

Acta Crystallographica Section E

Structure Reports

Online

ISSN 1600-5368

6-(4-Chlorophenyl)-3-methylimidazo-[2,1-*b*]thiazole

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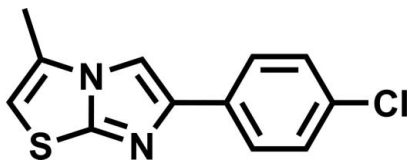
Received 17 October 2013; accepted 20 October 2013

Key indicators: single-crystal X-ray study; $T = 120$ K; mean $\sigma(\text{C}-\text{C}) = 0.002$ Å; R factor = 0.038; wR factor = 0.093; data-to-parameter ratio = 20.3.

In the title compound, $\text{C}_{12}\text{H}_9\text{ClN}_2\text{S}$, the imidazo[2,1-*b*]thiazole fragment is planar (r.m.s. deviation = 0.003 Å), and the benzene ring is twisted slightly [by 5.65 (6)°] relative to this moiety. In the crystal, molecules are linked by π - π stacking interactions into columns along [010]. The molecules within the columns are arranged alternatively by their planar rotation of 180°. Thus, in the columns, there are the two types of π - π stacking interactions, namely, (i) between two imidazo[2,1-*b*]thiazole fragments [interplanar distance = 3.351 (2) Å] and (ii) between an imidazo[2,1-*b*]thiazole fragment and the phenyl ring [interplanar distance = 3.410 (5) Å]. There are no short contacts between the columns.

Related literature

For the synthesis and properties of related compounds containing an imidazo[2,1-*b*]thiazole moiety, see: Raeymaekers *et al.* (1966); Metaye *et al.* (1992); Carpenter *et al.* (2003); Milne *et al.* (2007); Scribner *et al.* (2008); Chorell *et al.* (2010); Guzeldemirci & Kucukbasmaci (2010); Budriesi *et al.* (2011); Yousefi *et al.* (2011).



Experimental

Crystal data

$\text{C}_{12}\text{H}_9\text{ClN}_2\text{S}$
 $M_r = 248.73$
 Triclinic, $P\bar{1}$
 $a = 7.0624$ (5) Å
 $b = 7.7132$ (5) Å
 $c = 10.3460$ (7) Å
 $\alpha = 93.353$ (1)°
 $\beta = 90.107$ (1)°
 $\gamma = 98.832$ (1)°
 $V = 555.92$ (7) Å³
 $Z = 2$
 Mo $K\alpha$ radiation
 $\mu = 0.50$ mm⁻¹
 $T = 120$ K
 $0.30 \times 0.20 \times 0.20$ mm

Data collection

Bruker APEXII CCD diffractometer
 Absorption correction: multi-scan (SADABS; Bruker, 2003)
 $T_{\min} = 0.864$, $T_{\max} = 0.906$
 6927 measured reflections
 2963 independent reflections
 2306 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.032$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.038$
 $wR(F^2) = 0.093$
 $S = 1.05$
 2963 reflections
 146 parameters
 H-atom parameters constrained
 $\Delta\rho_{\text{max}} = 0.38$ e Å⁻³
 $\Delta\rho_{\text{min}} = -0.22$ e Å⁻³

Data collection: APEX2 (Bruker, 2005); cell refinement: SAINT (Bruker, 2001); data reduction: SAINT; program(s) used to solve structure: SHELXTL (Sheldrick, 2008); program(s) used to refine structure: SHELXTL; molecular graphics: SHELXTL; software used to prepare material for publication: SHELXTL.

The authors are grateful to the Ministry of Education and Science of the Russian Federation (State program No. 3.1168.2011).

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: RK2417).

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supplementary materials

Acta Cryst. (2013). E69, o1701 [doi:10.1107/S1600536813028833]

6-(4-Chlorophenyl)-3-methylimidazo[2,1-*b*]thiazole

Alexander S. Bunev, Elena V. Sukhonosova, Vladimir E. Statsyuk, Gennady I. Ostapenko and Victor N. Khrustalev

1. Comment

Many natural products and biologically active compounds containing imidazo[2,1-*b*]thiazole moieties have been discovered and synthesized so far (Metaye *et al.*, 1992; Guzeldemirci & Kucukbasmaci, 2010; Budriesi *et al.*, 2011). As some typical examples, anthelmintics tetramisole (Raeymaekers *et al.*, 1966), thieno(3,2-*d*)pyrimidinone (Carpenter *et al.*, 2003), 5,6-diarylimidazo[2,1-*b*](1,3)thiazoles (Scribner *et al.*, 2008), C-2 aryl-substituted pilicides (Chorell *et al.*, 2010), and ¹³C-labeled imidazo[2,1-*b*]benzothiazoles (Yousefi *et al.*, 2011) all showed effective biological and medicinal activity. Milne and co-authors (Milne *et al.*, 2007) described the identification and characterization of a molecule bearing imidazo[2,1-*b*]thiazole as an activator of SIRT1, which was structurally unrelated to, and 1000-fold more potent than, resveratrol. And it can bind to the SIRT1 enzyme-peptide substrate complex at an allosteric site amino terminal to the catalytic domain and lower the Michaelis constant for acetylated substrates.

In this work, a 6-(4-chlorophenyl)-3-methylimidazo[2,1-*b*]thiazole, C₁₂H₉ClN₂S, **I**, was prepared by the reaction of 4-methyl-2-aminothiazole with 2-bromo-1-(4-chlorophenyl)ethanone (Fig. 1), and its structure was unambiguously established by the X-ray diffraction study (Fig. 2).

The imidazo[2,1-*b*]thiazole fragment in **I** is planar (r.m.s. deviation is 0.003 Å), and the phenyl ring is slightly twisted in relative to this fragment by 5.65 (6)°.

In the crystal, the molecules of **I** are linked by the intermolecular $\pi\cdots\pi$ -stacking interactions into columns along [010] (Fig. 3). The molecules within the columns are arranged alternatively by their planar rotation of 180° (Fig. 3). Thus, in the columns of **I**, there are the two types of $\pi\cdots\pi$ -stacking interactions, namely, (i) between two imidazo[2,1-*b*]thiazole fragments (the interplane distance is 3.351 (2) Å) and (ii) between imidazo[2,1-*b*]thiazole fragment and phenyl ring (the interplane distance is 3.410 (5) Å). There are no any short contacts between the columns (Fig. 4).

2. Experimental

A mixture of 4-methyl-2-aminothiazole (5.0 g, 43.8 mmol) and 2-bromo-1-(4-chlorophenyl)ethanone (10.2 g, 43.8 mmol) was dissolved in acetone (40 mL). The reaction mixture was stirred for 24 h. The resulting precipitate was collected, suspended in 2*N* HCl (70 mL) and heated under reflux. The warm solution basified with 20% NH₄OH yielded the expected imidazo[2,1-*b*]thiazole after cooling upto room temperature. The residue crystallized from *N,N*-dimethylformamide. Yield is 78%. The single crystal of the product was obtained by slow crystallization from *N,N*-dimethylformamide. M.p. = 397-399 K. IR (KBr), ν/cm^{-1} : ¹H NMR (500 MHz, DMSO-*d*₆, 304 K): 2.43 (s, 3H, CH₃), 6.91 (s, 1H, H5), 7.46 (d, 2H, *J* = 8.55, H11,13), 7.87 (d, 2H, *J* = 8.55, H10,14), 8.31 (s, 1H, H2). Anal. Calcd for C₁₂H₉ClN₂S: C, 57.95; H, 3.65. Found: C, 57.91; H, 3.59.

3. Refinement

All hydrogen atoms were placed in the calculated positions with $C-H = 0.95\text{\AA}$ (for CH-groups) and 0.98\AA (for CH_3 -group) and refined in the riding model with fixed isotropic displacement parameters: $U_{iso}(H) = 1.5U_{eq}(C)$ for the CH_3 -group and $U_{iso}(H) = 1.2U_{eq}(C)$ for the other CH-groups.

Computing details

Data collection: *APEX2* (Bruker, 2005); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT* (Bruker, 2001); program(s) used to solve structure: *SHELXTL* (Sheldrick, 2008); program(s) used to refine structure: *SHELXTL* (Sheldrick, 2-methyl-2-aminothiazole with 2-bromo-1-(4-chlorophenyl)ethanone.

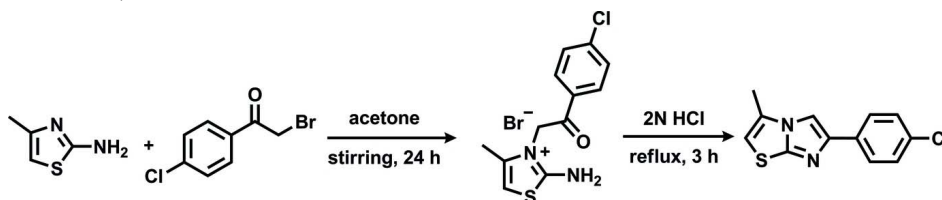


Figure 1

The reaction of 4-methyl-2-aminothiazole with 2-bromo-1-(4-chlorophenyl)ethanone.

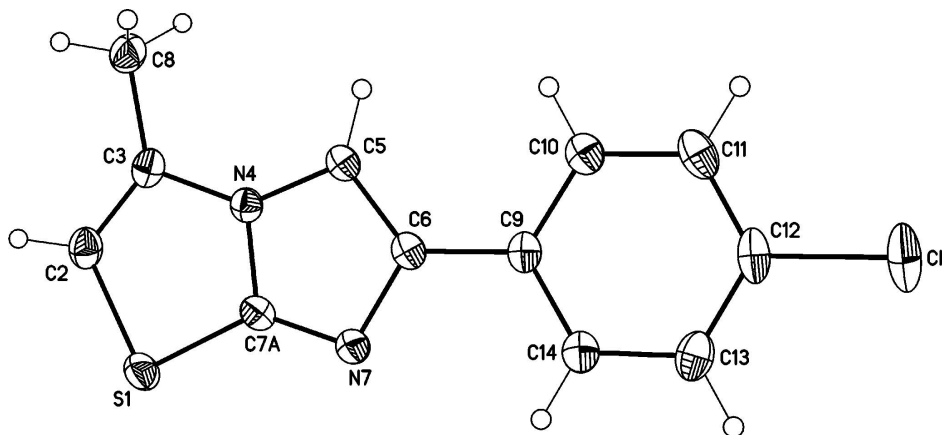


Figure 2

Molecular structure of **I** with the atom numbering scheme. Displacement ellipsoids are presented at the 50% probability level. H atoms are depicted as small spheres of arbitrary radius.

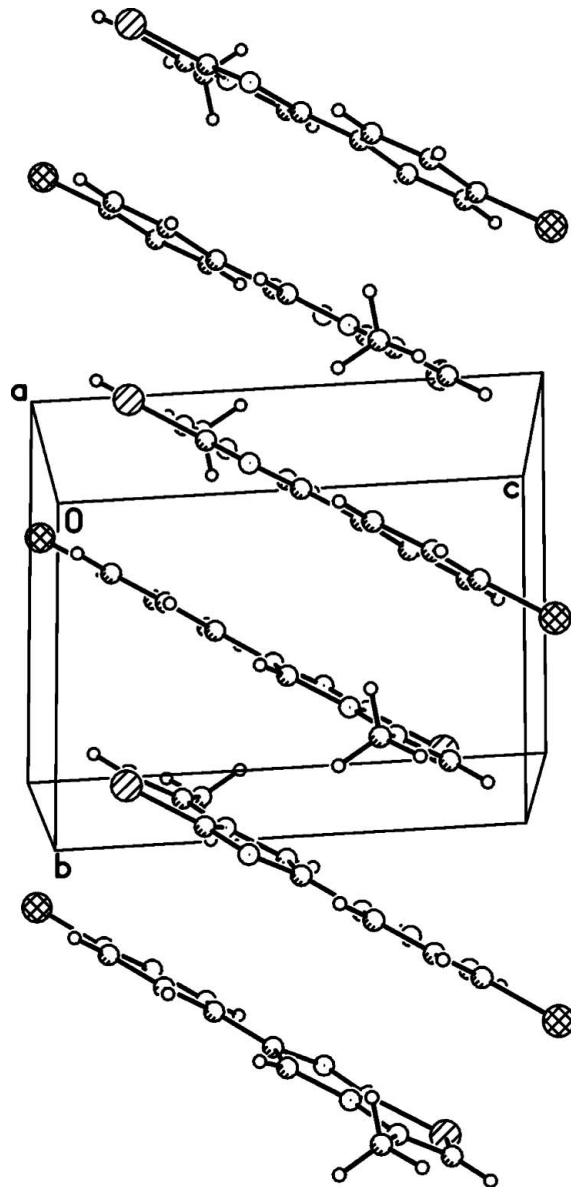


Figure 3

The $\pi\cdots\pi$ -bonded column of **I** along [010].

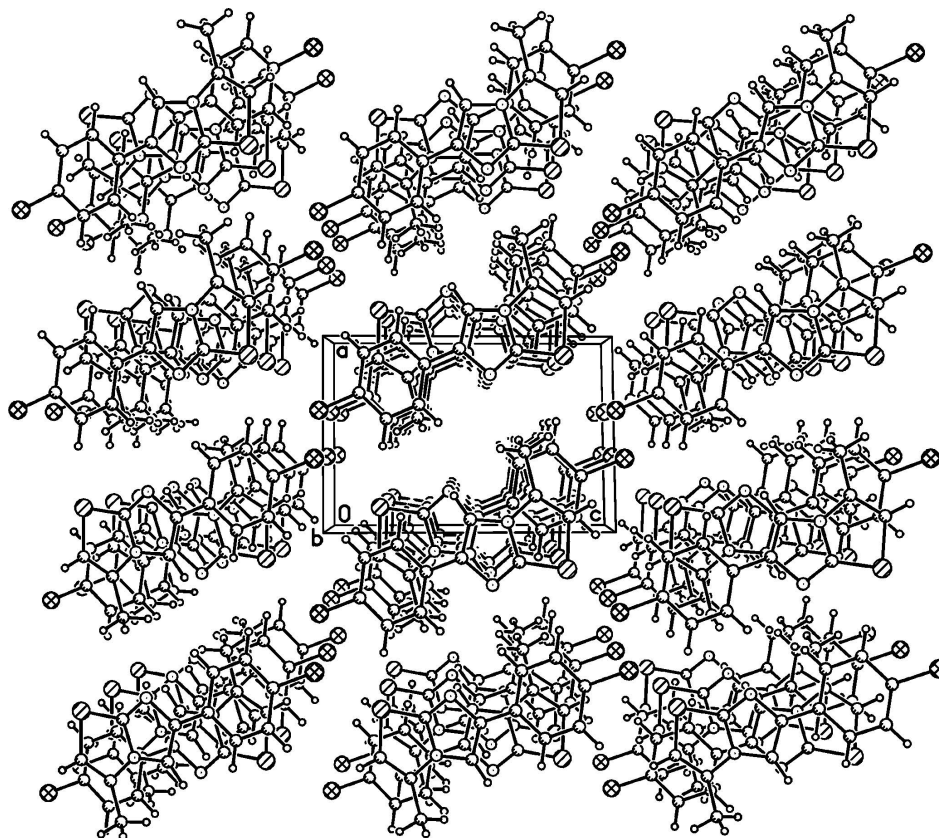


Figure 4

The crystal packing of **I** along the *b* axis.

6-(4-Chlorophenyl)-3-methylimidazo[2,1-*b*]thiazole

Crystal data

$C_{12}H_9ClN_2S$

$M_r = 248.73$

Triclinic, $P\bar{1}$

Hall symbol: -P 1

$a = 7.0624$ (5) Å

$b = 7.7132$ (5) Å

$c = 10.3460$ (7) Å

$\alpha = 93.353$ (1)°

$\beta = 90.107$ (1)°

$\gamma = 98.832$ (1)°

$V = 555.92$ (7) Å³

$Z = 2$

$F(000) = 256$

$D_x = 1.486$ Mg m⁻³

Melting point = 397–399 K

Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å

Cell parameters from 2226 reflections

$\theta = 2.7$ – 30.6 °

$\mu = 0.50$ mm⁻¹

$T = 120$ K

Prism, colourless

$0.30 \times 0.20 \times 0.20$ mm

Data collection

Bruker APEXII CCD
diffractometer

Radiation source: fine-focus sealed tube

Graphite monochromator

φ and ω scans

Absorption correction: multi-scan

(*SADABS*; Bruker, 2003)

$T_{\min} = 0.864$, $T_{\max} = 0.906$

6927 measured reflections

2963 independent reflections

2306 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.032$

$\theta_{\text{max}} = 29.0$ °, $\theta_{\text{min}} = 2.0$ °

$h = -9 \rightarrow 9$

$k = -10 \rightarrow 10$

$l = -14 \rightarrow 14$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.038$

$wR(F^2) = 0.093$

$S = 1.05$

2963 reflections

146 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

H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0461P)^2 + 0.0291P]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} = 0.001$

$\Delta\rho_{\max} = 0.38 \text{ e } \text{\AA}^{-3}$

$\Delta\rho_{\min} = -0.22 \text{ e } \text{\AA}^{-3}$

Special details

Geometry. All s.u.'s (except the s.u. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell s.u.'s are taken into account individually in the estimation of s.u.'s in distances, angles and torsion angles; correlations between s.u.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell s.u.'s is used for estimating s.u.'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 $F^2 > 2\sigma(F^2)$ 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 (\AA^2)

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
C11	0.38211 (8)	0.73973 (6)	1.00250 (4)	0.04269 (15)
S1	0.13039 (6)	0.04797 (6)	0.19530 (4)	0.02548 (12)
C2	-0.1162 (2)	-0.0288 (2)	0.18876 (16)	0.0239 (3)
H2	-0.1768	-0.1011	0.1184	0.029*
C3	-0.2120 (2)	0.0238 (2)	0.29218 (15)	0.0203 (3)
N4	-0.08638 (17)	0.12958 (16)	0.37993 (12)	0.0180 (3)
C5	-0.0956 (2)	0.21865 (19)	0.49862 (14)	0.0189 (3)
H5	-0.2063	0.2255	0.5495	0.023*
C6	0.0896 (2)	0.29557 (19)	0.52765 (14)	0.0190 (3)
N7	0.21503 (18)	0.25589 (17)	0.42952 (12)	0.0204 (3)
C7A	0.1018 (2)	0.1576 (2)	0.34408 (15)	0.0201 (3)
C8	-0.4178 (2)	-0.0182 (2)	0.32472 (17)	0.0258 (3)
H8A	-0.4875	-0.0863	0.2518	0.039*
H8B	-0.4704	0.0911	0.3422	0.039*
H8C	-0.4314	-0.0873	0.4017	0.039*
C9	0.1606 (2)	0.40574 (19)	0.64315 (14)	0.0188 (3)
C10	0.0334 (2)	0.4576 (2)	0.73671 (15)	0.0230 (3)
H10	-0.1006	0.4220	0.7246	0.028*
C11	0.1012 (3)	0.5600 (2)	0.84631 (16)	0.0272 (4)
H11	0.0142	0.5955	0.9087	0.033*
C12	0.2971 (3)	0.6103 (2)	0.86436 (15)	0.0271 (4)
C13	0.4260 (2)	0.5626 (2)	0.77325 (16)	0.0265 (4)
H13	0.5598	0.5985	0.7860	0.032*
C14	0.3567 (2)	0.4617 (2)	0.66341 (15)	0.0222 (3)
H14	0.4445	0.4298	0.6002	0.027*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C11	0.0636 (3)	0.0379 (3)	0.0254 (2)	0.0095 (2)	-0.0140 (2)	-0.01208 (19)
S1	0.0251 (2)	0.0306 (2)	0.0207 (2)	0.00669 (17)	0.00010 (15)	-0.00563 (16)
C2	0.0266 (8)	0.0227 (8)	0.0224 (8)	0.0048 (7)	-0.0059 (6)	-0.0019 (6)
C3	0.0214 (7)	0.0173 (7)	0.0225 (8)	0.0040 (6)	-0.0064 (6)	0.0014 (6)
N4	0.0190 (6)	0.0166 (6)	0.0190 (6)	0.0045 (5)	-0.0015 (5)	0.0008 (5)
C5	0.0220 (7)	0.0181 (7)	0.0172 (7)	0.0053 (6)	0.0011 (6)	0.0017 (6)
C6	0.0230 (8)	0.0173 (7)	0.0176 (7)	0.0054 (6)	0.0003 (6)	0.0019 (6)
N7	0.0199 (6)	0.0221 (6)	0.0191 (6)	0.0034 (5)	0.0004 (5)	-0.0007 (5)
C7A	0.0211 (7)	0.0215 (7)	0.0187 (7)	0.0064 (6)	0.0011 (6)	0.0007 (6)
C8	0.0212 (8)	0.0263 (8)	0.0292 (9)	0.0027 (7)	-0.0041 (6)	-0.0027 (7)
C9	0.0253 (8)	0.0142 (7)	0.0172 (7)	0.0028 (6)	-0.0018 (6)	0.0031 (6)
C10	0.0275 (8)	0.0190 (7)	0.0230 (8)	0.0049 (6)	0.0014 (6)	0.0027 (6)
C11	0.0417 (10)	0.0228 (8)	0.0192 (8)	0.0107 (7)	0.0030 (7)	0.0021 (6)
C12	0.0438 (10)	0.0193 (7)	0.0178 (7)	0.0047 (7)	-0.0072 (7)	-0.0019 (6)
C13	0.0321 (9)	0.0218 (8)	0.0249 (8)	0.0010 (7)	-0.0067 (7)	0.0027 (7)
C14	0.0262 (8)	0.0199 (7)	0.0200 (7)	0.0019 (6)	0.0000 (6)	0.0022 (6)

Geometric parameters (\AA , $^\circ$)

C11—C12	1.7450 (17)	C8—H8A	0.9800
S1—C7A	1.7399 (16)	C8—H8B	0.9800
S1—C2	1.7512 (17)	C8—H8C	0.9800
C2—C3	1.343 (2)	C9—C14	1.397 (2)
C2—H2	0.9500	C9—C10	1.404 (2)
C3—N4	1.4018 (19)	C10—C11	1.384 (2)
C3—C8	1.483 (2)	C10—H10	0.9500
N4—C7A	1.3685 (19)	C11—C12	1.388 (2)
N4—C5	1.3782 (19)	C11—H11	0.9500
C5—C6	1.376 (2)	C12—C13	1.385 (2)
C5—H5	0.9500	C13—C14	1.383 (2)
C6—N7	1.3996 (18)	C13—H13	0.9500
C6—C9	1.466 (2)	C14—H14	0.9500
N7—C7A	1.315 (2)		
C7A—S1—C2	89.68 (7)	H8A—C8—H8B	109.5
C3—C2—S1	113.96 (12)	C3—C8—H8C	109.5
C3—C2—H2	123.0	H8A—C8—H8C	109.5
S1—C2—H2	123.0	H8B—C8—H8C	109.5
C2—C3—N4	110.46 (14)	C14—C9—C10	118.13 (14)
C2—C3—C8	130.15 (15)	C14—C9—C6	120.96 (14)
N4—C3—C8	119.35 (13)	C10—C9—C6	120.91 (14)
C7A—N4—C5	106.48 (12)	C11—C10—C9	120.71 (16)
C7A—N4—C3	115.56 (13)	C11—C10—H10	119.6
C5—N4—C3	137.96 (13)	C9—C10—H10	119.6
C6—C5—N4	105.33 (12)	C10—C11—C12	119.54 (15)
C6—C5—H5	127.3	C10—C11—H11	120.2
N4—C5—H5	127.3	C12—C11—H11	120.2

C5—C6—N7	111.17 (13)	C13—C12—C11	121.06 (15)
C5—C6—C9	128.03 (14)	C13—C12—C11	119.50 (14)
N7—C6—C9	120.79 (14)	C11—C12—C11	119.43 (13)
C7A—N7—C6	103.37 (12)	C14—C13—C12	118.94 (16)
N7—C7A—N4	113.65 (13)	C14—C13—H13	120.5
N7—C7A—S1	136.01 (12)	C12—C13—H13	120.5
N4—C7A—S1	110.33 (11)	C13—C14—C9	121.60 (15)
C3—C8—H8A	109.5	C13—C14—H14	119.2
C3—C8—H8B	109.5	C9—C14—H14	119.2
C7A—S1—C2—C3	-0.51 (13)	C3—N4—C7A—S1	-0.54 (16)
S1—C2—C3—N4	0.30 (17)	C2—S1—C7A—N7	179.01 (17)
S1—C2—C3—C8	-177.40 (14)	C2—S1—C7A—N4	0.57 (12)
C2—C3—N4—C7A	0.17 (19)	C5—C6—C9—C14	174.39 (15)
C8—C3—N4—C7A	178.15 (13)	N7—C6—C9—C14	-5.4 (2)
C2—C3—N4—C5	-179.57 (16)	C5—C6—C9—C10	-5.4 (2)
C8—C3—N4—C5	-1.6 (3)	N7—C6—C9—C10	174.78 (14)
C7A—N4—C5—C6	-0.14 (16)	C14—C9—C10—C11	-0.6 (2)
C3—N4—C5—C6	179.61 (16)	C6—C9—C10—C11	179.28 (14)
N4—C5—C6—N7	-0.20 (17)	C9—C10—C11—C12	-0.7 (2)
N4—C5—C6—C9	-179.99 (14)	C10—C11—C12—C13	1.2 (2)
C5—C6—N7—C7A	0.46 (16)	C10—C11—C12—C11	179.89 (12)
C9—C6—N7—C7A	-179.73 (13)	C11—C12—C13—C14	-0.6 (2)
C6—N7—C7A—N4	-0.56 (17)	C11—C12—C13—C14	-179.23 (12)
C6—N7—C7A—S1	-178.95 (14)	C12—C13—C14—C9	-0.7 (2)
C5—N4—C7A—N7	0.46 (17)	C10—C9—C14—C13	1.2 (2)
C3—N4—C7A—N7	-179.35 (12)	C6—C9—C14—C13	-178.60 (14)
C5—N4—C7A—S1	179.27 (10)		
