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First total syntheses of dihydroflustramine C and flustramine E, alkaloids from the marine bryozoan *Flustra foliacea*

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Abstract—We have developed a simple and practical method for providing the common tricyclic skeleton of physostigmine type alkaloids, and demonstrated its utility for indole alkaloid synthesis. Thus, we achieved the first total syntheses of (±)-dihydroflustramine C and (±)-flustramine E, as well as the total syntheses of their debromoanalogues from the corresponding 2-hydroxyindolenines in five steps with 31, 27, 39 and 23% overall yields, respectively. The structures of some intermediates were confirmed by single crystal X-ray diffraction analyses.

1. Introduction

In recent years, a number of brominated indole alkaloids were isolated from bryozoans of the family Flustridae (*Flustra foliacea*). Among these, the marine alkaloids dihydroflustramine C (**1**) and flustramine E (**2**) were isolated from *F. foliacea* collected in the Minas Basin, Nova Scotia[1] and in the North Sea,[2] respectively. These alkaloids have proven to show antibacterial activity against *Bacillus subtilis*, *Botrytis cinerea*, *Rhizotonia solani*, *Enterobacter cloacea*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Salmonella tryphimurium*, *Serratia marcescens*, *Staphylococcus aureus*, and *Staphylococcus epidermidis*.[1,2] While possessing the physostigmine skeleton,[3] dihydroflustramine C (**1**) contains an inverted prenyl unity at the 3a position instead of the prenyl group of flustramine E (**2**). Although to date no published syntheses for these alkaloids exist, for their debromoanalogues few are reported. Thus, the synthesis of debromodihydroflustramine C (**3**) has been performed via a thio-Claisen type rearrangement strategy from a sulphonium cation of 2-methylthioindole derivative.[4] An alternative approach to **3** has been reported by reduction of the marine alkaloid flustramine C.[5] For debromoflustramine E (**4**), two syntheses have been recently described involving either a Claisen type rearrangement as the key step of 2-allyloxy-3-(2-nitrovinyl)indole,[6] or via a C-3 alkylation–cyclization of the methylamide of indole-3-acetic acid as the key reaction.[7]

We report herein the first total syntheses of dihydroflustramine C (**1**) and flustramine E (**2**), and the total syntheses of their debrominated analogues **3** and **4** (Fig. 1) by applying a highly efficient version of the synthetic methodology that we firstly employed for the total syntheses of flustramines A (**5**) and B (**6**), flustramides A (**7**) and B (**8**) and debromoflustramine B (**9**),[8] as well as for the formal total syntheses of physostigmine (**10**) and physovenine (**11**)[9] (Fig. 2). It is remarkable to point out that this synthetic strategy requires only minor variation to be adapted for the synthesis of this class of compounds, which differ mainly for variation in appendages. To achieve this aim, the corresponding 2-hydroxyindolenines **12a** or **12b** were converted to the key tricyclic precursor(s) **13a** and **14a** or **13b** and **14b** in a combined yield of 76% (53:47 ratio) or 77% (61:39 ratio), respectively, via a one step Grignard alkylation and lactonization.[8] The 2-oxofuroindolines thus obtained can be easily decyanated[10] by reacting with wet alumina to

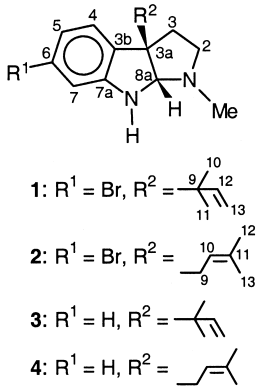

Figure 1.

Keywords: dihydroflustramine C; flustramine E; indole alkaloids; total synthesis.

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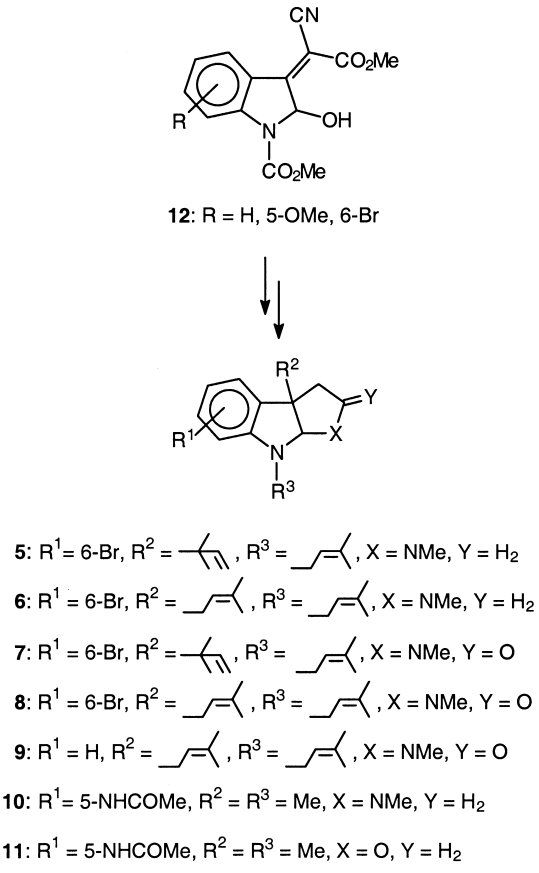


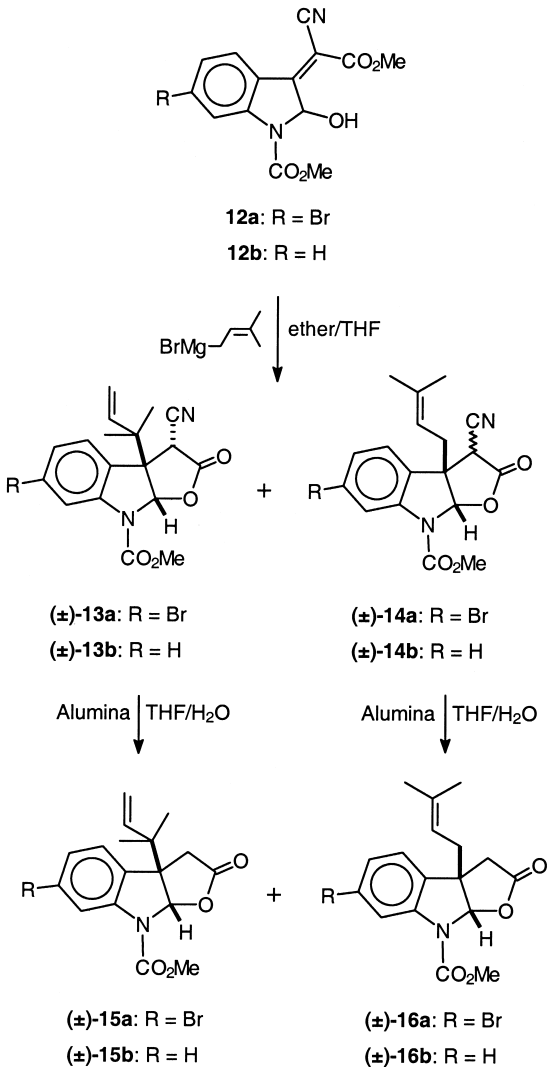
Figure 2. Versatile intermediate **12**, for the synthesis of physostigmine type alkaloids.

give the intermediates **15a**, **16a**, **15b**, and **16b** in 89, 83, 95 and 86% yield, respectively (Scheme 1).

2. Results and discussion

The structure and relative stereochemistry of the tricyclic precursors **13a**, **13b** and **14b** were unambiguously determined by X-ray crystallography, namely **13a** and **13b** were 3*S**, 3a*S**, 8a*R** and **14b** was 3*S**, 3a*R**, 8a*R** (Fig. 3). These structures are characterized by a folded shape along the C-3a–C-8a bond, with the CN group at C-3 and the corresponding alkyl group at C-3a arranged in an *anti* relationship with each other. In DMSO-d_6 solution,[11] the ^{1}H NMR spectra of **13a** and **13b** indicate that these compounds exist as single isomers with the CN group and the 1,1-dimethylallyl group at C-3a in an *anti* orientation, whereas for **14b**, the populations of the *anti–syn* isomers were found by ^{1}H NMR to be in an equilibrated 12:1 ratio. NOE experiments on **14b** support the stereochemical preference, since irradiation of the signal centered at δ 2.64 ppm (methylene protons of the prenyl group) enhances the signals at δ 7.58 (H-4), δ 6.42 (H-8a) and δ 5.18 ppm (exchangeable H-3) by 5, 16, and 17%, respectively.

After decyanation, the starting *N*-protected 2-oxofuroindolines **15a**, **15b**, **16a** and **16b** were converted into deprotected analogues **17a**, **17b**, **18a** and **18b**, respectively, by cleavage of the indoline ester group with MeONa/MeOH at reflux. The resulting unstable lactones were isolated pure-enough



Scheme 1. Key synthetic strategy of precursors **15a**, **15b**, **16a** and **16b**. Compounds **14a** and **14b** are *anti–syn* mixtures.

to be used in the next step, without recourse to chromatographic procedures. The latter was inferred from the ^{1}H NMR spectra of the respective crude reaction mixtures. The kind of solvent used for NMR measurements has an important effect on the speed of decomposition. DMSO-d_6 and $CDCl_3$ lead to fast decomposition, whereas in CD_3OD this effect is slower. Thus, the ^{1}H NMR spectrum of **18a** measured in CD_3OD allows to observe two singlets at δ 1.09 and 0.97 ppm of the allylic methyl groups, the AB pattern of the carboxymethylenic protons appears at δ 3.16 and 2.76 ppm (geminal coupling constant of 17.9 Hz). In addition, the H-8a signal and the aromatic protons H-7 and H-5 *ortho* and *para* to the NH, respectively, are shifted highfield to δ 5.98, 6.67 and 6.78 ppm with respect to the same protons of **16a** ($\delta_{\text{DMSO-}d6}$ 6.29, 7.67 and 7.13 ppm, respectively).[8b]

Since lactones **17a**, **17b**, **18a** and **18b** proved to decompose slowly on standing at room temperature they were immediately transformed to the corresponding lactams **19a**, **19b**, **20a** and **20b**, respectively, by reaction with methylamine in MeOH at room temperature, in nearly quantitative yields for the two steps (Scheme 2). A readily

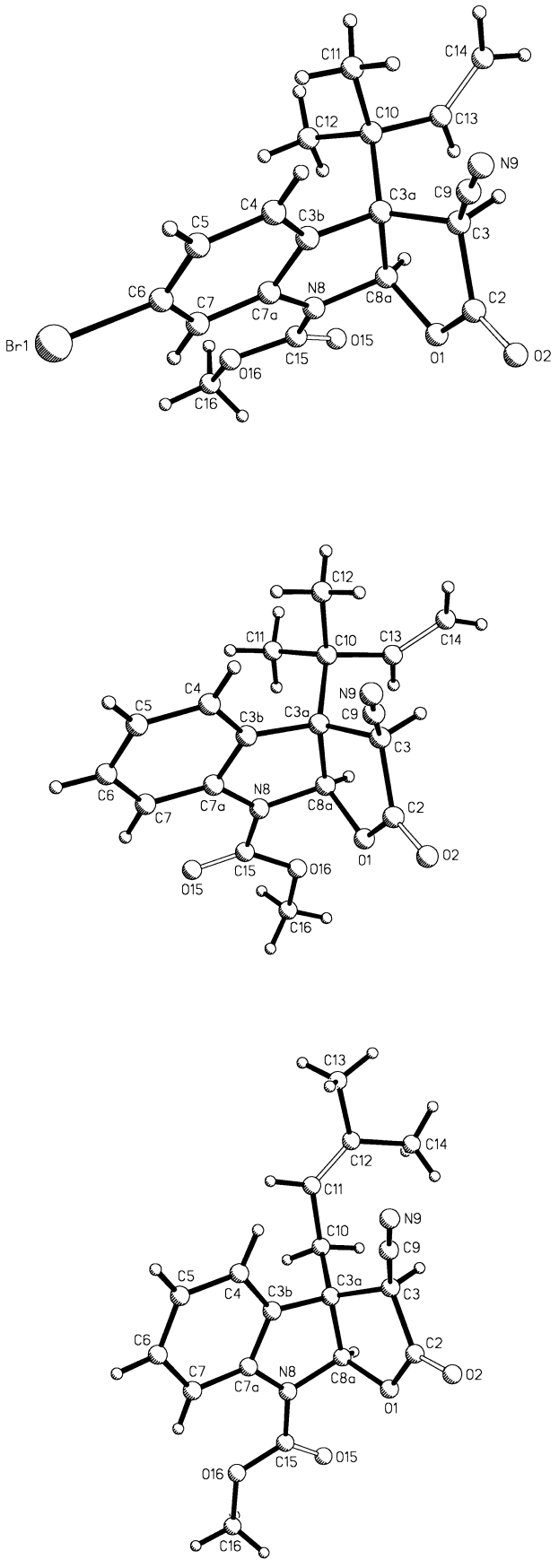
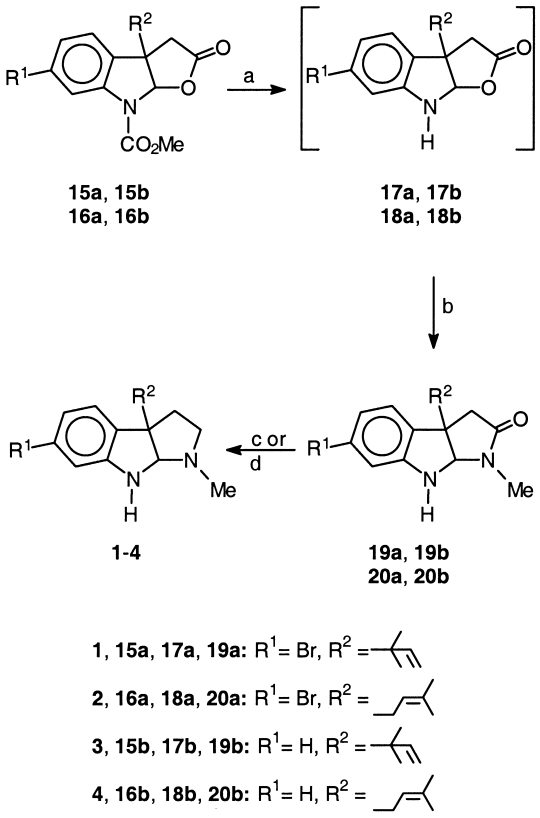


Figure 3. X-Ray structures of **13a** (top), **13b** (center), and **14b** (bottom).



Scheme 2. Synthesis of dihydroflustramine E and their debrominated analogues (**1-4**). (a) MeONa/MeOH. (b) $MeNH_2$/MeOH. (c) **19a** and **20a**: $EtN(Me)_2{\cdot}AlH_3$/THF. (d) **19b** and **20b**: $LiAlH_4$/THF.

recognizable characteristic feature in all lactams is the observation of three-bond HMBC correlations between the *N*-Me signal at δ_H 2.6 with the carbon signals at δ_C 171 (C-2) and 79–81 (C-8a) ppm. Other ^{13}C NMR signals also matched literature data.[12]

The final reduction of **19a** and **20a** turned out to be somewhat delicate due to the inherent lability of the aromatic bromides toward the non-selective nature of $LiAlH_4$.[13] Thus, conversion of brominated lactams **19a** and **20a** into the corresponding natural products **1** and **2** was therefore accomplished by treatment with alane-*N*,*N*-dimethylethylamine complex at room temperature for 45 min in excellent yields (90 and 93%, respectively). This completes the total synthesis of dihydroflustramine C (**1**) and flustramine E (**2**). The spectral properties of **1** and **2** are identical (IR, EIMS, ^1H and ^{13}C NMR) to those reported for the marine natural products dihydroflustramine C[1] and flustramine E,[2] except for the optical activity.

The analogues debrominated lactams **19b** and **20b**[7] were reduced with $LiAlH_4$ in refluxing THF to give debromodihydroflustramine C (**3**) and debromoflustramine E (**4**) in 90 and 92% yield, respectively. The spectral properties of **3** and **4** are identical (IR, EIMS, ^1H and ^{13}C NMR) to those reported for the unnatural products.[4–7]

3. Conclusions

In summary, as an extension of our ongoing work on the

total synthesis of indole alkaloids, we have now exploited the application of the convertible 2-hydroxyindolenine approach in order to synthesize dihydroflustramine C (**1**) and flustramine E (**2**) alkaloids from marine bryozoan *F. foliacea*.

4. Experimental

4.1. General experimental procedures

Melting points were uncorrected. IR spectra were recorded on a Perkin Elmer 16F PC FT spectrophotometer. ^{1}H and ^{13}C NMR spectra were measured on Varian XL-300GS and Mercury spectrometers working at 300 and 75 MHz, respectively. Chemical shifts are reported in ppm downfield from tetramethylsilane. EIMS were obtained on Hewlett Packard 5989A or Varian Saturn 2000 mass spectrometers. HRMS were measured on a Jeol JMS-SX 102A spectrometer. Analytical thin-layer chromatography was performed on silica gel F_{254} coated aluminium sheets. Flash chromatography was performed using silica gel 60 (230–400 mesh) from Aldrich.

4.1.1. 6-Bromo-1-methyl-3a-(2-methyl-3-buten-2-yl)-2-oxo-2,3,3a,8a-tetrahydro-8*H*-pyrrolo[2,3-*b*]indole (19a). To a solution of the lactone **15a** (230 mg, 0.60 mmol) in MeOH (15 mL) at 0°C was added NaH (1.20 mmol). The mixture was heated at reflux for 2 h, and the volatiles were evaporated. The residue was dissolved in EtOAc (100 mL) and saturated aqueous NH_4Cl (5 mL). The organic phase was washed with brine (3×20 mL), and the combined aqueous phases were extracted with EtOAc (3×20 mL). The combined organic layers were dried over Na_2SO_4 and evaporated to give **17a** which was used without purification. To the crude compound **17a** in MeOH (10 mL) was added $MeNH_2$ (3 mL of a 2.0 M solution in MeOH, 6 mmol), the reaction mixture was stirred for 20 h at room temperature, the volatiles were evaporated, and the resultant crude product was purified by silica gel flash column chromatography (1:1 EtOAc/hexane) to give lactam **19a** as colorless solid (193 mg, 96%): mp 199–201°C (Et_2O/hexane); R_f 0.16 (1:1 EtOAc/hexane). IR ($CHCl_3$) ν_{max} 3432, 3008, 1682, 1598, 1482 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.02 (1H, br s, N-*H*), 7.01 (1H, d, *J*=7.8 Hz, H-4), 6.75 (1H, dd, *J*=8.0, 1.8 Hz, H-5), 6.65 (1H, d, *J*=1.8 Hz, H-7), 5.93 (1H, dd, *J*=17.3, 10.9 Hz, H-12), 5.11 (1H, d, *J*=1.7 Hz, H-8a), 5.07 (1H, dd, *J*=10.9, 1.4 Hz, H-13), 5.01 (1H, dd, *J*=17.3, 1.4 Hz, H-13′), 2.75 and 2.35 (1H each, AB, *J*=17.3 Hz, H-3, H-3′), 2.66 (3H, s, *N*-Me), 0.96 and 0.89 (3H each, both s, Me-10 and Me-11); ^{13}C NMR (DMSO-d_6) δ 170.9 (s, C=O), 151.3 (s, C-7a), 143.8 (d, C-12), 131.5 (s, C-3b), 126.8 (d, C-4), 121.2 (s, C-6), 119.7 (d, C-5), 114.1 (t, C-13), 111.4 (d, C-7), 79.1 (d, C-8a), 55.7 (s, C-3a), 40.7 (s, C-9), 39.0 (t, C-3), 26.0 (q, *N*-Me), 22.3 and 21.5 (both q, Me-10 and Me-11); EIMS *m/z* (relative intensity) 334/336 (M^+, 11/11), 265/267 (100/96), 208/210 (82/79); HRMS (FAB) *m/z* 335.0770 (MH^+, $C_{16}H_{19}BrN_2O$ requires 335.0759).

4.1.2. 1-Methyl-3a-(2-methyl-3-buten-2-yl)-2-oxo-2,3,3a,8a-tetrahydro-8*H*-pyrrolo[2,3-*b*]indole (19b). This compound was prepared from **15b** (180 mg, 0.60 mmol) as described above for **19a**. Extractive workup and purification by flash column chromatography (1:1 EtOAc/hexane) gave lactam **19b** as colorless crystals (148 mg, 97%); mp 167–168°C (EtOAc/hexane); R_f 0.40 (EtOAc). IR ($CHCl_3$) ν_{max} 3428, 3006, 1674, 1606, 1484 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.09 (1H, d, *J*=7.4 Hz, H-4), 7.02 (1H, td, *J*=7.6, 1.3 Hz, H-6), 6.67 (1H, d, *J*=2.5 Hz, *N*-H), 6.64 (1H, td, *J*=7.4, 1.1 Hz, H-5), 6.54 (1H, d, *J*=7.8 Hz, H-7), 5.97 (1H, dd, *J*=17.3, 10.9 Hz, H-12), 5.10 (1H, dd, *J*=10.8, 1.4 Hz, H-13), 5.08 (1H, d, *J*=2.1 Hz, H-8a), 5.03 (1H, dd, *J*=17.3, 1.4 Hz, H-13′), 2.76 and 2.37 (1H each, AB, *J*=17.3 Hz, H-3, H-3′), 2.67 (3H, s, *N*-Me), 0.99 and 0.89 (3H each, both s, Me-10 and Me-11); ^{13}C NMR (DMSO-d_6) δ 171.2 (s, C=O), 149.5 (s, C-7a), 144.2 (d, C-12), 132.1 (s, C-3b), 128.4 (d, C-6), 125.1 (d, C-4), 117.7 (d, C-5), 113.9 (t, C-13), 109.4 (d, C-7), 79.0 (d, C-8a), 56.1 (s, C-3a), 40.8 (s, C-9), 39.3 (t, C-3), 26.0 (q, *N*-Me), 22.3 and 21.7 (both q, Me-10 and Me-11); EIMS *m/z* (relative intensity) 256 (M^+, 19), 187 (92), 130 (100); HRMS (FAB) *m/z* 257.1649 (MH^+, $C_{16}H_{20}N_2O$ requires 257.1654).

4.1.3. 6-Bromo-1-methyl-3a-(3-methyl-2-buten-1-yl)-2-oxo-2,3,3a,8a-tetrahydro-8*H*-pyrrolo[2,3-*b*]indole (20a). This compound was prepared from **16a** (230 mg, 0.60 mmol) as described above for **19a**. Extractive workup and purification by flash column chromatography (1:1 EtOAc/hexane) gave lactam **20a** as colorless crystals (197 mg, 98%): mp 168–169°C (Et_2O); R_f 0.12 (1:1 EtOAc/hexane). IR ($CHCl_3$) ν_{max} 3432, 3018, 1682, 1600, 1482 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.02 (1H, d, *J*=7.8 Hz, H-4), 7.02 (1H, br d, *J*=1.2 Hz, *N*-H), 6.75 (1H, dd, *J*=7.9, 1.8 Hz, H-5), 6.66 (1H, d, *J*=1.8 Hz, H-7), 5.07 (1H, br t, *J*=7.3 Hz, H-10), 4.93 (1H, d, *J*=1.7 Hz, H-8a), 2.67 (3H, s, *N*-Me), 2.57 and 2.46 (1H each, AB, *J*=17.0 Hz, H-3, H-3′), 2.35 (1H, dd, *J*=14.6, 8.1 Hz, H-9), 2.29 (1H, dd, *J*=14.6, 6.7 Hz, H-9′), 1.65 (3H, s, Me-12), 1.49 (3H, s, Me-13); ^{13}C NMR (DMSO-d_6) δ 171.3 (s, C=O), 150.4 (s, C-7a), 134.4 (s, C-11), 133.7 (s, C-3b), 125.2 (d, C-4), 120.9 (s, C-6), 120.1 (d, C-5), 118.8 (d, C-10), 111.3 (d, C-7), 81.3 (d, C-8a), 49.6 (s, C-3a), 41.1 (t, C-3), 35.8 (t, C-9), 26.2 (q, *N*-Me), 25.7 (q, Me-12), 17.8 (q, Me-13); EIMS *m/z* (relative intensity) 334/336 (M^+, 28/29), 265/267 (100/94), 208/210 (91/91); HRMS (FAB) *m/z* 335.0773 (MH^+, $C_{16}H_{19}BrN_2O$ requires 335.0759).

4.1.4. 1-Methyl-3a-(3-methyl-2-buten-1-yl)-2-oxo-2,3,3a,8a-tetrahydro-8*H*-pyrrolo[2,3-*b*]indole, debromoflustramide E (20b). This compound was prepared from **16b** (180 mg, 0.60 mmol) as described above for **19a**. Extractive workup and purification by flash column chromatography (1:1 EtOAc/hexane) gave lactam **20b** (150 mg, 98%) as colorless oil (lit.[7] yellow oil); R_f 0.38 (EtOAc). IR 3428, 3008, 1682, 1608, 1484 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.08 (1H, d, 7.4 Hz, H-4), 6.99 (1H, td, *J*=7.6, 1.3 Hz, H-6), 6.69 (1H, br d, *J*=1.7 Hz, *N*-H), 6.63 (1H, td, *J*=7.4, 1.0 Hz, H-5), 6.54 (1H, d, *J*=7.6 Hz, H-7), 5.09 (1H, br t, *J*=6.6 Hz, H-10), 4.90 (1H, d, *J*=2.1 Hz, H-8a), 2.67 (3H, s *N*-Me), 2.57 and 2.46 (1H each, AB, *J*=16.9 Hz, H-3 and H-3′), 2.36 (1H, dd, *J*=14.2, 7.5 Hz, H-9), 2.29 (1H, dd, *J*=14.2, 6.3 Hz, H-9′), 1.65 (3H, s, Me-12), 1.50 (3H, s, Me-13); ^{13}C NMR (DMSO-d_6) δ 171.4 (s, C-2), 148.5 (s, C-7a), 134.4 (s, C-3b), 134.1 (s, C-11), 128.1 (d,

C-6), 123.4 (d, C-4), 119.2 (d, C-10), 118.0 (d, C-5), 109.2 (d, C-7), 81.1 (d, C-8a), 50.1 (s, C-3a), 41.3 (t, C-3), 36.0 (t, C-9), 26.2 (q, *N*-Me), 25.7 (q, Me-12), 17.8 (q, Me-13); EIMS *m/z* (relative intensity) 256 (M^+, 81), 187 (100), 130 (98); HRMS (FAB) *m/z* 257.1653 (MH^+, $C_{16}H_{20}N_2O$ requires 257.1654).

4.1.5. 6-Bromo-1-methyl-3a-(2-methyl-3-buten-2-yl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole, dihydroflustramine C (1). To a stirred solution of **19a** (64 mg, 0.19 mmol) in 10 mL of dry THF was added alane-*N*,*N*-dimethylethylamine complex (0.6 mL of a 0.5 M solution in toluene, 0.3 mmol) and the reaction mixture was stirred for 45 min at ambient temperature. The reaction was quenched by adding slowly a mixture of THF–H_2O (1:1, 10 mL) followed by EtOAc (70 mL). The insoluble part was removed by filtration and washed with EtOAc (3×10 mL). The combined organic phases were washed with brine, dried over Na_2SO_4 and evaporated to afford the crude alkaloid **1**, which was purified by flash chromatography on silica gel (EtOAc). Colorless solid (56 mg, 90%): mp 82–84°C (lit.[1a] mp 82–84°C); R_f 0.29 (1:9 MeOH/$CHCl_3$); HRMS (FAB) *m/z* 321.0958 (MH^+, $C_{16}H_{21}BrN_2$ requires 321.0966). The IR, EIMS, ^1H and ^{13}C NMR spectral data were identical to those of the known sample.[1a]

4.1.6. 6-Bromo-1-methyl-3a-(3-methyl-2-buten-1-yl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole, flustramine E (2). This compound was prepared from **20a** (64 mg, 0.19 mmol) in a similar manner to that described previously for **1**. Extractive workup and purification by flash column chromatography (EtOAc) gave **2** as colorless solid (58 mg, 93%): mp 82–85°C (on standing) (lit.[2] brown oil); R_f 0.28 (1:9 MeOH/$CHCl_3$); HRMS (FAB) *m/z* 321.0956 (MH^+, $C_{16}H_{21}BrN_2$ requires 321.0966). The IR, EIMS, ^1H and ^{13}C NMR spectral data were identical to those of the known sample.[2]

4.1.7. 1-Methyl-3a-(2-methyl-3-buten-2-yl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole, debromodihydroflustramine C (3). To a stirred suspension of LAH (2.5 mmol in 10 mL of dry THF) was added lactam **19b** (84 mg, 0.31 mmol) in THF (5 mL), and the mixture was heated at reflux for 3 h. After the mixture was cooled to 0°C, the reaction was quenched by adding dropwise EtOAc (120 mL), washed with brine, dried over Na_2SO_4, and evaporated. The resultant crude tetrahydropyrrole **3** was purified by silica gel flash column chromatography (EtOAc) to give colorless solid (68 mg, 90%): mp 57–59°C (on standing) (lit.[4] colorless oil); R_f 0.17 (1:9 MeOH/$CHCl_3$); HRMS (FAB) *m/z* 243.1855 (MH^+, $C_{16}H_{22}N_2$ requires 243.1861). The IR, EIMS, ^1H and ^{13}C NMR spectral data were identical to those of the known sample.[4]

4.1.8. 1-Methyl-3a-(3-methyl-2-buten-1-yl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole, debromoflustramine E (4). This compound was prepared from **20b** (84 mg, 0.31 mmol) in a similar manner to that described previously for **3**. Extractive workup and purification by flash column chromatography (EtOAc) gave **4** as colorless solid (69 mg, 92%): mp 57–59°C (on standing) (lit.[6] mp 57–59°C); R_f 0.27 (1:9 MeOH/$CHCl_3$); HRMS (FAB) *m/z* 243.1864 (MH^+, $C_{16}H_{22}N_2$ requires 243.1861). The IR, EIMS, ^1H and ^{13}C NMR spectral data were identical to those of the known sample.[7]

4.2. X-Ray structure determination of 13a

X-Ray data for **13a** were collected on a Bruker Smart 6000 CCD diffractometer. Single crystals of **13a** were grown from hexane–CH_2Cl_2. A total of 1321 frames were collected at a scan width of 0.3° and an exposure time of 10 s/frame. The frames were processed with the SAINT software package, provided by the diffractometer manufacturer, by using a narrow-frame integration algorithm, and the structure was solved and refined by using SHELX97. An empirical absorption correction was applied. Pertinent crystal data, collection and refinement parameters are given in Table 1. The CCDC deposition number is 176720.

Table 1. X-Ray data collection and processing parameters for **13a**, **13b** and **14b**

Compound	**13a**	**13b**	**14b**
Formula	$C_{18}H_{17}BrN_2O_4$	$C_{18}H_{18}N_2O_4$	$C_{18}H_{18}N_2O_4$
Size (mm^3)	0.34×0.10×0.05	0.20×0.08×0.40	0.30×0.12×0.50
Crystal system	Monoclinic	Triclinic	Triclinic
Space group	$P2_1/n$	$P\bar{1}$	$P\bar{1}$
a (Å)	13.0749(5)	7.761(2)	8.946(2)
b (Å)	9.2227(3)	13.092(2)	9.733(2)
c (Å)	15.5121(6)	8.180(1)	11.055(2)
α (°)	90.000	87.843(8)	77.58(1)
β (°)	112.410(1)	90.453(8)	77.53(1)
γ (°)	90.000	84.673(9)	64.19(1)
V (Å^3)	1729.28	826.96	838.01
D_{calcd} (g cm^{-3})	1.56	1.31	1.29
Z-value	4	2	2
μ (mm^{-1})	2.4(Mo K_α)	0.73(Cu K_α)	0.76(Cu K_α)
T (K)	293	298	298
$2\theta_{range}$ (°)	3.48–46.56	3–110	3–110
Total reflections	8813	2313	2332
Unique reflections	2492	2078	2117
R_{int} (%)	4.0	1.1	8.0
$I \geq 3\sigma(I)$	1859	1863	1930
Parameters	229	217	217
R (%), R_w (%)	3.2, 7.3	4.6, 5.8	5.4, 6.9
ρ_{max} (eÅ^{-3})	0.36	0.35	0.35

4.3. X-Ray structure determination of 13b and 14b

X-Ray data for **13b** and **14b** were collected on a Nicloet R3m diffractometer. Single crystals of **13b** and **14b** were grown from hexane–Et_2O and Et_2O solutions, respectively. The measured data were corrected for Lorentz and polarization effects and for absorption. The structures were solved by direct methods using SHELX86. For the structural refinement, the non-hydrogen atoms were treated anisotropically, and the hydrogen atoms, included in the structure factor calculation, were refined isotropically. Crystal data, collection and refinement parameters are given in Table 1. The CCDC deposition numbers are 176719 and 176716, respectively.

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References

1. (a) Wright, J. L. C. *J. Nat. Prod.* **1984**, *47*, 893. (b) Laycock, M. V.; Wright, J. L. C.; Findlay, J. A.; Patil, A. D. *Can. J. Chem.* **1986**, *64*, 1312.
2. Holst, P. B.; Anthoni, U.; Christophersen, C.; Nielsen, P. H. *J. Nat. Prod.* **1994**, *57*, 997.
3. Pauling, P.; Petcher, T. J. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1342.
4. Takase, S.; Uchida, I.; Tanaka, H.; Aoki, H. *Tetrahedron* **1986**, *42*, 5879.
5. Carlé, J. S.; Christophersen, C. *J. Org. Chem.* **1981**, *46*, 3440.
6. Somei, M.; Yamada, F.; Izumi, T.; Nakajou, M. *Heterocycles* **1997**, *45*, 2327.
7. Jensen, J.; Anthoni, U.; Christophersen, C.; Nielsen, P. H. *Acta Chem. Scand.* **1995**, *49*, 68.
8. (a) Morales-Ríos, M. S.; Suárez-Castillo, O. R.; Joseph-Nathan, P. *J. Org. Chem.* **1999**, *64*, 1086. (b) Morales-Ríos, M. S.; Suárez-Castillo, O. R.; Trujillo-Serrato, J. J.; Joseph-Nathan, P. *J. Org. Chem.* **2001**, *66*, 1186.
9. (a) Morales-Ríos, M. S.; Santos-Sánchez, N. F.; Joseph-Nathan, P. *J. Nat. Prod.* **2002** in press. For synthetic routes to furo[2,3-*b*]indoles: see (b) Morales-Ríos, M. S.; Suárez-Castillo, O. R.; Joseph-Nathan, P. *Trends Heterocycl. Chem.* **1999**, *6*, 111.
10. Morales-Ríos, M. S.; Suárez-Castillo, O. R.; García-Martínez, C.; Joseph-Nathan, P. *Synthesis* **1998**, 1755.
11. Morales-Ríos, M. S.; Suárez-Castillo, O. R.; Joseph-Nathan, P. *J. Chem. Soc., Perkin Trans. 2* **2000**, 769.
12. Morales-Ríos, M. S.; Espiñeira, J.; Joseph-Nathan, P. *Magn. Reson. Chem.* **1987**, *25*, 377.
13. Brown, H. C.; Krishnamurthy, S. *J. Org. Chem.* **1969**, *34*, 3918.