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Benzoin 4-ethylthiosemicarbazone

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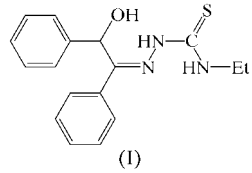
In the title compound, 2-hydroxy-1,2-diphenylethanone 4-ethylthiosemicarbazone, $C_{17}H_{19}N_3OS$, the thiosemicarbazone moiety is planar and has an *E* configuration. The planar phenyl rings make dihedral angles of 82.34 (8) and 8.07 (17)° with the plane of the thiosemicarbazone moiety. The crystal structure contains two intramolecular (N—H···O and N—H···N) and one intermolecular interaction (O—H···S), as well as two C—H···π(benzene) interactions. Molecules are stacked in columns running along the *a* axis. Molecules in each column are connected to each other by means of linear O—H···S hydrogen bonds and C—H···π interactions. In addition, there are also C—H···π(benzene) interactions between the columns.

Comment

Recently, there has been considerable interest in the coordination chemistry of thiosemicarbazones because of their biological and carcinostatic activities (Liu, Lin *et al.*, 1995; Lukevics *et al.*, 1996) and their non-linear optical properties (Tian *et al.*, 1997; Liu *et al.*, 1999). These biological activities include antitumour and antileukaemic properties (French & Blanz, 1966; Agarwal *et al.*, 1972), antibacterial and antiviral activities (Nandi *et al.*, 1986; Chattopadhyay *et al.*, 1987), infertility properties (Nagarajan *et al.*, 1984), and anticancer (Ali & Livingstone, 1974) and antimalarial activities (Klayman *et al.*, 1979). These properties are thought to arise from the metal-chelating ability of these ligands. In almost all cases, the ligands are bidentate and bind to the metal through the S and hydrazinic N atoms, although there are examples of them acting as monodentate ligands binding only through sulfur (Valdes-Martines *et al.*, 1996). It has been postulated that extensive electron delocalization in the thiosemicarbazone moiety helps the free thiosemicarbazone ligands and their metal complexes to exhibit second-harmonic generation (SHG) efficiency (Tian *et al.*, 1997; Liu *et al.*, 1999).

Due to its critical role in DNA synthesis and proliferation, iron is a potential target for the treatment of cancer (Richardson, 2002). To this end, the cellular antiproliferative effects of a number of iron-specific chelators and their complexes have been examined. A class of chelators with pronounced and selective activity against tumour cells are the thiosemicarbazones. The antitumour properties of heterocyclic thiosemicarbazones are partly related to their ability to inhibit the ribonucleoside diphosphate reductase enzyme (Cory *et al.*, 1995; Liu, Lin & Sartorelli, 1995), which is essential in DNA synthesis (Moore *et al.*, 1970). The mechanism by which these compounds act is still not well understood, but chelation of intracellular iron and other metal ions is believed to be important. 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, and also to compare the values obtained with reported structural results.



(I)

The molecular structure of (I), together with the atom-labelling scheme and the intramolecular hydrogen bonding, is shown in Fig. 1. As seen from the structure of the molecule, chirality is present around atom C5. In the crystallization procedure, only one enantiomer of the molecule has been crystallized. The thiosemicarbazone moiety shows an *E* configuration about both the C2—N2 and C1—N1 bonds, as found previously (Mathew & Palenik, 1971; Tian, Wu *et al.*, 1999; Tian, Yu *et al.*, 1999). The C—S bond distance of 1.691 (3) Å agrees well with similar bonds in related

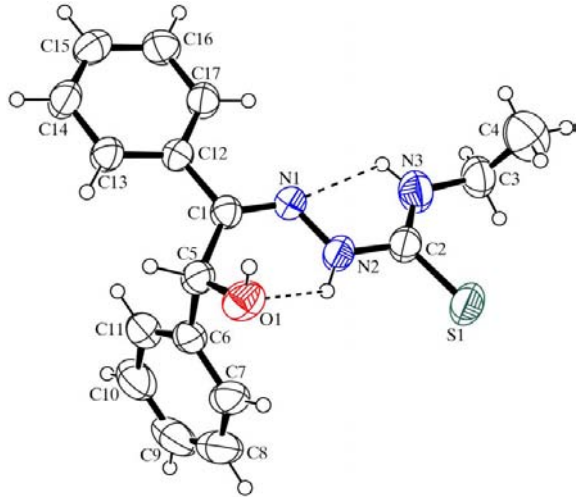


Figure 1
A view of the title compound, (I), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 40% probability level and H atoms are shown as small spheres of arbitrary radii. Intramolecular N—H···O and N—H···N hydrogen bonds are represented by dashed lines.

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compounds, being intermediate between 1.82 Å for a C—S single bond and 1.56 Å for a C═S double bond (Wu *et al.*, 2000). The corresponding C2—N2 bond distance of 1.356 (3) Å is indicative of some double-bond character, suggesting extensive electron delocalization in the whole molecule. It has been reported (Tian *et al.*, 1997; Liu *et al.*, 1999) that this type of structure helps thiosemicarbazone complexes to exhibit SHG efficiency. In this case, the non-centrosymmetry of the space group can allow the compound to exhibit SHG efficiency. The C2—N3 bond distance of 1.330 (4) Å is also indicative of some double-bond character. The C2—S1 and C2—N2 bond lengths indicate intermediate character between thione and thiol structures. The bond lengths of the thiosemicarbazone moiety (Table 1) show resonance character when compared with typical single- and double-bond lengths in cyclohexanone thiosemicarbazone (Casas *et al.*, 2001). Atoms C1, N1, N2, C2, N3 and S1 are coplanar [the maximum deviation from the plane is −0.0499 (19) Å for atom N2 and this clearly supports the resonance effect in this moiety.

The C6–C11 (*A*) and C12–C17 (*B*) phenyl rings are planar and are oriented at angles of 82.34 (8) and 8.07 (17)°, respectively, to the plane of the thiosemicarbazone moiety. These values indicate that the plane of the thiosemicarbazone moiety is almost parallel to the plane of ring *B*, while it is almost perpendicular to the plane of ring *A*. However, the four-membered bridge linking the phenyl rings to each other is not planar; the Φ_{CC} torsion angle (C6—C5—C1—C12) is 101.3 (2)°, showing that the conformation about the C1—C5 bond is (+)anticlinal. The plane of ring *A* is nearly perpendicular to that of ring *B*, the corresponding dihedral angle being 79.87 (9)°. The greatest deviation from an ideal trigonal–planar geometry is at atom C1, where steric repulsion between the phenyl–methanol group and the phenyl ring contracts the N1—C1—C12 angle to 115.3 (2)°. In addition, the N2—C2—N3 angle [116.8 (3)°] indicates that there is also steric repulsion between the ethyl group and the thiocarbonyl S atom.

The potential donors N2 and O1 are found in a *syn* disposition, as a result of an intramolecular hydrogen bond [H2N···O1 = 2.10 Å and N2···O1 = 2.705 (3) Å]. Typically for this type of molecule, the S and hydrazinic N atoms are mutually *trans*, which allows for a weak intramolecular hydrogen bond between atoms N3 and N1 [H3N···N1 = 2.22 Å, N3···N1 = 2.626 (3) Å and N3—H3N···N1 = 109°]. Such contacts have been observed in other derivatives (Park & Ahn, 1985; Parsons *et al.*, 2000). The first of these intramolecular interactions leads to the formation of a six-membered ring, while the second leads to the formation of a five-membered ring which is fused with the six-membered ring (Fig. 1). Although the five-membered ring is close to being planar, with a maximum deviation of 0.0338 (15) Å for atom C2, the six-membered ring is not, the maximum deviation being 0.3545 (15) Å for atom O1.

Molecules of the title compound are packed in columns running along the *a* axis. The molecules in each column are connected to each other in a zigzag arrangement by means of linear O—H···S hydrogen bonds and C—H···π(benzene) interactions (Fig. 2 and Table 2). In these C—H···π interactions, atom C13 forms a C—H···π contact with the centroid, *Cg*1, of the C6–C11 ring of the molecule at $(x+1, y, z)$. In addition, there are also C—H···π(benzene) interactions between the columns. In these C—H···π interactions, atom C9 forms a C—H···π contact with the centroid, *Cg*2, of the C12–C17 ring of the molecule at $(1-x, \frac{1}{2}+y, -z)$. Although N—H···S hydrogen bonds leading to the formation of dimers are a common feature previously observed in similar thiosemicarbazone compounds (Palenik *et al.*, 1974; Restivo & Palenik, 1970; Dinçer *et al.*, 2005), this type of interaction is not observed in the crystal structure of (I). The full geometry of the intra- and intermolecular interactions is given in Table 2. There are no other significant interactions, such as π–π stacking, in the crystal structure.

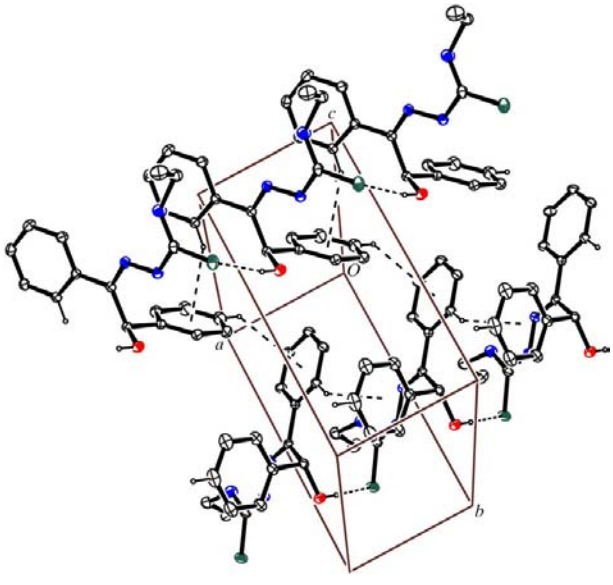

Figure 2
The molecular packing of (I). Dashed lines show the O—H···S and C—H···π(benzene) interactions. For clarity, only H atoms involved in hydrogen bonding have been included.

Experimental

A solution of 2-hydroxy-1,2-diphenylethanone (benzoin) (2.122 g, 10 mmol) and 4-ethylthiosemicarbazide (1.192 g, 10 mmol) in absolute ethanol (50 ml) was refluxed in the presence of *p*-toluenesulfonic acid as catalyst (0.005 g) with continuous stirring. The course of the reaction was monitored using IR spectroscopy. On cooling to room temperature, the target product was precipitated by the slow addition of water, filtered, washed with copious cold ethanol and dried in air. Shiny crystals of (I) suitable for X-ray analysis were obtained by slow evaporation from an alcoholic solution (yield 2.65 g, 84.6%; m.p. 434 K). IR (KBr, ν, cm^{-1}): 3415 (–OH), 3337 and 3291 (–NH–), 1600 (C═N); ^{1}H NMR ($CDCl_3$, TMS): δ 1.19 (*t*, J = 6.95 Hz, 3H, –CH_3), 3.63 (*m*, 2H, –CH_2–), 6.08 (*s*, 1H, >CH–), 6.23 (*s*, 1H, –OH), 7.19–7.62 (*m*, 13H, aromatics plus –NH–), 11.83 (*s*, 1H, –NH–, D_2O exchangeable); ^{13}C NMR ($CDCl_3$, TMS): δ 14.65 (C_1), 39.44 (C_2), 176.71 (C_3), 149.08 (C_4), 136.80 (C_5), 129.75 (C_6), 128.55 (C_7), 130.47 (C_8), 75.34 (C_9), 149.07 (C_{10}), 127.15 (C_{11}), 128.81 (C_{12}), 127.36 (C_{13}).

Crystal data

$C_{17}H_{19}N_3OS$
M_r = 313.41
Monoclinic, $P2_1$
a = 5.5803 (3) Å
b = 11.5739 (10) Å
c = 13.1420 (8) Å
β = 98.660 (5)°
V = 839.11 (10) Å^3
Z = 2
D_x = 1.240 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 18162 reflections
θ = 2.4–27.9°
μ = 0.20 mm^{-1}
T = 296 K
Rod, colourless
0.80 × 0.42 × 0.16 mm

Data collection

Stoe IPDS-2 diffractometer
ω scans
Absorption correction: integration (*X-RED32*; Stoe & Cie, 2002)
T_{min} = 0.864, T_{max} = 0.968
14309 measured reflections
3958 independent reflections
2723 reflections with $I > 2\sigma(I)$
R_{int} = 0.095
θ_{max} = 27.8°
$h = -7 \rightarrow 7$
$k = -15 \rightarrow 15$
$l = -17 \rightarrow 17$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.048
$wR(F^2)$ = 0.135
S = 1.02
3958 reflections
193 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0682P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.35 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}
Absolute structure: Flack (1983), with 1559 Friedel pairs
Flack parameter: −0.12 (10)

Table 1
Selected geometric parameters (Å, °).

O1—C5	1.421 (3)	C1—C12	1.495 (3)
N1—C1	1.287 (3)	C1—C5	1.532 (3)
N1—N2	1.370 (3)	C3—C4	1.456 (5)
N3—C3	1.489 (4)	C5—C6	1.517 (4)
C1—N1—N2	118.3 (2)	O1—C5—C6	109.4 (2)
C2—N2—N1	119.1 (2)	O1—C5—C1	112.6 (2)
C2—N3—C3	126.8 (3)	C6—C5—C1	110.3 (2)
N1—C1—C5	124.6 (2)	C11—C6—C5	120.0 (3)
N3—C2—S1	125.0 (2)	C7—C6—C5	121.2 (3)
N2—C2—S1	118.1 (2)	C13—C12—C1	122.4 (2)
C4—C3—N3	109.8 (3)	C17—C12—C1	119.6 (2)
C1—N1—N2—C2	179.9 (2)	C3—N3—C2—S1	4.9 (5)
N2—N1—C1—C12	178.9 (2)	N1—N2—C2—N3	−7.8 (4)
N2—N1—C1—C5	−0.9 (4)	N1—N2—C2—S1	174.54 (18)
C3—N3—C2—N2	−172.6 (3)	C2—N3—C3—C4	−86.3 (4)

H atoms were positioned geometrically and refined with a riding model, fixing the bond lengths at 0.98, 0.97, 0.96, 0.93, 0.86 and 0.82 Å for CH, CH_2, CH_3, aromatic CH, NH and OH groups, respectively. The displacement parameters of the H atoms were constrained as $U_{iso}(H) = 1.2U_{eq}$(parent), or $1.5U_{eq}(C)$ for methyl H atoms. Refinement of the absolute structure parameter (Flack, 1983) yielded a value of −0.12 (10).

Data collection: *X-AREA* (Stoe & Cie, 2002); cell refinement: *X-AREA*; data reduction: *X-RED32* (Stoe & Cie, 2002); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999) and *PLATON* (Spek, 2003).

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

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2N···O1	0.86	2.10	2.705 (3)	127
N3—H3N···N1	0.86	2.22	2.626 (3)	109
O1—H1···S1^{i}	0.82	2.39	3.202 (2)	168

Symmetry code: (i) $x + 1, y, z$.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SF1021). Services for accessing these data are described at the back of the journal.

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