HETEROCYCLES, Vol. 57, No. 12, 2002, pp. 2279 – 2297, Received, 26th August, 2002

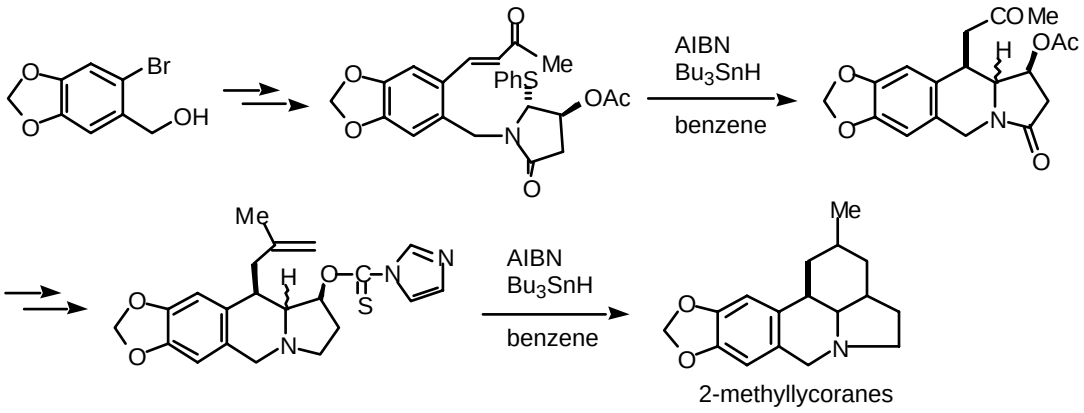
SYNTHESIS OF OPTICALLY ACTIVE 2-ACETOXY-3-ALKYLIDENE-α-LYCORANES FOR A SYNTHETIC APPROACH TOWARD (+)-LYCORINE BY RADICAL REACTION

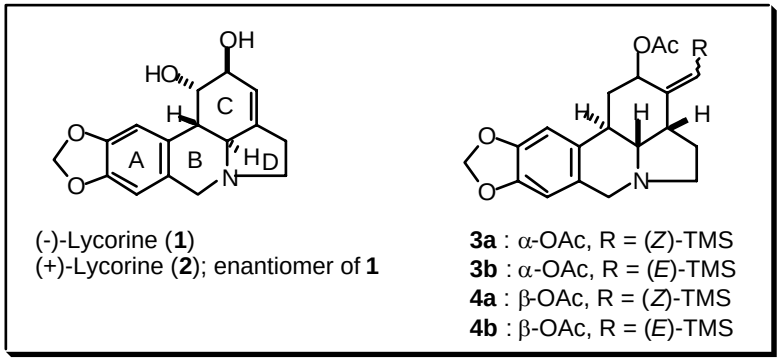
Miyuki Ishizaki,* Yuichiro Kai, and Osamu Hoshino*

Faculty of Pharmaceutical Sciences, Tokyo University of Science, 12, Ichigaya Funagawara-machi, Shinjuku-ku, Tokyo 162-0826, Japan

Abstract – A radical-mediated synthesis of optically active 2α- and 2β-trimethylsilylmethyene-α-lycoranes (**3**,**4**), which are key intermediates for synthesis of (+)-lycorine (**2**), is described. Thus, both B and C rings in lycorine (**2**) were constructed by 6-exo mode radical cyclization. The former ring formation was performed in diastereoselective manner by radical cyclization *via* α-acylamino radical of (4*S*,5*R*)-4-acetoxy-*N*-(2-methoxy-, benzyloxy-, and *tert*-butoxycarbonylethenyl-4,5-methylenedioxybenzyl)- or (4*S*,5*R*)-*N*-(2-*tert*-butoxycarbonylethenyl-4,5-methylenedioxybenzyl)-4-triethylsilyloxy-5-phenylselenyl-2-pyrrolidinones (**10**-**12** or **19**). The latter ring formation was accomplished by the reaction of (1*S*,10*R*,10a*R*,2'*S*)- and (1*S*,10*R*,10a*R*,2'*R*)-10-(2'-acetoxy-4'-trimethylsilyl-3'-butynyl)-1-imidazolylthiocarbonyloxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidines (**28**).

The *Amaryllidaceae* alkaloids[1] have been focused as central role in the development of alkaloid chemistry. Among them, (-)-lycorine (**1**), which is one of representative alkaloids in this family, has pentacyclic structure contains in all *trans* oriented four contiguous chiral carbon centers. Moreover, it shows interesting and potential biological activities such as antineoplastic,[2a,b] antiviral,[2c,d] anti-inflammatory activities,[2e] inhibitory effect on tumour cell apoptosis,[2f,g] and DNA binding activity[2h] is also reported. Therefore, in past three decades, considerable synthetic studies have been reported.[3-8] However, most of them[3-7] were performed as racemic form except for only two papers[3a,8] on a synthesis of (-)-lycorine (**1**)[3a] and (+)-lycorine (**2**).[8]



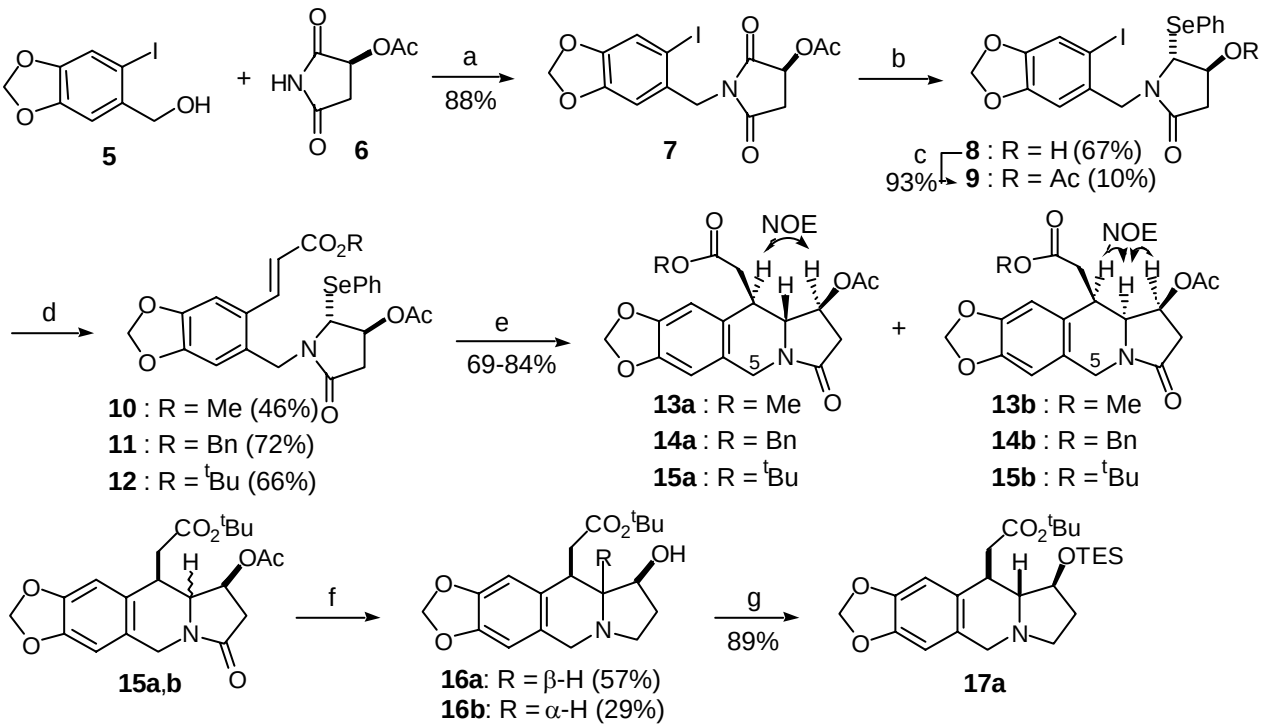


Scheme 1.

In continuation of our studies[4,9] on the synthesis of *Amaryllidaceae* alkaloids, we have recently reported synthesis of optically active 2-methyllycoranes using combination of 6-exo and -endo mode radical reactions (Scheme 1).[10] The methodology suggested a promise to make a potential intermediate for synthesis of optically active lycorine. In this paper, we describe the radical-mediated synthesis of optically active functionallized α-lycoranes (**3**,**4**) as candidates for synthesis of (+)-lycorine (**2**).

Synthesis of radical precursors (**11**-**13**) was as follows (Scheme 2). Reaction of 6-iodopiperonyl alcohol (**5**) and (3*S*)-acetoxy-2,5-pyrrolidinedione (**6**)[12] under Mitsunobu conditions gave an imide (**7**) in 88% yield. Reduction of **8** with $NaBH_4$ followed by phenylselenenylation afforded seleno-alcohol (**8**) and -acetate (**9**) in 67 and 10% yields, respectively. The alcohol (**8)** was converted to the acetate (**9**) in 93% yield by conventional way. In order to examine the steric effect of ester moiety on diastereoselectivity in radical reaction, three kinds of radical precursors (**10**-**12**) were synthesized in 46-72% yields by Heck reaction of **9** with methyl, benzyl or *tert*-butyl acrylate.

All radical reactions were performed with AIBN and Bu_3SnH in boiling benzene using syringe pump technique to give unseparable mixture of diastereomers (Table 1). As a result, the selenide (**12**) bearing *tert*-butyl ester gave the best result to form products (**15a**,**b**) in both diastereoselectivity and chemical yield, although the diastereoselectivity was not affected by the bulkiness of ester group. Stereochemistry of cyclized products (**13**-**15**) was determined by NOE experiments. In all cases, only two of possible four diastereomers were obtained as similarly observed in our previous report.[10] From above results,



Scheme 2. Reagents and conditions: a) DEAD, PPh_3, THF, rt; b) $NaBH_4$, THF-EtOH, 0 ÞC; PhSeH,*p*-TsOH, rt; c) Ac_2O, Py, rt; d) acrylates, $Pd(OAc)_2$, PPh_3, EtCN, 100 ÞC; e) AIBN, Bu_3SnH, benzene, Δ (Table 1); f) BH_3•THF, THF, rt; TMEDA, rt; NaOMe, MeOH, rt; g) TESCl, imidazole, DMF, rt

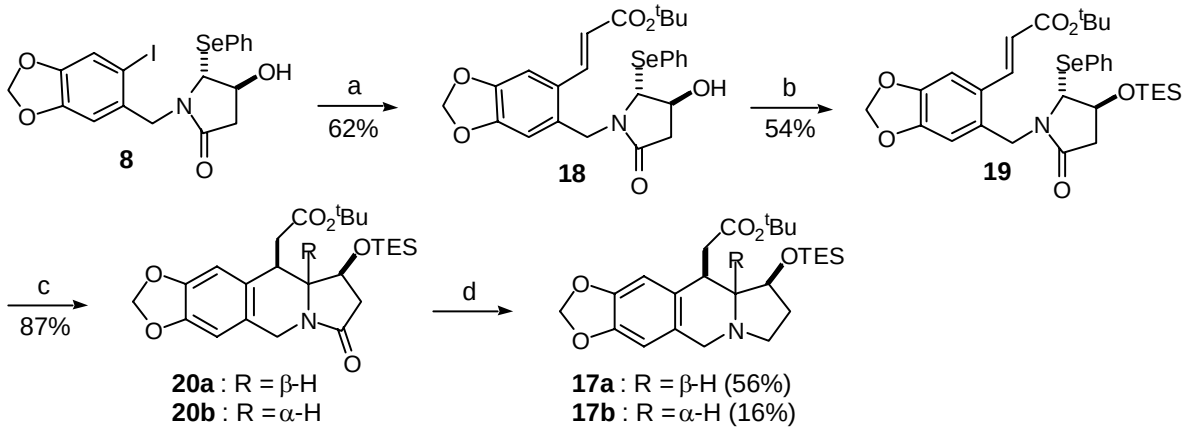
Table 1. Radical reaction of selenides (**11-13**).

Run	Substrate	Time (h)	Yield (%)[a]	Ratio (**a**:**b**)[b]
1	**11**	3.5	84	1.6 : 1
2	**12**	2.5	69	2.0 : 1
3	**13**	3	84	2.0 : 1

a) Combined isolated yield of cyclized products (**a**,**b**).
b) Determined by ^{1}H-NMR spectral analysis.

diastereomeric mixture of lactams (**15**) was reduced with BH_3 followed by treatment with TMEDA and methanolysis to give separable amino alcohols (**16a**) and (**16b**) in 57 and 29% yields, respectively. The former (**16a**), which could be led to (+)-lycorine (**2**), was converted to TES ether (**17a**) in 89% yield.

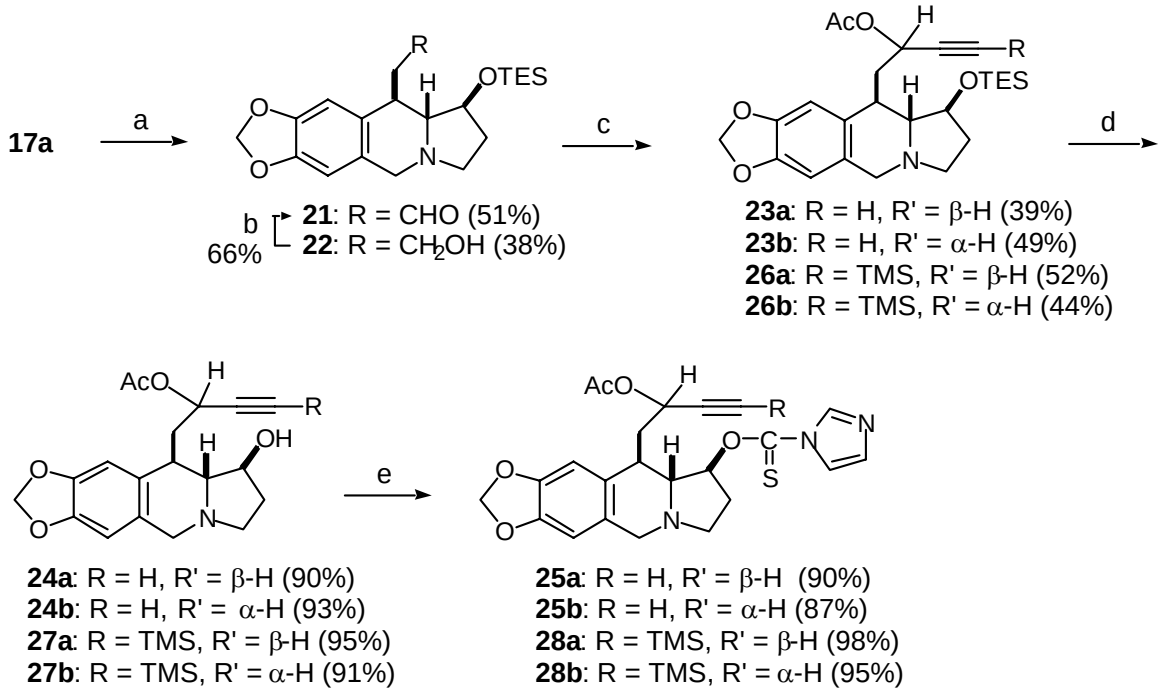
Although TES ether (**17a**) was produced, unexpected low diastereoselectivity in radical reaction and number of steps promoted us to plan an alternative approach to TES ether (**17a**) as depicted in Scheme 3.



Scheme 3. Reagents and conditions: a) *tert*-butyl acrylate, $Pd(OAc)_2$, PPh_3, EtCN, 100 ÞC; b) TESCl, imidazole DMF, rt; c) AIBN, Bu_3SnH, benzene, Δ; d) BH_3•THF, THF, rt; TMEDA, rt

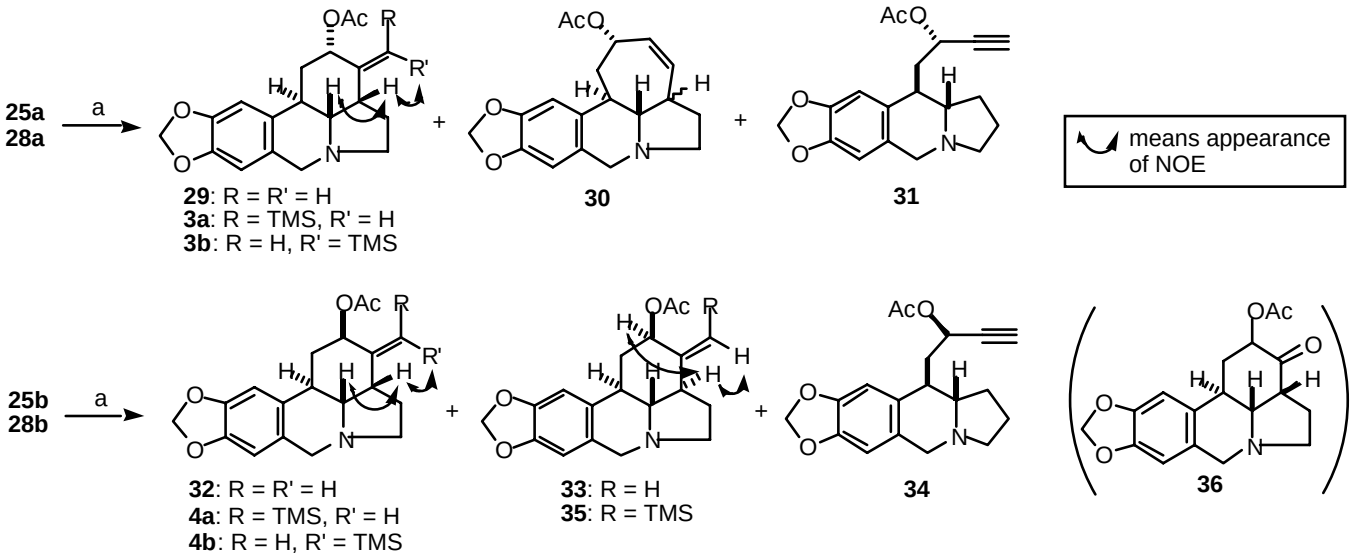
In this route, we anticipated that introduction of bulky silyl ether group would raise diastereoselectivity by its interaction with *tert*-butyl ester moiety in radical reaction. Thus, the iodide (**8**) was converted to *tert*-butyl ester (**18**) in 62% yield. As expected, radical reaction of **19**, which was obtained by triethylsilylation of **18**, gave 3.4 : 1 mixture of diastereomers (**20a**,**b**) in 87% yield.[13] The lactams (**20a**,**b**) were led to **17a** and **17b** in 51 and 16% yields, respectively, by transformation similar to that described for **13**, in which improved synthesis of **17a** was achieved.

Furthermore, **17a** was transformed to radical precursor for construction of C ring. Reduction of *tert*-butyl ester (**17a**) with DIBAH gave aldehyde (**21**) and alcohol (**22**) in 51 and 38% yields, respectively, along with unchanged **17a** (4%). The alcohol (**22**) could be recycled to **21** in 66% yield by Dess-Martin oxidation. Treatment of aldehyde (**21**) with ethynylmagnesium bromide followed by acetylation furnished separable propargyl acetates (**23a**) and (**23b**) in 39 and 49% yields, respectively. Stereochemistry of **23a**,**b** was determined by further conversion as described below. Desilylation of **23a**,**b** with 1 N HCl gave alcohols (**24a**,**b**), treatment of which with *N*, *N'*-thiocarbonyldiimidazole in refluxing benzene furnished radical precursors (**25a**,**b**) (Scheme 4).



Scheme 4. Reagents and conditions: a) DIBAH, THF, -78 ÞC; b) Dess-Martin periodinane, rt; c) RC≡ CM (R = H, M = MgBr or R = TMS, M = Li), THF; Ac_2O, Py d) 1 N HCl, THF, rt; e) *N*, *N'*-thiocarbonyldiimidazole, benzene

With radical precursors (**25**) in hand, we examined their radical cyclization. Initially, radical reaction of **25a** was performed under various conditions using syringe pump technique (Table 2). Unfortunately, the reaction produced not only desired 6-exo cyclized product (**29a**) but also 7-endo cyclization product (**30**) (runs 1-6). The reaction in boiling benzene afforded 18% yield of reduced product (**31**), while that in boiling toluene diminished formation of **31**. The reaction with tricyclohexyltin hydride [Cy_3SnH][14] instead



Scheme 5. Reagents and conditions: a) AIBN, Bu_3SnH or Cy_3SnH, benzene or toluene, Δ (Table 2)

Table 2. Radical reaction of imidazolides (**28a**,**b and 29a**,**b**).[a]

			Product (%)										
Run	Substrate	Reagent	**29**	**30**	**31**	**32**	**33**	**34**	**3a**	**3b**	**4a**	**4b**	**35**
1	**25a**	Bu_3SnH[b]	29	21	18								
2	**25a**	Cy_3SnH[c]	29	14	18								
3	**25a**	Bu_3SnH[c]	36	-[d]	-[e]								
4	**25a**	Bu_3SnH	27	15	-[e]								
5	**25a**	Cy_3SnH[f]	34	24	-[e]								
6	**25a**	Cy_3SnH	37	14	-[e]								
7	**25b**	Bu_3SnH[f]				23	24	3					
8	**25b**	Bu_3SnH				28	28	3					
9	**25b**	Cy_3SnH[f]				17	12	3					
10	**25b**	Cy_3SnH				23	20	2					
11	**28a**	Bu_3SnH							31	33			
12	**28a**	Cy_3SnH							42	42			
13	**28b**	Bu_3SnH									27	16	10
14	**28b**	Cy_3SnH									27	14	12

a. Reaction was carried out in 0.01 M toluene solution for 0.5 h, unless otherwise noted.
b. In 0.02 M benzene solution for 1 h.
c. In 0.02 M benzene solution for 0.5 h.
d. Not isolated.
e. Determined as a trace amount.
f. In 0.02 M toluene solution for 0.5 h.

of Bu_3SnH in boiling toluene (0.01 M) gave the best result, in which desired product (**29**) was formed in 37% yield (run 6). Stereochemistry in each product was determined by NOE experiment. Interestingly, in similar reaction of **25b** only 6-exo mode cyclization occurred to afford α-lycorane (**32**) and β-lycorane (**33**) along with reduced product (**34**). These results indicated that acetoxy group attached to propargyl carbon affected the course of the radical reaction.

We next turned our attention to use radical precursors with TMS group[11c] at terminal alkynyl moiety, because TMS group seemed to be bulky enough to suppress 7-endo cyclization. Synthesis of radical precursors (**28a**,**b**) was performed *via* **26** and **27** from **21** by the procedure similar to that described for conversion of **21** to **25a**,**b** (Scheme 4).

As expected, radical reaction of **28a** with Cy_3SnH in boiling toluene (0.01 M) proceeded in only 6-exo mode cyclization to give α-lycoranes (**3a**,**b**) in each 42% yield as separable geometric isomers (Table 2, run 12). On the other hand, radical reaction of **28b** with Bu_3SnH or Cy_3SnH afforded α-lycoranes (**4a**,**b**) in moderate yield along with about 10% yield of β-lycorane (**35**).

Unfortunately, further conversion of *exo*-alkene products (**3**,**4**,**29**) to keto compounds (**36**) by ozonolysis[15a] or osmium oxidation[15b] gave intractable mixture, in which the corresponding ketones (**36**) could not be determined at all. Also, desilylation of **3** or **4** under various conditions[16] did not proceed without decomposition.

In conclusion, synthesis of optically active 2-acetoxy-3-alkylidene-α-lycoranes (**3**,**4**,**29**) by radical-mediated reaction was accomplished. For the construction of B ring, TES ether (**19**) was the best radical precursor to give the products (**17a**,**b**). TMS substituted acetylenes (**28a**,**b**), which were obtained from **17a**, smoothly formed C ring by radical reaction to give functionallized α-lycoranes (**3**,**4**) in moderate to high yield. Further transformation of **3**, **4**, or **29** to (+)-lycorine (**2**) is now in progress.

EXPERIMENTAL

General. All melting points were measured on a Büchi or a Yanagimoto (hot plate) melting point apparatus and are uncorrected. IR spectra were performed with a Hitachi 260-10 spectrophotometer in $CHCl_3$ solution. ^1H and ^{13}C NMR spectra were taken with a JEOL EX-270 (270 MHz) spectrometer in $CDCl_3$ solution with tetramethylsilane as an internal standard. MS and HRMS spectra were measured on a Hitachi M-80 or a JEOL JMS D-300 spectrometer. Elementary analysis was performed with a Heraeus CHN-O-RAPID. Column chromatography was performed over silica gel (Merck Kiegelsel 60). Preparative TLCs were run on Merck 5744 or Merck 5715 plates. Organic extracts were dried over K_2CO_3, unless otherwise noted.

(3*S*)-3-Acetoxy-*N*-(2-iodo-4,5-methylenedioxybenzyl)-2,5-pyrrolidinedione (7). To a stirred solution of 6-iodopiperonyl alcohol (**5**) (26.41 g, 95 mmol), (3*S*)-acetoxy-2,5-pyrrolidinedione (**6**)[12] (15.70 g, 100

mmol), and PPh_3 (26.3 g, 100 mmol) in THF (150 mL) at 0˚C was added DEAD (16 mL, 101.6 mmol) over a period of 20 min. After being stirred at rt for 1 h, the solvent was evaporated *in vacuo* to give a residue, to which was added benzene to form a precipitate. The precipitate was removed by suction filtration. The filtrate was evaporated *in vacuo* to give a residue, which was purified by column chromatography (benzene : AcOEt = 5 : 1) to afford **7** (34.96 g, 88%); mp 127-128˚C (AcOEt-hexane); $[\alpha]_D^{24}$ -30.4˚ (c 1.01, $CHCl_3$); ^{1}H NMR δ 7.25, 6.69 (each 1H, s), 5.96 (2H, s), 5.44 (1H, dd, *J* = 5, 8.9 Hz), 4.70 (2H, s), 3.21 (1H, dd, *J* = 8.9, 18.5 Hz), 2.78 (1H, dd, *J* = 5, 18.5 Hz), 2.17 (3H, s); IR 1751, 1724 cm^{-1}; EI MS *m/z* 417 (M^+); Anal. Calcd for $C_{14}H_{12}NO_6I$: C, 40.31; H, 2.90; N, 3.36. Found: C, 40.02; H, 2.88; N, 3.63.

(4*S*,5*R*)-4-Hydroxy- and (4*S*,5*R*)-4-Acetoxy-*N*-(2-iodo-4,5-methylenedioxybenzyl)-5-phenylselenyl-2-pyrrolidinone (8 and 9). To a stirred solution of **7** (30.0 g, 71.9 mmol) in THF (250 mL) and EtOH (120 mL) at 0˚C was added $NaBH_4$ (2.78 g, 73 mmol) in small portions. After being stirred for 1.5 h, the reaction was quenched with water. The product was taken up in $CHCl_3$, and the extracts were washed with 3N HCl and brine, successively, dried (Mg_2SO_4), and evaporated under reduced pressure to give crude alcohol. To the alcohol in CH_2Cl_2 (250 mL) were added PhSeH (9.9 mL, 93.3 mmol) and *p*-TsOH•H_2O (1.37 g, 7.2 mmol). After being stirred for 2 h, the reaction was quenched with water. The mixture was extracted with $CHCl_3$. The organic extracts were washed with brine, dried ($MgSO_4$), and evaporated *in vacuo* to give a residue, which was purified by column chromatography (hexane : AcOEt = 1 : 1 then AcOEt) to afford **8** (24.93 g, 67%) and **9** (3.86 g, 10%) as amorphous solid. A mixture of **8** (15.78 g, 30.4 mmol) and Ac_2O (5.5 mL) in pyridine (18 mL) was stirred for 12 h. Usual work-up gave a residue, which was purified by column chromatography (hexane : AcOEt = 10 : 1) to give **9** (15.80 g, 93%). **8**; $[\alpha]_D^{23}$ -43.2˚ (c 1.06, $CHCl_3$); ^{1}H NMR δ 7.52-7.55 (2H, m), 7.23-7.55 (4H, m), 6.85 (1H, s), 5.95 (2H, s), 4.97, 4.31 (each 1H, d, *J* = 15.2 Hz), 4.58-4.70 (2H, m), 1.95-2.20 (2H, m); EI MS *m/z* 517 $(M)^+$; HRMS *m/z* calcd for $C_{18}H_{17}NO_4Se$ (M^+) 517.9368, found: 517.9358. **9**; $[\alpha]_D^{29}$ -39.8˚ (c 1.0, $CHCl_3$); ^{1}H NMR δ 7.25-7.61 (5H, m), 7.26, 6.77 (each 1H, s), 5.97, 5.96 (each 1H, d, *J* = 2 Hz), 5.47 (1H, d, *J* = 5.4 Hz), 4.99, 4.30 (each 1H, d, *J* = 18.4 Hz), 4.64 (1H, s), 2.21 (1H, d, *J* = 18.4 Hz), 2.01 (1H, dd, *J* = 5.4, 18.4 Hz,), 2.01 (3H, s); IR 1741, 1701 cm^{-1}; FAB MS *m/z* 560 $[(M+H)^+]$; HR FAB MS *m/z* calcd for $C_{20}H_{19}NO_5ISe$ $[(M+H)^+]$ 559.9473, found: 559.9483.

General procedure for Heck reaction of aryl iodides (8,9). A solution of **8** or **9** (1 eq.), $Pd(OAc)_2$ (3 mol%), PPh_3 (12 mol%), Et_3N (2.5 eq.), and methyl, benzyl or *tert*-butyl acrylate (5 eq.) in propionitrile was heated at 100˚C under an argon atmosphere. The solvent was evaporated *in vacuo* to give a residue, which was purified by column chromatography ($CHCl_3$: AcOEt = 50 : 1 for **11** and **12**; hexane : AcOEt = 1 : 1 for **10** and **18**) to afford esters **(10-12,18)**.

(4*S*,5*R*)-(*E*)-4-Acetoxy-*N*-(2-methoxycarbonylethenyl-4,5-methylenedioxybenzyl)-5-phenylselenyl-2-pyrrolidinone (10); from **9** (0.993 g, 1.78 mmol) in propionitrile (30 mL) for 17 h, **10** (0.420 g, 46%) as an oil and **9** (0.250 g, 25%) were obtained; $[\alpha]_D^{27}$ -23.6˚ (c 1.02, $CHCl_3$); ^{1}H NMR δ 7.91, 6.20 (each 1H, d, *J* = 15.7 Hz), 7.56 (2H, d, *J* = 8.3 Hz), 7.30-7.41 (3H, m), 7.04, 6.75 (each 1H, s), 6.00 (2H, s), 5.42 (1H, d, *J* = 5.9 Hz), 5.21, 4.26 (each 1H, d, *J* = 15.1 Hz), 4.54 (1H, s), 3.80 (3H, s), 2.01-2.21 (2H, m), 1.94 (3H, s); IR 1743, 1693 cm^{-1}; FAB MS *m/z* 538 [(M+Na)$^+$]; HR FAB MS *m/z* calcd for $C_{24}H_{23}NO_7NaSe$ [(M+Na)$^+$] 538.0546, found: 538.0543.

(4*S*,5*R*)-(*E*)-4-Acetoxy-*N*-(2-benzyloxycarbonylethenyl-4,5-methylenedioxybenzyl)-5-phenylselenyl-2-pyrrolidinone (11); from **9** (1.937 g, 3.47 mmol) in propionitrile (40 mL) for 14 h, **11** (1.48 g, 72%) was obtained as an oil; ^{1}H NMR δ 7.94, 6.24 (each 1H, d, *J* = 15.7 Hz), 7.25-7.61 (2H, m), 7.20-7.43 (8H, m), 7.04, 6.74 (each 1H, s), 6.00, 5.99 (each 1H, d, *J* = 1.3 Hz), 5.40 (1H, d, *J* = 5.6 Hz), 5.27, 4.22 (each 1H, d, *J* = 12.5 Hz), 5.21, 4.24 (each 1H, d, *J* = 15.2 Hz), 4.57 (1H, s), 1.96-2.09 (2H, m), 1.87 (3H, s, Ac); IR 1743 cm^{-1}; FAB MS *m/z* 594 [(M+H)$^+$]; HR FAB MS *m/z* calcd for $C_{30}H_{28}NO_7Se$ [(M+H)$^+$] 594.0986, found: 594.0987.

(4*S*,5*R*)-(*E*)-4-Acetoxy-*N*-(2-*tert*-butoxycarbonylethenyl-4,5-methylenedioxybenzyl)-5-phenylselenyl-2-pyrrolidinone (12); from **9** (6.235 g, 11.2 mmol) in propionitrile (230 mL) for 24 h, **12** (4.13 g, 66%) was obtained as an oil; $[\alpha]_D^{27}$ -15.2˚ (c 1.02, $CHCl_3$); ^{1}H NMR δ 7.76, 6.11 (each 1H, d, *J* = 15.5 Hz), 7.56 (2H, d, *J* = 8.3 Hz), 7.26-7.40 (3H, m), 7.03, 6.75 (each 1H, s), 6.00, 5.99 (each 1H, d, *J* = 1.4 Hz), 5.41 (1H, d, *J* = 5.9 Hz), 5.23, 4.22 (each 1H, d, *J* = 15.1 Hz), 4.48 (1H, s), 2.01-2.18 (2H, m), 1.94 (3H, s), 1.53 (9H, s); IR 1743, 1709 cm^{-1}; FAB MS *m/z* 558 [(M+H)$^+$]; HR FAB MS *m/z* calcd for $C_{27}H_{30}NO_7Se$ [(M+H)$^+$] 558.1195, found: 558.1180.

(4*S*,5*R*)-(*E*)-*N*-(2-*tert*-Butoxycarbonylethenyl-4,5-methylenedioxybenzyl)-4-hydroxy-5-phenylselenyl-2-pyrrolidinone (18); from **8** (8.78 g, 17.0 mmol) in propionitrile (300 mL) for 9 h, **18** (5.41 g, 62%) was obtained as crystals; mp 171-172.5˚C (AcOEt-hexane); $[\alpha]_D^{24}$ -12.4˚ (c 1.01, $CHCl_3$); ^{1}H NMR δ 7.83, 6.15 (each 1H, d, *J* = 15.8 Hz), 7.50 (2H, d, *J* = 7.9 Hz), 7.26-7.38 (3H, m), 7.02, 6.80 (each 1H, s), 5.97 (2H, s), 5.17, 4.27 (each 1H, d, *J* = 15.3 Hz), 4.58 (1H, t, *J* = 5.3 Hz), 4.54 (1H, s), 2.57 (1H, d, *J* = 5.3 Hz), 2.14 (1H, d, *J* = 17.7 Hz), 1.99 (1H, dd, *J* = 5.3, 17.7 Hz), 1.52 (9H, s); IR 3400, 1697, 1632 cm^{-1}; MS *m/z* 517 (M$^+$); HRMS *m/z* calcd for $C_{25}H_{27}NO_6Se$ (M$^+$) 517.1004, found: 517.1022.

General procedure for radical reaction of selenides (10-12,19). To a refluxed solution of selenides (**10-12**, **19**) (1 eq.) in benzene (32 mL per 1 mmol of selenide) was added a solution of AIBN (0.5 eq.) and Bu_3SnH (3 eq.) in benzene (18 mL per 1 mmol of selenide) using syringe pump. After the mixture was refluxed for additional 1 h, the solvent was removed *in vacuo* to give a residue, which was purified by column chromatography (hexane : AcOEt = 30 : 1 then 1 : 1) to afford cyclized products (**13-15**,**20**). Attempts to separate the diastereomeric mixtures were unsuccessful.

(1*S*,10*R*,10a*R*)- and (1*S*,10*R*,10a*S*)-1-Acetoxy-10-methoxycarbonylmethyl-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidin-3-ones (13a,b); from **10** (1.298 g, 2.50 mmol), **13a**,**b** (0.757 g, 84%) was obtained as amorphous solid (addition time; 2.5 h); ^{1}H NMR δ 6.66, 6.34 (1H, each s), 6.59, 6.56 (1H, each s), 5.93-5.95 (2H, m), 5.19-5.25 (1H, m), 4.94, 4.15 (each 0.36H, d, *J* = 16.5 Hz, H-5), 4.80, 4.27 (each 0.64H, d, *J* = 17.3 Hz, H-5), 3.71, 3.65 (3H, each s), 3.55-3.91 (1H, m), 2.80-3.21 (3H, m), 2.20-2.60 (2H, m), 2.10, 2.09 (3H, each s); IR 1738, 1687 cm^{-1}; MS *m/z* 361 (M$^+$); HRMS *m/z* calcd for $C_{18}H_{19}NO_7$ (M$^+$) 361.1159, found: 361.1158.

(1*S*,10*R*,10a*R*)- and (1*S*,10*R*,10a*S*)-1-Acetoxy-10-benzyloxycarbonylmethyl-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidin-3-ones (14a,b); from **11** (0.711 g, 1.2 mmol), **14a**,**b** (0.360 g, 69%) was obtained as an oil (addition time; 2 h); ^{1}H NMR δ 7.18-7.36 (5H, m), 6.63, 6.62 (1H, each s), 6.56, 6.54 (1H, each s), 5.89-5.92 (2H, m), 5.02-5.22 (3H, m), 4.93, 4.10 (each 0.67H, d, *J* = 16.5 Hz, H-5), 4.79, 4.25 (each 0.33H, d, *J* = 17.5 Hz, H-5), 3.47-3.88 (2H, m), 2.81-3.17 (3H, m), 2.25-2.54 (1H, m), 2.08, 2.06 (3H, each s); IR 1736, 1689 cm^{-1}; MS *m/z* 437 (M$^+$); HRMS *m/z* calcd for $C_{24}H_{23}NO_7$ (M$^+$) 437.1475, found: 437.1487.

(1*S*,10*R*,10a*R*)- and (1*S*,10*R*,10a*S*)-1-Acetoxy-10-(*tert*-butoxycarbonylmethyl)-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidin-3-ones (15a,b); from **12** (4.02 g, 7.20 mmol), **15a**,**b** (2.443 g, 84%) was obtained as amorphous solid (addition time; 2 h); ^{1}H NMR δ 6.69, 6.67 (1H, each s), 6.58, 6.56 (1H, each s), 5.92, 5.91 (2H, each s), 5.20-5.25 (1H, m), 4.94, 4.14 (each 0.63H, d, *J* = 16.5 Hz, H-5), 4.84, 4.24 (each 0.37H, d, *J* = 17.4 Hz, H-5), 3.76-3.89 (1H, m), 3.51-3.69 (1H, m), 2.69-3.15 (3H, m), 2.32-2.55 (1H, m), 2.10, 2.08 (3H, each s,), 1.42, 1.41 (9H, each s); IR 1731, 1686 cm^{-1}; MS *m/z* 403 (M$^+$); HRMS *m/z* calcd for $C_{21}H_{25}NO_7$ (M$^+$) 403.1631, found: 403.1633.

(1*S*,10*R*,10a*R*)- and (1*S*,10*R*,10a*S*)-10-(*tert*-Butoxycarbonylmethyl)-1-triethylsilyloxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidin-3-ones (20a,b); from **19** (3.76 g, 5.97 mmol), **20a,b** (2.47 g, 87%) was obtained as amorphous solid (addition time; 3 h); ^{1}H NMR δ 6.68, 6.67 (1H, each s), 6.58, 6.56 (1H, each s), 5.89-5.88 (2H, m), 4.82, 4.16 (each 0.77H, d, *J* = 16.7 Hz, H-5), 4.76, 4.27 (each 0.23H, d, *J* = 15.5 Hz, H-5), 4.26-4.35 (1H, m), 3.76 (0.46H, t, *J* = 3.0 Hz), 3.56 (1.54H, dd, *J* = 3.6, 9.9 Hz), 3.41-3.47, 2.90-3.08 (1H, each m), 2.04-2.94 (4H, m), 1.43, 1.41 (9H, each s), 0.98, 0.97 (9H, each t, *J* = 7.9 Hz), 0.65, 0.62 (6H, each t, *J* = 7.9 Hz); IR 1728, 1693, cm^{-1}; MS *m/z* 475 (M$^+$) ; HRMS *m/z* calcd for $C_{25}H_{37}NO_6Si$ (M$^+$) 475.2389, found: 475.2382.

(1*S*,10*R*,10a*R*)- and (1*S*,10*R*,10a*S*)-10-(*tert*-Butoxycarbonylmethyl)-1-hydroxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine (16a and 16b). To a stirred solution of **15a,b** (2.00 g, 4.96 mmol) in THF (140 mL) at rt was added BH_3•THF (20 mL, 20 mmol, 1 M in THF) over a period of 5 min. After being stirred for 2 h, TMEDA (4.5 mL) was added to the mixture, and the mixture was stirred for overnight. Water was added to the mixture and the product was extracted with $CHCl_3$. The extracts

were washed with saturated $NaHCO_3$ and brine, successively, dried, and evaporated under reduced pressure to give a residue, which was taken up in Et_2O and the solid was filtered off. The filtrate was evaporated *in vacuo* to afford a residue, which was treated with NaOMe (0.603 g, 11.2 mmol) in MeOH (40 mL) at rt for 1 h. Then, the reaction was quenched with water and extracted with $CHCl_3$. The extracts were washed with brine, dried, and evaporated under reduced pressure to give a residue, which was subjected to column chromatography (AcOEt : MeOH = 50 : 1 the 10 : 1) to afford **16a** (0.985 g, 57%) and **16b** (0.505 g, 29%). **16a**; oil; $[\alpha]_D^{26}$ +85.9˚ (c 1.0, $CHCl_3$); ^{1}H NMR δ 6.77, 6.49 (each 1H, s), 5.90 (2H, s), 4.20 (1H, ddd, *J* = 3.3, 5.6, 8.7 Hz), 3.87, 3.45 (each 1H, d, *J* = 14.2 Hz), 3.19 (1H, dt, *J* = 5.5, 9.9 Hz), 3.11 (1H, t, *J* = 8.7 Hz), 2.83 (1H, dd, *J* = 5.8, 15.3 Hz), 2.72 (1H, dd, *J* = 4.8, 15.3 Hz), 2.53 (1H, q, *J* = 8.9 Hz), 2.18-2.356 (2H, m), 1.66-1.77 (1H, m), 1.41 (9H, s); IR 3400, 1703 cm^{-1}; MS *m/z* 347 (M^+); HRMS *m/z* calcd for $C_{19}H_{25}NO_5$ (M^+) 347.1734, found: 347.1748. **16b**; oil; $[\alpha]_D^{28}$ +42.2˚ (c 1.15, $CHCl_3$); ^{1}H NMR δ 6.56, 6.39 (each 1H, s), 5.82 (2H, s), 3.85, 3.27 (each 1H, d, *J* = 14.2 Hz), 3.79 (1H, dd, *J* = 7.9, 15.8 Hz), 3.36 (1H, dt, *J* = 4.6, 12.6 Hz), 3.16 (1H, dt, *J* = 4.6, 12.6 Hz), 2.73 (1H, dd, *J* = 9.9, 18.2 Hz), 2.44 (1H, dd, *J* = 6.9, 9.9 Hz), 2.38 (1H, dd, *J* = 3.6, 7.5 Hz), 2.26 (1H, dd, *J* = 2.4, 18.0 Hz), 2.04-2.18 (1H, m), 1.63-1.77 (1H, m), 1.40 (9H, s); IR 3500, 1705 cm^{-1}; MS *m/z* 347 (M^+); HRMS *m/z* calcd for $C_{19}H_{25}NO_5$ (M^+) 347.1734, found: 347.1737.

(1*S*,10*R*,10a*R*)-10-(*tert*-Butoxycarbonylmethyl)-1-triethylsilyloxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine (17a). To a stirred solution of **16a** (0.635 g, 1.83 mmol) and imidazole (0.436 g, 6.41 mmol) in DMF (16 mL) at rt was added a solution of chlorotriethylsilane (0.689 g, 16.6 mmol) in DMF (1 mL) over a period of 5 min. After being stirred for 0.5 h, the reaction was quenched with saturated aqueous $NaHCO_3$. The mixture was extracted with ether. The extracts were washed with brine, dried, and evaporated under reduced pressure to give a residue, which was purified by column chromatography (benzene : AcOEt = 3 : 1 then 1 : 1) to afford **17a** (0.753 g, 89%) as an oil; $[\alpha]_D^{22}$ +63.1˚ (c 1.27, $CHCl_3$); ^{1}H NMR δ 6.67, 6.47 (each 1H, s), 5.87, 5.86 (each 1H, d, *J* = 1.3 Hz), 4.16 (1H, ddd, *J* = 4.5, 6.4, 8.6 Hz), 3.81, 3.43 (each 1H, d, *J* = 14.2 Hz), 3.27 (1H, t, *J* = 8.3 Hz), 3.10 (1H, dt, *J* = 2.6, 8.8 Hz), 3.03 (1H, dd, *J* = 2.6, 16.9 Hz), 2.52 (1H, dd, *J* = 7.3, 16.9 Hz), 2.47-2.56 (1H, m), 2.18-2.29 (2H, m), 1.60-1.70 (1H, m), 1.41 (9H, s), 0.97 (9H, t, *J* = 7.9 Hz), 0.62 (6H, t, *J* = 7.9 Hz); IR 1720 cm^{-1}; MS *m/z* 461 (M^+); HRMS *m/z* calcd for $C_{25}H_{39}NO_5Si$ (M^+) 461.2598, found: 461.2605.

(4*S*,5*R*)-(*E*)-*N*-[(2-(*tert*-Butoxycarbonylethenyl)-4,5-methylenedioxybenzyl)-4-triethylsilyloxy-5-phenylselenylpyrrolidin-2-one (19). To a stirred solution of **18** (5.72 g, 11.1 mmol) and imidazole (1.89 g, 27.8 mmol) in DMF (80 mL) was added a solution of chlorotriethylsilane (2.50 g, 16.6 mmol) in DMF (15 mL) at rt over a period of 5 min. After being stirred for 2 h, similar work-up as described above gave a residue, which was purified by column chromatography (benzene : AcOEt = 40 : 1 then 10 : 1) to afford **19** (3.76 g, 54%); $[\alpha]_D^{24}$ +5.1˚ (c 0.35, $CHCl_3$); ^{1}H NMR δ 7.88, 6.16 (each 1H, d, *J* = 15.5 Hz), 7.54 (2H,

d, *J* = 7.9 Hz), 7.30-7.37 (3H, m), 7.04, 6.83 (each 1H, s), 5.95, 5.96 (each 1H, d, *J* = 1.5 Hz), 5.16, 4.31 (each 1H, d, *J* = 15.5 Hz), 4.49 (1H, t, *J* = 2.6 Hz), 4.47 (1H, s), 2.10 (2H, d, *J* = 2.6 Hz), 1.53 (9H, s), 0.78 (9H, t, *J* = 7.9 Hz), 0.39 (6H, t, *J* = 7.9 Hz); IR 1709, 1630 cm^{-1}; FAB MS *m/z* 632 [$(M+H)^+$]; HR FAB MS *m/z* calcd for $C_{31}H_{42}NO_6SeSi$ [$(M+H)^+$] 632.1947, found: 632.1950.

Reduction of 20a,b. To a stirred solution of **20a,b** (2.30 g, 4.84 mmol) in THF (140 mL) at rt was added BH_3•THF (20 mL, 19.3 mmol, 0.92 M in THF) over a period of 10 min. After being stirred for 3.5 h, TMEDA (4.5 mL) was added to the mixture, and the mixture was stirred for overnight. Similar work-up as described above gave a residue, which was subjected to column chromatography (hexane : AcOEt = 10 : 1 the 4 : 1) to afford **17a** (1.250 g, 56%) and **17b** (0.0358 g, 16%). ^{1}H-NMR spectrum of **17a** was identical with that of **17a** obtained from **16a**.

(1*S*,10*R*,10a*S*)-10-(*tert*-Butoxycarbonylmethyl)-1-triethylsilyloxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine (17b); oil; $[\alpha]_D^{32}$ +107.1˚ (c 1.05, $CHCl_3$); ^{1}H NMR δ 6.71, 6.48 (each 1H, s), 5.88 (2H, s), 4.19 (1H, ddd, *J* = 2.8, 5.1, 7.9 Hz), 3.96, 3.42 (each 1H, d, *J* = 14.5 Hz), 3.28 (1H, t, *J* = 7.9 Hz), 3.07 (1H, dt, *J* = 1.8, 8.2 Hz), 2.58 (1H, dd, *J* = 4.3, 8.2 Hz), 2.44-2.53 (2H, m), 2.36 (1H, dd, *J* = 7.9, 15.5 Hz), 1.96-2.11 (1H, m), 1.62-1.74 (1H, m), 1.43 (9H, s), 0.97 (9H, t, *J* = 7.9 Hz), 0.61 (6H, q, *J* = 7.9 Hz); IR 1728 cm^{-1}; MS *m/z* 461 (M^+); HRMS *m/z* calcd for $C_{25}H_{39}NO_5Si$ (M^+) 461.2597, found: 461.2599.

(1*S*,10*R*,10a*R*)-1-Triethylsilyloxy-10-formylmethyl- and (1*S*,10*R*,10a*S*)-1-Triethylsilyloxy-10-hydroxyethyl-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine (21 and 22). To a solution of **17a** (1.313 g, 2.85 mmol) in CH_2Cl_2 (110 mL) at -78˚C was added DIBAH (8.5 mL, 8.5 mmol, 1 M in hexane) over a period of 15 min. After being stirred for 1 h, further DIBAH (6 mL, 6 mmol) was added over a period of 8 min and the mixture was stirred for additional 1 h. Then, the reaction was quenched with water. The mixture was extracted with $CHCl_3$. Usual work-up gave a residue, which was purified by column chromatography (AcOEt : hexane = 1 : 3 then 1 : 3 then AcOEt : MeOH = 10 : 1) to afford **21** (0.567 g, 51%), **22** (0.420 g, 38%), and **17a** (0.058 g, 4.4%). **21**; $[\alpha]_D^{24}$ +94.4˚ (c 1.01, $CHCl_3$); ^{1}H NMR δ 9.79 (1H, t, *J* = 1.5 Hz), 6.56, 6.48 (each 1H, s), 5.88, 5.87 (each 1H, d, *J* = 1.3 Hz), 4.15 (1H, ddd, *J* = 4.6, 6.5, 8.8 Hz), 3.84, 3.42 (each 1H, d, *J* = 13.7 Hz), 3.35-3.41 (1H, m), 3.09-3.20 (2H, m), 2.89 (1H, ddd, *J* = 1.5, 5.6, 19.7 Hz), 2.52 (1H, q, *J* = 8.8 Hz), 2.16-2.30 (2H, m), 1.60-1.74 (1H, m), 0.95 (9H, t, *J* = 7.7 Hz), 0.60 (6H, q, *J* = 7.7 Hz); IR 1722 cm^{-1}; MS *m/z* 389 (M^+); HRMS *m/z* calcd for $C_{21}H_{31}NO_4Si$ (M^+) 389.2022, found: 389.2032. **22**; oil; $[\alpha]_D^{26}$ +94.2˚ (c 1.02, $CHCl_3$); ^{1}H NMR δ 6.70, 6.46 (each 1H, s), 5.87 (2H, s), 4.08 (1H, ddd, *J* = 4.4, 7.3, 8.6 Hz), 3.52 (2H, t, *J* = 6.1 Hz), 3.72, 3.49 (each 1H, d, *J* = 14.5 Hz), 2.92-3.05 (3H, m), 2.62 (1H, q, *J* = 8.6 Hz), 2.48 (1H, t, *J* = 7.3 Hz), 2.08-2.27 (3H, m), 1.60-1.71 (1H, m), 0.96 (9H, t, *J* = 7.8 Hz), 0.62 (6H, q, *J* = 7.8 Hz); IR 3500, 1738 cm^{-1}; MS *m/z* 391 (M^+); HRMS *m/z* calcd for $C_{21}H_{33}NO_4Si$ (M^+) 391.2179, found: 391.2188.

Dess-Martin Oxidation of Alcohol (22). To a stirred suspension of **22** (0.696 g, 1.78 mmol) and $NaHCO_3$ (0.748 g, 8.89 mmol) in CH_2Cl_2 (40 mL) at rt was added Dess-Martin periodinane (1.608 g, 3.56 mmol) in one portion. After being stirred for 1 h, the mixture was washed with 10% aqueous $Na_2S_2O_3$ and brine, successively. Usual work-up gave a residue, which was purified by column chromatography (AcOEt : hexane = 1 : 1) to afford **21** (0.457 g, 66%). Its ^{1}H NMR spectral data were identical with those for the product obtained from **17a**.

(1*S*,10*R*,10a*R*,2'*S*)- and (1*S*,10*R*,10a*R*,2'*R*)-10-(2'-Acetoxy-3'-butynyl)-1-triethylsilyloxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine (23a and 23b). To a solution of **21** (0.495 g, 1.27 mmol) in THF (20 mL) was added 0.5 M ethynylmagnesium bromide in THF (5 mL, 2.5 mmol) at 0˚C over a period of 4 min. After being stirred for 30 min, the reaction was quenched with water. The mixture was extracted with $CHCl_3$. Usual work-up gave an alcohol (0.567 g, 100%), which was treated with Ac_2O (0.404 g, 3.96 mmol) in pyridine (2.5 mL) for 20 h. Work-up as usual gave a residue, which was purified by preparative TLC (AcOEt : hexane = 1 : 1, two times) to afford **23a** (0.226 g, 39%) and **23b** (0.284 g, 49%). **23a**; mp 78-79˚C (hexane); $[\alpha]_D^{31}$ +53.9˚ (c 1.05, $CHCl_3$); ^{1}H NMR δ 6.78, 6.49 (each 1H, s), 5.89 (2H, s), 5.60 (1H, ddd, *J* = 2, 4.8, 9.2 Hz), 4.07 (1H, dd, *J* = 6.6, 12.9 Hz), 3.55, 3.48 (each 1H, d, *J* = 14.2 Hz), 2.95-3.02 (2H, m), 2.48-2.68 (3H, m), 2.46 (1H, d, *J* = 2 Hz), 2.31 (1H, dt, *J* = 5.3, 14.9 Hz), 2.14 (1H, dt, *J* = 8.1, 12.9 Hz), 1.82 (3H, s), 1.64-1.75 (1H, m), 0.99 (9H, t, *J* = 7.8 Hz), 0.50 (6H, q, *J* = 7.8 Hz); IR 1736 cm^{-1}; MS *m/z* 457 (M^+); HRMS *m/z* calcd for $C_{25}H_{35}NO_5Si$ (M^+) 457.2282, found: 457.2295. **23b**; oil; $[\alpha]_D^{32}$ +76.9˚ (c 1.0, $CHCl_3$); ^{1}H NMR δ 6.83, 6.51 (each 1H, s), 5.92, 5.91 (each 1H, d, *J* = 1.5 Hz), 5.42 (1H, dt, *J* = 2.0, 7.7 Hz), 4.07 (1H, dd, *J* = 6.3, 13.2 Hz), 3.70, 3.54 (each 1H, d, *J* = 14.4 Hz), 2.90-3.03 (2H, m), 2.66 (1H, q, *J* = 8.2 Hz), 2.22-2.50 (3H, m), 2.47 (1H, d, *J* = 2.0 Hz), 2.06 (3H, s), 2.06-2.18 (1H, m), 1.65-1.82 (1H, m), 0.99 (9H, t, *J* = 7.9 Hz), 0.65 (6H, q, *J* = 7.9 Hz); IR 1738 cm^{-1}; MS *m/z* 457 (M^+); MS *m/z* 457 (M^+); HRMS *m/z* calcd for $C_{25}H_{35}NO_5Si$ (M^+) 457.2282, found: 457.2288.

(1*S*,10*R*,10a*R*,2'*S*)-10-(2'-Acetoxy-3'-butynyl)-1-hydroxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine (24a). A solution of **23a** (0.226 g, 0.49 mmol) and 1 N HCl (3 mL, 3 mmol) in THF (10 mL) was stirred at rt for 15 min. The mixture was diluted with $CHCl_3$ and saturated aqueous $NaHCO_3$ was added. Usual work-up gave a residue, which was purified by column chromatography (AcOEt then AcOEt : MeOH = 10 : 1) to afford **24a** (0.153 g, 90%); mp 61-62˚C (AcOEt-hexane); $[\alpha]_D^{28}$ +71.6˚ (c 0.43, $CHCl_3$); ^{1}H NMR δ 6.86, 6.49 (each 1H, s), 5.90 (2H, s), 5.71 (1H, dt, *J* = 2.0, 6.6 Hz), 4.20 (1H, ddd, *J* = 2.6, 5.6, 11.2 Hz), 3.82, 3.46 (each 1H, d, *J* = 14.5 Hz), 2.97-3.08 (2H, m), 2.85 (1H, br s), 2.58 (1H, d, *J* = 2.0 Hz), 2.54 (1H, dd, *J* = 8.9, 14.9 Hz), 2.23-2.35 (4H, m), 2.01 (3H, s), 1.66-1.77 (1H, m); IR 3305, 1736 cm^{-1}; MS *m/z* 343 (M^+); HRMS *m/z* calcd for $C_{19}H_{21}NO_5$ (M^+) 343.1417, found: 343.1407.

(1*S*,10*R*,10a*R*,2'*R*)-10-(2'-Acetoxy-3'-butynyl)-1-hydroxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine (24b). A solution of **23b** (0.284 g, 0.62 mmol) and 1 N HCl (4 mL, 4 mmol) in THF (12 mL) was stirred at rt for 15 min. Similar work-up as described above gave a residue, which was purified by column chromatography (AcOEt then AcOEt : MeOH = 10 : 1) to afford **24b** (0.201 g, 93%); mp 94-95˚C (AcOEt-hexane); $[\alpha]_D^{28}$ +83.8˚ (c 0.25, $CHCl_3$); ^{1}H NMR δ 6.84, 6.50 (each 1H, s), 5.92, 5.91 (each 1H, d, *J* = 1.3 Hz), 5.63 (1H, dt, *J* = 2.0, 7.1 Hz), 4.19 (1H, ddd, *J* = 3.1, 5.4, 8.6 Hz), 3.82, 3.49 (each 1H, d, *J* = 14.2 Hz), 3.05 (1H, dt, *J* = 2.5, 8.7 Hz), 2.97 (1H, dd, *J* = 4.5, 9.2 Hz), 2.58 (1H, q, *J* = 8.7 Hz), 2.49 (1H, d, *J* = 2 Hz), 2.35-2.40 (2H, m), 2.25-2.29 (3H, m), 2.11 (3H, s), 1.67-1.77 (1H, m); IR 3305, 1738 cm^{-1}; MS *m/z* 343 (M^+); HRMS *m/z* calcd for $C_{19}H_{21}NO_5$ (M^+) 343.1417, found: 343.1427.

General procedure for synthesis of imidazolides (25,28) A solution of alcohol (**24** or **27**) (1 eq.) and and *N*, *N'*-thiocarbonyldiimidazole (2 eq.) in benzene (25 mL per 1 mmol of alcohol) was refluxed for 1 h. Removal of the solvent under reduced pressure gave a residue, which was purified by preparative TLC (AcOEt for **25**; hexane : AcOEt = 1 : 5 for **28**) to afford corresponding imidazolides (**25**,**28**).

(1*S*,10*R*,10a*R*,2'*S*)-10-(2'-Acetoxy-3'-butynyl)-1-imidazolylthiocarbonyloxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine (25a); from **24a** (0.065 g, 0.19 mmol), **25a** 0.077 g, 90%) was obtained as an oil; $[\alpha]_D^{28}$ +97.1˚ (c 0.90, $CHCl_3$); ^{1}H NMR δ 8.39, 7.68, 7.05, 6.82, 6.53 (each 1H, s) 5.92 (2H, s), 5.68 (1H, ddd, *J* = 2.6, 5.4, 8.1 Hz), 5.52 (1H, dt, *J* = 2.0, 7.1 Hz), 3.89, 3.58 (each 1H, *J* = 14.3 Hz), 3.13-3.20 (2H, m), 2.92 (1H, dd, *J* = 5.9, 9.6 Hz), 2.53-2.65 (2H, m), 2.45 (1H, d, *J* = 2.0 Hz), 2.39 (1H, ddd, *J* = 5.3, 7.1, 14.9 Hz), 2.22 (1H, ddd, *J* = 4.3, 7.1, 14.9 Hz), 1.89-1.96 (1H, m), 1.88 (3H, s); IR 1740 cm^{-1}; MS *m/z* 453 (M^+); HRMS *m/z* calcd for $C_{25}H_{23}N_3O_5Si$ (M^+) 453.1359, found: 453.1352.

(1*S*,10*R*,10a*R*,2'*R*)-10-(2'-Acetoxy-3'-butynyl)-1-imidazolylthiocarbonyloxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine (25b); from **24b** (0.068 g, 0.20 mmol), **25b** (0.078 g, 87%) was obtained as an oil; $[\alpha]_D^{26}$ +110.9˚ (c 1.38, $CHCl_3$); ^{1}H NMR δ 8.37, 7.67, 7.06, 6.86, 6.53 (each 1H, s), 5.94 (2H, s), 5.71 (1H, ddd, *J* = 2.6, 5.2, 7.9 Hz), 5.45 (1H, dt, *J* = 2, 7.3 Hz), 3.90, 3.57 (each 1H, *J* = 14.2 Hz), 3.08-3.20 (2H, m), 2.84 (1H, dd, *J* = 5.6, 9.2 Hz), 2.52-2.66 (2H, m), 2.45 (1H, d, *J* = 2 Hz), 2.23-2.30 (2H, m), 2.06 (3H, s), 1.91-1.97 (1H, m); IR 1741 cm^{-1}; MS *m/z* 453 (M^+); HRMS *m/z* calcd for $C_{25}H_{23}N_3O_5Si$ (M^+) 453.1359, found: 453.1346.

(1*S*,10*R*,10a*R*,2'*S*)-10-(2'-Acetoxy-4'-trimethylsilyl-3'-butynyl)-1-imidazolylthiocarbonyloxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine (28a); from **27a** (0.202 g, 0.49 mmol), **28a** (0.250 g, 98%) was obtained as amorphous solid; $[\alpha]_D^{27}$ +57.2˚ (c 1.02, $CHCl_3$); ^{1}H NMR δ 8.39, 7.68, 7.04, 6.86, 6.51 (5H, each s), 5.90 (2H, s), 5.64 (1H, ddd, *J* = 2.6, 5.9, 7.9 Hz), 5.53 (1H, t, *J* = 7.4 Hz), 3.87, 3.55 (each 1H, *J* = 14.1 Hz), 3.07-3.18 (2H, m), 2.98 (1H, dd, *J* = 5.9, 9.6 Hz), 2.49-2.65 (2H, m), 2.30 (1H, ddd, *J* = 5.6, 7.4, 14.5 Hz), 2.17 (1H, ddd, *J* = 4, 7.4, 14.5 Hz), 1.87-1.98 (1H, m), 1.85 (3H, s),

0.12 (9H, s); IR 2179, 1740 cm^{-1}; MS *m/z* 525 (M^+); HRMS *m/z* calcd for $C_{26}H_{31}N_3O_5SSi$ (M^+) 525.1754, found: 525.1750.

(1*S*,10*R*,10a*R*,2'*R*)-10-(2'-Acetoxy-4'-trimethylsilyl-3'-butynyl)-1-imidazolylthiocarbonyloxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine (28b); from **27b** (0.140 g, 0.34 mmol), **28b** (0.169 g, 95%) was obtained as amorphous solid; $[\alpha]_D^{27}$ +111.7˚ (c 1.16, $CHCl_3$); ^{1}H NMR δ 8.35, 7.64, 7.04, 6.90, 6.51 (5H, each s), 5.92, 5.91 (each 1H, d, *J* = 1.3 Hz), 5.71 (1H, ddd, *J* = 3, 5.5, 7.4 Hz), 5.51 (1H, t, *J* = 7.1 Hz), 3.89, 3.59 (each 1H, d, *J* = 14.3 Hz), 3.06-3.16 (2H, m), 2.82 (1H, dd, *J* = 5.5, 9.2 Hz), 2.43-2.65 (2H, m), 2.09-2.27 (2H, m), 2.03 (3H, s), 1.92-2.01 (1H, m), 0.12 (9H, s); IR 2179, 1740 cm^{-1}; MS *m/z* 525 (M^+); HRMS *m/z* calcd for $C_{26}H_{31}N_3O_5SSi$ (M^+) 525.1754, found: 525.1756.

Radical reaction of 25a,b. To a solution of **25a** or **25b** (0.041 g, 0.09 mmol) in benzene or toluene under reflux was added a solution of AIBN (0.007 g, 0.54 mmol) and Bu_3SnH (0.055 g, 0.18 mmol) or Cy_3SnH (0.067 g, 0.18 mmol) in benzene or toluene using syringe pump over a period of 30 min. Then, the solvent was removed *in vacuo* to give a residue, which was purified by column chromatography (hexane then $CHCl_3$: MeOH = 30 : 1) and preparative TLC (AcOEt : Et_3N = 25 : 2) to afford **29**-**31** or **32**-**34**.

2α-Acetoxy-3-methylene-α-lycorane (29); oil; $[\alpha]_D^{28}$ +42.0˚ (c 1.03, $CHCl_3$); ^{1}H NMR δ 6.66, 6.62 (each 1H, s), 5.91 (2H, s), 5.60 (1H, t, *J* = 4.0 Hz), 5.23, 5.11 (each 1H, s), 4.13, 3.84 (each 1H, d, *J* = 14.9 Hz), 3.15 (1H, q, *J* = 8.9 Hz), 3.02 (1H, dt, *J* = 7.6, 9.2 Hz), 2.93 (1H, dt, *J* = 3.6, 8.9 Hz), 2.80 (1H, dt, *J* = 4, 11 Hz), 2.67 (1H, dd, *J* = 7.6, 11 Hz), 2.44, 1.74 (each 1H, dt, *J* = 4, 13.5 Hz), 2.10 (3H, s), 1.99-2.20 (2H, m); ^{13}C NMR δ 170.0, 146.6, 145.8, 143.9, 132.6, 128.1, 115.4, 107.1, 104.5, 100.8, 72.7, 64.9, 54.0, 53.8, 43.3, 31.8, 30.1, 29.3, 21.5; IR 1738 cm^{-1}; MS *m/z* 327 (M^+); HRMS *m/z* calcd for $C_{19}H_{21}NO_4$ (M^+) 327.1471, Found: 327.1476.

18-Acetoxy-12-aza-5,7-dioxapentacyclo[10.7.1.0<2,10>.0<4,8>.0<15,20>]licosa-[2(10),3,8(9),16-tetraene (30); amorphous solid; ^{1}H NMR δ 6.74, 6.49 (each 1H, s), 5.89, 5.88 (each 1H, d, *J* = 1.3 Hz), 5.51-5.66 (3H, m), 3.97, 3.44 (each 1H, d, *J* = 14.9 Hz), 3.15-3.25 (2H, m), 2.87-2.98 (1H, m), 2.15-2.34 (3H, m), 2.09 (3H, s), 1.72-1.95 (3H, m); IR 1726 cm^{-1}; MS *m/z* 327 (M^+); HRMS *m/z* calcd for $C_{19}H_{21}NO_4$ (M^+) 327.1471, found: 327.1472.

(10*R*,10a*R*,2'*S*)-10-(2'-Acetoxy-3'-butynyl)-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydro-benz[*f*]indolizidine (31); oil; ^{1}H NMR δ 6.84 6.50 (each 1H, s), 5.91, 5.90 (each 1H, d, *J* = 1.3 Hz), 5.49 (1H, ddd, *J* = 2, 6.5, 8.6 Hz), 3.91, 3.34 (each 1H, d, *J* = 14 Hz), 3.20 (1H, dt, *J* = 2.6, 8.5 Hz), 2.85-2.95 (1H, m), 2.53 (1H, d, *J* = 2 Hz), 1.50-2.37 (7H, m), 2.00 (3H, s, Ac), 1.25-1.40 (1H, m); IR 2121, 1740 cm^{-1}; MS *m/z* 327 (M^+); HRMS *m/z* calcd for $C_{19}H_{21}NO_4$ (M^+) 327.1471, found: 327.1471.

2β-Acetoxy-3-methylene-α-lycorane (32); oil; $[\alpha]_D^{29}$ +22.9˚ (c 1.13, $CHCl_3$); ^{1}H NMR δ 6.65, 6.60 (each 1H, s, arom. Hx2), 5.91 (2H, s, OCH_2O), 5.59 (1H, dd, *J* = 6.4, 8.0 Hz, H-2), 5.12, 5.04 (each 1H, s, olefinic Hx2), 4.09, 3.83 (each 1H, d, *J* = 15.0 Hz, H-7x2), 2.93 (1H, dt, *J* = 3.6, 8.9 Hz, H-5), 3.20 (1H, q,

J = 8.3 Hz, H-3a), 3.10 (1H, q, *J* = 8.9 Hz, H-5), 2.70 (1H, ddd, *J* = 3.4, 6.4, 12 Hz, H-1), 2.68 (1H, dd, *J* = 8.3, 12 Hz, H-11c), 2.56 (1H, dt, *J* = 3.4, 12 Hz, H-11b), 2.13 (3H, s, Ac), 1.95-2.10 (2H, m, H-4x2), 1.42 (1H, dt, *J* = 8, 12 Hz, H-1); ^{13}C NMR δ 170.3 (s), 146.3 (s), 145.8 (s), 145.1 (s), 132.3 (s), 128.5 (s), 111.6 (t), 107.0 (d), 104.5 (d), 100.8 (t), 72.7 (d), 65.0 (d), 54.3 (t), 53.5 (t), 43.4 (d), 33.4 (d), 32.7 (t), 28.6 (t), 21.3 (q); IR 1740 cm^{-1}; MS *m/z* 327 (M^+); HRMS *m/z* calcd for $C_{19}H_{21}NO_4$ (M^+) 327.1471, found: 327.1476.

2β-Acetoxy-3-methylene-β-lycorane (33); oil; ^{1}H NMR δ 6.80, 6.67 (each 1H, s, arom. Hx2), 5.91, 5.90 (each 1H, d, *J* = 1.3 Hz, OCH_2O), 5.48 (1H, dd, *J* = 5.3, 11.2 Hz, H-2), 4.92, 4.80 (each 1H, s, olefinic Hx2), 4.09, 3.39 (each 1H, d, *J* = 14.5 Hz, H-7x2), 3.50 (1H, ddd, *J* = 5.7, 8.2, 9.8 Hz, H-5), 2.81 (1H, t, *J* = 10.9 Hz, H-11b), 2.67 (1H, ddd, *J* = 4.3, 5, 11.9 Hz, H-1), 2.33-2.50 (2H, m, H-3a, H-5), 2.18 (3H, s, Ac), 1.90-2.09 (2H, m, H-4x2), 1.69 (1H, t, *J* = 10.7 Hz, H-11c), 1.42 (1H, q, *J* = 11.8 Hz, H-1); ^{13}C NMR δ 170.1 (s), 146.5 (s), 146.1 (s), 146.0 (s), 129.4 (s), 128.4 (s), 107.0 (d), 105.3 (d), 102.7 (t), 100.9 (t), 73.8 (d), 71.8 (d), 57.0 (t), 54.2 (t), 46.1 (d), 38.8 (d), 35.6 (t), 23.4 (t), 21.1 (q); IR 1743 cm^{-1}; MS *m/z* 327 (M^+); HRMS *m/z* calcd for $C_{19}H_{21}NO_4$ (M^+) 327.1471, found: 327.1473.

(10*R*,10a*R*,2'*R*)-10-(2'-Acetoxy-3'-butynyl)-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine (34); oil; ^{1}H NMR δ 6.83, 6.50 (each 1H, s, arom. Hx2), 5.91, 5.90 (each 1H, d, *J* = 1.3 Hz, OCH_2O), 5.44 (1H, ddd, *J* = 2, 5.3, 8.7 Hz, C<u>H</u>OAc), 3.91, 3.30 (each 1H, d, *J* = 14 Hz, H-5x2), 3.20 (1H, dt, *J* = 2.6, 8.5 Hz), 2.78-2.88 (1H, m), 2.48 (1H, d, *J* = 2 Hz, C≡CH), 1.57-2.48 (7H, m), 2.09 (3H, s, Ac), 1.25-1.36 (1H, m); IR 2121, 1740 cm^{-1}; MS *m/z* 327 (M^+); HRMS *m/z* calcd for $C_{19}H_{21}NO_4$ (M^+) 327.1471, found: 327.1470.

(1*S*,10*R*,10a*R*,2'*S*)- and (1*S*,10*R*,10a*R*,2'*R*)-10-(2'-Acetoxy-4'-trimethylsilyl-3'-butynyl)-1-triethyl-silyloxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidines (26a and 26b). To a stirred solution of trimethylsilylacetylene (0.54 mL, 3.82 mmol) in THF (20 mL) at 0˚C was added 1.54 M BuLi in hexane (2.3 mL, 3.54 mmol) over a period of 3 min. After being stirred for 10 min, a solution of **21** (0.671 g, 1.72 mmol) in THF (8 mL) was added over a period of 5 min and stirring was continued for additional 30 min. Then, Ac_2O (0.5 mL) was added and the mixture was stirred for 10 min. The reaction was quenched with saturated NH_4Cl. The mixture was extracted with Et_2O. Usual work-up gave a residue, which was purified by column chromatography (AcOEt : hexane = 3 : 1 to 1 : 1) to afford **26a** (0.476 g, 52%) and **26b** (0.400 g, 44%) as each oil. **26a**; $[\alpha]_D^{27}$ +21.9˚ (c 1.02, $CHCl_3$); ^{1}H NMR δ 6.80, 6.45 (each 1H, s), 5.85 (2H, s), 5.65 (1H, dd, *J* = 4.4, 9 Hz), 4.08 (1H, ddd *J* = 5, 5.9, 7.9 Hz), 3.69, 3.43 (each 1H, d, *J* = 14.5 Hz), 2.93-3.04 (2H, m), 2.43-2.61 (3H, m), 2.28 (1H, dt, *J* = 5, 14.9 Hz), 2.14 (1H, ddd, *J* = 9, 12.9, 16.4 Hz), 1.75 (3H, s), 1.66 (1H, ddd, *J* = 4.4, 8.2, 16.4 Hz), 0.97 (9H, t, *J* = 7.8 Hz), 0.48 (6H, q, *J* = 7.8 Hz), 0.13 (9H, s); IR 2181, 1745 cm^{-1}; MS *m/z* 529 (M^+); HRMS *m/z* calcd for $C_{28}H_{43}NO_5Si_2$ (M^+) 529.2680, found: 529.2674. **26b**; $[\alpha]_D^{27}$ +74.4˚ (c 1.03, $CHCl_3$); ^{1}H NMR δ 6.85, 6.48

(each 1H, s), 5.90, 5.88 (each 1H, d, *J* = 1.5 Hz), 5.50 (1H, t, *J* = 8.0 Hz), 4.11(1H, ddd, *J* = 5.3, 6.3, 7.4 Hz), 3.71, 3.48 (each 1H, d, *J* = 14.2 Hz), 2.89-3.00 (2H, m), 2.59 (1H, q, *J* = 8.4 Hz), 2.08-2.40 (4H, m), 2.04 (3H, s), 1.67 (1H, ddd, *J* = 4.3, 8.0, 16.8 Hz), 0.98 (9H, t, *J* = 7.8 Hz), 0.65 (6H, q, *J* = 7.8 Hz), 0.13 (9H, s); IR 2179, 1747 cm^{-1}; MS *m/z* 529 (M^+); HRMS *m/z* calcd for $C_{28}H_{43}NO_5Si_2$ (M^+) 529.2680, found: 529.2670.

(1*S*,10*R*,10a*R*,2'*S*)-10-(2'-Acetoxy-4'-trimethylsilyl-3'-butynyl)-1-hydroxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine (27a). A solution of **26a** (0.292 g, 0.55 mmol) and 1N HCl (3 mL, 3 mmol) in THF (10 mL) was stirred at rt for 15 min. Similar work-up as described above gave a residue, which was purified by preparative TLC (AcOEt : MeOH = 25 : 1) to afford **27a** (0.216 g, 95%) as amorphous solid; $[\alpha]_D^{27}$ -16.4˚ (c 1.17, $CHCl_3$); ^{1}H NMR δ 6.89, 6.44 (each 1H, s), 5.85 (2H, s), 5.63 (1H, t, *J* = 7.6 Hz), 4.19 (1H, ddd, *J* = 2.3, 5.6, 10.9 Hz), 3.79, 3.41 (each 1H, d, *J* = 13.9 Hz), 3.15 (1H, br s), 2.87-23.15 (2H, m), 2.48 (1H, q, *J* = 8.8 Hz), 2.15-2.31 (4H, m), 1.99 (3H, s), 1.60-1.73 (1H, m), 0.14 (9H, s); IR 2179, 1734 cm^{-1}; MS *m/z* 415 (M^+); HRMS *m/z* calcd for $C_{22}H_{29}NO_5Si$ (M^+) 415.1815, found: 415.1819**.**

(1*S*,10*R*,10a*R*,2'*R*)-10-(2'-Acetoxy-4'-trimethylsilyl-3'-butynyl)-1-hydroxy-7,8-methylenedioxy-1,2,3,5,10,10a-hexahydrobenz[*f*]indolizidine (27b). A solution of **26b** (0.244 g, 0.46 mmol) and 1N HCl (3 mL, 3 mmol) in THF (10 mL) was stirred at rt for 15 min. Similar work-up as described above gave a residue, which was purified by preparative TLC (AcOEt : MeOH = 25 : 1) to afford **27b** (0.174 g, 91%) as amorphous solid; $[\alpha]_D^{27}$ +97.2˚ (c 1.13, $CHCl_3$); ^{1}H NMR δ 6.85, 6.45 (each 1H, s), 5.86 (2H, s), 5.64 (1H, t, *J* = 6.9 Hz), 4.14 (1H, ddd, *J* = 2.6, 5.6, 12.9 Hz), 3.79, 3.43 (each 1H, d, *J* = 14.2 Hz), 3.01 (1H, t, *J* = 8.3 Hz), 2.81-3.04 (4H, m), 2.51 (1H, q, *J* = 8.8 Hz), 2.12-2.39 (3H, m), 2.07 (3H, s), 1.58-1.71 (1H, m), 0.11 (9H, s); IR 2177, 1740 cm^{-1}; MS *m/z* 415 (M^+); HRMS *m/z* calcd for $C_{22}H_{29}NO_5Si$ (M^+) 415.1815, found: 415.1813.

Radical reaction of 28a (Table 2, run 12). To a solution of **28a** (0.1053 g, 0.2 mmol) in toluene (13 mL) under reflux was added a solution of AIBN (0.016 g, 0.1 mmol) and tricyclohexyltin hydride (0.134 g, 0.36 mmol) in toluene (7 mL) over a period of 1 h. Then, the solvent was removed *in vacuo* to give a residue, which was purified by column chromatography (hexane then $CHCl_3$: MeOH = 10 : 1), followed by preparative TLC ($CHCl_3$: MeOH = 15 : 1) to afford **3a** (0.0334 g, 42%) and **3b** (0.0336 g, 42%).

(3*Z*)-2α-Acetoxy-3-trimethylsilylmethylene-α-lycorane (3a); $[\alpha]_D^{25}$ -0.77˚ (c 1.51, $CHCl_3$); ^{1}H NMR δ 6.64, 6.62 (each 1H, s, arom. Hx2), 5.89, 5.88 (each 1H, d, *J* = 1.6 Hz, OCH_2O), 5.73 (1H, t, *J* = 3 Hz, H-2), 5.72 (1H, s, olefinic H), 4.24, 3.73 (each 1H, d, *J* = 15.3 Hz, H-7x2), 3.34 (1H, q, *J* = 8.6 Hz, H-5), 3.03 (1H, ddd, *J* = 5.7, 8.6, 11.2 Hz, H-3a), 2.84 (1H, dt, *J* = 3.6, 8.6 Hz, H-5), 2.73 (1H, dd, *J* = 8.6, 10 Hz, H-11c), 2.71 (1H, dd, *J* = 10, 12.6 Hz, H-11b), 2.66 (1H, dt, *J* = 3, 13.7 Hz, H-1), 2.18-2.34 (1H, m, H-4), 2.04 (3H, s, Ac), 1.90-2.02 (1H, m, H-4), 1.49 (1H, ddd, *J* = 3, 12.6, 13.7 Hz, H-1), 0.13 (9H, s,

$SiMe_3$); ^{13}C NMR δ 169.7, 151.3, 146.2, 145.4, 134.6, 133.0, 128.5, 106.8, 103.9, 100.5, 72.3, 64.9, 53.9, 53.6, 49.2, 30.7, 29.8, 27.2, 21.4, -0.1; IR 1736 cm^{-1}; MS *m/z* 339 (M^+); HRMS m/z calcd for $C_{22}H_{29}NO_4Si$ (M^+) 339.1866, found: 339.1866.

(3*E*)-2α-Acetoxy-3-trimethylsilylmethylene-α-lycorane (3b); $[\alpha]_D^{25}$ -29.6˚ (c 1.03, $CHCl_3$); ^1H NMR δ 6.65, 6.62 (each 1H, s, arom. Hx2), 5.89 (2H, s, OCH_2O), 5.80 (1H, s, olefinic H), 5.54 (1H, t, *J* = 2.8 Hz, H-2), 4.29, 3.76 (each 1H, d, *J* = 15.5 Hz, H-7x2), 3.39 (1H, q, *J* = 8.6 Hz, H-5), 3.21 (1H, ddd, *J* = 6, 8.6, 10.6 Hz, H-3a), 2.80-2.91 (2H, m, H-5, H-11b), 2.69 (1H, dd, *J* = 6, 10.6 Hz, H-11c), 2.52 (1H, dt, *J* = 2.8, 13.9 Hz, H-1), 2.14-2.28 (1H, m, H-4), 1.91-2.01 (1H, m, H-4), 2.04 (3H, s, Ac), 1.55 (1H, ddd, *J* = 2.8, 12.9, 13.9 Hz, H-1), 0.12 (9H, s, $SiMe_3$); ^{13}C NMR δ 169.8, 151.3, 146.3, 145.5, 134.9, 133.1, 128.6, 106.9, 103.9, 100.6, 77.6, 64.9, 53.9, 53.5, 43.9, 31.2, 29.5, 26.9, 21.6, -0.1; IR 1738 cm^{-1}; MS *m/z* 339 (M^+); HRMS m/z calcd for $C_{22}H_{29}NO_4Si$ (M^+) 339.1866, found: 339.1849.

Radical reaction of 28b (Table 2, Run 13). To a solution of **28b** (0.042 g, 0.08 mmol) in toluene (5 mL) under reflux was added a solution of AIBN (0.007 g, 0.04 mmol) and Bu_3SnH (0.047 g, 0.15 mmol) in toluene (3 mL) using syringe pump over a period of 30 min. Then, the solvent was removed *in vacuo* to give a residue, which was purified by column chromatography (hexane then $CHCl_3$: MeOH = 10 : 1), followed by preparative TLC (AcOEt : MeOH = 30 : 1) to afford **4a** (0.009 g, 27%), **4b** (0.005 g, 16%) and **35** (0.003 g, 10%).

(3*Z*)-2β-Acetoxy-3-trimethylsilylmethylene-α-lycorane (4a); $[\alpha]_D^{25}$ +37.5˚ (c 1.09, $CHCl_3$); ^1H NMR δ 6.65, 6.54 (each 1H, s, arom. Hx2), 5.89, 5.88 (each 1H, d, *J* = 1.3 Hz, OCH_2O), 5.76 (1H, dd, *J* = 3.2, 8.5 Hz, H-2), 5.64 (1H, d, *J* = 2.3 Hz, olefinic H), 3.98, 3.76 (each 1H, d, *J* = 14.9 Hz, H-7x2), 3.19 (1H, q, *J* = 8.6 Hz, H-5), 3.06 (1H, ddd, *J* = 2.3, 6.4, 8.7 Hz, H-3a), 2.86 (1H, dt, *J* = 5.0, 8.5, 13.8 Hz, H-1), 2.56-2.67 (2H, m, H-5, H-11c), 2.35 (1H, dt, *J* = 5, 12 Hz, H-11b), 2.02 (3H, s, Ac), 1.93-2.12 (2H, m, H-4x2), 1.45 (1H, dt, *J* = 3.2, 13.8 Hz, H-1), 0.14 (9H, s, $SiMe_3$); ^{13}C NMR δ 170.2, 153.1, 146.4, 145.9, 131.9, 128.9, 128.6, 106.9, 105.5, 100.9, 73.4, 65.2, 55.1, 53.0, 41.6, 35.8, 31.2, 28.2, 21.4, 0.3; IR 2924, 1716, 1621 cm^{-1}; MS *m/z* 339 (M^+); HRMS m/z calcd for $C_{22}H_{29}NO_4Si$ (M^+) 339.1866, found: 339.1870.

(3*E*)-2β-Acetoxy-3-trimethylsilylmethylene-α-lycorane (4b); $[\alpha]_D^{27}$ -41.5˚ (c 0.56, $CHCl_3$); ^1H NMR δ 6.63, 6.61 (each 1H, s, arom. Hx2), 5.89 (2H, s, OCH_2O), 5.50-5.56 (2H, m, H-2, olefinic H), 4.27, 3.73 (each 1H, d, *J* = 15.8 Hz, H-7x2), 3.34-3.47 (2H, m, H-3a, H-5), 2.79-2.88 (1H, m, H-5), 2.66-2.76 (2H, m, H-11b, H-11c), 2.56 (1H, ddd, *J* = 2.6, 4.3, 12.5 Hz, H-1), 2.19 (3H, s, Ac), 1.94-2.08 (2H, m, H-4x2), 1.35-1.51 (1H, m, H-1), 0.13 (9H, s, $SiMe_3$); ^{13}C NMR δ 170.4, 152.5, 146.6, 145.8, 133.0, 128.0, 122.2, 107.2, 104.2, 101.0, 73.0, 65.5, 54.0, 53.8, 45.8, 33.2, 31.8, 29.0, 21.4, 0.4; IR 1737 cm^{-1}; MS *m/z* 339 (M^+); HRMS m/z calcd for $C_{22}H_{29}NO_4Si$ (M^+) 339.1866, found: 339.1874.

(3*Z*)-2β-Acetoxy-3-trimethylsilylmethylene-β-lycorane (35); $[\alpha]_D^{27}$ +19.0˚ (c 0.41, $CHCl_3$); ^1H NMR δ 6.65, 6.50 (each 1H, s, arom. Hx2), 5.89, 5.88 (each 1H, d, *J* = 1.3 Hz, OCH_2O), 5.56 (1H, dd, *J* = 4.5, 11

Hz, H-2), 5.29 (1H, s, olefinic H), 4.07, 3.38 (each 1H, d, *J* = 14.9 Hz, H-7x2), 3.48 (1H, dt, *J* = 5.6, 8.9 Hz, H-5), 2.36-2.53 (2H, m, H-3a, H-5), 2.87 (1H, t, *J* = 11 Hz, H-11b), 2.72 (1H, dt, *J* = 4.5, 11 Hz, H-1), 2.18 (3H, s, Ac), 1.84-2.12 (2H, m, H-4x2), 2.87 (1H, t, *J* = 11 Hz, H-11c), 1.36 (1H, q, *J* = 11 Hz, H-1), 0.13 (9H, s, $SiMe_3$); ^{13}C NMR δ 170.2, 153.7, 146.2, 146.0, 129.5, 128.3, 117.5, 106.9, 105.3, 100.9, 77.2, 72.2, 57.2, 54.2, 49.2, 39.0, 36.1, 23.5, 22.1, 1.5; IR 1732 cm^{-1}; MS *m/z* 339 (M^+); HRMS m/z calcd for $C_{22}H_{29}NO_4Si$ (M^+) 339.1866, found: 339.1875.

ACKNOWLEDGEMENTS

The authors are grateful to Mrs. F. Hasegawa of this faculty for her MS spectral measurement.

REFERENCES AND NOTES

1. For reviews; (a) S. F. Martin, 'The Alkaloids; Chemistry and Biology,' Vol. 30, Academic Press, New York, 1987, p. 251. (b) O. Hoshino, 'The Alkaloids; Chemistry and Biology,' Vol. 51, Academic Press, New York, 1998, p. 323.
2. (a) G. R. Pettit, V. Gaddamidi, A. Goswami, and G. M. Cragg, *J. Nat. Prod*., 1984, **47**, 796. (b) B. Gabrielsen, T. P. Monath, J. W. Huggins, D. F. Kefauver, G. R. Pettit, G. Groszek, M. Hollingshead, J. Kirsi, W. M. Shannon, E. M. Schubert, J. Dare, B. Ugarkar, M. A. Ussery, and M. Phelan, *J. Nat. Prod*., 1992, **55**, 1569. (c) E. Furusawa, S. Furusawa, S. Morimoto, and W. Cutting, *Proc. Sci. Exp. Biol. Med*., 1971, **136**, 1168. (d) E. Furusawa, N. Suzuki, S. Ramanathan, S. Furusawa, and W. Cutting, *Proc. Sci. Exp. Biol. Med*., 1972, **140**, 1034. (e) G. Citoglu, M. Tanker, and B. Gumusel, *Phytother. Res.*, 1998, **12**, 205. (f) A. Yui, M. Mikami, M. Kitahara, and M. Yamazaki, *Immunopharmacology*, 1998, **40**, 151. (g) M. Mikami, M. Kitahara, M. Kitano, Y. Ariki, Y. Mimaki, Y. Sashida, M. Yamazaki, and S. Yui, *Biol. Pharm. Bull*., 1999, **22**, 674. (h) G. Schmeda-Hirschmann, L. Astudillo, J. Bastida, F. Viladomat, and C. Codina, *Bol. Soc. Chil. Quim.*, 2000, **45**, 515.
3. (a) Y. Tsuda, T, Sano, J. Taga, K. Isobe, J. Toda, H. Irie, H. Tanaka, S. Takagi, M. Yamaki, and M. Murata, *J. Chem. Soc., Chem. Commun.*, 1975, 933. (b) Y. Tsuda, T. Sano, J. Taga, K. Isobe, J. Toda, S. Takagi, M. Yamaki, M. Murata, H. Irie, and H. Tanaka, *J. Chem. Soc., Perkin Trans. 1*, 1978, 1358. (c) H. Irie, Y. Nagai, K. Tamoto, and H. Tanaka, *Chem. Commun.*, 1973, 302. (d) T. Sano, N. Kashiwaba, J. Toda, Y. Tsuda, and H. Irie, *Heterocycles*, 1980, **14**, 1097.
4. (a) B. Umezawa, O. Hoshino, S. Sawaki, H. Sashida, and K. Mori, *Heterocycles*, 1979, **12**, 1475. (b) B. Umezawa, O. Hoshino, S. Sawaki, H. Sashida, K. Mori, Y. Hamada, K. Kotera, and Y. Iitaka, *Tetrahedron*, 1984, **40**, 1783. (c) O. Hoshino, M. Ishizaki, K. Kamei, M. Taguchi, N. Nagao, K. Iwaoka, S. Sawaki, B. Umezawa, and Y. Iitaka, *Chem. Lett.*, 1991, 1365. (d) O. Hoshino, M. Ishizaki,

K. Kamei, M. Taguchi, T. Nagao, K. Iwaoka, S. Sawaki, B. Umezawa, and Y. Iitaka, *J. Chem. Soc., Perkin Trans. 1,* 1996, 571.

5. O. Møller, E.-M. Steinberg, and K. Torssell, *Acta Chem. Scand. B32*, 1978, 98.
6. (a) S. F. Martin and C. Tu, *J. Org. Chem.,* 1981, **46**, 3763. (b) S. F. Martin, C. Tu, M. Kimura, and S. H. Simonsen, *J. Org. Chem.,* 1982, **47,** 3634.
7. R. K. Boeckman Jr., S. W. Goldstein, and M. A. Walters, *J. Am. Chem. Soc.,* 1988, **110**, 8250.
8. A. G. Schultz, M. A. Hploboski, and M. S. Smyth, *J. Am. Chem. Soc.,* 1996, **118**, 6210.
9. (a) O. Hoshino, M. Ishizaki, K. Saito, and K. Yumoto, *J. Chem. Soc., Chem. Commun.,* 1990, 420. (b) O. Hoshino and M. Ishizaki, *Chem. Lett.,* 1990, 1817. (c) M. Ishizaki, O. Hoshino, and Y. Iitaka, *Tetrahedron Lett.,* 1991, **32**, 7079. (d) M. Ishizaki, O. Hoshino, and Y. Iitaka, *J. Org. Chem.,* 1992, **57**, 7285. (e) M. Ishizaki, K. Kurihara, E. Tanazawa, and O. Hoshino, *J. Chem. Soc., Perkin Trans. 1,* 1993, 101. (f) M. Ishizaki, K. Ozaki, A. Kanematsu, K. Isoda, and O. Hoshino, *J. Org. Chem.,* 1993, **58**, 3877. (g) O. Hoshino and M. Ishizaki, *J. Synth. Org. Chem. Jpn.,* 1994, **52**, 207.
10. M. Ishizaki, Y. Kai, Y. Makanae, and O. Hoshino, *ACH Model in Chemistry*, 1998, **132**, 529.
11. (a) D. J. Hart and Y.-M. Tsai, *J. Am. Chem. Soc.,* 1984, **106**, 8209. (b) D. A. Burnett, J.-K. Choi, D. J. Hart, and Y.-M. Tsai, *J. Am. Chem. Soc.,* 1984, **106**, 8201. (c) J.-K. Choi and D. J. Hart, *Tetrahedron,* 1985, **41**, 3959.
12. A. R. Chamberlin and J. Y. L. Chung, *J. Am. Chem. Soc.,* 1983, **105**, 3653.
13. Similar reaction of TBS ether afforded 2.9 : 1 mixture of cyclized products in 92% yield.
14. Cy_3SnH is known as superior reagent to Bu_3SnH in radical cyclization reaction to alkynyl group; E. J. Corey and M. M. Mehrotra, *Tetrahedron Lett.,* 1988, **29**, 57.
15. (a) G. Büchi and H. Wüest, *J. Org. Chem.,* 1979, **44**, 546. (b) P. C. P. Page and S. Rosenthal, *Tetrahedron,* 1990, **46**, 2573.
16. (a) HI; K. Utimoto, M. Kitai, and H. Nozaki, *Tetrahedron Lett.,* 1975, 2825. (b) $PhSO_2H$; G. Büchi and H. Wüest, *Tetrahedron Lett.,* 1977, 4305. (c) TsOH; S. Fujioka, M. Inoue, K. Utimoto, and H. Nozaki, *Tetrahedron Lett.,* 1984, **25**, 1999. (d) TBAF and related reagents; S. D. Burke, A. D. Piscopio, B. E. Marron, M. A. Matulanko, and G. Pan, *Tetrahedron Lett.,* 1991, **32**, 857; T. H. Chan and W. Mychajlowskij, *Tetrahedron Lett.,* 1974, 3479. (e) TFA; T. Sato, K. Okamoto, Y. Nakano, J. Uenishi, and M. Ikeda, *Heterocycles,* 2001, **54**, 747.