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Crystalline form B of risperidone

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Key indicators

Single-crystal X-ray study
T = 298 K
Mean σ(C–C) = 0.004 Å
R factor = 0.064
wR factor = 0.151
Data-to-parameter ratio = 15.9

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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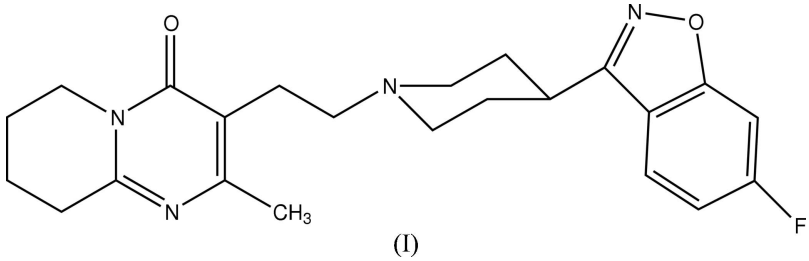
The asymmetric unit of the title compound {systematic name: 4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-hydroxy-1-[2-(2-methyl-4-oxo-3,4,6,7,8,9-hexahydro-2*H*-pyrido[1,2-*a*]pyrimidin-3-yl)-ethyl]piperidine}, $C_{23}H_{27}FN_4O_2$, contains two independent risperidone molecules. The piperidine and the tetrahydropyridine rings adopt chair and sofa conformations, respectively.

Comment

Risperidone is a relative new antipsychotic agent, belonging to a new chemical class of the benzisoxazole derivatives, available worldwide since the early 1990s (Callaghan *et al.*, 1999; Kennedy *et al.*, 2001; Tandon, 2002). It has useful central nervous system activity and shows a wide range of therapeutic effects. Up to now, six crystalline forms of risperidone have been reported (Krochmal *et al.*, 2004; Reddy *et al.*, 2004; Strelice & Nijmegen, 2004) and characterized by X-ray powder diffraction patterns, but only two of their crystal structures (Form A and risperidone hydrochloride hemipentahydrate) have been determined (Peeters *et al.*, 1993; Wang & Pan, 2006). We report here the crystal structure of form B.



(I)

In the molecule of the title compound, (I) (Fig. 1), the bond lengths and angles are within normal ranges (Allen *et al.*, 1987). The asymmetric unit contains two independent risperidone molecules. The molecule contains a piperdine ring, with one end connected to a pyridopyrimidine group *via* an ethylene bridge, while the other end is connected to an almost planar fluorobenzisoxazole ring system. The molecular conformation of (I) is in agreement with that of the previously reported risperidones (Peeters *et al.*, 1993; Wang & Pan, 2006; Ravikumar *et al.*, 2005).

The rings *C* (N12/C8–C12), *C*′ (N22/C31—C35), *E* (N13/C17–C21) and *E*′ (N23/C40–C44) are not planar, having total puckering amplitudes Q_T of 1.068 (2), 1.034 (3), 0.275 (2) and 0.382 (2) Å, respectively, and chair and sofa conformations [φ = 27.11 (5)°, θ = 57.00 (3)°; φ = 29.24 (9)°, θ = 56.72 (4)°; φ =

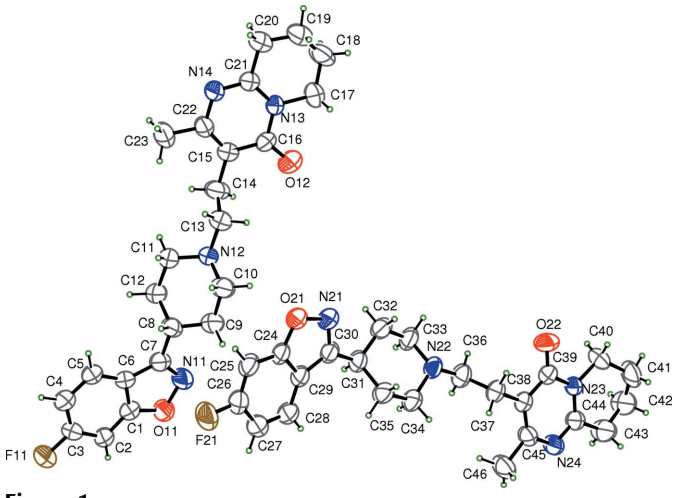


Figure 1
The asymmetric unit of (I), with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

158.9 (3)°, θ = 47.7 (2)°; and φ = 142.0 (2)°, θ = 50.4 (2)°; Cremer & Pople, 1975]. Rings *A* (C1–C6), *B* (N11/O11/C1/C6/C7), *D* (N13/N14/C15/C16/C21/C22), *A*′ (C24–C29), *B*′ (N21/O21/C24/C29/C30) and *D*′ (N23/N24/C38/C39/C44/C45) are, of course, planar and the dihedral angles between them are *A*/*B* = 3.07 (2)° and *A*′/*B*′ = 0.50 (3)°. The ethylene bridges between rings *C* and *D*, and between *C*′ and *D*′, adopt antiperiplanar conformations with the torsion angles N12—C13—C14—C15 = 178.1 (2)° and N22—C36—C37—C38 = 176.1 (2)°.

Experimental

The crude risperidone product was supplied by Zhejiang Huahai Pharmaceutical Co. Ltd. It was recrystallized from a mixed solvent of ethanol and water (2:5), with the pH adjusted to 7, giving colorless crystals of (I) suitable for X-ray diffraction.

Crystal data

$C_{23}H_{27}FN_4O_2$
M_r = 410.49
Triclinic, $P\overline{1}$
a = 9.938 (4) Å
b = 11.016 (6) Å
c = 20.274 (9) Å
α = 75.240 (17)°
β = 79.514 (13)°
γ = 81.397 (17)°
V = 2097.8 (17) Å^3
Z = 4
D_x = 1.300 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 298 (1) K
Needle, colorless
0.29 × 0.16 × 0.12 mm

Data collection

Rigaku R-AXIS RAPID diffractometer
ω scans
Absorption correction: none
20587 measured reflections
9462 independent reflections
3536 reflections with $F^2 > 2\sigma(F^2)$
R_{int} = 0.051
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.064
$wR(F^2)$ = 0.151
S = 1.05
9462 reflections
596 parameters
All H-atom parameters refined
$w = 1/[0.0003F_o^2 + 1\sigma(F_o^2)]/(4F_o^2)$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.60 e Å^{-3}
$\Delta\rho_{min}$ = −0.68 e Å^{-3}
Extinction correction: Larson (1970)
Extinction coefficient: 1.6 (2) × 10^2

Table 1
Selected torsion angles (°).

C5—C6—C7—C8	0.6 (6)	N21—C30—C31—C32	−3.2 (4)
N11—C7—C8—C9	−20.7 (4)	C29—C30—C31—C32	174.4 (2)
C6—C7—C8—C12	−78.7 (4)	C29—C30—C31—C35	−62.3 (3)

H atoms were positioned geometrically, with C—H = 0.93, 0.98, 0.97 and 0.96 Å for aromatic, methine, methylene and methyl H atoms, respectively, and constrained to ride on their parent atoms, with U_{iso}(H) = 1.2U_{eq}(C).

Data collection: *PROCESS-AUTO* (Rigaku, 1998); cell refinement: *PROCESS-AUTO*; data reduction: *CrystalStructure* (Rigaku/MSC, 2004); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *CrystalStructure*.

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