Crystal structure and Hirshfeld surface analysis of 5-(5-phenyl-1,2-oxazol-3-yl)-1,3,4-thiadiazol-2-amine

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The title compound, C11H8N4OS, crystallizes with two independent molecules in the asymmetric unit. In the crystal, the N–H···N and C–H···N hydrogen bonds connect the molecules, generating double layers parallel to the (001) plane. The layers are joined by C–H···π interactions to form a three-dimensional supramolecular structure.

1. Chemical context

Compounds with the five-membered isoxazole, isothiazole and 1,3,4-thiadiazole heterocycles possess high potential for biological activity and are privileged scaffolds for the development of pharmaceutical agents (Das & Chanda, 2021; Kletskov et al., 2020; Khalilullah et al., 2014; Yadigarov et al., 2009; Safavora et al., 2019; Zubkov et al., 2014). In particular, isoxazoles are able to enhance the action of ‘first-line’ antitumor substances, which makes it possible to reduce their therapeutic doses and thus reduce toxic side effects (Khalilov et al., 2021; Kulchitsky et al., 2012; Naghiyev et al., 2020). The combination of the pharmacophore fragments of isoxazole and thiadiazole in one molecule increases the variability of its binding to the key sites of enzymes regulating the biological action. The presence of an amino group additionally increases the biopotential of the molecule, and the introduction of an aromatic fragment makes it possible to implement binding with a biotarget by π-stacking (Shixaliyev et al., 2014, 2018; Mahmudov et al., 2011, 2013; Gurbanov et al., 2017, 2018a,b). To assess the biological potential of a molecule in silico and the molecular docking procedure, which is widely used for the development of new pharmaceuticals, information about the structures of promising molecules is needed. All this initiated our research on the synthesis of 5-(5-phenylisoxazol-3-yl)-1,3,4-thiadiazol-2-amine (1) and the further determination of the accurate structure of its molecule. The synthesis and structure of the compound has not published before. There are many approaches for building a thiadiazole heterocycle based on the use of carboxylic acids (Bhinge et al., 2015; Nayak et al., 2014), carbonyl chlorides (Sun et al., 2001; Kudelko et al., 2020), aldehydes (Shivakumara et al., 2019; Wang et al., 2019),
We chose here a method based on the transformation of carbonitriles (as shown in the scheme) as the shortest and most convenient way to achieve this purpose (Sakthivel et al., 2016; et al.; Abdelhamid et al., 2011). Its efficacy has recently been demonstrated by one of us (Petkevich et al., 2021). The synthetic procedure involves the interaction of 5-phenylisoxazole-3-carbonitrile with thiosemicarbazide. The starting 5-phenylisoxazole-3-carbonitrile was obtained according to the previously described method (Kulchitsky et al., 2012; Bumagin et al., 2018).

2. Structural commentary

The title compound I crystallizes in the orthorhombic space group Pca2₁, with two independent molecules (I with S1 and II with S2) in the asymmetric unit (Fig. 1). The oxazole (O1/N2/C3/C4/C5 and O12/N13/C14/C15/C16) and thiadiazole (S1/N3/C1/C2 and S2/N14/N15/C12/C13) rings are essentially planar and inclined to one another by 18.8 (3) and 14.6 (3)° in molecules I and II, respectively. The phenyl rings (C6–C11 and C17–C22) make dihedral angles of 24.6 (3) and 26.8 (3)° with the oxazole rings in molecules I and II, respectively. Fig. 2 shows the overlay of molecules I and II in the asymmetric unit, with an r.m.s. deviation of 0.087 Å. The C—N bond distances to the amino N atom of 1.330 (6) and 1.328 (6) Å, respectively, in molecules I and II indicate strong conjugation of the amino groups with the thiadiazole π-systems.

3. Supramolecular features

In the crystal, molecules are linked by N—H···N and C—H···N hydrogen bonds (Table 1, Figs. 3 and 4), forming double layers of cross-linked molecules parallel to the (001) plane.
The molecules within a layer are further linked by \(\pi-\pi\) stacking interactions between the thiadiazole rings \([Cg1\cdots Cg4(x, y, z) = 3.636 (3) \text{ Å}, \text{slippage } = 1.283 \text{ Å}, \text{where } Cg1 \text{ and } Cg4 \text{ are the centroids of the } S1/N3/N4/C1/C2 \text{ and } S2/N14/N15/C12/C13, \text{respectively}]. \) The layers are linked by van der Waals interactions (Table 2), forming a three-dimensional supramolecular structure (Fig. 5).

4. Hirshfeld surface analysis

Crystal Explorer 17 (Turner et al., 2017) was used to construct Hirshfeld surfaces for both independent molecules in the asymmetric unit of the title compound. The \(d_{\text{norm}}\) mappings for molecule I were performed in the range of \(-0.5418\) to 1.2328 a.u., and for molecule II in the range of \(-0.5446\) to 1.1988 a.u.

On the \(\text{on the } d_{\text{norm}}\) surfaces, bold red circles show the locations of \(\text{N} \cdots \text{H} \cdots \text{N} \) interactions. Smaller red spots are caused by \(\text{C} \cdots \text{H} \cdots \text{N} \) interactions (Fig. 6a,b for molecule I and Fig. 6c,d for molecule II).

Fingerprint plots (Fig. 7) reveal that while \(\text{H} \cdots \text{H} \) (26.6% for molecule I and 25.3% for molecule II) interactions make the largest contributions to the surface contacts (Table 2), \(\text{N} \cdots \text{H}/\text{H} \cdots \text{N} \) (24.1% for I and 24.1% for II) and \(\text{C} \cdots \text{H}/\text{H} \cdots \text{C} \) (19.3% for I and 21.0% for II) contacts are also significant. The contributions of other, less noteworthy contacts are listed in Table 3. The environments of molecules I and II are quite similar, as indicated in Table 3.

5. Database survey

The only hit related to the title compound found in a search of the Cambridge Structural Database (CSD, Version 5.42; May 2021; Groom et al., 2016) was 1-[(3-thiophen-2-yl)-4,5-dihydro-1,2-oxazol-5-yl]methyl]-1H-indole-2,3-dione (NAQQOO; Rayni et al., 2017). In the structure of NAQQOO, the indole ring system is almost planar as expected. The dihedral angle between this plane and that of the thiophene ring is 2.01 (2)°. The mean plane of the isoxazole ring is inclined by 19.78 (14) and 20.83 (12)° to the thiophene and indoline mean planes, respectively. In the crystal, the
Combination of C—H···O hydrogen bonds forms stepped layers two molecules thick, or slabs, which are oriented parallel to (103). These layers are associated through offset π-stacking interactions, involving inversion-related indole rings in adjacent layers [interplanar distance of 3.479 (1) Å], forming a supramolecular three-dimensional structure.

6. Synthesis and crystallization

5-(5-Phenylisoxazol-3-yl)-1,3,4-thiadiazol-2-amine:
Thiosemicarbazide (1.0 g, 11 mmol) was added at r.t to a solution of 5-phenylisoxazole-3-carbonitrile (1.70 g, 10 mmol) in CF₃CO₂H (10 mL), and the resulting mixture was heated under reflux for 6 h. After cooling, the mixture was poured into water (150 mL) and basified with 25% aqueous ammonia to pH ~8. The precipitate was filtered off, washed with warm H₂O (3 × 30 mL) and dried under reduced pressure over P₂O₅. The obtained solid product was recrystallized from MeOH giving light-yellow cubic crystals, yield 2.37 g (97%), m.p. = 501–503 K. IR (KBr), ν (cm⁻¹): 3413, 3278, 3147, 3125, 2927, 1615, 1592, 1575, 1508, 1450, 1436, 1417, 1323, 1260, 1140, 1068, 947, 931, 817, 763, 686, 661, 575. ¹H NMR (DMSO-d₆, 500 MHz, 301 K): δ = 7.51–7.58 (m, 4H, 3HAr + 1H-isox), 7.80 (br.s, 2H, NH₂), 7.92–7.98 (m, 2HAr). ¹³C NMR (DMSO-d₆, 125 MHz, 301 K): δ = 184.7–186.3 (s, C=O), 178.93–179.05 (s, C=O), 159.41–159.56 (s, C=O), 146.98–147.04 (s, C=O), 145.71–145.75 (s, C=O), 136.65–136.71 (s, C=O). Mass-spectrum, m/z (Irel, %): 267 [M+Na⁺]⁺ (5), 245 [M+H⁺]⁺ (100). Elemental analysis calculated for C₁₁H₈N₄OS (%): C 54.09, H 3.30, N 22.94, S 13.12; found (%): C 54.21, H 3.11, N 22.99, S 13.18.

Figure 7
The two-dimensional fingerprint plots for molecules I and II of the title compound showing (a) all interactions, and delineated into (b) H···H, (c) N···H···H···N and (d) C···H···H···C interactions. The dᵢ and dₑ values are the closest internal and external distances (in Å) from given points on the Hirshfeld surface.

7. Refinement
Crystal data, data collection and structure refinement details are summarized in Table 4. All H atoms were positioned geometrically (N—H = 0.88 Å, C—H = 0.95 Å) and refined using a riding model with \(U_{eq}(H) = 1.2U_{eq}(N, C)\).

Acknowledgements
The authors’ contributions are as follows: Conceptualization, EVN, MA and SM; synthesis, EVN, EKP, SKP and EAA; X-ray analysis, STC, VNK and MA; writing (review and editing of the manuscript), EVN, STC, MA and SM; funding acquisition, EVN, SKP, EAA and SM; supervision, MA, SKP and SM.
**Table 4**

Experimental details.

| Crystal data | Chemical formula | Chemical formula | M, g mol⁻¹ | Measured intensity | Refinement of structure factors | R factors | b/a, c (Å) | Space group | Temperature (K) | a, b, c (Å) | Refinement | Starting parameters | Source data | Crystal size (mm) | Radiation type | μ (mm⁻¹) | Data collection | Diffractometer |
|--------------|------------------|------------------|------------|-------------------|--------------------------------|-----------|-------------|-------------|----------------|----------------|-------------|-------------------|-------------|----------------|---------------|------------|-----------------|--------------|
| C₁₀H₁₃N₂O₂ | 2234.72           | Orthorhombic, Pca₂ | 100        | 11.142 (2) 7.25555 (15) 27.333 (6) | 2209.6 (8) | 2           | Mo Kα      | 0.28          | 0.24 × 0.18 × 0.02 | Multi-scan (SADABS) | Bruker D8 QUEST PHOTON-III CCD | Kα | 0.28 | Multi-scan (SADABS) |
|              |                  |                  |            |                   |                                |          |             |              |               |               |             |                  |             |                |               |          |                 |              |

**Funding information**

EVN is grateful to the Russian Foundation for Basic Research (RFBR) (award No. 19–53-04002, Bel_mol_a) and the Belarusian Republican Foundation for Fundamental Research (BRFFR) (award No. X20PM-056) for financial support of this research.

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Crystal structure and Hirshfeld surface analysis of 5-(5-phenyl-1,2-oxazol-3-yl)-1,3,4-thiadiazol-2-amine

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Computing details

Data collection: *APEX3* (Bruker, 2018); cell refinement: *SAINT* (Bruker, 2013); data reduction: *SAINT* (Bruker, 2013); program(s) used to solve structure: *SHELXT* (Sheldrick, 2015a); program(s) used to refine structure: *SHELXL* (Sheldrick, 2015b); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 2012); software used to prepare material for publication: *PLATON* (Spek, 2020).

5-(5-Phenyl-1,2-oxazol-3-yl)-1,3,4-thiadiazol-2-amine

Crystal data

| Symbol  | Value                      |
|---------|----------------------------|
| C_{11}H_{8}N_{4}OS | Mr = 244.27                |
| Orthorhombic, Pca2_1 |                          |
| a = 11.142 (2) Å |                          |
| b = 7.2555 (15) Å |                          |
| c = 27.333 (6) Å |                          |
| V = 2209.6 (8) Å³ |                          |
| Z = 8 |                          |
| F(000) = 1008 |                          |

Cell parameters from 5781 reflections

θ = 2.8–28.1°
μ = 0.28 mm⁻¹

Data collection

Bruker D8 QUEST PHOTON-III CCD
diffractometer

| Value                      |
|---------------------------|
| 6442 independent reflections |
| 4347 reflections with I > 2σ(I) |
| R_{int} = 0.110             |
| θ_{max} = 30.0°, θ_{min} = 2.8° |
| h = -15→15                 |
| k = -10→10                 |
| l = -38→38                 |

Refinement

Refinement on F^2

| Value                      |
|---------------------------|
| Least-squares matrix: full |
| R[F^2 > 2σ(F^2)] = 0.053  |
| wR(F^2) = 0.125            |
| S = 1.03                   |
| 6442 reflections           |
| 307 parameters             |
| 1 restraint                |

Primary atom site location: difference Fourier map

Secondary atom site location: difference Fourier map

Hydrogen site location: inferred from neighbouring sites

H-atom parameters constrained

w = 1/[σ(F^2) + 0.1115P]

where P = (F^2 + 2F_c^2)/3

〈Δρ〉_{max} < 0.001

Δρ_{max} = 0.32 e Å⁻³

Δρ_{min} = -0.34 e Å⁻³
Absolute structure: Flack $x$ determined using 1699 quotients $[(I')-(I')]/[(I')+(I')]$ (Parsons et al., 2013)
Absolute structure parameter: 0.44 (7)

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 ($\AA^2$)

|   | x   | y   | z   | $U_{eq}$/$U_{eq}$ |
|---|-----|-----|-----|-------------------|
| S1 | 0.55238 (9) | 0.15104 (17) | 0.56580 (4) | 0.0346 (3) |
| O1 | 0.4133 (3) | 0.6622 (5) | 0.63143 (14) | 0.0407 (8) |
| N1 | 0.5629 (3) | −0.1735 (6) | 0.51880 (17) | 0.0411 (11) |
| H1A | 0.5313 | −0.2668 | 0.5028 | 0.049* |
| H1B | 0.6408 | −0.1700 | 0.5241 | 0.049* |
| N2 | 0.4659 (3) | 0.5198 (6) | 0.60417 (16) | 0.0404 (10) |
| N3 | 0.3753 (3) | −0.0298 (6) | 0.52886 (16) | 0.0368 (10) |
| N4 | 0.3268 (3) | 0.1278 (6) | 0.54882 (15) | 0.0363 (9) |
| C1 | 0.4931 (4) | −0.0378 (7) | 0.53495 (18) | 0.0337 (11) |
| C2 | 0.4066 (3) | 0.2358 (7) | 0.56877 (18) | 0.0324 (10) |
| C3 | 0.3784 (4) | 0.4041 (7) | 0.59427 (18) | 0.0325 (10) |
| C4 | 0.2667 (4) | 0.4653 (7) | 0.61365 (18) | 0.0339 (10) |
| H4 | 0.1905 | 0.4077 | 0.6107 | 0.041* |
| C5 | 0.2934 (4) | 0.6234 (7) | 0.63716 (19) | 0.0353 (11) |
| C6 | 0.2228 (4) | 0.7554 (7) | 0.66463 (18) | 0.0381 (11) |
| C7 | 0.1161 (4) | 0.6999 (7) | 0.68654 (19) | 0.0400 (11) |
| H7 | 0.0917 | 0.5746 | 0.6847 | 0.048* |
| C8 | 0.0454 (5) | 0.8268 (9) | 0.7110 (2) | 0.0547 (16) |
| H8 | −0.0272 | 0.7883 | 0.7261 | 0.066* |
| C9 | 0.0801 (6) | 1.0089 (10) | 0.7136 (2) | 0.0622 (17) |
| H9 | 0.0305 | 1.0958 | 0.7299 | 0.075* |
| C10 | 0.1865 (6) | 1.0655 (9) | 0.6926 (2) | 0.0586 (16) |
| H10 | 0.2103 | 1.1910 | 0.6949 | 0.070* |
| C11 | 0.2591 (5) | 0.9399 (7) | 0.66806 (19) | 0.0435 (12) |
| H11 | 0.3325 | 0.9788 | 0.6538 | 0.052* |
| S2 | 0.25267 (9) | 0.34769 (16) | 0.43188 (5) | 0.0345 (3) |
| O12 | 0.3748 (3) | −0.1645 (5) | 0.36528 (14) | 0.0414 (8) |
| N12 | 0.2466 (3) | 0.6713 (6) | 0.47918 (16) | 0.0401 (10) |
| H12A | 0.2801 | 0.7631 | 0.4952 | 0.048* |
| H12B | 0.1686 | 0.6711 | 0.4740 | 0.048* |
| N13 | 0.3275 (3) | −0.0167 (6) | 0.39175 (17) | 0.0406 (10) |
| N14 | 0.4322 (3) | 0.5220 (6) | 0.46910 (15) | 0.0354 (9) |
| N15 | 0.4782 (3) | 0.3622 (5) | 0.44954 (15) | 0.0336 (9) |
| C12 | 0.3137 (4) | 0.5330 (7) | 0.46289 (18) | 0.0325 (11) |
| C13 | 0.3977 (3) | 0.2571 (7) | 0.42917 (19) | 0.0324 (10) |
|     |     |     |     |     |
|-----|-----|-----|-----|-----|
| C14 | 0.4201 (4) | 0.0858 (7) | 0.40348 (19) | 0.0339 (11) |
| C15 | 0.5296 (4) | 0.0103 (7) | 0.38637 (18) | 0.0355 (11) |
| H15 | 0.6085 | 0.0576 | 0.3907 | 0.043* |
| C16 | 0.4959 (4) | −0.1445 (7) | 0.36254 (19) | 0.0348 (10) |
| C17 | 0.5587 (4) | −0.2878 (7) | 0.33530 (18) | 0.0354 (11) |
| C18 | 0.6693 (4) | −0.2494 (8) | 0.31302 (18) | 0.0403 (12) |
| H18 | 0.7024 | −0.1289 | 0.3145 | 0.048* |
| C19 | 0.7299 (5) | −0.3898 (8) | 0.2886 (2) | 0.0487 (14) |
| H19 | 0.8046 | −0.3646 | 0.2733 | 0.058* |
| C20 | 0.6826 (5) | −0.5652 (9) | 0.2866 (2) | 0.0519 (14) |
| H20 | 0.7252 | −0.6607 | 0.2704 | 0.062* |
| C21 | 0.5732 (5) | −0.6019 (8) | 0.3082 (2) | 0.0492 (14) |
| H21 | 0.5400 | −0.7223 | 0.3063 | 0.059* |
| C22 | 0.5121 (5) | −0.4653 (7) | 0.3324 (2) | 0.0422 (12) |
| H22 | 0.4372 | −0.4923 | 0.3474 | 0.051* |

Atomic displacement parameters (Å²)

|     |     |     |     |     |
|-----|-----|-----|-----|-----|
| S1  | 0.0126 (4) | 0.0464 (6) | 0.0447 (7) | −0.0005 (4) | −0.0026 (4) | −0.0051 (6) |
| O1  | 0.0207 (14) | 0.047 (2) | 0.055 (2) | −0.0023 (14) | 0.0010 (14) | −0.0061 (18) |
| N1  | 0.0154 (16) | 0.047 (3) | 0.061 (3) | 0.0009 (17) | −0.0043 (17) | −0.011 (2) |
| N2  | 0.0187 (18) | 0.049 (3) | 0.053 (3) | −0.0012 (17) | 0.0002 (17) | −0.006 (2) |
| N3  | 0.0159 (17) | 0.047 (2) | 0.048 (3) | −0.0013 (16) | −0.0018 (16) | −0.002 (2) |
| N4  | 0.0162 (17) | 0.050 (3) | 0.043 (2) | 0.0009 (17) | −0.0030 (15) | 0.0001 (19) |
| C1  | 0.0166 (19) | 0.047 (3) | 0.037 (3) | −0.0025 (18) | 0.0005 (18) | 0.000 (2) |
| C2  | 0.0130 (16) | 0.048 (3) | 0.036 (3) | 0.0006 (17) | −0.0018 (18) | 0.003 (2) |
| C3  | 0.0170 (19) | 0.044 (3) | 0.036 (3) | −0.0025 (18) | −0.0032 (17) | 0.003 (2) |
| C4  | 0.0175 (19) | 0.045 (3) | 0.039 (3) | −0.0010 (19) | −0.0010 (18) | 0.001 (2) |
| C5  | 0.0191 (19) | 0.050 (3) | 0.037 (3) | −0.0005 (18) | −0.0018 (19) | 0.006 (2) |
| C6  | 0.031 (2) | 0.049 (3) | 0.034 (3) | 0.006 (2) | −0.0073 (19) | 0.000 (2) |
| C7  | 0.028 (2) | 0.059 (3) | 0.033 (3) | 0.008 (2) | −0.005 (2) | −0.001 (2) |
| C8  | 0.038 (3) | 0.086 (5) | 0.040 (3) | 0.012 (3) | 0.002 (2) | −0.004 (3) |
| C9  | 0.062 (4) | 0.071 (4) | 0.053 (4) | 0.020 (3) | 0.003 (3) | −0.021 (3) |
| C10 | 0.064 (4) | 0.056 (4) | 0.056 (4) | 0.005 (3) | −0.002 (3) | −0.012 (3) |
| C11 | 0.044 (3) | 0.048 (3) | 0.039 (3) | 0.003 (2) | −0.003 (2) | −0.003 (2) |
| S2  | 0.0129 (4) | 0.0473 (6) | 0.0433 (6) | −0.0003 (5) | −0.0025 (4) | −0.0049 (6) |
| O12 | 0.0193 (15) | 0.049 (2) | 0.056 (2) | −0.0022 (14) | −0.0014 (15) | −0.0103 (18) |
| N12 | 0.0158 (17) | 0.051 (3) | 0.053 (3) | 0.0013 (17) | −0.0033 (16) | −0.013 (2) |
| N13 | 0.0206 (19) | 0.048 (3) | 0.054 (3) | 0.0026 (18) | −0.0004 (18) | −0.007 (2) |
| N14 | 0.0158 (17) | 0.047 (2) | 0.044 (2) | −0.0001 (15) | −0.0025 (15) | −0.0051 (19) |
| N15 | 0.0155 (16) | 0.044 (2) | 0.041 (2) | −0.0003 (15) | −0.0010 (14) | −0.0016 (18) |
| C12 | 0.0150 (19) | 0.043 (3) | 0.039 (3) | −0.0015 (18) | −0.0035 (17) | 0.000 (2) |
| C13 | 0.0147 (16) | 0.044 (3) | 0.039 (3) | −0.0014 (17) | −0.0005 (18) | 0.005 (2) |
| C14 | 0.0138 (18) | 0.046 (3) | 0.041 (3) | 0.0009 (18) | −0.0021 (17) | 0.004 (2) |
| C15 | 0.0135 (18) | 0.051 (3) | 0.042 (3) | 0.0038 (19) | −0.0004 (18) | 0.002 (2) |
| C16 | 0.0163 (19) | 0.051 (3) | 0.037 (2) | 0.0032 (19) | −0.0007 (17) | 0.005 (2) |
| C17 | 0.025 (2) | 0.048 (3) | 0.033 (3) | 0.003 (2) | −0.0036 (19) | 0.004 (2) |

*sup-3*
| | | | | | | |
|---|---|---|---|---|---|
| C18 | 0.021 (2) | 0.056 (3) | 0.044 (3) | 0.005 (2) | -0.0004 (18) | 0.004 (2) |
| C19 | 0.033 (3) | 0.070 (4) | 0.042 (3) | 0.014 (2) | 0.008 (2) | 0.009 (3) |
| C20 | 0.051 (3) | 0.061 (4) | 0.044 (3) | 0.018 (3) | 0.003 (3) | -0.002 (3) |
| C21 | 0.052 (4) | 0.050 (3) | 0.045 (3) | 0.002 (3) | 0.003 (3) | 0.000 (3) |
| C22 | 0.035 (3) | 0.052 (3) | 0.039 (3) | 0.001 (2) | -0.001 (2) | 0.000 (2) |

**Geometric parameters (Å, °)**

| Bond/Angle | Distance/Angle |
|---|---|
| S1—C1 | 1.739 (5) |
| S1—C2 | 1.739 (4) |
| O1—C5 | 1.374 (5) |
| O1—N2 | 1.342 (5) |
| N1—C1 | 1.330 (6) |
| N1—H1A | 0.8800 |
| N1—H1B | 0.8800 |
| C5—O1—N2 | 108.4 (3) |
| C1—N3—N4 | 112.0 (4) |
| C3—N2—O1 | 105.7 (4) |
| C1—N3—N4 | 112.0 (4) |
| C2—N4—N3 | 113.4 (4) |
| C3—N2—O1 | 105.7 (4) |
| C1—N3—N4 | 112.0 (4) |
| C2—N4—N3 | 113.4 (4) |
| C3—N2—O1 | 105.7 (4) |
| C1—N3—N4 | 112.0 (4) |
| C2—N4—N3 | 113.4 (4) |

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N4—C2—S1 113.9 (4) N15—C13—S2 113.5 (4)
C3—C2—S1 121.7 (3) C14—C13—S2 120.2 (3)
N2—C3—C4 111.9 (4) N13—C14—C15 112.2 (5)
N2—C3—C2 118.6 (4) N13—C14—C13 117.9 (4)
C4—C3—C2 129.4 (4) C15—C14—C13 129.8 (4)
C5—C4—C3 104.4 (4) C16—C15—C14 103.9 (4)
C5—C4—H4 127.8 C16—C15—H15 128.0
C3—C4—H4 127.8 C14—C15—H15 128.0
C4—C5—O1 109.6 (4) C15—C16—O12 109.8 (4)
C4—C5—C6 133.6 (4) C15—C16—C17 134.9 (4)
O1—C5—C6 116.8 (4) O12—C16—C17 115.4 (4)
C7—C6—C11 119.6 (5) C22—C17—C18 119.2 (5)
C7—C6—C5 119.7 (5) C22—C17—C16 120.6 (5)
C11—C6—C5 120.6 (5) C18—C17—C16 120.1 (5)
C8—C7—C6 120.1 (5) C19—C18—C17 119.2 (5)
C8—C7—H7 119.9 C19—C18—H18 120.4
C6—C7—H7 119.9 C17—C18—H18 120.4
C9—C8—C7 120.2 (6) C20—C19—C18 120.6 (5)
C9—C8—H8 119.9 C20—C19—H19 119.7
C8—C9—C10 120.4 (6) C18—C19—H19 119.7
C8—C9—H9 119.8 C19—C20—C21 119.9 (5)
C10—C9—H9 119.8 C19—C20—H20 120.0
C9—C10—C11 120.3 (6) C21—C20—H20 120.0
C9—C10—C11 119.8 C22—C21—C20 120.4 (6)
C11—C10—C11 119.8 C22—C21—H21 119.8
C11—C10—C11 119.4 (5) C21—C22—C17 120.7 (5)
C10—C11—C6 120.3 C21—C22—H22 119.7
C6—C11—H11 120.3 C17—C22—H22 119.7
C5—O1—N2—C3 0.5 (5) C16—O12—N13—C14 0.4 (5)
C1—N3—N4—C2 0.8 (6) C12—N14—N15—C13 0.3 (6)
N4—N3—C1—N1 −179.2 (5) N15—N14—C12—N12 178.6 (5)
N4—N3—C1—S1 −0.2 (5) N15—N14—C12—S2 −0.7 (5)
C2—S1—C1—N3 −0.2 (4) C13—S2—C12—N12 −178.6 (5)
C2—S1—C1—N1 178.7 (5) C13—S2—C12—N14 0.7 (4)
N3—N4—C2—C3 −176.7 (5) N14—N15—C13—C14 176.6 (5)
N3—N4—C2—S1 −1.0 (6) N14—N15—C13—S2 0.3 (6)
C1—S1—C2—C3 0.7 (4) C12—S2—C13—N15 −0.5 (4)
C1—S1—C2—N4 176.5 (4) C12—S2—C13—C14 −177.1 (4)
O1—N2—C3—C4 0.7 (6) O12—N13—C14—C15 −0.9 (6)
O1—N2—C3—C2 −176.3 (4) O12—N13—C14—C13 176.6 (4)
N4—C2—C3—N2 −166.4 (5) N15—C13—C14—N13 169.7 (5)
S1—C2—C3—N2 18.2 (7) S2—C13—C14—N13 −14.2 (7)
N4—C2—C3—C4 17.1 (9) N15—C13—C14—C15 −13.3 (9)
S1—C2—C3—C4 −158.3 (4) S2—C13—C14—C15 162.9 (4)
N2—C3—C4—C5 −1.7 (6) N13—C14—C15—C16 1.1 (6)
C2—C3—C4—C5 174.9 (5) C13—C14—C15—C16 −176.1 (5)
| C3—C4—C5—O1 | 2.0 (6) | C14—C15—C16—O12 | −0.7 (6) |
| C3—C4—C5—C6 | −180.0 (5) | C14—C15—C16—C17 | 178.6 (6) |
| N2—O1—C5—C4 | −1.7 (6) | N13—O12—C16—C15 | 0.2 (6) |
| N2—O1—C5—C6 | 179.9 (4) | N13—O12—C16—C17 | −179.2 (4) |
| C4—C5—C6—C7 | 24.7 (9) | C15—C16—C17—C22 | 152.5 (6) |
| C14—C15—C16—O12 | −0.7 (6) | C15—C16—C17—C22 | 28.2 (7) |
| C4—C5—C6—C11 | −153.3 (6) | C15—C16—C17—C18 | −25.4 (9) |
| O1—C14—C15—C16 | 24.5 (7) | O12—C16—C17—C18 | 154.0 (5) |
| C11—C6—C7—C8 | 0.9 (8) | C22—C17—C18—C19 | −0.2 (7) |
| C5—C6—C7—C8 | −177.2 (5) | C16—C17—C18—C19 | 177.7 (5) |
| C6—C7—C8—C9 | 0.3 (8) | C17—C18—C19—C20 | −0.4 (8) |
| C7—C8—C9—C10 | −1.2 (10) | C18—C19—C20—C21 | 1.0 (9) |
| C8—C9—C10—C11 | 0.8 (10) | C19—C20—C21—C22 | −1.1 (9) |
| C9—C10—C11—C6 | 0.4 (9) | C20—C21—C22—C23 | 0.5 (9) |
| C7—C6—C11—C10 | −1.2 (8) | C18—C17—C22—C21 | 0.1 (8) |
| C5—C6—C11—C10 | 176.8 (5) | C16—C17—C22—C21 | −177.8 (5) |

**Hydrogen-bond geometry (Å, °)**

$Cg_4$ and $Cg_6$ are the centroids of the S2/N14/N15/C12/C13 and C17–C22 rings, respectively.

| D—H···A | D—H | H···A | D···A | D—H···A |
|---------|------|------|-------|---------|
| N1—H1.4···N14 | 0.88 | 2.10 | 2.974 (6) | 172 |
| N1—H1B···N4 | 0.88 | 2.20 | 3.071 (6) | 169 |
| N12—H12A···N3 | 0.88 | 2.06 | 2.933 (6) | 174 |
| N12—H12B···N15 | 0.88 | 2.24 | 3.108 (5) | 170 |
| C4—H4···N2 | 0.95 | 2.56 | 3.363 (6) | 142 |
| C15—H15···N13 | 0.95 | 2.46 | 3.323 (6) | 151 |
| C8—H8···Cg6 | 0.95 | 2.98 | 3.774 (6) | 142 |
| C22—H22···Cg4 | 0.95 | 2.95 | 3.648 (6) | 132 |

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