

Crystal structure of 4-methylsulfanyl-2-(2H-tetrazol-2-yl)pyrimidine

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The title compound, C₆H₆N₆S, crystallized with two independent molecules (*A* and *B*) in the asymmetric unit. The conformation of the two molecules differs slightly. While the tetrazole ring is inclined to the pyrimidine ring by 5.48 (7) and 4.24 (7)° in molecules *A* and *B*, respectively, the N–C–S–C torsion angles of the thiomethyl groups differ by *ca* 180°. In the crystal, the *A* and *B* molecules are linked *via* a C–H⋯N hydrogen bond. They stack along the *b*-axis direction forming columns within which there are weak π – π interactions present [shortest inter-centroid distance = 3.6933 (13) Å].

Keywords: crystal structure; tetrazole; pyrimidine; thio; heterocycles; S_NAr reactions; π – π interactions.

CCDC reference: 1441424

1. Related literature

For applications of tetrazolyl-substituted aromatic systems in metal–ligand research, see: Kim *et al.* (2008); Stoessel *et al.* (2010); in drug development, see: Pasternak *et al.* (2012); Biswas *et al.* (2015); in polymer synthesis, see: Yu *et al.* (2008); Sengupta *et al.* (2010). For the synthesis of 4-methylsulfanyl-2-(1H-tetrazol-1-yl)pyrimidine and the title compound, see: Thomann *et al.* (2014).

2. Experimental

2.1. Crystal data

C ₆ H ₆ N ₆ S	$\gamma = 102.695 (8)^\circ$
$M_r = 194.23$	$V = 819.9 (4) \text{ \AA}^3$
Triclinic, $P\bar{1}$	$Z = 4$
$a = 6.3001 (17) \text{ \AA}$	Mo $K\alpha$ radiation
$b = 7.393 (2) \text{ \AA}$	$\mu = 0.35 \text{ mm}^{-1}$
$c = 18.159 (5) \text{ \AA}$	$T = 143 \text{ K}$
$\alpha = 91.407 (7)^\circ$	$0.22 \times 0.22 \times 0.01 \text{ mm}$
$\beta = 95.864 (7)^\circ$	

2.2. Data collection

Bruker APEXII CCD diffractometer	15501 measured reflections
Absorption correction: multi-scan (SADABS; Bruker, 2010)	4581 independent reflections
$T_{\min} = 0.716$, $T_{\max} = 0.746$	3596 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.028$

2.3. Refinement

$R[F^2 > 2\sigma(F^2)] = 0.034$	283 parameters
$wR(F^2) = 0.086$	All H-atom parameters refined
$S = 1.01$	$\Delta\rho_{\text{max}} = 0.35 \text{ e \AA}^{-3}$
4581 reflections	$\Delta\rho_{\text{min}} = -0.30 \text{ e \AA}^{-3}$

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

<i>D</i> –H⋯ <i>A</i>	<i>D</i> –H	H⋯ <i>A</i>	<i>D</i> ⋯ <i>A</i>	<i>D</i> –H⋯ <i>A</i>
C2–H1⋯N9 ⁱ	0.89 (2)	2.58 (2)	3.203 (2)	129 (2)

Symmetry code: (i) $x - 1, y, z$.

Data collection: APEX2 (Bruker, 2010); cell refinement: SAINT (Bruker, 2010); data reduction: SAINT; program(s) used to solve structure: SHELXS97 (Sheldrick 2008); program(s) used to refine structure: SHELXL2014 (Sheldrick, 2015); molecular graphics: PLATON (Spek, 2009); software used to prepare material for publication: SHELXL2014 and PLATON.

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Supporting information for this paper is available from the IUCr electronic archives (Reference: SU5253).

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supporting information

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Crystal structure of 4-methylsulfanyl-2-(2*H*-tetrazol-2-yl)pyrimidine

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S1. Comment

4-tetrazolylpyrimidines are well reported scaffolds in many bioactive entities. Besides synthetic chemistry, tetrazolyl substituted aromatic systems are also of high interest for example, in metal-ligand research (Kim *et al.*, 2008; Stoessel *et al.*, 2010), drug development (Pasternak *et al.*, 2012; Biswas *et al.*, 2015) and polymer discovery (Yu *et al.*, 2008; Sengupta *et al.*, 2010). Thus, the knowledge of the three dimensional structure of these moieties is of crucial importance for the rational design in these fields of research. Recently, we have reported a novel method to synthesize such compounds (Thomann *et al.*, 2014). We have reported the synthesis of 4-(methylthio)-2-(1*H*-tetrazol-1-yl)pyrimidine (**1**). Interestingly, when scaling up the reaction, another product was found in small amounts. NMR analytical characterization revealed the compound to be the 2-tetrazolyl regioisomer (**2**). To determine unequivocally proof of the structure of this compound, we determined its crystal structure.

The title compound (**2**), crystallized with two independent molecules (A and B) in the asymmetric unit (Fig. 1). Interestingly, the two molecules differ in their conformation. While the tetrazole moieties are arranged similarly, with the tetrazole ring is inclined to the pyrimidine ring by 5.48 (7) and 4.24 (7) ° in molecules A and B, respectively, the thio-methyl groups have a difference of the torsion angle about the C_{ar}...S bond of *ca* 180° [for example, torsion angle N5—C4—S1—C6 = 0.89 (12) °, compared to torsion angle N11—C10—S2—C12 = -176.78 (10) °] indicating higher rotational freedom than the tetrazoles (Fig. 1). The latter finding is of importance for computational chemists in medicinal chemistry, as the polarized hydrogen at atom C5 of the tetrazole ring is able to form non-classical hydrogen bonds. Therefore, the results from the crystal structure may favour this conformational isomer for *in silico* predictions.

In the crystal, the A and B molecules are linked *via* a C—H...N hydrogen bond (Table 1 and Fig. 2). They stack along the *b* axis direction forming columns within which there are weak π - π interactions present [shortest inter-centroid distance is Cg2...Cg4ⁱ = 3.6918 (5) Å; Cg2 and Cg4 are the centroids of rings N5/N6/C1—C4 and N11/N12/C7—C10, respectively; symmetry code: (i) *x*, *y* + 1, *z*].

S2. Synthesis and crystallization

The title compound (**2**), was synthesized following a previously reported procedure (Thomann *et al.*, 2014). A mixture of 4-chloro-2-(methylthio)pyrimidine, 1*H*-tetrazole and triethylamine, in the ratio 1:1:1, was stirred under microwave irradiation at 50 W, 353 K for 1 h. The crude product was purified by flash chromatography (hexane:ethyl acetate, 8:2, *R_f* = 1/4) to yield a white solid (9%). Crystals formed at 294 K after 16 h from a saturated solution of **2** in ethyl acetate. ¹H NMR (CDCl₃, 300 MHz) 8.80 (dd, *J* = 5.3, 0.6 Hz, 1 H), 8.77 (s, 1 H), 7.77 (dd, *J* = 5.3, 0.7 Hz, 1 H), 2.69 p.p.m. (d, *J* = 0.7 Hz, 3 H).

S3. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. H atoms were located in a difference Fourier map and freely refined.

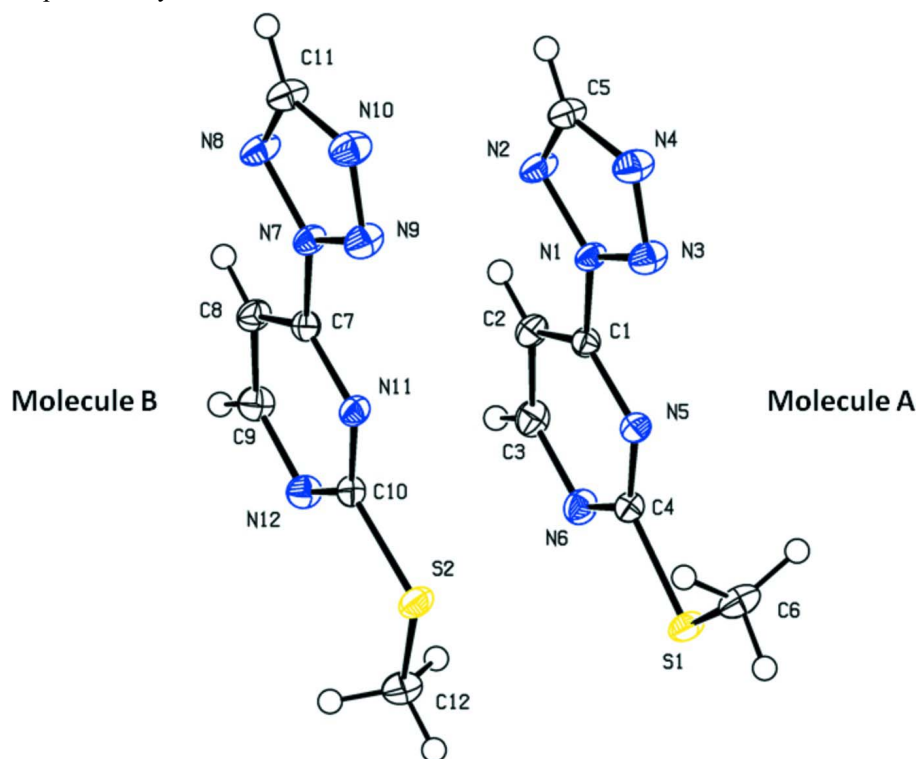


Figure 1

The molecular structure of the two independent molecules (*A* and *B*) of the title compound (2), with atom labelling. Displacement ellipsoids are drawn at the 50% probability level.

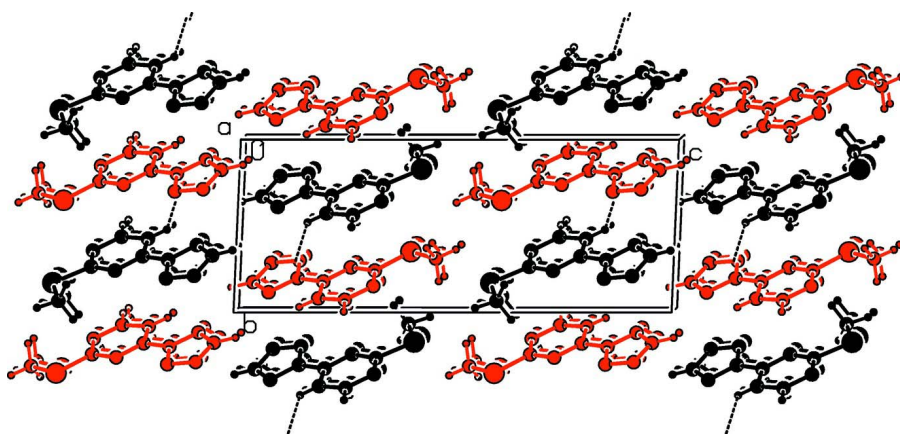


Figure 2

The crystal packing of the two independent molecules (*A* black; *B* red) of the title compound (2), viewed along the *a* axis. Hydrogen bonds are shown as dashed lines (see Table 1).

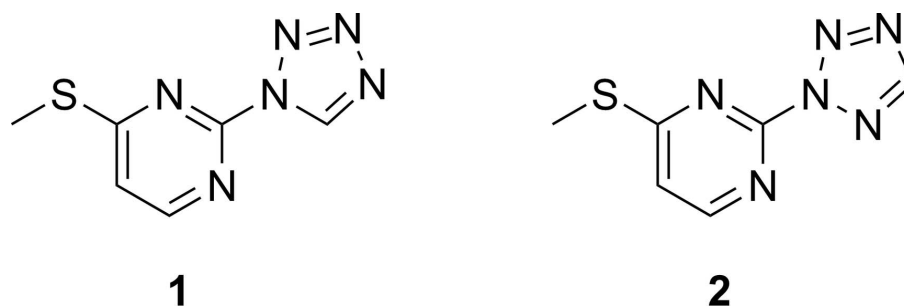


Figure 3
Compounds (1) and (2).

4-Methylsulfonyl-2-(2H-tetrazol-2-yl)pyrimidine

Crystal data

$C_6H_6N_6S$
 $M_r = 194.23$
 Triclinic, $P\bar{1}$
 $a = 6.3001$ (17) Å
 $b = 7.393$ (2) Å
 $c = 18.159$ (5) Å
 $\alpha = 91.407$ (7)°
 $\beta = 95.864$ (7)°
 $\gamma = 102.695$ (8)°
 $V = 819.9$ (4) Å³

$Z = 4$
 $F(000) = 400$
 $D_x = 1.574$ Mg m⁻³
 Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
 Cell parameters from 728 reflections
 $\theta = 3.6$ – 24.3 °
 $\mu = 0.35$ mm⁻¹
 $T = 143$ K
 Cuboid, colourless
 $0.22 \times 0.22 \times 0.01$ mm

Data collection

Bruker APEXII CCD
 diffractometer
 φ and ω scans
 Absorption correction: multi-scan
 (SADABS; Bruker, 2010)
 $T_{\min} = 0.716$, $T_{\max} = 0.746$
 15501 measured reflections

4581 independent reflections
 3596 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.028$
 $\theta_{\max} = 29.6$ °, $\theta_{\min} = 2.3$ °
 $h = -8 \rightarrow 8$
 $k = -10 \rightarrow 10$
 $l = -24 \rightarrow 25$

Refinement

Refinement on F^2
 Least-squares matrix: full
 $R[F^2 > 2\sigma(F^2)] = 0.034$
 $wR(F^2) = 0.086$
 $S = 1.01$
 4581 reflections
 283 parameters
 0 restraints

Hydrogen site location: difference Fourier map
 All H-atom parameters refined
 $w = 1/[\sigma^2(F_o^2) + (0.0376P)^2 + 0.2718P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} = 0.001$
 $\Delta\rho_{\max} = 0.35$ e Å⁻³
 $\Delta\rho_{\min} = -0.30$ e Å⁻³

Special details

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.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
S1	0.84117 (6)	0.83334 (5)	0.58281 (2)	0.01975 (9)
N1	1.04303 (18)	0.69484 (15)	0.84617 (6)	0.0152 (2)
N2	1.00906 (19)	0.60999 (17)	0.90974 (6)	0.0208 (3)
N3	1.24517 (19)	0.79683 (17)	0.84553 (7)	0.0209 (3)
N4	1.3498 (2)	0.77865 (18)	0.91059 (7)	0.0233 (3)
N5	0.93885 (18)	0.76012 (15)	0.72442 (6)	0.0159 (2)
N6	0.56784 (19)	0.65519 (16)	0.66803 (7)	0.0200 (3)
C1	0.8749 (2)	0.67900 (17)	0.78527 (7)	0.0148 (3)
C2	0.6647 (2)	0.58341 (19)	0.79335 (8)	0.0184 (3)
C3	0.5146 (2)	0.5770 (2)	0.73096 (8)	0.0203 (3)
C4	0.7801 (2)	0.74205 (18)	0.66783 (8)	0.0162 (3)
C5	1.2034 (2)	0.6651 (2)	0.94818 (8)	0.0209 (3)
C6	1.1309 (2)	0.9298 (2)	0.60068 (9)	0.0230 (3)
H1	0.629 (3)	0.532 (2)	0.8352 (10)	0.028 (5)*
H2	0.366 (3)	0.512 (2)	0.7313 (9)	0.023 (4)*
H3	1.235 (3)	0.634 (2)	0.9944 (11)	0.030 (5)*
H4	1.204 (3)	0.833 (2)	0.6178 (10)	0.032 (5)*
H5	1.160 (3)	1.037 (2)	0.6366 (10)	0.030 (5)*
H6	1.172 (3)	0.969 (3)	0.5531 (11)	0.040 (5)*
S2	0.91337 (6)	0.35407 (5)	0.59998 (2)	0.02003 (10)
N7	1.07557 (18)	0.19569 (15)	0.85809 (6)	0.0156 (2)
N8	1.0376 (2)	0.11547 (17)	0.92240 (7)	0.0219 (3)
N9	1.28032 (19)	0.29223 (17)	0.85739 (7)	0.0218 (3)
N10	1.3817 (2)	0.27602 (18)	0.92304 (7)	0.0241 (3)
N11	0.97742 (18)	0.26119 (15)	0.73636 (6)	0.0159 (2)
N12	0.60819 (19)	0.16413 (16)	0.67866 (7)	0.0192 (2)
C7	0.9101 (2)	0.18161 (17)	0.79690 (7)	0.0146 (3)
C8	0.6975 (2)	0.08981 (19)	0.80433 (8)	0.0181 (3)
C9	0.5511 (2)	0.0862 (2)	0.74162 (8)	0.0204 (3)
C10	0.8194 (2)	0.24779 (18)	0.67912 (8)	0.0162 (3)
C11	1.2311 (2)	0.1686 (2)	0.96118 (8)	0.0218 (3)
C12	0.6629 (3)	0.3216 (2)	0.53901 (9)	0.0256 (3)
H7	0.658 (3)	0.041 (2)	0.8462 (10)	0.028 (5)*
H8	0.400 (3)	0.022 (2)	0.7410 (10)	0.027 (4)*
H9	1.264 (3)	0.138 (3)	1.0104 (11)	0.035 (5)*
H10	0.564 (3)	0.385 (2)	0.5600 (10)	0.035 (5)*
H11	0.702 (3)	0.373 (3)	0.4949 (11)	0.037 (5)*
H12	0.600 (3)	0.192 (3)	0.5294 (10)	0.038 (5)*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.02103 (18)	0.02210 (18)	0.01490 (18)	0.00253 (13)	-0.00004 (13)	0.00614 (13)
N1	0.0152 (5)	0.0167 (5)	0.0130 (5)	0.0007 (4)	0.0036 (4)	0.0040 (4)
N2	0.0216 (6)	0.0250 (6)	0.0152 (6)	0.0020 (5)	0.0040 (5)	0.0078 (5)

N3	0.0155 (6)	0.0260 (6)	0.0190 (6)	-0.0011 (5)	0.0024 (5)	0.0049 (5)
N4	0.0203 (6)	0.0295 (7)	0.0186 (6)	0.0031 (5)	0.0005 (5)	0.0046 (5)
N5	0.0166 (5)	0.0159 (5)	0.0149 (6)	0.0028 (4)	0.0030 (4)	0.0019 (4)
N6	0.0182 (6)	0.0193 (6)	0.0212 (6)	0.0019 (4)	0.0009 (5)	0.0034 (5)
C1	0.0155 (6)	0.0138 (6)	0.0150 (6)	0.0030 (5)	0.0025 (5)	0.0011 (5)
C2	0.0186 (7)	0.0180 (7)	0.0181 (7)	0.0012 (5)	0.0057 (5)	0.0042 (5)
C3	0.0168 (7)	0.0200 (7)	0.0232 (8)	0.0008 (5)	0.0039 (6)	0.0026 (5)
C4	0.0181 (6)	0.0149 (6)	0.0157 (7)	0.0034 (5)	0.0026 (5)	0.0020 (5)
C5	0.0221 (7)	0.0251 (7)	0.0153 (7)	0.0044 (6)	0.0022 (6)	0.0045 (5)
C6	0.0203 (7)	0.0305 (8)	0.0190 (7)	0.0053 (6)	0.0042 (6)	0.0093 (6)
S2	0.02219 (18)	0.02074 (18)	0.01648 (18)	0.00230 (13)	0.00321 (14)	0.00600 (13)
N7	0.0134 (5)	0.0181 (5)	0.0149 (6)	0.0015 (4)	0.0037 (4)	0.0045 (4)
N8	0.0203 (6)	0.0281 (7)	0.0170 (6)	0.0028 (5)	0.0044 (5)	0.0090 (5)
N9	0.0152 (6)	0.0265 (6)	0.0213 (6)	-0.0005 (5)	0.0014 (5)	0.0057 (5)
N10	0.0182 (6)	0.0316 (7)	0.0203 (7)	0.0015 (5)	-0.0004 (5)	0.0048 (5)
N11	0.0159 (5)	0.0160 (5)	0.0155 (6)	0.0021 (4)	0.0029 (4)	0.0033 (4)
N12	0.0170 (6)	0.0214 (6)	0.0184 (6)	0.0020 (5)	0.0026 (5)	0.0016 (5)
C7	0.0139 (6)	0.0142 (6)	0.0160 (6)	0.0039 (5)	0.0019 (5)	0.0008 (5)
C8	0.0171 (7)	0.0200 (7)	0.0170 (7)	0.0018 (5)	0.0056 (5)	0.0036 (5)
C9	0.0164 (7)	0.0233 (7)	0.0206 (7)	0.0019 (5)	0.0034 (6)	0.0014 (5)
C10	0.0189 (7)	0.0139 (6)	0.0160 (7)	0.0039 (5)	0.0023 (5)	0.0008 (5)
C11	0.0188 (7)	0.0294 (8)	0.0168 (7)	0.0039 (6)	0.0023 (6)	0.0060 (6)
C12	0.0305 (8)	0.0281 (8)	0.0181 (8)	0.0075 (7)	-0.0006 (6)	0.0034 (6)

Geometric parameters (Å, °)

S1—C4	1.7453 (15)	S2—C10	1.7487 (15)
S1—C6	1.8004 (16)	S2—C12	1.7992 (16)
N1—N3	1.3311 (16)	N7—N9	1.3314 (16)
N1—N2	1.3412 (16)	N7—N8	1.3421 (16)
N1—C1	1.4347 (17)	N7—C7	1.4291 (17)
N2—C5	1.3207 (19)	N8—C11	1.3182 (19)
N3—N4	1.3176 (17)	N9—N10	1.3148 (17)
N4—C5	1.356 (2)	N10—C11	1.3566 (19)
N5—C1	1.3267 (17)	N11—C7	1.3237 (17)
N5—C4	1.3412 (17)	N11—C10	1.3496 (17)
N6—C3	1.3336 (19)	N12—C10	1.3377 (18)
N6—C4	1.3506 (18)	N12—C9	1.3393 (19)
C1—C2	1.3815 (19)	C7—C8	1.3837 (19)
C2—C3	1.393 (2)	C8—C9	1.386 (2)
C2—H1	0.885 (19)	C8—H7	0.886 (19)
C3—H2	0.951 (17)	C9—H8	0.965 (18)
C5—H3	0.891 (19)	C11—H9	0.940 (19)
C6—H4	0.974 (17)	C12—H10	0.955 (19)
C6—H5	0.988 (17)	C12—H11	0.93 (2)
C6—H6	0.96 (2)	C12—H12	0.957 (19)
C4—S1—C6	101.92 (7)	C10—S2—C12	101.37 (8)

N3—N1—N2	113.78 (11)	N9—N7—N8	113.63 (11)
N3—N1—C1	123.45 (11)	N9—N7—C7	123.40 (11)
N2—N1—C1	122.75 (11)	N8—N7—C7	122.96 (11)
C5—N2—N1	101.28 (11)	C11—N8—N7	101.34 (12)
N4—N3—N1	105.82 (12)	N10—N9—N7	105.89 (12)
N3—N4—C5	106.17 (12)	N9—N10—C11	106.19 (12)
C1—N5—C4	114.47 (12)	C7—N11—C10	114.67 (12)
C3—N6—C4	115.71 (12)	C10—N12—C9	115.82 (12)
N5—C1—C2	125.31 (12)	N11—C7—C8	125.20 (12)
N5—C1—N1	115.33 (12)	N11—C7—N7	115.25 (12)
C2—C1—N1	119.36 (12)	C8—C7—N7	119.55 (12)
C1—C2—C3	114.59 (13)	C7—C8—C9	114.40 (13)
C1—C2—H1	122.4 (11)	C7—C8—H7	122.5 (11)
C3—C2—H1	123.0 (12)	C9—C8—H7	123.1 (12)
N6—C3—C2	123.19 (13)	N12—C9—C8	123.46 (14)
N6—C3—H2	116.5 (10)	N12—C9—H8	116.1 (11)
C2—C3—H2	120.3 (10)	C8—C9—H8	120.5 (11)
N5—C4—N6	126.72 (13)	N12—C10—N11	126.44 (13)
N5—C4—S1	119.87 (10)	N12—C10—S2	119.96 (10)
N6—C4—S1	113.41 (10)	N11—C10—S2	113.60 (10)
N2—C5—N4	112.96 (13)	N8—C11—N10	112.94 (13)
N2—C5—H3	124.0 (12)	N8—C11—H9	124.6 (12)
N4—C5—H3	123.0 (12)	N10—C11—H9	122.5 (12)
S1—C6—H4	108.9 (11)	S2—C12—H10	109.7 (11)
S1—C6—H5	110.3 (10)	S2—C12—H11	105.7 (12)
H4—C6—H5	112.5 (14)	H10—C12—H11	110.6 (16)
S1—C6—H6	103.5 (11)	S2—C12—H12	110.3 (11)
H4—C6—H6	110.8 (15)	H10—C12—H12	111.9 (16)
H5—C6—H6	110.4 (15)	H11—C12—H12	108.4 (16)

Hydrogen-bond geometry (Å, °)

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
C2—H1...N9 ⁱ	0.89 (2)	2.58 (2)	3.203 (2)	129 (2)

Symmetry code: (i) $x-1, y, z$.