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4-Chloro-2-{3-chloro-2-[(3,5-dimethylpiperidin-1-yl)methyl]phenylsulfanyl}-6-methoxypyrimidine

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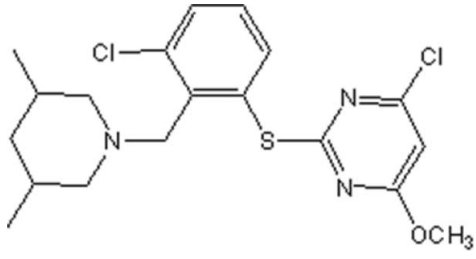
Key indicators: single-crystal X-ray study; T = 296 K; mean σ(C–C) = 0.005 Å; R factor = 0.041; wR factor = 0.119; data-to-parameter ratio = 16.2.

In the title compound, $C_{19}H_{23}Cl_2N_3OS$, the dihedral angle between the benzene ring and the pyrimidine ring is 86.6 (9)°. The piperidine ring adopts a chair conformation.

Related literature

For the biological activity of pyrimidine derivatives, see: Joffe *et al.* (1989); Petersen & Schmidt (2003); Blum (2001); Gompper *et al.* (2004); Michael (2005); Nadal & Olavarria (2004).



Experimental

Crystal data

$C_{19}H_{23}Cl_2N_3OS$
M_r = 412.36
Triclinic, $P\overline{1}$
a = 8.000 (4) Å
b = 11.454 (6) Å
c = 12.001 (7) Å
α = 87.820 (7)°
β = 76.084 (6)°
γ = 77.700 (6)°
V = 1042.9 (10) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.42 mm^{-1}
T = 296 K
0.39 × 0.37 × 0.25 mm

Data collection

Bruker SMART APEXII CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.852, T_{max} = 0.901
7861 measured reflections
3848 independent reflections
2553 reflections with $I > 2\sigma(I)$
R_{int} = 0.019

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.119
S = 1.03
3848 reflections
238 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.30 e Å^{-3}
$\Delta\rho_{min}$ = −0.31 e Å^{-3}

Data collection: *APEX2* (Bruker, 2004); cell refinement: *SAINT* (Bruker, 2004); data reduction: *SAINT*; 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* and *PLATON* (Spek, 2009).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: PB2021).

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supporting information

Acta Cryst. (2010). E**66**, o650 [doi:10.1107/S1600536810004599]

4-Chloro-2-{3-chloro-2-[(3,5-dimethylpiperidin-1-yl)methyl]phenylsulfanyl}-6-methoxypyrimidine

Guanglong Zou and Mei Zhu

S1. Comment

Pyrimidine derivatives are widespread in medicinal and natural products chemistry. A number of natural products, pharmaceuticals, and functional materials incorporate this heterocycle (Michael, 2005. Several examples of pharmaceutically important compounds include trimethoprim (Joffe *et al.*, 1989), sulfadiazine (Petersen & Schmidt, 2003),Gleevec (imatinib mesilate) (Nadal & Olavarria, 2004), and Xeloda (capecitabine) (Blum, 2001). Natural and unnatural polymers also contain pyrimidine derivatives (Gompper *et al.*, 2004). The potent physiological properties of these pyrimidine derivatives led to vast research of their use as medicines in the field of pharmaceutical chemistry. So in the recent decades, many chemists have been attracted by the synthesis of pyrimidines. In this context, we report the synthesis ofthe title compound.

The molecular structure is shown in Fig. 1. The bond lengths and angles are within normal ranges. The pyrimidine ring makes dihedral angles of 86.6 (9)° with the benzene ring. In the crystal structure,The cyclohexyl groups display chair-type conformation.

S2. Experimental

To a solution of 2,4-dichloro-6-methoxypyrimidine (0.5 mmol) and 3-chloro-2-((3,5-dimethylpiperidin-1-yl)methyl)-benzenethiol (0.5 mmol) in dry methylbenzene was added NaH (0.6 mmol). The mixture was stirred for 12 h at room temperature. After evaporation of the solvent, the residue was purified by column chromatography on silica gel to afford the title compound as a colorless solid (yield 78%). The title compound was recrystallized from CH_2Cl_2 at room temperature to give the desired crystals suitable for single-crystal X-ray diffraction.

S3. Refinement

All H atoms were positioned geometrically and treated as riding, with C—H bond lengths constrained to 0.93 Å (aromatic CH) or 0.97 Å (methylene CH_2), and with *U*ĩso~(H) = 1.2Ueq(C) or 1.5Ueq(methylene C).

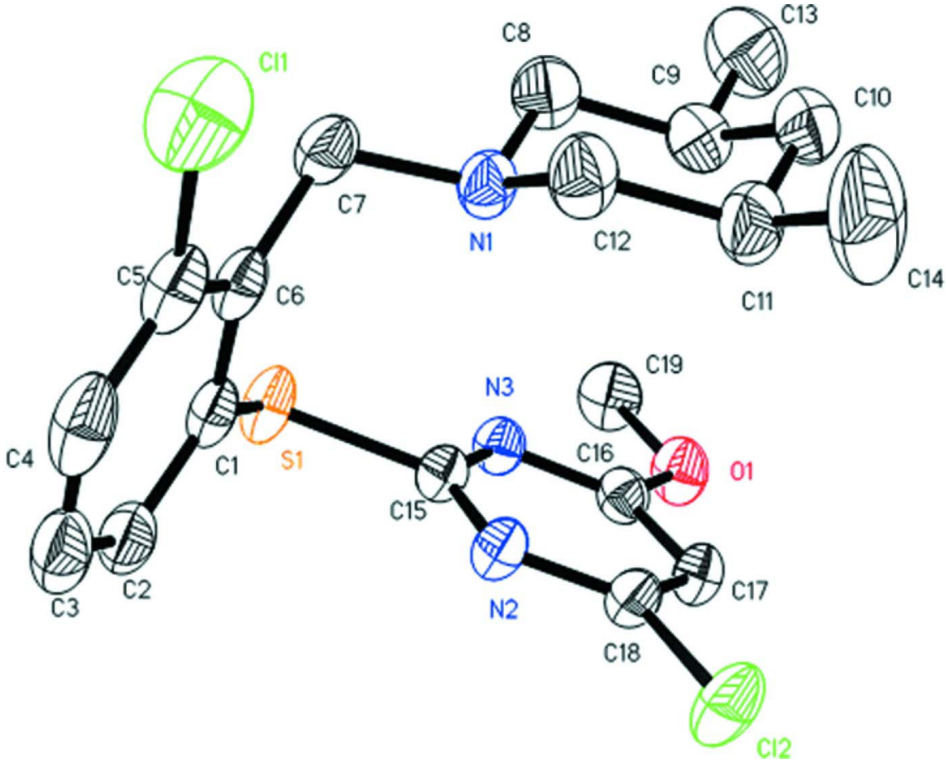

Figure 1

View of the molecular structure of (I) with atom numbering scheme and 30% probability displacement ellipsoids.

4-Chloro-2-{3-chloro-2-[(3,5-dimethylpiperidin-1-yl)methyl]phenylsulfanyl}- 6-methoxypyrimidine

Crystal data

$C_{19}H_{23}Cl_2N_3OS$
$M_r = 412.36$
Triclinic, $P\overline{1}$
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$c = 12.001$ (7) Å
$\alpha = 87.820$ (7)°
$\beta = 76.084$ (6)°
$\gamma = 77.700$ (6)°
$V = 1042.9$ (10) Å^3
$Z = 2$
$F(000) = 432$
$D_x = 1.313$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 2557 reflections
$\theta = 2.5$–25.9°
$\mu = 0.42$ mm^{-1}
$T = 296$ K
Block, colourless
0.39 × 0.37 × 0.25 mm

Data collection

Bruker SMART APEXII CCD area-detector diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
phi and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{min} = 0.852$, $T_{max} = 0.901$
7861 measured reflections
3848 independent reflections
2553 reflections with $I > 2\sigma(I)$
$R_{int} = 0.019$
$\theta_{max} = 25.5°$, $\theta_{min} = 2.5°$
$h = -9 \rightarrow 9$
$k = -13 \rightarrow 13$
$l = -14 \rightarrow 14$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.041$
$wR(F^2) = 0.119$
$S = 1.03$
3848 reflections
238 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
$w = 1/[\sigma^2(F_o^2) + (0.0498P)^2 + 0.3748P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.30$ e Å^{-3}
$\Delta\rho_{min} = -0.31$ e Å^{-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 $F^2 > 2\text{sigma}(F^2)$ 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 (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.8993 (3)	0.4679 (2)	0.3790 (2)	0.0511 (6)
C2	0.7914 (4)	0.5783 (3)	0.4072 (2)	0.0639 (7)
H2	0.8031	0.6417	0.3572	0.077*
C3	0.6657 (4)	0.5951 (3)	0.5096 (3)	0.0772 (10)
H3	0.5913	0.6695	0.5281	0.093*
C4	0.6503 (4)	0.5026 (4)	0.5841 (3)	0.0765 (10)
H4	0.5657	0.5136	0.6533	0.092*
C5	0.7618 (4)	0.3926 (3)	0.5555 (2)	0.0649 (8)
C6	0.8897 (3)	0.3706 (2)	0.4527 (2)	0.0517 (6)
C7	1.0146 (4)	0.2522 (3)	0.4215 (2)	0.0613 (7)
H7A	1.1342	0.2648	0.3977	0.074*
H7B	1.0071	0.2019	0.4886	0.074*
C8	1.1282 (4)	0.1048 (3)	0.2685 (3)	0.0722 (8)
H8A	1.1601	0.0419	0.3206	0.087*
H8B	1.2269	0.1439	0.2432	0.087*
C9	1.0929 (4)	0.0498 (3)	0.1644 (3)	0.0773 (9)
H9	1.0612	0.1145	0.1126	0.093*
C10	0.9343 (4)	−0.0090 (3)	0.2069 (3)	0.0838 (10)
H10A	0.9048	−0.0403	0.1418	0.101*
H10B	0.9647	−0.0753	0.2562	0.101*
C11	0.7761 (4)	0.0801 (3)	0.2730 (3)	0.0867 (10)

H11	0.7438	0.1436	0.2202	0.104*
C12	0.8245 (4)	0.1367 (3)	0.3699 (3)	0.0757 (9)
H12A	0.7247	0.1972	0.4083	0.091*
H12B	0.8503	0.0761	0.4256	0.091*
C13	1.2537 (5)	−0.0357 (3)	0.1000 (3)	0.1102 (13)
H13A	1.3485	0.0055	0.0749	0.165*
H13B	1.2284	−0.0676	0.0345	0.165*
H13C	1.2871	−0.0998	0.1494	0.165*
C14	0.6166 (5)	0.0238 (4)	0.3187 (5)	0.151 (2)
H14A	0.6428	−0.0360	0.3738	0.226*
H14B	0.5894	−0.0124	0.2562	0.226*
H14C	0.5174	0.0844	0.3547	0.226*
C15	0.9754 (3)	0.4023 (2)	0.14901 (19)	0.0466 (6)
C16	1.0372 (3)	0.3253 (2)	−0.0292 (2)	0.0483 (6)
C17	0.8596 (3)	0.3280 (2)	−0.0188 (2)	0.0528 (6)
H17	0.8179	0.3030	−0.0778	0.063*
C18	0.7513 (3)	0.3697 (2)	0.0833 (2)	0.0500 (6)
C19	1.3329 (4)	0.2760 (3)	−0.1362 (3)	0.0729 (8)
H19A	1.3525	0.3554	−0.1317	0.109*
H19B	1.3998	0.2398	−0.2085	0.109*
H19C	1.3695	0.2292	−0.0749	0.109*
Cl1	0.73889 (14)	0.27940 (11)	0.65587 (8)	0.1117 (4)
Cl2	0.52759 (9)	0.37327 (8)	0.10766 (6)	0.0780 (3)
N1	0.9758 (3)	0.19101 (19)	0.32894 (19)	0.0585 (6)
N2	0.8031 (3)	0.40866 (18)	0.16994 (16)	0.0497 (5)
N3	1.0978 (3)	0.36245 (17)	0.05379 (16)	0.0480 (5)
O1	1.1505 (2)	0.28158 (17)	−0.12653 (14)	0.0651 (5)
S1	1.06955 (9)	0.45367 (7)	0.25092 (6)	0.0613 (2)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0428 (14)	0.0719 (18)	0.0443 (13)	−0.0167 (13)	−0.0152 (11)	−0.0130 (13)
C2	0.0580 (18)	0.0735 (19)	0.0658 (18)	−0.0100 (15)	−0.0263 (15)	−0.0174 (15)
C3	0.0500 (18)	0.095 (2)	0.088 (2)	−0.0002 (16)	−0.0258 (17)	−0.043 (2)
C4	0.0440 (17)	0.127 (3)	0.0581 (18)	−0.0211 (19)	−0.0025 (13)	−0.0381 (19)
C5	0.0497 (16)	0.102 (2)	0.0489 (15)	−0.0256 (16)	−0.0123 (12)	−0.0129 (15)
C6	0.0387 (14)	0.0765 (18)	0.0458 (14)	−0.0172 (13)	−0.0144 (11)	−0.0118 (13)
C7	0.0502 (16)	0.0762 (19)	0.0630 (17)	−0.0127 (14)	−0.0235 (13)	−0.0044 (14)
C8	0.0544 (18)	0.075 (2)	0.086 (2)	−0.0077 (15)	−0.0158 (15)	−0.0109 (16)
C9	0.088 (2)	0.0613 (19)	0.084 (2)	−0.0076 (17)	−0.0285 (18)	−0.0092 (16)
C10	0.090 (2)	0.063 (2)	0.104 (3)	−0.0093 (18)	−0.038 (2)	−0.0161 (18)
C11	0.069 (2)	0.078 (2)	0.126 (3)	−0.0152 (17)	−0.044 (2)	−0.019 (2)
C12	0.0523 (18)	0.080 (2)	0.096 (2)	−0.0149 (15)	−0.0165 (16)	−0.0183 (17)
C13	0.120 (3)	0.099 (3)	0.097 (3)	−0.015 (2)	−0.003 (2)	−0.023 (2)
C14	0.081 (3)	0.149 (4)	0.234 (6)	−0.048 (3)	−0.028 (3)	−0.070 (4)
C15	0.0469 (15)	0.0525 (15)	0.0424 (13)	−0.0118 (12)	−0.0128 (11)	−0.0016 (11)
C16	0.0533 (16)	0.0477 (14)	0.0413 (13)	−0.0097 (11)	−0.0065 (11)	−0.0045 (11)

C17	0.0575 (16)	0.0600 (16)	0.0461 (14)	−0.0163 (13)	−0.0179 (12)	−0.0061 (12)
C18	0.0462 (15)	0.0567 (15)	0.0498 (14)	−0.0110 (12)	−0.0159 (12)	−0.0012 (12)
C19	0.0481 (17)	0.087 (2)	0.0704 (19)	−0.0035 (15)	0.0056 (14)	−0.0227 (16)
Cl1	0.1161 (8)	0.1555 (10)	0.0669 (5)	−0.0582 (7)	−0.0048 (5)	0.0201 (6)
Cl2	0.0450 (4)	0.1197 (7)	0.0740 (5)	−0.0198 (4)	−0.0189 (3)	−0.0135 (4)
N1	0.0447 (13)	0.0622 (14)	0.0712 (14)	−0.0079 (11)	−0.0197 (11)	−0.0128 (11)
N2	0.0428 (12)	0.0640 (13)	0.0436 (11)	−0.0108 (10)	−0.0120 (9)	−0.0063 (9)
N3	0.0459 (12)	0.0536 (12)	0.0436 (11)	−0.0111 (9)	−0.0076 (9)	−0.0041 (9)
O1	0.0607 (12)	0.0770 (13)	0.0517 (11)	−0.0109 (10)	−0.0021 (9)	−0.0198 (9)
S1	0.0499 (4)	0.0947 (6)	0.0468 (4)	−0.0301 (4)	−0.0108 (3)	−0.0118 (3)

Geometric parameters (Å, º)

C1—C2	1.374 (4)	C11—C14	1.527 (5)
C1—C6	1.400 (4)	C11—H11	0.9800
C1—S1	1.778 (3)	C12—N1	1.451 (3)
C2—C3	1.378 (4)	C12—H12A	0.9700
C2—H2	0.9300	C12—H12B	0.9700
C3—C4	1.367 (5)	C13—H13A	0.9600
C3—H3	0.9300	C13—H13B	0.9600
C4—C5	1.381 (4)	C13—H13C	0.9600
C4—H4	0.9300	C14—H14A	0.9600
C5—C6	1.392 (4)	C14—H14B	0.9600
C5—Cl1	1.744 (3)	C14—H14C	0.9600
C6—C7	1.504 (4)	C15—N2	1.327 (3)
C7—N1	1.462 (3)	C15—N3	1.336 (3)
C7—H7A	0.9700	C15—S1	1.759 (2)
C7—H7B	0.9700	C16—N3	1.327 (3)
C8—N1	1.450 (3)	C16—O1	1.334 (3)
C8—C9	1.531 (4)	C16—C17	1.390 (3)
C8—H8A	0.9700	C17—C18	1.356 (3)
C8—H8B	0.9700	C17—H17	0.9300
C9—C13	1.501 (5)	C18—N2	1.331 (3)
C9—C10	1.533 (4)	C18—Cl2	1.735 (3)
C9—H9	0.9800	C19—O1	1.423 (3)
C10—C11	1.517 (4)	C19—H19A	0.9600
C10—H10A	0.9700	C19—H19B	0.9600
C10—H10B	0.9700	C19—H19C	0.9600
C11—C12	1.518 (4)		
C2—C1—C6	122.1 (2)	C10—C11—H11	107.8
C2—C1—S1	118.1 (2)	C14—C11—H11	107.8
C6—C1—S1	119.5 (2)	N1—C12—C11	112.1 (3)
C1—C2—C3	120.0 (3)	N1—C12—H12A	109.2
C1—C2—H2	120.0	C11—C12—H12A	109.2
C3—C2—H2	120.0	N1—C12—H12B	109.2
C4—C3—C2	120.1 (3)	C11—C12—H12B	109.2
C4—C3—H3	119.9	H12A—C12—H12B	107.9

C2—C3—H3	119.9	C9—C13—H13A	109.5
C3—C4—C5	119.2 (3)	C9—C13—H13B	109.5
C3—C4—H4	120.4	H13A—C13—H13B	109.5
C5—C4—H4	120.4	C9—C13—H13C	109.5
C4—C5—C6	122.9 (3)	H13A—C13—H13C	109.5
C4—C5—Cl1	116.9 (2)	H13B—C13—H13C	109.5
C6—C5—Cl1	120.1 (2)	C11—C14—H14A	109.5
C5—C6—C1	115.7 (3)	C11—C14—H14B	109.5
C5—C6—C7	123.5 (3)	H14A—C14—H14B	109.5
C1—C6—C7	120.8 (2)	C11—C14—H14C	109.5
N1—C7—C6	112.1 (2)	H14A—C14—H14C	109.5
N1—C7—H7A	109.2	H14B—C14—H14C	109.5
C6—C7—H7A	109.2	N2—C15—N3	127.9 (2)
N1—C7—H7B	109.2	N2—C15—S1	120.94 (18)
C6—C7—H7B	109.2	N3—C15—S1	111.10 (18)
H7A—C7—H7B	107.9	N3—C16—O1	119.2 (2)
N1—C8—C9	111.9 (2)	N3—C16—C17	122.8 (2)
N1—C8—H8A	109.2	O1—C16—C17	118.0 (2)
C9—C8—H8A	109.2	C18—C17—C16	115.4 (2)
N1—C8—H8B	109.2	C18—C17—H17	122.3
C9—C8—H8B	109.2	C16—C17—H17	122.3
H8A—C8—H8B	107.9	N2—C18—C17	124.9 (2)
C13—C9—C8	111.4 (3)	N2—C18—Cl2	115.60 (19)
C13—C9—C10	112.8 (3)	C17—C18—Cl2	119.48 (19)
C8—C9—C10	107.9 (3)	O1—C19—H19A	109.5
C13—C9—H9	108.2	O1—C19—H19B	109.5
C8—C9—H9	108.2	H19A—C19—H19B	109.5
C10—C9—H9	108.2	O1—C19—H19C	109.5
C11—C10—C9	111.0 (3)	H19A—C19—H19C	109.5
C11—C10—H10A	109.4	H19B—C19—H19C	109.5
C9—C10—H10A	109.4	C8—N1—C12	111.5 (2)
C11—C10—H10B	109.4	C8—N1—C7	111.9 (2)
C9—C10—H10B	109.4	C12—N1—C7	111.8 (2)
H10A—C10—H10B	108.0	C15—N2—C18	113.9 (2)
C12—C11—C10	110.0 (3)	C16—N3—C15	115.1 (2)
C12—C11—C14	110.9 (3)	C16—O1—C19	118.0 (2)
C10—C11—C14	112.3 (3)	C15—S1—C1	103.40 (12)
C12—C11—H11	107.8		

C6—C1—C2—C3	−1.7 (4)	N3—C16—C17—C18	−1.0 (4)
S1—C1—C2—C3	−175.51 (19)	O1—C16—C17—C18	178.0 (2)
C1—C2—C3—C4	1.2 (4)	C16—C17—C18—N2	1.2 (4)
C2—C3—C4—C5	0.0 (4)	C16—C17—C18—Cl2	−178.17 (19)
C3—C4—C5—C6	−0.7 (4)	C9—C8—N1—C12	59.6 (3)
C3—C4—C5—Cl1	178.5 (2)	C9—C8—N1—C7	−174.4 (2)
C4—C5—C6—C1	0.1 (4)	C11—C12—N1—C8	−57.7 (3)
Cl1—C5—C6—C1	−178.95 (17)	C11—C12—N1—C7	176.2 (2)
C4—C5—C6—C7	178.6 (2)	C6—C7—N1—C8	157.2 (2)

Cl1—C5—C6—C7	−0.5 (3)	C6—C7—N1—C12	−76.9 (3)
C2—C1—C6—C5	1.0 (3)	N3—C15—N2—C18	−0.1 (4)
S1—C1—C6—C5	174.74 (17)	S1—C15—N2—C18	178.03 (18)
C2—C1—C6—C7	−177.5 (2)	C17—C18—N2—C15	−0.7 (4)
S1—C1—C6—C7	−3.8 (3)	Cl2—C18—N2—C15	178.70 (18)
C5—C6—C7—N1	109.8 (3)	O1—C16—N3—C15	−178.6 (2)
C1—C6—C7—N1	−71.8 (3)	C17—C16—N3—C15	0.4 (3)
N1—C8—C9—C13	177.8 (3)	N2—C15—N3—C16	0.2 (4)
N1—C8—C9—C10	−57.8 (3)	S1—C15—N3—C16	−178.04 (17)
C13—C9—C10—C11	179.1 (3)	N3—C16—O1—C19	0.5 (3)
C8—C9—C10—C11	55.6 (4)	C17—C16—O1—C19	−178.5 (2)
C9—C10—C11—C12	−54.9 (4)	N2—C15—S1—C1	15.0 (2)
C9—C10—C11—C14	−178.9 (3)	N3—C15—S1—C1	−166.64 (18)
C10—C11—C12—N1	55.2 (4)	C2—C1—S1—C15	−95.9 (2)
C14—C11—C12—N1	180.0 (3)	C6—C1—S1—C15	90.2 (2)