

$S = 2.410$
1632 reflections
154 parameters
H-atom parameters not refined
Unit weights applied

Atomic scattering factors
from *International Tables for Crystallography* (1992), Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters (\AA^2)

$$U_{eq} = (1/3)\sum_i \sum_j U_{ij} a_i^* a_j^* a_i \cdot a_j$$

	x	y	z	U_{eq}
Br(1)	0.13557 (5)	0.07867 (4)	0.28446 (4)	0.0447 (1)
O(1)	0.41124 (3)	0.2746 (3)	0.0691 (2)	0.0429 (9)
N(1)	0.3574 (3)	0.2900 (3)	0.2433 (3)	0.0269 (9)
C(2)	0.3599 (4)	0.3356 (4)	0.1356 (3)	0.029 (1)
C(3)	0.2998 (5)	0.4527 (4)	0.1125 (3)	0.035 (1)
C(4)	0.2433 (5)	0.5129 (4)	0.1886 (4)	0.036 (1)
C(5)	0.2436 (4)	0.4626 (4)	0.2961 (4)	0.034 (1)
C(6)	0.3012 (4)	0.3529 (4)	0.3207 (3)	0.031 (1)
C(1')	0.4153 (4)	0.1689 (4)	0.2724 (4)	0.035 (1)
C(2')	0.3049 (4)	0.0735 (4)	0.2215 (3)	0.033 (1)
C(3')	0.3227 (4)	-0.0056 (4)	0.1453 (4)	0.034 (1)
C(1'')	0.2354 (4)	-0.1045 (3)	0.0824 (3)	0.030 (1)
C(2'')	0.3038 (4)	-0.1748 (3)	0.0142 (4)	0.033 (1)
C(3'')	0.2279 (5)	-0.2650 (4)	-0.0536 (4)	0.038 (1)
C(4'')	0.0833 (5)	-0.2880 (4)	-0.0545 (4)	0.040 (1)
C(5'')	0.0151 (5)	-0.2206 (4)	0.0130 (4)	0.043 (1)
C(6'')	0.0894 (5)	-0.1303 (4)	0.0810 (4)	0.040 (1)

Table 2. Selected geometric parameters (\AA , $^\circ$)

Br(1)—C(2')	1.918 (4)	C(1')—C(2')	1.511 (6)
O(1)—C(2)	1.241 (5)	C(1'')—C(3')	1.473 (6)
N(1)—C(1')	1.473 (5)	C(2')—C(3')	1.315 (6)
C(1')—N(1)—C(2)	118.0 (3)	Br(1)—C(2')—C(1')	111.7 (3)
C(1')—N(1)—C(6)	119.6 (3)	Br(1)—C(2')—C(3')	123.5 (3)
N(1)—C(1')—C(2')	112.3 (3)	C(1')—C(2')—C(3')	124.7 (4)
C(2'')—C(1'')—C(3')	116.6 (4)	C(1'')—C(3')—C(2')	135.8 (4)
C(3')—C(1'')—C(6'')	125.7 (4)		

The θ scan width used was $(1.10 + 0.3\tan\theta)^\circ$ at a speed of $16.0^\circ \text{ min}^{-1}$ (in ω). The weak reflections were rescanned a maximum of four times and the counts accumulated to ensure good counting statistics. Stationary background counts were made on each side of the reflection with a 2:1 ratio of peak to background counting time. H atoms were located from a difference map and fixed at ideal positions with $U_{iso} = 1.2U_{eq}(C)$. The structure was solved by Patterson methods and expanded using Fourier techniques (Beurskens *et al.*, 1992). All calculations were performed using *TEXSAN* (Molecular Structure Corporation, 1993).

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1993). Program(s) used to refine structure: *TEXSAN*. Software used to prepare material for publication: *TEXSAN*.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: AS1181). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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(+)-(S)-1-{4-[(2-Benzothiazolyl)(methyl)-amino]piperidyl}-3-(3,4-difluorophenoxy)-2-propanol (Lubeluzole)†

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Abstract

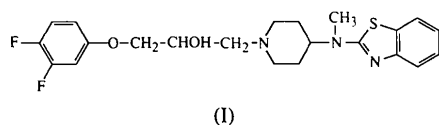
The crystal structure and absolute configuration of the (+) enantiomer of the title compound, $C_{22}H_{25}F_2N_3O_2S$, have been determined. The absolute configuration is S.

† Internal code of the Janssen Research Foundation: R87926.

The asymmetric unit contains two molecules having different conformations of the chain bridging the piperidyl and difluorophenyl rings. In one molecule the bridge is folded, while in the other it is fully extended.

Comment

Lubeluzole, (I), is the (+) enantiomer of a novel benzothiazole compound proposed for use in the acute treatment of ischemic stroke. Lubeluzole reduces infarct size, accelerates recovery of tissue in the penumbra and potentially protects neurologic function when administered intravenously following neocortical infarcts in rats. In contrast, the (−) isomer of lubeluzole is virtually inactive with respect to this model (De Ryck, Keersmaekers, Clincke, Janssen & Van Reet, 1994).



In order to determine the absolute configuration of lubeluzole, its crystal structure was solved. The asymmetric unit contains two molecules and corresponding bond lengths and angles within these molecules do not deviate significantly from each other or from those listed by Allen *et al.* (1987). Molecule A shows rotational disorder of the difluorophenyl moiety. The principal difference between the two molecules is the conformation of the chain bridging the piperidyl and

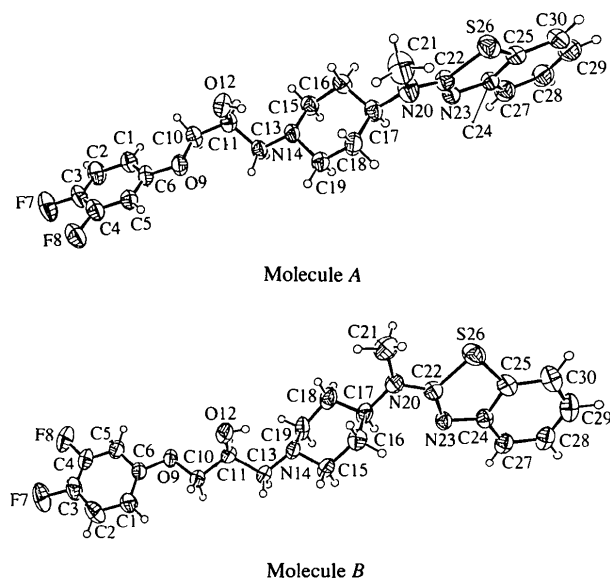


Fig. 1. Perspective views of the molecules of the title compound with the atomic numbering scheme. Displacement ellipsoids are drawn at the 40% probability level. The major component of the rotationally disordered difluorophenyl moiety of molecule A is shown.

difluorophenyl rings. The conformation is *ap/sc/ap* in molecule A and *ap/ap/ap* in molecule B (*ap* is antiplanar and *sc* is synclinal). In both molecules, the hydroxy O atom is *−sc* with respect to the piperidyl N atom. This conformation is stabilized by an O—H···N intramolecular hydrogen bond [O12A—H12A 0.820, H12A···N14A 2.23, O12A···N14A 2.706 (2) Å and O12A—H12A···N14A 117.5°; O12B—H12B 0.820, H12B···N14B 2.21, O12B···N14B 2.704 (2) Å and O12B—H12B···N14B 118.6°]. The packing of the molecules is due purely to van der Waals forces. The absolute configuration was established to be *S* according to the procedure of Flack (1983).

Experimental

Crystal data

C₂₂H₂₅F₂N₃O₂S

M_r = 433.51

Orthorhombic

*P*2₁2₁2₁

a = 8.5973 (5) Å

b = 16.5920 (8) Å

c = 30.202 (2) Å

V = 4308.2 (4) Å³

Z = 8

D_x = 1.337 Mg m^{−3}

D_m = 1.331 Mg m^{−3}

D_m measured by flotation in *n*-heptane/CCl₄

Cu Kα radiation

λ = 1.54184 Å

Cell parameters from 40 reflections

θ = 10–28°

μ = 1.690 mm^{−1}

T = 293 K

Prism

0.61 × 0.46 × 0.14 mm

Pale orange

Data collection

Siemens P4 four-circle diffractometer

ω/2θ scans

Absorption correction:

ψ scan (XEMP; Siemens, 1989)

T_{min} = 0.157, *T_{max}* = 0.235

7673 measured reflections

5825 independent reflections

5185 observed reflections [*F*² > 2σ(*F*²)]

R_{int} = 0.0578

θ_{max} = 57.10°

h = −9 → 9

k = −18 → 18

l = −32 → 32

3 standard reflections monitored every 100 reflections

intensity decay: < 4.0%

Refinement

Refinement on *F*²

R [*F*² > 2σ(*F*²)] = 0.0524

wR (*F*²) = 0.1541

S = 1.039

5824 reflections

619 parameters

H-atom parameters not refined

w = 1/[σ²(*F_o*²) + (0.0942*P*)² + 1.1464*P*]

where *P* = (*F_o*² + 2*F_c*²)/3

(Δ/σ)_{max} = −0.153

Δρ_{max} = 0.23 e Å^{−3}

Δρ_{min} = −0.25 e Å^{−3}

Extinction correction:

SHELXL93 (Sheldrick, 1993)

Extinction coefficient: 0.00086 (7)

Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, Tables 2.2B and 2.3.1)

Absolute configuration: χ = −0.01 (3) (Flack, 1983)

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters (\AA^2)
$$U_{\text{eq}} = (1/3)\sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$$

	x	y	z	U_{eq}
C1A1†	0.8515 (4)	0.3679 (2)	0.7087 (1)	0.068 (1)
C2A1†	0.8477 (5)	0.3965 (3)	0.6652 (1)	0.083 (1)
C3A1†	0.9843 (5)	0.4102 (2)	0.6430 (1)	0.081 (1)
C4A1†	1.1206 (5)	0.3977 (2)	0.6637 (1)	0.072 (1)
C5A1†	1.1283 (4)	0.3690 (2)	0.7062 (1)	0.065 (1)
C6A1†	0.9943 (4)	0.3547 (2)	0.72862 (9)	0.058 (1)
F7A1†	0.9786 (4)	0.4374 (2)	0.60067 (7)	0.123 (1)
F8A1†	1.2500 (3)	0.4123 (1)	0.64017 (7)	0.0931 (8)
C1A2†	0.852 (1)	0.3682 (7)	0.7085 (3)	0.069 (3)
C2A2†	0.849 (1)	0.3953 (8)	0.6657 (3)	0.082 (3)
C3A2†	0.981 (1)	0.4098 (7)	0.6429 (3)	0.076 (2)
C4A2†	1.122 (1)	0.3991 (6)	0.6633 (3)	0.069 (2)
C5A2†	1.129 (1)	0.3688 (7)	0.7064 (3)	0.064 (3)
C6A2†	0.990 (1)	0.3548 (6)	0.7288 (3)	0.063 (3)
F7A2†	0.978 (1)	0.4370 (5)	0.6005 (2)	0.109 (3)
F8A2†	0.7143 (6)	0.4086 (4)	0.6443 (2)	0.087 (2)
O9A	1.0109 (2)	0.3244 (1)	0.77073 (5)	0.0658 (5)
C10A	0.8721 (3)	0.2970 (2)	0.79220 (7)	0.0636 (8)
C11A	0.9117 (3)	0.2501 (1)	0.83290 (7)	0.0570 (7)
O12A	0.9953 (2)	0.1796 (1)	0.82120 (5)	0.0701 (6)
C13A	0.9995 (3)	0.2966 (1)	0.86803 (7)	0.0580 (7)
N14A	1.0491 (2)	0.2408 (1)	0.90282 (5)	0.0520 (5)
C15A	0.9228 (3)	0.2134 (2)	0.93095 (7)	0.0629 (7)
C16A	0.9766 (3)	0.1468 (2)	0.96195 (8)	0.0653 (8)
C17A	1.1169 (3)	0.1719 (1)	0.98885 (7)	0.0576 (7)
C18A	1.2406 (3)	0.2080 (2)	0.95917 (7)	0.0686 (8)
C19A	1.1724 (3)	0.2743 (2)	0.93048 (8)	0.0676 (8)
N20A	1.1762 (3)	0.1062 (1)	1.01677 (6)	0.0701 (7)
C21A	1.2492 (4)	0.0370 (2)	0.9957 (1)	0.097 (1)
C22A	1.1370 (3)	0.1030 (1)	1.06023 (7)	0.0536 (7)
N23A	1.0635 (2)	0.1590 (1)	1.08151 (6)	0.0530 (5)
C24A	1.0446 (2)	0.1371 (1)	1.12578 (7)	0.0507 (6)
C25A	1.1062 (3)	0.0627 (1)	1.13744 (7)	0.0566 (7)
S26A	1.19255 (8)	0.01752 (3)	1.09162 (2)	0.0697 (2)
C27A	0.9736 (3)	0.1841 (2)	1.15806 (7)	0.0629 (8)
C28A	0.9596 (3)	0.1549 (2)	1.20046 (8)	0.0763 (9)
C29A	1.0182 (3)	0.0814 (2)	1.21184 (8)	0.081 (1)
C30A	1.0945 (3)	0.0336 (2)	1.18109 (9)	0.0766 (9)
C1B	1.1315 (3)	0.3946 (1)	0.20901 (8)	0.0671 (8)
C2B	1.1558 (4)	0.4198 (2)	0.16512 (9)	0.086 (1)
C3B	1.0298 (4)	0.4304 (2)	0.13811 (8)	0.083 (1)
C4B	0.8862 (3)	0.4198 (2)	0.15307 (8)	0.0701 (8)
C5B	0.8572 (3)	0.3936 (2)	0.19471 (8)	0.0644 (8)
C6B	0.9831 (3)	0.3810 (1)	0.22284 (7)	0.0560 (8)
F7B	1.0541 (3)	0.4549 (1)	0.09534 (5)	0.1327 (9)
F8B	0.7643 (2)	0.4325 (1)	0.12535 (5)	0.1099 (7)
O9B	0.9426 (2)	0.3526 (1)	0.26367 (5)	0.0695 (5)
C10B	1.0612 (3)	0.3371 (2)	0.29547 (7)	0.0606 (8)
C11B	0.9833 (3)	0.2921 (2)	0.33215 (7)	0.0615 (8)
O12B	0.9623 (2)	0.2115 (1)	0.31860 (5)	0.0936 (6)
C13B	1.0771 (3)	0.2930 (2)	0.37506 (7)	0.0606 (7)
N14B	1.0117 (2)	0.2355 (1)	0.40604 (5)	0.0537 (6)
C15B	1.1225 (3)	0.2112 (2)	0.43992 (8)	0.0635 (7)
C16B	1.0569 (3)	0.1442 (2)	0.46858 (8)	0.0631 (8)
C17B	0.9026 (3)	0.1668 (1)	0.48893 (7)	0.0574 (7)
C18B	0.7928 (3)	0.1991 (2)	0.45356 (7)	0.0703 (9)
C19B	0.8694 (3)	0.2657 (2)	0.42776 (8)	0.0708 (8)
N20B	0.8352 (3)	0.1007 (1)	0.51488 (6)	0.0663 (7)
C21B	0.7603 (4)	0.0327 (2)	0.49305 (9)	0.094 (1)
C22B	0.8751 (3)	0.0936 (1)	0.55887 (7)	0.0554 (7)
N23B	0.9521 (2)	0.1475 (1)	0.58107 (5)	0.0493 (5)
C24B	0.9656 (3)	0.1228 (1)	0.62527 (7)	0.0512 (7)
C25B	0.8986 (3)	0.0480 (1)	0.63522 (7)	0.0577 (7)
S26B	0.81367 (8)	0.00745 (3)	0.58841 (2)	0.0718 (2)
C27B	1.0342 (3)	0.1678 (2)	0.65843 (7)	0.0597 (7)
C28B	1.0400 (3)	0.1369 (2)	0.70092 (8)	0.0725 (9)
C29B	0.9781 (4)	0.0631 (2)	0.71050 (8)	0.080 (1)
C30B	0.9059 (3)	0.0167 (2)	0.67829 (9)	0.0745 (9)

† Partially occupied site of the rotationally disordered difluorophenyl moiety of molecule A (see below).

Table 2. Selected geometric parameters (\AA , $^\circ$)

C1A1—C2A1	1.398 (5)	C1B—C2B	1.406 (4)
C1A1—C6A1	1.385 (5)	C1B—C6B	1.361 (4)
C2A1—C3A1	1.371 (6)	C2B—C3B	1.368 (4)
C3A1—C4A1	1.345 (6)	C3B—C4B	1.327 (4)
C3A1—F7A1	1.357 (4)	C3B—F7B	1.370 (3)
C4A1—C5A1	1.370 (5)	C4B—C5B	1.354 (3)
C4A1—F8A1	1.342 (4)	C4B—F8B	1.358 (3)
C5A1—C6A1	1.358 (5)	C5B—C6B	1.392 (4)
C6A1—O9A	1.375 (3)	C6B—O9B	1.365 (3)
C1A2—C2A2	1.37 (1)		
C1A2—C6A2	1.36 (1)		
C2A2—C3A2	1.34 (1)		
C2A2—F8A2	1.35 (1)		
C3A2—C4A2	1.37 (1)		
C3A2—F7A2	1.36 (1)		
C4A2—C5A2	1.40 (1)		
C5A2—C6A2	1.39 (1)		
C6A2—O9A	1.375 (8)		
O9A—C10A	1.432 (3)	O9B—C10B	1.424 (3)
C10A—C11A	1.494 (3)	C10B—C11B	1.495 (3)
C11A—O12A	1.417 (3)	C11B—O12B	1.411 (3)
C11A—C13A	1.513 (3)	C11B—C13B	1.527 (3)
C13A—N14A	1.464 (3)	C13B—N14B	1.449 (3)
N14A—C15A	1.452 (3)	N14B—C15B	1.455 (3)
N14A—C19A	1.460 (3)	N14B—C19B	1.476 (3)
C15A—C16A	1.521 (3)	C15B—C16B	1.517 (4)
C16A—C17A	1.513 (4)	C16B—C17B	1.510 (4)
C17A—C18A	1.514 (3)	C17B—C18B	1.523 (3)
C17A—N20A	1.469 (3)	C17B—N20B	1.467 (3)
C18A—C19A	1.518 (4)	C18B—C19B	1.503 (4)
N20A—C21A	1.455 (4)	N20B—C21B	1.456 (4)
N20A—C22A	1.356 (3)	N20B—C22B	1.377 (3)
C22A—N23A	1.295 (3)	C22B—N23B	1.298 (3)
C22A—S26A	1.771 (2)	C22B—S26B	1.766 (2)
N23A—C24A	1.395 (3)	N23B—C24B	1.401 (3)
C24A—C25A	1.389 (3)	C24B—C25B	1.401 (3)
C24A—C27A	1.390 (3)	C24B—C27B	1.381 (3)
C25A—S26A	1.740 (2)	C25B—S26B	1.728 (2)
C25A—C30A	1.408 (3)	C25B—C30B	1.402 (3)
C27A—C28A	1.374 (3)	C27B—C28B	1.383 (3)
C28A—C29A	1.364 (4)	C28B—C29B	1.366 (4)
C29A—C30A	1.386 (4)	C29B—C30B	1.388 (4)
C2A1—C1A1—C6A1	118.9 (3)	C2B—C1B—C6B	118.6 (2)
C1A1—C2A1—C3A1	119.7 (3)	C1B—C2B—C3B	118.9 (3)
C2A1—C3A1—F7A1	119.0 (4)	C2B—C3B—F7B	118.7 (3)
C2A1—C3A1—C4A1	119.6 (3)	C2B—C3B—C4B	121.1 (3)
C4A1—C3A1—F7A1	121.4 (4)	C4B—C3B—F7B	120.2 (3)
C3A1—C4A1—F8A1	116.7 (3)	C3B—C4B—F8B	119.2 (2)
C3A1—C4A1—C5A1	122.1 (4)	C3B—C4B—C5B	122.0 (3)
C5A1—C4A1—F8A1	121.3 (3)	C5B—C4B—F8B	118.7 (2)
C4A1—C5A1—C6A1	119.2 (3)	C4B—C5B—C6B	118.2 (2)
C1A1—C6A1—C5A1	120.5 (3)	C1B—C6B—C5B	121.1 (2)
C5A1—C6A1—O9A	115.9 (3)	C5B—C6B—O9B	113.8 (2)
C1A1—C6A1—O9A	123.5 (3)	C1B—C6B—O9B	125.0 (2)
C6A1—O9A—C10A	116.7 (2)	C6B—O9B—C10B	119.2 (2)
C2A2—C1A2—C6A2	119.7 (8)		
C1A2—C2A2—F8A2	121.4 (8)		
C1A2—C2A2—C3A2	121.8 (8)		
C3A2—C2A2—F8A2	116.7 (8)		
C2A2—C3A2—F7A2	121.9 (8)		
C2A2—C3A2—C4A2	119.4 (8)		
C4A2—C3A2—F7A2	118.6 (8)		
C3A2—C4A2—C5A2	120.2 (8)		
C4A2—C5A2—C6A2	118.5 (8)		
C1A2—C6A2—C5A2	120.2 (8)		
C5A2—C6A2—O9A	113.7 (7)		
C1A2—C6A2—O9A	126.0 (8)		
C6A2—O9A—C10A	115.3 (4)		
O9A—C10A—C11A	110.4 (2)	O9B—C10B—C11B	105.6 (2)
C10A—C11A—C13A	115.1 (2)	C10B—C11B—C13B	112.8 (2)
C10A—C11A—O12A	109.9 (2)	C10B—C11B—O12B	108.4 (2)
O12A—C11A—C13A	110.1 (2)	O12B—C11B—C13B	108.8 (2)
C11A—C13A—N14A	109.1 (2)	C11B—C13B—N14B	109.7 (2)
C13A—N14A—C19A	112.4 (2)	C13B—N14B—C19B	112.7 (2)
C13A—N14A—C15A	113.6 (2)	C13B—N14B—C15B	112.5 (2)

C15A—N14A—C19A	109.1 (2)	C15B—N14B—C19B	108.9 (2)
N14A—C15A—C16A	111.1 (2)	N14B—C15B—C16B	111.2 (2)
C15A—C16A—C17A	111.9 (2)	C15B—C16B—C17B	112.2 (2)
C16A—C17A—N20A	112.4 (2)	C16B—C17B—N20B	112.2 (2)
C16A—C17A—C18A	110.5 (2)	C16B—C17B—C18B	110.3 (2)
C18A—C17A—N20A	112.9 (2)	C18B—C17B—N20B	113.2 (2)
C17A—C18A—C19A	110.7 (2)	C17B—C18B—C19B	110.6 (2)
N14A—C19A—C18A	109.3 (2)	N14B—C19B—C18B	110.1 (2)
C17A—N20A—C22A	119.9 (2)	C17B—N20B—C22B	118.7 (2)
C17A—N20A—C21A	119.0 (2)	C17B—N20B—C21B	120.8 (2)
C21A—N20A—C22A	119.9 (2)	C21B—N20B—C22B	118.8 (2)
N20A—C22A—S26A	118.9 (2)	N20B—C22B—S26B	118.8 (2)
N20A—C22A—N23A	125.0 (2)	N20B—C22B—N23B	124.5 (2)
N23A—C22A—S26A	116.1 (2)	N23B—C22B—S26B	116.7 (2)
C22A—N23A—C24A	110.2 (2)	C22B—N23B—C24B	109.4 (2)
N23A—C24A—C27A	125.3 (2)	N23B—C24B—C27B	124.6 (2)
N23A—C24A—C25A	115.5 (2)	N23B—C24B—C25B	115.4 (2)
C25A—C24A—C27A	119.2 (2)	C25B—C24B—C27B	119.9 (2)
C24A—C25A—C30A	121.0 (2)	C24B—C25B—C30B	120.6 (2)
C24A—C25A—S26A	110.1 (2)	C24B—C25B—S26B	110.1 (2)
S26A—C25A—C30A	128.9 (2)	S26B—C25B—C30B	129.3 (2)
C22A—S26A—C25A	88.0 (1)	C22B—S26B—C25B	88.4 (1)
C24A—C27A—C28A	119.7 (2)	C24B—C27B—C28B	119.2 (2)
C27A—C28A—C29A	121.2 (2)	C27B—C28B—C29B	121.0 (2)
C28A—C29A—C30A	121.2 (3)	C28B—C29B—C30B	121.6 (3)
C25A—C30A—C29A	117.7 (2)	C25B—C30B—C29B	117.7 (2)

C6A1—O9A—C10A—C11A	167.8 (2)
C6A2—O9A—C10A—C11A	168.1 (4)
O9A—C10A—C11A—O12A	-63.7 (2)
O9A—C10A—C11A—C13A	61.3 (3)
C10A—C11A—C13A—N14A	-172.1 (2)
O12A—C11A—C13A—N14A	-47.3 (2)
C6B—O9B—C10B—C11B	-169.0 (2)
O9B—C10B—C11B—O12B	77.3 (2)
O9B—C10B—C11B—C13B	-162.1 (2)
C10B—C11B—C13B—N14B	-168.5 (2)
O12B—C11B—C13B—N14B	-48.1 (2)

Molecule A shows rotational disorder of the difluorophenyl moiety. The atoms were split and refined using the *SAME*, *DELU* and *SIMU* restraint facilities of *SHELXL93* (Sheldrick, 1993). The sum of the occupancy factors was constrained to 1. The occupancy factor for atoms C1A1–F8A1 refined to 0.732 (2). H atoms were calculated in geometrical positions and allowed to ride on their parent atom.

Data collection: *XSCANS* (Siemens, 1993). Cell refinement: *XSCANS*. Data reduction: *XSCANS*. Program(s) used to solve structure: *DIRDIF* (Beurskens *et al.*, 1992). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *ORTEX2.1* (McArdle, 1994). Software used to prepare material for publication: *PARST* (Nardelli, 1983).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: NA1175). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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1-[(4-Fluorophenyl)methyl]-N-[1-[2-(4-methoxyphenyl)ethyl]-4-piperidyl]-1H-benzimidazol-2-amine (Astemizole)†

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Abstract

Astemizole, C₂₈H₃₁FN₄O, is a non-sedating H₁ antihistamine. The crystal structure contains two molecules in the asymmetric unit related by a pseudo centre of symmetry. The conformations of the methoxyphenylethyl side chains are different. N—H···N intermolecular hydrogen bonds link the molecules into infinite chains in the *c* direction of the *Cc* space group.

Comment

Astemizole, (I), was developed from a series of structurally novel antihistamines. The oral antiallergic activity of astemizole in laboratory animals was found to be expressed at low doses of the order of 0.1 mg kg⁻¹ and to be of long duration. Tight binding of astemizole (and a major metabolite, desmethylastemizole) to H₁ receptors and little penetration into the brain sus-

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