

## A simple synthesis of the lamellarin analogues from 3-nitro-2-(trifluoromethyl)-2H-chromenes and 1-benzyl-3,4-dihydroisoquinolines

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### Experimental

14-(3',4'-Dimethoxyphenyl)-2,11,12-trimethoxy-6-(trifluoromethyl)-8,9-dihydro-6H-chromeno[4',3':4,5]pyrrolo[2,1-a]isoquinoline **4b**. Yield 66%, mp 174–175 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 3.05 (t, 2H, CH<sub>2</sub>, *J* 5.8 Hz), 3.36, 3.47, 3.86, 3.94 (all s, 3H, MeO), 3.7–4.0 (m, 4H, MeO, CHHN), 4.07 (dt, 1H, CHHN, *J* 12.2, 5.8 Hz), 5.70 (q, 1H, H-6, <sup>3</sup>*J*<sub>H,F</sub> 6.2 Hz), 6.52 (d, 1H, H-1, *J* 3.0 Hz), 6.54 (dd, 1H, H-3, *J* 8.7, 3.0 Hz), 6.59 (s, 1H, H-13), 6.69 (s, 1H, H-10), 6.8–7.2 (br m, 3H, Ar), 6.90 (d, 1H, H-4, *J* 8.7 Hz). <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ: 83.52 (br d, CF<sub>3</sub>, <sup>3</sup>*J*<sub>F,H</sub> 6.2 Hz). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 28.95, 42.01, 55.11, 55.16, 55.93, 56.09, 56.13, 69.89 (q, C-6, <sup>2</sup>*J*<sub>C,F</sub> 33.9 Hz), 107.39, 107.73, 111.02, 111.78, 114.03 (br s), 115.33, 115.69, 116.27, 116.52, 120.86, 121.57, 123.34 (q, CF<sub>3</sub>, <sup>1</sup>*J*<sub>C,F</sub> 287.6 Hz), 123.46 (br s), 123.89, 128.81, 128.90, 143.90, 147.37, 147.59, 148.49, 149.47, 154.55. IR (KBr, ν<sub>cm<sup>-1</sup></sub>): 1613, 1581, 1558, 1544, 1516, 1488. Found (%): C, 65.45; H, 4.62; N, 2.52. Calc. for C<sub>31</sub>H<sub>28</sub>F<sub>3</sub>NO<sub>6</sub> (%): C, 65.60; H, 4.97; N, 2.47.

2-Bromo-14-(3',4'-dimethoxyphenyl)-11,12-dimethoxy-6-(trifluoromethyl)-8,9-dihydro-6H-chromeno[4',3':4,5]pyrrolo[2,1-a]isoquinoline **4c**. Yield 92%, mp 204–205 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 3.05 (t, 2H, CH<sub>2</sub>, *J* 5.9 Hz), 3.36, 3.86, 3.96 (all s, 3H, MeO), 3.8–4.0 (m, 4H, MeO, CHHN), 4.07 (dt, 1H, CHHN, *J* 12.2, 5.9 Hz), 5.74 (q, 1H, H-6, <sup>3</sup>*J*<sub>H,F</sub> 6.1 Hz), 6.55 (s, 1H, H-13), 6.69 (s, 1H, H-10), 6.7–7.2 (br s, 3H, Ar), 6.85 (d, 1H, H-4, *J* 8.3 Hz), 7.07 (d, 1H, H-1, *J* 2.4 Hz), 7.08 (dd, 1H, H-3, *J* 8.3, 2.4 Hz). <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ: 83.38 (d, CF<sub>3</sub>, <sup>3</sup>*J*<sub>F,H</sub> 6.1 Hz). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 28.91, 42.08, 55.16, 55.93, 56.16, 56.19, 70.07 (q, C-6, <sup>2</sup>*J*<sub>C,F</sub> 34.3 Hz), 107.50, 111.01, 111.87, 113.98 (br s), 114.12, 114.82, 115.42, 116.33, 117.70, 121.32, 122.36, 123.40 (br s), 123.13 (q, CF<sub>3</sub>, <sup>1</sup>*J*<sub>C,F</sub> 287.3 Hz), 123.96, 125.43, 128.07, 128.90, 129.32, 147.53, 147.63, 148.77, 149.01, 154.60. IR (KBr, ν<sub>cm<sup>-1</sup></sub>): 1602, 1576, 1545, 1516, 1502, 1486. Found (%): C, 58.50; H, 3.99; N, 2.45. Calc. for C<sub>30</sub>H<sub>25</sub>BrF<sub>3</sub>NO<sub>5</sub> (%): C, 58.45; H, 4.09; N, 2.27.

14-(3',4'-Diethoxyphenyl)-11,12-diethoxy-2-methoxy-6-(trifluoromethyl)-8,9-dihydro-6H-chromeno[4',3':4,5]pyrrolo[2,1-a]isoquinoline **4e**. Yield 71%, mp 146–147 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 1.17, 1.43, 1.49 (all t, 3H, Me, *J* 7.0 Hz), 1.3–1.5 (br s, 3H, Me), 3.00–3.05 (m, 2H, CH<sub>2</sub>), 3.45 (s, 3H, MeO), 3.52–3.62 (m, 2H, CH<sub>2</sub>O), 3.92–4.02 (m, 2H, CH<sub>2</sub>O), 4.06 (q, 4H, 2 CH<sub>2</sub>O, *J* 7.0 Hz), 4.15 (br q, 2H, CH<sub>2</sub>O, *J* 7.0 Hz), 5.69 (q, 1H, H-6, <sup>3</sup>*J*<sub>H,F</sub> 6.4 Hz), 6.50 (d, 1H, H-1, *J* 3.0 Hz), 6.52 (dd, 1H, H-3, *J* 8.6, 3.0 Hz), 6.61 (br s, 1H, H-13), 6.69 (s, 1H, H-10), 6.8–7.2 (br m, 3H, Ar), 6.88 (d, 1H, H-4, *J* 8.6 Hz). <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ: 83.50 (br d, CF<sub>3</sub>, <sup>3</sup>*J*<sub>F,H</sub> 6.0

Hz).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 14.47, 14.73, 14.82 (2C), 28.88, 41.99, 55.08, 63.61, 64.48 (br s), 64.61, 64.81, 69.88 (q, C-6,  $^2J_{\text{C,F}}$  33.8 Hz), 107.56, 108.92, 111.82, 113.11, 114.19 (br s), 115.30, 115.49, 115.88 (br s), 116.27, 116.43, 120.87, 121.65, 123.22 (br s), 123.32 (q,  $\text{CF}_3$ ,  $^1J_{\text{C,F}}$  287.7 Hz), 123.69, 128.90, 129.01 (br s), 143.83, 146.90, 147.14, 148.01, 149.35, 154.51. IR (KBr,  $\nu/\text{cm}^{-1}$ ): 1613, 1578, 1562, 1544, 1515. Found (%): C, 67.14; H, 5.66; N, 2.22. Calc. for  $\text{C}_{35}\text{H}_{36}\text{F}_3\text{NO}_6$  (%): C, 67.41; H, 5.82; N, 2.25.

*2-Bromo-14-(3',4'-diethoxyphenyl)-11,12-diethoxy-6-(trifluoromethyl)-8,9-dihydro-6H-chromeno[4',3':4,5]pyrrolo[2,1-a]isoquinoline 4f*. Yield 64%, mp 166–167 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 1.17 (t, 3H, Me,  $J$  7.0 Hz), 1.43 (t, 6H, 2 Me,  $J$  7.0 Hz), 1.50 (t, 3H, Me,  $J$  7.0 Hz), 2.98–3.06 (m, 2H,  $\text{CH}_2$ ), 3.51–3.63 (m, 2H,  $\text{CH}_2\text{N}$ ), 3.92–3.98 (m, 2H,  $\text{CH}_2\text{O}$ ), 4.06 (q, 4H, 2  $\text{CH}_2\text{O}$ ,  $J$  7.0 Hz), 4.18 (br q, 2H,  $\text{CH}_2\text{O}$ ,  $J$  7.0 Hz), 5.73 (q, 1H, H-6,  $^3J_{\text{H,F}}$  6.0 Hz), 6.58 (br s, 1H, H-13), 6.68 (s, 1H, H-10), 6.75–6.90 (br m, 1H, Ar), 6.84 (d, 1H, H-4,  $J$  8.5 Hz), 6.95–7.20 (br m, 2H, Ar), 7.03 (d, 1H, H-1,  $J$  2.4 Hz), 7.07 (dd, 1H, H-3,  $J$  8.5, 2.4 Hz).  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$ : 83.36 (d,  $\text{CF}_3$ ,  $^3J_{\text{F,H}}$  6.0 Hz).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 14.51, 14.80, 14.85 (2C), 28.88, 42.10, 63.68, 64.66, 64.75 (br s), 64.90, 70.09 (q, C-6,  $^2J_{\text{C,F}}$  34.2 Hz), 109.07, 113.11, 114.15, 114.49 (br s), 114.82, 115.26, 116.09 (br s), 116.38, 117.64, 121.44, 122.43, 123.13 (q,  $\text{CF}_3$ ,  $^1J_{\text{C,F}}$  287.2 Hz), 123.37 (br s), 123.78, 125.44, 128.31, 128.80, 129.34, 147.11, 147.23, 148.39, 148.99, 149.49. IR (KBr,  $\nu/\text{cm}^{-1}$ ): 1606, 1577, 1541, 1513, 1501, 1475. Found (%): C, 60.75; H, 5.05; N, 2.16. Calc. for  $\text{C}_{34}\text{H}_{33}\text{BrF}_3\text{NO}_5$  (%): C, 60.75; H, 4.95; N, 2.08.