research communications

Crystal structure of N-(4-hydroxybenzyl)acetone thiosemicarbazone

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The structure of the title compound, $C_{11}H_{15}N_3OS$, shows the flexibility due to the methylene group at the thioamide N atom in the side chain, resulting in the molecule being non-planar. The dihedral angle between the plane of the benzene ring and that defined by the atoms of the thiosemicarbazide arm is 79.847 (4)°. In the crystal, the donor–acceptor hydrogen-bond character of the –OH group dominates the intermolecular associations, acting as a donor in an O—H⋯S hydrogen bond, as well as being a double acceptor in a centrosymmetric cyclic bridging N—H⋯O,O′ interaction [graph set $R_2^2(4)$]. The result is a one-dimensional duplex chain structure, extending along [111]. The usual N—H⋯S hydrogen-bonding association common in thiosemicarbazone crystal structures is not observed.

1. Chemical context

Thiosemicarbazones (TSCs) are an interesting group of compounds because they show diverse biological properties (Serda et al., 2012) and pharmacological activities (Lukman-tara et al., 2013). They can be easily functionalized to yield different supramolecular arrays through intermolecular hydrogen-bonding interactions (Nuñez-Montenegro et al., 2017), by selection of suitable aldehyde or ketone reagents. In addition, metal coordination may be used to orient some of their substituents to optimize the interaction with biomole-cules (e.g. see Nuñez-Montenegro et al., 2014). In the present paper, we describe the synthesis and crystal structure of a TSC derivative (Figs. 1), namely N-(4-hydroxybenzyl)acetone thiosemicarbazone (acTSC), having a 4-hydroxybenzyl substituent at the thioamide N atom (N1), in which the –CH₂– group provides more flexibility to establish intermolecular associations.
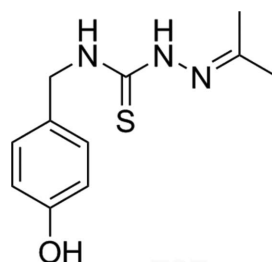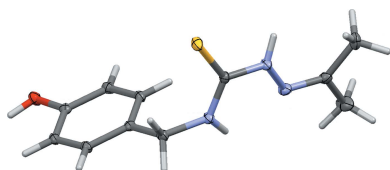
2. Structural commentary

In the acTSC molecule (Fig. 2), the bond lengths (S1=C1 and C10=N3) and angles in the thiosemicarbazide arm are similar to those observed in other thiosemicarbazones, suggesting that the thione form is predominant. This arm is almost planar, probably due to some π-delocation (r.m.s. deviation of 0.0516 Å for the plane defined by atoms S1/C1/N1/N2/N3).
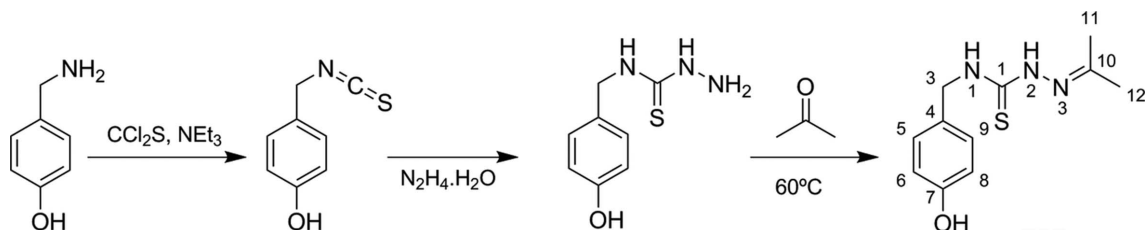
Figure 1
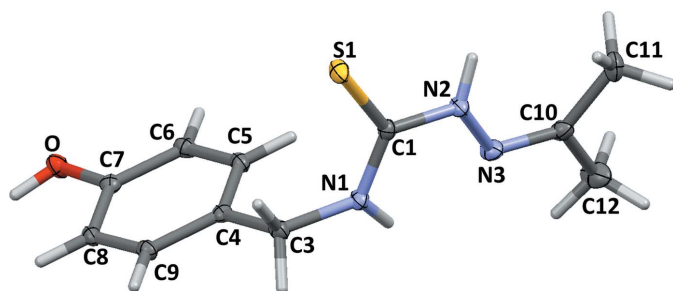Reaction scheme for the synthesis of acTSC.

Figure 2
The molecular structure of acTSC, with displacement ellipsoids drawn at the 40% probability level.

Nevertheless, the ethylene group at N1 allows an almost orthogonal orientation relative to the phenolic substituent group, with a dihedral angle between the two planes of 79.847 (4)°. The interatomic distance N1⋯N3 interaction [2.6074 (18) Å] suggests some kind of intramolecular interaction.

Table 1
Hydrogen-bond geometry (Å, °).

$D—H\cdots A$	$D—H$	$H\cdots A$	$D\cdots A$	$D—H\cdots A$
N2—H2⋯O^i	0.848 (17)	2.292 (17)	2.9955 (15)	140.6 (14)
N2—H2⋯O^{ii}	0.848 (17)	2.434 (16)	3.1333 (15)	140.3 (14)
O—H0⋯S1^{iii}	0.857 (19)	2.299 (19)	3.1349 (10)	165.2 (16)

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

hydrogen-bonding interactions with different phenolic O-atom acceptors. The shortest of these is N2—H2⋯O^i (Table 1), which generates a centrosymmetric cyclic $R_2^2(4)$ ring-motif association (Etter, 1990) and also forms a conjoined cyclic $R_2^2(6)$ association *via* an O—H⋯S interaction (see Fig. 3). The second of the three-centre hydrogen-bonding interactions (N2—H2⋯O^{ii}) extends the structure into one-dimensional duplex chains along [111] (Fig. 3).

3. Supramolecular features

The association of the molecules is strongly affected by the donor–acceptor character of the –OH group, while the usual N—H⋯S hydrogen bonds observed in most TSC structures (Nuñez-Montenegro *et al.*, 2017; Pino-Cuevas *et al.*, 2014) are absent. The phenolic –OH group forms an intermolecular hydrogen bond with a S-atom acceptor (O—H0⋯S1^{iii}; Table 1), while the N2—H group establishes two different

4. Database survey

For related structures of thiosemicarbazones derived from acetone, see: Yamin *et al.* (2014); Basu & Das (2011); Venkatraman *et al.* (2005); Jian *et al.* (2005). For the metal-coordination properties of thiosemicarbazones, see: Paterson & Donnelly (2011); Casas *et al.* (2000). For acetone derivatives, see, for example, Su *et al.* (2013); Nuñez-Montenegro *et al.* (2014); Swesi *et al.* (2006); Paek *et al.* (1997).
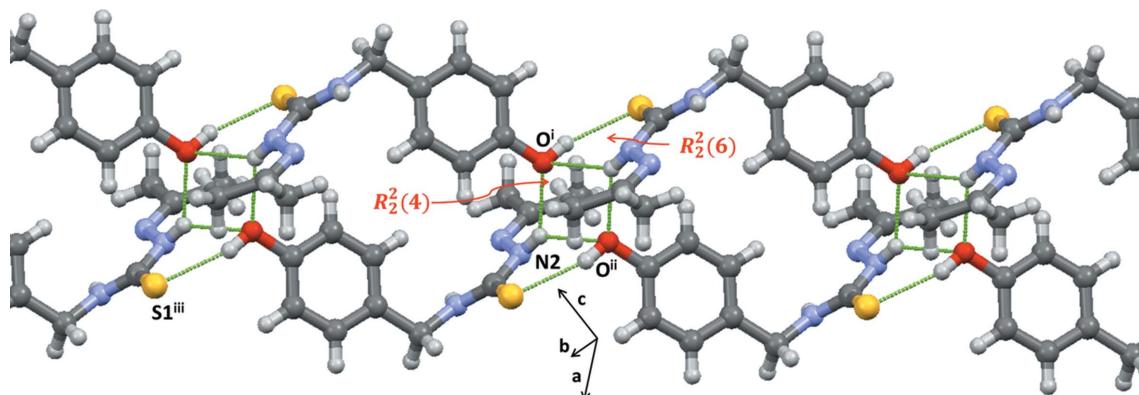

Figure 3
Intermolecular hydrogen-bonding associations between molecules in the crystal structure of acTSC, shown as dashed lines.

5. Synthesis and crystallization

The reaction scheme for the synthesis of the title compound is shown in Fig. 1. The primary amine 4-hydroxybenzylamine was converted to the corresponding isothiocyanate by reaction with thiophosgene (Sharma, 1978). This isothiocyanate was treated with hydrazide to form the thiosemicarbazide, as described previously (Reis *et al.*, 2011). Finally, this compound was reacted with acetone in order to synthesize the desired thiosemicarbazone. In a typical synthesis, 3.4 g (0.017 mol) of thiosemicarbazide was dissolved in acetone (20 ml) and heated to 60°C for 20 min (Fig. 1). This solution was concentrated and the resultant residue was purified using a silica column (AcOEt–hexane 30%). This solution was vacuum dried giving 1.96 g of acTSC. The solution was also used to obtain single crystals by slow evaporation (yield 48%; m.p. 165°C). $C_{11}H_{15}N_3OS$ requires: C 55.7, H 6.4, N 17.7%; found C 55.8, H 7.1, N 16.9%. MS–ESI [*m/z* (%)]: 238 (100) $[M + H]^+$. IR (ATR, ν/cm^{-1}): 3241 (*b*) ν(NH, OH); 1536 (*w*), 1508 (*s*) ν(C=N); 784 (*w*) ν(C=S). ^{1}H NMR (DMSO-d_6): 9.95 (*s*, 1H, N2H), 9.26 (*s*, 1H, OH), 8.46 (*t*, $^3J_{\text{H-NH}}$ = 6.2 Hz, 1H, N1H), 7.15 (*d*, $^3J_{\text{H-H}}$ = 8.5 Hz, 2H, C5H, C9H), 6.70 (*d*, $^3J_{\text{H-H}}$ = 8.5 Hz, 2H, C6H, C8H), 4.65 (*d*, $^3J_{\text{H-H}}$ = 6.2 Hz, 2H, C3H), 1.92 (*d*, $^3J_{\text{H-H}}$ = 8.5 Hz, 6H, C11H, C12H).

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. Interactive H atoms on O and N atoms were located in difference Fourier analyses and were allowed to freely refine, with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{O,N})$ and riding. Other H atoms were included at calculated sites and allowed to ride, with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}$(aromatic and methylene C) or $1.5U_{\text{eq}}$(methyl C).

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Crystal data	
Chemical formula	$C_{11}H_{15}N_3OS$
M_r	237.32
Crystal system, space group	Triclinic, $P\bar{1}$
Temperature (K)	100
a, b, c (Å)	8.2799 (8), 8.9169 (9), 9.7451 (10)
α, β, γ (°)	104.597 (3), 112.569 (3), 105.220 (3)
V (Å^3)	588.7 (1)
Z	2
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.26
Crystal size (mm)	$0.18 \times 0.11 \times 0.11$
Data collection	
Diffractometer	Bruker D8 Venture Photon 100 CMOS
Absorption correction	Multi-scan (*SADABS*; Bruker, 2014)
$T_{\min}$, $T_{\max}$	0.638, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	17083, 2911, 2562
R_{int}	0.043
$(\sin\theta/\lambda)_{\max}$ (Å^{-1})	0.667
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.032, 0.082, 1.00
No. of reflections	2911
No. of parameters	156
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{\max}$, $\Delta\rho_{\min}$ (e Å^{-3})	0.29, −0.28

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Computing details

Data collection: *APEX3* (Bruker, 2014); cell refinement: *SAINT* (Bruker, 2014); data reduction: *SAINT* (Bruker, 2014); program(s) used to solve structure: *SHELXS2013* (Sheldrick, 2015a); program(s) used to refine structure: *SHELXL2013* (Sheldrick, 2015b); molecular graphics: *Mercury* (Bruno *et al.*, 2002); software used to prepare material for publication: *SHELXL2013* (Sheldrick, 2015b).

(I)

Crystal data

$C_{11}H_{15}N_3OS$	$F(000) = 252$
$M_r = 237.32$	$D_x = 1.339$ Mg m^{-3}
Triclinic, $P\bar{1}$	Melting point: 438 K
$a = 8.2799\ (8)$ Å	Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
$b = 8.9169\ (9)$ Å	Cell parameters from 9917 reflections
$c = 9.7451\ (10)$ Å	$\theta = 2.5\text{–}28.3°$
$\alpha = 104.597\ (3)°$	$\mu = 0.26$ mm^{-1}
$\beta = 112.569\ (3)°$	$T = 100$ K
$\gamma = 105.220\ (3)°$	Prism, colourless
$V = 588.7\ (1)$ Å^3	$0.18 \times 0.11 \times 0.11$ mm
$Z = 2$	

Data collection

Bruker D8 Venture Photon 100 CMOS diffractometer	2911 independent reflections
	2562 reflections with $I > 2\sigma(I)$
φ and ω scans	$R_{int} = 0.043$
Absorption correction: multi-scan (SADABS; Bruker, 2014)	$\theta_{max} = 28.3°$, $\theta_{min} = 2.5°$
	$h = -11 \rightarrow 11$
$T_{min} = 0.638$, $T_{max} = 0.746$	$k = -11 \rightarrow 11$
17083 measured reflections	$l = -12 \rightarrow 13$

Refinement

Refinement on F^2	Hydrogen site location: mixed
Least-squares matrix: full	H atoms treated by a mixture of independent
$R[F^2 > 2\sigma(F^2)] = 0.032$	and constrained refinement
$wR(F^2) = 0.082$	$w = 1/[\sigma^2(F_o^2) + (0.0325P)^2 + 0.3538P]$
$S = 1.00$	where $P = (F_o^2 + 2F_c^2)/3$
2911 reflections	$(\Delta/\sigma)_{max} < 0.001$
156 parameters	$\Delta\rho_{max} = 0.29$ e Å^{-3}
0 restraints	$\Delta\rho_{min} = -0.28$ e Å^{-3}

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($Å^2$)

	x	*y*	*z*	U_{iso}*/U_{eq}
C12	0.5032 (2)	−0.1953 (2)	0.3563 (2)	0.0345 (4)
H12A	0.6301	−0.1042	0.4309	0.052*
H12B	0.5165	−0.2971	0.3036	0.052*
H12C	0.4356	−0.2199	0.4166	0.052*
C11	0.1912 (2)	−0.26338 (16)	0.10998 (17)	0.0243 (3)
H11A	0.1070	−0.2506	0.1562	0.036*
H11B	0.1842	−0.3793	0.0828	0.036*
H11C	0.1508	−0.2401	0.0118	0.036*
S1	0.33739 (4)	0.28903 (4)	0.00401 (4)	0.02014 (10)
O	0.96910 (14)	0.95385 (12)	0.83590 (11)	0.0206 (2)
H0	1.063 (3)	1.046 (2)	0.864 (2)	0.031*
N2	0.37419 (16)	0.05734 (13)	0.12372 (13)	0.0170 (2)
H2	0.254 (2)	0.024 (2)	0.0853 (19)	0.020*
N1	0.65479 (15)	0.27673 (13)	0.21157 (13)	0.0163 (2)
H1	0.701 (2)	0.225 (2)	0.2663 (19)	0.020*
N3	0.47907 (15)	0.00499 (14)	0.23774 (13)	0.0194 (2)
C6	0.79084 (18)	0.67223 (16)	0.64146 (15)	0.0173 (2)
H6	0.7308	0.6484	0.7038	0.021*
C3	0.77639 (18)	0.44581 (15)	0.24342 (15)	0.0171 (2)
H3A	0.7100	0.4789	0.1551	0.021*
H3B	0.8951	0.4438	0.2427	0.021*
C1	0.46524 (17)	0.20611 (15)	0.12097 (14)	0.0147 (2)
C4	0.82883 (17)	0.57817 (15)	0.40388 (14)	0.0148 (2)
C7	0.92864 (17)	0.83296 (15)	0.69457 (14)	0.0158 (2)
C9	0.96926 (17)	0.73918 (15)	0.46107 (15)	0.0170 (2)
H9	1.0319	0.7622	0.4003	0.020*
C8	1.01956 (17)	0.86683 (15)	0.60508 (15)	0.0164 (2)
H8	1.1150	0.9760	0.6419	0.020*
C5	0.74164 (17)	0.54680 (15)	0.49646 (15)	0.0162 (2)
H5	0.6466	0.4376	0.4600	0.019*
C10	0.39253 (19)	−0.14134 (17)	0.23078 (16)	0.0197 (3)

Atomic displacement parameters ($Å^2$)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C12	0.0274 (8)	0.0421 (9)	0.0502 (10)	0.0188 (7)	0.0187 (7)	0.0374 (8)
C11	0.0297 (7)	0.0153 (6)	0.0263 (7)	0.0065 (5)	0.0131 (6)	0.0090 (5)
S1	0.01646 (16)	0.01708 (15)	0.02248 (17)	0.00497 (12)	0.00379 (13)	0.01202 (12)
O	0.0182 (5)	0.0184 (4)	0.0173 (4)	0.0022 (4)	0.0071 (4)	0.0030 (4)

N2	0.0138 (5)	0.0164 (5)	0.0197 (5)	0.0056 (4)	0.0053 (4)	0.0104 (4)
N1	0.0152 (5)	0.0145 (5)	0.0182 (5)	0.0059 (4)	0.0059 (4)	0.0083 (4)
N3	0.0174 (5)	0.0228 (5)	0.0238 (6)	0.0108 (4)	0.0097 (5)	0.0157 (5)
C6	0.0154 (6)	0.0201 (6)	0.0178 (6)	0.0059 (5)	0.0085 (5)	0.0101 (5)
C3	0.0151 (6)	0.0164 (6)	0.0187 (6)	0.0042 (5)	0.0081 (5)	0.0076 (5)
C1	0.0163 (6)	0.0135 (5)	0.0139 (5)	0.0060 (5)	0.0075 (5)	0.0046 (4)
C4	0.0131 (5)	0.0158 (5)	0.0161 (6)	0.0072 (5)	0.0055 (5)	0.0082 (5)
C7	0.0134 (5)	0.0169 (6)	0.0144 (6)	0.0067 (5)	0.0036 (5)	0.0065 (4)
C9	0.0154 (6)	0.0182 (6)	0.0202 (6)	0.0065 (5)	0.0094 (5)	0.0110 (5)
C8	0.0131 (5)	0.0146 (5)	0.0194 (6)	0.0041 (4)	0.0056 (5)	0.0086 (5)
C5	0.0131 (5)	0.0154 (5)	0.0186 (6)	0.0042 (4)	0.0060 (5)	0.0087 (5)
C10	0.0213 (6)	0.0225 (6)	0.0263 (7)	0.0131 (5)	0.0155 (5)	0.0152 (5)

Geometric parameters (Å, º)

S1—C1	1.6959 (14)	C8—C9	1.3914 (18)
O—C7	1.3708 (16)	C10—C11	1.498 (2)
O—H0	0.86 (2)	C10—C12	1.495 (2)
N1—C3	1.4527 (19)	C3—H3A	0.9900
N1—C1	1.3328 (19)	C3—H3B	0.9900
N2—N3	1.3929 (17)	C5—H5	0.9500
N2—C1	1.3554 (19)	C6—H6	0.9500
N3—C10	1.284 (2)	C8—H8	0.9500
N1—H1	0.839 (18)	C9—H9	0.9500
N2—H2	0.849 (18)	C11—H11A	0.9800
C3—C4	1.5186 (18)	C11—H11B	0.9800
C4—C5	1.391 (2)	C11—H11C	0.9800
C4—C9	1.395 (2)	C12—H12A	0.9800
C5—C6	1.3914 (19)	C12—H12B	0.9800
C6—C7	1.392 (2)	C12—H12C	0.9800
C7—C8	1.391 (2)		
C7—O—H0	111.1 (13)	N1—C3—H3B	109.00
C1—N1—C3	124.73 (12)	C4—C3—H3A	109.00
N2—N3—C10	116.82 (12)	C4—C3—H3B	109.00
S1—C1—N1	124.19 (11)	H3A—C3—H3B	108.00
S1—C1—N2	119.75 (11)	C4—C5—H5	119.00
C1—N1—H1	115.1 (12)	C6—C5—H5	119.00
C3—N1—H1	119.1 (12)	C5—C6—H6	120.00
N1—C1—N2	116.05 (12)	C7—C6—H6	120.00
N3—N2—H2	120.9 (12)	C7—C8—H8	120.00
C1—N2—H2	116.2 (13)	C9—C8—H8	120.00
N1—C3—C4	113.39 (12)	C4—C9—H9	119.00
C3—C4—C5	122.91 (12)	C8—C9—H9	119.00
C5—C4—C9	118.17 (12)	C10—C11—H11A	109.00
C3—C4—C9	118.92 (12)	C10—C11—H11B	109.00
C4—C5—C6	121.31 (13)	C10—C11—H11C	109.00
C5—C6—C7	119.54 (13)	H11A—C11—H11B	109.00

O—C7—C6	117.57 (13)	H11A—C11—H11C	109.00
C6—C7—C8	120.21 (12)	H11B—C11—H11C	109.00
O—C7—C8	122.21 (12)	C10—C12—H12A	109.00
C7—C8—C9	119.30 (13)	C10—C12—H12B	109.00
C4—C9—C8	121.46 (13)	C10—C12—H12C	109.00
N3—C10—C12	116.82 (14)	H12A—C12—H12B	109.00
C11—C10—C12	116.61 (14)	H12A—C12—H12C	109.00
N3—C10—C11	126.57 (13)	H12B—C12—H12C	109.00
N1—C3—H3A	109.00		
C3—N1—C1—S1	10.03 (19)	C3—C4—C9—C8	178.25 (13)
C3—N1—C1—N2	−171.02 (12)	C3—C4—C5—C6	−178.75 (14)
C1—N1—C3—C4	97.14 (15)	C9—C4—C5—C6	0.6 (2)
C1—N2—N3—C10	−175.62 (14)	C5—C4—C9—C8	−1.1 (2)
N3—N2—C1—S1	−170.98 (10)	C4—C5—C6—C7	0.7 (2)
N3—N2—C1—N1	10.02 (19)	C5—C6—C7—C8	−1.4 (2)
N2—N3—C10—C12	−178.18 (13)	C5—C6—C7—O	178.34 (13)
N2—N3—C10—C11	1.5 (2)	O—C7—C8—C9	−178.83 (13)
N1—C3—C4—C9	169.60 (13)	C6—C7—C8—C9	0.9 (2)
N1—C3—C4—C5	−11.0 (2)	C7—C8—C9—C4	0.4 (2)

Hydrogen-bond geometry (Å, °)

D—H⋯A	D—H	H⋯A	D⋯A	D—H⋯A
N2—H2⋯O^i	0.848 (17)	2.292 (17)	2.9955 (15)	140.6 (14)
N2—H2⋯O^ii	0.848 (17)	2.434 (16)	3.1333 (15)	140.3 (14)
O—H0⋯S1^iii	0.857 (19)	2.299 (19)	3.1349 (10)	165.2 (16)

Symmetry codes: (i) −x+1, −y+1, −z+1; (ii) x−1, y−1, z−1; (iii) x+1, y+1, z+1.