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(*S*)-(−)-2,3-Methylenedioxy-8-oxoberbine

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.002 Å
R factor = 0.031
wR factor = 0.085
Data-to-parameter ratio = 9.8

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

In the title optically active protoberberine derivative, $C_{18}H_{15}NO_3$, the absolute configuration has been confirmed as 13a*S*. The H atom at the asymmetric centre assumes an α orientation and occupies a bisectional position relative to the tetrahydropyridine ring, and is axial to the tetrahydropyridinone ring.

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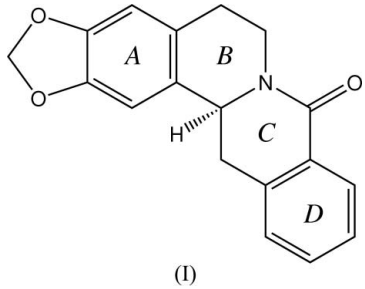
Comment

As a continuation of our study of stereoselective syntheses of isoquinoline alkaloids based on the addition of carbon nucleophiles to imines (Brózda *et al.*, 2001), we extended this approach to the synthesis of the protoberberine system. The key step of the synthesis, in which the new stereogenic centre at C13a was created, involved the addition of laterally metallated chiral *o*-toluamides to cyclic imines. We were interested in performing the first asymmetric synthesis of gusanlung D, using this metallation methodology. (−)-Gusanlung D isolated from *Acangelisia gusanlung* H. S. Lo by Zhang *et al.* (1995) is the first optically active natural protoberberine alkaloid unoxygenated at ring *D*, to which the structure of (*S*)-(−)-2,3-methylenedioxy-8-oxoberbine was assigned on the basis of spectroscopic analysis. We have obtained (*S*)-(−)-2,3-methylenedioxy-8-oxoberbine, (I), and its (*R*)-enantiomer, each with enantiomeric excess >99%, in the reactions of 6,7-methylenedioxy-3,4-dihydroisoquinoline with laterally lithiated *o*-toluamides in which the amine group was derived from (1*S*,2*S*)-thiomicamine or (1*R*,2*S*)-2-amino-1-phenylpropanol, respectively (Chrzanowska *et al.*, 2004). However our synthetic compound (I) differed significantly in its physical data, *viz.* specific rotation, melting point and spectroscopic data, from those reported for gusanlung D (Zhang *et al.*, 1995), but are in line with those reported for racemic 2,3-methylenedioxy-8-oxoberbine (Kessar *et al.*, 1992; Reimann *et al.*, 2003). In order to clarify this ambiguity, we have undertaken an X-ray crystallographic study to confirm the correctness of the absolute configuration of synthesized (*S*)-(−)-2,3-methylenedioxy-8-oxoberbine.



(I)

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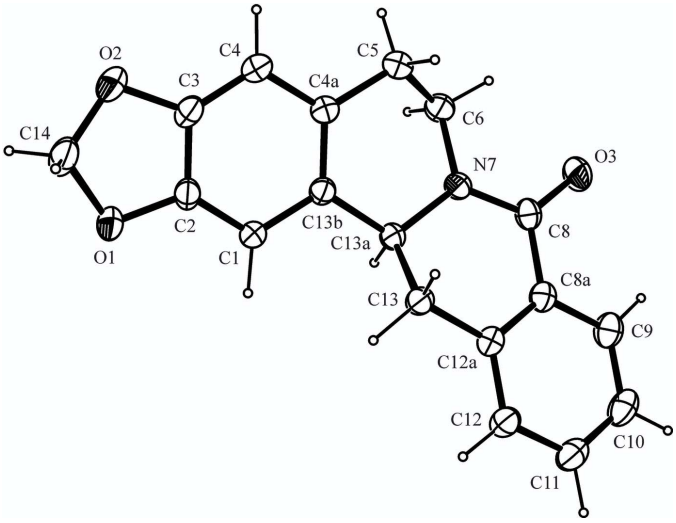

Figure 1
The molecular structure of (I), showing the atomic labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

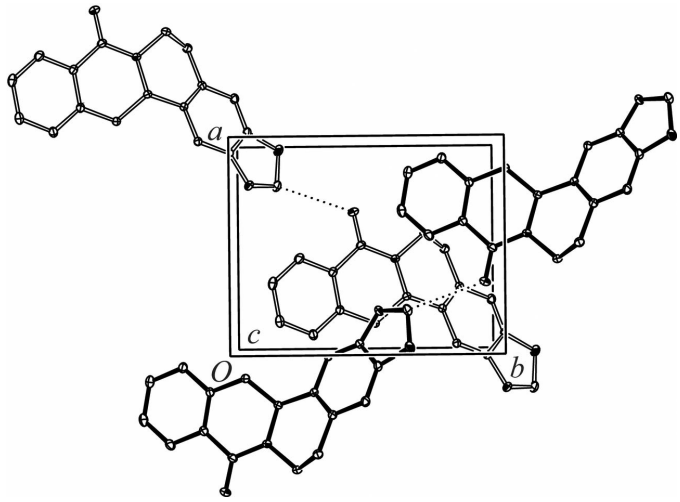

Figure 2
The hydrogen bonding in the crystal structure of (I). The molecular layers at the front and back are drawn with filled and open bonds, respectively. Dashed lines indicate hydrogen bonds.

The results of the X-ray study have confirmed the absolute configuration of (I) as *S* (Fig. 1), as proposed earlier on the basis of spectroscopic data (Chrzanowska *et al.*, 2004). The H atom at the asymmetric centre C13a assumes an α configuration and a bisectional position relative to ring *B*, and is axial to ring *C*. The torsion angles H13a—C13a—N7—C6 and H13a—C13a—N7—C8 are 90.1 (10) and −74.6 (10)°, respectively.

Compound (I) is a δ-lactam. As expected, the C8—N7 bond distance of 1.353 (2) Å is comparable with the normal length of the Csp^2—N bond of 1.352 (3) Å (Allen *et al.*, 1987) for the lactam group C*—N(—C*)—C═O, where C* = Csp^3. The five-membered heterocyclic ring attached to the six-membered ring *A* has the envelope conformation [puckering parameters (Cremer & Pople, 1975) Q = 0.135 (2) Å and φ = 325.6 (8)°], with atom C14 deviating from the planar system defined by the other four atoms by 0.215 (3) Å. The six-membered ring *B* assumes an envelope conformation [Q = 0.493 (2) Å, θ = 122.7 (2)° and φ = 241.5 (2)°], while ring *C* has a skew boat conformation distorted towards an envelope [Q = 0.453 (2) Å, θ = 60.9 (3)° and φ = 275.7 (2)°]. The difference in the puckering of rings *B* and *C* is thought to be mainly a consequence of the presence of the carbonyl group in the latter. The Cambridge Structural Database (CSD, version 5.26; Allen, 2002) contains only one protoberberine alkaloid of a δ-lactam type unsubstituted at rings *B* and *C* (Aree *et al.*, 2003). In that compound, ring *B* assumes a conformation intermediate between an envelope and a skew boat, while ring *C* has the conformation of a distorted skew boat. Furthermore, the dihedral angle between the least-squares planes through rings *B* and *C* is 27.93 (6)°. The dihedral angle made by the planes of the benzene rings *A* and *D* is 25.16 (7)°.

The molecules in the crystal structure of (I) are linked *via* non-classical C—H···O hydrogen bonds into chains aligned alternately along the different diagonals in the *ab* plane (Table 1, Fig. 2).

Experimental

Compound (I) was synthesized according to the literature procedure of Chrzanowska *et al.* (2004); mp. 468–470 K; $[\alpha]_D$ = −432.6° (*c* 0.80, $CHCl_3$). Single crystals were grown by slow evaporation of a methanol solution of (I) kept at room temperature. The enantiomeric excess of (I) was established to be >99% by high-performance liquid chromatography analysis using a Chiracel OD-H column.

Crystal data

$C_{18}H_{15}NO_3$
M_r = 293.31
Orthorhombic, $P2_12_12_1$
a = 7.3551 (19) Å
b = 9.2458 (12) Å
c = 20.332 (3) Å
V = 1382.7 (4) Å^3
Z = 4
D_x = 1.409 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 56 reflections
θ = 10.1–26.4°
μ = 0.79 mm^{-1}
T = 293 (2) K
Lath, colourless
0.55 × 0.17 × 0.08 mm

Data collection

Kuma KM-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
2750 measured reflections
2554 independent reflections
2284 reflections with $I > 2\sigma(I)$
R_{int} = 0.028
θ_{max} = 70.1°
$h = -8 \rightarrow 8$
$k = 0 \rightarrow 11$
$l = 0 \rightarrow 24$
2 standard reflections every 100 reflections intensity decay: 1.4%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.031
$wR(F^2)$ = 0.085
S = 1.07
2554 reflections
260 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0547P)^2 + 0.0905P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ < 0.001
$\Delta\rho_{max}$ = 0.16 e Å^{-3}
$\Delta\rho_{min}$ = −0.11 e Å^{-3}
Extinction correction: *SHELXL97* (Sheldrick, 1997)
Extinction coefficient: 0.0042 (5)
Absolute structure: Flack (1983), with 1025 Friedel pairs
Flack parameter: 0.0 (2)

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

D—H···A	D—H	H···A	D···A	D—H···A
C6—H61···O3	1.02 (2)	2.27 (2)	2.722 (2)	105 (1)
C14—H142···O3^{i}	0.99 (3)	2.35 (3)	3.323 (3)	168 (2)

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

All H atoms were located in difference Fourier maps and refined freely; the range of C—H distances was 0.94 (2)–1.03 (2) Å.

Data collection: *KM-4 Software* (Kuma, 1996); cell refinement: *KM-4 Software*; data reduction: *KM-4 Software*; 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: *WinGX* (Farrugia, 1999).

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