

1-(3-Bromo-1-phenylsulfonyl-1*H*-indol-2-ylmethyl)pyrrolidine-2,5-dione

T. Ravishankar,^a
K. Chinnakali,^{a†}
N. Arumugam,^b
P. C. Srinivasan,^c
Anwar Usman^d and
Hoong-Kun Fun^{d*}

^aDepartment of Physics, Anna University, Chennai 600 025, India, ^bR and D Department, Amrutanjan Ltd, Chennai 600 004, India, ^cDepartment of Organic Chemistry, University of Madras, Guindy Campus, Chennai 600 025, India, and ^dX-ray Crystallography Unit, School of Physics, Universiti Sains Malaysia, 11800 USM, Penang, Malaysia

† Additional correspondence author, email: kali@annauniv.edu

Correspondence e-mail: hkfun@usm.my

Key indicators

Single-crystal X-ray study

$T = 293\text{ K}$

Mean $\sigma(\text{C}-\text{C}) = 0.003\text{ \AA}$

R factor = 0.025

wR factor = 0.071

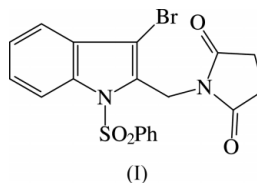
Data-to-parameter ratio = 18.1

For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.

In the title compound, $\text{C}_{19}\text{H}_{15}\text{BrN}_2\text{O}_4\text{S}$, the indole ring system is planar and the S atom has a distorted tetrahedral configuration. The dihedral angle between the sulfonyl-bound phenyl ring and the indole ring system is $71.19(8)^\circ$. The orientations of the phenylsulfonyl and methylpyrrolidine-2,5-dione substituents with respect to the indole moiety are influenced by intramolecular $\text{C}-\text{H}\cdots\text{O}$ and $\text{C}-\text{H}\cdots\text{Br}$ interactions. The pyrrolidine ring adopts an extremely flattened envelope conformation. Weak $\text{C}-\text{H}\cdots\text{O}$ interactions generate rings of motifs $S(5)$, $S(6)$, $R_2^1(5)$ and $R_2^2(9)$.

Comment

Indole derivatives have been found to exhibit antibacterial, antifungal (Wang & Ng, 2002; Singh *et al.*, 2000; Tsotinis *et al.*, 1997; Quetin-Leclercq *et al.*, 1995) and antitumor activities (Andreani *et al.*, 2001; Bradlow *et al.*, 1999; Cirrincione *et al.*, 1999; Tiwari *et al.*, 1994; Dashwood *et al.*, 1994). Poly-halogenated indole derivatives exhibit marked antimicrobial activity against Gram-positive and Gram-negative bacteria, also fungi (Piscopo *et al.*, 1990; Piscopo *et al.*, 1990). Some of the indole alkaloids extracted from plants possess interesting cytotoxic, antitumor or antiparasitic properties (Quetin-Leclercq, 1994; Mukhopadhyay *et al.*, 1981). The title compound, (I), an indole derivative, dissolved in ethyl acetate is found to exhibit relative antibacterial activity against *E. coli* with MIC (Minimum Inhibitory Concentration) of 1024 and $2048\text{ }\mu\text{g ml}^{-1}$ (Ravishankar, Chinnakali, Arumugam & Srinivasan, 2003). As part of our investigations on indole derivatives, we have undertaken the X-ray structural analysis of (I).



The indole ring system in (I) (Fig. 1) is planar, with a maximum deviation of $0.033(1)\text{ \AA}$ for atom C1. The $\text{N}-\text{Csp}^2$ bond lengths, *viz.* $\text{N1}-\text{C1}$ [$1.4258(18)\text{ \AA}$] and $\text{N1}-\text{C8}$ [$1.4175(18)\text{ \AA}$], are longer than the mean value reported for N atoms with planar [$1.355(14)\text{ \AA}$] and pyramidal [$1.416(18)\text{ \AA}$] configurations (Allen *et al.*, 1987). This bond length increase may be a result of the electron-withdrawing character of the phenylsulfonyl group. The bond angles at atoms C3–C8 of the indole moiety show the same trend as that observed by Benassi *et al.* (1991) in benzocyclopentanes; these values also

Received 8 October 2003

Accepted 29 October 2003

Online 8 November 2003

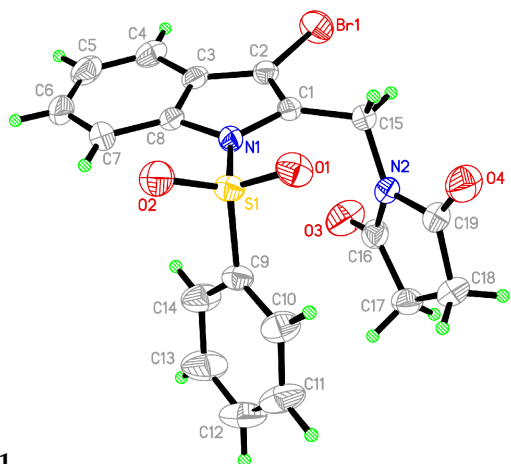


Figure 1
The structure of the title compound, showing the atom-numbering scheme and 50% probability displacement ellipsoids.

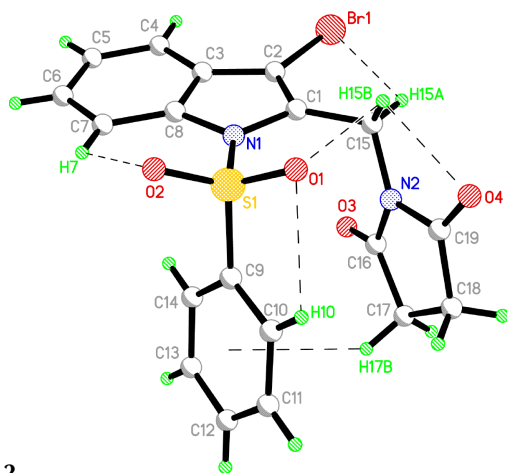


Figure 2
A view of the intramolecular interactions in the title compound.

agree with the corresponding values in other indole derivatives (Sankaranarayanan *et al.*, 2001; Seshadri *et al.*, 2002).

As a result of the repulsive interaction between the short S=O bonds, atom S1 has a distorted tetrahedral configuration, with angles O2–S1–O1 [119.03 (8)°] and N1–S1–C9 [106.02 (7)°] deviating significantly from ideal tetrahedral values. The orientation of the phenylsulfonyl group with respect to the indole moiety is described by the torsion angles O1–S1–N1–C1 = 23.50 (14)°, O2–S1–N1–C8 = –23.42 (14)° and N1–S1–C9–C10 = 141.57 (13)°. This orientation may be influenced by the weak intramolecular C–H···O interactions, C7–H7···O2, C15–H15B···O1 and C10–H10···O1 (Table 2), involving sulfonyl atoms O1 and O2; the latter deviate by 0.724 (1) and 0.775 (1) Å, respectively, from the plane of the indole system. As seen in Fig. 2, each of these interactions generates rings of graph-set motif $S(5)$ or $S(6)$ (Bernstein *et al.*, 1995; Etter, 1990). The dihedral angle between the sulfonyl-bound phenyl ring and the indole ring system is 71.19 (8)°. The S–N, S–O and S–C distances are comparable with the values reported for related phenylsulfonylindoles (Ravishankar, Chinnakali, Arumugam, Srinivasan *et al.*, 2003; Sankaranarayanan *et al.*, 2001; Seshadri *et al.*, 2002).

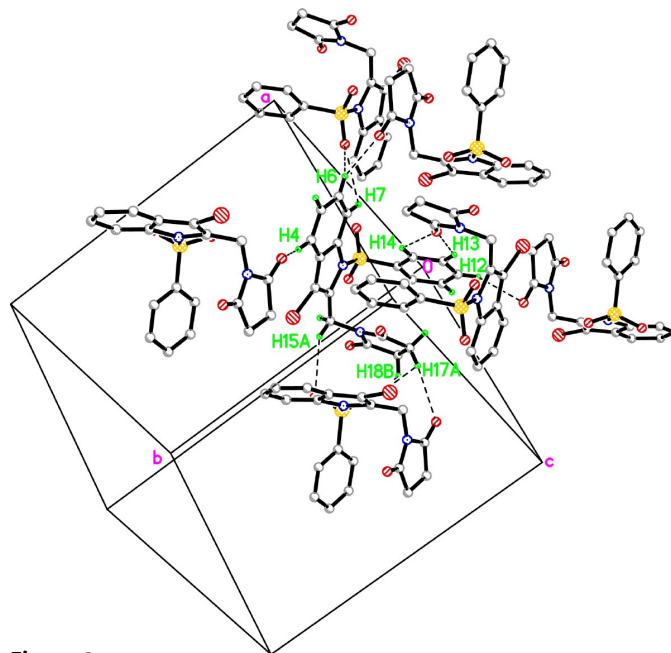


Figure 3
A view of the intermolecular C–H···O interactions in the title compound. Only the H atoms involved in the interactions are labeled.

The torsion angle N1–C1–C15–N2 of 57.7 (2)° describes the orientation of the methyl pyrrolidine-2,5-dione substituent with respect to the indole ring system. This orientation may be influenced by the weak intramolecular interactions, C15–H15A···Br1, C15–H15B···O4 and C15–H15B···O1, which generate rings of graph-set motif $S(5)$ or $S(6)$ (Fig. 2). The pyrrolidine ring adopts an extremely flattened envelope conformation, with atom C16 deviating by 0.148 (2) Å from the mean plane through the remaining atoms in that ring. The sum of the angles around N2 is 359.1°, indicating sp^2 hybridization. However, the N2–C19 [1.3871 (19) Å] and N2–C16 [1.390 (2) Å] distances are intermediate between the average C_{ar} – N_{sp^3} (pyramidal) [1.419 (17) Å] and C_{ar} – N_{sp^2} (planar) [1.353 (7) Å] distances reported by Allen *et al.* (1987). The dihedral angle between the mean planes through the pyrrolidine ring and the phenyl ring of the phenylsulfonyl group is 11.42 (10)°; the centroids of these rings are separated by 3.843 (1) Å. An intramolecular C–H··· π interaction is observed between these two rings, with atom H17B separated by 2.87 Å (Table 2) from the centroid of phenyl ring C9–C14.

The crystal structure is stabilized by weak C–H···O interactions (Table 2 and Fig. 3). The C–H···O interactions involving symmetry-related O1, O2 and O3 atoms constitute pairs of bifurcated acceptor bonds, generating rings of graph-set motif $R_2^1(5)$ (Table 3); two $R_2^2(9)$ motifs are also formed. In addition to these interactions, a short intermolecular contact of 2.958 (2) Å is observed between atom O1 and symmetry-related atom C16 at $(x, \frac{1}{2} - y, z - \frac{1}{2})$.

Experimental

To a solution of 1-phenylsulfonyl-3-phenylthioindol-2-ylmethanol (5 mmol) in chloroform (40 ml), a solution of succinimide (5 mmol)

in the same solvent was added, followed by anhydrous magnesium sulfate (4 g) and boron trifluoride etherate (0.5 ml). The resulting solution was refluxed for 3 h. Water (10 ml) was then added and the organic layer was separated. 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 hexane–benzene (1:1), benzene and finally with acetone–benzene (1:9). The acetone–benzene eluant yielded the title compound, which was then crystallized from ethyl acetate–hexane (2:1).

Crystal data

$C_{19}H_{15}BrN_2O_4S$	$D_x = 1.636 \text{ Mg m}^{-3}$
$M_r = 447.30$	Mo $K\alpha$ radiation
Monoclinic, $P2_1/c$	Cell parameters from 6536 reflections
$a = 11.4561 (5) \text{ \AA}$	$\theta = 2.4\text{--}28.2^\circ$
$b = 15.1588 (7) \text{ \AA}$	$\mu = 2.41 \text{ mm}^{-1}$
$c = 11.6819 (5) \text{ \AA}$	$T = 293 (2) \text{ K}$
$\beta = 116.493 (1)^\circ$	Block, yellow
$V = 1815.65 (14) \text{ \AA}^3$	$0.58 \times 0.42 \times 0.40 \text{ mm}$
$Z = 4$	

Data collection

Siemens SMART CCD area-detector diffractometer	4435 independent reflections
ω scans	3837 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (SADABS; Sheldrick, 1996)	$R_{\text{int}} = 0.016$
$T_{\text{min}} = 0.287$, $T_{\text{max}} = 0.382$	$\theta_{\text{max}} = 28.3^\circ$
11117 measured reflections	$h = -13 \rightarrow 15$
	$k = -20 \rightarrow 13$
	$l = -15 \rightarrow 15$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0359P)^2 + 0.5632P]$
$R[F^2 > 2\sigma(F^2)] = 0.026$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.071$	$(\Delta/\sigma)_{\text{max}} = 0.001$
$S = 1.05$	$\Delta\rho_{\text{max}} = 0.28 \text{ e \AA}^{-3}$
4435 reflections	$\Delta\rho_{\text{min}} = -0.44 \text{ e \AA}^{-3}$
245 parameters	Extinction correction: <i>SHELXTL</i>
H-atom parameters constrained	Extinction coefficient: 0.0086 (6)

Table 1

Selected geometric parameters (\AA , $^\circ$).

Br1–C2	1.8726 (15)	O4–C19	1.210 (2)
S1–O2	1.4256 (12)	N1–C8	1.4175 (18)
S1–O1	1.4273 (12)	N1–C1	1.4258 (18)
S1–N1	1.6665 (12)	N2–C19	1.3871 (19)
S1–C9	1.7633 (15)	N2–C16	1.390 (2)
O3–C16	1.201 (2)	N2–C15	1.4666 (19)
O2–S1–O1	119.03 (8)	C16–N2–C15	124.56 (13)
O2–S1–N1	106.30 (7)	C4–C3–C8	119.93 (15)
O1–S1–N1	107.43 (7)	C4–C3–C2	133.34 (15)
O2–S1–C9	108.86 (7)	C8–C3–C2	106.72 (13)
O1–S1–C9	108.46 (8)	C5–C4–C3	118.08 (17)
N1–S1–C9	106.02 (7)	C4–C5–C6	121.43 (16)
C8–N1–C1	108.45 (11)	C7–C6–C5	121.73 (16)
C8–N1–S1	124.60 (10)	C6–C7–C8	116.94 (16)
C1–N1–S1	126.82 (10)	C7–C8–C3	121.88 (14)
C19–N2–C16	112.81 (13)	C7–C8–N1	130.87 (14)
C19–N2–C15	121.68 (13)	C3–C8–N1	107.24 (12)
O2–S1–N1–C8	–23.42 (14)	O2–S1–C9–C10	–104.44 (14)
O1–S1–N1–C8	–151.86 (12)	O1–S1–C9–C10	26.45 (15)
O2–S1–N1–C1	151.95 (12)	C19–N2–C15–C1	–140.86 (14)
O1–S1–N1–C1	23.50 (14)	C16–N2–C15–C1	51.1 (2)
O2–S1–C9–C14	70.94 (16)	C2–C1–C15–N2	–123.55 (16)
O1–S1–C9–C14	–158.16 (15)	N1–C1–C15–N2	57.7 (2)

Table 2

Hydrogen-bonding geometry (\AA , $^\circ$).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
C7–H7 \cdots O2	0.93	2.36	2.901 (2)	117
C10–H10 \cdots O1	0.93	2.55	2.911 (2)	104
C15–H15A \cdots Br1	0.97	2.83	3.349 (1)	115
C15–H15B \cdots O1	0.97	2.50	2.900 (2)	105
C15–H15B \cdots O4	0.97	2.48	2.857 (2)	103
C4–H4 \cdots O4 ⁱ	0.93	2.70	3.541 (2)	152
C7–H7 \cdots O2 ⁱⁱ	0.93	2.82	3.333 (3)	115
C6–H6 \cdots O2 ⁱⁱ	0.93	2.88	3.377 (2)	115
C6–H6 \cdots O4 ⁱⁱⁱ	0.93	2.68	3.478 (2)	145
C12–H12 \cdots O4 ^{iv}	0.93	2.70	3.500 (3)	144
C14–H14 \cdots O3 ^v	0.93	2.79	3.317 (2)	117
C13–H13 \cdots O3 ^v	0.93	2.50	3.181 (2)	131
C15–H15A \cdots O2 ^{vi}	0.97	2.67	3.481 (2)	142
C17–H17A \cdots O1 ^{vi}	0.97	2.67	3.053 (2)	104
C17–H17A \cdots O4 ^{vi}	0.97	2.67	3.603 (3)	162
C18–H18B \cdots O1 ^{vi}	0.97	2.81	3.189 (2)	104
C17–H17B \cdots Cg4	0.97	2.87	3.635 (2)	136

Symmetry codes: (i) $1+x, \frac{1}{2}-y, \frac{1}{2}+z$; (ii) $1-x, -y, -z$; (iii) $1-x, y-\frac{1}{2}, \frac{1}{2}-z$; (iv) $-x, y-\frac{1}{2}, \frac{1}{2}-z$; (v) $1-x, -y, 1-z$; (vi) $x, \frac{1}{2}-y, \frac{1}{2}+z$. Cg4 is the centroid of phenyl ring C9–C14.

Table 3

List of graph-set motifs generated by pairs of hydrogen bonds.

Hydrogen bond 1	Hydrogen bond 2	Ring
C7–H7 \cdots O2		S(6)
C10–H10 \cdots O1		S(5)
C15–H15A \cdots Br1		S(5)
C15–H15B \cdots O1		S(6)
C15–H15B \cdots O4		S(5)
C7–H7 \cdots O2 ⁱⁱ	C6–H6 \cdots O2 ⁱⁱ	$R_2^2(5)$
C14–H14 \cdots O3 ^v	C13–H13 \cdots O3 ^v	$R_2^2(5)$
C17–H17A \cdots O1 ^{vi}	C18–H18B \cdots O1 ^{vi}	$R_2^2(5)$
C15–H15A \cdots O2 ^{vi}	C17–H17A \cdots O1 ^{vi}	$R_2^2(9)$
C15–H15A \cdots O2 ^{vi}	C18–H18B \cdots O1 ^{vi}	$R_2^2(9)$

Symmetry codes are as given in Table 2.

H atoms were positioned geometrically and were treated as riding on their parent C atoms, with C–H distances of 0.93 (aromatic) and 0.97 \AA (methylene), and $U_{\text{iso}}(\text{H})$ values set at $1.2U_{\text{eq}}(\text{C})$.

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, 2003).

AU thanks Universiti Sains Malaysia for a Visiting Post-doctoral Fellowship. HKF thanks the Malaysian Government and Universiti Sains Malaysia for research grant R&D No. 305/PFIZIK/610961.

References

- Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.
- Andreani, A., Granaiola, M., Leoni, A., Locatelli, A., Morigi, R., Rambaldi, M., Giorgi, G., Salvini, L. & Garaliene, V. (2001). *Anticancer Drug Des.* **16**, 167–174.
- Benassi, R., Ianelli, S., Nardelli, M. & Taddei, F. (1991). *J. Chem. Soc. Perkin Trans. 2*, pp. 1381–1386.

- Bernstein, J., Davis, R. E., Shimon, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
- Bradlow, H. L., Sepkovic, D. W., Telang, N. T. & Osborne, M. P. (1999). *Ann. N. Y. Acad. Sci.* **889**, 204–213.
- Cirrincone, G., Almerico, A. M., Barraja, P., Diana, P., Lauria, A., Passannanti, A., Musiu, C., Pani, A., Murtas, P., Minnei, C., Marongiu, M. E. & La Colla, P. (1999). *J. Med. Chem.* **42**, 2561–2568.
- Dashwood, R. H., Fong, A. T., Arbogast, D. N., Bjeldanes, L. F., Hendricks, J. D. & Bailey, G. S. (1994). *Cancer Res.* **54**, 3617–3619.
- Etter, M. C. (1990). *Acc. Chem. Res.* **23**, 120–126.
- Mukhopadhyay, S., Handy, G. A., Funayama, S. & Cordell, G. A. (1981). *J. Nat. Prod.* **44**, 696–700.
- Nardelli, M. (1995). *J. Appl. Cryst.* **28**, 659.
- Piscopo, E., Diurno, M. V., Mazzoni, O., Ciaccio, A. M. (1990). *Boll. Soc. Ital. Biol. Sper.* **66**, 1181–1186.
- Piscopo, E., Diurno, M. V., Mazzoni, O., Ciaccio, A. M. & Veneruso, G. (1990). *Boll. Soc. Ital. Biol. Sper.* **66**, 1187–1191.
- Quetin-Leclercq, J. (1994). *J. Pharm. Belg.* **49**, 181–192.
- Quetin-Leclercq, J., Favel, A., Balansard, G., Regli, P. & Angenot, L. (1995). *Planta Med.* **61**, 475–477.
- Ravishankar, T., Chinnakali, K., Arumugam, N. & Srinivasan, P. C. (2003). Unpublished results.
- Ravishankar, T., Chinnakali, K., Arumugam, N. & Srinivasan, P. C., Usman, A. & Fun, H.-K. (2003). *Acta Cryst. C* **59**, o137–o140.
- Sankaranarayanan, R., Velmurugan, D., Shanmuga Sundara Raj, S., Fun, H.-K., Narasinga Rao, S., Kannadasan, S. & Srinivasan, P. C. (2001). *Acta Cryst. C* **57**, 569–571.
- Seshadri, P. R., Velmurugan, D., Govindaraj, J., Kannadasan, S., Srinivasan, P. C., Shanmuga Sundara Raj, S., Fun, H.-K. & Kim, M. J. (2002). *Acta Cryst. C* **58**, o700–o703.
- Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.
- Sheldrick, G. M. (1997). *SHELXTL*. Version 5.1. Bruker AXS Inc., Madison, Wisconsin, USA.
- Siemens (1996). *SMART* and *SAINT*. Versions 4.0. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
- Singh, U. P., Sarma, B. K., Mishra, P. K. & Ray, A. B. (2000). *Folia Microbiol.* **45**, 173–176.
- Spek, A. L. (2003). *PLATON*. University of Utrecht, The Netherlands.
- Tiwari, R. K., Guo, L., Bradlow, H. L., Telang, N. T. & Osborne, M. P. (1994). *J. Natl Cancer Inst.* **86**, 126–131.
- Tsotinis, A., Varvaresou, A., Calogeropoulou, T., Siatra-Papastaikoudi, T. & Tiligada, A. (1997). *Arzneim. Forsch.* **47**, 307–310.
- Wang, H. X. & Ng, T. B. (2002). *Comput. Biochem. Physiol. C, Toxicol. Pharmacol.* **132**, 261–268.