

## Total Synthesis of Debromoflustramine B via Biomimetic Alkylative Cyclization

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Supporting information.

**Synthesis of carbamate 1.** Tryptamine (2.40 g, 15 mmol) was dissolved in a water (30 mL) and dichloromethane (30 mL) mixture and treated with NaCl (3.75 g) and NaHCO<sub>3</sub> (1.28 g, 22.5 mmol) at 0 °C. Ethyl chloroformate (1.65 mL, 22.5 mmol) was added dropwise via a syringe, and the reaction stirred for 3 h (monitored by TLC, 1:1 EtOAc:Hex). The organic layer was then separated and the aqueous layer washed with dichloromethane (2 × 20 mL). The combined organic extract was washed with brine (2 × 20 mL), dried, concentrated and purified by column chromatography (silica, 1:2 EtOAc:Hex) to yield **1** as a pale yellow viscous oil (2.94 g, 12.7 mmol, 84%). IR 3313, 1688 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) 8.07 (1H, br s, CNHCH), 7.61 (1H, d, J 8.1 Hz, CCHCH), 7.37 (1H, d, J 7.4 Hz, CCHCH), 7.21 (1H, t, J 7.4 Hz, CHCHCH), 7.13 (1H, t, J 6.5 Hz, CHCHCH), 7.04 (1H, s, NHCH), 4.70 (1H, br s, NHC=O), 4.11 (2H, q, J 7.4 Hz, CH<sub>2</sub>CH<sub>3</sub>), 3.51 (2H, t, NHCH<sub>2</sub>CH<sub>2</sub>), 2.97 (2H, t, J 6.5 Hz, NHCH<sub>2</sub>CH<sub>2</sub>), 1.23 (3H, t, J 7.4 Hz, CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) 156.8 (C), 136.4 (C), 127.3 (C), 122.2 (CH), 122.1 (CH), 119.2 (CH), 118.7 (CH), 112.1 (C), 111.2 (CH), 60.8 (CH<sub>2</sub>), 41.2 (CH<sub>2</sub>), 25.8 (CH<sub>2</sub>), 14.7 (CH<sub>3</sub>); ESI+ MS *m/z* 233 ([M+H]<sup>+</sup>, 23%), 255 (14), 487 (50). Spectroscopic data was identical to that reported in the literature.

**Synthesis of hexahydropyrrolo[2,3-*b*]indoline 3.** Carbamate **2** (0.200 g, 0.86 mmol) was added to a mixture of zinc triflate (0.313 g, 0.86 mmol), tetra-butyl ammonium iodide (0.635 g, 1.72 mmol), *N,N*-diisopropylethylamine (0.330 mL, 1.89 mmol) and toluene (5 mL) under a nitrogen atmosphere at room temperature. The mixture was stirred for 15 mins before dropwise addition of prenyl bromide (0.397 mL, 3.44 mmol). The reaction mixture was stirred for 3 h and monitored by TLC (2:1). Upon completion, the reaction was quenched with saturated NH<sub>4</sub>Cl (5 mL), diluted with H<sub>2</sub>O (5 mL) and extracted with ether (2 × 5 mL). The resulting organic layer was washed with water, dried, concentrated and purified by column chromatography (silica, 1:5 EtOAc:Hex), to yield **3** as a pale yellow oil (0.220 g, 0.60 mmol, 70%). IR 1693, 1604, 1486 cm<sup>-1</sup>; <sup>1</sup>H

NMR (400 MHz, CDCl<sub>3</sub>) 7.06 (1H, dt, J 7.8, 1.3 Hz, CHCHCH), 6.97 (1H, d, J 7.0 Hz, NCCHCH), 6.65 (1H, t, J 7.4 Hz, CHCHCH), 6.36 (1H, d, J 7.4 Hz, CCHCH), 5.35 (1H, s, NCHN), 5.16 (1H, t, J 7.0 Hz, CHCH<sub>2</sub>N), 5.06 (1H, t, J 7.0 Hz, CCH<sub>2</sub>CH), 4.15 (2H, q, J 6.8 Hz, CH<sub>3</sub>CH<sub>2</sub>O), 3.96 (2H, d, J 7.0 Hz, NCH<sub>2</sub>CH), 3.70-3.78 (1H, m, NCHHCH<sub>2</sub>), 3.05 (1H, dt, J 8.4, 9.5 Hz, NCHHCH<sub>2</sub>), 2.38 (2H, d, J 7.5 Hz, CCH<sub>2</sub>CH), 2.02 (2H, dd, J 6.0, 8.3 Hz, NCH<sub>2</sub>CH<sub>2</sub>), 1.74 (3H, s, CHCCH<sub>3</sub>), 1.68 (6H, s, CHC(CH<sub>3</sub>)<sub>2</sub>), 1.55 (3H, s, CHCCH<sub>3</sub>), 1.26 (3H, t, J 6.8 Hz, OCH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 150.2 (C), 134.6 (C), 133.2 (C), 128.4(CH), 124.3 (CH), 122.7 (CH), 121.4 (CH), 119.5 (CH), 117.0 (CH), 106.4 (CH), 84.4 (CH), 61.0 (CH), 56.2 (C), 45.4 (CH<sub>2</sub>), 44.2 (CH<sub>2</sub>), 37.0 (CH<sub>2</sub>), 36.9 (CH<sub>2</sub>), 36.8 (CH<sub>2</sub>), 25.9 (CH<sub>3</sub>), 25.7 (CH<sub>3</sub>), 18.0 (CH<sub>3</sub>), 14.7 (CH<sub>3</sub>); ESI+ MS *m/z* 759.3 [2M + Na<sup>+</sup>, 95%].

**Synthesis of debromoflustramine B.** To carbamate **3** (0.368 g, 1.00 mmol) in toluene (5 mL) was added Red-Al (10.0 mmol, 0.195 mL of Aldrich 65+ wt.% solution in toluene). The reaction mixture was refluxed under nitrogen for 24 h until completion, as monitored by TLC (1:2 EtOAc:Hex). The reaction mixture was then treated with EtOAc (200 mL) and washed with water (50 mL), brine (20 mL), dried and concentrated. Purification by column chromatography (silica, EtOAc) afforded debromoflustramine B as a pale yellow oil (0.300 g, 0.97 mmol, 96%). IR 1670, 1601, 1485 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) 7.04 (1H, td, J 8.0, 1.5 Hz, CHCHCH), 6.97 (1H, dd, J 7.3, 1.3 Hz, NCCHCH), 6.64 (1H, td, J 7.5, 1.0 Hz, CHCHCH), 6.41 (1H, br d, J 7.8 Hz, CCHCH), 5.17 (1H, br t, J 4.4 Hz, CHCH<sub>2</sub>N), 4.97 (1H, br t, J 5.6 Hz, CCH<sub>2</sub>CH), 4.26 (1H, s, NCHN); 3.92 (1H, dd, J 16.0, 5.8 Hz, NCHHCH), 3.80 (1H, dd, J 16.0, 7.2 Hz, NCHHCH), 2.67 (1H, ddd, J 9.3, 6.5, 3.3 Hz, NCHHCHH), 2.56 (1H, ddd, J 9.0, 5.8, 9.3 Hz, NCHHCHH), 2.48 (3H, s, NCH<sub>3</sub>), 2.42 (2H, d, J 7.0 Hz, CCH<sub>2</sub>CH), 2.00-2.08 (1H, m, NCHHCHH), 1.88-1.93 (1H, m, NCHHCHH), 1.71 (3H, s, NCH<sub>2</sub>CHC(CH<sub>3</sub>)<sub>2</sub>), 1.70 (3H, s, CHC(CH<sub>3</sub>)<sub>2</sub>), 1.65 (3H, s, CHC(CH<sub>3</sub>)<sub>2</sub>), 1.58 (3H, s, NCH<sub>2</sub>CHC(CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 150.9 (C), 134.7 (C), 133.0 (C), 132.4(C), 126.5 (CH), 121.8 (CH), 120.4 (CH), 119.8 (CH), 116.4 (CH), 106.3 (CH), 90.4 (C), 56.1 (C), 51.8 (CH<sub>2</sub>), 45.8 (CH<sub>2</sub>), 38.0 (CH<sub>2</sub>), 37.5 (CH<sub>2</sub>), 37.0 (CH<sub>3</sub>), 24.9 (CH<sub>3</sub>), 24.7 (CH<sub>3</sub>), 17.1 (CH<sub>3</sub>), 17.0 (CH<sub>3</sub>); ESI+ MS *m/z*

311 ( $[M+H]^+$ , 100%), 325 (30). Spectroscopic data was identical to that reported in the literature.