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(10a*S*)-7-Methoxy-1,10a-dihydropyrrolo[1,2-*b*]-isoquinoline-3,10(2*H*,5*H*)-dione

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Key indicators

Single-crystal X-ray study
T = 296 K
Mean σ(C–C) = 0.004 Å
R factor = 0.043
wR factor = 0.111
Data-to-parameter ratio = 9.0

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

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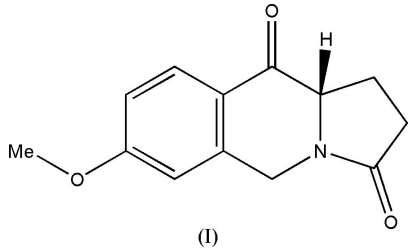
The crystal structure of the title compound, $C_{13}H_{13}NO_3$, is stabilized by dipole–dipole and van der Waals forces. The pyrrolidine ring is almost planar, while the central six-membered ring of the indolizine moiety adopts a sofa conformation.

Comment

Indolizine derivatives are found in medically important compounds, such as calcium channel blockers, cardiovascular agents, spectral sensitizers and novel dyes (Gubin *et al.*, 1992; Poty *et al.*, 1994; Hema *et al.*, 2003). Several polyhydroxylated indolizines are interesting as inhibitors of glycosides (Hempel *et al.*, 1993;Brandi *et al.*, 1995). Furthermore, indolizines have also been tested as antimycobacterial agents against mycobacterial tuberculosis (Gundersen *et al.*, 2003). The structural investigation of the title compound, (I), has been undertaken as part of our study on the conformational changes caused by different substituents on the indolizine ring system. The absolute configuration is known from the synthesis and is depicted in the scheme and figures.



(I)

The crystal structure of (I) (Fig. 1) is stabilized by van der Waals forces; the shortest intermolecular contacts are 3.347 (2) Å for C1···O15($-x+1$, $y-\frac{1}{2}$, $-z$) and 3.298 (4) Å

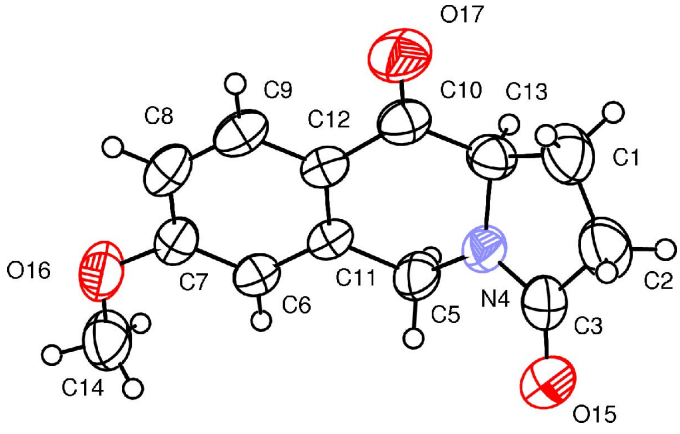


Figure 1
The molecular structure of (I) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

for C5···O17($x+1$, y, z). The isoquinoline moiety is not completely planar, the central *N*-heterocyclic ring being distorted towards a sofa conformation (Nardelli, 1983), with atom N4 displaced by 0.515 (2) Å from the mean plane defined by atoms C5/C11/C12/C10/C13. The oxopyrrolidine ring is almost planar. Atom N4 is sp^2-hybridized, as evidenced by the sum of the valence angles around it (360.0°). These data are consistent with conjugation of the lone-pair electrons on N4 with the adjacent carbonyl, similar to what is observed for amides. The bond length of the carbonyl groups C10═O17 and C3═O15 of 1.219 (2) and 1.225 (3) Å, respectively, are somewhat longer than typical carbonyl bonds. This may be due to the fact that atoms O17 and O15 participate in intermolecular van der Waals forces.

Experimental

The title compound was prepared by intramolecular Friedel–Crafts acylation of the chloride of the starting enantiopure 5-oxoproline derivative, which in turn was obtained from (*S*)-glutamic acid (Marchalín *et al.*, 1998). A stirred solution of (*S*)-(+)-*N*-(3-methoxybenzyl)-5-oxoproline (2.5 g, 10 mmol) in dry dichloromethane (30 ml) was treated rapidly with thionyl chloride (1.3 g, 11 mmol). After being refluxed overnight the chilled solution was treated in portions over 2 h with high-purity aluminium trichloride (4.0 g, 31 mmol) with stirring and external cooling (268–273 K). The mixture was stirred with cooling for 1 h and then for 2 h at room temperature. The mixture was chilled with ice–water and the reaction was quenched by cautious addition of ice chips and then diluted with water. Dichloromethane was added and the mixture was agitated thoroughly until all the solid dissolved. The phases were separated and the aqueous phase was extracted with dichloromethane (50 ml). The combined organic phase was washed with water and saturated brine, dried ($MgSO_4$), filtered and concentrated *in vacuo* to give a solid residue. Colorless block-shaped single crystals were obtained by recrystallization from ethanol in 56% yield (1.3 g) (m.p. 402–404 K); $[\alpha]_D^{25}$ = +8.2° (*c* 1, ethanol). Analysis calculated for $C_{13}H_{13}NO_3$: C 67.52, H 5.67, N 6.06%; found: C 67.27, H 5.59, N 6.33%. IR (KBr, ν cm^{-1}): 2839, 1689 (C═O), 1670 (C═O); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.30–2.60 (*m*, 4H, H-1, H-2), 3.88 (*s*, 3H, CH_3O), 4.31 (*d*, 1H, J = 17.1 Hz, H-5ax), 4.20–4.33 (*m*, 1H, H-10*a*), 5.21 (*d*, 1H, J = 17.1 Hz, H-5eq), 6.74 (*d*, 1H, J = 2.6 Hz, H-aromatic), 6.75 (*dd*, 1H, J = 9.0 Hz, J = 2.6 Hz, H-aromatic), 8.03 (*d*, 1H, J = 8.5 Hz, H-aromatic); ^{13}C NMR ($CDCl_3$,75 MHz): δ 20.7 (C-1), 30.0 (C-2), 41.6 (C-5), 55.7 (CH_3O–), 61.6 (C-10*a*), 110.3 (C-aromatic), 114.5 (C-aromatic), 123.6 (C-aromatic), 130.1 (C-aromatic), 142.2 (C-aromatic), 164.3 (C-aromatic), 173.9 (C-3), 193.0 (C-10); EIMS, *m*/*z* (%): 231 (M^+, 89), 203 (39), 202 (17), 189 (44), 176 (5), 148 (100), 132 (5), 121 (11), 120 (22), 105 (6), 91 (10), 89 (6), 77 (12).

Crystal data

$C_{13}H_{13}NO_3$	D_x = 1.357 Mg m^{-3}
M_r = 231.24	Mo $K\alpha$ radiation
Monoclinic, $P2_1$	Cell parameters from 864 reflections
a = 7.423 (1) Å	θ = 3.0–29.9°
b = 7.034 (1) Å	μ = 0.10 mm^{-1}
c = 10.998 (1) Å	T = 296.1 (2) K
β = 99.67 (1)°	Block, colorless
V = 566.08 (12) Å^3	0.60 × 0.40 × 0.30 mm
Z = 2	

Data collection

Oxford Diffraction Xcalibur CCD diffractometer	864 reflections with $I > 2\sigma(I)$
ω and φ scans	R_{int} = 0.025
Absorption correction: none	θ_{max} = 27.5°
3959 measured reflections	$h = -9 \rightarrow 9$
1380 independent reflections	$k = -9 \rightarrow 5$
	$l = -13 \rightarrow 14$

Refinement

Refinement on F^2	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.043	$w = 1/[\sigma^2(F_o^2) + (0.0589P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2)$ = 0.111	$(\Delta/\sigma)_{max} < 0.001$
S = 1.00	$\Delta\rho_{max}$ = 0.16 e Å^{-3}
1380 reflections	$\Delta\rho_{min}$ = −0.17 e Å^{-3}
154 parameters	

Table 1
Selected geometric parameters (Å, °).

C3—O15	1.225 (4)	C7—O16	1.363 (3)
C3—N4	1.345 (4)	C10—O17	1.219 (3)
N4—C5	1.441 (3)	C11—C12	1.391 (3)
N4—C13	1.450 (3)	C14—O16	1.433 (3)
C2—C1—C13	105.8 (2)	C5—N4—C13	120.1 (2)
O15—C3—N4	124.7 (3)	O17—C10—C12	122.4 (2)
O15—C3—C2	126.9 (3)	O17—C10—C13	120.7 (2)
C3—N4—C5	124.8 (2)	C7—O16—C14	117.9 (2)
C3—N4—C13	115.1 (2)		
C1—C2—C3—O15	−175.4 (3)	O17—C10—C13—N4	156.8 (3)
C7—C6—C11—C5	−179.8 (3)	C12—C10—C13—N4	−26.5 (4)
O17—C10—C12—C9	1.1 (6)	C8—C7—O16—C14	178.8 (3)

All H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms, with C—H distances in the range 0.93–0.98 Å and U_{iso}(H) = 1.2U_{eq}(C), or 1.5U_{eq}(C) for methyl. The absolute configuration could not be reliably determined for this compound using Mo radiation and has been assigned based on that of the synthetic precursor. Friedel pairs have been merged.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2002); cell refinement: *CrysAlis CCD*; data reduction: *CrysAlis RED* (Oxford Diffraction, 2002); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

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