



SUPPLEMENTARY MATERIAL TO
**Synthesis of 2-oxo-azetidine derivatives of 2-amino thiazole
and their biological activity**

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ANALYTICAL AND SPECTRAL DATA OF THE SYNTHESIZED COMPOUNDS

2-[(2-Chloroethyl)amino]thiazole (1). Yield: 56.0 g, 70 %; m.p. 66–70 °C; Anal. Calcd. for $C_5H_7ClN_2S$: C, 36.92; H, 4.33; N, 17.22 %. Found: C, 36.89; H, 4.30; N, 17.18 %; IR (KBr, cm^{-1}): 740 (C–Cl), 878 (C–S), 1336 (N–CH₂), 1564 (C=C), 2888, 3086 (CH), 3388 (NH); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.42 (2H, *t*, *J* = 7.50 Hz, CH₂–Cl), 3.94 (2H, *m*, N–CH₂), 6.80 (1H, *d*, *J* = 4.70 Hz, C5–H of thiazole), 7.18 (1H, *d*, *J* = 4.70 Hz, C4–H of thiazole), 7.70 (1H, *s*, NH); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 46.8 (CH₂–Cl), 56.1 (N–CH₂), 109.9 (C5 of thiazole), 139.9 (C4 of thiazole), 169.8 (C2 of thiazole).

N-(2-Hydrazinylethyl)-2-thiazolamine (2). Yield: 43.0 g, 80 %; m.p. 60–61 °C; Anal. Calcd. for $C_5H_{10}N_4S$: C, 37.95; H, 6.37; N, 20.26 %. Found: C, 37.91; H, 6.35; N, 20.22 %; IR (KBr, cm^{-1}): 878 (C–S), 1248 (C–N), 3378 (NH), 3429 (NH₂); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.32 (2H, *m*, CH₂–N), 3.89 (2H, *m*, N–CH₂), 5.56 (2H, *s*, NH₂), 6.76 (1H, *d*, *J* = 5.0 Hz, C5–H of thiazole), 7.15 (1H, *d*, *J* = 5.0 Hz, C4–H of thiazole), 7.63 (1H, *s*, NH), 7.72 (1H, *s*, NH); ¹³C-NMR (75 MHz, CDCl₃, δ / pm): 49.1 (CH₂–N), 54.7 (N–CH₂), 109.8 (C5 of thiazole), 138.7 (C4 of thiazole), 168.6 (C2 of thiazole); Mass (FAB).

Benzaldehyde 2-[2-(2-thiazolylamino)ethyl]-hydrazone (3a). Yield: 3.27 g, 60 %; m.p. 79–80 °C; Anal. Calcd. for $C_{12}H_{14}N_4S$: C, 58.51; H, 5.72; N, 22.74 %. Found: C, 58.45; H, 5.67; N, 22.70 %; IR (KBr, cm^{-1}): 3374 (NH), 1557 (N=CH); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.41 (2H, *m*, CH₂–N), 3.96 (2H, *m*, N–CH₂), 6.64 (1H, *d*, *J* = 4.95 Hz, C5–H of thiazole), 7.29 (1H, *d*, *J* = 4.95 Hz, C4–H of thiazole), 7.56 (1H, *s*, NH), 7.82 (1H, *s*, N=CH), 7.98 (1H,

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s, NH), 6.40–7.11 (5H, *m*, Ar–H); ^{13}C -NMR (75 MHz, CDCl_3 , δ / ppm): 49.5 ($\text{CH}_2\text{-N}$), 55.4 (N-CH_2), 112.8 (C5 of thiazole), 141.5 (C4 of thiazole), 152.2 (N=CH), 170.1 (C2 of thiazole), 124.6, 127.8, 131.8, 137.8 (Ar).

4-Chlorobenzaldehyde 2-[2-(2-thiazolylamino)ethyl]hydrazone (3b). Yield: 4.23 g, 68 %; m.p. 80–83 °C; Anal. Calcd. for $\text{C}_{12}\text{H}_{13}\text{ClN}_4\text{S}$: C, 51.33; H, 4.66; N, 19.95 %. Found: C, 51.30; H, 4.62; N, 19.92 %; IR (KBr, cm^{-1}): 3378 (NH), 1569 (N=CH), 747 (C–Cl); ^1H -NMR (300 MHz, CDCl_3 , δ / ppm): 3.53 (2H, *m*, $\text{CH}_2\text{-N}$), 3.94 (2H, *m*, N-CH_2), 7.16 (1H, *d*, $J = 5.0$ Hz, C5–H of thiazole), 7.40 (1H, *d*, $J = 5.0$ Hz, C4–H of thiazole), 7.55 (1H, *s*, NH), 7.82 (1H, *s*, NH), 7.94 (1H, *s*, N=CH), 6.68–7.81 (4H, *m*, Ar–H); ^{13}C -NMR (75 MHz, CDCl_3 , δ / ppm): 49.4 ($\text{CH}_2\text{-N}$), 57.8 (N-CH_2), 115.8 (C5 of thiazole), 143.9 (C4 of thiazole), 155.6 (N=CH), 172.9 (C2 of thiazole), 125.5, 129.6, 134.9, 140.4 (Ar).

3-Chlorobenzaldehyde 2-[2-(2-thiazolylamino)ethyl]hydrazone (3c). Yield: 4.17 g, 67 %; m.p. 77–79 °C; Anal. Calcd. for $\text{C}_{12}\text{H}_{13}\text{ClN}_4\text{S}$: C, 51.33; H, 4.66; N, 19.95 %. Found: C, 51.28; H, 4.60; N, 19.90 %; IR (KBr, cm^{-1}): 745 (C–Cl), 1566 (N=CH), 3378 (NH); ^1H -NMR (300 MHz, CDCl_3 , δ / ppm): 3.51 (2H, *m*, $\text{CH}_2\text{-N}$), 3.96 (2H, *m*, N-CH_2), 7.17 (1H, *d*, $J = 5.10$ Hz, C5–H of thiazole), 7.31 (1H, *d*, $J = 5.10$ Hz, C4–H of thiazole), 7.65 (1H, *s*, NH), 7.85 (1H, *s*, NH), 7.92 (1H, *s*, N=CH), 7.10–7.82 (4H, *m*, Ar–H); ^{13}C -NMR (75 MHz, CDCl_3 , δ / ppm): 47.4 ($\text{CH}_2\text{-N}$), 57.5 (N-CH_2), 114 (C5 of thiazole), 142.8 (C4 of thiazole), 157.4 (N=CH), 171.5 (C2 of thiazole), 126.8, 128.7, 130.8, 132.6, 136.7, 137.8 (Ar).

2-Chlorobenzaldehyde 2-[2-(2-thiazolylamino)ethyl]hydrazone (3d). Yield: 4.0 g, 65 %; m.p. 77–78 °C; Anal. Calcd. for $\text{C}_{12}\text{H}_{13}\text{ClN}_4\text{S}$: C, 51.33; H, 4.66; N, 19.95 %. Found: C, 51.25; H, 4.61; N, 19.93 %; IR (KBr, cm^{-1}): 748 (C–Cl), 1560 (N=CH), 3375 (NH); ^1H -NMR (300 MHz, CDCl_3 , δ / ppm): 3.48 (2H, *m*, $\text{CH}_2\text{-N}$), 3.80 (2H, *m*, N-CH_2), 7.17 (1H, *d*, $J = 5.0$ Hz, C5–H of thiazole), 7.36 (1H, *d*, $J = 5.0$ Hz, C4–H of thiazole), 7.53 (1H, *s*, NH), 7.79 (1H, *s*, NH), 7.89 (1H, *s*, N=CH), 7.20–7.92 (4H, *m*, Ar–H); ^{13}C -NMR (75 MHz, CDCl_3 , δ / ppm): 48.6 ($\text{CH}_2\text{-N}$), 58.2 (N-CH_2), 112.9 (C5 of thiazole), 142.9 (C4 of thiazole), 154.6 (N=CH), 170.6 (C2 of thiazole), 126.8, 128.6, 128.9, 129.8, 132.7, 139.6 (Ar); Mass (FAB).

4-Bromobenzaldehyde 2-[2-(2-thiazolylamino)ethyl]hydrazone (3e). Yield: 4.96 g, 69 %; m.p. 80–81 °C; Anal. Calcd. for $\text{C}_{12}\text{H}_{13}\text{BrN}_4\text{S}$: C, 44.31; H, 4.02; N, 17.22 %. Found: C, 44.21; H, 3.96; N, 17.15 %; IR (KBr, cm^{-1}): 642 (C–Br), 1552 (N=CH), 3360 (NH); ^1H -NMR (300 MHz, CDCl_3 , δ / ppm): 3.49 (2H, *m*, $\text{CH}_2\text{-N}$), 3.76 (2H, *m*, N-CH_2), 7.09 (1H, *d*, $J = 5.0$ Hz, C5–H of thiazole), 7.28 (1H, *d*, $J = 5.0$ Hz, C4–H of thiazole), 7.59 (1H, *s*, NH), 7.75 (1H, *s*, NH), 7.94 (1H, *s*, N=CH) 7.39–7.68 (4H, *m*, Ar–H); ^{13}C -NMR (75 MHz, CDCl_3 , δ / ppm): 48.2 ($\text{CH}_2\text{-N}$), 56.5 (N-CH_2), 111.8 (C5 of thiazole), 140.9 (C4 of thiazole), 154.6 (N=CH), 169.9 (C2 of thiazole), 126.9, 129.8, 133.9, 137.8 (Ar).

3-Bromobenzaldehyde 2-[2-(2-thiazolylamino)ethyl]hydrazone (3f). Yield: 4.82 g, 67 %; m.p. 82–83 °C; Anal. Calcd. for C₁₂H₁₃BrN₄S: C, 44.31; H, 4.02; N, 17.22 %. Found: C, 44.23; H, 3.96; N, 17.16 %; IR (KBr, cm⁻¹): 636 (C–Br), 1568 (N=CH), 3369 (NH); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.50 (2H, *m*, CH₂–N), 3.98 (2H, *m*, N–CH₂), 7.10 (1H, *d*, *J* = 5.0 Hz, C5–H of thiazole), 7.30 (1H, *d*, *J* = 5.0 Hz, C4–H of thiazole), 7.55 (1H, *s*, NH), 7.73 (1H, *s*, NH), 7.92 (1H, *s*, N=CH), 7.23–7.90 (4H, *m*, Ar–H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 47.8 (N–CH₂), 59.4 (CH₂–N), 112.8 (C5 of thiazole), 141.6 (C4 of thiazole), 151.8 (N=CH), 172.8 (C2 of thiazole), 124.8, 126.9, 129.6, 131.8, 137.9, 141.8 (Ar).

2-Bromobenzaldehyde 2-[2-(2-thiazolylamino)ethyl]hydrazone (3g). Yield: 4.46 g, 62 %; m.p. 79–81 °C; Anal. Calcd. for C₁₂H₁₃BrN₄S: C, 44.31; H, 4.02; N, 17.22 %. Found: C, 44.20; H, 3.95; N, 17.18 %; IR (KBr, cm⁻¹): 632 (C–Br), 1573 (N=CH), 3374 (NH); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.31 (2H, *m*, CH₂–N), 3.77 (2H, *m*, N–CH₂), 7.12 (1H, *d*, *J* = 5.0 Hz, C5–H of thiazole), 7.32 (1H, *d*, *J* = 5.0 Hz, C4–H of thiazole), 7.49 (1H, *s*, NH), 7.85 (1H, *s*, NH), 8.01 (1H, *s*, N=CH), 7.31–7.63 (4H, *m*, Ar–H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 50.1 (CH₂–N), 59.4 (N–CH₂), 109.9 (C5 of thiazole), 140.2 (C4 of thiazole), 154.6 (N=CH), 171.8 (C2 of thiazole), 126., 128.8, 129.7, 131.8, 133.8, 141.8 (Ar).

4-Nitrobenzaldehyde 2-[2-(2-thiazolylamino)ethyl]hydrazone (3h). Yield: 4.19 g, 65 %; m.p. 84–86 °C; Anal. Calcd. for C₁₂H₁₃N₅O₂S: C, 49.47; H, 4.49; N, 24.03 %. Found: C, 49.42; H, 4.45; N, 24.00 %; IR (KBr, cm⁻¹): 852 (C–N), 1542 (N=O), 1575 (N=CH), 3379 (NH); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.59 (2H, *m*, CH₂–N), 3.94 (2H, *m*, N–CH₂), 7.14 (1H, *s*, NH), 7.22 (1H, *d*, *J* = 5.0 Hz, C5–H of thiazole), 7.41 (1H, *s*, NH), 7.52 (1H, *d*, *J* = 5.0 Hz, C4–H of thiazole), 8.12 (1H, *s*, N=CH), 7.32–7.91 (4H, *m*, Ar–H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 48.3 (CH₂–N), 58.3 (N–CH₂), 112.9 (C5 of thiazole), 141.6 (C4 of thiazole), 155.8 (N=CH), 171.5 (C2 of thiazole), 124.8, 129.7, 138.8, 147.6 (Ar).

3-Nitrobenzaldehyde 2-[2-(2-thiazolylamino)ethyl]hydrazone (3i). Yield: 4.38 g, 68 %; m.p. 85–87 °C; Anal. Calcd. for C₁₂H₁₃N₅SO₂: C, 49.47; H, 4.49; N, 24.03 %. Found: C, 49.40; H, 4.47; N, 23.98 %; IR (KBr, cm⁻¹): 3365 (NH), 1534 (N=O), 1579 (N=CH), 858 (C–N); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.26 (2H, *m*, CH₂–N), 3.92 (2H, *m*, N–CH₂), 7.08 (1H, *s*, NH), 7.17 (1H, *d*, *J* = 5.0 Hz, C5–H of thiazole), 7.42 (1H, *d*, *J* = 5.0 Hz, C4–H of thiazole), 7.72 (1H, *s*, NH), 7.92 (1H, *s*, N=CH), 7.21–7.86 (4H, *m*, Ar–H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 47.2 (CH₂–N), 57.8 (N–CH₂), 154.5 (N=CH), 171.6 (C2 of thiazole), 112.8 (C5 of thiazole), 140.6 (C4 of thiazole), 122.7, 125.5, 128.7, 133.8, 137.7, 150.8 (Ar).

2-Nitrobenzaldehyde 2-[2-(2-thiazolylamino)ethyl]hydrazone (3j). Yield: 4.20 g, 65 %; m.p. 80–81 °C; Anal. Calcd. for C₁₂H₁₃N₅O₂S: C, 49.47; H, 4.49; N, 24.03 %. Found: C, 49.43; H, 4.44; N, 23.97 %; IR (KBr, cm⁻¹): 852 (C–N), 1541 (N=O), 1578 (N=CH), 3359 (NH); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.35 (2H, *m*, CH₂–N), 3.96 (2H, *m*, N–CH₂), 7.15 (1H, *s*, NH), 7.18 (1H, *d*, *J* = 4.90 Hz, C5–H of thiazole), 7.36 (1H, *d*, *J* = 4.90 Hz, C4–H of thiazole), 7.53 (1H, *s*, NH), 8.12 (1H, *s*, N=CH), 7.26–7.99 (4H, *m*, Ar–H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 47.6 (CH₂–N), 57.4 (N–CH₂), 110.7 (C5 of thiazole), 139.6 (C4 of thiazole), 155.8 (N=CH), 171.8 (C2 of thiazole), 122.8, 125.8, 127.8, 133.6, 137.7, 149.6 (Ar).

4-Methoxybenzaldehyde 2-[2-(2-thiazolylamino)ethyl]hydrazone (3k). Yield: 3.91 g, 64 %; m.p. 73–74 °C; Anal. Calcd. for C₁₃H₁₆N₄OS: C, 56.49; H, 5.83; N, 20.27 %. Found: C, 56.40; H, 5.78; N, 20.22 %; IR (KBr, cm⁻¹): 1568 (N=CH), 2949 (OCH₃), 3361 (NH); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.28 (2H, *m*, CH₂–N), 3.52 (3H, *s*, OCH₃), 3.67 (2H, *m*, N–CH₂), 7.20 (1H, *d*, *J* = 4.95 Hz, C5–H of thiazole), 7.39 (1H, *d*, *J* = 4.95 Hz, C4–H of thiazole), 7.45 (1H, *s*, NH), 7.85 (1H, *s*, N=CH), 7.98 (1H, *s*, NH), 7.34–7.52 (4H, *m*, Ar–H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 46.6 (CH₂–N), 55.5 (N–CH₂), 54.7 (OCH₃), 110.1 (C5 of thiazole), 138.6 (C4 of thiazole), 154.7 (N=CH), 170.6 (C2 of thiazole), 114.8, 128.8, 130.7, 159.9 (Ar).

4-Methylbenzaldehyde 2-[2-(2-thiazolylamino)ethyl]hydrazone (3l). Yield: 3.45 g, 60 %; m.p. 66–67 °C; Anal. Calcd. for C₁₃H₁₆N₄S: C, 59.97; H, 6.19; N, 21.51 %. Found: C, 59.92; H, 6.15; N, 21.44 %; IR (KBr, cm⁻¹): 1545 (N=CH), 2914 (CH₃), 3348 (NH); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.32 (2H, *m*, CH₂–N), 2.62 (3H, *s*, CH₃), 3.82 (2H, *m*, N–CH₂), 6.87 (1H, *d*, *J* = 4.85 Hz, C5–H of thiazole), 7.25 (1H, *d*, *J* = 4.85 Hz, C4H of thiazole), 7.38 (1H, *s*, NH), 7.82 (1H, *s*, NH), 7.89 (1H, *s*, N=CH), 7.39–7.79 (4H, *m*, Ar–H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 24.9 (CH₃), 45.3 (CH₂–N), 54.7 (N–CH₂), 151.6 (N=CH), 171.5 (C2 of thiazole), 111.5 (C5 of thiazole), 140.4 (C4 of thiazole), 127.9, 129.8, 134.5, 139.8 (Ar).

4-Hydroxybenzaldehyde 2-[2-(2-thiazolylamino)ethyl]hydrazone (3m). Yield: 3.60 g, 62 %; m.p. 66–67 °C; Anal. Calcd. for C₁₂H₁₄N₄OS: C, 54.94; H, 5.37; N, 21.35 %. Found: C, 54.90; H, 5.32; N, 21.31 %; IR (KBr, cm⁻¹): 1565 (N=CH), 3388 (NH), 3477 (OH); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.37 (2H, *m*, CH₂–N), 3.89 (2H, *m*, N–CH₂), 4.12 (1H, *s*, OH), 7.12 (1H, *d*, *J* = 4.85 Hz, C5–H of thiazole), 7.35 (1H, *d*, *J* = 4.85 Hz, C4–H of thiazole), 7.42 (1H, *s*, NH), 7.76 (1H, *s*, NH), 8.06 (1H, *s*, N=CH), 7.32–7.79 (4H, *m*, Ar–H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 48.1 (CH₂–N), 57.6 (N–CH₂), 108.8 (C5 of thiazole), 138.9 (C4 of thiazole), 154.6 (N=CH), 169.8 (C2 of thiazole), 115.7, 126.6, 130.8, 154.9 (Ar).

3-Chloro-4-phenyl-1-[[2-(2-thiazolylamino)ethyl]amino]-2-azetidinone (4a). Yield: 2.44 g, 62 %; m.p. 78–80 °C; Anal. Calcd. for C₁₄H₁₅ClN₄OS: C, 52.08; H, 4.68; N, 17.35 %. Found: C, 52.02; H, 4.63; N, 17.31%; IR (KBr, cm⁻¹): 1337 (C–N), 2917 (CH–Cl), 1741 (CO, cyclic); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.30 (2H, *m*, CH₂–N), 3.90 (2H, *m*, N–CH₂), 4.26 (1H, *d*, *J* = 4.90 Hz, CH–Cl), 4.72 (1H, *d*, *J* = 4.90 Hz, N–CH), 7.15 (1H, *d*, *J* = 4.95 Hz, C5–H of thiazole), 7.23 (1H, *d*, *J* = 4.95 Hz, C4–H of thiazole), 7.35 (1H, *s*, NH), 7.70 (1H, *s*, NH), 6.85–7.72 (5H, *m*, Ar–H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 41.2 (CH₂–N), 50.6 (N–CH₂), 54.6 (CH–Cl), 62.7 (N–CH), 111.7 (C5 of thiazole), 139.8 (C4 of thiazole), 171.5 (C2 of thiazole), 173.7 (CO, cyclic), 124.6, 128.9, 132.8, 137.9 (Ar).

3-Chloro-4-(4-chlorophenyl)-1-[[2-(2-thiazolylamino)ethyl]amino]-2-azetidinone (4b). Yield: 3.54 g, 68 %; m.p. 80–82 °C; Anal. Calcd. for C₁₄H₁₄Cl₂N₄OS: C, 47.06; H, 3.94; N, 15.68 %. Found: C, 47.00; H, 3.91; N, 15.64 %; IR (KBr, cm⁻¹): 769 (C–Cl), 1342 (C–N), 1752 (CO, cyclic), 2921 (CH–Cl); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.36 (2H, *m*, CH₂–N), 3.94 (2H, *m*, N–CH₂), 4.21 (1H, *d*, *J* = 4.95 Hz, CH–Cl), 4.86 (1H, *d*, *J* = 4.95 Hz, N–CH), 7.12 (1H, *d*, *J* = 5.0 Hz, C5–H of thiazole), 7.29 (1H, *d*, *J* = 5.0 Hz, C4–H of thiazole), 7.45 (1H, *s*, NH), 7.86 (1H, *s*, NH), 6.86–7.72 (4H, *m*, Ar–H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 42.3 (CH₂–N), 51.1 (N–CH₂), 53.5 (CH–Cl), 63.8 (N–CH), 113.6 (C5 of thiazole), 142.8 (C4 of thiazole), 172.6 (C2 of thiazole), 176.2 (CO, cyclic), 127.8, 130.7, 136.4, 140.5 (Ar).

3-Chloro-4-(3-chlorophenyl)-1-[[2-(2-thiazolylamino)ethyl]amino]-2-azetidinone (4c). Yield: 3.30 g, 65 %; m.p. 78–79 °C; Anal. Calcd. for C₁₄H₁₄Cl₂N₄OS: C, 47.06; H, 3.94; N, 15.68 %. Found: C, 47.02; H, 3.85; N, 15.62 %; IR (KBr, cm⁻¹): 778 (C–Cl), 1345 (C–N), 1745 (C=O, cyclic), 2919 (CH–Cl); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.32 (2H, *m*, CH₂–N), 3.96 (2H, *m*, N–CH₂), 4.38 (1H, *d*, *J* = 5.05 Hz, CH–Cl), 4.86 (1H, *d*, *J* = 5.05 Hz, N–CH), 7.15 (1H, *d*, *J* = 4.90 Hz, C5–H of thiazole), 7.24 (1H, *d*, *J* = 4.90 Hz, C4–H of thiazole), 7.46 (1H, *s*, NH), 7.80 (1H, *s*, NH), 6.79–7.64 (4H, *m*, Ar–H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 41.8 (CH₂–N), 51.9 (N–CH₂), 54.8 (CH–Cl), 65.7 (N–CH), 112.8 (C5 of thiazole), 142.4 (C4 of thiazole), 172.6 (C2 of thiazole), 175.5 (CO, cyclic), 126.8, 128.9, 129.7, 132.7, 135.6, 139.6 (Ar).

3-Chloro-4-(2-chlorophenyl)-1-[[2-(2-thiazolylamino)ethyl]amino]-2-azetidinone (4d). Yield: 3.18 g, 66 %; m.p. 74–75 °C; Anal. Calcd. for C₁₄H₁₄Cl₂N₄OS: C, 47.06; H, 3.94; N, 15.68 %. Found: C, 47.00; H, 3.89; N, 15.64 %; IR (KBr, cm⁻¹): 778 (C–Cl), 1339 (C–N), 1750 (C=O, cyclic), 2925 (CH–Cl); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.36 (2H, *m*, CH₂–N), 3.94 (2H, *m*, N–CH₂), 4.33 (1H, *d*, *J* = 5.0 Hz, CH–Cl), 4.86 (1H, *d*, *J* = 5.0 Hz, N–CH), 7.12 (1H, *d*, *J* = 4.85 Hz, C5–H of thiazole), 7.27 (1H, *d*, *J* = 4.85 Hz, C4–H of thiazole), 7.43 (1H, *s*, NH), 7.82 (1H, *s*, NH), 6.81–7.62 (4H, *m*, Ar–H); ¹³C-NMR

(75 MHz, CDCl₃, δ / ppm): 43.4 (CH₂-N), 52.9 (N-CH₂), 53.8 (CH-Cl), 63.4 (N-CH), 112.6 (C5 of thiazole), 141.7 (C4 of thiazole), 172.6 (C2 of thiazole), 174.2 (CO, cyclic), 126.4, 128.4, 129.5, 130.8, 133.9, 137.8 (Ar).

4-(4-Bromophenyl)3-chloro-1-[[2-(2-thiazolylamino)ethyl]amino]-2-azetidione (4e). Yield: 3.50 g, 60 %; m.p. 83–84 °C; Anal. Calcd. for C₁₄H₁₄BrClN₄O₂S: C, 41.85; H, 3.51; N, 13.94 %. Found: C, 41.82; H, 3.45; N, 13.90 %; IR (KBr, cm⁻¹): 572 (C-Br), 1310 (C-N), 1748 (CO cyclic), 2896 (CH-Cl); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.33 (2H, *m*, CH₂-N), 3.95 (2H, *m*, N-CH₂), 4.30 (1H, *d*, *J* = 5.0 Hz, CH-Cl), 4.92 (1H, *d*, *J* = 5.0 Hz, N-CH), 7.14 (1H, *d*, *J* = 4.95 Hz, C5-H of thiazole), 7.32 (1H, *d*, *J* = 4.95 Hz, C4-H of thiazole), 7.46 (1H, *s*, NH), 7.88 (1H, *s*, NH), 7.35–7.95 (4H, *m*, Ar-H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 43.0 (CH₂-N), 52.1 (N-CH₂), 53.6 (CH-Cl), 62.7 (N-CH), 112.6 (C5 of thiazole), 140.9 (C4 of thiazole), 171.2 (C2 of thiazole), 171.9 (CO, cyclic), 122.5, 128.8, 134.7, 137.8 (Ar).

4-(3-Bromophenyl)3-chloro-1-[[2-(2-thiazolylamino)ethyl]amino]-2-azetidione (4f). Yield: 3.60 g, 65 %; m.p. 81–82 °C; Anal. Calcd. for C₁₄H₁₄BrClN₄O₂S: C, 41.85; H, 3.51; N, 13.94 %. Found: C, 41.82; H, 3.48; N, 13.91 %; IR (KBr, cm⁻¹): 578 (C-Br), 1328 (C-N), 1744 (CO, cyclic), 2892 (CH-Cl); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.29 (2H, *m*, CH₂-N), 3.91 (2H, *m*, N-CH₂), 4.29 (1H, *d*, *J* = 5.10 Hz, CH-Cl), 4.97 (1H, *d*, *J* = 5.10 Hz, N-CH), 7.00 (1H, *d*, *J* = 4.90 Hz, C5-H of thiazole), 7.30 (1H, *d*, *J* = 4.90 Hz, C4-H of thiazole), 7.39 (1H, *s*, NH), 7.91 (1H, *s*, NH), 7.31–7.92 (4H, *m*, Ar-H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 42.5 (CH₂-N), 51.9 (N-CH₂), 52.7 (CH-Cl), 621.9 (N-CH), 112.6 (C5 of thiazole), 141.7 (C4 of thiazole), 171.9 (C2 of thiazole), 175.3 (CO, cyclic), 123.5, 125.6, 129.8, 130.7, 132.8, 139.2 (Ar).

4-(2-Bromophenyl)3-chloro-1-[[2-(2-thiazolylamino)ethyl]amino]-2-azetidione (4g). Yield: 3.30 g, 64 %; m.p. 80–81 °C; Anal. Calcd. for C₁₄H₁₄BrClN₄O₂S: C, 41.85; H, 3.51; N, 13.94 %. Found: C, 41.80; H, 3.50; N, 13.92 %; IR (KBr, cm⁻¹): 569 (C-Br), 1329 (C-N), 1750 (CO, cyclic), 2888 (CH-Cl); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.33 (2H, *m*, CH₂-N), 3.97 (2H, *m*, N-CH₂), 4.34 (1H, *d*, *J* = 5.10 Hz, CH-Cl), 4.95 (1H, *d*, *J* = 5.10 Hz, N-CH), 7.97 (1H, *d*, *J* = 4.90 Hz, C5-H of thiazole), 7.29 (1H, *d*, *J* = 4.90 Hz, C4-H of thiazole), 7.48 (1H, *s*, NH), 7.94 (1H, *s*, NH), 7.27–7.84 (4H, *m*, Ar-H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 42.4 (CH₂-N), 51.7 (N-CH₂), 51.7 (CH-Cl), 61.9 (N-CH), 111.8 (C5 of thiazole), 140.8 (C4 of thiazole), 170.8 (C2 of thiazole), 174.5 (CO, cyclic), 121.4, 125.7, 127.9, 131.3, 133.4, 142.6 (Ar).

3-Chloro-4-(4-nitrophenyl)-1-[[2-(2-thiazolylamino)ethyl]amino]-2-azetidione (4h). Yield: 3.40 g, 68 %; m.p. 88–90 °C; Anal. Calcd. for C₁₄H₁₄ClN₅O₃S: C, 45.71; H, 3.83; N, 19.04 %. Found: C, 45.66; H, 3.80; N, 19.00 %; IR (KBr, cm⁻¹): 878 (C-NO), 1548 (NO₂), 1744 (CO, cyclic), 2927 (CH-Cl); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.34 (2H, *m*, CH₂-N), 3.96 (2H,

m, N-CH₂), 4.30 (1H, *d*, *J* = 4.85 Hz, CH-Cl), 4.93 (1H, *d*, *J* = 5.10 Hz, N-CH), 7.30 (1H, *d*, *J* = 4.80 Hz, C4-H of thiazole), 7.81 (1H, *d*, *J* = 4.80 Hz, C5-H of thiazole), 7.45 (1H, *s*, NH), 7.87 (1H, *s*, NH), 7.13–7.71 (4H, *m*, Ar-H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 43.1 (CH₂-N), 52.6 (N-CH₂), 51.3 (CH-Cl), 64.8 (N-CH), 112.8 (C5 of thiazole), 140.9 (C4 of thiazole), 170.4 (C2 of thiazole), 171.3 (CO, cyclic), 125.7, 127.8, 137.9, 147.8 (Ar).

3-Chloro-4-(3-nitrophenyl)-1-[[2-(2-thiazolylamino)ethyl]amino]-2-azetidione (4i). Yield: 3.37 g, 65 %; m.p. 86–87 °C; Anal. Calcd. for C₁₄H₁₄ClN₅O₃S: C, 45.71; H, 3.83; N, 19.04 %. Found: C, 45.66; H, 3.80; N, 19.02 %; IR (KBr, cm⁻¹): 869 (C-NO), 1549 (NO₂), 1741 (CO, cyclic), 2924 (CH-Cl); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.35 (2H, *m*, CH₂-N), 3.98 (2H, *m*, N-CH₂), 4.37 (1H, *d*, *J* = 5.0 Hz, CH-Cl), 4.92 (1H, *d*, *J* = 5.0 Hz, N-CH), 6.94 (1H, *d*, *J* = 4.85 Hz, C5-H of thiazole), 7.20 (1H, *d*, *J* = 4.85 Hz, C4-H of thiazole), 7.46 (1H, *s*, NH), 7.83 (1H, *s*, NH), 7.16–7.79 (4H, *m*, Ar-H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 43.1 (CH₂-N), 53.7 (N-CH₂), 54 (CH-Cl), 62.8 (N-CH), 112.6 (C5 of thiazole), 141.2 (C4 of thiazole), 171.3 (C2 of thiazole), 172.3 (CO, cyclic), 120.5, 123.9, 128.6, 138.4, 139.6, 149.8 (Ar).

3-Chloro-4-(2-nitrophenyl)-1-[[2-(2-thiazolylamino)ethyl]amino]-2-azetidione (4j). Yield: 3.34 g, 61 %; m.p. 73–74 °C; Anal. Calcd. for C₁₄H₁₄ClN₅O₃S: C, 45.71; H, 3.83; N, 19.04 %. Found: C, 45.63; H, 3.79; N, 18.96 %; IR (KBr, cm⁻¹): 879 (C-NO), 1548 (NO₂), 1740 (CO, cyclic), 2923 (CH-Cl); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.30 (2H, *m*, CH₂-N), 3.97 (2H, *m*, N-CH₂), 4.30 (1H, *d*, *J* = 5.10 Hz, CH-Cl), 4.94 (1H, *d*, *J* = 5.10 Hz, N-CH), 6.90 (1H, *d*, *J* = 4.85 Hz, C5-H of thiazole), 7.22 (1H, *d*, *J* = 4.85 Hz, C4-H of thiazole), 7.49 (1H, *s*, NH), 7.89 (1H, *s*, NH), 7.05–7.71 (4H, *m*, Ar-H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 43.4 (CH₂-N), 53.4 (N-CH₂), 52.6 (CH-Cl), 63.8 (N-CH), 112.3 (C5 of thiazole), 140.7 (C4 of thiazole), 171.8 (C2 of thiazole), 173.2 (CO, cyclic), 123.8, 127.9, 129.8, 132.8, 135.9, 145.8 (Ar).

3-Chloro-4-(4-methoxyphenyl)-1-[[2-(2-thiazolylamino)ethyl]amino]-2-azetidione (4k). Yield: 2.75 g, 60 %; m.p. 72–74 °C; Anal. Calcd. for C₁₅H₁₇ClN₄O₂S: C, 51.06; H, 4.85; N, 15.87 %. Found: C, 51.00; H, 4.80; N, 15.82 %; IR (KBr, cm⁻¹): 1160 (C-O), 1323 (N-C), 1726 (CO, cyclic), 2890 (CH-Cl); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 3.29 (2H, *m*, CH₂-N), 3.95 (2H, *m*, N-CH₂), 3.60 (3H, *s*, OCH₃), 4.21 (1H, *d*, *J* = 5.15 Hz, CH-Cl), 4.79 (1H, *d*, *J* = 5.15 Hz, N-CH), 6.92 (1H, *d*, *J* = 4.95 Hz, C5-H of thiazole), 7.27 (1H, *d*, *J* = 4.95 Hz, C4-H of thiazole), 7.44 (1H, *s*, NH), 7.80 (1H, *s*, NH), 7.26–7.92 (4H, *m*, Ar-H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 40.9 (CH₂-N), 50.8 (N-CH₂), 50.7 (CH-Cl), 54.3 (OCH₃), 61.4 (N-CH), 111.6 (C5 of thiazole), 139.8 (C4 of thiazole), 169.7 (C₂ of thiazole), 171.5 (CO, cyclic), 113.4, 127.2, 131.7, 160.2 (Ar).

3-Chloro-4-(4-methylphenyl)-1-[[2-(2-thiazolylamino)ethyl]amino]-2-azetidione (4l). Yield: 2.30 g, 56 %; m.p. 69–70 °C; Anal. Calcd. for C₁₅H₁₇ClN₄O₂S: C, 53.48; H, 5.08; N, 16.63 %. Found: C, 53.43; H, 5.05; N, 16.60 %; IR (KBr, cm⁻¹): 1742 (CO, cyclic), 2880 (CH–Cl), 2928 (CH₃); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 2.61 (3H, *s*, CH₃), 3.32 (2H, *m*, CH₂–N), 3.94 (2H, *m*, N–CH₂), 4.13 (1H, *d*, *J* = 5.05 Hz, CH–Cl), 4.72 (1H, *d*, *J* = 5.05 Hz, N–CH), 6.80 (1H, *d*, *J* = 4.90 Hz, C5–H of thiazole), 7.18 (1H, *d*, *J* = 4.90 Hz, C4–H of thiazole), 7.36 (1H, *s*, NH), 7.82 (1H, *s*, NH), 7.28–7.98 (4H, *m*, Ar–H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 24.8 (CH₃), 40.1 (CH₂–N), 50.0 (N–CH₂), 49.7 (CH–Cl), 60.8 (N–CH), 111.6 (C5 of thiazole), 138.7 (C4 of thiazole), 169.8 (CO, cyclic), 170.5 (C2 of thiazole), 126.8, 129.5, 134.8, 137.7 (Ar).

3-Chloro-4-(4-hydroxyphenyl)-1-[[2-(2-thiazolylamino)ethyl]amino]-2-azetidione (4m). Yield: 2.65 g, 64 %; m.p. 65–67 °C; Anal. Calcd. for C₁₄H₁₅ClN₄O₂S: C, 49.62; H, 4.46; N, 16.53 %. Found: C, 49.55; H, 4.41; N, 16.50 %; IR (KBr, cm⁻¹): 1750 (CO, cyclic), 2925 (CH–Cl), 3462 (OH); ¹H-NMR (300 MHz, CDCl₃, δ / ppm): 4.18 (1H, *s*, OH), 3.35 (2H, *m*, CH₂–N), 3.98 (2H, *m*, N–CH₂), 4.28 (1H, *d*, *J* = 5.10 Hz, CH–Cl), 4.98 (1H, *d*, *J* = 5.10 Hz, N–CH), 6.92 (1H, *d*, *J* = 4.85 Hz, C5–H of thiazole), 7.32 (1H, *d*, *J* = 4.85 Hz, C4–H of thiazole), 7.39 (1H, *s*, NH), 7.85 (1H, *s*, NH), 7.09–8.12 (4H, *m*, Ar–H); ¹³C-NMR (75 MHz, CDCl₃, δ / ppm): 41.5 (CH₂–N), 51.8 (N–CH₂), 53.6 (CH–Cl), 63.9 (N–CH), 112.6 (C5 of thiazole), 139.8 (C4 of thiazole), 169.8 (C2 of thiazole), 176.4 (CO, cyclic), 113.8, 122.9, 138.8, 153.8 (Ar).