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(*S*)-(–)-2,3-Dimethoxy-8-oxoberbine

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In the title optically active protoberberine derivative [systematic name: (*S*)-(−)-2,3-dimethoxy-5,6,13,13a-tetrahydro-8*H*-dibenzo[*a*,*g*]quinolizin-8-one], $C_{19}H_{19}NO_3$, the key intermediate in the synthesis of enantiomerically pure (*S*)-(−)-*O*-methylbharatamine, the absolute configuration of the asymmetric centre at the 13a position has been confirmed as *S* by crystal structure refinement. The H atom at the asymmetric centre assumes an α-orientation and occupies a pseudo-axial position relative to the central non-planar rings of the tetracyclic skeleton.

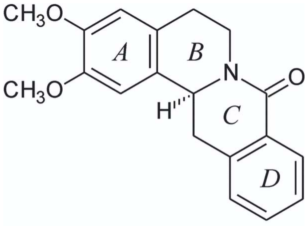
Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.002 Å
R factor = 0.038
wR factor = 0.093
Data-to-parameter ratio = 13.5

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

Comment

(*S*)-(−)- and (*R*)-(+)-2,3-dimethoxy-8-oxoberbine are the key intermediates in the syntheses of the enantiomerically pure (*S*)-(−)- and (*R*)-(+)-*O*-methylbharatamine, performed by Chrzanowska & Dreas (2004). They are derivatives of bharatamine, a protoberberine alkaloid, which was isolated in its racemic form from *Alangium lamarckii* Thw. (Alangiaceae) by Pakrashi *et al.* (1983). Racemic *O*-methylbharatamine and its 8-oxo-derivative served for many years as model compounds in designing new methods of synthesis of the protoberberine skeleton [see literature summary by Chrzanowska & Dreas (2004) and references therein].



(I)

(*S*)-(−)-2,3-Dimethoxy-8-oxoberbine, (I), was obtained with 82% enantiomeric excess (ee) in the addition reaction of (4*S*)-2,2-dimethyl-3-*o*-toluoyl-4-benzyloxazolidine with 6,7-dimethoxy-3,4-dihydroisoquinoline, which proceeded with a simultaneous cyclization of the addition product. Recrystallization from diethyl ether/methanol led to pure (*S*)-(−)-2,3-dimethoxy-8-oxoberbine, (I), with ee > 99% (Chrzanowska & Dreas, 2004). The value of the specific rotation measured for the pure enantiomer (ee > 99%) reached $[\alpha]_D$ = −413.8 (*c* 0.359, chloroform) and differs from $[\alpha]_D$ = −372.4 (*c* 0.359, chloroform) reported by Warrener *et al.* (1997) for the sample with 97% ee of (I). Therefore, in order to obtain additional confirmation of the absolute configuration of the synthesized (−)-2,3-dimethoxy-8-oxoberbine, a single crystal X-ray diffraction study has been undertaken.

The results obtained for the title compound confirmed the absolute configuration as 13a*S* (Fig. 1), as proposed earlier on the basis of the sign of specific rotation (Chrzanowska & Dreas, 2004, and references therein). The H atom at the stereogenic C13*a* centre exhibits an α-orientation and occupies a pseudo-axial position with respect to the *B* and *C* rings [the angles of the H13*a*—C13*a* bond vector to the Cremer & Pople *B* and *C* ring plane normals are 25.23 (5) and 1.74 (5)°, respectively (Cremer & Pople, 1975; Spek, 2003)].

In the solid state, the non-planar *B* ring has an envelope conformation distorted towards a half-chair [Cremer & Pople (1975) puckering parameters are Q = 0.470 (2) Å, Θ = 130.2 (2)° and Φ = 231.7 (2)°], whereas ring *C* has a conformation intermediate between envelope and twist-boat [Q = 0.411 (1) Å, Θ = 59.8 (2)° and Φ = 285.7 (2)°]. The dihedral angle between the least-squares planes of the central rings *B* and *C* of the tetracyclic skeleton is 24.27 (5)°. The dihedral angle between the outer rings *A*/*D* is 20.66 (6)°.

The Me groups of the methoxy substituents are not very significantly displaced from the plane of the aromatic ring *A*. The vectors of the O1—C14 and O2—C15 bonds are inclined to the least-squares plane of this ring by 17.06 (12) and 4.40 (8)° respectively.

In the *C* ring the N7—C8 bond distance, 1.3558 (17) Å, is comparable with the normal length of the Csp^2—N bond of 1.352 (3) Å for the lactam group C*—N(—C*)—C=O, where C* = Csp^3 (Allen *et al.*, 1987).

The majority of the bond lengths and angles in the title molecule are consistent with those found in 8-oxotetrahydrothalifendine (Aree *et al.*, 2003) and (*S*)-(−)- and (*R*)-(+)-2,3-methylenedioxy-8-oxoberbine (Gzella *et al.*, 2005*a*,*b*).

Experimental

Compound (I) (m.p. 442–445 K; $[\alpha]_D$ = −413.8°; c 0.359, $CHCl_3$) was synthesized according to the procedure reported by Chrzanowska & Dreas (2004). Single crystals were grown by slow evaporation of solvent from a diethyl ether/methanol solution of (I) at room temperature. According to the high-performance liquid chromatography on Chiralcel OD-H column, the resulting crystals contain almost exclusively enantiomer *S* (ee > 99%).

Crystal data

$C_{19}H_{19}NO_3$
M_r = 309.35
Monoclinic, $P2_1$
a = 7.9530 (12) Å
b = 7.7145 (12) Å
c = 12.7627 (12) Å
β = 95.76 (1)°
V = 779.08 (18) Å^3
Z = 2
D_x = 1.319 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 53 reflections
θ = 12.8–30.1°
μ = 0.72 mm^{-1}
T = 293 (2) K
Block, colourless
0.52 × 0.16 × 0.12 mm

Data collection

Kuma Diffraction KM-4 diffractometer
ω–2θ scans
Absorption correction: none
2960 measured reflections
2849 independent reflections
2801 reflections with $I > 2\sigma(I)$
$R_{\rm int}$ = 0.121
$\theta_{\rm max}$ = 70.1°
$h = -9 \rightarrow 9$
$k = -9 \rightarrow 9$
$l = 0 \rightarrow 15$
2 standard reflections every 100 reflections intensity decay: 2%

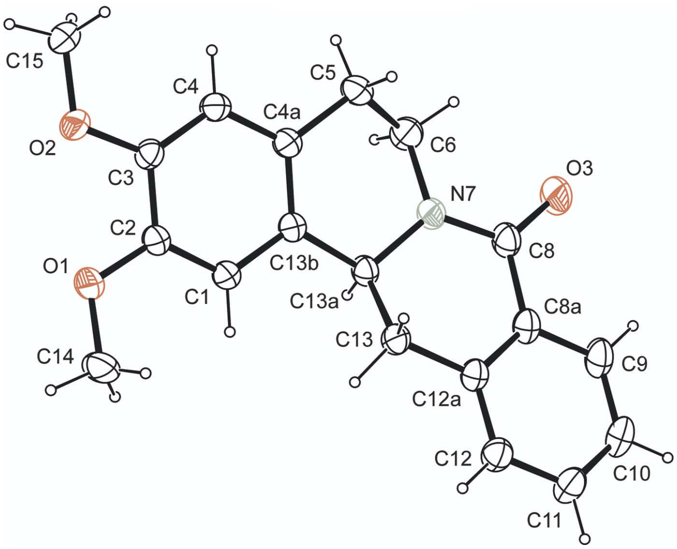


Figure 1
The molecular structure of (I), showing the atomic labelling scheme. Non-H atoms are drawn as 30% probability displacement ellipsoids; H atoms are shown as small spheres of arbitrary radius.

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.093
S = 1.10
2849 reflections
211 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0621P)^2 + 0.0533P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta\rho_{\rm max}$ = 0.16 e Å^{-3}
$\Delta\rho_{\rm min}$ = −0.20 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.081 (4)
Absolute structure: Flack (1983), 1239 Friedel reflections
Flack parameter: 0.08 (18)

The high $R_{\rm int}$ value results from the relatively poor quality of the crystal and the fact that the data collection was performed at room temperature. All H atoms were located in difference Fourier maps and refined in a riding-model approximation with $U_{\rm iso}$ constrained to be 1.2 (1.5 for methyl groups) times $U_{\rm eq}$ of the parent atom. The methyl H atoms were refined as rigid groups, which were allowed to rotate. The range of C–H distances was 0.93–0.98 Å. The absolute configuration of (I) was established by refinement of the Flack (1983) parameter. The rather large s.u. of the Flack parameter is due to the small contribution of atoms with measurable anomalous dispersion effects; refinement of the inverse structure of (I) leads to a value close to 1 [x = 0.91 (18)], which provides additional proof of the correct assignment of the absolute configuration.

Data collection: *KM-4 Software* (Kuma Diffraction, 1996); cell refinement: *KM-4 Software*; data reduction: *KM-4 Software*; program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1993); 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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Acta Cryst. (2006). E**62**, o598–o600 Gzella *et al.* • $C_{19}H_{19}NO_3$ **o599**

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