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SUPPLEMENTARY MATERIAL TO

Synthesis and *in vitro* anti-breast cancer activity of some novel 1,5-benzothiazepine derivatives

K. L. AMETA*, NITU S. RATHORE and BIRESH KUMAR

Department of Chemistry, FASC, Mody Institute of Technology and Science (Deemed University) Lakshmangarh, Rajasthan-332311, India

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ANALYTICAL AND SPECTRAL DATA OF THE NEWLY SYNTHESIZED COMPOUNDS

*2,4-Dibromo-6-(2-phenyl-2,3-dihydro-1,5-benzothiazepin-4-yl)benzene-1,3--diol (**3a**)*. Yield: 78 %; m.p.: 80–81 °C; Anal. Calcd. for $C_{21}H_{15}Br_2NO_2S$ (FW 504.80): C, 49.92; H, 2.97; O, 6.34; N, 2.77 %. Found: C, 49.86; H, 2.92; O, 6.40; N, 2.82 %; IR (KBr, cm^{-1}): 3372 (O–H stretching), 3289 (aliphatic C–H stretching), 3059–3008 (aromatic C–H stretching), 1606 (C=N), 1575 (C=C), 862 (C–Br), 666 (C–S); ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 9.2–8.7 (2H, *brs*, aromatic-OH), 7.86 (1H, *s*, aromatic), 7.56–7.10 (9H, *m*, aromatic), 4.9 (1H, *t*, J = 11.2 Hz, CH), 3.35 (2H, *d*, J = 12.2 Hz, CH_2); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 162.52 (C=N), 158.59 (C–OH), 155.42 (C'–OH), 140.62, 131.49, 129.62, 128.57, 126.50, 116.99 (aromatic-C), 140.54 (C–S), 108.81 (C'–Br), 94.60 (C–Br), 55.37 (CH_2), 52.63 (CH); MS (*m*/*z*): 506.80 $[M+2+H]^+$.

*2,4-Dibromo-6-[2-(2-chlorophenyl)-2,3-dihydro-1,5-benzothiazepin-4-yl]-benzene-1,3-diol (**3b**)*. Yield: 82 %; m.p.: 82–83 °C. Anal. Calcd. for $C_{21}H_{14}Br_2ClNO_2S$ (FW 539.30): C, 46.73; H, 2.60; O, 5.94; N, 2.60 %. Found: C, 46.80; H, 2.67; O, 5.90; N, 2.53 %; IR (KBr, cm^{-1}): 3378 (O–H stretching), 3298 (aliphatic C–H stretching), 3061–3018 (aromatic C–H stretching), 1629 (C=N), 1571 (C=C), 862 (C–Br), 753 (C–Cl stretching of chlorine), 666 (C–S); ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 9.5–8.4 (2H, *brs*, aromatic–OH), 7.86 (1H, *s*, aromatic), 7.45–7.15 (8H, *m*, aromatic), 4.98 (1H, *t*, J = 11.1 Hz, CH), 3.54 (2H, *d*, J = 12.2 Hz, CH_2); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 165.50 (C=N), 158.53 (C–OH), 154.52 (C'–OH), 140.44 (C–S),139.51, 131.49, 129.93, 128.07, 127.85, 126.50, 116.99 (aromatic-C), 131.48 (C–Cl), 107.80 (C'–Br), 94.51 (C–Br), 53.63 (CH_2), 49.39 (CH); MS (*m*/*z*): 541.30 $[M+2+H]^+$.

* Corresponding author. E-mail: klameta77@yahoo.co.in

2,4-Dibromo-6-[2-(2,4-dichlorophenyl)-2,3-dihydro-1,5-benzothiazepin-4--yl]benzene-1,3-diol (***3c***). Yield: 84 %; m.p.: 89–90 °C. Anal. Calcd. for $C_{21}H_{13}Br_2Cl_2NO_2S$ (FW 573.80): C, 43.92; H, 2.26; O, 5.58; N, 2.44 %. Found: C, 43.86; H, 2.21; O, 5.54; N, 2.50 %; IR (KBr, cm^{-1}): 3370 (O–H stretching), 3288 (aliphatic C–H stretching), 3060 (aromatic C–H stretching), 2830 (OCH_3), 848–825 (C–Cl stretching of chlorine), 1606 (C=N), 1564 (C=C), 862 (C–Br), 665 (C–S), ^{1}H-NMR (500 MHz, $CDCl_3$ δ / ppm): 9.6–8.53 (2H, *brs*, aromatic–OH), 7.86 (1H, *s*, aromatic), 7.50–7.16 (7H, *m*, aromatic), 4.97 (1H, *t*, *J* = 11.2 Hz, CH), 3.46 (2H, *d*, *J* = 12.3 Hz, CH_2); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 166.43 (C=N), 159.76 (C–OH), 156.26 (C'–OH), 139.63 (C–S),133.66, 131.69, 129.11, 128.07, 127.75, 126.50 (aromatic-C), 132.71 (C–Cl), 109.38 (C'–Br), 95.31 (C–Br), 54.46 (CH_2), 50.35 (CH); MS (*m*/*z*): 575.80 $[M+2+H]^+$.

2,4-Dibromo-6-[2-(2-fluorophenyl)-2,3-dihydro-1,5-benzothiazepin-4-yl]-benzene-1,3-diol (***3d***). Yield: 83 %; m.p.: 81–82 °C. Anal. Calcd. for $C_{21}H_{14}Br_2FNO_2S$ (FW 522.80): C, 48.20; H, 2.68; O, 6.12; N, 2.68 %. Found: C, 48.27; H, 2.61; O, 6.06; N, 2.72 %; IR (KBr, cm^{-1}): 3368 (O–H stretching), 3284 (aliphatic C–H stretching), 3056–3005 (aromatic C–H stretching), 1605 (C=N), 1581 (C=C), 1244 (C–F stretching), 862 (C–Br), 660 (C–S); ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 9.8–8.54 (2H, *brs*, aromatic–OH), 7.82 (1H, *s*, aromatic), 7.30–6.85 (8H, *m*, aromatic), 5.01(1H, *t*, *J* = 11.1 Hz, CH), 3.45 (2H, *d*, *J* = 12.2 Hz, CH_2); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 166.78 (C=N), 150.56 (C–OH), 148.66 (C'–OH), 138.93 (C–S), 136.66, 132.02, 130.98, 128.77, 125.92, 116.74,115.63 (aromatic-C), 108.08 (C'–Br), 95.35 (C–Br), 55.51 (CH_2), 53.71 (CH); MS (*m*/*z*): 524.80 $[M+2+H]^+$.

2,4-Dibromo-6-[2-(4-fluorophenyl)-2,3-dihydro-1,5-benzothiazepin-4-yl]-benzene-1,3-diol (***3e***). Yield: 86 %; m.p.: 87–88 °C. Anal. Calcd. for $C_{21}H_{14}Br_2FNO_2S$ (FW 522.80): C, 48.21; H, 2.68; O, 6.12; N, 2.68 %. Found: C, 48.16; H, 2.75; O, 6.18; N, 2.61 %; IR (KBr, cm^{-1}): 3368 (O–H stretching), 3284 (aliphatic C–H stretching), 3058–3005 (aromatic C–H stretching), 1605 (C=N), 1581 (C=C), 1244 (C–F stretching), 862 (C–Br), 660 (C–S); ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 9.6–8.42 (2H, *brs*, aromatic–OH), 7.86 (1H, *s*, aromatic), 7.39–6.85 (8H, *m*, aromatic), 4.98 (1H, *t*, *J* = 11.3 Hz, CH), 3.25 (2H, *d*, *J* = 12.1 Hz, CH_2); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 165.93 (C=N), 162.42 (C–F), 158.56 (C–OH), 157.79 (C'–OH), 139.57 (C–S), 136.56, 132.42, 129.53, 128.77, 125.98, 117.98, 116.99 (aromatic-C), 108.98 (C'–Br), 96.32 (C–Br), 54.52 (CH_2), 51.29 (CH); MS (*m*/*z*): 524.80 $[M+2+H]^+$.

2,4-Dibromo-6-[2-(4-chlorophenyl)-2,3-dihydro-1,5-benzothiazepin-4-yl]-benzene-1,3-diol (***3f***). Yield: 80 %; m.p.: 90–91 °C. Anal. Calcd. for $C_{21}H_{14}Br_2ClNO_2S$ (FW 539.30): C, 46.73; H, 2.60; O, 5.93; N, 2.59 %. Found: C, 46.78; H, 2.64; O, 5.87; N, 2.64 %; IR (KBr, cm^{-1}): 3372 (O–H stretching), 3291 (aliphatic C–H stretching), 3060–3009 (aromatic C–H stretching), 1606

(C=N), 1581 (C=C), 862 (C–Br), 848 (C–Cl stretching of chlorine), 666 (C–S); ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 9.40–8.57 (2H, *brs*, aromatic–OH), 7.72 (1H, *s*, aromatic), 7.20–7.15 (8H, *m*, aromatic), 5.14 (1H, *t*, *J* = 11.4 Hz, CH), 3.44 (2H, *d*, *J* = 12.3 Hz, CH_2); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 164.77 (C=N), 159.06 (C–OH), 156.29 (C'–OH), 141.97 (C–S), 138.36, 131.97, 129.63, 130.23, 128.37, 127.78,116.72, 115.63 (aromatic-C), 131.72 (C–Cl), 109.63 (C'–Br), 95.32 (C–Br), 55.02 (CH_2), 49.73 (CH); MS (*m*/*z*): 541.30 $[M+2+H]^+$.

2,4-Dibromo-6-[2-(4-methoxyphenyl)-2,3-dihydro-1,5-benzothiazepin-4-yl]-benzene-1,3-diol (***3g***). Yield: 89 %; m.p.: 82–83 °C. Anal. Calcd. for $C_{22}H_{17}Br_2NO_3S$ (FW 534.80): C, 49.36; H, 3.18; O, 8.97; N, 2.62 %. Found: C, 49.31; H, 3.25; O, 8.91; N, 2.65 %; IR (KBr, cm^{-1}): 3377 (O–H stretching), 3298 (aliphatic C–H stretching), 3061– 3018 (aromatic C–H stretching), 2830 (OCH_3), 1611 (C=N), 1581 (C=C), 862 (C–Br), 671 (C–S); ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 9.6–8.34 (2H, *brs*, aromatic–OH), 7.76 (1H, *s*, aromatic), 7.41–7.19 (8H, *m*, aromatic), 5.16 (1H, *t*, *J* = 11.2 Hz, CH), 3.87 (3H, *s*, OCH_3), 3.32 (2H, *d*, *J* = 12.2 Hz, CH_2); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 34.77 (OCH_3), 164.07 (C=N), 159.96 (C–OH), 158.02 (C'–OH), 159.14, 131.85, 129.62, 128.64, 127.78, 113.74 (aromatic-C), 139.93 (C–S), 107.97 (C'–Br), 96.23 (C–Br), 55.92 (CH_2), 54.03 (CH); MS (*m*/*z*): 536.80 $[M+2+H]^+$.

2,4-Dibromo-6-[2-(4-methylphenyl)-2,3-dihydro-1,5-benzothiazepin-4-yl]-benzene-1,3-diol (***3h***). Yield: 81 %; m.p.: 85–86 °C. Anal. Calcd. for $C_{22}H_{17}Br_2NO_2S$ (FW 518.80): C, 50.88; H, 3.28; O, 6.17; N, 2.70 %. Found: C, 50.83; H, 3.32; O, 6.20; N, 2.74 %; IR (KBr, cm^{-1}): 3371 (O–H stretching), 3289 (aliphatic C–H stretching), 3008–3059 (aromatic C–H stretching), 2913 (CH_3), 1606 (C=N), 1581 (C=C), 862 (C–Br), 627 (C–S); ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 9.5–8.52 (2H, *brs*, aromatic–OH), 7.76 (1H, *s*, aromatic), 7.22–6.96 (8H, m, aromatic), 5.21 (1H, *t*, *J* = 11.3 Hz, CH), 3.38 (2H, *d*, *J* = 12.1 Hz, CH_2), 2.63 (3H, *s*, $-CH_3$); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 165.93 C=N), 159.06 (C–OH), 157.53 (C'–OH), 139.52, 131.65, 129.32, 126.89, 117.06, 105.71 (aromatic-C), 141.03 (C–S), 107.91 (C'–Br), 96.93 (C–Br), 55.27 (CH_2), 51.93 (CH), 21.18 (CH_3); MS (*m*/*z*): 520.80 $[M+2+H]^+$.

2,4-Dibromo-6-[2-(4-hydroxy-3-methoxyphenyl)-2,3-dihydro-1,5-benzothiazepin-4-yl]benzene-1,3-diol (***3i***). Yield: 79 %; m.p.: 78–79 °C. Anal. Calcd. for $C_{22}H_{17}Br_2NO_4S$ (FW 550.80): C, 47.93; H, 3.09; O, 11.62; N, 2.54 %. Found: C, 47.89; H, 3.14; O, 11.66; N, 2.46 %; IR (KBr, cm^{-1}): 3373 (O–H stretching), 3291 (aliphatic C–H stretching), 3060–3009 (aromatic C–H stretching), 2848 (OCH_3), 1606 (C=N), 1581 (C=C), 862 (C–Br), 665 (C–S); ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 9.96 (1H, *s*, aromatic–OH), 9.0–8.32 (2H, *brs*, aromatic–OH), 7.82 (1H, *s*, aromatic), 7.26–7.16 (7H, *m*, aromatic), 5.26 (1H, *t*, *J* = 11.1 Hz, CH), 3.87 (3H, *s*, $-OCH_3$), 3.37 (2H, *d*, *J* = 12.4 Hz, CH_2); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 35.40 (OCH_3), 167.53 C=N), 159.77 (C–OH), 156.67 (C'–OH),

150.13, 145.00, 131.93, 129.62, 128.09, 121.04, 122.35, 116.37, 111.95 (aromatic-C), 141.03 (C–S), 108.51 (C'–Br), 97.07 (C–Br), 55.78 (CH_2), 54.47 (CH); MS (*m*/*z*): 552.80 $[M+2+H]^+$.

2,4-Dibromo-6-[2-(4-bromophenyl)-2,3-dihydro-1,5-benzothiazepin-4-yl]-benzene-1,3-diol ***(3j)***. Yield: 90 % m.p.: 93–94 °C. Anal. Calcd. for $C_{21}H_{14}Br_3NO_2S$ (FW 583.70): C, 43.17; H, 2.40; O, 5.48; N, 2.40 %. Found: C, 43.11; H, 2.45; O, 5.41; N, 2.39 %; IR (KBr, cm^{-1}): 3377 (O–H stretching), 3298 (aliphatic C–H stretching), 3061–3018 (aromatic C–H stretching), 2830 (OCH_3), 1611 (C=N), 1581 (C=C), 869 (C–Br), 671 (C–S); ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 9.7–8.42 (2H, *brs*, aromatic–OH), 7.82 (1H, *s*, aromatic), 7.52–6.99 (8H, *m*, aromatic), 5.18 (1H, *t*, J = 11.2 Hz, CH), 3.52 (2H, *d*, J = 12.3 Hz, CH_2); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 166.03 (C=N), 159.37 (C–OH), 157.47 (C'–OH), 141.03 (C–S), 137.43, 131.43, 130.96, 129.62, 128.69, 121.45 (aromatic-C), 108.51 (C'–Br), 97.07 (C–Br), 54.98 (CH_2), 51.47 (CH); MS (*m*/z): 585.70 $[M+2+H]^+$.