Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: FG1122). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Acta Cryst. (1996). C**52**, 2939-2941

A Potential Antiprotozoal Drug Containing Acridine and Thiadiazole Moieties

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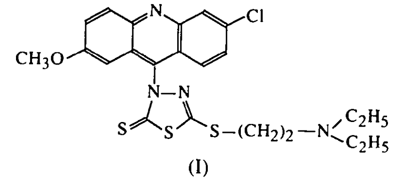
(*Received 16 January 1996; accepted 30 May 1996*)

Abstract

The title compound, 3-(6-chloro-2-methoxy-9-acridinyl)-5-[2-(diethylamino)ethylthio]-1,3,4-thiadiazol-2(3*H*)-one, $C_{22}H_{23}ClN_4OS_3$, belongs to a series of new potential antiprotozoal drugs containing the acridine and thiadiazole systems. These two quasi-planar moieties are bonded together and are almost perpendicular to one another because of steric hindrance.

Comment

In the course of our research on antiprotozoal (Bsiri *et al.*, 1995) and antimicrobial drugs (Crèmieux *et al.*, 1994), we synthesized derivatives with two active pharmacophoric moieties in order to produce a heteroaromatic acridine nucleus with a basic [(diethylamino)ethylthio]thiadiazole substituent. The title product, (I), was obtained by the attack of 9-chloroacridine at an unexpected point on the thiadiazole and we have investigated its crystal structure in order to confirm ^{13}C NMR results (Amiel *et al.*, 1995).



(I)

The title molecule can be described in terms of two parts corresponding to the two pharmacophoric moieties (Fig. 1). The heterocyclic nucleus of the 9-substituted acridine is not completely planar and the three unsaturated aromatic rings look like a very flattened boat, with a dihedral angle of 2.5 (3)° between the external rings. This conformation is in agreement with data obtained from the Cambridge Structural Database (Allen & Kennard, 1993) for 51 compounds containing the 9-substituted acridine moiety. The thiadiazole substituent is directly attached to the acridine system *via* the C9′—N3*a* bond. The five-membered heteroatomic ring is almost planar, the largest deviation from the mean plane being only 0.013 (2) Å for the C2*a* atom. The thiadiazole ring is almost perpendicular to the acridine nucleus, forming a dihedral angle of 74.1 (1)° with it.

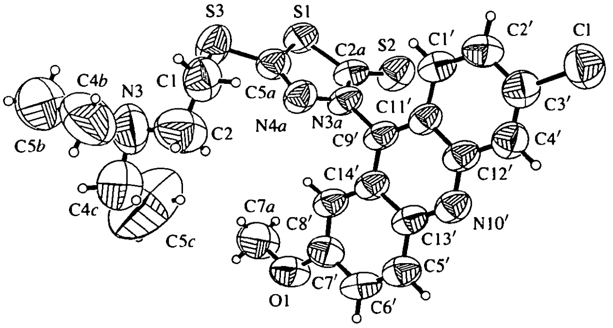


Fig. 1. The molecular structure of (I) showing 50% probability displacement ellipsoids.

The geometry of the diethylaminoethyl substituent on the S3 atom is unreliable because of the high displacement parameters for these atoms, which may be genuinely dynamic or may mask some degree of static disorder. Low-temperature data collection was unfortunately not possible because the crystals cracked on cooling.

The acridine nuclei are stacked parallel in columns along the *b* axis, with a closest spacing of 3.40 (4) Å. This value corresponds to a stabilizing hydrophobic interaction. There are no intermolecular contacts shorter than the sum of the van der Waals radii.

We have previously reported the structure of the thiadiazole starting material (Amiel *et al.*, 1995). The geometric features of the thiadiazole ring are comparable, except that the S2—C2*a* and C2a—N3*a* bond lengths differ in the two structures; S2—C2*a* is shorter [1.646 (5) *versus* 1.667 (5) Å] and C2*a*—N3*a* is longer [1.345 (5) *versus* 1.316 (7) Å] in the present structure. Substitution of the H atom on the N3*a* atom by the acridine nucleus with its greater electronegativity thus enhances the C═S double-bond and C—N single-bond characters.

Experimental

The synthesis of (I) was achieved by heating 2(3*H*)-thioxo-5-[2-(diethylamino)ethylthio]-1,3,4-thiadiazole hydrochloride (1 g, 3.5 mmol) and 2-methoxy-6,9-dichloroacridine (0.98 g, 3.5 mmol) in anhydrous pyridine (50 ml) under nitrogen for 5 h at 383 K. The compound was recrystallized from diethyl ether–light petroleum (1:1). Crystals suitable for X-ray analysis were obtained by crystallization from ethanol by slow evaporation at room temperature.

Crystal data

$C_{22}H_{23}ClN_4OS_3$
$M_r = 491.07$
Orthorhombic
Pbca
$a = 20.977 (4)$ Å
$b = 8.943 (2)$ Å
$c = 25.504 (5)$ Å
$V = 4784.5 (17)$ Å^3
$Z = 8$
$D_x = 1.363$ Mg m^{-3}
D_m not measured

Cu *Kα* radiation
$\lambda = 1.54178$ Å
Cell parameters from 25 reflections
$\theta = 5–65°$
$\mu = 4.04$ mm^{-1}
$T = 293 (2)$ K
Thin plate
0.50 × 0.40 × 0.10 mm
Yellow

Data collection

Kuma KM-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: empirical *via* ψ scan (North, Phillips & Mathews, 1968)
$T_{\min} = 0.26$, $T_{\max} = 0.67$
2380 measured reflections
2380 independent reflections

1621 observed reflections $[I > 2\sigma(I)]$
$\theta_{\max} = 81.02°$
$h = -26 \rightarrow 0$
$k = -11 \rightarrow 0$
$l = -32 \rightarrow 0$
2 standard reflections frequency: 100 min intensity decay: 2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.0640$
$wR(F^2) = 0.1745$
$S = 1.075$
2380 reflections
281 parameters
H atoms: see below

$\Delta\rho_{\max} = 0.608$ e Å^{-3}
$\Delta\rho_{\min} = -0.278$ e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.00016 (7)

$w = 1/[\sigma^2(F_o^2) + (0.1456P)^2 + 2.287P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.193$

Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

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}
Cl	0.97028 (7)	−0.1512 (2)	0.68150 (6)	0.1233 (5)
C1′	0.8759 (2)	0.0128 (5)	0.5599 (2)	0.091 (2)
C2′	0.8907 (2)	−0.0642 (5)	0.6034 (2)	0.094 (2)
C3′	0.9530 (2)	−0.0497 (6)	0.6251 (2)	0.092 (2)
C4′	0.9976 (2)	0.0346 (5)	0.6017 (2)	0.091 (2)
C5′	1.0632 (2)	0.3737 (5)	0.4695 (2)	0.092 (2)
C6′	1.0517 (2)	0.4577 (5)	0.4274 (2)	0.095 (2)
C7′	0.9910 (2)	0.4580 (5)	0.4040 (2)	0.091 (2)
O1	0.9865 (2)	0.5528 (4)	0.36204 (14)	0.1080 (12)
C7*a*	0.9254 (3)	0.5750 (8)	0.3391 (3)	0.145 (3)
C8′	0.9423 (2)	0.3737 (5)	0.4232 (2)	0.0834 (14)
C9′	0.9074 (2)	0.1905 (5)	0.4903 (2)	0.0774 (13)
N10′	1.0296 (2)	0.2018 (4)	0.53430 (14)	0.0844 (12)
C11′	0.9206 (2)	0.1072 (5)	0.5350 (2)	0.0728 (12)
C12′	0.9834 (2)	0.1145 (5)	0.5561 (2)	0.0820 (14)
C13′	1.0153 (2)	0.2805 (5)	0.4920 (2)	0.0783 (13)
C14′	0.9531 (2)	0.2822 (5)	0.4673 (2)	0.0765 (13)
S1	0.72860 (5)	0.2083 (2)	0.44705 (5)	0.0916 (4)
S2	0.78856 (6)	0.3573 (2)	0.54038 (6)	0.1047 (5)
S3	0.74935 (7)	0.0242 (2)	0.35006 (5)	0.1139 (5)
C2*a*	0.7929 (2)	0.2521 (5)	0.4875 (2)	0.0781 (13)
N3*a*	0.8448 (2)	0.1852 (4)	0.46733 (14)	0.0792 (11)
N4*a*	0.8384 (2)	0.1048 (4)	0.42083 (14)	0.0845 (11)
C5*a*	0.7800 (2)	0.1090 (5)	0.4059 (2)	0.0850 (14)
C1	0.8180 (2)	−0.0768 (7)	0.3272 (2)	0.118 (2)
C2	0.8594 (3)	0.0019 (9)	0.2918 (3)	0.166 (3)
N3	0.8246 (3)	0.0521 (9)	0.2435 (2)	0.184 (2)
C4*b*	0.8194 (5)	−0.0535 (11)	0.2075 (3)	0.234 (4)
C5*b*	0.7762 (4)	−0.0419 (11)	0.1657 (3)	0.238 (4)
C4*c*	0.8752 (4)	0.1484 (12)	0.2161 (4)	0.223 (3)
C5*c*	0.8818 (6)	0.2841 (11)	0.2343 (6)	0.385 (7)

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

C9′—N3*a*	1.438 (4)	N4*a*—C5*a*	1.284 (5)
S1—C2*a*	1.744 (4)	C1—C2	1.436 (7)
S1—C5*a*	1.748 (5)	C2—N3	1.502 (9)
S2—C2*a*	1.646 (5)	N3—C4*b*	1.321 (10)
S3—C5*a*	1.737 (5)	N3—C4*c*	1.534 (10)
S3—C1	1.797 (5)	C4*b*—C5*b*	1.403 (11)
C2*a*—N3*a*	1.345 (5)	C4*c*—C5*c*	1.307 (13)
N3*a*—N4*a*	1.393 (5)		
C2*a*—S1—C5*a*	89.6 (2)	C5*a*—N4*a*—N3*a*	109.2 (3)
C5*a*—S3—C1	100.9 (2)	N4*a*—C5*a*—S3	125.8 (4)
N3*a*—C2*a*—S2	127.8 (3)	N4*a*—C5*a*—S1	115.2 (3)
N3*a*—C2*a*—S1	107.4 (3)	S3—C5*a*—S1	119.1 (2)
S2—C2*a*—S1	124.8 (2)	C4*b*—N3—C2	113.4 (7)
C2*a*—N3*a*—N4*a*	118.6 (3)	C4*b*—N3—C4*c*	98.1 (6)
C2*a*—N3*a*—C9′	124.6 (3)	C2—N3—C4*c*	101.9 (6)
N4*a*—N3*a*—C9′	116.8 (3)		

The title structure was solved by direct methods. The isotropic displacement parameters for all H atoms were held at 1.5 times the respective U_{eq} values of the parent C atoms.

Data collection: *Kuma KM-4 Software* (Kuma, 1992). Cell refinement: *Kuma KM-4 Software*. Data reduction: *DATARED* (Pèpe, 1979) in *Kuma KM-4 Software*. Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990*a*). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *SHELXTL/PC* (Sheldrick, 1990*b*). Software used to prepare material for publication: *SHELXL*93.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: CF1083). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Acta Cryst. (1996). C**52**, 2941-2942

N′-[Bis(methylthio)methylene]cyanoacetohydrazide

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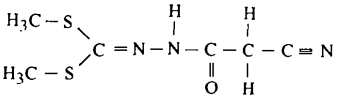
(*Received 17 January 1996; accepted 30 May 1996*)

Abstract

The title compound, $C_6H_9N_3OS_2$, forms chains of hydrogen-bonded molecules along the [100] direction, the chains being held together by van der Waals interactions. Bond lengths and angles are in good agreement with standard literature values.

Comment

In the course of a project aimed at finding possible new products, attention has been focused on the use of cyanoacetohydrazide derivatives as drugs (Negwer, 1987). In this context, the title compound, (I), has been synthesized and characterized.



$$(H_3C{-}S)_2C{=}N{-}NH{-}C({=}O){-}CH_2{-}C{\equiv}N$$

(I)

The title compound was obtained from cyanoacetohydrazide by adding carbon disulfide and methyl iodide at room temperature (Napoles, Peseke & Quincoces, 1987), and displays biological activity against fungus and parasites of bovine cattle (Napoles, 1993). The product of the above reaction was characterized by quantitative analysis, IR and proton-NMR spectroscopy, and mass spectrometry (Napoles, 1993), and its crystal structure was determined by single-crystal X-ray diffraction (Fig. 1).

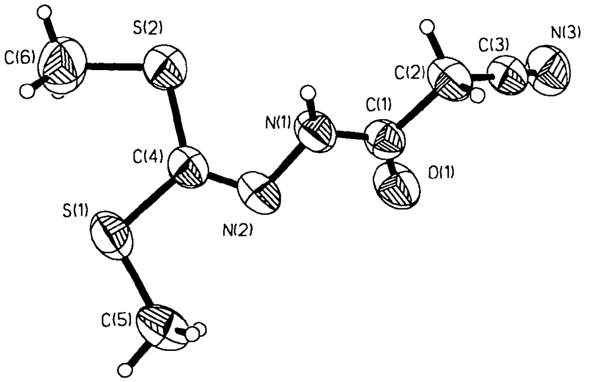


Fig. 1. The molecular structure of (I) with 50% probability displacement ellipsoids.

Bond lengths and angles in (I) are all in good agreement with literature values. In particular, those of the cyanoacetohydrazide moiety are very similar to the corresponding values found in α-cyanoacetohydrazide itself (Chieh, 1973). The only significant difference is in the C(2)—C(1)—N(1)—N(2) torsion angle [165.9 (5) in the title compound and 172.6° in α-cyanoacetohydrazide]. This is probably as a result of the substituent on the N(2) atom causing the molecule to deviate from planarity; the dihedral angle between the planes of the $(MeS)_2CN$ and $HNC({=}O)CH_2CN$ moieties is 55.8 (5)°.

The crystal packing includes infinite chains of hydrogen-bonded molecules along the [100] direction (Fig. 2). The amine N(1) atom of each molecule is hydrogen bonded to the carbonyl O(1) atom of the molecule of the next unit cell (Table 2). The chains are held together in the crystal by means of van der Waals interactions.

Acta Crystallographica Section C
ISSN 0108-2701 © 1996