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## Structure of 1-(2-Chloro-4,5-dimethoxyphenyl)-2-(isopropylamino)ethanol

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**Abstract.**  $C_{13}H_{20}ClNO_3$ ,  $M_r = 273.8$ , monoclinic,  $P2_1/a$ ,  $a = 8.389$  (3),  $b = 18.39$  (1),  $c = 9.395$  (2) Å,  $\beta = 94.46$  (3)°,  $V = 1445.4$  Å<sup>3</sup>,  $Z = 4$ ,  $D_x = 1.26$  g cm<sup>-3</sup>,  $\lambda(\text{Mo } K\alpha) = 0.71073$  Å,  $\mu = 2.2$  cm<sup>-1</sup>,  $F(000) = 584$ ,  $T = 298$  K,  $R = 0.0318$  for 2018 unique reflections. The ethylamine side chain is oriented perpendicular to the plane of the phenyl ring; the isopropyl group is *trans* to the chiral centre of the molecule. The molecules form a one-dimensional chain linked by O–H...N hydrogen bonds.

**Introduction.** The title compound is one of a series of structurally related  $\beta$ -adrenoceptor blocking drugs, studied by molecular-mechanics calculations in this laboratory (Squier, Van der Schyf, Venter, Oliver, Van Rooyen & Dillen, 1986). Synthesis and pharmacological results are reported in the literature (Squier, Van der Schyf, Oliver & Venter, 1986).

**Experimental.** Colourless regular shaped crystal,  $ca$   $0.3 \times 0.3 \times 0.4$  mm used for data collection. Intensities measured at 298 K; Enraf–Nonius CAD-4 diffractometer; graphite-monochromated Mo  $K\alpha$  radiation;  $\omega$  scan; variable scan speed with a maximum of  $5.49^\circ \text{ min}^{-1}$ , and a minimum corresponding to a measuring time of 50 s per reflection;  $\omega$ -scan angle changed as  $(0.63 + 0.34 \tan\theta)^\circ$ , horizontal aperture as  $(1.17 + 0.77 \tan\theta)$  mm, limited to 1.3–5.0 mm; vertical slit fixed to 4 mm. Unit-cell parameters determined with 25 reflections in the  $\theta$  range 7–19°; total exposure time 18.3 h; intensity control every hour using three standard reflections ( $2\bar{5}1$ ,  $1\bar{5}2$ ,  $0\bar{5}3$ ), no significant loss in intensity; orientation control every 200 reflections, allowed deviation  $0.1^\circ$ . Monoclinic data set collected up to  $(\sin\theta)/\lambda = 0.595$  Å<sup>-1</sup> ( $h = 0 \rightarrow 9$ ,  $k =$

$0 \rightarrow 21$ ,  $l = -11 \rightarrow 11$ ) resulting in 2650 reflections of which 311 were unobserved [ $I < \sigma(I)$ ]. Data corrected for Lorentz and polarization effects;  $\psi$ -scan empirical absorption correction (transmission 94.29 to 99.27%).

The structure was solved by direct methods (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), all H atoms were located from subsequent Fourier maps. Non-H atoms were refined anisotropically, H atoms with a common isotropic temperature factor  $U = 0.079$  (2) Å<sup>2</sup>; *SHELX76* (Sheldrick, 1976); full-matrix method with  $1/\sigma^2(F)$  weights; 2018 unique reflections used for 224 refined parameters;  $R_{\text{int}} = 0.0195$ ,  $(\Delta/\sigma)_{\text{max}} = 0.59$ ;  $(\Delta\rho)_{\text{max}} = 0.36$ ,  $(\Delta\rho)_{\text{min}} = -0.33$  e Å<sup>-3</sup>;  $R = 0.0318$ ,  $wR = 0.0478$ ; atomic scattering factors from *International Tables for X-ray Crystallography* (1974).

**Discussion.** Table 1\* lists final refined positional parameters with equivalent isotropic temperature factors. The coordinates refer to the (*R*)-enantiomer of the compound, hereafter referred to as (1). Selected bond lengths and torsion angles are given in Table 2. A view of the molecule is given in Fig. 1.

The phenyl ring is planar; the r.m.s. deviation of the C atoms is 0.002 Å. The methoxy substituents are coplanar with the ring. The ethylamine side chain adopts a perpendicular-*trans* conformation. This is the conformation which occurs most frequently in crystalline phenylethanolamine derivatives (Murray-Rust,

\* Lists of structure factors, anisotropic thermal parameters, bond lengths and valence angles, and H-atom data have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44576 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Murray-Rust, Hartley, Hallett & Clifton, 1984), and is also the form that is calculated by molecular mechanics to be the most stable (Squier, Van der Schyf, Venter, Oliver, Van Rooyen & Dillen, 1986).

The conformation about the C(9)–N(10) bond is (+)-antiperiplanar, in contrast to the (–)-synclinal form observed in the related hydrochloride (Koorts & Cairn, 1985*b*), hereafter referred to as (2). In the very similar 2-(2-chloro-3,4-dimethoxyphenyl)-*N*-isopropyl-

Table 1. Fractional coordinates ( $\times 10^4$ ,  $\times 10^5$  for Cl) and equivalent isotropic temperature factors ( $\text{\AA}^2 \times 10^3$ ,  $\times 10^4$  for Cl)

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

	x	y	z	$U_{eq}$
C(1)	–628 (3)	–1554 (1)	–5671 (3)	45 (1)
C(2)	–1508 (3)	–912 (2)	–5785 (3)	49 (1)
C(3)	–2017 (3)	–554 (1)	–4617 (3)	49 (1)
C(4)	–1640 (3)	–859 (1)	–3245 (3)	49 (1)
C(5)	–781 (3)	–1487 (2)	–3117 (3)	49 (1)
C(6)	–278 (3)	–1832 (1)	–4325 (3)	48 (1)
C(7)	–24 (3)	–1903 (2)	–6996 (3)	49 (1)
O(8)	–1169 (2)	–1845 (1)	–8189 (2)	56 (1)
C(9)	–8533 (4)	–1503 (2)	–7382 (3)	58 (1)
N(10)	–7865 (3)	–1845 (1)	–8629 (2)	50 (1)
C(11)	–6920 (4)	–1325 (2)	–9420 (3)	60 (1)
C(12)	–6440 (5)	–1702 (2)	–760 (4)	83 (1)
C(13)	–5473 (4)	–1074 (2)	–8504 (4)	78 (1)
O(14)	–2887 (2)	71 (1)	–4630 (2)	63 (1)
C(15)	–3175 (4)	433 (2)	–5961 (4)	69 (1)
O(16)	–2199 (2)	–476 (1)	–2138 (2)	64 (1)
C(17)	–1832 (5)	–779 (2)	–755 (4)	80 (1)
Cl(18)	–91843 (10)	–26329 (4)	–40577 (8)	760 (2)

Table 2. Selected bond lengths ( $\text{\AA}$ ) and torsion angles ( $^\circ$ )

C(1)–C(7)	1.522 (5)	C(6)–Cl(18)	1.743 (4)
C(7)–C(8)	1.422 (5)	C(3)–O(14)	1.361 (5)
C(7)–C(9)	1.519 (6)	O(14)–C(15)	1.420 (6)
C(9)–N(10)	1.477 (5)	C(4)–O(16)	1.368 (4)
N(10)–C(11)	1.480 (6)	O(16)–C(17)	1.425 (6)
C(6)–C(1)–C(7)–C(9)	–97.6 (3)	O(8)–C(7)–C(9)–N(10)	–61.8 (3)
C(1)–C(7)–C(9)–N(10)	177.6 (2)	C(9)–N(10)–C(11)–C(12)	–174.0 (3)
C(6)–C(1)–C(7)–O(8)	144.4 (2)	C(9)–N(10)–C(11)–C(13)	64.3 (3)
C(7)–C(9)–N(10)–C(11)	154.7 (2)		

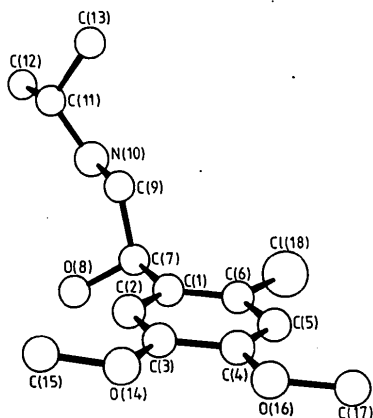


Fig. 1. View of the title compound showing atom numbering.

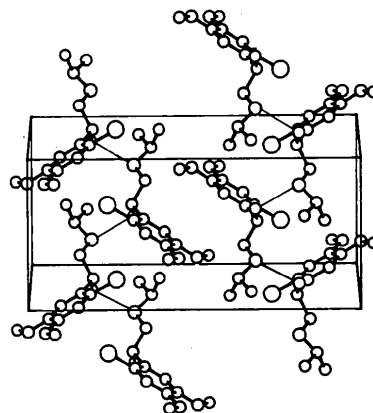


Fig. 2. Crystal packing. Hydrogen bonds are indicated by fine lines.

2-methoxyethylamine hydrochloride (Koorts & Cairn, 1985*a*) and 2-(2-chloro-3,4-dimethoxyphenyl)-2-hydroxy-*N*-isopropylethylamine hydrochloride (Koorts, Cairn & Venter, 1986), the conformations are found to be respectively (+)-anticlinal and (+)-antiperiplanar.

Differences in bond lengths compared with (2) are found for C(9)–N(10) and N(10)–C(11), where shorter distances are observed for (1), indicating a weakening of the bonds in (2) as a result of the protonation of N(10).

Crystal packing and hydrogen bonds are shown in Fig. 2. The hydroxyl hydrogen at O(8) acts as a donor to N(10) [ $\frac{1}{2} + x, \frac{1}{2} - y, z$ ];  $r(\text{N} \cdots \text{O}) = 2.812$ ,  $r(\text{N} \cdots \text{H}) = 1.963 \text{ \AA}$ . The mean distance of the Cl atom from the atoms of the phenyl ring at [ $\frac{1}{2} + x, \frac{1}{2} - y, z$ ] is  $3.647 \text{ \AA}$ , which is nearly equal to the sum of the van der Waals radii.

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