



SUPPLEMENTARY MATERIAL TO
**Synthesis of some novel 7-(1*H*-benzimidazol-2-ylazo)-1,3-
-dimethyl-6,8-disubstituted-1*H*-pyrimido[4,5-*b*][1,4]
diazepine-2,4-diones as potential anti-anxiety agents**

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ANALYTICAL AND SPECTRAL DATA FOR THE COMPOUNDS **3a–c**, **4a–c** AND **5a–i**

3-[(1*H*-Benzimidazol-2-yl)hydrazono]pentane-2,4-dione (**3a**). Yield: 94 %; m.p. 160–162 °C; Anal. Calcd. for C₁₂H₁₂N₄O₂: C, 59.01; H, 4.91; N, 22.95 %. Found: C, 59.03; H, 4.95; N, 22.91 %; IR (KBr, cm⁻¹): 1620 (C=N), 1680 (C=O), 3205 (NH benz.), 3050 (NH-hydrazono); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 1.56 (3H, *s*, CH₃), 1.75 (3H, *s*, CH₃), 7.12–8.56 (4H, *m*, Ar-H), 9.51 (1H, *s*, NH benz.), 10.52 (1H, *s*, NH hydrazono); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 29.8 (CH₃), 30.5 (CH₃), 116.5–135.8 (Ar-C), 162.4 (C=N), 178.2 (C=O), 180.1 (C=O); MS (*m/z*): 244 (M⁺).

2-[(1*H*-Benzimidazol-2-yl)hydrazono]-1-phenylbutane-1,3-dione (**3b**). Yield: 95 %; m.p. 182–183 °C; Anal. Calcd. for C₁₇H₁₄N₄O₂: C, 66.66; H, 4.57; N, 18.30 %. Found: C, 66.70; H, 4.53; N, 18.34 %; IR (KBr, cm⁻¹): 1610 (C=N), 1685 (C=O), 3080 (NH-hydrazono), 3215 (NH benz.); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 1.65 (3H, *s*, -CH₃), 6.95–8.09 (9H, *m*, Ar-H), 9.45 (1H, *s*, NH benz.), 10.62 (1H, *s*, NH hydrazono); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 31.2 (CH₃), 115.2–137.6 (Ar-C), 160.4 (C=N), 175.0 (C=O), 182.3 (C=O); MS (*m/z*): 306 (M⁺).

2-[(1*H*-Benzimidazol-2-yl)hydrazono]-4,4,4-trifluoro-1-phenyl-butane-1,3-dione (**3c**) Yield: 92 %; m.p. 145–147 °C; Anal. Calcd. for C₁₇H₁₁N₄O₂F₃: C, 56.66; H, 3.05; N, 15.55 %. Found: C, 56.69; H, 3.08; N, 15.58 %; IR (KBr, cm⁻¹): 1618 (C=N), 1690 (C=O), 3200 (NH benz.), 3020 (NH-hydrazono); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 6.85–8.02 (9H, *m*, Ar-H), 9.46 (1H, *s*, NH benz.), 10.54 (1H, *s*, NH hydrazono); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 115.4 (CF₃), 116.2–137.8 (Ar-C), 164.2 (C=N), 175.3 (C=O), 181.4 (C=O); MS (*m/z*): 360 (M⁺).

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7-(1H-Benzimidazol-2-ylazo)-1,3,6,8-tetramethyl-1H-pyrimido[4,5-b][1,4]-diazepine-2,4(3H,5H)-dione (**4a**). Yield: 92 %; m.p. 220–222 °C; Anal. Calcd. for C₁₈H₁₈N₈O₂: C, 57.14; H, 4.76; N, 29.62 %. Found: C, 57.18; H, 4.80; N, 29.60 %; IR (KBr, cm⁻¹): 1560 (N=N), 1626 (C=N), 1700 (C=O), 1720 (C=O), 3220 (NH benz.), 3340 (NH diazepine); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 1.54 (3H, s, CH₃), 1.68 (3H, s, CH₃), 3.32 (3H, s, NCH₃), 3.63 (3H, s, NCH₃), 6.89–7.86 (4H, m, Ar-H), 8.46 (1H, s, NH diazepine), 9.51 (1H, s, NH benz.); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 28.4 (CH₃), 30.2 (CH₃), 33.5 (NCH₃), 34.9 (NCH₃), 115.6–138.4 (Ar-C), 190.2 (C=O), 195.1 (C=O); MS (m/z): 378 (M⁺).

7-(1H-Benzimidazol-2-ylazo)-1,3,8-trimethyl-6-phenyl-1H-pyrimido[4,5-b][1,4]diazepine-2,4(3H,5H)-dione (**4b**). Yield: 95 %; m.p. 239–240 °C; Anal. Calcd. for C₂₃H₂₀N₈O₂: C, 62.72; H, 4.54; N, 25.45 %. Found: C, 62.75, H, 4.58, N, 25.48 %; IR (KBr, cm⁻¹): 1540 (N=N), 1628 (C=N), 1700 (C=O), 1725 (C=O), 3212 (NH benz.), 3350 (NH diazepine); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 1.60 (3H, s, CH₃), 3.26 (3H, s, NCH₃), 3.78 (3H, s, NCH₃), 6.56–7.84 (9H, m, Ar-H), 8.39 (1H, s, NH diazepine), 9.53 (1H, s, NH benz.); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 29.3 (CH₃), 33.6 (NCH₃), 34.8 (NCH₃), 115.8–137.9 (Ar-C); 189.4 (C=O), 194.3 (C=O); MS (m/z): 440 (M⁺).

7-(1H-Benzimidazol-2-ylazo)-1,3-dimethyl-6-phenyl-8-(trifluoromethyl)-1H-pyrimido[4,5-b][1,4]diazepine-2,4(3H,5H)-dione (**4c**). Yield: 94 %; m.p. 189–191 °C; Anal. Calcd. for C₂₃H₁₇N₈O₂F₃: C, 55.87; H, 3.44; N, 22.67 %. Found: C, 55.83; H, 3.47; N, 22.70 %; IR (KBr, cm⁻¹): 1560 (N=N), 1630 (C=N), 1710 (C=O), 1730, 3205 (NH benz.), 3345 (NH diazepine); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.25 (3H, s, NCH₃), 3.80 (3H, s, NCH₃), 6.59–7.78 (9H, m, Ar-H), 8.42 (1H, s, NH diazepino), 9.48 (1H, s, NH benz.); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 34.1 (NCH₃), 35.2 (NCH₃), 115.2 (CF₃), 116.2–138.5 (Ar-C), 185.5 (C=O), 196.2 (C=O); MS (m/z): 494 (M⁺).

1,3,6,8-Tetramethyl-7-[(1-methyl-1H-benzimidazol-2-yl)azo]-1H-pyrimido[4,5-b][1,4]diazepine-2,4(3H,5H)-dione (**5a**). Yield: 92 %; m.p. 170–172 °C; Anal. Calcd. for C₁₉H₂₀N₈O₂: C, 58.16; H, 5.10; N, 28.57 %. Found: C, 58.20; H, 5.13; N, 28.53 %; IR (KBr, cm⁻¹): 1560 (N=N), 1610 (C=N), 1695 (C=O), 1720 (C=O), 3320 (NH diazepine); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 1.73 (3H, s, CH₃), 1.86 (3H, s, CH₃), 3.38 (3H, s, NCH₃), 3.52 (3H, s, NCH₃), 3.69 (3H, s, NCH₃), 6.56–7.92 (4H, m, Ar-H), 8.61 (1H, s, NH diazepine); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 28.2 (CH₃), 30.6 (CH₃), 33.3 (NCH₃), 34.8 (NCH₃), 35.6 (NCH₃), 117.2–139.2 (Ar-C), 189.4 (C=O), 194.2 (C=O); MS (m/z): 392 (M⁺).

1,3,8-Trimethyl-7-[(1-methyl-1H-benzimidazol-2-yl)azo]-6-phenyl-1H-pyrimido[4,5-b][1,4]diazepine-2,4(3H,5H)-dione (**5b**). Yield: 92 %; m.p. 191–192 °C; Anal. Calcd. for C₂₄H₂₂N₈O₂: C, 63.43; H, 4.894; N, 24.66 %. Found: C, 63.40; H, 4.82; N, 24.70 %; IR (KBr, cm⁻¹): 1550 (N=N), 1610 (C=N), 1705

(C=O), 1730 (C=O), 3360 (NH diazepine); $^1\text{H-NMR}$ (300 MHz, CDCl_3 , δ / ppm): 1.68 (3H, s, CH_3), 3.41 (3H, s, NCH_3), 3.56 (3H, s, NCH_3), 3.72 (3H, s, NCH_3), 6.78–8.02 (9H, m, Ar-H), 8.47 (1H, s, NH diazepine); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , δ / ppm): 28.6 (CH_3), 33.7 (NCH_3), 34.6 (NCH_3), 35.8 (NCH_3), 116.2–138.6 (Ar-C), 190.3 (C=O), 193.6 (C=O); MS (m/z): 454 (M^+).

7-[(1-Benzyl-1H-benzimidazol-2-yl)azo]-1,3,6,8-tetramethyl-1H-pyrimido[4,5-b][1,4]diazepine-2,4(3H,5H)-dione (**5c**). Yield: 95 %; m.p. 126–128 °C; Anal. Calcd. for $\text{C}_{25}\text{H}_{24}\text{N}_8\text{O}_2$: C, 64.10; H, 5.12; N, 23.93 %. Found: C, 64.14; H, 5.15; N, 23.90 %; IR (KBr, cm^{-1}): 1560 (N=N), 1620 (C=N), 1720 (C=O), 1735 (C=O), 3310 (NH diazepine); $^1\text{H-NMR}$ (300 MHz, CDCl_3 , δ / ppm): 1.69 (3H, s, CH_3); 1.78 (3H, s, CH_3), 3.31 (3H, s, NCH_3), 3.59 (3H, s, NCH_3), 4.02 (2H, s, CH_2), 6.75–7.86 (9H, m, Ar-H), 8.68 (1H, s, NH diazepine); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , δ / ppm): 28.4 (CH_3), 30.5 (CH_3), 33.8 (NCH_3), 34.5 (NCH_3), 43.8 (NCH_2Ph), 115.8–138.7 (Ar-C), 186.5 (C=O), 192.4 (C=O); MS (m/z): 468 (M^+).

7-[(1-Benzyl-1H-benzimidazol-2-yl)azo]-1,3,8-trimethyl-6-phenyl-1H-pyrimido[4,5-b][1,4]diazepine-2,4(3H,5H)-dione (**5d**). Yield: 94 %; m.p. 139–140 °C; Anal. Calcd. for $\text{C}_{30}\text{H}_{26}\text{N}_8\text{O}_2$: C, 67.92; H, 4.90; N, 21.13 %. Found: C, 67.90; H, 4.94; N, 21.17 %; IR (KBr, cm^{-1}): 1580 (N=N), 1625 (C=N), 1710 (C=O), 1730 (C=O), 3315 (NH diazepine); $^1\text{H-NMR}$ (300 MHz, CDCl_3 , δ / ppm): 1.80 (3H, s, CH_3), 3.34 (3H, s, NCH_3), 3.68 (3H, s, NCH_3), 4.12 (2H, s, CH_2), 6.69–8.02 (14H, m, Ar-H), 8.92 (1H, s, NH diazepine); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , δ / ppm): 29.2 (CH_3), 33.5 (NCH_3), 34.8 (NCH_3), 43.4 (NCH_2Ph), 116.2–137.8 (Ar-C), 190.8 (C=O), 197.2 (C=O); MS (m/z): 530 (M^+).

7-[[1-(Chloroacetyl)-1H-benzimidazol-2-yl]azo]-1,3,6,8-tetramethyl-1H-pyrimido[4,5-b][1,4]diazepine-2,4(3H,5H)-dione (**5e**). Yield: 93 %; m.p. 143–145 °C; Anal. Calcd. for $\text{C}_{20}\text{H}_{19}\text{N}_8\text{O}_3\text{Cl}$: C, 52.80; H, 4.18; N, 24.64 %. Found: C, 52.84; H, 4.14; N, 24.68 %; IR (KBr, cm^{-1}): 1540 (N=N), 1625 (C=N), 1680 (C=O), 1710 (C=O), 1725 (C=O), 3320 (NH diazepine); $^1\text{H-NMR}$ (300 MHz, CDCl_3 , δ / ppm): 1.65 (3H, s, CH_3), 1.70 (3H, s, CH_3), 3.42 (3H, s, NCH_3), 3.64 (3H, s, NCH_3), 4.23 (2H, s, CH_2Cl), 6.78–7.78 (9H, m, Ar-H), 8.92 (1H, s, NH diazepine); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3 , δ / ppm): 28.6 (CH_3), 30.8 (CH_3), 33.5 (NCH_3), 34.9 (NCH_3), 46.4 (CH_2Cl), 116.5–137.6 (Ar-C), 182.2 (C=O), 190.4 (C=O), 196.3 (C=O); MS (m/z): 454.5 (M^+).

7-[[1-(Dimethylamino)methyl-1H-benzimidazol-2-yl]azo]-1,3,8-trimethyl-6-phenyl-1H-pyrimido[4,5-b][1,4]diazepine-2,4(3H,5H)-dione (**5f**). Yield: 92 %; m.p. 128–130 °C; Anal. Calcd. for $\text{C}_{26}\text{H}_{27}\text{N}_9\text{O}_2$: C, 62.77; H, 5.43; N, 25.35 %. Found: C, 62.79; H, 5.41; N, 25.38 %; IR (KBr, cm^{-1}): 1580 (N=N), 1630 (C=N), 1705 (C=O), 1720 (C=O), 3330 (NH diazepine); $^1\text{H-NMR}$ (300 MHz, CDCl_3 , δ / ppm): 1.76 (3H, s, CH_3), 3.40 (3H, s, NCH_3), 3.52 (6H, s, $\text{N}(\text{CH}_3)_2$), 3.69 (3H, s, NCH_3), 4.21 (2H, s, $\text{NCH}_2\text{-N}$), 6.75–7.98 (9H, m, Ar-H), 8.96 (1H, s,

NH diazepine); ^{13}C -NMR (75 MHz, CDCl_3 , δ / ppm): 29.5 (CH_3), 33.4 (NCH_3), 34.7 ($-\text{NCH}_3$), 35.4 ($\text{N}(\text{CH}_2\text{CH}_3)_2$), 116.8–137.8 (Ar-C), 191.5 ($\text{C}=\text{O}$), 194.3 ($\text{C}=\text{O}$), 168.2 (NCH_2N); MS (m/z): 497 (M^+).

7- $\{[1-(\text{Diethylamino})\text{methyl}-1\text{H}-\text{benzimidazol}-2\text{-yl}]\text{azo}\}-1,3,8\text{-trimethyl}-6\text{-phenyl}-1\text{H}-\text{pyrimido}[4,5\text{-b}][1,4]\text{-diazepine}-2,4(3\text{H},5\text{H})\text{-dione}$ (**5g**). Yield: 94 %; m.p. 135–136 °C; Anal. Calcd. for $\text{C}_{28}\text{H}_{31}\text{N}_9\text{O}_2$: C, 64.00; H, 5.90; N, 24.00 %. Found: C, 64.04; H, 5.92; N, 24.03 %; IR (KBr, cm^{-1}): 1560 ($\text{N}=\text{N}$), 1628 ($\text{C}=\text{N}$), 1710 ($\text{C}=\text{O}$), 1725 ($\text{C}=\text{O}$), 3318 (NH diazepine); ^1H -NMR (300 MHz CDCl_3 , δ / ppm): 1.26 (6H, *t*, $J = 7.0$ Hz, $\text{N}(\text{CH}_2\text{CH}_3)_2$), 1.60 (3H, *s*, CH_3), 3.50 (4H, *q*, $J = 7.0$ Hz, $\text{N}(\text{CH}_2\text{CH}_3)_2$), 3.62 (3H, *s*, NCH_3), 3.79 (3H, *s*, NCH_3), 4.42 (2H, *s*, $\text{NCH}_2\text{-N}$), 6.68–7.89 (9H, *m*, Ar-H), 8.67 (1H, *s*, NH diazepine); ^{13}C -NMR (75 MHz, CDCl_3 , δ / ppm): 28.4 ($\text{N}(\text{CH}_2\text{CH}_3)_2$), 29.2 (CH_3), 34.3 (NCH_3), 34.9 (NCH_3), 116.5–137.8 (Ar-C), 126.2 ($\text{N}(\text{CH}_2\text{CH}_3)_2$), 169.8 ($\text{N}-\text{CH}_2\text{-N}$), 189.8 ($\text{C}=\text{O}$), 193.2 ($\text{C}=\text{O}$); MS (m/z): 525 (M^+).

1,3,6,8-Tetramethyl-7- $\{[1\text{-trifluoroacetyl}-1\text{H}-\text{benzimidazol}-2\text{-yl}]\text{azo}\}-1\text{H}-\text{pyrimido}[4,5\text{-b}][1,4]\text{-diazepine}-2,4(3\text{H},5\text{H})\text{-dione}$ (**5h**). Yield: 95 %; m.p. 120–122 °C; Anal. Calcd. for $\text{C}_{20}\text{H}_{17}\text{N}_8\text{O}_3\text{F}_3$: C, 50.63; H, 3.58; N, 23.62 %. Found: C, 50.65; H, 3.54; N, 23.64 %; IR (KBr, cm^{-1}): 1565 ($\text{N}=\text{N}$), 1620 ($\text{C}=\text{N}$), 1680 (COCF_3), 1700 ($\text{C}=\text{O}$), 1720 ($\text{C}=\text{O}$), 3310 (NH diazepine); ^1H -NMR (300 MHz, CDCl_3 , δ / ppm): 1.75 (3H, *s*, CH_3), 1.85 (3H, *s*, CH_3), 3.50 (3H, *s*, NCH_3), 3.67 (3H, *s*, NCH_3), 6.58–7.87 (4H, *m*, Ar-H), 8.86 (1H, *s*, NH diazepine); ^{13}C -NMR (75 MHz, CDCl_3 , δ / ppm): 28.2 (CH_3), 30.4 (CH_3), 34.8 ($-\text{NCH}_3$), 35.6 (NCH_3), 116.2 (CF_3), 116.8–138.2 (Ar-C), 187.6 (COCF_3), 190.3 ($\text{C}=\text{O}$), 193.2 ($\text{C}=\text{O}$); MS (m/z): 474 (M^+).

1,3,8-Trimethyl-6-phenyl-7- $\{[1\text{-trifluoroacetyl}-1\text{H}-\text{benzimidazol}-2\text{-yl}]\text{azo}\}-1\text{H}-\text{pyrimido}[4,5\text{-b}][1,4]\text{-diazepine}-2,4(3\text{H},5\text{H})\text{-dione}$ (**5i**). Yield: 97 %; m.p. 108–109 °C; Anal. Calcd. for $\text{C}_{25}\text{H}_{19}\text{N}_8\text{O}_3\text{F}_3$: C, 55.97; H, 3.54; N, 20.89 %. Found: C, 55.94; H, 3.52; N, 20.86 %; IR (KBr, cm^{-1}): 3300 (NH diazepine), 1545 ($\text{N}=\text{N}$), 1625 ($\text{C}=\text{N}$), 1685 (COCF_3), 1710 ($\text{C}=\text{O}$), 1725 ($\text{C}=\text{O}$); ^1H -NMR (300 MHz, CDCl_3 , δ / ppm): 1.79 (3H, *s*, CH_3), 3.52 (3H, *s*, NCH_3), 3.68 (3H, *s*, NCH_3), 6.56–7.88 (9H, *m*, Ar-H), 8.88 (1H, *s*, NH diazepine); ^{13}C -NMR (75 MHz, CDCl_3 , δ / ppm): 29.4 (CH_3), 34.4 (NCH_3), 35.2 (NCH_3), 116.0 (CF_3), 116.4–138.9 (Ar-C), 187.2 (COCF_3), 190.2 ($\text{C}=\text{O}$), 194.0 ($\text{C}=\text{O}$); MS (m/z): 536 (M^+).