Pd-Catalyzed Alkyl to Aryl Migration and Cyclization: An Efficient Synthesis of Fused Polycycles via Multiple C-H Activation

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General procedures. All ^1H and ^{13}C NMR spectra were recorded at 300 and 75.5 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), 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] and/or an acidic *p*-anisaldehyde stain [657 mL of EtOH (99 %) + 25 mL of conc. H_2SO_4 + 7.5 mL of glacial $\text{CH}_3\text{CO}_2\text{H}$ + 10.5 mL of *p*-anisaldehyde]. High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV. 2-Iodo-5-methoxyphenol,¹ 2-iodo-5-nitrophenol,² 2,5-diiodo-1,4-dihydroquinone³ and compound **22**⁴ were prepared according to literature procedures.

3-Phenyl-3-buten-1-ol. This compound was prepared by a modified literature procedure.⁵ To a stirred mixture of $\text{Pd(PPh}_3)_4$ (0.346 g, 0.3 mmol), Na_2CO_3 (2 M aq

solution, 10 mL, 20 mmol), benzene (20 mL) and 3-bromo-3-buten-1-ol (1.51 g, 10 mmol) was added dropwise a clear solution of PhB(OH)₂ (1.57 g, 13 mmol) in EtOH (10 mL) at 25 °C. The resulting mixture was then heated to reflux under an Ar atmosphere (oil bath temperature is 70 °C). After 12 h, the mixture was cooled to 25 °C and 1.5 mL of 30 % aq H₂O₂ was added dropwise. The resulting mixture was stirred at 25 °C for 30 min, diluted with Et₂O (30 mL) and washed with brine (50 mL). The organic layer was dried over Na₂SO₄, concentrated, and the residue was chromatographed (2:1 hexane/EtOAc) to afford 1.16 g of the indicated compound (78 % yield) as a yellow oil: ¹H NMR (CDCl₃) δ 1.42 (s, 1H), 2.80 (t, *J* = 6.4 Hz, 2H), 3.73 (t, *J* = 6.4 Hz, 2H), 5.17 (d, *J* = 0.8 Hz, 1H), 5.42 (d, *J* = 0.8 Hz, 1H), 7.26-7.36 (m, 3H), 7.41-7.43 (m, 2H).

3-Phenyl-3-butenyl tosylate. To a solution of TsCl (0.96 g, 5.05 mmol) in CH₂Cl₂ (10 mL) was added dropwise a solution of 3-phenyl-3-buten-1-ol (0.74 g, 5.0 mmol) in CH₂Cl₂ (5 mL) at 0 °C under an Ar atmosphere. Et₃N (0.7 mL, 5.05 mol) was added slowly and the reaction mixture was stirred at 25 °C until the reaction reached completion as indicated by thin layer chromatography. The reaction mixture was diluted with Et₂O (20 mL), washed with brine (30 mL), and the organic layer was dried over Na₂SO₄. The solvent was removed under reduced pressure and the residue was chromatographed (5:1 hexane/EtOAc) to afford 1.23 g of the indicated compound (82 % yield) as a brown oil: ¹H NMR (CDCl₃) δ 2.44 (s, 3H), 2.86 (dt, *J* = 0.8, 7.2 Hz, 2H), 4.10 (t, *J* = 7.2 Hz, 2H), 5.08 (s, 1H), 5.34 (s, 1H), 7.25-7.31 (m, 7H), 7.72-7.74 (m, 2H); ¹³C NMR (CDCl₃) δ 21.8, 35.0, 68.9, 115.5, 126.2, 128.0, 128.1, 128.7, 130.0, 133.3, 139.9, 143.0, 144.9.

2-Iodophenyl 3-phenyl-3-butenyl ether (1). To a suspension of NaH (60 % in mineral oil, 44 mg, 1.12 mmol) in dry DMF (1.5 mL) was added a solution of 2-

iodophenol (0.23 g, 1.02 mmol) in dry DMF (2.0 mL) at 0 °C under an Ar atmosphere. Lots of bubbles were generated. After 20 min, a solution of 3-phenyl-3-butenyl tosylate (0.28 g, 0.93 mmol) in dry DMF (2.0 mL) was added slowly. The reaction mixture was allowed to warm to and stirred at 25 °C for 1 d, diluted with Et₂O (20 mL), and washed with brine (20 mL). The organic layer was dried over Na₂SO₄, filtered, and concentrated under reduce pressure. The residue was chromatographed (35:1 hexane/EtOAc) to afford 0.15 g of the indicated compound (46 % yield) as a yellow oil: ¹H NMR (CDCl₃) δ 3.07 (dt, *J* = 0.9, 6.9 Hz, 2H), 4.10 (t, *J* = 6.9 Hz, 2H), 5.25-5.27 (m, 1H), 5.43 (d, *J* = 1.2 Hz, 1H), 6.65-6.71 (m, 1H), 6.73 (dd, *J* = 1.2, 8.4 Hz, 1H), 7.21-7.37 (m, 4H), 7.45-7.48 (m, 2H), 7.76 (dd, *J* = 2.0, 8.4 Hz, 1H); ¹³C NMR (CDCl₃) δ 35.3, 68.2, 86.9, 112.5, 115.2, 122.7, 126.4, 127.9, 128.7, 129.6, 139.7, 140.8, 144.5, 157.6; IR (neat, cm⁻¹) 3080, 3056, 2946, 1581, 1464; HRMS Calcd for C₁₆H₁₅IO: 350.0168. Found: 350.0171.

***N*-(2-Iodophenyl)-*N*-(3-phenyl-3-butenyl)methanesulfonamide (**3**).** To a stirred mixture of 3-phenyl-3-buten-1-ol (0.296 g, 1.3 mmol), PPh₃ (0.34 g, 1.3 mmol), *N*-(2-iodophenyl)methanesulfonamide (0.297 g, 1.0 mmol) and CH₂Cl₂ (10 mL) was added slowly a solution of diethyl azodicarboxylate (DEAD) (0.20 mL, 1.3 mmol) in CH₂Cl₂ (2 mL) at 0 °C under an Ar atmosphere. The resulting yellow solution was stirred at 0 °C for 2 h, diluted with Et₂O (20 mL), and washed with brine (20 mL). The organic layer was dried over Na₂SO₄ and the solvent was removed under reduced pressure. The

residue was chromatographed (3:1 hexane/EtOAc) to afford 0.14 g of the indicated compound (34 % yield) as a colorless oil: ^1H NMR (CDCl_3) δ 2.77-2.92 (m, 2H), 3.04 (s, 3H), 3.59-3.68 (m, 1H), 3.79-3.88 (m, 1H), 5.07 (s, 1H), 5.35 (s, 1H), 7.07-7.12 (m, 1H), 7.25-7.33 (m, 5H), 7.40-7.44 (m, 1H), 7.47 (dd, $J = 1.6, 7.6$ Hz, 1H), 7.94-7.96 (m, 1H); ^{13}C NMR (CDCl_3) δ 34.8, 41.0, 50.9, 101.6, 114.5, 126.1, 128.0, 128.7, 129.5, 130.4, 132.7, 140.0, 140.7, 141.2, 144.7; IR (CDCl_3 , cm^{-1}) 3081, 3055, 3023, 2932, 1763, 1721, 1626, 1466, 1340; HRMS Calcd for $\text{C}_{17}\text{H}_{18}\text{INO}_2\text{S}$: 427.0103. Found: 427.0114.

Diethyl 2-(2-iodobenzyl)-2-(2-phenylallyl)malonate (5). Using the procedure used to prepare compound **1**, but employing diethyl 2-(2-iodobenzyl)malonate and 2-phenylallyl bromide, afforded compound **5** in an 82 % yield (19:1 hexane/EtOAc) as a yellow oil: ^1H NMR (CDCl_3) δ 1.05 (t, $J = 7.2$ Hz, 6H), 3.33 (s, 2H), 3.40 (s, 2H), 3.76-3.90 (m, 4H), 5.80 (d, $J = 1.2$ Hz, 1H), 5.28 (d, $J = 1.2$ Hz, 1H), 6.81-6.87 (m, 1H), 7.17-7.36 (m, 7H), 7.79 (dd, $J = 1.2, 8.1$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 13.9, 39.6, 43.0, 58.3, 61.5, 103.4, 118.7, 127.0, 127.7, 128.1, 128.2, 128.3, 130.0, 139.8, 140.5, 141.7, 144.4, 170.7; IR (CDCl_3 , cm^{-1}) 3057, 2981, 1728, 1626, 1468, 1444; HRMS Calcd for $\text{C}_{23}\text{H}_{25}\text{IO}_4$: 492.0798. Found: 492.0809.

3-(2-Naphthyl)-3-buten-1-ol. Using the procedure used to prepare 3-phenyl-3-buten-1-ol, but employing 3-bromo-3-buten-1-ol and 2-naphthylboronic acid, afforded the indicated compound in a 76 % yield (4:1 hexane/EtOAc) as a yellow solid: mp 45-46 °C; ¹H NMR (CDCl₃) δ 1.58 (br s, 1H), 2.92 (dt, *J* = 0.9, 6.4 Hz, 2H), 3.79 (t, *J* = 6.4 Hz, 2H), 5.28 (d, *J* = 1.0 Hz, 1H), 5.57 (d, *J* = 1.0 Hz, 1H), 7.45-7.52 (m, 2H), 7.59 (dd, *J* = 1.7, 8.7 Hz, 1H), 7.80-7.85 (m, 4H); ¹³C NMR (CDCl₃) 38.8, 61.3, 115.4, 124.7, 125.1, 126.3, 126.5, 127.8, 128.3, 128.4, 133.1, 133.6, 137.8, 144.8.

3-(2-Naphthyl)-3-butenyl tosylate. Using the procedure used to prepare 3-phenyl-3-butenyl tosylate, but employing 3-(2-naphthyl)-3-buten-1-ol, afforded the indicated compound in a 60 % yield (7:3 hexane/EtOAc) as a yellow oil: ¹H NMR (CDCl₃) δ 2.35 (s, 3H), 2.98 (dt, *J* = 0.9, 6.9 Hz, 2H), 4.15 (t, *J* = 6.9 Hz, 2H), 5.19 (d, *J* = 0.9 Hz, 1H), 5.49 (s, 1H), 7.17-7.20 (m, 2H), 7.42-7.48 (m, 3H), 7.66-7.69 (m, 3H), 7.73-7.78 (m, 3H); ¹³C NMR (CDCl₃) δ 21.7, 35.0, 68.9, 116.1, 124.4, 124.9, 126.3, 126.5, 127.2, 127.7, 128.0, 128.3, 128.3, 129.9, 133.1, 133.4, 137.0, 142.8, 144.8.

2-Iodophenyl 3-(2-naphthyl)-3-butenyl ether (7). Using the procedure used to prepare compound **1**, but employing 2-iodophenol and 3-(2-naphthyl)-3-butenyl tosylate, afforded the indicated compound in a 58 % yield (30:1 hexane/EtOAc) as a colorless oil:

^1H NMR (CDCl_3) δ 3.18 (t, $J = 6.9$ Hz, 2H), 4.14 (t, $J = 6.9$ Hz, 2H), 5.36 (s, 1H), 5.57 (s, 1H), 6.64-6.72 (m, 2H), 7.18-7.23 (m, 1H), 7.44-7.48 (m, 2H), 7.62 (dd, $J = 1.5, 8.4$ Hz, 1H), 7.73-7.88 (m, 5H); ^{13}C NMR (CDCl_3) 35.3, 68.3, 86.9, 112.5, 115.7, 122.7, 124.8, 125.0, 126.2, 126.4, 127.7, 128.2, 128.4, 129.6, 133.1, 133.6, 137.9, 139.7, 144.3, 157.6; IR (CHCl_3 , cm^{-1}) 3056, 3009, 2931, 1581, 1477, 1459; HRMS Calcd for $\text{C}_{20}\text{H}_{17}\text{IO}$: 400.0324. Found: 400.0332.

2-Iodo-5-methoxyphenyl 3-(2-naphthyl)-3-butenyl ether (9). Using the procedure used to prepare compound **1**, but employing 2-iodo-5-methoxyphenol¹ and 3-(2-naphthyl)-3-butenyl tosylate, afforded the indicated compound in a 56 % yield (24:1 hexane/EtOAc) as a white solid: mp 72-73 °C; ^1H NMR (CDCl_3) δ 3.18 (t, $J = 7.2$ Hz, 2H), 3.70 (s, 3H), 4.11 (t, $J = 7.2$ Hz, 2H), 5.36 (s, 1H), 5.57 (s, 1H), 6.28 (dd, $J = 1.6, 8.4$ Hz, 1H), 6.31 (d, $J = 2.8$ Hz, 1H), 7.42-7.49 (m, 2H), 7.59 (d, $J = 8.8$ Hz, 1H), 7.62 (dd, $J = 1.6, 8.8$ Hz, 1H), 7.79-7.84 (m, 3H), 7.88 (s, 1H); ^{13}C NMR (CDCl_3) 35.1, 55.5, 68.1, 75.5, 100.2, 107.4, 115.6, 124.6, 124.9, 126.1, 126.3, 127.6, 128.1, 128.3, 132.9, 133.4, 137.7, 139.2, 144.0, 158.2, 161.3; IR (CHCl_3 , cm^{-1}) 3057, 3013, 2937, 1577, 1483, 1304; HRMS Calcd for $\text{C}_{21}\text{H}_{19}\text{IO}_2$: 430.0430. Found: 430.0435.

2-Iodo-5-nitrophenyl 3-(2-naphthyl)-3-butenyl ether (11). Using the procedure used to prepare compound **1**, but employing 2-iodo-5-nitrophenol² and 3-(2-naphthyl)-3-butenyl tosylate, afforded the indicated compound in a 30 % yield (35:1 hexane/EtOAc) as a pale yellow solid: mp 94-96 °C; ^1H NMR (CDCl_3) δ 3.23 (t, $J = 6.6$ Hz, 2H), 4.24 (t, $J = 6.6$ Hz, 2H), 5.39 (d, $J = 0.6$ Hz, 1H), 5.60 (s, 1H), 7.43-7.56 (m, 4H), 7.62 (dd, $J = 1.8, 9.7$ Hz, 1H), 7.81-7.94 (m, 5 H); ^{13}C NMR (CDCl_3) δ 35.1, 68.9, 95.7, 106.2, 116.2, 117.0, 124.7, 125.1, 126.3, 126.6, 127.8, 128.4, 128.4, 133.1, 133.6, 137.6, 139.9, 143.9,

149.3, 158.2; IR (CHCl₃, cm⁻¹) 3018, 2927, 1569, 1525, 1349; HRMS Calcd for C₂₀H₁₆INO₅: 445.0175. Found: 445.0186.

2-Iodo-1-(methoxymethoxy)naphthalene. To a stirred solution of 1-(methoxymethoxy)naphthalene (1.75 g, 9.3 mmol) in dry THF (45 mL) was added *n*-BuLi (2.5 M in hexane, 4.5 mL, 11.2 mmol) at -78 °C under an Ar atmosphere. The reaction mixture was then warmed to and stirred at 25 °C. After 30 min, the resulting deep orange solution was cooled to -78 °C and a solution of I₂ (4.0 g, 11.2 mmol) in dry THF (20 mL) was added dropwise. The resulting deep blue solution was stirred at -78 °C for another 10 min and then warmed to 25 °C. The reaction mixture was diluted with Et₂O (30 mL) and excess I₂ was destroyed by satd aq Na₂S₂O₃ (30 mL). The organic layer was dried over Na₂SO₄ and the solvent was removed under reduced pressure. The residue was chromatographed (19:1 hexane/EtOAc) on silica gel to afford 2.0 g of the indicated compound in a 68 % yield as a yellow oil: ¹H NMR (CDCl₃) δ 3.76 (s, 3H), 5.25 (s, 2H), 7.39 (s, *J* = 8.7 Hz, 1H), 7.48-7.54 (m, 2H), 7.79 (d, *J* = 8.7 Hz, 1H), 7.81-7.83 (m, 1H), 8.15-8.19 (m, 1H).

2-Iodo-1-naphthol. To a stirred mixture of NaI (0.91 mg, 6.0 mmol), 2-iodo-1-(methoxymethoxy)naphthalene (0.96 g, 3.0 mmol) and CH₃CN (30 mL) was added dropwise TMSCl (0.57 mL, 4.5 mmol) at 0 °C under an Ar atmosphere. The mixture was stirred at 0 °C for 10 min and then warmed to 25 °C. As the reaction proceeded, the reaction mixture became more and more cloudy. After 2 h, the reaction was diluted with Et₂O (30 mL) and washed with satd aq Na₂S₂O₃ (30 mL). The organic layer was dried over Na₂SO₄, filtered, and the solvent was removed under reduced pressure. The residue was chromatographed (4:1 hexane/EtOAc) on silica gel to afford 0.35 g of the indicated compound in a 43 % yield as a yellow solid: mp 54-55 °C; ¹H NMR (CDCl₃) δ 5.72 (s, 1H), 7.20 (d, *J* = 8.7 Hz, 1H), 7.46-7.54 (d, *J* = 2 H), 7.61 (d, *J* = 9.7 Hz, 1H), 7.75-7.79 (m, 1H), 8.22-8.25 (m, 1H); ¹³C NMR (CDCl₃) δ 79.5, 122.2, 122.8, 123.9, 126.3, 127.3, 127.7, 133.8, 134.7, 151.3.

2-Iodonaphth-1-yl 3-phenyl-3-butenyl ether (13). Using the procedure used to prepare compound **1**, but employing 2-iodo-1-naphthol and 3-phenyl-3-butenyl tosylate, afforded compound **13** in a 36 % yield (49:1 hexane/EtOAc) as a white solid: mp 74-75 °C; ¹H NMR (CDCl₃) δ 3.26 (dt, *J* = 0.9, 6.9 Hz, 2H), 4.15 (t, *J* = 6.9 Hz, 2H), 5.31 (d, *J* = 1.2 H, 1H), 5.48 (d, *J* = 1.2 Hz, 1H), 7.27-7.49 (m, 6H), 7.51-7.55 (m, 2H), 7.74 (d, *J* = 8.7 Hz, 1H), 7.77-7.80 (m, 1H), 7.91-7.94 (m, 1H); ¹³C NMR (CDCl₃) δ 36.3, 73.0, 87.8, 114.9, 122.4, 125.8, 126.4, 126.7, 126.9, 127.9, 128.1, 128.7, 128.7, 134.9, 135.4, 140.7, 144.7, 155.6; IR (CHCl₃, cm⁻¹) 3056, 3016, 2928, 1598, 1497, 1361; HRMS Calcd for C₂₀H₁₇IO: 400.0324. Found: 400.0331.

3-Benzofuran-2-yl-3-buten-1-ol. Using the procedure used to prepare 3-phenyl-3-buten-1-ol, but employing benzofuran-2-boronic acid and 3-bromo-3-buten-1-ol, afforded the indicated compound in a 78 % yield (4:1 hexane/EtOAc) as a yellow oil: ^1H NMR (CDCl_3) δ 1.83 (br s, 1H), 2.73 (t, J = 5.6 Hz, 2H), 3.87 (dt, J = 0.8, 5.6 Hz, 2H), 5.27 (s, 1H), 5.94 (s, 1H), 6.69 (s, 1H), 7.19-7.22 (m, 1H), 7.26-7.30 (m, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H); ^{13}C NMR (CDCl_3) 36.7, 61.6, 103.2, 111.2, 114.9, 121.2, 123.0, 124.9, 129.0, 134.1, 154.9, 155.9.

***N*-(3-Benzofuran-2-yl-3-butenyl)-*N*-(2-iodophenyl)methanesulfonamide (15).**

Using the procedure used to prepare compound **3**, but employing 3-benzofuran-2-yl-3-buten-1-ol and *N*-(2-iodophenyl)methanesulfonamide, afforded the indicated compound in a 78 % yield (3:1 hexane/EtOAc) as a yellow oil: ^1H NMR (CDCl_3) δ 2.72-2.80 (m, 1H), 2.84-2.91 (m, 1H), 3.10 (s, 3H), 3.70-3.74 (m, 1H), 3.97-4.02 (m, 1H), 5.18 (s, 1H), 5.85 (s, 1H), 6.68 (s, 1H), 7.11-7.15 (m, 1H), 7.17-7.21 (m, 1H), 7.24-7.28 (m, 1H), 7.41 (dd, J = 0.4, 8.0 Hz, 1H), 7.44-7.48 (m, 1H), 7.52-7.54 (m, 2H), 7.98 (dd, J = 1.2, 8.0 Hz, 1H); ^{13}C NMR (CDCl_3) 33.4, 41.2, 51.7, 101.3, 103.4, 111.1, 114.9, 121.4, 123.0, 125.0,

129.0, 129.6, 130.6, 132.9, 133.9, 140.8, 141.1, 154.9, 155.4; IR (neat, cm^{-1}) 3060, 2980, 1799, 1722, 1467, 1339; HRMS Calcd for $\text{C}_{19}\text{H}_{18}\text{INO}_3\text{S}$: 467.0052. Found: 467.0062.

3-Iodo-4-(methoxymethoxy)phenyl phenyl ether. Using the procedure used to prepare 2-iodo-1-(methoxymethoxy)naphthalene, but employing 4-(methoxymethoxy)phenyl phenyl ether, afforded the indicated compound in a 70 % yield (15:1 hexane/EtOAc) as a colorless oil: ^1H NMR (CDCl_3) δ 3.53 (s, 3H), 5.20 (s, 2H), 6.95-6.99 (m, 3H), 7.04 (d, $J = 8.8$ Hz, 1H), 7.07-7.11 (m, 1H), 7.30-7.34 (m, 2H), 7.45 (d, $J = 2.8$ Hz, 1H); ^{13}C NMR (CDCl_3) 56.7, 87.5, 95.8, 115.9, 118.4, 120.4, 123.4, 130.0, 130.3, 152.1, 152.7, 157.8.

2-Iodo-4-phenoxyphenol. Using the procedure used to prepare 2-iodo-1-naphthol, but employing 3-iodo-4-(methoxymethoxy)phenyl phenyl ether, afforded the indicated compound in a 100 % yield (7:1 hexane/EtOAc) as a yellow oil: ^1H NMR (CDCl_3) δ 5.11 (s, 1H), 6.93-6.97 (m, 4H), 7.05-7.11 (m, 1H), 7.29-7.35 (m, 3H); ^{13}C NMR (CDCl_3) 85.3, 115.5, 118.1, 121.8, 123.2, 129.0, 130.0, 150.8, 151.5, 158.1.

2-Iodo-4-phenoxyphenyl 3-methyl-3-butenyl ether (17). Using the procedure used to prepare compound **1**, but employing 2-iodo-4-phenoxyphenol and 3-methyl-3-butenyl tosylate, afforded compound **17** in a 62 % yield (30:1 hexane/EtOAc) as a yellow oil: ^1H NMR (CDCl_3) δ 1.85 (s, 3H), 2.57 (t, J = 6.8 Hz, 2H), 4.10 (t, J = 6.8 Hz, 2H), 6.78 (d, J = 9.2 Hz, 1H), 6.93-6.96 (m, 2H), 6.99 (dd, J = 2.8, 9.2 Hz, 1H), 7.05-7.09 (m, 1H), 7.30-7.34 (m, 2H), 7.47 (d, J = 2.8 Hz, 1H); ^{13}C NMR (CDCl_3) δ 23.3, 37.4, 68.9, 86.9, 112.6, 112.7, 118.1, 120.5, 123.1, 129.9, 130.7, 142.3, 150.9, 154.3, 158.1; IR (neat, cm^{-1}) 3072, 2967, 1649, 1587, 1482; HRMS Calcd for $\text{C}_{17}\text{H}_{17}\text{IO}_2$: 380.0273. Found: 380.0282.

1,4-Diiodo-2,5-bis(3-phenyl-3-butenyloxy)benzene (19). Using the procedure used to prepare compound **1**, but employing 2,5-diiodo-1,4-diphenol³ and 3-phenyl-3-butenyl tosylate, afforded compound **19** in a 44 % yield (9:1 hexane/EtOAc) as a white solid: mp 118-119 °C; ^1H NMR (CDCl_3) δ 3.02 (t, J = 6.8 Hz, 4H), 4.00 (t, J = 6.8 Hz, 4H), 5.23 (s, 2H), 5.41 (s, 2H), 7.08 (s, 2H), 7.26-7.29 (m, 2H), 7.32-7.36 (m, 4H), 7.44 (d, J = 7.6 Hz, 4H); ^{13}C NMR (CDCl_3) δ 35.3, 69.2, 86.5, 115.2, 123.2, 126.4, 127.9, 128.7, 140.6, 144.3, 152.9; IR (CHCl_3 , cm^{-1}) 3089, 3019, 2933, 2914, 1622, 1571, 1484, 1448; HRMS Calcd for $\text{C}_{26}\text{H}_{24}\text{IO}_2$: 621.9866. Found: 621.9880.

2-Iodophenyl 3-methyl-3-butenyl ether (24). Using the procedure used to prepare compound **1**, but employing 2-iodophenol and 3-methyl-3-butenyl tosylate, afforded compound **24** in an 80 % yield (30:1 hexane/EtOAc) as a colorless oil: ^1H NMR (CDCl_3) δ 1.84 (s, 3H), 2.57 (t, J = 6.9 Hz, 2H), 4.12 (t, J = 6.9 Hz, 2H), 4.84-4.85 (m, 1H), 4.85-4.86 (m, 1H), 6.70 (dt, J = 1.5, 7.5 Hz, 1H), 6.81 (dd, J = 1.2, 8.4 Hz, 1H), 7.25-7.31 (m, 1H), 7.76 (dd, J = 1.5, 7.8 Hz, 1H); ^{13}C NMR (CDCl_3) δ 23.2, 37.3, 68.2, 86.9, 112.3, 112.6, 122.7, 129.6, 139.7, 142.3, 157.7; IR (CHCl_3 , cm^{-1}) 3021, 1610; HRMS Calcd for $\text{C}_{11}\text{H}_{13}\text{IO}$: 273.9855. Found: 273.9860.

General procedure for the 1,4-palladium alkyl to aryl migration. A mixture of aryl halide (0.25 mmol), $\text{Pd}(\text{OAc})_2$ (2.8 mg, 0.0125 mmol), *bis*(diphenylphosphino)methane (4.8 mg, 0.0125 mmol), cesium pivalate (0.1170 g, 0.5 mmol), and the indicated amounts of alkene (if employed) in dry DMF (4 mL) was quickly flushed with argon and stirred at the indicated reaction temperature. The reaction was monitored by TLC and gas chromatographic analysis. After the reaction was complete, it was diluted with ethyl ether, washed with satd aq NaHCO_3 , dried over Na_2SO_4 , concentrated, and purified by flash chromatography on silica gel.

10b-Methyl-1,10b-dihydro-2H-indeno[1,2,3-*de*]chromene (2). The reaction mixture was chromatographed using 40:1 hexane/EtOAc to afford 49 mg of the indicated compound (88 % yield) as a white solid: mp 51-53 °C; ^1H NMR (CDCl_3) δ 1.46 (s, 3H), 1.63-1.70 (ddd, J = 8.0, 11.2, 11.2 Hz, 1H), 2.29-2.33 (ddd, J = 0.8, 8.0, 11.2 Hz, 1H), 4.56 (ddd, J = 0.8, 8.0, 13.2 Hz, 1H), 4.65 (ddd, J = 8.0, 11.2, 13.2 Hz, 1H), 6.71-6.75 (m, 1H), 7.22-7.26 (m, 2H), 7.29 (dd, J = 1.2, 7.2 Hz, 1H), 7.33-7.37 (m, 1H), 7.42-7.44 (m, 1H), 7.69-7.72 (m, 1H); ^{13}C NMR (CDCl_3) δ 25.7, 31.0, 42.6, 65.7, 112.5, 113.8, 121.3, 123.2, 127.1, 127.5, 129.5, 134.9, 140.4, 140.6, 153.0, 153.9; IR (CHCl_3 , cm^{-1}) 3053, 3010, 2963, 2919, 1614, 1592, 1486, 1447; HRMS Calcd for $\text{C}_{16}\text{H}_{14}\text{O}$: 222.1045. Found: 222.1048.

10b-Methyl-3-trifluoromethanesulfonyl-1,2,3,10b-tetrahydroindeno[1,2,3-*de*]quinoline (4). The reaction mixture was chromatographed using 40:1 hexane/EtOAc to afford 71 mg of the indicated compound (95 % yield) as a white solid: mp 111-112 °C; ^1H NMR (CDCl_3) δ 1.42 (s, 3H), 1.45-1.58 (m, 1H), 2.49-2.55 (m, 1H), 3.94-4.11 (m, 2H), 7.29-7.40 (m, 3H), 7.43-7.45 (m, 2H), 7.57 (d, J = 8.1 Hz, 1H), 7.71-7.74 (m, 1H); ^{13}C NMR (CDCl_3) δ 22.7, 31.9, 37.7, 44.5, 45.4, 115.8, 118.1, 121.2, 123.1, 127.6, 127.8, 129.4, 134.4, 139.6, 139.8, 152.6 (one sp^2 carbon missing due to overlap); IR (CHCl_3 ,

cm⁻¹) 3023, 2967, 2927, 1591, 1451, 1346; HRMS Calcd for C₁₇H₁₇NO₂S: 299.0980.

Found: 299.0987.

Dimethyl 10b-methyl-3,10b-dihydrofluoranthene-2,2(1H)-dicarboxylate (6). The reaction mixture was chromatographed using 15:1 hexane/EtOAc to afford 75 mg of the indicated compound (82 % yield) as a colorless oil: ¹H NMR (CDCl₃) δ 1.06 (t, *J* = 6.9 Hz, 3H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.89 (d, *J* = 14.7 Hz, 1H), 3.09 (d, *J* = 14.7 Hz, 1H), 3.47 (d, *J* = 1.2 Hz, 2H), 3.90-4.00 (m, 2H), 4.32 (dq, *J* = 1.2, 7.2 Hz, 2H), 7.15 (d, *J* = 7.5 Hz, 1H), 7.25-7.37 (m, 3H), 7.48-7.51 (m, 1H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.70-7.72 (m, 1H); ¹³C NMR (CDCl₃) δ 14.0, 14.3, 24.3, 33.3, 38.6, 46.2, 56.6, 61.7, 62.0, 118.8, 121.0, 123.4, 126.0, 127.3, 127.5, 128.0, 132.6, 138.2, 140.2, 149.4, 154.4, 172.0, 172.9; IR (neat, cm⁻¹) 2978, 2930, 1732, 1446; HRMS Calcd for C₂₃H₂₄O₄: 364.1674. Found: 364.1684.

12b-Methyl-1,12b-dihydro-2H-benzo[5,6]indeno[1,2,3-*de*]chromene (8). The reaction mixture was chromatographed using 30:1 hexane/EtOAc to afford 57 mg of the

indicated compound (84 % yield) as a white solid: mp 154-156 °C; ^1H NMR (CDCl_3) δ 1.52 (s, 3H), 1.76-1.87 (m, 1H), 2.41 (dd, $J = 3.6, 12.9$ Hz, 1H), 4.59 (dd, $J = 6.0, 11.4$ Hz, 1H), 4.63-4.73 (m, 1H), 6.76 (d, $J = 11.1$ Hz, 1H), 7.25-7.30 (m, 1H), 7.37 (d, $J = 7.5$ Hz, 1H), 7.45-7.48 (m, 2H), 7.81 (s, 1H), 7.81-7.85 (m, 1H), 7.88-7.91 (m, 1H), 8.11 (s, 1H); ^{13}C NMR (CDCl_3) δ 26.9, 31.5, 42.1, 65.6, 113.1, 114.3, 119.5, 121.6, 125.9, 125.9, 128.1, 128.5, 129.7, 133.1, 133.6, 135.4, 139.1, 140.0, 151.9, 153.0; IR (CHCl_3 , cm^{-1}) 3017, 2965, 1614, 1591, 1484; HRMS Calcd for $\text{C}_{20}\text{H}_{16}\text{O}$: 272.1201. Found: 272.1208.

5-Methoxy-12b-methyl-1,12b-dihydro-2H-benzo[5,6]indeno[1,2,3-de]chromene

(10). The reaction mixture was chromatographed using 10:1 hexane/EtOAc to afford 69 mg of the indicated compound (91 % yield) as a white solid: mp 58-61 °C; ^1H NMR (CDCl_3) δ 1.50 (s, 3H), 1.71-1.83 (m, 1H), 2.34-2.39 (m, 1H), 4.53-4.58 (m, 1H), 4.61-4.70 (m, 1H), 6.36 (d, $J = 2.1$ Hz, 1H), 6.95 (d, $J = 2.1$ Hz, 1H), 7.44-7.47 (m, 2H), 7.78 (s, 1H), 7.81-7.84 (m, 1H), 7.87-7.91 (m, 1H), 8.07 (s, 1H); ^{13}C NMR (CDCl_3) δ 27.1, 31.9, 41.6, 56.0, 65.8, 99.1, 100.4, 119.5, 121.6, 125.9, 126.0, 128.2, 128.5, 133.2, 133.6, 139.1, 140.4, 152.4, 153.5, 162.2 (one sp^2 carbon missing due to overlap); IR (CHCl_3 , cm^{-1}) 3018, 2963, 2922, 1612, 1596, 1483; HRMS Calcd for $\text{C}_{21}\text{H}_{18}\text{O}_2$: 302.1307. Found: 302.1312.

12b-Methyl-5-nitro-1,12b-dihydro-2H-benzo[5,6]indeno[1,2,3-*de*]chromene (12).

The reaction mixture was chromatographed using 15:1 hexane/EtOAc to afford 18 mg of the indicated compound (21 % yield) as a yellow solid: mp 192-194 °C; ¹H NMR (CDCl₃) δ 1.55 (s, 3H), 1.79-1.90 (m, 1H), 2.50 (dd, *J* = 3.3, 12.9 Hz, 1H), 4.65-4.79 (m, 2H), 7.50-7.55 (m, 1H), 7.65 (d, *J* = 1.5 Hz, 1H), 7.87-7.89 (m, 2H), 7.94-7.97 (m, 1H), 8.22-8.23 (m, 2H); ¹³C NMR (CDCl₃) δ 26.7, 31.0, 42.5, 66.3, 108.5, 110.2, 120.8, 122.1, 126.5, 126.8, 128.2, 128.8, 133.5, 133.6, 137.0, 140.5, 141.6, 150.3, 150.9, 152.8; IR (CHCl₃, cm⁻¹) 3019, 2971, 1617, 1525; HRMS Calcd for C₂₀H₁₅O₃: 317.1052. Found: 317.1058.

3a-Methyl-3,3a-dihydro-2H-benzo[*h*]indeno[1,2,3-*de*]chromene (14).

The reaction mixture was chromatographed using 19:1 hexane/EtOAc to afford 65 mg of the indicated compound (95 % yield) as a yellow oil: ¹H NMR (CDCl₃) δ 1.50 (s, 3H), 1.73-1.84 (m, 1H), 2.36-2.42 (m, 1H), 4.72-4.87 (m, 2H), 7.29-7.48 (m, 5H), 7.67 (s, 1H), 7.81-7.88 (m, 2H), 8.10-8.13 (m, 1H); ¹³C NMR (CDCl₃) δ 27.0, 31.2, 42.2, 66.1, 110.8, 121.3, 121.8, 123.5, 124.5, 124.9, 126.0, 127.7, 127.8, 128.0, 128.6, 135.8, 138.8, 140.0,

147.6, 154.2; IR (CDCl₃, cm⁻¹) 3053, 2963, 2920, 1646, 1587, 1509; HRMS Calcd for C₂₀H₁₄O: 272.1201. Found: 272.1207.

6a-Methyl-4-(trifluoromethanesulfonyl)-4,5,6,6a-tetrahydro[1]benzofuro[3',2':4,5]cyclopenta[1,2,3-*de*]quinoline (16). The reaction mixture was chromatographed using 4:1 hexane/EtOAc to afford 65 mg of the indicated compound (76 % yield) as a yellow oil: ¹H NMR (CDCl₃) δ 1.55-1.62 (m, 4H), 2.58 (dd, *J* = 1.2 Hz, 5.7 Hz, 1H), 3.95-4.11 (m, 2H), 7.31-7.38 (m, 4H), 7.51-7.58 (m, 2H), 7.77-7.81 (m, 1H); ¹³C NMR (CDCl₃) δ 19.3, 30.4, 38.0, 41.3, 44.9, 112.7, 115.7, 116.9, 120.3, 122.3, 123.6, 123.8, 124.2, 129.5, 134.2, 135.2, 138.2, 160.5, 172.2; IR (CHCl₃, cm⁻¹) 3020, 2927, 1722, 1610, 1592, 1487; HRMS Calcd for C₁₉H₁₇O₃SN: 339.0929. Found: 339.0935.

1,1-Dimethyl-2,3-dihydro-1H-[1]benzofuro[3,2-*f*]chromene (16). The reaction mixture was chromatographed using 30:1 hexane/EtOAc to afford 52 mg of the indicated compound (83 % yield) as a colorless oil: ¹H NMR (CDCl₃) δ 1.69 (s, 6H), 1.98-2.02 (m,

2H), 4.14-4.18 (m, 2H), 7.99 (d, $J = 9.0$ Hz, 1H), 7.34 (d, $J = 9.0$ Hz, 1H), 7.31-7.36 (m, 1H), 7.40-7.46 (m, 1H), 7.55-7.58 (m, 1H), 8.21 (dd, $J = 0.9, 8.4$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 28.4, 31.7, 41.6, 62.9, 110.7, 112.0, 118.2, 122.0, 122.0, 124.1, 125.8, 126.3, 126.4, 150.5, 151.8, 157.0; IR (neat, cm^{-1}) 3069, 2959, 1622, 1585, 1472, 1415; HRMS Calcd for $\text{C}_{17}\text{H}_{16}\text{O}_2$: 252.1150. Found: 252.1156.

3a,10a-Dimethyl-2,3,3a,9,10,10a-hexahydro-1,8-dioxarubicen-21 and 22. The reaction mixture was chromatographed using 30:1 hexane/EtOAc to afford 52 mg of the indicated compounds as a 60:40 mixture (48 % yield) as a yellow solid. Compound **21** was confirmed by enantiomeric separation on HPLC using Cyclobond I 2000 RSP (250 x 4.6 mm). Compound **21**: ^1H NMR (CDCl_3) δ 1.53 (s, 6H), 1.64 (ddd, $J = 6.0, 13.2, 13.2$ Hz, 2H), 2.30 (dd, $J = 3.0, 13.2$ Hz, 2H), 4.62 (dd, $J = 6.0, 10.4$ Hz, 2H), 4.69-4.79 (m, 2H), 7.20-7.25 (m, 2H), 7.31-7.36 (m, 2H), 7.40 (d, $J = 7.5$ Hz, 2H), 7.96 (d, $J = 7.5$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 26.2, 31.6, 43.5, 65.3, 122.9, 123.9, 126.2, 126.9, 127.9, 136.9, 139.5, 143.9, 153.9; IR (CDCl_3 , cm^{-1}) 2956, 1505, 1437; HRMS Calcd for $\text{C}_{26}\text{H}_{22}\text{O}_2$: 366.1620. Found: 366.1626. Compound **22**: ^1H NMR (CDCl_3) δ 1.46 (s, 6H), 1.83-1.94 (m, 2H), 2.39 (ddd, $J = 1.2, 3.6, 13.2$ Hz, 2H), 4.59-4.79 (m, 4H), 7.18-7.26 (m, 2H),

7.31-7.36 (m, 2H), 7.40 (d, $J = 7.5$ Hz, 2H), 7.93 (d, $J = 7.5$ Hz, 2H); HRMS Calcd for $C_{26}H_{22}O_2$: 366.1620. Found: 366.1626.

8-Methyl-1H-indole[1,2-*b*]benzo[*d*]isothiazole-10-(endo-norbornan-2-yl)-5,5-dioxide (23). Compound **22**⁴ (99.3 mg, 0.25 mmol) and norbornene (25.9 mg, 0.275 mmol) were allowed to react under our standard reaction conditions for 1 d. The reaction mixture was diluted with diethyl ether (30 mL) and washed with brine (30 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure to afford 68.0 g (75 % yield) of the indicated compound **23** as a yellow solid, which is easily recrystallized from $CHCl_3$ /hexanes: mp 255-256 °C; 1H NMR ($CDCl_3$) δ 1.42-1.49 (m, 3H), 1.71-1.75 (m, 2H), 1.89-1.94 (m, 2H), 2.07-2.08 (m, 1H), 2.51 (br s, 4H), 2.65 (br s, 1H), 3.28-3.31 (m, 1H), 7.18-7.23 (m, 1H), 7.26-7.28 (m, 1H), 7.31-7.36 (m, 1H), 7.60 (s, 1H), 7.68-7.72 (m, 2H), 7.83 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 22.3, 29.4, 30.7, 36.5, 37.8, 37.9, 41.1, 42.7, 112.0, 122.6, 122.8, 123.0, 123.2, 123.5, 125.5, 128.7, 129.2, 132.2, 133.0, 135.5, 145.0 (one sp^2 carbon missing due to overlap); IR (neat, cm^{-1}) 2952, 2866, 1597, 1326, 1179; HRMS Calcd for $C_{22}H_{21}NO_2S$: 363.1293. Found: 363.1300.

Ethyl (2E)-3-(4,4-dimethyl-3,4-dihydro-2H-chromen-5-yl)propenoate (25).

Compound **24** (68.5 mg, 0.25 mmol) and ethyl acrylate (0.375 mmol) were allowed to react under our standard reaction conditions for 18 h. The reaction mixture was diluted with diethyl ether (30 mL) and washed with brine (30 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. The residue was chromatographed (8:1 hexane/EtOAc) to afford 40.3 mg of the indicated compound (62 % yield) as a yellow oil: ^1H NMR (CDCl_3) δ 1.34 (t, $J = 7.2$ Hz, 3H), 1.46 (s, 6H), 1.84 (t, $J = 7.2$ Hz, 2H), 4.15 (t, $J = 7.2$ Hz, 1H), 4.27 (q, $J = 7.2$ Hz, 2H), 6.18 (d, $J = 15.6$ Hz, 1H), 6.84 (dd, $J = 1.5, 7.5$ Hz, 1H), 6.98-7.10 (m, 2H), 8.32 (d, $J = 15.6$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 14.5, 30.4, 31.6, 41.1, 60.7, 62.5, 119.5, 119.6, 121.6, 127.4, 129.9, 136.0, 146.3, 154.7, 169.2; IR (CHCl_3 , cm^{-1}) 3018, 2966, 1712; HRMS Calcd for $\text{C}_{16}\text{H}_{20}\text{O}_3$: 260.1412. Found: 260.1416.

(3E)-4-(4,4-Dimethyl-3,4-dihydro-2H-chromen-5-yl)but-3-en-2-one (26).

Compound **24** (68.5 mg, 0.25 mmol) and methyl vinyl ketone (0.375 mmol) were allowed to react under our standard reaction conditions for 18 h. The reaction mixture was diluted with diethyl ether (30 mL) and washed with brine (30 mL). The organic

layer was dried (Na₂SO₄), filtered and the solvent removed under reduced pressure. The residue was chromatographed (3:1 hexane/EtOAc) to afford 42.0 mg of the indicated compound (73 % yield) as a yellow oil: ¹H NMR (CDCl₃) δ 1.47 (s, 6H), 1.85 (t, *J* = 5.2 Hz, 2H), 2.38 (s, 3H), 4.15 (t, *J* = 5.2 Hz, 2H), 6.47 (d, *J* = 15.0 Hz, 1H), 6.86 (dd, *J* = 0.9, 6.0 Hz, 1H), 7.01 (dd, *J* = 1.2, 5.7 Hz, 1H), 7.09 (t, *J* = 5.7 Hz, 1H), 8.17 (d, *J* = 15.0 Hz, 1H); ¹³C NMR (CDCl₃) δ 28.2, 30.5, 31.6, 41.1, 62.5, 119.8, 121.6, 127.5, 128.3, 130.1, 135.9, 144.8, 154.7, 198.3; IR (CHCl₃, cm⁻¹) 3020, 2964, 1705; HRMS Calcd for C₁₅H₁₈O₂: 230.1307. Found: 230.1311.

References

- (1) Tsukayama, M.; Utsumi, H.; Kunugi, A.; Nozaki, H. *Heterocycles* **1997**, *45*, 1131.
- (2) Zhu, G.-D.; Staeger, M. A.; Boyd, S. A. *Org. Lett.* **2000**, *2*, 3345.
- (3) Ramos, A. M.; Rispens, M. T.; van Duren, J. K. J.; Hummelen, J. C.; Janssen, R. A. J. *J. Am. Chem. Soc.* **2001**, *123*, 6714.
- (4) (a) Campo, M. A.; Larock, R. C. *Org. Lett.* **2000**, *2*, 3675. (b) Campo, M. A.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 5616.
- (5) Padwa, A.; Brodney, M. A.; Dimitroff, M.; Liu, B.; Wu, T. *J. Org. Chem.* **2001**, *66*, 3119.

data/dat2/nmr300/qh737-3.fid

data/dat2/nmr300/qh772-1.fid

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