The protonation of O(18) and the relatively strong hydrogen bond O(18)—H(18)···O(1) = 2·506 (5) Å with the hydrogensulfate anion decrease the electronegativity of O(18) and contribute to the enhancement of the attractive force between O(16) and O(18) [2·55 (3) Å in khellinium hydrogensulfate and 2·79 (2) Å in khellin] and narrow the angle C(5)—C(4)—O(16) to 116·6 (2)°. The bond length C(10)—O(18) = 1·288 (3) Å in khellinium, longer than in khellin [1·229 (3) Å], is in agreement with this protonation.

The bonds C(8)—C(9) = 1·329 (4) and 1·335 (3) Å and C(9)—C(10) = 1·405 (4) and 1·446 (4) Å in khellinium and khellin, respectively, show a small variation which can be explained by delocalized double bonds in the C(8)—C(9)—C(10) group at the carbonium ion.

The crystalline cohesion is ensured by a strong hydrogen bond between the benzofuran and the anion: O(18)—H(18)···O(1) = 2·506 (5) Å and an intermediate one O(2)—H(2)···O(4) ($-x, y-1/2, 1/2-z$) = 2·68 (5) Å between two hydrogensulfate anions. The angles of these bonds are 166 (4) and 176 (3)°, respectively. The anions and the cations are on separate planes parallel to (001).

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Structure of Tetrahydrozoline Hydrochloride

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Abstract. 2-(1,2,3,4-Tetrahydro-1-naphthyl)-4,5-dihydro-1*H*-imidazole hydrochloride, $C_{13}H_{17}N_2^+.Cl^-$, $M_r = 236{\cdot}77$, triclinic, $P\bar{1}$, $a = 9{\cdot}9932\ (9)$, $b = 8{\cdot}0417\ (5)$, $c = 7{\cdot}9269\ (5)$ Å, $\alpha = 106{\cdot}68\ (1)$, $\beta = 86{\cdot}32\ (1)$, $\gamma = 98{\cdot}73\ (1)°$, $V = 603{\cdot}01\ (8)$ Å^3, $Z = 2$, $D_x = 1{\cdot}304$ g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 26{\cdot}089$ cm^{-1}, $F(000) = 252$, room temperature, $R = 0{\cdot}079$ for 1891 observed reflections. The imidazole ring is involved in protonation and the structure is stabilized by hydrogen bonds of the form N(1)—N(1H)···Cl···N(2H)—N(2) that link the molecules in continuous chains parallel to the *b* axis. The dihedral angle between the aromatic and the imidazole rings is 88·2 (2)°. Structural differences between the phenethylamines and the α-adrenergic imidazoli(di)ne agonists and antagonists are discussed.

Introduction. Most of the sympathomimetic amines influence both the α- and the β-adrenergic receptors, but the ratio of α to β activity varies between drugs from almost pure α activity to almost pure β activity (Weiner, 1985). The adrenergic action of the 2-substituted imidazoli(di)nes is selective for the α-adrenergic receptors only. Structurally, a typical adrenergic imidazoli(di)ne consists of a substituted phenyl ring separated from an imidazole ring by a carbon or nitrogen bridge. The title compound, tetrahydrozoline hydrochloride, is an imidazole ring containing an α-sympathomimetic amine. When applied topically to the nasal mucosa, it causes vasoconstriction. It is also useful in a 0·05% solution as an ocular decongestant (Weiner, 1985). The crystal structure analysis of the title compound has been undertaken in order to obtain an idea of the structural and conformational differences, if any, between the phenethylamines and the α-adrenergic imidazoli(di)ne agonists and antagonists.

Experimental. Commercially available compound recrystallized at 277 K, from a solution of dilute

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HCl. Crystal size 0·25 × 0·12 × 0·08 mm; Philips PW 1100 diffractometer, graphite-monochromatized Cu $K\alpha$ radiation; cell dimensions from the least-squares fit of angular 2θ positions of 82 reflections within $\theta < 45°$; intensities up to $\theta_{max} = 65°$, hkl: $h = 0$ to 11, $k = -9$ to 9, $l = -9$ to 9; $\omega/2\theta$ scans, 1·6° scan width. Of 2063 independent reflections, 1891 observed with $I \geq 2\sigma(I)$; two standard reflections, remeasured every 90 min, showed no significant intensity variation; Lp but no absorption corrections. Structure solved by *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980); all H atoms from a difference map and included with an isotropic temperature factor of the bonded non-H atom in subsequent calculations, but not refined. Least-squares calculations, $\sum w(\Delta F)^2$ minimized, $w = 1/\sigma^2(F)$, for 16 anisotropically refined non-H atoms and 17 isotropically fixed H atoms. $R = 0{\cdot}079$, $wR = 0{\cdot}070$, $S = 1{\cdot}51$, $(\Delta/\sigma)_{max} = 0{\cdot}72$ in last cycle, $(\Delta\rho)_{max} = 0{\cdot}56$ and $(\Delta\rho)_{min} = -0{\cdot}60$ e Å^{-3} in final ΔF map. The final R value was somewhat high, since the quality of the crystals was rather poor. Scattering factors from *International Tables for X-ray Crystallography* (1974); *XRAY ARC* program system (Vickery, Bright & Mallinson, 1971) used for most of the calculations.

Discussion. The final atomic parameters are given in Table 1* and the bond lengths and angles in Table 2. The structure of the compound and the numbering scheme are shown in Fig. 1. The aromatic ring [C(8)–C(13)] is planar within the limits of experimental error and the atoms C(5) and C(6) (of the saturated ring) show maximum deviations from this plane of −0·516 (6) and 0·217 (7) Å, respectively. The dihedral angle between the aromatic ring and the imidazole ring is 88·2 (2)°.

The imidazole part of the molecule is protonated. Consequently, the two N atoms are chemically equivalent. The two C(3)—N bonds, 1·321 (7) and 1·311 (7) Å, are shorter than the C(1)—N(1) = 1·463 (7) and C(2)—N(2) = 1·477 (7) Å bonds; their values are intermediate between a double bond (1·265 Å) and a single bond (1·470 Å). This result indicates a delocalization of the positive charge on the two N atoms of the imidazole ring. Both N(1) and N(2) participate in hydrogen bonding. N(1)—N(1H)···Cl ($-x+1$, $-y+1$, $-z$) = 3·150 (5) [N(1H)···Cl = 2·17 Å] and N(2)—N(2H)···Cl($-x+1$, $-y$, $-z+1$) = 3·130 (5) [N(2H)···Cl = 2·25 Å], and

* Lists of structure factors, anisotropic thermal parameters, coordinates and isotropic thermal parameters of the H atoms, and least-squares-planes data have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51903 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Fractional atomic coordinates and equivalent isotropic temperature factors* (Å^2) *for non-*H *atoms with e.s.d.'s in parentheses*

$B_{eq} = \frac{4}{3}\sum_i\sum_j\beta_{ij}(\mathbf{a}_i.\mathbf{a}_j)$.

	x	y	z	B_{eq}
Cl	0·1591 (2)	0·1991 (2)	0·7743 (2)	4·28 (5)
N(1)	0·9453 (4)	0·4504 (5)	0·2254 (7)	4·0 (2)
N(2)	0·9550 (5)	0·1926 (5)	0·2548 (7)	3·8 (2)
C(1)	1·0891 (6)	0·4660 (7)	0·2613 (8)	4·3 (2)
C(2)	1·0973 (6)	0·2761 (7)	0·2808 (8)	4·4 (2)
C(3)	0·8764 (5)	0·2956 (7)	0·2221 (7)	3·2 (2)
C(4)	0·7299 (5)	0·2414 (7)	0·1882 (7)	3·2 (2)
C(5)	0·6451 (6)	0·3736 (7)	0·3100 (8)	4·1 (2)
C(6)	0·4954 (6)	0·3080 (8)	0·2726 (8)	4·7 (2)
C(7)	0·4637 (6)	0·2954 (8)	0·0840 (9)	4·9 (3)
C(8)	0·5724 (5)	0·2297 (7)	−0·0520 (7)	3·4 (2)
C(9)	0·6991 (5)	0·2048 (6)	−0·0052 (7)	2·9 (2)
C(10)	0·7939 (6)	0·1468 (7)	−0·1348 (7)	3·3 (2)
C(11)	0·7642 (6)	0·1036 (7)	−0·3141 (8)	3·9 (2)
C(12)	0·6401 (6)	0·1288 (7)	−0·3629 (8)	4·2 (2)
C(13)	0·5455 (6)	0·1876 (7)	−0·2331 (8)	4·2 (2)

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

N(1)—C(1)	1·463 (7)	C(7)—C(8)	1·522 (8)
N(1)—C(3)	1·321 (7)	C(8)—C(9)	1·400 (7)
N(2)—C(2)	1·477 (7)	C(4)—C(9)	1·518 (8)
N(2)—C(3)	1·311 (7)	C(9)—C(10)	1·380 (8)
C(1)—C(2)	1·593 (8)	C(10)—C(11)	1·403 (8)
C(3)—C(4)	1·482 (7)	C(11)—C(12)	1·383 (8)
C(4)—C(5)	1·537 (8)	C(12)—C(13)	1·381 (8)
C(5)—C(6)	1·527 (8)	C(13)—C(8)	1·411 (8)
C(6)—C(7)	1·520 (9)		

C(1)—N(1)—C(3)	113·8 (5)	C(6)—C(7)—C(8)	114·8 (5)
C(2)—N(2)—C(3)	112·6 (5)	C(7)—C(8)—C(9)	122·6 (5)
N(1)—C(1)—C(2)	100·8 (5)	C(7)—C(8)—C(13)	119·7 (5)
N(2)—C(2)—C(1)	101·8 (5)	C(8)—C(9)—C(4)	119·3 (5)
N(1)—C(3)—N(2)	111·0 (5)	C(4)—C(9)—C(10)	120·9 (5)
N(1)—C(3)—C(4)	126·0 (5)	C(8)—C(9)—C(10)	119·8 (5)
N(2)—C(3)—C(4)	123·1 (5)	C(9)—C(10)—C(11)	121·4 (5)
C(3)—C(4)—C(5)	111·2 (5)	C(10)—C(11)—C(12)	119·5 (5)
C(3)—C(4)—C(9)	111·9 (4)	C(11)—C(12)—C(13)	118·9 (6)
C(5)—C(4)—C(9)	112·9 (5)	C(12)—C(13)—C(8)	122·6 (6)
C(4)—C(5)—C(6)	108·8 (5)	C(9)—C(8)—C(13)	117·6 (5)
C(5)—C(6)—C(7)	111·1 (5)		

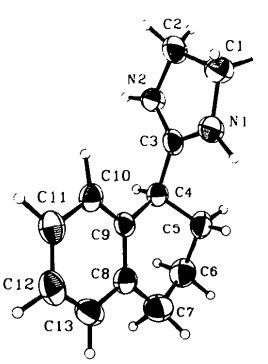

Fig. 1. *ORTEP* (Johnson, 1965) plot of the molecule with the atom-numbering scheme.

the N—H···Cl angles are 166·3 (3) and 163·2 (3)°, respectively. The crystal packing is dominated by hydrogen bonds that form infinite chains of the type N(1)—N(1H)···Cl···N(2H)—N(2) parallel to the *b* axis (Fig. 2).

Certain structural and conformational differences have been observed between these adrenergic imidazoli(di)nes and the flexible phenethylamines. With few exceptions, the phenethylamines adopt a perpendicular *trans* conformation (Carlström, Bergin & Falkenberg, 1973; Herbert, 1979; Duax, 1978) in which the torsion angle τ_1 involving the atoms C(8)—C(9)—C(4)—C(3) is about ±90° and τ_2 involving C(9)—C(4)—C(3)—N(1) is about ±180°. Although some of the adrenergic imidazoli(di)nes also exhibit this conformation, *e.g.* xylometazoline hydrochloride (Ghose & Dattagupta, 1986) where $\tau_1 = 75{\cdot}7$ and $\tau_2 = -143°$ and clonidine hydrochloride (Cody & DeTitta, 1979) where $\tau_1 = 76$ and $\tau_2 = 178°$, there are notable contrasts too. For example, in the present structure $\tau_1 = -151{\cdot}4\ (5)$ and $\tau_2 = 74{\cdot}9\ (7)°$, in naphazoline hydrochloride (Podder, Mukhopadhyay, Dattagupta & Saha, 1983) $\tau_1 = 176{\cdot}8$ and $\tau_2 = -93{\cdot}6°$, and in tolazoline hydrochloride (Ghose & Dattagupta, 1989) $\tau_1 = 179{\cdot}4$ and $\tau_2 = -91{\cdot}0°$. Although there is a wide variation in the torsion angles, all of these adrenergic imidazoli(di)nes show a striking conformational similarity in that the aromatic and imidazole rings are oriented more or less perpendicularly. So for the adrenergic imidazoli(di)nes, unlike the phenethylamines, it is possible that a dihedral angle of about 90° between the aromatic and imidazole rings (irrespective of the values of τ_1 and τ_2) may be important for their interaction at the α-adrenergic receptor site.

Another significant difference has been observed between the crystal structures of the α-adrenergic imidazoli(di)ne agonists and antagonists concerning the C(3)—N bond lengths. In agonists like xylometazoline (Ghose & Dattagupta, 1986) they are 1·309 (4) and 1·304 (4) Å; in clonidine (Cody & DeTitta, 1979) 1·323 (3) and 1·318 (3) Å; in naphazoline (Podder *et al.*, 1983) 1·310 (5) and 1·309 (4) Å; and in the present compound 1·311 (7) and 1·321 (7) Å; *i.e.* the two C(3)—N bonds in the structures are very similar in length. In the antagonists like tolazoline (Ghose & Dattagupta, 1989) the C(3)–N bond lengths are 1·352 (8) and 1·289 (8) Å, and in phentolamine (Leger, Dubost, Colleter & Carpy, 1983) 1·316 (5) and 1·294 (5) Å; *i.e.* the two corresponding C(3)—N bonds are dissimilar (the difference is more than three times the standard deviation). This may imply that in the agonist the positive charge is more or less evenly distributed in the N(1)—C(3)—N(2) region, while in the antagonists there is a gradation of the positive-charge distribution in the corresponding region of the imidazole ring. This may be one of the factors which influence their mode of interaction at the α-adrenergic receptors.

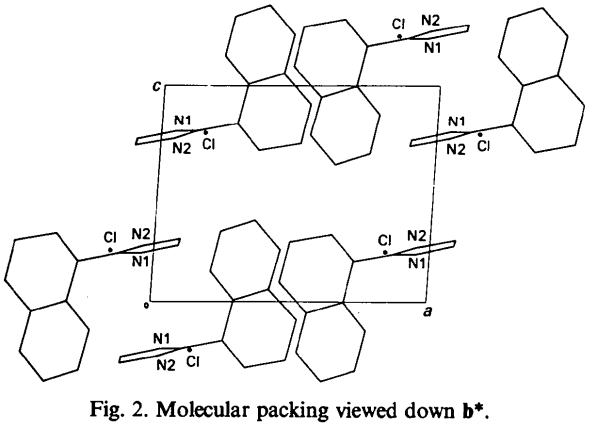

Fig. 2. Molecular packing viewed down **b***.

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