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

Okan Simsek, a* Muharrem Dincer, a Necmi Dege, a Eiad Saif, b,c* Ibrahim Yılmaz d and Alaaddin Cukoovalı e

*Department of Physics, Faculty of Arts and Sciences, Ondokuz Mayıs University, 55139, Samsun, Turkey, bDepartment of Computer and Electronic Engineering Technology, Sanaa Community College, Sanaa, Yemen, cOndokuz Mayıs University, Faculty of Engineering, Department of Electrical and Electronic Engineering, 55139, Samsun, Turkey, dDepartment of Chemistry, Kamıl Özdag Science, Karamanoğlu Mehmetbey University, 70200, Karaman, Turkey, and eDepartment of Chemistry, Sciences Faculty, Fırat University, 23119, Elazıg, Turkey. *Correspondence e-mail: okan.simsek@omu.edu.tr, eiad.saif@scc.edu.ye

The title cyclobutyl compound, C18H18N2O3S, was synthesized by the interaction of 4-(3-methyl-3-phenylcyclobutyl)thiazol-2-amine and maleic anhydride, and crystallizes in the orthorhombic space group P212121 with Z' = 1. The molecular geometry is partially stabilized by an intramolecular N—H/C1/C1/C1O hydrogen bond forming an S11(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/C1/C1/C1N hydrogen bonds, forming supramolecular ribbons with C11(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/C1/C1/C1H (43%), C/C1/C1/C1H (18%), O/C1/C1/C1H (17%) and N/C1/C1/C1H (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 (Dincer 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 P212121 space group with Z' = 1. Its molecular structure is...
3. Supramolecular features

The crystal packing of the title compound (Fig. 2) features intermolecular hydrogen bonds (C16—H16⋯O1' and O3—H3A⋯N1") 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(9) motifs. Adjacent ribbons are connected by C16—H16⋯O1 hydrogen bonds, leading to the formation of layers lying parallel to the bc plane.

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-y]lamin]-4-oxobutanoic acid dihydrate (CIBQIP; Se n et al., 2013), 2-[4-(2.5-dimethylphenyl)-3-methylcyclobutyl]-1,3-thiazol-2-yl]-1H-isoinodole-1,3(2H)-dione (HAMAKA; ¨Oz demir et al., 2010), 2-chloro-N-[4-(3-methyl-3-phenylcyclobutyl)-1,3-thiazol-2-yl]-N’-(naphthalen-1-ylmethylidene)acetohydrazide (IJULIL; Inkaya et al., 2011a), N-[4-(3-methyl-3-phenylcyclobutyl)-1,3-thiazol-2-yl]acetamide (LUXDU; 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)benzyliden]-N-[4-(3-methyl-3-phenylcyclobutyl)-1,3-thiazol-2-yl]acetohydrazide (QAKFU; Inkaya et al., 2011b), 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; Se n 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

Table 1

| D—H⋯A | D—H | H⋯A | D⋯A | D—H⋯A |
|-------|-----|-----|-----|-------|
| C16⋯H16⋯O1' | 0.93 | 2.35 | 3.233 (4) | 159 |
| N2⋯H2A⋯O2' | 0.86 | 1.83 | 2.651 (4) | 158 |
| O3⋯H3A⋯N1" | 0.82 | 1.81 | 2.607 (3) | 165 |

Symmetry codes: (i) x + 1/2, y + 1/2, z + 1; (ii) x + 1/2, y + 1/2, z + 1.
θ = 15.83 (5)°]. The cyclobutane ring is puckered, with a dihedral angle of 25.20 (5)° in IJULII (Inkaya et al., 2011a) and 22.99 (47)° in QAKFUF (Inkaya et al., 2011b). 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.

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 (Althamili 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. 4. 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
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==N), 1569 ν(=C≡N azomethine), 699 ν(C–S–C). Characteristic 1H NMR shifts (THF-d₈ + acetone-d₆, TMS, ppm): 1.26 (s, 3H, –CH₃), 2.15–2.20 (m, 2H, –CH₂– in cyclobutane ring), 2.31–2.36 (m, 2H, –CH₂– 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, 2H, aromatics). –OH and –NH– protons are 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. 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 Uiso(H) = 1.5Ueq(0), and N–H = 0.86 Å and Uiso(H) = 1.2Ueq(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 Uiso(H) = 1.5Ueq(C) for methyl H atoms and 1.2Ueq(C) for other H atoms.

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. 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 Uiso(H) = 1.5Ueq(0), and N–H = 0.86 Å and Uiso(H) = 1.2Ueq(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 Uiso(H) = 1.5Ueq(C) for methyl H atoms and 1.2Ueq(C) for other H atoms.

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Author contributions are as follows. Conceptualization, OS, MD, AC and ES; synthesis, AC and IY; writing (review and editing of the manuscript) OS, ND and AC; formal analysis, AC, OS, ND and MD; crystal-structure determination, OS, AC and ND; validation, AC, MD, ND and ES; project administration, AC, OS, ES and IY.

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Table 2

| Crystal data |
|-------------|
| Chemical formula | C₁₈H₁₈N₂O₃S |
| M_r | 342.40 |
| Crystal system, space group | Orthorhombic, P2₁,2₁,2₁ |
| Temperature (K) | 296 |
| a, b, c (Å) | 5.9685 (4), 11.0580 (9), 26.215 (2) |
| V (Å³) | 1730.2 (2) |
| Z | 4 |
| Radiation type | Mo Kα |
| 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) |
| No. of measured, independent and observed | 7546, 3338, 2648 |
| No. of reflections | 3338 |
| No. of parameters | 218 |
| H-atom treatment | H-atom parameters constrained |
| Δρmax, Δρmin (e Å⁻³) | 0.20, –0.16 |
| Absolute structure | Flack determined using 907 quotients [(I)–(I)]/[I] + [(I)+(I)] (Parsons et al., 2013) |
| Absolute structure parameter | −0.05 (8) |

Computer programs: X-AREA and X-RED32 (Stoe & Cie, 2002). SHELXTL2014/5 (Sheldrick, 2015a). SHELXL2017/1 (Sheldrick, 2015b), ORTEP-3 for Windows and WinGX (Farrugia, 2012) and PLATON (Spek, 2020).

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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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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

\[ \text{C}_{18}\text{H}_{18}\text{N}_{2}\text{O}_{3}\text{S} \]
\[ M_r = 342.40 \]

Orthorhombic, \( P2_12_12_1 \)

\( a = 5.9685 \) (4) Å
\( b = 11.0580 \) (9) Å
\( c = 26.215 \) (2) Å

\( V = 1730.2 \) (2) Å\(^3\)

\( Z = 4 \)

\( F(000) = 720 \)

Density:

\( D_x = 1.314 \) Mg m\(^{-3}\)

Melting point:

460 K

Cell parameters from 7998 reflections

\( \theta = 1.6 - 27.3^\circ \)

\( \mu = 0.21 \) mm\(^{-1}\)

\( T = 296 \) K

Prism, light yellow

\( 0.78 \times 0.71 \times 0.59 \) mm

Data collection

Stoe IPDS 2 diffractometer

Radiation source: sealed X-ray tube, 12 x 0.4 mm long-fine focus

Detector resolution: 6.67 pixels mm\(^{-1}\)

Rotation method scans

Absorption correction: integration (X-RED32; Stoe & Cie, 2002)

\( T_{\text{min}} = 0.832, T_{\text{max}} = 0.899 \)

7546 measured reflections

3338 independent reflections

2648 reflections with \( I > 2\sigma(I) \)

\( R_{\text{int}} = 0.058 \)

\( \theta_{\text{max}} = 26.0^\circ, \theta_{\text{min}} = 1.6^\circ \)

\( h = -7 \rightarrow 7 \)

\( k = -13 \rightarrow 12 \)

\( l = -32 \rightarrow 30 \)

Refinement

Refinement on \( F^2 \)

Least-squares matrix: full

\[ R[F^2 > 2\sigma(F^2)] = 0.045 \]

\[ wR(F^2) = 0.113 \]

\( S = 0.97 \)

3338 reflections

218 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

\[
w = \frac{1}{\sigma^2(Fo^2)} + 0.000002F^2
\]

where \( P = (Fo^2 + 2Fc^2)/3 \)

\[\Delta/\sigma_{\text{max}} = 0.001\]

\[\Delta \rho_{\text{max}} = 0.20 \text{ e Å}^{-3}\]

\[\Delta \rho_{\text{min}} = -0.16 \text{ e Å}^{-3}\]

Extinction correction: SHELXL2017/1 (Sheldrick 2015b),

\[Fc^2 = kFc[1 + 0.001xFc^2/\sin(2\theta)]^{1/4}\]

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 (Å²)

|    | x      | y      | z      | U_{iso}/U_{eq} |
|----|--------|--------|--------|----------------|
| C1 | 0.4002 | 0.8359 | 0.8058 | 0.0711 (8)     |
| H1 | 0.2742 | 0.7945 | 0.7943 | 0.085*         |
| C2 | 0.4122 | 0.8741 | 0.8563 | 0.0839 (11)    |
| H2 | 0.2936 | 0.8586 | 0.8784 | 0.101*         |
| C3 | 0.5971 | 0.9343 | 0.8739 | 0.0897 (12)    |
| H3 | 0.6044 | 0.9589 | 0.9077 | 0.108*         |
| C4 | 0.7710 | 0.9581 | 0.8415 | 0.0877 (11)    |
| H4 | 0.8964 | 0.9993 | 0.8533 | 0.105*         |
| C5 | 0.7611 | 0.9208 | 0.7910 | 0.0764 (9)     |
| H5 | 0.8804 | 0.9374 | 0.7693 | 0.092*         |
| C6 | 0.5764 | 0.8595 | 0.7725 | 0.0626 (7)     |
| C7 | 0.5717 | 0.8175 | 0.7177 | 0.0642 (8)     |
| C8 | 0.6388 | 0.9135 | 0.6772 | 0.0751 (9)     |
| H8A| 0.6282 | 0.9960 | 0.6894 | 0.090*         |
| H8B| 0.7834 | 0.8985 | 0.6612 | 0.090*         |
| C9 | 0.4381 | 0.8741 | 0.6437 | 0.0695 (8)     |
| H9 | 0.4860 | 0.8149 | 0.6181 | 0.083*         |
| C10| 0.3400 | 0.8091 | 0.6912 | 0.0706 (9)     |
| H10A| 0.2234 | 0.8546 | 0.7084 | 0.085*         |
| H10B| 0.2917 | 0.7268 | 0.6846 | 0.085*         |
| C11| 0.7026 | 0.6997 | 0.7118 | 0.0864 (10)    |
| H11A| 0.6981 | 0.6741 | 0.6768 | 0.130*         |
| H11B| 0.8553 | 0.7124 | 0.7219 | 0.130*         |
| H11C| 0.6365 | 0.6384 | 0.7329 | 0.130*         |
| C12| 0.2935 | 0.9681 | 0.6200 | 0.0664 (8)     |
| C13| 0.3006 | 1.0888 | 0.6265 | 0.0823 (10)    |
| H13| 0.4080 | 1.1288 | 0.6459 | 0.099*         |
| C14| −0.0010 | 1.0208 | 0.5734 | 0.0636 (8)     |
| C15| −0.3247 | 1.0930 | 0.5267 | 0.0682 (8)     |
| C16| −0.5193 | 1.0635 | 0.4943 | 0.0712 (9)     |
| H16| −0.6226 | 1.1261 | 0.4917 | 0.085*         |
# Atomic displacement parameters (Å²)

| Atom | $U^{11}$   | $U^{22}$   | $U^{33}$   | $U^{13}$   | $U^{12}$   | $U^{23}$   |
|------|------------|------------|------------|------------|------------|------------|
| 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, °)

| 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) |
| Bond/Angle | Distance/Angle |
|------------|---------------|
| C3—H3      | 0.9300        |
| C4—C5      | 1.386 (5)     |
| C4—H4      | 0.9300        |
| C5—C6      | 1.382 (5)     |
| C5—H5      | 0.9300        |
| C6—C7      | 1.511 (4)     |
| C7—C11     | 1.526 (5)     |
| C7—C10     | 1.550 (4)     |
| C7—C8      | 1.553 (4)     |
| C8—C9      | 1.547 (5)     |
| C8—H8A     | 0.9700        |
| C8—H8B     | 0.9700        |
| C9—C12     | 1.488 (5)     |
| C9—C10     | 1.553 (5)     |
| C9—H9      | 0.9800        |
| C10—H10A   | 0.9700        |
| C6—C1—C2   | 120.0 (4)     |
| C6—C1—H1   | 120.0         |
| C2—C1—H1   | 120.0         |
| C3—C2—C1   | 120.6 (4)     |
| C3—C2—H2   | 119.7         |
| C1—C2—H2   | 119.7         |
| C4—C3—C2   | 119.9 (3)     |
| C4—C3—H3   | 120.1         |
| C2—C3—H3   | 120.1         |
| C3—C4—C5   | 120.2 (4)     |
| C3—C4—H4   | 119.9         |
| C5—C4—H4   | 119.9         |
| C6—C5—C4   | 121.0 (3)     |
| C6—C5—H5   | 119.5         |
| C4—C5—H5   | 119.5         |
| C5—C6—C1   | 118.3 (3)     |
| C5—C6—C7   | 120.0 (3)     |
| C1—C6—C7   | 121.7 (3)     |
| C6—C7—C11  | 110.4 (3)     |
| C6—C7—C10  | 117.4 (3)     |
| C11—C7—C10 | 111.1 (3)     |
| C6—C7—C8   | 115.8 (3)     |
| C11—C7—C8  | 112.5 (3)     |
| C10—C7—C8  | 88.0 (2)      |
| C9—C8—C7   | 89.8 (2)      |
| C9—C8—H8A  | 113.7         |
| C7—C8—H8A  | 113.7         |
| C9—C8—H8B  | 113.7         |
| C7—C8—H8B  | 113.7         |
| H8A—C8—H8B | 110.9         |
| C12—C9—C8  | 119.3 (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)  C8—C9—C12—N1  178.4 (3)
C3—C4—C5—C6  0.1 (6)  C10—C9—C12—C13  97.8 (4)
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—C10  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, °)

| D—H···A   | D—H | H···A | D···A   | D—H···A |
|-----------|-----|-------|---------|---------|
| C16—H16···O1i | 0.93 | 2.35  | 3.233 (4) | 159 |
| N2—H2A···O2  | 0.86 | 1.83  | 2.651 (4) | 158 |
| O3—H3A···N1ii | 0.82 | 1.81  | 2.607 (3) | 165 |

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