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(10a*S*)-6-Methoxy-1,10a-dihydropyrrolo[1,2-*b*]isoquinoline-3,10(2*H*,5*H*)-dione

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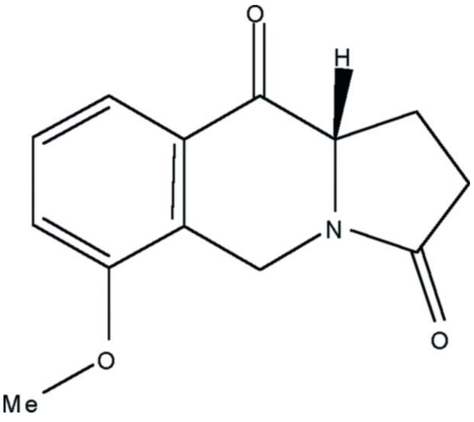
Key indicators: single-crystal X-ray study; T = 298 K; mean σ(C–C) = 0.003 Å; R factor = 0.031; wR factor = 0.087; data-to-parameter ratio = 8.6.

In the title compound, $C_{13}H_{13}NO_3$, the central six-membered ring of the indolizine system adopts a sofa conformation. The conformation of the oxopyrrolidine ring is envelope. The crystal structure is stabilized by van der Waals forces.

Related literature

For related literature, see: Camus *et al.* (2000, 2003); Guarna *et al.* (2001); Harris & Kozarich (1997); Kubo *et al.* (2000); Lokaj *et al.* (1999); Marchalín *et al.* (1998); Nardelli (1983).



Experimental

Crystal data

$C_{13}H_{13}NO_3$
M_r = 231.24
Orthorhombic, $P2_12_12_1$
a = 6.1806 (1) Å
b = 9.2755 (2) Å
c = 19.4579 (4) Å
V = 1115.49 (4) $Å^3$
Z = 4
Mo $K\alpha$ radiation
μ = 0.10 mm^{-1}
T = 298 (2) K
0.5 × 0.3 × 0.2 mm

Data collection

Oxford Diffraction Gemini R CCD area-detector diffractometer
Absorption correction: analytical (Clark & Reid, 1995)
T_{min} = 0.948, T_{max} = 0.978
20403 measured reflections
1340 independent reflections
1188 reflections with $I > 2\sigma(I)$
R_{int} = 0.017

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.031
$wR(F^2)$ = 0.087
S = 1.05
1340 reflections
156 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.12 e $Å^{-3}$
$\Delta\rho_{min}$ = −0.11 e $Å^{-3}$

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2006); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2006); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *DIAMOND* (Brandenburg, 2002); software used to prepare material for publication: *SHELXL97*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: CI2358).

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supplementary materials

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(10a*S*)-6-Methoxy-1,10a-dihydropyrrolo[1,2-*b*]isoquinoline-3,10(2*H*,5*H*)-dione

L. Svorc, **V. Vrábel**, **J. Kozísek**, **S. Marchalín** and **J. Zúziová**

Comment

Isoquinolizine derivatives continue to attract the attention of organic and medicinal chemists because of their potential application as pharmaceutical drugs for the treatment of diabetes (Kubo *et al.*, 2000). Benzoquinolizine derivatives are interesting as selective non-steroidal inhibitors of steroid 5α-reductase-1 (Guarna *et al.*, 2001). Selective inhibition of 5αR-1 is currently investigated as a potential therapeutic tool for the treatment of dihydrotestosterone-related skin disorders, such as acne, alopecia, male baldness and hirsutism (Harris & Kozarich, 1997). The structural investigation of the title compound, (I), has been undertaken as part of our study of 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 figure.

The crystal structure of (I) (Fig. 1) is stabilized by van der Waals forces; the shortest intermolecular contacts are 3.395 (3) Å for C1···O3(-1+x, y, z) and 3.350 (2) Å for C5···O3(-1/2+x, 3/2-y, 2-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 0.485 (3) Å from the mean plane defined by atoms C11/C5/C13/C10/C12. Atom N4 is sp^2-hybridized, as evidenced by the sum of the valence angles around it (359.7°). 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 oxopyrrolidine ring adopts a flat-envelope conformation, with C1 on

the flap; the deviation of atom C1 from the N4/C13/C2/C3 plane is 0.350 (1) Å.

The bond lengths of the carbonyl groups C10═O2 and C3═O3 are 1.217 (2) and 1.230 (2) Å, respectively, somewhat longer than typical carbonyl bonds. This may be due to the fact that atoms O2 and O3 participate in intermolecular van der Waals forces. Bond lengths and angles in the indolizine ring system are in good agreement with values from the literature (Camus *et al.*, 2000, 2003; Lokaj *et al.*, 1999).

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*-(2-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 a period of 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 (MgSO4), filtered and concentrated in vacuo to give a solid residue. Colourless block-shaped single crystals were obtained by recrystallization from ethanol (yield 65%, 1.5 g; m.p. 447–449 K).

Refinement

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

Figures

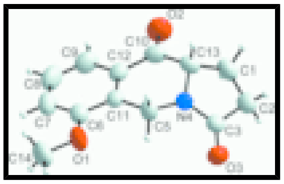

Fig. 1. The molecular structure of (I), with the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

(10aS)-6-Methoxy-1,10a-dihydropyrrolo[1,2-b]isoquinoline-3,10(2*H*,5H)-dione

Crystal data

$C_{13}H_{13}NO_3$
M_r = 231.24
Orthorhombic, $P2_12_12_1$
Hall symbol: P 2ac 2ab
a = 6.1806 (1) Å
b = 9.2755 (2) Å
c = 19.4579 (4) Å
V = 1115.49 (4) Å^3
Z = 4

F_{000} = 488
D_x = 1.377 Mg m^{-3}
Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 13309 reflections
θ = 4.2–26.3°
μ = 0.10 mm^{-1}
T = 298 (2) K
Block, colourless
0.5 × 0.3 × 0.2 mm

Data collection

Oxford Gemini R CCD area-detector diffractometer
Radiation source: fine-focus sealed tube
Monochromator: graphite
Detector resolution: 10.4340 pixels mm^{-1}
T = 298(2) K
ω and φ scans
Absorption correction: analytical (Clark & Reid, 1995)
T_{min} = 0.948, T_{max} = 0.978
20403 measured reflections

1340 independent reflections
1188 reflections with $I > 2\sigma(I)$
R_{int} = 0.017
θ_{max} = 26.4°
θ_{min} = 4.1°
$h = -7 \rightarrow 7$
$k = -9 \rightarrow 11$
$l = -24 \rightarrow 24$

Refinement

Refinement on F^2	H-atom parameters constrained
Least-squares matrix: full	$w = 1/[\sigma^2(F_o^2) + (0.0428P)^2 + 0.1859P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.031$	$(\Delta/\sigma)_{max} = 0.001$
$wR(F^2) = 0.087$	$\Delta\rho_{max} = 0.12$ e Å^{-3}
$S = 1.05$	$\Delta\rho_{min} = -0.11$ e Å^{-3}
1340 reflections	Extinction correction: SHELXL97 (Sheldrick, 1997), $Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
156 parameters	Extinction coefficient: 0.021 (3)
Primary atom site location: structure-invariant direct methods	
Secondary atom site location: difference Fourier map	
Hydrogen site location: inferred from neighbouring sites	

Special details

Experimental. face-indexed (CrysAlis RED; Oxford Diffraction, 2006)

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.1338 (3)	0.9055 (2)	0.86422 (11)	0.0599 (6)
H1A	0.1529	0.9140	0.8149	0.072*
H1B	−0.0130	0.9332	0.8760	0.072*
C2	0.2964 (4)	0.9972 (2)	0.90225 (12)	0.0600 (5)
H2A	0.3516	1.0731	0.8727	0.072*
H2B	0.2308	1.0409	0.9425	0.072*
C3	0.4738 (3)	0.8963 (2)	0.92269 (10)	0.0501 (5)
C5	0.5222 (3)	0.6327 (2)	0.93118 (10)	0.0517 (5)
H5A	0.4716	0.5969	0.9752	0.062*
H5B	0.6746	0.6558	0.9357	0.062*
C6	0.6387 (3)	0.4031 (2)	0.87544 (10)	0.0520 (5)
C7	0.6177 (4)	0.2969 (2)	0.82579 (11)	0.0647 (6)
H7	0.7170	0.2217	0.8237	0.078*
C8	0.4488 (5)	0.3033 (3)	0.77955 (11)	0.0700 (7)
H8	0.4342	0.2313	0.7466	0.084*
C9	0.3036 (4)	0.4131 (2)	0.78132 (10)	0.0631 (6)
H9	0.1907	0.4159	0.7498	0.076*
C10	0.1595 (3)	0.6372 (2)	0.83345 (10)	0.0547 (5)
C11	0.4937 (3)	0.5179 (2)	0.87746 (9)	0.0450 (4)
C12	0.3240 (3)	0.5219 (2)	0.83063 (9)	0.0486 (4)
C13	0.1826 (3)	0.7511 (2)	0.88860 (10)	0.0492 (5)
H13	0.0872	0.7272	0.9272	0.059*
C14	0.9445 (4)	0.2899 (3)	0.92832 (15)	0.0789 (7)

H14A	1.0217	0.2821	0.8857	0.118*
H14B	0.8668	0.2021	0.9368	0.118*
H14C	1.0451	0.3067	0.9650	0.118*
N4	0.4035 (3)	0.76077 (17)	0.91305 (8)	0.0475 (4)
O1	0.7955 (3)	0.40722 (15)	0.92447 (8)	0.0673 (4)
O2	0.0057 (3)	0.6414 (2)	0.79442 (9)	0.0842 (6)
O3	0.6514 (2)	0.92868 (17)	0.94671 (9)	0.0706 (5)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0507 (11)	0.0656 (13)	0.0635 (11)	0.0183 (11)	−0.0045 (10)	0.0036 (10)
C2	0.0583 (12)	0.0506 (10)	0.0710 (12)	0.0064 (10)	0.0026 (11)	0.0103 (10)
C3	0.0451 (10)	0.0492 (10)	0.0561 (10)	0.0004 (9)	0.0030 (9)	−0.0012 (8)
C5	0.0499 (11)	0.0500 (10)	0.0553 (10)	0.0111 (9)	−0.0132 (9)	−0.0048 (8)
C6	0.0557 (11)	0.0477 (10)	0.0527 (9)	0.0046 (10)	0.0047 (9)	0.0021 (8)
C7	0.0797 (15)	0.0491 (11)	0.0653 (12)	0.0053 (12)	0.0153 (13)	−0.0075 (10)
C8	0.0928 (18)	0.0597 (13)	0.0574 (11)	−0.0107 (14)	0.0065 (13)	−0.0164 (10)
C9	0.0737 (14)	0.0660 (13)	0.0496 (10)	−0.0143 (13)	−0.0063 (11)	−0.0057 (10)
C10	0.0480 (10)	0.0632 (11)	0.0528 (10)	−0.0051 (10)	−0.0089 (9)	0.0056 (9)
C11	0.0480 (10)	0.0425 (9)	0.0444 (8)	−0.0029 (9)	0.0014 (8)	0.0014 (7)
C12	0.0524 (10)	0.0485 (9)	0.0450 (9)	−0.0079 (9)	−0.0022 (9)	0.0034 (8)
C13	0.0364 (9)	0.0594 (11)	0.0517 (10)	0.0041 (9)	−0.0029 (8)	0.0031 (9)
C14	0.0712 (15)	0.0642 (14)	0.1013 (17)	0.0284 (13)	0.0037 (15)	0.0095 (13)
N4	0.0400 (8)	0.0454 (8)	0.0571 (8)	0.0054 (7)	−0.0098 (7)	−0.0033 (7)
O1	0.0679 (9)	0.0569 (8)	0.0769 (9)	0.0250 (8)	−0.0132 (8)	−0.0062 (8)
O2	0.0711 (11)	0.0890 (12)	0.0924 (11)	0.0036 (10)	−0.0415 (10)	−0.0081 (10)
O3	0.0513 (8)	0.0622 (9)	0.0984 (12)	−0.0056 (8)	−0.0119 (8)	−0.0093 (9)

Geometric parameters (Å, °)

C1—C2	1.510 (3)	C7—C8	1.379 (3)
C1—C13	1.539 (3)	C7—H7	0.93
C1—H1A	0.97	C8—C9	1.358 (3)
C1—H1B	0.97	C8—H8	0.93
C2—C3	1.496 (3)	C9—C12	1.398 (3)
C2—H2A	0.97	C9—H9	0.93
C2—H2B	0.97	C10—O2	1.217 (2)
C3—O3	1.230 (2)	C10—C12	1.477 (3)
C3—N4	1.344 (3)	C10—C13	1.512 (3)
C5—N4	1.441 (2)	C11—C12	1.390 (3)
C5—C11	1.502 (2)	C13—N4	1.449 (3)
C5—H5A	0.97	C13—H13	0.98
C5—H5B	0.97	C14—O1	1.427 (3)
C6—O1	1.361 (2)	C14—H14A	0.96
C6—C7	1.386 (3)	C14—H14B	0.96
C6—C11	1.393 (3)	C14—H14C	0.96
C2—C1—C13	104.08 (16)	C7—C8—H8	119.5

C2—C1—H1A	110.9	C8—C9—C12	119.9 (2)
C13—C1—H1A	110.9	C8—C9—H9	120.0
C2—C1—H1B	110.9	C12—C9—H9	120.0
C13—C1—H1B	110.9	O2—C10—C12	122.5 (2)
H1A—C1—H1B	109.0	O2—C10—C13	119.6 (2)
C3—C2—C1	105.39 (17)	C12—C10—C13	117.86 (16)
C3—C2—H2A	110.7	C12—C11—C6	119.16 (17)
C1—C2—H2A	110.7	C12—C11—C5	121.76 (16)
C3—C2—H2B	110.7	C6—C11—C5	119.07 (16)
C1—C2—H2B	110.7	C11—C12—C9	119.9 (2)
H2A—C2—H2B	108.8	C11—C12—C10	120.94 (16)
O3—C3—N4	124.73 (19)	C9—C12—C10	119.10 (19)
O3—C3—C2	127.1 (2)	N4—C13—C10	111.43 (16)
N4—C3—C2	108.15 (17)	N4—C13—C1	103.18 (17)
N4—C5—C11	110.74 (14)	C10—C13—C1	114.39 (16)
N4—C5—H5A	109.5	N4—C13—H13	109.2
C11—C5—H5A	109.5	C10—C13—H13	109.2
N4—C5—H5B	109.5	C1—C13—H13	109.2
C11—C5—H5B	109.5	O1—C14—H14A	109.5
H5A—C5—H5B	108.1	O1—C14—H14B	109.5
O1—C6—C7	125.15 (19)	H14A—C14—H14B	109.5
O1—C6—C11	114.64 (16)	O1—C14—H14C	109.5
C7—C6—C11	120.2 (2)	H14A—C14—H14C	109.5
C8—C7—C6	119.7 (2)	H14B—C14—H14C	109.5
C8—C7—H7	120.2	C3—N4—C5	124.97 (16)
C6—C7—H7	120.2	C3—N4—C13	114.13 (16)
C9—C8—C7	121.1 (2)	C5—N4—C13	120.61 (16)
C9—C8—H8	119.5	C6—O1—C14	118.34 (18)

C13—C1—C2—C3	21.1 (2)	O2—C10—C12—C9	0.1 (3)
C1—C2—C3—O3	169.8 (2)	C13—C10—C12—C9	178.36 (18)
C1—C2—C3—N4	−12.8 (2)	O2—C10—C13—N4	−159.6 (2)
O1—C6—C7—C8	178.8 (2)	C12—C10—C13—N4	22.1 (2)
C11—C6—C7—C8	−1.8 (3)	O2—C10—C13—C1	−43.0 (3)
C6—C7—C8—C9	0.8 (3)	C12—C10—C13—C1	138.68 (18)
C7—C8—C9—C12	0.0 (3)	C2—C1—C13—N4	−21.6 (2)
O1—C6—C11—C12	−178.38 (17)	C2—C1—C13—C10	−142.78 (17)
C7—C6—C11—C12	2.2 (3)	O3—C3—N4—C5	1.9 (3)
O1—C6—C11—C5	0.4 (3)	C2—C3—N4—C5	−175.59 (18)
C7—C6—C11—C5	−179.08 (19)	O3—C3—N4—C13	175.80 (19)
N4—C5—C11—C12	−18.7 (3)	C2—C3—N4—C13	−1.7 (2)
N4—C5—C11—C6	162.57 (16)	C11—C5—N4—C3	−140.97 (19)
C6—C11—C12—C9	−1.5 (3)	C11—C5—N4—C13	45.5 (2)
C5—C11—C12—C9	179.83 (19)	C10—C13—N4—C3	138.26 (18)
C6—C11—C12—C10	176.51 (17)	C1—C13—N4—C3	15.1 (2)
C5—C11—C12—C10	−2.2 (3)	C10—C13—N4—C5	−47.6 (2)
C8—C9—C12—C11	0.4 (3)	C1—C13—N4—C5	−170.79 (17)
C8—C9—C12—C10	−177.60 (19)	C7—C6—O1—C14	−3.7 (3)
O2—C10—C12—C11	−177.9 (2)	C11—C6—O1—C14	176.89 (18)
C13—C10—C12—C11	0.4 (3)		

Fig. 1