organic compounds

(Z)-2-(3-Methoxybenzylidene)-1-aza-bicyclo[2.2.2]octan-3-one

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The crystal structure of the title compound, $C_{15}H_{17}NO_2$, contains two nearly identical but crystallographically independent molecules, each with a double bond connecting an azabicyclic ring system to a 3-methoxybenzylidene moiety. The space group is triclinic $P\bar{1}$. The benzene ring is twisted by 18.44 (5) and 22.35 (4)° with respect to the plane of the double bond connected to the azabicyclic ring system for the two molecules. In addition to $C-H\cdots\pi$ interactions, molecules are held together in the solid state by van der Waals interactions.

Comment

1-Azabicyclo[2.2.2]octane ring systems linked to five- or six-membered heteroaromatics are known to be muscarinic agonists (Nilsson *et al.*, 1995). Also, the 5-HT-3 receptor antagonist zacopride contains a 1-azabicyclo[2.2.2]octane moiety (Paulis *et al.*, 1997). In continuation of our work with 1-azabicyclo[2.2.2]octan-3-ones as precursors of medicinal agents, we synthesized a series of 2-(substituted benzylidene/ hetero-3-arylmethylene)-1-azabicyclo[2.2.2]octan-3-ones (Sonar *et al.*, 2004), and their crystal structures were determined in order to confirm the geometry and to establish the conformations of the molecules. The title compound, (I), was prepared by condensation of 3-methoxybenzaldeyde with 1-azabicyclo[2.2.2]octan-3-one under base catalysis, to afford a single geometrical isomer, *viz.* (Z)-2-(3-methoxybenzylidene)-1-azabicyclo[2.2.2]octan-3-one. In order to confirm the geometry of this compound, and to obtain more detailed information on the structural conformation of the molecule, its X-ray structure determination has been carried out and the results are presented here.

The asymmetric unit of (I) contains two independent molecules, A and B (Fig. 1), with very similar geometries (Table 1). The molecule contains a double bond between atoms C7 and C8 that connects a 1-azabicyclo[2.2.2]octan-3-one ring system to a 3-methoxybenzylidene group, and has a Z geometry in which the C1—C7 bond is in the *trans* position with respect to the C8—C9 bond. The C7═C8 bond is essentially planar,

since the r.m.s. deviations from the mean planes passing through atoms N1, C8, C9, C7 and C1 are 0.0270 (5) and 0.0060 (5)° for molecules A and B, respectively.
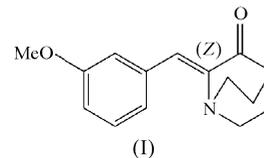
Deviations from ideal geometry are observed in the bond angles around atoms C1, C7, C8 and C9. While the C7═C8—C9 angle [121.27 (7)° in A and 121.07 (7)° in B] is close to the ideal angle of 120°, the C2═C1—C7, C1—C7═C8, N1—C8═C7, C8—C9—C10 and N1—C8—C9 angles [124.25 (7), 130.35 (8), 125.30 (8), 110.88 (7) and 113.24 (7)° in molecule A, and 123.93 (7), 130.65 (8), 125.36 (8), 110.59 (7) and 113.54 (7)° in molecule B, respectively] are more distorted, a consequence of the strain induced by the double-bond linkage at atoms C8 and C9. These deviations in the angles contribute to the release of the intramolecular non-bonded interactions within the 1-azabicyclo[2.2.2]octane ring. In both cases, Csp^2 atoms replace Csp^3 atoms and, as a result, atoms N1, C8, C9 and C10 assume a planar configuration [the N1—C8—C9—C10 torsion angle is −4.81 (9)° in A and −0.55 (9)° in B], with partial conjugation between the double bond and the carbonyl group, as indicated by the significant shortening of the C8—C9 single bonds [1.4807 (12) Å in A and 1.4883 (12) Å in B]. The values of the C2═C1—C7═C8 torsion angles [−19.25 (13)° in A and −21.74 (13)° in B] indicate a deviation of the benzene ring from the plane of the double bond connected to the azabicyclic ring. The observed O2—C5 [1.3710 (10) Å in A and 1.3762 (10) Å in B] and O2—C15 [1.4287 (11) Å in A and 1.4255 (11) Å in B] bond lengths are comparable to values found for aromatic methoxy groups in the literature (Domiano *et al.*, 1979).

In addition to the C—H⋯π interaction shown in Fig. 1 (H12C⋯Cg = 2.80 Å, C12B⋯Cg = 3.701 Å and C12B—H12C⋯Cg = 154°; Cg is the centroid of the C1A—C6A ring), molecules are held together in the solid state by van der Waals interactions.
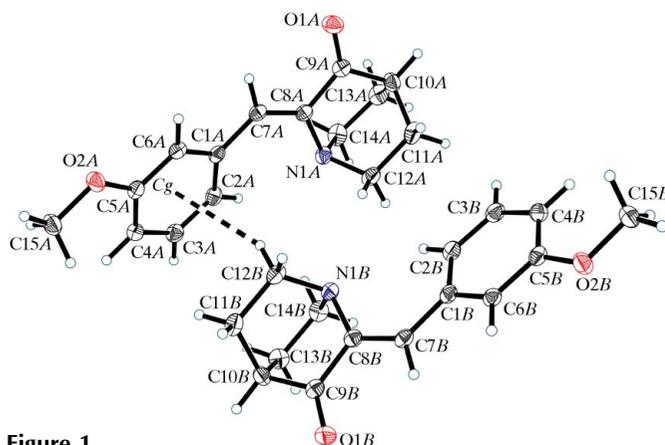
Figure 1
A view of the two independent molecules of the title compound, A and B, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

Experimental

A mixture of 3-methoxybenzaldehyde (0.409 g, 3 mmol) and 1-aza-bicyclo[2.2.2]octan-3-one hydrochloride (0.483 g, 3 mmol) was dissolved in 10% methanolic KOH (10 ml) and the solution was refluxed for 5 h. The cooled reaction mixture was poured onto crushed ice (100 g), and the yellow solid that separated was collected by filtration and dried. Recrystallization from ethyl acetate afforded (I) as a yellow crystalline product suitable for X-ray analysis. ^{1}H NMR (300 MHz, CDCl$_3$): δ 2.03 (td, J = 7.95 and 2.7 Hz, 4H), 2.63 (p, J = 3 Hz, 1H), 2.95–3.06 (m, 2H), 3.12–3.22 (m, 2H), 3.83 (s, 3H), 6.91 (dd, J = 8.25 and 2.7 Hz, 1H), 6.98 (s, 1H), 7.29 (t, J = 8.1 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H), 7.80 (q, J = 1.5 Hz, 1H). ^{13}C NMR (75 MHz, CDCl$_3$): δ 26.2, 40.5, 47.7, 55.5, 115.5, 117.2, 125.1, 125.1, 129.4, 135.3, 145.0, 159.4, 206.4.

Crystal data

C$_{15}$H$_{17}$NO$_2$	$Z = 4$
$M_r = 243.30$	$D_x = 1.326$ Mg m^{-3}
Triclinic, $P\bar{1}$	Cu $K\alpha$ radiation
$a = 5.8860$ (2) Å	Cell parameters from 6692
$b = 10.4741$ (4) Å	reflections
$c = 20.2724$ (8) Å	$\theta = 1.0$–68.0°
$\alpha = 81.090$ (2)°	$\mu = 0.70$ mm^{-1}
$\beta = 89.223$ (2)°	$T = 90.0$ (2) K
$\gamma = 80.845$ (2)°	Plate fragment, yellow
$V = 1218.92$ (8) Å^3	0.15 × 0.05 × 0.03 mm

Data collection

Bruker–Nonius X8 Proteum diffractometer	13961 independent reflections
ω and φ scans	11234 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (TWINABS; Bruker–Nonius, 2004)	$R_{int} = 0.057$
	$\theta_{max} = 68.1°$
	$h = -7 \rightarrow 7$
$T_{min} = 0.803$, $T_{max} = 0.979$	$k = -12 \rightarrow 12$
13961 measured reflections	$l = -24 \rightarrow 24$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0809P)^2]$
$R[F^2 > 2\sigma(F^2)] = 0.042$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.114$	$(\Delta/\sigma)_{max} = 0.001$
$S = 0.97$	$\Delta\rho_{max} = 0.37$ e Å^{-3}
13961 reflections	$\Delta\rho_{min} = -0.27$ e Å^{-3}
351 parameters	Extinction correction: SHELXL97
Only H-atom coordinates refined	Extinction coefficient: 0.0022 (4)

The crystals are non-merohedral twins, in which two components with nearly equal abundances of 51.5 and 48.5% are related by a twofold operation in which the components are related by the twin-law matrix (1.00 $\overline{0.18}$ 0.00, 0.00 $\overline{1}$.00 0.00, 0.00 0.00 $\overline{1}$.00).

Data collection: APEX2 (Bruker–Nonius, 2004); cell refinement: APEX2; data reduction: SAINT-Plus (Bruker–Nonius, 2004);

Table 1
Selected geometric parameters (Å, °).

N1A—C8A	1.4443 (10)	N1B—C8B	1.4465 (10)
N1A—C14A	1.4782 (11)	N1B—C14B	1.4803 (11)
N1A—C12A	1.4807 (11)	N1B—C12B	1.4827 (10)
O1A—C9A	1.2261 (10)	O1B—C9B	1.2230 (10)
O2A—C5A	1.3710 (10)	O2B—C5B	1.3762 (10)
O2A—C15A	1.4287 (11)	O2B—C15B	1.4255 (11)
C7A—C8A	1.3426 (12)	C7B—C8B	1.3431 (12)
C5A—O2A—C15A	116.68 (6)	C5B—O2B—C15B	116.86 (7)
O2A—C5A—C6A	115.62 (7)	O2B—C5B—C6B	115.35 (7)
O2A—C5A—C4A	124.12 (8)	O2B—C5B—C4B	124.21 (8)
O1A—C9A—C8A	124.99 (7)	O1B—C9B—C8B	125.02 (7)
C2A—C1A—C7A—C8A	−19.25 (13)	C2B—C1B—C7B—C8B	−21.74 (13)
C1A—C7A—C8A—C9A	−174.31 (7)	C1B—C7B—C8B—C9B	179.61 (7)
C7A—C8A—C9A—O1A	−8.26 (13)	C7B—C8B—C9B—O1B	−1.78 (12)

program(s) used to solve structure: SHELXS97 (Sheldrick, 1997); program(s) used to refine structure: SHELXL97 (Sheldrick, 1997); molecular graphics: XP in SHELXTL/PC (Sheldrick, 1995); software used to prepare material for publication: SHELXL97 and local procedures.

References

Bruker–Nonius (2004). APEX2, SAINT-Plus and TWINABS. Bruker–Nonius AXS Inc., Madison, Wisconsin, USA.

Domiano, P., Nardelli, M., Balsamo, A., Macchia, B. & Macchia, F. (1979). Acta Cryst. B35, 1363–1372.

Nilsson, B. M., Sundquist, S., Johansson, G., Nordvall, G., Glas, G., Nilvebrant, L. & Hacksell, U. (1995). J. Med. Chem. 38, 473–487.

Paulis, T., Hewlett, W. A., Schimidt, D. E., Mason, N. S., Trivedi, B. L. & Ebert, M. H. (1997). Eur. J. Med. Chem. 32, 385–396.

Sheldrick (1995). XP in SHELXTL/PC. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Sheldrick, G. M. (1997). SHELXS97 and SHELXL97. University of Göttingen, Germany.

Sonar, V. N., Parkin, S. & Crooks, P. A. (2004). Acta Cryst. C60, o659–o661.