Fawcettimine-Related Alkaloids from *Lycopodium serratum*

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Five new *Lycopodium* alkaloids (**1**−**5**) having the fawcettimine skeleton were isolated from *Lycopodium serratum*. The structures of the alkaloids were elucidated on the basis of spectroscopic analysis. Some alkaloids isolated in this and previous studies (**1**, **2**, **5**, and **10**) were assayed for acetylcholine esterase (AChE) inhibitory activity.

Plants belonging to genus *Lycopodium* are known to contain alkaloids having unique skeletal characteristics and activities such as acetylcholine esterase (AChE) inhibition.[1] This has inspired many groups to investigate the alkaloid constituents in those plants, resulting in the discovery of a number of novel alkaloids in recent years.[2] We have reported previously the isolation and structure elucidation of novel *Lycopodium* alkaloids having various kinds of skeletons.[3] In this paper, we describe the isolation and structure elucidation of new alkaloids from *L. serratum*. The AChE inhibitory activities of some alkaloids are also reported.

Results and Discussion

The whole plant of *Lycopodium serratum* Thunb. collected at Mt. Kiyosumi, Chiba Prefecture, Japan, was dried, pulverized, and extracted with MeOH. The alkaloid fraction was obtained by acid−base extraction, and the crude base was separated by column chromatography to afford five new alkaloids (**1**−**5**), together with known alkaloids, lycothunine (**6**),[4,5] serratine (**7**),[6,7] and serratanidine (**8**).[8,9]

Compound **1**, 11α-hydroxyfawcettidine, was obtained as a colorless solid. High-resolution FABMS analysis gave *m*/*z* 262.1805 (M + H, Δ −0.2 mmu) and established the molecular formula as $C_{16}H_{23}NO_2$. IR absorption bands at 1732 and 3454 cm^{-1} implied the presence of a ketone and a hydroxy group, respectively. ^1H and ^{13}C NMR and HMQC analyses indicated the presence of one ketone (δ_C 217.1), one oxygenated methine (δ_H 3.87, 1H, br s), a trisubstituted olefinic function (δ_H 5.97, 1H, d, J = 5.2 Hz), one sp^3 methyl group (δ_H 1.09, 3H, d, J = 7.1 Hz), two sp^3 aminomethylene carbons (δ_C 61.3 and 45.8), three sp^3 methines, and five sp^3 methylenes (Table 1). $^1H-^1H$ COSY analysis gave three fragments [**a**: $-CH_2CH_2CH_2CH-$, **b**: $-CH_2CHCH_2CH(CH_3)CH-$, **c**: $-CH_2CH_2CH-$]. The planar structure of **1** was elucidated by HMBC analysis as follows. Correlations between the two hydrogens attached to the carbon adjacent to the terminal carbon of fragments **a** and **b** [δ_H 1.43 (Hβ-3) on fragment **a** and 2.80 (H-7) on fragment **b**] and the carbonyl carbon [δ_C 217.1 (C-5)] as well as quaternary carbon [δ_C 52.4 (C-12)] indicated the presence of a cyclopentanone ring system. The connectivity of the aminomethylene carbons on the termini of fragments **a** and **c** [δ_C 61.3 (C-1) and 45.8 (C-9)] with the same nitrogen atom was revealed by correlations between the aminomethylene hydrogen [δ_H 3.00 (Hβ-1)] and the aminomethylene carbon [δ_C 45.8 (C-9)]. A similar correlation between H-9 and C-1 was also observed. The enamino group was elucidated on the basis of correlations between two hydrogens [δ_H 3.00 (Hβ-1) and 5.97 (H-14)] and an olefinic carbon [δ_C 141.9 (C-13)]. Finally, the piperidine ring system (C-9−C-13 and a nitrogen atom) was determined on the basis of correlations between the oxygenated methine hydrogen [δ_H 3.87 (H-11)] and two carbons [δ_C 52.4 (C-12) and 141.9 (C-13)]. These data indicated that **1** possessed the fundamental backbone of the known alkaloid fawcettidine (**9**).[10] The relative configuration of **1** was found to be the same as that of **9** by NOESY analysis [correlations H-4/H-11, H-7/H-11, and Hβ-6/H-15]. NOESY correlations between the oxymethine hydrogen (H-11) and two adjacent hydrogens (H_2-10) indicated that H-11 has a gauche relationship with the two methylene hydrogens on C-10. Furthermore, the broadened singlet of H-11 also implied the gauche relationship described above. These results indicated that the C-11 hydroxy group occupied the α-axial position in the piperidine ring system. Thus, we proposed **1** to be the 11-hydroxy derivative of fawcettidine (**9**), i.e., 11α-hydroxyfawcettidine, as shown in Figures 1 and 2.

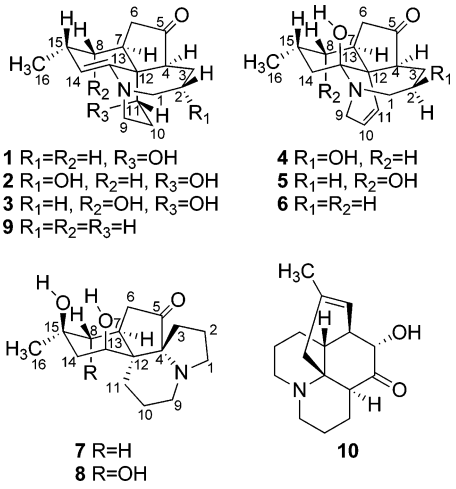

Figure 1. New and related known alkaloids.

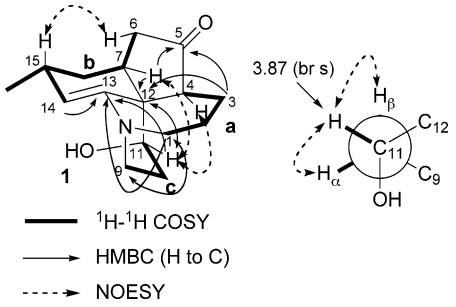

Figure 2. Selected 2D NMR data and configurational analysis of **1**.

Compound **2**, 2α,11α-dihydroxyfawcettidine, was obtained as a colorless solid. High-resolution FABMS analysis gave *m*/*z* 278.1775 (M + H, Δ +1.9 mmu) and established the molecular

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Table 1. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) Data for **1**−**3** in $CDCl_3$

	1		**2**		**3**	
position	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1α	3.15 (br d, 14.3)	61.3	3.15 (d, 15.1)	65.9	3.12 (ddd, 13.8, 2.8, 2.8)	60.8
1*β*	3.00 (ddd, 12.9, 12.9, 3.5)		3.23 (dd, 15.3, 2.7)		3.03 (m)	
2α	1.70 (m)	31.3	3.99 (d, *J* = 6.6)	70.6	1.77 (m)	31.6
2*β*	1.76 (m)				1.77 (m)	
3α	2.32 (m)	29.2	2.34 (m)	34.8	2.17 (m)	30.8
3*β*	1.43 (m)		1.67 (dd, 13.4, 13.4)		1.51 (m)	
4	2.04 (m)	55.1	2.53 (d, 12.3)	47.4	2.17 (m)	56.0
5		217.1		219.8		217.4
6α	2.72 (dd, 16.7, 7.9)	43.8	2.80 (m)	44.2	2.51 (m)	40.7
6*β*	2.06 (m)		2.07 (d, 17.0)		2.51 (m)	
7	2.80 (m)	30.9	2.85 (m)	30.3	2.70 (ddd, 7.5, 7.5, 7.5)	30.7
8α	1.25 (m)	34.2	1.22 (ddd, 13.3, 13.3, 5.3)	34.1	3.59 (dd, 4.9, 4.9)	70.4
8*β*	1.40 (m)		1.42 (br d, 12.3)			
9α	3.35 (ddd, 14.0, 14.0, 3.8)	45.8	3.33 (ddd, 13.4, 13.4, 3.7)	46.6	3.45 (ddd, 13.9, 13.9, 4.0)	45.7
9*β*	2.83 (dd, 14.5, 6.0)		2.85 (m)		2.80 (dd, 14.2, 5.2)	
10α	1.65 (m)	30.0	1.50 (ddd, 13.7, 3.5, 3.5)	28.0	1.63 (ddd, 14.5, 3.2, 3.2)	29.9
10*β*	2.23 (dddd, 13.9, 13.9, 6.3, 2.6)		2.80 (m)		2.17 (m)	
11	3.87 (br s)	71.8	3.91 (s)	71.6	3.79 (br s)	73.5
12		52.4		53.2		51.4
13		141.9		141.4		143.0
14	5.97 (d, 5.2)	132.9	5.95 (d, 5.5)	131.9	5.65 (d, 3.2)	128.1
15	2.32 (m)	27.9	2.31 (m)	28.2	2.51 (m)	31.8
16	1.09 (d, 7.1)	21.0	1.10 (d, 7.1)	21.0	1.14 (d, 7.1)	16.2

formula as $C_{16}H_{23}NO_3$, which was one oxygen atom more than that of **1**. IR absorption bands at 1731 and 3444 cm^{-1} implied the presence of a ketone and a hydroxy group, respectively. ^{1}H and ^{13}C NMR spectra of **2** were similar to those of **1** except for the presence of one additional oxygenated methine function instead of one methylene function (Table 1). This led us to assume that **2** was an oxygenated derivative of **1**. The presence of the −CH_2CH-(OH)CH_2CH− fragment inferred from ^{1}H−^{1}H COSY and HMQC spectra, as well as HMBC correlations such as H-2/C-4, H-1/C-9, H-1/C-13, H-3/C-5, and H-3/C-12, indicated that the additional hydroxy group was located at C-2. The configuration of this stereocenter was elucidated by NOESY analysis (Figure 3). Correlations between H*β*-1 (δ_H 3.23) and H*β*-3 (δ_H 1.67) as well as H*β*-1 and H-14 (δ_H 5.95) indicated that H*β*-1 and H*β*-3 occupied quasi-axial positions on the azepine ring system (C-1−C-4, C-12−C-13, and nitrogen atom). Correlations between H-2 (δ_H 3.99) and four neighboring hydrogens (H_2-1 and H_2-3) implied that the secondary C-2 hydroxy group also occupied an axial position. Moreover, a decoupling experiment of H-2 (δ_H 3.99, d, *J* = 6.6 Hz) indicated that this hydrogen coupled with Hα-3. Dreiding models regarding the dihedral angles (gauche relationships of H*β*-2 and both hydrogens on C-1, 30° between H*β*-2 and Hα-3, and 90° between H*β*-2 and H*β*-3) also supported the result from NOESY analysis. From these data, we proposed that **2** is the 2α-hydroxy derivative of **1**, i.e., 2α,11α-dihydroxyfawcettidine, as shown in Figures 1 and 3.

Compound **3**, 8α,11α-dihydroxyfawcettidine, showed the protonated molecular ion at *m*/*z* 278.1769 (M + H) that established the molecular formula as $C_{16}H_{23}NO_3$ (Δ +1.3 mmu), which was identical with that of **2**. Comparison of ^{1}H and ^{13}C NMR data with those of **2** suggested that the two alkaloids were regioisomers with respect to the secondary hydroxy group (Table 1). ^{1}H−^{1}H COSY and HMQC analyses indicated that this hydroxy group was located at C-8 instead of C-2 in **2** because an oxymethine resonance (δ_H 3.59, H-8) coupled with a methine hydrogen (δ_H 2.51, H-15), which further coupled with methyl hydrogens (δ_H 1.14, H_3-16). The orientation of the 8-hydroxy group was elucidated from NOESY correlations between H-8 and two adjacent hydrogens (H*β*-6 and H-15) as well as the *J* value of H-8 (dd, *J* = 4.9 and 4.9 Hz), which was typical of a gauche relationship with neighboring hydrogens (H-7 and H-15). From these results, we confirmed that **3** was the 8α-hydroxylated derivative of **1**, i.e., 8α,11α-dihydroxyfawcettidine, as shown in Figures 1 and 3.

The CD spectra of **1**, **2**, **3**, and fawcettidine (**9**), the absolute configuration of which was elucidated by means of correlation with literature data,[10e] were almost the same, as shown in Figure 4, allowing us to determine the absolute configuration of the new alkaloids **1**, **2**, and **3**.

Compound **4**, 2*β*-hydroxylycothunine, was obtained as a colorless, amorphous powder. High-resolution FABMS analysis gave *m*/*z* 278.1740 (M + H, Δ −1.6 mmu) and established the molecular

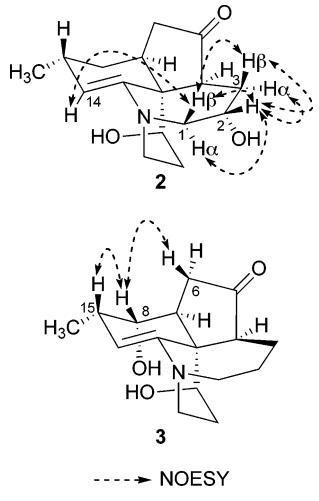

Figure 3. NOESY analyses of **2** and **3**.

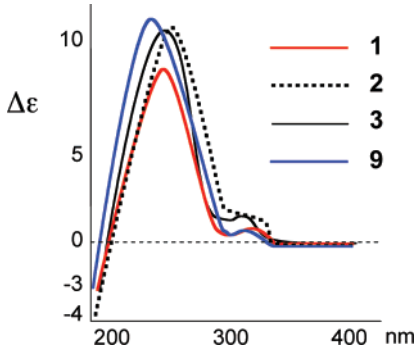

Figure 4. CD spectra of **1**, **2**, **3**, and fawcettidine (**9**) in MeOH.

Table 2. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) Data for **4**−**6** in $CDCl_3$

	4		**5**		**6**	
position	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1α	2.83 (d, 14.0)	60.6	2.82 (dd, 14.5, 4.1)	54.6	2.80 (d, 14.5)	54.6
1*β*	3.27 (dd, 14.1, 10.5)		3.27 (dd, 12.7, 12.7)		3.33 (dd, 13.3, 13.3)	
2α	4.22 (dddd, 11.8, 10.4, 2.7, 2.7)	65.1	1.35 (m)	23.6	1.36 (m)	23.5
2*β*			2.01 (m)		1.99 (m)	
3α	2.26 (m)	37.8	2.19 (m)	28.8	2.18 (m)	28.8
3*β*	2.10 (m)		1.97 (m)		1.97 (m)	
4	2.28 (m)	54.8	2.27 (m)	56.9	2.23 (m)	57.3
5		218.4		217.9		219.8
6α	2.19 (m)	39.9	2.30 (m)	39.5	2.18 (m)	40.2
6*β*	2.54 (dd, 18.1, 12.6)		2.34 (m)		2.54 (dd, 17.8, 12.9)	
7	2.15 (m)	43.4	2.32 (m)	50.4	2.11 (m)	43.5
8α	1.20 (ddd, 13.0, 13.0, 5.2)	32.6	3.75 (br s)	72.3	1.20 (ddd, 13.0, 13.0, 4.8)	32.5
8*β*	1.61 (d, 15.6)				1.60 (d, 13.5)	
9α	3.83 (d, 19.2)	51.4	3.91 (d, 19.5)	51.2	3.82 (ddd, 19.4, 2.1, 2.1)	51.2
9*β*	3.33 (dd, 19.3, 3.9)		3.22 (dd, 19.3, 3.7)		3.23 (br d, 19.2)	
10	5.84 (ddd, 9.8, 3.8, 1.6)	128.4	5.80 (dd, 10.7, 3.0)	127.0	5.80 (ddd, 9.9, 3.9, 1.8)	127.8
11	5.53 (d, 9.8)	135.0	5.75 (d, 9.8)	136.3	5.53 (ddd, 9.9, 2.0, 2.0)	135.5
12		49.7		49.0		50.1
13		87.2		87.5		88.0
14α	1.71 (dd, 12.9, 12.9)	44.5	2.23 (m)	38.1	1.70 (dd, 13.6, 12.2)	45.2
14*β*	1.32 (d, 13.7)		1.09 (m)		1.36 (m)	
15	1.99 (m)	22.7	2.25 (m)	27.1	1.99 (m)	22.6
16	0.92 (d, 6.5)	21.7	1.01 (d, 6.3)	17.3	0.92 (d, 6.6)	21.8

formula as $C_{16}H_{23}NO_3$, which was identical with those of **2** and **3**. ^{1}H and ^{13}C NMR data suggested the presence of one disubstituted olefinic function [δ_H 5.84 (1H, ddd, J = 9.8, 3.8, 1.6 Hz), 5.53 (1H, d, J = 9.8 Hz), δ_C 135.0 and 128.4], one aminoacetal [δ_C 87.2], one oxymethine [δ_H 4.22 (1H, dddd, J = 11.8, 10.4, 2.7, 2.7 Hz), δ_C 65.1], and one secondary methyl group [δ_H 0.92 (3H, d, J = 6.5 Hz)] (Table 2). ^{1}H−^{1}H COSY and HMQC analyses gave three fragments [**a**: −$CH_2CH(OH)CH_2CH$−, **b**: −$CH_2CHCH_2CH(CH_3)CH_2$−, and **c**: −CH_2CH═CH−]. Further, HMBC correlations between one aminomethylene hydrogen [δ_H 2.83 (Hα-1)] and one aminomethylene carbon [δ_C 51.4 (C-9)] suggested that C-1 (δ_C 60.6) and C-9 were attached to the same nitrogen atom, implying that **4** had the fawcettimine-type skeleton with one external hydroxy group at C-2 and one disubstituted olefinic function at C-10 and C-11. The positions of the hydroxy group and the disubstituted olefinic function were inferred from chemical shifts and HMBC analyses as follows. Correlation between the olefinic hydrogen on fragment **c** [δ_H 5.84 (H-10)] and the quaternary carbon [δ_C 49.7 (C-12)] implied that the quaternary carbon (C-12) was connected to the olefinic carbon [δ_C 135.0 (C-11)] at the terminus of fragment **c**. Further correlations between the terminal olefinic hydrogen on fragment **c** [δ_H 5.53 (H-11)] and two carbons [δ_C 43.4 (C-7) and 87.2 (C-13)] as well as correlations between the terminal methine hydrogen on fragment **a** [δ_H 2.28 (H-4)] and the C-12 and C-13 permitted confirmation of the positions of the C-2 hydroxy group and one disubstituted olefinic function at C-10 in the fawcettimine-type skeleton. The relative configuration was elucidated on the basis of NOESY analysis. The configurations of the five asymmetric carbons (C-4, -7, -12, -13, and -15) were found to be the same as that of the related known alkaloid lycothunine (**6**) on the basis of NOESY correlations such as H-4/H-11, H-7/H-11, and H-6*β*/H-15, as shown in Figure 5. The NOESY correlation between H-2 and H-4 indicated that these two hydrogens are oriented on the same side. The large coupling constants between H-2 and two anti-hydrogens (H*β*-1 and H*β*-3) supported the *β*-orientation of the hydroxyl group on C-2. Thus, we concluded that **4** is 2*β*-hydroxylycothunine, as depicted in Figures 1 and 5.

Compound **5**, 8α-hydroxylycothunine, was obtained as a colorless solid. High-resolution FABMS analysis gave *m*/*z* 278.1762 (M + H, Δ +0.6 mmu) and established the molecular formula as $C_{16}H_{23}NO_3$, which was identical with that of compound **4**. The NMR spectrum of **5** was similar to that of **4** except for the oxymethine resonances at δ_H 3.75 (H-8) and δ_C 72.3 (C-8), implying that **5** is a regioisomer of **4** (Table 2). ^{1}H−^{1}H COSY and HMQC analyses gave three fragments [**a**: −$CH_2CH_2CH_2CH$−, **b**: −CH_2-$CHCH(OH)CH(CH_3)CH_2$−, and **c**: −CH_2CH═CH−], which implied that **5** had a secondary hydroxy group at C-8 (Figure 5). HMBC correlations such as H-1/C-9, H-1/C-13, H-3/C-5, H-3/C-12, H-4/C-5, H-6/C-5, H-8/C-12, H-11/C-12, and H-11/C-13 demonstrated that **5** had the same backbone as **4**. The stereostructure of **5** was deduced to be the same as that of **4** on the basis of NOESY correlations, particularly H-4/H-11, H-6/H-15, and H-7/H-11. The orientation of the secondary C-8 hydroxy group was assigned by coupling constant analysis as in the case of **3**, since the C-8 hydrogen was observed as a broadened singlet (small coupling constants), which indicated its equatorial orientation. Thus, the C-8 hydroxy group occupied the axial position in the cyclohexane ring system consisting of C-7−C-8 and C-12−C-15, causing a steric (*γ*-gauche) effect on C-14 and C-16 (the resonances were shifted upfield by 6.4 and 4.4 ppm, respectively, compared with those of **4**). These results allowed the structure of **5** to be assigned as 8α-hydroxylycothunine.

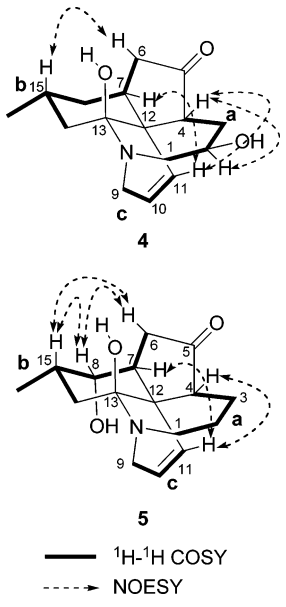

Figure 5. Selected 2D NMR data of **4** and **5**.

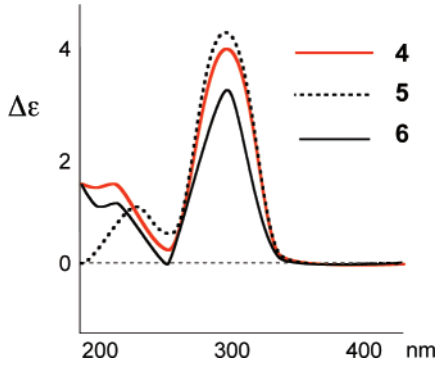

Figure 6. CD spectra of **4**, **5**, and **6** in MeOH.

Comparing the CD spectra (Figure 6) of **4** and **5** with that of lycothunine (**6**), the absolute configuration of which was elucidated by means of comparison with fawcettimine,[5b] we concluded the absolute configuration of **4** and **5** to be the same as **6**.

The AChE inhibitory activity of **1**, **2**, **5**, and lycoposerramine-H[3c] was assayed using the Ellman method.[11] **2** and **10** inhibited AChE (IC_{50} 27.9 and 16.7 μM, respectively), whereas **1** and **5** did not show such activity.

Experimental Section

General Experimental Procedures. Optical rotations were measured with a JASCO P-1020 polarimeter. CD was recorded on a JASCO J-720WI spectrometer. IR spectra were recorded on a JASCO FT/IR-230 spectrophotometer. NMR spectroscopic data were recorded on JEOL JNM ECP-600 and JNM A-500 spectrometers, where *J* values are given in Hz. EIMS was recorded on a JEOL JMS GC-mate spectrometer with direct probe insertion at 70 eV. FABMS and HRFABMS were recorded on a JEOL AX-500 spectrometer and a JEOL JMS-HX110 spectrometer, respectively. X-ray crystallographic analysis was conducted on a Rigaku AFC7S diffractometer with graphite-monochromated Mo Kα radiation (λ = 1.54178 Å). TLC was done on precoated silica gel 60 F254 plates (Merck, 0.25 mm thick). Column chromatography was carried out over silica gel 60 (Merck, 70−230 mesh). Medium-pressure liquid column chromatography was carried out over silica gel prepacked columns (Kusano CPS-HS-221-05).

Plant Material. The club moss *Lycopodium serratum* Thunb. was collected at Kiyosumi Mountains in 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 Science, Chiba University (20010512tn).

Extraction and Isolation of Alkaloids. The air-dried club moss (95.7 g) was extracted with MeOH (5 × 5.0 L), and the extracts were filtered. The combined filtrates were concentrated under reduced pressure to give the crude extract (37.6 g), which was suspended in 2% tartaric acid and filtered. The aqueous filtrate was washed with petroleum ether, rendered basic with Na_2CO_3 (pH 10), and exhaustively extracted with 5% MeOH/$CHCl_3$. The organic layer was dried over $MgSO_4$ and evaporated to give the crude alkaloid fraction (628 mg). The crude base was roughly separated by silica gel column chromatography using a $CHCl_3$ to 30% MeOH/$CHCl_3$ gradient, 30% MeOH/$CHCl_3$ saturated with NH_4OH, and MeOH to give six fractions (A−F). The 10−20% MeOH/$CHCl_3$ eluate (fraction C) was rechromatographed over SiO_2 using 0−100% MeOH/EtOAc to give nine fractions (C1−C9). The 15−20% MeOH/EtOAc eluate (fraction C5) was further purified by SiO_2 column chromatography using 5% MeOH/$CHCl_3$ to afford 6.6 mg of 11α-hydroxyfawcettidine (**1**), 4.3 mg of 2α,11α-dihydroxyfawcettidine (**2**), 1.2 mg of 8α,11α-dihydroxyfawcettidine (**3**), and 1.9 mg of 2β-hydroxylycothunine (**4**) together with 9.5 mg of lycothunine (**6**), 11.7 mg of serratine (**7**), and 1.4 mg of serratanidine (**8**). The 20% MeOH/$CHCl_3$ to 30% MeOH in $CHCl_3$ saturated with NH_4OH eluate (fraction D) was rechromatographed over an Al_2O_3 column using 0−100% MeOH/$CHCl_3$ (D1−D5). The 5−15% MeOH/$CHCl_3$ eluate (fraction D2) was further purified by Al_2O_3 column chromatography using 1% MeOH/AcOEt to give 7.1 mg of 8α-hydroxylycothunine (**5**).

11α-Hydroxyfawcettidine (1): colorless solid; CD (*c* 0.35 mmol/L, MeOH, 24 °C), λ nm ($\Delta\epsilon$) 316 (0), 294 (+0.7), 272 (+0.5), 230 (+8.7); $[\alpha]^{23}_D$ +134.2 (*c* 0.28, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3454, 1732 cm^{-1}; NMR data, see Table 1; FABMS (NBA) *m/z* 262 $[M + H]^+$; HRFABMS (NBA/PEG) *m/z* 262.1805 (M + H, calcd for $C_{16}H_{24}NO_2$, 262.1807).

2α, 11α-Dihydroxyfawcettidine (2): colorless solid; CD (*c* 0.21 mmol/L, MeOH, 24 °C), λ nm ($\Delta\epsilon$) 316 (0), 298 (+0.9), 279 (+1.3), 232 (+11.8); $[\alpha]^{23}_D$ +84.7 (*c* 0.20, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3444, 1731 cm^{-1}; NMR data, see Table 1; FABMS (NBA) *m/z* 278 $[M + H]^+$; HRFABMS (NBA/PEG) *m/z* 278.1775 (M + H, calcd for $C_{16}H_{24}NO_3$, 278.1756).

8α, 11α-Dihydroxyfawcettidine (3): colorless solid; CD (*c* 0.43 mmol/L, MeOH, 24 °C), λ nm ($\Delta\epsilon$) 324 (0), 292 (+1.1), 281 (+0.9), 230 (+10.9); IR ($CHCl_3$) ν_{max} 3399, 1731 cm^{-1}; NMR data, see Table 1; FABMS (NBA) *m/z* 278 $[M + H]^+$; HRFABMS (NBA/PEG) *m/z* 278.1769 (M + H, calcd for $C_{16}H_{24}NO_3$, 278.1756).

2β-Hydroxylycothunine (4): colorless, amorphous powder; CD (*c* 0.41 mmol/L, MeOH, 24 °C), λ nm ($\Delta\epsilon$) 323 (0), 286 (+4.2), 247 (+0.3), 215 (+1.6); IR ($CHCl_3$) ν_{max} 3389, 1731 cm^{-1}; NMR data, see Table 2; FABMS (NBA) *m/z* 278 $[M + H]^+$; HRFABMS (NBA/PEG) *m/z* 278.1740 (M + H, calcd for $C_{16}H_{24}NO_3$, 278.1756).

8α-Hydroxylycothunine (5): colorless solid; CD (*c* 0.33 mmol/L, MeOH, 24 °C), λ nm ($\Delta\epsilon$) 319 (+0.1), 284 (+4.7), 253 (+1.0), 231 (+1.5); $[\alpha]^{21}_D$ +72.2 (*c* 0.26, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3309, 1733 cm^{-1}; NMR data, see Table 2; FABMS (NBA) *m/z* 278 $[M + H]^+$; HRFABMS (NBA/PEG) *m/z* 278.1762 (M + H, calcd for $C_{16}H_{24}NO_3$, 278.1756).

Lycothunine (6): colorless, amorphous powder; CD (*c* 0.36 mmol/L, MeOH, 24 °C), λ nm ($\Delta\epsilon$) 318.8 (0), 286.2 (+3.5), 246.6 (+0.2), 220.2 (+1.3); $[\alpha]_D^{23}$ +153.5 (*c* 0.21, EtOH); IR ($CHCl_3$) ν_{max} 3418, 1730 cm^{-1}; NMR data, see Table 2; EIMS (%) *m/z* 261 (M^+, 100), 220 (12.7), 243 (16.1)

Serratine (7): colorless pillars (recrystallized from EtOAc, mp 249 °C); $[\alpha]^{24}_D$ −11.8 (*c* 0.39, EtOH); IR (KBr) ν_{max} 3288, 1737 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.36 (1H, s), 3.62 (1H, s), 2.97 (2H, m), 2.70 (5H, m), 2.24 (1H, dd, *J* = 11.4, 11.4), 2.08 (1H, m), 1.74−1.94 (8H, m), 1.57 (2H, m), 1.25 (3H, s), 1.08 (1H, m); ^{13}C NMR (150 MHz, $CDCl_3$) δ 214.8, 77.4, 75.2, 72.2, 52.1, 50.3, 45.2, 39.4, 38.1, 35.4, 32.6, 31.0, 25.3, 21.6, 21.1, 21.0; EIMS (%) 279 (M^+, 5.5), 251 (89.9), 152 (100). Crystal data: triclinic, $C_{16}H_{25}NO_3$ (MW 279.38), space group *P*1 with *a* = 7.708(1) Å, *b* = 24.878(4) Å, *c* = 7.597(2) Å, *V* = 1456.9(5) $Å^3$, *Z* = 4, and D_{calc} = 1.274 g/cm^3. The structure was solved by direct methods (SIR97) and expanded using Fourier techniques (DIRDIF94). The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement was based on 4887 reflections ($I > 3.00\sigma(I)$, $2\theta < 137.99$) and 723 variable parameters and converted with unweighted and weighted agreement factors of *R* = 0.050 and R_w = 0.073.

Serratanidine (8): colorless solid; $[\alpha]^{26}_D$ −31.0 (*c* 0.049, EtOH); ^1H NMR (500 MHz, $CDCl_3$) δ 4.05 (1H, dd, *J* = 6.1, 11.5), 3.59 (1H, d, *J* = 10.9), 3.14 (1H, ddd, *J* = 7.9, 7.9, 7.9), 3.05 (1H, m), 2.90 (1H, br d, *J* = 7.9), 2.66 (1H, br dd, *J* = 12.5, 12.5), 2.56 (1H, m), 2.48 (2H, m), 2.32 (1H, br s), 2.22 (1H, dd, 7.0, 13.1), 2.10 (1H, m), 1.94−1.81 (3H, m), 1.75−1.69 (2H, m), 1.58 (1H, m), 1.36 (1H, ddd, 4.5, 14.0, 14.0), 1.19 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.4, 79.1, 75.8, 74.8, 72.3, 49.9, 46.9, 45.6, 43.4, 42.6, 39.8, 37.8, 31.0, 22.5, 19.5, 19.2; FABMS (NBA) *m/z* 296 $[M + H]^+$.

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References and Notes

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