

Palladium-Catalyzed Synthesis of N-Aryl-2-Benzylindolines via Tandem Arylation of 2-Allylaniline: Control of Selectivity Through *in situ* Catalyst Modification

Ricardo Lira and John P. Wolfe*

Department of Chemistry, University of Michigan, 930 N. University Avenue, Ann Arbor, Michigan 48109-1055

Supporting Information

Experimental procedures and characterization data for new compounds in Tables 1 and 2 (11 pages).

General All reactions were carried out under a nitrogen atmosphere in oven or flame dried glassware. Tris(dibenzylideneacetone)dipalladium (0) and all phosphine ligands were purchased from Strem Chemical Co. and used without further purification. All aryl bromides except for 4-bromobenzoic acid *tert*-butyl ester were obtained from commercial sources (Aldrich Chemical CO or Acros Chemical CO) and were used as obtained. 4-Bromobenzoic acid *tert*-butyl ester,¹ 2-allylaniline,² and 2-allyl-5-methoxyaniline³ were prepared according to literature procedures. Toluene was purified using a GlassContour solvent purification system. Yields refer to isolated yields of compounds estimated to be $\geq 95\%$ pure as determined by ^1H NMR, and/or combustion analysis. The yields reported in the supporting information describe the result of a single experiment, whereas the yields reported in Tables

1 and 2 are average yields of two or more experiments. Thus, the yields reported in the supporting information may differ from those shown in Tables 1 and 2.

General procedure for the one-pot palladium-catalyzed synthesis of N-aryl-2-benzylindolines using two equivalents of a single aryl bromide (Table 1). An oven or flame-dried Schlenk tube was cooled under a stream of nitrogen and charged with $\text{Pd}_2(\text{dba})_3$ (1 mol % complex, 2 mol % Pd), dpe-phos (2 mol %), NaOtBu (2.2 equiv), and the aryl bromide (2.05 equiv). The tube was purged with nitrogen and a solution of the aniline substrate (1.0 equiv) in toluene (4 mL/mmol substrate) was added. The mixture was placed in a pre-heated oil bath at 105 °C with stirring until the starting material had been consumed as judged by GC or ^1H NMR analysis. The reaction mixture was cooled to room temperature, quenched with saturated aqueous NH_4Cl (2 mL) and diluted with ethyl acetate (10 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (2 X 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude product was then purified by flash chromatography on silica gel.

2-Benzyl-1-phenyl-2,3-dihydro-1H-indole (Table 1, Entry 1). Reaction of 34 mg (0.25 mmol) of 2-allylaniline with 4-bromobenzene (54 μL , 0.51 mmol) and NaOtBu (53 mg, 0.55 mmol) following the general procedure afforded 65 mg (91 %) of the title compound as a pale yellow viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.39-7.35 (m, 2 H), 7.32-7.26 (m, 4 H), 7.22-7.16 (m, 3 H), 7.08-7.04 (m, 2 H), 7.01 (t, J = 7.6 Hz, 1 H), 6.84 (d, J = 8.4 Hz, 1 H), 6.70 (d, J = 7.6 Hz, 1 H), 4.50 (m, 1 H), 3.20–3.16 (dd, J = 3.6, 13.6 Hz, 1 H), 3.10-3.04 (dd, J = 8.8, 15.6 Hz, 1 H), 2.88-2.83 (dd, J = 6.8, 15.6 Hz, 1 H), 2.74-2.68 (dd, J = 10.0, 13.6 Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.4, 143.5, 138.3, 129.4, 129.3, 128.5, 127.1, 126.4, 125.0, 122.9, 121.4, 119.0, 108.6, 65.5, 39.6, 34.1, (two of the

aromatic signals are incidentally equivalent); IR (film) 1592, 1498 cm^{-1} . Anal calcd for $\text{C}_{21}\text{H}_{19}\text{N}$: C, 88.38; H, 6.71; N, 4.91. Found: C, 88.57; H, 6.69; N, 4.95.

1-Pyridin-3-yl-2-pyridin-3-ylmethyl-2,3-dihydro-1H-indole (Table 1, Entry 2). Reaction of 34 mg (0.25 mmol) of 2-allylaniline with 3-bromopyridine (50 μL , 0.51 mmol) and NaOtBu (53 mg, 0.55 mmol) following the general procedure afforded 63 mg (87 %) of the title compound as a pale yellow viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 8.57 (d, $J = 2.4$ Hz, 1 H), 8.43-8.42 (dd, $J = 2.0$, 6.8 Hz, 1 H), 8.41 (d, $J = 2.0$ Hz, 1 H), 8.27-8.26 (dd, $J = 1.6$, 4.8 Hz, 1 H), 7.55-7.51 (ddd, $J = 1.2$, 2.8, 8.0 Hz, 1 H), 7.45-7.43 (m, 1 H), 7.26-7.22 (dd, $J = 4.8$, 8.4 Hz, 1 H), 7.18-7.15 (dd, $J = 4.8$, 12.4 Hz, 1 H), 7.08 (d, $J = 7.2$ Hz, 1 H), 7.02 (t, $J = 8.0$ Hz, 1 H), 6.83 (d, $J = 8.0$ Hz, 1 H), 6.75 (t, $J = 7.2$ Hz, 1 H), 4.54-4.47 (m, 1 H), 3.18-3.12 (dd, $J = 8.8$, 15.6 Hz, 1 H), 3.09-3.05 (dd, $J = 4.4$, 14.0 Hz, 1 H), 2.85-2.77 (m, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 150.5, 148.1, 147.1, 143.7, 143.0, 140.0, 136.7, 133.0, 129.1, 127.3, 127.2, 125.2, 123.8, 123.4, 120.2, 109.1, 64.7, 36.7, 34.1; IR (film) 1500 cm^{-1} . MS (EI) m/z 287.1418 (287.1422 calcd for $\text{C}_{19}\text{H}_{17}\text{N}_3$).

1-Naphthalen-1-yl-2-naphthalenylmethyl-2,3-dihydro-1H-indole (Table 1, Entry 3). Reaction of 34 mg (0.25 mmol) of 2-allylaniline with 1-bromonaphthalene (71 μL , 0.51 mmol) and NaOtBu (53 mg, 0.55 mmol) following the general procedure afforded 90 mg (93 %) of the title compound as a colorless viscous oil. This material was obtained as a 2.3:1 mixture of rotamers as judged by ^1H NMR. The signals for the two rotamers coalesced when dissolved in d^8 -toluene and heated to 75 $^\circ\text{C}$. Major rotamer: ^1H NMR (400 MHz, CDCl_3) δ 8.29 (d, $J = 8.0$ Hz, 0.7 H), 7.94 (d, $J = 7.6$ Hz, 0.7 H), 7.87-7.65 (m, 4 H), 7.60 (t, $J = 7.2$ Hz, 0.7 H), 7.58-7.47 (m, 2 H), 7.45-7.39 (m, 1.4 H), 7.35-7.29 (m, 2 H), 7.11-6.98 (m, 1.4 H), 6.84 (t, $J = 8.0$ Hz, 0.7 H), 6.64 (t, $J = 6.8$ Hz, 0.7 H), 5.88 (d, $J = 8.0$ Hz, 0.7 H), 4.91-4.78 (m, 1 H), 3.62-3.58 (dd, $J = 4.0$, 17.6 Hz, 0.7 H), 3.27-2.91 (m,

3.3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 152.3, 141.2, 134.6, 134.5, 133.8, 132.5, 132.0, 128.8, 128.2, 127.2, 126.45, 126.41, 126.28, 126.12, 125.83, 125.76, 125.5, 125.4, 124.5, 124.2, 123.5, 121.3, 118.2, 108.3, 67.5, 37.6, 35.7 (two of the aromatic signals are incidentally equivalent); IR (film) 1499 cm^{-1} . Anal calcd for $\text{C}_{29}\text{H}_{23}\text{N}$: C, 90.35; H, 6.01; N, 3.63. Found: C, 90.29; H, 5.96; N, 3.63.

1-Biphenyl-4-yl-2-biphenyl-4-ylmethyl-2,3-dihydro-1H-indole (Table 1, Entry 4). Reaction of 34 mg (0.25 mmol) of 2-allylaniline with 4-bromobiphenyl (117 mg, 0.51 mmol) and NaOtBu (53 mg, 0.55 mmol) following the general procedure afforded 98 mg (85 %) of the title compound as a colorless viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.62-7.50 (m, 8 H), 7.44-7.36 (m, 6 H), 7.33-7.22 (m, 4 H), 7.12-7.10 (d, $J = 7.6\text{ Hz}$, 1 H), 7.06 (t, $J = 7.6\text{ Hz}$, 1 H), 6.96-6.94 (d, $J = 8.0\text{ Hz}$, 1 H), 6.74 (t, $J = 7.2\text{ Hz}$, 1 H), 4.62-4.57 (m, 1 H), 3.28-3.24 (dd, $J = 3.6, 13.6\text{ Hz}$, 1 H), 3.19-3.13 (dd, $J = 8.8, 15.2\text{ Hz}$, 1 H), 2.94-2.89 (dd, $J = 6.4, 15.6\text{ Hz}$, 1 H), 2.82-2.76 (dd, $J = 9.6, 13.6\text{ Hz}$, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.0, 142.8, 140.9, 140.7, 139.3, 137.3, 135.3, 129.8, 129.5, 128.8, 128.7, 128.0, 127.21, 127.17, 127.0, 126.8, 126.7, 125.1, 121.1, 119.2, 108.9, 65.3, 39.3, 34.2, (two of the aromatic signals are incidentally equivalent); IR (film) 1485 cm^{-1} . Anal calcd for $\text{C}_{33}\text{H}_{27}\text{N}$: C, 90.58; H, 6.22; N, 3.20. Found: C, 90.63; H, 6.21; N, 3.16.

2-(4-Methylbenzyl)-1-*p*-tolyl-2,3-dihydro-1H-indole (Table 1, Entry 5). Reaction of 68 mg (0.5 mmol) of 2-allylaniline with 4-bromotoluene (135 μL , 1.1 mmol) and NaOtBu (110 mg, 1.2 mmol) following the general procedure afforded 114 mg (72 %) of the title compound as a pale yellow gum. ^1H NMR (400 MHz, CDCl_3) δ 7.22 (br s, 4 H), 7.11-7.05 (m, 5 H), 7.00 (t, $J = 8.0\text{ Hz}$, 1 H), 6.72 (d, $J = 8.4\text{ Hz}$, 1 H), 6.68 (dt, $J = 1.2, 7.6\text{ Hz}$, 1 H), 4.48-4.40 (m, 1 H), 3.15-3.11 (dd, $J = 3.6, 13.6\text{ Hz}$, 1 H), 3.08-3.02 (dd, $J = 8.4, 15.6\text{ Hz}$, 1 H), 2.89-2.84 (dd, $J = 7.6, 16.0\text{ Hz}$, 1 H), 2.70-2.64 (dd, $J = 10.0, 13.2\text{ Hz}$, 1 H), 2.36 (s, 3 H), 2.32 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.4, 140.9, 135.8,

135.3, 132.9, 130.0, 129.20, 129.16, 129.10, 127.1, 124.8, 122.5, 118.4, 108.0, 65.9, 39.2, 34.2, 21.0, 20.9; IR (film) 1638 cm^{-1} . Anal calcd for $\text{C}_{23}\text{H}_{23}\text{N}$: C, 88.13; H, 7.40; N, 4.47; Found: C, 88.26; H, 7.49; N, 4.41.

{4-[1-(4-Benzoylphenyl)-2,3-dihydro-1*H*-indol-2-ylmethyl]phenyl}phenylmethanone

(Table 1, Entry 6). Reaction of 34 mg (0.25 mmol) of 2-allylaniline with 4-bromobenzophenone (133 mg, 0.51 mmol) and NaOtBu (53 mg, 0.55 mmol) following the general procedure afforded 120 mg (97 %) of the title compound as a bright yellow viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.84 (td, J = 2.4, 9.2 Hz, 2 H), 7.78-7.70 (m, 6 H), 7.58-7.51 (m, 2 H), 7.46-7.43 (m, 4 H), 7.31-7.27 (m, 4 H), 7.24-7.22 (m, 1H), 7.17-7.11 (dd, J = 7.6, 16.0 Hz, 2 H), 6.85 (dt, J = 0.4, 7.2 Hz, 1 H), 4.68-4.62 (m, 1 H), 3.27-3.21 (m, 2 H), 2.90-2.80 (m, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 196.3, 195.0, 147.4, 144.8, 142.5, 138.4, 137.6, 136.1, 132.4, 131.7, 130.6, 130.4, 130.0, 129.6, 129.40, 129.37, 128.3, 128.2, 127.7, 125.6, 121.2, 115.9, 111.6, 64.6, 39.4, 33.9, (two of the aromatic signals are incidentally equivalent); IR (film) 1650, 1588 cm^{-1} . Anal calcd for $\text{C}_{35}\text{H}_{27}\text{NO}_2$: C, 85.15; H, 5.51; N, 2.84. Found: C, 84.74; H, 5.46; N, 2.58.

2-(4-Methoxybenzyl)-1-(4-methoxyphenyl)-2,3-dihydro-1*H*-indole (Table 1, Entry 7).

Reaction of 34 mg (0.25 mmol) of 2-allylaniline with 4-bromoanisole (64 μL , 0.51 mmol) and NaOtBu (53 mg, 0.55 mmol) following the general procedure using xantphos in place of dpe-phos afforded 37 mg (43 %) of the title compound as a pale yellow viscous oil. N-(4-methoxyphenyl)-2-methylindole was also isolated in 25 % yield. Major product: ^1H NMR (400 MHz, CDCl_3) δ 7.26-7.22 (m, 2 H), 7.08-7.05 (m, 3 H), 7.00-6.95 (m, 3 H), 6.83-6.81 (m, 2 H), 6.67 (t, J = 7.6 Hz, 1 H), 6.53 (d, J = 8.0 Hz, 1 H), 4.36-4.29 (m, 1 H), 3.83 (s, 3H), 3.78 (s, 3H), 3.08-3.00 (m, 2 H), 2.89-2.83 (dd, J = 8.4, 15.6 Hz, 1 H), 2.70-2.65 (dd, J = 9.6, 13.2 Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 158.1, 156.5,

150.7, 136.7, 130.4, 130.2, 128.7, 127.1, 125.6, 124.6, 118.2, 114.7, 113.8, 107.6, 67.0, 55.4, 55.2, 38.8, 34.3; IR (film) 1610, 1510 cm^{-1} . Anal calcd for $\text{C}_{23}\text{H}_{23}\text{NO}_2$: C, 79.97; H, 6.71; N, 4.05. Found: C, 80.01; H, 6.76; N, 4.09.

2-(4-carbo-*tert*-butoxybenzyl)-1-(4-carbo-*tert*-butoxyphenyl)-6-methoxy-2,3-dihydro-1*H*-indole (Table 1, Entry 8). Reaction of 41 mg (0.25 mmol) of 2-allyl-5-methoxyaniline with 4-bromobenzoic acid *tert*-butyl ester (131 mg, 0.51 mmol) and NaOtBu (53 mg, 0.55 mmol) following the general procedure afforded 100 mg (78 %) of the title compound as a colorless viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.98 (d, J = 8.8 Hz, 2 H), 7.92 (d, J = 8.4 Hz, 2 H), 7.28-7.22 (m, 4 H), 7.01 (d, J = 8.0 Hz, 1 H), 6.70 (d, J = 2.0 Hz, 1 H), 6.37-6.34 (dd, J = 2.8, 8.8 Hz, 1 H), 4.64-4.57 (m, 1 H), 3.75 (s, 3H), 3.23–3.19 (dd, J = 3.6, 13.6 Hz, 1 H), 3.09-3.03 (dd, J = 8.8, 16.0 Hz, 1 H), 2.81-2.71 (m, 2 H), 1.59 (s, 9 H), 1.58 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.55, 165.46, 159.7, 146.9, 146.7, 142.6, 131.0, 130.4, 129.7, 129.2, 125.5, 124.6, 122.2, 117.6, 104.8, 97.9, 80.9, 80.5, 65.3, 55.4, 39.1, 32.9, 28.24, 28.15; IR (film) 1707, 1598 cm^{-1} . Anal calcd for $\text{C}_{32}\text{H}_{37}\text{NO}_5$: C, 74.54; H, 7.23; N, 2.72. Found: C, 74.50; H, 7.22; N, 2.77.

2-(4-Chlorobenzyl)-1-(4-chlorophenyl)-6-methoxy-2,3-dihydro-1*H*-indole (Table 1, Entry 9). Reaction of 41 mg (0.25 mmol) of 2-allyl-5-methoxyaniline with 4-bromochlorobenzene (98 mg, 0.51 mmol) and NaOtBu (53 mg, 0.55 mmol) following the general procedure afforded 65 mg (68 %) of the title compound as a colorless viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.33-7.30 (m, 2 H), 7.24-7.17 (m, 4 H), 7.06-7.04 (m, 2 H), 6.95 (d, J = 8.0 Hz, 1 H), 6.33 (d, J = 2.4 Hz, 1 H), 6.27-6.24 (dd, J = 2.4, 8.0 Hz, 1 H), 4.45-4.38 (m, 1 H), 3.70 (s, 3 H), 3.06–2.97 (m, 2 H), 2.77-2.65 (m, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.7, 149.4, 141.8, 136.4, 132.3, 130.6, 129.5, 128.6, 128.2, 125.1,

123.1, 121.4, 103.5, 96.2, 66.1, 55.4, 38.8, 33.3; IR (film) 1495 cm^{-1} . Anal calcd for $\text{C}_{22}\text{H}_{19}\text{Cl}_2\text{NO}$: C, 68.76; H, 4.98; N, 3.64. Found: C, 68.67; H, 5.00; N, 3.62.

6-Methoxy-1-naphthalen-2-yl-2-naphthalen-2-ylmethyl-2,3-dihydro-1H-indole (Table 1, Entry 10). Reaction of 41 mg (0.25 mmol) of 2-allyl-5-methoxyaniline with 2-bromonaphthalene (106 mg, 0.51 mmol) and NaOtBu (53 mg, 0.55 mmol) following the general procedure afforded 85 mg (82 %) of the title compound as a pale yellow viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.90 (d, J = 8.8 Hz, 1 H), 7.85-7.78 (m, 5 H), 7.43 (d, J = 2.0 Hz, 1 H), 7.64 (s, 1 H), 7.61-7.58 (dd, J = 2.0, 8.8 Hz, 1 H), 7.52-7.41 (m, 4 H), 7.35-7.33 (dd, J = 1.6, 8.4 Hz, 1 H), 7.02 (d, J = 8.0 Hz, 1 H), 6.56 (d, J = 2.0 Hz, 1 H), 6.33-6.30 (dd, J = 2.4, 8.0 Hz, 1 H), 4.82-4.75 (m, 1 H), 3.75 (s, 3 H), 3.42-3.38 (dd, J = 3.6, 13.6 Hz, 1 H), 3.12-3.06 (dd, J = 8.8, 15.6 Hz, 1 H), 2.99-2.92 (m, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.7, 149.9, 140.8, 135.8, 134.3, 133.5, 132.2, 130.3, 129.2, 128.1, 127.8, 127.7, 127.65, 127.61, 127.4, 127.1, 126.4, 126.0, 125.4, 125.1, 124.7, 122.3, 121.7, 118.5, 103.3, 96.0, 66.3, 55.4, 39.8, 33.5; IR (film) 1494 cm^{-1} . Anal calcd for $\text{C}_{30}\text{H}_{25}\text{NO}$: C, 86.71; H, 6.06; N, 3.37. Found: C, 86.32; H, 6.18; N, 3.45.

General procedure for the one-pot palladium-catalyzed synthesis of N-aryl-2-benzylindolines using two different aryl bromides (Table 2). An oven or flame-dried Schlenk tube was cooled under a stream of nitrogen and charged with $\text{Pd}_2(\text{dba})_3$ (0.5 mol % complex, 1 mol % Pd), $t\text{-Bu}_2\text{P}(o\text{-biphenyl})$ (2 mol %), NaOtBu (2.1 equiv), and the first aryl bromide (1.0 equiv). The tube was purged with nitrogen and a solution of the aniline substrate (1.0 equiv) in toluene (4 mL/mmol substrate) was added. The mixture was placed in a pre-heated oil bath at 80 $^\circ\text{C}$ with stirring until the starting material had been consumed as judged by GC or ^1H NMR analysis. While maintaining the reaction mixture at 80 $^\circ\text{C}$, a solution of a catalytic amount (2 mol %) of dpe-phos in toluene (0.5 mL)

was added to the reaction mixture, and after 10 min of stirring at 80 °C, the second aryl halide (1.0 equiv) was added neat. When the intermediate arylamine had been consumed (as judged by GC or ¹H NMR analysis), the reaction mixture was cooled to room temperature, quenched with saturated aqueous NH₄Cl (2 mL) and diluted with ethyl acetate (10 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (2 X 10 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude product was then purified by flash chromatography on silica gel.

2-Naphthalen-2-ylmethyl-1-phenyl-2,3-dihydro-1H-indole (Table 2, Entry 1). Reaction of 68 mg (0.50 mmol) of 2-allylaniline with 4-bromobenzene (53 μ L, 0.50 mmol), 2-bromonaphthalene (104 mg, 0.50 mmol), and NaOtBu (100 mg, 1.05 mmol) following the general procedure afforded 135 mg (80 %) of the title compound as a pale yellow viscous oil. ¹H NMR (400 MHz, CDCl₃) δ 7.86-7.81 (m, 3 H), 7.66 (s, 1 H), 7.53-7.41 (m, 6 H), 7.37-7.35 (dd, J = 2.0, 8.4, 1 H), 7.17-7.12 (m, 2 H), 7.08 (t, J = 7.2 Hz, 1 H), 6.92 (d, J = 7.6 Hz, 1 H), 6.79-6.75 (dt, J = 0.4, 8.0 Hz, 1 H), 4.71-4.64 (m, 1 H), 3.42-3.38 (dd, J = 3.2, 13.2 Hz, 1 H), 3.15-3.09 (dd, J = 8.8, 15.6 Hz, 1 H), 3.00–2.90 (m, 2 H); ¹³C NMR (100 MHz, CDCl₃) δ 148.5, 143.5, 135.8, 133.5, 132.1, 129.4, 129.3, 128.1, 127.73, 127.66, 127.62, 127.4, 127.1, 126.0, 125.4, 125.0, 123.0, 121.0, 118.9, 108.5, 65.4, 39.7, 34.1; IR (film) 1499 cm⁻¹. Anal calcd for C₂₅H₂₁N: C, 89.51; H, 6.31; N, 4.18. Found: C, 89.52; H, 6.45; N, 4.22.

1-Biphenyl-4-yl-2-pyridin-3-ylmethyl-2,3-dihydro-1H-indole (Table 2, Entry 2). Reaction of 68 mg (0.50 mmol) of 2-allylaniline with 4-bromobiphenyl (116 mg, 0.50 mmol), 3-bromopyridine (50 μ L, 0.50 mmol), and NaOtBu (100 mg, 1.05 mmol) following the general procedure afforded 153 mg (84 %) of the title compound as a colorless viscous oil. ¹H NMR (400 MHz, CDCl₃) δ 8.47-8.45 (m, 2 H), 7.63-7.59 (m, 4 H), 7.51-7.48 (td, J = 2.0, 7.6 Hz, 1 H), 7.45-7.42 (m, 2 H), 7.36-7.30 (m, 3

H), 7.21-7.18 (dd, $J = 4.8, 7.6$ Hz, 1 H), 7.10 (d, $J = 7.2$ Hz, 1 H), 7.05 (t, $J = 8.0$ Hz, 1 H), 6.91 (d, $J = 8.0$ Hz, 1 H), 6.76-6.72 (dt, $J = 0.4, 7.6$ Hz, 1 H), 4.63-4.55 (m, 1 H), 3.19-3.13 (m, 2 H), 2.89-2.82 (m, 2 H), ^{13}C NMR (100 MHz, CDCl_3) δ 150.6, 148.0, 147.9, 142.5, 140.5, 136.8, 135.6, 133.4, 129.0, 128.7, 128.0, 127.2, 126.9, 126.6, 125.0, 123.3, 121.2, 119.3, 108.9, 64.7, 36.6, 33.9; IR (film) 1486 cm^{-1} . Anal calcd for $\text{C}_{26}\text{H}_{22}\text{N}_2$: C, 86.15; H, 6.12; N, 7.73. Found: C, 85.76; H, 6.04; N, 7.75.

4-[2-(4-Chlorobenzyl)-2,3-dihydroindol-1-yl]benzoic acid *tert*-butyl ester (Table 2, Entry 3). Reaction of 68 mg (0.50 mmol) of 2-allylaniline with 4-bromobenzoic acid *tert*-butyl ester (128 mg, 0.50 mmol), 4-bromochlorobenzene (95 mg, 0.50 mmol), and NaOtBu (100 mg, 1.05 mmol) following the general procedure afforded 180 mg (86 %) of the title compound as a colorless viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.98-7.94 (td, $J = 2.4, 9.2$ Hz, 2 H), 7.26-7.22 (m, 4 H), 7.40-7.07 (m, 5 H), 6.83-6.79 (dt, $J = 1.6, 6.8$ Hz, 1 H), 4.57-4.50 (m, 1 H), 3.18-3.10 (m, 2 H), 2.81-2.76 (dd, $J = 4.0, 15.6$ Hz, 1 H), 2.73-2.68 (dd, $J = 9.6, 14.0$ Hz, 1 H), 1.59 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.5, 147.0, 145.6, 136.1, 132.4, 131.0, 130.7, 130.1, 128.7, 127.2, 125.4, 124.2, 120.5, 116.9, 110.6, 80.4, 64.6, 38.5, 33.7, 28.3; IR (film) 1641 cm^{-1} . Anal calcd for $\text{C}_{26}\text{H}_{26}\text{ClNO}_2$: C, 74.36; H, 6.24; N, 3.34. Found: C, 74.27; H, 6.26; N, 3.28.

4-[1-(4-Benzoylphenyl)-2,3-dihydro-1*H*-indol-2-ylmethyl]benzonitrile (Table 2, Entry 4). Reaction of 68 mg (0.50 mmol) of 2-allylaniline with 4-bromobenzophenone (130 mg, 0.50 mmol), 4-bromobenzonitrile (91 mg, 0.50 mmol), and NaOtBu (100 mg, 1.05 mmol) following the general procedure afforded 98 mg (46 %) of the title compound as a yellow viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.86-7.82 (m, 2 H), 7.78-7.75 (m, 2 H), 7.57-7.54 (m, 3 H), 7.49-7.45 (m, 2 H), 7.31-7.24 (m, 4 H), 7.22-7.20 (m, 1 H), 7.16-7.12 (m, 2 H), 6.88-6.84 (dt, $J = 0.8, 7.2$ Hz, 1 H), 4.66-4.60 (m, 1 H), 3.28-3.20 (m, 2 H), 2.92-2.86 (dd, $J = 8.8, 13.6$ Hz, 1 H), 2.79-2.75 (dd, $J = 3.2, 15.0$ Hz, 1 H); ^{13}C

NMR (100 MHz, CDCl_3) δ 195.0, 147.3, 144.8, 143.1, 138.3, 133.6, 132.34, 132.26, 131.8, 130.2, 129.6, 128.2, 127.3, 125.6, 121.3, 118.7, 116.0, 111.6, 110.6, 64.3, 39.5, 33.8 (two of the aromatic signals are incidentally equivalent); IR (film) 2228, 1644 cm^{-1} . Anal calcd for $\text{C}_{29}\text{H}_{22}\text{N}_2\text{O}$: C, 84.03; H, 5.35; N, 6.76. Found: C, 83.79; H, 5.32; N, 6.79.

4-[1-(4-Chlorophenyl)-6-methoxy-2,3-dihydro-1*H*-indol-2-ylmethyl]benzoic acid *tert*-butyl ester (Table 2, Entry 5). Reaction of 82 mg (0.50 mmol) of 2-allyl-5-methoxyaniline with 4-bromochlorobenzene (96 mg, 0.50 mmol), 4-bromobenzoic acid *tert*-butyl ester (129 mg, 0.50 mmol), and NaOtBu (100 mg, 1.05 mmol) following the general procedure afforded 198 mg (88 %) of the title compound as a clear viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.88 (d, J = 8.4 Hz, 2 H), 7.32 (d, J = 8.8 Hz, 2 H), 7.20-7.18 (m, 4 H), 6.94 (d, J = 8.4 Hz, 1 H), 6.34 (d, J = 2.4 Hz, 1 H), 6.26-6.23 (dd, J = 2.4, 8.0 Hz, 1 H), 4.49-4.42 (m, 1 H), 3.70 (s, 3 H), 3.14-3.10 (dd, J = 4.0, 13.2 Hz, 1 H), 3.00-2.94 (dd, J = 8.0, 15.2 Hz, 1H), 2.78-2.71 (m, 2 H), 1.56 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.6, 159.8, 149.4, 142.8, 141.7, 130.3, 129.6, 129.5, 129.1, 128.2, 125.1, 123.2, 121.31, 103.5, 96.1, 80.9, 66.1, 55.4, 39.5, 33.3, 28.2; IR (film) 1641 cm^{-1} . Anal calcd for $\text{C}_{27}\text{H}_{28}\text{ClNO}_3$: C, 72.07; H, 6.27; N, 3.11. Found: C, 71.95; H, 6.26; N, 3.10.

4-[2-(4-Benzoylbenzyl)-6-methoxy-2,3-dihydroindol-1-yl]benzoic acid *tert*-butyl ester (Table 2, Entry 6). Reaction of 64 mg (0.40 mmol) of 2-allyl-5-methoxyaniline, 4-bromobenzoic acid *tert*-butyl ester (103 mg, 0.40 mmol), 4-bromobenzophenone (105 mg, 0.40 mmol), and NaOtBu (81 mg, 0.84 mmol) following the general procedure afforded 160 mg (78 %) of the title compound as a pale yellow viscous oil. ^1H NMR (400 MHz, CDCl_3) δ 7.95 (d, J = 8.8 Hz, 2 H), 7.75-7.69 (m, 4 H), 7.55 (t, J = 7.2 Hz, 1 H), 7.47-7.43 (m, 2 H), 7.27-7.22 (m, 4 H), 7.00 (d, J = 8.0 Hz, 1 H), 6.69 (d, J = 2.0 Hz, 1 H), 6.35-6.32 (dd, J = 2.0, 8.0 Hz, 1 H), 4.66-4.60 (m, 1 H), 3.73 (s, 3 H), 3.22-3.18 (dd, J =

4.0, 17.6 Hz, 1 H), 3.15-3.09 (dd, $J = 8.8, 15.6$ Hz, 1 H), 2.87-2.81 (dd, $J = 8.8, 13.2$ Hz, 1 H), 2.79-2.74 (dd, $J = 4.4, 15.2$ Hz, 1 H), 1.56 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ 196.3, 165.5, 159.6, 146.9, 146.8, 142.7, 137.6, 135.9, 132.3, 131.0, 130.3, 130.0, 129.3, 128.2, 125.5, 124.6, 122.3, 117.4, 104.8, 98.1, 80.5, 65.2, 55.5, 39.4, 33.2, 28.2; IR (film) 1702, 1657 cm^{-1} . Anal calcd for $\text{C}_{34}\text{H}_{33}\text{NO}_4$: C, 78.59; H, 6.40; N, 2.70. Found: C, 78.55; H, 6.42; N, 2.70.

¹ Francis, J. E.; Webb, R. L.; Ghai, G. R.; Hutchinson, A. J.; Moskal, M. A.; deJesus, R.; Yokoyama, R.; Rovinski, S. L.; Contardo, N.; Dotson, R.; Barclay, B.; Stone, G. A.; Jarvis, M. F. *J. Med. Chem.* **1991**, 34, 8, 2570-2579.

² Organ, M. G.; Xu, J.; N'Zemba, B. *Tetrahedron Lett.* **2002**, 43, 8177-8180.

³ Anderson, W. K.; Lai, G. F. *Synthesis* **1995**, 1287-1290.