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Key indicators

Single-crystal X-ray study
T = 293 K
Mean $\sigma(\text{C}-\text{C}) = 0.002 \text{ \AA}$
R factor = 0.027
wR factor = 0.080
Data-to-parameter ratio = 9.6

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

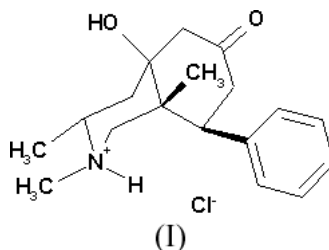
4a-Hydroxy-2,3,8a-trimethyl-6-oxo-8-phenyl-perhydroisoquinolinium chloride

The title compound, $\text{C}_{18}\text{H}_{26}\text{ClNO}_2$, is one of a group of decahydroisoquinoline derivatives that are known to exhibit a diverse range of bioactivities. The piperidine and cyclohexanone rings exist in chair conformations and form a *cis*-fused decalin-type bicyclic framework. In the crystal structure, infinite zigzag chains oriented along the *b* axis are formed by $\text{O}-\text{H} \cdots \text{O}$ intermolecular hydrogen bonds.

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Comment

The title compound, (I), is one of a group of decahydroisoquinoline derivatives that are known to exhibit a diverse range of bioactivities, including antibacterial and, most importantly, antimalarial activities (Nakagawa, 2000). Considerable effort has been made in these areas to design new analgetic drugs (Menard *et al.*, 1974; Ripka, 1978, 1979, 1984). There are also studies devoted to the discovery of novel classes of NMDA receptor antagonists (Hansen *et al.*, 1998) and selective iGluR5 receptor antagonists (Martinelli *et al.*, 1998, 2001).



Compound (I) was produced in a one-pot cascade Michael addition intramolecular aldol reaction sequence and isolated in the form of the salt with hydrochloric acid. The bicyclic part of (I) takes the form of a *cis*-fused decalin-type framework (Fig. 1). Both six-membered rings have chair conformations. All methyl groups attached to the piperidine ring and the phenyl group attached to the cyclohexanone ring occupy equatorial positions. The chloride anion is connected to the nearest H atom at the piperidine N atom *via* a hydrogen bond (Table 1). There is an intermolecular hydrogen bond between the hydroxy group and carbonyl atom O1 at $(-x, \frac{1}{2} + y, \frac{1}{2} - z)$, forming infinite zigzag chains along the *b* axis (Fig. 2).

Experimental

Sodium hydride (65% suspension in mineral oil, 0.42 g) was added in small portions, with constant stirring, to a solution of 1,2,5-trimethylpiperidin-4-one (1.5 g, 0.01 mol) in anhydrous dimethylformamide (30 ml). One hour later, benzalacetone (1.16 g, 0.008 mol) was added dropwise, with stirring, at room temperature and a solution of enolate was obtained. The reaction mixture was allowed to stand for 3 d. Addition of water, extraction with benzene, washing with water

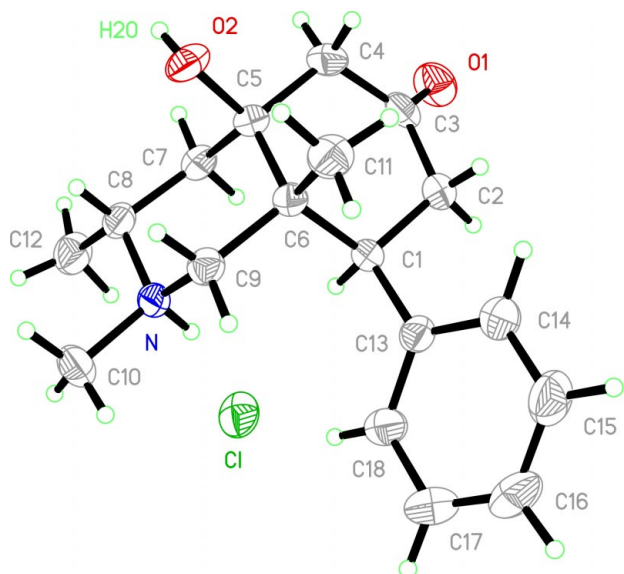


Figure 1

The molecular structure of (I), showing the atom labeling scheme. Displacement ellipsoids are drawn at the 50% probability level.

and recrystallization from cyclohexane gave 0.8 g (27.8% yield) of the base compound of (I) (m.p. 439–441 K). Crystals of the chloride, (I), were obtained by the addition of diethyl ether/HCl to the solution of the base in diethyl ether (m.p. 518–520 K). Analysis calculated: C 63.17, H 7.89, N 4.09, Cl 10.38%; found: C 63.72, H 7.98, N 4.33, Cl 10.79%. IR (cm^{-1}): 1705 (C=O), 3300–3500 (OH). ^1H NMR (250 MHz, DMSO- d_6 , p.p.m.): 0.92 [s, 3H, C(8a)CH $_3$], 1.42 [d, 3H, C(3)CH $_3$], 1.68 [d, 1H, He(4)], 1.93 [dd, 1H, Ha(4)], 2.09 [dd, 1H, He(7)], 2.18 [d, 1H, He(5)], 2.62 [d, 1H, He(1)], 2.76 (d, 3H, N-CH $_3$), 2.95 [dd, 1H, Ha(1)], 3.09 [d, 1H, Ha(5)], 3.42 [dd, 1H, Ha(7)], 3.55 [dq, 1H, Ha(3)], 3.82 [dd, 1H, Ha(8)], 5.69 (s, 1H, OH), 7.2–7.75 (m, 5H, Ar-H), 10.02 (dq, 1H, NHa).

Crystal data

$\text{C}_{18}\text{H}_{26}\text{NO}_2^+\cdot\text{Cl}^-$
 $M_r = 323.85$
 Monoclinic, $P2_1/c$
 $a = 15.149$ (3) Å
 $b = 9.339$ (2) Å
 $c = 12.227$ (2) Å
 $\beta = 106.87$ (3)°
 $V = 1655.4$ (6) Å 3
 $Z = 4$

$D_x = 1.299$ Mg m $^{-3}$
 Mo $K\alpha$ radiation
 Cell parameters from 24 reflections
 $\theta = 11.2$ – 12.5 °
 $\mu = 0.24$ mm $^{-1}$
 $T = 293$ (2) K
 Prism, colorless
 $0.56 \times 0.48 \times 0.25$ mm

Data collection

Enraf–Nonius CAD-4 diffractometer
 θ – 2θ scans
 Absorption correction: none
 3059 measured reflections
 2906 independent reflections
 2215 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.022$

$\theta_{\text{max}} = 25.0$ °
 $h = -17 \rightarrow 17$
 $k = 0 \rightarrow 11$
 $l = 0 \rightarrow 14$
 3 standard reflections
 frequency: 60 min
 intensity decay: none

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.027$
 $wR(F^2) = 0.080$
 $S = 1.05$
 2906 reflections
 304 parameters
 All H-atom parameters refined

$w = 1/[\sigma^2(F_o^2) + (0.0447P)^2 + 0.3033P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\text{max}} = 0.001$
 $\Delta\rho_{\text{max}} = 0.26$ e Å $^{-3}$
 $\Delta\rho_{\text{min}} = -0.20$ e Å $^{-3}$
 Extinction correction: SHELXL97
 Extinction coefficient: 0.0052 (15)

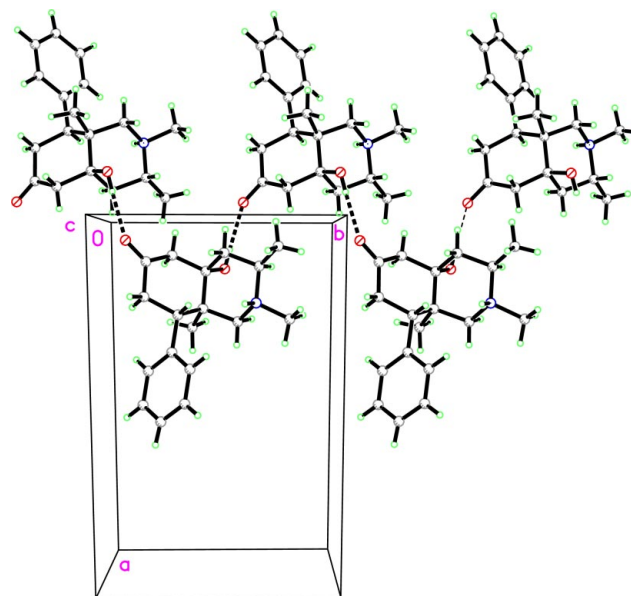


Figure 2

The crystal structure of (I). The broken lines indicate hydrogen bonds.

Table 1

Hydrogen-bonding geometry (Å, °).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$N-H1N\cdots Cl$	0.90 (2)	2.22 (2)	3.092 (1)	163 (2)
$O2-H2O\cdots O1^i$	0.82 (2)	2.09 (2)	2.906 (2)	174 (2)

Symmetry code: (i) $-x, \frac{1}{2} + y, \frac{1}{2} - z$.

All H atoms were located in difference syntheses and refined isotropically. The C–H, N–H and O–H bond lengths are 0.926 (17)–0.980 (19), 0.901 (18) and 0.82 (2) Å, respectively.

Data collection: CAD-4 Diffractometer Program (Schagen *et al.*, 1988); cell refinement: CAD-4 Diffractometer Program; data reduction: XCAD4 (Harms, 1997); program(s) used to solve structure: SHELXS97 (Sheldrick, 1997); program(s) used to refine structure: SHELXL97 (Sheldrick, 1997); molecular graphics: SHELXL97; software used to prepare material for publication: SHELXL97.

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