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(2*S*,3*S*,5*R*)-2-(3-Chlorophenyl)-2-hydroxy-3,5-dimethyl-2-morpholinium chloride

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Key indicators

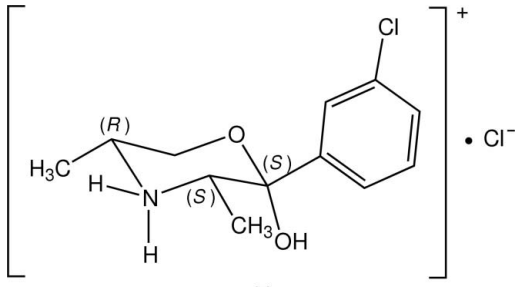
Single-crystal X-ray study
T = 294 K
Mean σ(C–C) = 0.004 Å
R factor = 0.035
wR factor = 0.081
Data-to-parameter ratio = 16.9

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

The title compound, $C_{12}H_{17}ClNO_2^+\cdot Cl^-$, was synthesized by the reaction of (*R*)-(−)-2-amino-1-propanol and 2-bromo-1-(3-chlorophenyl)propan-1-one. The morpholine ring has a chair conformation; the 3,5-dimethyl and 2-hydroxy groups are on the same side of the morpholine ring with the 2-(3-chlorophenyl) group on the opposite side.

Comment

2-Morpholinol derivatives exhibit pharmacological activities, including antidepressant (Kelley *et al.*, 1996), analeptic (Kelley *et al.*, 1992), anorectic (Meyer *et al.*, 1981), adrenergic-blocking and antifungal activities (Asselin & Humber, 1977). 2-Morpholinol derivatives have also been used to treat human diseases such as tardive dyskinesia (TD), minimal brain dysfunction (MBD) (Mehta & Smyser, 1986), obesity, migraine, sexual dysfunction, chronic fatigue, Parkinson's disease (Ascher *et al.*, 2003) and so on. We report here the synthesis and structure of the title 2-morpholinol derivative, (I).



(I)

The molecular structure of (I) is illustrated in Fig. 1. The morpholine ring (C1/C2/C3/C4/N1/O2) is in a chair conformation; the dihedral angle between the C1/C2/O2 and C2/O2/C4/N1 planes and between the C3/C4/N1 and C2/02/C4/N1 planes are 51.8 (3)° and 48.7 (2)°, respectively. The 3,5-dimethyl and 2-hydroxy groups are on the same side of the morpholine ring, but the 2-(3-chlorophenyl) group is on the opposite side.

The chloride anion links with the morpholinonium cation through hydrogen bonding (Table 1).

Experimental

2-Bromo-1-(3-chlorophenyl)propan-1-one (0.01 mol) was added to a solution of (*R*)-(−)-2-amino-1-propanol (0.04 mol) in 10 ml *N*-methyl-2-pyrrolone (Perrine *et al.*, 2000), and stirred for 1 h at room temperature. The mixture was diluted with 30 ml water, and extracted

with 30 ml diethyl ether. The aqueous layer was extracted further with 15 ml diethyl ether three times. The extracts were combined, washed with 10 ml water three times, and dried over anhydrous Na_2SO_4 and filtered. The filtrate was stirred in an ice bath and the pH adjusted to acidity by passing anhydrous HCl through slowly, yielding a white crystalline substance which was filtered, washed with acetone and dried to give the title compound. Spectroscopic analysis: ^{1}H NMR (CD_3SOCD_3, 400 MHz): 0.97 (*d*, *J* = 6.4 Hz, 3H, CH_3), 1.23 (*d*, *J* = 6.4 Hz, 3H, CH_3), 3.40–3.60 (*br m*, 2H, morpholine ring 3,5-H), 3.85–3.95 (*m*, 2H, morpholine ring 6-H), 7.47–7.58 (*m*, 4H, C_6H_4), 7.89 (*s*, 1H, OH), 8.78, 10.39 (2 × *br*, 2H, NH, HCl). Single crystals of (I) were obtained from the filtrate by slow evaporation of a solution in a mixture of ethanol and diethyl ether (4:1).

Crystal data

$C_{12}H_{17}ClNO_2^+\cdot Cl^-$
M_r = 278.17
Orthorhombic, $P2_12_12$
a = 8.718 (2) Å
b = 20.264 (6) Å
c = 7.882 (2) Å
V = 1392.5 (6) Å^3
Z = 4
D_x = 1.327 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 2751 reflections
θ = 2.8–25.1°
μ = 0.46 mm^{-1}
T = 294 (2) K
Block, colorless
0.26 × 0.22 × 0.20 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2002)
T_{min} = 0.880, T_{max} = 0.913
7875 measured reflections
2836 independent reflections
2233 reflections with $I > 2\sigma(I)$
R_{int} = 0.029
θ_{max} = 26.4°
$h = -10 \rightarrow 9$
$k = -23 \rightarrow 25$
$l = -9 \rightarrow 9$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.081
S = 1.03
2836 reflections
168 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0336P)^2 + 0.2878P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.19 e Å^{-3}
$\Delta\rho_{min}$ = −0.25 e Å^{-3}
Absolute structure: Flack (1983), 1669 Friedel Pairs
Flack parameter: −0.02 (6)

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

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···Cl2	0.80 (3)	2.29 (3)	3.074 (2)	166 (2)
N1—H1A···Cl2^{i}	0.92 (2)	2.27 (2)	3.183 (2)	171.3 (19)
N1—H1B···Cl2^{ii}	0.88 (3)	2.34 (3)	3.142 (2)	151 (2)

Symmetry codes: (i) $x-\frac{1}{2}, -y+\frac{3}{2}, -z$; (ii) $x-1, y, z$.

H atoms were positioned geometrically with C—H = 0.98 (CH), 0.96 (CH_3), 0.97 (CH_2) or 0.93 Å (aromatic), and treated as riding, U_{iso}(H)= 1.2U_{eq}(C), or 1.5U_{eq}(C) for the methyl groups. O—H and N—H were freely refined.

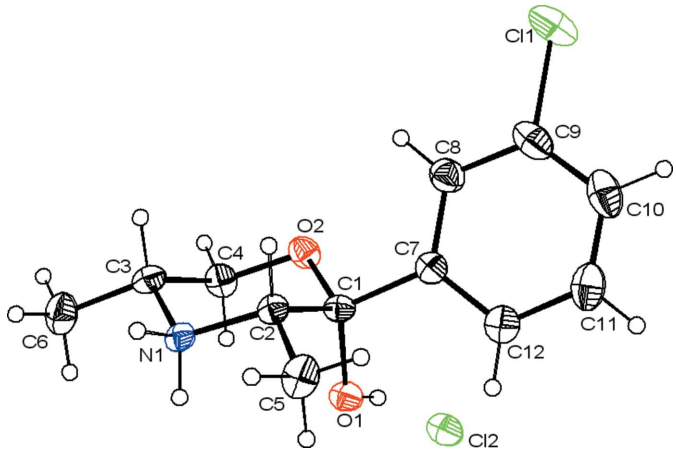


Figure 1
The molecular structure of (I) with 30% probability displacement ellipsoids (arbitrary spheres for H atoms).

Data collection: *SMART* (Bruker, 1997); cell refinement: *SAINT* (Bruker, 1997); data reduction: *SAINT*; 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: *SHELXTL* (Bruker, 1997).

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