Novel Synthesis of 2-Aryl and 2,3-Disubstituted Indoles by Modified Double Elimination Protocol

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Supporting Information

Novel Synthesis of 2-Aryl and 2,3-Disubstituted Indoles by Modified Double Elimination protocol

Compound **1**: A 300 mL flask was charged with 2-nitro-benzylchloride (8.56 g, 49.8 mmol), benzenesulfinic acid sodium salt dihydrate (9.82 g, 59.8 mmol) and DMF (200 mL). After the mixture had been stirred at 80 °C for 12 h, the reaction mixture was cooled to room temperature and poured into cold water. The product thus precipitated was filtered, washed with water, dried in vacuo and recrystallized from dichloromethane-hexane to give 13.39 g of 2-nitro-benzylsulfone¹ (97 %) as a colorless solid. ¹H NMR (500 MHz, CDCl₃) δ : 7.91 (dd, 1H, *J* = 8.5, 1.5 Hz), 7.69-7.45 (m, 8H), 4.95 (s, 2H); ¹³C NMR (125 MHz, CDCl₃) δ : 149.1, 137.7, 134.2, 134.1, 133.3, 130.0, 129.2, 128.3, 125.4, 122.9, 58.4.

A 200 mL flask was charged with 2-nitro-benzylsulfone (5.54 g, 20 mmol), tin (10 g, 84.2 mmol) in methanol (50 mL) and con. HCl (50 mL). After the mixture had been stirred at 40 °C for 6 h, the reaction mixture was cooled to room temperature and poured into the mixture of ice and 10% NaOH solution (500 mL). The product thus precipitated was filtered, washed with water, dried in vacuo and recrystallized from ethyl acetate-ethanol (1:1) to give 4.49 g of **1**² (91 %) as a colorless solid. ¹H NMR (500 MHz, CDCl₃) δ : 7.75 (d, 2H, *J* = 7.0 Hz), 7.64 (t, 1H, *J* = 7.5 Hz), 7.51 (t, 2H, *J* = 7.5 Hz), 7.13 (t, 1H, *J* = 7.5 Hz), 6.76 (d, 1H, *J* = 7.5 Hz), 6.60 (t, 1H, *J* = 7.5 Hz), 6.53 (d, 1H, *J* = 7.5 Hz), 4.35 (s, 2H), 4.27 (s, 2H); ¹³C NMR (125 MHz, CDCl₃) δ : 146.8, 137.6, 133.8, 132.7, 130.0, 128.9, 128.4, 119.1, 117.7, 113.9, 60.0.

Compound **2**: A 100 mL flask was charged with **1** (1.24 g, 5.03 mmol) and

pyridine (1.22 mL, 15.11 mmol) in CH_2Cl_2 (30 mL). Trifluoroacetic anhydride (1.54 mL, 11.06 mmol) was added at 0 °C. After the mixture had been stirred at room temperature for 2 h, the reaction mixture was quenched by the addition of aqueous NH_4Cl . After extraction with ethyl acetate, the organic layer was dried over MgSO_4 and filtered. The solvent was evaporated and the residue was chromatographed (4:6 ethyl acetate / hexane) to give 1.63 g of **2** (95 %) as a colorless solid. ^1H NMR (500 MHz, CDCl_3) δ : 9.81 (s, 1H), 7.81 (d, 1H, J = 8.0 Hz), 7.75 (d, 2H, J = 7.5 Hz), 7.70 (t, 1H, J = 7.5 Hz), 7.55 (d, 2H, J = 8.0 Hz), 7.45 (dt, 1H, J = 8.0, 1.0 Hz), 7.14 (t, 1H, J = 7.5 Hz), 6.85 (d, 1H, J = 8.0 Hz), 4.37 (s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 156.3 (q, J = 38.1 Hz), 136.8, 134.6, 134.5, 132.8, 130.2, 129.3, 128.3, 127.2, 125.9, 121.2, 117.1 (q, J = 288.8 Hz), 59.6.

Compound **3a**: LHMDS (1.0M in THF, 6.8 mL, 6.8 mmol) was added to a THF solution (30 mL) of sulfone **2** (1.16 g, 3.39 mmol) at -78 °C, and the mixture was stirred for 30 min. Benzaldehyde (0.790 g, 7.45 mmol) in THF (6 mL) was added dropwise at this temperature. After an additional 1h, CIP(O)(OEt)_2 (1.07 mL, 7.45 mmol) was added at -78 °C and the mixture was stirred at room temperature for 2h. Potassium *t*-butoxide (1.65 g, 13.56 mmol) was added at 0 °C. After the mixture had been stirred at the same temperature for 1h, the reaction mixture was quenched by the addition of aqueous NH_4Cl . After extraction with ethyl acetate, the organic layer was dried over MgSO_4 and filtered. The solvent was evaporated, and the residue was chromatographed (2.5:7.5 ethylacetate / hexane) to give 1.33 g of **3a** (91 %) as a colorless solid. ^1H NMR (500 MHz, CDCl_3) δ : 9.11 (s, 1H), 8.24 (s, 1H), 8.03 (d, 1H, J = 8.5 Hz), 7.63 (m, 3H), 7.49 (m, 3H), 7.31-7.18 (m, 3H), 7.08-6.99 (m, 3H), 6.62 (dd, 1H, J = 8.0, 1.5 Hz); ^{13}C NMR (125 MHz, CDCl_3) δ : 155.5 (q, J = 36.5 Hz), 140.7, 136.7, 136.3, 134.3, 133.9, 132.0, 131.4, 131.0, 130.8, 130.2, 129.0, 128.5, 128.4, 126.9, 124.2, 123.9, 118.9 (q, J = 278.6 Hz).

Compound **4a**³: A 100 mL flask was charged with **3a** (0.367 g, 0.85 mmol), potassium carbonate (0.587 g, 4.25 mmol), water (2 mL) and methanol (40 mL). After the mixture had been refluxed for 1 h, the reaction mixture was quenched by the addition of aqueous NH_4Cl . After extraction with ethyl acetate, the organic layer was dried over MgSO_4 and filtered. The solvent was evaporated, and the residue was chromatographed (2.5:7.5 ethylacetate / hexane) to give 0.162 g of **4a** (98 %) as a colorless solid. ^1H NMR (500 MHz, CDCl_3) δ : 8.32 (s, 1H), 7.66 (d, 2H, J = 7.5 Hz), 7.63 (d, 1H, J = 7.5 Hz), 7.45 (m, 3H), 7.33 (t, 1H, J = 7.5 Hz), 7.20 (dt, 1H, J = 8.0, 1.0 Hz), 7.13 (t, 1H, J = 7.5 Hz), 6.82 (d, 1H, J = 1.5 Hz).

Compound **3b**: LHMDS (1.0M in THF, 3.9mL, 3.9 mmol) was added to a THF solution (20 mL) of sulfone **2** (0.677 g, 1.97 mmol) at -78 °C, and the mixture was stirred for 30 min. Thiophene-2-carboxaldehyde (0.331 g, 2.95 mmol) in THF (6 mL) was added dropwise at this temperature. After an additional 1 h, CIP(O)(OEt)_2 (0.427 mL, 2.95 mmol) was added at -78 °C and the mixture was stirred at room temperature for 2 h. Potassium *t*-butoxide (0.722 g, 5.91 mmol) was added at 0 °C. After the

mixture had been stirred at the same temperature for 1 h, the reaction mixture was quenched by the addition of aqueous NH_4Cl . After extraction with ethyl acetate, the organic layer was dried over MgSO_4 and filtered. The solvent was evaporated and the residue was chromatographed (3:7 ethyl acetate / hexane) to give 0.714 g of **3b** (83 %) as a light yellow solid. ^1H NMR (500 MHz, CDCl_3) δ : 9.17 (s, 1H), 8.25 (s, 1H), 8.13 (d, 1H, J = 8.0 Hz), 7.65-7.28 (m, 8H), 7.12 (t, 1H, J = 7.5 Hz), 7.00 (m, 1H), 6.58 (dd, 1H, J = 7.5, 1.5 Hz); ^{13}C NMR (125 MHz, CDCl_3) δ : 155.3 (q, J = 38.1 Hz), 137.1, 135.5, 135.2, 135.0, 134.2, 133.9, 133.0, 132.7, 132.5, 131.4, 129.1, 128.5, 127.4, 127.1, 124.3, 122.8, 116.8 (q, J = 287.8 Hz).

Compound **4b**⁴: A 100 mL flask was charged with **3b** (0.270 g, 0.617 mmol), potassium carbonate (0.426 g, 3.08 mmol), water (1.5 mL) and methanol (20 mL). After the mixture had been refluxed for 1 h, the reaction mixture was quenched by the addition of aqueous NH_4Cl . After extraction with ethyl acetate, the organic layer was dried over MgSO_4 and filtered. The solvent was evaporated, and the residue was chromatographed (2.5:7.5 ethyl acetate / hexane) to give 0.098 g of **4b** (80 %) as a colorless solid. ^1H NMR (500 MHz, CDCl_3) δ : 8.20 (s, 1H), 7.59 (d, 1H, J = 8.0 Hz), 7.37 (d, 1H, J = 8.5 Hz), 7.28 (d, 1H, J = 5.0 Hz), 7.26 (d, 1H, J = 5.0 Hz), 7.20 (t, 1H, J = 7.5 Hz), 7.12 (m, 2H), 6.72 (s, 1H).

Compound **3c**: LHMDS (1.0 M in THF, 1.48 mL, 1.48 mmol) was added to a THF solution (6 mL) of sulfone **2** (0.231 g, 0.672 mmol) at -78°C , and the mixture was stirred for 30 min. Cinnamaldehyde (0.195 g, 1.48 mmol) in THF (4 mL) was added dropwise at this temperature. After an additional 1h, ClP(O)(OEt)_2 (0.214 mL, 1.48 mmol) was added at -78°C and the mixture was stirred at room temperature for 2 h. Potassium *t*-butoxide (0.328 g, 2.68 mmol) was added at 0°C . After the mixture had been stirred at the same temperature for 1h, the reaction mixture was quenched by the addition of aqueous NH_4Cl . After extraction with ethyl acetate, the organic layer was dried over MgSO_4 and filtered. The solvent was evaporated, and the residue was chromatographed (2.5:7.5 ethyl acetate / hexane) to give 0.243 g of **3c** (79 %) as a colorless solid. ^1H NMR (500 MHz, CDCl_3) δ : 9.28 (s, 1H), 8.04 (d, 1H, J = 8.5 Hz), 7.83 (d, 1H, J = 11.5 Hz), 7.62 (m, 3H), 7.49 (m, 3H), 7.29 (s, 5H), 7.14 (d, 1H, J = 15.5 Hz), 7.09 (d, 1H, J = 7.5 Hz), 6.63 (dd, 1H, J = 7.5, 1.0 Hz), 6.30 (dd, 1H, J = 15.5, 11.5 Hz); ^{13}C NMR (125 MHz, CDCl_3) δ : 155.9 (q, J = 37.5 Hz), 145.3, 141.7, 137.6, 136.1, 135.0, 134.7, 133.8, 132.8, 130.7, 130.0, 129.0, 128.8, 128.2, 127.7, 126.3, 124.1, 123.4, 121.2, 119.1 (q, J = 286.8 Hz).

Compound **4c**⁵: A 100 mL flask was charged with **3c** (0.236 g, 0.517 mmol), potassium carbonate (0.357 g, 2.58 mmol), water (1.5 mL) and methanol (20 mL). After the mixture had been refluxed for 3 h, the reaction mixture was quenched by the addition of aqueous NH_4Cl . After extraction with ethyl acetate, the organic layer was dried over MgSO_4 and filtered. The solvent was evaporated, and the residue was chromatographed (2.5:7.5 ethyl acetate / hexane) to give 0.061 g of **4c** (54 %) as a colorless solid. ^1H NMR (500 MHz, CDCl_3) δ : 8.24 (s, 1H), 7.58 (d, 1H, J = 8.0 Hz), 7.50 (d, 2H, J = 7.5 Hz), 7.38 (m, 3H), 7.28 (d, 1H, J = 7.5 Hz), 7.20 (t, 1H, J = 8.0 Hz), 7.14 (d, 1H, J = 16.5 Hz), 7.09 (d, 1H, J = 7.5 Hz), 6.92 (d, 1H, J = 16.5 Hz), 6.61 (s, 1H).

Compound **6**⁶: A 300 mL flask was charged with lithium aluminium hydride (3.68 g, 97 mmol) in THF (80 mL) and cooled to 0 °C. *N*-Methyl anthranillic acid methyl ester **5** (10.69 g, 64.7 mmol) in THF (20 mL) was added dropwise. After the mixture had been stirred at room temperature for 3 h, the reaction was quenched by the dropwise addition of cold water and extracted with ethyl acetate. The extract was washed with brine, dried over MgSO₄ and filtered. The solvent was evaporated and the residue was chromatographed (4:6 ethyl acetate / hexane) to give 7.80 g of **6** (88 %) as a yellow oil. ¹H NMR (500 MHz, CDCl₃) δ : 7.27 (m, 1H), 7.06 (d, 1H, *J* = 7.5 Hz), 6.68 (m, 2H), 4.65 (s, 2H), 2.87 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ : 148.4, 129.6, 128.8, 124.2, 116.3, 110.0, 64.6, 30.2.

Compound **7**⁶: A 200 mL flask was charged with **6** (7.62 g, 55.6 mmol) in THF (70 mL) and (BOC)₂O (13.3 g, 61.2 mmol) in THF (30 mL) was added. After the mixture had been refluxed for 5.5 h, stirring was continued at room temperature for 12 h. The solvent was evaporated and the residue was chromatographed (3.5:6.5 ethyl acetate / hexane) to give 10.01 g of **7** (76 %) as a yellow liquid. ¹H NMR (500 MHz, CDCl₃) δ : 7.53 (m, 1H), 7.32- 7.06 (m, 3H), 4.60 & 4.45 (br, 2H), 3.50 (br, 1H), 3.20 (s, 3H), 1.53 & 1.33 (br, 9H).

Compound **8**⁶: A 300 mL flask was charged with **7** (9.85 g, 41.5 mmol) and triphenylphosphine (13.08 g, 49.8 mmol) in THF (180 mL) and cooled to 0 °C. *N*-Bromosuccinimide (8.87 g, 49.8 mmol) was added at this temperature and the stirring was continued at room temperature for 2 h. The solid formed was filtered and washed with ethyl acetate. The filtrate was evaporated and the residue was chromatographed (2.5: 7.5 ethyl acetate / hexane) to give 10.45 g of **8** (84 %) as a colorless solid. ¹H NMR (500 MHz, CDCl₃) δ : 7.45 (m, 1H), 7.31- 7.26 (m, 2H), 7.11 (br, 1H), 4.52 (d, 1H, *J* = 10.5 Hz), 4.39 (d, 1H, *J* = 10.0 Hz), 3.22 (s, 3H), 1.53 & 1.33 (br, 9H).

Compound **9**: A 200 mL flask was charged with **8** (10.16 g, 33.8 mmol), benzenesulfinic acid sodium salt dihydrate (6.67 g, 40.6 mmol) and DMF (120 mL). After the mixture had been stirred at 80 °C for 12 h, the reaction mixture was cooled to room temperature. After usual workup with water and ethyl acetate, the solvent was evaporated and the residue was chromatographed (3.5:6.5 ethyl acetate / hexane) to give 10.75 g of **9** (88 %) as a colorless solid. ¹H NMR (500 MHz, CDCl₃) δ : 7.70 (d, 2H, *J* = 7.5 Hz), 7.63 (t, 1H, *J* = 7.5 Hz), 7.50-7.06 (m, 6H), 4.49 (d, 1H, *J* = 12.0 Hz), 4.18 (d, 1H, *J* = 12.0 Hz), 2.97 & 2.76 (br, 3H), 1.49 & 1.27 (br, 9H); ¹³C NMR (125 MHz, CDCl₃) δ : 154.4, 143.5, 138.6, 133.6, 131.9, 131.4, 129.7, 128.9, 128.4, 127.0, 126.7, 125.8, 80.2, 58.6, 57.4, 37.7, 36.8, 28.0.

Compound **10**: BuLi (1.33 M in hexane, 2.75 mL, 3.65 mmol) was added to a THF solution (35 mL) of sulfone **9** (1.20 g, 3.32 mmol) at -78 °C, and the mixture was stirred for 30 min. Benzaldehyde (0.422 g, 3.98 mmol) in THF (8 mL) was added dropwise at this temperature. After an additional 1 h, CIP(O)(OEt)₂ (0.57 mL, 3.98 mmol) was added at -78 °C and the mixture was stirred at room temperature for 2 h. Potassium *t*-butoxide (1.21 g, 9.96 mmol) was added at 0 °C. After the mixture had been stirred at

the same temperature for 1 h, the solvent was evaporated and the residue was dissolved in a premixed solution of ethyl acetate (56 mL) / 12M HCl (24 mL) and stirred at room temperature for 2 h. The reaction mixture was neutralized with solid NaHCO₃, extracted with ethyl acetate, dried over MgSO₄ and filtered. The solvent was evaporated and the residue was chromatographed (2.5:7.5 ethyl acetate / hexane) to give 1.06 g of **10** (92 %) as a yellow solid. ¹H NMR (500 MHz, CDCl₃) δ : 8.05 (s, 1H), 7.66 (dd, 2H, *J* = 8.5, 1.5 Hz), 7.56 (m, 1H), 7.42 (t, 2H, *J* = 8.0 Hz), 7.29-7.17 (m, 6H), 6.59-6.48 (m, 3H), 3.98 (br, 1H), 2.57 (d, 3H, *J* = 3.5 Hz); ¹³C NMR (125 MHz, CDCl₃) δ : 147.9, 139.6, 138.2(2), 133.2, 132.5, 131.3, 130.8, 130.5, 130.2, 128.7, 128.6, 128.5, 116.7, 115.4, 110.2, 30.4.

Compound **11a**⁷: A 50 mL flask was charged with **10** (0.288 g, 0.82 mmol) in THF (15 mL) and cooled to 0 °C. LHMDS (1M in THF, 1.23 mL, 1.23 mmol) was added slowly. After the mixture had been stirred at 0 °C for 1 h, and then at room temperature for 10 min., methyl iodide (0.154 mL, 2.47 mmol) was added. After the mixture had been stirred at room temperature for 1 h, the reaction was quenched by the addition of aqueous NH₄Cl and extracted with ethyl acetate. The extract was dried over MgSO₄ and filtered. The solvent was evaporated and chromatographed (2.5:7.5 CH₂Cl₂ / hexane) to give 0.149 g of **11a** (82 %) as a colorless solid. ¹H NMR (500 MHz, CDCl₃) δ : 7.61 (d, 1H, *J* = 7.5 Hz), 7.50 (t, 2H, *J* = 7.5 Hz), 7.42 (m, 3H), 7.34 (d, 1H, *J* = 8.5 Hz), 7.27 (t, 1H, *J* = 8.0 Hz), 7.17 (t, 1H, *J* = 8.0 Hz), 3.61 (s, 3H), 2.28 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ : 137.6, 137.1, 132.0, 130.6, 128.3, 128.2, 127.7, 121.6, 119.0, 118.7, 109.1, 108.5, 30.9, 9.3.

Compound **11b**⁷: A 50 mL flask was charged with **10** (0.300 g, 0.86 mmol) in THF (15 mL) and cooled to 0 °C. LHMDS (1 M in THF, 1.30 mL, 1.29 mmol) was added slowly. After the mixture had been stirred at 0 °C for 1 h, and then at room temperature for 10 min., ethyl iodide (0.355 mL, 3.44 mmol) was added. After the mixture had been stirred at room temperature for 1 h, the reaction was quenched by the addition of aqueous NH₄Cl and extracted with ethyl acetate. The extract was dried over MgSO₄ and filtered. The solvent was evaporated and chromatographed (2.5:7.5 CH₂Cl₂ / hexane) to give 0.173 g of **11b** (86 %) as a colorless liquid. ¹H NMR (500 MHz, CDCl₃) δ : 7.66 (d, 1H, *J* = 8.0 Hz), 7.48- 7.33 (m, 6H), 7.26 (m, 1H), 7.16 (m, 1H), 3.57 (s, 3H), 2.73 (q, 2H, *J* = 8.0 Hz), 1.24 (t, 3H, *J* = 8.0 Hz); ¹³C NMR (125 MHz, CDCl₃) δ : 137.2, 137.1, 132.2, 130.5, 128.2, 127.8, 127.3, 121.5, 119.0, 115.3, 109.3, 30.7, 17.8, 16.0.

Compound **11c**⁸: A 50 mL flask was charged with **10** (0.283 g, 0.81 mmol) in THF (15 mL) and cooled to 0 °C. LHMDS (1 M in THF, 1.21 mL, 1.21 mmol) was added slowly. After the mixture had been stirred at 0 °C for 1 h, and then at room temperature for 10 min., propyl iodide (0.316 mL, 3.24 mmol) was added. After the mixture had been stirred at room temperature for 1 h, the reaction was quenched by the addition of aqueous NH₄Cl and extracted with ethyl acetate. The extract was dried over MgSO₄ and filtered. The solvent was evaporated and chromatographed (2.5:7.5 CH₂Cl₂ / hexane) to give 0.169 g of **11c** (84 %) as a colorless liquid. ¹H NMR (500 MHz, CDCl₃) δ : 7.65 (d, 1H, *J* = 8.0 Hz), 7.49- 7.32 (m, 6H), 7.24 (t, 1H, *J* = 4.0 Hz), 7.15 (t, 1H, *J* = 7.5 Hz), 3.57 (s, 3H), 2.67 (t, 2H, *J* = 8.0 Hz), 1.67 (m, 2H), 0.89 (t, 3H, *J* = 7.5 Hz); ¹³C NMR (125 MHz, CDCl₃) δ : 137.6, 137.1, 132.9, 130.6, 128.2, 127.8, 127.7,

121.5, 119.1, 118.9, 113.6, 109.2, 30.7, 26.7, 24.4, 14.2.

Compound 11d: A 50 mL flask was charged with **10** (0.282 g, 0.80 mmol) in THF (15 mL) and cooled to 0 °C. LHMDS (1 M in THF, 1.21 mL, 1.21 mmol) was added slowly. After the mixture had been stirred at 0 °C for 1 h, and then at room temperature for 10 min., allyl iodide (0.295 mL, 3.23 mmol) was added. After the mixture had been stirred at room temperature for 1 h, the reaction was quenched by the addition of aqueous NH₄Cl and extracted with ethyl acetate. The extract was dried over MgSO₄ and filtered. The solvent was evaporated and chromatographed (2.5:7.5 CH₂Cl₂ / hexane) to give 0.167 g of **11d** (84 %) as a colorless liquid. ¹H NMR (500 MHz, CDCl₃) δ : 7.63 (d, 1H, *J* = 7.5 Hz), 7.49- 7.39 (m, 5H), 7.35 (d, 1H, *J* = 8.5 Hz), 7.27 (t, 1H, *J* = 7.5 Hz), 7.15 (t, 1H, *J* = 7.5 Hz), 6.05 (m, 1H), 5.05 (m, 2H), 3.62 (s, 3H), 3.44 (d, 2H, *J* = 6.0 Hz); ¹³C NMR (125 MHz, CDCl₃) δ : 138.0, 137.9, 137.2, 131.7, 130.5, 128.2, 127.9, 127.7, 121.6, 119.2, 119.1, 114.5, 110.5, 109.3, 30.8, 29.2. Anal. Calcd for C₁₈H₁₇N: C, 87.41; H, 6.93; N, 5.66; Found C, 87.12; H, 7.12, N, 5.57.

Compound 11e: A 50 mL flask was charged with **10** (0.277 g, 0.79 mmol) in THF (15 mL) and cooled to 0 °C. LHMDS (1 M in THF, 1.20 mL, 1.20 mmol) was added slowly. After the mixture had been stirred at 0 °C for 1 h, and then at room temperature for 10 min., ethyl bromoacetate (0.352 mL, 3.17 mmol) was added. After the mixture had been stirred at room temperature for 1 h, the reaction was quenched by the addition of aqueous NH₄Cl and extracted with ethyl acetate. The extract was dried over MgSO₄ and filtered. The solvent was evaporated and chromatographed (1.5:8.5 ethyl acetate / hexane) to give 0.188 g of **11e** (81 %) as a yellow liquid. ¹H NMR (500 MHz, CDCl₃) δ : 7.66 (d, 1H, *J* = 8.0 Hz), 7.51- 7.43 (m, 5H), 7.35 (d, 1H, *J* = 8.0 Hz), 7.28 (dd, 1H, *J* = 7.0, 1.0 Hz), 7.18 (dt, 1H, *J* = 8.0, 1.0 Hz), 4.15 (q, 2H, *J* = 7.0 Hz), 3.65 (s, 2H), 3.62 (s, 3H), 1.25 (t, 3H, *J* = 7.0 Hz); ¹³C NMR (125 MHz, CDCl₃) δ : 172.3, 139.2, 137.1, 131.1, 130.6, 128.3, 128.2, 127.5, 121.9, 119.6, 119.0, 109.4, 105.7, 60.6, 31.1, 30.9, 14.1. Anal. Calcd for C₁₉H₁₉NO₃: C, 77.79; H, 6.53; N, 4.77; Found C, 77.74; H, 6.66, N, 4.77.

Compound 11f: A 50 mL flask was charged with **10** (0.284 g, 0.81 mmol) in THF (15 mL) and cooled to 0 °C. LHMDS (1 M in THF, 1.21 mL, 1.21 mmol) was added slowly. After the mixture had been stirred at 0 °C for 1 h, and then at room temperature for 10 min., *N,N*-diethyl chloroacetamide (0.446 mL, 3.24 mmol) was added. After the mixture had been stirred at room temperature for 1 h, the reaction was quenched by the addition of aqueous NH₄Cl and extracted with ethyl acetate. The extract was dried over MgSO₄ and filtered. The solvent was evaporated and chromatographed (2.5:7.5 ethyl acetate / hexane) to give 0.223 g of **11f** (86 %) as a colorless solid. ¹H NMR (500 MHz, CDCl₃) δ : 7.75 (d, 1H, *J* = 8.0 Hz), 7.51- 7.41 (m, 5H), 7.34 (d, 1H, *J* = 8.0 Hz), 7.25 (t, 1H, *J* = 8.0 Hz), 7.15 (t, 1H, *J* = 8.0 Hz), 3.72 (s, 2H), 3.62 (s, 3H), 3.33 (q, 2H, *J* = 7.0 Hz), 3.11 (q, 2H, *J* = 7.0 Hz), 1.06 (t, 3H, *J* = 7.0 Hz), 0.86 (t, 3H, *J* = 7.0 Hz); ¹³C NMR (125 MHz, CDCl₃) δ : 170.4, 138.2, 137.2, 131.4, 130.5, 128.4, 128.1, 127.6, 121.8, 119.6, 119.5, 109.1, 107.0, 41.9, 40.7, 31.0, 30.9, 13.8, 12.9. Anal. Calcd for C₂₁H₂₄N₂O: C, 78.71; H, 7.55, N, 8.74; Found C, 78.57; H, 7.56; N, 8.60.

Compound 11g⁹: A 50 mL flask was charged with **10** (0.281 g, 0.80 mmol) in THF (15

mL) and cooled to 0 °C. LHMDs (1 M in THF, 1.20 mL, 1.20 mmol) was added slowly. After the mixture had been stirred at 0 °C for 1 h, and then at room temperature for 10 min., benzoyl chloride (0.467 mL, 4.02 mmol) was added. After the mixture had been stirred at room temperature for 1 h, LHMDs (1 M in THF, 4.0 mL, 4.02 mmol) was added and stirred at room temperature for 1 h. The reaction was quenched by the addition of aqueous NH₄Cl and extracted with ethyl acetate. The extract was dried over MgSO₄ and filtered. The solvent was evaporated and chromatographed (1.5:8.5 ethyl acetate / hexane) to give 0.212 g of **11g** (85 %) as a colorless solid. ¹H NMR (500 MHz, CDCl₃) δ : 8.02 (d, 1H, *J* = 8.0 Hz), 7.52- 7.23 (m, 11H), 7.13 (t, 2H, *J* = 7.5 Hz), 3.68 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ : 198.8, 146.3, 140.0, 137.1, 130.8(2), 130.6, 129.1, 128.6, 127.9, 127.5, 127.4, 123.1, 122.2, 121.8, 114.4, 109.7, 31.2.

Compound **12**: BuLi (1.33 M in hexane, 1.45 mL, 1.93 mmol) was added to a THF solution (20 mL) of sulfone **9** (0.636 g, 1.76 mmol) at -78 °C, and the mixture was stirred for 30 min. 4-Chloro-benzaldehyde (0.296 g, 2.11 mmol) in THF (8 mL) was added dropwise at this temperature. After an additional 1 h, ClP(O)(OEt)₂ (0.305 mL, 2.11 mmol) was added at -78 °C and the mixture was stirred at room temperature for 2 h. Potassium *t*-butoxide (0.645 g, 5.28 mmol) was added at 0 °C. After the mixture had been stirred at the same temperature for 1 h, the solvent was evaporated and the residue was dissolved in a premixed solution of ethyl acetate (29.4 mL) / 12M HCl (12.6 mL) and stirred at room temperature for 2 h. The reaction mixture was neutralized with solid NaHCO₃, extracted with ethyl acetate, dried over MgSO₄ and filtered. The solvent was evaporated and the residue was chromatographed (2.5:7.5 ethyl acetate / hexane) to give 0.614 g of **12** (91 %) as a yellow solid. ¹H NMR (500 MHz, CDCl₃) δ : 7.99 (s, 1H), 7.65 (dd, 2H, *J* = 8.5, 1.5 Hz), 7.57 (m, 1H), 7.42 (t, 2H, *J* = 8.5 Hz), 7.28 (m, 1H), 7.18 (d, 2H, *J* = 8.5 Hz), 7.10 (d, 2H, *J* = 8.5 Hz), 6.58 (d, 1H, *J* = 8.0 Hz), 6.55 (dt, 1H, *J* = 7.0, 1.0 Hz), 6.47 (dd, 1H, *J* = 7.0, 1.0 Hz), 3.97 (b, 1H), 2.57 (d, 3H, *J* = 5.0 Hz); ¹³C NMR (125 MHz, CDCl₃) δ : 147.9, 139.0, 138.2, 138.0, 136.5, 133.3, 131.4, 131.2, 131.1, 131.0, 128.9, 128.8, 128.6, 116.8, 115.0, 110.4, 30.4.

Compound **14**¹⁰: A 50 mL flask was charged with **12** (0.306 g, 0.79 mmol) in THF (15 mL) and cooled to 0 °C. LHMDs (1 M in THF, 1.20 mL, 1.19 mmol) was added slowly. After the mixture had been stirred at 0 °C for 1 h, and then at room temperature for 10 min., **13** (0.566 g, 3.18 mmol) was added. After the mixture had been stirred at room temperature for 1 h, the reaction was quenched by the addition of aqueous NH₄Cl and extracted with ethyl acetate. The extract was dried over MgSO₄ and filtered. The solvent was evaporated and chromatographed (3:7 ethyl acetate / hexane) to give 0.244 g of **14** (80 %) as a colorless solid. ¹H NMR (500 MHz, CDCl₃) δ : 7.68 (d, 1H, *J* = 7.5 Hz), 7.47 (d, 2H, *J* = 8.5 Hz), 7.40 (d, 2H, *J* = 8.5 Hz), 7.33 (d, 1H, *J* = 8.5 Hz), 7.25 (m, 1H), 7.14 (t, 1H, *J* = 8.0 Hz), 3.68 (s, 2H), 3.60 (s, 3H), 3.26 (t, 2H, *J* = 7.5 Hz), 3.10 (t, 2H, *J* = 7.5 Hz), 1.53 (m, 4H), 0.83 (t, 3H, *J* = 7.5 Hz), 0.74 (t, 3H, *J* = 7.5 Hz); ¹³C NMR (125 MHz, CDCl₃) δ : 170.7, 137.3, 137.1, 134.3, 131.8, 129.9, 128.6, 127.6, 122.0, 119.6, 119.4, 109.3, 107.6, 49.6, 47.8, 30.9, 30.5, 22.1, 20.8, 11.3, 11.0.

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