

(Z)-2-[(1-Phenylsulfonyl-1*H*-indol-3-yl)methylene]-1-azabicyclo[2.2.2]octan-3-one semicarbazoneVijayakumar N. Sonar,^a M. Venkatraj,^a Sean Parkin^b and Peter A. Crooks^{a*}^aDepartment of Pharmaceutical Sciences, College of Pharmacy, University of Kentucky, Lexington, KY 40536, USA, and ^bDepartment of Chemistry, University of Kentucky, Lexington, KY 40506, USA

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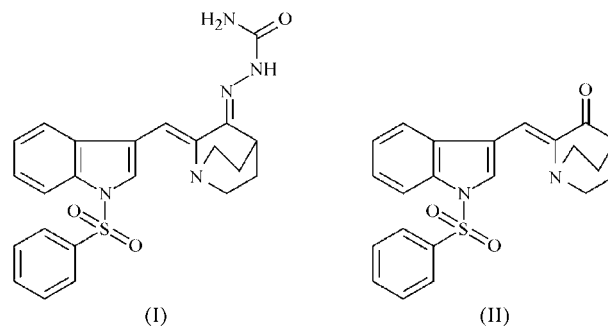
In crystals of the title compound, C₂₃H₂₃N₅O₃S, the indole system is planar and the phenyl ring of the phenylsulfonyl group makes a dihedral angle with the best plane of the indole system of 77.18 (4)°. The olefinic bond connecting the azabicyclic and indole systems has *Z* geometry. The geometry adopted by the C=O bond with respect to the N—N bond is *trans*. The O atom of the carbonyl group of each molecule is hydrogen bonded to the hydrazidic H atom of an adjacent molecule to form an eight-membered-ring dimeric structure.

Comment

Radiotherapy is the treatment of cancer and other diseases with ionizing radiation. The technique is successful because ionizing radiation kills dividing cells and is thus slightly more toxic to fast-growing cancer cells than to normal cells. Radiotherapy may be used to treat localized solid tumours, such as cancers of the skin, tongue, larynx, brain, breast, uterus or cervix. Agents which are used to potentiate the effectiveness of radiation therapy in destroying unwanted cells are radio-sensitizing agents. Recently, we have reported (Sekhar *et al.*, 2007) the radio-sensitizing activity of *N*-arylsulfonyl-substituted (*Z*)-(\pm)-2-(1*H*-indol-3-ylmethylene)-1-azabicyclo[2.2.2]octan-3-ols. Systematic structural modification of the active molecule (*Z*)-2-(1-phenylsulfonyl-1*H*-indol-3-ylmethylene)-1-azabicyclo[2.2.2]octan-3-one, (II), was carried out and the title compound, (I), was synthesized as a structural analogue of (II). In order to confirm the double-bond geometry, and to determine the molecular conformation in the crystal structure, the X-ray crystallographic analysis of (I) has been carried out and the results are presented here.

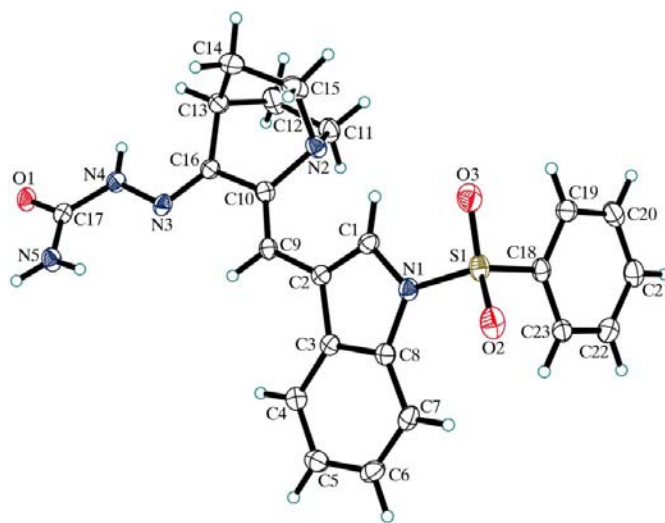
X-ray crystallography confirmed the molecular structure and atom connectivity for (I), as illustrated in Fig. 1. Selected geometric parameters are presented in Table 1. The indole ring is planar, with bond distances and angles comparable with

those previously reported for other indole derivatives (Mason *et al.*, 2003; Zarza *et al.*, 1988).



In compound (I), atom N1 lies only very slightly [0.0555 (15) Å] out of the plane of the connecting atoms S1, C1 and C8, the sum of the angles about N1 being 359.58 (11)°. In a previous study, 21 structurally related indole analogues bearing *N*-arylsulfonyl groups were analyzed (Beddoes *et al.*, 1986) (available in the Cambridge Structural Database; Allen, 2002), and the sums of the three angles around the N atom were determined, to assess planarity. It was found that only two of the 21 compounds had values that were outside the range 359.0–360°, the farthest value from the perfectly planar situation being 357.2°. This is in general agreement with our current observation with compound (I). However, it should be noted that in at least one case, *i.e.* in a moiety consisting of a pyrrolidine N atom bearing a tolylsulfonyl group, atom N1 can exist significantly out of the plane of the connecting atoms S1, C1 and C4 (335.1°), indicating pyrimidalization at the N atom (Helliwell *et al.*, 1997).

The sulfonyl group of (I) has a distorted tetrahedral geometry, with widening of the O2—S1—O3 angle [120.99 (7)°] and a resultant narrowing of the N1—S1—C18 angle [104.88 (7)°] from ideal tetrahedral values. This type of

**Figure 1**

A view of the molecule of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

deviation in the sulfonyl group has been reported previously (Beddoes *et al.*, 1994; Govindasamy *et al.*, 1998; Zhao *et al.*, 1997, 1999) and is due to the repulsive interaction between the short S=O bonds. The S—O, S—C and S—N distances are comparable with those found in *N*-phenylsulfonamides (Gomes *et al.*, 1993). The orientation of the phenylsulfonamide group with respect to the planar indole system [r.m.s. deviation = 0.0172 (13) Å] is described by the torsion angles O3—S1—N1—C1, O2—S1—N1—C8 and N1—S1—C18—C19 (Table 1). The phenyl ring linked to the sulfonyl group is orthogonal to the indole system, forming a dihedral angle of 77.18 (4)°.

Compound (I) is the *Z* isomer and the C10—C16 bond is in a *trans* disposition with respect to the C2—C9 bond. The double bond has a nearly planar arrangement, since the r.m.s. deviation from the best plane passing through atoms N2/C10/C16/C9/C2 is 0.0195 (9) Å. Deviations from ideal geometry are observed in the bond angles around atoms C2, C9 and C10. While the C9—C10—C16 angle is close to the ideal value of 120°, the C1—C2—C9, C2—C9—C10 and N2—C10—C16 angles are more distorted, as a consequence of the strain induced by the double-bond linkage at C9—C10. The azabicyclic system presents very small distortions around atoms N2, C11, C12, C13, C14 and C15. The value of the C1—C2—C9—C10 torsion angle [25.1 (3)°] indicates a deviation of the indole ring from the plane of the double bond connected to the azabicyclic ring. However, the C2—C9 bond length [1.455 (2) Å], when compared with the standard value for a single bond connecting a C_{ar} atom to a Csp² atom [1.470 (15) Å; Wilson, 1992], suggests extensive conjugation, beginning at atom N5 of the semicarbazone group and

extending through to the indole ring in (I), which is also evident from the C10—C16 and C16—N3 bond lengths.

The mode of packing of (I), as viewed down the crystallographic *b* axis, is shown in Fig. 2. The molecules are linked by two types of hydrogen bonding. Atoms N4 and O1 are mutually hydrogen bonded to an inversion-related molecule at (−*x*, −*y*, −*z*), leading to dimers, and atom N5 is hydrogen bonded to sulfonyl atom O2 of a different inversion-related molecule at (−*x* + 1, −*y*, −*z* + 1). In addition to hydrogen bonding, π–π interactions between phenyl rings [3.433 (1) Å] of inversion-related molecules at (1 − *x*, 1 − *y*, 1 − *z*) and between different inversion-related indole rings at (1 − *x*, −*y*, 1 − *z*) (3.343 Å) link these dimers in an extended fashion parallel to the *b* axis.

Experimental

The starting material, (II) (see scheme), was prepared according to the previously reported procedure of Sonar *et al.* (2004). The title compound, (I), was prepared by the reaction of (II) with semicarbazide to afford a single geometric isomer. Crystallization from methanol afforded yellow crystals. ¹H NMR (DMSO-*d*₆): δ 1.70 (*m*, 4H), 2.81 (*m*, 2H), 3.16 (*m*, 2H), 3.40 (*s*, 1H), 6.51 (*b*, 2H), 7.13 (*s*, 1H), 7.34 (*m*, 2H), 7.59 (*t*, 2H), 7.69 (*t*, 1H), 7.92 (*d*, 3H) 8.07 (*d*, 1H), 8.42 (*s*, 1H), 9.54 (*s*, 1H); ¹³C NMR (DMSO-*d*₆): δ 24.63, 25.13, 46.62, 105.47, 112.94, 117.65, 120.31, 123.33, 124.94, 125.99, 126.38, 129.77, 130.18, 133.52, 134.54, 136.59, 146.02, 148.47, 157.27.

Crystal data

C ₂₃ H ₂₃ N ₅ O ₃ S	<i>V</i> = 2124.75 (7) Å ³
<i>M_r</i> = 449.52	<i>Z</i> = 4
Monoclinic, <i>P</i> 2 ₁ / <i>c</i>	Mo <i>K</i> α radiation
<i>a</i> = 11.2058 (2) Å	<i>μ</i> = 0.19 mm ^{−1}
<i>b</i> = 12.7677 (2) Å	<i>T</i> = 90.0 (2) K
<i>c</i> = 15.0499 (3) Å	0.30 × 0.20 × 0.20 mm
<i>β</i> = 99.3278 (9)°	

Data collection

Nonius KappaCCD area-detector diffractometer	9258 measured reflections
Absorption correction: multi-scan (SCALEPACK; Otwinowski & Minor, 1997)	4851 independent reflections
<i>T_{min}</i> = 0.945, <i>T_{max}</i> = 0.963	3681 reflections with <i>I</i> > 2σ(<i>I</i>)
	<i>R_{int}</i> = 0.027

Refinement

<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)] = 0.040	289 parameters
<i>wR</i> (<i>F</i> ²) = 0.111	H-atom parameters constrained
<i>S</i> = 1.06	Δρ _{max} = 0.32 e Å ^{−3}
4851 reflections	Δρ _{min} = −0.38 e Å ^{−3}

Table 1

Selected geometric parameters (Å, °).

S1—O2	1.4307 (12)	N3—C16	1.292 (2)
S1—N1	1.6668 (13)	N3—N4	1.3844 (17)
S1—C18	1.7514 (17)	N5—C17	1.344 (2)
O1—C17	1.2394 (18)	C9—C10	1.337 (2)
C2—C9	1.455 (2)	C10—C16	1.476 (2)
C1—C2—C9	129.03 (14)	C9—C10—N2	122.99 (14)
C10—C9—C2	127.85 (14)	N2—C10—C16	112.84 (13)
O3—S1—N1—C1	27.83 (14)	C9—C10—C16—N3	−3.7 (2)
O2—S1—N1—C8	−31.08 (15)	N1—S1—C18—C19	107.79 (13)

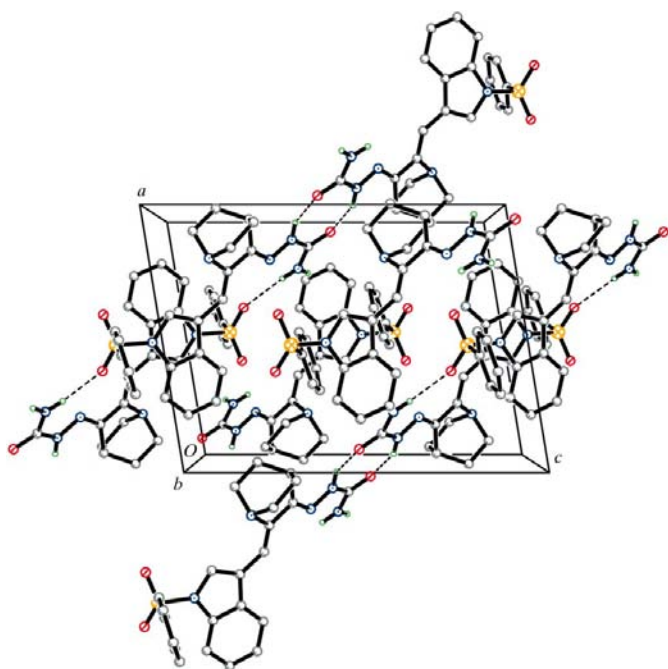


Figure 2

A packing diagram for (I), viewed down the *b* axis, showing the hydrogen-bonding interactions (dashed lines). For clarity, only those H atoms involved in hydrogen bonding are shown.

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

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$N4-H4A\cdots O1^i$	0.88	2.06	2.8785 (17)	154
$N5-H5B\cdots O2^{ii}$	0.88	2.25	3.0651 (17)	154

Symmetry codes: (i) $-x, -y, -z$; (ii) $-x + 1, -y, -z + 1$.

H atoms were found in difference Fourier maps and subsequently placed in idealized positions, with constrained distances of 0.95 (Csp^2), 0.99 (CH_2), 1.00 (CH) and 0.88 Å (NH). $U_{iso}(H)$ values were set at $1.2U_{eq}$ of the attached atom.

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO-SMN* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *XP* in *SHELXTL* (Sheldrick, 1995); software used to prepare material for publication: *SHELXL97* and local programs.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: HJ3030). Services for accessing these data are described at the back of the journal.

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