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1-(3-Chlorophenyl)-4-(3-chloropropyl)-piperazinium chloride

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
Disorder in main residue
R factor = 0.047
wR factor = 0.130
Data-to-parameter ratio = 17.1

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

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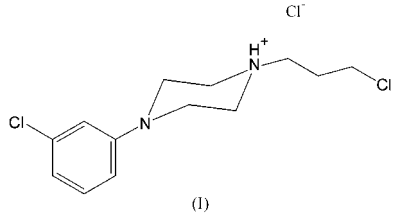
The title compound, $C_{13}H_{19}Cl_2N_2^+\cdot Cl^-$, exhibits stereochemical features that are deemed necessary for 5-HT_1 subtype serotonin receptor interaction. A distance of 5.69 (1) Å is observed between the protonated nitrogen and the centroid of the phenyl ring. The piperazine ring adopts a chair conformation and the protonated nitrogen is involved in hydrogen bonding to the chloride counter-ion. The chlorophenyl moiety is disordered, with the major conformer adopting a *trans, trans* geometry while the minor conformer is *trans, gauche*.

Comment

The stereochemical requirements of the 5-HT_1 (5-hydroxytryptamine$_1$) subtype serotonin receptors dictate that drugs exhibit several common features. General characteristics which persist are: (*a*) an amine nitrogen, either protonated or available for protonation, separated by a short chain of 3–4 atoms from an aromatic ring (as a conformational constraint at least two atoms of the chain should be embedded in a ring); (*b*) a nitrogen to aromatic ring centroid distance of 5–6 Å and, to a lesser extent; (*c*) to a lesser extent, the presence of long bulky chain substituents on an amine nitrogen (Dalpiaz *et al.*, 1996, Chilmonczyk *et al.*, 1995). The three-dimensional structure of 1-(3-chlorophenyl)-4-(3-chloropropyl)piperazine hydrochloride, (I), was determined in order to compare its conformation to other compounds of this type.



(I)

The piperazine ring in (I) adopts a chair conformation, with N1 and N2 out-of-plane deviations of 0.678 (3) and 0.643 (3) Å, respectively. The ring is protonated at N2 and it is this nitrogen that is involved in hydrogen bonding to Cl1 [3.048 (2) Å, 171°]. A distance of 5.69 (1) Å is observed between N2 and the centroid of the phenyl ring in (I). This is consistent with known 5–HT_1 receptor ligands such as 1-[3-(3,4-methylenedioxyphenoxy)propyl]-4-phenylpiperazinium chloride (5.68 Å; Okamoto *et al.*, 1993), eltoprazine (5.65 Å; Verdonk *et al.*, 1992) and 1-(2-methoxyphenyl)-4-[4-(2-phthalimido)butyl]piperazinium bromide (5.66 Å; Dalpiaz *et al.*, 1996).

The chloropropyl moiety in (I) is disordered over two principal conformations. The major conformer is fully extended with a *trans, trans* geometry about C11—C12 and C12—C13 (torsion angles of −178.7 (4)° and −172.3 (4)°, respectively). The minor conformer is folded with a *trans, gauche* geometry about C11′—C12′ and C12′—C13′ (torsion angles of −175 (1)° and 67 (2)°, respectively.

Experimental

Crystals of (I) were obtained as colorless irregular blocks from slow evaporation of alcoholic solutions maintained at room temperature.

Crystal data

$C_{13}H_{19}Cl_2N_2^+\cdot Cl^-$
M_r = 309.65
Monoclinic, $P2_1/c$
a = 10.856 (2) Å
b = 9.815 (2) Å
c = 14.052 (3) Å
β = 93.07 (3)°
V = 1495.1 (5) Å^3
Z = 4
D_x = 1.376 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 40 reflections
θ = 5.0–15.0°
μ = 0.60 mm^{-1}
T = 293 (2) K
Irregular block, colorless
0.55 × 0.55 × 0.50 mm

Data collection

Siemens $P3$ diffractometer
θ–2θ scans
Absorption correction: none
3573 measured reflections
3403 independent reflections
2409 reflections with $I > 2\sigma(I)$
R_{int} = 0.026
θ_{max} = 27.6°
$h = 0 \rightarrow 14$
$k = 0 \rightarrow 12$
$l = -18 \rightarrow 18$
3 standard reflections
every 300 reflections
intensity decay: 4.1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.130
S = 1.02
3403 reflections
199 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0526P)^2 + 0.7734P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.36 e Å^{-3}
$\Delta\rho_{min}$ = −0.36 e Å^{-3}

The position of H1 was located directly from a difference map at an N—H distance of 1.09 Å, then adjusted to a more acceptable distance of 0.87 Å and held at this distance in subsequent refinements. The remaining H atoms were placed in calculated positions and treated with a riding model. All H-atom isotropic displacement parameters were defined as $1.2U_{eq}$ of the parent atom. The chloropropyl moiety shows disorder over two principal conformations. Refinement of the anisotropic displacement parameters, although still exhibiting signs of unresolved disorder proceeded the most satisfactorily when occupancies where held at at 70:30.

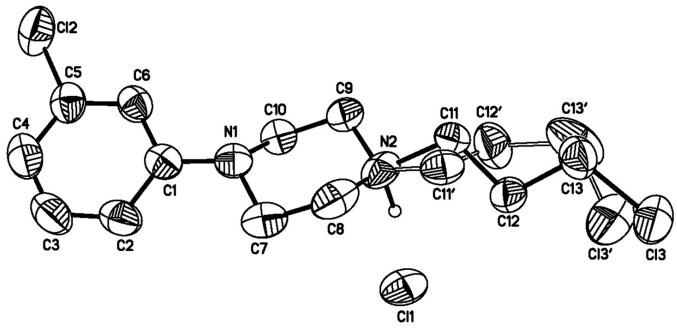


Figure 1
Structure of (I), showing 50% probability displacement ellipsoids and the atomic numbering scheme. The minor conformer of the disordered chloropropyl group is drawn with open bonds. For clarity, all H atoms with the exception of the one involved in hydrogen bonding have been omitted.

Data collection: *P3*/*P4*-*PC* (Siemens, 1989); cell refinement: *P3*/*P4*-*PC*; data reduction: *XDISK* (Siemens, 1989); program(s) used to solve structure: *SHELXTL* (Bruker, 1998); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

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