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2-{2-[2-(4-Methoxybenzoyl)ethylamino]-4-nitroanilino}ethyl acetate: complex sheets built from five independent hydrogen bonds

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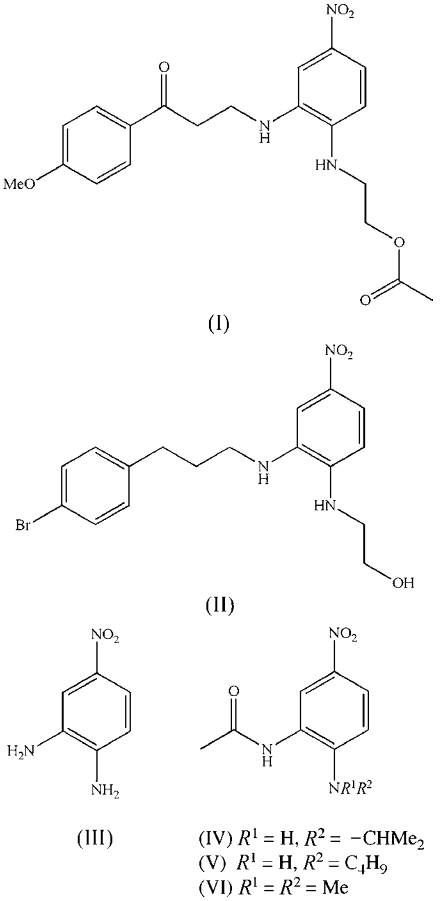
The molecules of the title compound, $C_{20}H_{23}N_3O_6$, are almost completely planar, apart from the H atoms bonded to tetrahedral C atoms. A combination of five hydrogen bonds, one of the N—H···O type and two each of the C—H···O and C—H···π(arene) types, links the molecules into complex sheets.

Comment

Benzodiazepines are a very commonly prescribed class of psychoactive drugs with varying sedative, hypnotic, anxiolytic (anti-anxiety), anticonvulsant, muscle-relaxant and amnesic properties. As part of a programme for the synthesis of new derivatives of this type, we have developed the reaction between 2-(2-amino-4-nitroanilino)ethanol and the α,β-unsaturated ketone precursor 3-dimethylamino-4-methoxypropiophenone and, from this procedure, we have now isolated the title compound, (I), as a reaction intermediate, along with other products. We report here the molecular and supramolecular structure of (I) and we compare its structure with that of analogue (II) (Low *et al.*, 2003), as well as with those of unsubstituted 2-amino-4-nitroaniline, (III) (Kolev *et al.*, 2007), and the *N*-acetyl derivatives (IV)–(VI) (Clark *et al.*, 2000) (see scheme).

The non-H atoms in the molecules of compound (I) are almost coplanar, as indicated by the relevant torsion angles (Table 1). The r.m.s deviation of the non-H atoms from the mean plane through all of the non-H atoms is only 0.067 Å, and the biggest individual deviations are 0.156 (3) Å for atom C13 and 0.138 (2) Å for atom C16, on opposite sides of the mean plane. For the peripheral substituents, methoxy atom C17 deviates from the plane of the C11–C16 ring by only 0.002 (3) Å, while nitro atoms O51 and O52 deviate from the plane of the C31–C36 ring by −0.007 (2) and 0.029 (2) Å, respectively. By contrast, the torsion angle defining the orientation of the 2-hydroxyethyl substituent in compound (II), analogous to the C32—N21—C22—C23 torsion angle in (I), is 83.1 (3)°, indicating an overall conformation far from planarity.



The bond distances involving the trisubstituted aryl ring show a number of unusual values. Firstly, in the nitro group the C35—N51 bond is short for its type (standard value = 1.468 Å; Allen *et al.*, 1987), while the N51—O51 and N51—O52 bonds are both somewhat long (standard value = 1.217 Å; Allen *et al.*, 1987). Secondly, the two exocyclic bonds, C31—N31 and C32—N21, differ somewhat in length. These values are consistent with the quinonoid behaviour often observed in 4-nitroaniline derivatives (Ferguson *et al.*, 2001; Glidewell *et al.*, 2002, 2004, 2005; Howie *et al.*, 2004), but the C—C distances within the C31–C36 ring of (I) do not support this, as the shortest C—C distance is for the C34—C35 bond, while the longest is for the C31—C32 bond. Although the original report on (II) (Low *et al.*, 2003) did not discuss the intramolecular geometry, the corresponding bond distances show a pattern very similar to that in (I). For compounds (IV)–(VI), the authors reported that all bond distances were close to standard values (Clark *et al.*, 2000). In fact, the same behaviour for the exocyclic bonds is observed in (IV)–(VI) as is found in (I) and (II), but with the interesting qualifier that the C—C distances in the rings clearly support the quininoid form in (V) and (VI), but not in (IV). In unsubstituted compound

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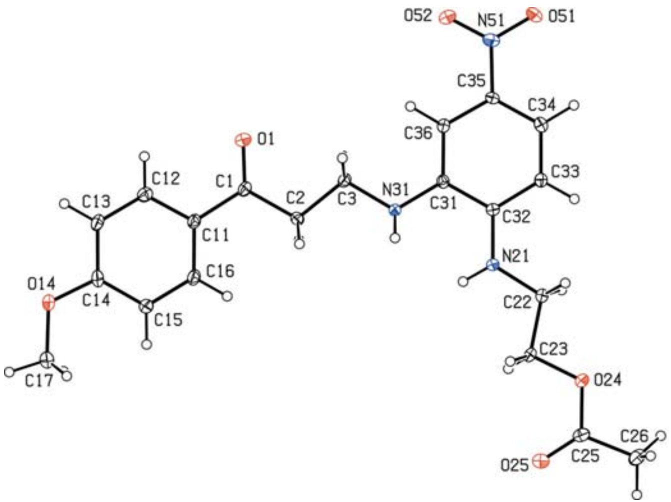

Figure 1
The molecular structure of compound (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

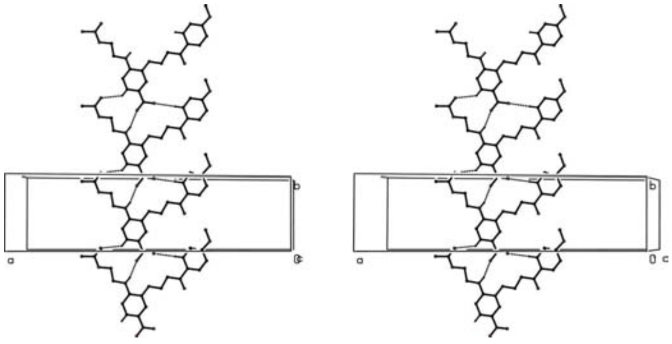

Figure 2
A stereoview of part of the crystal structure of (I), showing the formation of a chain of rings running parallel to the [010] direction and containing two C—H$\cdots\pi$(arene) hydrogen bonds. For the sake of clarity, H atoms bonded to N atoms and to C atoms not involved in the motifs shown have been omitted.

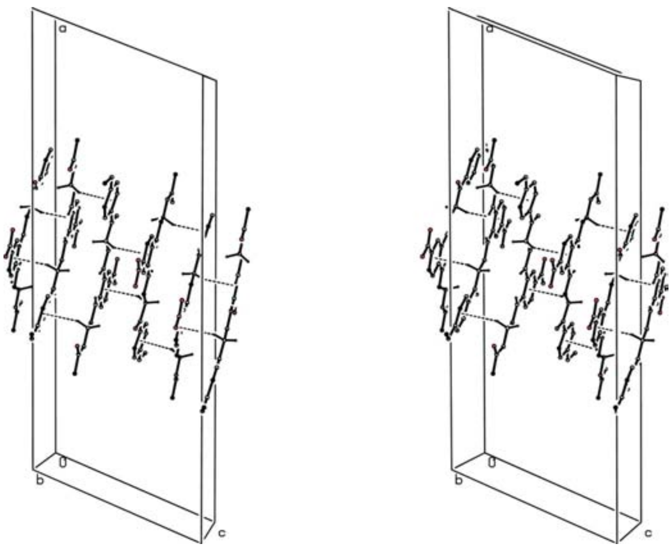

Figure 3
A stereoview of part of the crystal structure of (I), showing the formation of a chain of rings running parallel to the [001] direction and containing two C—H$\cdots\pi$(arene) hydrogen bonds. For the sake of clarity, H atoms bonded to N atoms and to C atoms not involved in the motifs shown have been omitted.

(III), the quinonoid form is dominant in the electronic ground state, but with classical aromatic delocalization dominant in the first electronic excited state (Kolev *et al.*, 2007).

Methoxy atom C17 in (I) is coplanar with the adjacent aryl ring, within experimental uncertainty. Accordingly, the two exocyclic angles at atom C14 differ by *ca* 9.0°, as is usual (Seip & Seip, 1973; Ferguson *et al.*, 1996), while the C—O—C angle in the methoxy group is significantly larger than the tetrahedral value.

The supramolecular aggregation in compound (I) depends upon five hydrogen bonds of the N—H$\cdots$O, C—H$\cdots$O and C—H$\cdots\pi$(arene) types (Table 2), and these combine to generate sheets of considerable complexity. However, the formation of the sheets can readily be analysed in terms of two one-dimensional substructures. The first is built from N—H$\cdots$O and C—H$\cdots$O hydrogen bonds, while the second is formed solely by the two C—H$\cdots\pi$(arene) hydrogen bonds. In the first substructure the N—H$\cdots$O hydrogen bond links molecules related by translation into a $C(8)$ (Bernstein *et al.*, 1995) chain running parallel to the [010] direction (Fig. 2). By contrast, a chain of rings is present in the structure of compound (IV); here molecules related by an *n*-glide plane in the space group $P2_1/n$ are linked into a $C(4)C(7)[R^1_2(7)]$ chain of rings, although the aggregation was not described as such by the original authors (Clark *et al.*, 2000), and this may be contrasted with the simple translational chain in compound (I). Similarly, the two independent molecules in the structure of compound (V) form an exactly analogous motif, but this time built from molecules related by translation. The chain in compound (I) is augmented by the two C—H$\cdots$O hydrogen bonds to form a chain containing fused $R^2_2(12)$ and $R^2_2(14)$ rings (Fig. 2). Just as the individual molecules of (I) are effectively planar, so too is the chain formed from molecules related by translation; the broad chain runs parallel to [010] and its plane lies approximately parallel to $(10\overline{2})$.

In the second substructure, atom C2 in the molecule at (x, y, z) acts as hydrogen-bond donor to the C31–C36 ring in the molecule at $(1 - x, 1 - y, -z)$, so linking a pair of molecules related by inversion. Similarly, atom C23 at (x, y, z) acts as hydrogen-bond donor to the C11–C16 ring in the molecule at $(1 - x, y, \frac{1}{2} - z)$, thereby linking a pair of molecules related by the twofold rotation axis along $(\frac{1}{2}, y, \frac{1}{4})$. Propagation of these two hydrogen bonds thus generates a chain of edge-fused rings running parallel to the [001] direction, in which the component molecules are related by the inversion centres at $(\frac{1}{2}, \frac{1}{2}, \frac{n}{2})$, where n represents an integer, and by the twofold rotation axes along $(\frac{1}{2}, y, \frac{1}{4} + \frac{n}{2})$, where again n represents an integer (Fig. 3). The combination of the ribbon along [010] and the chain of rings along [001] generates a complex sheet lying parallel to (100). Two such sheets, related to one another by the *C*-centring operation, pass through each unit cell, but there are no direction-specific interactions between adjacent sheets. In particular, aromatic π–π stacking interactions are absent.

The constitution of compound (II) differs from that of (I) in two significant ways. Firstly, the ester function is absent, so that a free hydroxyl group is present, and secondly, the compound crystallizes as a stoichiometric 1:1 solvate with dimethylformamide (Low *et al.*, 2003). The two N—H bonds are utilized in linking the major component to the solvent molecule, but they play no further role in the hydrogen-bonding scheme. The supramolecular aggregation is thus dominated by an O—H···O hydrogen bond, which is necessarily absent from the structure of (I), and this, together, with three C—H···O hydrogen bonds, generates a ribbon containing no fewer than five types of ring, two of them centrosymmetric. Again, aromatic π–π stacking interactions are absent, as are significant C—H···π(arene) hydrogen bonds, so that the hydrogen-bonded structure of (II) is one-dimensional, as opposed to the two-dimensional structure of (I). The molecules of (VI) (Clark *et al.*, 2000) are linked into the $C(4)$ chain characteristic of simple amides, while in (III), a combination of four N—H···O hydrogen bonds and one N—H···N hydrogen bond links the molecules into a complex three-dimensional framework structure (Kolev *et al.*, 2007).

Experimental

A solution containing equimolar quantities (3.55 mmol of each reagent) of 2-(2-amino-4-nitroanilino)ethanol and 3-dimethylamino-4-methoxypropiophenone in acetic acid (5 ml) was heated under reflux for 25 min. The mixture was then cooled to ambient temperature and the solvent was removed. The resulting solid products were separated by column chromatography on silica gel, using dichloromethane–ethyl acetate (3:2 *v*/*v*) as eluent. The title compound, (I), was obtained from the last fraction (yield 20%, m.p. 420–421 K). Analysis found: C 59.6, H 6.0, N 10.2%; $C_{20}H_{23}N_3O_6$ requires: C 59.8, H 5.8, N 10.5%. Crystals of (I) suitable for single-crystal X-ray diffraction were grown by slow evaporation of a solution in ethanol.

Crystal data

$C_{20}H_{23}N_3O_6$
$M_r = 401.41$
Monoclinic, $C2/c$
$a = 34.3729\ (17)$ Å
$b = 8.7718\ (5)$ Å
$c = 13.6662\ (9)$ Å
$\beta = 111.847\ (2)^\circ$
$V = 3824.6\ (4)$ Å^3
$Z = 8$
Mo $K\alpha$ radiation
$\mu = 0.10$ mm^{-1}
$T = 120$ K
0.31 × 0.24 × 0.18 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{\min} = 0.928$, $T_{\max} = 0.981$
11193 measured reflections
4308 independent reflections
2277 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.086$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.062$
$wR(F^2) = 0.160$
$S = 1.00$
4308 reflections
270 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{\max} = 0.30$ e Å^{-3}
$\Delta\rho_{\min} = -0.33$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

C31—C32	1.419 (3)	C31—N31	1.388 (3)
C32—C33	1.395 (3)	C32—N21	1.370 (3)
C33—C34	1.376 (3)	C35—N51	1.437 (3)
C34—C35	1.373 (3)	N51—O51	1.237 (3)
C35—C36	1.392 (3)	N51—O52	1.226 (3)
C36—C31	1.382 (3)		
C12—C11—C1—C2	176.8 (2)	C31—C32—N21—C22	179.4 (2)
C11—C1—C2—C3	−177.4 (2)	C32—N21—C22—C23	174.9 (2)
C1—C2—C3—N31	178.13 (18)	N21—C22—C23—O24	−178.53 (18)
O1—C1—C11—C12	−3.0 (3)	C22—C23—O24—C25	−172.8 (2)
C2—C3—N31—C31	−179.82 (19)	C23—O24—C25—O25	0.1 (4)
C3—N31—C31—C32	178.7 (2)	C23—O24—C25—C26	−179.4 (2)
C13—C14—O14—C17	178.8 (2)	C34—C35—N51—O51	−0.8 (3)
C15—C14—O14—C17	−2.1 (3)	C34—C35—N51—O52	179.4 (2)

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

*Cg*1 and *Cg*2 are the centroids of the C11–C16 and C31–C36 rings, respectively.

D—H···A	D—H	H···A	D···A	D—H···A
N21—H21···O51$^{\rm i}$	0.85 (3)	2.16 (3)	2.959 (3)	155 (2)
C16—H16···O52$^{\rm i}$	0.95	2.58	3.508 (4)	166
C34—H34···O25$^{\rm ii}$	0.95	2.52	3.244 (4)	133
C2—H2*B*···*Cg*2$^{\rm iii}$	0.99	2.66	3.455 (3)	138
C23—H23*B*···*Cg*1$^{\rm iv}$	0.99	2.70	3.602 (3)	151

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

All H atoms were located in difference maps. H atoms bonded to C atoms were then treated as riding atoms in geometrically idealized positions, with C—H distances of 0.95 (aromatic), 0.98 (CH_3) or 0.99 Å (CH_2), and with $U_{\rm iso}({\rm H}) = kU_{\rm eq}({\rm C})$, where $k = 1.5$ for the methyl groups, which were permitted to rotate but not to tilt, and 1.2 for all other H atoms bonded to C atoms. For the H atoms bonded to N atoms, the coordinates were freely refined, with $U_{\rm iso}({\rm H}) = 1.2U_{\rm eq}({\rm N})$, giving N—H distances of 0.80 (2) and 0.85 (3) Å.

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *DIRAX*/*LSQ* (Duisenberg *et al.*, 2000); data reduction: *EVALCCD* (Duisenberg *et al.*, 2003); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXL97* and *PLATON*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SF3112). Services for accessing these data are described at the back of the journal.

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