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2,3-BENZODIAZEPINE-1-THIONE IN THE SYNTHESIS OF SUBSTITUTED AND HETERO-ANNELATED 2,3-BENZODIAZEPINES

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A series of S-substituted and 1,2-annelated derivatives of 2,3-benzodiazepine has been obtained on the basis of 2,3-benzodiazepine-1-thione.

Keywords: 2,3-benzodiazepin-1-one, 2,3-benzodiazepine-1-thione, 4-(4-methoxyphenyl)-5H-1,2,4-triazolo-2,3-benzodiazepin-1-ylhydrazine, alkylation, acylation, cyclization.

In current medicinal chemistry the modification of the structure of 2,3-benzodiazepine is considered to be one of the promising directions for the creation of new medicinal substances, stimulating the higher nervous activity (brain integrative functions) – intellect, memory, ability to learn, increased stability of the organism in extreme conditions [1, 2]. In contrast to 1,4- and 1,5-benzodiazepines, long known as neuroleptics and sedatives, tranquilizers and anxiolytics based on 2,3-benzodiazepines do not as a rule possess sedative and narcopotentiating properties, they show nootropic properties.

Most of the successes in the chemistry and pharmacology of derivatives of 2,3-benzodiazepines are based on modification of 1-aryl-2,3-benzodiazepin-4-ones at the N(3)–C(4) fragment of the seven-membered ring [3,4]. In contrast, compounds with the isomeric structure – 4-aryl-2,3-benzodiazepin-1-ones – remain practically uninvestigated until now: only their synthesis and bromination are known [6]. In the present work the possibility of functionalization and annelation in the 2,3-benzodiazepine series based on 4-aryl-2,3-benzodiazepine-1-thione has been studied.

4-(4-Methoxyphenyl)-2,5-dihydro-5H-2,3-benzodiazepin-1-one (**2**) was obtained by recyclization of isocoumarin **1** with hydrazine hydrate. Attempts to replace the oxygen atom of the amide fragment with an atom of sulfur in the benzodiazepinone **2** using phosphorus sulfide in pyridine did not lead to the expected thio-derivative probably because of the constriction of the seven-membered ring which occurs readily in acid media [7]. On the other hand, use of the Lawson's reagent in toluene gave 4-(4-methoxyphenyl)-2,5-dihydro-5H-2,3-benzodiazepine-1-thione (**3**) in 95% yield. Substitution of the sulfur atom in the thione **3** with the hydrazine unit occurs practically quantitatively on boiling with hydrazine hydrate to give the benzodiazepin-4-ylhydrazine **4**.

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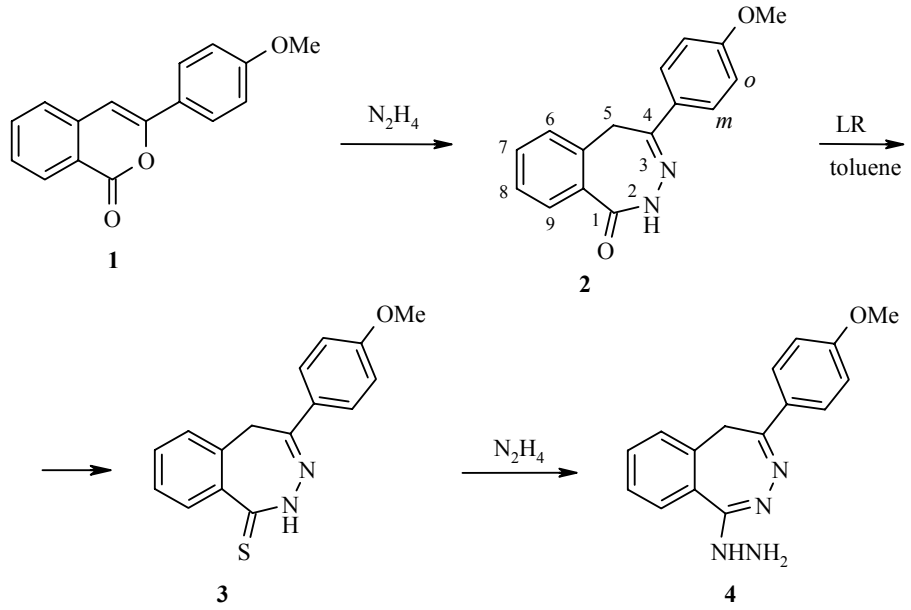
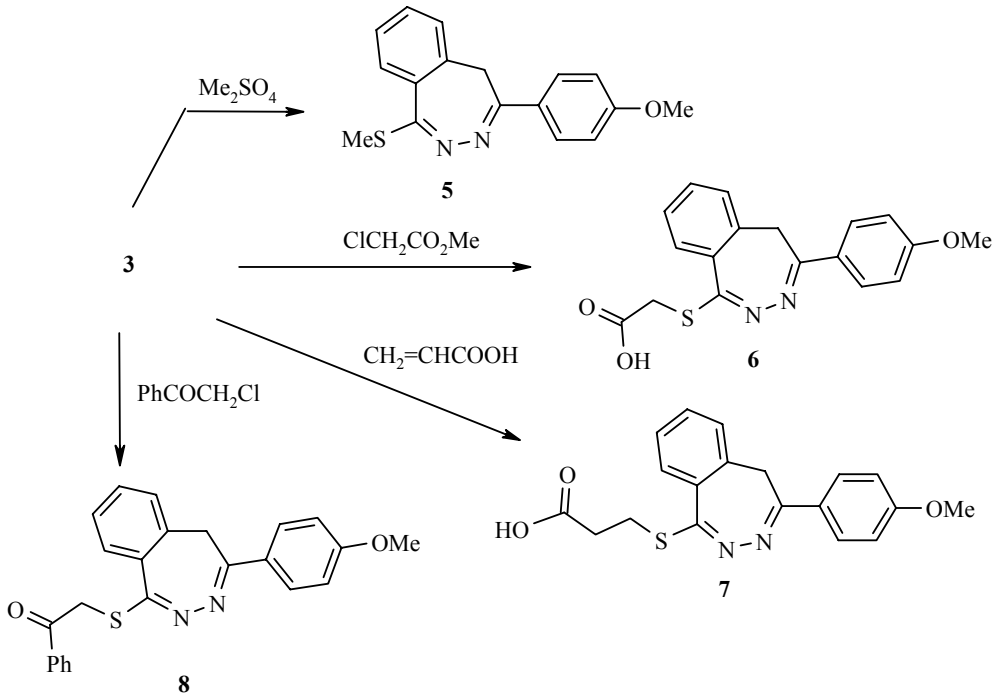
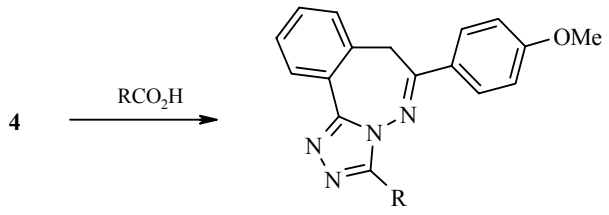


LR = Lawson's reagent

The sulfur atom in thione **3** is readily alkylated with dimethyl sulfate, haloalkanes (methyl chloroacetate, ω-chloroacetophenone), and acrylic acid. The product of alkylation with ethyl chloroacetate was isolated from the reaction in the form of the acid **6**.



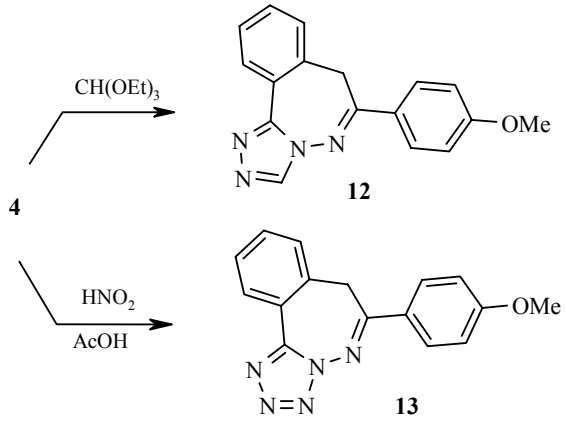
The reactions of compound **4** with a variety of reagents were studied. On reaction with aliphatic acids it formed 3-R-6-(4-methoxyphenyl)-7H-1,2,4-triazolo[3,4-*a*][2,3]benzodiazepines **9-11**. Identification of the products of the reaction of hydrazine **4** with aromatic acids under the same conditions was unsuccessful.



9–11

9 R = Me, **10** R = Et, **11** R = 3,4-$(MeO)_2C_6H_3CH_2$

Reaction of hydrazine **4** with triethyl orthoformate gave 6-(4-methoxyphenyl)-7H-1,2,4-triazolo-[3,4 *a*][2,3]benzodiazepine (**12**). Nitrosation of the hydrazine **4** with acetic acid–sodium nitrite led to intramolecular cyclization to 6-(4-methoxyphenyl)-7H-tetrazolo[5,4-*a*][2,3]benzodiazepine (**13**).



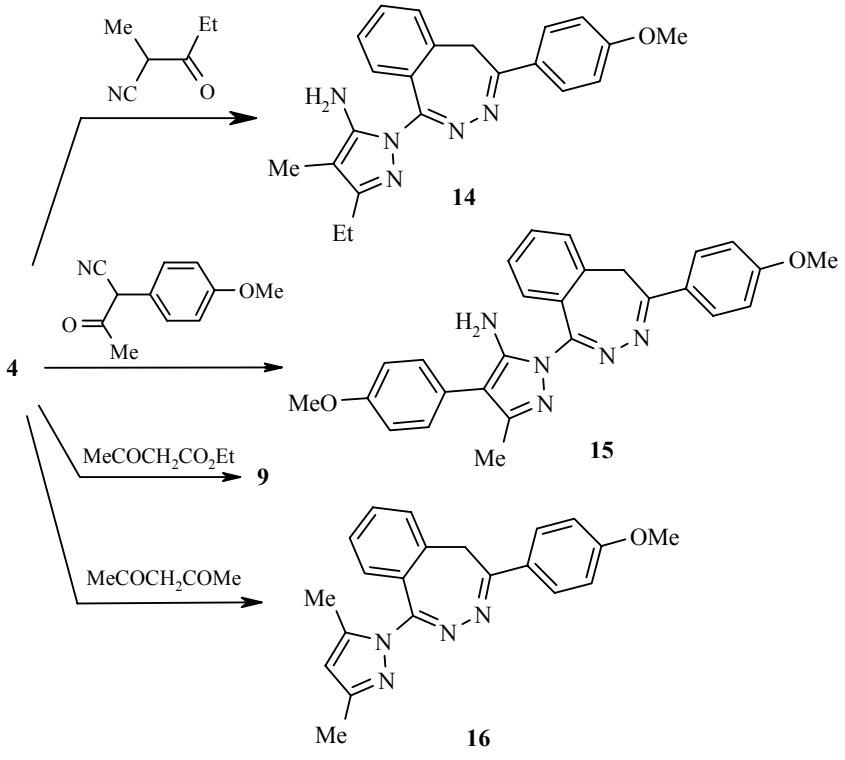
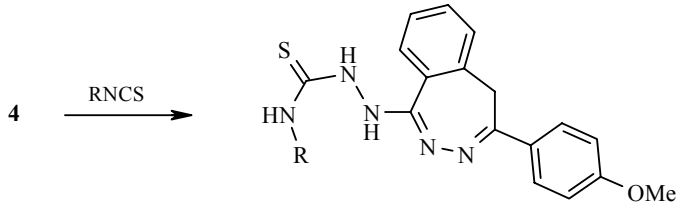


Table 1. IR Spectra of Compounds **2-18**

Compound	ν, cm^{-1}
2	3170 (C=O), 3050 (C–N), 2900, 1640 (C=N), 1600 (C=C), 1340, 1250
3	2920 (C=S), 1600 (C=C), 1350, 1250, 1190, 1025, 825, 780
4	2960 (C=N), 2840 (C=N), 1600 (C=C), 1350, 1250, 1140, 1020, 820
5	3050 (C=N), 3000 (C=N), 2910 (C–S), 2820 (C–S), 1600 (C=C), 1510, 1250, 1180, 1010, 770
6	2920 (C–S), 1735, 1600 (C=C), 1490, 1250, 1010, 760
7	2920 (C–S), 1710, 1600 (C=C), 1300, 1250, 1190, 1010, 760
8	3065 (C=N), 2945 (C–S), 1680, 1600 (C=C), 1320, 1250, 1190, 1040, 990, 775
9	3050 (C=N), 2900 (C=N), 2820 (C=N), 1600 (C=C), 1460, 1250, 1150
10	2960 (C=N), 2920 (C=N), 2810 (C=N), 1600 (C=C), 1450, 1250, 1150
11	2900 (C=N), 2820 (C=N), 1600 (C=C), 1500, 1450, 1250, 1010
12	3050 (C=N), 2920 (C=N), 2820 (C=N), 1600 (C=C), 1480, 1360, 1250, 1170, 1030
13	2900 (C=N); 2830 (C=N), 1600 (C=C), 1250, 1180, 1010
14	2950 (C=N), 2900 (C=N), 1600 (C=C), 1400, 1250, 1010
15	2920 (C=N), 2830 (C=N), 1600 (C=C), 1400, 1250, 1180, 1010
16	2900 (C=N), 1600 (C=C), 1390, 1250, 1010
17	3120 (C=N), 2900 (C=S), 1600 (C=C), 1250, 1010, 800, 760
18	1600 (C=C), 1520, 1410, 1250, 1370, 1010, 820, 700

Reaction of diazepin-1-ylhydrazine **4** with 2-methyl-3-oxopentane nitrile or 2-(4-methyoxyphenyl)-3-oxobutyronitrile gave the aminotriazoles **14** and **15**, and with acetylacetone gave the pyrazole **16**. Reaction with ethyl acetoacetate did not give the expected pyrazalone, but the triazolodiazepine **9** was isolated from the reaction mixture in high yield.

The reaction of *p*-tolyl isothiocyanate and benzoyl isothiocyanate with diazepin-1-ylhydrazine **4** gave the thiosemicarbazides **17** and **18**, but attempts at further cyclization by standard methods did not give the expected derivatives of triazolobenzodiazepine.



17, 18

17 R = 4-MeC_6H_4, **18** R = PhCO

The results obtained indicate the promise of using derivatives of 2,3-benzodiazepin-1-one(thione) in the synthesis of new heterocyclic systems and new pharmacologically attractive compounds, suitable for modification by the methods of combinatorial chemistry.

EXPERIMENTAL

^{1}H NMR spectra were measured in DMSO-d_6 with TMS as internal standard with a Varian Gemini (200 MHz) instrument and IR spectra in KBr tablets were measured with an IR-75 instrument. Melting points were measured with a Boetius instrument and were not corrected. 3-(4-Methoxyphenyl)isocoumarin (**1**) was prepared by a method described in [8].

Table 2. ^{1}H NMR Spectra of Compounds **2-18**

Compound	Chemical shifts, δ, ppm (*J*, Hz)
2	3.8 (3H, s, OCH_3); 4.0 (2H, s, H-5); 6.0 (2H, d, *J* = 8.8, H-*o*); 7.6-7.25 (3H, m, H-6,7,8); 7.8 (1H, d, *J* = 7.3, H-9); 7.83 (2H, d, *J* = 8.8, H-*m*); 10.95 (1H, s, NH)
3	3.7 (2H, s, H-5); 3.8 (3H, s, OCH_3); 7.0 (2H, d, *J* = 8.8, H-*o*); 7.6-7.2 (3H, m, H-6,7,8); 7.95 (2H, d, *J* = 8.8, H-*m*); 8.1 (1H, d, *J* = 7.3, H-9); 13.2 (1H, s, NH)
4	3.8 (3H, s, OCH_3); 4.0 (2H, s, H-5); 6.6 (3H, br. s, $NH-NH_2$); 6.9 (2H, d, *J* = 8.8, H-*o*); 7.45-7.15 (3H, m, H-6,7,8); 7.65 (1H, d, *J* = 7.3, H-9); 7.8 (2H, d, *J* = 8.8, H-*m*)
5	2.6 (3H, s, SCH_3); 3.1 (1H, d, *J* = 13.3, H-5); 3.8 (3H, s, OCH_3); 4.2 (1H, d, *J* = 13.3, H-5); 6.9 (2H, d, *J* = 8.8, H-*o*); 7.55-7.3 (3H, m, H-6,7,8); 7.65 (1H, d, *J* = 7.3, H-9); 7.85 (2H, d, *J* = 8.8, H-*m*)
6	3.1 (1H, d, *J* = 13.3, H-5); 3.8 (3H, s, OCH_3); 4.2 (1H, d, *J* = 13.3, H-5); 6.9 (2H, d, *J* = 8.8, H-*o*); 7.55-7.3 (3H, m, H-6,7,8); 7.65 (1H, d, *J* = 7.3, H-9); 7.85 (2H, d, *J* = 8.8, H-*m*)
7	2.76 (2H, t, *J* = 6.9, CH_2); 3.1 (1H, d, *J* = 12.9, H-5); 3.36 (2H, t, *J* = 6.9, CH_2); 3.8 (3H, s, OCH_3); 4.2 (1H, d, *J* = 12.9, H-5); 6.9 (2H, d, *J* = 8.8, H-*o*); 7.55-7.3 (3H, m, H-6,7,8); 7.67 (1H, d, *J* = 5.6, H-9); 7.85 (2H, d, *J* = 8.8, H-*m*)
8	3.1 (1H, d, *J* = 13.3, H-5); 3.8 (3H, s, OCH_3); 4.2 (1H, d, *J* = 13.3, H-5); 4.8 (2H, dd, J_1 = 17.7, J_2 = 6.6, CH_2); 7.8 (2H, d, *J* = 8.8, H-*o*); 7.65-7.25 (6H, m, H arom); 7.68 (1H, d, *J* = 7.3, H-9); 7.8 (2H, d, *J* = 8.8, H-*m*); 8.1 (2H, d, *J* = 8.8, H arom)
9	2.56 (3H, s, CH_3); 3.85 (3H, s, OCH_3); 4.05 (2H, s, H-5); 7.0 (2H, d, *J* = 8.8, H-*o*); 7.65-7.35 (3H, m, H-6,7,8); 7.95 (1H, d, *J* = 7.3, H-9); 8.05 (2H, d, *J* = 8.8, H-*m*)
10	1.44 (3H, t, *J* = 6.8, CH_3); 2.95 (2H, q, *J* = 6.8, CH_2); 3.85 (3H, s, OCH_3); 4.05 (2H, s, H-5); 7.0 (2H, d, *J* = 7.3, H-*o*); 7.65-7.35 (3H, m, H-6,7,8); 7.95 (1H, d, *J* = 7.3, H-9); 8.05 (2H, d, *J* = 8.2, H-*m*)
11	3.68 (3H, s, OCH_3); 3.72 (3H, s, OCH_3); 3.85 (3H, s, OCH_3); 3.97 (2H, s, CH_2); 4.22 (2H, s, H-5); 6.9-6.7 (3H, m, H arom); 7.0 (2H, d, *J* = 7.3, H-*o*); 7.65-7.35 (3H, m, H arom); 7.95 (1H, d, *J* = 7.3, H-9); 8.05 (2H, d, *J* = 8.2, H-*m*)
12	3.85 (3H, s, OCH_3); 4.1 (2H, s, CH_2); 7.05 (2H, d, *J* = 8.8, H-*o*); 7.7-7.4 (3H, m, H-6,7,8); 8.0 (1H, d, *J* = 7.3, H-9); 8.1 (2H, d, *J* = 8.8, H-*m*); 8.9 (1H, s, H arom)
13	3.85 (3H, s, OCH_3); 4.15 (2H, s, H-5); 7.05 (2H, d, *J* = 8.8, H-*o*); 7.8-7.5 (3H, m, H-6,7,8); 8.1 (1H, d, *J* = 7.3, H-9); 8.2 (2H, d, *J* = 8.8, H-*m*)
14	1.1 (3H, t, *J* = 6.8, CH_3); 1.89 (3H, s, CH_3); 2.38 (2H, q, *J* = 6.8, CH_2); 3.15 (1H, d, *J* = 14, H-5); 3.8 (3H, s, OCH_3); 4.4 (1H, d, *J* = 14, H-5); 5.91 (2H, s, NH_2); 6.95 (2H, d, *J* = 8.8, H-*o*); 7.6-7.33 (4H, m, H-6,7,8); 7.95 (2H, d, *J* = 8.8, H-*m*)
15	2.08 (3H, s, CH_3); 3.15 (1H, d, *J* = 13.3, H-5); 3.8 (3H, s, OCH_3); 4.4 (1H, d, *J* = 13.3, H-5); 6.05 (2H, s, NH_2); 6.9 (2H, d, *J* = 6.6, CH); 6.95 (2H, d, *J* = 8.8, H-*o*); 7.6-7.33 (4H, m, H-6,7,8); 7.95 (2H, d, *J* = 8.8, H-*m*)
16	2.15 (3H, s, CH_3); 2.65 (3H, s, CH_3); 3.05 (1H, d, *J* = 13.3, 5-CH); 3.8 (3H, s, OCH_3); 4.5 (1H, d, *J* = 13.3, 5-CH); 6.05 (1H, s, CH); 6.95 (2H, d, *J* = 8.8, CH); 7.15 (1H, d, *J* = 7.3, 6-CH); 7.4-7.35 (3H, m, 7,8,9-CH); 7.95 (2H, d, *J* = 8.8, CH)
17	3.8 (3H, s, OCH_3); 4.1 (2H, s, H-5); 7.0 (2H, d, *J* = 8.8, H-*o*); 7.06 (2H, d, *J* = 4, CH); 7.34 (2H, d, *J* = 4, CH); 7.66-7.38 (3H, m, H-6,7,8); 7.86 (1H, d, *J* = 7.3, H-9); 8.35 (2H, d, *J* = 8.8, H-*m*); 9.4 (1H, s, NH); 13.8 (1H, s, NH)
18	3.8 (3H, s, OCH_3); 4.1 (2H, s, H-5); 6.7 (2H, d, *J* = 8.8, H-*o*); 7.8-7.3 (7H, m, CH); 7.86 (2H, d, *J* = 8.8, H-*m*); 8.04 (2H, d, *J* = 7.4, CH); 10.4 (1H, s, NH); 11.1 (1H, s, NH); 12.84 (1H, s, NH)

4-(4-Methoxyphenyl)-2,5-dihydro-5H-2,3-benzodiazepin-1-one (2). A mixture of isocoumarin **1** (25.2 g, 100 mmol), 2-propanol (100 ml), and hydrazine hydrate (6 ml, 120 mmol) was boiled for 2 h. After cooling, the precipitate was filtered off, washed with 2-propanol, and dried to give diazepinone **2** (25.2 g, 94%); mp 190-191°C. Found, %: C 72.10; H 5.3; N 10.40. $C_{16}H_{14}N_2O_2$. Calculated, %: C 72.17; H 5.30; N 10.52.

4-(4-Methoxyphenyl)-2,5-dihydro-5H-2,3-benzodiazepine-1-thione (3). A mixture of compound **2** (30 g, 112 mmol) in toluene (200 ml) was heated to boiling and Lawson's reagent (22 g) was added. The undissolved compound **2** relatively rapidly dissolved and thione **3** began to precipitate. The mixture was boiled for 30 min, cooled, compound **3** was filtered off and washed on the filter with toluene. Yield 30 g (95%); mp 205-206°C. Found, %: C 67.80; H 4.90; N 9.90; S 11.30. $C_{16}H_{14}N_2OS$. Calculated, %: C 68.06; H 5.00; N 9.92; S 11.36.

4-(4-Methoxyphenyl)-2,5-dihydro-5H-2,3-benzodiazepin-1-ylhydrazine (4). A mixture of thione **3** (1 g, 3.5 mmol) and hydrazine hydrate (5 ml) were boiled for 30 min, cooled, the precipitate was filtered off, washed with water and a small amount of methanol, to give the hydrazine **4** (0.9 g, 91%); mp 153-154°C. Found, %: C 68.40; H 5.80; N 20.10; $C_{16}H_{16}N_4O$. Calculated, %: C 68.55; H 5.75; N 19.99.

3-R-6-(4-Methoxyphenyl)-7H-1,2,4-triazolo[3,4-*a*][2,3]benzodiazepines 9-11 (General Method). A mixture of hydrazine **4** (0.6 g, 2.15 mmol), 1 drop conc. HCl, 2-propanol (2 ml) and the corresponding acid (2.6 mmol) was boiled for 6 h and poured into water (50 ml), and made basic with NaOH to pH 9-10. The oil which precipitated crystallized rapidly. The crystalline precipitate was filtered off, dried, and recrystallized from 1:1 benzene–hexane.

6-(4-Methoxyphenyl)-3-methyl-7H-1,2,4-triazolo[3,4-*a*]benzodiazepine (9). Yield 0.325 g (49%); mp 184-185°C. Found, %: C 70.95; H 5.2; N 18.3. $C_{18}H_{16}N_4O$. Calculated, %: C 71.04; H 5.30; N 18.41.

3-Ethyl-6-(methoxyphenyl)-7H-1,2,4-triazolo[3,4-*a*][2,3]benzodiazepine (10). Yield 0.323 g (48%); mp 130-131°C. Found, %: C 71.65; H 5.75; N 17.50. $C_{19}H_{18}N_4O$. Calculated, %: C 71.68; H 5.70; N 17.60.

3-(3,4-Dimethoxybenzyl)-6-(4-methoxyphenyl)-7H-1,2,4-triazolo[3,4-*a*][2,3]benzodiazepine (11). Yield 0.325 g (30%); mp 130-131°C. Found, %: C 70.90; H 5.52; N 12.68. $C_{26}H_{24}N_4O_3$. Calculated, %: C 70.89; H 5.49; N 12.72.

6-(4-Methoxyphenyl)-7H-1,2,4-triazolo[3,4-*a*][2,3]benzodiazepine (12). A mixture of compound **4** (0.5 g, 1.8 mmol) and trimethyl orthoformate (5 ml, 33.8 mmol) was boiled for 4 h. A fine crystalline precipitate separated during this time. After cooling the precipitate was filtered off and washed with a small amount of methanol to give compound **12** (0.4 g, 77%); mp 218-219°C. Found, %: C 70.40; H 4.83; N 19.40. $C_{17}H_{14}N_4O$. Calculated, %: C 70.33; H 4.86; N 19.30.

6-(4-Methoxyphenyl)-7H-tetrazolo[5,4-*a*][2,3]benzodiazepine (13). To a solution of hydrazine **4** (0.25 g, 0.9 mmol) in acetic acid (3 ml) $NaNO_2$ (0.07 g, 1 mmol) was added with vigorous stirring, the flask was closed tightly, and stirring was continued. After 30 min the precipitate formed was filtered off, washed with water and a small amount of methanol to give compound **13** (0.12 g, 46%); mp 139-141°C. Found, %: C 65.94; H 4.52; N 24.00. $C_{16}H_{13}N_5O$. Calculated, %: C 65.97; H 4.50; N 24.04.

1-(3,5-Dimethyl-1H-pyrazol-1-yl)-4-(4-methoxyphenyl)-5H-2,3-benzodiazepine (16). A mixture of compound **4** (1 g, 3.6 mmol), dioxane (5 ml), and acetylacetone (0.5 ml, 5 mmol) was boiled for 30 min and then poured into water (40 ml). The precipitate formed was filtered off, dried, and crystallized from 2-propanol to give compound **16** (0.9 g, 76%); mp 208-209°C. Found, %: C 73.21; H 5.83; N 16.25. $C_{21}H_{20}N_4O$. Calculated, %: C 73.23; H 5.85; N 16.27.

1-(5-Amino-3-ethyl-4-methylpyrazol-1-yl)-4-(4-methoxyphenyl)-5H-2,3-benzodiazepine (14) and 1-(5-Amino-4-(4-methoxyphenyl)-3-methylpyrazol-1-yl)-4-(4-methoxyphenyl)-5H-2,3-benzodiazepine (15) (General Method). A mixture of compound **4** (1 g, 3.6 mmol), 1 drop conc. HCl, 2-propanol (5 ml), and 2-methyl-3-oxopentonitrile (3.8 mmol) or 2-(4-methoxyphenyl)-3-oxobutyronitrile (3.8 mmol) was boiled for 3 h and then poured into water (30 ml). The crystalline precipitate was filtered off, dried, and crystallized from benzene.

1-(5-Amino-3-ethyl-4-methylpyrazol-1-yl)-4-(4-methoxyphenyl)-5H-2,3-benzodiazepine (14). Yield 0.9 g, 67%); mp 195-196°C. Found, %: C 70.74; H 6.20; N 18.73. $C_{22}H_{23}N_5O$. Calculated, %: C 70.76; H 6.21; N 18.75.

1-(5-Amino-4-(4-methoxyphenyl)-3-methylpyrazol-1-yl)-4-(4-methoxyphenyl)-5H-2,3-benzodiazepine (15). Yield 1 g (62%); mp 177-179°C. Found, %: C 71.81; H 5.55; N 15.53. $C_{27}H_{25}N_5O_2$. Calculated, %: C 71.82; H 5.58; N 15.51.

4-(4-Methoxyphenyl)-1-(methylthio)-5H-2,3-benzodiazepine (5). Dimethyl sulfate (0.4 ml) was added with vigorous stirring to a mixture of compound **3** (1 g, 3.6 mmol) and ground KOH (0.5 g) in acetone (10 ml), stirring was continued for 1 h, and then poured into water (50 ml). The precipitate formed was filtered off, washed with water and a small amount of methanol to give compound **5** (0.95 g, 90%); mp 170-171°C. Found, %: C 68.87; H 5.42; N 9.50; S 10.79. $C_{17}H_{16}N_2OS$. Calculated, %: C 68.89; H 5.44; N 9.45; S 10.82.

[4-(4-methoxyphenyl)-5H-2,3-benzodiazepin-1-yl]thioacetic Acid (6). Methyl monochloroacetate (0.6 ml, 5.5 mmol) was added with vigorous stirring to a mixture of compound **3** (1 g, 3.6 mmol) and ground NaOH (0.44 g) in acetone (10 ml), stirring was continued for 1 h, then the mixture was added to water (50 ml). The solution was acidified with acetic acid (2 ml), the precipitate which formed was filtered off and washed with water to give compound **6** (1.1 g, 92%); mp 127-128°C. Found, %: C 63.50; H 4.72; N 8.25; S 9.41. $C_{18}H_{16}N_2O_3S$. Calculated, %: C 63.51; H 4.74; N 8.23; S 9.42.

3-[4-(4-Methoxyphenyl)-5H-2,3-benzodiazepin-1-yl]thiopropionic acid (7). A mixture of compound **3** (1g, 3.6 mmol) and acrylic acid (0.5 ml, 7 mmol) was boiled in toluene (5 ml), the solvent was evaporated, methanol (3 ml) was added to the residue, the mixture was heated to boiling then cooled to room temperature. The fine white precipitate was filtered off and washed with a small amount of methanol to give compound **7** (1.1 g, 87%); mp 158-159°C. Found, %: C 64.41; H 5.14; N 7.88; S 9.06. $C_{19}H_{18}N_2O_3S$. Calculated, %: C 64.39; H 5.12; N 7.90; S 9.05.

2-[4-(4-Methoxyphenyl)-5H-2,3-benzodiazepin-1-yl]thio-1-phenylethanone (8). γ-Chloroacetophenone (0.6 g, 3.9 mmol) was added with vigorous stirring to a mixture of compound **3** (1 g, 3.6 mmol) and ground KOH (0.4 g) in acetone (10 ml), stirring was continued for 1 h and the mixture added to water (50 ml). The precipitate formed was filtered off, washed with water and a small amount of methanol to give compound **8** (1.2 g, 84%); mp 135-136°C. Found, %: C 72.00; H 5.05; N 7.01; S 9.06. $C_{24}H_{20}N_2O_2S$. Calculated, %: C 71.98; H 5.03; N 6.99; S 7.94.

2-[4-(4-Methoxyphenyl)-5H-2,3-benzodiazepin-1-yl]-N-(4-methylphenyl)hydrazincarbothioamide (17). A mixture of compound **4** (1 g, 3.6 mmol), 4-methylphenylisothocyanate (0.6 g, 4 mmol), and 1 drop of triethylamine was boiled for 8 h. After cooling the crystals which formed were filtered off and washed with a small amount of 2-propanol to give compound **17** (1 g, 67%); mp 170-171°C. Found, %: C 67.12; H 5.38; N 16.33; S 7.47. $C_{24}H_{23}N_5OS$. Calculated, %: C 67.11; H 5.40; N 16.30; S 7.46.

1-({2-[4-(4-Methoxyphenyl)-5H-2,3-benzodiazepin-1-yl]hydrazino}carbothioyl)benzamide (18). Benzoyl chloride (0.7 ml) was added to a mixture of KCNS (0.52 g) and anhydrous acetonitrile (10 ml) and stirred for 30 min. Then compound **4** (1.5 g, 5.4 mmol) was added to the mixture and stirring was continued for a further 2 h. The mixture was poured into water (50 ml) and the yellow residue was filtered off, It was washed with water and a small amount of methanol, and dried to give compound **18** (2.1 g, 88%); mp 142-144°C. Found, %: C 65.01; H 4.75; N 15.80; S 7.20. $C_{24}H_{21}N_5O_2S$. Calculated, %: C 64.99; H 4.77; N 15.79; S 7.22.

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