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Crystal structure of Brinzolamide: a carbonic anhydrase inhibitor

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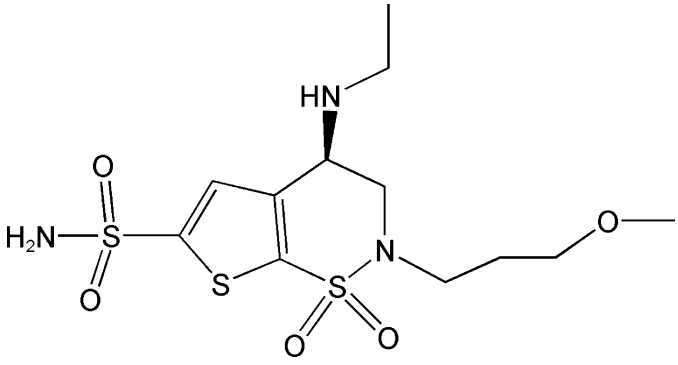
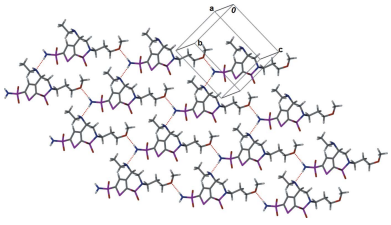
In crystal structure of the title compound, $C_{12}H_{21}N_3O_5S_3$ [systematic name: (*R*)-4-ethylamino-2-(3-methoxypropyl)-3,4-dihydro-2*H*-thieno[3,2-*e*][1,2]thiazine-6-sulfonamide 1,1-dioxide], there exist three kinds of hydrogen-bonding interactions. The sulfonamide group is involved in hydrogen bonding with the secondary amine and the methoxy O atom, resulting in the formation of layers parallel to the *bc* plane. The layers are linked by an N—H···O hydrogen bond involving a sulfonamide O atom as acceptor and the secondary amine H atom as donor, which gives rise to the formation of a unique bilayer structure. The absolute structure of the molecule in the crystal was determined by resonant scattering [Flack parameter = 0.01 (4)].

1. Chemical context

The crystal structures of organic solids are dominated mainly by hydrogen-bonding interactions (Steiner, 2002). Hydrogen bonding plays a crucial role in polymorphism of active pharmaceutical ingredients (Vippagunta *et al.*, 2001). Brinzolamide (Conrow *et al.*, 1999), is a carbonic anhydrase inhibitor used for the treatment of open-angle glaucoma or ocular hypertension (March & Ochsner, 2000). Herein,we report on the crystal structure of Brinzolamide and the hydrogen-bonding interactions present in the crystal packing.





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2. Structural commentary

The molecular structure of the title compound is shown in Fig. 1. The six-membered thiazine ring has an envelope conformation with the N atom, N2, as the flap. The 3-methoxypropyl chain has a twisted conformation with torsion angles N2—C7—C8—C9, C7—C8—C9—O5 and C8—C9—O5—C10 being 71.66 (18), 166.76 (14) and 82.04 (19)°, respectively. The ethylamino group (N3/C11/C12) is normal to

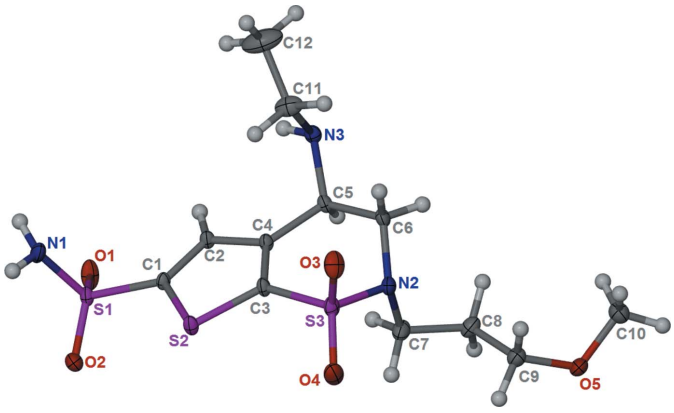

Figure 1
The molecular structure of the title compound, showing the atom labelling and 30% displacement ellipsoids.

the mean plane of the five planar atoms of the thiazine ring (S3/C3–C6), making a dihedral angle of 84.4 (3)°. The three main functional groups (the sulfonamide, the secondary amine and the methoxy group) extend themselves in different directions, which facilitates the formation of a hydrogen-bonded network.

3. Supramolecular features

There are three kinds of hydrogen-bonding interactions in the crystal of Brinzolamide (Table 1 and Figs. 2 and 3). The sulfonamide group is involved in hydrogen bonding [N1···N3 = 2.886 (2) Å, Table 1] with the secondary amine, forming a *C*(8) chain along the *b*-axis direction. The sulfonamide group is also involved in hydrogen bonding with the methoxy group

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*B*···O5^{i}	0.87 (1)	1.98 (1)	2.841 (2)	177 (2)
N1—H1*A*···N3^{ii}	0.87 (1)	2.03 (1)	2.886 (2)	171 (2)
N3—H3···O1^{iii}	0.86 (1)	2.26 (1)	3.042 (2)	151 (2)

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

[N1···O5 = 2.841 (2) Å, Table 1], linking the chains to form sheets parallel to the *bc* plane (Fig. 2 and Table 1). There also exists another hydrogen bond between the sulfonamide and the secondary amine [N3···O1 = 3.042 (2) Å, Table 1], linking the sheets to form a unique bilayer structure (Fig. 3).

4. Database survey

A search of the Cambridge Structural Database (CSD, Version 5.37, last update February 2016; Groom *et al.*, 2016) revealed no hits for Brinzolamide. A search for the fused six- and five-membered ring system, *viz.* 3,4-dihydro-2λ^2-thieno-[3,2-*e*][1,2]thiazine 1,1-dioxide, gave only two hits: 8b-bromo-2-(bromomethyl)-4-methyl-3a-phenyl-1,3a,4,8b-tetrahydro-2*H*-furo[2,3-*c*]thieno[3,2-*e*][1,2]thiazine 5,5-dioxide (BUFQIE; Barange *et al.*, 2014) and (*S*)-6,6-dimethyl-4a,5,6,7-tetrahydro-4*H*-pyrrolo[1,2-*b*]thieno[3,2-*e*][1,2]thiazine 9,9-dioxide (BUXDEE; Zeng & Chemler, 2007). The latter crystallizes in the chiral monoclinic space group $P2_1$, with four independent molecules in the asymmetric unit. However, in both compounds the six-membered thiazine ring is also fused to a second five-membered ring; a tetrahydrofuro ring in the case of BUFQIE, fused to the C—C bond, and a pyrrolo ring

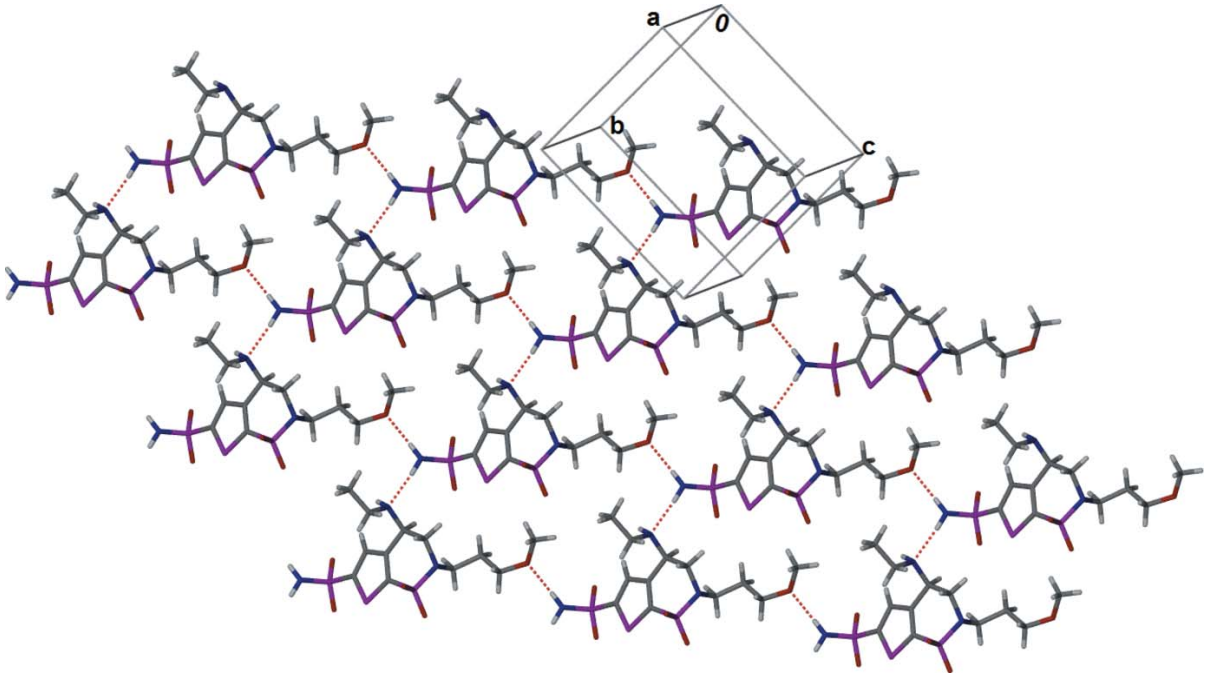

Figure 2
A view along the *a* axis of the two-dimensional hydrogen-bonded network in the crystal of the title compound. The hydrogen bonds are shown as dashed lines (see Table 1 for details).

in the case of BUXDEE, fused to the N—C bond. The thiazine ring in BUFQIE has a distorted twist-boat conformation, while in BUFQIE all four independent molecules have half-chair conformations. This is in contrast to the situation in the title compound where the thiazine ring has an envelope conformation with the N atom as the flap.

5. Synthesis and crystallization

The enantioselective synthesis of Brinzolamide has been reported by Conrow *et al.*, (1999). It is marketed under the trade name of Azopt by Alcon Laboratories, Inc., Fort Worth, Texas 76134, USA. Colourless prismatic crystals of Brinzolamide (383 mg, 1 mmol) were obtained by slow evaporation of a solution in chloroform (15 ml).

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. The NH and NH_2 H atoms were located in difference Fourier maps and refined with distance restraints of N—H = 0.87 (1) Å for NH and 0.86 (1) Å for NH_2 H atoms. The C-bound H atoms were included in calculated positions and treated as riding atoms: C—H = 0.95–1.00 Å with U_{iso}(H) = 1.5U_{eq}(C-methyl) and 1.2U_{eq}(C) for other H atoms. The absolute structure of the molecule in the crystal was determined by resonant scattering [Flack parameter = 0.01 (4)].

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{12}H_{21}N_3O_5S_3$
M_r	383.50
Crystal system, space group	Monoclinic, $P2_1$
Temperature (K)	293
a, b, c (Å)	9.698 (2), 8.8127 (19), 10.133 (2)
β (°)	92.248 (3)
V (Å^3)	865.4 (3)
Z	2
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.46
Crystal size (mm)	0.35 × 0.35 × 0.20
Data collection	
Diffractometer	Rigaku Mercury CCD
Absorption correction	Multi-scan (*CrystalClear*; Rigaku, 2000)
T_{min}, T_{max}	0.853, 0.913
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	6608, 3684, 3612
R_{int}	0.010
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.649
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.022, 0.059, 1.04
No. of reflections	3684
No. of parameters	222
No. of restraints	4
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.21, −0.19
Absolute structure	1595 Friedel pairs; Flack (1983)
Absolute structure parameter	0.01 (4)

Computer programs: *CrystalClear* (Rigaku, 2000), *SHELXS97* and *SHELXL97* (Sheldrick, 2008), *X-SEED* (Barbour, 2001) and *PLATON* (Spek, 2009).

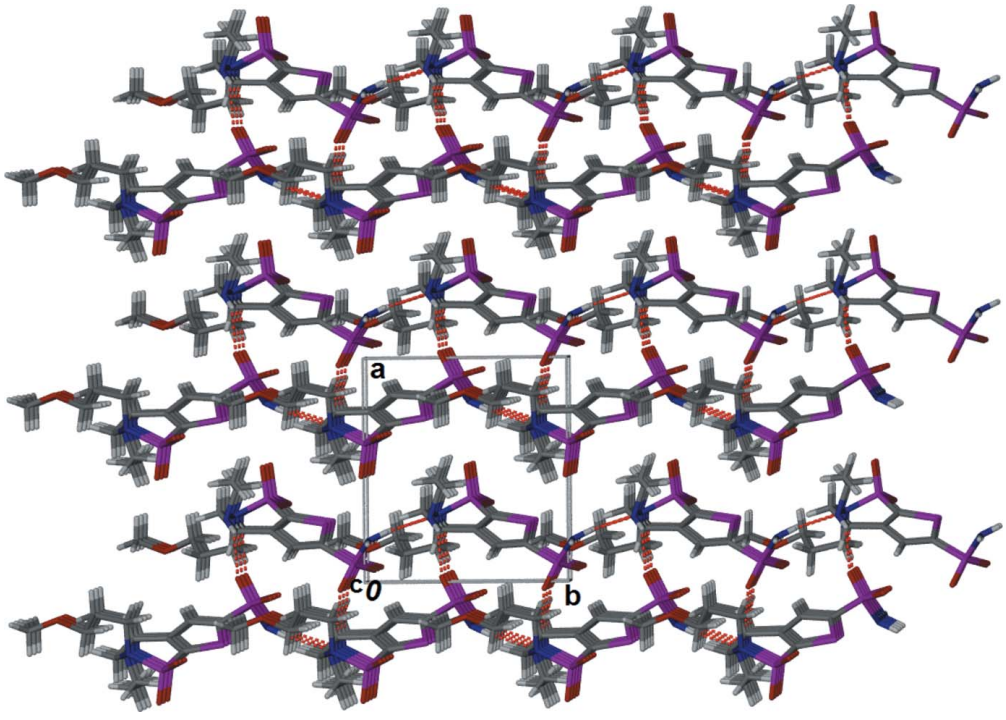

Figure 3
A view along the *c* axis of the crystal packing of the title compound, showing the hydrogen bonded bilayer structure. The hydrogen bonds are shown as dashed lines (see Table 1 for details).

Acknowledgements

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References

Barange, D. K., Kavala, V., Kuo, C.-W., Wang, C.-C., Rajawinslin, R. R., Donala, J. & Yao, C.-F. (2014). *Tetrahedron*, **70**, 7598–7605.
Barbour, L. J. (2001). *J. Supramol. Chem.* **1**, 189–191.
Conrow, R. E., Dean, W. D., Zinke, P. W., Deason, M. E., Sproull, S. J., Dantanarayana, A. P. & DuPriest, M. T. (1999). *Org. Process Res. Dev.* **3**, 114–120.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Groom, C. R., Bruno, I. J., Lightfoot, M. P. & Ward, S. C. (2016). *Acta Cryst.* B**72**, 171–179.
March, W. F. & Ochsner, K. I. (2000). *Am. J. Ophthalmol.* **129**, 136–143.
Rigaku (2000). *CrystalClear*. Rigaku Corporation, Tokyo, Japan.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Spek, A. L. (2009). *Acta Cryst.* D**65**, 148–155.
Steiner, T. (2002). *Angew. Chem. Int. Ed.* **41**, 48–76.
Vippagunta, S. R., Brittain, H. G. & Grant, D. J. W. (2001). *Adv. Drug Deliv. Rev.* **48**, 3–26.
Zeng, W. & Chemler, S. R. (2007). *J. Am. Chem. Soc.* **129**, 12948–12949.

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Computing details

Data collection: *CrystalClear* (Rigaku, 2000); cell refinement: *CrystalClear* (Rigaku, 2000); data reduction: *CrystalClear* (Rigaku, 2000); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *X-SEED* (Barbour, 2001); software used to prepare material for publication: *SHELXL97* (Sheldrick, 2008) and *PLATON* (Spek, 2009).

(5*R*)-5-ethylamino-3-(3-methoxypropyl)-2,2-dioxo-2,9-dithia-3-azabicyclo[4.3.0]nona-1(6)7-diene-8-sulfonamide

Crystal data

$C_{12}H_{21}N_3O_5S_3$
M_r = 383.50
Monoclinic, $P2_1$
Hall symbol: P 2yb
a = 9.698 (2) Å
b = 8.8127 (19) Å
c = 10.133 (2) Å
β = 92.248 (3)°
V = 865.4 (3) Å^3
Z = 2
$F(000)$ = 404
D_x = 1.472 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 2619 reflections
θ = 2.1–27.5°
μ = 0.46 mm^{-1}
T = 293 K
Prism, colourless
0.35 × 0.35 × 0.20 mm

Data collection

Rigaku Mercury CCD diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
Detector resolution: 14.6306 pixels mm^{-1}
CCD_Profile_fitting scans
Absorption correction: multi-scan (*CrystalClear*; Rigaku, 2000)
T_{min} = 0.853, T_{max} = 0.913
6608 measured reflections
3684 independent reflections
3612 reflections with $I > 2\sigma(I)$
R_{int} = 0.010
θ_{max} = 27.5°, θ_{min} = 2.0°
h = −12→12
k = −11→11
l = −13→13

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.022
$wR(F^2)$ = 0.059
S = 1.03
3684 reflections
222 parameters
4 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

$w = 1/[\sigma^2(F_o^2) + (0.0403P)^2 + 0.0611P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.21$ e Å^{-3}
$\Delta\rho_{min} = -0.19$ e Å^{-3}
Absolute structure: 1595 Friedel pairs; Flack (1983)
Absolute structure parameter: 0.01 (4)

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}
S1	0.08557 (3)	0.95125 (4)	0.63688 (3)	0.02705 (9)
S2	0.26509 (4)	0.81437 (4)	0.85525 (3)	0.02964 (9)
S3	0.37674 (4)	0.52417 (4)	0.99143 (4)	0.03230 (9)
O1	−0.02692 (13)	0.88932 (16)	0.55817 (13)	0.0482 (3)
O2	0.05935 (13)	1.05211 (14)	0.74416 (12)	0.0409 (3)
O3	0.51842 (12)	0.50532 (17)	0.96186 (14)	0.0482 (3)
O4	0.34354 (16)	0.59370 (17)	1.11319 (11)	0.0504 (3)
O5	0.14543 (15)	0.01552 (16)	1.26375 (12)	0.0472 (3)
N1	0.19095 (16)	1.02862 (18)	0.54219 (13)	0.0365 (3)
N2	0.30128 (13)	0.35864 (15)	0.97875 (12)	0.0310 (3)
N3	0.29017 (12)	0.32938 (16)	0.60656 (12)	0.0285 (3)
C1	0.17016 (14)	0.79352 (17)	0.70936 (12)	0.0241 (3)
C2	0.16170 (15)	0.64755 (17)	0.66712 (13)	0.0262 (3)
H2	0.1130	0.6168	0.5884	0.031*
C3	0.29337 (15)	0.62151 (18)	0.85939 (14)	0.0269 (3)
C4	0.23410 (14)	0.54569 (18)	0.75421 (13)	0.0248 (3)
C5	0.23691 (15)	0.37508 (18)	0.73479 (14)	0.0262 (3)
H5	0.1394	0.3386	0.7368	0.031*
C6	0.31904 (17)	0.29191 (18)	0.84604 (15)	0.0312 (3)
H6A	0.2895	0.1844	0.8473	0.037*
H6B	0.4182	0.2939	0.8264	0.037*
C7	0.15834 (18)	0.3485 (2)	1.02768 (17)	0.0410 (4)
H7A	0.0916	0.3777	0.9557	0.049*
H7B	0.1486	0.4212	1.1012	0.049*
C8	0.12434 (19)	0.1893 (2)	1.07530 (16)	0.0409 (4)
H8A	0.0237	0.1818	1.0872	0.049*
H8B	0.1489	0.1149	1.0069	0.049*
C9	0.2000 (2)	0.1493 (2)	1.20395 (16)	0.0414 (4)
H9A	0.2988	0.1329	1.1873	0.050*
H9B	0.1935	0.2355	1.2661	0.050*
C10	0.1941 (2)	−0.1233 (3)	1.2128 (2)	0.0497 (5)

H10A	0.1556	−0.1381	1.1229	0.074*
H10B	0.1652	−0.2072	1.2690	0.074*
H10C	0.2950	−0.1209	1.2114	0.074*
C11	0.42904 (19)	0.3825 (3)	0.57763 (18)	0.0499 (5)
H11A	0.4982	0.3234	0.6305	0.060*
H11B	0.4386	0.4905	0.6033	0.060*
C12	0.4563 (3)	0.3657 (5)	0.4339 (2)	0.0923 (12)
H12A	0.4480	0.2586	0.4087	0.138*
H12B	0.5497	0.4016	0.4175	0.138*
H12C	0.3890	0.4258	0.3816	0.138*
H3	0.2359 (17)	0.369 (2)	0.5477 (16)	0.038 (5)*
H1A	0.228 (2)	1.1141 (16)	0.566 (2)	0.044 (6)*
H1B	0.174 (2)	1.024 (3)	0.4577 (10)	0.046 (5)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.03112 (17)	0.02019 (17)	0.02929 (17)	0.00014 (14)	−0.00565 (13)	0.00508 (14)
S2	0.04226 (19)	0.01977 (18)	0.02583 (16)	−0.00143 (14)	−0.01218 (13)	−0.00112 (14)
S3	0.0398 (2)	0.0277 (2)	0.02842 (17)	0.00293 (16)	−0.01163 (13)	0.00436 (15)
O1	0.0434 (7)	0.0388 (7)	0.0599 (8)	−0.0078 (6)	−0.0284 (6)	0.0154 (6)
O2	0.0534 (7)	0.0300 (7)	0.0398 (6)	0.0094 (5)	0.0096 (5)	0.0022 (5)
O3	0.0345 (6)	0.0476 (8)	0.0612 (8)	0.0005 (6)	−0.0145 (5)	0.0135 (7)
O4	0.0838 (10)	0.0383 (7)	0.0280 (6)	0.0073 (7)	−0.0134 (6)	−0.0016 (5)
O5	0.0716 (9)	0.0387 (7)	0.0326 (6)	0.0081 (7)	0.0188 (6)	0.0074 (6)
N1	0.0563 (8)	0.0259 (8)	0.0274 (6)	−0.0088 (7)	0.0012 (5)	0.0046 (6)
N2	0.0382 (6)	0.0250 (7)	0.0297 (6)	0.0047 (5)	0.0010 (5)	0.0062 (5)
N3	0.0306 (6)	0.0254 (7)	0.0291 (6)	−0.0013 (5)	−0.0040 (4)	−0.0020 (5)
C1	0.0283 (6)	0.0219 (8)	0.0216 (6)	−0.0007 (5)	−0.0055 (5)	0.0033 (5)
C2	0.0324 (7)	0.0211 (7)	0.0246 (6)	−0.0015 (5)	−0.0064 (5)	0.0004 (6)
C3	0.0328 (7)	0.0196 (8)	0.0276 (7)	0.0021 (6)	−0.0074 (5)	0.0031 (6)
C4	0.0279 (6)	0.0205 (7)	0.0257 (6)	0.0010 (5)	−0.0037 (5)	0.0025 (6)
C5	0.0280 (6)	0.0202 (7)	0.0301 (7)	0.0013 (5)	−0.0034 (5)	0.0005 (6)
C6	0.0394 (7)	0.0217 (8)	0.0322 (7)	0.0059 (6)	−0.0008 (6)	0.0026 (6)
C7	0.0414 (8)	0.0419 (11)	0.0402 (8)	0.0084 (7)	0.0087 (6)	0.0116 (7)
C8	0.0458 (9)	0.0453 (11)	0.0317 (7)	−0.0054 (8)	0.0035 (6)	0.0066 (8)
C9	0.0549 (10)	0.0368 (10)	0.0327 (8)	0.0009 (8)	0.0042 (7)	0.0026 (7)
C10	0.0651 (12)	0.0380 (10)	0.0462 (10)	0.0054 (9)	0.0051 (8)	−0.0013 (9)
C11	0.0390 (9)	0.0666 (13)	0.0444 (9)	−0.0152 (9)	0.0070 (7)	−0.0117 (10)
C12	0.0653 (15)	0.153 (4)	0.0599 (14)	−0.0316 (19)	0.0227 (11)	−0.0246 (18)

Geometric parameters (Å, º)

S1—O1	1.4338 (12)	C4—C5	1.517 (2)
S1—O2	1.4346 (13)	C5—C6	1.540 (2)
S1—N1	1.5834 (14)	C5—H5	1.0000
S1—C1	1.7600 (15)	C6—H6A	0.9900
S2—C1	1.7205 (13)	C6—H6B	0.9900

S2—C3	1.7219 (16)	C7—C8	1.524 (3)
S3—O4	1.4256 (14)	C7—H7A	0.9900
S3—O3	1.4274 (14)	C7—H7B	0.9900
S3—N2	1.6349 (15)	C8—C9	1.513 (2)
S3—C3	1.7592 (14)	C8—H8A	0.9900
O5—C10	1.416 (2)	C8—H8B	0.9900
O5—C9	1.436 (2)	C9—H9A	0.9900
N1—H1A	0.866 (10)	C9—H9B	0.9900
N1—H1B	0.866 (9)	C10—H10A	0.9800
N2—C6	1.484 (2)	C10—H10B	0.9800
N2—C7	1.493 (2)	C10—H10C	0.9800
N3—C11	1.466 (2)	C11—C12	1.497 (3)
N3—C5	1.4731 (19)	C11—H11A	0.9900
N3—H3	0.856 (9)	C11—H11B	0.9900
C1—C2	1.357 (2)	C12—H12A	0.9800
C2—C4	1.4245 (19)	C12—H12B	0.9800
C2—H2	0.9500	C12—H12C	0.9800
C3—C4	1.365 (2)		

O1—S1—O2	120.25 (9)	N2—C6—H6A	108.9
O1—S1—N1	108.78 (8)	C5—C6—H6A	108.9
O2—S1—N1	109.28 (8)	N2—C6—H6B	108.9
O1—S1—C1	105.28 (7)	C5—C6—H6B	108.9
O2—S1—C1	105.47 (7)	H6A—C6—H6B	107.7
N1—S1—C1	106.95 (8)	N2—C7—C8	112.05 (14)
C1—S2—C3	89.70 (7)	N2—C7—H7A	109.2
O4—S3—O3	118.92 (9)	C8—C7—H7A	109.2
O4—S3—N2	109.63 (8)	N2—C7—H7B	109.2
O3—S3—N2	108.14 (8)	C8—C7—H7B	109.2
O4—S3—C3	109.63 (8)	H7A—C7—H7B	107.9
O3—S3—C3	108.34 (8)	C9—C8—C7	112.58 (16)
N2—S3—C3	100.62 (7)	C9—C8—H8A	109.1
C10—O5—C9	114.96 (14)	C7—C8—H8A	109.1
S1—N1—H1A	118.3 (14)	C9—C8—H8B	109.1
S1—N1—H1B	118.6 (15)	C7—C8—H8B	109.1
H1A—N1—H1B	112 (2)	H8A—C8—H8B	107.8
C6—N2—C7	114.80 (13)	O5—C9—C8	112.38 (16)
C6—N2—S3	110.94 (10)	O5—C9—H9A	109.1
C7—N2—S3	116.48 (11)	C8—C9—H9A	109.1
C11—N3—C5	116.46 (13)	O5—C9—H9B	109.1
C11—N3—H3	105.9 (14)	C8—C9—H9B	109.1
C5—N3—H3	106.0 (14)	H9A—C9—H9B	107.9
C2—C1—S2	113.32 (10)	O5—C10—H10A	109.5
C2—C1—S1	126.55 (10)	O5—C10—H10B	109.5
S2—C1—S1	119.95 (9)	H10A—C10—H10B	109.5
C1—C2—C4	112.31 (12)	O5—C10—H10C	109.5
C1—C2—H2	123.8	H10A—C10—H10C	109.5
C4—C2—H2	123.8	H10B—C10—H10C	109.5

C4—C3—S2	113.72 (11)	N3—C11—C12	111.18 (16)
C4—C3—S3	121.46 (12)	N3—C11—H11A	109.4
S2—C3—S3	124.60 (9)	C12—C11—H11A	109.4
C3—C4—C2	110.94 (13)	N3—C11—H11B	109.4
C3—C4—C5	125.25 (13)	C12—C11—H11B	109.4
C2—C4—C5	123.73 (13)	H11A—C11—H11B	108.0
N3—C5—C4	113.21 (12)	C11—C12—H12A	109.5
N3—C5—C6	109.05 (12)	C11—C12—H12B	109.5
C4—C5—C6	112.84 (13)	H12A—C12—H12B	109.5
N3—C5—H5	107.1	C11—C12—H12C	109.5
C4—C5—H5	107.1	H12A—C12—H12C	109.5
C6—C5—H5	107.1	H12B—C12—H12C	109.5
N2—C6—C5	113.55 (12)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*B*···O5^{i}	0.87 (1)	1.98 (1)	2.841 (2)	177 (2)
N1—H1*A*···N3^{ii}	0.87 (1)	2.03 (1)	2.886 (2)	171 (2)
N3—H3···O1^{iii}	0.86 (1)	2.26 (1)	3.042 (2)	151 (2)

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