Ten New Lycopodium Alkaloids Having the Lycopodane Skeleton Isolated from *Lycopodium serratum* THUNB.

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Ten new alkaloids, lycoposerramines-F (1), -G (2), -H (3), -I (4), -J (5), -K (6), -L (7), -M (8), -N (9), and -O (10), having lycopodine-related structures, were isolated from the club moss *Lycopodium serratum* THUNB. and their structures were elucidated on the basis of spectroscopic analysis and/or chemical transformation.

Key words alkaloid; *Lycopodium*; structure elucidation; X-ray crystal structure; NMR; chemical transformation

Lycopodium alkaloids[1—3] isolated from club mosses of the genus *Lycopodium* (Lycopodiaceae) exhibit fascinating complex structures and have attracted the attention of synthetic organic chemists[4—10] as well as pharmacologists because of such potent biological activities as an inhibitory effect on acetylcholinesterase.[11] Recent extensive studies on the chemical constituents in *Lycopodium* plants have resulted in the isolation of a number of new alkaloids having novel and diverse structures.[12—26] Recently, we have also isolated several new alkaloids having fawcettimine-related structures from *Lycopodium serratum* THUNB.[27—29] In our continuing investigation of the structurally unique Lycopodium alkaloids from this plant, we have purified and identified ten new alkaloids possessing lycopodine-related skeletons. We report herein the structure elucidation of those alkaloids.

The crude basic fraction obtained by a conventional procedure from the MeOH extract of the club moss *L. serratum* collected in Boso Peninsula, Japan, was purified by repeated chromatography over SiO_2 to afford new alkaloids, lycoposerramines-F (**1**, 0.03% based on the crude base), -G (**2**, 0.13%), -H (**3**, 0.29%), -I (**4**, 0.14%), -J (**5**, 0.08%), -K (**6**, 0.05%), -L (**7**, 0.10%), -M (**8**, 0.10%), -N (**9**, 0.03%), and -O (**10**, 0.06%), along with known alkaloids belonging to the lycopodine group, *i.e.*, lycopodine,[30] lucidioline (**11**),[31] L.20 (**12**),[15,32,33] lycodoline,[15,24,30,34] deacetyllycoclavine (**15**),[35,36] acetyllycoclavine (**17**),[37] serratidine,[38] and serratezomine C.[15]

Compound **1**, named lycoposerramine-F, was obtained as colorless prisms (mp >300 °C). High-resolution fast atom bombardment mass spectrometry (HR-FAB-MS) analysis gave *m/z* 296.1848 $(M+H)^+$ (Δ −1.4 mmu) and established the molecular formula as $C_{16}H_{25}NO_4$. IR absorption implied the presence of hydroxyl (3403 cm^{-1}) and ketone (1713 cm^{-1}) groups. ^{1}H- and ^{13}C-NMR spectra (see Table 1) as well as distorsionless enhancement by polarization transfer (DEPT) spectra suggested the presence of one ketone, two sp^3 quaternary carbons having an oxygen function, one sp^3 quaternary carbon, two sp^3 methines, nine sp^3 methylenes, and one methyl group. ^{1}H–^{1}H correlation spectroscopy (COSY) and ^{1}H-detected heteronuclear multiple quantum coherence (HMQC) spectra indicated the presence of the following three fragments: $-CH_2CH_2CH_2-$ (C1—C3), $-CH_2CH_2CH_2-$ (C9—C11), and $-CH_2CHCH_2CH(CH_3)CH_2-$ (C6—C8—C15(C16)—C14), as shown by a bold line in Fig. 1. ^{1}H-Detected heteronuclear multiple bond connectivity (HMBC) correlations between the protons (δ 2.14, 3.24, H-6) at the terminal carbon (C-6) and the carbonyl carbon (C-5, δ 207.3) as well as an oxygenated quaternary carbon (C-4, δ 73.6) indicated the presence of an α-hydroxyketone residue. Further, HMBC correlations between the protons at the same terminal carbon (C-6) and the other oxygenated quaternary carbon (C-12, δ 78.9) and between the protons (δ 2.62, 1.84, H-14) at the other terminal carbon (C-14) and a quaternary carbon (C-13), C-4 and C-12 indicated the presence of a bicyclo[3.3.1]nonane system including a ketone and two tertiary hydroxyl groups. HMBC correlations between the protons (δ 2.93, 3.52, H-1) at the methylene carbon (C-1) bearing a nitrogen and a methylene carbon (C-9, δ 64.9) as well as a quaternary carbon (C-13, δ 75.0) indicated that these three carbons were connected by a nitrogen atom. All of these data indicated that **1** had lycopodane skeleton. The molecular formula and the ^{13}C chemical shifts of the nitrogen bearing carbons (C-1, C-9, C-13) implied that **1** existed as an *N*-oxide. The structure inferred by spectroscopic analysis was confirmed by X-ray crystallographic analysis (Fig. 2). To the best our knowledge, this is the first example of a lycopodine-type alkaloid existing as an *N*-oxide in nature.

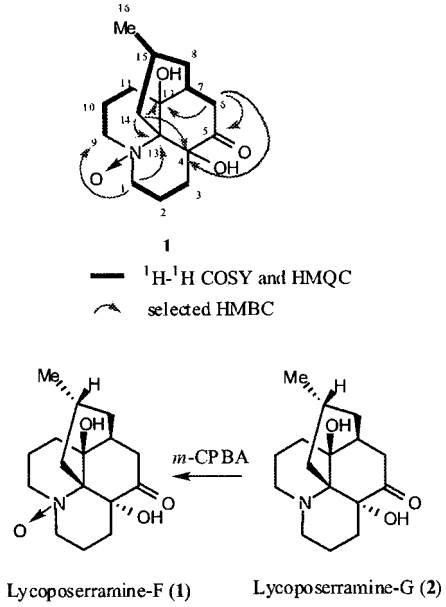

Fig. 1

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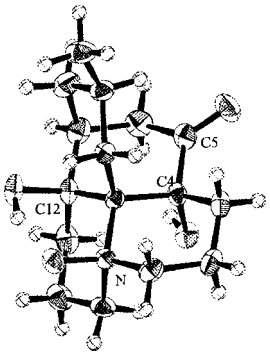
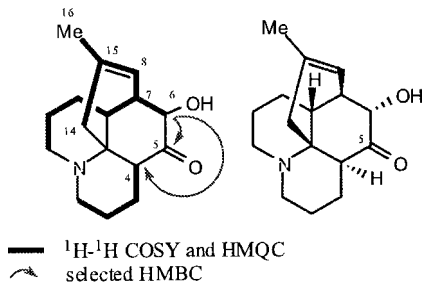


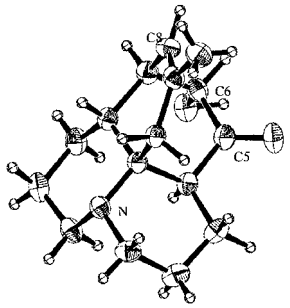
Fig. 2. ORTEP Drawing (X-Ray Analysis) of Lycoposerramine-F (**1**)

Lycoposerramine-G (**2**) was obtained as a colorless amorphous powder. HR-FAB-MS analysis gave *m/z* 280.1893 $(M+H)^+$ (Δ −2.0 mmu) and established the molecular formula as $C_{16}H_{25}NO_3$, which was one oxygen atom less than **1** described above. The ^{1}H- and ^{13}C-NMR (Table 1) spectra of **2**, which resembled those of **1** except for the chemical shifts of the carbons adjacent to nitrogen, indicated that **1** was an *N*-oxide derivative of **2**. Actually, when **2** was treated with one equivalent of *m*-CPBA, lycoposerramine-F (**1**) was obtained in 63% yield, thereby establishing the structure of the new alkaloid as formula **2**.

Lycoposerramine-H (**3**) was obtained as colorless prisms (mp 227—228 °C, sublimation). HR-FAB-MS analysis gave *m/z* 262.1809 $(M+H)^+$ (Δ +0.2 mmu) and established the molecular formula as $C_{16}H_{23}NO_2$, which indicated that **3** had one extra unsaturated number compared to common lycopodine-type alkaloids. ^{1}H- and ^{13}C-NMR spectra (see Table 1) as well as DEPT spectra suggested the presence of one ketone, a trisubstituted olefin bearing a methyl group, one sp^3 quaternary carbon, four sp^3 methines (one of which had a hydroxyl function), and seven sp^3 methylenes. ^{1}H–^{1}H COSY and HMQC spectra revealed connectivities as shown by the bold line in Fig. 3. Further, allyl couplings between the olefinic proton (δ 5.35, H-8) and methyl protons (δ 1.58, H-16) and methylene protons (δ 1.98, 2.70, H-14), as well as homoallyl coupling between the methyl protons (H-16) and the methine proton (δ 2.52, H-7), indicated the presence of a double bond at the C-8 (δ 121.6)–C-15 (δ 135.9) position of the lycopodine skeleton. The location of the secondary hydroxyl group was inferred from the HMBC cross-peaks between the proton at δ 3.78 (d, J=2.7 Hz) and the carbonyl carbon (δ 212.4, C-5) and the methine carbon at δ 38.7 (C-4). The structure including the stereochemistry of the secondary hydroxyl group at C-6 was determined by X-ray analysis as formula **3** (Fig. 3). This is the first example of a lycopodine-type alkaloid that has a double bond at the C-8–C-15 position.

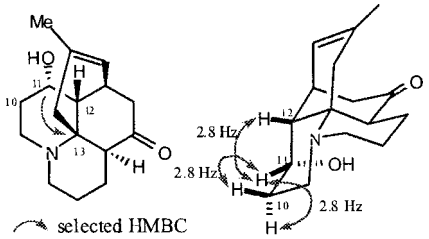
Lycoposerramine-I (**4**) showed a molecular ion peak at *m/z* 261 and the molecular formula, $C_{16}H_{23}NO_2$, which was established by HR-FAB-MS [*m/z* 262.1802 $(M+H)^+$, Δ −0.5 mmu], was identical with that of **3** described above. Comparison of its ^{1}H- and ^{13}C-NMR spectra (see Table 1) with those of **3** suggested that the two alkaloids were isomers at the position of the secondary hydroxyl group. The chemical shifts at C-10 (δ 35.5), C-11 (δ 69.2), and C-12 (δ 44.6) in **4** as well as the HMBC cross-peak (Fig. 4) between the low-field proton (δ 4.34) and the quaternary carbon at C-13



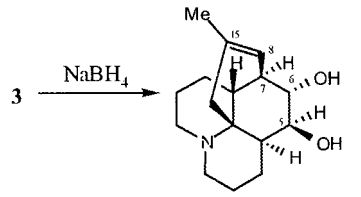


Lycoposerramine-H(**3**)

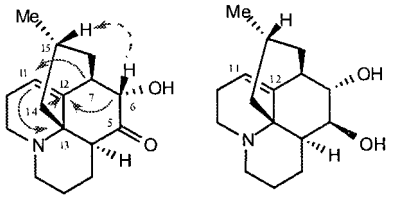
Fig. 3. Selected 2D NMR Correlations and ORTEP Drawing (X-Ray Analysis) for Lycoposerramine-H (**3**)



Lycoposerramine-I (**4**)



Lycoposerramine-J (**5**)



Lycoposerramine-K (**6**) Lucidioline (**11**)

Fig. 4

(δ 59.7) indicated that the hydroxyl group existed at the C-11 position. The stereochemistry of the hydroxyl group at this position was deduced to be α-axial orientation based on the coupling constants (ddd, J=2.8, 2.8, 2.8 Hz) (Fig. 4) of the proton at C-11.

Lycoposerramine-J (**5**) was obtained as a colorless amorphous powder. HR-FAB-MS analysis gave *m/z* 264.1965 $(M+H)^+$ (Δ +0.1 mmu) and established the molecular formula as $C_{16}H_{25}NO_2$, which indicated that **5** was a dihydro derivative of lycoposerramine-H (**3**). As in the case of **3**, this compound had a double bond at the C-8–C-15 position, which was revealed by ^{1}H- and ^{13}C-NMR spectral data (δ_H 1.69, 3H, s, δ_H 5.72, 1H, dd-like, δ_C 125.6, δ_C 136.8). However, the ^{13}C-NMR spectrum did not show any signals ascribable to the carbonyl function. Instead, two methine carbons (δ 73.1, 77.5) bearing an oxygen function were observed, indicating that the carbonyl, which was commonly present at C-5 in lycopodine alkaloids, was displaced by a hydroxyl function in the new alkaloid **5**. Actually, when **3** was reduced with $NaBH_4$ in MeOH, **5** was obtained in quantitative yield as the sole product. (Fig. 4) The stereochemistry of the secondary hydroxyl group at C5 was deduced to be β-axial configuration based on observations of the W-configuration long-range coupling between H-5 and H-7 as well as the previously reported fact[37,39] that the reduction of the carbonyl group at C-5 in the lycopodine group occurred diastereoselectively from the α face.

Lycoposerramine-K (**6**) showed a pseudomolecular ion peak at *m/z* 262 and the molecular formula, $C_{16}H_{23}NO_2$, which was established by HR-FAB-MS [*m/z* 262.1788 $(M+H)^+$, Δ −1.9 mmu], was identical with that of lycoposerramine-H (**3**). The position of the double bond in **6** was deduced to be C-11 (δ 121.1)–C-12 (δ 139.3) from the HMBC cross-peaks (H-7/C-11, H-6/C-12, H-14/C-12, H-11/C-13) (Fig. 4) and by comparing the ^{13}C chemical shifts (see Table 1) with those of lucidioline (**11**),[31] a known alkaloid that was simultaneously isolated from this plant. Both the stereochemistry at C-6 (δ 78.2) having a secondary hydroxyl group and the C-15 methine carbon could be elucidated from the observed nuclear Overhauser effect (NOE) between H-6 (δ 3.85) and H-15 (δ 1.51).

Lycoposerramine-L (**7**) was obtained as an amorphous powder. HR-FAB-MS analysis gave *m/z* 264.1968 $(M+H)^+$ (Δ +0.4 mmu) and established the molecular formula as $C_{16}H_{25}NO_2$. The ^{13}C-NMR spectrum (Table 1), clearly indicating the presence of one ketone (δ 214.1) and a secondary hydroxyl group (δ_H 4.24, δ_C 73.7), as well as the analysis of ^{1}H–^{1}H COSY and HMQC spectra revealed that **7** had the fundamental lycopodane skeleton. The HMBC cross-peak (Fig. 5) between the proton (δ 4.24) and the carbonyl carbon (C-5) indicated the presence of a hydroxyl group at the C-6 position. From these data, lycoposerramine-L was deduced to be 6-hydroxylycopodine, which corresponded to a known alkaloid, L20,[15,32,33] *i.e.*, 6-α-hydroxylycopodine (**12**). The ^{1}H- and ^{13}C-NMR spectra of **7** and L.20 (**12**) were very similar with the exception of the chemical shifts at C-6 (δ 73.7) and C-8 (δ 35.0), suggesting that they were stereoisomers at the C-6 position. The observed NOE between H-6 (δ 4.24) and H-4 (δ 3.02) revealed that the structure of new alkaloid **7** was 6-β-hydroxylycopodine.

Lycoposerramine-M (**8**) showed a molecular ion peak at *m/z* 263 and the molecular formula, $C_{16}H_{25}NO_2$, which was established by HR-FAB-MS [*m/z* 264.1969 $(M+H)^+$, Δ +0.5 mmu], was identical with that of **7** described above. Comparison of its ^{1}H- and ^{13}C-NMR spectra (Table 1) with those of **7** suggested that the two alkaloids were isomers at the position of the secondary hydroxyl group. The chemical

Table 1. ^{13}C-NMR Spectral Data of Lycoposerramines and Their Related Alkaloids in $CDCl_3$

Position	**1**[a]	**2**	**3**	**4**	**5**	**6**	**11**[b]	**7**	**12**	**8**	**9**	**17**	**10**
1	64.9	46.0	47.0	47.4	48.0	47.7	47.6	46.6	46.7	47.1	46.6	47.0	47.1
2	19.2	15.5	17.8	18.6	19.7	22.7	25.1	18.1	18.6	19.3	18.0	19.9	20.0
3	25.6[c]	27.9	18.9	19.5	23.6	19.4	23.2	19.3	19.5	19.7	19.7	22.2	22.3
4	73.6	78.8	38.7	46.4	29.1	49.6	43.1	40.8	39.2	45.8	42.4	28.7	28.5
5	207.3	208.9	212.4	213.9	77.5	210.9	72.5	214.1	213.6	215.7	213.4	72.4	72.6
6	41.0	40.6[c]	[d]	44.4	73.1	78.2	77.7	73.7	78.1	44.9	45.2	[d]	[d]
7	42.5	40.5[c]	42.7	36.8	42.6	48.0	47.4	43.1	42.3	35.9	38.9	40.3	40.2
8	36.1	35.3	121.6	126.9	125.6	39.1	40.9	35.0	39.6	44.1	37.3	39.7	39.6
9	64.9	48.5	47.4	41.0	47.2	45.0	44.7	47.3	47.6	41.4	41.9	47.0	47.0
10	17.4	20.8	26.6	35.5	26.9	26.4	26.1	25.1[c]	26.7	35.3	27.1	26.5	26.7
11	32.0	31.2	25.8	69.2	26.0	121.1	115.0	26.1	26.4	69.8	75.2	25.6	25.8
12	78.9	70.1	42.1	44.6	42.4	139.3	143.8	45.8	44.6	47.5	69.7	44.1	44.2
13	75.0	61.2	61.0	59.7	54.5	59.8	55.8	61.0	60.0	59.2	60.7	54.9	54.5
14	33.4	38.7	40.7	41.6	42.1	37.0	34.3	43.2	42.9	43.5	37.1	42.3	42.5
15	25.7[c]	24.3	135.9	132.0	136.8	25.6	22.6	25.0[c]	26.1	25.4	24.1	24.0	24.0
16	23.2	22.9	22.9	22.5	22.9	22.7	23.5	22.9	23.1	22.7	22.4	24.1	24.0
$\underline{C}OCH_3$											169.5	169.7[e]	169.3
$CO\underline{C}H_3$											21.9	21.1[e]	21.4
$\underline{C}OCH_3$												169.2[f]	
$CO\underline{C}H_3$												21.3[f]	
17													171.8
18													36.7
19													30.7
20													132.1
21													110.9
22													146.5
23													144.1
24													114.0
25													120.8

a) In CD_3OD. *b*) In DMSO-d_6. *c*) Interchangeable in each vertical column. *d*) Overlapped with $CDCl_3$. *e*) C5-OAc. *f*) C6-OAc.

shifts at C-10 (δ 35.3), C-11 (δ 69.8) and C-12 (δ 47.5) as well as the observed HMBC cross-peak (Fig. 5) between the low-field proton (δ 4.22) and the quaternary carbon at C-13 (δ 59.2) indicated that the hydroxyl group existed at the C-11 position. The stereochemistry at this position was deduced to be α-axial orientation based on the coupling constants (δ 4.22, ddd, J=2.8, 2.8, 2.8 Hz) of the proton at C-11, as in the case of **4**.

Lycoposerramine-N (**9**) was revealed to have the molecular formula, $C_{18}H_{27}NO_4$, by HR-FAB-MS [*m/z* 322.2011 $(M+H)^+$, Δ −0.7 mmu]. ^{1}H- and ^{13}C-NMR spectra as well as DEPT spectra showed some characteristic signals, *i.e.*, one ketone (δ 213.4), one sp^3 quaternary carbon bearing an oxygen (δ 69.7), one sp^3 oxymethine (δ 75.2), and one acetoxy function [δ_H 2.07 (3H, s), δ_C 169.5, δ_C 21.9], along with one sp^3 quaternary carbon, three sp^3 methines, eight sp^3 methylenes, and one methyl group. Among them, two methylenes (δ 46.6, 41.9) and one quaternary carbon (δ 60.7) were ascribed to those bearing nitrogen. ^{1}H–^{1}H COSY and HMQC spectra indicated the presence of the following three fragments: –$CH_2CH_2CH_2CH$– (C1—C4), –CH_2CH_2CH– (C9—C11), and –$CH_2CHCH_2CH(CH_3)CH_2$– (C6—C8—C15 (C16)—C14), implying that **9** had the tetracyclic lycopodane skeleton possessing a carbonyl function at C-5. HMBC correlations between the quaternary carbon (δ 69.7) having an oxygen function and H-6, H-8, and H-14 (Fig. 5) indicated the presence of a hydroxyl function at C-12 (δ 69.7). The low-field proton at δ 4.98 exhibited HMBC cross-peaks with C-12, C-13 and the carbonyl of the ester group, suggesting that the acetoxy group existed at C-11 (δ 75.2). The stereochemistry at C-11 was deduced to be α-axial orientation based on the coupling constants (δ 4.98, dd, J=2.7, 2.7 Hz) of the proton at C-11, as in the case of **4**.

Lycoposerramine-O (**10**) was obtained as an amorphous powder. HR-FAB-MS analysis gave *m/z* 486.2866 $(M+H)^+$ (Δ +1.0 mmu) and established the molecular formula as $C_{28}H_{39}NO_6$. ^{13}C-NMR spectra (Table 1) suggested the presence of sixteen carbons ascribable to the lycopodane framework (*vide infra*) and two additional ester groups. ^{1}H–^{1}H COSY and HMQC spectra indicated the presence of the following three fragments in the alkaloid portion: **a**, –$CH_2CH_2CH_2CHCH$– (C1—C5); **b**, –$CH_2CH_2CH_2CH$– (C9—C12); and **c**, –$CHCHCH_2CH(CH_3)CH_2$– (C6—C8—C15(C16)—C14). Partial units **a** and **c** as well as **b** and **c** could be connected by the HMBC cross-peaks (H-5/C-6, H-5/C-7, H-6/C-5, H-6/C-4) and (H-14/C-12, H-6/C-12), respectively (Fig. 6). These three units could be further linked through the nitrogen atom on the basis of the following HMBC correlations: H-1/C-13, H-9/C-13, H-5/C-13, and H-14/C-13. These data suggested that **10** had the basic lycopodane skeleton; however, the functional group at C-5 was replaced from an ordinary ketone with an ester group, as shown by the ^{1}H-NMR spectrum of the signal at C-5 (δ_H 5.06, δ_C 72.6). The presence of an acetoxy group at C-6 was also elucidated from the following NMR spectra [δ_H 4.60 (1H, s, H-6), δ_H 2.04 (3H, s), δ_C 169.3 (CO_2), δ_C 21.4 (CH_3), and the HMBC cross-peak of δ_H 4.60 (H-6) and δ_C 169.3 (CO_2)]. The structure of the second ester group on C-5 was elucidated as follows. ^{1}H- and ^{13}C-NMR spectra showed the presence of an ethane fragment, a methoxy group, a phenolic hydroxyl function, and a benzene ring, on which the first

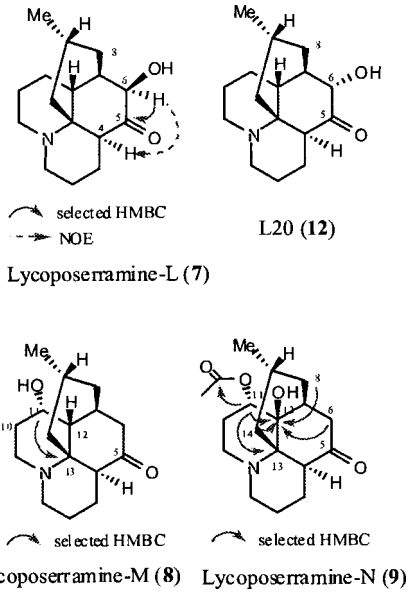
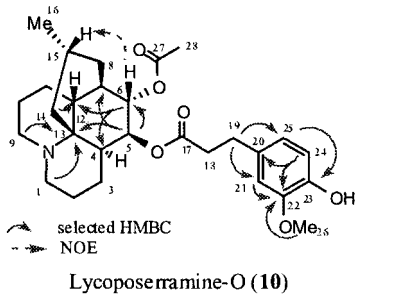


Fig. 5



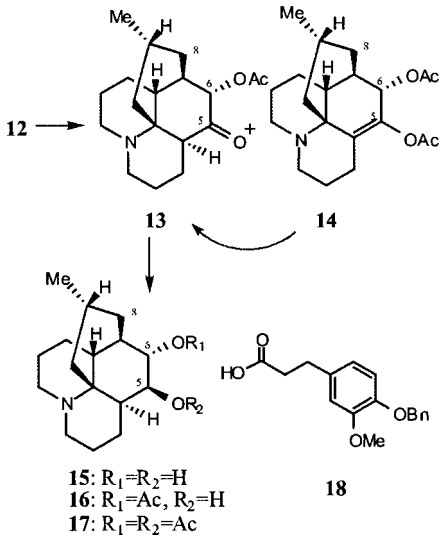


Fig. 6

three groups were located in a 1,2,4-substitution mode, as inferred from the splitting pattern of the protons on the benzene ring. The positions of these three functions were elucidated from the HMBC correlations as shown in the Fig. 6, and indicated the presence of a dihydroferulate as the ester structure on C-5. The relative stereochemistries at C-5 and C-6 were deduced from the NOE correlation and by comparing the coupling constants of the corresponding protons with

those of a known alkaloid, as follows. Thus, the NOE cross-peak of H-6/H-15 suggested an α-orientation of the acetoxy group at C-6. Further, the coupling constants of the protons at H-5 (d, J=7.0 Hz) and H-6 (broad, s) strongly resembled those of a known alkaloid, acetyllycoclavine (**17**),[37] indicating the stereochemistry at C-5 was a β-axial configuration. To confirm the structure inferred from the spectroscopic analysis above, we attempted to synthesize **10** from a known alkaloid. Initially, the hydroxyl group in L.20 (**12**) was acetylated under conventional conditions (Ac_2O and pyridine) to give the desired acetate (**13**)[33] in 46% yield together with the enol acetate (**14**)[33] in 50% yield, which could be converted into **13** by hydrolysis under acidic conditions (1 N HCl, MeOH, rt). The carbonyl function in **13** was reduced with $NaBH_4$ in MeOH to give the alcohol derivative (**16**) as the sole product. Partial acetylation (one equivalent of Ac_2O and excess pyridine in CH_2Cl_2) of the diol in a known alkaloid, deacetyllycoclavine (**15**), afforded the same product as that obtained by reduction of **13** above, demonstrating the stereochemistry of the hydroxyl group at C-5 in **16** to be β-orientation. The thus-obtained C-6 monoacetylated compound (**16**) was subjected to esterification with *O*-benzyl 3-(4-hydroxy-3-methoxylphenyl)propanoic acid (**18**),[40] which was prepared from commercially available ferulic acid. Finally, the protecting group on the phenol group was removed by hydrogenolysis to furnish the target compound, which was found to be completely identical with natural **10** by comparison of their chromatographic behavior and spectroscopic data including $[\alpha]_D$. Therefore, the structure of lycoposerramine-O was determined to be formula **10**.

Experimental

General Experimental Procedures UV: recorded in MeOH on a JASCO V-560 instrument. IR: recorded on a JASCO FT/IR-230 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra: recorded on a JEOL JNM A-400, JNM A-500, JNM ECP-400, or JNM ECP-600 spectrometer, where J values are given in Hz. EI-MS: direct probe insertion at 70 eV recorded on a JEOL JMS GC-mate spectrometer. FAB-MS: recorded on a JEOL JMS-HX110 mass spectrometer. Optical rotation: measured using a JASCO P-1020 polarimeter. CD: recorded on a JASCO J-720WI spectrometer. TLC: precoated Kieselgel 60 F_{254} plates (Merck, 0.25 mm thick). Column chromatography: Kieselgel 60 [Merck, 70—230 (for open chromatography) and 230—400 mesh (for flash chromatography)], medium pressure liquid column chromatography: silica gel prepacked column Kusano CPS-HS-221-05.

Plant Material The club moss *Lycopodium serratum* Thunb. was collected in Boso Peninsula, Chiba Prefecture in May and identified by Mr. Tamotsu Nose, a member of the Botanical Society of Chiba Prefecture, Japan. A voucher specimen was deposited at the Herbarium of the Faculty of Pharmaceutical Sciences, Chiba University.

Extraction and Isolation of Alkaloids The air-dried club moss (1.45 kg) was extracted with MeOH (7.7 l) four times and the extracts were filtered. The combined filtrates were concentrated under reduced pressure to give the crude extract (336 g), which was then suspended in 2% tartaric acid and filtered. The aqueous filtrate was extracted with petroleum ether, rendered basic with Na_2CO_3 (pH 10), and then exhaustively extracted with 5% MeOH–$CHCl_3$. The organic layer was dried over $MgSO_4$ and evaporated to give the crude alkaloidal fraction (3.23 g). A portion of the crude base (3.18 g) was roughly separated by silica gel flash column chromatography using a $CHCl_3$ to 30% MeOH/$CHCl_3$ gradient, 30% MeOH in $CHCl_3$ saturated with NH_4OH, and then MeOH to give five fractions (A—E). The 5% MeOH/$CHCl_3$ eluate (fraction B) was rechromatographed over SiO_2 using 5—15% MeOH in AcOEt to give six fractions (B1—B6). The 5% MeOH in AcOEt eluate (fraction B2) was further purified by SiO_2 column chromatography using 3% MeOH in $CHCl_3$ to afford 1.6 mg of lycoposerramine-K (**6**) together with 3.9 mg of serratidine. The 10—20% MeOH in $CHCl_3$ eluate (fraction C) was rechromatographed over SiO_2 using 5—15% MeOH in AcOEt, 20% MeOH in $CHCl_3$, and then MeOH to give eight fractions (C1—C8). The 15% MeOH in AcOEt to 20% MeOH in $CHCl_3$ eluate (fraction C5) was further purified by SiO_2 column chromatography using 3% MeOH in $CHCl_3$ to afford 9.1 mg of lycoposerramine-H (**3**) and 1.1 mg of lycoposerramine-N (**9**). The 20% MeOH in $CHCl_3$ eluate (fraction C6) was rechromatographed over SiO_2 using 5% MeOH in $CHCl_3$ to give 3.1 mg of lycoposerramine-L (**7**) together with 5.5 mg of lycopodine. The 20% MeOH in $CHCl_3$–MeOH eluate (fraction C7) was further purified by SiO_2 column chromatography using 10% MeOH in AcOEt to afford 1.3 mg of acetyllycoclavine (**17**). The 30% MeOH in $CHCl_3$ saturated with NH_4OH eluate (fraction D) was rechromatographed over SiO_2 using 0—20% MeOH in AcOEt to give six fractions (D1—D6). The 5—10% MeOH in AcOEt eluate (fraction D3) was further purified by SiO_2 column chromatography using 5% MeOH in $CHCl_3$ to afford 4.4 mg of lycoposerramine-I (**4**), 1.9 mg of lycoposerramine-O (**10**) together with 21.6 mg of L.20 (**12**). The 10—15% MeOH in AcOEt eluate (fraction D4) was purified by SiO_2 using 5% MeOH in $CHCl_3$ to afford 3.2 mg of lycoposerramine-M (**8**) together with 4.5 mg of lycodoline. The MeOH eluate (fraction E) was rechromatographed over SiO_2 using 100% AcOEt to MeOH : AcOEt : NH_4OH=25 : 75 : 2.5 to give five fractions (E1—E5). The MeOH : AcOEt : NH_4OH=15 : 85 : 0.1—20 : 80 : 0.1 eluate (fraction E2) was further purified by SiO_2 column chromatography using 0—30% MeOH in $CHCl_3$, 30% MeOH in $CHCl_3$ saturated with NH_4OH, and then MeOH to afford 1.1 mg of lycoposerramine-F (**1**), 4.1 mg of lycoposerramine-G (**2**), 2.4 mg of lycoposerramine-J (**5**), 2.4 mg of lucidioline (**11**), and 6.4 mg of serratezomine-C. The MeOH : AcOEt : NH_4OH= 20 : 80 : 2—25 : 75 : 2.5 (fraction E3) was further purified over Al_2O_3 column chromatography using 5% MeOH in AcOEt to give 27.4 mg of deacetyllycoclavine (**15**).

Lycoposerramine-F (**1**): Colorless prisms, mp >300 °C (MeOH–AcOEt); $[\alpha]_D^{24}$ −15.2° (c=0.06, MeOH); IR (KBr) ν_{max} 3403 (hydroxyl group), 1713 (ketone) cm^{-1}; ^{1}H-NMR (CD_3OD, 500 MHz) δ: 4.89 (1H, ddd, J=4.0, 10.2, 15.4 Hz, H-9), 3.52 (1H, ddd, J=4.2, 13.8, 13.8 Hz, H-1), 3.24 (1H, m, H-6), 2.93 (3H, m, H-1, 9, 11), 2.62 (2H, m, H-10, 14), 2.14 (1H, dd, J=2.0, 16.0 Hz, H-6), 2.05 (2H, m, H-2, 3), 1.93 (2H, m, H-7, 8), 1.84 (1H, dd, J=5.0, 13.9 Hz, H-14), 1.75 (2H, m, H-2, 3), 1.64 (1H, m, H-10), 1.60 (1H, m, H-15), 1.30 (2H, m, H-8, 11), 0.84 (3H, d, J=6.1 Hz, H-16); ^{13}C-NMR data (Table 1); FAB-MS (NBA) m/z 296 $[M+H]^+$; HR-FAB-MS (NBA) m/z 298.1848 (M+H; Calcd for $C_{16}H_{26}NO_4$, 296.1862).

The Crystal Data for **1**: Data were acquired with a Rigaku/MSC Mercury CCD diffractometer Mo-Kα radiation (λ=0.71069 Å), graphite monochromated, orthorhombic, $C_{16}H_{25}NO_4$ (Mw: 295.38), space group $P2_12_12_1$ with a=9.150(12) Å, b=11.839(2) Å, c=13.146(2) Å, V=1424.0(4) Å^3, Z=4, and D_{calc}=1.378 g/cm^3 The final R value was 0.046 (R_w=0.053) for 1750 reflections ($I>1\sigma(I)$).

Lycoposerramine-G (**2**): Colorless amorphous powder; CD (0.64 mM, MeOH, 25 °C) nm ($\Delta\varepsilon\lambda$) 344 (0), 322 (+0.6), 292 (0), 239 (−1.7), 212 (0); IR ($CHCl_3$) ν_{max} 3385 (hydroxyl group), 1707 (ketone) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 3.99 (1H, ddd, J=4.6, 10.9, 13.1 Hz, H-9), 3.35 (1H, ddd, J=3.9, 14.0, 14.0 Hz, H-1), 3.29 (1H, ddd, J=1.5, 5.8, 15.9 Hz, H-6), 2.91 (1H, ddd, J=5.2, 13.1, 13.1 Hz, H-11), 2.56 (1H, m, H-1), 2.55 (1H, m, H-9), 2.28 (1H, ddddd, J=5.2, 5.2, 13.7, 13.7, 13.7 Hz, H-2), 2.23 (1H, dd, J=2.1, 15.9 Hz, H-6), 2.17 (1H, m, H-3), 2.10 (3H, m, H-7, 10, 14), 2.00 (1H, dddd, J=1.4, 4.1, 12.4, 12.4 Hz, H-8), 1.73 (2H, m, H-3, 10), 1.54 (1H, dd, J=13.1, 13.1 Hz, H-14), 1.44 (3H, m, H-2, 11, 15), 1.37 (1H, m, H-8), 0.85 (3H, d, J=6.1 Hz, H-16); ^{13}C-NMR data (Table 1); EI-MS (%) m/z 279 ($[M]^+$, 33.5), 262 (100); HR-FAB-MS (NBA/PEG) m/z 280.1893 (M+H; Calcd for $C_{16}H_{26}NO_3$, 280.1913).

***m*-CPBA Oxidation of Lycoposerramine-G (2)** To a stirred solution of **2** (1.8 mg, 0.00645 mmol) in dry CH_2Cl_2 (0.5 ml) was added *m*-CPBA (1.5 mg, 0.00669 mmol) at 0 °C under argon atmosphere. After the reaction mixture was stirred at 0 °C for 2.5 h, it was directly subjected to Al_2O_3 column chromatography (0—100% MeOH in $CHCl_3$) to give 1.2 mg (yield 63%) of **1**. All the spectroscopic data (^{1}H- and ^{13}C-NMR, MS and $[\alpha]_D$) were identical with those of natural **1**.

Lycoposerramine-H (**3**): Colorless prisms, mp 227—228 °C (Sublimation, crystallized from MeOH); CD (0.37 mM, MeOH, 25 °C) nm ($\Delta\varepsilon\lambda$) 341 (0), 306 (+4.9), 268 (0), 234 (−3.7), 213 (0), 210 (+1.7); IR (KBr) ν_{max} 3099 (hydroxyl group), 1714 (ketone) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 5.35 (1H, d, J=5.2 Hz, H-8), 3.78 (1H, d, J=2.7 Hz, H-6), 3.65 (1H, dd, J=5.8, 9.5 Hz, H-4), 3.20 (1H, m, H-9), 3.18 (1H, m, H-1), 2.70 (1H, d, J=18.3 Hz, H-14), 2.62 (1H, m, H-9), 2.59 (1H, m, H-1), 2.52 (1H, br s, H-7), 2.45 (1H, dddd, J=3.7, 13.4, 13.4, 13.4 Hz, H-11), 1.98 (1H, m, H-14), 1.95 (1H, m, H-12), 1.88 (1H, m, H-2), 1.86 (1H, m, H-3), 1.85 (1H, m, H-10), 1.79 (1H, m, H-3), 1.69 (1H, m, H-11), 1.63 (1H, m, H-10), 1.58 (3H, s, H-16), 1.34 (1H, br d, J=12.2 Hz, H-2), ^{13}C-NMR data (Table 1); EI-MS (%) m/z 261 ($[M]^+$, 100), 232 (87.5), 190 (66.7), 160 (52.9), 137 (69.2); HR-FAB-MS

(NBA/PEG) *m/z* 262.1809 (M+H; Calcd for $C_{16}H_{24}NO_2$, 262.1807).

The Crystal Data for **3**: Data were acquired with a Rigaku RAXIS-II diffractometer Mo-Kα radiation (λ=0.71070 Å), graphite monochromated, orthorhombic, $C_{16}H_{23}NO_2$ (Mw: 261.36), space group $P2_12_12_1$ with a=18.53(2) Å, b=7.22(1) Å, c=10.483(5) Å, V=1401(2) Å^3, Z=4, and D_{calc}=1.238 g/cm^3. The final R value was 0.069 (R_w=0.088) for 1273 reflections ($I>1.50\sigma(I)$).

Lycoposerramine-I (**4**): Colorless amorphous powder, CD (1.47 mM, MeOH, 25 °C) nm ($\Delta\varepsilon\lambda$) 320 (0), 291 (+5.0), 261 (0), 229 (−5.3), 208 (0), IR ($CHCl_3$) ν_{max} 3420 (hydroxyl group), 1697 (ketone) cm^{-1}, ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 5.49 (1H, d, J=5.2 Hz, H-8), 4.34 (1H, ddd, J=2.8, 2.8, 2.8 Hz, H-11), 3.63 (1H, dd, J=3.5, 12.1 Hz, H-4), 3.58 (1H, ddd, J=2.3, 12.7, 12.7 Hz, H-9), 3.45 (1H, dd, J=5.2, 13.4 Hz, H-6), 3.18 (1H, ddd, J=3.5, 14.0, 14.0 Hz, H-1), 2.73 (1H, d, J=18.0 Hz, H-14), 2.63 (1H, m, H-7), 2.61 (1H, m, H-1), 2.46 (1H, ddd, J=2.8, 4.2, 12.0 Hz, H-9), 2.08 (2H, m, H-6, 10), 1.94 (1H, d, J=17.7 Hz, H-14), 1.87 (1H, m, H-12), 1.85 (1H, m, H-2), 1.80 (2H, m, H-3, 10), 1.69 (1H, m, H-3), 1.57 (3H, s, H-16), 1.35 (1H, br d, J=14.6 Hz, H-2), ^{13}C-NMR data (Table 1); EI-MS (%) *m/z*: 261 ([M]$^+$, 100), 244 (28.6), 206 (34.7), 218 (29.8); HR-FAB-MS (NBA/PEG): 262.1802 (M+H; Calcd for $C_{16}H_{24}NO_2$, 262.1807).

Lycoposerramine-J (**5**): Colorless solid; $[\alpha]_D^{22}$ −67.7 (c=0.11, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2875 (hydroxyl group) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 5.72 (1H, dd-like, J=1.5, 6.4 Hz, H-8), 3.90 (1H, s, H-6), 3.56 (1H, dd-like, J=4.2, 11.1 Hz, H-5), 3.27 (1H, ddd, J=3.4, 13.4, 13.4 Hz, H-1), 3.22 (1H, ddd, J=2.4, 12.2, 12.2 Hz, H-9), 2.96 (1H, d, J=18.3 Hz, H-14), 2.64 (1H, br d, J=14.0 Hz, H-1), 2.59 (1H, m, H-4), 2.54 (1H, br d, J=12.5 Hz, H-9), 2.37 (1H, d, J=4.9 Hz, H-7), 2.17 (1H, dddd, J=3.5, 13.3, 13.3, 13.3 Hz, H-11), 2.05 (1H, m, H-14), 2.00 (2H, m, H-2, 3), 1.85 (1H, d, J=11.0 Hz, 5-OH), 1.78 (1H, m, H-12), 1.74 (1H, m, H-10), 1.69 (3H, s, H-16), 1.56 (1H, m, H-10), 1.55 (1H, m, H-3), 1.50 (1H, m, H-11), 1.38 (1H, br d, J=10.4 Hz, H-2), ^{13}C-NMR data (Table 1); EI-MS (%) *m/z* 263 ([M]$^+$, 93.9), 230 (70.3), 203 (100), 188 (88.7), 137 (74.0); HR-FAB-MS (NBA/PEG) *m/z* 264.1965 (M+H; Calcd for $C_{16}H_{26}NO_2$, 264.1964).

$NaBH_4$ Reduction of Lycoposerramine-H (3) To a stirred solution of **3** (2.9 mg, 0.0111 mmol) in dry MeOH (0.5 ml) was added $NaBH_4$ (4.9 mg, 0.0544 mmol) at 0 °C under argon atmosphere. After the reaction mixture was stirred at 0 °C for 9.5 h, it was poured onto ice-cold water and was extracted with $CHCl_3$. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by Al_2O_3 column chromatography (0—5% MeOH in AcOEt) to give **5** (3.0 mg, quantitative yield) as a colorless solid. All the spectroscopic data (^{1}H-, ^{13}C-NMR, MS and $[\alpha]_D$) were identical with those of natural **5**.

Lycoposerramine-K (**6**): Colorless amorphous powder; IR ($CHCl_3$) ν_{max} 3384 (hydroxyl group), 1714 (ketone) cm^{-1}; CD (0.52 mM, MeOH, 25 °C) nm ($\Delta\varepsilon\lambda$): 338 (0), 312 (+0.7), 274 (0), 254 (−0.5), 248 (0), 224 (+1.3); ^{1}H-NMR ($CDCl_3$, 600 MHz,) δ: 5.73 (1H, dd, J=3.8, 3.8 Hz, H-11), 3.85 (1H, d, J=2.4 Hz, H-6), 3.08 (1H, dd, J=12.5, 12.5 Hz, H-1), 2.99 (1H, br d, J=9.5 Hz, H-4), 2.86 (1H, m, H-9), 2.71 (1H, m, H-9), 2.68 (1H, ddd, J=2.4, 2.4, 4.9 Hz, H-7), 2.62 (1H, m, H-1), 2.37 (1H, dd, J=3.4, 13.4 Hz, H-14), 2.34 (2H, m, H-12), 1.98 (1H, br d, J=11.0 Hz, H-3), 1.83 (1H, dddd, J=2.1, 2.1, 4.2, 13.4 Hz, H-8), 1.69 (1H, m, H-2), 1.60 (1H, m, H-2), 1.51 (2H, m, H-3, 15), 1.32 (1H, ddd, J=4.9, 13.1, 13.1 Hz, H-8), 1.10 (1H, m, H-14), 0.84 (3H, d, J=6.1 Hz, H-16); ^{13}C-NMR (Table 1); FAB-MS (NBA) *m/z* 262 [M+H]$^+$; HR-FAB-MS (NBA/PEG) *m/z* 262.1788 (M+H; Calcd for $C_{16}H_{24}NO_2$, 262.1807).

Lycoposerramine-L (**7**): Yellowish amorphous powder; IR ($CHCl_3$) ν_{max} 2869 (hydroxyl group), 1698 (ketone) cm^{-1}; CD (0.47 mM, MeOH, 24 °C) nm ($\Delta\varepsilon\lambda$): 331 (0), 287 (+2.3), 259 (0), 224 (−3.1); ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 4.24 (1H, dd, J=1.5, 6.4 Hz, H-6), 3.38 (1H, ddd, J=3.7, 14.0, 14.0 Hz, H-1), 3.12 (1H, ddd, J=2.7, 11.9, 11.9 Hz, H-9), 3.02 (1H, br d, J=11.9 Hz, H-4), 2.66 (1H, m, H-9), 2.63 (1H, dd, J=4.6, 13.4 Hz, H-14), 2.53 (1H, dd, J=4.9, 14.6 Hz, H-1), 2.41 (1H, br s, H-7), 2.10 (1H, br d, J=16.8 Hz, H-8), 2.04 (1H, br d, J=10.7 Hz, H-3), 1.86 (1H, m, H-2), 1.73 (1H, m, H-3), 1.60—1.86 (5H, m, H-10, 10, 11, 11, 12), 1.37 (1H, br d, J=14.6 Hz, H-2), 1.22 (1H, m, H-15), 1.01 (1H, ddd, J=4.1, 12.9, 12.9 Hz, H-8), 0.91 (1H, m, H-14), 0.83 (3H, d, J=6.1 Hz, H-16); ^{13}C-NMR (Table 1) FAB-MS (Glycerol) *m/z* 264 [M+H]$^+$; HR-FAB-MS (NBA/PEG): 264.1968 (M+H; Calcd for $C_{16}H_{26}NO_2$ 264.1964).

Lycoposerramine-M (**8**): Colorless solid; IR ($CHCl_3$) ν_{max} 3363 (hydroxyl group), 1685 (ketone) cm^{-1}; CD (0.53 mM, MeOH, 24 °C) nm ($\Delta\varepsilon\lambda$): 325 (0), 289 (+2.0), 258 (0), 223 (−2.9); ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 4.22 (1H, ddd, J=2.8, 2.8, 2.8 Hz, H-11), 3.54 (1H, ddd, J=2.3, 12.7, 12.7 Hz, H-9), 3.50 (1H, m, H-4), 3.36 (1H, ddd, J=3.7, 14.3, 14.3 Hz, H-1), 3.31 (1H, dd, J=6.0, 15.1 Hz, H-6, 9), 2.64 (1H, dd, J=4.4, 13.6 Hz, H-14), 2.57 (1H, dd, J=4.4, 14.2 Hz, H-1), 2.48 (1H, m, H-9), 2.33 (1H, m, H-7), 2.16 (1H, d, J=16.2 Hz, H-6), 2.05 (2H, m, H-3, 10), 1.87 (1H, ddddd, J=4.9, 4.9, 13.7, 13.7, 13.7 Hz, H-2), 1.75 (1H, dddd, J=2.7, 2.7, 2.7, 14.0 Hz, H-10), 1.68 (1H, br d, J=12.8 Hz, H-8), 1.53 (3H, m, H-3, 12, 15), 1.40 (1H, br d, J=14.3 Hz, H-2), 1.28 (1H, ddd, J=3.7, 12.5, 12.5 Hz, H-8), 0.85 (1H, m, H-14), 0.85 (3H, d, J=6.1 Hz, H-16). ^{13}C-NMR (Table 1); EI-MS *m/z* (%): 263 ([M]$^+$, 25.6), 246 (2.5), 207 (39.5), 58 (100). HR-FAB-MS (NBA/PEG) *m/z* 264.1969 (M+H; Calcd for $C_{16}H_{26}NO_2$, 264.1964).

Lycoposerramine-N (**9**): Colorless amorphous powder, IR ($CHCl_3$) ν_{max} 1734 (ester), 1697 (ketone) cm^{-1}, CD (0.38 mM, MeOH, 25 °C) nm ($\Delta\varepsilon\lambda$): 330 (0), 292 (+3.1), 263 (0), 231 (−4.7); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 4.98 (1H, dd, J=2.7, 2.7 Hz, H-11), 3.44 (1H, dd, J=3.7, 11.9 Hz, H-4), 3.33 (1H, ddd, J=3.1, 12.8, 12.8 Hz, H-9), 3.22 (1H, ddd, J=3.8, 14.2, 14.2 Hz, H-1), 2.97 (1H, s, –O<u>H</u>), 2.85 (1H, dd, J=6.9, 17.2 Hz, H-6), 2.49 (1H, dd, J=5.2, 14.7 Hz, H-1), 2.46 (1H, m, H-9), 2.42 (1H, m, H-10), 2.38 (1H, m, H-14), 2.32 (1H, dd, J=1.2, 17.4 Hz, H-6), 2.20 (1H, dd, J=3.5, 3.5 Hz, H-8), 2.10 (1H, br d, J=12.5 Hz, H-3), 2.07 (3H, s, –$OCOCH_3$), 2.00 (1H, ddd, J=4.0, 13.1, 13.1 Hz, H-8), 1.90 (1H, ddddd, J=5.4, 5.4, 13.7, 13.7, 13.7 Hz, H-2), 1.75 (1H, dddd, J=2.5, 2.5, 2.5, 15.0 Hz, H-10), 1.66 (1H, m, H-3), 1.48 (1H, m, H-15), 1.40 (1H, br d, J=15.0 Hz, H-2), 1.31 (1H, br d, J=11.9 Hz, H-8), 1.26 (1H, dd, J=13.1, 1.31 Hz, H-14), 0.87 (3H, d, J=6.1 Hz, H-16). ^{13}C-NMR (Table 1); FAB-MS (NBA) *m/z* 322 [M+H]$^+$ HR-FAB-MS (NBA/PEG) *m/z* 322.2011 (M+H; Calcd for $C_{18}H_{28}NO_4$, 322.2018).

Lycoposerramine-O (**10**): Colorless amorphous powder; $[\alpha]_D^{23}$ −27.8° (c=0.06, $CHCl_3$); IR ($CHCl_3$) ν_{max} 1733 (ester) cm^{-1}, ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 6.85 (1H, d, J=7.6 Hz, H-24), 6.70 (1H, s, H-21), 6.69 (1H, dd, J=1.8, 8.2 Hz, H-25), 5.06 (1H, d, J=7.0 Hz, H-5), 4.60 (1H, s, H-6), 3.89 (3H, s, H-28), 3.37 (1H, ddd, J=3.5, 14.2, 14.2 Hz, H-2), 3.16 (1H, ddd, J=2.4, 12.2, 12.2 Hz, H-9), 2.88 (2H, dd, J=7.8, 7.8 Hz, H-19), 2.66 (1H, ddd, J=2.7, 8.5, 11.3 Hz, H-4), 2.61 (2H, dd, J=7.6, 7.6 Hz, H-18), 2.61 (1H, m, H-14), 2.53 (1H, m, H-9), 2.52 (1H, m, H-1), 2.35 (1H, m, H-15), 2.04 (3H, s, H-27), 1.92 (1H, ddddd, J=4.7, 4.7, 13.6, 13.6, 13.6 Hz, H-2), 1.86 (1H, br s, H-7), 1.76 (1H, m, H-11), 1.74 (3H, m, H-8, 10, 10), 1.47 (1H, m, H-3), 1.42 (1H, m, H-12), 1.30 (2H, m, H-3, 11), 1.28 (1H, m, H-2), 1.23 (1H, m, H-8), 0.88 (3H, d, J=6.4 Hz, H-16), 0.85 (1H, m, H-14); ^{13}C-NMR (Table 1); EI-MS *m/z* (%): 485 (M$^+$, 5.7), 428 (11.2), 230 (100); HR-FAB-MS (NBA/PEG) 486.2866 (M+H; Calcd for $C_{28}H_{40}NO_6$, 486.2856).

Serratidine: IR ($CHCl_3$) ν_{max} 3404 (hydroxyl group) 1702 (ketone) cm^{-1}; CD (0.46 mM, MeOH, 25 °C) nm ($\Delta\varepsilon\lambda$): 322 (0), 296 (+0.8), 268 (0), 241 (−1.0), 230 (0), 217 (+0.4); ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 5.90 (1H, dd, J=4.0, 4.0 Hz, H-11), 3.05 (1H, ddd, J=3.7, 12.6, 12.6 Hz, H-1), 2.77 (2H, m, H-9), 2.67 (1H, m, H-6), 2.60 (1H, m, H-1), 2.58 (1H, m, H-6), 2.52 (1H, m, H-4), 2.33 (2H, m, H-10, 14), 2.23 (1H, m, H-10), 2.06 (1H, br d, J=11.9 Hz, H-3), 1.93 (1H, dd, J=4.3, 11.9 Hz, H-8), 1.63 (2H, m, H-2), 1.51 (2H, m, H-3, 15), 1.23 (1H, dd, J=12.2, 12.2 Hz, H-8), 1.11 (1H, dd, J=12.7, 12.7 Hz, H-14), 0.88 (3H, d, J=6.4 Hz, H-16); ^{13}C-NMR 208.6 (C-5), 144.7 (C-12), 114.6 (C-11), 73.3 (C-7), 59.4 (C-13), 55.3 (C-6), 53.8 (C-4), 51.6 (C-8), 48.3 (C-1), 45.2 (C-9), 36.2 (C-14), 25.9 (C-10), 25.3 (C-15), 22.9 (C-2), 22.1 (C-16), 19.7 (C-3); FAB-MS (NBA) *m/z* 262 [M+H]$^+$.

Acetyllycoclavine (**17**): $[\alpha]_D^{23}$ −14.0° (c=0.15, $CHCl_3$); IR ($CHCl_3$) ν_{max} 1734 (ester); ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 5.08 (1H, d, J=7.3 Hz, H-5), 4.67 (1H, s, H-6), 3.42 (1H, ddd, J=3.4, 14.0, 14.0 Hz, H-9), 3.20 (1H, ddd, J=1.9, 12.1, 12.1 Hz, H-1), 2.70 (2H, m, H-1, 4), 2.65 (1H, m, H-14), 2.57 (1H, m, H-9), 2.41 (1H, m, H-15), 2.07 (3H, s, 5-$OCOCH_3$), 2.05 (3H, s, 6-$OCOCH_3$), 1.96 (1H, m, H-2), 1.89 (1H, br s, H-7), 1.83 (1H, m, H-8), 1.80 (1H, d, J=2.7 Hz, H-14), 1.78 (1H, m, H-11), 1.74 (1H, m, H-10), 1.66 (2H, m, H-3, 10), 1.50 (1H, m, H-12), 1.43 (1H, m, H-3), 1.37 (1H, m, H-2), 1.33 (1H, m, H-11), 1.28 (1H, dd, J=5.0, 13.3 Hz, H-8), 0.91 (3H, d, J=6.4 Hz, H-16); ^{13}C-NMR (Table 1); FAB-MS (Glycerol) *m/z* 350 [M+H]$^+$.

Acetylation of L.20 (12) To a stirred solution of **12** (10.0 mg, 0.0380 mmol) in dry pyridine (0.28 ml) was added acetic anhydride (0.15 ml) at 0 °C under argon atmosphere. After the reaction mixture was stirred at room temperature for 8 h, it was evaporated under reduced pressure. The residue was diluted with chilled sat. $NaHCO_3$ solution and was extracted with 5% MeOH in $CHCl_3$. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by SiO_2 column chromatography (10% MeOH in AcOEt) to give **13** (5.3 mg, yield 46%) and **14** (6.6 mg, yield 50%) as an amorphous powder, respectively.

13: Colorless amorphous powder; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.91 (1H, br s), 3.37 (1H, ddd, J=3.7, 14.1, 14.1 Hz), 3.25 (1H, dd, J=11.7, 11.7 Hz), 3.17 (1H, ddd, J=3.3, 12.3, 12.3 Hz), 2.74 (1H, br d, J=9.7 Hz), 2.61 (2H, m), 2.22 (1H, br s), 2.07 (3H, s), 2.10—1.20 (12H, m), 1.03 (1H, m), 0.87 (3H, d, J=5.7 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 207.8, 169.1,

77.8, 60.6, 47.4, 46.8, 44.0, 42.1, 41.4, 40.4, 38.8, 26.1, 25.9, 25.8, 23.0, 21.1, 19.3, 18.4; EI-MS (%) 305 (M^+, 25.1), 248 (52.2), 245 (46.0), 160 (100).

14: ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.07 (1H, d, J=2.4 Hz), 3.47 (1H, dd, J=13.5, 13.5 Hz), 2.96 (1H, ddd, J=2.9, 11.6, 11.6 Hz), 2.70 (1H, br d, J=13.2 Hz), 2.63 (1H, br d, J=11.5 Hz), 2.13 (3H, s), 2.06 (3H, s), 2.1—1.6 (10H, m), 1.53 (1H, br d, J=13.2 Hz), 1.40 (1H, br d, J=13.0 Hz) 1.30 (1H, m), 1.18 (1H, ddd, J=4.9, 13.0, 13.0 Hz), 0.92 (1H, m), 0.92 (3H, d, J=6.2 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 170.5, 168.7, 139.5, 127.9, 71.3, 59.0, 49.3, 46.3, 42.8, 42.3, 40.6, 39.2, 26.8, 26.2, 25.8, 22.1, 21.2, 20.4, 20.4, 16.6; FAB-MS (NBA): 348 $[M+H]^+$.

Hydrolysis of Enol Acetate (14) To a solution of **14** (7.9 mg, 0.0228 mmol) in MeOH (0.28 ml) was added 1 N HCl solution (50 μl) under argon atmosphere. After the reaction mixture was stirred at room temperature for 47.5 h, it was evaporated to dryness. The residue was diluted with chilled sat. $NaHCO_3$ solution and was extracted with 5% MeOH in $CHCl_3$. The combined organic phase was washed with brine, dried over $MgSO_4$ and evaporated. The residue was separated by SiO_2 column chromatography (13% MeOH in AcOEt) to give **13** (1.9 mg, yield 27%) as an amorphous powder.

Reduction of L.20 Acetate (13) To a solution of **13** (11.5 mg, 0.0337 mmol) in dry EtOH (1.0 ml) was added $NaBH_4$ (2.6 mg, 0.0687 mmol) at 0 °C under argon atmosphere. After the reaction mixture was stirred at 0 °C for 8.5 h, it was poured into ice-cold water and was extracted with 5% MeOH in $CHCl_3$. The combined organic phase was washed with brine, dried over $MgSO_4$ and evaporated. The residue was separated by Al_2O_3 column chromatography (0—5% MeOH in AcOEt) to give **16** (4.2 mg, yield 36%) as an amorphous powder.

16: Colorless amorphous powder; $[\alpha]_D^{24}$ −29.3° (c=0.24, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 4.60 (1H, br s), 3.74 (1H, d, J=6.7 Hz), 3.40 (1H, ddd, J=3.1, 13.7, 13.7 Hz), 3.15 (1H, m), 2.40—2.70 (4H, m), 1.98 (3H, s), 1.20—1.95 (14H, m), 0.87 (3H, d, J=6.1 Hz), 0.80 (1H, m); ^{13}C-NMR: 170.2, 80.1, 72.6, 47.0, 46.9, 44.1, 42.0, 40.2, 39.9, 29.3, 25.4, 24.0, 23.6, 22.7, 22.5, 21.4, 20.5, 14.1; EI-MS (%) 307 (M^+, 36.8), 250 (100), 247 (76.5), 230 (29.6), 205 (70.7), 190 (81.3); HR-FAB-MS (NBA/PEG) m/z 308.2210 (M+H; Calcd for $C_{18}H_{30}NO_3$, 308.2226).

Partial Acetylation of Deacetyllycoclavine (15) To a solution of **15** (9.4 mg, 0.0355 mmol) in dry CH_2Cl_2 (0.5 ml) was added dry Ac_2O (3.3 μl, 0.0355 mmol) and dry pyridine (28 μl, 0.173 mmol) at 0 °C under argon atmosphere. After the reaction mixture was stirred at room temperature for 20.5 h, it was warmed to 40 °C and stirred for further 97.5 h. Then the reaction mixture was cooled to room temperature and evaporated to dryness. The residue was poured into chilled sat. $NaHCO_3$ solution and was extracted with 5% MeOH in $CHCl_3$. The combined organic phase was washed with brine, dried over $MgSO_4$ and evaporated. The residue was separated by SiO_2 column chromatography (0—20% MeOH in $CHCl_3$) to give **16** (1.4 mg, yield 13%) as an amorphous powder.

Preparation of Lycoposerramine-O (10) from 16 To a solution of **16** (2.1 mg, 0.0068 mmol) in dry CH_2Cl_2 (0.5 ml) was successively added DMAP (2.2 mg, 0.018 mmol), **18** (5.9 mg, 0.0206 mmol), and DCC (4.2 mg, 0.0204 mmol) at room temperature under argon atmosphere. After the reaction mixture was stirred at 40 °C for 10 h, it was cooled to room temperature and poured into chilled sat. $NaHCO_3$ solution and was extracted with 5% MeOH in $CHCl_3$. The combined organic phase was dried over $MgSO_4$ and evaporated. The residue was separated by SiO_2 column chromatography (0—10% MeOH in $CHCl_3$) to give ester (2.0 mg, yield 51%) as an colorless amorphous powder; $[\alpha]_D^{23}$ −10.3° (c=0.22, $CHCl_3$); IR cm^{-1} 1734 (ester); ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.26—7.44 (5H, m), 6.82 (1H, d, J=8.2 Hz), 6.73 (1H, d, J=1.9 Hz), 6.66 (1H, dd, J=1.9, 8.2 Hz), 5.13 (2H, s), 5.11 (1H, d, J=9.2 Hz), 4.60 (1H, s), 3.88 (3H, s), 3.46 (1H, br dd, J=13.4, 13.4 Hz), 3.27 (1H, br dd, J=11.3, 11.3 Hz), 2.89 (2H, dd, J=7.6, 7.6 Hz), 2.70—2.61 (6H, m), 2.47 (1H, m), 2.37 (1H, m), 2.05 (3H, s), 1.25—1.91 (11H, m), 0.92 (3H, d, J=6.2 Hz), 0.88 (1H, m); ^{13}C-NMR (100 MHz, $CDCl_3$): 171.6, 169.0, 149.7, 146.8, 137.2, 133.1, 128.5, 127.8, 127.2, 120.1, 114.2, 112.2, 76.1, 71.5, 71.1, 56.0, 47.0, 46.7, 42.9, 40.1, 38.8, 36.9, 36.3, 31.9, 29.2, 24.1, 22.7, 21.3, 19.3, 14.1; EI-MS (%) 575 (M^+, 45.1), 518 (62.9), 230 (100), 190 (73.2); HR-FAB-MS (NBA/PEG) m/z 576.3312 (M+H; Calcd for $C_{35}H_{46}NO_6$ 576.3325). A solution of the ester (9.4 mg, 0.016 mmol) in dry EtOH (0.5 ml) was hydrogenated in the presence of 10% Pd on carbon (4.6 mg) for 1 h at room temperature. The catalyst was removed by filtration and the solvent was evaporated. The residue was separated by amino silica gel column chromatography (20% Me_2CO in n-hex) to give **10** (2.6 mg, yield 33%) as an amorphous powder. All the spectroscopic data including ^{1}H- and ^{13}C-NMR, MS and $[\alpha]_D$ were identical with those of natural **10**.

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