Supporting Information

An Efficient Direct Amination of Cyclic Amides and Cyclic Ureas

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Materials and Methods:

All reagents and solvents were purchased from commercial sources and used without further purification. Reactions were performed under nitrogen, and monitored by LCMS. Flash chromatography was performed on Isco systems, and HPLC was performed on Gilson systems with solvents indicated. LCMS yield was calibrated by using diphenyl ether (Ph₂O) as an internal standard. ¹H and ¹³C NMR spectra were recorded on a Bruker 400 MHz spectrometer. Chemical shifts in ¹H NMR were reported in parts per million (ppm) on the δ scale from an internal standard of residual chloroform (7.26 ppm) or DMSO (2.54 ppm). Data from ¹³C NMR spectra were reported in terms of chemical shift in ppm from the center peak of CDCl₃ (77.36 ppm) or DMSO (40.45 ppm).¹

General Procedure A: To a solution of a cyclic amide (typically 0.5 mmol), Ph₂O² (85.1 mg, 0.5 mmol) and BOP (287 mg, 0.65 mmol) was added DBU (112 μ L, 0.75 mmol) at room temperature. The resultant mixture was stirred for 5–10 min, after which the nucleophile, i.e. n-Bu-NH₂ (75 μ L, 0.75 mmol) was added drop-wise. The reaction was monitored by LCMS until complete disappearance of starting material was observed. The solvent was removed under vacuum, and the crude reaction mixture was purified either by flash chromatography on a SiO₂ column with hexanes/EtOAc or MeOH/EtOAc solvent system, or by HPLC with MeCN/H₂O affording the desired product in high purity. A reference standard sample of a 1:1 mixture of pure product and Ph₂O was made, and an LCMS calibration was performed to allow calculation of the LCMS yield.³

General Procedure B: To a solution of a cyclic amide (typically 0.5 mmol), Ph₂O² (73 mg, 0.5 mmol) and BOP (287 mg, 0.65 mmol) was added DBU (112 μ L, 0.75 mmol) at room temperature. The resultant mixture was stirred for 5 – 10 min, after which the nucleophile, i.e. *t*-Bu-NH₂ (150 μ L, 1.50 mmol) was added drop-wise. The reaction mixture was stirred at room temperature overnight, then heated to 60 °C and monitored by LCMS until complete disappearance of starting material was observed. The solvent was removed under vacuum, and the crude reaction mixture was purified either by flash chromatography on SiO₂ column eluted with hexanes/EtOAc or MeOH/EtOAc solvent system or by HPLC with MeCN/H₂O to give the desired product in high purity. A reference standard sample of a 1:1 mixture of pure product and Ph₂O was made, and an LCMS calibration was performed to allow calculation of the LCMS yield.³

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(1) Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, 62, 7512.

(2) Internal standard when LCMS yield was reported.

(3) The lower isolated yield was occasionally lower, due to low solubility of these heterocyclic products that sometimes precipitate out on SiO₂ column and subsequently led to incomplete elution.

Butyl-quinazolin-4-yl-amine (2a): Synthesized according to general procedure A (rt, 2 h) from 4-hydroxyquinazoline **1a** (73 mg, 0.5 mmol), Ph₂O (85.1 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and n-BuNH₂ (75 μ L, 0.75 mmol) in acetonitrile (2.5 mL) and purified by flash chromatography as a white solid (86 mg, 86%; 99% by LCMS). Mp: 111 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 8.67 (s, 1H), 7.83 (dd, J = 1.2, 8.4 Hz, 1H), 7.74-7.70 (m, 2H), 7.47-7.45 (m, 1H), 5.87 (br s, 1H), 3.66 (td, J = 5.5, 7.3 Hz, 2H), 1.75-1.68 (m, 2H), 1.52-1.43 (m, 2H), 0.97 (t, J = 7.3 Hz, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 159.5, 155.4, 149.2, 132.5, 128.4, 125.9, 120.4, 114.9, 41.1, 31.4, 20.4, 20.2, 13.8. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₂H₁₅N₃ 202.1338, found 202.1339.

Butyl-(7-trichloromethyl-quinazolin-4-yl)-amine (2b): Synthesized according to general procedure A (rt, overnight) from **1b** (95 mg, 0.5 mmol), Ph₂O (85.1 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and n-BuNH₂ (75 μ L, 0.75 mmol) in acetonitrile (2.5 mL), purified by HPLC as a white solid (118 mg, 99%; 100% by LCMS). Mp: 113-114 °C. ¹H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 8.80 (t, J = 5.5 Hz, 1H), 8.36 (dd, J = 8.3, 0.5 Hz, 1H), 7.83-7.91 (m, 2H), 7.65-7.69 (m, 1H), 3.64 (q, J = 7.2 Hz, 2H), 1.68-1.75 (m, 2H), 1.36-1.45 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H). ¹³C NMR (DMSO-*d*₆, 100 MHz): δ (ppm) 161.5, 161.4, 148.2, 113.4, 129.2, 128.3, 123.8, 114.6, 99.3, 40.3, 31.3, 20.5, 14.6. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₃H₁₄N₃Cl₃ 318.0326, found 318.0333.

Butyl-(7-bromo-quinazolin-4-yl)-amine (2c): Synthesized according to general procedure A (rt, overnight) from **1c** (214 mg, 1.0 mmol), Ph₂O (170.2 mg, 1.0 mmol), BOP (580 mg, 1.3 mmol), DBU (224 μ L, 1.5 mmol) and n-BuNH₂ (150 μ L, 1.5 mmol) in acetonitrile (5 mL), triturated by DMSO/water as a white solid (268 mg, 95%, 99% by LCMS). Mp: 261 °C (softening). ¹H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 8.49 (s, 1H), 8.43 (t, J = 5.3 Hz, 1H), 8.24 (d, J = 8.9 Hz, 1H), 7.89 (d, J = 1.9 Hz, 1H), 7.70 (dd, J = 8.9, 1.9 Hz, 1H), 3.55 (q, J = 7.0 Hz, 2H), 1.62-1.69 (m, 2H), 1.36-1.45 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H). ¹³C NMR (DMSO-*d*₆, 100 MHz): δ (ppm) 160.2, 157.2, 151.3, 130.4, 123.4, 126.8, 125.9, 114.8, 41.2, 31.5, 20.7, 14.7. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₂H₁₄BrN₃ 280.0444, found 280.0447.

Butyl-(6-chloro-quinazolin-4-yl)-amine (2d): Synthesized according to general procedure A (rt, 3 h) from 7-chloro-4-hydroxyquinazoline **1d** (150 mg, 0.83mmol and BuNH₂ (415 μ L, 4.15 mmol), purified by flash chromatography as a white solid (169 mg, 86%). Mp: 150 °C. ¹H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 8.51-8.42 (m, 2H), 8.30 (t, *J* = 4.8 Hz), 7.83-7.67 (m, 2H), 3.52 (td, *J* = 5.5, 6.8 Hz), 1.66-1.59 (m, 2H), 1.42-1.33 (m, 2H), 0.92 (t, *J* = 7.3 Hz). ¹³C NMR (DMSO-*d*₆, 100 MHz): δ (ppm) 158.5, 155.4, 147.7, 132.6, 129.5, 129.4, 121.9, 155.7, 40.2, 30.4, 19.6, 13.6. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₄H₁₄N₃Cl 236.0949, found 236.0949.

Butyl-(2-methyl-quinazolin-4-yl)-amine (2e): Synthesized according to general procedure A (rt, overnight) from **1e** (80 mg, 0.5 mmol), Ph₂O (85.1 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and n-BuNH₂ (75 μ L, 0.75 mmol) in acetonitrile (2.5 mL), purified by HPLC as a white solid (112 mg, 99%; 100% by LCMS). Mp: 112-114 °C. ¹H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 14.02 (br, s, 1H), 10.04 (t, *J* = 5.3 Hz, 1H), 8.47 (d, *J* = 7.7 Hz, 1H), 8.03-8.07 (m, 1H), 7.76-7.80 (m, 1H), 7.75 (d, *J* = 7.3 Hz, 1H), 3.75 (q, *J* = 7.0 Hz, 2 H), 2.67 (s, 3H), 1.68-1.75 (m, 2H), 1.38-1.47 (m, 2H), 0.98 (t, *J* = 7.3 Hz). ¹³C NMR (DMSO-*d*₆, 100 MHz): δ (ppm) 162.5, 161.0, 139.0, 136.9, 128.8, 125.0, 119.6, 112.5, 42.4, 31.2, 23.6, 20.6, 14.7. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₃H₁₇N₃ 216.1495, found 216.1596.

Butyl-(2-dimethylamino-quinazolin-4-yl)-amine (2f): Synthesized according to general procedure A (rt, overnight) from **1f** (95 mg, 0.5 mmol), Ph₂O (85.1 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and n-BuNH₂ (75 μ L, 0.75 mmol) in acetonitrile (2.5 mL), purified by HPLC as a white solid (118 mg, 97%;100% by LCMS). Mp: 174-177 °C. ¹H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 11.51 (br, s, 1H), 9.42 (t, *J* = 5.3 Hz, 1H), 8.26 (d, *J* = 7.4 Hz, 1H), 7.85 (dt, *J* = 7.4, 1.1 Hz, 1H), 7.4 (d, *J* = 7.8 Hz, 1H), 7.48 (dt, *J* = 7.8, 0.9 Hz, 1H), 3.64 (q, *J* = 6.8 Hz, 2H), 3.31 (s, 6H), 1.66-1.74 (m, 2H), 1.37-1.46 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (DMSO-*d*₆, 100 MHz): δ (ppm) 159.7, 153.20, 140.4, 135.9, 125.5, 124.7, 118.4, 110.6, 42.0, 38.6, 31.1, 20.7, 14.7. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₄H₂₀N₄ 245.1761, found 245.1762.

Butyl-(2-phenyl-quinazolin-4-yl)-amine (2g): Synthesized according to general procedure A (rt, 3h) from **1g** (111.1 mg, 0.5 mmol), Ph₂O (85.1 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and n-BuNH₂ (75 μ L, 0.75 mmol) in acetonitrile (2.5 mL), purified by SiO₂ column eluted with hexanes/EtOAc as a white solid (137 mg, 99%; 100% by LCMS). Mp: 104-105 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 8.56-8.59 (m, 2H), 9.2 (dd, J = 8.3, 0.5 Hz, 1H), 7.67-7.75 (m, 2H), 7.42-7.50 (m, 4H), 5.67 (t, J = 1.6 Hz, 1H), 3.80-3.85 (m, 2H), 1.75-1.85 (m, 2H), 1.48-1.56 (m, 2H), 1.03 (t, J = 7.4 Hz, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 161.0, 160.0, 151.0, 139.5, 132.8, 130.4, 129.4, 128.8, 125.7, 120.7, 114.1, 41.5, 32.0, 20.7, 14.4. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₈H₁₉N₃ 264.0879278.1652, found 278.1655.

Ethyl 4-(butylamino)quinazoline-2-carboxylate (2h): Synthesized according to general procedure A (rt, 2h) from **1g** (225 mg, 1.0 mmol), BOP (575 mg, 1.3 mmol), DBU (224 μ L, 1.5 mmol) and n-BuNH₂ (150 μ L, 1.5 mmol) in acetonitrile (5 mL), purified by SiO₂ column eluted with hexanes/EtOAc as a white solid (235 mg, 86%). Mp: 104-106 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.95 (dd, J = 8.3, 0.7 Hz, 1H), 7.91 (dd, J = 8.4, 0.7 Hz, 1H), 7.66-7.70 (m, 1H), 7.42-7.46 (m, 1H), 6.31 (t, J = 5.3 Hz, 1H), 4.46 (q, J = 7.2 Hz, 2H), 3.65-3.70 (m, 2H), 1.56-1.64 (m, 2H), 1.38 (t, J = 7.2 Hz, 3H), 1.28-1.37 (m, 2H), 0.85 (t, J = 7.3 Hz, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 165.6, 160.9, 153.9, 149.5, 133.3, 129.6, 127.8, 121.6, 115.4, 62.7, 41.5, 31.6, 20.5, 14.6, 14.1. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₅H₁₉N₃O₂ 274.1550, found 274.1553.

Ethyl 2-(4-(butylamino)quinazolin-2-yl)acetate (2i): Synthesized according to general procedure A (rt, 3h) from **1g** (138.2 mg, 0.5 mmol), Ph₂O (85.1 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and n-BuNH₂ (75 μ L, 0.75 mmol) in acetonitrile (2.5 mL), purified by SiO₂ column eluted with hexanes/EtOAc as a light yellow solid (160 mg, 96%; 100% by LCMS). Mp: 79-81 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.10 (s, 1H), 6.90 (s, 1H), 6.07 (s, 2H), 4.21 (q, 7.1 Hz, 2H), 3.86 (s, 2H), 3.56-3.61 (m, 2H), 5.24 (t, J = 4.8 Hz, 1H), 1.61-1.68 (m, 2H), 1.38-1.47 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H), 0.97 (t, J = 7.3 Hz, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 171.0, 159.7, 159.3, 152.5, 148.6, 108.4, 105.7, 102.2, 97.4, 61.2, 46.2, 41.3, 31.8, 31.7, 20.5, 14.6, 14.2. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₇H₂₁N₃O₄ 332.1605, found 332.1609.

(E)-N-Butyl-2-styrylquinazolin-4-amine (2j): Synthesized according to general procedure A (rt, 3h) from **1g** (124.2 mg, 0.5 mmol), Ph₂O (85.1 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and n-BuNH₂ (75 μ L, 0.75 mmol) in acetonitrile (2.5 mL), purified by SiO₂ column eluted with hexanes/EtOAc as a yellow oil (140.1 mg, 92%; 99% by LCMS). Mp: 98-99 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 8.04 (d, J = 15.8 Hz, 1H), 7.78-7.82 (m, 1H, 7.64-7.72 (m, 4H), 7.33-7.43 (m, 4H), 7.22 (d, J = 15.8 Hz, 1H), 5.88 (t, J = 5.3 Hz, 1H), 3.77-3.82 (m, 2H), 1.74-1.82 (m, 2H), 1.48-1.57 (m, 2H), 1.04 (t, J = 7.3 Hz, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 161.2, 159.4, 150.6, 137.5, 137.0, 132.8, 129.5, 129.0, 128.7, 128.6, 127.9, 125.6, 120.8, 114.2, 41.3, 31.8, 20.6, 14.2. HRMS (ES-MS) [(M+H)⁺]: calcd for C₂₀H₂₁N₃ 304.1808, found 304.1814.

N-Butyl-2-(3-fluorobenzylthio)quinazolin-4-amine (2k): Synthesized according to general procedure A (rt, 3h) from **1g** (50 mg, 0.175 mmol), Ph₂O (29.7 mg, 0.175 mmol), BOP (100.6 mg, 0.228 mmol), DBU (26.1 μ L, 0.228 mmol) and n-BuNH₂ (29.8 μ L, 0.228 mmol) in acetonitrile (1.5 mL), purified by SiO₂ column eluted with hexanes/EtOAc as a white solid (xxmg, 90%; 99% by LCMS). Mp: 68-70 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 7.64-7.70 (m, 2H), 7.57 (d, J = 8.0 Hz, 1H), 7.31-7.35 (m, 1H), 7.21-7.26 (m, 3H), 6.88-6.93 (m, 1H), 5.62 (t, J = 5.3 Hz, 1H), 4.48 (s, 2H), 3.60-3.64 (m, 2H), 1.63-1.70 (m, 2H), 1.38-1.48 (m, 2H), 0.96 (t, J = 7.3 Hz, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 167.0, 162.7 (d, J = 244 Hz), 159.1, 150.5, 142.0 (d, J = 14.1 Hz), 133.1, 130.0 (d, J = 20.8 Hz), 127.50, 124.9, 120.9, 116.2 (d, J = 53.8 Hz), 114.0 (d, J = 53.8 Hz), 113.2, 41.4, 34.9, 31.7, 20.5, 14.2. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₉H₂₀FN₃S 342.1435, found 342.1440.

N-(4-(4-(Butylamino)quinazolin-2-yl)phenyl)-3-oxo-3-phenylpropanamide (2l): Synthesized according to general procedure A (rt, overnight) from **1g** (191.7 mg, 0.5 mmol), Ph₂O (85.1 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and n-BuNH₂ (75 μ L, 0.75 mmol) in acetonitrile (2.5 mL), purified by SiO₂ column eluted with hexanes/EtOAc as a white solid (148.5 mg, 85%; 95% by LCMS). Mp: 177-178 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 9.6 (br, s, 1H), 8.56-8.60 (m, 2H), 8.05-8.07 (m, 2H), 7.89 (d, J = 8.4 Hz, 1H), 7.64-7.74 (m, 5H), 7.52-7.56 (m, 2H), 7.38-7.43 (m, 1H), 5.66 (t, J = 5.3 Hz, 1H), 4.16 (s, 2H), 3.78-3.84 (m, 2H), 1.75-1.80 (m, 2H), 1.49-1.57 (m, 2H), 1.02 (t, J = 7.3 Hz, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 197.0, 163.9, 160.3,

160.0, 151.0, 139.6, 136.4, 135.6, 134.8, 132.7, 129.6, 129.4, 129.32, 129.0, 125.5, 120.6, 119.8, 114.0, 45.9, 41.4, 31.9, 20.7, 14.3. HRMS (ES-MS) $[(M+H)^+]$: calcd for $C_{27}H_{26}N_4O_2$ 439.2129, found 439.2140.

4-(Benzotriazol-1-yloxy)-quinazoline (3a): Synthesized according to general procedure A (rt, 20 min) from 4-hydroxyquinazoline **1a** (73 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol), purified by flash chromatography as a white solid (115 mg, 87%). Mp: 169 $^{\circ}$ C. ^1H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 8.76 (s, 1H), 8.60 (d, J = 4.0 Hz, 1H), 8.25-8.16 (m, 3H), 8.00 (t, J = 8.0 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.67 (t, J = 8.0 Hz, 1H), 7.58 (t, J = 8.0 Hz, 1H). ^{13}C NMR (DMSO-*d*₆, 100 MHz): 165.7, 153.2, 151.9, 143.1, 136.1, 129.6, 128.8, 128.1, 125.7, 123.0, 120.3, 113.1, 110.0. HRMS (ES-MS) $[(M+H)^+]$: calcd for $C_{14}H_9N_5O$ 264.0879, found 264.0879.

tert-Butyl-quinazolin-4-yl-amine (3b): Synthesized according to general procedure B (rt, overnight, then 60 $^{\circ}$ C 36 h) from 4-hydroxyquinazoline **1a** (73 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and *t*-BuNH₂ (65 μ L, 0.65 mmol), purified by flash chromatography as a white solid (64 mg, 64%). Mp: 136 $^{\circ}$ C. ^1H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 8.48 (s, 1H), 8.38 (d, J = 7.6 MHz, 1H), 7.74-7.65 (m, 2H), 7.48 (t, J = 6.8, 1H), 7.29 (s, 1H), 1.55 (s, 9H). ^{13}C NMR (DMSO-*d*₆, 100 MHz): δ (ppm) 159.4, 154.6, 149.4, 132.5, 127.8, 125.5, 123.5, 115.752.5, 28.8. HRMS (ES-MS) $[(M+H)^+]$: calcd for $C_{12}H_{15}N_3$ 202.1338, found 202.1336.

4-Piperidin-1-yl-quinazoline (3c): Synthesized according to general procedure A (rt, 10 h) from 4-hydroxyquinazoline **1a** (73 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and piperidine (63 μ L, 0.75 mmol), purified by flash chromatography as a light yellow oil (94 mg, 88%). ^1H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 8.61 (s, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.80-7.77 (m, 1H), 7.55-7.51 (m, 2H), 3.68 (s, 4H), 1.70 (s, 6H). ^{13}C NMR (DMSO-*d*₆, 100 MHz): 164.2, 15.0, 151.6, 132.8, 128.2, 125.7, 125.6, 116.2, 50.6, 25.8, 24.5. HRMS (ES-MS) $[(M+H)^+]$: calcd for $C_{13}H_{15}N_5O$ 214.1338, found 214.1335.

(Quinazolin-4-ylamino)-acetic acid methyl ester (3d): Synthesized according to general procedure A (rt, overnight) from 4-hydroxyquinazoline **1a** (73 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (86 μ L, 0.5 mmol) and glycine methyl ester hydrogen chloride (188 mg, 3 mmol check!), purified by flash chromatography as white solid (90 mg, 84%). Mp: 139 °C. ^1H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 8.78 (t, J = 6.0 Hz, 1H), 8.47 (s, 1H), 8.25 (dd, J = 0.4, 8.4 Hz, 1H), 7.81-7.72 (m, 2H), 7.57 (t, J = 6.8 Hz, 1H), 4.27 (d, J = 5.6 Hz, 2H), 3.66 (s, 3H). ^{13}C NMR (DMSO-*d*₆, 100 MHz): 170.4, 159.3, 154.6, 148.9, 132.7, 127.4, 125.8, 122.5, 114.6, 51.6, 42.1. HRMS (ES-MS) $[(\text{M}+\text{H})^+]$: calcd for $\text{C}_{11}\text{H}_{11}\text{N}_3\text{O}_2$ 218.0924, found 218.0921.

3-Phenyl-2-(quinazolin-4-ylamino)-propionic acid methyl ester (3e): Synthesized according to general procedure B (rt, overnight, then 60 °C, 2d) from 4-hydroxyquinazoline **1a** (73 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (82 μ L, 0.55 mmol) and L-phenylalanine methyl ester (108 mg, 1.2 mmol), purified by flash chromatography as yellow oil (115 mg, 75%). ^1H NMR (CDCl_3 , 400 MHz): δ (ppm) 8.68 (s, 1H), 7.85 (d, J = 8.4 Hz, 1H), 7.77-7.75 (m, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.47 (t, J = 6.8 Hz, 1H), 7.28-7.25 (m, 3H), 7.14-7.12 (m, 2H), 6.23 (d, J = 6.8 Hz, 1H), 5.33 (q, J = 6 Hz, 1H), 3.79 (s, 3H), 3.36 (qd, J = 5.6, 12.0 Hz, 2H). ^{13}C NMR (CDCl_3 , 100 MHz): δ (ppm) 172.47, 158.4, 155.0, 149.3, 135.8, 132.9, 129.3, 128.6, 128.4, 127.2, 126.3, 120.6, 114.7, 54.4, 52.4, 37.5. HRMS (ES-MS) $[(\text{M}+\text{H})^+]$: calcd for $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_2$ 308.1393, found 308.1393.

Phenyl-quinazolin-4-yl-amine⁴ (3f): Synthesized according to general procedure B (rt, overnight, then 60 °C, 10 h) from 4-hydroxyquinazoline **1a** (73 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and aniline (63 μ L, 0.75 mmol), purified by flash chromatography as a white solid (86 mg, 78%). Mp: 206-208 °C. ^1H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 9.38 (s, 1H), 8.66-8.57 (m, 2H), 7.88-7.89 (m, 4H), 7.64 (t, J = 1.2 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.15 (t, J = 7.6 Hz, 1H). ^{13}C NMR (DMSO-*d*₆, 100 MHz): 157.9, 154.5, 149.6, 139.2, 131.1, 128.6, 127.8, 126.5, 123.9, 123.1, 122.6, 115.2. HRMS (ES-MS) $[(\text{M}+\text{H})^+]$: calcd for $\text{C}_{14}\text{H}_{11}\text{N}_3$ 222.1025, found 222.1023.

(4) Szczepankiewicz, w.; Suwinski, J. *Tetrahedron Lett.* **1998**, 39, 1785.

4-Imidazol-1-yl-quinazoline (3g): Synthesized according to general procedure B (rt, overnight, then 80 °C, 4 h) from 4-hydroxyquinazoline **1a** (73 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and imidazole (156 mg, 2.25 mmol), purified by flash chromatography as a white solid (90 mg, 92%). Mp: 98 °C. ^1H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 9.26 (s, 1H), 8.51 (s, 1H), 8.23-8.14 (m, 3H), 7.97 (s, 1H), 7.89-7.85 (m, 1H), 7.30 (s, 1H). ^{13}C NMR (DMSO-*d*₆, 100 MHz): 155.2, 154.1, 152.2, 138.1, 135.2, 130.1, 129.4, 128.5, 124.8, 120.5, 117.5. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₁H₈N₄ 197.0821, found 197.0818.

4-Phenylsulfanyl-quinazoline (3h): Synthesized according to general procedure A (rt, 10 h) from 4-hydroxyquinazoline **1a** (73 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and thiophenol (77 μ L, 0.75 mmol), purified by flash chromatography as a white solid (110 mg, 93%). Mp: 118 °C. ^1H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 8.74 (s, 1H), 8.39 (d, J = 7.6 Hz, 1H), 8.05-8.02 (m, 2H), 7.80 (t, J = 5.5 Hz, 1H), 7.52 (t, J = 6.8 Hz, 2H), 7.37-7.35 (m, 3H). ^{13}C NMR (DMSO-*d*₆, 100 MHz): 166.7, 154.2, 152.5, 151.4, 134.9, 130.0, 128.4, 127.8, 126.2, 123.7, 122.4, 115.9. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₄H₁₀N₂S 239.0564, found 239.0635.

4-Phenoxy-quinazoline⁵ (3i): Synthesized according to general procedure A (rt, 10 h) from 4-hydroxyquinazoline **1a** (73 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and phenol (67 μ L, 0.75 mmol), purified by flash chromatography as a white solid (93 mg, 84%). Mp: 59 °C. ^1H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 8.85 (s, 1H), 8.26 (d, J = 8.2 Hz, 1H), 8.05-8.00 (m, 2H), 7.80 (t, J = 6.3 Hz, 1H), 7.68-7.66 (m, 2H), 7.56-7.54 (m, 3H). ^{13}C NMR (DMSO-*d*₆, 100 MHz): 170.6, 153.8, 148.1, 136.1, 134.9, 130.2, 129.9, 128.8, 128.7, 126.8, 123.9, 122.7. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₄H₁₀N₂O 223.0861, found 223.0862.

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(5) Morley, J. S.; Simpson, J. C. E. *J. Chem. Soc.* **1949**, 1354.

Butyl-(7H-purin-6-yl)-amine (5a): Synthesized according to general procedure B (rt, 2d; 60 °C, 2 h) from hypoxanthine **4a** (68 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), Ph₂O (80 μL, 0.5 mmol), DBU (0.75 mmol, 112 μL) and butylamine (2.50 mmol, 250 μL) in DMF (5 mL) in 79% yield as judged by LCMS analysis. An analytical sample was obtained by flash chromatography with MeOH/EtOAc (1:10) as a white solid. ¹H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 13.05 (s, 1H), 8.16 (s, 1H), 8.06 (s, 1H), 7.58-7.56 (m, 1H), 3.46 (s br, 2H), 1.61-1.53 (m, 2H), 1.38-1.29 (m, 2H), 0.90 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (DMSO-*d*₆, 100 MHz): δ (ppm) 156.2, 155.6, 154.1, 132.1, 99.7, 30.9, 19.6, 13.6. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₉H₁₃N₅ 192.1243 found 192.1241.

Butyl-(1H-pyrazolo[3,4-d]pyrimidin-4-yl)-amine(5b): Synthesized according to general procedure B (rt, 2d; 60 °C, 2 h) from **4b** (68mg, 0.5mmol), BOP (287 mg, 0.65 mmol), Ph₂O (80 μL, 0.5 mmol), DBU (0.75 mmol, 112 μL) and butylamine (0.75 mmol, 75 μL) in DMF (10 mL) in 86% yield as judged by LCMS analysis. An analytical sample was obtained by flash chromatography as a white solid. ¹H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 13.25 (s, 1H), 8.21 (s, 1H), 8.13-8.11 (m, 2H), 3.57-3.46 (m, 2H), 1.66-1.55 (m, 2H), 1.45-1.31 (m, 2H), 0.92 (td, *J* = 7.6 Hz, 3H). ¹³C NMR (DMSO-*d*₆, 100 MHz): δ (ppm) 156.6, 156.0, 154.6, 132.5, 100.2, 40.4, 31.3, 20.0, 14.0. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₉H₁₃N₅ 192.1243 found 192.1241.

Butyl-thieno[2,3-d]pyrimidin-4-yl-amine (5c): Synthesized according to general procedure A (rt, 2 h) from theino[2,3-*d*]pyrimidin-4(3*H*)-one **4c** (76 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol) and Ph₂O (80 μL, 0.5 mmol), DBU (0.75 mmol, 112 μL) and butylamine (0.75 mmol, 75 μL) in MeCN (5 mL), purified by column chromatophy with EtOAc/hexane (35:100) as a white solid (98 mg, 94%; 99% by LCMS analysis). Mp: 104 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 8.51 (s, 1H), 7.27 (d, *J* = 6.0 Hz, 1H), 7.14 (d, *J* = 6.2 Hz, 1H), 5.23 (s, 1H), 3.63 (td, *J* = 5.6, 7.2 Hz, 2H), 1.74-1.65 (m, 2H), 1.27-1.24 (m, 2 H), 0.98 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 166.3, 157.2, 154.1, 122.9, 116.8, 116.1, 40.9, 31.6, 20.1, 13.8. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₀H₁₃N₃S₁ 208.0903 found 208.0912.

4-Butylamino-5-methyl-thieno[2,3-d]pyrimidine-6-carboxylic acid methyl ester (5d):

Synthesized according to general procedure A (rt, 1 h) from **4d** (112 mg, 0.5 mmol), DBU (0.75 mmol, 112 μ L) and butylamine (0.75 mmol, 75 μ L), purified by column chromatography with EtOAc/hexane (35:100) as a white solid (112 mg, 81%). Mp: 106 °C. ^1H NMR (CDCl_3 , 400 MHz): δ (ppm) 8.48 (s, 1H), 5.70 (s, 1H), 3.90 (s, 3H), 3.63 (td, $J = 5.2, 7.2$ Hz, 2H), 2.97 (s, 3H), 1.73-1.64 (m, 2H), 1.51-1.41 (m, 2H), 0.996 (t, $J = 7.6$ Hz, 3H). ^{13}C NMR (CDCl_3 , 100 MHz): δ (ppm) 167.1, 163.3, 159.1, 156.2, 138.1, 121.9, 116.9, 52.2, 41.0, 31.3, 20.3, 15.7, 13.8. HRMS (ES-MS) $[(\text{M}+\text{H})^+]$: calcd for $\text{C}_{13}\text{H}_{17}\text{N}_3\text{O}_2\text{S}$ 280.1114 found 280.1112.

Butyl-thieno[3,2-d]pyrimidin-4-yl-amine (5e): Synthesized according to general procedure A (rt, 1 h) from **4e** (76mg, 0.5 mmol), DBU (0.75 mmol, 112 μ L) and butylamine (0.75 mmol, 75 μ L), purified by column chromatography with EtOAc/hexane (35:100) as a white solid (98mg, 81%) Mp: 206 °C. ^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ (ppm) 8.43 (s, 1H), 8.09-8.07 (m, 1H), 7.83 (t, $J = 5.2$ Hz, 1H), 7.36 (d, $J = 5.2$ Hz, 1H), 3.48 (td, $J = 5.6, 7.2$ Hz, 2H), 1.63-1.55 (m, 2H), 1.40-1.31 (m, 2H), 0.91 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR ($\text{DMSO}-d_6$, 100 MHz): δ (ppm) 159.8, 157.2, 154.8, 133.0, 124.7, 114.9, 40.2, 31.2, 20.0, 14.1. HRMS (ES-MS) $[(\text{M}+\text{H})^+]$: calcd for $\text{C}_{10}\text{H}_{13}\text{N}_3\text{S}$ 208.0903 found 208.090.

(5f): Synthesized according to general procedure A (rt, 1 h) from **4f** (15 mg, 0.06 mmol), BOP (36 mg, 0.08 mmol), DBU (15 μ L, 0.09 mmol) and butylamine (0.30 mmol, 32 μ L), purified by column chromatography as colorless oil (17 mg, 95%). ^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ (ppm) 8.78 (s, 1H), 8.39 (d, $J = 5.6$ Hz, 1H), 6.80 (d, $J = 5.6$ Hz, 1H), 4.80-4.79 (m, 1H), 3.67 (td, $J = 5.6, 7.2$ Hz, 2H), 3.15 (s, 6H), 1.75-1.98 (m, 2H), 1.50-1.45 (m, 2H), 0.99 (t, $J = 7.6$ Hz, 3H). ^{13}C NMR ($\text{DMSO}-d_6$, 100 MHz): δ (ppm) 168.8, 157.5, 156.9, 154.6, 154.0, 150.3, 117.8, 111.9, 107.4, 44.0, 41.1, 32.2, 20.1, 13.8. HRMS (ES-MS) $[(\text{M}+\text{H})^+]$: calcd for $\text{C}_{15}\text{H}_{19}\text{N}_5\text{S}$ 302.1434 found 302.1432.

5-Butylamino-[1,2,3]triazolo[1,5-a]quinazoline-3-carboxylic acid ethyl ester (5g): Synthesized according to general procedure A (rt, 1 h) from **4g** (25 mg, 0.09 mmol), BOP (56 mg, 0.125 mmol), DBU (22 μ L, 0.1444 mmol) and butylamine (0.48 mmol, 48 μ L), purified by trituration with EtOAc as white solid (28 mg, 94%). Mp: xx. ^1H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 8.73 (t, J = 5.3 Hz, 1H), 8.45 (d, J = 8.40 Hz, 2H), 8.01 (t, J = 7.2 Hz, 1H), 7.76 (t, J = 7.1 Hz, 1H), 4.31 (q, J = 7.0 Hz, 2H), 3.63 (q, J = 6.9 Hz, 2H), 1.74-1.67 (m, 2H), 1.46-1.32 (m, 5H), 0.95 (t, J = 7.3 Hz, 3H). ^{13}C NMR (DMSO-*d*₆, 100 MHz): δ (ppm) 161.1, 155.9, 142.7, 134.6, 133.3, 127.9, 125.0, 124.7, 116.1, 111.9, 62.5, 41.0, 30.6, 20.1, 14.5, 14.0. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₆H₁₉N₅O₂ 364.1611 found 364.1610.

1-Benzyl-4-butylamino-1H-pyrimidin-2-one (5h): Synthesized according to general procedure A (rt, 3d) from **4h** (60 mg, 0.29 mmol), BOP (66 mg, 0.377 mmol), DBU (65 μ L, 0.43 mmol) and butylamine (59 μ L, 0.58 mmol), purified by column chromatography with 3% MeOH/EtOAc as a white solid (54 mg, 73%, a tautomeric mixture). ^1H NMR (DMSO-*d*₆, 400 MHz): δ (ppm): 7.52-7.22 (m, 6H), 6.07 (s, 0.3H), 5.65-5.55 (m, 1H), 5.28 (s, 0.7H), 4.98 (s, 1H), 3.48-3.45 (m, 1.4H), 3.19 (s, 1H), 1.82-1.51 (m, 2H), 1.40-1.31 (m, 2H), 0.91 (t, J = 7.6 Hz). ^{13}C NMR (DMSO-*d*₆, 100 MHz): δ (ppm) 136.7, 145.8, 128.8, 128.1, 127.9, 95.2, 52.0, 4.06, 31.3, 20.1, 13.8. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₅H₁₉N₃O₁ 258.1600 found 258.1597.

4-Butylamino-6-methyl-1-phenyl-1H-pyrimidin-2-one (5i): Synthesized according to general procedure A (rt, 3d) from **4i** (60 mg, 0.29 mmol), BOP (166 mg, 0.38mmol), DBU (65 μ L, 0.43 mmol) and butylamine (43 μ L, 0.43 mmol), purified by flash chromatography as a white solid (60 mg, 81%, a tautomeric mixture). ^1H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 10.40 (s, 0.57H), 9.65 (t, J = 6.5 Hz), 7.58-7.47 (m, 5H), 6.58 (s, 0.43H), 6.23 (s, 0.57H), 3.42 (m, 2H), 1.96 (s, 1.29H), 1.88 (s, 1.71H), 1.59-1.54 (m, 2H), 1.41-1.34 (m, 2H), 0.94-0.90 (m, 3H). ^{13}C NMR (DMSO-*d*₆, 100 MHz): δ (ppm) 161.0, 157.3, 156.7, 156.4, 149.7, 148.1, 136.3, 136.0, 130.0, 129.9, 129.7, 128.8, 128.7, 94.1, 90.7, 42.3, 41.8, 30.8, 30.3, 21.7, 21.8, 19.6, 19.5, 13.8. HRMS (ES-MS) [(M+H)⁺]: for C₁₅H₁₉N₃O₁ 258.1600 found 258.1600.

N-Butyl-[1,3,5]triazine-2,4-diamine (5j): Synthesized according to general procedure B (rt, overnight; 60 °C, 4 h) from **4j** (112 mg, 1.00 mmol), BOP (575 mg, 1.3 mmol), Ph₂O (170 mg, 1.0 mmol), DBU (224 μL, 1.5 mmol) and butylamine (200 μL, 2.0 mmol) in 82% yield as judged by LCMS analysis. An analytical sample was obtained by flash chromatography as a white solid (a tautomeric mixture). ¹H NMR (DMSO-*d*₆, 400 MHz): δ (ppm): 7.99 (s, 0.4H), 7.87 (s, 0.6H), 7.19 (s, 0.6H), 7.04 (s, 0.4H), 6.72 (s, 1H), 6.59 (s, 1H), 3.29-3.15 (m, 2H), 1.91-1.41 (m, 2H), 1.33-1.26 (m, 2H), 0.87 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (DMSO-*d*₆, 100 MHz): δ (ppm) 167.3, 166.7, 166.4, 165.6, 165.5, 165.4, 31.3, 19.6, 14.0. HRMS (ES-MS) [(M+H)⁺]: calcd for C₁₇H₁₃N₅ 168.1243 found 168.1241.

Butyl-(6-chloro-pyrimidin-4-yl)-amine (5k): Synthesized according to general procedure A (rt, 2d) from **4k** (13 mg, 0.1 mmol), BOP (53 mg, 0.12 mmol) and Ph₂O (16 μL, 0.1 mmol) DIPEA (20 μL, 0.12 mmol) and butylamine (30 μL, 0.30 mmol) in DCM (2 mL) in 75% yield as judged by LCMS analysis. An analytical sample was obtained by flash chromatography eluted with EtOAc/Hexane (25: 100) as a white solid. Mp: 90 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 8.32 (s, 1H), 6.32 (s, 1H), 5.36 (s, 1H), 3.27 (s br, 2H), 1.79-1.95 (m, 2H), 1.46-1.39 (m, 2H), 0.96 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 163.3, 158.4, 41.3, 31.2, 20.3, 13.7. HRMS (ES-MS) [(M+H)⁺]: calcd for C₈H₁₂N₃Cl₁ 186.0792 found 186.0789.

(5-Bromo-pyrimidin-2-yl)-butyl-amine (5l): Synthesized according to general procedure A (rt, 10 h) from **5f** (87 mg, 0.50 mmol), BOP (287 mg, 0.65 mmol), Ph₂O (85.1 mg, 0.5 mmol) and butylamine (150 μL, 1.00 mmol) in 95% yield as judged by LCMS analysis. An analytic sample was obtained by flash chromatography with EtOAc/Hexane (25:100) as colorless oil that solidifies upon standing at room temperature. Mp: 78 °C. ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 8.48 (s, 2H), 5.17 (s br, 1H), 3.36 (td, *J* = 5.4, 6.8 Hz, 2H), 1.60-1.54 (m, 2H), 1.45-1.37 (m, 2H), 0.94 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ (ppm) 160.7, 158.2, 106.2, 41.47, 31.53, 20.06, 13.81. HRMS (ES-MS) [(M+H)⁺]: calcd for C₈H₁₂N₃Br₁ 230.0287 found 230.0287.

Butyl-(4-methyl-pyrimidin-2-yl)-amine (5m): Synthesized according to general procedure A (rt, 8 h) from 2-hydroxy-4-methylpyrimidine hydrogen chloride (**4m**) (146 mg, 1.00 mmol), DBU (450 μ L, 3.00 mmol) and butylamine (200 μ L, 2.00 mmol), purified by column chromatography eluted with EtOAc/Hexane (35:100) as colorless oil (111 mg, 68%). ^1H NMR (CDCl_3 , 400 MHz): δ 8.12 (d, $J = 4.8$ Hz, 1H), 6.37 (d, $J = 4.8$ Hz, 1H), 5.25 (s br, 1H), 3.41 (td, $J = 6.0, 7.2$ Hz, 2H), 2.31 (s, 3H), 1.61-1.54 (m, 2H), 1.45-1.36 (m, 2H), 0.940 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (CDCl_3 , 100 MHz): δ (ppm) 168.17, 162.08, 157.8, 110.2, 41.4, 32.1, 24.47, 20.45, 14.19. HRMS (ES-MS) $[(\text{M}+\text{H})^+]$: calcd for $\text{C}_9\text{H}_{15}\text{N}_3$ 116.3338 found 116.3335.

Kinetin⁶ (6): Synthesized according to general procedure A (rt, 3d) from hypoxanthine **4a** (68 mg, 0.5 mmol), BOP (287 mg, 0.65 mmol), Ph_2O (85 mg, 0.65 mmol), DBU (112 μ L, 0.75 mmol) and fufurylamine (141 μ L, 1.5 mmol) in DMF (10 mL) in 90% yield as judged by LCMS analysis. An analytic sample was obtained by column chromatography with 10% MeOH/EtOAc as a white solid. Mp: 265-267 $^\circ\text{C}$. Lit. 270 $^\circ\text{C}$. ^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ (ppm) 12.92 (s, 1H), 8.21-8.09 (m, 3H), 7.54 (s, 1H), 6.36 (s, 1H), 6.24 (s, 1H), 4.74 (s, 2H). ^{13}C NMR ($\text{DMSO}-d_6$, 100 MHz): δ (ppm) 154.3, 153.2, 152.3, 151.9, 141.9, 139.1, 137.8, 110.5, 106.7, 36.5. HRMS (ES-MS) $[(\text{M}+\text{H})^+]$: calcd for $\text{C}_{10}\text{H}_{19}\text{N}_5\text{O}_1$ 216.0879 found 216.0877.

Olomoucine (8): To a mixture of **7** (66 mg, 0.4 mmol), BOP (265 mg, 0.6 mmol) and DBU (119 μ L, 0.8 mmol) in DMF/DMSO (1:1, 4 mL) was added BnNH_2 (131 μ L, 1.2 mmol) at room temperature. The resultant mixture was stirred at room temperature for 2 days, then heated to 60 $^\circ\text{C}$ for 2 hrs. The crude mixture was purified by HPLC ($\text{MeCN}/\text{H}_2\text{O}/\text{HCO}_2\text{H}$) and then neutralized by aqueous NH_3 , the precipitate was collected by filtration as a white solid (90.5mg, 89%). Mp: 209-211 $^\circ\text{C}$. ^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ (ppm) 7.72 (br, s, 1H), 7.70 (s, 1H), 7.30-7.38 (m, 4H), 7.21-7.25 (m, 1H), 5.88

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(s, 2H), 4.68 (br, s, 2H), 3.78 (s, 3H). ^{13}C NMR (DMSO-*d*₆, 100 MHz): δ (ppm) 161.3, 155.8, 153.1, 141.7, 138.8, 129.1, 128.2, 127.4, 114.2, 30.0. HRMS (ES-MS) [(M+H)⁺]: for C₁₃H₁₄N₆ 255.1353 found 255.1353.

A portion of above product (76 mg, 0.3 mmol) was suspended in MeOH (2 mL). To this was added HOAc (26.5 mL, 0.45 mmol) and aldehyde (95 mL, 0.45 mmol) and NaBH₃CN (19 mg, 0.3 mmol). The resultant mixture was stirred at room temperature for 2 days, followed by addition of 10% aq. HCl (0.5 mL). The mixture was then stirred for 30 min and basified with aqueous NH₃, the precipitate was collected and washed with water. The crude product was purified by HPLC (MeCN/H₂O/HCO₂H), and basified with aqueous NH₃. The product was collected by filtration as a white solid (xx mg, 90%). Mp: 121-123 °C. Lit. 120.9-125.8 °C;⁷ 125-126 °C.⁸ ^1H NMR (DMSO-*d*₆, 400 MHz): δ (ppm) 7.84 (br, s, 1H), 7.70 (s, 1H), 7.30-7.39 (m, 4H), 7.22-7.25 (m, 1H), 6.21 (br, s, 2H), 4.47 (br, s, 3H: CH₂ + OH), 3.58 (s, 3H), 3.50-3.54 (m, 2H), 3.33-3.38 (m, 2H). ^{13}C NMR (DMSO-*d*₆, 100 MHz): δ (ppm) 160.4, 155.5, 152.5, 141.8, 138.8, 129.1, 128.4, 127.5, 114.2, 61.4, 45.0, 43.7, 29.9. HRMS (ES-MS) [(M+H)⁺]: for C₁₅H₁₈N₆O 299.1615 found 299.1618.

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