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4-Allyl-2-(morpholin-4-ylmethyl)-5-(pyridin-4-yl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione

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In the title compound, $C_{15}H_{19}N_5OS$, the morpholine ring adopts a chair conformation. The mean plane of the pyridine ring makes a dihedral angle of 35.16 (7)° with the triazole ring plane.

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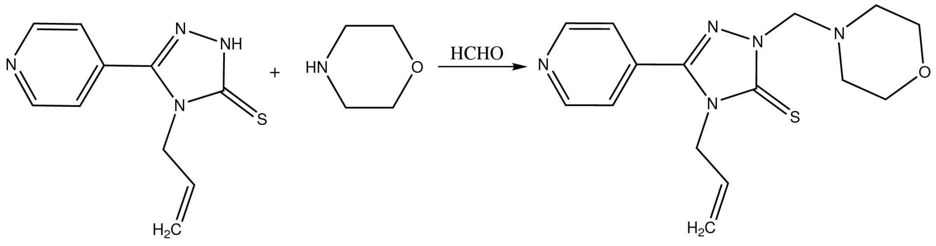
Key indicators

Single-crystal X-ray study
T = 296 K
Mean σ(C–C) = 0.002 Å
R factor = 0.040
wR factor = 0.115
Data-to-parameter ratio = 22.4

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Comment

Derivatives of 1,2,4-triazole are known to exhibit anti-inflammatory (Unangst *et al.*, 1992; Mullican *et al.*, 1993), antiviral (Jones *et al.*, 1965), analgesic (Sughen & Yoloye, 1978), antimicrobial (Shams El-Dine & Hazzaa, 1974; Misato *et al.*, 1977; Cansız *et al.*, 2001), anticonvulsant (Stillings *et al.*, 1986) and antidepressant activities (Kane *et al.*, 1988), this last being usually explored by the forced swim test (Porsolt *et al.*, 1977; Vamvakides, 1990). Among the pharmacological profiles of 1,2,4-triazoles, their antimicrobial, anticonvulsant and antidepressant properties seem to be the best documented. Derivatives of 4,5-disubstituted 1,2,4-triazole are synthesized by intramolecular cyclization of 1,4-disubstitued thiosemicarbazides (Zamani *et al.*, 2003; Cansız *et al.*, 2004; Koparır *et al.*, 2005). Furthermore, pyridine derivatives are of special interest, because they represent an example where a high level of predictability of potential supramolecular arrangements is achieved (Moulton & Zaworotko, 2001).



(II) (I)

In the present study, the title compound, (I), was synthesized by the reaction of formaldehyde and morpholine with 4-allyl-5-pyridin-4-yl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione, (II), which was synthesized by the reaction of 3-isothiocyanatoprop-1-ene and isonicotinohydrazide through *N*-allyl-2-isonicotinoylhydrazinecarbothioamide (Çetin, 2004). Base-catalysed intramolecular dehydrative cyclization of this intermediate furnished 4,5-disubstituted 1,2,4-triazole-3-thione, (II), in good yield (75–85%). The reaction sequence depicted in the scheme was followed to obtain the new compound, (I). The structures of these compounds have been confirmed by IR, ^{1}H NMR and ^{13}C NMR spectroscopy.

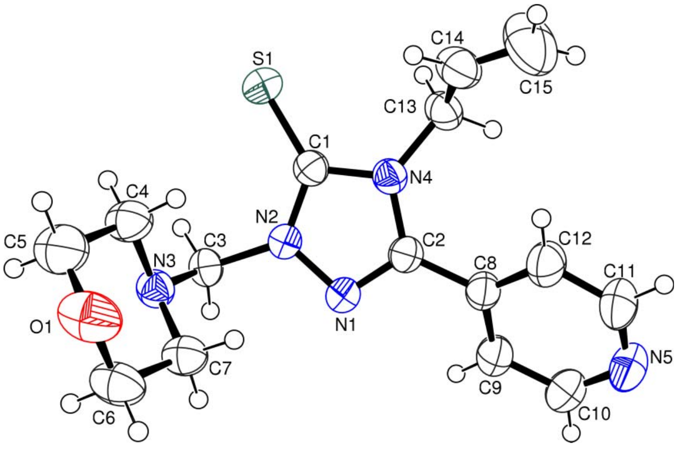


Figure 1
A drawing of (I), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 40% probability level and H atoms are shown as small spheres of arbitrary radii.

Previously, we have reported a 1,2,4-triazole derivative, namely 4-ethyl-5-(2-hydroxyphenyl)-2*H*-1,2,4-triazole-3(4*H*)-thione, (III) (Dege *et al.*, 2005). As a continuation of our investigation of the structures of 1,2,4-triazole compounds, we describe here the structure of the title compound, (I). The aim of the present investigation is to study the differences between the structures of (I) and (III), and also to establish the conformational features of various functional groups.

The molecular structure of (I) is shown in Fig. 1. Atoms S1, C3, C8 and C13 are coplanar with the triazole ring, the maximum deviation from the least-squares planes being 0.0795 (8) Å for atom C13. Atoms N3 and C14 are in axial positions with respect to the triazole ring plane. The Φ_{CC} torsion angle (N4—C13—C14—C15) is 134.8 (2)°, which shows that the conformation about the C13—C14 bond is (+)-anticlinal.

The interatomic distances within the triazole ring are not equal, ranging from 1.301 (2) to 1.373 (2) Å, and agree with the values observed in (III) (Dege *et al.*, 2005). The N1═C2 bond length is 1.3006 (15) Å and this corresponds with the average value of the lengths of the analogous bonds in related triazole-thiones [1.300 (2) Å; Cambridge Structural Database, Version 5.26; *ConQuest*, Version 3.6; Allen, 2002]. In the triazole ring, the C1—N2 bond distance is significantly shorter than the C1—N4 and C2—N4 bonds. This is attributed to the presence of delocalization between the lone pair on atom N2 and the C1═S1 double bond, and also to electronic factors associated with the large electron-dense substituents. This suggests that the bond length is more affected by electronic effects than by the steric hindrance of the ring substituents. The N2—C3 and N4—C13 bonds are almost the same length, thus confirming the absence of important conjugation effects. The geometry around atom N4, carrying the allyl group, is essentially planar, the sum of the three bond angles around it being 359.3°.

The morpholine ring adopts a chair conformation, as is evident from the puckering parameters (Cremer & Pople, 1975), Q = 0.5662 (16) Å, q_2 = 0.0034 (16) Å, q_3 = 0.5661 (16) Å, θ = 1.15 (16)° and φ_2 = 150 (3)° for the atom sequence N3/C4/C5/O1/C6/C7. Atoms N3 and O1 are on opposite sides of the C4/C5/C6/C7 plane and displaced from it by 0.2371 (10) and 0.2338 (13) Å, respectively. The mean plane of the pyridine ring makes a dihedral angle of 35.16 (7)° with respect to the triazole ring plane.

Experimental

A slurry consisting of 4-allyl-5-pyridin-4-yl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione, (II) (0.02 mol, 0.436 g), dimethylformamide (10 ml) and 37% formalin (0.04 mol, 0.356 ml) was prepared. To this, morpholine (0.02 mol, 0.174 g) was added dropwise, with cooling and shaking. The reaction mixture was allowed to stand at room temperature for 1 h with occasional shaking, after which it was warmed over a steam bath for 30 min. At the end of this period, the contents were cooled and the product, (I), was obtained. Compound (I) was then recrystallized from a mixture of acetone–petroleum ether (1:2) (yield 55%, m.p. 407 K). Spectroscopic analysis: IR (KBr, ν, cm^{-1}): 3099–2970 (Ar and allyl C—H), 2960–2829 (aliphatic C—H), 1660 (C═C, *cis*) 1614 (C═N), 1598 (Ar C═C), 1186 (C—O—C); ^{1}H NMR (400 MHz, DMSO-d_6, δ, p.p.m.): 2.70 (*t*, J = 4.40 Hz, 4H, CH_2—N—CH_2), 3.31 (*s*, 2H, NH—CH_2—CH), 3.54 (*t*, J = 4.40 Hz, 4H, CH_2—O—CH_2), 4.81 (*dd*, 1H, J_{cis} = 8.23 and 1.10 Hz, NH—CH_2—CH═CH_2), 4.86 (*d*, J_{trans} = 15.30 Hz, 1H, NH—CH_2—CH═CH_2), 5.81 (*dq*, 1H, J = 9.90 and 5.13 Hz, NH—CH_2—CH═CH_2), 5.14 (*s*, 2H, N—CH_2—N), 7.55 (*dd*, J = 5.23 and 1.83 Hz, 2H, Ar C—CH), 8.55 (*dd*, J = 5.23 and 1.47 Hz, 2H, Ar N—CH); ^{13}C NMR (100 MHz, DMSO-d$_6$, δ, p.p.m.): 169.83 (C_5), 151.22 (C_2), 148.74 (C_4), 133.72 (C_3), 132.12 (C_7), 123.06 (C_1), 117.15 (C_8), 69.82 (C_9), 66.74 (C_{11}), 50.95 (C_{10}), 47.74 (C_6).

Crystal data

$C_{15}H_{19}N_5OS$
M_r = 317.41
Triclinic, $P\bar{1}$
a = 8.9387 (7) Å
b = 9.1043 (7) Å
c = 10.6069 (8) Å
α = 88.509 (6)°
β = 85.498 (6)°
γ = 80.661 (6)°
V = 849.05 (11) Å^3

Z = 2
D_x = 1.242 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 11208 reflections
θ = 1.9–29.0°
μ = 0.20 mm^{-1}
T = 296 K
Prism, colourless
0.62 × 0.42 × 0.20 mm

Data collection

Stoe IPDS-2 diffractometer
ω scans
Absorption correction: integration (*X-RED32*; Stoe & Cie, 2002)
T_{min} = 0.886, T_{max} = 0.967
11655 measured reflections
4462 independent reflections

3716 reflections with $I > 2\sigma(I)$
R_{int} = 0.034
θ_{max} = 29.0°
h = −12 → 12
k = −12 → 12
l = −14 → 13

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.115
S = 1.05
4462 reflections
199 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0603P)^2 + 0.0942P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.28 e Å^{-3}
$\Delta\rho_{min}$ = −0.23 e Å^{-3}

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Table 1
Selected geometric parameters (Å, °).

S1—C1	1.6676 (12)	N3—C4	1.4566 (17)
O1—C5	1.413 (2)	N3—C7	1.4607 (16)
O1—C6	1.419 (2)	N4—C2	1.3711 (14)
N1—C2	1.3006 (15)	N4—C1	1.3734 (15)
N1—N2	1.3719 (13)	N4—C13	1.4654 (15)
N2—C1	1.3526 (15)	N5—C10	1.325 (2)
N2—C3	1.4773 (15)	N5—C11	1.325 (2)
N3—C3	1.4278 (15)		
C5—O1—C6	110.12 (13)	C4—N3—C7	110.46 (11)
C2—N1—N2	104.48 (9)	C2—N4—C1	107.67 (9)
C1—N2—N1	112.54 (9)	C10—N5—C11	116.20 (14)
C1—N2—C3	128.11 (10)	N2—C1—N4	103.84 (10)
N1—N2—C3	119.25 (9)	N1—C2—N4	111.46 (10)
C3—N3—C7	114.45 (10)	N3—C3—N2	116.37 (9)

H atoms were positioned geometrically and treated using a riding model, fixing the bond lengths at 0.97 Å for CH_2 and for the pyridine ring, and at 0.93 Å for atoms C14 and C15. The displacement parameters of the H atoms were constrained as $U_{iso}(H) = 1.2U_{eq}$ of the carrier atom.

Data collection: *X-AREA* (Stoe & Cie, 2002); cell refinement: *X-AREA*; data reduction: *X-RED32* (Stoe & Cie, 2002); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* for Windows (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999) and *PLATON* (Spek, 2003).

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