Direct C-H Bond Arylation: Selective Palladium-Catalyzed C2-Arylation of *N*-Substituted Indoles

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General Procedures:

All reactions were performed under an atmosphere of argon, which was passed through Drierite. Nuclear Magnetic Resonance spectra were recorded at 298° K on a Bruker Avance DPX 300 Fourier Transform NMR. Spectra recorded in CDCl₃ solutions were referenced to TMS; spectra recorded in acetone-*d*₆ were referenced to residual solvent peaks. IR spectra were taken neat as thin films on NaCl plates using a Perkin-Elmer 1600 FTIR spectrophotometer. Mass spectra were recorded on a JEOL LCmate instrument (Ionization mode: APCI+). All HPLC analysis was conducted on a Waters Millennium³² Analytical system with a 996 photodiode array detector; all runs were analyzed at 254 nm, with a Zorbax Rx-C18 Column (4.6 mm x 25 cm). All HPLC methods were conducted using 30% acetonitrile / water (with 0.1 % trifluoroacetic acid) with a linear gradient to 100 % acetonitrile over 20 minutes; this was followed by a 5 minute wash of 100% acetonitrile and a 5 minute re-equilibration time; analyte concentrations were determined versus benzoic acid as an internal standard. Flash chromatography was carried out on SILICYCLE silica gel (230-400 mesh), with a gradient elution of 100 % hexanes to 30 % ethyl acetate / 70 % hexanes.

Materials:

All materials were used as received unless otherwise noted. Palladium acetate (98%) was purchased from Strem. 5-nitroindole, and 5-cyanoindole were purchased from Alfa Aesar. 4-hydroxyindole and 1H-pyrrolo[2,3-*b*]pyridine were purchased from TCI America. 1-(Phenylsulfonyl)indole was purchased from Lancaster. Triphenylphosphine (99%), iodobenzene (98%), cesium acetate (99.9%), dicyclohexylphenylphosphine (95%), dimethylacetamide (99.8 %, anhydrous), and benzoic acid (99.5%) were purchased from Aldrich. 1-Methylindole was also purchased from Aldrich, but was purified via fractional distillation onto 4 Å molecular sieves and stored under argon in the dark prior to use. Chloroform-*d* and acetone-*d*₆ were purchased from Cambridge Isotope Laboratories.

Part A: Optimization of Catalyst Loading

Introduction:

In the initial reaction conditions (5 mol % Pd(OAc)₂, CsOAc as a base), biphenyl formation was a real issue. For reasons discussed in the text, it was hypothesized, that by reducing the catalyst loading, biphenyl formation could be decreased. The following investigation, summarized in Figure S1, was conducted to address this issue.

Figure S1. Catalyst loading optimization at a substrate concentration of 2.54 M. Yield determined by HPLC vs. an internal standard. Yield of biphenyl is relative to the amount of Ph-I used.

Experimental Procedure:

In 8 mL vials, sealed with an open-top closure fitted with Teflon septa, CsOAc (350 mg, 1.824 mmol) was dried under high vacuum at 125° C for 2 hours. After the CsOAc was

fully dried (no longer the appearance of moisture inside the vessels), the vials were then cooled to room temperature under argon. For the reactions with 5 to 0.75 mol % Pd(OAc)₂, the corresponding amounts of metal and ligand were added under argon, followed by 120 μ L of anhydrous dimethylacetamide (DMA; anhydrous Aldrich). For all other reactions, the catalyst was added as a solution; in a separate flame-dried flask, Pd(OAc)₂ (41.7 mg, 0.186 mmol) and PPh₃ (200 mg, 0.763 mmol) was mixed with 5 ml of anhydrous DMA under argon. Each of these reactions (ones that used 0.5 to 0.005 mol % of Pd(OAc)₂) received a portion of the palladium solution proportional to the desired catalyst loading, followed by an injection of additional DMA so that the total volume of solvent used was 120 μ L. The following portions were used in these experiments:

catalyst mol %	Pd(OAc) ₂ (mg)	PPh ₃ (mg)	catalyst mol %	μ L of catalyst solution	μ L of DMA
5.0	10.2	48	0.50	120	0
2.5	5.1	24	0.25	60	60
1.0	2	9.6	0.10	24	96
0.75	1.5	7.2	0.05	12	108
			0.01	2.4	117.6
			0.005	1.2	118.8

After addition of the catalyst solution was complete, 1-methylindole (119.5 mg, 0.912 mmol) and Ph-I (223.3 mg, 1.09 mmol) were added consecutively to the reactions via syringe. The solution was then heated for 24 hours at 125° C in the sealed vial with an argon atmosphere. Subsequently, the mixtures were diluted with methanol (to 20 mL), and benzoic acid (111.4 mg, 0.912 mmol) was added. An aliquot of this solution was analyzed by HPLC versus the internal standard (benzoic acid).

Figure S2. Sample HPLC traces, the internal standard and analytes are identified on the traces.

Figure S2 Continued.

To prove that the ratio of biphenyl to arylated indole obtained is independent of the substrate concentration, the following additional set of experiments was conducted, Figure S3. The same procedure was used as above except the concentration of substrate was diluted so that the total solvent used was 3.35 mL. The yields obtained in these experiments are identical to the ones shown above, even though the overall concentration of the substrate was an order of magnitude smaller (concentration = 0.254 M). This illustrates the importance of careful control over relative reaction rates in this system; in other words, the catalyst/substrate ratio (the catalyst loading) is more important in these arylations than the overall reaction concentration.

Figure S3. Catalyst loading optimization at a substrate concentration of 0.254 M. Yield determined by HPLC vs. an internal standard. Yield of biphenyl is relative to the amount of Ph-I used.

Part B: Optimization of Base

The proper choice of base in this reaction is critical. Figure S4 depicts the arylation of 1-methylindole with iodobenzene in the presence of different bases; these include a variety of acetate bases and cesium bases (inset). This reaction is sensitive to both the cation and anion of the salt. Only cesium acetate provides reasonable yields out of the acetate salts examined. In addition, the counter ion to cesium is also essential; for example, the carbonate salt provides marginal yields of 1-methyl-2-phenylindole.

Figure S4. Optimization of base in arylation conditions.

Experimental Procedure:

In 8 mL vials, sealed with an open-top closure fitted with Teflon septa, 1.824 mmol of each base was dried under dynamic vacuum at 125° C for 2 hours; the amounts used for each reaction are listed in the table below.

base	amount used (mg)	base	amount used (mg)
LiOAc	120.3	Ba(OAc) ₂	465.7
NaOAc	149.6	Zn(OAc) ₂	334.6
KOAc	178.9	Bi(OAc) ₃	704.3
CsOAc	350.0	CsOPiv ^a	426.9
Mg(OAc) ₂	259.6	CsTFA ^b	245.9
Ca(OAc) ₂	288.4	Cs ₂ CO ₃	594.3

^a CsOPiv is cesium pivalate.¹ ^b CsTFA is cesium trifluoromethylacetate.²

After the bases were fully dried (no longer the appearance of moisture inside the vessels), the vials were then cooled to room temperature under argon. Pd(OAc)₂ (1 mg, 0.0046 mmol) and PPh₃ (4.8 mg, 0.018 mmol) were added under argon, followed by 120 μL of anhydrous dimethylacetamide (DMA). After addition of the catalyst was complete, 1-

methylindole (119.5 mg, 0.912 mmol) and Ph-I (223.3 mg, 1.09 mmol) were added consecutively to the reactions. The solution was then heated for 24 hours at 125° C in the sealed vial with an argon atmosphere. After the reaction was complete, the mixtures were diluted with methanol (to 20 mL), and benzoic acid (111.4 mg, 0.912 mmol) was added. An aliquot of this solution was analyzed by HPLC versus the internal standard (benzoic acid).

Part C: Synthesis of Substrates

The following substrates were prepared according to literature procedure: 1-phenylindole,³ 1-*iso*-propylindole,⁴ and 1-benzylindole.⁵ The synthesis of the other substrates is described below.

1-methylpyrrolo[2,3-*b*]pyridine. A flame dried flask is charged with pyrrolo[2,3-*b*]pyridine (729 mg, 6.17 mmol) and 60 % NaH (296 mg 7.41 mmol) in oil. The flask is then flushed with argon and cooled to 0° C. Once cool, dimethylformamide (15 mL) is added, and the reaction is allowed to stir until the evolution of hydrogen is complete. Iodomethane (875.9 mg, 6.17 mmol) is then added dropwise, and the reaction is allowed to slowly come to room temperature. After complete, the solvent is removed and the product (709 mg) is isolated by flash chromatography (8:1.8:0.2 = hex:EtOAc:CH₂Cl₂) in 87 % yield. ¹H NMR (300 MHz, CDCl₃) δ 3.89 (s, 3H), 6.44 (d, J = 3.3 Hz, 1H), 7.04 (dd, J = 7.8, 4.7 Hz, 1H), 7.17 (d, J = 3.6 Hz, 1H), 7.89 (dd, J = 7.8, 1.5 Hz, 1H), 8.33 (dd, J = 4.8, 1.5 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 31.7, 99.7, 115.9, 129.0, 129.0, 129.6, 143.5, 162.8; IR (NaCl plate, cm⁻¹) ν_{max} 2920.5, 2850.4, 1731.0, 1596.5, 1466.1, 1346.9, 1126.5; MS: calculated for C₈H₈N₂ 132.07, observed (APCI+): [M⁺+1] 133.15 m/z.

4-methoxy-1-methylindole. A flame dried flask is charged with 4-hydroxyindole (468 mg, 3.52 mmol) and 60 % NaH (338 mg, 8.5 mmol) in oil. The flask is then flushed with argon and cooled to 0° C. Once cool, dimethylformamide (15 mL) is added, and the reaction is allowed to stir until the evolution of hydrogen is complete. Iodomethane (1.099 g, 7.74 mmol) is then added dropwise, and the reaction is allowed to slowly come to room temperature. After complete, the solvent is removed and the product (419 mg) is isolated by flash chromatography (10% EtOAc/Hex) in 74 % yield. ¹H NMR (300 MHz, CDCl₃) δ 3.78 (s, 3H), 3.98 (s, 3H), 6.55 (d, J = 7.7 Hz, 1H), 6.61 (d, J = 3.2 Hz, 1H), 6.98 (m, 2H), 7.17 (t, J = 7.8 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 33.5, 55.7, 98.6, 99.6, 103.1, 119.4, 122.7, 127.7, 138.8, 154.1; IR (NaCl plate, cm⁻¹) ν_{max} 2956.5, 2840.8, 1611.9, 1581.8, 1500.5, 1292.6, 1260.2, 1184.0, 1061.7; MS: calculated for C₁₀H₁₁NO 161.08, observed (APCI+): [M⁺+1] 162.13 m/z.

5-cyano-1-methylindole. A flame dried flask is charged with 5-cyanoindole (500 mg, 3.52 mmol) and 60 % NaH (169 mg, 4.23 mmol) in oil. The flask is then flushed with argon and cooled to 0° C. Once cool, dimethylformamide (8 mL) is added, and the reaction is allowed to stir until the evolution of hydrogen is complete. Iodomethane (550 mg, 3.87 mmol) is then added dropwise, and the reaction is allowed to slowly come to room temperature. After complete, the solvent is removed and the product (489 mg) is isolated by flash chromatography (10% EtOAc/Hex) in 89 % yield. ¹H NMR (300MHz, CDCl₃) δ 3.83 (s, 3H), 6.55 (d, J = 3.2 Hz, 1H), 7.16 (d, J = 3.2 Hz, 1H), 7.35 (d, J = 8.5 Hz, 1H), 7.44 (dd, J = 8.5, 1.4 Hz, 1H), 7.96 (d, 0.8 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 33.5, 102.5,

102.6, 110.5, 121.4, 124.7, 126.8, 128.7, 131.6, 138.6; IR (NaCl plate, cm^{-1}) ν_{max} 2947.3, 2341.6, 2219.9, 1610.5, 1513.0, 1450.5, 1341.9, 1292.3, 1248.9, 1151.6, 1089.6; MS: calculated for $\text{C}_{10}\text{H}_8\text{N}_2$ 156.07, observed (APCI+) $[\text{M}^++1]$ 157.12 m/z.

5-nitro-1-methylindole. A flame dried flask is charged with 5-nitroindole (1 g, 6.17 mmol) and 60 % NaH (296.3 mg, 7.41 mmol) in oil. The flask is then flushed with argon and cooled to 0° C. Once cool, dimethylformamide (15 mL) is added, and the reaction is allowed to stir until the evolution of hydrogen is complete. Iodomethane (963.5 mg, 6.79 mmol) is then added dropwise, and the reaction is allowed to slowly come to room temperature. After complete, the solvent is removed and the product (999 mg) is isolated by flash chromatography (20 % EtOAc/Hex) in 92 % yield. ^1H NMR (300MHz, CDCl_3) δ 3.86 (s, 3H), 6.67 (d, J = 3.2 Hz, 1H), 7.19 (d, J = 3.2 Hz, 1H), 7.33 (d, J = 9.0 Hz, 1H), 8.12 (dd, 9.0, 2.3 Hz, 1H), 8.58 (d, J = 2.2 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 33.7, 104.2, 109.5, 117.6, 118.5, 128.1, 132.5, 139.8, 141.9; IR (NaCl plate, cm^{-1}) ν_{max} 2987.0, 2305.9, 1422.0, 1332.2, 1265.1; MS: calculated for $\text{C}_9\text{H}_8\text{N}_2\text{O}_2$ 176.06, observed (APCI+) $[\text{M}^++1]$ 177.09 m/z.

1-(4'-cyanophenyl)-indole. Procedure was adopted from Professor Hartwig's work.⁶ A 250 ml flask is charged with Cs_2CO_3 (1.68 g, 5.16 mmol), 4-iodobenzonitrile (1.18 g, 5.16 mmol), indole (500 mg, 4.3 mmol), $\text{Pd}(\text{OAc})_2$ (9.7 mg, 0.043 mmol), and DPPF (35.8 mg, 0.065 mmol). The flask is purged with argon, followed by the addition of 130 mL of toluene. The reaction mixture is heated to 100° C for 12 hours.

After the reaction is complete, the crude material is adsorbed onto silica and purified by flash chromatography (gradient elution, 0 to 15 % EtOAc/Hex). The final product is obtained in 65 % yield, 218 mg. Before being used in arylation reactions, the material is re-crystallized under an atmosphere of argon from CH_2Cl_2 layered with hexanes. ^1H NMR (300MHz, CDCl_3) δ 6.87 (d, J = 3.3 Hz, 1H), 7.32-7.45 (m, 3H), 7.69-7.73 (m, 3H), 7.82 (d, J = 7.2 Hz, 1H), 7.88 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 106.2, 109.9, 110.8, 119.0, 121.8, 122.0, 123.7, 124.2, 127.5, 130.4, 134.2, 135.6, 144.0; IR (NaCl plate, cm^{-1}) ν_{max} 3108.4, 3056.5, 2225.7, 1602.9, 1517.0, 1455.9, 1334.9, 1234.8, 1209.7, 1135.8; MS: calculated for $\text{C}_{15}\text{H}_{10}\text{N}_2$ 218.08, observed (APCI+) $[\text{M}^+ + 1]$ 219.03 m/z.

5-benzenesulfonamido-1-methylindole. This material was synthesized in two steps from 5-nitro-1-methylindole. A hydrogenation apparatus was charged with 5-nitro-1-methylindole (500 mg, 2.84 mmol), approximately 100 mL of ethanol (or until everything dissolves; mild heating and stirring may be required).

To the substrate solution was added 20 mg of Raney® 2800 nickel. The vessel was sealed and pressurized with 40 psi of H_2 ; the reaction was allowed to stir for 3-5 hours or until the solution was colorless. After the reaction was complete, the solution was filtered through celite and the solvent was removed with a rotavapor. The material, 5-amino-1-methylindole, was used in the next step without further purification or characterization. (CAUTION: 5-amino-1-methylindole is very prone to oxidation. It should be used immediately in the next step and stored under argon! Do not expose the

material to acetone; 5-amino-1-methylindole will react with it.⁷⁾ The 5-amino-1-methylindole from the previous step was mixed with a catalytic amount of dimethylaminopyridine in 6 mL of pyridine under an argon atmosphere. The solution was cooled to 0° C and benzenesulfonyl chloride (552 mg, 3.1 mmol) was added dropwise. The reaction was allowed to reach ambient temperature with stirring, and continued stirring until the reaction was complete. The solvent was removed under vacuum with a rotavapor, and the final product (68 % yield, 552 mg) was purified via flash chromatography (10 to 35 % EtOAc/Hex gradient elution). ¹H NMR (300MHz, CDCl₃) δ 3.75 (s, 3H), 6.38 (d, J = 2.8 Hz, 1H), 6.47 (s, 1H), 6.89 (dd, J = 8.6, 1.6, 1H), 7.03 (d, J = 2.9 Hz, 1H), 7.15 (d, J = 8.6Hz, 1H), 7.29 (d, J = 1.3 Hz, 1H), 7.38 (t, J = 7.5 Hz, 2H), 7.49 (t, J = 7.3 Hz, 1H), 7.69 (d, J = 7.4 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 33.6, 101.5, 110.1, 117.4, 119.5, 127.8, 128.2, 128.9, 129.2, 130.4, 133.1, 135.7, 139.5; IR (NaCl plate, CM⁻¹) ν_{max} 3259.3, 2922.7, 2852.1, 1476.6, 1446.6, 1326.0, 1164.5, 1091.6; MS: calculated for C₁₅H₁₄N₂O₂S 286.08, observed (APCI+) [M⁺+1] 287.12 m/z.

4-methoxybenzyl 2'-iodophenylether. A flame dried flask is charged with 2-iodophenol (2 g, 9.09 mmol), a catalytic amount of KI and K₂CO₃ (1.93 g, 18.2 mmol). The flask is then flushed with argon and acetone (5 mL) is added, and the reaction is allowed to stir until all the 2-iodophenol is dissolved. 4-Methoxybenzyl chloride (1.57 g, 9.99 mmol) is then added dropwise, and the reaction is allowed to stir until completion. The solvent is removed and the product (2.7 g) is isolated by flash chromatography (10 % EtOAc/Hex) in 88 % yield. ¹H NMR (300MHz, CDCl₃) δ 3.92 (s, 3H), 5.18 (s, 2H), 6.82 (t, J = 7.5 Hz, 1H), 6.97 (d, J = 7.5 Hz, 1H), 7.03 (d, J = 8.7 Hz, 2H), 7.37 (t, J = 7.7 Hz, 1H), 7.52 (d, J = 8.7 Hz, 2H), 7.90 (d, J = 7.5 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 55.7, 71.1, 87.9, 113.4, 114.4, 123.2, 128.8, 129.1, 129.8, 139.9, 157.5, 159.8; IR (NaCl plate, cm⁻¹) ν_{max} 3002.0, 2933.2, 2834.3, 1611.6, 1581.2, 1515.9, 1464.6, 1375.7, 1281.7, 1253.5, 1180.0, 1116.3, 1031.1.

4-methoxybenzyl 2'-iodophenylether continued.

Part D: Arylation Protocol

General procedure for arylation of alkyl indoles:

In an 8 mL vial, sealed with an open-top closure fitted with Teflon septa, cesium acetate (350 mg, 1.8 mmol) was dried for at least 2 hours under dynamic vacuum at 125° C. Once dried, the base was cooled to ambient temperature, then palladium acetate (1 mg, 4.6 x 10⁻³ mmol) and triphenylphosphine (4.8 mg, 1.8 x 10⁻² mmol) were added under argon on a bench-top. To this mixture was then added 120 µL of dimethylacetamide, followed by 1-methylindole (119.5 mg, (0.91 mmol) and iodobenzene (223.3 mg, 1.1 mmol). The mixture was then heated to 125° C with stirring for 24 hrs. Upon completion, the reaction was diluted with dichloromethane (15 mL), filtered through celite, and the solvent was evaporated. The final product was isolated by flash column chromatography (5% ethylacetate, 95 % hexane) to give 88 % yield (0.8 mmol) of 2-phenyl-1-methylindole. All spectra matched literature values.⁸

The spectra for the following compounds matched literature values: 1-methyl-2-(4'-cyanophenyl)-indole,⁹ 1-methyl-2-(3'-pyridyl)-indole,⁹ 1,2-diphenylindole.¹⁰ Full characterization of the other arylation products is shown below. All compounds were purified by flash chromatography using the gradient elution mentioned in the general procedure. If additional purification was used, it is stated in the compound characterization data.

1-methyl-2-(4'-trifluoromethylphenyl)-indole. ¹H NMR (300MHz, CDCl₃) δ 3.87 (s, 3H), 6.74 (s, 1H), 7.27 (t, J = 7.5 Hz, 1H), 7.39 (t, J = 7.5 Hz, 1H), 7.49 (d, J = 7.5 Hz, 1H), 7.73 (d, J = 7.5 Hz, 1H), 7.77 (d, J = 8.5 Hz, 2H) 7.83 (d, J = 8.5 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 32.0, 103.3, 110.2, 120.8, 121.2, 122.9, 126.0, 128.1, 129.4 (q, 172.5 Hz, 1C) 129.9, 136.8, 139.3, 140.6; IR (NaCl plate, cm⁻¹) ν_{max} 2925.0, 1616.8, 1465.0, 1323.5, 1168.3, 1128.4, 1069.3; MS: calculated for C₁₆H₁₂F₃N 275.09, observed (APCI+) [M⁺+1] 276.09 m/z.

1-methyl-2-(4'-acetophenone)-indole. ^1H NMR (300MHz, CDCl_3) δ 2.77 (s, 3H), 3.88 (s, 3H), 6.77 (s, 1H), 7.28 (t, $J = 7.0$ Hz, 1H), 7.40 (t, $J = 7.0$ Hz, 1H), 7.49 (d, $J = 7.8$ Hz, 1H), 7.72 (d, $J = 8.1$ Hz, 2H), 7.77 (d, $J = 7.8$ Hz, 1H) 8.15 (d, $J = 8.1$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 26.9, 32.0, 103.4, 110.2, 120.6, 121.2, 122.8, 128.2, 129.0, 129.6, 136.7, 137.9, 139.4, 140.8, 198.1; IR (NaCl plate, cm^{-1}) ν_{max} 2915.4, 2360.0, 1682.5, 1604.3, 1464.4, 1267.2; MS: calculated for $\text{C}_{17}\text{H}_{15}\text{NO}$ 249.12, observed (APCI+) $[\text{M}^+ + 1]$ 250.11 m/z.

1-methyl-2-phenylpyrrolo[2,3-b]pyridine. ^1H NMR (300MHz, CDCl_3) δ 3.91 (s, 3H), 6.51 (s, 1H), 7.08 (dd, $J = 7.8, 4.7$ Hz, 1H), 7.40-7.58 (m, 5H), 7.89 (dd, $J = 7.8, 1.5$ Hz, 1H), 8.33 (dd, $J = 4.8, 1.5$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 30.2, 99.9, 116.5, 121.0, 128.5, 128.7, 128.9, 129.0, 129.6, 132.9, 143.1, 149.9; IR (NaCl plate, CM^{-1}) ν_{max} 3051.6, 2850.4, 1731.0, 1483.7, 1403.1, 1317.8, 1295.4, 1225.7; MS: calculated for $\text{C}_{14}\text{H}_{12}\text{N}_2$ 208.10, observed (APCI+) $[\text{M}^+ + 1]$ 209.13 m/z.

4-methoxy-1-methyl-2-phenylindole. ^1H NMR (300MHz, CDCl_3) δ 3.74 (s, 3H), 3.98 (s, 3H), 6.58 (d, $J = 7.7$ Hz, 1H), 6.58 (s, 1H), 7.00 (d, $J = 8.2$ Hz, 1H), 7.18 (t, $J = 8.0$ Hz, 1H), 7.36-7.53 (m, 5H); ^{13}C NMR (75 MHz, CDCl_3) δ 31.9, 55.8, 99.3, 100.3, 103.6, 119.2, 122.9, 128.1, 128.9, 129.8, 133.4, 140.2, 140.9, 153.9; IR (NaCl plate, cm^{-1}) ν_{max} 2945.3, 2835.9, 1584.8, 1481.8, 1351.3, 1253.5, 1071.6; MS: calculated for $\text{C}_{16}\text{H}_{15}\text{NO}$ 237.12, observed (APCI+) $[\text{M}^+ + 1]$ 238.09 m/z. Re-crystallized from hexanes.

5-cyano-1-methyl-2-phenylindole. ^1H NMR (300MHz, CDCl_3) δ 3.77 (s, 3H), 6.61 (s, 1H), 7.25-7.49 (m, 7H), 7.95 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 31.8, 102.7, 103.2, 110.8, 121.3, 124.9, 126.3, 128.1, 129.1, 129.1, 129.8, 132.0, 140.1, 144.2; IR (NaCl plate, cm^{-1}) ν_{max} 2947.5, 2361.3, 2217.0, 1607.2, 1475.8, 1335.6, 1287.5; MS: calculated for $\text{C}_{16}\text{H}_{12}\text{N}_2$ 232.10, observed (APCI+) $[\text{M}^+ + 1]$ 233.11 m/z. Re-crystallized from hexanes / dichloromethane.

1-methy-5-nitro-2-phenylindole. ^1H NMR (300MHz, CDCl_3) δ 3.79 (s, 3H), 6.71 (s, 1H), 7.37 (d, $J = 9.0$ Hz, 1H), 7.42-7.51 (m, 5H), 8.12 (dd, $J = 9.0, 2.3$ Hz, 1H), 8.57 (d, $J = 2.2$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 32.0, 104.2, 109.8, 117.7, 118.0, 127.6, 129.2, 129.8, 131.9, 141.5, 142.2, 145.8; IR (NaCl plate, cm^{-1}) ν_{max} 2918.3, 2849.8, 1699.8, 1517.0, 1461.3, 1335.8, 1265.0, 1171.5, 1139.8; MS: calculated for $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_2$ 252.09, observed (APCI+) $[\text{M}^++1]$ 253.07 m/z.

5-benzenesulfonamide-1-methy-2-phenylindole. ^1H NMR (300MHz, CDCl_3) δ 3.70 (s, 3H), 6.45 (s, 1H), 6.46 (s, 1H), 6.92 (dd, $J = 8.6, 2.0$ Hz, 1H), 7.30 (d, $J = 8.6$ Hz, 1H), 7.30 (d, $J = 2.0$ Hz, 1H), 7.37-7.59 (m, 8H), 7.72 (d, $J = 7.8$ Hz, 2H); ^{13}C NMR (75 MHz, d_6 -acetone) δ 31.1, 101.9, 110.6, 115.1, 118.2, 127.5, 128.4, 128.6, 128.9, 129.1, 129.6, 130.2, 132.8, 133.0, 137.0, 140.7, 142.9; IR (NaCl plate, cm^{-1}) ν_{max} 3253.4, 2921.5, 1476.1, 1446.1, 1325.9, 1163.1, 1091.5; MS: calculated for $\text{C}_{21}\text{H}_{18}\text{N}_2\text{O}_2\text{S}$ 362.11, observed $[\text{M}^++1]$ 363.11 m/z. Re-crystallized from hexanes / dichloromethane.

1-benzyl-2-phenylindole. ^1H NMR (300MHz, CDCl_3) δ 5.51 (s, 2H), 6.80 (s, 1H), 7.17 (d, $J = 7.2$ Hz, 2H), 7.26-7.43 (m, 6H), 7.48-7.62 (m, 5H), 7.79-7.82 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 48.3, 102.9, 111.0, 120.6, 121.0, 122.5, 126.4, 127.6, 128.4, 128.9, 129.0, 129.2, 129.7, 133.2, 138.4, 138.8, 142.2; IR (NaCl plate, cm^{-1}) ν_{max} 3058.1, 3029.3, 1603.3, 1495.3, 1416.9, 1345.9; MS: calculated for $\text{C}_{21}\text{H}_{17}\text{N}$ 283.14, observed (APCI+) $[\text{M}^++1]$ 284.18 m/z. Re-crystallized from hexanes / dichloromethane.

1-iso-propyl-2-phenylindole. ^1H NMR (300MHz, CDCl_3) δ 1.81 (d, $J = 7.0$ Hz, 6H), 4.88 (h, $J = 7.0$ Hz, 1H), 6.66 (s, 1H), 7.31 (dt, $J = 7.2$, 1.0 Hz, 1H), 7.39 (dt, $J = 7.5$, 1.5 Hz, 1H), 7.55-7.70 (m, 5H), 7.81 (t, $J = 7.41$, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 22.0, 48.4, 102.7, 112.9, 119.9, 121.4, 121.5, 128.4, 128.9, 129.8, 130.1, 134.3, 135.9, 141.9; IR (NaCl plate, cm^{-1}) ν_{max} 3053.0, 2971.8, 2932.2, 1455.9, 1368.7, 1303.1; MS: calculated for $\text{C}_{17}\text{H}_{17}\text{N}$ 235.14, observed (APCI+) $[\text{M}^++1]$ 236.19 m/z. Re-crystallized from hexanes / dichloromethane.

1-(4'-cyanophenyl)-2-phenylindole. ^1H NMR (300MHz, CDCl_3) δ 6.93 (s, 1H), 7.30-7.46 (m, 10H), 7.74-7.81 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 106.0, 110.5, 110.9, 118.8, 121.4, 122.0, 123.5, 128.3, 128.7, 128.9, 129.1, 129.4, 132.2, 133.7, 138.6, 140.7, 143.0; IR (NaCl plate, cm^{-1}) ν_{max} 3059.4, 2228.2, 1601.3, 1510.4, 1454.8, 1379.8, 1348.3; MS: calculated for $\text{C}_{21}\text{H}_{14}\text{N}_2$ 294.12, observed (APCI+) $[\text{M}^++1]$ 295.14 m/z. Re-crystallized from hexanes / dichloromethane.

1-methyl-2-(2'-*para*-methoxybenzylphenylether)-indole. ^1H NMR (300MHz, CDCl_3) δ 3.69 (s, 3H), 3.88 (s, 3H), 5.10 (s, 2H), 6.63 (s, 1H), 6.89 (d, $J = 8.7$ Hz, 2H), 7.15-7.26 (m, 5H), 7.34 (t, $J = 8.8$ Hz, 1H), 7.43-7.52 (m, 3H), 7.44 (d, $J = 9$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 31.9, 55.7, 70.8, 102.3, 109.8, 113.9, 114.3, 119.7, 120.8, 121.6, 123.4, 128.5, 129.0, 129.5, 130.4, 133.1, 138.2, 139.1, 155.2, 159.8; IR (NaCl plate, cm^{-1}) ν_{max} 3054.2, 2935.1, 2835.7, 1612.0, 1580.9, 1514.9, 1465.9, 1451.3, 1383.9, 1312.7, 1244.8, 1175.2, 1115.6, 1033.4; MS: calculated for $\text{C}_{23}\text{H}_{21}\text{NO}_2$ 343.16, observed (APCI+) $[\text{M}^++1]$ 344.02 m/z. Re-crystallized from hexanes; caution, air sensitive.

1-methyl-3-(2'-para-methoxybenzylphenylether)-indole. ^1H NMR (300MHz, CDCl_3) δ 3.89 (s, 3H), 3.90 (s, 3H), 5.14 (s, 2H), 6.95 (d, $J = 8.6$ Hz, 2H), 7.15-7.39 (m, 7H), 7.45 (d, $J = 8.2$ Hz, 1H), 7.51 (s, 1H), 7.81 (d, $J = 3.7$ Hz, 1H), 7.96 (d, $J = 7.9$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 33.1, 56.0, 70.9, 109.9, 112.0, 114.0, 114.2, 120.1, 121.2, 121.8, 122.2, 126.0, 127.3, 127.5, 129.3, 130.2, 131.1, 137.5, 139.8, 156.3, 159.9; IR (NaCl plate, cm^{-1}) ν_{max} 2932.2, 1612.5, 1543.3, 1514.0, 1465.1, 1375.6, 1329.0, 1234.9, 1174.3, 1118.8, 1087.6, 1033.8; MS: calculated for $\text{C}_{23}\text{H}_{21}\text{NO}_2$ 343.16, observed (APCI+) $[\text{M}^+ + 1]$ 344.03 m/z. Recrystallized from hexanes; caution, air sensitive.

References:

- (1) Made by mixing 6.14 mmol of Cs_2CO_3 (2.00 g) with 12.44 mmol of trimethylacetic acid (1.27 g) in 1.2 mL of water and heating to 50°C for 10 minutes. After the acid/base reaction is complete, the water is removed and the salt dried under vacuum at 125°C for 24 hours.
- (2) Made by mixing 6.14 mmol of Cs_2CO_3 (2.00 g) with 12.44 mmol of trifluoroacetic acid (1.42 g) in 1.2 mL of water and heating to 50°C for 10 minutes. After the acid/base reaction is complete, the water is removed and the salt dried under vacuum at 125°C for 24 hours.
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