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N-{4-Bromo-2-[(3-bromo-1-phenylsulfonyl-1*H*-indol-2-yl)methyl]-5-methoxyphenyl}acetamide

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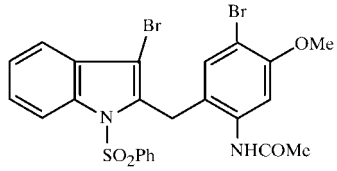
In the title compound, $C_{24}H_{20}Br_2N_2O_4S$, the indole ring system is planar and the S atom has a distorted tetrahedral configuration. The sulfonyl-bound phenyl ring is orthogonal to the indole ring system and the conformation of the phenylsulfonyl substituent with respect to the indole moiety is influenced by intramolecular C—H···O hydrogen bonds involving the two sulfonyl O atoms. The mean plane through the acetylamido group makes a dihedral angle of 57.0 (1)° with the phenyl ring of the benzyl moiety. In the crystal, glide-related molecules are linked together by N—H···O hydrogen bonds and C—H···π interactions to form molecular chains, which extend through the crystal. Inversion-related chains are interlinked by C—H···π interactions to form molecular layers parallel to the *bc* plane. These layers are interconnected through π–π interactions involving the five- and six-membered rings of the indole moiety.

Comment

Indole derivatives have been found to exhibit interesting antibacterial and antifungal properties (Wang & Ng, 2002; Singh *et al.*, 2000; Tsotinis *et al.*, 1997; Quetin-Leclercq *et al.*, 1995). Polyhalogenated indole derivatives exhibit marked antimicrobial activity against Gram-positive and Gram-negative bacteria and fungi (Piscopo, Diurno, Mazzoni, Ciaccio & Veneruso, 1990; Piscopo, Diurno, Mazzoni & Ciaccio, 1990). Pyrido[1,2-*a*]indole derivatives have been identified as potent inhibitors of human immunodeficiency virus type 1 (Taylor *et al.*, 1999), and 5-chloro-3-(phenylsulfonyl)indole-2-carboxamide is reported to be a highly potent non-nucleoside inhibitor of HIV-1 reverse transcriptase (Williams *et al.*, 1993). Indole derivatives also exhibit antitumour activities (Andreani *et al.*, 2001; Bradlow *et al.*, 1999; Cirrincione *et al.*, 1999; Tiwari *et al.*, 1994; Dashwood *et al.*, 1994). Some of the indole alkaloids extracted from plants possess interesting cytotoxic, antitumour and antiparasitic properties (Quetin-Leclercq, 1994; Mukhopadhyay *et al.*, 1981). In view of this wide range of biological activities associated with indole derivatives, we have undertaken the X-ray structure analysis of the title compound, (I), in order to study its conformation in the solid state.



(I)

In compound (I), the indole ring system is planar, with atom C4 deviating by a maximum of 0.022 (4) Å from the weighted least-squares plane through that ring; the dihedral angle formed by the planes of the benzene and pyrrole rings is 1.0 (2) Å. The angles at the fused benzene ring of the indole moiety show the same trend as that observed by Benassi *et al.* (1991) in benzocyclopentanes (average values given in square brackets): C8—C3—C4 120.2 (3) and C3—C8—C7 121.4 (3)° [α 120.6 (6)°], C3—C4—C5 118.4 (4) and C8—C7—C6 116.5 (4)° [β 118.6 (2)°], C4—C5—C6 120.9 (4) and C5—C6—C7 122.6 (4)° [γ 120.8 (2)°], C2—C3—C8 106.6 (3) and N1—C8—C3 107.3 (3)° [ε 110.4 (1)°], and C2—C3—C4 133.2 (3) and N1—C8—C7 131.3 (3)° [δ 128.9 (4)°].

As observed in other related structures (Yokum & Fronczek, 1997; Sankaranarayanan *et al.*, 2000), atom N1 is slightly out of the plane defined by atoms S1, C1 and C8 [deviation 0.141 (2) Å]. The N—Csp^2 bond lengths, *viz.* N1—C1 [1.423 (4) Å] and N1—C8 [1.422 (4) Å], are longer than the mean value reported for N atoms with planar [1.355 (14) Å] and pyramidal [1.416 (18) Å] configurations (Allen *et al.*, 1987). This bond-length increase may be a result of the electron-withdrawing character of the phenylsulfonyl group.

Atom S1 has a distorted tetrahedral configuration, with the angles O2—S1—O1 [120.1 (2)°] and N1—S1—C9 [104.5 (1)°] deviating significantly from ideal tetrahedral values. Similar distortions in the sulfonyl group have been reported and are attributed to the repulsive interaction between the short S=O bonds (Sankaranarayanan *et al.*, 2001; Seshadri *et al.*, 2002). The conformation of the phenylsulfonyl group with respect to the indole moiety is described by the torsion angles O1—S1—N1—C1 [36.3 (3)°], O2—S1—N1—C8 [−35.2 (3)°] and N1—S1—C9—C10 [116.1 (3)°]. This conformation is influenced by the intramolecular C—H···O hydrogen bonds, C7—H7···O2 and C15—H15*A*···O1, involving sulfonyl atoms O1 and O2, which lie almost in the plane of the indole system (Fig. 1 and Table 2). The sulfonyl-bound phenyl ring is orthogonal to the

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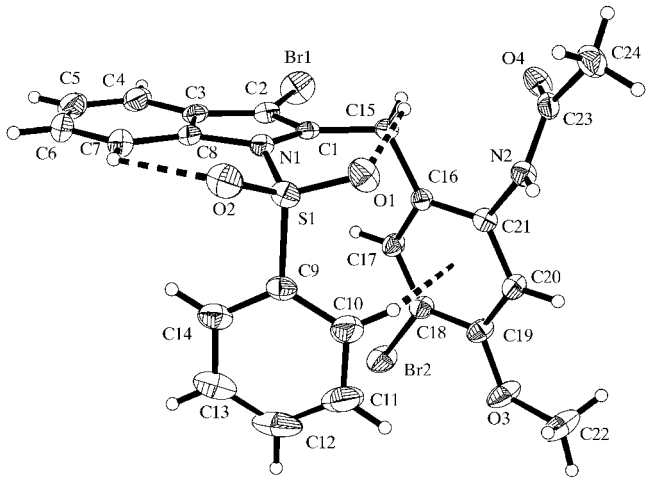

Figure 1
The molecular structure of (I), showing the intramolecular interactions (dashed lines). Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

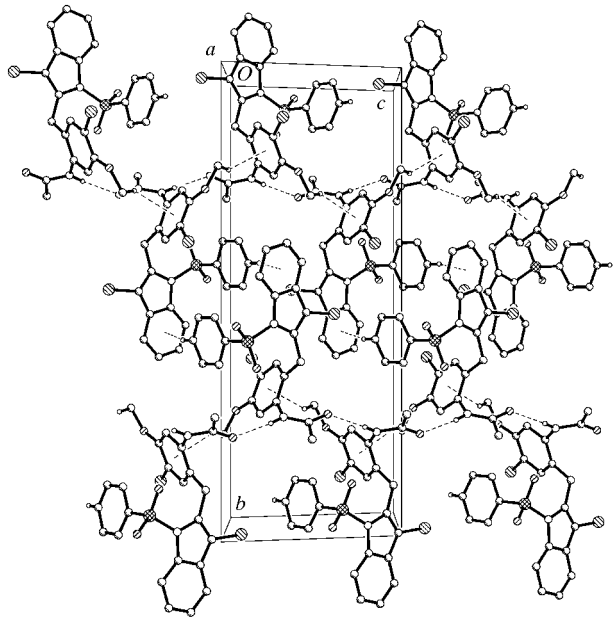

Figure 2
A view of the molecular network of (I) down the *a* axis. For clarity, only the H atoms involved in the hydrogen bonds (dashed lines) are shown.

indole ring system, forming a dihedral angle of 89.09 (8)°. The S—N, S—O and S—C distances are comparable with the values reported for related phenylsulfonylindoles (Sankaranarayanan *et al.*, 2001; Seshadri *et al.*, 2002)

The conformation of the attachment of the benzyl substituent to the indole ring system is described by the N1—C1—C15—C16 torsion angle of 85.9 (3)°; the C1—C15—C16—C17 torsion angle of 38.6 (4)° shows how the phenyl ring of the benzyl moiety is oriented. The mean plane through the acetylamido group makes a dihedral angle of 57.0 (1)° with the phenyl ring of the benzyl moiety. The low value [10.1 (5)°] of the C20—C19—O3—C22 torsion angle is in agreement with the tendency shown by the methoxy group to be coplanar with phenyl, as is usually seen in all the anisoles (Domiano *et al.*, 1979). The sum of the angles around atom N2 is 360°, indicating sp^2 hybridization. The N2—C21 bond length of 1.420 (4) Å is closer to the average C_{ar}—Nsp^3(pyramidal) value of 1.419 (17) Å than to the C_{ar}—Nsp^2(planar) value of 1.353 (7) Å (Allen *et al.*, 1987). This is probably due to some lack of accuracy in the previous data, while the lack of π conjugation of the N atom with the phenyl ring is indicated by the lack of coplanarity of the acetylamido group and the phenyl ring of the benzyl moiety. The mean planes through the phenyl rings of the benzyl and phenylsulfonyl groups are tilted by 28.7 (1)° and the centroids of these rings are separated by 4.095 (2) Å, indicating the absence of π–π interactions. However, a weak intramolecular C—H$\cdots\pi$ interaction is observed between these rings, with atoms C10 and H10 separated from the centroid of the phenyl ring of the benzyl moiety by 3.244 (4) and 2.92 Å, respectively, with the angle subtended at atom H10 being 102°.

In the crystal of (I), glide-related molecules are linked together by N—H$\cdots$O hydrogen bonds (Table 2) to form molecular chains which extend through the crystal. The molecular chain structure is further stabilized by C—H$\cdots\pi$ interactions involving atom C22 and the phenyl ring of the benzyl moiety of the symmetry-related molecule at (x, $\frac{3}{2}-y$, $z-\frac{1}{2}$). Neighbouring inversion-related chains are interlinked by C—H$\cdots\pi$ interactions involving atom C12 and the benzene ring of the indole moiety at ($-x$, $1-y$, $-z$), to form layers parallel to the *bc* plane (Fig. 2). This interaction results in the formation of centrosymmetrically C—H$\cdots\pi$-bonded dimeric pairs (Table 2). Since the sulfonyl phenyl ring is orthogonal to the indole moiety, the benzene ring of the indole moiety and the symmetry-related phenyl rings are arranged to form a T-shaped structure, with their centroids separated by

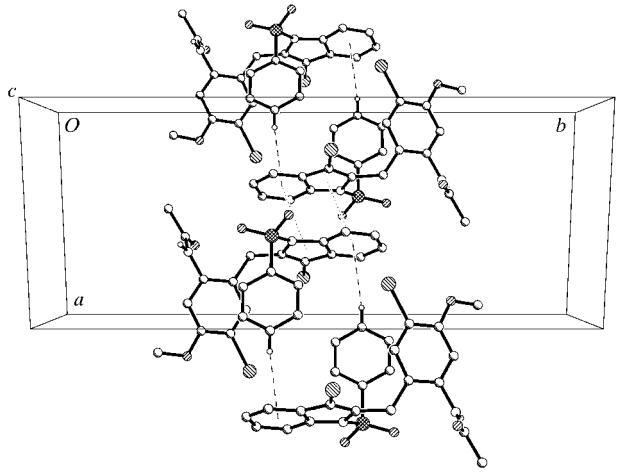

Figure 3
A view of the C—H$\cdots\pi$ hydrogen-bonded dimers and π–π interactions in (I).

5.123 (2) Å. This distance is slightly larger than the separation of 5.10 Å reported for normal T-shaped π–π-stacking interactions (Hobza *et al.*, 1994). These dimeric pairs are packed along the cell diagonal such that the indole moieties of the $(1-x, 1-y, 1-z)$ adjacent pairs face each other, with the centroids of the five- and six-membered rings separated by 3.769 (2) Å, an indication for π–π interactions (Fig. 3). In addition to these interactions, a short intermolecular contact of 3.247 (4) Å is observed between atom Br1 and atom C13 of the molecule translated one unit along the *c* axis.

Experimental

To a solution of [3-bromo-1-(phenylsulfonyl)indol-2-yl]methanol (3.6 g, 10 mmol) in chloroform (200 ml) was added a solution of 4-bromo-3-methoxyacetanilide (2.34 g, 10 mmol) in the same solvent (25 ml), followed by anhydrous magnesium sulfate (10 g) and boron trifluoride etherate (2.0 ml). The resulting solution was refluxed for 3 h. Water (100 ml) was then added, and the organic layer was separated and washed with 20% hydrochloric acid (1 × 50 ml), followed by washing with water and saturated bicarbonate solution. The solvent was removed by distillation after drying over anhydrous sodium sulfate. The residue was chromatographed on a silica-gel column (350 mesh) and eluted successively with 20% ethyl acetate in hexane, followed by 25% and then finally with 30%. The 30% ethyl acetate in hexane eluant gave 2-arylmethylindole, which was then crystallized from hexane–chloroform (2:1) to give crystals of (I) (m.p. 455–457 K).

Crystal data

$C_{24}H_{20}Br_2N_2O_4S$
M_r = 592.30
Monoclinic, $P2_1/c$
a = 10.2647 (11) Å
b = 24.976 (3) Å
c = 9.7963 (11) Å
β = 104.760 (2)°
V = 2428.6 (5) Å^3
Z = 4
D_x = 1.620 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4221 reflections
θ = 2.3–25.0°
μ = 3.46 mm^{-1}
T = 293 (2) K
Block, colourless
0.34 × 0.30 × 0.24 mm

Table 1
Selected geometric parameters (Å, °).

S1—O2	1.419 (2)	N1—C8	1.422 (4)
S1—O1	1.425 (2)	N1—C1	1.423 (4)
S1—N1	1.675 (3)	N2—C23	1.350 (4)
S1—C9	1.759 (3)	N2—C21	1.420 (4)
O4—C23	1.221 (4)		
O2—S1—O1	120.06 (15)	N1—S1—C9	104.48 (14)
O2—S1—N1	106.12 (15)	C5—C6—C7	122.6 (4)
O1—S1—N1	106.70 (13)	C6—C7—C8	116.5 (4)
O2—S1—C9	109.40 (15)	C1—C15—C16	115.9 (2)
O1—S1—C9	108.91 (16)		
O2—S1—N1—C8	−35.2 (3)	O2—S1—C9—C10	−130.6 (3)
O1—S1—N1—C8	−164.4 (2)	O1—S1—C9—C10	2.4 (3)
O2—S1—N1—C1	165.4 (2)	N1—C1—C15—C16	85.9 (3)
O1—S1—N1—C1	36.3 (3)	C1—C15—C16—C17	38.6 (4)
O2—S1—C9—C14	49.4 (3)	C22—O3—C19—C20	10.1 (5)
O1—S1—C9—C14	−177.6 (3)		

Data collection

Siemens SMART CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.343, T_{max} = 0.436
15 276 measured reflections
5984 independent reflections
3727 reflections with $I > 2\sigma(I)$
R_{int} = 0.031
θ_{max} = 28.3°
$h = -13 \rightarrow 11$
$k = -33 \rightarrow 17$
$l = -12 \rightarrow 11$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.097
S = 1.00
5984 reflections
301 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0316P)^2 + 2.3420P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.85 e Å^{-3}
$\Delta\rho_{min}$ = −0.74 e Å^{-3}
Extinction correction: *SHELXTL* (Sheldrick, 1997)
Extinction coefficient: 0.0023 (3)

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

*Cg*1 and *Cg*2 denote the centroids of the C3–C8 and C16–C21 rings, respectively.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C7—H7···O2	0.93	2.35	2.928 (5)	120
C10—H10···O1	0.93	2.50	2.886 (5)	105
C15—H15*A*···O1	0.97	2.34	2.886 (4)	115
C15—H15*A*···N2	0.97	2.50	2.936 (4)	107
C15—H15*B*···Br1	0.97	2.89	3.346 (3)	110
N2—H2N···O4^{i}	0.86	2.05	2.843 (3)	154
C10—H10···Cg2	0.93	2.92	3.244 (5)	102
C22—H22*B*···*Cg*2^{i}	0.96	2.85	3.661 (6)	143
C12—H12···*Cg*1^{ii}	0.93	2.88	3.784 (5)	164

Symmetry codes: (i) $x, \frac{3}{2}-y, z-\frac{1}{2}$; (ii) $-x, 1-y, -z$.

The H atoms were fixed geometrically and allowed to ride on the corresponding non-H atoms, with an N—H distance of 0.86 Å and C—H distances in the range 0.93–0.96 Å. The isotropic displacement parameters were set equal to $1.5U_{eq}$(C) for methyl H atoms and $1.2U_{eq}$(C) for all other H atoms. Rotating group refinement was used for the methyl groups.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*, *PARST* (Nardelli, 1995) and *PLATON* (Spek, 2002).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: NA1592). Services for accessing these data are described at the back of the journal.

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