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Crystal structure of 5-(β-D-glucopyranosylthio)-*N*-(4-methylphenyl)-1,3,4-thiadiazol-2-amine

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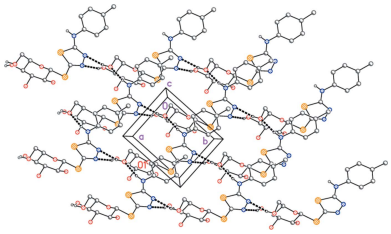
In the structure of the title compound, $C_{15}H_{19}N_3O_5S_2$, the bond lengths at the linking sulfur atom are significantly different [1.7473 (17) and 1.811 (2) Å], and the angle at the exocyclic nitrogen atom is wide at 128.45 (18)°. The interplanar angle between the tolyl and thiadiazole rings is 9.2 (1)°. The complex hydrogen-bonding pattern, involving five donors and five acceptors, can be broken down into a one-dimensional ribbon parallel to the *b* axis, involving hydrogen bonds of the sugar residues only, and a two-dimensional layer structure parallel to the *ab* plane, based on the N—H···O and O—H···N hydrogen bonds.

1. Chemical context

There has been considerable recent interest in the chemistry of compounds involving both heterocyclic and carbohydrate moieties (Lopes *et al.*, 2021). Heterocyclic thioglycosides are promising candidates in synthetic carbohydrate research, and some of these compounds have displayed various antagonistic activities (Abu-Zaied *et al.*, 2011, 2019; Khedr *et al.*, 2022). 1,3,4-Thiadiazoles are an important class of heterocycles that have found diverse applications in organic synthesis, biological applications, and pharmaceuticals (Sun *et al.*, 2011), thus motivating researchers to prepare many derivatives of these compounds (Matysiak, 2015). Our interest in synthesizing novel active heterocycles (Khedr *et al.*, 2022; Hebishy *et al.*, 2022; Abdallah *et al.*, 2022) and their glycosylic derivatives (Azzam *et al.*, 2022*a*,*b*) led us to expect that 1,3,4-thiazole compounds and their sugar-linked products could be valuable systems for designing novel cytotoxic agents (Yang *et al.*, 2012). In our previous work, many antiviral heterocyclic thioglycosides, such as azole and azine thioglycosides, were synthesized and found to display effective cytotoxicities (Elgemeie *et al.*, 2016, 2017*a*,*b*, 2018; Elgemeie & Mohamed-Ezzat, 2022*a*,*b*). We have also reported that dihydropyridine thioglycosides can be used as inhibitors of the glycosylation of proteins (Scala *et al.*, 1997).

In the current study, we have designed a facile synthesis of 1,3,4-thiadiazole thioglucosides by coupling of potassium 1,3,4-thiadiazolates and protected α-D-glucopyranosyl bromide. Our target derivative was synthesized by the reaction of the thiosemicarbazide derivative **1** with carbon disulfide in boiling KOH/EtOH to afford the corresponding potassium 1,3,4-thiadiazole thiolate **2** in good yield (Fig. 1). Compound **2** was then coupled with acetylated α-D-glucopyranose bromide **3** in DMF at room temperature to give a product that could in



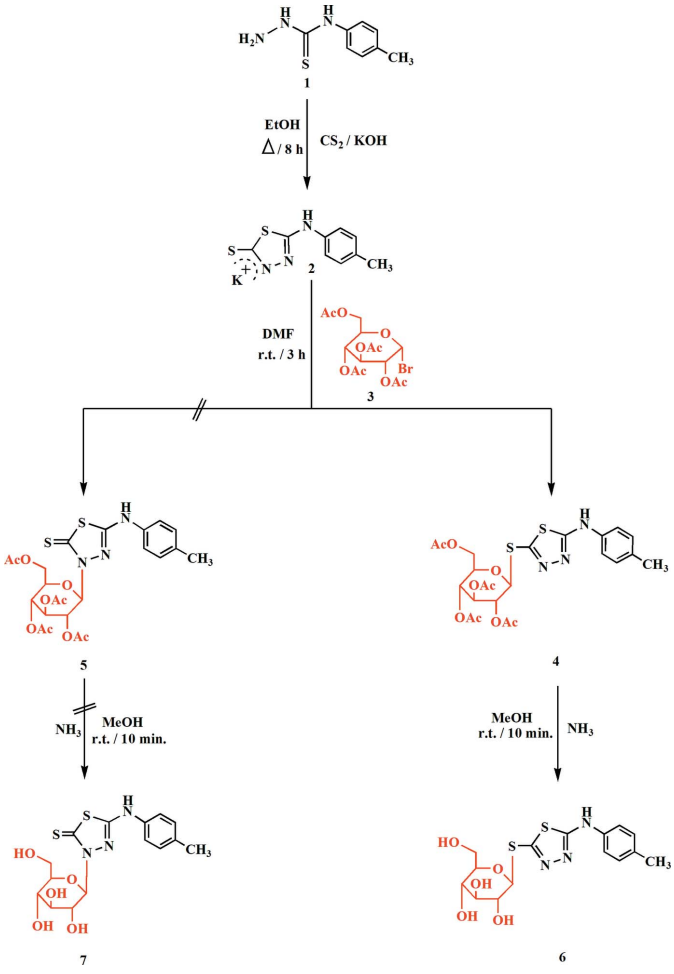
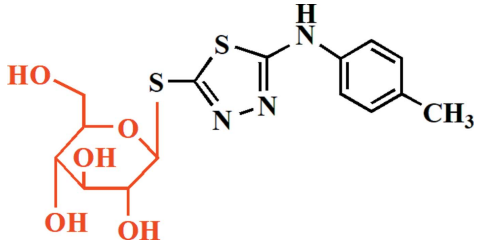


Figure 1
Reaction scheme for the synthesis of **6**.

principle be either the 1,3,4-thiadiazole *S*-glucoside **4** or the isomeric *N*-glucoside **5**, corresponding to two different modes of glycosylation. Deprotection then provided a final product that should be either the 1,3,4-thiadiazole *S*-glucoside **6** or the isomeric *N*-glucoside **7**. Spectroscopic data cannot distinguish these two structures with absolute certainty, although it had already been proposed that a simple S_{N^2} reaction between **2** and **3** would give the *β*-glucoside product **4** (Masoud *et al.*, 2017; Hammad *et al.*, 2018), which would imply the final formation of **6**.



This is consistent with the spectroscopic data; thus the ^{1}H NMR spectrum of **6** showed the signal of the anomeric proton as a doublet at *δ* 4.72 ($J_{1',2'}$ = 10.8 Hz), strongly implying a *β*-D-configuration. The ^{13}C NMR spectrum exhibited a signal at *δ* 86.89 corresponding to C-1′, whereas the signals at *δ* 61.34, 70.00, 73.07 and 78.32, 81.42 were allocated to C-6′, C-4‘, C-2′, C-3′ and C-5′. The X-ray structure determination, presented here, unambiguously shows the isolated product to be the 1,3,4-thiadiazole-5-thioglucoside **6** (Fig. 1).

Table 1
Selected geometric parameters (Å, °).

S1—C2	1.7322 (19)	N4—C5	1.309 (3)
S1—C5	1.7525 (18)	C5—N1	1.358 (2)
C2—N3	1.298 (2)	C11—S2	1.811 (2)
C2—S2	1.7473 (17)	N1—C21	1.411 (2)
N3—N4	1.397 (2)		
C2—S1—C5	86.59 (9)	C5—N4—N3	111.44 (15)
N3—C2—S1	114.31 (13)	N4—C5—N1	128.67 (17)
N3—C2—S2	119.74 (14)	N4—C5—S1	114.15 (14)
S1—C2—S2	125.88 (10)	N1—C5—S1	117.17 (15)
C2—N3—N4	113.29 (16)	C5—N1—C21	128.45 (18)
S2—C11—O1—C15	177.11 (10)	O1—C11—S2—C2	−55.86 (12)
N3—C2—S2—C11	−164.51 (14)	C12—C11—S2—C2	−174.12 (11)
S1—C2—S2—C11	18.65 (13)		

2. Structural commentary

The molecular structure of compound **6** is shown in Fig. 2. Note that the standard sugar numbering has been slightly modified (to C11–16) for the crystallographic numbering. Molecular dimensions (Table 1) may be regarded as normal; *e.g.* the bond lengths at S2 are significantly different, consistent with the different hybridization of the carbon atoms [C2—S2 = 1.7473 (17), C11—S2 = 1.811 (2) Å], and the angle C5—N1—C21 is wide at 128.45 (18)°. The interplanar angle between the tolyl and thiadiazole rings is 9.2 (1)°. The *β* (equatorial) position of the substituent at the glucose ring is confirmed by the torsion angle C15—O1—C11—S2 of 177.11 (10)°. The absolute configuration was confirmed by the Flack parameter, with chiralities *S*,*R*,*S*,*S*,*R* at C11–15 respectively consistent with the presence of D-glucose.

3. Supramolecular features

With five classical hydrogen bonds (Table 2), the molecular packing of **6** might be expected to be three-dimensional and

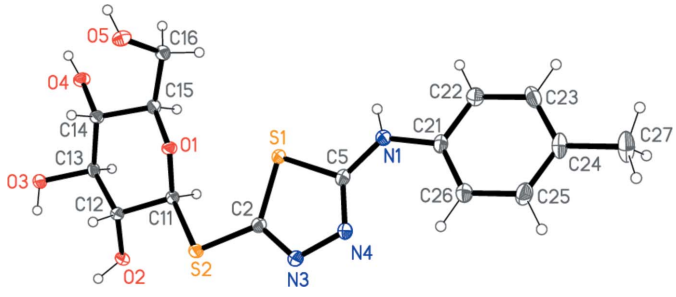


Figure 2
The molecule of compound **6** in the crystal. Ellipsoids represent 50% probability levels.

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O2—H02···O3^{i}	0.82 (2)	1.87 (2)	2.6846 (19)	174 (3)
O3—H03···O4^{i}	0.84 (2)	1.93 (2)	2.7375 (18)	161 (3)
O4—H04···N3^{ii}	0.81 (2)	2.06 (2)	2.848 (2)	162 (3)
O5—H05···N4^{ii}	0.83 (2)	2.11 (2)	2.899 (2)	159 (3)
O5—H05···N3^{ii}	0.83 (2)	2.60 (2)	3.282 (2)	141 (2)
N1—H01···O5^{iii}	0.84 (3)	2.05 (3)	2.853 (2)	158 (2)
C14—H14···S1^{iv}	1.00	2.74	3.7044 (18)	163
C16—H16B···S2^{v}	0.99	2.71	3.570 (2)	145

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

complex, and this is indeed the case. However, the packing may be analysed in terms of more easily assimilable substructures. One, formally one-dimensional, substructure involving the sugar residues can readily be identified (Fig. 3), the hydrogen bonds O2—H02···O3 and O3—H03···O4($-x+3, y+\frac{1}{2}, -z+1$ for both) combine *via* the 2_1 screw axis to form ribbons of molecules parallel to the *b* axis. The ribbons lie in layers roughly parallel to (105). The OH group at C16 is directed away from its layer to form contacts to the neighbouring layer.

A second, two-dimensional, substructure (Fig. 4) is based on the remaining three hydrogen bonds (of the types O—H···N and N—H···O), and connects the molecules first by translation (both O—H···N hydrogen bonds; $x+1, y-1, z$) to form chains parallel to (1$\bar{1}$0) (horizontal in the Figure), and secondly by *a*-axis translation (the N—H···O hydrogen bond; $x-1, y, z$). The overall effect is to create layers parallel to the *ab* plane.

The contact O5—H05···N3($x+1, y-1, z$) may be regarded as the second, weaker, branch of a three-centre

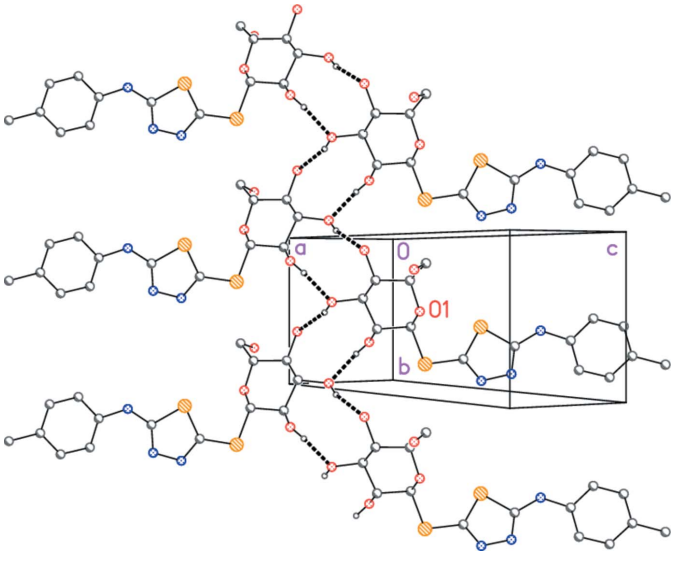


Figure 3
Packing diagram of compound **6**: the glucose-based substructure involving two O—H···O hydrogen bonds (indicated by thick dashed lines). The view direction is perpendicular to the plane (105). The labelled atom (O1) indicates the asymmetric unit.

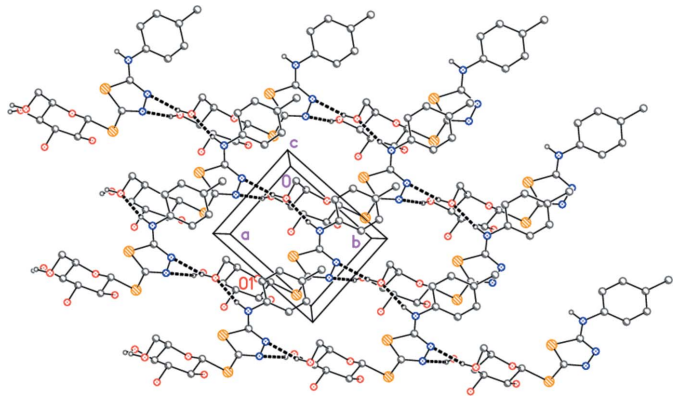


Figure 4
Packing diagram of compound **6**: the layer substructure involving the O—H···N and N—H···O hydrogen bonds (indicated by thick dashed lines). The view direction is perpendicular to the *ab* plane. The labelled atom (O1) indicates the asymmetric unit.

interaction, but this contact is omitted from the packing diagrams for clarity. Similarly, the two C—H···S interactions are probably interpretable as 'weak' hydrogen bonds, but we do not discuss their structural role in detail.

4. Database survey

The search employed the routine ConQuest (Bruno *et al.*, 2002), part of Version 2022.3.0 of the Cambridge Structural Database (Groom *et al.*, 2016). We searched for pyranose sugars attached by a sulfur atom to heterocycles containing more than one heteroatom (a larger subset of hits was edited by hand). The six structures thus found were derivatives of 1,2,4-triazole (refcode HEKPUL; El Ashry *et al.*, 2018), 1,3,4-oxadiazole (IZAJEY; Qiu & Xu, 2004), benzoxazole (JIPYUD and JIPZAK; Kamat *et al.*, 2007), 1,3,5-oxathiazole, involving a spiro junction at the sugar C1 atom (PIWVIA; Praly *et al.*, 1994) and 1,3,4-thiadiazole (SASXIU; Qiu *et al.*, 2005). In all except PIWVIA, the sugar OH groups were substituted with ester functions. The structure SASXIU, despite having the same heterocycle as **6**, (but with a 2-phenyl substituent), has a markedly different relative orientation of the glucose and heterocyclic rings, with a torsion angle C_{gluc}—S_{gluc}—C_{hetero}—S_{hetero} of 78.10 (10)° compared to the value of 18.65 (13)° for **6**.

5. Synthesis and crystallization

Preparation of intermediate **4**: A solution of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**3**) (10 mmol) in dry DMF (15 mL) was added dropwise over 30 min to a solution of the potassium thiolate **2** (10 mmol) in 20 mL of DMF. The reaction mixture was stirred at room temperature until completion (monitored by TLC), then the mixture was poured into ice–water, and the resulting precipitate was collected by filtration, dried, and crystallized from ethanol to give the acetylated glucoside **4**.

N·B.: The NMR data, as given here and in Section 1, refer to sugar numbering C1′–C6′, which is different from the crystallographic numbering of the glucose moiety in **6** (C11–C16).

White powder (EtOH); yield 93%; m.p. 479–481 K; IR (cm^{-1}): υ 3360 (NH), 2949 (CH_3), 1741 (C═O); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.91–2.05 (4*s*, 12H, 4 × OAc), 2.27 (*s*, 3H, CH_3), 4.07–4.19 (*m*, 3H, H-6′, H-6″, H-5′), 4.90–4.98 (*m*, 2H, H-4′, H-2′), 5.39 (*t*-like, 1H, J = 10.8 Hz, H-3′), 5.40 (*d*, 1H, $J_{1'-2'}$ = 7.1 Hz, H-1′), 7.16 (*d*, 2H, J = 8.0 Hz, Ar-H), 7.46 (*d*, 2H, J = 7.2 Hz, Ar-H), 10.45 (*s*, D_2O exchangeable, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 20.70, 20.81, 20.90 (5 × CH_3), 62.20 (C-6′), 68.23 (C-4′), 70.04 (C-2′), 73.14 (C-3′), 75.17 (C-5′), 82.99 (C-1′), 118.35 (2C, Ar-C), 130.05 (2C, Ar-C), 131.99 (Ar-C), 138.30 (Ar-C), 145.21 (C-2), 167.88 (C-5), 169.50, 169.74, 169.98, 170.48 (4C═O). Analysis calculated for $C_{23}H_{27}N_3O_9S_2$ (553.61): C 49.90, H 4.92, N 7.59, S 11.58. Found: C 49.82, H 4.81, N 7.52, S 11.46%.

Preparation of title compound **6**: In a 50 mL flask, the tetraacetylated glucoside derivative **4** (0.01 mol) was dissolved in 20 mL of dry methanol, and then ammonia gas was passed through the solution at 273 K for 10 min. The mixture was then stirred until the reaction was complete (monitored by TLC using chloroform/methanol 9:1). The solution was concentrated under reduced pressure to afford a solid residue, which was washed several times with boiling chloroform. The residue was dried, purified and recrystallized from ethanol to give the corresponding free glucoside **6**.

Colourless crystals (EtOH); yield 62%; m.p. 472–474 K; IR (cm^{-1}): ν 3271 (OH), 2921 (CH); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.25 (*s*, 3H, CH_3), 3.11–3.22 (*m*, 2H, H-6′, H-6″), 3.23–3.29 (*m*, 2H, H-5′, H-4′), 3.49–3.56 (*m*, 1H, H-3′), 3.71–3.76 (*m*, 1H, H-2′), 4.59 (*t*, 1H, $J_{OH-H-6''}$ = 3.6 Hz, D_2O-exchangeable, 6″-OH), 4.72 (*d*, 1H, $J_{1'-2'}$ = 10.8 Hz, H-1′), 5.05 (d, 1H, J = 6.4 Hz, D_2O-exchangeable, OH), 5.17 (*d*, 1H, J = 6.4 Hz, D_2O-exchangeable, OH), 5.53 (*d*, 1H, J = 8.0 Hz, D_2O-exchangeable, OH), 7.14 (*d*, 2H, J = 11.2 Hz, Ar-H), 7.47 (*d*, 2H, J = 12.4 Hz, Ar-H), 10.32 (*s*, D_2O exch., 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 20.82 (CH_3), 61.34 (C-6′), 70.00 (C-4′), 73.07 (C-2′), 78.32 (C-3′), 81.42 (C-5′), 86.89 (C-1′), 117.98 (2C, Ar-C), 129.96 (2C, Ar-C), 131.33 (Ar-C), 138.50 (Ar-C), 150.03 (C-2), 166.90 (C-5). Analysis calculated for $C_{15}H_{19}N_3O_5S_2$ (385.08): C 46.75, H 4.94, N 10.91, S 16.62. Found: C 46.6, H 4.8, N 10.9, S 16.5%.

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 3. Hydrogen atoms of the NH and OH groups were refined freely, the latter however with O—H distances restrained to be approximately equal (command SADI). The methyl group was included as an idealized rigid group allowed to rotate but not tip (C—H = 0.98 Å, H—C—H = 109.5°). Other hydrogen atoms were included using a riding model starting from calculated positions (C—$H_{aromatic}$ 0.95 Å, C—$H_{methine}$ 1.00 Å, C—$H_{methylene}$ 0.99 Å). The U(H) values were fixed at 1.5 × U_{eq} of the parent carbon atoms for the methyl group and 1.2 × U_{eq} for other hydrogens. An extinction correction was performed; the extinction parameter as defined by Sheldrick (2015*a*) refined to 0.0009 (3). The absolute configuration (corresponding to D-glucose) was confirmed by the Flack parameter of −0.006 (5).

Table 3
Experimental details.

Crystal data	
Chemical formula	$C_{15}H_{19}N_3O_5S_2$
M_r	385.45
Crystal system, space group	Monoclinic, $P2_1$
Temperature (K)	100
a, b, c (Å)	6.23840 (6), 7.4355 (1), 18.32032 (17)
β (°)	91.4183 (8)
V (Å^3)	849.54 (2)
Z	2
Radiation type	Cu $K\alpha$
μ (mm^{-1})	3.14
Crystal size (mm)	0.10 × 0.08 × 0.02
Data collection	
Diffractometer	XtaLAB Synergy
Absorption correction	Multi-scan (*CrysAlis PRO*; Rigaku OD, 2021)
T_{min}, T_{max}	0.851, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	70354, 3520, 3502
R_{int}	0.030
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.633
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.019, 0.050, 1.03
No. of reflections	3520
No. of parameters	248
No. of restraints	7
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.30, −0.21
Absolute structure	Flack x determined using 1554 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter	−0.006 (5)

Computer programs: *CrysAlis PRO* (Rigaku OD, 2021), *SHELXT* (Sheldrick, 2015*b*), *SHELXL2018/3* (Sheldrick, 2015*a*) and *XP* (Siemens, 1994).

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supporting information

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Crystal structure of 5-(*β*-D-glucopyranosylthio)-*N*-(4-methylphenyl)-1,3,4-thiadiazol-2-amine

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Computing details

Data collection: *CrysAlis PRO* (Rigaku OD, 2021); cell refinement: *CrysAlis PRO* (Rigaku OD, 2021); data reduction: *CrysAlis PRO* (Rigaku OD, 2021); program(s) used to solve structure: *SHELXT* (Sheldrick, 2015b); program(s) used to refine structure: *SHELXL2018/3* (Sheldrick, 2015a); molecular graphics: *XP* (Siemens, 1994); software used to prepare material for publication: *SHELXL2018/3* (Sheldrick, 2015a).

5-[(*β*-*D*-Glucopyranosyl)sulfanyl]-*N*-(4-methylphenyl)-1,3,4-thiadiazol-2-amine

Crystal data

$C_{15}H_{19}N_3O_5S_2$
M_r = 385.45
Monoclinic, $P2_1$
a = 6.23840 (6) Å
b = 7.4355 (1) Å
c = 18.32032 (17) Å
β = 91.4183 (8)°
V = 849.54 (2) Å^3
Z = 2
$F(000)$ = 404
D_x = 1.507 Mg m^{-3}
Cu $K\alpha$ radiation, λ = 1.54184 Å
Cell parameters from 61296 reflections
θ = 2.4–77.5°
μ = 3.14 mm^{-1}
T = 100 K
Plate, colourless
0.10 × 0.08 × 0.02 mm

Data collection

XtaLAB Synergy diffractometer
Radiation source: micro-focus sealed X-ray tube, PhotonJet (Cu) X-ray Source
Mirror monochromator
Detector resolution: 10.0000 pixels mm^{-1}
ω scans
Absorption correction: multi-scan (CrysAlisPro; Rigaku OD, 2021)
T_{min} = 0.851, T_{max} = 1.000
70354 measured reflections
3520 independent reflections
3502 reflections with $I > 2\sigma(I)$
R_{int} = 0.030
θ_{max} = 77.3°, θ_{min} = 2.4°
h = −7→7
k = −9→8
l = −23→23

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.019
$wR(F^2)$ = 0.050
S = 1.03
3520 reflections
248 parameters
7 restraints
Primary atom site location: dual
Hydrogen site location: mixed
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0289P)^2 + 0.2573P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.30 e Å^{-3}

$\Delta\rho_{min}$ = −0.21 e Å^{-3}
Extinction correction: SHELXL-2018/3 (Sheldrick, 2015a), $Fc^{*}=kFc[1+0.001xFc^{2}\lambda^{3}/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.0009 (3)
Absolute structure: Flack *x* determined using 1554 quotients $[(I^{+})-(I^{-})]/[(I^{+})+(I^{-})]$ (Parsons *et al.*, 2013)
Absolute structure parameter: −0.006 (5)

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.
Least-squares planes (x,y,z in crystal coordinates) and deviations from them (* indicates atom used to define plane)
3.7080 (0.0039) x + 2.0545 (0.0042) y + 13.5622 (0.0105) z = 13.7691 (0.0045)
* 0.0205 (0.0007) S1 * -0.0130 (0.0010) C2 * -0.0030 (0.0011) N3 * 0.0244 (0.0010) N4 * -0.0289 (0.0010) C5 -0.1014 (0.0026) N1 0.0173 (0.0026) S2
Rms deviation of fitted atoms = 0.0201
3.4518 (0.0038) x + 1.0131 (0.0062) y + 14.7993 (0.0080) z = 13.9365 (0.0076)
Angle to previous plane (with approximate esd) = 9.200 (0.107)
* 0.0048 (0.0012) C21 * -0.0074 (0.0013) C22 * 0.0034 (0.0013) C23 * 0.0035 (0.0014) C24 * -0.0062 (0.0014) C25 * 0.0020 (0.0013) C26 0.0546 (0.0026) N1 0.0234 (0.0033) C27
Rms deviation of fitted atoms = 0.0049
3.6049 (0.0167) x + 0.8656 (0.1231) y + 14.5324 (0.0137) z = 13.6402 (0.0694)
Angle to previous plane (with approximate esd) = 1.978 (0.397)
* 0.0000 (0.0000) H01 * 0.0000 (0.0000) C5 * 0.0000 (0.0000) C21 0.0965 (0.0103) N1
Rms deviation of fitted atoms = 0.0000

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

	x	*y*	*z*	U_{iso}*/U_{eq}
S1	0.68679 (6)	0.56520 (6)	0.74337 (2)	0.01368 (10)
C2	0.7401 (3)	0.7619 (2)	0.69652 (9)	0.0141 (4)
N3	0.6138 (2)	0.8948 (2)	0.71166 (8)	0.0164 (3)
N4	0.4594 (2)	0.8505 (2)	0.76262 (8)	0.0164 (3)
C5	0.4713 (3)	0.6807 (3)	0.78116 (9)	0.0141 (3)
C11	1.0267 (2)	0.5674 (3)	0.61331 (9)	0.0129 (3)
H11	0.908249	0.505970	0.585259	0.015*
C12	1.2263 (3)	0.5825 (3)	0.56692 (9)	0.0125 (3)
H12	1.336334	0.656908	0.593626	0.015*
C13	1.3196 (3)	0.3958 (3)	0.55237 (9)	0.0132 (3)
H13	1.225617	0.331025	0.516019	0.016*
C14	1.3421 (3)	0.2844 (3)	0.62159 (9)	0.0129 (3)
H14	1.457744	0.336867	0.653816	0.015*
C15	1.1297 (3)	0.2862 (3)	0.66200 (9)	0.0135 (3)
H15	1.014260	0.235018	0.629328	0.016*
C16	1.1351 (3)	0.1833 (3)	0.73351 (10)	0.0159 (3)
H16A	1.005890	0.214160	0.761185	0.019*
H16B	1.129897	0.052814	0.722861	0.019*
O1	1.07795 (19)	0.47115 (17)	0.67845 (7)	0.0135 (3)
O2	1.1689 (2)	0.66863 (19)	0.50027 (7)	0.0153 (3)
H02	1.264 (4)	0.740 (4)	0.4908 (15)	0.038 (8)*
O3	1.52906 (19)	0.41758 (19)	0.52349 (7)	0.0168 (3)

H03	1.522 (4)	0.482 (4)	0.4857 (13)	0.029 (7)*
O4	1.3989 (2)	0.10451 (18)	0.60228 (7)	0.0162 (3)
H04	1.471 (4)	0.067 (4)	0.6365 (12)	0.030 (7)*
O5	1.3225 (2)	0.22073 (19)	0.77822 (7)	0.0178 (3)
H05	1.382 (4)	0.122 (3)	0.7831 (14)	0.032 (8)*
N1	0.3417 (2)	0.5861 (2)	0.82558 (8)	0.0156 (3)
H01	0.353 (4)	0.473 (4)	0.8230 (13)	0.020 (6)*
C21	0.1567 (3)	0.6454 (3)	0.86130 (9)	0.0154 (3)
C22	0.0393 (3)	0.5129 (3)	0.89691 (10)	0.0191 (4)
H22	0.082328	0.390608	0.894194	0.023*
C23	−0.1396 (3)	0.5595 (3)	0.93618 (10)	0.0221 (4)
H23	−0.216466	0.468512	0.960842	0.027*
C24	−0.2085 (3)	0.7375 (3)	0.94008 (11)	0.0220 (4)
C25	−0.0925 (3)	0.8667 (3)	0.90351 (11)	0.0230 (4)
H25	−0.138366	0.988413	0.905038	0.028*
C26	0.0901 (3)	0.8234 (3)	0.86446 (10)	0.0195 (4)
H26	0.167780	0.914713	0.840330	0.023*
S2	0.94984 (6)	0.79473 (6)	0.63645 (2)	0.01473 (10)
C27	−0.4029 (3)	0.7886 (4)	0.98327 (13)	0.0322 (5)
H27A	−0.533285	0.765916	0.953762	0.048*
H27B	−0.395250	0.916469	0.996023	0.048*
H27C	−0.406140	0.716487	1.028010	0.048*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.01271 (18)	0.0111 (2)	0.01736 (19)	0.00212 (16)	0.00360 (13)	0.00076 (16)
C2	0.0134 (8)	0.0129 (10)	0.0161 (8)	0.0005 (6)	0.0007 (6)	−0.0002 (7)
N3	0.0159 (7)	0.0146 (8)	0.0188 (7)	0.0029 (6)	0.0043 (6)	0.0020 (6)
N4	0.0147 (7)	0.0164 (8)	0.0183 (7)	0.0024 (6)	0.0050 (6)	0.0016 (6)
C5	0.0127 (8)	0.0155 (9)	0.0140 (8)	0.0021 (7)	0.0004 (6)	−0.0013 (7)
C11	0.0123 (7)	0.0115 (8)	0.0149 (7)	0.0006 (7)	0.0020 (6)	0.0008 (7)
C12	0.0122 (7)	0.0120 (8)	0.0133 (7)	0.0005 (7)	0.0016 (5)	0.0015 (7)
C13	0.0114 (8)	0.0139 (9)	0.0145 (8)	0.0002 (6)	0.0031 (6)	−0.0006 (7)
C14	0.0141 (7)	0.0103 (8)	0.0145 (7)	0.0010 (7)	0.0031 (6)	0.0000 (7)
C15	0.0140 (7)	0.0103 (8)	0.0163 (7)	0.0011 (7)	0.0034 (6)	−0.0013 (7)
C16	0.0154 (8)	0.0153 (9)	0.0174 (8)	0.0007 (7)	0.0033 (6)	0.0017 (7)
O1	0.0160 (6)	0.0102 (6)	0.0144 (6)	0.0027 (5)	0.0040 (4)	0.0010 (5)
O2	0.0146 (6)	0.0151 (7)	0.0162 (6)	−0.0009 (5)	0.0017 (4)	0.0053 (5)
O3	0.0147 (6)	0.0166 (7)	0.0194 (6)	0.0030 (5)	0.0074 (5)	0.0049 (5)
O4	0.0202 (6)	0.0122 (7)	0.0163 (6)	0.0046 (5)	0.0039 (5)	0.0000 (5)
O5	0.0211 (7)	0.0135 (7)	0.0188 (6)	0.0027 (5)	−0.0010 (5)	0.0006 (5)
N1	0.0149 (7)	0.0127 (9)	0.0193 (7)	0.0012 (6)	0.0035 (5)	0.0009 (6)
C21	0.0120 (8)	0.0208 (10)	0.0136 (7)	0.0020 (7)	0.0007 (6)	−0.0009 (7)
C22	0.0177 (8)	0.0202 (10)	0.0195 (8)	0.0008 (7)	0.0013 (7)	0.0005 (7)
C23	0.0157 (8)	0.0301 (11)	0.0207 (8)	−0.0037 (9)	0.0038 (6)	0.0027 (9)
C24	0.0141 (8)	0.0309 (12)	0.0211 (9)	0.0000 (7)	0.0035 (7)	−0.0081 (8)
C25	0.0197 (9)	0.0225 (11)	0.0271 (10)	0.0042 (8)	0.0049 (8)	−0.0046 (8)

C26	0.0177 (8)	0.0194 (11)	0.0217 (8)	0.0012 (7)	0.0046 (7)	0.0001 (8)
S2	0.01492 (19)	0.0101 (2)	0.01939 (19)	0.00117 (15)	0.00557 (14)	0.00078 (16)
C27	0.0195 (9)	0.0386 (13)	0.0389 (11)	−0.0030 (10)	0.0112 (8)	−0.0133 (11)

Geometric parameters (Å, º)

S1—C2	1.7322 (19)	C16—O5	1.438 (2)
S1—C5	1.7525 (18)	C16—H16A	0.9900
C2—N3	1.298 (2)	C16—H16B	0.9900
C2—S2	1.7473 (17)	O2—H02	0.82 (2)
N3—N4	1.397 (2)	O3—H03	0.84 (2)
N4—C5	1.309 (3)	O4—H04	0.81 (2)
C5—N1	1.358 (2)	O5—H05	0.83 (2)
C11—O1	1.421 (2)	N1—C21	1.411 (2)
C11—C12	1.529 (2)	N1—H01	0.84 (3)
C11—S2	1.811 (2)	C21—C26	1.389 (3)
C11—H11	1.0000	C21—C22	1.398 (3)
C12—O2	1.417 (2)	C22—C23	1.387 (3)
C12—C13	1.531 (3)	C22—H22	0.9500
C12—H12	1.0000	C23—C24	1.394 (3)
C13—O3	1.4311 (19)	C23—H23	0.9500
C13—C14	1.518 (2)	C24—C25	1.386 (3)
C13—H13	1.0000	C24—C27	1.513 (2)
C14—O4	1.431 (2)	C25—C26	1.397 (2)
C14—C15	1.534 (2)	C25—H25	0.9500
C14—H14	1.0000	C26—H26	0.9500
C15—O1	1.446 (2)	C27—H27A	0.9800
C15—C16	1.517 (2)	C27—H27B	0.9800
C15—H15	1.0000	C27—H27C	0.9800
C2—S1—C5	86.59 (9)	O5—C16—C15	113.27 (15)
N3—C2—S1	114.31 (13)	O5—C16—H16A	108.9
N3—C2—S2	119.74 (14)	C15—C16—H16A	108.9
S1—C2—S2	125.88 (10)	O5—C16—H16B	108.9
C2—N3—N4	113.29 (16)	C15—C16—H16B	108.9
C5—N4—N3	111.44 (15)	H16A—C16—H16B	107.7
N4—C5—N1	128.67 (17)	C11—O1—C15	110.51 (13)
N4—C5—S1	114.15 (14)	C12—O2—H02	108 (2)
N1—C5—S1	117.17 (15)	C13—O3—H03	109.9 (19)
O1—C11—C12	109.56 (13)	C14—O4—H04	106 (2)
O1—C11—S2	109.19 (11)	C16—O5—H05	104 (2)
C12—C11—S2	106.59 (13)	C5—N1—C21	128.45 (18)
O1—C11—H11	110.5	C5—N1—H01	115.6 (16)
C12—C11—H11	110.5	C21—N1—H01	113.9 (17)
S2—C11—H11	110.5	C26—C21—C22	119.40 (17)
O2—C12—C11	108.70 (13)	C26—C21—N1	124.47 (17)
O2—C12—C13	110.40 (13)	C22—C21—N1	116.11 (17)
C11—C12—C13	110.38 (15)	C23—C22—C21	120.26 (19)

O2—C12—H12	109.1	C23—C22—H22	119.9
C11—C12—H12	109.1	C21—C22—H22	119.9
C13—C12—H12	109.1	C22—C23—C24	121.12 (19)
O3—C13—C14	107.70 (13)	C22—C23—H23	119.4
O3—C13—C12	108.45 (14)	C24—C23—H23	119.4
C14—C13—C12	112.14 (14)	C25—C24—C23	117.89 (17)
O3—C13—H13	109.5	C25—C24—C27	120.9 (2)
C14—C13—H13	109.5	C23—C24—C27	121.2 (2)
C12—C13—H13	109.5	C24—C25—C26	122.0 (2)
O4—C14—C13	108.79 (13)	C24—C25—H25	119.0
O4—C14—C15	110.46 (15)	C26—C25—H25	119.0
C13—C14—C15	109.59 (13)	C21—C26—C25	119.31 (18)
O4—C14—H14	109.3	C21—C26—H26	120.3
C13—C14—H14	109.3	C25—C26—H26	120.3
C15—C14—H14	109.3	C2—S2—C11	102.94 (8)
O1—C15—C16	107.46 (13)	C24—C27—H27A	109.5
O1—C15—C14	107.97 (14)	C24—C27—H27B	109.5
C16—C15—C14	114.29 (14)	H27A—C27—H27B	109.5
O1—C15—H15	109.0	C24—C27—H27C	109.5
C16—C15—H15	109.0	H27A—C27—H27C	109.5
C14—C15—H15	109.0	H27B—C27—H27C	109.5

C5—S1—C2—N3	2.54 (14)	O1—C15—C16—O5	−74.18 (17)
C5—S1—C2—S2	179.52 (13)	C14—C15—C16—O5	45.6 (2)
S1—C2—N3—N4	−0.4 (2)	C12—C11—O1—C15	−66.50 (18)
S2—C2—N3—N4	−177.57 (12)	S2—C11—O1—C15	177.11 (10)
C2—N3—N4—C5	−3.0 (2)	C16—C15—O1—C11	−168.02 (13)
N3—N4—C5—N1	−175.82 (17)	C14—C15—O1—C11	68.24 (16)
N3—N4—C5—S1	4.95 (19)	N4—C5—N1—C21	2.2 (3)
C2—S1—C5—N4	−4.30 (14)	S1—C5—N1—C21	−178.54 (14)
C2—S1—C5—N1	176.37 (14)	C5—N1—C21—C26	−9.0 (3)
O1—C11—C12—O2	176.33 (14)	C5—N1—C21—C22	172.65 (16)
S2—C11—C12—O2	−65.64 (15)	C26—C21—C22—C23	−1.2 (3)
O1—C11—C12—C13	55.11 (18)	N1—C21—C22—C23	177.18 (16)
S2—C11—C12—C13	173.14 (11)	C21—C22—C23—C24	1.1 (3)
O2—C12—C13—O3	72.56 (16)	C22—C23—C24—C25	−0.1 (3)
C11—C12—C13—O3	−167.24 (13)	C22—C23—C24—C27	−179.64 (18)
O2—C12—C13—C14	−168.64 (13)	C23—C24—C25—C26	−0.9 (3)
C11—C12—C13—C14	−48.44 (18)	C27—C24—C25—C26	178.71 (19)
O3—C13—C14—O4	−69.37 (17)	C22—C21—C26—C25	0.3 (3)
C12—C13—C14—O4	171.39 (13)	N1—C21—C26—C25	−177.94 (17)
O3—C13—C14—C15	169.77 (14)	C24—C25—C26—C21	0.7 (3)
C12—C13—C14—C15	50.53 (19)	N3—C2—S2—C11	−164.51 (14)
O4—C14—C15—O1	−178.61 (13)	S1—C2—S2—C11	18.65 (13)
C13—C14—C15—O1	−58.76 (17)	O1—C11—S2—C2	−55.86 (12)
O4—C14—C15—C16	61.89 (19)	C12—C11—S2—C2	−174.12 (11)
C13—C14—C15—C16	−178.26 (16)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H02···O3^{i}	0.82 (2)	1.87 (2)	2.6846 (19)	174 (3)
O3—H03···O4^{i}	0.84 (2)	1.93 (2)	2.7375 (18)	161 (3)
O4—H04···N3^{ii}	0.81 (2)	2.06 (2)	2.848 (2)	162 (3)
O5—H05···N4^{ii}	0.83 (2)	2.11 (2)	2.899 (2)	159 (3)
O5—H05···N3^{ii}	0.83 (2)	2.60 (2)	3.282 (2)	141 (2)
N1—H01···O5^{iii}	0.84 (3)	2.05 (3)	2.853 (2)	158 (2)
C14—H14···S1^{iv}	1.00	2.74	3.7044 (18)	163
C15—H15···O2^{v}	1.00	2.66	3.577 (2)	153
C11—H11···O3^{iii}	1.00	2.68	3.652 (2)	164
C16—H16*B*···S2^{vi}	0.99	2.71	3.570 (2)	145

Symmetry codes: (i) −*x*+3, *y*+1/2, −*z*+1; (ii) *x*+1, *y*−1, *z*; (iii) *x*−1, *y*, *z*; (iv) *x*+1, *y*, *z*; (v) −*x*+2, *y*−1/2, −*z*+1; (vi) *x*, *y*−1, *z*.