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Hydrochlorothiazide dimethyl sulfoxide solvate

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Key indicators

Single-crystal X-ray study
$T = 123$ K
Mean σ(C–C) = 0.003 Å
R factor = 0.040
wR factor = 0.110
Data-to-parameter ratio = 15.7

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Hydrochlorothiazide forms a 1:1 solvate with dimethyl sulfoxide, $C_7H_8ClN_3O_4S_2 \cdot C_2H_6OS$. The crystal structure contains a hydrogen-bonding network comprising three N—H$\cdots$O contacts.
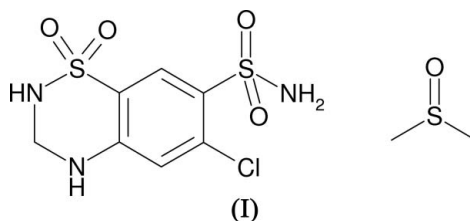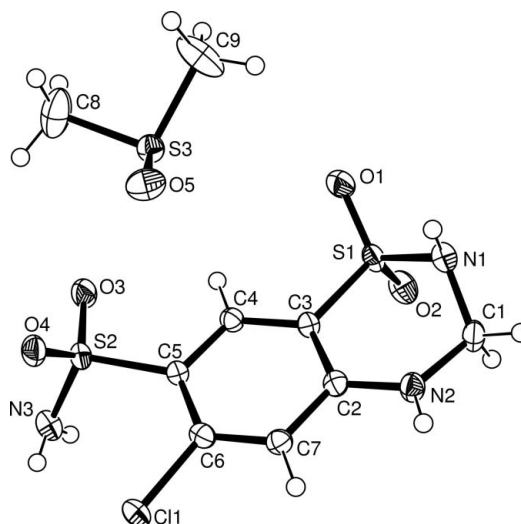
Comment

Hydrochlorothiazide (HCT) is a thiazide diuretic which is known to crystallize in at least two non-solvated forms; form I (Dupont & Dideberg, 1972) and form II (Florence *et al.*, 2005). The dimethyl sulfoxide (DMSO) solvate, (I), was produced during an automated parallel crystallization polymorph search on HCT. The sample was identified as a new form using multi-sample X-ray powder diffraction analysis of all recrystallized samples (Florence *et al.*, 2003). Subsequent manual recrystallization by slow evaporation of a saturated DMSO solution at 278 K yielded samples of (I) suitable for single-crystal X-ray analysis (Fig. 1).

In (I), the six-membered ring N1—S1—C3—C2—N2—C1 in HCT displays a puckered conformation, atom N1 having a

Figure 1
Plot of the asymmetric-unit contents with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

Experimental

A single-crystal sample of the title compound was recrystallized by slow evaporation of a dimethyl sulfoxide solution at 278 K.

Crystal data

$C_7H_8ClN_3O_4S_2 \cdot C_2H_6OS$	$V = 749.23\ (7)$ Å^3
$M_r = 375.86$	$Z = 2$
Triclinic, $P\bar{1}$	$D_x = 1.666$ Mg m^{-3}
$a = 7.5068\ (4)$ Å	Mo $K\alpha$ radiation
$b = 9.8272\ (5)$ Å	$\mu = 0.70$ mm^{-1}
$c = 10.7311\ (6)$ Å	$T = 123\ (2)$ K
$\alpha = 85.639\ (3)°$	Cut fragment, colourless
$\beta = 73.896\ (3)°$	$0.28 \times 0.28 \times 0.10$ mm
$\gamma = 80.246\ (3)°$	

Data collection

Nonius KappaCCD diffractometer	3267 independent reflections
φ and ω scans	2669 reflections with $I > 2\sigma(I)$
Absorption correction: none	$R_{int} = 0.055$
10594 measured reflections	$\theta_{max} = 27.2°$

Refinement

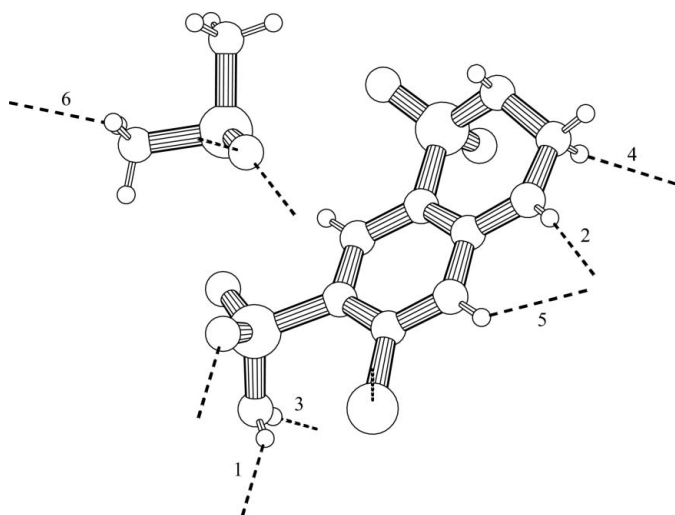|	
Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0592P)^2$
$R[F^2 > 2\sigma(F^2)] = 0.040$	$+ 0.534P]$
$wR(F^2) = 0.110$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.03$	$(\Delta/\sigma)_{max} = 0.001$
3267 reflections	$\Delta\rho_{max} = 0.47$ e Å^{-3}
208 parameters	$\Delta\rho_{min} = -0.48$ e Å^{-3}
H atoms treated by a mixture of independent and constrained refinement	

Figure 2
Intermolecular interactions in (I). Dashed lines indicate hydrogen bonds and unique contacts are labelled as follows: 1 = N3···O4, 3.004 (3)Å, O4 in the molecule at $(-x, 2-y, 2-z)$; 2 = N2···O5, 2.806 (3)Å, O5 in the molecule at $(1-x, 1-y, 2-z)$; 3 = N3···O5, 2.776 (3)Å; O5 in the molecule at $(-1+x, y, z)$; 4 = C1···O4, 3.347 (3)Å, O4 in the molecule at $(x, -1+y, z)$; 5 = C7···O5, 3.289 (3)Å, O5 in the molecule at $(1-x, 1-y, 2-z)$; 6 = C8···O3, 3.228 (4)Å, O3 in the molecule at $(1-x, 2-y, 1-z)$. Contacts calculated and illustrated using *PLATON* (Spek, 2003; program version 150306)
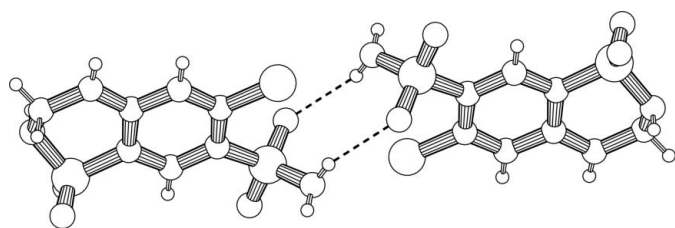

Figure 3
The $R_2^2(8)$ hydrogen-bonded motif in the crystal structure of (I).

deviation of 0.622 (2) Å from the least-squares plane through atoms C2–C7. The sulfonamide side chain adopts an N3—S2—C5—C6 torsion angle of −62.0 (2)°, such that O3 eclipses H4, and atoms O4 and N3 are staggered with respect to Cl1.

The crystal structure is stabilized by three N—H···O hydrogen bonds interconnecting (*a*) HCT molecules (Fig. 2, contact 1) and forming an $R_2^2(8)$ (Etter, 1990) centrosymmetric dimer (Fig. 3), and (*b*) HCT and two DMSO molecules (Fig. 2, contacts 2 and 3).

The aromatic ring formed by atoms C2–C7 is involved in two offset face-to-face π–π interactions between nearest-neighbour HCT molecules with centroid–centroid distances/perpendicular distances between the corresponding planes equal to 4.354 (2)/3.58 Å (centroid at $-x, 1-y, 2-z$) and 4.466 (2)/3.57 Å (centroid at $1-x, 1-y, 2-z$). The HCT aromatic rings form a stacked arrangement in the direction of the *a* axis. The structure also contains three C—H···O contacts between HCT and HCT (Fig.2, contact 4) and between HCT and DMSO (contacts 5 and 6).

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

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N3—H4$N\cdots$O4^i	0.80 (3)	2.27 (3)	3.004 (3)	153 (3)
N2—H2$N\cdots$O5^{ii}	0.81 (3)	2.02 (3)	2.806 (3)	164 (3)
N3—H3$N\cdots$O5^{iii}	0.83 (3)	1.95 (3)	2.776 (3)	172 (3)
C1—H1$A\cdots$O4^{iv}	0.99	2.46	3.347 (3)	149
C7—H7$\cdots$O5^{ii}	0.95	2.56	3.289 (3)	134
C8—H8$B\cdots$O3^v	0.98	2.53	3.228 (4)	128

Symmetry codes: (i) $-x, -y+2, -z+2$; (ii) $-x+1, -y+1, -z+2$; (iii) $x-1, y, z$; (iv) $x, y-1, z$; (v) $-x+1, -y+2, -z+1$.

H atoms bonded to N atoms were found in difference maps and refined isotropically, but all other H atoms were constrained to idealized geometry using a riding model; $U_{iso}(H) = 1.2U_{eq}(C)$ and C—H = 0.95 (CH group) or 0.99 Å (CH$_2$ groups).

Data collection: *COLLECT* (Hooft, 1988) and *DENZO* (Otwinowski & Minor, 1997); cell refinement: *DENZO* and *COLLECT*; data reduction: *DENZO*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

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Control and Prediction of the Organic Solid State (URL: www.cposs.org.uk).

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supporting information

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Crystal data

$C_7H_8ClN_3O_4S_2 \cdot C_2H_6OS$	$Z = 2$
$M_r = 375.86$	$F(000) = 388$
Triclinic, $P\bar{1}$	$D_x = 1.666$ Mg m^{-3}
Hall symbol: -P 1	Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
$a = 7.5068$ (4) Å	Cell parameters from 2971 reflections
$b = 9.8272$ (5) Å	$\theta = 2.9–27.1°$
$c = 10.7311$ (6) Å	$\mu = 0.70$ mm^{-1}
$\alpha = 85.639$ (3)°	$T = 123$ K
$\beta = 73.896$ (3)°	Cut fragment, colourless
$\gamma = 80.246$ (3)°	$0.28 \times 0.28 \times 0.10$ mm
$V = 749.23$ (7) Å^3	

Data collection

Nonius KappaCCD diffractometer	2669 reflections with $I > 2\sigma(I)$
	$R_{int} = 0.055$
Radiation source: fine-focus sealed tube	$\theta_{max} = 27.2°$, $\theta_{min} = 2.9°$
Graphite monochromator	$h = -9 \rightarrow 9$
φ and ω scans	$k = -11 \rightarrow 12$
10594 measured reflections	$l = -13 \rightarrow 13$
3267 independent reflections	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	
$R[F^2 > 2\sigma(F^2)] = 0.040$	Hydrogen site location: inferred from neighbouring sites
$wR(F^2) = 0.110$	
$S = 1.04$	H atoms treated by a mixture of independent and constrained refinement
3267 reflections	
208 parameters	$w = 1/[\sigma^2(F_o^2) + (0.0592P)^2 + 0.534P]$ where $P = (F_o^2 + 2F_c^2)/3$
0 restraints	
Primary atom site location: structure-invariant direct methods	$(\Delta/\sigma)_{max} = 0.001$
	$\Delta\rho_{max} = 0.47$ e Å^{-3}
	$\Delta\rho_{min} = -0.48$ e Å^{-3}

Special details

Experimental. Although no formal absorption correction was applied, the standard Kappa CCD methodology involves collecting a large number of redundant reflections and processing *via SCALEPACK*. This effectively introduces a multi-scan type correction suitable for weakly absorbing molecules.

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}
Cl1	0.02575 (8)	0.73342 (6)	1.11711 (6)	0.02319 (16)
S1	0.51163 (9)	0.34312 (6)	0.67153 (6)	0.02145 (16)
S2	0.15774 (9)	0.85850 (6)	0.81869 (6)	0.02141 (16)
S3	0.69526 (9)	0.76246 (6)	0.63385 (6)	0.02243 (17)
O1	0.6400 (3)	0.41391 (19)	0.57579 (18)	0.0319 (4)
O2	0.3873 (3)	0.27152 (19)	0.63320 (18)	0.0300 (4)
O3	0.2162 (3)	0.86589 (18)	0.67974 (17)	0.0295 (4)
O4	0.2406 (3)	0.93652 (17)	0.89048 (18)	0.0267 (4)
O5	0.7163 (3)	0.7637 (2)	0.77073 (17)	0.0322 (4)
N1	0.6358 (3)	0.2308 (2)	0.7473 (2)	0.0245 (5)
N2	0.4255 (3)	0.2776 (2)	0.9606 (2)	0.0225 (5)
N3	−0.0632 (3)	0.9093 (2)	0.8633 (2)	0.0248 (5)
C1	0.5231 (4)	0.1724 (2)	0.8661 (2)	0.0236 (5)
H1A	0.4299	0.1247	0.8446	0.028*
H1B	0.6056	0.1030	0.9050	0.028*
C2	0.3507 (3)	0.4058 (2)	0.9263 (2)	0.0182 (5)
C3	0.3807 (3)	0.4550 (2)	0.7960 (2)	0.0181 (5)
C4	0.3152 (3)	0.5911 (2)	0.7652 (2)	0.0190 (5)
H4	0.3415	0.6224	0.6770	0.023*
C5	0.2114 (3)	0.6819 (2)	0.8622 (2)	0.0179 (5)
C6	0.1710 (3)	0.6301 (2)	0.9914 (2)	0.0192 (5)
C7	0.2385 (3)	0.4977 (2)	1.0242 (2)	0.0193 (5)
H7	0.2103	0.4671	1.1127	0.023*
C8	0.6947 (6)	0.9341 (3)	0.5754 (3)	0.0489 (9)
H8A	0.5787	0.9911	0.6223	0.073*
H8B	0.7023	0.9384	0.4826	0.073*
H8C	0.8029	0.9687	0.5888	0.073*
C9	0.9207 (5)	0.6894 (4)	0.5400 (3)	0.0517 (10)
H9A	1.0142	0.7440	0.5485	0.078*
H9B	0.9206	0.6894	0.4487	0.078*
H9C	0.9518	0.5942	0.5710	0.078*
H1N	0.729 (5)	0.264 (3)	0.758 (3)	0.036 (9)*
H2N	0.407 (4)	0.261 (3)	1.038 (3)	0.023 (7)*
H3N	−0.131 (4)	0.872 (3)	0.831 (3)	0.023 (8)*
H4N	−0.107 (4)	0.923 (3)	0.939 (3)	0.026 (8)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0229 (3)	0.0246 (3)	0.0208 (3)	0.0002 (2)	−0.0042 (2)	−0.0075 (2)
S1	0.0253 (3)	0.0181 (3)	0.0191 (3)	0.0034 (2)	−0.0060 (2)	−0.0041 (2)
S2	0.0236 (3)	0.0151 (3)	0.0238 (3)	0.0000 (2)	−0.0048 (2)	−0.0020 (2)
S3	0.0241 (3)	0.0226 (3)	0.0207 (3)	−0.0030 (2)	−0.0065 (2)	−0.0015 (2)
O1	0.0332 (11)	0.0284 (10)	0.0257 (10)	0.0020 (8)	0.0022 (8)	−0.0011 (8)
O2	0.0321 (10)	0.0292 (10)	0.0316 (10)	−0.0003 (8)	−0.0132 (8)	−0.0109 (8)
O3	0.0374 (11)	0.0212 (9)	0.0238 (10)	0.0024 (8)	−0.0035 (8)	0.0026 (7)
O4	0.0271 (10)	0.0185 (8)	0.0346 (10)	−0.0042 (7)	−0.0066 (8)	−0.0057 (7)
O5	0.0353 (11)	0.0433 (11)	0.0196 (9)	−0.0103 (9)	−0.0088 (8)	0.0038 (8)
N1	0.0244 (11)	0.0207 (10)	0.0276 (12)	0.0008 (9)	−0.0076 (9)	−0.0026 (9)
N2	0.0292 (12)	0.0183 (10)	0.0194 (11)	−0.0009 (8)	−0.0075 (9)	−0.0001 (8)
N3	0.0245 (12)	0.0245 (11)	0.0262 (13)	0.0015 (9)	−0.0100 (10)	−0.0064 (9)
C1	0.0305 (14)	0.0148 (11)	0.0252 (13)	−0.0007 (10)	−0.0089 (11)	0.0001 (9)
C2	0.0172 (11)	0.0178 (11)	0.0214 (12)	−0.0040 (9)	−0.0068 (9)	−0.0022 (9)
C3	0.0195 (11)	0.0159 (11)	0.0189 (12)	−0.0012 (9)	−0.0058 (9)	−0.0024 (9)
C4	0.0196 (12)	0.0189 (11)	0.0177 (11)	−0.0017 (9)	−0.0045 (9)	−0.0012 (9)
C5	0.0184 (11)	0.0156 (11)	0.0189 (11)	−0.0015 (9)	−0.0042 (9)	−0.0019 (9)
C6	0.0168 (11)	0.0211 (11)	0.0209 (12)	−0.0047 (9)	−0.0043 (9)	−0.0064 (9)
C7	0.0208 (12)	0.0203 (11)	0.0173 (11)	−0.0047 (9)	−0.0048 (9)	−0.0014 (9)
C8	0.086 (3)	0.0267 (15)	0.0400 (18)	−0.0107 (16)	−0.0281 (18)	0.0061 (13)
C9	0.0374 (18)	0.072 (2)	0.0395 (19)	0.0171 (17)	−0.0091 (15)	−0.0262 (17)

Geometric parameters (Å, º)

Cl1—C6	1.749 (2)	N3—H4N	0.80 (3)
S1—O2	1.4195 (19)	C1—H1A	0.9900
S1—O1	1.427 (2)	C1—H1B	0.9900
S1—N1	1.638 (2)	C2—C3	1.413 (3)
S1—C3	1.758 (2)	C2—C7	1.422 (3)
S2—O3	1.4327 (19)	C3—C4	1.393 (3)
S2—O4	1.4443 (19)	C4—C5	1.394 (3)
S2—N3	1.595 (2)	C4—H4	0.9500
S2—C5	1.771 (2)	C5—C6	1.409 (3)
S3—O5	1.5213 (18)	C6—C7	1.371 (3)
S3—C8	1.754 (3)	C7—H7	0.9500
S3—C9	1.774 (3)	C8—H8A	0.9800
N1—C1	1.458 (3)	C8—H8B	0.9800
N1—H1N	0.85 (3)	C8—H8C	0.9800
N2—C2	1.358 (3)	C9—H9A	0.9800
N2—C1	1.457 (3)	C9—H9B	0.9800
N2—H2N	0.81 (3)	C9—H9C	0.9800
N3—H3N	0.83 (3)		
O2—S1—O1	119.64 (12)	N2—C2—C3	123.0 (2)
O2—S1—N1	107.28 (12)	N2—C2—C7	119.7 (2)

O1—S1—N1	107.26 (12)	C3—C2—C7	117.3 (2)
O2—S1—C3	108.77 (11)	C4—C3—C2	121.4 (2)
O1—S1—C3	110.26 (11)	C4—C3—S1	119.71 (18)
N1—S1—C3	102.16 (11)	C2—C3—S1	118.87 (17)
O3—S2—O4	118.94 (12)	C3—C4—C5	120.8 (2)
O3—S2—N3	107.80 (13)	C3—C4—H4	119.6
O4—S2—N3	106.60 (12)	C5—C4—H4	119.6
O3—S2—C5	105.53 (11)	C4—C5—C6	117.7 (2)
O4—S2—C5	107.25 (11)	C4—C5—S2	118.49 (18)
N3—S2—C5	110.66 (12)	C6—C5—S2	123.52 (17)
O5—S3—C8	105.16 (14)	C7—C6—C5	122.4 (2)
O5—S3—C9	104.42 (14)	C7—C6—Cl1	117.17 (19)
C8—S3—C9	99.1 (2)	C5—C6—Cl1	120.43 (18)
C1—N1—S1	113.31 (18)	C6—C7—C2	120.2 (2)
C1—N1—H1N	113 (2)	C6—C7—H7	119.9
S1—N1—H1N	111 (2)	C2—C7—H7	119.9
C2—N2—C1	122.8 (2)	S3—C8—H8A	109.5
C2—N2—H2N	116 (2)	S3—C8—H8B	109.5
C1—N2—H2N	121 (2)	H8A—C8—H8B	109.5
S2—N3—H3N	118 (2)	S3—C8—H8C	109.5
S2—N3—H4N	116 (2)	H8A—C8—H8C	109.5
H3N—N3—H4N	113 (3)	H8B—C8—H8C	109.5
N2—C1—N1	112.2 (2)	S3—C9—H9A	109.5
N2—C1—H1A	109.2	S3—C9—H9B	109.5
N1—C1—H1A	109.2	H9A—C9—H9B	109.5
N2—C1—H1B	109.2	S3—C9—H9C	109.5
N1—C1—H1B	109.2	H9A—C9—H9C	109.5
H1A—C1—H1B	107.9	H9B—C9—H9C	109.5
O2—S1—N1—C1	−63.1 (2)	S1—C3—C4—C5	−179.87 (18)
O1—S1—N1—C1	167.15 (17)	C3—C4—C5—C6	−1.8 (4)
C3—S1—N1—C1	51.2 (2)	C3—C4—C5—S2	172.14 (19)
C2—N2—C1—N1	37.5 (3)	O3—S2—C5—C4	8.1 (2)
S1—N1—C1—N2	−61.1 (3)	O4—S2—C5—C4	−119.65 (19)
C1—N2—C2—C3	−8.2 (4)	N3—S2—C5—C4	124.5 (2)
C1—N2—C2—C7	172.6 (2)	O3—S2—C5—C6	−178.3 (2)
N2—C2—C3—C4	−174.4 (2)	O4—S2—C5—C6	53.9 (2)
C7—C2—C3—C4	4.7 (3)	N3—S2—C5—C6	−62.0 (2)
N2—C2—C3—S1	3.1 (3)	C4—C5—C6—C7	3.7 (4)
C7—C2—C3—S1	−177.79 (17)	S2—C5—C6—C7	−169.91 (19)
O2—S1—C3—C4	−92.3 (2)	C4—C5—C6—Cl1	−174.82 (18)
O1—S1—C3—C4	40.7 (2)	S2—C5—C6—Cl1	11.6 (3)
N1—S1—C3—C4	154.5 (2)	C5—C6—C7—C2	−1.3 (4)
O2—S1—C3—C2	90.2 (2)	Cl1—C6—C7—C2	177.25 (18)
O1—S1—C3—C2	−136.8 (2)	N2—C2—C7—C6	176.3 (2)
N1—S1—C3—C2	−23.0 (2)	C3—C2—C7—C6	−2.9 (3)
C2—C3—C4—C5	−2.4 (4)		

Hydrogen-bond geometry (Å, º)

D—H···A	D—H	H···A	D···A	D—H···A
N3—H4N···O4^i	0.80 (3)	2.27 (3)	3.004 (3)	153 (3)
N2—H2N···O5^{ii}	0.81 (3)	2.02 (3)	2.806 (3)	164 (3)
N3—H3N···O5^{iii}	0.83 (3)	1.95 (3)	2.776 (3)	172 (3)
C1—H1A···O4^{iv}	0.99	2.46	3.347 (3)	149
C7—H7···O5^{ii}	0.95	2.56	3.289 (3)	134
C8—H8B···O3^v	0.98	2.53	3.228 (4)	128

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