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N-Cyclohexyl-2-[5-(4-pyridyl)-4-(*p*-tolyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]-acetamide dihydrate

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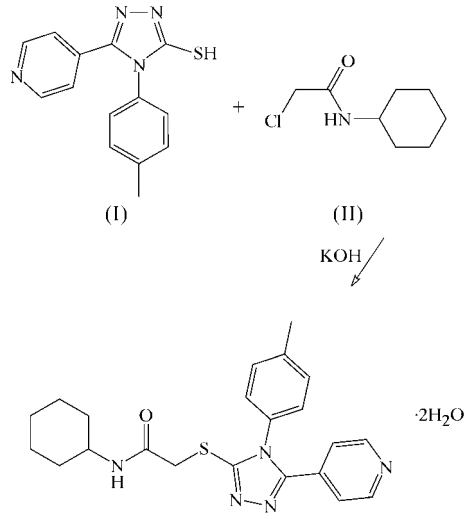
In the title compound, $C_{22}H_{25}N_5OS\cdot 2H_2O$, the molecules are stacked in columns running along the *b* axis. In this arrangemant, the molecules are linked to each other by a combination of one two-centre N—H···O hydrogen bond and four two-centre O—H···O hydrogen bonds containing two types of ring motif, *viz*. $R_4^4(10)$ and $R_3^3(11)$. In the crystal structure, centrosymmetric π–π interactions between the triazole rings, with a distance of 3.691 (2) Å between the ring centroids, also affect the packing of the molecules.

Comment

1,2,4-Triazole and its derivatives represent one of the most biologically active classes of compounds, possessing a wide spectrum of activities, including antibacterial, antifungal, antiviral, anti-inflammatory, anticonvulsant, antidepressant, antihypertensive, analgesic and hypoglycaemic properties (Abbas & Khalil, 2005; Holla *et al.*, 1998; Hovsepian *et al.*, 2004). In addition to these important biological applications, mercapto-1,2,4-triazoles are also of great utility in preparative organic chemistry, and triazolothiadiazines, for example, in the presence of various reagents, undergo different types of reaction to yield other heterocyclic compounds, *e.g.* thiazolotriazoles, triazolothiadizoles and triazolothiazepines. The amino and mercapto groups of these compounds serve as readily accessible nucleophilic centres for the preparation of N-bridged heterocycles (Shaker, 2006). Furthermore, there have been some studies of the electronic structures and thiol–thione tautomeric equilibrium of heterocyclic thione derivatives (Koparır, Çetin & Cansız, 2005; Coyanis *et al.*, 2002). Substituted 1,2,4-triazoles have been actively studied as bridging ligands coordinating through their vicinal N atoms (Mills *et al.*, 2002; Li *et al.*, 2003, 2006; Zaleski *et al.*, 2005). It is of interest that some complexes containing 1,2,4-triazole ligands have particular structures and specific magnetic properties (Vreugdenhil *et al.*, 1987; van Albada *et al.*, 1984; Vos *et al.*, 1983; Kahn & Martinez, 1998). Taking into account these important properties, the present single-crystal X-ray diffraction study of the title compound, (III), was carried out and the results are presented here.



(I) (II) (III)

In the present study, the reaction of 5-(4-pyridyl)-4-(*p*-tolyl)-4*H*-1,2,4-triazole-3-thiol, (I), with 2-chloro-*N*-cyclohexylacetamide, (II), in a basic medium gave the corresponding *N*-cyclohexyl-2-[5-(4-pyridyl)-4-(*p*-tolyl)-4*H*-1,2,4-triazol-3-ylsulfanyl]acetamide dihydrate, (III), in almost quantitative yield (65%) (Hovsepian *et al.*, 2004). The reaction sequences depicted in the scheme above were followed to obtain the new compound, whose structure has been confirmed by IR and ^{1}H NMR spectroscopic analyses.

A view of the hydrogen-bonded structure of (III) and its atom-numbering scheme are shown in Fig. 1. Selected geometric parameters are listed in Table 1. The asymmetric unit of (III) is made up of just one organic moiety and two water molecules. The organic component is composed of a central 1,2,4-triazole ring, with a (cyclohexylaminocarbonyl)methylsulfanyl group connected to the 3-position of the ring, a *p*-tolyl group in the 4-position and a 4-pyridyl ring in the 5-position. As expected, the 1,2,4-triazole and pyridine rings are planar, as are all similar fragments reported in the Cambridge Structural Database (CSD, Version 5.26; *CONQUEST*, Version 3.6; Allen, 2002), which can be attributed to a wide range of electron delocalization [maximum deviations of 0.0015 (11) and −0.0067 (17) Å for atoms N4 and N5, respectively]. The cyclohexane ring adopts a chair conformation, as is evident from the puckering parameters for the atom sequence C33—C34—C35—C36—C37—C38 [Q = 0.578 (3) Å, θ = 180 (3)° and φ = 360 (3)°; Cremer & Pople, 1975]. Atoms C33 and C36 are on opposite sides of the C33—C34—C35—C36—C37—C38 plane and are displaced from it by −0.234 (2) and 0.243 (2) Å, respectively. The benzene ring is twisted out of the plane of the triazole ring. The dihedral angle between these planes is 74.12 (7)°. The dihedral angle between the triazole and pyridine rings is 28.55 (10)°. A non-

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planar disposition of the three rings has been observed in similar 1,2,4-triazole derivatives (Zhu *et al.*, 2000; Bruno *et al.*, 2003; Yılmaz *et al.*, 2005). The sulfanylacetamide bridge linking the triazole ring with the cyclohexane ring is not planar, and the Φ_{CC} torsion angle (S3—C31—C32—N3) is 164.05 (15)°, which shows that the conformation about the C31—C32 bond is (+)-antiperiplanar.

The interatomic distances within the triazole ring are not equal, ranging from 1.308 (2) to 1.388 (2) Å. The C—N bonds in the ring are classified into localized single (*e.g.* N4—C3 and N4—C5) and double bonds (*e.g.* N1═C5 and N2═C3). The N4—C5 single bond is associated with a larger *endo* angle, N4—C5—C51, whereas the N1═C5 double bond has a smaller *exo* angle, N1═C5—C51. The difference between the S3—C3 and S3—C31 bond distances [1.7319 (18) and 1.7880 (19) Å, respectively] can be attributed to the different hybridization of the Csp^2 and Csp^3 atoms. The N1═C5 and N2═C3 bond distances are in good agreement with those found for structures containing the 1,2,4-triazole ring (Wang *et al.*, 1998; Özbey *et al.*, 1999; Zhu *et al.*, 2000; Bruno *et al.*, 2003; Dinçer *et al.*, 2005). The N—N bond length is 1.388 (2) Å, which is smaller than a pure single bond (1.41 Å; Burke-Laing & Laing, 1976). The fact that the C3—N4 and C5—N4 bond distances are shorter than the C41—N4 bond distance can be considered as possible evidence of conjugation over the whole of the triazole moiety. Furthermore, the C—N bond distances in the sulfanylacetamide linkage are quite different. The C32—N3 bond length [1.314 (2) Å] is significantly shorter than the C33—N3 bond [1.460 (2) Å], which is indicative of the usual delocalized amide bond character. The remaining bond lengths in (III) show no unusual values.

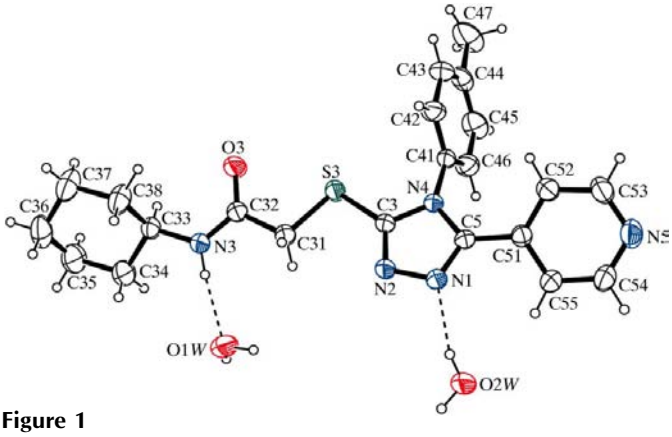

Figure 1
The molecule of the title compound, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii. Hydrogen bonds are indicated by broken lines.

In the crystal structure of (III), the molecules are packed in columns running along the *b* axis, and linked to each other by a combination of one two-centre N—H···O hydrogen bond and four two-centre O—H···O hydrogen bonds, in which the solvent water molecules lead to a number of intermolecular hydrogen bonds (Table 2). Considering these entities alone first, the water (O2*W*) molecule at (*x*, *y*, *z*) participates in O2*W*—H21*W*···N1 and O2*W*—H22*W*···N2^{i} hydrogen bonds [symmetry code: (i) $-x+1, -y, -z+1$], forming a centrosymmetric $R_4^4(10)$ ring (Bernstein *et al.*, 1995). Another ring forms from a combination of hydrogen bonds [N3—H3···O1*W*, O1*W*—H11*W*···O2*W*^{i} and O2*W*^{i}—H22*W*^{i}···N2]. Together, these form an $R_3^3(11)$ ring (Fig. 2).

In addition to these hydrogen bonds occurring between molecules in inversion-related columns, there are also O—H···O hydrogen bonds between the molecules in each column. In this interaction, the water molecule (O1*W*) at (*x*, *y*, *z*) acts as a hydrogen-bond donor to carbonyl atom O3 at (x, $y-1$, z). This hydrogen bond, together with N3—H3···O1*W*, links the molecules in each column in a zigzag arrangement.

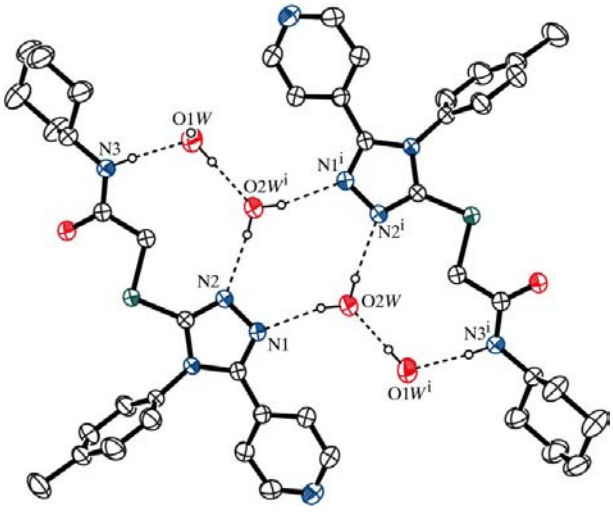

Figure 2
Part of the crystal structure of (III), showing the formation of $R_4^4(10)$ and $R_3^3(11)$ rings. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii. For the sake of clarity, H atoms not involved in the motif shown have been omitted. [Symmetry code: (i) $-x+1, -y, -z+1$.]

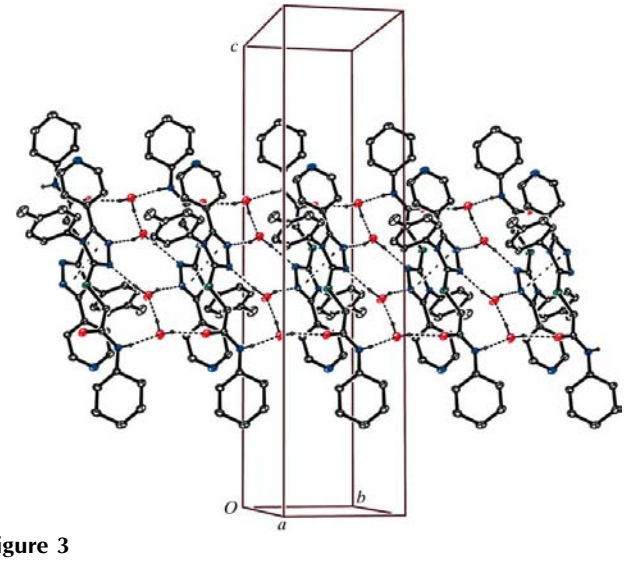

Figure 3
A packing diagram for compound (III), showing the N—H···O, O—H···O, O—H···N and π–π interactions (dashed lines). For clarity, only H atoms involved in hydrogen bonding have been included.

Water is potentially capable of participating in four hydrogen bonds but frequently shows a three-coordinate configuration (Jeffrey & Maluszynska, 1990). This is illustrated in the case of (III), where atoms O1*W* and O2*W* donate two hydrogen bonds but accept one. A centrosymmetric π–π stacking interaction involving pairs of overlaid triazole rings also plays a part in the crystal packing. The triazole rings of the molecules at (x, y, z) and $(-x+1, -y+1, -z+1)$ are strictly parallel, with an interplanar spacing of 3.343 (2) Å. The ring-centroid separation is 3.691 (2) Å, corresponding to a near-ideal ring offset of 1.564 (2) Å (Fig. 3).

Experimental

Compounds (I) and (II) were prepared according to previously reported methods (Çetin, 2004; Koparır, Cansız & Çetin, 2005). Triazole (I) (2 mmol, 0.536 g) was dissolved in a solution of KOH (2 mmol, 0.112 g) in methanol (15 ml) at 313 K. 2-Chloro-*N*-cyclohexylacetamide, (II) (0.002 mmol, 0.365 g), was added to the solution obtained and the mixture was refluxed for 2 h. After cooling, the precipitated product, (III), was filtered off and recrystallized from ethanol (yield 65%; m.p. 450–451 K). IR (ν, cm^{-1}): 3446–3340 (*s*, N—H, O—H), 3160–3020 (*b*, Ar C—H), 2980–2930 (*b*, Alk C—H), 1680 (*s*, C═O), 1618 (*m*, C═N); ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.25–1.89 (*m*, 10H, cyclohexyl CH_2), 2.47 (*s*, 3H, CH_3), 3.71–3.73 (*m*, 1H, cyclohexyl N—CH), 7.11–7.61 (*m*, 7H, Ar CH, NH), 7.78–7.80 (*d*, 2H, J = 6.23 Hz, pyridine N—CH).

Crystal data

$C_{22}H_{25}N_5OS\cdot 2H_2O$
M_r = 443.56
Monoclinic, $P2_1/c$
a = 12.3634 (10) Å
b = 6.8031 (4) Å
c = 28.077 (2) Å
β = 90.306 (7)°
V = 2361.5 (3) Å^3
Z = 4
D_x = 1.248 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.17 mm^{-1}
T = 296 K
Prism, colourless
0.68 × 0.43 × 0.15 mm

Data collection

Stoe IPDS-II diffractometer
ω scans
Absorption correction: integration (*X-RED32*; Stoe & Cie, 2002)
T_{min} = 0.921, T_{max} = 0.979
26676 measured reflections
4135 independent reflections
2947 reflections with $I > 2\sigma(I)$
R_{int} = 0.048
θ_{max} = 25.0°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.107
S = 1.03
4135 reflections
298 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0634P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.17 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}
Extinction correction: *SHELXL97* (Sheldrick, 1997)
Extinction coefficient: 0.0066 (10)

The coordinates of the H atoms of the water molecules were determined from a difference map and were then allowed to refine isotropically, while the coordinates of atom H12*W* were refined isotropically subject to a DFIX restraint of O—H = 0.82 Å. All other H atoms were positioned geometrically and refined with a riding model, fixing the bond lengths at 0.98, 0.97, 0.96, 0.93 and 0.86 Å for CH, CH_2, CH_3, aromatic CH and NH groups, respectively. The displacement parameters of the H atoms were constrained to U_{iso}(H) = 1.2U_{eq}(parent), or 1.5U_{eq}(C) for methyl H atoms. Riding methyl H atoms were allowed to rotate freely during refinement using the AFIX 137 command of *SHELXL97* (Sheldrick, 1997). Examination of the refined structure using *PLATON* (Spek, 2003) revealed the presence of void spaces having a total volume of 20.9 Å^3 (0.9%) per unit cell.

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).

Table 1
Selected geometric parameters (Å, °).

O3—C32	1.230 (2)	N4—C5	1.371 (2)
N1—C5	1.308 (2)	N4—C41	1.443 (2)
N2—C3	1.308 (2)	C5—C51	1.470 (2)
N4—C3	1.369 (2)	C31—C32	1.513 (2)
C3—S3—C31	98.69 (8)	N1—C5—N4	109.51 (15)
C5—N1—N2	108.27 (13)	N4—C5—C51	126.68 (15)
C3—N2—N1	106.72 (14)	N1—C5—C51	123.79 (15)
C32—N3—C33	123.56 (16)	C32—C31—S3	107.43 (13)
C3—N4—C5	104.98 (14)	O3—C32—N3	124.11 (17)
N2—C3—N4	110.52 (15)	O3—C32—C31	120.80 (17)
N2—C3—S3	128.92 (14)	N3—C32—C31	115.09 (16)
N4—C3—S3	120.55 (12)		
C3—S3—C31—C32	176.56 (15)	C33—N3—C32—C31	177.03 (17)
C33—N3—C32—O3	−2.9 (3)	S3—C31—C32—O3	−16.0 (3)

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

D—H···A	D—H	H···A	D···A	D—H···A
O1*W*—H11*W*···O2*W*^{i}	0.87 (3)	1.90 (3)	2.763 (3)	172 (3)
N3—H3···O1*W*	0.86	1.97	2.827 (2)	171
O2*W*—H22*W*···N2^{i}	0.86 (3)	2.03 (3)	2.873 (2)	167 (3)
O2*W*—H21*W*···N1	0.83 (4)	2.01 (4)	2.819 (2)	165 (3)
O1*W*—H12*W*···O3^{ii}	0.84 (2)	2.09 (2)	2.905 (3)	164 (5)

Symmetry codes: (i) $-x+1, -y, -z+1$; (ii) $x, y-1, z$.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SF3017). Services for accessing these data are described at the back of the journal.

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