A Two-Step Synthesis of 1*H*-Tetrazolyl-1*H*-1,4-benzonitriles and 1*H*-Tetrazolyl-benzo[*b*][1,4]diazepines

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Abstract: A two-step synthetic protocol for the title heteroannulated diazepines has been developed. The approach includes a pseudo five-component isocyanide-based condensation reaction between diamines, ketones, isocyanides and trimethylsilyl azide and proceeds in good yields.

Key words: diazepine, tetrazole, multicomponent reactions, isocyanide

The benzodiazepine moiety appears as an important structural component in both biological and medicinal compounds.[1] For instance, benzodiazepine compounds **I**, **II**, and **III** have a variety of pharmaceutical proprieties including anxiolytic, anticonvulsant, hypnotic, sedative, skeletal muscle relaxant, amnestic, diabetic nephropathy or glomerulosclerosis and peptide hormones properties (Figure 1).[1–5] Because of these properties of benzodiazepines, a variety of synthetic methods have been developed by different research groups.[6]

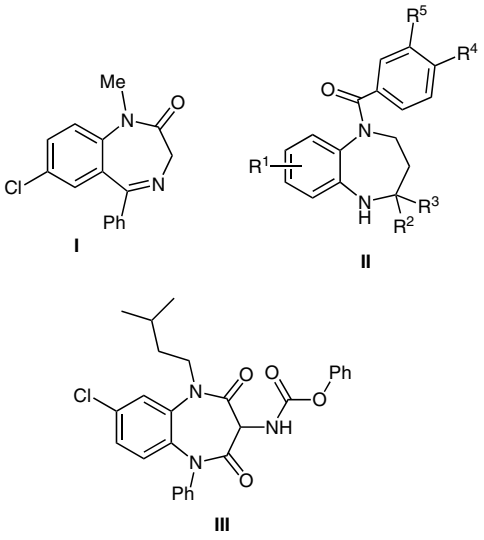


Figure 1 Examples of medicinal benzodiazepine derivatives

Tetrazole compounds also show diverse biological activities.[7] This moiety is a bioisostere of carboxylic acid that does not show acidic properties.[8] Introducing a tetrazole group instead of a carboxylic moiety can reduce the toxic properties of drugs.[9] 1,5-Disubstituted tetrazoles have a wide range of applications in the drug industry.[10] Glucokinase activators,[11] NAD(P)H oxidase inhibitors,[12] antimigraine agents,[13] and hepatitis C virus serine protease NS3 inhibitors are some of the uses of 1,5-disubstituted tetrazole containing compounds.[14] Losartan **IV**, angiotensin II antagonist,[15] pentylenetetrazole (PTZ) **V**,[16] and tetrazole **VI** also show some biological activities (Figure 2).[17]

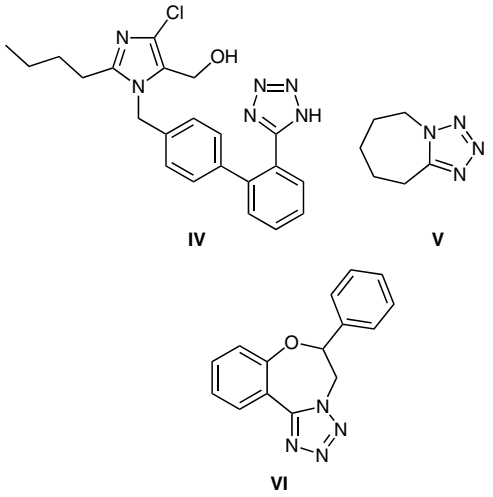
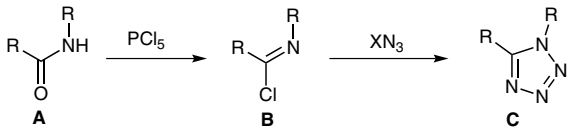


Figure 2 Examples of medicinal tetrazole derivatives

A general and efficient method to protected tetrazoles is required in medicinal chemistry. The cyanoethyl group can be used to protect tetrazoles and mild conditions allow for subsequent deprotection (aqueous hydroxide, r.t.). General and efficient methods for the synthesis of tetrazole compounds involve the conversion of a secondary amide **A** into the corresponding imidoyl chloride **B** followed by treatment with sodium azide (Scheme 1, X = Na)[18a,b] or hydrazoic acid (Scheme 1, X = H)[18c,d] to afford the desired tetrazole **C**. In recent years, the employment of trimethylsilyl azide in conjunction with imidoyl chlorides has been reported for the synthesis of *N*-alkyl and *N*-aryl tetrazoles.[19]



Scheme 1 Tetrazole synthesis *via* imidoyl chlorides

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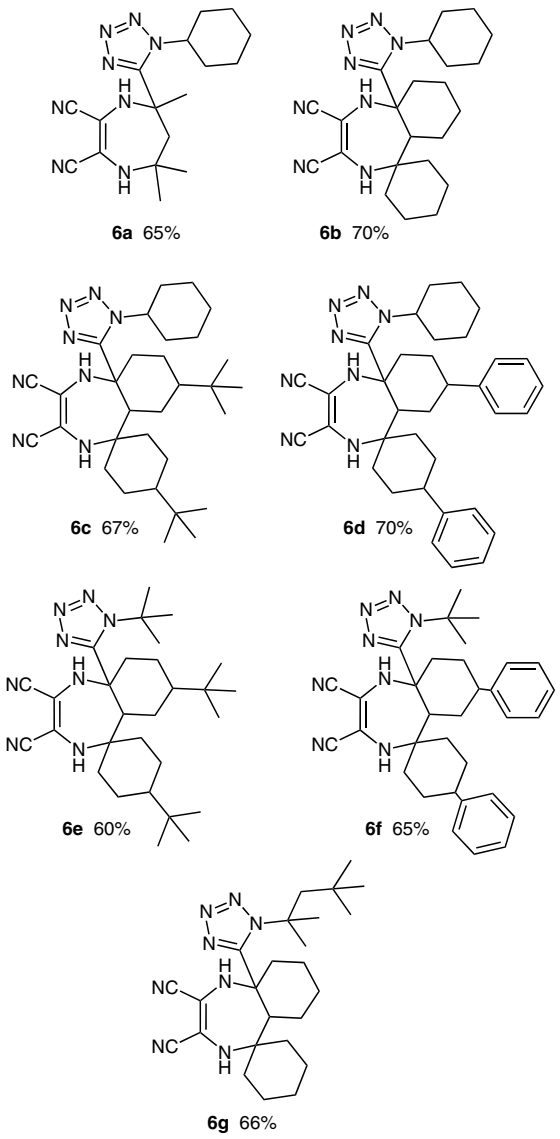


Figure 3 Structures of 1*H*-tetrazolyl-1*H*-1,4-diazepine-2,3-dicarbonitrile derivatives

In view of our current interest in isocyanide-based multicomponent reaction (IMCR) of diamines[20] and the potential use of 1,4-benzodiazepines and tetrazoles, we wished to investigate the possibility of synthesizing a new class of tetrazole-containing diazepine compounds 1*H*-tetrazolyl-1*H*-1,4-diazepine-2,3-dicarbonitriles **6a–g** and 1*H*-tetrazolyl-benzo[*b*][1,4]diazepines **7a–f** with regiochemical control, through a condensation reaction between 2,3-diaminomaleonitrile **1** or *o*-phenylenediamines **2**, ketones **3**, isocyanides **4** and $TMSN_3$ (**5**) *via* a two-step route (Scheme 2). To the best of our knowledge, this is the first report of the synthesis of 1*H*-tetrazol-1*H*-1,4-diazepine-2,3-dicarbonitrile and 1*H*-tetrazolyl-benzo[*b*][1,4]diazepine derivatives using a two-step IMCR strategy, and this new reaction opens an important field to the use of MCR strategies in heterocyclic synthesis.

In a pilot experiment, 2,3-diaminomaleonitrile and ketones were stirred in methanol at ambient temperature with a catalytic amount of *p*-toluenesulfonic acid. The progress of the reaction was monitored by TLC. After 4 h, isocyanides and water were added to the reaction mixture and stirring was continued for 12 h. After completion of the reaction, an aqueous workup afforded compounds **8a–g**.[20a] The use of phosphorus pentachloride, trimethylsilyl azide and pyridine as a catalyst successively under reflux conditions provided **6a–g** in good yields (Figure 3). The structures of compounds **6a–g** were deduced from their IR, mass, ^{1}H NMR, and ^{13}C NMR spectral data.

To investigate the scope and limitations of this reaction, we decided to extend it to aromatic 1,2-diamines **2** instead of 2,3-diaminomaleonitrile **1** and synthesize compounds **9a–f** and subsequently **7a–f** in good yields (Scheme 3).[20d] As indicated in Figure 4, the reaction proceeded efficiently and led to the regioselective formation of 1*H*-tetrazolyl-benzo[*b*][1,4]diazepine derivatives **7a–f** in good yields.

A possible mechanism for the formation of products **6a–g** and **7a–f** is shown in Scheme 4. It is conceivable that the initial event is the formation of diimine **10** from condensation between diamines and ketones.[21,22] Then, an intramolecular imine–enamine cyclization of **11** affords seven-membered ring **12**.[23] On the basis of the well-established chemistry of the reaction of isocyanides with imines,[21] intermediate **13** could be produced by nucleophilic attack of isocyanide **4** to iminium **12** followed by nucleophilic attack of a water molecule on the nitrilium moiety and production of compound **14**. Subsequent, tautomerization of intermediate **14** produces compounds **8a–g** and **9a–f**. Intermediate **15** can be produced by reaction of amide **8a–g** and **9a–f** and PCl_5. Nucleophilic attack of

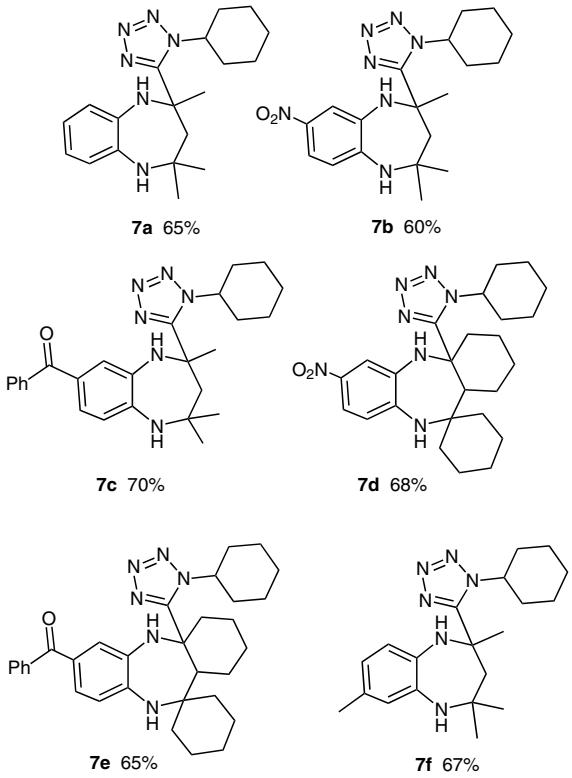
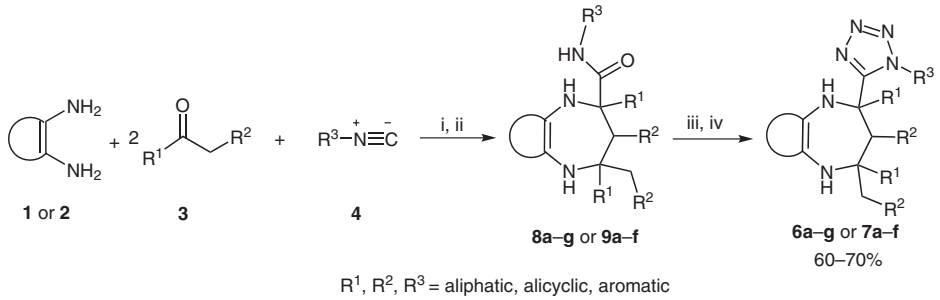
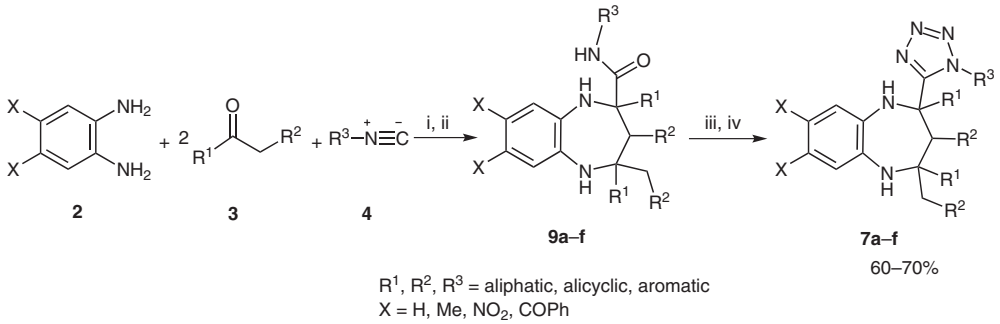


Figure 4 Structures of 1*H*-tetrazolyl-benzo[*b*][1,4]diazepine derivatives



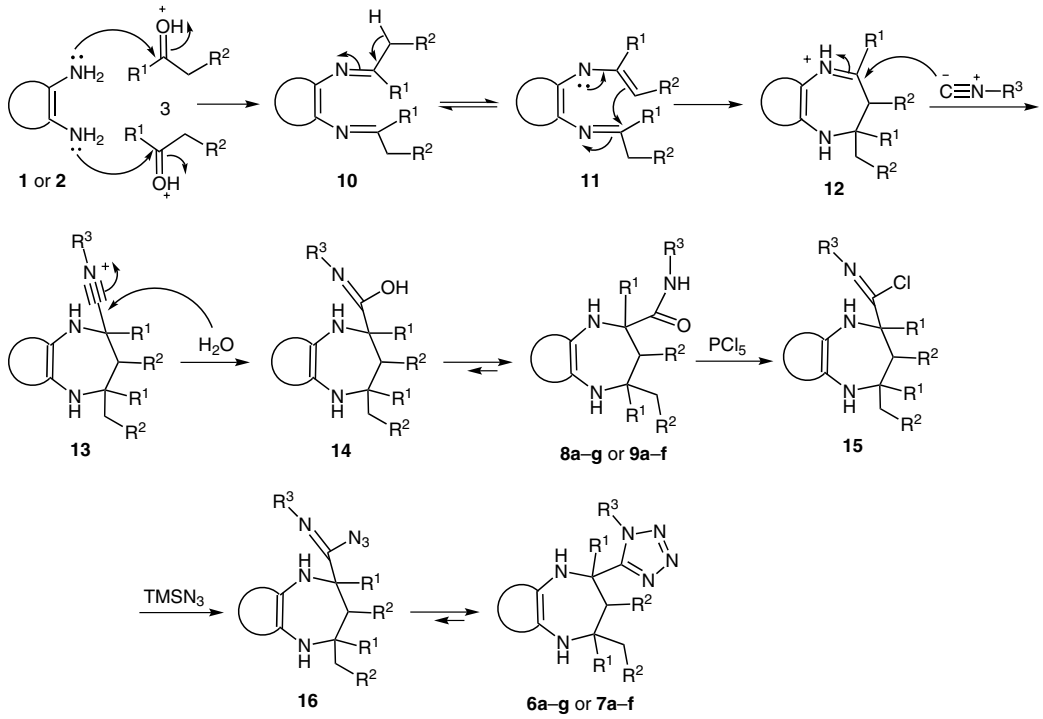
Scheme 2 Synthesis of 1*H*-tetrazolyl-1*H*-1,4-diazepine-2,3-dicarbonitriles **6a**–**g** and 1*H*-tetrazolyl-benzo[*b*][1,4]diazepines **7a**–**f**. *Reagents and conditions*: (i) **1** (or **2**) + **3**, MeOH, TsOH·H_2O, r.t., 4 h; (ii) **4**, H_2O, r.t., 12 h; (iii) CH_2Cl_2, pyridine, PCl_5, reflux, 6 h; (iv) **5**, r.t. 24 h.



Scheme 3 Synthesis of 1*H*-tetrazolyl-benzo[*b*][1,4]diazepines **7a**–**f**. *Reagents and conditions*: (i) **2** + **3**, MeOH, TsOH·H_2O, r.t., 4 h; (ii) **4**, H_2O, r.t., 12 h; (iii) CH_2Cl_2, pyridine, PCl_5, reflux, 6 h; (iv) **5**, r.t. 24 h.

azide ion **5** on the imidoyl chloride **15** and production of compound **16**. Finally, a [3+2] intramolecular cycloaddition reaction between the C=N and N_3 group of intermediate **16** takes place to produce 1*H*-tetrazolyl-1*H*-1,4-diazepine-2,3-dicarbonitriles **6a**–**g** or 1*H*-tetrazolyl-benzo[*b*][1,4]diazepines **7a**–**f**.[24]

In summary, we have developed a straightforward procedure for the synthesis of a new class of substituted 1*H*-tetrazolyl-1*H*-1,4-diazepine-2,3-dicarbonitrile and 1*H*-tetrazolyl-benzo[*b*][1,4]diazepine derivatives with regiochemical control, using a two-step protocol centered on condensation reactions between *o*-phenylenediamines or



Scheme 4 Possible mechanism for the formation of products **6a**–**g** and **7a**–**f**

2,3-diaminomaleonitrile, ketones, various isocyanides and trimethylsilyl azide.[25] This reaction can be regarded as a new approach to the preparation of synthetically and pharmaceutically important 1*H*-tetrazolyl-1*H*-1,4-diazepine-2,3-dicarbonitrile and 1*H*-tetrazolyl-benzo[*b*][1,4]diazepine derivatives, especially, spirocyclic compounds. This reaction benefits from some important aspects such as the easy workup procedure, high atom economy, regioselectivity, very good yields, combinatorial diversity in good yields and mild reaction conditions.

Acknowledgment

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(25) Melting points were measured with an Electrothermal 9200 apparatus. Mass spectra were recorded with a Finnigan-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded with a Shimadzu IR-470 spectrometer. ^{1}H NMR spectra were recorded with a Bruker DRX-300 Avance spectrometer at 300.13 MHz; chemical shifts (δ) are reported in units of parts per million(ppm). ^{1}H NMR spectra are reported in the order: multiplicity, approximate coupling constant (*J* value) in hertz (Hz), and integration. ^{13}C NMR spectra were recorded at 75.47 MHz; chemical shifts (δ) are reported in ppm. Elemental analyses were performed with an Elementar Analysensysteme GmbH VarioEL. All the products are new compounds, which were characterized by IR, ^{1}H and ^{13}C NMR spectra and Mass spectral data.

Synthesis of 1*H*-tetrazolyl-1*H*-1,4-diazepine-2,3-dicarbonitriles 6a–g and 1*H*-tetrazolyl-benzo[*b*]-[1,4]diazepines 7a–f; General Procedure: A solution of the diamine (1.00 mmol) and ketone (2.20 mmol) in the presence of *p*-TsOH·H_2O (0.095 g, 5 mol%) was stirred for 4 h in MeOH (5 mL) at ambient temperature. After completion of the reaction, as indicated by TLC (EtOAc–*n*-hexane, 3:1), the isocyanide (1.00 mmol) and H_2O (0.50 mL) were added to the reaction mixture. The resulting mixture was stirred for 12 h at ambient temperature. After completion of the reaction, as indicated by TLC (EtOAc–*n*-hexane, 4:1), the product was filtered off, washed further with H_2O, and then crystallized from acetone to give the 1,4-diazepine derivative.

To a solution of the 1,4-diazepine (0.50 mmol) and pyridine (3.00 mmol) in CH_2Cl_2 (5.00 mL) was added PCl_5 (0.75 mmol) and the resulting mixture was heated to reflux. After 6 h the reaction mixture was cooled to ambient temperature and $TMSN_3$ (2.00 mmol) was added and stirred for 24 h at ambient temperature. After completion of the reaction, as indicated by TLC (EtOAc–*n*-hexane, 4:1), the product was filtered off, washed further with H_2O and MeOH, and then crystallized from acetone to give **6a–g** and **7a–f**.

5-(1-Cyclohexyl-1*H*-tetrazol-5-yl)-5,7,7-trimethyl-4,5,6,7-tetrahydro-1*H*-1,4-diazepine-2,3-dicarbonitrile (6a): Colorless crystals; mp 229–231 °C. IR (KBr): 3350, 3135, 3078, 2940, 2865, 2213, 1656, 1625, 1478, 1390 cm^{-1}. ^{1}H NMR (300.13 MHz, DMSO-d_6): δ = 1.00–2.10 (m, 20 H, 5 × CH_2 of *c*-Hex, 3 × CH_3 and 1 H CH), 2.79 (AB_q, *J* = 14.2 Hz, 1 H, CH_2), 4.75 (m, 1 H, CH of *c*-Hex), 5.75 (s, 1 H, NH), 6.78 (s, 1 H, NH). ^{13}C NMR (75.47 MHz, DMSO-d_6): δ = 25.0, 25.3, 30.5, 31.6, 31.8, 33.9, 34.2, 46.5, 54.8, 56.8, 58.1, 106.0, 109.7, 116.3, 116.8, 158.8. MS: *m*/*z* = 340 (20) [M]$^+$, 258 (15), 189 (55), 173 (20), 153 (20), 133 (100), 111 (15), 83 (20), 56 (65). Anal. Calcd for $C_{17}H_{24}N_8$: C, 59.98; H, 7.11; N, 32.92. Found: C, 59.92; H, 7.00; N, 32.82.

9a-(1-Cyclohexyl-1*H*-tetrazol-5-yl)-1,4,5a,6,7,8,9,9a-octahydrospiro[benzo[*e*][1,4]diazepine-5,1′-cyclohexane]-2,3-dicarbonitrile (6b): Colorless crystals; mp >300 °C. IR (KBr): 3345, 3135, 2983, 2935, 2857, 2225, 2206, 1622, 1495, 1454, 1404, 1297 cm^{-1}. ^{1}H NMR (300.13 MHz, DMSO-d_6): δ = 1.00–2.10 (m, 28 H, 14 × CH_2 of *c*-Hex), 2.64 (m, 1 H, CH), 4.69 (m, 1 H, CH of *c*-Hex), 4.80 (s, 1 H, NH), 6.85 (s, 1 H, NH). ^{13}C NMR (75.47 MHz, DMSO-d_6): δ = 19.0, 20.9, 21.6, 25.0, 25.4, 30.5, 34.2, 34.8, 37.4, 46.2, 49.0, 56.5, 57.9, 59.8, 61.2, 106.1, 110.0, 116.1, 116.5, 161.1. Anal. Calcd for $C_{23}H_{32}N_8$: C, 65.69; H, 7.67; N, 26.64. Found: C, 65.60; H, 7.60; N, 26.55.

4′,7-di-*tert*-Butyl-9a-(1-cyclohexyl-1*H*-tetrazol-5-yl)-1,4,5a,6,7,8,9,9a-octahydrospiro[benzo[*e*][1,4]-diazepine-5,1′-cyclohexane]-2,3-dicarbonitrile (6c): Colorless crystals; mp >300 °C. IR (KBr): 3358, 3128, 3072, 2941, 2867, 2217, 1657, 1620, 1473, 1398, 1294 cm^{-1}. ^{1}H NMR (300.13 MHz, DMSO-d_6): δ = 0.76 (s, 9 H, 4 × CH_3), 0.85 (s, 9 H, 4 × CH_3), 1.10–2.70 (m, 27 H, 12 × CH_2 of *c*-Hex and 3 × CH), 4.56 (s, 1 H, NH), 4.67 (m, 1 H, CH of *c*-Hex), 6.71 (s, 1 H, NH). Anal. Calcd for $C_{31}H_{48}N_8$: C, 69.89; H, 9.08; N, 21.03. Found: C, 69.79; H, 9.01; N, 21.00.

9*a*-(1-Cyclohexyl-1*H*-tetrazol-5-yl)-4′,7-diphenyl-1,4,5*a*,6,7,8,9,9*a*-octahydrospiro[benzo[*e*][1,4]-diazepine-5,1′-cyclohexane]-2,3-dicarbonitrile (6d): Brown powder; mp >300 °C. IR (KBr): 3419, 3351, 3090, 3021, 2938, 2862, 1619, 1495, 1453, 1398 cm^{-1}. ^{1}H NMR (300.13 MHz, DMSO-d_6): δ = 1.00–2.20 (m, 24 H, 12 × CH_2 of *c*-Hex), 2.43 (m, 1 H, CH), 2.64 (m, 1 H, CH), 3.10 (m, 1 H, CH), 4.79 (m, 1 H, CH of *c*-Hex), 5.02 (s, 1 H, NH), 7.03 (s, 1 H, NH), 7.00–7.15 (m, 3 H, ArH), 7.15–7.30 (m, 3 H, ArH), 7.32 (m, 4H, ArH). ^{13}C NMR (75.47 MHz, DMSO-d_6): δ = 25.1, 25.4, 28.1, 28.5, 29.2, 30.4, 33.4, 34.2, 34.9, 42.7, 43.0, 46.4, 58.1, 59.2, 106.2, 110.3, 116.1, 116.5, 126.3, 126.6, 127.0, 127.2, 128.7, 128.9, 146.8, 147.3, 161.1. MS: *m*/*z* = 421 (10) [M$^+$ – 151], 309 (30), 227 (35), 184 (15), 145 (35), 117 (45), 91 (100), 55 (23). Anal. Calcd for $C_{35}H_40N_8$: C, 73.40; H, 7.04; N, 19.56. Found: C, 73.33; H, 7.00; N, 19.46.

4′,7-di-*tert*-Butyl-9a-(1-*tert*-butyl-1*H*-tetrazol-5-yl)-1,4,5a,6,7,8,9,9a-octahydrospiro[benzo[*e*][1,4]-diazepine-5,1′-cyclohexane]-2,3-dicarbonitrile (6e): Colorless crystals; mp 170–171 °C. IR (KBr): 3340, 3089, 2935, 2856, 2215, 1570, 1545, 1450 cm^{-1}. ^{1}H NMR (300.13 MHz, DMSO-d_6): δ = 0.80–2.40 (m, 43 H, 7 × CH_2 of *c*-Hex, 9 × CH_3 and 2 × CH), 3.03 (m, 1 H, CH), 4.70 (s, 1 H, NH), 6.67 (s, 1 H, NH). ^{13}C NMR (75.47 MHz, DMSO-d_6): δ = 21.8, 22.1, 22.8, 26.1, 27.5, 27.8, 31.5, 32.5, 32.8, 33.0, 33.7, 46.9, 57.3, 60.6, 65.1, 104.1, 105.8, 110.6, 115.3, 163.4. Anal. Calcd for $C_{29}H_{46}N_8$: C, 68.74; H, 9.15; N, 22.11. Found: C, 68.62; H, 9.05; N, 22.07.

9a-(1-*tert*-Butyl-1*H*-tetrazol-5-yl)-4′,7-diphenyl-1,4,5a,6,7,8,9,9a-octahydrospiro[benzo[*e*][1,4]-diazepine-5,1′-cyclohexane]-2,3-dicarbonitrile (6f). Brown powder; mp >300 °C. IR (KBr): 3406, 3236, 3160, 3040, 3021, 2926, 2850, 2219, 2194, 1634, 1544, 1443, 1366, 1316 cm^{-1}. ^1H NMR (300.13 MHz, DMSO-d_6): δ = 1.00–2.20 (m, 23 H, 7 × CH_2 of *c*-Hex and 3 × CH_3), 2.40 (m, 1 H, CH), 2.64 (m, 1 H, CH), 3.30 (m, 1 H, CH), 4.92 (s, 1 H, NH), 6.92 (s, 1 H, NH), 7.16 (m, 3 H, ArH), 7.18 (m, 3 H, ArH), 7.32 (m, 4 H, ArH). ^{13}C NMR (75.47 MHz, DMSO-d_6): δ = 27.9, 28.6, 29.3, 30.8, 31.6, 33.4, 37.7, 42.9, 43.1, 48.8, 60.7, 61.2, 65.2, 105.8, 111.6, 116.6, 117.0, 126.3, 126.6, 127.1, 127.2, 128.6, 128.8, 146.9, 147.4, 163.5. Anal. Calcd for $C_{33}H_{38}N_8$: C, 72.50; H, 7.01; N, 20.50. Found: C, 72.42; H, 6.91; N, 20.41.

9a-(1-(2,4,4-Trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)-1,4,5a,6,7,8,9,9a-octahydrospiro[benzo[*e*][1,4]-diazepine-5,1′-cyclohexane]-2,3-dicarbonitrile (6g): Colorless crystals; mp 167–169 °C. IR (KBr): 3406, 3282, 3128, 3021, 2946, 2850, 2215, 2200, 1618, 1529, 1454, 1304 cm^{-1}. ^1H NMR (300.13 MHz, DMSO-d_6): δ = 1.00–2.10 (m, 35 H, 9 × CH_2 of *c*-Hex, 1 × CH_2 and 5 × CH_3), 2.94 (m, 1 H, CH), 4.69 (s, 1 H, NH), 6.70 (s, 1 H, NH). ^{13}C NMR (75.47 MHz, DMSO-d_6): δ = 20.6, 20.7, 21.1, 21.6, 24.7, 25.4, 25.5, 25.6, 31.1, 31.2, 31.5, 48.8, 61.0, 61.8, 65.1, 105.7, 107.1, 111.2, 116.5, 163.4. Anal. Calcd for $C_{25}H_{38}N_8$: C, 66.63; H, 8.50; N, 24.87. Found: C, 66.58; H, 8.41; N, 24.77.

2-(1-Cyclohexyl-1*H*-tetrazol-5-yl)-2,4,4-trimethyl-2,3,4,5-tetrahydro-1*H*-benzo[*b*][1,4]diazepine (7a): Colorless crystals; mp 241–242 °C. IR (KBr): 3383, 2924, 2861, 1600, 1508, 1478, 1450, 1302, 1259 cm^{-1}. ^1H NMR (300.13 MHz, DMSO-d_6): δ = 1.00–2.00 (m, 20 H, 5 × CH_2 of *c*-Hex, 3 × CH_3 and 1 × CH), 2.80 (AB_q, *J* = 13.8 Hz, 1 H, CH_2), 3.99 (br s, 1 H, NH), 4.96 (t, *J* = 10.9 Hz, 1 H, CH of *c*-Hex), 5.88 (br s, 1 H, NH), 6.40–6.50 (m, 2 H, ArH), 6.57 (dd, *J* = 6.8, 7.4 Hz, 1 H, ArH), 6.73 (AB_q, *J* = 7.6 Hz, 1 H, ArH). ^{13}C NMR (75.47 MHz, DMSO-d_6): δ = 25.0, 25.4, 31.6, 32.0, 32.5, 32.9, 34.3, 51.5, 53.2, 55.8, 57.9, 117.3, 119.2, 120.7, 120.9, 135.2, 136.9, 160.1. MS: *m*/*z* = 440 (75) $[M]^+$, 189 (80), 173 (100), 133 (80), 90 (10), 55 (15). Anal. Calcd for $C_{19}H_{28}N_6$: C, 67.03; H, 8.29; N, 24.68. Found: C, 69.90; H, 8.22; N, 24.60.

4-(1-Cyclohexyl-1*H*-tetrazol-5-yl)-2,2,4-trimethyl-7-nitro-2,3,4,5-tetrahydro-1*H*-benzo[*b*][1,4]diazepine (7b): Red powder; mp 196–198 °C. IR (KBr): 3400, 3374, 2928, 2859, 1644, 1594, 1530, 1461, 1404, 1309 cm^{-1}. ^1H NMR (300.13 MHz, DMSO-d_6): δ = 1.00–2.10 (m, 20 H, 5 × CH_2 of *c*-Hex, 3 × CH_3 and 1 × CH), 3.09 (AB_q, *J* = 13.2 Hz, 1 H, CH_2), 4.67 (m, 1 H, CH of *c*-Hex), 5.75 (br s, 1 H, NH), 6.50 (br s, 2 H, ArH and AB_q, *J* = 9.3 Hz, ArH), 6.38 (AB_q, *J* = 7.7 Hz, 1 H, ArH), 7.76 (br s, 1 H, NH). ^{13}C NMR (75.47 MHz, DMSO-d_6): δ = 24.7, 24.9, 25.2, 31.0, 32.5, 33.0, 33.6, 34.4, 49.2, 53.8, 55.8, 57.7, 112.9, 116.8, 117.9, 134.7, 138.9, 144.2, 159.6. MS: *m*/*z* = 385 (50) $[M]^+$, 234 (65), 218 (100), 177 (50), 132 (45), 83 (10), 55 (35). Anal. Calcd for $C_{19}H_{27}N_7O_2$: C, 59.20; H, 7.06; N, 25.44. Found: C, 59.07; H, 7.01; N, 25.34.

(4-(1-Cyclohexyl-1*H*-tetrazol-5-yl)-2,2,4-trimethyl-2,3,4,5-tetrahydro-1*H*-benzo[*b*][1,4]diazepin-7-yl)(phenyl)methanone (7c): Yellow powder; mp 293–295 °C. IR (KBr): 3349, 3084, 3040, 2970, 2935, 2850, 1631, 1570, 1492, 1402, 1342, 1301 cm^{-1}. ^1H NMR (300.13 MHz, DMSO-d_6): δ = 1.28 (br s, 3 H, CH_3), 1.32 (br s, 3 H, CH_3), 1.44 (br s, 3 H, CH_3), 1.00–2.00 (m, 11 H, 5 × CH_2 of *c*-Hex and 1 × CH), 3.08 (AB_q, *J* = 13.5 Hz, 1 H, CH_2), 4.69 (m, 1 H, CH of *c*-Hex), 5.16 (br s, 1 H, NH), 6.30 (br s, 1 H, NH), 6.47 (AB_q, *J* = 8.1 Hz, 1 H, ArH), 6.83 (AB_q, *J* = 7.5 Hz, 1 H, ArH), 7.41 (s, 1 H, ArH), 7.45–7.60 (m, 5 H, ArH). ^{13}C NMR (75.47 MHz, DMSO-d_6): δ = 24.9, 25.0, 25.1, 31.2, 32.4, 33.1, 33.4, 34.5, 49.9, 53.5, 55.8, 57.6, 118.1, 119.2, 123.9, 127.7, 128.6, 129.2, 131.6, 135.1, 139.3, 141.8, 160.0, 194.2. Anal. Calcd for $C_{26}H_{32}N_6O$: C, 70.24; H, 7.26; N, 18.90. Found: C, 70.15; H, 7.20; N, 18.81.

4a′-(1-Cyclohexyl-1*H*-tetrazol-5-yl)-7′-nitro-1′,2′,3′,4′,4a′,5′,10′,11a′-octahydrospiro[cyclohexane-1,11′-dibenzo[*b*,*e*][1,4]diazepine] (7d): Red powder; mp >300 °C. IR (KBr): 3394, 3368, 3065, 2932, 2857, 1594, 1524, 1493, 1467, 1327, 1272 cm^{-1}. ^1H NMR (300.13 MHz, DMSO-d_6): δ = 1.00–2.10 (m, 28 H, 14 × CH_2 of *c*-Hex), 2.86 (m, 1 H, CH), 4.55 (m, 1 H, CH of *c*-Hex), 5.08 (br s, 1 H, NH), 6.39 (br s, 1 H, NH), 6.65 (AB_q, *J* = 8.7 Hz, 1H, ArH), 7.37 (AB_q, *J* = 6.6 Hz, 1 H, ArH), 7.72 (br s, 1 H, ArH). ^{13}C NMR (75.47 MHz, DMSO-d_6): δ = 21.2, 21.3, 21.5, 24.8, 24.9, 25.2, 25.4, 25.8, 31.1, 34.7, 49.0, 57.8, 58.4, 58.7, 59.4, 111.0, 115.6, 118.4, 137.6, 140.2, 141.8, 162.3. Anal. Calcd for $C_{25}H_{35}N_7O_2$: C, 64.49; H, 7.58; N, 21.06. Found: C, 64.39; H, 7.48; N, 21.01.

{4a′-(1-Cyclohexyl-1*H*-tetrazol-5-yl)-1′,2′,3′,4′,4a′,5′,10′,11a′-octahydrospiro[cyclohexane-1,11′-dibenzo[*b*,*e*][1,4]-diazepine]-7′-yl}(phenyl)methanone (7e): Yellow powder; mp >300 °C. IR (KBr): 3381, 3354, 2926, 2856, 1625, 1575, 1500, 1445, 1398, 1336 cm^{-1}. ^1H NMR (300.13 MHz, DMSO-d_6): δ = 1.00–2.10 (m, 28 H, 14 × CH_2 of *c*-Hex), 2.86 (m, 1 H, CH), 4.59 (m, 2 H, CH of *c*-Hex and NH), 6.13 (br s, 1 H, NH), 6.60 (AB_q, *J* = 7.7 Hz, 1 H, ArH), 6.83 (AB_q, *J* = 8.1 Hz, 1 H, ArH), 7.38 (s, 1 H, ArH), 7.50–7.60 (m, 5 H, ArH). ^{13}C NMR (75.47 MHz, DMSO-d_6): δ = 21.4, 21.5, 25.0, 25.3, 25.5, 25.9, 32.0, 32.9, 34.8, 37.8, 49.6, 57.6, 58.4, 58.9, 117.7, 119.7, 122.8, 128.7, 129.3, 131.7, 137.7, 139.2, 139.4, 162.7, 194.3. Anal. Calcd for $C_{32}H_{40}N_6O$: C, 73.25; H, 7.68; N, 16.02. Found: C, 73.14; H, 7.58; N, 15.93.

2-(1-Cyclohexyl-1*H*-tetrazol-5-yl)-2,4,4,7-tetramethyl-2,3,4,5-tetrahydro-1*H*-benzo[*b*][1,4]diazepine (7f): White powder; mp 202–204 °C. IR (KBr): 3381, 3306, 2928, 2862, 1600, 1525, 1478, 1451, 1398, 1309 cm^{-1}. ^1H NMR (300.13 MHz, DMSO-d_6): δ = 1.00–2.10 (m, 23 H, 5 × CH_2 of *c*-Hex, 4 × CH_3 and 1 × CH), 2.78 (AB_q, *J* = 14.1 Hz, 1 H, CH_2), 4.96 (m, 1 H, CH of *c*-Hex), 5.69 (br s, 1 H, NH), 6.37 (br s, 1 H, ArH), 6.38 (AB_q, *J* = 7.7 Hz, 1 H, ArH), 6.56 (br s, 1 H, NH), 6.62 (AB_q, *J* = 7.7 Hz, 1 H, ArH). ^{13}C NMR (75.47 MHz, DMSO-d_6): δ = 20.6, 20.8, 25.1, 25.4, 31.5, 31.6, 31.8, 32.0, 32.3, 32.9, 34.3, 51.6, 53.1, 55.8, 57.9, 117.7, 121.2, 121.4, 127.8, 134.4, 135.3, 160.1. MS: *m*/*z* = 354 (80) $[M]^+$, 203 (80), 187 (100), 147 (80), 55 (23). Anal. Calcd for $C_{20}H_{30}N_6$: C, 67.76; H, 8.53; N, 23.71. Found: C, 67.69; H, 8.45; N, 23.61.

