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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}-*N*-phenylacetamide

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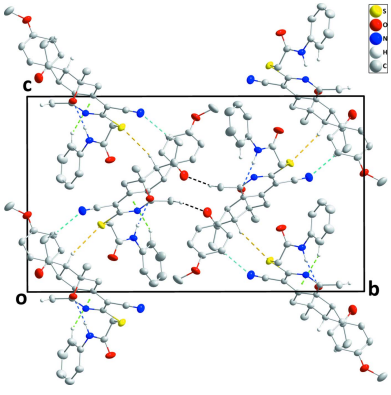
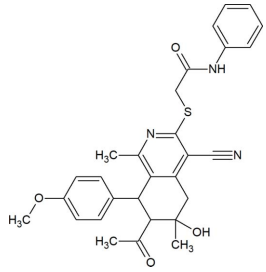
The title molecule, $C_{29}H_{29}N_3O_4S$, adopts a conformation with the two phenyl substituents disposed on opposite sides of the mean plane of the isoquinoline unit. In the crystal, corrugated layers of molecules are formed by N—H···O, C—H···N and C—H···S hydrogen bonds together with C—H···π(ring) interactions. These layers are connected by C—H···O contacts. The Hirshfeld surface analysis of the crystal structure indicates that the most important contributions for the crystal packing are from H···H (45.2%), C···H/H···C (20.2%), O···H/H···O (15.8%) and N···H/H···N (11.0%) interactions.

1. Chemical context

Many tetrahydroisoquinolines have medicinal importance as potent selective and orally active aldosterone synthase (CYP11B2) inhibitors (Martin *et al.*, 2016). There are many natural and modified natural products that contain annulated pyridine rings such as the fatty acid bending protein inhibitor, (−)-oxerine, (−)-actinidine, indicaine, and other compounds that are derived from flavouring agents, namely (*s*)-(−)-perillaldehyde and (1*R*)-myrtenal (Uredi *et al.*, 2019). In C—H activation reactions, the pyridine ring acts as the directing group (Zhang *et al.*, 2014).

Tienopyridine derivatives show diverse pharmacological activities including antibacterial activity against a drug-resistant *S. epidermidis* clinical strain (Leal *et al.*, 2008) and cytotoxic activity against human hepatocellular liver carcinoma (HepG2) (Hassan *et al.*, 2013) and are used as antiplatelet drugs for the treatment of acute coronary syndromes (Peters *et al.*, 2003).





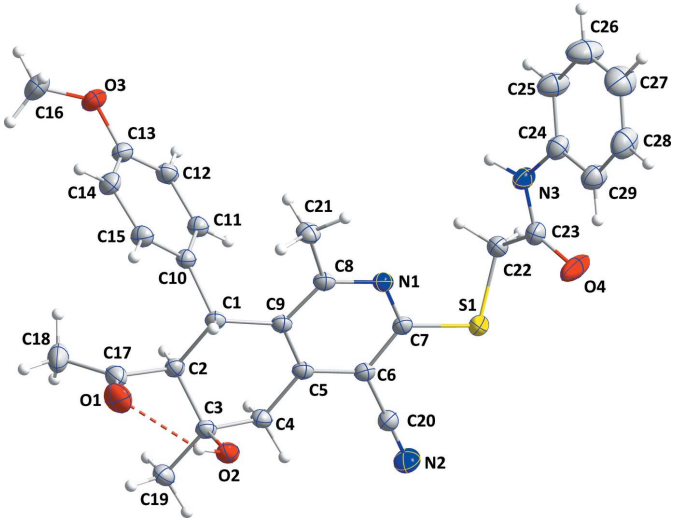


Figure 1
The title molecule with the atom-labelling scheme and 50% probability ellipsoids. The intramolecular hydrogen bond is depicted by a dashed line.

2. Structural commentary

The title molecule adopts a conformation in which the C24–C29 phenyl group is on the same side of the mean plane of tetrahydroisoquinoline core as the O2–H2*A* hydroxy group, while the 4-methoxyphenyl group is situated on the opposite side (Fig. 1). There is an intramolecular O2—H2*A*···O1 hydrogen bond, which controls the orientation of the acetyl group. Puckering analysis (Cremer & Pople, 1975) shows that the conformation of the C1–C5/C9 ring is close to half-chair with the C2 atom as the flap. The mean planes of the C10–C15 and C24–C29 rings are inclined to that of the pyridine N1/C5–C9 ring by 77.17 (3) and 67.93 (5)°, respectively. All bond lengths and angles appear normal for the given formulation.

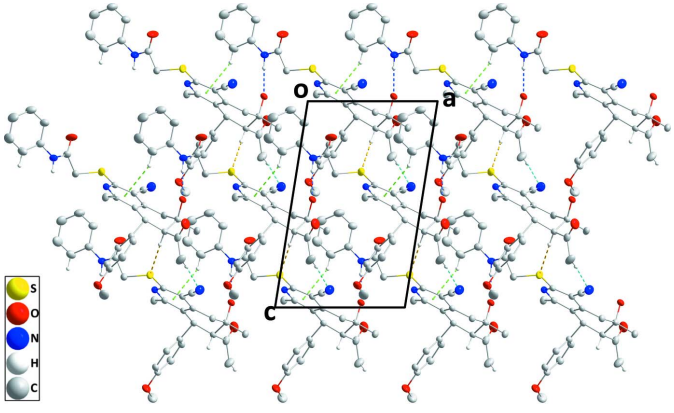


Figure 2
View of a portion of one layer seen along the *b*-axis direction. N—H···O, C—H···N and C—H···S hydrogen bonds are depicted, respectively, by dark-blue, light-blue and yellow dashed lines. C—H···π(ring) interactions are depicted by green dashed lines.

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

*Cg*1 is the centroid of the N1/C–C9 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2*A*···O1	0.87	2.13	2.8343 (14)	138
N3—H3*A*···O2^{i}	0.91	2.03	2.9335 (14)	174
C2—H2···S1^{ii}	1.00	2.86	3.8269 (12)	163
C18—H18*A*···N2^{ii}	0.98	2.52	3.493 (2)	170
C21—H21*C*···O1^{iii}	0.98	2.39	3.3593 (16)	169
C25—H25···*Cg*1^{i}	0.95	2.79	3.6141 (18)	146

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

3. Supramolecular features

In the crystal, N3—H3*A*···O2 hydrogen bonds and C25—H25···*Cg*1 interactions form chains of molecules extending along the *a*-axis direction, which are linked into corrugated layers parallel to (010) by C18—H18*A*···N2 and C2—H2···S1 hydrogen bonds (Table 1 and Fig. 2). The layers are connected by inversion-related C21—H21*C*···O1 contacts into the three-dimensional structure (Table 1 and Fig. 3).

4. Hirshfeld surface analysis

Hirshfeld surface calculations (Spackman & Jayatilaka, 2009) were performed in order to further characterize the supramolecular association in the title compound. The Hirshfeld surface plotted over $d_{\rm norm}$ in the range −0.5236 to +1.6751 a.u. and two-dimensional fingerprint plots (McKinnon *et al.*, 2007) prepared using *CrystalExplorer 17.5* (Turner *et al.*, 2017) are

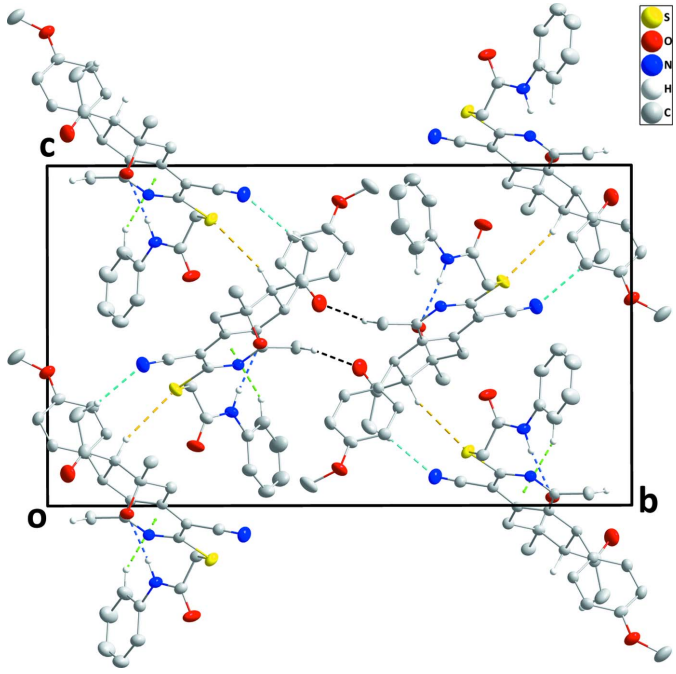


Figure 3
View of portions of two layers showing their connection by C—H···O hydrogen bonds (black dashed lines). Other intermolecular interactions are depicted as in Fig. 2.

Table 2
Summary of short intermolecular contacts (Å) in the title structure.

Contact	Distance	Symmetry operation
N2···H18*A*	2.52	$-\frac{1}{2}+x, \frac{1}{2}-y, -\frac{1}{2}+z$
H21*C*···O1	2.39	$2-x, 1-y, 1-z$
O2···H3*A*	2.03	$1+x, y, z$
O3···H27	2.70	$1+x, y, 1+z$
N2···H16*B*	2.69	$\frac{3}{2}-x, -\frac{1}{2}+y, \frac{3}{2}-z$
N2···H12	2.61	$\frac{1}{2}+x, \frac{1}{2}-y, -\frac{1}{2}+z$
H26···H18*C*	2.49	$1-x, 1-y, 1-z$
H27···H16*B*	2.47	$-x, 1-y, 1-z$

shown in Figs. 4 and 5, respectively. The red spots on the Hirshfeld surface represent strong intermolecular interactions (Table 2), whereas the blue colour represents a lack of interactions. The fingerprint plots (Fig. 5) reveal that H···H (45.2%), C···H/H···C (20.2%), O···H/H···O (15.8%) and N···H/H···N (11.0%) interactions make the greatest contributions to the surface contacts. The lowest contributions are from S···H/H···S (6.2%), O···C/C···O (1.2%), N···C/C···N (0.3%) and C···C (0.1%) contacts.

5. Database survey

Nine comparable tetrahydroisoquinoline derivatives are: NAQRIJ (Mague *et al.*, 2017), KUGLIK (Langenohl *et al.*, 2020), DUSVIZ (Selvaraj *et al.*, 2020), AKIVUO (Al-Taifi *et al.*, 2021), ULUTAZ (Naghiyev *et al.*, 2021), CARCOQ (Lehmann *et al.*, 2017), POPYEB (Ben Ali & Retailleau, 2019), ENOCIU (Naicker *et al.*, 2011) and NIWPAL (Bouasla *et al.*, 2008).

In the crystal of NAQRIJ, dimers are formed through complementary sets of inversion-related O—H···O and C—H···O hydrogen bonds, which are further connected into zigzag chains by pairwise C—H···N interactions that also form inversion dimers. In KUGLIK, the heterocyclic amines are alternately connected by hydrogen bonds thus forming syndiotactic polymeric chains. The hydrogen-bonding network of water molecules forms planes parallel to (100). In the crystal of DUSVIZ, molecules are linked *via* C—H···O hydrogen bonds. For the major disorder component, they form

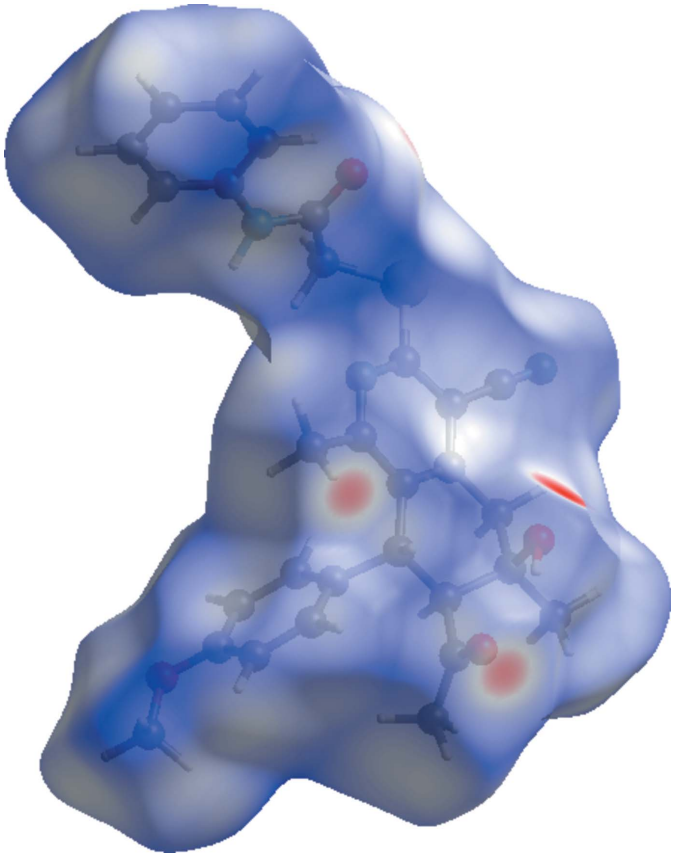


Figure 4
A view of the three-dimensional Hirshfeld surface of the title molecule plotted over d_{norm} in the range −0.5236 to +1.6751 a.u.

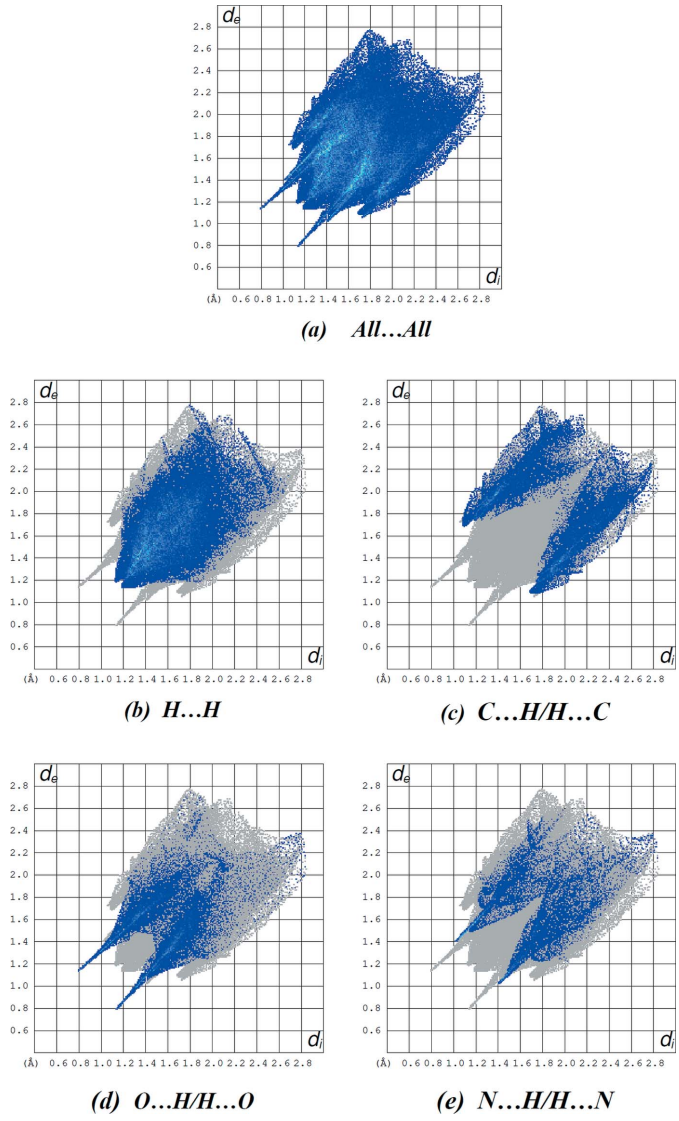


Figure 5
A view of the two-dimensional fingerprint plots for the title compound, showing (*a*) all interactions, and those delineated into (*b*) H···H, (*c*) C···H/H···C, (*d*) O···H/H···O and (*e*) N···H/H···N interactions. The d_i and d_e values are the closest internal and external distances (in Å) from given points on the Hirshfeld surface.

C(11) chains that propagate parallel to the *a* axis. In AKIVUO, a layer structure with the layers parallel to (10$\bar{1}$) is generated by O—H···O and C—H···O hydrogen bonds. In ULUTAZ, the molecules are linked *via* N—H···O and C—H···N hydrogen bonds into a three-dimensional network. Furthermore, the crystal packing is dominated by C—H···π contacts involving the phenyl H atoms. In CARCOQ, molecules are linked by an O—H···O hydrogen bond, forming chains propagating along the *a*-axis direction. The chains are linked by C—H···F hydrogen bonds, forming layers lying parallel to (001). In POPYEB, molecules are packed in a herringbone manner parallel to (103) and (10$\bar{3}$) *via* weak C—H···O and C—H···π(ring) interactions. In ENOCIU, various C—H···π and C—H···O bonds link the molecules together. In NIWPAL, the molecules are linked by N—H···O intermolecular hydrogen bonds involving the sulfonamide function to form an infinite two-dimensional network parallel to (001).

6. Synthesis and crystallization

A mixture of 7-acetyl-4-cyano-1,6-dimethyl-6-hydroxy-8-(4-methoxyphenyl)-5,6,7,8-tetrahydroisoquinoline-3(2*H*)-thione (10 mmol), *N*-(phenyl)-2-chloroacetamide (10 mmol) and sodium acetate trihydrate (1.77 g, 13 mmol) in ethanol (100 ml) was heated under reflux for 1 h. The reaction mixture was allowed to stand at room temperature overnight. The precipitate that formed was collected and recrystallized from ethanol giving colourless crystals of the title compound, m.p.: 508–510 K, yield 84%. Its IR spectrum showed characteristic absorption bands at 3474 cm^{-1} (OH); 3311 cm^{-1} (NH); 3023 cm^{-1} (C-H aromatic); 2910, 2956 cm^{-1} (C—H aliphatic); 1800, 1900 cm^{-1} (overtones of phenyl group); 2220 cm^{-1} (C≡N) and 1694 cm^{-1} (C=O). Its ^{1}H NMR (500 MHz, DMSO-d_6) spectrum exhibited the following signals: δ 10.21 (*s*, 1H, NH), 7.48–7.49 (*d*, 2H, *J* = 5 Hz, Ar-H); 7.22–7.25 (*t*, 2H, Ar-H); 6.97–7.00 (*t*, 1H, Ar-H); 6.89–6.91 (*d*, *J* = 10 Hz, 2H, Ar-H); 6.75–6.77 (*d*, *J* =10 Hz, 2H, Ar-H); 4.84 (*s*, 1H, OH); 4.41–4.43 (*d*, *J* = 10 Hz, 1H, CH at C-8); 4.04–4.11 (*dd*, 2H, SCH_2); 3.66 (*s*, 3H, OCH_3); 3.20–3.24 (*d*, *J* = 20 Hz, 1H, CH of cyclohexene ring); 2.83–2.85 (*d*, *J* = 10 Hz, 1H, CH at C-7); 2.81–2.84 (*d*, *J* = 15 Hz, 1H, CH of cyclohexene ring); 2.08 (*s*, 3H, $COCH_3$); 1.86 (*s*, 3H, CH_3 attached to pyridine ring) and 1.21 (*s*, 3H, CH_3 at C-6).

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 those attached to O and N atoms were positioned from a difference map, refined for a few cycles to ensure that reasonable displacement parameters could be achieved, and then their coordinates were adjusted to give O—H = 0.87 and N—H = 0.91 Å. All H atoms were refined using a riding model with isotropic displacement parameters 1.2–1.5 times those of the parent atoms.

Table 3
Experimental details.

Crystal data	
Chemical formula	$C_{29}H_{29}N_3O_4S$
M_r	515.61
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	150
a, *b*, *c* (Å)	8.4506 (16), 23.112 (5), 13.601 (3)
β (°)	99.021 (3)
V (Å^3)	2623.5 (9)
Z	4
Radiation type	Mo *K*α
μ (mm^{-1})	0.16
Crystal size (mm)	0.39 × 0.25 × 0.14
Data collection	
Diffractometer	Bruker *SMART APEX* CCD
Absorption correction	Multi-scan (*SADABS*; Krause *et al.*, 2015)
T_{min}, T_{max}	0.89, 0.98
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	50421, 7039, 5632
R_{int}	0.034
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.684
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*	0.043, 0.126, 1.10
No. of reflections	7039
No. of parameters	338
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.49, −0.20

Computer programs: *APEX3* (Bruker, 2016), *SAINT* (Bruker, 2016), *SHELXT* (Sheldrick, 2015*a*), *SHELXL2018/1* (Sheldrick, 2015*b*), *DIAMOND* (Brandenburg & Putz, 2012), *SHELXTL* (Sheldrick, 2008).

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Author contributions are as follows. Conceptualization, SKM and EAB; methodology, JTM, EAB and MA; investigation, EMS, RH and EAB; writing (original draft), JTM, MA and SKM; writing (review and editing of the manuscript), SKM, EAB and NF; visualization, SKM, EAB, MA and JTM; funding acquisition, SAHA; resources, SKM, EAB, JTM and RH; supervision, EAB and SKM.

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supporting information

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Computing details

Data collection: *APEX3* (Bruker, 2016); cell refinement: *SAINT* (Bruker, 2016); data reduction: *SAINT* (Bruker, 2016); program(s) used to solve structure: *SHELXT* (Sheldrick, 2015*a*); program(s) used to refine structure: *SHELXL2018/1* (Sheldrick, 2015*b*); molecular graphics: *DIAMOND* (Brandenburg & Putz, 2012); software used to prepare material for publication: *SHELXTL* (Sheldrick, 2008).

2-{[7-Acetyl-4-cyano-6-hydroxy-8-(4-methoxyphenyl)-1,6-dimethyl-5,6,7,8-tetrahydroisoquinolin-3-yl]sulfanyl}-*N*-phenylacetamide

Crystal data

$C_{29}H_{29}N_3O_4S$
M_r = 515.61
Monoclinic, $P2_1/n$
a = 8.4506 (16) Å
b = 23.112 (5) Å
c = 13.601 (3) Å
β = 99.021 (3)°
V = 2623.5 (9) Å^3
Z = 4
$F(000)$ = 1088
D_x = 1.305 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 9458 reflections
θ = 2.3–29.1°
μ = 0.16 mm^{-1}
T = 150 K
Block, colourless
0.39 × 0.25 × 0.14 mm

Data collection

Bruker SMART APEX CCD diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
Detector resolution: 8.3333 pixels mm^{-1}
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Krause *et al.*, 2015)
T_{min} = 0.89, T_{max} = 0.98
50421 measured reflections
7039 independent reflections
5632 reflections with $I > 2\sigma(I)$
R_{int} = 0.034
θ_{max} = 29.1°, θ_{min} = 1.8°
h = −11→11
k = −31→31
l = −18→18

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.126
S = 1.10
7039 reflections
338 parameters
0 restraints

Primary atom site location: dual
Secondary atom site location: difference Fourier map
Hydrogen site location: mixed
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0798P)^2 + 0.1546P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.49$ e Å^{-3}
$\Delta\rho_{min} = -0.20$ e Å^{-3}

Special details

Experimental. The diffraction data were obtained from 3 sets of 400 frames, each of width 0.5° in ω, collected at φ = 0.00, 90.00 and 180.00° and 2 sets of 800 frames, each of width 0.45° in φ, collected at ω = –30.00 and 210.00°. The scan time was 20 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 $F^2 > 2\text{sigma}(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger. 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 (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
S1	0.49743 (4)	0.21951 (2)	0.34201 (2)	0.02816 (10)
O1	1.20833 (12)	0.46549 (4)	0.59462 (8)	0.0424 (3)
O2	1.15692 (10)	0.36411 (4)	0.47667 (6)	0.02629 (19)
H2A	1.193331	0.399275	0.484612	0.039*
O3	0.60807 (11)	0.50037 (4)	0.89281 (7)	0.0355 (2)
O4	0.22412 (14)	0.25356 (5)	0.17522 (7)	0.0472 (3)
N1	0.55129 (11)	0.32668 (4)	0.41455 (7)	0.0221 (2)
N2	0.89889 (15)	0.16351 (5)	0.41504 (9)	0.0376 (3)
N3	0.11079 (13)	0.31512 (5)	0.27523 (7)	0.0283 (2)
H3A	0.123005	0.327808	0.339295	0.034*
C1	0.89205 (13)	0.40578 (4)	0.57616 (8)	0.0193 (2)
H1	0.912963	0.436858	0.528669	0.023*
C2	1.05704 (13)	0.38474 (5)	0.63229 (8)	0.0205 (2)
H2	1.037934	0.365533	0.695266	0.025*
C3	1.14103 (13)	0.34073 (5)	0.57288 (8)	0.0216 (2)
C4	1.03246 (13)	0.28858 (5)	0.55317 (9)	0.0225 (2)
H4A	1.079572	0.261207	0.509824	0.027*
H4B	1.026798	0.268725	0.617023	0.027*
C5	0.86588 (13)	0.30393 (5)	0.50451 (8)	0.0193 (2)
C6	0.77354 (13)	0.26220 (5)	0.44664 (8)	0.0204 (2)
C7	0.61510 (13)	0.27491 (5)	0.40627 (8)	0.0208 (2)
C8	0.64077 (13)	0.36804 (5)	0.46651 (8)	0.0207 (2)
C9	0.79759 (13)	0.35800 (4)	0.51612 (8)	0.0187 (2)
C10	0.80553 (13)	0.43324 (5)	0.65445 (8)	0.0204 (2)
C11	0.71854 (14)	0.39936 (5)	0.71205 (9)	0.0225 (2)

H11	0.704102	0.359333	0.697472	0.027*
C12	0.65289 (14)	0.42303 (5)	0.79006 (9)	0.0251 (2)
H12	0.592213	0.399454	0.827603	0.030*
C13	0.67580 (14)	0.48133 (5)	0.81346 (9)	0.0263 (2)
C14	0.76132 (15)	0.51598 (5)	0.75698 (9)	0.0284 (3)
H14	0.776837	0.555878	0.772287	0.034*
C15	0.82427 (14)	0.49165 (5)	0.67751 (9)	0.0249 (2)
H15	0.881237	0.515577	0.638293	0.030*
C16	0.6676 (2)	0.55312 (7)	0.93842 (12)	0.0465 (4)
H16A	0.784465	0.550913	0.955575	0.070*
H16B	0.620648	0.559492	0.999005	0.070*
H16C	0.638604	0.585256	0.892094	0.070*
C17	1.16474 (14)	0.43673 (5)	0.66046 (10)	0.0286 (3)
C18	1.21626 (19)	0.44933 (7)	0.76823 (11)	0.0431 (4)
H18A	1.267619	0.414967	0.801321	0.065*
H18B	1.122528	0.459723	0.798737	0.065*
H18C	1.292503	0.481576	0.775466	0.065*
C19	1.30468 (14)	0.32302 (6)	0.62869 (9)	0.0290 (3)
H19A	1.293501	0.310103	0.695891	0.044*
H19B	1.377685	0.356189	0.633079	0.044*
H19C	1.347991	0.291385	0.592961	0.044*
C20	0.84162 (14)	0.20690 (5)	0.43026 (9)	0.0247 (2)
C21	0.56021 (15)	0.42595 (5)	0.46529 (10)	0.0265 (2)
H21A	0.519924	0.431841	0.528302	0.040*
H21B	0.470632	0.427392	0.410039	0.040*
H21C	0.637465	0.456448	0.456723	0.040*
C22	0.29909 (14)	0.24507 (5)	0.35184 (9)	0.0257 (2)
H22A	0.234973	0.212181	0.370639	0.031*
H22B	0.307145	0.274003	0.406068	0.031*
C23	0.21135 (15)	0.27208 (5)	0.25746 (9)	0.0273 (3)
C24	−0.00831 (16)	0.34254 (5)	0.20589 (9)	0.0285 (3)
C25	−0.13620 (19)	0.36782 (6)	0.24298 (11)	0.0396 (3)
H25	−0.141122	0.365874	0.312204	0.047*
C26	−0.2556 (2)	0.39563 (8)	0.18009 (13)	0.0514 (4)
H26	−0.343050	0.412373	0.206057	0.062*
C27	−0.2491 (2)	0.39938 (7)	0.07906 (12)	0.0492 (4)
H27	−0.331596	0.418599	0.035625	0.059*
C28	−0.1216 (2)	0.37489 (7)	0.04246 (11)	0.0437 (4)
H28	−0.115917	0.377920	−0.026552	0.052*
C29	−0.00134 (18)	0.34587 (6)	0.10445 (10)	0.0351 (3)
H29	0.084748	0.328480	0.077982	0.042*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.02272 (16)	0.03016 (17)	0.03103 (18)	0.00082 (11)	0.00246 (12)	−0.01154 (12)
O1	0.0374 (5)	0.0381 (5)	0.0533 (6)	−0.0143 (4)	0.0119 (5)	0.0018 (5)
O2	0.0251 (4)	0.0342 (4)	0.0211 (4)	−0.0026 (3)	0.0085 (3)	0.0007 (3)

O3	0.0362 (5)	0.0424 (5)	0.0303 (5)	−0.0006 (4)	0.0130 (4)	−0.0128 (4)
O4	0.0612 (7)	0.0552 (6)	0.0236 (5)	0.0261 (5)	0.0014 (5)	−0.0100 (4)
N1	0.0203 (5)	0.0248 (4)	0.0216 (5)	0.0017 (4)	0.0043 (4)	−0.0006 (4)
N2	0.0387 (6)	0.0308 (5)	0.0423 (7)	0.0087 (5)	0.0035 (5)	−0.0053 (5)
N3	0.0318 (6)	0.0322 (5)	0.0209 (5)	0.0055 (4)	0.0039 (4)	−0.0030 (4)
C1	0.0191 (5)	0.0201 (5)	0.0194 (5)	−0.0001 (4)	0.0051 (4)	0.0011 (4)
C2	0.0203 (5)	0.0231 (5)	0.0186 (5)	−0.0001 (4)	0.0044 (4)	0.0003 (4)
C3	0.0193 (5)	0.0275 (5)	0.0186 (5)	0.0013 (4)	0.0048 (4)	0.0005 (4)
C4	0.0193 (5)	0.0238 (5)	0.0244 (6)	0.0038 (4)	0.0034 (4)	−0.0004 (4)
C5	0.0186 (5)	0.0222 (5)	0.0181 (5)	0.0013 (4)	0.0061 (4)	0.0019 (4)
C6	0.0209 (5)	0.0215 (5)	0.0196 (5)	0.0024 (4)	0.0054 (4)	−0.0002 (4)
C7	0.0199 (5)	0.0244 (5)	0.0188 (5)	−0.0002 (4)	0.0052 (4)	−0.0015 (4)
C8	0.0202 (5)	0.0222 (5)	0.0206 (5)	0.0016 (4)	0.0058 (4)	0.0015 (4)
C9	0.0183 (5)	0.0206 (5)	0.0180 (5)	0.0006 (4)	0.0054 (4)	0.0014 (4)
C10	0.0194 (5)	0.0209 (5)	0.0210 (5)	0.0015 (4)	0.0034 (4)	−0.0004 (4)
C11	0.0222 (5)	0.0216 (5)	0.0238 (5)	0.0002 (4)	0.0046 (4)	0.0005 (4)
C12	0.0224 (6)	0.0291 (6)	0.0247 (6)	−0.0012 (4)	0.0065 (5)	0.0006 (4)
C13	0.0222 (6)	0.0334 (6)	0.0237 (6)	0.0037 (5)	0.0045 (4)	−0.0058 (5)
C14	0.0297 (6)	0.0234 (5)	0.0319 (6)	0.0006 (5)	0.0049 (5)	−0.0058 (5)
C15	0.0250 (6)	0.0219 (5)	0.0287 (6)	−0.0007 (4)	0.0074 (5)	0.0010 (4)
C16	0.0458 (9)	0.0524 (9)	0.0426 (8)	−0.0003 (7)	0.0107 (7)	−0.0253 (7)
C17	0.0217 (6)	0.0272 (6)	0.0359 (7)	0.0009 (4)	0.0016 (5)	−0.0037 (5)
C18	0.0401 (8)	0.0420 (8)	0.0420 (8)	0.0037 (6)	−0.0101 (6)	−0.0156 (6)
C19	0.0202 (6)	0.0375 (7)	0.0285 (6)	0.0038 (5)	0.0011 (5)	−0.0028 (5)
C20	0.0243 (6)	0.0260 (5)	0.0236 (6)	0.0017 (4)	0.0030 (5)	−0.0023 (4)
C21	0.0230 (6)	0.0220 (5)	0.0335 (6)	0.0044 (4)	0.0017 (5)	0.0026 (5)
C22	0.0217 (5)	0.0305 (6)	0.0248 (6)	−0.0004 (5)	0.0035 (4)	−0.0037 (5)
C23	0.0275 (6)	0.0301 (6)	0.0236 (6)	0.0000 (5)	0.0026 (5)	−0.0054 (5)
C24	0.0332 (7)	0.0260 (6)	0.0261 (6)	0.0022 (5)	0.0037 (5)	−0.0003 (5)
C25	0.0448 (8)	0.0434 (7)	0.0323 (7)	0.0137 (6)	0.0118 (6)	0.0066 (6)
C26	0.0488 (9)	0.0588 (10)	0.0482 (9)	0.0255 (8)	0.0126 (8)	0.0086 (7)
C27	0.0509 (10)	0.0524 (9)	0.0413 (8)	0.0168 (7)	−0.0023 (7)	0.0072 (7)
C28	0.0532 (9)	0.0480 (8)	0.0277 (7)	0.0080 (7)	−0.0006 (6)	0.0016 (6)
C29	0.0394 (7)	0.0394 (7)	0.0264 (6)	0.0052 (6)	0.0052 (6)	−0.0020 (5)

Geometric parameters (Å, º)

S1—C7	1.7661 (12)	C11—H11	0.9500
S1—C22	1.8018 (12)	C12—C13	1.3911 (17)
O1—C17	1.2176 (16)	C12—H12	0.9500
O2—C3	1.4414 (13)	C13—C14	1.3884 (18)
O2—H2A	0.8696	C14—C15	1.3955 (16)
O3—C13	1.3711 (14)	C14—H14	0.9500
O3—C16	1.4233 (17)	C15—H15	0.9500
O4—C23	1.2182 (15)	C16—H16A	0.9800
N1—C7	1.3245 (14)	C16—H16B	0.9800
N1—C8	1.3482 (15)	C16—H16C	0.9800
N2—C20	1.1463 (15)	C17—C18	1.4908 (19)

N3—C23	1.3545 (16)	C18—H18A	0.9800
N3—C24	1.4164 (16)	C18—H18B	0.9800
N3—H3A	0.9097	C18—H18C	0.9800
C1—C10	1.5216 (15)	C19—H19A	0.9800
C1—C9	1.5229 (15)	C19—H19B	0.9800
C1—C2	1.5587 (15)	C19—H19C	0.9800
C1—H1	1.0000	C21—H21A	0.9800
C2—C17	1.5198 (16)	C21—H21B	0.9800
C2—C3	1.5399 (15)	C21—H21C	0.9800
C2—H2	1.0000	C22—C23	1.5128 (17)
C3—C4	1.5129 (16)	C22—H22A	0.9900
C3—C19	1.5255 (16)	C22—H22B	0.9900
C4—C5	1.5011 (15)	C24—C25	1.3911 (19)
C4—H4A	0.9900	C24—C29	1.3923 (18)
C4—H4B	0.9900	C25—C26	1.375 (2)
C5—C9	1.3958 (15)	C25—H25	0.9500
C5—C6	1.4021 (16)	C26—C27	1.386 (2)
C6—C7	1.3964 (16)	C26—H26	0.9500
C6—C20	1.4334 (15)	C27—C28	1.378 (2)
C8—C9	1.4088 (15)	C27—H27	0.9500
C8—C21	1.5006 (15)	C28—C29	1.387 (2)
C10—C15	1.3894 (16)	C28—H28	0.9500
C10—C11	1.3957 (15)	C29—H29	0.9500
C11—C12	1.3847 (16)		

C7—S1—C22	100.59 (6)	C15—C14—H14	120.3
C3—O2—H2A	108.6	C10—C15—C14	121.50 (11)
C13—O3—C16	117.10 (11)	C10—C15—H15	119.3
C7—N1—C8	118.87 (10)	C14—C15—H15	119.3
C23—N3—C24	127.59 (10)	O3—C16—H16A	109.5
C23—N3—H3A	115.3	O3—C16—H16B	109.5
C24—N3—H3A	117.1	H16A—C16—H16B	109.5
C10—C1—C9	114.12 (9)	O3—C16—H16C	109.5
C10—C1—C2	106.17 (9)	H16A—C16—H16C	109.5
C9—C1—C2	112.94 (8)	H16B—C16—H16C	109.5
C10—C1—H1	107.8	O1—C17—C18	122.75 (13)
C9—C1—H1	107.8	O1—C17—C2	118.98 (12)
C2—C1—H1	107.8	C18—C17—C2	118.24 (12)
C17—C2—C3	110.33 (9)	C17—C18—H18A	109.5
C17—C2—C1	109.33 (9)	C17—C18—H18B	109.5
C3—C2—C1	113.55 (9)	H18A—C18—H18B	109.5
C17—C2—H2	107.8	C17—C18—H18C	109.5
C3—C2—H2	107.8	H18A—C18—H18C	109.5
C1—C2—H2	107.8	H18B—C18—H18C	109.5
O2—C3—C4	106.15 (9)	C3—C19—H19A	109.5
O2—C3—C19	110.25 (9)	C3—C19—H19B	109.5
C4—C3—C19	110.59 (10)	H19A—C19—H19B	109.5
O2—C3—C2	110.17 (9)	C3—C19—H19C	109.5

C4—C3—C2	107.61 (9)	H19A—C19—H19C	109.5
C19—C3—C2	111.88 (9)	H19B—C19—H19C	109.5
C5—C4—C3	112.99 (9)	N2—C20—C6	177.76 (14)
C5—C4—H4A	109.0	C8—C21—H21A	109.5
C3—C4—H4A	109.0	C8—C21—H21B	109.5
C5—C4—H4B	109.0	H21A—C21—H21B	109.5
C3—C4—H4B	109.0	C8—C21—H21C	109.5
H4A—C4—H4B	107.8	H21A—C21—H21C	109.5
C9—C5—C6	118.41 (10)	H21B—C21—H21C	109.5
C9—C5—C4	122.51 (10)	C23—C22—S1	114.22 (9)
C6—C5—C4	119.07 (9)	C23—C22—H22A	108.7
C7—C6—C5	119.41 (10)	S1—C22—H22A	108.7
C7—C6—C20	120.66 (10)	C23—C22—H22B	108.7
C5—C6—C20	119.93 (10)	S1—C22—H22B	108.7
N1—C7—C6	122.32 (10)	H22A—C22—H22B	107.6
N1—C7—S1	119.46 (9)	O4—C23—N3	124.77 (12)
C6—C7—S1	118.22 (8)	O4—C23—C22	122.14 (11)
N1—C8—C9	122.85 (10)	N3—C23—C22	112.92 (10)
N1—C8—C21	114.24 (10)	C25—C24—C29	119.47 (12)
C9—C8—C21	122.90 (10)	C25—C24—N3	117.25 (11)
C5—C9—C8	117.89 (10)	C29—C24—N3	123.27 (12)
C5—C9—C1	121.24 (10)	C26—C25—C24	120.45 (14)
C8—C9—C1	120.80 (9)	C26—C25—H25	119.8
C15—C10—C11	118.02 (10)	C24—C25—H25	119.8
C15—C10—C1	120.86 (10)	C25—C26—C27	120.43 (14)
C11—C10—C1	120.80 (10)	C25—C26—H26	119.8
C12—C11—C10	121.20 (11)	C27—C26—H26	119.8
C12—C11—H11	119.4	C28—C27—C26	119.13 (14)
C10—C11—H11	119.4	C28—C27—H27	120.4
C11—C12—C13	119.99 (11)	C26—C27—H27	120.4
C11—C12—H12	120.0	C27—C28—C29	121.28 (14)
C13—C12—H12	120.0	C27—C28—H28	119.4
O3—C13—C14	124.61 (11)	C29—C28—H28	119.4
O3—C13—C12	115.51 (11)	C28—C29—C24	119.22 (13)
C14—C13—C12	119.87 (11)	C28—C29—H29	120.4
C13—C14—C15	119.40 (11)	C24—C29—H29	120.4
C13—C14—H14	120.3		

C10—C1—C2—C17	−73.07 (11)	C2—C1—C9—C5	−7.81 (14)
C9—C1—C2—C17	161.14 (9)	C10—C1—C9—C8	53.90 (13)
C10—C1—C2—C3	163.24 (9)	C2—C1—C9—C8	175.28 (9)
C9—C1—C2—C3	37.45 (12)	C9—C1—C10—C15	−145.75 (11)
C17—C2—C3—O2	−68.34 (12)	C2—C1—C10—C15	89.18 (12)
C1—C2—C3—O2	54.80 (12)	C9—C1—C10—C11	40.85 (14)
C17—C2—C3—C4	176.35 (9)	C2—C1—C10—C11	−84.22 (12)
C1—C2—C3—C4	−60.51 (11)	C15—C10—C11—C12	−0.12 (17)
C17—C2—C3—C19	54.68 (13)	C1—C10—C11—C12	173.46 (10)
C1—C2—C3—C19	177.82 (9)	C10—C11—C12—C13	−1.27 (18)

O2—C3—C4—C5	−64.32 (11)	C16—O3—C13—C14	−19.52 (18)
C19—C3—C4—C5	176.09 (9)	C16—O3—C13—C12	161.09 (12)
C2—C3—C4—C5	53.62 (12)	C11—C12—C13—O3	−179.06 (10)
C3—C4—C5—C9	−26.75 (15)	C11—C12—C13—C14	1.52 (18)
C3—C4—C5—C6	154.50 (10)	O3—C13—C14—C15	−179.75 (11)
C9—C5—C6—C7	−2.77 (16)	C12—C13—C14—C15	−0.39 (18)
C4—C5—C6—C7	176.02 (10)	C11—C10—C15—C14	1.28 (17)
C9—C5—C6—C20	177.84 (10)	C1—C10—C15—C14	−172.30 (11)
C4—C5—C6—C20	−3.36 (16)	C13—C14—C15—C10	−1.03 (18)
C8—N1—C7—C6	−2.18 (16)	C3—C2—C17—O1	59.92 (14)
C8—N1—C7—S1	177.89 (8)	C1—C2—C17—O1	−65.65 (14)
C5—C6—C7—N1	4.95 (17)	C3—C2—C17—C18	−118.40 (12)
C20—C6—C7—N1	−175.67 (11)	C1—C2—C17—C18	116.04 (12)
C5—C6—C7—S1	−175.12 (8)	C7—S1—C22—C23	103.44 (9)
C20—C6—C7—S1	4.25 (15)	C24—N3—C23—O4	7.0 (2)
C22—S1—C7—N1	−22.84 (10)	C24—N3—C23—C22	−168.25 (11)
C22—S1—C7—C6	157.23 (9)	S1—C22—C23—O4	36.74 (17)
C7—N1—C8—C9	−2.71 (16)	S1—C22—C23—N3	−147.86 (9)
C7—N1—C8—C21	176.15 (10)	C23—N3—C24—C25	155.07 (13)
C6—C5—C9—C8	−1.73 (15)	C23—N3—C24—C29	−25.9 (2)
C4—C5—C9—C8	179.52 (10)	C29—C24—C25—C26	0.4 (2)
C6—C5—C9—C1	−178.72 (9)	N3—C24—C25—C26	179.45 (14)
C4—C5—C9—C1	2.53 (16)	C24—C25—C26—C27	−0.7 (3)
N1—C8—C9—C5	4.65 (16)	C25—C26—C27—C28	0.0 (3)
C21—C8—C9—C5	−174.11 (10)	C26—C27—C28—C29	1.0 (3)
N1—C8—C9—C1	−178.34 (10)	C27—C28—C29—C24	−1.3 (2)
C21—C8—C9—C1	2.90 (16)	C25—C24—C29—C28	0.6 (2)
C10—C1—C9—C5	−129.19 (11)	N3—C24—C29—C28	−178.39 (13)

Hydrogen-bond geometry (Å, º)

*Cg*1 is the centroid of the N1/C–C9 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2*A*···O1	0.87	2.13	2.8343 (14)	138
N3—H3*A*···O2^{i}	0.91	2.03	2.9335 (14)	174
C2—H2···S1^{ii}	1.00	2.86	3.8269 (12)	163
C18—H18*A*···N2^{ii}	0.98	2.52	3.493 (2)	170
C21—H21*C*···O1^{iii}	0.98	2.39	3.3593 (16)	169
C25—H25···*Cg*1^{i}	0.95	2.79	3.6141 (18)	146

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