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Studies on Constituents of Crude Drugs. VII.[1] Syneilesine and Acetylsyneilesine from *Syneilesis palmata*

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Two new alkaloids, syneilesine and acetylsyneilesine, together with senecionine have been isolated from the roots and aerial parts of *Syneilesis palmate* Maxim. (Compositae). The structures of syneilesine and acetylsyneilesine were shown to be (12*R*), (13*R*), (14*R*)-15-ethyl-12,14-dihydroxy-4,12,13-trimethyl-8-oxo-4,8-secosenec-1-enine and (12*R*), (13*R*), (14*R*)-14-acetoxy-15-ethyl-12-hydroxy-4,12,13-trimethyl-8-oxo-4,8-secosenec-1-enine, respectively.

In a preliminary communication,[3] we have reported the isolation of syneilesine (**1**), a new cytotoxic secopyrrolizidine alkaloid from the roots of *Syneilesis palmata* Maxim. (Japanese name: Yaburegasa, the tribe Senecioneae of Compositae) which is spread widely throughout Japan. The young leaves are used for foods in various districts. We have now isolated a new secopyrrolizidine alkaloid named acetylsyneilesine (**2**) accompanied with senecionine (**3**) from the same plant. Based on the chemical and physicochemical evidence, we have elucidated that **2** is 14-O-acetylsyneilesine. The present paper deals with the full account on the structure elucidation of syneilesine (**1**), acetylsyneilesine (**2**) and senecionine (**3**).

The crude alkaloids obtained from the methanol extracts of the roots and the aerial parts were chromatographed on silica gel column using $CHCl_3$–MeOH–NH_4OH as a solvent system to afford three alkaloids (**1**), (**2**) and (**3**). The first alkaloid (**1**), colorless needles mp 195.0° ($C_{19}H_{29}O_7N$ by high resolution mass spectroscopy), shows 19 detectable signals of carbon in ^{13}C–NMR. Signals at δ 134.2, 136.0, 171.4, 176.7 and 189.4 ppm were easily assigned.[4] The signals at 171.4 and 176.7 ppm indicate the presence of two ester carbonyl carbons[5] which were also ascertained by infrared (IR) absorptions at 1720 and 1735 cm^{-1}. The signals at 134.2, 136.0 and 189.4 ppm are responsible for α,β-unsaturated carbonyl group. A significant high field shift of the signal due to carbonyl carbon at 189.4 ppm, relative to the ordinary α,β-unsaturated carbonyl carbons, would be caused by effects of transannular interactions of the nitrogen atom in the necine moiety of the secopyrrolizidine alkaloid.[6] A positive circular dichroism(CD) curve at 243 and 278 nm (in methylcyclohexane) suggests characteristic otonecine diester alkaloid.[7] All the signals of carbon atoms were assigned by the aid of proton noise decoupling and off resonance methods. The proton magnetic resonance (PMR) spectrum of **1** shows a typical pattern of twelve membered macrocyclic secopyrrolizidine alkaloid, a singlet at δ 2.07 ppm corresponds to $\underline{CH_3}$–N< at N-4, two broad singlets at 6.08 and 5.07 to the olefinic proton at C-2 and methine proton at C-7, respectively. The signals of the

1) Part VI: T. Furuya, M. Hikichi and Y. Iitaka, *Chem. Pharm. Bull.* (Tokyo), **24**, 1120 (1976).
2) Location: *Shirogane Minato-ku, Tokyo, 108, Japan.*
3) M. Hikichi and T. Furuya, *Tetrahedron Letters*, **1974**, 3657.
4) M. Tanaka, S. Toda, T. Nagata, K. Kanoda, J. Saito, T. Mitsuishi, S. Hashimoto, Y. Shimizu, and H. Kigasawa, *Japan Analyst*, **21**, 41 (1972).
5) G.C. Levy and G.L. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists", J. Wily & Sons, Inc., N.Y., 1972, Chap. 5, p. 109.
6) C.C.J. Culvenor, J.M. O'Donovan, and L.W. Smith, *Aust. J. Chem.*, **20**, 801 (1967).
7) K.B. Birmbaum, A. Klasek, P. Sedmera, G. Snatzke, L.F. Johnson and F. Šantavý, *Tetrahedron Letters*, **1971**, 3421. C.C.J. Culvenor, D.H.G. Crout, W. Klyne, W.P. Mose, J.D. Renivick and P.M. Scopes, *J. Chem. Soc.*, (*C*), **1971**, 3653.

geminal methylene protons at C-9 appeared as a pair of doublets at 5.52 and 4.30 (J=11.5 Hz each other). From the appreciable difference of the shift (ΔH=1.22 ppm) between two protons at C-9 and the coupling constant (J=11.5 Hz), **1** is classified as a characteristic twelve membered macrocyclic secopyrrolizidine alkaloid.[8] Other assignable signals are at 0.91 for $C\underline{H}_3$–CH_2– and at 1.05 for $C\underline{H}_3$–CH, respectively. The complicated peaks at 2.00 to 3.70 are due to the methylene protons at C-3, C-5 and C-6 and the methine protons at C-13, C-14 and C-15. From the above data, the structure of **1** was estimated to be 15-ethyl-12,14-dihydroxy-4,12,13-trimethyl-8-oxo-4,8-secosenec-1-enine.

The absolute configurations of asymmetric carbons at C-7, C-12, C-13 and C-14 of **1** were revealed by chemical hydrolysis and hydrogenolysis of **1**. The alkaline hydrolysis of **1** gave three lactones, named syneilesinolide-A(**4a**) syneilesinolide-B(**5**) and syneilesinolide-C(**6**). **4a** was easily obtained by crystallization of the chloroform extract from the reaction mixture, and **5** and **6** were separated by silica gel column chromatography from the mother liquor of the crystallization of **4a**. The high resolution mass spectra of **5** and **6** showed the parent peaks at m/e: 198 ($C_{10}H_{14}O_4$), while the highest mass number of **4a** was observed at m/e: 172 (M^+-CO_2). Monomethyl ester (**4b**) derived from **4a** with diazomethane, was shown to possess empirical formula $C_{11}H_{18}O_5$ (M^+ 230). The IR absorptions of **4a** (1790 cm^{-1}), **5** (1740 cm^{-1}) and **6** (1745 and 1790 cm^{-1}) indicate the existence of γ-lactone, α,β-unsaturated δ-lactone and γ,δ-dilactone derivatives, respectively. The structures of **4a**, **5** and **6** are shown to be 2-ethyl-5-hydroxy-4,5-dimethylhexanoic acid-6,3-olide, 5-carboxy-2-ethyl-4,5-dimethyl-2-pentene-5-olide and 2-ethyl-4,5-dimethylhexane-1,5: 6,3-diolide, respectively. Hydrogenation of **5** gave dihydrosyneilesinolide-B (**7**), whose negative CD curve at 238 nm indicated that the configuration at C-5 in **5** was the same with that[9] at C-2 in (2R)-dihydrosenecic acid lactone and also the formation of **6** (γ,δ-dilactone) from **1** suggests the configuration at C-3 in **6** is R. As the δ-lactone conformation of **6** is restricted to be half chair form[10] and the ethyl group at C-2 is faced toward more stable quasi-equatorial orientation. The coupling constant J=5.4 Hz,[11] indicates that the dihedral angle between C-3 and C-4 protons is about 36° and the R configurations of C-2 and C-4 were established. Therefore the structure of **6** is shown to be (2R),(3R),-(4R),(5R)-2-ethyl-4,5-dimethylhexane-1,5: 6,3-diolide. The structures of **4a** and **5** are also

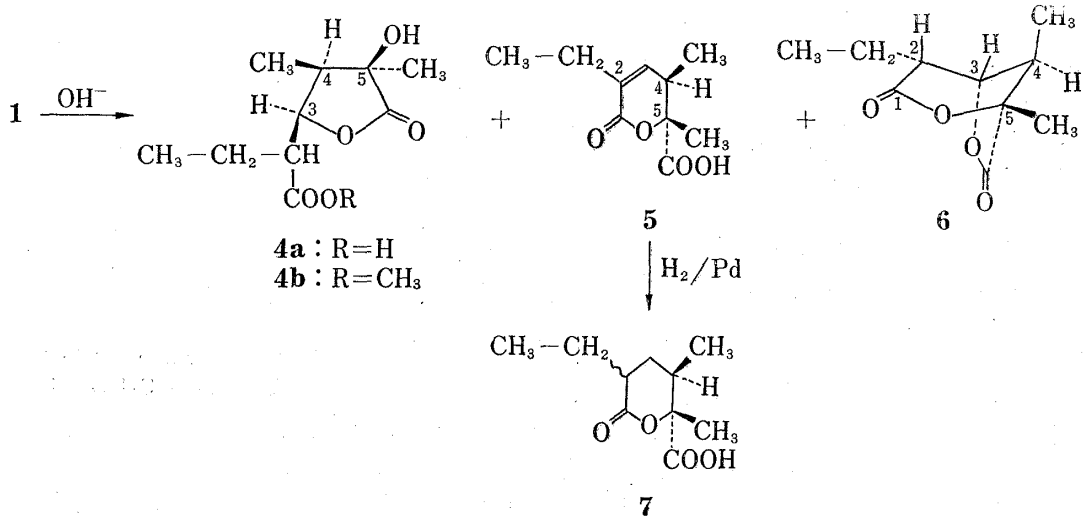


Chart 1

8) L.H. Briggs, R.C. Cambie, B.J. Candy, J.M. O'Donovan, R.H. Russell and R.N. Sulye, *J. Chem. Soc.*, **1965**, 2492.
9) O. Cervinka, L. Hub, A. Klasek, and F. Šantavý, *Chem. Comm.*, **1968**, 261.
10) A. Jch. Mathieson, *Tetrahedron Letters*, **1963**, 81.
11) M. Karplus, *J. Am. Chem. Soc.*, **85**, 2870 (1963).

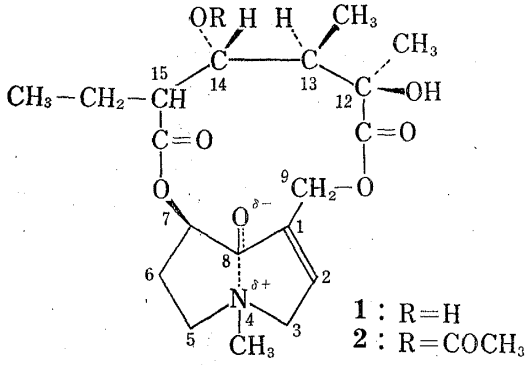


Fig. 1

shown to be (3*R*), (4*R*), (5*R*)-2-ethyl-5-hydroxy-4,5-dimethylhexanoic acid-6,3-olide and(4*R*), (5*R*)-2-ethyl-5-carboxy-4,5-dimethyl-2-pentene-5-olide, respectively. As **5** and **6** were formed by acid treatment of **4a**, the chirarities of C-3, C-4 and C-5 were preserved during the saponification with alkali.

On the other hand, the formation of dihydrodesoxysyneilesine-11,14-olide (**8**) derived from the hydrogenolysis of **1** over Adam's catalyst in dil.HCl solution, proves an evidence on the connection of the necine and the necic acid. **8** was hydrolyzed with alkali to give necic acids, **4a**, **5** and small amount of **6** and dihydrodesoxyotonecine (**9**).[6]

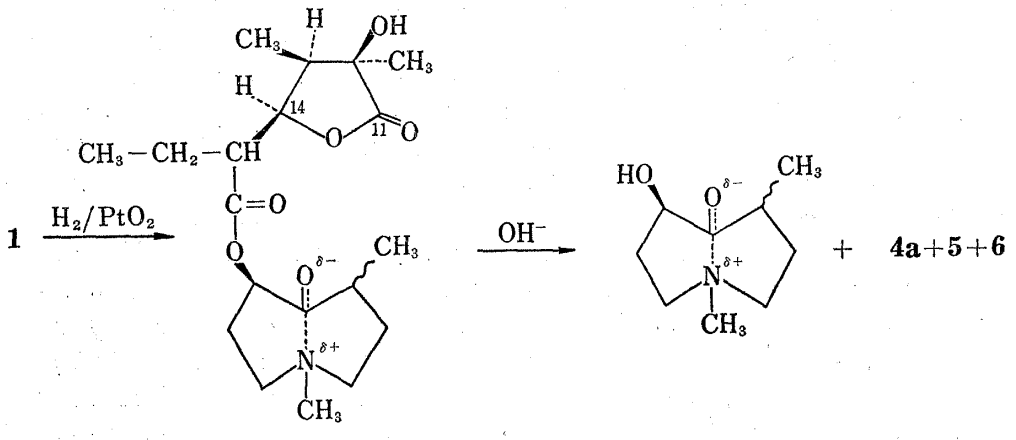


Chart 2

The structure of the basic moiety and the acidic moiety and the formation of **8** lead to the conclusion that the structure of **1** is (12*R*),(13*R*),(14*R*)-15-ethyl-12,14-dihydroxy-4,12,13-trimethyl-8-oxo-4,8-secosenec-1-enine.

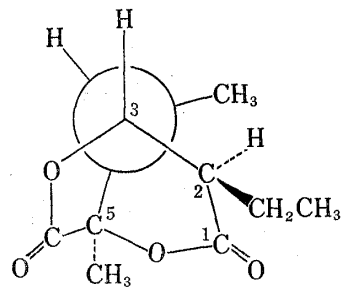


Fig. 2. Newman Projection of **6** about C-3—C-4 Bond

The second alkaloid (**2**), colorless oil $C_{21}H_{31}O_7N$, showed similar IR, PMR and mass spectra to those of **1**, except singlet at δ 2.20 (3H) and one broad doublet at δ 5.07 (1H) in the PMR spectrum, suggesting the presence of acetoxy group. The positive at 243 and 278 nm (in methylcyclohexane) showed **2** to be diester otonecine alkaloid, probably. The alkaline hydrolysis of the hydrogenolysis product from **2** yielded the necine, dihydrodesoxyotonecine, and three lactones, **4a**, **5** and **6**. From above data, **2** is shown to be (12*R*),(13*R*),(14*R*)-14-acetoxy-15-ethyl-12-hydroxy-4,12,13-trimethyl-8-oxo-4,8-secosenec-1-enine, which was further confirmed by the acetylation of **1** with Ac_2O and AcONa to give **2**.

High resolution mass spectrometric studies on **1** and **2** showed[12] that the fragment ions at *m/e*: 168 ($C_9H_{14}O_2N$), 152 ($C_9H_{14}ON$), 151 ($C_9H_{13}ON$), 122 (C_7H_8ON) and 110 (C_6H_8ON) are in good agreement with the characteristic secopyrrolizidine alkaloids. The significant frag-

12) M.P. Cava, K.V. Rao, J.A. Weisbach, R.F. Raffaul, and B. Douglas, *J. Org. Chem.*, 33, 3570 (1968).

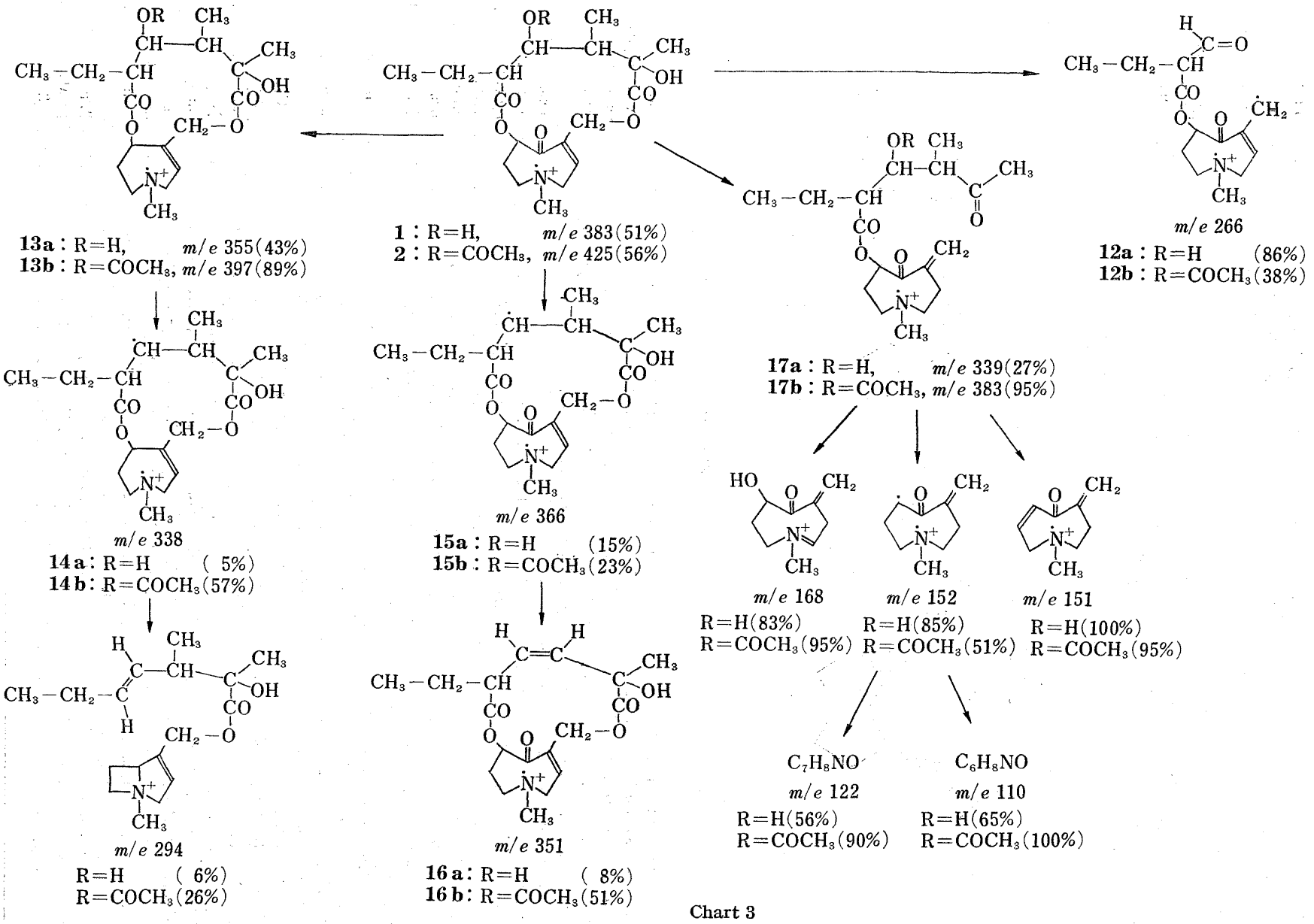
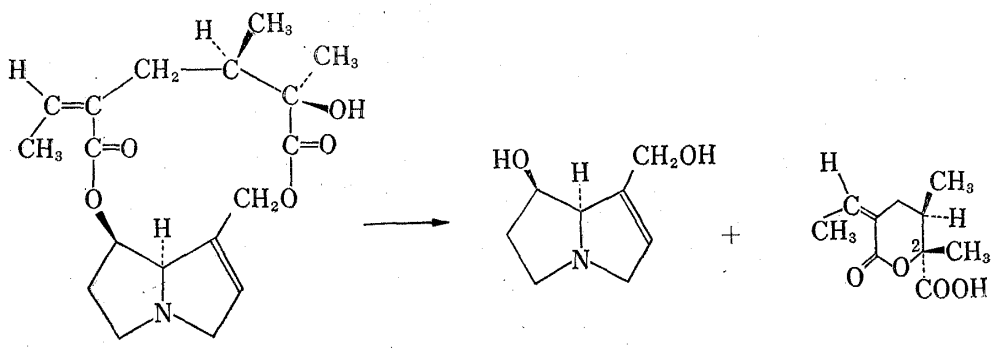


Chart 3

ment ion at *m/e*: 355 (**13a**) or 397 (**13b**), 338 (**14a** and **14b**), 366 (**15a** and **15b**), 351 (**16a** and **16b**) and 266 (**12a** and **12b**) indicate that the O-functional group are located at C-12 in the necic acid moiety. Other fragment patterns of **1** and **2** are in full agreement with the proposed structure as shown in Chart 3.

The third alkaloid (**3**), colorless needles, mp 231.5° was identified with senecionine by the IR, Mass and PMR spectral data and the chemical hydrolysis with alkali to give (+)-retronecine (**10**)[13] and senecic acid lactone (**11**).[14]

The cytotoxic bioassay of **1**, **2** and **3** is now in progress.



3 **10** **11**

Chart 4

Experimental

Mps were taken on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were recorded with a Shimadzu IR 27G spectrometer. The CMR and PMR spectra were obtained with a JEOL PS-100 Fourier-Transform Spectrometer with 8K data table for acquisition of free induction decay and TMS as in internal standard. High resolution mass spectra were obtained with a JEOL JMS OlS mass spectrometer. CD data were obtained with a JASCO Model ORD/CD-6.

Extraction of Crude Alkaloids——The air dried powdered roots and aerial parts of Syneilesis palmata collected near the Sagamiko, Kanagawa-ken in July, 1973 were percolated in hot with MeOH for three times, respectively. The solvent from the combined MeOH extract was removed *in vacuo* below 45° to yield viscous mass, which was extracted with 0.5N H_2SO_4 for several times. The acid soluble fraction was extracted with $CHCl_3$ three times and the $CHCl_3$ extract contained mainly nonbasic materials. The aqueous acidic soln. was then made alkaline to phenolphthalein with 28% NH_4OH and extracted with $CHCl_3$ five times. A crude alkaloid was obtained after evaporating the solvent. The aerial parts (9.5 kg) and the roots (4.0 kg) yield 5.4 g (0.057%) and 8.8 g (0.22%) of crude alkaloid, respectively.

Separation of Alkaloids——The crude alkaloid (10.1 g) was submitted to silica gel (1.2 kg) column chromatography. On the eluation with mixed solvent ($CHCl_3$: MeOH: 28% NH_4OH=100: 10: 1), the alkaloid **3** (0.1 g), **2** (0.8 g), and **1** (1.5 g) were present in fraction 46—56, 97—107, and 110—121, respectively. The physical properties and the spectral data of the each alkaloids are as follows.

1: Colorless needles, mp 194.5—195° (light petroleum); M^+ 383.197 (383.199 Calcd for $C_{19}H_{29}O_7N$); CD$[\theta]^{25}_{max}$ (MeOH) +20500 (232 nm), +43500 (275 nm), $[\theta]^{25}_{max}$ (methylcyclohexane) +11200 (225 nm), +14800 (275 nm); IR ν^{KBr}_{max} 3500 cm^{-1}, 1735, 1720, 1660, 1580; CMR (δ ppm in $CDCl_3$) 189.4 (-C̲O-C=CH- at C-8), 176.7 (C̲OO- at C-11), 171.4 (-COO- at C-16), 136.0 (-C̲H=C< at C-2), 134.2 (>C̲=CH at C-1), 78.9 (>C̲< at C-12), 74.3 (>C̲H-OCO at C-7), 73.3 (>C̲-OH at C-14), 63.6 (-C̲H_2-N at C-3), 59.2 (-C̲H_2N at C-5), 53.5 (>N-C̲H_3), 41.2, and 40.4 (-C̲H< at C-13 and C-15), 37.3 (-C̲H_2- at C-6), 24.3 (C̲H_3-C-12), 23.0 and 5.8 (C̲H_3-C̲H_2-C-15), 11.8 (C̲H_3-C-13), 78.4 (-C̲H_2-OCO- at C-9): PMR (δ ppm in $CDCl_3$) 0.91 (3H, t, J=7.5 Hz), 1.05 (3H, d, J= Hz), 1.34 (3H, s), 2.07 (3H, s), 3.41 (2H, broad s), 3.65 (1H, d, J=10.0 Hz), 4.30 (1H, d, J=11.5 Hz), 5.52 (1H, d, J=11.5 Hz), 5.07 (1H, broad s), 6.08 (1H, broad s) and 1.50—3.00 (complicated peaks).

2: Colorless oil; M^+ 425.215 (425.210 Calcd. for $C_{21}H_{31}O_8N$); CD$[\theta]^{16}_{max}$ (MeOH) +22100 (225 nm), $[\theta]^{21}_{max}$ (methylcyclohexane) +14300 (243 nm), +19800 (278 nm); IR ν^{KBr}_{max} 3430 cm^{-1}, 1735, 1650, 1615; PMR (δ ppm in $CDCl_3$), 0.85 (3H, t. J=10.0 Hz), 1.10 (3H, d, J=11.5 Hz), 1.27 (3H, s), 2.20 (3H, s), 2.08 (3H, s), 4.27

13) T. Furuya and M. Hikichi, *Phytochemistry*, **10**, 217 (1971).
14) C.C.J. Culvenor and L.W. Smith, *Aust. J. Chem.*, **8**, 556 (1955). T. Furuya, K. Murakami, and M. Hikichi, *Phytochemistry*, **10**, 3306 (1971).

(1H, d, J=12.0 Hz), 5.07 (1H, d, J=11.0 Hz), 5.10 (1H, broad s), 5.50 (1H, d, J=12.0 Hz), 6.18 (1H, broad s), and 1.50—3.40 (complicated peaks).

3: Colorless prisms, mp 230.5—231.5° (from acetone); $[\alpha]_D^{20}$ −61° (c=1 in $CHCl_3$); M^+ 335.179 (335.173 Calcd. for $C_{18}H_{25}O_5N$); IR ν_{max}^{KBr} 3420 cm^{-1}, 1735, 1710, 1655; PMR (δ ppm in $CDCl_3$) 0.92 (3H, d, J=6.0 Hz), 1.30 (3H, s), 1.82 (3H, d, J=8.2 Hz), 4.02 (1H, d, J=12.0 Hz), 5.50 (1H, d, J=12.0 Hz), 5.75 (1H, q of d, J=8.2 Hz and 1.5), 6.20 (1H, broad s), 5.01 (1H, broad s), 4.28 (1H, broad s) and 1.90—3.50 (complicated peaks).

Hydrolysis of 1——EtOH solution (5.0 ml) of **1** (0.11 g) was mixed with 10% KOH (2.0 ml) at room temp. After allowing to stand for 20 hr, 30 ml of H_2O was added into the reaction mixture and EtOH and H_2O were evaporated to the half volume *in vacuo*. The basic solution was acidified to Congo red with 20%HCl and continuously extracted with $CHCl_3$ by use of Asahina's extractor. The $CHCl_3$ extract yielded white solid which gave **4a** as colorless needles by crystallization from the mixture solvent of *n*-hexane and benzene. The mother liquor of the crystallization of **4a** was then evaporated to dryness to give white solid which was then chromatographed on silica gel (20 g) column eluting with benzene–AcOEt (10: 1). Fraction 5—10 and 15—21 contained 0.015 g of **6** and 0.035 g of **5**, respectively. The physical properties and the spectral data of the necic acids are described as follows.

4a: Colorless needles mp 133.0—134.0° (from *n*-hexane–benzene); CD $[\theta]_{max}^{16}$ (MeOH) +3700 (215 nm); Mass Spectrum *m/e*: 172.112 (M^+-CO_2); IR ν_{max}^{KBr} 3400 cm^{-1}, 1790, 1700; PMR (δ ppm in $CDCl_3$), 1.04 (3H,t, J=7.5 Hz), 1.00 (3H, d, J=6.2 Hz), 1.52 (3H, s), 4.58 (1H, d of d, J=10.0 Hz, and 5.2).

5: Colorless needles mp 120.0—121.0° (*n*-hexane–benzene); CD $[\theta]_{max}^{15}$ (MeOH) −82500 (203 nm), −61000 (223 nm), −6600 (257 nm); M^+ 198.093 (198.089 Calcd. for $C_{10}H_{14}O_4$); IR ν_{max}^{KBr} 3300 cm^{-1}, 1740, 1090; PMR (δ ppm in $CDCl_3$), 0.98 (3H, d, J=6.5 Hz), 1.09 (3H, t, J=8.0 Hz), 1.58 (3H, s), 2.30 (2H, broad q, J=8.0 Hz), 2.88 (1H, d of q, J=7.5 Hz and 6.5), and 6.45 (1H, broad d, J=7.5 Hz).

6: Colorless wooly crystals mp 85.0—86.0° (from *n*-hexane); CD $[\theta]_{max}^{15}$ (MeOH) +9800 (210 nm); M^+ 198.095 (198.089 Calcd. for $C_{10}H_{14}O_4$); IR ν_{max}^{KBr} 1790 cm^{-1}, 1745; PMR (δ ppm in $CDCl_3$), 0.92 (3H, t, J=7.5 Hz), 0.98 (3H, d, J=8.0 Hz), 1.50 (3H, s), 2.42 (1H, t of d, J=11.0 Hz and 2.4), 4.75 (1H, d of d, J=5.4 and 2.4) and 1.60—2.00 (3H, complicated peaks).

Treatment of 4a with Diazomethane——Into the ether solution of **4a** (0.02 g) was added an etheral solution of diazomethane. After allowing to stand for 1 hr, the excess of diazomethane was decomposed with small portion of AcOH. Evaporating of the solvent *in vacuo* yield colorless solid which was recrystallized to give **4b**, colorless needles, mp 124.0—124.5° (from *n*-hexane–benzene). CD $[\theta]_{max}^{16}$ (MeOH) +2600 (212 nm). M^+ 230.118 (230.115 Calcd for $C_{11}H_{18}O_5$); IR ν_{max}^{KBr} 3420 cm^{-1}, 1760, 1740, PMR (δ ppm in C_6D_6), 0.72 (3H, d, J= 7.5 Hz), 0.80 (3H, t, J=7.0 Hz), 1.10 (3H, s), 1.20 (2H, m), 1.86 (1H, d of q, J=5.1 Hz and 7.5), 2.51 (1H, t of d, J=11.0 Hz and 8.5), 3.38 (3H, s), 3.31 (1H, broad s) and 4.38 (1H, d. of d, J=5.1 and 8.5), (δ ppm in $CDCl_3$), 0.95 (3H, t, J=7.0 Hz), 0.97 (3H, d, J=7.5 Hz), 1.44 (3H, s), 1.52 (2H, t, J=11.2 Hz and 8.5), 2.4—2.60 (4H, m), 3.71 (3H, s) and 4.52 (1H, d of d, J=8.5 Hz and 5.1).

Hydrogenation of 5——In 10 ml of MeOH, **5** (0.06 g) was dissolved, 0.05 g of 5% Pd/C catalyst was added and the solution was hydrogenated for 1.5 hr under normal atmospheric pressure. After hydrogenation, the catalyst was filtered off, the filtrate was evaporated under reduced presure and the oily residue was distilled to yield white solid, 177—180°/0.7 mmHg, which was recrystallized to give colorless prisms (**7**), mp 86.0—88.0° (light petroleum), CD $[\theta]_{max}^{25}$ (MeOH) −2400 (238 mm); M^+ 200.107 (200.105 Calcd. for $C_{10}H_{16}O_4$); IR ν_{max}^{KBr} 3450 cm^{-1}, 1750, 1690.

Acid Treatment of 4a——A solution of **4a** (0.08 g) in 5% HCl was allowed to stand for 2 days at room temp. and the reaction mixture was extracted with $CHCl_3$ by use of Asahina's extractor. The $CHCl_3$ extract gave white amorphous solid, which was chromatographed on silica gel column eluting with benzene–AcOEr (10: 1) to yield **5** amd **6**.

Hydrogenolysis of 1——A solution of **1** (0.15 g) in 0.5N HCl (30 ml) was shaken with hydrogen over Adam's catalyst, 25 ml of hydrogen was absorved. The catalyst was removed by filtration and the filtrate was then evaporated to dryness *in vacuo*. White solid obtained was then chromatographed on silica gel (15 g) eluting with $CHCl_3$: MeOH: 28%NH_4OH (100: 10: 1). **8** was obtained from fraction 20—35 as white gum, which was recrystallized from light petroleum to give **8** colorless needles, mp 108.0—109.0, M^+ 369.225 (369.220 Calcd for $C_{19}H_{31}O_6N$); CD $[\theta]_{max}^{16}$ (MeOH) +17500 (230 nm); IR ν_{max}^{KBr}; 3450 cm^{-1}, 1770, 1740, 1620. PMR (δ ppm in CD_3OD), 0.97 (3H, t, J=7.0 Hz), 1.04 (3H, s), 1.06 (3H, d, J=11.5 Hz), 1.45 (3H, s), 2.10 (3H, s), 4.70 (1H, d of d, J=11.0 and 5.4 Hz), 5.05 (1H, broad s), 1.60—2.80 (complicated peaks).

Hydrolysis of 8——To the EtOH solution (10 ml) of **8** (0.10 g) was added 5% KOH (2 ml) at room temp. After allowing to stand for 30 min, 50 ml of H_2O was added into the reaction mixture and extracted with $CHCl_3$ three times. The $CHCl_3$ extract gave pale yellow oil which was distilled to give **9** colorless oil (0.03 g), bp 133—135°/15 mmHg, M^+ 171.128 (171.126 Calcd. for $C_9H_{17}O_2N$), picrate, mp 218.0—220.0° (from EtOH). (Found: C, 44.80; H, 5.20; N, 14.00. Calcd. for $C_{15}H_{20}O_9N_4$: C, 44.99; H, 5.04; N, 13.96%. HCl salt, mp 238.0—240.0° (from EtOH), $[\alpha]_D^{20}$ −35.1° which was shown to be identical with an authentic sample of dihydrodesoxyothonecine HCl by mmp and IR and $[\alpha]_D$. The aq. basic solution was then acidified to congo red with 20%HCl and extracted with $CHCl_3$ by use of Asahina's extractor. The $CHCl_3$ ext. yields **4a** (0.02 g), **5** (0.01 g) and small portion of **6** (0.002 g).

Hydrogenolysis and Hydrolysis of 2——A solution of **2** (0.15 g) in 0.5N HCl (20 ml) was shaken with hydrogen over Adam's catalyst, 20 ml of hydrogen was absorbed. The catalyst was removed by filtration. The filtrate was then evaporated to dryness *in vacuo*. To the white gum obtained was then added 10 ml of 5%-KOH. After allowing to stand for 3 hr at room temp. the reaction mixture was extracted with $CHCl_3$ for three times. Pale yellow oil was obtained after evaporation of the solvent and distilled to give colorless oil, bp 130—135°/15 mmHg, which was identical with authentic sample of dihydrodesoxyotonecine (**9**) by all spectral data.

The residual basic layer was then acidified to congo red with 20%HCl and continuously extracted with $CHCl_3$ by use of Asahina's extractor, **4a** (0.03 g), **5** (0.015 g) and **6** (0.01 g) were obtained from the $CHCl_3$ ext. by use of silica gel column chromatography.

Acetylation of 1——A solution of **1** (0.1 g) in Ac_2O (5 ml) was heated to 80° for 3 hr, the reaction mixture was then poured into ice water and made alkaline with ammonia and extracted with $CHCl_3$ for five times. The $CHCl_3$ extract gave pale brown oil, which was treated with silica gel (10 g) column chromatography eluting with $CHCl_3$: MeOH: 28%NH_4OH (100: 10: 1) to give colorless oil. Its IR and CD spectra were in full agreement with those of **2**.

Hydrolysis of 3——Barium hydroxide (1 g) and **3** (0.1 g) were refluxed in H_2O (10 ml) for 1.5 hr. After saturating CO_2 gas, the solution was filtered, the filtrate was acidified to congo red and extracted with ether for several times. The ether extract yielded a gum which was dissolved in conc. HCl and evaporated to dryness *in vacuo* to give white solid. Recrystallization from benzene gave **11**, colorless prisms, mp 154.5—156.0°, $[\alpha]_D^{20}$ +36.0° (c=1, EtOH) which was identical with an authentic sample of senecic acid lactone by mmp, IR spectra and $[\alpha]_D$.

The residual hydrolysed solution was made alkaline with NaOH (1.0 g) and evaporated to dryness. The residue, extracted with EtOH, gave crystals which was recrystallized from acetone to give **10**, colorless prisms mp 117.0—118.0°, $[\alpha]_D^{20}$ +49.6° (EtOH). This base was identical with the authentic sample of retrenecine by mmp, IR and $[\alpha]_D$.

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