

## **Supporting Information**

### **Microwave-Assisted Synthesis Utilizing Supported Reagents: A Rapid and Efficient Acylation Procedure**

**Daryl R. Sauer\*, Douglas Kalvin, and Kathleen M. Phelan**

*High-Throughput Organic Synthesis Group, Global Pharmaceutical Research and Development, Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064-6113.*

## General Experimental for microwave synthesis

All reagents were obtained from commercial suppliers and were used without further purification. All microwave reactions were performed using an Emrys<sup>TM</sup> Optimizer in a septa capped 2-5 mL Smith<sup>TM</sup> process vial with stirring. Initial heating of 300W was used to bring the reaction to desired temperature. Power required to maintain target temperature was controlled by Emrys<sup>TM</sup> Optimizer Software (version 2.5.0.10). The time reported for the reaction includes the time required to reach the target temperature. Compounds **4** and **8** were purified by MPLC on an Analogix IntelliFlash 280 (0-100% EtOAc/hexanes) using Analogix RS-4 cartridges. All isolated compounds were homogenous by LC/MS with four methods of detection (UV 220 & 254 nM, ELSD, and ion chromatograph).

## Spectroscopic Data

**1-Methyl-1H-indole-3-carboxylic acid benzylamide (2):** <sup>1</sup>H NMR: (400 MHz, DMSO-d<sub>6</sub>) δ 3.82 (s, 3H, Indole-N-CH<sub>3</sub>), 4.47 (d, 2H, *J* = 6.0 Hz, CO-NH-CH<sub>2</sub>-Ar), 7.14 (d t, 1H, *J* = 2.0, 8.0 Hz, ArH), 7.20–7.25 (m, 2H, ArH), 7.30–7.35 (m, 4H, ArH), 7.48 (d, 1H, *J* = 9.0 Hz, ArH), 8.30 (s, 1H, Indole ArH), 8.15 (d, 1H, *J* = 9.0 Hz, 1H), 8.39 (br t, 1H, *J* = 8.0 Hz, -CO-NH-); <sup>13</sup>C NMR: (100 MHz, DMSO-d<sub>6</sub>) δ 164.1, 140.4, 136.6, 131.7, 128.1, 127.1, 126.5, 126.4, 121.9, 121.1, 120.5, 110.1, 109.5, 41.8, 32.9; MS (ESI), *m/z* 265.0 (100%) [*M*+*H*]; HRMS (EI) calcd for C<sub>17</sub>H<sub>16</sub>N<sub>2</sub>O 264.1263, found 264.1266.

**1-Methyl-1H-indole-3-carboxylic acid phenylamide (4):** <sup>1</sup>H NMR: (400 MHz, DMSO-d<sub>6</sub>) δ 3.87 (s, 3H, Indole-N-CH<sub>3</sub>), 7.13 (t, 1H, *J* = 6.0 Hz, ArH), 7.20 (t, 1H; *J* = 6.0 Hz, ArH), 7.25 (t, 1H, *J* = 8.0 Hz, 1H ArH), 7.33 (t, 2H, *J* = 8.0 Hz, ArH), 7.53 (d, 1H, *J* = 8.0 Hz, ArH), 7.77 (d, 2H, *J* = 8.0 Hz, ArH), 8.20 (d, 1H, *J* = 8.0 Hz, ArH), 8.25 (s, 1H, Indole ArH), 9.70 δ (s, 1H, CO-NH-); <sup>13</sup>C NMR: (100 MHz, DMSO-d<sub>6</sub>) δ 32.8, 109.5, 110.3, 119.6, 119.9, 120.9, 121.2, 122.2, 122.6, 126.7, 128.5, 128.6, 132.4, 136.8, 139.8, 162.9; MS (ESI), *m/z* 251.1 (100%) [*M*+*H*]; HRMS (EI) calcd for C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>O 250.1106, found 250.1104.

**1-Methyl-1H-indole-3-carboxylic acid N-methyl-phenethylamide (5):** <sup>1</sup>H NMR: (400 MHz, DMSO-d<sub>6</sub>) δ 2.87 (t, 2H, *J* = 8.0 Hz; CH<sub>2</sub>-), 3.08 (s, 3H, CONCH<sub>3</sub>), 3.69 (t, 2H, *J* = 8.0 Hz; CH<sub>2</sub>), 3.80 (s, 3H, Indole-N-CH<sub>3</sub>), 7.10 (dt, 1H, *J* = 1.0, 8.0 Hz; ArH), 7.19-7.31 (m, 6H, ArH), 7.46 (d, 1H, *J* = 8.0 Hz, ArH), 7.57 (br s, 1H, Indole ArH), 7.70 (d, 1H, *J* = 8.0 Hz, ArH); <sup>13</sup>C NMR: (100 MHz, DMSO-d<sub>6</sub>) δ 32.6, 33.4, 39.31, 50.1, 109.1, 110.0, 120.2, 120.8, 121.8, 126.1, 126.8, 128.3, 128.7, 131.2, 136.0, 139.2, 165.8; MS (ESI), *m/z* 293.2 (100%) [*M*+*H*]; HRMS (EI) calcd for C<sub>19</sub>H<sub>20</sub>N<sub>2</sub>NaO 315.1468, found 315.1265.

**(1-Methyl-1H-indol-3-yl)-morpholin-4-yl-methanone (6):** <sup>1</sup>H NMR: (400 MHz, DMSO-d<sub>6</sub>) δ 3.60 (s, 8H), 3.82 (s, 3H, Indole-N-CH<sub>3</sub>), 7.15 (t, 1H, *J* = 8.0 Hz, ArH), 7.22 (t, 1H, *J* = 8.0 Hz, ArH), 7.49 (d, 1H, *J* = 8.0 Hz, ArH), 7.71 (d, 1H, *J* = 8.0 Hz, ArH),

7.75 (s, 1H, Indole ArH);  $^{13}\text{C}$  NMR: (100 MHz, DMSO- $\text{d}_6$ )  $\delta$  32.7, 66.3, 108.3, 110.3, 120.3, 120.4, 121.9, 126.3, 132.1, 136.2, 165.3; MS (ESI),  $m/z$  245.1 (100%)  $[\text{M}+\text{H}]$ ; HRMS (EI) calcd for  $\text{C}_{14}\text{H}_{16}\text{N}_2\text{NaO}_2$  267.1109, found 267.1110.

**1-Methyl-1H-indole-3-carboxylic acid methyl-(2-pyridin-2-yl-ethyl)-amide (7):**  $^1\text{H}$  NMR: (400 MHz, DMSO- $\text{d}_6$ )  $\delta$  3.03 (t, 2H,  $J=7.0$  Hz;  $\text{CH}_2$ ), 3.07 (s, 3H,  $\text{CONCH}_3$ ), 3.80 (s, 3H, Indole-N- $\text{CH}_3$ ), 3.83 (t, 2H,  $J=7.0$  Hz;  $\text{CH}_2$ ); 7.10 (dd, 1H,  $J=1.0, 8.0$  Hz, ArH), 7.18-7.23 (m, 2H, ArH), 7.28 (d, 1H,  $J=8.0$  Hz, ArH), 7.46 (dt, 1H,  $J=1.0, 8.0$  Hz, ArH), 7.65 (s, 1H, Indole ArH), 7.67-7.71 (m, 2H, ArH), 8.47 (dd; 1H;  $J=1.0, 4.0$  Hz, ArH);  $^{13}\text{C}$  NMR: (100 MHz, DMSO- $\text{d}_6$ )  $\delta$  32.6, 35.8, 39.3, 48.6, 109.1, 110.0, 120.2, 120.8, 121.5, 121.8, 123.2, 126.8, 131.3, 136.0, 136.4, 149.0, 159.0, 165.7; MS (ESI),  $m/z$  294.2 (100%)  $[\text{M}+\text{H}]$ ; HRMS (EI) calcd for  $\text{C}_{18}\text{H}_{19}\text{N}_3\text{NaO}$  315.1426, found 315.1422.

**1-Methyl-1H-indole-3-carboxylic acid dibenzylamide (8):**  $^1\text{H}$  NMR: (400 MHz, DMSO- $\text{d}_6$ )  $\delta$  3.75 (s, 3H, Indole-N- $\text{CH}_3$ ), 4.65 (s, 4H,  $\text{ArCH}_2\text{N}$ ), 7.15 (dt, 1H,  $J=2.0, 8.0$  Hz., ArH), 7.20-7.30 (m, 7H, ArH), 7.35 (m, 4H, ArH), 7.48 (d, 1H,  $J=8.0$  Hz, ArH), 7.62 (s, 1H, Indole ArH), 7.83 (d, 1H,  $J=8.0$  Hz, ArH);  $^{13}\text{C}$  NMR: (100 MHz, DMSO- $\text{d}_6$ )  $\delta$  32.7, 56.2, 108.3, 110.2, 120.5, 122.1, 127.0, 127.1, 127.2, 128.6, 130.8, 136.2, 137.6, 166.6; MS (ESI),  $m/z$  355.1 (100%)  $[\text{M}+\text{H}]$ ; HRMS (EI) calcd for  $\text{C}_{24}\text{H}_{22}\text{N}_2\text{NaO}$  377.1630, found 377.1629.