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Crystal structure of 5-{4′-[(2-{2-[2-(2-ammonioethoxy)ethoxy]ethoxy}ethyl)carbamoyl]-4-methoxy-[1,1′-biphenyl]-3-yl}-3-oxo-1,2,5-thiadiazolidin-2-ide 1,1-dioxide: a potential inhibitor of the enzyme protein tyrosine phosphatase 1B (PTP1B)

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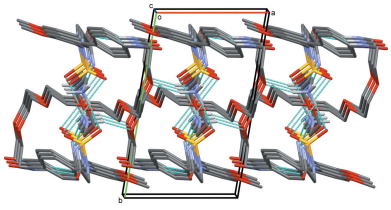
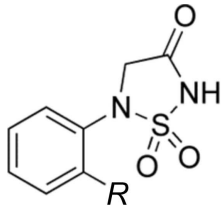
The title compound, $C_{24}H_{32}N_4O_8S$, (I), crystallizes as a zwitterion. The terminal amine N atom of the [(2-{2-[2-(2-ammonioethoxy)ethoxy]ethoxy}ethyl)carbamoyl] side chain is protonated, while the 1,2,5-thiadiazolidin-3-one 1,1-dioxide N atom is deprotonated. The side chain is turned over on itself with an intramolecular N—H···O hydrogen bond. The 1,2,5-thiadiazolidin-3-one 1,1-dioxide ring has an envelope conformation with the aryl-substituted N atom as the flap. Its mean plane is inclined by 62.87 (8)° to the aryl ring to which it is attached, while the aryl rings of the biphenyl unit are inclined to one another by 20.81 (8)°. In the crystal, molecules are linked by N—H···O and N—H···N hydrogen bonds, forming slabs lying parallel to (010). Within the slabs there are C—H···O and C—H···N hydrogen bonds and C—H···π interactions present.

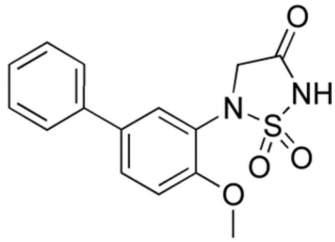
1. Chemical context

A variety of 5-aryl-1,2,5-thiadiazolidin-3-one 1,1-dioxides have been developed as inhibitors of the enzyme protein tyrosine phosphatase 1B (PTP1B) (Combs, 2010). In this capacity, the 5-aryl-1,2,5-thiadiazolidin-3-one 1,1-dioxide core serves as a structural mimic of the phosphoryl tyrosine unit that is present in the endogenous substrates of the enzyme. The parent compound, 5-phenyl-1,2,5-thiadiazolidin-3-one 1,1-dioxide **1** (Fig. 1), is a rather weak inhibitor of PTP1B, displaying a K_i value of approximately 2 m*M* (Black *et al.*, 2005). Docking studies predicted that this compound must bind to the enzyme active site in a conformation where the planes of the 1,2,5-thiadiazolidin-3-one 1,1-dioxide and aryl





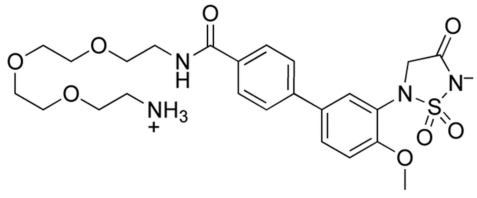
1 *R* = H
2 *R* = CH_3
3 *R* = OCH_3



4

Figure 1
The parent compound **1** and related compounds.

rings are twisted, rather than co-planar (Black *et al.*, 2005). It was further anticipated that installation of substituents such as methyl or methoxy groups on the aryl ring at the position *ortho* to the 1,2,5-thiadiazolidin-3-one 1,1-dioxide substituent would bias the conformation of the free ligand toward the twisted form, thus serving to 'pre-organize' the compounds for binding to the enzyme active site (Black *et al.*, 2005). Indeed, compounds **2** and **3** (K_i values of 100 and 70 μ*M*, respectively**)** display substantially higher affinities for PTP1B than does **1** (Black *et al.*, 2005). X-ray crystal structure analysis confirmed the twisted conformation of the 1,2,5-thiadiazolidin-3-one 1,1-dioxide and aryl ring systems in the protein–ligand co-crystal structure of **4** bound to PTP1B (Black *et al.*, 2005). The planes of these two rings are nearly perpendicular in the protein–ligand complex (dihedral angle of *ca* 88°, see: pdb code 2bgd). The ability of methyl and methoxy substituents to favor the twisted relationship between the 1,2,5-thiadiazolidin-3-one 1,1-dioxide and aryl rings in compounds like **2** and **3** has been studied computationally and the twisted relationship of these rings has been experimentally observed in the protein–ligand co-crystal structure of **4** with the enzyme PTP1B. However, to the best of our knowledge no crystal structures of free 5-aryl-1,2,5-thiadiazolidin-3-one 1,1-dioxides have been published. Herein, we describe the crystal structure of the title compound (I), shown in the scheme below, a derivative of compound **4**.



2. Structural commentary

The title compound (I), crystallized as a zwitterion (Fig. 2). The terminal amine N atom, N4, is protonated and the 1,2,5-thiadiazolidin-3-one 1,1-dioxide nitrogen atom, N1, is deprotonated. The [(2-{2-[2-(2-ammonioethoxy)ethoxy]ethoxy}ethyl)carbamoyl] side chain is folded over on itself with an intramolecular N—H···O hydrogen bond involving the ammonium group, N4, and an ether O atom, O7 (Table 1 and Fig. 2). The aryl rings of the biphenyl unit (C3–C8 and C9–C14) are inclined to one another by 20.81 (8)°. The 1,2,5-thiadiazolidin-3-one 1,1-dioxide ring (S1/N1/N2/C1/C2) has a shallow envelope conformation with nitrogen atom N2 as the flap. Its mean plane is inclined to the benzene ring to which it is attached (C3–C8) by 62.87 (8)°. This twisted relationship between the planes of the 1,2,5-thiadiazolidin-3-one 1,1-dioxide and aryl rings is substantially less than that seen in the protein–ligand co-crystal structure of **4** bound to PTP1B (Black *et al.*, 2005), where these two rings are nearly perpendicular to one another with a dihedral angle of *ca* 88° (see: Protein Data Bank entry: code 2bgd).

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

*Cg*1 is the centroid of the C3–C8 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H1*N*3···O3^{i}	0.82 (2)	2.22 (3)	3.012 (2)	161 (2)
N4—H1*N*4···O1^{ii}	0.93 (3)	2.29 (3)	3.010 (2)	133 (2)
N4—H1*N*4···O7	0.93 (3)	2.49 (3)	3.106 (2)	124 (2)
N4—H2*N*4···N1^{i}	1.03 (3)	1.82 (3)	2.821 (2)	163 (2)
N4—H3*N*4···O6^{iii}	0.98 (3)	1.99 (3)	2.942 (2)	162 (3)
C2—H2*B*···O3^{iv}	0.99	2.30	3.267 (2)	166
C18—H18*A*···N1^{i}	0.99	2.57	3.545 (2)	168
C22—H22*A*···O8^{ii}	0.99	2.63	3.343 (3)	129
C24—H24*A*···O5^{iii}	0.99	2.58	3.298 (2)	129
C21—H21*B*···*Cg*1^{ii}	0.99	2.70	3.555 (2)	165

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

3. Supramolecular features

In the crystal of (I), molecules are linked by N—H···O and N—H···N hydrogen bonds, forming slabs lying parallel to the ac plane (Fig. 3 and Table 1). Within the slabs there are also

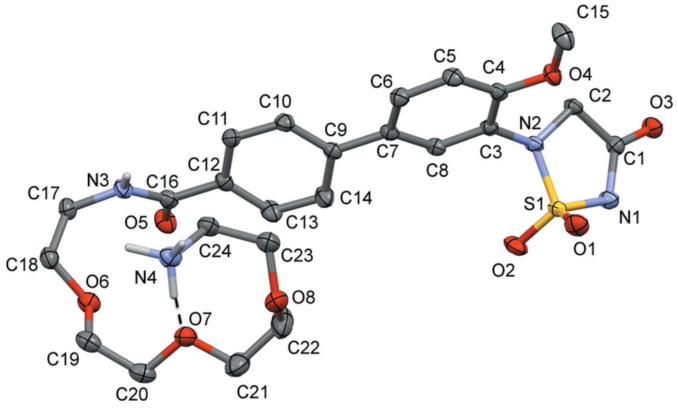


Figure 2
A view of the molecular structure of the title compound (I), showing the atom labelling. Displacement ellipsoids are drawn at the 50% probability level. The intramolecular N—H···O hydrogen bond is shown as a dashed line (see Table 1 for details) and C-bound H atoms have been omitted for clarity.

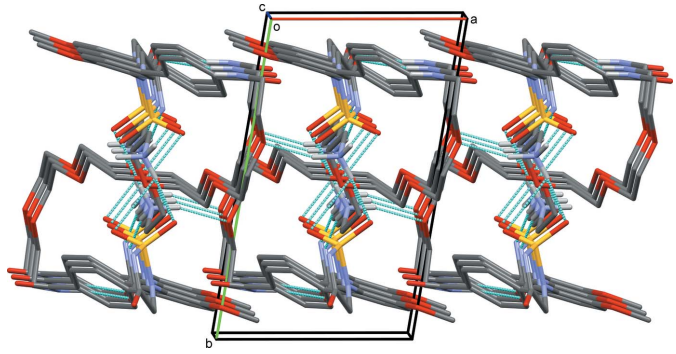


Figure 3
A view along the *c* axis of the crystal packing of the title compound. The N—H···O and N—H···O hydrogen bonds are shown as dashed lines (see Table 1 for details) and C-bound H atoms have been omitted for clarity.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{24}H_{32}N_4O_8S$
M_r	536.59
Crystal system, space group	Triclinic, $P\overline{1}$
Temperature (K)	100
a, b, c (Å)	7.3483 (2), 12.2233 (3), 13.9847 (4)
α, β, γ (°)	95.323 (1), 90.281 (2), 99.802 (1)
V (Å^3)	1232.16 (6)
Z	2
Radiation type	Cu $K\alpha$
μ (mm^{-1})	1.67
Crystal size (mm)	0.15 × 0.15 × 0.02
Data collection	
Diffractometer	Bruker APEXII CCD area detector
Absorption correction	Multi-scan (*SADABS*; Bruker, 2008)
T_{min}, T_{max}	0.89, 0.97
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	15014, 4539, 4292
R_{int}	0.017
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.617
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.039, 0.111, 1.03
No. of reflections	4539
No. of parameters	351
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.56, −0.33

Computer programs: *APEX2* and *SAINT* (Bruker, 2008), *SHELXS2013* (Sheldrick, 2008), *SHELXL2013* (Sheldrick, 2015) and *Mercury* (Macrae *et al.*, 2008).

C—H···O and C—H···N hydrogen bonds and C—H···π interactions present reinforcing the two-dimensional structure (Table 1).

4. Database survey

A search of the Cambridge Structural Database (Version 5.36; Groom & Allen, 2014) revealed no crystal structures of free 5-aryl-1,2,5-thiadiazolidin-3-one 1,1-dioxides. It did reveal the presence of five 1,2,5-thiadiazolidin-3-one 1,1-dioxide compounds substituted at the N atom in the 2-position. In the majority of these compounds, the five-membered 1,2,5-thiadiazolidine rings also have envelope conformations, with the N atom in the 5-position, as in compound (I), as the flap.

5. Synthesis and crystallization

The title compound was synthesized by amide bond formation between *tert*-butyl (2-{2-[2-(2-aminoethoxy)ethoxy]ethoxy}ethyl)carbamate and 3′-(1,1-dioxido-4-oxo-1,2,5-thiadiazolidin-2-yl)-4′-methoxy-[1,1′-biphenyl]-4-carboxylic acid *via* (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate. The precursors were synthesized according to published procedures (Black *et al.*, 2005; Schwabacher *et al.*, 1998). Full synthetic details will be published elsewhere. Single crystals of the title compound (I) were obtained by slow evaporation of a solution of (I) in methanol.

6. Refinement details

Crystal data, data collection and structure refinement details are summarized in Table 2. The N-bound H atoms were located in a difference Fourier map and freely refined. The C-bound H atoms were included in calculated positions and treated as riding: C—H = 0.95–0.99 Å with U_{iso}(H) = 1.5U_{eq}(C) for methyl H atoms and = 1.2U_{eq}(C) for other H atoms.

Acknowledgements

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supporting information

Acta Cryst. (2015). E**71**, 336-338 [doi:10.1107/S2056989015003850]

Crystal structure of 5-{4′-[(2-{2-[2-(2-ammonioethoxy)ethoxy]ethoxy}ethyl)-carbamoyl]-4-methoxy-[1,1′-biphenyl]-3-yl}-3-oxo-1,2,5-thiadiazolidin-2-ide 1,1-dioxide: a potential inhibitor of the enzyme protein tyrosine phosphatase 1B (PTP1B)

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Computing details

Data collection: *APEX2* (Bruker, 2008); cell refinement: *SAINT* (Bruker, 2008); data reduction: *SAINT* (Bruker, 2008); program(s) used to solve structure: *SHELXS2013* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL2013* (Sheldrick, 2015); molecular graphics: *Mercury* (Macrae *et al.*, 2008); software used to prepare material for publication: *SHELXL2013* (Sheldrick, 2015).

5-{4′-[(2-{2-[2-(2-Ammonioethoxy)ethoxy]ethoxy}ethyl)carbamoyl]-4-methoxy-[1,1′-biphenyl]-3-yl}-3-oxo-1,2,5-thiadiazolidin-2-ide 1,1-dioxide

Crystal data

$C_{24}H_{32}N_4O_8S$
$M_r = 536.59$
Triclinic, $P\overline{1}$
$a = 7.3483$ (2) Å
$b = 12.2233$ (3) Å
$c = 13.9847$ (4) Å
$\alpha = 95.323$ (1)°
$\beta = 90.281$ (2)°
$\gamma = 99.802$ (1)°
$V = 1232.16$ (6) Å^3
$Z = 2$
$F(000) = 568$
$D_x = 1.446$ Mg m^{-3}
Cu $K\alpha$ radiation, $\lambda = 1.54178$ Å
Cell parameters from 8971 reflections
$\theta = 3.2$–$71.7°$
$\mu = 1.67$ mm^{-1}
$T = 100$ K
Plate, colourless
0.15 × 0.15 × 0.02 mm

Data collection

Bruker APEXII CCD area-detector diffractometer
Radiation source: Incoatec microfocus Cu tube
ω and phi scans
Absorption correction: multi-scan (SADABS; Bruker, 2008)
$T_{min} = 0.89$, $T_{max} = 0.97$
15014 measured reflections
4539 independent reflections
4292 reflections with $I > 2\sigma(I)$
$R_{int} = 0.017$
$\theta_{max} = 72.1°$, $\theta_{min} = 3.2°$
$h = -8 \rightarrow 7$
$k = -15 \rightarrow 15$
$l = -16 \rightarrow 16$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.039$
$wR(F^2) = 0.111$
$S = 1.03$
4539 reflections

351 parameters	$w = 1/[\sigma^2(F_o^2) + (0.0647P)^2 + 0.8661P]$
0 restraints	where $P = (F_o^2 + 2F_c^2)/3$
Hydrogen site location: mixed	$(\Delta/\sigma)_{max} < 0.001$
H atoms treated by a mixture of independent and constrained refinement	$\Delta\rho_{max} = 0.56$ e Å^{-3}
	$\Delta\rho_{min} = -0.33$ e Å^{-3}

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. Maximum electron density of 0.56 e is in the vicinity of C21 in the extended chain and may represent very minor disorder.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
S1	0.52151 (5)	0.68948 (3)	0.09933 (3)	0.01945 (13)
O1	0.65998 (19)	0.61868 (11)	0.09811 (10)	0.0305 (3)
O2	0.35802 (18)	0.64660 (11)	0.14874 (10)	0.0317 (3)
O3	0.52042 (18)	0.86988 (10)	−0.09372 (9)	0.0266 (3)
O4	0.97456 (17)	0.88464 (10)	0.17601 (9)	0.0242 (3)
O5	−0.07338 (17)	0.81837 (11)	0.69084 (9)	0.0296 (3)
O6	−0.04449 (18)	0.63027 (11)	0.85611 (9)	0.0279 (3)
O7	0.16486 (19)	0.49974 (10)	0.73225 (10)	0.0305 (3)
O8	0.5123 (2)	0.49283 (11)	0.63370 (10)	0.0359 (3)
N1	0.4761 (2)	0.71885 (12)	−0.00657 (10)	0.0239 (3)
N2	0.6032 (2)	0.81729 (11)	0.14491 (10)	0.0221 (3)
N3	0.1468 (2)	0.84118 (12)	0.80862 (11)	0.0232 (3)
H1N3	0.256 (3)	0.8427 (18)	0.8228 (16)	0.027 (6)*
N4	0.5520 (3)	0.58747 (14)	0.82658 (12)	0.0291 (3)
H1N4	0.474 (4)	0.520 (3)	0.812 (2)	0.052 (8)*
H2N4	0.510 (3)	0.621 (2)	0.8909 (19)	0.041 (6)*
H3N4	0.685 (5)	0.585 (2)	0.831 (2)	0.058 (8)*
C1	0.5371 (2)	0.82684 (14)	−0.01819 (12)	0.0206 (3)
C2	0.6324 (2)	0.89346 (13)	0.07032 (11)	0.0198 (3)
H2A	0.7659	0.9167	0.0595	0.024*
H2B	0.5769	0.9607	0.0878	0.024*
C3	0.6802 (2)	0.83838 (13)	0.23985 (12)	0.0187 (3)
C4	0.8705 (2)	0.87285 (13)	0.25612 (12)	0.0204 (3)
C5	0.9381 (2)	0.89174 (14)	0.35051 (13)	0.0229 (4)
H5	1.0668	0.9150	0.3628	0.028*
C6	0.8188 (2)	0.87689 (14)	0.42708 (12)	0.0224 (3)
H6	0.8679	0.8896	0.4909	0.027*
C7	0.6289 (2)	0.84384 (13)	0.41224 (12)	0.0193 (3)
C8	0.5638 (2)	0.82427 (13)	0.31696 (12)	0.0197 (3)
H8	0.4352	0.8005	0.3047	0.024*
C9	0.4964 (2)	0.83521 (13)	0.49259 (12)	0.0195 (3)
C10	0.5441 (2)	0.88953 (14)	0.58384 (12)	0.0223 (3)

H10	0.6661	0.9293	0.5958	0.027*
C11	0.4178 (2)	0.88685 (14)	0.65740 (12)	0.0230 (4)
H11	0.4549	0.9235	0.7190	0.028*
C12	0.2375 (2)	0.83098 (13)	0.64171 (12)	0.0204 (3)
C13	0.1889 (3)	0.77461 (16)	0.55146 (13)	0.0282 (4)
H13	0.0665	0.7354	0.5396	0.034*
C14	0.3165 (3)	0.77503 (16)	0.47882 (13)	0.0281 (4)
H14	0.2816	0.7338	0.4187	0.034*
C15	1.1677 (3)	0.92460 (19)	0.18946 (15)	0.0334 (4)
H15A	1.1870	0.9942	0.2319	0.050*
H15B	1.2233	0.9383	0.1272	0.050*
H15C	1.2255	0.8687	0.2185	0.050*
C16	0.0893 (2)	0.82919 (14)	0.71575 (13)	0.0226 (4)
C17	0.0153 (3)	0.82894 (15)	0.88628 (13)	0.0270 (4)
H17A	−0.1093	0.8332	0.8612	0.032*
H17B	0.0500	0.8914	0.9369	0.032*
C18	0.0089 (3)	0.71993 (16)	0.92983 (13)	0.0273 (4)
H18A	0.1319	0.7157	0.9570	0.033*
H18B	−0.0813	0.7146	0.9822	0.033*
C19	0.0108 (3)	0.52875 (16)	0.87786 (14)	0.0294 (4)
H19A	−0.0770	0.4912	0.9229	0.035*
H19B	0.1350	0.5449	0.9090	0.035*
C20	0.0145 (3)	0.45443 (15)	0.78734 (15)	0.0303 (4)
H20A	0.0284	0.3787	0.8026	0.036*
H20B	−0.1026	0.4487	0.7505	0.036*
C21	0.1833 (3)	0.42988 (19)	0.64803 (17)	0.0431 (5)
H21A	0.0660	0.4151	0.6101	0.052*
H21B	0.2117	0.3577	0.6651	0.052*
C22	0.3357 (4)	0.4859 (2)	0.58984 (17)	0.0510 (6)
H22A	0.3335	0.4440	0.5256	0.061*
H22B	0.3141	0.5621	0.5807	0.061*
C23	0.6108 (3)	0.60309 (16)	0.65657 (15)	0.0344 (4)
H23A	0.5972	0.6482	0.6026	0.041*
H23B	0.7437	0.6005	0.6651	0.041*
C24	0.5416 (3)	0.65799 (15)	0.74680 (14)	0.0297 (4)
H24A	0.6178	0.7324	0.7631	0.036*
H24B	0.4123	0.6680	0.7366	0.036*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.0198 (2)	0.0170 (2)	0.0207 (2)	−0.00143 (15)	−0.00151 (15)	0.00555 (14)
O1	0.0350 (8)	0.0252 (6)	0.0340 (7)	0.0097 (5)	0.0005 (6)	0.0085 (5)
O2	0.0250 (7)	0.0316 (7)	0.0353 (7)	−0.0080 (5)	0.0031 (6)	0.0098 (6)
O3	0.0334 (7)	0.0249 (6)	0.0221 (6)	0.0042 (5)	−0.0041 (5)	0.0077 (5)
O4	0.0183 (6)	0.0312 (6)	0.0231 (6)	0.0026 (5)	0.0036 (5)	0.0060 (5)
O5	0.0197 (7)	0.0391 (7)	0.0312 (7)	0.0057 (5)	0.0018 (5)	0.0076 (6)
O6	0.0264 (7)	0.0275 (6)	0.0308 (7)	0.0055 (5)	0.0002 (5)	0.0065 (5)

O7	0.0299 (7)	0.0246 (6)	0.0351 (7)	0.0004 (5)	0.0045 (6)	0.0007 (5)
O8	0.0422 (8)	0.0267 (7)	0.0368 (7)	0.0029 (6)	0.0066 (6)	−0.0014 (6)
N1	0.0289 (8)	0.0204 (7)	0.0217 (7)	0.0008 (6)	−0.0043 (6)	0.0044 (6)
N2	0.0275 (8)	0.0182 (7)	0.0188 (7)	−0.0036 (5)	−0.0031 (6)	0.0064 (5)
N3	0.0194 (8)	0.0262 (8)	0.0237 (7)	0.0021 (6)	0.0040 (6)	0.0032 (6)
N4	0.0342 (10)	0.0243 (8)	0.0300 (8)	0.0068 (7)	−0.0004 (7)	0.0049 (6)
C1	0.0199 (8)	0.0219 (8)	0.0206 (8)	0.0042 (6)	−0.0002 (6)	0.0039 (6)
C2	0.0218 (8)	0.0176 (7)	0.0201 (8)	0.0006 (6)	−0.0006 (6)	0.0069 (6)
C3	0.0212 (8)	0.0158 (7)	0.0188 (8)	0.0015 (6)	−0.0018 (6)	0.0042 (6)
C4	0.0214 (9)	0.0180 (7)	0.0226 (8)	0.0035 (6)	0.0029 (7)	0.0049 (6)
C5	0.0166 (8)	0.0252 (8)	0.0263 (9)	0.0009 (6)	−0.0020 (7)	0.0035 (7)
C6	0.0219 (9)	0.0237 (8)	0.0212 (8)	0.0023 (6)	−0.0033 (7)	0.0026 (6)
C7	0.0206 (9)	0.0174 (7)	0.0205 (8)	0.0031 (6)	0.0002 (6)	0.0050 (6)
C8	0.0176 (8)	0.0189 (8)	0.0225 (8)	0.0015 (6)	−0.0012 (6)	0.0051 (6)
C9	0.0202 (9)	0.0188 (8)	0.0207 (8)	0.0039 (6)	−0.0003 (6)	0.0065 (6)
C10	0.0200 (9)	0.0226 (8)	0.0230 (8)	−0.0006 (6)	−0.0004 (7)	0.0031 (6)
C11	0.0266 (9)	0.0205 (8)	0.0210 (8)	0.0014 (6)	0.0001 (7)	0.0019 (6)
C12	0.0216 (9)	0.0201 (8)	0.0212 (8)	0.0052 (6)	0.0012 (6)	0.0072 (6)
C13	0.0204 (9)	0.0373 (10)	0.0251 (9)	−0.0017 (7)	−0.0024 (7)	0.0052 (7)
C14	0.0251 (10)	0.0365 (10)	0.0202 (8)	−0.0020 (7)	−0.0017 (7)	0.0019 (7)
C15	0.0175 (9)	0.0517 (12)	0.0328 (10)	0.0062 (8)	0.0031 (8)	0.0133 (9)
C16	0.0229 (10)	0.0196 (8)	0.0258 (9)	0.0033 (6)	0.0030 (7)	0.0053 (6)
C17	0.0255 (9)	0.0293 (9)	0.0252 (9)	0.0032 (7)	0.0081 (7)	0.0006 (7)
C18	0.0241 (9)	0.0340 (10)	0.0231 (8)	0.0022 (7)	0.0040 (7)	0.0038 (7)
C19	0.0231 (9)	0.0292 (9)	0.0367 (10)	0.0016 (7)	−0.0006 (8)	0.0131 (8)
C20	0.0226 (9)	0.0249 (9)	0.0438 (11)	0.0018 (7)	0.0007 (8)	0.0094 (8)
C21	0.0386 (12)	0.0417 (12)	0.0427 (12)	−0.0026 (9)	0.0010 (10)	−0.0108 (10)
C22	0.0471 (14)	0.0703 (17)	0.0295 (11)	−0.0007 (12)	0.0019 (10)	−0.0079 (10)
C23	0.0421 (12)	0.0263 (9)	0.0336 (10)	0.0014 (8)	0.0054 (9)	0.0049 (8)
C24	0.0369 (11)	0.0225 (9)	0.0296 (9)	0.0024 (7)	0.0016 (8)	0.0065 (7)

Geometric parameters (Å, º)

S1—O2	1.4341 (13)	C8—H8	0.9500
S1—O1	1.4429 (13)	C9—C10	1.397 (2)
S1—N1	1.6025 (14)	C9—C14	1.402 (3)
S1—N2	1.6429 (14)	C10—C11	1.388 (2)
O3—C1	1.237 (2)	C10—H10	0.9500
O4—C4	1.365 (2)	C11—C12	1.390 (2)
O4—C15	1.425 (2)	C11—H11	0.9500
O5—C16	1.226 (2)	C12—C13	1.395 (3)
O6—C19	1.428 (2)	C12—C16	1.505 (2)
O6—C18	1.435 (2)	C13—C14	1.386 (3)
O7—C21	1.410 (2)	C13—H13	0.9500
O7—C20	1.414 (2)	C14—H14	0.9500
O8—C22	1.419 (3)	C15—H15A	0.9800
O8—C23	1.424 (2)	C15—H15B	0.9800
N1—C1	1.345 (2)	C15—H15C	0.9800

N2—C3	1.425 (2)	C17—C18	1.509 (3)
N2—C2	1.454 (2)	C17—H17A	0.9900
N3—C16	1.351 (2)	C17—H17B	0.9900
N3—C17	1.459 (2)	C18—H18A	0.9900
N3—H1N3	0.82 (2)	C18—H18B	0.9900
N4—C24	1.481 (2)	C19—C20	1.491 (3)
N4—H1N4	0.93 (3)	C19—H19A	0.9900
N4—H2N4	1.03 (3)	C19—H19B	0.9900
N4—H3N4	0.98 (3)	C20—H20A	0.9900
C1—C2	1.515 (2)	C20—H20B	0.9900
C2—H2A	0.9900	C21—C22	1.496 (3)
C2—H2B	0.9900	C21—H21A	0.9900
C3—C8	1.385 (2)	C21—H21B	0.9900
C3—C4	1.401 (2)	C22—H22A	0.9900
C4—C5	1.393 (2)	C22—H22B	0.9900
C5—C6	1.393 (2)	C23—C24	1.505 (3)
C5—H5	0.9500	C23—H23A	0.9900
C6—C7	1.394 (2)	C23—H23B	0.9900
C6—H6	0.9500	C24—H24A	0.9900
C7—C8	1.399 (2)	C24—H24B	0.9900
C7—C9	1.490 (2)		

O2—S1—O1	113.21 (8)	C14—C13—H13	119.5
O2—S1—N1	112.24 (8)	C12—C13—H13	119.5
O1—S1—N1	111.49 (8)	C13—C14—C9	121.12 (17)
O2—S1—N2	109.69 (8)	C13—C14—H14	119.4
O1—S1—N2	111.90 (8)	C9—C14—H14	119.4
N1—S1—N2	97.26 (7)	O4—C15—H15A	109.5
C4—O4—C15	117.63 (14)	O4—C15—H15B	109.5
C19—O6—C18	112.83 (14)	H15A—C15—H15B	109.5
C21—O7—C20	111.72 (15)	O4—C15—H15C	109.5
C22—O8—C23	115.10 (18)	H15A—C15—H15C	109.5
C1—N1—S1	111.85 (12)	H15B—C15—H15C	109.5
C3—N2—C2	125.75 (13)	O5—C16—N3	123.27 (16)
C3—N2—S1	120.81 (11)	O5—C16—C12	120.31 (16)
C2—N2—S1	111.22 (11)	N3—C16—C12	116.41 (16)
C16—N3—C17	121.27 (16)	N3—C17—C18	112.19 (15)
C16—N3—H1N3	120.7 (16)	N3—C17—H17A	109.2
C17—N3—H1N3	116.9 (15)	C18—C17—H17A	109.2
C24—N4—H1N4	108.5 (17)	N3—C17—H17B	109.2
C24—N4—H2N4	113.3 (14)	C18—C17—H17B	109.2
H1N4—N4—H2N4	107 (2)	H17A—C17—H17B	107.9
C24—N4—H3N4	102.2 (17)	O6—C18—C17	108.55 (14)
H1N4—N4—H3N4	117 (2)	O6—C18—H18A	110.0
H2N4—N4—H3N4	109 (2)	C17—C18—H18A	110.0
O3—C1—N1	124.30 (16)	O6—C18—H18B	110.0
O3—C1—C2	121.76 (15)	C17—C18—H18B	110.0
N1—C1—C2	113.94 (14)	H18A—C18—H18B	108.4

N2—C2—C1	104.42 (13)	O6—C19—C20	109.31 (15)
N2—C2—H2A	110.9	O6—C19—H19A	109.8
C1—C2—H2A	110.9	C20—C19—H19A	109.8
N2—C2—H2B	110.9	O6—C19—H19B	109.8
C1—C2—H2B	110.9	C20—C19—H19B	109.8
H2A—C2—H2B	108.9	H19A—C19—H19B	108.3
C8—C3—C4	119.87 (15)	O7—C20—C19	108.74 (15)
C8—C3—N2	118.94 (15)	O7—C20—H20A	109.9
C4—C3—N2	121.19 (15)	C19—C20—H20A	109.9
O4—C4—C5	125.49 (16)	O7—C20—H20B	109.9
O4—C4—C3	115.86 (15)	C19—C20—H20B	109.9
C5—C4—C3	118.65 (15)	H20A—C20—H20B	108.3
C6—C5—C4	120.62 (16)	O7—C21—C22	109.08 (18)
C6—C5—H5	119.7	O7—C21—H21A	109.9
C4—C5—H5	119.7	C22—C21—H21A	109.9
C5—C6—C7	121.50 (16)	O7—C21—H21B	109.9
C5—C6—H6	119.3	C22—C21—H21B	109.9
C7—C6—H6	119.3	H21A—C21—H21B	108.3
C6—C7—C8	117.06 (15)	O8—C22—C21	112.5 (2)
C6—C7—C9	122.74 (15)	O8—C22—H22A	109.1
C8—C7—C9	120.11 (15)	C21—C22—H22A	109.1
C3—C8—C7	122.29 (16)	O8—C22—H22B	109.1
C3—C8—H8	118.9	C21—C22—H22B	109.1
C7—C8—H8	118.9	H22A—C22—H22B	107.8
C10—C9—C14	117.26 (16)	O8—C23—C24	111.71 (16)
C10—C9—C7	121.45 (15)	O8—C23—H23A	109.3
C14—C9—C7	121.26 (15)	C24—C23—H23A	109.3
C11—C10—C9	121.63 (16)	O8—C23—H23B	109.3
C11—C10—H10	119.2	C24—C23—H23B	109.3
C9—C10—H10	119.2	H23A—C23—H23B	107.9
C10—C11—C12	120.59 (16)	N4—C24—C23	109.41 (16)
C10—C11—H11	119.7	N4—C24—H24A	109.8
C12—C11—H11	119.7	C23—C24—H24A	109.8
C11—C12—C13	118.37 (16)	N4—C24—H24B	109.8
C11—C12—C16	123.98 (16)	C23—C24—H24B	109.8
C13—C12—C16	117.63 (16)	H24A—C24—H24B	108.2
C14—C13—C12	120.93 (17)		

O2—S1—N1—C1	121.10 (13)	C9—C7—C8—C3	175.66 (14)
O1—S1—N1—C1	−110.68 (13)	C6—C7—C9—C10	19.1 (2)
N2—S1—N1—C1	6.33 (14)	C8—C7—C9—C10	−157.39 (16)
O2—S1—N2—C3	68.27 (15)	C6—C7—C9—C14	−162.95 (16)
O1—S1—N2—C3	−58.24 (15)	C8—C7—C9—C14	20.6 (2)
N1—S1—N2—C3	−174.93 (14)	C14—C9—C10—C11	−1.7 (3)
O2—S1—N2—C2	−127.73 (12)	C7—C9—C10—C11	176.34 (15)
O1—S1—N2—C2	105.76 (13)	C9—C10—C11—C12	−1.1 (3)
N1—S1—N2—C2	−10.94 (13)	C10—C11—C12—C13	2.2 (2)
S1—N1—C1—O3	179.31 (14)	C10—C11—C12—C16	−176.56 (15)

S1—N1—C1—C2	0.00 (19)	C11—C12—C13—C14	−0.6 (3)
C3—N2—C2—C1	174.45 (15)	C16—C12—C13—C14	178.28 (17)
S1—N2—C2—C1	11.42 (16)	C12—C13—C14—C9	−2.3 (3)
O3—C1—C2—N2	173.35 (16)	C10—C9—C14—C13	3.4 (3)
N1—C1—C2—N2	−7.3 (2)	C7—C9—C14—C13	−174.70 (17)
C2—N2—C3—C8	127.60 (17)	C17—N3—C16—O5	7.3 (3)
S1—N2—C3—C8	−70.86 (19)	C17—N3—C16—C12	−173.40 (14)
C2—N2—C3—C4	−52.4 (2)	C11—C12—C16—O5	151.68 (17)
S1—N2—C3—C4	109.13 (16)	C13—C12—C16—O5	−27.1 (2)
C15—O4—C4—C5	−3.1 (2)	C11—C12—C16—N3	−27.6 (2)
C15—O4—C4—C3	177.13 (15)	C13—C12—C16—N3	153.56 (16)
C8—C3—C4—O4	−179.96 (14)	C16—N3—C17—C18	105.25 (19)
N2—C3—C4—O4	0.1 (2)	C19—O6—C18—C17	157.75 (15)
C8—C3—C4—C5	0.3 (2)	N3—C17—C18—O6	−59.8 (2)
N2—C3—C4—C5	−179.71 (15)	C18—O6—C19—C20	−159.42 (15)
O4—C4—C5—C6	−179.90 (15)	C21—O7—C20—C19	176.42 (17)
C3—C4—C5—C6	−0.2 (2)	O6—C19—C20—O7	70.69 (19)
C4—C5—C6—C7	−0.6 (3)	C20—O7—C21—C22	176.10 (19)
C5—C6—C7—C8	1.1 (2)	C23—O8—C22—C21	−119.2 (2)
C5—C6—C7—C9	−175.45 (15)	O7—C21—C22—O8	69.3 (3)
C4—C3—C8—C7	0.3 (2)	C22—O8—C23—C24	78.5 (2)
N2—C3—C8—C7	−179.69 (14)	O8—C23—C24—N4	55.8 (2)
C6—C7—C8—C3	−1.0 (2)		

Hydrogen-bond geometry (Å, º)

Cg1 is the centroid of the C3–C8 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H1*N*3···O3^{i}	0.82 (2)	2.22 (3)	3.012 (2)	161 (2)
N4—H1*N*4···O1^{ii}	0.93 (3)	2.29 (3)	3.010 (2)	133 (2)
N4—H1*N*4···O7	0.93 (3)	2.49 (3)	3.106 (2)	124 (2)
N4—H2*N*4···N1^{i}	1.03 (3)	1.82 (3)	2.821 (2)	163 (2)
N4—H3*N*4···O6^{iii}	0.98 (3)	1.99 (3)	2.942 (2)	162 (3)
C2—H2*B*···O3^{iv}	0.99	2.30	3.267 (2)	166
C18—H18*A*···N1^{i}	0.99	2.57	3.545 (2)	168
C22—H22*A*···O8^{ii}	0.99	2.63	3.343 (3)	129
C24—H24*A*···O5^{iii}	0.99	2.58	3.298 (2)	129
C21—H21*B*···*Cg*1^{ii}	0.99	2.70	3.555 (2)	165

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