Crystal structure and Hirshfeld surface analysis of 2-{{[7-acetyl-4-cyano-6-hydroxy-8-(4-methoxyphenyl)-1,6-dimethyl-5,6,7,8-tetrahydroisoquinolin-3-yl]sulfanyl}acetic acid ethyl ester

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Crystal structure and Hirshfeld surface analysis of 2-{{[7-acetyl-4-cyano-6-hydroxy-8-(4-methoxyphenyl)-1,6-dimethyl-5,6,7,8-tetrahydroisoquinolin-3-yl]sulfanyl}acetic acid ethyl ester

In the title molecule, C_{25}H_{28}N_{2}O_{5}S, (alternative name ethyl 2-[[7-acetyl-4-cyano-6-hydroxy-8-(4-methoxyphenyl)-1,6-dimethyl-5,6,7,8-tetrahydroisoquinolin-3-yl]sulfanyl]acetate) the 4-methoxyphenyl group is disposed on one side of the bicyclic core and the oxygen atoms of the hydroxyl and acetyl groups are disposed on the other side. In the crystal, a layered structure parallel to the ac plane is generated by O—H⋯O and C—H⋯O hydrogen bonds plus C—H⋯π(ring) interactions.

1. Chemical context

Some tetrahydroisoquinoline (THISQ) based compounds are of medicinal and biological importance, being used as antitumoral (Pingaew et al., 2014; Castillo et al., 2018), antifungal (Scott et al., 2002) and anti-inflammatory agents (Siegfried et al., 1989). Other tetrahydroisoquinolines were used as inhibitors including B-rafV600E or p38 kinase inhibitors (Lu et al., 2016; Rosales et al., 2007). The THISQ core can easily be functionalized to build other heterocyclic rings on the carbocyclic ring (Xu et al., 2002; Carroll et al., 2007; Demers et al., 2008, Marae et al., 2021a). Recently, we have used some compounds related to THISQ as durable fluorescent dyes for cotton (Marae et al., 2021b). The widespread importance of these compounds motivated us to further study the THISQ core. Here we report the synthesis and crystal structure determination of the title compound.
2. Structural commentary

The ethyl sulfanylacetate, acetyl and cyano groups and both methyl groups (C19 and C21) are in equatorial positions with respect to the bicyclic core, while the hydroxyl and anisole groups on the cyclohexane ring occupy an axial and bisectioanal position, respectively (Fig. 1). The C10–C15 benzene ring is inclined to the N1/C5–C9 pyridine ring by 82.57 (6)°. The C1–C5/C9 cyclohexane ring is in an envelope conformation, with atom C3 at the flap position [deviation from best plane = 0.367 (1) Å] and puckering parameters (Cremer & Pople, 1975) $Q_T = 0.5180$ (12) Å, $\theta = 53.85$ (13)° and $\varphi = 109.07$ (17)°.

3. Supramolecular features

In the crystal of the title compound, chains of molecules extending along the $a$-axis direction are formed by O3–

Table 1

| Hydrogen-bond geometry (Å, °). |
|-----------------------------|
| $D$–H···$A$ | $D$–H | $H$···$A$ | $D$–···$A$ |
|-----------------------------|
| O3–H3···O1$^a$ | 0.90 (2) | 2.05 (2) | 2.9283 (12) | 164 (2) |
| C16–H16C···O2$^u$ | 0.98 | 2.47 | 3.1566 (15) | 127 |
| C21–H21A···O2$^u$ | 0.98 | 2.51 | 3.3956 (15) | 150 |
| C22–H22A···O3$^v$ | 0.99 | 2.44 | 3.1815 (15) | 131 |
| C22–H22B···Cg1$^v$ | 0.99 | 2.58 | 3.4559 (15) | 147 |
| C24–H24B···O4$^v$ | 0.99 | 2.52 | 3.442 (2) | 154 |

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

4. Hirshfeld surface analysis

Hirshfeld surface analysis (Spackman & Jayatilaka, 2009) was carried out using CrystalExplorer17.5 (Turner et al., 2017). The Hirshfeld surface and their associated two-dimensional fingerprint plots were used to quantify the various intermolecular interactions in the title compound. In the Hirshfeld surface plotted over $d_{norm}$ in the range $-0.4903$ (red) to +1.6396 (blue) a.u. (Fig. 4), the white areas indicate contacts with distances equal to the sum of van der Waals radii, and the red and blue areas indicate distances shorter (in close contact) or longer (distinct contact) than the van der Waals radii, respectively (Venkatesan et al., 2016). The bright-red spots indicate their roles as the respective donors and/or acceptors.

Fingerprint plots (Fig. 5b–c; Table 2) reveal that H···H (47.6%), O···H/H···O (19.7%), C···H/H···C (12.5%) and N···H/H···N (11.6%) interactions make the greatest contributions to the surface contacts. S···H/H···S (6.4%), N···C/C···N (0.7%), O···C/C···O (0.5%), O···O (0.5%) and C···C (0.4%) contacts also contribute to the overall crystal packing of the title compound. The Hirshfeld surface analysis confirms the importance of H-atom contacts in establishing the packing. The large number of H···H, O···H, C···H and N···H interactions suggest that van der Waals interactions and hydrogen...
bonding play the major roles in the crystal packing (Hathwar et al., 2015).

5. Database survey
A search of the Cambridge Structural Database (CSD version 5.42, updated September 2021; Groom et al., 2016) for tetra-hydroisoquinoline derivatives gave nine compounds very similar to the title compound. In the crystal of NAQRIJ (Mague et al., 2017), dimers form through complementary sets of inversion-related O—H···O and C—H···O hydrogen bonds. These are connected into zigzag chains along the c-axis direction by pairwise C—H···N interactions that also form inversion dimers. In KUGLIK (Langenhohl et al., 2020), the heterocyclic amines are alternately connected to the hydrogen-bonding system along the c-axis, which leads to the formation of syndiotactic polymer chains in this direction. In DUSVIZ (Selvaraj et al., 2020), molecules are linked via C—H···O hydrogen bonds. In AKIVUO (Al-Taifi et al., 2021), a layered structure with layers parallel to (101) is generated by O—H···O and C—H···O hydrogen bonds. In ULUTAZ (Naghiyev et al., 2021), molecules are linked via N—H···O and C—H···N hydrogen bonds, forming a three-dimensional network, and the crystal packing is dominated by C—H···π bonds. In CARCOQ (Lehmann et al., 2017), molecules are linked by O—H···O hydrogen bonds, forming layers lying parallel to the ab plane. In POPYEB (Ben Ali et al., 2019), molecules are packed in a herringbone manner parallel to (103) and (103) via weak C—H···O and C—H···π (ring) interactions. In ENOCIU (Naicker et al., 2011) various C—H···π and C—H···O bonds link the molecules together. In NIWPAL (Bouasla et al., 2008), the molecules are linked by N—H···O intermolecular hydrogen bonds involving the sulfonamide function to form an infinite two-dimensional network parallel to the (001) plane.

6. Synthesis and crystallization
7-Acetyl-4-cyano-1,6-dimethyl-6-hydroxy-8-(4-methoxyphenyl)-5,6,7,8-tetrahydro-isoquinoline-3(2H)-thione (5 mmol,
research communications

Table 3
Experimental details.

| Crystal data | Chemical formula | C_{13}H_{20}N_{2}O_{5}S |
|--------------|------------------|------------------------|
| M, g·mol⁻¹  |                  | 468.55                 |
| Crystal system, space group |               | Triclinic, P\(\bar{T}\) |
| Temperature (K) |                | 150                    |
| \(a, b, c (\text{Å})\) |                 | 10.0643 (6), 10.3592 (7), 12.0685 (8) |
| \(V (\text{Å}^3)\) |       | 1199.23 (13)          |
| \(\alpha, \beta, \gamma (°)\) |       | 83.296 (1), 80.770 (1), 75.638 (1) |
| Z |              | 2                      |
| \(\mu (\text{mm}^{-1})\) |          | 0.17                   |
| Crystal size (mm) |         | 0.29 × 0.27           |

Data collection

Diffractometer | Bruker SMART APEX CCD
Absorption correction | Multi-scan (SADABS; Krause et al., 2015)
\(T_{\text{min}}, T_{\text{max}}\) | 0.82, 0.96
No. of measured, independent and observed \([I > 2\sigma(I)]\) reflections | 22695, 6509, 5177
\(R_{\text{int}}\) | 0.023
\(\sin \theta/\lambda_{\text{max}} (\text{Å}^{-1})\) | 0.695

Refinement

\(R(F^2 > 2\sigma(F^2)), wR(F^2), S\) | 0.045, 0.133, 1.11
No. of reflections | 6509
No. of parameters | 305
H-atom treatment | H atoms treated by a mixture of independent and constrained refinement
\(\Delta p_{\text{max}}, \Delta p_{\text{min}} (\text{e Å}^{-3})\) | 0.71, -0.22


1.91 g) and sodium acetate trihydrate (1.36 g, 10 mmol) were suspended in 50 ml of absolute ethanol, then 0.55 ml of ethyl chloroacetate (5.3 mmol) were added and the mixture was refluxed for one h. During reflux, the yellow colour disappeared gradually over time to afford a colourless reaction mixture. The reaction mixture was then left to cool at room temperature and the formed precipitate was collected by filtration, washed with water, dried in air and recrystallized from ethanol to give the title compound as cubic crystals, yield 2.11 g (94%); m.p. 453–455 K. IR (cm⁻¹): 3454 (O–H); 3048 (C–H aromatic); 2970, 2913 (C–H aliphatic); 2215 (C=O); 1743 (C==O, ester); 1697 (C==O, acetyl). ¹H NMR (CDCl₃, 400 MHz) δ: 6.80–6.86 (dd, J = 8 Hz, 4H, ArH), 4.24–4.26 (d, J = 8 Hz, 1H, C₅H), 3.12–3.14 (q, J = 6 Hz, 2H, OCH₂), 3.89–3.92 (dd, J = 12 Hz, 2H, SCH₂), 3.78 (s, 3H, OCH₃), 3.38 (s, 1H, OH), 3.09–3.12 (d, J = 12 Hz, 1H, C₆H), 3.03–3.05 (d, J = 8 Hz, 1H, C₇H), 2.89–2.92 (d, J = 12 Hz, 1H, C₈H), 1.90 (s, 3H, CH₃ at C-1), 1.80 (s, 3H, COCH₃), 1.34 (s, 3H, CH₁ at C-6), 1.18–1.21 (t, J = 6 Hz, 3H, CH₂ of ester group).

7. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 3. All C-bound H atoms were placed in geometrically idealized positions (C–H = 0.95–1.00 Å) while the hydrogen atom attached to O3 was found from a difference map, and was subsequently refined isotropically [O3–H3 = 0.903 (17) Å] with \(U_{eq}(\text{H}) = 1.5U_{eq}(\text{O})\). All C-bound H atoms were included as riding contributions with isotropic displacement parameters 1.2 times those of the parent atoms (1.5 for methyl groups).

Acknowledgements

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Crystal structure and Hirshfeld surface analysis of 2-[[7-acetyl-4-cyano-6-hydroxy-8-(4-methoxyphenyl)-1,6-dimethyl-5,6,7,8-tetrahydroisoquinolin-3-yl]sulfanyl]acetic acid ethyl ester

Elham A. Al-Taifi, Islam S. Marae, Yasser A. El-Ossaily, Shaaban K. Mohamed, Joel T. Mague, Mehmet Akkurt and Etify A. Bakhite

Crystal data

\[ \text{C}_{25}\text{H}_{28}\text{N}_{2}\text{O}_{5}\text{S} \]

\[ M_r = 468.55 \]

Triclinic, \( P \overline{1} \)

\[ a = 10.0643 (6) \text{ Å} \]

\[ b = 10.3592 (7) \text{ Å} \]

\[ c = 12.0685 (8) \text{ Å} \]

\[ \alpha = 83.296 (1) \text{°} \]

\[ \beta = 80.770 (1) \text{°} \]

\[ \gamma = 75.638 (1) \text{°} \]

\[ V = 1199.23 (13) \text{ Å}^3 \]

Cell parameters from 9995 reflections

\[ \theta = 2.5–29.5 \text{°} \]

\[ \mu = 0.17 \text{ mm}^{-1} \]

\[ T = 150 \text{ K} \]

Block, colourless

\[ 0.35 \times 0.29 \times 0.27 \text{ mm} \]

Data collection

Bruker SMART APEX CCD diffractometer

Radiation source: fine-focus sealed tube

Graphite monochromator

Detector resolution: 8.3333 pixels mm\(^{-1}\)

\( \phi \) and \( \omega \) scans

Absorption correction: multi-scans

\( \text{(SADABS; Krause et al., 2015)} \)

\[ T_{\text{min}} = 0.82, T_{\text{max}} = 0.96 \]

22695 measured reflections

6509 independent reflections

5177 reflections with \( I > 2\sigma(I) \)

\[ R_{\text{int}} = 0.023 \]

\[ \theta_{\text{max}} = 29.6 \text{°}, \theta_{\text{min}} = 1.7 \text{°} \]

\[ h = -13\rightarrow13 \]

\[ k = -14\rightarrow14 \]

\[ l = -16\rightarrow16 \]
Supporting Information

Refinement

Refinement on \(F^2\)
Least-squares matrix: full
\(R[F^2 > 2\sigma(F^2)] = 0.045\)
\(wR(F^2) = 0.133\)
\(S = 1.11\)

6509 reflections
305 parameters
0 restraints

Primary atom site location: dual
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

\(w = 1/[\sigma^2(F_o^2) + (0.0848P)^2 + 0.0389P]\)
where \(P = (F_o^2 + 2F_c^2)/3\)

\((\Delta/\sigma)_{max} < 0.001\)
\(\Delta\rho_{max} = 0.71\) e Å\(^{-3}\)
\(\Delta\rho_{min} = -0.22\) e Å\(^{-3}\)

Special details

Experimental. The diffraction data were obtained from 3 sets of 400 frames, each of width 0.5° in \(\omega\), collected at \(\varphi = 0.00, 90.00\) and 180.00° and 2 sets of 800 frames, each of width 0.45° in \(\varphi\), collected at \(\omega = -30.00\) and 210.00°. The scan time was 10 sec/frame.

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 \(F^2 > 2\sigma(F^2)\) 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. H-atoms attached to carbon were placed in calculated positions (C—H = 0.95 - 1.00 Å) while that attached to oxygen was placed in a location derived from a difference map and its coordinates adjusted to give O—H = 0.87 %A. All were included as riding contributions with isotropic displacement parameters 1.2 - 1.5 times those of the attached atoms.

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

| x          | y          | z          | Uiso /*\Ueq |
|------------|------------|------------|-------------|
| S1         | 0.40179 (4)| 0.33194 (3)| 0.67126 (2) | 0.02919 (11) |
| O1         | -0.01601 (8)| 0.26808 (9)| -0.00282 (7)| 0.0261 (2)   |
| O2         | 0.65454 (10)| 0.31103 (10)| -0.03628 (7)| 0.0325 (2)   |
| O3         | 0.76674 (8)| 0.24179 (8)| 0.18545 (7) | 0.02199 (18) |
| H3         | 0.8202 (16)| 0.2524 (10)| 0.1190 (13) | 0.033*       |
| O4         | 0.08897 (11)| 0.46076 (12)| 0.66388 (9) | 0.0455 (3)   |
| O5         | 0.13749 (11)| 0.65264 (10)| 0.58156 (8) | 0.0357 (2)   |
| N1         | 0.35085 (10)| 0.41231 (10)| 0.46279 (8) | 0.0208 (2)   |
| N2         | 0.67128 (14)| 0.03469 (14)| 0.60676 (11)| 0.0424 (3)   |
| C1         | 0.46954 (11)| 0.29768 (11)| 0.16884 (9) | 0.0159 (2)   |
| H1         | 0.500590    | 0.379658    | 0.134272    | 0.019*       |
| C2         | 0.57706 (11)| 0.17513 (11)| 0.12120 (9) | 0.0173 (2)   |
| H2         | 0.531350    | 0.098468    | 0.129582    | 0.021*       |
| C3         | 0.70498 (11)| 0.13262 (11)| 0.18391 (9) | 0.0193 (2)   |
| C4         | 0.65493 (12)| 0.09343 (12)| 0.30675 (10)| 0.0223 (2)   |
| H4A        | 0.620266    | 0.011333    | 0.310543    | 0.027*       |
| H4B        | 0.734138    | 0.072924    | 0.350225    | 0.027*       |
| C5         | 0.54209 (11)| 0.20148 (11)| 0.35998 (9) | 0.0179 (2)   |
| C6         | 0.52467 (11)| 0.20985 (12)| 0.47729 (9) | 0.0199 (2)   |
| Atomic displacement parameters (Å²) | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
|-----------------------------------|----------|----------|----------|----------|----------|----------|
| S1      | 0.0375 (2) | 0.03615 (19) | 0.01391 (15) | −0.00874 (14) | −0.00410 (13) | −0.00088 (12) |
| O1      | 0.0185 (4) | 0.0418 (5) | 0.0196 (4) | −0.0100 (4) | −0.0083 (3) | 0.0052 (4) |
### Geometric parameters (Å, °)

| Bond/Distance | Length (Å) | Angle (°) |
|---------------|-----------|-----------|
| S1—C7         | 1.7672 (11) | C10—C11  | 1.3927 (15) |
| S1—C22        | 1.7966 (14) | C11—C12  | 1.3882 (16) |
| O1—C13        | 1.3742 (14) | C11—H11  | 0.9500     |
| O1—C16        | 1.4355 (14) | C12—C13  | 1.3940 (15) |
| O2—C17        | 1.2116 (15) | C12—H12  | 0.9500     |
| O3—C3         | 1.4223 (14) | C13—C14  | 1.3863 (16) |
| O3—H3         | 0.903 (17)  | C14—C15  | 1.3944 (16) |
| O4—C23        | 1.2046 (17) | C14—H14  | 0.9500     |
| O5—C23        | 1.3298 (17) | C15—H15  | 0.9500     |
| O5—C24        | 1.457 (2)   | C16—H16A | 0.9800     |
| N1—C7         | 1.3240 (15) | C16—H16B | 0.9800     |
| N1—C8         | 1.3439 (14) | C16—H16C | 0.9800     |
| N2—C20        | 1.1443 (17) | C17—C18  | 1.4956 (18) |
| C1—C9         | 1.5206 (14) | C18—H18A | 0.9800     |
C1—C10 1.5278 (15) C18—H18B 0.9800
C1—C2 1.5501 (15) C18—H18C 0.9800
C1—H1 1.0000 C19—H19A 0.9800
C2—C17 1.5258 (15) C19—H19B 0.9800
C2—C3 1.5421 (15) C19—H19C 0.9800
C2—H2 1.0000 C21—H21A 0.9800
C3—C4 1.5290 (16) C21—H21B 0.9800
C3—C19 1.5311 (15) C21—H21C 0.9800
C4—C5 1.5028 (16) C22—C23 1.5093 (19)
C4—H4A 0.9900 C22—H22A 0.9900
C4—H4B 0.9900 C22—H22B 0.9900
C5—C9 1.3941 (15) C24—C25 1.488 (3)
C5—C6 1.4087 (15) C24—H24A 0.9900
C6—C7 1.3972 (16) C24—H24B 0.9900
C6—C20 1.4369 (16) C25—H25A 0.9800
C8—C9 1.4057 (15) C25—H25B 0.9800
C8—C21 1.4957 (15) C25—H25C 0.9800
C10—C15 1.3893 (15)

C7—S1—C22 98.39 (6) C13—C14—C15 119.48 (10)
C13—O1—C16 116.26 (9) C13—C14—H14 120.3
C3—O3—H3 109.5 C15—C14—H14 120.3
C23—O5—C24 115.10 (12) C10—C15—C14 121.43 (11)
C7—N1—C8 119.27 (10) C10—C15—H15 119.3
C9—C1—C10 113.57 (9) C14—C15—H15 119.3
C9—C1—C2 113.46 (9) O1—C16—H16A 109.5
C10—C1—C2 106.92 (8) O1—C16—H16B 109.5
C9—C1—H1 107.5 H16A—C16—H16B 109.5
C10—C1—H1 107.5 O1—C16—H16C 109.5
C2—C1—H1 107.5 H16C—C16—H16B 109.5
C17—C2—C3 112.73 (9) O2—C17—C2 118.78 (11)
C17—C2—C1 108.37 (9) O2—C17—C18 121.16 (12)
C3—C2—C1 112.73 (9) O2—C17—C2 120.04 (11)
C3—C2—H2 108.1 C18—C17—C2 118.78 (11)
C3—C2—H2 108.1 C17—C18—H18A 109.5
C1—C2—H2 108.1 C17—C18—H18B 109.5
O3—C3—C4 106.22 (9) H18A—C18—H18B 109.5
O3—C3—C19 110.37 (9) C17—C18—H18C 109.5
O3—C3—C19 109.61 (10) H18A—C18—H18C 109.5
O3—C3—C2 111.05 (9) H18B—C18—H18C 109.5
O3—C3—C2 107.54 (9) C3—C19—H19A 109.5
C19—C3—C2 111.84 (9) C3—C19—H19B 109.5
C5—C4—C3 112.68 (9) H19A—C19—H19B 109.5
C5—C4—H4A 109.1 C3—C19—H19C 109.5
C3—C4—H4A 109.1 H19A—C19—H19C 109.5
C5—C4—H4B 109.1 H19B—C19—H19C 109.5
C3—C4—H4B 109.1 N2—C20—C6 177.83 (14)
H4A—C4—H4B 107.8 C8—C21—H21A 109.5
C9—C5—C6 118.33 (10)  C8—C21—H21B 109.5
C9—C5—C4 121.92 (10)  H21A—C21—H21B 109.5
C6—C5—C4 119.67 (10)  C8—C21—H21C 109.5
C7—C6—C5 119.09 (10)  H21B—C21—H21C 109.5
C7—C6—C20 119.89 (10)  C23—C22—S1 114.39 (9)
C5—C6—C20 121.00 (11)  H21A—C21—H21B 109.5
N1—C7—C6 122.29 (10)  C23—C22—H22A 108.7
N1—C7—C5 116.98 (9)  H21A—C21—H21C 109.5
C6—C7—C5 120.69 (9)  S1—C22—H22A 108.7
C7—C6—C20 119.89 (10)  H21B—C21—H21C 109.5
C5—C6—C20 121.00 (11)  C23—C22—H22B 108.7
C15—C10—C11 119.5  H22A—C22—H22B 107.6
C15—C10—C1 120.46 (10)  C23—C22—H22C 109.5
C11—C10—C1 121.02 (9)  C9—C8—C21 123.45 (10)  O4—C23—O5 124.65 (13)
C12—C11—C10 121.02 (10)  O4—C23—C22 124.79 (13)
C15—C10—C11 118.27 (10)  C23—C22—S1 114.39 (9)
C11—C10—C1 122.66 (10)  H21A—C21—H21B 109.5
C9—C1—C2—C17 −159.86 (9)  C2—C1—C9—C5 3.61 (14)
C10—C1—C2—C17 74.15 (10)  C10—C1—C9—C8 −58.88 (13)
C9—C1—C2—C3 −36.30 (12)  C2—C1—C9—C8 178.74 (9)
C10—C1—C2—C3 −162.29 (9)  C9—C1—C10—C15 143.67 (11)
C17—C2—C3—O3 67.55 (12)  C11—C12—C13—C14 −2.44 (18)
C17—C2—C3—C4 −176.63 (9)  O1—C13—C14—C15 −178.52 (11)
C1—C2—C3—O3 −54.40 (12)  C12—C13—C14—C15 1.34 (18)
C1—C2—C3—C4 61.42 (12)  O3—C3—C4—C5 −159.86 (9)
C17—C2—C3—C4 −176.63 (9)  C2—C1—C9—C5 3.61 (14)
C1—C2—C3—C4 −56.24 (13)  C2—C1—C9—C8 −58.88 (13)
C1—C2—C3—C19 −56.24 (13)  C10—C1—C9—C5 125.98 (11)
C11—C12—C13—C14 124.12 (10)  C2—C1—C9—C8 178.74 (9)
C11—C12—C13—C15 119.91 (10)  C9—C1—C10—C15 143.67 (11)
C11—C12—H12 120.0  C2—C1—C9—C5 3.61 (14)
C9—C1—C10—C15 119.5  H24A—C24—C25 108.5
C10—C1—C10—C15 −90.40 (12)  C15—C10—C11—C12 0.81 (17)
C11—C12—C13—C14 124.12 (10)  O5—C24—C25 107.60 (17)
O1—C13—C14−112.0  H25A—C25—C26 109.5
O1—C13—C12 116.04 (10)  C24—C25—C26 109.5
C14—C13—C12 119.84 (10)  C24—C25—H25A 109.5

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C8—N1—C7—S1 179.98 (8)  C11—C10—C15—C14  172.40 (10)
C5—C6—C7—N1  −1.67 (18)  C1—C10—C15—C14  0.87 (18)
C20—C6—C7—N1  177.03 (11)  C13—C14—C15—C10  −73.61 (14)
C5—C6—C7—S1  −179.50 (8)  C3—C2—C17—O2  50.84 (14)
C22—S1—C7—N1  −15.41 (11)  C3—C2—C17—O2  107.90 (13)
C22—S1—C7—C6  162.54 (10)  C1—C2—C17—O2  −127.65 (12)
C7—N1—C8—C9  0.94 (17)  C13—C14—C15—C10  69.08 (10)
C7—N1—C8—C21  −177.79 (10)  C24—O5—C23—O4  −3.71 (19)
C6—C5—C9—C8  4.47 (16)  C24—O5—C23—C22  178.31 (11)
C4—C5—C9—C8  −172.42 (10)  C1—C2—C17—C18  36.21 (17)
C6—C5—C9—C1  179.69 (10)  S1—C22—C23—C25  −145.80 (9)
C4—C5—C9—C1  2.79 (16)  S1—C22—C23—O4  15.41 (11)
N1—C8—C9—C5  −4.26 (16)  C22—H22A···Cg1iv  0.99  2.52  3.442 (2)  154

Hydrogen-bond geometry (Å, º)

|                  | D—H  | H···A | D···A | D—H···A |
|------------------|------|------|-------|---------|
| O3—H3···O1i      | 0.90 (2) | 2.05 (2) | 2.9283 (12) | 164 (2) |
| C16—H16C···O2ii | 0.98  | 2.47  | 3.1566 (15) | 127     |
| C21—H21A···O2iii | 0.98  | 2.51  | 3.3956 (15) | 150     |
| C22—H22A···O3iv | 0.99  | 2.44  | 3.1815 (15) | 131     |
| C22—H22B···Cg1iv| 0.99  | 2.58  | 3.4559 (15) | 147     |
| C24—H24B···O4v  | 0.99  | 2.52  | 3.442 (2) | 154     |

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