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Crystal structure of (*E*)-2-[(2*S*,5*R*)-2-isopropyl-5-methylcyclohexylidene]-hydrazine-1-carbothioamide

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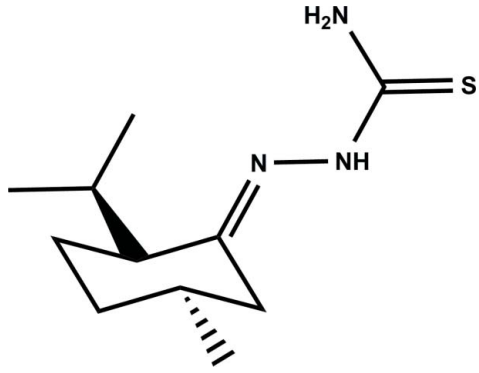
The title compound, $C_{11}H_{21}N_3S$, consists of a menthone moiety attached to an extended thiosemicarbazone group with the N—N—C—N torsion angle being 11.92 (16)°. The cyclohexane ring has a chair conformation and the conformation about the C=N bond is *E*. In the crystal, molecules are linked *via* pairs of N—H···S hydrogen bonds, forming chains along the *a* axis. The absolute structure could be assigned with reference to the starting material, *i.e.* enantiopure (−)-menthone [Flack parameter = 0.05 (5)].

Keywords: thiocarbazone; hydrogen-bonding polymer; crystal structure.

CCDC reference: 1012829

1. Related literature

For one of the first reports of the synthesis of thiosemicarbazone derivatives, see: Freund & Schander (1902). For a report of the anti-HIV activity of thiosemicarbazone derivatives of menthone, see: Mishra *et al.* (2012).



2. Experimental

2.1. Crystal data

$C_{11}H_{21}N_3S$
M_r = 227.37
Orthorhombic, $P2_12_12_1$
a = 8.2139 (1) Å
b = 11.6117 (2) Å
c = 13.8820 (2) Å
V = 1324.03 (3) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.22 mm^{-1}
T = 123 K
0.54 × 0.10 × 0.06 mm

2.2. Data collection

Nonius KappaCCD diffractometer
Absorption correction: analytical (Alcock, 1970)
T_{min} = 0.890, T_{max} = 0.988
22998 measured reflections
3033 independent reflections
2848 reflections with $I > 2\sigma(I)$
R_{int} = 0.046

2.3. Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.025
$wR(F^2)$ = 0.060
S = 1.05
3033 reflections
220 parameters
All H-atom parameters refined
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}
Absolute structure: Flack (1983)
Absolute structure parameter: 0.05 (5)

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

D—H···A	D—H	H···A	D···A	D—H···A
N2—H*N*2···S1^{i}	0.858 (17)	2.525 (18)	3.3551 (11)	163.1 (15)
N3—H*N*3*A*···S1^{ii}	0.794 (19)	2.52 (2)	3.3104 (12)	173.0 (17)

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

Data collection: *COLLECT* (Nonius, 1998); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *DIAMOND* (Brandenburg, 2006); software used to prepare material for publication: *publCIF* (Westrip, 2010).

Acknowledgements

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Supporting information for this paper is available from the IUCr electronic archives (Reference: SU2751).

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supporting information

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Crystal structure of (*E*)-2-[(2*S*,5*R*)-2-isopropyl-5-methylcyclohexylidene]hydrazine-1-carbothioamide

Adriano Bof de Oliveira, Johannes Beck, Jörg Daniels, Renan Lira de Farias and Adelino Vieira de Godoy Netto

S1. Structural commentary

Several thiosemicarbazone derivatives have a wide range of pharmacological properties. For example, some thiosemicarbazone derivatives of the peppermint essential oil show anti-HIV activity (Mishra *et al.*, 2012). As part of our studies on synthesis and structural chemistry of thiosemicarbazone derivatives of natural products, we report herein the crystal structure of (-)-3-menthone thiosemicarbazone.

In the molecular structure of the title compound, Fig, 1, the thiosemicarbazone unit is not completely planar, but shows a torsion angle N1–N2–C11–N3 of 11.92 (16)°. The cyclohexane ring of the menthone unit is in the chair conformation. The molecule, shows also a *trans* conformation about the N1—N2 bond.

For the synthesis, enantiopure (-)-menthone was used. No change in chirality occurred in the course of the reaction with thiosemicarbazide and the obtained product emerged as chiral crystals in the non-centrosymmetric space group $P2_12_12_1$.

In the crystal, molecules are connected by a pair of N—H···S hydrogen bonds, with bridging sulfur atoms, into a one-dimensional chain along the *a*-axis (Fig. 2 and Table 1).

S2. Synthesis and crystallization

The synthesis of the title compound was adapted from a previously reported procedure (Freund & Schander, 1902). In a hydrochloric acid catalyzed reaction, a mixture of (-)-menthone (10 mmol) and thiosemicarbazide (10 mmol) in ethanol (80 ml) was refluxed for 5 h. After cooling and filtering, the title compound was obtained. Colourless needles were obtained by slow evaporation of a solution in the solvent DMSO.

S3. Refinement

All the H atoms were located in a difference Fourier map and freely refined. The assignment of the correct absolute configuration was assured by the Flack parameter of 0.05 (5).

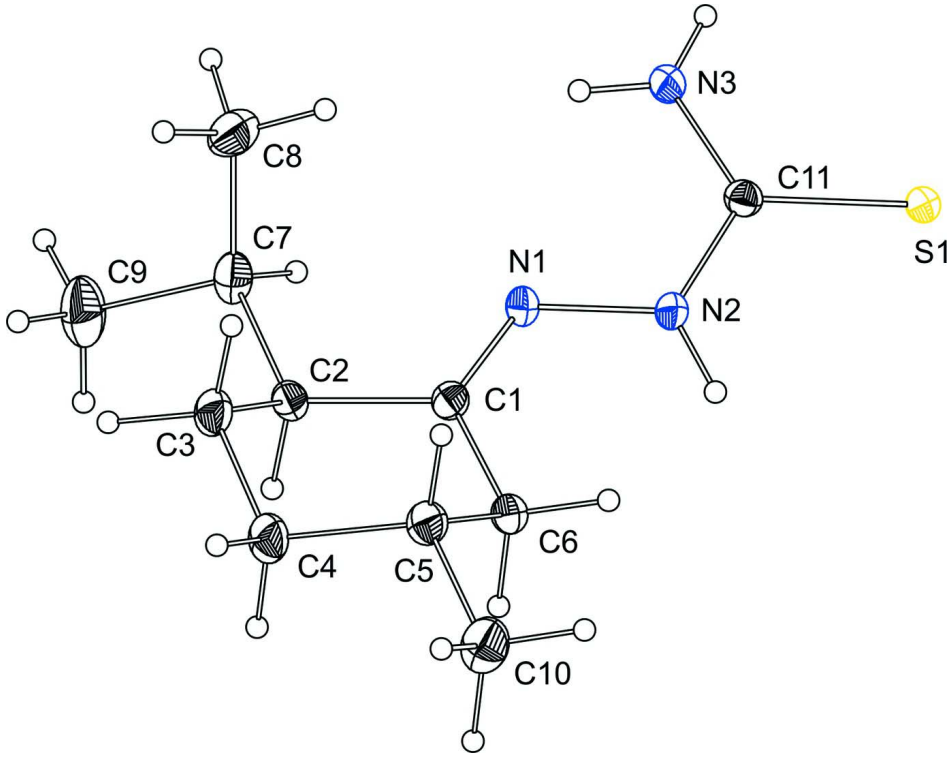

Figure 1

The molecular structure of the title molecule, with atom labelling. Displacement ellipsoids are drawn at the 40% probability level.

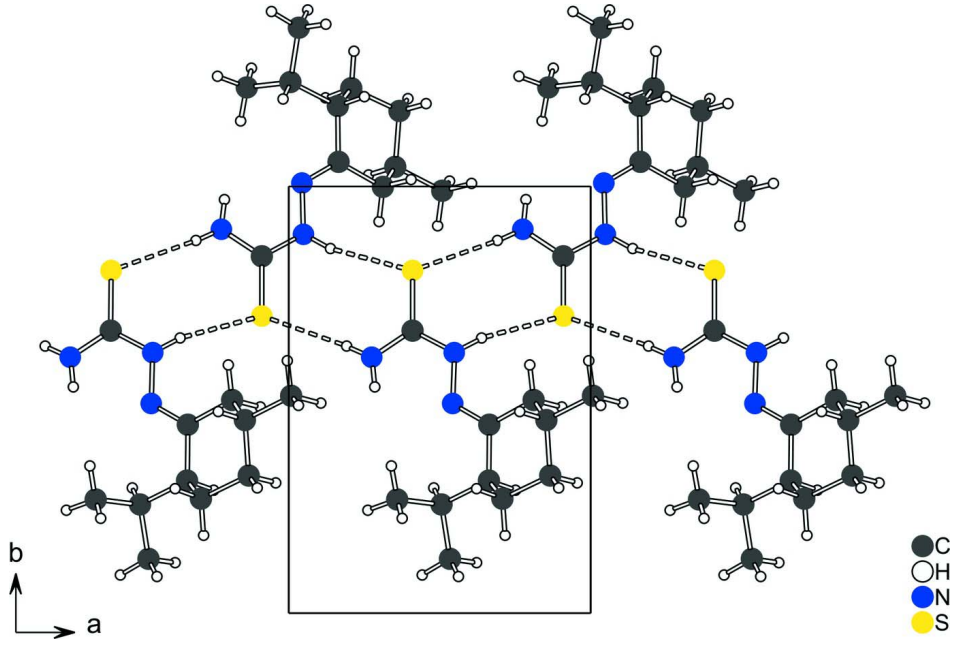

Figure 2

A partial view along the *c*-axis of the crystal structure of the title compound, showing the hydrogen bonded chains (hydrogen bonds are shown as dashed lines; see Table 1 for details).

(*E*)-2-[(2*S*,5*R*)-2-Isopropyl-5-methylcyclohexylidene]hydrazine-1-carbothioamide

Crystal data

$C_{11}H_{21}N_3S$
$M_r = 227.37$
Orthorhombic, $P2_12_12_1$
Hall symbol: P 2ac 2ab
$a = 8.2139$ (1) Å
$b = 11.6117$ (2) Å
$c = 13.8820$ (2) Å
$V = 1324.03$ (3) Å^3
$Z = 4$
$F(000) = 496$
$D_x = 1.141$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 37558 reflections
$\theta = 2.9$–$27.5°$
$\mu = 0.22$ mm^{-1}
$T = 123$ K
Needle, colourless
0.54 × 0.10 × 0.06 mm

Data collection

Nonius KappaCCD diffractometer
Radiation source: fine-focus sealed tube, Nonius KappaCCD
Graphite monochromator
Detector resolution: 9 pixels mm^{-1}
CCD rotation images, thick slices scans
Absorption correction: analytical (Alcock, 1970)
$T_{min} = 0.890$, $T_{max} = 0.988$
22998 measured reflections
3033 independent reflections
2848 reflections with $I > 2\sigma(I)$
$R_{int} = 0.046$
$\theta_{max} = 27.5°$, $\theta_{min} = 2.9°$
$h = -10 \rightarrow 10$
$k = -15 \rightarrow 15$
$l = -17 \rightarrow 18$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.025$
$wR(F^2) = 0.060$
$S = 1.05$
3033 reflections
220 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0305P)^2 + 0.1951P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.15$ e Å^{-3}
$\Delta\rho_{min} = -0.19$ e Å^{-3}
Absolute structure: Flack (1983), **???? Friedel pairs**
Absolute structure parameter: 0.05 (5)

Special details

Experimental. Alcock, N. W., 1970

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

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness 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 threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating R-factors(gt) *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 (Å^2)

	x	y	z	U_{iso}*/U_{eq}
S1	−0.08952 (3)	−0.30315 (2)	0.48771 (2)	0.02034 (8)
N1	0.04374 (12)	0.00856 (9)	0.41416 (7)	0.0177 (2)

N2	0.04891 (13)	−0.11130 (9)	0.42555 (8)	0.0186 (2)
N3	−0.22424 (13)	−0.09979 (10)	0.45259 (9)	0.0231 (2)
C1	0.16488 (14)	0.05821 (10)	0.37313 (8)	0.0168 (2)
C2	0.16273 (15)	0.18913 (11)	0.36955 (8)	0.0192 (2)
C3	0.20800 (17)	0.23095 (11)	0.26796 (10)	0.0238 (3)
C4	0.36682 (16)	0.17718 (11)	0.23241 (11)	0.0263 (3)
C5	0.35351 (16)	0.04665 (11)	0.22932 (9)	0.0217 (3)
C6	0.31196 (15)	−0.00025 (11)	0.32996 (9)	0.0193 (2)
C7	0.00597 (17)	0.24498 (11)	0.40902 (10)	0.0244 (3)
C8	−0.14038 (18)	0.23265 (14)	0.34230 (13)	0.0337 (3)
C9	0.0343 (3)	0.37222 (13)	0.43286 (15)	0.0406 (4)
C10	0.50872 (19)	−0.00988 (14)	0.19164 (12)	0.0320 (3)
C11	−0.09004 (15)	−0.16286 (9)	0.45455 (8)	0.0166 (2)
HN2	0.139 (2)	−0.1453 (14)	0.4388 (12)	0.030 (4)*
HN3A	−0.308 (2)	−0.1263 (15)	0.4708 (13)	0.038 (5)*
HN3B	−0.214 (2)	−0.0304 (16)	0.4401 (12)	0.032 (4)*
H2	0.2510 (19)	0.2111 (14)	0.4104 (11)	0.025 (4)*
H3A	0.1221 (19)	0.2081 (13)	0.2244 (11)	0.026 (4)*
H3B	0.2167 (19)	0.3172 (14)	0.2688 (11)	0.026 (4)*
H4A	0.395 (2)	0.2061 (14)	0.1673 (12)	0.038 (4)*
H4B	0.4556 (19)	0.1942 (14)	0.2754 (11)	0.027 (4)*
H5	0.2651 (19)	0.0275 (13)	0.1881 (11)	0.022 (4)*
H6A	0.2988 (18)	−0.0818 (14)	0.3277 (11)	0.024 (4)*
H6B	0.4050 (19)	0.0163 (12)	0.3714 (10)	0.021 (3)*
H7	−0.0193 (19)	0.2058 (13)	0.4704 (11)	0.032 (4)*
H8A	−0.124 (2)	0.2778 (16)	0.2830 (13)	0.046 (5)*
H8B	−0.237 (2)	0.2586 (16)	0.3744 (12)	0.040 (5)*
H8C	−0.160 (2)	0.1543 (16)	0.3249 (12)	0.033 (4)*
H9A	−0.058 (2)	0.4100 (15)	0.4585 (12)	0.037 (5)*
H9B	0.123 (3)	0.3810 (18)	0.4819 (17)	0.067 (6)*
H9C	0.063 (2)	0.4138 (15)	0.3757 (14)	0.045 (5)*
H10A	0.606 (2)	0.0073 (14)	0.2334 (12)	0.039 (4)*
H10B	0.494 (2)	−0.0917 (18)	0.1884 (13)	0.041 (5)*
H10C	0.533 (2)	0.0126 (17)	0.1271 (15)	0.053 (6)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.01461 (12)	0.01597 (13)	0.03044 (16)	−0.00151 (11)	−0.00087 (12)	0.00710 (12)
N1	0.0187 (5)	0.0138 (5)	0.0206 (5)	−0.0008 (4)	−0.0011 (4)	0.0037 (4)
N2	0.0155 (5)	0.0140 (5)	0.0264 (6)	−0.0001 (4)	0.0001 (4)	0.0059 (4)
N3	0.0150 (5)	0.0163 (5)	0.0380 (7)	−0.0007 (4)	0.0031 (5)	0.0053 (5)
C1	0.0183 (5)	0.0171 (6)	0.0151 (5)	−0.0002 (5)	−0.0028 (5)	0.0026 (4)
C2	0.0201 (5)	0.0157 (5)	0.0217 (6)	−0.0026 (5)	−0.0036 (5)	0.0016 (5)
C3	0.0251 (6)	0.0191 (6)	0.0272 (6)	0.0005 (5)	0.0023 (6)	0.0079 (5)
C4	0.0263 (7)	0.0213 (7)	0.0314 (7)	−0.0008 (5)	0.0073 (6)	0.0095 (5)
C5	0.0219 (6)	0.0219 (6)	0.0213 (6)	−0.0003 (5)	0.0018 (5)	0.0048 (5)
C6	0.0183 (5)	0.0174 (6)	0.0223 (6)	−0.0014 (5)	0.0000 (5)	0.0053 (5)

C7	0.0301 (7)	0.0171 (6)	0.0259 (7)	0.0015 (5)	0.0053 (6)	0.0013 (5)
C8	0.0249 (7)	0.0326 (8)	0.0435 (9)	0.0071 (6)	0.0017 (6)	0.0066 (7)
C9	0.0557 (11)	0.0205 (7)	0.0455 (10)	0.0015 (7)	0.0114 (8)	−0.0055 (7)
C10	0.0324 (7)	0.0295 (8)	0.0342 (8)	0.0045 (6)	0.0108 (7)	0.0073 (6)
C11	0.0159 (5)	0.0174 (5)	0.0165 (5)	−0.0012 (5)	−0.0010 (5)	0.0007 (4)

Geometric parameters (Å, º)

S1—C11	1.6928 (11)	C4—H4B	0.963 (16)
N1—C1	1.2833 (15)	C5—C10	1.5264 (19)
N1—N2	1.4015 (14)	C5—C6	1.5377 (17)
N2—C11	1.3502 (15)	C5—H5	0.951 (15)
N2—HN2	0.858 (17)	C6—H6A	0.954 (16)
N3—C11	1.3237 (16)	C6—H6B	0.976 (15)
N3—HN3A	0.794 (19)	C7—C8	1.524 (2)
N3—HN3B	0.829 (18)	C7—C9	1.5318 (19)
C1—C6	1.5098 (17)	C7—H7	0.988 (16)
C1—C2	1.5211 (16)	C8—H8A	0.984 (19)
C2—C3	1.5372 (17)	C8—H8B	0.961 (19)
C2—C7	1.5423 (18)	C8—H8C	0.955 (18)
C2—H2	0.955 (15)	C9—H9A	0.947 (18)
C3—C4	1.5282 (18)	C9—H9B	1.00 (2)
C3—H3A	0.966 (16)	C9—H9C	0.96 (2)
C3—H3B	1.004 (16)	C10—H10A	1.008 (19)
C4—C5	1.5202 (17)	C10—H10B	0.96 (2)
C4—H4A	0.991 (16)	C10—H10C	0.95 (2)
C1—N1—N2	118.21 (10)	C1—C6—C5	112.27 (10)
C11—N2—N1	116.64 (10)	C1—C6—H6A	111.6 (9)
C11—N2—HN2	117.4 (11)	C5—C6—H6A	110.3 (9)
N1—N2—HN2	120.5 (11)	C1—C6—H6B	107.7 (8)
C11—N3—HN3A	120.0 (13)	C5—C6—H6B	107.0 (8)
C11—N3—HN3B	117.0 (12)	H6A—C6—H6B	107.6 (12)
HN3A—N3—HN3B	122.3 (17)	C8—C7—C9	109.98 (13)
N1—C1—C6	126.49 (10)	C8—C7—C2	113.76 (11)
N1—C1—C2	117.03 (11)	C9—C7—C2	110.83 (12)
C6—C1—C2	116.47 (10)	C8—C7—H7	108.4 (9)
C1—C2—C3	110.06 (10)	C9—C7—H7	106.8 (9)
C1—C2—C7	114.73 (10)	C2—C7—H7	106.7 (9)
C3—C2—C7	113.27 (10)	C7—C8—H8A	110.6 (11)
C1—C2—H2	103.8 (10)	C7—C8—H8B	110.0 (10)
C3—C2—H2	106.1 (9)	H8A—C8—H8B	109.4 (16)
C7—C2—H2	108.1 (9)	C7—C8—H8C	112.0 (10)
C4—C3—C2	111.94 (11)	H8A—C8—H8C	108.5 (15)
C4—C3—H3A	108.0 (9)	H8B—C8—H8C	106.2 (15)
C2—C3—H3A	108.1 (9)	C7—C9—H9A	113.9 (10)
C4—C3—H3B	110.5 (9)	C7—C9—H9B	110.8 (12)
C2—C3—H3B	108.8 (9)	H9A—C9—H9B	106.3 (15)

H3A—C3—H3B	109.4 (12)	C7—C9—H9C	110.1 (10)
C5—C4—C3	110.80 (10)	H9A—C9—H9C	106.0 (15)
C5—C4—H4A	109.2 (9)	H9B—C9—H9C	109.5 (16)
C3—C4—H4A	110.8 (10)	C5—C10—H10A	112.4 (10)
C5—C4—H4B	106.1 (10)	C5—C10—H10B	109.9 (11)
C3—C4—H4B	111.2 (9)	H10A—C10—H10B	108.7 (15)
H4A—C4—H4B	108.6 (13)	C5—C10—H10C	112.4 (12)
C4—C5—C10	112.23 (11)	H10A—C10—H10C	108.5 (15)
C4—C5—C6	110.09 (10)	H10B—C10—H10C	104.6 (16)
C10—C5—C6	110.15 (11)	N3—C11—N2	116.90 (10)
C4—C5—H5	107.7 (9)	N3—C11—S1	122.69 (9)
C10—C5—H5	109.3 (9)	N2—C11—S1	120.37 (9)
C6—C5—H5	107.2 (9)		

C1—N1—N2—C11	−169.70 (11)	C3—C4—C5—C6	−58.39 (15)
N2—N1—C1—C6	3.59 (18)	N1—C1—C6—C5	133.17 (12)
N2—N1—C1—C2	−174.83 (9)	C2—C1—C6—C5	−48.41 (14)
N1—C1—C2—C3	−133.96 (11)	C4—C5—C6—C1	52.25 (14)
C6—C1—C2—C3	47.46 (14)	C10—C5—C6—C1	176.53 (11)
N1—C1—C2—C7	−4.82 (15)	C1—C2—C7—C8	−73.69 (14)
C6—C1—C2—C7	176.60 (11)	C3—C2—C7—C8	53.83 (15)
C1—C2—C3—C4	−52.04 (14)	C1—C2—C7—C9	161.77 (12)
C7—C2—C3—C4	178.03 (11)	C3—C2—C7—C9	−70.71 (15)
C2—C3—C4—C5	59.56 (15)	N1—N2—C11—N3	11.92 (16)
C3—C4—C5—C10	178.54 (12)	N1—N2—C11—S1	−170.14 (8)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H*N*2···S1^{i}	0.858 (17)	2.525 (18)	3.3551 (11)	163.1 (15)
N3—H*N*3*A*···S1^{ii}	0.794 (19)	2.52 (2)	3.3104 (12)	173.0 (17)

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