# Synthesis, crystal structure and Hirshfeld surface analysis of diethyl 2,6-dimethyl-4-(thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

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In the title compound, $C_{17}H_{21}NO_4S$, the 1,4-dihydropyridine ring has an envelope conformation with the $Csp^3$ atom at the flap. The thiophene ring is nearly perpendicular to the best plane through the 1,4-dihydropyridine ring, the dihedral angle being 82.19 (13)°. In the crystal, chains running along the $b$-axis direction are formed through N—H···O interactions between the 1,4-dihydropyridine N atom and one of the O atoms of the ester groups. Neighbouring chains are linked by C—H···O and C—H···$\pi$ interactions. A Hirshfeld surface analysis shows that the most prominent contributuion to the surface contacts are H···H contacts (55.1%).

## 1. Chemical context

1,4-Dihydropyridine derivatives exhibit a large range of biological activities (Stout & Meyers, 1982; Wei et al., 1989; Bossert & Vater, 1989; Mauzerall & Westheimer, 1955). They have been used as anticonvulsant, antidepressive, antianxiety, analgesic, antitumoral, vasodilator and anti-inflammatory agents (Sausins & Duburs, 1988; Boecker & Guenguerich, 1986; Godfraind et al., 1986). Some of them, such as amlodipine, felodipine and isradipine are drugs effective as calcium-channel blockers for the treatment of cardiovascular diseases and hypertension (Bossert et al., 1981; Nakayama & Kanoaka, 1996; Gordeev et al., 1996). 1,4-Dihydropyridines are also good precursors of the corresponding substituted pyridine derivatives and constitute useful reducing agents for imines in the presence of a catalytic amount of Lewis acid (Xia & Wang, 2005; Heravi et al., 2005; Bagley & Lubinu, 2006).
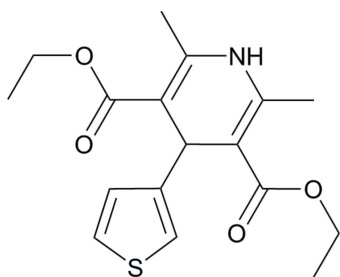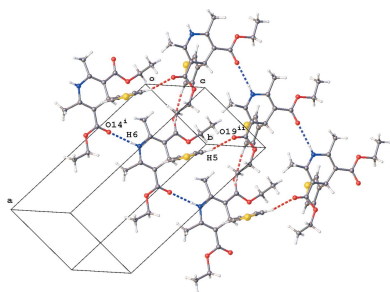


As a continuation of our research on the chemical and physical properties of novel polythiophenes (Nguyen et al., 2016; Vu et al., 2016), some new thiophene monomers have
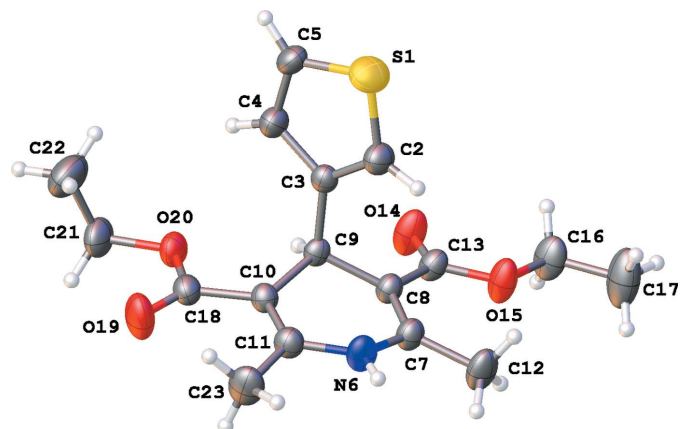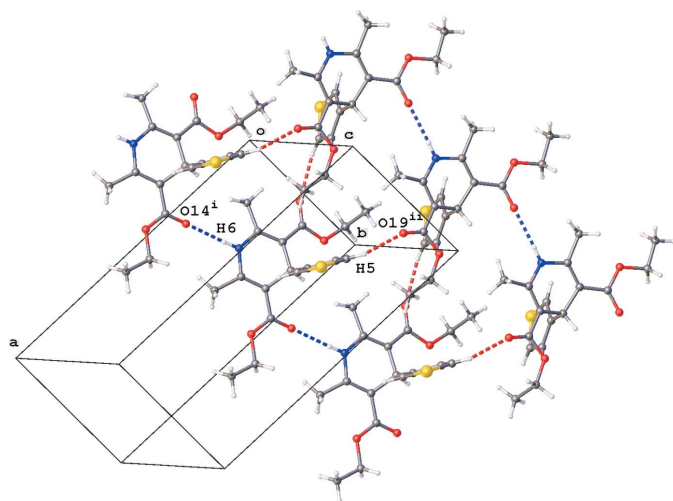
**Figure 1**
A view of the molecular structure of the title compound, with atom labels and displacement ellipsoids drawn at the 50% probability level. H atoms are shown as small circles of arbitrary radii.

been prepared (Vu *et al.*, 2017, 2018, 2019; Nguyen *et al.*, 2017). In this study, the synthesis and crystal structure of diethyl 2,6-dimethyl-4-(thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate are presented together with a Hirshfeld surface analysis and non-covalent interaction plots.

## 2. Structural commentary

The title compound crystallizes in the monoclinic space group $P2_1/c$ with one molecule in the asymmetric unit (Fig. 1). The 1,4-dihydropyridine ring (N6,C7–C11) has an envelope conformation with atom C9 at the flap [puckering parameters: $Q = 0.300$ (3) Å, $\theta = 73.9$ (6)°, $\varphi = 182.0$ (5)°]. The best plane through the 1,4-dihydropyridine ring makes an angle of 82.19 (13)° with the plane through the thiophene ring (S1/C2–C5; r.m.s. deviation = 0.001 Å). Both methyl C atoms are closer to the best plane through the 1,4-dihydropyridine

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

$Cg1$ is the centroid of the thiophene S1/C2–C5 ring.

| $D-\mathrm{H}\cdots A$ | $D-\mathrm{H}$ | $\mathrm{H}\cdots A$ | $D\cdots A$ | $D-\mathrm{H}\cdots A$ |
|---|---|---|---|---|
| N6—H6···O14$^i$ | 0.82 (4) | 2.19 (4) | 3.010 (3) | 176 (3) |
| C5—H5···O19$^{ii}$ | 0.93 | 2.52 | 3.220 (4) | 133 |
| C9—H9···O20 | 0.98 | 2.36 | 2.739 (3) | 102 |
| C12—H12$B$···O15 | 0.96 | 2.33 | 2.768 (3) | 107 |
| C23—H23$C$···O19 | 0.96 | 2.42 | 2.826 (4) | 105 |
| C17—H17$C$···$Cg1^{iii}$ | 0.96 | 2.79 | 3.720 (4) | 162 |

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

[deviations: C12 − 0.164 (3) Å, C23 − 0.162 (3) Å] than the C atoms of the two ester substituents [deviations: C13 − 0.363 (3) Å, C18 − 0.446 (2) Å]. All four of these C atoms are at the opposite sides with respect to the thiophene substituent which is in an axial position. Atoms O15, O19 and O20 are involved in intramolecular short contacts (Table 1). Both ester groups have a different conformation as illustrated by torsion angles C13—O15—C16—C17 [177.2 (3)°, +ap] and C18—O20—C21—C22 [85.3 (8)°, +sc].

## 3. Supramolecular features and Hirshfeld surface analysis

In the crystal, the 1,4-dihydropyridine N6 atom acts as a hydrogen-bond donor to the O14 atom of one of the ester groups, resulting in chain formation along the *b*-axis direction (Fig. 2, Table 1). Parallel chains are linked by C—H···O hydrogen bonds between the thiophene H5 atom and the carbonyl O19 atom of the second ester group (Fig. 2, Table 1). In addition, inversion dimers are formed by C—H···π interactions (Fig. 3, Table 1). No voids are observed in the crystal packing of the title compound.



**Figure 2**
Partial crystal packing of the title compound, showing the chain formation along the *b* axis by N—H···O interactions (blue dashed lines). Parallel chains are linked by C—H···O interactions (red dashed lines; see Table 1 for symmetry codes).
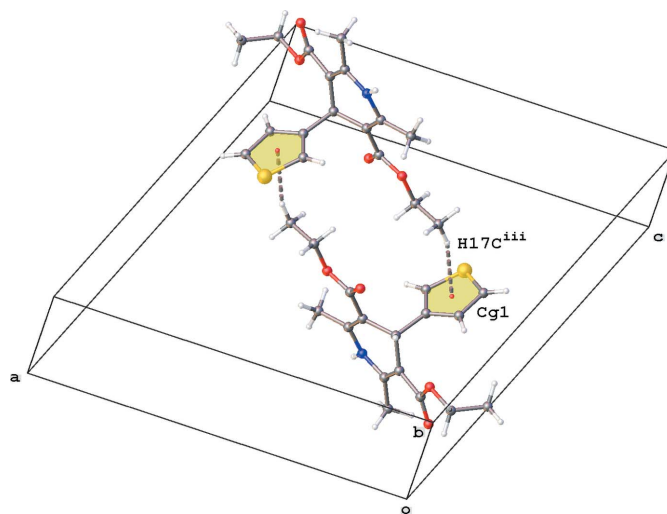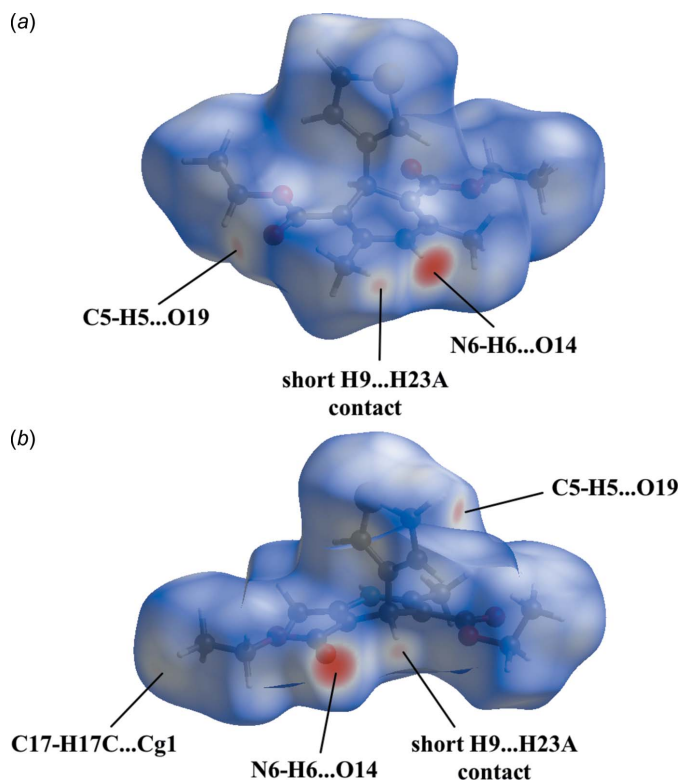


**Figure 3**
Partial crystal packing of the title compound, showing the inversion dimer formation through C—H···π interactions (grey dashed lines; $Cg1$ is the centroid of the S1/C2–C5 ring; see Table 1 for symmetry code).

**Table 2**
Enrichment ratios for the title compound.

| Parameter | Ratio |
|---|---|
| H···H | 0.94 |
| C···H | 1.23 |
| O···H | 1.24 |
| N···H | 1.30 |
| S···H | 1.11 |
| S···C | 0.96 |
| S···O | 0.82 |

In order to gain further insight into the packing, the Hirshfeld surface and fingerprint plots were calculated using *CrystalExplorer* (Turner *et al.*, 2017). The Hirshfeld surface (Spackman & Jayatilaka, 2009) mapped over $d_{norm}$ in Fig. 4 shows bright-red spots near the atoms participating in the already discussed intermolecular interactions. In addition a faint-red spot is present near atoms H9 and H23*A* indicating a short H9···H23*A*[iv] contact distance of 2.276 Å [symmetry code: (iv) *x*, *y* + 1, *z*]. The associated two-dimensional fingerprint plots (McKinnon *et al.*, 2007) are shown in Fig. 5 and give additional information about the intermolecular contacts. H···H Van der Waals contacts dominate (55.1%) and appear in the middle of the scattered points in the fingerprint plot (Fig. 5*b*). The contribution (16.4%) from the O···H/H···O contacts shows a pair of sharp spikes corresponding to the N—H···O interactions (Fig. 5*c*). In addition, C···H/H···C and S···H/H···S contacts contribute 15.7 and 9.6%, respectively, to the Hirshfeld surface. A further small contribution is from



*(a)*



*(b)*

**Figure 4**
Two views of the Hirshfeld surface mapped over $d_{norm}$ for the title compound in the range −0.4662 to +1.2830 arbitrary units.
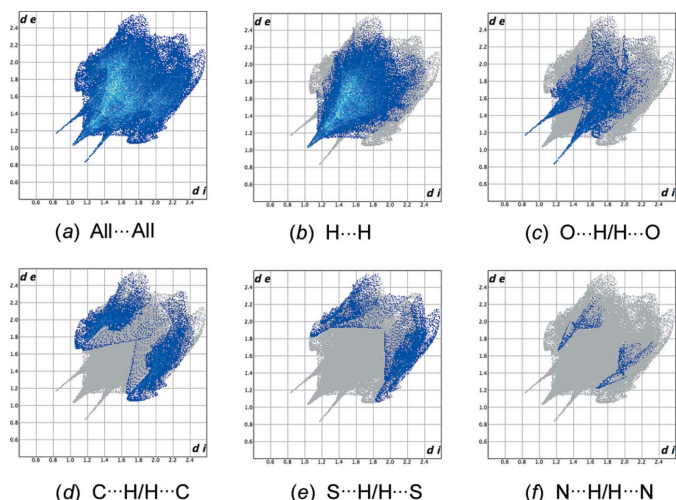


**Figure 5**
Full two-dimensional fingerprint plots for the title compound, showing (*a*) all interactions, and delineated into (*b*) H···H, (*c*) O···H/H···O, (*d*) C···H/H···C, (*e*) S···H/H···S, (*f*) N···H/H···N interactions. The $d_i$ and $d_e$ values are the closest internal and external distances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

N···H/H···N contacts (1.5%, Fig. 5*f*). The percentage contributions of the other contact types are negligible.

Enrichment ratios (Table 2) were calculated according to the method described by Jelsch *et al.* (2014). A ratio $E_{XY}$ greater than unity for a pair of elements *X* and *Y* indicates a high likelihood of forming *X*···*Y* contacts in the crystal packing. The favourable O···H and H···$\pi$ contacts in the crystal packing are reflected in the enrichment ratios $E_{OH}$ of 1.24 and $E_{CH}$ of 1.23 for these contacts. The slight $E_{SH}$ enrichment (1.11) refers to the multiple S···H contacts between S1 and neighbouring methyl groups (S···H distances ranging from 3.01 to 3.50 Å). However, the high enrichment ratio $E_{NH}$ must be interpreted with caution as it results from the quotient of two small numbers (Jelsch *et al.*, 2014).

## 4. Database survey

A search of the Cambridge Structural Database (CSD, Version 5.40, update of May 2019; Groom *et al.*, 2016) for diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate derivatives with a ring substituent at C4 results in 70 hits for which coordinates are available. Most similar to the title compound is the 4-(2-thienyl) derivative (refcode QIWWEY; Caignan *et al.*, 2000; refcode QIWWEY01; Huang & Cui, 2016). In these compounds the thienyl group is disordered over two sets of sites with an occupancy ratio of 0.51:0.49. An overlay between the title compound and QIWWEY excluding the thiophene ring gives an r.m.s. deviation of 0.318 Å. In QIWWEY, the 1,4-dihydropyridine and thiophene rings make an angle of 83.19 (17)°. Fig. 6 shows the four possible orientations of the two C=O substituents on the 1,4-dihydropyridine ring. Most popular are the *s-trans/s-cis* (35%), the *s-cis/s-cis* (31%) and the *s-cis/s-trans* conformation (29%). The *s-trans/s-trans* conformation occurs only for 5% of the deriv-
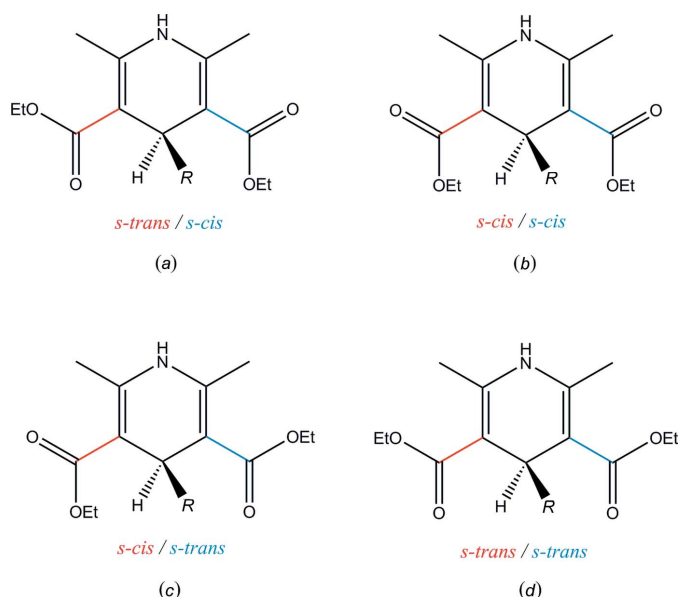
**Figure 6**
Four possible orientations of the C=O groups for diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate derivatives with a ring substituent ($R$) at C4.

atives. In the title compound, both C=O substituents are present in an *s-trans/s-cis* conformation.

## 5. Synthesis and crystallization

The reaction scheme for the synthesis of the title compound is given in Fig. 7.

**Synthesis of diethyl 2,6-dimethyl-4-(thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate:**

A mixture of thiophene-3-carbaldehyde (3 mmol), ethyl acetoacetate (6 mmol) and $NH_4OAc$ (3 mmol) in ethanol (10 mL) was exposed to microwave radiation for 3 min. at a power of 450W. The reaction mixture was cooled down and the solid product was separated by filtration and purified by recrystallization in ethanol to give the compound as yellowish transparent crystals (yield 82%), m.p. 423 K. IR (KBr, cm$^{-1}$): 3346, 3244 (NH), 3099, 2979 (C–H), 1699 (C=O), 1490 (C=C). $^1$H NMR [Bruker XL-500, 500 MHz, $d_6$-CDCl$_3$, $\delta$ (ppm), $J$ (Hz), see Fig. 7 for numbering scheme]: 7.12 ($m$, 1H, $J$ = 4.5, H$^4$), 6.99 ($m$, 1H, $J$ = 4.5, H$^5$), 6.91 ($d$, 1H,, $J$ = 2.5, H$^2$), 5.93 ($s$, 1H, H$^9$), 5.14 ($s$, 1H, H$^6$), 4.13 ($m$, 4H, $J$ = 7.5Hz, H$^{13,13'}$), 2.30 ($s$, 6H, H$^{10,10'}$), 1.25 ($m$, 6H, $J$ = 7.25 H$^{14,14'}$). $^{13}$C NMR [Bruker XL-500, 125 MHz, $d_6$-CDCl$_3$, (ppm)]: 19.4 (C$^{10,10'}$), 14.3 (C$^{14,14'}$), 34.6 (C$^6$), 59.7 (C$^{13,13'}$), 103.4 (C$^{7,7'}$), 120.3 (C$^2$), 124.6 (C$^4$), 127.6 (C$^5$), 144.4 (C$^3$), 147.9 (C$^8$,C$^{8'}$), 167.7 (C$^{11,11'}$). Calculated for C$_{17}$H$_{21}$NO$_4$S: $M^{[+H]}$ = 335.4 au.
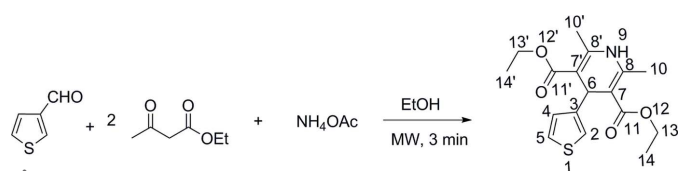


**Figure 7**
Reaction scheme for the synthesis of the title compound.

**Table 3**
Experimental details.

| | |
|---|---|
| Crystal data | |
| Chemical formula | C$_{17}$H$_{21}$NO$_4$S |
| $M_r$ | 335.41 |
| Crystal system, space group | Monoclinic, $P2_1/c$ |
| Temperature (K) | 293 |
| $a, b, c$ (Å) | 15.6801 (8), 7.4311 (3), 15.5968 (8) |
| $\beta$ (°) | 111.424 (6) |
| $V$ (Å$^3$) | 1691.77 (16) |
| $Z$ | 4 |
| Radiation type | Mo $K\alpha$ |
| $\mu$ (mm$^{-1}$) | 0.21 |
| Crystal size (mm) | 0.5 × 0.2 × 0.05 |
| | |
| Data collection | |
| Diffractometer | Rigaku Oxford Diffraction Super-Nova, single source at offset/far, Eos |
| Absorption correction | Multi-scan (*CrysAlis PRO*; Rigaku OD, 2018) |
| $T_{min}$, $T_{max}$ | 0.555, 1.000 |
| No. of measured, independent and observed [$I > 2\sigma(I)$] reflections | 19775, 3446, 2805 |
| $R_{int}$ | 0.027 |
| $(\sin \theta/\lambda)_{max}$ (Å$^{-1}$) | 0.625 |
| | |
| Refinement | |
| $R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, $S$ | 0.061, 0.187, 1.05 |
| No. of reflections | 3446 |
| No. of parameters | 216 |
| H-atom treatment | H atoms treated by a mixture of independent and constrained refinement |
| $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å$^{-3}$) | 0.53, −0.47 |

Computer programs: *CrysAlis PRO* (Rigaku OD, 2018), *SHELXT2014* (Sheldrick, 2015a), *SHELXL2016* (Sheldrick, 2015b) and *OLEX2* (Dolomanov *et al.*, 2009).

## 6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 3. H atom H6 was found in a difference electron-density map and refined freely. The other H atoms were placed in idealized positions and included as riding contributions with $U_{iso}$(H) values of 1.2$U_{eq}$ or 1.5$U_{eq}$ of the parent atoms, with C—H distances of 0.93 (aromatic), 0.98 (CH), 0.97 (CH$_2$) and 0.96 Å (CH$_3$). In the final cycles of refinement, four outlying reflections were omitted.

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# Synthesis, crystal structure and Hirshfeld surface analysis of diethyl 2,6-dimethyl-4-(thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate

**Trung Vu Quoc, Duong Tran Thi Thuy, Thanh Phung Ngoc, Manh Vu Quoc, Hien Nguyen, Linh Duong Khanh, Anh Tu Quang and Luc Van Meervelt**

**Computing details**

Data collection: *CrysAlis PRO* (Rigaku OD, 2018); cell refinement: *CrysAlis PRO* (Rigaku OD, 2018); data reduction: *CrysAlis PRO* (Rigaku OD, 2018); program(s) used to solve structure: SHELXT2014 (Sheldrick, 2015a); program(s) used to refine structure: *SHELXL2016* (Sheldrick, 2015b); molecular graphics: *OLEX2* (Dolomanov *et al.*, 2009); software used to prepare material for publication: *OLEX2* (Dolomanov *et al.*, 2009).

**Diethyl 2,6-dimethyl-4-(thiophen-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate**

*Crystal data*

| | |
|---|---|
| $C_{17}H_{21}NO_4S$ | $F(000) = 712$ |
| $M_r = 335.41$ | $D_x = 1.317$ Mg m$^{-3}$ |
| Monoclinic, $P2_1/c$ | Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å |
| $a = 15.6801$ (8) Å | Cell parameters from 8195 reflections |
| $b = 7.4311$ (3) Å | $\theta = 3.1$–27.9° |
| $c = 15.5968$ (8) Å | $\mu = 0.21$ mm$^{-1}$ |
| $\beta = 111.424$ (6)° | $T = 293$ K |
| $V = 1691.77$ (16) Å$^3$ | Block, colourless |
| $Z = 4$ | $0.5 \times 0.2 \times 0.05$ mm |

*Data collection*

| | |
|---|---|
| Rigaku Oxford Diffraction SuperNova, single source at offset/far, Eos diffractometer | $T_{min} = 0.555$, $T_{max} = 1.000$ |
| | 19775 measured reflections |
| | 3446 independent reflections |
| Radiation source: micro-focus sealed X-ray tube, SuperNova (Mo) X-ray Source | 2805 reflections with $I > 2\sigma(I)$ |
| | $R_{int} = 0.027$ |
| Mirror monochromator | $\theta_{max} = 26.4°$, $\theta_{min} = 2.6°$ |
| Detector resolution: 15.9631 pixels mm$^{-1}$ | $h = -19 \rightarrow 19$ |
| $\omega$ scans | $k = -9 \rightarrow 9$ |
| Absorption correction: multi-scan (CrysAlis PRO; Rigaku OD, 2018) | $l = -19 \rightarrow 19$ |

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | 216 parameters |
| Least-squares matrix: full | 0 restraints |
| $R[F^2 > 2\sigma(F^2)] = 0.061$ | Hydrogen site location: mixed |
| $wR(F^2) = 0.187$ | H atoms treated by a mixture of independent and constrained refinement |
| $S = 1.05$ | |
| 3446 reflections | |

$w = 1/[\sigma^2(F_o^2) + (0.0981P)^2 + 1.416P]$
   where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$

$\Delta\rho_{max} = 0.53$ e Å$^{-3}$
$\Delta\rho_{min} = -0.46$ e Å$^{-3}$

*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)*

|  | $x$ | $y$ | $z$ | $U_{iso}$*/$U_{eq}$ |
|---|---|---|---|---|
| S1 | 0.23846 (6) | 0.68160 (12) | 0.53767 (5) | 0.0587 (3) |
| C2 | 0.28608 (18) | 0.6398 (4) | 0.45764 (17) | 0.0407 (6) |
| H2 | 0.340156 | 0.575481 | 0.470126 | 0.049* |
| C3 | 0.23681 (15) | 0.7104 (3) | 0.37324 (15) | 0.0293 (5) |
| C4 | 0.15812 (17) | 0.8010 (4) | 0.37597 (18) | 0.0405 (6) |
| H4 | 0.115977 | 0.858331 | 0.325101 | 0.049* |
| C5 | 0.14966 (17) | 0.7959 (4) | 0.46445 (18) | 0.0393 (6) |
| H5 | 0.102525 | 0.847582 | 0.478796 | 0.047* |
| N6 | 0.32530 (15) | 0.3391 (3) | 0.28906 (16) | 0.0406 (5) |
| H6 | 0.346 (2) | 0.236 (5) | 0.297 (2) | 0.053 (9)* |
| C7 | 0.39001 (16) | 0.4737 (3) | 0.31863 (17) | 0.0351 (5) |
| C8 | 0.36158 (15) | 0.6465 (3) | 0.31363 (16) | 0.0302 (5) |
| C9 | 0.26034 (14) | 0.6872 (3) | 0.28729 (15) | 0.0273 (5) |
| H9 | 0.246735 | 0.800269 | 0.252562 | 0.033* |
| C10 | 0.20195 (15) | 0.5392 (3) | 0.22653 (15) | 0.0303 (5) |
| C11 | 0.23455 (16) | 0.3689 (3) | 0.23509 (17) | 0.0359 (5) |
| C12 | 0.48666 (18) | 0.4023 (4) | 0.3531 (2) | 0.0533 (8) |
| H12A | 0.509780 | 0.397134 | 0.419186 | 0.080* |
| H12B | 0.524659 | 0.480463 | 0.333367 | 0.080* |
| H12C | 0.487105 | 0.283768 | 0.328792 | 0.080* |
| C13 | 0.42150 (16) | 0.8049 (3) | 0.33895 (17) | 0.0348 (5) |
| O14 | 0.39447 (13) | 0.9578 (2) | 0.32155 (16) | 0.0545 (6) |
| O15 | 0.50981 (12) | 0.7683 (2) | 0.38631 (16) | 0.0516 (5) |
| C16 | 0.57344 (18) | 0.9188 (4) | 0.4152 (2) | 0.0532 (7) |
| H16A | 0.553963 | 1.002135 | 0.452336 | 0.064* |
| H16B | 0.575719 | 0.982674 | 0.361883 | 0.064* |
| C17 | 0.6646 (2) | 0.8441 (5) | 0.4697 (3) | 0.0831 (13) |
| H17A | 0.683923 | 0.764533 | 0.431803 | 0.125* |
| H17B | 0.661164 | 0.778721 | 0.521443 | 0.125* |
| H17C | 0.707965 | 0.940521 | 0.491285 | 0.125* |
| C18 | 0.10811 (16) | 0.5808 (4) | 0.16274 (16) | 0.0363 (5) |
| O19 | 0.05131 (14) | 0.4733 (3) | 0.11903 (16) | 0.0646 (7) |
| O20 | 0.09182 (12) | 0.7592 (2) | 0.15614 (12) | 0.0410 (4) |
| C21 | 0.00100 (19) | 0.8172 (5) | 0.0952 (2) | 0.0525 (7) |
| H21A | −0.020354 | 0.738253 | 0.042024 | 0.063* |
| H21B | 0.005081 | 0.938003 | 0.073416 | 0.063* |

| | | | |
|---|---|---|---|
| C22 | −0.0661 (3) | 0.8156 (6) | 0.1416 (3) | 0.0767 (11) |
| H22A | −0.124239 | 0.858116 | 0.099750 | 0.115* |
| H22B | −0.044950 | 0.892617 | 0.194641 | 0.115* |
| H22C | −0.072715 | 0.695134 | 0.160476 | 0.115* |
| C23 | 0.1849 (2) | 0.2020 (4) | 0.1900 (2) | 0.0542 (8) |
| H23A | 0.218986 | 0.098199 | 0.220459 | 0.081* |
| H23B | 0.178354 | 0.200892 | 0.126401 | 0.081* |
| H23C | 0.125325 | 0.199968 | 0.194332 | 0.081* |

*Atomic displacement parameters (Å$^2$)*

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
|---|---|---|---|---|---|---|
| S1 | 0.0677 (5) | 0.0662 (6) | 0.0442 (4) | 0.0079 (4) | 0.0228 (4) | 0.0059 (3) |
| C2 | 0.0385 (13) | 0.0430 (14) | 0.0386 (13) | 0.0084 (11) | 0.0117 (10) | 0.0040 (11) |
| C3 | 0.0288 (10) | 0.0250 (11) | 0.0327 (11) | −0.0019 (8) | 0.0094 (9) | −0.0028 (8) |
| C4 | 0.0339 (12) | 0.0462 (14) | 0.0391 (13) | 0.0080 (11) | 0.0104 (10) | −0.0014 (11) |
| C5 | 0.0313 (12) | 0.0424 (14) | 0.0466 (14) | 0.0033 (10) | 0.0169 (11) | −0.0069 (11) |
| N6 | 0.0372 (11) | 0.0225 (10) | 0.0547 (13) | 0.0035 (8) | 0.0082 (10) | 0.0007 (9) |
| C7 | 0.0298 (11) | 0.0306 (12) | 0.0422 (13) | 0.0026 (9) | 0.0101 (10) | 0.0014 (10) |
| C8 | 0.0266 (11) | 0.0267 (11) | 0.0362 (11) | 0.0012 (8) | 0.0100 (9) | 0.0014 (9) |
| C9 | 0.0269 (10) | 0.0209 (10) | 0.0333 (11) | 0.0021 (8) | 0.0098 (9) | 0.0024 (8) |
| C10 | 0.0289 (11) | 0.0289 (11) | 0.0314 (11) | −0.0019 (9) | 0.0091 (9) | 0.0004 (9) |
| C11 | 0.0350 (12) | 0.0312 (12) | 0.0399 (12) | −0.0025 (10) | 0.0116 (10) | −0.0027 (10) |
| C12 | 0.0359 (14) | 0.0342 (14) | 0.080 (2) | 0.0093 (11) | 0.0095 (13) | −0.0009 (14) |
| C13 | 0.0295 (11) | 0.0292 (12) | 0.0465 (13) | 0.0007 (9) | 0.0146 (10) | 0.0007 (10) |
| O14 | 0.0375 (10) | 0.0254 (9) | 0.0918 (15) | 0.0001 (7) | 0.0134 (10) | 0.0048 (9) |
| O15 | 0.0300 (9) | 0.0301 (9) | 0.0830 (15) | −0.0027 (7) | 0.0068 (9) | 0.0011 (9) |
| C16 | 0.0378 (14) | 0.0339 (14) | 0.081 (2) | −0.0091 (11) | 0.0137 (13) | 0.0000 (14) |
| C17 | 0.0435 (17) | 0.056 (2) | 0.124 (3) | −0.0095 (15) | 0.0001 (19) | 0.009 (2) |
| C18 | 0.0321 (11) | 0.0432 (14) | 0.0312 (11) | 0.0001 (10) | 0.0084 (9) | −0.0009 (10) |
| O19 | 0.0429 (11) | 0.0552 (13) | 0.0715 (14) | −0.0041 (10) | −0.0079 (10) | −0.0129 (11) |
| O20 | 0.0338 (9) | 0.0420 (10) | 0.0395 (9) | 0.0080 (7) | 0.0043 (7) | 0.0042 (7) |
| C21 | 0.0391 (14) | 0.0634 (19) | 0.0449 (15) | 0.0146 (13) | 0.0035 (12) | 0.0102 (13) |
| C22 | 0.055 (2) | 0.091 (3) | 0.084 (3) | 0.0277 (19) | 0.0258 (18) | 0.005 (2) |
| C23 | 0.0489 (16) | 0.0326 (14) | 0.073 (2) | −0.0062 (12) | 0.0128 (14) | −0.0139 (13) |

*Geometric parameters (Å, º)*

| | | | |
|---|---|---|---|
| S1—C2 | 1.701 (3) | C12—H12C | 0.9600 |
| S1—C5 | 1.674 (3) | C13—O14 | 1.208 (3) |
| C2—H2 | 0.9300 | C13—O15 | 1.338 (3) |
| C2—C3 | 1.364 (3) | O15—C16 | 1.456 (3) |
| C3—C4 | 1.420 (3) | C16—H16A | 0.9700 |
| C3—C9 | 1.525 (3) | C16—H16B | 0.9700 |
| C4—H4 | 0.9300 | C16—C17 | 1.479 (4) |
| C4—C5 | 1.434 (4) | C17—H17A | 0.9600 |
| C5—H5 | 0.9300 | C17—H17B | 0.9600 |
| N6—H6 | 0.82 (4) | C17—H17C | 0.9600 |

| N6—C7 | 1.379 (3) | C18—O19 | 1.205 (3) |
|---|---|---|---|
| N6—C11 | 1.381 (3) | C18—O20 | 1.347 (3) |
| C7—C8 | 1.352 (3) | O20—C21 | 1.459 (3) |
| C7—C12 | 1.507 (3) | C21—H21A | 0.9700 |
| C8—C9 | 1.518 (3) | C21—H21B | 0.9700 |
| C8—C13 | 1.468 (3) | C21—C22 | 1.479 (5) |
| C9—H9 | 0.9800 | C22—H22A | 0.9600 |
| C9—C10 | 1.521 (3) | C22—H22B | 0.9600 |
| C10—C11 | 1.353 (3) | C22—H22C | 0.9600 |
| C10—C18 | 1.477 (3) | C23—H23A | 0.9600 |
| C11—C23 | 1.496 (3) | C23—H23B | 0.9600 |
| C12—H12A | 0.9600 | C23—H23C | 0.9600 |
| C12—H12B | 0.9600 | | |
| | | | |
| C5—S1—C2 | 94.05 (12) | H12B—C12—H12C | 109.5 |
| S1—C2—H2 | 123.5 | O14—C13—C8 | 123.8 (2) |
| C3—C2—S1 | 113.10 (19) | O14—C13—O15 | 121.5 (2) |
| C3—C2—H2 | 123.5 | O15—C13—C8 | 114.7 (2) |
| C2—C3—C4 | 110.2 (2) | C13—O15—C16 | 118.0 (2) |
| C2—C3—C9 | 124.8 (2) | O15—C16—H16A | 110.2 |
| C4—C3—C9 | 124.9 (2) | O15—C16—H16B | 110.2 |
| C3—C4—H4 | 123.1 | O15—C16—C17 | 107.4 (2) |
| C3—C4—C5 | 113.8 (2) | H16A—C16—H16B | 108.5 |
| C5—C4—H4 | 123.1 | C17—C16—H16A | 110.2 |
| S1—C5—H5 | 125.6 | C17—C16—H16B | 110.2 |
| C4—C5—S1 | 108.88 (18) | C16—C17—H17A | 109.5 |
| C4—C5—H5 | 125.6 | C16—C17—H17B | 109.5 |
| C7—N6—H6 | 115 (2) | C16—C17—H17C | 109.5 |
| C7—N6—C11 | 123.8 (2) | H17A—C17—H17B | 109.5 |
| C11—N6—H6 | 120 (2) | H17A—C17—H17C | 109.5 |
| N6—C7—C12 | 112.6 (2) | H17B—C17—H17C | 109.5 |
| C8—C7—N6 | 118.9 (2) | O19—C18—C10 | 126.2 (2) |
| C8—C7—C12 | 128.5 (2) | O19—C18—O20 | 121.9 (2) |
| C7—C8—C9 | 119.7 (2) | O20—C18—C10 | 111.8 (2) |
| C7—C8—C13 | 125.5 (2) | C18—O20—C21 | 117.0 (2) |
| C13—C8—C9 | 114.60 (19) | O20—C21—H21A | 109.2 |
| C3—C9—H9 | 108.4 | O20—C21—H21B | 109.2 |
| C8—C9—C3 | 110.47 (18) | O20—C21—C22 | 112.2 (3) |
| C8—C9—H9 | 108.4 | H21A—C21—H21B | 107.9 |
| C8—C9—C10 | 110.90 (18) | C22—C21—H21A | 109.2 |
| C10—C9—C3 | 110.21 (18) | C22—C21—H21B | 109.2 |
| C10—C9—H9 | 108.4 | C21—C22—H22A | 109.5 |
| C11—C10—C9 | 119.68 (19) | C21—C22—H22B | 109.5 |
| C11—C10—C18 | 120.6 (2) | C21—C22—H22C | 109.5 |
| C18—C10—C9 | 119.6 (2) | H22A—C22—H22B | 109.5 |
| N6—C11—C23 | 113.4 (2) | H22A—C22—H22C | 109.5 |
| C10—C11—N6 | 118.6 (2) | H22B—C22—H22C | 109.5 |
| C10—C11—C23 | 128.0 (2) | C11—C23—H23A | 109.5 |

| | | | |
|---|---|---|---|
| C7—C12—H12A | 109.5 | C11—C23—H23B | 109.5 |
| C7—C12—H12B | 109.5 | C11—C23—H23C | 109.5 |
| C7—C12—H12C | 109.5 | H23A—C23—H23B | 109.5 |
| H12A—C12—H12B | 109.5 | H23A—C23—H23C | 109.5 |
| H12A—C12—H12C | 109.5 | H23B—C23—H23C | 109.5 |
| | | | |
| S1—C2—C3—C4 | 0.1 (3) | C9—C3—C4—C5 | 177.0 (2) |
| S1—C2—C3—C9 | −177.09 (17) | C9—C8—C13—O14 | −16.0 (4) |
| C2—S1—C5—C4 | −0.1 (2) | C9—C8—C13—O15 | 161.9 (2) |
| C2—C3—C4—C5 | −0.2 (3) | C9—C10—C11—N6 | −9.6 (4) |
| C2—C3—C9—C8 | −23.5 (3) | C9—C10—C11—C23 | 172.7 (3) |
| C2—C3—C9—C10 | 99.4 (3) | C9—C10—C18—O19 | −170.8 (3) |
| C3—C4—C5—S1 | 0.2 (3) | C9—C10—C18—O20 | 10.6 (3) |
| C3—C9—C10—C11 | −93.6 (3) | C10—C18—O20—C21 | −179.8 (2) |
| C3—C9—C10—C18 | 82.7 (2) | C11—N6—C7—C8 | 15.7 (4) |
| C4—C3—C9—C8 | 159.7 (2) | C11—N6—C7—C12 | −164.1 (3) |
| C4—C3—C9—C10 | −77.4 (3) | C11—C10—C18—O19 | 5.5 (4) |
| C5—S1—C2—C3 | 0.0 (2) | C11—C10—C18—O20 | −173.1 (2) |
| N6—C7—C8—C9 | 7.6 (4) | C12—C7—C8—C9 | −172.6 (3) |
| N6—C7—C8—C13 | −177.6 (2) | C12—C7—C8—C13 | 2.2 (4) |
| C7—N6—C11—C10 | −14.7 (4) | C13—C8—C9—C3 | −80.8 (2) |
| C7—N6—C11—C23 | 163.4 (3) | C13—C8—C9—C10 | 156.7 (2) |
| C7—C8—C9—C3 | 94.5 (3) | C13—O15—C16—C17 | 177.2 (3) |
| C7—C8—C9—C10 | −28.0 (3) | O14—C13—O15—C16 | −1.1 (4) |
| C7—C8—C13—O14 | 169.0 (3) | C18—C10—C11—N6 | 174.1 (2) |
| C7—C8—C13—O15 | −13.1 (4) | C18—C10—C11—C23 | −3.6 (4) |
| C8—C9—C10—C11 | 29.0 (3) | C18—O20—C21—C22 | 85.3 (3) |
| C8—C9—C10—C18 | −154.6 (2) | O19—C18—O20—C21 | 1.5 (4) |
| C8—C13—O15—C16 | −179.1 (2) | | |

*Hydrogen-bond geometry (Å, °)*

*Cg*1 is the centroid of the thiophene S1/C2–C5 ring.

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| N6—H6···O14[i] | 0.82 (4) | 2.19 (4) | 3.010 (3) | 176 (3) |
| C5—H5···O19[ii] | 0.93 | 2.52 | 3.220 (4) | 133 |
| C9—H9···O20 | 0.98 | 2.36 | 2.739 (3) | 102 |
| C12—H12*B*···O15 | 0.96 | 2.33 | 2.768 (3) | 107 |
| C23—H23*C*···O19 | 0.96 | 2.42 | 2.826 (4) | 105 |
| C17—H17*C*···*Cg*1[iii] | 0.96 | 2.79 | 3.720 (4) | 162 |

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