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Methyl 4-Diethylamino-2-formamidothieno[2,3-*d*]pyrimidine-6-carboxylate

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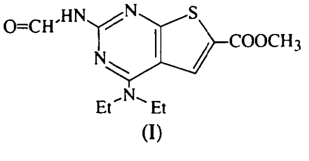
Abstract

The crystal structure of the thienopyrimidine derivative methyl 4-diethylamino-2-formamidothieno[2,3-*d*]pyrimidine-6-carboxylate, $C_{13}H_{16}N_4O_3S$, displays a strong stacking interaction between the two crystallographically independent, almost planar molecules of the asymmetric unit.

Comment

Thieno[2,3-*d*]pyrimidine was first prepared in 1953 (Baker, Joseph, Shaub, McEroy & Williams, 1953). Diaminothieno[2,3-*d*]pyrimidines are known to possess antimalarial, antibacterial and antihelmentic activities (Rosowsky, Chaykowsky, Chen, Lin & Modest, 1973; Chaykowsky, Lin, Rosowsky & Modest, 1973; Rosowsky, Chen & Lin, 1973).

Copper(II) complexes of these interesting ligands (Jakovidis, Varvounis & Hadjiliadis, 1988), as well as cobalt(II) and nickel(II) complexes, have also been reported (Tsiveriotis, Varvounis, Papadimitriou & Hadjiliadis, 1994). During an attempt to prepare Co^{II} and Ni^{II} complexes of the corresponding ligand methyl 2-amino-4-diethylaminothieno[2,3-*d*]pyrimidine-6-carboxylate in the presence of tetraethylorthoformate (TEOF), crystals of methyl 4-diethyl-2-formamidoaminothieno[2,3-*d*]pyrimidine-6-carboxylate, (I), were precipitated. The structure of this compound was solved by X-ray diffraction methods.



(I)

The two independent molecules, *A* and *B*, are almost planar and arranged in a head-to-tail fashion. The two thieno[2,3-*d*]pyrimidine planes are almost parallel, the dihedral angle being 178.1 (5)°.

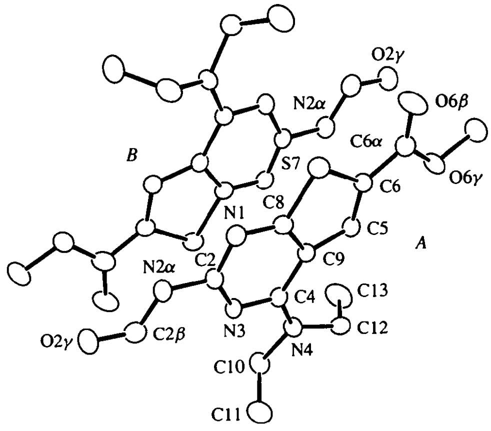


Fig. 1. *ORTEP* representation of the two crystallographically independent molecules showing the labelling scheme for *A*. Displacement ellipsoids are plotted at the 40% probability level.

The molecular packing is enhanced by a stacking interaction, of an average distance of 3.51 Å between *A* and *B*, and by a hydrogen-bonding scheme between the amido N2α and O2γ atoms of the formamido groups of adjacent molecules.

The shortest van der Waals contact is between O6β*A* and C13*B*($1 - x$, $\frac{1}{2} + y$, $2 - z$) and is 3.311 (4) Å, while the distance between O6β*B* and C13*A*($1 - x$, $-\frac{1}{2} + y$, $1 - z$) is 3.402 (4) Å.

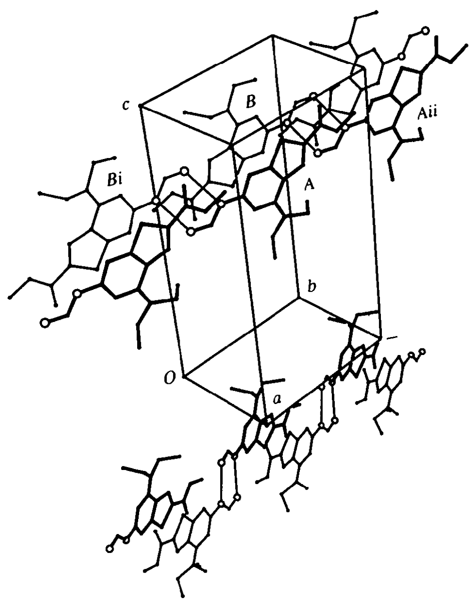


Fig. 2. *ORTEP* packing diagram in the unit cell showing the hydrogen-bonding scheme. Bond lengths and angles are $N2\alpha\cdots O2\gamma_{i}$ = 2.935 (4), $HN2\alpha\cdots O2\gamma_{i}$ = 2.00 Å, $N2\alpha—HN2\alpha\cdots O2\gamma_{i}$ = 160°, from *A* to *B* (x, $-1 + y$, z), and $N2\alpha\cdots O2\gamma_{ii}$ = 2.907 (4), $HN2\alpha\cdots O\gamma_{ii}$ = 1.96 Å, $N2\alpha—HN2\alpha\cdots O2\gamma_{ii}$ = 166°, from *B* to *A* (x, $1 + y$, z).

The bond distances and angles are within the expected ranges. They are slightly different in the two independent molecules. The C6—S7—C8 angle [90.7 (2)°] and the corresponding C—S bonds [1.732 (3) and 1.730 (3) Å], are in agreement with single-bond values. They are comparable with the corresponding values for thiazole in thiamine derivatives (Louloudi, Hadjiliadis, Feng, Sukumar & Bau, 1990; Cramer, Kirkup & Carrie, 1988), where the S atom is known not to interact with metal ions, due to the participation of the sulfur lone electron pair in the ring resonance.

Experimental

Crystal data

$C_{13}H_{16}N_4O_3S$
$M_r = 308.36$
Monoclinic
$P2_1$
$a = 7.214\,(1)$ Å
$b = 10.513\,(1)$ Å
$c = 19.459\,(2)$ Å
$\beta = 90.81\,(1)°$
$V = 1475.7\,(5)$ Å^3
$Z = 4$
$D_x = 1.388$ Mg m^{-3}

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 25 reflections
$\theta = 11.5$–$17.6°$
$\mu = 0.224$ mm^{-1}
$T = 293$ K
Rectangular
0.50 × 0.20 × 0.15 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
ω–2θ scans
Absorption correction: ψ scan (North, Phillips & Mathews, 1968)
$T_{\min} = 0.979$, $T_{\max} = 0.999$
3224 measured reflections
3224 independent reflections

2983 observed reflections [$I > 2\sigma(I)$]
$\theta_{\max} = 24°$
$h = 0 \rightarrow 8$
$k = -9 \rightarrow 12$
$l = -22 \rightarrow 22$
3 standard reflections
frequency: 120 min
intensity decay: 0.3%

Refinement

Refinement on F
$R = 0.021$
$wR = 0.025$
$S = 0.85$
2983 reflections
378 parameters
H-atom parameters not refined
Unit weights applied

$(\Delta/\sigma)_{\max} = 0.006$
$\Delta\rho_{\max} = 0.15$ e Å^{-3}
$\Delta\rho_{\min} = -0.23$ e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

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

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

	x	y	z	$U_{\rm eq}$
S7A	0.7491 (1)	0.5000	0.85413 (4)	4.18 (5)
S7B	0.2198 (1)	0.4325 (1)	0.64001 (4)	4.11 (5)
O6βA	0.8138 (4)	0.7638 (3)	0.9091 (1)	6.8 (2)
O6βB	0.1598 (4)	0.1663 (3)	0.5878 (1)	6.0 (2)
O6γA	0.8540 (3)	0.8546 (2)	0.8066 (1)	5.0 (1)
O6γB	0.0629 (3)	0.0877 (3)	0.6886 (1)	5.2 (1)
O2γA	0.4806 (3)	−0.0522 (2)	0.6564 (1)	5.6 (2)
O2γB	0.4093 (3)	1.0031 (3)	0.8353 (1)	6.2 (2)
N1A	0.6701 (3)	0.2931 (3)	0.7800 (1)	3.8 (2)
N1B	0.2890 (3)	0.6422 (3)	0.7143 (1)	3.8 (2)
N3A	0.6625 (3)	0.3042 (3)	0.6570 (1)	3.3 (1)
N3B	0.2756 (3)	0.6345 (3)	0.8376 (1)	3.8 (2)
N2αA	0.5761 (3)	0.1227 (3)	0.7147 (1)	4.0 (2)
N2αB	0.3469 (3)	0.8203 (3)	0.7786 (1)	4.4 (2)
N4A	0.7319 (3)	0.4787 (3)	0.5930 (1)	3.8 (2)
N4B	0.2376 (3)	0.4541 (3)	0.9006 (1)	4.0 (2)
C8A	0.7189 (4)	0.4162 (3)	0.7782 (1)	3.4 (2)
C8B	0.2515 (3)	0.5175 (4)	0.7154 (1)	3.4 (2)
C9A	0.7430 (3)	0.4922 (3)	0.7205 (1)	3.1 (2)
C9B	0.2277 (3)	0.4417 (3)	0.7740 (1)	3.2 (2)
C5A	0.7805 (4)	0.6217 (3)	0.7399 (2)	3.5 (2)
C5B	0.1777 (4)	0.3150 (3)	0.7553 (2)	3.7 (2)
C6A	0.7880 (4)	0.6392 (3)	0.8085 (2)	3.5 (2)
C6B	0.1690 (4)	0.2958 (3)	0.6865 (2)	3.7 (2)
C6αA	0.8188 (4)	0.7562 (4)	0.8479 (2)	4.2 (2)
C6αB	0.1300 (4)	0.1783 (4)	0.6487 (2)	4.4 (2)
C6δA	0.8865 (5)	0.9754 (4)	0.8412 (2)	5.7 (2)
C6δB	0.0200 (5)	−0.0314 (4)	0.6553 (2)	6.2 (2)
C2A	0.6410 (4)	0.2477 (3)	0.7165 (2)	3.5 (2)
C2B	0.3001 (4)	0.6912 (3)	0.7763 (2)	3.7 (2)
C4A	0.7144 (4)	0.4273 (4)	0.6555 (1)	3.3 (2)
C4B	0.2474 (4)	0.5074 (4)	0.8381 (1)	3.3 (2)
C2βA	0.5466 (4)	0.0551 (4)	0.6576 (2)	4.6 (2)
C2βB	0.3623 (5)	0.8930 (4)	0.8351 (2)	5.3 (2)
C10A	0.6714 (4)	0.4072 (3)	0.5313 (1)	4.4 (2)
C10B	0.2198 (4)	0.5349 (4)	0.9619 (2)	5.0 (2)
C11A	0.8177 (5)	0.3177 (4)	0.5048 (2)	6.3 (2)
C11B	0.4060 (5)	0.5745 (4)	0.9933 (2)	7.6 (3)
C12A	0.8118 (4)	0.6047 (3)	0.5797 (2)	4.1 (2)
C12B	0.2594 (5)	0.3168 (4)	0.9132 (2)	5.1 (2)
C13A	0.6630 (5)	0.7063 (4)	0.5718 (2)	6.4 (2)
C13B	0.0787 (5)	0.2484 (4)	0.9251 (2)	6.5 (3)

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

S7A—C8A	1.732 (3)	S7B—C8B	1.730 (3)
C8A—C9A	1.391 (4)	C8B—C9B	1.404 (4)
C9A—C5A	1.437 (5)	C9B—C5B	1.427 (5)
C5A—C6A	1.348 (4)	C5B—C6B	1.354 (4)
C6A—S7A	1.737 (3)	C6B—S7B	1.739 (4)
C6A—C6αA	1.464 (5)	C6B—C6αB	1.463 (5)
C6αA—O6βA	1.195 (4)	C6αB—O6βB	1.214 (4)
C6αA—O6γA	1.336 (4)	C6αB—O6γB	1.325 (4)
O6γA—C6δA	1.455 (4)	O6γB—C6δB	1.442 (4)
C8A—N1A	1.342 (4)	C8B—N1B	1.339 (5)
N1A—C2A	1.338 (4)	N1B—C2B	1.314 (4)
C2A—N3A	1.313 (4)	C2B—N3B	1.346 (4)
N3A—C4A	1.348 (4)	N3B—C4B	1.352 (5)
C4A—C9A	1.449 (4)	C4B—C9B	1.431 (4)
C2A—N2αA	1.395 (4)	C2B—N2αB	1.399 (4)
N2αA—C2βA	1.334 (4)	N2αB—C2βB	1.342 (5)
C2βA—O2γA	1.225 (4)	C2βB—O2γB	1.206 (5)
C4A—N4A	1.339 (4)	C4B—N4B	1.341 (4)
N4A—C10A	1.477 (4)	N4B—C10B	1.472 (4)
C10A—C11A	1.511 (5)	C10B—C11B	1.525 (5)
N4A—C12A	1.469 (4)	N4B—C12B	1.472 (5)
C12A—C13A	1.521 (5)	C12B—C13B	1.510 (5)

C6A—S7A—C8A	90.7 (2)
S7A—C8A—C9A	112.4 (3)
C8A—C9A—C5A	110.9 (3)
C9A—C5A—C6A	113.3 (3)
C5A—C6A—S7A	112.7 (2)
C9A—C8A—N1A	127.7 (3)
C8A—N1A—C2A	110.9 (3)
N1A—C2A—N3A	129.4 (3)
C2A—N3A—C4A	119.3 (3)
N3A—C4A—C9A	118.0 (3)
C4A—C9A—C8A	114.6 (3)
S7A—C8A—N1A	119.8 (2)
C5A—C9A—C4A	134.4 (3)
C5A—C6A—C6αA	129.6 (3)
S7A—C6A—C6αA	117.7 (2)
C6A—C6αA—O6βA	124.8 (3)
C6A—C6αA—O6γA	111.3 (3)
O6βA—C6αA—O6γA	123.8 (3)

C6α*A*—O6γ*A*—C6δ*A*	115.4 (2)
N1*A*—C2*A*—N2α*A*	114.0 (3)
N3*A*—C2*A*—N2α*A*	116.6 (3)
C2*A*—N2α*A*—C2β*A*	124.9 (3)
N2α*A*—C2β*A*—O2γ*A*	124.4 (3)
N3*A*—C4*A*—N4*A*	115.9 (3)
C9*A*—C4*A*—N4*A*	126.1 (3)
C4*A*—N4*A*—C10*A*	120.2 (3)
C4*A*—N4*A*—C12*A*	124.5 (3)
C10*A*—N4*A*—C12*A*	115.3 (2)
N4*A*—C10*A*—C11*A*	113.3 (2)
N4*A*—C12*A*—C13*A*	111.9 (3)
C6*B*—S7*B*—C8*B*	90.7 (2)
S7*B*—C8*B*—C9*B*	112.3 (3)
C8*B*—C9*B*—C5*B*	110.8 (3)
C9*B*—C5*B*—C6*B*	113.6 (3)
C5*B*—C6*B*—S7*B*	112.6 (3)
C9*B*—C8*B*—N1*B*	126.5 (3)
C8*B*—N1*B*—C2*B*	112.2 (3)
N1*B*—C2*B*—N3*B*	129.3 (3)
C2*B*—N3*B*—C4*B*	117.8 (3)
N3*B*—C4*B*—C9*B*	118.9 (3)
C4*B*—C9*B*—C8*B*	115.0 (3)
S7*B*—C8*B*—N1*B*	121.1 (2)
C5*B*—C9*B*—C4*B*	134.0 (3)
C5*B*—C6*B*—C6α*B*	128.9 (3)
S7*B*—C6*B*—C6α*B*	118.4 (2)
C6*B*—C6α*B*—O6β*B*	122.9 (3)
C6*B*—C6α*B*—O6γ*B*	112.4 (3)
O6β*B*—C6α*B*—O6γ*B*	124.7 (3)
C6α*B*—O6γ*B*—C6δ*B*	116.0 (3)
N1*B*—C2*B*—N2α*B*	114.9 (3)
N3*B*—C2*B*—N2α*B*	115.9 (3)
C2*B*—N2α*B*—C2β*B*	126.6 (3)
N2α*B*—C2β*B*—O2γ*B*	124.7 (4)
N3*B*—C4*B*—N4*B*	115.5 (3)
C9*B*—C4*B*—N4*B*	125.7 (3)
C4*B*—N4*B*—C10*B*	120.0 (3)
C4*B*—N4*B*—C12*B*	123.6 (3)
C10*B*—N4*B*—C12*B*	116.2 (2)
N4*B*—C10*B*—C11*B*	113.3 (3)
N4*B*—C12*B*—C13*B*	113.8 (3)

Data collection was performed using *CAD*-4 *Software* (Enraf–Nonius, 1989). *PROCESS* in *MolEN* (Fair, 1990) was used for data reduction. The structure was determined by direct methods using *SHELXS*86 (Sheldrick, 1985) and refined by full-matrix least-squares techniques (*SHELX*76; Sheldrick, 1976). All H atoms were located from a difference Fourier map and kept fixed (C—H = N—H = 0.97 Å). *R* values for both enantiomers were similar. The absolute structure was chosen by comparing the values of F_c/F_o for Bijvoet pairs and by considering the Flack (1983) parameters [0.10 (8) and 0.69 (9)]. All calculations were made on a MicroVAX 3400 computer. Molecular graphics were produced using *ORTEP* (Johnson, 1965).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and least-squares-planes data have been deposited with the IUCr (Reference: HR1004). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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The Cyclic Depsipeptide Backbone of the Didemnins

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Abstract

An X-ray crystal analysis of φ-lactone *N*-{1-{*N*-{4-{[3-hydroxy-5-methyl-1-oxo-4-(*N*-L-threonylamino)heptyl]-oxy}-2,5-dimethyl-1,3-dioxohexyl}-L-leucyl}-L-prolyl}-*N*,*O*-dimethyl-L-tyrosine hydrobromide hydrate (1*a*), $C_{42}H_{66}N_5O_{11}^+.Br^-.H_2O$, was obtained in order to determine the backbone folding of the macrocycle and to compare the results obtained with those reported previously for the natural product didemnin B (1*b*). Some differences were noted in the torsion angles of the two conformers of the hydrobromide salt, denoted (1*a*) and (1*a*′). The conformation of (1*a*′) resembled the conformation of (1*b*) more closely than did that of (1*a*). Certain regions of both crystal backbones were more flexible than those in didemnin B; however, the transannular hydrogen bonds in both (1*a*) and (1*a*′) were somewhat stronger than in (1*b*).

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