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(6*R*,7*R*)-3-Hydroxymethyl-7-(2-phenylacetamido)-3-cephem-4-carboxylic acid lactone

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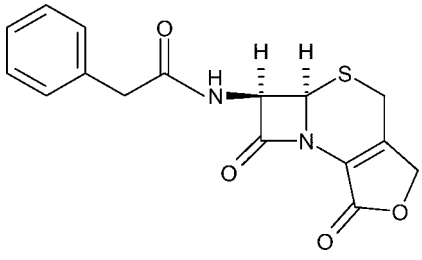
Key indicators: single-crystal X-ray study; T = 113 K; mean σ(C–C) = 0.002 Å; R factor = 0.027; wR factor = 0.065; data-to-parameter ratio = 19.9.

In the title compound {systematic name: *N*-[(4*R*,5*R*)-3,11-dioxo-10-oxa-6-thia-2-azatricyclo[6.3.0.0^{2,5}]undec-1(8)-en-4-yl]-2-phenylacetamide}, $C_{16}H_{14}N_2O_4S$, the four- and five-membered rings adopt planar conformations (with r.m.s. deviations of 0.0349 and 0.0108 Å respectively) while the six-membered ring adopts a half-chair, or envelope-like, conformation with the S atom in the flap position. In the crystal, molecules are linked by N—H···O hydrogen bonds.

Related literature

For standard bond lengths, see: Allen *et al.* (1987) and for ring puckering parameters, see: Cremer & Pople (1975). The title compound is an important synthetic intermediate for cephalosporins. For its synthesis, see: Yu *et al.* (2009).



Experimental

Crystal data

$C_{16}H_{14}N_2O_4S$
M_r = 330.35
Orthorhombic, $P2_12_12_1$
a = 9.1300 (13) Å
b = 9.7060 (14) Å
c = 16.701 (2) Å
V = 1480.0 (3) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.24 mm^{-1}
T = 113 K
0.26 × 0.24 × 0.22 mm

Data collection

Rigaku Saturn724 CCD diffractometer
Absorption correction: multi-scan (*CrystalClear-SM Expert*; Rigaku, 2009)
T_{min} = 0.940, T_{max} = 0.949
21123 measured reflections
4249 independent reflections
3823 reflections with $I > 2\sigma(I)$
R_{int} = 0.043

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.027
$wR(F^2)$ = 0.065
S = 1.02
4249 reflections
213 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.29 e Å^{-3}
Absolute structure: Flack (1983), 1803 Friedel pairs
Flack parameter: −0.02 (4)

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

D—H···A	D—H	H···A	D···A	D—H···A
N2—H1···O4^{i}	0.778 (15)	2.276 (15)	3.0506 (14)	173.5 (14)

Symmetry code: (i) $-x+1, y+\frac{1}{2}, -z+\frac{1}{2}$.

Data collection: *CrystalClear-SM Expert* (Rigaku, 2009); cell refinement: *CrystalClear-SM Expert*; data reduction: *CrystalClear-SM Expert*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *CrystalStructure* (Rigaku, 2009); software used to prepare material for publication: *CrystalStructure*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: ZJ2026).

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supporting information

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(6*R*,7*R*)-3-Hydroxymethyl-7-(2-phenylacetamido)-3-cephem-4-carboxylic acid lactone

Xiao-Liang Zhou, Hao Wang, Yan Wang and Pei-Ji Shi

S1. Comment

The title compound is a lactone derivative of cephalosporin, which was fond originally as an impurity in the synthetic process, but now has become an useful intermediate, because the lactone ring enhances the stability of the molecule and adds new sites for structure reformation.There is one molecule in the asymmetric unit of the title compound. The absolute configuration has been determined by refinement of the Flack parameter (Flack, 1983) which converged to -0.02 (4). The ring A (N1—C1—C2—C3) and ring C (C4—C5—O3—C6—C7) adopt planer conformation with the r.m.s. deviation were 0.0349 and 0.0108 respectively, the ring B (S1—C3—N1—C4—C7—C8) displays half chair conformation with atom S1 in the flap position [the displacement from the C-atom mean plane is 0.3949 (6) Å], with the r.m.s. deviation was 0.2468 and with puckering parameters (Cremer and Pople, 1975) of Q (total puckering amplitude) = 0.6064 (10) Å, θ (azimuthal angle) = 127.68 (10)°, φ (phase angle) = 188.04 (15)°. The dihedral angle between ring A and ring B was 36.45 (7) °, and the dihedral angle between ring B and ring C was 10.34 (7) °. The spatial orientation of the phenyl ring can be described by the dihedral angle between the phenyl ring and the ring A [42.06 (6)]. The torsion angle of C4—N1—C3—S1 was -39.63 (13)°, and the torsion angle of N2—C2—C3—N1 was 120.16 (10)°. In the crystal, molecules are linked by N—H···O [N2—H1···O4=173.5 (14)°, N2···O4=3.0506 (14) Å] hydrogen bonds.

S2. Experimental

The title compound was synthesized according to the literature method (Yu *et al.* (2009). Colorless Prism-shaped single crystals suitable for X-ray structure determination were recrystallized from acetone by the slow evaporation of the solvent at room temperature after several days.

S3. Refinement

H atoms were positioned geometrically (with C—H = 0.95 for aromatic and 0.99–1.00 for others) and refined in a riding model (except for H1, whose position was freely refined). All H atoms were refined with U_{iso}(H) values equal to 1.2 U_{eq} of the C atom. As the molecule contains S atom (heavier than Si), anomalous scattering can be used to determine the absolute configuration, and 1803 Friedel pairs were used to determine the absolute configuration.

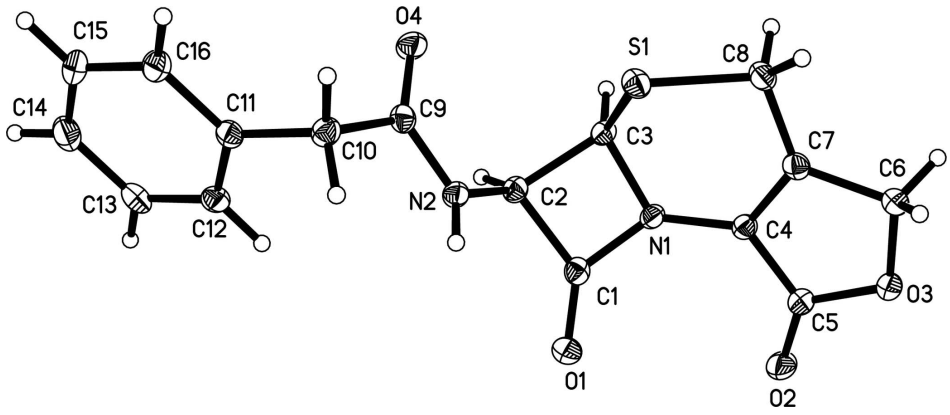

Figure 1

Molecular structure of the title compound with the atomic numbering scheme and displacement ellipsoids drawn at the 50% probability level.

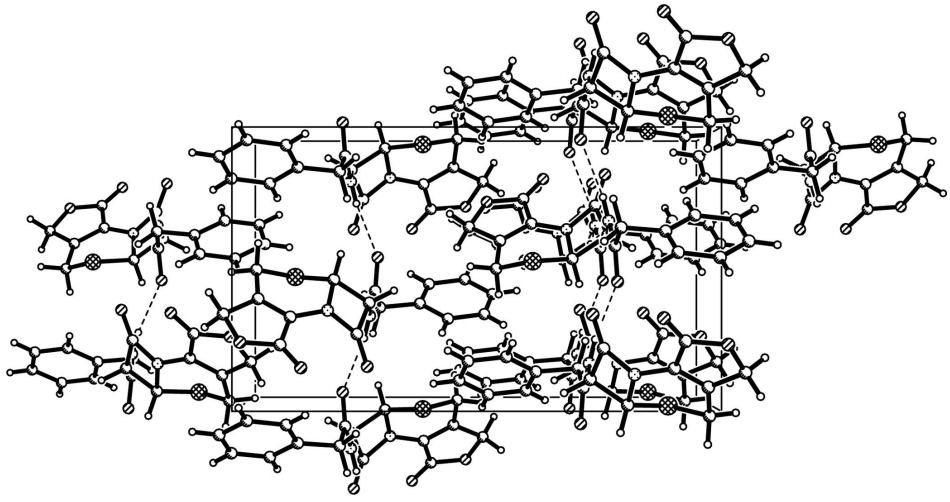

Figure 2

The crystal packing of the title compound viewed along the *a* axis, hydrogen bonds are shown as dashed lines.

***N*-[(4*R*,5*R*)-3,11-Dioxo-10-oxa-6-thia-2- azatricyclo[6.3.0.0^{2,5}]undec-1(8)-en-4-yl]-2-phenylacetamide**

Crystal data

$C_{16}H_{14}N_2O_4S$
M_r = 330.35
Orthorhombic, $P2_12_12_1$
Hall symbol: P 2ac 2ab
a = 9.1300 (13) Å
b = 9.7060 (14) Å
c = 16.701 (2) Å
V = 1480.0 (3) Å^3
Z = 4
F(000) = 688
D_x = 1.483 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71075 Å
Cell parameters from 5950 reflections
θ = 1.2–29.9°
μ = 0.24 mm^{-1}
T = 113 K
Prism, colourless
0.26 × 0.24 × 0.22 mm

Data collection

Rigaku Saturn724 CCD diffractometer
Radiation source: rotating anode
Multilayer monochromator
Detector resolution: 14.222 pixels mm^{-1}
ω scans
Absorption correction: multi-scan (*CrystalClear-SM Expert*; Rigaku, 2009)
T_{min} = 0.940, T_{max} = 0.949

21123 measured reflections
4249 independent reflections
3823 reflections with $I > 2\sigma(I)$
R_{int} = 0.043
θ_{max} = 30.0°, θ_{min} = 2.4°
h = −12→12
k = −13→13
l = −23→22

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.027
$wR(F^2)$ = 0.065
S = 1.02
4249 reflections
213 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
$w = 1/[\sigma^2(F_o^2) + (0.0358P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.29 e Å^{-3}
Extinction correction: *SHELXL97* (Sheldrick, 2008), $Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.0067 (12)
Absolute structure: Flack (1983), 1803 Friedel pairs
Absolute structure parameter: −0.02 (4)

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.

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}
S1	0.67754 (3)	0.52846 (3)	0.117029 (18)	0.01734 (8)
O1	0.88288 (11)	0.84664 (9)	0.27380 (5)	0.0225 (2)
O2	1.16829 (11)	0.84019 (9)	0.14678 (5)	0.0244 (2)
O3	1.13554 (11)	0.75318 (9)	0.02326 (5)	0.0200 (2)
O4	0.49856 (10)	0.45642 (8)	0.28773 (5)	0.0208 (2)
N1	0.91224 (11)	0.64624 (10)	0.19268 (6)	0.0154 (2)
N2	0.58912 (12)	0.67140 (11)	0.27251 (6)	0.0160 (2)
C1	0.85344 (13)	0.73156 (12)	0.25163 (7)	0.0160 (2)
C2	0.73837 (13)	0.62194 (12)	0.27474 (7)	0.0157 (2)
H2	0.7621	0.5770	0.3270	0.019*
C3	0.79901 (12)	0.53771 (12)	0.20224 (7)	0.0145 (2)
H3	0.8404	0.4462	0.2180	0.017*

C4	0.97995 (13)	0.66890 (12)	0.11842 (7)	0.0148 (2)
C5	1.10260 (14)	0.76339 (12)	0.10264 (7)	0.0173 (3)
C6	1.03597 (15)	0.65749 (13)	−0.01579 (7)	0.0184 (3)
H6A	1.0906	0.5813	−0.0415	0.022*
H6B	0.9764	0.7051	−0.0569	0.022*
C7	0.94119 (14)	0.60460 (13)	0.05064 (7)	0.0160 (3)
C8	0.82046 (14)	0.50169 (12)	0.04180 (7)	0.0175 (2)
H8A	0.8610	0.4076	0.0475	0.021*
H8B	0.7772	0.5097	−0.0124	0.021*
C9	0.47668 (14)	0.58147 (13)	0.28174 (7)	0.0163 (2)
C10	0.32515 (14)	0.64414 (12)	0.28916 (7)	0.0176 (2)
H10A	0.2560	0.5957	0.2532	0.021*
H10B	0.3279	0.7425	0.2735	0.021*
C11	0.27483 (13)	0.63045 (12)	0.37592 (8)	0.0159 (2)
C12	0.35751 (14)	0.68729 (12)	0.43847 (8)	0.0182 (3)
H12	0.4433	0.7385	0.4263	0.022*
C13	0.31636 (15)	0.67012 (13)	0.51797 (7)	0.0206 (3)
H13	0.3739	0.7093	0.5595	0.025*
C14	0.19037 (15)	0.59516 (14)	0.53662 (8)	0.0243 (3)
H14	0.1618	0.5824	0.5908	0.029*
C15	0.10737 (15)	0.53953 (14)	0.47505 (8)	0.0257 (3)
H15	0.0213	0.4889	0.4875	0.031*
C16	0.14795 (13)	0.55650 (13)	0.39503 (8)	0.0207 (3)
H16	0.0895	0.5179	0.3536	0.025*
H1	0.5708 (16)	0.7467 (16)	0.2600 (8)	0.021 (4)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.01461 (14)	0.02029 (15)	0.01712 (13)	0.00003 (12)	−0.00149 (12)	−0.00324 (12)
O1	0.0267 (5)	0.0206 (4)	0.0201 (4)	−0.0045 (4)	0.0017 (4)	−0.0043 (4)
O2	0.0271 (5)	0.0249 (5)	0.0213 (4)	−0.0103 (5)	0.0002 (4)	−0.0028 (4)
O3	0.0252 (5)	0.0186 (4)	0.0162 (4)	−0.0050 (4)	0.0036 (4)	−0.0004 (4)
O4	0.0214 (4)	0.0130 (4)	0.0278 (5)	0.0011 (4)	0.0042 (4)	0.0025 (4)
N1	0.0166 (5)	0.0162 (5)	0.0135 (5)	−0.0044 (4)	0.0004 (4)	0.0002 (4)
N2	0.0170 (5)	0.0122 (5)	0.0188 (5)	0.0014 (4)	0.0027 (4)	0.0023 (4)
C1	0.0175 (6)	0.0184 (6)	0.0119 (5)	−0.0009 (5)	−0.0013 (4)	0.0007 (4)
C2	0.0165 (6)	0.0161 (5)	0.0145 (6)	−0.0006 (5)	0.0007 (5)	0.0013 (5)
C3	0.0152 (6)	0.0142 (5)	0.0143 (5)	−0.0020 (5)	−0.0003 (4)	0.0017 (4)
C4	0.0153 (5)	0.0144 (5)	0.0149 (5)	−0.0005 (5)	0.0004 (5)	0.0008 (5)
C5	0.0192 (6)	0.0153 (6)	0.0173 (6)	−0.0006 (5)	0.0015 (5)	0.0010 (5)
C6	0.0228 (6)	0.0166 (6)	0.0158 (6)	−0.0008 (5)	0.0021 (5)	−0.0015 (5)
C7	0.0170 (6)	0.0142 (6)	0.0168 (6)	0.0035 (5)	0.0005 (5)	0.0005 (5)
C8	0.0166 (5)	0.0193 (6)	0.0166 (5)	−0.0005 (5)	0.0009 (5)	−0.0047 (4)
C9	0.0191 (6)	0.0173 (6)	0.0126 (5)	0.0001 (5)	0.0018 (5)	0.0000 (5)
C10	0.0174 (6)	0.0165 (6)	0.0190 (6)	−0.0002 (5)	0.0013 (5)	0.0024 (5)
C11	0.0155 (6)	0.0134 (5)	0.0188 (6)	0.0040 (5)	0.0015 (5)	0.0009 (5)
C12	0.0178 (6)	0.0132 (5)	0.0237 (6)	0.0023 (5)	0.0014 (5)	−0.0005 (5)

C13	0.0231 (6)	0.0189 (6)	0.0198 (6)	0.0059 (6)	−0.0004 (5)	−0.0048 (5)
C14	0.0274 (7)	0.0247 (7)	0.0210 (6)	0.0045 (6)	0.0064 (6)	−0.0013 (5)
C15	0.0203 (6)	0.0286 (7)	0.0282 (7)	−0.0048 (6)	0.0104 (5)	−0.0030 (6)
C16	0.0152 (6)	0.0229 (6)	0.0238 (7)	−0.0007 (5)	0.0018 (5)	−0.0029 (5)

Geometric parameters (Å, º)

S1—C3	1.8065 (12)	C6—H6A	0.9900
S1—C8	1.8300 (12)	C6—H6B	0.9900
O1—C1	1.2070 (14)	C7—C8	1.4949 (17)
O2—C5	1.2079 (15)	C8—H8A	0.9900
O3—C5	1.3630 (14)	C8—H8B	0.9900
O3—C6	1.4540 (15)	C9—C10	1.5164 (18)
O4—C9	1.2341 (14)	C10—C11	1.5258 (17)
N1—C1	1.3940 (15)	C10—H10A	0.9900
N1—C4	1.4030 (15)	C10—H10B	0.9900
N1—C3	1.4846 (15)	C11—C16	1.3997 (16)
N2—C9	1.3563 (16)	C11—C12	1.4019 (17)
N2—C2	1.4452 (16)	C12—C13	1.3900 (17)
N2—H1	0.778 (15)	C12—H12	0.9500
C1—C2	1.5443 (17)	C13—C14	1.3963 (19)
C2—C3	1.5623 (16)	C13—H13	0.9500
C2—H2	1.0000	C14—C15	1.3868 (19)
C3—H3	1.0000	C14—H14	0.9500
C4—C7	1.3401 (17)	C15—C16	1.3966 (17)
C4—C5	1.4713 (17)	C15—H15	0.9500
C6—C7	1.4978 (17)	C16—H16	0.9500
C3—S1—C8	96.33 (5)	C4—C7—C6	108.27 (11)
C5—O3—C6	110.17 (9)	C8—C7—C6	125.58 (10)
C1—N1—C4	134.50 (10)	C7—C8—S1	111.29 (8)
C1—N1—C3	94.44 (9)	C7—C8—H8A	109.4
C4—N1—C3	120.87 (9)	S1—C8—H8A	109.4
C9—N2—C2	119.79 (10)	C7—C8—H8B	109.4
C9—N2—H1	118.2 (11)	S1—C8—H8B	109.4
C2—N2—H1	121.4 (11)	H8A—C8—H8B	108.0
O1—C1—N1	132.89 (11)	O4—C9—N2	121.31 (12)
O1—C1—C2	135.44 (11)	O4—C9—C10	122.38 (11)
N1—C1—C2	91.67 (9)	N2—C9—C10	116.21 (11)
N2—C2—C1	113.96 (10)	C9—C10—C11	108.50 (10)
N2—C2—C3	119.21 (10)	C9—C10—H10A	110.0
C1—C2—C3	85.74 (9)	C11—C10—H10A	110.0
N2—C2—H2	111.8	C9—C10—H10B	110.0
C1—C2—H2	111.8	C11—C10—H10B	110.0
C3—C2—H2	111.8	H10A—C10—H10B	108.4
N1—C3—C2	87.64 (8)	C16—C11—C12	118.53 (12)
N1—C3—S1	112.21 (8)	C16—C11—C10	120.69 (11)
C2—C3—S1	114.77 (8)	C12—C11—C10	120.75 (11)

N1—C3—H3	113.3	C13—C12—C11	121.27 (12)
C2—C3—H3	113.3	C13—C12—H12	119.4
S1—C3—H3	113.3	C11—C12—H12	119.4
C7—C4—N1	123.87 (11)	C12—C13—C14	119.88 (12)
C7—C4—C5	109.87 (11)	C12—C13—H13	120.1
N1—C4—C5	126.25 (11)	C14—C13—H13	120.1
O2—C5—O3	121.94 (11)	C15—C14—C13	119.19 (12)
O2—C5—C4	130.79 (12)	C15—C14—H14	120.4
O3—C5—C4	107.27 (10)	C13—C14—H14	120.4
O3—C6—C7	104.35 (9)	C14—C15—C16	121.24 (12)
O3—C6—H6A	110.9	C14—C15—H15	119.4
C7—C6—H6A	110.9	C16—C15—H15	119.4
O3—C6—H6B	110.9	C15—C16—C11	119.88 (12)
C7—C6—H6B	110.9	C15—C16—H16	120.1
H6A—C6—H6B	108.9	C11—C16—H16	120.1
C4—C7—C8	126.11 (11)		

C4—N1—C1—O1	−30.8 (2)	N1—C4—C5—O2	−1.1 (2)
C3—N1—C1—O1	−173.70 (14)	C7—C4—C5—O3	−0.01 (14)
C4—N1—C1—C2	148.54 (13)	N1—C4—C5—O3	179.44 (11)
C3—N1—C1—C2	5.61 (9)	C5—O3—C6—C7	−2.54 (13)
C9—N2—C2—C1	171.83 (10)	N1—C4—C7—C8	1.1 (2)
C9—N2—C2—C3	72.89 (15)	C5—C4—C7—C8	−179.45 (11)
O1—C1—C2—N2	53.78 (19)	N1—C4—C7—C6	178.94 (11)
N1—C1—C2—N2	−125.50 (10)	C5—C4—C7—C6	−1.59 (14)
O1—C1—C2—C3	173.95 (15)	O3—C6—C7—C4	2.50 (14)
N1—C1—C2—C3	−5.33 (9)	O3—C6—C7—C8	−179.63 (11)
C1—N1—C3—C2	−5.55 (9)	C4—C7—C8—S1	26.83 (16)
C4—N1—C3—C2	−155.48 (10)	C6—C7—C8—S1	−150.67 (10)
C1—N1—C3—S1	110.30 (9)	C3—S1—C8—C7	−49.31 (9)
C4—N1—C3—S1	−39.63 (13)	C2—N2—C9—O4	−4.00 (18)
N2—C2—C3—N1	120.16 (10)	C2—N2—C9—C10	172.50 (10)
C1—C2—C3—N1	5.01 (8)	O4—C9—C10—C11	69.25 (15)
N2—C2—C3—S1	6.73 (13)	N2—C9—C10—C11	−107.21 (12)
C1—C2—C3—S1	−108.42 (9)	C9—C10—C11—C16	−119.87 (12)
C8—S1—C3—N1	56.24 (9)	C9—C10—C11—C12	57.76 (14)
C8—S1—C3—C2	154.26 (9)	C16—C11—C12—C13	0.65 (17)
C1—N1—C4—C7	−130.03 (14)	C10—C11—C12—C13	−177.03 (11)
C3—N1—C4—C7	5.52 (18)	C11—C12—C13—C14	−0.08 (19)
C1—N1—C4—C5	50.6 (2)	C12—C13—C14—C15	−0.42 (19)
C3—N1—C4—C5	−173.86 (11)	C13—C14—C15—C16	0.3 (2)
C6—O3—C5—O2	−177.82 (12)	C14—C15—C16—C11	0.2 (2)
C6—O3—C5—C4	1.67 (13)	C12—C11—C16—C15	−0.72 (18)
C7—C4—C5—O2	179.42 (14)	C10—C11—C16—C15	176.96 (12)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H1···O4^{i}	0.778 (15)	2.276 (15)	3.0506 (14)	173.5 (14)

Symmetry code: (i) −*x*+1, *y*+1/2, −*z*+1/2.