Table 2. *Selected geometric parameters* (Å, °)

F—C9	1.421 (3)	C8—C9	1.535 (3)
O1—C3	1.219 (4)	C9—C11	1.536 (3)
O2—C21	1.345 (3)	C9—C10	1.563 (3)
O2—C11	1.452 (3)	C10—C19	1.549 (4)
O3—C17	1.212 (3)	C11—C12	1.534 (3)
O4—C21	1.197 (4)	C12—C13	1.522 (4)
C1—C2	1.310 (4)	C13—C17	1.517 (4)
C1—C10	1.503 (3)	C13—C14	1.533 (3)
C2—C3	1.454 (5)	C13—C18	1.547 (4)
C3—C4	1.454 (4)	C14—C15	1.530 (3)
C4—C5	1.326 (4)	C15—C16	1.542 (4)
C5—C6	1.489 (4)	C16—C20	1.517 (4)
C5—C10	1.519 (3)	C16—C17	1.531 (4)
C6—C7	1.524 (4)	C21—C22	1.436 (4)
C7—C8	1.531 (3)	C22—C23	1.180 (4)
C8—C14	1.526 (3)	C23—C24	1.459 (4)
C21—O2—C11	118.8 (2)	C19—C10—C9	113.7 (2)
C2—C1—C10	124.7 (3)	O2—C11—C12	107.5 (2)
C1—C2—C3	121.7 (3)	O2—C11—C9	107.6 (2)
O1—C3—C2	122.3 (3)	C12—C11—C9	114.2 (2)
O1—C3—C4	121.4 (3)	C13—C12—C11	112.0 (2)
C2—C3—C4	116.3 (3)	C17—C13—C12	116.2 (2)
C5—C4—C3	123.6 (3)	C17—C13—C14	98.8 (2)
C4—C5—C6	122.9 (2)	C12—C13—C14	108.9 (2)
C4—C5—C10	121.7 (3)	C17—C13—C18	104.2 (2)
C6—C5—C10	115.4 (2)	C12—C13—C18	113.7 (2)
C5—C6—C7	110.9 (2)	C14—C13—C18	114.2 (2)
C6—C7—C8	113.8 (2)	C8—C14—C15	120.3 (2)
C14—C8—C7	110.6 (2)	C8—C14—C13	114.2 (2)
C14—C8—C9	109.0 (2)	C15—C14—C13	104.1 (2)
C7—C8—C9	111.7 (2)	C14—C15—C16	102.6 (2)
F—C9—C8	107.0 (2)	C20—C16—C17	110.9 (3)
F—C9—C11	101.9 (2)	C20—C16—C15	114.3 (3)
C8—C9—C11	112.9 (2)	C17—C16—C15	104.7 (2)
F—C9—C10	104.5 (2)	O3—C17—C13	126.0 (3)
C8—C9—C10	113.0 (2)	O3—C17—C16	125.5 (3)
C11—C9—C10	116.1 (2)	C13—C17—C16	108.5 (2)
C1—C10—C5	112.0 (2)	O4—C21—O2	124.0 (3)
C1—C10—C19	106.7 (2)	O4—C21—C22	126.3 (2)
C5—C10—C19	107.9 (2)	O2—C21—C22	109.6 (3)
C1—C10—C9	110.6 (2)	C23—C22—C21	174.8 (3)
C5—C10—C9	106.0 (2)	C22—C23—C24	179.0 (3)

Data collection: CAD-4-VAX diffractometer software (Enraf–Nonius, 1988). Cell refinement: CAD-4-VAX diffractometer software. Program(s) used to solve structure: *SHELXTL/PC* (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: CR1188). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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2-[2-(2-Ethyl-2,3-dihydrobenzofuranyl)]-2-imidazoline Hydrobromide

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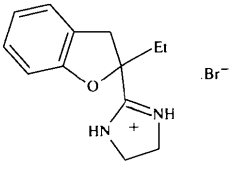
Abstract

The isomorphous structures of 2-[2-(2-ethyl-2,3-dihydro-2-benzofuranyl)]-2-imidazolinium [(+)-efaroxan cation] chloride, $C_{13}H_{17}N_2O^+.Cl^-$, and bromide, $C_{13}H_{17}N_2O^+.Br^-$, have been determined. The absolute configuration of the active molecule (efaroxan) could be resolved only in the hydrobromide salt, the structure of which is reported. (+)-Efaroxan has the *R* configuration.

Comment

Efaroxan {(±)-2-[2-(2-ethyl-2,3-dihydro-2-benzofuranyl)]-2-imidazoline (CAS Registery Number 99197–32–0)} is a potent and highly selective α-2-adrenoreceptor antagonist. Efaroxan has one asymmetric C atom on the dihydrobenzofuranyl ring [C(2)] and therefore exhibits two enantiomers. It has long been recognized that many receptor systems are highly isomerically selective and compounds possessing a chiral centre should be resolved so that the configuration of the active isomer may be established. The *R* configuration of the molecule of the title compound, (I), is shown in Fig. 1 and the crystal packing of the structure is represented in Fig. 2.



(I)

The sums of the angles around each N atom are close to 360°, as is the sum of angles around the H atom attached to N(14), which is involved in weak hydrogen bonding to the Br anion and to O(1). The other weak hydrogen bond involves the H atom attached to N(11) and is almost linear. Knowledge of the true configuration of (+)-efaroxan hydrobromide and thus of the chloride analogue prepared from the same base, may aid understanding of its structure–therapeutic activity correlation. Furthermore, it is now expected that the active substance may be prepared by a convenient and more economical asymmetric synthesis.

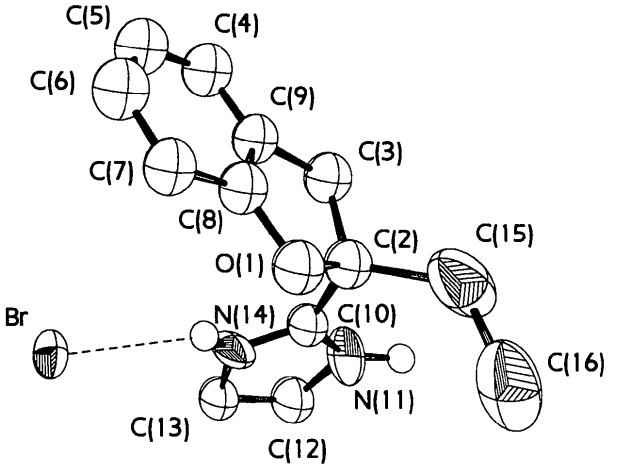


Fig. 1. Molecular structure of efaroxan hydrobromide showing 50% probability displacement ellipsoids. For clarity, some H atoms have been omitted.

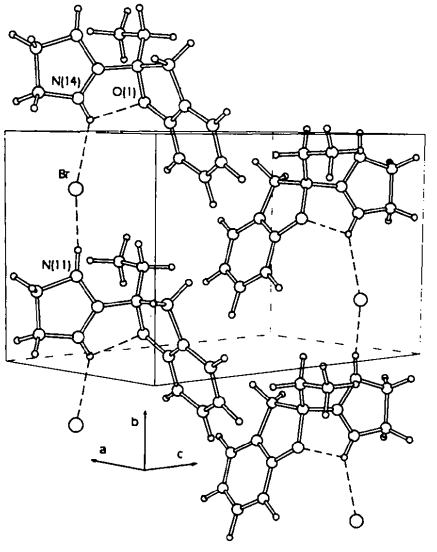


Fig. 2. Packing diagram of efaroxan hydrobromide in the monoclinic cell. The hydrogen bond is represented as a dashed line.

Experimental

Separation of the (+) and (−) isomers of efaroxan from the racemic mixture was achieved by fractional crystallization of the (+)- and (−)-dibenzoyl tartrate salts. This resolution method afforded good yields (80%) of both enantiomers and high levels of enantiomeric purity (>99.8%). The enantiomeric purity was checked by chiral chromatography with a Cyclobond 1 2000 Astec column. Only (+)-efaroxan is pharmacologically active as an $\alpha 2$ antagonist; in order to improve its poor water solubility, (+)-efaroxan hydrochloride was prepared from the free base and crystallized. It crystallizes in the non-centrosymmetric monoclinic space group $P2_1$ with a = 7.023 (2), b = 8.229 (2), c = 11.490 (3) Å and β = 102.58 (2)°; the structure was refined to $R(F)$ = 0.043, but its absolute configuration could not be resolved. Since the imaginary part of the anomalous-scattering factor of Br is larger than that of Cl with Mo $K\alpha$, it was decided to prepare the (+)-efaroxan hydrobromide salt from the same free base as the hydrochloride salt.

Crystal data

$C_{13}H_{17}N_2O^+.Br^-$
M_r = 297.18
Monoclinic
$P2_1$
a = 7.181 (2) Å
b = 8.485 (3) Å
c = 11.446 (3) Å
β = 103.11 (2)°
V = 679.3 (3) Å^3
Z = 2
D_x = 1.453 Mg m^{-3}
Mo $K\alpha$ radiation
λ = 0.7107 Å
Cell parameters from 25 reflections
θ = 6.8–20.8°
μ = 2.929 mm^{-1}
T = 298 K
Needle
0.305 × 0.100 × 0.075 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
ω–2θ scans
Absorption correction: numerical (*SHELX*76; Sheldrick, 1976)
T_{min} = 0.720, T_{max} = 0.908
3264 measured reflections
2894 independent reflections
983 observed reflections [$I > 3\sigma(I)$]
R_{int} = 0.0148
θ_{max} = 27°
h = −9 → 9
k = −10 → 10
l = −14 → 14
3 standard reflections
monitored every 50 reflections
intensity decay: <0.5%

Refinement

Refinement on F
R = 0.0391
wR = 0.0494
S = 0.87
983 reflections
101 parameters
$w = 1/[\sigma^2(F) + 0.0035F^2]$
$(\Delta/\sigma)_{max}$ = 0.10
$\Delta\rho_{max}$ = 0.67 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}
Extinction correction: none
Atomic scattering factors from Cromer & Mann (1968)

Table 1. *Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters* (Å^2)

$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$ for Br, N(11), N(14), C(15) and C(16).

	x	y	z	U_{iso}/U_{eq}
Br	0.7757 (1)	0.2310	0.1091 (1)	0.0596 (4)
O(1)	0.726 (1)	0.6013 (9)	0.3255 (7)	0.050 (2)
C(2)	0.648 (1)	0.750 (1)	0.2611 (7)	0.048 (2)

C(3)	0.429 (1)	0.754 (1)	0.2515 (9)	0.055 (2)
C(4)	0.229 (1)	0.507 (1)	0.2987 (9)	0.066 (2)
C(5)	0.249 (2)	0.353 (1)	0.344 (1)	0.071 (3)
C(6)	0.421 (1)	0.287 (1)	0.384 (1)	0.070 (3)
C(7)	0.588 (1)	0.362 (1)	0.3823 (8)	0.053 (2)
C(8)	0.570 (1)	0.516 (1)	0.3370 (9)	0.049 (2)
C(9)	0.399 (1)	0.585 (1)	0.2953 (8)	0.050 (2)
C(10)	0.693 (1)	0.737 (2)	0.1438 (7)	0.041 (2)
N(11)	0.704 (2)	0.862 (1)	0.0743 (9)	0.059 (3)
C(12)	0.735 (2)	0.813 (1)	−0.045 (1)	0.055 (3)
C(13)	0.757 (2)	0.634 (1)	−0.026 (1)	0.046 (2)
N(14)	0.719 (1)	0.611 (1)	0.087 (1)	0.051 (3)
C(15)	0.743 (2)	0.886 (2)	0.337 (1)	0.089 (3)
C(16)	0.957 (2)	0.893 (1)	0.359 (1)	0.091 (3)

Table 2. *Selected geometric parameters* (Å, °)

C(10)—N(14)	1.28 (2)	C(9)—C(3)	1.55 (2)
C(13)—N(14)	1.40 (2)	C(5)—C(4)	1.40 (2)
H(N14)—N(14)	0.94 (6)	C(6)—C(5)	1.34 (2)
C(10)—N(11)	1.34 (2)	C(7)—C(6)	1.36 (2)
C(12)—N(11)	1.49 (2)	C(7)—C(8)	1.40 (1)
H(N11)—N(11)	0.94 (4)	C(2)—C(3)	1.55 (1)
C(8)—O(1)	1.36 (2)	C(15)—C(2)	1.51 (3)
C(2)—O(1)	1.51 (2)	C(10)—C(2)	1.45 (1)
C(4)—C(5)	1.40 (2)	C(16)—C(15)	1.51 (3)
C(8)—C(9)	1.35 (1)	C(13)—C(12)	1.53 (2)
Br···H(N14)	2.54 (5)	Br···H(N11^{i})	2.25 (4)
O(1)···H(N14)	2.24 (7)		
C(10)—N(14)—C(13)	116 (1)	O(1)—C(8)—C(7)	122 (1)
C(10)—N(14)—H(N14)	110 (4)	C(9)—C(8)—C(7)	122 (1)
C(13)—N(14)—H(N14)	133 (4)	C(9)—C(3)—C(2)	100 (1)
C(10)—N(11)—C(12)	111 (1)	O(1)—C(2)—C(3)	108 (1)
C(10)—N(11)—H(N11)	134 (5)	O(1)—C(2)—C(15)	107 (1)
C(12)—N(11)—H(N11)	115 (5)	O(1)—C(2)—C(10)	105 (1)
C(2)—O(1)—C(8)	106 (1)	C(3)—C(2)—C(15)	110 (1)
C(4)—C(9)—C(8)	121 (1)	C(3)—C(2)—C(10)	112 (1)
C(4)—C(9)—C(3)	129 (1)	C(15)—C(2)—C(10)	115 (1)
C(8)—C(9)—C(3)	109 (1)	C(2)—C(15)—C(16)	116 (2)
C(9)—C(4)—C(5)	116 (1)	N(14)—C(10)—N(11)	109 (1)
C(4)—C(5)—C(6)	122 (1)	N(14)—C(10)—C(2)	128 (2)
C(5)—C(6)—C(7)	123 (1)	N(11)—C(10)—C(2)	123 (2)
C(6)—C(7)—C(8)	116 (1)	N(11)—C(12)—C(13)	100 (1)
O(1)—C(8)—C(9)	116 (1)	N(14)—C(13)—C(12)	103 (1)
Br···H(N14)—O(1)	116 (3)	Br···H(N14)—N(14)	133 (5)
O(1)···H(N14)—N(14)	110 (5)	Br···H(N11^{i})—N(11^{i})	170 (7)

Symmetry code: (i) $x, y-1, z$.

Enraf–Nonius (1989) *CAD-4 Software* was used for data collection and reduction. The structure was solved by direct methods using *SHELXS*86 (Sheldrick, 1985) and refinement was carried out using *SHELX*76 (Sheldrick, 1976) with anisotropic displacement parameters for Br, ethyl C, and N atoms. H atoms were included as fixed atoms in idealized positions with C_{sp^2}—H = 0.97 and C_{sp^3}—H = 0.98 Å. An attempt to freely refine H atoms attached to N atoms was not satisfactory; these H atoms could be fairly well positioned by constraining the N—H bond length to 0.94 Å, a value which has been found in histamine (Bonnet & Ibers, 1973) and in protonated histamine (Veidis, Palenik, Schaffin & Trotter, 1969). The ellipsoid plot was drawn using *ORTEP*II (Johnson, 1976); the packing diagram was obtained using *ATOMS* (Dowty, 1993). All computations were carried out on a Pentium 90 computer.

The authors thank Mr Serge Brunel for technical assistance.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: PA1181). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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1,2,3,4,6,7-Hexahydro-10-chloronaphtho-[3,2-*c*]acridine

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Abstract

The title molecule, $C_{21}H_{18}ClN$, shows conformational flexibility; each of the two unsaturated rings present in the structure adopts two conformations, a major

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