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Synthesis and Mass Spectrometric Analysis of Cyclostellettamines H, I, K and L

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Very recently the new cyclostellettamines H, I, K and L were identified from a Brazilian sponge of the genus *Pachychalina*. They were isolated together with the known cyclostellettamines A–G in a mixture of only 1.5 mg. To obtain further material for biological investigations, the synthesis of the four new cyclostellettamines has been carried out. Since mass spectrometry plays an essential role in identifying these compounds a systematic analysis of the cyclostellettamines is discussed.

Introduction

Piperidine and pyridine (pyridinium) alkaloids are widely distributed in marine sponges of different genera.[1] The order Haplosclerida (genera *Haliclona*, *Xestospongia* and *Amphimedon*) has proved to be a particularly rich source of alkaloids containing 1,3-dialkylpyridine or piperidine motifs,[2] many of which have quite complex structures. Members of this alkaloid class with a lower structural complexity are the halitoxins,[3] the haliclamines[4] and the cyclostellettamines.[5] The first six members of the cyclostellettamines (A to F) were reported by Fusetani and co-workers in 1994.[5a] They differ in the lengths of the alkyl chains − the chain length varies from 12 to 14 carbon atoms − that connect the two pyridinium rings in positions 1 and 3. Very recently, we have identified eleven cyclostellettamines from a sample of a Brazilian sponge of the genus *Pachychalina*, of which cyclostellettamines A–G (**2**)[6] were already known.[5c] The chain lengths of the new cyclostellettamines H (**1**), I (**3**), K (**4**) and L (**5**) were identified as 10 to 14.[7] Since it was not possible to get pure samples of the new compounds a synthetic approach was carried out. Furthermore, the as yet unknown cyclostellettamine Q (**6**) is also discussed in this manuscript.[8] Cyclostellettamines I (**3**), K (**4**) and L (**5**) are the first members of this family in which the chain length of the two alkyl chains differs by more than two carbon atoms (Figure 1). A difference of three in the chain lengths is known for the structurally related haliclamines (tetrahydropyridine derivatives of the cyclostellettamines).[4a]

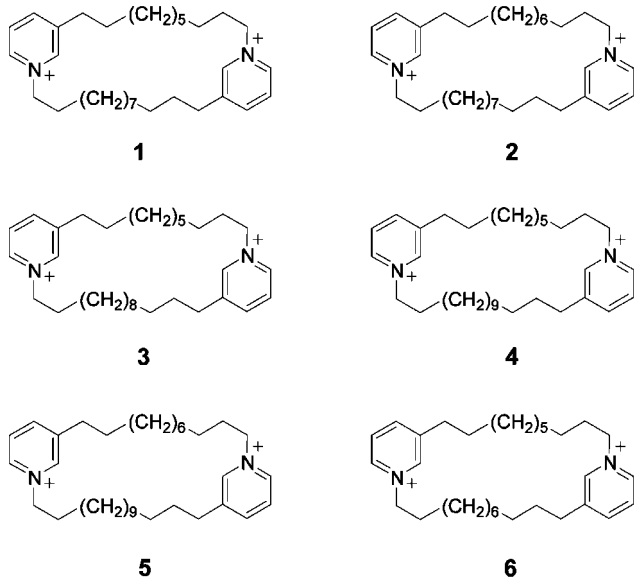

Figure 1. Cyclostellettamines H (**1**), G (**2**), I (**3**), K (**4**), L (**5**) and Q (**6**).

Methods and Results

Cyclostellettamines G (**2**), H (**1**), I (**3**), K (**4**), L (**5**) and Q (**6**) were synthesised following a procedure developed by Baldwin et al.[9] Depending on the commercial availability of the starting material, pyridyl alcohol monomers **12** were prepared in three to five steps, starting either from the diacid (C_{14}), the diol (C_{10}, C_{11}, C_{13}) or the bromo alcohol (C_{12}). The diacid **7a** was reduced to the diol **8a** by treatment with $BH_3{\cdot}SMe_2$. Monobromination[10] of the diols **8a**,**b**,**d**,**e** yielded the bromo alcohols **9a**,**b**,**d**,**e**, which were then protected as the THP ethers **10a**–**e** and coupled with 3-picoline to give the protected 3-alkylpyridines **11a**–**e**. Deprotection

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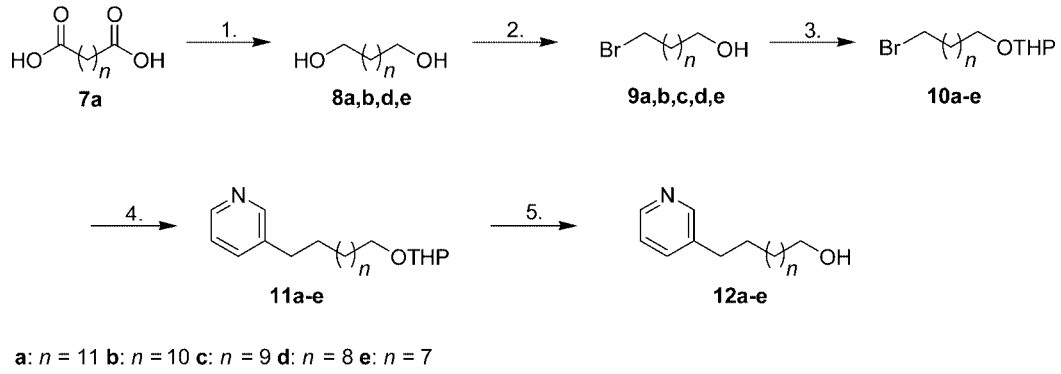


Figure 2. Preparation of the monomeric building block **12**: 1) 4 equiv. $BH_3{\cdot}SMe_2$, THF, 0 °C to room temp.; 2) 1.1 equiv. HBr, toluene, Δ, $-H_2O$; 3) 1.5 equiv. DHP, PPTS, DCM, room temp.; 4) 2 equiv. picoline, LDA, THF, –78 °C to room temp.; 5) 2 equiv. HCl, MeOH, room temp.

with HCl gave monomers **12a**–**e** in 18 to 39% yield (see Figure 2).

Prior to dimerisation, one monomer was activated by converting the alcohol into a chloride with $SOCl_2$, followed by protection of the nitrogen as the *N*-oxide by treatment with *m*-CPBA (see Figure 3). Coupling of **12** and **14** was achieved by treatment with NaI (nucleophilic addition). The resulting dimer was activated and deprotected in one step with PBr_3. Cyclisation to the target compounds was performed under pseudo high dilution conditions by slowly adding the bromo dimer with a syringe pump to a refluxing solution of NaI in butan-2-one to give cyclostellettamines G (**2**), H (**1**), I (**3**), K (**4**), L (**5**) and Q (**6**) in 28 to 61% yield (not optimised) starting from monomers **12** and **14** (see Figure 4).

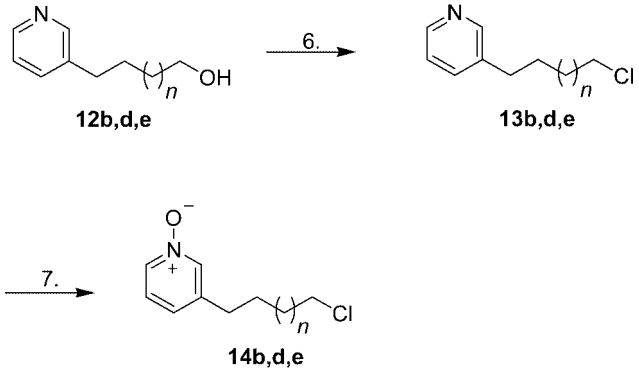


Figure 3. Activation of the monomeric building block **12**: 6) 1.2 equiv. $SOCl_2$, dioxane, 0 °C–room temp.; 7) 1.1 equiv. *m*-CPBA, DCM, 0 °C to room temp.

MS and MS/MS methods are essential for the structure elucidation of cyclstellettamines since the NMR spectra of these compounds are very similar to each other. Determination of the high resolution masses of cyclostellettamines and generation of the corresponding molecular fragments was achieved with an ESI-oTOF mass spectrometer. Even with low fragmentation energy the molecules underwent mass spectral cleavage, which allowed MS/MS analysis without fragmentation with an ion trap or a triple quadrupole as analyzer (Figure 5). Molecular fragments of cyclostellettamines were generated in the ion-transfer unit of the orthogonal-TOF by setting a voltage difference between the capillary exit and the skimmer. In this setup API-CID (atmospheric pressure ionisation – collision induced dissociation) was carried out with a non-mass-selected ion stream, which made it necessary to work with pure compounds.

The fragmentation patterns under API-CID and CID-MS/MS conditions were compared. The results of the MS and API-CID-MS/MS analysis of cyclostellettamines H (**1**), G (**2**), I (**3**), K (**4**), L (**5**) and Q (**6**) are given in Table 1. The average mass deviation of the TOF instrument was 0.84 amu with a standard deviation of 0.49 amu (largest mass deviation was 1.9 amu).

In order to understand the fragmentation pattern of cyclostellettamines, MS^n spectra of cyclostellettamine Q (**6**) were recorded with an ion-trap mass spectrometer (see Figure 6). Three fragmentation pathways are possible for cyclostellettamine Q (**6**): an onium reaction, a Hofmann fragmentation[2d] and a McLafferty rearrangement (see Figure 7). The two main fragments at m/z = 218 and 232 are both generated from the doubly charged precursor ion (m/z = 225, see Figure 6c), the mono iodide salt (m/z = 577, see Figure 6b) and from the m/z = 449 fragment (not shown) in an onium reaction. In this reaction a proton remains at the pyridine nitrogen to form a quaternary ammonium ion, while the localisation of the double bond in the alkyl chain is variable.[11]

In MS/MS spectra of the cyclostellettamines the fragments have a typical difference of 14 amu. This indicates the stepwise cleavage of the alkyl chain. The daughter ions obtained in the MS/MS spectra of the m/z = 225 fragment, i.e. m/z = 162 and 176, are doubly and singly charged, respectively. This leads to the assumption that the doubly charged M^{2+} ion also undergoes an onium reaction and splits in the alkyl chain. The doubly charged daughter ions at m/z = 197, 183 and 169 could arise from a McLafferty-type rearrangement of the m/z = 225 fragment, where a methyl group remains at the pyridine nitrogen. Duffield et al. have shown for *N*-butyl- and *N*-pentylpyrroles that a hydrogen transfer occurs from C-3 of the alkyl chain via a six-

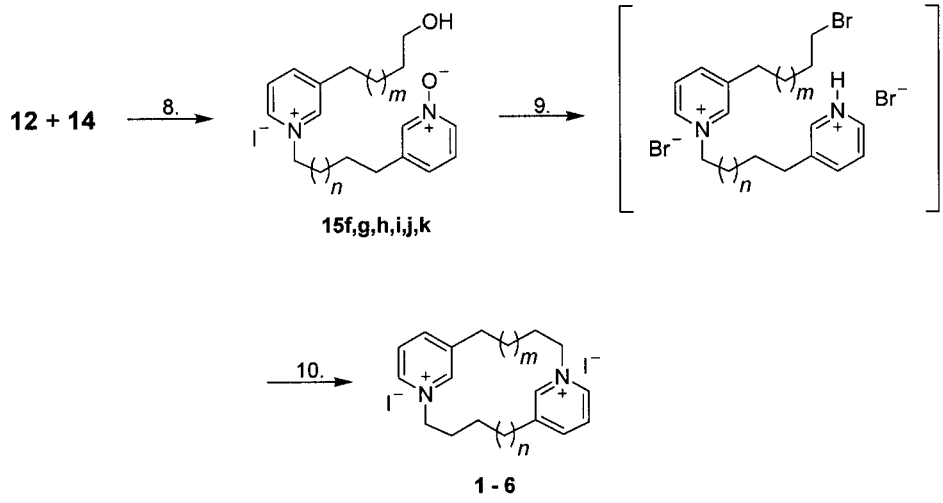


Figure 4. Dimerisation and cyclisation of the monomeric building blocks **12** and **14**: 8) 1.2 equiv. NaI, butan-2-one, Δ; 9) 4 equiv. PBr_3, $CHCl_3$, 0 °C to room temp.; 10) 2.2 equiv. NaI, butan-2-one, Δ.

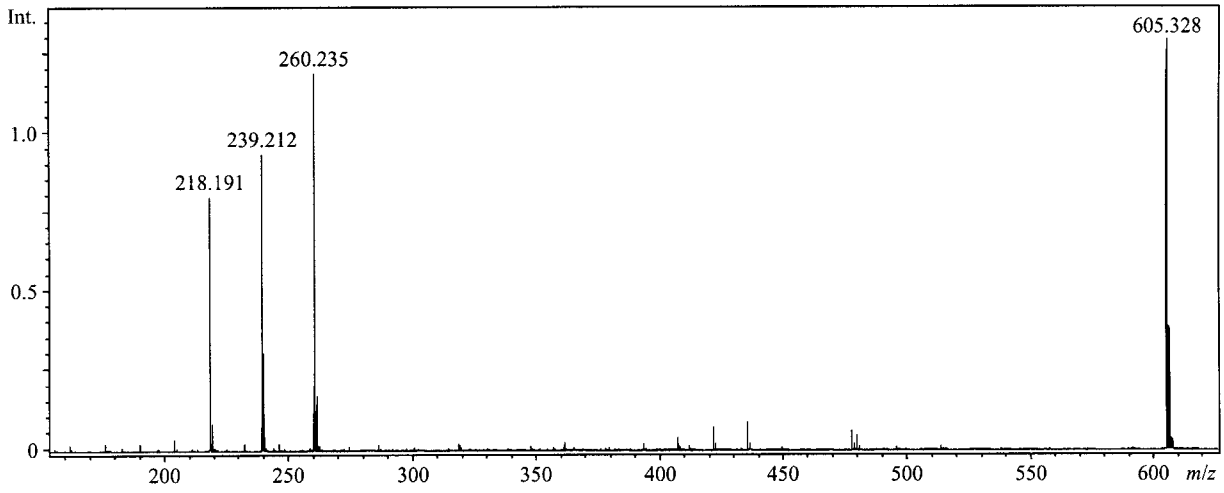


Figure 5. API-CID-MS/MS spectrum of cyclostellettamine I (**3**). The two daughter ions at *m*/*z* = 218 and 260 arise from the doubly charged precursor ion (*m*/*z* = 239) and the mono iodide salt (*m*/*z* = 605).

membered transition state to an α-carbon of the heterocycle with a synchronous α,β-carbon bond cleavage.[12] An analogous pathway with a following re-aromatisation could be possible for the cyclostellettamines (see Figure 8). A γ-cleavage that leads to a 1,2-dimethylene-1,2-dihydropyridinium ion has been described by Spiteller for alkylpyridines.[13] A 1-azoniabicyclo[4.2.0]octa-1(6),2,4-triene, which has a similar structure to the cyclostellettamines, is formed as an intermediate in this reaction (see Supporting Information). The intensity of the McLafferty fragments is lower than the fragments due to the onium reaction.

The $[M - 2I - H]^+$ fragment typically observed for the cyclostellettamines is only formed from the mono iodide salt at *m*/*z* = 577 in a so-called Hofmann fragmentation. The appearance of this Hofmann fragment seems to depend on the anion as this fragment is observed with chloride,[2d] bromide, iodide and nitrate as anion, whereas with triflate[2d] no Hofmann fragmentation is observed. Under API-CID conditions, and only in the presence of formic acid, an $[M - 2I + H]^+$ fragment is also formed. Other acids, for example acetic acid or ascorbic acid, do not lead to the observed $[M - 2I + H]^+$ fragment. This fragment is probably generated by a reduction of the unsaturated alkyl chain with formic acid as reducing agent.

Discussion and Conclusion

Since the new cyclostellettamines H, I, K and L were obtained in a 1.5 mg mixture of 11 derivatives, a synthetic approach was deemed necessary to obtain pure compounds for further biological studies. The synthetic approach intro-

Table 1. MS and MS/MS results for compounds **1**–**6**.

		HRMS	Fragment 1	Fragment 2
1	calcd.	232.2060, $C_{32}H_{52}N_2$	218.1902, $C_{15}H_{24}N$ (C_{10})	246.2216, $C_{17}H_{28}N$ (C_{12})
	exp.	232.2054, Δm = 2.7 ppm	218.1913, Δm = 4.5 ppm	246.2210, Δm = 2.6 ppm
		FWHM: 0.0418	FWHM: 0.0399	FWHM: 0.0439
2	calcd.	239.2138, $C_{33}H_{54}N_2$	232.2060, $C_{16}H_{26}N$ (C_{11})	246.2216, $C_{17}H_{28}N$ (C_{12})
	exp.	239.2135, Δm = 1.1 ppm	232.2064, Δm = 1.8 ppm	246.2211, Δm = 2.0 ppm
		FWHM: 0.0450	FWHM: 0.0366	FWHM: 0.0381
3	calcd.	239.2138, $C_{33}H_{54}N_2$	218.1902, $C_{15}H_{24}N$ (C_{10})	260.2373, $C_{18}H_{30}N$ (C_{13})
	exp.	239.2136, Δm = 1.0 ppm	218.1914, Δm = 5.2 ppm	260.2364, Δm = 3.2 ppm
		FWHM: 0.0457	FWHM: 0.0353	FWHM: 0.0399
4	calcd.	246.2216, $C_{34}H_{56}N_2$	218.1903, $C_{15}H_{24}N$ (C_{10})	274.2529, $C_{18}H_{30}N$ (C_{14})
	exp.	246.2205 Δm = 4.5 ppm	218.1915, Δm = 5.5 ppm	274.2519, Δm = 3.8 ppm
		FWHM: 0.0430	FWHM: 0.0394	FWHM: 0.0479
5	calcd.	253.2295, $C_{35}H_{58}N_2$	232.2060, $C_{16}H_{26}N$ (C_{11})	274.2529, $C_{18}H_{30}N$ (C_{14})
	exp.	253.2279, Δm = 6.2 ppm	232.2059, Δm = 0.4 ppm	274.2510, Δm = 6.9 ppm
		FWHM: 0.0462	FWHM: 0.0414	FWHM: 0.0476
6	calcd.	225.1982, $C_{31}H_{50}N_2$	218.1902, $C_{15}H_{24}N$ (C_{10})	232.2060, $C_{16}H_{26}N$ (C_{11})
	exp.	225.1992, Δm = 4.9 ppm	218.1914, Δm = 5.1 ppm	232.2061, Δm = 0.4 ppm
		FWHM: 0.0339	FWHM: 0.0339	FWHM: 0.0366

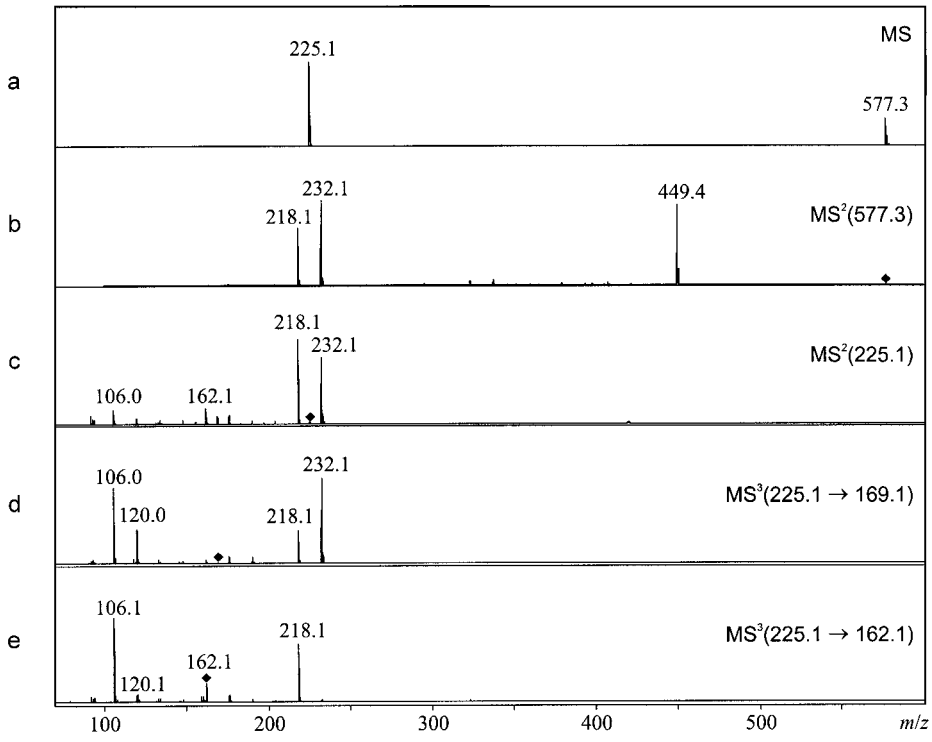


Figure 6. MS and MS^n spectra of cyclostellettamine Q (**6**): a) MS spectrum of **6** with the doubly charged ion at m/z = 225 and the mono iodide salt (m/z = 577); b) MS/MS spectrum of the mono iodide salt as precursor ion; c) MS/MS spectrum of the doubly charged ion at m/z = 225 as precursor ion; d) MS/MS spectrum of the doubly charged ion at m/z = 169, which arises as a daughter ion from the m/z = 225 fragment; e) MS/MS spectrum of the doubly charged ion at m/z = 162, which arises as a daughter ion from the m/z = 225 fragment.

duced by Baldwin et al. proved to be an effective access to cyclostellettamines. The structure elucidation of cyclostellettamines, and 3-alkylpyridine alkaloids in general, depends strongly on mass spectrometry as the NMR spectra of these compounds are very similar to each other due to a considerable overlap of the aliphatic protons (about 50% of the proton resonances have the same resonance frequency). This investigation has described a systematic analysis of ESI-HRMS, ESI-API-CID-MS/MS and ESI-CID-MS/MS spectra. The high resolution masses could be measured with the high accuracy required for the unambiguous identification of cyclostellettamines. The results show comparable fragmentation behaviour under ESI-API-CID-MS/MS and ESI-CID-MS/MS conditions. An advantage of API-CID-MS/MS with an oTOF is the determination of high resolution masses. Analysis of the fragments generated allows a fast and easy identification of the alkyl chain lengths of the cyclostellettamines, thus facilitating the structure elucida-

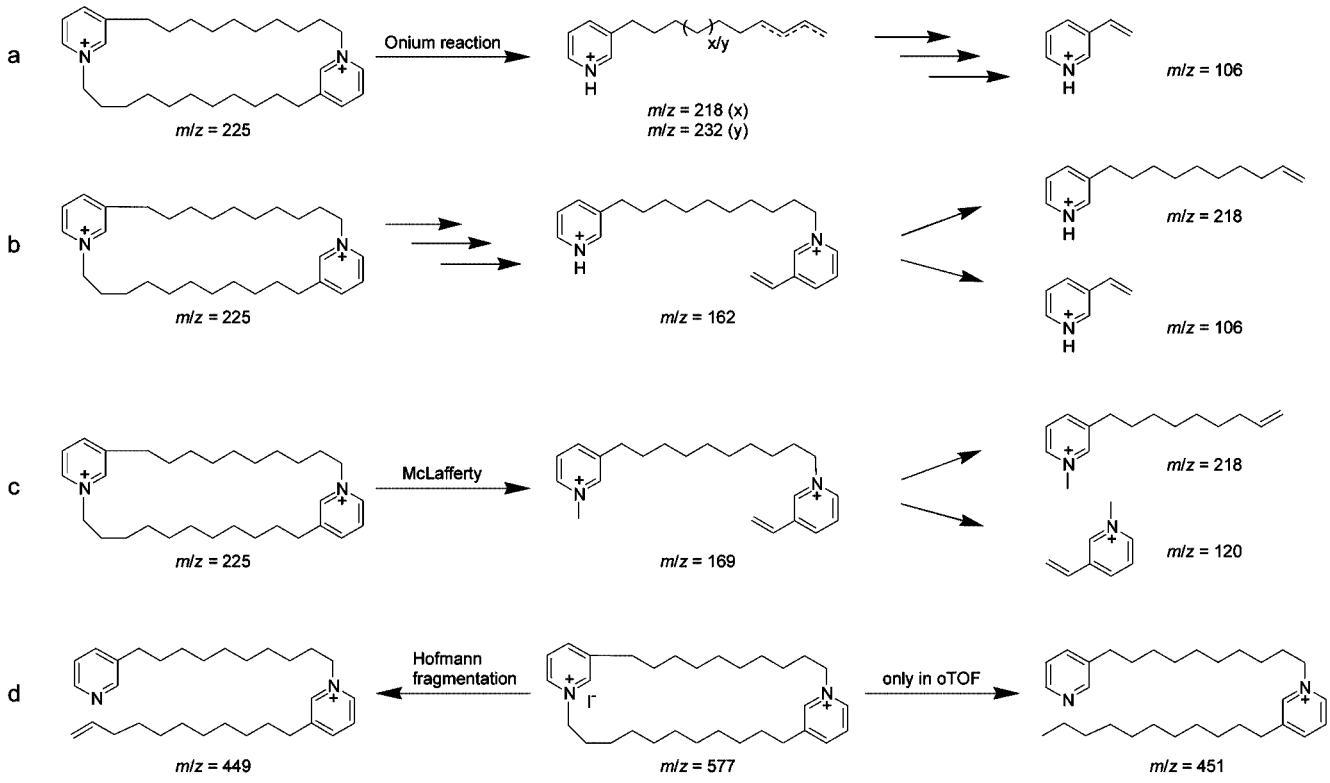


Figure 7. Proposed fragmentation pathways of cyclostellettamine Q (**6**) according to MS/MS analysis. The doubly charged precursor ion (m/z = 225) undergoes an onium reaction which leads to singly (a) as well as doubly (b) charged ions. Another possible fragmentation reaction of the precursor ion is the McLafferty rearrangement (c). The mono iodide salt reacts in a so-called Hofmann fragmentation and only in oTOF to a reduced form of the Hofmann fragment (d).

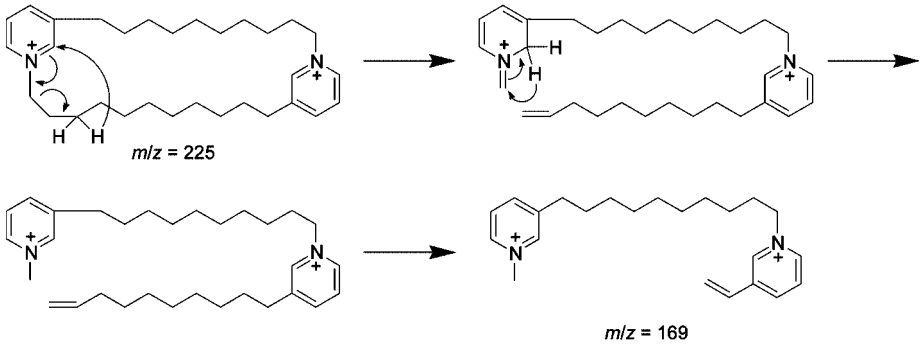


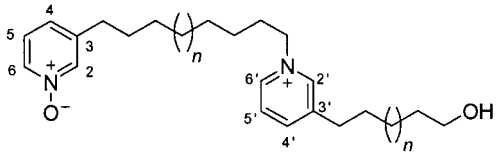
Figure 8. Possible fragmentation mechanism for cyclostellettamines related to the McLafferty rearrangement. Initially, a hydrogen transfer from C-3 of the alkyl chain via a six-membered transition state to an α-carbon of the heterocycle with a synchronous α,β-carbon bond cleavage occurs. The obtained 1-methylene-1,2-dihydropyridinium cation can undergo a re-aromatisation to form a methylpyridinium ion, which splits in the alkyl chain.

tion. Furthermore, the systematic investigation will promote a better understanding of the fragmentation patterns of these kinds of molecules in the future.

Experimental Section

General: NMR spectra were recorded with a Bruker AM 250 (250 MHz) spectrometer. Chemical shifts are quoted in ppm and are referenced to the appropriate solvent signal. The samples were injected into a HPLC System 1100 Series (Agilent) equipped with a photodiode-array detector (Agilent) and a microTOF$_{LC}$ mass spectrometer (Bruker Daltonik). The detection with the DAD was performed at a wavelength of 260 nm. For HPLC separation an XTerra RP-18 column (3.0×150 mm, 3.5 μm, Waters) was used. Separation was achieved by applying a gradient from 20% acetonitrile/80% formic acid (0.1%) to 80% acetonitrile/20% formic acid (0.1%) in 30 min and in 35 min back to the initial conditions. Total analysis time was 45 minutes with a flow rate of 0.4 mL min^{-1} and an oven temperature of 30 °C. Mass spectra were acquired with a microTOF$_{LC}$ mass spectrometer equipped with an ESI source (Bruker Daltonik). The following ESI inlet conditions were applied: dry gas temperature: 180 °C; dry gas flow: 10 L min^{-1}; nebulizer pressure: 1.5 bar; capillary voltage: 4500 V. For fragmentation the voltage of the capillary exit was set to 150% of the normal voltage and the voltage of skimmer 1 was set to 133% of the nor-

mal voltage. The system was calibrated in positive mode by external calibration with sodium formiate clusters. The following reference masses were used for calibration: 226.9515, 362.9263, 430.9138, 498.9012, 566.8886, 634.8760, 702.8635 and 770.8509. Before the measurements the calibration was renewed. The standard deviation of the calibration curve (quadratic calibration) was 1.51. MS^n spectra were acquired with an Esquire HCT ion trap in the positive mode equipped with an ESI source (Bruker Daltonik). FT-IR spectra were recorded on a Perkin–Elmer 1600 series spectrometer. Absorption maxima are reported in wavenumbers and the following abbreviations are used s: strong, m: medium, w: weak Elemental analysis was performed with a Heraeus CHN Rapid. Melting points were obtained with a Kofler melting point apparatus and are uncorrected. Column chromatography was performed on silica gel 60 (Merck, particle size 0.04–0.063 mm) or basic alumina. TLC was performed on aluminium plates precoated with Merck silica 60. Compounds were visualised by UV irradiation (254 nm) or dying with $KMnO_4$ solution (1% $KMnO_4$, 6.6% K_2CO_3, 2% 5% NaOH solution in 100 mL of water). All solvents were purified by simple distillation, except for THF, which was distilled from sodium/benzophenone under argon. Chemicals were used as purchased. LDA solution was purchased from Fluka. The assignment of protons and carbons in the dimers is as follows:



1,13-Tridecanediol (8a): A solution of $BH_3{\cdot}SMe_2$ (36.83 mmol, 3.76 mL 94%) in 10 mL of THF was added within 10 min, at 0 °C, to a suspension of tridecanoic diacid (3 g, 12.27 mmol) in 40 mL of dry THF under argon in a three-necked flask equipped with a dropping funnel and a silver-coated Vigreux column. After the addition was complete and gas evolution had almost stopped the ice bath was removed, the mixture was heated to reflux and SMe_2 was distilled off. When the temperature in the column head had reached 66 °C, indicating that all SMe_2 had been removed, the mixture was refluxed for an additional 30 min. It was then cooled down to room temperature and 30 mL of MeOH was slowly added (gas evolution). The solvent was removed and the residue was twice coevaporated with 30 mL of MeOH to give a grey solid, which was recrystallised from hexane to yield 2.2 g (83%) of **8a** as white crystals. M.p. 77 °C (ref.[14] 76–77 °C). ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.18–1.25 (br. s, 18 H, 9×CH_2), 1.36–1.41 (m, 4 H, CH_2CH$_2$OH), 3.36 (m and t, J = 6.5 Hz, 4 H, CH_2OH), 4.32 (t, J = 5.0 Hz, 2 H, OH; interchangeable with D_2O) ppm. IR (KBr): $\tilde{\nu}$ = 3299 cm^{-1} s, 2917 s, 2849 s, 1462 s, 1407 m, 1344 m, 1296 w, 1257 w, 1187 w, 1123 s, 1058 s, 1036 m, 1002 w, 958 m, 919 m, 831 w, 732 m. $C_{13}H_{28}O_2$ (216.21): calcd. C 72.17, H 13.04; found C 72.31, H 13.26.

13-Bromotridecan-1-ol (9a): To a suspension of tridecandiol **8a** (2.2 g, 10.16 mmol) in 80 mL of toluene in a round-bottomed flask equipped with a water extractor and a cooler was added hydrobromic acid (1.7 mL 48% aqueous solution, 15.25 mmol). The mixture was refluxed for 16 h. After cooling, the solution was consecutively washed with 20 mL of 1 M HCl, 2 M NaOH, water and brine. The organic layer was dried with $MgSO_4$ and the solvent was evaporated. Flash chromatography of the residue on silica (4:1 hexane/ethyl acetate) yielded 1.53 g (54%) of **9a** as a white solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.16–1.41 (m, 18 H, 9×CH_2), 1.42–1.58 (m, 2 H, CH_2–CH$_2$–OH), 1.72–1.84 (m, 2 H, CH_2–CH$_2$–Br), 3.39 (t, J = 7.0 Hz, 2 H, CH_2OH), 3.57 (t, J = 6.5 Hz, 2 H, CH_2–Br) ppm. IR (KBr): $\tilde{\nu}$ = 3425 cm^{-1} s, 2920 s, 2850 s, 1467 s, 1355 m, 1252 w, 1229 w, 1204 w, 1058 s, 970 w, 722 m, 645 s. $C_{13}H_{27}BrO$ (279.26): calcd. C 55.91, H 9.75; found C 56.03, H 9.90. M.p. 56 °C (ref.[14] 56–57 °C).

12-Bromododecanol (9b): Prepared from dodecanediol (5 g, 24.7 mmol) and hydrobromic acid (3.1 mL 48% aqueous solution, 27.5 mmol) in the same way as **9a**. The crude product was purified by kugelrohr distillation (150 °C/0.4 mbar) and yielded 4.0 g (60%) of **9b** as a colourless oil. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.22–1.48 (m, 18 H, 9×CH_2), 1.80 (pseudo quint, J = 7.0 Hz, 2 H, CH_2CH$_2$OH), 3.36 (t, J = 6.4 Hz, 2 H, CH_2Br), 3.52 (t, J = 6.6 Hz, 2 H, CH_2OH), 4.31 (t, J = 6.6 Hz, 1 H, OH; interchangeable with D_2O) ppm. IR (NaCl): $\tilde{\nu}$ = 3298 cm^{-1} s, 2918 s, 2849 s, 1462 s, 1334 w, 1206 m, 1072 s, 1030 s, 938 m, 729 m, 651 s. $C_{12}H_{25}BrO$ (265.23): calcd. C 54.34, H 9.50; found C 54.48, H 9.60.

10-Bromodecanol (9d): Prepared from decanediol (5 g, 28.7 mmol) and hydrobromic acid (3.6 mL 48% aqueous solution, 31.6 mmol) in the same way as **9a**. The crude product was purified by kugelrohr distillation (120 °C/0.5 mbar) and yielded 6.05 g (89%) of **9d** as a colourless oil. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.26–1.48 (m, 14 H, 7×CH_2), 1.80 (pseudo quint, J = 6.9 Hz, 2 H, CH_2CH$_2$OH), 3.38 (t, J = 6.4 Hz, 2 H, CH_2Br), 3.52 (t, J = 6.7 Hz, 2 H, CH_2OH), 3.68 (br. s, 1 H, OH; interchangeable with D_2O) ppm. IR (NaCl): $\tilde{\nu}$ = 3332 cm^{-1} s, 2926 s, 2853 s, 1464 s, 1370 w, 1256 m, 1056 s, 722 w, 644 w. $C_{10}H_{21}BrO$ (237.18): calcd. C 50.64, H 8.92; found C 50.39, H 8.85.

9-Bromononanol (9e): Prepared from nonanediol (5 g, 31.2 mmol) and hydrobromic acid (3.9 mL 48% aqueous solution, 34.3 mmol) in the same way as **9a**. Kugelrohr distillation (120 °C/0.66 mbar) yielded 5.98 g (86%) of **9e** as a colourless oil. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.23–1.45 (m, 12 H, 6×CH_2), 1.80 (quint, J = 6.9 Hz, 2 H, CH_2CH$_2$OH), 3.39 (t, J = 6.4 Hz, 2 H, CH_2Br), 3.53 (t, J = 6.7 Hz, 2 H, CH_2OH), 3.8 (br. s, 1 H, OH; interchangeable with D_2O) ppm. IR (KBr): $\tilde{\nu}$ = 3364 cm^{-1} m, 2929 s, 2854 s, 1465 m, 1348 w, 1253 w, 1216 w, 1056 m, 1013 w, 726 w, 646 m, 562 w. $C_9H_{19}BrO$ (223.15): calcd. C 48.44, H 8.58; found C 48.59, H 8.67.

2-(13-Bromotridecyloxy)tetrahydro-2*H*-pyran (10a): DHP (0.74 mL, 8.05 mmol) and PPTS (13.5 mg, 0.05 mmol) were added to a solution of **9a** (1.5 g, 5.37 mmol) in 50 mL of CH_2Cl_2 and the mixture was stirred at room temperature for 16 h. The solution was then washed with 2 M Na_2CO_3 (2×15 mL) and the organic layer was dried with $MgSO_4$. Evaporation of the solvent yielded crude **10a** as a yellow oil. Flash chromatography (19:1 hexane/ethyl acetate) yielded 1.52 g (78%) of **10a** as a colourless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.15–1.85 (m, 28 H, 14×CH_2), 3.26–3.48 (m, 4 H, CH_2Br, CHH′O), 3.61–3.86 (m, 2 H, CH$H′$–O), 4.50 (pseudo t, J = 3.5 Hz, 1 H, CH) ppm. IR (NaCl): $\tilde{\nu}$ = 2926 cm^{-1} s, 2853 s, 1465 m, 1352 m, 1260 w, 1200 m, 1136 m, 1120 m, 1078 m, 1034 s, 987 w, 905 w, 869 m, 815 w, 722 w, 645 w. $C_{18}H_{35}BrO_2$ (363.37): calcd. C 59.50, H 9.71; found C 59.67, H 9.88.

2-(12-Bromododecyloxy)tetrahydro-2*H*-pyran (10b): Prepared from **9b** (3 g, 11.3 mmol), DHP (1.54 mL, 17.0 mmol) and PPTS (0.03 g, 0.11 mmol) in the same way as **10a**. Flash chromatography (19:1 hexane/ethyl acetate) yielded 3.5 g (90%) of **10b** as a colourless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.25–1.96 (m, 26 H, 13×CH_2), 3.36–3.57 (m, 4 H, CH_2Br, CHH′O), 3.70–3.96 (m, 2 H, CH$H′$O), 4.60 (pseudo t, J = 3.5 Hz, 1 H, CH) ppm. IR (NaCl): $\tilde{\nu}$ = 2926 cm^{-1} s, 2854 s, 1465 m, 1352 m, 1260 w, 1200 m, 1120 m, 1078 m, 1034 s, 986 w, 905 w, 869 w, 815 w, 722 w. $C_{17}H_{33}BrO_2$ (349.35): calcd. C 58.45, H 9.52; found C 58.60, H 9.43.

2-(11-Bromoundecyloxy)tetrahydro-2*H*-pyran (10c): Prepared from bromoundecanol (2 g, 7.96 mmol), DHP (1.1 mL, 11.9 mmol) and PPTS (20 mg, 0.08 mmol) in the same way as **10a**. Flash chromatography (19:1 hexane/ethyl acetate) yielded 2.5 g (93%) of **10c** as a colourless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.25–1.91 (m, 24 H, 12×CH_2), 3.33–3.56 (m, 4 H, C*H*$_2$Br, C*H*H′O), 3.68–3.93 (m, 2 H, CH*H*′O), 4.57 (pseudo t, *J* = 3.5 Hz, 1 H, C*H*) ppm. IR (NaCl): $\tilde{\nu}$ = 2925 cm^{-1} s, 2853 s, 1465 m, 1440 m, 1352 m, 1260 w, 1200 m, 1120 s, 1078 s, 1033 s, 988 w, 905 m, 869 m, 815 m, 722 w, 646 w. $C_{16}H_{31}BrO_2$ (335.32): calcd. C 57.31, H 9.32; found C 57.50, H 9.13.

2-(10-Bromodecyloxy)tetrahydro-2*H*-pyran (10d): Prepared from **9d** (4 g, 17 mmol), DHP (2.32 mL, 25.5 mmol) and PPTS (0.04 g, 0.17 mmol) in the same way as **10a**. Flash chromatography (19:1 hexane/ethyl acetate; R_f = 0.28) yielded 4.4 g (80%) of **10d** as a colourless oil. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.25–1.86 (m, 22 H, 11×CH_2), 3.27–3.79 (m, 6 H, C*H*$_2$Br, 2×C*H*$_2$O), 4.51–4.56 (m, 1 H, C*H*) ppm. IR (NaCl): $\tilde{\nu}$ = 2927 cm^{-1} s, 2854 s, 1465 m, 1440 m, 1352 m, 1260 m, 1200 m, 1120 m, 1078 m, 1033 s, 988 m, 905 w, 869 w, 815 w, 722 w. $C_{15}H_{29}BrO_2$ (321.29): calcd. C 56.07, H 9.10; found C 56.18, H 9.18.

2-(9-Bromononyloxy)tetrahydro-2*H*-pyran (10e): Prepared from **9e** (4 g, 17.89 mmol) DHP (2.46 mL, 26.9 mmol) and PPTS (0.045 g, 0.18 mmol) in the same way as **10a**. Flash chromatography (19:1 hexane/ethyl acetate; R_f = 0.3) yielded 4.42 g (80%) of **10e** as a colourless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28–1.93 (m, 20 H, 10×CH_2), 3.36–3.94 (m, 6 H, C*H*$_2$Br, 2×C*H*$_2$O), 4.58–4.61 (m, 1 H, C*H*) ppm. IR (NaCl): $\tilde{\nu}$ = 2932 cm^{-1} s, 2855 s, 1718 w, 1458 m, 1352 m, 1260 m, 1200 m, 1120 m, 1078 m, 1033 s, 989 w, 905 w, 869 w, 815 w. $C_{14}H_{27}BrO_2$ (307.27): calcd. C 54.72, H 8.86; found C 54.82, H 8.88.

3-[14-(Tetrahydro-2*H*-pyran-2-yloxy)tetradecyl]pyridine (11a): A solution of 3-picoline (14.3 mmol, 1.4 mL) in 20 mL of dry THF at –80 °C under argon was treated with LDA (7.15 mL of a 2 M solution in 10 mL of THF) over a period of 10 min. After 30 min of stirring a solution of **10a** (7.15 mmol, 2.6 g) in 20 mL of dry THF was added within 10 min. Stirring was continued for 14 h during which time the mixture was warmed up to room temperature. After addition of 20 mL of sat. NH_4Cl solution and 20 mL of water the layers were separated and the aqueous layer was extracted twice with 25 mL of ethyl acetate. The combined organic layers were dried with $MgSO_4$. After evaporation of the solvent flash chromatography of the crude product (2:1 hexane/ethyl acetate; R_f = 0.36) afforded 1.45 g (54%) of pure **11a** as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.22–1.39 (m, 22 H, 11×CH_2), 1.47–1.92 (m, 8 H, py-CH_2C*H*$_2$, C*H*$_2$CH$_2$O and OCHC*H*$_2$CH$_2$C*H*$_2$), 2.59 (t, *J* = 7.7 Hz, 2 H, py-C*H*$_2$), 3.34–3.54 (m, 2 H, OC*H*H′), 3.67–3.92 (m, 2 H, OCH*H*′), 4.57 (pseudo t, *J* = 3.5 Hz, OC*H*O), 7.19 (dd, *J* = 7.7, *J* = 4.8 Hz, 1 H, py*H5*), 7.46 (dt, *J* = 7.8, *J* = 1.7 Hz, 1 H, py*H4*), 8.40–8.46 (m, 2 H, py*H2* and py*H6*) ppm. IR (NaCl): $\tilde{\nu}$ = 2925 cm^{-1} s, 2853 s, 1576 w, 1466 m, 1421 m, 1352 w, 1322 w, 1260 w, 1200 w, 1121 m, 1078 m, 1033 s, 989 w, 905 w, 869 w, 814 w, 714 m. $C_{24}H_{41}NO_2$ (375.59): calcd. C 76.75, H 11.00, N 3.73; found C 76.71, H 11.21, N 3.84.

3-[13-(Tetrahydro-2*H*-pyran-2-yloxy)tridecyl]pyridine (11b): Prepared from 3-picoline (17.3 mmol, 1.68 mL), LDA (8.6 mL of a 2 M solution) and **10b** (5.75 mmol, 2 g) in the same way as **11a**. Flash chromatography of the crude product (2:1 hexane/ethyl acetate; R_f = 0.26) afforded 1.45 g (70%) of pure **11b** as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.24–1.40 (m, 20 H, 10×CH_2), 1.48–1.89 (m, 8 H, py-CH_2C*H*$_2$, C*H*$_2$CH$_2$O and OCHC*H*$_2$CH$_2$C*H*$_2$), 2.62 (t, *J* = 7.7 Hz, 2 H, py-C*H*$_2$), 3.35–3.56 (m, 2 H, OC*H*H′), 3.70–3.94 (m, 2 H, OCH*H*′), 4.60 (pseudo t, *J* = 3.5 Hz, OC*H*O), 7.21 (dd, *J* = 7.8, *J* = 4.7 Hz, 1 H, py*H5*) 7.51 (dt, *J* = 7.8, *J* = 2.0 Hz, 1 H, py*H4*), 8.42–8.48 (m, 2 H, py*H2* and py*H6*) ppm. IR (NaCl): $\tilde{\nu}$ = 2922 cm^{-1} s, 2853 s, 1574 m, 1465 m, 1422 m, 1352 m, 1260 w, 1200 m, 1135 s, 1078 s, 1033 s, 987 w, 905 w, 869 w, 815 w, 714 s. $C_{23}H_{39}NO_2$ (361.56): calcd. C 76.4, H 10.87, N 3.87; found C 76.41, H 10.93, N 3.89.

3-[12-(Tetrahydro-2*H*-pyran-2-yloxy)dodecyl]pyridine (11c): Prepared from 3-picoline (14.9 mmol, 1.5 mL), LDA (7.45 mL 2 M solution) and **10c** (2.5 g, 7.45 mmol) in the same way as **11a**. Flash chromatography of the crude product (2:1 hexane/ethyl acetate) afforded 1.44 g (59%) of pure **11c** as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.21–1.40 (m, 18 H, 9×CH_2), 1.45–1.90 (m, 8 H, py-CH_2C*H*$_2$, C*H*$_2$CH$_2$O and OCHC*H*$_2$CH$_2$C*H*$_2$), 2.60 (t, *J* = 7.7 Hz, 2 H, py-C*H*$_2$), 3.33–3.54 (m, 2 H, OC*H*H′), 3.68–3.92 (m, 2 H, OCH*H*′), 4.57 (pseudo t, *J* = 3.5 Hz, OC*H*O), 7.19 (dd, *J* = 7.8, *J* = 4.8 Hz, 1 H, py*H5*), 7.48 (dt, *J* = 7.8, *J* = 2.2 Hz, 1 H, py*H4*), 8.40–8.45 (m, 2 H, py*H2* and py*H6*) ppm. IR (NaCl): $\tilde{\nu}$ = 2926 cm^{-1} s, 2854 s, 1576 w, 1466 w, 1421 w, 1352 w, 1200 w, 1136 m, 1120 m, 1078 m, 1034 m, 869 w, 815 w, 714 m. $C_{22}H_{37}NO_2$ (347.53): calcd. C 76.03, H 10.73, N 4.03; found C 75.66, H 10.96, N 4.40.

3-[11-(Tetrahydro-2*H*-pyran-2-yloxy)undecyl]pyridine (11d): Prepared from 3-picoline (12.4 mmol, 1.2 mL), LDA (6.2 mL of a 2 M solution) and **10d** (6.2 mmol, 2 g) in the same way as **11a**. Flash chromatography of the crude product (2:1 hexane/ethyl acetate; R_f = 0.35) afforded 1.45 g (70%) of pure **11d** as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.32 (br. s, 16 H, 8×CH_2), 1.48–1.89 (m, 8 H, py-CH_2C*H*$_2$, C*H*$_2$CH$_2$O and OCHC*H*$_2$CH$_2$C*H*$_2$), 2.61 (t, *J* = 7.7 Hz, 2 H, py-C*H*$_2$), 3.35–3.56 (m, 2 H, OC*H*H′), 3.70–3.94 (m, 2 H, OCH*H*′), 4.59 (pseudo t, *J* = 3.5 Hz, OC*H*O), 7.21 (dd, *J* = 7.6 Hz, 1 H, py*H5*) 7.51 (dt, *J* = 7.8, *J* = 1.9 Hz, 1 H, py*H4*), 8.43–8.47 (m, 2 H, py*H2* and py*H6*) ppm. IR (NaCl): $\tilde{\nu}$ = 2926 cm^{-1} s, 2853 s, 1574 m, 1465 m, 1421 m, 1352 m, 1260 w, 1200 w, 1120 m, 1078 m, 1033 s, 986 w, 905 m, 869 m, 815 m, 713 s. $C_{21}H_{35}NO_2$ (333.51): calcd. C 75.63, H 10.58, N 4.20; found C 75.78, H 10.67, N 4.37.

3-[10-(Tetrahydro-2*H*-pyran-2-yloxy)decyl]pyridine (11e): Prepared from 3-picoline (2.85 mL, 29.3 mmol), LDA (14.7 mL of a 2 M solution) and **10e** (3 g, 9.76 mmol) as described above for **11a**. Flash chromatography of the crude product (2:1 hexane/ethyl acetate; R_f = 0.35) afforded 1.82 g (57%) of pure **11e** as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (br. s, 14 H, 7×CH_2), 1.47–1.87 (m, 8 H, py-CH_2C*H*$_2$, C*H*$_2$CH$_2$O and OCHC*H*$_2$CH$_2$C*H*$_2$), 2.59 (t, *J* = 7.7 Hz, 2 H, py-C*H*$_2$), 3.32–3.53 (m, 2 H, OC*H*H′), 3.67–3.91 (m, 2 H, OCH*H*′), 4.56 (pseudo t, *J* = 3.5 Hz, OC*H*O), 7.19 (dd, *J* = 7.8, *J* = 4.8 Hz, 1 H, py*H5*), 7.47 (dt, *J* = 7.8, *J* = 1.9 Hz, 1 H, py*H4*), 8.40–8.43 (m, 2 H, py*H2* and py*H6*) ppm. IR (NaCl): $\tilde{\nu}$ = 2927 cm^{-1} s, 2854 s, 1575 w, 1465 m, 1422 m, 1352 m, 1260 w, 1200 m, 1120 m, 1078 m, 1033 s, 905 w, 869 w, 814 w, 714 m. $C_{20}H_{33}NO_2$ (319.48): calcd. C 75.19, H 10.41, N 4.38; found C 74.93, H 10.28, N 4.58.

14-(Pyridin-3-yl)tetradecanol (12a): Compound **11a** (1.29 g, 3.44 mmol) was dissolved in 50 mL of methanol and 6.9 mL of 1 M HCl was added. After stirring for 12 h at room temperature the solution was concentrated to 1/4 of its volume. The pH was brought to 10 by addition of 2 M NaOH and the solution was extracted three times with 10 mL of ethyl acetate. The combined organic layers were dried with $MgSO_4$ and the solvent removed to yield 0.96 g (96%) of **12a**. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.18–1.46 (m, 22 H, 11×CH_2), 1.48–1.64 (m, 2 H, C*H*$_2$CH$_2$OH), 2.57 (t, *J* = 7.6 Hz, 2 H, py-C*H*$_2$), 3.37 (dt and t, *J* = 6.2, *J* = 5.1 Hz, 2 H,

CH_2OH), 4.31 (t, J = 5.1 Hz, 1 H, OH; interchangeable with D_2O), 7.28 (dd, J = 7.8, J = 4.8 Hz, 1 H, py*H5*), 7.60 (dt, J = 7.7, J = 2.2 Hz, 1 H, py*H4*), 8.38 (dd, J = 4.8, J = 1.7 Hz, 1 H, py*H6*), 8.40 (d, J = 1.7 Hz, 1 H, py*H2*) ppm. IR (KBr): $\tilde{\nu}$ = 3334 cm^{-1} s, 2917 s, 2849 s, 1578 m, 1472 s, 1423 s, 1338 m, 1228 w, 1186 w, 1114 w, 1070 m, 1029 w, 1011 w, 964 w, 928 m, 888 w, 831 w, 802 m, 716 s, 640 m. $C_{19}H_{33}NO$ (291.47): calcd. C 78.29, H 11.41, N 4.81; found C 78.03, H 11.39, N 4.77. M.p. 61 °C (ref.[9] 61–62 °C).

13-(Pyridin-3-yl)tridecanol (12b): Prepared from **11b** (1.45 g, 4.0 mmol) and 8.0 mL of 1 M HCl as described above for **12a**. Recrystallisation from 1:1 hexane/ethyl acetate yielded 0.84 g (76%) of **12b**. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.14–1.33 (m, 18 H, 9 × CH_2), 1.33–1.48 (m, 2 H, C$H_2$$CH_2$py), 1.48–1.64 (m, 2 H, C$H_2$$CH_2$OH), 2.58 (t, J = 7.5 Hz, 2 H, py-CH_2), 3.36–3.42 (m, 2 H, CH_2OH), 4.32 (t, J = 5.1 Hz, 2 H, OH; interchangeable with D_2O), 7.29 (dd, J = 7.8, J = 4.7 Hz, 1 H, py*H5*), 7.61 (dt, J = 7.8, J = 1.9 Hz, 1 H, py*H4*), 8.39 (dd, J = 4.7, J = 1.6 Hz, 1 H, py*H6*), 8.42 (d, J = 1.6 Hz, 1 H, py*H2*) ppm. IR (KBr): $\tilde{\nu}$ = 3241 cm^{-1} m, 2923 s, 2848 s, 1574 m, 1470 m, 1420 m, 1378 w, 1186 w, 1078 s, 1025 m, 908 w, 802 m, 707 m, 634 w. $C_{18}H_{31}NO$ (277.44): calcd. C 77.92, H 11.26, N 5.05; found C 77. 66, H 11.33, N 4.86. M.p. 48 °C (ref.[9] 48–50 °C).

12-(Pyridin-3-yl)dodecanol (12c): Prepared from **11c** (2.16 g, 6.63 mmol) and 13.3 mL of 1 M HCl as described above for **12a**. Recrystallisation from 1:1 hexane/ethyl acetate yielded 1.36 g (78%) of **12c**. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.21–1.39 (m, 16 H, 8 × CH_2), 1.50–1.68 (m, 4 H, C$H_2$$CH_2py, CH_2$$CH_2$OH), 2.59 (t, J = 7.6 Hz, 2 H, py-CH_2), 3.36 (t, J = 6.6 Hz, 2 H, CH_2OH), 7.19 (dd, J = 4.8, J = 7.8 Hz, 1 H, py*H5*), 7.48 (dt, J = 7.8, J = 1.8 Hz, 1 H, py*H*4), 8.40–8.45 (m, 2 H, py*H*2, py*H6*) ppm. IR (KBr): $\tilde{\nu}$ = 3334 cm^{-1} s, 2918 s, 2850 s, 1578 m, 1472 m, 1423 m, 1335 w, 1186 w, 1113 w, 1071 m, 1027 w, 990 w, 947 w, 903 w, 830 w, 803 m, 715 s, 639 m. $C_{17}H_{29}NO$ (263.42): calcd. C 77.51, H 11.10, N 5.32; found C 77.54, H 11.27, N 5.46. M.p. 48–49 °C (ref.[15] 48–50 °C).

11-(Pyridin-3-yl)undecanol (12d): Prepared from **11d** (1.45 g, 4.35 mmol) and 8.7 mL of 1 M HCl as described above for **12a**. Drying under high vacuum yielded 0.87 g (80%) of **12d**. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.14–1.46 (m, 16 H, 8 × CH_2), 1.50–1.63 (m, 2 H, C$H_2$$CH_2$OH), 2.59 (t, J = 7.6 Hz, 2 H, py-CH_2), 3.34–3.41 (m, 2 H, CH_2OH), 4.33 (t, J = 5.1 Hz, 1 H, OH; interchangeable with D_2O), 7.30 (dd, J = 7.8, J = 4.8 Hz, 1 H, py*H5*), 7.62 (dt, J = 7.8, J = 1.9 Hz, 1 H, py*H4*), 8.39 (dd, J = 4.8, J = 1.6 Hz, 1 H, py*H6*), 8.43 (d, J = 2 Hz, 1 H, py*H2*) ppm. IR (KBr): $\tilde{\nu}$ = 3245 cm^{-1} m, 2926 s, 2852 s, 1576 m, 1466 m, 1420 s, 1376 w, 1188 m, 1078 s, 1019 m, 934 w, 801 m, 709 s, 635 m. $C_{16}H_{27}NO$ (249.39): calcd. C 77.06, H 10.91, N 5.62; found C 76.88, H 10.91, N 5.85.

10-(Pyridin-3-yl)decanol (12e): Prepared from **11e** (1.8 g, 5.63 mmol) and HCl (11.2 mL 1 M solution) in the same way as **12a**. Flash chromatography (19:1 CH_2Cl_2/methanol; R_f = 0.37) of the crude product gave 1.23 g (93%) of **12e** as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.22–1.40 (m, 12 H, 6 × CH_2), 1.49–1.67 (m, 4 H, C$H_2$$CH_2$OH and py-$CH_2CH_2$), 1.90 (br. s, 1 H, O*H*), 2.59 (t, J = 7.7 Hz, 2 H, py-CH_2), 3.63 (t, J = 6.6 Hz, 2 H, CH_2OH), 7.19 (dd, J = 7.8, J = 4.8 Hz, 1 H, py*H5*), 7.48 (dt, J = 7.8, J = 1.9 Hz, 1 H, py*H4*), 8.39–8.44 (m, 2 H, py*H6* and py*H2*) ppm. IR (NaCl): $\tilde{\nu}$ = 3331 cm^{-1} s, 2925 s, 2853 s, 1576 m, 1465 s, 1423 s, 1369 w, 1190 w, 1058 s, 1028 s, 924 w, 794 m, 713 s. $C_{15}H_{25}NO$ (235.37): calcd. C 76.55, H 10.71, N 5.95; found C 76.62, H 10.89, N 6.16.

3-(13-Chlorotridecyl)pyridine (13b): A solution of **12b** (1.0 g, 3.6 mmol) in 5 mL of dioxane was added to $SOCl_2$ (0.32 mL, 4.3 mmol) at 0 °C within 10 min. After stirring at room temperature for 1 h, 10 mL of ethanol was added and the mixture was heated to reflux for 10 min. The solvent was evaporated and the residue dissolved in 10 mL of CH_2Cl_2. The solution was washed three times with 10 mL of 2 M Na_2CO_3, the organic layer dried with $MgSO_4$ and the solvent removed. Flash chromatography (3:1 hexane/ethyl acetate; R_f = 0.24) of crude **13b** gave 753 mg (71%) of the pure compound as a slightly yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.25–1.50 (m, 18 H, 9 × CH_2), 1.55–1.85 (m, 4 H, py-CH_2CH_2 and C$H_2$$CH_2$Cl), 2.63 (t, J = 7.7 Hz, 2 H, py-CH_2), 3.55 (t, J = 6.7 Hz, 2 H, CH_2Cl), 7.23 (dd, J = 7.8, J = 4.7 Hz, 1 H, py*H5*), 7.51 (dt, J = 7.8, J = 1.9 Hz, 1 H, py*H4*), 8.43–8.49 (m, 2 H, py*H6* and py*H2*) ppm. IR (NaCl): $\tilde{\nu}$ = 2926 cm^{-1} s, 2853 s, 2365 w, 1574 m, 1465 m, 1421 m, 1308 w, 1189 w, 1127 w, 1026 m, 793 w, 714 m. $C_{18}H_{30}ClN$ (295.89): calcd. C 73.07, H 10.22, N 4.73; found C 73.24, H 10.32, N 4.70.

3-(11-Chloroundecyl)pyridine (13d): Prepared from **12d** (0.8 g, 3.21 mmol) and $SOCl_2$ (0.28 mL, 3.85 mmol) as described above for **13b**. Flash chromatography (2:1 hexane/ethyl acetate; R_f = 0.33) of crude **13d** gave 645 mg (75%) of the pure compound as a slightly brown oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.23–1.47 (m, 14 H, 7 × CH_2), 1.55–1.67 (m, 2 H, py-CH_2CH_2), 1.76 (quint, J = 7.1 Hz, 2 H, C$H_2$$CH_2$Cl), 2.59 (t, J = 7.7 Hz, 2 H, py-CH_2), 3.53 (t, J = 6.7 Hz, 2 H, CH_2Cl), 7.20 (dd, J = 7.8, J = 4.8 Hz, 1 H, py*H5*), 7.49 (dt, J = 7.8, J = 1.9 Hz, 1 H, py*H4*), 8.41–8.45 (m, 2 H, py*H6* and py*H2*) ppm. IR (NaCl): $\tilde{\nu}$ = 2926 cm^{-1} s, 2853 s, 1710 w, 1574 s, 1465 s, 1422 s, 1308 m, 1189 w, 1128 w, 1026 s, 793 m, 714 s, 651 m. $C_{16}H_{26}ClN$ (267.84): calcd. C 71.75, H 9.78, N 5.23; found C 71.83, H 9.86, N 5.35

3-(10-Chlorodecyl)pyridine (13e): Prepared from **12e** (1.56 g, 6.62 mmol) and $SOCl_2$ (0.72 mL, 9.93 mmol) as described above for **13b**. Flash chromatography (2:1 hexane/ethyl acetate; R_f = 0.45) of crude **12e** gave 1.32 g (79%) of pure **13e** as an orange oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.18–1.41 (m, 12 H, 6 × CH_2), 1.46–1.61 (m, 2 H, py-CH_2CH_2), 1.63–1.79 (m, 2 H, C$H_2$$CH_2$Cl), 2.53 (t, J = 7.7 Hz, 2 H, py-CH_2), 3.46 (t, J = 6.7 Hz, 2 H, CH_2Cl), 7.13 (dd, J = 4.8, J = 7.8 Hz, 1 H, py*H5*), 7.41 (dt, J = 1.7, J = 7.8 Hz, 1 H, py*H4*), 8.34–8.39 (m, 2 H, py*H6*, py*H2*) ppm. IR (NaCl): $\tilde{\nu}$ = 2926 cm^{-1} s, 2853 s, 2216 m, 1734 w, 1574 s, 1464 s, 1422 s, 1308 m, 1189 m, 1128 w, 1107 w, 1026 s, 910 s, 793 m, 732 s, 713 s, 649 m. $C_{15}H_{24}ClN$ (253.81): calcd. C 70.98, H 9.53, N 5.52; found C 70.89, H 9.54, N 5.63

3-(13-Chlorotridecyl)pyridine 1-Oxide (14b): *m*-Chloroperbenzoic acid (710 mg, 2.78 mmol, 77% active) was added to a solution of **13b** (750 mg, 2.53 mmol) in 20 mL of CH_2Cl_2 at 0 °C and the mixture was stirred for 1 h. After concentrating the solution to approximately 2 mL it was column-filtered through basic Al_2O_3 (40 g, 19:1 CH_2Cl_2/methanol). Evaporation of the solvent gave 739 mg (93%) of **14b** as a white solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.22–1.50 (m, 18 H, 9 × CH_2), 1.57–1.68 (m, 2 H, py-CH_2CH_2), 1.79 (quint, J = 7.1 Hz, 2 H, C$H_2$$CH_2$Cl), 2.59 (t, J = 7.7 Hz, 2 H, py-CH_2), 3.55 (t, J = 6.7 Hz, 2 H, CH_2Cl), 7.10–7.25 (m, 2 H, py*H5* and py*H4*), 8.08–8.12 (m, 2 H, py*H6* and py*H2*) ppm. IR (KBr): $\tilde{\nu}$ = 3084 cm^{-1} m, 2918 s, 2850 s, 1599 m, 1560 m, 1472 s, 1420 s, 1329 w, 1262 s, 1207 w, 1151 s, 1014 s, 939 s, 856 m, 793 m, 718 s, 678 s. $C_{18}H_{30}ClNO$ (311.89): calcd. C 69.32, H 9.70, N 4.39; found C 69.31, H 9.77, N 4.39. M.p. 63 °C (ref.[9] 62–63 °C).

3-(11-Chloroundecyl)pyridine *N*-Oxide (14d): Prepared from **13d** (471 mg, 1.76 mmol) and *m*-chloroperbenzoic acid (434 mg, 1.94 mmol, 77% active) as described above for **14b**. Evaporation of the solvent gave 404 mg (81%) of **14d** as a white solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.23–1.47 (m, 14 H, 7 × CH_2), 1.59–1.67

(m, 2 H, py-CH_2CH_2), 1.79 (quint, J = 7.1 Hz, 2 H, CH_2CH_2Cl), 2.60 (t, J = 7.7 Hz, 2 H, py-CH_2), 3.56 (t, J = 6.7 Hz, 2 H, CH_2Cl), 7.10–7.25 (m, 2 H, py*H5* and py*H4*), 8.05–8.13 (m, 2 H, py*H6* and py*H2*) ppm. IR (KBr): $\tilde{\nu}$ = 3084 cm^{-1} m, 2982 s, 2851 s, 1599 m, 1560 m, 1472 s, 1420 s, 1309 m, 1268 s, 1213 m, 1152 s, 1010 s, 940 s, 862 m, 794 m, 718 s, 677 s. $C_{16}H_{26}ClNO$ (283.84): calcd. C 67.70, H 9.23, N 4.93; found C 67.70, H 8.97, N 4.77. M.p. 49–50 °C.

3-(10-Chlorodecyl)pyridine *N*-Oxide (14e): Prepared from **13e** (1.46 g, 5 mmol) and *m*-chloroperbenzoic acid (1.29 g, 7.5 mmol, 77% active) as described above for **14b**. Evaporation of the solvent gave 1.14 g (83%) of **14e** as a slightly yellow oil. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.23–1.48 (m, 12 H, 6×CH_2), 1.51–1.68 (m, 2 H, py-CH_2CH_2), 1.70–1.83 (m, 2 H, CH_2CH_2Cl), 2.56 (t, J = 7.6 Hz, 2 H, py-CH_2), 3.52 (t, J = 6.7 Hz, 2 H, CH_2Cl), 7.05–7.21 (m, 2 H, py*H5* and py*H4*), 8.03–8.10 (m, 2 H, py*H6* and py*H2*) ppm. IR (NaCl): $\tilde{\nu}$ = 3064 cm^{-1} w, 2227 s, 2854 s, 1602 m, 1506 m, 1480 w, 1436 s, 1273 s, 1159 s, 1014 s, 966 w, 862 w, 793 w, 761 w, 722 w, 681 m. $C_{15}H_{24}ClNO$ (269.81): calcd. C 66.77, H 8.97, N 5.19 calcd. **13e**·0.25 H_2O: calcd. C 65.68, H 9.00, N 5.11; found C 65.69, H 9.15, N 5.13.

3-(12-Hydroxydodecyl)-1-[10-(1-oxidopyridin-3-yl)decyl]pyridinium Iodide (15f): Compound **14e** (830 mg, 3.07 mmol) was added to a solution of **12c** (0.81 g, 3.07 mmol) and NaI (552 mg, 3.7 mmol) in 30 mL of butan-2-one and the mixture was refluxed for 40 h. The solvent was then removed and the residue was adsorbed on SiO_2. Flash chromatography on SiO_2 (9:1 CH_2Cl_2/methanol) yielded 1.27 g (66%) of **15f** as a waxy solid. ^1H NMR (250 MHz, [D_6]DMSO): δ = 1.11–1.71 (m, 34 H, 17×CH_2), 1.84–1.99 (m, 2 H, NCH_2CH_2), 2.53 (t, J = 7.5 Hz, 2 H, 3-CH_2), 2.80 (t, J = 7.5 Hz, 2 H, 3′-CH_2), 3.32–3.40 (m, 2 H, CH_2OH), 4.33 (t, J = 5.0 Hz, 1 H, OH; interchangeable with D_2O), 4.56 (t, J = 7.3 Hz, 2 H, NCH_2), 7.19 (d, J = 7.8 Hz, 1 H, H4), 7.34 (t, J = 7.2 Hz, 1 H, H5), 8.03–8.14 (m, 3 H, H2, H2′ and H5′), 8.49 (d, J = 8.0 Hz, 1 H, H4′), 8.95 (d, J = 6.0 Hz, 1 H, H6′), 9.05 (s, 1 H, H2′) ppm. ^{13}C NMR (62.5 MHz, [D_6]DMSO): δ = 25.3, 25.4, 28.15, 28.20, 28.25, 28.55, 28.60, 28.65, 28.80, 28.85, 28.90 and 29.0 (12×CH_2), 29.6 (3′-CH_2CH_2), 29.8 (3-CH_2CH_2), 30.5 (CH_2CH_2N), 31.5 (3′-CH_2 + 3-CH_2), 32.4 (CH_2CH_2OH), 60.6 (CH_2OH, CH_2N), 125.4 (C4), 125.9 (C5), 127.5 (C5′), 136.1 (C6), 138.0 (C2), 141.3 (C3′), 142.1 (C6′), 142.9 (C3), 143.8 (C2′), 145.0 (C4′) ppm. IR (KBr): $\tilde{\nu}$ = 3422 cm^{-1} s, 3029 w, 2924 s, 2849 s, 1630 w, 1570 w, 1500 m, 1459 m, 1353 w, 1259 m, 1166 s, 1107 w, 1060 m, 1023 w, 953 w, 810 m, 761 m, 725 w, 689 m. HRMS: calcd. for $C_{32}H_{53}N_2O_2^+$ 497.4102; found 497.4108.

3-(10-Hydroxydecyl)-1-[13-(1-oxidopyridin-3-yl)tridecyl]pyridinium Iodide (15g): Prepared from **12e** (0.67 g, 2.86 mmol), **14b** (0.89 g, 2.86 mmol) and NaI (0.51 g, 3.4 mmol) as described above for **15f**. Flash chromatography on SiO_2 (9:1 CH_2Cl_2/methanol) yielded 1.1 g (60%) of **15g** as orange solid. ^1H NMR (250 MHz, [D_6] DMSO): δ = 1.11–1.45 (m, 32 H, 16×CH_2), 1.46–1.71 (m, 4 H, 3′-CH_2–CH_2, 3-CH_2–CH_2), 1.83–1.98 (m, 2 H, NCH_2CH_2), 2.53 (t, J = 7.4 Hz, 2 H, 3-CH_2), 2.79 (t, J = 7.6 Hz, 2 H, 3′-CH_2), 3.32–3.40 (m, 2 H, CH_2OH), 4.30 (t, J = 5.1 Hz, 1 H, OH; interchangeable with D_2O), 4.55 (t, J = 7.3 Hz, 2 H, NCH_2), 7.19 (dt, J = 7.8, J = 1.3 Hz, 1 H, H4), 7.34 (dd, J = 7.5, J = 6.5 Hz, 1 H, H5), 8.02–8.12 (m, 3 H, H2, H2′ and H5′), 8.48 (d, J = 8.2 Hz, 1 H, H4′), 8.93 (d, J = 6.0 Hz, 1 H, H6′), 9.03 (s, 1 H, H2′) ppm. ^{13}C NMR (62.5 MHz, [D_6]DMSO): δ = 25.2, 25.4, 28.1, 28.2, 28.3, 28.60, 28.65, 28.75, 28.80 and 28.9 (10×CH_2), 29.6 (3′-CH_2CH_2), 29.8 (3-CH_2CH_2), 30.5 (CH_2CH_2N), 31.5 (3′-CH_2 + 3-CH_2), 32.4 (CH_2CH_2OH), 60.6 (CH_2OH + CH_2N), 125.4 (C4), 125.9 (C5), 127.5 (C5′), 136.5 (C6), 138.0 (C2), 141.3 (C3′), 142.1(C6′), 142.9 (C3), 143.8 (C2′), 145.5 (C4′) ppm. IR (KBr): $\tilde{\nu}$ = 3422 cm^{-1} s, 2922 s, 2851 s, 1629 w, 1560 w, 1507 w, 1468 m, 1438 w, 1260 m, 1160 m, 1063 w, 1020 w, 962 w, 791 w, 760 w, 719 w, 678 m. HRMS: calcd. for $C_{33}H_{55}N_2O_2^+$ 511.4258; found 511.4262.

3-(14-Hydroxytetradecyl)-1-[10-(1-oxidopyridin-3-yl)decyl]pyridinium Iodide (15h): Prepared from **12a** (0.9 g, 3.08 mmol), **14e** (0.83 g, 3.08 mmol) and NaI (0.55 g, 3.7 mmol) as described above for **15f**. Flash chromatography on SiO_2 (9:1 CH_2Cl_2/methanol) yielded 1.57 g (78%) of **15h** as a yellow solid. ^1H NMR (250 MHz, [D_6] DMSO): δ = 1.18–1.72 (m, 38 H, 19×CH_2), 1.83–1.98 (m, 2 H, NCH_2CH_2), 2.53 (t, J = 7.3 Hz, 2 H, 3-CH_2), 2.78 (t, J = 7.5 Hz, 2 H, 3′-CH_2), 3.31–3.40 (m, 2 H, CH_2OH), 4.32 (t, J = 5.1 Hz, 1 H, OH; interchangeable with D_2O), 4.56 (t, J = 7.3 Hz, 2 H, NCH_2), 7.19 (d, J = 8.0 Hz, 1 H, H4), 7.32 (dd, J = 7.6, J = 6.6 Hz, 1 H, H5), 8.02–8.13 (m, 3 H, H2, H2′ and H5′), 8.49 (d, J = 8.0 Hz, 1 H, H4′), 8.95 (d, J = 6.0 Hz, 1 H, H6′), 9.05 (s, 1 H, H2′) ppm. ^{13}C NMR (62.5 MHz, [D_6]DMSO): δ = 25.2, 25.4, 28.15, 28.20, 28.25, 28.55, 28.60, 28.62, 28.66, 28.80, 28.85, 28.94 and 29.0 (13×CH_2), 29.6 (3′-CH_2CH_2), 29.8 (3-CH_2CH_2), 30.5 (CH_2CH_2N), 31.5 (3′-CH_2 + 3-CH_2), 32.4 (CH_2CH_2OH), 60.5 (CH_2OH + CH_2N), 125.4 (C4), 125.9 (C5), 127.5 (C5′), 136.2 (C6), 138.0 (C2), 141.3 (C3′), 142.1 (C6′), 142.9 (C3), 143.8 (C2′), 145.0 (C4′) ppm. IR (KBr): $\tilde{\nu}$ = 3384 cm^{-1} s, 3046 m, 2918 s, 2850 s, 1734 w, 1630 m, 1604 m, 1570 w, 1505 w, 1466 s, 1438 m, 1364 w, 1314 w, 1263 s, 1161 s, 1054 m, 1019 w, 964 w, 917 w, 804 m, 761 w, 721 m, 683 s. HRMS: calcd. for $C_{34}H_{57}N_2O_2^+$ 525.4415; found 525.4381.

3-(12-Hydroxydodecyl)-1-[11-(1-oxidopyridin-3-yl)undecyl]pyridinium Iodide (15i): Prepared from **12c** (0.74 g, 2.82 mmol), **14d** (0.8 g, 2.82 mmol) and NaI (0.51 g, 3.4 mmol) as described above for **15f**. Filtration of the precipitate yielded 1.53 g (85%) of **15i** as an off-white solid. ^1H NMR (250 MHz, [D_6]DMSO): δ = 1.15–1.71 (m, 36 H, 18×CH_2), 1.83–1.98 (m, 2 H, NCH_2CH_2), 2.51 (t, J = 8.2 Hz, 2 H, 3-CH_2), 2.79 (t, J = 7.5 Hz, 2 H, 3′-CH_2), 3.34–3.40 (m, 2 H, CH_2OH), 4.38 (t, J = 4.5 Hz, 1 H, OH; interchangeable with D_2O), 4.58 (t, J = 7.3 Hz, 2 H, NCH_2), 7.19 (dt, J = 8.1, J = 1.3 Hz, 1 H, H4), 7.32 (dd, J = 6.5, J = 7.5 Hz, 1 H, H5), 8.02–8.12 (m, 3 H, H2, H2′ and H5′), 8.49 (d, J = 8.1 Hz, 1 H, H4′), 9.00 (d, J = 6.0 Hz, 1 H, H6′), 9.10 (s, 1 H, H2′) ppm. ^{13}C NMR (62.5 MHz, [D_6]DMSO): δ = 25.2, 25.4, 28.2, 28.3, 28.55, 28.60, 28.66, 28.73, 28.77, 28.82, 28.85, 28.90 and 29.0 (14×CH_2), 29.6 (3′-CH_2CH_2), 29.8 (3-CH_2CH_2), 30.5 (CH_2CH_2N), 31.5 (3′-CH_2 + 3-CH_2), 32.4 (CH_2CH_2OH), 60.5 (CH_2OH + CH_2N), 125.4 (C4), 125.9 (C5), 127.5 (C5′), 136.2 (C6), 138.1 (C2), 141.3 (C3′), 142.2 (C6′), 142.9 (C3), 143.9 (C2′), 145.0 (C4′) ppm. IR (KBr): $\tilde{\nu}$ = 3256 cm^{-1} m, 3067 w, 2917 s, 2848 s, 1630 w, 1603 w, 1560 w, 1492 w, 1468 m, 1431 m, 1330 w, 1269 m, 1215 m, 1156 s, 1079 m, 1016 w, 965 m, 906 w, 817 w, 801 w, 760 w, 720 w, 682 m. HRMS: calcd. for $C_{33}H_{55}N_2O_2^+$ 511.4258; found 511.4254.

3-(14-Hydroxytetradecyl)-1-[11-(1-oxidopyridin-3-yl)undecyl]-pyridinium Iodide (15j): Prepared from **12a** (0.7 g, 2.4 mmol), **14d** (0.68 g, 2.4 mmol) and NaI (0.43 g, 2.88 mmol) as described above for **15f**. Flash chromatography on SiO_2 (9:1 CH_2Cl_2/methanol) yielded 0.85 g (53%) of **15h** as a yellow solid. ^1H NMR (250 MHz, [D_6]DMSO): δ = 1.15–1.72 (m, 40 H, 20×CH_2), 1.82–1.98 (m, 2 H, NCH_2CH_2), 2.52 (t, J = 7.7 Hz, 2 H, 3-CH_2), 2.78 (t, J = 7.5 Hz, 2 H, 3′-CH_2), 3.32–3.40 (m, 2 H, CH_2OH), 4.38 (t, J = 5.1 Hz, 1 H, OH; interchangeable with D_2O), 4.55 (t, J = 7.3 Hz, 2 H, NCH_2), 7.19 (d, J = 8.0 Hz, 1 H, H4), 7.32 (dd, J = 6.4, J = 7.6 Hz, 1 H, H5), 8.02–8.13 (m, 3 H, H2, H2′ and H5′), 8.48 (d, J = 8.1 Hz, 1 H, H4′), 8.94 (d, J = 6.0 Hz, 1 H, H6′), 9.04 (s, 1 H, H2′) ppm. ^{13}C NMR (62.5 MHz, [D_6]DMSO): δ = 25.2, 25.4, 28.15, 28.23,

28.27, 28.61, 28.66, 28.74, 28.77, 28.83, 28.86, 28.94 and 29.0 (13 × CH_2), 29.6 (3′-CH_2CH_2), 29.8 (3-CH_2CH_2), 30.5 (CH_2CH_2N), 31.5 (3′-CH_2 + 3-CH_2), 32.4 (CH_2CH_2OH), 60.5 (CH_2OH + CH_2N), 125.4 (C4), 125.9 (C5), 127.5 (C5′), 136.2 (C6), 138.1 (C2), 141.3 (C3′), 142.1 (C6′), 142.9 (C3), 143.8 (C2′), 145.0 (C4′) ppm. IR (KBr): $\tilde{\nu}$ = 3405 cm^{-1} s, 3048 w, 2918 s, 2850 s, 1629 w, 1604 w, 1560 w, 1507 w, 1466 m, 1438 w, 1351 w, 1263 s, 1161 s, 1054 m, 1019 w, 961 w, 800 w, 762 w, 721 w, 683 m. HRMS: calcd. for $C_{35}H_{59}N_2O_2^+$ 539.4571; found 539.4519.

3-(10-Hydroxydecyl)-1-[11-(1-oxidopyridin-3-yl)undecyl]pyridinium Iodide (15k): Prepared from **12d** (0.66 g; 2.79 mmol) and **14e** (0.79 g; 2.79 mmol) as described for **15f**. Flash chromatography on SiO_2 (9:1 CH_2Cl_2/methanol) yielded 1.2 g (70%) of **15k** as a waxy solid. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.14–1.72 (m, 32 H, 16 × CH_2), 1.84–1.97 (m, 2 H, NCH_2CH_2), 2.54 (t, J = 7.5 Hz, 2 H, 3-CH_2), 2.80 (t, J = 7.5 Hz, 2 H, 3′-CH_2), 3.32–3.40 (m, 2 H, CH_2OH), 4.32 (br. s, 1 H, OH; interchangeable with D_2O), 4.58 (t, J = 7.2 Hz, 2 H, NCH_2), 7.21 (d, J = 7.8 Hz, 1 H, H4), 7.33 (t, J = 7.0 Hz, 1 H, H5), 8.04–8.12 (m, 3 H, H2, H2′ and H5′), 8.50 (d, J = 8.0 Hz, 1 H, H4′), 8.96 (d, J = 6.0 Hz, 1 H, H6′), 9.08 (s, 1 H, H2′) ppm. ^{13}C NMR (62.5 MHz, [D$_6$]DMSO): δ = 25.3, 25.5, 28.27, 28.30, 28.33, 28.70, 28.72, 28.80, 28.84, 28.86, 28.90 and 29.0 (13 × CH_2), 29.7 (3′-CH_2CH_2), 29.9 (3-CH_2CH_2), 30.6 (CH_2CH_2N), 31.6 (3′-CH_2 + 3-CH_2), 32.5 (CH_2CH_2OH), 60.7 (CH_2OH, CH_2N), 125.6 (C4), 126.0 (C5), 127.5 (C5′), 136.2 (C6), 138.0 (C2), 141.5 (C3′), 142.2 (C6′), 143.0 (C3), 143.9 (C2′), 145.1 (C4′) ppm. IR (KBr): $\tilde{\nu}$ = 3451 cm^{-1} s, 3219 s, 2922 s, 2850 s, 1602 m, 1563 w, 1466 m, 1437 m, 1343 w, 1268 m, 1154 s, 1058 m, 1027 m, 965 m, 874 w, 812 m, 759 m, 721 w, 681 m. HRMS: calcd. for $C_{31}H_{51}N_2O_2^+$ 483.3945; found 483.3939.

Cyclostellettamine H (1): A suspension of **15f** (1.0 g, 1.6 mmol) in 15 mL of $CHCl_3$ under argon at 0 °C was treated with PBr_3 (0.6 mL, 6.4 mmol) over a period of 10 min. After stirring at 0 °C for an additional 15 min the mixture was heated to reflux for 1 h. It was then cooled to room temperature, poured into an ice-water solution (30 mL) and stirred until the ice had melted. The layers were separated and the aqueous layer was extracted three times with 20 mL of CH_2Cl_2. The combined organic phases were neutralised by washing three times with 20 mL of saturated $NaHCO_3$ solution and dried with $MgSO_4$. Most of the solvent was removed, leaving about 2 mL of bromide-containing solution, which was diluted with 13 mL of 2-butanone. The resulting mixture was added to a refluxing solution of NaI (0.53 g, 3.5 mmol) in 250 mL of 2-butanone with a syringe pump at a rate of approximately 0.6 mL per hour. Refluxing was continued for 4 d. The solvent was then removed to yield a brown oil, which solidified upon trituration with Et_2O. Recrystallisation from methanol/Et_2O yielded 810 mg (70%) of **1** as an orange solid. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.00–1.37 (m, 28 H, 14 × CH_2), 1.54–1.74 (m, 4 H, 3-CH_2CH_2), 1.81–2.00 (m, 4 H, NCH_2CH_2), 2.73–2.89 (m, 4 H, 3-CH_2), 4.59 (t, J = 6.3 Hz, 4 H, NCH_2), 8.10 (dd, J = 6.1, J = 7.8 Hz, 2 H, H5), 8.49 (d, J = 7.5 Hz, 2 H, H4), 8.97 (d, J = 6.0 Hz, 2 H, H6), 9.09 (s, 2 H, H2) ppm. ^{13}C NMR (62.5 MHz, [D$_6$]DMSO): δ = 24.8, 25.0, 27.4, 27.6, 28.0 28.3, 28.4, 28.5, 28.7 and 28.9 (10 × CH_2) 29.3 and 29.6 (3-CH_2CH_2), 30.2 and 30.4 (NCH_2CH_2), 31.2 and 31.3 (3-CH_2), 60.4 (NCH_2), 127.7 (C5), 142.4 (C6), 142.7 (C3), 144.0 (C2), 145.4 (C4) ppm. IR (KBr): $\tilde{\nu}$ = 3014 cm^{-1} m, 2921 s, 2850 s, 1625 s, 1582 w, 1500 s, 1467 s, 1438 s, 1367 w, 1305 w, 1233 w, 1207 w, 1153 m, 1106 w, 1007 w, 926 w, 813 m, 765 w, 721 m, 696 s. HRMS: calcd. for $C_{32}H_{52}IN_2^+$ 591.3170; found 591.3155. calcd. for $C_{32}H_{52}N_2^{2+}$ 232.2060 (found 232.2061), $C_{17}H_{28}N^+$ 246.2216 (246.2217), $C_{15}H_{24}N^+$ 218.1903 (218.1919).

Cyclostellettamine I (3): Prepared from **15g** (1 g, 1.56 mmol), PBr_3 (0.58 mL, 6.3 mmol) and NaI (0.47 g, 3.12 mmol) as described above for **1**. Compound **3** (0.75 g, 66%) was isolated as an off-white solid. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.04–1.31 (m, 30 H, 15 × CH_2), 1.57–1.70 (m, 4 H, 3-CH_2CH_2), 1.82–1.99 (m, 4 H, NCH_2CH_2), 2.81 (t, J = 6.0 Hz, 4 H, 3-CH_2), 4.59 (t, J = 6.2 Hz, 4 H, NCH_2), 8.09 (pseudo t, J = 6.9 Hz, 2 H, H5), 8.50 (d, J = 7.8 Hz, 2 H, H4), 8.96 (d, J = 5.5 Hz, 2 H, H6), 9.08 (s, 2 H, H2) ppm. ^{13}C NMR (62.5 MHz, [D$_6$]DMSO): δ = 24.9, 25.2, 27.6, 27.9, 28.3, 28.5, 28.7 and 28.9 (8 × CH_2), 29.3 and 29.8 (3-CH_2CH_2), 30.1 and 30.5 (NCH_2CH_2), 31.0 and 31.5 (3-CH_2), 60.6 (NCH_2), 127.7 (C5), 142.3 (C6), 142.8 (C3), 143.9 (C2), 145.4 (C4) ppm. IR (KBr): $\tilde{\nu}$ = 3011 cm^{-1} m, 2921 s, 2851 s, 1625 m, 1583 w, 1500 s, 1467 m, 1439 w, 1364 w, 1326 w, 1240 w, 1208 w, 1152 w, 924 w, 835 m, 801 w, 722 w, 696 s. HRMS: calcd. for $C_{33}H_{54}IN_2^+$ 605.3363 (found 605.3308), $C_{33}H_{54}N_2^{2+}$ 239.2138 (239.2136), $C_{18}H_{30}N^+$ 260.2373 (260.2364), $C_{15}H_{24}N^+$ 218.1903 (218.1914).

Cyclostellettamine K (4): Prepared from **15h** (1 g, 1.53 mmol), PBr_3 (0.57 mL, 6.2 mmol) and NaI (0.51 g, 3.36 mmol) as described above for **1**. Compound **4** (0.81 g, 71%) was isolated as a slightly yellow solid. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.01–1.32 (m, 32 H, 16 × CH_2), 1.55–1.74 (m, 4 H, 3-CH_2CH_2), 1.83–1.99 (m, 4 H, NCH_2CH_2), 2.74–2.88 (m, 4 H, 3-CH_2), 4.60 (t, J = 5.8 Hz, 4 H, NCH_2), 8.10 (dd, J = 6.0, J = 7.9 Hz, 2 H, H5), 8.50 (d, J = 8.0 Hz, 2 H, H4), 8.99 (d, J = 5.8 Hz, 2 H, H6), 9.10 (s, 2 H, H2) ppm. ^{13}C NMR (62.5 MHz, [D$_6$]DMSO): δ = 24.6, 25.1, 27.2, 27.9, 28.0, 28.3, 28.5, 28.6, 28.8 and 28.9 (10 × CH_2), 29.0 and 29.7 (3-CH_2CH_2), 29.9 and 30.4 (NCH_2CH_2), 31.0 and 31.4 (3-CH_2), 60.4 (NCH_2), 127.7 (C5), 142.2 (C6), 142.6 (C3), 143.8 (C2), 145.2 (C4) ppm. IR (KBr): $\tilde{\nu}$ = 3023 cm^{-1} m, 2921 s, 2850 s, 1718 w, 1629 m, 1500 s, 1466 s, 1364 w, 1321 w, 1238 w, 1202 w, 1150 w, 1029 w, 905 w, 827 w, 721 w, 688 s. HRMS: calcd. for $C_{34}H_{56}N_2^{2+}$ 246.2216 (found 246.2195), $C_{19}H_{32}N^+$ 274.2529 (274.2503), $C_{15}H_{24}N^+$ 218.1903 (218.1912).

Cyclostellettamine G (2): Prepared from **15i** (1 g, 1.56 mmol), PBr_3 (0.58 mL, 6.3 mmol) and NaI (0.47 g, 3.12 mmol) as described above for **1**. Compound **2** (0.819 g, 72%) was isolated as a light-brown solid. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.02–1.38 (m, 30 H, 15 × CH_2), 1.55–1.74 (m, 4 H, 3-CH_2CH_2), 1.82–2.00 (m, 4 H, NCH_2CH_2), 2.81 (t, J = 6.1 Hz, 4 H, 3-CH_2), 4.63 (t, J = 6.1 Hz, 4 H, NCH_2), 8.1 (dd, J = 6.1, J = 7.7 Hz, 2 H, H5), 8.51 (d, J = 7.9 Hz, 2 H, H4), 9.03 (d, J = 5.9 Hz, 2 H, H6), 9.1 (s, 2 H, H2) ppm. ^{13}C NMR (62.5 MHz, [D$_6$]DMSO): δ = 24.7, 24.9, 27.3, 27.7, 28.0, 28.3, 28.4, 28.6, 28.70, 28.75 and 28.80 (11 × CH_2), 29.2 and 29.4 (3-CH_2CH_2), 30.1 and 30.2 (NCH_2CH_2), 31.1 and 31.4 (3-CH2), 60.4 (NCH_2), 127.6 (C5), 142.2 (C6), 142.6 (C3), 143.9 (C2), 145.2 (C4) ppm. IR (KBr): $\tilde{\nu}$ = 3013 cm^{-1} m, 2921 s, 2851 s,1719 w, 1626 m, 1501 s, 1467 s, 1444 m, 1364 w, 1314 w, 1238 w, 1206 w, 1153 w, 924 w, 816 m, 697 s. HRMS: calcd. for $C_{33}H_{54}IN_2^+$ 605.3363 (found 605.3317), $C_{33}H_{54}N_2^{2+}$ 239.2138 (239.2135), $C_{17}H_{28}N^+$ 246.2216 (246.2211), $C_{16}H_{26}N^+$ 232.2060 (232.2064).

Cyclostellettamine L (5): Prepared from **15j** (0.8 g, 1.29 mmol), PBr_3 (0.45 mL, 4.8 mmol) and NaI (0.4 g, 2.64 mmol) as described above for **1**. Compound **5** (0.65 g, 66%) was isolated as a yellow solid. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 1.02–1.37 (m, 34 H, 17 × CH_2), 1.56–1.74 (m, 4 H, 3-CH_2CH_2), 1.82–1.99 (m, 4 H, NCH_2CH_2), 2.73–2.88 (m, 4 H, 3-CH_2), 4.59 (t, J = 6.3 Hz, 4 H, NCH_2), 8.11 (dd, J = 6.0, J = 7.7 Hz, 2 H, H5), 8.50 (d, J = 7.8 Hz, 2 H, H4), 8.97 (d, J = 5.7 Hz, 2 H, H6), 9.08 (s, 2 H, H2) ppm.^{13}C NMR (62.5 MHz, [D$_6$]DMSO): δ = 24.7, 25.0, 27.3, 27.7, 28.0, 28.3, 28.45, 28.50, 28.65, 28.70, 28.77, 28.80 and 28.88 (13 × CH_2), 29.1 and 29.4 (3-CH_2CH_2), 29.9 and 30.2 (NCH_2CH_2), 31.2 and

31.3 (3-CH_2), 60.4 (N–CH_2), 127.6 (C5), 142.2 (C6), 142.6 (C3), 143.8 (C2), 145.3 (C4) ppm. IR (KBr): $\tilde{\nu}$ = 3016 cm^{-1} m, 2921 s, 2851 s, 1727 w, 1627 m, 1502 s, 1466 s, 1362 w, 1320 w, 1237 w, 1204 w, 1152 w, 1111 w, 1030 w, 927 w, 818 m, 720 m, 693 s. HRMS: calcd. for $C_{35}H_{58}N_2^{2+}$ 253.2295 (found 253.2264), $C_{19}H_{32}N^+$ 274.2529 (274.2499), $C_{16}H_{26}N^+$ 232.2060 (232.2049).

Cyclostellettamine Q (6): Prepared from **15k** (1.27 g, 2.08 mmol), PBr_3 (0.78 mL, 8.3 mmol) and NaI (0.69 g, 4.58 mmol) as described above for **1**. Compound **6** (0.59 g, 40%) was isolated as an off-white solid. ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ = 0.99–1.30 (m, 26 H, 13 × CH_2), 1.55–1.71 (m, 4 H, 3-CH_2CH_2), 1.82–1.98 (m, 4 H, NCH_2CH_2), 2.80 (t, J = 6.3 Hz, 4 H, 3-CH_2), 4.60 (t, J = 5.9 Hz, 4 H, NCH_2), 8.10 (t, J = 6.9 Hz, 2 H, H5), 8.50 (d, J = 8.0 Hz, 2 H, H4), 9.05 (d, J = 5.8 Hz, 2 H, H6), 9.20 (s, 2 H, H2) ppm. ^{13}C NMR (62.5 MHz, [D$_6$]DMSO): δ = 24.9, 25.0, 27.5, 27.7, 28.0, 28.2, 28.4, 28.5, 28.6, 28.7, 28.8, 28.9 and 29.0 (13 × CH_2), 29.4 and 29.6 (3-CH_2CH_2), 30.2 and 30.4 (NCH_2CH_2), 31.2 and 31.4 (3-CH_2), 60.4 (NCH_2), 127.7 (C5), 142.4 (C6), 142.7 (C3), 144.0 (C2), 145.3 (C4) ppm. IR (KBr): $\tilde{\nu}$ = 3013 cm^{-1} m, 2923 s, 2852 s, 1627 m, 1583 w, 1500 s, 1467 m, 1439 w, 1368 w, 1321 w, 1241 w, 1205 w, 1154 w, 823 m, 758 w, 724 w, 697 m. HRMS: calcd. for $C_{31}H_{50}IN_2^+$ 577.3019 (found 577.3012), $C_{31}H_{50}N_2^{2+}$ 225.1982 (225.1991).

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[6] A 1.5 mg sample of the mixture was obtained from this sponge and analysed. The 1D ^{1}H NMR spectrum of the mixture showed no indication of compounds other than the cyclostellettamines. The compounds were identified by their characteristic UV maximum at a wavelength of 267 nm, the measured high resolution mass and their MS fragmentation pattern.

[7] Due to an overlap in publishing the results with Fusetani's work (ref.[5b]) the name cyclostellettamine G has already been given to the chain length combination 11 and 12, which would have been cyclostellettamine H in our nomenclature.

[8] This compound is a synthetic precursor of haliclamine D and has not yet been isolated as a natural product. The name cyclostellettamine Q was chosen because it is probable that further derivatives will be isolated in the future. Cyclostellettamines M, N, O, P and R are reserved for the chain length combinations 9/9, 9/10, 10/10, 9/11 and 11/11, respectively.

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