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# *t*-3-Isopropyl-1-methyl-*r*-2,*c*-6-diphenylpiperidin-4-one thiosemicarbazone

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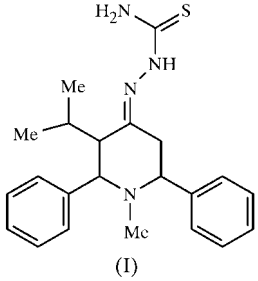
The piperidine ring in the title compound, $C_{22}H_{28}N_4S$, exhibits a chair conformation. The thiosemicarbazone moiety adopts an extended conformation, and the planar phenyl rings are oriented equatorially with respect to the piperidine ring. Two intermolecular hydrogen bonds involving the S atom form molecular pairs, and the crystal structure is stabilized by weak C—H$\cdots\pi$ interactions in addition to van der Waals forces.

## Comment

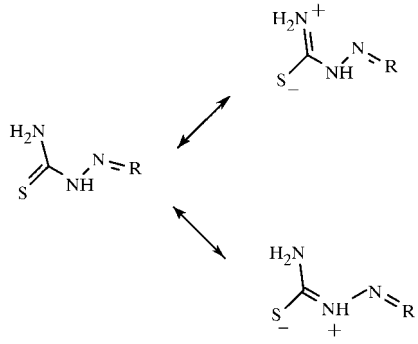
Thiosemicarbazone derivatives of Schiff base compounds containing *N*,*S*-donor chromophores and metal complexes exhibit non-linear optical properties (Tian *et al.*, 1997; Duan *et al.*, 1996; Liu *et al.*, 1999). These substituted thiosemicarbazones possess a wide range of biological activities, including antitumour and antileukemic properties (French & Blanz, 1966; Agarwal *et al.*, 1972), antibacterial and antiviral activities (Nandi *et al.*, 1986; Chattopadhyay *et al.*, 1987), and antimalarial activities (Klayman *et al.*, 1979). The antitumour properties of heterocyclic thiosemicarbazones are partly related to their ability to inhibit the ribonucleoside diphosphate reductase enzyme, which is essential in DNA synthesis



(I)

(Moore *et al.*, 1970). The biological activity of these *N*,*S*-donor ligands has been correlated with their metal-chelating abilities (Kirschner *et al.*, 1966) and reductive capacity (Palenik *et al.*, 1974). As part of our study of thiosemicarbazone derivatives, the title compound, (I), was prepared and the crystal structure determined in order to establish the conformational features of various functional groups.

The bond lengths of the thiosemicarbazone moiety (Fig. 1 and Table 1) show resonance character when compared with typical single- and double-bond lengths in cyclohexanone thiosemicarbazone (Casas *et al.*, 2001). Atoms C4, N10, N11, C12, N13 and S1 are coplanar [the maximum deviation from the plane is −0.064 (19) Å] and this clearly supports the resonance effect in this moiety (see *Scheme* below). The thiosemicarbazone moiety adopts an extended conformation, as evidenced by the torsion angles listed in Table 1. The *trans* configuration of the thiocarbonyl S atom with respect to the hydrazine N atom is evident from the S1—C12—N11—N10 torsion angle of −175.54 (15)°, in accordance with the unprotonated thiosemicarbazone compounds available in the literature (Chattopadhyay *et al.*, 1987).



The C14–C19 (*A*) and C20–C25 (*B*) phenyl rings are planar and are oriented at angles of 63.4 (7) and 81.8 (3)°, respectively, to the plane of the piperidine ring. The torsion angles,

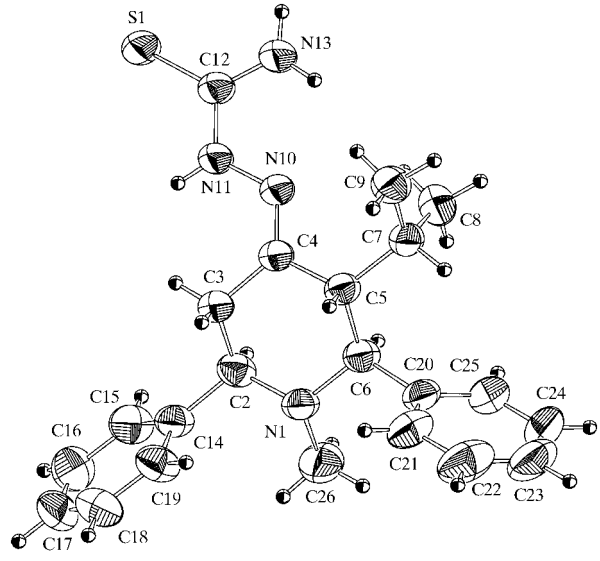



**Figure 1**
*ZORTEP* (Zsolnai, 1998) diagram of (I), showing displacement ellipsoids at the 50% probability level.

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asymmetry parameters and least-squares plane calculations show that the piperidine ring adopts a chair conformation ($Q_T = 0.534$; Nardelli, 1995). Atoms N1, C2, C4 and C5 constitute the best-fitting plane of the piperidine ring, and atoms C3 and C6 deviate by 0.652 (2) and −0.607 (2) Å, respectively, on either side of this plane.

The isopropyl group is equatorially substituted at the 5-position of the piperidine ring, as confirmed by the torsion angles (Table 1). The imine N atom is *cis* with respect to the isopropyl group, and the *N*-methyl group is equatorially substituted at the 1-position of the piperidine ring. Parthasarathi *et al.* (1986) reported a related structure with similar substitution, which leads to an equatorial orientation.

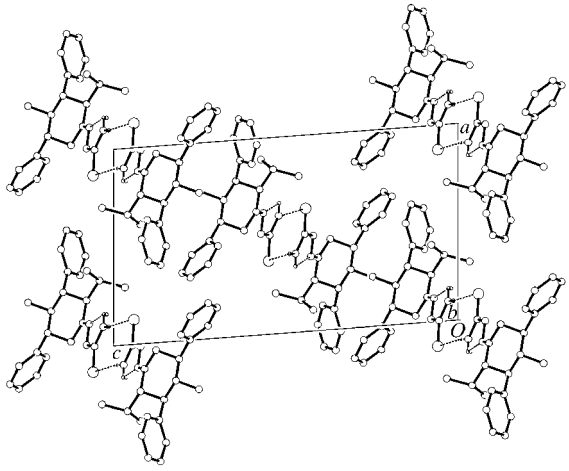


**Figure 2**
The crystal packing of (I), viewed along the *b* axis. Dashed lines represent hydrogen bonds.

Pairs of intermolecular N—H···S hydrogen bonds across the center of inversion (Fig. 2) result in the formation of dimers, a common feature that is observed in similar thiosemicarbazone compounds (Palenik *et al.*, 1974; Restivo & Palenik, 1970). An intramolecular N13—H13*A*···N10 hydrogen bond (Table 2) leads to the formation of a five-membered ring. Two C—H···$\pi$ (Desiraju, 1989) interactions stabilize the crystal structure in (I), *viz*. the C8—H8···*Cg*1$^{ii}$ and C24—H24···*Cg*1$^{iii}$ interactions (see Table 2 for symmetry codes and geometric parameters), where *Cg*1 is the centroid of ring *A*.

## Experimental

The title compound, (I), was synthesized by the Mannich condensation reaction. Benzaldehyde, 2-methylpentan-4-one and methylamine in a 2:1:1 molar ratio were treated (Noller & Baliah, 1948) in ethyl alcohol (99%), refluxed for 1 h and left overnight. Colorless crystals were recrystallized from ethanol. The resulting compound was treated with thiosemicarbazide (1 mol) in ethanol and refluxed for 6 h. A purified sample of (I) was recrystallized from ethanol by slow evaporation, and good quality crystals were selected for structural studies.

*Crystal data*

$C_{22}H_{28}N_4S$
$M_r = 380.55$
Monoclinic, $P2_1/n$
$a = 11.1794$ (17) Å
$b = 10.0720$ (16) Å
$c = 19.591$ (3) Å
$\beta = 94.317$ (3)°
$V = 2199.7$ (6) Å$^3$
$Z = 4$
$D_x = 1.149$ Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 4891 reflections
$\theta = 2.0$–27.9°
$\mu = 0.16$ mm$^{-1}$
$T = 293$ (2) K
Needle, colorless
0.40 × 0.36 × 0.24 mm

*Data collection*

Siemens SMART CCD area-detector diffractometer
$\omega$ scans
23 481 measured reflections
4891 independent reflections
3490 reflections with $I > 2\sigma(I)$
$R_{int} = 0.053$
$\theta_{max} = 27.9°$
$h = -14 \rightarrow 14$
$k = -12 \rightarrow 13$
$l = -25 \rightarrow 24$

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.064$
$wR(F^2) = 0.154$
$S = 1.07$
4891 reflections
244 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0674P)^2 + 0.3252P]$ where $P = (F_o^2 + 2F_c^2)/3'$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.31$ e Å$^{-3}$
$\Delta\rho_{min} = -0.14$ e Å$^{-3}$

**Table 1**
Selected geometric parameters (Å, °).

| | | | |
|---|---|---|---|
| S1—C12 | 1.673 (2) | N11—C12 | 1.350 (2) |
| C4—N10 | 1.278 (2) | C12—N13 | 1.319 (3) |
| N10—N11 | 1.382 (2) | | |
| | | | |
| C4—N10—N11 | 119.13 (16) | N13—C12—S1 | 124.78 (16) |
| C12—N11—N10 | 118.66 (17) | N11—C12—S1 | 119.47 (16) |
| N13—C12—N11 | 115.74 (18) | | |
| | | | |
| C26—N1—C2—C3 | −176.42 (18) | C7—C5—C6—C20 | 56.1 (2) |
| N10—C4—C5—C7 | 2.8 (3) | C4—N10—N11—C12 | 177.1 (2) |
| C3—C4—C5—C7 | −177.23 (18) | N10—N11—C12—N13 | 3.1 (3) |
| C26—N1—C6—C5 | 174.69 (18) | N10—N11—C12—S1 | −175.54 (15) |
| C7—C5—C6—N1 | 178.01 (16) | | |

**Table 2**
Hydrogen-bonding geometry (Å, °).

*Cg*1 is the centroid of the C14–C19 ring.

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| N13—H13*B*···S1$^{i}$ | 0.86 | 2.52 | 3.362 (2) | 167 |
| N13—H13*A*···N10 | 0.86 | 2.21 | 2.587 (3) | 106 |
| C8—H8*A*···*Cg*1$^{ii}$ | 0.96 | 3.21 | 4.00 | 142 |
| C24—H24···*Cg*1$^{iii}$ | 0.93 | 3.07 | 3.88 | 148 |

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

All the H atoms were fixed geometrically and allowed to ride on their parent atoms.

Data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT* (Bruker, 2000); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine

structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ZORTEP* (Zsolnai, 1998) and *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL*97 and *PARST* (Nardelli, 1995).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: OB1115). Services for accessing these data are described at the back of the journal.

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