organic compounds

(S)-2,3,5,10,11,11a-Hexahydro-1H-pyrrolo[2,1-c][1,4]benzodiazepine-3,11-dione

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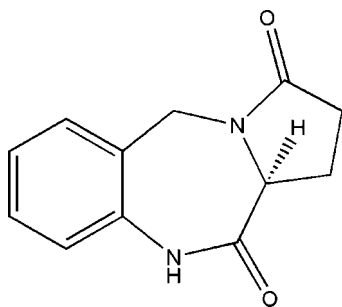
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The title chiral compound, $C_{12}H_{12}N_2O_2$, was prepared by an intramolecular cyclization reaction of (S)-methyl 1-(2-nitrobenzyl)-5-oxopyrrolidine-2-carboxylate in the presence of EtOH/Fe. In the molecule, the seven-membered ring adopts a twist-boat conformation, while the five-membered ring shows a typical envelope conformation. The crystal structure is stabilized by intermolecular N—H···O hydrogen bonding.

Related literature

For general background, see: Kamal et al. (2002); Mérour et al. (1994); Mishra et al. (2007); Thurston & Bose (1994). For a related structure, see: Arora (1979).

Experimental

Crystal data

$C_{12}H_{12}N_2O_2$	$a = 16.280$ (2) Å
$M_r = 216.24$	$b = 6.2848$ (9) Å
Monoclinic, $C2$	$c = 11.1016$ (15) Å
$\beta = 112.810$ (2)°	$\mu = 0.10$ mm^{-1}
$V = 1047.0$ (3) Å^3	$T = 187$ (2) K
$Z = 4$	$0.36 \times 0.17 \times 0.13$ mm
Mo $K\alpha$ radiation	

Data collection

Bruker SMART APEX CCD area-detector diffractometer	1089 independent reflections
Absorption correction: none	1046 reflections with $I > 2\sigma(I)$
2870 measured reflections	$R_{int} = 0.021$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.036$	1 restraint
$wR(F^2) = 0.093$	H-atom parameters constrained
$S = 1.17$	$\Delta\rho_{max} = 0.20$ e Å^{-3}
1089 reflections	$\Delta\rho_{min} = -0.17$ e Å^{-3}
145 parameters	

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

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N2—H2···O2^i	0.88	2.06	2.871 (2)	153

Symmetry code: (i) $-x + 1, y, -z + 1$.

Data collection: SMART (Bruker, 1997); cell refinement: SAINT (Bruker, 1999); data reduction: SAINT; program(s) used to solve structure: SHELXS97 (Sheldrick, 1997); program(s) used to refine structure: SHELXL97 (Sheldrick, 1997); molecular graphics: SHELXTL-Plus (Siemens, 1990); software used to prepare material for publication: SHELXL97.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: XU2346).

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supplementary materials

(*S*)-2,3,5,10,11,11a-Hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-3,11-dione

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Comment

Pyrrolo[2,1-*c*][1,4]benzodiazepines (PBDs) are naturally occurring compounds isolated from various streptomyces (Kamal *et al.*, 2002; Thurston & Bose, 1994). Such compounds have potential as regulators of gene expression with possible application as therapeutic agents in the treatment of certain genetic disorders including some cancers (Mishra *et al.*, 2007; Mérour *et al.*, 1994). As PBDs compounds are of great pharmaceutical importance, we determined the title chiral compound's crystal structure.

The molecular is shown in Fig. 1. The bond lengths and angles are within normal ranges. PBD ring involves in a twisted conformation (Arora, 1979). The seven-membered ring C6—C11—C12—N1—C4—C5—N2 (substituted diazepine) is far from planar, and its shape approximates to a twist boat. In this description applied to the title compound (Fig. 1), atoms C5, C12, N1 and N2 form the bottom of the boat (deviation from the mean C5/N1/C12/N2 plane = 0.090 (2) Å), C4 the prow, and C6 and C11 the stern [deviations from the C5/C12/N1/N2 mean plane = 0.655, 0.951, 0.932 Å, respectively]. The bond length of the carbonyl groups C1=O1 and C5=O2 of 1.213 (3) and 1.224 (3) Å, respectively, are somewhat longer than typical carbonyl bonds. This may be due to the fact that atoms O1 and O2 participate in intermolecular van der Waals forces. The five-membered ring N1—C1—C2—C3—C4 (substituted pyrrole) is non-planar and adopts nearly envelope conformation (deviation from the mean C4/N1/C1/C2 plane = 0.013 (5) Å). The C3 atom is located above the plane [deviations from the C4/N1/C1/C2 mean plane = 0.378 Å]. Atom C4 of the title molecule is chiral: S configuration was assigned to this atom based on the known chirality of the equivalent atom in the starting material.

The molecules are linked by an intermolecular hydrogen bond between N2–H2 and O2 (–*X*+1, *y*, *z*) (Table 1, Fig. 2).

Experimental

(*S*)-1-(2-Nitrobenzyl)-5-oxopyrrolidine-2-carboxylic acid methyl ester (5.56 g, 20 mmol) was dissolved in ethanol (100 ml). Fe (2.51 g, 45 mmol) was added and the solution was heated to reflux for 30 min. The mixture was filtered and the filtrate was concentrated under vacuum. The pure product was obtained through silica gel chromatography (eluant: petroleum ether/ethyl acetate, 1:1). Single crystals suitable for X-ray diffraction were obtained by slow evaporation of a dilute solution of the title compound in ethyl acetate at room temperature.

Refinement

All H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms, with N—H = 0.88 Å, C—H = 0.95, 0.99 and 1.00 Å for phenyl, methylene and tertiary H atoms, respectively, U_{iso}(H) = 1.2U_{eq}(C,*N*). Based on known chirality of the equivalent atom in the starting material, the S chirality at C4 was assigned. Friedels pairs were merged.
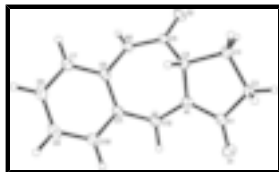
supplementary materials

Figures

Fig. 1. The structure of the title compound(I), showing 30% probability displacement ellipsoids and the atom-numbering scheme.

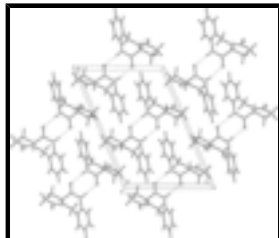
Fig. 2. The molecular packing of (I), the molecular packing viewed along the *b* axis, H atoms not involved in hydrogen bonding have been omitted.

(*S*)-2,3,5,10,11,11*a*-Hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-3,11-dione

Crystal data

$C_{12}H_{12}N_2O_2$	$F_{000} = 456$
$M_r = 216.24$	$D_x = 1.372$ Mg m^{-3}
Monoclinic, *C*2	Mo *K*α radiation λ = 0.71073 Å
a = 16.280 (2) Å	Cell parameters from 1769 reflections
b = 6.2848 (9) Å	θ = 2.7–25.5º
c = 11.1016 (15) Å	μ = 0.10 mm^{-1}
β = 112.810 (2)º	*T* = 187 (2) K
V = 1047.0 (3) Å^3	Block, colorless
Z = 4	0.36 × 0.17 × 0.13 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer	1046 reflections with $I > 2\sigma(I)$
Radiation source: fine-focus sealed tube	$R_{int} = 0.021$
Monochromator: graphite	θ$_{max}$ = 25.6º
T = 187(2) K	θ$_{min}$ = 2.0º
φ and ω scans	*h* = −19→16
Absorption correction: none	*k* = −7→7
2870 measured reflections	*l* = −8→13
1089 independent reflections	

Refinement

Refinement on F^2	Hydrogen site location: inferred from neighbouring sites
Least-squares matrix: full	H-atom parameters constrained

$R[F^2 > 2\sigma(F^2)] = 0.036$

$wR(F^2) = 0.093$

$S = 1.17$

1089 reflections

145 parameters

1 restraint

Primary atom site location: structure-invariant direct methods

Secondary atom site location: difference Fourier map

$w = 1/[\sigma^2(F_o^2) + (0.0528P)^2 + 0.3158P]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} < 0.001$

$\Delta\rho_{max} = 0.20$ e Å^{-3}

$\Delta\rho_{min} = -0.17$ e Å^{-3}

Extinction correction: none

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating R-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

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

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.65320 (15)	0.9090 (4)	0.9102 (2)	0.0281 (5)
C2	0.61760 (16)	0.7804 (4)	0.9947 (2)	0.0313 (6)
H2A	0.5689	0.8577	1.0083	0.038*
H2B	0.6654	0.7504	1.0809	0.038*
C3	0.58320 (16)	0.5751 (4)	0.9194 (2)	0.0308 (6)
H3A	0.5181	0.5825	0.8688	0.037*
H3B	0.5964	0.4517	0.9795	0.037*
C4	0.63361 (15)	0.5576 (4)	0.8278 (2)	0.0249 (5)
H4	0.6886	0.4700	0.8700	0.030*
C5	0.57841 (15)	0.4697 (4)	0.6922 (2)	0.0251 (5)
C6	0.71544 (15)	0.4757 (4)	0.6450 (2)	0.0251 (5)
C7	0.76369 (16)	0.3207 (4)	0.6119 (2)	0.0294 (5)
H7	0.7352	0.1945	0.5686	0.035*
C8	0.85484 (18)	0.3519 (5)	0.6431 (3)	0.0342 (6)
H8	0.8885	0.2463	0.6212	0.041*
C9	0.89569 (16)	0.5354 (5)	0.7053 (3)	0.0366 (6)
H9	0.9577	0.5556	0.7273	0.044*
C10	0.84635 (16)	0.6912 (5)	0.7360 (2)	0.0330 (6)
H10	0.8749	0.8179	0.7783	0.040*
C11	0.75563 (15)	0.6642 (4)	0.7055 (2)	0.0270 (5)
C12	0.70051 (17)	0.8408 (4)	0.7277 (2)	0.0301 (5)
H12A	0.7392	0.9658	0.7643	0.036*

H12B	0.6540	0.8834	0.6428	0.036*
N1	0.65789 (13)	0.7786 (3)	0.81665 (19)	0.0268 (5)
N2	0.62252 (12)	0.4396 (4)	0.61258 (18)	0.0274 (5)
H2	0.5911	0.3934	0.5331	0.033*
O1	0.67442 (13)	1.0953 (3)	0.9227 (2)	0.0395 (5)
O2	0.49882 (10)	0.4306 (3)	0.65628 (16)	0.0328 (4)

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0213 (10)	0.0298 (14)	0.0313 (12)	0.0030 (10)	0.0081 (9)	−0.0003 (10)
C2	0.0262 (11)	0.0376 (14)	0.0336 (12)	−0.0003 (11)	0.0155 (10)	−0.0049 (12)
C3	0.0291 (12)	0.0369 (14)	0.0314 (12)	−0.0040 (11)	0.0170 (10)	−0.0015 (11)
C4	0.0241 (11)	0.0252 (12)	0.0261 (11)	−0.0006 (10)	0.0105 (9)	0.0013 (10)
C5	0.0244 (11)	0.0233 (11)	0.0284 (11)	−0.0005 (9)	0.0111 (9)	0.0035 (10)
C6	0.0250 (11)	0.0316 (13)	0.0207 (10)	−0.0004 (10)	0.0110 (9)	0.0025 (10)
C7	0.0319 (12)	0.0311 (14)	0.0289 (11)	−0.0022 (11)	0.0157 (9)	0.0000 (10)
C8	0.0323 (12)	0.0407 (15)	0.0353 (13)	0.0066 (11)	0.0193 (10)	0.0057 (11)
C9	0.0223 (11)	0.0529 (18)	0.0368 (13)	−0.0018 (12)	0.0140 (10)	0.0063 (13)
C10	0.0291 (12)	0.0385 (14)	0.0317 (13)	−0.0098 (11)	0.0121 (10)	0.0011 (12)
C11	0.0285 (12)	0.0300 (14)	0.0263 (11)	−0.0016 (11)	0.0147 (9)	0.0035 (10)
C12	0.0363 (12)	0.0253 (12)	0.0328 (12)	−0.0040 (11)	0.0178 (10)	0.0013 (10)
N1	0.0283 (10)	0.0248 (10)	0.0291 (10)	−0.0020 (8)	0.0131 (8)	0.0006 (9)
N2	0.0223 (9)	0.0354 (11)	0.0235 (9)	−0.0055 (9)	0.0078 (7)	−0.0047 (9)
O1	0.0433 (11)	0.0269 (10)	0.0508 (11)	−0.0014 (8)	0.0210 (9)	−0.0054 (9)
O2	0.0199 (8)	0.0461 (11)	0.0329 (8)	−0.0053 (8)	0.0107 (6)	−0.0001 (9)

Geometric parameters (Å, °)

C1—O1	1.213 (3)	C6—C11	1.393 (3)
C1—N1	1.348 (3)	C6—N2	1.431 (3)
C1—C2	1.514 (4)	C7—C8	1.401 (4)
C2—C3	1.521 (4)	C7—H7	0.9500
C2—H2A	0.9900	C8—C9	1.376 (4)
C2—H2B	0.9900	C8—H8	0.9500
C3—C4	1.538 (3)	C9—C10	1.390 (4)
C3—H3A	0.9900	C9—H9	0.9500
C3—H3B	0.9900	C10—C11	1.392 (3)
C4—N1	1.462 (3)	C10—H10	0.9500
C4—C5	1.527 (3)	C11—C12	1.507 (4)
C4—H4	1.0000	C12—N1	1.463 (3)
C5—O2	1.224 (3)	C12—H12A	0.9900
C5—N2	1.351 (3)	C12—H12B	0.9900
C6—C7	1.387 (4)	N2—H2	0.8800
O1—C1—N1	125.2 (3)	C6—C7—C8	119.4 (3)
O1—C1—C2	127.2 (3)	C6—C7—H7	120.3
N1—C1—C2	107.6 (2)	C8—C7—H7	120.3
C1—C2—C3	105.10 (19)	C9—C8—C7	120.0 (2)

C1—C2—H2A	110.7	C9—C8—H8	120.0
C3—C2—H2A	110.7	C7—C8—H8	120.0
C1—C2—H2B	110.7	C8—C9—C10	120.1 (2)
C3—C2—H2B	110.7	C8—C9—H9	120.0
H2A—C2—H2B	108.8	C10—C9—H9	120.0
C2—C3—C4	104.26 (19)	C9—C10—C11	120.9 (3)
C2—C3—H3A	110.9	C9—C10—H10	119.5
C4—C3—H3A	110.9	C11—C10—H10	119.5
C2—C3—H3B	110.9	C10—C11—C6	118.5 (2)
C4—C3—H3B	110.9	C10—C11—C12	120.9 (2)
H3A—C3—H3B	108.9	C6—C11—C12	120.5 (2)
N1—C4—C5	109.59 (19)	N1—C12—C11	112.4 (2)
N1—C4—C3	102.69 (19)	N1—C12—H12A	109.1
C5—C4—C3	114.64 (18)	C11—C12—H12A	109.1
N1—C4—H4	109.9	N1—C12—H12B	109.1
C5—C4—H4	109.9	C11—C12—H12B	109.1
C3—C4—H4	109.9	H12A—C12—H12B	107.8
O2—C5—N2	121.6 (2)	C1—N1—C12	122.7 (2)
O2—C5—C4	122.5 (2)	C1—N1—C4	114.5 (2)
N2—C5—C4	115.91 (18)	C12—N1—C4	121.72 (19)
C7—C6—C11	121.1 (2)	C5—N2—C6	126.30 (18)
C7—C6—N2	118.3 (2)	C5—N2—H2	116.9
C11—C6—N2	120.6 (2)	C6—N2—H2	116.9

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2···O2[i]	0.88	2.06	2.871 (2)	153

Symmetry codes: (i) −*x*+1, *y*, −*z*+1.

Fig. 1

Fig. 2