O5A—H5OA···O7B^{i}	2.13	2.914 (3)	160
N1A—H1NA···O1^{ii}	1.90	2.800 (3)	179
O7A—H7OA···O4^{ii}	1.94	2.658 (3)	145
N1A—H2NA···O7A^{ii}	2.05	2.876 (3)	153
N1B—H1NB···O3^{iii}	1.95	2.848 (2)	172
O3B—H3OB···O1^{iv}	1.86	2.641 (3)	158
O7B—H7OB···O3B^{iv}	2.15	2.754 (3)	131
O5B—H5OB···O3A^{v}	2.26	2.798 (3)	123

Symmetry codes: (i) $1+x, 1+y, z$; (ii) $1-x, 1-y, 1-z$; (iii) $1-x, 1-y, 2-z$; (iv) $-x, 1-y, 2-z$; (v) $x-1, y-1, z$.

All of the H atoms were placed in geometrically calculated positions with average distances C—H 0.956, N—H 0.90 and O—H 0.82 Å. All hydrogen bond calculations were made using *PARST* (Nardelli, 1983).

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *SDP* (Enraf–Nonius, 1985). Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1985). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *ORTEX* (McArdle, 1993). Software used to prepare material for publication: *SHELXL93*.

The authors acknowledge National Diffractometer Facility (DST) at the Department of Biophysics, AIIMS, New Delhi, for intensity data collection.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: VJ1027). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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An α-Adrenergic Agonist: Protonated Oxymetazoline Hydrochloride Monohydrate

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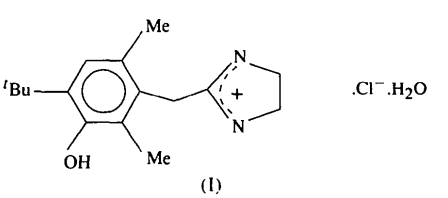
Abstract

The title compound, 2-[4-*tert*-butyl-2,6-dimethyl-3-hydroxyphenyl)methyl]-4,5-dihydro-1*H*,3*H*$^+$-imidazolium chloride monohydrate, $C_{16}H_{25}N_2O^+.Cl^-.H_2O$, is a sympathomimetic amine containing an imidazole ring. The ring is protonated with the positive charge dispersed over both of the N atoms, which are involved in hydrogen bonding, one with the Cl^- ion and the other with a water-O atom. The dihedral angle between the phenyl and imidazole rings is 86.3 (3)°.

Comment

The adrenergic imidazoli(di)nes are generally selective for α-adrenergic receptors. Oxymetazoline hydrochloride belongs to this class of compound and acts as an α-adrenergic agonist. It is clinically used as a nasal decongestant. The crystal structure analysis of the title compound (I) has been undertaken to compare its conformation with those of a few similar drug molecules and with a view to gain insight into the nature of the interaction of these drugs at α-adrenergic receptors.



(I)

The C16—N1 and C16—N2 bond lengths in the imidazole ring are 1.30 (1) and 1.29 (1) Å, respectively. These values, which are comparable within experimental error, are intermediate between those for a single and a double bond, indicating dispersion of positive charge over both N atoms in the imidazole ring. This has been seen in the case of other α-adrenergic agonists like xylometazoline hydrochloride (Ghose & Dattagupta, 1986), clonidine hydrochloride (Cody & DeTitta, 1979), naphazoline hydrochloride

(Podder, Mukhopadhyay, Dattagupta & Saha, 1983), tetrahydrozoline hydrochloride (Ghose & Dattagupta, 1989*a*). But in the case of antagonists like tolazoline hydrochloride (Ghose & Dattagupta, 1989*b*) and phentolamine (Leger, Dubost, Colleter & Carpy, 1983) the two corresponding C—N bonds have significantly different lengths. This may imply that in agonists the positive charge is more or less evenly distributed over the N1—C16—N2 region whereas in antagonists there is an uneven distribution.

The C2—C3—C8—C16 and C3—C8—C16—N1 torsion angles have values of 78.6 (8) and −143.9 (7)°, respectively. Although in some of the adrenergic imidazolines like clonidine hydrochloride (Cody & De-Titta, 1979) and xylometazoline hydrochloride (Ghose & Dattagupta, 1986) these torsion angles show similar values, in many like naphazoline hydrochloride (Podder, Mukhopadhyay, Dattagupta & Saha, 1983), tolazoline hydrochloride (Ghose & Dattagupta, 1989*b*) and tetrahydrozoline hydrochloride (Ghose & Dattagupta, 1989*a*) the corresponding angles have opposite values. In spite of variations in torsion angle values in all imidazolines, the aromatic and the imidazole rings are oriented more or less perpendicularly. In the present case, the dihedral angle is 86.3 (3)°. This near orthogonal orientation may be necessary for the interaction of this class of drugs at the α-adrenergic receptor site.

The crystal structure contains a network of hydrogen bonds. Both of the N atoms and the OH group of the cation, the Cl^- ion and the solvent water molecule participate in hydrogen bonding.

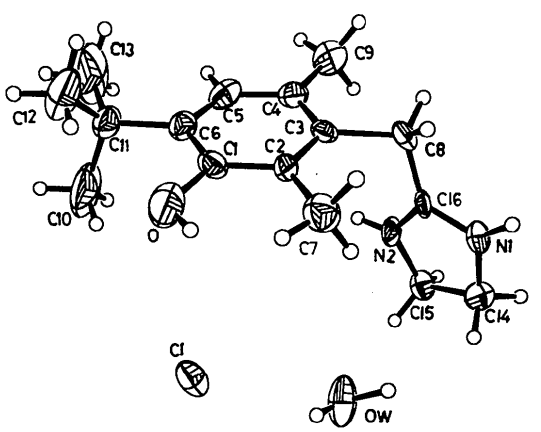


Fig. 1. *ORTEX* (McArdle, 1993) drawing of the protonated oxymetazoline hydrochloride monohydrate with the atom-numbering scheme. Thermal ellipsoids are drawn at the 40% probability level.

Experimental

The title compound was prepared by evaporation of aqueous solution.

Crystal data

$C_{16}H_{25}N_2O^+.Cl^-.H_2O$
M_r = 314.85
Orthorhombic
Pbca
a = 9.708 (2) Å
b = 14.039 (1) Å
c = 26.302 (2) Å
V = 3584.7 (8) Å^3
Z = 8
D_x = 1.167 Mg m^{-3}
D_m = 1.188 Mg m^{-3}
D_m measured by flotation method
Cu $K\alpha$ radiation
λ = 1.54178 Å
Cell parameters from 25 reflections
θ = 18–40°
μ = 1.930 mm^{-1}
T = 293 (2) K
Rectangular
0.80 × 0.40 × 0.10 mm
White

Data collection

CAD-4 diffractometer
$\theta/2\theta$ scans
Absorption correction: none
1308 measured reflections
1308 independent reflections
1221 observed reflections [$I > 2\sigma(I)$]
θ_{max} = 50°
$h = 0 \rightarrow 6$
$k = 0 \rightarrow 13$
$l = 0 \rightarrow 26$
3 standard reflections monitored every 200 reflections
intensity decay: not significant

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.079
$wR(F^2)$ = 0.219
S = 1.131
1308 reflections
191 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F_o^2) + (0.1291P)^2 + 11.9249P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = −0.028
$\Delta\rho_{max}$ = 0.768 e Å^{-3}
$\Delta\rho_{min}$ = −0.283 e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2)*

$U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
Cl	0.1698 (2)	0.5663 (1)	0.2926 (7)	0.0548 (9)
O	0.2494 (7)	0.6574 (4)	0.4000 (2)	0.084 (3)
OW	0.3695 (7)	0.6538 (4)	0.2096 (2)	0.078 (3)
N1	0.7155 (7)	0.8091 (4)	0.2572 (2)	0.044 (3)
N2	0.5412 (7)	0.8994 (4)	0.2712 (2)	0.041 (3)
C1	0.3280 (9)	0.7398 (5)	0.4017 (3)	0.042 (3)
C2	0.4527 (9)	0.7447 (5)	0.3760 (2)	0.038 (3)
C3	0.5238 (8)	0.8297 (5)	0.3769 (2)	0.035 (3)
C4	0.4769 (10)	0.9068 (5)	0.4042 (3)	0.043 (4)
C5	0.3513 (10)	0.8976 (6)	0.4293 (3)	0.053 (4)
C6	0.2748 (9)	0.8162 (5)	0.4295 (2)	0.043 (3)
C7	0.5052 (10)	0.6566 (5)	0.3490 (3)	0.062 (4)
C8	0.6612 (8)	0.8355 (5)	0.3472 (3)	0.046 (3)
C9	0.5557 (10)	0.9995 (6)	0.4083 (3)	0.072 (4)
C10	0.0226 (12)	0.8006 (11)	0.4223 (4)	0.141 (7)
C11	0.1369 (10)	0.8107 (6)	0.4587 (3)	0.058 (4)
C12	0.1380 (12)	0.7265 (8)	0.4948 (4)	0.115 (6)
C13	0.1124 (13)	0.8927 (9)	0.4920 (5)	0.157 (8)
C14	0.6668 (8)	0.8310 (5)	0.2062 (2)	0.046 (3)
C15	0.5517 (9)	0.9014 (5)	0.2166 (2)	0.043 (3)
C16	0.6370 (9)	0.8484 (5)	0.2914 (3)	0.033 (3)

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

D—H···*A*	H···*A*	*D*···*A*	*D*—H···*A*
O—H1O···Cl	2.73	3.197 (6)	118
OW—H1*OW*···Cl	2.52	3.168 (6)	134
N1—H1N···*OW*^{i}	2.01	2.785 (8)	150
OW—H2*OW*···Cl^{i}	2.18	3.165 (7)	166
N2—H2N···Cl^{ii}	2.41	3.163 (7)	146

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

With the poor crystal quality, data collection had to be restricted to $\theta = 50°$, beyond which intensity decreased rapidly. All of the H atoms were placed in geometrically calculated positions (with average distances C—H 0.961, N—H 0.86 and O—H 0.82 Å), except for the two H atoms of the solvent water molecule which were located from a difference Fourier map. All hydrogen bond calculations were made using *PARST* (Nardelli, 1983).

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software* (Enraf–Nonius, 1989). Data reduction: *SDP* (Enraf–Nonius, 1985). Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1985). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *ORTEX* (McArdle, 1993). Software used to prepare material for publication: *SHELXL93*.

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4,4′-Dichloro-2,2′-iminodibenzoic Acid

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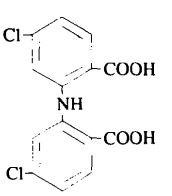
Abstract

Both rings in the title compound, $C_{14}H_9Cl_2NO_4$, are essentially planar, the r.m.s. deviation being 0.007 Å. The dihedral angle between the two planes is 44.8 (3)°. Dimerization occurs through hydrogen bonding of the carboxylic groups.

Comment

Lobenzarit acid (4-chloro-2,2′-iminodibenzoic acid) is an intermediate compound in the synthesis of lobenzarit disodium (CCA, disodium 4-chloro-2,2′-iminodibenzoate) which is an anti-rheumatic drug (Suzuki *et al.*, 1984; Pellón, 1990, 1993). We have carried out the crystallographic characterization of both compounds (Novoa, Duque, Pomés & Pellón, 1995) in the course of a crystallographic investigation of CCA analogues. Although the pharmacological activity of the title compound, (I), has not been tested, the substituents bonded to the diphenylamine skeleton makes this compound an analogue of lobenzarit acid.



(I)

Fig. 1 shows the atom-numbering scheme used. The aromatic rings are planar and the dihedral angle between the two planes is 44.8 (3)°. An internal N—H···O bifurcated hydrogen bond with the imino N atom as donor and carbonyl O atoms as acceptors is present [H(1)···O(1) 2.12 (6) Å, N(1)—H(1)···O(1) 129 (6)° and H(1)···O(4) 2.16 Å, N(1)—H(1)···O(4) 124 (6)°]. The imino group is not involved in intermolecular interactions, which is a common feature of related compounds such as fenamates (Dhanaraj & Vijayan,