organic compounds

1-(1*H*-Indol-3-ylcarbonyl)-*N*-(4-methoxybenzyl)formamide

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In the title compound, $C_{18}H_{16}N_2O_3$, the indole ring is planar and the two adjacent carbonyl groups are mutually *trans* oriented with a torsion angle of 144.8 (3)°. The single C—C bond linking the two carbonyl functionalities is 1.539 (4) Å. Molecules are linked into a two-dimensional network by intermolecular N—H···O hydrogen bonds.

Comment

N-(Indol-3-ylglyoxylyl)benzylamine derivatives exhibit high affinity for the benzodiazepine receptor (BzR), with K_i values ranging from 67 to 11 nM (Da Settimo *et al.*, 1996). In addition to their biological activities, these *N*-(indol-3-ylglyoxylyl)-benzylamines are very good synthons for the preparation of *N*-benzyl-substituted tryptamines (Da Settimo *et al.*, 1996). The title compound, (I), is a synthetic intermediate in the preparation of *N*-(4-methoxybenzyl)tryptamine and is prepared by treating indole with oxalyl chloride followed by quenching with 4-methoxybenzylamine. The product was characterized by spectroscopic analysis and its X-ray structure determination was carried out to study the conformation of the molecule.

X-ray crystallography confirmed the molecular structure and atom connectivity for (I), and selected geometric parameters are listed in Table 1. The indole ring is planar, with

(I)
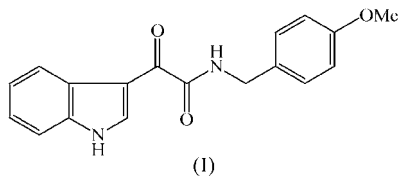
bond distances and angles comparable to those previously reported for indole derivatives (Mason *et al.*, 2003). The two carbonyl groups are in a *trans* orientation, with an O1—C9—C10—O2 torsion angle of 144.8 (3)°. Since the C9=O1 group is coplanar with the indole nucleus, extended conjugation is present, from atom O1 through to the indole ring. This is also

evident from the C2—C9 bond length [1.437 (4) Å], which is shortened in comparison with the standard value for a single bond connecting a C_{ar} atom to a Csp^2 atom [1.470 (15) Å; Wilson, 1992]. Because of the above, the C9—C10 bond length of 1.539 (4) Å is longer than expected, the characteristic value for a Csp^2—Csp^2 bond being 1.50 Å (Zukerman-Schpector *et al.*, 1994).

The C10—N11 bond length [1.337 (4) Å] and the bond angles around atom N11 suggest that the lone pair of electrons on N11 undergoes delocalization, affording double-bond character to the C10—N11 bond and forcing the O2/C10/N11/C12 atoms into an almost planar conformation. The 4-methoxyphenyl ring makes a dihedral angle of 74.55 (12)° with the amide group. The observed O3—C16 [1.376 (3) Å] and O3—C19 [1.428 (3) Å] bond lengths are comparable with values found for aromatic methoxy O—CH$_3$ bonds. There is an asymmetry of the exocyclic angles at C16 for (I) [O3—C16—C15 = 115.1 (3)° and O3—C16—C17 = 124.8 (3)°], as is typical of anisoles. This is caused by the tendency of the methoxy group to be coplanar with the benzene ring, due to conjugation of the O3 lone pair with the benzene ring (Domiano *et al.*, 1979).
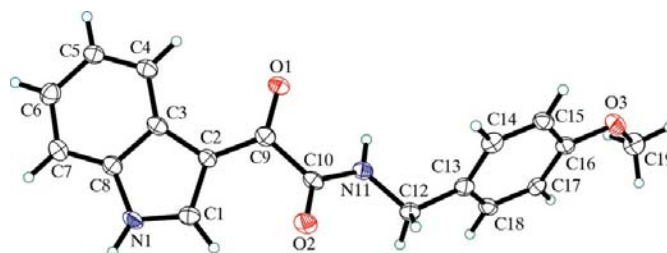

Figure 1
A view of the asymmetric unit of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.
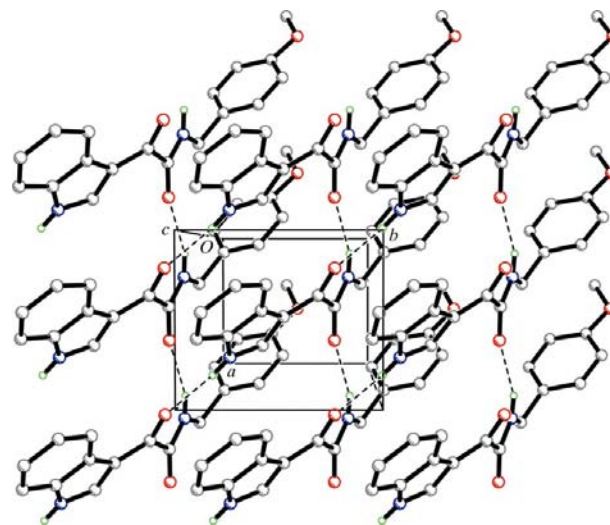

Figure 2
A packing diagram for (I), viewed approximately down the *c* axis, showing the hydrogen-bonding interactions (dashed lines). For clarity, only those H atoms involved in hydrogen bonding are shown.

organic compounds

The packing of compound (I), as viewed down the *c* axis, is illustrated in Fig. 2. Amides participate in extensive hydrogen bonding, but here, in addition to secondary amide functionality, a carbonyl group acts as a hydrogen-bond acceptor and the glyoxylamide torsion angle is variable. The molecules are linked by intermolecular hydrogen bonds [N1—H1N···O1[i] and N11—H11···O2[ii]; symmetry codes: (i) $1 + x$, $y - 1$, z; (ii) $x - 1$, y, z], resulting in a two-dimensional network, details of which are given in Table 2. In addition, two weak intramolecular hydrogen bonds (N11—H11···O1 and C1—H1···O2; Table 2) form five- and six-membered rings, respectively. These weak hydrogen bonds introduce rigidity into the system (Black *et al.*, 1996).

Experimental

The title compound was prepared according to the previously reported procedure of Da Settimo *et al.* (1996). The compound was obtained as pale-yellow crystals. ^{1}H NMR (DMSO): δ 3.73 (*s*, 3H), 4.35 (*d*, 2H), 6.90 (*d*, 2H), 7.20–7.30 (*m*, 4H), 7.6 (*m*, 1H), 8.3 (*m*, 1H), 8.76 (*d*, 1H), 9.23 (*t*, 1H), 12.22 (*s*, 1H); ^{13}C NMR (DMSO): δ 41.5, 55.0, 112.1, 112.4, 113.6, 121.1, 122.4, 123.3, 126.0, 128.6, 130.8, 136.1, 138.3, 158.1, 163.3, 181.9.

Crystal data

$C_{18}H_{16}N_2O_3$	$D_x = 1.407$ Mg m^{-3}
$M_r = 308.33$	Mo $K\alpha$ radiation
Monoclinic, Pn	Cell parameters from 1741
$a = 4.9402$ (2) Å	reflections
$b = 5.6847$ (3) Å	$\theta = 1.0$–27.5°
$c = 25.9862$ (13) Å	$\mu = 0.10$ mm^{-1}
$\beta = 94.495$ (2)°	$T = 90.0$ (2) K
$V = 727.54$ (6) Å^3	Slab, colourless
$Z = 2$	$0.25 \times 0.22 \times 0.08$ mm

Data collection

Nonius KappaCCD area-detector diffractometer	1663 independent reflections
ω scans at fixed $\chi = 55°$	1336 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (*SCALEPACK*; Otwinowski & Minor, 1997)	$R_{int} = 0.037$
	$\theta_{max} = 27.5°$
	$h = -6 \rightarrow 6$
$T_{min} = 0.976$, $T_{max} = 0.992$	$k = -7 \rightarrow 7$
3052 measured reflections	$l = -33 \rightarrow 33$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0385P)^2$
$R[F^2 > 2\sigma(F^2)] = 0.039$	$+ 0.1457P]$
$wR(F^2) = 0.091$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.07$	$(\Delta/\sigma)_{max} < 0.001$
1663 reflections	$\Delta\rho_{max} = 0.21$ e Å^{-3}
210 parameters	$\Delta\rho_{min} = -0.21$ e Å^{-3}
H-atom parameters constrained	Extinction correction: *SHELXL97*
	Extinction coefficient: 0.019 (5)

All H atoms were located in difference Fourier syntheses, and were subsequently positioned geometrically and refined with a riding model. Bond distances to parent atoms were set at 0.95 (C_{ar}—H), 0.98 (C_{Me}—H), 0.99 (C_{sec}—H) or 0.88 Å (N—H), with U_{iso}(H) = $1.2U_{eq}$(C_{ar}—H, C_{sec}—H or N—H) or $1.5U_{eq}$(C_{Me}—H). Friedel opposites were merged before the final cycles of least-squares refinement.

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction:

Table 1
Selected geometric parameters (Å, °).

O1—C9	1.234 (4)	C2—C9	1.437 (4)
O2—C10	1.235 (3)	C9—C10	1.539 (4)
O3—C16	1.376 (3)	C10—N11	1.337 (4)
O3—C19	1.428 (3)	N11—C12	1.466 (4)
C16—O3—C19	117.1 (2)	O2—C10—N11	123.2 (3)
C1—C2—C9	127.2 (3)	O2—C10—O9	121.9 (2)
O1—C9—C2	124.2 (3)	N11—C10—C9	114.9 (2)
O1—C9—C10	118.8 (3)	C10—N11—C12	119.9 (2)
C2—C9—C10	117.0 (2)	N11—C12—C13	112.3 (2)
C1—C2—C9—O1	175.5 (3)	O1—C9—C10—O2	144.8 (3)
C3—C2—C9—O1	−0.2 (5)	O1—C9—C10—N11	−35.2 (4)

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1N···O1[i]	0.88	2.08	2.944 (3)	165
N11—H11···O2[ii]	0.88	2.04	2.881 (3)	159
N11—H11···O1	0.88	2.49	2.787 (3)	100
C1—H1···O2	0.95	2.36	2.888 (4)	115

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

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/PC* (Siemens, 1995); software used to prepare material for publication: *SHELXL97* and local procedures.

References

Black, D. C., Craig, D. C. & McConnell, D. B. (1996). *J. Am. Chem. Soc.* **118**, 8148–8149.

Da Settimo, A., Primofiore, G., Da Settimo, F., Marini, A. M., Novellino, E., Greco, G., Martini, C., Giannaccini, G. & Lucacchini, A. (1996). *J. Med. Chem.* **39**, 5083–5091.

Domiano, P., Nardelli, M., Balsamo, A., Macchia, B. & Macchia, F. (1979). *Acta Cryst.* B**35**, 1363–1372.

Mason, M. R., Barnard, T. S., Segla, M. F., Xie, B. & Kirschbaum, K. (2003). *J. Chem. Crystallogr.* **33**, 531–540.

Nonius (1999). *COLLECT*. Nonius BV, Delft, The Netherlands.

Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.

Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.

Siemens (1995). *XP* in *SHELXTL/PC*. Release 5.03. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Wilson, A. J. C. (1992). Editor. *International Tables for Crystallography*, Vol. C, Table 9.5.1.1. Dordrecht: Kluwer Academic Publishers.

Zukerman-Schpector, J., Pinto, A. Da C., Da Silva, J. F. M. & Da Silva, R. B. (1994). *Acta Cryst.* C**50**, 87–88.