Supporting Information

New Organolithium Addition Methodology to Diversely Functionalized Indoles

Claire M. Coleman and Donal F. O'Shea*

Centre for Synthesis and Chemical Biology, Conway Institute, Department of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland.

Materials and Methods

Reagents and Solvents. All commercially available solvents and reagents were used as supplied by Aldrich Chemical Co. unless otherwise stated. Diethyl ether was distilled from sodium benzophenone ketyl, under nitrogen, immediately before use. TMEDA and nitriles were dried over 4Å molecular sieves. Reactions were carried out in oven or flame dried glassware. *t*-BuLi was purchased as 1.7M in pentane, *s*-BuLi 1.4M in cyclohexane, *n*-BuLi 2.5M in hexanes. Exact concentration of organolithiums were determined by titration in THF with diphenylacetic acid as an indicator prior to use.¹ Low reaction temperatures were obtained with an acetone/solid CO₂ bath. Chromatography was performed on Merck silica gel 60 PF₂₅₄. ¹H NMR and ¹³C were recorded on a Varian 300MHz instrument. GC-MS spectra were recorded using a ThermoQuest 2000 instrument. High resolution mass spectra were performed by the Kent Mass Spectroscopy Service, Kent, U.K. using a Micromass magnetic sector mass spectrometer and by the Mass Spectroscopy Centre, Trinity College Dublin using a Micromass LCT electrospray spectrometer.

1. Kofron, W.G., Baclawski, L.M. *J. Org. Chem.* **1976**, *41*, 1879.

Representative Procedure for Synthesis of Indoles 4a, c, d, f, g.

(2-Vinylphenyl)carbamic acid *tert*-butyl ester (2.0 mmol) was dissolved in dry diethyl ether (25 mL) and cooled to -78 °C under nitrogen. *t*-BuLi or *s*-BuLi (8.0 mmol) was added drop-wise via syringe over 30 min. The orange-red solution was stirred for a further 1.5 h at -78 °C. Anhydrous DMF (20 mmol) was added and stirring continued for 10 min. 2M HCl (25 mL) was added and the solution warmed to room temperature. The diethyl ether was evaporated, replaced with THF (20 mL) and stirred at room temperature for 5 h under nitrogen. The THF was evaporated and

the residue extracted with diethyl ether (2 x 20 mL), dried over sodium sulphate and solvent evaporated. Chromatography (hexanes/diethyl ether as eluent) gave the purified product.

Representative Procedure for Synthesis of Indoles 4b, e, h.

(2-Vinylphenyl)carbamic acid *tert*-butyl ester (2.0 mmol) and TMEDA (4.0 mmol) was dissolved in dry diethyl ether (25 mL) and cooled to -78 °C under nitrogen. *n*-BuLi (8.0 mmol) was added drop-wise via syringe over 30 min. The temperature was warmed to -25 °C with stirring for 2 h during which time an orange-red color developed. The solution was re-cooled to -78 °C and anhydrous DMF (20 mmol) was added and stirring continued for 10 min. 2M HCl (25 mL) was added and the solution warmed to room temperature. The diethyl ether was evaporated, replaced with THF (20 mL) and stirred at room temperature for 5 h. The THF was evaporated and the residue extracted with diethyl ether (3x10 mL), dried over sodium sulphate and solvent evaporated. Chromatography (hexanes/diethyl ether as eluent) gave the purified product.

Representative Deprotection Procedure for Synthesis of Indoles 5a-h.

N-Boc indole **4a-h** (0.25 mmol) was dissolved in a premixed solution of ethyl acetate (4.2 mL) / 12M HCl (1.8 mL) and stirred at room temperature, under nitrogen, for 1-12 h monitoring the reaction by TLC until judged complete. The reaction mixture was washed with sodium hydrogen carbonate (1M, 2x50 mL), extracted with ethyl acetate (3x10 mL), dried over sodium sulphate and concentrated to give the product.

Representative Procedure for Synthesis of Indoles 8a, b, e, g.

(2-Vinylphenyl)carbamic acid *tert*-butyl ester (2.0 mmol) was dissolved in dry diethyl ether (25 mL) and cooled to -78 °C under nitrogen. *t*-BuLi (8.0 mmol) was added drop-wise via syringe over 30 min. The orange-red solution was stirred for a further 1 h at -78 °C. Anhydrous nitrile (20 mmol) was added and the solution warmed to -25 °C with stirring continued for 3 h. The reaction was cooled to -78 °C, 2M HCl (25 mL) added and the solution warmed to room temperature. The reaction mixture was extracted with ethyl acetate (3x10 mL) and the organic

layer dried over sodium sulfate and solvent evaporated. The residue was dissolved in a premixed solution of ethyl acetate (8.4 mL) / 12M HCl (3.6 mL) and stirred at room temperature for 16 h under nitrogen. The reaction mixture was washed with sodium hydrogen carbonate (1M, 2x50 mL), extracted with ethyl acetate (3x10 mL), dried over sodium sulphate and solvent evaporated. Chromatography (hexanes/diethyl ether as eluent) gave the purified product.

Representative Procedure for Synthesis of Indoles 8c, d, f, h.

(2-Vinylphenyl)carbamic acid *tert*-butyl ester (2.0 mmol) and TMEDA (4.0 mmol) was dissolved in dry diethyl ether (25 mL) and cooled to -78 °C under nitrogen. *n*-BuLi (8.0 mmol) was added drop-wise via syringe over 30 min. The temperature was warmed to -25 °C with stirring for 2 h during which time an orange-red color developed. The mixture was re-cooled to -78 °C and anhydrous nitrile (20 mmol) was added, the temperature raised to -25 °C and stirring continued for 3 h. The reaction was cooled to -78 °C, 2M HCl (25 mL) added and the solution warmed to room temperature. The reaction mixture was extracted with ethyl acetate (3x10 mL) and the organic layer dried over sodium sulfate and solvent evaporated. The residue was dissolved in a premixed solution of ethyl acetate (8.4 mL) / 12M HCl (3.6 mL) and stirred at room temperature for 16 h under nitrogen. The reaction mixture was washed with sodium hydrogen carbonate (1M, 2x50 mL), extracted with ethyl acetate (3x10 mL), dried over sodium sulphate and solvent evaporated. Chromatography (hexanes/diethyl ether as eluent) gave the purified product.

3-(2,2-Dimethyl-propyl)-indole-carboxylic acid *tert*-butyl ester 4a.

Colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 0.89 (s, 9H), 1.59 (s, 9H), 2.49 (s, 2H), 7.13-7.15 (m, 2H), 7.26 (s, 1H), 7.44 (d, $J = 7.0$ Hz, 1H), 8.05 (bs, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 27.2, 28.7, 30.9, 37.6, 82.3, 114.0, 117.6, 118.8, 121.1, 122.8, 123.2, 131.1, 134.1, 148.9. IR (NaCl plate, neat): 2951, 1729 cm^{-1} . EI-MS: m/z 287.3. HRMS (M) $^+$: 287.1884, $\text{C}_{18}\text{H}_{25}\text{NO}_2$ requires 287.1885. Anal. calcd for $\text{C}_{18}\text{H}_{25}\text{NO}_2$: C, 75.22; H, 8.77; N, 4.87. Found: C, 74.95; H, 9.07; N 4.66.

3-Pentyl-indole-1-carboxylic acid *tert*-butyl ester 4b.

Colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 0.95-1.0 (m, 3H), 1.42-1.47 (m, 4H), 1.72 (s, 9H), 1.74-1.79 (m, 2H), 2.72 (t, $J = 7.8$ Hz, 2H), 7.28-7.41 (m, 3H), 7.57 (d, $J = 6.8$ Hz, 1H), 8.16 (bs, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 14.3, 22.8, 25.2, 28.5, 29.2, 32.0, 83.4, 115.5, 119.3, 121.8, 122.5, 124.1, 124.4, 131.2, 135.9, 150.2. IR (NaCl plate, neat): 2957, 1731 cm^{-1} . EI-MS: m/z 287.2. HRMS (M) $^+$: 287.1881, $\text{C}_{18}\text{H}_{25}\text{NO}_2$ requires 287.1885. Anal. calcd for $\text{C}_{18}\text{H}_{25}\text{NO}_2$: C, 75.22; H, 8.77; N, 4.87. Found C, 75.55; H, 8.98; N, 4.63.

3-(2-Methyl-butyl)-indole-1-carboxylic acid *tert*-butyl ester 4c.

Colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 0.90-0.95 (m, 6H), 1.15-1.29 (m, 1H), 1.40-1.54 (m, 1H), 1.66 (s, 9H), 1.71-1.82 (m, 1H), 2.43 (dd, $J = 8.05, 14.3$ Hz, 1H), 2.68 (dd, $J = 6.0$ Hz, 14.3 Hz, 1H), 7.18-7.33 (m, 3H), 7.50 (d, $J = 7.0$ Hz, 1H), 8.10 (bs, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 11.8, 19.7, 28.5, 29.8, 32.5, 35.1, 83.5, 115.4, 119.5, 120.4, 122.4, 123.3, 124.4, 131.5, 136.1, 150.2. IR (NaCl plate, neat): 2966, 1736 cm^{-1} . EI-MS: m/z 287.3. HRMS ($\text{M}+\text{Na}$) $^+$: 310.1780, $\text{C}_{18}\text{H}_{25}\text{NO}_2\text{Na}$ requires 310.1783. Anal. calcd for $\text{C}_{18}\text{H}_{25}\text{NO}_2$: C, 75.22; H, 8.77; N, 4.87. Found C, 74.97; H, 8.67; N, 4.80.

3-(2,2-Dimethyl-propyl)-5-fluoro-indole-1-carboxylic acid *tert* butyl ester 4d.

Pale yellow solid, m.p. 70-71 °C. ¹H NMR (300 MHz, CDCl₃): δ 0.96 (s, 9H), 1.66 (s, 9H), 2.51 (s, 2H), 6.95-7.05 (m, 1H), 7.16 (d, *J* = 9.2 Hz, 1H), 7.36 (s, 1H), 8.1 (bs, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 27.1, 28.6, 30.9, 37.6, 82.5, 104.3 (d, *J*_{CF} = 23.6 Hz), 110.5 (d, *J*_{CF} = 25.2 Hz), 114.9 (d, *J*_{CF} = 9.2 Hz), 117.3 (d, *J*_{CF} = 4.6 Hz), 124.7, 130.5, 132.3 (d, *J*_{CF} = 9.9 Hz), 148.6, 156.6 (d, *J*_{CF} = 238.8 Hz). IR (KBr disk): 2966, 1732 cm⁻¹. EI-MS: *m/z* 305.4. HRMS (M)⁺: 305.1787, C₁₈H₂₄FNO₂ requires 305.1791. Anal. calcd for C₁₈H₂₄FNO₂: C, 70.79; H, 7.92; F, 6.22; N, 4.59. Found: C, 70.49; H, 7.94; F, 6.48; N, 4.52.

5-Fluoro-3-pentyl-indole-1-carboxylic acid *tert*-butyl ester 4e.

Pale yellow solid, m.p. 40-41 °C. ¹H NMR (300 MHz, CDCl₃): δ 0.89-0.94 (m, 3H), 1.35-1.39 (m, 4H), 1.66 (s, 9H), 1.70-1.73 (m, 2H), 2.60 (t, *J* = 7.7 Hz, 2H), 6.97-7.03 (m, 1H), 7.15 (d, *J* = 8.9 Hz, 1H), 7.36 (s, 1H), 8.05 (bs, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 14.2, 22.7, 25.0, 28.4, 29.0, 31.9, 83.7, 104.9 (d, *J*_{CF} = 23.7 Hz), 111.9 (d, *J*_{CF} = 25.2 Hz), 116.4 (d, *J*_{CF} = 9.2 Hz), 121.5 (d, *J*_{CF} = 4.57 Hz), 124.0, 132.1 (d, *J*_{CF} = 9.1 Hz), 149.9, 157.8 (d, *J*_{CF} = 239.5 Hz). IR (KBr disk): 2929, 1726 cm⁻¹. EI-MS: *m/z* 305.3. HRMS (M)⁺: 305.1786, C₁₈H₂₄FNO₂ requires 305.1791. Anal. calcd for C₁₈H₂₄FNO₂: C, 70.79; H, 7.92; F, 6.22; N, 4.59. Found: C, 70.74; H, 7.88; F, 6.39; N, 4.60.

5-Fluoro-3-(2-methyl-butyl)-indole-1-carboxylic acid *tert*-butyl ester 4f.

Colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 0.90-0.96 (m, 6H), 1.14-1.26 (m, 1H), 1.39-1.52 (m, 1H), 1.66 (s, 9H), 1.69-1.87 (m, 1H), 2.40 (dd, *J* = 8.05, 14.4 Hz, 1H), 2.64 (dd, *J* = 6.1 Hz, 14.4 Hz, 1H), 6.97-7.04 (m, 1H), 7.15 (d, *J* = 8.9 Hz, 1H), 7.36 (s, 1H), 8.05 (bs, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 11.8, 19.6, 28.4, 29.7, 32.4, 35.1, 83.7, 105.0 (d, *J*_{CF} = 23.6 Hz), 111.9 (d, *J*_{CF} = 25.3 Hz), 116.3 (d, *J*_{CF} = 9.2 Hz), 120.1 (d, *J*_{CF} = 4.0 Hz), 124.8, 132.0, 132.3 (d, *J*_{CF} = 9.7 Hz), 149.8, 159.3 (d, *J*_{CF} = 238.7 Hz). IR (NaCl plate, neat): 2968, 1741 cm⁻¹. EI-MS: *m/z* 305.3. HRMS (M+Na)⁺: 328.1696, C₁₈H₂₄FNO₂Na requires 328.1689. Anal. calcd for C₁₈H₂₄FNO₂: C, 70.79; H, 7.92; F, 6.22; N, 4.59. Found: C, 71.04; H, 7.97; F, 6.62; N, 4.34.

3-(2,2-Dimethyl-propyl)-5-methoxy-indole-1-carboxylic acid *tert*-butyl ester 4g.

Colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 0.97 (s, 9H), 1.66 (s, 9H), 2.53 (s, 2H), 3.85 (s, 3H), 6.87-6.98 (m, 2H), 7.31 (s, 1H), 8.05 (bs, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 28.5, 29.9, 32.2, 38.9, 55.9, 83.4, 103.2, 112.4, 115.9, 118.6, 125.2, 130.1, 133.2, 150.1, 155.8. IR (NaCl plate, neat): 2945, 1735 cm^{-1} . EI-MS: m/z 317.2. HRMS (M) $^+$: 317.1993, $\text{C}_{19}\text{H}_{27}\text{NO}_3$ requires 317.1990. Anal. calcd for $\text{C}_{19}\text{H}_{27}\text{NO}_3$: C, 71.89; H, 8.57; N, 4.41. Found C, 72.0; H, 8.57; N, 4.35.

5-Methoxy-3-pentyl-indole-1-carboxylic acid *tert*-butyl ester 4h.

White solid, m.p. 54-55 $^{\circ}\text{C}$. ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ 0.88 (t, $J = 7.0$ Hz, 3H), 1.24-1.37 (m, 4H), 1.61 (s, 9H), 1.62-1.68 (m, 2H), 2.62 (t, $J = 7.3$ Hz, 2H), 3.80 (s, 3H), 6.93 (dd, $J = 2.5, 8.9$ Hz, 1H), 7.06 (d, $J = 2.5$ Hz, 1H), 7.38 (s, 1H), 7.90 (d, $J = 8.9$ Hz, 1H). ^{13}C NMR (CDCl_3): δ 14.2, 22.7, 25.1, 28.5, 29.0, 32.0, 56.0, 83.2, 102.3, 112.6, 116.1, 118.6, 125.3, 130.1, 133.2, 150.1, 155.9. IR (KBr disk): 2998, 1721 cm^{-1} . EI-MS: m/z 317.3. HRMS ($\text{M}+\text{H}$) $^+$: 318.2080, $\text{C}_{19}\text{H}_{28}\text{NO}_3$ requires 317.1990. Anal. calcd for $\text{C}_{19}\text{H}_{27}\text{NO}_3$: C, 71.89; H, 8.57; N, 4.41. Found C, 71.94; H, 8.60; N, 4.33.

3-(2,2-Dimethyl-propyl)-1*H*-indole 5a.

White solid, m.p. 36-37 $^{\circ}\text{C}$. ^1H NMR (300 MHz, CDCl_3): δ 0.96 (s, 9H), 2.64 (s, 2H), 6.93 (d, $J = 2.2$ Hz, 1H), 7.06-7.19 (m, 2H), 7.33 (d, $J = 7.4$ Hz, 1H), 7.60 (d, $J = 7.8$ Hz, 1H), 7.92 (bs, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 29.9, 32.4, 39.4, 111.2, 114.5, 119.4, 119.9, 121.7, 123.3, 129.2, 136.2. IR (KBr disk): 3437, 2966 cm^{-1} . EI-MS: m/z 187.3. HRMS (M) $^+$: 187.1359, $\text{C}_{13}\text{H}_{17}\text{N}$ requires 187.1361. Anal. calcd for $\text{C}_{13}\text{H}_{17}\text{N}$: C, 83.37; H, 9.15; N, 7.48. Found C, 83.08; H, 9.16; N, 7.33.

Rainier, J.D., Kennedy, A.R. *J. Org. Chem.* **2000**, 65, 6213.

3-Pentyl-1*H*-indole 5b.

White solid, m.p. 41-42 °C. ¹H NMR (300 MHz, CDCl₃): δ 0.93 (t, *J* = 6.7 Hz, 3H), 1.40-1.46 (m, 4H), 1.74-1.79 (m, 2H), 2.77 (t, *J* = 7.6 Hz, 2H), 7.0 (d, *J* = 1.0 Hz, 1H), 7.12-7.24 (m, 2H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 7.4 Hz, 1H), 7.87 (bs, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 14.3, 22.8, 25.4, 30.1, 32.1, 111.2, 117.4, 119.2, 119.3, 121.2, 122.0, 127.9, 136.4. IR (KBr disk): 3395, 2923 cm⁻¹. EI-MS: *m/z* 187.2.

Fukuyama, T., Chen, X., Peng, G. *J. Am. Chem. Soc.* **1994**, *116*, 3127.

3-(2-Methyl-butyl)-1*H*-indole 5c.

Colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 0.90 (d, *J* = 6.6 Hz, 3H), 0.93 (t, *J* = 7.3 Hz, 3H), 1.15-1.27 (m, 1H), 1.39-1.53, (m, 1H), 1.69-1.81 (m, 1H), 2.50 (dd, *J* = 7.7, 14.3 Hz, 1H), 2.75 (dd, *J* = 6.15, 14.3 Hz, 1H), 6.91 (d, *J* = 1.8 Hz, 1H), 7.07-7.2 (m, 2H), 7.31 (d, *J* = 7.3 Hz, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.72 (bs, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 11.9, 19.7, 29.8, 32.7, 35.9, 111.2, 116.0, 119.3, 119.4, 121.9, 122.1, 128.3, 136.5. IR (KBr disk): 3422, 2958 cm⁻¹. EI-MS: *m/z* 187.3. HRMS (M+H)⁺: 188.1445, C₁₃H₁₈N requires 188.1439.

3-(2,2-Dimethyl-propyl)-5-fluoro-1*H*-indole 5d.

Colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 0.93 (s, 9H), 2.56 (s, 2H), 6.86-6.92 (m, 1H), 6.98 (d, *J* = 2.2 Hz, 1H), 7.19-7.24 (m, 2H), 7.96 (bs, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 29.8, 32.4, 39.3, 104.7 (d, *J*_{CF} = 23.4 Hz), 110.0 (d, *J*_{CF} = 26.4 Hz), 111.6 (d, *J*_{CF} = 9.3 Hz), 114.6 (d, *J*_{CF} = 4.7 Hz), 125.1, 129.6 (d, *J*_{CF} = 9.4 Hz), 132.6, 157.9 (d, *J*_{CF} = 232.9 Hz). IR (NaCl plate, neat): 3432, 2951 cm⁻¹. EI-MS: *m/z* 205.2. HRMS (M+H)⁺: 206.1350, C₁₃H₁₇FN requires 206.1345. Anal. calcd for C₁₃H₁₆FN; C, 76.06; H, 7.86; F, 9.26; N, 6.82. Found C, 76.02; H, 7.83; F, 9.36; N, 6.69.

5-Fluoro-3-pentyl-1*H*-indole 5e.

Yellow oil. ^1H NMR (300 MHz, CDCl_3): δ 0.90 (t, $J = 6.9$ Hz, 3H), 1.33-1.42 (m, 4H), 1.63-1.73 (m, 2H), 2.68 (t, $J = 7.5$ Hz, 2H), 6.88-6.95 (m, 1H), 7.01 (d, $J = 2.2$ Hz, 1H), 7.21-7.26 (m, 2H), 7.87 (bs, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 14.3, 22.8, 25.3, 30.0, 32.0, 104.1 (d, $J_{\text{CF}} = 23.0$ Hz), 110.3 (d, $J_{\text{CF}} = 26.4$ Hz), 111.8 (d, $J_{\text{CF}} = 9.2$ Hz), 117.6 (d, $J_{\text{CF}} = 4.6$ Hz), 123.1, 128.2 (d, $J_{\text{CF}} = 9.8$ Hz), 133.0, 157.9 (d, $J_{\text{CF}} = 233.6$ Hz). IR (NaCl plate, neat): 3435, 2955 cm^{-1} . EI-MS: m/z 205.2. HRMS ($\text{M}+\text{H}^+$): 206.1351, $\text{C}_{13}\text{H}_{17}\text{FN}$ requires 206.1345.

5-Fluoro-3-(2-methyl-butyl)-1*H*-indole 5f.

Colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 0.92 (d, $J = 8.6$ Hz, 3H), 0.93 (t, $J = 7.0$ Hz, 3H), 1.12-1.26 (m, 1H), 1.38-1.49 (m, 1H), 1.65-1.74 (m, 1H), 2.46 (dd, $J = 7.9, 14.4$ Hz, 1H), 2.69 (dd, $J = 6.1, 14.4$ Hz, 1H), 6.87-6.94 (m, 1H), 6.98 (d, $J = 2.2$ Hz, 1H), 7.19-7.24 (m, 2H), 7.86 (bs, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 11.8, 19.6, 29.7, 32.7, 35.8, 104.2 (d, $J_{\text{CF}} = 23.0$ Hz), 110.3 (d, $J_{\text{CF}} = 26.5$ Hz), 111.7 (d, $J_{\text{CF}} = 9.7$ Hz), 116.2 (d, $J_{\text{CF}} = 4.6$ Hz), 124.0, 128.6, (d, $J_{\text{CF}} = 9.2$ Hz), 133.0, 157.8 (d, $J_{\text{CF}} = 234.1$ Hz). IR (NaCl plate, neat): 3434, 2959 cm^{-1} . EI-MS: m/z 205.3. HRMS ($\text{M}+\text{H}^+$): 206.1344, $\text{C}_{13}\text{H}_{17}\text{FN}$ requires 206.1345.

3-(2,2-Dimethyl-propyl)-5-methoxy-1*H*-indole 5g.

Tan solid, m.p. 40-41 $^{\circ}\text{C}$. ^1H NMR (300 MHz, CDCl_3): δ 0.88 (s, 9H), 2.51 (s, 2H), 3.77 (s, 3H), 6.75 (dd, $J = 2.3, 8.7$ Hz, 1H), 6.82 (d, $J = 2.0$ Hz, 1H), 6.96 (d, $J = 2.3$ Hz, 1H), 7.11 (d, $J = 8.7$ Hz, 1H), 7.80 (bs, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 29.9, 32.5, 39.4, 56.2, 102.0, 111.6, 111.7, 114.2, 124.3, 129.5, 131.4, 154.0. IR (KBr disk): 3408, 2950 cm^{-1} . EI-MS: m/z 217.3. HRMS ($\text{M}+\text{H}^+$): 218.1540, $\text{C}_{14}\text{H}_{20}\text{NO}$ requires 218.1545.

5-Methoxy-3-pentyl-1*H*-indole 5h.

Light yellow oil. ^1H NMR (300 MHz, CDCl_3): δ 0.85-0.94 (m, 3H), 1.27-1.42 (m, 4H), 1.61-1.74 (m, 2H), 2.70 (t, $J = 7.9$ Hz, 2H), 3.86 (s, 3H), 6.85 (dd, $J = 2.3, 8.8$ Hz, 1H), 6.95 (s, 1H), 7.05 (d, $J = 2.3$ Hz, 1H), 7.25 (d, $J = 8.8$ Hz, 1H), 7.78 (bs, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 14.3, 22.8, 25.3, 29.9, 32.1, 56.2, 101.2, 111.9, 112.1, 117.1, 122.1, 128.2, 132.0, 153.9. IR (NaCl plate, neat): 3419, 2952 cm^{-1} . EI-MS: m/z 217.2.

Caubere, C., Caubere, P., Ianelli, S., Nardelli, M., Jamart-Gregoire, B. *Tetrahedron* **1994**, 50, 11904.

3-(2,2-Dimethyl-propyl)-2-phenyl-1*H*-indole 8a.

White solid, m.p. 94-95 °C. ^1H NMR (300 MHz, CDCl_3): δ 0.74 (s, 9H), 2.86 (s, 2H), 7.07-7.17 (m, 2H), 7.24-7.33 (m, 2H), 7.37-7.42 (m, 2H), 7.48-7.52 (m, 2H), 7.60-7.65 (m, 1H) 7.83 (bs, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 30.3, 34.5, 37.6, 110.9, 111.6, 119.6, 120.6, 122.1, 127.8, 129.0, 129.1, 130.8, 135.1, 135.9, 136.2. IR (KBr disk): 3396, 2956 cm^{-1} . EI-MS: m/z 263.3. HRMS (M) $^+$: 263.1670, $\text{C}_{19}\text{H}_{21}\text{N}$ requires 263.1673. Anal. calcd for $\text{C}_{19}\text{H}_{21}\text{N}$: C, 86.65; H, 8.04; N, 5.32. Found C, 86.36; H, 8.14; N, 5.27.

2-*tert*-Butyl-3-(2,2-dimethyl-propyl)-1*H*-indole 8b.

White solid, m.p. 61-62 °C. ^1H NMR (300 MHz, CDCl_3): δ 0.92 (s, 9H), 1.34 (s, 9H), 2.87 (s, 2H), 6.92-6.99 (m, 2H), 7.08-7.10 (m, 1H), 7.46-7.50 (m, 1H), 7.83 (bs, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 31.5, 31.8, 33.6, 34.1, 37.7, 109.2, 109.9, 118.6, 120.7, 121.1, 130.9, 134.8, 142.6. IR (KBr disk): 3147, 2960 cm^{-1} . EI-MS: m/z 243.2. HRMS (M) $^+$: 243.1982, $\text{C}_{17}\text{H}_{25}\text{N}$ requires 243.1986. Anal. calcd for $\text{C}_{17}\text{H}_{25}\text{N}$: C, 83.89; H, 10.35; N, 5.75. Found C, 83.59; H, 10.15; N, 5.42.

1-(3-Pentyl-1*H*-indol-2-yl)-ethanone 8c.

White solid, m.p. 77-78 °C. ¹H NMR (300 MHz, CDCl₃): δ 0.9 (t, *J* = 7.1 Hz, 3H), 1.25-1.47 (m, 4H), 1.66-1.76 (m, 2H), 2.65 (s, 3H), 3.09 (t, *J* = 8.0 Hz, 2H), 7.10-7.15 (m, 1H), 7.30-7.37 (m, 2H), 7.70 (d, *J* = 8.1 Hz, 1H), 8.91 (bs, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 14.2, 22.7, 25.7, 28.5, 31.7, 32.3, 112.0, 120.2, 121.6, 124.5, 126.6, 129.1, 132.2, 136.3, 190.6. IR (KBr disk): 3332, 2951, 1637 cm⁻¹. EI-MS: *m/z* 229.3. HRMS (M)⁺: 229.1465, C₁₅H₁₉NO requires 229.1466. Anal. calcd for C₁₅H₁₉NO: C, 78.56; H, 8.35; N, 6.10. Found C, 78.44; H, 8.35; N, 6.07.

3-(2,2-Dimethyl-propyl)-2-thiophen-2-yl-1*H*-indole 8d.

Yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 0.88 (t, *J* = 7.1 Hz, 3H), 1.31-1.44 (m, 4H), 1.54-1.75 (m, 2H), 2.92 (t, *J* = 7.8 Hz, 2H), 7.07-7.17 (m, 4H), 7.18-7.31 (m, 2H), 7.59 (m, 1H), 7.95 (bs, 1H). ¹³C NMR (75 MHz, CDCl₃): 14.4, 22.9, 25.1, 30.7, 32.4, 110.9, 115.4, 119.5, 119.9, 122.9, 124.4, 125.2, 127.8, 128.2, 129.6, 135.4, 136.2. IR (NaCl plate, neat): 3055, 2987 cm⁻¹. EI-MS: *m/z* 269.2. HRMS (M)⁺: 269.1223, C₁₇H₁₉NS requires 269.1238.

3-(2,2-Dimethyl-propyl)-5-fluoro-2-phenyl-1*H*-indole 8e.

White solid, m.p. 100-101 °C. ¹H NMR (300 MHz, CDCl₃): δ 0.73 (s, 9H), 2.8 (s, 2H), 6.86-6.92 (m, 1H), 7.18-7.36 (m, 2H), 7.39-7.52 (m, 5H), 7.9 (bs, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 30.1, 34.4, 37.6, 105.3 (d, *J*_{CF} = 23.6 Hz), 110.2, (d, *J*_{CF} = 25.9 Hz), 111.4 (d, *J*_{CF} = 9.9 Hz), 111.8 (d, *J*_{CF} = 4.5 Hz), 128.0, 128.9, 129.0, 131.2 (d, *J*_{CF} = 9.9 Hz), 132.3, 134.6, 138.0, 158.1 (d, *J*_{CF} = 233.4 Hz). IR (KBr disk): 3429, 2960 cm⁻¹. EI-MS: *m/z* 281.3. HRMS (M)⁺: 281.1577, C₁₉H₂₀FN requires 281.1579. Anal. calcd for C₁₉H₂₀FN: C, 81.11; H, 7.16; F, 6.75; N, 4.98. Found: C, 81.0; H, 7.45; F, 6.48; N, 4.90.

2-tert-Butyl-5-fluoro-3-pentyl-1H-indole 8f.

Colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 0.92 (t, $J = 7.0$ Hz, 3H), 1.37-1.43 (m, 4H), 1.44 (s, 9H), 1.57-1.67 (m, 2H), 2.77 (t, $J = 8.0$ Hz, 2H), 6.79-6.86 (m, 1H), 7.10-7.22 (m, 2H), 7.67 (bs, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 14.3, 22.8, 25.8, 30.7, 31.3, 32.7, 33.2, 103.3 (d, $J_{\text{CF}} = 23.6$ Hz), 109.1 (d, $J_{\text{CF}} = 25.9$ Hz), 111.0 (d, $J_{\text{CF}} = 9.8$ Hz), 111.9 (d, $J_{\text{CF}} = 4.5$ Hz), 130.6 (d, $J_{\text{CF}} = 9.9$ Hz), 143.2, 143.5, 158.3 (d, $J_{\text{CF}} = 233.2$ Hz). IR (NaCl plate, neat): 3477, 2958 cm^{-1} . EI-MS m/z : 261.3. HRMS ($\text{M}+\text{H}$) $^+$: 262.1927, $\text{C}_{17}\text{H}_{25}\text{FN}$ requires 262.1971.

3-(2,2-Dimethyl-propyl)-5-methoxy-2-phenyl-1H indole 8g.

White solid, m.p. 116-117 $^{\circ}\text{C}$. ^1H NMR (300 MHz, CDCl_3): δ 0.75 (s, 9H), 2.85 (s, 2H), 3.87 (s, 3H), 6.85 (dd, $J = 2.4, 8.6$ Hz, 1H), 7.07 (d, $J = 2.4$ Hz, 1H), 7.22 (d, $J = 8.6$ Hz, 1H), 7.33-7.36 (m, 1H), 7.40-7.45 (m, 2H), 7.54 (m, 2H), 7.88 (bs, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 30.2, 34.3, 37.5, 56.2, 102.7, 111.4, 111.5, 112.0, 127.7, 128.8, 128.9, 131.1, 131.2, 135.8, 137.8, 154.0. IR (KBr disk): 3424, 2954 cm^{-1} . EI-MS m/z : 293.4. HRMS ($\text{M}+\text{H}$) $^+$: 294.1851, $\text{C}_{20}\text{H}_{24}\text{NO}$ requires 294.1858. Anal. calcd for $\text{C}_{20}\text{H}_{23}\text{NO}$; C, 81.87; H, 7.90; N, 4.77. Found C, 81.49; H, 7.89; N, 4.62.

5-Methoxy-3-pentyl-2-phenyl-1H-indole 8h.

White solid, m.p. 65-66 $^{\circ}\text{C}$. ^1H NMR (300 MHz, CDCl_3): δ 0.88 (t, $J = 7.3$ Hz, 3H), 1.30-1.41 (m, 4H), 1.66-1.74 (m, 2H), 2.83 (t, $J = 8.0$ Hz, 2H), 3.89 (s, 3H), 6.86 (dd, $J = 2.4, 8.8$ Hz, 1H), 7.07 (d, $J = 2.4$ Hz, 1H), 7.24-7.56 (m, 6H), 7.85 (bs, 1H). ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$): δ 14.6, 22.6, 24.7, 30.8, 32.1, 56.1, 101.1, 112.1, 112.5, 112.7, 127.7, 128.2, 129.3, 129.7, 131.9, 134.0, 135.2, 153.8. IR (KBr disk): 3383, 2957 cm^{-1} . EI-MS m/z : 293.3. HRMS (M) $^+$: 293.1773, $\text{C}_{20}\text{H}_{23}\text{NO}$ requires 293.1779.