Condensation of Anthranilic Acids with Pyridines to Pyridoquinoxazolones via Pyridines Dearomatization

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Contents

I. General Considerations .......................................................... S2
II. Experimental Data ............................................................. S2
III. References ........................................................................ S24
IV. 1H, 13C and 19F NMR Spectra of Compounds ...................... S25
**General Comments**

All reactions were carried out under dry O$_2$ or dry air with dry solvents under anhydrous conditions unless otherwise noted. 4-Aminobenzo[d][1,3]dioxole-5-carboxylic acid,\(^1\) 2-amino-4-benzyloxy -5-methoxybenzoic acid,\(^1\) substituted carboline \(^2\) and substituted 3,4-dihydro-\(\beta\)-carboline \(^3\) were prepared according to the reported procedures. All other reagents used for experiments were purchased from Alfa Aesar, TCI, Sigma-Aldrich Co. CH$_2$Cl$_2$ was distilled from CaH$_2$ under nitrogen and stored under nitrogen. NMR spectra were obtained on a Bruker AVANCE 400 (400 MHz for \(^1\)H NMR; 100 MHz for \(^13\)C NMR; 377 MHz for \(^19\)F NMR) spectrometer. HRMS were obtained on an Agilent Technologies 6224 TOF LC/MS equipped with an ESI source or HEXIN 10000 TOF-MS equipped with an API source.

**General Experimental Procedure**

For compounds 3a-n and 4a-u: A 25 mL of Schlenk tube equipped with a stir bar was charged with 2-amino-6-methyl-benzoic acid (60.5 mg, 0.4 mmol, 1.0 equiv), EDCI (153.4 mg, 0.8 mmol, 2.0 equiv), pyridine (0.29 mL, 3.6 mmol, 9.0 equiv), CH$_2$Cl$_2$ (2.0 mL), was added in turn to the Schlenk tube through the rubber septum using syringes, Then, the tube was evacuated and refilled with O$_2$ for three times. Finally, the septum was replaced with a Teflon screwcap under O$_2$ flow. After 4 hours, the reaction mixture was diluted with 30 mL of CH$_2$Cl$_2$. Then it was washed with saturated aqueous NaHCO$_3$ (20 mL), H$_2$O (20 mL), and brine (20 mL). The organic phase was dried over Na$_2$SO$_4$, filtered, concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel to provide the corresponding product.

For compounds 5a-r: A 25 mL of Schlenk tube equipped with a stir bar was charged with 2-Amino-4,5-dimethoxybenzoic acid (70.9 mg, 0.36 mmol), 4,9-dihydro-6-methoxy-3H-pyrido[3,4-b]indole (60.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml) was added in turn to the Schlenk tube through the rubber septum using syringes. Then, the tube was stirred at 80°C under air. After 4 hours, the
reaction mixture was concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel to provide the corresponding product.

**The Characterization of Products**

1-Methyl-11H-pyrido[2,1-b]quinazolin-11-one  (3a): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH₂Cl₂ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH₂Cl₂=100:10) to afford a yellow solid (73.9 mg, 88% yield). ¹H NMR (400MHz, CDCl₃): δ 8.78 (d, J = 8.0 Hz, 1H), 7.63-7.53 (m, 2H), 7.45-7.37 (m, 2H), 7.15 (d, J = 4.0 Hz, 1H), 6.78-6.75 (m, 1H), 2.92 (s, 3H); ¹³C NMR (100MHz, CDCl₃): δ 158.90, 150.00, 147.54, 141.53, 134.10, 134.04, 127.45, 126.52, 125.98, 125.00, 115.03, 112.11, 23.63; HRMS (ESI) m/z calcd. for C₁₃H₁₁N₂O [M+H]+ 211.08659, found 211.08626.

2-Methyl-11H-pyrido[2,1-b]quinazolin-11-one  (3b): Following the general procedure with 2-Amino-5-methylbenzoic acid (60.4 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH₂Cl₂ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (77.3 mg, 92% yield). ¹H NMR(400MHz, CDCl₃) : δ 8.87 (d, J = 8.0 Hz, 1H), 7.62-7.50 (m, 2H), 7.49-7.46 (m, 1H), 7.15 (d, J = 4.0 Hz, 1H), 6.86-6.82 (m, 1H), 2.54 (s, 3H); ¹³C NMR (100MHz, CDCl₃) : δ 158.89, 147.12, 146.68, 136.92, 135.38, 133.51, 126.72, 126.63, 126.32, 126.22, 116.04, 112.31, 21.37; HRMS (ESI) m/z calcd. for C₁₃H₁₁N₂O [M+H]+ 211.08659, found 211.08620.

3-Methyl-11H-pyrido[2,1-b]quinazolin-11-one  (3c): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH₂Cl₂ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (73.9 mg, 88% yield). ¹H NMR (400MHz, CDCl₃): δ 8.78 (d, J = 8.0 Hz, 1H), 7.63-7.53 (m, 2H), 7.45-7.37 (m, 2H), 7.15 (d, J = 4.0 Hz, 1H), 6.78-6.75 (m, 1H), 2.92 (s, 3H); ¹³C NMR (100MHz, CDCl₃): δ 158.90, 150.00, 147.54, 141.53, 134.10, 134.04, 127.45, 126.52, 125.98, 125.00, 115.03, 112.11, 23.63; HRMS (ESI) m/z calcd. for C₁₃H₁₁N₂O [M+H]+ 211.08659, found 211.08626.
**11H-pyrido[2,1-b]quinazolin-11-one (3c):** Following the general procedure with 2-Amino-5-methylbenzoic acid (54.8 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH₂Cl₂ (2.0 mL). The reaction mixture was stirred at 80°C under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (55.7 mg, 71% yield).

**1H NMR (400MHz, CDCl₃):** \(\delta 8.89 (d, J = 8.0 \text{ Hz}, 1H), 8.46 (d, J = 8.0 \text{ Hz}, 1H), 7.87-7.78 (m, 2H), 7.52-7.49 (m, 2H), 6.88-6.86 (m, 2H);\)

**13C NMR (100MHz, CDCl₃):** δ 158.99, 148.57, 147.69, 135.05, 134.07, 127.29, 126.89, 126.69, 126.34, 125.20, 116.28, 112.47; HRMS (ESI) m/z calcd. for C₁₂H₉N₂O [M+H]+ 197.07094, found 197.07043.

![Diagram 3c](image)

**4-Methyl-11H-pyrido[2,1-b]quinazolin-11-one (3d):** Following the general procedure with 2-Amino-3-methylbenzoic acid (60.4 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH₂Cl₂ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH₂Cl₂=100:10) to afford a yellow solid (50.4 mg, 60% yield).

**1H NMR (400MHz, CDCl₃):** \(\delta 8.83 (d, J = 7.3 \text{ Hz}, 1H), 8.28 (d, J = 8.1 \text{ Hz}, 1H), 7.66 (d, J = 7.0 \text{ Hz}, 1H), 7.51 (d, J = 9.1 \text{ Hz}, 1H), 7.44 (dd, J = 8.2 and 7.2 \text{ Hz}, 1H), 7.34 (t, J = 7.6 \text{ Hz}, 1H), 6.81 (t, J = 6.8 Hz, 1H), 2.68 (s, 3H);\)

**13C NMR (100MHz, CDCl₃):** δ 159.30, 147.3, 146.64, 135.35, 135.03, 133.35, 126.88, 125.50, 124.89, 124.74, 116.19, 112.35, 17.66; HRMS (ESI) m/z calcd. for C₁₃H₁₁N₂O [M+H]+ 211.08659, found 211.08624.

![Diagram 3d](image)

**2-Methoxy-11H-pyrido[2,1-b]quinazolin-11-one (3e):** Following the general procedure with 2-Amino-3-methoxybenzoic acid (66.8 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH₂Cl₂ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH₂Cl₂=100:10) to afford a yellow solid (65.1 mg, 72% yield).

**1H NMR (400MHz, CDCl₃):** \(\delta 8.82 (d, J = 8.0 \text{ Hz}, 1H), 7.70 (s, 1H), 7.45-7.41 (m, 3H), 6.83-6.79 (m, 1H), 3.93 (s, 3H);\)

**13C NMR (100MHz, CDCl₃):** δ 158.57, 157.29, 145.98, 143.63, 143.63, 132.74, 128.62, 126.70, 126.35, 126.33, 116.80, 112.50, 105.07, 55.80; HRMS (ESI) m/z calcd. for C₁₃H₁₁N₂O₂ [M+H]+ 227.08150, found 227.08104.
**2,3-Dimethoxy-11H-pyrido[2,1-b]quinazolin-11-one (3f):** Following the general procedure with 2-Amino-4,5-dimethylbenzoic acid (78.8 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH₂Cl₂ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH₂Cl₂ = 100:10) to afford a yellow solid (82.9 mg, 81% yield).

1H NMR (400MHz, CDCl₃): δ 8.91 (d, J = 8.0 Hz, 1H), 7.73 (s, 1H), 7.48 (s, 2H), 7.17 (s, 1H), 6.89-6.86 (m, 1H), 4.05 (s, 6H);

13C NMR (100MHz, CDCl₃): δ 157.82, 156.24, 148.60, 146.86, 145.54, 133.19, 126.58, 125.87, 112.35, 109.81, 106.46, 105.16, 56.34, 56.31; HRMS (ESI) m/z calcd. for C₁₄H₁₃N₂O₃ [M+H]+ 257.09207, found 257.09161.

**12H-Benzoo[gi]pyrido[2,1-b]quinazolin-12-one (3g):** Following the general procedure with 3-amino-2-naphthoic acid (74.4 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH₂Cl₂ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH₂Cl₂ = 100:10) to afford a yellow solid (73.8 mg, 75% yield).

1H NMR (400MHz, CDCl₃): δ 9.11 (s, 1H), 8.78 (d, J = 8.0 Hz, 1H), 8.28 (s, 1H), 8.10 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.64-7.60 (m, 1H), 7.54-7.50 (m, 1H), 7.42 (m, 2H), 6.73 (m, 1H); 13C NMR (100MHz, CDCl₃): δ 159.86, 147.13, 143.49, 137.34, 133.65, 130.62, 129.37, 129.00, 128.59, 127.77, 126.52, 126.34, 125.64, 123.89, 116.28, 111.32; HRMS (ESI) m/z calcd. for C₁₆H₁₁N₂O [M+H]+ 247.08659, found 247.08618.

**3-Fluoro-11H-pyrido[2,1-b]quinazolin-11-one (3h):** Following the general procedure with 2-Amino-4-fluorobenzoic acid (62.0 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH₂Cl₂ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate = 100:50) to afford a yellow solid (40.2 mg, 47% yield).

1H NMR (400MHz, CDCl₃): δ 8.83 (d, J = 8.0 Hz, 1H), 8.04 (dd, J = 8.0 and 4.0 Hz, 1H), 7.88 (dd, J = 8.0 and 4.0 Hz, 1H), 7.78 (dd, J = 8.0 and 4.0 Hz, 1H), 7.60-7.47 (m, 3H), 7.20-6.86 (m, 1H); 13C NMR (100MHz, CDCl₃): δ 160.89, 158.36, 147.03, 133.49, 133.74, 133.65, 130.62, 129.37, 129.00, 128.59, 127.77, 126.52, 126.34, 125.64, 123.89, 116.28, 111.32; HRMS (ESI) m/z calcd. for C₁₂H₈N₂OF [M+H]+ 215.06152, found 215.06108.
**1-Fluoro-11H-pyrido[2,1-b]quinazolin-11-one (3i):** Following the general procedure with 2-Amino-6-fluorobenzoic acid (62.0 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH₂Cl₂ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (59.9 mg, 70% yield). ¹H NMR (400MHz, CDCl₃): δ 8.90 (d, \( J = 8.0 \) Hz, 1H), 7.78-7.73 (m, 1H), 7.59-7.47 (m, 3H), 7.12-7.08 (m, 1H), 6.92-6.88 (m, 1H); ¹³C NMR (100MHz, CDCl₃): δ 162.96, 160.31, 150.41, 148.41, 135.19, 135.09, 126.58, 126.11, 122.75, 112.79, 110.87, 110.67; HRMS (ESI) m/z calcd.for C₁₂H₈N₂O₃ [M+H]+ 215.06152, found 215.06111.

**2-Bromo-11H-pyrido[2,1-b]quinazolin-11-one (3j):** Following the general procedure with 2-Amino-5-bromobenzoic acid (86.4 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH₂Cl₂ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (60.3 mg, 55% yield). ¹H NMR (400MHz, CDCl₃): δ 8.87 (d, \( J = 8.0 \) Hz, 1H), 8.57 (d, \( J = 4.0 \) Hz, 1H), 7.89 (dd, \( J = 8.0 \) and 4.0 Hz, 1H), 7.65 (d, \( J = 8.0 \) Hz, 1H), 7.58-7.49 (m, 2H), 6.92-6.89 (m, 1H); ¹³C NMR (100MHz, CDCl₃): δ 157.82, 147.79, 147.26, 138.17, 134.47, 129.45, 128.74, 126.70, 117.34, 112.96; HRMS (ESI) m/z calcd.for C₁₂H₈N₂OBr [M+H]+ 274.98145, found 274.98114.

**1-Chloro-11H-pyrido[2,1-b]quinazolin-11-one (3k):** Following the general procedure with 2-Amino-6-chlorobenzoic acid (68.8 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH₂Cl₂ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (55.2 mg, 60% yield). ¹H NMR (400MHz, CDCl₃): δ 8.90 (d, \( J = 4.0 \) Hz, 1H), 7.68-7.67 (m, 1H), 7.58-7.54 (m, 1H), 7.48-7.46 (m, 2H), 6.92-6.88 (m, 1H); ¹³C NMR (100MHz, CDCl₃): δ 156.87, 150.82, 148.10, 135.03, 134.39, 134.10, 127.51, 126.47, 126.20, 126.02, 113.41, 112.86; HRMS (ESI) m/z calcd.for C₁₂H₈N₂OCl [M+H]+ 240.04408, found 240.04406.
2-Trifluoromethyl-11\(H\)-pyrido[2,1-b]quinazolin-11-one (3l): Following the general procedure with 2-Amino-5-trifluoromethylbenzoic acid (82.0 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH\(_2\)Cl\(_2\) (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O\(_2\). After 4 hours, the reaction mixture was diluted with 30 mL of CH\(_2\)Cl\(_2\). Then it was washed with saturated aqueous NaHCO\(_3\) (20 mL), H\(_2\)O (20 mL), and brine (20 mL). The organic phase was dried over Na\(_2\)SO\(_4\), filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (52.8 mg, 50% yield). \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 8.30 (s, 1H), 8.21 (d, \(J = 4.0\) Hz, 1H), 8.04-8.03 (m, 3H), 7.54 (d, \(J = 8.0\) Hz, 1H), 7.01 (d, \(J = 8.0\) Hz, 1H); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 157.90, 157.61, 153.69, 148.79, 132.74, 132.72, 128.01, 126.42, 126.39, 124.98, 124.95, 117.57, 106.83; HRMS (ESI) m/z calcd for C\(_{13}\)H\(_8\)N\(_2\)OF\(_3\) [M+H]\(^+\) 265.05832, found: 265.05780.

3-Chloro-11\(H\)-pyrido[2,1-b]quinazolin-11-one (3m): Following the general procedure with 2-Amino-4-chlorobenzoic acid (68.8 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH\(_2\)Cl\(_2\) (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O\(_2\). After 4 hours, the reaction mixture was diluted with 30 mL of CH\(_2\)Cl\(_2\). Then it was washed with saturated aqueous NaHCO\(_3\) (20 mL), H\(_2\)O (20 mL), and brine (20 mL). The organic phase was dried over Na\(_2\)SO\(_4\), filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (40.5 mg, 44% yield). \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 8.78 (dd, \(J = 4.0\) and 8.0 Hz, 1H), 8.28 (d, \(J = 8.0\) Hz, 1H), 7.78-7.74 (m, 2H), 7.52-7.48 (m, 2H), 7.11-7.08 (m, 1H); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 158.37, 149.10, 148.58, 135.11, 128.73, 126.71, 125.99, 125.85, 114.40, 113.04; HRMS (ESI) m/z calcd for C\(_{12}\)H\(_8\)N\(_2\)OCl [M+H]\(^+\) 231.03171, found: 231.03197.

10-Oxo-10\(H\)-pyrido[1,2-\(a\)]thieno[3,2-\(d\)]pyrimidine (3n): Following the general procedure with 3-Amino-2-thiopheneacetic acid (57.2 mg, 0.4 mmol), pyridine (0.29 mL, 3.6 mmol), EDCI (153.4 mg, 0.8 mmol), and CH\(_2\)Cl\(_2\) (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O\(_2\). After 4 hours, the reaction mixture was diluted with 30 mL of CH\(_2\)Cl\(_2\). Then it was washed with saturated aqueous NaHCO\(_3\) (20 mL), H\(_2\)O (20 mL), and brine (20 mL). The organic phase was dried over Na\(_2\)SO\(_4\), filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH\(_2\)Cl\(_2\)=100:10) to afford a yellow solid (34.8 mg, 43% yield). \(^1\)H NMR (400MHz, CDCl\(_3\)) \(\delta\) 9.5 (d, \(J = 8.0\) Hz, 1H), 7.7.98 (d, \(J = 4.0\) Hz, 1H), 7.7.98 (d, \(J = 8.0\) Hz, 1H), 7.7.98 (d, \(J = 8.0\) Hz, 1H); \(^{13}\)C NMR (100MHz, CDCl\(_3\)) \(\delta\) 158.37, 149.10, 148.58, 141.51 135.11, 128.73, 126.71, 125.99, 125.85, 114.40, 113.04; HRMS (ESI) m/z calcd for C\(_{12}\)H\(_8\)N\(_2\)OCl [M+H]\(^+\) 231.03171, found: 231.03197.
$^{1}H$ NMR (500MHz, DMSO-$d_6$): $\delta$ 7.25-7.21 (m, 2H), 7.15 (d, $J = 5.0$ Hz, 1H), 6.71 (d, $J = 10.0$ Hz, 1H), 6.63 (d, $J = 5.0$ Hz, 1H), 6.10-6.06 (m, 1H), 6.56-6.51 (m, 2H), 6.30-6.27 (m, 1H), 2.54 (s, 3H); $^{13}C$ NMR (125MHz, DMSO-$d_6$): $\delta$ 161.40, 148.07, 141.87, 133.87, 123.66, 123.46, 122.42, 119.04, 114.02, 113.82, 103.66, 66.19, 22.67; HRMS (ESI) m/z calcld for C$_{13}$H$_{13}$N$_2$O $[M+H]^+$ 213.10224, found 213.10167.

1,7-Dimethyl-11H-pyrido[2,1-b]quinazolin-11-one (4a): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), 4-methylpyridine (111.6 mg, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH$_2$Cl$_2$ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O$_2$. After 4 hours, the reaction mixture was diluted with 30 mL of CH$_2$Cl$_2$. Then it was washed with saturated aqueous NaHCO$_3$ (20 mL), H$_2$O (20 mL), and brine (20 mL). The organic phase was dried over Na$_2$SO$_4$, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH$_2$Cl$_2$ = 100:10) to afford a yellow solid (65.4 mg, 73% yield). $^{1}H$ NMR (400MHz, CDCl$_3$): $\delta$ 8.68 (d, $J = 8.0$ Hz, 1H), 7.61-7.57 (m, 1H), 7.52 (d, $J = 8.0$ Hz, 1H), 7.16-7.12 (m, 2H), 6.61 (dd, $J = 4.0$ and 8.0 Hz, 1H), 2.92 (s, 3H), 2.35 (s, 3H); $^{13}C$ NMR (100MHz, CDCl$_3$): $\delta$ 158.98, 150.37, 147.68, 145.79, 141.53, 134.08, 127.01, 125.79, 124.82, 123.34, 115.21, 114.77, 23.66, 21.35; HRMS (ESI) m/z calcld for C$_{14}$H$_{13}$N$_2$O $[M+H]^+$ 225.10224, found 225.10188.

1-Methyl-7-ethyl-11H-pyrido[2,1-b]quinazolin-11-one (4b): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), 4-ethylpyridine (128.4 mg, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH$_2$Cl$_2$ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O$_2$. After 4 hours, the reaction mixture was diluted with 30 mL of CH$_2$Cl$_2$. Then it was washed with saturated aqueous NaHCO$_3$ (20 mL), H$_2$O
(20 mL), and brine (20 mL). The organic phase was dried over Na$_2$SO$_4$, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH$_2$Cl$_2$=100:10) to afford a yellow solid (68.5 mg, 72% yield). $^1$H NMR (400MHz, CDCl$_3$): $\delta$ 8.71 (d, $J$ = 8.0 Hz, 1H), 7.62-7.58 (m, 1H), 7.53 (d, $J$ = 8.0 Hz, 1H), 7.18 (s, 1H), 2.93 (s, 3H), 2.67 (q, $J$ = 8.0 Hz, 2H), 1.29 (t, $J$ = 8.0 Hz, 3H); $^{13}$C NMR (100MHz, CDCl$_3$): $\delta$ 159.01, 151.25, 150.46, 147.91, 141.50, 134.01, 126.96, 125.88, 124.85, 121.77, 114.81, 114.25, 28.17, 23.60, 12.87; HRMS (ESI) m/z calcd. for C$_{15}$H$_{15}$N$_2$O [M+H]$^+$ 239.11789, found 239.11739.

1-Methyl-7-tert-Butyl-11H-pyrido[2,1-b]quinazolin-11-one (4c): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), 4-tert-butylpyridine (0.2 mL, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH$_2$Cl$_2$ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O$_2$. After 4 hours, the reaction mixture was diluted with 30 mL of CH$_2$Cl$_2$. Then it was washed with saturated aqueous NaHCO$_3$ (20 mL), H$_2$O (20 mL), and brine (20 mL). The organic phase was dried over Na$_2$SO$_4$, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH$_2$Cl$_2$=100:10) to afford a yellow solid (60.6 mg, 57% yield). $^1$H NMR (400MHz, CDCl$_3$): $\delta$ 8.75 (d, $J$ = 8.0 Hz, 1H), 7.63-7.54 (m, 2H), 7.32 (d, $J$ = 0.8 Hz, 1H), 7.15 (d, $J$ = 8.0 Hz, 1H), 6.8 (dd, $J$ = 8.0 Hz, 1H), 2.94 (s, 3H), 1.35 (s, 9H); $^{13}$C NMR (100MHz, CDCl$_3$): $\delta$ 158.95, 158.02, 150.52, 148.04, 141.50, 134.04, 126.99, 125.89, 119.80, 114.8, 111.94, 35.11, 29.66, 29.45, 23.72, 23.54; HRMS (ESI) m/z calcd. for C$_{17}$H$_{19}$N$_2$O [M+H]$^+$ 267.14919, found 267.14862.

1-Methyl-7-phenyl-11H-pyrido[2,1-b]quinazolin-11-one (4d): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), 4-phenylpyridine (186.3 mg, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH$_2$Cl$_2$ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O$_2$. After 4 hours, the reaction mixture was diluted with 30 mL of CH$_2$Cl$_2$. Then it was washed with saturated aqueous NaHCO$_3$ (20 mL), H$_2$O (20 mL), and brine (20 mL). The organic phase was dried over Na$_2$SO$_4$, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH$_2$Cl$_2$=100:10) to afford a yellow solid (62.9 mg, 55% yield). $^1$H NMR (400MHz, CDCl$_3$): $\delta$ 8.89 (dd, $J$ = 8.0 and 0.8 Hz, 1H), 7.74-7.72 (m, 2H), 7.66-7.61 (m, 3H), 7.52-7.47 (m, 3H), 7.13 (d, $J$ = 8.0 Hz, 1H), 7.12 (dd, $J$ = 8.0 and 2.0 Hz, 1H), 2.98 (s, 3H); $^{13}$C NMR (100MHz, CDCl$_3$): $\delta$ 158.95, 158.02, 150.52, 148.04, 141.50, 134.04, 126.99, 125.89, 119.80, 114.8, 111.94, 35.11, 29.66, 29.45, 23.72, 23.54; HRMS (ESI) m/z calcd. for C$_{19}$H$_{15}$N$_2$O [M+H]$^+$ 287.11789, found 287.11728.
1-Methyl-7-trifluoromethyl-11H-pyrido[2,1-b]quinazolin-11-one (4e): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), 4-trifluoromethylpyridine (0.2 mL, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH$_2$Cl$_2$ (1.0 mL). The reaction mixture was stirred at room temperature under 1 atm O$_2$. After 4 hours, the reaction mixture was diluted with 30 mL of CH$_2$Cl$_2$. Then it was washed with saturated aqueous NaHCO$_3$ (20 mL), H$_2$O (20 mL), and brine (20 mL). The organic phase was dried over Na$_2$SO$_4$, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH$_2$Cl$_2$=100:10) to afford a yellow solid (55.6 mg, 50% yield).

$^1$H NMR (400MHz, CDCl$_3$): δ 8.84 (d, $J$ = 8.0 Hz, 1H), 7.71-7.67 (m, 2H), 7.60 (d, $J$ = 8.0 Hz, 1H), 7.28-7.26 (m, 1H), 6.84 (dd, $J$ = 8.0 Hz, 1H), 2.94 (s, 3H);

$^{13}$C NMR(100MHz, CDCl$_3$): δ 158.34, 149.56, 145.87, 141.84, 134.60, 128.84, 128.46, 125.53, 124.69, 115.63, 106.86, 106.83, 23.52; HRMS (ESI) m/z calcd. for C$_{14}$H$_{10}$N$_2$OF$_3$ [M+H]$^+$ 279.07397, found 279.07339.

1-Methyl-7-iodo-11H-pyrido[2,1-b]quinazolin-11-one (4f): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), 4-iodopyridine (164.0 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O$_2$. After 4 hours, the reaction mixture was diluted with 30 mL of CH$_2$Cl$_2$. Then it was washed with saturated aqueous NaHCO$_3$ (20 mL), H$_2$O (20 mL), and brine (20 mL). The organic phase was dried over Na$_2$SO$_4$, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH$_2$Cl$_2$=100:10) to afford a yellow solid (84.7 mg, 63% yield).

$^1$H NMR (400MHz, CDCl$_3$): δ 8.46 (d, $J$ = 8.0 Hz, 1H), 7.89 (d, $J$ = 4.0 Hz, 1H), 7.67-7.63 (m, 1H), 7.55 (d, $J$ = 8.0 Hz, 1H), 7.22 (d, $J$ = 8.0 Hz, 1H), 7.99 (dd, $J$ = 8.0 Hz, 1H), 2.93 (s, 1H);

$^{13}$C NMR(100MHz, CDCl$_3$): δ 158.70, 149.78, 146.76, 141.82, 134.68, 134.53, 128.06, 126.47, 125.28, 120.93, 115.24, 102.64, 23.55; HRMS (ESI) m/z calcd. for C$_{13}$H$_{10}$N$_2$I [M+H]$^+$ 336.98323, found 336.98248.

1-Methyl-8H-isoquinolino[1,2-b]quinazolin-8-one (4g): Following the general procedure with 2-Amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), isoquinoline (103.2 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O$_2$. After 4 hours, the reaction mixture was diluted with 30 mL of CH$_2$Cl$_2$. Then it was washed with saturated aqueous NaHCO$_3$ (20 mL), H$_2$O (20 mL), and brine (20 mL). The organic phase was dried over Na$_2$SO$_4$, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: CH$_2$Cl$_2$=100:10) to afford a yellow solid (57.2 mg, 55% yield).

$^1$H NMR (400MHz, CDCl$_3$): δ 8.95 (d, $J$ = 8.0 Hz, 1H), 8.54 (d, $J$ = 8.0 Hz, 1H), 7.68-7.54 (m, 5H), 7.20 (d, $J$ = 8.0 Hz, 1H), 6.92 (d, $J$ = 8.0 Hz, 1H), 2.96 (s, 1H);

$^{13}$C NMR(100MHz, CDCl$_3$): δ 159.49, 149.78, 146.76, 141.82, 134.68, 134.53, 128.06, 126.47, 125.28, 120.93, 115.24, 102.64, 23.55; HRMS (ESI) m/z calcd. for C$_{17}$H$_{13}$N$_2$O [M+H]$^+$ 336.98323, found 336.98248.
2,6,8-Trimethyl-11H-pyrido[2,1-b]quinazolin-11-one (4h): Following the general procedure with 2-Amino-5-methylbenzoic acid (60.4 mg, 0.4 mmol), 3,5-dimethylpyridine (128.4 mg, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH₂Cl₂ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (67.6 mg, 71% yield).

1H NMR (400MHz, CDCl₃): δ 8.60 (s, 1H), 8.21 (s, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.22 (s, 1H), 2.57 (s, 3H), 2.52 (s, 3H), 2.31 (s, 3H);

13C NMR (100MHz, CDCl₃): δ 159.20, 146.30, 146.23, 136.32, 135.17, 134.92, 133.73, 127.19, 126.04, 121.69, 121.51, 115.79, 21.36, 18.41, 18.32; HRMS (ESI) m/z calcd. for [M+H]+ 239.11789 C₁₅H₁₅N₂O, found 239.11736.

2-Methyl-6-fluoro-11H-pyrido[2,1-b]quinazolin-11-one (4i): Following the general procedure with 2-Amino-5-methylbenzoic acid (60.4 mg, 0.4 mmol), 3-fluoropyridine (349.2 mg, 3.6 mmol), and EDCI (153.4 mg, 0.8 mmol). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (50.2 mg, 55% yield).

1H NMR (400MHz, CDCl₃): δ 8.67 (d, J = 8.0 Hz, 1H), 8.22 (s, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 6.78-6.73 (m, 1H), 2.54 (s, 3H); 13C NMR (100MHz, CDCl₃): δ 158.36, 155.31, 152.75, 145.60, 137.19, 136.49, 126.92, 126.32, 122.77, 116.40, 114.40, 109.85, 21.41; HRMS (ESI) m/z calcd. for C₁₃H₁₀N₂OF [M+H]+ 229.07717, found: 229.07687.

2,3,7-Trimethoxy-11H-pyrido[2,1-b]quinazolin-11-one (4o): Following the general procedure with 2-Amino-4,5-dimethoxybenzoic acid (78.8 mg, 0.4 mmol), 4-methoxypyridine (82.7 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (52.6 mg, 46% yield).

1H NMR (400MHz, CDCl₃): δ 8.80 (d, J = 8.0 Hz, 1H), 7.65 (s, 1H), 7.05 (s, 1H), 6.67 (d, J = 4.0 Hz, 1H), 7.60-7.58 (m, 1H), 4.03 (s, 3H), 4.02 (s, 3H), 3.94 (s, 3H);
\[ 13C \text{ NMR (100MHz, CDCl}_3\text{): } \delta 163.11, 157.89, 156.31, 148.87, 147.78, 146.36, 126.79, 108.78, 108.72, 105.92, 105.35, 100.01, 56.26, 56.26, 56.01; \text{HRMS (ESI) m/z calcld. for C}_{16}H_{15}N_2O_4 [M+H]^+ 287.10263, found 287.10205. \]

![Image 4k](9-methyl-8H-phthalazino[1,2-b]quinazolin-8-one (4q): Following the general procedure with 2-amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), phthalazine (104.0 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O\textsubscript{2}. After 4 hours, the reaction mixture was diluted with 30 mL of CH\textsubscript{2}Cl\textsubscript{2}. Then it was washed with saturated aqueous NaHCO\textsubscript{3} (20 mL), H\textsubscript{2}O (20 mL), and brine (20 mL). The organic phase was dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: ethyl acetate=100:40) to afford a yellow solid (55.3 mg, 53% yield). \textsuperscript{1}H NMR (500MHz, CDCl\textsubscript{3}): \delta 8.92 (d, \textit{J} = 5.0 Hz, 1H), 8.66 (s, 1H), 8.32 (s, 1H), 7.88 (t, \textit{J} = 5.0 Hz, 1H), 7.83 (t, \textit{J} = 5.0 Hz, 1H), 7.76 (t, \textit{J} = 10.0 Hz, 2H), 7.66 (d, \textit{J} = 10.0 Hz, 1H), 2.54 (s, 3H); \textsuperscript{13}C NMR (125MHz, CDCl\textsubscript{3}): \delta 159.08, 145.31, 144.59, 142.57, 136.77, 136.51, 133.34, 132.74, 129.13, 127.30, 127.12, 127.07, 126.01, 124.96, 120.00, 21.41; HRMS (ESI) m/z calcld. for C\textsubscript{16}H\textsubscript{12}N\textsubscript{3}O [M+H]^+ 262.09804, found 262.09598.

![Image 4l](9-methyl-10H-pyridazino[6,1-b]quinazolin-10-one (4r): Following the general procedure with 2-amino-6-methylbenzoic acid (60.4 mg, 0.4 mmol), pyridazine (64.0 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O\textsubscript{2}. After 4 hours, the reaction mixture was diluted with 30 mL of CH\textsubscript{2}Cl\textsubscript{2}. Then it was washed with saturated aqueous NaHCO\textsubscript{3} (20 mL), H\textsubscript{2}O (20 mL), and brine (20 mL). The organic phase was dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: ethyl acetate=100:40) to afford a yellow solid (38.8 mg, 46% yield). \textsuperscript{1}H NMR (500MHz, CDCl\textsubscript{3}): \delta 8.45 (s, 1H), 8.35 (s, 1H), 7.72 (s, 3H), 7.25 (s, 1H), 2.56 (s, 3H); \textsuperscript{13}C NMR (125MHz, CDCl\textsubscript{3}): \delta 158.61, 145.37, 144.59, 142.57, 136.77, 136.51, 133.34, 132.74, 129.13, 127.30, 127.11, 127.01, 124.80, 119.32, 21.48; HRMS (ESI) m/z calcld. for C\textsubscript{12}H\textsubscript{10}N\textsubscript{3}O [M+H]^+ 212.08184, found 212.08124.

![Image 4m](7-acetyl-2-methyl-11H-pyrido[2,1-b]quinazolin-11-one (4t): Following the general procedure with 2-Amino-5-methylbenzoic acid (60.4 mg, 0.4 mmol), 4-acetylpyridine (96.8 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O\textsubscript{2}. After 4 hours, the reaction mixture was diluted with 30 mL of CH\textsubscript{2}Cl\textsubscript{2}. Then it was washed with saturated aqueous NaHCO\textsubscript{3} (20 mL), H\textsubscript{2}O (20 mL), and brine (20 mL). The organic phase was dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, concentrated under reduced
pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (48.4 mg, 48% yield). $^1$H NMR (400MHz, CDCl$_3$): $\delta$ 8.88-8.86 (m, 1H), 8.29-8.28 (m, 1H), 8.03-8.02 (m, 1H), 7.77-7.76 (m, 2H), 7.30-7.28 (m, 1H), 2.69-2.68 (m, 3H), 2.58 (s, 3H); $^{13}$C NMR (100MHz, CDCl$_3$): $\delta$ 196.43, 158.55, 146.72, 146.52, 140.01, 137.25, 137.07, 129.13, 127.31, 127.26, 126.55, 116.94, 108.71, 29.73, 21.56; HRMS (ESI) m/z calcd. for [M+H]$^+$ 253.09715 C$_{15}$H$_{13}$N$_2$O$_2$, found 253.09636.

methyl 2-methyl-11-oxo-11$H$-pyrido[2,1-b]quinazoline-7-carboxylate (4u): Following the general procedure with 2-Amino-5-methylbenzoic acid (60.4 mg, 0.4 mmol), Methyl isonicotinate (109.6 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O$_2$. After 4 hours, the reaction mixture was diluted with 30 mL of CH$_2$Cl$_2$. Then it was washed with saturated aqueous NaHCO$_3$ (20 mL), H$_2$O (20 mL), and brine (20 mL). The organic phase was dried over Na$_2$SO$_4$, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (45.0 mg, 42% yield). $^1$H NMR (400MHz, CDCl$_3$): $\delta$ 8.85 (dd, $J$ = 8.0 and 4.0 Hz, 1H), 8.27-8.26 (s, 1H), 8.17-8.16 (m, 1H), 7.77-7.72 (m, 2H), 7.25 (dd, $J$ = 8.0 and 4.0 Hz, 1H), 4.00 (s, 3H), 2.56 (s, 3H); $^{13}$C NMR (100MHz, CDCl$_3$): $\delta$ 164.39, 158.59, 146.55, 146.36, 136.84, 134.52, 129.83, 127.35, 127.20, 126.41, 116.77, 110.28, 53.07, 21.54; HRMS (ESI) m/z calcd. for [M+H]$^+$ 269.09207 C$_{15}$H$_{13}$N$_3$O$_3$, found 269.09128.

2-Methyl-8$H$-isoquinolino[1,2-b]quinazolin-8-one (4j): Following the general procedure with 2-Amino-5-methylbenzoic acid (60.4 mg, 0.4 mmol), isoquinoline (103.2 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O$_2$. After 4 hours, the reaction mixture was diluted with 30 mL of CH$_2$Cl$_2$. Then it was washed with saturated aqueous NaHCO$_3$ (20 mL), H$_2$O (20 mL), and brine (20 mL). The organic phase was dried over Na$_2$SO$_4$, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (62.4 mg, 60% yield). $^1$H NMR (400MHz, CDCl$_3$): $\delta$ 9.07 (d, $J$ = 8.0 Hz, 1H), 8.66 (d, $J$ = 8.0 Hz, 1H), 8.25 (s, 1H), 7.81 (d, $J$ = 8.0 Hz, 1H), 7.72-7.64 (m, 4H), 7.02 (d, $J$ = 8.0 Hz, 1H), 2.55 (s, 3H); $^{13}$C NMR (100MHz, CDCl$_3$): $\delta$ 159.38, 145.55, 145.46, 136.48, 135.91, 132.68, 131.90, 128.37, 127.53, 127.31, 127.02, 126.37, 121.96, 117.46, 112.98, 21.39; HRMS (ESI) m/z calcd. for C$_{17}$H$_{13}$N$_2$O$_2$ [M+H]$^+$ 261.10224, found 261.10224.
6,8-Dimethyl-11H-pyrido[2,1-b]quinazolin-11-one (4k): Following the general procedure with 2-Aminobenzoic acid (54.8 mg, 0.4 mmol), 3,5-dimethylpyridine (128.4 mg, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH$_2$Cl$_2$ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O$_2$. After 4 hours, the reaction mixture was diluted with 30 mL of CH$_2$Cl$_2$. Then it was washed with saturated aqueous NaHCO$_3$ (20 mL), H$_2$O (20 mL), and brine (20 mL). The organic phase was dried over Na$_2$SO$_4$, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (60.9 mg, 68% yield).$^1$H NMR (400MHz, CDCl$_3$): δ 8.61 (s, 1H), 8.43 (d, $J = 8.0$ Hz, 1H), 7.82-7.78 (m, 2H), 7.46-7.43 (m, 1H), 2.58 (s, 3H), 2.32 (s, 3H); $^{13}$C NMR (100MHz, CDCl$_3$): δ 159.28, 148.14, 146.74, 135.38, 133.78, 133.32, 127.34, 127.10, 123.40, 121.72, 121.69, 116.02, 18.41, 18.31; HRMS (ESI) m/z calcd. for C$_{14}$H$_{13}$N$_2$O $[M+H]^+$ 225.10224, found 225.10176.

8H-isoquinolinol[1,2-b]quinazolin-8-one (4l): Following the general procedure with 2-Aminobenzoic acid (60.4 mg, 0.4 mmol), isoquinoline (103.2 mg, 2.0 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O$_2$. After 4 hours, the reaction mixture was diluted with 30 mL of CH$_2$Cl$_2$. Then it was washed with saturated aqueous NaHCO$_3$ (20 mL), H$_2$O (20 mL), and brine (20 mL). The organic phase was dried over Na$_2$SO$_4$, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (59.0 mg, 60% yield).$^1$H NMR (400MHz, CDCl$_3$): δ 9.10 (d, $J = 8.0$ Hz, 1H), 8.67 (d, $J = 8.0$ Hz, 1H), 8.45 (d, $J = 8.0$ Hz, 1H), 7.90-7.87 (m, 2H), 7.75-7.66 (m, 3H), 7.54-7.51 (m, 1H), 7.05 (d, $J = 8.0$Hz, 1H); $^{13}$C NMR (100MHz, CDCl$_3$): δ 159.43, 147.49, 146.10, 134.75, 132.82, 132.12, 128.43, 127.49, 127.41, 126.40, 125.71, 121.87, 117.72, 113.12; HRMS (ESI) m/z calcd. for C$_{16}$H$_{11}$N$_2$O $[M+H]^+$ 247.08659, found 247.08607.

2,3-Dimethoxy-7-phenyl-11H-pyrido[2,1-b]quinazolin-11-one (4m): Following the general procedure with 2-Amino-4,5-dimethoxybenzoic acid (78.8, 0.4 mmol), 4-phenylpyridine (124.0 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O$_2$. After 4 hours, the reaction mixture was diluted with 30 mL of CH$_2$Cl$_2$. Then it was washed with saturated aqueous NaHCO$_3$ (20 mL), H$_2$O (20 mL), and brine (20 mL). The organic phase was dried over Na$_2$SO$_4$, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (110.2 mg, 83% yield).$^1$H NMR (400MHz, CDCl$_3$): δ 8.94 (d, $J = 8.0$ Hz, 1H), 7.73-7.67 (m, 4H), 7.54-7.46 (m, 3H), 7.17-7.14 (m, 2H), 4.04 (s, 3H), 4.04 (s, 3H); $^{13}$C NMR (100MHz, CDCl$_3$): δ 157.70, 156.28, 148.52, 147.14, 145.98, 145.16, 136.53, 129.35, 129.35, 129.33 126.81, 126.77, 126.77, 112.15, 109.70, 106.42, 105.25, 56.33, 56.33; HRMS (ESI) m/z calcd. for C$_{20}$H$_{13}$N$_2$O $[M+H]^+$ 333.12337, found 333.12259.
2,3-Dimethoxy-6,8-dimethyl-11H-pyrido[2,1-b]quinazolin-11-one (4n): Following the general procedure with 2-Amino-4,5-dimethoxybenzoic acid (78.8 mg, 0.4 mmol), 3,5-dimethylpyridine (128.4 mg, 1.2 mmol), EDCI (153.4 mg, 0.8 mmol), and CH₂Cl₂ (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (79.5 mg, 70% yield). ¹H NMR (400MHz, CDCl₃): δ 8.62 (s, 1H), 7.69 (s, 1H), 7.22 (s, 1H), 7.18 (s, 1H), 4.05 (s, 3H), 4.03 (s, 3H), 2.57 (s, 3H), 2.32 (s, 3H); ¹³C NMR (100MHz, CDCl₃): δ 158.14, 155.82, 148.38, 145.95, 145.11, 134.95, 133.24, 121.72, 121.53, 109.64, 106.85, 105.04, 56.32, 56.27, 18.38, 18.32; HRMS (ESI) m/z calcd.for C₁₆H₁₇N₂O₃ [M+H]⁺ 285.12337, found 285.12277.

2,3-Dimethoxy-8H-isouquinolino[1,2-b]quinazolin-8-one (4p): Following the general procedure with 2-Amino-4,5-dimethoxybenzoic acid (78.8 mg, 0.4 mmol), isoquinoline (103.2 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether: ethyl acetate=100:50) to afford a yellow solid (79.6 mg, 65% yield). ¹H NMR (400MHz, CDCl₃): δ 9.02 (d, J = 8.0 Hz, 1H), 8.67 (d, J = 8.0 Hz, 1H), 7.74-7.62 (m, 4H), 7.27 (s, 1H), 7.03 (d, J = 8.0 Hz, 1H), 4.08 (s, 3H), 4.04 (s, 3H); ¹³C NMR(100MHz, CDCl₃): δ 158.14, 155.82, 148.38, 145.11, 134.95, 133.24, 121.72, 121.53, 109.64, 106.85, 105.04, 56.32, 56.27, 18.38, 18.32; HRMS (ESI) m/z calcd.for C₁₈H₁₅N₂O₃ [M+H]+ 307.10772, found 307.10712.

13,13a-dihydro-13-methylisouquinolino[1,2-b]quinazolin-8-one (4s): Following the general procedure with 2-(N-methylamino)benzoic acid (60.4 mg, 0.4 mmol), isoquinoline (103.2 mg, 0.8 mmol), EDCI (153.4 mg, 0.8 mmol), and DMF (2.0 mL). The reaction mixture was stirred at room temperature under 1 atm O₂. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane: ethyl acetate=100:40) to
afford a yellow solid (67.1 mg, 64% yield). \(^{1}\)H NMR (500 MHz, CDCl\(_3\)) : δ 8.09 (d, \(J = 5.0\) Hz, 1H), 7.54 (t, \(J = 5.0\) Hz, 1H), 7.46 (d, \(J = 10.0\) Hz, 1H), 7.28-7.20 (m, 4H), 7.06 (d, \(J = 10.0\) Hz, 1H), 6.46 (s, 1H), 5.72 (d, \(J = 10.0\) Hz, 1H), 2.64 (s, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) : δ 162.09, 150.59, 134.34, 131.76, 129.36, 129.33, 127.92, 127.39, 126.84, 124.20, 123.44, 122.96, 106.09, 72.24, 36.80; HRMS (ESI) m/z calcd for C\(_{17}\)H\(_{15}\)N\(_2\)O\(_2\)[M+H]+ 263.11844, found 263.11652.

**The synthesis of substituted anthranilic Acids:**

\( \text{O} \) \( \text{O} \) \( \text{O} \)

\( \text{H} \) \( \text{N} \) \( \text{O} \)

\( \text{O} \) \( \text{O} \) \( \text{N} \) \( \text{O} \)

\( \text{O} \)

\( \text{O} \) \( \text{O} \)

\( \text{H} \) \( \text{N} \)

\( 4\text{-Aminobenzo}[d][1,3]\text{dioxole-5-carboxylic acid} \)

To a solution of 65% HNO\(_3\) (10 mL, 102 mmol) at 0°C (ice-salt bath) was added benzo[d][1,3]dioxole-5-carboxylic acid (1.0 g, 6.0 mmol). After the resulting mixture was kept at 0°C for 1 h, then the solution was generally raised to room temperature for 1 h. Ice water (50g) was added to the solution. The solid was filtered, washed by water, and dried to afford a yellow solid (1.136g, 89.7%). \(^{1}\)H NMR (500 MHz, CDCl\(_3\)): δ 7.31 (s, 2H), 6.27 (s, 2H).

To a solution of concentration HCl (10 mL, 140 mmol) at 0°C (ice-salt bath) was added 4-nitrobenzo[d][1,3]dioxole-5-carboxylic acid (1.0 g, 4.7 mmol) and SnCl\(_2\)·2H\(_2\)O (3.17, 14.1 mmol). After the resulting mixture was kept at 0°C for 4 h, then ice water (50g) was added to the solution. The solution was adjusted to pH=5 with NaOH, and concentrated under vacuum. The residue was re-dissolved in methanol (100 ml). The solid was filtered, washed by methanol. The filtrate was dried and concentrated to afford a brown solid (619 mg, 72.8%). \(^{1}\)H NMR (400 MHz, CD\(_3\)OD): δ 7.17 (s, 1H), 6.27 (s, 1H), 5.86 (s, 2H).

\( \text{O} \) \( \text{Me} \) \( \text{O} \) \( \text{B} \) \( \text{O} \)

\( \text{O} \) \( \text{O} \) \( \text{H} \) \( \text{N} \)

\( 2\text{-Amino-4-(benzyloxy)-5-methoxybenzoic acid} \)

To a solution of methyl 4-(benzyloxy)-3-methoxybenzoate (8.76 g, 32.17 mmol) in CH\(_2\)Cl\(_2\) at -20°C was added a fresh prepared mixture consisting of tin (IV) chloride (40 ml of 1M in CH\(_2\)Cl\(_2\), 40 mmol) and fuming nitric acid (2.14 ml, 51 mmol) in 10 min. The mixture was kept at -20°C for 50 min, Water (100 ml) was added to the reaction and separated. The aqueous phase was extracted by ethyl acetate (3 × 60 mL) and the combined organic phases were washed with brine and dried under sodium sulfate. Concentration under vacuum then gave a residue that was triturated with methanol to generate a product (9.72 g, 95.2%). \(^{1}\)H NMR (400 MHz, CD\(_3\)OD): δ 7.17 (s, 1H), 6.27 (s, 1H), 5.86 (s, 2H).

To a solution of methyl 4-(benzyloxy)-5-methoxy-2-nitrobenzoate (6.34 g, 19.98 mmol) in CH\(_2\)Cl\(_2\) (100 ml) and MeOH (50 ml) was added nickel (II) chloride hexahydrate (1.5 g, 6.3 mmol). Sodium borohydride (2.5 g, 66 mmol) was then added in portions to the reaction at 0-5°C in 30 min. The solvents were evaporated under vacuum and to the resulting residue was added cold 2N HCl (100 ml). The mixture was extracted with ethyl acetate (3 × 60 mL). After washing with brine and drying, the organic layer was evaporated under vacuum. Recrystallization of
the residue gave a product (5.43 g, 94.5%). A solution of methyl 2-amino-4-(benzyloxy)-5-methoxybenzoate (4.88 g, 16.98 mmol) in 2N NaOH (60 ml) and methanol (60 ml) was heated at reflux for 1 h. Methanol was removed by a rotary evaporator and the aqueous residue was acidified to pH 2 with cold concentrated HCl. Filtration and washing with water then gave the target compound (4.26 g, 91.8%).

\[ \text{\(^1\)H NMR (500MHz, DMSO-} d_{6}) \ delta 7.43-7.34 \text{ (m, 5H), 7.15 (s, 1H), 6.42 (s, 1H), 5.42 (s, 2H), 3.63 (s, 3H).} \]

**The synthesis of substituted carboline:**

![Chemical structure](image)

4,9-dihydro-6-methoxy-3H-pyrido[3,4-b]indole

A solution of 5-methoxyltryptamine (1.90 g, 10 mmol) in 10 mL ethyl formate was heated at reflux for 10 h. Evaporation under vacuum gave a product (2.18 g, 100% yield). To the cooled solution of N-formyltryptamine (0.96 g, 5 mmol) in 3 mL of CH\(_2\)Cl\(_2\) was added POCl\(_3\) (1.25 mL) drop wise at 0~5 °C. After the addition, the reaction mixture was stirred at r.t. for another 2 hrs. Then it was concentrated in vacuo to remove unconsumed POCl\(_3\) and CH\(_2\)Cl\(_2\). The dark solid residue was suspended in ethyl acetate (50 mL) and extracted with 10% AcOH/water (4 × 30 mL). The combined AcOH extracts were basified with conc. aqueous ammonia until pH 9. The precipitated solid was extracted with CH\(_2\)Cl\(_2\) (3× 30 mL) to give the product as yellow foam (793 mg, 92.8%). ESI-MS: 201.1061[M+H].

6-methoxy-9H-pyrido[3,4-b]indole

A solution of 4,9-dihydro-6-methoxy-3H-pyrido[3,4-b]indole (0.40 g, 2 mmol) and 10% palladium on carbon (100 mg) in 20 mL toluene was heated at reflux for 24 h. The reaction was cooled, filtrated through celite, washed with CH\(_2\)Cl\(_2\), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford a yellow solid (0.25 g, 64%). \(^1\)H NMR (500MHz, DMSO-\(d_6\)): \( \delta \) 11.38 (s, 1H), 8.84 (s, 1H), 8.27(d, J = 5.0 Hz, 1H), 8.07(d, J = 5.0 Hz, 1H), 7.77 (s, 1H), 7.50-7.49 (m, 1H), 7.18-7.17 (m, 1H), 3.85 (s, 3H).

**Rutacearpine (5a):** Following the general procedure with 2-Aminobenzoic acid (1.13 g, 8.23 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (1.40g, 8.23 mmol), EDCI (2.20 g, 11.5 mmol), and DMF (20 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The
residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$: MeOH=100:1) to afford a yellow solid (2.0 g, 85% yield). $^1$H NMR (400MHz, CDCl$_3$): $\delta$ 9.41 (s, 1H), 8.32 (d, $J$ = 8.0 Hz, 1H), 7.72-7.69 (m, 1H), 7.66-7.62 (m, 2H), 7.44-7.37 (m, 2H), 7.32-7.30 (m, 1H), 7.19-7.16 (m, 1H), 4.59 (t, $J$ = 8.0 Hz, 2H), 3.23 (t, $J$ = 8.0 Hz, 2H);
$^{13}$C NMR (100MHz, CDCl$_3$): $\delta$ 161.62, 147.49, 145.07, 138.35, 134.36, 127.27, 127.16, 126.57, 126.23, 125.63, 125.60, 121.18, 120.63, 120.09, 118.43, 112.12, 41.16, 19.68; HRMS (API) m/z calcd. for C$_{18}$H$_{14}$N$_3$O$_2$ [M+H]$^+$ 288.1123, found 288.1131.

Euxylophoricine D (5b): Following the general procedure with 2-Amino-4,5-dimethoxybenzoic acid (70.9 mg, 0.36 mmol), 4,9-dihydro-6-methoxy-3H-pyrido[3,4-b]indole (60.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$: MeOH=100:1) to afford a yellow solid (61.2 mg, 54% yield). $^1$H NMR (500MHz, DMSO-d$_6$): $\delta$ 11.61 (s, 1H), 7.47 (s, 1H), 7.35 (d, $J$ = 10.0 Hz, 1H), 7.10 (s, 1H), 7.05 (s, 1H), 6.89 (d, $J$ = 10.0 Hz, 1H), 4.42 (t, $J$ = 5.0 Hz, 2H), 3.92 (s, 3H), 3.88 (s, 3H), 3.79 (s, 3H), 3.13 (t, $J$ = 5.0 Hz, 2H); $^{13}$C NMR (125MHz, DMSO-d$_6$): $\delta$ 159.94, 154.56, 153.78, 148.15, 144.17, 143.39, 133.79, 127.70, 125.21, 116.55, 115.61, 113.63, 113.36, 107.06, 105.87, 100.43, 55.83, 55.78, 55.36, 40.83, 19.09; HRMS (ESI) m/z calcd. for C$_{21}$H$_{20}$N$_3$O$_4$ [M+H]$^+$ 378.14483, found 378.14331.

Hortiacine (5c): Following the general procedure with 2-Aminobenzoic acid (49.3 mg, 0.36 mmol), 4,9-dihydro-6-methoxy-3H-pyrido[3,4-b]indole (60.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$: MeOH=100:1) to afford a yellow solid (75.4 mg, 79% yield). $^1$H NMR (400MHz, CDCl$_3$): $\delta$ 9.14 (s, 1H), 8.30 (d, $J$ = 8.0 Hz, 1H), 7.72-7.65 (m, 2H), 7.42-7.31 (m, 2H), 7.01 (s, 2H), 4.58 (t, $J$ = 8.0 Hz, 2H), 3.38 (s, 3H), 3.20 (t, $J$ = 8.0 Hz, 2H); $^{13}$C NMR (125MHz, CDCl$_3$): $\delta$ 161.65, 154.68, 147.57, 144.92, 134.34, 133.50, 127.67, 127.22, 126.61, 126.14, 125.88, 121.09, 117.83, 116.72, 112.95, 100.61, 55.78, 55.12, 41.16, 19.73; HRMS (ESI) m/z calcd. for C$_{19}$H$_{16}$N$_3$O$_2$ [M+H]$^+$ 318.12370, found 318.12216.
Euxylophoricine A (5d): Following the general procedure with 2-Amino-4,5-dimethoxybenzoic acid (70.9 mg, 0.36 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (51.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$: MeOH=100:1) to afford a yellow solid (90.8 mg, 87% yield). $^1$H NMR (500MHz, DMSO-$_d_6$): $\delta$ 11.72 (s, 1H), 7.58 (s, 1H), 7.42 (d, $J$ = 10.0 Hz, 2H), 7.21 (s, 1H), 7.02 (d, $J$ = 10.0 Hz, 2H), 4.39 (s, 2H), 3.88 (s, 3H), 3.84 (s, 3H), 3.11 (s, 2H); $^{13}$C NMR (125MHz, DMSO-$_d_6$): $\delta$ 159.93, 154.57, 148.22, 144.13, 143.34, 138.54, 127.38, 125.04, 124.52, 119.88, 119.74, 116.96, 113.72, 112.53, 107.11, 105.88, 55.85, 55.79, 40.80, 19.03; HRMS (API) m/z calcd. for C$_{21}$H$_{20}$N$_3$O$_4$[M+H]$^+$ 348.1348, found 348.1343.

Euxylophoricine C (5e): Following the general procedure with 6-aminobenzo[d][1,3]dioxole-5-carboxylic acid (65.2 mg, 0.36 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (51.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$: MeOH=100:1) to afford a yellow solid (41.8 mg, 42% yield). $^1$H NMR (500MHz, DMSO-$_d_6$): $\delta$ 7.63 (d, $J$ = 8.0 Hz, 1H), 7.48 (d, $J$ = 4.0 Hz, 2H), 7.08 (d, $J$ = 4.0 Hz, 2H), 6.21 (s, 2H), 4.42 (t, $J$ = 8.0 Hz, 2H), 3.15 (t, $J$ = 4.0 Hz, 2H); $^{13}$C NMR (125MHz, DMSO-$_d_6$): $\delta$ 159.90, 153.17, 146.76, 145.07, 144.27, 138.62, 127.16, 124.98, 124.61, 119.93, 119.77, 117.27, 115.39, 112.60, 104.66, 103.28, 102.53, 40.86, 19.01; HRMS (ESI) m/z calcd. for C$_{19}$H$_{14}$N$_3$O$_3$[M+H]$^+$ 332.10297, found 332.10165.

1-Methoxyrutaecarpine (5f): Following the general procedure with 2-Amino-3-methoxybenzoic acid (60.1 mg, 0.36 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (51.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$: MeOH=100:1) to afford a yellow solid (45.8 mg, 48% yield). $^1$H NMR (400MHz, Acetone-$_d_6$+CDCl$_3$): $\delta$ 9.95 (s, 1H), 7.90 (d, $J$ = 4.0 Hz, 1H), 7.61 (d, $J$ = 4.0 Hz, 1H), 7.42-7.30 (m, 3H), 7.16 (d, $J$ = 8.0 Hz, 2H), 4.57 (t, $J$ = 8.0 Hz, 2H), 4.01 (s, 3H), 3.21 (t, $J$ = 8.0 Hz, 2H); $^{13}$C NMR (125MHz, Acetone-$_d_6$+CDCl$_3$): $\delta$ 161.40, 153.96, 144.44, 146.76, 145.07, 144.27, 138.62, 127.16, 124.61, 119.93, 119.77, 117.27, 115.39, 112.60, 104.66, 103.28, 102.53, 40.86, 19.01; HRMS (ESI) m/z calcd. for C$_{19}$H$_{16}$N$_3$O$_2$[M+H]$^+$ 318.12370, found 318.12268.
2-Methoxyrutaecarpine (5g): Following the general procedure with 2-Amino-4-methoxybenzoic acid (60.1 mg, 0.36 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (51.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$: MeOH=100:1) to afford a yellow solid (61.1 mg, 64% yield). $^1$H NMR (500MHz, DMSO-$d_6$): $\delta$ 11.85 (s, 1H), 8.09 (d, $J$ = 10.0 Hz, 1H), 7.67 (d, $J$ = 10.0 Hz, 1H), 7.51 (d, $J$ = 5.0 Hz, 2H), 3.94 (s, 5H); $^{13}$C NMR(125MHz, DMSO-$d_6$): $\delta$ 164.05, 160.27, 149.53, 145.95, 138.71, 128.39, 127.18, 124.97, 124.87, 120.08, 119.86, 118.01, 115.40, 114.27, 112.64, 107.65, 55.67, 40.68, 19.04; HRMS (ESI) m/z calcd. for C$_{19}$H$_{16}$N$_3$O$_2$ [M+H]$^+$ 318.12370, found 318.12274.

Euxylophoricine F (5h): Following the general procedure with 2-Amino-4-benzyloxy-5-methoxybenzoic acid (98.3 mg, 0.36 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (51.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in methanol (5 ml). After addition of 10% palladium on carbon (10 mg) and ammonium formate (0.3 g), the mixture was heated to reflux for 1 hour. The reaction was cooled, filtrated through celite, washed with methanol, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$: MeOH=100:1) to afford a yellow solid (31.1 mg, 31% yield). $^1$H NMR (500MHz, CDCl$_3$+CD$_3$OD): $\delta$ 7.63 (m, 2H), 7.47 (d, $J$ = 8.0 Hz, 1H), 7.34 (m, 1H), 7.17 (m, 1H), 7.05 (s, 1H), 4.56 (t, $J$ = 8.0 Hz, 2H), 4.01 (s, 3H); $^{13}$C NMR(125MHz, CDCl$_3$+CD$_3$OD): $\delta$ 161.19, 153.12, 147.81, 144.37, 143.24, 138.41, 126.55, 125.37, 125.17, 120.36, 119.84, 118.22, 113.42, 112.17, 109.70, 106.37, 56.10, 41.19, 19.55; HRMS (ESI) m/z calcd. for C$_{19}$H$_{16}$N$_3$O$_3$ [M+H]$^+$ 334.11862, found 334.11771.

3-Methoxyrutaecarpine (5i): Following the general procedure with 2-Amino-5-methoxybenzoic acid (60.1 mg, 0.36 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (51.0 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$: MeOH=100:1) to afford a yellow solid (54.4 mg, 57% yield). $^1$H NMR (400MHz, DMSO-$d_6$): $\delta$ 11.81 (s, 1H), 7.62 (d, $J$ = 8.0 Hz, 1H), 7.51 (d, $J$ = 5.0 Hz, 2H), 3.94 (s, 5H); $^{13}$C NMR(125MHz, DMSO-$d_6$): $\delta$ 155.88, 150.57, 149.53, 145.95, 138.71, 128.39, 127.18, 124.97, 124.87, 120.08, 119.86, 118.01, 115.40, 114.27, 112.64, 107.65, 55.67, 40.68, 19.04; HRMS (ESI) m/z calcd. for C$_{19}$H$_{16}$N$_3$O$_2$ [M+H]$^+$ 318.12370, found 318.12274.
2H), 7.55 (s, 1H), 7.47-7.41 (m, 2H), 7.24 (t, \(J = 4.0\) Hz, 1H), 7.07 (t, \(J = 4.0\) Hz, 1H), 4.43 (t, \(J = 8.0\) Hz, 2H), 3.88 (s, 3H), 3.16 (t, \(J = 8.0\) Hz, 2H); \(^{13}\)C NMR (125MHz, DMSO-\(d_6\)): \(\delta 164.73, 149.22, 136.92, 133.95, 131.09, 128.46, 126.42, 122.34, 120.75, 119.69, 119.37, 118.70, 117.92, 112.13, 111.96, 70.23, 41.36, 36.91, 19.95; HRMS (ESI) m/z calcd. for C\(_{19}\)H\(_{16}\)N\(_3\)O\(_2\) [M+H]+ 318.12370, found 318.12225.

Evodiamine (5j): Following the general procedure with 2-Methylaminobenzoic acid (49.2 mg, 0.33 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (51 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and CH\(_2\)Cl\(_2\) (3 ml). The reaction mixture was stirred at room temperature under air. After 4 hours, the reaction mixture was diluted with 10 mL of CH\(_2\)Cl\(_2\), filtered through a pad of silica gel, followed by washing the pad of the silica gel with the same solvent (40 mL). The filtrate was extracted three times with 30 mL of water. The organic phase was dried over Na\(_2\)SO\(_4\), filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH\(_2\)Cl\(_2\): MeOH=100:1) to afford a yellow solid (75.4 mg, 83% yield). \(^1\)H NMR (400MHz, CDCl\(_3\)): \(\delta 8.22\) (s, 1H), 8.12 (d, \(J = 8.0\) Hz, 1H), 7.60 (d, \(J = 8.0\) Hz, 1H), 7.51-7.47 (m, 1H), 7.42 (d, \(J = 8.0\) Hz, 1H), 7.28-7.13 (m, 4H), 5.92 (s, 1H), 4.89-4.85 (m, 1H), 3.33-3.26 (m, 1H), 2.98 (s, 2H), 2.50 (s, 3H); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)): \(\delta 164.73, 149.22, 136.92, 133.95, 131.10, 128.46, 126.42, 122.34, 120.75, 119.69, 119.37, 118.70, 117.92, 112.13, 111.96, 70.22, 41.36, 36.91, 19.95. HRMS (ESI) m/z calcd. for C\(_{19}\)H\(_{18}\)N\(_3\)O [M+H]+ 304.14444, found 304.14343.

7,8-Dehydrorutaecarpine (5k): Following the general procedure with 2-Amino-benzoic acid (49.3 mg, 0.36 mmol), 9H-pyrido[3,4-b]indole (50.4 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and CH\(_2\)Cl\(_2\) (3 ml). The reaction mixture was stirred at room temperature under air. After 4 hours, the reaction mixture was diluted with 10 mL of CH\(_2\)Cl\(_2\), filtered through a pad of silica gel, followed by washing the pad of the silica gel with the same solvent (40 mL). The filtrate was extracted three times with 30 mL of water. The organic phase was dried over Na\(_2\)SO\(_4\), filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH\(_2\)Cl\(_2\): MeOH=100:1) to afford a white solid (75.4 mg, 83% yield). \(^1\)H NMR (400MHz, CDCl\(_3\)): \(\delta 10.23\) (s, 1H), 8.76 (d, \(J = 8.0\) Hz, 1H), 8.51 (d, \(J = 8.0\) Hz, 1H), 8.02 (d, \(J = 8.0\) Hz, 1H), 7.81 (d, \(J = 4.0\) Hz, 2H), 7.54 (d, \(J = 8.0\) Hz, 1H), 7.49-7.46 (m, 3H), 7.35-7.31 (m, 1H); \(^{13}\)C NMR (125MHz, CDCl\(_3\)): \(\delta 159.38, 147.81, 140.33, 139.44, 134.92, 129.48, 127.78, 127.25, 126.19, 124.81, 122.57, 121.21, 120.90, 118.73, 116.57, 112.24, 107.67; HRMS (ESI) m/z calcd. for C\(_{18}\)H\(_{12}\)N\(_3\)O [M+H]+ 286.09749, found 286.09665.
Euxylophoricine B (5l): Following the general procedure with 2-Amino-4,5-dimethoxybenzoic acid (70.9 mg, 0.36 mmol), 9H-pyrido[3,4-b]indole (50.4 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$: MeOH=100:1) to afford a yellow solid (89.0 mg, 86% yield). 

$^1$H NMR(400MHz, CDCl$_3$+CD$_3$OD): $\delta$ 8.73 (d, $J = 8.0$ Hz, 1H), 8.02 (d, $J = 8.0$ Hz, 1H), 7.72 (s, 1H), 7.65 (d, $J = 8.0$ Hz, 1H), 7.59-7.50 (m, 2H), 7.36-7.31 (m, 2H), 7.11 (s, 1H), 4.07 (s, 3H), 4.04 (s, 3H); $^{13}$C NMR(100MHz, CDCl$_3$ and CD$_3$OD): $\delta$ 162.28, 160.14, 158.31, 152.19, 148.24, 143.60, 131.04, 126.10, 124.88, 124.55, 122.99, 122.13, 117.46, 116.24, 113.45, 111.69, 109.55, 109.17, 60.10. HRMS (ESI) m/z calcd.for C$_{20}$H$_{16}$N$_3$O$_3$[M+H]$^+$ 346.11862, found 346.11746.

Euxylophoricine E (5m): Following the general procedure with 2-Amino-benzoic acid (49.3 mg, 0.36 mmol), 9H-6-methoxy-pyrido[3,4-b]indole (59.4 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and CH$_2$Cl$_2$ (3 ml). The reaction mixture was stirred at room temperature under air. After 4 hours, the reaction mixture was diluted with 10 mL of CH$_2$Cl$_2$, filtered through a pad of silica gel, followed by washing the pad of the silica gel with the same solvent (40 mL). The filtrate was extracted three times with 30 mL of water. The organic phase was dried over Na$_2$SO$_4$, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$: MeOH=100:1) to afford a yellow solid (84.4 mg, 89% yield).

$^1$H NMR (400MHz, DMSO-$d_6$): $\delta$ 12.54 (s, 1H), 8.57 (d, $J = 4.0$ Hz, 1H), 8.34 (d, $J = 8.0$ Hz, 1H), 7.89 (d, $J = 8.0$ Hz, 1H), 7.81 (t, $J = 4.0$ Hz, 2H), 7.68 (s, 1H), 7.56 (d, $J = 12.0$ Hz, 1H), 7.50 (t, $J = 8.0$ Hz, 1H), 7.12 (d, $J = 12.0$ Hz, 1H), 3.86 (s, 3H); $^{13}$C NMR (125MHz, DMSO-$d_6$): $\delta$ 159.13, 154.74, 148.07, 140.65, 135.51, 135.33, 130.05, 127.55, 126.66, 124.98, 122.62, 120.11, 118.05, 117.61, 116.42, 114.10, 108.74, 102.22, 55.97; HRMS (ESI) m/z calcd.for C$_{19}$H$_{14}$N$_3$O$_2$ [M+H]$^+$ 316.10805, found 316.10706.

2-Hydroxy-3-Methoxy-7,8-Dehydrorutaecarpine (5n): Following the general procedure with 2-Amino-4-benzyloxy-5-methoxybenzoic acid (98.3 mg, 0.36 mmol), 9H-pyrido[3,4-b]indole (50.4 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3 ml). The reaction mixture was stirred at 80°C under air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in methanol (5 ml). After addition of 10% palladium on carbon (10 mg) and ammonium formate (0.3 g), the mixture was heated to reflux for 1 hour. The reaction was cooled, filtrated through celite, washed with methanol, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH$_2$Cl$_2$: MeOH=100:1) to afford a yellow solid (45.8 mg, 46% yield). 

$^1$H NMR (400MHz, DMSO-$d_6$): $\delta$ 12.55 (s, 1H), 8.58 (d, $J = 4.0$ Hz, 1H), 8.34 (d, $J = 8.0$ Hz, 1H), 7.89 (d, $J = 8.0$ Hz, 1H), 7.81 (t, $J = 4.0$ Hz, 2H), 7.68 (s, 1H), 7.56 (d, $J = 12.0$ Hz, 1H), 7.50 (t, $J = 8.0$ Hz, 1H), 7.12 (d, $J = 12.0$ Hz, 1H), 3.86 (s, 3H); $^{13}$C NMR (125MHz, DMSO-$d_6$): $\delta$ 157.92, 154.93, 148.03, 148.83, 140.21, 139.50, 129.91, 126.83, 122.39, 121.25, 120.89, 119.51, 118.07, 113.14, 109.98, 109.00, 107.94, 106.31, 56.24; HRMS
1-Methoxy-7,8-dehydrorutaecarpine (5o): Following the general procedure with 2-Amino-3-methoxybenzoic acid (60.1 mg, 0.36 mmol), 9H-pyrido[3,4-b]indole (50.4 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and CH₂Cl₂ (3 ml). The reaction mixture was stirred at room temperature under air. After 4 hours, the reaction mixture was diluted with 10 mL of CH₂Cl₂, filtered through a pad of silica gel, followed by washing the pad of the silica gel with the same solvent (40 mL). The filtrate was extracted three times with 30 mL of water. The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH₂Cl₂: MeOH=100:1) to afford a yellow solid (51.2 mg, 54% yield).

1H NMR (400MHz, DMSO-d₆): δ 12.53 (s, 1H), 8.62 (d, J = 4.0 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 4.0 Hz, 1H), 7.85 (d, J = 4.0 Hz, 1H), 7.74 (d, J = 4.0 Hz, 1H), 7.49 (t, J = 4.0 Hz, 2H), 7.29 (t, J = 4.0 Hz, 1H), 4.02 (s, 3H);

13C NMR (125MHz, DMSO-d₆): δ 158.94, 154.36, 140.46, 139.55, 139.24, 130.12, 127.08, 122.27, 121.29, 121.04, 120.25, 118.44, 118.15, 117.27, 114.69, 113.49, 108.83, 56.34; HRMS (ESI) m/z calcd for C₁₉H₁₄N₃O₃[M+H]⁺ 332.10297, found 332.10129.

3-Methoxy-7,8-dehydrorutaecarpine (5p): Following the general procedure with 2-Amino-5-methoxybenzoic acid (60.1 mg, 0.36 mmol), 9H-pyrido[3,4-b]indole (50.4 mg, 0.3 mmol), EDCI (80.5 mg, 0.42 mmol), and DMF (3.0 ml). The reaction mixture was stirred at 80°C under dry air. After 4 hours, the reaction mixture was concentrated under reduced pressure. The residue was dried with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH₂Cl₂: MeOH=100:1) to afford a yellow solid (82.2 mg, 87% yield).

1H NMR (400MHz, DMSO-d₆): δ 12.62 (s, 1H), 8.59 (d, J = 8.0 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.80-7.78 (m, 2H), 7.68-7.66 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H), 7.49-7.45 (m, 1H), 7.29-7.25 (m, 1H), 3.91 (s, 3H);

13C NMR (100MHz, DMSO-d₆): δ 158.66, 156.84, 142.96, 140.25, 139.04, 130.02, 128.55, 126.84, 126.21, 122.39, 121.20, 120.93, 119.46, 117.99, 116.95, 113.18, 108.59, 106.12, 56.10. HRMS (ESI) m/z calcd for C₁₉H₁₄N₃O₃[M+H]⁺ 316.10805, found 316.10696.

7,8,13,13b-Tetrahydro-5H-benzo[5',6'][1,3]thiazino[3',2':1,2]-pyrido[3,4-b]indol-5-one (5q): Following the general procedure with 2-Mercaptobenzoic acid (184.8 mg, 1.2 mmol), 4,9-dihydro-3H-pyrido[3,4-b]indole (170.0 mg, 1.0 mmol), EDCI (268.4 mg, 1.4 mmol), and CH₂Cl₂ (3.0 ml). The reaction mixture was stirred at room
temperature. After 4 hours, the reaction mixture was diluted with 30 mL of CH₂Cl₂. Then it was washed with saturated aqueous NaHCO₃ (20 mL), H₂O (20 mL), and brine (20 mL). The organic phase was dried over Na₂SO₄, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH₂Cl₂: MeOH=100:1) to afford a yellow solid (198.9 mg, 65% yield). ¹H NMR (400MHz, CDCl₃): δ 8.22 (d, J = 8.0 Hz, 1H), 8.10 (s, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.44-7.34 (m, 2H), 7.34 (m, 2H), 7.28-7.26 (m, 1H), 7.19-7.17 (m, 1H), 6.35 (s, 1H), 4.85-4.82 (m, 1H), 3.49-3.47 (m, 1H), 3.04 (s, 2H); ¹³C NMR (100MHz, CDCl₃): δ 164.83, 137.25, 136.07, 132.58, 131.12, 129.42, 128.25, 127.57, 126.86, 126.04, 122.70, 119.59, 118.96, 112.11, 110.57, 56.82, 40.43, 20.58. HRMS (API) m/z calcd. for C₁₈H₁₅N₂O₅ [M+H]⁺ 307.0900, found 307.0910.

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