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Synthesis of New Analogues of the Tetraponerines

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To evaluate the influences of the tetraponerine alkyl chains and tricyclic ring systems on their cytotoxic activities, we have prepared a series of alkyl derivatives (**3a**, **3b** and **4a**–**f**) of the non-natural tricyclic skeletons decahydro-2*H*,6*H*-dipyrido[1,2-*a*:1′,2′-*c*]pyrimidine (**3**, 6–6–6 skeleton) and dodecahydro-2*H*-1,8a-diazaphenanthrene (**4**, iso-6–6–6 skeleton). In this study, two ways to synthesise the 6–6–6 analogues have been developed and compared. One is based on the condensation of α-tripiperideine with diethyl malonate (DEM) in water at pH 11. This yielded oxo ester **11**, precursor of the amino nitrile **8**, but only in moderate yield. In the second pathway, the key intermediate **8** was more efficiently synthesised by starting from 2-(2-piperidyl)ethanol. Treatment of **8** with alkyl Grignard reagents led to the 6–6–6 analogues **3a** and **3b**. When the one-pot reaction between α-tripiperideine and DEM was performed in water at pH 8, the lactam **12**, precursor of the iso-6–6–6 skeleton, was obtained in a yield of 76 %. The same lactam was also obtained in a yield of 86 % by treatment of tetrahydroanabasine **14** with DEM in water at pH 8. Lactam **12** was transformed into the iso-6–6–6 analogues **4a**–**4f**. The cytotoxic activities of the 6–6–6 and iso-6–6–6 analogues against HT29 cancer cells were compared with those of the 5–6–5 and 6–6–5 tetraponerines and with those of solenopsin analogues.

Introduction

Pseudomyrmecine ants of the genus *Tetraponera* utilise their modified stings to smear enemies with a contact poison that contains a mixture of eight tricyclic alkaloids.[1–3] These alkaloids, named tetraponerines T-1 to T-8, can be divided into two structural families, based either on the decahydrodipyrrolo[1,2-*a*:1′,2′-*c*]pyrimidine skeleton (**1**, 5–6–5 skeleton, Figure 1) or on the decahydro-5*H*-pyrido[1,2-*c*]-pyrrolo[1′,2′-*a*]pyrimidine skeleton (**2**, 6–6–5 skeleton). In each family, the compounds differ from each other in the lengths (*n*-Pr or *n*-pentyl) and the stereochemistries of the alkyl chains attached at C-5.[1–3]

In the context of a program involving the search for bioactive compounds in insects, preliminary tests indicated that the tetraponerines and some of their derivatives presented interesting cytotoxic activities. It has also been shown that these molecules possess neurotoxic[4] and insecticidal activities.[1] To evaluate the influences of the alkyl chains and of the tricyclic ring systems on the cytotoxic activity, we decided to prepare a series of 6-alkyl derivatives of the non-natural tricyclic skeleton decahydro-2*H*,6*H*-dipyrido[1,2-*a*:1′,2′-*c*]pyrimidine (**3**, 6–6–6 skeleton). In this study we have compared two pathways starting from Δ^1-piperideine that permit access to these derivatives. In addition, we also found a simple and effective way to synthesise 9-alkyl derivatives of the isomeric dodecahydro-2*H*-1,8a-diazaphenanthrene skeleton (**4**, iso-6–6–6 skeleton).

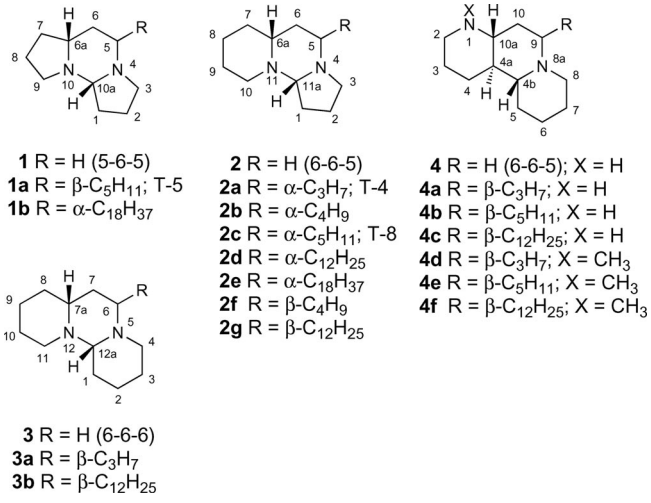

Figure 1. Structures of the tricyclic skeletons of the tetraponerines and their analogues.

Results and Discussion

Several syntheses of derivatives based on the 5–6–5 (**1**) and 6–6–5 (**2**) skeletons and substituted at C-5 have been reported.[2,3,5,6] In particular, a short and practical synthesis of compound **5** (Scheme 1), a pivotal intermediate in the synthesis of derivatives related to the 5–6–5 skeleton and

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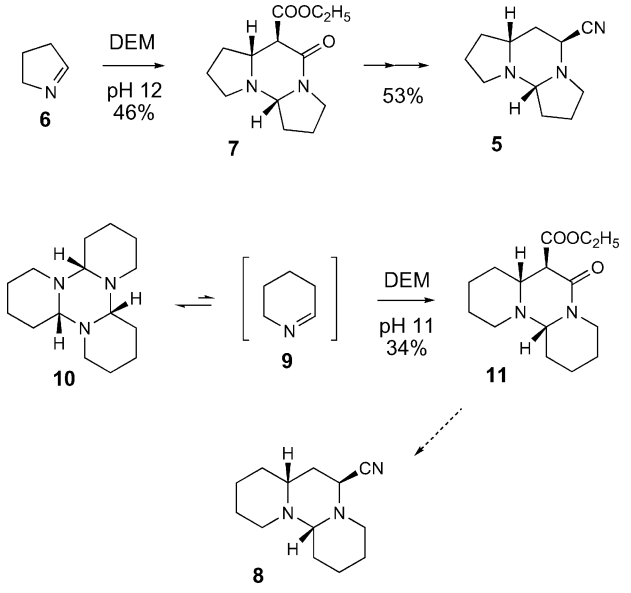
alkylated at C-5, has been achieved.[6] The key step of this synthesis was a one-pot stereoselective process in which two molecules of Δ^1-pyrroline (**6**) react with one molecule of diethyl malonate (DEM) to afford the tricyclic lactam ester **7**. Hydrolysis of the ethoxycarbonyl group and subsequent decarboxylation yielded a lactam that was then converted into the α-amino nitrile **5** (Scheme 1).

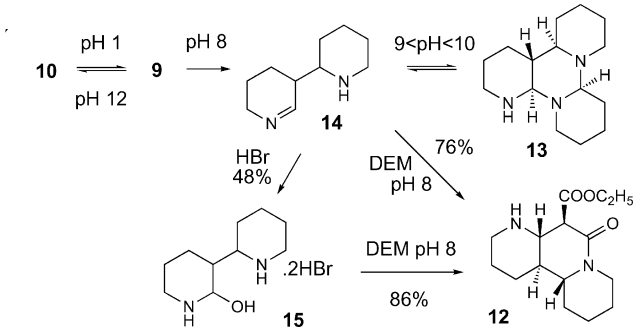


Scheme 1. Synthesis of the key intermediates **8** and **11**.

To synthesise the 6–6–6 derivative **8** corresponding to **5**, we decided to follow the same pathway but with the replacement of Δ^1-pyrroline by Δ^1-piperideine (**9**, Scheme 1). Because this compound is unstable, it must be prepared in situ. Three different methods for generating Δ^1-piperideine were attempted: treatment of lysine with NBS,[7] dehydrohalogenation of *N*-chloropiperidine[8] and detrimerisation of α-tripiperideine (**10**).[9]

Numerous assays were carried out to study the influence of different parameters – such as temperature, proportion of reactants, method of formation of **9** and pH – on the outcomes of the reactions. The best yield (34%) of the lactam ester **11** (Scheme 1) was obtained by generation of **9** by slow detrimerisation of α-tripiperideine in water at pH 11 and simultaneous addition of DEM (2 equiv.). As observed by Plehiers et al.[6] for the formation of **7**, only one diastereoisomer of **11** was obtained, possessing *trans* stereochemistry at both ring junctions and an equatorial ethoxycarbonyl group at C-7. These configurations were assigned on the basis of the coupling constant data for 7-H, 7a-H and 12a-H (see Exp. Sect.), which were consistent with the presence of axial protons.

To understand why the yield is at its optimum at pH 11, we have to take into account the pH-sensitive isomerisation of α-tripiperideine (**10**) into isotripiperideine (**13**), which implies the occurrence of the transient dimer **14**, tetrahydroanabasine (Scheme 2). Indeed, Schöpf et al.[10,11] have shown that the trimer **10** is stable at pH values above 12, whereas at pH values below 2 the monomer **9** is quickly formed. Moreover, they observed that Δ^1-piperideine dimerises to form tetrahydroanabasine (**14**), which may further react with a third molecule of **9** to generate trimer **13**. The rate of formation of tetrahydroanabasine (**14**) is at its maximum at pH 8 and that of isotripiperideine (**13**) at pH values between 9 and 10. In view of these results, we have to admit that pH 11 is probably the best compromise between the rate of formation of Δ^1-piperideine (**9**) and its undesired transformation into dimer **14**, and thus that it is at this pH that the conditions are the most appropriate for the condensation of two molecules of **9** with one of DEM to form the amide **11**. It should be noted that, in addition to compound **11**, several derivatives originating from competing reactions were identified. Malonic acid monoester and malonic acid, resulting from the hydrolysis of DEM, isotripiperideine (**13**) from isomerisation of α-tripiperideine (**10**) and high-molecular-weight material from polymerisation of Δ^1-piperideine (**9**), for instance, were also isolated from the reaction mixture. This could explain the low yield of compound **11**.

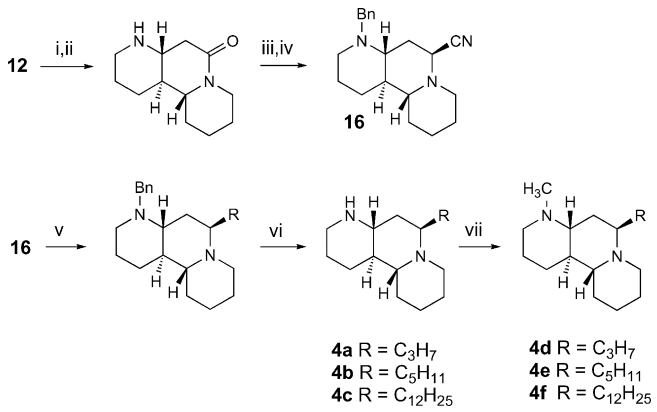


Scheme 2. Synthesis of the key intermediate **12**.

Moreover, during this reaction we isolated also small amounts (4% yield) of an isomer of the amide **11**, the spectral properties of which indicated that it was the iso-6–6–6 derivative **12**. Again, only one diastereoisomer was obtained, corresponding to the most stable configuration (*trans* ring junctions and equatorial ethoxycarbonyl group). It is reasonable to assume that amide **12** results from the reaction between traces of tetrahydroanabasine (**14**) and 1 equiv. of DEM through a Robinson–Schöpf condensation. To support this hypothesis, α-tripiperideine (**10**) was detrimerised in HCl (1 M). The pH was then raised to 8 and maintained at this value for 5 h to generate dimer **14**, avoiding the formation of trimer **13**. DEM was then added, and the mixture was further left at pH 8 for 17 h. This afforded amide **12** in 76% yield. Compound **11** was not formed under these conditions. Moreover, when the bis(hydrobromide) of 2-hydroxy-3-[2-piperidyl]piperidine (**15**), prepared according to Schöpf et al.[12] from α-tripiperideine (**10**), was condensed at pH 8 with DEM, we obtained compound **12** in 86% yield.

By application to **12** of a procedure similar to that utilised the transformation of **7** into **5**, the amino nitrile **16** was obtained in an overall yield of 52% (Scheme 3). Treatment of this compound with appropriate Grignard reagents,

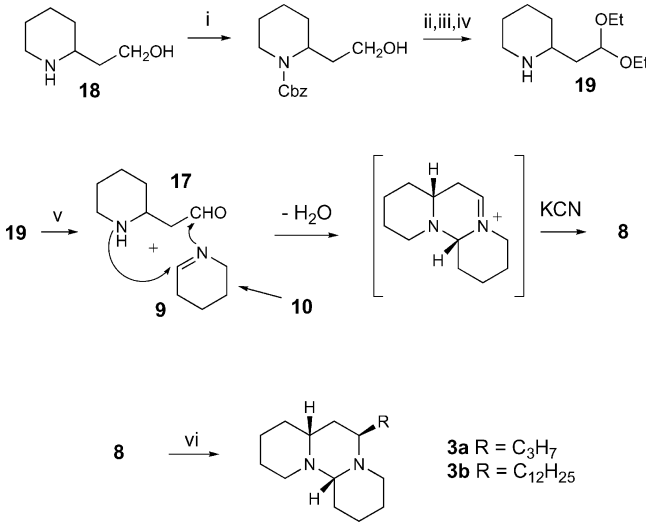
followed by removal of the protecting group, led stereoselectively to the alkylated compounds **4a**–**c**. Methylation of the secondary amine through a modified Eschweiler–Clarke reaction provided compounds **4d**–**f**. This represents a particularly attractive route for the synthesis of such derivatives (26% yield from **12**).



Scheme 3. Synthesis of the iso-6–6–6 analogues **4a**–**4f**. Reagents and conditions: (i) 5% KOH/MeOH, 20 °C, 2 h; (ii) (a) 10% HCl → pH 4–5, 0 °C, (b) 70 °C, 2 h, 85%; (iii) Na_2CO_3, BnBr, CH_2Cl_2/H_2O, reflux, 3 h, 98%; (iv) (a) Dibal-H (1 equiv.)/hexane, –78 °C, Et_2O, 3 h, (b) 10% $HClO_4$/EtOH → pH 3, (c) KCN (5.5 equiv.)/H_2O, room temp. overnight, 60%; (v) RMgBr (5 equiv.), Et_2O/THF, –10 °C to room temp., 40 h, average yield: 90%; (vi) H_2, 10% Pd/C, MeOH/12.5 M HCl (98:2), atmospheric pressure, 20 °C, 16 h, average yield: 97%; (vii) (a) 37% aq. HCHO (11.6 equiv.), MeOH, reflux, 20 h, (b) room temp., $NaBH_4$ (3.9 equiv.), 2 h, average yield: 65%.

It is notable that, despite our efforts, the two other means to obtain Δ^1-piperideine – namely treatment of lysine with NBS and the use of a solution of **9** freshly prepared by dehydrohalogenation of *N*-chloropiperidine under conditions avoiding its trimerisation – led to very low yields not only of **11** but also of **12**. Nevertheless, in one set of experiments by using *N*-chloropiperidine as starting material with maintenance of the pH between 6 to 12, a yield of about 20% of compound **12** could be isolated, suggesting the formation of relatively small amounts of tetrahydroanabasine (**14**) under these conditions. In addition, to improve the yields of **11**, we carried out the condensation between **10** and DEM in organic solvents instead of water; similar condensations of activated methylene compounds with Δ^1-piperideine generated by detrimerisation of α-tripiperideine (**10**) in organic solvents have been reported to proceed with good yields.[13–15] Unfortunately, though, none of our attempts led to the desired compound **11**. In CH_2Cl_2 or EtOH/EtONa, for example, in addition to unchanged α-tripiperideine (**10**), the α-tripiperideine isomer **13** was obtained in 47 and 70% yields, respectively, and in EtOH compound **12** was formed (20% yield). These results suggested that in these organic solvents the formation of dimer **14** is favoured.

At this point, because the yields in preparing the 6–6–6 derivatives were not very satisfactory, another approach was used to prepare the key derivative **8**. This approach consisted of condensation of Δ^1-piperideine (**9**) with the amino aldehyde **17**, which can be easily prepared from the commercially available amino alcohol **18** as shown in Scheme 4 by successive protection of the secondary amine, oxidation of the primary hydroxy group, transformation of the resulting aldehyde into an acetal and subsequent deprotection of the amino group by catalytic hydrogenolysis. By this pathway, the key compound **8** was obtained in an overall yield of 38% from **18**. No other diastereoisomers were detected. This high stereoselectivity is probably the result of thermodynamic control that leads to the more stable diastereoisomer in which the ring junctions are *trans* and the cyano group occupies an axial position, forced by the anomeric effect. These configurations are deduced from the coupling constants of 6-H, 7a-H and 12a-H (see the Experimental Section). Subsequent alkylation of the amino nitrile **8** with appropriate alkylmagnesium bromides led via iminium ions to the 6-alkylated 6–6–6 derivatives **3a** and **3b**. This last scheme thus appears to be the most convenient and effective method to prepare 6–6–6 derivatives alkylated at C-6.



Scheme 4. Synthesis of the 6–6–6 analogues **3a** and **3b**. Reagents and conditions: (i) $ClCO_2Bn$, K_2CO_3, EtOH/H_2O, 0 °C to room temp., 2.5 h, 99%; (ii) PCC/Al_2O_3, room temp., 6 h, 71%; (iii) EtOH abs., *p*TosOH, molecular sieves (3 Å), 35 °C, 40 h, 63%; (iv) H_2, 10% Pd/C, EtOH, atmospheric pressure, 20 °C, 16 h, 98%; (v) (a) 5% aq. HCl, room temp., 16 h, (b) α-tripiperideine, pH→2.5, 1 h, (c) KCN, $2 \leq pH \leq 3$, room temp., 21 h, 88%; (vi) RMgBr (5 equiv.), Et_2O/THF, –10 °C to room temp., 40 h, average yield: 78%.

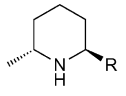
Now having several analogues, differing in their alkyl substituents, at our disposal for each of the tricyclic skeletons [5–6–5, 6–6–5, 6–6–6, and iso-6–6–6], we compared their cytotoxicities against HT29 cancer cells. The measured IC_{50} values are collected in Table 1. Compounds **1a** and **1b** were prepared as reported by Plehiers et al.[6] and compounds **2a**–**2g** by the procedure described by Devijver et al.[2] The syntheses of **3a**, **3b** and **4a**–**4f** are described in this paper. The results clearly indicated that the cytotoxicities are highly sensitive to the size of the alkyl substituents, whereas the natures of the tricycle ring systems have no significant effect. Indeed, the long-chain derivatives system-

atically display the lowest IC_{50} values over all four types of skeletons. It is also interesting to point out that the toxic activities are not sensitive to the stereochemistries of the alkyl substituents. This is also true for alkylation of the secondary amine in the iso-6–6–6 series.

Table 1. IC_{50} values of compounds **1**–**4**, **20** and **21** [μM] against HT29 cancer cells.

Compound	R	X	IC_{50} [μM]
1a, T-5	β-C_5H_{11}	–	>10
1b	α-$C_{18}H_{37}$	–	5
2a, T-4	α-C_3H_7	–	>100
2b	α-C_4H_9	–	100
2c, T-8	α-C_5H_{11}	–	50
2d	α-$C_{12}H_{25}$	–	2
2e	α-$C_{18}H_{37}$	–	20
2f	β-C_4H_9	–	100
2g	β-$C_{12}H_{25}$	–	2
3a	β-C_3H_7	–	>10
3b	β-$C_{12}H_{25}$	–	5
4a	β-C_3H_7	H	>10
4b	β-C_5H_{11}	H	>10
4c	β-$C_{12}H_{25}$	H	2
4d	β-C_3H_7	CH_3	>10
4e	β-C_5H_{11}	CH_3	>10
4f	β-$C_{12}H_{25}$	CH_3	6
20	β-C_5H_{11}	–	>10
21	β-$C_{15}H_{31}$	–	10

In addition, we have observed that the influence of the size of the alkyl chain on the cytotoxicity is comparable to that observed for the solenopsins, a group of 6-alkyl-2-methylpiperidines that are the main constituents of the venom of fire ants.[16] Indeed, the natural derivative **21** (solenopsin C, Figure 2) is cytotoxic against HT29 cells, whereas the short-chain derivative **22** is inactive (Table 1). These two derivatives were prepared starting from 2,6-dimethylpyridine by the route described by MacConnell et al.[17] In the case of the solenopsins, it has been demonstrated that their cytotoxicities are linked to their amphiphilic characters, which lead to breaking of the plasma membranes of cells. It follows from our results that a similar mechanism of action could also be proposed for the long-chain derivatives of the tetraponerines and their analogues. Such a mechanism would also be in good agreement with the fact that the structures of the tricyclic moieties of these compounds have almost no influence on their toxicity potency.



20 R = C_5H_{11}
21 R = $C_{15}H_{31}$

Figure 2. Structures of the solenopsin analogues.

Experimental Section

General: EIMS and EIHRMS were performed with a Fisons VG Micromass Autospec instrument (70 eV). In all cases, peak intensities are expressed as % values relative to the base peak. The ^1H NMR spectra were recorded in $CDCl_3$ at 300 MHz with a Bruker Avance TM 300 or at 600 MHz with a Varian Unity 600 instrument and are reported in ppm from internal TMS on the δ scale. Data are reported as follows: chemical shift [multiplicity (s: singlet, d: doublet, dd: double doublet, ddd: double double doublet, t: triplet, dt: double triplet, tt: triple triplet, q: quartet, m: multiplet), coupling constants in Hz, integration, assignment]. The ^{13}C NMR spectra were recorded in $CDCl_3$ at 75.4 MHz with a Bruker Avance TM 300 instrument. The IR spectra were recorded with a Bruker IFS 25 instrument as films on an NaCl disk. Thin layer chromatography (TLC) was performed with 0.25 mm Polygram silica gel SILG/UV254 precoated plates (Macherey–Nagel). Chromatography was performed on silica gel columns (MN Kieselgel 60 0.04–0.063 mm) by the flash technique or on basic alumina (MN Aluminiumoxid, basisch, Activity 1).

Δ^1-Piperideine (9): Fresh solutions of Δ^1-piperideine were prepared according to the procedure of Bender et al.[8] Piperidine (1.29 g, 15.18 mmol) was added to a solution of *N*-chlorosuccinimide (3.752 g, 28.21 mmol) in diethyl ether (100 mL). The solution was stirred at room temp. for 1 h. After filtration and rinsing of the precipitate with diethyl ether (10 mL), the diethyl ether solution was washed with water (2 × 100 mL) and brine (50 mL) and then dried with $MgSO_4$. Just before dehydrohalogenation, the *N*-chloropiperidine solution was filtered and concentrated at reduced pressure to about 20 mL. The resulting solution was added dropwise to a solution of KOH (85%, 1 g, 15.16 mmol) in absolute ethanol (16 mL), while the temp. was maintained between 5 and 10 °C. After addition, the mixture was stirred at room temp. for 24 h and filtered, and the precipitate was rinsed with absolute ethanol (15 mL).

α-Tripiperideine (10): α-Tripiperideine was prepared according to the procedure of Claxton et al.,[9] starting from a solution of *N*-chloropiperidine prepared as described above. This solution was added dropwise to a boiling solution of KOH (85%, 2 g, 30.32 mmol) in absolute ethanol (32 mL). The mixture was heated at reflux for 2.5 h and was then allowed to stand at room temp. for 36 h. The precipitate was removed by filtration and washed with absolute ethanol. The washes and the filtrate were combined, and the solvent was removed by distillation. The residue and the precipitate were then combined and dissolved in water (50 mL). The resulting solution was extracted with diethyl ether. The diethyl ether extract was dried with $MgSO_4$, filtered and concentrated in vacuo. The resulting oily residue was dissolved in acetone (3 mL), and the solution was cooled to –20 °C and left overnight. The crystals were filtered off and washed with cold acetone. This afforded **10** with a mean yield of 37% (minimum yield 32%, maximum yield 42%). The spectral properties of the crystals were identical to those reported by Kessler et al. for α-tripiperideine.[18]

Condensation between Δ^1-Piperideine (9) and Diethyl Malonate (DEM): A fresh solution of Δ^1-piperideine in ethanol/diethyl ether was concentrated to dryness, and the residue was dissolved in water (10 mL). Aqueous HCl (1 M) was added dropwise at 0 °C until the desired pH was reached, and diethyl malonate (1.266 g, 7.91 mmol, or 2.532 g, 15.83 mmol) was then poured into the solution in one portion. The mixture was stirred under nitrogen at room temp. overnight. The pH was then brought to 8 with ammonia, and the solution was extracted with CH_2Cl_2. The combined organic phases were dried, and the solvents were removed to dryness to give a crude product that was flash-chromatographed on silica gel [CH_2Cl_2/CH_3OH (99:1) + 1% NH_4OH]. The following yields of **11** and **12** were obtained: at pH 14 and with 1 equiv. of DEM 4 and

0%, respectively, at pH 13 and with 2 equiv. of DEM 1 and 0%, respectively, at pH 12 and with 2 equiv. of DEM 0 and 22%, respectively, and at pH 6 and with 2 equiv. of DEM 0 and 17%, respectively.

Oxo Ester 11: Diethyl malonate (2.841 g, 17.76 mmol) was added to a solution of α-tripiperideine (**10**, 1.46 g, 5.86 mmol) dispersed in a buffer solution [Na_2HPO_4 (0.15 M, 340 mL), NaOH (0.1 M, 160 mL), pH 11.3, 100 mL]. The pH of the mixture was maintained at 11.3 by regular addition of aqueous NaOH. The mixture was stirred at room temp. for 18 h and was then extracted with CH_2Cl_2 (3 × 100 mL). The combined organic phases were dried and concentrated to give a crude product that was flash-chromatographed on silica gel [CH_2Cl_2/CH_3OH (99:1) + 1% concd. NH_4OH] to afford **11** (841.3 mg, 3.01 mmol, 34%) as white crystals. ^1H NMR (600 MHz, $CDCl_3$): δ = 1.26 (m, 2 H, 1-H, 8-H), 1.30 (t, J = 7.2 Hz, 3 H, 3′-H_3, m, 1 H, 9-H), 1.36 (qt, J = 13.2, 3.6 Hz, 1 H, 3-H), 1.45 (qt, J = 13.2, 3.6 Hz, 1 H, 2-H), 1.58 (m, 1 H, 10-H), 1.65 (m, 1 H, 3-H), 1.70 (m, 3 H, 8-H, 9-H, 10-H), 1.88 (br. dd, J = 13.0, 2.0 Hz, 1 H, 2-H), 2.14 (m, 2 H, 1-H, 11-H), 2.45 (td, J = 13.0, 2.0 Hz, 1 H, 4-H), 2.84 (br. t, J = 11.0 Hz, 1 H, 7a-H), 3.10 (br. d, J = 11.0 Hz, 1 H, 11-H), 3.27 (d, J = 10.2 Hz, 1 H, 7-H), 3.62 (dd, J = 10.0, 2.0 Hz, 1 H, 12a-H), 4.19, 4.28 (m, 2 H, 2′-H_2), 4.76 (dt, J = 13.0, 2.0 Hz, 1 H, 4-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 14.3 (C-3′), 22.6 (C-9), 23.5 (C-2), 24.8 (C-3), 25.3 (C-10), 30.8 (C-8), 32.4 (C-1), 42.2 (C-4), 49.8 (C-11), 55.0 (C-7), 56.7 (C-7a), 61.2 (C-2′), 78.0 (C-12a), 164.1 (C-6), 169.4 (C-1′) ppm. IR (KBr): $\tilde{\nu}$ = 2944, 2857, 2805, 1733, 1652, 1454, 1393, 1372, 1347, 1177, 1125, 1006, 729 cm^{-1}. EIMS: m/z (%) = 280 (46) $[M]^{+\cdot}$, 251 (30), 238 (13), 223 (8), 207 (59), 197 (12), 179 (8), 169 (25), 123 (100), 84 (51). EIHRMS: m/z (%) = 280.1781 (calcd. for $C_{15}H_{24}N_2O_3$ 280.1787), 279.1704 (calcd. for $C_{15}H_{23}N_2O_3$ 279.1709), 251.1394 (calcd. for $C_{13}H_{19}N_2O_3$ 251.1396), 238.1313 (calcd. for $C_{12}H_{18}N_2O_3$ 238.1317), 207.1492 (calcd. for $C_{12}H_{19}N_2O$ 207.1497), 197.1047 (calcd. for $C_{10}H_{15}NO_3$ 197.1052), 123.0920 (calcd. for $C_7H_{11}N_2$ 123.0922), 84.0814 (calcd. for $C_5H_{10}N$ 84.0813).

Oxo Ester 12 from α-Tripiperideine (10): A buffer solution [Na_2HPO_4 (0.2 M, 486 mL), citric acid (0.1 M, 14 mL), pH 7.8, 200 mL] was added to a solution of α-tripiperideine (1.53 g, 6.15 mmol) in HCl 1 M (20 mL). The mixture was stirred at room temp. under nitrogen. After 5 h, diethyl malonate (2.949 g, 18.43 mmol) was added, and the mixture was stirred for additional 16 h. The mixture was then basified by addition of NH_4OH (pH 10) and extracted with CH_2Cl_2. The combined organic phases were dried and the solvents were removed to dryness to give a yellow oil that was flash-chromatographed [CH_2Cl_2/CH_3OH (98:2) + 1% concd. NH_4OH]. This afforded **12** (1.95 g, 6.96 mmol, 76%) as a colourless oil. ^1H NMR (600 MHz, $CDCl_3$): δ = 1.04–1.16 (qd, J = 12.6, 3.6 Hz, 2 H, 4-H, 5-H), 1.31 (t, J = 6.6 Hz, 3 H, 3′-H), 1.32 (m, 1 H, 4a-H), 1.34 (m, 1 H, 7-H), 1.38 (br. d, J = 13.0 Hz, 1 H, 6-H), 1.51 (qt, J = 13.2, 3.6 Hz, 1 H, 3-H), 1.70 (m, 1 H, 7-H), 1.72 (m, 1 H, 3-H), 1.87 (br. d, J = 11.0 Hz, 1 H, 6-H), 2.02 (br. d, J = 13.0 Hz, 2 H, 4-H, 5-H), 2.40 (br. t, J = 13.0 Hz, 1 H, 8-H), 2.63 (td, J = 12.0, 2.4 Hz, 1 H, 2-H), 2.87 (td, J = 11.4, 2.4 Hz, 1 H, 4b-H), 2.96 (t, J = 11.1 Hz, 1 H, 10a-H), 3.05 (br. d, J = 12.0 Hz, 1 H, 2-H), 3.22 (d, J = 11.4 Hz, 1 H, 10-H), 4.20, 4.33 (m, 2 H, 2′-H), 4.74 (br. d, J = 14.0 Hz, 1 H, 8-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 14.2 (C-3′), 24.3 (C-6), 25.1 (C-7), 25.6 (C-3), 28.4 (C-4), 31.9 (C-5), 42.6 (C-8), 43.3 (C-4a), 45.9 (C-2), 55.4 (C-10a), 56.6 (C-10), 61.0 (C-4b), 61.3 (C-2′), 164.5 (C-9), 170.0 (C-1′) ppm. IR (NaCl): $\tilde{\nu}$ = 2934, 2854, 1735, 1643, 1443, 1369, 1314, 1264, 1173, 1132 cm^{-1}. EIMS: m/z (%) = 281 (20) $[M^{+\cdot} + H^{\cdot}]$, 280 (8) $[M]^{+\cdot}$, 279 (10) $[M^{+\cdot} - H^{\cdot}]$, 235 (6), 207 (100), 165 (11), 152 (6), 123 (4), 84 (5). EIHRMS: m/z (%) = 280.1771 (calcd. for $C_{15}H_{24}N_2O_3$ 280.1786), 207.1488 (calcd. for $C_{12}H_{19}N_2O$ 207.1497).

Oxo Ester 12 from 15: A solution of **15**[12] (200 mg, 0.58 mmol) and diethyl malonate (186 mg, 1.16 mmol, 2 equiv.) dissolved in a buffer solution (pH 7.8, 20 mL) was stirred under nitrogen at room temp. for 16 h. The pH was brought to 10 by addition of NH_4OH,and the resulting aqueous solution was extracted with CH_2Cl_2. The combined organic layers were filtered through a WA filter paper, and the solvent was evaporated in vacuo to give a residue that was flash-chromatographed on silica gel [CH_2Cl_2/CH_3OH (98:2) + 1% concd. NH_4OH]. This afforded **12** (140 mg, 0.50 mmol, 86%) as a colourless oil.

Dodecahydro-2*H*-1,8a-diazaphenanthren-9-one: Compound **12** (204.7 g, 0.73 mmol) was dissolved in aqueous KOH (5%, 7 mL), and the mixture was stirred at 20 °C for 4 h. HCl (10%) was then added dropwise at 0 °C until pH 2.5 was reached. The resulting mixture was heated at 70 °C for 2 h, basified with NH_4OH and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were filtered through a WA filter paper, and the solvents were evaporated in vacuo to yield an oily residue that was flash-chromatographed on silica gel [CH_2Cl_2/MeOH/10% NH_4OH (95:5:0.1 to 9:1:0.1)]. This afforded dodecahydro-2*H*-1,8a-diazaphenanthren-9-one (129 g, 0.62 mmol, 85%). ^1H NMR (600 MHz, $CDCl_3$): δ = 1.1 (m, 2 H, 4-H, 5-H), 1.22 (m, 1 H, 4a-H), 1.38 (m, 2 H, 6-H, 7-H), 1.53 (q, J = 13.2 Hz, 1 H, 3-H), 1.69 (br. d, J = 11.0 Hz, 1 H, 7-H), 1.74 (br. d, J = 13.0 Hz, 1 H, 3-H), 1.86 (br. d, J = 11.0 Hz, 1 H, 6-H), 2.01 (m, 1 H, 4-H), 2.05 (m, 1 H, 5-H), 2.21 (t, J = 16.2 Hz, 1 H, 10-H), 2.36 (t, J = 12.1 Hz, 1 H, 8-H), 2.50 (dd, J = 16.8, 3.6 Hz, 1 H, 10-H), 2.58 (td, J = 10.2, 4.2 Hz, 1 H, 10a-H), 2.63 (t, J = 12.0 Hz, 1 H, 2-H), 2.82 (t, J = 10.5 Hz, 1 H, 4b-H), 3.06 (br. d, J = 11.0 Hz, 1 H, 2-H), 4.78 (d, J = 13.2 Hz, 1 H, 8-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 24.0 (C-6), 24.8 (C-7), 25.5 (C-3), 27.9 (C-4), 31.5 (C-5), 39.4 (C-10), 41.8 (C-8), 44.4 (C-4a), 45.6 (C-2), 53.0 (C-10a), 60.8 (C-4b), 167.4 (C-9) ppm. IR (NaCl): $\tilde{\nu}$ = 2936, 2855, 2791, 1642, 1444, 1263 cm^{-1}. EIMS: m/z (%) = 208 (13) $[M]^{+\cdot}$, 207 (22) $[M^{+\cdot} - H^{\cdot}]$, 165 (7), 150 (12), 122 (8), 110 (5), 97 (60) $[C_6H_{11}N]^+$, 84 (100) $[C_5H_{10}N]^+$, 68 (8), 55 (10).

1-Benzyl-dodecahydro-2*H*-1,8a-diazaphenanthren-9-one: A solution of Na_2CO_3 (113 mg, 1.07 mmol) in water (0.5 mL) and benzyl bromide (64 μL, 0.54 mmol) was added to a solution of dodecahydro-2*H*-1,8a-diazaphenanthren-9-one (113 mg, 0.54 mmol) in CH_2Cl_2 (1 mL). The mixture was heated at reflux for 3 h and was then extracted with CH_2Cl_2 (3 × 1 mL). The combined organic layers were filtered through a WA filter paper, and the solvent was evaporated in vacuo to give a solid residue that was flash-chromatographed on silica gel [CH_2Cl_2/MeOH/10% NH_4OH (99:1:0.1)]. This afforded 1-benzyl-dodecahydro-2*H*-1,8a-diazaphenanthren-9-one (0.157 g, 0.53 mmol, 98%) as a colourless oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.85 (qd, J = 12.1, 4.4 Hz, 1 H, 4-H), 1.14 (qd, J = 11.6, 3.7 Hz, 1 H, 5-H), 1.35–1.78 (m, 6 H, 3-H_2, 4a-H, 6-H, 7-H_2), 1.80–2.0 (m, 3 H, 2-H, 5-H, 6-H), 2.03 (br. d, J = 13.0 Hz, 1 H, 4-H), 2.20 (td, J = 9.8, 3.6 Hz, 1 H, 10-H), 2.33 (m, 1 H, 10a-H), 2.39 (td, J = 12.5, 2.7 Hz, 1 H, 8-H), 2.80 (m, 2 H, 2-H, 4b-H), 3.07 (dd, J = 15.9, 3.7 Hz, 1 H, 10-H), 3.18 (d, J = 13.5 Hz, 1 H, CH_2Ph), 4.04 (d, J = 13.5 Hz, 1 H, CH_2Ph), 4.83 (d, J = 12.0 Hz, 1 H, 8-H), 7.29 (m, 5 H, Ar-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 24.3 (C-6), 24.7, 25.0 (C-3, C-7), 28.1 (C-4), 32.1 (C-5), 38.1 (C-10), 42.0 (C-8), 44.3 (C-4a), 52.2 (C-2), 57.3 (CH_2Ph), 58.0 (C-4b), 60.8 (C-10a), 126.8, 128.1, 129.1, 138.2 (Ar-C), 167.6 (C-9) ppm. IR (film): $\tilde{\nu}$ = 3084, 3060, 3026, 2934, 2855, 2793, 1645, 1444 cm^{-1}. EIMS: m/z (%) = 298 (56) $[M]^{+\cdot}$, 255 (18), 239 (14), 221 (11) $[M^{+\cdot} - C_6H_5^{\cdot}]$, 212 (13), 207 (54), 186 (51), 172 (35), 91 (100) $[C_7H_7]^+$, 84 (36) $[C_5H_{10}N]^+$.

1-Benzyl-9-cyano-dodecahydro-2*H*-1,8a-diazaphenanthrene (16): A solution of DIBALH (1 M) in hexane (0.36 mL, 0.36 mmol) was added to the protected lactam (107 mg, 0.36 mmol) dissolved in anhydrous diethyl ether (5 mL). The mixture was stirred under nitrogen at –78 °C for 3 h. The mixture was then acidified with an ethanolic perchloric acid solution (10%) until pH 3 was reached. KCN (128 mg, 1.97 mmol) dissolved in H_2O (1 mL) was added, and the mixture was left at 20 °C overnight. After addition of a satd. $NaHCO_3$ solution (pH 8), the mixture was extracted three times with CH_2Cl_2. The combined organic layers were filtered through a WA filter paper, and the solvents were evaporated in vacuo. Chromatography on a silica gel column [hexane/acetone/10% NH_4OH (9:1:0.1)] yielded nitrile **16** (66.9 mg, 0.22 mmol, 60%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.90 (qd, J = 12.6, 4.2 Hz, 1 H, 4-H), 1.07 (qd, J = 13.2, 3.6 Hz, 1 H, 5-H), 1.20–1.29 (m, 2 H, 4a-H, 6-H), 1.53 (qt, J = 12.6, 3.6 Hz, 2 H, 3-H, 7-H), 1.61 (br. d, J = 13.0 Hz, 1 H, 3-H), 1.67 (br. d, J = 13.0 Hz, 1 H, 7-H), 1.78 (m, 1 H, 6-H), 1.80 (m, 1 H, 10-H), 1.85 (dd, J = 10.8, 1.8 Hz, 1 H, 4-H), 1.95 (br. d, J = 13.0 Hz, 1 H, 5-H), 2.00 (td, J = 12.0, 3.0 Hz, 1 H, 2-H), 2.03 (td, J = 10.2, 2.4 Hz, 1 H, 4b-H), 2.27 (td, J = 9.0, 3.0 Hz, 1 H, 10a-H), 2.38 (dt, J = 13.2, 3.0 Hz, 1 H, 10-H), 2.44 (td, J = 12.0, 2.4 Hz, 1 H, 8-H), 2.70 (br. d, J = 11.0 Hz, 1 H, 8-H), 2.81 (br. d, J = 11.0 Hz, 1 H, 2-H), 3.25 (d, J = 13.8 Hz, 1 H, CH_2Ph), 3.88 (br. t, J = 4.0 Hz, 1 H, 9-H), 3.99 (d, J = 13.8 Hz, 1 H, CH_2Ph), 7.23, 7.30 (m, 5 H, Ar-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 23.9 (C-6), 25.1 (C-3), 25.4 (C-7), 26.6 (C-4), 29.8 (C-5), 32.8 (C-10), 46.1 (C-4a), 53.4 (C-2), 54.2 (C-8), 55.1 (C-9), 57.4 (CH_2Ph), 60.3 (C-4b), 61.6 (C-10a), 117.2 (CN), 126.9, 127.9, 128.8, 139.4 (Ar-C) ppm. IR (NaCl): $\tilde{\nu}$ = 3084, 3060, 3026, 2932, 2855, 2793, 2219, 1645, 1442 cm^{-1}. EIMS: m/z (%) = 309 (15) $[M]^{+\cdot}$, 281 (41), 226 (20), 218 (97) $[M^{+\cdot} - CH_2C_6H_5^{\cdot}]$, 191 (39), 173 (15), 134 (45), 110 (37), 91 (69) $[C_7H_7]^+$, 84 (100) $[C_5H_{10}N]^+$.

1-Benzyl-9-propyl-dodecahydro-2*H*-1,8a-diazaphenanthrene: A solution of propylmagnesium bromide, prepared from magnesium (18 mg, 0.74 mmol) and propyl bromide (67 μL, 0.74 mmol) in diethyl ether (1 mL), was added at –10 °C to a solution of α-amino nitrile **16** (46.1 mg, 0.15 mmol) in THF (1 mL). The mixture was stirred at room temp. for 40 h, treated with a satd. aqueous solution of NH_4Cl and extracted three times with CH_2Cl_2. The combined organic phases were dried, and the solvents were removed to dryness, leading to a yellow oil that was flash-chromatographed on silica gel [CH_2Cl_2/MeOH/10% NH_4OH (95:5:0.1)] to give 1-benzyl-9-propyl-dodecahydro-*2H*-1,8a-diazaphenanthrene (41.8 mg, 0.128 mmol, 86%) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (m, 1 H, 4-H), 0.95 (t, J = 6.6 Hz, 3 H, 3′-H), 1.07–1.78 (m, 13 H), 1.80–2.02 (m, 3 H), 2.03–2.23 (m, 3 H), 2.53 (m, 1 H, 8-H), 2.66 (d, J = 13.5 Hz, 1 H, CH_2Ph), 2.71 (br. d, J = 10.0 Hz, 1 H, 8-H), 2.81 (br. d, J = 12.0 Hz, 1 H, 2-H), 2.93 (m, 1 H, 9-H), 4.52 (d, J = 13.5 Hz, 1 H, CH_2Ph), 7.21–7.29 (m, 5 H, Ar-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 14.5 (C-3′), 21.1, 24.1 (C-6, C-1′), 25.0 (C-3), 25.8 (C-7), 26.6 (C-4), 27.3 (C-5), 30.4 (C-10), 32.0 (C-2′), 46.0 (C-4a), 52.2 (C-8), 53.5 (C-2), 56.9 (CH_2Ph), 58.0 (C-4b), 60.0 (C-10a), 60.5 (C-9), 126.7, 128.2, 129.0, 139.9 (Ar-C) ppm. IR (NaCl): $\tilde{\nu}$ = 3084, 3060, 3026, 2931, 2871, 2793, 1494, 1452, 1372, 1122, 974, 736, 698 cm^{-1}. EIMS: m/z (%) = 326 (8) $[M]^{+\cdot}$, 283 (33) $[M^{+\cdot} - C_3H_5^{\cdot}]$, 235 (99) $[M^{+\cdot} - CH_2C_6H_5^{\cdot}]$, 152 (6), 138 (10), 207 (54), 110 (100).

1-Benzyl-9-pentyl-dodecahydro-2*H*-1,8a-diazaphenanthrene: This compound was prepared according to the same procedure as utilised for preparing the corresponding propyl derivative but by starting from pentylmagnesium bromide (yield 90%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.85 (m, 1 H, 4-H), 0.91 (t, J = 6.6 Hz, 3 H, 5′-H_3), 1.18–1.27 (m, 2 H, 5-H, 6-H), 1.29–1.35 (m, 6 H, 2′-H_2, 3′-H_2, 4′-H_2), 1.47 (m, 2 H, 1′-H, 4a-H), 1.53 (m, 2 H, 3-H_2), 1.67 (m, 2 H, 7-H, 1′-H), 1.75 (m, 2 H, 6-H, 7-H), 1.85 (td, J = 2.4, 12.6 Hz, 2 H, 4-H, 10-H), 1.95–1.99 (m, 2 H, 2-H, 5-H), 2.10 (td, J = 9.0, 3.0 Hz, 1 H, 10a-H), 2.19 (br. d, J = 13.1 Hz, 1 H, 10-H), 2.27 (m, 1 H, 4b-H), 2.58 (td, J = 2.4, 10.8 Hz, 1 H, 8-H), 2.64 (d, J = 13.2 Hz, CH_2Ph), 2.78 (br. d, J = 11.0 Hz, 1 H, 8-H), 2.82 (br. d, J = 11.0 Hz, 1 H, 2-H), 3.00 (m, 1 H, 9-H), 4.50 (d, J = 13.2 Hz, 1 H, CH_2Ph), 7.23, 7.30 (m, 5 H, Ar-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 14.1 (C-5′), 22.7 (C-3′), 23.8 (C-6), 24.3 (C-1′), 24.9 (C-3), 25.3 (C-7), 27.2 (C-4), 27.4 (C-4′), 29.9 (C-5), 31.6 (C-10), 32.1 (C-2′), 45.6 (C-4a), 52.2 (C-8), 53.4 (C-2), 56.8 (CH_2Ph), 58.3 (C-4b), 59.7 (C-10a), 60.9 (C-9), 126.7, 128.2, 129.0, 139.7 (Ar-C) ppm. IR (NaCl): $\tilde{\nu}$ = 3081, 3061, 3025, 2929, 2854, 2791, 1494, 1452, 1371, 1122, 1028, 968, 736, 698 cm^{-1}. EIMS: m/z (%) = 354 (5) $[M]^{+\cdot}$, 283 (33) $[M^{+\cdot} - C_5H_{11}^{\cdot}]$, 263 (83) $[M^{+\cdot} - C_7H_7^{\cdot}]$, 166 (11), 110 (100) $[C_7H_{12}N]^+$, 91 (37) $[C_7H_7]^+$, 84 (12) $[C_5H_{10}N]^+$, 55 (10).

1-Benzyl-9-dodecyl-dodecahydro-2*H*-1,8a-diazaphenanthrene: This compound was prepared according to the same procedure as utilised for preparing the corresponding propyl derivative but by starting from dodecylmagnesium bromide (yield 90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80 (m, 1 H), 0.88 (t, J = 6.2 Hz, 3 H, 3′-H_3), 1.27 (br. s, 23 H), 1.41 (m, 1 H), 1.48–2.02 (m, 10 H), 2.08 (td, J = 4.0, 11.9 Hz, 1 H, 10a-H), 2.20 (m, 2 H, 4b-H, 10-H), 2.55 (m, 1 H, 8-H), 2.68 (d, J = 13.4 Hz, 1 H, CH_2Ph), 2.73 (br. d, J = 11.0 Hz, 1 H, 8-H), 2.82 (br. d, J = 12.0 Hz, 1 H, 2-H), 2.94 (m, 1 H, 9-H), 4.51 (d, J = 13.4 Hz, 1 H, CH_2Ph), 7.22–7.29 (m, 5 H, Ar-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 14.2 (C-12′), 22.8, 23.9, 24.2, 24.9, 25.5, 27.2, 27.8, 29.4, 29.7, 29.7, 29.8, 29.8, 29.9, 30.0, 31.7, 32.0, 45.7 (C-4a), 52.1 (C-8), 53.4 (C-2), 56.9 (CH_2Ph), 58.0 (C-4b), 59.8 (C-10a), 60.7 (C-9), 126.8, 128.2, 129.1, 139.5 (Ar-C) ppm. IR (NaCl): $\tilde{\nu}$ = 3085, 3065, 3025, 2926, 2854, 2791, 1494, 1453, 1118, 735, 695 cm^{-1}. EIMS: m/z (%) = 452 (33) $[M]^{+\cdot}$, 361 (64) $[M^{+\cdot} - CH_2C_6H_5^{\cdot}]$, 283 (36) $[M^{+\cdot} - C_{12}H_{25}^{\cdot}]$, 191 (6) $[M^{+\cdot} - CH_2C_6H_5^{\cdot} - C_{12}H_{25}^{\cdot}]$, 110 (100) $[C_7H_{12}N]^+$, 91 (23) $[C_7H_7]^+$, 84 (8) $[C_5H_{10}N]^+$.

9-Propyl-dodecahydro-2*H*-1,8a-diazaphenanthrene (4a): 1-Benzyl-9-propyl-dodecahydro-2*H*-1,8a-diazaphenanthrene (51.9 mg, 0.12 mmol) dissolved in MeOH/12.5 M HCl (98:2, 6 mL) was stirred under hydrogen in the presence of Pd/C (10%, 30 mg) at atmospheric pressure and room temp. for 16 h. The mixture was filtered through Celite and concentrated in vacuo, and the solid residue was flash-chromatographed on silica gel [CH_2Cl_2/MeOH/10% NH_4OH (9:1:0.1)]. This yielded **4a** (36.1 mg, 0.15 mmol, 96%) as a colourless solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.93 (t, J = 7.2 Hz, 3 H, 3′-H_3), 0.98 (qd, J = 12.0, 3.6 Hz, 1 H, 4-H), 1.13–1.17 (m, 2 H, 5-H, 6-H), 1.22 (m, 2 H, 4a-H, 2′-H), 1.38 (m, 2 H, 1′-H, 2′-H), 1.60 (m, 4 H, 3-H, 7-H_2, 1′-H), 1.70 (m, 2 H, 3-H, 6-H), 1.78 (td, J = 4.8, 12.0 Hz, 1 H, 10-H), 1.84 (m, 3 H, 4-H, 5-H, 10-H), 2.12 (br. t, J = 7.0 Hz, 1 H, 4b-H), 2.51 (br. t, J = 2.0, 11.4 Hz, 2 H, 8-H, 10a-H), 2.66 (m, 2 H, 2-H, 8-H), 2.89 (m, 1 H, 9-H), 3.16 (br. d, J = 11.0 Hz, 1 H, 2-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 14.4 (C-3′), 20.9 (C-2′), 24.0 (C-6), 25.9 (C-3), 26.0 (C-7), 26.4 (C-1′), 26.6 (C-4), 30.0 (C-5), 34.1 (C-10), 46.2 (C-2), 46.7 (C-4a), 52.1 (C-8), 54.8 (C-10a), 57.5 (C-4b), 60.3 (C-9) ppm. IR (NaCl): $\tilde{\nu}$ = 3391, 2932, 2855, 2802, 1447, 1373, 1146, 1122 cm^{-1}. EIMS: m/z (%) = 236 (7) $[M]^{+\cdot}$, 221 (2) $[M^{+\cdot} - CH_3^{\cdot}]$, 207 (2) $[M^{+\cdot} - C_2H_5^{\cdot}]$, 193 (76) $[M^{+\cdot} - C_3H_7^{\cdot}]$, 138 (8), 124 (6), 110 (100) $[C_7H_{12}N]^+$, 96 (10), 84 (14).

9-Pentyl-dodecahydro-2*H*-1,8a-diazaphenanthrene (4b): This compound was prepared according to the same procedure as utilised for preparing the corresponding propyl derivative **4a** (yield 95%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, J = 6.5 Hz, 3 H, 5′-H_3), 0.96–2.22 (m, 21 H), 2.26 (br. t, J = 9.0 Hz, 1 H, 4b-H), 2.55 (m, 1 H, 8-H or 10a-H), 2.77 (m, 3 H, 2-H, 8-H, 10a-H or 8-H), 2.95 (m, 1 H, 9-H), 3.36 (br. d, J = 12.0 Hz, 1 H, 2-H), 7.2 (br. s, 1 H, NH) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 14.2 (C-5′), 22.6, 23.4, 24.0, 25.5, 25.5, 27.2, 29.4, 31.7, 32.0, 43.6 (C-4a), 44.9 (C-2), 52.0 (C-8), 55.0 (C-10a), 57.4 (C-4b), 60.5 (C-9) ppm. IR (NaCl): $\tilde{\nu}$ = 3402, 2933, 2856, 2805, 2529, 1593, 1456, 1374, 1243, 1123, 1061 cm^{-1}. EIMS: m/z (%) = 264 (46) [M]$^{+\cdot}$, 249 (5) [$M^{+\cdot}$ – $CH_3^{\cdot}$], 235 (5) [$M^{+\cdot}$ – $C_2H_5^{\cdot}$], 220 (10) [$M^{+\cdot}$ – $H^{\cdot}$ – $C_3H_7^{\cdot}$], 206 (16) [$M^{+\cdot}$ – $H^{\cdot}$ – $C_4H_9^{\cdot}$], 193 (68) [$M^{+\cdot}$ – $C_5H_{11}^{\cdot}$], 110 (100), 96 (6), 84 (8).

9-Dodecyl-dodecahydro-2*H*-1,8a-diazaphenanthrene (4c): This compound was prepared according to the same procedure as utilised for preparing the corresponding propyl derivative **4a** (yield 99%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.2 Hz, 3 H, 12′-H_3), 0.93–1.43 (m, 25 H), 1.51–1.97 (m, 10 H), 2.13 (m, 1 H, 4b-H), 2.53 (br. t, J = 2.0, 10.0 Hz, 2 H, 8-H, 10a-H), 2.68 (m, 2 H, 2-H, 8-H), 2.86 (m, 1 H, 9-H), 3.18 (br. d, J = 12.0 Hz, 1 H, 2-H), 4.57 (br. s, 1 H, NH) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 14.2 (C-12′), 22.8, 23.9, 24.2, 25.8, 25.9, 26.5, 27.8, 29.5, 29.8, 29.9, 30.0, 32.0, 34.0 (C-10), 46.1 (C-2), 46.5 (C-4a), 52.1 (C-8), 54.8 (C-10a), 57.5 (C-4b), 60.7 (C-9) ppm. IR (NaCl): $\tilde{\nu}$ = 3397, 2926, 2853, 2804, 1463, 1372, 1306, 1123, 1062 cm^{-1}. EIMS: m/z (%) = 362 (57) [M]$^{+\cdot}$, 361 (48) [$M^{+\cdot}$ – $H^{\cdot}$], 347 (6) [$M^{+\cdot}$ – $CH_3^{\cdot}$], 333 (4) [$M^{+\cdot}$ – $C_2H_5^{\cdot}$], 318 (12) [$M^{+\cdot}$ – $H^{\cdot}$ – $C_3H_7^{\cdot}$], 304 (22) [$M^{+\cdot}$ – $H^{\cdot}$ – $C_4H_9^{\cdot}$], 290 (6) [$M^{+\cdot}$ – $H^{\cdot}$ – $C_5H_{11}^{\cdot}$], 278 (34) [M + H^+ – $C_6H_{13}^{\cdot}$], 264 (59) [M + H^+ – $C_7H_{15}^{\cdot}$], 250 (4) [M + H^+ – $C_8H_{17}^{\cdot}$], 236 (4) [M + H^+ – $C_9H_{19}^{\cdot}$], 221 (15) [$M^{+\cdot}$ – $C_{10}H_{21}^{\cdot}$], 207 (15) [$M^{+\cdot}$ – $C_{11}H_{23}^{\cdot}$], 193 (100) [$M^{+\cdot}$ – $C_{12}H_{25}^{\cdot}$], 110 (84), 97 (14), 84 (14).

***N*-Methyl Derivative 4d:** Aqueous formaldehyde (37%, 55 μL, 0.74 mmol) was added to a solution of **4a** (13 mg, 0.054 mmol) in MeOH (0.5 mL). The mixture was heated at reflux for 3 h and was then allowed to cool to room temp. $NaBH_4$ (8 mg, 0.21 mmol) was then added. After stirring at room temp., for 2 h the mixture was extracted with CH_2Cl_2. The combined organic layers were filtered through a WA filter paper, and the solvent was evaporated in vacuo to give a residue that was flash-chromatographed on silica gel [CH_2Cl_2/MeOH/10% NH_4OH (97:3:0.1)]. This afforded **4d** (10 mg, 0.039 mmol, 72%) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (m, 1 H), 0.94 (t, J = 7.1 Hz, 3 H, 3′-H_3), 1.00–1.76 (m, 14 H), 1.86 (br. t, J = 12.0 Hz, 2 H), 1.95–2.13 (m, 3 H), 2.2 (s, 3 H, NCH_3), 2.50 (td, J = 3.8, 10.9 Hz, 1 H, 8-H), 2.65 (m, 1 H, 8-H), 2.87 (m, 2 H, 2-H, 9-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 14.6 (C-3′), 21.0, 24.3, 25.5, 26.1, 26.4, 27.2, 30.7, 31.9, 42.4 (NCH_3), 46.1 (C-4a), 52.2 (C-8), 57.6 (C-2), 57.7 (C-4b), 60.1 (C-9), 62.1 (C-10a) ppm. IR (NaCl): $\tilde{\nu}$ = 2931, 2871, 2856, 2776, 1456, 1373, 1126 cm^{-1}. EIMS: m/z (%) = 250 (11) [M]$^{+\cdot}$, 235 (3) [$M^{+\cdot}$ – $CH_3^{\cdot}$], 221 (2) [$M^{+\cdot}$ – $C_2H_5^{\cdot}$], 207 (51) [$M^{+\cdot}$ – $C_3H_7^{\cdot}$], 178 (6), 138 (10), 124 (10), 110 (100), 96 (6), 84 (11).

***N*-Methyl Derivative 4e:** This compound was prepared according to the same procedure as utilised for preparing the corresponding propyl derivative **4d** (yield 62%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (m, 1 H), 0.90 (t, J = 7.1 Hz, 3 H, 5′-H_3), 1.00–1.45 (m, 10 H), 1.47–1.78 (m, 8 H), 1.86 (td, J = 2.8, 12.6 Hz, 2 H), 2.06 (m, 3 H), 2.23 (s, 3 H, NCH_3), 2.49 (td, J = 3.8, 10.9 Hz, 1 H, 8-H), 2.66 (br. d, J = 11.0 Hz, 1 H, 8-H), 2.87 (m, 2 H, 2-H, 9-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 14.2 (C-5′), 22.8, 24.0, 24.3, 25.5, 26.1, 27.2, 27.5, 30.6, 31.8, 32.3, 42.4 (NCH_3), 46.1 (C-4a), 52.2 (C-8), 57.6 (C-2), 57.8 (C-4b), 60.4 (C-9), 62.1 (C-10a) ppm. IR (NaCl): $\tilde{\nu}$ = 2930, 2853, 2775, 1464, 1373, 1126 cm^{-1}. EIMS: m/z (%) = 278 (5) [M]$^{+\cdot}$, 207 (24) [$M^{+\cdot}$ – $C_5H_{11}^{\cdot}$], 193 (9), 166 (8), 110 (100), 96 (7), 84 (9).

***N*-Methyl Derivative 4f:** This compound was prepared according to the same procedure as utilised for preparing the corresponding propyl derivative **4d** (yield 60%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (br. t, J = 6.0 Hz, 4 H, 12′-H_3), 0.9–1.18 (m, 3 H), 1.27 (s, 20 H), 1.36–1.79 (m, 9 H), 1.86 (br. t, J = 11.0 Hz, 2 H), 2.04 (m, 3 H), 2.23 (s, 3 H, NCH_3), 2.48 (td, J = 3.6, 7.4 Hz, 1 H, 8-H), 2.65 (br. d, J = 11.3 Hz, 1 H, 8-H), 2.87 (m, 2 H, 2-H, 9-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 14.3 (C-12′), 22.8, 24.0, 24.3, 25.5, 26.1, 27.2, 27.8, 29.5, 29.8, 29.8, 30.1, 30.7, 31.9, 32.1, 42.5 (NCH_3), 46.2 (C-4a), 52.2 (C-8), 57.6 (C-2), 57.8 (C-4b), 60.4 (C-9), 62.1 (C-10a) ppm. IR (NaCl): $\tilde{\nu}$ = 2924, 2852, 2775, 1461, 1371, 1126 cm^{-1}. EIMS: m/z (%) = 376 (7) [M]$^{+\cdot}$, 264 (6) [$M^{+\cdot}$ – $C_8H_{17}^{\cdot}$], 207 (80) [$M^{+\cdot}$ – $C_{12}H_{25}^{\cdot}$], 149 (8), 136 (7), 124 (12), 110 (100), 96 (7), 84 (20).

2-[2-(1-Benzyloxycarbonyl)piperidyl]ethanol: A solution of K_2CO_3 (1.074 g, 7.8 mmol) in water (5 mL) was added to a solution of 2-(2-piperidyl)ethanol (**18**, 496.4 mg, 3.85 mmol) in ethanol (5 mL). The reaction mixture was cooled in an ice bath, and benzyl chloroformate (650 μL, 4.6 mmol) was added with vigorous stirring. The ice bath was maintained for 15 min. The mixture was then allowed to warm progressively to room temp. After 3 h, the mixture was extracted with CH_2Cl_2, the combined organic layers were filtered through a WA filter paper, and the solvent was evaporated in vacuo to give a residue that was flash-chromatographed on silica gel [hexane/AcOEt (8:2)]. This afforded 2-[2-(1-benzyloxycarbonyl)piperidyl]ethanol (1002 mg, 3.81 mmol, 99%) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.3–1.85 (m, 7 H, 3-H_2, 4-H_2, 5-H_2, 7-H), 1.95 (br. t, J = 12.0 Hz, 1 H, 7-H), 2.77 (t, J = 13.4 Hz, 1 H, 6-H), 3.39 (m, 1 H, 8-H), 3.57 (m, 1 H, 8-H), 4.05 (br. d, J = 13.0 Hz, 1 H, 6-H), 4.47 (m, 1 H, 2-H), 5.13 (br. s, 2 H, 10-H_2), 7.35 (m, 5 H, Ar-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 19.0, 25.4, 29.1, 32.3, 39.3, 53.5 (C-2), 60.4 (C-8), 67.3 (C-10), 127.8, 128.1, 128.5, 136.6 (C-11), 171.1 (C-9) ppm. IR (NaCl): $\tilde{\nu}$ = 3446, 3093, 3068, 3034, 2948, 2900, 1699, 1435, 1270, 1058, 763 cm^{-1}. EIMS: m/z (%) = 263 (7) [M]$^{+\cdot}$, 218 (68), 174 (99), 156 (20), 126 (18), 108 (32), 91 (100), 79 (46), 65 (34), 55 (24).

2-[2-(1-Benzyloxycarbonyl)piperidyl]ethanal: PCC (547 mg, 2.54 mmol) and neutral alumina (360 mg, previously dried under reduced pressure at room temp. for 1 d) were ground together and placed under nitrogen in freshly distilled dichloromethane (3 mL). 2-[2-(1-Benzyloxycarbonyl)piperidyl]ethanol (221.6 mg, 0.84 mmol) dissolved in CH_2Cl_2 (3 mL) was quickly added with vigorous stirring. The progress of the reaction was monitored by TLC on silica gel [hexane/EtOAc (7:3)]. After 6 h at room temp., the mixture was filtered through a Florisil column and eluted with diethyl ether. This yielded 2-[2-(1-benzyloxycarbonyl)piperidyl]ethanal (156 mg, 0.60 mmol, 71%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.45–1.74 (m, 6 H, 3-H_2, 4-H_2, 5-H_2), 2.54–2.79 (m, 2 H, 7-H_2), 2.85 (t, J = 13.4 Hz, 1 H, 6-H), 4.05 (br. d, J = 14.0 Hz, 1 H, 6-H), 4.91 (m, 1 H, 2-H), 5.12 (s, 2 H, 10-H_2), 7.34 (m, 5 H, Ar-H), 9.68 (s, 1 H, 8-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 18.7, 25.1, 28.6 (C-3, C-4, C-5), 39.5, 44.4 (C-6, C-7), 46.1 (C-2), 67.1 (C-10), 127.8, 127.9, 128.4, 136.6 (C-11), 155.1 (C-9), 200.4 (C-8) ppm. IR (NaCl): $\tilde{\nu}$ = 3092, 3063, 3035, 2942, 2865, 2731, 1729, 1692, 1421, 1258, 1056 cm^{-1}. EIMS: m/z (%) = 261 (6) [M]$^{+\cdot}$, 233 (32), 219 (25), 218 (174), 170 (16), 126 (43), 108 (26), 91 (100), 84 (15), 77 (13), 65 (51).

1-Benzyloxycarbonyl-2-(2,2-diethoxyethyl)piperidine: 2-[2-(1-Benzyloxycarbonyl)piperidyl]ethanal (1.523 g, 5.84 mmol) dissolved in dry ethanol (17 mL) was stirred under nitrogen at 35 °C in the presence of *p*-toluenesulfonic acid monohydrate (56 mg, 0.3 mmol) and molecular sieves (3 Å) for 17 h. Dry ethanol (10 mL) was added,

and the mixture was further stirred at 35 °C for 22 h. The disappearance of the aldehyde was complete after 40 h. The mixture was filtered through Celite, and the filtrate was concentrated in vacuo. The solid residue was washed with a satd. aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined organic phases were dried, and the solvents were removed to dryness. The crude product was then flash-chromatographed on silica gel [hexane/AcOEt (9:1 to 7:3)] to afford 1-benzyloxycarbonyl-2-(2,2-diethoxyethyl)piperidine (1.217 g, 3.63 mmol, 63%) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (t, J = 7.0 Hz, 6 H, 18-H_3, 20-H_3), 1.53–1.62 (m, 6 H, 3-H_2, 4-H_2, 5-H_2), 1.68–1.79 (m, 1 H, 7-H), 2.04 (m, 1 H, 7-H), 2.88 (t, J = 13.1 Hz, 1 H, 6-H), 3.38–3.64 (m, 4 H, 17-H_2, 19-H_2), 4.06 (br. d, J = 13.0 Hz, 1 H, 6-H), 4.46 (m, 2 H, 2-H, 8-H), 5.12 (s, 2 H, 10-H_2), 7.31–7.36 (m, 5 H, Ar-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 15.3 (C-18, C-20), 19.0, 25.6, 29.1 (C-3, C-4, C-5), 34.2, 39.3 (C-6, C-7), 47.9 (C-2), 60.6, 62.0 (C-17, C-19), 67.0 (C-10), 101.3 (C-8), 127.8, 127.9, 128.4 (C-12–16), 137.0 (C-11), 155.4 (C-9) ppm. IR (NaCl): $\tilde{\nu}$ = 3089, 3065, 3033, 2977, 2937, 2870, 1694, 1419, 1256, 1057 cm^{-1}. EIMS: m/z (%) = 335 (10) $[M]^{+\cdot}$, 306 (29), 290 (9), 262 (14), 218 (35), 198(73), 174 (59), 154 (100), 126 (13), 91 (88), 65 (11).

2-(2,2-Diethoxyethyl)piperidine (19): 1-Benzyloxycarbonyl-2-(2,2-diethoxyethyl)piperidine (545.2 mg, 1.63 mmol) dissolved in ethanol (50 mL) was stirred under hydrogen in the presence of Pd/C (10%, 57 mg) at atmospheric pressure and room temp. for 21 h. The mixture was filtered through Celite, and the filtrate was concentrated in vacuo. Flash chromatography on neutral alumina [CH_2Cl_2/MeOH (9:1)] gave **19** (319.1 mg, 1.59 mmol, 98%) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, J = 7.1 Hz, 6 H, 10-H_3, 12-H_3), 1.32–1.79 (m, 8 H, 3-H_2, 4-H_2, 5-H_2, 7-H_2), 2.29 (br. s, 1 H, NH), 2.61–2.67 (m, 2 H, 2-H, 6-H), 3.03 (br. d, J = 11.0 Hz, 1 H, 6-H), 3.42–3.70 (m, 4 H, 9-H_2, 11-H_2), 4.62 (t, J = 5.5 Hz, 1 H, 8-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 15.1, 15.2 (C-10, C-12), 24.7, 25.9, 33.0, 40.4, 46.6, 53.5 (C-2), 61.0, 61.5 (C-9, C-11), 101.5 (C-8) ppm. IR (NaCl): $\tilde{\nu}$ = 3353, 2976, 2931, 2857, 1456, 1373, 1124, 1061 cm^{-1}. EIMS: m/z (%) = 201 (2) $[M]^{+\cdot}$, 172 (5), 156 (29), 136 (31), 126 (14), 110 (5), 103 (12), 84 (100), 75 (13), 56 (16).

6-Cyano-decahydro-2*H*,6*H*-dipyrido[1,2-*a*:1′,2′-*c*]pyrimidine (8): A solution of **19** (57.5 mg, 0.29 mmol) in aqueous HCl (5%, 995 μL) was stirred at room temp. overnight. Ground α-tripiperideine (**10**, 42 mg, 0.17 mmol) was then added to this solution. The pH was then raised to 2.5 by slow addition of satd. aqueous $NaHCO_3$, and this pH was maintained for 1 h. Potassium cyanide (33 mg, 0.51 mmol) was then slowly added, while the pH was maintained between 2 and 3 by regular addition of diluted aqueous HCl. After 21 h at room temp., the mixture was basified (pH 8) by addition of a satd. aqueous $NaHCO_3$ solution and was then extracted with CH_2Cl_2/EtOH (3:2). The organic phases were combined and dried, and the solvents were removed to dryness. The resulting yellow oil was flash-chromatographed on silica gel [CH_2Cl_2/CH_3OH (99:1) + 1% concd. NH_4OH]. This yielded **8** (54.9 mg, 0.25 mmol, 88%) as a colourless oil. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.27–1.37 (ms, 4 H, 1-H, 2-H, 8-H, 9-H), 1.52–1.65 (ms, 4 H, 3-H_2, 8-H, 10-H), 1.65–1.73 (ms, 2 H, 9-H, 10-H), 1.76 (m, 1 H, 7-H), 1.81 (m, 1 H, 2-H), 1.87 (td, J = 2.4, 12 Hz, 1 H, 11-H), 1.98 (td, J = 4.8, 13.2 Hz, 1 H, 7-H), 2.17 (m, 1 H, 1-H), 2.3 (t, J = 10.8 Hz, 1 H, 7a-H), 2.53 (td, J = 3.0, 11.4 Hz, 1 H, 4-H), 2.72 (td, J = 3.0, 9.6 Hz, 1 H, 4-H), 2.74 (dd, J = 3.0, 9.6 Hz, 1 H, 12a-H), 3.17 (br. d, J = 11.0 Hz, 1 H, 11-H), 3.84 (dd, J = 1.8, 4.8 Hz, 1 H, 6-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 23.1 (C-2), 23.6 (C-9), 24.8 (C-3), 25.7 (C-10), 29.3 (C-1), 32.8 (C-8), 34.4 (C-7), 48.3 (C-11), 53.5 (C-4), 54.5 (C-6), 57.0 (C-7a), 77.6 (C-12a), 116.9 (CN) ppm. IR (NaCl): $\tilde{\nu}$ = 2933, 2858, 2796, 2730, 2221, 1455, 1287, 1246, 1113 cm^{-1}. EIHRMS: m/z (%) = 219.1722 (calcd. for $C_{13}H_{21}N_3$ 219.1735), 192.1618 (calcd. for $C_{12}H_{20}N_2$ 192.1626), 163.1176 (calcd. for $C_{10}H_{15}N_2$ 163.1235), 152.1320 (calcd. for $C_9H_{16}N_2$ 152.1313).

Propyl Derivative 3a: A solution of propylmagnesium bromide, prepared from magnesium (31 mg, 1.28 mmol) and propyl bromide (116 μL, 1.28 mmol) in diethyl ether (2 mL), was added to a solution of α-amino nitrile **8** (53 mg, 0.24 mmol) in THF (1 mL) and cooled to –10 °C. The mixture was stirred at room temp. for 40 h and was then hydrolysed by addition of a satd. aqueous NH_4Cl solution and extracted three times with CH_2Cl_2. The organic phases were combined and dried, and the solvents were removed to dryness. This afforded a yellow oil that was flash-chromatographed on silica gel [CH_2Cl_2/MeOH/10% NH_4OH (95:5:0.1)] to give **3a** (45 mg, 0.19 mmol, 79%) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, J = 7.2 Hz, 3 H, 3′-H_3), 1.17–1.38 (m, 8 H), 1.40–1.76 (m, 12 H), 1.89 (td, J = 2.4, 12.0 Hz, 1 H, 11-H), 2.15 (br. t, J = 10.0 Hz, 1 H, 7a-H), 2.47 (m, 1 H, 4-H), 2.64 (m, 1 H, 4-H), 3.01 (br. d, J = 11.0 Hz, 1 H, 12a-H), 3.10 (m, 2 H, 6-H, 11-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 14.3 (C-3′), 20.7, 20.8, 24.5, 26.2, 26.3, 28.9, 30.4, 32.6, 33.9, 49.3 (C-4), 50.2 (C-11), 57.1 (C-6), 59.2 (C-7a), 73.2 (C-12a) ppm. IR (NaCl): $\tilde{\nu}$ = 2930, 2858, 2796, 2730, 1442, 1373, 1316, 1226, 1134 cm^{-1}. EIMS: m/z (%) = 236 (36) $[M]^{+\cdot}$, 207 (100) $[M^{+\cdot} - C_2H_5^{\cdot}]$, 193 (11) $[M^{+\cdot} - C_3H_7^{\cdot}]$, 179 (20), 166 (23), 152 (28), 138 (22), 124 (9), 110 (25), 84 (32).

Dodecyl Derivative 3b: This compound was prepared according to the same procedure as utilised for preparing the corresponding propyl derivative **3a** (yield 76%) but by using dodecylmagnesium bromide. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (t, J = 6.1 Hz, 3 H, 12′-H_3), 1.23 (br. s, 24 H), 1.32–1.72 (m, 12 H), 1.86 (td, J = 2.4, 12.0 Hz, 1 H, 11-H), 2.14 (br. t, J = 10.0 Hz, 1 H, 7a-H), 2.45 (m, 1 H, 4-H), 2.60 (m, 1 H, 4-H), 2.98 (br. d, J = 11.0 Hz, 1 H, 12a-H), 3.09 (m, 2 H, 6-H, 11-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 14.2 (C-12′), 20.7, 22.8, 24.5, 26.1, 26.2, 27.6, 28.1, 28.9, 29.4, 29.7, 29.8, 29.9, 32.0, 32.5, 33.8, 49.2 (C-4), 50.2 (C-11), 57.1 (C-6), 59.5 (C-7a), 73.3 (C-12a) ppm. IR (NaCl): $\tilde{\nu}$ = 2928, 2853, 1455, 1377, 1317, 1229, 1137 cm^{-1}. EIMS: m/z (%) = 362 (20) $[M]^{+\cdot}$, 333 (5) $[M^{+\cdot} - C_2H_5^{\cdot}]$, 305 (6) $[M^{+\cdot} - C_4H_9^{\cdot}]$, 277 (7) $[M^{+\cdot} - C_6H_{13}^{\cdot}]$, 264 (7) $[M^{+\cdot} - C_7H_{15}^{\cdot}]$, 249 (8) $[M^{+\cdot} - C_8H_{17}^{\cdot}]$, 235 (5) $[M^{+\cdot} - C_9H_{19}^{\cdot}]$, 221 (13) $[M^{+\cdot} - C_{10}H_{21}^{\cdot}]$, 207 (100) $[M^{+\cdot} - C_{11}H_{23}^{\cdot}]$, 194 (34), 179 (11), 166 (23), 152 (34), 138 (11), 124 (11), 110 (31), 84 (38).

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