SUPPORTING INFORMATION

Synthesis of 3-Substituted 4-Aroylisoquinolines via Pd-Catalyzed Carbonylative Cyclization of 2-(1-Alkynyl)benzaldimines

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Preparation of Starting Materials

2-(1-Alkynyl)benzaldimines **1**, **23**, **25**, **34** and **37** have been reported previously.^{1,2}
The following new 2-(1-alkynyl)benzaldimines were prepared using our previously reported procedure.¹

***N*-tert-Butyl-2-(5-cyano-1-pentynyl)benzalimine (27).** A yellow oil: ¹H NMR (CDCl₃) δ 1.32 (s, 9H), 2.00 (quintet, *J* = 6.8 Hz, 2H), 2.59 (t, *J* = 6.8 Hz, 2H), 2.68 (t, *J* = 6.8 Hz, 2H), 7.31-7.34 (m, 2H), 7.40-7.43 (m, 1H), 8.01-8.03 (m, 1H), 8.75 (s, 1H); ¹³C NMR (CDCl₃) δ 16.49, 18.88, 24.90, 29.93, 57.91, 79.97, 92.62, 119.12, 123.96, 126.16, 128.58, 129.88, 132.65, 137.97, 154.08; IR (CHCl₃) 3031, 2963, 2312, 2200, 1699 cm⁻¹; HRMS 252.1262 (calcd C₁₇H₂₀N₂ 252.1259).

***N*-tert-Butyl-2-(3-methoxy-1-propynyl)benzalimine (29).** A yellow oil: ¹H NMR (CDCl₃) δ 1.31 (s, 9H), 3.48 (s, 3H), 4.39 (s, 2H), 7.31-7.37 (m, 2H), 7.46-7.48 (m, 1H), 8.03-8.05 (m, 1H), 8.79 (s, 1H); ¹³C NMR (CDCl₃) δ 29.93, 57.85, 57.96, 60.62, 83.97,

90.59, 123.42, 126.15, 128.98, 129.86, 132.73, 138.16, 154.12; IR (CHCl₃) 3027, 2983, 2200, 1695 cm⁻¹; HRMS 229.1145 (calcd C₁₅H₁₉NO, 229.1142).

N-tert-Butyl-6-(phenylethynyl)piperonaldimine (31). A white solid: mp 88-90 °C; ¹H NMR (CDCl₃) δ 1.32 (s, 9H), 6.01 (s, 2H), 6.96 (s, 1H), 7.35-7.38 (m, 3H), 7.49-7.52 (m, 2H), 7.56 (s, 1H), 8.84 (s, 1H); ¹³C NMR (CDCl₃) δ 30.04, 57.77, 86.93, 93.85, 101.89, 105.93, 111.29, 118.57, 123.37, 128.58, 128.68, 131.54, 134.05, 148.82, 149.22, 153.70; IR (CHCl₃) 3018, 2970, 2200, 1695 cm⁻¹; HRMS 305.1420 (calcd C₂₀H₁₉NO₂, 305.1416).

3-Substituted 4-Aroylisoquinolines Prepared. For the preparation and characterization of compounds **2**, **5**, **6**, **10**, **15**, **18**, **19**, **24** and **26**, see the Supporting Information in reference 1.

4-(4-Methylbenzoyl)-3-phenylisoquinoline (7). The reaction mixture was chromatographed using 4:1 hexanes/EtOAc to yield a yellow solid: mp 120-121 °C (hexanes); ¹H NMR (CDCl₃) δ 2.30 (s, 3H), 7.07 (d, *J* = 8.0 Hz, 2H), 7.21-7.29 (m, 3H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.63-7.68 (m, 4H), 7.72 (d, *J* = 7.2 Hz, 1H), 8.07-8.09 (m, 1H), 9.45 (s, 1H); ¹³C NMR (CDCl₃) δ 21.86, 124.76, 127.09, 127.72, 128.09, 128.43, 128.55, 129.08, 129.45, 129.67, 129.92, 131.57, 134.33, 135.17, 139.82, 144.87, 149.82, 153.43, 197.76; IR (CHCl₃) 3018, 1658 cm⁻¹; HRMS 323.1315 (calcd for C₂₃H₁₇NO 323.1310).

4-(3-Methylbenzoyl)-3-phenylisoquinoline (8). The reaction mixture was chromatographed using 4:1 hexanes/EtOAc to yield a yellow solid: mp 124-125 °C (hexanes); ¹H NMR (CDCl₃) δ 2.26 (s, 3H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.20-7.30 (m, 4H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.54 (s, 1H), 7.61-7.63 (m, 2H), 7.65-7.70 (m, 2H), 7.73-7.75

(m, 1H), 8.09-8.11 (m, 1H), 9.47 (s, 1H); ^{13}C NMR (CDCl_3) δ 21.38, 124.80, 127.16, 127.33, 127.81, 128.19, 128.48, 128.58, 128.62, 129.11, 129.72, 130.08, 131.71, 134.40, 134.71, 137.58, 138.52, 139.83, 150.05, 153.56, 198.38; IR (CHCl_3) 3019, 1659 cm^{-1} ; HRMS 323.1315 (calcd for $\text{C}_{23}\text{H}_{17}\text{NO}$ 323.1310).

4-(2-Methylbenzoyl)-3-phenylisoquinoline (9). The reaction mixture was chromatographed using 4:1 hexanes/EtOAc to yield a yellow solid: mp 99-100 $^{\circ}\text{C}$ (hexanes); ^1H NMR (CDCl_3) δ 2.58 (s, 3H), 6.90 (t, $J = 5.7$ Hz, 1H), 7.06 (d, $J = 5.7$ Hz, 1H), 7.10 (d, $J = 5.7$ Hz, 1H), 7.18-7.28 (m, 4H), 7.51-7.53 (m, 2H), 7.67 (td, $J = 6.0, 0.9$ Hz, 1H), 7.73 (td, $J = 6.0, 0.9$ Hz, 1H), 7.92 (d, $J = 6.0$ Hz, 1H), 8.10 (d, $J = 8.0$ Hz, 1H), 9.44 (s, 1H); ^{13}C NMR (CDCl_3) δ 21.84, 124.77, 125.58, 127.26, 127.81, 128.19, 128.31, 128.53, 129.55, 130.59, 131.84, 131.87, 132.08, 132.52, 134.51, 137.47, 140.15, 140.37, 150.67, 153.54, 199.84; IR (CHCl_3) 3019, 1659 cm^{-1} ; HRMS 323.1315 (calcd for $\text{C}_{23}\text{H}_{17}\text{NO}$ 323.1310).

4-(1-Naphthoyl)-3-phenylisoquinoline (11). The reaction mixture was chromatographed using 3:1 hexanes/EtOAc to yield a yellow solid: mp 160-161 $^{\circ}\text{C}$ (hexanes); ^1H NMR (CDCl_3) δ 7.01 (t, $J = 7.6$ Hz, 1H), 7.08-7.16 (m, 3H), 7.35 (d, $J = 7.2$ Hz, 1H), 7.53-7.60 (m, 3H), 7.67-7.74 (m, 3H), 7.80 (d, $J = 8.4$ Hz, 1H), 7.85 (d, $J = 8.0$ Hz, 1H), 7.87 (d, $J = 8.0$ Hz, 1H), 8.12 (d, $J = 8.0$ Hz, 1H), 9.12 (d, $J = 8.4$ Hz, 1H), 9.48 (s, 1H); ^{13}C NMR (CDCl_3) δ 124.21, 124.82, 126.22, 126.74, 127.24, 127.83, 128.16, 128.27, 128.31, 128.54, 128.75, 129.53, 130.80, 131.10, 131.96, 132.42, 133.90, 134.50, 134.80, 135.00, 139.98, 150.89, 153.66, 199.79; IR (CHCl_3) 3019, 1657, 1216 cm^{-1} ; HRMS 359.1315 (calcd $\text{C}_{26}\text{H}_{17}\text{NO}$, 359.1310).

3-Phenyl-4-(2-thienylcarbonyl)isoquinoline (12). The reaction mixture was chromatographed using 4:1 hexanes/EtOAc to yield a yellow solid: mp 117-118 °C (hexanes); ^1H NMR (CDCl_3) δ 6.84 (dd, $J = 5.2, 3.6$ Hz, 1H), 7.11 (dd, $J = 3.6, 1.2$ Hz, 1H), 7.24-7.28 (m, 1H), 7.30-7.34 (m, 2H), 7.55 (dd, $J = 5.2, 1.2$ Hz, 1H), 7.65 (td, $J = 8.0, 1.2$ Hz, 1H), 7.71-7.73 (m, 3H), 7.87 (d, $J = 8.0$ Hz, 1H), 8.08 (d, $J = 8.0$ Hz, 1H), 9.45 (s, 1H); ^{13}C NMR (CDCl_3) δ 124.62, 129.09, 127.86, 128.10, 128.30, 128.57, 128.71, 128.74, 129.67, 131.80, 134.08, 135.42, 135.61, 139.83, 145.09, 149.89, 153.78, 190.03; IR (CHCl_3) 3019, 1640, 1216 cm^{-1} ; HRMS 315.0723 (calcd $\text{C}_{20}\text{H}_{13}\text{NOS}$ 315.0718).

3-Phenyl-4-(3-thienylcarbonyl)isoquinoline (13). The reaction mixture was chromatographed using 4:1 hexanes/EtOAc to yield a yellow solid: mp 153-154 °C (hexanes); ^1H NMR (CDCl_3) δ 7.16 (dd, $J = 5.4, 3.0$ Hz, 1H), 7.24-7.35 (m, 3H), 7.41 (dd, $J = 5.1, 1.2$ Hz, 1H), 7.57 (dd, $J = 3.0, 1.2$ Hz, 1H), 7.64-7.70 (m, 4H), 7.73 (dd, $J = 6.9, 1.5$ Hz, 1H), 7.84 (d, $J = 7.8$ Hz, 1H), 8.08-8.11 (m, 1H), 9.45 (s, 1H); ^{13}C NMR (CDCl_3) δ 124.71, 126.69, 127.18, 127.42, 127.87, 128.16, 128.60, 128.74, 129.56, 129.71, 131.79, 134.08, 135.62, 139.88, 143.19, 149.84, 153.67, 191.63; IR (CHCl_3) 3019, 1641, 1216 cm^{-1} ; HRMS 315.0723 (calcd $\text{C}_{20}\text{H}_{13}\text{NOS}$ 315.0718).

4-(4-Bromobenzoyl)-3-phenylisoquinoline (14). The reaction mixture was chromatographed using 3:1 hexanes/EtOAc to yield a yellow solid: mp 139-140 °C (hexanes); ^1H NMR (CDCl_3) δ 7.25-7.32 (m, 3H), 7.41 (d, $J = 8.8$ Hz, 2H), 7.52 (d, $J = 8.4$ Hz, 2H), 7.61 (d, $J = 6.4$ Hz, 2H), 7.66-7.53 (m, 3H), 8.12 (d, $J = 7.2$ Hz, 1H), 9.48 (s, 1H); ^{13}C NMR (CDCl_3) δ 124.52, 127.18, 127.97, 128.28, 128.30, 128.63, 128.90,

129.20, 129.75, 131.14, 131.93, 132.07, 134.24, 136.36, 139.64, 150.24, 153.89, 197.22; IR (CHCl₃) 3019, 1658, 1216 cm⁻¹; HRMS 387.0266 (calcd C₂₂H₁₄BrNO 387.0259).

3-Phenyl-4-(3-trifluoromethylbenzoyl)isoquinoline (17). The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to yield a yellow solid: mp 130-131 °C; ¹H NMR (CDCl₃) δ 7.20-7.28 (m, 3H), 7.37 (t, *J* = 8.0 Hz, 1H), 7.55-7.58 (m, 2H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.69-7.78 (m, 3H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.90 (s, 1H), 8.15 (dd, *J* = 3.2, 1.2 Hz, 1H), 9.51 (s, 1H); ¹³C NMR (CDCl₃) δ 127.23 (q, *J* = 273.1, 1C, including 121.804, 125.421, 129.034), 124.39, 126.33 (q, *J* = 3.9 Hz, 1C, including 126.26, 126.31, 126.36, 126.41), 127.26, 127.79, 128.07, 128.41, 128.62, 128.96, 129.25, 129.82, 129.90 (q, *J* = 3.6 Hz, 1C, including 129.881, 129.928, 129.975), 131.16 (q, *J* = 33.1 Hz, 1C, including 130.50, 130.94, 131.38, 131.81), 132.12, 132.71-132.73 (m, 1C, including 132.71, 132.73), 134.22, 138.04, 139.64, 150.78, 154.25, 196.80; IR (CHCl₃) 3019, 1671, 1323, 1216 cm⁻¹; HRMS *m/z* 377.1031 (calcd for C₂₃H₁₄F₃NO, 377.1028).

4-(3-Nitrobenzoyl)-3-phenylisoquinoline (21). The reaction mixture was chromatographed using 2:1 hexanes/ethyl acetate to yield a yellow solid: mp 128-129 °C; ¹H NMR (CDCl₃) δ 7.18-7.27 (m, 3H), 7.43 (t, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 2H), 7.70-7.79 (m, 2H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 7.6 Hz, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 8.22 (dt, *J* = 8.0, 1.2 Hz, 1H), 8.40 (s, 1H), 9.54 (s, 1H); ¹³C NMR (CDCl₃) δ 124.19, 124.26, 127.30, 127.31, 127.69, 128.28, 128.55, 128.73, 129.15, 129.80, 129.87, 132.34, 134.14, 134.87, 138.83, 139.51, 148.27, 150.89, 154.53, 195.86; IR (CHCl₃) 3021, 1667, 1619, 1534 cm⁻¹; HRMS *m/z* 354.1008 (calcd for C₂₂H₁₄N₂O₃, 354.1004).

4-Benzoyl-3-(3-cyanopropyl)isoquinoline (28). The reaction mixture was chromatographed using 1:1 hexanes/ethyl acetate to yield a yellow oil: ^1H NMR (CDCl_3) δ 2.15 (quintet, $J = 7.2$ Hz, 2H), 2.36 (t, $J = 7.2$ Hz, 2H), 2.86 (t, $J = 7.2$ Hz, 2H), 7.45-7.50 (m, 3H), 7.59-7.66 (m, 3H), 7.82 (d, $J = 7.2$ Hz, 2H), 8.01-8.06 (m, 1H), 9.32 (s, 1H); ^{13}C NMR (CDCl_3) δ 16.88, 25.39, 34.69, 119.62, 124.34, 126.88, 127.58, 128.14, 129.28, 129.59, 129.95, 131.57, 133.87, 134.67, 137.38, 149.34, 153.49, 198.14; IR (CHCl_3) 3064, 2234, 1667 cm^{-1} ; HRMS m/z 300.1266 (calcd for $\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}$, 300.1263).

4-Benzoyl-3-(methoxymethyl)isoquinoline (30). The reaction mixture was chromatographed using 1:1 hexanes/ethyl acetate to yield a white solid: mp 99-100 $^\circ\text{C}$; ^1H NMR (CDCl_3) δ 3.18, (s, 3H), 4.66 (s, 3H), 7.45 (t, $J = 8.0$ Hz, 2H), 7.58-7.64 (m, 4H), 7.82 (d, $J = 7.2$ Hz, 2H), 8.04-8.06 (m, 1H), 9.34 (s, 1H); ^{13}C NMR (CDCl_3) δ 58.80, 124.58, 127.70, 127.88, 128.19, 128.98, 129.32, 129.56, 131.61, 133.93, 134.14, 137.99, 148.30, 153.24, 197.01; IR (CHCl_3) 3064, 1659 cm^{-1} ; HRMS m/z 277.1106 (calcd for $\text{C}_{18}\text{H}_{15}\text{NO}_2$, 277.1103).

8-(4-Methoxybenzoyl)-7-phenyl-[1,3]dioxolo[4,5-g]isoquinoline (32). The reaction mixture was chromatographed using 1:1 hexanes/ethyl acetate to yield a yellow solid: mp 160-161 $^\circ\text{C}$; ^1H NMR (CDCl_3) δ 3.75 (s, 3H), 6.06 (s, 2H), 6.73 (d, $J = 8.8$ Hz, 2H), 7.00 (s, 1H), 7.19-7.27 (m, 3H), 7.59-7.64 (m, 4H), 9.15 (s, 1H); ^{13}C NMR (CDCl_3) δ 55.57, 101.23, 102.08, 103.47, 113.94, 124.73, 128.34, 128.91, 129.50, 130.68, 132.20, 132.66, 139.99, 148.72, 149.14, 150.94, 152.05, 164.07, 196.75; IR (CHCl_3) 3019, 1654 cm^{-1} ; HRMS m/z 383.1164 (calcd for $\text{C}_{24}\text{H}_{17}\text{NO}_3$, 383.1158).

7-Phenyl-8-(3-trifluoromethylbenzoyl)-[1,3]dioxolo[4,5-g]isoquinoline (33). The reaction mixture was chromatographed using 1:1 hexanes/ethyl acetate to yield a yellow solid: mp 139-140 °C; ¹H NMR (CDCl₃) δ 7.10 (s, 1H), 7.17-7.26 (m, 3H), 7.32-7.37 (m, 2H), 7.49-7.52 (m, 2H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.84 (s, 1H), 9.21 (s, 1H); ¹³C NMR (CDCl₃) δ 100.89, 102.30, 103.77, 124.93, 127.23 (q, *J* = 272.9 Hz, 1C, including 121.81, 125.43), 126.35 (q, *J* = 3.85 Hz, 1C, including 126.727, 126.32, 126.37, 126.42), 127.54, 128.54, 128.76, 129.19, 129.71, 129.82 (q, *J* = 3.62 Hz, 1C, including 129.75, 129.79, 129.84, 129.89), 130.65 (q, *J* = 33.0 Hz, 1C, including 130.87, 131.30), 132.65-132.70 (m, 1C, including 132.65, 132.70), 138.12, 139.80, 145.29, 149.00, 150.25, 151.78, 152.62, 197.08; IR (CHCl₃) 3019, 1654 cm⁻¹; HRMS *m/z* 383.1164 (calcd for C₂₄H₁₄NO₃F₃, 383.1158).

4-(4-Methoxybenzoyl)-4-(4-methoxyphenyl)isoquinoline (35). The reaction mixture was chromatographed using 1:1 hexanes/ethyl acetate to yield a yellow solid: mp 141-142 °C; ¹H NMR (CDCl₃) δ 3.77 (s, 3H), 3.80 (s, 3H), 6.77 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 7.61-7.73 (m, 7H), 8.08 (d, *J* = 7.6 Hz, 1H), 9.44 (s, 1H); ¹³C NMR (CDCl₃) δ 55.37, 55.61, 113.96, 114.02, 124.70, 126.92, 127.46, 128.11, 128.45, 130.75, 131.02, 131.52, 132.26, 132.48, 134.48, 149.37, 153.29, 159.94, 164.13, 196.87; IR (CHCl₃) 3019, 1654, 1216 cm⁻¹; HRMS *m/z* 369.1370 (calcd for C₂₄H₁₉NO₃, 369.1365).

4-(4-Ethoxycarbonylbenzoyl)-4-(4-methoxyphenyl)isoquinoline (36). The reaction mixture was chromatographed using 1:1 hexanes/ethyl acetate to yield a yellow solid: mp 152-153 °C; ¹H NMR (CDCl₃) δ 1.38 (t, *J* = 7.2 Hz, 3H), 3.72 (s, 3H), 4.33 (q, *J* = 7.2 Hz, 2H), 6.78 (dt, *J* = 8.8, 2.4 Hz, 2H), 7.33 (t, *J* = 8.0 Hz, 1H), 7.66 (dt, *J* = 8.8,

2.4 Hz, 2H), 7.64 (td, $J = 8.0, 1.2$ Hz, 1H), 7.69 (td, $J = 8.0, 1.2$ Hz, 1H), 7.76 (d, $J = 8.4$ Hz, 1H), 7.79 (dt, $J = 8.0, 1.2$ Hz, 1H), 8.09 (dd, $J = 8.0, 1.2$ Hz, 2H), 8.34 (t, $J = 1.2$ Hz, 1H), 9.46 (s, 1H); ^{13}C NMR (CDCl_3) δ 14.43, 55.34, 61.47, 114.02, 124.30, 126.96, 127.46, 127.63, 128.30, 128.82, 130.61, 131.11, 131.15, 131.82, 132.34, 133.70, 134.31, 134.37, 137.64, 150.11, 153.88, 160.07, 165.68, 197.54; IR (CHCl_3) 3064, 1720, 1667 cm^{-1} ; HRMS m/z 411.1478 (calcd for $\text{C}_{26}\text{H}_{21}\text{NO}_4$, 411.1471).

References

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Table 2, Compound **11**

Table 2, Compound **12**