Synthesis of 6-oxopyrimidin-1(6H)-yl benzamide derivatives and evaluation of their antibacterial and cytotoxic activity

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5-(4-bromophenyl)-1,3,4-oxadiazol-2-amine (1): To a stirred solution of ethyl 4-bromobenzoate **I** (50 g, 0.218 mol) in Ethanol (750 mL) was added hydrazine hydrate (50 mL, 1 vol) and stirred at reflux temp for 16 h. The solvent was evaporated, the residue was triturated with pet ether to give hydrazide. The hydrazide was taken in in Ethanol (500 mL) and added cyanogen bromide (34 g, 0.327 mmol) and stirred at RT for 16 h. After completion, the solvent was evaporated and the residue was poured into ice water and filtered the solid to obtain oxadiazole **1** (37.7 g, 72%, over two steps) as a white solid; m. p. 270-272 °C; IR (KBr) ν : 3292, 3110, 1660 cm^{-1} ; ^1H NMR (DMSO- d_6 , 300 MHz): δ 7.75 (t, 4H, Phenyl), 7.35 (s, 2H, -NH₂) ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 163.7, 156.6, 132.3, 126.9, 123.7, 123.4; ^{Lit-35} ^1H NMR (CDCl₃): δ 7.25-7.69 (dd, 4H, J = 2.6, 5.6 Hz, Ar-H), 7.75 (s, 2H, NH); ^{13}C NMR (CDCl₃): 144-130 (Ar-C). LC-MS: m/z 240.09 (M+H). HRMS. Calcd. for C₈H₇BrN₃O: 240.0875, Found: 240.0879.

2-(4-bromophenyl)-7-hydroxy-5H-[1,3,4]oxadiazolo[3,2-a] pyrimidin-5-one (2): To a stirred solution of 5-(4-bromophenyl)-1,3,4-oxadiazol-2-amine (**1**) (20 g, 83.2 mmol) in Chlorobenzene (400 mL) was added Bis(1,3,5, trichlorophenyl)malonate (38.4 g, 83.2 mmol) at 100 °C and the mixture was refluxed under stirring for 1 h. The reaction mixture was cooled and diluted with pet. ether, solid that precipitated was filtered, washed with pet ether to give pyrimidinone derivative **2** (23.6, 92%) as a pale yellow solid; m. p. 290-292 °C; IR (KBr) ν : 3447, 3087, 2923 cm^{-1} ; ^1H NMR (DMSO- d_6 , 300 MHz): δ 12.03 (s, 1H, -OH), 7.98-7.87 (m, 4H, Phenyl), 5.36 (s, 1H, pyrimidine); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 169.3, 156.9, 156.1, 155.2, 132.7, 128.7, 127.1, 121.4, 84.7; LC-MS: m/z 308.4 (M+H). HRMS. Calcd. for C₁₁H₇BrN₃O₃: 308.4012, Found: 308.4017.

2-(4-bromophenyl)-7-chloro-5H-[1,3,4]oxadiazolo[3,2-a] pyrimidin-5-one (3): A solution of 2-(4-bromophenyl)-7-hydroxy-5H-[1,3,4]oxadiazolo[3,2-a]pyrimidin-5-one **2** (20 g, 64.8 mmol) in POCl₃ (100 mL) refluxed under stirring for 2 h. The reaction mixture was cooled and poured into ice water (500 mL), solid that precipitated was filtered, washed with pet ether to give chloro pyrimidinone derivative **3** (19.9 g, 94%) as pale yellow solid; m.p 210-212 °C; IR (KBr) ν : 3422, 3089, 2921 cm^{-1} ; ^1H NMR (DMSO- d_6 , 300 MHz): δ 8.01 (d, 2H, Phenyl), 7.75 (d, 2H, Phenyl), 6.51 (s, 1H, pyrimidine); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 159.1, 157.7, 154.1, 133.1, 129.7, 128.9, 119.7, 107.9; LC-MS: m/z 326 (M+H). HRMS. Calcd. for C₁₁H₆BrClN₃O₂: 326.0016, Found: 326.0012.

4-bromo-N-(4-chloro-2-morpholino-6-oxopyrimidin-1(6H)-yl)benzamide (5a): Off white solid (494 mg, 78%), m.p. 240-242 °C; IR (KBr) ν : 3295, 1662, 1541 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz): δ 10.24 (s, 1H, $-\text{CO}-\text{NH}-$), 7.62 (d, 2H, $J = 8.0$ Hz, Phenyl), 7.47 (d, 2H, $J = 8.0$ Hz, Phenyl), 6.12 (s, 1H, pyrimidine- C_5H), 3.78-3.63 (m, 6H, Morpholine), 3.49 (t, 2H, $J = 13.1$ Hz, Morpholine); ^{13}C NMR ($\text{DMSO}-d_6$, 75 MHz): δ 164.1, 160.6, 156.8, 156.3, 131.9, 130.0, 129.7, 126.8, 102.5, 65.6, 48.6; HRMS. Calcd. for $\text{C}_{15}\text{H}_{15}\text{BrClN}_4\text{O}_3$: 413.0016, Found: 413.0168.

4-bromo-N-(4-chloro-6-oxo-2-(2,2,2 trifluoroethylamino) pyrimidin-1(6H)-yl) benzamide (5b): Off white solid (497 mg, 76%), m.p. 242-244 °C; IR (KBr) ν : 3446, 1687, 1667 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz): δ 9.02 (s, 1H, $-\text{CO}-\text{NH}-$), 7.82 – 7.72 (d, 2H, $J = 8.9$ Hz, Phenyl), 7.58 (d, 2H, $J = 8.9$ Hz, Phenyl), 6.06 (s, 1H, pyrimidine- C_5H), 5.94 (t, 1H, $J = 7.3$ Hz, $\text{CF}_3\text{CH}_2\text{-NH}$), 4.15 (p, 2H, $J = 8.4$ Hz, $\text{CF}_3\text{-CH}_2$); ^{13}C NMR ($\text{DMSO}-d_6$, 75 MHz): δ 165.3, 158.3, 157.5, 154.2, 131.6, 130.3, 126.6, 125.8, 123.1, 100.7, 41.9; LC-MS : m/z 425.01. HRMS. Calcd. for $\text{C}_{13}\text{H}_{10}\text{BrClF}_3\text{N}_4\text{O}_2$: 425.0099, Found: 425.0103.

N-(2-(allylamino)-4-chloro-6-oxopyrimidin-1(6H)-yl)-4-bromo benzamide (5c): Off white solid (418 mg, 71%), m.p. 199-201 °C; IR (KBr) ν : 3293, 1677, 1574 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz): δ 9.46 (s, 1H, $-\text{CO}-\text{NH}-$), 7.80-7.68 (d, 2H, Phenyl), 7.56-7.46 (m, 2H, Phenyl), 5.95 (s, 1H, pyrimidine- C_5H), 5.86 (m, 1H, $\text{CH}_2=\text{C-H}$), 5.75 (t, 1H, $J = 5.6$ Hz, Allyl-NH), 5.27-5.16 (m, 2H, $\text{CH}=\text{CH}_2$), 4.08 (m, 2H, $\text{CH}_2\text{-CH}$); ^{13}C NMR ($\text{DMSO}-d_6$, 75 MHz): δ 165.3, 158.7, 158.0, 153.6, 134.2, 131.5, 130.5, 130.2, 126.4, 115.3, 98.8, 42.7; LC-MS : m/z 383.03. HRMS. Calcd. for $\text{C}_{14}\text{H}_{13}\text{BrClN}_4\text{O}_2$: 383.0014, Found: 383.0021.

4-bromo-N-(4-chloro-2-(isopropylamino)-6-oxo pyrimidin-1(6H)-yl) benzamide (5d): Off white solid (428 mg, 72%), m.p. 143-145 °C; IR (KBr) ν : 3335, 1683, 1669, 1567 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz): δ 9.72 (s, 1H, $-\text{CO}-\text{NH}-$), 7.77-7.65 (d, 2H, Phenyl), 7.52-7.41 (d, 2H, Phenyl), 5.89 (s, 1H, pyrimidine- C_5H), 5.45 (d, 1H, $J = 7.9$ Hz, isopropyl-NH), 4.32-4.12 (m, 1H, $(\text{CH}_3)_2\text{-C-H}$), 1.22 (d, 6H, $J = 6.5$ Hz, $\text{CH-(CH}_3)_2$); ^{13}C NMR ($\text{DMSO}-d_6$, 75 MHz): δ 165.8, 160.9, 160.5, 152.0, 131.8, 129.4, 128.5, 128.0, 99.8, 44.2, 29.6, 22.3; LC-MS : m/z 385.08. HRMS. Calcd. for $\text{C}_{14}\text{H}_{15}\text{BrClN}_4\text{O}_2$: 385.0061, Found: 385.0066.

4-bromo-N-(4-chloro-2-(cyclopropylamino)-6-oxo pyrimidin -1(6H)-yl)benzamide (5e): Off white solid (581 mg, 82%), m.p. 246-248 °C; IR (KBr) ν : 3343, 1693, 1666, 1567 cm^{-1} ; ^1H NMR

(CDCl₃, 400 MHz): δ 9.62 (s, 1H, –CO-NH-), 7.69 (d, 2H, J = 8.2 Hz, Phenyl), 7.53-7.39 (d, 2H, J = 8.2 Hz, Phenyl), 5.96 (s, 1H, pyrimidine-C₅H), 5.82 (s, 1H, cyclopropyl-NH), 2.82 (tq, 1H, J = 7.0, 3.6 Hz cyclopropyl-CH), 0.95-0.77 (m, 2H, cyclopropyl), 0.64-0.52 (m, 2H, cyclopropyl); ¹³C NMR (DMSO-*d*₆, 75 MHz): δ 165.3, 158.3, 158.0, 155.0, 131.4, 130.6, 130.3, 126.4, 99.2, 24.3, 6.2, 5.8; LC-MS : m/z 382.8. HRMS. Calcd. for C₁₄H₁₃BrClN₄O₂: 382.9924, Found: 383.9921.

4-bromo-N-(4-chloro-2-(cyclopentylamino)-6-oxo pyrimidin-1 (6H)-yl)benzamide (5f): Off white solid (470 mg, 74%), m.p. 186-188 °C; IR (KBr) ν : 3329, 1684, 1667, 1569 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 9.74 (s, 1H, –CO-NH-), 7.71 (d, 2H, J = 8.2 Hz, Phenyl), 7.47 (d, 2H, J = 8.6 Hz, Phenyl), 5.89 (s, 1H, pyrimidine-C₅H), 5.58 (d, 1H, J = 7.1 Hz, cyclopentyl-NH), 4.30 (m, 1H, J = 7.1 Hz, cyclopentyl), 2.08 (m, 2H, cyclopentyl), 1.64 (m, 4H, cyclopentyl), 1.48-1.31 (m, 2H, cyclopentyl); ¹³C NMR (DMSO-*d*₆, 75 MHz): δ 165.8, 160.9, 160.4, 152.4, 131.8, 129.3, 128.6, 128.0, 99.8, 53.6, 32.7, 23.5; HRMS. Calcd. for C₁₆H₁₇BrClN₄O₂: 411.0223. Found: 411.0233.

4-bromo-N-(4-chloro-2-(2-cyclohexylethylamino)-6-oxopyrimidin-1(6H)-yl)benzamide (5g): Off white solid (566 mg, 81%), m.p. 198-200 °C; IR (KBr) ν : 3312, 1681, 1667, 1577 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 9.67 (s, 1H, –CO-NH-), 7.71 (d, 2H, J = 8.5, Phenyl), 7.47 (d, 2H, J = 6.7 Hz, Phenyl), 5.90 (s, 1H, pyrimidine-C₅H), 5.61 (t, 1H, J = 5.5 Hz, -C-NH-), 3.43 (m, 2H, J = 7.6 Hz, -C-CH₂-N-), 1.66 (m, 5H, cyclohexyl), 1.50-1.40 (m, 2H, cyclohexyl), 1.21 (m, 3H, cyclohexyl), 1.03-0.78 (m, 3H, cyclohexyl); ¹³C NMR (DMSO-*d*₆, 75 MHz): δ 165.2, 158.7, 158.0, 153.6, 131.5, 130.6, 130.2, 126.4, 99.3, 36.1, 34.5, 32.6, 26.0, 25.7; LC-MS: m/z 453.15. HRMS. Calcd. for C₁₉H₂₃BrClN₄O₂: 453.0687, Found: 453.0691.

4-bromo-N-(4-chloro-2-(dimethylamino)-6-oxopyrimidin-1(6H)-yl)benzamide (5h): Off white solid (434 mg, 76%), m.p. 197-199 °C; IR (KBr) ν : 3207, 1701, 1673, 1575 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ 10.71 (s, 1H –CO-NH-), 7.63 (d, 2H, J = 8.1 Hz, Phenyl), 7.41 (d, 2H, J = 8.1 Hz, Phenyl), 6.01 (d, 1H, J = 1.4 Hz, pyrimidine-C₅H), 3.12 (s, 6H, -N(CH₃)₂); ¹³C NMR (DMSO-*d*₆, 75 MHz): δ 164.3, 160.7, 156.9, 156.4, 131.9, 129.9, 129.8, 126.7, 100.2, 40.8; HRMS. Calcd. for C₁₃H₁₃BrClN₄O₂: 370.9910, Found: 370.9933.

4-bromo-N-(4-chloro-6-oxo-2-(piperidin-1-yl)pyrimidin-1(6H)-yl) benzamide (5i): Off white solid (495 mg, 78%), m.p. 177-179 °C; IR (KBr) ν : 3421, 1706, 1664, 1559 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz): δ 10.65 (s, 1H, $-\text{CO}-\text{NH}-$), 7.61 (d, 2H, $J = 8.1$ Hz, Phenyl), 7.42 (d, 2H, $J = 7.9$ Hz, Phenyl), 6.05 (s, 1H, pyrimidine- C_5H), 3.69-3.36 (m, 4H, piperidine), 1.67-1.49 (m, 6H, piperidine); ^{13}C NMR ($\text{DMSO}-d_6$, 75 MHz): δ 164.0, 163.3, 159.7, 156.2, 131.7, 128.9, 128.6, 127.8, 102.0, 49.9, 25.5, 23.9; HRMS. Calculated for $\text{C}_{16}\text{H}_{17}\text{BrClN}_4\text{O}_2$: 411.0223, Found: 411.0236.

4-bromo-N-(4-chloro-2-(ethylamino)-6-oxopyrimidin-1(6H)-yl) benzamide (5j): Off white solid (451 mg, 79%), m.p. 253-255 °C; IR (KBr) ν : 3340, 1693, 1666 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ ppm: 9.62 (s, 1H $-\text{CO}-\text{NH}-$), 7.72 (d, 2H, $J = 7.9$ Hz, Phenyl), 7.54-7.42 (d, 2H, $J = 7.9$ Hz, Phenyl), 5.92 (s, 1H, pyrimidine- C_5H), 5.67 (t, 1H, $J = 5.8$ Hz Ethyl-NH), 3.58-3.36 (m, 2H, Ethyl- CH_2), 1.22 (t, 3H, $J = 7.3$ Hz, Ethyl- CH_3); ^{13}C NMR ($\text{DMSO}-d_6$, 75 MHz): δ 165.3, 158.7, 158.6, 153.5, 131.5, 130.5, 130.26, 126.4, 98.4, 35.8, 14.35; LC-MS : m/z 371.06. HRMS. Calcd. for $\text{C}_{13}\text{H}_{12}\text{BrClN}_4\text{O}_2\text{Na}$: 392.9724, Found: 392.9727.

(S)-N-(2-(3-aminopyrrolidin-1-yl)-4-chloro-6-oxopyrimidin-1(6H)-yl)-4-

bromobenzamide(5k): Off white solid (443 mg, 70%), m.p. 296-298 °C; IR (KBr) ν : 3432, 1669, 1591 cm^{-1} ; ^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ 11.57 (d, 1H, $J = 3.8$ Hz, $-\text{CO}-\text{NH}-$), 8.17 (s, 3H, $-\text{NH}_2$), 7.91 (d, 2H, $J = 8.4$ Hz, Phenyl), 7.85-7.77 (d, 2H, $J = 8.4$ Hz, Phenyl), 6.00 (d, 1H, $J = 1.5$ Hz, pyrimidine- C_5H), 3.98 -3.52 (m, 6H, Pyrrolidine), 2.19 (m, 1H, Pyrrolidine), 1.98 (m, 1H, Pyrrolidine); ^{13}C NMR ($\text{DMSO}-d_6$, 75 MHz): δ 165.2, 159.8, 156.9, 153.1, 131.7, 130.0, 126.7, 99.5, 53.4, 52.7, 48.8, 48.2, 28.6; HRMS. Calcd. for $\text{C}_{15}\text{H}_{16}\text{BrClN}_5\text{O}_2$: 411.9659, Found: 411.9643.

4-bromo-N-(2,4-dimorpholino-6-oxopyrimidin-1(6H)-yl) benzamide (6a): Off white solid (543 mg, 77%), m.p. 290-292 °C; IR (KBr) ν : 3467, 1697, 1647, 1588 cm^{-1} ; ^1H NMR ($\text{DMSO}-d_6$, 300 MHz): δ 11.24 (s, 1H, $-\text{CO}-\text{NH}-$), 7.88-7.71 (m, 4H, phenyl), 5.12 (s, 1H, pyrimidine- C_5H), 3.68-3.38 (m, 14H, morpholine), 3.25 (m, 2H, morpholine); ^{13}C NMR ($\text{DMSO}-d_6$, 75 MHz): δ 164.2, 161.8, 159.8, 156.2, 131.8, 130.7, 129.6, 126.3, 78.9, 65.8, 65.6, 48.6, 44.1; HRMS. Calcd. for $\text{C}_{19}\text{H}_{23}\text{BrN}_5\text{O}_4$: 464.0933, Found: 464.0926.

4-bromo-N-(6-oxo-2,4-bis(2,2,2-trifluoro ethylamino) pyrimidin-1(6H)-yl)benzamide (6b):

Off white solid (565 mg, 76%), m.p. 223-225 °C; IR (KBr) ν : 3312, 1669, 1574 cm^{-1} ; ^1H NMR (DMSO- d_6 , 400 MHz): δ 10.89 (s, 1H, $-\text{CO}-\text{NH}-$), 8.11 (t, 1H, $J = 6.4$ Hz, $\text{CF}_3\text{CH}_2-\text{NH}$), 7.92 (d, 2H, $J = 8.2$ Hz, Phenyl), 7.79 (d, 2H, $J = 8.2$ Hz, Phenyl), 7.42 (s, 1H, $\text{CF}_3\text{CH}_2-\text{NH}$), 4.91 (s, 1H, pyrimidine- C_5H), 4.12 (m, 4H, CF_3-CH_2); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 165.7, 161.6, 159.3, 153.9, 131.4, 130.9, 130.2, 129.3, 129.0, 126.6, 126.2, 123.8, 123.4, 120.6, 77.3, 42.1, 41.8, 41.4, 41.1; LC-MS : m/z 487.95. HRMS. Calcd. for $\text{C}_{15}\text{H}_{13}\text{BrF}_6\text{N}_5\text{O}_2$: 488.0151, Found: 488.0155.

N-(2,4-bis(allylamino)-6-oxopyrimidin-1(6H)-yl)-4-bromo benzamide (6c):

Off white solid (437 mg, 70%), m.p. 218-220 °C; IR (KBr) ν : 3417, 3387, 1692, 1639 cm^{-1} ; ^1H NMR (DMSO- d_6 , 400 MHz): δ 10.72 (s, 1H, $-\text{CO}-\text{NH}-$), 8.00-7.87 (d, 2H, $J = 8.4$ Hz, phenyl), 7.83-7.71 (d, 2H, $J = 8.4$ Hz, phenyl), 7.61 (s, 1H, allyl-NH-), 6.80 (s, 1H, allyl-NH-), 5.84 (m, 2H, $\text{C}=\text{CH}-\text{C}-$), 5.24-4.97 (m, 4H, $-\text{C}=\text{CH}_2$), 4.61 (s, 1H, pyrimidine- C_5H), 3.85 (m, 2H, $\text{C}=\text{C}-\text{CH}_2-$), 3.76 (s, 2H, $\text{C}=\text{C}-\text{CH}_2-$); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 165.7, 161.6, 159.7, 153.2, 135.4, 131.3, 130.2, 125.9, 115.2, 114.9, 74.5, 42.6; LC-MS : m/z 404.03. HRMS. Calcd. for $\text{C}_{17}\text{H}_{19}\text{BrN}_5\text{O}_2$: 404.0716, Found: 404.0720.

N-(2,4-bis(isopropylamino)-6-oxopyrimidin-1(6H)-yl)-4-bromobenzamide (6d):

Off white solid (424 mg, 69%), m.p. 209-210 °C; IR (KBr) ν : 3308, 1674, 1581 cm^{-1} ; ^1H NMR (DMSO- d_6 , 300 MHz): δ 10.51 (s, 1H, $-\text{CO}-\text{NH}-$), 7.87 (d, 2H, $J = 7.8$ Hz, phenyl), 7.71 (d, 2H, $J = 7.9$ Hz, Phenyl), 6.81 (s, 1H, isopropyl-NH), 5.76 (s, 1H, isopropyl-NH), 4.91 (s, 1H, pyrimidine- C_5H), 3.91 (m, 1H, isopropyl), 1.34 (d, 6H, $J = 6.8$ Hz, isopropyl), 1.28 (d, 6H, $J = 6.6$ Hz, isopropyl); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 167.1, 163.8, 158.9, 152.1, 134.3, 132.1, 129.7, 124.6, 79.2, 43.2, 41.8, 28.1, 27.2, 22.7, 22.4; LC-MS: m/z 408.16. HRMS. Calcd. for $\text{C}_{17}\text{H}_{23}\text{BrN}_5\text{O}_2$: 408.0951, Found: 413.0946.

N-(2,4-bis(cyclopropylamino)-6-oxopyrimidin-1(6H)-yl)-4-bromobenzamide (6e):

Off white solid (500 mg, 82%), m.p. 201-203 °C; IR (KBr) ν : 3302, 1670, 1588 cm^{-1} ; ^1H NMR (DMSO- d_6 , 400 MHz): δ 10.59 (s, 1H, $-\text{CO}-\text{NH}-$), 7.91 (d, 2H, $J = 7.9$ Hz, phenyl), 7.75 (d, 2H, $J = 8.0$ Hz, Phenyl), 7.33 (s, 1H, cyclopropyl-NH), 6.83 (s, 1H, cyclopropyl-NH), 4.88 (s, 1H, pyrimidine- C_5H), 2.68 (m, 1H, cyclopropyl), 2.35 (m, 1H, cyclopropyl), 0.76-0.58 (m, 4H, cyclopropyl),

0.57-0.41 (m, 4H, cyclopropyl); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 165.7, 162.7, 159.6, 154.3, 131.3, 131.2, 130.3, 125.9, 75.4, 24.0, 23.4, 6.5, 6.3, 5.9; LC-MS: m/z 404.03. HRMS. Calcd. for $\text{C}_{17}\text{H}_{19}\text{BrN}_5\text{O}_2$: 404.0624, Found: 404.0619.

N-(2,4-bis(cyclopentylamino)-6-oxopyrimidin-1(6H)-yl)-4-bromobenzamide (6f): Off white solid (559 mg, 79%), m.p. 206-208 °C; IR (KBr) ν : 3355, 1654, 1590 cm^{-1} ; ^1H NMR (DMSO- d_6 , 400 MHz): δ 10.53 (s, 1H, $-\text{CO}-\text{NH}-$), 7.93 (d, 2H, $J = 7.8$ Hz, Phenyl), 7.76 (d, 2H, $J = 7.9$ Hz, Phenyl), 6.98 (s, 1H, cyclopentyl-NH), 6.52 (s, 1H, cyclopentyl-NH), 4.59 (s, 1H, pyrimidine- C_5H), 4.22 (m, 2H, cyclopentyl), 1.87 (m, 4H, cyclopentyl), 1.74-1.39 (m, 12H, cyclopentyl); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 165.8, 161.2, 159.5, 153.0, 131.3, 131.2, 130.2, 125.8, 74.4, 52.3, 32.4, 31.6, 23.5; Calcd. for $\text{C}_{21}\text{H}_{27}\text{BrN}_5\text{O}_2$: 460.1348, Found: 460.1339.

N-(2,4-bis(2-cyclohexylethylamino)-6-oxopyrimidin-1(6H)-yl)-4-bromobenzamide (6g): Off white solid (518 mg, 62%), m.p. 186-188 °C; IR (KBr) ν : 3431, 1648, 1582 cm^{-1} ; ^1H NMR (DMSO- d_6 , 300 MHz): δ 11.12 (s, 1H, $-\text{CO}-\text{NH}-$), 7.91-7.75 (m, 4H, phenyl), 5.11 (s, 1H, pyrimidine- C_5H), 2.65-2.59 (m, 4H, $-\text{CH}_2-$), 1.69-1.59 (m, 10H, cyclohexyl), 1.55-1.42 (m, 16H, cyclohexyl); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 165.2, 163, 162.2, 154.5, 131.8, 131.5, 129.8, 126.2, 78.3, 39.7, 36.8, 35.6, 35.2, 33.5, 33.1, 33.0, 29.1, 28.9, 28.2, 27.9; LC-MS: m/z 544.31. HRMS. Calcd. for $\text{C}_{27}\text{H}_{39}\text{BrN}_5\text{O}_2$: 544.3204, Found: 544.3198.

N-(2,4-bis(dimethylamino)-6-oxopyrimidin-1(6H)-yl)-4-bromobenzamide (6h): Off white solid (436 mg, 75%), m.p. 250-252 °C; IR (KBr) ν : 3448, 1686, 1643, 1591 cm^{-1} ; ^1H NMR (DMSO- d_6 , 400 MHz): δ : 11.16 (s, 1H, $-\text{CO}-\text{NH}-$), 7.87 (d, 2H, $J = 8.4$ Hz, Phenyl), 7.78 (d, 2H, $J = 8.2$ Hz, phenyl), 4.84 (s, 1H, pyrimidine- C_5H), 2.99 (s, 3H, Dimethyl), 2.92 (s, 9H, Dimethyl); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 164.3, 161.6, 160.2, 156.2, 131.7, 130.7, 129.7, 126.2, 76.5, 40.3, 37.0; HRMS. Calcd. for $\text{C}_{15}\text{H}_{19}\text{BrN}_5\text{O}_2$: 380.0722, Found: 380.0733.

4-bromo-N-(6-oxo-2,4-di(piperidin-1-yl)pyrimidin-1(6H)-yl)benzamide (6i): Off white solid (516 mg, 73%), m.p. 259-261 °C; IR (KBr) ν : 3447, 1703, 1646, 1591 cm^{-1} ; ^1H NMR (DMSO- d_6 , 400 MHz): δ 11.21 (s, 1H, $-\text{CO}-\text{NH}-$), 7.92-7.73 (m, 4H, phenyl), 5.05 (s, 1H, pyrimidine- C_5H), 3.50 (m, 4H, Piperidine), 3.43-3.33 (m, 2H, Piperidine), 3.25 (m, 2H, Piperidine), 1.72-1.30 (m, 12H, Piperidine); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 163.9, 162.1, 159.4, 156.5, 131.7,

130.9, 129.6, 126.2, 77.9, 49.1, 44.8, 25.1, 24.0, 23.8; HRMS. Calcd. for $C_{21}H_{27}BrN_5O_2$: 460.1348. Found: 460.1334.

N-(2,4-bis(ethylamino)-6-oxopyrimidin-1(6H)-yl)-4-bromo benzamide (6j): Off white solid (421 mg, 73%), m.p. 220-222 °C; IR (KBr) ν : 3317, 1685, 1652 cm^{-1} ; 1H NMR (DMSO- d_6 , 300 MHz): δ 10.63 (s, 1H, -CO-NH-), 8.01 (t, 1H, J = 6.3 Hz, CH_3CH_2 -NH), 7.85 (d, 2H, J = 8.0 Hz, Phenyl), 7.61 (d, 2H, J = 7.9 Hz, Phenyl), 7.36 (s, 1H, CH_3CH_2 -NH), 5.04 (s, 1H, pyrimidine- C_5H), 3.67-3.41 (m, 4H, CH_3 - CH_2), 1.45-1.21 (m, 6H, Ethyl- CH_3); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 163.1, 161.6, 158.9, 153.4, 131.1, 130.5, 129.2, 128.7, 128.3, 126.4, 126.2, 123.4, 123.1, 120.6, 75.3, 35.9, 35.1, 14.38, 14.32; LC-MS : m/z 380.14. HRMS. Calcd. for $C_{15}H_{19}BrN_5O_2$: 380.0730, Found: 380.0727.

N-(2,4-bis((S)-3-aminopyrrolidin-1-yl)-6-oxopyrimidin-1 (6H)-yl)-4-bromobenzamide (6k): Off white solid (439 mg, 62%), m.p. 330-332 °C; IR (KBr) ν , cm^{-1} : 3435, 1681, 1645, 1560; 1H NMR (D_2O , 400 MHz) δ ppm: 7.89-7.72 (m, 4H, phenyl), 4.17 – 3.48 (m, 10H, Pyrrolidine), 2.52-2.28 (m, 2H, Pyrrolidine), 2.27-2.00 (m, 2H, Pyrrolidine); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 164.2, 160.7, 159.7, 153.1, 131.4, 129.9, 126.8, 78.9, 53.4, 53.2, 52.7, 52.6, 48.8, 48.2, 28.3; HRMS. Calcd. for $C_{19}H_{25}BrN_7O_2$: 462.0777, Found: 462.0761.

Figure S1. ^1H NMR Spectrum of **1** (300 MHz, $\text{DMSO-}d_6$, 298K).

Figure S2. ¹³C NMR Spectrum of **1** (75 MHz, DMSO-*d*₆, 298K).

Figure S3. ^1H NMR Spectrum of **2** (300 MHz, $\text{DMSO-}d_6$, 298K).

Figure S4. ¹³C NMR Spectrum of **2** (75 MHz, DMSO-*d*₆, 298K).

Figure S5. ^1H NMR Spectrum of **3** (300 MHz, CDCl_3 , 298K).

Figure S6. ^{13}C NMR Spectrum of **3** (75 MHz, CDCl_3 , 298K).

Figure S7. ^1H NMR Spectrum of **5A** (300 MHz, CDCl_3 , 298K).

Figure S8. ¹³C NMR Spectrum of **5A** (75 MHz, DMSO-*d*₆, 298K).

Figure S9. ¹H NMR Spectrum of **5b** (400 MHz, CDCl₃, 298 K).

Figure S10. ¹³C NMR Spectrum of **5b** (75 MHz, DMSO-*d*₆, 298 K).

Figure S11. ^1H NMR Spectrum of **5c** (400 MHz, CDCl_3 , 298 K).

Figure S12. ¹³C NMR Spectrum of **5c** (75 MHz, DMSO-*d*₆, 298 K).

Figure S13. ^1H NMR Spectrum of **5d** (400 MHz, CDCl_3 , 298 K).

Figure S14. ¹³C NMR Spectrum of **5d** (75 MHz, CDCl₃, 298 K).

Figure S15. ^1H NMR Spectrum of **5e** (400 MHz, CDCl_3 , 298 K).

Figure S16. ¹³C NMR Spectrum of **5e** (75 MHz, DMSO-*d*₆, 298 K).

Figure S17. ¹H NMR Spectrum of **5f** (400 MHz, CDCl₃, 298 K).

Figure S18. ^{13}C NMR Spectrum of **5f** (75 MHz, CDCl_3 , 298 K).

Figure S19. ¹H NMR Spectrum of **5g** (400 MHz, CDCl₃, 298 K).

Figure S20. ¹³C NMR Spectrum of **5G** (75 MHz, DMSO-*d*₆, 298 K).

Figure S21. ^1H NMR Spectrum of **5h** (400 MHz, CDCl_3 , 298 K).

Figure S22. ¹³C NMR Spectrum of **5h** (75 MHz, DMSO-*d*₆, 298 K).

Figure S23. ¹H NMR Spectrum of **5i** (400 MHz, CDCl₃, 298 K).

Figure S24. ^{13}C NMR Spectrum of **5i** (75 MHz, CDCl_3 , 298 K).

Figure S25. ^1H NMR Spectrum of **5i** (400 MHz, CDCl_3 , 298 K).

Figure S26. ¹³C NMR Spectrum of **5j** (75 MHz, DMSO-*d*₆, 298 K).

Figure S27. ^1H NMR Spectrum of **5k** (400 MHz, CDCl_3 , 298 K).

Figure S28. ^{13}C NMR Spectrum of **5k** (75 MHz, $\text{DMSO-}d_6$, 298 K).

Figure S29. ^1H NMR Spectrum of **6a** (300 MHz, CDCl_3 , 298 K).

Figure S30. ^{13}C NMR Spectrum of **6a** (75 MHz, CDCl_3 , 298 K).

Figure S31. ^1H NMR Spectrum of **6b** (400 MHz, $\text{DMSO-}d_6$, 298 K).

Figure S32. ¹³C NMR Spectrum of **6b** (75 MHz, DMSO-*d*₆, 298 K).

Figure S33. ^1H NMR Spectrum of **6c** (400 MHz, $\text{DMSO-}d_6$, 298 K).

Figure S34. ^{13}C NMR Spectrum of **6c** (75 MHz, $\text{DMSO-}d_6$, 298 K).

Figure S35. ^1H NMR Spectrum of **6e** (400 MHz, $\text{DMSO}-d_6$, 298 K).

Figure S36. ¹³C NMR Spectrum of **6e** (75 MHz, DMSO-*d*₆, 298 K).

Figure S37. ^1H NMR Spectrum of **6f** (400 MHz, $\text{DMSO-}d_6$, 298 K).

Figure S38. ¹³C NMR Spectrum of **6f** (75 MHz, DMSO-*d*₆, 298 K).

Figure S39. ¹H NMR Spectrum of **6h** (400 MHz, DMSO-*d*₆, 298 K).

Figure S40. ¹³C NMR Spectrum of **6h** (75 MHz, DMSO-*d*₆, 298 K).

Figure S41. ^1H NMR Spectrum of **6i** (400 MHz, $\text{DMSO-}d_6$, 298 K).

Figure S42. ¹³C NMR Spectrum of **6i** (75 MHz, DMSO-*d*₆, 298 K).