IUCrData

ISSN 2414-3146

rac-2,3-Diphenyl-2,3-dihydro-4*H*-pyrido[3,2-e]-[1,3]thiazin-4-one 1-oxide

Hemant P. Yennawar,[a] Duncan J. Noble,[b] Ziwei Yang[b] and Lee J. Silverberg[b]*

[a]Department of Biochemistry and Molecular Biology, Pennsylvania State University, University Park PA 16802, and [b]Pennsylvania State University, Schuylkill Campus, 200 University Drive, Schuylkill Haven, PA 17972, USA. *Correspondence e-mail: ljs43@psu.edu

Received 21 June 2017
Accepted 27 July 2017

Edited by H. Stoeckli-Evans, University of Neuchâtel, Switzerland

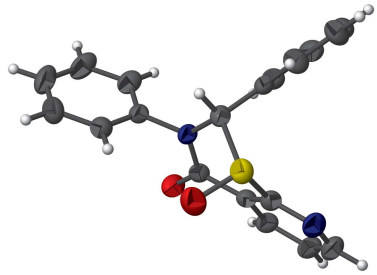
Keywords: crystal structure; pyridothiazine; benzothiazine; screw-boat puckering; C–H···O hydrogen bonding..

CCDC reference: 1565252

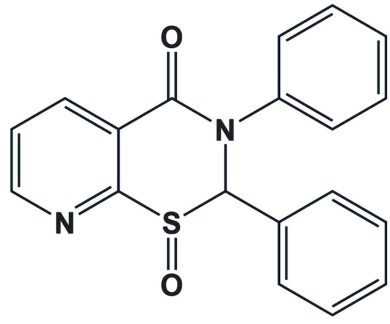
Structural data: full structural data are available from iucrdata.iucr.org

In the title compound, $C_{19}H_{14}N_2O_2S$, the thiazine ring exhibits a screw-boat pucker. The oxygen atom on the sulfur atom of the ring is pseudo-axial on the thiazine ring. In the crystal, 2_1 screw-related molecules are linked by C—H···$O_{carbonyl}$ hydrogen bonds, forming helices propagating along the *b*-axis direction.

3D view



Chemical scheme



Structure description

Pyridothiazinones (including different positions of the pyridine nitrogen) exhibit a variety of different of biological activities (Arya *et al.*, 2014). The number of 3-aryl-2,3-dihydro-4*H*-pyrido[3,2-*e*]thiazin-4-ones reported in the literature is small. One such compound is 2,3-diphenyl-2,3-dihydro-4*H*-pyrido[3,2-*e*][1,3]thiazin-4-one (**II**) (Fig. 1), whose crystal structure we have previously reported (Yennawar *et al.*, 2014). Herein, we report on the crystal structure of that compound's sulfoxide, (**I**), prepared using the method we have reported for oxidation of five-membered 1,3-thiazolidin-4-ones (Cannon *et al.*, 2015; Silverberg *et al.*, 2015). To the best of our knowledge, this is the first report of an *S*-oxide of a 2,3-dihydro-4*H*-pyrido[3,2-*e*]thiazin-4-one, despite the evidence of enhanced activity in similar 2,3,5,6-tetrahydro-4*H*-1,3-thiazin-4-ones (Surrey *et al.*, 1958; Surrey, 1963, US Patent 3082209) and in 1,3-thiazolidin-4-ones (Gududuru *et al.* 2004.)

Although the chemical structure of the title compound, (**I**) (Fig. 2), differs slightly from the structure of 2,3-diphenyl-2,3-dihydro-4*H*-1,3-benzothiazin-4-one 1-oxide (**III**) (Yennawar *et al.* 2017), both compounds crystallize in the monoclinic space group $P2_1/n$, with very similar unit-cell parameters. Their crystal structures are nearly identical. The thiazine ring in both compounds has a screw-boat conformation [puckering parameters for (**I**): (Q) = 0.6996 (13) Å, θ = 114.66 (12)° and φ = 205.32 (14)°; puckering parameters for (**III**): (Q) = 0.686 (2) Å, θ = 114.37 (17)° and φ = 210.6 (2) °]. Atom O1, on the sulfur

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

D—H···A	D—H	H···A	D···A	D—H···A
C1—H1···O2^{i}	0.98	2.30	3.249 (2)	163

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

atom, S1, of the thiazine ring is pseudo-axial on the thiazine ring and *trans* to the phenyl ring on C1, as observed for (**III**) and 2,3-diphenyl-2,3,5,6-tetrahydro-4*H*-1,3-thiazin-4-one 1-oxide (**IV**) (Yennawar *et al.*, 2016).

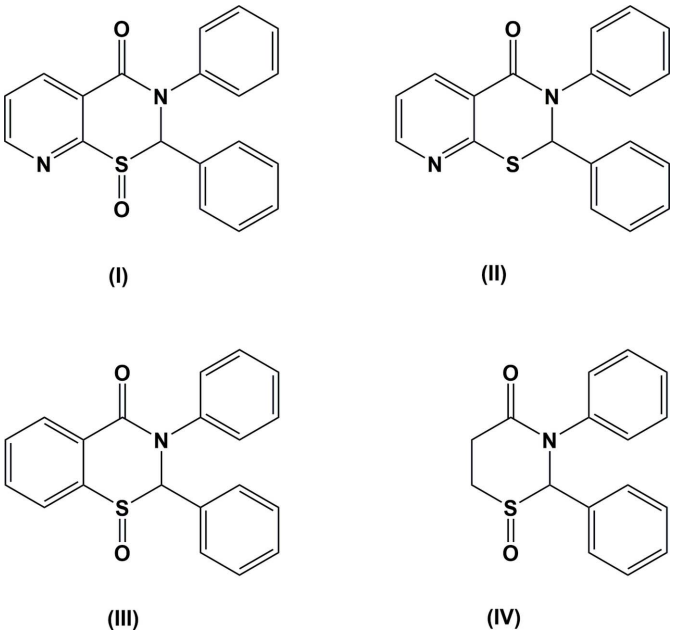


Figure 1
The title compound (**I**) and related compounds.

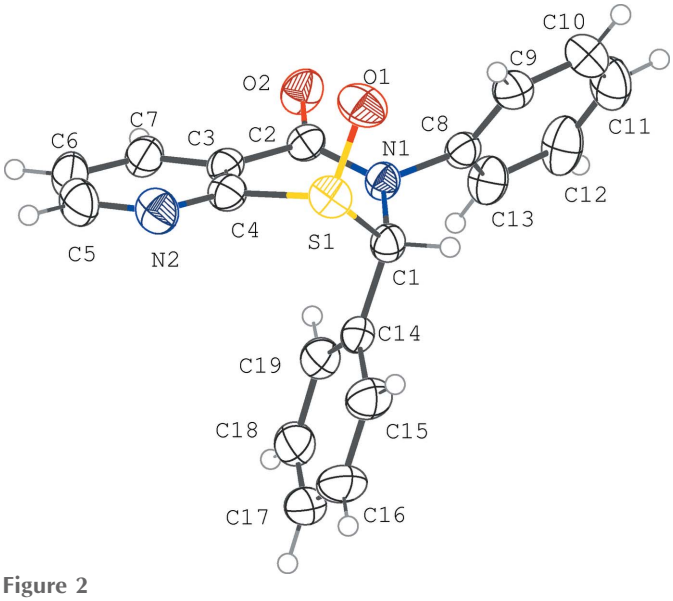


Figure 2
The molecular structure of the title compound, with displacement ellipsoids drawn at the 50% probability level..

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{19}H_{14}N_2O_2S$
M_r	334.38
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	298
a, b, c (Å)	9.1633 (15), 11.0861 (18), 16.250 (3)
β (°)	104.011 (3)
V (Å^3)	1601.7 (5)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.22
Crystal size (mm)	0.29 × 0.15 × 0.05
Data collection	
Diffractometer	Bruker CCD area detector
Absorption correction	Multi-scan (*SADABS*; Bruker, 2001)
T_{min}, T_{max}	0.794, 0.9
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	10735, 3917, 3163
R_{int}	0.024
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.667
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.049, 0.150, 1.07
No. of reflections	3917
No. of parameters	217
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.38, −0.34

Computer programs: *SMART* and *SAINT* (Bruker, 2001), *SHELXS* and *SHELXL* (Sheldrick, 2008) and *OLEX2* (Dolomanov *et al.*, 2009).

The crystal packing of the title compound (**I**), is identical to that observed for compound (**III**), hence the supramolecular

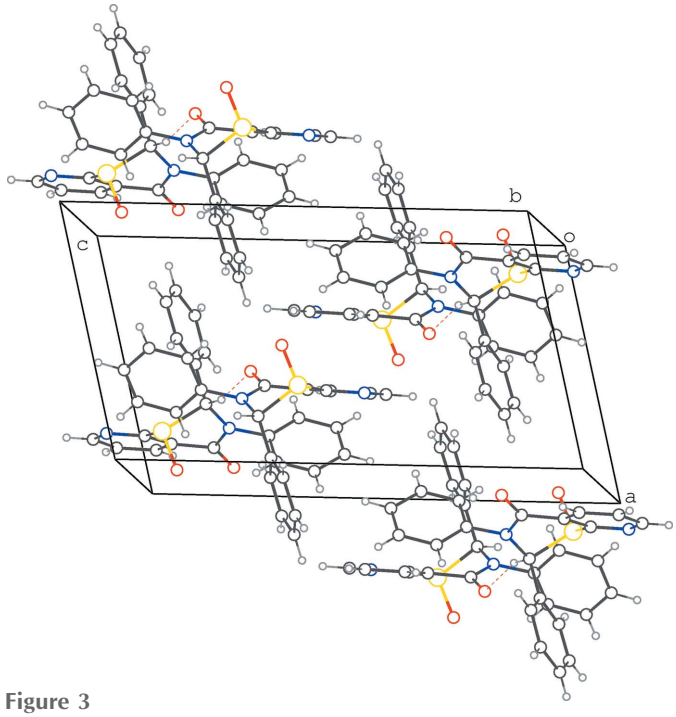


Figure 3
Crystal packing diagram showing C—H···O contacts as dotted red lines between molecules of (**I**), which form helical chains along *b*-axis direction.

features are common to both. Molecules related by a 2_1 screw axis are linked by C1—H1···O2^{i} hydrogen bonds, forming helices propagating along the *b*-axis direction (Table 1 and Fig. 3). While C—H···O type interactions are also present in compound (**IV**), here the oxygen at position 1 (···O═S) is the acceptor of the H atom at the chiral C atom, thus forming helices propagating along the *c*-axis direction. The helices are linked by C—H···π interactions forming a three-dimensional supramolecular structure. In compound (**II**), there are no C—H···O hydrogen bonds present, only C—H..π interactions.

Synthesis and crystallization

A 5 ml round-bottom flask was charged with 49.5 mg of 2,3-diphenyl-2,3-dihydro-4*H*-pyrido[3,2-*e*][1,3]thiazin-4-one and 1 ml of methanol and the mixture stirred. A solution of 75.5 mg Oxone® and 0.63 ml of distilled water was added dropwise, and the mixture was stirred until the reaction was complete, as determined by TLC. The solids were dissolved by addition of 6.3 ml distilled water. The solution was extracted twice with dichloromethane. The combined organic phases were washed with a sat. sodium chloride solution. The solution was dried over Na_2SO_4 and concentrated under vacuum to give a crude solid. Recrystallization from CH_2Cl_2/hexanes gave 35.5 mg of the title compound (68% yield, m.p. 450–551 K). Colourless thin plate-like crystals, suitable for X-ray diffraction analysis, were grown by slow evaporation of a solution in toluene.

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2.

Acknowledgements

We thank Penn State Schuylkill for financial support and NSF funding (CHEM-0131112) for the X-ray diffractometer.

References

Arya, K., Tomar, P. & Singh, J. (2014). *RSC Adv.* **4**, 3060–3064.
Bruker (2001). *SMART*, *SAINT* and *SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA.
Cannon, K., Gandla, D., Lauro, S., Silverberg, L., Tierney, J. & Lagalante, A. (2015). *Intl. J. Chem. (Toronto, ON, Can.)*, **7**(2), 73–84.
Dolomanov, O. V., Bourhis, L. J., Gildea, R. J., Howard, J. A. K. & Puschmann, H. (2009). *J. Appl. Cryst.* **42**, 339–341.
Gududuru, V., Hurh, E., Dalton, J. T. & Miller, D. D. (2004). *Bioorg. Med. Chem. Lett.* **14**, 5289–5293.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Silverberg, L. J., Pacheco, C. N., Lagalante, A., Cannon, K. C., Bachert, J. T., Xie, Y., Baker, L. & Bayliff, J. A. (2015). *Intl. J. Chem. (Toronto, ON, Can.)*, **7**(2), 150-162.
Surrey, A. R. (1963). US Patent 3082209.
Surrey, A. R., Webb, W. G. & Gesler, R. M. (1958). *J. Am. Chem. Soc.* **80**, 3469–3471.
Yennawar, H. P., Fox, R., Moyer, Q. J., Yang, Z. & Silverberg, L. J. (2017). *Acta Cryst.* E**73** 1189–1191.
Yennawar, H. P., Singh, H. & Silverberg, L. J. (2014). *Acta Cryst.* E**70**, o638.
Yennawar, H. P., Yang, Z. & Silverberg, L. J. (2016). *Acta Cryst.* E**72**, 1541–1543.

full crystallographic data

IUCrData (2017). **2**, x171112 [https://doi.org/10.1107/S2414314617011129]

rac-2,3-Diphenyl-2,3-dihydro-4*H*-pyrido[3,2-*e*][1,3]thiazin-4-one 1-oxide

Hemant P. Yennawar, Duncan J. Noble, Ziwei Yang and Lee J. Silverberg

2,3-Diphenyl-2,3-dihydro-4H-pyrido[3,2-e][1,3]thiazin-4-one 1-oxide

Crystal data

$C_{19}H_{14}N_2O_2S$
M_r = 334.38
Monoclinic, $P2_1/n$
a = 9.1633 (15) Å
b = 11.0861 (18) Å
c = 16.250 (3) Å
β = 104.011 (3)°
V = 1601.7 (5) Å^3
Z = 4
$F(000)$ = 696
D_x = 1.387 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 3767 reflections
θ = 2.3–28.2°
μ = 0.22 mm^{-1}
T = 298 K
Plate, colorless
0.29 × 0.15 × 0.05 mm

Data collection

Bruker CCD area detector diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
phi and ω scans
Absorption correction: multi-scan (SADABS; Bruker, 2001)
T_{min} = 0.794, T_{max} = 0.9
10735 measured reflections
3917 independent reflections
3163 reflections with $I > 2\sigma(I)$
R_{int} = 0.024
θ_{max} = 28.3°, θ_{min} = 2.3°
h = −7→12
k = −14→14
l = −21→20

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.049
$wR(F^2)$ = 0.150
S = 1.07
3917 reflections
217 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
$w = 1/[\sigma^2(F_o^2) + (0.1P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.38 e Å^{-3}
$\Delta\rho_{min}$ = −0.34 e Å^{-3}

Special details

Experimental. The data collection nominally covered a full sphere of reciprocal space by a combination of 4 sets of ω scans each set at different φ and/or 2θ angles and each scan (5 s exposure) covering -0.300° degrees in ω. The crystal to detector distance was 5.82 cm.

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	0.30471 (18)	0.62077 (13)	0.18068 (9)	0.0335 (3)
H1	0.3135	0.5530	0.2203	0.040*
C2	0.15996 (18)	0.81146 (13)	0.16516 (9)	0.0324 (3)
C3	0.17155 (17)	0.81522 (14)	0.07510 (9)	0.0323 (3)
C4	0.18742 (18)	0.71236 (14)	0.02869 (9)	0.0349 (3)
C5	0.1838 (2)	0.81999 (19)	−0.09076 (11)	0.0518 (5)
H5	0.1890	0.8227	−0.1472	0.062*
C6	0.1664 (2)	0.92662 (17)	−0.05124 (11)	0.0495 (5)
H6	0.1588	0.9992	−0.0807	0.059*
C7	0.16044 (19)	0.92452 (15)	0.03313 (10)	0.0405 (4)
H7	0.1491	0.9958	0.0612	0.049*
C8	0.19571 (18)	0.70036 (13)	0.29588 (9)	0.0337 (3)
C9	0.0847 (2)	0.62118 (17)	0.30533 (11)	0.0438 (4)
H9	0.0341	0.5745	0.2598	0.053*
C10	0.0496 (2)	0.6120 (2)	0.38294 (12)	0.0572 (5)
H10	−0.0258	0.5596	0.3898	0.069*
C11	0.1271 (3)	0.6812 (2)	0.45089 (13)	0.0600 (6)
H11	0.1016	0.6766	0.5028	0.072*
C12	0.2407 (3)	0.75606 (17)	0.44173 (11)	0.0562 (5)
H12	0.2939	0.8003	0.4879	0.067*
C13	0.2770 (2)	0.76636 (15)	0.36422 (10)	0.0450 (4)
H13	0.3547	0.8168	0.3580	0.054*
C14	0.46180 (18)	0.65049 (15)	0.17426 (9)	0.0359 (4)
C15	0.5491 (2)	0.56025 (18)	0.15151 (12)	0.0520 (5)
H15	0.5098	0.4829	0.1407	0.062*
C16	0.6938 (2)	0.5836 (2)	0.14464 (14)	0.0641 (6)
H16	0.7504	0.5229	0.1278	0.077*
C17	0.7537 (2)	0.6968 (2)	0.16282 (13)	0.0647 (6)
H17	0.8515	0.7125	0.1589	0.078*
C18	0.6701 (2)	0.7872 (2)	0.18682 (12)	0.0563 (5)
H18	0.7115	0.8635	0.1996	0.068*
C19	0.5238 (2)	0.76419 (17)	0.19187 (10)	0.0445 (4)
H19	0.4668	0.8258	0.2072	0.053*
N1	0.22476 (15)	0.71606 (11)	0.21339 (7)	0.0322 (3)
N2	0.19379 (18)	0.71156 (14)	−0.05230 (9)	0.0463 (4)
O1	0.03546 (15)	0.55035 (11)	0.09257 (8)	0.0509 (3)

O2	0.09481 (14)	0.89182 (10)	0.19355 (7)	0.0454 (3)
S1	0.18764 (5)	0.56726 (3)	0.07754 (2)	0.03877 (16)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0385 (9)	0.0304 (7)	0.0330 (7)	0.0053 (6)	0.0113 (6)	0.0025 (6)
C2	0.0319 (8)	0.0317 (7)	0.0320 (7)	0.0013 (6)	0.0048 (6)	−0.0022 (5)
C3	0.0278 (8)	0.0365 (8)	0.0310 (7)	0.0015 (6)	0.0039 (6)	0.0005 (5)
C4	0.0320 (8)	0.0404 (8)	0.0311 (7)	−0.0022 (6)	0.0049 (6)	−0.0026 (6)
C5	0.0521 (12)	0.0710 (13)	0.0306 (8)	−0.0095 (9)	0.0069 (8)	0.0035 (8)
C6	0.0508 (11)	0.0540 (11)	0.0411 (9)	−0.0012 (8)	0.0059 (8)	0.0150 (8)
C7	0.0400 (9)	0.0399 (9)	0.0397 (9)	0.0026 (7)	0.0060 (7)	0.0053 (6)
C8	0.0340 (8)	0.0374 (8)	0.0298 (7)	0.0072 (6)	0.0079 (6)	0.0017 (6)
C9	0.0359 (9)	0.0560 (11)	0.0388 (9)	0.0003 (8)	0.0080 (7)	0.0035 (7)
C10	0.0489 (12)	0.0719 (13)	0.0566 (12)	0.0021 (10)	0.0240 (9)	0.0140 (10)
C11	0.0822 (16)	0.0649 (13)	0.0404 (10)	0.0178 (11)	0.0294 (11)	0.0062 (8)
C12	0.0882 (16)	0.0459 (10)	0.0332 (8)	0.0089 (10)	0.0121 (9)	−0.0040 (7)
C13	0.0566 (12)	0.0395 (9)	0.0372 (8)	0.0010 (8)	0.0082 (8)	−0.0012 (7)
C14	0.0337 (8)	0.0458 (9)	0.0282 (7)	0.0070 (7)	0.0073 (6)	0.0077 (6)
C15	0.0470 (11)	0.0553 (11)	0.0552 (11)	0.0148 (8)	0.0155 (9)	0.0038 (8)
C16	0.0433 (11)	0.0910 (17)	0.0621 (13)	0.0241 (11)	0.0205 (10)	0.0110 (11)
C17	0.0348 (10)	0.1087 (19)	0.0510 (11)	0.0082 (11)	0.0109 (9)	0.0279 (11)
C18	0.0426 (11)	0.0740 (13)	0.0483 (10)	−0.0096 (10)	0.0034 (9)	0.0169 (9)
C19	0.0396 (10)	0.0509 (10)	0.0411 (9)	−0.0019 (8)	0.0060 (7)	0.0068 (7)
N1	0.0369 (7)	0.0322 (6)	0.0280 (6)	0.0052 (5)	0.0090 (5)	0.0007 (5)
N2	0.0489 (9)	0.0564 (9)	0.0328 (7)	−0.0077 (7)	0.0084 (6)	−0.0068 (6)
O1	0.0439 (8)	0.0531 (7)	0.0565 (8)	−0.0150 (6)	0.0139 (6)	−0.0074 (6)
O2	0.0553 (8)	0.0407 (6)	0.0408 (6)	0.0153 (5)	0.0128 (6)	−0.0013 (5)
S1	0.0433 (3)	0.0331 (2)	0.0410 (2)	−0.00253 (16)	0.01232 (19)	−0.00753 (15)

Geometric parameters (Å, º)

C1—C14	1.505 (2)	C8—C13	1.387 (2)
C1—N1	1.4573 (19)	C8—N1	1.4391 (19)
C1—S1	1.8550 (15)	C9—C10	1.379 (2)
C2—C3	1.493 (2)	C10—C11	1.390 (3)
C2—N1	1.3639 (19)	C11—C12	1.367 (3)
C2—O2	1.2232 (18)	C12—C13	1.383 (3)
C3—C4	1.394 (2)	C14—C15	1.386 (2)
C3—C7	1.382 (2)	C14—C19	1.384 (2)
C4—N2	1.331 (2)	C15—C16	1.382 (3)
C4—S1	1.7936 (16)	C16—C17	1.373 (3)
C5—C6	1.373 (3)	C17—C18	1.374 (3)
C5—N2	1.348 (2)	C18—C19	1.386 (3)
C6—C7	1.386 (2)	O1—S1	1.4847 (13)
C8—C9	1.380 (2)		

C14—C1—S1	111.16 (10)	C9—C10—C11	119.90 (19)
N1—C1—C14	116.13 (13)	C12—C11—C10	120.29 (18)
N1—C1—S1	109.24 (10)	C11—C12—C13	120.44 (18)
N1—C2—C3	117.41 (13)	C12—C13—C8	118.99 (18)
O2—C2—C3	120.42 (14)	C15—C14—C1	118.95 (16)
O2—C2—N1	122.16 (14)	C19—C14—C1	122.48 (15)
C4—C3—C2	123.29 (14)	C19—C14—C15	118.56 (18)
C7—C3—C2	119.59 (14)	C16—C15—C14	120.9 (2)
C7—C3—C4	117.07 (14)	C17—C16—C15	119.7 (2)
C3—C4—S1	118.89 (12)	C16—C17—C18	120.4 (2)
N2—C4—C3	125.13 (15)	C17—C18—C19	119.8 (2)
N2—C4—S1	115.85 (12)	C14—C19—C18	120.65 (18)
N2—C5—C6	123.61 (16)	C2—N1—C1	122.68 (12)
C5—C6—C7	119.04 (16)	C2—N1—C8	118.43 (12)
C3—C7—C6	119.15 (15)	C8—N1—C1	118.34 (12)
C9—C8—C13	120.92 (16)	C4—N2—C5	115.99 (15)
C9—C8—N1	119.23 (14)	C4—S1—C1	92.96 (7)
C13—C8—N1	119.84 (15)	O1—S1—C1	104.62 (7)
C10—C9—C8	119.36 (17)	O1—S1—C4	106.59 (8)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C1—H1···O2^{i}	0.98	2.30	3.249 (2)	163

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