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

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

	x	y	z	U_{eq}
O14	0.5472 (2)	0.3763 (1)	−0.0494 (2)	0.0538
O23	0.9604 (2)	0.2414 (1)	0.5088 (3)	0.0641
O32	0.4332 (2)	0.1238 (1)	0.5279 (3)	0.0610
C1	0.4883 (2)	0.2469 (2)	0.2384 (3)	0.0384
C2	0.5495 (2)	0.3166 (2)	0.2174 (3)	0.0382
C3	0.6685 (2)	0.3317 (2)	0.3205 (3)	0.0399
C4	0.7292 (2)	0.2741 (2)	0.4408 (3)	0.0390
C5	0.6698 (2)	0.2042 (2)	0.4636 (3)	0.0386
C6	0.5491 (2)	0.1918 (2)	0.3625 (3)	0.0375
C7	0.3608 (2)	0.2295 (1)	0.1289 (3)	0.0376
C8	0.3516 (3)	0.2097 (2)	−0.0617 (3)	0.0460
C9	0.2343 (3)	0.1900 (2)	−0.1608 (4)	0.0564
C10	0.1279 (3)	0.1890 (2)	−0.0721 (4)	0.0578
C11	0.1348 (3)	0.2088 (2)	0.1157 (4)	0.0543
C12	0.2513 (3)	0.2291 (2)	0.2167 (4)	0.0461
C13	0.4881 (2)	0.3757 (2)	0.0790 (3)	0.0410
C15	0.3582 (3)	0.4334 (2)	0.1113 (5)	0.0592
C16	0.7280 (2)	0.4112 (2)	0.3133 (3)	0.0416
C17	0.8535 (3)	0.4033 (2)	0.2621 (4)	0.0578
C18	0.9087 (3)	0.4787 (3)	0.2698 (5)	0.0736
C19	0.8391 (4)	0.5618 (3)	0.3277 (5)	0.0724
C20	0.7147 (4)	0.5706 (2)	0.3733 (4)	0.0617
C21	0.6584 (3)	0.4957 (2)	0.3655 (3)	0.0498
C22	0.8589 (3)	0.2873 (2)	0.5547 (3)	0.0434
C24	0.8527 (3)	0.3564 (2)	0.7238 (4)	0.0598
C25	0.7336 (2)	0.1439 (2)	0.5959 (3)	0.0409
C26	0.7225 (3)	0.1713 (2)	0.7814 (4)	0.0519
C27	0.7799 (3)	0.1152 (3)	0.9038 (5)	0.0675
C28	0.8457 (3)	0.0331 (3)	0.8424 (6)	0.0752
C29	0.8578 (3)	0.0046 (2)	0.6587 (6)	0.0745
C30	0.8012 (3)	0.0606 (2)	0.5348 (5)	0.0602
C31	0.4845 (2)	0.1168 (2)	0.3896 (3)	0.0420
C33	0.4893 (4)	0.0370 (2)	0.2421 (5)	0.0628

Table 2. *Geometric parameters* (Å, °)

C1—C2	1.402 (3)	C3—C16	1.501 (3)
C1—C6	1.397 (3)	C4—C5	1.398 (3)
C1—C7	1.498 (3)	C4—C22	1.517 (3)
C2—C3	1.398 (3)	C5—C6	1.398 (3)
C2—C13	1.519 (3)	C5—C25	1.504 (3)
C3—C4	1.403 (3)	C6—C31	1.514 (3)
C2—C1—C6	118.9 (2)	C3—C4—C5	120.9 (2)
C1—C2—C3	120.8 (2)	C4—C5—C6	118.9 (2)
C2—C3—C4	119.1 (2)	C1—C6—C5	121.3 (2)

Sample preparation involved refluxing a hexane solution (25 cm^{-3}) of 4-phenylbut-3-yn-2-one (0.13 mol) and a catalytic amount of (η^5-indenyl)bis(ethylene)rhodium (0.58 mmol) for 6 h under an atmosphere of argon. The product, which was a mixture containing 1,2,4-triacetyltriphenylbenzene and 1,3,5-triacetyltriphenylbenzene (3:1 ratio), precipitated from solution as a yellow solid in 76% yield. Repeated washing with diethyl ether removed the 1,2,4 isomer, and repeated recrystallization of the residual 1,3,5 isomer from dry acetone, followed by dry flash chromatography (silica GF_{254} Fluka, eluents hexane/ethyl acetate) gave crystals of the pure 1,3,5 isomer.

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 71209 (37 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: AL1046]

References

Bart, J. C. J. (1968). *Acta Cryst.* B**24**, 1277–1287.
CSSR (1984). *Crystal Structure Search and Retrieval Instruction Manual.* SERC Daresbury Laboratory, Warrington, England.
Gilmore, C. J. (1984). *J. Appl. Cryst.* **17**, 42–46.
Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Lin, Y. C. & Williams, D. E. (1975). *Acta Cryst.* B**31**, 318–320.
Molecular Structure Corporation (1985). *TEXSAN. TEXRAY Structure Analysis Package.* MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
Molecular Structure Corporation (1988). *MSC/AFC Diffractometer Control Software.* MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
O'Connor, B. H. (1973). *Acta Cryst.* B**29**, 1893–1903.
O'Connor, B. H. & Moore, F. H. (1973). *Acta Cryst.* B**29**, 1903–1909.
Romero, A., Vegas, A., Santos, A. & Lopez de Lerma, J. (1987). *Acta Cryst.* C**43**, 2186–2189.

Acta Cryst. (1993). C**49**, 1698–1700

Structure of 3-{2-[4-(6-Fluoro-1,2-benzisoxazol-3-yl)piperidino]ethyl}-6,7,8,9-tetrahydro-2-methyl-4*H*-pyrido-[1,2-*a*]pyrimidin-4-one (Risperidone)

O. M. Peeters, N. M. Blaton and C. J. De Ranter*

Laboratorium voor Analytische Chemie en Medicinale Fysicochemie, Instituut voor Farmaceutische Wetenschappen, Katholieke Universiteit Leuven, Van Evenstraat 4, B-3000 Leuven, Belgium

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Abstract

The benzisoxazole and pyrimidine moieties are essentially planar and the dihedral angle between these planes is 5.6 (1)°. The piperidine ring is in a slightly distorted chair conformation, while the tetrahydropyridine moiety shows a half-chair conformation. The crystal stucture is stabilized by a hydrogen bond between the H atom on position 4 of the benzisoxazole and the O atom of the pyrimidinone of a translated (x, $y-1$, z) molecule [C···O = 3.372 (7), H···O = 2.327 Å, C—H···O = 161.6°].

Comment

Risperidone is an antipsychotic drug with serotonin-S_2 and dopamine-D_2 antagonistic properties (Janssen *et al.*, 1988). The determination was undertaken to compare the structural features with other known serotonin and dopamine antagonists in the hope of obtaining a better in-

sight into its mechanism. Bond distances and angles agree with those of Lisgarten & Palmer (1988) for the benzisoxazole moiety and with those of Sasvari & Simon (1973) for the pyridopyrimidinone moiety. The tetrahydropyridine ring is in a half-chair conformation with a twofold axis intersecting N21—C22.

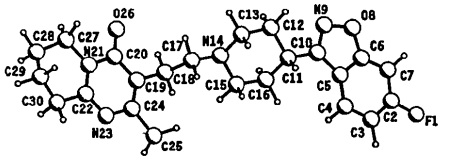

Fig. 1. Perspective view (Motherwell & Clegg, 1978) of the molecule with atomic numbering scheme.

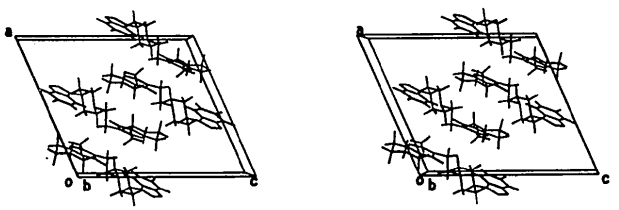

Fig. 2. Stereoscopic packing diagram (Motherwell & Clegg, 1978) of the molecules in the unit cell.

Experimental

Crystal data

$C_{23}H_{27}FN_4O_2$
M_r = 410.49
Monoclinic
$P2_1/n$
a = 14.24 (1) Å
b = 9.767 (7) Å
c = 16.59 (1) Å
β = 113.74 (6)°
V = 2112 (3) Å^3
Z = 4
D_x = 1.2912 Mg m^{-3}
Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 24 reflections
θ = 19.00–22.00°
μ = 0.0846 mm^{-1}
T = 293 K
Dipyramid
0.40 × 0.40 × 0.40 mm
Colourless

Data collection

Stoe Stadi-4 four-circle diffractometer
ω scans
Absorption correction: empirical (North, Phillips & Mathews, 1968)
T_{min} = 0.624, T_{max} = 0.660
7773 measured reflections
3402 independent reflections
1710 observed reflections [$I > 2.0\sigma(I)$]
R_{int} = 0.0232
θ_{max} = 24.95°
$h = 0 \rightarrow 17$
$k = -12 \rightarrow 12$
$l = -20 \rightarrow 20$
4 standard reflections
frequency: 60 min
intensity variation: 8.5%

Refinement

Refinement on F
Final R = 0.0475
wR = 0.0635
S = 1.53
1710 reflections
271 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F) + 0.00120F^2]$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, Tables 2.2B and 2.3.1)

Data collection: *DIF4* (Stoe & Cie, 1988). Cell refinement: *DIF4*. Data reduction: locally adapted *REDU4* (Stoe & Cie, 1988). Program(s) used to solve structure: *NRCVAX* (Gabe, Le Page, Charland, Lee & White, 1989). Program(s) used to refine structure: *NRCVAX*. Molecular graphics: *PLUTO* (Motherwell & Clegg, 1978). Software used to prepare material for publication: *PARST* (Nardelli, 1983).

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

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

	x	y	z	U_{eq}
F1	0.9592 (3)	0.1274 (3)	0.4481 (2)	0.099 (2)
C2	0.9463 (4)	0.2562 (5)	0.4153 (3)	0.068 (2)
C3	0.9836 (4)	0.2843 (4)	0.3516 (3)	0.070 (2)
C4	0.9732 (3)	0.4148 (4)	0.3169 (3)	0.062 (2)
C5	0.9237 (3)	0.5134 (4)	0.3468 (3)	0.051 (2)
C6	0.8872 (3)	0.4773 (4)	0.4093 (3)	0.054 (2)
C7	0.8960 (3)	0.3480 (5)	0.4462 (3)	0.061 (2)
O8	0.8421 (2)	0.5863 (3)	0.4297 (2)	0.067 (2)
N9	0.8485 (3)	0.6994 (4)	0.3765 (3)	0.065 (2)
C10	0.8959 (3)	0.6553 (4)	0.3292 (3)	0.053 (2)
C11	0.9168 (3)	0.7505 (4)	0.2671 (3)	0.055 (2)
C12	0.8698 (3)	0.8915 (5)	0.2620 (3)	0.067 (2)
C13	0.8942 (3)	0.9834 (5)	0.1990 (3)	0.070 (2)
N14	1.0054 (3)	0.9980 (3)	0.2264 (2)	0.057 (2)
C15	1.0515 (3)	0.8639 (4)	0.2288 (3)	0.068 (2)
C16	1.0312 (3)	0.7666 (4)	0.2914 (3)	0.068 (2)
C17	1.0279 (3)	1.0927 (4)	0.1688 (3)	0.061 (2)
C18	1.1374 (3)	1.1491 (4)	0.2094 (3)	0.062 (2)
C19	1.1627 (3)	1.2349 (4)	0.1449 (3)	0.052 (2)
C20	1.1386 (3)	1.3781 (4)	0.1391 (3)	0.054 (2)
N21	1.1633 (3)	1.4527 (3)	0.0786 (2)	0.051 (1)
C22	1.2063 (3)	1.3916 (4)	0.0282 (3)	0.058 (2)
N23	1.2268 (3)	1.2604 (3)	0.0326 (2)	0.064 (2)
C24	1.2035 (3)	1.1817 (4)	0.0906 (3)	0.056 (2)
C25	1.2300 (4)	1.0328 (5)	0.0894 (3)	0.078 (3)
O26	1.0983 (3)	1.4372 (3)	0.1827 (2)	0.079 (2)
C27	1.1353 (4)	1.6004 (4)	0.0700 (3)	0.069 (2)
C28	1.1827 (5)	1.6787 (5)	0.0177 (4)	0.106 (4)
C29	1.1815 (5)	1.6073 (6)	−0.0600 (4)	0.108 (4)
C30	1.2359 (4)	1.4764 (5)	−0.0340 (4)	0.081 (3)

Table 2. *Geometric parameters* (Å, °)

F1—C2	1.353 (5)	N14—C17	1.457 (6)
C2—C3	1.388 (8)	C15—C16	1.519 (7)
C2—C7	1.369 (7)	C17—C18	1.530 (6)
C3—C4	1.381 (6)	C18—C19	1.512 (6)
C4—C5	1.397 (6)	C19—C20	1.435 (5)
C5—C6	1.380 (7)	C19—C24	1.357 (7)
C5—C10	1.438 (5)	C20—N21	1.395 (6)
C6—C7	1.387 (6)	C20—O26	1.234 (6)
C6—O8	1.354 (5)	N21—C22	1.358 (6)
O8—N9	1.440 (5)	N21—C27	1.488 (5)
N9—C10	1.297 (6)	C22—N23	1.309 (5)
C10—C11	1.505 (6)	C22—C30	1.509 (8)
C11—C12	1.519 (6)	N23—C24	1.372 (6)
C11—C16	1.520 (6)	C24—C25	1.504 (6)
C12—C13	1.520 (7)	C27—C28	1.505 (9)
C13—N14	1.467 (5)	C28—C29	1.460 (9)
N14—C15	1.459 (5)	C29—C30	1.468 (7)

F1—C2—C7	117.8 (5)	N14—C15—C16	111.8 (4)
F1—C2—C3	117.3 (5)	C11—C16—C15	111.2 (4)
C3—C2—C7	124.9 (5)	N14—C17—C18	113.2 (4)
C2—C3—C4	119.3 (5)	C17—C18—C19	112.2 (4)
C3—C4—C5	118.3 (5)	C18—C19—C24	123.1 (4)
C4—C5—C10	136.8 (4)	C18—C19—C20	118.0 (4)
C4—C5—C6	119.1 (4)	C20—C19—C24	118.9 (4)
C6—C5—C10	104.1 (4)	C19—C20—O26	124.9 (4)
C5—C6—O8	110.2 (4)	C19—C20—N21	115.8 (4)
C5—C6—C7	124.7 (5)	N21—C20—O26	119.3 (4)
C7—C6—O8	125.0 (4)	C20—N21—C27	116.1 (4)
C2—C7—C6	113.6 (5)	C20—N21—C22	121.3 (4)
C6—O8—N9	107.3 (4)	C22—N21—C27	122.5 (4)
O8—N9—C10	107.0 (4)	N21—C22—C30	119.9 (4)
C5—C10—N9	111.4 (4)	N21—C22—N23	122.7 (4)
N9—C10—C11	120.2 (4)	N23—C22—C30	117.3 (5)
C5—C10—C11	128.4 (4)	C22—N23—C24	118.5 (4)
C10—C11—C16	111.6 (4)	C19—C24—N23	122.7 (4)
C10—C11—C12	113.2 (4)	N23—C24—C25	113.6 (4)
C12—C11—C16	108.8 (4)	C19—C24—C25	123.7 (4)
C11—C12—C13	110.8 (4)	N21—C27—C28	112.5 (4)
C12—C13—N14	111.2 (4)	C27—C28—C29	114.7 (5)
C13—N14—C17	110.7 (4)	C28—C29—C30	109.8 (5)
C13—N14—C15	109.8 (4)	C22—C30—C29	114.8 (6)
C15—N14—C17	111.8 (4)		

N9—C10—C11—C12	−4.8 (6)	C17—C18—C19—C24	−89.7 (6)
C5—C10—C11—C12	176.4 (5)	C20—N21—C27—C28	168.7 (4)
N9—C10—C11—C16	118.4 (5)	C22—N21—C27—C28	−14.2 (7)
C5—C10—C11—C16	−60.3 (6)	C27—N21—C22—C30	5.3 (7)
C13—N14—C17—C18	161.0 (4)	N21—C22—C30—C29	−22.4 (8)
C15—N14—C17—C18	−76.2 (5)	N23—C22—C30—C29	159.6 (5)
C17—N14—C15—C16	178.0 (4)	N21—C27—C28—C29	41.3 (7)
N14—C17—C18—C19	173.8 (4)	C27—C28—C29—C30	−58.4 (7)
C17—C18—C19—C20	87.8 (5)	C28—C29—C30—C22	47.5 (7)

Intensity data were collected using an ω scan with variable scan speed 0.6–2.4°min^{-1}. The scan width was (60 + N) steps of 0.02° with N the number of extra steps to take the $\alpha_1 - \alpha_2$ splitting into account. The number of steps for background counts was 10 on each side of the scan.

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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 71224 (26 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: NA1034]

References

Gabe, E. J., Le Page, Y., Charland, J.-P., Lee, F. L. & White, P. S. (1989). *J. Appl. Cryst.* **22**, 384–387.

Janssen, P. A. J., Niemegeers, C. J. E., Awouters, F., Schellekens, K. H. L., Meegens, A. A. H. P. & Meert, T. F. (1988). *J. Pharmacol. Exp. Ther.* **244**, 685–693.

Lisgarten, J. N. & Palmer, R. A. (1988). *Acta Cryst.* C**44**, 2013–2016.

Motherwell, W. D. S. & Clegg, W. (1978). *PLUTO. Program for Plotting Molecular and Crystal Structures.* Univ. of Cambridge, England.

Nardelli, M. (1983). *Comput. Chem.* **7**, 95–98.

North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* A**24**, 351–359.

Sasvari, K. & Simon, K. (1973). *Acta Cryst.* B**29**, 1245–1250.

Stoe & Cie (1988). *DIF4. Diffractometer Control Program.* Version 6.2. Stoe & Cie, Darmstadt, Germany.

Stoe & Cie (1988). *REDU4. Data Reduction Program.* Version 6.2. Stoe & Cie, Darmstadt, Germany.

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Structure of a 4-Phenyl-1,4-dihydropyridine Derivative Containing a Nitrooxyalkyl Ester at the 3-Position

T. Ogawa, K. Matsumoto,* K. Hatayama and K. Kitamura

Research Center, Taisho Pharmaceutical Co. Ltd, 1-403 Yoshino-cho, Ohmiya 330, Japan

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Abstract

In the title compound, (*R*)-(+)-3-nitrooxypropyl 2-methoxyethyl 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylate, $[\alpha]_D^{20°C} = +21.4°$ (*c.* 0.5, MeOH), the phenyl ring linked to C4 is perpendicular to the dihydropyridine ring. The orientations of the carbonyl groups at C3 and C5 are antiperiplanar to the C2=C3 double bond and synperiplanar to the C5=C6 double bond.

Comment

In the last decade, synthetic studies on Hantzsch-type 1,4-dihydropyridines (Bossert, Meyer & Wehinger, 1981; Jolly, Hardman & Gross, 1981; Meyer, Bossert, Wehinger, Stoepel & Vater, 1981) have been carried out in many research institutes all over the world because of their vasodilator properties as calcium antagonists. When this work was initiated, nifedipine was the only known compound used clinically for the treatment of *angina pectoris* (Ellrodt, Chew & Singh, 1980; Leonard & Talbert, 1982; Spivack, Ocken & Frishman, 1983; Theroux, Taeymans & Waters, 1983; Vater *et al.*, 1972), and it was also known that nicardipine had been developed in preclinical studies for the treatment of hypertension (Iwanami *et al.*, 1979; Seki & Takenaka, 1977; Takenaka, Miyazaki, Asano, Higuchi & Maeno, 1982; Takenaka, Usuda, Nomura, Maeno & Sado, 1976). The aim of our work was to produce a drug with improved duration of activity. We were interested in the phenomenon that some organic nitro compounds, including nitroglycerine and nicorandil, increase the level of cyclic guanosine 5′-monophosphate (cyclic GMP) produced in various vascular smooth muscle tissues and promote relaxation (Holzmann, 1983; Waldman & Murad, 1988). So the combination of nitro-like and calcium-blocking active sites in a single molecule was expected to realize a vasodilating activity. Therefore, we synthesized novel dihydropyridine derivatives having a nitrate moiety in one of the ester chains.