SUPPORTING INFORMATION

Synthesis of 4-(1-Alkenyl)isoquinolines by Palladium(II)-catalyzed Cyclization/Olefination

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General. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz or 400 and 100 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) and a basic KMnO_4 solution [3 g of KMnO_4 + 20 g of K_2CO_3 + 5 mL of NaOH (5 %) + 300 mL of H_2O].

Reagents. All reagents were used directly as obtained commercially unless otherwise noted. All palladium salts were donated by Johnson Matthey Inc. and Kawaken Fine Chemicals Co. Ltd. Aryldimines **1**,¹ **10**,¹ **12**,¹ **14**,¹ **20**,¹ **52**,¹ **53**,² **54**,¹ 4-dimethylamino-2-iodobenzaldehyde,³ 5-dimethylamino-2-iodobenzaldehyde,³ 2-iodo-3,4,5-trimethoxybenzaldehyde,³ and *N*-(benzo[1,3]dioxol-5-ylmethylene)-*tert*-butylamine⁴ were prepared according to previous literature procedures. The following starting materials were prepared as indicated.

2-Methoxyphenyl trimethylsilyl acetylene. To a solution of 2-iodoanisole (4.68 g, 20 mmol) and trimethylsilylacetylene (24 mmol, 1.2 equiv) in Et_3N (60 mL) were added $\text{PdCl}_2(\text{PPh}_3)_2$ (0.281 mg, 2 mol %) and CuI (38.2 mg, 1 mol %). The resulting mixture was then heated under an Ar atmosphere at 55 °C. The reaction was complete in 2 h. The mixture was allowed to cool to room temperature, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (15:1 hexane/ EtOAc) to afford 4.05 g of the indicated product in 100 % yield as a yellow liquid: ^1H NMR (CDCl_3) δ 0.27 (s, 9H), 3.87 (s, 3H), 6.85 (d, J = 8.8 Hz, 1H), 6.89 (dd, J = 0.8, 7.6 Hz, 1H), 7.25-7.30 (m, 1H), 7.44 (dd, J = 1.6, 7.6 Hz, 1H); ^{13}C NMR (CDCl_3) δ 0.3, 56.0, 98.7, 101.4, 110.8, 112.4, 120.5, 130.2, 134.4, 160.5.

2-Methoxyphenylacetylene. A solution of KOH (5.06 g, 10 mmol) in 4 mL of water was added dropwise to 2-methoxyphenyl trimethylsilyl acetylene (2.04 g, 10 mmol) in 40 mL of CH₃OH under an Ar atmosphere at 25 °C. The mixture was stirred for another 0.5 h at 25 °C, and the CH₃OH was removed under vacuum. The residue was added to 20 mL of brine solution, and the mixture was extracted with EtOAc (3 x 20 mL), dried (Na₂SO₄), filtered, and the solvent removed under vacuum. Purification by flash chromatography (7:1 hexane/EtOAc) afforded 1.15 g (10 mmol) of the indicated compound in a 100 % yield as a yellow liquid: ¹H NMR (CDCl₃) δ 3.31 (s, 1H), 3.88 (s, 3H), 6.86 (d, *J* = 8.4 Hz, 1H), 6.90 (dd, *J* = 0.8, 7.6 Hz, 1H), 7.28-7.32 (m, 1H), 7.46 (dd, *J* = 1.6, 7.6 Hz, 1H); ¹³C NMR (CDCl₃) δ 55.9, 80.2, 81.3, 110.7, 111.3, 120.5, 130.4, 134.3, 160.7.

***N*-[4,5-Dimethoxy-2-(phenylethynyl)benzylidene]-*tert*-butylamine (16).** To a solution of 2-bromo-4,5-dimethoxybenzaldehyde (1.23 g, 5.0 mmol) and phenylacetylene (0.62 g, 6.0 mmol) in Et₃N (20 mL) were added PdCl₂(PPh₃)₂ (70 mg, 2 mol %) and CuI (10 mg, 1 mol %). The resulting mixture was then heated under an Ar atmosphere at 55 °C. The reaction was monitored by TLC to establish completion. When the reaction was complete, the reaction mixture was allowed to cool to 25 °C, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford the corresponding arylalkyne. To the purified arylalkyne in a 4 dram vial was added *t*-BuNH₂ (12 equiv). The mixture was then stirred under an Ar atmosphere at 25 °C for 24 h. The resulting mixture was extracted with ether. The combined organic layers were dried (Na₂SO₄) and filtered. Removal of the solvent afforded 1.32 g of the indicated arylaldimine in a 82 % overall yield as a yellow solid: mp 137-140 °C; ¹H NMR (CDCl₃) δ 1.35 (s, 9H), 3.95 (s, 3H), 4.00 (s, 3H), 7.01 (s, 1H), 7.36-7.38 (m, 3H), 7.52-7.55 (m, 2H), 7.63 (s, 1H), 8.86 (s, 1H); ¹³C NMR (CDCl₃) δ 30.1, 56.2, 56.3, 57.8, 86.9, 93.8, 107.9, 113.9, 117.1, 123.5, 128.5, 128.7, 131.5, 132.1, 149.9, 150.5, 153.9; IR (CHCl₃, cm⁻¹) 3019, 2969, 1681, 1593, 1507; HRMS Calcd for C₂₁H₂₃O₂N: 321.1729. Found: 321.1735.

***N*-[2-(*o*-Methoxyphenylethynyl)benzylidene]-*tert*-butylamine (22).** Using the procedure used to prepare arylaldimine **16**, 2-bromobenzaldehyde (0.93 g, 5.0 mmol) and *o*-methoxyphenylacetylene (0.79 g, 6.0 mmol) were employed to afford 1.06 g of the

indicated arylaldimine in a 90 % overall yield as a yellow oil: ^1H NMR (CDCl_3) δ 1.35 (s, 9H), 3.91 (s, 3H), 6.92 (d, $J = 7.8$ Hz, 1H), 6.97 (dd, $J = 0.9, 7.5$ Hz, 1H), 7.25-7.36 (m, 3H), 7.50 (dd, $J = 1.8, 7.5$ Hz, 1H), 7.55-7.58 (m, 1H), 8.06-8.09 (m, 1H), 9.01 (s, 1H); ^{13}C NMR (CDCl_3) δ 30.0, 55.9, 57.9, 90.9, 91.5, 110.9, 112.5, 120.7, 124.6, 126.0, 128.6, 129.8, 130.2, 132.4, 133.6, 137.9, 155.0, 160.2; IR (CHCl_3 , cm^{-1}) 3063, 3015, 2969, 2837, 1693, 1635; HRMS Calcd for $\text{C}_{20}\text{H}_{21}\text{ON}$: 291.1623. Found: 291.1626.

***N*-[4,5-Dimethoxy-2-(*o*-methoxyphenylethynyl)benzylidene]-*tert*-butylamine (29).**

Using the procedure used to prepare arylaldimine **16**, 2-bromo-4,5-dimethoxybenzaldehyde (1.23 g, 5.0 mmol) and *o*-methoxyphenylacetylene (0.79 g, 6.0 mmol) were employed to afford 1.23 g of the indicated arylaldimine in a 70 % overall yield as a yellow solid: mp 124-126 °C; ^1H NMR (CDCl_3) δ 1.35 (s, 9H), 3.92 (s, 3H), 3.94 (s, 3H), 3.99 (s, 3H), 6.92-6.99 (m, 2H), 7.03 (s, 1H), 7.30-7.35 (m, 1H), 7.50 (d, $J = 7.5$ Hz, 1H), 7.61 (s, 1H), 8.93 (s, 1H); ^{13}C NMR (CDCl_3) δ 30.2, 55.9, 56.2, 57.6, 90.2, 91.3, 107.8, 110.8, 112.7, 113.9, 117.6, 120.7, 129.9, 132.0, 133.4, 149.8, 150.5, 154.6, 160.0 (one methoxy carbon is missing due to overlap); IR (CHCl_3 , cm^{-1}) 3019, 2967, 2838, 1634, 1598, 1507; HRMS Calcd for $\text{C}_{22}\text{H}_{25}\text{O}_3\text{N}$: 351.1834. Found: 351.1839.

***N*-[6-(*o*-Methoxy)phenylethynylbenzo[1,3]dioxol-5-ylmethylene]-*tert*-butylamine (33).** Using the procedure used to prepare arylaldimine **16**, 6-bromo-1,3-benzodioxole-5-carboxaldehyde (1.15 g, 5 mmol) and *o*-methoxyphenylacetylene (0.70 g, 6 mmol) were employed to afford 1.12 g of the indicated arylaldimine in a 67 % overall yield after recrystallization (EtOAc /hexane) as a yellow solid: mp 87-89 °C; ^1H NMR (CDCl_3) δ 1.33 (s, 9H), 3.90 (s, 3H), 6.00 (s, 2H), 6.90-6.97 (m, 2H), 6.98 (s, 1H), 7.30-7.33 (m, 1H), 7.47 (d, $J = 7.6$ Hz, 1H), 7.57 (s, 1H), 8.92 (s, 1H); ^{13}C NMR (CDCl_3) δ 30.1, 55.9, 57.7, 90.2, 90.9, 101.8, 105.7, 110.8, 111.3, 112.6, 119.0, 120.7, 129.9, 133.4, 133.8, 148.6, 149.1, 154.3, 160.1; IR (CHCl_3 , cm^{-1}) 3017, 2968, 1612, 1476; HRMS Calcd for $\text{C}_{21}\text{H}_{21}\text{O}_3\text{N}$: 335.1521. Found: 335.1526.

***N*-[4-Dimethylamino-2-(*o*-methoxyphenylethynyl)benzylidene]-*tert*-butylamine (37).** Using the procedure used to prepare arylaldimine **16**, 4-dimethylamino-2-iodobenzaldehyde³ (1.38 g, 5 mmol) and *o*-methoxyphenylacetylene (0.70 g, 6 mmol) were employed to afford 1.57 g of the indicated arylaldimine in a 94 % overall yield as a yellow solid: mp 102-104 °C; ^1H NMR (CDCl_3) δ 1.34 (s, 9H), 3.02 (s, 6H), 3.92 (s, 3H),

6.72 (dd, $J = 2.4, 8.8$ Hz, 1H), 6.82 (d, $J = 2.8$ Hz, 1H), 6.91-6.97 (m, 2H), 7.30-7.35 (m, 1H), 7.52 (dd, $J = 1.6, 7.6$ Hz, 1H), 8.00 (br s, 1H), 8.90 (s, 1H); ^{13}C NMR (CDCl_3) δ 30.2, 40.5, 55.9, 57.3, 90.2, 91.8, 110.8, 112.6, 113.1, 114.5, 120.7, 125.6, 126.1, 127.2, 130.0, 133.6, 151.4, 155.0, 160.2; IR (CHCl_3 , cm^{-1}) 3018, 2968, 2400, 1596; HRMS Calcd for $\text{C}_{22}\text{H}_{16}\text{ON}_2$: 334.2045. Found: 334.2050.

***N*-[5-Dimethylamino-2-(*o*-methoxyphenylethynyl)benzylidene]-*tert*-butylamine (40).** Using the procedure used to prepare arylaldimine **16**, 5-dimethylamino-2-iodobenzaldehyde³ (1.38 g, 5 mmol) and *o*-methoxyphenylacetylene (0.70 g, 6 mmol) were employed to afford 1.48 g of the indicated arylaldimine in a 89 % overall yield as a yellow solid: mp 118-120 °C; ^1H NMR (CDCl_3) δ 1.35 (s, 9H), 3.03 (s, 6H), 3.92 (s, 3H), 6.72 (dd, $J = 2.8, 8.4$ Hz, 1H), 6.90 (d, $J = 8.4$ Hz, 1H), 6.91-6.95 (m, 1H), 7.25-7.29 (m, 1H), 7.38 (br s, 1H), 7.44 (d, $J = 8.8$ Hz, 1H), 7.48 (dd, $J = 1.6, 7.6$ Hz, 1H), 8.99 (s, 1H); ^{13}C NMR (CDCl_3) δ 30.1, 40.6, 55.9, 57.7, 89.1, 92.3, 108.4, 110.8, 112.2, 113.5, 114.2, 120.7, 129.2, 133.2, 133.5, 138.7, 150.4, 155.8, 159.7; IR (CHCl_3 , cm^{-1}) 3017, 2969, 1638, 1602; HRMS Calcd for $\text{C}_{22}\text{H}_{16}\text{ON}_2$: 334.2045. Found: 334.2050.

***N*-[2-(Phenylethynyl)-3,4,5-trimethoxybenzylidene]-*tert*-butylamine (43).** Using the procedure used to prepare arylaldimine **16**, 2-iodo-3,4,5-trimethoxybenzaldehyde³ (1.61 g, 5.0 mmol) and phenylacetylene (0.62 g, 6.0 mmol) were employed to afford 1.42 g of the indicated arylaldimine in a 81 % overall yield as a yellow oil: ^1H NMR (CDCl_3) δ 1.33 (s, 9H), 3.92 (s, 3H), 3.97 (s, 3H), 4.03 (s, 3H), 7.35-7.38 (m, 3H), 7.43 (s, 1H), 7.52-7.55 (m, 2H), 8.85 (s, 1H); ^{13}C NMR (CDCl_3) δ 30.1, 56.4, 58.0, 61.4, 61.7, 82.8, 98.1, 104.6, 112.4, 123.7, 128.5, 128.7, 131.5, 134.5, 144.1, 153.9, 154.3, 154.6; IR (neat, cm^{-1}) 3079, 3056, 2966, 2872, 2837, 1687, 1640, 1585, 1493; HRMS Calcd for $\text{C}_{22}\text{H}_{25}\text{O}_3\text{N}$: 351.1834. Found: 351.1839.

4-Iodo-1,3-benzodioxole-5-carboxaldehyde. To a solution of *N*-(benzo[1,3]dioxol-5-ylmethylene)-*tert*-butylamine⁴ (1.03 g, 5.0 mmol) in 40 mL of THF at -78 °C was added 5.25 mmol of *n*-BuLi (2.5 M in hexane) dropwise over a 5 min period. The solution was stirred for 30 min at -78 °C and a solution of I_2 (2.68 g, 7.5 mmol) in 15 mL of THF was added dropwise. The resulting solution was warmed to 25 °C and stirred for 2 h. The reaction mixture was then quenched with water, extracted with ether, washed with satd aq $\text{Na}_2\text{S}_2\text{O}_3$, dried (Na_2SO_4), filtered, and the solvent was removed under

reduced pressure. The residue was chromatographed using 3:1 hexane/EtOAc to afford 1.01 g of the indicated compound in a 70 % yield as a white solid: mp 130-132 °C; ¹H NMR (CDCl₃) δ 6.16 (s, 2H), 6.86 (dd, *J* = 0.3, 8.1 Hz, 1H), 7.53 (d, *J* = 8.1 Hz, 1H), 9.90 (d, *J* = 0.6 Hz, 1H); ¹³C NMR (CDCl₃) δ 76.0, 101.5, 108.3, 127.5, 128.8, 150.3, 150.9, 192.8.

***N*-(4-Phenylethynylbenzo[1,3]dioxol-5-ylmethylene)-*tert*-butylamine (48).** Using the procedure used to prepare arylaldimine **16**, 4-iodo-1,3-benzodioxole-5-carboxaldehyde (1.45 g, 5 mmol) and phenylacetylene (0.61 g, 6 mmol) were employed to afford 1.52 g of the indicated arylaldimine in a 100 % overall yield as a yellow solid: mp 128-129 °C; ¹H NMR (CDCl₃) δ 1.34 (s, 9H), 6.10 (s, 2H), 6.84 (d, *J* = 8.0 Hz, 1H), 7.37-7.39 (m, 3H), 7.55-7.57 (m, 2H), 7.64 (d, *J* = 8.0 Hz, 1H), 8.77 (s, 1H); ¹³C NMR (CDCl₃) δ 30.0, 57.8, 80.8, 98.8, 102.1, 106.1, 109.0, 120.6, 122.9, 128.6, 128.9, 131.7, 131.8, 148.9, 153.4 (one sp² carbon missing due to overlap); IR (CHCl₃, cm⁻¹) 3018, 2969, 1644, 1616, 1458; HRMS Calcd for C₂₀H₁₉O₂N: 305.1416. Found: 305.1420.

General procedure A for the palladium-catalyzed formation of isoquinolines.

Dried DMSO (3 mL), PdBr₂ (6.7 mg, 0.025 mmol), Cu(OAc)₂ (0.091 g, 0.50 mmol), NaOAc (0.062 g, 0.75 mmol) and the benzaldimine (0.25 mmol) were placed in a 4 dram vial. The contents were then stirred for 1 min, and the appropriate olefin (1.25 mmol) was added. The vial was sealed carefully and heated in an oil bath at 70 °C for the indicated period of time. The reaction was monitored by TLC to establish completion. The reaction mixture was cooled to 25 °C, diluted with 20 mL of EtOAc, washed with 20 mL of brine, dried (Na₂SO₄), and filtered. The solvent was evaporated under reduced pressure, and the product was isolated by chromatography on a silica gel column.

General procedure B for the palladium-catalyzed formation of isoquinolines.

Dried DMSO (3 mL), PdBr₂ (6.7 mg, 0.025 mmol), CuCl₂ (3.4 mg, 0.025 mmol), NaHCO₃ (0.063 g, 0.75 mmol) and the benzaldimine (0.25 mmol) were placed in a 4 dram vial. The contents were then stirred for 1 min, and the appropriate olefin (1.25 mmol) was added. The vial was flushed with O₂ and heated in an oil bath at 70 °C or 90 °C under an O₂ balloon for the indicated period of time. The reaction was monitored by TLC to establish completion. The reaction mixture was cooled to 25 °C, diluted with 20 mL of EtOAc, washed with 20 mL of brine, dried (Na₂SO₄), and filtered. The solvent

was evaporated under reduced pressure, and the product was isolated by chromatography on a silica gel column.

Methyl (*E*)-3-(3-phenylisoquinolin-4-yl)acrylate (2). The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 44 mg of the indicated compound in a 61 % yield as a yellow oil: ¹H NMR (CDCl₃) δ 3.81 (s, 3H), 6.31 (d, *J* = 16.4 Hz, 1H), 7.41-7.49 (m, 3H), 7.61-7.63 (m, 2H), 7.63-7.68 (m, 1H), 7.77-7.80 (m, 1H), 8.02 (d, *J* = 16.0 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 8.24 (dd, *J* = 0.8, 8.8 Hz, 1H), 9.30 (s, 1H); ¹³C NMR (CDCl₃) δ 52.1, 123.9, 124.4, 126.3, 127.5, 127.6, 128.5, 128.5, 128.6, 130.6, 131.5, 134.5, 140.2, 141.6, 152.0, 152.9, 166.8; IR (CHCl₃, cm⁻¹) 3018, 2924, 2852, 1717, 1638; HRMS Calcd for C₁₉H₁₅O₂N: 289.1103. Found: 289.1108.

***n*-Butyl (*E*)-3-(3-phenylisoquinolin-4-yl)acrylate (5).** The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 51 mg (Table 3, entry 2) or 46 mg (entry 3) of the indicated compound as a yellow oil in a 61 % or a 56 % yield using Procedure A or B, respectively: ¹H NMR (CDCl₃) δ 0.96 (t, *J* = 7.2 Hz, 3H), 1.37-1.46 (m, 2H), 1.64-1.72 (m, 2H), 4.23 (t, *J* = 6.8 Hz, 2H), 6.32 (d, *J* = 16.4 Hz, 1H), 7.42-7.49 (m, 3H), 7.63-7.68 (m, 3H), 7.76-7.80 (m, 1H), 7.99 (d, *J* = 16.4 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 8.26 (d, *J* = 8.8 Hz, 1H), 9.31 (s, 1H); ¹³C NMR (CDCl₃) δ 13.9, 19.4, 30.9, 64.8, 123.9, 124.4, 126.6, 127.4, 127.6, 128.4, 128.5, 128.5, 130.6, 131.5, 134.4, 140.2, 141.3, 152.0, 152.8, 166.4; IR (neat, cm⁻¹) 3058, 2958, 2872, 1716, 1636, 1570; HRMS Calcd for C₂₂H₂₁O₂N: 331.1572. Found: 331.1577.

***t*-Butyl (*E*)-3-(3-phenylisoquinolin-4-yl)acrylate (6).** The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 41 mg of the indicated compound as a yellow oil in a 50 % yield: ¹H NMR (CDCl₃) δ 1.50 (s, 9H), 6.22 (d, *J* = 16.4 Hz, 1H), 7.38-7.49 (m, 3H), 7.62-7.67 (m, 3H), 7.75-7.80 (m, 1H), 7.85 (d, *J* = 16.4 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 9.27 (s, 1H); ¹³C NMR (CDCl₃) δ 28.4, 81.0, 124.1, 124.6, 127.4, 127.6, 128.3, 128.4, 128.5, 130.6, 131.4, 134.4, 140.2, 140.3, 151.9, 152.7, 165.7 (one sp² carbon missing due to overlap); IR (CHCl₃, cm⁻¹) 3058, 2977, 2931, 1708, 1634, 1617, 1572, 1553; HRMS Calcd for C₂₂H₂₁O₂N: 331.1572. Found: 331.1577.

3-Phenyl-4-[(*E*)-2-phenylethen-1-yl]isoquinoline (7). The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 41 mg of the indicated compound as

a yellow oil in a 53 % yield: ^1H NMR (CDCl_3) δ 6.89 (d, $J = 16.8$ Hz, 1H), 7.25-7.47 (m, 9H), 7.60-7.65 (m, 1H), 7.71-7.74 (m, 3H), 8.03 (d, $J = 7.8$ Hz, 1H), 8.38 (d, $J = 8.4$ Hz, 1H), 9.27 (s, 1H); ^{13}C NMR (CDCl_3) δ 124.7, 125.2, 126.6, 126.7, 127.1, 127.9, 127.9, 128.2, 128.2, 128.2, 128.9, 130.6, 130.8, 135.1, 136.8, 137.3, 141.1, 150.8, 151.4; IR (CHCl_3 , cm^{-1}) 3058, 3024, 2972, 1697, 1666, 1617, 1495; HRMS Calcd for $\text{C}_{23}\text{H}_{17}\text{N}$: 307.1361. Found: 307.1366.

(E)-2-Methyl-4-(3-phenylisoquinolin-4-yl)-3-buten-2-ol (8). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 26 mg of the indicated compound as a white solid in a 34 % yield: mp 178-179 °C; ^1H NMR (CDCl_3) δ 1.34 (s, 6H), 1.55 (br s, 1H), 5.92 (d, $J = 16.5$ Hz, 1H), 6.83 (d, $J = 16.5$ Hz, 1H), 7.32-7.38 (m, 1H), 7.40-7.45 (m, 2H), 7.60-7.65 (m, 3H), 7.70-7.76 (m, 1H), 8.01 (d, $J = 7.5$ Hz, 1H), 8.17 (dd, $J = 0.9, 8.7$ Hz, 1H), 9.25 (s, 1H); ^{13}C NMR (CDCl_3) δ 29.6, 71.5, 121.7, 124.8, 126.7, 127.1, 127.6, 127.7, 128.1, 128.1, 130.7, 130.7, 135.3, 141.2, 145.9, 150.9, 151.2; IR (CHCl_3 , cm^{-1}) 3650, 3019, 2975, 2400, 1521; HRMS Calcd for $\text{C}_{20}\text{H}_{19}\text{ON}$: 289.1467. Found: 289.1471.

4-(1-*n*-Butoxyethen-1-yl)-3-phenylisoquinoline (9). The reaction mixture was chromatographed using 7:1 hexane/EtOAc to afford 24 mg of the indicated compound as a yellow oil in a 31 % yield: ^1H NMR (CDCl_3) δ 0.93 (t, $J = 7.6$ Hz, 3H), 1.33-1.43 (m, 2H), 1.64-1.72 (m, 2H), 3.87 (t, $J = 2.8$ Hz, 2H), 4.13 (d, $J = 2.4$ Hz, 1H), 4.48 (d, $J = 2.4$ Hz, 1H), 7.35-7.45 (m, 3H), 7.59-7.63 (m, 1H), 7.72-7.76 (m, 1H), 7.77-7.79 (m, 2H), 8.00 (d, $J = 8.0$ Hz, 1H), 8.08 (dd, $J = 0.8, 8.8$ Hz, 1H), 9.33 (s, 1H); ^{13}C NMR (CDCl_3) δ 14.1, 19.6, 31.2, 67.7, 89.6, 125.5, 127.2, 127.2, 127.4, 127.7, 127.9, 128.1, 129.4, 130.9, 135.9, 141.2, 151.4, 152.5, 157.5; IR (CHCl_3 , cm^{-1}) 3060, 3015, 2960, 2873, 1621, 1564, 1497; HRMS Calcd for $\text{C}_{21}\text{H}_{21}\text{ON}$: 303.1623. Found: 303.1627.

***n*-Butyl (E)-3-(3-cyclohexen-1-ylisoquinolin-4-yl)acrylate (11).** The reaction mixture was chromatographed using 3:1 hexane/EtOAc to afford 34 mg of the indicated compound as a yellow oil in a 41 % yield: ^1H NMR (CDCl_3) δ 0.99 (t, $J = 7.2$ Hz, 3H), 1.43-1.53 (m, 2H), 1.68-1.76 (m, 4H), 1.83-1.86 (m, 2H), 2.25-2.27 (m, 2H), 2.47-2.49 (m, 2H), 4.27 (t, $J = 6.8$ Hz, 2H), 5.85 (t, $J = 1.6$ Hz, 1H), 6.40 (d, $J = 16.4$ Hz, 1H), 7.58-7.61 (m, 1H), 7.71-7.75 (m, 1H), 7.98 (d, $J = 8.0$ Hz, 1H), 8.08 (d, $J = 16.4$ Hz, 1H), 8.21 (d, $J = 8.4$ Hz, 1H), 9.19 (s, 1H); ^{13}C NMR (CDCl_3) δ 13.9, 19.5, 22.2, 23.1, 25.9, 28.8,

30.9, 64.7, 122.9, 124.4, 124.9, 126.9, 127.4, 128.4, 131.2, 132.7, 134.4, 138.0, 141.6, 152.5, 155.1, 166.8; IR (neat, cm^{-1}) 2932, 2872, 1712, 1632; HRMS Calcd for $\text{C}_{22}\text{H}_{25}\text{O}_2\text{N}$: 335.1885. Found: 335.1892.

***n*-Butyl (*E*)-3-(3-phenyl-2,6-naphthyridin-4-yl)acrylate (13).** The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 42 mg of the indicated compound as a yellow solid in a 51 % yield: mp 86-88 °C; ^1H NMR (CDCl_3) δ 0.96 (t, J = 7.2 Hz, 3H), 1.37-1.48 (m, 2H), 1.65-1.74 (m, 2H), 4.24 (t, J = 6.9 Hz, 2H), 6.44 (d, J = 16.5 Hz, 1H), 7.44-7.53 (m, 3H), 7.64 (dd, J = 1.5, 8.1 Hz, 2H), 7.85 (d, J = 5.7 Hz, 1H), 7.97 (d, J = 16.5 Hz, 1H), 8.79 (d, J = 5.7 Hz, 1H), 9.39 (s, 1H), 9.74 (s, 1H); ^{13}C NMR (CDCl_3) δ 13.9, 19.4, 30.8, 65.0, 119.4, 123.7, 128.1, 128.6, 128.7, 129.0, 129.2, 130.5, 139.2, 139.3, 144.8, 150.0, 152.0, 153.4, 165.9; IR (CHCl_3 , cm^{-1}) 3019, 2965, 2874, 1712, 1638; HRMS Calcd for $\text{C}_{21}\text{H}_{20}\text{O}_2\text{N}_2$: 332.1525. Found: 332.1531. Anal. Calcd: C, 75.88; H, 6.07; N, 8.43. Found: C, 76.21; H, 6.09; N, 8.08.

***n*-Butyl (*E*)-3-(7-phenyl-1,3-dioxolo[4,5-*g*]isoquinolin-8-yl)acrylate (15).** The reaction mixtures were chromatographed using 2:1 hexane/EtOAc to afford 40 mg or 45 mg of the indicated compound as a yellow solid in a 43 % (entry 10) or 48 % (entry 11) yield: mp 73-76 °C; ^1H NMR (CDCl_3) δ 0.95 (t, J = 7.2 Hz, 3H), 1.36-1.44 (m, 2H), 1.62-1.70 (m, 2H), 4.20 (t, J = 6.8 Hz, 2H), 6.14 (s, 2H), 6.23 (d, J = 16.4 Hz, 1H), 7.24 (s, 1H), 7.38-7.46 (m, 3H), 7.51 (s, 1H), 7.56-7.59 (m, 2H), 7.90 (d, J = 16.4 Hz, 1H), 9.02 (s, 1H); ^{13}C NMR (CDCl_3) δ 13.9, 19.3, 30.8, 64.8, 101.1, 102.1, 103.8, 123.7, 125.1, 126.1, 128.3, 130.4, 132.8, 140.3, 141.8, 148.4, 150.4, 151.3, 152.2, 166.4 (one sp^2 carbon missing due to overlap); IR (CHCl_3 , cm^{-1}) 3018, 2962, 1708, 1615; HRMS Calcd for $\text{C}_{23}\text{H}_{21}\text{O}_4\text{N}$: 375.1471. Found: 375.1475.

***t*-Butyl (*E*)-3-(6,7-dimethoxy-3-phenylisoquinolin-4-yl)acrylate (17).** The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 50 mg of the indicated compound as a yellow solid in a 51 % yield: mp 157-159 °C; ^1H NMR (CDCl_3) δ 1.51 (s, 9H), 4.04 (s, 3H), 4.06 (s, 3H), 6.20 (d, J = 16.4 Hz, 1H), 7.26 (s, 1H), 7.37-7.48 (m, 4H), 7.60 (d, J = 6.8 Hz, 2H), 7.86 (d, J = 16.4 Hz, 1H), 9.08 (s, 1H); ^{13}C NMR (CDCl_3) δ 28.4, 56.3, 56.3, 80.9, 103.0, 106.0, 123.0, 123.8, 127.6, 128.2, 130.5, 131.0, 140.5, 140.9, 150.0, 150.4, 150.9, 153.8, 165.8 (one sp^2 carbon missing due to overlap); IR (CHCl_3 , cm^{-1}) 3020, 2972, 2934, 2840, 1700, 1503; HRMS Calcd for $\text{C}_{24}\text{H}_{25}\text{O}_4\text{N}$:

391.1784. Found: 391.1792. Anal. Calcd: C, 73.64; H, 6.44; N, 3.58. Found: C, 73.52; H, 6.38; N, 3.54.

***N,N*-Dimethyl (*E*)-3-(6,7-dimethoxy-3-phenylisoquinolin-4-yl)acrylamide (18).**

The reaction mixture was chromatographed using 1:3 hexane/EtOAc and 50:1 CHCl₃/CH₃OH to afford 46 mg of the indicated compound as a yellow solid in a 51 % yield: mp 150-151 °C; ¹H NMR (CDCl₃) δ 2.72 (s, 3H), 3.00 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.41 (d, *J* = 16.0 Hz, 1H), 7.26 (s, 1H), 7.32-7.38 (m, 2H), 7.41-7.44 (m, 2H), 7.57-7.59 (m, 2H), 8.07 (d, *J* = 16.0 Hz, 1H), 9.07 (s, 1H); ¹³C NMR (CDCl₃) δ 35.9, 37.0, 56.3, 56.4, 102.7, 105.8, 123.6, 124.0, 126.8, 127.7, 128.3, 130.3, 131.7, 137.9, 141.3, 149.5, 150.4, 150.8, 153.6, 166.2; IR (CHCl₃, cm⁻¹) 3444, 3006, 2934, 1649, 1618, 1505, 1467; HRMS Calcd for C₂₂H₂₂O₃N₂: 362.1630. Found: 362.1635.

6,7-Dimethoxy-3-phenyl-4-[(*E*)-2-methylsulfonylethen-1-yl]isoquinoline (19).

The reaction mixture was chromatographed using 1:3 hexane/EtOAc to afford 25 mg of the indicated compound as a yellow solid in a 27 % yield: mp 196-198 °C; ¹H NMR (CDCl₃) δ 2.80 (s, 3H), 4.06 (s, 3H), 4.07 (s, 3H), 6.47 (d, *J* = 15.6 Hz, 1H), 7.24 (s, 1H), 7.29 (s, 1H), 7.39-7.42 (m, 1H), 7.46-7.48 (m, 2H), 7.52-7.54 (m, 2H), 8.03 (d, *J* = 16.0 Hz, 1H), 9.12 (s, 1H); ¹³C NMR (CDCl₃) δ 42.6, 56.4, 56.5, 101.9, 106.1, 120.8, 123.6, 128.5, 128.6, 130.4, 131.1, 134.4, 140.4, 140.8, 150.7, 150.8, 151.3, 154.3; IR (CHCl₃, cm⁻¹) 3019, 2974, 2399, 1621, 1508; HRMS Calcd for C₂₀H₁₉O₄SN: 369.1035. Found: 369.1041.

***n*-Butyl (*E*)-3-[3-(*p*-methoxyphenyl)isoquinolin-4-yl]acrylate (21).** The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 32 mg of the indicated compound as a yellow oil in a 35 % yield: ¹H NMR (CDCl₃) δ 0.96 (t, *J* = 7.5 Hz, 3H), 1.36-1.49 (m, 2H), 1.64-1.74 (m, 2H), 3.87 (s, 3H), 4.24 (t, *J* = 6.6 Hz, 2H), 6.36 (d, *J* = 16.5 Hz, 1H), 6.98-7.01 (m, 2H), 7.58-7.66 (m, 3H), 7.74-7.78 (m, 1H), 8.97 (d, *J* = 16.5 Hz, 1H), 8.03 (d, *J* = 8.1 Hz, 1H), 8.25 (d, *J* = 8.7 Hz, 1H), 9.28 (s, 1H); ¹³C NMR (CDCl₃) δ 14.0, 19.4, 30.9, 55.6, 64.8, 113.9, 123.4, 124.4, 126.3, 127.2, 127.4, 128.5, 131.5, 132.1, 132.7, 134.5, 141.7, 151.7, 152.8, 160.0, 166.6; IR (neat, cm⁻¹) 3057, 2958, 2872, 2836, 1708, 1633, 1607, 1552, 1463; HRMS Calcd for C₂₃H₂₃O₃N: 361.1678. Found: 361.1682.

***n*-Butyl (*E*)-3-[3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylate (23).** The reaction mixtures were chromatographed using 2:1 hexane/EtOAc to afford 59 mg (entry 16) or 58 mg (entry 17) of the indicated compound as a yellow oil in a 65 % or a 64 % yield, respectively: ^1H NMR (CDCl_3) δ 0.91 (t, J = 7.2 Hz, 3H), 1.31-1.37 (m, 2H), 1.57-1.64 (m, 2H), 3.72 (s, 3H), 4.13 (t, J = 6.8 Hz, 2H), 6.07 (d, J = 16.4 Hz, 1H), 6.94 (d, J = 8.0 Hz, 1H), 7.03-7.07 (m, 1H), 7.35-7.39 (m, 2H), 7.60-7.64 (m, 1H), 7.71-7.75 (m, 1H), 7.92 (d, J = 16.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 8.14 (d, J = 8.8 Hz, 1H), 9.27 (s, 1H); ^{13}C NMR (CDCl_3) δ 13.9, 19.3, 30.8, 55.5, 64.6, 111.2, 121.0, 124.3, 125.3, 125.6, 127.4, 127.6, 128.3, 129.4, 130.1, 131.2, 131.6, 134.2, 141.2, 149.7, 152.6, 156.4, 166.6; IR (neat, cm^{-1}) 3059, 2958, 2872, 2835, 1716, 1638, 1601, 1494; HRMS Calcd for $\text{C}_{23}\text{H}_{23}\text{O}_3\text{N}$: 361.1678. Found: 361.1682.

***t*-Butyl (*E*)-3-[3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylate (24).** The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 61 mg of the indicated compound as a yellow oil in a 68 % yield: ^1H NMR (CDCl_3) δ 1.47 (s, 9H), 3.74 (s, 3H), 6.04 (d, J = 16.4 Hz, 1H), 6.96 (d, J = 8.8 Hz, 1H), 7.06-7.09 (m, 1H), 7.38-7.42 (m, 2H), 7.61-7.65 (m, 1H), 7.73-7.77 (m, 1H), 7.82 (d, J = 16.4 Hz, 1H), 8.02 (d, J = 8.0 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H), 9.28 (s, 1H); ^{13}C NMR (CDCl_3) δ 28.3, 55.5, 80.7, 111.2, 121.0, 124.4, 125.7, 127.0, 127.3, 127.6, 128.3, 129.5, 130.0, 131.1, 131.6, 134.2, 140.1, 149.7, 152.4, 156.4, 165.8; IR (neat, cm^{-1}) 3059, 2977, 2934, 2835, 1708, 1636, 1601, 1494; HRMS Calcd for $\text{C}_{23}\text{H}_{23}\text{O}_3\text{N}$: 361.1678. Found: 361.1682.

3-(*o*-Methoxyphenyl)-4-[(*E*)-2-phenylethen-1-yl]isoquinoline (25). The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 54 mg of the indicated compound as a yellow oil in a 64 % yield: ^1H NMR (CDCl_3) δ 3.71 (s, 3H), 6.71 (d, J = 16.4 Hz, 1H), 6.94 (d, J = 8.4 Hz, 1H), 7.04-7.07 (m, 1H), 7.21-7.26 (m, 2H), 7.31-7.37 (m, 5H), 7.40 (dd, J = 1.6, 7.6 Hz, 1H), 7.59-7.64 (m, 1H), 7.69-7.74 (m, 1H), 8.02 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 8.8 Hz, 1H), 9.25 (s, 1H); ^{13}C NMR (CDCl_3) δ 55.7, 111.3, 120.9, 124.3, 124.9, 126.5, 127.0, 127.9, 128.1, 128.2, 128.8, 129.6, 130.4, 130.6, 131.7, 134.9, 135.8, 137.6, 149.1, 151.0, 156.6 (one sp^2 carbon missing due to overlap); IR (neat, cm^{-1}) 3057, 3025, 2957, 2935, 2833, 2214, 1617, 1494; HRMS Calcd for $\text{C}_{24}\text{H}_{19}\text{ON}$: 337.1467. Found: 337.1473.

3-(*o*-Methoxyphenyl)-4-[(*E*)-2-phenylsulfonylethen-1-yl]isoquinoline (26). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 20 mg of the indicated compound as a yellow oil in a 20 % yield: ^1H NMR (CDCl_3) δ 3.58 (s, 3H), 6.45 (d, J = 15.6 Hz, 1H), 6.71 (d, J = 8.4 Hz, 1H), 6.96-7.00 (m, 1H), 7.27-7.31 (m, 2H), 7.50 (t, J = 8.0 Hz, 2H), 7.61-7.70 (m, 4H), 7.78-7.82 (m, 1H), 8.02-8.08 (m, 3H), 9.30 (s, 1H); ^{13}C NMR (CDCl_3) δ 55.5, 111.3, 121.1, 123.6, 123.7, 127.4, 127.7, 127.8, 128.5, 128.9, 129.5, 130.1, 131.3, 131.7, 133.4, 133.8, 134.0, 139.0, 140.4, 149.5, 153.3, 155.8; IR (neat, cm^{-1}) 3060, 2938, 2836, 1619, 1600, 1494; HRMS Calcd for $\text{C}_{24}\text{H}_{19}\text{O}_3\text{NS}$: 401.1086. Found: 401.1093.

***N,N*-Dimethyl (*E*)-3-[3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylamide (27).** The reaction mixture was chromatographed using 1:1 hexane/EtOAc and pure EtOAc to afford 54 mg of the indicated compound as a yellow oil in a 65 % yield: ^1H NMR (CDCl_3) δ 2.66 (s, 3H), 2.96 (s, 3H), 3.74 (s, 3H), 6.33 (d, J = 15.6 Hz, 1H), 6.95 (d, J = 8.0 Hz, 1H), 7.05-7.08 (m, 1H), 7.34-7.38 (m, 1H), 7.41 (dd, J = 1.6, 7.6 Hz, 1H), 7.62-7.66 (m, 1H), 7.73-7.77 (m, 1H), 8.01 (d, J = 7.6 Hz, 1H), 8.03 (d, J = 15.6 Hz, 1H), 8.16 (d, J = 8.8 Hz, 1H), 9.28 (s, 1H); ^{13}C NMR (CDCl_3) δ 35.8, 37.0, 55.7, 111.3, 121.0, 124.3, 125.3, 126.7, 127.3, 127.4, 128.1, 129.6, 130.3, 130.9, 131.4, 134.7, 137.3, 148.8, 151.9, 156.3, 166.3; IR (CHCl_3 , cm^{-1}) 3468, 3058, 3004, 2935, 2835, 2234, 1651, 1613; HRMS Calcd for $\text{C}_{21}\text{H}_{20}\text{O}_2\text{N}_2$: 332.1525. Found: 332.1531.

(*E*)-2-Methyl-4-[3-(*o*-methoxyphenyl)isoquinolin-4-yl]-3-buten-2-ol (28). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 20 mg of the indicated compound as a yellow oil in a 25 % yield: ^1H NMR (CDCl_3) δ 1.20 (s, 6H), 3.74 (s, 3H), 5.75 (d, J = 16.0 Hz, 1H), 6.77 (d, J = 16.0 Hz, 1H), 6.93 (d, J = 8.0 Hz, 1H), 7.01-7.05 (m, 1H), 7.32-7.37 (m, 2H), 7.58-7.62 (m, 1H), 7.68-7.73 (m, 1H), 7.99 (d, J = 8.0 Hz, 1H), 8.08 (d, J = 8.4 Hz, 1H), 9.24 (s, 1H) (the hydrogen from the OH group is missing); ^{13}C NMR (CDCl_3) δ 29.6, 55.6, 71.2, 111.0, 120.7, 121.1, 124.6, 127.0, 127.6, 128.1, 128.3, 129.3, 130.5, 130.7, 131.6, 134.9, 144.8, 148.9, 150.9, 156.5; IR (CHCl_3 , cm^{-1}) 3650, 3018, 2973, 1496; HRMS Calcd for $\text{C}_{21}\text{H}_{21}\text{O}_2\text{N}$: 319.1572. Found: 319.1576.

***t*-Butyl (*E*)-3-[6,7-dimethoxy-3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylate (30).** The reaction mixture was chromatographed using 1:3 hexane/EtOAc to afford 94 mg of

the indicated compound as a yellow oil in a 92 % yield: ^1H NMR (CDCl_3) δ 1.46 (s, 9H), 3.74 (s, 3H), 4.04 (s, 6H), 6.01 (d, J = 16.4 Hz, 1H), 6.94 (d, J = 8.8 Hz, 1H), 7.05-7.08 (m, 1H), 7.25 (s, 1H), 7.36-7.40 (m, 3H), 7.82 (d, J = 16.4 Hz, 1H), 9.08 (s, 1H); ^{13}C NMR (CDCl_3) δ 14.3, 28.3, 55.4, 56.2, 56.3, 80.6, 102.8, 105.8, 111.0, 120.9, 123.8, 124.5, 126.2, 129.7, 130.8, 131.5, 140.6, 148.6, 149.8, 150.3, 153.6, 156.3, 165.9; IR (neat, cm^{-1}) 3060, 3004, 2975, 2835, 2255, 2211, 1701, 1624, 1578, 1505; HRMS Calcd for $\text{C}_{25}\text{H}_{27}\text{O}_5\text{N}$: 421.1889. Found: 421.1895.

***N,N*-Dimethyl (*E*)-3-[6,7-dimethoxy-3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylamide (31).** The reaction mixture was chromatographed using pure EtOAc and 50:1 $\text{CHCl}_3/\text{CH}_3\text{OH}$ to afford 95 mg of the indicated compound as a yellow solid in a 97 % yield: mp 124-126 $^\circ\text{C}$; ^1H NMR (CDCl_3) δ 2.63 (s, 3H), 2.96 (s, 3H), 3.74 (s, 3H), 4.05 (s, 6H), 6.29 (d, J = 15.6 Hz, 1H), 6.93 (d, J = 8.4 Hz, 1H), 7.03-7.07 (m, 1H), 7.25 (s, 1H), 7.30-7.37 (m, 2H), 7.41 (dd, J = 1.6, 7.2 Hz, 1H), 8.02 (d, J = 15.6 Hz, 1H), 9.07 (s, 1H); ^{13}C NMR (CDCl_3) δ 35.7, 36.9, 55.7, 56.2, 56.4, 102.5, 105.7, 111.2, 121.0, 123.6, 124.7, 125.5, 129.3, 130.7, 131.4, 131.4, 137.6, 147.8, 149.4, 150.4, 153.4, 156.2, 166.3; IR (CHCl_3 , cm^{-1}) 3547, 3011, 2937, 2836, 1649, 1618, 1499; HRMS Calcd for $\text{C}_{23}\text{H}_{24}\text{O}_4\text{N}_2$: 392.1736. Found: 392.1742.

6,7-Dimethoxy-3-phenyl-4-[(*E*)-2-methanesulfonylthien-1-yl]isoquinoline (32). The reaction mixture was chromatographed using 1:3 hexane/EtOAc to afford 51 mg of the indicated compound as a pale yellow solid in a 52 % yield: mp 212-214 $^\circ\text{C}$; ^1H NMR (CDCl_3) δ 2.66 (s, 3H), 3.77 (s, 3H), 4.06 (s, 3H), 4.06 (s, 3H), 6.34 (d, J = 15.6 Hz, 1H), 6.96 (d, J = 8.0 Hz, 1H), 7.07-7.11 (m, 1H), 7.14 (s, 1H), 7.28 (s, 1H), 7.37-7.43 (m, 2H), 8.02 (d, J = 15.6 Hz, 1H), 9.12 (s, 1H); ^{13}C NMR (CDCl_3) δ 42.7, 55.8, 56.3, 56.5, 101.9, 105.9, 111.3, 121.3, 122.3, 123.6, 129.6, 130.0, 130.8, 131.6, 132.5, 140.5, 148.1, 150.6, 150.7, 154.0, 156.0; IR (CHCl_3 , cm^{-1}) 3020, 2963, 2838, 1622, 1579; HRMS Calcd for $\text{C}_{21}\text{H}_{21}\text{O}_5\text{SN}$: 399.1140. Found: 399.1148.

***t*-Butyl (*E*)-3-{7-(*o*-methoxyphenyl)-1,3-dioxolo[4,5-*g*]isoquinolin-8-yl}acrylate (34).** The reaction mixtures were chromatographed using 1:1 hexane/EtOAc to afford 62 mg or 83 mg of the indicated compound as a pale yellow solid in a 61 % (entry 26) or an 82 % (entry 27) yield: mp 151-152 $^\circ\text{C}$; ^1H NMR (CDCl_3) δ 1.47 (s, 9H), 3.74 (s, 3H), 5.97 (d, J = 16.4 Hz, 1H), 6.11 (s, 2H), 6.94 (d, J = 8.0 Hz, 1H), 7.03-7.07 (m, 1H), 7.23

(s, 1H), 7.35-7.40 (m, 2H), 7.44 (s, 1H), 7.73 (d, $J = 16.4$ Hz, 1H), 9.01 (s, 1H); ^{13}C NMR (CDCl_3) δ 28.3, 55.4, 80.6, 101.0, 101.9, 103.6, 111.1, 120.9, 125.1, 125.4, 126.6, 129.5, 129.9, 131.5, 132.6, 140.5, 148.3, 148.9, 150.1, 151.8, 156.4, 165.8; IR (CHCl_3 , cm^{-1}) 2977, 2835, 1704, 1640; HRMS Calcd for $\text{C}_{24}\text{H}_{23}\text{O}_5\text{N}$: 405.1576. Found: 405.1584. Anal. Calcd: C, 71.10; H, 5.72; N, 3.46. Found: C, 71.00; H, 5.62; N, 3.43.

***N,N*-Dimethyl (*E*)-3-{7-(*o*-methoxyphenyl)-1,3-dioxolo[4,5-*g*]isoquinolin-8-yl}acrylamide (35).** The reaction mixture was chromatographed using 1:3 hexane/EtOAc and pure EtOAc to afford 61 mg of the *E* isomer as a yellow oil and 23 mg of the *Z* isomer as a yellow oil in a 89 % overall yield. The following characterization data is for the pure major *E* isomer: ^1H NMR (CDCl_3) δ 2.64 (s, 3H), 2.95 (s, 3H), 3.74 (s, 3H), 6.12 (s, 2H), 6.26 (d, $J = 15.6$ Hz, 1H), 6.93 (d, $J = 8.4$ Hz, 1H), 7.03-7.06 (m, 1H), 7.23 (s, 1H), 7.32-7.36 (m, 1H), 7.39 (dd, $J = 1.6, 7.6$ Hz, 1H), 7.41 (s, 1H), 7.90 (d, $J = 15.6$ Hz, 1H), 9.01 (s, 1H); ^{13}C NMR (CDCl_3) δ 35.8, 37.0, 55.8, 100.9, 102.0, 103.5, 111.3, 121.0, 124.9, 125.1, 126.5, 129.5, 130.5, 131.4, 133.3, 137.7, 148.2, 148.5, 149.7, 151.8, 156.3, 166.3; IR (CHCl_3 , cm^{-1}) 3006, 2937, 2836, 1650, 1614; HRMS Calcd for $\text{C}_{22}\text{H}_{20}\text{O}_4\text{N}_2$: 376.1423. Found: 376.1431.

4-{7-(*o*-Methoxyphenyl)-1,3-dioxolo[4,5-*g*]isoquinolin-8-yl}butan-2-one (36). The reaction mixture was chromatographed using 1:3 hexane/EtOAc to afford 42 mg of the indicated compound as a yellow solid in a 48 % yield: mp 174-175 $^\circ\text{C}$; ^1H NMR (CDCl_3) δ 2.02 (s, 3H), 2.57-2.65 (m, 2H), 2.91-3.01 (m, 1H), 3.06-3.16 (m, 1H), 3.75 (s, 3H), 6.12 (s, 2H), 6.99 (d, $J = 8.4$ Hz, 1H), 7.02-7.07 (m, 1H), 7.23-7.25 (m, 3H), 7.36-7.41 (m, 1H), 8.94 (s, 1H); ^{13}C NMR (CDCl_3) δ 23.3, 29.8, 43.7, 55.6, 99.8, 101.8, 104.0, 111.2, 120.9, 125.4, 128.5, 129.6, 130.3, 130.9, 133.3, 148.0, 148.5, 149.4, 151.6, 156.7, 207.9; IR (CHCl_3 , cm^{-1}) 3018, 2963, 2837, 1713, 1603; HRMS Calcd for $\text{C}_{21}\text{H}_{19}\text{O}_4\text{N}$: 349.1314. Found: 349.1320.

***t*-Butyl (*E*)-3-[6-dimethylamino-3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylate (38).** The reaction mixtures were chromatographed using pure EtOAc to afford 70 mg or 68 mg of the indicated compound as a yellow oil in a 69 % (entry 30) or a 67 % (entry 31) yield: ^1H NMR (CDCl_3) δ 1.45 (s, 9H), 3.14 (s, 6H), 3.74 (s, 3H), 6.02 (d, $J = 16.4$ Hz, 1H), 6.93 (d, $J = 8.8$ Hz, 1H), 7.02-7.07 (m, 2H), 7.20 (dd, $J = 2.0, 8.8$ Hz, 1H), 7.35-7.38 (m, 2H), 7.79 (d, $J = 16.4$ Hz, 1H), 7.83 (d, $J = 9.2$ Hz, 1H), 8.99 (s, 1H); ^{13}C NMR

(CDCl₃) δ 28.3, 40.5, 42.8, 55.5, 80.3, 101.0, 111.0, 116.2, 120.9, 123.5, 125.3, 129.6, 129.6, 130.2, 131.5, 136.2, 141.1, 150.1, 151.3, 151.8, 156.4, 166.3; IR (CHCl₃, cm⁻¹) 2975, 2834, 1698, 1613; HRMS Calcd for C₂₅H₂₈O₃N₂: 404.2100. Found: 404.2107.

***N,N*-Dimethyl 3-[6-dimethylamino-3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylamide (39).** The reaction mixture was chromatographed using pure EtOAc and 10:1 CHCl₃/CH₃OH to afford 65 mg of a 91:9 *E/Z* mixture as determined by ¹H NMR spectroscopy of a yellow oil in 89 % overall yield. ¹H NMR (CDCl₃) for the major *E* isomer: δ 2.63 (s, 3H), 2.95 (s, 3H), 3.13 (s, 6H), 3.73 (s, 3H), 6.28 (d, *J* = 15.6 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.93 (s, 1H), 7.02-7.05 (m, 1H), 7.19 (dd, *J* = 1.6, 9.2 Hz, 1H), 7.31-7.35 (m, 1H), 7.38 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.82 (d, *J* = 9.2 Hz, 1H), 7.98 (d, *J* = 15.6 Hz, 1H), 8.96 (s, 1H); additional ¹³C NMR (CDCl₃) for the *E/Z* mixture δ 35.7, 36.9, 40.5, 40.6, 41.1, 55.7, 100.7, 111.3, 116.3, 120.7, 120.8, 120.9, 124.0, 124.5, 129.3, 129.4, 131.3, 136.8, 138.1, 149.1, 150.8, 151.7, 156.3, 166.6 (except for two sp³ carbons from the minor *Z* isomer, all other carbons are from the major *E* isomer); IR (CHCl₃, cm⁻¹) for the *E/Z* mixture 3006, 2937, 2836, 1650, 1614; HRMS Calcd for C₂₃H₂₅O₂N₃: 375.1947. Found: 375.1953.

***t*-Butyl (*E*)-3-[7-dimethylamino-3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylate (41).** The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 71 mg of the indicated compound as a yellow solid in a 71 % yield: mp 163-166 °C; ¹H NMR (CDCl₃) δ 1.47 (s, 9H), 3.09 (s, 6H), 3.73 (s, 3H), 6.05 (d, *J* = 16.4 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 7.00 (s, 1H), 7.03-7.07 (m, 1H), 7.36-7.38 (m, 3H), 7.78 (d, *J* = 16.4 Hz, 1H), 8.06 (d, *J* = 9.2 Hz, 1H), 9.10 (s, 1H); ¹³C NMR (CDCl₃) δ 28.3, 40.7, 55.4, 80.5, 105.4, 111.1, 120.7, 120.9, 125.2, 125.3, 126.3, 126.7, 129.6, 129.6, 129.8, 131.8, 140.8, 146.1, 149.1, 150.9, 156.6, 166.1; IR (CHCl₃, cm⁻¹) 3018, 2979, 2836, 1702, 1621; HRMS Calcd for C₂₅H₂₈O₃N₂: 404.2100. Found: 404.2107.

***N,N*-Dimethyl (*E*)-3-[7-dimethylamino-3-(*o*-methoxyphenyl)isoquinolin-4-yl]acrylamide (42).** The reaction mixture was chromatographed using pure EtOAc and 20:1 CHCl₃/CH₃OH to afford 66 mg of the indicated compound as a yellow solid in a 70 % yield: mp 171-174 °C; ¹H NMR (CDCl₃) δ 2.65 (s, 3H), 2.95 (s, 3H), 3.09 (s, 6H), 3.73 (s, 3H), 6.31 (d, *J* = 15.6 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.99 (d, *J* = 2.8 Hz, 1H), 7.02-7.06 (m, 1H), 7.31-7.40 (m, 3H), 8.00 (d, *J* = 15.6 Hz, 1H), 8.02 (d, *J* = 9.6 Hz, 1H),

9.09 (s, 1H); ^{13}C NMR (CDCl_3) δ 35.8, 37.0, 40.7, 55.7, 105.2, 111.2, 120.5, 120.9, 124.7, 125.1, 126.2, 127.3, 129.2, 129.3, 130.7, 131.6, 137.8, 145.1, 149.2, 150.4, 156.4, 166.5; IR (CHCl_3 , cm^{-1}) 3017, 2837, 2399, 1650, 1621, 1581; HRMS Calcd for $\text{C}_{23}\text{H}_{25}\text{O}_2\text{N}_3$: 375.1947. Found: 375.1953. Anal. Calcd: C, 73.58; H, 6.71; N, 11.19. Found: C, 73.19; H, 6.69; N, 10.98.

***n*-Butyl (*E*)-3-(3-phenyl-5,6,7-trimethoxyisoquinolin-4-yl)acrylate (44).** The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 52 mg of the indicated compound as a yellow oil in a 51 % yield: ^1H NMR (CDCl_3) δ 0.93 (t, J = 7.6 Hz, 3H), 1.32-1.39 (m, 2H), 1.57-1.63 (m, 2H), 3.81 (s, 3H), 4.02 (s, 3H), 4.04 (s, 3H), 4.12 (t, J = 6.4 Hz, 2H), 5.49 (d, J = 16.0 Hz, 1H), 7.12 (s, 1H), 7.28-7.32 (m, 1H), 7.36-7.40 (m, 2H), 7.52 (d, J = 7.6 Hz, 2H), 8.57 (d, J = 16.4 Hz, 1H), 9.09 (s, 1H); ^{13}C NMR (CDCl_3) δ 13.9, 19.3, 30.9, 56.3, 61.0, 61.4, 64.3, 102.6, 123.3, 123.7, 125.0, 127.1, 127.7, 128.2, 130.5, 140.8, 145.7, 146.6, 149.0, 150.3, 150.7, 154.0, 166.8; IR (CHCl_3 , cm^{-1}) 3058, 2960, 2871, 1709, 1636, 1612, 1483; HRMS Calcd for $\text{C}_{25}\text{H}_{27}\text{O}_5\text{N}$: 421.1889. Found: 421.1897.

***t*-Butyl (*E*)-3-(3-phenyl-5,6,7-trimethoxyisoquinolin-4-yl)acrylate (45).** The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 63 mg of the indicated compound as a yellow oil in a 62 % yield: ^1H NMR (CDCl_3) δ 1.45 (s, 9H), 3.81 (s, 3H), 4.02 (s, 3H), 4.03 (s, 3H), 5.41 (d, J = 16.0 Hz, 1H), 7.11 (s, 1H), 7.29-7.33 (m, 1H), 7.37-7.40 (m, 2H), 7.53-7.55 (m, 2H), 8.46 (d, J = 16.4 Hz, 1H), 9.07 (d, 1H); ^{13}C NMR (CDCl_3) δ 28.3, 56.3, 60.9, 61.3, 80.2, 102.5, 123.8, 124.9, 125.0, 127.2, 127.6, 128.1, 130.6, 140.9, 144.6, 146.5, 149.0, 150.2, 150.6, 154.0, 166.0; IR (neat, cm^{-1}) 3058, 2976, 2937, 2840, 2253, 1698, 1636, 1611, 1484; HRMS Calcd for $\text{C}_{25}\text{H}_{27}\text{O}_5\text{N}$: 421.1889. Found: 421.1895.

***N,N*-Dimethyl (*E*)-3-[3-phenyl-5,6,7-trimethoxyisoquinolin-4-yl]acrylamide (46).** The reaction mixture was chromatographed using 1:1 hexane/EtOAc and 20:1 $\text{CHCl}_3/\text{CH}_3\text{OH}$ to afford 49 mg of the indicated compound as a white solid in a 50 % yield: mp 169-171 $^\circ\text{C}$; ^1H NMR (CDCl_3) δ 2.43 (s, 3H), 2.92 (s, 3H), 3.90 (s, 3H), 4.02 (s, 3H), 4.04 (s, 3H), 5.90 (d, J = 15.6 Hz, 1H), 7.11 (s, 1H), 7.28-7.31 (m, 1H), 7.36-7.40 (m, 2H), 7.53-7.55 (m, 2H), 8.43 (d, J = 15.6 Hz, 1H), 9.07 (s, 1H); ^{13}C NMR (CDCl_3) δ 35.6, 36.7, 56.3, 61.3, 61.3, 102.4, 124.7, 124.9, 125.1, 127.3, 127.3, 128.2, 130.7, 141.7,

141.8, 146.6, 149.4, 150.0, 150.8, 154.0, 166.8; IR (CHCl₃, cm⁻¹) 3017, 2941, 1648, 1611, 1580; HRMS Calcd for C₂₃H₂₄O₄N₂: 392.1736. Found: 392.1742.

5,6,7-Trimethoxy-3-phenyl-4-[(E)-2-phenylethen-1-yl]isoquinoline (47). The reaction mixture was chromatographed using 2:1 hexane/EtOAc to afford 77 mg of the indicated compound as a yellow solid in a 78 % yield: mp 133-135 °C; ¹H NMR (CDCl₃) δ 3.74 (s, 3H), 4.02 (s, 3H), 4.03 (s, 3H), 6.12 (d, *J* = 16.4 Hz, 1H), 7.11 (s, 1H), 7.17-7.28 (m, 6H), 7.32-7.35 (m, 2H), 7.59-7.61 (m, 2H), 7.86 (d, *J* = 16.4 Hz, 1H), 9.06 (s, 1H); ¹³C NMR (CDCl₃) δ 56.2, 61.4, 61.4, 102.7, 125.4, 126.1, 126.2, 127.1, 127.3, 127.6, 128.0, 128.3, 128.7, 130.6, 133.9, 138.2, 141.9, 146.6, 149.4, 149.7, 151.0, 153.7; IR (CHCl₃, cm⁻¹) 3018, 2940, 1612, 1482; HRMS Calcd for C₂₆H₂₃O₃N: 397.1678. Found: 397.1685. Anal. Calcd: C, 78.57; H, 5.83; N, 3.52. Found: C, 78.20; H, 5.69; N, 3.47.

4-{8-Phenyl-1,3-dioxolo[4,5-f]isoquinolin-9-yl}butan-2-one (49). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 41 mg of the indicated compound as a yellow solid in a 50 % yield: mp 161-164 °C; ¹H NMR (CDCl₃) δ 2.06 (s, 3H), 2.69 (dd, *J* = 6.0, 8.1 Hz, 2H), 3.31-3.36 (m, 2H), 6.17 (s, 2H), 7.27-7.32 (m, 1H), 7.40-7.47 (m, 5H), 7.63 (d, *J* = 8.4 Hz, 1H), 9.04 (s, 1H); ¹³C NMR (CDCl₃) δ 23.5, 28.6, 44.5, 100.6, 110.6, 121.6, 122.9, 123.2, 124.2, 126.8, 127.3, 128.1, 139.6, 139.7, 146.8, 149.5, 151.5, 206.6; IR (CHCl₃, cm⁻¹) 3018, 1709, 1632, 1572, 1503; HRMS Calcd for C₂₀H₁₇O₄N: 319.1208. Found: 319.1212.

1-Phenyl-3-{8-phenyl-1,3-dioxolo[4,5-f]isoquinolin-9-yl}propan-1-one (50). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 34 mg of the indicated compound as a yellow solid in a 36 % yield: mp 184-186 °C; ¹H NMR (CDCl₃) δ 3.20-3.34 (m, 2H), 3.50-3.54 (m, 2H), 6.10 (s, 2H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.37-7.54 (m, 8H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.80-7.82 (m, 2H), 9.06 (s, 1H); ¹³C NMR (CDCl₃) δ 25.3, 40.8, 101.9, 111.8, 122.9, 124.1, 124.7, 125.4, 128.0, 128.2, 128.6, 128.7, 129.3, 133.1, 136.8, 140.9, 140.9, 148.0, 150.7, 152.8, 199.1; IR (CHCl₃, cm⁻¹) 3018, 1685, 1632, 1598, 1580, 1503; HRMS Calcd for C₂₅H₁₉O₃N: 381.1365. Found: 381.1373.

6-{8-Phenyl-1,3-dioxolo[4,5-f]isoquinolin-9-yl}hexan-2-one (51). The reaction mixture was chromatographed using 1:1 hexane/EtOAc to afford 24 mg of the indicated compound as a yellow oil in a 27 % yield: ¹H NMR (CDCl₃) δ 1.54-1.58 (m, 4H), 2.06

(s, 3H), 2.29 (t, $J = 7.2$ Hz, 2H), 3.04 (t, $J = 7.6$ Hz, 2H), 6.20 (s, 2H), 7.26-7.31 (m, 1H), 7.41-7.50 (m, 5H), 7.60 (d, $J = 8.4$ Hz, 1H), 9.02 (s, 1H); ^{13}C NMR (CDCl_3) δ 23.6, 29.7, 29.8, 31.4, 43.1, 101.5, 111.5, 122.8, 123.7, 125.2, 125.7, 127.6, 128.1, 129.3, 140.8, 141.0, 147.7, 150.1, 152.0, 208.9; IR (CHCl_3 , cm^{-1}) 3017, 2959, 1711, 1632, 1571, 1503, 1503; HRMS Calcd for $\text{C}_{22}\text{H}_{21}\text{O}_3\text{N}$: 347.4130. Found: 347.4136.

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data/drxl/nmr400/qh163-1.fid

Compound **32**, Table **3**

9.063
7.887
7.846
7.611
7.608
7.590
7.353
7.335
7.315
7.280
7.269
7.254
7.245
7.227
7.209
7.199
7.188
7.113
6.136
6.095

4.030
4.024
3.742

Compound 47, Table 3