Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

Benzoin thiosemicarbazone

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Key indicators

Single-crystal X-ray study
T = 296 K
Mean σ(C–C) = 0.003 Å
R factor = 0.036
wR factor = 0.107
Data-to-parameter ratio = 17.6

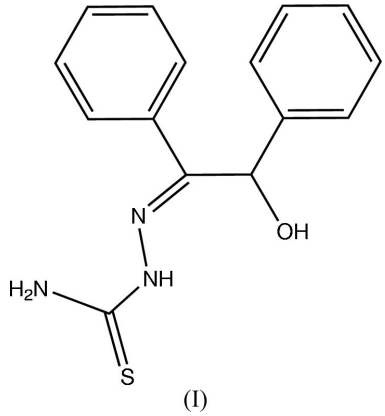
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 21 February 2005
Accepted 1 March 2005
Online 11 March 2005

In the title compound, $C_{15}H_{15}N_3OS$, the thiosemicarbazone moiety is planar, with a maximum deviation of 0.0369 (11) Å, and has an *E* configuration. The planar phenyl rings make dihedral angles of 26.56 (9) and 81.20 (5)° with the plane of the thiosemicarbazone moiety. In the molecule, there are two intramolecular interactions of types N—H···O and N—H···N. In the crystal structure, there are two intermolecular interactions of types O—H···S and N—H···S, leading to the formation of dimers.

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 SHG (second harmonic generation) efficiency (Tian *et al.*, 1997; Liu *et al.*, 1999).



(I)

Due to its critical role in DNA synthesis and proliferation, iron is a potential target for the treatment of cancer

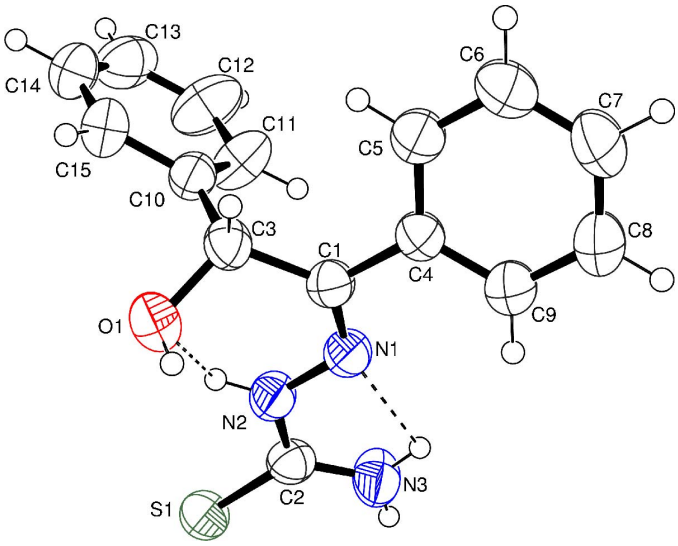


Figure 1
An *ORTEP-3* drawing (Farrugia, 1997) of the title compound, showing the atomic numbering scheme. Displacement ellipsoids of non-H atoms are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. The intramolecular N—H···O and N—H···N hydrogen bonds are represented by dashed lines.

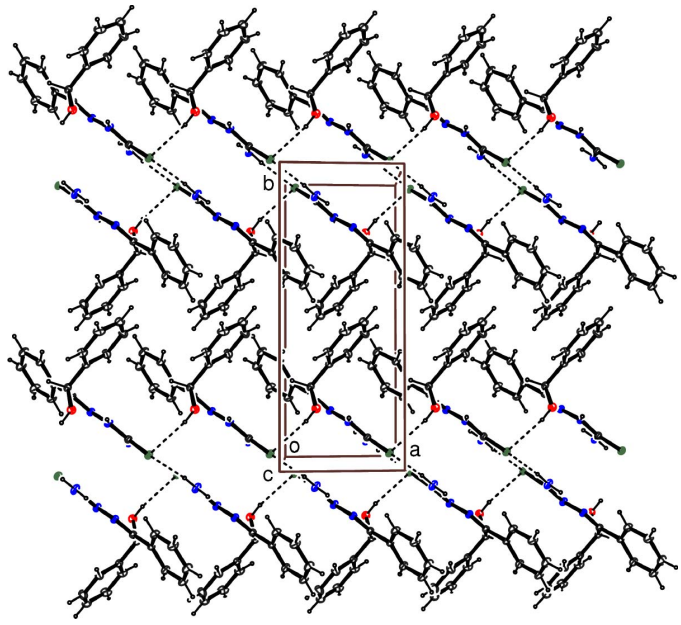


Figure 2
A projection of the crystal structure of (I) along the *c* axis. Dashed lines show the N—H···S and O—H···S interactions.

(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. Taking into account the importance of the thiosemicarbazones, we have undertaken the X-ray diffraction study of the title compound, (I), in order to establish the conformational features of various functional groups and to compare the values obtained with reported structural results.

The molecular structure of (I), together with the atom-labelling scheme and the intramolecular hydrogen bonding, is shown in Fig. 1. 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 1.6907 (14) Å agrees well with similar bonds in related 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 1.3451 (19) 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; however, in this case, the centrosymmetry of the space group does not allow the compound to exhibit any SHG efficiency. The C2—N3 bond distance of 1.3127 (19) Å is also indicative of some double-bond character. The bond lengths C2—S1 and C2—N2 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 0.0369 (11) Å] and this clearly supports the resonance effect in this moiety.

The C4–C9 (*A*) and C10–C15 (*B*) phenyl rings are planar and are oriented at angles of 26.56 (9) and 81.20 (5)°, 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 *A*, while it is almost perpendicular to the plane of ring *B*. However, the four-membered bridge linking the phenyl rings to each other is not planar, the C4—C1—C3—C10 torsion angle being 97.06 (15)°. The plane of ring *A* is also perpendicular to the plane of ring *B*, the corresponding dihedral angle being 88.65 (6)°.

In the molecular structure, an intramolecular N3—H3*A*···N1 hydrogen bond leads to the formation of a five-membered ring, while an intramolecular N2—H2···O1 hydrogen bond leads to the formation of a six-membered ring which is fused with the five-membered ring (Fig. 1). Although the five-membered ring is close to being planar, with a maximum deviation of −0.0269 (10) Å for atom N2, the six-membered ring is not, the maximum deviation being 0.3309 (8) Å for atom O1. The geometry of the intra- and intermolecular interactions is given in Table 2.

In the crystal structure, pairs of intermolecular N—H···S hydrogen bonds across a centre of inversion result in the formation of dimers, generating an $R_2^2(8)$ ring (Fig. 2). This is a common feature previously observed in similar thiosemicarbazone compounds (Palenik *et al.*, 1974; Restivo & Palenik, 1970). The dimers are connected to each other by pairs of intermolecular O—H···S hydrogen bonds. This arrangement leads to the formation of another larger dimeric structure with an $R_4^4(20)$ ring (Fig. 2). The thiocarbonyl S atom acts as a single acceptor for both hydrogen bonds. As can be seen in Fig. 2, the repeat of the dimeric structures formed by the N—H···S and O—H···S intermolecular hydrogen bonds resembles steps extending along the *a* axis of the crystal. In addition, a C—H···π(phenyl) interaction is also observed in the structure. Atom C6 forms a C—H···π contact with the centroid, *Cg*1, of the C10–C15 ring of the molecule at position $(2-x, 1-y, 1-z)$. Such C—H···π contacts serve to link the chains of dimers, which extend in the [100] direction, so generating sheets of molecules in planes normal to the *c* axis at $z = 0, \frac{1}{2}, 1$, *etc*. There are no other significant interactions, such as π–π stacking, in the crystal structure.

Experimental

A solution of 2-hydroxy-1,2-diphenylethanone (benzoin; 2.122 g, 10 mmol) and thiosemicarbazide (0.91 g, 10 mmol) in absolute ethanol (50 ml) was maintained at 313–323 K, in the presence of *p*-toluenesulfonic acid (0.005 g) as catalyst, with continuous stirring. The course of the reaction was monitored by IR spectroscopy. The reaction was complete after *ca* 2 h. On cooling to room temperature, the target product, (I), precipitated, was filtered off, washed with copious cold ethanol and dried in air. Shiny crystals of (I) suitable for X-ray analysis were obtained by slow evaporation of a solution in ethanol (yield: 2.71 g, 95%; m.p. 449 K). IR (ν, cm^{-1}): 3252 and 3154 (—NH_2), 3408 (—OH), 1603 (C═N), 903 (C═S); ^{1}H NMR (DMSO-d_6, TMS): δ 4.48 (*s*, 1H, —OH), 6.28 (*d, J* = 3.67 Hz, 1H, >CH—), 7.25–7.369 (*m*, 8H, aromatic), 7.89–7.92 (*m*, 2H, aromatic), 7.99 (*s*, 1H, —NH—, from —NH_2, D_2O exchangeable), 8.42 (*s*, 1H, —NH—, from —NH_2, D_2O exchangeable), these —NH— singlets indicate the intramolecular hydrogen bonding of H···S, 11.67 (*s*, 1H, —NH—, D_2O exchangeable); ^{13}C NMR (DMSO-d_6, TMS): δ 72.97 (C1), 140.14 (C2), 127.05 (C3), 129.37 (C4), 128.61 (C5), 148.36 (C6), 136.61 (C7), 127.81 (C8), 129.10 (C9), 129.96 (C10), 178.41 (C11).

Crystal data

$C_{15}H_{15}N_3OS$
M_r = 285.36
Monoclinic, $P2_1/c$
a = 6.0440 (4) Å
b = 14.6516 (9) Å
c = 16.8653 (11) Å
β = 100.266 (5)°
V = 1469.58 (16) Å^3
Z = 4
D_x = 1.290 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 15 282 reflections
θ = 1.4–27.2°
μ = 0.22 mm^{-1}
T = 296 K
Lath, colourless
0.80 × 0.45 × 0.24 mm

Data collection

Stoe IPDS-2 diffractometer
ω scans
Absorption correction: by integration (*X-RED32*; Stoe &; Cie, 2002)
T_{min} = 0.878, T_{max} = 0.962
16 115 measured reflections
3207 independent reflections
2398 reflections with $I > 2\sigma(I)$
R_{int} = 0.091
θ_{max} = 27.0°
$h = -7 \rightarrow 7$
$k = -18 \rightarrow 18$
$l = -21 \rightarrow 21$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.036
$wR(F^2)$ = 0.107
S = 1.03
3207 reflections
182 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0593P)^2 + 0.0081P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.19 e Å^{-3}
$\Delta\rho_{min}$ = −0.14 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.010 (2)

Table 1
Selected geometric parameters (Å, °).

S1—C2	1.6907 (14)	N3—C2	1.3127 (19)
O1—C3	1.4343 (17)	C1—C4	1.4803 (18)
N1—C1	1.2853 (18)	C1—C3	1.5262 (19)
N1—N2	1.3747 (16)	C3—C10	1.512 (2)
N2—C2	1.3451 (19)		
C1—N1—N2	118.42 (12)	O1—C3—C10	107.32 (11)
C2—N2—N1	118.52 (12)	O1—C3—C1	112.07 (11)
N1—C1—C4	115.47 (12)	C10—C3—C1	113.15 (12)
N1—C1—C3	125.55 (12)	C9—C4—C1	120.53 (13)
C4—C1—C3	118.98 (12)	C5—C4—C1	121.21 (13)
N3—C2—N2	117.31 (13)	C11—C10—C3	123.74 (13)
N3—C2—S1	124.16 (12)	C15—C10—C3	118.52 (15)
N2—C2—S1	118.54 (11)		
C1—N1—N2—C2	179.44 (14)	N1—N2—C2—S1	175.39 (10)

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

*Cg*1 is the centroid of the C10–C15 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2···O1	0.86	2.06	2.6738 (18)	128
N3—H3*A*···N1	0.86	2.25	2.6057 (18)	105
O1—H1···S1^{i}	0.82	2.43	3.2370 (12)	169
N3—H3B···S1^{ii}	0.86	2.54	3.3840 (14)	168
C6—H6···*Cg*1^{i}	0.93	2.83	3.665 (2)	150

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

H atoms were positioned geometrically and refined with a riding model, fixing the bond lengths at 0.98, 0.93, 0.86 and 0.82 Å for CH, CH(aromatic), NH and OH groups, respectively, with U_{iso}(H) = 1.2U_{eq}(carrier atom).

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).

This study was supported financially by the Research Center of Ondokuz Mayıs University (project No. F-276).

References

Agarwal, K. C., Cushley, R. J., Lipsky, S. R., Wheaton, J. R. & Sartorelli, A. C. (1972). *J. Med. Chem.* **15**, 192–195.
Ali, M. A. & Livingstone, S. E. (1974). *Coord. Chem. Rev.* **13**, 101–132.
Casas, J. S., Castineiras, A., Lobana, T. S., Sanchez, A., Sordo, J. & Garcia-Tasende, M. S. (2001). *J. Chem. Crystallogr.* **31**, 329–332.

Chattopadhyay, D., Banerjee, T., Mazumdar, S. K., Ghosh, S. & Kuroda, R. (1987). *Acta Cryst.* C**43**, 974–977.
Cory, J. G., Cory, A. H., Rappa, G., Lorico, A., Liu, M. C., Lin, T. S. & Sartorelli, A. C. (1995). *Adv. Enzyme Regul.* **35**, 55–68.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
French, F. A. & Blanz, E. J. Jr (1966). *J. Med. Chem.* **9**, 585–589.
Klayman, D. L., Bartosevich, J. F., Griffin, T. S., Mason, C. J. & Scovill, J. P. (1979). *J. Med. Chem.* **22**, 855–862.
Liu, M.-C., Lin, T.-S., Penketh, P. & Sartorelli, P. (1995). *J. Med. Chem.* **38**, 4234–4241.
Liu, M. C., Lin, T. S. & Sartorelli, A. C. (1995). *Prog. Med. Chem.* **32**, 1–35.
Liu, Z.-H., Duan, C.-Y., Hu, J. & You, X.-Z. (1999). *Inorg. Chem.* **38**, 1719–1724.
Lukevics, E., Jansone, D., Rubina, K., Abele, E., Germane, S., Leite, L., Shymanska, M. & Popelis, J. (1996). *Eur. J. Med. Chem.* **30**, 983–990.
Mathew, M. & Palenik, G. J. (1971). *Acta Cryst.* B**27**, 59–66.
Moore, E. C., Zedek, M. S., Agarwal, K. C. & Sartorelli, A. C. (1970). *Biochemistry*, **9**, 4492–4498.
Nagarajan, K., Talwaker, P. K.,Kulkarni, C. L., Venkateswarlu, A., Prabhu, S. S. & Nayak, G. V. (1984). *Indian J. Chem.* **23**, 1243–1257.
Nandi, A. K., Sheldrick, W. S. & Ghosh, S. (1986). *Acta Cryst.* C**42**, 1570–1573.
Palenik, G. J., Rendle, D. F. & Carter, W. S. (1974). *Acta Cryst.* B**30**, 2390–2395.
Restivo, R. & Palenik, G. J. (1970). *Acta Cryst.* B**26**, 1397–1402.
Richardson, D. R. (2002). *Crit. Rev. Oncol. Hematol.* **42**, 267–281.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Stoe & Cie (2002). *X-AREA* (Version 1.18) and *X-RED32* (Version 1.04). Stoe & Cie, Darmstadt, Germany.
Tian, Y.-P., Duan, C.-Y., Chao, C.-Y., You, X.-Z., Zhang, Z.-Y. & Mak, T. C. W. (1997). *Inorg. Chem.* **36**, 1247–1251.
Tian, Y.-P., Wu, J.-Y., Xie, F.-X., Shanmuga Sundara Raj, S., Yang, P. & Fun, H.-K. (1999). *Acta Cryst.* C**55**, 1641–1644.
Tian, Y.-P., Yu, W.-T., Jiang, M.-H., Shanmuga Sundara Raj, S., Yang, P. & Fun, H.-K. (1999). *Acta Cryst.* C**55**, 1639–1641.
Valdes-Martines, J., Enriquez, A., Cabrera, A. & Espinosa-Perez, G. (1996). *Polyhedron*, **15**, 897–901.
Wu, D., He, C., Duan, C. & You, X. (2000). *Acta Cryst.* C**56**, 1336–1337.