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Indole-3-spiro-*N*-methyl-2′-pyrrolidine-3′-spiro-9″-anthracene-2,10″-dione

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.002 Å
R factor = 0.044
wR factor = 0.124
Data-to-parameter ratio = 14.4

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

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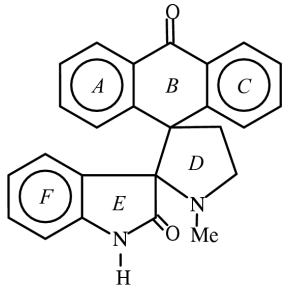
The asymmetric unit of the title compound, $C_{25}H_{20}N_2O_2$, contains an enantiomeric pair of molecules, which are linked by N—H···O hydrogen bonds involving N—H and C=O groups of the pyrrole ring. In both molecules, the central six-membered ring of the anthrone moiety adopts a boat conformation, the pyrrolidine ring adopts an envelope conformation and the five-membered ring in the oxindole moiety is slightly distorted from planarity. Both the anthrone and oxindole moieties are almost perpendicular to the pyrrolidine ring.

Comment

Anthrone derivatives are used to study the reaction rate of acid catalysts (Ghosh *et al.*, 1993). The indole ring system is present in a number of natural products (Nigović *et al.*, 2000), many of which are found to possess psychotropic (Grinev *et al.*, 1978) and antidepressant (Grinev *et al.*, 1984) properties. They also exhibit antimicrobial (El-Sayed *et al.*, 1986; Gadaginamath & Patil, 1999), antitumor (Schollmeyer *et al.*, 1995), antibacterial (Okabe & Adachi, 1998) and anti-inflammatory (Rodriguez *et al.*, 1985; Polletto *et al.*, 1974) activities. They have been proven to display high aldose reductase inhibitory activity (Rajeswaran *et al.*, 1999). The pyrrolidine skeleton occurs in many families of biologically important compounds. The resulting functionality, due to ease of substitution and therefore modification at several positions (Baldwin *et al.*, 1994*a*,*b*), has been utilized to synthesize compounds with varying properties. For example, several unusual amino acids, which contain the pyrrolidine motif, were investigated (Galeazzi *et al.*, 1999) and optically active pyrrolidines have been used as intermediates in controlled asymmetric synthesis (Suzuki *et al.*, 1994). In view of its medicinal importance, the crystal and molecular structure determination of the title compound, (I), was carried out by X-ray diffraction.



(I)

The asymmetric unit of (I) contains two crystallographically independent molecules (1 and 2), with almost identical

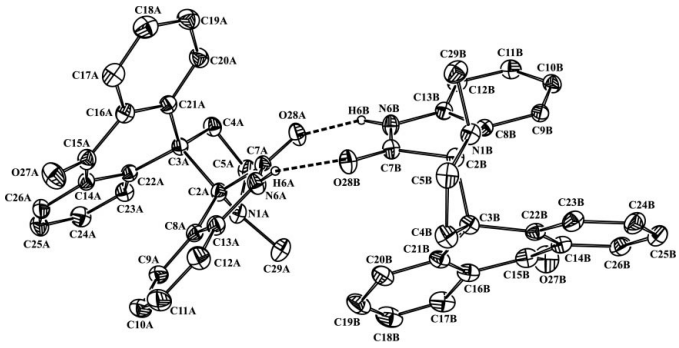


Figure 1
The structures of the two independent molecules of the title compound, showing 30% probability displacement ellipsoids and the atom-numbering scheme for the non-H atoms, and illustrating the N—H···O hydrogen-bonded dimer.

geometry. The superposition of molecule 1 and the inverted image of molecule 2, using *BIOSYM* (Biosym/MSI, 1995), shows that the r.m.s. deviation for all the non-H atoms in the molecules is 0.19 Å. The bond lengths in the pyrrolidine moiety are slightly longer than the normal values and are comparable with those already reported (Jeyabharathi *et al.*, 2001; Gzella & Wrzeciono, 1990). This may be due to the spiro-atom character and the steric effect of the bulky groups substituted at C2 and C3. In the benzene ring of the oxindole system, the endocyclic C—C—C angles at C12 and C9 are slightly narrowed from 120°, while those at C11 and C13 are slightly widened from 120°. This effect may be caused by the fusion of the smaller pyrrole ring to the six-membered benzene ring. A similar effect has also been observed by Sivaraman *et al.* (1994*a*,*b*, 1996), Govindasamy *et al.* (1999) and Sankaranarayanan *et al.* (2000, 2001).

In both the molecules, ring *B* adopts a boat conformation and ring *D* is in an envelope conformation. Ring *E* in molecule 1 is planar, and in molecule 2 it is slightly twisted along the C7*B*—C2*B* bond. The conformations were confirmed by their puckering parameters (Cremer & Pople, 1975): for ring *B*, q_2 = 0.303 (1), q_3 = 0.049 (1), Q_T = 0.307 (1) Å and φ_2 = −4.2 (3)° for molecule 1, and q_2 = 0.373 (2), q_3 = −0.071 (1), Q_T = 0.380 (2) Å and φ_2 = −177.5 (2)° for molecule 2; for ring *D*, q_2 = 0.418 (1) Å and φ_2 = 143.6 (2)° for molecule 1, and q_2 = 0.407 (2) Å and φ_2 = −39.7 (2)° for molecule 2.

The oxindole moiety is not strictly planar and the dihedral angle formed by the pyrrole and benzene planes is 5.56 (5)° for molecule 1 and 4.90 (6)° for molecule 2. A similar effect has also been observed in related indoles (Sankaranarayanan *et al.*, 2001; Yokum & Fronczek, 1997; Beddoes *et al.*, 1986). The anthrone moiety is folded about the line passing through atoms C3 and C15, and the dihedral angle between the two halves is 22.79 (3) and 29.59 (3)° for molecules 1 and 2, respectively. The dihedral angles between the outer rings *A* and *C* of the anthrone moiety is 22.23 (5) and 29.83 (6)° for molecules 1 and 2, respectively. The pyrrolidine moiety makes dihedral angles of 83.62 (4) and 80.84 (5)° with the oxindole rings in molecules 1 and 2, respectively, corresponding to nearly perpendicular configurations. The anthrone ring is also nearly perpendicular to the pyrrolidine ring, with dihedral angles of 76.36 (4) and 74.42 (5)° in molecules 1 and 2, respectively. The dihedral angles between the anthrone and oxindole moieties are 53.08 (3) and 40.02 (3)° in molecules 1 and 2, respectively. In the crystal, the molecules 1 and 2 form an enantiomeric pair linked by N—H···O hydrogen bonds involving N—H and C=O groups of the pyrrole ring. The dimers are interlinked by a network of weak C—H···O hydrogen bonds (Jeffrey, 1997) (see Table 1).

Experimental

A mixture of 9-methylene-anthrone (3 mmol) in sarcosine (4.5 mml) and isatin (3 mmol) was refluxed for 6.5 h until the starting material had disappeared, as evidenced by thin-layer chromatography. After the reaction, the solvent was evaporated *in vacuo* and the resulting crude product was purified by column chromatography, using a hexane–ethyl acetate mixture (8:2). Crystals (m.p. 445–447 K) suitable for X-ray diffraction studies were grown by slow evaporation from a chloroform–methanol (2:1) solvent system.

Crystal data

$C_{25}H_{20}N_2O_2$
M_r = 380.43
Monoclinic, $P2_1/c$
a = 8.338 (1) Å
b = 28.339 (4) Å
c = 17.045 (2) Å
β = 108.18 (1)°
V = 3826.5 (9) Å^3
Z = 8
D_x = 1.321 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 15–30°
μ = 0.67 mm^{-1}
T = 293 (2) K
Needle, orange
0.36 × 0.30 × 0.13 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
ω–2θ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.794, T_{max} = 0.918
8049 measured reflections
7521 independent reflections
6411 reflections with $I > 2\sigma(I)$
R_{int} = 0.025
θ_{max} = 72.0°
$h = 0 \rightarrow 10$
$k = -34 \rightarrow 0$
$l = -21 \rightarrow 19$
3 standard reflections
frequency: 120 min
intensity decay: <1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.044
$wR(F^2)$ = 0.124
S = 1.04
7521 reflections
524 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.068P)^2 + 0.7213P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.21 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0047 (2)

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N6*A*—H6*A*···O28*B*	0.86	2.00	2.832 (2)	161
N6*B*—H6*B*···O28*A*	0.86	2.08	2.883 (2)	155
C23*A*—H23*A*···O28*A*	0.93	2.49	3.000 (2)	115
C23*B*—H23*B*···O28*B*	0.93	2.74	3.093 (2)	104
C20*A*—H20*A*···O27*A*^{i}	0.93	2.85	3.641 (2)	144
C5*A*—H5*B*···O27*A*^{i}	0.97	2.95	3.872 (2)	159
C11*A*—H11*A*···O27*A*^{ii}	0.93	2.74	3.461 (2)	135
C12*A*—H12*A*···O27*B*^{iii}	0.93	2.88	3.702 (2)	149
C18*B*—H18*B*···O28*A*^{iv}	0.93	2.95	3.643 (2)	133
C19*B*—H19*B*···O27*B*^{v}	0.93	2.56	3.403 (2)	151

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

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *SDP* (Frenz, 1978); data reduction: *CAD*-4 *Software*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ZORTEP* (Zsolnai, 1997); software used to prepare material for publication: *PARST*97 (Nardelli, 1995).

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