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SUPPLEMENTARY MATERIAL TO

Antimicrobial and anticancer evaluation of a novel synthetic tetracyclic system obtained by Dimroth rearrangement

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ANALYTICAL AND SPECTRAL DATA OF THE SYNTHESIZED COMPOUNDS

*7,9-Bis(4-methoxyphenyl)pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidin-4(3*H*)-one (**2**)*. Yield: 70 %; m.p.: 224 °C; Anal. Calcd. for $C_{23}H_{17}N_3O_3S$ (FW: 415.46): C, 66.49; H, 4.12; N, 10.11 %. Found: C, 66.27; H, 4.29; N, 10.03 %. IR (KBr, cm^{-1}): 3154 (NH), 1664 (C=O), 1600 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): = 3.83 (3H, *s*, OCH_3), 3.86 (3H, *s*, OCH_3), 7.03–8.27 (8H, *m*, Ar-H), 7.88 (1H, *s*, pyridine-H5), 8.12 (1H, *s*, pyrimidine-H2), 12.79 (1H, *s*, D_2O exchangeable, NH); MS (70 eV, *m*/*z* (relative abundance, %)): 415 (M^+, 100), 256 (16), 129 (29), 57 (85).

*4-Hydrazinyl-7,9-bis(4-methoxyphenyl)pyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidine (**4**)*. Yield: 71 %; m.p.: 240–242 °C; Anal. Calcd. for $C_{23}H_{19}N_5O_2S$ (FW: 429.49): C, 64.32; H, 4.46; N, 16.31 %. Found: C, 64.18; H, 4.31; N, 16.10 %; IR (KBr, cm^{-1}): 3424–3291 (NH_2 and NH), 1605 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6 δ / ppm): 3.85 (6H, *s*, $2OCH_3$), 5.01 (2H, *s*, NH_2, D_2O exchangeable), 7.06–8.35 (10H, *m*, Ar-H, pyridine-H5 and pyrimidine-H2), 9.02 (1H, *s*, NH, D_2O exchangeable); MS (70 eV, *m*/*z* (relative abundance, %)): 429 (M^+, 16), 358 (100), 285 (60), 57 (22).

N′*-(2-Cyano-4,6-bis(4-methoxyphenyl)thieno[2,3-*b*]pyridin-3-yl)-*N,N*-dimethylformimidamide (**5**)*. Yield: 72 %; m.p.: 200–202 °C; Anal. Calcd. for $C_{25}H_{22}N_4O_2S$ (FW: 442.53): C, 67.85; H, 5.01; N, 12.66 %. Found: C, 67.69; H, 5.13; N, 12.48 %; IR (KBr, cm^{-1}): 3097 (=C–H), 2924 (C–H), 2191 (CN), 1627(C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 2.64 (6H, *s*, $N(CH_3)_2$), 2.87 (6H, *s*, $N(CH_3)_2$), 3.88 (3H, *s*, OCH_3), 3.89 (3H, *s*, OCH_3), 6.94–8.10 (9H,

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m, Ar-H and CH=N), 7.57 (1H, *s*, pyridine-H5); MS (70 eV, *m*/*z* (relative abundance, %)): 443 (M^++1, 30), 442 (M^+, 100), 383 (54), 221 (7), 59 (49).

4-Imino-7,9-bis(4-methoxyphenyl)pyrido[3′,2′:4,5]thieno[3,2-d*]pyrimidin--3(4*H*)-amine (**6**)*. Yield: 74 %; m.p.: 264–266 °C; Anal. Calcd. for $C_{23}H_{19}N_5O_2S$ (FW: 429.49): C, 64.32; H, 4.46; N, 16.31 %. Found: C, 64.20; H, 4.34; N, 16.17 %; IR (KBr, cm^{-1}): 3472, 3341, 3220 (NH_2 and NH), 1605 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.82 (3H, *s*, OCH_3), 3.85 (3H, *s*, OCH_3), 4.92 (2H, *s*, NH_2, D_2O exchangeable), 7.02–8.23 (9H, *m*, Ar-H and pyridine-H5), 8.44 (1H, *s*, pyrimidine-H2), 9.02 (1H, *s*, NH, D_2O exchangeable); MS (70 eV, *m*/*z* (relative abundance, %)): 429 (M^+, 97), 399 (100), 355 (23), 192 (22), 58 (7).

Benzaldehyde, 2-(7,9-bis(4-methoxyphenyl)pyrido[3′,2′:4,5]thieno[3,2-d*]-pyrimidin-4-yl)hydrazone (**8a**)*. Yield: 78 %; white solid; m.p.: 312–314 °C; Anal. calcd. for $C_{30}H_{23}N_5O_2S$ (FW: 517.60): C, 69.61; H, 4.48; N, 13.53%. Found: C, 69.48; H, 4.32; N, 13.27 %; IR (KBr, cm^{-1}): 3440 (NH), 3049 (=CH), 2932 (CH), 1605 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.84 (6H, *s*, $2OCH_3$), 7.04–7.65 (13H, *m*, Ar-H), 7.88 (1H, *s*, pyridine-H2), 8.22 (1H, *s*, pyrimidine-H5), 8.82 (1H, *s*, N=CH), 12.16 (1H, *s*, NH, D_2O exchangeable); MS (70 eV, *m*/*z* (relative abundance, %)): 517 (M^+, 15), 516 (100), 421 (63), 311 (81), 240 (42), 130 (26), 77 (12).

4-Methylbenzaldehyde, 2-(7,9-bis(4-methoxyphenyl)pyrido-[3′,2′:4,5]thieno-[3,2-d*]pyrimidin-4-yl)hydrazone (**8b**)*. Yield: 73 %; white solid; m.p.: 330–332 °C; Anal. Calcd. for $C_{31}H_{25}N_5O_2S$ (FW: 531.63): C, 70.04; H, 4.74; N, 13.17 %. Found: C, 69.91; H, 4.70; N, 13.03 %; IR (KBr, cm^{-1}): 3432 (NH), 3044 (=CH), 2911 (CH), 1605 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 2.37 (3H, *s*, CH_3), 3.84 (6H, *s*, $2OCH_3$), 7.05–7.71 (12H, *m*, Ar-H), 7.79 (1H, *s*, pyridine--H5), 8.21 (1H, *s*, pyrimidine-H2), 8.42 (1H, *s*, N=CH), 12.12 (1H, *s*, NH, D_2O exchangeable); MS (70 eV, *m*/*z* (relative abundance, %)): 531 (M^+, 12), 424 (38), 232 (76), 137 (59), 91 (90), 53 (100).

4-Methoxybenzaldehyde, 2-(7,9-bis(4-methoxyphenyl)pyrido-[3′,2′:4,5]thieno[3,2-d*]pyrimidin-4-yl)hydrazone (**8c**)*. Yield: 70 %; pale yellow solid; m.p.: 334–335 °C; Anal. Calcd. for $C_{31}H_{25}N_5O_3S$ (FW: 547.63): C, 67.99; H, 4.60; N, 12.79 %. Found: C, 67.75; H, 4.48; N, 12.54 %. IR (KBr, cm^{-1}): 3435 (NH), 3045 (=CH), 2953 (CH), 1605 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.86 (9H, *s*, $3OCH_3$), 7.09–7.71 (12H, *m*, Ar-H), 7.84 (1H, *s*, pyridine-H5), 8.28 (1H, *s*, pyrimidine-H2), 8.43 (s, 1H, N=CH), 12.06 (s, D_2O exchangeable, 1H, NH); MS (70 eV, *m*/*z* (relative abundance, %)): 547 (M^+, 6), 258 (31), 179 (100), 143 (84), 57 (16).

4-Chlorobenzaldehyde, 2-(7,9-bis(4-methoxyphenyl)pyrido[3′,2′:4,5]thieno-[3,2-d*]pyrimidin-4-yl)hydrazone (**8d**)*. Yield: 78 %; white solid; m.p.: 338––340 °C; Anal. Calcd. for $C_{30}H_{22}ClN_5O_2S$ (FW: 552.05): C, 65.27; H, 4.02; N, 12.69 %. Found: C, 65.13; H, 4.14; N, 12.43 %; IR (KBr, cm^{-1}): 3421 (NH),

3044 (=CH), 2908 (CH), 1599 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.84 (6H, *s*, 2OCH_3), 7.07–7.71 (12H, *m*, Ar-H), 7.83 (1H, *s*, pyridine-H5), 8.22 (1H, *s*, pyrimidine-H2), 8.42 (1H, *s*, N=CH), 12.10 (1H, *s*, NH, D_2O exchangeable); MS (70 eV, *m*/*z* (relative abundance, %)): 554 (M^++2, 3), 552 (M^+, 10), 447 (100), 330 (28), 272 (65), 142 (73), 57 (79).

*4-Nitrobenzaldehyde, 2-(7,9-Bis(4-methoxyphenyl)pyrido[3',2':4,5]thieno-[3,2-*d*]pyrimidin-4-yl)hydrazone (**8e**)*. Yield: 76 %; pale yellow solid; m.p.: 342––344 °C; Anal. Calcd. for $C_{30}H_{22}N_6O_4S$ (FW: 562.60): C, 64.05; H, 3.94; N, 14.94 %. Found: C, 64.17; H, 3.82; N, 14.72 %; IR (KBr, cm^{-1}): 3418 (NH), 3040 (=CH), 2909 (CH), 1599 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / pm): 3.85 (3H, *s*, OCH_3), 3.87 (3H, *s*, OCH_3), 7.03–8.31 (12H, *m*, Ar-H), 7.88 (1H, *s*, pyridine-H5), 8.39 (1H, *s*, pyrimidine-H2), 8.51 (1H, s, N=CH), 11.91 (s, 1H, NH, D_2O exchangeable); MS (70 eV, *m*/*z* (relative abundance, %)): 562 (M^+, 21), 444 (19), 415 (100), 388 (56), 120 (49), 56 (73).

*4-Hydroxybenzaldehyde, 2-(2-(7,9-Bis(4-methoxyphenyl)pyrido[3',2':4,5]-thieno[3,2-*d*]pyrimidin-4-yl)hydrazine (**8f**)*. Yield: 73 %; brown solid; m.p.: 286––288 °C; Anal. Calcd. for $C_{30}H_{23}N_5O_3S$ (FW: 533.60): C, 67.53; H, 4.34; N, 13.12 %. Found: C, 67.43; H, 4.19; N, 13.03 %; IR (KBr, cm^{-1}): 4425 (OH and NH), 3044 (=CH), 2908 (CH),1604 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / / ppm): 3.85 (3H, *s*, OCH_3), 3.86 (s, 3H, OCH_3), 6.94–8.28 (12H, *m*, Ar-H), 7.87 (1H, *s*, pyridine-H5), 8.43 (1H, *s*, pyrimidine-H2), 8.58 (1H, *s*, N=CH), 10.12 (1H, *s*, OH, D_2O exchangeable), 12.11 (1H, *s*, NH, D_2O exchangeable); MS (70 eV, *m*/*z* (relative abundance, %)): 533 (M^+, 2), 429 (100), 415 (42), 272 (75), 121 (39), 58 (68).

*4-Dichlorobenzaldehyde, 2-(7,9-bis(4-methoxyphenyl)pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-4-yl)hydrazine (**8g**)*. Yield: 76 %; white solid; m.p.: 350––352 °C; Anal. Calcd. for $C_{30}H_{21}Cl_2N_5O_2S$ (FW: 586.49): C, 61.44; H, 3.61; N, 11.94 %. Found: C, 61.31; H, 3.32; N, 11.75 %; IR (KBr, cm^{-1}): 3425 (NH), 3055 (=CH), 2910 (CH), 1599 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.84 (3H, *s*, OCH_3), 3.89 (3H, *s*, OCH_3), 7.04–7.77 (11H, *m*, Ar-H), 7.91 (1H, *s*, pyridine-H5), 8.23 (1H, *s*, pyrimidine-H2), 8.54 (1H, *s*, N=CH), 12.12 (1H, *s*, NH, D_2O exchangeable); MS (70 eV, *m*/*z* (relative abundance, %)): 586 (M^+, 2), 388 (100), 359 (45), 273 (39), 178 (47), 59 (77).

*Acetaldehyde, 2-(7,9-bis(4-methoxyphenyl)pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-4-yl)hydrazine (**8h**)*. Yield: 84 %; green solid; m.p.: 240–241 °C; Anal. Calcd. for $C_{25}H_{21}N_5O_2S$ (FW: 455.53): C, 65.92; H, 4.65; N, 15.37 %. Found: C, 65.75; H, 4.60; N, 15.14 %; IR (KBr, cm^{-1}): 3375 (NH), 3047 (=CH), 2939 (CH), 1608 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 1.42 (3H, *d*, J = = 5.7 Hz, CH_3), 3.89 (3H, *s*, OCH_3), 3.92 (3H, *s*, OCH_3), 7.03 (1H, *q*, J = 5.7 Hz, N=CH), 7.26–8.17 (8H, *m*, Ar-H), 7.71 (1H, *s*, pyridine-H5), 7.99 (1H, *s*,

pyrimidine-H2), 12.17 (1H, *s*, NH, D_2O exchangeable); MS (70 eV, *m*/*z* (relative abundance, %)): 455 (M^+, 3), 415 (100), 388 (38), 207 (11), 136 (14), 56 (12).

*7,9-Bis(4-methoxyphenyl)-3-phenylpyrido[3',2':4,5]thieno[2,3-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (**9a**)*. Yield: 67 %; orange solid; m.p.: 354 °C (dioxane); Anal. Calcd. for $C_{30}H_{21}N_5O_2S$ (FW: 515.59): C, 69.89; H, 4.11; N, 13.58 %; Found: C, 69.79; H, 4.02; N, 13.44 %; IR (KBr, cm^{-1}): 3060, 3000 (=C–H), 2935 (C–H), 1604 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.81 (3H, *s*, OCH_3), 3.97 (3H, *s*, OCH_3), 7.04–8.23 (14H, *m*, Ar-H and pyridine-H5), 9.20 (1H, *s*, pyrimidine-H2); MS (70 eV, *m*/*z* (relative abundance, %)): 515 (M^+, 51), 485 (18), 380 (10), 121 (100), 50 (93).

*7,9-Bis(4-methoxyphenyl)-3-*p*-tolylpyrido[3',2':4,5]thieno[2,3-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine (**9b**)*. Yield: 70 %; yellow solid; m.p.: 318 °C (dioxane); Anal. Calcd. for $C_{31}H_{23}N_5O_2S$ (FW: 529.61): C, 70.30; H, 4.38; N, 13.22 %. Found: C, 70.27; H, 4.19; N, 13.03 %; IR (KBr, cm^{-1}): 3060, 3010 (=C–H), 2958, 2932 (C–H), 1606 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 2.42 (3H, *s*, CH_3), 3.82 (3H, *s*, OCH_3), 3.88 (3H, *s*, OCH_3), 7.04–8.25 (13H, *m*, Ar-H and pyridine-H5), 9.18 (1H, *s*, pyrimidine-H2); MS (70 eV, *m*/*z* (relative abundance, %)): 529 (M^+, 18), 511 (23), 247 (100), 205 (40), 118 (36), 92 (49), 77 (69).

*3,7,9-Tris(4-methoxyphenyl)pyrido[3',2':4,5]thieno[2,3-*e*][1,2,4]triazolo-[4,3-*c*]pyrimidine (**9c**)*. Yield: 69 %; yellow solid; m.p.: 326–328 °C (dioxane); Anal. Calcd. for $C_{31}H_{23}N_5O_3S$ (FW: 545.61): C, 68.24; H, 4.25; N, 12.84 %. Found: C, 68.11; H, 4.20; N, 12.72 %; IR (KBr, cm^{-1}): 3063, 2999 (=C–H), 2932(C–H), 1607 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.83 (3H, *s*, OCH_3), 3.86 (3H, *s*, OCH_3), 3.89 (3H, *s*, OCH_3), 7.06–8.43 (13H, *m*, Ar-H and pyridine-H5), 9.16 (1H, *s*, pyrimidine-H2); MS (70 eV, *m*/*z* (relative abundance, %)):= 545 (M^+, 3), 444 (100), 388 (48), 108 (59).

*3-(4-Chlorophenyl)-7,9-bis(4-methoxyphenyl)pyrido[3',2':4,5]thieno[2,3-*e*]-[1,2,4]triazolo[4,3-*c*]pyrimidine (**9d**)*. Yield: 73 %; reddish-brown solid; m.p.: 346–348 °C (dioxane); Anal. Calcd. for $C_{30}H_{20}ClN_5O_2S$ (FW: 550.03): C, 65.51; H, 3.67; N, 12.73 %. Found: C, 65.38; H, 3.61; N, 12.54 %; IR (KBr, cm^{-1}): 3067, 3001 (=C–H), 2958, 2933 (C–H), 1606 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.82 (3H, *s*, OCH_3), 3.87 (3H, *s*, OCH_3), 7.01–8.31 (13H, *m*, Ar-H and pyridine-H5), 9.14 (1H, *s*, pyrimidine-H2); MS (70 eV, *m*/*z* (relative abundance, %)): 552 (M^++2, 19), 550 (M^+, 59), 414 (44), 388 (53), 247 (14), 178 (100), 77 (56).

*7,9-Bis(4-methoxyphenyl)-3-(4-nitrophenyl)pyrido[3',2':4,5]thieno[2,3-*e*]-[1,2,4]triazolo[4,3-*c*]pyrimidine (**9e**)*. Yield: 73 %; brown solid; m.p.: 312–314 °C; (DMF); Anal. Calcd. for $C_{30}H_{20}N_6O_4S$ (FW: 560.58): C, 64.28; H, 3.60; N, 14.99 %. Found: C, 64.20; H, 3.47; N, 14.76 %; IR (KBr, cm^{-1}): 3074, 3005 (=C–H), 2937 (C–H), 1605 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm):

3.83 (3H, *s*, OCH_3), 3.86 (3H, *s*, OCH_3), 7.00–8.28 (13H, *m*, Ar-H and pyridine--H5), 9.15 (1H, *s*, pyrimidine-H2); MS (70 eV, *m*/*z* (relative abundance, %)): 560 (M^+, 20), 433 (31), 354 (47), 247 (14), 44 (100).

*2-(7,9-Bis(4-methoxyphenyl)pyrido[3',2':4,5]thieno[2,3-*e*][1,2,4]triazolo-[4,3-*c*]pyrimidin-3-yl)phenol* (***9f***). Yield: 72 %; brown solid; m.p.: 284–286 °C (dioxane); Anal. Calcd. for $C_{30}H_{21}N_5O_3S$ (FW: 531.58): C, 67.78; H, 3.98; N, 13.17 %. Found: C, 67.63; H, 3.69; N, 13.08 %; IR (KBr, cm^{-1}): 3064 (=C–H), 2955 (C–H), 1605 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.84 (3H, *s*, OCH_3), 3.85 (3H, *s*, OCH_3), 7.03–8.29 (13H, *m*, Ar-H and pyridine-H5), 9.08 (1H, *s*, pyrimidine-H2), 11.24 (1H, *s*, OH, D_2O exchangeable); MS (70 eV, *m*/*z* (relative abundance, %)): 531 (M^+, 5), 432 (31), 309 (94), 247 (78), 92 (71), 40 (100).

*3-(2,4-Dichlorophenyl)-7,9-bis(4-methoxyphenyl)pyrido[3',2':4,5]thieno-[2,3-*e*][1,2,4]triazolo[4,3-*c*]pyrimidine* (***9g***). Yield: 70 %; brown solid; m.p.: 318 °C (dioxane); Anal. Calcd. for $C_{30}H_{19}Cl_2N_5O_2S$ (FW: 584.48): C, 61.65; H, 3.28; N, 11.98 %. Found: C, 61.66; H, 3.20; N, 11.75 %; IR (KBr, cm^{-1}): 3066, 3000 (=C–H), 2953, 2931 (C–H), 1606 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.85 (3H, *s*, OCH_3), 3.94 (3H, *s*, OCH_3), 7.06–8.25 (12H, *m*, Ar-H and pyridine-H5), 9.03 (1H, *s*, pyrimidine-H2); MS (70 eV, *m*/*z* (relative abundance, %)): 584 (M^+, 12), 531 (40), 354 (78), 279 (51), 193 (39), 173 (91), 40 (100).

*7,9-Bis(4-methoxyphenyl)-3-methylpyrido[3',2':4,5]thieno[2,3-*e*][1,2,4]tri-azolo[4,3-*c*]pyrimidine* (***9h***). Yield: 76 %; green solid; m.p.: 312–314 °C (ethanol); Anal. Calcd. for $C_{25}H_{19}N_5O_2S$ (FW: 453.52): C, 66.21; H, 4.22; N, 15.44 %. Found: C, 66.39; H, 4.15; N, 15.31 %; IR (KBr, cm^{-1}): 3062, 2998 (=C–H), 2930 (C–H), 1605 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6. δ / ppm): 2.74 (3H, *s*, CH_3), 3.83 (3H, *s*, OCH_3), 3.92 (3H, *s*, OCH_3), 7.04–8.34 (9H, *m*, Ar-H and pyridine-H5), 9.15 (1H, *s*, pyrimidine-H2); MS (70 eV, *m*/*z* (relative abundance, %)): 453 (M^+, 34), 309 (62), 281 (100), 239 (68), 92 (62), 44 (52).

*7,9-Bis(4-methoxyphenyl)-2-phenylpyrido[3',2':4,5]thieno[2,3-*e*][1,2,4]tri-azolo[1,5-*c*]pyrimidine* (***10a***). Yield: 66 %; orange solid; m.p.: 351–353 °C; Anal. Calcd. for $C_{30}H_{21}N_5O_2S$ (FW: 515.59): C, 69.89; H, 4.11; N, 13.58 %. Found: C, 69.68; H, 4.00; N, 13.39 %; IR (KBr, cm^{-1}): 3044 (=C–H), 2911 (C–H), 1600 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.81 (3H, *s*, OCH_3), 3.87 (3H, *s*, OCH_3), 7.04–8.27 (14H, *m*, Ar-H and pyridine-H5), 8.45 (1H, *s*, pyrimidine-H2); MS (70 eV, *m*/*z* (relative abundance, %)): 515 (M^+, 51), 413 (18), 350 (21), 149 (22), 93 (58), 65 (100).

*7,9-Bis(4-methoxyphenyl)-2-*p*-tolylpyrido[3',2':4,5]thieno[2,3-*e*][1,2,4]tri-azolo[1,5-*c*]pyrimidine* (***10b***). Yield: 65 %; yellow solid; m.p.: 308–310 °C; Anal. Calcd. for $C_{31}H_{23}N_5O_2S$ (FW: 529.61): C, 70.30; H, 4.38; N, 13.22 %. Found: C, 70.21; H, 4.23; N, 13.01 %; IR (KBr, cm^{-1}): 3048 (=C–H), 2934 (C–H), 1602 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 2.36 (3H, *s*,

CH_3), 3.81 (3H, *s*, OCH_3), 3.85 (3H, *s*, OCH_3), 6.79–8.32 (13H, *m*, Ar-H and pyridine-H5), 8.40 (1H, *s*, pyrimidine-H2); MS (70 eV, *m*/*z* (relative abundance, %)): 529 (M^+, 37), 447 (65), 378 (100), 198 (91), 142 (55), 50 (62).

*2,7,9-Tris(4-methoxyphenyl)pyrido[3′,2′:4,5]thieno[2,3-*e*][1,2,4]triazolo-[1,5-*c*]pyrimidine (**10c**)*. Yield: 69 %; yellow solid; m.p.: 326–328 °C; Anal. Calcd. for $C_{31}H_{23}N_5O_3S$ (FW: 545.61): C, 68.24; H, 4.25; N, 12.84 %. Found: C, 68.07; H, 4.22; N, 12.57 %; IR (KBr, cm^{-1}): 3046 (=C–H), 2909 (C–H), 1601 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.83 (3H, *s*, OCH_3), 3.87 (3H, *s*, OCH_3), 3.89 (3H, *s*, OCH_3), 7.05–8.44 (13H, *m*, Ar-H and pyridine-H5), 9.09 (1H, *s*, pyrimidine-H2); MS (70 eV, *m*/*z* (relative abundance, %)): 545 (M^+, 32), 413 (45), 262 (27), 149 (81), 65 (100).

*2-(4-Chlorophenyl)-7,9-bis(4-methoxyphenyl)pyrido[3′,2′:4,5]thieno[2,3-*e*]-[1,2,4]triazolo[1,5-*c*]pyrimidine (**10d**)*. Yield: 69 %; brown solid; m.p.: 346–348 °C; Anal. Calcd. for $C_{30}H_{20}ClN_5O_2S$ (FW: 550.03): C, 65.51; H, 3.67; N, 12.73 %. Found: C, 65.31; H, 3.59; N, 12.50 %; IR (KBr, cm^{-1}): 3050 (=C–H), 2911 (C–H), 1603 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.80 (3H, *s*, OCH_3), 3.89 (3H, *s*, OCH_3), 7.07–8.29 (13H, *m*, Ar-H and pyridine-H5), 9.04 (1H, *s*, pyrimidine-H2); MS (70 eV, *m*/*z* (relative abundance, %)): 552 (M^++2, 11), 550 (M^+, 39), 414 (100), 387 (49), 274 (41), 137 (35).

*7,9-Bis(4-methoxyphenyl)-2-(4-nitrophenyl)pyrido[3′,2′:4,5]thieno[2,3-*e*]-[1,2,4]triazolo[1,5-*c*]pyrimidine (**10e**)*. Yield: 67 %; brown solid; m.p.: 312–314 °C; Anal. Calcd. for $C_{30}H_{20}N_6O_4S$ (FW: 560.58): C, 64.28; H, 3.60; N, 14.99 %. Found: C, 64.25; H, 3.42; N, 14.79 %; IR (KBr, cm^{-1}): 3050 (=C–H), 2911 (C–H), 1602 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.82 (3H, *s*, OCH_3), 3.86 (3H, *s*, OCH_3), 7.03–8.52 (13H, *m*, Ar-H and pyridine-H5), 9.35 (1H, *s*, pyrimidine-H2); MS (70 eV, *m*/*z* (relative abundance, %)): 560 (M^+, 28), 494 (39), 388 (100), 344 (43), 193 (10), 64 (53).

*2-(7,9-Bis(4-methoxyphenyl)pyrido[3′,2′:4,5]thieno[2,3-*e*][1,2,4]triazolo-[1,5-*c*]pyrimidin-2-yl)phenol (**10f**)*. Yield: 68 %; brown solid; m.p.: 284–286 °C; Anal. Calcd. for $C_{30}H_{21}N_5O_3S$ (FW: 531.58): C, 67.78; H, 3.98; N, 13.17 %. Found: C, 67.69; H, 3.64; N, 13.00 %; IR (KBr, cm^{-1}): 3461 (OH), 3047 (=C–H), 2930 (C–H), 1606 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.85 (3H, *s*, OCH_3), 3.92 (3H, *s*, OCH_3), 6.73–8.58 (13H, *m*, Ar-H and pyridine-H5), 9.10 (1H, *s*, pyrimidine-H2), 10.12 (1H, *s*, OH, D_2O exchangeable); MS (70 eV, *m*/*z* (relative abundance, %)): 531 (M^+, 17), 444 (32), 299 (56), 149 (72), 92 (79), 65 (100).

*2-(2,4-Dichlorophenyl)-7,9-bis(4-methoxyphenyl)pyrido[3′,2′:4,5]thieno-[2,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine (**10g**)*. Yield: 64 %; brown solid; m.p.: 318–320 °C; Anal. Calcd. for $C_{30}H_{19}Cl_2N_5O_2S$ (FW: 584.48): C, 61.65; H, 3.28; N, 11.98 %. Found: C, 61.62; H, 3.24; N, 11.70 %; IR (KBr, cm^{-1}): 3062 (=C–H), 2930 (C–H), 1605 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 3.83 (3H, *s*,

OCH_3), 3.87 (3H, *s*, OCH_3), 7.01–8.58 (12H, *m*, Ar-H and pyridine-H5), 9.09 (1H, *s*, pyrimidine-H2); MS (70 eV, *m*/*z* (relative abundance, %)): 584 (M^+, 13), 414 (100), 344 (61), 193 (72), 76 (68).

*7,9-Bis(4-methoxyphenyl)-2-methylpyrido[3′,2′:4,5]thieno[2,3-*e*][1,2,4]triazolo[1,5-*c*] pyrimidine (**10h**)*. Yield: 69 %; green solid; m.p.: 182–184 °C; Anal. Calcd. for $C_{25}H_{19}N_5O_2S$ (FW: 453.52): C, 66.21; H, 4.22; N, 15.44 %. Found: C, 66.31; H, 4.12; N, 15.28 %; IR (KBr, cm^{-1}): 3049 (=C–H), 2928 (C–H), 1606 (C=N); ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 2.50 (3H, *s*, CH_3), 3.82 (3H, *s*, OCH_3), 3.84 (3H, *s*, OCH_3), 7.03–8.18 (9H, *m*, Ar-H and pyridine-H5), 9.15 (1H, *s*, pyrimidine-H2); MS (70 eV, *m*/*z* (relative abundance, %)): 453 (M^+, 100), 334 (56), 270 (59), 193 (43), 76 (60).

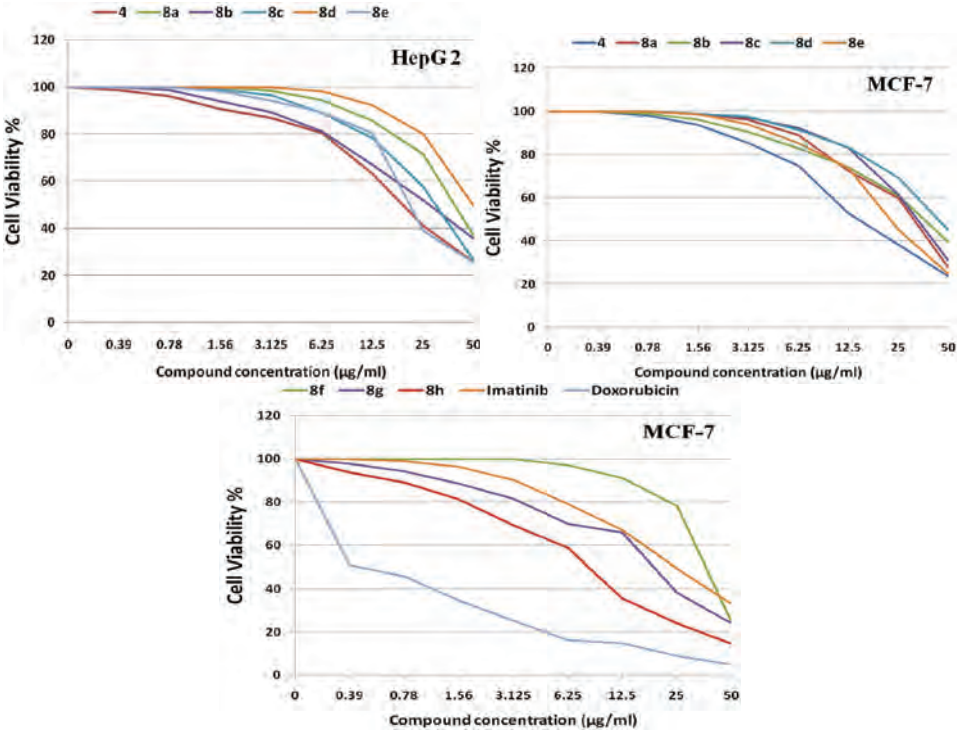

Fig. S-1. The dose response curves showing the *in vitro* inhibitory activity of compounds of the **8** series (**8a**–**h**) against hepatocellular carcinoma HepG2 and breast carcinoma MCF-7 cell lines.

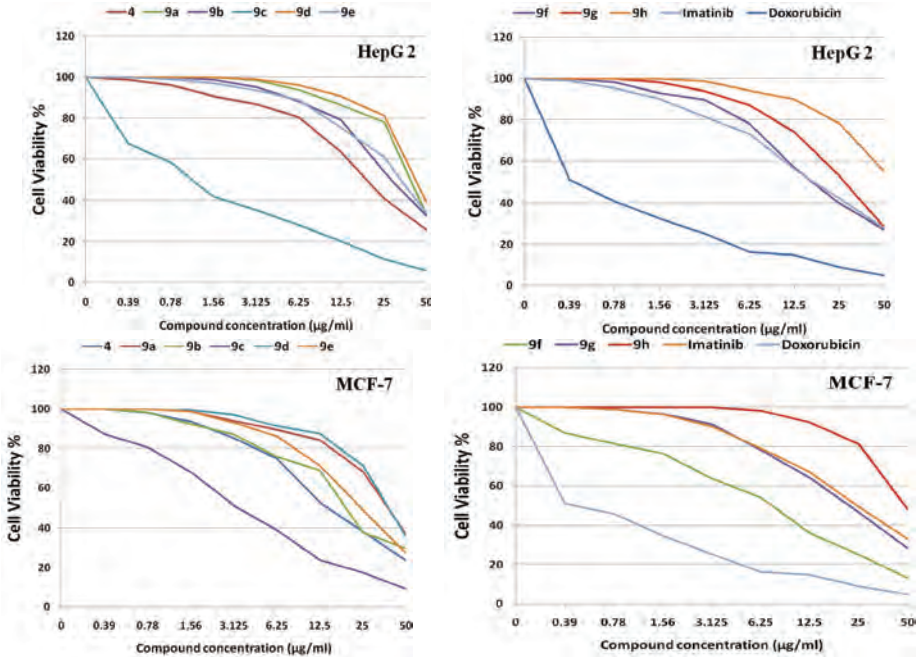

Fig. S-2. The dose response curves showing the *in vitro* inhibitory activity of compounds of the **9** series (**9a**–**9h**) against hepatocellular carcinoma HepG2 and breast carcinoma MCF-7 cell lines.

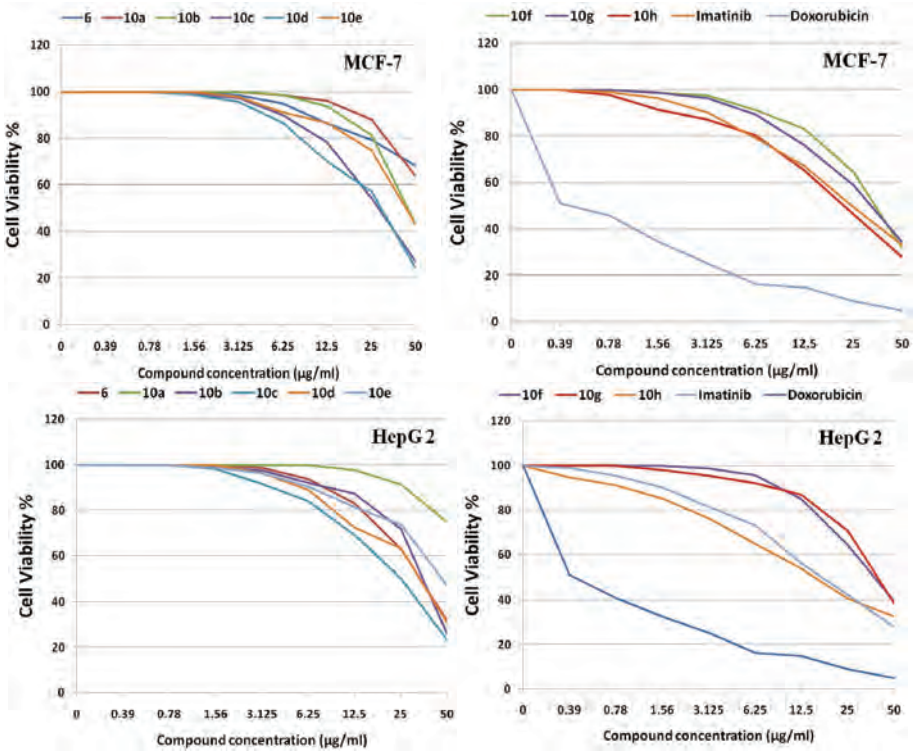

Fig. S-3. The dose response curves showing the *in vitro* inhibitory activity of compounds of the **10** series (**10a**–**10h**) against hepatocellular carcinoma (HepG2) and breast carcinoma (MCF-7) cell lines.