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2-Methyl-4-(4-methyl-1-piperazinyl)-10*H*-thieno[2,3-*b*][1,5]benzodiazepine methanol solvate

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Key indicators

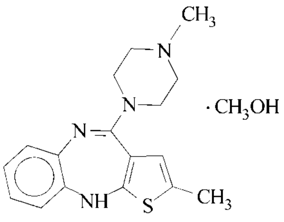
Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.009 Å
R factor = 0.063
wR factor = 0.276
Data-to-parameter ratio = 17.9

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

The title compound, $C_{17}H_{20}N_4S{\cdot}CH_4O$, is an olanzapine 1:1 methanol solvate. A pair of olanzapine molecules forms a centrosymmetric dimer with intermolecular C—H⋯π interactions. Intermolecular host–host N—H⋯N hydrogen bonds were not found. The guest molecule is linked to host molecules through O—H⋯N, N—H⋯O and C—H⋯O hydrogen bonds.

Comment

This work is a continuation of our studies on olanzapine (Wawrzycka-Gorczyca *et al.*, 2003). Olanzapine is an atypical antipsychotic agent used in the treatment of schizophrenia and other psychotic disorders (Tandon & Jibson, 2003; Kennedy *et al.*, 2001; Callaghan *et al.*, 1999). Thus far, procedures for obtaining five polymorphic forms of olanzapine and three alcoholates have been patented (Bunnell *et al.*, 1997, 1998, Hamied *et al.*, 2002). Recently, the crystal structure of olanzapine methanol solvate monohydrate, (I*a*), has been reported by Capuano *et al.* (2003). To prepare microcrystalline olanzapine methanolate, (I), Bunnell *et al.* (1997) cooled both an ethyl acetate/methanol/olanzapine mixture and a methanol/water/olanzapine mixture. Crystals of (I*a*) have been obtained, by the diffusion method, from a methanol solution of the compound layered on to water (Capuano *et al.*, 2003). In contrast to these methods, we have used slow evaporation of the solvent from an anhydrous methanol solution of olanzapine. The crystals formed in such conditions are an olanzapine methanol solvate (1:1) and are identical with the microcrystalline solid prepared by Bunnell *et al.* (1997). The identity of these solids was proved by comparison of the calculated X-ray powder diffraction pattern with the experimental one (Bunnell *et al.*, 1997).



(I)

In (I) and (I*a*), the diazepine ring adopts a boat conformation, where N4 is the 'bow' and N1 and C7 constitute the 'stern' (Fig. 1). The benzene and thiophene systems, fused with the central 1,5-diazepine ring, are planar. The dihedral angle between the planes of these two aromatic rings is 124.3 (2)°, and is larger than 117.67 (5)° observed for (I*a*) (Capuano *et al.*, 2003).

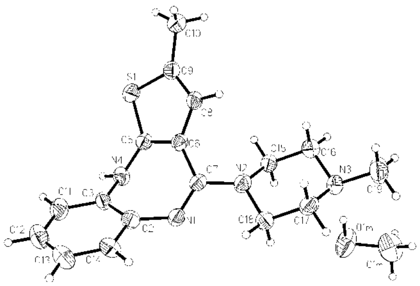


Figure 1
Perspective view of (I). Displacement ellipsoids are drawn at the 30% probability level.

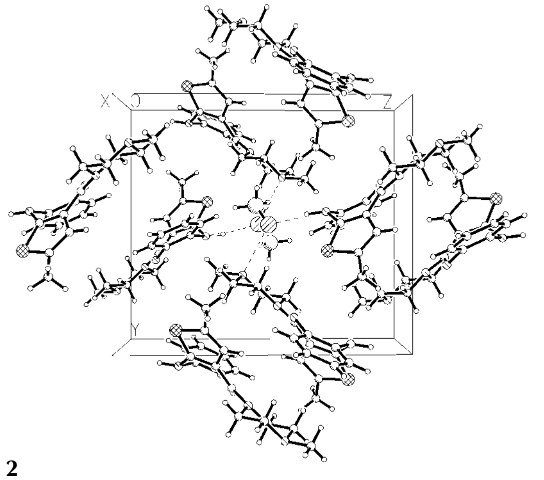


Figure 2
The packing arrangement of molecules, viewed along the *a* axis.

Molecules of olanzapine form centrosymmetric dimers in which C—H$\cdots\pi$ interactions (Umezawa *et al.*, 1999) are observed (Table 2). The geometry of these contacts is very similar to those found for the unsolvated olanzapine crystal structure (Wawrzycka-Gorczyca *et al.*, 2003). Moreover, the observed host–host interactions are: (i) C—H$\cdots\pi$ contacts (C10—H$\cdots$C2 and C10—H$\cdots$C3) for which the H$\cdots\pi_C$ distances are shorter than the sum of the van der Waals radii (Bondi, 1964); (ii) a three-centre C—H$\cdots$N, methyl(C10)$\cdots$diazepine(N4) hydrogen bond.

However, no N_{host}—H$\cdots$$N_{host}$ hydrogen bonds are observed. The dimers in the crystal structure are arranged in columns and form channels, filled with guest molecules, along the *a* axis. The methanol molecule acts both as donor and acceptor in strong intermolecular N_{host}—H$\cdots$$O_{guest}$–H$\cdots$$N_{host}$ hydrogen bonds; it links together the diazepine N4 and piperazine N3 atoms from neighbouring columns (Fig. 2). The same pattern of hydrogen bonds was formed in the crystal structure of (I*a*), involving a water molecule as a bridging unit, while methanol was bonded to atom N1. In the crystal structure of (I), the hydroxyl group of the guest molecule is involved in C—H$\cdots$O interactions with the host benzene atom C11 (Table 2).

Experimental

Well shaped yellow prismatic crystals were obtained by slow evaporation of methanol at room temperature. Thermomicroscopic analysis showed desolvation in the range 343–375 K and a melting point of 464–468 K.

Crystal data

$C_{17}H_{20}N_4S\cdot CH_4O$
M_r = 344.47
Monoclinic, $P2_1/c$
a = 10.207 (3) Å
b = 12.440 (4) Å
c = 14.278 (5) Å
β = 92.60 (3)°
V = 1811.1 (10) Å^3
Z = 4
D_x = 1.263 Mg m^{-3}
Cu *K*α radiation
Cell parameters from 43 reflections
θ = 8–16°
μ = 1.68 mm^{-1}
T = 293 (2) K
Prism, yellow
0.26 × 0.19 × 0.15 mm

Data collection

Kuma KM-4 four-circle diffractometer
ω–2θ scans
Absorption correction: none
4123 measured reflections
3913 independent reflections
1140 reflections with $I > 2\sigma(I)$
R_{int} = 0.080
θ_{max} = 80.2°
$h = -13 \rightarrow 0$
$k = 0 \rightarrow 15$
$l = -18 \rightarrow 18$
3 standard reflections every 100 reflections intensity decay: 8.7%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.063
$wR(F^2)$ = 0.276
S = 1.02
3913 reflections
218 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1344P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.49 e Å^{-3}
$\Delta\rho_{min}$ = −0.44 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0042 (9)

Table 1
Selected geometric parameters (Å, °).

N1—C7	1.298 (7)	N4—C5	1.392 (7)
N1—C2	1.394 (7)	C5—C6	1.369 (7)
C2—C3	1.410 (8)	C6—C7	1.458 (8)
C3—N4	1.428 (7)	C7—N2	1.380 (7)
C5—N4—C3	114.3 (4)	C7—N2—C15	122.0 (4)
C7—N2—C18	119.9 (5)	C18—N2—C15	112.0 (5)
C7—N1—C2—C3	41.2 (9)	N4—C5—C6—C7	2.3 (9)
N1—C2—C3—N4	−4.6 (9)	C2—N1—C7—N2	171.4 (5)
C2—C3—N4—C5	−57.9 (7)	C2—N1—C7—C6	−2.8 (9)
C3—N4—C5—C6	58.8 (8)	C5—C6—C7—N1	−36.4 (9)

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

D—H$\cdots$*A*	*D*—H	H$\cdots$*A*	*D*$\cdots$*A*	*D*—H$\cdots$*A*
O1*M*—H1O$\cdots$N3	1.01	1.79	2.788 (7)	169
N4—H4N$\cdots$O1M^{i}	0.96	1.99	2.941 (6)	173
C10—H101$\cdots$N4^{i}	0.96	3.00	3.486 (8)	113
C10—H103$\cdots$N4^{i}	0.96	3.10	3.486 (8)	106
C11—H11$\cdots$O1M^{i}	0.93	2.70	3.405 (9)	133
C10—H101$\cdots$C2^{i}	0.96	2.74	3.660 (8)	161
C10—H101$\cdots$C3^{i}	0.96	2.78	3.488 (8)	131
C16—H162$\cdots$C13^{ii}	0.97	3.34	4.213 (9)	151
C16—H162$\cdots$C14^{ii}	0.97	3.19	4.144 (9)	167
C17—H171$\cdots$C5^{ii}	0.97	3.18	4.101 (9)	159
C17—H171$\cdots$C6^{ii}	0.97	3.34	4.177 (8)	145
C17—H171$\cdots$C8^{ii}	0.97	3.34	3.944 (9)	122
C18—H182$\cdots$C8^{ii}	0.97	3.02	3.676 (9)	126
C18—H182$\cdots$C9^{ii}	0.97	2.93	3.687 (9)	136
C19—H193$\cdots$C11^{ii}	0.96	3.23	4.184 (11)	176
C19—H193$\cdots$C12^{ii}	0.96	3.31	4.184 (11)	153

Symmetry codes: (i) $2 - x, \frac{1}{2} + y, \frac{3}{2} - z$; (ii) $2 - x, 2 - y, 1 - z$.

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H atoms bonded to C were positioned geometrically, while those bonded to non-C atoms were found in ΔF maps. C—H distances were in the range 0.93–0.97 Å, N—H was set to 0.96 Å and O—H to 1.02 Å. The H atoms were included in the refinement in the riding-model approximation, with $U_{\rm iso}$ values constrained to be $1.2U_{\rm eq}$(C, N or O).

Data collection: *KM*4 *Software* (Kuma Diffraction, 1991); cell refinement: *KM*4 *Software*; data reduction: *KM*4 *Software*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL/PC* (Sheldrick, 1990); software used to prepare material for publication: *SHELXL*97.

References

Bondi, A. (1964). *J. Phys. Chem.* **68**, 441–451.

Bunnell, C. A., Hendriksen, B. A. & Larsen, S. D. (1998). US Patent No. 5 736 541 (Eli Lilly and Company, USA; Lilly Industries Ltd, England).

Bunnell, C. A., Hotten, T. M., Larsen, S. D. & Tupper, D. E. (1997). US Patent No. 5 703 232 (Eli Lilly and Company, USA).

Callaghan, J. T., Bergstrom, R. F., Ptak, L. R. & Beasley, C. M. (1999). *Clin. Pharm.* **37**, 177–193.

Capuano, B., Crosby, I. T., Fallon, G. D., Lloyd, E. J., Yuriev, E. & Egan, S. J. (2003). *Acta Cryst.* E**59**, o1367–o1369.

Hamied, Y. K., Kankan, R. N. & Rao, D. R. (2002). US Patent No. 6,348,458 (U and I Pharmaceuticals Ltd, USA).

Kennedy, J. S., Bymaster, F. P., Schuh L., Calligaro, D. O., Nomikos, G., Felder, C. C., Bernauer, M., Kinon, B. J., Baker, R. W., Hay, D., Roth, H. J., Dossenbach, M., Kaiser, C., Beasley, C. M., Holcombe, J. H., Effron, M. B. & Breier, A. (2001). *Int. J. Geriatr. Psych. Suppl. 1*, **16**, S33—S61.

Kuma Diffraction (1991). *KM*4 *Software*. Kuma Diffraction, Wrocław, Poland.

Sheldrick, G. M. (1990). *SHELXTL/PC. Users Manual.* Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Sheldrick, G. M. (1997). *SHELXS*97 and *SHELXL*97. University of Göttingen, Germany.

Tandon, R. & Jibson, M. D. (2003). *Psychoneuroendocrinology*, **28**, 9–26.

Umezawa, Y., Tsuboyama, S., Takahashi, H., Uzawa, J. & Nishio M. (1999). *Tetrahedron*, **55**, 10047–10056.

Wawrzycka-Gorczyca, I., Koziol, A. E., Glice, M. & Cybulski, J. (2003). *Acta Cryst.* E**59**, o69–o71.

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