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4-Morpholinyl{2-[1-(2-pyridinyl)ethylidene]diazan-2-iumylidene}methanethiolate

Hoong-Kun Fun,[a]* Suchada Chantrapromma,[b]‡ V. Suni,[c] A. Sreekanth,[c] S. Sivakumar[c] and M. R. Prathapachandra Kurup[c]

[a]X-ray Crystallography Unit, School of Physics, Universiti Sains Malaysia, 11800 USM, Penang, Malaysia, [b]Department of Chemistry, Faculty of Science, Prince of Songkla University, Hat-Yai, Songkhla 90112, Thailand, and [c]Department of Applied Chemistry, Cohin University of Science and Technology, Kochi 682022, India

‡ Additional correspondence author, email: suchada.c@psu.ac.th

Correspondence e-mail: hkfun@usm.my

Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
R factor = 0.044
wR factor = 0.125
Data-to-parameter ratio = 16.4

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

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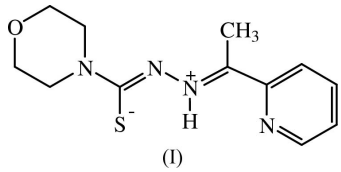
The title compound, $C_{12}H_{16}N_4OS$, is zwitterionic and exists in the *EZ* configuration of thiosemicarbazones. The thiocarbonyl S atom and coordinating pyridyl N atom are aligned *cis* to each other, avoiding the possibility of a structural reorientation upon coordination. Two crystallographically independent molecules, *A* and *B*, are observed in the asymmetric unit, with the morpholyl ring adopting a chair conformation in both molecules. N—H···N and N—H···S intramolecular hydrogen bonds are observed in the molecular structure, generating four rings of motif $R_1^2(5)$. There is zigzag packing in the unit cell, involving both intra- and intermolecular hydrogen-bonding interactions.

Comment

Thiosemicarbazones coordinate *in vivo* to metallic cations by binding through the thioketo S and hydrazinic N atoms. A broad spectrum of medicinal properties of this class of compounds has been studied for activity against tuberculosis, leprosy, psoriasis, rheumatism and coccidiosis (Demertzi *et al.*, 1997). Some thiosemicarbazones show selective inhibition of herpes simplex virus (HSV) infection *in vitro* and thiosemicarbazones are active inhibitors of *in vivo* HSV genital infection. The effect of thiosemicarbazones against the human immunodeficiency virus (HIV) has also been reported (Logan *et al.*, 1975). It is implicit from the literature that the presence of a bulky group at the terminal N3 atom enhances biological activity. For instance, the anti-smallpox activity of metal complexes of thiosemicarbazones is observed to depend upon the group at the N3 position (Durham *et al.*, 1974). Thiosemicarbazones derived from 2-acetylpyridine have been shown to have substantial clinical significance, such as antileprotic activity and ribonucleotide diphosphate reductase (RDR) activity (Dobek *et al.*, 1980). In view of these potential antimicrobial properties of heterocyclic thiosemicarbazones, for the past decade we have synthesized and characterized a wide variety of compounds of this class (Sreekanth *et al.*, 2004; Joseph *et al.*, 2004; Philip *et al.*, 2004; John *et al.*, 2003; Usman, Razak, Chantrapromma, Fun, Philip *et al.*, 2002; Usman, Razak, Chantrapromma, Fun, Sreekanth *et al.*, 2002; Bindu *et al.*, 1999; Garg *et al.*, 1988) and we report here the distinctive structural features of the title compound, (I).



(I)

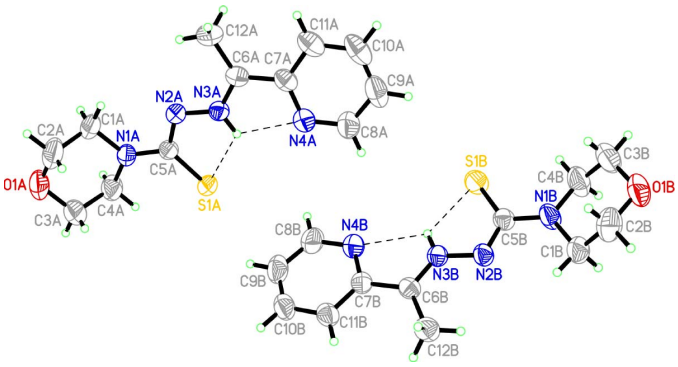


Figure 1
The structure of the asymmetric unit of (I), showing 50% probability displacement ellipsoids and the atom-numbering scheme. Dashed lines indicate intramolecular hydrogen bonds.

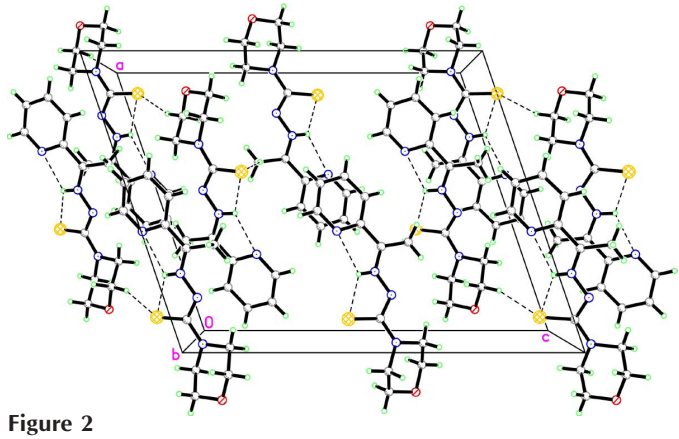


Figure 2
The packing of (I), viewed down the *b* axis. Hydrogen bonds are shown as dashed lines.

A report of the crystal structure of (I) has already been published (Nomiya *et al.*, 2004), but limited details of the molecular geometry were presented and the hydrogen bonding was not discussed. In that paper, it was reported that solution NMR spectra revealed the presence of three tautomers (*E*, *E*′ and *Z* forms), whereas solid-state NMR showed a single species, *viz*. the *E*′ form; this latter form was confirmed by the X-ray crystallographic study.

Two crystallographically independent molecules *A* and *B* constitute the asymmetric unit of (I), and the geometric parameters of each are almost identical. Bond lengths and angles in (I) have normal values (Allen *et al.*, 1987), except for N1—C5, C5—S1, C5═N2 and N2—N3. In each independent molecule, the N2—N3 distance [1.350 (2) Å in molecule *A* and 1.354 (2) Å in molecule *B*] is intermediate between an N—N single bond and an N═N double bond; this agrees well with the situation in similar thiosemicarbazones (Palenik *et al.*, 1974). Also, the C—S distance of 1.713 (2) Å observed in both molecules *A* and *B* is intermediate between a single C—S and C═S bond, (1.82 and 1.56 Å, respectively; Huheey *et al.*, 1993). The C5═N2 [1.352 (2) and 1.350 (3) Å] and N1—C5 [1.353 (3) and 1.350 (3) Å] distances are also intermediate between single- and double-bond values. In summary, there appears to be extensive delocalization of the electron density of the thiosemicarbazone group.

Fig. 1 shows a perspective view of the asymmetric unit of (I), together with the atomic labelling scheme. Except for the morpholinyl ring, each molecule is essentially planar. For the thiosemicarbazone group, the maximum deviation from the mean plane is 0.031 (2) Å for atom N1*A*. In each molecule, the morpholinyl ring adopts a chair conformation.

Torsion angle values of −0.9 (3) and 179.57 (2)° in molecule *A*, and −3.1 (3) and 176.28 (2)° in molecule *B*, for C12—C6—N3—N2 and N3—N2—C5—N1, respectively, reveal the *cis* and *trans* alignments of the methyl and morpholinyl moieties with respect to the thiosemicarbazone chain. The pyridyl ring and the methyl group are aligned at a C12—C6—C7—N4 torsion angle of 178.0 (2)° in molecule *A* and −177.9 (2)° in molecule *B*. With respect to the C6═N3 and C5═N2 bonds, both molecules adopt *E* and *Z* configurations, respectively. Values of −3.8 (2) and −0.8 (3)° for S1—C5—N2—N3 in molecules *A* and *B*, respectively, show that the thiocarbonyl S1 atom is *cis* -positioned with respect to the hydrazinic N atom. Thiosemicarbazone ligands with pyridyl rings in the keto part commonly exhibit a configuration in which the coordinating pyridyl N is aligned *trans* to the thiocarbonyl S atom. During their coordination to metallic cations, these thiosemicarbazones undergo a structural reorientation, resulting in *cis* alignment of the coordinating thiolate S and pyridyl N atoms. However, in the present compound, the thiosemicarbazone ligand as such remains in the *cis* configuration with respect to the pyridyl N and thiocarbonyl S atoms; this is a unique structural attribute of (I).

An extensive network of intra- and intermolecular interactions contributes towards the stability of the molecule in the crystal structure (Table 2). A packing diagram is depicted in Fig. 2. Four prominent intramolecular hydrogen bonds are observed (Table 2), and these give rise to four five-membered rings of motif $R_1^1(5)$ (Etter *et al.*, 1990), *viz*. N4*A*/H1N3/N3*A*/C6*A*/C7*A*, S1*A*/H1N3/N3*A*/N2*A*/C5*A*, N4*B*/H2N3/N3*B*/C6*B*/C7*B* and S1*B*/H2N3/N3*B*/N2*B*/C5*B*. Weak intermolecular C—H···N and C—H···S interactions are also observed in the crystal structure (Table 2). Molecules *A* and *B* are arranged in an offset fashion, and adjacent units are linked *via* C2*A*—H2*AC*···S1*B* interactions, resulting in a zigzag packing in the unit cell. These intra- and intermolecular hydrogen-bonding interactions are responsible for the packing of the molecules in the unit cell.

Experimental

A solution of 4-methyl-4-pyridyl-3-thiosemicarbazide (1 g, 5.52 mmol) in acetonitrile (5 ml) was treated with morpholine (480 mg, 5.52 mmol) and 2-acetylpyridine (668 mg, 5.52 mmol). The solution was heated at reflux for 15 min and then chilled, and the crystals that separated were collected and washed well with acetonitrile. This afforded 850 mg of stout yellow blocks of (I). The compound was recrystallized from methanol. Single crystals suitable for X-ray diffraction were grown by slow evaporation of a dilute solution in methanol at room temperature (m.p. 461 K). Yield is *ca* 58%.

Crystal data

$C_{12}H_{16}N_4OS$	D_x = 1.323 Mg m^{-3}
M_r = 264.35	Mo $K\alpha$ radiation
Monoclinic, $P2_1/c$	Cell parameters from 14 456 reflections
a = 14.158 (9) Å	θ = 2.2–26.5°
b = 11.075 (7) Å	μ = 0.24 mm^{-1}
c = 17.877 (1) Å	T = 293 (2) K
β = 108.776 (1)°	Block, yellow
V = 2654 (2) Å^3	0.64 × 0.44 × 0.40 mm
Z = 8	

Data collection

Siemens SMART CCD area-detector diffractometer	5503 independent reflections
	4012 reflections with $I > 2\sigma(I)$
ω scans	R_{int} = 0.020
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)	θ_{max} = 26.5°
	$h = -12 \rightarrow 17$
T_{min} = 0.882, T_{max} = 0.909	$k = -13 \rightarrow 13$
14 456 measured reflections	$l = -22 \rightarrow 22$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0543P)^2 + 1.0486P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.044	
$wR(F^2)$ = 0.125	
S = 1.05	$(\Delta/\sigma)_{max}$ = 0.001
5503 reflections	$\Delta\rho_{max}$ = 0.21 e Å^{-3}
335 parameters	$\Delta\rho_{min}$ = −0.21 e Å^{-3}
H atoms treated by a mixture of independent and constrained refinement	

Table 1
Selected geometric parameters (Å, °).

S1*A*—C5*A*	1.713 (2)	S1*B*—C5*B*	1.713 (2)
O1*A*—C2*A*	1.416 (4)	O1*B*—C3*B*	1.416 (3)
O1*A*—C3*A*	1.422 (3)	O1*B*—C2*B*	1.421 (3)
N1*A*—C5*A*	1.353 (3)	N1*B*—C5*B*	1.350 (3)
N1*A*—C4*A*	1.451 (3)	N1*B*—C4*B*	1.454 (3)
N1*A*—C1*A*	1.460 (3)	N1*B*—C1*B*	1.463 (3)
N2*A*—N3*A*	1.350 (2)	N2*B*—C5*B*	1.350 (3)
N2*A*—C5*A*	1.352 (2)	N2*B*—N3*B*	1.354 (2)
N3*A*—C6*A*	1.299 (2)	N3*B*—C6*B*	1.294 (3)
N4*A*—C8*A*	1.334 (3)	N4*B*—C8*B*	1.328 (3)
N4*A*—C7*A*	1.340 (3)	N4*B*—C7*B*	1.345 (3)
N3*A*—N2*A*—C5*A*—N1*A*	176.28 (17)	N3*B*—N2*B*—C5*B*—N1*B*	179.20 (18)
N3*A*—N2*A*—C5*A*—S1*A*	−3.8 (2)	N3*B*—N2*B*—C5*B*—S1*B*	−0.8 (3)
N2*A*—N3*A*—C6*A*—C12*A*	−3.1 (3)	N2*B*—N3*B*—C6*B*—C12*B*	−0.9 (3)
C12*A*—C6*A*—C7*A*—N4*A*	178.0 (2)	C12*B*—C6*B*—C7*B*—N4*B*	−177.9 (2)

Table 2
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3*A*—H1N3···S1*A*^{i}	0.90 (2)	2.33 (2)	2.837 (2)	116 (2)
N3*A*—H1N3···N4*A*^{i}	0.90 (2)	2.20 (3)	2.626 (3)	109 (2)
N3*B*—H2N3···S1*B*^{i}	0.86 (2)	2.31 (2)	2.835 (2)	120 (2)
N3*B*—H2N3···N4*B*^{i}	0.86 (2)	2.26 (2)	2.639 (3)	106 (2)
C1*A*—H1*AB*···N2*A*^{i}	0.97	2.27	2.703 (3)	106
C2*A*—H2*AC*···S1*B*^{ii}	0.97	2.74	3.673 (3)	161
C4*A*—H4*AB*···S1*A*^{i}	0.97	2.56	3.081 (3)	114
C1*B*—H1*BB*···N2*B*^{i}	0.97	2.28	2.714 (3)	106
C12*A*—H12*A*···N2*A*^{i}	0.96	2.36	2.811 (3)	108
C12*B*—H12*D*···N2*B*^{i}	0.96	2.39	2.804 (3)	105
C4*B*—H4*BB*···S1*B*^{i}	0.97	2.56	3.077 (3)	113

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

H atoms were placed in calculated positions, with an N—H distance of 0.86 Å and C—H distances in the range 0.93–0.97 Å. The H atoms attached to N3*A* and N3*B* were freely refined; the others were refined in a riding-model approximation, with U_{iso}(H) constrained to be 1.5U_{eq} of the carrier atom for methyl H atoms and 1.2U_{eq} for the remaining H atoms.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL* and *PLATON* (Spek, 2003).

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