A novel one-pot pseudo five-component condensation reaction towards bifunctional diazepine-tetrazole containing compounds: Synthesis of 1H-tetrazolyl-1H-1,4-diazepine-2,3-dicarbonitriles and 1H-tetrazolyl-benzo[b][1,4]diazepines

Hamid Mofakham, a Ahmad Shaabani,*a Sajjad Mousavifaraz, a Fatemeh Hajishaabanha, a
Shabnam Shaabani a and Seik Weng Ng b

aDepartment of Chemistry, Shahid Beheshti University, 19396-4716, Tehran, Iran
a-shaabani@cc.sbu.ac.ir

bDepartment of Chemistry, University of Malaya, 50603, Kuala Lumpur, Malaysia

R¹, R² and R³ = aliphatic, alicyclic and aromatic
6a-g or 7a-i 75-90%
EXPERIMENTAL PROCEDURES

General

Melting points were measured on an Electrothermal 9200 apparatus. Mass spectra were recorded on a Shimadzu GCMS-QP1100EX mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrometer. $^1$H NMR Spectra were recorded on a Bruker DRX-300 Avance spectrometer 300.13 MHz; chemical shifts ($\delta$ scale) are reported in parts per million (ppm). $^1$H NMR Spectra are reported in order: number of protons, multiplicity and approximate coupling constant ($J$ value) in hertz (Hz); signals were characterized as s (singlet), d (doublet), t (triplet), m (multiplet), br s (broad signal) and Ar (aryl). The $^{13}$C NMR spectra were recorded at 75.47 MHz; chemical shifts ($\delta$ scale) are reported in parts per million (ppm). The elemental analyses were performed with an Elementar Analysensysteme GmbH VarioEL. All the products are new compounds, which were characterized by IR, $^1$H NMR and $^{13}$C NMR spectra and Mass spectral data.

**General procedure for the preparation of products 6a–g and 7a–i:** A solution of diamine (1.00 mmol) and ketone (2.20 mmol) was stirred for 4 h in the presence of $p$-TsOH$\cdot$H$_2$O (0.09 g, 5 mol%) in 5 mL of methanol at room temperature. After completion of the reaction, as indicated by TLC (ethyl acetate/$n$-hexane, 2/1) after 4 h, isocyanide (1.00 mmol) and trimethylsilyl azide (1.50 mmol) were added to the reaction mixture and stirred at room temperature. After completion of the reaction, as indicated by TLC (ethyl acetate/$n$-hexane, 3/1) after 6 h, the precipitate was filtered off and washed with water and methanol, and then crystallized from acetone to give products 6a–g and 7a–i.

**General procedure for the preparation of products 7a–e:** A solution of $o$-phenylenediamine (1.00 mmol) and 3-oxopentanedioic acid (2.20 mmol) was stirred in CHCl$_3$ (2.00 mL) for 8 h in
the presence of 10% HCl (200 µL) at room temperature. After completion of the reaction, as indicated by TLC (ethyl acetate/n-hexane, 3/1), 5 mL of methanol, isocyanide (1.00 mmol), trimethylsilyl azide (1.50 mmol) and p-TsOH·H2O (0.095 g, 5 mol %) were added to the reaction mixture and stirred at room temperature. After completion of the reaction, as indicated by TLC (ethyl acetate/n-hexane, 3/1) after 6 h, the precipitate was filtered off and washed with water and methanol, and then crystallized from acetone to give products 7a–e.

**General procedure for the preparation of products 16a and 16b:** A solution of o-phenylenediamine (2.00 mmol) and 3-oxopentanedioic acid (4.40 mmol) was stirred in CHCl3 (4.00 mL) for 8 h in the presence of 10% HCl (1600 µL) at room temperature. After completion of the reaction, as indicated by TLC (ethyl acetate/n-hexane, 3/1), isocyanide (2.00 mmol) and water (1.0 mL) were added to the reaction mixture. Then the resulting mixture was stirred for 4 h at ambient temperature. After completion of the reaction, as indicated by TLC (ethyl acetate/n-hexane, 3/1) the precipitate was filtered off and washed with ethyl acetate, and then crystallized from acetone to give products 16a and 16b.
Compounds Characterization Data

5-(1-Cyclohexyl-1H-tetrazol-5-yl)-5,7,7-trimethyl-4,5,6,7-tetrahydro-1H-1,4-diazepine-2,3-dicarbonitrile (6a): Colorless crystals; mp 229–231°C. IR (KBr) cm⁻¹: 3350, 3135, 3078, 2940, 2865, 2213, 1656, 1625, 1478, 1390. ¹H NMR (300.13 MHz, DMSO-d₆) δ: 1.00-2.10 (20H, m, 5CH₂ of cyclohexyl, 3CH₃ and 1H CH), 2.79 (1H, ABq, J = 14.2, CH₂), 4.75 (1H, m, CH of cyclohexyl), 5.75 (1H, s, NH), 6.78 (1H, s, NH). ¹³C NMR (75.47 MHz, DMSO-d₆) 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 (M⁺, 20), 258 (15), 189 (55), 173 (20), 153 (20), 133 (100), 111 (15), 83 (20), 56 (65). Anal. Calcd for C₁₇H₂₄N₈: C, 59.98; H, 7.11; N, 32.92; found C, 59.92; H, 7.00; N, 32.82

4',7-di-tert-Butyl-9a-(1-cyclohexyl-1H-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) cm⁻¹: 3358, 3128, 3072, 2941, 2867, 2217, 1657, 1620, 1473, 1398, 1294. ¹H NMR (300.13 MHz, DMSO-d₆) δ: 0.76 (9H, s, 4CH₃), 0.85 (9H, s, 4CH₃), 1.10-2.70 (27H, m, 12CH₂ of cyclohexyl and 3CH), 4.56 (1H, s, NH), 4.67 (1H, m, CH of cyclohexyl), 6.71 (1H, s, NH). Anal. Calcd for C₃₁H₄₈N₈: C, 69.89; H, 9.08; N, 21.03; found C, 69.79; H, 9.01; N, 21.00.

9a-(1-Cyclohexyl-1H-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) cm⁻¹: 3345, 3135, 2983, 2935, 2857, 2225, 2206, 1622, 1495, 1454, 1404, 1297. ¹H NMR (300.13 MHz, DMSO-d₆) δ: 1.00-2.10 (28H, m, 14CH₂ of cyclohexyl), 2.64 (1H, m, CH), 4.69 (1H, m, CH of cyclohexyl), 4.80 (1H, s, NH), 6.85 (1H, s, NH). ¹³C NMR (75.47 MHz, DMSO-d₆) 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 C₂₃H₃₂N₈: C, 65.69; H, 7.67; N, 26.64; found C, 65.60; H, 7.60; N, 26.55.
ORTEP diagram for 6c; summary of data: The Cambridge Crystallographic Data Centre (CCDC) no.: 814967; unit cell parameters: a 9.8399(6) b 13.7523(9) c 20.5139(13) alpha 82.638(1) beta 77.064(1) gamma 72.281(1) space group P-1. (Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk or www.ccdc.cam.ac.uk).

9a-(1-(2,4,4-Trimethylpentan-2-yl)-1H-tetrazol-5-yl)-1,4,5a,6,7,8,9,9a-octahydrospiro[benzo[e][1,4]diazepine-5,1'-cyclohexane]-2,3-dicarbonitrile (6d): Colorless crystals; mp 167-169 °C. IR (KBr) cm⁻¹: 3406, 3282, 3128, 3021, 2946, 2850, 2215, 2200, 1618, 1529, 1454, 1304. ¹H NMR (300.13 MHz, DMSO-d₆) δ: 1.00-2.10 (35H, m, 9CH₂ of cyclohexyl, 1CH₂ and 5CH₃), 2.94 (1H, m, CH), 4.69 (1H, s, NH), 6.70 (1H, s, NH). ¹³C NMR (75.47 MHz, DMSO-d₆) 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 C₂₅H₃₈N₈: C, 66.63; H, 8.50; N, 24.87; found C, 66.58; H, 8.41; N, 24.77.

9a-(1-Cyclohexyl-1H-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 (6e): Brown powder; mp > 300 °C. IR (KBr) cm⁻¹: 3419, 3351, 3090, 3021, 2938, 2862, 1619, 1495, 1453, 1398. ¹H NMR (300.13 MHz, DMSO-d₆) δ: 1.00-2.20 (24H, m, 12CH₂ of cyclohexyl), 2.43 (1H, m, CH), 2.64 (1H, m, CH), 3.10 (1H, m, CH), 4.79 (1H, m, CH of cyclohexyl), 5.02 (1H, s, NH), 7.03 (1H, s, NH). ¹³C NMR (75.47 MHz, DMSO-d₆) 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 (M⁺-151, 10), 309 (30), 227 (35), 184 (15), 145 (35), 117 (45), 91 (100), 55 (23). Anal. Calcd for C₃₅H₄₀N₈: 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-1H-tetrazol-5-yl)-1,4,5a,6,7,8,9,9a-octahydrospiro[benzo[e][1,4]diazepine-5,1′-cyclohexane]-2,3-dicarbonitrile (6f): Colorless crystals; mp 170-171°C. IR (KBr) cm⁻¹: 3340, 3089, 2935, 2856, 2215, 1570, 1545, 1450. ¹H NMR (300.13 MHz, DMSO-d₆) δ: 0.80-2.40 (43H, m, 7CH₂ of cyclohexyl, 9CH₃ and 2CH), 3.03 (1H, m, CH), 4.70 (1H, s, NH), 6.67 (1H, s, NH). ¹³C NMR (75.47 MHz, DMSO-d₆) 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 C₂₉H₄₆N₈: C, 68.74; H, 9.15; N, 22.11; found C, 68.62; H, 9.05; N, 22.07.

9a-(1-tert-Butyl-1H-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 (6g): Brown powder; mp > 300 °C. IR (KBr) cm⁻¹: 3406, 3236, 3160, 3040, 3021, 2926, 2850, 2219, 2194, 1634, 1544, 1443, 1366, 1316. ¹H NMR (300.13 MHz, DMSO-d₆) δ: 1.00-2.20 (23H, m, 7CH₂ of cyclohexyl and 3CH₃), 2.40 (1H, m, CH), 2.64 (1H, m, CH), 3.30 (1H, m, CH), 4.92 (1H, s, NH), 6.92 (1H, s, NH) 7.16 (3H, m, H-Ar), 7.18 (3H, m, H-Ar), 7.32 (4H, m, H-Ar). ¹³C NMR (75.47 MHz, DMSO-d₆) 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 C₃₃H₃₈N₈: C, 72.50; H, 7.01; N, 20.50; found C, 72.42; H, 6.91; N, 20.41.

2-(1-Cyclohexyl-1H-tetrazol-5-yl)-2,4,4-trimethyl-2,3,4,5-tetrahydro-1H-benzo[b][1,4]diazepine (7a): Colorless crystals; mp 241–242°C. IR (KBr) cm⁻¹: 3383, 2924, 2861, 1600, 1508, 1478, 1450, 1302, 1259. ¹H NMR (300.13 MHz, DMSO-d₆) δ: 1.00-2.00 (20H, m, 5CH₂ of cyclohexyl, 3CH₃ and 1CH), 2.80 (1H, ABq, J = 13.8 Hz, CH₂), 3.99 (1H, br s, NH), 4.96 (1H, t, J = 10.9 Hz, CH of cyclohexyl), 6.40-6.50 (2H, m, H-Ar), 6.57 (1H, dd, J = 6.8 Hz and J = 7.4 Hz, H-Ar), 6.73 (1H, ABq, J = 7.6 Hz, H-Ar). ¹³C NMR (75.47 MHz, DMSO-d₆) 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 (M⁺, 75), 189 (80), 173 (100), 133 (80), 90 (10), 55 (15). Anal. Calcd for C₁₉H₂₈N₆: C, 67.03; H, 8.29; N, 24.68; found C, 69.90; H,
4-(1-Cyclohexyl-1H-tetrazol-5-yl)-2,2,4-trimethyl-7-nitro-2,3,4,5-tetrahydro-1H-benzo[b][1,4]diazepine (7b): Red powder; mp 196–198 °C. IR (KBr) cm⁻¹: 3400, 3374, 2928, 2859, 1644, 1594, 1530, 1461, 1404, 1309. ¹H NMR (300.13 MHz, DMSO-d₆) δ: 1.00-2.10 (20H, m, 5CH₂ of cyclohexyl, 3CH₃ and 1CH), 3.09 (1H, ABq, J = 13.2 Hz, CH₂), 4.67 (1H, m, CH of cyclohexyl), 5.75 (1H, br s, NH), 6.50 (1H, br s, H-Ar and 1H, ABq, J = 9.3 Hz, H-Ar), 6.38 (1H, ABq, J = 7.7 Hz, H-Ar), 7.76 (1H, br s, NH). ¹³C NMR (75.47 MHz, DMSO-d₆) 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 (M⁺, 50), 234 (65), 218 (100), 177 (50), 132 (45), 83 (10), 55 (35). Anal. Calcd for C₁₉H₂₇N₇O₂: C, 59.20; H, 7.06; N, 25.44; found C, 59.07; H, 7.01; N, 25.34.

2-(1-cyclohexyl-1H-tetrazol-5-yl)-2,4,4,7-tetramethyl-2,3,4,5-tetrahydro-1H-benzo[b][1,4]diazepine (7c): White powder; mp 202–204°C. IR (KBr) cm⁻¹: 3381, 3306, 2928, 2862, 1600, 1525, 1478, 1451, 1398, 1309. ¹H NMR (300.13 MHz, DMSO-d₆) δ: 1.00-2.10 (23H, m, 5CH₂ of cyclohexyl, 4CH₃ and 1CH), 2.78 (1H, ABq, J = 14.1 Hz, CH₂), 4.96 (1H, m, CH of cyclohexyl), 5.69 (1H, br s, NH), 6.37 (1H, br s, H-Ar), 6.38 (1H, ABq, J = 7.7 Hz, H-Ar), 6.56 (1H, br s, NH), 6.62 (1H, ABq, J = 7.7 Hz, H-Ar). ¹³C NMR (75.47 MHz, DMSO-d₆) 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 (M⁺, 80), 203 (80), 187 (100), 147 (80), 55 (23). Anal. Calcd for C₂₀H₃₀N₆: C, 67.76; H, 8.53; N, 23.71; found C, 67.69; H, 8.45; N, 23.61.
(4-(1-Cyclohexyl-1H-tetrazol-5-yl)-2,2,4-trimethyl-2,3,4,5-tetrahydro-1H-benzo[b][1,4]diazepin-7-yl)(phenyl)methanone (7d): Yellow powder; mp 293-295 °C.
IR (KBr) cm⁻¹: 3349, 3084, 3040, 2970, 2935, 2850, 1631, 1570, 1492, 1402, 1342, 1301. ¹H NMR (300.13 MHz, DMSO-d₆) δ: 1.28 (3H, br s, CH₃), 1.32 (3H, br s, CH₃), 1.44 (3H, br s, CH₃), 1.00-2.00 (11H, m, 5CH₂ of cyclohexyl and 1CH), 3.08 (1H, AB q, J = 13.5 Hz, CH₂), 4.69 (1H, m, CH of cyclohexyl), 5.16 (1H, br s, NH), 6.30 (1H, br s, NH), 6.47 (1H, ABq, J = 8.1 Hz, H-Ar), 6.83 (1H, ABq, J = 7.5 Hz, H-Ar), 7.41 (1H, br s, H-Ar), 7.45-7.60 (5H, m, H-Ar). ¹³C NMR (75.47 MHz, DMSO-d₆) 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 C₂₆H₃₂N₆O: C, 70.24; H, 7.26; N, 18.90; found C, 70.15; H, 7.20; N, 18.81.

2,2,4-Trimethyl-7-nitro-4-(1-(tosylmethyl)-1H-tetrazol-5-yl)-2,3,4,5-tetrahydro-1H-benzo[b][1,4]diazepine (7e): Red powder; mp 196–198 °C. IR (KBr) cm⁻¹: 3381, 2920, 2850, 1625, 1600, 1530, 1505, 1493, 1462, 1448. ¹H NMR (300.13 MHz, DMSO-d₆) δ: 1.19 (6H, br s, 2CH₃), 2.08 (3H, br s, CH₃), 2.28 (3H, br s, CH₃), 2.72 (1H, s, CH), 2.88 (1H, s, CH), 4.94 (2H, CH₂), 6.41 (1H, br s, NH), 6.51 (1H, ABq, J = 8.5 Hz, H-Ar), 7.20-7.40 (5H, m, H-Ar). ¹³C NMR (75.47 MHz, DMSO-d₆) δ: 21.4, 26.3, 31.2, 37.8, 50.7, 62.4, 106.8, 113.6, 122.9, 129.1, 129.8, 136.4, 136.6, 143.0, 144.8, 160.7. Anal. Calcd for C₂₁H₂₅N₇O₄S: C, 53.49; H, 5.34; N, 20.79; found C, 53.35; H, 5.25; N, 20.69.

7',8'-Dichloro-4a'-(1-cyclohexyl-1H-tetrazol-5-yl)-1',2',3',4',4a',5',10',11a'-octahydrospiro[cyclohexane-1,11'-dibenzo[b,e][1,4]diazepine] (7f): Black powder; mp > 300 °C. IR (KBr) cm⁻¹: 3411, 3368, 2928, 2863, 1625, 1595, 1493, 1462, 1448. ¹H NMR (300.13 MHz, DMSO-d₆) δ: 1.00-1.90 (28H, m, 14CH₂ of cyclohexyl), 2.82 (1H, m, CH), 4.14 (1H, br s, NH), 4.59 (1H, m, CH of cyclohexyl), 6.18 (1H, br s, NH), 6.76 (1H, br s, H-Ar), 6.93 (1H, br s, H-Ar). MS m/z: 490 (M⁺, 37Cl, 1), 488 (M⁺, 35Cl, 3), 337 (20),
293 (10), 256 (15), 213 (100). Anal. Calcd for C_{25}H_{34}Cl_{2}N_{6}: C, 61.34; H, 7.00; N, 17.17; found C, 61.30; H, 6.91; N, 17.10.

4a’-(1-Cyclohexyl-1H-tetrazol-5-yl)-7’-nitro-1’,2’,3’,4’,4a’,5’,10’,11a’-octahydrospiro[cyclohexane-1,11’-dibenzo[b,e][1,4]diazepine] (7g): Red powder; mp > 300 °C. IR (KBr) cm⁻¹: 3394, 3368, 3065, 2932, 2857, 1594, 1524, 1493, 1467, 1327, 1272. \(^{1}H\) NMR (300.13 MHz, DMSO-\(d_{6}\)) \(\delta\): 1.00-2.10 (28H, m, 14CH\(_{2}\) of cyclohexyl), 2.86 (1H, CH), 4.55 (1H, m, CH of cyclohexyl), 5.08 (1H, br s, NH), 6.39 (1H, br s, NH), 6.65 (1H, AB\(_{q}\), \(J = 8.7\) Hz, H-Ar), 7.37 (1H, AB\(_{q}\), \(J = 6.6\) Hz, H-Ar), 7.72 (1H, br s, H-Ar). \(^{13}C\) NMR (75.47 MHz, DMSO-\(d_{6}\)) \(\delta\): 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\(_{7}\)O\(_{2}\): C, 64.49; H, 7.58; N, 21.06; found C, 64.39; H, 7.48; N, 21.01.

(4a’-(1-Cyclohexyl-1H-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 (7h): Yellow powder; mp > 300 °C. IR (KBr) cm⁻¹: 3381, 3354, 2926, 2856, 1625, 1575, 1500, 1445, 1398, 1336. \(^{1}H\) NMR (300.13 MHz, DMSO-\(d_{6}\)) \(\delta\): 1.00-2.10 (28H, m, 14CH\(_{2}\) of cyclohexyl), 2.86 (1H, m, CH), 4.59 (2H, m, CH of cyclohexyl and NH), 6.13 (1H, br s, NH), 6.60 (1H, AB\(_{q}\), \(J = 7.7\) Hz, H-Ar), 6.83 (1H, AB\(_{q}\), \(J = 8.1\) Hz, H-Ar), 7.38 (1H, s, H-Ar), 7.50-7.60 (5H, m, H-Ar). \(^{13}C\) NMR (75.47 MHz, DMSO-\(d_{6}\)) \(\delta\): 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\(_{6}\)O: C, 73.25; H, 7.68; N, 16.02; found C, 73.14; H, 7.58; N, 15.93.

2’,4-di-tert-Butyl-4a’-(1-cyclohexyl-1H-tetrazol-5-yl)-7’-nitro-1’,2’,3’,4’,4a’,5’,10’,11a’-octahydrospiro[cyclohexane-1,11’-dibenzo[b,e][1,4]diazepine] (7i): Red powder; mp > 300 °C. IR (KBr) cm⁻¹: 3400, 3368, 2937, 2857, 1650, 1587, 1524, 1472, 1327, 1284. \(^{1}H\) NMR (300.13 MHz, DMSO-\(d_{6}\)) \(\delta\): 1.00-2.10 (44H, m, 12CH\(_{2}\) of cyclohexyl, 6CH\(_{3}\) and 2CH), 2.93 (1H, CH),
4.56 (1H, m, CH of cyclohexyl), 5.14 (1H, br s, NH), 6.38 (1H, br s, NH), 6.59 (1H, AB₃, J = 8.8 Hz, H-Ar), 7.38 (1H, AB₄, J = 8.3 Hz, H-Ar), 7.71 (1H, br s, H-Ar). MS m/z: 578 (M⁺+1, 4), 478 (1), 426 (6), 410 (4), 368 (4), 326 (5), 309 (1), 289 (10), 232 (10), 190 (100), 57 (5). Anal. Calcd for C₃₅H₅₁N₇O₂: C, 68.60; H, 8.90; N, 16.97; found C, 68.55; H, 8.80; N, 16.87.

*N-Cyclohexyl-2,4,4-trimethyl-2,3,4,5-tetrahydro-1*H*-benzo[b][1,4]diazepine-2-carboxamide* (16a): Colorless crystals; mp 210–211°C. IR (KBr) cm⁻¹: 3375, 3330, 2930, 2862, 1602, 1502, 1478. "H NMR (300.13 MHz, DMSO-d₆) δ: 1.00–2.00 (21H, m, 5CH₂ of cyclohexyl and 3CH₃), 2.28 (2H, s, CH₂), 4.12 (m, br s, CH of cyclohexyl), 6.57 (1H, br s, NH), 6.70–6.80 (2H, m, H-Ar), 7.12 (1H, d, J = 7.2 Hz, H-Ar), 7.50 (1H, d, J = 7.2 Hz, H-Ar), 8.86 (1H, d, J = 7.9 Hz, NH), 11.56 (1H, br s, NH). "C NMR (75.47 MHz, DMSO-d₆) δ: 21.2, 24.7, 24.9, 25.1, 31.1, 52.0, 53.0, 118.8, 123.3, 123.9, 125.9, 126.5, 128.6, 134.5, 159.8. MS m/z: 440 (M⁺, 21), 189 (47), 173 (100), 90 (25), 55 (35), 37 (24). Anal. Calcd for C₁₉H₂₉N₅O: C, 72.34; H, 9.27; N, 13.32; found C, 72.34; H, 9.20; N, 13.42.

ORTEP diagram for 6c; summary of data: The Cambridge Crystallographic Data Centre (CCDC) no.: 814967; unit cell parameters: a 9.2850(6) b 10.5724(6) c 11.2667(7) alpha 73.463(1) beta 68.702(1) gamma 67.344(1) space group P-1. (Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk or www.ccdc.cam.ac.uk).
8-Benzoyl-\textit{N}-cyclohexyl-2,4,4-trimethyl-2,3,4,5-tetrahydro-1\textit{H}-benzo[\textit{b}][1,4]diazepine-2-carboxamide (16b): Yellow crystals; mp > 300 °C. IR (KBr) cm\(^{-1}\): 3375, 3330, 2925, 2861, 1620, 1577, 1510, 1450, 1398. \(^1\)H NMR (300.13 MHz, DMSO-\textit{d}\(_6\)) \(\delta\): 1.00-2.00 (21H, m, 5CH\(_2\) of cyclohexyl, 3CH\(_3\) and CH\(_2\)), 4.42 (m, br s, CH of cyclohexyl), 6.96 (1H, br s, NH), 7.12 (1H, d, \(J = 8.2\) Hz, H-Ar), 7.50-7.60 (2H, m, H-Ar), 7.60-7.70 (3H, m, H-Ar), 7.86 (1H, d, \(J = 8.0\) Hz, H-Ar), 9.36 (1H, d, \(J = 8.0\) Hz, NH), 12.40 (1H, br s, NH). \(^1\)C NMR (75.47 MHz, DMSO-\textit{d}\(_6\)) \(\delta\): 24.6, 25.1, 25.4, 31.1, 52.7, 53.1, 116.0, 118.0, 120.9, 127.2, 128.9, 129.8, 132.8, 134.4, 137.9, 160.3, 195.4. MS \textit{m/z}: Anal. Calcd for C\(_{26}\)H\(_{33}\)N\(_3\)O\(_2\): C, 74.43; H, 7.93; N, 10.02; found C, 74.33; H, 7.95; N, 10.00.
$^1$H NMR of 6d
$^1$H NMR of 6f
13C NMR of 6f
$^{13}$C NMR of 6g
$^1$H NMR of 7a
$^{13}$C NMR of 7a
\[ \text{H NMR of 7b} \]
1H NMR of 7c
$^1$H NMR of 7e
$^1$H NMR of $^7T$
$^{13}$C NMR of $7g$
$^{13}C$ NMR of 16b