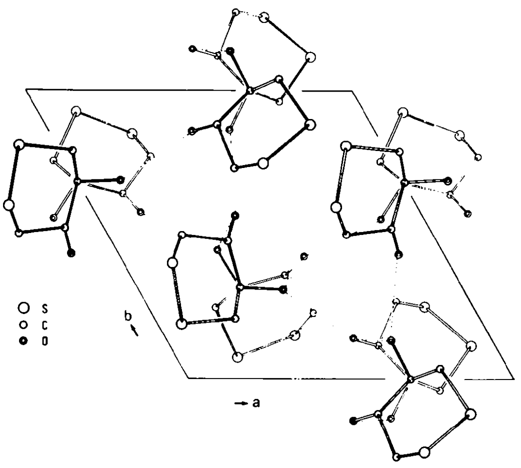

Fig. 2. Projection of the crystal structure along the *c* axis. Broken lines indicate hydrogen bonds.

The positions of the H atoms do not allow the formation of an intramolecular hydrogen bond between the two OH groups in the *cis* position.

In the crystal (Fig. 2), the molecules are fully hydrogen bonded. Each hydroxyl group is involved in two linear hydrogen bonds to symmetry-related molecules. O(1) is the donor to O(2) across the diad axis [O(1)···O(2) 2·85, H(1)···O(2) 2·15 Å, O(1)···H(1)···O(2) 163°], giving rise to dimeric molecules which are bonded helically, *via* the O(2) donor bonds, along the screw axes [O(1)···O(2) 2·86, H(2)···O(1) 2·00 Å, O(1)···H(2)···O(2) 162°]. The packing distances fall within the normal range except for the S(1) atom which is involved in a rather short intermolecular contact [S(1)(x,y,z); S(1)($x-y, -y, \frac{2}{3}-z$)] of 3·37 Å, which is well below the sum of the van der Waals radii (3·7 Å).

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Structure of *p*-Hydroxyephedrine Hydrochloride

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Abstract. $C_{10}H_{15}NO_2.HCl$, $M_r = 217·7$, orthorhombic, $P2_12_12_1$, $a = 6·388\,(3)$, $b = 7·555\,(3)$, $c = 23·854\,(5)$ Å, $V = 1151·23$ Å^3, $Z = 4$, $D_m = 1·26$, $D_c = 1·26$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, μ(Cu $K\alpha$) = 2·773 mm^{-1}. The structure was solved by direct methods and refined to an R value of 0·047 for 1088 diffractometer data using block-diagonal least-squares methods. The ethylamine side chain is in the extended form, the C—C—C—N$^+$ torsion angle being 178·1°. The mean plane through these atoms makes an angle of 81·1° with the plane of the phenol ring. The distance of the amino N atom from the centre of the phenyl ring is 5·16 Å. The crystal structure is stabilized by a network of N—H···Cl, O—H···Cl and O—H···O hydrogen bonds.

Introduction. *p*-Hydroxyephedrine, *p*-hydroxy-α-[1-(methylamino)ethyl]benzyl alcohol, a sympathomimetic amine, pharmacologically resembles *p*-aminoephedrine which is about twice as active, and half as toxic, as ephedrine (McLean, 1960). Since such biogenic amines are found to assume a favoured conformation (Carlström, Bergin & Falkenberg, 1973), it was thought worthwhile to determine the crystal structure of *p*-hydroxyephedrine hydrochloride.

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Single crystals were grown by slow evaporation of an aqueous solution of the title compound. The unit-cell dimensions were first determined from rotation and Weissenberg photographs and later more accurately on a Stoe four-circle single-crystal diffractometer using Cu $K\alpha$ radiation. Systematic absences indicate the space group $P2_12_12_1$.

X-ray intensities were collected using a crystal of dimensions 0·10 × 0·15 × 0·35 mm in the $2\theta/\omega$ scan mode on an automated Stoe diffractometer and corrected for geometrical factors but not for absorption. Altogether 1093 reflections were measured and three check reflections monitored every 100 measurements showed no significant change in intensity. The structure was solved with *MULTAN* (Main, Germain & Woolfson, 1970). Full-matrix isotropic refinement and block-diagonal anisotropic refinement converged at $R = \sum||F_o| - |F_c||/\sum |F_o|$ = 0·10 for all 1093 measured data. The function minimized was $\sum w(|F_o| - |F_c|)^2$ with $w = 1/\sigma^2(F)$. Scattering factors were taken from *International Tables for X-ray Crystallography* (1974). H atoms were located at this stage from a difference Fourier map, utilizing stereochemical considerations as an additional aid. They were assigned fixed isotropic thermal parameters of 4·0 Å^2, and their locations were not varied; the non-H atoms, however, were refined anisotropically. A prominent extinction effect was observed at this stage for five reflections and these were excluded from subsequent refinement which was stopped when the average parameter shifts were less than their standard deviations; the last cycle gave an R value of 0·047 for 1088 reflections. The positional parameters of the atoms along with their e.s.d.'s are given in Table 1.*

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

	x	y	z	B_{iso} (Å^2)
Cl	1405 (2)	198 (2)	482 (1)	3·2 (1)
N	4740 (8)	864 (6)	−484 (2)	2·8 (3)
O(1)	544 (6)	327 (6)	−3588 (1)	3·6 (3)
O(2)	1178 (8)	2162 (6)	−983 (2)	3·9 (3)
C(1)	287 (10)	856 (9)	−2076 (2)	3·2 (4)
C(2)	−298 (10)	500 (9)	−2627 (2)	3·5 (4)
C(3)	1181 (10)	675 (8)	−3047 (2)	3·3 (4)
C(4)	3237 (10)	1188 (8)	−2927 (2)	3·3 (4)
C(5)	3762 (10)	1557 (8)	−2370 (2)	3·4 (4)
C(6)	2299 (10)	1372 (7)	−1940 (2)	3·5 (4)
C(7)	2956 (10)	1800 (8)	−1337 (2)	3·5 (4)
C(8)	4109 (9)	254 (8)	−1071 (2)	3·5 (4)
C(9)	2821 (11)	−1452 (8)	−1025 (3)	3·9 (4)
C(10)	6563 (10)	−157 (9)	−239 (3)	4·5 (4)

Discussion. The intramolecular bond distances and angles are listed in Table 2. The numbering scheme is indicated in Fig. 1. The individual values for intramolecular bond lengths and angles are normal and do not show any remarkable deviation from the average model (Hebert, 1979) obtained by averaging pertinent bond lengths and angles for 34 similar compounds. The aromatic C—C bond distances in the molecule vary from 1·381 to 1·399 Å, the average being 1·392 Å. The C(8)—N and C(10)—N bond distances are larger than the corresponding values in similar compounds but are not significantly different from a standard C—N$^+$ bond length 1·505 Å (Hahn, 1957). An observation to be noted is the slightly distorted tetrahedral arrangement around the C(7), C(8) and N atoms with significant deviation of the angles O(2)—C(7)—C(8), C(7)—C(8)—C(9), C(7)—C(8)—N and C(8)—N—C(10) from 109°. A comparison of some relevant intramolecular angles in various ephedrine structures is made in Table 3 and it is interesting that similar distortions [angles O(2)—C(7)—C(8), C(7)—C(8)—N are smaller and angles C(7)—C(8)—C(9), C(8)—N—C(10) are larger than standard values] are present in nearly all the ephedrine compounds studied so far. Interactions between neighbouring groups may be responsible for such deviations.

Table 2. *Bond lengths* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

O(1)—C(3)	1·377 (6)	C(1)—C(6)	1·381 (9)
C(1)—C(2)	1·392 (8)	C(6)—C(7)	1·534 (8)
C(2)—C(3)	1·385 (8)	C(7)—C(8)	1·520 (8)
C(3)—C(4)	1·399 (9)	C(8)—C(9)	1·533 (9)
C(4)—C(5)	1·397 (8)	N—C(8)	1·527 (7)
C(5)—C(6)	1·395 (8)	N—C(10)	1·515 (8)
O(1)—C(3)—C(2)	117·3 (5)	C(1)—C(6)—C(7)	122·3 (5)
O(1)—C(3)—C(4)	121·6 (5)	C(5)—C(6)—C(7)	119·1 (5)
C(2)—C(3)—C(4)	121·2 (5)	O(2)—C(7)—C(6)	112·0 (5)
C(2)—C(1)—C(6)	121·7 (6)	O(2)—C(7)—C(8)	106·5 (5)
C(1)—C(2)—C(3)	118·8 (6)	C(6)—C(7)—C(8)	111·2 (5)
C(3)—C(4)—C(5)	118·5 (5)	N—C(8)—C(7)	106·1 (4)
C(4)—C(5)—C(6)	121·2 (6)	N—C(8)—C(9)	109·3 (5)
C(1)—C(6)—C(5)	118·6 (5)	C(7)—C(8)—C(9)	114·6 (5)
C(8)—N—C(10)	113·8 (4)		

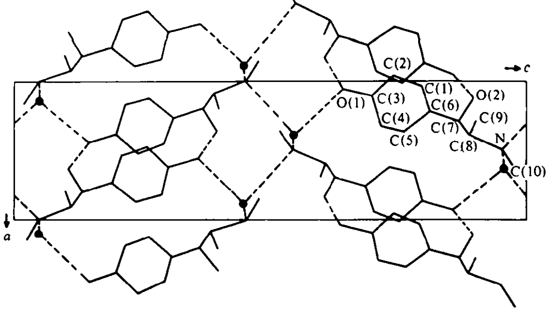

Fig. 1. Crystal structure projected down **b**. Filled circles denote chloride ions and broken lines indicate hydrogen bonds.

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* Lists of structure factors, anisotropic thermal parameters, H atom coordinates and least-squares planes have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35988 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 3. *Comparison of some intramolecular angles* (°) *in various ephedrine structures*

Numbering schemes of the other compounds included in the table are according to that of the present structure.

Compound	O(2)–C(7)–C(8)	C(7)–C(8)–C(9)	C(8)–N–C(10)	C(7)–C(8)–N	References
p-Hydroxyephedrine hydrochloride	106·5 (5)	114·6 (5)	113·8 (4)	106·1 (4)	(1)
(−)-Ephedrine hydrochloride	105·7 (3)	113·2 (3)	115·0 (3)	107·8 (2)	(2)
(−)-Ephedrine dihydrogen phosphate	107·6 (4)	112·9 (4)	117·0 (4)	108·0 (4)	(3)
(+)-Pseudoephedrine with Cu *K*α	106·2 (4)	111·1 (4)	113·7 (4)	107·7 (4)	(4)
(+)-Pseudoephedrine with Mo *K*α	106·1 (5)	111·9 (5)	114·3 (5)	108·0 (5)	
(+)-Pseudoephedrine hydrochloride (with Mo *K*α)	107·8 (9)	108·1 (9)	110·2 (8)	105·7 (9)	(4)
Ephedrine monohydrogen phosphate monohydrate Mol. *A*	111·2 (3)	114·6 (3)		107·1 (3)	(5)
Ephedrine monohydrogen phosphate monohydrate Mol. *B*	110·3 (3)	112·5 (3)		108·4 (3)	
Norephedrine hydrochloride Mol. *A*	107·4 (3)	114·5 (3)		108·3 (3)	(6)
Norephedrine hydrochloride Mol. *B*	109·9 (3)	115·6 (3)		109·6 (3)	

References: (1) Present study; (2) Bergin (1971); (3) Hearn & Bugg (1972); (4) Mathew & Palenik (1977); (5) Hearn, Freeman & Bugg (1973); (6) Hebert (1979).

Atoms O(1) and C(7) are on the same side of the least-squares plane of the benzene ring and a similar observation has been made in the case of tyramine hydrochloride (Podder, Dattagupta & Saha, 1979) and octopamine hydrochloride (Paxton & Hamor, 1977) which also have a hydroxy group attached to the phenyl ring at the *para* position. The ethylamine side chain is coplanar and is in the extended form and the dihedral angle between this plane and the plane of the phenyl ring is 81·1°. The conformation can be described in terms of the torsion angles in Table 4. The O(2)—C(7)—C(8)—N torsion angle is −59·7° which is a common conformation for O—C—C—N^+ groupings (Paxton & Hamor, 1977).

The distance, D_N, of the N atom from the centre of the ring is 5·16 Å. In other similar biologically active amines D_N has been found to be around 5 Å (Hebert, 1979; Post & Kennard, 1974; Giesecke, 1973) and this appears to be a significant requirement for a compound to have sympathomimetic property. Hydrogen-bond distances are given in Table 5. Molecules and their packing within the unit cell as viewed down **b** are shown in Fig. 1. All the four H atoms available for hydrogen-bond formation, two from the N^+H_2 group and two from the ethanol and hydroxyl OH groups, take part in formation of hydrogen bonds and the structure is stabilized by a three-dimensional network of hydrogen bonds of the types N—H···Cl, O—H···Cl and O—H···O.

Table 4. *Selected torsion angles* (°)

Mean standard deviation is 0·8°. Sign convention as defined by Klyne & Prelog (1960).

C(6)–C(7)–C(8)–N	178·1	C(7)–C(8)–N–C(10)	−157·7
C(1)–C(6)–C(7)–C(8)	100·1	C(9)–C(8)–N–C(10)	78·2
C(6)–C(7)–C(8)–C(9)	−61·2	O(2)–C(7)–C(8)–N	−59·7
C(1)–C(6)–C(7)–O(2)	−18·8	O(2)–C(7)–C(8)–C(9)	61·0

Table 5. *Hydrogen-bond distances* (Å)

D–H···*A*	Position of acceptor atom	*D*···*A*
N–HN*A*···Cl	x,y,z	3·178 (5)
N–HN*B*···Cl	$\frac{1}{2}+x, \frac{1}{2}-y, -z$	3·159 (5)
O(1)–HO(1)···Cl	$\frac{1}{2}-x, -y, z-\frac{1}{2}$	2·981 (4)
O(2)–HO(2)···O(1)	$-x, y-\frac{1}{2}, -z-\frac{1}{2}$	2·825 (6)

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