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Key indicators

Single-crystal X-ray study

$T = 90\text{ K}$

Mean $\sigma(\text{C}-\text{C}) = 0.002\text{ \AA}$

R factor = 0.047

wR factor = 0.130

Data-to-parameter ratio = 16.7

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

(Z)-2-(2,4-Dimethoxybenzylidene)-1-azabicyclo[2.2.2]octan-3-ol

The title compound, $\text{C}_{16}\text{H}_{21}\text{NO}_3$, crystallizes in the monoclinic space group $P2_1/c$. The 2,4-dimethoxyphenyl ring is twisted by -39.8 (2)^\circ with respect to the plane of the double bond connected to the azabicyclic ring system. In addition to intermolecular hydrogen bonding, molecules are held together in the solid state by van der Waals interactions.

Comment

In the course 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/heteroar-3-ylmethylene)-1-azabicyclo[2.2.2]octan-3-ones (Sonar *et al.*, 2003*a,b*), and their crystal structures were determined to confirm the geometry and to establish the conformation of the molecules. It was observed that hydrogen bonding plays an important role in establishing the conformation of the molecules and strongly influences the crystal packing.

(Z)-2-(2,4-Dimethoxybenzylidene)-1-azabicyclo[2.2.2]octan-3-ol, (I), was prepared by condensation of 2,4-dimethoxybenzaldehyde, (III), with 1-azabicyclo[2.2.2]octan-3-one, (IV), under base catalysis, affording a single geometrical isomer, *viz.* (Z)-2-(2,4-dimethoxybenzylidene)-1-azabicyclo[2.2.2]octan-3-one, (II). Compound (II) was reacted with sodium borohydride in methanol, affording a single isomer, (I), which was initially identified by NMR spectroscopy. In order to confirm the geometry, and to obtain more detailed information on the structural conformation of the molecule, its crystal structure determination has been carried out and the results are presented here.

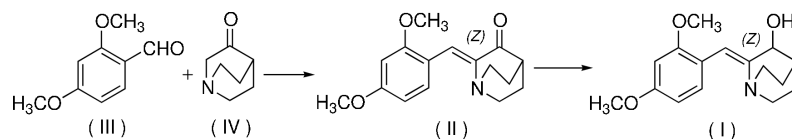


Fig. 1 shows a displacement ellipsoid plot of (I) and selected geometrical parameters are presented in Table 1. In the title compound, the C6—C9 bond is in a *trans* disposition with respect to the C10—C15 bond. The double bond and its attached atoms are nearly coplanar, the r.m.s. deviation of atoms N11, C10, C15, C9 and C6 from the mean plane passing through them being 0.0116 (9) Å. As expected, deviations from ideal bond-angle geometry around the Csp^2 atoms of the double bonds are observed. While the C9—C10—C15 angle shows a value of 121.62 (13)^\circ , close to the ideal geometry (120°), the N11—C10—C15, C9—C10—N11 and C10—C9—C6 angles [114.01 (12)^\circ , 124.37 (13)^\circ and 130.41 (14)^\circ respectively] are distorted because of steric hindrance of the double bond linking the two ring systems. These deviations contribute

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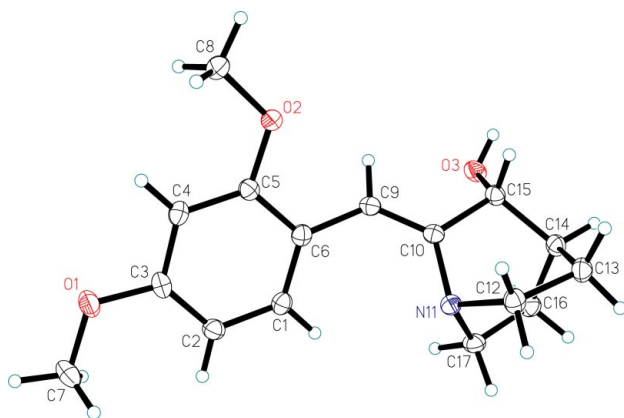


Figure 1

A view of the title compound, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

significantly to the relief of the intramolecular non-bonded interactions present in this portion of the molecule. The C1—C6—C9—C10 torsion angle [$-39.8(2)^\circ$] indicates a deviation of the 2,4-dimethoxyphenyl group from the plane of the double bond connected to the azabicyclic ring system. The C6—C9 bond length [$1.471(2) \text{ \AA}$] suggests conjugation of the C9=C10 bond π electrons with those of the 2,4-dimethoxyphenyl ring (Allen *et al.*, 1987).

The mode of packing of (I) along the **a** direction is illustrated in Fig. 2. In addition to intermolecular hydrogen bonding, van der Waals forces contribute to the stabilization of the crystal structure.

Experimental

A mixture of 2,4-dimethoxybenzaldehyde (0.499 g, 3 mmol) and 1-azabicyclo[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 into crushed ice (100 g) and the yellow crystalline solid, (II), that separated was collected by filtration and dried. To a stirred solution of (II) (0.547 g, 2 mmol) in methanol (25 ml) at 273 K was added NaBH_4 (0.758 g, 20 mmol) over a period of 15 min, and stirring was continued for 2 h at room temperature. Water (50 ml) was added, and the mixture was extracted with CHCl_3 ($3 \times 20 \text{ ml}$). The combined organic layers were dried over Na_2SO_4 and evaporated, affording (I) as a colorless solid; crystallization from methanol afforded colorless needles that were suitable for X-ray analysis. ^1H NMR (CDCl_3): δ 1.42–1.57 (*m*, 2H), 1.58–1.78 (*m*, 2H), 1.91–1.96 (*m*, 1H), 2.04–2.08 (*p*, 1H), 2.78–2.83 (*m*, 1H), 2.91–3.05 (*m*, 3H), 3.82 (*d*, 6H), 4.33 (*t*, 1H), 6.42 (*d*, 1H), 6.49 (*dd*, 1H), 6.59 (*d*, 1H), 8.21 (*d*, 1H); ^{13}C NMR (CDCl_3): δ 19.3, 25.4, 30.8, 47.5, 48.3, 55.6, 55.7, 71.7, 98.0, 104.5, 115.6, 117.6, 131.5, 150.4, 157.7, 159.9.

Crystal data

$\text{C}_{16}\text{H}_{21}\text{NO}_3$
 $M_r = 275.34$
 Monoclinic, $P2_1/c$
 $a = 6.20610(10) \text{ \AA}$
 $b = 14.0232(3) \text{ \AA}$
 $c = 15.8208(4) \text{ \AA}$
 $\beta = 101.0515(10)^\circ$
 $V = 1351.34(5) \text{ \AA}^3$
 $Z = 4$

$D_x = 1.353 \text{ Mg m}^{-3}$
 Mo $K\alpha$ radiation
 Cell parameters from 3205 reflections
 $\theta = 1.0\text{--}27.5^\circ$
 $\mu = 0.09 \text{ mm}^{-1}$
 $T = 90.0(2) \text{ K}$
 Semi-regular block, colorless
 $0.25 \times 0.18 \times 0.10 \text{ mm}$

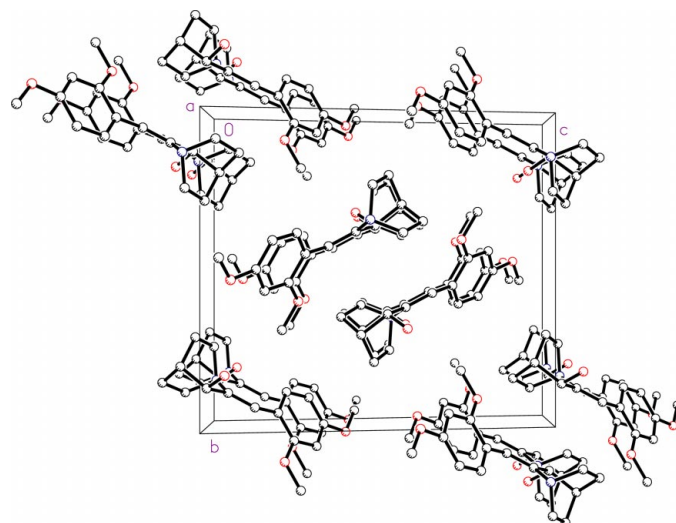


Figure 2

The crystal packing of (I), viewed along the **a** axis. H atoms have been omitted for clarity.

Data collection

Nonius KappaCCD diffractometer
 ω scans at fixed $\chi = 55^\circ$
 5998 measured reflections
 3074 independent reflections
 2241 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.030$
 $\theta_{\text{max}} = 27.4^\circ$
 $h = -8 \rightarrow 8$
 $k = -17 \rightarrow 18$
 $l = -20 \rightarrow 20$

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.047$
 $wR(F^2) = 0.130$
 $S = 1.49$
 3074 reflections
 184 parameters
 H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0764P)^2 + 0.0831P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\text{max}} = 0.001$
 $\Delta\rho_{\text{max}} = 0.26 \text{ e \AA}^{-3}$
 $\Delta\rho_{\text{min}} = -0.26 \text{ e \AA}^{-3}$

Table 1

Selected geometric parameters (\AA , $^\circ$).

O1—C3	1.3691 (17)	O3—H3	0.8400
O1—C7	1.4270 (18)	C6—C9	1.471 (2)
C1—C6	1.387 (2)	C9—C10	1.333 (2)
O3—C15	1.4245 (17)	C10—C15	1.529 (2)
C3—O1—C7	117.34 (12)	C9—C10—N11	124.37 (13)
C1—C6—C9	124.17 (14)	N11—C10—C15	114.01 (12)
C10—C9—C6	130.41 (14)	N11—C17—C16	112.54 (12)
C1—C6—C9—C10	$-39.8(2)$	C6—C9—C10—N11	$-2.1(3)$

Table 2

Hydrogen-bonding geometry (\AA , $^\circ$).

$D\cdots H\cdots A$	$D\cdots H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O3—H3 \cdots N11 ¹	0.84	2.04	2.8610 (16)	165

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

H atoms were located from difference electron-density maps, and were subsequently placed at calculated positions and treated using a riding model. C—H distances were in the range 0.95–1.00 \AA and the O—H distance was set to 0.84 \AA . U_{iso} was constrained to be 1.2 (1.5 for O) times U_{eq} of the parent atom.

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO-SMN*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *XP* in *SHELXTL* (Sheldrick, 1995); software used to prepare material for publication: *SHELXL97* and local procedures.

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