

1-[1-[4-(4-Fluorophenyl)-4-oxobutyl]-1,2,3,6-tetrahydro-4-pyridyl]-1,3-dihydro-2H-benzimidazol-2-one Dihydrate (Dehydrobenzperidol®)

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Abstract. $C_{22}H_{22}FN_3O_2 \cdot 2H_2O$, $M_r = 415.45$, monoclinic, $P2_1/n$, $a = 9.693(2)$, $b = 10.811(3)$, $c = 20.442(5)$ Å, $\beta = 79.16(2)^\circ$, $V = 2104(1)$ Å³, $D_m = 1.32$, $D_c = 1.31$ Mg m⁻³, $Z = 4$, $\lambda(\text{Cu } K\alpha) = 1.5418$ Å, $\mu(\text{Cu } K\alpha) = 0.82$ mm⁻¹; $F(000) = 880$, final conventional $R = 6.2\%$ for 1421 reflections with $(\sin \theta/\lambda)_{\max} = 0.459$ Å⁻¹. Owing to the presence of two water molecules an extensive network of hydrogen bonds is formed.

Introduction. The title compound, also called droperidol, is a potent neuroleptic. Crystals were grown at room temperature by slow evaporation from a water-methanol solution.

The cell dimensions were obtained from a least-squares fit to the setting angles of 23 reflections. Intensity measurements were made on a Syntex $P2_1$ diffractometer with graphite-monochromated $\text{Cu } K\alpha$ radiation. During the collection of data, three reference reflections (measured every 50 reflections) showed a nearly linear intensity decrease of approximately 30% with time (θ - 2θ scan technique). Intensities were measured for all independent reflections (1912) with $2\theta < 90^\circ$. Of these, 1421 were considered as observed [$I_{\text{rel}} > 3.0\sigma(I_{\text{rel}})$] and used in the refinement. The data were corrected for Lorentz-polarization effects, but not for absorption.

The structure was solved by direct methods using *MULTAN* (Main, Woolfson, Lessinger, Germain & Declercq, 1974). All non-hydrogen atoms were located in the resultant E map. Refinement of the positional and anisotropic thermal parameters of the 17 non-hydrogen atoms by block-diagonal least-squares methods (*CRYLSQ* link of the *XRAY* system; Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976) resulted in $R = 9.7\%$. The H atoms were then located from a difference synthesis and were included as a fixed-atom contribution with the overall temperature factor. Further refinement converged at $R =$

6.2%.† The weighting scheme employed was $w = (3.0 + |F_o| + 0.1|F_o|^2)^{-1}$. The overall parameter shift during the final cycle was 0.5σ . The scattering factors of Cromer & Mann (1968) were used for the non-hydrogen atoms, those of Stewart, Davidson & Simpson (1965) for H.

The final positional parameters and their e.s.d.'s are given in Table 1. A view of the molecule with the atom-numbering system is shown in Fig. 1.

† Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35459 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

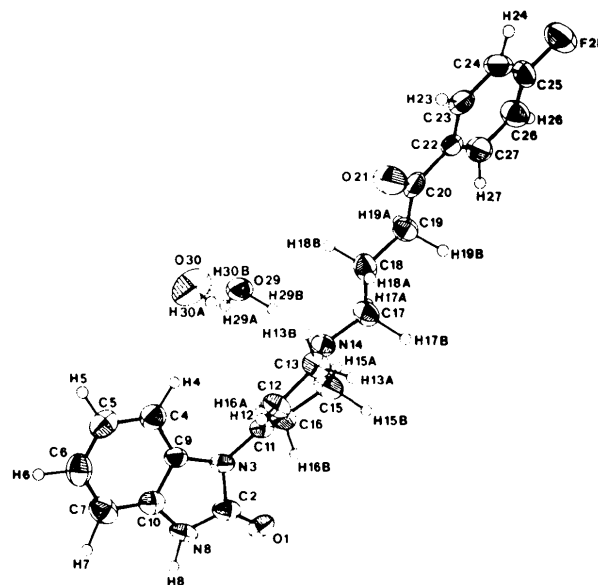


Fig. 1. General view of the molecule.

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Table 1. Atomic coordinates ($\times 10^4$) and equivalent isotropic thermal parameters with *e.s.d.*'s of the refined parameters in parentheses

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> (Å ²)
O(1)	220 (3)	6323 (3)	2813 (1)	4.07 (9)
C(2)	683 (4)	6913 (4)	2310 (2)	3.77 (3)
N(3)	2023 (3)	7436 (3)	2135 (1)	3.10 (10)
C(4)	3242 (5)	8690 (4)	1140 (2)	3.89 (14)
C(5)	2999 (5)	9200 (4)	550 (2)	4.45 (15)
C(6)	1723 (5)	9090 (4)	343 (2)	4.68 (16)
C(7)	612 (5)	8429 (4)	730 (2)	4.54 (15)
N(8)	9 (3)	7212 (3)	1796 (1)	3.83 (11)
C(9)	2146 (4)	8058 (4)	1524 (1)	3.00 (13)
C(10)	854 (4)	7918 (3)	1320 (2)	3.37 (13)
C(11)	3036 (4)	7459 (4)	2562 (2)	3.00 (12)
C(12)	3602 (4)	8518 (4)	2707 (2)	3.69 (14)
C(13)	4738 (4)	8578 (4)	3117 (2)	3.81 (13)
N(14)	5416 (3)	7377 (3)	3161 (1)	3.14 (10)
C(15)	4332 (5)	6422 (4)	3350 (2)	4.73 (15)
C(16)	3441 (5)	6244 (4)	2813 (2)	3.97 (14)
C(17)	6334 (5)	7400 (4)	3650 (2)	3.83 (14)
C(18)	7498 (4)	8350 (4)	3503 (2)	3.88 (14)
C(19)	8592 (4)	8124 (4)	3940 (2)	3.51 (13)
C(20)	9642 (5)	9153 (4)	3917 (2)	3.56 (13)
O(21)	9575 (3)	10082 (3)	3578 (1)	5.73 (11)
C(22)	10799 (4)	9048 (4)	4302 (1)	2.90 (12)
C(23)	11732 (4)	10029 (4)	4287 (2)	3.51 (13)
C(24)	12760 (4)	9995 (4)	4661 (2)	4.10 (14)
C(25)	12815 (5)	8969 (4)	5060 (2)	4.12 (14)
C(26)	11960 (5)	7976 (4)	5085 (2)	4.55 (15)
C(27)	10914 (5)	8030 (4)	4703 (2)	4.00 (14)
F(28)	13845 (3)	8962 (3)	5436 (1)	6.29 (9)
O(29)	7048 (3)	6992 (3)	1903 (1)	4.47 (10)
O(30)	6731 (4)	9495 (3)	1336 (2)	7.10 (13)
H(4)	4193	8769	1335	3.69
H(5)	3813	9761	234	3.69
H(6)	1570	9412	-146	3.69
H(7)	-527	8302	604	3.69
H(8)	-988	7059	1747	3.69
H(12)	3166	9463	2545	3.69
H(13A)	4344	9042	3607	3.69
H(13B)	5519	9262	2890	3.69
H(15A)	4954	5643	3425	3.69
H(15B)	3618	6841	3914	3.69
H(16A)	3872	5591	2406	3.69
H(16B)	2390	5659	3083	3.69
H(17A)	6711	6509	3664	3.69
H(17B)	5595	7562	4229	3.69
H(18A)	7084	9174	3578	3.69
H(18B)	8080	8334	2986	3.69
H(19A)	9005	7120	3847	3.69
H(19B)	8040	7956	4489	3.69
H(23)	11594	10886	4006	3.69
H(24)	13534	10588	4685	3.69
H(26)	12066	7026	5334	3.69
H(27)	10115	7233	4838	3.69
H(29A)	6682	6176	1739	3.69
H(29B)	6468	7059	2397	3.69
H(30A)	6244	10000	1642	3.69
H(30B)	6769	8529	1593	3.69

Discussion. The title compound, which crystallized with two water molecules, shows a normal molecular conformation. Bond lengths and angles are listed in Table 2. The crystal structure is closely related to that

Table 2. Bond lengths (Å) and angles (°)

O(1)—C(2)	1.220 (5)	N(14)—C(15)	1.472 (6)
C(2)—N(3)	1.400 (5)	N(14)—C(17)	1.459 (6)
C(2)—N(8)	1.376 (6)	C(15)—C(16)	1.531 (7)
N(3)—C(9)	1.404 (5)	C(17)—C(18)	1.514 (6)
N(3)—C(11)	1.432 (6)	C(18)—C(19)	1.530 (6)
C(4)—C(5)	1.387 (6)	C(19)—C(20)	1.503 (6)
C(4)—C(9)	1.377 (6)	C(20)—O(21)	1.229 (6)
C(5)—C(6)	1.386 (8)	C(20)—C(22)	1.490 (6)
C(6)—C(7)	1.406 (6)	C(22)—C(23)	1.390 (6)
C(7)—C(10)	1.386 (6)	C(22)—C(27)	1.389 (6)
N(8)—C(10)	1.378 (5)	C(23)—C(24)	1.365 (7)
C(9)—C(10)	1.401 (6)	C(24)—C(25)	1.385 (6)
C(11)—C(12)	1.327 (6)	C(25)—C(26)	1.351 (7)
C(11)—C(16)	1.489 (6)	C(25)—F(28)	1.369 (6)
C(12)—C(13)	1.505 (7)	C(26)—C(27)	1.394 (7)
C(13)—N(14)	1.466 (6)		
O(1)—C(2)—N(3)	127.1 (4)	C(4)—C(9)—C(10)	121.4 (4)
O(1)—C(2)—N(8)	127.8 (4)	C(7)—C(10)—N(8)	131.3 (4)
N(3)—C(2)—N(8)	105.1 (3)	C(7)—C(10)—C(9)	121.5 (3)
C(2)—N(3)—C(9)	109.9 (3)	N(8)—C(10)—C(9)	107.2 (3)
C(2)—N(3)—C(11)	124.1 (3)	N(3)—C(11)—C(12)	120.7 (4)
C(9)—N(3)—C(11)	125.5 (3)	N(3)—C(11)—C(16)	116.7 (3)
C(5)—C(4)—C(9)	117.0 (4)	C(12)—C(11)—C(16)	122.5 (4)
C(4)—C(5)—C(6)	122.6 (4)	C(11)—C(12)—C(13)	122.5 (4)
C(5)—C(6)—C(7)	120.3 (4)	C(12)—C(13)—N(14)	112.3 (3)
C(6)—C(7)—C(10)	117.1 (4)	C(13)—N(14)—C(15)	109.3 (3)
C(2)—N(8)—C(10)	111.4 (3)	C(13)—N(14)—C(17)	111.5 (3)
N(3)—C(9)—C(4)	132.2 (4)	C(15)—N(14)—C(17)	109.3 (3)
N(3)—C(9)—C(10)	106.4 (3)	N(14)—C(15)—C(16)	111.8 (3)
C(11)—C(16)—C(15)	110.9 (4)	C(20)—C(22)—C(27)	121.5 (3)
N(14)—C(17)—C(18)	113.7 (3)	C(23)—C(22)—C(27)	119.6 (3)
C(17)—C(18)—C(19)	110.3 (3)	C(22)—C(23)—C(24)	120.5 (4)
C(18)—C(19)—C(20)	113.7 (3)	C(23)—C(24)—C(25)	117.7 (4)
C(19)—C(20)—O(21)	121.1 (4)	C(24)—C(25)—C(26)	124.6 (4)
C(19)—C(20)—C(22)	120.0 (4)	C(24)—C(25)—F(28)	116.6 (4)
O(21)—C(20)—C(22)	119.0 (4)	C(26)—C(25)—F(28)	118.8 (4)
C(20)—C(22)—C(23)	118.8 (3)	C(25)—C(26)—C(27)	116.9 (4)
		C(22)—C(27)—C(26)	120.7 (4)

Table 3. Torsion angles (°) defining the conformation of the side chain and the tetrahydropyridyl ring

O(21)—C(20)—C(22)—C(23)	2.6 (6)
O(21)—C(20)—C(19)—C(18)	1.0 (6)
C(20)—C(19)—C(18)—C(17)	-169.5 (4)
C(19)—C(18)—C(17)—N(14)	-167.3 (4)
C(18)—C(17)—N(14)—C(13)	-59.3 (4)
C(18)—C(17)—N(14)—C(15)	179.7 (4)
C(16)—C(11)—N(3)—C(2)	56.8 (5)
C(13)—N(14)—C(15)—C(16)	64.6 (5)
C(13)—N(12)—C(11)—C(16)	2.2 (6)
C(12)—C(11)—C(16)—C(15)	11.3 (6)
C(12)—C(11)—N(3)—C(2)	-124.9 (5)
C(11)—C(12)—C(13)—N(14)	17.0 (6)
C(11)—C(16)—C(15)—N(14)	-44.4 (5)

of benperidol, a similar neuroleptic drug (Declercq, Germain & Koch, 1973). The benzimidazole group is planar and makes an angle of 48.1° with the mean plane of the tetrahydropyridyl ring. The conformation of the molecule may be described in terms of the torsion angles listed in Table 3.

The crystal structure is stabilized by an extensive hydrogen-bonding network (Fig. 2). The first water molecule O(29) acts both as a donor in two hydrogen

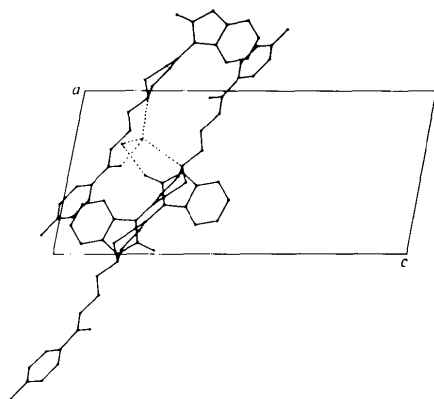


Fig. 2. Unit cell of droperidol viewed along the *b* axis (the hydrogen bonds are shown with broken lines).

bonds with N(14) and a screw-axis-related (*y* direction) O(21) atom, and as an acceptor with the second water molecule O(30) and a translation-equivalent (*x* direction) imidazolic NH group.

The second water molecule O(30) forms, in addition to the hydrogen bond with O(29) mentioned above, a second hydrogen bond with a symmetry-related (screw axis) O(1).

Table 4 gives relevant hydrogen-bond distances and angles.

We thank Janssen Pharmaceutica, Belgium, for supplying the droperidol sample.

Table 4. Hydrogen-bond distances (Å) and angles (°)

<i>A</i> - <i>B</i> ... <i>C</i>	$\angle A$ - <i>B</i> ... <i>C</i>	<i>A</i> - <i>B</i>	<i>B</i> ... <i>C</i>	<i>A</i> ... <i>C</i>
O(29)-H(29 <i>A</i>)...O(21) ⁽ⁱ⁾	158.0	1.03	1.89	2.880 (5)
O(29)-H(29 <i>B</i>)...N(14)	171.0	1.06	1.73	2.785 (4)
O(30)-H(30 <i>A</i>)...O(1) ⁽ⁱⁱⁱ⁾	165.7	0.89	2.17	3.044 (5)
O(30)-H(30 <i>B</i>)...O(29)	171.9	1.17	1.81	2.982 (5)
N(8) ⁽ⁱⁱⁱ⁾ -H(8)...O(29)	162.9	1.00	1.87	2.847 (5)

Symmetry code

(i) $\frac{1}{2} - x, -\frac{1}{2} + y, \frac{1}{2} - z$

(ii) $\frac{1}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z$

(iii) $1 + x, y, z$

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3-[Bis(trimethylsilyl)aminofluoro(methyl)silyl]-2,2,4,4,6,8,8-heptamethyl-5,7-bis(trimethylsilyl)-1,3,5,7-tetraaza-2,4,6,8-tetrasilabicyclo[4.2.0]octane

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(Received 10 June 1980; accepted 1 July 1980)

Abstract. C₂₀H₆₀FN₄Si₅, *M_r* = 642.6, monoclinic, *P*2₁/*c*, *a* = 14.107 (4), *b* = 9.468 (3), *c* = 29.874 (8) Å, β = 102.41 (2)°, *U* = 3896.9 Å³, *Z* = 4, *D_x* = 1.095 Mg m⁻³; final *R* = 0.061 for 4889 reflexions. The molecule contains an almost planar Si₂N₂ ring fused to a Si₃N₃ ring which approximates to a boat conformation.

Introduction. This structure was determined as part of a study of Si-N ring compounds. Air-stable, colour-

less crystals were obtained from a solution in light petrol. The preparation has been described (Skoda, Klingebiel & Meller, 1980).

Intensities were measured with graphite-monochromated Mo *K*α radiation (λ = 0.71069 Å) and a Stoe-Siemens AED diffractometer by a profile-fitting procedure (Clegg, 1981). 4889 reflexions with 7 ≤ 2θ ≤ 60° and *I* ≥ 2σ(*I*) were collected. No corrections were made for absorption (μ = 0.32 mm⁻¹). Cell dimensions were obtained by least squares from the setting angles of 24 reflexions with 20 ≤ 2θ ≤ 25°.

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