

Supporting Information

Synthesis of Rutaecarpine Alkaloids via Electrochemical Cross Dehydrogenation Coupling Reaction

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1. General Information

Unless otherwise noted, all reagents and solvents were obtained commercially and used without further purification. Column chromatography on silica gel (300-400 mesh) was carried out using technical grade 60-90 °C petroleum ether and analytical grade EtOAc (without further purification). ¹H and ¹³C spectra were recorded on a 400 MHz, 500 MHz or 600 MHz spectrometer. Chemical shifts were reported in ppm. ¹H NMR spectra were referenced to CDCl₃ (7.26 ppm) or *d*₆-DMSO (2.50 ppm), and ¹³C NMR spectra were referenced to CDCl₃ (77.0 ppm) or *d*₆-DMSO (39.5 ppm). Peak multiplicities were designated by the following abbreviations: s, singlet; d, doublet; t, triplet; m, multiplet; brs, broad singlet and J, coupling constant in Hz. HRMS spectra were recorded with Micromass QTOF2 Quadrupole/Time-of-Flight Tandem mass spectrometer using electron spray ionization. All devices of the electrolysis were purchased according to our previous work.

2. Experimental Section

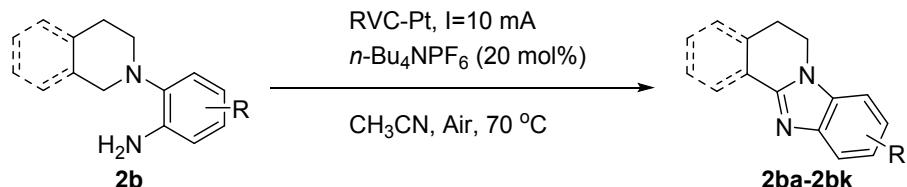
2.1 Optimization of phosphates and other electrolytes

Table S1. Optimization of reaction conditions^{a,b}

Entry	Deviation from standard condition	Yield (%) ^b
1	none	85
2	Na ₃ PO ₄ ·12H ₂ O as the electrolyte	NR
3	Na ₂ HPO ₄ ·5H ₂ O as the electrolyte	NR
4	K ₂ HPO ₄ ·3H ₂ O as the electrolyte	Trace
5	Pb Pt	60
6	RVC Pb	36

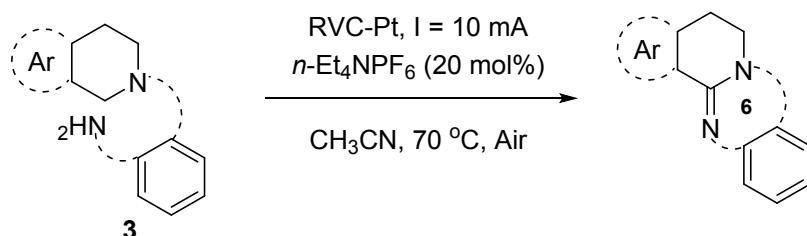
^a Reaction conditions: RVC anode (100 PPI, 1 cm × 1 cm × 1.2 cm), Pt plate cathode (1 cm × 1 cm), undivided cell, constant current = 10 mA, **2b** (0.3 mmol), *n*-Bu₄NPF₆ (20 mol%), and CH₃CN (5 mL), under air atmosphere at 70 °C for 4 h. ^b Isolated yield.

2.2 Synthesis of benzimidazole by dehydrogenation cross-coupling



2b (0.3 mmol, 1.0 equiv) and *n*-Bu₄NPF₆ (20 mol%) were placed in 10 mL three-necked round-bottomed flask. A RVC (100 PPI, 1 cm x 1 cm x 1.2 cm) anode and a platinum plate (1 cm x 1 cm) cathode, CH₃CN (5.0 mL) were added. The electrolysis was carried out at 70 °C using a constant current of 10 mA until complete consumption of the substrate (monitored by TLC). The reaction mixture was concentrated and the residue was chromatographed through silica gel eluting with ethyl acetate/petroleum ether to give the products **2ba-2bk**.

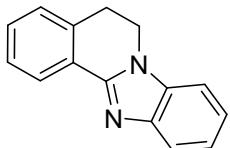
2.3 Synthesis of benzoquinolinone by dehydrogenation cross-coupling



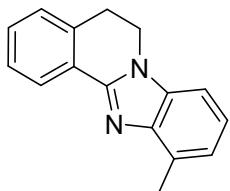
3 (0.3 mmol, 1.0 equiv) and *n*-Bu₄NPF₆ (20 mol%) were placed in 10 mL three-

necked round-bottomed flask. A RVC (100 PPI, 1 cm x 1 cm x 1.2 cm) anode and a platinum plate (1 cm x 1 cm) cathode, CH₃CN (5.0 mL) were added. The electrolysis was carried out at 70 °C using a constant current of 10 mA until complete consumption of the substrate (monitored by TLC). The reaction mixture was concentrated and the residue was chromatographed through silica gel eluting with ethyl acetate/petroleum ether to give the products.

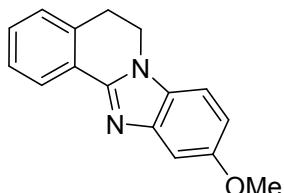
3. ^1H and ^{13}C NMR of all products



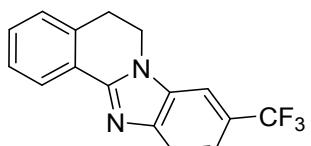
5,6-Dihydrobenzo[4,5]imidazo[2,1-*a*]isoquinoline (2ba) White solid, mp 146.5 – 147.8 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.32 – 8.27 (m, 1H), 7.85 – 7.80 (m, 1H), 7.43 – 7.37 (m, 2H), 7.36 – 7.27 (m, 4H), 4.30 (t, J = 6.8 Hz, 2H), 3.26 (t, J = 6.8 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 149.1, 143.9, 134.6, 134.2, 130.1, 128.0, 127.7, 126.6, 125.6, 122.6, 122.4, 119.7, 109.0, 40.3, 28.2. HRMS (m/z) (ESI) calculated for $\text{C}_{15}\text{H}_{13}\text{N}_2^+$ 221.1073 [M+H $^+$]; found: 221.1071.



11-Methyl-5,6-dihydrobenzo[4,5]imidazo[2,1-*a*]isoquinoline (2bb) White solid, mp 134.5 – 136.2 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.35 (d, J = 7.3 Hz, 1H), 7.44 – 7.35 (m, 2H), 7.30 (d, J = 7.0 Hz, 1H), 7.19 (d, J = 4.2 Hz, 2H), 7.11 – 7.06 (m, 1H), 4.29 (t, J = 6.8 Hz, 2H), 3.26 (t, J = 6.8 Hz, 2H), 2.75 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 148.4, 143.3, 134.3, 134.1, 129.9, 127.9, 127.6, 126.9, 125.7, 122.7, 122.5, 106.4, 40.4, 28.3, 16.8. HRMS (m/z) (ESI) calculated for $\text{C}_{16}\text{H}_{15}\text{N}_2^+$ 235.1230 [M+H $^+$]; found: 235.1206.

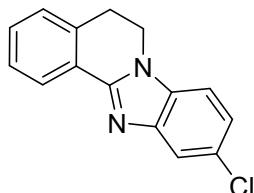


10-methoxy-5,6-dihydrobenzo[4,5]imidazo[2,1-*a*]isoquinoline (2bc) White solid, mp 155.1 – 156.9 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.29 – 8.24 (m, 1H), 7.44 – 7.36 (m, 2H), 7.34 – 7.29 (m, 2H), 7.24 (d, J = 8.8 Hz, 1H), 6.94 (dd, J = 8.7, 2.3 Hz, 1H), 4.30 (t, J = 6.9 Hz, 2H), 3.88 (s, 3H), 3.28 (t, J = 6.8 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 156.4, 149.3, 144.6, 133.9, 129.9, 129.3, 128.0, 127.7, 126.7, 125.4, 112.8, 109.4, 101.9, 55.8, 40.5, 28.2. HRMS (m/z) (ESI) calculated for $\text{C}_{16}\text{H}_{15}\text{N}_2\text{O}^+$ 251.1179 [M+H $^+$]; found: 251.1179.

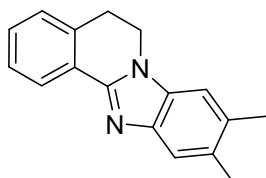


9-(Trifluoromethyl)-5,6-dihydrobenzo[4,5]imidazo[2,1-*a*]isoquinoline (2bd) White solid, mp 185.1 – 186.7 °C; ^1H NMR (400 MHz, CDCl_3)

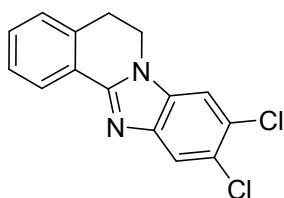
δ 8.27–8.22 (m, 1H), 7.83 (d, J = 8.5 Hz, 1H), 7.60 (s, 1H), 7.50 (dd, J = 8.5, 1.2 Hz, 1H), 7.42–7.36 (m, 2H), 7.30–7.25 (m, 1H), 4.31 (t, J = 6.9 Hz, 2H), 3.27 (t, J = 6.9 Hz, 2H). **^{13}C NMR** (100 MHz, CDCl_3) δ 151.4, 146.0, 134.4, 134.0, 130.8, 128.1, 127.7, 125.8, 125.8, 124.8 (q, J = 271.1 Hz), 124.5 (q, J = 31.8 Hz), 119.8, 119.3 (q, J = 3.6 Hz), 106.7 (q, J = 4.4 Hz), 40.5, 27.9. **HRMS** (m/z) (ESI) calculated for $\text{C}_{16}\text{H}_{12}\text{F}_3\text{N}_2^+$ 289.0947 [M+H $^+$]; found: 289.0938.



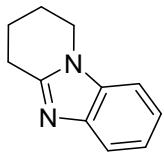
10-Chloro-5,6-dihydrobenzo[4,5]imidazo[2,1-a]isoquinoline (2be) Yellow solid, mp 176.3 – 178.1 °C; **^1H NMR** (500 MHz, CDCl_3) δ 8.25–8.20 (m, 1H), 7.68 (d, J = 10 Hz, 1H), 7.40–7.36 (m, 2H), 7.30 (d, J = 1.9 Hz, 1H), 7.29–7.26 (m, 1H), 7.21 (dd, J = 8.6, 2.0 Hz, 1H), 4.24 (t, J = 6.9 Hz, 2H), 3.25 (t, J = 6.9 Hz, 2H). **^{13}C NMR** (125 MHz, CDCl_3) δ 149.8, 142.4, 135.2, 134.1, 130.4, 128.2, 128.1, 127.7, 126.2, 125.6, 123.0, 120.4, 109.2, 40.4, 28.0. **HRMS** (m/z) (ESI) calculated for $\text{C}_{15}\text{H}_{12}\text{ClN}_2^+$ 255.0684 [M+H $^+$]; found: 255.0678.



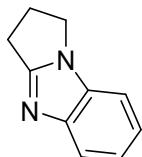
9,10-Dimethyl-5,6-dihydrobenzo[4,5]imidazo[2,1-a]isoquinoline (2bf) White solid, mp 195.9 – 198.1 °C; **^1H NMR** (500 MHz, CDCl_3) δ 8.26 (dd, J = 7.5, 1.4 Hz, 1H), 7.57 (s, 1H), 7.40–7.34 (m, 2H), 7.30–7.27 (m, 1H), 7.11 (s, 1H), 4.26 (t, J = 6.9 Hz, 2H), 3.24 (t, J = 6.8 Hz, 2H), 2.40 (s, 3H), 2.39 (s, 3H). **^{13}C NMR** (125 MHz, CDCl_3) δ 148.3, 142.5, 134.0, 133.2, 131.8, 131.2, 129.7, 127.9, 127.6, 126.9, 125.4, 119.8, 109.3, 40.3, 28.3, 20.6, 20.4. **HRMS** (m/z) (ESI) calculated for $\text{C}_{17}\text{H}_{17}\text{N}_2^+$ 249.1386 [M+H $^+$]; found: 249.1379.



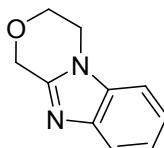
9,10-Dichloro-5,6-dihydrobenzo[4,5]imidazo[2,1-a]isoquinoline (2bg) White solid, mp 157.1 – 159.0 °C; **^1H NMR** (500 MHz, CDCl_3) δ 8.26–8.19 (m, 1H), 7.85 (s, 1H), 7.45–7.39 (m, 3H), 7.33–7.30 (m, 1H), 4.27 (t, J = 6.9 Hz, 2H), 3.29 (t, J = 6.9 Hz, 2H). **^{13}C NMR** (125 MHz, CDCl_3) δ 150.9, 143.2, 134.2, 133.9, 130.8, 128.2, 127.9, 126.5, 126.3, 125.9, 125.8, 120.7, 110.4, 40.6, 28.0. **HRMS** (m/z) (ESI) calculated for $\text{C}_{15}\text{H}_{11}\text{Cl}_2\text{N}_2^+$ 289.0294 [M+H $^+$]; found: 289.0274.



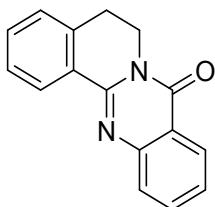
1,2,3,4-Tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (2bh) White solid, mp 62.0 – 64.6 °C; **¹H NMR** (400 MHz, CDCl₃) δ 7.61 (dd, *J* = 6.3, 2.5 Hz, 1H), 7.24 – 7.20 (m, 1H), 7.19 – 7.13 (m, 2H), 4.01 (t, *J* = 6.1 Hz, 2H), 3.02 (t, *J* = 6.4 Hz, 2H), 2.10 – 2.02 (m, 2H), 1.99 – 1.92 (m, 2H). **¹³C NMR** (100 MHz, CDCl₃) δ 151.7, 142.8, 134.6, 122.1, 121.6, 118.9, 108.7, 42.4, 25.4, 22.7, 20.8. **HRMS (m/z) (ESI)** calculated for C₁₁H₁₃N₂⁺ 173.1073 [M+H⁺]; found: 173.1068.



2,3-Dihydro-1H-benzo[d]pyrrolo[1,2-a]imidazole (2bi) White solid, mp 106.7 – 107.3 °C; **¹H NMR** (500 MHz, CDCl₃) δ 7.71 – 7.67 (m, 1H), 7.30 – 7.27 (m, 1H), 7.23 – 7.17 (m, 2H), 4.09 (t, *J* = 6.1 Hz, 2H), 3.05 (t, *J* = 6.8 Hz, 2H), 2.74 – 2.67 (m, 2H). **¹³C NMR** (125 MHz, CDCl₃) δ 161.1, 148.8, 132.3, 121.7, 121.6, 119.5, 109.4, 42.7, 26.0, 23.4. **HRMS (m/z) (ESI)** calculated for C₁₀H₁₁N₂⁺ 159.0917 [M+H⁺]; found: 159.0912.

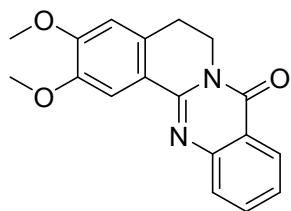


3,4-dihydro-1H-benzo[4,5]imidazo[2,1-c][1,4]oxazine (2bj) White solid, mp 73.7 – 75.6 °C; **¹H NMR** (600 MHz, CDCl₃) δ 7.75 – 7.71 (m, 1H), 7.36 – 7.32 (m, 1H), 7.31 – 7.27 (m, 2H), 5.04 (s, 2H), 4.22 – 4.19 (m, 2H), 4.19 – 4.16 (m, 2H). **¹³C NMR** (150 MHz, CDCl₃) δ 147.8, 142.6, 134.0, 122.6, 122.3, 119.5, 108.7, 65.5, 64.0, 42.0. **HRMS (m/z) (ESI)** calculated for C₁₀H₁₁N₂O⁺ 175.0866 [M+H⁺]; found: 175.0860.

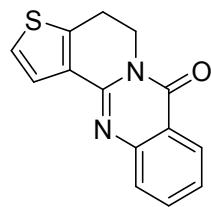


5,6-Dihydro-8H-isoquinolino[1,2-b]quinazolin-8-one (3aa) White solid, mp 193.8 – 195.0 °C; **¹H NMR** (600 MHz, CDCl₃) δ 8.49 (dd, *J* = 7.6, 1.0 Hz, 1H), 8.32 (dd, *J* = 11.1, 3.8 Hz, 1H), 7.79 – 7.73 (m, 2H), 7.50 – 7.42 (m, 3H), 7.29 (d, *J* = 7.3 Hz, 1H), 4.42 (t, *J* = 6.0 Hz, 2H), 3.10 (t, *J* = 6.5 Hz, 2H). **¹³C NMR** (150 MHz, CDCl₃) δ 161.7, 149.4, 147.8, 137.0, 134.2, 131.7, 129.5, 128.0, 127.6, 127.6, 127.5, 126.8,

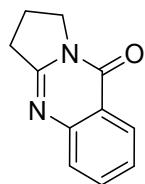
126.5, 120.7, 39.6, 27.4. **HRMS** (*m/z*) (ESI) calculated for C₁₆H₁₃N₂O⁺ 249.1022 [M+H⁺]; found: 249.1008.



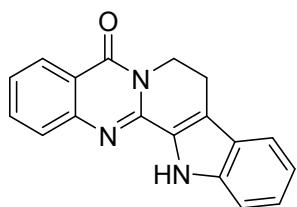
2,3-Dimethoxy-5,6-dihydro-8H-isoquinolino[1,2-*b*]quinazolin-8-one (3ab) White solid, mp 207.7 – 209.1 °C; **¹H NMR** (400 MHz, CDCl₃) δ 8.30 (d, *J* = 8.4 Hz, 1H), 7.99 (s, 1H), 7.77 – 7.71 (m, 2H), 7.45 – 7.41 (m, 1H), 6.74 (s, 1H), 4.43 – 4.38 (m, 2H), 4.04 (s, 3H), 3.97 (s, 3H), 3.04 (t, *J* = 6.5 Hz, 2H). **¹³C NMR** (100 MHz, CDCl₃) δ 161.8, 152.2, 149.5, 148.6, 147.9, 134.2, 131.0, 127.3, 126.9, 126.1, 121.8, 120.5, 110.0, 109.7, 56.2, 39.7, 29.7, 27.1. **HRMS** (*m/z*) (ESI) calculated for C₁₈H₁₇N₂O₃⁺ 309.1234 [M+H⁺]; found: 309.1240.



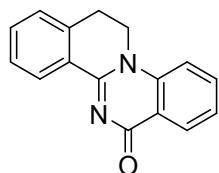
4,5-Dihydro-7H-thieno[3',2':3,4]pyrido[2,1-*b*]quinazolin-7-one (3ac) Light yellow solid, mp 184.4 – 186.0 °C; **¹H NMR** (600 MHz, CDCl₃) δ 8.28 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.75 – 7.66 (m, 3H), 7.45 – 7.40 (m, 1H), 7.23 (d, *J* = 5.2 Hz, 1H), 4.53 (t, *J* = 13.8 Hz, 2H), 3.21 (t, *J* = 13.8 Hz, 2H). **¹³C NMR** (150 MHz, CDCl₃) δ 161.7, 147.7, 146.8, 143.0, 134.2, 132.2, 127.2, 126.9, 126.3, 125.9, 124.4, 120.8, 40.6, 23.3. **HRMS** (*m/z*) (ESI) calculated for C₁₄H₁₁ON₂S⁺ 255.0587 [M+H⁺]; found: 255.0574.



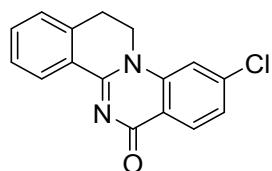
2,3-Dihdropyrrolo[2,1-*b*]quinazolin-9(1*H*)-one (3ad) White solid, mp 112.1 – 113.3 °C; **¹H NMR** (400 MHz, d₆-DMSO) δ 8.11 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.81 – 7.73 (m, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 7.47 (t, *J* = 12.0 Hz, 1H), 4.05 (t, *J* = 7.9 Hz, 2H), 3.08 (t, *J* = 7.9 Hz, 2H), 2.21 – 2.13 (m, 2H). **¹³C NMR** (100 MHz, d₆-DMSO) δ 160.4, 160.0, 149.0, 134.0, 126.6, 125.9, 125.7, 120.1, 46.3, 31.8, 18.9. **HRMS** (*m/z*) (ESI) calculated for C₁₁H₁₁N₂O⁺ 187.0866 [M+H⁺]; found: 187.0853.



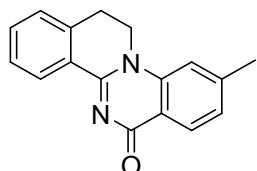
8,13-Dihydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(7*H*)-one (2ae) White solid, mp 270.9 – 273.2 °C; **¹H NMR** (400 MHz, CDCl₃) δ 9.52 (s, 1H), 8.33 (dd, J = 8.0, 1.1 Hz, 1H), 7.73 – 7.60 (m, 3H), 7.45 – 7.28 (m, 3H), 7.20 – 7.15 (m, 1H), 4.59 (t, J = 6.9 Hz, 2H), 3.24 (t, J = 6.9 Hz, 2H). **¹³C NMR** (100 MHz, CDCl₃) δ 161.6, 147.5, 145.0, 138.3, 134.4, 127.3, 127.2, 126.6, 126.2, 125.7, 125.6, 121.2, 120.6, 120.1, 118.4, 112.1, 41.2, 19.7. **HRMS (m/z)** (ESI) calculated for C₁₈H₁₄N₃O⁺ 288.1131 [M+H⁺]; found: 288.1115.



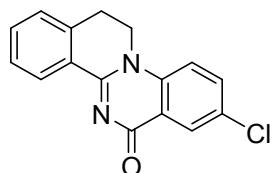
12,13-Dihydro-6H-isoquinolino[2,1-*a*]quinazolin-6-one (3ba) White solid, mp 260.3 – 261.9 °C; **¹H NMR** (400 MHz, CDCl₃) δ 8.54 (dd, J = 7.9, 0.9 Hz, 1H), 8.39 (dd, J = 7.9, 1.5 Hz, 1H), 7.75 – 7.71 (m, 1H), 7.56 – 7.36 (m, 4H), 7.27 (d, J = 2.0 Hz, 1H), 4.34 (t, J = 6.7 Hz, 2H), 3.25 (t, J = 6.7 Hz, 2H). **¹³C NMR** (100 MHz, CDCl₃) δ 169.3, 155.0, 140.7, 135.7, 133.7, 132.7, 129.6, 129.1, 128.9, 127.8, 126.9, 125.7, 120.4, 113.8, 43.2, 27.1. **HRMS (m/z)** (ESI) calculated for C₁₆H₁₃N₂O⁺ 249.1022 [M+H⁺]; found: 249.1027.



9-chloro-12,13-dihydro-6H-isoquinolino[2,1-*a*]quinazolin-6-one (3ca) Light yellow solid, mp 223.3 – 225.4 °C; **¹H NMR** (400 MHz, CDCl₃) δ 8.48 (t, J = 7.6 Hz, 2H), 7.79 (s, 1H), 7.66 (d, J = 7.9 Hz, 1H), 7.52 (t, J = 7.0 Hz, 1H), 7.39 (t, J = 7.2 Hz, 1H), 7.31 (d, J = 7.1 Hz, 1H), 4.39 (t, J = 6.1 Hz, 2H), 3.32 (d, J = 5.8 Hz, 2H). **¹³C NMR** (100 MHz, CDCl₃) δ 168.2, 156.0, 140.8, 135.8, 133.2, 130.1, 129.8, 128.6, 127.9, 127.1, 122.4, 122.1, 122.0, 111.5, 43.6, 27.0. **HRMS (m/z)** (ESI) calculated for C₁₆H₁₂ClN₂O⁺ 283.0633 [M+H⁺]; found: 283.0645.



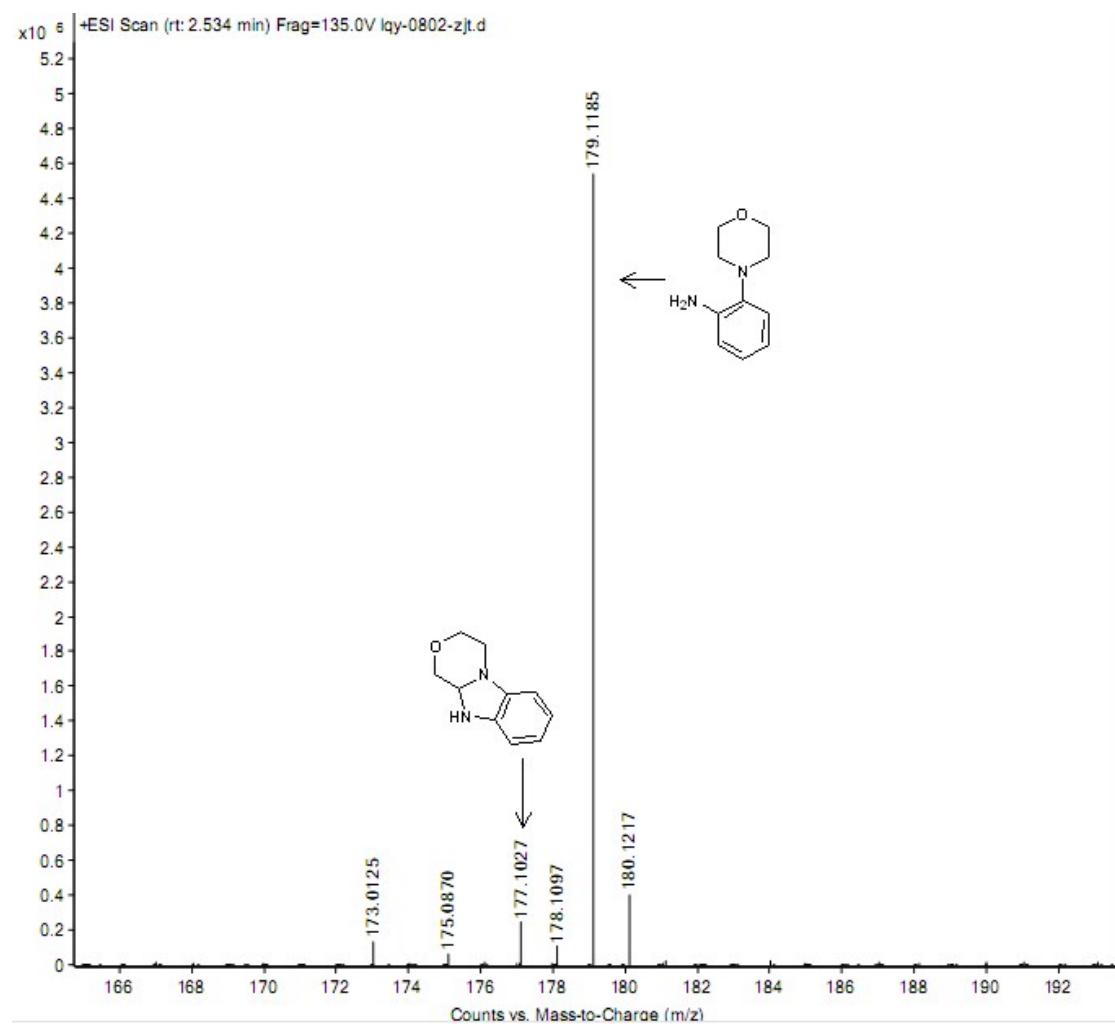
9-Methyl-12,13-dihydro-6*H*-isoquinolino[2,1-*a*]quinazolin-6-one (3da) White solid, mp 261.4 – 263.0 °C; **¹H NMR** (400 MHz, CDCl₃) δ 8.51 (d, *J* = 7.8 Hz, 1H), 8.24 (d, *J* = 8.1 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.36 (t, *J* = 16.0 Hz, 1H), 7.29 (d, *J* = 20.0 Hz, 2H), 7.24 (t, *J* = 20.0 Hz, 1H), 4.32 (t, *J* = 6.7 Hz, 2H), 3.24 (t, *J* = 6.7 Hz, 2H), 2.51 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ 169.3, 154.8, 144.7, 140.7, 135.7, 132.5, 129.4, 129.1, 128.6, 127.6, 127.1, 126.9, 118.1, 113.9, 43.1, 27.0, 22.3. **HRMS** (*m/z*) (ESI) calculated for C₁₇H₁₅N₂O⁺ 263.1179 [M+H⁺]; found: 263.1170.



8-Chloro-12,13-dihydro-6*H*-isoquinolino[2,1-*a*]quinazolin-6-one (3ea) White solid, mp 221.6 – 223.0 °C; **¹H NMR** (400 MHz, CDCl₃) δ 8.53 (d, *J* = 7.8 Hz, 1H), 8.37 (d, *J* = 7.9 Hz, 1H), 7.76 – 7.69 (m, 1H), 7.53 (d, *J* = 8.6 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.27 (d, *J* = 2.0 Hz, 1H), 4.34 (t, *J* = 6.7 Hz, 2H), 3.26 (t, *J* = 6.6 Hz, 2H). **¹³C NMR** (100 MHz, CDCl₃) δ 140.7, 135.7, 133.7, 132.7, 129.6, 129.0, 128.9, 128.2, 127.8, 126.9, 125.8, 120.4, 113.8, 43.2, 27.1. **HRMS** (*m/z*) (ESI) calculated for C₁₆H₁₂ClN₂O⁺ 283.0633 [M+H⁺]; found: 283.0651.

4. ESI-HRMS analysis for the 2bj-1

HRMS (m/z) (ESI): calculated for $C_{10}H_{13}N_2O^+$ 177.1022 [M+H] $^+$; found: 177.1027.



5. Copies of ^{13}C and ^1H NMR spectra for all products

