Tetrahedron Vol. 49, No. 48, pp. 11205-11212, 1993
Printed in Great Britain

0040-4020/93 $6.00+.00

A SHORT, PRACTICAL SYNTHESIS OF THE ANT VENOM ALKALOID, THREE (3*R*,5*S*,8a*S*)-3-ALKYL-5-METHYLINDOLIZIDINES[1]

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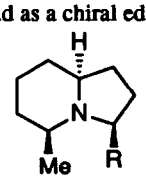
(*Received in Japan* 13 *September* 1993)

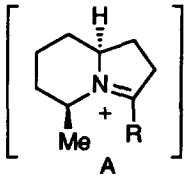
Abstract: A short, practical and diastereoselective method for preparing the ant venom alkaloid, three (3*R*,5*S*,8a*S*)-3-alkyl-5-methylindolizidines (**1-3**), has been developed. The stereoselective intramolecular amidomercuration of the *N*-alkenylurethane **4** followed by oxidative demercuration provides the piperidine alcohol *cis*-**6** as a major product. Thereafter, oxidation of *cis*-**6** followed by the Horner-Emmons elongation of the ring appendages affords the enones **8**, **10**, and **11**, which are stereoselectively converted into **1**, **2**, and **3**, respectively, by catalytic hydrogenation.

Indolizidine alkaloids offer attractive targets for synthesis because of their unique structures and intriguing biological activities.[2] Three are found in ant venom: (+)-monomorine I (**1**), with a trail-following activity and isolated from *Monomorium pharaonis*,[3] 5-ethyl-3-methylindolizidine (**2**), produced by *Solenopsis* (*Diplorhoptrum*) *conjurata*,[4] and 5-hexyl-3-methylindolizidine (**3**), derived from *Solenopsis* (*Diplorhoptrum*) species AA.[4] With respect to monomorine I, both the determination of its absolute configuration[5] and the asymmetric synthesis[6] have been reported. However, the absolute configuration of two indolizidines **2** and **3** remain unknown due to their poor supply from natural sources. Additionally, their chiral synthesis has never been performed to date. So far, the synthesis of **1** has been reported several times since 1988[5] in its scalemic form,[7] but most of the syntheses reported are those by relatively multi-step procedures. Accordingly, we were stimulated to the development of a comprehensive synthetic program for these alkaloids. Our interest in this field has been focused on the synthetic utilization of electrophile-induced olefin heterocyclization,[8] as employed for the stereoselective construction of nitrogen and oxygen heterocycles leading to natural products.[9] In this paper, we disclose a short, practical synthesis of **1-3** *via* the 2,6-*cis*-disubstituted piperidine, a common building block prepared by stereoselective intramolecular amidomercuration of a homochiral *N*-alkenylurethane available from an α–amino acid as a chiral educt.



1 R= $(CH_2)_3CH_3$
2 R= CH_2CH_3
3 R= $(CH_2)_5CH_3$

Our tactics for construction of an indolizidine (**1-3**) having the 3*R*,5*S*,8a*S* configuration involves two critical steps ((1) **4** → **6**; (2) **8**, **10**, and **11** → **1**, **2**, and **3**). The elaboration of the *cis* arrangement of the C5 and C8a hydrogens is assumed on the basis of the protocol developed for the synthesis of (-)-pinidine,[10] where the thermodynamically controlled intramolecular amidomercuration[11] of an α-alkylated 5-hexenylcarbamate has effected the purpose. The stereoselective construction of the bicyclic skeleton is presumed to be performed *via* catalytic hydrogenation, with its least hindered side (α) attacked, of the iminium intermediate A from debenzyloxycarbonylation and subsequent intramolecular carbonyl condensation.

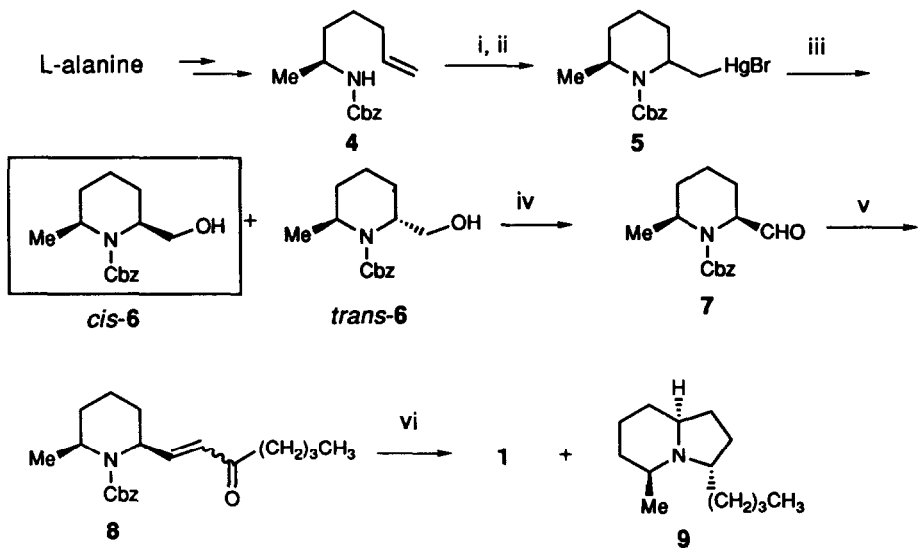


A

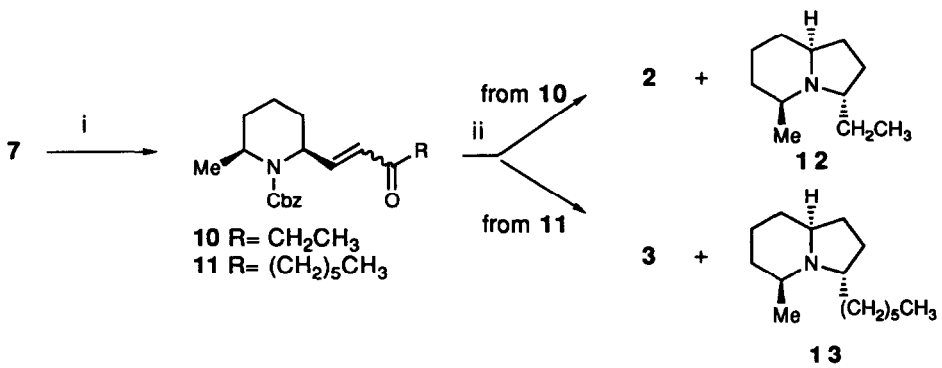
Although the occurrence of *cis*- and *trans*-2,6-disubstituted piperidines in ants is well known, there have been no reports of that of *cis*-2,5-dialkylpyrrolidines.[12] Consideration of the stereochemistry of the indolizidines **1-3** suggests that, in the biogenetic cyclization forming an indolizidine skeleton, the six-membered ring may be first formed and followed by formation of its fused five-membered ring. Accordingly, it is considered that our protocol starting from a *cis*-disubstituted piperidine would be a biomimetic model.[4,13]

Our synthesis of **1** began with the intramolecular amidomercuration of (*S*)-*N*-(benzyloxycarbonyl)-1-methyl-5-hexenylamine (**4**)[10], readily available from L-alanine (Scheme 1). The unsaturated carbamate **4** underwent the cyclization induced by mercuric trifluoroacetate in nitromethane followed by treatment with sodium bromide to afford the organomercurial bromide **5**, which was oxidatively demercurated[14] to provide a 5.6:1 (*cis*:*trans*) mixture of diastereomeric 2,6-disubstituted piperidines **6**. The pure *cis*-diastereomer (*cis*-**6**) was isolated by chromatography in 53% yield from **4**. The Swern oxidation of *cis*-**6** gave the aldehyde **7**, which on subsequent Horner-Emmons reaction with dimethyl (2-oxohexyl)phosphonate provided the α,β-unsaturated ketone **8** (*E*:*Z*= 8:1) in 77% overall yield from *cis*-**6**. Exposure of **8** to an atmosphere of hydrogen in the presence of palladium hydroxide as a catalyst in methanol caused simultaneous reduction of its double bond, debenzyloxycarbonylation, annulative imination, and reduction of the resulting iminium intermediate to give stereoselectively the desired indolizidine monomorine I (**1**) ($[\alpha]_D^{24}$ +34.0° (*c* 0.975, hexane) lit.[6] $[\alpha]_D^{24}$ +34.2° (c 1.02, hexane)) (59%) along with its C3-epimer, indolizidine 195B (**9**), isolated from *Dendrobates histrionicus*[15] (17%). Spectral data (^{1}H and ^{13}C NMR) for **1** and **9** were completely identical with those reported.[6,16]

Having obtained these results, we next undertook the synthesis of **2** and **3** (Scheme 2). Our synthesis of **2** and **3** was initiated with the Horner-Emmons reaction of the aldehyde **7** with dimethyl (2-oxobutyl)phosphonate and dimethyl (2-oxooctyl)phosphonate, respectively. This time the elongation of the ring appendage was performed according to the Masamune-Roush procedure to afford the α,β-unsaturated ketones **10** and **11** in 73 and 86% yields from cis-**6**, respectively. Construction of the bicyclic ring from **10** by catalytic hydrogenation provided the desired indolizidine **2** ($[\alpha]_D^{24}$ +65.1° (*c* 1.99, hexane) along with its C3-epimer **12** in 76% and 8% yields, respectively. A similar procedure for **11** gave **3** {$[\alpha]_D^{24}$ +27.9° (*c* 1.335, hexane)} and its C3-epimer **13**, in 82% and 12% yields, respectively. Spectral data (^{1}H and ^{13}C NMR) for both **2** and **3** were in agreement with those reported.[4]



Scheme 1 *Reagents* i, $Hg(OCOCF_3)_2$, CH_3NO_2; ii, NaBr, $NaHCO_3$; iii, O_2, $NaBH_4$, DMF; iv, $(COCl)_2$, DMSO, Et_3N; v, $(H_3CO)_2POCH_2CO(CH_2)_3CH_3$, NaH, THF; vi, H_2, $Pd(OH)_2$, MeOH



Scheme 2 *Reagents* i, $(H_3CO)_2POCH_2COCH_2CH_3$ for **10** or $(H_3CO)_2POCH_2CO(CH_2)_5CH_3$ for**11**, LiCl/*i*-Pr_2NEt; ii, H_2, $Pd(OH)_2$, MeOH

In summary, starting from the homochiral *N*-alkenylurethane **4**, available from L-alanine, three 3-alkyl-5-methylindolizidines **1-3** found in ant venom were stereoselectively prepared *via* the biogenetic cyclization using the common precursor *cis*-**6**. Further application of our procedure to the preparation of other scare, chiral pyrrolizidines and indolizidines are under study, and the results will be described in due course.

EXPERIMENTAL

Microanalyses were performed by Microanalysis Center of Toyama Medical & Pharmaceutical University. Infrared spectra (IR) were measured with a JASCO A 102 spectrophotometer or Perkin-Elmer 1600 series FTIR spectrophotometer. Proton magnetic resonance (^{1}H NMR) spectra were recorded either at 60 MHz on a JEOL PMX-60 instrument or at 270 MHz on a JEOL-FX270 instrument with tetramethylsilane as an internal standard. Carbon-13 NMR spectra were determined on a Varian XL-200 or a JEOL-FX270 instrument with tetramethylsilane as an internal standard unless otherwise specified. Mass spectra (MS) and high resolution mass spectra (HRMS) were measured on a JEOL JMS D-200 spectrometer. Optical rotations were measured on a JASCO DIP-140 instrument. Column chromatography was performed on silica gel (Fuji-Davision BW-200 or Merck 60 (No 9385) with a medium pressure apparatus and a mixture of ethyl acetate/hexane was used as eluant unless otherwise specified. The extracts were dried over Na_2SO_4 unless otherwise specified.

(2*R*,6*S*)-1-Benzyloxycarbonyl-2-hydroxymethyl-6-methylpiperidine [*trans*-(6)] and (2*S*,6*S*)-1-Benzyloxycarbonyl-2-hydroxymethyl-6-methylpiperidine [*cis*-(6)] . To a solution of **4** (667 mg, 2.70 mmol) in CH_3NO_2 (46 mL) was added mercuric trifluoroacetate (1.73g, 4.05 mmol) and the reaction mixture was stirred for 20 h at room temperature. Saturated $NaHCO_3$ was added to the mixture with ice-cooling. After 30 min of stirring, saturated KBr (20 mL) was added to the mixture. After 2 h of stirring, organic layer was separated. The aqueous layer was extracted with ethyl acetate three times. The combined organic layers were washed with brine and dried. After evaporation, the resulting residue was purified by column chromatography to yield the organomercurial bromide **5** (1.39 g, 98%) as an oil. Oxygen (O_2) was bubbled into a suspension of $NaBH_4$ (153 mg, 4.05 mmol) in DMF (36 mL) for 1 h, and to this was added dropwise a solution of 5 in DMF (120 mL) over 3 h with continuous introduction of O_2. The bubbling of O_2 into the mixture was continued for 1 h, and ether was added. The reaction mixture was filtered through Celite, and the filtrate was evaporated *in vacuo*. The residue was chromatographed to yield *trans*-**6** (75.3 mg, 10.6%) and *cis*-**6** (419 mg, 59%).

trans-**6**: $[\alpha]_D^{26}$ +34.7° (*c* 1.23, MeOH); IR (neat) 3432, 1678, 1586, 1498, 1268 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.22 (3 H, t, *J*= 6.8 Hz), 1.49-1.88 (6 H, m), 3.42 (1 H, br s), 3.66-3.81 (3 H, m), 4.30 (1 H, m), 5.10, 5.16 (each 1 H, ABq, *J*= 12.4 Hz), 7.35 (5 H, m). Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.42; H, 8.04; N, 5.32. Found: C, 68.61; H, 8.22; N, 5.33.

cis-**6**: $[\alpha]_D^{26}$ +13.5° (*c* 1.25, MeOH); IR (neat) 3400, 2830, 1760-1580(br) cm^{-1};^{1}H NMR ($CDCl_3$) δ 1.16 (3 H, d, *J*= 7.1 Hz), 1.45-1.87 (6 H, m), 2.54 (1 H, br s), 363 (2 H, dd, *J*= 12.9, 5.6 Hz), 4.29-4.40 (1 H, m), 5.13, 5.17 (each 1 H, ABq, *J*= 12.4 Hz), 7.35 (5 H, m). Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.42; H, 8.04; N, 5.32. Found: C, 68.25; H, 8.18; N, 5.60.

(2*S*,6*S*)-1-Benzyloxycarbonyl-2-(3-oxo-1-heptenyl)-6-methylpiperidine (8). To a solution of oxalyl chloride (1.49 μL, 1.71 mmol) in CH_2Cl_2 (1. 5 mL) was added dropwise a mixture of DMSO (1.62 μL, 2.28 mmol) in CH_2Cl_2 (1.5 mL) of - 78 °C. After being stirred at the same temperature, a solution of *cis*-**6** (300 mg, 1.14 mmol) in CH_2Cl_2 (6 mL) was added to the mixture. After being stirred for 30 min, triethylamine (715 μL, 5.13 mmol) was added to the mixture. The resulting mixture was stirred for 3 h, and then quenched with 20% $KHSO_3$. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The

combined organic layers were successively washed with saturated $NaHCO_3$ and brine, dried, and evaporated to leave a crude product (**7**) as an oil. To a suspension of sodium hydride (68 mg, 1.71 mmol) in THF (2.4 mL) was added dimethyl (2-oxohexyl)phosphonate (315 mL, 1.71 mmol) over 5 min at 0 °C. After being stirred for 10 min, a solution of **7** (298 mg, 1.14 mmol) in THF (1 mL) was added to the mixture, and the whole mixture was stirred for 1.5 h at 0 °C Saturated NH_4Cl was added to the reaction mixture . After separation of organic layer, the aqueous phase was extracted with ether three times. The organic layer and extracts were combined, washed with brine, dried, and evaporated to give an oil, which was chromatographed to afford **8** (303 mg, 77%) (*E*:*Z*=8:1) as an oil. (*E*)-**8**: $[\alpha]_D^{24}$ - 54.5° (*c* 1.405, $CHCl_3$); IR (neat) 1694, 1628 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (3 H, t, *J*= 7.3 Hz), 1.16 (3 H, d, *J*= 6.9 Hz), 1.45-1.98 (10 H, m), 2.49 (2 H, t, *J*= 7.4 Hz), 4.45 (1 H, m), 4.93 (1 H, m), 5.16 (2 H, m), 6.13 (1 H, dd, *J*= 16.1, 2.0 Hz), 6.81 (1 H, dd, *J*= 16.1, 5.1 Hz), 7.35 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 13.88, 14.46, 20.50, 22.40 26.26 27.93, 29.92, 40.40, 46.62, 50.71, 67.270, 127.97, 128.86, 129.59, 136.76, 147.01, 155.68, 200.48; HRMS calcd for $C_{21}H_{29}NO_3$: 343.2145. found: 343.2104.

(3*R*,5*S*,9*S*)-3-Butyl-5-methylindolizidine (Monomorine I, 1) and (3*S*,5*S*,9*S*)-3-Butyl-5-methylindolizidine (Indolizidine 195B, 9). A suspension of **8** (303 mg, 0.882 mmol) and palladium hydroxide (30 mg) in methanol (8 mL) was stirred under a hydrogen atmosphere for 20 h. The insoluble materials were removed by filtration, and the filtrate was evaporated to give a residue, which was fractionated by chromatography on basic alumina using a mixture of n-hexane and $CHCl_3$ (1:3) as eluant to afford **1** (102 mg, 59%) and **9** (30 mg, 17%) as oils.

1: $[\alpha]_D^{24}$ + 34.0° (*c* 0.975, n-hexane); lit.[6] $[\alpha]_D^{24}$ + 34.2° (*c* 1.02, n-hexane); IR (neat) 2958, 2957, 2859, 1654, 1560, 1508, 1458, 1478 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (3 H, t, *J*= 6.8 Hz), 1.12-1.95 (16 H, m, containing 1.13 (3 H, d, *J*= 6.3 Hz)), 2.07 (1 H, br s), 2.21 (1 H, br s), 2.47 (1 H, br s), 3.26 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 22.92, 24.94, 29.40, 29.78, 30.35, 30.93, 35.85, 37.12, 60.30, 62.95, 67.21; HRMS calcd for $C_{13}H_{25}N$: 195.1987. found: 195.2008. Anal. Calcd for $C_{13}H_{25}N$: C, 79.93; H, 12.90; N, 7.17. Found: C, 80.33; H, 12.65; N, 7.25.

9: $[\alpha]_D^{24}$ + 87.6° (*c* 0.39, MeOH), lit. [16] $[\alpha]_D^{24}$ + 98.0° (*c* 0.39, MeOH); IR (neat) 2959, 2926, 2869, 2856, 2787, 1654, 1458, 1375, 1132, 1052 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (3 H, t, *J*= 6.9 Hz), 0.98-1.99 (16 H, m, containing 3 H, d, *J*= 6.1 Hz), 2.38 (1 H, m), 2.52 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 14.20, 20.39, 23.01, 24.71, 24.97, 26.32, 29.14, 29.98, 32.28, 34.44, 52.09, 58.92, 59.00. HRMS calcd for $C_{13}H_{25}N$: 195.1987. found: 195.2008.

(2*S*,6*S*)-1-Benzyloxycarbonyl-2-(3-oxo-1-pentenyl)-6-methylpiperidine (10). According to the procedure described for **8**, treatment of **4** (321 mg, 1.22 mmol) with oxalyl chloride (213 μL, 2.44 mmol), DMSO (260 μL, 3.67 mmol), and triethylamine (767 μL, 5.50 mmol) in CH_2Cl_2 (7 mL) gave the crude aldehyde **5**. To a stirred suspension of LiCl (62 mg, 1.47 mmol) in CH_3CN (5 mL) at room temperature were added dimethyl (2-oxobutyl)phosphonate (330 mg, 1.83 mmol), *N*,*N*-diisopropylethylamine (212 μL, 1.47 mmol), and finally a solution of the aldehyde **5** (318 mg, 1.22 mmol) in CH_3CN (1.5 mL). The reaction mixture was stirred for 8 h at room temperature. Saturated NH_4Cl was added to the mixture, and the solvent was removed under reduced pressure. The residue was extracted with ether. The extracts were combined, washed with brine, dried, and evaporated to leave an oil, which was chromatographed to yield **10** (83 mg, 73%)

(*E*:*Z*=8:1) as an oil. (*E*)-**10**; $[\alpha]_D^{24}$ - 72.8° (*c* 2.32, $CHCl_3$); IR (neat) 1694, 1628 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (3 H, t, *J*= 7.1 Hz), 1.16 (3H, d, *J*= 7.3 Hz), 1.45-1.96 (6 H, m), 2.55 (2 H, q, *J*= 7.3 Hz), 4.47 (1 H, m), 4.93 (1 H, m), 5.16 (2 H, m), 6.15 (1 H, d, *J*= 16.3 Hz), 6.82 (1 H, dd, *J*= 16.3, 5.1 Hz), 7.39 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 7.98, 14.43, 20.50, 27.90, 29.89, 33.78, 46.62, 50.68, 67.24, 127.94, 128.03, 128.52, 129.30, 136.73, 146.95; HRMS calcd for $C_{19}H_{25}NO_3$; 315.1835. found: 315.1836.

(2*S*,6*S*)-1-Benzyloxycarbonyl-2-(3-oxo-1-nonenyl)-6-methylpiperidine (11). According to the procedure described for **8**, treatment of **4** (293 mg, 1.13 mmol) with oxalyl chloride (194 μL, 2.23 mmol), DMSO (237 μL, 3.34 mmol), and triethylamine (698 μL, 5.01 mmol) in CH_2Cl_2 (7 mL) gave the crude aldehyde **5**. In a similar procedure described for **10**, **5** (1.13 mmol) in CH_3 CN (1.3 mL) was treated dimethyl (2-oxooctyl)phosphonate (349 μL, 1.67 mmol), *N*,*N*-diisopropylethylamine (194 μL, 1.34 mmol), and LiCl (57 mg, 1.34 mmol) in CH_3CN (5 mL) to give **11** (357 mg, 86%) (*E*:*Z*=8:1) as an oil. (*E*)-**11**; $[\alpha]_D^{24}$ - 54.5° (*c* 1.405, $CHCl_3$); IR (neat) 1694, 1628 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (3 H, t, *J*= 65 Hz), 1.16 (3 H, d, *J*= 7.1 Hz), 1.20-1.38 (6 H, m), 1.41-1.95 (8 H, m), 2.49 (2 H, t, *J*= 7.4 Hz), 4.45 (1 H, m), 4.93 (1 H, br s), 5.16 (2 H, m), 6.13 (1 H, dd, *J*= 16.1, 1.8 Hz), 6.80 (1 H, dd, *J*= 16.1, 5.1 Hz), 7.35 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 14.02, 14.43, 20.50, 22.49, 24.10, 27.90, 28.94, 29.89, 31.62, 40.72, 46.62, 50.68, 67.24, 127.94, 128.03, 128.52, 129.59, 147.01, 200.74; HRMS calcd for $C_{23}H_{33}NO_3$: 371.2459. found: 371.2459.

(3*R*,5*S*,9*S*)-3-Ethyl-5-methylindolizidine (2) and (3*S*,5*S*,9*S*)-3-Ethyl-5-methylindolizidine (12). According to the procedure described for **1** and **9**, treatment of **10** (230 mg, 0.729 mmol) with $Pd(OH)_2$ (23 mg) in MeOH (5 mL) provided **2** (93 mg, 76%) and **12** (9 mg, 7.5%) as oils.

2: $[\alpha]_D^{24}$ + 65.1° (*c* 1.99, n-hexane); IR (neat) 2959, 2930, 1718, 1654, 1560 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (3 H, t, *J*= 5 Hz), 1.04-1.91 (12 H, m, containing 1.12 (3 H, d, *J*= 6.4 Hz)), 2.08 (1 H, m), 2.21 (1 H, m), 2.41 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 11.14, 22.87, 24.94, 29.23, 30.32, 30.96, 32.37, 35.88, 60.19, 64.51, 67.27. HRMS calcd for $C_{11}H_{21}N$: 167.1672. found: 167.1652. Anal. Calcd for $C_{11}H_{21}N$: C, 78.97; H, 12.65; N, 8.37. Found: C, 78.65; H, 12.98; N, 8.02.

12: $[\alpha]_D^{24}$ + 60.3° (*c* 1.025, $CHCl_3$); IR (neat) 2961, 2927, 1718, 1654, 1560 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (3 H, t, *J*= 6.7 Hz), 0.92-1.96 (12 H, m, containing 1.11 (3 H, d, *J*= 6.4 Hz)), 2.49 (1 H, m), 2.53 (1 H, m), 3.28 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 9.99, 19.24, 23.61, 24.62, 28.68, 28.85, 31.07, 33.29, 51.14, 57.97, 59.67. HRMS calcd for $C_{11}H_{21}N$: 167.1672. found: 167.1712. $C_{11}H_{21}N$: C, 78.97; H, 12.65; N, 8.37. Found: C, 78.57; H, 12.89; N, 8.14.

(3*R*,5*S*,9*S*)-3-Hexyl-5-methylindolizidine (3) and (3*S*,5*S*,9*S*)-3-Hexyl-5-methylindolizidine (13). In a similar procedure described for **1** and **9**, **11** (234 mg, 0.63 mmol) was treated with $Pd(OH)_2$ (24 mg) in MeOH (6 mL) to give **3** (115 mg, 82%) and **13** (17 mg, 12%) as oils.

3: $[\alpha]_D^{24}$ + 27.9° (*c* 1.355, n-hexane); IR (neat) 2926, 2857, 1654, 1458 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (3 H, t, *J*= 6.8 Hz), 0.97-1.95 (20 H, m, containing 1.13 (3 H, d, *J*= 6.3 Hz)), 2.07 (1 H, m), 2.21 (1 H, m), 2.49 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 14.14, 22.66, 22.84, 24.91, 27.18, 29.55, 29.78, 30.32, 30.87, 31.96, 35.82, 39.94, 60.34, 63.07, 67.33. HRMS calcd for $C_{15}H_{29}N$: 223.2298. found: 223.2287.

13: $[\alpha]_D^{24}$ + 90.1° (*c* 0.285, MeOH); IR (neat) 2926, 2364, 2344, 1654, 1560, 1542, 1508, 1458 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (3 H, t, *J*= 6.5 Hz), 0.95-198 (20 H, m, counting 1.11 (3 H, d, *J*= 6.4 Hz)), 2.38 (1 H,

m), 2.53 (1 H, m), 3.28 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 14.11, 20.33, 22.66, 24.68, 25.28, 26.29, 26.87, 29.63, 29.92, 31.96, 32.17, 34.35, 52.18, 58.89, 59.06;.HRMS calcd for $C_{15}H_{29}N$: 223.2298. found: 223.2277.

ACKNOWLEDGMENT.

This work was partially supported by a research grant from Toyama First Bank Foundation for which we are grateful.

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