).

There is considerable distortion from ideal sp^2 hybridization at C9=C12, the double bond fusing the bicyclo[2.2.1]hepta-2,5-diene with the six-membered ring; the bond angle C13—C12—C16 is 94.76 (6)°. This degree of distortion is expected to cause this double bond to be exceptionally reactive.

The six-membered ring adopts a chair conformation. The bond angle exocyclic to the fulvene, C7—C6—C11, is 112.69 (7)° which is the same as the analogous bond angle of the precursor difulvene, 112.71 (9)° (McLaughlin, Cronan & Fronczek, 1988).

A linear C—H...O intermolecular contact exists involving carbonyl oxygen O2 and fulvene carbon C5 at x , $1-y$, z . The C...O distance is 3.351 (2) Å, the O...H distance is 2.35 (2) Å, and the angle at H is 177 (2)°. The other carbonyl oxygen, O4, has a closer intermolecular distance, 3.307 (2) Å, to the methylene

C7 at $2-x$, $-y$, $2-z$, but the H atom does not point at oxygen: O...H is 2.68 (2) Å, and the angle at H is 118 (2)°.

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Structure of *O,S*-Diacylthiamin

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Abstract. 3-Acetylthio-4-{*N*-[4-amino-2-methyl-5-pyrimidinyl)methyl]formamido}-3-penten-1-yl acetate, C₁₆H₂₂N₄O₄S, $M_r = 366.45$, monoclinic, $P2_1/n$ with $a = 9.086$ (2), $b = 19.096$ (5), $c = 11.084$ (3) Å, $\beta = 98.49$ (3)°, $V = 1902.1$ (9) Å³, $Z = 4$, $D_x = 1.279$ g cm⁻³, $\lambda(\text{Cu K}\alpha) = 1.5418$ Å, $\mu = 16.45$ cm⁻¹, $F(000) = 776$, $T = 295$ K, $R = 0.069$ for 1341 reflections with $I \geq 2\sigma(I)$. The pyrimidine, *N*-formyl and ethylenic groups are nearly perpendicular to each other and the N(3)—C(4) bond retains single-bond character. The conformation of the molecule is stabilized by an intramolecular N(4' α)—H...O(2 α) hydrogen bond [2.950 (10) Å]. The overall conformation is somewhat different from that of its congener *O,S*-dibenzoyl-

thiamin. The molecules related by a center of symmetry form a dimer *via* N(4' α)—H...N(3') hydrogen bonds [3.049 (10) Å].

Introduction. Thiamin (vitamin B₁) is labile against acid, alkali and heat (Dwidevi & Arnold, 1973). The thiazolium ring in thiamin is easily hydrolyzed in mildly alkaline solution to give various thiol or disulfide derivatives which, in turn, can easily be converted to thiamin upon acidification (Hopmann, 1982). Treatment of a thiol derivative of thiamin with an acylating agent such as acetic anhydride or benzoyl chloride yields the *O,S*-diacylthiamin such as *O,S*-diacylthiamin (DAT) or *O,S*-dibenzoylthiamin (DBT). These *O,S*-diacylthiamins as well as the disulfide derivatives are potential prodrugs because they pass through

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biological membranes more easily than thiamin itself (Duclos & Haake, 1974).

Thus far, crystal structures of four disulfide or thiol derivatives of thiamin have been reported. These include thiamin propyl disulfide (TPD; Nishikawa, Kamiya, Asahi & Matsumura, 1969), thiamin tetrahydrofurfuryl disulfide (TTFD; Shin & Kim, 1986a), thiamin disulfide dinitrate (TDD; Shin & Chun, 1987) and DBT (Shin, 1988). In an effort to investigate the structural characteristics of this class of compounds, X-ray analysis of DAT has been undertaken.

Experimental. DAT prepared following the reported procedures (Matsukawa & Kawasaki, 1953). Colorless tabular crystals obtained from a benzene solution of DAT by slow evaporation at room temperature; crystal *ca* 0.2 × 0.3 × 0.5 mm, Rigaku AFC diffractometer, graphite-monochromated Cu K α radiation, $2\theta < 115^\circ$, ω - 2θ scan, scan speed 2° min^{-1} in 2θ , ω -scan width $(1.5 + 0.24 \tan \theta)^\circ$, background measured for 10 s on either side of the peak; cell parameters by least-squares fit to observed 2θ values for 25 centered reflections with $17 < 2\theta < 52^\circ$; intensity checks for three standard reflections showed little ($\pm 3\%$) variation; 2602 independent reflections (h -9 to 9, k 0 to 20, l 0 to 12), 1341 (51.5%) observed with $I \geq 2\sigma(I)$ and used in refinement; Lp corrections, no absorption or extinction correction. Structure solved by direct methods and refined by full-matrix least squares on F with anisotropic thermal parameters using *SHELX76* (Sheldrick, 1976); H atoms identified on a difference map and refined isotropically. $\sum w(|F_o| - |F_c|)^2$ minimized, with $w = k/[\sigma^2(F_o) + gF_o^2]$, $\sigma(F)$ from counting statistics, k and g optimized in the least-squares procedure ($k = 1.43$, $g = 0.0022$); $wR = 0.0690$ for 1341 observed reflections, 292 variables, $R = 0.199$ for all data, $S = 2.175$, $(\Delta/\sigma)_{\text{max}} = 0.705$ [thermal parameter of C(7)] in final refinement cycle; max. and min. heights in final difference map 0.30 and $-0.30 \text{ e } \text{ \AA}^{-3}$, respectively. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974) as incorporated in *SHELX76*.

Discussion. Final atomic parameters are in Table 1.* A view of the DAT molecule with the atomic numbering scheme is shown in Fig. 1. Bond lengths, angles and selected torsion angles are listed in Table 2. The molecular dimensions of DAT are reasonable within experimental errors. A stereoscopic packing diagram is shown in Fig. 2. There is only one unique hydrogen

*Lists of structure factors, anisotropic thermal parameters, coordinates of H atoms, bond distances and angles involving H atoms, and least-squares planes have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51753 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Atomic coordinates ($\times 10^4$) and thermal factors ($\text{\AA}^2 \times 10^3$) of DAT

$$U_{eq} = \frac{1}{3}(\sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j).$$

	x	y	z	U_{eq}
S(1)	4965 (2)	9077 (1)	4753 (2)	46
C(6)	3840 (11)	9044 (5)	3315 (8)	64
C(7)	3961 (13)	9699 (6)	2551 (11)	82
O(6)	3084 (8)	8542 (4)	2963 (6)	92
C(2)	6569 (11)	7869 (4)	3546 (9)	60
O(2 α)	7589 (7)	7997 (3)	2970 (5)	75
N(3)	6747 (7)	7774 (3)	4766 (6)	46
C(4)	5465 (9)	7721 (4)	5369 (6)	43
C(4 α)	5270 (12)	7009 (5)	5958 (9)	62
C(5)	4523 (9)	8253 (4)	5377 (7)	45
C(5 α)	3165 (9)	8234 (5)	5947 (9)	53
C(5 β)	3171 (12)	8724 (6)	7009 (9)	66
O(5 γ)	4486 (6)	8579 (3)	7889 (6)	67
C(8)	4572 (13)	8854 (6)	8993 (9)	73
C(9)	5987 (17)	8691 (8)	9796 (13)	102
O(8)	3597 (11)	9180 (5)	9307 (7)	144
C(3,5')	8244 (10)	7743 (5)	5492 (9)	53
N(1')	9105 (9)	8978 (4)	8166 (5)	69
C(2')	9638 (10)	9513 (5)	7584 (8)	56
C(2' α)	10214 (16)	10117 (6)	8363 (10)	89
N(3')	9682 (7)	9552 (3)	6403 (6)	49
C(4')	9219 (8)	9001 (5)	5706 (8)	47
N(4' α)	9320 (8)	9050 (4)	4530 (7)	62
C(5')	8662 (8)	8395 (4)	6235 (8)	43
C(6')	8650 (10)	8432 (5)	7427 (9)	58

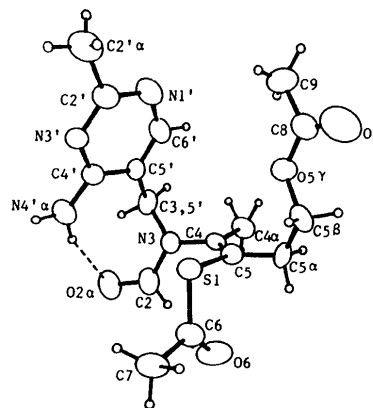


Fig. 1. An ORTEP (Johnson, 1976) view and the atomic numbering scheme for *O,S*-diacetylthiamin. The broken line denotes the hydrogen bond.

bond in the crystal lattice [$\text{N}(4'\alpha) \cdots \text{N}(3')(2-x, 2-y, 1-z) = 3.049$ (10), $\text{N}(4'\alpha) - \text{H}(4'2) = 0.96$ (9), $\text{H} \cdots \text{N}(3') = 2.10$ (9) \AA , $\text{N} - \text{H} \cdots \text{N} = 170$ (7) $^\circ$]. This hydrogen bond produces a molecular dimer around a center of symmetry at $(\frac{1}{2}, \frac{1}{2}, 0)$, forming a pyrimidine base pair. This kind of base pairing is frequently observed in the crystal structures of thiamin and its derivatives (Shin & Lah, 1987). DBT has the same hydrogen-bonding pattern. There are only van der Waals interactions between the molecular dimers.

The pyrimidine ring is planar with a maximum deviation of 0.019 (9) \AA . The five atoms around N(3) including the formyl group are also planar with a maximum deviation of 0.069 (8) \AA . N(3) is only

Table 2. Bond lengths (Å), angles (°) and selected torsion angles (°) of DAT

S(1)—C(6)	1.764 (9)	S(1)—C(5)	1.787 (8)
C(6)—C(7)	1.524 (15)	C(6)—O(6)	1.209 (12)
C(2)—O(2 α)	1.225 (11)	C(2)—N(3)	1.350 (12)
N(3)—C(4)	1.429 (10)	N(3)—C(3,5')	1.477 (11)
C(4)—C(4 α)	1.530 (12)	C(4)—C(5)	1.330 (11)
C(5)—C(5 α)	1.466 (12)	C(5 α)—C(5 β)	1.504 (14)
C(5 β)—O(5 γ)	1.454 (12)	O(5 γ)—C(8)	1.323 (12)
C(8)—C(9)	1.485 (19)	C(8)—O(8)	1.177 (15)
C(3,5')—C(5')	1.509 (12)	N(1')—C(2')	1.337 (12)
N(1')—C(6')	1.351 (12)	C(2')—C(2' α)	1.489 (15)
C(2')—N(3')	1.318 (11)	N(3')—C(4')	1.336 (11)
C(4')—N(4' α)	1.323 (12)	C(4')—C(5')	1.424 (12)
C(5')—C(6')	1.325 (13)		
C(7)—C(6)—S(1)	113.2 (7)	O(6)—C(6)—S(1)	123.1 (7)
O(6)—C(6)—C(7)	123.7 (9)	N(3)—C(2)—O(2 α)	124.1 (9)
C(4)—N(3)—C(2)	119.5 (7)	C(4)—C(5)—S(1)	119.2 (6)
C(4 α)—C(4)—N(3)	114.6 (7)	C(5)—S(1)—C(6)	100.6 (4)
C(5)—C(4)—N(3)	121.3 (7)	C(5)—C(4)—C(4 α)	124.1 (8)
C(5 α)—C(5)—S(1)	116.2 (6)	C(5 α)—C(5)—C(4)	124.5 (7)
C(5 β)—C(5 α)—C(5)	114.5 (8)	O(5 γ)—C(5 β)—C(5 α)	108.3 (8)
C(8)—O(5 γ)—C(5 β)	118.4 (8)	C(9)—C(8)—O(5 γ)	113.5 (10)
O(8)—C(8)—O(5 γ)	122.6 (10)	O(8)—C(8)—C(9)	123.8 (10)
C(3,5')—N(3)—C(2)	121.1 (7)	C(3,5')—N(3)—C(4)	119.4 (6)
C(2' α)—C(2')—N(1')	115.8 (8)	N(3')—C(2')—N(1')	126.0 (8)
N(3')—C(2')—C(2' α)	118.2 (8)	C(4')—N(3')—C(2')	118.5 (7)
C(4')—C(5')—C(3,5')	121.5 (8)	N(4' α)—C(4')—N(3')	117.0 (8)
C(5')—C(3,5')—N(3)	113.7 (7)	C(5')—C(4')—N(3')	120.2 (8)
C(5')—C(4')—N(4' α)	122.9 (8)	C(5')—C(6')—N(1')	126.9 (9)
C(6')—N(1')—C(2')	113.4 (7)	C(6')—C(5')—C(3,5')	123.4 (8)
C(6')—C(5')—C(4')	115.0 (8)		
C(4')—C(5')—C(3,5')—N(3)	81.7 (9)	C(4)—C(5)—S(1)—C(6)	-101.0 (7)
C(5')—C(3,5')—N(3)—C(4)	72.7 (8)	C(5)—S(1)—C(6)—C(7)	-179.1 (8)
C(3,5')—N(3)—C(4)—C(5)	-115.0 (10)	C(4)—C(5)—C(5 α)—C(5 β)	-115.1 (11)
N(3)—C(4)—C(5)—S(1)	6.3 (5)	C(5)—C(5 α)—C(5 β)—O(5 γ)	54.9 (8)

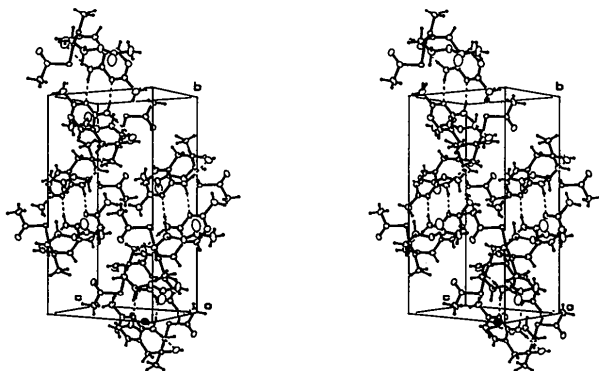


Fig. 2. Stereoscopic ORTEP (Johnson, 1976) packing drawing of O,S-diacetylthiamin. The broken lines denote the hydrogen bonds.

0.007 (6) Å from the plane formed by C(2), C(4) and C(3,5') and the sum of the valence angles around N(3) is 360.0°. These are indicative of a near- sp^2 hybridization of N(3). The bond lengths around N(3) indicate that the lone-pair electrons of N(3) are delocalized mainly through the C(2)—N(3) [1.350 (12) Å] bond for conjugation with the formyl group, but only slightly through the N(3)—C(3,5') [1.477 (11) Å] and the N(3)—C(4) [1.429 (10) Å] bonds. The C(4)=C(5) ethylenic double bond and the four atoms attached to it

are also planar with a maximum deviation of 0.084 (10) Å.

All of the dihedral angles between these three planar groups are near 113°. Mutually perpendicular arrangement of the three π -electron systems located in close proximity is a characteristic feature in the conformations of the ring-opened derivatives of thiamin, although the detailed geometries are slightly different as can be seen in the comparison of the dihedral angles listed in Table 3. The conformation of DAT is stabilized by an intramolecular N(4' α)—H...O(2 α) hydrogen bond [2.950 (10) Å] which is also present in TPD, TTFD and TDD. In DBT, N(4' α) is too far from O(2 α) [3.539 (5) Å] for hydrogen-bonding interaction, although a favorable N—H...O geometry is maintained. The conformation of this portion of the DAT molecule is more similar to those of disulfide TPD and TTFD rather than that of its congener DBT.

The S-acetyl group and the side chain at C(5 α) in DAT are nearly planar with maximum deviations of 0.01 (1) and 0.15 (1) Å, respectively. They are perpendicular to the ethylenic plane with dihedral angles of 97 and 95°, respectively, and placed opposite across the plane. The most significant difference between the conformations of DAT and DBT is the relative orientation of these side chains with respect to the ethylenic plane. In DAT the S-acetyl group and the pyrimidine ring are *anti* whereas the corresponding substituent at S(1), and the ring are all *syn* related in DBT, TPD and TTFD.

It is interesting to note that the conformational characteristics of thiamin and its ring-opened derivatives are very similar. Numerous crystal-structure analyses show that in terms of the relative orientation of the pyrimidine and thiazolium rings thiamin assumes a relatively rigid conformation despite apparent freedom of rotation about the two bonds to the methylene bridge C, but the conformation of the 5-(β -hydroxyethyl) side chain is subject to the crystal-packing forces (Shin, Pletcher, Blank & Sax, 1977). In the ring-opened derivatives, the conformation of the portion essential for the formation of intact thiamin, including the pyrimidine, N-formyl and ethylenic groups, is also relatively rigid despite apparently large freedom of rotation, but the conformations of the side chains at S(1) and C(5 α) are variable depending on the crystal packing.

It has been pointed out that the great reactivity of the ring-opened derivatives towards the formation of the thiazolium ring results from the preserved capability of easy rotation about the N(3)—C(4) single bond (Shin & Kim, 1986a). The N(3)—C(4) bond remains an easily rotatable single bond since the interaction between the lone-pair electrons of N(3) and the ethylenic π orbital is practically forbidden owing to the perpendicular arrangement of the two planar groups. In addition to this, nonbonded intramolecular attraction between S(1) and C(2), already present in the relatively rigid

Table 3. Comparison of the dihedral angles ($^{\circ}$) between the planar groups in related compounds

	DAT	DBT	TPD	TTFD	TDD
(a)/(b)	113.0	94.7	110.1	112.9	103.3
(a)/(c)	113.4	108.3	113.6	116.5	137.5
(b)/(c)	113.9	127.6	117.0	111.2	197.6

Notes: (a) six-atom plane of the pyrimidine ring; (b) five-atom plane around the N(3)-formyl group; (c) six-atom plane of the ethylenic group.

structure, may also facilitate the ring closure. The S(1)···C(2) separation in DAT is 3.132 (9) Å which is much shorter than the expected van der Waals contact of 3.50 Å (Bondi, 1964). The S···C distances are 3.004 (3), 3.10 (1), 3.10 (1) and 3.414 (6) Å in DBT, TPD, TTFD and TDD, respectively. Since rotations about the two single bonds around C(3,5') are not likely to occur owing to the presence of the intramolecular N—H···O hydrogen bond during the ring-closing reaction, simple rotation about the N(3)—C(4) bond by *ca* 60° may be sufficient for the formation of the thiazolium ring. The C(2)—N(3)—C(4)—C(5) torsion angle is 63.4 (9), 54.7 (3), 68 (1), 69 (1) and 82.2 (6)°, for DAT, DBT, TPD, TTFD and TDD, respectively.

The C(2)—N(3)—C(3,5')—C(5') and N(3)—C(3,5')—C(5')—C(4') torsion angles correspond to φ_T and φ_P which have been used for the description of the conformation of the thiamin molecule (Pletcher, Sax, Blank & Wood, 1977). The angles of 106 (1) and -82 (2)° in DAT are comparable to those ($\varphi_T = 104$, $\varphi_P = -74$)° in thiamin thiazolone, which is a transition-state analogue of thiamin and the only example found in the V form with an intramolecular N—H···O hydrogen

bond (Shin & Kim, 1986b). This similarly suggests that the conformation of the pseudo base intermediate for the ring opening-closing reaction of the thiazolium ring may be the similar V form.

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Chloro-2 (Nitro-3 phényl)-3 Phényl-1 Aziridinecarboxylate-2 de Méthyle

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Abstract. C₁₆H₁₃ClN₂O₄, *M_r* = 332.5, triclinic, *P* $\bar{1}$, *a* = 8.4645 (8), *b* = 10.2718 (13), *c* = 11.2804 (11) Å, α = 74.47 (1), β = 66.96 (1), γ = 63.37 (1)°, *V* = 801.7 Å³, *Z* = 2, *D_x* = 1.377 Mg m⁻³, λ (Cu *K*α) =

1.54184 Å, μ = 23.6 mm⁻¹, *F*(000) = 344, *T* = 293 K, *R* = 0.049 (*wR* = 0.054) for 2119 unique reflections [*I* > 3σ(*I*)]. The molecular geometry shows that the two aryl groups are in a *trans* configuration relative to the

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