

Structure of an Antihistaminic Drug, Tripeleennamine Hydrochloride

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Abstract. *N'*-Benzyl-*N,N*-dimethyl-*N'*-2-pyridinyl-1,2-ethanediamine hydrochloride, $C_{16}H_{22}N_3^+Cl^-$, $M_r = 219.826$, triclinic, $P\bar{1}$, $a = 10.548$ (4), $b = 10.912$ (4), $c = 14.031$ (3) Å, $\alpha = 94.17$ (2), $\beta = 92.57$ (2), $\gamma = 94.57$ (3)°, $V = 1604$ (2) Å³, $Z = 4$, $D_x = 1.21$, $D_m = 1.20$ Mg m⁻³, $\lambda(Mo K\alpha) = 0.71073$ Å, $\mu = 0.23$ mm⁻¹, $F(000) = 624$, $T = 293$ (1) K, $R = 0.035$ for 3991 observed data with $I > 3\sigma(I)$. There are two independent molecules in the asymmetric unit. Both molecules adopt the *trans* configuration about the C(6)–C(7) bonds. The orientation of the pyridine and benzyl groups is opposite in the two molecules as expressed by the torsion angles C(1)N(2)–C(10)C(11) of 93.3 (2) and –91.2 (2)° in molecules *A* and *B*, respectively. The cations are protonated at the terminal dimethylamino group and are hydrogen bonded to the anions, Cl^- , $N\cdots Cl$ 3.027 (1) and 2.992 (1) Å in molecules *A* and *B*, respectively.

Introduction. Several derivatives of alkyldiamines are known to act as antiallergic agents (Wilhelm, 1961). Tripeleennamine is a potent antihistaminic drug which is widely prescribed for hay fever and other allergies (Witiak, 1970). The mechanism of action of these drugs is not clearly understood. Therefore, the crystal and molecular structure of tripeleennamine hydrochloride has been determined to establish its solid-state conformation as part of a program investigating relationships between conformation and biological activity in this series of compounds.

Experimental. Colorless prismatic crystals of tripeleennamine hydrochloride (Sigma Inc.) grown from acetone by slow evaporation at room temperature, approximate crystal dimensions 0.14 × 0.40 × 0.60 mm. D_m by flotation. Enraf–Nonius CAD-4 diffractometer, graphite-monochromatized $Mo K\alpha$ radiation, lattice constants and orientation matrix from 25 reflections with $10 < \theta < 15^\circ$, $2 < \theta < 25^\circ$ intensity data, $\omega/2\theta$ scans, ω -scan width $(0.70 + 0.35 \tan \theta)^\circ$, h –12→12, k –13→13, l 0→16, 5624 unique reflections, 3991 with $I > 3\sigma(I)$, where $\sigma^2(I) = S + 2B + [0.04(S-B)]^2$, S = scan count and B = time-averaged background count, no significant variation in intensities of three standard reflections measured every 2 h, L_p correction, empirical absorption correction (North, Phillips &

Mathews, 1968), min. and max. correction factors 0.9876 and 1.0000. Structure solved by heavy-atom method, refinement by full-matrix least-squares calculations on F^2 s, H atoms from ΔF map, non-H atoms anisotropic, H-atoms isotropic. Final $R = 0.035$, $wR = 0.047$, $w = [\sigma^2(F_o) + (0.05F_o)^2]^{-1}$, $(\Delta/\sigma)_{\max} < 0.01$, $\Delta\rho = \pm 0.3$ e Å⁻³ in final difference map, goodness of fit = 1.44. Scattering factors from Cromer & Mann (1968) and Stewart, Davidson & Simpson (1965), allowance made for anomalous dispersion (Cromer & Liberman, 1970). Computer programs from the Enraf–Nonius *Structure Determination Package* (B. A. Frenz & Associates Inc., 1985), *ORTEP* (Johnson, 1976).

Discussion. Final fractional coordinates and equivalent isotropic thermal parameters with estimated standard deviations are given in Table 1.* Table 2 contains molecular dimensions. Fig. 1 shows the molecular structure of the two independent cations in the asymmetric unit with the crystallographic numbering scheme. The crystal structure is shown in Fig. 2.

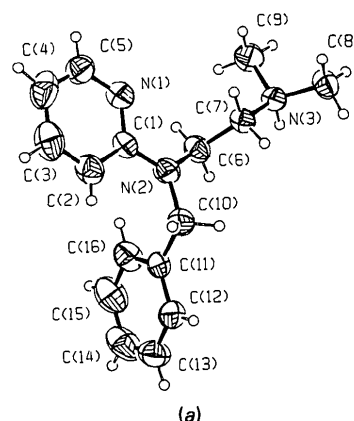
The diaminoethyl chain is fully extended in each molecule and the plane of the side chain comprising N(2), C(6), C(7), N(3), C(8) is perpendicular to the plane of the pyridine ring (mean interplanar angles are 95.5 and 83.5° in molecules *A* and *B*, respectively). The side chain is inclined at 65.3° to the benzyl group in molecule *A* and at 71.0° in molecule *B*. Moreover, the pyridine and the phenyl rings in molecules *A* and *B* are inclined at 89.3 and 79.1° respectively. Both molecules adopt the *trans* configuration about the C(6)–C(7) bonds. However, the most striking features in which the two molecules differ from each other are: the conformations of the pyridine rings, and the orientation of the pyridine and the benzyl groups about the N(2)–C(10) bonds. In molecule *A*, the pyridine N(1) atom is *cis* to C(6) while it is *trans* to C(6) in molecule *B*, i.e. the pyridine ring in molecule *B* is rotated ~180° about the N(2)–C(1) bond with respect

* Lists of anisotropic thermal parameters, H-atom coordinates, molecular dimensions involving H atoms, least-squares-planes data and structure factors have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43848 (53 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

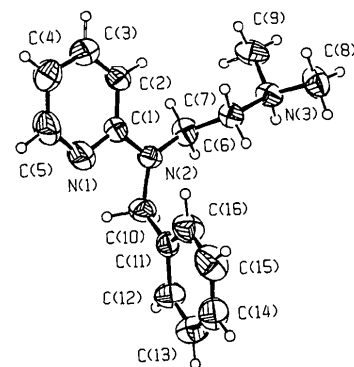
Table 1. *Final fractional coordinates and equivalent isotropic thermal parameters (\AA^2) with e.s.d.'s in parentheses*

$$B_{\text{eq}} = \frac{1}{3}[a^2B(1,1) + b^2B(2,2) + c^2B(3,3) + ab(\cos\gamma)B(1,2) + ac(\cos\beta)B(1,3) + bc(\cos\alpha)B(2,3)].$$

	x	y	z	B_{eq}
Cl(A)	1.05549 (4)	0.71601 (4)	1.05563 (4)	4.34 (1)
Cl(B)	0.53125 (5)	-0.24250 (4)	-0.05247 (4)	4.90 (1)
N(1A)	1.2600 (2)	0.3332 (2)	1.3412 (1)	4.57 (4)
N(2A)	1.0698 (1)	0.3547 (1)	1.2566 (1)	4.07 (3)
N(3A)	1.2506 (1)	0.5296 (1)	1.0768 (1)	3.25 (3)
C(1A)	1.1349 (2)	0.3006 (2)	1.3271 (1)	3.55 (4)
C(2A)	1.0738 (2)	0.2147 (2)	1.3804 (2)	4.65 (4)
C(3A)	1.1429 (3)	0.1608 (2)	1.4466 (2)	5.98 (6)
C(4A)	1.2702 (2)	0.1906 (2)	1.4609 (2)	6.10 (6)
C(5A)	1.3238 (2)	0.2774 (2)	1.4082 (2)	5.38 (5)
C(6A)	1.1283 (2)	0.4617 (2)	1.2139 (1)	4.02 (4)
C(7A)	1.1930 (2)	0.4219 (2)	1.1240 (1)	3.39 (4)
C(8A)	1.2799 (2)	0.4929 (2)	0.9767 (1)	4.57 (4)
C(9A)	1.3644 (2)	0.5900 (2)	1.1312 (2)	4.96 (5)
C(10A)	0.9407 (2)	0.3131 (2)	1.2247 (1)	4.16 (4)
C(11A)	0.8381 (2)	0.3792 (2)	1.2739 (1)	3.67 (4)
C(12A)	0.7122 (2)	0.3468 (2)	1.2454 (1)	4.61 (4)
C(13A)	0.6167 (2)	0.4080 (2)	1.2864 (2)	6.07 (5)
C(14A)	0.6454 (2)	0.5009 (2)	1.3555 (2)	7.07 (6)
C(15A)	0.7708 (3)	0.5336 (2)	1.3856 (2)	6.67 (6)
C(16A)	0.8659 (2)	0.4724 (2)	1.3446 (2)	5.00 (5)
N(1B)	0.6144 (2)	0.1706 (2)	-0.4186 (1)	5.62 (4)
N(2B)	0.6063 (1)	0.0299 (1)	-0.3012 (1)	3.80 (3)
N(3B)	0.7298 (1)	-0.0311 (1)	-0.0543 (1)	3.64 (3)
C(1B)	0.6747 (2)	0.1174 (2)	-0.3482 (1)	3.50 (4)
C(2B)	0.7995 (2)	0.1493 (2)	-0.3232 (1)	4.15 (4)
C(3B)	0.8655 (2)	0.2352 (2)	-0.3703 (2)	5.44 (5)
C(4B)	0.8087 (2)	0.2898 (2)	-0.4422 (2)	5.98 (5)
C(5B)	0.6835 (2)	0.2561 (2)	-0.4645 (2)	6.29 (6)
C(6B)	0.6688 (2)	-0.0343 (2)	-0.2279 (1)	3.95 (4)
C(7B)	0.6796 (2)	0.0402 (2)	-0.1321 (1)	3.49 (4)
C(8B)	0.7296 (2)	0.0411 (2)	0.0400 (1)	5.12 (5)
C(9B)	0.8567 (2)	-0.0730 (2)	-0.0719 (2)	5.07 (5)
C(10B)	0.4794 (2)	-0.0181 (2)	-0.3378 (1)	4.19 (4)
C(11B)	0.3708 (2)	0.0492 (2)	-0.2993 (1)	3.41 (4)
C(12B)	0.2482 (2)	-0.0034 (2)	-0.3169 (2)	4.51 (4)
C(13B)	0.1455 (2)	0.0554 (2)	-0.2845 (2)	5.54 (5)
C(14B)	0.1646 (2)	0.1667 (2)	-0.2336 (2)	5.52 (5)
C(15B)	0.2852 (2)	0.2199 (2)	-0.2161 (2)	6.04 (6)
C(16B)	0.3881 (2)	0.1617 (2)	-0.2485 (2)	5.03 (5)



(a)



(b)

Fig. 1. ORTEP (Johnson, 1976) drawings of the two cations in the asymmetric unit: (a) molecule A, (b) molecule B.

Table 2. *Bond lengths (\AA), bond angles ($^\circ$) and torsion angles ($^\circ$)*

Molecule			Molecule			Molecule		
	A	B		A	B		A	B
N(1)–C(1)	1.342 (2)	1.344 (2)	C(1)–C(2)	1.379 (2)	1.358 (3)	C(11)–C(16)	1.373 (3)	1.368 (2)
N(1)–C(5)	1.341 (2)	1.355 (3)	C(2)–C(3)	1.353 (3)	1.352 (3)	C(12)–C(13)	1.376 (3)	1.380 (3)
N(2)–C(1)	1.373 (2)	1.375 (2)	C(3)–C(4)	1.358 (3)	1.350 (3)	C(13)–C(14)	1.357 (4)	1.359 (3)
N(2)–C(6)	1.457 (2)	1.450 (2)	C(4)–C(5)	1.349 (3)	1.358 (3)	C(14)–C(15)	1.380 (4)	1.360 (3)
N(2)–C(10)	1.442 (2)	1.455 (2)	C(6)–C(7)	1.512 (2)	1.514 (2)	C(15)–C(16)	1.373 (3)	1.379 (3)
N(3)–C(7)	1.492 (2)	1.489 (2)	C(10)–C(11)	1.512 (2)	1.509 (2)	Cl1...N(3)	3.027 (1)	2.992 (1)
N(3)–C(8)	1.486 (2)	1.490 (2)	C(11)–C(12)	1.380 (2)	1.377 (2)	Cl1...H(N3)	2.11 (2)	2.09 (2)
N(3)–C(9)	1.475 (2)	1.473 (2)						
C(1)–N(1)–C(5)	117.3 (2)	117.3 (2)	N(2)–C(1)–C(2)	121.1 (2)	120.7 (2)	C(10)–C(11)–C(16)	122.2 (2)	123.0 (2)
C(1)–N(2)–C(6)	120.4 (2)	120.1 (1)	C(1)–C(2)–C(3)	118.8 (2)	119.9 (2)	C(12)–C(11)–C(16)	118.7 (2)	118.1 (2)
C(1)–N(2)–C(10)	122.4 (1)	120.3 (1)	C(2)–C(3)–C(4)	120.9 (2)	120.6 (2)	C(11)–C(12)–C(13)	120.5 (2)	121.1 (2)
C(6)–N(2)–C(10)	117.2 (2)	118.3 (1)	C(3)–C(4)–C(5)	117.5 (2)	117.7 (2)	C(12)–C(13)–C(14)	120.2 (2)	120.0 (2)
C(7)–N(3)–C(8)	110.8 (1)	110.5 (1)	N(1)–C(5)–C(4)	124.1 (2)	123.2 (2)	C(13)–C(14)–C(15)	120.0 (2)	119.4 (2)
C(7)–N(3)–C(9)	112.3 (1)	113.1 (2)	N(2)–C(6)–C(7)	110.4 (1)	111.8 (1)	C(14)–C(15)–C(16)	119.7 (3)	120.8 (2)
C(8)–N(3)–C(9)	111.1 (2)	111.3 (2)	N(3)–C(7)–C(6)	111.8 (1)	111.9 (1)	C(11)–C(16)–C(15)	120.9 (3)	120.5 (2)
N(1)–C(1)–N(2)	117.6 (1)	118.1 (2)	N(2)–C(10)–C(11)	115.7 (2)	115.8 (1)	Cl1...H(N3)...N(3)	177 (1)	174 (1)
N(1)–C(1)–C(2)	121.3 (2)	121.2 (2)	C(10)–C(11)–C(12)	119.1 (2)	118.9 (2)			
C(5)N(1)–C(1)C(2)	1.1 (3)	0.9 (3)	N(1)C(1)–C(2)C(3)	-1.5 (3)	-0.6 (3)	C(16)C(11)–C(12)C(13)	0.9 (3)	-0.1 (3)
C(1)N(1)–C(5)C(4)	0.6 (3)	-0.4 (3)	C(1)C(2)–C(3)C(4)	0.2 (3)	-0.2 (3)	C(12)C(11)–C(16)C(15)	-0.8 (3)	0.2 (3)
C(6)N(2)–C(1)N(1)	-12.9 (3)	177.0 (2)	C(2)C(3)–C(4)C(5)	1.4 (3)	0.7 (4)	C(11)C(12)–C(13)C(14)	-0.1 (3)	-0.4 (3)
C(6)N(2)–C(1)C(2)	167.9 (2)	-3.4 (3)	C(3)C(4)–C(5)N(1)	-1.8 (4)	-0.4 (4)	C(12)C(13)–C(14)C(15)	-0.7 (4)	0.7 (3)
C(10)N(2)–C(1)N(1)	170.0 (2)	10.3 (3)	N(2)C(10)–C(11)C(16)	-0.3 (3)	12.6 (3)	C(13)C(14)–C(15)C(16)	0.7 (4)	-0.6 (3)
C(10)N(2)–C(1)C(2)	-9.2 (3)	-170.1 (2)	C(10)C(11)–C(12)C(13)	-177.8 (2)	-179.0 (2)	C(14)C(15)–C(16)C(11)	0.1 (4)	0.2 (4)
C(1)N(2)–C(10)C(11)	93.3 (2)	-91.2 (2)						

The sign convention for the torsion angles is that of Klyne & Prelog (1960).

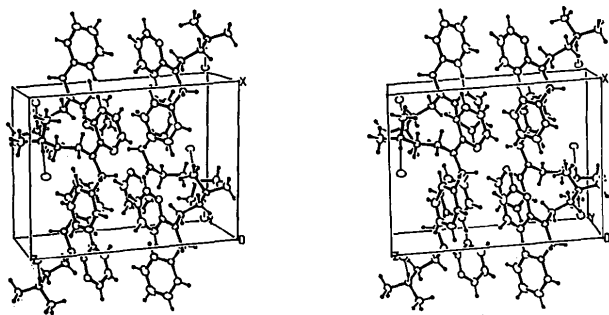


Fig. 2. A stereoview of the unit cell showing hydrogen bonds.

to the pyridine ring in molecule *A* [torsion angle C(6)N(2)—C(1)C(2) is 167.9 (2) in molecule *A* and -3.4 (3) $^\circ$ in molecule *B*]. The benzyl group in molecule *B* is also rotated around the N(2)—C(10) bond resulting in a rather extended conformation of the two six-membered rings as compared with the conformation of molecule *A* wherein the two rings are *cis* about the N(2)—C(10) bond [torsion angle C(1)N(2)—C(10)—C(11) is 93.3 (2) and -91.2 (2) $^\circ$ in molecules *A* and *B*, respectively].

Bond lengths and angles in the two molecules (Table 2) are normal. There are, however, slight differences in the bond lengths and angles between the two independent molecules. For example, the N(1)—C(5) bond in molecule *B* [1.355 (3) Å] is significantly longer than the N—C bonds in the pyridine rings of the two molecules, which range between 1.341 (2) and 1.344 (2) Å. This significantly long bond in molecule *B* is matched by a similar lengthening of the C(1)—C(2) bond in molecule *A* [1.379 (4) Å]; the rest of the C—C bonds in the pyridine moieties of the two molecules range between 1.349 (2) and 1.358 (3) Å. The N(2)—C(10) bond in molecule *B* [1.455 (2) Å] is 0.013 Å longer than the

corresponding bond in molecule *A* which could be a consequence of the conformation adopted by molecule *B* about this bond; the strong interactions thus originating from this conformation seem to influence the C(14)—C(15) bond length in molecule *B* which is significantly shorter than the C(14)—C(15) bond in molecule *A*. The effects of different conformations are also manifested in small but significant differences in angles between the two molecules, *e.g.* the angle C(1)—N(2)—C(10) is 122.4 (1) and 120.3 (1) $^\circ$ in molecules *A* and *B*, respectively.

The phenyl and pyridine rings are planar to within 0.011 (2) Å. Each of the cations contains one H atom, H(N3), on the dimethylamino group which forms a relatively strong hydrogen bond to the Cl[−] ion. The N...Cl distances are 3.027 (1) and 2.992 (1) Å, the H(N3)...Cl distances are 2.11 (2) and 2.09 (2) Å, and the Cl...H(N3)...N(3) angles are 177 (1) and 174 (1) $^\circ$ for cations *A* and *B*, respectively. There are no unusual intermolecular distances less than van der Waals distances and the crystal appears to be composed of hydrogen-bonded cation–anion species (Fig. 2).

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Structure of 1-(1-Hydroxy-1-methylethyl)-1-vinyl-3,5-dioxatricyclo[5.4.1.0^{2,6}]dodeca-8,10-dien-12-ol

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Abstract. C₁₇H₂₄O₄, *M*_r = 292.38, monoclinic, *P*2₁/*n*, *a* = 16.499 (4), *b* = 8.422 (5), *c* = 11.173 (2) Å, β = 93.96 (2) $^\circ$, *V* = 1548.9 Å³, *Z* = 4, *D*_x = 1.254 g cm^{−3}, λ(Mo Kα) = 0.71073 Å, μ = 0.82 cm^{−1}, *F*(000) = 632,

0108-2701/87/071410-03\$01.50

T = 293 K, *R* = 0.050 for 1354 observed reflections. The seven-membered ring has an envelope conformation with C(2) 0.906 (3) Å out of the plane described by the remaining atoms of the ring. The five-membered

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