Acta Cryst E CRYSTALLOGRAPHIC COMMUNICATIONS

OPEN ACCESS

ISSN 2056-9890

Crystal structure of [(*E*)-({2-[3-(2-{(1*E*)-[(carbamothioylamino)imino]methyl}-phenoxy)propoxy]phenyl}methylidene)-amino]thiourea with an unknown solvate

Joel T. Mague,[a] Shaaban K. Mohamed,[b,c] Mehmet Akkurt,[d] Sabry H. H. Younes[e] and Mustafa R. Albayati[f]*

[a]Department of Chemistry, Tulane University, New Orleans, LA 70118, USA, [b]Faculty of Science & Engineering, School of Healthcare Science, Manchester Metropolitan University, Manchester M1 5GD, England, [c]Chemistry Department, Faculty of Science, Minia University, 61519 El-Minia, Egypt, [d]Department of Physics, Faculty of Sciences, Erciyes University, 38039 Kayseri, Turkey, [e]Chemistry Department, Faculty of Science, Sohag University, 82524 Sohag, Egypt, and [f]Kirkuk University, College of Education, Department of Chemistry, Kirkuk, Iraq. *Correspondence e-mail: shaabankamel@yahoo.com

Received 22 June 2015; accepted 23 June 2015

Edited by W. T. A. Harrison, University of Aberdeen, Scotland

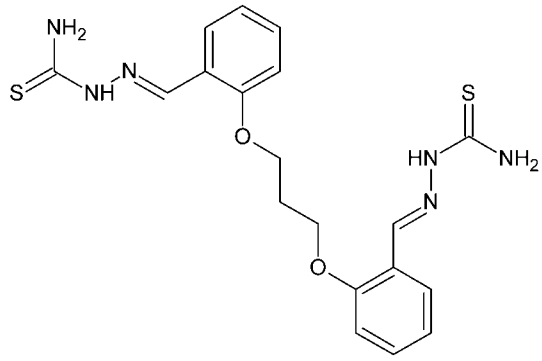
The title molecule, $C_{19}H_{22}N_6O_2S_2$, has crystallographically imposed C_2 symmetry, with the central C atom lying on the rotation axis. The O—C—C—C torsion angle for the central chain is −59.22 (16)° and the dihedral angle between the planes of the benzene rings is 75.20 (7)°. In the crystal, N—H···O and N—H···S interactions link the molecules, forming a three-dimensional network encompassing channels running parallel to the *c* axis, which account for about 20% of the unit-cell volume. The contribution to the scattering from the highly disordered solvent molecules in these channels was removed with the SQUEEZE routine [Spek (2015). *Acta Cryst.* C**71**, 9–18] in *PLATON*. The stated crystal data for M_r, μ *etc.* do not take these into account.

Keywords: crystal structure; bis-thiosemicarbazones; biological activity; SQUEEZE.

CCDC reference: 1408451

1. Related literature

For the various biological activities of bis-thiosemicarbazones, see: Singh *et al.* (2001); Offiong & Martelli (1997). For general synthesis and assessment of the pharmaceutical properties of thiosemicarbazone scaffold compounds, see: Greenbaum *et al.* (2004); Finch *et al.* (1999); Wilson *et al.* (1974); Du *et al.* (2002); Desai *et al.* (1984); Shucla *et al.* (1984); Vrdoljak *et al.* (2010); Belicchi-Ferrari *et al.* (2010); Marzano *et al.* (2009). For use of the SQUEEZE routine in *PLATON* to remove the contribution of disordered solvents, see: Spek (2009, 2015).



2. Experimental

2.1. Crystal data

$C_{19}H_{22}N_6O_2S_2$
M_r = 430.55
Monoclinic, $C2/c$
a = 19.3941 (5) Å
b = 12.7110 (3) Å
c = 10.1450 (3) Å
β = 103.306 (2)°
V = 2433.79 (11) Å^3
Z = 4
Cu $K\alpha$ radiation
μ = 2.19 mm^{-1}
T = 150 K
0.44 × 0.23 × 0.05 mm

2.2. Data collection

Bruker D8 VENTURE PHOTON 100 CMOS diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2014)
T_{min} = 0.71, T_{max} = 0.91
8997 measured reflections
2365 independent reflections
1886 reflections with $I > 2\sigma(I)$
R_{int} = 0.042

2.3. Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.112
S = 1.06
2365 reflections
135 parameters
1 restraint
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.24 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1*A*···N3	0.91	2.27	2.631 (2)	103
N1—H1*A*···S1^{i}	0.91	2.64	3.3393 (16)	135
N1—H1*B*···O1^{ii}	0.91	2.20	3.1046 (19)	176
N2—H2*A*···S1^{iii}	0.91	2.49	3.3909 (16)	171

Symmetry codes: (i) $x, -y+1, z-\frac{1}{2}$; (ii) $-x+\frac{1}{2}, y+\frac{1}{2}, -z+\frac{3}{2}$; (iii) $-x+\frac{1}{2}, -y+\frac{1}{2}, -z+2$.

Data collection: *APEX2* (Bruker, 2014); cell refinement: *SAINT* (Bruker, 2014); data reduction: *SAINT*; program(s) used to solve structure: *SHELXT* (Sheldrick, 2015*a*); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2015*b*); molecular graphics: *DIAMOND* (Brandenburg & Putz, 2012) and *ORTEP-3 for Windows* (Farrugia, 2012); software used to prepare material for publication: *SHELXTL* (Sheldrick, 2008) and *WinGX* (Farrugia, 2012).

Acknowledgements

The support of NSF–MRI (grant No. 1228232) for the purchase of the diffractometer and Tulane University for support of the Tulane Crystallography Laboratory are gratefully acknowledged.

Supporting information for this paper is available from the IUCr electronic archives (Reference: HB7453).

References

Belicchi-Ferrari, M., Bisceglie, F., Buschini, A., Franzoni, S., Pelosi, G., Pinelli, S., Tarasconi, P. & Tavone, M. (2010). *J. Inorg. Biochem.* **104**, 199–206.
Brandenburg, K. & Putz, H. (2012). *DIAMOND*. Crystal Impact GbR, Bonn, Germany.
Bruker (2014). *APEX2*, *SAINT* and *SADABS*. Bruker AXS, Inc., Madison, Wisconsin, USA.
Desai, N. C., Shucla, H. K., Parekh, B. R. & Thaker, K. A. (1984). *J. Indian Chem. Soc.* **61**, 455–457.
Du, X., Guo, C., Hansell, E., Doyle, P. S., Caffrey, C. R., Holler, T. P., McKerrow, J. H. & Cohen, F. E. (2002). *J. Med. Chem.* **45**, 2695–2707.
Farrugia, L. J. (2012). *J. Appl. Cryst.* **45**, 849–854.
Finch, R. A., Liu, M. C., Cory, A. H., Cory, J. G. & Sartorelli, A. C. (1999). *Adv. Enzyme Regul.* **39**, 3–12.
Greenbaum, D. C., Mackey, Z., Hansell, E., Doyle, P., Gut, J., Caffrey, C. R., Lehrman, J., Rosenthal, P. J., McKerrow, J. H. & Chibale, K. (2004). *J. Med. Chem.* **47**, 3212–3219.
Marzano, C., Pellei, M., Tisato, F. & Santini, C. (2009). *Anticancer Agents Med. Chem.* **9**, 185–211.
Offiong, O. E. & Martelli, S. (1997). *Transition Met. Chem.* **22**, 263–269.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Sheldrick, G. M. (2015*a*). *Acta Cryst.* A**71**, 3–8.
Sheldrick, G. M. (2015*b*). *Acta Cryst.* C**71**, 3–8.
Shucla, H. K., Desai, N. C., Astik, R. R. & Thaker, K. A. (1984). *J. Indian Chem. Soc.* **61**, 168–171.
Singh, N. K., Singh, S. B., Shrivastav, A. & Singh, S. M. (2001). *J. Chem. Sci.* **113**, 257–273.
Spek, A. L. (2009). *Acta Cryst.* D**65**, 148–155.
Spek, A. L. (2015). *Acta Cryst.* C**71**, 9–18.
Vrdoljak, V., Đilović, I., Rubčić, M., Kraljević Pavelić, S., Kralj, M., Matković–Čalogović, D., Piantanida, I., Novak, P., Rožman, A. & Cindrić, M. (2010). *Eur. J. Med. Chem.* **45**, 38–48.
Wilson, H. R., Revankar, G. R. & Tolman, R. L. (1974). *J. Med. Chem.* **17**, 760–761.

supporting information

Acta Cryst. (2015). E**71**, o530–o531 [doi:10.1107/S2056989015012074]

Crystal structure of [(*E*)-({2-[3-(2-{(1*E*)-[(carbamothioylamino)imino]methyl}-phenoxy)propoxy]phenyl}methylidene)amino]thiourea with an unknown solvate

Joel T. Mague, Shaaban K. Mohamed, Mehmet Akkurt, Sabry H. H. Younes and Mustafa R. Albayati

S1. Comment

Currently, bis-thiosemicarbazones is considerable interest in their biological activity (Singh *et al.*, 2001; Offiong & Martelli, 1997) and have been known for over 50 years. Thiosemicarbazones have been reported to exhibit antivirals and as anticancer therapeutics, as well as for their parasiticidal action against Plasmodium falciparum and Trypanasoma cruzi which are the causative agents of malarya and Chagas′ disease, respectively (Greenbaum *et al.*, 2004; Finch *et al.*, 1999; Wilson *et al.*, 1974; Du *et al.*, 2002). In addition, in the last few years there has been a growing attention towards thiosemicarbazones related to their range of biological properties, as antituberculosis activity (Desai *et al.*, 1984; Shucla *et al.*, 1984), antitumor (Vrdoljak *et al.*, 2010), antiproliferative (Belicchi-Ferrari *et al.*, 2010), and anticancer agents (Marzano *et al.*, 2009). Such facts inspired us to synthesis and study the crystal structure determination of the title compound.

The title molecule has crystallographically imposed C_2 symmetry (Fig. 1). The dihedral angle between the planes of the benzene rings is 75.20 (7)°. Significant N1—H1B···O1^{i} (i: 1.5 - *x*, -1/2 + *y*, 1/2 - *z*) hydrogen bonds are formed in the crystal as well as weaker N2—H2A···S1^{ii} (ii: 1.5 - *x*, 1.5 - *y*, -*z*) and N1—H1A···S1^{iii} (iii: *x* 1 - *y*, 1/2 + *z*) interactions (Fig. 2). These lead to the formation of channels running parallel to the *c* axis (Fig. 3).

S2. Experimental

A mixture of 0.5 mmol (142 mg) of 2,2′-[ethane-1,2-diylbis(oxy)]dibenzaldehyde and 1 mmol (91 mg) of thiosemicarbazide in ethanol (10 ml) was heated under reflux for 4 h in the presence of a catalytic amount of acetic acid. After cooling, the reaction mixture was poured into an ice-water. The resulting solid product was then filtered off, washed with water, dried and crystallized from dimethylformamide to afford the title compound. Mp 488 K.

S3. Refinement

The H-atom (H10A) attached to C10 was located from a difference Fourier map and refined with restraint C—H = 0.99 (2) Å using a riding model, with U_{iso}(H) = 1.2 U_{eq}(C). The other H-atoms attached to carbon were placed in calculated positions (C—H = 0.95 - 0.99 Å) while those attached to nitrogen were placed in locations derived from a difference map and their parameters adjusted to give N—H = 0.91 Å. All were included as riding contributions with isotropic displacement parameters 1.2 times those of the attached atoms. A region of density amounting to the scattering from approximately 1.5 carbon atoms, apparently disordered about the twofold axis and well removed from the main molecule was removed with *PLATON SQUEEZE* (Spek, 2009) after it proved impossible to identify it with any reasonable solvent or byproduct molecule.

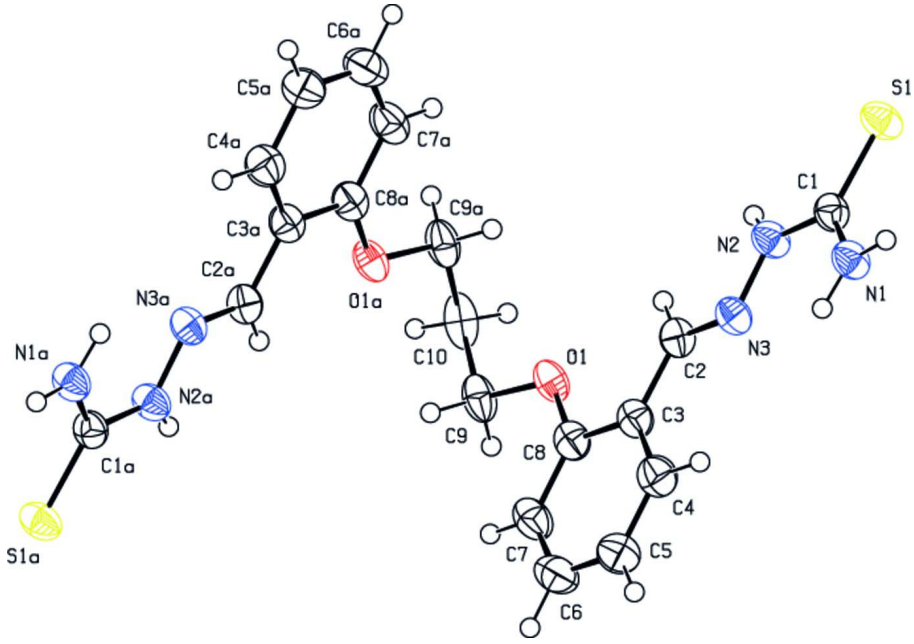


Figure 1

The title molecule with labeling scheme and 50% probability ellipsoids. Atoms with the suffix a are related to their counterparts by the crystallographic twofold axis passing through C10.

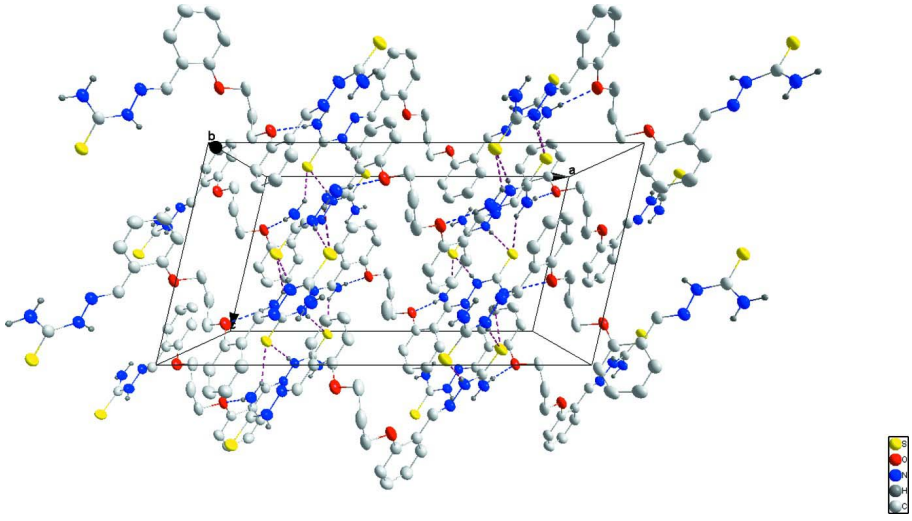


Figure 2

Packing viewed down the *b* axis. N—H···O and N—H···S hydrogen bonds are shown, respectively, as blue and purple dotted lines.

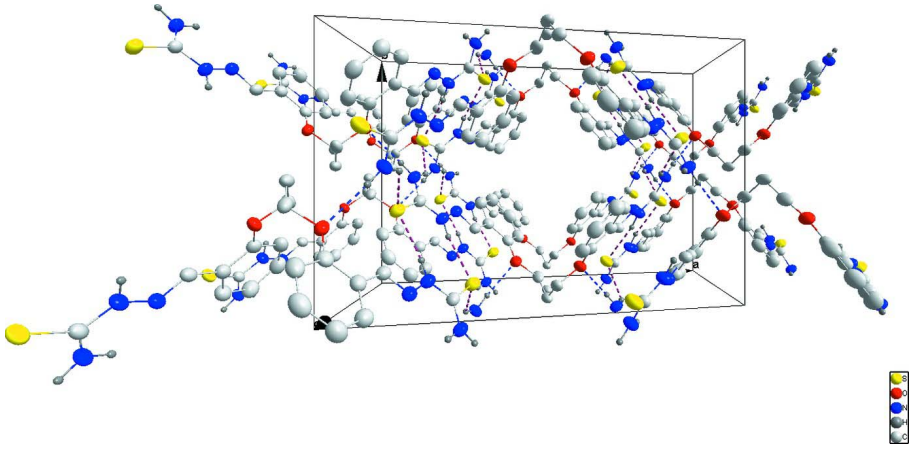


Figure 3

Packing viewed down the the *c* axis showing the one-dimensonal channels.

[(*E*)-({2-[3-(2-{(1*E*)-[(Carbamothioylamino)imino]methyl}phenoxy)propoxy]phenyl}methylidene)amino]thiourea

Crystal data

$C_{19}H_{22}N_6O_2S_2$
$M_r = 430.55$
Monoclinic, *C*2/*c*
Hall symbol: -C 2yc
$a = 19.3941\ (5)$ Å
$b = 12.7110\ (3)$ Å
$c = 10.1450\ (3)$ Å
$\beta = 103.306\ (2)°$
$V = 2433.79\ (11)$ Å^3
$Z = 4$
$F(000) = 904$
$D_x = 1.175$ Mg m^{-3}
Cu $K\alpha$ radiation, $\lambda = 1.54178$ Å
Cell parameters from 5935 reflections
$\theta = 4.2–72.3°$
$\mu = 2.19$ mm^{-1}
$T = 150$ K
Plate, colourless
0.44 × 0.23 × 0.05 mm

Data collection

Bruker D8 VENTURE PHOTON 100 CMOS diffractometer
Radiation source: INCOATEC IμS micro–focus source
Mirror monochromator
Detector resolution: 10.4167 pixels mm^{-1}
ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2014)
$T_{min} = 0.71$, $T_{max} = 0.91$
8997 measured reflections
2365 independent reflections
1886 reflections with $I > 2\sigma(I)$
$R_{int} = 0.042$
$\theta_{max} = 72.4°$, $\theta_{min} = 4.7°$
$h = -23\rightarrow21$
$k = -15\rightarrow15$
$l = -12\rightarrow11$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.040$
$wR(F^2) = 0.112$
$S = 1.06$
2365 reflections
135 parameters
1 restraint
Hydrogen site location: mixed
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0642P)^2 + 0.5713P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.24$ e Å^{-3}
$\Delta\rho_{min} = -0.22$ e Å^{-3}

Special details

Geometry. Bond distances, angles *etc*. have been calculated using the rounded fractional coordinates. All su's are estimated from the variances of the (full) variance-covariance matrix. The cell e.s.d.'s are taken into account in the estimation of distances, angles and torsion angles

Refinement. Refinement on F^2 for ALL reflections except those flagged by the user for potential systematic errors. Weighted *R*-factors *wR* and all goodnesses of fit *S* are based on F^2, conventional *R*-factors *R* are based on *F*, with *F* set to zero for negative F^2. The observed criterion of $F^2 > \sigma(F^2)$ is used only for calculating -*R*-factor-obs *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on *F*, and *R*-factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
S1	0.16947 (3)	0.37583 (4)	1.00065 (5)	0.0410 (2)
O1	0.41803 (6)	0.15260 (9)	0.63827 (14)	0.0374 (4)
N1	0.18026 (8)	0.48300 (11)	0.78226 (16)	0.0378 (5)
N2	0.24940 (8)	0.33630 (12)	0.82840 (15)	0.0362 (5)
N3	0.27239 (8)	0.35523 (11)	0.71219 (16)	0.0355 (4)
C1	0.20151 (9)	0.40093 (13)	0.86192 (18)	0.0338 (5)
C2	0.31703 (9)	0.28864 (13)	0.68644 (18)	0.0343 (5)
C3	0.34370 (10)	0.29762 (13)	0.56355 (19)	0.0356 (5)
C4	0.31914 (10)	0.37535 (16)	0.4677 (2)	0.0437 (6)
C5	0.34321 (11)	0.38278 (17)	0.3499 (2)	0.0493 (7)
C6	0.39290 (12)	0.31119 (18)	0.3267 (2)	0.0499 (7)
C7	0.41864 (11)	0.23341 (16)	0.4199 (2)	0.0443 (6)
C8	0.39431 (10)	0.22645 (13)	0.53912 (19)	0.0358 (5)
C9	0.47639 (10)	0.08725 (14)	0.6228 (2)	0.0421 (6)
C10	0.50000	0.0236 (2)	0.75000	0.0468 (9)
H1A	0.19900	0.49480	0.70920	0.0450*
H1B	0.15310	0.53380	0.80830	0.0450*
H2	0.33300	0.23270	0.74800	0.0410*
H2A	0.26650	0.27530	0.87040	0.0430*
H4	0.28500	0.42450	0.48350	0.0520*
H5	0.32590	0.43640	0.28560	0.0590*
H6	0.40940	0.31570	0.24570	0.0600*
H7	0.45280	0.18470	0.40310	0.0530*
H9A	0.51590	0.13150	0.60780	0.0500*
H9B	0.46130	0.04000	0.54380	0.0500*
H10A	0.4614 (9)	−0.0236 (16)	0.755 (2)	0.0560*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.0497 (3)	0.0379 (3)	0.0406 (3)	0.0112 (2)	0.0209 (2)	0.0037 (2)
O1	0.0372 (7)	0.0318 (6)	0.0488 (8)	0.0044 (5)	0.0212 (6)	−0.0030 (5)
N1	0.0403 (9)	0.0350 (8)	0.0413 (9)	0.0098 (6)	0.0161 (7)	0.0036 (6)
N2	0.0410 (9)	0.0330 (7)	0.0378 (9)	0.0080 (6)	0.0158 (7)	0.0024 (6)
N3	0.0367 (8)	0.0332 (7)	0.0393 (8)	0.0023 (6)	0.0146 (7)	−0.0007 (6)
C1	0.0325 (9)	0.0315 (8)	0.0385 (10)	0.0019 (7)	0.0107 (7)	−0.0044 (7)

C2	0.0339 (9)	0.0283 (8)	0.0418 (10)	0.0015 (7)	0.0110 (8)	−0.0017 (7)
C3	0.0353 (9)	0.0333 (9)	0.0399 (10)	−0.0033 (7)	0.0121 (7)	−0.0043 (7)
C4	0.0433 (11)	0.0426 (11)	0.0467 (11)	0.0020 (8)	0.0134 (9)	0.0004 (8)
C5	0.0510 (12)	0.0548 (12)	0.0437 (11)	−0.0029 (9)	0.0143 (9)	0.0068 (9)
C6	0.0555 (13)	0.0580 (13)	0.0411 (11)	−0.0120 (10)	0.0215 (9)	−0.0062 (9)
C7	0.0452 (11)	0.0439 (10)	0.0493 (12)	−0.0058 (8)	0.0224 (9)	−0.0119 (9)
C8	0.0361 (9)	0.0316 (9)	0.0415 (10)	−0.0068 (7)	0.0128 (8)	−0.0078 (7)
C9	0.0348 (10)	0.0339 (9)	0.0626 (13)	0.0007 (7)	0.0217 (9)	−0.0127 (8)
C10	0.0335 (14)	0.0252 (12)	0.086 (2)	0.0000	0.0227 (14)	0.0000

Geometric parameters (Å, º)

S1—C1	1.6945 (19)	C5—C6	1.384 (3)
O1—C8	1.375 (2)	C6—C7	1.380 (3)
O1—C9	1.441 (2)	C7—C8	1.399 (3)
N1—C1	1.326 (2)	C9—C10	1.503 (2)
N2—N3	1.374 (2)	C2—H2	0.9500
N2—C1	1.341 (2)	C4—H4	0.9500
N3—C2	1.280 (2)	C5—H5	0.9500
N1—H1A	0.9100	C6—H6	0.9500
N1—H1B	0.9100	C7—H7	0.9500
C2—C3	1.460 (3)	C9—H9A	0.9900
N2—H2A	0.9100	C9—H9B	0.9900
C3—C4	1.391 (3)	C10—H10A	0.970 (19)
C3—C8	1.398 (3)	C10—H10A^{i}	0.970 (19)
C4—C5	1.383 (3)		
C8—O1—C9	116.91 (14)	O1—C9—C10	107.97 (14)
N3—N2—C1	119.38 (15)	C9—C10—C9^{i}	114.84 (19)
N2—N3—C2	115.31 (15)	N3—C2—H2	120.00
S1—C1—N1	122.17 (14)	C3—C2—H2	120.00
S1—C1—N2	120.20 (13)	C3—C4—H4	119.00
N1—C1—N2	117.62 (16)	C5—C4—H4	119.00
H1A—N1—H1B	119.00	C4—C5—H5	120.00
C1—N1—H1B	120.00	C6—C5—H5	120.00
C1—N1—H1A	120.00	C5—C6—H6	120.00
C1—N2—H2A	127.00	C7—C6—H6	120.00
N3—N2—H2A	113.00	C6—C7—H7	120.00
N3—C2—C3	120.78 (16)	C8—C7—H7	120.00
C4—C3—C8	118.49 (17)	O1—C9—H9A	110.00
C2—C3—C8	120.12 (16)	O1—C9—H9B	110.00
C2—C3—C4	121.38 (17)	C10—C9—H9A	110.00
C3—C4—C5	121.55 (19)	C10—C9—H9B	110.00
C4—C5—C6	119.26 (19)	H9A—C9—H9B	108.00
C5—C6—C7	120.71 (19)	C9—C10—H10A	107.0 (12)
C6—C7—C8	119.81 (19)	C9—C10—H10A^{i}	112.0 (12)
O1—C8—C3	116.25 (16)	C9^{i}—C10—H10A	112.0 (12)
C3—C8—C7	120.18 (17)	H10A—C10—H10A^{i}	103.6 (17)

O1—C8—C7	123.57 (17)	C9^{i}—C10—H10A^{i}	107.0 (12)
C9—O1—C8—C3	−172.46 (16)	C2—C3—C8—O1	−2.2 (3)
C9—O1—C8—C7	6.8 (3)	C2—C3—C8—C7	178.46 (18)
C8—O1—C9—C10	172.29 (14)	C4—C3—C8—O1	178.61 (16)
C1—N2—N3—C2	−178.70 (16)	C4—C3—C8—C7	−0.7 (3)
N3—N2—C1—S1	177.07 (13)	C3—C4—C5—C6	0.0 (3)
N3—N2—C1—N1	−2.2 (2)	C4—C5—C6—C7	−0.3 (3)
N2—N3—C2—C3	177.81 (16)	C5—C6—C7—C8	0.1 (3)
N3—C2—C3—C4	−3.1 (3)	C6—C7—C8—O1	−178.85 (18)
N3—C2—C3—C8	177.76 (17)	C6—C7—C8—C3	0.4 (3)
C2—C3—C4—C5	−178.67 (18)	O1—C9—C10—C9^{i}	−59.22 (16)
C8—C3—C4—C5	0.5 (3)		

Symmetry code: (i) −*x*+1, *y*, −*z*+3/2.

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*A*···N3	0.91	2.27	2.631 (2)	103
N1—H1*A*···S1^{ii}	0.91	2.64	3.3393 (16)	135
N1—H1*B*···O1^{iii}	0.91	2.20	3.1046 (19)	176
N2—H2*A*···S1^{iv}	0.91	2.49	3.3909 (16)	171

Symmetry codes: (ii) *x*, −*y*+1, *z*−1/2; (iii) −*x*+1/2, *y*+1/2, −*z*+3/2; (iv) −*x*+1/2, −*y*+1/2, −*z*+2.