Crystal structure of {2-[4-(4-chlorophenyl)-4-hydroxy-1-piperidinyl-methyl]cyclopentyl}-(4-fluorophenyl)-methanone, $C_{24}H_{27}ClFNO_2$

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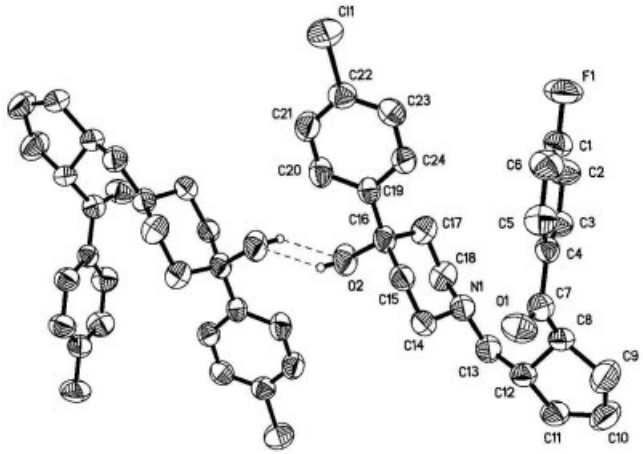

Abstract

$C_{24}H_{27}ClFNO_2$, triclinic, $P\bar{1}$ (No. 2), a = 9.494(2) Å, b = 10.769(2) Å, c = 11.377(3) Å, α = 87.18(3)°, β = 67.27(3)°, γ = 88.01(3)°, V = 1071.4 Å^3, Z = 2, $R_{gt}(F)$ = 0.076, $wR_{obs}(F^2)$ = 0.302, T = 293 K.

Source of material

The title compound was synthetized with a 86% yield by refluxing for 20 h in benzene 4-(4-chlorophenyl)-4-hydroxy-piperidine and [2-(bromomethyl)cyclopentyl]-(4-fluoro-phenyl)-methanone [1] in 2:1 molar ratio and was then recrystallized from methanol (mp 377 K – 379 K).

Experimental details

The H atom of the OH group was easily located on the Fourier electron density map and was included in the refinement, while the other H atoms were introduced in calculated positions. The *hkl* set consists of a great number of reflections with low or very low intensities for which the percentage of estimated errors is high. This is probably due to the poor quality of the crystal studied. All recorded reflections were used in calculating the electron density maps. However, in order to limit the use of data possibly affected by errors, a part of the low intensities was excluded from the refinement through the criterium of choice of the observable reflections, which was $6{\cdot}\sigma(I_{obs})$. The used intensities were in any case more than sufficient (12 data per parameter refined) to ensure the success of the proceeding.

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Discussion

The title compound is an analogue of haloperidol [2], one of the most widely prescribed neuroleptics for treatment of psychotic syndromes, where the α and β carbons of the haloperidol propyl chain were included in a cyclopentane ring, in order to obtain a semi-rigid model of this class of compounds. The six-membered heterocycle has the expected chair conformation while the cyclopentane ring adopts a regular envelope conformation, with C(8) clearly displaced from the plane of the other four carbon atoms. Relevant bond distances (Å) are: C—Cl, 1.736(4); C—F, 1.363(4); C = O (chetonic), 1.212(5); C—OH, 1.440(5); N—C, 1.465 (mean). In general, these and all other structural details agree well with the corresponding values determined for haloperidol. The major structural difference between the two structures, due to the constraint imposed by the presence of the cyclopentane ring, is the overall molecular conformation. This is completely extended in haloperidol and angled in the title compound, with the two phenylene rings facing each other with a perpendicular orientation. Two relatively short OH···O contacts of 2.46 Å connect pairs of adjacent molecules through H bonding.

Table 1. Data collection and handling.

Crystal:	colorless prism, size 0.12 × 0.15 × 0.20 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	2.07 cm^{-1}
Diffractometer, scan mode:	Bruker, $\theta/2\theta$
$2\theta_{max}$:	60°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	4298, 4049
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 6\ \sigma(I_{obs})$, 3032
$N(param)_{refined}$:	265
Programs:	SHELXS-86 [3], SHELXL-93 [4]

Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{iso}
HO(2)	2*i*	0.979(5)	0.108(4)	–0.031(5)	0.08
H(2)	2*i*	0.2645(5)	0.1581(5)	–0.1636(5)	0.08
H(3)	2*i*	0.4954(5)	0.2159(4)	–0.3214(4)	0.08
H(5)	2*i*	0.4927(5)	0.5183(4)	–0.1323(4)	0.08
H(6)	2*i*	0.2600(5)	0.4599(5)	0.0254(5)	0.08
H(8)	2*i*	0.6622(4)	0.3004(4)	–0.4794(4)	0.08
H(91)	2*i*	0.6357(7)	0.4797(6)	–0.5862(5)	0.08
H(92)	2*i*	0.7671(7)	0.5464(6)	–0.5625(5)	0.08
H(101)	2*i*	0.9116(7)	0.4869(6)	–0.7543(5)	0.08
H(102)	2*i*	0.7974(7)	0.3830(6)	–0.7510(5)	0.08

Table 2. Continued.

Atom	Site	x	y	z	U_{iso}
H(111)	2*i*	1.0543(5)	0.3446(6)	–0.7088(4)	0.08
H(112)	2*i*	0.9347(5)	0.2420(6)	–0.6971(4)	0.08
H(121)	2*i*	0.9534(4)	0.3805(4)	–0.5000(4)	0.08
H(131)	2*i*	0.8628(5)	0.1329(4)	–0.4974(4)	0.08
H(132)	2*i*	1.0178(5)	0.1727(4)	–0.4928(4)	0.08
H(141)	2*i*	0.9535(4)	0.3369(4)	–0.3073(4)	0.08
H(142)	2*i*	1.0244(4)	0.2089(4)	–0.2831(4)	0.08
H(151)	2*i*	0.9011(4)	0.3039(4)	–0.0895(4)	0.08
H(152)	2*i*	0.7489(4)	0.3142(4)	–0.1129(4)	0.08

Table 2. Continued.

Atom	Site	x	y	z	U_{iso}
H(171)	2*i*	0.7047(5)	–0.0225(4)	–0.0970(4)	0.08
H(172)	2*i*	0.6175(5)	0.0980(4)	–0.1167(4)	0.08
H(181)	2*i*	0.9090(6)	0.0201(4)	–0.2882(4)	0.08
H(182)	2*i*	0.7587(6)	0.0190(4)	–0.3151(4)	0.08
H(201)	2*i*	0.8176(5)	0.0680(4)	0.1651(4)	0.08
H(211)	2*i*	0.6489(5)	0.0846(4)	0.3709(4)	0.08
H(231)	2*i*	0.3441(5)	0.2520(4)	0.2517(4)	0.08
H(241)	2*i*	0.5142(4)	0.2371(4)	0.0441(4)	0.08

Table 3. Atomic coordinates and displacement parameters (in $Å^2$).

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Cl(1)	2*i*	0.3516(2)	0.1770(2)	0.4876(1)	0.0946(9)	0.140(1)	0.0672(8)	0.0050(8)	–0.0120(6)	–0.0162(7)
F(1)	2*i*	0.1101(3)	0.2682(4)	0.0346(3)	0.070(2)	0.163(3)	0.072(2)	–0.020(2)	0.004(1)	–0.016(2)
O(1)	2*i*	0.7367(3)	0.4975(3)	–0.3185(3)	0.074(2)	0.077(2)	0.092(2)	–0.009(2)	–0.018(2)	–0.016(2)
O(2)	2*i*	0.9284(4)	0.0683(4)	–0.0677(3)	0.072(2)	0.114(3)	0.079(2)	0.043(2)	–0.033(2)	–0.015(2)
N(1)	2*i*	0.8398(4)	0.1902(3)	–0.3250(3)	0.062(2)	0.073(2)	0.059(2)	0.006(2)	–0.022(2)	–0.011(2)
C(1)	2*i*	0.2454(4)	0.3044(5)	–0.0578(4)	0.056(2)	0.097(3)	0.062(2)	0.005(2)	–0.015(2)	–0.010(2)
C(2)	2*i*	0.3109(5)	0.2310(5)	–0.1580(5)	0.073(3)	0.097(3)	0.071(3)	–0.023(2)	–0.015(2)	–0.015(2)
C(3)	2*i*	0.4487(5)	0.2663(4)	–0.2523(4)	0.068(2)	0.085(3)	0.058(2)	–0.007(2)	–0.014(2)	–0.019(2)
C(4)	2*i*	0.5179(4)	0.3745(3)	–0.2456(4)	0.055(2)	0.060(2)	0.058(2)	0.005(2)	–0.023(2)	–0.004(2)
C(5)	2*i*	0.4468(5)	0.4459(4)	–0.1399(4)	0.083(3)	0.072(2)	0.072(3)	–0.001(2)	–0.022(2)	–0.017(2)
C(6)	2*i*	0.3081(5)	0.4112(5)	–0.0449(5)	0.075(3)	0.092(3)	0.072(3)	0.017(2)	–0.011(2)	–0.026(2)
C(7)	2*i*	0.6671(5)	0.4178(4)	–0.3446(4)	0.065(2)	0.062(2)	0.068(2)	0.003(2)	–0.025(2)	–0.004(2)
C(8)	2*i*	0.7273(4)	0.3680(4)	–0.4769(4)	0.054(2)	0.093(3)	0.051(2)	–0.010(2)	–0.013(2)	0.006(2)
C(9)	2*i*	0.7349(7)	0.4677(6)	–0.5808(5)	0.108(4)	0.121(4)	0.078(3)	0.021(3)	–0.031(3)	0.017(3)
C(10)	2*i*	0.8491(7)	0.4196(6)	–0.7027(5)	0.114(4)	0.110(4)	0.062(3)	–0.014(3)	–0.029(3)	0.020(3)
C(11)	2*i*	0.9474(5)	0.3228(6)	–0.6689(4)	0.068(2)	0.125(4)	0.050(2)	–0.011(2)	–0.011(2)	–0.003(2)
C(12)	2*i*	0.8934(4)	0.3209(4)	–0.5229(4)	0.059(2)	0.087(3)	0.054(2)	–0.008(2)	–0.016(2)	–0.002(2)
C(13)	2*i*	0.9101(5)	0.1944(4)	–0.4656(4)	0.067(2)	0.087(3)	0.063(2)	0.010(2)	–0.024(2)	–0.013(2)
C(14)	2*i*	0.9293(4)	0.2541(4)	–0.2682(4)	0.055(2)	0.087(3)	0.065(2)	–0.002(2)	–0.023(2)	–0.003(2)
C(15)	2*i*	0.8396(4)	0.2631(4)	–0.1267(4)	0.056(2)	0.069(2)	0.063(2)	–0.002(2)	–0.025(2)	–0.007(2)
C(16)	2*i*	0.7924(4)	0.1369(4)	–0.0594(4)	0.056(2)	0.068(2)	0.066(2)	0.019(2)	–0.028(2)	–0.007(2)
C(17)	2*i*	0.7179(5)	0.0626(4)	–0.1309(4)	0.089(3)	0.054(2)	0.069(3)	0.000(2)	–0.034(2)	–0.002(2)
C(18)	2*i*	0.8123(6)	0.0629(4)	–0.2728(4)	0.094(3)	0.064(2)	0.068(3)	0.007(2)	–0.032(2)	–0.016(2)
C(19)	2*i*	0.6852(4)	0.1485(3)	0.0786(4)	0.057(2)	0.053(2)	0.063(2)	0.008(1)	–0.028(2)	–0.005(2)
C(20)	2*i*	0.7221(5)	0.1047(4)	0.1813(4)	0.070(2)	0.076(2)	0.072(2)	0.017(2)	–0.037(2)	–0.013(2)
C(21)	2*i*	0.6214(5)	0.1146(4)	0.3045(4)	0.078(3)	0.090(3)	0.063(2)	0.009(2)	–0.035(2)	–0.010(2)
C(22)	2*i*	0.4804(5)	0.1683(4)	0.3308(4)	0.065(2)	0.072(2)	0.062(2)	–0.004(2)	–0.018(2)	–0.010(2)
C(23)	2*i*	0.4395(5)	0.2146(4)	0.2339(4)	0.057(2)	0.078(3)	0.077(3)	0.010(2)	–0.022(2)	–0.006(2)
C(24)	2*i*	0.5419(4)	0.2048(4)	0.1096(4)	0.058(2)	0.079(2)	0.068(2)	0.012(2)	–0.025(2)	0.003(2)

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