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Crystal structure and Hirshfeld surface analysis of (Z)-4-{[4-(3-methyl-3-phenylcyclobutyl)thiazol-2-yl]amino}-4-oxobut-2-enoic acid

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The title cyclobutyl compound, $C_{18}H_{18}N_2O_3S$, was synthesized by the interaction of 4-(3-methyl-3-phenylcyclobutyl)thiazol-2-amine and maleic anhydride, and crystallizes in the orthorhombic space group $P2_12_12_1$ with $Z' = 1$. The molecular geometry is partially stabilized by an intramolecular N—H⋯O hydrogen bond forming an $S_1^1(7)$ ring motif. The molecule is non-planar with a dihedral angle of 88.29 (11)° between the thiazole and benzene rings. In the crystal, the molecules are linked by O—H⋯N hydrogen bonds, forming supramolecular ribbons with $C_1^1(9)$ chain motifs. To further analyze the intermolecular interactions, a Hirshfeld surface analysis was performed. The results indicate that the most important contributions to the overall surface are from H⋯H (43%), C⋯H (18%), O⋯H (17%) and N⋯H (6%), interactions.

1. Chemical context

Cyclobutanes are four-membered carbocycles, which present a unique structural feature in bioactive natural products. Many natural cyclobutanes contain various substituents (Hui *et al.*, 2021). Complex derivatives of cyclobutanes have an important place in biology and biotechnology (Dinçer *et al.*, 2004). In addition, it has been shown that 3-substituted cyclobutane carboxylic acid derivatives exhibit anti-inflammatory and antidepressant activities (Dehmlow & Schmidt, 1990), and can also form liquid crystals (Coghi *et al.*, 1976). In addition, thiazole is a heterocyclic organic compound that has a five-membered ring containing three carbon, one sulfur, and one nitrogen atoms. Thiazoles are found in many potent biologically active compounds, such as sulfathiazole (antimicrobial drug), ritonavir (antiretroviral drug), abafungin (antifungal drug), bleomycine, and tiazofurin (antineoplastic drug) (Kashyap *et al.*, 2012; Mohapatra *et al.*, 2019). In this study, (Z)-4-{[4-(3-methyl-3-phenylcyclobutyl)thiazol-2-yl]amino}-4-oxobut-2-enoic acid was synthesized from 4-(3-methyl-3-phenylcyclobutyl)thiazol-2-amine and maleic anhydride and was characterized by single crystal X-ray diffraction and the crystal packing was analyzed using Hirshfeld surface analysis.

2. Structural commentary

The title cyclobutyl derivative crystallizes in the orthorhombic $P2_12_12_1$ space group with $Z' = 1$. Its molecular structure is
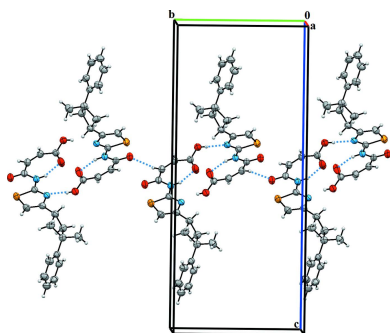
illustrated in Fig. 1, showing the intramolecular N—H⋯O hydrogen bond forming an $S_1^1(7)$ ring motif. The molecule is non-planar as the thiazole and benzene rings are twisted with respect to each other, subtending a dihedral angle of 88.29 (11)°. In addition, the cyclobutyl ring is twisted by 58.1 (2) and 40.2 (2)°, with respect to the thiazole, and benzene rings. In the thiazole ring, the C12—N1 bond length is 1.386 (4) Å and classified as a single bond.
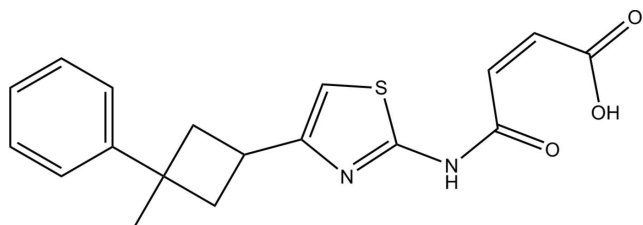
The cyclobutane adopts a puckered (butterfly) conformation. The average carbon–carbon (C—C) bond lengths within the ring is 1.5506 Å, with average C—C—C bond angles of 88.89°, while the average torsion angle within the C_4 ring is 15.83°. When these parameters are compared with the recently published cyclobutane derivatives (Gumus *et al.*, 2021), it is seen that there are no considerable differences. The S1—C13 and S1—C14 bond lengths are 1.727 (4) and 1.716 (3) Å, typical of a single bond. These values are comparable to those reported previously [1.718 (4) Å (Kansiz *et al.*, 2021) and 1.727 (9) Å (Qadir *et al.*, 2021)], but are longer than the values of 1.685 (4) and 1.698 (3) Å reported by Albayati *et al.* (2020).

3. Supramolecular features

The crystal packing of the title compound (Fig. 2) features intermolecular hydrogen bonds (C16—H16⋯O1^i and O3—H3A⋯N1^{ii}; symmetry codes are given in Table 1). In the crystal, the molecules are linked by O3—H3A⋯N1 hydrogen bonds forming supramolecular ribbons *via* $C_1^1(9)$ motifs. Adjacent ribbons are connected by C16—H16⋯O1 hydrogen bonds, leading to the formation of layers lying parallel to the *bc* plane.
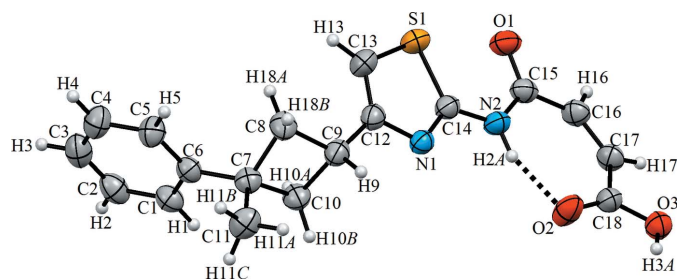

Figure 1
The molecular structure of the title compound with displacement ellipsoids drawn at the 40% probability level. Dashed lines denote the intramolecular N—H⋯O hydrogen bonds forming an $S_1^1(7)$ ring motif.

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

D—H⋯A	D—H	H⋯A	D⋯A	D—H⋯A
C16—H16⋯O1^i	0.93	2.35	3.233 (4)	159
N2—H2A⋯O2	0.86	1.83	2.651 (4)	158
O3—H3A⋯N1^{ii}	0.82	1.81	2.607 (3)	165

Symmetry codes: (i) $x - \frac{1}{2}, -y + \frac{5}{2}, -z + 1$; (ii) $x - \frac{1}{2}, -y + \frac{3}{2}, -z + 1$.

4. Database survey

A search of the Cambridge Structural Database (CSD Version 5.42, update of September 2021; Groom *et al.*, 2016) for the 4-(3-methyl-3-phenylcyclobutyl)thiazole moiety gave several hits including 4-{[4-(3-mesityl-3-methylcyclobutyl)-1,3-thiazol-2-yl]amino}-4-oxobutanoic acid dihydrate (CIBQIP; Şen *et al.*, 2013), 2-[4-(3-(2,5-dimethylphenyl)-3-methylcyclobutyl)-1,3-thiazol-2-yl)-1H-isoindole-1,3(2H)-dione (HAMKAJ; Öz-demir *et al.*, 2010), 2-chloro-N-[4-(3-methyl-3-phenylcyclo-butyl)-1,3-thiazol-2-yl]-N'-(naphthalen-1-ylmethylidene)ace-tohydrazide (IJULIJ; Inkaya *et al.*, 2011*a*), N-[4-(3-methyl-3-phenylcyclobutyl)-1,3-thiazol-2-yl]acetamide (LUXDIU; Ekici *et al.*, 2020), N'-benzylidene-2-chloro-N-[4-(3-methyl-3-phenylcyclobutyl)-1,3-thiazol-2-yl]acetohydrazide (PICZUY; Demir *et al.*, 2012), 2-chloro-N'-[4-(dimethylamino)benzyl-idene]-N-[4-(3-methyl-3-phenylcyclobutyl)-1,3-thiazol-2-yl]-acetohydrazide (QAKFUF; Inkaya *et al.*, 2011*b*), 2-chloro-N'-(2-furylmethylene)-N-[4-(3-methyl-3-phenylcyclobutyl)-1,3-thiazol-2-yl]acetohydrazide (URECEB; Demir *et al.*, 2016) and 4-[4-(3-mesityl-3-methylcyclobutyl)-1,3-thiazol-2-yl]-1-thia-4-azaspiro[4.5]decan-3-one (VOXBER; Şen *et al.*, 2015). In LUXDIU (Ekici *et al.*, 2020), the cyclobutyl ring has puckering parameters Q = 0.240 (4) Å and θ = 17.67 (2)°, that are close to those for the title compound [Q = 0.216 (2) Å and
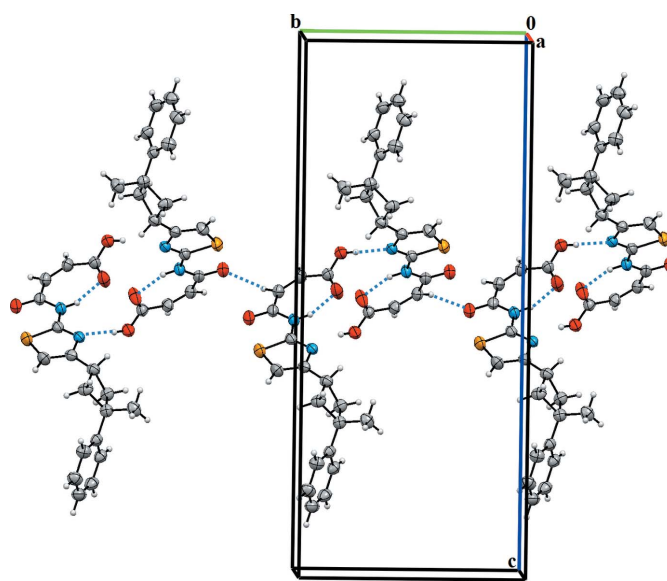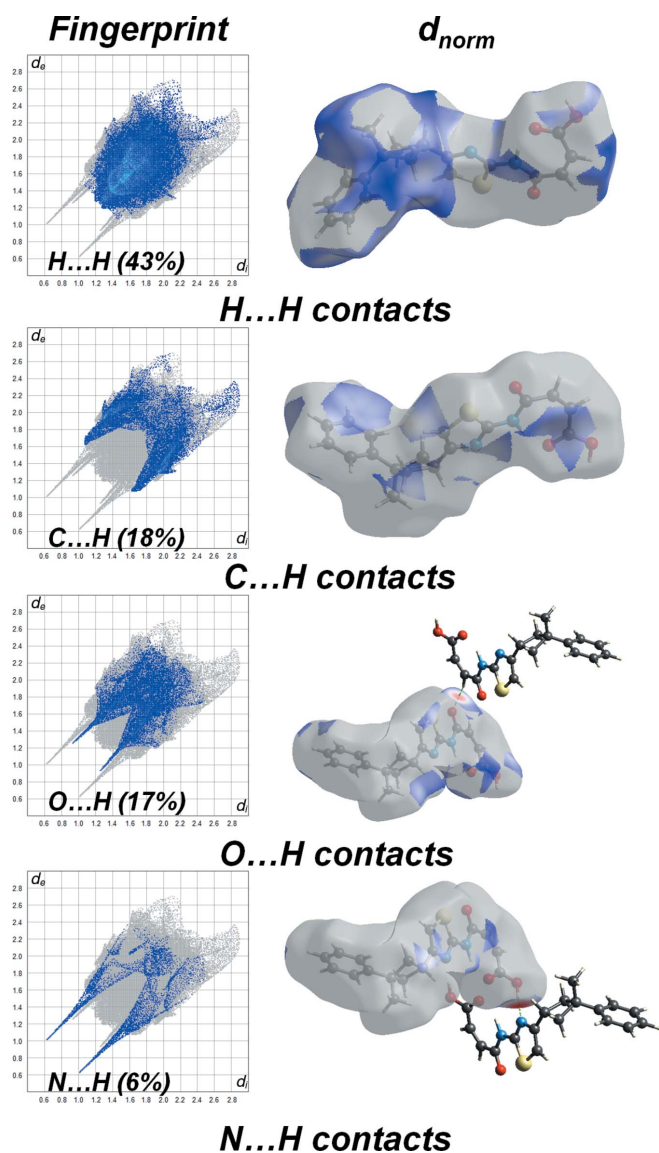

Figure 2
A view of the crystal packing of the title compound. Blue dashed lines denote the intermolecular O3—H3A⋯N1 hydrogen bonds forming a $C_1^1(9)$ motif (Table 1).

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$\theta = 15.83\,(5)°$]. The cyclobutane ring is puckered, with a dihedral angle of 25.20 (5)° in IJULIJ (Inkaya *et al.*, 2011*a*) and 22.99 (47)° in QAKFUF (Inkaya *et al.*, 2011*b*). In HAMKAJ (Özdemir *et al.*, 2010), the cyclobutane ring has a puckered conformation with 28.84 (22)°. This value is significantly bigger than those in the literature; 20.03 (3)° (PICZUY; Demir *et al.*, 2012) and 18.9 (3)° (CIBQIP; Şen *et al.*, 2013). In the title compound, the C—S bond lengths within the thiazole ring are 1.727 (4) and 1.716 (3) Å, which are congruent with similar examples from the literature, 1.697 (6) and 1.739 (6) Å (VOXBER; Şen *et al.*, 2015) and 1.701 (4) and 1.726 (2) Å (URECEB; Demir *et al.*, 2016). These values are shorter than the standard value for a Csp^2—S single bond (1.76 Å). In all structures, the phenyl and thiazole rings are *cis*-related with respect to the cyclobutane ring. The asymmetric units in all above-mentioned examples contain only one molecule.
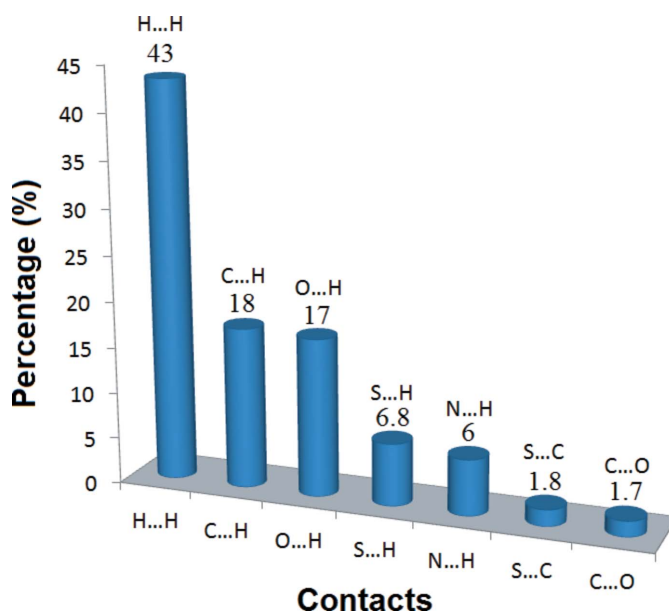

Figure 3
The Hirshfeld surface analysis of the title compound mapped with d_{norm} over the range −0.763 to 1.558 showing C—H⋯O and O—H⋯N hydrogen-bonded contacts.

5. Hirshfeld surface analysis

To compare quantitatively the different intermolecular interactions affecting the molecular packing in the studied compound, the Hirshfeld surface analysis was employed. The strength of the present intermolecular interactions can be displayed on the Hirshfeld surface (Spackman & Jayatilaka, 2009) generated by *CrystalExplorer17* (Turner *et al.*, 2017), here indicated by the red spots (Fig. 3). Furthermore, the Hirshfeld surface analysis is a valuable tool for predicting the properties of a crystal and its potential applications (Al-thamili *et al.*, 2020; Ilmi *et al.*, 2020). The contributions of the different types of intermolecular interactions for the title compound are shown in the two-dimensional fingerprint plots in Fig. 3. Fig. 4 displays the diverse contacts and their percentages observed in the crystal structure of the $C_{18}H_{18}O_3S$ compound based on the Hirshfeld calculations. The molecular packing of the title compound is mainly controlled by relatively strong O⋯H (17%) and N⋯H (6%) interactions ions and by abundant, but weaker, H⋯H (43%) and C⋯H (18%) 8%) van der Waals type interactions. S⋯H (6.8%), S⋯C (1.8%), C⋯O (1.7%), C⋯C (1.7%) and C⋯N (1.5%) contacts are also present. The corresponding fingerprint plots and decomposed d_{norm} maps for these interactions are shown in Fig. 3. The results also indicate the presence of N—H⋯O, C—H⋯O and O—H⋯N hydrogen bonds.

6. Synthesis and crystallization

A mixture of 4-(3-methyl-3-phenylcyclobutyl)thiazol-2-amine (2.4436 g, 10 mmol) and maleic anhydride (0.9806 g, 10 mmol) in 20 mL of dry toluene under argon atmosphere was refluxed for 12 h (monitored by TLC). Solvent was removed under reduced pressure and the residue crystallized from ethanol in the form of brilliant yellow crystals. The reaction scheme is

Figure 4
Intermolecular interactions and their percentages in $C_{18}H_{18}N_2O_3S$.
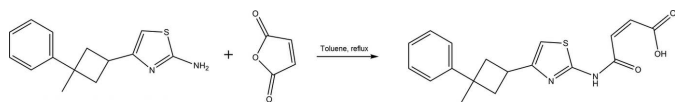
Figure 5
The synthesis of (Z)-4-{[4-(3-methyl-3-phenylcyclobutyl)thiazol-2-yl]amino}-4-oxobut-2-enoic acid.

shown in Fig. 5. Yield 94%, m.p. 460 K. Characteristic IR bands (cm^{-1}): 2975–2855 ν(C—H aliphatics), 1670 ν(C=O), 1626 ν(C=O), 1569 ν(C=N azomethine), 699 ν(C—S—C). Characteristic ^{1}H NMR shifts (THF-d_8 + acetone-d_6, TMS, ppm): 1.26 (s, 3H, –CH$_3$), 2.15–2.20 (m, 2H, –CH$_2$– in cyclobutane ring), 2.31–2.36 (m, 2H, –CH$_2$– in cyclobutane ring), 3.48 (quint, J = 9.2 Hz, 2H, >CH– in cyclobutane ring), 6.10 (d, J = 12.8 Hz, 1H, –CH=), 6.27 (d, J = 12.4 Hz, 1H, =CH–), 6.50 (s, 1H, S—CH= in thiazole ring), 6.89–6.92 (m, 3H, aromatics), 7.00 (m, 2H, aromatics). –OH and –NH– protons of this molecule have not been determined in the ^{1}H NMR spectrum. Characteristic ^{13}C NMR shifts (THF-d_8 + acetone-d_6, TMS, ppm): 165.30, 162.65, 156.96, 154.69, 152.29, 132.00, 130.84, 127.71, 124.81, 124.21, 107.19, 40.25, 38.16, 30.20, 29.35.

7. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. Although the acidic protons from the O–H and N–H bonds could be located in the difference-Fourier map, even very strong distance restraints were not sufficient to obtain proper distances between the parent atom and hydrogen. Therefore, both protons were refined in geometrical positions using the corresponding AFIX instructions with O—H = 0.82 Å and U_{iso}(H) = 1.5U_{eq}(O), and N—H = 0.86 Å and U_{iso}(H) = 1.2U_{eq}(N), respectively. The C-bound H atoms were positioned geometrically (C—H = 0.93, 0.96, 0.97 and 0.98 Å) and refined using a riding model, with U_{iso}(H) = 1.5U_{eq}(C) for methyl H atoms and 1.2U_{eq}(C) for other H atoms.

Table 2
Experimental details.

Crystal data	
Chemical formula	C$_{18}$H$_{18}$N$_2$O$_3$S
M_r	342.40
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	296
a, b, c (Å)	5.9685 (4), 11.0580 (9), 26.215 (2)
V (Å^3)	1730.2 (2)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.21
Crystal size (mm)	0.78 × 0.71 × 0.59
Data collection	
Diffractometer	Stoe IPDS 2
Absorption correction	Integration (X-RED32; Stoe & Cie, 2002)
T_{min}, T_{max}	0.832, 0.899
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	7546, 3338, 2648
R_{int}	0.058
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.617
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.045, 0.113, 0.97
No. of reflections	3338
No. of parameters	218
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.20, −0.16
Absolute structure	Flack x determined using 907 quotients [$(I^+)-(I^-)$]/[$(I^+)+(I^-)$] (Parsons et al., 2013)
Absolute structure parameter	−0.05 (8)

Computer programs: X-AREA and X-RED32 (Stoe & Cie, 2002), SHELXT2014/5 (Sheldrick, 2015a), SHELXL2017/1 (Sheldrick, 2015b), ORTEP-3 for Windows and WinGX (Farrugia, 2012) and PLATON (Spek, 2020).

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supporting information

Crystal structure and Hirshfeld surface analysis of (*Z*)-4-{[4-(3-methyl-3-phenyl-cyclobutyl)thiazol-2-yl]amino}-4-oxobut-2-enoic acid

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Computing details

Data collection: *X-AREA* (Stoe & Cie, 2002); cell refinement: *X-AREA* (Stoe & Cie, 2002); data reduction: *X-RED32* (Stoe & Cie, 2002); program(s) used to solve structure: *SHELXT2014/5* (Sheldrick, 2015a); program(s) used to refine structure: *SHELXL2017/1* (Sheldrick, 2015b); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 2012); software used to prepare material for publication: *WinGX* (Farrugia, 2012) and *PLATON* (Spek, 2020).

(*Z*)-4-{[4-(3-Methyl-3-phenylcyclobutyl)thiazol-2-yl]amino}-4-oxobut-2-enoic acid

Crystal data

$C_{18}H_{18}N_2O_3S$	$D_x = 1.314$ Mg m^{-3}
$M_r = 342.40$	Melting point: 460 K
Orthorhombic, $P2_12_12_1$	Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
$a = 5.9685$ (4) Å	Cell parameters from 7998 reflections
$b = 11.0580$ (9) Å	$\theta = 1.6$–$27.3°$
$c = 26.215$ (2) Å	$\mu = 0.21$ mm^{-1}
$V = 1730.2$ (2) Å^3	$T = 296$ K
$Z = 4$	Prism, light yellow
$F(000) = 720$	$0.78 \times 0.71 \times 0.59$ mm

Data collection

Stoe IPDS 2 diffractometer	7546 measured reflections
Radiation source: sealed X-ray tube, 12 x 0.4 mm long-fine focus	3338 independent reflections
	2648 reflections with $I > 2\sigma(I)$
Detector resolution: 6.67 pixels mm^{-1}	$R_{int} = 0.058$
rotation method scans	$\theta_{max} = 26.0°$, $\theta_{min} = 1.6°$
Absorption correction: integration (X-RED32; Stoe & Cie, 2002)	$h = -7 \rightarrow 7$
	$k = -13 \rightarrow 12$
$T_{min} = 0.832$, $T_{max} = 0.899$	$l = -32 \rightarrow 30$

Refinement

Refinement on F^2	0 restraints
Least-squares matrix: full	Primary atom site location: structure-invariant direct methods
$R[F^2 > 2\sigma(F^2)] = 0.045$	
$wR(F^2) = 0.113$	Secondary atom site location: difference Fourier map
$S = 0.97$	
3338 reflections	Hydrogen site location: inferred from neighbouring sites
218 parameters	

H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0679P)^2]$
    where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.20$ e Å^{-3}
$\Delta\rho_{min} = -0.16$ e Å^{-3}

Extinction correction: SHELXL2017/1
    (Sheldrick 2015b),
    $Fc^* = kFc[1+0.001 \text{x} Fc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.014 (3)
Absolute structure: Flack x determined using
    907 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter: −0.05 (8)

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.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	y	z	U_{iso}*/U_{eq}
C1	0.4002 (6)	0.8359 (3)	0.80585 (12)	0.0711 (8)
H1	0.274222	0.794587	0.794336	0.085*
C2	0.4122 (8)	0.8741 (4)	0.85639 (13)	0.0839 (11)
H2	0.293567	0.858606	0.878430	0.101*
C3	0.5971 (8)	0.9343 (4)	0.87390 (14)	0.0897 (12)
H3	0.604483	0.958968	0.907768	0.108*
C4	0.7710 (7)	0.9581 (4)	0.84151 (14)	0.0877 (11)
H4	0.896441	0.999348	0.853340	0.105*
C5	0.7611 (6)	0.9208 (4)	0.79108 (13)	0.0764 (9)
H5	0.880417	0.937415	0.769367	0.092*
C6	0.5764 (5)	0.8595 (3)	0.77256 (11)	0.0626 (7)
C7	0.5717 (5)	0.8175 (3)	0.71772 (11)	0.0642 (8)
C8	0.6388 (6)	0.9135 (4)	0.67725 (13)	0.0751 (9)
H8A	0.628167	0.996095	0.689444	0.090*
H8B	0.783448	0.898561	0.661620	0.090*
C9	0.4381 (6)	0.8741 (3)	0.64378 (12)	0.0695 (8)
H9	0.486075	0.814897	0.618184	0.083*
C10	0.3400 (5)	0.8091 (4)	0.69128 (12)	0.0706 (9)
H10A	0.223403	0.854686	0.708437	0.085*
H10B	0.291717	0.726837	0.684630	0.085*
C11	0.7026 (7)	0.6997 (4)	0.71183 (14)	0.0864 (10)
H11A	0.698104	0.674197	0.676846	0.130*
H11B	0.855370	0.712428	0.721945	0.130*
H11C	0.636589	0.638486	0.732996	0.130*
C12	0.2935 (6)	0.9681 (3)	0.62006 (11)	0.0664 (8)
C13	0.3006 (7)	1.0888 (3)	0.62654 (14)	0.0823 (10)
H13	0.408013	1.128814	0.645944	0.099*
C14	−0.0010 (6)	1.0208 (3)	0.57345 (11)	0.0636 (8)
C15	−0.3247 (6)	1.0930 (3)	0.52675 (12)	0.0682 (8)
C16	−0.5193 (6)	1.0635 (3)	0.49439 (13)	0.0712 (9)
H16	−0.622658	1.126176	0.491776	0.085*

C17	−0.5769 (6)	0.9646 (3)	0.46806 (12)	0.0710 (8)
H17	−0.714462	0.969359	0.451502	0.085*
C18	−0.4561 (6)	0.8490 (3)	0.46116 (12)	0.0674 (8)
N1	0.1187 (4)	0.9299 (2)	0.58924 (9)	0.0609 (6)
N2	−0.1832 (5)	1.0037 (2)	0.54206 (10)	0.0677 (7)
H2A	−0.209319	0.931474	0.531402	0.081*
O1	−0.2951 (5)	1.1985 (2)	0.54005 (10)	0.0859 (7)
O2	−0.3074 (5)	0.8116 (2)	0.48857 (12)	0.0998 (9)
O3	−0.5286 (4)	0.7906 (2)	0.42168 (8)	0.0776 (7)
H3A	−0.459781	0.726735	0.418911	0.116*
S1	0.0856 (2)	1.16026 (8)	0.59435 (4)	0.0829 (3)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0678 (18)	0.073 (2)	0.0730 (18)	0.0039 (18)	0.0067 (16)	0.0099 (16)
C2	0.093 (3)	0.088 (3)	0.0708 (19)	0.018 (2)	0.018 (2)	0.0131 (17)
C3	0.104 (3)	0.098 (3)	0.067 (2)	0.025 (3)	−0.006 (2)	−0.0036 (18)
C4	0.082 (2)	0.100 (3)	0.082 (2)	0.007 (2)	−0.016 (2)	−0.012 (2)
C5	0.0613 (18)	0.092 (3)	0.076 (2)	0.0016 (18)	−0.0035 (16)	−0.0028 (17)
C6	0.0600 (16)	0.0635 (19)	0.0644 (15)	0.0079 (16)	−0.0002 (14)	0.0052 (13)
C7	0.0552 (16)	0.070 (2)	0.0676 (16)	−0.0017 (16)	0.0036 (13)	0.0008 (14)
C8	0.0637 (19)	0.095 (3)	0.0663 (18)	−0.0158 (17)	0.0057 (14)	0.0062 (16)
C9	0.0714 (18)	0.075 (2)	0.0626 (16)	−0.0095 (17)	−0.0003 (15)	−0.0063 (14)
C10	0.0590 (17)	0.077 (2)	0.0757 (18)	−0.0103 (16)	−0.0003 (15)	0.0048 (16)
C11	0.076 (2)	0.087 (3)	0.096 (2)	0.012 (2)	0.0016 (19)	−0.016 (2)
C12	0.0735 (19)	0.071 (2)	0.0550 (15)	−0.0107 (17)	0.0018 (15)	−0.0046 (13)
C13	0.095 (3)	0.073 (3)	0.079 (2)	−0.015 (2)	−0.015 (2)	−0.0097 (17)
C14	0.073 (2)	0.058 (2)	0.0592 (15)	−0.0101 (15)	0.0050 (14)	−0.0059 (13)
C15	0.083 (2)	0.0537 (19)	0.0677 (18)	−0.0004 (16)	0.0095 (16)	0.0001 (13)
C16	0.077 (2)	0.060 (2)	0.0762 (19)	0.0093 (16)	−0.0005 (16)	0.0013 (15)
C17	0.0756 (19)	0.061 (2)	0.0759 (18)	0.0136 (17)	−0.0069 (17)	0.0009 (15)
C18	0.0757 (19)	0.0570 (18)	0.0696 (17)	−0.0036 (16)	−0.0085 (16)	−0.0025 (15)
N1	0.0687 (15)	0.0577 (15)	0.0565 (13)	−0.0073 (12)	0.0034 (12)	−0.0068 (11)
N2	0.0778 (16)	0.0501 (14)	0.0753 (15)	−0.0039 (13)	−0.0071 (14)	−0.0072 (12)
O1	0.1089 (18)	0.0548 (14)	0.0940 (15)	−0.0059 (13)	0.0042 (14)	−0.0051 (12)
O2	0.1046 (19)	0.0668 (16)	0.128 (2)	0.0217 (15)	−0.0505 (18)	−0.0262 (14)
O3	0.0922 (16)	0.0679 (14)	0.0727 (13)	0.0082 (12)	−0.0112 (12)	−0.0049 (11)
S1	0.1047 (7)	0.0564 (5)	0.0875 (6)	−0.0127 (5)	−0.0120 (5)	−0.0076 (4)

Geometric parameters (Å, º)

C1—C6	1.391 (5)	C10—H10B	0.9700
C1—C2	1.393 (5)	C11—H11A	0.9600
C1—H1	0.9300	C11—H11B	0.9600
C2—C3	1.368 (6)	C11—H11C	0.9600
C2—H2	0.9300	C12—C13	1.346 (5)
C3—C4	1.366 (6)	C12—N1	1.386 (4)

C3—H3	0.9300	C13—S1	1.727 (4)
C4—C5	1.386 (5)	C13—H13	0.9300
C4—H4	0.9300	C14—N1	1.301 (4)
C5—C6	1.382 (5)	C14—N2	1.377 (4)
C5—H5	0.9300	C14—S1	1.716 (3)
C6—C7	1.511 (4)	C15—O1	1.230 (4)
C7—C11	1.526 (5)	C15—N2	1.360 (4)
C7—C10	1.550 (4)	C15—C16	1.475 (5)
C7—C8	1.553 (4)	C16—C17	1.338 (5)
C8—C9	1.547 (5)	C16—H16	0.9300
C8—H8A	0.9700	C17—C18	1.479 (5)
C8—H8B	0.9700	C17—H17	0.9300
C9—C12	1.488 (5)	C18—O2	1.215 (4)
C9—C10	1.553 (5)	C18—O3	1.295 (4)
C9—H9	0.9800	N2—H2A	0.8600
C10—H10A	0.9700	O3—H3A	0.8200
C6—C1—C2	120.0 (4)	C9—C10—H10A	113.7
C6—C1—H1	120.0	C7—C10—H10B	113.7
C2—C1—H1	120.0	C9—C10—H10B	113.7
C3—C2—C1	120.6 (4)	H10A—C10—H10B	110.9
C3—C2—H2	119.7	C7—C11—H11A	109.5
C1—C2—H2	119.7	C7—C11—H11B	109.5
C4—C3—C2	119.9 (3)	H11A—C11—H11B	109.5
C4—C3—H3	120.1	C7—C11—H11C	109.5
C2—C3—H3	120.1	H11A—C11—H11C	109.5
C3—C4—C5	120.2 (4)	H11B—C11—H11C	109.5
C3—C4—H4	119.9	C13—C12—N1	113.6 (3)
C5—C4—H4	119.9	C13—C12—C9	128.5 (3)
C6—C5—C4	121.0 (3)	N1—C12—C9	117.8 (3)
C6—C5—H5	119.5	C12—C13—S1	111.6 (3)
C4—C5—H5	119.5	C12—C13—H13	124.2
C5—C6—C1	118.3 (3)	S1—C13—H13	124.2
C5—C6—C7	120.0 (3)	N1—C14—N2	121.2 (3)
C1—C6—C7	121.7 (3)	N1—C14—S1	115.3 (2)
C6—C7—C11	110.4 (3)	N2—C14—S1	123.5 (3)
C6—C7—C10	117.4 (3)	O1—C15—N2	121.1 (3)
C11—C7—C10	111.1 (3)	O1—C15—C16	119.0 (3)
C6—C7—C8	115.8 (3)	N2—C15—C16	119.9 (3)
C11—C7—C8	112.5 (3)	C17—C16—C15	132.8 (3)
C10—C7—C8	88.0 (2)	C17—C16—H16	113.6
C9—C8—C7	89.8 (2)	C15—C16—H16	113.6
C9—C8—H8A	113.7	C16—C17—C18	130.1 (3)
C7—C8—H8A	113.7	C16—C17—H17	114.9
C9—C8—H8B	113.7	C18—C17—H17	114.9
C7—C8—H8B	113.7	O2—C18—O3	123.1 (3)
H8A—C8—H8B	110.9	O2—C18—C17	125.4 (3)
C12—C9—C8	119.3 (3)	O3—C18—C17	111.5 (3)

C12—C9—C10	116.1 (3)	C14—N1—C12	111.3 (3)
C8—C9—C10	88.1 (2)	C15—N2—C14	124.5 (3)
C12—C9—H9	110.5	C15—N2—H2A	117.7
C8—C9—H9	110.5	C14—N2—H2A	117.7
C10—C9—H9	110.5	C18—O3—H3A	109.5
C7—C10—C9	89.7 (2)	C14—S1—C13	88.22 (18)
C7—C10—H10A	113.7		
C6—C1—C2—C3	−0.4 (6)	C8—C9—C10—C7	−15.9 (3)
C1—C2—C3—C4	0.5 (6)	C8—C9—C12—C13	−5.7 (5)
C2—C3—C4—C5	−0.3 (6)	C10—C9—C12—C13	97.8 (4)
C3—C4—C5—C6	0.1 (6)	C8—C9—C12—N1	178.4 (3)
C4—C5—C6—C1	0.0 (5)	C10—C9—C12—N1	−78.1 (4)
C4—C5—C6—C7	−178.7 (3)	N1—C12—C13—S1	0.4 (4)
C2—C1—C6—C5	0.1 (5)	C9—C12—C13—S1	−175.7 (3)
C2—C1—C6—C7	178.8 (3)	O1—C15—C16—C17	168.3 (4)
C5—C6—C7—C11	80.9 (4)	N2—C15—C16—C17	−12.7 (6)
C1—C6—C7—C11	−97.7 (4)	C15—C16—C17—C18	−2.2 (7)
C5—C6—C7—C10	−150.3 (3)	C16—C17—C18—O2	19.8 (6)
C1—C6—C7—C10	31.1 (5)	C16—C17—C18—O3	−160.4 (4)
C5—C6—C7—C8	−48.3 (4)	N2—C14—N1—C12	179.7 (3)
C1—C6—C7—C8	133.0 (3)	S1—C14—N1—C12	−0.1 (3)
C6—C7—C8—C9	−135.5 (3)	C13—C12—N1—C14	−0.2 (4)
C11—C7—C8—C9	96.2 (3)	C9—C12—N1—C14	176.4 (3)
C10—C7—C8—C9	−15.8 (3)	O1—C15—N2—C14	1.0 (5)
C7—C8—C9—C12	134.9 (3)	C16—C15—N2—C14	−178.0 (3)
C7—C8—C9—C10	15.8 (3)	N1—C14—N2—C15	175.5 (3)
C6—C7—C10—C9	134.0 (3)	S1—C14—N2—C15	−4.7 (4)
C11—C7—C10—C9	−97.6 (3)	N1—C14—S1—C13	0.3 (3)
C8—C7—C10—C9	15.8 (3)	N2—C14—S1—C13	−179.5 (3)
C12—C9—C10—C7	−137.8 (3)	C12—C13—S1—C14	−0.4 (3)

Hydrogen-bond geometry (Å, º)

D—H⋯A	D—H	H⋯A	D⋯A	D—H⋯A
C16—H16⋯O1[i]	0.93	2.35	3.233 (4)	159
N2—H2A⋯O2	0.86	1.83	2.651 (4)	158
O3—H3A⋯N1[ii]	0.82	1.81	2.607 (3)	165

Symmetry codes: (i) $x-1/2, -y+5/2, -z+1$; (ii) $x-1/2, -y+3/2, -z+1$.