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1,4-Bis[(*Z*)-2-(3-mesityl-3-methylcyclobutyl)-2-(thiosemicarbazono)ethyl]piperazine dimethyl sulfoxide disolvate

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.006 Å
Disorder in solvent or counterion
R factor = 0.058
wR factor = 0.174
Data-to-parameter ratio = 15.7

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

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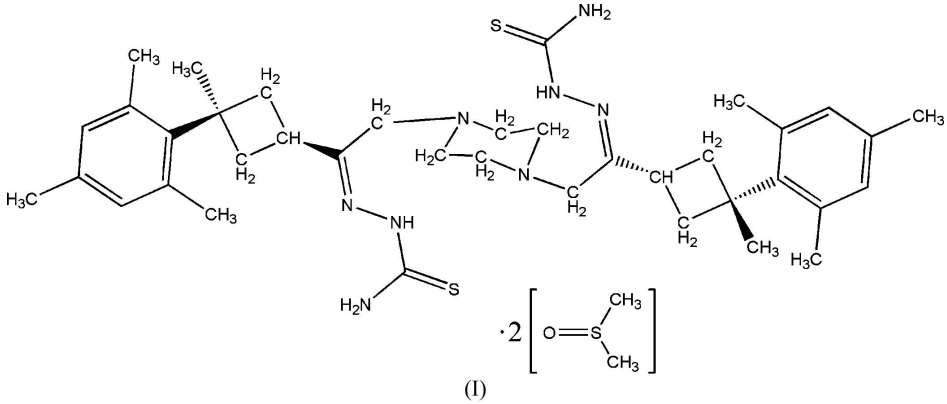
The structure of the title compound, $C_{38}H_{56}N_8S_2\cdot 2C_2H_6OS$, has been determined by single-crystal diffractometry and is compared with the structures of other compounds containing the thiosemicarbazide group. The structure is stabilized by N—H···S hydrogen bonding, resulting in the formation of infinite chains parallel to the [010] axis. The thiosemicarbazone group has an *E* configuration.

Comment

Thiosemicarbazones represent an important class of potential ligands for complexing metal cations to obtain coordination compounds of biomedical relevance (Forni & Gradinaru, 2002). In the solid state, thiosemicarbazones, N^1H_2–N^2H–C(=S)–N^4H_2 (thsc), exist in the thione form and are almost planar. In solution, however, they are known to tautomerize into the thiol form. In thsc (Andreetti *et al.*, 1970) and its derivatives, the S atom is *trans* to the hydrazine atom N^1, thus placing the atoms N^1 and N^4 in suitable positions for intramolecular hydrogen bonding (Chattopadhyay *et al.*, 1989; Casas *et al.*, 2000). The molecule of the title compound, (I), contains two thsc groups, one piperazine ring and two cyclobutyl rings. Some piperazine-containing derivatives constitute a novel class of mixed D2/D4 receptor antagonists (Zhao *et al.*, 2002), and *N*,*N*′-disubstitued piperazine derivatives are antifilarial, antiamoebic and spermicidal agents (Yogavel *et al.*, 2003; Sonurlikar *et al.*, 1977).



(I)

The crystal structure determination of the title compound, (I) (Fig. 1), was carried out in order to determine the strength of the hydrogen-bond capability of the thsc groups, as well as to establish the molecular arrangement; the aim was also to compare the geometry of the thsc group in (I) with those found in other molecules containing this group (Table 2). The structure of (I) contains five rings, namely two cyclobutane

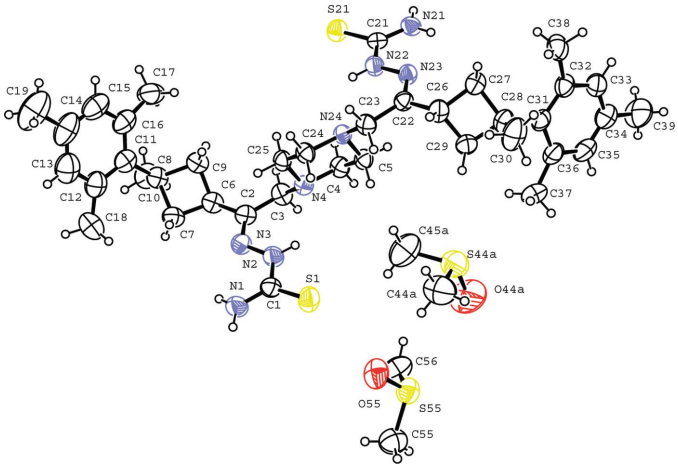


Figure 1
The asymmetric unit of (I), with the atom-numbering scheme and 40% probability displacement ellipsoids. For clarity, the minor component of the disordered part of the solvent has been omitted.

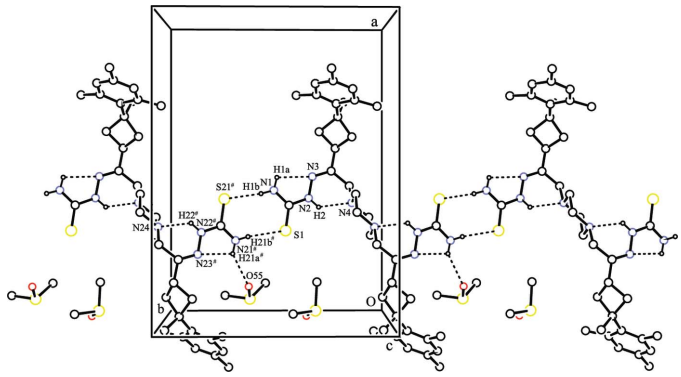


Figure 2
A view, down the *c* axis, of the chains of $R_2^2(8)$ rings in (I). Atoms labelled with a hash (#) are at the symmetry position $(x, 1 + y, z)$. For clarity, H atoms bonded to C atoms and the minor component of the disordered DMSO have been omitted.

rings (C6–C9 and C26–C29), two 1,3,5-trimethylbenzene rings and an *N*,*N*′-disubstituted piperazine ring. There is a pseudo-centre of symmetry at the centre of the piperazine ring. Additionally, there are two dimethylsulfoxide (DMSO) molecules in the asymmetric unit.

A comparison of the bond lengths and angles of the thsc group for related compounds is listed in Table 2. All bond lengths and angles, except for N2—N3, are in agreement with the literature values; in the present study, N2—N3 is somewhat longer. The *Z* configuration of thsc is preferred by most molecules in the solid state, as mentioned above. In the thsc group in (I), the S atom is *trans* to the hydrazine N atom, which has also been observed in other related compounds (Table 2).

An inspection of the structures reported in Table 2 indicates that, in all cases, the *E* configuration should allow the formation of one or more intramolecular N—H···N hydrogen bonds. Intramolecular interactions are also found in (I). Analysis of the crystal packing and comparison with the tabulated structures shows significant differences. The molecules of (I) are linked head-to-head by N—H···S hydrogen bonding. This configuration is characterized by an $R_2^2(8)$ graph set (Bernstein *et al.*, 1995). Propagation by translation in the *b* direction results in polymeric chains approximately along the *b* axis in the crystal structure, as illustrated in Fig. 2. Head-to-head intermolecular N—H···S hydrogen-bonding interactions have not been reported for the other structures considered in Table 2. There is also an intermolecular N—H···O hydrogen-bonding interaction between the thsc group and a DMSO molecule (Table 2, Fig. 2). All these interactions stabilize the crystal structure of (I).

The piperazine ring adopts an almost perfect chair conformation, with puckering parameters (Cremer & Pople, 1975) Q_T = 0.582 (3) Å, θ = 179.4 (4)° and φ = 98 (22)°. Literature values for the puckering of the cyclobutane ring are 23.5° (Swenson *et al.*, 1997) and 29.0 (1)° (Yüksektepe *et al.*, 2004). In this study, the C27/C26/C29 plane forms a dihedral angle of 28.16 (3)° with the C27/C28/C29 plane, and the C7/C6/C9 plane forms a dihedral angle of 27.03 (3)° with the C7/C8/C9 plane, which deviates from the values reported in the previous studies.

Experimental

A mixture of 1-mesityl-1-methyl-3-(2-chloro-1-oxoethyl)cyclobutane (5.29 g, 20 mmol), piperazine (0.86 g, 10 mmol) and K_2CO_3 (1.38 g, 10 mmol) in absolute ethanol (50 ml) was refluxed for 90 min, and the progress of the reaction was monitored by IR spectroscopy. After completion of the reaction, thiosemicarbazide (1.82 g, 20 mmol), with *p*-toluenesulfonic acid (0.002 g) as catalyst, was added portionwise and the mixture stirred at room temperature for 10 min. The resulting solid, 1,4-bis{[(2*Z*)-2-(3-mesityl-3-methylcyclobutyl)-2-one thiosemicarbazono]ethyl}piperazine, was separated from the reaction mixture by suction. Shiny crystals of (I) suitable for X-ray analysis were obtained from a solution in DMSO by slow evaporation at room temperature (yield 88%; m.p. 501 K).

Crystal data

$C_{38}H_{56}N_8S_2{\cdot}2C_2H_6OS$
M_r = 845.28
Monoclinic, $P2_1/n$
a = 17.861 (11) Å
b = 13.386 (6) Å
c = 20.451 (13) Å
β = 91.744 (5)°
V = 4887 (5) Å^3
Z = 4
D_x = 1.149 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3897 reflections
θ = 1.5–27.2°
μ = 0.24 mm^{-1}
T = 293 (2) K
Prism, yellow
0.34 × 0.30 × 0.21 mm

Data collection

Stoe IPDS-2 diffractometer
ω scans
Absorption correction: integration (*X-RED32*; Stoe & Cie, 2002)
T_{min} = 0.876, T_{max} = 0.953
25636 measured reflections
8599 independent reflections
4458 reflections with $I > 2\sigma(I)$
R_{int} = 0.057
θ_{max} = 25.0°
h = −21 → 21
k = −15 → 15
l = −24 → 24

Refinement

Refinement on F^2	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.058$	$w = 1/[\sigma^2(F_o^2) + (0.0946P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.174$	$(\Delta/\sigma)_{max} = 0.009$
$S = 0.94$	$\Delta\rho_{max} = 0.80$ e Å^{-3}
8599 reflections	$\Delta\rho_{min} = -0.29$ e Å^{-3}
548 parameters	

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1A···N3	0.86	2.26	2.629 (4)	106
N1—H1B···S21^{i}	0.86	2.56	3.407 (4)	167
N2—H2···N4	0.86	2.14	2.747 (4)	127
N21—H21A···O55^{ii}	0.86	2.27	2.983 (5)	140
N21—H21A···N23	0.86	2.29	2.649 (4)	105
N21—H21B···S1^{ii}	0.86	2.49	3.344 (4)	172
N22—H22···N24	0.86	2.08	2.701 (4)	128
C6—H6···S21^{iii}	0.98	2.81	3.700 (4)	152
C24—H24A···O55^{iv}	0.97	2.47	3.413 (5)	163
C44A—H44B···O55	0.96	2.59	3.553 (9)	175
C55—H55B···O44A^{v}	0.96	2.57	3.425 (9)	149
C56—H56C···O44A^{v}	0.96	2.41	3.297 (9)	154

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

Table 2
Comparative geometrical parameters (Å, °) in the thsc moiety.

Compound	N1—C1	C1—S1	N2—C1	N2—N3	S1—C1—N1	Ref.
(I)	1.321 (5)	1.669 (4)	1.352 (5)	1.390 (4)	125.3 (3)	(*a*)
(II)	1.325 (3)	1.688 (2)	1.343 (3)	1.374 (2)	123.1 (2)	(*b*)
(III)	1.353 (3)	1.689 (2)	1.353 (3)	1.373 (2)	122.6 (2)	(*c*)
(IV)	1.342 (2)	1.696 (2)	1.342 (2)	1.342 (2)	122.5 (1)	(*d*)
(V)	1.319 (3)	1.674 (2)	1.352 (2)	1.373 (2)	123.3 (2)	(*e*)
(VI)	1.319 (3)	1.673 (2)	1.350 (2)	1.382 (2)	124.8 (2)	(*f*)

References: (*a*) This work (averaged values), (I), $C_{42}H_{68}N_8O_2S_4$, 1,4-bis[[(2*Z*)-2-(3-mesityl-3-methylcyclobutyl)-2-one thiosemicarbazone]ethyl]piperazine dimethyl sulfoxide disolvate; (*b*) Kokila *et al.* (1995), (II), $C_{11}H_{17}N_3O_4S$, 3,4,5-trimethoxybenzaldehyde thiosemicarbazone monohydrate; (*c*) Zhu *et al.* (1999), (III), $C_{22}H_{32}N_6O_4S_4$, 2,2′-ethylenedioxydibenzaldehyde bis(thiosemicarbazone) bis(dimethyl sulfoxide); (*d*) Moers *et al.* (1999), (IV), $C_{16}H_{34}N_6O_4S_2$, 1,4,7,10-tetraoxacyclododecane-acetone thiosemicarbazone (1/2); (*e*) Wu *et al.* (2000), (V), $C_{16}H_{26}N_8O_2S_2$, terephthaldehyde thiosemicarbazone bis-*N*,*N*-dimethylformamide; (*f*) Sampath *et al.* (2003), (VI), $C_{22}H_{28}N_4S$, 1-*N*-methyl-*t*-3-isopropyl-*r*-2,*c*-6-diphenylpiperidone thiosemicarbazone.

H atoms were treated as riding, with N—H = 0.86 Å and C—H = 0.93–0.96 Å, and with U_{iso}(H) = 1.2 or 1.5U_{eq} of the parent atom. One DMSO molecule was disordered, such that atoms S44, O44, C44 and C45 show positional disorder over two sites, with site occupancy factors of 0.834 (9) and 0.179 (9).

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: *ORTEP3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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