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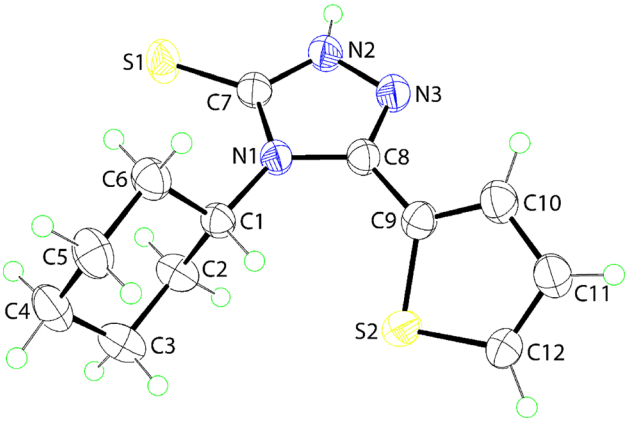
Crystal structure of 4-cyclohexyl-5-(thiophen-2-yl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione, $C_{12}H_{15}N_3S_2$



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Abstract

$C_{12}H_{15}N_3S_2$, monoclinic, $P2_1/n$ (no. 14), a = 5.51310(10) Å, b = 15.4525(4) Å, c = 15.9261(4) Å, β = 99.844(2)°, V = 1336.79(5) Å^3, Z = 4, $R_{gt}(F)$ = 0.0359, $wR_{ref}(F^2)$ = 0.1009, T = 160 K.

CCDC no.: 2450625

Table 1: Data collection and handling.

Crystal:	Colourless prism
Size:	0.22 × 0.11 × 0.05 mm
Wavelength:	Cu*Kα* radiation (1.54184 Å)
μ:	3.46 mm^{-1}
Diffractometer, scan mode:	Rigaku Synergy, ω scan
θ_{max}, completeness:	74.5°, 100 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	14587, 2725, 0.051
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2,403
$N(param)_{refined}$:	196
Programs:	Rigaku,[1] SHELX,[2,3] WinGX[4]

1 Source of material

A mixture of thiophene-2-carbohydrazide (1.42 g, 0.01 mol) and cyclohexyl isothiocyanate (1.41 g, 0.01 mol), in ethanol (10 mL), was heated under reflux for 30 min, and the solvent was then distilled off under vacuum. Sodium hydroxide in a 10 % aqueous solution (8 mL) was then added to the residue, and the mixture was heated under reflux for 2 h, then filtered hot. On cooling, the mixture was acidified with hydrochloric acid (pH 1–2) and the precipitated crude product was filtered, washed with water, dried and crystallised from aqueous ethanol to yield 2.28 g (86 %) of the title compound as colourless prisms. Single crystals suitable for X-ray diffraction were obtained by slow evaporation of a solution of the title compound in EtOH/$CHCl_3$ (2:1, v/v) held at room temperature for 2 days. **M. pt**: 469–471 K (uncorrected). **^{1}H NMR** ($CDCl_3$, 500.13 MHz): δ 13.6 (s, 1H, NH), 6.98 (t, 1H, Thiophene–H, J = 4.2 Hz), 7.10 (d, 1H, Thiophene–H, J = 4.2 Hz), 7.18 (d, 1H, Thiophene–H, J = 4.2 Hz), 2.54–2.68 (m, 1H, Cyclohexyl–H), 1.50–1.72 (m, 4H, Cyclohexyl–H), 1.12–1.44 (m, 6H, Cyclohexyl–H). **^{13}C NMR** ($CDCl_3$, 125.76 MHz): δ 169.26 (C=S), 148.66 (Triazole–C5), 124.62, 126.04, 127.88, 128.0 (Thiophene–C), 24.44, 25.98, 30.88, 66.62 (Cyclohexyl–C).

2 Experimental details

The C-bound H atoms were geometrically placed (C–H = 0.95–1.00 Å) and refined as riding with U_{iso}(H) = 1.2U_{eq}(C). The N-bound H atom was refined freely. The S2-containing thiophen-2-yl ring was disordered over two co-planar orientations, each of which was refined independently. The major component of the disorder had a site occupancy factor = 0.544(2).

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3 Discussion

The 1,2,4-triazole scaffold is recognised as an essential component of several biologically interesting drugs and exhibits a wide range of chemotherapeutic properties.[5,6] Marketed triazole-based drugs are extensively used as advantageous anti-fungal,[7] anti-cancer,[8] anti-bacterial[9] and anti-viral[10] agents. In addition, the thiophene heterocycle constitutes a main building block of many drugs.[11]

The molecular structure of the title triazole-thiophene hybrid molecule, (I), is shown in figure (50 % probability ellipsoids; only the major component of the disordered S2-containing thiophen-2-yl ring is shown for reasons of clarity). The molecule comprises a central 1,2,4-triazole-3-thione group connected at the 4-position to a cyclohexyl ring, and at the 5-position to a thiophen-2-yl ring; the dihedral angle between the two five-membered rings is 35.9(3)° consistent with a splayed orientation. Within the 1,2,4-triazole ring, the lengthening of the formally C8–N3 [1.3041(19) Å] double bond and the shortening, for example, of the formally N2–N3 [1.3640(18) Å] and C8–N1 [1.3854(18) Å] single bonds indicate significant delocalisation of π-electron density over the constituent atoms.

In the crystallographic literature, there are two related N-alkyl structures available for comparison, namely alkyl = ethyl[12] and cyclohexyl,[13] hereafter (II) and (III), respectively. Each of (II) and (III) exhibit similar patterns in the bond lengths within the 1,2,4-triazole ring as for (I). The relative orientations of the five-membered rings differ, however. Thus, in (II) and (III), the dihedral angles are 13.53(12) and 6.19(7)°, respectively, indicating closer to co-planar orientations than for (I). This difference is likely to arise due to steric considerations in (I). The separation between the methine–C–H and the thiophen-2-yl–C–H atoms of the disordered component of the ring is 2.25 Å which would contract if a more co-planar orientation was adopted.

In the molecular packing, the most prominent intermolecular interactions correspond to amine–N–H···S(thione) hydrogen-bonding [N2–H2*n*···S1^{i}: H2*n*···S1^{i} = 2.38(2) Å, N2···S1^{i} = 3.2511(14) Å with angle at H2*n* = 169.1(19)° for symmetry operation (i) 2 − x, 1 − y, 1 − z]. The hydrogen bonds occur within a centrosymmetric aggregate through an eight-membered $\{\cdots HNCS\}_2$ synthon. Similar synthons are noted in the crystals of (II) and (III).

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Conflict of interest: The authors declare no conflicts of interest.

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