Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD1010). Services for accessing these data are described at the back of the journal.

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7,11b-Dihydro-9,10-dimethoxy-3,11b-diphenyl[1,2,4]oxadiazolo[5,4-*a*]-[2,3]benzodiazepin-6(5*H*)-one

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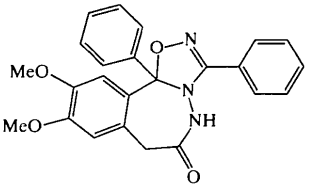
Abstract

This paper represents one of the few structural reports on 2,3-benzodiazepines. The title compound, $C_{24}H_{21}N_3O_4$, consists of a benzodiazepine moiety and an oxadiazole ring fused together, with the seven-membered ring in a 'boat' conformation. The molecules are linked into pairs by N—H···O hydrogen bonds. The title compound is an interesting antagonist at non-NMDA (*N*-methyl-D-aspartate) receptors.

Comment

The unusual biological activities shown by benzodiazepine derivatives containing an additional heterocyclic ring fused to different edges of the heptatomic nucleus (Chimirri *et al.*, 1993) have stimulated the exploitation of the chemistry of this class of compounds. Previous reports claim that the biological activity of benzodiazepines can be correlated to the conformational mobility of the seven-membered ring and therefore the fusion of a heterocyclic ring can lead to an enhancement of the ring inversion barrier, thus determining a higher activity and/or specificity of action.

On this basis, in the course of our studies on structure–activity relationships of cyclofunctionalized benzodiazepines, with particular reference to their anticonvulsant effects (De Sarro *et al.*, 1992, 1993), we reported the synthesis of a series of 1,2,4-oxadiazolo-[5,4-*a*][2,3]benzodiazepine derivatives (De Sarro *et al.*, 1995), as potential antagonists at non-NMDA receptors, which constitute new interesting targets for anti-epileptic therapy (Chimirri *et al.*, 1999). In this paper, we report the results of the X-ray structure determination of 7,11b-dihydro-9,10-dimethoxy-3,11b-diphenyl[1,2,4]oxadiazolo[5,4-*a*][2,3]benzodiazepin-6(5*H*)-one, (I), in order to study the geometry of this new class of annelated 2,3-benzodiazepines. We then compare the structure of (I) with those of other known non-NMDA antagonists in order to clarify which structural elements are necessary for anticonvulsant activity.



(I)

There are several reports in the literature describing benzodiazepines, but only a few refer to 1,2- or 2,3-benzodiazepines (Allen & Kennard, 1993). In this paper we report the crystal structure of a 2,3-benzodiazepine which reveals that in the solid state a strong hydrogen bond occurs between molecules related by an inversion centre (see Table 2). Such interaction may be described in terms of the graph set $R_2^2(8)$ (Bernstein *et al.*, 1995), which is typical for carboxylic acids, amides and their supramolecular association complexes (Walsh *et al.*, 1997).

The title compound consists of three fused rings: the five-membered ring has a twisted envelope conformation [$\varphi_2 = -130.8(4)°$] whereas the seven-membered ring shows the usual 'boat' conformation [$\varphi_2 = 100.98(9)°$, $\varphi_3 = 159.6(4)°$, $Q = 0.9688(17)$ Å, $\theta = 78.37(10)°$; Cremer & Pople, 1975]. The disposition of the rings is shown by the torsion angles

C4—C5—C6—C7 = 4.0 (2) and N2—N3—C4—O14 = −118.46 (15)°. The seven-membered ring may be considered as being formed of two parts: the first is coplanar with the dimethoxybenzene ring and the second C1,N2,N3 forms an angle of 81.6 (1)° with the six-membered ring. Geometrical parameters of the seven-membered ring are within the range of values reported for analogous compounds; the single N—N bond length [1.4016 (18) Å] is comparable with the value reported for 1-(3,4-dimethoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5*H*-2,3-benzodiazepine hydrobromide (Fogassy *et al.*, 1986) and is slightly smaller than the value found in 6-(*p*-chlorophenyl)-3-(*p*-chlorobenzoyl)-4*H*-pyrazolo[4,3-*d*][2,3]benzodiazepine (Laskos *et al.*, 1995).

The sum of the valency bond angles around N3 is 346.70 (13)° demonstrating its pyramidalization; the orientation of its lone pair favours the interaction with H14 and H26 (see Table 2). The phenyl substitutent at C4 is arranged in such a way to allow an intramolecular interaction between O14 and H18 (see Table 2). The carbonyl double bond and C1—N2 [1.2305 (19) and 1.346 (2) Å, respectively] are indicative of the slight electronic delocalization favoured by hydrogen-bond formation.

The relative disposition of the six- and seven-membered rings is determined by the benzenic bond between C5 and C6, while the disposition of the oxadiazole with respect to the 2,3-diazepine ring is determined by the presence of the phenyl substituent at C4. The distances in the five-membered ring are in good agreement with those reported in the literature, showing the presence of a double bond between C12 and N13 [1.285 (2) Å].

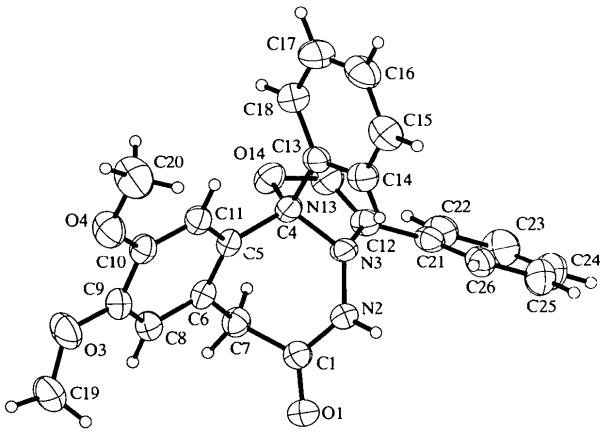


Fig. 1. A view of (I) showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level for non-H atoms.

Experimental

The title compound was synthesized as described in De Sarro *et al.* (1995) and recrystallized from ethanol.

Crystal data

$C_{24}H_{21}N_3O_4$
M_r = 415.44
Triclinic
$P\bar{1}$
a = 9.308 (2) Å
b = 10.6395 (19) Å
c = 11.225 (2) Å
α = 86.959 (16)°
β = 70.753 (19)°
γ = 79.375 (18)°
V = 1031.5 (4) Å^3
Z = 2
D_x = 1.338 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 30 reflections
θ = 5.65–14.84°
μ = 0.093 mm^{-1}
T = 294 (2) K
Irregular
0.26 × 0.24 × 0.12 mm
Colourless

Data collection

Siemens *R3m/V* diffractometer
ω–2θ scans
Absorption correction: none
3889 measured reflections
3644 independent reflections
2167 reflections with $I > \sigma(I)$

R_{int} = 0.035
θ_{max} = 25.05°
h = 0 → 11
k = −12 → 12
l = −12 → 13
3 standard reflections
every 197 reflections
intensity decay: 2.48%

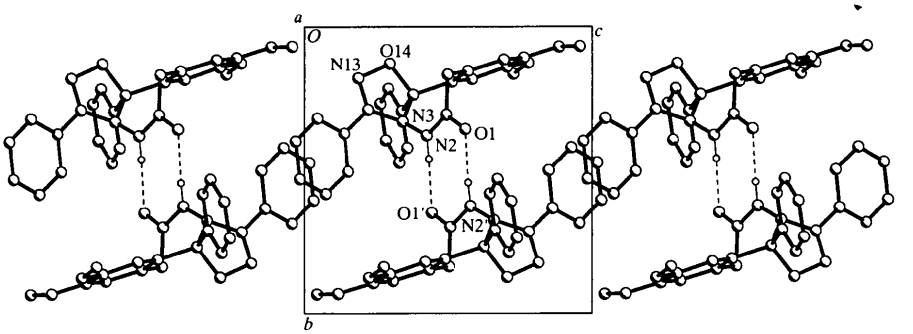


Fig. 2. The molecular packing in (I) viewed down the *a* axis. Only the H atoms involved in hydrogen bonding (indicated as dashed lines) are shown, for clarity.

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.034$
$wR(F^2) = 0.080$
$S = 0.796$
3644 reflections
285 parameters
H atoms: see below
$w = 1/[\sigma^2(F_o^2) + (0.045P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.180$ e Å^{-3}
$\Delta\rho_{min} = -0.130$ e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.0146 (16)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °)*

O1=C1	1.2305 (19)	C9—O3	1.356 (2)
C1—N2	1.346 (2)	C10—O4	1.369 (2)
N2—N3	1.4016 (18)	C12=N13	1.285 (2)
N3—C12	1.405 (2)	N13—O14	1.4429 (18)
N3—C4	1.484 (2)	O3—C19	1.414 (2)
C4—O14	1.4492 (19)	O4—C20	1.413 (2)
O1=C1—N2	120.79 (16)	C12—N3—C4	104.02 (13)
O1=C1—C7	122.66 (15)	C12=N13—O14	106.41 (13)
N2—C1—C7	116.17 (15)	N13—O14—C4	106.78 (11)
C1—N2—N3	124.67 (15)	C9—O3—C19	117.87 (15)
N2—N3—C12	118.12 (13)	C10—O4—C20	117.72 (14)
N2—N3—C4	124.56 (13)		

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2···O1^{i}	0.859 (17)	1.983 (18)	2.830 (2)	168.5 (17)
C14—H14···N3	0.93	2.54	2.819 (2)	98
C26—H26···N3	0.93	2.65	2.944 (2)	99
C18—H18···O14	0.93	2.50	2.806 (2)	99

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

Reflection intensities were evaluated by profile fitting of a 96-step peak scan in shells of 2θ (Diamond, 1969) and then corrected for Lorentz–polarization effects. Standard deviations $\sigma(I)$ were estimated from counting statistics. All non-H atoms were refined anisotropically. H atoms were located in idealized positions (except H2 which was refined isotropically) and allowed to ride on the coordinates of their parent C atoms with a common isotropic displacement parameter ($U_{iso} = 0.06$ Å^2). All calculations were performed on a MicroVAX 3400 and an AXP DecStation 3000/400.

Data collection: *P3/V Control Software* (Siemens, 1989). Cell refinement: *P3/V Control Software*. Data reduction: *SHELXTL-Plus* (Sheldrick, 1990). Program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994). Program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997). Molecular graphics: *XPW* (Siemens, 1996). Software used to prepare material for publication: *PARST*97 (Nardelli, 1995) and *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: NA1353). Services for accessing these data are described at the back of the journal.

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(1*S*,*R*$_S$)-6,7-Dimethoxy-*N*-methyl-1-(*p*-tolylsulfinylmethyl)-1-trifluoromethyl-1,2,3,4-tetrahydroisoquinoline

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Abstract

The title compound, $C_{21}H_{24}F_3NO_3S$, is an intermediate in the synthesis of enantiomerically pure alkaloids; the molecular structure has been determined to establish its stereochemistry. The molecular conformation is largely determined by intramolecular interactions, while the