Supporting Information for:

CuI-Catalyzed Domino Reactions for the Synthesis of Benzoxazine-Fused Isoquinolines under Microwave Irradiation

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General: Analytical TLC was carried out on precoated silica gel plates. Column chromatography was conducted with 300–400 mesh silica gel. NMR spectra were recorded at 500 MHz for ¹H NMR using SiMe₄ as an internal standard in CDCl₃ and 125 MHz for ¹³C NMR. Infrared (IR) data were recorded using a Nicolet Av360 instrument. Microwave irradiation was performed by single mode microwave synthesis system (CEM Discover). *o*-Alkynyl aldehydes were prepared according to the reported procedures.^[1] Unless otherwise stated, all chemicals were purchased as the highest purity commercially available and were used without further purification.

Typical procedure: To a solution of *o*-alkynyl aldehydes **1a** (103 mg, 0.5 mmol) in ethanol (3 mL) was added **2a** (92 mg, 0.75 mmol) and CuI (9.5 mg, 0.05 mmol), the mixture was stirred under microwave irradiation at 70 °C until all starting material has been consumed. The solvent was removed under reduced pressure. The residue was purified by silica gel flash column chromatography to afford product **3a**.

*12-Phenyl-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-*a*]-isoquinoline (3a)*,^[2] pale yellow solid. ¹H NMR (500 MHz, CDCl₃) δ 7.42 (d, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.23-7.17 (m, 7H), 7.05 (d, *J* = 7.5 Hz, 1H), 6.92 (t, *J* = 7.5 Hz, 1H), 6.78 (t, *J* = 7.5 Hz, 1H), 6.22 (d, *J* = 8.0 Hz, 1H), 6.09 (s, 1H), 5.96 (s, 1H), 5.26 (d, *J* = 14.5 Hz, 1H), 5.09 (d, *J* = 14.5 Hz, 1H). ¹³C NMR

(125 MHz, CDCl₃) δ 140.8, 139.9, 136.9, 132.4, 129.0, 128.6, 128.5, 128.0, 127.9, 126.8, 126.0, 125.8, 124.7, 124.3, 123.8, 122.5, 105.7, 85.0, 68.0.

3-Methyl-12-phenyl-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-a]-isoquinoline (3b), pale yellow solid (**3b**), m.p. 122~123 °C; IR (KBr) cm⁻¹ 3030, 2853, 1604, 1504, 1487, 1446, 1384, 1286, 1099, 819, 747. ¹H NMR (500 MHz, CDCl₃) δ 7.25 – 7.21 (m, 6H), 7.13 (d, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 7.5 Hz, 1H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.77 (t, *J* = 7.5 Hz, 1H), 6.21 (d, *J* = 8.0 Hz, 1H), 6.05 (s, 1H), 5.96 (s, 1H), 5.24 (d, *J* = 14.5 Hz, 1H), 5.08 (d, *J* = 14.5 Hz, 1H), 2.36 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 139.9, 137.0, 135.9, 129.8, 129.7, 128.5, 128.3, 128.0, 127.7, 127.0, 125.8, 124.7, 124.3, 123.6, 122.3, 106.0, 85.1, 67.9, 21.3. HRMS calcd for C₂₃H₂₁NO[M+H]⁺ 326.1545, found 326.1539.

3-Chloro-12-phenyl-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-a]-isoquinoline (3c), pale yellow solid, m.p. 137~138 °C; IR (KBr) cm⁻¹ 3037, 2856, 1602, 1552, 1446, 1383, 1286, 1196, 777, 759, 747. ¹H NMR (500 MHz, CDCl₃) δ 7.39 (s, 1H), 7.25 (m, 6H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 7.5 Hz, 1H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.78 (t, *J* = 7.5 Hz, 1H), 6.20 (d, *J* = 8.0 Hz, 1H), 6.01 (s, 1H), 5.95 (s, 1H), 5.20 (d, *J* = 14.5 Hz, 1H), 5.06 (d, *J* = 14.5 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃) δ 141.0, 139.3, 136.6, 131.1, 131.0, 129.1, 128.5, 128.4, 128.1, 128.1, 128.0, 126.6, 126.0, 125.5, 124.8, 123.4, 122.5, 105.3, 84.5, 67.9. HRMS calcd for C₂₂H₁₇ClNO[M+H]⁺ 346.0999, found 346.0993.

3-Nitro-12-phenyl-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-a]-isoquinoline (3d), pale yellow solid, m.p. 165~166 °C; IR (KBr) cm⁻¹ 3032, 2834, 1607, 1566, 1492, 1317, 1274, 1190, 1033, 888, 750. ¹H NMR (500 MHz, CDCl₃) δ 8.29 (s, 1H), 8.20 – 8.11 (m, 1H), 7.32 – 7.20 (m, 6H), 7.08 (d, *J* = 7.5 Hz, 1H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.82 (t, *J* = 7.5 Hz, 1H), 6.25 (d, *J* = 8.0 Hz, 1H), 6.09 (s, 1H), 5.94 (s, 1H), 5.28 (d, *J* = 14.5 Hz, 1H), 5.12 (d, *J* = 14.5 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃) δ 145.2, 145.0, 138.8, 136.0, 128.7, 128.5, 128.2, 126.1, 126.0, 125.0, 124.4, 124.3, 124.1, 123.7, 123.4, 103.5, 84.2, 68.3. HRMS calcd for C₂₂H₁₇N₂O₃[M+H]⁺ 357.1239, found 357.1234.

12-(4-Methylphenyl)-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-a]-isoquinoline (3e), pale yellow solid, m.p. 150~151 °C; IR (KBr) cm⁻¹ 3026, 2853, 1601, 1479, 1380, 1279, 1134, 1094, 807, 746, 708. ¹H NMR (500 MHz, CDCl₃) δ 7.43 – 7.38 (m, 1H), 7.32–7.7.29 (m, 1H), 7.23 – 7.15

(m, 2H), 7.11 (d, $J = 4.0$ Hz, 2H), 7.03 (d, $J = 4.0$ Hz, 3H), 6.90 (dd, $J = 8.5, 5.5$ Hz, 1H), 6.80 (d, $J = 7.5$ Hz, 1H), 6.33 - 6.16 (m, 1H), 6.06 (s, 1H), 5.94 (s, 1H), 5.23 (d, $J = 14.5$ Hz, 1H), 5.07 (d, $J = 14.5$ Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 140.8, 139.9, 137.7, 134.0, 132.5, 129.0, 128.7, 128.5, 128.4, 126.9, 126.7, 125.94, 125.8, 124.7, 124.3, 123.8, 122.4, 105.5, 85.0, 68.0, 21.3. HRMS calcd for $\text{C}_{23}\text{H}_{21}\text{NO}[\text{M}+\text{H}]^+$ 326.1545, found 326.1539.

12-(4-chlorophenyl)-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-a]-isoquinoline (3f), pale yellow solid, m.p. 132~133 °C; IR (KBr) cm^{-1} 3035, 2850, 1606, 1480, 1379, 1285, 1131, 1087, 1011, 814, 738. ^1H NMR (500 MHz, CDCl_3) δ 7.40 (d, $J = 7.5$ Hz, 1H), 7.31 (t, $J = 7.5$ Hz, 1H), 7.25 - 7.12 (m, 6H), 7.04 (d, $J = 7.5$ Hz, 1H), 6.93 (t, $J = 7.5$ Hz, 1H), 6.82 (t, $J = 7.5$ Hz, 1H), 6.20 (d, $J = 8.0$ Hz, 1H), 6.05 (s, 1H), 5.93 (s, 1H), 5.23 (d, $J = 14.5$ Hz, 1H), 5.07 (d, $J = 14.5$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 137.8, 133.7, 132.0, 130.4, 128.1, 127.3, 126.7, 126.5, 125.2, 125.1, 124.5, 124.3, 123.1, 122.7, 121.9, 121.0, 104.4, 83.2, 66.3. HRMS calcd for $\text{C}_{22}\text{H}_{17}\text{ClNO}[\text{M}+\text{H}]^+$ 346.0999, found 346.0993.

3-Methyl-12-(4-Methylphenyl)-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-a]-isoquinoline (3g): pale yellow solid, m.p. 140~141 °C; IR (KBr) cm^{-1} 3021, 2965, 2851, 1064, 1485, 1387, 1290, 1132, 1103, 822, 751. ^1H NMR (500 MHz, CDCl_3) δ 7.22 (s, 1H), 7.12 - 7.00 (m, 7H), 6.88 (t, $J = 7.5$ Hz, 1H), 6.78 (t, $J = 7.5$ Hz, 1H), 6.23 (d, $J = 8.0$ Hz, 1H), 6.03 (s, 1H), 5.94 (s, 1H), 5.21 (d, $J = 14.5$ Hz, 1H), 5.06 (d, $J = 14.5$ Hz, 1H), 2.35 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 140.0, 139.9, 137.6, 135.8, 134.1, 129.9, 129.8, 128.7, 128.4, 128.2, 127.1, 126.9, 125.9, 124.6, 124.3, 123.6, 122.2, 105.8, 85.2, 67.9, 21.4, 21.3. HRMS calcd for $\text{C}_{24}\text{H}_{22}\text{NO}[\text{M}+\text{H}]^+$ 340.1701, found 340.1696.

12-(4-chlorophenyl)-3-Methyl-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-a]-isoquinoline (3h): pale yellow solid, m.p. 160~161 °C; IR (KBr) cm^{-1} 3023, 2973, 2849, 1604, 1487, 1385, 1288, 1087, 1012, 826, 756. ^1H NMR (500 MHz, CDCl_3) δ 7.22 (s, 1H), 7.19 (d, $J = 8.5$ Hz, 2H), 7.13 (d, $J = 8.5$ Hz, 3H), 7.07 (d, $J = 7.5$ Hz, 1H), 7.05 - 7.02 (m, 1H), 6.91 (t, $J = 7.5$ Hz, 1H), 6.81 (t, $J = 8.0$ Hz, 1H), 6.19 (d, $J = 8.0$ Hz, 1H), 6.02 (s, 1H), 5.93 (s, 1H), 5.21 (d, $J = 14.5$ Hz, 1H), 5.06 (d, $J = 14.5$ Hz, 1H), 2.35 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 139.6, 138.7, 136.2, 135.5, 133.6, 129.9, 129.8, 129.4, 128.3, 128.2, 127.1, 126.0, 124.8, 124.4, 123.5, 122.5, 106.5, 85.1, 67.9, 21.4. HRMS calcd for $\text{C}_{23}\text{H}_{19}\text{ClNO}[\text{M}+\text{H}]^+$ 360.1155, found 360.1150.

3-Chloro-12-(4-Methylphenyl)-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-a]-isoquinoline (3i), pale yellow solid, m.p. 135~136 °C; IR (KBr) cm^{-1} 3037, 2909, 2854, 1602, 1490, 1385, 1281, 1135, 1106, 826, 746. ^1H NMR (500 MHz, CDCl_3) δ 7.38 (s, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.13 – 7.02 (m, 6H), 6.90 (t, J = 7.5 Hz, 1H), 6.80 (t, J = 7.5 Hz, 1H), 6.22 (d, J = 8.0 Hz, 1H), 5.99 (s, 1H), 5.94 (s, 1H), 5.18 (d, J = 14.5 Hz, 1H), 5.05 (d, J = 14.5 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 141.0, 139.4, 138.0, 133.6, 131.1, 131.0, 129.0, 128.8, 128.6, 128.3, 128.1, 126.4, 126.1, 125.4, 124.7, 123.4, 122.4, 105.1, 84.5, 67.9, 21.3. HRMS calcd for $\text{C}_{23}\text{H}_{19}\text{ClNO}[\text{M}+\text{H}]^+$ 360.1155, found 360.1150.

3-Chloro-12-(4-chlorophenyl)-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-a]-isoquinoline (3j), pale yellow solid, m.p. 140~141 °C; IR (KBr) cm^{-1} 3038, 2841, 1609, 1489, 1413, 1382, 1285, 1087, 1008, 825, 754. ^1H NMR (500 MHz, CDCl_3) δ 7.38 (d, J = 1.5 Hz, 1H), 7.26 (dd, J = 8.0, 1.5 Hz, 1H), 7.21 (d, J = 8.5 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.0 Hz, 1H), 7.05 (d, J = 7.5 Hz, 1H), 6.93 (t, J = 7.5 Hz, 1H), 6.83 (t, J = 7.5 Hz, 1H), 6.18 (d, J = 8.0 Hz, 1H), 5.98 (s, 1H), 5.93 (s, 1H), 5.18 (d, J = 14.5 Hz, 1H), 5.06 (d, J = 14.5 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 138.1, 137.3, 133.3, 132.3, 129.7, 129.0, 127.9, 127.4, 126.8, 126.6, 126.5, 124.8, 124.5, 123.9, 123.2, 121.6, 121.0, 104.0, 82.7, 66.2. HRMS calcd for $\text{C}_{22}\text{H}_{16}\text{Cl}_2\text{NO}[\text{M}+\text{H}]^+$ 380.0609, found 380.0604.

6-Phenyl-benzo[4,5]imidazo[2,1-a]isoquinoline (3k),^[3] ^1H NMR (500 MHz, CDCl_3) δ 8.89 (m, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.71 – 7.58 (m, 8H), 7.38 (t, J = 7.5 Hz, 1H), 7.00 (m, 1H), 6.89 (s, 1H), 6.48 (d, J = 8.5 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 148.3, 144.2, 137.5, 134.6, 131.5, 130.7, 130.1, 129.9, 129.4, 129.0, 127.9, 126.6, 125.1, 124.2, 122.9, 121.2, 119.7, 114.1, 112.5.

Reference

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Copies of ^1H and ^{13}C NMR spectra for all compounds