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(–)-(1′*S*,4a*S*,7*R*,8a*R*)-4a-Ethyl-7-hydroxy-1-(1′-phenylethyl)-perhydroquinolinium bromide

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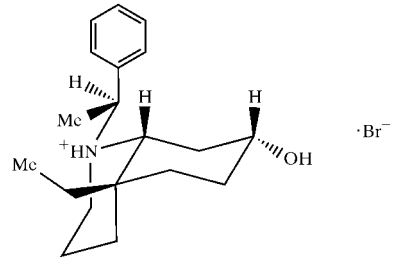
In the structure of the title compound, $C_{19}H_{30}NO^{+}\cdot Br^{-}$, the rings of the perhydroquinolinium moiety are *cis* fused. The successful reduction of the ketone functionality of the quinolinone used as starting material is confirmed by the hydroxy C—O bond length of 1.428 (3) Å.

Comment

In the course of the total synthesis of a natural product, is it essential to check carefully the configuration of the generated stereogenic centres, in order to obtain the expected final product with the correct configuration. In spite of sophisticated tools available in the form of modern NMR techniques, dubious or even incorrect configurations can be deduced from these spectroscopic data. The best way to determine the absolute configuration of a chiral molecule is still to use anomalous X-ray methods, providing that at least one heavy atom ($Z \geq 14$ for Mo radiation) is present and that a large fraction of Friedel pairs have been measured.

It has long been known that the treatment of non-chiral endocyclic enamines with methyl vinyl ketone affords a racemic mixture of *cis*-fused perhydroquinolin-7-ones. However, the separation of this mixture into the corresponding enantiomers is a very laborious process. We recently reported a diastereoselective synthesis of 4a-ethyl-1-(1′-phenylethyl)octahydroquinolin-7-ones (Vázquez *et al.*, 2001). Both diastereoisomers were easily separated by chromatography, and their relative absolute configurations were assigned by NMR experiments. These chiral non-racemic compounds are versatile starting materials for the synthesis of aspidosperma alkaloids if the bicycle is *cis* fused (Meyers & Berney, 1989; Schultz & Pettus, 1997; Iyengar *et al.*, 2000; Toczko & Heathcock, 2000).

In order to establish unambiguously the absolute configuration of the two chiral centres belonging to the octahydroquinoline moiety, we used the following procedure. The ketone group of chiral non-racemic (−)-(1′*S*,4a*S*,8a*R*)-4a-ethyl-1-(1′-phenylethyl)perhydroquinolin-7-one was reduced, giving a diastereoisomeric mixture of perhydroquinolin-7-ols (see *Experimental*). The main diastereoisomer was easily separated by chromatography, and its bromide salt, (I), was crystallized and characterized by X-ray diffraction methods.



(I)

The structure of (I) (Fig. 1 and Table 1) clearly shows that the two six-membered cycles of the perhydroquinoline moiety adopt chair conformations. The puckering angles θ (Cremer & Pople, 1975) are 175.2 and 2.64° for the N1/C2/C3/C4/C4a/C8a and C4a/C5/C6/C7/C8/C8a rings, respectively (Spek, 1998). These rings are *cis* fused, with the ethyl group on C4a and the H atom on C8a oriented toward the same face of the bicycle.

The hydroxy group generated during the reduction step is characterized by a C7—O15 bond length of 1.428 (3) Å, with the hydroxy group in an equatorial position. The crystallization of (I) as a bromide salt allows the determination of the absolute configuration for the five chiral centres. The final value of the Flack (1983) parameter, *viz*. 0.002 (8), determines the configurations unambiguously as N1*S*, C1′*S*, C4a*S*, C8a*R* and C7*R*. This assignation is in agreement with the configuration of the chiral inductor, (−)-(*S*)-1-phenylethylamine, which is retained as 1′*S*.

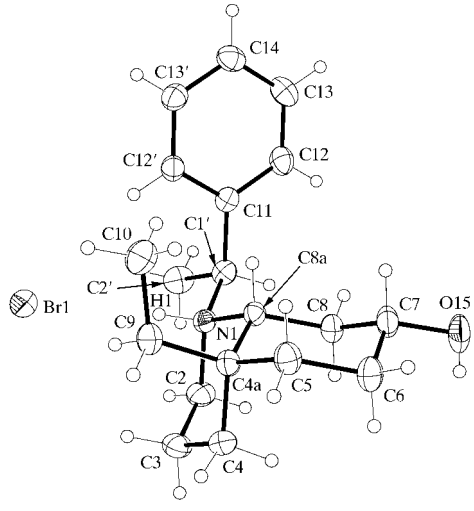


Figure 1
A view of the structure of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

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Finally, as expected, the structure of (I) is stabilized in the solid state through moderate hydrogen bonds involving Br1 as the acceptor and N1—H1 and O15—H15 as donor groups, with approximately linear X—H···Br angles (Table 2). These interactions link alternating cations and anions into chains running parallel to the b axis.

Experimental

(−)-(1′*S*,4a*S*,8a*R*)-4a-Ethyl-1-(1′-phenylethyl)perhydroquinolin-7-one (0.091 g, 0.32 mmol) was dissolved in tetrahydrofuran (30 ml) and $NaBH_4$ (0.024 g, 0.63 mmol) was added. A solution of NaOH (5%, 3.5 ml) and H_2O (3.5 ml) was added to the mixture, which was then refluxed for 8 h. After cooling, the mixture was extracted (× 5) with Et_2O, and the organic phases were combined, dried over Na_2SO_4 and evaporated to dryness, yielding 0.090 g (98%) of a diastereoisomeric mixture of alcohols. This crude product was easily separated by chromatography (Al_2O_3, *n*-hexane/AcOEt), giving pure diastereoisomers in a 7:3 ratio. The main diastereoisomer was treated with HBr, yielding (I), which was crystallized from AcOEt/MeOH.

Crystal data

$C_{19}H_{30}NO^+\cdot Br^-$
M_r = 368.35
Monoclinic, $P2_1$
a = 9.6977 (8) Å
b = 9.2191 (7) Å
c = 10.3008 (8) Å
β = 92.624 (7)°
V = 919.97 (13) Å^3
Z = 2
D_x = 1.330 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 61 reflections
θ = 4.5–12.5°
μ = 2.24 mm^{-1}
T = 300 (1) K
Block, colourless
0.62 × 0.60 × 0.40 mm

Data collection

Bruker *P*4 diffractometer
$2\theta/\omega$ scans
Absorption correction: ψ scan (30 ψ scans with *XSCANS*; Siemens, 1996)
T_{min} = 0.292, T_{max} = 0.409
6148 measured reflections
4443 independent reflections
3804 reflections with $I > 2\sigma(I)$
R_{int} = 0.028
θ_{max} = 28°
$h = -12 \rightarrow 12$
$k = -12 \rightarrow 12$
$l = -13 \rightarrow 13$
3 standard reflections
every 97 reflections
intensity decay: 2.5%

Table 1
Selected geometric parameters (Å, °) for (I).

N1—C8a	1.538 (3)	C4a—C9	1.548 (3)
C4a—C5	1.538 (3)	C7—O15	1.428 (3)
C4a—C8a	1.548 (3)	C8—C8a	1.532 (3)
C4—C4a—C5	109.9 (2)	C8a—C4a—C9	112.7 (2)
C4—C4a—C8a	109.32 (19)	O15—C7—C6	112.3 (2)
C5—C4a—C8a	108.21 (19)	O15—C7—C8	109.6 (2)
C4—C4a—C9	108.6 (2)	C6—C7—C8	111.7 (2)
C5—C4a—C9	108.0 (2)		

Table 2
Hydrogen-bonding geometry (Å, °) for (I).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···Br1	0.91	2.62	3.492 (2)	161
O15—H15···Br1^{i}	0.74	2.75	3.491 (3)	179

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

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.033
$wR(F^2)$ = 0.079
S = 1.02
4443 reflections
199 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0358P)^2 + 0.1874P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.28 e Å^{-3}
$\Delta\rho_{min}$ = −0.29 e Å^{-3}
Absolute structure: Flack (1983); 2088 Friedel pairs
Flack parameter = 0.002(8)

In order to refine the Flack (1983) parameter accurately, 2088 Friedel pairs were collected, corresponding to 88% of the accessible pairs. Atoms H1 (bonded to N1) and H15 (bonded to O15) were localized in difference maps and their positions refined freely. The remaining H atoms, bonded to sp^2- and sp^3-hybridized C atoms, were placed in idealized positions. In the final cycles, the hydroxy H atom was allowed to refine as part of a rigid rotating group, while the other H atoms were constrained to ride on their parent atoms, with $U_{iso}(H) = xU_{eq}$(parent), where x = 1.5 for methyl and hydroxy H atoms, and 1.2 for all others. Constrained distances were O—H = 0.74, N—H = 0.91, aryl C—H = 0.93, methine C—H = 0.98, methylene C—H = 0.97 and methyl C—H = 0.96 Å.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXTL-Plus* (Sheldrick, 1998); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL-Plus*; software used to prepare material for publication: *SHELXL*97.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM1506). Services for accessing these data are described at the back of the journal.

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