organic compounds

Salicylaldehyde 4,4′-(hexane-1,6-diyl)-thiosemicarbazone

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The title compound, $C_{14}H_{19}N_3OS$, is in the thioketo form, with the thione S and hydrazine N atoms *cis* with respect to each other so that the S atom is involved in inter- and intramolecular hydrogen bonds simultaneously. Intermolecular $C—H\cdots S$ and $C—H\cdots O$ hydrogen bonds result in one-dimensional polymeric chains of molecules along the *a* axis. A weak $C—H\cdots\pi$ ring interaction binds the polymeric chains together.

Comment

Thiosemicarbazones are considered as an important class of nitrogen–sulfur donor ligands because of their highly interesting chemical, biological and medicinal properties (Campbell, 1975; Scovill *et al.*, 1982). The biological activity of thiosemicarbazones is related to their chelating ability with transition metal ions, bonding through N, N and S atoms (Sartorelli *et al.*, 1977) or O, N and S atoms (Bindu *et al.*, 1997, 1999; Lu *et al.*, 1993; Dutta *et al.*, 1997). The presence of substituents at the 4-position has been shown to affect the activity of thiosemicarbazones and their metal complexes (Liberta & West, 1992). For example, metal complexes of 2-acetylpyridine thiosemicarbazones are found to exhibit increased antineoplastic activity when the N atom in the 4-position is part of a hexamethyleneiminyl ring instead of being a propyl- or dipropyl-carrying amine group (Kovala-Demertzi *et al.*, 1997). The 3-hexamethyleneiminyl thiosemicarbazone of 2-acetylpyridine has been screened against HSV-1, HSV-2 and leukemia P388 (Klayman *et al.*, 1983). The coordination chemistry of *O*,*N*,*S*-donor ligands has been of considerable interest because of their remarkable structural and biological properties (John *et al.*, 2002; Casas *et al.*, 2000). However, thiosemicarbazones of salicylaldehyde where the 4-position is part of a ring system have not been widely investigated. We have reported 2-hydroxyacetophenone-3-hexamethylene-iminyl thiosemicarbazone and its metal complexes (John *et al.*, 2002, 2003, 2004, 2005). We report here a new *O*,*N*,*S*-tridentate ligand, *viz.* the title compound, (I), shown in the scheme with the conventional numbering for thiosemicarbazones. Hereafter we use labels for (I) (Fig. 1) consistent with those used

for salicylaldehyde thiosemicarbazone (Chattopadhyay *et al.*, 1988).

Compound (I) adopts an *E* configuration about the N3—C8 and C7—N2 bonds relative to the N3—N2 bond (Fig. 1). The N3—N2—C7—S1 torsion angle of $-6.0\,(3)°$ indicates that the thione S1 and hydrazine N3 atoms are in the *Z* configuration with respect to the C7—N2 bond, similar to 2-pyridine-formamide 3-hexamethyleneiminyl thiosemicarbazone (Bermejo *et al.*, 2004) but in contrast to the parent salicylaldehyde thiosemicarbazone (Chattopadhyay *et al.*, 1988), where an *E* configuration exists. The *Z* configuration eliminates the possibility of any steric repulsion between the bulky rings. As a result, atom N3 lies *trans* to N1, with an N3—N2—C7—N1 torsion angle of 174.1 (2)°.

(I)
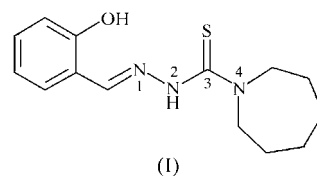
The C7—S1 and C7—N2 bond distances (Table 1) are similar to the C=S double and C—N single bonds in thiosemicarbazones (Usman *et al.*, 2002; Chattopadhyay *et al.*, 1988; Philip *et al.*, 2004) and suggest the thione form for (I). It is implicit from the literature that the delocalization of electron density along the thiosemicarbazide moiety is a characteristic of thiosemicarbazones. For instance, the C—S distance is always intermediate between a C—S single bond and a C=S double bond (1.82 and 1.56 Å, respectively; Huheey *et al.*, 1993). Palenik *et al.* (1974) pointed out that apparently the parent aldehyde or ketone moiety has a strong influence on the C—S bond distance. The C7—S1 bond length in (I) is in agreement with values in salicylaldehyde thiosemicarbazone (Chattopadhyay *et al.*, 1988) and does not differ significantly from the corresponding lengths in the thiosemicarbazones of some different aldehydes and ketones (Palenik *et al.*, 1974; Mathew & Palenik, 1971; Dincer *et al.*, 2005; Bain *et al.*, 1997; Sreekanth & Kurup, 2004; Sreekanth *et al.*, 2005; Rapheal *et al.*, 2005). The presence of electron density delocalization is again confirmed by the N3—N2, N2—C7 and C7—N1 bond lengths (Table 1). Of the two C7—N bonds of (I), C7—N1 is significantly shorter than C7—N2,
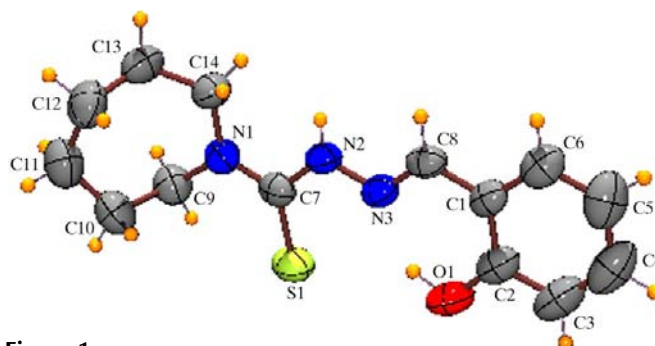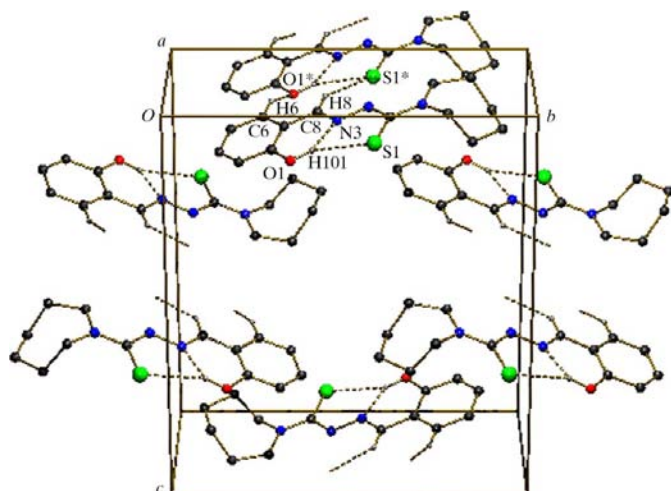
Figure 1
Compound (I), with 50% probability displacement ellipsoids and the atom-numbering scheme (Farrugia, 1997). H atoms are shown as small spheres of arbitrary radii.

Figure 2
The packing of (I), viewed along the *a* axis, showing intra- and intermolecular hydrogen bonds as broken lines.

suggesting greater double-bond character for the former bond and indicating an increased electron localization at this substituted end. This is confirmed by the typical double-bond nature [1.269 (3) Å] of the C8=N3 bond.

The salicylaldehyde thiosemicarbazone moiety, excluding atom N1, is almost planar, with a maximum deviation from the mean plane of 0.151 (1) Å for atom S1. The hexamethylene-iminyl ring adopts a chair conformation [the puckering para-meters (Cremer & Pople, 1975) are $Q_T = 0.799$ (3) Å, $\theta_2 = 38.4$ (3)°, $\varphi_2 = 45.6$ (3)° and $\varphi_3 = 73.95$ (3)°]. The *Cg*1 plane [comprising atoms C1–C6, with a maximum deviation of 0.003 (2) Å for atom C6] makes an angle of 40.59 (13)° with the mean plane through the hexamethyleneiminyl ring (atoms N1/C9–C14).

There are two intramolecular and two intermolecular hydrogen bonds (Table 2 and Fig. 2) in (I). The intramolecular N3···H1O1—O1 hydrogen bond is very strong, as indicated by the bond length of 1.76 (3) Å, which is shorter than the value of 1.96 (3) Å seen in salicylaldehyde thiosemicarbazone (Chattopadhyay *et al.*, 1988) and similar to the values in some hydrazones (Liu & Li, 2004; Ali *et al.*, 2005). Simultaneously, atom H1O1 is involved in a weaker hydrogen bond with atom S1, forming a five-membered ring, N3/H1O1/S1/C7/N2. The intermolecular hydrogen bonds involving atoms H6 and H8 with atoms O1$^{\mathrm{i}}$ and S1$^{\mathrm{i}}$ [symmetry code: (i) *x* + 1, *y*, *z*], respectively, form infinite one-dimensional chains of mol-ecules along the *a* axis. The strengths of these four hydrogen bonds have a direct influence on the angles subtended at atoms C2 and C7 (Table 2). The weak C9—H9B···π inter-action (Table 2) with *Cg*1 reinforces the packing stability along the *c* axis.

Experimental

4-Methyl-4-phenylthiosemicarbazide was prepared as described by Scovill (1991). A solution of 4-methyl-4-phenylthiosemicarbazide (1 g, 5.52 mmol) in acetonitrile (5 ml) was treated with salicylalde-hyde (0.58 ml, 5.52 mmol) and hexamethyleneimine (0.62 ml, 5.52 mmol) and refluxed for 15 min. The solution was allowed to cool

and fine colorless needles of the title compound separated out. These were filtered off, washed with cold acetonitrile and dried *in vacuo* over P_4O_{10}. Single crystals of (I) suitable for X-ray analysis were obtained by slow evaporation from an absolute ethanol solution. Elemental analysis found: C 60.25, H 7.37, N 15.08%; calculated: C 60.62, H 6.9, N 15.15%.

Crystal data

$C_{14}H_{19}N_3OS$	Mo $K\alpha$ radiation
$M_r = 277.38$	Cell parameters from 25
Monoclinic, $P2_1/n$	reflections
$a = 6.4480$ (11) Å	$\theta = 5.1–10.4°$
$b = 14.099$ (2) Å	$\mu = 0.22$ mm^{-1}
$c = 15.924$ (2) Å	$T = 293$ (2) K
$\beta = 94.617$ (12)°	Block, colorless
$V = 1443.0$ (4) Å^3	$0.35 \times 0.30 \times 0.25$ mm
$Z = 4$	
$D_x = 1.277$ Mg m^{-3}	

Data collection

Nonius MACH3 diffractometer	$h = -7 \rightarrow 0$
ω/θ scans	$k = -16 \rightarrow 0$
2764 measured reflections	$l = -18 \rightarrow 18$
2524 independent reflections	3 standard reflections
1290 reflections with $I > 2\sigma(I)$	every 200 reflections
$R_{int} = 0.020$	intensity decay: <3%
$\theta_{max} = 25.0°$	

Refinement

Refinement on F^2	H atoms treated by a mixture of
$R[F^2 > 2\sigma(F^2)] = 0.044$	independent and constrained
$wR(F^2) = 0.110$	refinement
$S = 0.98$	$w = 1/[\sigma^2(F_o^2) + (0.0454P)^2]$
2524 reflections	where $P = (F_o^2 + 2F_c^2)/3$
180 parameters	$(\Delta/\sigma)_{max} < 0.001$
	$\Delta\rho_{max} = 0.14$ e Å^{-3}
	$\Delta\rho_{min} = -0.16$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

S1—C7	1.684 (3)	N2—C7	1.362 (3)
N1—C7	1.336 (3)	N3—C8	1.269 (3)
N2—N3	1.356 (3)		
N3—N2—C7	119.3 (3)	N1—C7—N2	115.4 (2)
C8—N3—N2	120.0 (2)	N1—C7—S1	125.0 (2)
O1—C2—C3	117.8 (3)	N2—C7—S1	119.5 (2)
O1—C2—C1	122.5 (3)	N3—C8—C1	119.4 (2)
C3—C2—C1	119.6 (3)		

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

*Cg*1 is the centroid of the C1–C6 ring.

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1O1···N3	0.92 (3)	1.76 (3)	2.562 (3)	144 (3)
O1—H1O1···S1	0.92 (3)	2.82 (3)	3.600 (3)	143 (3)
C6—H6···O1$^{\mathrm{i}}$	0.93	2.42	3.239 (4)	147
C8—H8···S1$^{\mathrm{i}}$	0.93	2.87	3.706 (6)	150
C9—H9B···Cg1$^{\mathrm{ii}}$	0.97	2.96	3.758 (1)	141

Symmetry codes: (i) $x + 1, y, z$; (ii) $-x + 1, -y + 1, -z$.

All C-bound H atoms were positioned geometrically and treated as riding on their parent C atoms, with C—H distances of 0.93 and 0.97 Å, and with U_{iso}(H) values of 1.2U_{eq}(C). Atom H1O1 (on O1) and atom H2N (on N2) were located in difference maps and were refined with isotropic displacement parameters.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GA1110). Services for accessing these data are described at the back of the journal.

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