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ORIGINAL PAPER

Synthesis and Crystal Structure of Compound 1-Phenyl-2-(1H-1,2,4-triazolo-yl)-3-phenyl-propen-1-one and 1-Diphenyl-3-(1,2,4-triazolo-yl)-1H,4H-1,5-benzothiazepine

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Abstract The crystal structures of the compounds 1-phenyl-2-(1H-1,2,4-triazolo-yl)-3-phenyl-propen-1-one (**2**), and 2,4-diphenyl-3-(1,2,4-triazolo-yl)-1H,4H-1,5-benzothiazepine (**3**) were obtained by single crystal X-ray diffraction. Compound **2** crystallizes in the triclinic system with space group $P-1$, $a = 8.5553(17)$ Å, $b = 9.6229(19)$ Å, $c = 9.924(2)$ Å, $\alpha = 106.16(3)°$, $\beta = 108.03(3)°$, $\gamma = 105.14(3)°$, $V = 690.1(2)$ Å^3, $Z = 2$. The compound **3** crystallizes in the orthorhombic system with space group Pbca, $a = 12.904(3)$ Å, $b = 15.864(3)$ Å, $c = 19.140(4)$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$, $V = 3918.3(14)$ Å^3, $Z = 8$. H-bonds and π–π stacking are the main non-bonding interactions in the molecular structure. Details of the synthesis, structures, and spectroscopic properties of the two compounds are discussed.

Keywords 1,2,4-triazole · Benzothiazepine · Crystal structure

Introduction

Since biological and pharmacological activities have been noted for great number of heterocyclic aromatic cycles [1, 2], much attention has been paid to the synthesis of the heterocyclic compounds incorporating one or more seven membered rings [3]. Benzothiazepine compounds have confirmed known, bioactivity bioactivities, and many papers discussing the synthesis, structure–property relationships and the applications of such compounds have been published [4]. It has been reported that compounds bearing benzothiazepine moieties have shown anti-HIV [5], anti-hypertensive [6], anti-depressant [7], and anti-bacterial activity [8]. For instance, the drug diltiazem, which elicits anti-hypertensive effect, contains benzothiazepine as its structural subunit [9].

In addition, 1H-1,2,4-triazole derivatives represent an interesting class of heterocycles. Compounds containing 1H-1,2,4-triazole moiety have received considerable attention among medicinal chemists because molecules with these structural features have been found to show a broad range of potent biological activities, such as anti-hypertensive, antifungal [10] and antibacterial [11]. Compounds containing the 1H-1,2,4-triazole ring system are also well known to be highly active as fungicides [12], especially on the Basidiomycete and Ascomycete groups of fungi. In view of these facts and in order to search for new fused heterocyclic compounds with improved bioactivity, the present investigation deals with the synthesis of novel benzothiazepine system bearing 1,2,4-triazole moiety, as outlined in Scheme 1**,** which might have useful biological and therapeutic activities. The crystal structures of **2** and **3** determined by single-crystal X-ray diffraction are reported.

Experimental

Reagents and Apparatus

All reagents were of commercial availability. Reactions were monitored by thin-layer chromatography (TLC).

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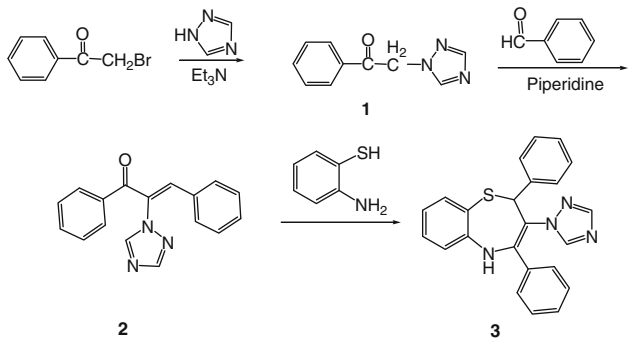

Scheme 1 Synthetic process of the title compound

Melting points were measured on a mettler FP-5 capillary melting point apparatus and were uncorrected. Elemental analyses were performed on a Perkin-Elmer 2400 elemental analyzer. The IR spectra were determined using potassium bromide pellets on a Bruker Equinox 55 FT-IR spectrophotometer. The ^{1}HNMR spectra were recorded on a Varian Inova-400 spectrophotometer using TMS as an internal standard. EI-ms spectra were recorded with an Agilent 5975 apparatus. X-ray crystal structures were obtained using R-AXIS SPIDER X-ray diffraction.

The Synthesis of α-Phenyl-2-(1H-1,2,4-triazolo-yl) ethanone **1**

Intermediate **1** was prepared according to the reported method [13].

Compound **1:** White crystals, Yield 65.92%, m.p.121.4–122.4 °C.

The Synthesis of 1-Phenyl-2-(1H-1,2,4-triazolo-yl)-3-phenyl-prop-en-1-one 2

The procedure according to the literature [14].A solution of benzaldehyde (0.02 mol), α-aryl-2-(1H-1,2,4-triazolo-1yl) ethanone(0.02 mol), and piperidine (0.5 mL) in toluene (80 mL) was refluxed for 7 hunder nitrogen atmosphere and during that time, the generated water was removed with a

Table 1 Summary of structure determination of compounds **2** and **3**

CCDC deposition number	762788	762789
Formula	C17H15N3O	C23H17N4S
Formula weight	277.32	381.47
Crystal size(mm)	0.690 × 0.580 × 0.270	0.691 × 0.374 × 0.060
Crystal colour	Colorless	Colorless
Crystal system	Triclinic	Orthorhombic
Space group	$P-1$	Pbca
Unit cell dimensions [A°] and angles (°)		
a (Å)	8.5553 (17)	12.904 (3)
b (Å)	9.6229 (19)	15.864 (3)
c (Å)	9.6229 (19)	19.140 (4)
α (°)	9.6229 (19)	90
β (°)	9.6229 (19)	90
γ (°)	9.6229 (19)	90
Volume (Å^3)	690.1 (2)	3918.3 (14)
Z	2	8
Density (calculated) (Mg/m^3)	1.335	1.293
Absorption coefficient (μ)	0.086	0.181
F(000)	292	1592
Theta range for data collection	3.57–25.03°	3.16–25.03°
Index ranges	$-10 \le h \le 10$, $-11 \le k \le 9$, $-11 \le l \le 11$	$-15 \le h \le 15$, $-18 \le k \le 18$, $-22 \le l \le 22$
Reflections collected/unique	5425/2423	27623/3461
R(int)	0.0425	0.0921
Absorption correction T(max), T(min)	0.9769; 0.9428	0.9513; 0.9085
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Goodness of fit ref	1.100	1.017
Final R indices [$I > 2.0\ \sigma(I)$]	$R1 = 0.0507$, $wR2 = 0.1511$	$R1 = 0.0625$, $wR2 = 0.1513$
R indices(all data)	$R1 = 0.0574$, $wR2 = 0.1578$	$R1 = 0.1124$, $wR2 = 0.1770$
Largest diff. Pesk and hole	0.162 and −0.512 e Å^{-3}	0.309 and −0.339 e Å^{-3}

Dean-Stark trap. After completion of the reaction, the solvent was evaporated off at reduced pressure. The residue was purified by silica gel column chromatography with ethyl acetate/light petroleum (V:V = 1:1). A colorless crystal of compound **2** was cultured from ethyl acetate and petroleum.

Compound **2**: colorless crystals, Yield 76.2%; m.p. 129.8–130.6 °C, ^{1}HNMR($CDCl_3$, 400 MHz) δ: 8.192(s, 1H, Triazole-H), 8.152(s, 1H, Triazole-H), 7.838(s, 1H, C=CH), 7.820 ~ 6.914 (m, 10H, Ar–H); IR(KBr) υ: 3112, 3062 (Ar–H), 1647(C=O), 1499, 1447, 1419(C=N, C=C) cm^{-1}; MS(EI) m/z(100%):275(M^+), 247, 178, 146, 116, 105(100%), 77.

Anal.Calcd. for $C_{17}H_{15}N_3O$: C, 74.17; H, 4.76; N, 15.26; O, 5.81; Found C, 15.28; H, 4.878; N, 15.28.

The Synthesis of Compound 2,4-Diphenyl-3-(1,2,4-triazolo-yl)-1H,4H-1,5-benzothiazepine 3

To a solution of chalcone (4.0 mmol) in methanol (60 mL) was added *o*-aminothiophenol (4.0 mmol). The reaction mixture was kept under stirring at room temperature for 0.5 h.The mixture was heated under reflux for 20–30 min and then added CF_3COOH (1.2 mL). The refluxing was continued for 5–6 h. About half of the solvent was distilled off and the resulting mixture was allowed to stand at room temperature. The crystalline solid product thus separated by filtered, washed by cold methanol and dried. The crude compound was recrystallized from methanol.

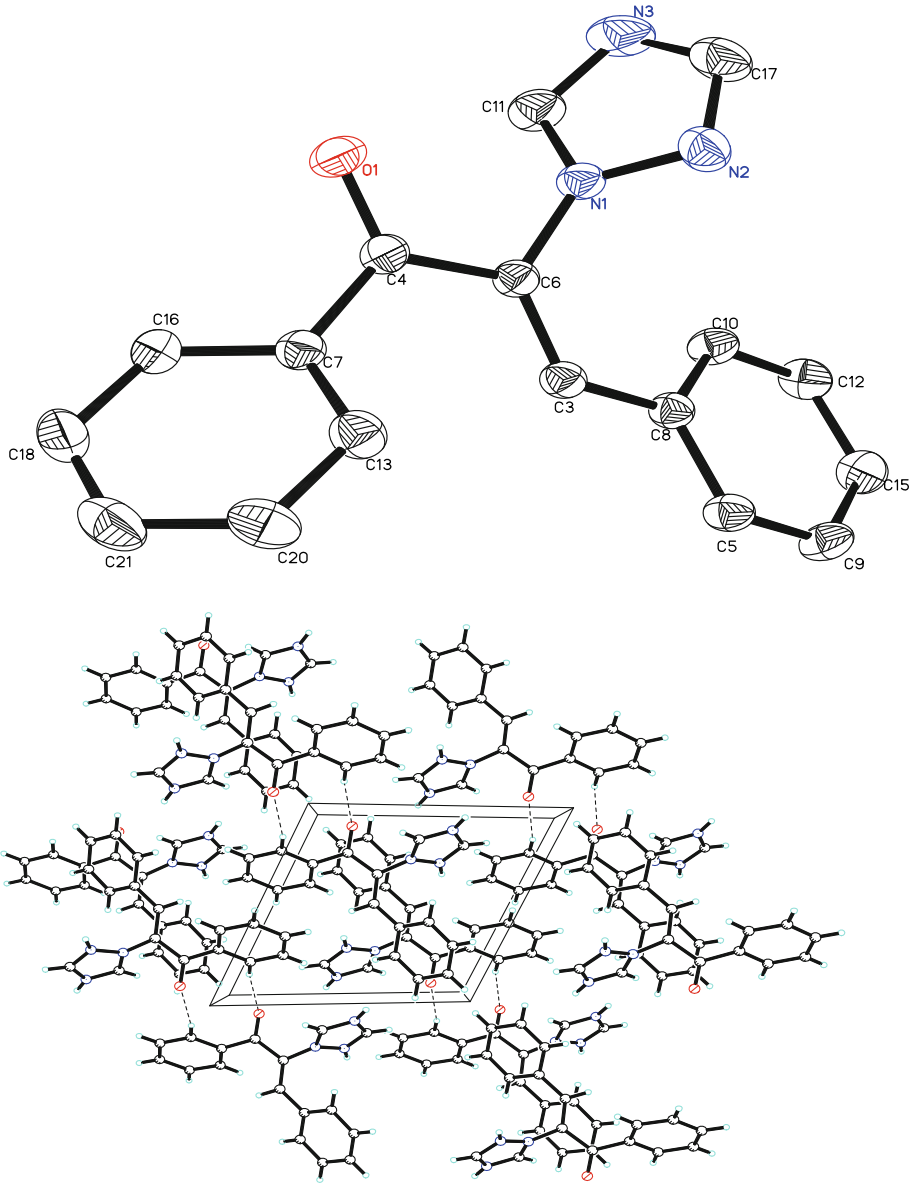

Fig. 1 **a** Molecular structure of **2**. **b** Packing diagram of **2**

Compound **3**: Colorless crystals, Yield 72.7%. m.p.209–211 °C. ^{1}HNMR ($CDCl_3$, 400 MHz) δ: 8.00–6.70 (m, 16H), 6.10(m, 0.5H), 5.88–5.85 (d, $J = 12.0$ Hz, 0.5H), 5.55–5.52 (d, $J = 12.0$ Hz, 0.5H), 5.43 (m, 0.5H); IR (KBr): 3244, 3050, 1672, 1587, 1475, 699 cm^{-1}; MS (70 eV) m/z (%): 382 (M^+), 313, 212 (100), 109, 65, 51;

Anal.Calcd. for $C_{23}H_{17}N_4S$: C, 72.22; H, 4.74; N, 14.65; Found C, 72.04; H, 4.817; N, 14.57;

X-ray Crystallography

The X-ray diffraction data of **2** and **3** were collected on crystals of approximate dimensions 0.690 × 0.580 × 0.270 mm and 0.691 × 0.374 × 0.060 mm respectively using a Rigaku *R*-axis Spider diffractometer with graphite-monochromated MoKa radiation at 293(2) K. All calculations were carried out with the aid of the SHELXS-97 [15]

Table 2 Selected bond lengths (Å), bond angles (°), and torsion angles (°) for compound **2** and **3**

Compound **2** [bond lengths (Å)]			
N(1)–C(11)	1.339(2)	C(3)–C(8)	1.471(2)
N(1)–N(2)	1.3517(18)	C(4)–C(6)	1.491(2)
N(1)–C(6)	1.4340(18)	C(4)–C(7)	1.495(2)
O(1)–C(4)	1.2172(18)	N(2)–C(17)	1.304(2)
C(3)–C(6)	1.335(2)	C(11)–N(3)	1.304(2)
N(3)–C(17)	1.343(3)	C(8)–C(10)	1.399(2)
Compound **3** [bond lengths (Å)]			
S(1)–C(6)	1.756(4)	N(1)–C(5)	1.417(4)
S(1)–C(7)	1.835(3)	N(3)–C(15)	1.318(4)
N(2)–C(16)	1.321(4)	N(4)–C(16)	1.315(4)
N(2)–N(3)	1.367(3)	N(4)–C(15)	1.339(4)
N(2)–C(8)	1.441(4)	C(7)–C(8)	1.502(4)
N(1)–C(23)	1.394(4)	C(8)–C(23)	1.339(4)
C(7)–C(9)	1.520(4)	C(11)–C(12)	1.373(6)
Compound **2** [bond angles (°)]			
C(11)–N(1)–N(2)	109.21(14)	O(1)–C(4)–C(6)	119.19(15)
C(11)–N(1)–C(6)	129.15(14)	O(1)–C(4)–C(7)	119.53(14)
N(2)–N(1)–C(6)	121.56(13)	C(6)–C(4)–C(7)	121.23(14)
C(6)–C(3)–C(8)	130.25(14)	C(3)–C(6)–N(1)	121.78(14)
C(3)–C(6)–C(4)	124.83(14)	N(1)–C(6)–C(4)	113.32(13)
C(11)–N(3)–C(17)	103.24(16)	C(17)–N(2)–N(1)	102.52(15)
N(2)–C(17)–N(3	114.94(17)	N(3)–C(11)–N(1)	110.07(17)
Compound **3** [bond angles (°)]			
C(6)–S(1)–C(7)	101.60(15)	C(8)–C(7)–C(9)	115.5(3)
C(23)–N(1)–C(5)	128.5(3)	C(8)–C(7)–S(1)	113.3(2)
C(6)–C(5)–N(1)	124.2(3)	C(9)–C(7)–S(1)	111.7(2)
C(5)–C(6)–S(1)	121.5(3)	C(23)–C(8)–N(2)	116.5(3)
C(23)–C(8)–C(7)	131.3(3)	N(2)–C(8)–C(7)	112.1(2)
C(8)–C(23)–N(1)	128.1(3)	C(8)–C(23)–C(17)	121.7(3)
Compound **2** [torsion angles (°)]			
C(11)–N(1)–C(6)–C(3)	116.8(2)	O(1)–C(4)–C(6)–N(1)	9.2(2)
C(11)–N(1)–C(6)–C(4)	−60.2(2)	C(7)–C(4)–C(6)–C(3)	9.6(2)
O(1)–C(4)–C(6)–C(3)	−167.72(15)	C(7)–C(4)–C(6)–N(1)	−173.40(12)
Compound **3** [torsion angles (°)]			
C(23)–N(1)–C(5)–C(6)	52.8(5)	C(6)–S(1)–C(7)–C(8)	69.5(2)
N(1)–C(5)–C(6)–S(1)	−2.3(4)	S(1)–C(7)–C(8)–C(23)	−28.8(4)
C(7)–S(1)–C(6)–C(5)	−59.6(3)	C(7)–C(8)–C(23)–N(1)	−4.7(6)
C(5)–N(1)–C(23)–C(8)	−24.8(5)	S(1)–C(7)–C(8)–N(2)	151.0(2)

Table 3

Intermolecular interactions (Å) in the compound **2**				
D–H···A	D–H	H···A	D···A	D–H···A
C(10)–H(10A)···N(1)	0.93	2.49	3.029(2)	117
C(16)–H(16A)···O(1)[a]	0.93	2.46	3.360(2)	164
Intermolecular interactions (Å) in the compound **3**				
D–H···A	D–H	H···A	D···A	D–H···A
N(1)–H(1A)···N(4)[b]	0.86	2.31	3.118(4)	156
C(10)–H(10A)···Cg(2)[c]	0.93	2.93	3.651(4)	136

[a] $1 - x, 2 - y, 2 - z$. [b] $5/2 - x, 1/2 + y, z$. [c] $2 - x, -1/2 + y, 1/2 - z$; Cg(2) is the center of gravity of ring C1–C6

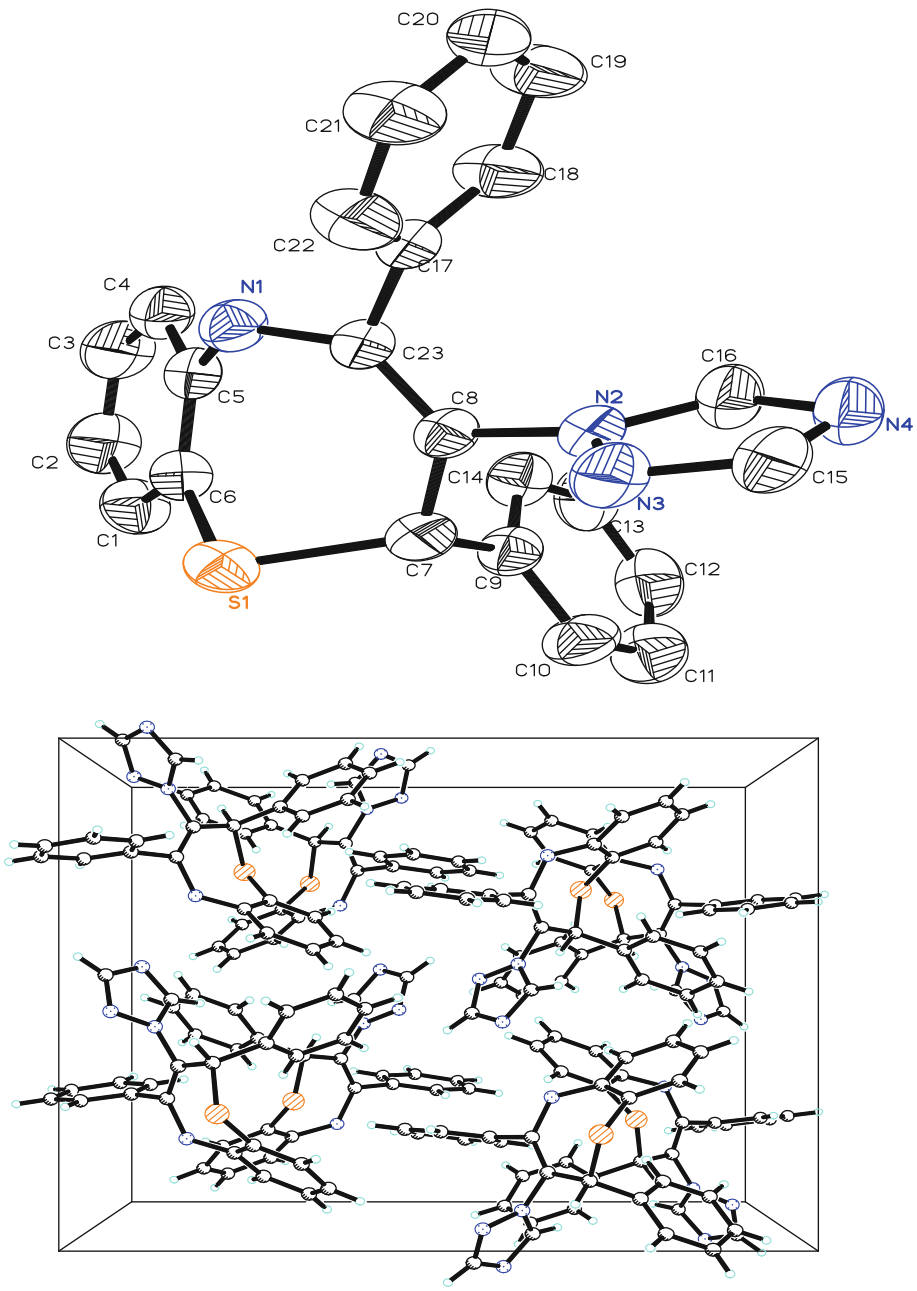

Fig. 2 **a** Molecular structure of **3**. **b** Packing diagram of **3**

and PLATON [16], programs and refinements on F^2 were performed by full-matrix least-squares techniques with equivalent isotropic displacement parameters for the non-hydrogen atoms. A summary of the crystallographic data and details of the structure refinements are listed in Table 1.

The X-ray data for compounds **2** and **3** respectively have been deposited with Cambridge Crystallographic Data Centre as CCDC 762788 and CCDC 762789. These data can be obtained free of charge from Cambridge Crystallographic Data Centre (CCDC)12 Union Road, Cambridge CB2 1EZ, UK; phone: +44(0)1223-336408;fax: +44(0)1223-336033; email: deposit@ccdc.cam.ac.uk; http://www.ccdc.cam.ac.uk.

Results and Discussion

The molecular structure of the compound **2** is exhibited in Fig. 1. The dihedral angle between the benzene ring plane (C7–C16) and the plane (O1–C4–C6–C3) is 49.3°, the plane (C8–C10) and the plane(O1–C4–C6–C3) is157.2°, while the triazole ring plane and the plane (O1–C4–C6–C3) is 61.5°. The bond length in this compound of C(3)–C(6), 1.335(2) Å, O(1)–C(4), 1.2172(18) Å, C(4)–C(6), 1.491(2) Å, C(4)–C(7), 1.495(2) Å and N(1)–C(6), 1.4340(18) Å, indicates it is a double bond between C(3) and C(6), as well as O(1) and C(4) (Table 2). Besides, the data of above suggests that the length of these two double bonds are much longer than the corresponding length of the normal double bond, and also demonstrates that the length of these three single bonds are a little shorter than the corresponding length of the normal single bond. In conclusion, there is, predicatively, a conjugate system in this molecule. In this molecule, the packing in this compound is held together by C–H···N, C–H···O hydrogen bonds and three C–H···Cg (π-Ring). In addition, existence weak π–π stacking interactions between triazole and benzene ring (C7–C16) of intermolecules are observed. The distance between the centroids of interacting rings is Cg(1)···Cg(1) = 3.9237(15) Å $(1 - x, 2 - y, 1 - z)$, Cg(3)···Cg(3) = 3.9035(14) Å $(1 - x, 1 - y, 2 - z)$ (Table 3). [Cg(1) = center of gravity of the triazole ring; Cg(3) = center of gravity of the benzene ring (C7–C16)].

The structure of the crystal **3** is displayed in Fig. 2. There is a seven-membered ring in the molecule. 1,5-Benzothiazepine ring is characterized by the endocyclic torsion angles (enumerated clockwise and starting with N(1)–C(5)–C(6)–S(1)): −2.3(4), 52.8 (5), −24.8(5), −4.7(6), −28.8(4), 69.5(2), −59.6(3) (Table 2). The four atoms of C(5), C(6), C(7) and C(8) are closely coplanar, while S(1), N(1) and C(23) are above the plane, with their deviations being 0.5905, 0.2790 and 0.1674 Å, respectively. Therefore, according to the data, the seven-membered ring adopts a boat-like conformation. The bond length in this ring of C(23)–C(8), 1.339(4) Å and C(7)–C(8), 1.502(4) Å, indicates it is a double bond between C(23) and C(8) (Table 2).

The dihedral angle between the benzene ring planes (C1–C6) and the thiazepine ring planes (N1–C5–C6–S1–C7–C8–C23) is 29.8°, while the angle is 67.8° between the benzene ring plane (C1–C6) and triazole ring plane. In this molecule, the packing in compound **3** is held together by a N–H···N hydrogen bond and a C–H···Cg (π-Ring). In addition, weak π–π stacking interactions are observed between triazole ring and benzene ring (C17–C22). The distance between the centroids of interacting rings is Cg(1)···Cg(4) = 4.104(2) Å (x, y, z) (Table 3). [Cg(1) = center of gravity of the triazole ring; Cg(4) = center of gravity of the benzene ring (C17–C22)]. The existence of H-bonding and weak π–π stacking interaction in the molecular structure is great helpful to stabilize the crystal packing.

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