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8-Methyl-6-(4-methylpiperazin-1-yl)-11*H*-pyrido[2,3-*b*][1,4]benzodiazepine

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
R factor = 0.050
wR factor = 0.106
Data-to-parameter ratio = 13.8

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

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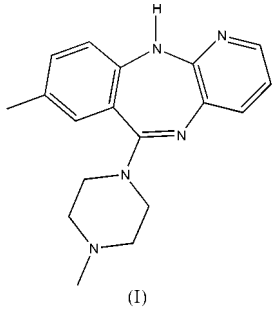
The conformation of the title compound, $C_{18}H_{21}N_5$, is very similar to that observed in other diaryldiazepine structures such as clozapine and clozapine dihydrobromide. N—H···H hydrogen-bond interactions result in the formation of a dimer.

Comment

The title compound binds to the dopamine *D*4 receptor with affinity up to 25 times superior to that for the dopamine *D*2 receptor and shows reduced affinities for other receptors (Liégeois *et al.*, 1995). As for clozapine in Parkinsonian patients, the title compound was shown to reduce L-3,4-dihydroxyphenylalanine (L-DOPA)-induced dyskinesias at low doses in Parkinsonian monkeys (Hadj Tahar *et al.*, 2000). The molecular conformation observed for the title compound (Fig. 1) is in agreement with the conformation described for two similar compounds, *viz*. $C_{18}H_{19}ClN_4$ (clozapine; Petcher & Weber, 1976) and $C_{18}H_{21}ClN_4Br_2$ (clozapine dihydrobromide; Fillers & Hawkinson, 1982). The diazepine moiety (central seven-membered heterocycle) is in a boat conformation. The dihedral angle between the planes of the aromatic rings is 122.21 (9)°. The piperazine side chain adopts a classical chair conformation. The distances between the basic N atom of the piperazine and the centres of each of the aromatic rings are 6.085 and 7.720 Å, respectively. Intermolecular contacts (Table 1) indicate N—H···N hydrogen bonding, with the formation of dimers, as shown in Fig. 2.



(I)

Experimental

The title compound was prepared according to methods described previously (Liégeois *et al.*, 1993). Briefly, a nitrobenzamide was first prepared by the reaction of 2-nitrobenzoyl chloride with 3-amino-2-chloropyridine. The nitro moiety was reduced using an acidic stannous chloride mixture to give an anthranilamide derivative. The diazepinone ring was then obtained by nucleophilic substitution of the Cl atom by heating in diethyleneglycol monomethylether. The lactam derivative was finally reacted with an excess of *N*-methylpiperazine and titanium tetrachloride in refluxing toluene to give the

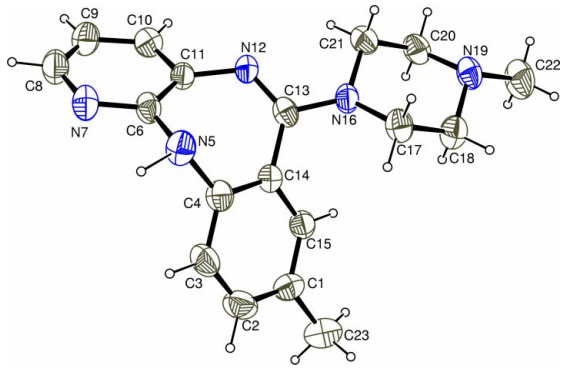


Figure 1
The title compound, with the atom-labelling scheme. Displacement ellipsoid are shown at the 50% probability level.

title compound. Single crystals suitable for X-ray analysis were grown from a solution in toluene.

Crystal data

$C_{18}H_{21}N_5$
M_r = 307.40
Orthorhombic, *Pbca*
a = 13.0331 (19) Å
b = 15.610 (3) Å
c = 16.514 (3) Å
V = 3359.7 (10) Å^3
Z = 8
D_x = 1.215 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 21 reflections
θ = 15.2–17.5°
μ = 0.08 mm^{-1}
T = 293 (2) K
Prism, yellow
0.35 × 0.30 × 0.25 mm

Data collection

Bruker *P*4 diffractometer
$2\theta/\omega$ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.915, T_{max} = 0.964
6621 measured reflections
2952 independent reflections
1441 reflections with $I > 2\sigma(I)$
R_{int} = 0.031
θ_{max} = 25.0°
$h = -1 \rightarrow 15$
$k = -1 \rightarrow 18$
$l = -1 \rightarrow 19$
3 standard reflections
every 97 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.050
$wR(F^2)$ = 0.106
S = 0.92
2952 reflections
214 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.034P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.15 e Å^{-3}

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N5—H5···N7^{i}	0.917 (16)	2.300 (17)	3.214 (3)	175 (2)

Symmetry code: (i) $1-x, -y, 1-z$.

All H atoms were located from difference Fourier maps. H atoms attached to C atoms were treated as riding [C—H = 0.93–0.97 Å and U_{iso}(H) = 1.5U_{eq}(C) (methyl groups) or 1.2U_{eq}(C) (other H atoms)],

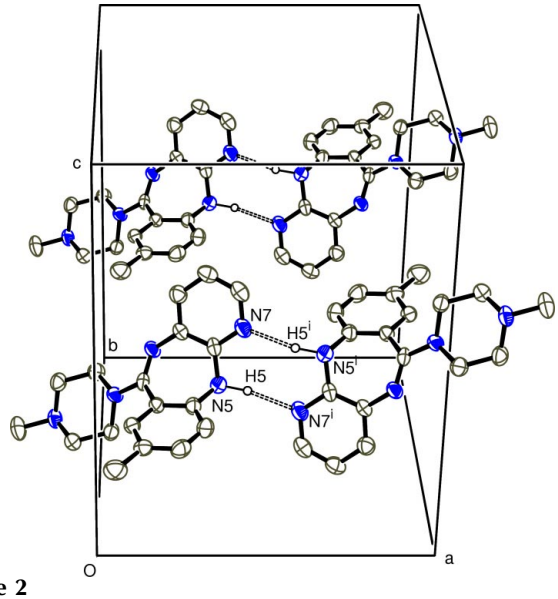


Figure 2
The N—H···N interactions, leading to the formation of dimers. [Symmetry code: (i) $-x+1, -y, -z+1$.]

and the coordinates and U_{iso}(H) value of that belonging to the NH group were refined with a restraint of N—H = 0.917 (16) Å.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *SHELXTL* (Siemens, 1991); program(s) used to solve structure: *SHELXTL*; program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 (Farrugia, 1997); software used to prepare material for publication: *SHELXTL*.

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