# Synthesis and Structure Characterization of New [1,2,4]Triazolo[5,4-*d*][1,5]benzothiazepine Derivatives Through 1,3-Dipolar Cycloaddition Reaction

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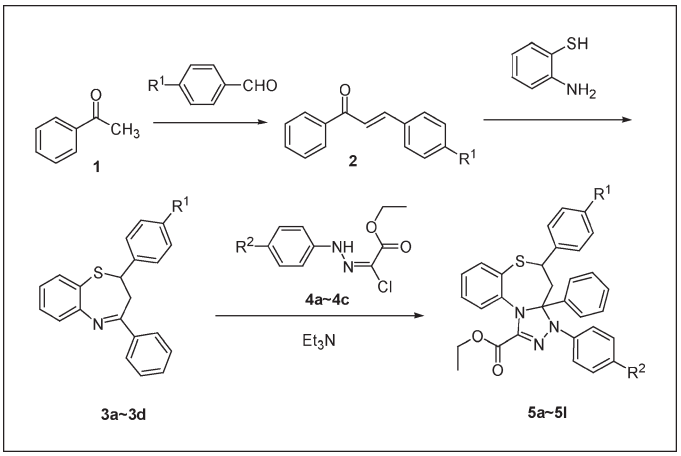


Reaction of 1,5-benzothiazepines **3**, obtained from chalcones **2** and *o*-aminobenzenthiol, with the (phenylhydrazino) chloromethylenecarboxylates **4** in the presence of $Et_3N$ leads to a series of new [1,2,4]triazolo[5,4-*d*][1,5]benzothiazepine derivatives **5**. Their structures were established using spectroscopic methods and that of compound **5d** was confirmed using X-ray diffraction analysis.

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## INTRODUCTION

The synthesis of benzothiazepine derivatives has attracted considerable attention of organic and medicinal chemists because of their broad spectrum of biological activities, such as cardiovascular modulator, coronary vasodilators, ACE inhibitors, anti-HIV, antihypertensive, antidepressant, and antibacterial and anticancer activity [1,2]. Recently, progress has been made into fix an additional heterocycle on the heptatomic nucleus of 1,5-benzothiazepine for the preparation of fused ring compounds. The presence of the conformational preferences of the seven-membered ring is possibly correlated with biological activity, and the fusion of a heterocyclic nucleus to the thiazepine system could induced an increase of the ring inversion barrier and consequently modify the activity profile [3,4].

Furthermore, 1,2,4-triazole derivatives have been reported to exhibit antifungal, anti-inflammatory, and antimicrobial activity [5]. For example, itraconazole and fluconazole are clinically used as antimicrobial drugs [6,7]. In addition, a 1,2,4-triazole is a key subunit in the structure of a potential anticancer and anti-HIV agents [8,9].

Inspired by the biological profile of 1,5-benzothiazepine and 1,2,4-triazole derivatives and in continuation of our interest in the synthesis of new 1,5-benzothiazepine derivatives [10,11], we reported herein the reaction of 1,5-benzothiazepines **3** with the nitrileimines **4** through 1,3-dipolar cycloaddition to afford a new series of [1,2,4]triazolo[5,4-*d*][1,5]benzothiazepine derivatives **5**. (Table 1). It was thought worthwhile to synthesize the title compounds with both active pharmacophores in a single molecular framework, which may have potential biological and medical applications.

## RESULTS AND DISCUSSION

The synthetic route used is shown in Scheme 1. The chalcones **2** were readily prepared by condensation of aryl aldehydes with acetophenone. The reaction of **2** with *o*-aminobenzenthiol, in methanol in the presence of acetic acid at reflux temperature for 4 h, to get the required 2,4-diaryl-2,3-dihydro-1,5-benzothiazepines **3** in good to excellent yields. 1,3-Dipolar cycloaddition reaction of **3** with nitrileimines, generated *in situ* from

**Table 1**

Physical and analytical data of compounds **5**.

| Entry | Comp. | $R^1$ | $R^2$ | mp (°C) | Yield (%) | Molecular formula | Analysis % (Calcd./Found) C | H | N |
|---|---|---|---|---|---|---|---|---|---|
| 1 | **5a** | H | H | 237–238 | 25 | $C_{31}H_{27}N_3O_2S$ | 73.64 | 5.38 | 8.31 |
| | | | | | | | 73.61 | 5.40 | 8.33 |
| 2 | **5b** | H | Cl | 199–200 | 31 | $C_{31}H_{26}ClN_3O_2S$ | 68.94 | 4.85 | 7.78 |
| | | | | | | | 68.92 | 4.86 | 7.80 |
| 3 | **5c** | H | $CH_3$ | 189–190 | 30 | $C_{32}H_{29}N_3O_2S$ | 73.96 | 5.62 | 8.09 |
| | | | | | | | 73.98 | 5.61 | 8.07 |
| 4 | **5d** | Cl | H | 217–218 | 26 | $C_{31}H_{26}ClN_3O_2S$ | 68.94 | 4.85 | 7.78 |
| | | | | | | | 68.95 | 4.82 | 7.79 |
| 5 | **5e** | Cl | Cl | 254–255 | 32 | $C_{31}H_{25}Cl_2N_3O_2S$ | 64.81 | 4.39 | 7.31 |
| | | | | | | | 64.79 | 4.40 | 7.34 |
| 6 | **5f** | Cl | $CH_3$ | 215–216 | 29 | $C_{32}H_{28}ClN_3O_2S$ | 69.36 | 5.09 | 7.58 |
| | | | | | | | 69.32 | 5.11 | 7.59 |
| 7 | **5g** | $OCH_3$ | H | 178–179 | 21 | $C_{32}H_{29}N_3O_3S$ | 71.75 | 5.46 | 7.84 |
| | | | | | | | 71.77 | 5.45 | 7.82 |
| 8 | **5h** | $OCH_3$ | Cl | 244–245 | 27 | $C_{32}H_{28}ClN_3O_3S$ | 67.42 | 4.95 | 7.37 |
| | | | | | | | 67.40 | 4.96 | 7.39 |
| 9 | **5i** | $OCH_3$ | $CH_3$ | 221–222 | 33 | $C_{33}H_{31}N_3O_3S$ | 72.11 | 5.68 | 7.64 |
| | | | | | | | 72.10 | 5.67 | 7.67 |
| 10 | **5j** | $NO_2$ | H | 179–180 | 22 | $C_{31}H_{26}N_4O_4S$ | 67.62 | 4.76 | 10.18 |
| | | | | | | | 67.61 | 4.75 | 10.21 |
| 11 | **5k** | $NO_2$ | Cl | 230–231 | 31 | $C_{31}H_{25}ClN_4O_4S$ | 63.64 | 4.31 | 9.58 |
| | | | | | | | 63.66 | 4.30 | 9.55 |
| 12 | **5l** | $NO_2$ | $CH_3$ | 170–171 | 28 | $C_{32}H_{28}N_4O_4S$ | 68.07 | 5.00 | 9.92 |
| | | | | | | | 68.08 | 4.99 | 9.94 |

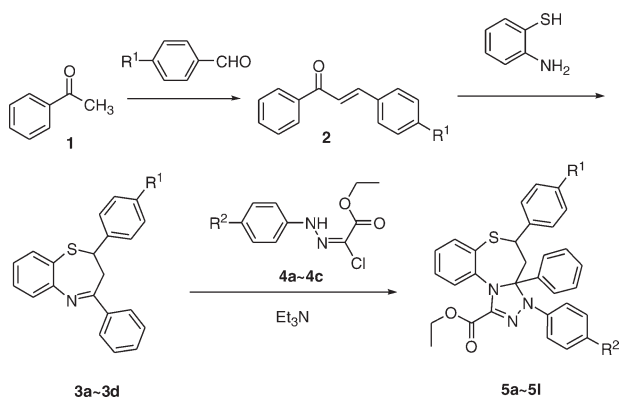
(phenylhydrazino) chloromethylenecarboxylates **4** in the presence of $Et_3N$, to yield the target compounds **5a–5l**.

The structures of the title compounds have been characterized by IR, $^1$H-NMR, MS, and elemental analysis. For example, the infrared spectra of these compounds showed a characteristic absorption band at 1730 $cm^{-1}$ because of the presence of the ester-carbonyl group. Also, their $^1$H-NMR spectra revealed multiplet between δ 7.60 and 6.60 ppm because of the aromatic protons, the signal for ethoxycarbonyl $CH_2$ and $CH_3$ appeared at δ 4.19–4.21 ppm and 1.19–1.20 ppm, respectively, and three distinct double doublets in the ABX system (a CH proton and tow anisochronous protons of a $CH_2$) appeared at δ 2.65–4.56 ppm, as has been observed in 2,3-dihydro-1,5-benaothiazepine. In MS spectra, the compounds exhibit a stable molecular ion, and the base peak is the [M-(EtOCO+$R_1C_6H_5CH{=}CH_2$)] ion in all the compounds analyzed. The relative abundance of the main fragmentation in the compounds has some common features. The most important ions are as follows: $M^+$, [M-77], [M-($R_1C_6H_5CH{=}CH_2$)], and [M-(EtO-CO+$R_1C_6H_5CH{=}CH_2$)]. The main fragmentation was consistent with the assigned structures.

Subsequently, the absolute configuration of the reaction products **5** has been further elucidated from X-ray diffraction analysis of a single crystal. The general view of the molecule **5d** and its principal characteristics are given in Figure 1. The higher occupancy in the three-dimensional packing arrangement is shown in Figure 2. The crystal data and structure refinement of **5d** are listed in Table 2. Selected bond distances and angles of **5d** are tabulated in Table 3.

Figure 1 is the stereostructure of compound **5d**. There is a five-membered ring in the molecule, resulting from the cycloaddition reaction. All atoms [N(1), C(7), N(2), N(3), and C(17)] in the ring are nearly coplanar with similar bond angles [N(1)—C(7)—N(2) 114.71(19)°, C(7)—N(2)—N(3) 106.34(17)°, N(2)—N(3)—C(17) 111.98(15)°, N(3)—C(17)—N(1) 97.98(15)°, and

**Scheme 1**



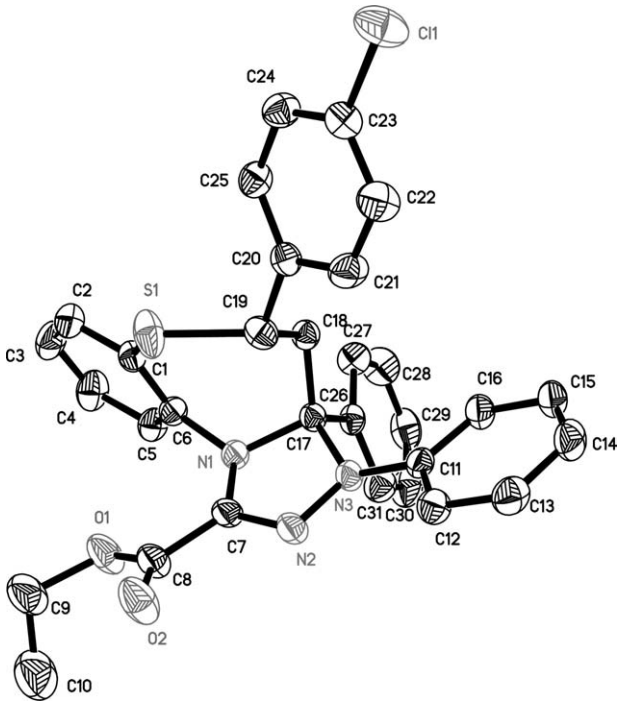



**Figure 1.** The molecular structure of the title compound **5d**.

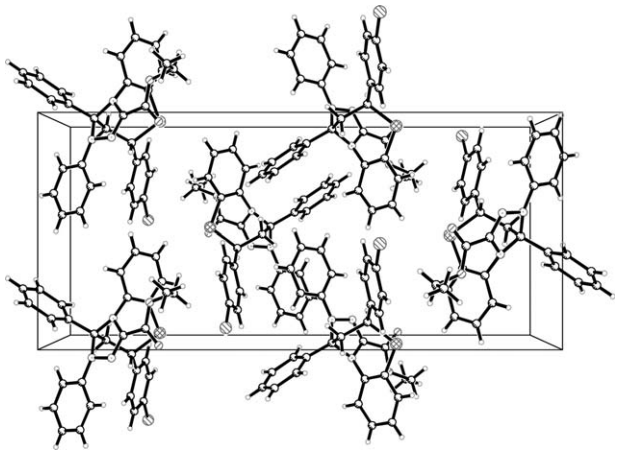


**Figure 2.** Packing of molecules in a unit cell of **5d**.

C(17)—N(1)—C(7) 107.28(16)°], indicating the ring is stable. The five-membered ring is characterized by the endocyclic torsion angles [enumerated clockwise and starting with C(7)—N(2)—N(3)—C(17)]: 7.5(3)°, 1.3(3)°, −9.4(3)°, 12.1(2)°, and −12.1(2)°. The five-membered ring plane adopts an envelope conformation with atom C(17) deviating from the plane defined by N(3), N(2), C(7), and N(1) of 0.0737 Å. The bond length of N(2)—C(7), 1.281(3) Å, indicates that it is a double bond.

There is also a seven-membered ring in the molecule. 1,5-Benzothiazepine ring is characterized by the endocyclic torsion angles (enumerated clockwise and starting with S(1)—C(1)—C(6)—N(1)): −1.9(3)°, 41.8(2)°, 11.2(2)°, −82.5(2)°, 56.0(2)°, 43.8(2)°, and −76.0(3)°. N(1), S(1), C(17), and C(19) are coplanar, whereas C(1), C(6), and C(18) are all below the plane, with their deviations being −0.4046, −0.2090, and −0.6481 Å. Therefore, the seven-membered ring adopts a boat-like conformation.

CCDC-769643 (for **5d**) contains the supplementary crystallographic data for this article. These data can be obtained free of charge at www.ccdc.cam.ac.uk/const/retrieving.html.

In conclusion, we have achieved an efficient one-step synthesis of new [1,2,4]triazolo[5,4-*d*][1,5]benzothiazepines **5a–5l** by way of highly regioselective 1,3-dipolar cycloaddition of the (phenylhydrazino) chloromethylenecarboxylates **4a–4c** to 2,4-diary-2,3-dihydro-1,5-benzothiazepines **3a–3d**.

## EXPERIMENTAL

All reagents were of commercial availability. Reactions were monitored by thin-layer chromatography (TLC). Melting points were measured on a mettler FP-5 capillary melting point

**Table 2**

Crystal data and structure refinement for compound **5d**.

| | | | |
|---|---|---|---|
| Empirical Formula | $C_{31}H_{26}ClN_3O_2S$ | $V$ (Å$^3$) | 2643.3(3) |
| Formula weight | 540.06 | $Z$ | 4 |
| Temperature | 293(2) K | $D_c$ (mg/m$^3$) | 1.357 |
| Wavelength | 0.71073 A | Crystal size (mm) | 0.72 × 0.45 × 0.10 |
| Crystal system | Orthorhombic | θ range (°) | 3.10–27.48 |
| Space group | $P2(1)2(1)2(1)$ | μ (mm$^{-1}$) | 0.258 |
| $a$ (Å) | 9.7747(7) | Reflections collected | 26123 |
| $b$ (Å) | 11.0448(8) | Independent reflection | 6060 [$R$(int) = 0.0353] |
| $c$ (Å) | 24.4840(17) | Data/restraints/parameters | 6060/0/344 |
| α (°) | 90 | Final $R$ indices [$I > 2\sigma(I)$] | $R_1 = 0.0445$, $wR_2 = 0.1125$ |
| β (°) | 90 | $R$ indices (all data) | $R_1 = 0.0628$, $wR_2 = 0.1309$ |
| γ (°) | 90 | | |

**Table 3**

Selected bond lengths (Å) and angles (°) of compounds **5d**.

| | | | |
|---|---|---|---|
| N(1)—C(7) | 1.388(3) | C(1)—S(1)—C(19) | 107.30(10) |
| N(2)—C(7) | 1.281(3) | C(7)—N(1)—C(6) | 124.45(18) |
| N(2)—N(3) | 1.392(2) | C(7)—N(1)—C(17) | 107.28(16) |
| N(1)—C(17) | 1.495(3) | N(2)—N(3)—C(11) | 116.82(17) |
| N(3)—C(17) | 1.493(3) | N(2)—C(7)—N(1) | 114.71(19) |
| O(1)—C(8) | 1.320(3) | O(2)—C(8)—C(7) | 123.4(2) |
| O(2)—C(8) | 1.206(3) | C(7)—N(2)—N(3) | 106.34(17) |
| C(7)—C(8) | 1.485(3) | O(2)—C(8)—O(1) | 124.7(2) |
| C(17)—C(26) | 1.322(3) | C(17)—C(18)—C(19) | 112.36(18) |

apparatus and were uncorrected. Elemental analyses were performed on a Perkin-Elmer 2400 elemental analyzer. The IR spectra were determined as potassium bromide pellet on a Bruker Equinox 55 FTIR spectrophotometer. The $^1$H-NMR 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 structure was obtained using R-AXIS SPIDER X-ray diffraction. Chalcones **2** were obtained according to the known procedure [12]. The (phenylhydrazino) chloromethylenecarboxylates **4a–4c** (**4a**: $R^2$ = H; **4b**: $R^2$ = Cl; **4c**: $R^2$ = $CH_3$) were obtained according to the known procedure [13].

**General procedure for the preparation of the 2,4-diaryl-2,3-dihydro-1,5-benzothiazepines (3a–3d).** Chalcones **2** (6 mmol) and *o*-aminobenzenthiol (6 mmol) were dissolved in 25 mL hot methanol [14]. After the mixture had cooled to room temperature and piperidine (five drops) was added, yellow solid appeared in 0.5 h, then a little methanol was added and the slurry heated until all material dissolved. Glacial acetic acid (2 mL) then was added, and the mixture was stirred under reflux for 4 h and allowed to stand overnight at a room temperature. The yellow precipitate formed was filtered, dried, and crystallized from anhydrous ethanol and benzene to give **3** as yellow crystals. Purity of the compounds was checked by TLC.

**3a**: Yield 86%, mp 113–115°C (lit. [14], 114–115°C), yellow crystals.

**3b**: Yield 72%, mp 137–139°C (lit. [15], 128°C), yellow crystals.

**3c**: Yield 81%, mp 128–130°C (lit. [15], 127–128°C), yellow crystals.

**3d**: Yield 43.2%, mp 201–202°C (lit. [16], 140°C; lit. [17], 185°C), yellow crystals.

**General procedure for the preparation of the ethyl 3a,4-dihydro-3a-phenyl-3,5-diaryl-5H-[1,2,4]triazolo[5,4-*d*][1,5] benzothiazepine-1-carboxylate (5a-5l).** To a stirred solution of 1,5-benzothiazepine derivatives **3** (1 mmol) and the (phenylhydrazino) chloromethylenecarboxylates **4** (1.5 mmol) in $CH_2Cl_2$ (20 mL), a solution of triethylamine (0.5 mL) in the same solvent (5 mL) was added dropwise over a few minutes. The reaction mixture was kept under stirring at room temperature for 3 days. After the removal of the solvent under reduced pressure, ethyl acetate was added to the residue and the triethylamine hydrochloride was filtered. The solvent was then evaporated off and the residue subjected to silica gel column chromatography with ethyl acetate/light petroleum (V:V = 1:8) as an eluent. A series of compounds **5** were cultured from ethyl acetate and light petroleum.

***Ethyl 3a,4-dihydro-3,3a,5-triphenyl-5H-[1,2,4]triazolo[5,4-d][1,5]benzothiazepine-1-carboxylate (5a).*** This compound was obtained as yellow crystals in 25% yield, mp 237–238°C. IR(KBr) υ: 3051, 1730, 758 cm$^{-1}$. $^1$H-NMR ($CDCl_3$, 400 MHz) δ: 7.60–6.60 (m, 19H, Ar-H), 4.55 (dd, 1H, H-5x, $J_{ax}$ = 1.56 Hz, $J_{bx}$ = 11.52 Hz), 4.20 (q, 2H, O—*CH*$_2$—$CH_3$), 2.86 (dd, 1H, H-4a, $J_{ax}$ = 1.56 Hz, $J_{ab}$ = 16 Hz), 2.71 (dd, 1H, H-4b, $J_{bx}$ = 11.52 Hz, $J_{ab}$ = 16 Hz), 1.19 (t, 3H, O—$CH_2$—*CH*$_3$). MS: *m/z* 505 ($M^+$). Anal. Calcd. for $C_{31}H_{27}N_3O_2S$: C, 73.64; H, 5.38; N, 8.31; Found: C, 73.61; H, 5.40; N, 8.33.

***Ethyl 3a,4-dihydro-3-(4-chlorophenyl)-3a,5-diphenyl-5H-[1,2,4]triazolo[5,4-d][1,5]benzothiazepine-1-carboxylate (5b).*** This compound was obtained as yellow crystals in 31% yield, mp 199–200°C. IR(KBr) υ: 3047, 1725, 763 cm$^{-1}$. $^1$H-NMR ($CDCl_3$, 400 MHz) δ: 7.60–6.60 (m, 18H, Ar-H), 4.52 (dd, 1H, H-5x, $J_{ax}$ = 1.60 Hz, $J_{bx}$ = 11.60 Hz), 4.21 (q, 2H, O—*C*$H_2$—$CH_3$), 2.87 (dd, 1H, H-4a, $J_{ax}$ = 1.60 Hz, $J_{ab}$ = 16 Hz), 2.77 (dd, 1H, H-4b, $J_{bx}$ = 11.60 Hz, $J_{ab}$ = 16 Hz), 1.20 (t, 3H, O—$CH_2$—C*H*$_3$). MS: *m/z* 539 ($M^+$). Anal. Calcd. for $C_{31}H_{26}ClN_3O_2S$: C, 68.94; H, 4.85; N, 7.78; Found: C, 68.92; H, 4.86; N, 7.80.

***Ethyl 3a,4-dihydro-3-(4-methylphenyl)-3a,5-diphenyl-5H-[1,2,4]triazolo[5,4-d][1,5]benzothiazepine-1-carboxylate (5c).*** This compound was obtained as yellow crystals in 30% yield, mp 189–190°C. IR(KBr) υ: 3043, 1721, 762 cm$^{-1}$. $^1$H-NMR ($CDCl_3$, 400 MHz) δ: 7.60–6.60 (m, 18H, Ar-H), 4.55 (dd, 1H, H-5x, $J_{ax}$ = 1.43 Hz, $J_{bx}$ = 11.77 Hz), 4.20 (q, 2H, O—*CH*$_2$—$CH_3$), 2.88 (dd, 1H, H-4a, $J_{ax}$ = 1.43 Hz, $J_{ab}$ = 16 Hz), 2.72 (dd, 1H, H-4b, $J_{bx}$ = 11.77 Hz, $J_{ab}$ = 16 Hz), 2.22 (s, 3H, Ar-$CH_3$), 1.20 (t, 3H, O—$CH_2$—C*H*$_3$). MS: *m/z* 519 ($M^+$). Anal. Calcd. for $C_{32}H_{29}N_3O_2S$: C, 73.96; H, 5.62; N, 8.09; Found: C, 73.98; H, 5.61; N, 8.07.

***Ethyl 3a,4-dihydro-3,3a-diphenyl-5-(4-chlorophenyl)-5H-[1,2,4]triazolo[5,4-d][1,5]benzothiazepine-1-carboxylate (5d).*** This compound was obtained as yellow crystals in 26% yield, mp 217–218°C. IR(KBr) υ: 3055, 1730, 765 cm$^{-1}$. $^1$H-NMR ($CDCl_3$, 400 MHz) δ: 7.60–6.60 (m, 18H, Ar-H), 4.53 (dd, 1H, H-5x, $J_{ax}$ = 1.45 Hz, $J_{bx}$ = 11.35 Hz), 4.20 (q, 2H, O—*CH*$_2$—$CH_3$), 2.86 (dd, 1H, H-4a, $J_{ax}$ = 1.45 Hz, $J_{ab}$ = 16 Hz), 2.70 (dd, 1H, H-4b, $J_{bx}$ = 11.35 Hz, $J_{ab}$ = 16 Hz), 1.20 (t, 3H, O—$CH_2$—*CH*$_3$). MS: *m/z* 539 ($M^+$). Anal. Calcd. for $C_{31}H_{26}ClN_3O_2S$: C, 68.94; H, 4.85; N, 7.78; Found: C, 68.95; H, 4.82; N, 7.79.

***Ethyl 3a,4-dihydro-3-(4-chlorophenyl)-3a-phenyl-5-(4-chlorophenyl)-5H-[1,2,4]triazolo[5,4-d][1,5]benzothiazepine-1-carboxylate (5e).*** This compound was obtained as yellow crystals in 32% yield, mp 254–255°C. IR(KBr) υ: 3062, 1733, 763 cm$^{-1}$. $^1$H-NMR ($CDCl_3$, 400 MHz) δ: 7.60–6.60 (m, 17H, Ar-H), 4.51 (dd, 1H, H-5x, $J_{ax}$ = 1.54 Hz, $J_{bx}$ = 11.68 Hz), 4.19 (q, 2H, O—*CH*$_2$—$CH_3$), 2.84 (dd, 1H, H-4a, $J_{ax}$ = 1.54 Hz, $J_{ab}$ = 16 Hz), 2.69 (dd, 1H, H-4b, $J_{bx}$ = 11.68 Hz, $J_{ab}$ = 16 Hz), 1.20 (t, 3H, O—$CH_2$—*CH*$_3$). MS: *m/z* 573 ($M^+$). Anal. Calcd. for $C_{31}H_{25}Cl_2N_3O_2S$: C, 64.81; H, 4.39; N, 7.31; Found: C, 64.79; H, 4.40; N, 7.34.

***Ethyl 3a,4-dihydro-3-(4-methylphenyl)-3a-phenyl-5-(4-chlorophenyl)-5H-[1,2,4]triazolo[5,4-d][1,5]benzothiazepine-1-carboxylate (5f).*** This compound was obtained as yellow crystals in 29% yield, mp 215–216°C. IR(KBr) υ: 3107, 1730, 762 cm$^{-1}$. $^1$H-NMR ($CDCl_3$, 400 MHz) δ: 7.59–6.60 (m, 17H, Ar-H), 4.54 (dd, 1H, H-5x, $J_{ax}$ = 1.42 Hz, $J_{bx}$ = 11.40 Hz), 4.20 (q, 2H, O—*CH*$_2$—$CH_3$), 2.85 (dd, 1H, H-4a, $J_{ax}$ = 1.42 Hz, $J_{ab}$

= 16 Hz), 2.73 (dd, 1H, H-4b, $J_{bx}$ = 11.40 Hz, $J_{ab}$ = 16 Hz), 2.20 (s, 3H, Ar-$CH_3$), 1.19 (t, 3H, O—$CH_2$—$CH_3$). MS: *m/z* 553 ($M^+$). Anal. Calcd. for $C_{32}H_{28}ClN_3O_2S$: C, 69.36; H, 5.09; N, 7.58; Found: C, 69.32; H, 5.11; N, 7.59.

***Ethyl 3a,4-dihydro-3,3a-diphenyl-5-(4-methoxyphenyl)-5H-[1,2,4]triazolo[5,4-d][1,5]benzothiazepine-1-carboxylate (5g).*** This compound was obtained as yellow crystals in 21% yield, mp 178–179°C. IR(KBr) υ: 3072, 1730, 765 $cm^{-1}$. $^1$H-NMR ($CDCl_3$, 400 MHz) δ: 7.60–6.60 (m, 18H, Ar-H), 4.56 (dd, 1H, H-5x, $J_{ax}$ = 1.54 Hz, $J_{bx}$ = 11.26 Hz), 4.21 (q, 2H, O—$CH_2$—$CH_3$), 3.73 (s, 3H, $OCH_3$), 2.86 (dd, 1H, H-4a, $J_{ax}$ = 1.54 Hz, $J_{ab}$ = 16 Hz), 2.70 (dd, 1H, H-4b, $J_{bx}$ = 11.26 Hz, $J_{ab}$ = 16 Hz), 1.20 (t, 3H, O—$CH_2$—$CH_3$). MS: *m/z* 535 ($M^+$). Anal. Calcd. for $C_{32}H_{29}N_3O_3S$: C, 71.75; H, 5.46; N, 7.84; Found: C, 71.77; H, 5.45; N, 7.82.

***Ethyl 3a,4-dihydro-3-(4-chlorophenyl)-3a-phenyl-5-(4-methoxyphenyl)-5H-[1,2,4]triazolo[5,4-d][1,5]benzothiazepine-1-carboxylate (5h).*** This compound was obtained as yellow crystals in 27% yield, mp 244–245°C. IR(KBr) υ: 3110, 1736, 763 $cm^{-1}$. $^1$H-NMR ($CDCl_3$, 400 MHz) δ: 7.60–6.60 (m, 17H, Ar-H), 4.55 (dd, 1H, H-5x, $J_{ax}$ = 1.62 Hz, $J_{bx}$ = 11.10 Hz), 4.20 (q, 2H, O—$CH_2$—$CH_3$), 3.72 (s, 3H, $OCH_3$), 2.85 (dd, 1H, H-4a, $J_{ax}$ = 1.62 Hz, $J_{ab}$ = 16 Hz), 2.72 (dd, 1H, H-4b, $J_{bx}$ = 11.10 Hz, $J_{ab}$ = 16 Hz), 1.20 (t, 3H, O—$CH_2$—$CH_3$). MS: *m/z* 569 ($M^+$). Anal. Calcd. for $C_{32}H_{28}ClN_3O_3S$: C, 67.42; H, 4.95; N, 7.37; Found: C, 67.40; H, 4.96; N, 7.39.

***Ethyl 3a,4-dihydro-3-(4-methylphenyl)-3a-phenyl-5-(4-methoxyphenyl)-5H-[1,2,4]triazolo[5,4-d][1,5]benzothiazepine-1-carboxylate (5i).*** This compound was obtained as yellow crystals in 33% yield, mp 221–222°C. IR(KBr) υ: 3102, 1720, 762 $cm^{-1}$. $^1$H-NMR ($CDCl_3$, 400 MHz) δ: 7.53–6.60 (m, 17H, Ar-H), 4.56 (dd, 1H, H-5x, $J_{ax}$ = 1.52 Hz, $J_{bx}$ = 11.29 Hz), 4.20 (q, 2H, O—$CH_2$—$CH_3$), 3.74 (s, 3H, $OCH_3$), 2.85 (dd, 1H, H-4a, $J_{ax}$ = 1.52 Hz, $J_{ab}$ = 16 Hz), 2.74 (dd, 1H, H-4b, $J_{bx}$ = 11.29 Hz, $J_{ab}$ = 16 Hz), 2.22 (s, 3H, Ar-$CH_3$), 1.19 (t, 3H, O—$CH_2$—$CH_3$). MS: *m/z* 549 ($M^+$). Anal. Calcd. for $C_{33}H_{31}N_3O_3S$: C, 72.11; H, 5.68; N, 7.64; Found: C, 72.10; H, 5.67; N, 7.67.

***Ethyl 3a,4-dihydro-3,3a-diphenyl-5-(4-nitrophenyl)-5H-[1,2,4]triazolo[5,4-d][1,5]benzothiazepine-1-carboxylate (5j).*** This compound was obtained as yellow crystals in 22% yield, mp 179–180°C. IR(KBr) υ: 3118, 1731, 764 $cm^{-1}$. $^1$H-NMR ($CDCl_3$, 400 MHz) δ: 7.60–6.60 (m, 18H, Ar-H), 4.52 (dd, 1H, H-5x, $J_{ax}$ = 1.48 Hz, $J_{bx}$ = 11.42 Hz), 4.19 (q, 2H, O—$CH_2$—$CH_3$), 2.87 (dd, 1H, H-4a, $J_{ax}$ = 1.48 Hz, $J_{ab}$ = 16 Hz), 2.70 (dd, 1H, H-4b, $J_{bx}$ = 11.42 Hz, $J_{ab}$ = 16 Hz), 1.20 (t, 3H, O—$CH_2$—$CH_3$). MS: *m/z* 550 ($M^+$). Anal. Calcd. for $C_{31}H_{26}N_4O_4S$: C, 67.62; H, 4.76; N, 10.18; Found: C, 67.61; H, 4.75; N, 10.21.

***Ethyl 3a,4-dihydro-3-(4-chlorophenyl)-3a-phenyl-5-(4-nitrophenyl)-5H-[1,2,4]triazolo[5,4-d][1,5]benzothiazepine-1-carboxylate (5k).*** This compound was obtained as yellow crystals in 31% yield, mp 230–231°C. IR(KBr) υ: 3075, 1733, 762 $cm^{-1}$. $^1$H-NMR ($CDCl_3$, 400 MHz) δ: 7.57–6.60 (m, 17H, Ar-H), 4.50 (dd, 1H, H-5x, $J_{ax}$ = 1.68 Hz, $J_{bx}$ = 11.36 Hz), 4.19 (q, 2H, O—$CH_2$—$CH_3$), 2.86 (dd, 1H, H-4a, $J_{ax}$ = 1.68 Hz, $J_{ab}$ = 16 Hz), 2.70 (dd, 1H, H-4b, $J_{bx}$ = 11.36 Hz, $J_{ab}$ = 16 Hz), 1.19 (t, 3H, O—$CH_2$—$CH_3$). MS: *m/z* 584 ($M^+$). Anal. Calcd. for $C_{31}H_{25}ClN_4O_4S$: C, 63.64; H, 4.31; N, 9.58; Found: C, 63.66; H, 4.30; N, 9.55.

***Ethyl 3a,4-dihydro-3-(4-methylphenyl)-3a-phenyl-5-(4-nitrophenyl)-5H-[1,2,4]triazolo[5,4-d][1,5]benzothiazepine-1-carboxylate (5l).*** This compound was obtained as yellow crystals in 28% yield, mp 170–171°C. IR(KBr) υ: 3097, 1745, 764 $cm^{-1}$. $^1$H-NMR ($CDCl_3$, 400 MHz) δ: 7.60–6.60 (m, 17H, Ar-H), 4.54 (dd, 1H, H-5x, $J_{ax}$ = 1.51 Hz, $J_{bx}$ = 11.29 Hz), 4.20 (q, 2H, O—$CH_2$—$CH_3$), 2.85 (dd, 1H, H-4a, $J_{ax}$ = 1.51 Hz, $J_{ab}$ = 16 Hz), 2.72 (dd, 1H, H-4b, $J_{bx}$ = 11.29 Hz, $J_{ab}$ = 16 Hz), 2.20 (s, 3H, Ar-$CH_3$), 1.20 (t, 3H, O—$CH_2$—$CH_3$). MS: *m/z* 564 ($M^+$). Anal. Calcd. for $C_{32}H_{28}N_4O_4S$: C, 68.07; H, 5.00; N, 9.92; Found: C, 68.08; H, 4.99; N, 9.94.

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