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(*Z*)-2-Thiophen-3-ylmethylene-1-aza-bicyclo[2.2.2]octan-3-one

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Key indicators

Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.002 Å
Disorder in main residue
R factor = 0.045
wR factor = 0.122
Data-to-parameter ratio = 17.1

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

The crystal structure of $C_{12}H_{13}NOS$, which was obtained in a base-catalysed condensation reaction of thiophene-3-carboxaldehyde with 1-aza-bicyclo[2.2.2]octan-3-one, is presented. The title compound, which contains a double bond connecting an azabicyclic ring system to a thiophen-3-ylmethylene moiety, crystallizes from solution in methanol and has a thienyl ring-flip disorder.

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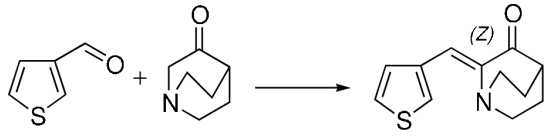
Comment

Thiophene derivatives have been found to exhibit a wide range of biological activity. Several reviews of biologically significant thiophene derivatives have been published. One review (Drehsen & Engel, 1983) provides detailed insights into the structure–activity relationships that have been developed for various thiophene congeners. Compounds active as chemotherapeutics, in the central nervous system (CNS) and in the cardiovascular system, as well as other miscellaneous derivatives were reported. 5-Bromothiophene-ethyl thioureas have been identified as potent inhibitors of HIV-1 strain $HTLV_{IIIB}$ in human peripheral blood mononuclear cells (Venkatachalam *et al.*, 2001). Thiophene derivatives also exhibit antitumor activity (Dallemagne *et al.*, 2002). 2–Amino-3-arylthiophenes have been reported to act as allosteric enhancers at the A_1 adenosine receptor (Baraldi *et al.*, 2003; Lutjens *et al.*, 2003). Recently, tryptamines have been found to be polyamine site antagonists at the *N*-methyl-D-asparatate receptor (Worthen *et al.*, 2001). As part of our synthetic strategy to obtain rigid analogs of tryptamine, we synthesized a series of 2-(heteroaryl-3-ylmethylene)-1-azabicyclo[2.2.2]octan-3-ones. The title compound, (I), was designed as a conformationally restrained thiophene-3-ethylamine analogue, and prepared by condensation of thiophene-3-carboxaldeyde 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-thiophen-3-ylmethylene-1-aza-bicyclo[2.2.2]octan-3-one, was initially identified by NMR spectroscopy. In order to confirm the geometry of this compound, and to obtain more detailed information of the structural conformation of the molecule that may be of value in structure–activity analysis, its X-ray structure determination has been carried out and the results are presented here.



(I)

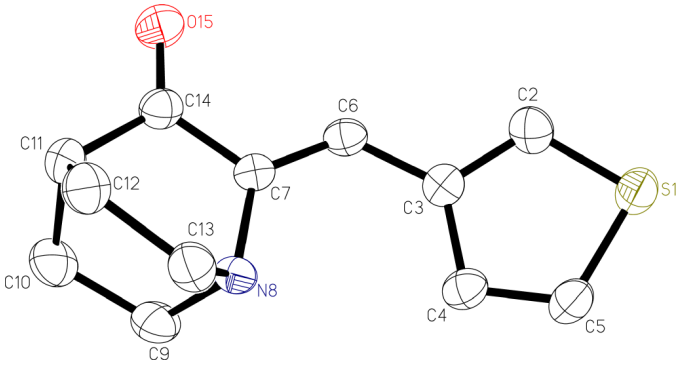


Figure 1
A view of (I). Displacement ellipsoids are drawn at the 50% probability level.

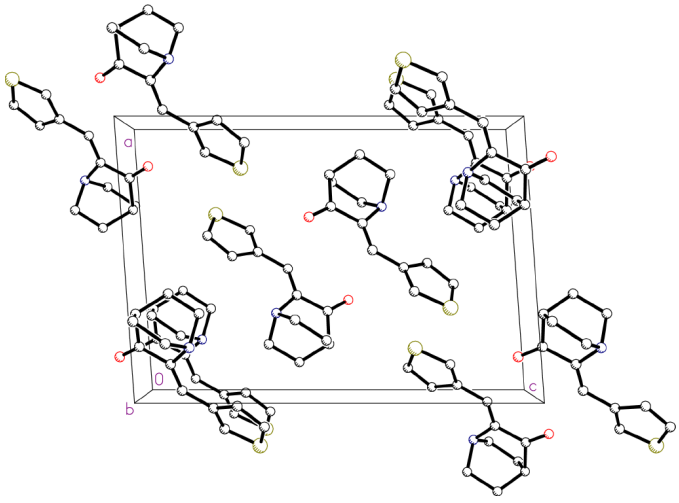


Figure 2
The packing of (I), viewed along *b*.

Fig. 1 shows an ellipsoid plot of (I) and selected geometrical parameters are presented in Table 1. In the title molecule, the C3—C6 bond is in a *trans* disposition with respect to the C7—C14 bond. The double bond is nearly planar in the molecule, as indicated by the value of 0.0004 (7) Å for the root-mean-square deviation of the atoms from the best plane passing through them. As expected, deviations from the ideal bond-angle geometry around the sp^2 C atoms of the double bonds are observed. While the C6—C7—C14 angle shows a value of 122.43 (14)°, close to ideal geometry (120°), the N8—C7—C14, C6—C7—N8 and C7—C6—C3 angles, because of steric hindrance of the double-linking two-ring systems, assume values of 113.26 (13)°, 124.03 (15)°, and 129.04 (15)°, respectively. These deviations contribute significantly to the release of the intramolecular non-bonded interactions present in this portion of the molecule. The thienyl-ring S atom is disordered over two positions by a twofold rotation about the C3—C6 bond. As a result, the geometry of this ring is somewhat distorted, and no particular significance is placed on bond parameters within this ring.

The mode of packing of compound (I), in projection along the **b** direction, is illustrated in Fig. 2.

Experimental

A mixture of thiophene-3-carboxaldeyde (0.337 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 crushed ice and the yellow crystalline solid that separated was collected by filtration and dried. Recrystallization from methanol afforded a yellow crystalline product, which was suitable for X-ray analysis. ^{1}H NMR ($CDCl_3$, p.p.m.): δ 2.02 (*m*, 4H), 2.62 (*p*, *J* = 3 Hz, 1H), 2.92–3.01(*m*, 2H), 3.10–3.20 (*m*, 2H), 7.07 (*s*, 1H), 7.28–7.31 (*m*, 1H), 7.77 (*d*, *J* = 5.1 Hz, 1H), 8.01 (*t*, 1H). ^{13}C NMR ($CDCl_3$, p.p.m.): δ 26.3, 40.7, 47.8, 119.3, 125.5, 130.1, 131.1, 135.9, 143.3, 206.4.

Crystal data

$C_{12}H_{13}NOS$	D_x = 1.363 Mg m^{-3}
M_r = 219.29	Mo $K\alpha$ radiation
Monoclinic, $P2_1/n$	Cell parameters from 6483 reflections
a = 11.3210 (10) Å	θ = 1.0–27.5°
b = 5.8790 (6) Å	μ = 0.27 mm^{-1}
c = 16.100 (2) Å	T = 173 (2) K
β = 94.058 (10)°	Rod, yellow
V = 1068.9 (2) Å^3	0.40 × 0.33 × 0.20 mm
Z = 4	

Data collection

Nonius KappaCCD diffractometer	2452 independent reflections
ω scans at fixed χ = 55°	1802 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (*SCALEPACK*; Otwinowski & Minor, 1997)	R_{int} = 0.042
	θ_{max} = 27.5°
	$h = -14 \rightarrow 14$
T_{min} = 0.899, T_{max} = 0.947	$k = -7 \rightarrow 7$
7996 measured reflections	$l = -20 \rightarrow 20$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0604P)^2 + 0.2115P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.045	$(\Delta/\sigma)_{max}$ = 0.002
$wR(F^2)$ = 0.122	$\Delta\rho_{max}$ = 0.24 e Å^{-3}
S = 1.03	$\Delta\rho_{min}$ = −0.25 e Å^{-3}
2452 reflections	Extinction correction: *SHELXL*
143 parameters	Extinction coefficient: 0.020 (3)
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °).

S1—C2	1.607 (3)	C6—C7	1.335 (2)
S1—C5	1.718 (8)	C7—N8	1.4456 (19)
C2—C3	1.399 (2)	C7—C14	1.483 (2)
C3—C4	1.407 (2)	N8—C13	1.476 (2)
C3—C6	1.452 (2)	N8—C9	1.480 (2)
C4—C5	1.395 (7)	C14—O15	1.2255 (19)
C2—C3—C6	121.44 (15)	N8—C9—C10	112.07 (14)
C4—C3—C6	127.22 (15)	C11—C10—C9	108.16 (14)
C7—C6—C3	129.04 (15)	C14—C11—C12	106.92 (14)
C6—C7—N8	124.03 (15)	C10—C11—C12	108.34 (15)
C6—C7—C14	122.43 (14)	C11—C12—C13	108.51 (14)
N8—C7—C14	113.26 (13)	N8—C13—C12	111.86 (13)
C7—N8—C13	107.99 (12)	O15—C14—C7	124.81 (16)
C7—N8—C9	108.39 (13)	O15—C14—C11	124.58 (16)
C13—N8—C9	108.48 (14)	C7—C14—C11	110.58 (13)

H atoms were located in a difference electron density map and subsequently placed at calculated positions (C—H 0.95–1.00 Å), with U_{iso} values set to 1.2 times U_{eq} of the parent atom.

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 (Sheldrick, 1997) and local procedures.

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