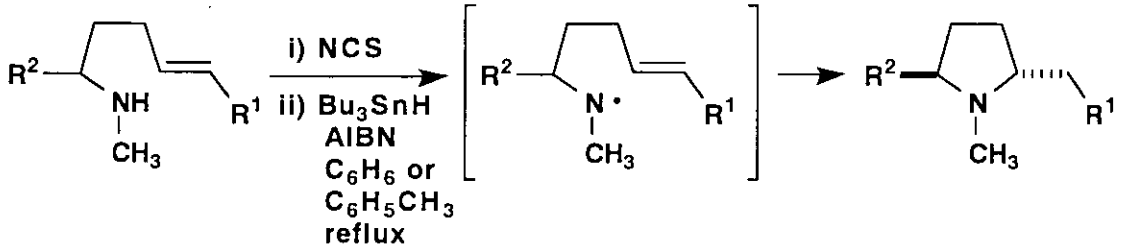
NEW STEREOSELECTIVE SYNTHESIS OF (±)-*trans*-2-BUTYL-5-HEPTYL-1-METHYLPYRROLIDINE, ANT VENOM ALKALOID, BY AMINYL RADICAL CYCLIZATION

Hisanori Senboku,* Hikaru Hasegawa, Kazuhiko Orito, and Masao Tokuda*

Laboratory of Organic Synthesis, Division of Molecular Chemistry,
Graduate School of Engineering, Hokkaido University, Sapporo 060-8628, Japan
E-Mail : senboku@- or tokuda@org-mc.eng.hokudai.ac.jp

Abstract - New synthesis of (±)-*trans*-2-butyl-5-heptyl-1-methylpyrrolidine (**1**), ant venom alkaloid, was achieved by the use of stereoselective cyclization of aminyl radicals. Thus, orthoester Claisen rearrangement of 1-hexen-3-ol (**2**) gave (*E*)-ethyl 4-octenoate (**3**). Reaction of ester (**3**) with 2-methylaminopyridine and $AlCl_3$ afforded the corresponding *N*-methyl-*N*-(2-pyridyl)amide (**4**), which was treated with heptylmagnesium iodide at -78°C to give (*E*)-4-pentadecen-8-one (**5**). Reductive amination of ketone (**5**) with methylamine gave *N*-methyl-1-heptyl-4-octenylamine (**6**). Treatment of amine (**6**) with NCS in toluene gave the corresponding *N*-chloroamine (**12**), and successive heating under reflux with Bu_3SnH and AIBN resulted in stereoselective cyclization of the aminyl radical to give (±)-*trans*-2-butyl-5-heptyl-1-methylpyrrolidine (**1**) in a 59 % yield. Similarly, 1-nonen-3-ol (**7**) was converted into *N*-methyl-1-butyl-4-undecenylamine (**11**), which was subjected to the aminyl radical cyclization to give **1** in a 49 % yield.

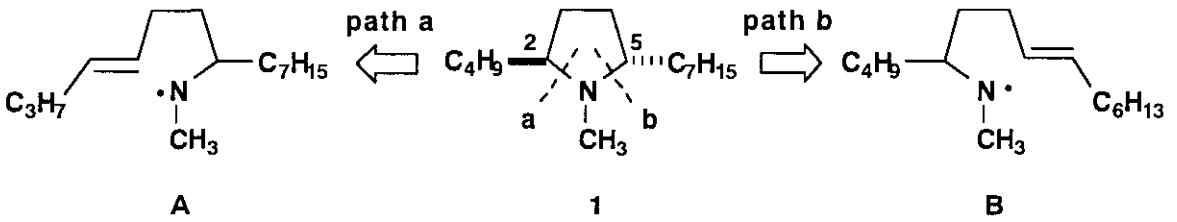
We previously reported a new stereoselective synthesis of *trans*-2,5-disubstituted pyrrolidines[1] and substituted pyrrolizidines[1,2] by cyclization of neutral aminyl radicals generated from *N*-chloroalk-4-enylamines and Bu_3SnH-AIBN in refluxing benzene[1] or in refluxing toluene[2] (Scheme 1).



Scheme 1

2,5-Disubstituted pyrrolidines are skeleton of some alkaloids and can be used as chemotherapeutic agents.[3] Actually, 2,5-disubstituted pyrrolidine alkaloids have recently been found in secretions of thief ants and fire

ants of the genera *Solenopsis, Monomorium*,[4] *Megalomyrmex*,[5] and have also been found in skin extracts of the poison frog *Dendrobates histrionicus*.[6] We selected (±)-*trans*-2-butyl-5-heptyl-1-methylpyrrolidine (**1**), isolated from *Monomorium latinode* in 1982,[7] as a synthetic target for an application of our stereoselective cyclization of aminyl radical. Here, we report the first stereoselective synthesis of (±)-*trans*-2-butyl-5-heptyl-1-methylpyrrolidine (**1**), ant venom alkaloid. Its synthesis has only been reported in one literature.[8] For a synthesis of pyrrolidine (**1**) by means of aminyl radical cyclization, two strategies were planned as outlined in Scheme 2. One is the C2-N bond formation (path a), and another method is C5-N bond formation (path b) of pyrrolidine (**1**) by aminyl radical cyclization.

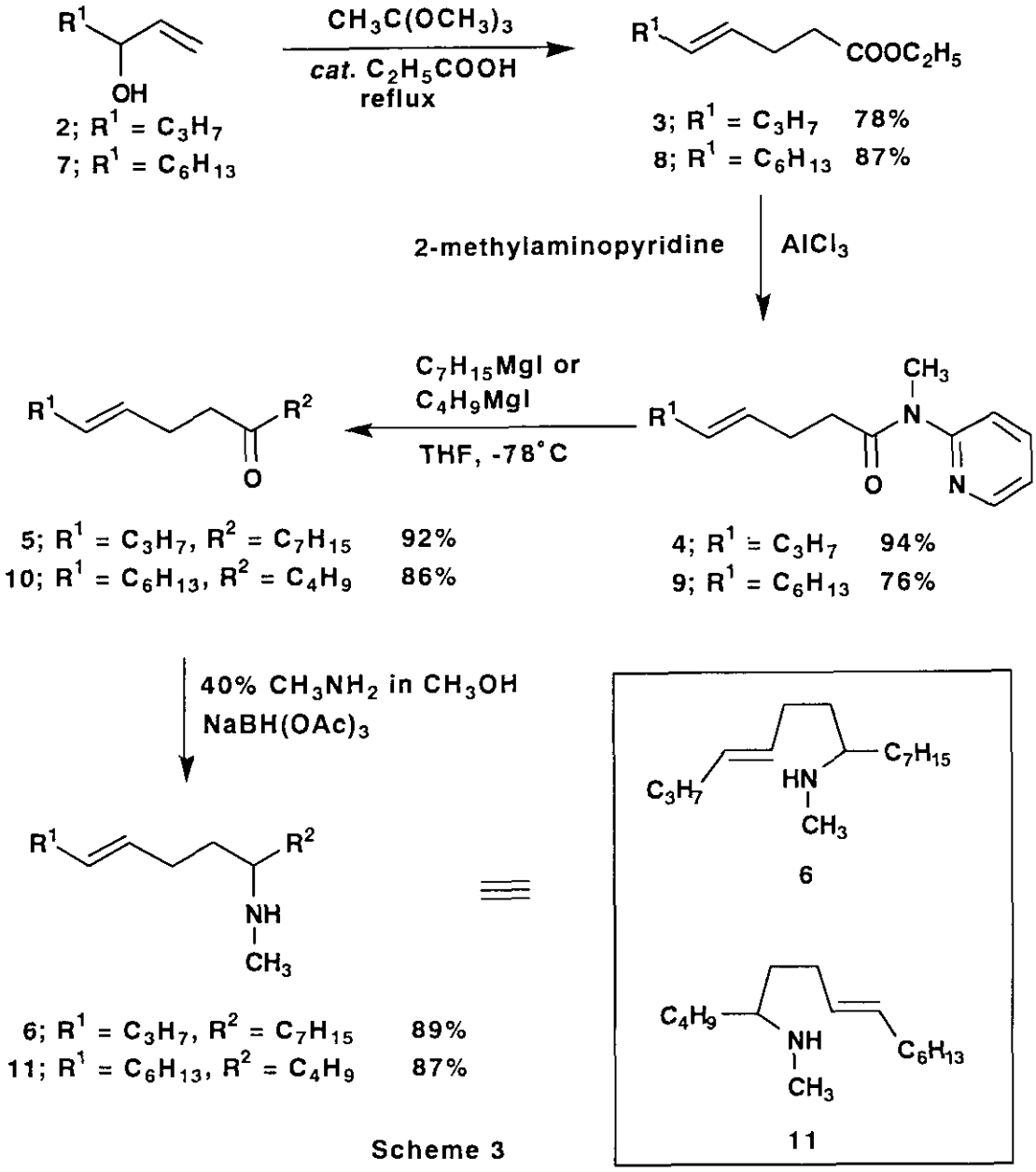


Scheme 2

Preparation of two different amines, the precursors of the corresponding aminyl radicals **A** and **B** leading to the pyrrolidine (**1**), was carried out according to Scheme 3. Starting amine (**6**) to generate the aminyl radical (**A**) was first prepared. Thus, 1-hexen-3-ol (**2**) was subjected to orthoester Claisen rearrangement according to our published method[9] and (*E*)-ethyl 4-octenoate (**3**) was obtained in a 78 % yield. Its geometry was confirmed to be exclusively (*E*) by ^{1}H NMR and capillary GLC analysis. Although various methods for transformation of ester into the corresponding ketone have been reported,[10] we selected the procedure of Meyers[11] to prepare ketone (**5**) from ester (**3**). Thus, ester (**3**) was converted into the corresponding *N*-methyl-*N*-(2-pyridyl)amide (**4**) in a 94 % yield by treatment of **3** with 2-methylaminopyridine and $AlCl_3$ in 1,2-dichloroethane.[12] *N*-(2-Pyridyl)amide (**4**) was treated with heptylmagnesium iodide in THF at -78°C, according to Meyers' procedure,[11] to give (*E*)-4-pentadecen-8-one (**5**) and recovered **4** in 92 and 6 % yields, respectively. Reductive amination of ketone (**5**) with methylamine and $NaBH(OAc)_3$ in 1,2-dichloroethane[13] followed by separation with preparative TLC (Al_2O_3) gave the amine (**6**) in a 89 % yield. Another amine (**11**) to generate the aminyl radical (**B**) was also prepared in a 49 % overall yield from 1-nonen-3-ol (**7**) by the same procedure (Scheme 3).

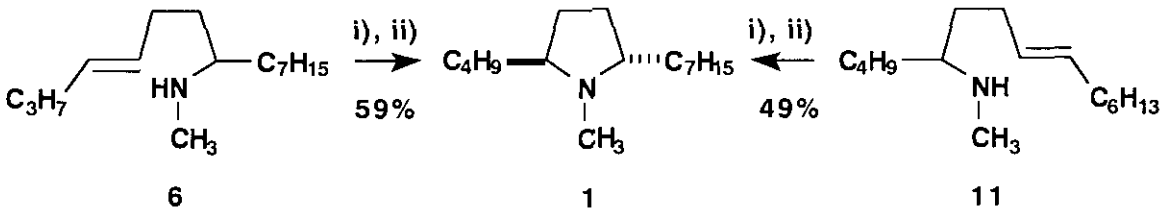
Stereoselective cyclization of aminyl radical for a synthesis of ant venom alkaloid (**1**) was carried out. A toluene solution of 4-alkenylamine (**6**) (0.02 M) was treated with *N*-chlorosuccinimide (NCS, 1.0 equiv.) for 30 min at room temperature to form the corresponding *N*-chloroamine quantitatively. Successive heating of the solution containing the *N*-chloroamine with Bu_3SnH (1.0 equiv.) and AIBN (0.2 equiv.) under reflux for 7 h resulted in stereoselective cyclization of the corresponding aminyl radical (**A**) to give (±)-*trans*-2-butyl-5-heptyl-1-methylpyrrolidine (**1**), ant venom alkaloid, in a 59 % yield as a single stereoisomer. *N*-Chloroamine (**12**) generated from amine (**6**) could be isolated by TLC (SiO_2) and was subjected to the radical reaction to give pyrrolidine (**1**) in an almost same yield. On the other hand, similar treatment of the amine (**11**) with NCS followed by the successive reaction with Bu_3SnH and AIBN also gave the ant venom alkaloid (**1**) stereoselectively in a 49 % yield *via* a cyclization of aminyl radical (**B**) (Scheme 4). The ^{1}H and

^{13}C NMR spectra of **1** were identical with those reported by Brossi[8] and the MS spectrum of **1** was also identical with that of previous report.[7]



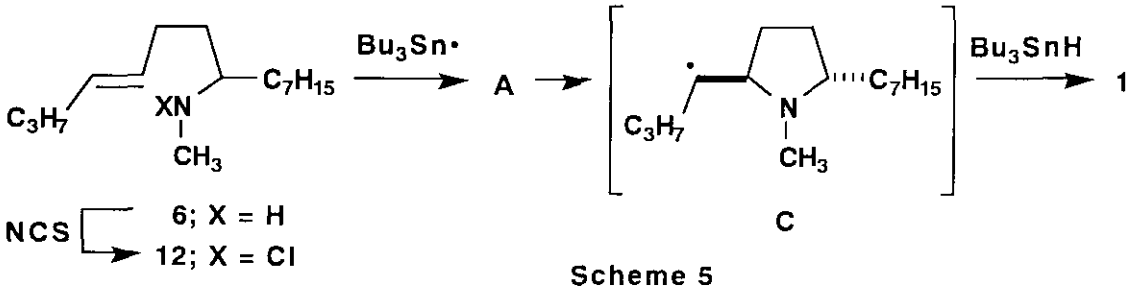
Scheme 3

Probable reaction pathways are shown in Scheme 5. Starting amine (**6**) is converted into the corresponding *N*-chloroamine (**12**) by the treatment with NCS in toluene. Chlorine abstraction from *N*-chloroamine (**12**) by $Bu_3Sn^{\bullet}$ generates the corresponding aminyl radical (**A**), which cyclizes stereoselectively to form the carbon radical intermediate having a *trans*-2,5-disubstituted pyrrolidine ring (**C**). Hydrogen abstraction of **C** from Bu_3SnH results in a cyclization product (**1**).



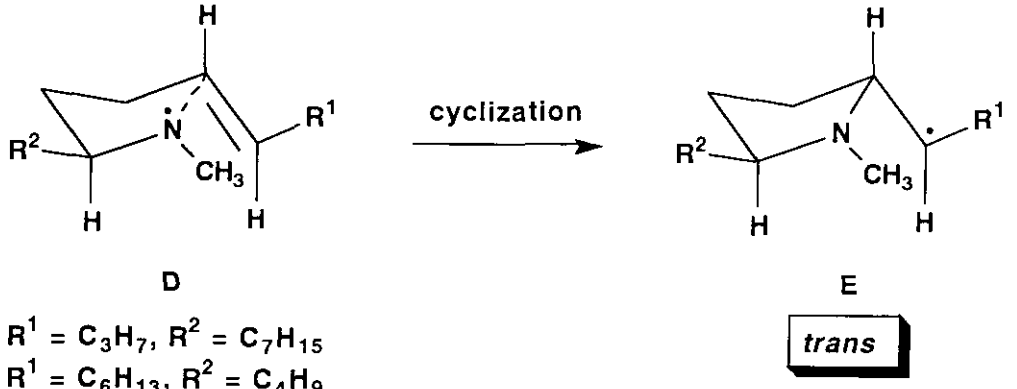
Reagents and Conditions; i) NCS (1.0 eq.) - toluene, rt, 30 min,
ii) Bu_3SnH (1.0 eq.), AIBN (0.2 eq.) - toluene, reflux, 7 h

Scheme 4



Scheme 5

Stereochemical outcome could be explained as outlined in Scheme 6. Aminyl radicals (**A**) or (**B**), generated from amine (**6**) or (**11**) respectively, probably have a transition structure of **D**, in which an alkyl group of R^2 is located in a pseudoequatrial position. Cyclization could take place *via* this stable 5-*exo*-chair-like transition structure (**D**) to give a carbon radical intermediate (**E**) having a *trans*-2,5-disubstituted pyrrolidine ring. This explanation is in good accordance with the theoretical calculation of the cyclization of 5-hexenyl radical.[14]



$R^1 = C_3H_7$, $R^2 = C_7H_{15}$
$R^1 = C_6H_{13}$, $R^2 = C_4H_9$

Scheme 6

In conclusion, synthesis of (±)-*trans*-2-butyl-5-heptyl-1-methylpyrrolidine (**1**), ant venom alkaloid, was achieved stereoselectively in a 35 % overall yield from 1-hexen-3-ol *via* 5 steps. Our study on a synthesis of various pyrrolidine alkaloids by using the aminyl radical cyclization as a key step is now in progress.

EXPERIMENTAL

IR spectra were determined in a neat form with a JASCO IR-810 infrared spectrophotometer. The ^1H and ^{13}C NMR spectra were determined in $CDCl_3$ ($SiMe_4$ as an internal reference) with a JEOL JNM EX-270 high-resolution spectrometer. The *J*-values are in Hz. The MS spectra were recorded using a JEOL JMS-DX303 or JMS-HX110 spectrometer (70 eV). Elemental analyses were performed by the staff of the analytical laboratory of the Faculty of Pharmaceutical Science. Preparative TLC was carried out with Merck Kiesel gel $60PF_{254}$ or Merck Alminium oxide $60PF_{254}$ (Type E).

Orthoester Claisen Rearrangement of Allyl Alcohols

(*E*)-Ethyl 4-Octenoate (3)

Commercially available 1-hexen-3-ol (**2**) (6.2 g, 61.6 mmol) in triethyl orthoacetate (80 mL) was heated with a catalytic amount of propionic acid (0.3 mL) at 130 °C for 3 h under an argon atmosphere. After excess triethyl orthoacetate was distilled off from the reaction mixture under a reduced pressure, the residue was distilled to give ester (**3**) (8.2 g, 78 %). bp 107 °C / 30 mmHg. ^1H NMR δ_H 0.87 (3H, t, *J*=7.3), 1.25 (3H, t, *J*=7.3), 1.35 (2H, sextet, *J*=7.3), 1.95 (2H, q, *J*=7.3), 2.2-2.4 (4H, m), 4.12 (2H, q, *J*=7.3), 5.3-5.5 (2H, m); ^{13}C NMR δ_C 13.60 (CH_3), 14.27 (CH_3), 22.55 (CH_2), 27.98 (CH_2), 34.47 (CH_2), 34.59 (CH_2), 60.23 (CH_2), 128.14 (CH), 131.61 (CH), 173.31 (C=O); IR 1740, 1372, 1249, 1165 cm^{-1}; MS (EI) *m/z* 170 (M^+, 18), 124 (63), 96 (64), 88 (89), 82 (100), 55 (70 %); HRMS Calcd for $C_{10}H_{18}O_2$ 170.1307. Found 170.1277.

(*E*)-Ethyl 4-Undecenoate (8)

Similar orthoester Claisen rearrangement of 1-nonen-3-ol (**7**) (11.0 g, 77.0 mmol), prepared in a 85 % yield from heptanal and vinylmagnesium bromide, with triethyl orthoacetate (99 mL) and propionic acid (0.3 mL) gave ester (**8**) (14.25 g, 87 %). bp 85 °C / 0.5 mmHg. ^1H NMR δ_H 0.88 (3H, t, *J*=7.3), 1.25 (3H, t, *J*=7.3), 1.2-1.4 (8H, m), 1.96 (2H, q, *J*=6.27), 2.2-2.4 (4H, m), 4.12 (2H, q, *J*=7.3), 5.3-5.5 (2H, m); ^{13}C NMR δ_C 14.07 (CH_3), 14.23 (CH_3), 22.61 (CH_2), 27.94 (CH_2), 28.77 (CH_2), 29.40 (CH_2), 31.72 (CH_2), 32.49 (CH_2), 34.43 (CH_2), 60.20 (CH_2), 127.89 (CH), 131.84 (CH), 173.28 (C=O); IR 1737, 1373, 1247 cm^{-1}; MS (EI) *m/z* 212 (M^+, 17), 166 (36), 149 (22), 124 (82), 96 (61), 88 (100 %); HRMS Calcd for $C_{13}H_{24}O_2$ 212.1776. Found 212.1769.

Transformation of Esters into N-*Methyl*-N-*2-(pyridyl)amides*

N-Methyl-*N*-(2-pyridyl)-4-octenamide (4)

To a stirred suspension of $AlCl_3$ (11.7 g, 88.0 mmol) in 1,2-dichloroethane (60 mL) was slowly added 2-methylaminopyridine (9.0 mL, 88.0 mmol) at 0 °C under an argon atmosphere. To this solution was added ester (**3**) (6.0 g, 35.2 mmol) at 0 °C. After the addition was completed, the reaction mixture was warmed up to rt and it was stirred at rt for 2 days. The reaction mixture was poured into ice-water (100 mL) and then extracted with CH_2Cl_2. The organic phase was washed with water and then dried over anhydrous $MgSO_4$. After evaporation of the solvent, the residue was distilled to give amide (**4**) (7.7 g, 94 %). bp 129-130 °C / 0.25 mmHg. ^1H NMR δ_H 0.85 (3H, t, *J*=7.3), 1.33 (2H, sextet, *J*=7.3), 1.8-2.0 (2H, m), 2.2-2.4 (4H, m), 3.37 (3H, s), 5.3-5.5 (2H, m), 7.20 (1H, ddd, *J*=1.0, 5.0, 7.3), 7.29 (1H, br d, *J*= 7.3), 7.75 (1H,

dt, *J*=2.0, 7.3) , 8.50 (1H, ddd, *J*= 1.0, 2.0, 5.0); ^{13}C NMR δ_C 13.59 (CH_3), 22.50 (CH_2), 28.30 (CH_2), 34.54 (CH_2), 34.93 (CH_2), 35.37 (CH_3), 120.70 (CH), 121.67(CH), 128.73 (CH), 131.14 (CH), 138.08 (CH), 148.91 (CH), 156.14 (C), 172.83 (C=O); IR 1665, 1587, 1472, 1436, 1379, 971 cm^{-1}; MS (EI) *m/z* 232 (M^+, 19), 203 (20), 189 (10), 161 (17), 150 (10), 108 (100 %); HRMS Calcd for $C_{14}H_{20}N_2O$ 232.1575. Found 232.1589. Anal. Calcd for $C_{14}H_{20}N_2O$: C, 72.38; H, 8.68; N, 12.06. Found: C, 72.28; H, 8.74; N, 12.07.

_N_-Methyl-_N_-(2-pyridyl)-4-undecenamide (9)

A similar reaction of ester (**8**) (5.0 g, 23.5 mmol) with 2-methylaminopyridine (4.8 mL, 47.0 mmol) and $AlCl_3$ (7.8 g, 58.8 mmol) in 1,2-dichloroethane (50 mL) gave, along with recovered ester (**8**) (600 mg, 12 %), amide (**9**) (4.9 g, 76 %; 85% based on reacted **8**). bp 150 °C / 0.1 mmHg. ^{1}H NMR δ_H 0.87 (3H, t, *J*=6.3), 1.2-1.4 (8H, m), 1.92 (2H, q, *J*=6.3), 2.3-2.4 (4H, m), 3.37 (3H, s), 5.3-5.5 (2H, m), 7.20 (1H, ddd, *J*=1.0, 5.0, 7.3), 7.29 (1H, br d, *J*=7.3), 7.75 (1H, dt, *J*=2.0, 7.3), 8.49 (1H, ddd, *J*=1.0, 2.0, 5.0); ^{13}C NMR δ_C 14.11 (CH_3), 22.62 (CH_2), 28.37 (CH_2), 28.82 (CH_2), 29.42 (CH_2), 31.73 (CH_2), 32.52 (CH_2), 35.02 (CH_2), 35.42 (CH_3), 120.75 (CH), 121.71 (CH), 128.57 (CH), 131.48 (CH), 138.11 (CH), 148.96 (CH), 156.19 (C), 172.88 (C=O); IR 1669, 1588, 1473-1379, 1135 cm^{-1}; MS (EI) *m/z* 274 (M^+, 8), 245 (4), 203 (12), 189 (7), 161 (13), 150 (11), 108 (100 %); HRMS Calcd for $C_{17}H_{26}N_2O$ 274.2045. Found 274.2059; Anal. Calcd for $C_{17}H_{26}N_2O$: C, 74.41; H, 9.55; N, 10.21. Found: C, 74.31; H, 9.66; N, 10.08.

Transformation of Amides into Ketones

4-Pentadecen-8-one (5)

To a stirred solution of amide (**4**) (710 mg, 3.1 mmol) in THF (10 mL) was added an etheral solution of heptylmagnesium iodide (3.6 mmol) at -78 °C under an argon atmosphere. After stirring for 3 h at -78 °C, 2N HCl (10 mL) was added to the reaction mixture at -78 °C and the solution was warmed up to rt. The reaction mixture was extracted with ether, and the etheral solution was washed with water and brine. After drying over anhydrous $MgSO_4$ followed by evaporation of the solvent, the residue was purified by TLC (SiO_2, hexane : AcOEt / 3 : 1) to afford, along with recovered amide (**4**) (42 mg, 6 %), ketone (**5**) (633 mg, 92 %; 98% based on reacted **4**). bp 87-90 °C / 0.15 mmHg; ^{1}H NMR δ_H 0.8-0.9 (6H, m), 1.2-1.4 (10H, m), 1.5-1.6 (2H, m), 1.9-2.0 (2H, m), 2.2-2.3 (2H, m), 2.38 (2H, t, *J*=7.3), 2.45 (2H, t, *J*=7.3), 5.3-5.5 (2H, m); ^{13}C NMR δ_C 13.64 (CH_3), 14.07 (CH_3), 22.59 (CH_2), 22.62 (CH_2), 23.85 (CH_2), 26.92 (CH_2), 29.09 (CH_2), 29.24 (CH_2), 31.70 (CH_2), 34.61 (CH_2), 42.66 (CH_2), 42.96 (CH_2), 128.59 (CH), 131.30 (CH), 211.01 (C=O); IR 1717 cm^{-1}; MS (EI) *m/z* 224 (M^+, 6), 181 (5), 140 (7), 127 (77), 109 (8), 97 (14), 82 (42), 57 (100 %); HRMS Calcd for $C_{15}H_{28}O$ 224.2140. Found 224.2138; Anal. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.08; H, 12.60.

8-Pentadecen-5-one (10)

Similar reaction of amide (**9**) (2.5 g, 9.1 mmol) with an etheral solution of butylmagnesium iodide (10.8 mmol) followed by TLC (SiO_2, hexane : AcOEt / 3 : 1) gave, along with recovered amide (**9**) (280 mg, 11 %), ketone (**10**) (1.8 g, 86 %; 96 % based on reacted **9**). ^{1}H NMR δ_H 0.8-0.9 (6H, m), 1.2-1.4 (10H, m), 1.5-1.6 (2H, m), 1.9-2.0 (2H, m), 2.2-2.3 (2H, m), 2.39 (2H, t, *J*=7.3), 2.45 (2H, t, *J*=7.3), 5.3-

5.5 (2H, m); ^{13}C NMR δ_C 13.87 (CH_3), 14.11 (CH_3), 22.39 (CH_2), 22.64 (CH_2), 25.93 (CH_2), 26.92 (CH_2), 28.82 (CH_2), 29.45 (CH_2), 31.75 (CH_2), 32.52 (CH_2), 42.66 (CH_2)x2, 128.34 (CH), 131.57 (CH), 210.96 (C=O); IR 1716 cm^{-1}; MS (EI) *m/z* 224 (M^+, 4), 182 (3), 167 (6), 139 (5), 124 (13), 113 (4), 96 (10), 85 (100), 57 (67 %); HRMS Calcd for $C_{15}H_{28}O$ 224.2140. Found 224.2134. Anal. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.37; H, 12.64.

Reductive Amination of Ketones

N-Methyl-1-heptyl-4-octenylamine (6)

To a solution of ketone (**5**) (500 mg, 2.2 mmol) and 40 % methanolic methylamine (0.4 mL, 3.3 mmol) in 1,2-dichloroethane (7 mL) were added AcOH (0.2 mL, 2.7 mmol) and $NaBH(OAc)_3$ (710 mg, 3.3 mmol). The mixture was stirred at rt under an argon atmosphere until the reactants were consumed as determined by TLC (for 36 h). The reaction mixture was quenched by 4N NaOH, and the product was extracted with ether. The organic phase was washed with water and brine, and dried over anhydrous $MgSO_4$. After evaporation of the solvent, the residue was purified by TLC (Al_2O_3, hexane : AcOEt / 30 : 1) to give amine (**6**) (474 mg, 89 %). ^{1}H NMR δ_H 0.88 (6H, br t, *J*=7.3), 1.2-1.5 (16H, m), 1.9-2.1 (4H, m), 2.37 (3H, s), 2.3-2.4 (1H, m), 5.3-5.5 (2H, m); ^{13}C NMR δ_C 13.64 (CH_3), 14.09 (CH_3), 22.66 (CH_2), 2, 25.63 (CH_2), 28.86 (CH_2), 29.31 (CH_2), 29.94 (CH_2), 31.86 (CH_2), 33.37 (CH_2), 33.44 (CH_2), 33.57 (CH_3), 34.68 (CH_2), 58.65 (CH), 130.26 (CH), 130.35 (CH); IR 3308, 1144, 1101, 967 cm^{-1}; MS (EI) *m/z* 239 (M^+, 3), 210 (4), 182 (3), 168 (3), 142 (100), 140 (87 %); HRMS Calcd for $C_{16}H_{33}N$ 239.2613. Found 239.2595.

N-Methyl-1-butyl-4-undecenylamine (11)

Amine (**11**) (154 mg, 67 %) was also obtained by a similar treatment of ketone (**10**) (215 mg, 1.0 mmol) with 40 % methylamine in MeOH (0.2 mL, 1.4 mmol), AcOH (0.1 mL, 1.4 mmol) and $NaBH(OAc)_3$ (410 mg, 1.9 mmol). ^{1}H NMR δ_H 0.8-1.0 (6H, m), 1.2-1.5 (16H, m), 1.9-2.1 (4H, m), 2.37 (3H, s), 2.3-2.4 (1H, m), 5.3-5.5 (2H, m); ^{13}C NMR δ_C 14.11 (CH_3×2), 22.64 (CH_2), 23.02 (CH_2), 27.84 (CH_2), 28.84 (CH_2×2), 29.56 (CH_2), 31.75 (CH_2), 32.58 (CH_2), 33.14 (CH_2), 33.39 (CH_2), 33.59 (CH_3), 58.64 (CH), 130.05 (CH), 130.62 (CH); IR 3294, 1458, 1144, 1099 cm^{-1}; MS (EI) *m/z* 239 (M^+, 1), 210 (1), 182 (64), 140 (10), 100 (100 %); HRMS Calcd for $C_{16}H_{33}N$ 239.2613. Found 239.2599.

Synthesis of trans-*2-Butyl-5-heptyl-1-methylpyrrolidine by Aminyl Radical Cyclization*

(i) from *N*-Methyl-1-heptyl-4-octenylamine (6)

To a toluene solution (16 mL, 0.02 M) of *N*-methyl-1-heptyl-4-octenylamine (**6**) (100 mg, 0.32 mmol) was added *N*-chlorosuccinimide (43 mg, 0.32 mmol), and the solution was stirred at rt for 30 min under an argon atmosphere. To this solution were added Bu_3SnH (0.086 mL, 0.32 mmol) and AIBN (11 mg, 0.064 mmol) and the reaction mixture was heated under reflux for 7 h under a nitrogen atmosphere. After evaporation of the solvent, ether (3 mL) and 10 % - KF aqueous solution (10 mL) were added and then stirred for a few hours. The precipitate was filtered off with celite and filtrate was extracted with ether. The organic phase was washed successively with water and brine, and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a residue, which was purified by TLC (Al_2O_3, hexane : AcOEt / 30 : 1) to give *trans*-2-butyl-5-heptyl-1-methylpyrrolidine (**1**) (59 mg, 59 %) as a single stereoisomer. ^{1}H NMR δ_H 0.8-1.0 (6H, m), 1.0-1.4 (16H, m), 1.4-1.5 (2H, m), 1.5-1.7 (2H, m), 1.8-2.0 (2H, m), 2.35 (3H, s),

2.7-2.8 (2H, m); ^{13}C NMR δ_C 14.12 (CH_3×2), 22.68 (CH_2), 23.05 (CH_2), 26.90 (CH_2), 28.68 (CH_2×2), 29.09 (CH_2), 29.34 (CH_2), 29.97 (CH_2), 30.19 (CH_2), 30.49 (CH_2), 31.86 (CH_2), 35.13 (CH_3), 63.43 (CH×2); MS (EI) *m/z* 240 [$(M+1)^+$, 2), 239 (M^+, 1), 238 (3), 208 (1), 182 (69), 141 (10), 140 (100), 96 (22), 84 (12), 83 916), 82 (30), 70 (12), 55 (17), 43 (22), 42 (18), 41 (29 %); HRMS Calcd for $C_{16}H_{33}N$ 239.2613. Found 239.2635.

(ii) from *N*-Methyl-1-butyl-4-undecenylamine (11)

Similar reaction of *N*-methyl-1-butyl-4-undecenylamine (**11**) (100 mg, 0.32 mmol) with *N*-chlorosuccinimide (43 mg, 0.32 mmol) followed by the reaction with Bu_3SnH (0.086 mL, 0.32 mmol) and AIBN (11 mg, 0.064 mmol) gave ant venom alkaloid (**1**) (49 mg, 49 %).

REFERENCES

1. M. Tokuda, H. Fujita, and H. Suginome, *J. Chem. Soc., Perkin Trans. 1.*, 1994, 777.
2. Y. Kajizuka, H. Senboku, H. Fujita, K. Orito, and M. Tokuda, *Book of Abstracts in 28th Congress of Heterocyclic Chemistry*, Shizuoka, Japan, 1997, 34.
3. M. Pichon and B. Figadère, *Tetrahedron Asymmetry*, 1996, **7**, 927.
4. G. Massiot and C. Delaude, 'Pyrrolidine Alkaloids' in *The Alkaloids*, Vol. 27, ed. by A. Brossi, Academic Press Inc, Orland, 1986, pp. 269-322.
5. T. H. Jones, M. S. Blum, H. M. Fales, C. R. F. Brandão, and J. Lattke, *J. Chem. Ecol.*, 1991, **17**, 1897.
6. J. W. Daly, T. F. Spande, N. Whittaker, R. J. Hight, D. Feigl, N. Nishimori, T. Tokuyama, and C. W. Myers, *J. Nat. Prod.*, 1986, **49**, 265.
7. T. H. Jones, M. S. Blum, and H. M. Fales, *Tetrahedron*, 1982, **38**, 1949.
8. W. Gessner, T. Takahashi, and A. Brossi, *Helv. Chim. Acta*, 1987, **70**, 2003.
9. H. Kaga, K. Goto, T. Takahashi, M. Hino, T. Tokuhashi, and K. Orito, *Tetrahedron*, 1996, **52**, 8451.
10. Transformation of ester into ketone (a) directly; F. Huet, G. Emptoz, and A. Jubier, *Tetrahedron*, 1973, **29**, 479; I. Kikkawa and T. Yorifuji, *Synthesis*, 1980, 877; (b) *via* thioester; T. Mukaiyama, M. Araki, and H. Takei, *J. Am. Chem. Soc.*, 1973, **95**, 4763; (c) *via* amide; S. Nahm and S. M. Weinreb, *Tetrahedron Lett.*, 1981, **22**, 3815; (d) *via* carboxylic acid; M. J. Jorgenson, *Org. React.*, 1970, **18**, 1, and references cited therein.
11. A. I. Meyers and D. L. Comins, *Tetrahedron Lett.*, 1978, 5179.
12. P. Lesimple and D. C. H. Bigg, *Synthesis*, 1991, 306.
13. A. F. Abdel-Magid, K. G. Carson, B. D. Harris, C. A. Maryanoff, and R. D. Shaf, *J. Org. Chem.*, 1996, **61**, 3849.
14. D. C. Spellmeyer and K. N. Houk, *J. Org. Chem.*, 1987, **52**, 959, and references cited therein.

Received, 6th July, 1998