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2-(Acridin-9-ylimino)-3-dimethylamino-1,3-thiazolidin-4-one

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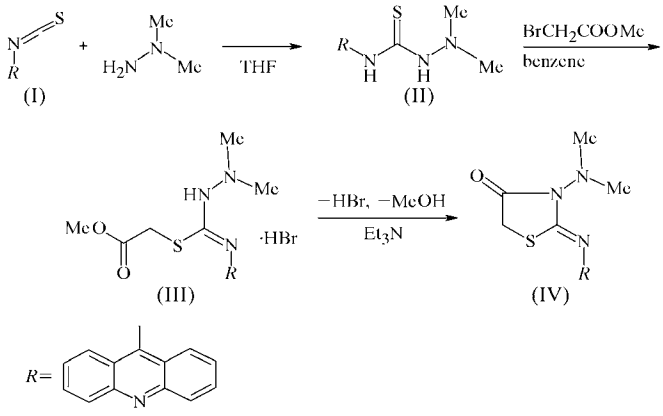
In the title compound, $C_{18}H_{16}N_4OS$, prepared by the reaction of 4-(acridin-9-yl)-1,1-dimethylthiosemicarbazide with methyl bromoacetate, the acridine and thiazolidine ring systems are both non-planar and, because of steric requirements, almost perpendicular, with a dihedral angle between their planes of 99.69 (6)°. C—H···O and C—H···π(arene) hydrogen bonds stabilize the crystal structure in the solid state.

Comment

Thiazole derivates, particularly 1,3-thiazolidin-4-ones, have a broad spectrum of biological activity (Singh *et al.*, 1998; Liu & Anthonsen, 2000). Our continuing interest in 9-substituted acridine compounds, which may possess anticancer, chemiluminescent and intercalating properties (Kristian *et al.*, 1998; Klika *et al.*, 2001; Bernát *et al.*, 2004; Demeunynck *et al.*, 2001), led us to the synthesis of new acridin-9-ylthiosemicarbazides and thiazolidinone derivatives. Besides the synthetic goal of this work, a presumed synergism of biological effects of both heterocyclic skeletons was another interesting point to study.

To obtain the target compounds, the reaction of acridin-9-yl isothiocyanate, (I), with 1,1- and 1,2-disubstituted hydrazines was used to give intermediate thiosemicarbazides, which were further cyclized with bromoacetate or bromide to obtain products of type (IV) (Fig. 1) (Vilková *et al.*, 2005). Because of the presence of four nucleophilic centres in thiosemicarbazides, at least six types of isomeric five-membered heterocyclic structures could possibly be formed from the terminal cyclization step and/or subsequent possible rearrangements of the Dimroth type. An NMR proof of these structures is questionable because of ambiguities in assignments of cross peaks from two-dimensional H,C-correlation and nuclear Overhauser effect spectroscopy (NOESY). Hence, we have determined the structure of the model title compound, (IV), obtained by the reaction of 4-(acridin-9-yl)-1,1-dimethylthiosemicarbazide, (II), with methyl bromoacetate. The preparation of the studied compound involved the alkylation of the thiosemicarbazide to afford 4-(acridin-9-yl)-1,1-dimethyl-*S*-(methoxycarbonylmethylene)isothiosemicarbazide hydrobromide, (III), by the attachment of the S atom of the thiosemicarbazide to a bromomethylene C atom.



A search of the Cambridge Structural Database (August 2004 release; Allen, 2002) showed that the title compound is the first example of a compound in which the acridine and thiazolidine ring systems are linked by an imine N atom. On the other hand, three derivatives of *N*-(acridin-9-yl)-1,4-benzoquinone monoimines have been structurally characterized (Clark *et al.*, 1993), and there are two entries containing an imino-1,3-thiazolidin-4-one ring (Deepthi *et al.*, 2001).

The acridine and thiazolidine ring systems in (IV) both deviate significantly from planarity. Atom C2 exhibits the greatest deviation [0.050 (3) Å] from the mean plane through the 14 atoms of the acridine ring system, while in the thiazolidine ring, atom C15 deviates most from the mean plane [0.079 (3) Å]. The geometric parameters for the acridine ring system are similar to those found in phenyl(acridin-9-yl)amine (Leardini *et al.*, 1998). The N2—C14 bond in the imine group is clearly shorter than the C9—N2 bond (Table 1), indicating the double-bond character of the former. Similar distances were found in *N*-(9-acridinyl)-2-methoxy-1,4-benzoquinone monoimine (Clark *et al.*, 1993). Owing to steric effects in (IV), the ring systems linked by imine atom N2 are almost

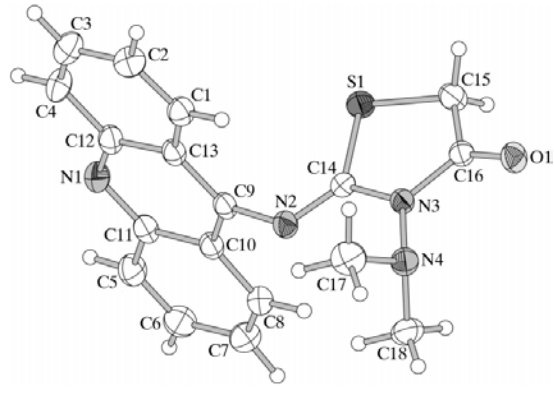


Figure 1
A view of the title compound, showing displacement ellipsoids at the 30% probability level and H atoms as spheres of arbitrary radii.

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perpendicular; the angle between the mean planes through the rings is 99.69 (6)°. The geometric parameters in the 1,3-thiazolidin-4-one ring are normal (Deepthi *et al.*, 2001).

The packing of the individual molecules in the solid state is governed by two intermolecular C—H···O hydrogen bonds (Table 2) and a C—H···π(arene) hydrogen bond. Pairs of molecules of (IV) are linked by C15—H15*A*···O1^{ii} [symmetry code: (ii) $-x, 1-y, -z$] hydrogen bonds, forming a ring that can be described by graph-set descriptor $R_2^2(8)$ (Bernstein *et al.*, 1995); moreover, each O1 atom participates in a C5—H5···O1^{i} [symmetry code: (i) $1+x, \frac{1}{2}-y, \frac{1}{2}+z$] hydrogen bond, linking pairs of molecules into deformed planes. Finally, the planes interact *via* C18—H18*B*···π(arene) hydrogen bonds.

Experimental

Single crystals of (IV) in the form of bright-yellow needles suitable for X-ray studies were prepared by the following procedure. Acridin-9-yl isothiocyanate [(I); 0.473 g, 2 mmol; Mazagová *et al.*, 1994] was added dropwise to a solution of 1,1-dimethylhydrazine (0.120 g, 2 mmol) in anhydrous tetrahydrofuran (THF, 5 ml). Dissolved in anhydrous THF (5 ml). The reaction mixture was stirred at room temperature until isothiocyanate disappeared (monitored by thin-layer chromatography; eluant cyclohexane–ethyl acetate, 3:1); a precipitate of 4-(acridin-9-yl)-1,1-dimethylthiosemicarbazide, (II), was filtered off, dried and recrystallized from methanol–diethyl ether (yield 60%, m.p. 466–469 K). ^{1}H NMR (DMSO-d_6): δ 2.76 (*s*, 6H, 2 × CH_3), 7.50–8.25 (*m*, 8H, acridinyl H), 9.59 (*br s*, 1H, NH), 10.40 (*br s*, 1H, NH). To a suspension of (II) (0.2 g, 0.67 mmol) in dry benzene (5 ml), methyl bromoacetate (0.103 g, 0.063 ml, 0.67 mmol) was added slowly. The solution was stirred at room temperature for 5 h, triethylamine (0.137 g, 0.188 ml, 1.35 mmol) was added and stirring was continued for a further 2 h. The solution was filtered, the filtrate was evaporated and the residue was chromatographed on a column filled with silica gel (Merck 109385, 0.040–0.063 mm, 230–400 mesh; eluant ethyl acetate–cyclohexane, 4:1). To a saturated solution of crude (IV) in hot ethyl acetate, *n*-heptane was added to first turbidity and the product was left to crystallize for 2 h (yield 31%, m.p. 475–477 K). ^{1}H NMR (DMSO-d_6): δ 3.16 (*s*, 6H, H-17,18), 3.93 (*s*, 2H, H-15), 7.53, 7.81, 8.00, 8.12 (*m*, 8H, acridinyl H); ^{13}C NMR: δ 30.8 (C-15), 42.7 (C-17,18), 117.0 (C-10,13), 123.9, 125.0, 129.2, 130.4 (acridinyl CH), 148.9 (C-11,12), 150.4 (C-9), 155.3 (C-14), 169.3 (C-16).

Crystal data

$C_{18}H_{16}N_4OS$
M_r = 336.42
Monoclinic, $P2_1/c$
a = 7.282 (5) Å
b = 19.456 (5) Å
c = 11.954 (5) Å
β = 105.326 (5)°
V = 1633.4 (14) Å^3
Z = 4
D_x = 1.368 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3118 reflections
θ = 2.1–25.0°
μ = 0.21 mm^{-1}
T = 298 (2) K
Prism, yellow
0.40 × 0.12 × 0.11 mm

Data collection

Bruker SMART 1000 diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 1999)
T_{min} = 0.787, T_{max} = 0.977
8245 measured reflections
2867 independent reflections
1776 reflections with $I > 2\sigma(I)$
R_{int} = 0.043
θ_{max} = 25.0°
$h = -8 \rightarrow 8$
$k = -23 \rightarrow 15$
$l = -14 \rightarrow 13$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.079
S = 0.87
2867 reflections
282 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0351P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.17 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.0023 (5)

Table 1
Selected geometric parameters (Å, °).

S1—C14	1.761 (2)	N2—C9	1.409 (2)
S1—C15	1.810 (2)	N3—C16	1.383 (2)
O1—C16	1.206 (2)	N3—C14	1.397 (2)
N1—C12	1.347 (2)	N3—N4	1.404 (2)
N1—C11	1.352 (3)	N4—C18	1.461 (3)
N2—C14	1.269 (2)	N4—C17	1.465 (3)
C14—S1—C15	91.81 (11)	C14—N3—N4	124.38 (16)
C12—N1—C11	117.71 (18)	N3—N4—C18	112.08 (18)
C14—N2—C9	120.77 (17)	N3—N4—C17	112.91 (19)
C16—N3—C14	116.84 (17)	C18—N4—C17	114.5 (2)
C16—N3—N4	118.78 (16)		

Table 2
Hydrogen-bonding geometry (Å, °).

Cg is the centroid of the C5–C11 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C5—H5···O1^{i}	0.93 (2)	2.42 (2)	3.311 (4)	161.7 (17)
C15—H15*A*···O1^{ii}	0.94 (2)	2.48 (2)	3.339 (4)	152.1 (16)
C18—H18*B*···*Cg*^{iii}	0.94 (3)	2.97 (3)	3.645 (4)	131 (2)

Symmetry codes: (i) $1+x, \frac{1}{2}-y, \frac{1}{2}+z$; (ii) $-x, 1-y, -z$; (iii) $x, \frac{1}{2}-y, z-\frac{1}{2}$.

H atoms were freely refined with isotropic displacement parameters [C—H = 0.927 (19)–0.99 (3) Å].

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINT* (Bruker, 1998); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS86* (Sheldrick, 1985); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *DIAMOND* (Crystal Impact, 2000); software used to prepare material for publication: *SHELXL97*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD1369). Services for accessing these data are described at the back of the journal.

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