Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

2-[4-(Acetamido)phenoxy]-*N*,*N*-dimethylacetamide: a potential anti-amnesic agent

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Key indicators

Single-crystal X-ray study
T = 298 K
Mean σ(C–C) = 0.003 Å
R factor = 0.050
wR factor = 0.127
Data-to-parameter ratio = 15.3

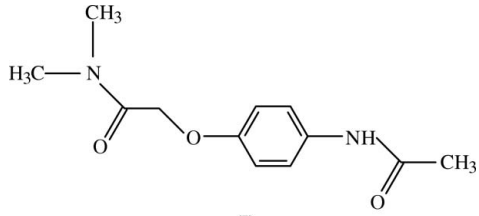
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 5 December 2005
Accepted 22 December 2005
Online 7 January 2006

For the title compound, $C_{12}H_{16}N_2O_3$, a potential anti-amnesic agent, the conformations of the molecule in the crystal structure and that of the energy-minimized free molecule do not differ significantly. Intermolecular N—H···O and C—H···O hydrogen bonds stabilize the crystal packing.

Comment

The conformations of molecules with anti-amnesic activity have attracted considerable interest (Amato *et al.*, 1991). The crystal structures of representatives from several new classes of anti-amnesic agents have been reported from our laboratory (Sundar *et al.*, 2005; Thamotharan *et al.*, 2003*a*,*b*,*c*,*d* and references therein) As a continuation of our investigation of a new class of anti-amnesic agents, the X-ray crystal structure determination of the title compound, (I), has been udertaken. The details of the synthesis of (I) and its biological activity will be published elsewhere (Malik & Piplani, 2006).



(I)

In the molecule (Fig. 1), the angle C1—N1—C11 of 129.72 (18)° is comparable with the corresponding angle of 130.06 (18)° in *N*-[4-(pyrrolidin-1-ylcarbonylmethoxy)phenyl]acetamide, (II) (Sundar *et al.*, 2005). A possible reason for the large value of this angle may be the short intramolecular contact O3···H2 (2.35 Å) which is less than the sum of the van der Waals radii (2.72 Å; Bondi, 1964), leading to an intramolecular C—H···O (Desiraju, 1997) interaction (Table 1). A similar short intramolecular O···H contact of 2.37 Å was

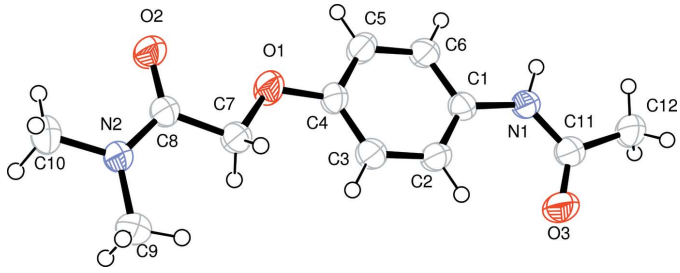


Figure 1
View of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are shown by circles of arbitrary radii.

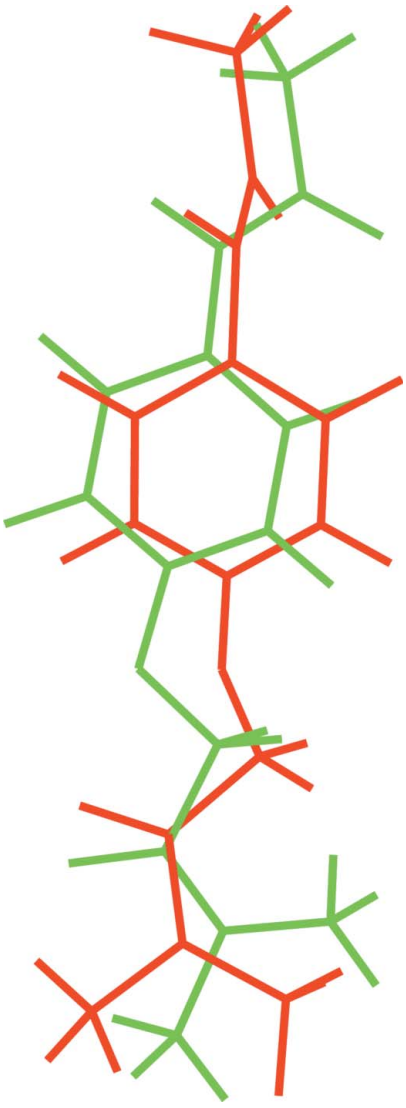


Figure 2
Superimposed fit of molecules of (I) in the crystal structure (green) and its energy-minimized counterpart (red).

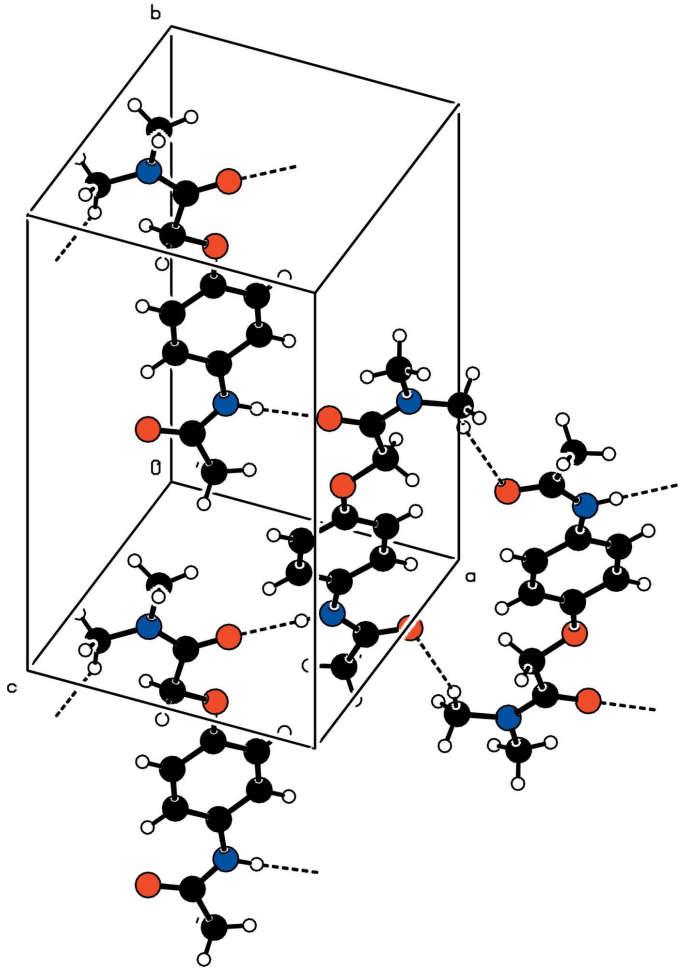


Figure 3
The crystal packing of (I), showing intermolecular N—H···O and C—H···O hydrogen bonds as dashed lines.

observed between the corresponding atoms in (II). This might be due to crystal packing effects.

In order to understand the influence of the packing on the molecular conformation, energy minimization was carried out on the isolated molecule using the *WinMopac* program (Shchepin & Litvinov, 1998). A least-squares fit of the energy-minimized molecule of (I) with its X-ray counterpart gives an r.m.s. deviation of 0.935 Å (Fig. 2). The conformation of the molecule in the crystal structure and that of the energy-minimized free molecule do not differ significantly. In the energy-minimized molecule, rotations about the C1–N1, N1–C11 and C4–O1 single bonds are possible; these might have reduced the strain due to the intermolecular short contacts observed in the molecules in the crystal structure. This can be seen in the lengthening of the intramolecular O3···H2 short contact from 2.35 Å in the crystal structure of (I) to 3.22 Å in the free molecule, thereby relieving the strain. In addition, the value of the angle C1—N1—C11 has decreased from 129.72 (18)° (crystal structure) to 124.47 (7)° (energy-minimized molecule).

In (I), the fragments C7/C8/O2/N2/C9/C10 (*A*), C1/C2/C3/C4/C5/C6/O1 (*B*) and N1/C11/O3/C12 (*C*) are each essentially planar, with r.m.s. deviations of 0.017, 0.007 and 0.002 Å, respectively. The dihedral angles *A*/*C* [2.4 (1)°], *A*/*B* [9.5 (1)°] and *B*/*C* [11.4 (2)°] show that these fragments are not coplanar in (I), whereas they are almost coplanar in (II). The superposition of non-H atoms common to structures (I) and (II) gives an r.m.s. deviation of 3.924 Å, showing there is a significant difference between the conformations of (I) and (II). On the other hand, superposition of the non-H atoms of the phenylacetamide groups of (I) and (II), with an r.m.s. deviation of 1.658 Å, suggests that the conformation of this group may be altered due to different types of bulky substituents at the *para* position of the phenyl ring.

In the crystal structure, intermolecular N—H···O hydrogen bonds (Table 1) link the molecules into linear *C*(10) chains extending along the *b* axis. The crystal packing (Fig. 3) is further stabilized by weak intermolecular C—H···O interactions (Table 1) of graph-set motif $R_2^2(26)$ (Bernstein *et al.*, 1995).

Experimental

An excess of *N*,*N*-dimethylamine was added to methyl 2-(4-acetamidophenoxy)acetate (1.0 g, 4.48 mmol) and stirred at room temperature. Crushed ice was added and the resulting solid was crystallized from acetone (yield = 420.0 mg, 39.7%; m.p. 432–434 K).

Crystal data

$C_{12}H_{16}N_2O_3$
M_r = 236.27
Monoclinic, $P2_1/c$
a = 8.350 (6) Å
b = 17.604 (9) Å
c = 8.197 (5) Å
β = 97.549 (18)°
V = 1194.5 (13) Å^3
Z = 4
D_x = 1.314 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 913 reflections
θ = 2.8–26.6°
μ = 0.10 mm^{-1}
T = 298 (2) K
Block, colourless
0.4 × 0.2 × 0.2 mm

Data collection

Bruker SMART CCD 1K diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.913, T_{max} = 0.998
14079 measured reflections
2563 independent reflections
1492 reflections with $I > 2\sigma(I)$
R_{int} = 0.068
θ_{max} = 26.5°
$h = -10 \rightarrow 10$
$k = -22 \rightarrow 22$
$l = -10 \rightarrow 10$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.050
$wR(F^2)$ = 0.127
S = 1.00
2468 reflections
161 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.057P)^2 + 0.178P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.14 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
C2—H2···O3	0.93	2.35	2.925 (3)	120
N1—H1···O2^{i}	0.87 (2)	2.04 (2)	2.911 (3)	178 (2)
C9—H9*A*···O3^{ii}	0.96	2.60	3.491 (3)	155

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

H1, attached to N1, was located in a difference Fourier map and refined freely. C-bound H atoms were placed in geometrically idealized positions (C—H = 0.93–0.97 Å) and constrained to ride on their parent atoms, with U_{iso}(H) = 1.5U_{eq}(C) for methyl H atoms and 1.2U_{eq}(C) for the others.

Data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT* (Bruker, 2000); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997), *PLATON* (Spek, 2003) and Qmol (Gans & Shalloway, 2001); software used to prepare material for publication: *SHELXL97* and *PARST* (Nardelli, 1995).

TVS thanks Dr. B. Walfort, Technische-Universität Chemnitz, Chemnitz, Germany, for his timely help and kind cooperation.

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