Supporting Information

for

The Efficient Palladium-Catalyzed N-Arylation of Indoles

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Complete experimental procedures and spectral data for ligands **2**–**4** and the compounds listed in Tables 1 and 2.

General. All reactions were performed under an argon atmosphere in oven-dried glassware and were assembled without the aid of a glovebox. Elemental analyses were performed by E&R Microanalytical Laboratory, Parsippany, NJ and Atlantic Microlab, Norcross, Ga. Toluene was distilled under nitrogen from molten sodium. THF was distilled under argon from sodium benzophenone ketyl. Dioxane, DMF and DME were purchased anhydrous from Aldrich Chemical Co. Substrates were purchased from Aldrich Chemical Co., with the following exceptions: 1-n-butyl-4-chlorotoluene, 2-(4-fluorophenyl)indole, 1-napthylboronic acid, 1-bromo-2-isopropylbenzene, and 3-chloroanisole, which were purchased from Lancaster; 3-bromopyridine and 4-bromoanisole, which were purchased from Alfa-Aesar; 2-bromopyridine, 2,3-dimethylindole, and 7-ethylindole, which were purchased from Acros. Methyl-[2-(trifluoromethylsulfonyl)oxy]benzoate was prepared from methyl-(2-hydroxy)benzoate and triflic anhydride. Sodium tert-butoxide was purchased from Aldrich Chemical Co. and stored in a Vacuum Atmospheres glovebox under nitrogen. Small amounts were removed from the glovebox as needed, stored in a dessicator for up to one week, and weighed in the air. Tribasic potassium phosphate was purchased from Fluka Chemical company. Tris(dibenzylideneacetone)dipalladium(0), dicyclohexylchlorophosphine, di-tert-butylchlorophosphine, and n-butyllithium were purchased from Strem Chemicals, Inc. tert-Butyllithium was purchased from Aldrich Chemical Co. Ligands **1**, **5** and **6** were prepared as previously described[1,2] or purchased from Strem Chemicals, Inc. All chemicals were used as supplied. Preparative flash chromatography was performed using ICN Flash Silica gel (230–400 mesh). The yields in Table 1 refer to isolated yields (average of two runs) of compounds estimated to be ≥95% pure as determined by ^{1}H NMR, GC analysis, and combustion analysis. The procedures described in the Experimental

Section are representative; thus, the yields may differ from those given in Tables 1 and 2.

Synthesis of ligands 2-4

1-(Di-tert-butylphosphino)-1'-(isopropyl)biphenyl (2)

2-Isopropylbromobenzene (4.0 g, 20.0 mmol) was loaded into an oven-dried flask which had been cooled to room temperature under an argon purge. The flask was capped with a septum, purged with argon and THF (80 mL) was added via syringe. The solution was cooled to –78 °C with stirring and then n-butyllithium (12.7 mL of a 1.65 M solution in hexanes, 21.0 mmol) was added dropwise. After the addition was complete, the reaction mixture was stirred at –78 °C for 60 min, at which point the aryllithium suspension was transferred via cannula to a separate flask containing a –78 °C solution of triisopropyl borate (9.2 mL, 40.0 mmol) in THF (40 mL). The reaction mixture was stirred at –78 °C for 15 min and was then warmed to room temperature and allowed to stir overnight (additional 14 h). The reaction mixture was quenched with 1 M aqueous HCl (250 mL) and was allowed to stir at room temperature for 15 min. The pH of the mixture was adjusted to pH 14 with 6 M aqueous NaOH, and the mixture was transferred to a separatory funnel. The reaction mixture was washed with ether (100 mL), and this organic extract was then discarded. The aqueous layer was adjusted to a pH 7 of with conc. aqueous HCl, and the organics were extracted with ether (2 x 150 mL). The combined organic layers were dried over anhydrous magnesium sulfate and were concentrated to half the volume in vacuo to give a light yellow solution. Pentane (100 mL) was added and approximately 90% of the solvents were removed in vacuo to give

2.4 g of (2-isopropylphenyl)boronic acid as a white crystalline material which was used without further purification.

To a flask containing tetrakis(triphenylphosphine)palladium (840 mg, 0.61 mmol, 5 mol % Pd) and K_3PO_4 (4.6 g, 21.9 mmol) was added the crude boronic acid (2.4g, 14.6 mmol). The flask was purged with argon and DMF (100 mL) and 2-bromoiodobenzene (1.88 mL, 14.6 mmol) were added via syringe. The reaction mixture was heated at reflux for 48 h. The reaction mixture was then cooled to room temperature, diluted with ether (200 mL), and poured into a separatory funnel. The layers were separated, and the aqueous layer was extracted with ether (200 mL). The combined organic layers were washed with 1 M aqueous NaOH (50 mL) and the aqueous layer was discarded. The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to give the crude material as yellow oil. Purification of the crude oil by flash chromatography (hexanes) afforded 1.5 g (37%) of 2-(bromo)-2'-(isopropyl)biphenyl as a colorless oil.

A flame-dried Schlenk tube was evacuated and backfilled with argon; this sequence was repeated an additional time. The flask was charged with 2-(bromo)-2'-(isopropyl)biphenyl (1.5 g, 5.45 mmol) and ether (15 mL). The reaction mixture was cooled to –78 °C, and t-BuLi (6.7 mL of a 1.7 M in pentane, 11.4 mmol) was added dropwise via syringe. Upon complete addition, the reaction mixture was allowed to stir for an additional 15 min at –78 °C. The cooling bath was removed and t-Bu_2PCl (1.24 mL, 6.54 mmol) was added dropwise by syringe. After reaching room temperature, the reaction mixture was heated to reflux for 48 h. The reaction mixture was cooled to room temperature, a saturated solution of aqueous ammonium chloride (10 mL) was added, and the resulting mixture was partitioned between ether (100 mL) and water (50 mL). The organic layer was dried over a 1:1 mixture of anhydrous magnesium

sulfate and sodium sulfate, filtered and concentrated in vacuo. The product was crystallized from hot methanol to afford 601 mg (30%) of 2-(di-tert-butylphosphino)-2'-(isopropyl)biphenyl as white needles, mp 89.5–91.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87–7.84 (m, 1H), 7.37–7.30 (m, 3H), 7.25–7.10 (m, 2H), 7.08–7.00 (m, 1H), 2.77–2.66 (m, 1H), 1.23 (d, J = 6.9 Hz, 3H), 1.18 (d, J = 11.6 Hz, 9H), 1.12 (d, J = 11.3 Hz, 9H), 1.04 (d, J = 6.7 Hz, 3H); ^{31}P NMR (121 MHz, $CDCl_3$) δ 20.0; ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.5, 150.0, 146.3, 146.2, 141.7, 141.6, 136.5, 136.1, 135.6, 135.5, 131.6, 131.2, 131.1, 128.2, 128.1, 127.5, 125.7, 124.9, 124.1, 33.6, 33.3, 32.8, 32.5, 31.6, 31.4, 30.9, 30.7, 30.2, 26.0, 23.0 (complex due to P–C splitting; definitive assignments have not been made); IR (neat, cm^{-1}) 2973, 2956, 2889, 2860, 1472, 1459, 1362, 758, 748; Anal. Calcd for $C_{23}H_{33}P$: C, 81.13; H, 9.77. Found: C, 81.04; H, 9.94.

2-(Dicyclohexylphosphino)-1,1'-binaphthyl (3)

An oven-dried Schlenk tube was cooled under argon and was charged with 2-bromo-1,1'-binaphthyl[3] (700 mg, 2.10 mmol) and THF (21 mL). The solution was cooled to –78 °C under argon, and n-BuLi (1.5 mL of a 1.6 M solution, 2.4 mmol) was added dropwise. After 1 h at –78 °C, chlorodicyclohexylphosphine (635 mg, 2.70 mmol) was added as a solution in THF (3 mL). The cooling bath was then removed and the reaction mixture was allowed to warm to room temperature overnight. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (10 mL) and then concentrated to remove THF. The resulting aqueous residue was extracted with Et_2O (2 X 100 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting crude solid was recrystallized from hot ethanol to afford 512 mg (54%) of the title compound as a white solid, mp 159–161 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96–7.87 (m, 4H), 7.77 (d, J = 8.5 Hz, 1H), 7.57 (t, J = 7.6

Hz, 1H), 7.46–7.39 (m, 2H), 7.34 (d, J = 6.8 Hz, 1H), 7.23–7.17 (m, 2H), 7.12–7.09 (m, 2H), 1.98–1.91 (m, 1H), 1.76–1.43 (m, 11H), 1.16–0.85 (m, 10H); ^{31}P NMR (121 MHz, $CDCl_3$) δ –10.4; ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.0, 146.6, 138.2, 134.3, 133.3, 133.2, 133.1, 129.1, 128.9, 128.1, 127.7, 127.5, 127.4, 127.3, 126.9, 126.2, 125.9, 125.5, 125.4, 124.7, 36.1, 35.8, 34.3, 34.1, 31.4, 31.1, 30.4, 30.2, 29.9, 29.7, 29.5, 27.5, 27.4, 27.2, 27.1, 27.0, 26.4, 26.3 (complex due to P–C splitting; definitive assignments have not been made); IR (neat, cm^{-1}) 3047, 2923, 2848, 1447, 820, 782, 747; Anal. Calcd for $C_{32}H_{35}P$: C, 85.30; H, 7.83. Found: C, 85.10; H, 7.83.

1-(2-bromophenyl)naphthalene[4]

Tetrakis(triphenylphosphine)palladium (0) (340 mg, 0.29 mmol, 5 mol % Pd) was suspended in DME (60 mL) in a 250 mL round-bottom flask. 2-Bromoiodobenzene (750 μL, 5.84 mmol) was added and the resulting mixture was stirred at room temperature for 15 min. 1-Naphthylboronic acid (1.0 g, 5.8 mmol) was added in a minimum volume of ethanol (ca. 2 mL), followed by aqueous Na_2CO_3 (6 mL of a 2 M solution, 12 mmol). The flask was fitted with a reflux condenser and the reaction mixture was refluxed overnight. The reaction was then cooled and concentrated in vacuo to remove the DME. The resulting residue was diluted with water (50 mL) and extracted with Et_2O (2 x 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. Triphenylphosphine was removed by crystallization from ethyl acetate/hexanes and the resulting crude solid was purified by flash chromotography (1% ethyl acetate-hexanes) to afford 1.35 g (82%) of the title compound as a white solid, mp 84–85 °C (lit.[4] mp 89–91.5 °C).

1-[2-(di-tert-butylphosphino)phenyl]naphthalene (4)

An oven-dried Schlenk tube was cooled under argon and charged with magnesium (56 mg, 2.30 mmol) and a crystal of iodine. The flask was sealed with a septum and a solution of 1-(2-bromophenyl)naphthalene (600 mg, 2.12 mmol) in THF (4 mL) was added via cannula. The reaction mixture was heated to reflux for 5 h. The resulting solution of Grignard reagent was cooled to room temperature and copper(I) chloride (220 mg, 2.20 mmol) was added. After purging the reaction vessel with argon, di-tert-butylchlorophosphine (500 μL, 2.60 mmol) was added and the reaction mixture was heated at reflux overnight. The reaction mixture was cooled and then diluted with hexanes/Et_2O (1:1 v/v, 30 mL) and stirred vigorously for 30 min. The solid was filtered and suspended in hexanes/Et_2O (1:1 v/v, 30 mL) and water (10 mL). A solution of 30% aqueous NH_4OH (10 mL) was added and the resulting mixture was stirred for 15 min, poured into a separatory funnel, and the layers were separated. The organic phase was washed with water and brine, dried over Na_2SO_4, filtered, and concentrated. The resulting crude solid was recrystallized from ethanol to afford 381 mg (52%) of the title compound as a white solid (in two crops), mp 107–108 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99–7.96 (m, 1H), 7.87–7.83 (m, 2H), 7.49–7.38 (m, 5H), 7.32–7.26 (m, 3H), 1.16 (d, J = 11.4 Hz, 9H), 1.05 (d, J = 11.6 Hz, 9H); ^{31}P NMR (121 MHz, $CDCl_3$) δ 20.5; ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.2, 148.7, 141.1, 141.0, 137.4, 137.0, 135.4, 135.3, 133.2, 132.5, 131.5, 131.4, 128.3, 128.2, 128.1, 128.0, 127.2, 127.1, 126.0, 125.2, 125.0, 124.4, 33.1, 32.8, 32.2, 31.9, 31.2, 31.0, 30.9, 30.7 (complex due to P–C splitting; definitive assignments have not been made); IR (neat, cm^{-1}) 2964, 1470, 1391, 801, 778; Anal. Calcd for $C_{24}H_{29}P$: C, 82.72; H, 8.39. Found: C, 82.63; H, 8.42.

N-arylation of Indoles.

General Procedure A: An oven-dried 16x100 mm test tube was charged with $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol, 1 mol % Pd), ligand **2** (4.9 mg, 0.0075 mmol, 1.5 mol %), indole reagent (0.51 mmol), and NaOt-Bu (67 mg, 0.7 mmol). The test tube was capped with a septum, purged with argon, then toluene (1.0 mL) and aryl halide or triflate (0.50 mmol) were added via syringe (indoles which are liquids at room temperature were added at this point). The reaction mixture was heated at 80 °C with stirring until the aryl halide or triflate had been consumed as judged by GC analysis. The reaction mixture was cooled to room temperature, diluted with diethyl ether, filtered through a pad of celite, and concentrated in vacuo. The crude residue was purified by flash chromatography on silica gel with an eluent of hexanes and ethyl acetate or toluene.

General Procedure B: An oven-dried 16x100 mm test tube was charged with $Pd_2(dba)_3$ (4.5 mg, 0.005 mmol, 1 mol % Pd), ligand **4** (2.5 mg, 0.0072 mmol, 1.5 mol %), indole substrate (1.02 mmol), and NaOt-Bu (135 mg, 1.4 mmol). The tube was capped with a septum, purged with argon, then toluene (2.0 mL) and aryl halide or triflate (1.0 mmol) were added via syringe (indoles which are liquids at room temperature were added at this point). The reaction mixture was heated at 100 °C with stirring until the aryl halide or triflate had been consumed as judged by GC analysis. The reaction mixture was cooled to room temperature, diluted with diethyl ether, filtered through a pad of celite, and concentrated in vacuo. The crude residue was purified by flash chromatography on silica gel with an eluent of hexanes and ethyl acetate or toluene.

N-(4-Methylphenyl)indole[5] (Table 1, Entry 1)

General procedure B was followed with $Pd_2(dba)_3$ (1.25 mol %), **1** (3.75 mol %), and toluene (1 mL) to afford 186 mg (90%) of the title compound as a colorless liquid.

N-(4-Methylphenyl)indole[5] (Table 1, Entry 2)

General procedure B was followed with $Pd_2(dba)_3$ (1.25 mol %), and **1** (3.75 mol %) to afford 191 mg (94%) of the title compound as a colorless liquid.

N-(4-Methylphenyl)indole[5] (Table 1, Entry 3)

General procedure A was followed with $Pd_2(dba)_3$ (1.25 mol %), **1** (3.75 mol %), and indole (1.02 mmol) at 100 °C to afford 95 mg (92%) of the title compound as a colorless liquid.

N-(4-t-Butylphenyl)indole (Table 1, Entry 4)

General procedure A was followed to afford 111 mg (90%) of the title compound as a white solid, mp 108–110 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69–7.66 (m, 1H), 7.57–7.50 (m, 3H), 7.44–7.41 (m, 2H), 7.33–7.31 (m, 1H), 7.24–7.12 (m, 2H), 6.66 (d, J = 3.3 Hz, 1H), 1.38 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.5, 137.3, 136.0, 129.3, 128.2, 126.6, 124.0, 122.3, 121.1, 120.3, 110.7, 103.3, 34.8, 31.6; IR (neat, cm^{-1}) 2960, 1519, 1457, 742; Anal. Calcd for $C_{18}H_{19}N$: C, 86.70; H 7.68. Found: C, 86.42; H 7.72.

N-(4-Methoxyphenyl)indole[5] (Table 1, Entry 5)

General procedure A was followed to afford 93 mg (84%) of the title compound as a white solid.

N-(4-N,N-dimethylaminophenyl)indole (Table 1, Entry 6)

General procedure A was followed to afford 100 mg (90%) of the title compound as a yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68–7.65 (m, 1H), 7.46–7.43 (m, 1H), 7.34–7.30 (m, 2H), 7.26–7.25 (m, 1H), 7.20–7.10 (m, 2H), 6.83–6.79 (m, 2H), 6.62 (d, J = 3.0 Hz, 1H), 2.99 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.4, 136.6, 129.1, 128.8, 128.6, 125.9, 121.9, 121.0, 119.9, 113.0, 110.6, 102.4, 40.9; IR (neat, cm^{-1}) 3047, 2802, 1523, 741; Anal. Calcd for $C_{16}H_{16}N_2$: C, 81.32; H 6.82. Found: C, 81.43; H 6.86.

N-(4-Fluorophenyl)indole[6] (Table 1, Entry 7)

General procedure A was followed with $Pd_2(dba)_3$ (2.5 mol %) and **1** (7.5 mol %) at 100 °C to afford 84 mg (79%) of the title compound as a colorless liquid. Data as below.

N-(4-Fluorophenyl)indole[6] (Table 1, Entry 8)

General procedure A was followed to afford 66 mg (63%) of the title compound as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69–7.67 (m, 1H), 7.47–7.42 (m, 3H), 7.28–7.14 (m, 5H), 6.68 (d, J = 3.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.2 (d, J_{CF} = 245 Hz), 136.2, 136.0, 129.3, 128.2, 126.4, 126.3, 122.6, 121.3, 120.6, 116.6 (d, J_{CF} = 23 Hz), 110.3, 104.1, 103.7; IR (neat, cm^{-1}) 3052, 1508, 1212, 741; Anal. Calcd for $C_{14}H_{10}NF$: C, 79.60; H 4.77. Found: C, 79.61; H 4.79.

N-(3,5-dimethylphenyl)indole (Table 1, Entry 9)

General procedure A was followed to afford 93 mg (84%) of the title compound as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68–7.65 (m, 1H), 7.57–

7.54 (m, 1H), 7.30–7.29 (m, 1H), 7.20–7.10 (m, 5H), 6.97 (broad s, 1H), 6.64 (d, J = 3.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.7, 139.4, 135.9, 129.3, 128.2, 128.1, 122.3, 122.2, 121.1, 120.3, 110.8. 103.3, 21.6; IR (neat, cm^{-1}) 2917, 1596, 1461, 1216, 760; Anal. Calcd for $C_{16}H_{15}N$: C, 86.84; H 6.83. Found: C, 86.91; H 6.83.

N-(3-pyridyl)indole[7] (Table 1, Entry 10)

General procedure A was followed using $Pd_2(dba)_3$ (1.5 mol %) and a reaction temperature of 100 °C to afford 88 mg (91%) of the title compound as a yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.84–8.83 (m, 1H), 8.62–8.60 (m, 1H), 7.86–7.82 (m, 1H), 7.72–7.69 (m, 1H), 7.54–7.44 (m, 2H), 7.33–7.18 (m, 3H), 6.74 (d, J = 3.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6, 145.7, 136.5, 135.8, 131.4, 129.5, 127.5, 124.2, 123.0, 121.5, 121.0, 110.1, 104.9; IR (neat, cm^{-1}) 3051, 1584, 1486, 739; Anal. Calcd for $C_{13}H_{10}N_2$: C, 80.39; H, 5.19. Found: C, 80.11; H 5.31.

N-(2,5-dimethylphenyl)indole (Table 1, Entry 11)

An oven-dried Schlenk flask was charged with $Pd_2(dba)_3$ (11.4 mg, 0.0125 mmol, 5 mol % Pd), **3** (16.0 mg, 0.0375 mmol, 7.5 mol %), indole (60 mg, 0.51 mmol), and NaOt-Bu (67 mg, 0.7 mmol). The flask was evacuated and backfilled with argon and fitted with a rubber septum. 2-Bromo-p-xylene (69 μL, 0.50 mmol) and toluene (1.0 mL) were added via syringe. The flask was sealed with a teflon screwcap and the reaction mixture was heated at 120 °C with stirring until the aryl bromide had been consumed as judged by GC analysis. The reaction mixture was cooled to room temperature, diluted with diethyl ether, filtered through a pad of celite, and concentrated in vacuo. The crude residue was purified by flash chromatography on silica gel with an eluent of 2.5% ethyl

acetate in hexanes to afford 107 mg (96%) of the title compound as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68–7.65 (m, 1H), 7.57–7.54 (m, 1H), 7.30–7.29 (m, 1H), 7.20–7.10 (m, 5H), 6.97 (broad s, 1H), 6.64 (d, J = 3.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.7, 139.4, 135.9, 129.3, 128.2, 128.1, 122.3, 122.2, 121.1, 120.3, 110.8. 103.3, 21.6; IR (neat, cm^{-1}) 2917, 1596, 1461, 1216, 760; Anal. Calcd for $C_{16}H_{15}N$: C, 86.84; H 6.83. Found: C, 86.91; H 6.83.

Methyl-4-(1-indolyl)benzoate (Table 1, Entry 12)

General procedure A was followed with $Pd_2(dba)_3$ (2.5 mol %), **1** (5.6 mol %), K_3PO_4 (0.7 mmol) as the base, and toluene (0.5 mL) at 100 °C to afford 108 mg (86%) of the title compound as a yellow liquid. Data as below (entry 17).

Methyl-4-(1-indolyl)benzoate (Table 1, Entry 13)

General procedure A was followed with K_3PO_4 (0.7 mmol) as the base and using a reaction temperature of 100 °C to afford 108 mg (86%) of the title compound as a yellow liquid. Data as below (entry 17).

Methyl-2-(1-indolyl)benzoate (Table 1, Entry 14)

An oven-dried Schlenk flask was charged with $Pd_2(dba)_3$ (6.9 mg, 0.0075 mmol, 3 mol % Pd), **3** (10.0 mg, 0.0225 mmol, 4.5 mol %), indole (60 mg, 0.51 mmol), and K_3PO_4 (148 mg, 0.7 mmol). The flask was evacuated and backfilled with argon and fitted with a rubber septum. Methyl-[2-[(trifluoromethylsulfonyl)oxy]benzoate (142 mg, 0.50 mmol) and toluene (1.0 mL) were added via syringe. The flask was sealed with a teflon screwcap and the reaction mixture was heated at 120 °C with stirring until the aryl triflate had been consumed as judged by GC analysis. The reaction mixture was cooled to room temperature, diluted with diethyl ether, filtered through a pad of celite, and

concentrated in vacuo. The crude residue was purified by flash chromatography on silica gel with an eluent of 7% ethyl acetate in hexanes to afford 105 mg (83%) of the title compound as a yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98–7.95 (m, 1H), 7.68–7.62 (m, 2H), 7.51–7.46 (m, 2H), 7.20–7.12 (m, 3H), 6.67 (d, J = 3.3 Hz, 1H), 1.54 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 138.8, 137.3, 132.9, 131.4, 129.0, 128.7, 128.6, 127.7, 122.4, 121.1, 120.2, 109.9, 130.3, 52.5; IR (neat, cm^{-1}) 2950, 1719, 1461, 1293, 740; Anal. Calcd for $C_{16}H_{13}NO_2$: C, 76.48; H 5.21. Found: C, 76.68; H 5.18.

N-(4-Methoxyphenyl)indole[5] (Table 1, Entry 15)

General procedure B was followed using $Pd_2(dba)_3$ (2.5 mol %), **1** (7.5 mol %), K_3PO_4 (0.7 mmol) as the base, and toluene (0.5 mL) to afford 197 mg (88%) of the title compound as a white solid.

N-(4-n-Butylphenyl)indole (Table 1, Entry 16)

General procedure A was followed with a reaction temperature of 100 °C to afford 112 mg (90%) of the title compound as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69–7.66 (m, 1H), 7.55–7.53 (m, 1H), 7.45–7.38 (m, 2H), 7.32–7.29 (m, 3H), 7.24–7.12 (m, 3H), 6.66 (d, J = 3.3 Hz, 1H), 2.68 (t, J = 7.8 Hz, 2H), 1.68–1.60 (m, 2H), 1.44–1.37 (m, 3H), 0.96 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.5, 137.6, 136.1, 129.6, 129.3, 128.2, 124.4, 122.3, 121.2, 120.3, 110.5, 103.3, 35.4, 33.8, 22.6, 14.2; IR (neat, cm^{-1}) 2956, 2929, 1519, 1457, 739; Anal. Calcd for $C_{18}H_{19}N$: C, 86.70; H 7.68. Found: C, 86.61; H 7.79.

Methyl-4-(1-indolyl)benzoate (Table 1, Entry 17)

General procedure A was followed using $Pd_2(dba)_3$ (1 mol %), and K_3PO_4 (0.7 mmol) as the base at 100 °C to afford 103 mg (61%) of the title compound as a yellow liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 8.20–8.18 (m, 2H), 7.70–7.58 (m, 4H), 7.38–7.37 (m, 1H), 7.26–7.19 (m, 2H), 6.73 (d, J = 3.3 Hz, 1H), 3.97 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 143.8, 135.5, 131.3, 129.8, 127.6, 127.5, 123.3, 123.0, 121.5, 121.0, 110.7, 105.0, 52.2; IR (neat, cm^{-1}) 3051, 1710, 1283, 721; Anal. Calcd for $C_{16}H_{10}NO_2$: C, 76.48; H, 5.21. Found: C, 76.23; H 5.27.

N-(4-t-Butylphenyl)-2-phenylindole (Table 2, Entry 1)

General procedure B was followed to afford 302 mg (95%) of the title compound as a white solid, mp 130–131 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 7.69–7.65 (m, 1H), 7.41–7.38 (m, 2H), 7.32–7.14 (m, 10H) 6.78 (d, J = 0.8 Hz, 1H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.1, 140.7, 139.0, 135.6, 132.6, 128.8, 128.1, 128.0, 127.4, 127.1, 126.0, 122.1, 120.5, 120.4, 110.7, 103.3, 34.7, 31.4; IR (neat, cm^{-1}) 2962, 1517, 1459, 843, 745; Anal. Calcd for $C_{24}H_{23}N$: C, 88.57; H, 7.12. Found: C, 88.60; H, 7.18.

N-(4-Methoxyphenyl)-2-phenylindole (Table 2, Entry 2)

General procedure A was followed using **4**, indole (0.52 mmol), and aryl halide (0.48 mmol) at 100 °C to afford 96 mg (67%) of the title compound as a white solid, mp 138–140 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.69–7.65 (m, 1H), 7.30–7.13 (m, 10H), 6.94–6.89 (m, 2H), 6.78 (s, 1H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.4, 140.8, 139.2, 132.5, 131.2, 129.1, 128.8, 128.1, 128.0, 127.1, 122.1, 120.4, 120.3, 114.4, 110.6, 103.0, 55.4; IR (neat, cm^{-1}) 2960, 1513, 1245, 751; Anal. calcd for $C_{21}H_{17}NO$: C, 84.25; H 5.72. Found: C, 83.96; H 5.79.

N-(3,5-Dimethylphenyl)-2-(4-fluorophenyl)indole (Table 2, Entry 3)

General procedure A was followed using **4**, indole (0.53 mmol), and aryl halide (0.52 mmol) at 100 °C to afford 120 mg (74%) of the title compound as a white solid, mp 140–141 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67–7.64 (m, 1H), 7.28–7.14 (m, 5H), 6.97–6.90 (m, 3H), 6.83 (broad s, 2H), 6.73 (s, 1H), 2.29 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9 (d, J_{CF} = 240 Hz), 139.5, 138.9, 138.0, 130.4, 130.3, 129.0, 128.7, 128.6, 128.0, 125.6, 122.1, 120.5, 120.3, 115.1 (d, J_{CF} = 21 Hz), 110.7, 103.1, 21.3; IR (neat, cm^{-1}) 2923, 1497, 1216, 749; Anal. Calcd for $C_{22}H_{18}NF$: C, 83.78; H, 5.75. Found: C, 83.57; H, 5.76.

3-(2-Methyl-1-indolyl)-1,3-dioxalane (Table 2, Entry 4)

General procedure A was followed using $Pd_2(dba)_3$ (1.5 mol %), and **5** (4.5 mol %) at 100 °C to afford 73 mg (52%) of the title compound as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57–7.49 (m, 4H), 7.37–7.35 (m, 1H), 7.15–7.08 (m, 3H), 6.39 (m, 1H), 5.87 (s, 1H), 4.15–4.05 (m, 4H), 2.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.7, 138.1, 138.0, 137.0, 129.6, 128.7, 128.3, 126.1, 125.9, 121.2, 120.1, 119.6, 110.1, 103.2, 101.5, 65.5, 13.6; IR (neat, cm^{-1}) 2887, 1459, 1075, 746; Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13. Found: C, 77.11; H, 6.11.

N-(4-Methylphenyl)-2-methylindole[8] (Table 2, Entry 5)

General procedure A was followed using $Pd_2(dba)_3$ (2.5 mol %), and **5** (7.5 mol %) at 100 °C to afford 47 mg (43%) of the title compound as a yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57–7.53 (m, 1H), 7.33–7.30 (m, 2H), 7.24–7.20 (m, 2H), 7.10–7.05 (m, 3H), 6.39–6.38 (m, 1H), 2.45 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4, 137.7, 137.5, 135.4, 130.2, 128.3, 127.9, 121.0,

120.0, 119.6, 110.2, 101.1, 21.4, 13.5; IR (neat, cm^{-1}) 3056, 2919, 1515, 746; Anal. Calcd for $C_{16}H_{15}N$: C, 86.84; H, 6.83. Found: C, 86.83; H, 6.93.

N-(2-pyridyl)-7-ethylindole (Table 2, Entry 6)

General Procedure B was followed using indole (1.08 mmol) and a reaction temperature of 80 °C to afford 209 mg (94%) of the title compound as a yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ 8.58 (ddd, J = 4.9, 1.9, 0.7 Hz, 1H), 7.84–7.78 (m, 1H), 7.53 (dd, J = 7.6, 1.3 Hz, 1H), 7.33–7.27 (m, 3H), 7.15 (t, J = 7.5 Hz, 1H), 7.09–7.07 (m, 1H), 6.68 (d, J = 3.3 Hz), 6.68 (d, J = 3.3 Hz, 1H), 2.54 (q, J = 7.5 Hz, 2H), 0.95 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.8, 148.9, 138.0, 134.4, 130.7, 130.0, 128.6, 123.4, 122.2, 121.2, 120.4, 119.0, 104.9, 26.3, 14.3; IR (neat, cm^{-1}) 2967, 1584, 1471, 1338, 1229, 721; Anal. Calcd for $C_{15}H_{14}N_2$: C, 81.05; H, 6.35. Found: C, 81.17; H, 6.38.

N-(3,5-Dimethylphenyl)-7-ethylindole (Table 2, Entry 7)

General Procedure B was followed using indole (1.08 mmol) and a reaction temperature of 60 °C to afford 132 mg (53%) of the title compound as a pale yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, J = 7.8 Hz, 1H), 7.12–6.99 (m, 6H), 6.60 (dd, J = 3.2, 1.1 Hz, 1H) 2.42 (q, J = 7.4 Hz, 2H), 2.36 (s, 6H), 0.97 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.6, 138.2, 134.8, 130.8, 129.7, 129.3, 128.2, 125.2, 122.4, 120.5, 118.7, 102.6, 24.9, 21.2, 14.8; IR (neat, cm^{-1}) 2968, 1596, 1484, 1347, 1196, 720; Anal. Calcd for $C_{18}H_{19}N$: C, 86.7; H 7.68. Found: C, 86.63; H 7.70.

N-(2,5-Dimethylphenyl)-5-fluoroindole (Table 2, Entry 8)

An oven-dried Schlenk flask was charged with $Pd_2(dba)_3$ (11.4 mg, 0.0125 mmol, 5 mol % Pd), **3** (16.0 mg, 0.0375 mmol, 7.5 mol %), 5-fluoroindole (69

mg, 0.51 mmol), and NaOt-Bu (67 mg, 0.7 mmol). The flask was evacuated and backfilled with argon and fitted with a rubber septum. 2-Bromo-p-xylene (69 μL, 0.50 mmol) and toluene (1.0 mL) were added via syringe. The flask was sealed with a teflon screwcap and the reaction mixture was heated at 120 °C with stirring until the aryl bromide had been consumed as judged by GC analysis. The reaction mixture was cooled to room temperature, diluted with diethyl ether, filtered through a pad of celite and concentrated in vacuo. The crude residue was purified by flash chromatography on silica gel with an eluent of 2% ethyl acetate in hexanes to afford 83 mg (69%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34–7.30 (m, 1H), 7.27–7.24 (m, 1H), 7.19–7.16 (m, 2H), 7.12–7.11 (m, 1H), 6.95–6.89 (m, 2H), 6.61 (d, J = 3.3 Hz, 1H), 2.38 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.2 (d, J = 225 Hz), 138.0, 136.9, 133.8, 132.6, 131.2, 130.4, 129.3, 128.7, 111.4, 111.3, 110.6, 110.4, 105.7 (d, J = 22 Hz), 102.4 (d, J = 5 Hz) , 20.96, 17.3; IR (NaCl, cm^{-1}) 2922, 1477, 1249, 798; Anal. Calcd for $C_{16}H_{14}NF$: C, 80.31; H 5.90. Found: C, 80.58; H 5.88.

N-(4-Fluorophenyl)-5-fluoroindole[9] (Table 2, Entry 9)

General procedure A was followed using $Pd_2(dba)_3$ (1.5 mol %), and indole (0.60 mmol) at 100 °C to afford 98 mg (85%) of the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45–7.16 (m ,7H), 6.99–6.92 (m, 1H), 6.62 (dd, J = 3.2, 0.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0 (d, J_{CF} = 245 Hz), 158.1 (d, J_{CF} = 234 Hz), 135.5, 132.6, 129.4, 129.3, 126.1, 126.0, 116.6, 116.3, 110.9, 110.8, 110.7 (d, J_{CF} = 19 Hz), 105.8 (d, J_{CF} = 23 Hz), 103.4, 103.3; IR (neat, cm^{-1}) 3076, 1511, 1474, 1210, 1138, 837; Anal. Calcd for $C_{14}H_9NF_2$: C, 73.36; H, 3.96. Found: C, 73.32; H, 3.88.

N-(4-Methylphenyl)-5-fluoroindole (Table 2, Entry 10)

General procedure A was followed using $Pd_2(dba)_3$ (2.5 mol %), and **1** (7.5 mol %) at 100 °C to afford 101 mg (88%) of the title compound as a yellow liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.43–7.28 (m ,7H), 6.97–6.90 (m, 1H), 6.61–6.60 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.3 (d, J_{CF} = 233 Hz),137.2, 136.8, 132.8, 130.4, 129.7, 129.6, 129.6, 124.4, 111.4, 111.3, 110.7 (d, J_{CF} = 26 Hz), 105.9 (d, J_{CF} = 24 Hz), 103.2, 103.2; IR (NaCl, cm^{-1}) 3036, 2921, 1519, 1474, 1249, 1140, 823; Anal. Calcd for $C_{15}H_{12}NF$: C, 79.98; H, 5.37. Found: C, 80.03; H, 5.37.

N-(3-Methoxyphenyl)-5-methoxyindole (Table 2, Entry 11)

General procedure A was followed using a reaction temperature of 100 °C to afford 118 mg (94%) of the title compound as a colorless liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.43–7.28 (m ,7H), 6.97–6.90 (m, 1H), 6.61–6.60 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7, 154.7, 141.2, 131.1, 130.5, 130.0, 128.5, 116.4, 112.6, 111.9, 111.6, 110.0, 103.4, 102.8, 56.0, 55.6; IR (neat, cm^{-1}) 2939, 2833, 1602, 1492, 1218, 694; Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97. Found: C, 75.67; H, 6.00.

N-(4-Methylphenyl)-5-methoxyindole (Table 2, Entry 12)

General procedure A was followed using $Pd_2(dba)_3$ (2.5 mol %), and **1** (7.5 mol %) at 100 °C to afford 99 mg (82%) of the title compound as a yellow liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.43–7.41 (m ,1H), 7.36–7.35 (m, 2H), 7.29–7.23 (m, 3H), 7.13–7.12 (m, 1H), 6.87–6.85 (m, 1H), 6.57 (d, J = 3.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.6, 137.5, 136.2, 131.3, 130.3, 129.8, 128.6, 124.1, 112.5, 111.5, 103.7, 102.7, 56.0, 21.2; IR (NaCl, cm^{-1}) 2942, 1518, 1476, 1258, 823; Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37. Found: C, 80.97; H, 6.31.

N-(3,5-dimethylphenyl)-2,3-dimethylindole (Table 2, Entry 13)

General procedure A was followed using **4**, indole (0.56 mmol), and aryl halide (0.52 mmol) at 100 °C to afford 125 mg (97%) of the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53–7.50 (m, 1H), 7.12–7.03 (m, 4H), 6.92 (broad s, 2H), 2.37 (broad s, 6H), 2.30 (broad s, 3H), 2.22 (broad s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9, 138.0, 137.2, 132.8, 129.0, 128.6, 125.6, 120.8, 119.2, 117.7, 109.8, 107.5, 21.3, 11.0, 8.9; IR (neat, cm^{-1}) 2917, 1598, 1465, 1364, 1233, 737; Anal. Calcd for $C_{18}H_{19}N$: C, 86.70; H, 7.68. Found: C, 86.85; H, 7.72.

N-(3,5-dimethylphenyl)-2,3-dimethylindole (Table 2, Entry 14)

General procedure A was followed using $Pd_2(dba)_3$ (1.0 mol %), **6** (3.0 mol %), indole (0.56 mmol), and aryl halide (0.52 mmol) at 100 °C to afford 116 mg (90%) of the title compound as a colorless oil. Data as above.

Ethyl-4-(2,3-dimethyl-1-indolyl)benzoate (Table 2, Entry 15)

An oven-dried Schlenk flask was charged with $Pd_2(dba)_3$ (11.4 mg, 0.0125 mmol, 5 mol % Pd), **3** (16.0 mg, 0.0375 mmol, 7.5 mol %), 2,3-dimethylindole (74 mg, 0.51 mmol), and K_3PO_4 (148 mg, 0.7 mmol). The flask was evacuated and backfilled with argon and fitted with a rubber septum. Ethyl-4-bromobenzoate (69 μL, 0.50 mmol) and dioxane (1.0 mL) were added via syringe. The flask was sealed with a teflon screwcap and the reaction mixture was heated at 100 °C with stirring until the aryl bromide had been consumed as judged by GC analysis. The reaction mixture was cooled to room temperature, diluted with diethyl ether, filtered through a pad of celite and concentrated in vacuo. The crude residue was purified by flash chromatography on silica gel with an eluent of 5% ethyl acetate in hexanes to afford 87 mg (59%) of the title

compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21–8.18 (m, 2H), 7.54–7.51 (m, 1H), 7.43–7.39 (m, 2H), 7.26–7.09 (m, 3H), 4.44 (q, J = 7.2 Hz, 2H), 2.31 (s, 3H), 2.26 (s, 3H), 1.43 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 142.6, 136.9, 132.4, 130.9, 129.3, 129.2, 127.6, 121.7, 120.1, 118.2, 109.8, 109.4, 61.4, 14.5, 11.3, 9.0; IR (neat, cm^{-1}) 2912, 1710, 1272, 742; Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53. Found: C, 77.53; H, 6.61.

Ethyl 3-[N-(4-methoxyphenyl)indolyl]acetate (Table 2, Entry 16)

General Procedure B was followed using **2**, indole (1.08 mmol), and K_3PO_4 (1.4 mmol) as the base to afford 270 mg (87%) of the title compound as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68–7.65 (m, 1H), 7.45–7.36 (m, 3H), 7.27 (s, 1H), 7.24–7.14 (m, 2H), 7.03–6.98 (m, 2H), 4.19 (q, J = 7.1 Hz, 2H), 3.86 (s, 3H), 3.81 (s, 2H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 158.0, 136.3, 132.5, 128.1, 127.0, 125.6, 122.3, 119.9, 119.1, 114.6, 110.4, 108.8, 60.8, 55.6, 31.4, 14.3; IR (neat, cm^{-1}) 2981, 1733, 1513, 1459, 1428, 1030, 741; Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19. Found: C, 73.68; H, 6.13.

Ethyl 3-[N-(3-acylphenyl)indolyl]acetate (Table 2, Entry 17)

General procedure A was followed using $Pd_2(dba)_3$ (1.0 mol %), and K_3PO_4 (0.7 mmol) as the base at 100 °C to afford 152 mg (95%) of the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07–8.06 (m, 1H), 7.92–7.89 (m, 1H), 7.72–7.60 (m, 3H), 7.57–7.51 (m, 1H), 7.38–7.37 (m, 1H), 7.27–7.17 (m, 2H), 4.18 (q, J = 7.2 Hz, 2H), 3.82 (s, 2H), 2.66 (s, 3H), 1.26 (t, J = 7.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.4, 171.8, 140.5, 138.7, 136.0, 130.1, 128.9, 128.6, 126.6, 126.2, 123.7, 123.1, 120.7, 119.6, 110.5, 110.4, 61.1, 31.4, 26.9, 14.4; IR (neat, cm^{-1}) 2981, 1733, 1686, 1459, 1262, 740; Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.15; H, 5.96. Found: C, 74.50; H, 6.10.

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