Total synthesis of flustramine C via dimethylallyl rearrangement

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Supporting Information: experimental procedures and characterization

General. NMR spectra were recorded on a Varian VRX 400S (399.9 MHz resp. 100.6 MHz) spectrometer, with the solvent used as internal standard. Mass spectra were recorded on Finnigan MAT95Q and Varian MAT-311 spectrometers. IR and UV spectra were recorded on Perkin-Elmer PE 1600 FT-IR and Perkin-Elmer UV/Vis-spectrometer Lambda 16, respectively. HPLC isolations were performed using Varian Prep Star 218, equipped with a Varian Pro Star 320 UV/Vis detector. A Merck LiChroprep RP-18 (25–40 µm, 250 × 210) semipreparative HPLC column was used. Elemental analyses were obtained from the Microanalytical Laboratory of the Faculty of Chemistry and Pharmacy (LMU Munich).

Nβ-Formyl-Nβ-methyltryptamine. A mixture of Ac2O and HCO2H (19.0 ml, 1:1) was stirred at 60 °C for 1 h. After cooling to rt a solution of Nβ-methyltryptamine (4, 10.0 g, 57.4 mmol) in DCM (100 ml) was added dropwise. After 90 min the reaction mixture was added to conc. NaOH (150 ml) and ice (150 g). The alkaline mixture was diluted with DCM (300 ml) and the aqueous layer was extracted twice with DCM (100 ml). The combined organic layers were washed with 2 m HCl (100 ml) and 3x with water, dried over Na2SO4, filtered and concentrated in vacuo. The resulting viscous oil was dried further by stirring at 70 °C in high vacuum. Et2O was added and concentrated in vacuo, affording the product (10.4 g, 51.7 mmol, 90%) as a brownish, semicrystalline oil. Rf (silica, EtOAc) = 0.3. Ratio of rotamers in
CDCl₃: 1.6:1. Major rotamer: ¹H NMR (400 MHz, CDCl₃): δ = 8.73 (s, 1 H, 1-H), 7.73 (s, 1 H, CHO), 7.55 (d, ³J = 7.8 Hz, 1 H, 7-H), 7.34 (d, ³J = 8.0 Hz, 1 H, 4-H), 7.19 (dd, ³J = 7.8, 7.0 Hz, 1 H, 6-H), 7.13 (dd, ³J = 8.0, 7.0 Hz, 1 H, 5-H), 6.90 (s, 1 H, 2-H), 3.51 (m, 2 H, 2'-H), 2.98 (m, 2 H, 1'-H), 2.93 (s, 3 H, NCH₃). ¹³C NMR (100 MHz, CDCl₃): δ = 163.4 (CHO), 136.9 (C-7a), 127.7 (C-3a), 122.9 (C-2), 122.5 (C-6), 119.8 (C-5), 118.9 (C-7), 113.3 (C-3), 111.8 (C-4), 50.5 (C-2'), 30.1 (CH₃), 24.7 (C-1'). Minor rotamer: ¹H NMR (400 MHz, CDCl₃): δ = 8.65 (s, 1 H, 1-H), 8.04 (s, 1 H, CHO), 7.64 (d, ³J = 7.8 Hz, 1 H, 7-H), 7.34 (d, ³J = 8.0 Hz, 1 H, 4-H), 7.16 (dd, ³J = 7.7, 7.0 Hz, 1 H, 6-H), 7.10 (dd, ³J = 7.7, 7.0 Hz, 1 H, 5-H), 6.98 (s, 1 H, 2-H), 3.66 (m, 2 H, 2'-H), 3.00 (m, 2 H, 1'-H), 2.87 (s, 3 H, NCH₃). ¹³C NMR (100 MHz, CDCl₃): δ = 163.2 (CHO), 136.8 (C-7a), 127.2 (C-3a), 122.6 (C-2), 122.3 (C-6), 119.7 (C-5), 118.5 (C-7), 112.7 (C-3), 111.6 (C-4), 45.4 (C-2'), 35.4 (NCH₃), 23.2 (C-1'). MS (EI, 70 eV): m/z (%) = 202 (8) [M⁺], 143 (78), 130 (100), 103 (5), 77 (5). HRMS (EI): calcd. 202.1106 (C₁₂H₁₄N₂O), found 202.1097. IR (KBr): ν ≈ 3275 cm⁻¹, 3010, 2964, 2934, 2884, 1658, 1617, 1492, 1451, 1434, 1397, 1368, 1350, 1335, 1249, 1230, 1179, 1099, 1076, 1061, 1008, 932, 876, 810, 766, 756, 628, 427. UV/Vis (CH₃CN): λ_max (ε) = 289 nm (5257 mol⁻¹ dm³ cm⁻¹), 280 (6165), 222 (36416). Calcd. for C₁₇H₂₂N₂O: C 71.26, H 6.98, N 13.85; found C 71.15, H 6.95, N 13.70.

*N-*{2'-[2-(1''-1H-indol-3-yl)-ethyl]-N-methylformamide (5). To a solution of *N*-Formyl-*N*-methyltryptamine (2.02 g, 10.0 mmol) in THF (36 ml) and Et₃N (1.66 ml, 12.0 mmol) was added t-BuOCl (1.36 ml, 12.0 mmol) at -78 °C. The colorless solution was stirred for 30 min at -78 °C, before a freshly prepared solution of prenyl-9-BBN (0.5 m, 40.0 ml, 20.0 mmol) in THF was added dropwise. It proved to be beneficial, if 1,1-dimethylallene and 9-BBN-H were allowed to react for 18 h at room temperature before use. After 30 min the yellow solution was allowed to warm to rt and was stirred for 1 h. Aqueous NaOH (3 m, 10 ml) and H₂O₂ (30%, 10 ml) were added dropwise. The mixture was stirred at
rt for 1 h and diluted in Et₂O (400 ml). The organic layer was washed three times with semisaturated solution of NaCl, dried over Na₂SO₄, filtered, and concentrated in vacuo. The residual oil was washed twice with Et₂O (10 ml) affording 5 (2.16 g, 8.0 mmol, 80%) as colorless solid. Further purification was possible by recrystallisation in n-heptane/toluene (5:1). M.p.: 146-147 °C. Rᶠ (silica, iso-hexane/EtOAc (1:1)) = 0.4. Ratio of rotamers in CDCl₃: 1.6:1. Major rotamer: ¹H NMR (400 MHz, CDCl₃): δ = 8.29 (s, 1 H, 1-H), 8.05 (s, 1 H, CHO), 7.65 (d, ²J = 7.2 Hz, 1 H, 7-H), 7.46 (d, ³J = 7.3 Hz, 1 H, 4-H), 7.35-7.08 (m, 2 H, 6-H, 5-H), 6.13 (dd, ³J = 17.4, 10.5 Hz, 1 H, 2''-H), 5.23-5.14 (m, 2 H, 3''-H), 3.49-3.42 (m, 2 H, 2'-H), 3.10-3.04 (m, 2 H, 1'-H), 2.99 (s, 3 H, NCH₃), 1.54 (s, 6 H, 4''-H, 5''-H). ¹³C NMR (100 MHz, CDCl₃): δ = 162.6 (CHO), 145.8 (C-2''), 140.2 (C-2), 134.3 (C-3a), 129.1 (C-7a), 121.6 (C-6), 119.4 (C-7), 117.5 (C-4), 111.9 (C-3''), 110.5 (C-5), 106.7 (C-3), 50.2 (C-2'), 38.8 (C-1''), 35.0 (NCH₃), 27.7 (C-4'', C-5'') 25.0 (C-1'). Minor rotamer: ¹H NMR (400 MHz, CDCl₃): δ = 8.16 (s, 1 H, CHO), 8.09 (s, 1 H, 1-H), 7.64 (d, ³J = 6.8 Hz, 1 H, 7-H), 7.46 (d, ³J = 6.9 Hz, 1 H, 4-H), 7.35-7.08 (m, 2 H, 6-H, 5-H), 6.14 (dd, ³J = 17.4, 10.5 Hz, 1 H, 2''-H), 5.23-5.14 (m, 2 H, 3''-H), 3.58-3.52 (m, 2 H, 2'-H), 3.10-3.04 (m, 2 H, 1'-H), 2.96 (s, 3 H, NCH₃), 1.57 (s, 6 H, 4''-H, 5''-H). ¹³C NMR (100 MHz, CDCl₃): δ = 162.4 (CHO), 145.9 (C-2''), 139.9 (C-2), 134.2 (C-3a), 129.5 (C-7a), 119.9 (C-6), 119.4 (C-7), 117.5 (C-4), 112.0 (C-3''), 110.8 (C-5), 107.6 (C-3), 45.5 (C-2''), 38.9 (C-1''), 30.0 (NCH₃), 27.6 (C-4'', C-5''), 22.7 (C-1'). MS (EI, 70 eV): m/z (%) = 270 (100) [M⁺], 211 (79), 199 (43), 196 (53), 183 (95), 168 (78), 154 (10), 130 (7), 72 (4), 44 (8). HRMS (EI): calcd. 270.1732 (C₁₇H₂₂N₂O₂, [M⁺]), found 270.1757. IR (KBr): ν = 3303 cm⁻¹, 3053, 2968, 2930, 2872, 1654, 1578, 1490, 1460, 1434, 1392, 1360, 1340, 1297, 1242, 1168, 1147, 1068, 1045, 1005, 914, 742, 724, 688, 583, 533, 423. UV/Vis (CH₃CN): λmax (ε) = 283 nm (3670 mol⁻¹dm³cm⁻¹), 226 (18949). Calcd. for C₁₇H₂₂N₂O₂: C 75.52, H 10.36, N 8.20; found C 75.12, H 10.20, N 8.20.
Flustrabromine (6). To a stirred solution of 5 (2.16 g, 8.0 mmol) in HOAc-HCO₂H (64 ml, 3:1) was added a solution of NBS (1.46 g, 8.2 mmol) in HOAc-HCO₂H (40 ml, 3:1). The solution was stirred at rt for 30 min, before the solution was added to a mixture of Et₂O (250 ml) and ice (250 g). It was diluted with Et₂O (300 ml). The organic layer was washed twice with H₂O (200 ml) and with aqueous NaOH (1 M, 150 ml). It was washed twice with H₂O (200 ml), dried over Na₂SO₄, filtered and concentrated in vacuo. The crude solid was washed 3× with MeOH (10 ml). Remaining solvent was removed under reduced pressure, affording 6 (1.71 g, 4.9 mmol, 61%) and 4-brominated side product as a colorless solids which were separated by chromatography. \( R_f = (\text{silica, iso-hexane/} \text{EtOAc (1:1)}): 0.43. \) Ratio of rotamers in CDCl₃: 1:0.8. Mp.: 218-220 °C. Major rotamer: \(^1\)H NMR (400 MHz, CDCl₃): \( \delta = 7.99 \) (s, 1 H, CHO), 7.91 (s, 1 H, 1-H), 7.49 (d, \( ^3J = 8.4 \) Hz, 1 H, 4-H), 7.46 (d, \( ^4J = 1.7 \) Hz, 1 H, 7-H), 7.20 (dd, \( ^3J = 8.4 \) Hz, \( ^4J = 1.7 \) Hz, 1 H, 5-H), 6.13-6.08 (dd, \( ^3J = 17.5, 10.4 \) Hz, 1 H, 2''-H), 5.21-5.15 (dd, \( ^3J = 17.5 \) Hz, \( ^2J = 1.2 \) Hz, 1 H, 3''-Hₓ), 3.53-3.38 (m, 2H, 2'-H), 3.06-2.99 (m, 2H, 1'-H), 2.96 (s, 3H, NC₃H₃), 1.52 (s, 6H, 4''-H, 5''-H). \(^{13}\)C NMR (100 MHz, DMSO-d₆): \( \delta = 162.5 \) (CHO), 145.5 (C-2''), 140.9 (C-2), 135.0 (C-7a), 128.1 (C-3a), 122.9 (C-5), 119.9 (C-4), 115.0 (C-6), 113.7 (C-7), 112.4 (C-3''), 107.1 (C-3), 50.2 (C-2'), 38.9 (C-1'''), 30.1 (NCH₃), 27.6 (C-5'', C-4''), 24.9 (C-1''). Minor rotamer: \(^1\)H NMR (400 MHz, CDCl₃): \( \delta = 8.07 \) (s, 1 H, CHO), 8.00 (s, 1 H, 1-H), 7.43 (d, \( ^4J = 1.7 \) Hz, 1 H, 7-H), 7.29 (d, \( ^3J = 8.4 \) Hz, 1 H, 4-H), 7.19 (d, \( ^3J = 8.4 \) Hz, \( ^4J = 1.7 \) Hz, 1 H, 5-H), 6.13-6.08 (dd, \( ^3J = 17.6, 10.4 \) Hz, 1 H, 2''-H), 5.21-5.15 (dd, \( ^3J = 17.6 \) Hz, \( ^2J = 1.2 \) Hz, 1 H, 3''-Hₓ), 3.53-3.38 (m, 2H, 2'-H), 3.06-2.99 (m, 2H, 1'-H), 2.95 (s, 3H, NCH₃), 1.55 (s, 6H, 4''-H, 5''-H). \(^{13}\)C NMR (100 MHz, CDCl₃): \( \delta = 162.5 \) (CHO), 145.5 (C-2''), 140.5 (C-2), 134.9 (C-7a), 128.5 (C-3a), 122.7 (C-5), 119.5 (C-4), 114.9 (C-6), 113.4 (C-7), 112.3 (C-3''), 108.0 (C-3), 45.5 (C-2''), 39.0 (C-1''), 35.1 (NCH₃), 27.6 (C-5'', C-4''), 22.6 (C-1''). MS (FAB+, NBA): \( m/z (\%) = 371/373 \) (6/6) [M⁺ + Na], 349/351 (36/33) [M⁺ + 1], 276/278 (29/26) [C₁₄H₁₄BrN⁺ + 1]. HRMS (EI): calcd.
348.0837 (C₁₇H₂₁⁷⁹BrN₂O, [M⁺]), found 348.0838. IR (KBr): ν = 3435 cm⁻¹, 2970, 2930, 2872, 1657, 1571, 1463, 1394, 1335, 1285, 1225, 1193, 1165, 1070, 909, 861, 803, 725, 696, 591. UV/Vis (CH₃CN): λ_max (ε) = 289 nm (5756 mol⁻¹dm³cm⁻¹), 232 (30906).

**Deformylflustrabromine (1).** To a solution of flustrabromine (6, 1.59 g, 5.0 mmol) in EtOH (400 ml) was added NaOH (32%, 15.3 ml). The reaction mixture was refluxed for 24 h, cooled to rt, and concentrated in vacuo to a volume of 50 ml. It was diluted with Et₂O (500 ml), washed four times with H₂O (100 ml), dried over Na₂SO₄, and filtered. The solvent was removed under reduced pressure affording 1 as a yellowish semi-crystalline oil (1.53 g, 4.8 mmol, 96%) which could be recrystallized from iso-hexane. Rf (silica, CHCl₃/MeOH (4:1)) = 0.4. ¹H NMR (400 MHz, CD₃OD): δ = 7.47 (d, 4J = 1.6 Hz, 1 H, 7-H), 7.31 (d, 3J = 8.4 Hz, 1 H, 4-H), 7.03 (dd, 3J = 8.4 Hz, 4J = 1.6 Hz, 1 H, 5-H), 6.06 (dd, 3J = 17.3, 10.6 Hz, 1 H, 2''-H), 5.04 (dd, 3J = 17.3 Hz, 2J = 1.1 Hz, 1 H, 3''-H₂), 5.02 (dd, 3J = 10.6 Hz, 2J = 1.1 Hz, 1 H, 3''-H₂), 4.88 (s, 1 H, NH), 2.90 (m, 2H, 1'-H), 2.65 (m, 2H, 2'-H), 2.31 (s, 3H, NCH₃), 1.46 (s, 6H, 4''-H, 5''-H). ¹³C NMR (400 MHz, CD₃OD): δ = 146.8 (C-2''), 141.2 (C-2), 136.2 (C-7a), 128.7 (C-3a), 121.6 (C-5), 118.6 (C-4), 114.0 (C-6), 113.6 (C-7), 110.9 (C-3''), 108.2 (C-3), 52.5 (C-2''), 48.3 (CH₃), 39.1 (C-1''), 27.4 (C-4'', C-5''), 24.8 (C-1''). ¹H, ¹⁵N-HMBC (600 MHz, CDCl₃): δ = 127 (indole-NH), 30 (side chain NH). MS (EI, 70 eV): m/z (%) = 320/322 (1/1) [M⁺], 277/279 (26/26), 261/263 (13/8) [C₁₃H₁₄BrN⁺], 194/196 (1/2) [C₈H₆BrN⁺], 167 (16). HRMS (EI): calcd. 320.0888 (C₁₄H₂₁⁷⁹BrN₂, [M⁺]); found 320.0881. IR (KBr): ν = 3447 cm⁻¹, 3247, 3082, 2969, 2929, 2873, 2800, 2447, 1634, 1612, 1566, 1463, 1413, 1382, 1363, 1336, 1306, 1286, 1217, 1182, 1142, 1100, 1051, 1008, 910, 852, 801, 756, 666, 592. UV/Vis (CH₃CN): λ_max (ε) = 297 nm (3989 mol⁻¹dm³cm⁻¹), 289 (4240), 232 (21827).

**Flustramine C (2).** To a solution of 1 (100 mg, 0.31 mmol) in THF (5 ml) was added NBS (55 mg, 0.31 mmol). The reaction mixture was stirred at rt for 2 h and diluted in diethyl ether (50 ml). The organic layer was washed with 2 N NaOH (10 ml) and twice with water (10 ml),
dried over Na₂SO₄, filtered and concentrated in vacuo. The residual oil was purified by column chromatography (silica, EtOAc) affording 2 (90 mg, 0.28 mmol, 90%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃): δ = 7.19 (dd, 3 ³J = 1.1 Hz, 4 ³J = 1.1 Hz, 1 H, 7-H), 6.89 (d, 3 ²J = 1.2 Hz, 1 H, 13-H₂), 5.99 (dd, 3 ³J = 17.3, 10.8 Hz, 1 H, 12-H), 5.05 (dd, 3 ³J = 10.8 Hz, 2 ²J = 1.2 Hz, 1 H, 13-H₂), 5.03 (dd, 3 ³J = 17.3 Hz, 2 ²J = 1.2 Hz, 1 H, 13-H₂), 3.93 (ddd, 2 ²J = 10.1 Hz, 3 ³J = 8.8, 6.5 Hz, 1 H, 2-Hₐ), 3.38 (ddd, 2 ²J = 10.1 Hz, 3 ³J = 10.1, 0.9 Hz, 1 H, 2-Hₖ), 3.00 (s, 3H, NCH₃), 2.32 (ddd, 2 ²J = 13.0 Hz, 3 ³J = 6.5, 0.9 Hz, 1 H, 3-Hₐ), 2.05 (ddd, 2 ²J = 13.0, 10.1 Hz, 3 ³J = 8.8 Hz, 1 H, 3-Hₖ), 0.98 (s, 3H, 10-H), 0.87 (s, 3H, 11-H). ¹³C NMR (75 MHz, CDCl₃): δ = 188.1 (C-8a), 163.5 (C-7a), 143.4 (C-12), 137.6 (C-3b), 124.2 (C-4), 122.0 (C-6), 121.9 (C-5), 119.1 (C-7), 113.5 (C-13), 65.8 (C-3a), 59.7 (C-2), 42.9 (C-9), 33.1 (NCH₃), 27.9 (C-3), 22.8 (C-10), 21.6 (C-11). ¹H,¹⁵N-HMBC (400 MHz, CDCl₃): δ = 217 (imine-N), 90 (NMe). MS (EI, 70 eV): m/z (%) = 320/318 (24/29) [M⁺], 251/249 (100/97) [C₁₁H₁₀N₂Br⁺], 170 (49) [C₁₁H₁₀N₂⁺], 129 (21). FTHRMS (ESI⁺): calcd. 319.0810 (C₁₆H₂₀N₂⁺Br, [M⁺+H]); found 319.0798. IR: ν = 2917 cm⁻¹, 1632 (s), 1582 (s), 1560 (s), 1452 (m), 1412 (m), 1394 (m), 1364 (w), 1300 (m), 1212 (w), 1153 (w), 1115 (w), 1056 (w), 1003 (w), 916 (w), 898 (w), 864 (m), 802 (w), 730 (w). UV/Vis (CH₃OH): λ max (λ) = 290 nm (7208 mol⁻¹dm³cm⁻¹), 232 (23412).

**Reaction of deformylflustrabromine with 1 equiv. of tBuOCl.** To a solution of 1 (100 mg, 0.31 mmol) in dry THF (2.5 ml) and triethylamine (52 µl, 0.37 mmol) was added t-BuOCl (35 µl, 0.31 mmol) at -78 °C. The reaction mixture was stirred at -78 °C for 30 min and was allowed to warm slowly to rt. It was diluted in Et₂O (50 ml). The organic layer was washed three times with water (10 ml), dried over Na₂SO₄, filtered and concentrated in vacuo, affording a 4:1 mixture of monochlorinated intermediate 7 and dichlorinated intermediate 11 as colorless oil. Data of N-chlorodeformylflustrabromine (7): ¹H NMR (600 MHz, CDCl₃): δ = 7.92 (br. s, 1 H, NH), 7.43 (d, ⁵J = 1.8 Hz, 1 H, 7-H), 7.40 (dd, ³J = 8.4 Hz, ⁵J = 1.8 Hz, 1
H, 4-H), 7.18 (d, $^3J = 8.4$ Hz, 1 H, 5-H), 6.09 (dd, $^3J = 18.0$, 10.4 Hz, 1 H, 2″-H), 5.17 (dd, $^3J = 10.4$ Hz, $^2J = 1.2$ Hz, 1 H, 3″-H$_2$), 5.16 (dd, $^3J = 18.0$ Hz, $^2J = 1.2$ Hz, 1 H, 3″-H$_2$), 3.17 (m, 2H, 1′-H$_2$), 3.08 (m, 2H, 2″-H$_2$), 2.99 (s, 3H, NCH$_3$), 1.54 (s, 6H, 2 CCH$_3$). 13C NMR (75 MHz, CDCl$_3$): $\delta = 145.4$ (C2″), 140.5 (C2), 134.9 (C7a), 128.5 (C3a), 122.5 (C5), 119.3 (C4), 114.8 (C6), 113.4 (C7), 112.4 (C3″), 107.8 (C3), 66.4 (C2′), 53.1 (NCH$_3$), 38.9 (C1″), 27.6 (2 CH$_3$), 23.8 (C1′). 1H,15N-HMBC (600 MHz, CDCl$_3$): $\delta = 127$ (indole-NH), 105 (side chain N-Cl). FTHRMS (ESI–): calcd. 389.0187 (C$_{16}$H$_{20}$79Br$_3$Cl$_2$N$_2$, [M+Cl]$^-$); found 389.0206. The mixture was stored in CDCl$_3$ (2.5 ml) at rt for 12 h. The solution was concentrated in vacuo and diluted with Et$_2$O (50 ml). The organic layer was washed with aqueous NaOH (2 M, 5 ml), three times with water (10 ml), dried over Na$_2$SO$_4$, filtered and concentrated in vacuo, affording flustramine C (2, 53 mg, 0.17 mmol, 60%) as a colorless oil. For data of 2 and 11, see there.

**Reaction of deformylflustrabromine with 2 equiv. of tBuOCl.** To a solution of 1 (550 mg, 1.71 mmol) in dry THF (14 ml) and triethylamine (0.52 ml, 3.77 mmol) was added t-BuOCl (0.38 ml, 3.42 mmol) at -78 °C. The reaction mixture was stirred at -78 °C for 30 min and was allowed to warm to rt. It was diluted in Et$_2$O (150 ml). The organic layer was washed three times with water (30 ml), dried over Na$_2$SO$_4$, filtered and concentrated in vacuo, affording chloroindolenine 11 as colorless oil (630 mg, 94 %) which was purified by chromatography (silica gel, petrol ether/EtOAc (15:1)). Data of chloroindolenine 11: 1H NMR (600 MHz, CDCl$_3$): $\delta = 7.66$ (d, $^4J = 1.7$ Hz, 1 H, 7-H), 7.38 (dd, $^3J = 7.9$ Hz, $^4J = 1.7$ Hz, 1 H, 5-H), 7.21 (d, $^3J = 7.9$ Hz, 1 H, 4-H), 6.37 (dd, $^3J = 17.4$, 10.6 Hz, 1 H, 2″-H), 5.26 (dd, $^3J = 17.4$ Hz, $^2J = 0.7$ Hz, 1 H, 3″-H$_2$), 5.19 (dd, $^3J = 10.6$ Hz, $^2J = 0.7$ Hz, 1 H, 3″-H$_2$), 2.83 (ddd, $^2J = 13.4$ Hz, $^3J = 10.4$, 5.1 Hz, 1 H, 1′-H$_a$), 2.74 (s, 3H, NCH$_3$), 2.67 (ddd, $^2J = 13.4$ Hz, $^3J = 10.4$, 4.5 Hz, 1 H, 1′-H$_b$), 2.30 (ddd, $^2J = 12.9$ Hz, $^3J = 10.4$, 5.1 Hz, 1 H, 2″-H$_a$), 2.24 (ddd, $^2J = 12.9$ Hz, $^3J = 10.4$, 4.5 Hz, 1 H, 2″-H$_b$), 1.62 (s, 3H, CH$_3$), 1.59 (s, 3H, CH$_3$). 13C NMR (100 MHz,
CDCl₃): δ = 188.2 (C2), 152.8 (C7a), 143.5 (C2"'), 138.5 (C3a), 129.7 (C5), 124.3 (C7), 123.5 (C6), 123.2 (C4), 113.6 (C3"'), 71.9 (C3), 60.5 (C2"'), 53.1 (NCH₃), 43.7 (C1"'), 37.7 (C1'), 28.1 (CCH₃), 27.2 (CCH₃). ¹H,¹⁵N-HMBC (600 MHz, CDCl₃): δ = 322 (indolenine-N), 101 (side chain N-Cl). FTHRMS (ESI+): calcd. 389.0187 (C₁₆H₂₀⁷⁹Br₃⁵Cl₂N₂, [M+H⁺]), found 389.0199. Chloroindolenine 11 (340 mg, 0.87 mmol) was heated in CHCl₃ (10 ml) at 55 °C for 17 h. The solution was concentrated in vacuo and diluted with Et₂O (50 ml). The organic layer was washed with aqueous NaOH (2 M, 25 ml), three times with water (10 ml), dried over Na₂SO₄, filtered and concentrated in vacuo. Column chromatography (silica gel, EtOAc) afforded flustramine C (2, 69 mg, 25%) and 5-chloroflustramine C (13, 92 mg, 30%) as colorless oils. Data of 5-chloroflustramine C (13): ¹H NMR (400 MHz, CDCl₃): δ = 7.27 (s, 1 H, 7-H), 7.10 (s, 1 H, 4-H), 5.96 (dd, ³J = 17.4, 10.8 Hz, 1 H, 12-H), 5.08 (dd, ³J = 10.8 Hz, ²J = 1.1 Hz, 1 H, 13-H₂), 5.04 (dd, ³J = 17.4 Hz, ²J = 1.1 Hz, 1 H, 13-H₂), 3.94 (ddd, ²J = 10.1 Hz, ²J = 8.8 Hz, 6.5 Hz, 1 H, 2-Hₐ), 3.39 (ddd, ²J = 10.1 Hz, ²J = 10.1 Hz, 0.9 Hz, 1 H, 2-Hₐ), 3.00 (s, 3H, NCH₃), 2.34 (ddd, ²J = 13.1 Hz, ²J = 13.1 Hz, 3J = 10.1 Hz, 1 H, 3-Hₐ), 0.98 (s, 3H, 10-H), 0.89 (s, 3H, 11-H). ¹³C NMR (100 MHz, CDCl₃): δ = 187.9 (C8a), 161.8 (C7a), 142.9 (C12), 139.3 (C3b), 124.7 (C4), 124.1 (C5), 121.6 (C6), 120.2 (C7), 114.0 (C13), 66.2 (C3a), 59.7 (C2), 43.0 (C9), 33.1 (NCH₃), 27.8 (C3), 22.8 (C11), 21.6 (C10). MS (EI, 70 eV): m/z (%) = 356/354/352 (7/28/22) [M⁺], 287/285/283 (27/50/100) [C₁₁H₁₀N₂Br⁺Cl⁻], 204/206 (6/18) [C₁₁H₉N₂Cl⁺], 169 (14) [C₁₁H₉N₂⁺]. HRMS (EI): calced. 352.0342 (C₁₆H₁₉N₂⁷⁹Br₃⁵Cl), found 352.0320. Following pages: NMR and MS spectra of compounds 1, 2, 5, 6, 7, 11, 13.
$^1$H NMR (CDCl$_3$, 400 MHz)

1: deformylflustrabromine
1: deformylflustrabromine

$^{13}$C NMR (CDCl$_3$, 100 MHz)
1H, 15N HMBC (CDCl₃, 600 MHz)

1: deformylflustrabromine

7.418/126.9

2.994/30.1 2.465/30.1

8.02, 7.78/126.9 (HSQC)  1.532/126.9
1: deformylfluustrabromine

\[ \text{Formula: } C_9H_{14}BrN_2 \]

**HREIMS**

- Mass: 217.0700
- Intensity: 364662.0
- Delta: 20.21
- P/M: 9.6

**Method:**
- Technique: GC-MS
- Operated: Turbo

**NMR Data**

- δ (ppm): 1.88 (s, 3H), 3.20 (s, 3H), 4.47 (s, 3H)
- J (Hz): 10.0, 13.0

**Time (min)**

- 5: 22.71
- 20: 22.66

**Relative Abundance**

- 0: 22.71
- 100: 22.66

**Relative Abundance (%)**

- 0: 22.71
- 100: 22.66
$^1$H NMR (CDCl$_3$, 300 MHz)

2: flustramine C
$^{13}$C NMR (CDCl$_3$, 75 MHz)

2: flustramine C
2: flustramine C

$^1H,^{15}N$ HMBC (CDCl$_3$, 400 MHz)

- 3.389/90.4
- 2.346/90.4
- 7.200/217.4
HRESIMS

2: flustramine C
1H NMR (CDCl3, 600 MHz)

Minor:

4:1
$^{13}$C NMR (CDCl$_3$, 75 MHz)
\[^1H,^{15}N\text{-HMBC (CDCl}_3, 600 \text{ MHz)}\]
HRESIMS

\[
\begin{align*}
N & \quad Cl \\
N & \quad Br
\end{align*}
\]

7
$\text{1H NMR (CDCl}_3, 600 \text{ MHz)}$
$^{1}H,^{15}N$-HMBC (CDCl$_3$, 600 MHz)

2.83, 2.74, 2.67, 2.40, 2.25/100.9

7.655/322.4
$^{1}$H NMR (CDCl$_3$, 400 MHz)

13
$^1$H NMR, CDCl$_3$, 400 MHz

5 (two rotamers)
$^{13}$C NMR, CDCl$_3$, 100 MHz

5 (two rotamers)
$^1$H NMR, CDCl$_3$, 400 MHz

6 (two rotamers)
$^{13}$C NMR, CDCl$_3$, 100 MHz

6 (two rotamers)
Br
\[
\begin{align*}
&NH_2

&H

&NO

&Br

\end{align*}
\]

6 (two rotamers)

HREIMS