Références

CARPY, A., COLLETER, J.-C. & LÉGER, J.-M. (1981). *Cryst. Struct. Commun.* **10**, 1391–1395.

DEMICHEL, P., GOMOND, P. & ROQUEBERT, J. (1981). *Br. J. Pharmacol.* **74**, 739–745.

DEMICHEL, P., GOMOND, P. & ROQUEBERT, J. (1982). *Br. J. Pharmacol.* **77**, 449–454.

EASSON, L. H. & STEADMAN, E. (1933). *Biochem. J.* **27**, 1257–1268.

FOCES-FOCES, C., CANO, F. H. & GARCÍA-BLANCO, S. (1976). *Acta Cryst.* B**32**, 3029–3033.

International Tables for X-ray Crystallography (1974). Tome IV. Birmingham: Kynoch Press.

MCGRATH, J. C. (1982). *Biochem. Pharmacol.* **4**, 467–484.

MAIN, P., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1978). *MULTAN*78. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. de York, Angleterre et Louvain, Belgique.

PULLMAN, B., COUBEILS, J.-L., COURRIÈRE, PH. & GERVOIS, J.-P. (1972). *J. Med. Chem.* **15**, 17–23.

ROQUEBERT, J., GOMOND, P. & DEMICHEL, P. (1981). *J. Pharmacol. (Paris)*, **12**, 393–403.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

Acta Cryst. (1984). C**40**, 154–156

Structure of 3,4-Dihydro-2-[(*p*-hydroxyphenethyl)aminomethyl]-1(2*H*)-naphthalenone Hydrochloride, BE-2254, $C_{19}H_{21}NO_2.HCl$

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Abstract. α_2-Adrenergic receptor blocking agent. Antihypertensive action. $M_r = 331{\cdot}8$, monoclinic, *Cc*, $a = 17{\cdot}759$ (3), $b = 13{\cdot}282$ (2), $c = 7{\cdot}521$ (1) Å, $\beta = 107{\cdot}09$ (1)°, $V = 1695{\cdot}7$ (3) Å^3, $Z = 4$, $D_x = 1{\cdot}30$ g cm^{-3}, Cu $K\bar{\alpha}$, $\lambda = 1{\cdot}54178$ Å, $\mu = 2{\cdot}06$ cm^{-1}, $F(000) = 704$, room temperature, $R = 0{\cdot}039$ for 1178 reflections. The bridge chain is in the fully extended conformation; the two aromatic ring systems are perpendicular. The quaternary nitrogen and the alcoholic function are involved in hydrogen bonds with the Cl^- ions.

Introduction. BE-2254, synthesized in the sixties (Hansen, 1969), attracted attention because of its marked antihypertensive activity in animal experiments. Following clarification of its mechanism of action, it was characterized as a potent relatively specific α-adrenergic receptor blocker. *In vitro*, BE-2254 proved to be a potent post-synaptic α-receptor blocker on the isolated anococcygeal muscle of the rat (Gillespie, 1971; Doxey, Smith & Walker, 1977) but exhibited also less presynaptic α-blocking properties (Doxey *et al.*, 1977). *In vivo*, BE-2254 was found to be nearly 200 times more potent at the cardiac presynaptic α_2-adrenoceptors than at the vascular smooth-muscle post-synaptic α_2-adrenoceptors (Hicks, 1981).

The solid-state structure of this drug was determined in order to see if there are conformational discriminating factors between α-agonists and antagonists.

Experimental. Small white blocks (from methanol), 0·20 × 0·13 × 0·10 mm, Enraf–Nonius CAD-4 diffractometer with graphite monochromator, 25 reflections ($7 < \theta < 40°$) used to refine orientation matrix, systematic absences: *hkl* for $h + k$ odd, *h*0*l* for *l* odd, 1268 ($\pm h,k,l$) independent with $\theta < 60°$, h −19 to +19, k 0 to +14, l 0 to +8, 1178 with $I \geq 3\sigma(I)$, Lp correction, absorption ignored; two check reflections ($20\bar{2}$, $2\bar{4}0$) every 5400 s showed no unusual variation (all within $\pm 3\sigma$); direct methods, *MULTAN* (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), anisotropic diagonal matrix, refinement on F using observed reflections, $w = 1$ if $|F_o| < P$, $P = (F_o{}^2{}_{max}/10)^{1/2}$, $w = (P/F_o)^2$ if $|F_o| > P$, H from ΔF synthesis, isotropic, $R = 0{\cdot}039$, $R_w = 0{\cdot}046$, $S = 0{\cdot}695$ (1178 reflections, 296 parameters), maximum $\Delta\rho$ excursion $\pm 0{\cdot}5$ e Å^{-3} in final ΔF map; in final cycle mean and max. $\Delta/\sigma = 0{\cdot}1$ and 0·3; H-atom form factors from Stewart, Davidson & Simpson (1965), all other form factors from *International Tables for X-ray Crystallography* (1974), IRIS80, CII, computer of the Centre Interuniversitaire de Calcul (Talence).

Discussion. Table 1 gives the atomic coordinates and Table 2 the bond distances and angles.* A diagram of the molecule with the atom numbering is shown in Fig. 1.

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38879 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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On checking the interatomic distances, one notices a shortening of the C(14)–C(13), C(19)–C(20) and C(20)–C(11) bond lengths, which indicates an important delocalization of π electrons in the naphthalenone ring. Other bond distances are consistent with expected values and will not be discussed. Except for C(12), all atoms of the naphthalenone ring are almost coplanar. C(12) is 0·607 (5) Å out of the least-squares mean plane. The two aromatic rings of the molecule are nearly perpendicular [89 (1)°]. The torsion angles associated with the bridge chain have the following values (±1°): C(2)–C(1)–C(7)–C(8) 163; C(1)–C(7)–C(8)–N(9) 180; C(7)–C(8)–N(9)–C(10) 178; C(8)–N(9)–C(10)–C(11) 175; N(9)–C(10)–C(11)–C(12) 253°.

Table 1. *Atomic coordinates* ($\times 10^4$) *and equivalent isotropic temperature factors*

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

	x	y	z	B_{eq}(Å^2)
C(1)	2510 (3)	4057 (3)	4487 (6)	3·2 (2)
C(2)	3134 (3)	4715 (4)	5266 (7)	3·8 (2)
C(3)	3892 (3)	4522 (4)	5194 (8)	4·1 (2)
C(4)	4041 (2)	3656 (3)	4325 (7)	3·3 (2)
C(5)	3447 (3)	3005 (4)	3528 (7)	3·5 (2)
C(6)	2679 (3)	3199 (4)	3616 (4)	3·4 (2)
C(7)	1711 (3)	4285 (4)	4723 (7)	3·9 (2)
C(8)	1046 (3)	3711 (4)	3384 (7)	3·6 (2)
N(9)	268 (2)	3977 (3)	3703 (5)	3·1 (1)
C(10)	−402 (3)	3444 (4)	2347 (8)	4·5 (2)
C(11)	−1186 (3)	3639 (4)	2764 (7)	3·8 (2)
C(12)	−1474 (3)	2714 (4)	3606 (8)	4·1 (2)
C(13)	−2242 (3)	2979 (4)	4044 (7)	4·3 (2)
C(14)	−2850 (3)	3387 (4)	2368 (7)	3·6 (2)
C(15)	−3653 (3)	3314 (4)	2233 (9)	4·8 (2)
C(16)	−4209 (3)	3706 (4)	771 (10)	5·3 (3)
C(17)	−4008 (3)	4190 (5)	−648 (10)	6·0 (3)
C(18)	−3221 (3)	4276 (4)	−555 (9)	5·1 (2)
C(19)	−2631 (3)	3895 (3)	976 (7)	3·4 (2)
C(20)	−1797 (3)	4018 (4)	1048 (8)	3·9 (2)
O(21)	−1617 (2)	4415 (3)	−233 (7)	6·1 (2)
O(22)	4804 (2)	3487 (3)	4316 (5)	4·6 (2)
Cl(23)	130 (1)	3706 (1)	7751 (2)	4·2 (0)

Table 2. *Bond distances* (Å) *and angles* (°)

C(1)–C(2)	1·397 (8)	C(11)–C(12)	1·538 (8)
C(1)–C(6)	1·390 (7)	C(11)–C(20)	1·508 (8)
C(1)–C(7)	1·512 (8)	C(12)–C(13)	1·534 (8)
C(2)–C(3)	1·386 (8)	C(13)–C(14)	1·500 (8)
C(3)–C(4)	1·386 (8)	C(14)–C(15)	1·404 (8)
C(4)–C(5)	1·360 (7)	C(14)–C(19)	1·393 (8)
C(4)–O(22)	1·377 (6)	C(15)–C(16)	1·347 (9)
C(5)–C(6)	1·408 (7)	C(16)–C(17)	1·38 (1)
C(7)–C(8)	1·514 (8)	C(17)–C(18)	1·38 (1)
C(8)–N(9)	1·512 (7)	C(18)–C(19)	1·404 (9)
N(9)–C(10)	1·498 (7)	C(19)–C(20)	1·475 (8)
C(10)–C(11)	1·536 (8)	C(20)–O(21)	1·220 (8)
C(2)–C(1)–C(6)	117·1 (5)	C(12)–C(11)–C(20)	112·1 (5)
C(2)–C(1)–C(7)	118·8 (5)	C(11)–C(12)–C(13)	109·3 (5)
C(6)–C(1)–C(7)	124·0 (5)	C(12)–C(13)–C(14)	111·6 (5)
C(1)–C(2)–C(3)	121·8 (5)	C(13)–C(14)–C(15)	120·1 (5)
C(2)–C(3)–C(4)	119·6 (5)	C(13)–C(14)–C(19)	121·0 (5)
C(3)–C(4)–C(5)	120·3 (5)	C(15)–C(14)–C(19)	118·8 (5)
C(3)–C(4)–O(22)	117·6 (5)	C(14)–C(15)–C(16)	121·1 (6)
C(5)–C(4)–O(22)	122·1 (5)	C(15)–C(16)–C(17)	121·2 (6)
C(4)–C(5)–C(6)	119·9 (5)	C(16)–C(17)–C(18)	119·1 (7)
C(1)–C(6)–C(5)	121·3 (5)	C(17)–C(18)–C(19)	120·8 (6)
C(1)–C(7)–C(8)	113·4 (5)	C(14)–C(19)–C(18)	119·0 (5)
C(7)–C(8)–N(9)	110·4 (4)	C(14)–C(19)–C(20)	121·6 (5)
C(8)–N(9)–C(10)	111·2 (4)	C(18)–C(19)–C(20)	119·3 (5)
N(9)–C(10)–C(11)	111·5 (5)	C(11)–C(20)–C(19)	117·2 (5)
C(10)–C(11)–C(12)	112·4 (5)	C(11)–C(20)–O(21)	122·0 (5)
C(10)–C(11)–C(20)	110·4 (5)		

The molecule of BE-2254 contains the phenethylamine skeleton which exists in noradrenaline and in various α ligands. α-Adrenergic receptor features postulated some ten years ago (Pullman, Coubeils, Courrière & Gervois, 1972) have been refined recently for a series of imidazoline agonists (Carpy, Léger, Leclerc, Decker, Rouot & Wermuth, 1982). The centers implicated in the interaction of α-ligands with their receptor are the quaternary N and the hydroxyphenyl ring.

The distance D between N(9) and the center π of the hydroxyphenyl ring is 5·23 (1) Å and the distance H between N(9) and the plane containing the ring is 0·248 (4) Å. These two distances are in good agreement with those found in some α-antagonists such as WB-4101 (Carpy, Colleter & Léger, 1981), raubasine (Dubost, Léger, Goursolle, Colleter & Carpy, 1984) or phentolamine (Léger, Dubost, Colleter & Carpy, 1983). In contrast, the H distance in α-agonists is much larger (≃1 Å) (Pullman *et al.*, 1972; Carpy *et al.*, 1982).

As we said earlier, there is another center of π electrons in the molecule which is probably the middle of the C(14)–C(19) bond. The distance between N(9) and this point is 5·13 (1) Å and the distance between N(9) and the mean plane of the naphthalenone ring is 0·549 (4) Å, these two values being very similar to D and H.

The crystalline cohesion is ensured by two hydrogen bonds involving N$^+$(9), O(22) and the Cl$^-$(23) ions: Cl(23)···N(9) (x, $1-y$, $\frac{1}{2}+z$) = 3·154 (4) Å, Cl(23)···H(91) = 2·25 (6) Å, Cl(23)···H(91)–N(9) = 171 (5)°; Cl(23)···O(22) ($-\frac{1}{2}+x$, $\frac{1}{2}-y$, $\frac{1}{2}+z$) = 3·256 (4) Å, Cl(23)···H(220) = 2·37 (7), Cl(23)···H(220)–O(22) = 167 (6)°, and by van der Waals contacts (Fig. 2).

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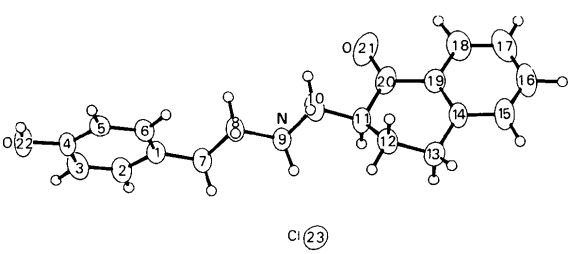

Fig. 1. Perspective view of the molecule showing the numbering of atoms. The bare numbers are for C atoms. H atoms are numbered such that Hmn is the nth H on Xm (X = O, N and C).

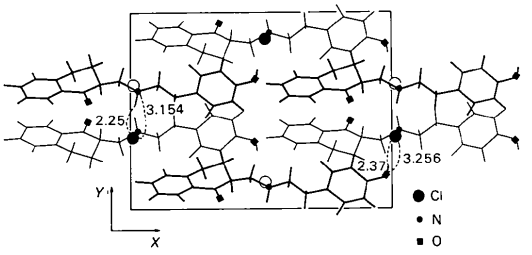

Fig. 2. Packing of the molecules projected on (001). (Distances in Å.)

References

CARPY, A., COLLETER, J.-C. & LÉGER, J.-M. (1981). *Cryst. Struct. Commun.* **10**, 1391–1395.

CARPY, A., LÉGER, J.-M., LECLERC, G., DECKER, N., ROUOT, B. & WERMUTH, C. G. (1982). *Mol. Pharmacol.* **21**, 400–408.

DOXEY, J. C., SMITH, C. F. C. & WALKER, J. M. (1977). *Br. J. Pharmacol.* **60**, 91–96.

DUBOST, J.-P., LÉGER, J.-M., GOURSOLLE, M., COLLETER, J.-C. & CARPY, A. (1984). *Acta Cryst.* C**40**, 152–154.

GILLESPIE, J. S. (1971). *Br. J. Pharmacol.* **43**, 430 P.

HANSEN, W. (1969). British Patent No. 1, 913, 199.

HICKS, P. E. (1981). *Br. J. Pharmacol.* **72**, 586 P.

International Tables for X-ray Crystallography. (1974). Vol. IV. Birmingham: Kynoch Press.

LÉGER, J.-M., DUBOST, J.-P., COLLETER, J.-C. & CARPY, A. (1983). *Acta Cryst.* C**39**, 1428–1430.

MAIN, P., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J. P. & WOOLFSON, M. M. (1978). *MULTAN*78. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.

PULLMAN, B., COUBEILS, J.-L., COURRIÈRE, PH. & GERVOIS, J.-P. (1972). *J. Med. Chem.* **15**, 17–23.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

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Hemanthamine, $C_{17}H_{19}NO_4$

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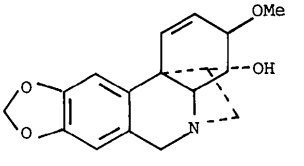
Abstract. (3*S*,11*S*)-3,4,4a,6-Tetrahydro-11-hydroxy-3-methoxy-5,10b-ethano-8,9-methylenedioxyphenanthridine, $M_r = 301{\cdot}34$, orthorhombic, $P2_12_12_1$, $a = 11{\cdot}006$ (2), $b = 14{\cdot}022$ (2), $c = 9{\cdot}582$ (2) Å, $V = 1478{\cdot}8$ (4) Å^3, $Z = 4$, $D_x = 1{\cdot}35$ Mg m^{-3}, Cu $K\alpha$, $\lambda = 1{\cdot}54178$ Å, $\mu = 0{\cdot}781$ mm^{-1}, $F(000) = 640$, room temperature, $R = 0{\cdot}070$ for 1486 unique reflections with $I > 3\sigma(I)$. The cyclohexene ring and the six-membered ring containing the N atom exist as 1,2-diplanar conformations while the five-membered methylenedioxy ring is a flattened envelope. The N-containing five-membered ring exhibits a slightly flattened half-chair conformation. The molecules are held together by hydrogen bonds between the hydroxyl of one molecule and the N of another, O···N = 2·693 (16) Å.

Introduction. Extracts of *Hippeastrum bicolor* (Amaryllidaceae) upon chromatography yielded several alkaloids including a few milligrams of a poorly crystalline material melting at 478 K with UV maxima at 240 and 296 nm. An X-ray diffraction study of an opaque crystal revealed the compound to be hemanthamine (1). Hemanthamine is a crinine-type alkaloid which has been isolated from other Amaryllidaceae. The absolute configuration was originally assigned through CD studies (Wildman & Bailey, 1969); however, further CD and ORD work brought the assignment into question (DeAngelis & Wildman, 1969; Kuriyama, Iwata, Moriyama, Kotera, Hameda, Mitsui & Takeda, 1967). A structural investigation of the *p*-bromobenzoate of hemanthamine confirmed the original assignment of configuration (Clardy, Hauser, Dahm, Jacobson & Wildman, 1970). The structure of crinamine, the C(3) epimer of hemanthamine, has also been reported (Roques, Declercq & Germain, 1977).



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