Lannotinidines H—J, New *Lycopodium* Alkaloids from *Lycopodium annotinum*

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Three new *Lycopodium* alkaloids, lannotinidines H—J (1—3), were isolated from the club moss *Lycopodium annotinum*. The structures and relative stereochemistry of 1—3 were elucidated on the basis of spectroscopic data and the absolute stereochemistry of 2 was assigned by chemical correlation. Lannotinidine H (1) is the first *Lycopodium* alkaloid possessing a lycopodane skeleton with an additional C_3 unit.

Key words *Lycopodium* alkaloid; *Lycopodium annotinum*; lannotinidine H; lannotinidine I; lannotinidine J

Club moss (Lycopodiaceae) is known to be a rich source of *Lycopodium* alkaloids[1,2] possessing unique heterocyclic ring systems such as $C_{16}N$, $C_{16}N_2$, and $C_{27}N_3$, which have attracted great interest from biogenetic,[3,4] synthetic,[5,6] and biological[7] points of view. Among them, huperzine A is a highly specific and potent inhibitor of acetylcholine esterase (AChE),[7] and the attractive biological profile has promoted the pursuit of the total synthesis and structure activity relationship (SAR) studies of huperzine A. In our continuing efforts to find structurally and biogenetically interesting *Lycopodium* alkaloids,[8—10] three new *Lycopodium* alkaloids, lannotinidines H (**1**), I (**2**), and J (**3**), were isolated from the club moss *Lycopodium annotinum* together with known alkaloids, lannotinidines A (**4**) and C (**5**).[11] In this paper, we describe the isolation and structure elucidation of **1**—**3**.

The club moss *L. annotinum* collected at Nayoro in Hokkaido was extracted with MeOH aq., and the extracts were partitioned between EtOAc and 3% tartaric acid. Water-soluble materials, adjusted at pH 9 with sat. Na_2CO_3 aq., were partitioned with $CHCl_3$. The $CHCl_3$-soluble materials were subjected to an amino silica gel column (*n*-hexane/EtOAc, 1 : 0→1 : 1 and then $CHCl_3$/MeOH, 1 : 0→1 : 1), from which a fraction eluted with $CHCl_3$/MeOH (1 : 0) was further purified with a silica gel column ($CHCl_3$/MeOH, 1 : 0→1 : 1) and a C_{18} column (MeCN/H_2O/trifluoroacetic acid (TFA), 20/80/0.1→80/20/0.1) chromatographies, followed by C_{18} HPLC (MeCN/H_2O/TFA, 12/88/0.1) to afford lannotinidine H (**1**, 0.57 mg, 0.00008%). The fraction eluted from an amino silica gel column with $CHCl_3$/MeOH (10 : 1) was purified by a silica gel column ($CHCl_3$/MeOH, 1 : 0→1 : 1) and then a C_{18} column (MeCN/H_2O/TFA, 20/80/0.1→100/0/0.1) chromatographies to get lannotinidine I (**2**, 14.2 mg, 0.002%), while a fraction eluted from an amino silica gel column with $CHCl_3$/MeOH (1 : 1) was purified by a C_{18} column (MeCN/H_2O/TFA, 100/0/0.1→0/100/0.1) and a silica gel column ($CHCl_3$/MeOH, 1 : 0→1 : 1) chromatographies, followed by C_{18} HPLC (MeCN/H_2O/TFA, 5/95/0.1) to give lannotinidine J (**3**, 1.71 mg, 0.0002%).

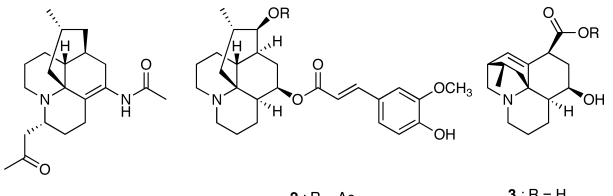

Chart 1

Lannotinidine H (**1**) {$[\alpha]_D^{23}$ −40.2 (c=0.2, MeOH)} showed the pseudomolecular ion peak at m/z 345 $(M+H)^+$ in the electrospray ionization (ESI)-MS, and the molecular formula, $C_{21}H_{32}N_2O_2$, was established by HR-ESI-MS [m/z 345.2541, $(M+H)^+$, Δ −0.1 mmu]. IR absorptions implied the presence of secondary amino (3358 cm^{-1}), keto carbonyl (1716 cm^{-1}), and amido carbonyl (1659 cm^{-1}) functionalities. Inspection of ^{1}H- and ^{13}C-NMR data (Table 1) and the heteronuclear multiple quantum coherence (HMQC) spectrum revealed that **1** possessed one keto carbonyl, one amide

Table 1. ^{1}H- and ^{13}C-NMR Data of Lannotinidine H (**1**) in CD_3OD

Position	δ_H	δ_C
1	4.46 (1H, m)	53.1 d
2	1.78 (2H, m)	23.9 t
3a	2.61 (1H, m)	22.4 t
3b	2.17 (1H, m)	
4	—	121.5 s
5	—	134.6 s
6a	2.58 (1H, m)	33.1 t
6b	1.92 (1H, dd, 18.6, 3.0)	
7	2.06 (1H, m)	35.1 d
8a	1.72 (1H, m)	43.0 t
8b	1.33 (1H, m)	
9	3.28 (2H, m)	45.1 t
10a	1.99 (1H, br d, 14.4)	23.6 t
10b	1.84 (1H, m)	
11a	1.68 (1H, dddd, 12.6, 12.6, 12.6, 3.6)	25.9 t
11b	1.58 (1H, br d, 12.6)	
12	1.88 (1H, m)	44.3 d
13	—	69.6 s
14a	2.63 (1H, m)	41.2 t
14b	1.27 (1H, m)	
15	1.84 (1H, m)	28.1 d
16	1.00 (3H, d, 6.6)	22.0 q
17	2.94 (2H, m)	44.9 t
18	—	206.5 s
19	2.21 (3H, s)	30.2 q
20	—	171.6 s
21	2.02 (3H, s)	22.8 q

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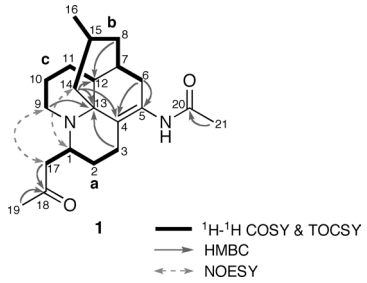

Fig. 1. Selected 2D NMR Correlations for Lannotinidine H (**1**)

carbonyl, two sp^2 quaternary carbons, one sp^3 quaternary carbon, four sp^3 methines, nine sp^3 methylenes, and three methyl groups. Among them, one sp^3 quaternary carbon (δ_C 69.6) and one sp^3 methine (δ_C 53.1) were attributed to carbons bearing a nitrogen atom. The gross structure of **1** was elucidated by analyses of 2 dimentional (2D) NMR data including the ^{1}H–^{1}H correlation spectroscopy (COSY), total correlation spectroscopy (TOCSY), HMQC, and heteronuclear multiple bond correlation (HMBC) spectra in CD_3OD (Fig. 1).

The ^{1}H–^{1}H COSY and TOCSY spectra of **1** revealed three structural units **a** (C-1—C-3, C-17), **b** (C-6—C-8, C-14—C-16), and **c** (C-9—C-12). HMBC correlations for H-17 (δ_H 2.94) and H-19 (δ_H 2.21) to a keto carbonyl carbon (δ_C 206.5) revealed that an acetyl group (C-18, C-19) was attached to C-17, while an HMBC cross-peak of H-9 (δ_H 3.28) to C-13 (δ_C 69.6) suggested that C-9 (δ_C 45.1) was connected to C-13 through N-9. The connectivity of C-7 and C-12 was elucidated by an HMBC correlation for H-8a to C-12. HMBC correlations for H-14b to C-4 and C-13, H-14a to C-12 suggested the connectivities of C-4, C-12, and C-14 *via* C-13. An HMBC cross-peak of H-3a to C-13 revealed that C-3 was connected to C-4 (δ_C 121.5). The connectivity of C-6 to C-5 (δ_C 134.6) was suggested by HMBC correlations for H-6b to C-4 and C-5. An HMBC correlation for H-21 (δ_H 2.02) to C-20 (δ_C 171.6) revealed that C-20 and C-21 (δ_C 22.8) composed an acetyl group. Nuclear Overhauser enhancement and exchange spectroscopy (NOESY) correlations for H-1/H-14a and H-9/H-17 suggested that C-1 was connected to N-9. Finally, molecular formula indicated that an acetyl amino group was attached to C-5. Thus, the gross structure of lannotinidine H was elucidated to be **1**.

The phase-sensitive NOESY spectrum of **1** showed cross-peaks as shown in computer-generated 3D drawing (Fig. 2). The chair form of cyclohexane ring (C-7, C-8, C-12—C-15) and the presence of *trans*-fused decahydroquinoline ring (C-7—C-15, N-9) were deduced from NOESY cross-peaks of H-12/H-8b and H-12/H-14b. The methyl group at C-15 was assigned as equatorial from a NOESY correlation for H-14b/H-16. A NOESY correlation for H-1/H-14a revealed chair form of the piperidine ring (C-1—C-4, C-13, N-9). ^3J value (12.6 Hz) between H-11a and H-12, and a NOESY correlation for H-6a/H-11a suggested that the piperidine ring (C-9—C-13, N-9) was chair form and the cyclohexene ring (C-4—C-7, C-12, C-13) was half-chair form. The α-orientation of C_3 unit (C-17—C-19) at C-1 was revealed by a NOESY correlation for H-9/H-17. Thus, the relative stereostructure of lannotinidine H (**1**) was elucidated to be shown in Fig. 2.

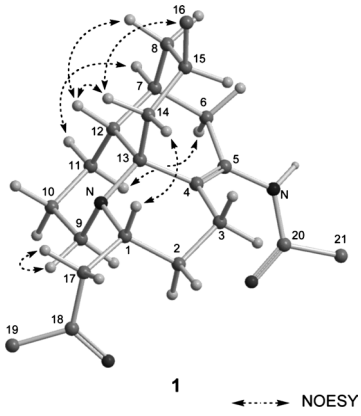

Fig. 2. Selected NOESY Correlations and Relative Stereochemistry for Lannotinidine H (**1**)

Hydrogen atoms of methyl groups were omitted.

Table 2. ^{1}H- and ^{13}C-NMR Data of Lannotinidine I (**2**) in $CDCl_3$

Position	δ_H	δ_C
1a	3.62 (1H, m)	47.0 t
1b	3.09 (1H, m)	
2a	1.93 (1H, m)	18.7 t
2b	1.85 (1H, m)	
3a	1.85 (1H, m)	20.7 t
3b	1.61 (1H, m)	
4	2.63 (1H, m)	32.5 d
5	5.34 (1H, dd, 6.9, 6.9)	67.1 d
6	1.97 (2H, m)	24.2 t
7	2.23 (1H, m)	37.0 d
8	4.65 (1H, dd, 10.9, 5.2)	78.4 d
9a	3.42 (1H, m)	46.6 t
9b	3.32 (1H, m)	
10a	2.16 (1H, m)	22.6 t
10b	1.92 (1H, m)	
11a	1.73 (1H, m)	22.0 t
11b	1.55 (1H, m)	
12	2.16 (1H, m)	40.7 d
13	—	61.4 s
14a	2.63 (1H, m)	36.9 t
14b	1.81 (1H, m)	
15	2.95 (1H, m)	28.9 d
16	1.07 (3H, d, 6.3)	19.7 q
17	—	166.2 s
18	6.20 (1H, d, 16.1)	114.6 d
19	7.59 (1H, d, 16.1)	145.9 d
20	—	126.4 s
21	7.01 (d, 1.7)	109.6 d
22	—	146.9 s
23	—	148.5 s
24	6.95 (d, 8.1)	115.0 d
25	7.09 (dd, 8.1, 1.8)	123.1 d
26	3.92 (3H, s)	56.0 q
27	—	170.5 s
28	2.01 (3H, s)	21.1 q

Lannotinidine I (**2**) {$[\alpha]_D^{22}$ +24.4 (c=0.4, MeOH)} showed the pseudomolecular ion peak at m/z 484 $(M+H)^+$ in the FAB-MS, and the molecular formula, $C_{28}H_{37}NO_6$, was established by HR-FAB-MS [m/z 484.2693, $(M+H)^+$, Δ −0.7 mmu]. The IR spectrum suggested the presence of hydroxy (3383 cm^{-1}), and carbonyl (1731, 1682 cm^{-1}) functionalities. ^{1}H- and ^{13}C-NMR data (Table 2) and the HMQC spectrum suggested that the structure of **2** was similar to lannotinidine C (**4**).[11] The gross structure of **2** was elucidated

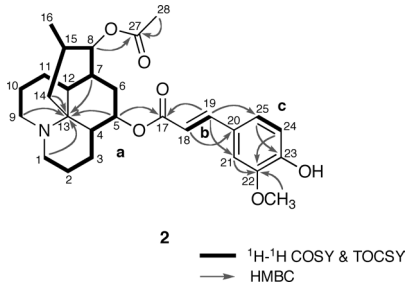

Fig. 3. Selected 2D NMR Correlations for Lannotinidine I (**2**)

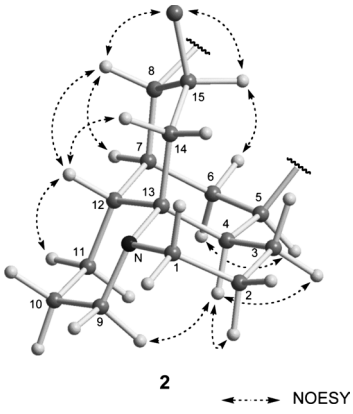

Fig. 4. Selected NOESY Correlations and Relative Stereochemistry for Lannotinidine I (**2**)

Hydrogen atoms of a methyl group and acyl groups were omitted.

by analyses of 2D NMR data including the ^{1}H–^{1}H COSY, TOCSY, HMQC, and HMBC spectra in $CDCl_3$ (Fig. 3).

The ^{1}H–^{1}H COSY and TOCSY spectra of **2** revealed three structural units **a** (C-1—C8, C-9—C-12, C-14—C-16), **b** (C-18, C-19), and **c** (C-24, C-25). HMBC correlations of H-1b (δ_H 3.09) and H-9b (δ_H 3.32) to C-13 (δ_C 61.4) revealed that C-1 (δ_C 47.0), C-9 (δ_C 46.6), and C-13 were connected through a nitrogen atom. The connectivities of C-4, C-12, and C-14 *via* C-13 were elucidated by HMBC correlations for H-5, H-7, and H-14 to C-13. HMBC correlations for H-8 (δ_H 4.65) and H-28 to C-27 (δ_C 170.5) revealed that an acetoxy group was connected to C-8 (δ_C 78.4). The presence of an *E*-3-methoxy-4-hydroxy cinnamoyl group was disclosed by HMBC cross-peaks depicted in Fig. 3 and a large coupling constant (16.1 Hz) for H-18 and H-19. Positions of an *E*-3-methoxy-4-hydroxy cinnamoyl group was assigned by an HMBC correlation for H-5 to C-17. Thus, the gross structure of lannotinidine I was elucidated to be **2**.

The relative stereochemistry of **2** was deduced as follows. ^3J value (10.9 Hz) between H-8 and H-15 and NOESY correlations for H-8/H-12, H-4/H-5 and H-4/H-9a suggested the relative stereochemistry of C-4, C-5, C-7, C-8, C-12, and C-15 to be as shown in Fig. 4. The β-orientation of an *E*-3-methoxy-4-hydroxy cinnamoyl group at C-5 was supported by ^3J values between H-4 and H-5, and H-5 and H-6 (both 6.9 Hz).

The absolute stereochemistry of **2** was elucidated by chemical correlation with lannotinidine C (**5**),[11] whose absolute stereochemistry has been established. Acetylation of **5** with acetic anhydride in pyridine gave a diacetyl derivative, whose aryl acetate was selectively deprotected using silica gel supported ammonium formate under micro wave irradiation[12] to obtaine **2**. The spectral data and the $[\alpha]_D$ value $\{[\alpha]_D^{22}$ +27.4 (c=0.4, MeOH)$\}$ of derived **2** were coincident with those of natural **2**. Thus, the absolute configurations at seven chiral centers of lannotinidine I (**2**) were assigned as 4*S*, 5*R*, 7*S*, 8*R*, 12*R*, 13*R*, and 15*S*.

Table 3. ^{1}H- and ^{13}C-NMR Data of Lannotinidine J (**3**) in CD_3OD

Position	δ_H	δ_C
1	3.41 (2H,m)	49.6 t
2	2.03 (2H, m)	24.5 t
3a	1.89 (1H, m)	20.2 t
3b	1.63 (1H, m)	
4	2.04 (1H, m)	42.0 d
5	4.21 (1H, m)	66.5 d
6a	2.54 (1H, m)	34.6 t
6b	1.29 (1H, ddd, 14.1, 14.1, 7.2)	
7	3.42 (1H, m)	41.9 d
8	—	175.0 s
9a	3.15 (1H, d, 12.0)	49.0 t
9b	3.00 (1H, d, 12.0)	
10	2.55 (1H, m)	35.6 d
11	6.54 (1H, dd, 6.9, 2.4)	130.4 d
12		141.4 s
13		62.7 s
14a	2.05 (1H, m)	28.3 t
14b	1.92 (1H, m)	
15	1.76 (1H, m)	30.2 d
16	1.19 (3H, d, 6.6)	17.3 q

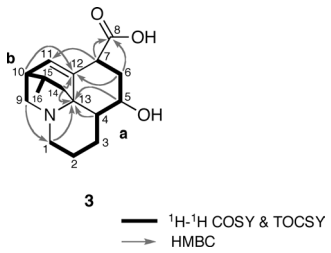

Fig. 5. Selected 2D NMR Correlations for Lannotinidine J (**3**)

Lannotinidine J (**3**) $\{[\alpha]_D^{23}$ +17.8 (c=0.7, MeOH)$\}$ showed the pseudomolecular ion peak at m/z 278 $(M+H)^+$ in the FAB-MS, and the molecular formula, $C_{16}H_{23}NO_3$, was established by HR-FAB-MS [m/z 278.1745, $(M+H)^+$, Δ +1.1 mmu]. IR absorptions implied the presence of hydroxy (3384 cm^{-1}) and carbonyl (1682 cm^{-1}) functionalities. ^{1}H- and ^{13}C-NMR data (Table 3) and the HMQC spectrum revealed the presence of 16 carbons due to one carbonyl carbon, one sp^2 quaternary carbon, one sp^3 quaternary carbon, one sp^2 methine, five sp^3 methines, six sp^3 methylenes, and one methyl group, in which one sp^3 methine (δ_C 66.5) was attributed to a carbon connected to a hydroxy group. The gross structure of **3** was elucidated by analyses of 2D NMR data including the ^{1}H–^{1}H COSY, TOCSY, HMQC, and HMBC spectra in CD_3OD (Fig. 5).

The ^{1}H–^{1}H COSY and TOCSY spectra of **3** revealed two structural units **a** (C-1—C-7) and **b** (C-9—C-11, C-14—C-16). HMBC correlations of H-9b (δ_H 3.00) to C-1 (δ_C 49.6) and H-1 (δ_H 3.41) to C-13 (δ_C 62.7) revealed that C-1, C-9 (δ_C 49.0), and C-13 were connected through a nitrogen atom. The presence of carboxylic acid at C-7 was suggested by HMBC cross-peaks of H-6b and H-7 to C-8 (δ_C 175.0). The

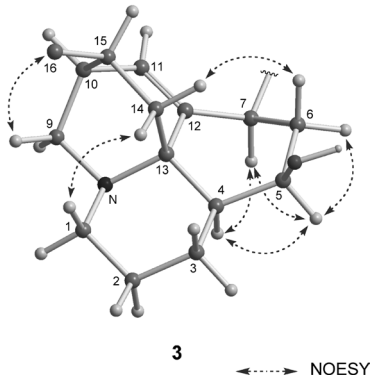

Fig. 6. Selected NOESY Correlations and Relative Stereochemistry for Lannotinidine J (**3**)

Hydrogen atoms of a methyl group and a carboxy group were omitted.

connectivity of C-7 (δ_C 41.9) and C-11 (δ_C 130.4) through C-12 (δ_C 141.4) was revealed by HMBC correlations for H-6b and H-10 to C-12. HMBC correlations for H-5 and H-14b to C-13, and H-14b to C-12 revealed that C-4, C-12, and C-14 were connected *via* C-13. Thus, the gross structure of lannotinidine J was elucidated to be **3**.

The relative stereochemistry of **3** was deduced from NOESY correlations as shown in computer-generated 3D drawing (Fig. 6). The α-configurations of H-4, H-5, and H-7 were revealed by NOESY correlations among H-4, H-5, and H-7, and twist-boat form of cyclohexene ring (C-4—C-7, C-12, C-13) was suggested by a NOESY correlation for H-4/H-7. NOESY correlations for H-1/H-14b, H-5/H-6a, and H-6b/H-14a supported the relative stereochemistry of C-13 and chair-form of a piperidine ring (C-1—C-4, C-13, N). The relative stereochemistry of C-15 was deduced by a NOESY cross-peak of H-9b/H-16. Thus, the structure of lannotinidine J was elucidated to be **3**, corresponding to free acid form of lannotinidine A (**4**).[11]

Lannotinidine H (**1**) is the first *Lycopodium* alkaloid possessing a lycopodane skeleton with an additional C_3 unit. Lannotinidines H—J (**1**—**3**) did not show cytotoxicities against P388 and L1210 murine leukemia, and KB human epidermoid carcinoma cells (IC_{50} >10.0 μg/ml) *in vitro*.

Experimental

General Methods Optical rotation was recorded on a JASCO P-1030 polarimeter. IR and UV spectra were recorded on JASCO FT/IR-230 and Shimadzu UV-1600PC spectrophotometer, respectively. ^{1}H-, ^{13}C-, and 2D-NMR spectra were recorded on a Bruker AMX-600 and a JEOL ECA-500 spectrometers. Each NMR sample of lannotinidines H (**1**) and J (**3**) was prepared by dissolving in 50 μl of CD_3OD in 2.5 mm micro cells (Shigemi Co., Ltd.) and chemical shifts were reported using residual CD_3OD (δ_H 3.31 and δ_C 49.0) as internal standard, while that of lannotinidine I (**2**) was prepared by dissolving in 500 μl of $CDCl_3$ in 5.0 mm micro cells (Shigemi Co., Ltd.) and chemical shifts reported using residual $CDCl_3$ (δ_H 7.26 and δ_C 77.0) as internal standard. Standard pulse sequences were employed for the 2D-NMR experiments. ^{1}H–^{1}H COSY, TOCSY, and NOESY spectra were measured with spectral widths of both dimensions of 4800 Hz, and 32 scans with two dummy scans were accumulated into 1K data points for each of 256 t_1 increments. NOESY and TOCSY spectra in the phase-sensitive mode were measured with a mixing time of 800 and 30 ms, respectively. For HMQC spectra in the phase-sensitive mode and HMBC spectra, a total of 256 increments of 1K data points were collected. For HMBC spetra in the phase-sensitive mode and HMBC spectra, a total of 256 increments of 1K data points were collected. For HMBC spectra with *Z*-axis PFG, 20 and 50 ms delay time were used for long-range C–H coupling. Zero-filling to 1K for F_1 and multiplication with squared cosine-bell windows shifted in both dimensions were performed prior to 2D Fourier transformation. ESI mass spectra were obtained on a JEOL JMS-700TZ spectrometer. FAB mass spectra were obtained on a JEOL JMS-HX110 spectrometer.

Plant Material The club moss *Lycopodium annotinum* was collected in Nayoro, Hokkaido in Japan, in 2007. The botanical identification was made by Dr. T. Shibata, Hokkaido Division, Research Center for Medicinal Plant Resources, National Institute of Biomedical Innovation. A voucher specimen has been deposited in the herbarium of Hokkaido University.

Extraction and Separation The club moss *L. annotinum* collected at Nayoro in Hokkaido was extracted with MeOH aq., and extracts were partitioned between EtOAc and 3% tartaric acid (pH 4). Water-soluble materials, adjusted at pH 9 with sat. Na_2CO_3 aq., were partitinoned with $CHCl_3$. $CHCl_3$-soluble materials were subjected to an amino silica gel column (*n*-hexane/EtOAc, 1 : 0→1 : 1 and then $CHCl_3$/MeOH, 1 : 0→1 : 1). A fraction eluted with $CHCl_3$/MeOH (1 : 1) was further purified by a silica gel column ($CHCl_3$/MeOH, 1 : 0→1 : 1) and then a C_{18} column (MeCN/H_2O/TFA, 20/80/0.1→80/20/0.1) chromatographies. A fraction eluted with MeCN/H_2O/TFA (20/80/0.1) was further purified by C_{18} HPLC (MeCN/H_2O/TFA, 12/88/0.1) to afford lannotinidine H (**1**, 0.57 mg, 0.00008%). A fraction eluted from an amino silica gel column with $CHCl_3$/MeOH (10 : 1) was purified by a silica gel column ($CHCl_3$/MeOH, 1 : 0→1 : 1) and then a C_{18} column (MeCN/H_2O/TFA, 20/80/0.1→100/0/0.1) chromatographies. A fraction eluted with MeCN/H_2O/TFA (40/60/0.1) afforded lannotinidine I (**2**, 14.2 mg, 0.002%). Finally, a fraction eluted from an amino silica gel column with $CHCl_3$/MeOH (1 : 1) was purified by a C_{18} column (MeCN/H_2O/TFA, 100/0/0.1→0/100/0.1) chromatography, from which a fraction eluted with (MeCN/H_2O/TFA, 20/80/0.1) was purified with a silica gel column ($CHCl_3$/MeOH, 1 : 0→1 : 1) chromatography and then C_{18} HPLC (MeCN/H_2O/TFA, 5/95/0.1) to afford lannotinidine J (**3**, 1.71 mg, 0.0002%).

Lannotinidine H (**1**): Colorless amorphous solids; $[\alpha]_D^{23}$ −40.2 (c=0.2, MeOH); IR (film) ν_{max} 3358, 2921, 2850, 1716, and 1659 cm^{-1}; ^{1}H- and ^{13}C-NMR see Table 1; ESI-MS *m/z* 345 $(M+H)^+$; HR-ESI-MS *m/z* 345.2541 (M+H; Calcd for $C_{21}H_{33}N_2O_2$, 345.2542).

Lannotinidine I (**2**): Colorless amorphous solids; $[\alpha]_D^{22}$ +24.4 (c=0.4, MeOH); UV (MeOH) λ_{max} 328 (ε 12500), 236 (7800), and 218 (9600) nm; IR (film) ν_{max} 3384, 2958, 1731, and 1682 cm^{-1}; ^{1}H- and ^{13}C-NMR see Table 2; FAB-MS *m/z* 484 $(M+H)^+$; HR-FAB-MS *m/z* 484.2693 (M+H; Calcd for $C_{28}H_{38}NO_6$, 484.2700).

Lannotinidine J (**3**): Colorless amorphous solids; $[\alpha]_D^{23}$ +17.8 (c=0.7, MeOH); IR (film) ν_{max} 3384, 2922, 2850, and 1682 cm^{-1}; ^{1}H- and ^{13}C-NMR see Table 3; ESI-MS *m/z* 278 $(M+H)^+$; HR-ESI-MS *m/z* 278.1745 (M+H; Calcd for $C_{16}H_{24}NO_3$, 278.1734).

Chemical Correlation of Lannotinidine C (5)[11] to Lannotinidine I (2) Lannotinidine C (**5**, 10.0 mg) was treated with Ac_2O (500 μl) and pyridine (500 μl) at room temperature for 22 h, then the mixture was concentrated *in vacuo* to afford diacetyl derivative of lannotinidine C (**5**) (8.2 mg). Diacetyl derivative of **5** (1.9 mg) was mixed with ammonium formate (2.4 mg) and silica gel (50 mg) in a glass tube, which was placed at the center of an almina bath. After irradiation of micro wave for 4 min, the glass tube was cooled to room temperature. The reaction mixture was extracted with EtOAc, and the extract was concentrated *in vacuo* and purified by a C_{18} HPLC [CAPCELL PAK AQ, Shiseido Co., Ltd., 10×250 mm; eluent, CH_3CN/H_2O/TFA, 12 : 88 : 0.1; flow rate, 2.0 ml/min; UV detection at 210 nm] to afford a reaction product (1.8 mg), whose spectral data and the $[\alpha]_D$ value {$[\alpha]_D^{22}$ +27.4 (c=0.4, MeOH)} were coincident with those of natural **2**.

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