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Efficient Synthesis of the Sponge Alkaloids Cyclostellettamines A-F

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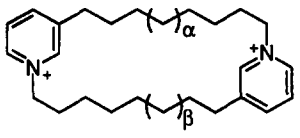
Abstract

The total synthesis of cyclostellettamines A-F is reported. The synthetic cyclostellettamines were reduced to the neutral *bis*-tetrahydropyridine compounds, and exact mass measurements of these reduced products provided unequivocal evidence for the cyclostellettamine structures.

Keywords: alkaloids; macrocycles; marine metabolites; sponges.

1. Introduction

In 1994, Fusetani *et al.* [1] isolated cyclostellettamines A-F (**1-6**) from the sponge *Stelletta maxima*[2] (Table 1). They were discovered because of their ability to inhibit effectively the binding of methyl quinuclidinyl benzylate to muscarinic acetylcholine receptors. Despite only very small amounts (<1mg) of the natural material being isolated, their structures were determined by a combination of NMR spectroscopy and mass spectrometry. The same group subsequently completed a synthesis of cyclostellettamine C adding credence to their proposed structures [2].



Cyclostellettamines A-F

Cyclostellettamine	α	β	Compound
A:	5	5	(1)
B:	5	6	(2)
C:	6	6	(3)
D:	5	7	(4)
E:	6	7	(5)
F:	7	7	(6)

Table 1.

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[2] It was reported recently [11] that the original *Stelletta maxima* sample was contaminated with *Haliclona*.

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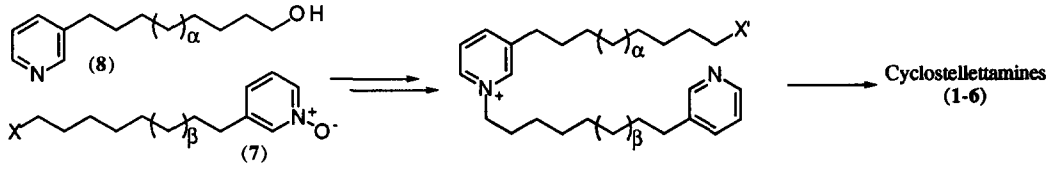
The cyclostellettamines consist of two 3-alkylpyridinium units, connected by C_{12}, C_{13} or C_{14} alkyl chains. Although structurally simple, they may be biogenetically related to many other more complex sponge metabolites, including the manzamine alkaloids [3-8]. Our continued interest in the biomimetic synthesis of these sponge alkaloids [9,10] prompted us to investigate the synthesis of the cyclostellettamines. Recently Wanner and Koomen [11] have reported the synthesis of cyclostellettamines A-F (**1-6**). In this paper we report our complementary total synthesis of the cyclostellettamines.

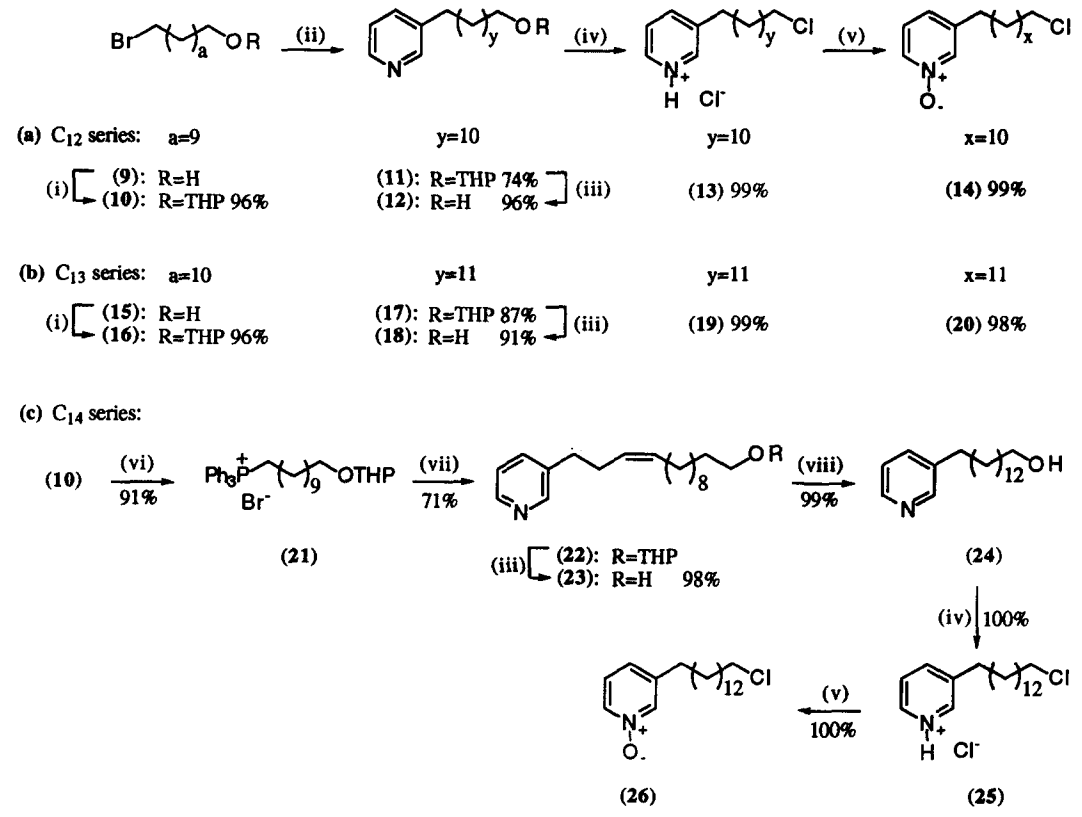
2. Results and discussion

We envisaged that the cyclostellettamines could be assembled by two controlled quaternisations of the pyridine rings from two 3-alkylpyridine subunits (Scheme 1). In order to achieve this (i) one pyridine subunit needs to be in a protected form (*e.g.* as the *N*-oxide **7**); (ii) the protected pyridine subunit (**7**) must have a leaving group (X) at the terminal position on its 3-alkyl chain; (iii) the other ("unprotected") pyridine subunit should have a masked leaving group (*e.g.* a hydroxyl group (**8**)) at the terminal position on its 3-alkyl chain. Once the first quaternisation has been achieved, deprotection, activation and a second quaternisation would complete the synthesis. This strategy was first demonstrated by Morimoto and Yokoe in the synthesis of haliclamine A [12].



Scheme 1

For the C_{12} alkylpyridine series (Scheme 2(a)), commercially available 11-bromoundecan-1-ol (**9**) was converted into its tetrahydropyranyl (THP) ether **10** in 96% yield [13]. Treatment of **10** with lithiated 3-methylpyridine [14] gave alkylpyridine **11** (74%). The THP group was removed with dilute hydrochloric acid in methanol to afford alcohol **12** (96%), the required "unprotected/unactivated" subunit. Activation of alcohol **12** was effected with $SOCl_2$ in 1,4-dioxane and the resultant chloroalkylpyridine **13** was isolated as its hydrochloride salt (99%). We found this process to be extremely convenient because the product was obtained as a crystalline solid which could be stored indefinitely. The free base, obtained from **13** by partitioning between CH_2Cl_2 and aqueous sodium carbonate, was oxidised with *m*CPBA to give *N*-oxide **14** (99%), the "protected/activated" subunit.



Scheme 2.

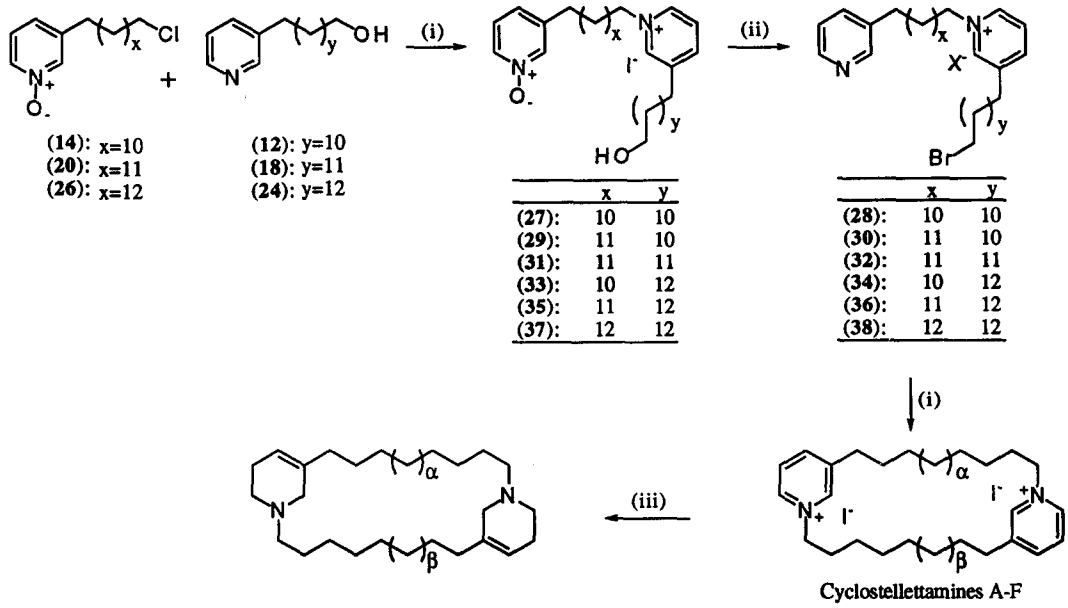
Reagents: (i) PPTS, 3,4-dihydro-2*H*-pyran, CH_2Cl_2; (ii) LDA, DMPU, 3-methylpyridine; (iii) 3M aq. HCl, MeOH; (iv) $SOCl_2$, 1,4-dioxane; (v) 2M aq. $NaCO_3$, then *m*CPBA, CH_2Cl_2; (vi) Ph_3P, MeCN; (vii) KHMDS then 3-pyridin-3-ylpropanal, THF; (viii) Pd/C, H_2, EtOH.

The C_{13} series of compounds was synthesised from 12-bromododecan-1-ol (**15**), obtained in 87% yield by monobromination of dodecan-1,12-diol with HBr [15]. Using the same sequence of reactions as described above, **15** was converted into **16** (96%), **17** (87%), **18** (91%), **19** (99%) and **20** (98%) (Scheme 2(b)).

Finally, the C_{14} alkylpyridine series was synthesised *via* a slightly different route (Scheme 2(c)), since tridecan-1,13-diol was not readily available. Triphenylphosphine and **10** were coupled to give the C_{11} phosphonium salt **21** (91%) which was used for Wittig olefination of 3-pyridin-3-ylpropanal to furnish **22** in 71% yield [16-18]. The THP group in **22** was removed with dilute hydrochloric acid in methanol to give alcohol **23** (98%). The double bond in **23** was saturated, by hydrogenation over 10% Pd/C, to afford **24** (99%) which was converted to **25** (100%) then **26** (100%) using the previously described protocol.

With the three pyridine subunits in hand, in "unprotected/unactivated" (**12**, **18** and **24**) and "protected/activated" (**14**, **20** and **26**) forms, the final steps in the synthesis were pursued. The requisite hydroxyalkylpyridine and chloroalkylpyridine-*N*-oxide were heated at reflux in butan-

2-one with sodium iodide (Scheme 3). The resulting mono-quaternised salt was treated with PBr_3 to effect a one-pot deoxygenation of the pyridine-*N*-oxide [19], and bromination of the alcohol.[1] The hydrobromide salt isolated was treated with solid K_2CO_3 to generate the free base which was immediately used in the macrocyclisation step. The free base was added slowly, using a syringe pump, to a refluxing solution of sodium iodide in butan-2-one, allowing the macrocyclisation to be conducted at a relatively high concentration (final concentration 10mM).



	x	y
(27):	10	10
(29):	11	10
(31):	11	11
(33):	10	12
(35):	11	12
(37):	12	12

	x	y
(28):	10	10
(30):	11	10
(32):	11	11
(34):	10	12
(36):	11	12
(38):	12	12

	α	β	Yield
(39):	5	5	81%
(40):	5	6	92%
(41):	6	6	96%
(42):	5	7	95%
(43):	6	7	92%
(44):	7	7	86%

Cyclostellettamines A-F

	α	β	Yield
(1):	5	5	65%
(2):	5	6	65%
(3):	6	6	64%
(4):	5	7	66%
(5):	6	7	62%
(6):	7	7	65%

Scheme 3.

Reagents: (i) NaI, butan-2-one, Δ; (ii) PBr_3, $CHCl_3$ then K_2CO_3; (iii) $NaBH_4$, MeOH, CH_2Cl_2, -78°C to 0°C.

Thus, as described above, cyclostellettamine A (**1**) was synthesised by the quaternisation of **12** with **14** to give **27**, which was then converted to **28** and this cyclised affording **1** in 65% yield. Reaction of **12** and **20** gave **29** which was converted to cyclostellettamine B (**2**) (65%) *via* **30**. Cyclostellettamine C (**3**) was obtained in 64% yield from **18** and **20** *via* **31** and **32**. Bromide **34**, prepared from **14** and **24** *via* **33**, was converted into cyclostellettamine D (**4**) (66%). Reaction of **20** and **24** afforded **35** which was converted into cyclostellettamine E (**5**)

[1] NMR analysis showed that *ca.* 10% of the product was present as the primary iodide, resulting from displacement of a leaving group by the iodide counter ion from the mono-quaternised starting material.

(62%) *via* **36**. Finally, macrocyclisation of bromide **38**, obtained from **24** and **26** *via* **37**, afforded cyclostellettamine F (**6**) (65%). All the cyclostellettamines were isolated as their diiodide salts and the yields quoted were calculated over the three steps.

The FAB mass spectra of the synthetic cyclostellettamines showed the $[M\text{-}I]^+$ ion consistent with literature observations [11]. However, unequivocal proof of the structures **1-6** was obtained by conversion of the cyclostellettamines into uncharged compounds, which were then subjected to mass spectrometry analysis. Thus **1, 2, 3, 4, 5** and **6** were reduced with $NaBH_4$ to produce the corresponding *bis*-tetrahydropyridine compounds **39** (81%), **40** (92%), **41** (96%), **42** (95%), **43** (92%) and **44** (86%) respectively. HRMS confirmed the identities of **39-44** and hence the structures of **1-6**.

3. Conclusion

In summary, we have achieved the total synthesis of cyclostellettamines A-F. The macrocyclisation strategy involving (i) the use of the pyridine-*N*-oxide as a protected form of the pyridine; and (ii) subsequent one-pot deprotection and activation with PBr_3 was found to be extremely effective. The synthesis utilised butan-2-one as the solvent in quaternisation reactions in place of the more toxic acetonitrile [11]. Moreover, the use of a syringe pump allowed the macrocyclisation to be conducted at relatively high concentrations utilising much less solvent. Finally, reduction of the synthetic cyclostellettamines produced neutral *bis*-tetrahydropyridines from which mass spectrometry proved conclusively the structures of compounds **1-6**.

4. Experimental

Melting Points were obtained using a Büchi 510 capillary melting point apparatus and are uncorrected. Microanalyses are quoted to the nearest 0.1% for all elements except for hydrogen which is quoted to the nearest 0.05%. Reported atomic percentages are within the error limits of ±0.4%. Infrared spectra were recorded on a Perkin-Elmer Paragon 1000 Fourier Transform spectrometer with internal referencing. Absorption maxima (ν_{max}) are reported in wavenumbers (cm^{-1}) and the following abbreviations are used: w, weak; m, medium; s, strong; br, broad. Proton magnetic resonance spectra were recorded on Varian Gemini 200 (200MHz), Bruker AC200 (200MHz) and Bruker DPX400 (400MHz) spectrometers. Chemical shifts (δ_H) are quoted in ppm and are referenced to the appropriate reşidual solvent peak. Coupling constants (J) are reported in hertz to the nearest 0.5Hz. Data are reported as follows: chemical shift, integration, multiplicity [br, broad; s, singlet; d, doublet; t, triplet; q, quartet; qui, quintet; m, multiplet; or as a combination of these (*e.g.* dd, dt, *etc.*)], coupling constant(s) and assignment. Diastereotopic protons are assigned as X and X', where the ' indicates the lower field proton. Carbon magnetic resonance spectra were recorded on Varian Gemini 200 (50.3MHz), Bruker

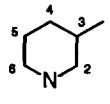
AC200 (50.3MHz) and Bruker DPX400 (100.6MHz) spectrometers. Chemical shifts (δ_C) are quoted in ppm to the nearest 0.1ppm (50.3MHz) or 0.01ppm (100.6MHz), and are referenced to the appropriate residual solvent peak. Low resolution mass spectra were recorded on Autospec (FAB/CI), BIO-Q (ES) and Micromass platform (APCI) spectrometers. Only molecular ions, fractions from molecular ions and other major peaks are reported. Reported exact mass values are within the error limits of ±10ppm mass units.

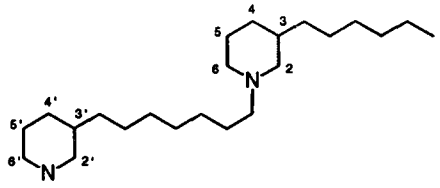
Column chromatography was carried out using Janssen silica 0.035-0.070mm or basic Laporte Actal U.G. alumina. Analytical TLC was performed on glass plates pre-coated with Merck silica gel 60 F_{254} or on aluminium sheets pre-coated with neutral aluminium oxide 60 F_{254} (type E). Visualisation was by the quenching of UV fluorescence (λ_{max}=254nm) or by staining with ammonium molybdate (10% w/v in 1M aq. sulfuric acid) or Dragendorff's reagent (0.08% w/v bismuth subnitrate and 2% w/v KI in 3M aq. AcOH). Retention factors (R_f) are quoted to 0.01. Kugelrohr distillations were performed using a Büchi GKR-50 distillation apparatus at the recorded pressure and oven temperature.

Anhydrous CH_2Cl_2, 1,4-dioxane and $^iPr_2NH$ were obtained by heating at reflux over calcium hydride followed by distillation under argon. Anhydrous $CHCl_3$ was obtained by heating at reflux over P_2O_5 followed by distillation under argon. Anhydrous THF was obtained by distillation from sodium/benzophenone ketyl under argon. PE 40-60 was distilled before use and refers to the fraction of light petroleum ether boiling between 40 and 60°C.

^{n}BuLi in hexane (Acros) and KHMDS in toluene (Aldrich) were titrated with 1,3-diphenylacetone-*para*-toluenesulfonylhydrazone before use. *m*CPBA was dissolved in CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*, then titrated with $KI/Na_2S_2O_3$. All other reagents were used as obtained from commercial sources.

For clarity the following numbering system has been consistently used for the pyridine ring system. Where two different pyridine ring systems appear in the same molecule, primed and unprimed locants have been used as shown below:





Synthesis of 1-bromo-11-tetrahydropyran-2-yloxyundecane (10)

A solution of 11-bromoundecan-1-ol (**9**) (25.0g, 99.5mmol), 3,4-dihydro-2*H*-pyran (13.6ml, 149mmol) and PPTS (250mg, 0.995mmol) in anhydrous CH_2Cl_2 (250ml) was stirred at room temperature for 18 hours. After washing with 2M aq. Na_2CO_3 (100ml) the organic phase was dried over K_2CO_3, filtered and concentrated *in vacuo*. The residual pale yellow oil was chromatographed (SiO_2; PE 40-60: EtOAc; 96:4) to yield *1-bromo-11-tetrahydropyran-2-yloxyundecane* (**10**) (32.0g, 96%) as a colourless oil; R_f 0.40 (SiO_2; PE 40-60: EtOAc; 96:4);

ν_{max} (thin film)/cm^{-1} 2926s, 2854s, 1135m, 1120m, 1078m, 1033m; δ_H (200MHz; $CDCl_3$) 1.53-1.90 (24H, m, CH_2), 3.30-3.53 (2H, m, OCHH'), 3.39 (2H, t, *J*7Hz, $BrCH_2$), 3.66-3.91 (2H, m, OCHH'), 4.56 (1H, dd, *J*4, 3Hz, OCHO); δ_C (50MHz; $CDCl_3$) 19.7, 25.5, 26.2, 28.1, 28.7, 29.4, 29.7, 30.7, 32.8, 34.0, 62.3 and 67.6 (12 x CH_2), 98.8 (CH); *m/z* (CI, NH_3) 337 (MH^+, ^{81}Br, 13%), 335 (MH^+, ^{79}Br, 27), 270 (27), 268 (29), 102 ($DHPOH_2^+$, 87), 85 ($DHPH^+$, 100).

Synthesis of 3-(12-tetrahydropyran-2-yloxydodecyl)pyridine (11)

To a solution of $^iPr_2NH$ (22.6ml, 161mmol) in THF (100ml) at 0°C in a 500ml two-necked flask, equipped with a magnetic stirrer, constant pressure addition funnel and a rubber septum, was added ^nBuLi (1.5M, 107ml, 161mmol) in hexane *via* a syringe. The resulting pale yellow solution was maintained at 0°C for 30 minutes, then treated with DMPU (19.5ml, 161mmol). The bright yellow solution was stirred at 0°C for 15 minutes, then treated over 10 minutes with a solution of 3-methylpyridine (15.7ml, 161mmol) in THF (50ml). After 30 minutes at 0°C, the mixture containing the lithiated 3-methylpyridine was cooled to -78°C and treated over 10 minutes with 1-bromo-11-tetrahydropyran-2-yloxyundecane (**10**) (18.0g, 53.8mmol) in THF (50ml). The resulting solution was stirred for 18 hours, being allowed to gradually warm to room temperature, and quenched with sat. aq. NH_4Cl (50ml) and water (50ml). The two-phase mixture was separated, and the aq. phase extracted with EtOAc (2 x 100ml). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated *in vacuo* to give a yellow oil. Flash chromatography (base-washed SiO_2; PE 40-60: EtOAc: Et_3N; 95:5:3) yielded *3-(12-tetrahydropyran-2-yloxydodecyl)pyridine* (**11**) (13.8g, 74%) as a pale yellow oil; R_f 0.27 (base-washed SiO_2; PE 40-60: EtOAc: Et_3N; 95:5:3); ν_{max} (thin film)/cm^{-1} 2926s, 2854s, 1575m, 1466m, 1421m, 1352m, 1200m, 1121m, 1078m, 1033m, 714m; δ_H (200MHz; $CDCl_3$) 1.25 (18H, br s, CH_2), 1.52-1.67 (8H, m, $pyCH_2CH_2$, CH_2CH_2O and $O_2CHCH_2CH_2CH_2$), 2.58 (2H, t, *J*7.5Hz, $pyCH_2$), 3.31-3.53 (2H, m, OCHH'), 3.66-3.89 (2H, m, OCHH'), 4.56 (1H, pseudo t, *J*3Hz, O_2CH), 7.17 (1H, dd, *J*7.5, 5Hz, C(5)H), 7.46 (1H, br d, *J*7.5Hz, C(4)H), 8.40-8.43 (2H, m, C(2)H and C(6)H); δ_C (50MHz; $CDCl_3$) 19.7, 25.5, 26.2, 29.1, 29.4, 29.5, 29.7, 30.7, 31.1, 33.0, 62.3 and 67.6 (12 x CH_2), 98.8, 123.1 and 135.7 (3 x CH), 137.9 (quaternary), 147.1 and 149.9 (2 x CH); *m/z* (APCI) 348 (MH^+, 47%), 264 ([MH_2-THP]$^+$, 100); HRMS found 348.2903, $C_{22}H_{38}NO_2$ (MH^+) requires 348.2903.

Synthesis of 12-pyridin-3-yldodecan-1-ol (12)

A solution of 3-(12-tetrahydropyran-2-yloxydodecyl)pyridine (**11**) (11.8g, 33.9mmol) and 3M aq. HCl (22.6ml, 67.8mmol) in MeOH (125ml) was stirred at room temperature for 15 hours. The mixture was concentrated *in vacuo* and basified with 2M aq. KOH (until pH=10). The aq. solution was extracted with EtOAc (3 x 50ml) and the organic phases were combined, dried over K_2CO_3, filtered and concentrated *in vacuo* to afford a yellow oil which slowly crystallised. Flash chromatography (SiO_2; PE 40-60: EtOAc: Et_3N; 70:20:10) yielded *12-*

pyridin-3-yldodecan-1-ol (**12**) (8.84g, 99%) as white crystals. The solid was recrystallised from PE 40-60: EtOAc to give *12-pyridin-3-yldodecan-1-ol* (**12**) (8.58g, 96%) as white crystals; m.p. 51-52°C (lit. [11] m.p. 48-50°C); R_f 0.23 (SiO_2; PE 40-60: EtOAc: Et_3N; 70:20:10); (Found: C, 77.7; H, 11.45; N, 5.2. $C_{17}H_{29}NO$ requires C, 77.5; H, 11.1; N, 5.3%); ν_{max} (KBr disk)/cm^{-1} 3332s br (OH), 2917s, 1578m, 1470m, 1423m, 1335m, 1070m, 1028m, 803m, 714s; δ_H (200MHz; $CDCl_3$) 1.27 (16H, br s, CH_2), 1.51-1.61 (5H, m, $pyCH_2CH_2$ and CH_2CH_2OH), 2.61 (2H, t, *J*7.5Hz, $pyCH_2$), 3.65 (2H, t, *J*6.5Hz, CH_2OH), 7.21 (1H, dd, *J*7.5, 5Hz, C(5)H), 7.50 (1H, br d, *J*7.5Hz, C(4)H), 8.41-8.45 (2H, m, C(2)H and C(6)H); δ_C (50MHz; $CDCl_3$) 25.7, 29.0, 29.3, 29.5, 31.0, 32.8, 32.9 and 62.5 (8 x CH_2), 123.5 and 136.2 (2 x CH), 138.3 (quaternary), 147.1 and 149.9 (2 x CH); *m/z* (APCI) 264 (MH^+, 100%), 246 ($[M\text{-}OH]^+$, 24); HRMS found 264.2336, $C_{17}H_{30}NO$ (MH^+) requires 264.2327.

Synthesis of 3-(12-chlorododecyl)pyridinium chloride (13)

A two-necked round-bottomed flask, equipped with a magnetic stirrer bar, reflux condenser and a pressure equalised dropping funnel was charged with $SOCl_2$ (1.00ml, 13.7mmol) at 0°C. 12-Pyridin-3-yldodecan-1-ol (**12**) (3.00g, 11.4mmol) in 1,4-dioxane (10ml) was added over 10 minutes [CAUTION: SO_2 gas evolved]. Once the addition was complete the ice bath was removed and the mixture stirred for 1 hour. After this time EtOH (10ml) was added and the mixture heated at reflux for 5 minutes. The solution was filtered while hot, allowed to cool and concentrated *in vacuo* to give white crystals, which were recrystallised from acetone: EtOH to give *3-(12-chlorododecyl)pyridinium chloride* (**13**) (3.59g, 99%) as white crystals; m.p. 111-112°C; (Found: C, 64.2; H, 9.3; N, 4.3. $C_{17}H_{29}Cl_2N$ requires C, 64.1; H, 9.2; N, 4.4%); R_f 0.58 (SiO_2; $CHCl_3$: EtOAc; 9:1); δ_H (200MHz; $CDCl_3$) 1.11 (16H, br s, CH_2), 1.46-1.66 (4H, m, $pyCH_2CH_2$ and CH_2CH_2Cl), 2.71 (2H, t, *J*7.5Hz, $pyCH_2$), 3.37 (2H, t, *J*6.5Hz, CH_2Cl), 7.86 (1H, dd, *J*8, 6Hz, C(5)H), 8.19 (1H, d, *J*8Hz, C(4)H), 8.53 (1H, s, C(2)H), 8.63 (1H, d, *J*6Hz, C(6)H); δ_C (50MHz; $CDCl_3$) 26.7, 28.7*, 29.0, 29.2, 30.2, 32.5, 32.6 and 45.1 (9 x CH_2), 126.9, 138.3 and 140.0 (3 x CH), 143.0 (quaternary), 145.6 (CH); *at this resonance two signals can be resolved; *m/z* (APCI) 284 ($[M\text{-}Cl]^+$, ^{37}Cl, 49%), 282 ($[M\text{-}Cl]^+$, ^{35}Cl, 100).

3-(12-Chlorododecyl)pyridine

3-(12-Chlorododecyl)pyridinium chloride (**13**) was neutralised by being dissolved in CH_2Cl_2 and washed with 2M aq. Na_2CO_3. The aq. phase was extracted with CH_2Cl_2 and the organic phases were combined, dried over K_2CO_3, filtered and concentrated *in vacuo* to afford *3-(12-chlorododecyl)pyridine* (quant.) as a colourless oil; R_f 0.44 (SiO_2; PE 40-60: EtOAc; 1:1; UV); ν_{max} (thin film)/cm^{-1} 2926s, 2854s, 1575m, 1478m, 1465m, 1422m, 1026m, 714m; δ_H (200MHz; $CDCl_3$) 1.28 (16H, br s, CH_2), 1.56-1.77 (4H, m, $pyCH_2CH_2$ and CH_2CH_2Cl), 2.59 (2H, t, *J*7.5Hz, $pyCH_2$), 3.51 (2H, t, *J*6.5Hz, CH_2Cl), 7.18 (1H, dd, *J*8, 5Hz, C(5)H), 7.47 (1H, d pseudo t, *J*8, 2Hz, C(4)H), 8.40-8.43 (2H, m, C(2)H and C(6)H); δ_C (50MHz; $CDCl_3$) 26.8,

28.8, 29.1, 29.5, 31.1, 32.6, 33.0 and 45.2 (8 x $\underline{C}H_2$), 123.2 and 135.7 (2 x $\underline{C}H$), 137.9 (quaternary), 147.1 and 149.9 (2 x $\underline{C}H$).

Synthesis of 3-(12-chlorododecyl)pyridine-N-oxide (14)

To a stirred solution of 3-(12-chlorododecyl)pyridine (1.49g, 5.27mmol) in CH_2Cl_2 (40ml) at 0°C was added *m*CPBA (89% active, 1.12g, 5.79mmol). The solution was stirred for 1 hour and then concentrated *in vacuo* behind a safety screen at 15°C. Flash chromatography (Al_2O_3; CH_2Cl_2: MeOH; 98:2) followed by concentration *in vacuo* and storage under high vacuum afforded *3-(12-chlorododecyl)pyridine-N-oxide* (**14**) (1.55g, 99%) as a hygroscopic white solid; R_f 0.63 (Al_2O_3; CH_2Cl_2: MeOH; 98:2; UV); ν_{max} ($CHCl_3$)/cm^{-1} 2924s, 2853s, 1604m, 1488m, 1468m, 1436m, 1269m, 1158m, 1015m; δ_H (200MHz; $CDCl_3$) 1.28 (16H, br s, $C\underline{H}_2$), 1.59-1.76 (4H, m, py$CH_2C\underline{H}_2$ and $C\underline{H}_2CH_2Cl$), 2.65 (2H, t, *J*7.5Hz, py$C\underline{H}_2$), 3.52 (2H, t, *J*6.5Hz, $C\underline{H}_2Cl$), 7.45-7.47 (2H, m, C(4)$\underline{H}$ and C(5)$\underline{H}$), 8.16-8.21 (2H, m, C(2)$\underline{H}$ and C(6)$\underline{H}$); δ_C (50MHz; $CDCl_3$) 26.5, 28.5, 28.6, 29.0, 29.2, 30.2, 32.0, 32.3 and 44.3 (9 x $\underline{C}H_2$), 126.1, 129.9, 136.4 and 138.4 (4 x $\underline{C}H$), 142.8(quaternary); *m/z* (APCI) 300 (MH^+, ^{37}Cl, 33%), 298 (MH^+, ^{35}Cl, 100); HRMS found 298.1947, $C_{17}H_{29}ClNO$ (MH^+, ^{35}Cl) requires 298.1938.

Synthesis of 1-bromo-12-tetrahydropyran-2-yloxydodecane (16)

The title compound was synthesised similarly to **10**, using 12-bromododecan-1-ol (**15**) (31.3g, 118mmol), 3,4-dihydro-2*H*-pyran (16.2ml, 177mmol) and PPTS (297mg, 1.18mmol) in anhydrous CH_2Cl_2 (300ml) to yield *1-bromo-12-tetrahydropyran-2-yloxydodecane* (**16**) (39.6g, 96%) as a colourless oil; R_f 0.42 (SiO_2; PE 40-60: Et_2O; 9:1); ν_{max} (thin film)/cm^{-1} 2927s, 2854s, 1465m, 1200m, 1135m, 1120m, 1078m, 1034m; δ_H (200MHz; $CDCl_3$) 1.24 (18H, br s, $C\underline{H}_2$), 1.35-1.58 (6H, m, $C\underline{H}_2CH_2O$ and $O_2CHC\underline{H}_2C\underline{H}_2C\underline{H}_2$), 1.72-1.85 (2H, m, $BrCH_2C\underline{H}_2$), 3.28-3.51 (2H, m, OC$\underline{H}$H'), 3.37 (2H, t, *J*7Hz, $BrC\underline{H}_2$), 3.64-3.89 (2H, m, OCH$\underline{H}$'), 4.54 (1H, pseudo t, *J*3.5Hz, OC$\underline{H}$O); δ_C (50MHz; $CDCl_3$) 19.6, 25.5, 26.2, 28.1, 28.7, 29.5, 29.7, 30.7, 32.8, 33.9, 62.2 and 67.6 (12 x $\underline{C}H_2$), 98.7 ($\underline{C}$H); *m/z* (CI, NH_3) 350 (MH^+, ^{81}Br, 13%), 348 (MH^+, ^{79}Br, 16), 102 ($DHPOH_2^+$, 72), 85 ($DHPH^+$, 100).

Synthesis of 3-(13-tetrahydropyran-2-yloxytridecyl)pyridine (17)

The title compound was synthesised similarly to **11**, using $^iPr_2NH$ (29.1ml, 207mmol), ^{n}BuLi (2.5M, 82.9ml, 207mmol) in hexane, DMPU (25.1ml, 207mmol), 3-methylpyridine (20.2ml, 207mmol) and 1-bromo-12-tetrahydropyran-2-yloxydodecane (**16**) (24.1g, 69.1mmol) in THF (250ml) to yield *3-(13-tetrahydropyran-2-yloxytridecyl)pyridine* (**17**) (21.7g, 87%) as a pale yellow oil; R_f 0.28 (base-washed SiO_2; PE 40-60: EtOAc: Et_3N; 95:5:3); ν_{max} (thin film)/cm^{-1} 2925s, 2854s, 1574m, 1466m, 1422m, 1352m, 1200m, 1120m, 1078m, 1034m, 714m; δ_H (200MHz; $CDCl_3$) 1.24 (20H, br s, $C\underline{H}_2$), 1.51-1.68 (8H, m, py$CH_2C\underline{H}_2$, $C\underline{H}_2CH_2O$

and $O_2CHCH_2CH_2CH_2$), 2.57 (2H, t, *J*7.5Hz, pyCH_2), 3.30-3.52 (2H, m, OCHH'), 3.65-3.90 (2H, m, OCHH'), 4.55 (1H, pseudo t, *J*3.5Hz, O_2CH), 7.16 (1H, dd, *J*8, 5Hz, C(5)H), 7.46 (1H, d, *J*7.5Hz, C(4)H), 8.39-8.42 (2H, m, C(2)H and C(6)H); δ_C (50MHz; $CDCl_3$) 19.7, 25.5, 26.2, 29.1, 29.4, 29.6, 29.7, 30.7, 31.1, 33.0, 62.3 and 67.6 (12 x CH_2), 98.8, 123.1 and 135.7 (3 x CH), 137.9 (quaternary), 147.1 and 150.0 (2 x CH); *m/z* (APCI) 362 (MH^+, 100%), 278 ([MH_2-THP]$^+$, 40); HRMS found 362.3069, $C_{23}H_{40}NO_2$ (MH^+) requires 362.3059.

Synthesis of 13-pyridin-3-yltridecan-1-ol (18)

The title compound was synthesised similarly to **12**, using 3-(13-tetrahydropyran-2-yloxytridecyl)pyridine (**17**) (21.5g, 59.6mmol) and 3M aq. HCl (40ml, 119mmol) in MeOH (150ml) to yield *13-pyridin-3-yltridecan-1-ol* (**18**) (15.0g, 91%) as white crystals. The solid was recrystallised from PE 40-60: EtOAc; m.p. 48-50°C (lit. [2] m.p. 44-47°C); R_f 0.25 (SiO_2; PE 40-60: EtOAc: Et_3N; 60:40:5); (Found: C, 78.1; H, 11.6; N, 4.7. $C_{18}H_{31}NO$ requires C, 77.9; H, 11.3; N, 5.1%); ν_{max} (KBr disk)/cm^{-1} 3271m br (OH), 2924s, 2852s, 1575m, 1467m, 1423m, 1074m, 1026m; δ_H (200MHz; $CDCl_3$) 1.14 (18H, br s, CH_2), 1.45-1.58 (4H, m, pyCH_2CH_2 and CH_2CH_2OH), 2.47 (2H, t, *J*7.5Hz, pyCH_2), 3.51 (2H, t, *J*6.5Hz, CH_2OH), 4.32 (1H, s, OH), 7.08 (1H, dd, *J*7.5, 5Hz, C(5)H), 7.37 (1H, d, *J*7.5Hz, C(4)H), 8.26-8.33 (2H, m, C(2)H and C(6)H); δ_C (50MHz; $CDCl_3$) 25.7, 28.9, 29.2, 29.4, 30.9, 32.7, 32.8 and 62.6 (8 x CH_2), 123.4 and 136.1 (2 x CH), 138.2 (quaternary), 147.1 and 149.9 (2 x CH); *m/z* (APCI) 278 (MH^+, 100%); HRMS found 278.2484, $C_{18}H_{32}NO$ (MH^+) requires 278.2484.

Synthesis of 3-(13-chlorotridecyl)pyridinium chloride (19)

The title compound was synthesised similarly to **13**, using $SOCl_2$ (2.48ml, 34.0mmol) and 13-pyridin-3-yltridecan-1-ol (**18**) (7.87g, 28.4mmol) in 1,4-dioxane (40ml) to give *3-(13-chlorotridecyl)pyridinium chloride* (**19**) (9.35g, 99%) as a white powder; m.p. 83-84°C; (Found: C, 64.9; H, 9.5; N, 4.1. $C_{18}H_{31}Cl_2N$ requires C, 65.1; H, 9.4; N, 4.2%); δ_H (200MHz; $CDCl_3$) 1.01 (18H, br s, CH_2), 1.44-1.54 (4H, m, pyCH_2CH_2 and CH_2CH_2Cl), 2.64 (2H, t, *J*7.5Hz, pyCH_2), 3.28 (2H, t, *J*6.5Hz, CH_2Cl), 7.84 (1H, dd, *J*8, 6Hz, C(5)H), 8.14 (1H, d, *J*8Hz, C(4)H), 8.47 (1H, s, C(2)H), 8.56 (1H, d, *J*6Hz, C(6)H); δ_C (50MHz; $CDCl_3$) 26.6, 28.6, 28.7, 29.0, 29.2, 30.2, 32.4, 32.5 and 45.0 (9 x CH_2), 126.9, 138.2 and 139.8 (3 x CH), 142.9 (quaternary), 145.7 (CH); *m/z* (APCI) 298 ([M-Cl]$^+$, ^{37}Cl, 44%), 296 ([M-Cl]$^+$, ^{35}Cl, 100).

3-(13-Chlorotridecyl)pyridine

3-(13-Chlorotridecyl)pyridinium chloride (**19**) was neutralised, in the same way as **13**, to afford *3-(13-chlorotridecyl)pyridine* (quant.) as a colourless oil; R_f 0.44 (SiO_2; PE 40-60: Et_2O; 1:1); ν_{max} (thin film)/cm^{-1} 2926s, 2854s, 1575m, 1478m, 1465m, 1422m, 1026m, 714m; δ_H (200MHz; $CDCl_3$) 1.24-1.43 (18H, br m, CH_2), 1.52-1.57 (2H, m, pyCH_2CH_2), 1.70 (2H,

pseudo qui, *J*6.5Hz, CH_2CH_2Cl), 2.57 (2H, t, *J*7.5Hz, $pyCH_2$), 3.50 (2H, t, *J*6.5Hz, CH_2Cl), 7.17 (1H, dd, *J*8, 5Hz, C(5)H), 7.46 (1H, d pseudo t, *J*8, 1.5Hz, C(4)H), 8.37-8.41 (2H, m, C(2)H and C(6)H); δ_C (50MHz; $CDCl_3$) 26.8, 28.8, 29.1, 29.4, 29.5, 31.1, 32.6, 33.0 and 45.1 (9 x CH_2), 123.2 and 135.7 (2 x CH), 137.9 (quaternary), 147.1 and 149.9 (2 x CH).

Synthesis of 3-(13-chlorotridecyl)pyridine-N-oxide (20)

The title compound was synthesised similarly to **14**, using 3-(13-chlorotridecyl)pyridine (3.00g, 10.2mmol) and *m*CPBA (89% active, 1.97g, 10.2mmol) in CH_2Cl_2 (40ml) to afford *3-(13-chlorotridecyl)pyridine-N-oxide* (**20**) (3.10g, 98%) as a white solid; m.p. 62-63°C; R_f 0.67 (Al_2O_3; CH_2Cl_2: MeOH; 98:2); ν_{max} ($CHCl_3$)/cm^{-1} 2917s, 2850s, 1472s, 1421m, 1262s, 1152s, 1014m, 718s; δ_H (200MHz; $CDCl_3$) 1.16-1.35 (18H, br m, CH_2), 1.47-1.54 (2H, m, $pyCH_2CH_2$), 1.66 (2H, pseudo qui, *J*7Hz, CH_2CH_2Cl), 2.47 (2H, t, *J*7.5Hz, $pyCH_2$), 3.42 (2H, t, *J*6.5Hz, CH_2Cl), 7.01-7.16 (2H, m, C(4)H and C(5)H), 7.95-7.99 (2H, m, C(2)H and C(6)H); δ_C (50MHz; $CDCl_3$) 26.7, 28.8, 29.2, 29.3, 29.4, 30.2, 32.5, 32.6 and 45.1 (9 x CH_2), 125.4, 126.7, 136.6 and 138.9 (4 x CH), 141.7(quaternary); *m/z* (APCI) 314 (MH^+, ^{37}Cl, 34%), 312 (MH^+, ^{35}Cl, 100); HRMS found 312.2095, $C_{18}H_{31}ClNO$ (MH^+, ^{35}Cl) requires 312.2094.

Synthesis of triphenyl-11-tetrahydropyran-2-yloxyundecylphosphonium bromide (21)

A solution of 1-bromo-11-tetrahydropyran-2-yloxyundecane (**10**) (15.0g, 44.7mmol) and Ph_3P (11.7g, 44.7mmol) in MeCN (100ml) was heated at reflux for 48h under argon. The solution was then concentrated *in vacuo* and chromatographed (SiO_2; CH_2Cl_2: MeOH; 95:5) to yield *triphenyl-11-tetrahydropyran-2-yloxyundecylphosphonium bromide* (**21**) (24.4g, 91%) as a colourless oil; R_f 0.23 (SiO_2; CH_2Cl_2: MeOH; 95:5); ν_{max} (thin film)/cm^{-1} 2927s, 2854s, 1587m, 1479s, 1438s, 1114s, 1077m, 1033s, 996m, 750m, 724s, 680s; δ_H (200MHz; $CDCl_3$) 1.13-1.75 (24H, br m, CH_2), 3.26-3.75 (6H, m, PCH_2 and $CH_2OCHOCH_2$), 4.47 (1H, dd, *J*4, 2.5Hz, OCHO), 7.58-7.78 (15H, m, phenyl CH); δ_C (50MHz; $CDCl_3$) 19.7 and 22.4 (2 x CH_2), 22.6 (d, *J*50Hz, C1), 25.4, 25.6, 26.1, 28.9, 29.0, 29.3, 29.6, 30.5, 30.7, 62.3 and 67.6 (11 x CH_2), 98.8 (CH), 118.1 (d, *J*86Hz, quaternary), 130.3, 130.6, 133.4, 133.6 and 135.0 (5 x CH); *m/z* (APCI) 517 ([M-Br]$^+$, 63%), 373 (36), 263 (100).

Synthesis of (Z)-3-(14-tetrahydropyran-2-yloxytetradec-3-enyl)pyridine (22)

A solution of triphenyl-11-tetrahydropyran-2-yloxyundecylphosphonium bromide (**21**) (21.7g, 36.4mmol) in THF (250ml) under argon was cooled to -78°C and a solution of 0.5M KHMDS in toluene (72.7ml, 36.4mmol) was added dropwise. The mixture was allowed to warm to room temperature over 1 hour to give a red solution. The mixture was cooled again to -78°C and a solution of 3-pyridin-3-ylpropanal (4.10g, 30.3mmol) in THF (20ml) was added *via* a cannula. The mixture was stirred at -78°C for 5 minutes and then allowed to warm to

room temperature over 2 hours. Water (100ml) was added to the black solution and the two yellow layers which formed were separated. The aq. layer was extracted with CH_2Cl_2 (2 x 100ml), dried with Na_2SO_4, filtered and concentrated *in vacuo* to give a yellow solid. Flash chromatography (base-washed SiO_2; PE 40-60: EtOAc: Et_3N; 95:5:3) yielded *(Z)-3-(14-tetrahydropyran-2-yloxytetradec-3-enyl)pyridine* (**22**) (8.04g, 71%, *Z:E*; 50:1 by proton NMR) as a colourless oil; R_f 0.27 (base-washed SiO_2; PE 40-60: EtOAc: Et_3N; 95:5:3; ammonium molybdate and UV); ν_{max} (thin film)/cm^{-1} 2925s, 2853s, 1574m, 1478m, 1422m, 1352m, 1200m, 1121m, 1078m, 1032m, 714m; δ_H (400MHz; C_6D_6) 1.14-1.41 (16H, br m, C$\underline{H}_2$), 1.53-1.64 (6H, m, C$\underline{H}_2$C$\underline{H}_2$O and O$_2$CHC$\underline{H}_2$C$\underline{H}_2$C$\underline{H}_2$), 1.82-1.89 (2H, m, py(CH$_2$)$_2$CH=CHC$\underline{H}_2$), 2.12-2.20 (2H, m, pyCH$_2$C$\underline{H}_2$), 2.34 (2H, t, *J*7.5Hz, pyC$\underline{H}_2$), 3.28-3.41 (2H, m, OC$\underline{H}$H'), 3.76-3.82 (2H, m, OCH$\underline{H}$'), 4.57 (1H, pseudo t, *J*3.5Hz, O$_2$C$\underline{H}$), 5.23-5.30 (1H, m, py(CH$_2$)$_2$C$\underline{H}$=CH), 5.34-5.40 (1H, m, py(CH$_2$)$_2$CH=C$\underline{H}$), 6.78 (1H, dd, *J*7.5, 4.5Hz, C(5)$\underline{H}$), 7.04 (1H, d pseudo t, *J*7.5, 2Hz, C(4)$\underline{H}$), 8.42 (1H, dd, *J*4.5, 1.5Hz, C(6)$\underline{H}$), 8.47 (1H, d, *J*2Hz, C(2)$\underline{H}$); δ_C (50MHz; C_6D_6) 19.7, 26.1, 26.9, 27.6, 29.1, 29.7, 30.0, 30.4, 31.2, 33.2, 61.6 and 67.6 (12 x $\underline{C}H_2$), 98.6, 123.1, 128.3, 131.4 and 135.4 (5 x $\underline{C}$H), 137.1 (quaternary), 147.9 and 150.7 (2 x $\underline{C}$H); *m/z* (APCI) 374 (MH$^+$, 24%), 290 ([MH$_2$-THP]$^+$, 100); HRMS found 374.3059, $C_{24}H_{40}NO_2$ (MH$^+$) requires 374.3059.

Synthesis of (Z)-14-pyridin-3-yltetradec-11-en-1-ol (23)

The title compound was synthesised similarly to **12**, using (Z)-3-(14-tetrahydropyran-2-yloxytetradec-3-enyl)pyridine (**22**) (7.38g, 19.8mmol) and 3M aq. HCl (13.2ml, 39.5mmol) in MeOH (100ml)to yield *(Z)-14-pyridin-3-yltetradec-11-en-1-ol* (**23**) (5.62g, 98%) as a colourless oil; R_f 0.22 (SiO_2; PE 40-60: EtOAc: Et_3N; 70:20:10); ν_{max} (thin film)/cm^{-1} 3339m br (OH), 3006m, 2925s, 2854s, 1579m, 1479m, 1424m, 1059m, 1030m, 714m; δ_H (200MHz; C_6D_6) 1.22-1.57 (14H, m, C$\underline{H}_2$), 1.60-1.71 (2H, m, C$\underline{H}_2$CH$_2$OH), 1.88 (2H, br d, *J*6.5Hz, py(CH$_2$)$_2$CH=CHC$\underline{H}_2$), 2.14 (2H, pseudo q, *J*7Hz, pyCH$_2$C$\underline{H}_2$), 2.31 (2H, t, *J*7Hz, pyC$\underline{H}_2$), 3.70 (2H, t, *J*6.5Hz, C$\underline{H}_2$OH), 4.08 (1H, br s, O$\underline{H}$), 5.21-5.47 (2H, m, C$\underline{H}$=C$\underline{H}$), 6.75 (1H, dd, *J*8, 5Hz, C(5)$\underline{H}$), 7.02 (1H, d pseudo t, *J*8, 2Hz, C(4)$\underline{H}$), 8.39 (1H, dd, *J*5, 1.5Hz, C(6)$\underline{H}$), 8.44 (1H, d, *J*2Hz, C(2)$\underline{H}$); δ_C (50MHz; C_6D_6) 26.5, 27.6, 29.1, 29.6, 30.0, 30.1, 30.2, 33.2, 33.6 and 62.5 (10 x $\underline{C}H_2$), 123.4, 128.2, 131.5 and 135.9 (4 x $\underline{C}$H), 137.4 (quaternary), 147.6 and 150.4 (2 x $\underline{C}$H); *m/z* (APCI) 290 (MH$^+$, 100%), 272 (16); HRMS found 290.2489, $C_{19}H_{32}NO$ (MH$^+$) requires 290.2484.

Synthesis of 14-pyridin-3-yltetradecan-1-ol (24)

To a solution of (Z)-14-pyridin-3-yltetradec-11-en-1-ol (**23**) (4.30g, 14.9mmol) in EtOH (50ml) was added 10% Pd-C (430mg, 10% w/w) and the mixture stirred under a hydrogen atmosphere for 10 hours at room temperature. The reaction mixture was filtered through a pad of Celite® and the filtrate was concentrated *in vacuo* to give *14-pyridin-3-yltetradecan-1-ol*

(**24**) (4.31g, 100%) as a white powder. The powder was recrystallised from PE 40-60: EtOAc to afford *14-pyridin-3-yltetradecan-1-ol* (**24**) (4.03g, 93%) as white crystals; m.p. 61-62°C (lit. [11] m.p. 57-59°C); R_f 0.33 (SiO_2; PE 40-60: EtOAc: Et_3N; 70:20:10); (Found: C, 78.0; H, 11.65; N, 4.7. $C_{19}H_{33}NO$ requires C, 78.3; H, 11.4; N, 4.8%); ν_{max} ($CHCl_3$)/cm^{-1} 3330m br (OH), 2915s, 2848s, 1578m, 1463s, 1424s, 1070s, 755s, 715s, 668s; δ_H (200MHz; $CDCl_3$) 1.22 (20H, br s, $C\underline{H}_2$), 1.47-1.57 (4H, m, $pyCH_2C\underline{H}_2$ and $C\underline{H}_2CH_2OH$), 2.56 (2H, t, *J*7.5Hz, $pyC\underline{H}_2$), 3.02 (1H, br s, O<u>H</u>), 3.60 (2H, t, *J*6.5Hz, $C\underline{H}_2OH$), 7.17 (1H, dd, *J*7.5, 5Hz, C(5)<u>H</u>), 7.46 (1H, br d, *J*8Hz, C(4)<u>H</u>), 8.35-8.38 (2H, m, C(2)<u>H</u> and C(6)<u>H</u>); δ_C (50MHz; $CDCl_3$) 25.8, 29.1, 29.3, 29.5, 29.6, 31.1, 32.8, 32.9 and 62.6 (9 x $\underline{C}H_2$), 123.3 and 135.9 (2 x <u>C</u>H), 138.0 (quaternary), 146.9 and 149.7 (2 x <u>C</u>H); *m/z* (APCI) 292 (MH^+, 100%), 274 (16); HRMS found 292.2640, $C_{19}H_{34}NO$ (MH^+) requires 292.2640.

Synthesis of 3-(14-chlorotetradecyl)pyridinium chloride (25)

The title compound was synthesised similarly to **13**, using $SOCl_2$ (0.30ml, 4.12mmol) and 14-pyridin-3-yltetradecan-1-ol (**24**) (1.00g, 3.43mmol) in 1,4-dioxane (5ml) to give *3-(14-chlorotetradecyl)pyridinium chloride* (**25**) (1.19g, 100%) as white crystals; m.p. 115-116°C; (Found: C, 66.1; H, 9.9; N, 4.1. $C_{19}H_{33}Cl_2N$ requires C, 65.9; H, 9.6; N, 4.0%); δ_H (200MHz; $CDCl_3$) 1.16 (20H, br s, $C\underline{H}_2$), 1.57-1.69 (4H, m, $pyCH_2C\underline{H}_2$ and $C\underline{H}_2CH_2Cl$), 2.77 (2H, t, *J*7.5Hz, $pyC\underline{H}_2$), 3.43 (2H, t, *J*6.5Hz, $C\underline{H}_2Cl$), 7.89 (1H, dd, *J*8, 5.5Hz, C(5)<u>H</u>), 8.22 (1H, d, *J*8Hz, C(4)<u>H</u>), 8.58 (1H, s, C(2)<u>H</u>), 8.67 (1H, d, *J*5.5Hz, C(6)<u>H</u>); δ_C (50MHz; $CDCl_3$) 26.7, 28.7, 29.0, 29.2, 29.3, 30.2, 32.4, 32.6 and 45.1 (9 x $\underline{C}H_2$), 127.0, 138.5 and 140.3 (3 x <u>C</u>H), 143.3 (quaternary), 145.8 (<u>C</u>H); *m/z* (APCI) 312 ([M-Cl]$^+$, ^{37}Cl, 48%), 310 ([M-Cl]$^+$, ^{35}Cl, 100).

3-(14-Chlorotetradecyl)pyridine

3-(14-Chlorotetradecyl)pyridinium chloride (**25**) was neutralised, in the same way as **13**, to afford *3-(14-Chlorotetradecyl)pyridine* (quant.) as a colourless oil; R_f 0.43 (SiO_2; PE 40-60: Et_2O; 1:1); ν_{max} (thin film)/cm^{-1} 2927s, 2854s, 1574m, 1478m, 1464m, 1422m, 1026m, 714m; δ_H (200MHz; $CDCl_3$) 1.25-1.44 (20H, br m, $C\underline{H}_2$), 1.57-1.64 (2H, m, $pyCH_2C\underline{H}_2$), 1.76 (2H, pseudo qui, *J*6.5Hz, $C\underline{H}_2CH_2Cl$), 2.59 (2H, t, *J*7.5Hz, $pyC\underline{H}_2$), 3.52 (2H, t, *J*6.5Hz, $C\underline{H}_2Cl$), 7.19 (1H, dd, *J*8, 5Hz, C(5)<u>H</u>), 7.48 (1H, d pseudo t, *J*8, 2Hz, C(4)<u>H</u>), 8.40-8.44 (2H, m, C(2)<u>H</u> and C(6)<u>H</u>); δ_C (50MHz; $CDCl_3$) 26.9, 28.9, 29.1, 29.5, 29.6, 31.1, 32.6, 33.0 and 45.2 (9 x $\underline{C}H_2$), 123.2 and 135.7 (2 x <u>C</u>H), 138.0 (quaternary), 147.1 and 149.9 (2 x <u>C</u>H).

Synthesis of 3-(14-chlorotetradecyl)pyridine-N-oxide (26)

The title compound was synthesised similarly to **14**, using 3-(14-chlorotetradecyl)pyridine (390mg, 1.25mmol) and *m*CPBA (89% active, 243mg, 1.25mmol) in CH_2Cl_2 (20ml)to afford

3-(14-chlorotetradecyl)pyridine-N-oxide (**26**) (408mg, 100%) as a hygroscopic white solid; R_f 0.44 (Al_2O_3; CH_2Cl_2: MeOH; 99:1); ν_{max} ($CHCl_3$)/cm^{-1} 2925s, 2853s, 1604m, 1482s, 1466m, 1438m, 1272m, 1159m, 1016m, 731m; δ_H (200MHz; $CDCl_3$) 1.06 (20H, br s, C$\underline{H}_2$), 1.35-1.58 (2H, m, pyCH$_2$C$\underline{H}_2$), 1.56 (2H, pseudo qui, *J*7Hz, C$\underline{H}_2$CH$_2$Cl), 2.38 (2H, t, *J*7.5Hz, pyC$\underline{H}_2$), 3.32 (2H, t, *J*6.5Hz, C$\underline{H}_2$Cl), 6.91-7.08 (2H, m, C(4)$\underline{H}$ and C(5)$\underline{H}$), 7.87-7.91 (2H, m, C(2)$\underline{H}$ and C(6)$\underline{H}$); δ_C (50MHz; $CDCl_3$) 26.6, 28.6, 29.0, 29.2, 29.3, 30.0, 32.4 and 44.9 (8 x $\underline{C}H_2$), 125.5, 126.6, 136.7 and 139.0 (4 x $\underline{C}$H), 141.8 (quaternary); *m/z* (APCI) 328 (MH$^+$, ^{37}Cl, 36%), 326 (MH$^+$, ^{35}Cl, 100), 310 (37); HRMS found 326.2252, $C_{19}H_{33}ClNO$ (MH$^+$, ^{35}Cl) requires 326.2251.

Synthesis of 3-(12-hydroxydodecyl)-1-[12-(N-oxidopyridin-3-yl)dodecyl]pyridinium iodide (27)

To a solution of 12-pyridin-3-yldodecan-1-ol (**12**) (970mg, 3.68mmol) and NaI (662mg, 4.42mmol) in butan-2-one (50ml) was added 3-(12-chlorododecyl)pyridine-*N*-oxide (**14**) (1.15g, 3.85mmol). The orange solution was heated at reflux for 24 hours, cooled to room temperature and then concentrated *in vacuo* to give an off-white solid. Flash chromatography (Al_2O_3; CH_2Cl_2: MeOH; 9:1) afforded *3-(12-hydroxydodecyl)-1-[12-(N-oxidopyridin-3-yl)dodecyl]pyridinium iodide* (**27**) (2.45g, quant.) as an off-white solid; m.p. 96-99°C, R_f 0.63 (Al_2O_3; CH_2Cl_2: MeOH; 9:1; UV); R_f 0.43 (SiO_2/NaBr [20]; CH_2Cl_2: MeOH; 9:1); ν_{max} (KBr disk)/cm^{-1} 3394m br (OH), 2919s, 2850s, 1467m, 1438m, 1267m, 1159m, 682m; δ_H (200MHz; $CDCl_3$) 1.09 (32H, br s, C$\underline{H}_2$), 1.32-1.67 (6H, m, C$\underline{H}_2$CH$_2$OH, C(3')CH$_2$C$\underline{H}_2$ and C(3)CH$_2$C$\underline{H}_2$), 1.86-1.98 (2H, m, C$\underline{H}_2$CH$_2$N), 2.43 (2H, t, *J*7.5Hz, C(3')C$\underline{H}_2$), 2.77 (2H, t, *J*7.5Hz, C(3)C$\underline{H}_2$), 3.16 (1H, br s, O$\underline{H}$), 3.45 (2H, t, *J*6.5Hz, C$\underline{H}_2$OH), 4.76 (2H, t, *J*7Hz, C$\underline{H}_2$N), 7.03-7.17 (2H, m, C(4')$\underline{H}$ and C(5')$\underline{H}$), 7.91-8.01 (3H, m, C(2')$\underline{H}$, C(5)$\underline{H}$ and C(6')$\underline{H}$), 8.20 (1H, d, *J*8Hz, C(4)$\underline{H}$), 9.12 (1H, d, *J*6Hz, C(6)$\underline{H}$), 8.22 (1H, s, C(2)$\underline{H}$); δ_C (50MHz; $CDCl_3$) 25.7, 25.9, 28.7, 28.9, 29.1 and 29.3 (6 x $\underline{C}H_2$), 30.2 and 30.3 (C(3')CH$_2$$\underline{C}H_2$ and C(3)CH$_2$$\underline{C}H_2$), 31.8 ($\underline{C}H_2CH_2$N), 32.5 (C(3')$\underline{C}H_2$ and C(3)$\underline{C}$H$_2$), 32.7 ($\underline{C}$H$_2$CH$_2$OH), 61.5 ($\underline{C}$H$_2$N), 62.3 ($\underline{C}$H$_2$OH), 125.7 (C5'), 127.2 (C4'), 128.1 (C5), 136.5 and 138.6 (C2' and C6'), 141.8 (C3'), 142.2 (C6), 143.9 (C2), 144.1 (C3), 144.9 (C4); *m/z* (ES) 525.5 ([M-I]$^+$, 100%); HRMS found 525.4417, $C_{34}H_{57}N_2O_2$ ([M-I]$^+$) requires 525.4420.

Synthesis of 3-(12-bromododecyl)-1-[12-(pyridin-3-io)dodecyl]pyridinium bromide

To a solution of 3-(12-hydroxydodecyl)-1-[12-(*N*-oxidopyridin-3-yl)dodecyl]pyridinium iodide (**27**) (2.03g, 3.11mmol) in $CHCl_3$ (60ml) at 0°C under argon was added phosphorus tribromide (1.17ml, 12.5mmol) dropwise. The solution was stirred for 15 minutes at 0°C, heated at reflux for 1 hour, cooled to room temperature and then poured into an ice: water solution (50ml). The two-phase mixture was stirred, until the ice melted, then separated. The aq. phase was extracted with CH_2Cl_2 (3 x 50ml), and the organic phases were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give *3-(12-bromododecyl)-1-[12-(pyridin-3-*

io)dodecyl]pyridinium bromide (2.32g, 98%) as a yellow oil; ν_{max} (thin film)/cm^{-1} 2924s, 2853s, 1630m, 1551m, 1504m, 1466m, 687m; δ_H (200MHz; $CDCl_3$) 1.09-1.18 (32H, br m, CH_2), 1.58-1.78 (6H, m, C(3')CH_2CH_2, C(3)CH_2CH_2 and CH_2CH_2Br), 1.88-1.95 (2H, m, CH_2CH_2N), 2.73-2.84 (4H, m, C(3')CH_2 and C(3)CH_2), 3.28 (2H, t, *J*7Hz, CH_2Br), 4.83 (2H, t, *J*7.5Hz, CH_2N), 7.98-8.09 (2H, m, C(5')H and C(5)H), 8.20 (1H, d, *J*8Hz, C(4)H), 8.38 (1H, d, *J*8Hz, C(4')H), 8.53 (1H, s, C(2')H), 8.65 (1H, br d, *J*5Hz, C(6')H), 9.20 (1H, d, *J*6Hz, C(6)H), 9.24 (1H, s, C(2)H); δ_C (50MHz; $CDCl_3$) 25.9, 28.0, 28.6, 28.9, 29.1 and 29.3 (6 x CH_2), 30.1 and 30.3 (C(3')CH_2CH_2 and C(3)CH_2CH_2), 31.9 (CH_2CH_2N), 32.6 (C(3')CH_2, C(3)CH_2 and CH_2CH_2Br), 34.2 (CH_2Br), 61.7 (CH_2N), 127.5 (C5'), 128.1 (C5), 138.0 (C6'), 139.4 (C2'), 142.3 (C6), 143.3 (C3'), 143.9 (C2), 144.1 (C3), 144.9 (C4), 146.8 (C4').

3-(12-Bromododecyl)-1-(12-pyridin-3-yldodecyl)pyridinium bromide (28)

3-(12-Bromododecyl)-1-[12-(pyridin-3-io)dodecyl]pyridinium bromide was neutralised by being dissolved in CH_2Cl_2 and dried over K_2CO_3, filtered and concentrated *in vacuo* to afford *3-(12-bromododecyl)-1-(12-pyridin-3-yldodecyl)pyridinium bromide* (**28**) (quant.) as a yellow oil; δ_H (200MHz; $CDCl_3$) 1.17-1.45 (32H, br m, CH_2), 1.54-1.91 (6H, m, C(3')CH_2CH_2, C(3)CH_2CH_2 and CH_2CH_2Br), 1.97-2.10 (2H, m, CH_2CH_2N), 2.61 (2H, t, *J*7.5Hz, C(3')CH_2), 2.90 (2H, t, *J*8Hz, C(3)CH_2), 3.40 (2H, t, *J*7Hz, CH_2Br), 4.95 (2H, t, *J*7.5Hz, CH_2N), 7.23-7.27 (1H, m, C(5')H), 7.56 (1H, d, *J*6.5Hz, C(4')H), 8.03 (1H, dd, *J*8, 6Hz, C(5)H), 8.24 (1H, d, *J*8Hz, C(4)H), 8.45 (2H, br s, C(2')H and C(6')H), 9.16 (1H, s, C(2)H), 9.25 (1H, d, *J*6Hz, C(6)H); *m/z* (FAB) 573.5 ([M-Br]$^+$, ^{81}Br, 95%), 571.5 ([M-Br]$^+$, ^{79}Br, 100), 328 ($C_{17}H_{29}NBr^+$, ^{81}Br, 16), 326 ($C_{17}H_{29}NBr^+$, ^{79}Br, 18), 246 ($C_{17}H_{28}N^+$, 50); HRMS found 573.3608, $C_{34}H_{56}BrN_2$ ([M-Br]$^+$, ^{81}Br) requires 573.3606.

Synthesis of cyclostellettamine A (1)

To a solution of NaI (1.01g, 6.75mmol) in butan-2-one (310ml) heated at reflux was added a solution of 3-(12-bromododecyl)-1-(12-pyridin-3-yldodecyl)pyridinium bromide (**28**) (2.00g, 3.07mmol) in butan-2-one (9ml) and $CHCl_3$ (1ml) at a rate of 0.01ml/minute over 24 hours. The orange solution was heated at reflux for 3 days, cooled to room temperature and then concentrated *in vacuo* to give an off-white powder. The powder was triturated with Et_2O (2 x 40ml), to remove any unreacted iodide. Flash chromatography (Al_2O_3; CH_2Cl_2: MeOH; 9:1) followed by recrystallisation from acetone afforded *cyclostellettamine A* (**1**) (1.52g, 66%) as an off-white powder; m.p. 218-220°C (lit. [11] m.p. 221-223°C); (Found: C, 54.6; H, 7.6; N, 3.7. $C_{34}H_{56}I_2N_2$ requires C, 54.7; H, 7.55; N, 3.8%); R_f 0.19 (Al_2O_3; CH_2Cl_2: MeOH; 9:1); ν_{max} (KBr disk)/cm^{-1} 3016m, 2921s, 2850s, 1626m, 1504s, 1465s, 692m; δ_H (200MHz; $CDCl_3$: CD_3OD; 9:1) 0.95-1.26 (32H, br m, CH_2), 1.56 (4H, br s, C(3)CH_2CH_2), 1.86 (4H, br s, NCH_2CH_2), 2.75 (4H, t, *J*7.5Hz, C(3)CH_2), 4.62 (4H, t, *J*7Hz, NCH_2), 7.89 (2H, dd, *J*8, 6Hz, C(5)H), 8.17 (2H, d, *J*8Hz, C(4)H), 8.82 (2H, d, *J*6Hz, C(6)H), 9.03 (2H, s, C(2)H); δ_C

(50MHz; $CDCl_3$: CD_3OD; 9:1) 26.9, 29.7, 29.9, 30.1, 30.2 and 30.7 (6 x $\underline{C}H_2$), 31.6 (C(3)$CH_2\underline{C}H_2$), 33.0 ($NCH_2\underline{C}H_2$), 33.8 (C(3)$\underline{C}H_2$), 63.2 ($N\underline{C}H_2$), 129.6 (C5), 143.4 (C6), 145.4 (C2), 145.8 (C3), 146.8 (C4); *m/z* (FAB) 619.5 ($[M-I]^+$, 100%), 246 ($[M-2I]^{2+}$, 28); HRMS found 619.3510, $C_{34}H_{56}IN_2$ ($[M-I]^+$) requires 619.3488.

Synthesis of 1,18-diazatricyclo[29.3.1.1^{14,18}]hexatriaconta-14,31-diene (39)

Cyclostellettamine A (**1**) (105mg, 0.14mmol) was dissolved in MeOH (40ml) and CH_2Cl_2 (10ml), then cooled to -78°C. $NaBH_4$ (32mg, 0.84mmol) was added and the mixture was stirred for 30 minutes, after which it was allowed to warm to 0°C over 1 hour. The mixture was concentrated *in vacuo* and then partitioned between sat. aq. $NaHCO_3$ (20ml) and CH_2Cl_2 (20ml). The two-phase solution was separated and the aq. phase extracted with CH_2Cl_2 (3 x 20ml). The combined organic phases were washed with sat. aq. NaCl (20ml), dried over $MgSO_4$, filtered and concentrated *in vacuo* to give a colourless oil. Flash chromatography (base-washed SiO_2; PE 40-60: EtOAc: Et_3N; 97:3:2) afforded *1,18-diazatricyclo[29.3.1.1^{14,18}]hexatriaconta-14,31-diene* (**39**) (57mg, 81%) (<4% of the tetrahydropyridine regioisomer) as a white solid; m.p. 89-90°C; R_f 0.28 (base-washed SiO_2; PE 40-60: EtOAc: Et_3N; 97:3:2); ν_{max} (KBr disk)/cm^{-1} 2917s, 2850s, 1471m; δ_H (200MHz; $CDCl_3$) 1.26 (36H, br s, $C\underline{H}_2$), 1.50-1.59 (4H, m, $NCH_2C\underline{H}_2CH_2$), 1.93 (4H, t, *J*7Hz, C(3)$C\underline{H}_2$), 2.14 (4H, br s, C(5)$\underline{H}_2$), 2.35-2.43 (4H, m, $NC\underline{H}_2(CH_2)_2$), 2.48 (4H, t, *J*6Hz, C(6)$\underline{H}_2$), 2.84 (4H, s, C(2)$\underline{H}_2$), 5.42 (2H, br s, C(4)$\underline{H}$); δ_C (50MHz; $CDCl_3$) 25.7, 26.8, 27.3, 27.7, 29.0, 35.4, 50.6, 55.2 and 58.2 (9 x $\underline{C}H_2$), 118.9 ($\underline{C}H$), 136.6 (quaternary); *m/z* (APCI) 499.5 (MH^+, 100%); HRMS found 499.4990, $C_{34}H_{63}N_2$ (MH^+) requires 499.4991.

Synthesis of 3-(12-hydroxydodecyl)-1-[13-(N-oxidopyridin-3-yl)tridecyl]pyridinium iodide (29)

The title compound was synthesised similarly to **27**, using 12-pyridin-3-yldodecan-1-ol (**12**) (498mg, 1.89mmol), 3-(13-chlorotridecyl)pyridine-*N*-oxide (**20**) (590mg, 1.89mmol) and NaI (340mg, 2.27mmol) in butan-2-one (10ml) to afford *3-(12-hydroxydodecyl)-1-[13-(N-oxidopyridin-3-yl)tridecyl]pyridinium iodide* (**29**) (1.23g, 97%) as an off-white powder; m.p. 100-103°C, R_f 0.65 (Al_2O_3; CH_2Cl_2: MeOH; 9:1; UV); R_f 0.24 (SiO_2/NaBr [20]; CH_2Cl_2: MeOH; 9:1); ν_{max} (KBr disk)/cm^{-1} 3370m br (OH), 2924s, 2853s, 1464m, 1436m, 1267m, 1159m, 734m, 684m; δ_H (200MHz; $CDCl_3$) 1.15 (34H, br s, $C\underline{H}_2$), 1.38-1.69 (6H, m, $C\underline{H}_2CH_2OH$, C(3')$CH_2C\underline{H}_2$ and C(3)$CH_2C\underline{H}_2$), 1.89-2.03 (2H, m, $C\underline{H}_2CH_2N$), 2.49 (2H, t, *J*7.5Hz, C(3')$C\underline{H}_2$), 2.82 (2H, t, *J*7.5Hz, C(3)$C\underline{H}_2$), 3.15 (1H, br s, O$\underline{H}$), 3.51 (2H, t, *J*6Hz, $C\underline{H}_2OH$), 4.85 (2H, t, *J*6.5Hz, $C\underline{H}_2N$), 7.06-7.17 (2H, m, C(4')$\underline{H}$ and C(5')$\underline{H}$), 7.98-8.06 (3H, m, C(2')$\underline{H}$, C(5)$\underline{H}$ and C(6')$\underline{H}$), 8.20 (1H, d, *J*7.5Hz, C(4)$\underline{H}$), 9.27 (2H, br s, C(2)$\underline{H}$ and C(6)$\underline{H}$); δ_C (50MHz; $CDCl_3$) 25.6, 25.9, 28.7, 28.8, 28.9, 29.0 and 29.2 (7 x $\underline{C}H_2$), 30.1 and 30.3 (C(3')$CH_2\underline{C}H_2$ and C(3)$CH_2\underline{C}H_2$), 31.8 ($\underline{C}H_2CH_2N$), 32.5 (C(3')$\underline{C}H_2$ and C(3)$\underline{C}H_2$), 32.7 ($\underline{C}H_2CH_2OH$), 61.7 ($\underline{C}H_2N$), 62.4 ($\underline{C}H_2OH$), 125.8 (C5'), 127.3 (C4'), 128.2 (C5), 136.7 and

138.9 (C2' and C6'), 142.0 (C3'), 142.7 (C6), 144.2 (C2), 144.3 (C3), 144.9 (C4); *m/z* (FAB) 539.5 ([M-I]$^+$, 100%), 523.5 ([M-IO]$^+$, 17); HRMS found 539.4579, $C_{35}H_{59}N_2O_2$ ([M-I]$^+$) requires 539.4577.

Synthesis of 3-(12-bromododecyl)-1-(13-pyridin-3-yltridecyl)pyridinium bromide (30)

The title compound was synthesised similarly to **28**, using 3-(12-hydroxydodecyl)-1-[13-(*N*-oxidopyridin-3-yl)tridecyl]pyridinium iodide (**29**) (1.17g, 1.75mmol) and phosphorus tribromide (0.66ml, 6.99mmol) in $CHCl_3$ (50ml) to give *3-(12-bromododecyl)-1-[13-(pyridin-3-io)tridecyl]pyridinium bromide* (1.29g, 99%) as a pale yellow oil; ν_{max} (thin film)/cm^{-1} 2925s, 2853s, 1631m, 1552m, 1504m, 1467m, 752m, 687m; δ_H (200MHz; $CDCl_3$) 1.13-1.21 (34H, br m, C$\underline{H}_2$), 1.61-1.82 (6H, m, C(3')CH$_2$C$\underline{H}_2$, C(3)CH$_2$C$\underline{H}_2$ and C$\underline{H}_2$CH$_2$Br), 1.94-2.05 (2H, m, C$\underline{H}_2$CH$_2$N), 2.76-2.87 (4H, m, C(3')C$\underline{H}_2$ and C(3)C$\underline{H}_2$), 3.31 (2H, t, *J*7Hz, C$\underline{H}_2$Br), 4.87 (2H, t, *J*7.5Hz, C$\underline{H}_2$N), 8.01-8.10 (2H, m, C(5')$\underline{H}$ and C(5)$\underline{H}$), 8.23 (1H, d, *J*8Hz, C(4)$\underline{H}$), 8.39 (1H, d, *J*8Hz, C(4')$\underline{H}$), 8.56 (1H, s, C(2')$\underline{H}$), 8.68 (1H, d, *J*5.5Hz, C(6')$\underline{H}$), 9.25 (1H, d, *J*6Hz, C(6)$\underline{H}$), 9.28 (1H, s, C(2)$\underline{H}$); δ_C (50MHz; $CDCl_3$) 25.9, 28.0, 28.6, 28.9, 29.1 and 29.3 (6 x $\underline{C}H_2$), 30.2 and 30.4 (C(3')CH$_2$$\underline{C}H_2$ and C(3)CH$_2$$\underline{C}H_2$), 31.9 ($\underline{C}H_2CH_2$N), 32.5 and 32.7 (C(3')$\underline{C}H_2$, C(3)$\underline{C}H_2$ and $\underline{C}$H$_2$CH$_2$Br), 34.2 ($\underline{C}$H$_2$Br), 61.7 ($\underline{C}$H$_2$N), 127.4 (C5'), 128.1 (C5), 138.1 (C6'), 139.5 (C2'), 142.3 (C6), 143.2 (C3'), 143.9 (C2), 144.1 (C3), 144.8 (C4), 146.6 (C4'). 3-(12-Bromododecyl)-1-[13-(pyridin-3-io)tridecyl]pyridinium bromide was neutralised to afford *3-(12-bromododecyl)-1-(13-pyridin-3-yltridecyl)pyridinium bromide* (**30**) (quant.) as a pale yellow oil; δ_H (200MHz; $CDCl_3$) 1.13-1.46 (34H, br m, C$\underline{H}_2$), 1.57-1.88 (6H, m, C(3')CH$_2$C$\underline{H}_2$, C(3)CH$_2$C$\underline{H}_2$ and C$\underline{H}_2$CH$_2$Br), 2.00-2.08 (2H, m, C$\underline{H}_2$CH$_2$N), 2.62 (2H, t, *J*7.5Hz, C(3')C$\underline{H}_2$), 2.90 (2H, t, *J*8Hz, C(3)C$\underline{H}_2$), 3.40 (2H, t, *J*7Hz, C$\underline{H}_2$Br), 4.96 (2H, t, *J*7.5Hz, C$\underline{H}_2$N), 7.26 (1H, dd, *J*7.5, 5Hz, C(5')$\underline{H}$), 7.55 (1H, d, *J*7.5Hz, C(4')$\underline{H}$), 8.02 (1H, dd, *J*8, 6Hz, C(5)$\underline{H}$), 8.24 (1H, d, *J*8Hz, C(4)$\underline{H}$), 8.42-8.45 (2H, m, C(2')$\underline{H}$ and C(6')$\underline{H}$), 9.12 (1H, s, C(2)$\underline{H}$), 9.26 (1H, d, *J*6Hz, C(6)$\underline{H}$); *m/z* (FAB) 587.5 ([M-Br]$^+$, ^{81}Br, 97%), 585.5 ([M-Br]$^+$, ^{79}Br, 100), 260 ($C_{18}H_{30}N^+$, 21); HRMS found 585.3783, $C_{35}H_{58}BrN_2$ ([M-Br]$^+$, ^{79}Br) requires 585.3783.

Synthesis of cyclostellettamine B (2)

The title compound was synthesised similarly to **1**, using 3-(12-bromododecyl)-1-(13-pyridin-3-yltridecyl)pyridinium bromide (**30**) (921mg, 1.38mmol) in butan-2-one (9ml) and $CHCl_3$ (1ml), and NaI (455mg, 3.04mmol) in butan-2-one (150ml) to afford *cyclostellettamine B* (**2**) (715mg, 68%) as an off-white powder; m.p. 222-224°C (lit. [11] m.p. 222-224°C); (Found: C, 55.2; H, 7.85; N, 3.7. $C_{35}H_{58}I_2N_2$ requires C, 55.3; H, 7.7; N, 3.7%); R_f 0.24 (Al_2O_3; CH_2Cl_2: MeOH; 9:1); ν_{max} (KBr disk)/cm^{-1} 3017m, 2921s, 2850s, 1627m, 1504s, 1464s, 691s; δ_H (200MHz; $CDCl_3$: CD_3OD; 9:1) 1.04-1.23 (34H, br m, C$\underline{H}_2$), 1.55 (4H, br s, C(3)CH$_2$C$\underline{H}_2$), 1.85 (4H, br s, NCH$_2$C$\underline{H}_2$), 2.75 (4H, t, *J*7Hz, C(3)C$\underline{H}_2$), 4.62 (4H, t, *J*7Hz,

$NC\underline{H}_2$), 7.91 (2H, dd, *J*8, 6Hz, C(5)H), 8.18 (2H, d, *J*8Hz, C(4)H), 8.84 (2H, d, *J*5.5Hz, C(6)H), 8.94 (2H, s, C(2)H); δ_C (50MHz; $CDCl_3$: CD_3OD; 9:1) 25.3, 25.5, 28.0, 28.1, 28.2, 28.3, 28.4, 28.7* and 28.9 (10 x $\underline{C}H_2$), 29.9 and 30.0 (C(3)$CH_2\underline{C}H_2$), 31.2 and 31.3 ($NCH_2\underline{C}H_2$), 32.1 and 32.2 (C(3)$\underline{C}H_2$), 61.7 ($N\underline{C}H_2$), 128.3 (C5), 142.1 (C6), 143.9 (C2), 144.4 (C3), 145.5 (C4); *at this resonance two signals can be resolved; *m/z* (FAB) 633.5 ($[M-I]^+$, 100%); HRMS found 633.3641, $C_{35}H_{58}IN_2$ ($[M-I]^+$) requires 633.3645.

Synthesis of 1,18-diazatricyclo[30.3.1.1^{14,18}]heptatriaconta-14,32-diene (40)

The title compound was synthesised similarly to **39**, using cyclostellettamine B (**2**) (95mg, 0.13mmol) and $NaBH_4$ (28mg, 0.75mmol) in MeOH (40ml) and CH_2Cl_2 (10ml), to afford *1,18-diazatricyclo[30.3.1.1^{14,18}]heptatriaconta-14,32-diene* (**40**) (59mg, 92%) (<7% of the tetrahydropyridine regioisomer) as a white solid; m.p. 52-55°C; R_f 0.29 (base-washed SiO_2; PE 40-60: EtOAc: Et_3N; 97:3:2); ν_{max} (KBr disk)/cm^{-1} 2917s, 2850s, 1471m; δ_H (200MHz; $CDCl_3$) 1.26 (38H, br s, $C\underline{H}_2$), 1.54 (4H, br s, $NCH_2C\underline{H}_2CH_2$), 1.93 (4H, t, *J*7Hz, C(3)$C\underline{H}_2$), 2.14 (4H, br s, C(5)$\underline{H}_2$), 2.37-2.44 (4H, m, $NC\underline{H}_2(CH_2)_2$), 2.50 (4H, t, *J*5.5Hz, C(6)$\underline{H}_2$), 2.85 (4H, br s, C(2)$\underline{H}_2$), 5.42 (2H, br s, C(4)H); δ_C (50MHz; $CDCl_3$) 25.7, 26.7, 27.3, 27.5, 27.7, 29.0, 29.3, 35.4, 35.6, 50.5, 50.7, 55.0, 55.1, 58.7 and 58.9 (15 x $\underline{C}H_2$), 119.0 and 119.1 (2 x $\underline{C}H$), 136.5 (quaternary); *m/z* (APCI) 513.5 (MH^+, 100%); HRMS found 513.5157, $C_{35}H_{65}N_2$ (MH^+) requires 513.5148.

Synthesis of 3-(13-hydroxytridecyl)-1-[13-(N-oxidopyridin-3-yl)tridecyl]pyridinium iodide (31)

The title compound was synthesised similarly to **27**, using 13-pyridin-3-yltridecan-1-ol (**18**) (218mg, 0.79mmol), 3-(13-chlorotridecyl)pyridine-*N*-oxide (**20**) (245mg, 0.79mmol) and NaI (141mg, 0.94mmol) in butan-2-one (10ml) to afford *3-(13-hydroxytridecyl)-1-[13-(N-oxidopyridin-3-yl)tridecyl]pyridinium iodide* (**31**) (524mg, 98%) as an off-white solid; m.p. 108-110°C, R_f 0.54 (Al_2O_3; CH_2Cl_2: MeOH; 9:1; UV); R_f 0.31 (SiO_2/NaBr [20]; CH_2Cl_2: MeOH; 9:1; UV); ν_{max} (KBr disk)/cm^{-1} 3396m br (OH), 2922s, 2850s, 1455m, 1436m, 1158m, 681m; δ_H (200MHz; $CDCl_3$) 1.20 (36H, br s, $C\underline{H}_2$), 1.44-1.74 (6H, m, $C\underline{H}_2CH_2OH$, C(3')$CH_2C\underline{H}_2$ and C(3)$CH_2C\underline{H}_2$), 1.96-2.04 (2H, m, $C\underline{H}_2CH_2N$), 2.53 (3H, t with a broad shoulder, *J*7.5Hz, C(3')$C\underline{H}_2$ and OH), 2.89 (2H, t, *J*6Hz, C(3)$C\underline{H}_2$), 3.56 (2H, t, *J*6Hz, $C\underline{H}_2OH$), 4.86 (2H, t, *J*7.5Hz, $C\underline{H}_2N$), 7.11-7.25 (2H, m, C(4')H and C(5')H), 8.03-8.10 (3H, m, C(2')H, C(5)H and C(6')H), 8.27 (1H, d, *J*8Hz, C(4)H), 9.16-9.21 (2H, m, C(2)H and C(6)H); δ_C (50MHz; $CDCl_3$: CD_3OD; 9:1) 25.5, 25.7, 28.6, 28.7, 28.9 and 29.2 (6 x $\underline{C}H_2$), 30.1* (C(3')$CH_2\underline{C}H_2$ and C(3)$CH_2\underline{C}H_2$), 31.5 ($\underline{C}H_2CH_2N$), 32.3 (C(3')$\underline{C}H_2$ and C(3)$\underline{C}H_2$), 32.4 ($\underline{C}H_2CH_2OH$), 61.8 ($\underline{C}H_2N$), 62.1 ($\underline{C}H_2OH$), 126.0 (C5'), 128.2 (C4'), 129.0 (C5), 136.5 and 138.7 (C2' and C6'), 142.2 (C6), 142.5 (C3'), 143.7 (C2), 144.5 (C3), 145.2 (C4); *at this resonance two signals can be resolved; *m/z* (FAB) 553.5 ($[M-I]^+$, 100%), 537.5 ($[M-IO]^+$, 12); HRMS found 553.4719, $C_{36}H_{61}N_2O_2$ ($[M-I]^+$) requires 553.4733.

Synthesis of 3-(13-bromotridecyl)-1-(13-pyridin-3-yltridecyl)pyridinium bromide (32)

The title compound was synthesised similarly to **28**, using 3-(13-hydroxytridecyl)-1-[13-(*N*-oxidopyridin-3-yl)tridecyl]pyridinium iodide (**31**) (503mg, 0.74mmol) and phosphorus tribromide (0.28ml, 2.96mmol) in $CHCl_3$ (10ml) to give *3-(13-bromotridecyl)-1-[13-(pyridin-3-io)tridecyl]pyridinium bromide* (584mg, quant.) as a yellow oil; ν_{max} (thin film)/cm^{-1} 2924s, 2854s, 1630m, 1552m, 1468m, 1242m, 752m; δ_H (200MHz; $CDCl_3$) 1.15-1.36 (36H, br m, $C\underline{H}_2$), 1.64-1.81 (6H, m, C(3')$CH_2C\underline{H}_2$, C(3)$CH_2C\underline{H}_2$ and $C\underline{H}_2CH_2Br$), 1.93-2.06 (2H, m, $C\underline{H}_2CH_2N$), 2.77-2.89 (4H, m, C(3')$C\underline{H}_2$ and C(3)$C\underline{H}_2$), 3.34 (2H, t, *J*7Hz, $C\underline{H}_2Br$), 4.91 (2H, t, *J*7.5Hz, $C\underline{H}_2N$), 8.02-8.11 (2H, m, C(5')$\underline{H}$ and C(5)$\underline{H}$), 8.24 (1H, d, *J*8Hz, C(4)$\underline{H}$), 8.40 (1H, d, *J*8Hz, C(4')$\underline{H}$), 8.61 (1H, s, C(2')$\underline{H}$), 8.72 (1H, br s, C(6')$\underline{H}$), 9.27 (2H, br s, C(2)$\underline{H}$ and C(6)$\underline{H}$); δ_C (50MHz; $CDCl_3$) 25.9, 28.0, 28.6, 28.9, 29.0, 29.1 and 29.4 (7 x $\underline{C}H_2$), 30.2 and 30.4 (C(3')$CH_2\underline{C}H_2$ and C(3)$CH_2\underline{C}H_2$), 31.9 ($\underline{C}H_2CH_2N$), 32.7 (C(3')$\underline{C}H_2$, C(3)$\underline{C}H_2$ and $\underline{C}H_2CH_2Br$), 34.1 ($\underline{C}H_2Br$), 61.7 ($\underline{C}H_2N$), 127.4 (C5'), 128.1 (C5), 138.1 (C6'), 139.6 (C2'), 142.4 (C6), 143.3 (C3'), 143.9 (C2), 144.1 (C3), 144.8 (C4), 146.6 (C4'). 3-(13-Bromotridecyl)-1-[13-(pyridin-3-io)tridecyl]pyridinium bromide was neutralised as before to afford *3-(13-bromotridecyl)-1-(13-pyridin-3-yltridecyl)pyridinium bromide* (**32**) (quant.) as a pale yellow oil; δ_H (200MHz; $CDCl_3$) 1.25 (36H, br s, $C\underline{H}_2$), 1.57-1.88 (6H, m, C(3')$CH_2C\underline{H}_2$, C(3)$CH_2C\underline{H}_2$ and $C\underline{H}_2CH_2Br$), 1.98-2.13 (2H, m, $C\underline{H}_2CH_2N$), 2.74 (2H, t, *J*8Hz, C(3')$C\underline{H}_2$), 2.90 (2H, t, *J*8Hz, C(3)$C\underline{H}_2$), 3.40 (2H, t, *J*7Hz, $C\underline{H}_2Br$), 4.98 (2H, t, *J*7.5Hz, $C\underline{H}_2N$), 7.50 (1H, dd, *J*7.5, 5.5Hz, C(5')$\underline{H}$), 7.81 (1H, d, *J*8Hz, C(4')$\underline{H}$), 8.04 (1H, dd, *J*8, 6Hz, C(5)$\underline{H}$), 8.24 (1H, d, *J*8Hz, C(4)$\underline{H}$), 8.48-8.59 (2H, m, C(2')$\underline{H}$ and C(6')$\underline{H}$), 9.24 (1H, s, C(2)$\underline{H}$), 9.33 (1H, d, *J*5.5Hz, C(6)$\underline{H}$); *m/z* (FAB) 601.5 ([M-Br]$^+$, ^{81}Br, 99%), 599.5 ([M-Br]$^+$, ^{79}Br, 100), 342 ($C_{18}H_{31}BrN^+$, ^{81}Br, 41), 340 ($C_{18}H_{31}BrN^+$, ^{79}Br, 33), 260 ($C_{18}H_{30}N^+$, 16); HRMS found 601.3921, $C_{36}H_{60}BrN_2$ ([M-Br]$^+$, ^{81}Br) requires 601.3919.

Synthesis of cyclostellettamine C (3)

The title compound was synthesised similarly to **1**, using 3-(13-bromotridecyl)-1-(13-pyridin-3-yltridecyl)pyridinium bromide (**32**) (485mg, 0.71mmol) in butan-2-one (9ml) and $CHCl_3$ (1ml), and NaI (235mg, 1.57mmol) in butan-2-one (80ml) to afford *cyclostellettamine C* (**3**) (357mg, 65%) as an off-white powder; m.p. 231-233°C (lit. [11] m.p. 233-236°C); (Found: C, 55.9; H, 8.05; N, 3.6. $C_{36}H_{60}I_2N_2$ requires C, 55.8; H, 7.8; N, 3.6%); R_f 0.27 (Al_2O_3; CH_2Cl_2: MeOH; 9:1); ν_{max} (KBr disk)/cm^{-1} 3016m, 2921s, 2851s, 1627m, 1504m, 1465m, 692m; δ_H (200MHz; $CDCl_3$: CD_3OD; 9:1) 1.00-1.21 (36H, br m, $C\underline{H}_2$), 1.59 (4H, br s, C(3)$CH_2C\underline{H}_2$), 1.88 (4H, br s, $NCH_2C\underline{H}_2$), 2.77 (4H, t, *J*7.5Hz, C(3)$C\underline{H}_2$), 4.60 (4H, t, *J*7Hz, $NC\underline{H}_2$), 7.89 (2H, dd, *J*8, 6.5Hz, C(5)$\underline{H}$), 8.18 (2H, d, *J*7.5Hz, C(4)$\underline{H}$), 8.75 (2H, d, *J*5.5Hz, C(6)$\underline{H}$), 8.89 (2H, s, C(2)$\underline{H}$); δ_C (50MHz; $CDCl_3$: CD_3OD; 9:1) 27.1, 29.9, 30.2 and 30.6 (4 x $\underline{C}H_2$), 31.5 (C(3)$CH_2\underline{C}H_2$), 32.8 ($NCH_2\underline{C}H_2$), 33.9 (C(3)$\underline{C}H_2$), 63.3 ($N\underline{C}H_2$), 129.7 (C5), 143.5 (C6), 145.3 (C2), 145.7 (C3), 146.8 (C4); *m/z* (FAB) 647.5 ([M-I]$^+$, 39%), 520.5 (28), 260 ([M-2I]$^{2+}$, 100); HRMS found 647.3781, $C_{36}H_{60}IN_2$ ([M-I]$^+$) requires 647.3801.

Synthesis of 1,19-diazatricyclo[31.3.1.1^{15,19}]octatriaconta-15,33-diene (41)

The title compound was synthesised similarly to **39**, using cyclostellettamine C (**3**) (59mg, 76μmol) and $NaBH_4$ (17mg, 450μmol) in MeOH (40ml) and CH_2Cl_2 (10ml), to afford *1,19-diazatricyclo[31.3.1.1^{15,19}]octatriaconta-15,33-diene* (**41**) (38mg, 96%) (<5% of the tetrahydropyridine regioisomer) as a white solid; m.p. 60-62°C; R_f 0.31 (base-washed SiO_2; PE 40-60: EtOAc: Et_3N; 97:3:2); ν_{max} (KBr disk)/cm^{-1} 2917s, 2850s, 1471m; δ_H (200MHz; $CDCl_3$) 1.26 (40H, br s, C$\underline{H}_2$), 1.47-1.56 (4H, m, NCH$_2$C$\underline{H}_2$CH$_2$), 1.94 (4H, t, *J*6.5Hz, C(3)C$\underline{H}_2$), 2.14 (4H, br s, C(5)$\underline{H}_2$), 2.35-2.43 (4H, m, NC$\underline{H}_2$(CH$_2$)$_2$), 2.48 (4H, t, *J*5.5Hz, C(6)$\underline{H}_2$), 2.83 (4H, br s, C(2)$\underline{H}_2$), 5.42 (2H, br s, C(4)$\underline{H}$); δ_C (50MHz; $CDCl_3$) 25.8, 26.7, 27.4, 27.6, 29.0, 29.1, 35.5, 50.6, 55.2 and 58.9 (10 x $\underline{C}H_2$), 119.0 ($\underline{C}$H), 136.6 (quaternary); *m/z* (APCI) 527.5 (MH$^+$, 100%); HRMS found 527.5307, $C_{36}H_{67}N_2$ (MH$^+$) requires 527.5304.

Synthesis of 3-(14-hydroxytetradecyl)-1-[12-(N-oxidopyridin-3-yl)dodecyl]pyridinium iodide (33)

The title compound was synthesised similarly to **27**, using 14-pyridin-3-yltetradecan-1-ol (**24**) (75mg, 0.26mmol), 3-(12-chlorododecyl)pyridine-*N*-oxide (**14**) (76mg, 0.26mmol) and NaI (47mg, 0.312mmol) in butan-2-one (5ml) to afford *3-(14-hydroxytetradecyl)-1-[12-(N-oxidopyridin-3-yl)dodecyl]pyridinium iodide* (**33**) (162mg, 93%) as a pale yellow solid; m.p. 94-98°C, R_f 0.61 (Al_2O_3; CH_2Cl_2: MeOH; 9:1; UV); R_f 0.20 (SiO_2/NaBr [20]; CH_2Cl_2: MeOH; 9:1); ν_{max} (KBr disk)/cm^{-1} 3388m br (OH), 2921s, 2852s, 1466m, 1264m, 1159m, 683m; δ_H (200MHz; $CDCl_3$) 1.30 (36H, br s, C$\underline{H}_2$), 1.50-1.68 (7H, m, C$\underline{H}_2$CH$_2$O$\underline{H}$, C(3')CH$_2$C$\underline{H}_2$ and C(3)CH$_2$C$\underline{H}_2$), 1.98-2.11 (2H, m, C$\underline{H}_2$CH$_2$N), 2.59 (2H, t, *J*7.5Hz, C(3')C$\underline{H}_2$), 2.92 (2H, t, *J*7.5Hz, C(3)C$\underline{H}_2$), 3.64 (2H, t, *J*6.5Hz, C$\underline{H}_2$OH), 4.95 (2H, t, *J*7.5Hz, C$\underline{H}_2$N), 7.17-7.27 (2H, m, C(4')$\underline{H}$ and C(5')$\underline{H}$), 8.00-8.10 (3H, m, C(2')$\underline{H}$, C(5)$\underline{H}$ and C(6')$\underline{H}$), 8.25 (1H, d, *J*8.5Hz, C(4)$\underline{H}$), 9.14 (1H, s, C(2)$\underline{H}$), 9.24 (1H, d, *J*6Hz, C(6)$\underline{H}$); δ_C (50MHz; $CDCl_3$) 25.7, 25.8, 28.7, 28.9, 29.3 and 29.4 (6 x $\underline{C}H_2$), 30.1 and 30.3 (C(3')CH$_2$$\underline{C}H_2$ and C(3)CH$_2$$\underline{C}H_2$), 31.8 ($\underline{C}H_2CH_2$N), 32.5 (C(3')$\underline{C}H_2$ and C(3)$\underline{C}$H$_2$), 32.7 ($\underline{C}$H$_2$CH$_2$OH), 61.7 ($\underline{C}$H$_2$N), 62.5 ($\underline{C}$H$_2$OH), 125.8 (C5'), 127.4 (C4'), 128.3 (C5), 136.8 and 139.0 (C2' and C6'), 142.1 (C3'), 142.5 (C6), 144.1 (C2), 144.5 (C3), 145.2 (C4); *m/z* (FAB) 553.5 ([M-I]$^+$, 100%), 537.5 ([M-IO]$^+$, 22); HRMS found 553.4716, $C_{36}H_{61}N_2O_2$ ([M-I]$^+$) requires 553.4733.

Synthesis of 3-(14-bromotetradecyl)-1-(12-pyridin-3-yldodecyl)pyridinium bromide (34)

The title compound was synthesised similarly to **28**, using 3-(14-hydroxytetradecyl)-1-[12-(*N*-oxidopyridin-3-yl)dodecyl]pyridinium iodide (**33**) (126mg, 0.19mmol) and phosphorus tribromide (70μl, 0.74mmol) in $CHCl_3$ (10ml) to give *3-(14-bromotetradecyl)-1-[12-(pyridin-3-io)dodecyl]pyridinium bromide* (135mg, 96%) as a pale yellow oil; ν_{max} (thin film)/cm^{-1} 2925s, 2853s, 1631m, 1552m, 1504m, 1467m, 727m, 687m; δ_H (200MHz; $CDCl_3$) 1.19 (36H,

br s, CH_2), 1.57-1.82 (6H, m, C(3')CH_2CH_2, C(3)CH_2CH_2 and CH_2CH_2Br), 1.94-2.04 (2H, m, CH_2CH_2N), 2.74-2.90 (4H, m, C(3')CH_2 and C(3)CH_2), 3.35 (2H, t, *J*7Hz, CH_2Br), 4.92 (2H, t, *J*7.5Hz, CH_2N), 8.00-8.10 (2H, m, C(5')H and C(5)H), 8.23 (1H, d, *J*8Hz, C(4)H), 8.33 (1H, d, *J*8Hz, C(4')H), 8.58 (1H, s, C(2')H), 8.68 (1H, br d, *J*5Hz, C(6')H), 9.32 (2H, br s, C(2)H and C(6)H); δ_C (50MHz; $CDCl_3$) 25.9, 28.0, 28.6, 28.9, 29.0, 29.1, 29.3 and 29.5 (8 x CH_2), 30.2 and 30.4 (C(3')CH_2CH_2 and C(3)CH_2CH_2), 32.0 (CH_2CH_2N), 32.7 (C(3')CH_2, C(3)CH_2 and CH_2CH_2Br), 34.1 (CH_2Br), 61.7 (CH_2N), 127.1 (C5'), 128.0 (C5), 138.8 (C6'), 140.4 (C2'), 142.5 (C6), 142.8 (C3'), 144.0 (C2), 144.1 (C3), 144.7 (C4), 145.7 (C4').3-(14-Bromotetradecyl)-1-[12-(pyridin-3-io)dodecyl]pyridinium bromide was neutralised as before to afford *3-(14-bromotetradecyl)-1-(12-pyridin-3-yldodecyl)pyridinium bromide* (**34**) (quant.) as a pale yellow oil; δ_H (200MHz; $CDCl_3$) 1.18 (36H, br s, CH_2), 1.55-1.81 (6H, m, C(3')CH_2CH_2, C(3)CH_2CH_2 and CH_2CH_2Br), 1.99-2.08 (2H, m, CH_2CH_2N), 2.70 (2H, t, *J*7.5Hz, C(3')CH_2), 2.84 (2H, t, *J*8Hz, C(3)CH_2), 3.33 (2H, t, *J*7Hz, CH_2Br), 4.90 (2H, t, *J*7.5Hz, CH_2N), 7.70 (1H, dd, *J*8, 5.5Hz, C(5')H), 7.88 (1H, d, *J*8Hz, C(4')H), 7.99-8.08 (1H, m, C(5)H), 8.20 (1H, d, *J*8Hz, C(4)H), 8.47-8.56 (2H, m, C(2')H and C(6')H), 8.99 (1H, s, C(2)H), 9.29 (1H, br s, C(6)H); *m/z* (FAB) 601.5 ($[M-Br]^+$, ^{81}Br, 98%), 599.5 ($[M-Br]^+$, ^{79}Br, 100), 356 ($C_{19}H_{33}BrN^+$, ^{81}Br, 65), 354 ($C_{19}H_{33}BrN^+$, ^{79}Br, 50), 246 ($C_{17}H_{28}N^+$, 16); HRMS found 599.3937, $C_{36}H_{60}BrN_2$ ($[M-Br]^+$, ^{79}Br) requires 599.3940.

Synthesis of cyclostellettamine D (4)

The title compound was synthesised similarly to **1**, using 3-(14-bromotetradecyl)-1-(12-pyridin-3-yldodecyl)pyridinium bromide (**34**) (89mg, 0.13mmol) in butan-2-one (9ml) and $CHCl_3$ (1ml), and NaI (43mg, 0.29mmol) in butan-2-one (30ml) to afford *cyclostellettamine D* (**4**) (75mg, 74%) as an off-white powder; m.p. 188-190°C (lit. [11] m.p. 188-192°C); (Found: C, 55.7; H, 8.0; N, 3.5. $C_{36}H_{60}I_2N_2$ requires C, 55.8; H, 7.8; N, 3.6%); R_f 0.24 (Al_2O_3; CH_2Cl_2: MeOH; 9:1); ν_{max} (KBr disk)/cm^{-1} 3017m, 2918s, 2850s, 1626m, 1504s, 1465s, 691s; δ_H (200MHz; $CDCl_3$: CD_3OD; 9:1) 1.10-1.26 (36H, br m, CH_2), 1.64 (4H, br s, C(3)CH_2CH_2), 1.90 (4H, br s, NCH_2CH_2), 2.79 (4H, t, *J*7.5Hz, C(3)CH_2), 4.62 (4H, t, *J*7Hz, NCH_2), 7.91 (2H, dd, *J*7.5, 6.5Hz, C(5)H), 8.19 (2H, d, *J*7.5Hz, C(4)H), 8.76 (1H, d, *J*6Hz, C(6)H), 8.79 (1H, d, *J*6Hz, C(6)H), 8.97 (2H, s, C(2)H); δ_C (100MHz; $CDCl_3$: CD_3OD; 9:1) 25.40, 28.09, 28.16, 28.24, 28.45, 28.63 and 28.72 (7 x CH_2), 29.86 and 29.97 (C(3)CH_2CH_2), 31.23 and 31.32 (NCH_2CH_2), 32.20 (C(3)CH_2), 61.69 (NCH_2), 127.88 (C5), 141.57 and 141.69 (C6), 143.65 and 143.73 (C2), 144.22 and 144.27 (C3), 145.04 (C4); *m/z* (FAB) 647.5 ($[M-I]^+$, 81%), 520.5 (80), 274 ($C_{19}H_{32}N^+$, 100), 260 ($[M-2I]^{2+}$, 81), 246 ($C_{17}H_{28}N^+$, 31); HRMS found 647.3785, $C_{36}H_{60}IN_2$ ($[M-I]^+$) requires 647.3801.

Synthesis of 1,18-diazatricyclo[31.3.1.1^{14,18}]octatriaconta-14,33-diene (42)

The title compound was synthesised similarly to **39**, using cyclostellettamine D (**4**) (40mg, 51μmol) and $NaBH_4$ (12mg, 310μmol) in MeOH (20ml) and CH_2Cl_2 (10ml), to afford *1,18-diazatricyclo[31.3.1.1^{14,18}]octatriaconta-14,33-diene* (**42**) (26mg, 95%) (<10% of the tetrahydropyridine regioisomer) as a colourless oil; R_f 0.28 (base-washed SiO_2; PE 40-60: EtOAc: Et_3N; 97:3:2); ν_{max} (thin film)/cm^{-1} 2917s, 2850s, 1472m; δ_H (200MHz; $CDCl_3$) 1.26-1.46 (40H, br m, C$\underline{H}_2$), 1.47-1.64 (4H, m, NCH$_2$C$\underline{H}_2$CH$_2$), 1.95 (4H, br s, C(3)C$\underline{H}_2$), 2.15 (4H, br s, C(5)$\underline{H}_2$), 2.35-2.57 (8H, m, NC$\underline{H}_2$(CH$_2$)$_2$ and C(6)$\underline{H}_2$), 2.84 (4H, br s, C(2)$\underline{H}_2$), 5.43 (2H, br s, C(4)$\underline{H}$); δ_C (50MHz; $CDCl_3$) 25.9, 26.9, 27.1, 27.4, 27.7, 27.8, 29.2, 29.6, 35.3, 35.5, 50.1, 50.6, 55.3, 55.9 and 58.8 (15 x $\underline{C}H_2$), 118.5 and 118.8 (2 x $\underline{C}H$), 136.4 (quaternary); *m/z* (APCI) 527.5 (MH$^+$, 100%); HRMS found 527.5299, $C_{36}H_{67}N_2$ (MH$^+$) requires 527.5304.

Synthesis of 3-(14-hydroxytetradecyl)-1-[13-(N-oxidopyridin-3-yl)tridecyl]pyridinium iodide (35)

The title compound was synthesised similarly to **27**, using 14-pyridin-3-yltetradecan-1-ol (**24**) (953mg, 3.27mmol), 3-(13-chlorotridecyl)pyridine-*N*-oxide (**20**) (1.02g, 3.27mmol) and NaI (588mg, 3.92mmol) in butan-2-one (50ml) to afford *3-(14-hydroxytetradecyl)-1-[13-(N-oxidopyridin-3-yl)tridecyl]pyridinium iodide* (**35**) (2.25g, 99%) as a white powder; m.p. 122-125°C, R_f 0.67 (Al_2O_3; CH_2Cl_2: MeOH; 9:1; UV); R_f 0.24 (SiO_2/NaBr [20]; CH_2Cl_2: MeOH; 9:1); ν_{max} (KBr disk)/cm^{-1} 3400m br (OH), 2920s, 2851s, 1468m, 1159m, 683m; δ_H (400MHz; $CDCl_3$) 1.09-1.30 (38H, br m, C$\underline{H}_2$), 1.39-1.50 (4H, m, C$\underline{H}_2$CH$_2$OH and C(3')CH$_2$C$\underline{H}_2$), 1.61 (2H, pseudo qui, *J*7Hz, C(3)CH$_2$C$\underline{H}_2$), 1.93 (2H, pseudo qui, *J*7Hz, C$\underline{H}_2$CH$_2$N), 2.46 (2H, t, *J*7.5Hz, C(3')C$\underline{H}_2$), 2.80 (2H, t, *J*7.5Hz, C(3)C$\underline{H}_2$), 2.93 (1H, br s, O$\underline{H}$), 3.48 (2H, t, *J*6.5Hz, C$\underline{H}_2$OH), 4.80 (2H, t, *J*7.5Hz, C$\underline{H}_2$N), 7.06 (1H, d, *J*8Hz, C(4')$\underline{H}$), 7.14 (1H, pseudo t, *J*7.5Hz, C(5')$\underline{H}$), 7.94-7.96 (2H, m, C(2')$\underline{H}$ and C(6')$\underline{H}$), 8.01 (1H, dd, *J*8, 6Hz, C(5)$\underline{H}$), 8.20 (1H, d, *J*8Hz, C(4)$\underline{H}$), 9.15 (1H, d, *J*6Hz, C(6)$\underline{H}$), 9.23 (1H, s, C(2)$\underline{H}$); δ_C (100MHz; $CDCl_3$) 25.74, 25.91, 28.76, 28.91, 28.94, 29.12, 29.23, 29.26, 29.35 and 29.43 (10 x $\underline{C}H_2$), 30.18 and 30.36 (C(3')CH$_2$$\underline{C}H_2$ and C(3)CH$_2$$\underline{C}H_2$), 31.86 ($\underline{C}H_2CH_2$N), 32.51 and 32.56 (C(3')$\underline{C}$H$_2$ and C(3)$\underline{C}$H$_2$), 32.75 ($\underline{C}$H$_2$CH$_2$OH), 61.63 ($\underline{C}$H$_2$N), 62.41 ($\underline{C}$H$_2$OH), 125.63 (C5'), 127.09 (C4'), 128.08 (C5), 136.51 and 138.70 (C2' and C6'), 141.82 (C3'), 142.28 (C6), 143.89 (C2), 144.14 (C3), 144.87 (C4); *m/z* (ES) 567.5 ([M-I]$^+$, 100%); HRMS found 567.4894, $C_{37}H_{63}N_2O_2$ ([M-I]$^+$) requires 567.4890.

Synthesis of 3-(14-bromotetradecyl)-1-(13-pyridin-3-yltridecyl)pyridinium bromide (36)

The title compound was synthesised similarly to **28**, using 3-(14-hydroxytetradecyl)-1-[13-(*N*-oxidopyridin-3-yl)tridecyl]pyridinium iodide (**35**) (1.33g, 1.91mmol) and phosphorus tribromide (0.72ml, 7.64mmol) in $CHCl_3$ to give *3-(14-bromotetradecyl)-1-[13-(pyridin-3-*

io)tridecyl]pyridinium bromide (1.46g, 99%) as a pale yellow oil; ν_{max} (thin film)/cm^{-1} 2925s, 2853s, 1630m, 1551m, 1504m, 1466m, 687m; δ_H (200MHz; $CDCl_3$) 1.17-1.46 (38H, br m, C$\underline{H}_2$), 1.70-1.90 (6H, m, C(3')CH$_2$C$\underline{H}_2$, C(3)CH$_2$C$\underline{H}_2$ and C$\underline{H}_2$CH$_2$Br), 1.94-2.12 (2H, m, C$\underline{H}_2$CH$_2$N), 2.83-2.93 (4H, m, C(3')C$\underline{H}_2$ and C(3)C$\underline{H}_2$), 3.39 (2H, t, *J*7Hz, C$\underline{H}_2$Br), 4.95 (2H, t, *J*7.5Hz, C$\underline{H}_2$N), 8.04-8.10 (2H, m, C(5')$\underline{H}$ and C(5)$\underline{H}$), 8.25 (1H, d, *J*8Hz, C(4)$\underline{H}$), 8.40 (1H, d, *J*8Hz, C(4')$\underline{H}$), 8.64 (1H, s, C(2')$\underline{H}$), 8.73 (1H, d, *J*5.5Hz, C(6')$\underline{H}$), 9.24 (1H, s, C(2)$\underline{H}$), 9.31 (1H, d, *J*6Hz, C(6)$\underline{H}$); δ_C (100MHz; $CDCl_3$) 25.91, 28.01, 28.60, 28.63, 28.89, 28.93, 29.05, 29.16, 29.21, 29.27, 29.37 and 29.44 (12 x $\underline{C}H_2$), 30.20 and 30.36 (C(3')CH$_2\underline{C}$H$_2$ and C(3)CH$_2\underline{C}$H$_2$), 31.90 ($\underline{C}$H$_2$CH$_2$N), 32.54 and 32.68 (C(3')$\underline{C}$H$_2$, C(3)$\underline{C}$H$_2$ and $\underline{C}$H$_2$CH$_2$Br), 34.16 ($\underline{C}$H$_2$Br), 61.66 ($\underline{C}$H$_2$N), 127.40 (C5'), 128.10 (C5), 138.37 (C6'), 139.75 (C2'), 142.40 (C6), 143.11 (C3'), 143.90 (C2), 144.11 (C3), 144.81 (C4), 146.43 (C4').3-(14-Bromotetradecyl)-1-[13-(pyridin-3-io)tridecyl]pyridinium bromide was neutralised as before to afford *3-(14-bromotetradecyl)-1-(13-pyridin-3-yltridecyl)pyridinium bromide* (**36**) (quant.) as a pale yellow oil; δ_H (200MHz; $CDCl_3$) 1.16-1.43 (38H, br m, C$\underline{H}_2$), 1.57-1.88 (6H, m, C(3')CH$_2$C$\underline{H}_2$, C(3)CH$_2$C$\underline{H}_2$ and C$\underline{H}_2$CH$_2$Br), 1.99-2.05 (2H, m, C$\underline{H}_2$CH$_2$N), 2.59 (2H, t, *J*7.5Hz, C(3')C$\underline{H}_2$), 2.89 (2H, t, *J*8Hz, C(3)C$\underline{H}_2$), 3.40 (2H, t, *J*7Hz, C$\underline{H}_2$Br), 4.96 (2H, t, *J*7.5Hz, C$\underline{H}_2$N), 7.20 (1H, dd, *J*8, 5Hz, C(5')$\underline{H}$), 7.49 (1H, d, *J*8Hz, C(4')$\underline{H}$), 8.02 (1H, dd, *J*8, 6Hz, C(5)$\underline{H}$), 8.23 (1H, d, *J*8Hz, C(4)$\underline{H}$), 8.40-8.43 (2H, m, C(2')$\underline{H}$ and C(6')$\underline{H}$), 9.15 (1H, s, C(2)$\underline{H}$), 9.28 (1H, d, *J*6Hz, C(6)$\underline{H}$); *m/z* (FAB) 615.5 ([M-Br]$^+$, ^{81}Br, 100%), 613.5 ([M-Br]$^+$, ^{79}Br, 98); HRMS found 613.4089, $C_{37}H_{62}BrN_2$ ([M-Br]$^+$, ^{79}Br) requires 613.4096.

Synthesis of cyclostellettamine E (5)

The title compound was synthesised similarly to **1**, using 3-(14-bromotetradecyl)-1-(13-pyridin-3-yltridecyl)pyridinium bromide (**36**) (1.31g, 1.89mmol) in butan-2-one (9ml) and $CHCl_3$ (1ml), and NaI (622mg, 4.15mmol) in butan-2-one (200ml) to afford *cyclostellettamine E* (**5**) (934mg, 63%) as an off-white powder; m.p. 222-224°C (lit. [11] m.p. 222-224°C); (Found: C, 56.0; H, 8.1; N, 3.5. $C_{37}H_{62}I_2N_2$ requires C, 56.4; H, 7.9; N, 3.6%); R_f 0.25 (Al_2O_3; CH_2Cl_2: MeOH; 9:1); ν_{max} (KBr disk)/cm^{-1} 3017m, 2922s, 2850s, 1627m, 1504m, 1464m, 691m; δ_H (200MHz; $CDCl_3$: CD_3OD; 9:1) 1.14-1.32 (38H, br m, C$\underline{H}_2$), 1.67 (4H, br s, C(3)CH$_2$C$\underline{H}_2$), 1.97 (4H, br s, NCH$_2$C$\underline{H}_2$), 2.86 (4H, t, *J*7.5Hz, C(3)C$\underline{H}_2$), 4.75 (4H, t, *J*7Hz, NC$\underline{H}_2$), 8.01 (2H, dd, *J*8, 6Hz, C(5)$\underline{H}$), 8.24 (2H, d, *J*8Hz, C(4)$\underline{H}$), 8.93-8.98 (2H, br m, C(6)$\underline{H}$), 9.04 (2H, s, C(2)$\underline{H}$); δ_C (50MHz; $CDCl_3$: CD_3OD; 9:1) 25.3, 25.5, 28.0, 28.2, 28.5 and 28.8 (6 x $\underline{C}H_2$), 29.9 and 30.1 (C(3)CH$_2\underline{C}$H$_2$), 31.2 and 31.6 (NCH$_2\underline{C}$H$_2$), 32.1 and 32.2 (C(3)$\underline{C}$H$_2$), 61.6 (N$\underline{C}$H$_2$), 128.3 (C5), 142.2 (C6), 143.9 (C2), 144.2 (C3), 145.4 (C4); *m/z* (FAB) 661.5 ([M-I]$^+$, 87%), 534.5 (99), 267 ([M-2I]$^{2+}$, 100); HRMS found 661.3963, $C_{37}H_{62}IN_2$ ([M-I]$^+$) requires 661.3958.

Synthesis of 1,19-diazatricyclo[32.3.1.1^{15,19}]nonatriaconta-15,34-diene (43)

The title compound was synthesised similarly to **39**, using cyclostellettamine E (**5**) (36mg, 46μmol) and $NaBH_4$ (10mg, 270μmol) in MeOH (20ml) and CH_2Cl_2 (10ml), to afford *1,19-diazatricyclo[32.3.1.1^{15,19}]nonatriaconta-15,34-diene* (**43**) (23mg, 92%) (<8% of the tetrahydropyridine regioisomer) as a white solid; m.p. 41-44°C; R_f 0.29 (base-washed SiO_2; PE 40-60: EtOAc: Et_3N; 97:3:2); ν_{max} (KBr disk)/cm^{-1} 2917s, 2850s, 1470m, 1176m, 1134m, 944m; δ_H (200MHz; $CDCl_3$) 1.26 (42H, br s, C$\underline{H}_2$), 1.45-1.56 (4H, m, NCH$_2$C$\underline{H}_2$CH$_2$), 1.93 (4H, br s, C(3)C$\underline{H}_2$), 2.15 (4H, br s, C(5)$\underline{H}_2$), 2.33-2.52 (8H, m, NC$\underline{H}_2$(CH$_2$)$_2$ and C(6)$\underline{H}_2$), 2.83 (4H, br s, C(2)$\underline{H}_2$), 5.42 (2H, br s, C(4)$\underline{H}$); δ_C (50MHz; $CDCl_3$) 25.7, 25.8, 26.8, 27.0, 27.5, 27.6, 29.1, 29.3, 29.5, 35.3, 50.1, 50.5, 55.3, 56.0 and 58.8 (15 x $\underline{C}H_2$), 118.7 and 119.1 (2 x $\underline{C}H$), 136.6 (quaternary); *m/z* (APCI) 541.5 (MH$^+$, 100%); HRMS found 541.5467, $C_{37}H_{69}N_2$ (MH$^+$) requires 541.5461.

Synthesis of 3-(14-hydroxytetradecyl)-1-[14-(N-oxidopyridin-3-yl)tetradecyl]pyridinium iodide (37)

The title compound was synthesised similarly to **27**, using 14-pyridin-3-yltetradecan-1-ol (**24**) (345mg, 1.18mmol), 3-(14-chlorotetradecyl)pyridine-*N*-oxide (**26**) (386mg, 1.18mmol) and NaI (213mg, 1.42mmol) in butan-2-one (10ml) to afford *3-(14-hydroxytetradecyl)-1-[14-(N-oxidopyridin-3-yl)tetradecyl]pyridinium iodide* (**37**) (837mg, 100%) as a white solid; m.p. 100-103°C, R_f 0.63 (Al_2O_3; CH_2Cl_2: MeOH; 9:1; UV); R_f 0.25 (SiO_2/NaBr [20]; CH_2Cl_2: MeOH; 9:1); ν_{max} (KBr disk)/cm^{-1} 3402m br (OH), 2920s, 2851s, 1468m, 1436m, 1265m, 1159m, 683m; δ_H (200MHz; $CDCl_3$) 1.21 (40H, br s, C$\underline{H}_2$), 1.49-1.74 (6H, m, C$\underline{H}_2$CH$_2$OH and C(3')CH$_2$C$\underline{H}_2$ and C(3)CH$_2$C$\underline{H}_2$), 1.94-2.08 (2H, m, C$\underline{H}_2$CH$_2$N), 2.23 (1H, br s, O$\underline{H}$), 2.55 (2H, t, *J*7.5Hz, C(3')C$\underline{H}_2$), 2.88 (2H, t, *J*7.5Hz, C(3)C$\underline{H}_2$), 3.59 (2H, t, *J*6.5Hz, C$\underline{H}_2$OH), 4.89 (2H, t, *J*7.5Hz, C$\underline{H}_2$N), 7.14-7.24 (2H, m, C(4')$\underline{H}$ and C(5')$\underline{H}$), 8.03-8.09 (3H, m, C(2')$\underline{H}$, C(5)$\underline{H}$ and C(6')$\underline{H}$), 8.26 (1H, d, *J*8Hz, C(4)$\underline{H}$), 9.21 (2H, br s, C(2)$\underline{H}$ and C(6)$\underline{H}$); δ_C (50MHz; $CDCl_3$) 25.7, 25.9, 28.8, 29.0, 29.2 and 29.4 (6 x $\underline{C}H_2$), 30.2 and 30.4 (C(3')CH$_2$$\underline{C}H_2$ and C(3)CH$_2$$\underline{C}H_2$), 31.9 ($\underline{C}H_2CH_2$N), 32.6 (C(3')$\underline{C}H_2$ and C(3)$\underline{C}$H$_2$), 32.7 ($\underline{C}$H$_2$CH$_2$OH), 61.8 ($\underline{C}$H$_2$N), 62.7 ($\underline{C}$H$_2$OH), 125.5 (C5'), 126.9 (C4'), 128.0 (C5), 136.6 and 138.8 (C2' and C6'), 141.8 (C3'), 142.3 (C6), 143.8 (C2), 144.2 (C3), 144.9 (C4); *m/z* (FAB) 581.5 ([M-I]$^+$, 100%), 565.5 ([M-IO]$^+$, 28); HRMS found 581.5054, $C_{38}H_{65}N_2O_2$ ([M-I]$^+$) requires 581.5046.

Synthesis of 3-(14-bromotetradecyl)-1-(14-pyridin-3-yltetradecyl)pyridinium bromide (38)

The title compound was synthesised similarly to **28**, using 3-(14-hydroxytetradecyl)-1-[14-(*N*-oxidopyridin-3-yl)tetradecyl]pyridinium iodide (**37**) (755mg, 1.06mmol) and phosphorus tribromide (0.40ml, 4.26mmol) in $CHCl_3$ (20ml) to give *3-(14-bromotetradecyl)-1-[14-(pyridin-3-io)tetradecyl]pyridinium bromide* (851mg, quant.) as a pale yellow oil which solidified on standing; ν_{max} (thin film)/cm^{-1} 2924s, 2853s, 1630m, 1552m, 1468m, 1258m,

1017m, 686m; δ_H (200MHz; $CDCl_3$) 1.09-1.40 (40H, br m, CH_2), 1.57-1.84 (6H, m, C(3')CH_2CH_2, C(3)CH_2CH_2 and CH_2CH_2Br), 2.00-2.09 (2H, m, CH_2CH_2N), 2.81-2.92 (4H, m, C(3')CH_2 and C(3)CH_2), 3.37 (2H, t, *J*7Hz, CH_2Br), 4.93 (2H, t, *J*7.5Hz, CH_2N), 8.05-8.12 (2H, m, C(5')H and C(5)H), 8.26 (1H, d, *J*8Hz, C(4)H), 8.41 (1H, d, *J*8Hz, C(4')H), 8.61 (1H, s, C(2')H), 8.72 (1H, d, *J*5.5Hz, C(6')H), 9.30 (2H, s, C(2)H and C(6)H); δ_C (50MHz; $CDCl_3$) 25.9, 28.0, 28.6, 28.9, 29.2, 29.4 and 29.5 (7 x CH_2), 30.2 and 30.4 (C(3')CH_2CH_2 and C(3)CH_2CH_2), 31.9 (CH_2CH_2N), 32.6 and 32.7 (C(3')CH_2, C(3)CH_2 and CH_2CH_2Br), 34.1 (CH_2Br), 61.7 (CH_2N), 127.4 (C5'), 128.1 (C5), 138.1 (C6'), 139.6 (C2'), 142.5 (C6), 143.3 (C3'), 143.9 (C2), 144.2 (C3), 144.8 (C4), 146.5 (C4'). 3-(14-Bromotetradecyl)-1-[14-(pyridin-3-io)tetradecyl]pyridinium bromide was neutralised as before to afford *3-(14-bromotetradecyl)-1-(14-pyridin-3-yltetradecyl)pyridinium bromide* (**38**) (quant.) as a pale yellow oil; δ_H (200MHz; $CDCl_3$) 1.23-1.42 (40H, br m, CH_2), 1.57-1.89 (6H, m, C(3')CH_2CH_2, C(3)CH_2CH_2 and CH_2CH_2Br), 1.98-2.10 (2H, m, CH_2CH_2N), 2.62 (2H, t, *J*7.5Hz, C(3')CH_2), 2.90 (2H, t, *J*8Hz, C(3)CH_2), 3.41 (2H, t, *J*7Hz, CH_2Br), 4.97 (2H, t, *J*7.5Hz, CH_2N), 7.27 (1H, dd, *J*8, 5.5Hz, C(5')H), 7.56 (1H, d, *J*8Hz, C(4')H), 8.02 (1H, dd, *J*8, 6Hz, C(5)H), 8.22 (1H, d, *J*8Hz, C(4)H), 8.43-8.46 (2H, m, C(2')H and C(6')H), 9.15 (1H, s, C(2)H), 9.27 (1H, d, *J*6Hz, C(6)H); *m/z* (FAB) 629.5 ($[M-Br]^+$, ^{81}Br, 96%), 627.5 ($[M-Br]^+$, ^{79}Br, 100), 274 ($C_{19}H_{32}N^+$, 24); HRMS found 629.4250, $C_{38}H_{64}BrN_2$ ($[M-Br]^+$, ^{81}Br) requires 629.4232.

Synthesis of cyclostellettamine F (6)

The title compound was synthesised similarly to **1**, using 3-(14-bromotetradecyl)-1-(14-pyridin-3-yltetradecyl)pyridinium bromide (**38**) (658mg, 0.93mmol) in butan-2-one (9ml) and $CHCl_3$ (1ml), and NaI (306mg, 2.04mmol) in butan-2-one (100ml) to afford *cyclostellettamine F* (**6**) (486mg, 65%) as an off-white powder; m.p. 225-227°C (lit. [11] m.p. 227-231°C); (Found: C, 56.7; H, 8.35; N, 3.5. $C_{38}H_{64}I_2N_2$ requires C, 56.9; H, 8.05; N, 3.5%); R_f 0.24 (Al_2O_3; CH_2Cl_2: MeOH; 9:1); ν_{max} (KBr disk)/cm^{-1} 3017m, 2921s, 2850s, 1627m, 1504m, 1465m, 691m; δ_H (200MHz; $CDCl_3$: CD_3OD; 9:1) 1.05-1.28 (40H, br m, CH_2), 1.65 (4H, br s, C(3)CH_2CH_2), 1.95 (4H, br s, NCH_2CH_2), 2.83 (4H, t, *J*7.5Hz, C(3)CH_2), 4.68 (4H, t, *J*7Hz, NCH_2), 7.96 (2H, dd, *J*8, 6Hz, C(5)H), 8.23 (2H, d, *J*8Hz, C(4)H), 8.86 (2H, d, *J*6Hz, C(6)H), 8.96 (2H, s, C(2)H); δ_C (50MHz; $CDCl_3$: CD_3OD; 9:1) 25.4, 28.1, 28.5 and 28.8 (4 x CH_2), 30.0 (C(3)CH_2CH_2), 31.2 (NCH_2CH_2), 32.2 (C(3)CH_2), 61.7 (NCH_2), 128.3 (C5), 142.2 (C6), 143.9 (C2), 144.4 (C3), 145.5 (C4); *m/z* (FAB) 675.5 ($[M-I]^+$, 19%), 548.5 (41), 274 ($[M-2I]^{2+}$, 100); HRMS found 675.4107, $C_{38}H_{64}IN_2$ ($[M-I]^+$) requires 675.4114.

Synthesis of 1,20-diazatricyclo[33.3.1.1^{16,20}]tetraconta-16,35-diene (44)

The title compound was synthesised similarly to **39**, using cyclostellettamine F (**6**) (88mg, 110μmol) and $NaBH_4$ (25mg, 660μmol) in MeOH (40ml) and CH_2Cl_2 (10ml), to afford *1,20-diazatricyclo[33.3.1.1^{16,20}]tetraconta-16,35-diene* (**44**) (53mg, 86%) (<6% of the tetrahydropyridine regioisomer) as a white solid; m.p. 87-89°C; R_f 0.27 (base-washed SiO_2; PE

40-60: EtOAc: Et_3N; 97:3:2); ν_{max} (KBr disk)/cm^{-1} 2917s, 2850s, 1471m, 1176m, 1134m, 944m; δ_H (200MHz; $CDCl_3$) 1.26 (44H, br s, CH_2), 1.46-1.50 (4H, m, $NCH_2CH_2CH_2$), 1.94 (4H, br t, *J*7Hz, C(3)CH_2), 2.15 (4H, br s, C(5)H_2), 2.35-2.43 (4H, m, $NCH_2(CH_2)_2$), 2.49 (4H, t, *J*5.5Hz, C(6)H_2), 2.83 (4H, br s, C(2)H_2), 5.43 (2H, br s, C(4)H); δ_C (50MHz; $CDCl_3$) 25.8, 26.9, 27.3, 27.7, 29.1, 29.2, 35.4, 50.6, 55.4 and 58.9 (10 x CH_2), 119.0 (CH), 136.6 (quaternary); *m/z* (APCI) 555.5 (MH^+, 100%); HRMS found 555.5612, $C_{38}H_{71}N_2$ (MH^+) requires 555.5617.

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