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**Structure and Absolute Configuration of Nebivolol: ( $\pm$ )-( $R^*\{S^*[S^*(-S^*)]\}$ )- $\alpha,\alpha'$ -[Iminobis(methylene)]bis(6-fluoro-3,4-dihydro-2H-1-benzopyran-2-methanol) (Nebivolol) Hydrochloride (I)<sup>†</sup> and (+)-( $S\{R[R-(R)]\}$ )-Nebivolol Hydrobromide Dihydrate (II)<sup>‡</sup>**

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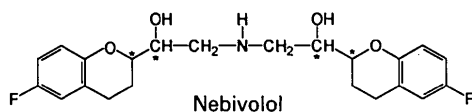
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**Abstract**

Both structures,  $C_{22}H_{26}F_2NO_4 \cdot Cl^-$  (I) and  $C_{22}H_{26}F_2NO_4 \cdot Br^- \cdot 2H_2O$  (II), have essentially the same conformation. The bridging chain between the two benzopyran moieties is nearly fully extended. In each molecule one O—C—C—O dihedral angle is synclinal and the other is antiperiplanar. One dihydropyran ring has a half-chair conformation while the other is halfway between half-chair and envelope. The structures are stabilized by hydrogen-bonding networks. The absolute configuration of the molecule was determined from the structure of (II).

**Comment**

Nebivolol contains four asymmetric C atoms in its structure and ten stereoisomers can exist. Nebivolol is a racemic mixture of two enantiomers, the *dextro d*-neбиволol [(+)-(*SRRR*) configuration] and the *levo l*-neбиволol [(-)-(*RSSS*) configuration]. Nebivolol, or strictly *dl*-neбиволol, has potent and selective  $\beta_1$ -adrenergic antagonist activity, exerts antihypertensive effects and can be distinguished in animals from other  $\beta$ -adrenergic antagonists by its haemodynamic profile. Pharmacological and clinical evidence demonstrates that the  $\beta_1$ -adrenergic antagonism of neбиволol resides in the (*SRRR*) enantiomer, whereas the distinctive haemodynamic profile can be largely attributed to the presence of (*RSSS*)-neбиволol (Janssens, Xhonneux & Janssen, 1991).



<sup>†</sup> Internal code of the Janssen Research Foundation: R67555.

<sup>‡</sup> Internal code of the Janssen Research Foundation: R74489.

A *PLUTO* diagram (Motherwell & Clegg, 1978) of (I) [(*RSSS*) configuration] with the atomic numbering scheme is shown in Fig. 1. The corresponding bond lengths in the two identical parts of the molecule agree to within three times the e.s.d.'s and are close to the average molecular dimensions of two stereoisomers of the defluorinated derivative of the title compound (Peeters, Verlinde, Blaton & De Ranter, 1989). Comparison of the equivalent bond angles shows significant differences at the primed and unprimed C3, C5, O6 and C10 atoms. The difference in the angles at C3 can be explained through the Räsänen rule (Räsänen, Aspiala, Homanen & Murto, 1982): 'If in a conformer of a primary alcohol or amine a C—C or C—H is *trans* to an X—H (X = O, N) bond, the corresponding X—C—C or X—C—H angle will be considerably smaller than for the other configurations'. The C2—C3—O4 angle, with the O4—H4 bond antiperiplanar to C2—C3, is smaller than the C2'—C3'—O4' angle with the O4'—H4' bond near 90°. The opening of the internal angles of the primed 3,4-dihydropyran ring at C5', O6' and C10' is related to the degree of pucker, which is less in the primed ring [ $Q_t = 0.481(8) \text{ \AA}$ ] than in the unprimed ring [ $Q_t = 0.510(7) \text{ \AA}$ ]. From the puckering parameters (Cremer & Pople, 1975) and asymmetry parameters (Nardelli, 1983*b*), and according to Boeyens (1978), the unprimed 3,4-dihydropyran ring adopts a half-chair conformation with a twofold axis intersecting C5—C10, while the primed ring is halfway between a half-chair and an envelope with its apex at C10'. This flattening allows the C—O—C angle to increase to 118.2(7)°. The deviation of the internal angles in the benzene moieties from the ideal value of 120° agrees very well with the combined angular substituent parameters for F, OMe and Me given by Domenicano & Murray-Rust (1979). The nearly fully extended conformation of the C—C—N—C—C bridging chain between the two benzopyran moieties is stabilized by two N—H...O intramolecular hydrogen bonds. Two non-classical C—H...O intramolecular hydrogen bonds keep the C2—C3—C5—O6 and C2'—C3'—C5'—O6' dihedral angles in a synclinal position. The packing of the molecules in the crystal results mainly from N—H...Cl, O—H...Cl and N—H...O intermolecular hydrogen bonds.

To obtain the absolute configuration, the structure of (+)-neбиволol hydrobromide, which crystallizes as a dihydrate, was determined. The conformation of the molecule

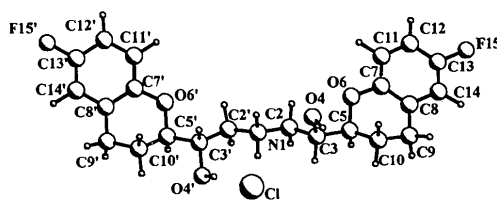


Fig. 1. A perspective view of the molecule of (I) with atomic numbering scheme.

is essentially the same as in structure (I). Unfortunately, due to the small dimensions and poor quality of the crystal, the errors on the positional parameters are rather high, especially in the *a* direction, and some anisotropic displacement factors do not represent ellipsoids. The geometric parameters will therefore not be discussed. However, the Bijvoet coefficient, calculated according to the selection procedure of Beurkens, Noordik & Beurskens (1980), was 0.865 (7) for 85 selected Friedel pairs after complete isotropic refinement ( $R = 0.11$ ) and 0.84 (1) for 101 Friedel pairs after anisotropic refinement. For more stringent selection parameters the Bijvoet coefficient becomes 1. This indicates that the configuration of (+)-neбиволол is (*SRRR*). To be sure that this indication is correct, the structure and absolute configuration of (-)- $\alpha$ -[(benzylamino)methyl]-6-fluoro-3,4-dihydro-2*H*-1-benzopyran-2-methanol hydrobromide was determined (Peeters, Blaton & De Ranter, 1993). This key intermediate in the synthesis of (-)-neбиволол shows the (*RS*) configuration which confirms that (-)-neбиволол has the (*RSSS*) configuration.

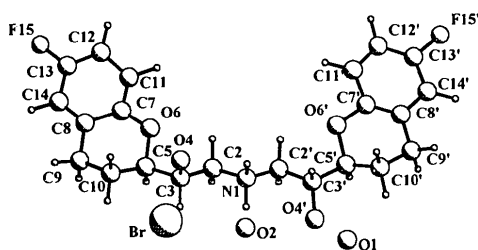


Fig. 2. A perspective view of the molecule of (II) with atomic numbering scheme.

## Experimental

### Compound (1)

#### Crystal data

$C_{22}H_{26}F_2NO_4 \cdot Cl^-$

$M_r = 442.91$

Triclinic

$P\bar{1}$

$a = 8.110$  (9) Å

$b = 9.07$  (1) Å

$c = 15.61$  (2) Å

$\alpha = 81.37$  (9)°

$\beta = 85.29$  (9)°

$\gamma = 68.61$  (9)°

$V = 1057$  (2) Å<sup>3</sup>

$Z = 2$

#### Data collection

Stoe Stadi-4 four-circle diffractometer

$2\theta/\omega$  scans (0.8–2.4° min<sup>-1</sup>)

Absorption correction: none

$D_x = 1.392$  Mg m<sup>-3</sup>

Cu  $K\alpha$  radiation

$\lambda = 1.54178$  Å

Cell parameters from 24 reflections

$\theta = 20$ – $25$ °

$\mu = 2.014$  mm<sup>-1</sup>

$T = 293$  K

Needle

$0.50 \times 0.20 \times 0.10$  mm

Colourless

$R_{int} = 0.0150$

$\theta_{max} = 64.48$ °

$h = -8 \rightarrow 9$

$k = 0 \rightarrow 10$

$l = -17 \rightarrow 18$

3812 measured reflections  
3109 independent reflections  
1858 observed reflections  
 $[I > 3.0\sigma(I)]$

#### Refinement

Refinement on  $F$

$R = 0.0464$

$wR = 0.0699$

$S = 1.10$

1858 reflections

271 parameters

H-atom parameters not refined

$w = 1/[\sigma^2(F) + 0.00300F^2]$

$(\Delta/\sigma)_{max} = 0.013$

4 standard reflections  
frequency: 60 min  
intensity variation: 0.6%

$\Delta\rho_{max} = 0.25$  e Å<sup>-3</sup>  
 $\Delta\rho_{min} = -0.26$  e Å<sup>-3</sup>

Extinction correction: none

Atomic scattering factors from *International Tables for X-ray Crystallography* [1974, Vol. IV, Tables 2.2B, 2.3.1 (Cl, N, C, O, F), 2.2B (H)]

Table 1. Fractional atomic coordinates and equivalent isotropic thermal parameters (Å<sup>2</sup>) for compound (1)

$$U_{eq} = \frac{1}{3} \sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$$

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{eq}$
Cl	0.4071 (2)	0.7088 (2)	0.56478 (9)	0.0706 (6)
N1	0.7842 (5)	0.7510 (4)	0.5103 (2)	0.044 (2)
C2	0.8592 (6)	0.7337 (5)	0.4206 (3)	0.044 (2)
C3	0.7991 (6)	0.6147 (5)	0.3849 (3)	0.041 (2)
O4	0.8511 (4)	0.4717 (3)	0.4443 (2)	0.044 (1)
C5	0.8765 (5)	0.5866 (5)	0.2941 (3)	0.040 (2)
O6	1.0669 (4)	0.5216 (4)	0.3013 (2)	0.043 (1)
C7	1.1604 (5)	0.4723 (5)	0.2263 (3)	0.037 (2)
C8	1.0816 (6)	0.4462 (5)	0.1573 (3)	0.042 (2)
C9	0.8901 (6)	0.4649 (6)	0.1613 (3)	0.052 (2)
C10	0.8150 (6)	0.4747 (6)	0.2539 (3)	0.045 (2)
C11	1.3397 (6)	0.4465 (6)	0.2244 (3)	0.047 (2)
C12	1.4432 (6)	0.3987 (6)	0.1520 (3)	0.055 (2)
C13	1.3647 (7)	0.3753 (6)	0.0835 (3)	0.055 (2)
C14	1.1881 (7)	0.3952 (6)	0.0842 (3)	0.052 (2)
F15	1.4663 (4)	0.3280 (4)	0.0116 (2)	0.078 (2)
C2'	0.8112 (6)	0.8812 (5)	0.5502 (3)	0.044 (2)
C3'	0.6932 (6)	0.9107 (5)	0.6316 (3)	0.042 (2)
O4'	0.5125 (4)	0.9774 (4)	0.6099 (2)	0.052 (1)
C5'	0.7280 (6)	1.0260 (5)	0.6827 (3)	0.040 (2)
O6'	0.9122 (4)	0.9570 (4)	0.7028 (2)	0.050 (1)
C7'	0.9684 (6)	1.0066 (5)	0.7706 (3)	0.048 (2)
C8'	0.8496 (7)	1.1045 (6)	0.8271 (3)	0.052 (2)
C9'	0.6542 (7)	1.1576 (7)	0.8162 (4)	0.061 (3)
C10'	0.6134 (6)	1.0479 (6)	0.7645 (3)	0.049 (2)
C11'	1.1484 (6)	0.9489 (6)	0.7821 (3)	0.055 (2)
C12'	1.2155 (7)	0.9904 (7)	0.8503 (4)	0.067 (3)
C13'	1.0982 (8)	1.0902 (7)	0.9030 (3)	0.068 (3)
C14'	0.9213 (8)	1.1472 (6)	0.8937 (3)	0.063 (2)
F15'	1.1647 (5)	1.1321 (5)	0.9697 (2)	0.100 (2)

Table 2. Geometric parameters (Å, °) for compound (1)

N1—C2	1.487 (5)	C13—F15	1.363 (5)
N1—C2'	1.504 (7)	C2'—C3'	1.522 (6)
C2—C3	1.524 (7)	C3'—O4'	1.415 (5)
C3—O4	1.423 (5)	C3'—C5'	1.521 (7)
C3—C5	1.521 (5)	C5'—O6'	1.434 (5)
C5—O6	1.445 (5)	C5'—C10'	1.511 (6)
C5—C10	1.511 (7)	O6'—C7'	1.380 (6)
O6—C7	1.381 (5)	C7'—C8'	1.402 (6)
C7—C8	1.388 (6)	C7'—C11'	1.377 (6)
C7—C11	1.384 (6)	C8'—C9'	1.495 (7)
C8—C9	1.496 (7)	C8'—C14'	1.397 (8)
C8—C14	1.402 (6)	C9'—C10'	1.508 (9)
C9—C10	1.523 (6)	C11'—C12'	1.391 (8)
C11—C12	1.377 (6)	C12'—C13'	1.366 (7)
C12—C13	1.368 (8)	C13'—C14'	1.348 (8)
C13—C14	1.377 (8)	C13'—F15'	1.371 (7)

C2—N1—C2'	114.6 (6)	N1—C2'—C3'	108.6 (6)
N1—C2—C3	108.3 (6)	C2'—C3'—C5'	112.4 (6)
C2—C3—C5	111.2 (6)	C2'—C3'—O4'	110.5 (5)
C2—C3—O4	107.3 (5)	O4'—C3'—C5'	107.1 (7)
O4—C3—C5	112.1 (6)	C3'—C5'—C10'	110.9 (6)
C3—C5—C10	113.4 (6)	C3'—C5'—O6'	106.0 (6)
C3—C5—O6	106.6 (5)	O6'—C5'—C10'	110.8 (6)
O6—C5—C10	110.2 (7)	C5'—O6'—C7'	118.2 (7)
C5—O6—C7	114.9 (6)	O6'—C7'—C11'	116.1 (6)
O6—C7—C11	116.2 (6)	O6'—C7'—C8'	122.3 (7)
O6—C7—C8	122.5 (7)	C8'—C7'—C11'	121.6 (6)
C8—C7—C11	121.4 (6)	C7'—C8'—C14'	117.4 (8)
C7—C8—C14	118.2 (7)	C7'—C8'—C9'	120.4 (6)
C7—C8—C9	121.4 (6)	C9'—C8'—C14'	122.2 (7)
C9—C8—C14	120.3 (6)	C8'—C9'—C10'	110.1 (7)
C8—C9—C10	110.9 (6)	C5'—C10'—C9'	110.4 (6)
C5—C10—C9	108.7 (6)	C7'—C11'—C12'	119.6 (7)
C7—C11—C12	120.3 (7)	C11'—C12'—C13'	118.0 (8)
C11—C12—C13	118.2 (8)	C12'—C13'—F15'	117.9 (8)
C12—C13—F15	118.6 (8)	C12'—C13'—C14'	123.6 (7)
C12—C13—C14	123.1 (6)	C14'—C13'—F15'	118.5 (8)
C14—C13—F15	118.3 (7)	C8'—C14'—C13'	119.8 (7)
C8—C14—C13	118.9 (6)		
C2—N1—C2'—C3'	167.0 (6)	O4—C3—C5—O6	-59.1 (8)
C2'—N1—C2—C3	-172.1 (6)	N1—C2'—C3'—C5'	172.9 (6)
N1—C2—C3—C5	-178.0 (6)	O4'—C3'—C5'—O6'	-179.2 (6)

Table 3. Hydrogen-bonding geometry (Å, °) for compound (1)

D	H	A	D—H	H...A	D...A	D—H...A
N1	H1B	Cl	1.045	2.317	3.249 (6)	147.6
O4'	H4'	Cl	1.048	2.062	3.049 (5)	156.1
N1	H1A	O4	1.048	2.405	2.732 (6)	96.7
N1	H1B	O4'	1.045	2.470	2.930 (6)	105.6
C2	H2B	O6	1.049	2.495	2.864 (6)	99.6
C2'	H2'A	O6'	1.069	2.440	2.835 (7)	100.4
N1	H1A	O4	1.048	2.304	2.982 (6)	121.0
O4	H4	Cl	0.911	2.209	3.116 (5)	173.4

**Compound (2)***Crystal data*C<sub>22</sub>H<sub>26</sub>F<sub>2</sub>NO<sub>4</sub>·Br<sup>-</sup>·2H<sub>2</sub>OM<sub>r</sub> = 522.38

Orthorhombic

P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>

a = 4.841 (4) Å

b = 14.617 (7) Å

c = 33.46 (1) Å

V = 2368. (2) Å<sup>3</sup>

Z = 4

D<sub>x</sub> = 1.465 Mg m<sup>-3</sup>*Data collection*

Stoe Stadi-4 four-circle diffractometer

2θ/ω scans (0.8–2.4° min<sup>-1</sup>)

Absorption correction: none

6139 measured reflections

2840 independent reflections

1088 observed reflections

[I &gt; 3.0σ(I)]

Cu Kα radiation

λ = 1.54178 Å

Cell parameters from 28 reflections

θ = 8–23°

μ = 2.835 mm<sup>-1</sup>

T = 293 K

Needle

0.38 × 0.06 × 0.04 mm

Colourless

R<sub>int</sub> = 0.050θ<sub>max</sub> = 59.18°

h = 0 → 5

k = 0 → 16

l = -29 → 37

3 standard reflections

frequency: 60 min

intensity variation: 9.1%

*Refinement*

Refinement on F

R = 0.0658

wR = 0.0833

S = 1.53

1088 reflections

289 parameters

H-atom parameters not refined

w = 1/[σ<sup>2</sup>(F) + 0.00200F<sup>2</sup>](Δ/σ)<sub>max</sub> = 0.092Δρ<sub>max</sub> = 0.54 e Å<sup>-3</sup>Δρ<sub>min</sub> = -0.57 e Å<sup>-3</sup>

Extinction correction: none

Atomic scattering factors

from *International Tables for X-ray Crystallography* [1974, Vol. IV, Tables 2.2B, 2.3.1 (Br, N, C, O, F), 2.2B (H)]

Absolute configuration: the Bijvoet coefficient was

0.84 (1) for the 101 most significant Bijvoet pairs.

With more stringent selection parameters it becomes equal to 1.

Table 4. Fractional atomic coordinates and equivalent isotropic thermal parameters (Å<sup>2</sup>) for compound (2)
$$U_{eq} = \frac{1}{3} \sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$$

	x	y	z	U <sub>eq</sub>
Br	-0.1944 (7)	1.0294 (3)	0.21313 (8)	0.084 (1)
N1	0.251 (5)	0.930 (1)	0.3401 (4)	0.058 (9)
C2	0.156 (5)	1.020 (2)	0.3562 (5)	0.042 (8)
C3	0.008 (5)	1.074 (2)	0.3252 (6)	0.04 (1)
O4	-0.226 (3)	1.025 (1)	0.3101 (3)	0.041 (5)
C5	-0.083 (5)	1.168 (2)	0.3445 (7)	0.041 (9)
O6	-0.253 (3)	1.141 (1)	0.3790 (4)	0.032 (5)
C7	-0.399 (5)	1.208 (2)	0.3963 (5)	0.03 (1)
C8	-0.466 (6)	1.295 (2)	0.3796 (8)	0.04 (1)
C9	-0.327 (6)	1.317 (2)	0.3408 (7)	0.05 (1)
C10	-0.249 (5)	1.229 (2)	0.3177 (7)	0.036 (8)
C11	-0.510 (5)	1.183 (2)	0.4317 (8)	0.04 (1)
C12	-0.700 (9)	1.242 (2)	0.4533 (7)	0.07 (1)
C13	-0.749 (7)	1.324 (2)	0.4362 (8)	0.07 (1)
C14	-0.624 (8)	1.353 (2)	0.400 (1)	0.08 (2)
F15	-0.913 (4)	1.383 (1)	0.4556 (5)	0.095 (8)
C2'	0.401 (6)	0.874 (2)	0.3701 (6)	0.06 (1)
C3'	0.511 (6)	0.788 (1)	0.3525 (6)	0.033 (9)
O4'	0.735 (4)	0.807 (1)	0.3284 (4)	0.046 (7)
C5'	0.618 (5)	0.723 (2)	0.3872 (7)	0.04 (1)
O6'	0.378 (4)	0.721 (1)	0.4163 (4)	0.041 (6)
C7'	0.420 (6)	0.657 (2)	0.4478 (5)	0.04 (1)
C8'	0.592 (6)	0.586 (2)	0.4468 (7)	0.04 (1)
C9'	0.772 (5)	0.570 (1)	0.4102 (6)	0.032 (8)
C10'	0.661 (4)	0.625 (2)	0.3741 (6)	0.032 (8)
C11'	0.230 (5)	0.677 (1)	0.4798 (6)	0.036 (9)
C12'	0.237 (7)	0.621 (2)	0.5121 (7)	0.07 (1)
C13'	0.427 (8)	0.549 (2)	0.5122 (7)	0.07 (1)
C14'	0.617 (5)	0.528 (2)	0.4805 (7)	0.047 (9)
F15'	0.458 (4)	0.493 (1)	0.5453 (4)	0.096 (7)
O1	0.710 (4)	0.681 (1)	0.2691 (4)	0.079 (8)
O2	0.295 (4)	0.903 (1)	0.2588 (4)	0.099 (9)

Table 5. Geometric parameters (Å, °) for compound (2)

N1—C2	1.49 (3)	C13—F15	1.34 (3)
N1—C2'	1.48 (3)	C2'—C3'	1.49 (3)
C2—C3	1.49 (3)	C3'—O4'	1.38 (3)
C3—O4	1.43 (2)	C3'—C5'	1.59 (3)
C3—C5	1.59 (3)	C5'—O6'	1.51 (2)
C5—O6	1.47 (2)	C5'—C10'	1.51 (3)
C5—C10	1.50 (3)	O6'—C7'	1.42 (2)
O6—C7	1.34 (2)	C7'—C8'	1.34 (3)
C7—C8	1.43 (3)	C7'—C11'	1.44 (3)
C7—C11	1.35 (3)	C8'—C9'	1.52 (3)
C8—C9	1.50 (3)	C8'—C14'	1.41 (3)
C8—C14	1.34 (4)	C9'—C10'	1.55 (2)
C9—C10	1.55 (3)	C11'—C12'	1.36 (3)
C11—C12	1.45 (4)	C12'—C13'	1.39 (4)
C12—C13	1.35 (4)	C13'—C14'	1.44 (3)
C13—C14	1.41 (4)	C13'—F15'	1.39 (2)

C2—N1—C2'	113 (2)	N1—C2'—C3'	112 (2)
N1—C2—C3	111 (2)	C2'—C3'—C5'	109 (2)
C2—C3—C5	108 (2)	C2'—C3'—O4'	109 (2)
C2—C3—O4	111 (2)	O4'—C3'—C5'	107 (2)
O4—C3—C5	111 (2)	C3'—C5'—C10'	114 (2)
C3—C5—C10	115 (2)	C3'—C5'—O6'	103 (2)
C3—C5—O6	104 (2)	O6'—C5'—C10'	106 (2)
O6—C5—C10	109 (2)	C5'—O6'—C7'	112 (2)
C5—O6—C7	116 (2)	O6'—C7'—C11'	109 (2)
O6—C7—C11	113 (2)	O6'—C7'—C8'	126 (2)
O6—C7—C8	127 (2)	C8'—C7'—C11'	125 (2)
C8—C7—C11	120 (2)	C7'—C8'—C14'	120 (2)
C7—C8—C14	119 (2)	C7'—C8'—C9'	120 (2)
C7—C8—C9	115 (2)	C9'—C8'—C14'	120 (2)
C9—C8—C14	125 (2)	C8'—C9'—C10'	111 (2)
C8—C9—C10	111 (2)	C5'—C10'—C9'	108 (2)
C5—C10—C9	109 (2)	C7'—C11'—C12'	117 (2)
C7—C11—C12	122 (2)	C11'—C12'—C13'	118 (2)
C11—C12—C13	115 (2)	C12'—C13'—F15'	121 (2)
C12—C13—F15	118 (3)	C12'—C13'—C14'	126 (2)
C12—C13—C14	124 (3)	C14'—C13'—F15'	113 (2)
C14—C13—F15	118 (3)	C8'—C14'—C13'	114 (2)
C8—C14—C13	120 (3)		
C2—N1—C2'—C3'	-176 (2)	O4—C3—C5—O6	65 (2)
C2'—N1—C2—C3	180 (2)	N1—C2'—C3'—C5'	-169 (2)
N1—C2—C3—C5	-179 (2)	O4'—C3'—C5'—O6'	169 (2)

The structure of (I) was solved by direct methods and that of (II) by a combination of Patterson functions and direct methods. Refinement was by full-matrix least-squares methods. H atoms were calculated, where possible, at geometrical positions. The hydroxyl H atoms in (I) were obtained from a difference Fourier synthesis and in (II) neither the hydroxyl nor the water H atoms could be located. Data collection: *DIF4* (Stoe & Cie, 1985a). Cell refinement: *DIF4*. Data reduction: *REDU4* (Stoe & Cie, 1985b). Program(s) used to solve structure: *MULTAN80* (Main *et al.*, 1980) for compound (1); *DIRDIF* (Beurskens *et al.*, 1992) for compound (II). Program(s) used to refine structure: *NRC-VAX* (Gabe, Le Page, Charland, Lee & White, 1989). Molecular graphics: *PLUTO* (Motherwell & Clegg, 1978). Software used to prepare material for publication: *PARST* (Nardelli, 1983a).

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Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and complete geometry have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71448 (31 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: NA1052]

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## Structure and Absolute Configuration of (–)-(RS)- $\alpha$ -[(Benzylamino)methyl]-6-fluoro-3,4-dihydro-2H-1-benzopyran-2-methanol Hydrobromide<sup>†</sup>

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## Abstract

The asymmetric unit of the title compound, C<sub>18</sub>H<sub>20</sub>FNO<sub>2</sub>·Br<sup>−</sup>, contains two molecules. The conformation of the bridging chain between the two rings is antiperiplanar/antiperiplanar/antiperiplanar in molecule *A* and antiperiplanar/synclinal/antiperiplanar in molecule *B*. The heterocyclic ring of the dihydrobenzopyran rings adopts a conformation halfway between a half-chair and an envelope with an apex at C10. The structure is stabilized by a network of hydrogen bonds between N, O and Br atoms. The absolute configuration is *R* for the asymmetric C atom in the dihydropyran ring and *S* for the hydroxyl-bearing C atom.

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