p-Hydroxy-m-methoxy-α-(methylaminomethyl)benzyl Alcohol Hydrochloride (DL-Metanephrine Hydrochloride), $C_{10}H_{16}NO_3^+.Cl^-$

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Abstract. $M_r = 233 \cdot 7$, triclinic, $P\bar{1}$, $a = 8 \cdot 359$ (2), $b = 9 \cdot 101$ (3), $c = 7 \cdot 847$ (3) Å, $\alpha = 87 \cdot 69$ (3), $\beta = 95 \cdot 19$ (2), $\gamma = 81 \cdot 43$ (2)°, $V = 587 \cdot 0$ Å³, $Z = 2$, $D_m = 1 \cdot 320$, $D_c = 1 \cdot 322$ Mg m⁻³, $\lambda(\text{Mo } K\alpha) = 0 \cdot 71069$ Å, $\mu(\text{Mo } K\alpha) = 0 \cdot 31$ mm⁻¹, $T = 298$ K, $R = 0 \cdot 065$, $R_w = 0 \cdot 040$ for 1758 reflections. The ethylamine side chain is oriented out of the plane of the benzene ring. The structure has a network of $NH \cdots Cl^-$, $OH \cdots Cl^-$ and $NH \cdots O$ hydrogen bonds.

Introduction. This compound (I) is one of the metabolites of catecholamines and is obtained when adrenaline is methylated by catechol O-methyl transferase (Barlow & Ing, 1964). It is also a naturally occurring derivative of epinephrine, found in urine and in certain tissues. It differs from adrenaline only in one methoxy group in place of a hydroxyl group at the *m* position. This analysis is to study the conformational changes due to this methoxylation.
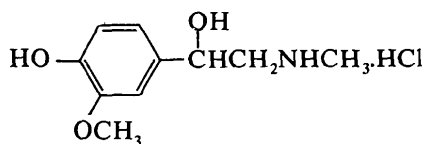
(I)

Experimental. Needle-shaped single crystals (Sigma Chemical Co.) grown by slow evaporation of an aqueous solution, density determined by flotation in a mixture of bromoform and benzene, cell dimensions measured on a CAD-4 diffractometer by least-squares refinement of seven selected Friedel pairs in the interval $0 \cdot 269 < \sin\theta/\lambda < 0 \cdot 421$ Å⁻¹, data collected with a crystal $0 \cdot 25 \times 0 \cdot 23 \times 0 \cdot 18$ mm, $2\theta/\omega$ scan mode, CAD-4 diffractometer, graphite-monochromatized radiation, data corrected for Lorentz and polarization factors but not for absorption; three standard reflections monitored after every 50 data reflections, intensities of standards showed gradual fluctuations of less than ±5% throughout the data collection of the 2118 independent reflections measured within the range $2° \le \theta \le 25°$; 360 were considered unobserved by the criterion $F < 2\sigma(F)$ where $\sigma(F)$ is the e.s.d. based on

counting statistics. Structure solved by direct methods with *MULTAN* (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978); although the $\langle |E^2| - 1 \rangle$, $\langle E \rangle$ and the $N(z)$ statistical distributions (Howells, Phillips & Rogers, 1950) indicated the noncentrosymmetric space group $P1$, a solution could be obtained only when the centrosymmetric space group was assumed; structure refined anisotropically by block-diagonal least-squares methods (*BLOCK*; *X-RAY ARC*, 1971) to $R = 0 \cdot 098$ and $R_w = 0 \cdot 080$, quantity minimized was $\sum w(|F_o| - |F_c|)^2$ with $w = 1/\sigma^2(F)$, scattering factors from *International Tables for X-ray Crystallography* (1974), H atoms located from a difference Fourier map, and placed in the stereochemically most likely positions; H atoms were assigned the isotropic temperature factors of the heavier atoms to which they are attached, and their inclusion with fixed parameters gave $R = 0 \cdot 065$ and $R_w = 0 \cdot 040$; refinement was stopped when the average parameter shifts were less than their standard deviations; final difference Fourier map featureless; $F(000) = 248$; the atomic parameters are given in Table 1.*

Discussion. The 50% probability thermal ellipsoids and the atomic numbering scheme are shown in Fig. 1. The bond lengths and angles are normal and do not show any remarkable deviation from the values obtained by averaging pertinent bond lengths and angles for 34 similar compounds (Hebert, 1979). There is a slightly distorted tetrahedral arrangement around C(7) and N atoms with deviations of the angles O(3)–C(7)–C(8), O(3)–C(7)–C(6) and C(8)–N–C(9) from 109°. The conformation of the side chain is described by the torsion angles shown in Fig. 1. This folded form of the side chain is different from that observed in adrenaline and in most of the other catecholamines (Hebert, 1979), where it is in the extended form. The distance of

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the N atom from the center of the ring is 3·73 (1) Å, whereas in typical catecholamines it is around 5 Å. The height of the N atom from the plane of the ring is 2·56 (1) Å. The hydrogen-bond distances are given in Table 2 and the molecular packing is shown in Fig. 2. All four H atoms available for hydrogen-bond formation participate in hydrogen bonding, forming a three-dimensional network of hydrogen bonds of types N—H···Cl, O—H···Cl and N—H···O. The N atom has two other close contacts with atoms O(1) and O(2), with N···O(1) = 2·349 (3) and N···O(2) = 2·913 (3) Å. The latter may be a weak hydrogen bond.

Table 1. *Fractional atomic coordinates* $(\times 10^4)$ *with e.s.d.'s in parentheses and isotropic thermal parameters* (Å^2)

$$B_{eq} = \tfrac{4}{3}\Sigma_i\Sigma_j\beta_{ij}(\mathbf{a}_i\cdot\mathbf{a}_j).$$

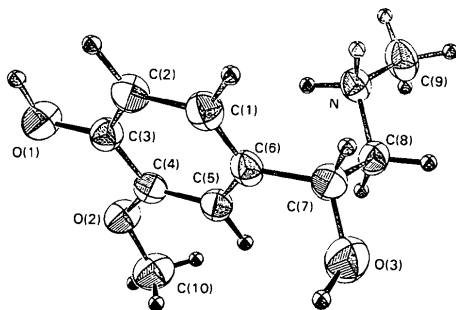|	x	y	z	B_{eq}
Cl	3813 (1)	−1882 (1)	−3410 (1)	4·3
N	−2424 (3)	−1972 (3)	−3211 (4)	3·2
O(1)	−1004 (3)	−6428 (3)	2834 (3)	4·0
O(2)	1300 (3)	−4857 (3)	2514 (3)	3·8
O(3)	−2076 (4)	466 (3)	328 (4)	5·8
C(1)	−3431 (4)	−3033 (4)	694 (5)	3·6
C(2)	−3048 (4)	−4457 (4)	1483 (5)	3·5
C(3)	−1458 (4)	−5035 (4)	2065 (5)	3·2
C(4)	−228 (4)	−4174 (4)	1867 (5)	3·1
C(5)	−597 (5)	−2759 (4)	1075 (5)	3·3
C(6)	−2212 (4)	−2199 (4)	476 (5)	3·3
C(7)	−2681 (5)	−681 (4)	−505 (5)	4·5
C(8)	−1938 (5)	−696 (4)	−2253 (5)	3·5
C(9)	−2095 (5)	−1879 (5)	−5050 (5)	5·1
C(10)	2572 (5)	−3949 (5)	2659 (6)	5·1

Fig. 1. A perspective view of the molecule with the atom-numbering scheme. Some torsion angles (Klyne & Prelog, 1960) are: C(1)–C(6)–C(7)–C(8) = −112·2, C(6)–C(7)–C(8)–N = 53·8, C(1)–C(6)–C(7)–O(3) = 131·1, O(3)–C(7)–C(8)–N = 176·0, C(7)–C(8)–N—C(9) = 167·0, C(10)–O(2)–C(4)–C(5) = 11·6°. The mean standard deviation in torsion angles is 0·8°.

Table 2. *Hydrogen-bond distances* (Å) *and angles* (°)

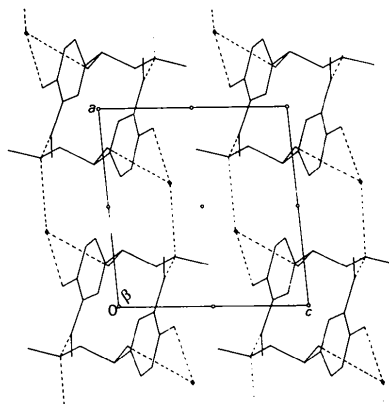| D—H···A	Position of acceptor atom	D···A	D···H	H···A	$\angle D$—H···A
N—H(N)···Cl	$x-1,y,z$	3·119 (3)	1·06	2·07	171·8
O(1)—H(O1)···Cl	$-x,-1-y,-z$	3·040 (3)	0·92	2·15	163·6
O(3)—H(O3)···Cl	$-x,-y,-z$	3·146 (3)	1·19	1·99	162·7
N—H'(N)···O(2)	$-x,-1-y,-z$	2·913 (3)	1·05	1·95	150·6

Fig. 2. The crystal structure projected down the b axis. Solid circles denote Cl⁻ ions and broken lines indicate hydrogen bonds.

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