Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

2-[(2,6-Dichlorobenzyl)amino]-*N*-(4-methylthiazol-2-yl)acetamide

Jie Luo,[a] Gui-Long Zhao,[b] Hua Shao,[b] Yu-Li Wang[a] and Bao-Han Qu[a]*

[a]College of Chemistry and Pharmaceutical Sciences, Qingdao Agricultural University, Qingdao 266109, People's Republic of China, and [b]Tianjin Key Laboratory of Molecular Design and Drug Discovery, Tianjin Institute of Pharmaceutical Research, Tianjin 300193, People's Republic of China
Correspondence e-mail: qubaohan2009@yahoo.cn

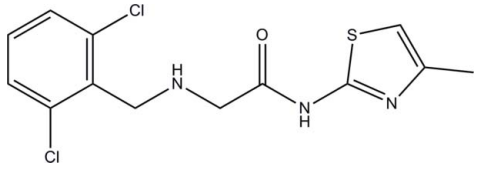
Received 27 December 2009; accepted 25 January 2010

Key indicators: single-crystal X-ray study; T = 113 K; mean σ(C–C) = 0.002 Å; R factor = 0.056; wR factor = 0.131; data-to-parameter ratio = 17.6.

In the title compound, $C_{13}H_{13}Cl_2N_3OS$, the thiazole and benzene rings are roughly parallel to one another in two layers [dihedral angle = 5.08 (2)°] because the N—C—C—N—C chain that links the two rings is folded [N—C—C—N torsion angle = 12.0 (2)°] rather than fully extended. An intramolecular N—H···N interaction occurs. In the crystal, weak intermolecular N—H···N and C—H···O interactions are present and π–π interactions are indicated by the short distances [3.507 (3)–3.665 (2) Å] between the centroids of the thiazole and benzene rings.

Related literature

For details of the biological activity of Dipeptidyl peptidase IV (DPP-IV) inhibitors, see: Cheon *et al.* (2005); Kondo *et al.* (2007); Sakashita *et al.* (2006); Zhan *et al.* (2009). For bond-length data, see: Allen *et al.* (1987).



Experimental

Crystal data

$C_{13}H_{13}Cl_2N_3OS$ M_r = 330.22
Monoclinic, $C2/c$
a = 14.008 (4) Å
b = 18.133 (5) Å
c = 11.390 (3) Å
β = 97.341 (3)°
V = 2869.4 (14) Å^3
Z = 8
Mo $K\alpha$ radiation
μ = 0.60 mm^{-1}
T = 113 K
0.22 × 0.18 × 0.16 mm

Data collection

Rigaku Saturn diffractometer
Absorption correction: multi-scan (*CrystalClear*; Rigaku, 2007)
T_{min} = 0.880, T_{max} = 0.911
11103 measured reflections
3371 independent reflections
3150 reflections with $I > 2\sigma(I)$
R_{int} = 0.036

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.056
$wR(F^2)$ = 0.131
S = 1.20
3371 reflections
191 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.65 e Å^{-3}
$\Delta\rho_{min}$ = −0.83 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N3—H3···N1^{i}	0.89 (2)	2.32 (2)	3.130 (2)	150.9 (17)
C7—H7B···O1^{ii}	0.99	2.53	3.3233 (19)	137
N2—H2···N3	0.84 (2)	2.26 (2)	2.6742 (19)	111 (2)

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

Data collection: *CrystalClear* (Rigaku, 2007); cell refinement: *CrystalClear*; data reduction: *CrystalClear*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL*.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: FL2286).

References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.
Cheon, H. G., Kim, S.-S., Kim, K.-R., Rhee, S. D., Yang, S.-D., Ahn, J. H., Park, S.-D., Lee, J. M., Jung, W. H., Lee, H. S. & Kim, H. Y. (2005). *Biochem. Pharmacol.* **70**, 22–29.
Kondo, T., Sugimoto, I., Nekado, T., Ochi, K., Ohtani, T., Tajima, Y., Yamamoto, S., Kawabata, K., Nakai, H. & Toda, M. (2007). *Bioorg. Med. Chem.* **15**, 2715–2735.
Rigaku (2007). *CrystalClear*. Rigaku Corporation, Tokyo, Japan.
Sakashita, H., Akahoshi, F., Kitajima, H., Tsutsumiuchi, R. & Hayashi, Y. (2006). *Bioorg. Med. Chem.* **14**, 3662–3671.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Zhan, F. X., Wang, Y. L., Zhao, G. L., Xu, W. R., Li, Y. L., Zou, M. X., Tang, L. D. & Wang, J. W. (2009). *Chin. J. Org. Chem.* **29**, 1236–1242

supporting information

Acta Cryst. (2010). E**66**, o518 [doi:10.1107/S1600536810003089]

2-[(2,6-Dichlorobenzyl)amino]-*N*-(4-methylthiazol-2-yl)acetamide

Jie Luo, Gui-Long Zhao, Hua Shao, Yu-Li Wang and Bao-Han Qu

S1. Comment

Dipeptidyl peptidase IV (DPP-IV) inhibitors are a new class of antidiabetic agents (Cheon *et al.*, 2005; Kondo *et al.*, 2007; Sakashita *et al.*, 2006) and the title compound was prepared as a novel DPP-IV inhibitor (Zhan *et al.*, 2009). We reported the crystal structure here.

In title compound, all bond lengths in the molecular are normal (Allen *et al.*, 1987). Atoms C4—C6/N2/N3/O1 lie in thiazole (C1—C3/N1/S1) plane with maximun least squares plane deviation for C4 0.065 (2) Å. Thiazole ring (C1—C3/N1/S1) and benzene ring (C8—C13) are essentially parallel to one another (dihedral angle of 5.08 (2) °) because the N—C—C—N—C chain that links the two rings is folded ((N—C—C—N torsion angle of 12.0 (2) °) rather than fully extended. *π*—*π* interactions are indicated by the short distance (Cg1···Cg1 distance of 3.665 (2) Å, symmetry code: 1-x,y,1/2-z; Cg1···Cg2 distance of 3.766 (3) Å, symmetry code: 1/2-x,1/2-y,-z; Cg1···Cg2 distance of 3.507 (3) Å, symmetry code: 1-x,y,-1/2-z) between the centroids of the thiazole rings C1—C3/N1/S1 (Cg1) and benzene rings C8—C13 (Cg2) (Table 1). There are intramolecular interaction and weaker N—H···N, C—H···O intermolecular interactions, which stabilized the structure (Table 1).

S2. Experimental

A round-bottomed flask was charged with [(2,6-dichlorophenyl)methyl]amine (1.76 g, 10 mmol), 2-[(2-chloroacetyl)-amino]-4-methylthiazole (1.91 g, 10 mmol), triethylamine (1.21 g, 12 mmol) and THF (20 ml), and the resulting mixture was stirred at room temperature over night. The reaction mixture was concentrated on a rotary evaporator and diluted with 100 ml of dichloromethane, and the organic solution thus obtained was washed with saturated brine, dried over sodium sulfate and evaporated on a rotary evaporator to afford a solid residue, which was triturated with a mixed solvent consisting of 5 ml of dichloromethane and 10 ml of ethyl acetate and filtered. The crystals were collected and dried to yield the title compound as colorless crystals 2.51 g (Yield 76.1%). Crystals suitable for single-crystal X-ray diffraction were obtained via slow evaporation at room temperature of a solution of the pure title compound in dichloromethane.

S3. Refinement

All H atoms were found on difference maps. The H atoms of secondary amine were refined freely, giveing 0.84 or 0.89 Å, and C—H hyrdogens in the final cycles of refinement using a riding model, giveing 0.95-0.99 Å, with U_{iso}(H) = 1.2U_{eq}(C) and 1.5U_{eq}(C) for the methyl H atoms.

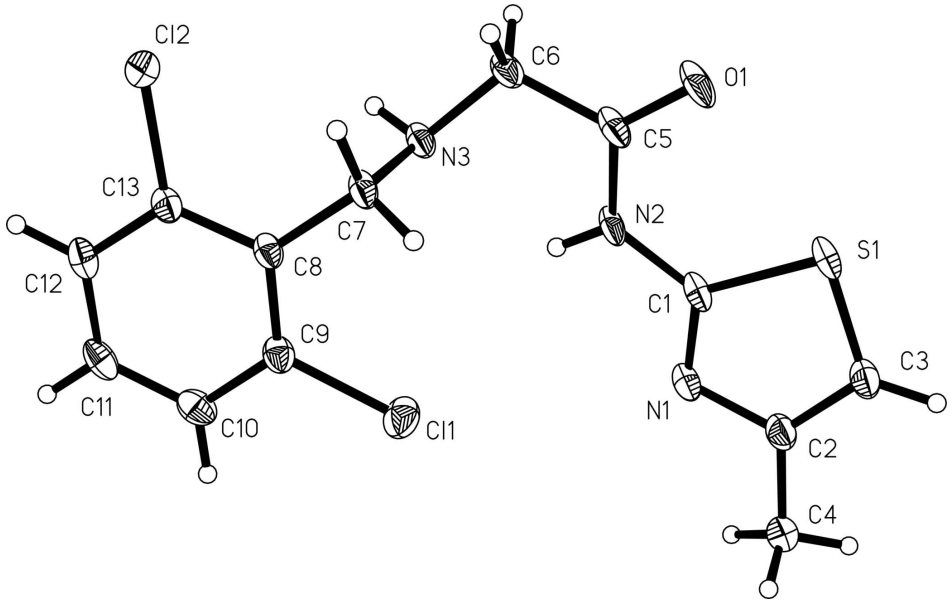


Figure 1

The molecular structure of (I), with atom labels and 40% probability displacement ellipsoids for non-H atoms.

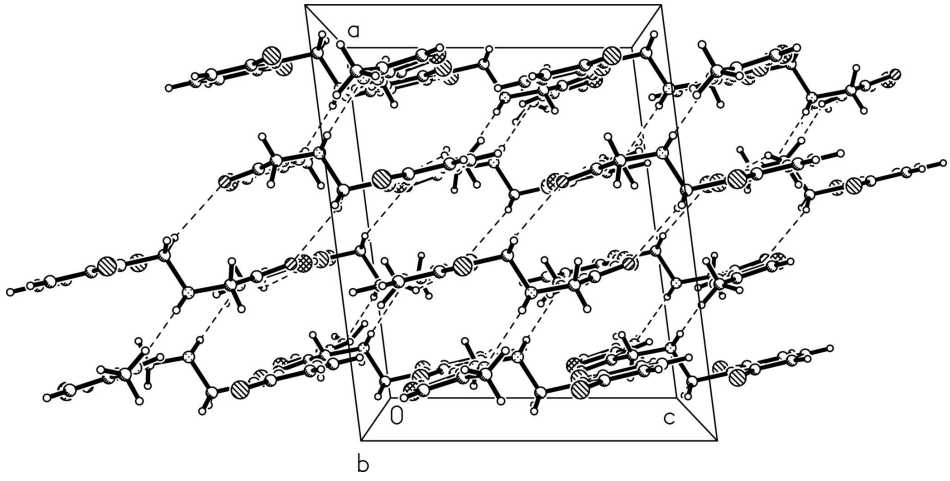


Figure 2

A packing diagram of the molecule of the title compound, view down b axis. Hydrogen bonds are shown as dashed lines.

2-[(2,6-Dichlorobenzyl)amino]-*N*-(4-methylthiazol-2-yl)acetamide

Crystal data

$C_{13}H_{13}Cl_2N_3OS$
$M_r = 330.22$
Monoclinic, *C*2/*c*
Hall symbol: -C 2yc
$a = 14.008\ (4)$ Å
$b = 18.133\ (5)$ Å
$c = 11.390\ (3)$ Å
$\beta = 97.341\ (3)°$
$V = 2869.4\ (14)$ Å^3
$Z = 8$
$F(000) = 1360$
$D_x = 1.529$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71075$ Å
Cell parameters from 5153 reflections
$\theta = 1.8–27.9°$
$\mu = 0.60$ mm^{-1}
$T = 113$ K
Prism, colorless
0.22 × 0.18 × 0.16 mm

Data collection

Rigaku Saturn diffractometer
Radiation source: rotating anode
Multilayer monochromator
Detector resolution: 14.63 pixels mm^{-1}
ω and φ scans
Absorption correction: multi-scan (*CrystalClear*; Rigaku, 2007)
T_{min} = 0.880, T_{max} = 0.911
11103 measured reflections
3371 independent reflections
3150 reflections with $I > 2\sigma(I)$
R_{int} = 0.036
θ_{max} = 27.9°, θ_{min} = 1.9°
h = −18→18
k = −23→18
l = −13→14

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.056
$wR(F^2)$ = 0.131
S = 1.20
3371 reflections
191 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 atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0837P)^2 + 0.6909P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.65 e Å^{-3}
$\Delta\rho_{min}$ = −0.83 e Å^{-3}
Extinction correction: *SHELXL97* (Sheldrick, 2008), $Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.086 (3)

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds 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}
Cl1	0.59889 (3)	0.30694 (2)	0.64087 (4)	0.03507 (18)
Cl2	0.60026 (3)	0.00844 (2)	0.65202 (3)	0.03000 (17)
S1	0.60179 (3)	0.37651 (2)	0.15270 (3)	0.02879 (17)
O1	0.59946 (9)	0.22476 (8)	0.16770 (10)	0.0371 (3)
N2	0.65223 (10)	0.28348 (8)	0.33975 (11)	0.0262 (3)
N1	0.66017 (10)	0.41118 (7)	0.37000 (11)	0.0260 (3)
N3	0.66669 (9)	0.15932 (7)	0.46748 (11)	0.0244 (3)
C1	0.64101 (10)	0.35505 (9)	0.29875 (12)	0.0242 (3)
C2	0.64316 (12)	0.47666 (9)	0.30816 (14)	0.0284 (3)
C3	0.61282 (13)	0.46827 (10)	0.19104 (15)	0.0325 (4)
H3A	0.5994	0.5080	0.1370	0.039*
C4	0.65614 (15)	0.54732 (10)	0.37486 (15)	0.0368 (4)
H4A	0.6702	0.5869	0.3211	0.055*
H4B	0.7097	0.5425	0.4387	0.055*

H4C	0.5971	0.5590	0.4087	0.055*
C5	0.63006 (11)	0.22221 (9)	0.27318 (13)	0.0282 (4)
C6	0.64796 (12)	0.15012 (9)	0.33971 (13)	0.0290 (4)
H6A	0.5911	0.1178	0.3207	0.035*
H6B	0.7037	0.1250	0.3119	0.035*
C7	0.57765 (11)	0.15610 (8)	0.52297 (13)	0.0239 (3)
H7A	0.5421	0.1103	0.4986	0.029*
H7B	0.5360	0.1986	0.4964	0.029*
C8	0.60135 (10)	0.15779 (8)	0.65549 (12)	0.0216 (3)
C9	0.61402 (11)	0.22376 (8)	0.71857 (13)	0.0251 (3)
C10	0.63758 (11)	0.22652 (10)	0.84107 (14)	0.0299 (4)
H10	0.6454	0.2726	0.8809	0.036*
C11	0.64947 (12)	0.16110 (10)	0.90375 (14)	0.0299 (4)
H11	0.6655	0.1622	0.9873	0.036*
C12	0.63813 (11)	0.09389 (9)	0.84525 (14)	0.0275 (3)
H12	0.6462	0.0488	0.8880	0.033*
C13	0.61481 (10)	0.09381 (8)	0.72306 (13)	0.0232 (3)
H2	0.6752 (16)	0.2782 (14)	0.411 (2)	0.049 (6)*
H3	0.7065 (14)	0.1245 (11)	0.5004 (18)	0.030 (5)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0473 (3)	0.0242 (2)	0.0324 (3)	−0.00894 (14)	−0.0001 (2)	0.00170 (13)
Cl2	0.0396 (3)	0.0237 (3)	0.0275 (3)	−0.00282 (13)	0.00714 (17)	0.00110 (12)
S1	0.0322 (3)	0.0420 (3)	0.0119 (2)	−0.00337 (14)	0.00174 (16)	0.00325 (13)
O1	0.0493 (8)	0.0486 (8)	0.0121 (5)	−0.0193 (5)	−0.0016 (5)	−0.0025 (5)
N2	0.0355 (7)	0.0315 (7)	0.0105 (6)	−0.0120 (5)	−0.0011 (5)	0.0016 (5)
N1	0.0302 (7)	0.0323 (7)	0.0157 (6)	−0.0046 (5)	0.0031 (5)	0.0022 (5)
N3	0.0305 (7)	0.0278 (7)	0.0147 (6)	−0.0082 (5)	0.0028 (5)	−0.0007 (4)
C1	0.0244 (7)	0.0353 (8)	0.0131 (7)	−0.0071 (6)	0.0029 (5)	0.0024 (5)
C2	0.0309 (8)	0.0345 (8)	0.0211 (8)	0.0034 (6)	0.0079 (6)	0.0043 (6)
C3	0.0397 (9)	0.0384 (9)	0.0200 (8)	0.0065 (7)	0.0066 (6)	0.0064 (6)
C4	0.0546 (11)	0.0321 (8)	0.0253 (8)	0.0080 (7)	0.0110 (7)	0.0037 (6)
C5	0.0331 (8)	0.0380 (8)	0.0134 (7)	−0.0158 (6)	0.0027 (6)	−0.0025 (6)
C6	0.0411 (9)	0.0298 (8)	0.0161 (8)	−0.0137 (6)	0.0033 (6)	−0.0048 (6)
C7	0.0282 (7)	0.0285 (8)	0.0146 (7)	−0.0088 (5)	0.0007 (5)	0.0015 (5)
C8	0.0222 (7)	0.0265 (8)	0.0160 (7)	−0.0061 (5)	0.0016 (5)	0.0002 (5)
C9	0.0271 (7)	0.0277 (7)	0.0201 (7)	−0.0056 (5)	0.0008 (6)	0.0005 (5)
C10	0.0297 (8)	0.0367 (8)	0.0226 (8)	−0.0045 (6)	0.0007 (6)	−0.0084 (6)
C11	0.0273 (8)	0.0471 (10)	0.0147 (7)	−0.0007 (6)	0.0007 (6)	−0.0007 (6)
C12	0.0262 (7)	0.0378 (9)	0.0190 (7)	0.0009 (6)	0.0042 (6)	0.0064 (6)
C13	0.0236 (7)	0.0272 (7)	0.0192 (7)	−0.0035 (5)	0.0044 (5)	0.0009 (5)

Geometric parameters (Å, º)

Cl1—C9	1.7480 (16)	C4—H4B	0.9800
Cl2—C13	1.7465 (16)	C4—H4C	0.9800

S1—C3	1.7222 (19)	C5—C6	1.516 (2)
S1—C1	1.7282 (15)	C6—H6A	0.9900
O1—C5	1.2238 (19)	C6—H6B	0.9900
N2—C5	1.359 (2)	C7—C8	1.5038 (19)
N2—C1	1.381 (2)	C7—H7A	0.9900
N2—H2	0.84 (2)	C7—H7B	0.9900
N1—C1	1.308 (2)	C8—C13	1.392 (2)
N1—C2	1.385 (2)	C8—C9	1.395 (2)
N3—C6	1.4550 (19)	C9—C10	1.393 (2)
N3—C7	1.470 (2)	C10—C11	1.384 (3)
N3—H3	0.89 (2)	C10—H10	0.9500
C2—C3	1.356 (2)	C11—C12	1.388 (2)
C2—C4	1.489 (3)	C11—H11	0.9500
C3—H3A	0.9500	C12—C13	1.388 (2)
C4—H4A	0.9800	C12—H12	0.9500

C3—S1—C1	88.07 (8)	C5—C6—H6A	108.9
C5—N2—C1	124.86 (13)	N3—C6—H6B	108.9
C5—N2—H2	118.5 (17)	C5—C6—H6B	108.9
C1—N2—H2	116.6 (17)	H6A—C6—H6B	107.7
C1—N1—C2	110.07 (13)	N3—C7—C8	109.89 (11)
C6—N3—C7	111.78 (12)	N3—C7—H7A	109.7
C6—N3—H3	111.3 (13)	C8—C7—H7A	109.7
C7—N3—H3	108.1 (13)	N3—C7—H7B	109.7
N1—C1—N2	121.05 (13)	C8—C7—H7B	109.7
N1—C1—S1	115.90 (12)	H7A—C7—H7B	108.2
N2—C1—S1	123.05 (11)	C13—C8—C9	115.51 (13)
C3—C2—N1	114.58 (15)	C13—C8—C7	122.35 (13)
C3—C2—C4	126.94 (15)	C9—C8—C7	122.11 (13)
N1—C2—C4	118.44 (14)	C10—C9—C8	123.02 (14)
C2—C3—S1	111.37 (12)	C10—C9—Cl1	118.29 (12)
C2—C3—H3A	124.3	C8—C9—Cl1	118.69 (11)
S1—C3—H3A	124.3	C11—C10—C9	118.91 (15)
C2—C4—H4A	109.5	C11—C10—H10	120.5
C2—C4—H4B	109.5	C9—C10—H10	120.5
H4A—C4—H4B	109.5	C10—C11—C12	120.41 (15)
C2—C4—H4C	109.5	C10—C11—H11	119.8
H4A—C4—H4C	109.5	C12—C11—H11	119.8
H4B—C4—H4C	109.5	C11—C12—C13	118.67 (14)
O1—C5—N2	122.92 (15)	C11—C12—H12	120.7
O1—C5—C6	122.55 (14)	C13—C12—H12	120.7
N2—C5—C6	114.51 (13)	C12—C13—C8	123.46 (14)
N3—C6—C5	113.47 (13)	C12—C13—Cl2	117.64 (12)
N3—C6—H6A	108.9	C8—C13—Cl2	118.89 (11)

C2—N1—C1—N2	−179.90 (14)	N3—C7—C8—C13	−91.91 (15)
C2—N1—C1—S1	0.25 (17)	N3—C7—C8—C9	86.22 (17)
C5—N2—C1—N1	176.97 (15)	C13—C8—C9—C10	−0.6 (2)

C5—N2—C1—S1	−3.2 (2)	C7—C8—C9—C10	−178.88 (14)
C3—S1—C1—N1	0.33 (13)	C13—C8—C9—Cl1	179.82 (11)
C3—S1—C1—N2	−179.52 (14)	C7—C8—C9—Cl1	1.57 (19)
C1—N1—C2—C3	−0.9 (2)	C8—C9—C10—C11	0.3 (2)
C1—N1—C2—C4	177.06 (14)	Cl1—C9—C10—C11	179.80 (12)
N1—C2—C3—S1	1.16 (19)	C9—C10—C11—C12	0.1 (2)
C4—C2—C3—S1	−176.61 (15)	C10—C11—C12—C13	0.1 (2)
C1—S1—C3—C2	−0.81 (13)	C11—C12—C13—C8	−0.5 (2)
C1—N2—C5—O1	1.8 (3)	C11—C12—C13—Cl2	−179.61 (12)
C1—N2—C5—C6	−179.27 (14)	C9—C8—C13—C12	0.8 (2)
C7—N3—C6—C5	90.42 (15)	C7—C8—C13—C12	179.01 (14)
O1—C5—C6—N3	−169.05 (15)	C9—C8—C13—Cl2	179.86 (11)
N2—C5—C6—N3	12.0 (2)	C7—C8—C13—Cl2	−1.90 (19)
C6—N3—C7—C8	174.04 (12)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H3···N1^{i}	0.89 (2)	2.32 (2)	3.130 (2)	150.9 (17)
C7—H7*B*···O1^{ii}	0.99	2.53	3.3233 (19)	137
N2—H2···N3	0.84 (2)	2.26 (2)	2.6742 (19)	111 (2)
*Cg*1···*Cg*1^{ii}			3.665 (2)	
*Cg*1···*Cg*2^{iii}			3.766 (3)	
*Cg*2···*Cg*2^{iv}			3.507 (3)	

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