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Seven new Lycopodium alkaloids, lycoposerramines-C, -D, -E, -P, -Q, -S, and -U, from *Lycopodium serratum* Thunb.

Hiromitsu Takayama,[a,*] Kazuaki Katakawa,[a] Mariko Kitajima,[a] Kentaro Yamaguchi[b] and Norio Aimi[a]

[a]*Graduate School of Pharmaceutical Sciences, Chiba University, 1-33 Yayoi-cho, Inage-ku, Chiba 263-8522, Japan*
[b]*Analysis Center, Chiba University, 1-33 Yayoi-cho, Inage-ku, Chiba 263-8522, Japan*

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Abstract—Seven new alkaloids, lycoposerramines-C, -D, -E, -P, -Q, -S, and -U, having novel fawcettimine-related structures, were isolated from the club moss *Lycopodium serratum* Thunb.

The genus *Lycopodium* (Lycopodiaceae), which produces a potential therapeutic agent, huperzine A, for the treatment of Alzheimer's disease, has been extensively studied in recent years,[1] resulting in the isolation of several new alkaloids having novel skeletons.[2] Recently, we have isolated a new type of Lycopodium alkaloid, lycoposerramine-A,[3] which has a 1,2,4-oxadiazolidin-5-one residue in the molecule, from *Lycopodium serratum* Thunb. In the continuing search for structurally unique Lycopodium alkaloids from this plant, we have purified a number of natural products including seven new alkaloids possessing fawcettimine-related skeletons. In this communication, we report the structure elucidation of these alkaloids.

The crude basic fraction obtained by the 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-C (**1**, 1.03% based on the crude base), -E (**6**, 0.31%), -D (**7**, 0.76%), -U (**8**, 0.03%), -P (**10**, 0.12%), -Q (**11**, 0.12%), and -S (**12**, 0.14%).

Compound **1**, named lycoposerramine-C, was obtained as colorless prisms (mp 164–165°C).[4] High-resolution FAB MS analysis gave m/z 262.1799 $(M+H)^+$ and established the molecular formula as $C_{16}H_{23}NO_2$. UV spectrum (λ_{max} 270 and 229 nm) as well as NMR data (δ_H 5.82 and δ_C 127.2, 183.9, and 209.9) indicated the presence of a trisubstituted α,β-unsaturated carbonyl residue. ^1H–^1H COSY and HMQC spectra indicated the presence of the following three fragments: $-CH_2CH_2CH_2CH-$ (C1–C4), $-CH_2CH_2CH_2-$ (C9–C11), and $-CH_2CH(CH_3)CH_2-$ (C8-C15(C16)-C14). Observation of a characteristic signal at δ_C 88.5 due to the aminoacetal carbon and the HMBC correlations as shown in Fig. 1 indicated that the fundamental skeleton of **1** is fawcettimine (**2**),[5] an alkaloid coexisting in this plant. The position of the double bond was easily assumed to be C6-C7 based on HMBC correlations between the olefinic proton (H6) and C4, C5, and C12. The structure inferred by spectroscopic analysis was confirmed by X-ray crystallographic analysis.[4] Treatment of lycoposerramine-C (**1**) with NaOMe in MeOH at room temperature gave two known alkaloids, phlegmariurines A (**3**)[6] and B (**4**),[2e,6,7] in 40.0% and 5.0% yields, respectively. The semi-synthetic phlegmariurine A and naturally occurring **3** simultaneously isolated from this plant showed the same CD curves, giving proof that new alkaloid **1** and phlegmariurine A have the same absolute configuration. The absolute configuration of **3** as determined by X-ray analysis[6] is shown in Fig. 1. However, the X-ray analysis was carried out using crystals that were free from heavy atoms. Therefore, to confirm the absolute configuration of **3**, we prepared secondary alcohol derivative (**5**) and subjected it to modified Mosher's method.[8] The secondary alcohol derivative having the β-configuration, which was stereoselectively prepared by $NaBH_4$ reduction of **3**, was converted into Mosher esters **5a** and **5b**. Calculation of $\Delta\delta_H = \delta_S - \delta_R$ by the Mosher method allowed assignment of the *R* configuration to C5, resulting in the establishment of the absolute configuration of **5**.

Keywords: alkaloids; *Lycopodium*; structure elucidation; X-ray crystal structures; NMR.

* Corresponding author. Tel./fax: (81) 43 2902902; e-mail: htakayam@p.chiba-u.ac.jp

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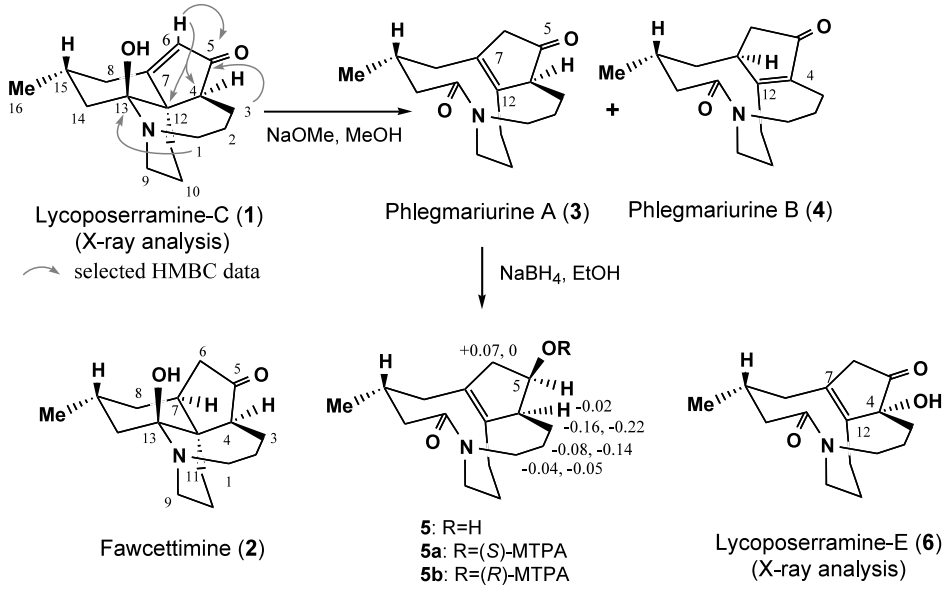

Figure 1.

Therefore, the absolute configuration of **1** was confirmed. It is possible that **1** is a biogenetic precursor of alkaloids **3** and **4**.

The new alkaloid (**6**), named lycoposerramine-E, was obtained as colorless needles (mp 259–262°C, sublimation).[9] High-resolution FAB MS analysis gave m/z 278.1779 $(M+H)^+$ and established the molecular formula as $C_{16}H_{23}NO_3$, which is one oxygen atom more than that of the known alkaloid, phlegmariurine A (**3**).[6] Actually, the ^{13}C NMR spectra of **6** and **3** are very similar with one exception, namely, **6** shows a carbon signal at δ_C 82.3 due to the introduction of a tertiary hydroxyl group at C4. The structure of **6** was finally established by X-ray crystallographic analysis.[9]

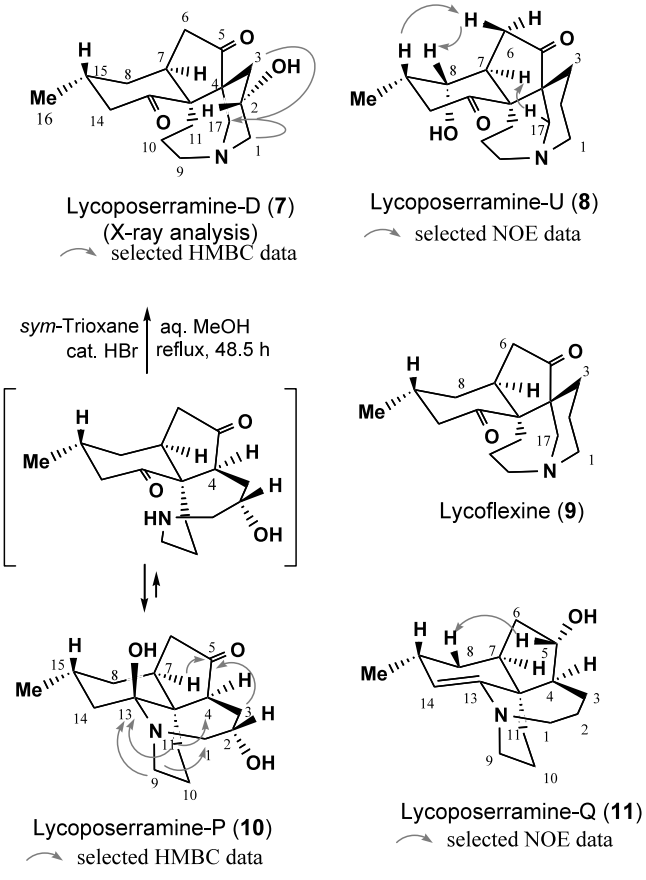

Figure 2.

The new alkaloid (**7**), named lycoposerramine-D, was obtained as colorless prisms (mp 173–176°C).[10] High-resolution FABMS analysis gave m/z 292.1914 $(M+H)^+$ and established the molecular formula as $C_{17}H_{25}NO_3$, which revealed that **7** has one excess carbon atom compared with common C16 type *Lycopodium* alkaloids. ^{13}C NMR data indicated the presence of a hydroxyl group (δ_C 61.9) and two ketones (δ_C 213.5 and 216.7) in the molecule. ^1H–^1H COSY and HMQC spectra revealed the presence of the following fragments: -CH_2CH-CH_2- (C1–C3), a three-carbon methylene chain (C9–C11), -CH_2CHCH_2CH(CH_3)CH_2- (C6–C8-C15(C16)-C14), and an isolated methylene unit (C17). HMBC analysis, particularly the correlations between the isolated methylene carbon (C17) and the protons on C1 and C3, as shown in Fig. 2, enabled the construction of the fundamental structure. The presence of a hydroxyl group at C2 was deduced from the chemical shift of the corresponding carbon atom (δ_C 61.9), and its stereochemistry was predicted from the observation of NOE between H2 and both H9 and H11. The structure inferred by spectroscopic analysis above was confirmed by X-ray crystallographic analysis.[10]

The new alkaloid (**8**), named lycoposerramine-U,[11] was obtained as a colorless amorphous powder. High-resolution FAB MS analysis gave m/z 292.1921 $(M+H)^+$ and established the molecular formula as $C_{17}H_{25}NO_3$, which is identical with that of lycoposerramine-D (**7**)

Table 1. ^{13}C NMR data of lycoposerramines and their related alkaloids in $CDCl_3$

Positions	**1**	**2**	**6**	**3**	**7**	**8**	**9**	**10**[a]	**11**	**12**
1	52.0	50.0	50.0	50.0	59.8	52.7	53.2	62.1	60.0	49.1
2	29.6	22.6	20.6	23.2	61.9	19.4	19.3	67.1	31.5	26.6
3	27.5	35.9	40.1	32.5	38.8	28.4	29.2	35.6*	33.1*	19.6
4	57.5	60.2	82.3	57.1	61.1	58.2	58.4	58.6	57.9	50.5
5	209.9	220.4	218.9	220.3	216.7	217.3	218.4	215.0	80.1	60.2
6	127.2	41.9	44.6	47.2	40.3	39.6	40.0	41.4	38.3	35.6
7	183.9	43.2	135.4	132.2	41.4	47.5	40.3	43.1	43.1	35.0
8	34.7	31.9	38.3	37.4	31.1	72.8	31.2	32.7	33.2*	33.0
9	49.4	53.4	50.8	50.7	57.2	57.4	56.6	51.7	52.4	56.8
10	22.5	28.8	23.9	24.1	26.0	28.0	25.9	21.6	24.2	22.0
11	35.3	28.2	23.7	27.4	36.4	40.8	36.2	35.7*	40.8	21.4
12	54.3	48.2	138.8	137.8	60.4	59.0	60.6	47.9	47.2	49.5
13	88.5	88[b]	172.7	172.4	213.5	213.2	213.8	88.8	147.2	59.0
14	42.9	44.4	40.4	40.3	46.9	42.4	46.7	43.7	127.6	33.7
15	29.0	23.7	28.4	28.4	27.9	30.9	28.0	24.6	27.0	20.7
16	21.8	21.8	23.5	23.3	22.3	18.0	22.4	22.2	21.3	22.1
17					52.6	55.6	53.4			
N-CH_3										44.5

[a] In acetone-d_6.
[b] Observed as broad signal (see Ref. 5d).
* Interchangeable within the vertical column.

described above. In analogy with **7**, lycoposerramine-U had a secondary hydroxyl group (δ_C 72.8) and two ketones (δ_C 213.2 and 217.3) as well as the characteristic fragments, i.e. -CH_2CH_2-CH_2- (C1–C3), a three-carbon methylene chain (C9–C11), -CH_2CHCHCH-(CH_3)CH_2- (C6–C8-C15(C16)-C14), and an isolated methylene unit (C17), thereby implying that **8** has the same skeleton as **7**. The ^{13}C NMR spectra of **8** and a known alkaloid, lycoflexine (**9**), are very similar with the exception that **8** exhibits a carbon signal at δ_C 72.8 due to the introduction of a secondary hydroxyl group at C8 in **9** (We isolated a known alkaloid, lycoflexine (**9**),[12] which was confirmed by direct comparison with an authentic sample provided by Dr. W. A. Ayer. The ^{13}C NMR data of **9** have not been published so far; thus, we present them in Table 1). The stereochemistry at C8 was deduced from the observation of NOE between H8 and H6β. We propose here the structure of lycoposerramine-U as formula **8**. The absolute configuration of **9** was established by chemical correlation with serratinine and fawcettimine (**2**).[13] The CD spectra of **9**, **8**, and **7** exhibited very similar curves, indicating that they have the same absolute configuration, as shown in Fig. 2.

The new alkaloid (**10**), named lycoposerramine-P,[14] was obtained as a colorless amorphous powder. High-resolution FAB MS analysis gave m/z 280.1916 $(M+H)^+$ and established the molecular formula as $C_{16}H_{25}NO_3$, which is one oxygen atom more than that of fawcettimine (**2**). ^{13}C NMR, ^1H–^1H COSY and HMQC spectra revealed the presence of a secondary hydroxyl group (δ_C 67.1), a ketone (δ_C 215.0), and an aminoacetal function (δ_C 88.8) as well as the fragments, i.e. -CH_2CHCH_2CH- (C1–C4), a three-carbon methylene chain (C9–C11), and -CH_2CHCH_2CH(CH_3)CH_2- (C6–C8-C15(C16)-C14). HMBC analysis as shown in Fig. 2, enabled the construction of the fundamental fawcettimine skeleton. The ^{13}C NMR spectra of **10** and fawcettimine (**2**) are very similar with the exception that **10** exhibits a carbon signal at δ_C 67.1 due to the introduction of a secondary hydroxyl group at C2 in **2**. When **10** was treated with *sym*-trioxane in the presence of catalytic amount of HBr in aqueous MeOH, lycoposerramine-D (**7**), whose structure was determined by X-ray analysis as above, could be obtained in 12% yield. The desired product would be formed by an intramolecular Mannich reaction,[12] i.e. insertion of formaldehyde between the secondary amine and C4 in the keto-amine equilibrium form of **10**. The semi-synthetic lycoposerramine-D (**7**) was completely identical with the naturally occurring **7** by comparison of their chromatographic behavior, as well as their mass, ^1H and ^{13}C NMR, and CD spectra. Therefore, the structure of lycoposerramine-P including the stereochemistry at C2 was formulated as **10**.

The new alkaloid (**11**), named lycoposerramine-Q,[15] was obtained as a colorless solid. High-resolution FABMS analysis gave m/z 248.2026 $(M+H)^+$ and established the molecular formula as $C_{16}H_{25}NO$. The presence of a secondary hydroxyl group (δ_H 3.96 and δ_C 80.1) and a trisubstituted olefin (δ_H 5.57 and δ_C 127.6 and 147.2) was revealed by ^1H and ^{13}C NMR data. ^1H–^1H COSY and HMQC spectra disclosed the presence of a three-carbon methylene chain (C9–C11) and a long connectivity, $CH_2CH_2CH_2CHCHCH_2CHCH_2$-$CH(CH_3)$CH- (C1–C8-C15(C16)-C14), thereby implying that the carbonyl group at C5 in the usual fawcettimine-type alkaloids converted into a secondary hydroxyl group as described above (δ_H 3.96 and δ_C 80.1). Comparison of the ^{13}C NMR data of **11** with those of fawcettimine (**2**) as well as the HMBC correlations between H14 and C13 and between H9 and C13 led to the elucidation of the molecular structure of lycoposerramine-Q (**11**). The stereochemistry at C5 was deduced from the observation of NOE between H5

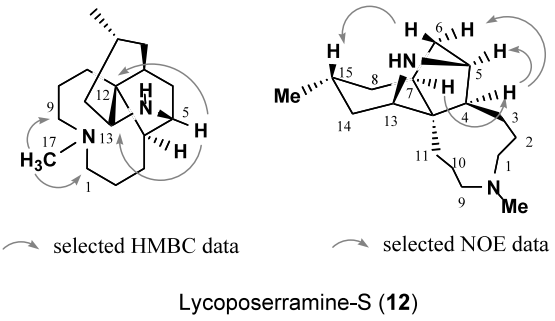

Figure 3.

and H8. This compound was previously prepared from fawcettimine (**2**) by the stereoselective reduction of the C5 carbonyl function and the dehydration at positions C13 and C14;[16] however, this is the first report of its isolation as a natural product.

The new compound (**12**), named lycoposerramine-S,[17] was obtained as a colorless amorphous powder. High-resolution FABMS analysis gave m/z 263.2485 $(M+H)^+$ and established the molecular formula as $C_{17}H_{30}N_2$, which has one extra carbon atom compared with common fawcettimine-type alkaloids. This carbon atom was easily deduced to be an *N*-Me function based on the signal at δ 2.24 (3H, s) in the ^{1}H NMR spectrum. ^{1}H–^{1}H COSY and HMQC spectra disclosed the presence of a three-carbon methylene chain (C9–C11) and a long connectivity, -$CH_2CH_2CH_2CHCHCH_2CHCH_2$-$CH(CH_3)CH_2CH$- (C1–C8-C15(C16)-C14-C13), thereby implying that position C5 in **12** is an sp^3 carbon atom, the chemical shifts (δ_H 3.00 and δ_C 60.2) of which indicate that a nitrogen function is attached to this position. In the HMBC spectrum, characteristic correlations between H5 and both C12 and C13 were observed, indicating that C5 and C13 are connected by a nitrogen bridge. The stereochemistry including positions C4 and C15 of the unprecedented pentacyclic alkaloid **12** was elucidated by NOE observations, as shown in Fig. 3.

Acknowledgements

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4. Lycoposerramine-C (**1**), colorless prisms, mp 164–165°C (from AcOEt/*n*-hexane), UV (EtOH) λ_{max} nm; 270, 229, FABMS; m/z 262 $(M+H)^+$, HRFAB MS; m/z 262.1799 (M+H; calcd for $C_{16}H_{24}NO_2$, 262.1807), CD (c 0.55 mM, MeOH); 322 (+4.2), 258 (+1.9), 227 (−10.8), ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.82 (1H, d, J=1.5 Hz, H-6), 3.43 (1H, ddd, J=4.6, 14.1, 14.1 Hz, H-1), 3.34 (1H, ddd, J=4.1, 14.6, 14.6 Hz, H-9), 2.98 (1H, dd, J=5.5, 14.6 Hz, H-9), 2.73 (1H, brd, J=14.1 Hz, H-1), 2.57 (1H, ddd, J=1.5, 4.3, 13.2 Hz, H-8), 2.35 (1H, dd, J=11.9, 14.0 Hz, H-14), 2.23 (1H, ddd, J=4.9, 13.6, 13.6 Hz, H-11), 2.14 (2H, m, H-3, 4), 2.05 (1H, ddd, J=1.7, 13.2, 13.2 Hz, H-8), 2.00 (2H, m, H-3, 15), 1.75 (3H, m, H-2, 2, 10), 1.53 (1H, brd, J=13.7 Hz, H-10), 1.31 (1H, dd, J=2.8, 14.0 Hz, H-14), 1.26 (1H, ddd, J=13.6, 2.3, 2.3 Hz, H-11), 1.01 (3H, d, J=6.1 Hz, H-16). The crystal data for **1**: data were acquired with a Rigaku RAXIS-II Imaging Plate diffractometer Mo–Kα radiation (λ=0.71070 Å), graphite monochromated, monoclinic, $C_{16}H_{23}NO_2$ (Mw: 261.36), space group $P2_1$ with a=7.440(2) Å, b=29.66(2) Å, c=12.96(1) Å, V=2837(3) Å^3, Z=8, and D_{calc}=1.223 g/cm^3 The final R value was 0.070 (R_w=0.069) for 3650 reflections (I>1.00$\sigma(I)$). The crystallographic data for compounds **1**, **6**, and **7** will be deposited with the Cambridge Crystallographic Data Centre.
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9. Lycoposerramine-E (**6**), colorless needles, mp 259–262°C (from AcOEt, sublimation), FABMS; m/z 278 $(M+H)^+$,

HRFABMS; m/z 278.1779 (M+H; calcd for $C_{16}H_{24}NO_3$, 278.1756), CD (c 0.40 mM, MeOH); 319 (–0.6), 243 (–3.9), 223 (–1.1), 207 (–3.7), ^{1}H NMR (600 MHz, $CDCl_3$) δ: 4.12 (1H, ddd, J=3.0, 13.9, 13.9 Hz, H-9), 4.00 (1H, ddd, J=13.8, 3.3, 3.3 Hz, H-1), 3.22 (1H, dd, J=2.6, 22.3 Hz, H-6), 3.18 (1H, brd, J=15.6 Hz, H-9), 2.77 (1H, ddd, J=4.2, 14.0, 14.0 Hz, H-11), 2.70 (1H, m, H-14), 2.65 (1H, m, H-6), 2.54 (3H, m, H-1,8,11), 2.39 (1H, m, H-15), 2.24 (1H, m, H-3), 2.14 (2H, m, H-3, 10), 2.02 (4H, m, H-2, 2, 8, 14), 1.70 (1H, ddd, J=15.3, 3.0, 3.0 Hz, H-10), 1.11 (3H, d, J=6.6 Hz, H-16). The crystal data for **6**: data were acquired with a same apparatus as compound **1**, orthorhombic, $C_{16}H_{23}NO_3$ (Mw: 277.36), space group $P2_12_12_1$ with a=11.918(4) Å, b=13.874(3) Å, c=8.729(4) Å, V=1443.22 Å^3, Z=4, and D_{calc}=1.276 g/cm^3 The final R value was 0.049 (R_w=0.060) for 879 reflections (I>0.00$\sigma(I)$).

10. Lycoposerramine-D (**7**), colorless prisms, mp 173–176°C (from AcOEt/Acetone), UV (EtOH) λ_{max} nm; 310, 235, FABMS; m/z 292 (M+H)$^+$, HRFAB MS; m/z 292.1914 (M+H; calcd for $C_{17}H_{26}NO_3$, 292.1913), CD (c 0.55 mM, MeOH); 307 (–0.8), 236 (+3.5), 211 (+1.0), ^{1}H NMR (600 MHz, $CDCl_3$) δ: 4.12 (1H, tt, J=5.1, 10.4 Hz, H-2), 3.09 (1H, d, J=14.2 Hz, H-17), 3.06 (1H, m, H-9), 2.99 (1H, dd, J=5.1, 13.5 Hz, H-1), 2.83 (1H, ddd, J=3.4, 6.7, 13.9 Hz, H-9), 2.71 (1H, dd, J=10.4, 13.5 Hz, H-1), 2.63 (1H, m, H-7), 2.57 (1H, d, J=14.2 Hz, H-17), 2.32 (1H, m, H-3), 2.30 (3H, m, H-6,14,14), 2.25 (1H, m, H-6), 2.20 (1H, m, H-11), 2.17 (1H, m, H-15), 2.05 (1H, dd, J=9.5, 14.7 Hz, H-11), 1.83 (1H, brd, J=11.4 Hz, H-8), 1.75 (2H, m, H-3, 10), 1.65 (2H, m, H-8, 10), 1.03 (3H, d, J=6.6 Hz, H-16). The crystal data for **7**: data were acquired with a Bruker SMART 1000 CCD diffractometer Mo–Kα radiation (λ=0.71069 Å), graphite monochromated, monoclinic, $C_{17}H_{25}NO_3$ (Mw: 291.39), space group $P2_1$ with a=8.6379(10) Å, b=9.8299(12) Å, c=9.1796(11) Å, V=740.8(1) Å^3, Z=2, and D_{calc}=1.306 g/cm^3. The final R value was 0.033 (R_w=0.038) for 1552 reflections (I>2.00$\sigma(I)$).

11. Lycoposerramine-U (**8**), amorphous powder, UV (EtOH) λ_{max} nm; 306(sh), 237(sh), EIMS; m/z (%) 291 (M^+, 39.4), 263 (17.8), 84 (100), HRFABMS; m/z 292.1921 (M+H; calcd for $C_{17}H_{26}NO_3$, 292.1913), CD (c 0.45 mM, MeOH); 302 (–1.5), 243 (+2.8), ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.86 (1H, t, J=2.4 Hz, H-8), 3.24 (1H, brd, J=14.3 Hz, H-17), 3.03 (1H, ddd, J=3.8, 9.5, 13.3 Hz, H-9), 2.95 (1H, ddd, J=3.7, 13.7, 13.7 Hz, H-1), 2.88 (2H, m, H-1, 9), 2.70 (1H, ddd, J=2.4, 8.2, 10.5 Hz, H-7), 2.66 (1H, m, H-17), 2.63 (1H, m, H-6), 2.53 (1H, dd, J=13.1, 18.0 Hz, H-14), 2.43 (1H, dd, J=9.3, 13.9 Hz, H-11), 2.20 (4H, m, H-10, 11, 14, 15), 2.03 (1H, dd, J=8.2, 18.2 Hz, H-6), 1.98 (2H, m, H-3, 3), 1.80 (2H, m, H-2, 10), 1.34 (1H, m, H-2), 1.06 (3H, d, J=6.4 Hz, H-16).
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14. Lycoposerramine-P (**10**), amorphous powder, EI MS; m/z (%) 279 (M^+, 64.7), 261 (10.6), 208 (11.5), 168 (20.6), 151 (24.3), 91 (52.3), 70 (100), HRFAB MS; m/z 280.1916 (M+H; calcd for $C_{16}H_{26}NO_3$, 280.1913), CD (c 0.32 mM, MeOH); 279 (+2.6), ^{1}H NMR (500 MHz, acetone-d_6) δ: 4.37 (1H, m, H-2), 3.57 (1H, dd, J=5.6, 13.9 Hz, H-1), 3.18 (1H, ddd, J=3.2, 14.3, 14.3 Hz, H-9), 2.70 (1H, dd, J=5.2, 14.3 Hz, H-9), 2.54 (1H, m, H-3), 2.37 (1H, dd, J=11.7, 17.9 Hz, H-6), 2.27 (2H, m, H-1, 11), 2.10 (1H, m, H-15), 2.04 (3H, m, H-6, 10, 14), 1.92 (3H, m, H-3, 4, 7), 1.53 (2H, m, H-8, 11), 1.38 (2H, m, H-8, 10), 1.30 (1H, m, H-14), 0.89 (3H, d, J=6.4 Hz, H-16).
15. Lycoposerramine-Q (**11**), colorless solid, EI MS; m/z (%) 247 (M^+, 37.7), 232 (39.7), 176 (29.3), 162 (39.0), 134 (43.1), 117 (42.5), 105 (57.4), 91 (100), 70 (86.5), HRFAB MS; m/z 248.2026 (M+H; calcd for $C_{16}H_{26}NO$, 248.2014), CD (c 1.00 mM, MeOH); 232 (+9.4), ^{1}H NMR (600 MHz, $CDCl_3$) δ: 5.57 (1H, d, J=3.4 Hz, H-14), 3.96 (1H, q, J=4.9 Hz, H-5), 3.09 (1H, brd, J=12.8 Hz, H-1), 2.97 (3H, m, H-1, 9, 9), 2.23 (1H, m, H-15), 2.13 (1H, m, H-7), 1.92 (2H, m, H-3, 10), 1.85 (2H, m, H-4, 11), 1.75 (3H, m, H-2, 6, 6), 1.69 (1H, m, H-2), 1.57 (1H, ddd, J=4.3, 12.5, 12.5 Hz, H-11), 1.51 (2H, m, H-8, 10), 1.35 (1H, q, J=12.7 Hz, H-3), 1.26 (1H, m, H-8), 0.98 (3H, d, J=7.0 Hz, H-16).
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17. Lycoposerramine-S (**12**), amorphous powder, EI MS; m/z 262 (M^+,100), 247 (42.0), 219 (96.7), HRFAB MS; m/z 263.2485 (M+H; calcd for $C_{17}H_{31}N_2$, 263.2487), $[\alpha]_D^{25}$ –37.8 (c 0.29, MeOH), ^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.00 (1H, brs, H-5), 2.97 (1H, brs, H-13), 2.68 (1H, ddd, J=4.1, 13.4, 13.4 Hz, H-1), 2.36 (1H, m, H-9), 2.24 (3H, s, N-CH_3), 2.21 (1H, m, H-9), 2.01 (1H, ddd, J=1.9, 4.8, 13.4 Hz, H-1), 1.94 (1H, m, H-7), 1.87 (1H, m, H-15), 1.75 (2H, m, H-3, 6), 1.69 (2H, m, H-2, 14), 1.57 (1H, m, H-4), 1.49 (1H, m, H-11), 1.48 (1H, m, H-10), 1.43 (2H, m, H-8, 11), 1.34 (3H, m, H-3, 6, 10), 1.20 (1H, m, H-2), 1.05 (1H, ddd, J=3.2, 13.0, 13.0 Hz, H-8), 1.00 (1H, ddd, J=2.7, 12.2, 12.2 Hz, H-14), 0.88 (3H, d, J=6.4 Hz, H-16).