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Key indicators

Single-crystal X-ray study
 $T = 170$ K
Mean $\sigma(\text{C}-\text{C}) = 0.005$ Å
Disorder in main residue
 R factor = 0.048
 wR factor = 0.123
Data-to-parameter ratio = 10.8

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

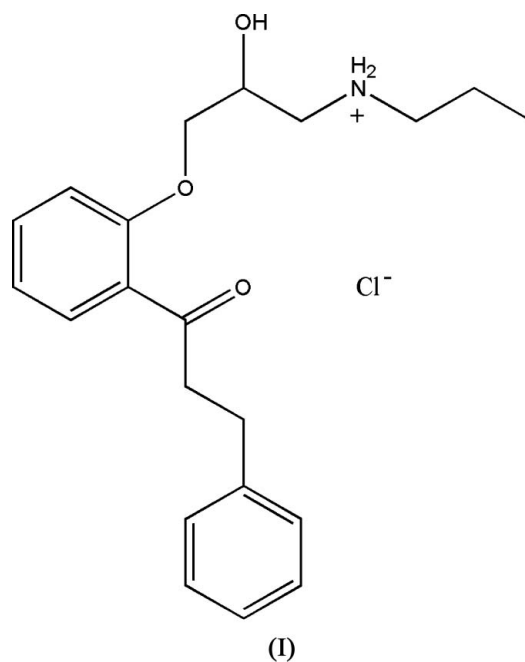
N-{(2*RS*)-2-Hydroxy-3-[2-(3-phenylpropanoyl)-phenoxy]propyl}propanaminium chloride

The title compound, propafenone hydrochloride, $\text{C}_{21}\text{H}_{28}\text{NO}_3^+\cdot\text{Cl}^-$, is a potent antiarrhythmic drug, which acts by blocking channels for sodium transport across cell borders. The crystal packing is essentially controlled by a system of hydrogen bonds involving the quaternary N atom, the (disordered) hydroxy group and the chloride ion.

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Comment

Propafenone, structurally similar to beta-blocking agents, is used in the treatment of ventricular and supraventricular arrhythmias (Harron & Brogden, 1987), being official in the European Pharmacopoeia 5th edition and in the United States Pharmacopoeia 29th edition. Its primary mechanism of action consists in blocking channels for sodium-ion transport across cell borders. It decreases the rate of cardiac conduction and increases the ventricular refractory period. It also has some β -adrenergic receptor-blocking properties and, to a lesser extent, a calcium-channel-blocking effect (Bryson *et al.*, 1993; Dollery, 1999). The solid-state structure of a drug may affect its stability and bioavailability, being also relevant to quality control and regulatory purposes (Datta & Grant, 2004). In view of this, the crystal structure of (I), propafenone hydrochloride, was determined.



In (I), the propafenone molecule is protonated (Fig. 1). Selected torsion angles are listed in Table 1. The hydroxy group is disordered over two possible sites, which are involved

in a hydrogen-bond system (Table 2), which extends along the *a* axis, with participation of the chloride ion and of the quaternary N atom (Fig. 2).

Experimental

Samples of (I) were kindly provided by SIMS srl, Reggello Firenze, Italy. Crystals suitable for X-ray analysis were obtained by slow evaporation of a methanol–butanol (1:1 v/v) solution.

Crystal data

$C_{21}H_{28}NO_3^+ \cdot Cl^-$	$Z = 4$
$M_r = 377.89$	$D_x = 1.275 \text{ Mg m}^{-3}$
Monoclinic, $P2_1/a$	Cu $K\alpha$ radiation
$a = 7.709 (1) \text{ \AA}$	$\mu = 1.88 \text{ mm}^{-1}$
$b = 15.959 (2) \text{ \AA}$	$T = 170 (2) \text{ K}$
$c = 16.007 (2) \text{ \AA}$	Elongated prism, colorless
$\beta = 90.49 (1)^\circ$	$0.80 \times 0.40 \times 0.20 \text{ mm}$
$V = 1969.2 (4) \text{ \AA}^3$	

Data collection

Oxford Diffraction Excalibur PX Ultra CCD diffractometer	$T_{\min} = 0.668$, $T_{\max} = 0.935$ (expected range = 0.491–0.687)
ω scans	15256 measured reflections
Absorption correction: multi-scan (<i>ABSPACK</i> ; Oxford Diffraction, 2006)	2676 independent reflections 1528 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.043$ $\theta_{\text{max}} = 58.0^\circ$

Refinement

Refinement on F^2	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.048$	$w = 1/[\sigma^2(F_o^2) + (0.0706P)^2]$
$wR(F^2) = 0.123$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 0.92$	$(\Delta/\sigma)_{\text{max}} < 0.001$
2676 reflections	$\Delta\rho_{\text{max}} = 0.24 \text{ e \AA}^{-3}$
247 parameters	$\Delta\rho_{\text{min}} = -0.23 \text{ e \AA}^{-3}$

Table 1

Selected torsion angles ($^\circ$).

C1–C2–C3–C16	–174.6 (3)	O2–C10–C11–C12	–62.9 (5)
C2–C1–C4–C5	12.5 (5)	C11–C12–N–C13	–178.9 (3)
C4–C5–O2–C10	171.5 (3)	C2–C3–C16–C17	–56.0 (4)

Table 2

Hydrogen-bond geometry (\AA , $^\circ$).

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
O31–H31O \cdots Cl	0.84	2.77	3.435 (5)	137
O32–H32O \cdots Cl ⁱ	0.84	2.41	3.038 (5)	132
N–H2N \cdots Cl	0.92	2.26	3.177 (3)	172
N–H1N \cdots Cl ⁱ	0.92	2.26	3.176 (3)	174

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

The crystal did not diffract strongly and it was deemed that collecting data at θ higher than 58° did not yield any improvement. H atoms were positioned geometrically, with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C}, \text{N})$, or $1.5U_{\text{eq}}(\text{C})$ for the methyl group. Assigned values of bond distances: secondary $\text{CH}_2 = 0.99 \text{ \AA}$, tertiary $\text{CH} = 1.00 \text{ \AA}$, methyl $\text{CH}_3 = 0.98 \text{ \AA}$, aromatic $\text{CH} = 0.95 \text{ \AA}$, $\text{N–H} = 0.92 \text{ \AA}$, $\text{O–H} = 0.84 \text{ \AA}$. The occupation factors of the two possible sites of the disordered hydroxy group, O31 and O32, are 0.534 (6) and 0.466 (6), respectively.

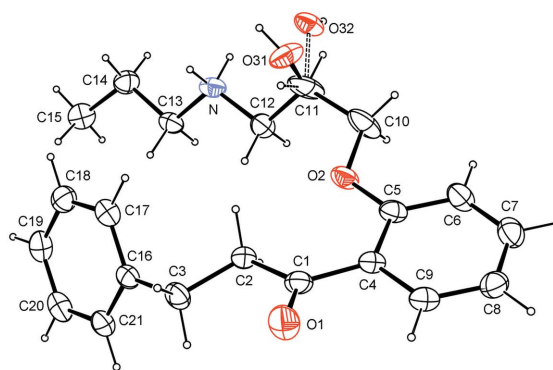


Figure 1

A view of the propafenone cation in (I). Displacement ellipsoids are at the 30% probability level. Bonds formed by the lower occupancy hydroxy component are indicated by dashed lines.

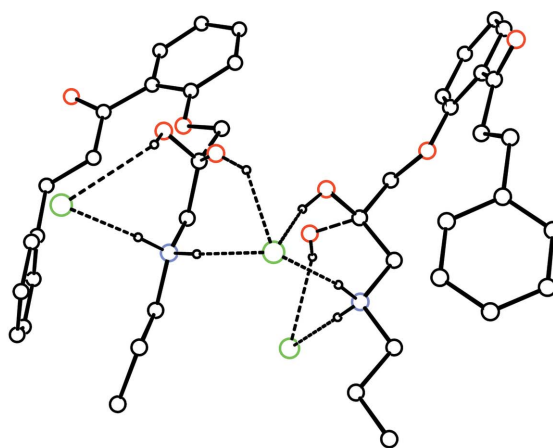


Figure 2

The essential part of the system of hydrogen bonds in (I). Dashed bonds are used for the minor hydroxy component and, with different dash size, for the hydrogen bonds. H atoms not involved in hydrogen bonding have been omitted.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2006); cell refinement: *CrysAlis CCD*; data reduction: *CrysAlis RED* (Oxford Diffraction, 2006); program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

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