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Synthesis of 5-hydroxy- and 5-sulfanyl-substituted [1,2,3]triazolo[4,5-*e*][1,4]diazepines

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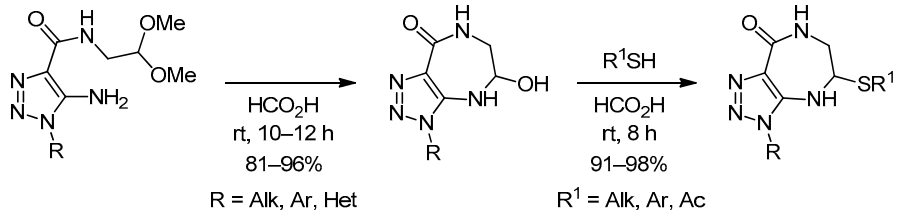


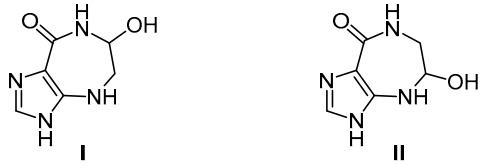
5-Amino-*N*-(2,2-dimethoxyethyl)-1*H*-1,2,3-triazole-4-carboxamides in formic acid were subjected to intramolecular cyclization to 5-hydroxy[1,2,3]triazolo[4,5-*e*][1,4]diazepines, which were converted by treatment with S-nucleophiles to 5-thio-functionalized derivatives.

Keywords: 5-amino-*N*-(2,2-dimethoxyethyl)-1*H*-1,2,3-triazole-4-carboxamides, [1,2,3]triazolo[4,5-*e*][1,4]diazepines, intramolecular cyclization, thiofunctionalization.

Heterocyclic systems containing [1,4]diazepine ring fused with azole ring are of importance due to their synthetic utility and potential biological activity.[1,2] Currently the most thoroughly studied examples of such compounds are [1,4]diazepine derivatives fused with pyrazole and imidazole rings. The pharmacological significance of pyrazolo[1,4]diazepines is obvious from their use as active substances in the anxiolytic drug zolazepam[3–5] and the antidepressant zometapine.[6,7] Besides that, selective phosphodiesterase inhibitors[8] and oxytocin receptor antagonists[9] have been identified in pyrazolo[1,4]-diazepine series.

From the viewpoint of medicinal chemistry, imidazo-[1,4]diazepines are no less valuable, especially the adenosine receptor antagonists[10] and inhibitors of the metalloenzyme guanase – the natural product azepinomycin[11] (**I**) (Fig. 1) and its synthetic analogs.[12–16] It has been recently shown[17] that some derivatives of isoazepinomycin (**II**) (5-hydroxy-4,5,6,7-tetrahydroimidazo-[4,5-*e*][1,4]diazepin-8-ol), which is a positional isomer of azepinomycin, can be used as guanase inhibitors. The authors of that study proposed that the inhibitory activity of these compounds was substantially affected by the hydrophobic cleft between the imidazole and diazepine ring nitrogen atoms. It could be expected that the structural changes in azole ring could also influence the inhibition of guanase – an enzyme catalyzing the hydrolytic deamination of guanine to xanthine.[18,19]

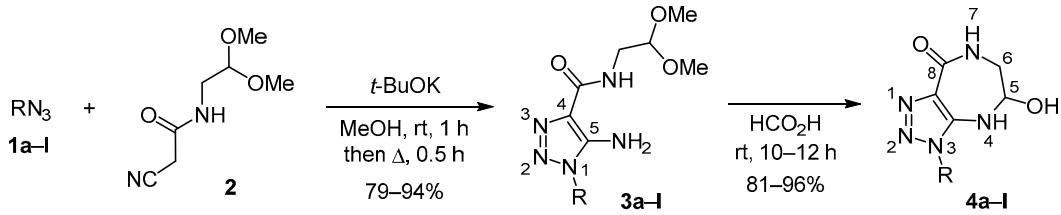
Taking all of this into account, it was considered worthwhile to develop a convenient method for the synthesis of isoelectronic isoazepinomycin analogs – derivatives of triazolo[4,5-*e*][1,4]diazepine. It should be noted that only a single literature source[20] describes the synthesis of tetrahydro[1,2,3]triazolo[4,5-*e*][1,4]diazepin-8-ol deriva-



I II

Figure 1. The molecular structures of azepinomycin (**I**) and isoazepinomycin (**II**).

Scheme 1



tives by cyclization of 5-amino-*N*-(2-chloroethyl)-1*H*-1,2,3-triazole-4-carboxamides in the presence of NaH.

The method previously proposed by our group[21] and by other authors[17] for the formation of hydroxydiazepine ring starting from 5-amino-*N*-(2,2-dialkoxyethyl)-1*H*-pyrazole-(imidazole)-4-carboxamides was found to be also suitable for the preparation of new triazolo[1,4]diazepine derivatives. The key starting materials for this reaction were 5-amino-*N*-(2,2-dimethoxyethyl)-1*H*-1,2,3-triazole-4-carboxamides **3a**–**l**, which were synthesized by us earlier using anionic cyclization of azides **1a**–**l** with 2-cyano-*N*-(2,2-dimethoxyethyl)acetamide (Scheme 1). This method was found to be generally applicable and could use alkyl-, aryl-, and hetaryl azides as starting materials for triazole ring formation under mild conditions in the presence of *t*-BuOK as base, giving compounds **3a**–**l** in 79–94% yields (Table 1). The obtained *N*-functionalized aminotriazole-carboxamides **3a**–**l** readily underwent intramolecular cyclization in formic acid at room temperature, forming 5-hydroxy-substituted triazolo[4,5-*e*][1,4]diazepines **4a**–**l** in nearly quantitative yields (Scheme 1, Table 1).

IR spectra of compounds **4a**–**l** featured a set of absorption bands corresponding to the stretching vibrations of C=O (1627–1636 cm^{-1}), N–H (3247–3312 cm^{-1}), and O–H bonds (3247–3312 cm^{-1}). ^{1}H NMR spectra contained the expected signals for substituents R, as well as multiplets of the 6-CH_2 protons at 2.98–3.38 ppm, 5-CH protons at 4.86–5.18 ppm, and the signals of NH protons: doublets at 7.26–8.01 ppm and multiplets at 7.13–7.66 ppm. ^{1}H NMR spectra of compounds **4a**–**l** did not show any changes after maintaining the samples in DMSO-d_6 solution for a week. This observation indicated that, in contrast to 7-hydroxypyrazolo[1,4]diazepines,[21] the more electron-withdrawing 1,2,3-triazole ring did not facilitate the elimination of water molecule from O,N-ketene acetal moiety in compounds **4** and establishment of equilibrium with the azomethine form. At the same time, a process of this type can easily proceed in acidic medium, which was used by us for selective functionalization of position 5 in triazolodiazepines with sulfur-containing groups.

We found that diazepines **4a**,**e**–**i**,**l** in the presence of S-nucleophilic reagents **5a**–**g** in formic acid at room temperature (method I) were readily converted to

Table 1. Yields of products **3**, **4 a**–**l**

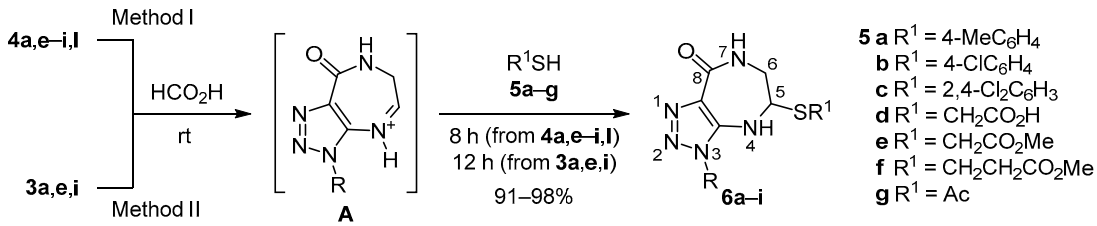
Azide	R	Product (yield, %)	Product (yield, %)
1a	Me_2CHCH_2	**3a** (79)	**4a** (81)
1b	$PhCH_2$	**3b** (85)	**4b** (89)
1c	4-$MeOC_6H_5CH_2$	**3c** (89)	**4c** (87)
1d	3-$ClC_6H_4CH_2$	**3d** (84)	**4d** (88)
1e	Ph	**3e** (81)	**4e** (92)
1f	4-ClC_6H_4	**3f** (93)	**4f** (95)
1g	4-MeC_6H_4	**3g** (88)	**4g** (91)
1h	4-$MeOC_6H_4$	**3h** (86)	**4h** (93)
1i	4-$O_2NC_6H_4$	**3i** (91)	**4i** (96)
1j	2,4-$F_2C_6H_3$	**3j** (91)	**4j** (90)
1k	2,4-$Me_2C_6H_3$	**3k** (81)	**4k** (89)
1l	1-Methylpyrazol-3-yl	**3l** (92)	**4l** (94)

5-sulfanyl-substituted triazolodiazepines **6a**–**i** in 91–98% yields (Scheme 2, Table 2). Studying this transformation in more detail in the case of compounds **6a**–**c**,**h** showed that they can be also obtained in a one-pot process from amides **3a**,**e**,**i** and sulfur-containing nucleophiles **5a**,**d**,**e**,**g** under analogous conditions, without isolation of 5-hydroxy-triazolodiazepine intermediates (method II) (Scheme 2, Table 2). Most probably, an acid-catalyzed formation of the cyclic iminium intermediate **A** occurred in both cases, and the reagents containing HS group added to this intermediate. It should be noted that alcohols as weaker

Table 2. Yields of compounds **6a**–**i**

Com-pound	R	R^1	Yield, % (method)
6a	Me_2CHCH_2	CH_2CO_2Me	96 (I) 92 (II)
6b	Me_2CHCH_2	Ac	98 (I) 95 (II)
6c	Ph	CH_2CO_2H	97 (I) 93 (II)
6d	4-ClC_6H_4	Ac	97 (I)
6e	4-MeC_6H_4	4-ClC_6H_4	96 (I)
6f	4-$MeOC_6H_4$	2,4-$Cl_2C_6H_3$	94 (I)
6g	4-$MeOC_6H_4$	Ac	98 (I)
6h	4-$NO_2C_6H_4$	4-MeC_6H_4	96 (I) 92 (II)
6i	1-Methylpyrazol-3-yl	$CH_2CH_2CO_2Me$	91 (I)

Scheme 2



nucleophiles were not effective in such reactions. Thus, LC-MS analysis indicated that the reactions with alcohols under analogous conditions did not produce more than 12–15% of 5-alkoxy derivatives.

Thus, our study has shown that intramolecular cyclization of 5-amino-*N*-(2,2-dimethoxyethyl)-1*H*-1,2,3-triazole-4-carboxamides in formic acid provides a convenient method for the synthesis of isoelectronic analogs of isoazepinomycin – 5-hydroxy[1,2,3]triazolo[4,5-*e*]-[1,4]diazepines, which are promising targets for synthetic and medicinal chemistry research.

Experimental

IR spectra were recorded on a Bruker Vertex 70 spectrometer for samples in the form of KBr pellets. ^{1}H NMR spectra were acquired in pulsed FT mode on Varian VXR-400 (400 MHz) and ^{13}C NMR spectra on Bruker Avance DRX-500 (125 MHz) spectrometers. The solvents were $CDCl_3$ (^{1}H and ^{13}C NMR spectra of compounds **3a**–**d**,**f**–**h**,**k**, ^{13}C NMR spectrum of compound **3e**) and DMSO-d_6 (^{1}H and ^{13}C NMR spectra of the rest of the compounds). The solvent signals were used as internal standards ($CDCl_3$: 7.26 ppm for ^{1}H nuclei, 77.0 ppm for ^{13}C nuclei; DMSO-d_6: 2.49 ppm for ^{1}H nuclei, 39.5 ppm for ^{13}C nuclei). Mass spectra were recorded on an Agilent LC/MSD SL instrument; the column was Zorbax SB-C18, 4.6 × 15 mm, 1.8 μm (PN 82(c)75-932); solvent DMSO, electrospray ionization at atmospheric pressure. Elemental analysis was performed on a PerkinElmer CHN Analyzer 2400 instrument. Melting points were determined on a Kofler bench and were not corrected.

Synthesis of compounds 3a–l (General method). A solution of cyanoacetamide **2** (1.89 g, 11 mmol) and *t*-BuOK (1.23 g, 11 mmol) in MeOH (20 ml) was treated by adding a MeOH solution (10 ml) of alkyl azide **1a**–**d**, obtained from 14 mmol of the respective alkyl halide according to a literature procedure[22] or aryl azide **1g**–**l** that was obtained from the respective arylamine according to another published procedure.[23] The mixture was stirred at room temperature for 1 h, then refluxed for 0.5 h. The reaction mixture was evaporated, the residue was treated with water (20 ml), the obtained precipitate was filtered off, washed with water (10 ml), dried, and recrystallized from MeOH.

5-Amino-*N*-(2,2-dimethoxyethyl)-1-isobutyl-1*H*-1,2,3-triazole-4-carboxamide (3a). Yield 2.35 g (79%), white powder, mp 162–163°C. IR spectrum, ν, cm^{-1}: 1646 (C=O), 3311, 3455 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.91 (6H, d, *J* = 6.4, $CH(C\underline{H}_3)_2$); 2.16–2.23 (1H, m, $CH_2C\underline{H}Me_2$); 3.37 (6H, s, $2OCH_3$); 3.52 (2H, d, *J* = 5.4, $C\underline{H}_2CH(OMe)_2$); 3.88 (2H, d, *J* = 7.2, $C\underline{H}_2CHMe_2$); 4.42 (1H, t, *J* = 5.2, $CH_2C\underline{H}(OMe)_2$); 5.18 (2H, s, NH_2); 7.01 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 19.9 (2C); 28.5; 40.1; 53.2; 54.3 (2C); 102.8; 122.9; 143.7; 162.7. Mass spectrum, *m*/*z* (I_{rel}, %): 270 $[M–H]^-$ (100). Found, %: C 48.61; H 7.96; N 25.94. $C_{11}H_{21}N_5O_3$. Calculated, %: C 48.70; H 7.80; N 25.81.

5-Amino-1-benzyl-*N*-(2,2-dimethoxyethyl)-1*H*-1,2,3-triazole-4-carboxamide (3b). Yield 2.85 g (85%), white powder, mp 144–145°C. IR spectrum, ν, cm^{-1}: 1647 (C=O), 3295, 3369 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.39 (6H, s, $2OCH_3$); 3.53 (2H, t, *J* = 5.4, $C\underline{H}_2CH(OMe)_2$); 4.43 (1H, t, *J* = 5.2, $CH_2C\underline{H}(OMe)_2$); 4.80 (2H, s, NH_2); 5.36 (2H, s, $C\underline{H}_2Ph$); 6.98 (1H, t, *J* = 5.4, NH); 7.18–7.38 (5H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 39.8; 49.1; 53.9 (2C); 102.2; 124.1 (2C); 128.7; 130.4 (2C); 139.4; 143.3; 147.1; 161.8. Mass spectrum, *m*/*z* (I_{rel}, %): 304 $[M–H]^-$ (97). Found, %: C 54.92; H 6.19; N 23.11. $C_{14}H_{19}N_5O_3$. Calculated, %: C 55.07; H 6.27; N 22.94.

5-Amino-*N*-(2,2-dimethoxyethyl)-1-(4-methoxybenzyl)-1*H*-1,2,3-triazole-4-carboxamide (3c). Yield 2.85 g (89%), white powder, mp 136–137°C. IR spectrum, ν, cm^{-1}: 1644 (C=O), 3283, 3394 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.43 (6H, s, $2OCH_3$); 3.59 (2H, t, *J* = 5.4, $C\underline{H}_2CH(OMe)_2$); 3.85 (3H, s, $ArOC\underline{H}_3$); 4.47 (1H, t, *J* = 5.2, $CH_2C\underline{H}(OMe)_2$); 5.27 (2H, s, NH_2); 5.30 (2H, s, $C\underline{H}_2Ar$); 6.88 (2H, d, *J* = 8.4, H Ar); 7.05 (1H, t, *J* = 5.2, NH); 7.18 (2H, d, *J* = 8.4, H Ar). ^{13}C NMR spectrum, δ, ppm: 40.3; 47.8; 54.3 (2C); 55.9; 102.8; 115.2 (2C); 122.9; 130.1 (2C); 134.7; 143.7; 162.7; 163.8. Mass spectrum, *m*/*z* (I_{rel}, %): 335 $[M–H]^-$ (100). Found, %: C 53.80; H 6.46; N 21.07. $C_{15}H_{21}N_5O_4$. Calculated, %: C 53.72; H 6.31; N 20.88.

5-Amino-1-(3-chlorobenzyl)-*N*-(2,2-dimethoxyethyl)-1*H*-1,2,3-triazole-4-carboxamide (3d). Yield 3.13 g (84%), beige powder, mp 129–130°C. IR spectrum, ν, cm^{-1}: 1645 (C=O), 3278, 3389 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.40 (6H, s, $2OCH_3$); 3.53 (2H, t, *J* = 5.4, $C\underline{H}_2CH(OMe)_2$); 4.44 (1H, t, *J* = 5.2, $CH_2C\underline{H}(OMe)_2$); 5.01 (2H, s, NH_2); 5.32 (2H, s, $C\underline{H}_2Ar$); 7.00–7.07 (2H, m, NH, H Ar); 7.18 (1H, s, H Ar); 7.25–7.30 (2H, m, H Ar). ^{13}C NMR spectrum, δ, ppm: 40.2; 49.4; 54.3 (2C); 102.7; 123.5; 125.3; 127.3; 128.9; 130.5; 135.2; 135.6; 143.9; 162.6. Mass spectrum, *m*/*z* (I_{rel}, %): 338 $[M–H]^-$ (100). Found, %: C 49.61; H 5.27; N 20.38. $C_{14}H_{18}ClN_5O_3$. Calculated, %: C 49.49; H 5.34; N 20.61.

5-Amino-*N*-(2,2-dimethoxyethyl)-1-phenyl-1*H*-1,2,3-triazole-4-carboxamide (3e). Yield 2.98 g (81%), white powder, mp 152–153°C. IR spectrum, ν, cm^{-1}: 1634 (C=O), 3275, 3382 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.29 (6H, s, $2OCH_3$); 3.58 (2H, t, *J* = 5.3, $C\underline{H}_2CH(OMe)_2$); 3.73 (3H, s, OCH_3); 5.17 (1H, t, *J* = 5.1, $CH_2C\underline{H}(OMe)_2$); 5.35 (2H, s, $C\underline{H}_2Ph$); 6.27 (2H, s, NH_2); 6.90 (2H, d, *J* = 7.2, H Ar); 7.21 (2H, d, *J* = 7.2, H Ar); 7.70 (1H, t, *J* = 5.2, NH). ^{13}C NMR spectrum, δ, ppm: 40.3; 54.3 (2C); 102.8; 122.6; 123.9 (2C); 129.6; 130.1 (2C); 134.7; 143.7; 162.7. Mass spectrum, *m*/*z* (I_{rel}, %): 290 $[M–H]^-$ (100). Found, %: C 53.81; H 5.76; N 23.85. $C_{13}H_{17}N_5O_3$. Calculated, %: C 53.60; H 5.88; N 24.04.

5-Amino-1-(4-chlorophenyl)-*N*-(2,2-dimethoxyethyl)-1*H*-1,2,3-triazole-4-carboxamide (3f). Yield 3.33 g (93%), yellow powder, mp 159–160°C. IR spectrum, ν, cm^{-1}: 1637 (C=O), 3281, 3396 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.43 (6H, s, $2OCH_3$); 3.58 (2H, t, *J* = 5.4, $C\underline{H}_2CH(OMe)_2$); 4.48 (1H, t, *J* = 5.2, $CH_2C\underline{H}(OMe)_2$); 5.31 (2H, s, NH_2); 7.03 (1H, t, *J* = 5.2, NH); 7.48–7.57 (4H, m, H Ar). ^{13}C NMR spectrum, δ, ppm: 40.3; 54.3 (2C); 102.8; 122.8; 125.1 (2C); 130.3 (2C); 133.2; 135.6; 143.7; 162.5. Mass spectrum, *m*/*z* (I_{rel}, %): 324 $[M–H]^-$ (100). Found, %:

C 47.78; H 4.84; N 21.76. $C_{13}H_{16}ClN_5O_3$. Calculated, %: C 47.93; H 4.95; N 21.50.

5-Amino-*N*-(2,2-dimethoxyethyl)-1-(4-methylphenyl)-1*H*-1,2,3-triazole-4-carboxamide (3g). Yield 295 g (88%), beige powder, mp 108–109°C. IR spectrum, ν, cm^{-1}: 1629 (C=O), 3294, 3405 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.44 (3H, s, ArC$\underline{H}_3$); 3.43 (6H, s, 2OCH_3); 3.60 (2H, t, *J* = 5.4, C$\underline{H}_2$CH$(OMe)_2$); 4.49 (1H, t, *J* = 5.2, $CH_2C\underline{H}(OMe)_2$); 5.25 (2H, s, NH_2); 7.30 (1H, t, *J* = 5.2, NH); 7.31–7.42 (4H, m, H Ar). ^{13}C NMR spectrum, δ, ppm: 21.3; 40.3; 54.3 (2C); 102.8; 122.5; 123.9 (2C); 130.6 (2C); 132.0; 139.9; 143.8; 162.7. Mass spectrum, *m*/*z* (I_{rel}, %): 304 $[M–H]^-$ (100). Found, %: C 55.26; H 6.14; N 23.16. $C_{14}H_{19}N_5O_3$. Calculated, %: C 55.07; H 6.27; N 22.94.

5-Amino-*N*-(2,2-dimethoxyethyl)-1-(4-methoxyphenyl)-1*H*-1,2,3-triazole-4-carboxamide (3h). Yield 3.04 g (86%), beige powder, mp 123–124°C. IR spectrum, ν, cm^{-1}: 1632 (C=O), 3282, 3398 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.42 (6H, s, 2OCH_3); 3.57 (2H, t, *J* = 5.4, C$\underline{H}_2$CH$(OMe)_2$); 3.86 (3H, s, ArOC$\underline{H}_3$); 4.46 (1H, t, *J* = 5.2, $CH_2C\underline{H}(OMe)_2$); 5.22 (2H, s, NH_2); 7.02–7.07 (3H, m, NH, H Ar); 7.42 (2H, d, *J* = 8.8, H Ar). ^{13}C NMR spectrum, δ, ppm: 40.3; 54.4 (2C); 55.7; 102.9; 115.2 (2C); 122.5; 125.8 (2C); 127.2; 143.9; 160.5; 162.7. Mass spectrum, *m*/*z* (I_{rel}, %): 320 $[M–H]^-$ (100). Found, %: C 52.56; H 5.74; N 21.58. $C_{14}H_{19}N_5O_4$. Calculated, %: C 52.33; H 5.96; N 21.79.

5-Amino-*N*-(2,2-dimethoxyethyl)-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-4-carboxamide (3i). Yield 3.47 g (91%), yellow powder, mp 174–175°C. IR spectrum, ν, cm^{-1}: 1637 (C=O), 3275, 3395 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.29 (6H, s, 2OCH_3); 3.36 (2H, t, *J* = 5.4, C$\underline{H}_2$CH$(OMe)_2$); 4.56 (1H, t, *J* = 5.2, $CH_2C\underline{H}(OMe)_2$); 6.71 (2H, s, NH_2); 7.93 (2H, d, *J* = 8.4, H Ar); 8.23 (1H, t, *J* = 5.2, NH); 8.44 (2H, d, *J* = 8.4, H Ar). ^{13}C NMR spectrum, δ, ppm: 41.3; 53.3 (2C); 102.2; 121.2; 124.9 (2C); 125.6 (2C); 140.4; 145.3; 147.3; 162.4. Mass spectrum, *m*/*z* (I_{rel}, %): 335 $[M–H]^-$ (97). Found, %: C 46.22; H 4.69; N 25.21. $C_{13}H_{16}N_6O_5$. Calculated, %: C 46.43; H 4.80; N 24.99.

5-Amino-1-(2,4-difluorophenyl)-*N*-(2,2-dimethoxyethyl)-1*H*-1,2,3-triazole-4-carboxamide (3j). Yield 3.27 g (91%), beige powder, mp 182–183°C. IR spectrum, ν, cm^{-1}: 1634 (C=O), 3275, 3395 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.30 (6H, s, 2OCH_3); 3.38 (2H, t, *J* = 5.4, C$\underline{H}_2$CH$(OMe)_2$); 4.56 (1H, t, *J* = 5.2, $CH_2C\underline{H}(OMe)_2$); 6.51 (2H, s, NH_2); 7.31–7.36 (1H, m, H Ar); 7.57–7.74 (2H, m, H Ar); 8.04 (1H, t, *J* = 5.2, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 40.4; 53.3 (2C); 102.2; 106.0 (d, $^2J_{CF}$ = 22.6, C-3'); 106.1 (d, $^2J_{CF}$ = 22.6, C-3'); 106.2 (d, $^2J_{CF}$ = 22.6, C-3'); 113.2 (dd, ^2J = 22.6, ^4J = 3.7, C-5'); 119.3 (dd, ^2J = 22.6, ^4J = 3.7, C-1'); 120.8; 131.3 (d, ^3J = 10.0, C-6'); 146.5; 157.6 (dd, ^1J = 253.6, ^3J = 13.8, C-4'); 162.6; 163.5 (dd, ^1J = 251.4, ^3J = 12.5, C-2'). Mass spectrum, *m*/*z* (I_{rel}, %): 326 $[M–H]^-$ (100). Found, %: C 47.97; H 4.49; N 21.17. $C_{13}H_{15}F_2N_5O_3$. Calculated, %: C 47.71; H 4.62; N 21.40.

5-Amino-*N*-(2,2-dimethoxyethyl)-1-(2,4-dimethylphenyl)-1*H*-1,2,3-triazole-4-carboxamide (3k). Yield 2.84 g (81%), beige powder, mp 133–134°C. IR spectrum, ν, cm^{-1}: 1638 (C=O), 3294, 3410 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.09 (3H, s, ArC$\underline{H}_3$); 2.40 (3H, s, ArC$\underline{H}_3$); 3.42 (6H, s, 2OCH_3); 3.58 (2H, t, *J* = 5.4, C$\underline{H}_2$CH$(OMe)_2$); 4.48 (1H, t, *J* = 5.2, $CH_2C\underline{H}(OMe)_2$); 5.03 (2H, s, NH_2); 7.15 (1H, t, *J* = 5.2, NH); 7.20 (2H, m, H Ar); 7.26 (1H, s, H Ar). ^{13}C NMR spectrum, δ, ppm: 17.4; 21.3; 40.3; 54.3 (2C); 102.9; 122.0; 127.0; 128.0; 130.2; 132.4; 135.8; 141.1; 144.5; 162.8. Mass spectrum, *m*/*z* (I_{rel}, %): 318 $[M–H]^-$ (100). Found, %: C 56.27; H 6.46; N 22.19. $C_{15}H_{21}N_5O_3$. Calculated, %: C 56.41; H 6.63; N 21.93.

5-Amino-*N*-(2,2-dimethoxyethyl)-1-(1-methylpyrazol-3-yl)-1*H*-1,2,3-triazole-4-carboxamide (3l). Yield 2.98 g (92%), white powder, mp 150–151°C. IR spectrum, ν, cm^{-1}: 1632 (C=O), 3291, 3407 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.27 (6H, d, 2OCH_3); 3.35 (2H, t, *J* = 5.4, C$\underline{H}_2$CH$(OMe)_2$); 3.92 (3H, s, NCH_3); 4.54 (1H, t, *J* = 5.2, $CH_2C\underline{H}(OMe)_2$); 6.59 (1H, s, H Ar); 6.63 (1H, s, NH_2); 7.91 (1H, s, H Ar); 8.11 (1H, t, *J* = 5.2, NH). ^{13}C NMR spectrum, δ, ppm: 38.5; 39.1; 53.3 (2C); 97.5; 102.2; 121.6; 133.5; 143.9; 145.4; 162.2. Mass spectrum, *m*/*z* (I_{rel}, %): 294 $[M–H]^-$ (100). Found, %: C 44.91; H 5.66; N 33.04. $C_{11}H_{17}N_7O_3$. Calculated, %: C 44.74; H 5.80; N 33.20 .

Synthesis of compounds 4a–l (General method). A solution of amide **3a–l** (7 mmol) in HCO_2H (10 ml) was stirred at room temperature for 10–12 h, diluted with water (10 ml), the obtained precipitate was filtered off, washed with water (50 ml), and air-dried.

5-Hydroxy-3-isobutyl-4,5,6,7-tetrahydro[1,2,3]triazolo-[4,5-*e*][1,4]diazepin-8(3*H*)-one (4a). Yield 1.28 g (81%), white powder, mp 241–244°C. IR spectrum, ν, cm^{-1}: 1632 (C=O), 3252, 3297 (N–H), 3347 (O–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.82–0.88 (6H, m, $CH_2CH(C\underline{H}_3)_2$); 2.04–2.11 (1H, m, $CH_2C\underline{H}Me_2$); 3.00–3.18 (1H, m) and 3.22–3.31 (1H, m, 6-CH_2); 3.92 (2H, d, *J* = 7.2, C$\underline{H}_2$CH$(CH_3)_2$); 4.97–5.02 (1H, m, 5-CH); 5.82 (1H, d, *J* = 4.4, OH); 7.35–7.39 (1H, m, NH); 7.73 (1H, d, *J* = 3.6, NH). ^{13}C NMR spectrum, δ, ppm: 19.5 (2C); 27.7; 44.9; 52.3; 74.0; 122.9; 144.7; 163.8. Mass spectrum, *m*/*z* (I_{rel}, %): 226 $[M+H]^+$ (100). Found, %: C 47.64; H 6.59; N 31.27. $C_9H_{15}N_5O_2$. Calculated, %: C 47.99; H 6.71; N 31.09.

3-Benzyl-5-hydroxy-4,5,6,7-tetrahydro[1,2,3]triazolo-[4,5-*e*][1,4]diazepin-8(3*H*)-one (4b). Yield 1.62 g (89%), white powder, mp 185–187°C. IR spectrum, ν, cm^{-1}: 1636 (C=O), 3256, 3299 (N–H), 3356 (O–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.02–3.09 (1H, m) and 3.18–3.31 (1H, m, 6-CH_2); 4.97–5.03 (1H, m, 5-CH); 5.41 (2H, s, C$\underline{H}_2$Ph); 5.92 (1H, br. s, OH); 7.18–7.41 (6H, m, NH, H Ph); 7.92 (1H, d, *J* = 3.6, NH). ^{13}C NMR spectrum, δ, ppm: 44.9; 48.5; 74.0; 127.1 (2C); 127.3; 127.7; 128.7 (2C); 135.8; 141.1; 163.6. Mass spectrum, *m*/*z* (I_{rel}, %): 260 $[M+H]^+$ (100). Found, %: C 55.33; H 4.96; N 27.27. $C_{12}H_{13}N_5O_2$. Calculated, %: C 55.59; H 5.05; N 27.01.

5-Hydroxy-3-(4-methoxybenzyl)-4,5,6,7-tetrahydro-[1,2,3]triazolo[4,5-*e*][1,4]diazepin-8(3*H*)-one (4c). Yield 1.78 g (87%), white powder, mp 180–182°C. IR spectrum, ν, cm^{-1}: 1631 (C=O), 3251, 3305 (N–H), 3360 (O–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.98–3.06

(1H, m) and 3.18–3.31 (1H, m, 6-CH_2); 3.72 (3H, s, OCH_3); 4.97–5.03 (1H, m, 5-CH); 5.31 (2H, s, C$\underline{H_2}$Ar); 5.88 (1H, br. s, OH); 6.89 (2H, d, *J* = 8.4, H Ar); 7.18 (2H, d, *J* = 8.4, H Ar); 7.39–7.46 (1H, m, NH); 7.90 (1H, d, *J* = 3.6, NH). ^{13}C NMR spectrum, δ, ppm: 45.3; 48.5; 55.5; 114.4 (2C); 123.6; 128.2 (2C); 141.3; 159.3; 163.9. Mass spectrum, *m*/*z* (I_{rel}, %): 290 $[M+H]^+$ (100). Found, %: C 54.19; H 5.29; N 24.47. $C_{13}H_{15}N_5O_3$. Calculated, %: C 53.97; H 5.23; N 24.21.

3-(3-Chlorobenzyl)-5-hydroxy-4,5,6,7-tetrahydro[1,2,3]-triazolo[4,5-*e*][1,4]diazepin-8(3*H*)-one (4d). Yield 1.81 g (88%), yellow powder, mp 176–178°C. IR spectrum, ν, cm^{-1}: 1634 (C=O), 3249, 3301 (N–H), 3361 (O–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.04–3.13 (1H, m) and 3.22–3.32 (1H, m, 6-CH_2); 4.98–5.05 (1H, m, 5-CH); 5.43 (2H, s, C$\underline{H_2}$Ar); 5.81 (1H, br. s, OH); 7.13–7.44 (5H, m, NH, H Ar); 7.82 (1H, d, *J* = 3.6, NH). ^{13}C NMR spectrum, δ, ppm: 45.3; 48.3; 74.6; 123.7; 126.4; 127.6; 128.2; 131.0; 133.6; 138.7; 141.6; 163.9. Mass spectrum, *m*/*z* (I_{rel}, %): 294 $[M+H]^+$ (100). Found, %: C 50.23; H 4.24; N 23.67. $C_{12}H_{12}ClN_5O_2$. Calculated, %: C 49.07; H 4.12; N 23.84.

5-Hydroxy-3-phenyl-4,5,6,7-tetrahydro[1,2,3]triazolo-[4,5-*e*][1,4]diazepin-8(3*H*)-one (4e). Yield 1.58 g (92%), white powder, mp 237–239°C. IR spectrum, ν, cm^{-1}: 1629 (C=O), 3253, 3307 (N–H), 3378 (O–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.11–3.19 (1H, m) and 3.32–3.38 (1H, m, 6-CH_2); 4.96–5.04 (1H, m, 5-CH); 5.72 (1H, d, *J* = 4.4, OH); 7.40–7.48 (1H, m, NH); 7.52–7.66 (6H, m, NH, H Ph). ^{13}C NMR spectrum, δ, ppm: 45.1; 74.4; 123.8; 125.5 (2C); 129.9; 130.5 (2C); 135.1; 141.5; 163.8. Mass spectrum, *m*/*z* (I_{rel}, %): 246 $[M+H]^+$ (100). Found, %: C 53.63; H 4.41; N 28.88. $C_{11}H_{11}N_5O_2$. Calculated, %: C 53.87; H 4.52; N 28.56.

3-(4-Chlorophenyl)-5-hydroxy-4,5,6,7-tetrahydro[1,2,3]-triazolo[4,5-*e*][1,4]diazepin-8(3*H*)-one (4f). Yield 1.96 g (95%), white powder, mp 258–260°C. IR spectrum, ν, cm^{-1}: 1630 (C=O), 3249, 3303 (N–H), 3371 (O–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.14–3.21 (1H, m) and 3.23–3.31 (1H, m, 6-CH_2); 4.92–5.00 (1H, m, 5-CH); 5.82 (1H, d, *J* = 4.4, OH); 7.49–7.55 (1H, m, NH); 7.57 (2H, d, *J* = 8.8, H Ar); 7.69 (2H, d, *J* = 8.8, H Ar); 7.75 (1H, *J* = 3.6, NH). ^{13}C NMR spectrum, δ, ppm: 45.1; 74.5; 123.8; 127.5 (2C); 130.3 (2C); 133.9; 134.4; 141.7; 163.7. Mass spectrum, *m*/*z* (I_{rel}, %): 280 $[M+H]^+$ (100). Found, %: C 47.47; H 3.53; N 24.84. $C_{11}H_{10}ClN_5O_2$. Calculated, %: C 47.24; H 3.60; N 25.04.

5-Hydroxy-3-(4-methylphenyl)-4,5,6,7-tetrahydro-[1,2,3]triazolo[4,5-*e*][1,4]diazepin-8(3*H*)-one (4g). Yield 1.65 g (91%), white powder, mp 197–199°C. IR spectrum, ν, cm^{-1}: 1628 (C=O), 3247, 3311 (N–H), 3366 (O–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.37 (3H, s, CH_3); 3.09–3.16 (1H, m) and 3.26–3.32 (1H, m, 6-CH_2); 4.93–5.02 (1H, m, 5-CH); 5.79 (1H, d, *J* = 4.4, OH); 7.38–7.48 (4H, m, H Ar); 7.49–7.51 (1H, m, NH); 7.59 (1H, d, *J* = 3.6, NH). ^{13}C NMR spectrum, δ, ppm: 21.2; 45.2; 74.4; 123.6; 125.4 (2C); 130.6 (2C); 132.6; 139.6; 141.5; 163.8. Mass spectrum, *m*/*z* (I_{rel}, %): 260 $[M+H]^+$ (99). Found, %: C 55.77; H 4.94; N 26.86. $C_{12}H_{13}N_5O_2$. Calculated, %: C 55.59; H 5.05; N 27.01.

5-Hydroxy-3-(4-methoxyphenyl)-4,5,6,7-tetrahydro-[1,2,3]triazolo[4,5-*e*][1,4]diazepin-8(3*H*)-one (4h). Yield 1.79 g (93%), white powder, mp 251–253°C. IR spectrum, ν, cm^{-1}: 1631 (C=O), 3251, 3308 (N–H), 3369 (O–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.07–3.15 (1H, m) and 3.24–3.33 (1H, m, 6-CH_2); 3.84 (3H, s, OCH_3); 4.91–4.97 (1H, m, 5-CH); 5.76 (1H, br. s, OH); 7.14 (2H, d, *J* = 8.8, H Ar); 7.40–7.48 (3H, m, NH, H Ar); 7.51 (1H, d, *J* = 3.6, NH). ^{13}C NMR spectrum, δ, ppm: 45.3; 56.5; 74.3; 115.2 (2C); 122.9; 130.1 (2C); 135.3; 141.0; 163.4; 164.6. Mass spectrum, *m*/*z* (I_{rel}, %): 276 $[M+H]^+$ (100). Found, %: C 52.07; H 4.55; N 25.69. $C_{12}H_{13}N_5O_3$. Calculated, %: C 52.36; H 4.76; N 25.44 .

5-Hydroxy-3-(4-nitrophenyl)-4,5,6,7-tetrahydro[1,2,3]-triazolo[4,5-*e*][1,4]diazepin-8(3*H*)-one (4i). Yield 1.95 g (96%), yellow powder, mp 242–244°C. IR spectrum, ν, cm^{-1}: 1628 (C=O), 3254, 3306 (N–H), 3361 (O–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.08–3.15 (1H, m) and 3.27–3.33 (1H, m, 6-CH_2); 4.97–5.02 (1H, m, 5-CH); 5.91 (1H, br. s, OH); 7.54–7.62 (1H, m, NH); 7.88 (2H, d, *J* = 8.8, H Ar); 8.01 (1H, d, *J* = 3.6, NH); 8.45 (2H, d, *J* = 8.8, H Ar). ^{13}C NMR spectrum, δ, ppm: 45.1; 74.7; 124.3; 125.7 (2C); 126.2 (2C); 140.3; 141.7; 147.6; 163.5. Mass spectrum, *m*/*z* (I_{rel}, %): 291 $[M+H]^+$ (100). Found, %: C 45.39; H 3.35; N 29.18. $C_{11}H_{10}N_6O_4$. Calculated, %: C 45.52; H 3.47; N 28.96.

3-(2,4-Difluorophenyl)-5-hydroxy-4,5,6,7-tetrahydro-[1,2,3]triazolo[4,5-*e*][1,4]diazepin-8(3*H*)-one (4j). Yield 1.77 g (90%), white powder, mp 223–225°C. IR spectrum, ν, cm^{-1}: 1634 (C=O), 3253, 3307 (N–H), 3368 (O–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.07–3.14 (1H, m) and 3.26–3.32 (1H, m, 6-CH_2); 4.90–4.98 (1H, m, 5-CH); 5.88 (1H, br. s, OH); 7.29–7.35 (1H, m, H Ar); 7.44–7.49 (1H, m, NH); 7.60–7.69 (2H, m, H Ar); 7.81–7.89 (1H, m, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 45.2; 74.4; 106.0 (d, $^2J_{CF}$ = 22.6, C-3'); 106.2 (d, $^2J_{CF}$ = 22.6, C-3'); 113.1 (dd, ^2J = 22.6, ^4J = 3.7, C-5'); 119.2 (dd, ^2J = 22.6, ^4J = 3.7, C-1'); 122.8; 131.6 (d, ^3J = 10.0, C-6'); 143.0; 157.6 (dd, ^1J = 253.6, ^3J = 13.8, C-4'); 163.7; 164.5 (dd, ^1J = 251.4, ^3J = 12.5, C-2'). Mass spectrum, *m*/*z* (I_{rel}, %): 282 $[M+H]^+$ (98). Found, %: C 47.19; H 3.13; N 24.76. $C_{11}H_9F_2N_5O_2$. Calculated, %: C 46.98; H 3.23; N 24.90.

3-(2,4-Dimethylphenyl)-5-hydroxy-4,5,6,7-tetrahydro-[1,2,3]triazolo[4,5-*e*][1,4]diazepin-8(3*H*)-one (4k). Yield 1.70 g (89%), beige powder, mp 258–260°C. IR spectrum, ν, cm^{-1}: 1627 (C=O), 3257, 3312 (N–H), 3379 (O–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.99 (3H, s, CH_3); 2.34 (3H, s, CH_3); 3.06–3.12 (1H, m) and 3.26–3.32 (1H, m, 6-CH_2); 4.89–4.93 (1H, m, 5-CH); 5.69 (1H, br. s, OH); 7.18–7.22 (2H, m, H Ar); 7.26–7.29 (2H, m, NH, H Ar); 7.38–7.42 (1H, m, NH). ^{13}C NMR spectrum, δ, ppm: 17.4; 21.2; 45.3; 74.2; 122.9; 128.1; 128.2; 131.1; 132.2; 135.9; 140.5; 142.2; 163.9. Mass spectrum, *m*/*z* (I_{rel}, %): 274 $[M+H]^+$ (97). Found, %: C 57.34; H 5.41; N 25.47. $C_{13}H_{15}N_5O_2$. Calculated, %: C 57.13; H 5.53; N 25.63.

5-Hydroxy-3-(1-methylpyrazol-3-yl)-4,5,6,7-tetrahydro-[1,2,3]triazolo[4,5-*e*][1,4]diazepin-8(3*H*)-one (4l). Yield 1.74 g (94%), white powder, mp 218–220°C. IR spectrum, ν, cm^{-1}: 1626 (C=O), 3254, 3298 (N–H), 3359 (O–H).

^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.13–3.19 (1H, m) and 3.21–3.33 (1H, m, 6-CH_2); 3.92 (3H, s, NCH_3); 5.12–5.18 (1H, m, 5-CH); 6.07 (1H, d, *J* = 4.4, OH); 6.59 (1H, s, H Ar); 7.50–7.57 (1H, m, NH); 7.87 (1H, d, *J* = 3.6, NH); 7.92 (1H, s, H Ar). ^{13}C NMR spectrum, δ, ppm: 45.0; 74.6; 98.0; 123.4; 133.7; 140.6; 145.2; 163.5; 163.6. Mass spectrum, *m*/*z* (I_{rel}, %): 250 $[M+H]^+$ (96). Found, %: C 43.19; H 4.36; N 39.71. $C_9H_{11}N_7O_2$. Calculated, %: C 43.37; H 4.45; N 39.34.

Synthesis of compounds 6a–i (General procedure). Method I. Thio derivative **5a**–**g** (4 mmol) was added to a solution of triazolodiazepine **4a**,**e**–**i**,**l** (4 mmol) in HCO_2H (10 ml), the reaction mixture was stirred at room temperature for 8 h, diluted with water (10 ml), the obtained precipitate was filtered off, washed with water (10 ml), dried, and recrystallized from MeCN.

Method II. Thio compound **5a**,**d**,**e**,**g** (5 mmol) was added to a solution of amide **3a**,**e**,**i** (5 mmol) in HCO_2H (15 ml), the reaction mixture was stirred at room temperature for 12 h, diluted with water (10 ml), the obtained precipitate was filtered off, washed with water (10 ml), dried, and recrystallized from MeCN.

Methyl [(3-isobutyl-8-oxo-3,4,5,6,7,8-hexahydro[1,2,3]-triazolo[4,5-*e*][1,4]diazepin-5-yl)sulfanyl]acetate (6a). Yield 1.20 g (96%, method I), 1.44 g (92%, method II), white powder, mp 239–240°C. IR spectrum, ν, cm^{-1}: 1670 (C=O), 1734–1756 (CO_2Me), 3321, 3415 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.79–0.88 (6H, m, $CH_2CH(C\underline{H}_3)_2$); 2.03–2.12 (1H, m, $CH_2C\underline{H}Me_2$); 3.35–3.62 (4H, m, 6-CH_2, SCH_2); 3.64 (3H, s, OCH_3); 3.95 (2H, d, *J* = 7.2, $C\underline{H}_2CHMe_2$); 5.09–5.19 (1H, m, 5-CH); 7.59–7.68 (1H, m, NH); 8.04 (1H, d, *J* = 3.6, NH). ^{13}C NMR spectrum, δ, ppm: 19.8 (2C); 27.9; 30.9; 44.8; 52.1; 52.4; 60.6; 123.4; 140.2; 163.3; 170.7. Mass spectrum, *m*/*z* (I_{rel}, %): 314 $[M+H]^+$ (100). Found, %: C 46.21; H 5.95; N 22.19. $C_{12}H_{19}N_5O_3S$. Calculated, %: C 45.99; H 6.11; N 22.35.

***S*-(3-Isobutyl-8-oxo-3,4,5,6,7,8-hexahydro[1,2,3]triazolo-[4,5-*e*][1,4]diazepin-5-yl)ethanethioate (6b)**. Yield 1.11 g (98%, method I), 1.35 g (95%, method II), white powder, mp 256–257°C. IR spectrum, ν, cm^{-1}: 1670 (C=O), 1715 (C=O), 3317, 3447 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.77–0.85 (6H, m, $CH_2CH(C\underline{H}_3)_2$); 1.97–2.05 (1H, m, $CH_2C\underline{H}Me_2$); 2.34 (3H, s, $COCH_3$); 3.31–3.53 (2H, m, 6-CH_2); 3.95 (2H, d, *J* = 7.2, $C\underline{H}_2CH(CH_3)_2$); 5.61–5.70 (1H, m, 5-CH); 7.72–7.79 (1H, m, NH); 8.07 (1H, d, *J* = 3.6, NH). ^{13}C NMR spectrum, δ, ppm: 19.7 (2C); 28.5; 31.4; 45.2; 52.8; 60.7; 123.6; 140.9; 163.4; 194.9. Mass spectrum, *m*/*z* (I_{rel}, %): 284 $[M+H]^+$ (100). Found, %: C 46.85; H 6.01; N 24.79. $C_{11}H_{17}N_5O_2S$. Calculated, %: C 46.63; H 6.05; N 24.72.

[(8-Oxo-3-phenyl-3,4,5,6,7,8-hexahydro[1,2,3]triazolo[4,5-*e*][1,4]diazepin-5-yl)sulfanyl]acetic acid (6c). Yield 1.24 g (97%, method I), 1.49 g (93%, method II), white powder, mp 206–208°C. IR spectrum, ν, cm^{-1}: 1675 (C=O), 2530–2851 (CO_2H), 3302, 3391 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.29–3.51 (4H, m, 6-CH_2, SCH_2); 4.97–5.04 (1H, m, 5-CH); 7.53–7.64 (5H, m, H Ph); 7.74–7.78 (1H, m, NH); 7.93 (1H, d, *J* = 3.6, NH); 12.59 (1H, br. s, CO_2H). ^{13}C NMR spectrum, δ, ppm: 31.7; 45.2; 61.5; 125.6 (2C); 130.0; 130.3 (2C); 134.9; 140.9; 163.6; 172.2. Mass spectrum, *m*/*z* (I_{rel}, %): 320 $[M+H]^+$ (96). Found, %: C 48.69; H 3.98; N 22.21. $C_{13}H_{13}N_5O_3S$. Calculated, %: C 48.90; H 4.10; N 21.93.

***S*-[3-(4-Chlorophenyl)-8-oxo-3,4,5,6,7,8-hexahydro-[1,2,3]triazolo[4,5-*e*][1,4]diazepin-5-yl]ethanethioate (6d)**. Yield 1.31 g (97%, method I), white powder, mp 272–274°C. IR spectrum, ν, cm^{-1}: 1668 (C=O), 1721 (C=O), 3323, 3449 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.33 (3H, s, $COCH_3$); 3.39–3.48 (1H, m) and 3.56–3.65 (1H, m, 6-CH_2); 5.57–5.62 (1H, m, 5-CH); 7.54 (2H, d, *J* = 8.8, H Ar); 7.66 (2H, d, *J* = 8.8, H Ar); 7.88–7.96 (1H, m, NH); 8.04 (1H, d, *J* = 3.6, NH). ^{13}C NMR spectrum, δ, ppm: 31.4; 44.8; 60.9; 123.8; 127.7 (2C); 130.3 (2C); 133.7; 134.6; 141.5; 163.1; 194.7. Mass spectrum, *m*/*z* (I_{rel}, %): 338 $[M+H]^+$ (100). Found, %: C 46.01; H 3.46; N 21.01. $C_{13}H_{12}ClN_5O_2S$. Calculated, %: C 46.23; H 3.58; N 20.73.

5-[(4-Chlorophenyl)sulfanyl]-3-(4-methylphenyl)-4,5,6,7-tetrahydro[1,2,3]triazolo[4,5-*e*][1,4]diazepin-8(3*H*)-one (6e). Yield 1.48 g (96%, method I), white powder, mp 281–284°C. IR spectrum, ν, cm^{-1}: 1658 (C=O), 3298, 3394 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.38 (3H, s, CH_3); 3.41–3.51 (1H, m) and 3.54–3.67 (1H, m, 6-CH_2); 5.23–5.31 (1H, m, 5-CH); 7.24–7.50 (9H, m, NH, H Ar); 7.85 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 21.4; 45.8; 64.1; 122.9; 123.2 (2C); 123.9; 127.8 (2C); 130.1 (2C); 130.9 (2C); 132.1; 133.4; 141.5; 163.1; 164.7. Mass spectrum, *m*/*z* (I_{rel}, %): 386 $[M+H]^+$ (99). Found, %: C 55.89; H 4.06; N 18.34. $C_{18}H_{16}ClN_5OS$. Calculated, %: C 56.03; H 4.18; N 18.15.

5-[(2,4-Dichlorophenyl)sulfanyl]-3-(4-methoxyphenyl)-4,5,6,7-tetrahydro[1,2,3]triazolo[4,5-*e*][1,4]diazepin-8(3*H*)-one (6f). Yield 1.64 g (94%, method I), white powder, mp 289–292°C. IR spectrum, ν, cm^{-1}: 1657 (C=O), 3309, 3407 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.45–3.54 (1H, m) and 3.60–3.71 (1H, m, 6-CH_2); 3.82 (3H, s, OCH_3); 5.32–5.43 (1H, m, 5-CH); 7.09 (2H, d, *J* = 8.4, H Ar); 7.31–7.47 (3H, m, H Ar); 7.65–7.77 (2H, m, H Ar); 7.81 (1H, d, *J* = 3.6, NH); 7.87–7.93 (1H, m, NH). ^{13}C NMR spectrum, δ, ppm: 45.7; 56.1; 64.2; 115.3 (2C); 123.9; 127.4; 127.7 (2C); 128.2; 129.6; 131.9; 133.6; 136.6; 137.6; 140.9; 160.5; 163.5. Mass spectrum, *m*/*z* (I_{rel}, %): 437 $[M+H]^+$ (99). Found, %: C 49.78; H 4.34; N 15.89. $C_{18}H_{15}Cl_2N_5O_2S$. Calculated, %: C 49.55; H 3.47; N 16.05.

***S*-[3-(4-Methoxyphenyl)-8-oxo-3,4,5,6,7,8-hexahydro-[1,2,3]triazolo[4,5-*e*][1,4]diazepin-5-yl]ethanethioate (6g)**. Yield 1.31 g (98%, method I), white powder, mp 265–267°C. IR spectrum, ν, cm^{-1}: 1658 (C=O), 1727 (C=O), 3323, 3452 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.33 (3H, s, $COCH_3$); 3.38–3.49 (1H, m) and 3.52–3.63 (1H, m, 6-CH_2); 3.84 (3H, s, OCH_3); 5.52–5.59 (1H, m, 5-CH); 7.13 (2H, d, *J* = 8.4, H Ar); 7.40 (2H, d, *J* = 8.4, H Ar); 7.79 (1H, d, *J* = 3.6, NH); 7.83–7.89 (1H, m, NH). ^{13}C NMR spectrum, δ, ppm: 30.6; 45.8; 56.1; 60.5; 60.9; 115.3 (2C); 123.5; 127.5 (2C); 141.4; 160.4; 163.2; 194.8. Mass spectrum, *m*/*z* (I_{rel}, %): 334 $[M+H]^+$ (99). Found, %: C 50.28; H 4.46; N 21.33. $C_{14}H_{15}N_5O_3S$. Calculated, %: C 50.44; H 4.54; N 21.01.

5-[(4-Methylphenyl)sulfanyl]-3-(4-nitrophenyl)-4,5,6,7-tetrahydro[1,2,3]triazolo[4,5-*e*][1,4]diazepin-8(3*H*)-one

(6h). Yield 1.52 g (96%, method I), 1.82 g (92%, method II), white powder, mp 275–278°C. IR spectrum, ν, cm^{-1}: 1662 (C=O), 3303, 3396 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.29 (3H, s, CH_3); 3.44–3.55 (1H, m) and 3.60–3.72 (1H, m, 6-CH_2); 5.20–5.29 (1H, m, 5-CH); 7.17 (2H, d, *J* = 8.0, H Ar); 7.37 (2H, d, *J* = 8.0, H Ar); 7.72 (2H, d, *J* = 8.8, H Ar); 7.91–7.99 (1H, m, NH); 8.20 (1H, d, *J* = 3.6, NH); 8.38 (2H, d, *J* = 8.8, H Ar). ^{13}C NMR spectrum, δ, ppm: 21.1; 45.5; 65.1; 124.7; 125.5 (2C); 129.8; 130.2 (2C); 134.0; 140.1; 140.9; 147.7; 163.4. Mass spectrum, *m*/*z* (I_{rel}, %): 397 $[M+H]^+$ (100). Found, %: C 54.29; H 3.98; N 21.44. $C_{18}H_{16}N_6O_3S$. Calculated, %: C 54.54; H 4.07; N 21.20.

Methyl 3-[3-(1-methyl-*1H*-pyrazol-3-yl)-8-oxo-3,4,5,6,7,8-hexahydro[1,2,3]triazolo[4,5-*e*][1,4]diazepin-5-yl)-sulfanyl]propanoate (6i). Yield 1.35 g (91%, method I), white powder, mp 269–272°C. IR spectrum, ν, cm^{-1}: 1669 (C=O), 1731–1764 (CO_2Me), 3319, 3420 (N–H). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.61–2.71 (2H, m, CH_2); 2.78–2.87 (2H, m, CH_2); 3.39–3.50 (1H, m) and 3.57–3.62 (1H, m, 6-CH_2); 3.55 (3H, s, OCH_3); 5.19–5.24 (1H, m, 5-CH); 6.60 (1H, s, H Ar); 7.69–7.75 (1H, m, NH); 7.95 (1H, s, H Ar); 8.16 (1H, d, *J* = 3.6, NH). ^{13}C NMR spectrum, δ, ppm: 24.6; 34.9; 45.5; 51.7; 51.9; 60.5; 98.7; 123.7; 133.8; 140.2; 144.6; 163.3; 172.5. Mass spectrum, *m*/*z* (I_{rel}, %): 352 $[M+H]^+$ (98). Found, %: C 44.29; H 4.76; N 28.13. $C_{13}H_{17}N_7O_3S$. Calculated, %: C 44.44; H 4.88; N 27.90.

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