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Studies on Constituents of Crude Drugs. XV.¹⁾ New Pyrrolizidine Alkaloids from *Ligularia dentata*

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Four new pyrrolizidine alkaloids, ligularidine, neoligularidine, ligularizine and ligularinine, were isolated together with the known compound clivorine from the roots and aerial parts of *Ligularia dentata*. Their structures were elucidated on the basis of the spectral data and chemical conversion of clivorine into these alkaloids. A useful epoxidation of pyrrolizidine alkaloids was achieved by using performic acid.

Keywords—*Ligularia dentata*; Compositae; pyrrolizidine alkaloid; ligularidine; neoligularidine; ligularizine; ligularinine; clivorine; epoxidation; chemical conversion

In a preliminary communication,²⁾ we reported the isolation of a new macrocyclic pyrrolizidine alkaloid, named ligularidine, from *Ligularia dentata* HARA (Japanese name: Maruba-dakebuki), the young plants of which are used as a food in rural areas in Japan. The presence of sesquiterpenes³⁾ and pyrrolizidine alkaloids⁴⁾ in this plant has already been reported. This paper describes the structure determination and chemical conversion of new pyrrolizidine alkaloids isolated from *Ligularia dentata*. The crude alkaloids obtained from the methanolic extracts of the roots and aerial parts were chromatographed on a silica gel column with C₆H₆ : AcOEt : Et₂NH as a solvent system to give five alkaloids, i.e., four new alkaloids (2), (3), (4), and (5) together with a known alkaloid, clivorine (1). The yields of alkaloids obtained from the roots and aerial parts are shown in Table I.

Alkaloid I (1), the main alkaloid, was obtained as colorless prisms (ether), mp 149—150 °C, $[\alpha]_D^{27} + 80^\circ$, C₂₁H₂₇NO₇ and identified as clivorine by mixed fusion, $[\alpha]_D$ and infrared (IR) spectral comparison with an authentic sample.

Alkaloid II (2), named ligularidine, was obtained as colorless needles (ether), mp 196 °C, $[\alpha]_D^{28} - 49.8^\circ$, C₂₁H₂₉NO₇. The IR spectrum of 2 shows absorptions at 1740 and 1730 (acetyl and ester carbonyl), 1700 (conjugated ester carbonyl) and 1610 cm⁻¹ ($\overset{\delta^+}{\text{N}}\text{---}\overset{\delta^-}{\text{C}}\text{---}\text{O}$). The molecular ion peak at m/z 407 in its mass spectrum (MS) suggests the introduction of two additional hydrogen atoms into 1, and other prominent peaks at m/z 168, 151, 110 and 96 indicate that 2 is a macrocyclic diester of otonecine. The proton nuclear magnetic resonance (¹H-NMR) spectrum of 2 also shows a typical macrocyclic diester pattern of otonecine⁵⁾ and is similar to that of clivorine (1). In the ¹H-NMR spectrum of 2, the signals of the vinyl group at C-15 in 1 had disappeared and the signals of an ethylidene group at C-15 appeared as follows: δ 1.78 (3H, d, $J=8$ Hz) for vinyl methyl protons at C-21 and δ 6.79 (1H, q, $J=8$ Hz) for an olefinic proton at C-20.

Alkaloid III (3), named neoligularidine, was obtained as colorless needles (*n*-hexane), mp 117—119 °C, $[\alpha]_D^{27} - 58^\circ$, C₂₁H₂₉NO₇. The mass spectrum of 3 shows the same molecular ion peak at m/z 407 as that of 2, and the fragmentation is similar to that of 2. The ¹H-NMR spectrum of 3 shows a doublet at δ 1.92 ppm corresponding to vinyl methyl protons at C-21 and a quartet at δ 5.87 due to an olefinic proton at C-20. The difference in the olefinic proton

TABLE I. Alkaloids Isolated from *Ligularia dentata*

Alkaloid	Aerial parts (17.7 kg)	Roots (8.8 kg)
Clivorine (1)	0.13%	0.26%
Ligularidine (2)	0.0018%	0.003%
Neoligularidine (3)	0.0002%	
Ligularizine (4)	0.006%	0.011%
Ligularinine (5)		0.004%

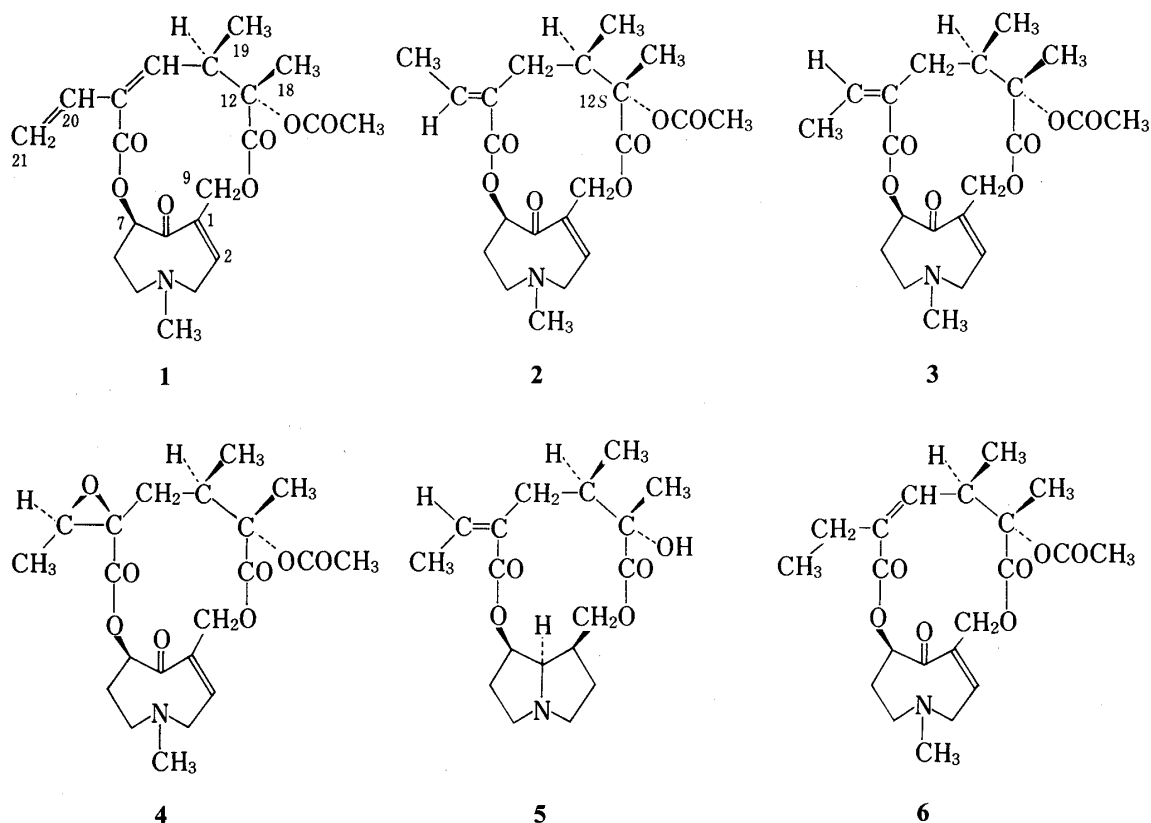


Chart 1

chemical shifts value between **2** and **3** is 0.92, which suggests that **3** is the *Z* isomer of **2**.⁶⁾

In order to confirm the structures of **2** and **3**, **1** was catalytically reduced with Pd-C to give **2**, **3** and **6** (Chart 2). From the spectral data and chemical transformation mentioned above, the structures of ligularidine and neoligularidine were determined as **2** and **3**, respectively.

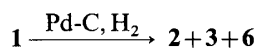


Chart 2

Alkaloid IV (**4**), named ligularizine, was isolated as the picrate, yellow needles, mp 210—211 °C (picrate, ethanol), $[\alpha]_D^{25} -24.5^\circ$, $\text{C}_{21}\text{H}_{29}\text{NO}_8 \cdot \text{C}_6\text{H}_3\text{N}_3\text{O}_7$. The MS of **4** shows a molecular ion peak at m/z 423 which is larger by 16 mass units than that of **2** or **3**, and other prominent peaks indicate that **4** is an epoxide of **2** or **3** (Chart 3). The ^1H -NMR spectrum of **4** is similar to that of **3**. The signals of the olefinic proton at C-20 and vinyl

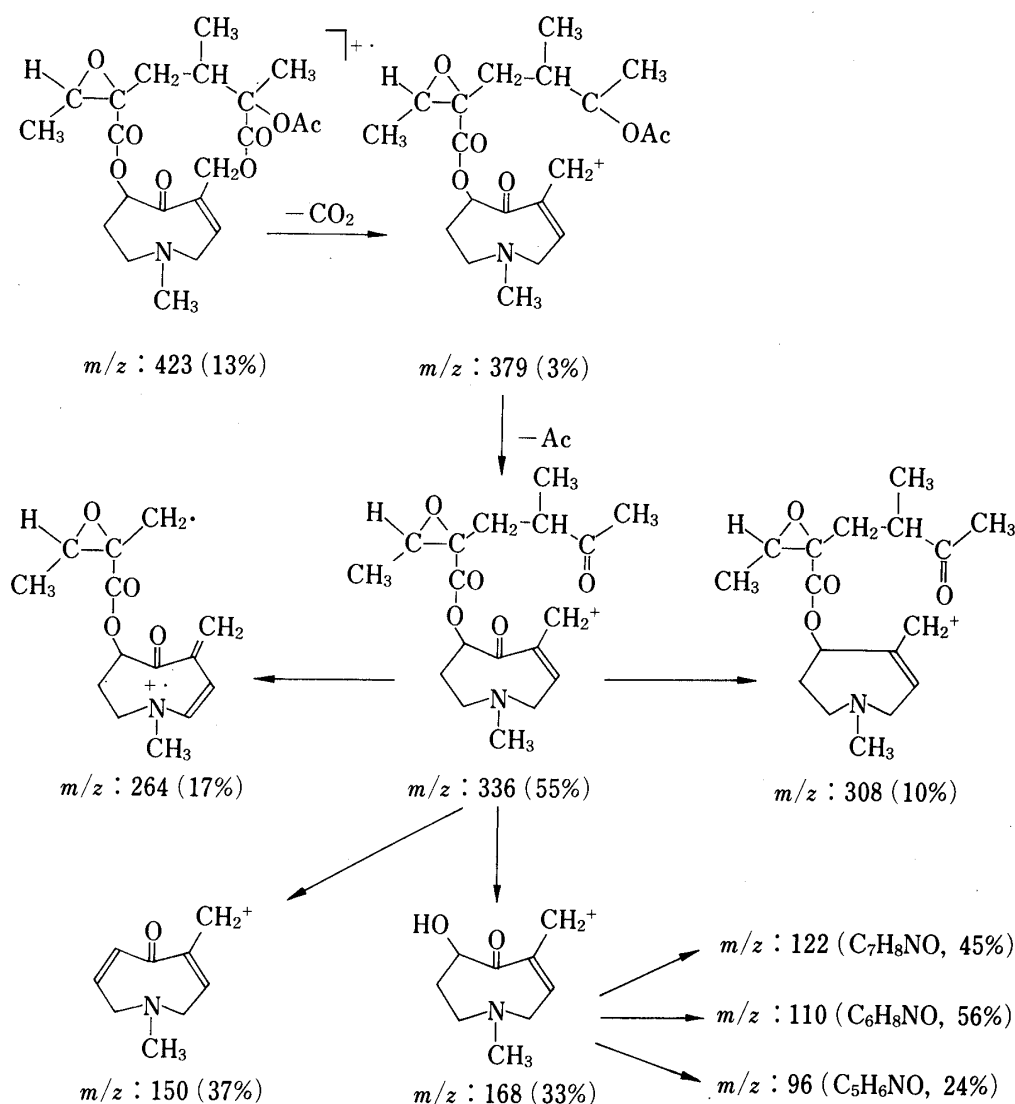


Chart 3

methyl protons at C-21 in **3** had disappeared and the signals of an epoxide methine proton δ 3.00 (1H, q, $J=6$ Hz) at C-20 and methyl protons δ 1.47 (3H, d, $J=6$ Hz) at C-21 appeared in **4**. Therefore the structure of **4** was presumed to be the 15,20-epoxide of **2** or **3**. The ^1H -NMR spectral data for florosenine (**7**),⁷⁾ acetylfukinotoxin (**8**),⁸⁾ and ligularizine (**4**), each containing a 15,20-epoxide group, are shown in Table II. From a comparison of chemical shift values at C-20 and C-21 in the ^1H -NMR spectra, ligularizine (**4**) was supposed to be the β -epoxide of neoligularidine (**3**). The carbon-13 nuclear magnetic resonance (^{13}C -NMR) spectral data for ligularizine (**4**) and acetylfukinotoxin (**8**) are shown in Table III. The chemical shift values of **4** are similar to those of **8** except for the chemical shift value at C-18. The ^{13}C -NMR spectral data suggest that **4** is an epimer of **8** at C-12.⁹⁾ In order to confirm the structure of ligularizine (**4**), the chemical transformation of neoligularidine (**3**) to **4** was performed by epoxidation with performic acid. We have already observed that acetylfukinotoxin (**8**), which is a β -epoxide, was mainly obtained on oxidizing acetylsenkirkine (**9**) with performic acid.¹⁰⁾ From the spectral data and chemical transformation mentioned above, the structure of ligularizine was determined to be **4**.

Alkaloid V (**5**), named ligularinine, was obtained as colorless prisms (ether), mp 103—104 °C, $[\alpha]_D^{24} -88^\circ$, $\text{C}_{18}\text{H}_{27}\text{NO}_5$. The MS of **5** shows a molecular ion peak at m/z 337 and its fragmentation is similar to that of platyphylline (**10**).¹¹⁾ This suggests that ligularinine (**5**) has

TABLE II. ^1H -NMR Spectral Data for 7, 8 and 4

Compound	$\text{C}_{20}\text{-H}$	$\text{C}_{21}\text{-H}$
Florosene (7)	2.95	1.24 (α -Epoxide)
Acetylfukinotoxin (8)	3.02	1.46 (β -Epoxide)
Ligularizine (4)	3.00	1.47 (β -Epoxide)

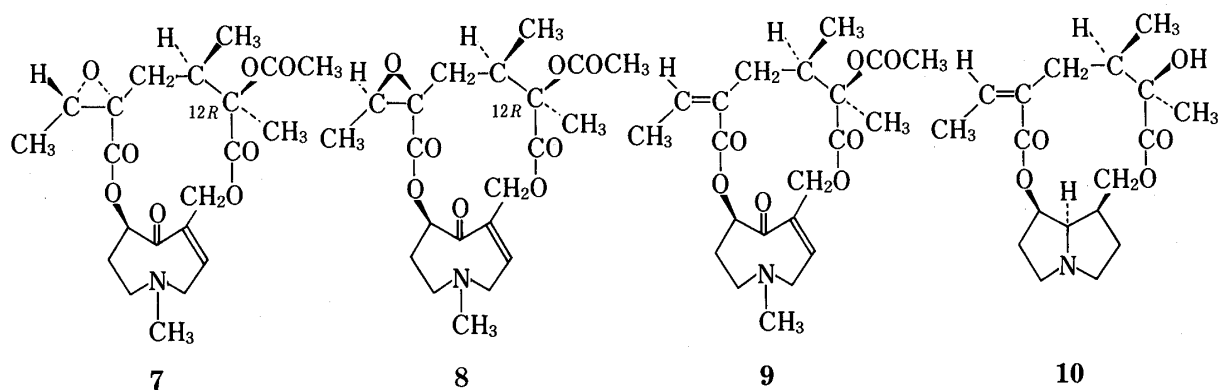


Chart 4

TABLE III. ^{13}C Chemical Shifts and Assignments^{a)}

Carbon	4	8	Carbon	4	8
1	133.5	133.3	14	36.9	37.0
2	138.3	138.7	15	62.2	62.6
3	63.7	64.1	16	166.0	166.3
5	53.2	53.1	18	14.4	21.5
6	35.8	36.5	19	13.9	13.0
7	77.4	77.3	20	61.4	61.4
8	190.2	190.0	21	15.5	15.6
9	58.9	58.9	N-CH ₃	40.1	40.0
11	171.2	170.5	-C=O	169.6	169.6
12	82.8	83.4	CH ₃	21.0	21.4
13	36.3	38.4			

^{a)} Chemical shifts in ppm downfield from tetramethylsilane (TMS); solvent CDCl_3 .

TABLE IV. ^{13}C Chemical Shifts and Assignments^{a)}

Carbon	5	10	Carbon	5	10
1	40.3	39.5	12	77.1	75.7
2	29.6	31.7	13	39.4	37.3
3	54.7	53.5	14	38.9	39.2
5	52.5	51.8	15	131.8	131.7
6	34.8	35.8	16	167.2	167.5
7	75.1	74.1	18	17.9	26.1
8	68.9	69.4	19	13.4	13.5
9	64.1	66.6	20	135.9	135.8
11	175.0	178.5	21	15.4	15.5

^{a)} Chemical shifts in ppm downfield from TMS; solvent CDCl_3 .

the same plane structure as platyphylline (10). The ^1H -NMR spectrum shows a typical pattern of a macrocyclic diester of platynecine (11) and is similar to that of 10. As shown in Table IV, the ^{13}C -NMR spectral data for 5 and 10 suggest that 5 is an epimer of 10 at C-12. Hydrolysis of ligularinine (5) afforded platynecine (11) and necic acid (12), which was identical with 12 obtained from the hydrolysis of neoligularidine (3) (Chart 5). From the spectral data and chemical study mentioned above, the structure was determined to be 5.

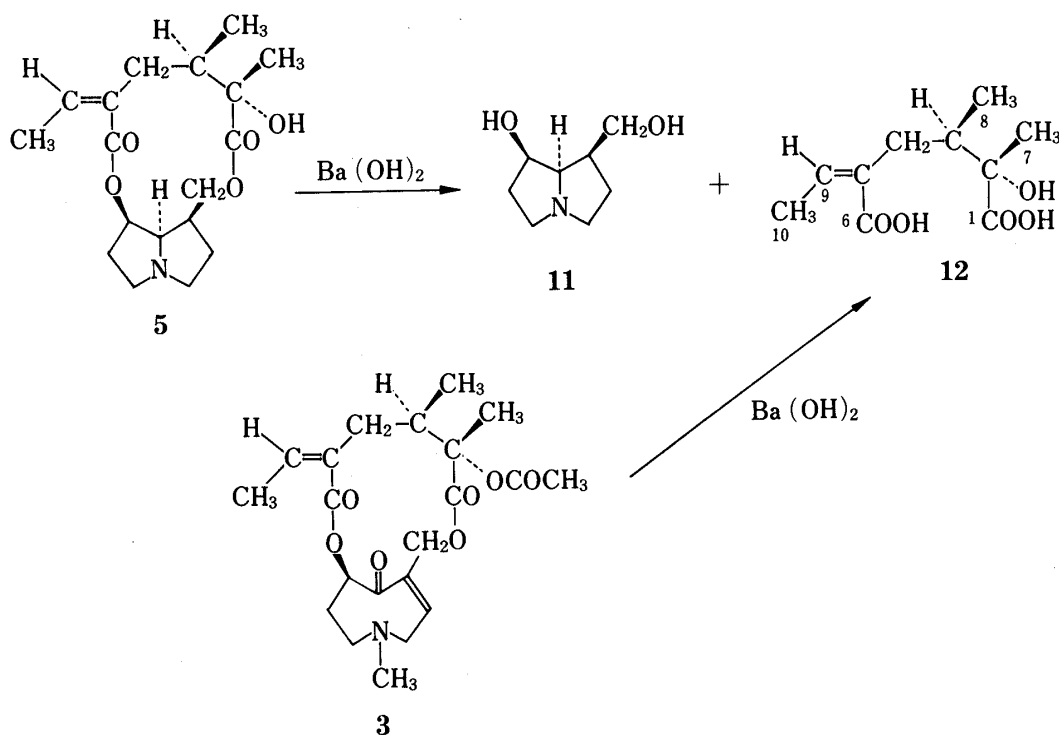


Chart 5

In conclusion, the structures of 2, 3 and 4 were determined by spectral analysis and chemical correlation with 1. The structure of 5 was also determined by spectral analysis and hydrolysis. The successful transformation of 3 to 4 using performic acid was carried out and it was demonstrated that performic acid oxidation is useful in compounds of this type to synthesize β -epoxides. The presence of 1, 2, 3, 4 and 5 having 12*S* configuration in *Ligularia dentata* is interesting in comparison with that of 8, 10 and senecionine having 12*R* configuration in *Ligularia japonica*⁸⁾ from chemotaxonomical and biosynthetic viewpoints. Further, it is known that some macrocyclic secopyrrolizidine alkaloids such as fukinotoxin¹²⁾ and clivorine (1)¹³⁾ are carcinogenic. Therefore tests for carcinogenicity, mutagenicity and other biological activities of the present compounds are in progress.

Experimental

Melting points were determined on a Büchi melting point apparatus and are uncorrected. IR spectra were recorded on Shimadzu IR 27G and JASCO IRA-I spectrometers. ^1H -NMR and ^{13}C -NMR spectra were taken on a JEOL PS 100 Fourier-transform spectrometer and chemical shifts are given on the δ (ppm) scale with tetramethylsilane as an internal standard. High resolution mass spectra were obtained with JEOL JMS-01SG and DX-300 mass spectrometers.

Extraction of Crude Alkaloids—The air-dried powdered aerial parts and roots of *Ligularia dentata* collected in Izu-kogen, Shizuoka Pref., were extracted with MeOH three times. The MeOH extract obtained from the aerial parts (17.7 kg) was extracted with 0.5 N H_2SO_4 several times. The acid-soluble fraction was extracted with CHCl_3 three

times. The aqueous acidic solution was then made alkaline with 28% NH_4OH and extracted with CHCl_3 six times to give 50 g of crude alkaloid. The MeOH extract obtained from the roots (8.8 kg) was extracted with 0.5 N H_2SO_4 several times. The acid-soluble fraction was extracted with CHCl_3 three times. The aqueous acidic solution was reduced with zinc dust and 18 N H_2SO_4 was added to make the solution 2 N with respect to acid. The aqueous acid solution was filtered, made alkaline with 28% NH_4OH and extracted with CHCl_3 six times to give 60.1 g of crude alkaloid.

Separation of Alkaloids—The crude alkaloid (50 g) obtained from the aerial parts was extracted with hot *n*-hexane : AcOEt = 1 : 1 and the residue obtained after evaporating off the solvent was recrystallized from ether to afford **1** (14.7 g). The residue (31.3 g) obtained from the mother liquor was subjected to silica gel (1.5 kg) column chromatography. On elution with a mixed solvent, C_6H_6 : AcOEt : Et_2NH = 72 : 20 : 8, **2** (209 mg), **4** (818 mg as the picrate) and **1** (7.92 g) were obtained in fractions 22–24, 26–29 and 30–81, respectively. The mixed alkaloid fractions (22–81) were chromatographed repeatedly on a silica gel column (solvent; C_6H_6 : AcOEt : Et_2NH = 75 : 20 : 5) and **2** (110 mg), **4** (874 mg as picrate) and **1** (736 mg) were obtained. Furthermore, a fraction consisting mainly of **3** was purified by semipreparative high performance liquid chromatography (HPLC) on a μ -Porasil column (solvent; CH_3CN : CHCl_3 : MeOH : Et_2NH = 300 : 300 : 6 : 1.6, flow rate; 2 ml/min) to give **3** (34.5 mg) after recrystallization from *n*-hexane. The crude alkaloid (60.1 g) obtained from the roots was extracted with hot *n*-hexane : AcOEt = 1 : 1 and the residue obtained after evaporating the solvent was recrystallized from ether to afford **1** (14.6 g). The purified residue (33.4 g) obtained from the mother liquor was subjected to silica gel (1.5 kg) column chromatography, and elution with a mixed solvent C_6H_6 : AcOEt : Et_2NH = 70 : 20 : 10 gave **2** (200 mg), **4** (1.361 g as the picrate) and **1** (7.25 g) in fractions 16–18, 20–22 and 23–40, respectively. The residue obtained from the mother liquor of **1** was extracted with hot *n*-hexane and the residue obtained after evaporating the solvent was recrystallized from ether to afford **5** (371 mg). The mixed alkaloid fractions (16–40) were chromatographed repeatedly on a silica gel column to give **2** (61 mg), **4** (170 mg as the picrate) and **1** (640 mg).

Clivorine (1): Colorless prisms, mp 149–150 °C (ether), $[\alpha]_D^{27} + 80.2^\circ$ ($c=0.99$, CHCl_3). *Anal.* Calcd for $\text{C}_{21}\text{H}_{27}\text{NO}_7$: C, 62.21; H, 6.71; N, 3.43. Found: C, 62.48; H, 6.83; N, 3.57. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1748, 1735, 1612. MS m/z (%): 405 (M^+ , 7), 361 ($\text{M}^+ - \text{CO}_2$, 3), 318 (9), 168 (19), 151 (27), 150 (17), 96 (5), 94 (15), 43 (100). $^1\text{H-NMR}$ (CDCl_3) δ : 1.18 (3H, d, $J=6$ Hz, $\text{C}_{19}\text{-H}$), 1.51 (3H, s, $\text{C}_{18}\text{-H}$), 2.04, 2.07 (each 3H, s, N-CH_3 , O-CO-CH_3), 2.84 (1H, dq, $J=11$, 6 Hz, $\text{C}_{13}\text{-H}$), 4.26 (1H, br d, $J=11$ Hz, $\text{C}_9\text{-Ha}$), 4.99 (1H, d, $J=17$ Hz, $\text{C}_{21}\text{-Ha}$), 5.03 (1H, d, $J=11$ Hz, $\text{C}_9\text{-Hb}$), 5.15 (1H, d, $J=10$ Hz, $\text{C}_{21}\text{-Hb}$), 5.19 (1H, m, $\text{C}_7\text{-H}$), 5.38 (1H, d, $J=11$ Hz, $\text{C}_{14}\text{-H}$), 5.99 (1H, br s, $\text{C}_2\text{-H}$), 6.26 (1H, dd, $J=17$, 10 Hz, $\text{C}_{20}\text{-H}$).

Ligularidine (2): Colorless needles, mp 196 °C (ether), $[\alpha]_D^{28} - 49.8^\circ$ ($c=1.02$, EtOH). *Anal.* Calcd for $\text{C}_{21}\text{H}_{29}\text{NO}_7$: C, 61.90; H, 7.17; N, 3.44. Found: C, 61.85; H, 7.05; N, 3.27. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1740, 1730, 1700, 1610. MS m/z (%): 407 (M^+ , 7), 379 ($\text{M}^+ - \text{CO}$, 2), 363 ($\text{M}^+ - \text{CO}_2$, 3), 320 (17), 303 (17), 249 (62), 221 (21), 168 (20), 166 (19), 153 (62), 151 (15), 110 (40), 96 (17), 94 (18), 43 (100). $^1\text{H-NMR}$ (CDCl_3) δ : 0.94 (3H, d, $J=6$ Hz, $\text{C}_{19}\text{-H}$), 1.45 (3H, s, $\text{C}_{18}\text{-H}$), 1.78 (3H, d, $J=8$ Hz, $\text{C}_{21}\text{-H}$), 2.00, 2.11 (each 3H, s, N-CH_3 , O-CO-CH_3), 4.38 (1H, br d, $J=12$ Hz, $\text{C}_9\text{-Ha}$), 4.92 (1H, t, $J=5$ Hz, $\text{C}_7\text{-H}$), 5.11 (1H, d, $J=12$ Hz, $\text{C}_9\text{-Hb}$), 6.16 (1H, br s, $\text{C}_2\text{-H}$), 6.79 (1H, q, $J=8$ Hz, $\text{C}_{20}\text{-H}$).

Neoligularidine (3): Colorless needles, mp 117–119 °C (*n*-hexane), $[\alpha]_D^{27} - 58^\circ$ ($c=0.13$, CHCl_3). *Anal.* Calcd for $\text{C}_{21}\text{H}_{29}\text{NO}_7$: C, 61.90; H, 7.17; N, 3.44. Found: C, 62.14; H, 7.22; N, 3.47. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1735, 1725, 1700, 1610. MS m/z (%): 407 (M^+ , 9), 320 (15), 303 (21), 249 (27), 221 (16), 168 (15), 166 (26), 153 (64), 110 (42), 84 (29), 83 (26), 43 (100). $^1\text{H-NMR}$ (CDCl_3) δ : 0.96 (3H, d, $J=7$ Hz, $\text{C}_{19}\text{-H}$), 1.40 (3H, s, $\text{C}_{18}\text{-H}$), 1.92 (3H, dd, $J=7.5$, 2 Hz, $\text{C}_{21}\text{-H}$), 2.01, 2.07 (each 3H, s, N-CH_3 , O-CO-CH_3), 4.32 (1H, br d, $J=11.5$ Hz, $\text{C}_9\text{-Ha}$), 4.94 (1H, t, $J=3.5$ Hz, $\text{C}_7\text{-H}$), 5.17 (1H, d, $J=11.5$ Hz, $\text{C}_9\text{-Hb}$), 5.87 (1H, q, $J=7.5$ Hz, $\text{C}_{20}\text{-H}$), 6.16 (1H, br s, $\text{C}_2\text{-H}$).

Ligularizine (4): Yellow needles (picrate), mp 210–211 °C, $[\alpha]_D^{25} - 24.5^\circ$ ($c=1.08$, CHCl_3 , picrate). *Anal.* Calcd for $\text{C}_{21}\text{H}_{29}\text{NO}_8 \cdot \text{C}_6\text{H}_3\text{N}_3\text{O}_7$: C, 49.70; H, 4.94; N, 8.54. Found: C, 49.76; H, 4.92; N, 8.47. IR (picrate) $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1745, 1735. MS m/z (%): 423 (M^+ , 13), 379 ($\text{M}^+ - \text{CO}_2$, 3), 336 (55), 319 (14), 308 (10), 304 (22), 264 (17), 250 (36), 238 (15), 168 (33), 150 (37), 122 (45), 110 (56), 96 (24), 94 (28), 43 (100). $^1\text{H-NMR}$ (CDCl_3) δ : 1.10 (3H, d, $J=7$ Hz, $\text{C}_{19}\text{-H}$), 1.38 (3H, s, $\text{C}_{18}\text{-H}$), 1.47 (3H, d, $J=6$ Hz, $\text{C}_{21}\text{-H}$), 2.02, 2.06 (each 3H, s, N-CH_3 , O-CO-CH_3), 3.00 (1H, q, $J=6$ Hz, $\text{C}_{20}\text{-H}$), 4.26 (1H, br d, $J=12.5$ Hz, $\text{C}_9\text{-Ha}$), 5.08 (1H, br s, $\text{C}_7\text{-H}$), 5.23 (1H, d, $J=12.5$ Hz, $\text{C}_9\text{-Hb}$), 6.18 (1H, br s, $\text{C}_2\text{-H}$).

Ligularinine (5): Colorless prisms, mp 103–104 °C, $[\alpha]_D^{24} - 88^\circ$ ($c=0.82$, CHCl_3). High resolution MS: Calcd for $\text{C}_{18}\text{H}_{27}\text{NO}_5$: 337.189. Found: 337.187. MS m/z (%): 337 (M^+ , 9), 266 (5), 211 (30), 140 (100), 138 (58), 123 (49), 122 (72), 96 (26), 95 (16), 82 (98). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3400, 1730, 1715. $^1\text{H-NMR}$ (CDCl_3) δ : 0.99 (3H, d, $J=6.5$ Hz, $\text{C}_{19}\text{-H}$), 1.24 (3H, s, $\text{C}_{18}\text{-H}$), 1.87 (3H, d, $J=7.5$ Hz, $\text{C}_{21}\text{-H}$), 3.43 (1H, dd, $J=7$, 5 Hz, $\text{C}_8\text{-H}$), 4.08 (1H, dd, $J=12$, 2 Hz, $\text{C}_9\text{-Ha}$), 4.57 (1H, dd, $J=12$, 8 Hz, $\text{C}_9\text{-Hb}$), 5.22 (1H, q, $J=5$ Hz, $\text{C}_7\text{-H}$), 5.81 (1H, q, $J=7.5$ Hz, $\text{C}_{20}\text{-H}$).

Catalytic Reduction of Clivorine (1) to Ligularidine (2), Neoligularidine (3) and 6—**1** (1 g) was dissolved in EtOH (10 ml) containing AcOH (0.1 ml) and shaken with Pd-C (100 mg) under an atmosphere of hydrogen at room temperature. The catalyst was removed by filtration and the filtrate was then evaporated to dryness *in vacuo* to give a mixture of dihydro derivatives (1.01 g). The mixture was dissolved in CHCl_3 and the solution was washed with water. The CHCl_3 layer was evaporated to give the residue (874 mg), which was recrystallized from acetone to give **2**

(188 mg). The residue obtained from the mother liquor of **2** was extracted with hot *n*-hexane and the solvent was evaporated. The residue was recrystallized from *n*-hexane to give **6** (199 mg). The mother liquor of **6** was separated by HPLC on a Senshu pack N505 column (solvent, CH₃CN : CHCl₃ : MeOH : Et₂NH = 300 : 300 : 5 : 0.8; flow rate, 6 ml/min) to afford **2** (36 mg), **3** (135 mg) and **6** (118 mg), respectively. **2** and **3** were identical with naturally occurring specimens on the basis of mixed fusion, $[\alpha]_D$ and other spectral data. **6**: Colorless prisms, mp 124–125°C (*n*-hexane), $[\alpha]_D^{25} + 135^\circ$ ($c = 1.04$, CHCl₃). *Anal.* Calcd for C₂₁H₂₉NO₇: C, 61.90; H, 7.17; N, 3.44. Found: C, 61.71; H, 7.17; N, 3.27. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1745, 1728, 1720, 1615. MS m/z (%): 407 (M⁺, 7), 363 (8), 320 (22), 304 (56), 168 (18), 166 (12), 153 (63), 137 (53), 125 (34), 122 (23), 110 (53), 43 (100). ¹H-NMR (CDCl₃) δ : 1.03 (3H, t, $J = 8$ Hz, C₂₁-H), 1.14 (3H, d, $J = 7.5$ Hz, C₁₉-H), 1.47 (3H, s, C₁₈-H), 2.02, 2.08 (each 3H, s, N-CH₃, O-CO-CH₃), 2.22 (1H, br q, $J = 8$ Hz, C₂₀-H), 4.23 (1H, br d, $J = 11$ Hz, C₉-Ha), 4.97 (1H, d, $J = 11$ Hz, C₉-Hb), 5.26 (1H, t, $J = 2$ Hz, C₇-H), 5.21 (1H, dt, $J = 12, 2, 2$ Hz, C₁₄-H), 6.05 (1H, br s, C₂-H).

Conversion of Neoligularidine (3) to Ligularizine (4)—**3** (40 mg) was dissolved in formic acid (0.5 ml). Thirty percent hydrogen peroxide (1.2 ml) was gently added to the above solution and the mixture was allowed to stand for 9 d at room temperature. The reaction mixture was diluted with water, made alkaline with 28% NH₄OH and extracted with CHCl₃ to afford a crude material (45 mg), which was converted to a crystalline picrate (39.7 mg). The residue obtained from the mother liquor of the picrate was chromatographed on Al₂O₃ with CHCl₃ to give the picrate (6.5 mg). The picrate of **4** was found to be identical with the picrate of naturally occurring ligularizine (**4**) on the basis of mixed fusion, $[\alpha]_D$ and other spectral data.

Hydrolysis of Ligularinine (5)—**5** (45 mg) in water (10 ml) was boiled under reflux with barium hydroxide octahydrate (234 mg) for 5 h. The solution was allowed to cool, treated with CO₂ gas, and filtrered, then the filtrate was acidified with HCl and extracted continuously with ether for 10 h. The ether extract was recrystallized from ether-*n*-hexane to give necic acid (**12**) (5 mg). The residual acidic solution was passed through a column of Amberlite IRA 400 ion-exchange resin (OH⁻ form, 5 g) and the eluate was evaporated to dryness. The residue was recrystallized from acetone to give platynecine (**11**) (10.2 mg). **12**: Colorless needles, mp 116–117°C (ether-*n*-hexane), $[\alpha]_D^{26} + 42.6^\circ$ ($c = 0.12$, EtOH). IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3450, 1725, 1690, 1675. MS m/z (%): 198 (M⁺ - H₂O, 12), 153 (M⁺ - H₂O - COOH, 81), 127 (79), 109 (87), 81 (100). ¹H-NMR (CD₃COCD₃) δ : 0.81 (3H, d, $J = 6$ Hz, C₈-H), 1.38 (3H, s, C₇-H), 1.95 (3H, d, $J = 7$ Hz, C₁₀-H), 5.98 (1H, q, $J = 7$ Hz, C₉-H). This necic acid (**12**) was identical with **12** obtained from neoligularidine (**3**) on the basis of mixed fusion, IR spectra and $[\alpha]_D$. **11**: Colorless prisms, mp 146–147°C (acetone), $[\alpha]_D^{24} - 63.4^\circ$ ($c = 0.15$, CHCl₃). *Anal.* Calcd for C₈H₁₅NO₂: C, 61.12; H, 9.62; N, 8.91. Found: C, 61.26; H, 9.61; N, 8.63. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3360, 1220, 1008, 735. MS m/z (%): 157 (M⁺, 21), 113 (40), 82 (100). This base was identical with an authentic sample of platynecine on the basis of mixed fusion, IR spectra and $[\alpha]_D$.

Hydrolysis of Neoligularidine (3)—**3** (50 mg) in water (10 ml) was boiled under reflux with barium hydroxide octahydrate (184 mg) for 5 h. The solution was allowed to cool, treated with CO₂ gas, and filtered, then the filtrate was acidified with HCl and extracted continuously with ether for 10 h. The ether extract was recrystallized from ether-*n*-hexane to give necic acid (**12**) (7.3 mg) which was identical with **12** obtained from **5** on the basis of mixed fusion, IR spectra and $[\alpha]_D$.

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