Stereoselective Synthesis and Stereochemical Determination of 2,5-Dialkylpyrrolidines and 2,6-Dialkylpiperidines

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ω-Alkyllactams **3** can be transformed into ω-alkyl cyclic β-enaminoesters **7** which are good precursors of insects venom alkaloids. A stereoselective synthesis of dialkylpyrrolidines and *Solenopsine A* is described followed by an easy stereochemical determination by ^{13}C nmr.

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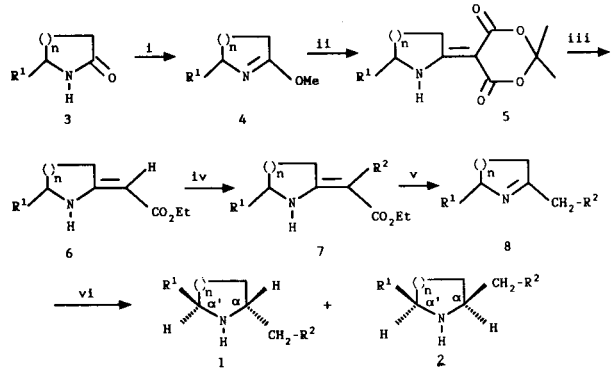
We have recently shown that the venom of the ant *Monomorium minutum* is composed of three 2,5-dialkylpyrrolidines **1** (n = 1) which exhibit a very broad and significant insecticidal activity [1]; the *trans* stereochemistry has been assigned by mass spectroscopy [2]. However, we looked to find a simple method of geometry determination of identically 2,5-disubstituted pyrrolidines, especially by nmr spectroscopy. A technique is to assign the *cis* stereochemistry to the major product of catalytic hydrogenation of the corresponding aromatic amine (pyrrole or pyridine). Assignments made on this basis cannot be considered as completely reliable, due to the stepwise nature of hydrogen addition, the possible isomerisation of olefins on catalyst [3] or the resulting possibility to obtain *trans* isomers as major products [4].

A non ambiguous stereochemistry determination has been achieved by ^1H nmr from the *N*-benzyl-2,6-dialkylpiperidine and 2,5-dialkylpyrrolidine derivatives [5] based on the non magnetic equivalence of the methylene protons of the benzyl radical; however, this method needs the preparation of *N*-benzyl derivatives.

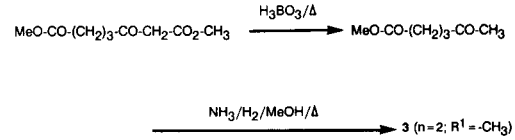
The single C=N catalytic hydrogenation of cyclic imines **8** is a stereospecific reduction which permitted us to assign a *cis* structure to heterocycles **2**. But a stereoselective chemical reduction of imines **8** was observed leading to a mixture of heterocycles **1** and **2**. However, sodium borohydride in acetic acid gives the best ratio (70:30) in favour of pyrrolidines **1** (n = 1) [6] and lithium aluminium hydride with trimethylaluminium in tetrahydrofuran leads to piperidines **1** (n = 2) with a good ratio (95:5) [7]. Also a general and regiospecific synthesis of such imines **8** with a decarboxylation of β-enaminoesters **6** issued from lactams **3** has been developped [8] (Scheme A).



Scheme A

Reaction conditions : i, Me_2SO_4; ii, Meldrum's acid/$Ni(acac)_2$/$CHCl_3$; iii, EtOH/Δ; iv, R^2-X/NaH/toluene; v, H_3BO_3/Δ; vi, catalytic or chemical reduction.

Generally, lactams are commercially available [9] like 2-pyrrolidinone **3** (n = 1, R^1 = H), 5-methyl-2-pyrrolidinone **3** (n = 1, R^1 = CH_3) and 2-piperidinone **3** (n = 2, R^1 = H), but 6-methyl-2-piperidinone **3** (n = 2, R^1 = CH_3) was prepared from dimethyl 3-oxoheptanedioate **9** by the following reactions (Scheme B).



Scheme B

The non ambiguous assignment of the chemical shifts of the α and α' carbons of *cis* heterocycles **2** permits us to assign these *trans* heterocycles **1** obtained by the chemical reduction (Table 1).

The tertiary carbon C-α of the monosubstituted pyrrolidine **2a** was found at δ = 59.3 ppm and permitted us to assign unambiguously the chemical shifts of the 2-undecyl-5-methylpyrrolidine **2b** (R^2 = $-(CH_2)_9-CH_3$, n = 1), δ = 59.9 ppm for C-α with the undecyl radical and δ = 54.6 ppm for C-α' bearing the methyl substituent. These two values were characteristic for a *cis* structure because compound **2b** was obtained by a stereospecific catalytic reduction of the corresponding imine. An extension of this result permitted us to assign *cis* stereochemistry to pyrrolidines **2c**, **2d** and **2e**.

A chemical reduction of cyclic imines **8** with sodium borohydride/acetic acid leads to a mixture of *trans* and *cis* pyrrolidines **1** and **2** (ratio: 70/30). Consequently, it is possible to assign the chemical shifts of tertiary carbons of

Table 1 : ^{13}C nmr chemical shifts of α and α' carbons of heterocycles **1** and **2**

Entry	n	R^1	R^2	2 Cis		1 Trans	
				C-α'	C-α	C-α'	C-α
a	1	-H	$-(CH_2)_9-CH_3$	46.5	59.3	----	----
b	1	$-CH_3$	$-(CH_2)_9-CH_3$	54.6	59.9	----	----
c	1	$-CH_3$	$-(CH_2)_7-CH_3$	54.6	59.9	53.2	58.1
d	1	$-CH_3$	$-(CH_2)_{13}-CH_3$	54.5	59.8	53.2	58.2
e	1	$-CH_3$	$-(CH_2)_8-CH=CH_2$	54.9	59.7	53.2	58.2
f	2	-H	$-(CH_2)_9-CH_3$	47.3	57.0	----	----
g	2	$-CH_3$	$-(CH_2)_9-CH_3$	52.5	57.2	----	----
g	2	$-CH_3$	$-(CH_2)_9-CH_3$	----	----	45.8	50.8

the *trans* products; ^{13}C resonance of compounds **1** appears at 1.5 ppm upfield from the corresponding *cis* deriatives. Similar results, according to the theoretical study of Beierbeck, *et al.* [10] were observed for piperidines **1g** and **2g**.

In conclusion, we report a stereoselective synthesis of 2,5-dialkylpyrrolidines and 2,6-dialkylpiperidines, especially *Solenopsine A* **1g**. An easy structural determination was performed by ^{13}C nmr.

EXPERIMENTAL

I. Methyl 5-Oxohexanoate (**10**).

Dimethyl 3-oxoheptanedioate (**9**) [11] was decarboxylated with boric acid as described by Werhli and Chu [12], yield 53%, bp 103°/15 mm Hg [13].

II. 6-Methyl-2-piperidone (**3**) (n = 2, $R^1 = CH_3$).

Methyl 5-oxohexanoate (**10**) (0.1 mmole), ammonia (0.5 mole) in methanol (125 ml) and Raney nickel (1 g) were hydrogenated (100 bar) for 5 hours at 160°. The solution was filtered, the solvent was evaporated and compound **3** was distilled, yield 82%, bp 140°/0.05 mm Hg [14]; ir (neat): ν 3200, 1690 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.00-1.60 (m, 2H), 1.25 (d, 3H, J = 6 Hz), 1.60-2.15 (m, 2H), 2.15-2.50 (m, 2H), 3.25-3.75 (m, 1H), 6.50 (s, 1H).

III. General Procedure for the preparation of Lactim Ethers **4**.

Lactam **3** (0.5 mole) and dimethyl sulfate (0.5 mole) were stirred for 12 hours at 60°. The mixture was then poured into a chilled potassium carbonate solution and extracted with ether (3 x 100 ml), dried with sodium sulfate and evaporated. The crude product was distilled to give **4**.

2-Methoxy-3,4-dihydro-5*H*-pyrrole (**4**) (R^1 = H, n = 1).

This compound was prepared as described by Wick *et al.* [15].

2-Methoxy-3,4,5,6-tetrahydropyridine (**4**) (R^1 = H, n = 2).

This compound was prepared as described by Oishi *et al.* [16].

2-Methoxy-5-methyl-3,4-dihydro-5*H*-pyrrole (**4**) ($R^1 = CH_3$, n = 1).

Compound **4** was obtained in a yield of 75%, bp 40°/25 mm Hg; ir (neat): ν 1650 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.20 (d, 3H, J = 6 Hz), 1.25-1.70 (m, 2H), 2.20-2.60 (m, 2H), 3.50-4.00 (m, 1H), 3.75 (s, 3H).

Anal. Calcd. for $C_6H_{11}NO$: C, 63.68; H, 9.80; N, 12.39. Found: C, 63.58; H, 9.72; N, 12.75.

2-Methoxy-6-methyl-3,4,5,6-tetrahydropyridine (**4**) ($R^1 = CH_3$, n = 2).

This compound was obtained in a yield of 84%, bp 55°/13 mm Hg; ir (neat): ν 1670 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.15 (d, 3H, J = 7 Hz), 1.50-1.90 (m, 4H), 1.90-2.90 (m, 2H), 3.10-3.70 (m, 1H), 3.50 (s, 3H).

Anal. Calcd. for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.01. Found: C, 65.98; H, 10.10; N, 11.35.

IV. General Procedure for Preparation of β-Enaminodiesters **5**.

This lactim ether **4** (0.15 mole), isopropylidene malonate (0.15 mole), and nickel acetylacetonate (0.5 g), were refluxed overnight in chloroform (100 ml). After evaporation of chloroform, the product was recrystallized [17,18].

Isopropylidine-α-(tetrahydro-2-pyrrolidinylidene)malonate (**5**) (R^1 = H, n = 1).

This compound was prepared as described by Célérier, *et al.* [18].

Isopropylidene-α-(hexahydro-2-pyridinylidene)malonate (**5**) (R^1 = H, n = 2).

This compound was prepared as described by Célérier *et al.* [18].

Isopropylidene-α-[5-methyl(tetrahydro-2-pyrrolidinylidene)]-

malonate (**5**) (R^1 = CH_3, n = 1).

This compound was obtained in a yield of 80%, mp 167° (ethanol); ir (bromoform): ν 3720, 1690, 1640, 1590 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.40 (d, 3H, J = 6 Hz), 1.65 (s, 6H), 2.00-2.50 (m, 2H), 3.10-3.60 (m, 2H), 4.00-4.30 (m, 1H), 9.75 (s, 1H).

Anal. Calcd. for $C_{11}H_{15}NO_4$: C, 58.65; H, 6.71; N, 6.22. Found: C, 58.42; H, 6.75; N, 5.97.

Isopropylidene-α-[6-methyl(hexahydro-2-pyridinylidene)]malonate (**5**) (R^1 = CH_3, n = 2).

This compound was obtained in a yield of 60%, mp 117° (ethanol); ir (bromoform): ν 3400, 1690, 1640, 1580 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.30 (d, 3H, J = 6 Hz), 1.50-2.20 (m, 4H), 1.60 (s, 6H), 2.90-3.40 (m, 2H), 3.40-3.80 (m, 1H), 10.75 (s, 1H).

Anal. Calcd. for $C_{12}H_{17}NO_4$: C, 60.24; H, 7.16; N, 5.85. Found: C, 60.56; H, 7.42; N, 5.63.

V. General Procedure for Preparation of β-Enaminoesters **6**.

β-Enaminodiester **5** (0.05 mole) and ethanol (60 ml) were heated in autoclave for 0.5 hour [19]. After evaporating ethanol, the crude product was distilled.

Ethyl α-(Tetrahydro-2-pyrrolidinylidene)acetate (**6**) (R^1 = H, n = 1).

This compound was prepared as described by Célérier *et al.* [18].

Ethyl α-(Hexahydro-2-pyridinylidene)acetate (**6**) (R^1 = H, n = 2).

This compound was prepared as described by Célérier *et al.* [18].

Ethyl α-[5-methyl(tetrahydro-2-pyrrolidinylidene)]acetate (**6**) (R^1 = CH_3, n = 1).

This compound was obtained in a yield of 85%, bp 86°/0.01 mm Hg; ir (neat): ν 3320, 1680, 1580 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.20 (t, 3H, J = 7 Hz), 1.30 (d, 3H, J = 6 Hz), 1.30-2.30 (m, 2H), 2.30-2.80 (m, 2H), 3.60-3.90 (m, 1H), 4.10 (q, 2H, J = 7 Hz), 4.40 (s, 1H), 7.90 (s, 1H).

Anal. Calcd. for $C_9H_{15}NO_2$: C, 63.88; H, 8.94; N, 8.28. Found: C, 63.79; H, 8.93; N, 8.45.

Ethyl-α-[6-Methyl(hexahydro-2-pyridinylidene)]acetate (**6**) (R^1 = CH_3, n = 2).

This compound was obtained in a yield of 70%, bp 85°/0.01 mm Hg; ir (neat): ν 3280, 1640, 1000 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.20 (t, 3H, J = 7 Hz), 1.30 (d, 3H, J = 6 Hz), 1.40-2.10 (m, 4H), 2.10-2.50 (m, 2H), 3.10-3.70 (m, 1H), 4.10 (Q, 2H, J = 7 Hz), 4.30 (s, 1H), 8.40 (s, 1H).

Anal. Calcd. for $C_{10}H_{17}NO_2$: C, 65.54; H, 9.35; N, 7.64. Found: C, 65.65; H, 9.28; N, 7.25.

VI. General Procedure for Preparation of *C*-Alkyl-β-enaminoesters **7**.

β-Enaminoester **6** (0.02 mole) was added to a suspension of sodium hydride (0.02 mole) in anhydrous toluene (50 ml). The mixture was refluxed until dissolution complete. To the cold solution was added, dropwise, the alkyl bromide (0.02 mole) in toluene (50 ml). After refluxing overnight, the mixture was hydrolysed and acidified with hydrochloric acid (10%) until *p*H = 6. The aqueous layer was extracted with chloroform (2 x 30 ml) and the organic layers were dried over sodium sulfate. After evaporation, the product was distilled or recrystallized.

Ethyl α-(Tetrahydro-2-pyrrolidinylidene)dodecanoate (**7a**) (R^1 = H, R^2 = $(CH_2)_9$-CH_3, n = 1).

This compound was obtained in a yield of 55%, bp 140°/0.05 mm Hg; ir (neat): ν 3360, 1650, 1580 cm^{-1}; ^1H nmr (carbon tetrachloride): δ 1.20 (t, 3H, J = 7 Hz), 0.80-2.20 (m, 23 H), 2.60 (m, 2H), 3.45 (m, 2H), 4.20 (q, 2H, J = 7 Hz), 8.20 (s, 1H).

Anal. Calcd. for $C_{18}H_{33}NO_2$: C, 73.17; H, 11.26; N, 4.74. Found: C, 72.95; H, 11.45; N, 4.79.

Ethyl α-[5-Methyl(tetrahydro-2-pyrrolidinylidene)]dodecanoate (**7b**) (R^1 = CH_3, R^2 = $(CH_2)_9$-CH_3, n = 1).

This compound was obtained in a yield of 60%, by 147°/0.01 mm Hg; ir (neat): ν 3310, 1600, 1580 cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.70-2.80 (m, 31H), 3.85 (m, 1H), 4.10 (q, 2H, J = 7 Hz), 8.15 (s, 1H).

Anal. Calcd. for $C_{19}H_{35}NO_2$: C, 73.73; H, 11.40; N, 4.53. Found: C, 73.56; H, 11.38; N, 4.49.

Ethyl α-[5-Methyl(tetrahydro-2-pyrrolidinylidene)]decanoate (**7c**) (R^1 = CH_3, R^2 = $(CH_2)_7$-CH_3, n = 1).

This compound was obtained in a yield of 66%, bp 137°/0.01 mm Hg; ir (neat): ν 3320, 1655, 1585 cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.75-2.80 (m, 27H), 3.85 (m, 1H), 4.10 (q, 2H, J = 7 Hz), 8.15 (s, 1H).

Anal. Calcd. for $C_{17}H_{31}NO_2$: C, 72.55; H, 11.10; N, 4.98. Found: C, 72.46; H, 11.19; N, 5.07.

Ethyl α-[5-Methyl(tetrahydro-2-pyrrolidinylidene)]-11-dodecenoate (**7d**) (R^1 = CH_3, R^2 = $(CH_2)_8$-CH=CH_2, n = 1).

This compound was obtained in a yield of 50%, bp 155°/0.01 mm Hg; ir (neat): ν 3310, 1650, 1580 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.20-2.80 (m, 23H), 1.35 (t, 3H, J = 7 Hz), 3.60-4.05 (m, 1H), 4.15 (q, 2H, J = 7 Hz), 4.70-6.10 (m, 3H), 7.80-8.20 (m, 1H).

Anal. Calcd. for $C_{19}H_{33}NO_2$: C, 74.22; H, 10.81; N, 4.56. Found: C, 74.41; H, 10.72; N, 4.49.

Ethyl α-[5-Methyl(tetrahydro-2-pyrrolidinylidene)]-11-dodecenoate (**7e**) (R^1 = CH_3, R^2 = $(CH_2)_8$-CH=CH_2, n = 1).

This compound was obtained in a yield of 50%, bp 155°/0.01 mm Hg; ir (neat): ν 3310, 1650, 1580 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.20-2.80 (m, 26H), 3.85 (m, 1H), 4.15 (q, 2H, J = 7 Hz), 4.70-6.10 (m, 3H), 8.00 (s, 1H).

Anal. Calcd. for $C_{19}H_{33}NO_2$: C, 74.22; H, 10.81; N, 4.56. Found: C, 74.18; H, 10.95; N, 4.52.

Ethyl α-(Hexahydro-2-pyridinylidene)dodecanoate (**7f**) (R^1 = H, R^2 = -$(CH_2)_9$-CH_3, n = 2).

This compound was obtained in a yield of 70%, bp 155°/0.01 mm Hg; ir (neat): ν 3220, 1630, 1590 cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.85 (m, 3H), 1.00-2.25 (m, 25H), 2.40 (m, 2H), 3.30 (m, 2H), 4.10 (m, 2H), 9.1 (s, 1H).

Anal. Calcd. for $C_{19}H_{35}NO_2$: C, 73.73; H, 11.40; N, 4.53. Found: C, 73.59; H, 11.56; N, 4.58.

Ethyl α-[6-Methyl(hexahydro-2-pyridinylidene)]dodecanoate (**7g**) (R^1 = CH_3, R^2 = $(CH_2)_9$-CH_3, n = 2).

This compound was obtained in a yield of 74%, bp 155°/0.01 mm Hg; ir (neat): ν 3200, 1730, 1590 cm^{-1}; ^1H nmr (deuterio-

chloroform): δ 0.90 (t, 3H, J = 6 Hz), 1.00-1.50 (m, 24H), 1.50-2.50 (m, 6H), 3.10-3.60 (m, 1H), 4.10 (q, 2H, J = 7 Hz), 8.80 (s, 1H).

Anal. Calcd. for $C_{20}H_{37}NO_2$: C, 74.25; H, 11.53; N, 4.33. Found: C, 74.14; H, 11.62; N, 4.19.

VII. General Procedure for Preparation of Cyclic Imines **8**:

β-Enaminoester **7** was heated with two equivalents of boric acid [20] at 180°. Within 1 hour, the distillate (mainly methanol) was collected. Then water was added until complete solubilisation and the solution was extracted with dichloromethane. The organic layers were dried with sodium sulfate and evaporated. The crude product was distilled.

5-Undecyl-3,4-dihydro-2*H*-pyrrole (**8a**) (R^1 = H, R^2 = $(CH_2)_9$-CH_3, n = 1).

This compound was obtained in a yield of 90%, bp 100°/0.01 mm Hg; ir (neat): ν 1640 cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.7-1.05 (m, 3H), 1.08-2.10 (m, 22H), 2.20-2.60 (m, 2H), 3.60-4.05 (m, 2H).

Anal. Calcd. for $C_{15}H_{29}N$: C, 80.64; H, 13.09; N, 6.27. Found: C, 80.52; H, 13.25; N, 6.11.

2-Methyl-5-undecyl-3,4-dihydro-2*H*-pyrrole (**8b**) (R^1 = CH_3, R^2 = $(CH_2)_9$-CH_3, n = 1).

This compound was obtained in a yield of 37%, bp 105°/0.01 mm Hg; ir (neat): ν 1640 cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.70-2.70 (m, 27H), 1.25 (d, 3H, J = 6 Hz), 4.05 (m, 1H).

Anal. Calcd. for $C_{16}H_{31}N$: C, 80.94; H, 13.16; N, 5.90. Found: C, 81.04; H, 13.07; N, 5.88.

2-Methyl-5-nonyl-3,4 dihydro-2*H*-pyrrole (**8c**) (R^1 = CH_3, R^2 = $(CH_2)_7$-CH_3, n = 1).

This compound was obtained in a yield of 60%, bp 95°/0.01 mm Hg; ir (neat): ν 1640 cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.70-2.70 (m, 23H), 1.23 (d, 3H, J = 6 Hz), 4.05 (m, 1H).

Anal. Calcd. for $C_{14}H_{27}N$: C, 80.31; H, 13.00; N, 6.69. Found: C, 80.62; H, 12.91; N, 6.78.

2-Methyl-5-pentadecyl-3,4 dihydro-2*H*-pyrrole (**8d**) (R^1 = CH_3, R^2 = $(CH_2)_{13}$-CH_3, n = 1).

This compound was obtained in a yield of 45% in two steps from **6d**, bp 160°/0.05 mm Hg; ir (neat): ν 1640 cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.70-2.70 (m, 35H), 1.25 (d, 3H, J = 6 Hz), 4.05 (m, 1H).

Anal. Calcd. for $C_{20}H_{39}N$: C, 81.83; H, 13.39; N, 4.77. Found: C, 81.99; H, 13.42; N, 4.53.

2-Methyl-5-(1-undecen-10-yl)-3,4-dihydro-2*H*-pyrrole (**8e**) (R^1 = CH_3, R^2 = $(CH_2)_8$-CH=CH_2, n = 1).

This compound was obtained in a yield of 80%, bp 103°/0.01 mm Hg; ir (neat): ν 1640, 1590 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.10-2.70 (m, 22H), 1.23 (d, 3H, J = 6 Hz), 4.10 (m, 1H), 4.80-5.20 (m, 2H), 5.50-6.10 (m, 1H).

Anal. Calcd. for $C_{16}H_{29}N$: C, 81.63; H, 12.42; N, 5.95. Found: C, 81.75; H, 12.56; N, 6.02.

6-Undecyl-2,3,4,5-tetrahydropyridine (**8f**) (R^1 = H, R^2 = $(CH_2)_9$-CH_3, n = 2).

This compound was obtained in a yield of 80%, bp 115°/0.01 mm Hg; ir (neat): ν 1660 cm^{-1}, ^1H nmr (deuteriochloroform): δ 0.7-1.1 (m, 3H), 1.15-1.90 (m, 24H), 1.95-2.35 (m, 2H), 3.40-3.75 (m, 2H).

Anal. Calcd. for $C_{16}H_{31}N$: C, 80.94; H, 13.16; N, 5.90. Found: C, 81.09; H, 13.11; N, 6.07.

2-Methyl-6-undecyl-2,3,4,5-tetrahydropyridine (**8g**) (R^1 = CH_3, R^2 = $(CH_2)_9$-CH_3, n = 2).

This compound was obtained in a yield of 80%, bp 130°/0.05 mm Hg; ir (neat): ν 1650 cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.80 (t, 3H, J = 7 Hz), 1.05-1.30 (m, 18H), 1.15 (d, 3H, J = 6 Hz), 1.35-1.55 (m, 2H), 1.60-1.70 (m, 2H), 1.90-2.00 (m, 2H), 2.05 (t, 2H, J = 6 Hz), 3.40 (s, 1H).

Anal. Calcd. for $C_{17}H_{33}N$: C, 81.20; H, 13.23; N, 5.57. Found: C, 81.15; H, 12.98; N, 5.69.

VIII. Reduction of Cyclic Imines **8**.

Method A.

The cyclic imine (8.5 10^{-3} mole) in 10% hydrochloric acid (4.5 ml) was hydrogenated at atmospheric pressure (24 hours) in presence of palladium-carbon (80 mg). The solution was then filtered neutralised and extracted with chloroform (3 x 5 ml). The organic layers were dried with sodium sulfate and evaporated, then the amine was distilled.

Method B.

The cyclic imine (6.4 10^{-3} mole) in dichloromethane (40 ml) was cooled at -80° under a nitrogen atmosphere. Diisobutylaluminium hydride (4 equivalents) was added and the solution was stirred until the temperature reached 20° (4 hours). The mixture was hydrolyzed with water (50 ml), acidified with hydrochloric acid until *p*H = 2 then saturated with potassium carbonate. Dichloromethane (50 ml) was added and the mixture was heated (40°) during 1/2 hour. The organic layer was separated and the aqueous layer extracted with dichloromethane (3 x 20 ml). The organic layers were dried over sodium sulfate, evaporated and the crude product was distilled.

Method C.

The cyclic imine (3.4 10^{-3} mole) was stirred in acetic acid (50 ml) at room temperature. Sodium borohydride (3 equivalents) was added in small portions and the mixture was stirred overnight. The work-up was then similar to method B.

Method D.

The cyclic imine (3.4 10^{-3} mole) was added to a suspension of lithium aluminium hydride (7 equivalents) in tetrahydrofuran (50 ml) at -80° under nitrogen. Trimethylaluminium (7 equivalents) was added dropwise and the mixture was stirred ½ hour at -80° then allowed to reach to room temperature. The work-up was similar to method B.

Only the *cis* compounds **2** are completely described; the spectral data of *trans* compounds **1** are given by comparison of mixtures spectra with pure *cis* compounds spectra.

2-Undecylpyrrolidine (**2a**) (R^1 = H, R^2 = $(CH_2)_9$-CH_3, n = 1).

This compound was obtained in a yield of 75% (Method C), bp 140°/0.01 mm Hg (kugelrohr); ir (neat): ν 3300 cm^{-1}; ^1H (carbon tetrachloride): δ 0.70-0.95 (m, 3H), 0.80-1.75 (m, 20H), 2.20-2.75 (m, 5H), 2.75-3.10 (m, 3H); ^{13}C nmr (deuteriochloroform): δ 14.0, 22.6, 25.3, 27.5, 29.2, 29.8, 30.8, 31.8, 36.9, 46.5, 59.3.

Anal. Calcd. for $C_{15}H_{31}N$: C, 79.92; H, 13.86; N, 6.21. Found: C, 80.22; H, 13.74; N, 6.27.

2-Undecyl-5-methylpyrrolidine (**2b**) ($R^1 = CH_3$, $R^2 = (CH_2)_9$-CH_3, n = 1).

This compound was obtained in a yield of 92% (Method A); bp 150°/0.01 mm Hg (kugelrohr); ir (neat): ν 3350 cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.70-1.00 (m, 3H), 1.16 (d, 3H, J = 6.5 Hz), 1.10-2.10 (m, 25H), 2.70-3.35 (m, 2H); ^{13}C nmr (deuteriochloroform): δ 14.1, 21.5, 22.7, 27.5, 29.4, 29.7, 29.9, 31.9, 33.3, 37.0, 54.6, 59.9,

Anal. Calcd. for $C_{16}H_{33}N$: C, 80.26; H, 13.89; N, 5.85. Found: C, 80.31; H, 13.78; N, 5.73.

2-Nonyl-5-methylpyrrolidines **2c** and **1c** ($R^1 = CH_3$, $R^2 = (CH_2)_7$-CH_3, n = 1).

Compound **2c** was obtained in a yield of 98% (Method B), bp 130°/0.01 mm Hg (kugelrohr); ir (neat): ν 3300 cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.70 (m, 3H), 1.16 (d, 3H, J = 6.5 Hz), 1.10-2.10 (m, 21H), 2.70-3.35 (m, 2H); ^{13}C-nmr (deuteriochloroform): δ 14.1, 22.2, 22.7, 27.4, 31.9, 33.3, 34.5, 37.4, 53.2, 58.1.

Anal. Calcd. for $C_{14}H_{29}N$: C, 79.54; H, 13.83; 6.63. Found: C, 79.37; H, 13.78; N, 6.54.

Compound (**1c**) had ^{13}C nmr (deuteriochloroform): δ 14.1, 21.5, 22.7, 27.5, 29.3, 29.6, 29.9, 31.9, 32.0, 33.3, 36.9, 54.6, 59.9.

The ration of **2c** to **1c** was 80/20 when obtained with lithium aluminium hydride (25 equivalents)/ether (Method D).

2-Pentadecyl-5-methylpyrrolidines (**2d**) and (**1d**) ($R^1 = CH_3$, $R^2 = (CH_2)_{13}$-CH_3, n = 1).

Compound **2d** was obtained in a yield of 90% (Method B), bp 170°/0.05 mm Hg (kugelrohr); ir (neat): ν 3250 cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.70-1.00 (m, 3H), 1.16 (d, 3H, J = 6.5 Hz), 1.00-2.00 (m, 33H), 2.80-3.10 (m, 2H); ^{13}C nmr (deuteriochloroform): δ 14.0, 22.1, 22.6, 29.3, 31.9, 34.5, 37.4, 58.1, 53.2.

Anal. Calcd. for $C_{20}H_{41}N$: C, 81.27; H, 13.98; N, 4.76. Found: C, 80.98; H, 140.6; N, 4.82.

Compound (**1d**) had ^{13}C nmr (deuteriochloroform): δ 14.0, 21.4, 22.7, 27.5, 29.3, 29.7, 29.8, 31.9, 33.3, 36.9, 54.5, 59.8.

The ratio of **2d** to **1d** was 30/70 when obtained with sodium borohydride (3 equivalents)/acetic acid (Method C).

2-(1-Undecen-10-yl)-5-methylpyrrolidines **2e** and **1e** ($R^1 = CH_3$, $R^2 = (CH_2)_8$-$CH=CH_2$, n = 1).

Compound **2e** was obtained in a yield of 93% (Method B), bp 115°/0.01 mm Hg; ir (neat): ν 3300, 3060, 1640 cm^{-1}; ^1H nmr (deuteriochloroform): 500 MHz, δ 1.11 (d, 3H, J = 6.3 Hz), 1.20-2.10 (m, 23H), 3.15 (m, 1H), 3.25 (m, 1H), 4.90-5.10 (m, 2H), 5.75-5.90 (m, 1H); ^{13}C nmr (deuteriochloroform): δ 22.2, 27.4, 29.0, 33.6, 33.8, 34.6, 37.4, 53.2, 58.2, 114, 139.0.

Anal. Calcd. for $C_{16}H_{31}N$: C, 80.94; H, 13.16; N, 5.90. Found: C, 81.11; H, 13.07; N, 6.04.

Compound **1e** had ^1H nmr (deuteriochloroform): 500 MHz, δ 1.16 (d, 3H, J = 6.3 Hz), 1.20-2.10 (m, 23H), 2.95 (m, 1H), 3.10 (m, 1H), 4.90-5.10 (m, 2H), 5.75-5.90 (m, 1H); ^{13}C nmr (deuteriochloroform): δ 21.3, 27.3, 29.0, 29.3, 29.7, 31.8, 33.1, 33.6, 36.8, 54.4, 59.7, 114.0, 139.0.

The ratio of **2e** to **1e** was 30/70 when obtained with sodium borohydride (3 equivalents)/acetic acid (Method C).

2-Undecylpiperidine (**2f**) ($R^1 = H$, $R^2 = (CH_2)_9$-CH_3, n = 2).

This compound was obtained in a yield of 95% (Method A), bp 145°/0.01 mm Hg (kugelrohr); ir (neat): ν 3300 cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.70-0.95 (m, 3H), 0.80-1.75 (m, 20H), 2.00-2.75 (m, 7H), 2.75-3.10 (m, 3H); ^{13}C nmr (deuteriochloroform): δ 14.1, 22.7, 25.0, 25.9, 26.8, 29.3, 29.6, 29.9, 31.9, 33.1, 37.6, 47.3, 57.0.

Anal. Calcd. for $C_{16}H_{33}N$: C, 80.26; H, 13.89; N, 5.85. Found: C, 80.32; H, 14.03; N, 5.58.

2-Undecyl-5-methylpiperidines (**2g**) and (**1g**) ($R^1 = CH_3$, $R^2 = (CH_2)_9$-CH_3, n = 2).

Compound **2g** was obtained in a yield of 93% (Method B), bp 150°/0.03 mm Hg; ir (neat): ν 3400 cm^{-1}; ^1H nmr (deuteriochloroform): 500 MHz, δ 0.85 (t, 3H, J = 7 Hz), 0.95-1.10 (m, 2H), 1.10 (d, 3H, J = 7 Hz), 1.20-1.40 (m, 23H), 1.55-1.65 (m, 1H), 1.70-1.80 (m, 1H), 2.40-2.50 (m, 1H), 2.65-2.75 (m, 1H); ^{13}C nmr (deuteriochloroform): δ 14.0, 22.7, 23.1, 24.9, 26.0, 29.3, 29.6, 29.9, 31.9, 32.3, 34.5, 37.5, 52.5, 57.2.

Anal. Calcd. for $C_{17}H_{35}N$: C, 70.43; H, 12.51; N, 4.83. Found: C, 70.38; H, 12.64; N, 4.57.

Compound **1g** (*Solenopsine A*) was obtained in a yield of 80% (Method D), bp 160°/0.05 mm Hg (kugelrohr); ir (neat): ν 3300 cm^{-1}; ^1H nmr (deuteriochloroform): 500 MHz, δ 0.85 (t, 3H, J = 7 Hz), 0.95-1.15 (m, 2H), 1.05 (d, 3H, J = 6 Hz), 1.20-1.45 (m, 22H), 1.55-1.80 (m, 2H), 2.00-2.10 (m, 1H), 2.80-2.90 (m, 1H), 3.05-3.15 (m, 1H); ^{13}C nmr (deuteriochloroform): 500 MHz, δ 14.1, 19.5, 21.1, 22.6, 26.4, 29.3, 29.6, 29.7, 30.6, 31.9, 32.8, 33.9, 45.8, 50.8.

Anal. Calcd. for $C_{17}H_{35}N$: C, 70.43; H, 12.51; N, 4.83. Found: C, 70.37; H, 12.42; N, 5.01.

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