(R)-(+)-2,3-Methylenedioxy-8-oxoberbine

Andrzej Gzella,ᵃ* Maria Chrzanowskaᵇ and Agnieszka Dreasᵇ

ᵃDepartment of Organic Chemistry, K. Marcinkowski University of Medical Sciences Poznań, ul. Grunwaldzka 6, 60-780 Poznań, Poland, and ᵇFaculty of Chemistry, A. Mickiewicz University, ul. Grunwaldzka 6, 60-780 Poznań, Poland

Correspondence e-mail: akgzella@amp.edu.pl

The title compound [systematic name: (R)-(+)-2,3-methylene-dioxy-5,6,13,13a-tetrahydro-8H-dibenzo[a,g]quinolizin-8-one], $C_{18}H_{15}NO_3$, an optically active protoberberine derivative, was synthesized and its absolute configuration has been additionally confirmed by this crystal structure refinement. The H atom at the asymmetric centre assumes a β configuration and is oriented in the bisectional position relative to the tetrahydropyridine ring and axial to the tetrahydropyridinone ring.

Comment

The asymmetric synthesis of (R)-(+)-2,3-methylenedioxy-8-oxoberbine, (I), a part of our study on stereoselective syntheses of isoquinoline alkaloids (Chrzanowska & Rozwadowska, 2004), is closely connected with the synthesis of a natural protoberberine alkaloid, (S)-(−)-2,3-methylenedioxy-8-oxoberbine, so-called gusanlung D. The crystal structure of synthesized (S)-(−)-2,3-methylenedioxy-8-oxoberbine has already been reported (Gzella et al., 2005). X-ray crystallographic studies have been undertaken to confirm the absolute configuration of synthesized (R)-(+)-2,3-methylenedioxy-8-oxoberbine.

(I)
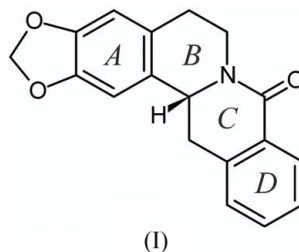
The results of the X-ray study have confirmed the absolute configuration (R) of (I) (Fig. 1), proposed earlier on the basis of spectroscopic data (Chrzanowska et al., 2004). The H atom at the asymmetric centre, C13a, assumes the β configuration. The torsion angles H13A—C13a—N7—C6 and H13A—C13a—N7—C8 are −89.1 (11) and 75.5 (11)°, respectively.

Other details concerning the structure analysis of (I) are the same as those of (S)-(-)-2,3-methylenedioxy-8-oxoberbine (Gzella et al., 2005).

Experimental

Compound (I) was synthesized according to the literature procedure of Chrzanowska et al., (2004); mp. 467–469 K; $[\alpha]_D$ = +415.3 (c 0.77, CHCl₃). The main concept of our synthetic strategy was based on the addition reaction of chiral carbon nucleophiles to cyclic imines, in which a new stereogenic centre was created. We were interested in performing the asymmetric synthesis of a protoberberine system

using lateral metallation methodology. Compound (I) was obtained in the reaction of 6,7-methylenedioxy-3,4-dihydroisoquinoline with laterally lithiated o-toluamide, in which the amine part was derived from (1S,2S)-thiomicamine, followed by a chromatographic separation of the diastereomeric addition products obtained, and a cyclization of a pure diastereomer characterized by a longer retention time on HPLC. The crystal was grown by slow evaporation of methanol from a methanolic solution kept at room temperature. The enantiomeric excess was established to be >99% by HPLC analysis using a Chiralcel OD–H column.

Crystal data

$C_{18}H_{15}NO_3$	Cu $K\alpha$ radiation
$M_r = 293.31$	Cell parameters from 61
Orthorhombic, $P2_12_12_1$	reflections
$a = 7.3595$ (8) Å	$\theta = 14.6$–$30.0°$
$b = 9.2465$ (14) Å	$\mu = 0.79$ mm^{-1}
$c = 20.323$ (3) Å	$T = 293$ (2) K
$V = 1383.0$ (3) Å^3	Pillar, colourless
$Z = 4$	$0.55 \times 0.15 \times 0.12$ mm
$D_x = 1.409$ Mg m^{-3}	

Data collection

Kuma KM-4 diffractometer	$\theta_{max} = 70.2°$
ω–2θ scans	$h = -8 \rightarrow 8$
Absorption correction: none	$k = 0 \rightarrow 11$
2673 measured reflections	$l = 0 \rightarrow 24$
2475 independent reflections	2 standard reflections
2311 reflections with $I > 2\sigma(I)$	every 100 reflections
$R_{int} = 0.019$	intensity decay: 3.8%

Refinement

Refinement on F^2	$(\Delta/\sigma)_{max} = 0.001$
$R[F^2 > 2\sigma(F^2)] = 0.031$	$\Delta\rho_{max} = 0.21$ e Å^{-3}
$wR(F^2) = 0.087$	$\Delta\rho_{min} = -0.15$ e Å^{-3}
$S = 1.05$	Extinction correction: SHELXL97
2475 reflections	Extinction coefficient: 0.0064 (7)
260 parameters	Absolute structure: Flack (1983),
All H-atom parameters refined	932 Friedel pairs
$w = 1/[\sigma^2(F_o^2) + (0.0667P)^2$	Flack parameter: 0.1 (2)
$+ 0.0526P]$	
where $P = (F_o^2 + 2F_c^2)/3$	

All H atoms were located in difference Fourier maps and refined freely; the range of C—H distances was 0.93 (2)–1.06 (2) Å. The rather large s.u. of the Flack (1983) parameter is due to the small anomalous dispersion effects; refinement of the inverse structure of (I) leads to a value close to 1 [$x = 0.9$ (2)].
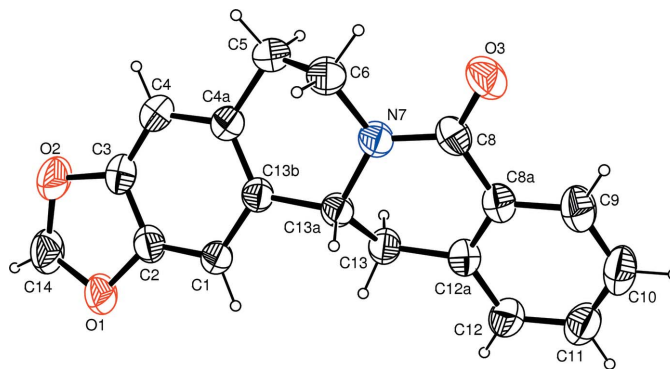

Figure 1
The molecular structure of (I), showing the atomic labelling scheme. Non-H atoms are drawn as 30% probability displacement ellipsoids.

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: *ORTEPIII* (Burnett & Johnson, 1996) and *ORTEP3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

References

Burnett, M. N. & Johnson, C. K.(1996) *ORTEPIII*. Report ORNL-6895. Oak Ridge National Laboratory, Oak Ridge, Tennessee, U. S.

Chrzanowska, M., Dreas A. & Rozwadowska, M. D. (2004). *Tetrahedron Asymmetry*, **15**, 1113–1120.

Chrzanowska, M. & Rozwadowska, M. D. (2004). *Chem. Rev.* **104**, 3341–3370 and references cited therein.

Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.

Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.

Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.

Gzella, A., Chrzanowska, M. & Dreas A. (2005). *Acta Cryst.* E**61**, o4001–4003.

Kuma (1996). *Kuma KM-4 User's Guide*. Version 8.0.1. Kuma Diffraction, Wrocław, Poland.

Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. Release 97-2. University of Göttingen, Germany.