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(*Z*)-2-(Benzo[*b*]thiophen-3-ylmethylene)-1-azabicyclo[2.2.2]octan-3-one

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Key indicators

Single-crystal X-ray study
T = 90 K
Mean σ(C–C) = 0.002 Å
R factor = 0.026
wR factor = 0.070
Data-to-parameter ratio = 16.6

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

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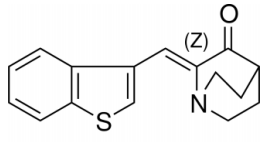
Crystals of the title compound, $C_{16}H_{15}NOS$, were obtained from a condensation reaction of benzo[*b*]thiophene-3-carboxaldehyde with 1-azabicyclo[2.2.2]octan-3-one and subsequent crystallization of the product from methanol. The title compound, containing a double bond that connects an azabicyclic ring system to a benzo[*b*]thiophen-3-ylmethylene group, was obtained as the *Z* geometric isomer, crystallizing in the triclinic space group *P*1.

Comment

A number of indole and benzo[*b*]thiophene analogs have been shown to possess interesting estrogenic and antiestrogenic effects. Some of these compounds inhibit estradiol with greater potency than tamoxifen, and inhibition of the growth of DMBA-induced mammary tumors by such compounds has been reported (Jones *et al.*, 1984). An *N*-protected analog of melatonin had comparable activity to melatonin, the fluoro derivative being the best in preventing ovulation in rats (Campaigne & Kim, 1983). Compounds containing the 3-aroyl-2-arylbenzo[*b*]thiophene ring system with methoxy substitution in the aryl moiety have been reported as anti-tubulin agents (Pinney *et al.*, 1999). Recently, tryptamine analogs have been found to be antagonists at the polyamine binding site on the *N*-methyl–D-aspartate receptor (Worthen *et al.*, 2001). As part of our synthetic strategy to obtain rigid analogues and isosteres of tryptamine, we synthesized a series of 2-(heteroaryl-3-ylmethylene)-1-azabicyclo[2.2.2]octan-3-ones (Sonar *et al.*, 2003*a*).



(I)

The title compound, (I), was designed as a conformationally restrained benzo[*b*]thiophene-3-ethylamine (a sulfur isostere of tryptamine) analog, and was prepared by the condensation of benzo[*b*]thiophene-3-carboxaldehyde with 1-azabicyclo[2.2.2]octan-3-one under base catalysis, to afford a single geometrical isomer. The structure of the product, (*Z*)-2-(benzo[*b*]thiophen-3-ylmethylene)-1-azabicyclo[2.2.2]octan-3-one, was initially identified by NMR spectroscopy. In order to confirm the geometry of the double bond in this compound, and to obtain more detailed information on the structural conformation of the molecule that may be of value in structure–activity analysis, an X-ray structure determination has been carried out, and the results are presented here.

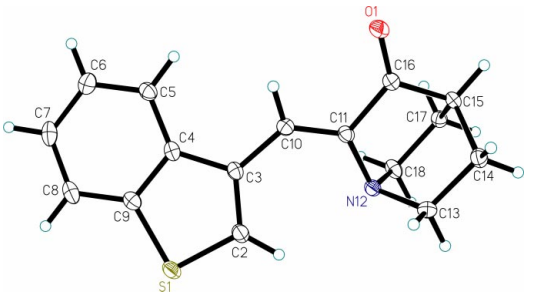


Figure 1
A view of the title compound, showing the atom-numbering scheme. Displacement ellipsoids for non-H atoms are drawn at the 50% probability level.

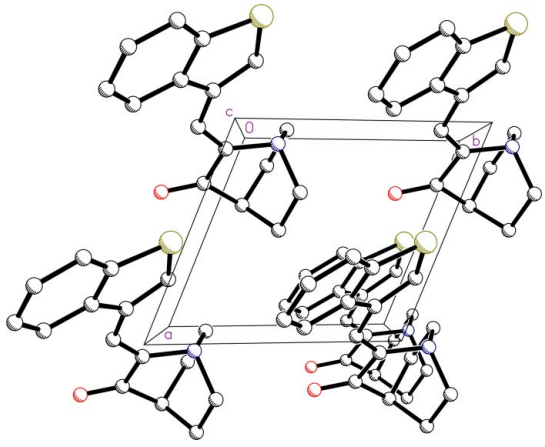


Figure 2
Crystal packing of (I), viewed down the *c* axis. H atoms have been omitted for clarity.

Fig. 1 shows a view of (I). Selected geometrical parameters are presented in Table 1. The C3—C10 bond is *trans* with respect to the C11—C16 bond. As expected, deviations from the ideal bond-angle geometry around the Csp^2 atoms of the double bonds are observed. While the C10—C11—C16 angle [120.76 (12)°] is very close to ideal geometry (120°), the C2—C3—C10, C3—C10—C11, C10—C11—N12, C11—C16—O1 and C15—C16—O1 angles assume values of 126.39 (13), 129.26 (12), 125.28 (12), 124.87 (12) and 125.04 (12)°, respectively, because of steric hindrance of the double bond linking the two-ring systems and distortion of the five-membered heterocyclic ring. Also, deviations from tetrahedral angles were observed for angles N12—C18—C17, N12—C13—C14 and N12—C11—C16 with values of 111.92 (11), 112.39 (11) and 113.80 (11)°, respectively. These deviations result from the intramolecular non-bonded interactions present in the aza-bicyclic moiety, and from the presence of the S atom in the five-membered ring of the benzo[*b*]thiophene nucleus. However, no ring flip was observed, as is seen in a related thiophene analog (Sonar *et al.*, 2003*b*). Fig. 2 shows the crystal packing of (I), viewed down the *c* axis.

Experimental

A mixture of benzo[*b*]thiophene-3-carboxaldeyde (0.487 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 refluxed for 5 h. The cooled reaction mixture was poured into 100 g of crushed ice and the yellow crystalline solid that separated out was collected by filtration and dried. Recrystallization from methanol afforded a yellow crystalline product, which was suitable for X-ray analysis. ^{1}H NMR ($CDCl_3$): δ 2.02–2.09 (*td*, J = 8.1, 3 Hz, 4H), 2.67 (*p*, J = 3 Hz, 1H), 2.98–3.08 (*m*, 2H), 3.15–3.24 (*m*, 2H), 7.36–7.48 (*m*, 3H), 7.88 (*d*, J = 7.2 Hz, 1H), 8.00 (*d*, J = 7.8 Hz, 1H), 8.89 (*s*, 1H). ^{13}C NMR ($CDCl_3$): δ 26.4, 40.6, 40.7, 47.6, 115.4, 115.5, 121.4, 122.9, 124.8, 129.0, 133.2, 133.3, 139.1, 139.3, 144.9, 206.0. HRMS calculated: 269.0869; found: 269.0870.

Crystal data

$C_{16}H_{15}NOS$
M_r = 269.35
Triclinic, *P*1
a = 6.21440 (10) Å
b = 6.80780 (10) Å
c = 8.4492 (2) Å
α = 102.8959 (9)°
β = 94.7214 (9)°
γ = 110.2617 (10)°
V = 321.860 (10) Å^3
Z = 1
D_x = 1.390 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1439 reflections
θ = 1.0–27.5°
μ = 0.24 mm^{-1}
T = 90.0 (2) K
Irregular block, yellow
0.30 × 0.30 × 0.15 mm

Data collection

Nonius KappaCCD diffractometer
ω scans at fixed χ = 55°
Absorption correction: multi-scan (*SCALEPACK*; Otwinowski & Minor)
T_{min} = 0.931, T_{max} = 0.965
7534 measured reflections
2858 independent reflections
2811 reflections with $I > 2\sigma(I)$
R_{int} = 0.029
θ_{max} = 27.5°
$h = -8 \rightarrow 8$
$k = -8 \rightarrow 8$
$l = -10 \rightarrow 10$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.026
$wR(F^2)$ = 0.070
S = 1.15
2858 reflections
172 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0582P)^2 + 0.0899P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.002
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}
Absolute structure: Flack (1983), 1389 Friedel pairs
Flack parameter = −0.03 (4)

Table 1
Selected geometric parameters (Å, °).

S1—C2	1.7259 (14)	C10—H10	0.9500
S1—C9	1.7404 (15)	C11—N12	1.4447 (17)
O1—C16	1.2174 (16)	C11—C16	1.4966 (17)
C2—C3	1.3631 (19)	N12—C18	1.4867 (18)
C3—C10	1.4598 (18)	C14—C15	1.5369 (18)
C10—C11	1.3374 (18)	C15—H15	1.0000
C2—S1—C9	91.66 (7)	C10—C11—N12	125.28 (12)
C3—C2—S1	113.61 (11)	N12—C11—C16	113.80 (11)
C2—C3—C4	111.74 (12)	N12—C13—C14	112.39 (11)
C2—C3—C10	126.39 (13)	O1—C16—C11	124.87 (12)
C8—C9—S1	126.86 (11)	O1—C16—C15	125.04 (12)
C11—C10—C3	129.26 (12)	N12—C18—C17	111.92 (11)

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO–SMN* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: XP in *SHELXTL* (Sheldrick, 1995); software used to prepare material for publication: *SHELX*97 and local procedures.

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