Table 3. *Mean bond lengths* (Å) *in acenaphthene compared with those in acenaphthylene, fluoranthene, and naphthalene as determined by neutron diffraction*

	Acenaphthene[a]	Acenaphthylene[b]	Fluoranthene[c]	Naphthalene[d]	Naphthalene[e]
C(1)–C(2)	1·380 (4)	1·381 (7)	1·361 (5)	1·373 (3)	1·381 (2)
C(2)–C(3)	1·423 (4)	1·424 (8)	1·433 (6)	1·410 (3)	1·421 (2)
C(3)–C(4)	1·388 (4)	1·382 (8)	1·383 (6)	1·373 (3)	1·381 (2)
C(4)–C(5)	1·427 (3)	1·433 (6)	1·415 (5)	1·423 (3)	1·426 (2)
C(5)–C(6)	1·398 (5)	1·386 (10)	1·413 (6)	1·420 (3)	1·432 (2)
C(1)–C(6)	1·422 (3)	1·441 (6)	1·415 (5)	1·423 (3)	1·426 (2)
C(1)–C(7)	1·507 (4)	1·466 (7)	1·498 (4)		
C(7)–C(7′)	1·573 (6)	1·395 (11)	1·408 (6)		

Notes: (*a*) this work, (*b*) 80 K, Wood, Welberry & Rae (1985), (*c*) Hazell, Jones & Sowden (1977), (*d*) Hazell (1980, unpublished, cited in Hazell & Mariezcurrena, 1980); new refinement with the data of Pawley & Yeats (1969), (*e*) 12 K, Natkaniec, Belushkin, Dyck, Fuess & Zeyen (1983).

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Structure of (±)-2-(2-Chloro-3,4-dimethoxyphenyl)-2-hydroxy-*N*-isopropylethylamine Hydrochloride

BY JACOBUS KOORTS AND MINO CAIRA

Crystallography Group, University of Port Elizabeth, PO Box 1600, *Port Elizabeth* 6000, *South Africa*

AND DANIEL P. VENTER

Department of Pharmacology, University of Potchefstroom for CHE, Potchefstroom 2520, *South Africa*

(*Received* 29 *October* 1985; *accepted* 11 *December* 1985)

Abstract. $C_{13}H_{21}ClNO_3^+.Cl^-$, $M_r = 310{\cdot}2$, triclinic $P\bar{1}$, $a = 7{\cdot}580\ (4)$, $b = 8{\cdot}566\ (5)$, $c = 12{\cdot}346\ (6)$ Å, $\alpha = 82{\cdot}57\ (2)$, $\beta = 101{\cdot}26\ (2)$, $\gamma = 94{\cdot}91\ (2)°$, $V = 778{\cdot}1\ (7)$ Å^3, $Z = 2$, $D_m = 1{\cdot}33\ (1)$, $D_x = 1{\cdot}324$ Mg m^{-3}, λ(Mo $K\alpha$) $= 0{\cdot}71069$ Å, $\mu = 0{\cdot}420$ mm^{-1}, $F(000) = 328{\cdot}0$, $T = 298$ K. Final $R = 0{\cdot}048$ for 1619 observed reflections. The main conformational features of the molecule are similar to those mostly observed for structurally related β-adrenergics. The molecular packing is determined by

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N–H···Cl^-, O–H···Cl^- and N–H···O hydrogen bonds which give rise to planar and non-planar pseudo-eight-membered hydrogen-bonded rings.

Introduction. Since β-adrenergic blocking agents enhance the respiratory difficulties in asthmatic patients (Murmann, 1969; Coleman & Somerville, 1977) it is important to develop cardioselective (β_1-selective) β-adrenergic blocking drugs with minimal bronchial (β_2-activity) side effects. The title compound is the third drug studied and exhibits a marked increase in β_1-adrenoceptor blocking activity as well as β_1-selectivity compared to the parent compound (±)-2-(3,4-dimethoxyphenyl)-2-hydroxy-*N*-isopropyl-ethylamine hydrochloride (Pratesi & Grana, 1965).

Table 1. *Fractional atomic coordinates* ($\times 10^4$) *and equivalent isotropic thermal parameters* (U_{iso} *for* H) (Å^2 × 10^3) *with e.s.d.'s in parentheses*

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

	x	y	z	U_{eq}
Cl(1)	8579 (1)	7158 (2)	6394 (1)	73 (1)
Cl(2)	8722 (1)	6354 (1)	10910 (1)	50 (1)
C(1)	5374 (5)	6173 (4)	7002 (3)	35 (1)
C(2)	6245 (4)	6816 (4)	6139 (3)	38 (1)
C(3)	5351 (5)	7211 (4)	5066 (3)	40 (2)
O(3)	6274 (3)	7729 (3)	4213 (2)	55 (1)
C(4)	3479 (5)	7011 (4)	4838 (3)	40 (2)
O(4)	2653 (4)	7492 (3)	3775 (2)	55 (1)
C(5)	2565 (5)	6357 (4)	5675 (3)	43 (2)
C(6)	3509 (5)	5955 (4)	6739 (3)	42 (2)
C(7)	6350 (5)	5689 (4)	8169 (3)	36 (1)
O(7)	5593 (4)	6430 (3)	8936 (2)	48 (1)
C(8)	6122 (5)	3903 (4)	8419 (3)	37 (1)
N(9)	7252 (4)	3361 (3)	9517 (2)	35 (1)
C(10)	6926 (5)	1644 (4)	9920 (3)	44 (2)
C(11)	8024 (6)	1337 (5)	11087 (3)	66 (2)
C(12)	7414 (6)	604 (4)	9123 (3)	56 (2)
C(13)	6416 (6)	9391 (5)	3947 (4)	73 (2)
C(14)	736 (6)	7600 (6)	3572 (3)	74 (2)
H(O)	6477 (56)	6563 (51)	9472 (34)	80†

† Not refined.

Table 2. *Selected bond lengths* (Å), *torsion angles* (°) *and hydrogen-bond data with e.s.d.'s in parentheses*

C(2)–Cl(1)	1·741 (3)	C(8)–N(9)	1·496 (4)
C(3)–O(3)	1·382 (5)	N(9)–C(10)	1·506 (4)
C(4)–O(4)	1·367 (4)	C(13)–O(3)	1·419 (5)
C(1)–C(7)	1·509 (5)	C(14)–O(4)	1·434 (6)
C(7)–O(7)	1·435 (5)	O(7)–H(O)	0·86 (4)
C(7)–C(8)	1·523 (5)		
C(6)–C(1)–C(7)–C(8) (τ_1)*	65·6 (5)	O(7)–C(7)–C(8)–N(9)	−67·3 (4)
C(1)–C(7)–C(8)–N(9) (τ_2)*	173·3 (3)	C(8)–N(9)–C(10)–C(11)	−174·1 (3)
C(2)–C(1)–C(7)–O(7)	127·1 (4)	C(8)–N(9)–C(10)–C(12)	62·9 (4)
C(1)–C(7)–O(7)–H(O)	−149 (3)	C(2)–C(3)–O(3)–C(13)	−98·5 (5)
C(7)–C(8)–N(9)–C(10)	171·7 (3)	C(3)–C(4)–O(4)–C(14)	−167·7 (4)
N(9)···Cl(2^i)	3·181 (4) Å	N(9)–H(9*A*)···Cl(2^i)	169°
H(9*A*)···Cl(2^i)	2·11		
O(7)···Cl(2)	3·049 (3)	O(7)–H(O)···Cl(2)	168 (4)
H(O)···Cl(2)	2·21 (4)		
N(9)···Cl(2)	3·267 (3)	N(9)–H(9*B*)···Cl(2)	130
H(9*B*)···Cl(2)	2·47		
N(9)···O(7^{ii})	3·177 (5)	N(9)–H(9*B*)···O(7^{ii})	125
H(9*B*)···O(7^{ii})	2·43		

Symmetry code: (i) $2-x, 1-y, 2-z$; (ii) $1-x, 1-y, 2-z$.

* See Murray-Rust, Murray-Rust, Hartley, Hallett & Clifton (1984).

Experimental. Colourless single crystals obtained by slow cooling from 2-propanol solution. Density determined by flotation in PhBr–PhCl mixture. Crystal system from Weissenberg and precession photographs with Cu $K\alpha$ radiation ($\lambda = 1{\cdot}5418$ Å). Crystal dimensions 0·24 × 0·20 × 0·18 mm, Philips PW 1100 four-circle diffractometer, graphite-monochromated Mo $K\alpha$ radiation. Cell constants by least-squares refinement of angular data for 25 reflections in range $8 < 2\theta < 24°$. Three standard reflections monitored after every 66 reflections; no significant intensity variation. 2161 reflections measured by ω–2θ technique, scan speed $0{\cdot}060°\theta\,s^{-1}$, scan width $1{\cdot}5°\theta$, θ range 3–23° (*hkl* limits ±8, ±9, 13); 2121 unique reflections ($R_{int} = 0{\cdot}051$) of which 502 reflections with $I_o < 2\sigma(I_o)$ omitted as unobserved [$\sigma(I_o)$ based on counting statistics]. Lorentz and polarization corrections applied, no absorption correction. Space group $P\bar{1}$ confirmed by Patterson analysis and intensity statistics. Structure solved by Patterson and Fourier methods and refined by full-matrix least squares, program *SHELX*76 (Sheldrick, 1976); $\sum w(|F_o| - |F_c|)^2$ minimized with $w = 1/\sigma^2(F_o)$ which yielded a constant distribution of $\langle w\Delta^2\rangle$ with $(\sin\theta)/\lambda$ and $[F_o/F_o(\text{max.})]^{1/2}$. All non-H atoms thermally anisotropic; all H atoms located in difference syntheses but [except for H(O) whose position was refined] included in idealized positions in a riding model (C–H, N–H = 1·08 Å) with common U_{iso} values for five groups of atoms [final values 0·047 (7)–0·13 (1) Å^2]. $R = 0{\cdot}048$, $wR = 0{\cdot}042$ for 1619 observations and 192 parameters, all $\Delta/\sigma < 10^{-3}$. Max. and min. peak heights in final difference map 0·24 and −0·28 e Å^{-3}. Scattering factors from *International Tables for X-ray Crystallography* (1974). Illustrations drawn with *CRISTEP* (De Wet, 1980). Geometrical calculations performed with *PARST* (Nardelli, 1983).

Discussion. Table 1* lists final refined atomic parameters. Selected bond lengths and torsion angles, and hydrogen-bond data are listed in Table 2.

The cation chosen for illustration in Fig. 1 has the *R* configuration associated with active dichloroisoproterenol analogues (Howe & Rao, 1968).

There are no significant differences between the bond lengths reported here and corresponding distances in (±)-2-(2-chloro-3,4-dimethoxyphenyl)-*N*-isopropyl-2-methoxyethylamine hydrochloride (1) (Koorts & Caira, 1985*a*), which differs only by substitution of a methyl group for H(O) of the hydroxy group. As in compound (1), the ethylamine side chain is extended (τ_2, Table 2),

* Lists of structure factors, calculated H-atom coordinates, anisotropic thermal parameters, bond lengths, bond angles, torsion angles and least-squares-planes' data have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42715 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

but a notable feature in the present case is the larger deviation of the plane of this side chain from perpendicularity with respect to the aromatic ring. Thus, τ_1 (Table 2) is 65·6 (5)° compared with the more typical values of 93·1 (4)° in (1) and −85·5 (4)° in (±)-2-(2-chloro-4,5-dimethoxyphenyl)-2-hydroxy-*N*-isopropylethylamine hydrochloride (2)(Koorts & Caira, 1985*b*), which is isomeric with the title compound. In this conformation, a significantly short contact, Cl(1)···H(7) 2·53 Å, occurs.

A second difference involves torsion about the C(8)–N(9) bond, where a *trans* conformation is adopted, in contrast to (+)-anticlinal and (−)-synclinal respectively for the *R* enantiomers of (1) and (2). Coupled with the torsion about N(9)–C(10), this results in the entire side chain [including the terminal isopropyl atom C(11)] being maximally extended. Atom N(9) is *gauche* with respect to O(7), as is typical for O–C–C–N^+ groupings (Paxton & Hamor, 1977).

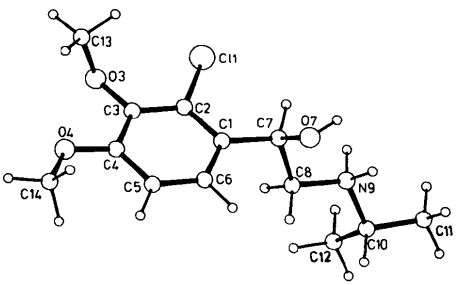

Fig. 1. Conformation of the (*R*)-enantiomeric cation showing atomic numbering.

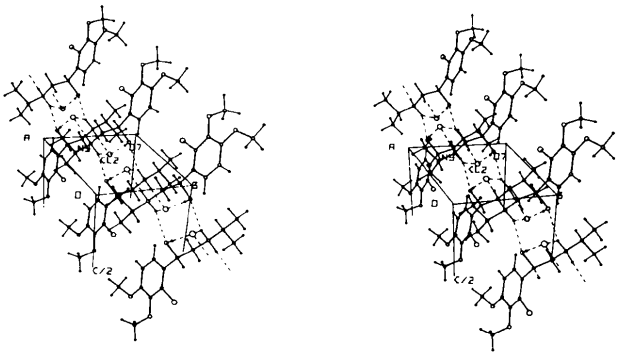

Fig. 2. Stereoview of the hydrogen-bonding geometry and crystal packing. The labelled molecule is at $x, y, z - 1$.

Important geometrical parameters, frequently cited in structure–activity relationships for drugs of this class, are for the title compound: (i) the non-bonded distance N(9)···O(7), 2·955 (4) Å, which lies in the reported range of 2·65–3·04 Å (Ammon, Balsamo, Macchia, Macchia, Howe & Keefe, 1975), (ii) the N···(centre of phenyl ring) distance, 5·12 (1) Å, which is consistent with values observed in related species containing the 2-phenylethylamine nucleus (Pattanayek, Dattagupta & Saha, 1983), and (iii) the displacement of N(9) from the phenyl ring, 1·480 (3) Å.

Crystal packing and the hydrogen-bonding interactions are shown in Fig. 2. The extended side-chain conformation is stabilized by intermolecular hydrogen bonding which links cations in two distinct arrangements. Pairs of cations, centrosymmetrically related by the inversion centre at $0,\frac{1}{2},0$, are linked *via* N–H···Cl^- hydrogen bonds involving both amino H atoms, while those related by the inversion centre at $\frac{1}{2},\frac{1}{2},0$ are linked by N–H···O hydrogen bonds. One amino H atom [H(9*B*)] thus participates in a bifurcated hydrogen bond, N–H···Cl^- and N–H···O. Each Cl^- ion engages in three distinct hydrogen bonds, two N–H···Cl^- and one O–H···Cl^-. The result is a continuous network consisting of alternating planar and non-planar pseudo-eight-membered hydrogen-bonded rings in bands parallel to *x*. The title compound is markedly less soluble in water than the isomeric salt (2) which has the same potential for hydrogen bonding. As the overall strengths of the hydrogen bonds in the two structures are comparable, the greater cohesion in the present case appears to be associated with the formation of the eight-membered hydrogen-bonded rings, which are lacking in crystals of (2).

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