Crystal structure of 2-[bis(benzylsulfanyl)methyl]-6-methoxyphenol

Abhinav Raghuvanshi, Lena Knauer, Lydie Viau, Michael Knorr, Carsten Strohmann

Crystal structure of 2-Hydroxy-3-methoxyphenyl-(bis(benzylthio))methane

Abhinav Raghuvanshi,[a]‡ Lena Knauer,[b] Lydie Viau,[a] Michael Knorr[a] and Carsten Strohmann[b]*

[a]Institut UTINAM UMR 6213 CNRS, Université Bourgogne Franche-Comté, 16, Route de Gray, 25030 Besançon Cedex, France, and [b]Anorganische Chemie, TU Dortmund University, Otto-Hahn-Str. 6/6a, D-44227 Dortmund, Germany

‡ Current address: Discipline of Chemistry, Indian Institute of Technology Indore, Khandwa Road, Simrol Indore 453552, M.P., India.

Correspondence e-mail: carsten.strohmann@tu-dortmund.de

Keywords

crystal structure; *ortho*-vanillin, thioacetal, dithioether; supramolecular network

Synopsis

The crystal structure of 2-hydroxy-3-methoxyphenyl-(bis(benzylthio))methane ($C_{22}H_{22}O_2S_2$) was determined at 100 K. Both weak intramolecular O—H···O and intermolecular O—H···S hydrogen bonding can be observed.

Abstract

The title compound **1**, 2-hydroxy-3-methoxyphenyl-(bis(benzylthio))methane ($C_{22}H_{22}O_2S_2$), represents an example of an *ortho*-vanillin-based functionalized dithioether, which could be useful as potential chelating ligand or bridging ligand for coordination chemistry. This dithioacetal **1**, crystallizes in the orthorhombic space group *Pbca*. The crystal structure, recorded at 100 K, displays both weak intramolecular O—H···O and intermolecular O—H···S hydrogen bonding.

1. Chemical context

Acyclic and cyclic dithioether compounds containing the -S-C(R)(H)-S- (R = H, alkyl, aryl) motif are synthesised by nucleophilic substitution of geminal dihalides X-C(R)(H)-X in the presence of thiolate RS^- (Murray *et al.*, 1981). Alternatively, they are readily accessible by treatment of aldehydes and ketones with thiols RSH and dithiols $HS(CH_2)_nSH$ (n = 2, 3) yielding geminal dithioethers, also called acyclic and cyclic thioacetals (1,3-dithiolanes, 1,3-dithianes) (Shaterian *et al.*, 2011). This type of organosulfur compounds is commonly used for Corey-Seebach umpolung reactions and the Mozingo reduction of dithioketals to hydrocarbons (Seebach *et al.*, 1975; Zhao *et al.*, 2017), but there are also numerous other transformations in organic chemistry such as their oxidation to sulfoxides and sulfones (Gasparrini *et al.*, 1984). They have furthermore been used in the past as monodentate, chelating or bridging ligands to construct both simple mono- and dinuclear coordination compounds or to assemble coordination networks of varying dimensionality ranging from 1D to 3D. Selected examples are $[(C_5H_5)Fe(CO)_2(\kappa^1\text{-}BzSCH_2SBz)]^+$, the 1:1 adduct $[Hg_2(NO_3)_2{\bullet}BzSCH_2SBz)]$, the dinuclear Pd(I) complex $[ClPd(\mu_2\text{-}BzSCH_2SBz)_2PdCl]$, or

the monodimensional coordination polymer $[Ag_2(BzSCH_2SBz)_2](ClO_4)_2$ built upon dinuclear $[Ag(\mu_2\text{-}BzSCH_2SBz)_2Ag]^{2+}$ units (Brodersen *et al.*, 1977; Fuchita *et al.*, 1991; Kuhn *et al.*, 1986; Li *et al.*, 2005).

In the context of our research interest in the assembly of molecular cluster compounds and coordination polymers by complexation of $ArSCH_2SAr$ or dithiolane- and dithiane-based thiaheterocycles, (Chaabéne *et al.*, 2016; Knauer *et al.*, 2020; Knorr *et al.*, 2014; Raghuvanshi *et al.*, 2017; Raghuvanshi *et al.*, 2019; Schlachter *et al.*, 2018), we have developed novel functionalized dithioether compounds such as ferrocenyl thioethers bearing a substituent at the alpha-carbon atom linking the two -SR groups. With the idea to design a functionalized thioacetal ligand bearing along with the two soft *S*-donor sites additional harder *O*-donor sites, we have chosen 2-hydroxy-3-methoxybenzaldehyde (ortho-vanillin) as starting material. This hydroxylated aldehyde is present in the extracts and essential oils of many plants. Several papers describe also its use (in its deprotonated vanillinato form or as Schiff base-derived ligand) in coordination chemistry (Andruh, 2015; Kirpik *et. al.*, 2019; Yu *et al.*, 2011). Its reaction with 2 equivalents of benzyl mercaptan affords the targeted dithioacetal 2-Hydroxy-3-methoxyphenyl-(bis(benzylthio))methane **1**, which was isolated in high yield as crystalline solid (Scheme 1).

This acyclic thioacetal contains, in addition to the benzylic thioether groups and the methoxy group prone to ligate metal centres, a phenolic hydroxyl group, which may allow additional interactions through hydrogen bonding.

2. Structural commentary

Compound **1** crystallizes from CH_2Cl_2/hexane in the orthorhomic crystal system, space group *Pbca*. The C1–S1 and C1–S2 bond lengths of 1.8133 (12) and 1.8192 (12) Å match with those of $[BzSC(H)(C_6H_4NO_2\text{-}p)SBz]$ (1.823 (3) and 1.8262 (19) Å), but elongated compared with those of bis(benzylsulfanyl)methane (CSD TUQPAX) (1.7988 (13) and 1.8013 (13) Å) (Yang *et al.*, 2010). The angle S1–C1–S2 is almost identical with that of 4-nitrophenyl-bis(benzylsulfanyl)methane (107.25 (6) *versus* 107.76°), but considerably more acute that of $[BzSCH_2SBz]$ (117.33 (7)°). There is a weak intramolecular O1–H2 contact of 2.166 (19) Å between the H atom of the phenolic hydroxyl group and the O-atom of the methoxy group (*d*O1–O2 = 2.6467 (13) Å; O2–H2–O1 = 115.2 (15)°). For the starting material 2-hydroxy-3-methoxybenzaldehyde, a similar intramolecular hydrogen bond seems to be absent, instead a rather strong intramolecular hydrogen bond between the O-H group and the carbonyl oxygen was evidenced (Iwaski *et al.*, 1976). The phenyl rings of the benzyl moieties (C10-C18) and (C17-C21) and the phenyl ring of the vanillin part (C2-C7) form dihedral angles of 35.391° and 100.230° respectively. Compared to the structurally very related compound 4-nitrophenyl-bis(benzylsulfanyl)methane $[BzSC(H)(C_6H_4NO_2\text{-}p)SBz]$ (CSD SUNMAQ) (Binkowska *et al.*, 2009), the coplanar and perpendicular arrangement of the phenyl rings is thus lost in **1** (Fig.1 and Fig.2)**.**

3. Supramolecular features

In the network, there is an intermolecular O–H···S hydrogen bond between the H2 atom of the phenolic hydroxyl group and the S1 atom of a neighbored molecule with distances (*d* H2···S1 = 2.434 (19) Å, *d* O2···S1 = 3.1318 (10) Å) similar to those reported for 4-

(1,3-dithian-2-yl)-1,2-benzenediol (*d* H···S = 2.44 Å, *d* O···S = 3.2417 (13) Å), while the O-H-S angle is more acute (∠O2-H2-S1 = 139.1 (16) *versus* 159.2°) (Fig. 3 and Table 2). This O2–H2···S1 interaction results in chain formation running along the *b* direction.

One of the benzylic methylene group near the sulfur atom S2 interacts with the π-cloud of the phenyl part of the vanillin moiety through C-H···π contacts. The geometrical parameters for this interaction are *d*(H16A···Cg) = 2.715 Å, *d*(C16···Cg) = 3.632 Å, and ∠ C16–H16···Cg = 154.21°. The second phenyl ring of the dithiane moiety also exhibits C-H···π interaction: the second methylene group near the sulfur atom S1 interacts with a phenyl carbon (*d*(H9A···C20) = 2.8630 (14) Å, *d*(C9···C20) = 3.5271 (18) Å and ∠C9–H9A···C20 = 125.15 (8)°). The third C-H···π contact involves H5 of one vanillin ring and the phenyl ring of an adjacent vanillin ring. The geometrical parameters for this interaction are *d*(H5···Cg) = 2.844 Å, *d*(C5···Cg) = 3.750 Å, and ∠ C5–H5···Cg = 159.71°.

4. Database survey

There are several other examples of structurally characterized related dithioethers bearing hydroxy substituents giving rise to formation of supramolecular networks. Selected examples found in the Cambridge Structural Database (CSD, version 5.40, update August 2019; Groom *et al.*, 2016) include 2-(2-Hydroxyphenyl)-1,3-dithiane (CSD WADROJ), 2-(3-Hydroxyphenyl)-1,3-dithiane (CSD KALJUD), 4,6-bis(1,3-dithian-2-yl)benzene-1,3-diol (CSD DITFIX), 4-(1,3-Dithian-2-yl)benzene-1,3-diol (CSD DITFOD), 2-phenyl-1,3-dithiepane-5,6-diol (CSD FIBTOC), and 2,2'-(((4-Methoxyphenyl)methylene)disulfanediyl)diethanol (CSD YISVUT) (Datta *et al.*, 2013; Ganguly *et al.*, 2005; Laskar *et al.*, 2013; Liu *et al.*, 2018; Usman *et al.*, 2003).

5. Synthesis and crystallization

3-Methoxysalicylaldehyde (1 mmol, 152 mg), benzyl mercaptan (2.5 mmol, 310 mg), and conc. HCl (2mL) were added to a flask at 0 °C. The mixture was stirred for 60 min at room temperature. After the reaction was completed, the resulting mixture was neutralized with 10% aq $NaHCO_3$ (10 mL) and extracted with dichloromethane (3 × 10 mL). The combined extracts were washed with H_2O (3 × 20 mL) and dried over Na_2SO_4. Evaporation of the solvent in vacuo gave a solid product, which was further purified by column chromatography. The product was obtained as a white solid, Yield: 83% (430 mg). X-ray quality crystals were obtained by keeping a dichloromethane:hexane (1:1) mixture of **1** at 273K for 3-4 days .^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.19 (m, 11H, Ph), 6.86 (t, *J* = 7.8 Hz, 1H, CH), 6.78 (d, *J* = 7.8 Hz, 1H, CH), 5.83 (s, 1H, OH), 5.13 (s, 1H CHS_2), 3.88 (s, 3H, OCH_3), 3.79 (d, *J* = 13.1 Hz, 2H, CH_2), 3.64 (d, *J* = 13.1 Hz, 2H, CH_2).^{13}C{^{1}H } NMR (101 MHz, $CDCl_3$) δ 146.5 (Cq_{OH}), 142.8 ($CqOCH_3$), 137.8 (SCH_2Cq), 129.1 (SCH_2CCH), 128.4 (SCH_2CCHCH), 126.9 ($SCH_2CCHCHCH$), 125.3 (S_2CHCq), 120.9 ($S_2CHCqCH$), 119.9 ($S_2CHCqCHCH$), 110.0 ($CHCqOCH_3$), 56.1 (OCH_3), 44.8 (S_2CH), 36.7 (S_2CH_2). IR (ATR) cm^{-1}: 3419 (O-H), 1430-1612 (C=C). 1054 and 1264 (C-O), 766 (C-S). HRMS: (ESI) m/z calculated for $C_{22}H_{22}O_2S_2Na$ $[M+Na]^+$ 405.0953, found 405.0965.

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 1.

All protons were refined independently.

Table 1 Experimental details

	mo_b0238_0m
Crystal data	
Chemical formula	$C_{22}H_{22}O_2S_2$
M_r	382.51
Crystal system, space group	Orthorhombic, *Pbca*
Temperature (K)	100
a, *b*, *c* (Å)	7.7418 (8), 13.856 (3), 36.197 (5)
V (Å^3)	3882.9 (10)
Z	8
Radiation type	Mo *K*α
μ (mm^{-1})	0.29
Crystal size (mm)	0.49 × 0.42 × 0.25
Data collection	
Diffractometer	Bruker D8 VENTURE area detector
Absorption correction	Multi-scan *SADABS2016* (Bruker, 2016) was used for absorption correction. wR2(int) was 0.1206 before and 0.0488 after correction. The ratio of minimum to maximum transmission is 0.9558. The λ/2 correction factor is not present.
T_{min}, T_{max}	0.713, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	107706, 5005, 4510
R_{int}	0.033

$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.684
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.033, 0.077, 1.09
No. of reflections	5005
No. of parameters	324
H-atom treatment	All H-atom parameters refined
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.34, −0.21

Computer programs: *APEX2* (Bruker, 2016), *SAINT* V8.35A (Bruker, 2016), SHELXT (Sheldrick, 2015), XL (Sheldrick, 2008), Olex2 1.3 (Dolomanov *et al.*, 2009).

Table 2 Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···S1^{i}	0.85 (2)	2.44 (2)	3.1317 (11)	139.5 (17)
O2—H2···O1	0.85 (2)	2.17 (2)	2.6469 (14)	115.2 (16)
Symmetry code: (i) −*x*+3/2, *y*−1/2, *z*.				

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Funding information

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Figures

Figure 1

Synthesis of 2-Hydroxy-3-methoxyphenyl-(bis(benzylthio))methane (**1**).

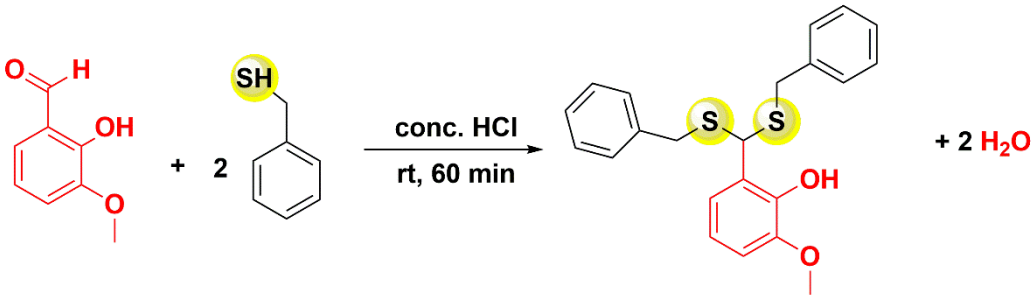


Figure 2

A displacement ellipsoid plot of **1** at the 50% probability level.

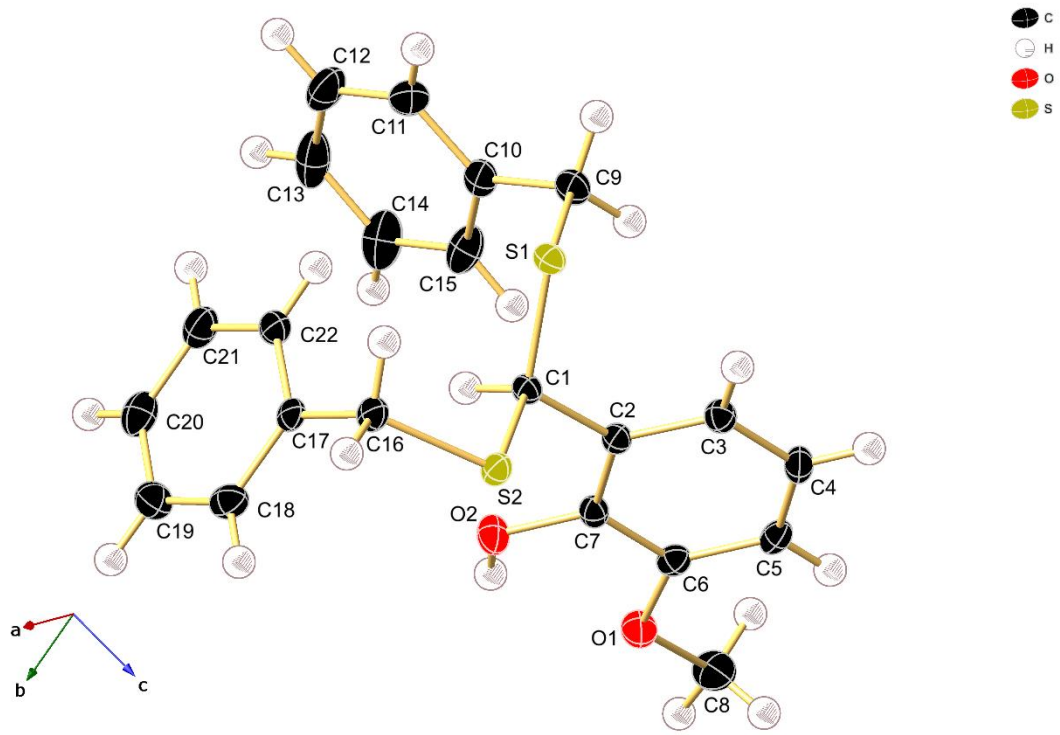


Figure 3

A view of the crystal packing of the title compound. For clarity, the H atoms have been omitted**.**

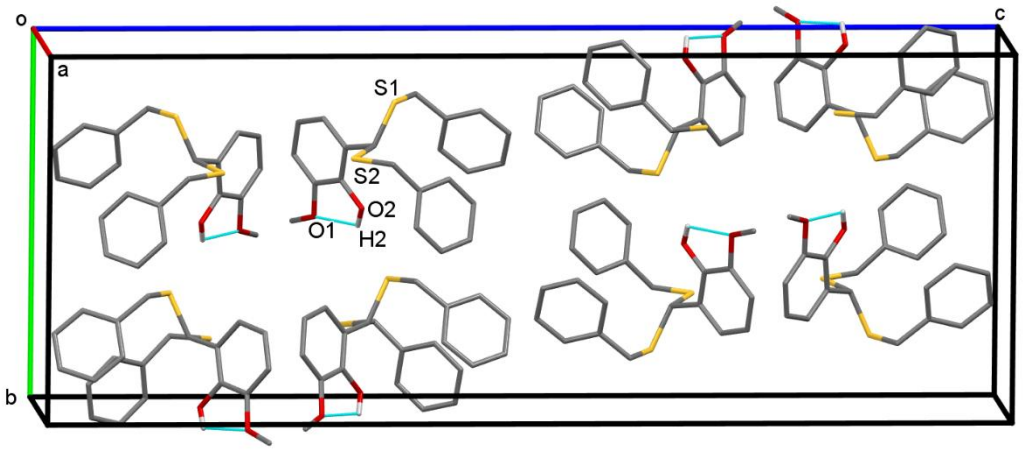
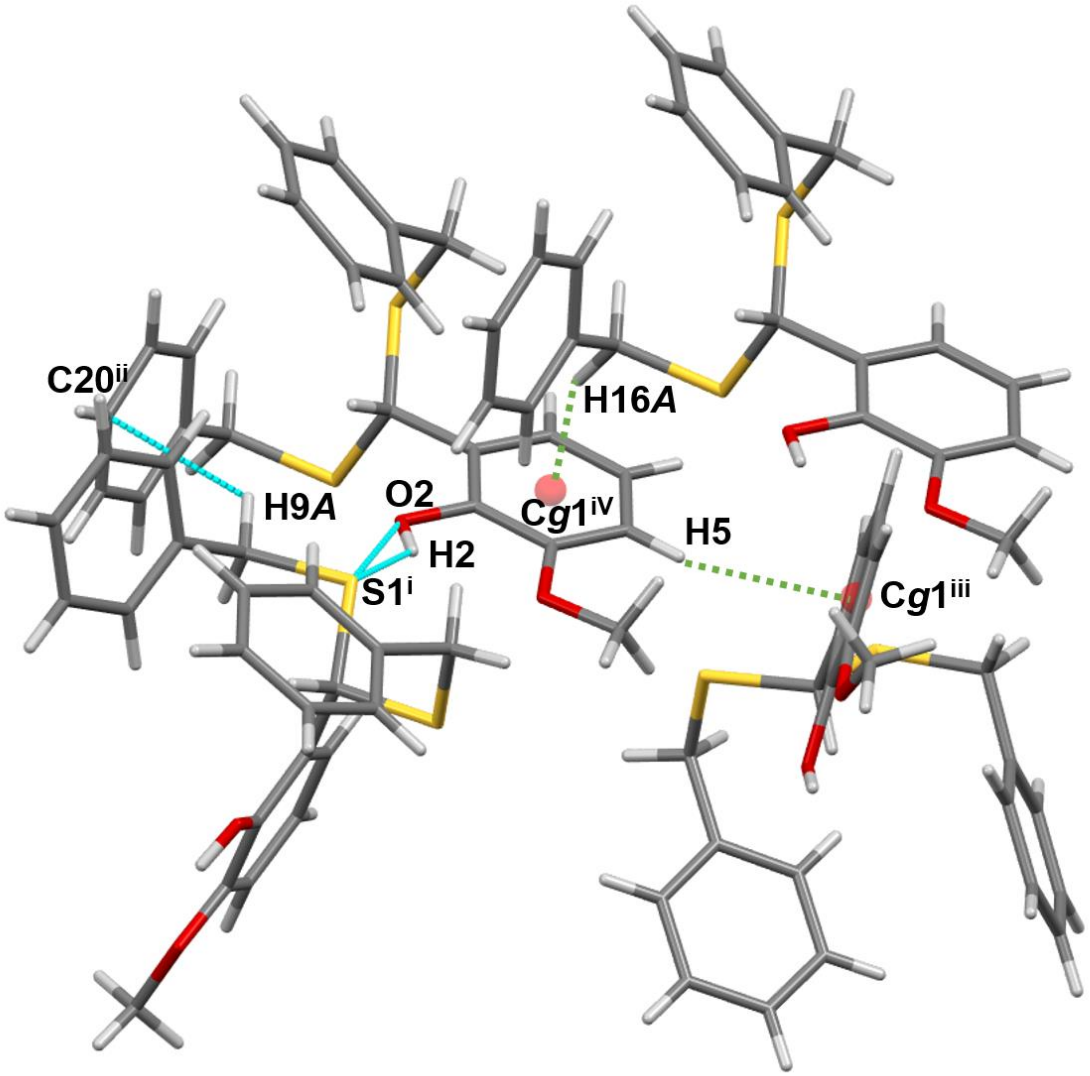


Figure 4

Intermolecular contacts of compound **1**.


C20ii
H9A
O2
H2
S1i
Cg1iv
H16A
H5
Cg1iii