Platinum(II)-Catalyzed Intermolecular Hydroarylation of Unactivated Alkenes with Indoles

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Supporting Information

Experimental procedures, analytical and spectroscopic data for products of catalytic reactions (11

pages).

General Methods. Pressurized reactions were performed behind a blast shield in a heavywalled pressure tube equipped with a pressure gauge and a valve that allowed the pressure to be regulated throughout the transformation. The pressure tubes were evacuated prior to pressurization by a single freeze-pump-thaw cycle at liquid nitrogen temperature. NMR spectra were obtained on a Varian spectrometer operating at 400 MHz for ¹H NMR and 100 MHz for ¹³C NMR in CDCl₃ unless noted otherwise. IR spectra were obtained on a Bomen MB-100 FT IR spectrometer. Gas chromatography was performed on a Hewlett-Parkard 5890 gas chromatograph equipped with a 25 m polydimethylsiloxane capillary column. Flash column chromatography was performed employing 200-400 mesh silica gel (EM). Thin layer chromatography (TLC) was performed on silica gel 60 F₂₅₄ eluting with a 5:1 mixture of hexanes and ethyl acetate unless noted otherwise. Elemental analyses were performed by Complete Analysis Laboratories (Parsippany, NJ).

1,4-Dioxane (Acros, anhydrous) was stored in an inert atmosphere glove box. $[PtCl_2(H_2C=CH_2)]_2$ (2), $PtCl_2$ (Strem), methanol, 1,2-dimethylindole (1), 4-chlorostyrene, 4trifluoromethylstyrene, 4-vinylanisole, *p*-benzoquinone, Pd/C (Aldrich), styrene, 4-methylstyrene, 4cyanostyrene (Acros), and 4-nitrostyrene (TCI) were used as received.

Catalytic hydroarylation

1,2-Dimethyl-3-ethylindole (3). A solution of **1** (0.29 g, 2.0 mmol), $[PtCl_2(H_2C=CH_2)]_2$ (**2**; 6.0 mg, 1.0×10^{-2} mmol) and dioxane (1 mL) in a pressure tube was evacuated via a freeze-pump-thaw cycle, pressurized with ethylene (50 psi), and heated at 90 °C for 6 h at constant ethylene pressure. The tube was cooled to room temperature, depressurized, and diluted with hexanes/ether (5:1, 10 mL). The resulting solution was filtered through a short plug of silica gel, concentrated, and chromatographed (hexanes–EtOAc = 50:1) to give **3** (0.34 g, 99%) as a colorless oil. TLC (hexanes–EtOAc = 30:1): R_f =

0.44. ¹H NMR: δ 7.68 (d, J = 7.6 Hz, 1 H), 7.35 (d, J = 8.0 Hz, 1 H), 7.29 (dt, J = 1.2, 6.8 Hz, 1 H), 7.19-7.23 (m, 1 H), 3.71 (s, 3 H), 2.89 (q, J = 7.6 Hz, 2 H), 2.45 (s, 3 H), 1.37 (t, J = 7.6 Hz, 3 H). ¹³C {¹H} NMR: δ 136.9, 132.4, 127.8, 120.7, 118.9, 118.3, 113.5, 108.9, 29.7, 18.0, 16.2, 10.3.

In a control experiment, treatment of 1-methylindole with ethylene (180 psi) and a catalytic amount of $HBF_4 \cdot OEt_2$ (5 mol %) in dioxane at 80 °C for 17 h led to no detectable consumption of 1-methylindole.

The remaining 3-ethylindoles were synthesized employing a procedure analogous to that used to synthesize **3**.

3-Ethyl-1,2-dimethyl-5-methoxyindole (**Table 1, entry 2**). Colorless oil. TLC (hexanes– EtOAc = 30:1): $R_f = 0.42$. ¹H NMR: δ 7.19 (d, J = 8.8 Hz, 1 H), 7.08 (d, J = 2.4 Hz, 1 H), 6.89 (dd, J = 2.4, 8.8 Hz, 1 H), 3.94 (s, 3 H), 3.65 (s, 3 H), 2.79 (q, J = 7.6 Hz, 2 H), 2.39 (s, 3 H), 1.29 (t, J = 7.6 Hz, 3 H). ¹³C{¹H} NMR: δ 153.9, 133.2, 132.2, 127.9, 113.1, 110.2, 109.4, 100.8, 56.4, 56.3, 29.8, 17.9, 15.9, 10.4. IR (neat, cm⁻¹): 2950, 2930, 1486, 1449, 1228. Anal. calcd (found) for C₁₃H₁₇NO: C, 76.81 (77.06); H, 8.43 (8.58); N, 6.89 (6.85).

3-Ethyl-1,2-dimethyl-5-chloroindole (Table 1, entry 3). Colorless oil. TLC (hexanes–EtOAc = 30:1): $R_f = 0.46$. ¹H NMR (Figure S1): δ 7.55-7.56 (dd, J = 0.8, 1.6 Hz, 1 H), 7.15 (dd, J = 0.8, 8.8 Hz, 1 H), 7.12 (dd, J = 1.6, 8.8 Hz, 1 H), 3.62 (s, 3 H), 2.75 (q, J = 7.6 Hz, 2 H), 2.39 (s, 3 H), 1.27 (t, J = 7.6 Hz, 3 H). ¹³C{¹H} NMR (Figure S2): δ 135.2, 134.0, 128.8, 124.5, 120.6, 117.6, 113.3, 109.7, 29.8, 17.8, 16.0, 10.3. IR (neat, cm⁻¹): 2961, 2929, 1573, 1479, 1370. HRMS calcd (found) for C₁₂H₁₄ClN (M⁺): 207.0815 (207.0811).

3-Ethyl-1-methyl-2-phenylindole (**Table 1, entry 4**). White solid. mp 58-60 °C. TLC (hexanes–EtOAc = 30:1): $R_f = 0.58$. ¹H NMR: δ 7.77 (d, J = 8.0 Hz, 1 H), 7.75-7.76 (m, 5 H), 7.42 (d, J = 8.0 Hz, 1 H), 7.33-7.37 (m, 1 H), 7.23-7.27 (m, 1 H), 3.65 (s, 3 H), 2.83 (q, J = 7.6 Hz, 2 H), 1.34 (t,

J = 7.6 Hz, 3H). ¹³C{¹H} NMR: δ 137.6, 132.6, 130.9, 128.6, 128.2, 127.8, 121.9, 119.4, 115.7, 109.7, 31.1, 18.3, 16.4. IR (neat, cm⁻¹): 3052, 2960, 1467, 1361. Anal. calcd (found) for C₁₈H₁₉N: C, 86.77 (86.71); H, 7.28 (7.20); N, 5.95 (5.83).

1,3-Diethyl-2-phenylindole (**Table 1, entry 5**). White solid. mp 65-66 °C. TLC (hexanes– EtOAc = 30:1): $R_f = 0.46$. ¹H NMR: δ 7.67 (qd, J = 0.8, 8.0 Hz, 1 H), 7.36-7.51 (m, 6 H), 7.24 (dt, J = 1.2, 8.0 Hz, 1 H), 7.13-7.17 (m, 1 H), 4.04 (q, J = 7.2 Hz, 2 H), 2.68 (q, J = 7.6 Hz, 2 H), 1.21 (t, J = 7.2 Hz, 3 H), 1.20 (t, J = 7.6 Hz, 3 H). ¹³C{¹H} NMR: δ 136.2, 132.8, 130.8, 128.6, 128.2, 127.9, 121.7, 119.4, 119.2, 115.8, 109.8, 38.7, 18.1, 16.2, 15.6. IR (neat, cm⁻¹): 3042, 2966, 2929, 1464, 1455, 1342. Anal. calcd (found) for C₁₈H₁₉N: C, 86.70 (86.83); H, 7.68 (7.67); N, 5.62 (5.50).

1-Methyl-3-ethylindole (**Table 1, entry 6**).^{S1} ¹H NMR: δ 7.65-7.67 (m, 1 H), 7.25-7.34 (m, 2 H), 7.13-7.17 (m, 1 H), 6.90 (s, 1 H), 3.77 (s, 3 H), 2.84 (dq, *J* = 0.8, 7.6 Hz, 2 H), 1.38 (t, *J* = 7.6 Hz, 3 H). ¹³C{¹H} NMR: δ 137.3, 128.0, 125.6, 121.7, 119.3, 118.7, 117.5, 109.3, 32.7, 18.5, 15.0.

Reaction of 1 with 1-butene. A solution of **1** (145 mg, 1.00 mmol), PtCl₂ (13 mg, 5.0×10^{-2} mmol), HCl (4 N in 1,4-dioxane, 12 µL, 0.05 mmol) in dioxane (0.5 mL) in a pressure tube was evacuated via a freeze-pump-thaw cycle, pressurized with 1-butene (30 psi), and heated at 90 ° C for 24 h at constant 1-butene pressure. The tube was cooled to room temperature, depressurized, and diluted with a mixture of hexanes/ether (3/1, 10 mL). The resulting solution was filtered through a short plug of silica gel, concentrated, and chromatographed (hexanes–EtOAc = 50:1) to give a 6:1 mixture of 3-*sec*-butyl-1,2-dimethylindole (**5a**)^{S2} and 3-butyl-1,2-dimethylindole (**5b**)^{S3} (148 mg, 74%) as a colorless oil. TLC (hexanes–EtOAc = 30:1): R_f = 0.48. ¹H NMR (**5a**): δ 7.81 (d, J = 8.0 Hz, 1 H), 7.37 (d, J = 8.0 Hz, 1 H), 7.28 (dt, J = 0.8, 6.8 Hz, 1 H), 7.19 (dt, J = 1.2, 8.0 Hz, 1 H), 3.72 (s, 3 H), 3.00-3.01 (m, 1 H), 2.48 (s, 3 H), 1.89-2.08 (m, 2 H), 1.59 (d, J = 6.8 Hz, 3 H), 0.99 (t, J = 7.6 Hz, 2 H), 2.47 (s, 3 H), 1.85

(quint, J = 7.6 Hz, 2 H), 1.53-1.65 (m, 2 H), 1.11 (t, J = 7.2 Hz, 3 H). ¹³C{¹H} NMR (**5a**): δ 137.2, 132.4, 126.8, 120.4, 119.9, 118.5, 116.0, 109.0, 34.1, 30.5, 29.7, 21.7, 13.4, 10.8. ¹³C{¹H} NMR (**5b**): δ 136.9, 132.9, 128.2, 120.7, 119.2, 118.9, 112.1, 108.8, 33.8, 25.5, 24.6, 23.1, 14.5, 10.5. Anal. calcd (found) for C₁₁H₁₈O₂: C, 83.53 (83.74); H, 9.51 (9.53); N, 6.96 (6.88).

In a control experiment, heating a solution of 1 (0.15 g, 1.0 mmol), HCl (4 N in dioxane, 12 μ L, 0.05 mmol) and 1-butene (20 psi) in dioxane (0.5 mL) at 90 °C for 18 h led to no detectable consumption of 1.

Reaction of 1 with propene. Platinum-catalyzed reaction of 1 with propene to form 3isopropyl-1,2-dimethylindole $(4a)^{S4}$ and 3-*n*-propyl-1,2-dimethylindole $(4b)^{S5}$ was performed employing a procedure analogous to that described for the reaction of 1 with 1-butene. TLC (hexanes–EtOAc = 30:1): $R_f = 0.51$. ¹H NMR (4a): δ 7.77 (dd, J = 0.8, 8.0 Hz, 1 H), 7.31 (dd, J = 0.8, 8.0 Hz, 1 H), 7.21 (dt, J = 0.8, 7.2 Hz, 1 H), 7.20-7.14 (m, 1 H), 3.67 (s, 3 H), 2.29 (hept, J = 7.2 Hz, 1 H), 2.43 (s, 3 H), 1.51 (d, J = 7.2 Hz, 6 H). ¹H NMR (4b): δ 7.60 (d, J = 7.6 Hz, 1 H), 7.10-7.30 (m, 3 H), 3.70 (s, 3 H), 2.78 (t, J = 7.2 Hz, 2 H), 2.41 (s, 3 H), 1.67-1.77 (m, 2 H), 1.03 (t, J = 7.2 Hz, 3 H). ¹³C{¹H} NMR: (4a) δ 137.1, 131.4, 126.6, 120.4, 119.7, 118.5, 117.4, 109.0, 26.6, 23.5, 10.7. ¹³C{¹H} NMR: (4b) δ 136.9, 133.0, 128.2, 120.6, 118.8, 118.4, 111.8, 108.7, 29.6, 26.8, 24.5, 14.4, 10.5. Anal. calcd (found) for C₁₁H₁₇N: C, 83.37 (83.58); H, 9.15 (9.22); N, 7.48 (7.25).

Reaction of 1 with *p***-chlorostyrene (Table 2, entry 3).** A mixture of **1** (72 mg, 0.50 mmol), *p*-chlorostyrene (0.14 g, 1.0 mmol), and PtCl₂ (6.7 mg, 2.5×10^{-2} mmol) in dioxane (1.0 mL) was stirred at 120 °C for 12 h. The resulting mixture was treated with *p*-benzoquinone (27 mg, 0.25 mmol) at 45 °C for 7 h, filtered through a plug of silica gel, and concentrated under vacuum. The residue was dissolved in methanol and treated with hydrogen (1 atm) and Pd/C (3.0 mg) at room temperature for 12 h. Evaporation of methanol followed by column chromatography of the residue (hexanes–EtOAc = 15:1)

gave an inseparable mixture of 1,2-dimethyl-3-[1-(4-chlorophenyl)ethyl]indole (**6a**) and 1,2-dimethyl-3-[2-(4-chlorophenyl)ethyl]indole (**6b**) (143 mg, 79%) as a pale yellow oil. TLC (hexanes-EtOAc = 5:1): $R_f = 0.74$. ¹H NMR (**6a**): δ 7.38-7.00 (m, 8 H), 4.42 (q, J = 7.2 Hz, 1 H), 3.66 (s, 3 H), 2.34 (s, 3 H), 1.76 (d, J = 7.6 Hz, 3 H). ¹H NMR (**6b**): δ 7.52-7.02 (m, 8 H), 3.62 (s, 3 H), 3.00-2.85 (m, 4 H), 2.11 (s, 3 H). ¹³C{¹H} NMR (**6a** + **6b**): δ 145.0, 141.1, 136.8, 133.4, 132.7, 131.6, 131.3, 130.2, 128.9, 128.4, 128.3, 127.6, 120.7, 119.4, 118.9, 118.0, 115.1, 110.1, 108.9, 108.8, 36.7, 35.3, 29.6, 27.0, 20.9, 18.3, 10.7, 10.1. IR (neat, cm⁻¹): 2916, 1648, 1489, 1471, 1369, 1091, 1012, 814, 737. Anal. calcd (found) for C₁₈H₁₈CIN: C, 76.18 (75.99); H, 6.39 (6.42); N, 4.94 (5.07).

In a control experiment, heating a solution of **1** (73 mg, 0.50 mmol), HCl (4 N in dioxane, 6.3 μ L, 2.5 × 10⁻² mmol), and *p*-chlorostyrene (140 mg, 1.0 mmol) in dioxane (1.0 mL) at 120 °C for 18 h led to no detectable consumption of **1** by GC analysis versus internal standard. Conversely, platinum (IV) compounds are also effective catalysts for the hydroarylation of indoles with vinyl arenes. For example, treatment of a 1:2 mixture of **1** and *p*-chlorostyrene with a catalytic amount of PtCl₄ (5 mol%) in dioxane at 120 °C for 12 h led to complete consumption of **1** with formation of a 4.3:7.1:1 mixture of **6a**, **6b**, and **6c** (Scheme S1).



Scheme S1

Hydroarylation of remaining vinyl arenes with 1 was performed in a manner analogous to that described for the hydroarylation of *p*-chlorostyrene with 1. A plot of the Markovnikov/*anti*-Markovnikov isomer ratio formed in the reaction of 1 with *p*-substituted vinyl arenes versus the Hammett σ -parameter is depicted in Figure S3.

1,2-Dimethyl-3-(1-phenylethyl)indole (7a) and 1,2-dimethyl-3-(2-phenylethyl)indole (7b). TLC (hexanes–dichloromethane = 5:1): $R_f = 0.54$. ¹H NMR (7**a**): δ 7.46-7.00 (m, 9 H), 4.49 (q, J = 7.2 Hz, 1 H), 3.67 (s, 3 H), 2.37 (s, 3 H), 1.82 (d, J = 7.2 Hz, 3 H). ¹H NMR (7**b**): δ 7.60-7.00 (m, 9 H), 3.64 (s, 3 H), 3.07-2.91 (m, 4 H), 2.17 (s, 3 H). ¹³C{¹H} NMR (7**a** + 7**b**): δ 154.5, 146.5, 142.7, 136.9, 133.3, 132.7, 128.8, 128.4, 128.3, 127.7, 127.5, 126.9, 125.9, 125.7, 120.6, 120.5, 119.5, 118.8, 118.7, 118.1, 115.6, 110.7, 108.9, 108.8, 37.6, 35.9, 29.6, 27.1, 20.9, 10.8, 10.1. IR (neat, cm⁻¹): 3054, 2931, 1601, 1580, 1563, 1493, 1471, 1369, 1332, 737, 700. Anal. calcd (found) for C₁₈H₁₉N: C, 86.70 (86.75); H, 7.68 (7.80); N, 5.62 (5.45).

1,2-Dimethyl-3-(1*-p***-tolylethyl)indole (8a) and 1,2-dimethyl-3-(2-p-tolylethyl)indole (8b).** TLC (hexanes-EtOAc = 5:1): $R_f = 0.67$. ¹H NMR (8a): δ 7.52-7.03 (m, 8 H), 4.50 (q, J = 7.2 Hz, 1 H), 3.69 (s, 3 H), 2.40 (s, 3 H), 2.37 (s, 3 H), 1.85 (d, J = 7.6 Hz, 3 H). ¹H NMR (8b): δ 7.66-7.03 (m, 8 H), 3.67 (s, 3 H), 3.09-2.91 (m, 4 H), 2.41 (s, 3 H), 2.24 (s, 3 H). ¹³C{¹H} NMR (8a + 8b): δ 143.5, 139.7, 136.9, 136.8, 135.3, 135.0, 133.2, 132.6, 129.1, 129.0, 128.6, 127.7, 127.4, 127.0, 120.6, 120.4, 119.6, 118.8, 118.7, 118.1, 115.7, 110.8, 108.8, 37.2, 35.5, 29.6, 27.3, 21.2, 21.1, 21.0, 10.7, 10.1. IR (neat, cm⁻¹): 2918, 2849, 1651, 1556, 1513, 1470, 1370, 1119, 817, 738. Anal. calcd (found) for C₁₉H₂₁N: C, 86.65 (86.45); H, 8.04 (7.92); N, 5.32 (5.63).

1,2-Dimethyl-3-[1-(4-cyanophenyl)ethyl]indole (9a) and **1,2-dimethyl-3-[2-(4-cyanophenyl)ethyl]indole** (9b). TLC (hexanes–EtOAc = 5:1): $R_f = 0.41$. ¹H NMR (9a): δ 7.54-7.00 (m, 8 H), 4.47 (q, J = 7.2 Hz, 1 H), 3.67 (s, 3 H), 2.35 (s, 3 H), 1.79 (d, J = 7.6 Hz, 3 H). ¹H NMR (9b):

δ 7.51-7.05 (m, 8 H), 3.60 (s, 3 H), 3.02-2.91 (m, 4 H), 2.04 (s, 3 H). ${}^{13}C{}^{1}H$ NMR (**9a** + **9b**): δ 148.3, 136.8, 133.4, 132.1, 129.7, 128.3, 127.5, 120.8, 119.4, 119.0, 117.8, 114.2, 109.7, 109.5, 109.0, 108.8, 37.5, 36.2, 29.7, 26.6, 20.5, 15.5, 10.7, 10.0. IR (neat, cm⁻¹): 2916, 2848, 2354, 2225, 1650, 1555, 1503, 1471, 1370, 738. Anal. calcd (found) for C₁₉H₁₈N₂: C, 83.18 (83.17); H, 6.61 (6.56); N, 10.21 (10.27).

1,2-Dimethyl-3-[1-(4-trifluoromethylphenyl)ethyl]indole (10a) and 1,2-dimethyl-3-[2-(4-trifluoromethylphenyl)ethyl]indole (10b). TLC (hexanes–EtOAc = 5:1): $R_f = 0.64$. ¹H NMR (10a): δ 7.53-7.00 (m, 8 H), 4.48 (q, J = 7.2 Hz, 1 H), 3.66 (s, 3 H), 2.34 (s, 3 H), 1.80 (d, J = 7.2 Hz, 3 H). ¹H NMR (10b): δ 7.51-7.06 (m, 8 H), 3.61 (s, 3 H), 3.02-2.91 (m, 4 H), 2.06 (s, 3 H). ¹³C{¹H} NMR (10a + 10b): δ 146.8, 145.1, 141.1, 136.8, 133.4, 132.7, 131.6, 131.3, 129.2, 128.9, 128.4, 128.3, 127.6, 125.2, 120.8, 119.0, 117.9, 115.1, 109.9, 108.9, 108.8, 37.3, 35.5, 29.7, 26.8, 20.9, 18.5, 10.6, 10.1. IR (neat, cm⁻¹): 2939, 2862, 1614, 1503, 1472, 1416, 1326, 1153, 1113, 825, 742. Anal. calcd (found) for C₁₉H₁₈F₃N: C, 71.79 (71.68); H, 5.72 (5.82); N, 4.41 (4.43).

1,2-Dimethyl-3-[1-(4-nitrophenyl)ethyl]indole (11a) and **1,2-dimethyl-3-[2-(4-nitrophenyl)ethyl]indole** (11b). TLC (hexanes–EtOAc = 5:1): R_f = 0.49. ¹H NMR (11a): δ 8.10-6.97 (m, 8 H), 4.50 (q, J = 7.2 Hz, 1 H), 3.66 (s, 3 H), 2.34 (s, 3 H), 1.81 (d, J = 7.2 Hz, 3 H). ¹H NMR (11b): δ 8.09-7.08 (m, 8 H), 3.61 (s, 3 H), 3.07-3.00 (m, 4 H), 2.07 (s, 3 H). ¹³C{¹H} NMR (11a + 11b): δ 150.5, 146.5, 136.8, 133.5, 129.7, 128.3, 127.5, 123.6, 120.9, 119.0, 117.8, 109.1, 108.9, 37.2, 36.1, 29.7, 26.6, 20.6, 16.8, 10.8, 10.1. IR (neat, cm⁻¹): 3051, 2944, 1601, 1560, 1515, 1473, 1344, 1109, 852, 739. Anal. calcd (found) for C₁₈H₁₈N₂O₂: C, 73.45 (73.48); H, 6.16 (6.15); N, 9.52 (9.69).





Figure S3. Hammett plot of the Markovnikov/*anti*-Markovnikov isomer ratio formed in the reaction of **1** with *p*-substituted vinyl arenes.



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