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8-Chloro-6-(3-dimethylaminopropylamino)-11*H*-pyrido[2,3-*b*][1,4]benzodiazepine

Léon Dupont,[a]* Laurence Eyrolles,[b] Guy Evrard,[c] Jacques Delarge[b] and Jean-François Liégeois[b]

[a]Unité de Cristallographie, Institut de Physique - Bât. B5, Université de Liège, Allée du 6 août 17, B-4000 Liège, Belgium, [b]Service de Chimie Pharmaceutique, Institut de Pharmacie - Bât. B36, Université de Liège, Avenue de l'Hôpital 1, B-4000 Liège, Belgium, and [c]Laboratoire de Chimie Moléculaire Structurale, Facultés Universitaires Notre-Dame de la Paix, Rue de Bruxelles 61, B-5000 Namur, Belgium

Correspondence e-mail: leon.dupont@ulg.ac.be

Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.003 Å
R factor = 0.044
wR factor = 0.122
Data-to-parameter ratio = 16.2

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

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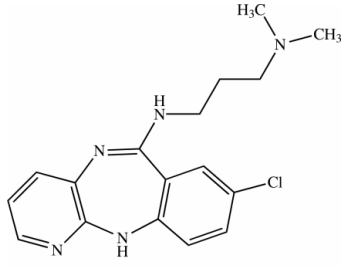
The crystal structure determination of the title compound, $C_{17}H_{20}ClN_5$, has been undertaken as part of studies on antipsychotic drugs. Its structure is compared with that of clozapine ($C_{18}H_{19}ClN_4$), a well known atypical antipsychotic drug. The side chain is more flexible than in the *N*-methylpiperazine analogues, but its folding is influenced by an intramolecular N—H···N hydrogen bond. The distances between the *N*-distal atom, a possible pharmacophore, and the centres of the two aromatic rings are significantly shorter than in clozapine. The crystal packing involves one N—H···N intermolecular hydrogen bond. The title compound showed no affinity for the receptors tested.

Comment

In the first part of our programme, biosteric analogues of dibenzoazepines were synthesized by modifying the tricyclic nucleus (Liégeois *et al.*, 1993, 1994). Later, new entities were further developed by modifying the *N*-methylpiperazine side chain either by varying the *N*-substituent or by replacing the piperazine ring by other nitrogen-containing rings or even by aliphatic diamines. The new compounds were used to explore the impact of such modifications on the binding affinities of these molecules for $D_{4.2}$, 5-HT_{2A} and D_{2L} receptors. The title compound, (I), showed no affinity for the receptors tested.



(I)

The flexibility of the side chain in the molecule is increased compared to the *N*-methylpiperazine analogues, such as 8-chloro-6-(4-methylpiperazin-1-yl)-11*H*-pyrido[2,3-*b*][1,4]-benzodiazepine [clozapine drug (II); Petcher & Weber, 1976]. Nevertheless, the folding of the side chain is determined by the existence of the intramolecular N16—H···N20(distal) hydrogen bond. In (I), the spatial position of the distal N atom, a possible pharmacophore, is modified and thus interaction with the receptor sites could be compromised. Some geometrical features may be compared between (I) and (II). The dihedral angles between the two aromatic rings are 134.6 (2) in (I) and 115.0 (4)° in (II). The distances *D*1 and *D*2

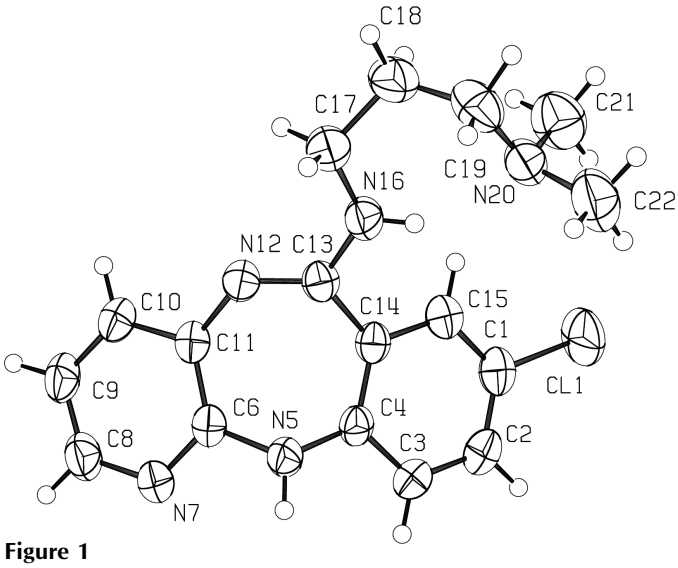


Figure 1
The molecular structure of (I) with the atom-labelling scheme. Displacement ellipsoids are shown at the 50% probability level.

between the N-distal atom and the the centres of the two aromatic rings are 4.754 (2) and 7.669 (2) Å in (I), and 5.972 (5) and 7.716 (5) Å in (II). In the crystal structure of (I), the side chain is more folded; in particular, *D*1 is shorter than in (II) and in other dibenzo- or pyridobenzoazepine derivatives. In the amidine moieties, the N=C double bond and C—N single bond are 1.295 (2) and 1.345 (2) Å in (I), and 1.293 (5) and 1.371 (5) in (II). The crystal packing is dominated by one intermolecular hydrogen bond, *viz*. N5—H···N12.

Experimental

The title compound was prepared according to previously described methods (Liégeois *et al.*, 1993) using a one-pot synthesis. A mixture of the lactam derivative, the corresponding amine, the titanium tetrachloride in toluene–anisole was refluxed for several hours. The product was extracted from the basic solution with chloroform and recrystallized from a methylene chloride/hexane mixture (Liégeois *et al.*, 2002).

Crystal data

$C_{17}H_{20}ClN_5$
M_r = 329.83
Monoclinic, $P2_1/n$
a = 9.001 (1) Å
b = 20.421 (3) Å
c = 9.935 (1) Å
β = 109.545 (6)°
V = 1720.9 (4) Å^3
Z = 4
D_x = 1.273 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 20–23°
μ = 0.23 mm^{-1}
T = 293 (2) K
Prism, yellow
0.50 × 0.50 × 0.50 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\theta/2\theta$ scans
Absorption correction: none
7197 measured reflections
3511 independent reflections
3036 reflections with $I > 2\sigma(I)$
R_{int} = 0.022
θ_{max} = 26.3°
$h = 0 \rightarrow 11$
$k = -25 \rightarrow 25$
$l = -12 \rightarrow 11$
3 standard reflections
every 200 reflections
intensity decay: 4%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.044
$wR(F^2)$ = 0.122
S = 1.11
3511 reflections
217 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0528P)^2 + 0.2131P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.34 e Å^{-3}
$\Delta\rho_{min}$ = −0.16 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.078 (4)

Table 1
Selected geometric parameters (Å, °).

C4—N5	1.407 (2)	C13—N16	1.345 (2)
N5—C6	1.4127 (19)	N16—C17	1.450 (2)
C6—N7	1.330 (2)	C19—N20	1.474 (3)
N7—C8	1.342 (2)	N20—C21	1.440 (3)
C11—N12	1.407 (2)	N20—C22	1.459 (3)
N12—C13	1.2945 (19)		
C4—N5—C6	119.04 (13)	C13—N16—C17	124.69 (15)
C6—N7—C8	117.74 (15)	C21—N20—C22	109.25 (19)
C13—N12—C11	123.16 (13)	C21—N20—C19	113.98 (19)
N12—C13—N16	119.18 (15)	C22—N20—C19	108.4 (2)
C14—C4—N5—C6	−53.9 (2)	C13—N16—C17—C18	168.89 (18)
C4—N5—C6—C11	53.3 (2)	N16—C17—C18—C19	51.8 (3)
N5—C6—C11—N12	9.8 (2)	C17—C18—C19—N20	−68.2 (3)
C6—C11—N12—C13	−40.5 (2)	C18—C19—N20—C21	−71.8 (2)
C11—N12—C13—N16	−179.23 (15)	C18—C19—N20—C22	166.35 (19)
N12—C13—N16—C17	−3.2 (3)		

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N5—H5···N12^{i}	0.87 (2)	2.49 (2)	3.332 (2)	162.9 (17)
N16—H16···N20	0.82 (2)	2.08 (2)	2.787 (2)	145 (2)

Symmetry code: (i) $x-\frac{1}{2}, \frac{1}{2}-y, z-\frac{1}{2}$.

All H atoms (with the exception of the nitrogen-bound atoms H5 and H16) were included in the refinement in the riding-model approximation, with isotropic displacement parameters fixed at $1.2U_{eq}$ of the parent atom ($1.5U_{eq}$ for methyl H-atoms). Atoms H5 and H16 were refined isotropically, their displacement parameters being fixed at $1.2U_{eq}$ of the N atom. The two methyl groups were allowed to rotate about their local threefold axis.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1992); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *HELENA* (Spek, 1997); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1993); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*III (Burnett & Johnson, 1996); software used to prepare material for publication: *SHELXL*97.

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