Studies on Nepalese Crude Drugs. XXI.[1] On the Diterpenoid Constituents of the Aerial Part of *Scutellaria discolor* COLEBR.

Akiko OHNO, Haruhisa KIZU, and Tsuyoshi TOMIMORI*

Faculty of Pharmaceutical Sciences, Hokuriku University, Ho-3, Kanagawa-machi, Kanazawa 920–11, Japan.
Received February 26, 1996; accepted April 11, 1996

From the aerial part of *Scutellaria discolor*, eight new neoclerodane diterpenes (compounds 3, 4, 6, 8, 9, 10, 11 and 12) were isolated together with clerodin, dihydroclerodin-I, clerodin hemiacetal (14-hydro-15β-hydroxyclerodin), jodrellin A, scutaltisin, squalene, 24-methylenecycloartanol and a mixture of 3-epioleanolic acid and 3-epiursolic acid. The structures of new compounds were determined by spectroscopic and chemical methods as follows: 3, 15β-ethoxy-14-hydroclerodin; 4, 15α-ethoxy-14-hydroclerodin; 6, (6α)-19-*O*-acetyl-4,18:11,16:15,16-triepoxyneoclerodane-6,15,19-triol (6-*O*-deacetyl-14-hydro-15-hydroxyclerodin); 8, 6α-*O*-acetyl-2,19:4,18:11,16:15,16-tetraepoxy-14-neoclerodene-6,19-diol (19-*O*-deacetyljodrellin A); 9, 10, 11 and 12, 6α-*O*-acetyl-15β,19β-di-*O*-ethyl-, 6α-*O*-acetyl-15α,19β-di-*O*-ethyl-, 6α-*O*-acetyl-19β-*O*-ethyl- and 6α,19-di-*O*-acetyl-2,19:4,18:11,16:15,16-tetraepoxyneoclerodane-6,15,19-triol, respectively.

Key words *Scutellaria discolor*; Labiatae; neoclerodane diterpene; triterpene

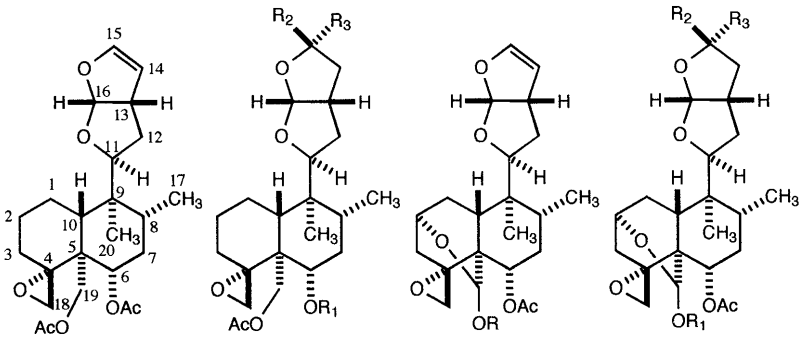
In a previous paper,[2] we reported the structural identification of ten flavonoids isolated from the aerial part of *Scutellaria discolor*. In our futher studies on the constituents of the aerial part of this plant, thirteen neoclerodane diterpenoids (**1**—**13**) and four triterpenoids (**14**—**17**) have been isolated as described in the experimental section. This paper deals with their structural identification.

Compounds **1**, **2**, **7**, **13**, **14** and **15** were identified as clerodin,[3] dihydroclerodin-I,[4] jodrellin A,[5] scutaltisin,[6] squalene[7] and 24-methylenecycloartanol,[8] respectively, based on spectral and physical data.

Compounds **16** and **17** were obtained as a mixture and were identified as 3-epioleanolic acid[9] and 3-epiursolic acid,[10] respectively from their retention times on HPLC and ^{1}H- and ^{13}C-NMR spectral data.

Compounds **3** and **4** were obtained as a white powder and colorless prisms (mp 152—154 °C), respectively. The molecular formula of both was determined as $C_{26}H_{40}O_8$ from elemental analysis, electron impact mass spectra (EIMS) and ^{13}C-NMR data. Their ^{1}H- and ^{13}C-NMR spectra were very similar to those of clerodin (**1**), except for the C_{14}–C_{15} part. The signals due to an olefinic group in **1** were absent in **3** and **4**, while those due to a hemiacetal [**3**: δ_H 5.32 (1H, br d, J=4.0 Hz), δ_C 104.2; **4**: δ_H 5.08 (1H, d, J=5.5 Hz), δ_C 104.3] and an ethoxy group [**3**: δ_H 1.12 (3H, t, J=7.0 Hz), 3.40, 3.76 (each 1H, dq, J=9.5, 7.0 Hz), δ_C 15.4, 62.8; **4**: δ_H 1.16 (3H, t, J=7.0 Hz), 3.39, 3.80 (each 1H, dq, J=9.5, 7.0 Hz), δ_C 15.3, 63.1] were observed, indicating that these compounds were 15-ethoxy-14-hydroclerodin isomers. The stereochemistry at the C-15 position in **3** was determined as the β form in a nuclear Overhauser effect (NOE) experiment, in which NOEs were observed between C_{15}-oxymethylene/H-16 and H-15/H-11, while that of **4** was the α form: an NOE was observed between C_{15}-oxymethylene and H-11. Furthermore, **3** and **4** were derived from **1** by treatment with 50% AcOH–EtOH, which afforded a 6:5 ratio of **3** and **4**.

Based on these findings, the structures of **3** and **4** were



1

	R_1	R_2	R_3
2	Ac	H	H
3	Ac	OEt	H
4	Ac	H	OEt
5a	Ac	OH	H
5b	Ac	H	OH
6a	H	OH	H
6b	H	H	OH

7: R = Ac
8: R = H

	R_1	R_2	R_3
9	Et	OEt	H
10	Et	H	OEt
11a	Et	OH	H
11b	Et	H	OH
12a	Ac	OH	H
12b	Ac	H	OH
13a	H	OH	H
13b	H	H	OH

Chart 1

* To whom correspondence should be addressed.

concluded to be 15β- and 15α-ethoxy-14-hydroclerodin, respectively.

Compound **5a** was obtained as colorless prisms (mp 188—191 °C) from acetone and was deduced to be a compound related to **3** from the NMR spectral data. Its ^{1}H- and ^{13}C-NMR spectra were very similar to those of **3**, except for the lack of ethoxy signals, showing that **5a** was 14-hydro-15β-hydroxyclerodin (clerodin hemiacetal).[3]

Although **5a** showed NMR signals due to one component immediately after being dissolved in pyridine-d_5, it gradually changed to **5b**. After 1 h, this solution reached equilibrium (**5a** : **5b** = *ca.* 1 : 1). Compound **5b** was deduced to be 14-hydro-15α-hydroxyclerodin by comparison of the ^{1}H- and ^{13}C-NMR spectra of an equilibrium mixture of **5a** and **5b** with those of **3** and **4** (Table 1).

These results were supported by the fact that treatment of **1** with 50% AcOH in tetrahydrofuran (THF)–H_2O gave an equilibrium mixture of **5a** and **5b**.

Compound **6** was obtained as a white powder and its IR spectrum revealed the presence of hydroxy (3488 cm^{-1}) and ester (1738 cm^{-1}) groups. The molecular formula was determined as $C_{22}H_{34}O_7$ from elemental analysis and EIMS data. The ^{1}H- and ^{13}C-NMR spectra of **6** were quite similar to those of **5**, suggesting that **6** was also an equilibrium mixture. The presence of only one acetyl group in **6** was confirmed from its NMR spectra. Comparison of the ^{1}H-NMR spectrum of **6** with that of **5** showed that the H-6 signal of **6** was at an upper field by 1.2 ppm than that of **5**. Consequently, a hydroxy group is present at the C-6 position and an acetoxy group at C-19.

Table 1. ^{13}C-NMR Spectral Data for **1**, **3**, **4**, **5** and **6** (100 MHz, Pyridine-d_5)

C No.	**1**[a]	**2**	**3**	**4**	**5a**	**5b**	**6a**	**6b**
1	22.5	22.5	22.4	22.5	22.5	22.5	22.4	22.4
2	25.2	25.3	25.1	25.3	25.2	25.3	25.3	25.3
3	33.1	33.1	33.1	33.2	33.2	33.2	32.6	32.7
4	65.3	65.3	65.3	65.3	65.3	65.3	67.3	67.3
5	46.1	46.1	46.0	46.1	46.1	46.1	46.0	46.0
6	72.2	72.2	72.2	72.3	72.2	72.4	73.4	73.3
7	33.8	33.9	33.8	34.0	34.0	34.0	35.4	35.4
8	36.2	35.8	35.9	36.2	36.0	36.3	36.2	35.9
9	40.3	40.8	40.3	40.5	40.5	40.5	40.8	40.8
10	48.8	48.4	48.6	48.6	48.7	48.7	47.7	47.5
11	84.9	85.4	83.7	83.7	83.8	83.4	83.6	84.0
12	31.4	32.8	32.4	33.0	32.6	33.0	32.7	33.0
13	46.5	42.5	40.5	41.1	41.0	41.7	41.0	41.7
14	102.5	32.7	38.3	39.7	39.9	40.7	39.9	40.6
15	147.2	68.4	104.2	104.3	99.3	98.7	99.3	98.7
16	108.3	108.2	107.7	109.6	107.6	109.5	107.6	109.4
17	16.5	16.6	16.5	16.6	16.6	16.6	16.9	16.9
18	48.3	48.3	48.3	48.3	48.3	48.3	48.9	48.9
19	61.9	61.9	61.8	62.0	61.9	62.0	62.6	62.5
20	14.2	14.1	14.1	14.3	14.2	14.2	14.6	14.5
Ac	170.6	170.6	170.7	170.6	170.6	170.6	170.8	170.8
	169.7	169.7	169.7	169.7	169.7	169.7		
	21.3	21.3	21.3	21.3	21.3	21.3	21.1	21.1
	21.2	21.2	21.2	21.3	21.3	21.3		
EtO			62.8	63.1				
			15.4	15.3				

a) Assignment was confirmed based on ^{1}H–^{1}H, ^{1}H–^{13}C and ^{1}H–^{13}C long-range COSY spectral data.

Table 2. ^{13}C-NMR Spectral Data for **7**—**12** and **13** (100 MHz)[a]

C No.	**7**[b]	**8**[c]	**8a**[b]	**8b**[b]	**8c**[b]	**9**[b]	**10**[b]	**11a**[b]	**11b**[b]	**12a**[b]	**12b**[b]	**13a**[b]	**13b**[b]
1	28.7	29.1	29.2	30.9	[d]	29.1	29.3	29.2	29.1	28.7	28.8	29.2	29.3
2	67.8	66.8	66.9	67.0	68.3	67.0	67.0	67.0	67.0	67.8	67.8	67.0	67.0
3	36.9	36.9	37.3	37.4	43.1	37.4	37.4	37.4	37.4	37.0	36.9	37.4	37.4
4	60.7	61.1	61.4	64.1	62.4	61.2	61.3	61.2	61.2	60.8	60.8	61.5	61.5
5	41.9	43.0	43.5	42.1	55.4	43.2	43.2	43.2	43.2	41.9	41.9	43.6	43.6
6	68.6	69.8	69.4	70.5	72.4	68.6	68.7	68.6	68.7	68.7	68.7	69.5	69.7
7	33.5	33.2	33.6	34.2	34.4	34.0	33.9	34.1	34.0	33.6	33.6	33.7	33.7
8	36.1	35.6	36.0	36.6	35.8	36.0	36.1	35.9	35.9	35.9	35.9	35.8	35.8
9	41.1	41.0	41.2	40.7	40.6	41.3	41.3	41.4	41.4	41.3	41.3	41.4	41.4
10	41.6	41.3	41.6	38.5	46.1	41.7	41.4	41.7	41.7	41.5	41.5	41.6	41.6
11	86.1	85.4	86.2	86.9	84.7	85.0	85.1	84.4	85.0	84.4	85.0	84.5	85.0
12	32.3	32.6	32.4	32.6	31.8	33.3	33.6	33.3	33.9	33.3	33.9	33.4	34.0
13	46.2	45.9	46.2	46.2	46.4	40.4	40.8	40.8	41.4	40.8	41.4	40.8	41.4
14	102.6	101.8	102.6	102.8	102.4	38.4	39.8	39.9	40.7	39.9	40.7	39.9	40.7
15	147.1	147.1	147.0	146.9	147.1	104.4	104.0	99.4	98.7	99.4	98.7	99.3	98.7
16	108.6	108.4	108.6	108.9	108.2	108.2	110.0	108.0	109.8	107.9	109.8	108.0	109.9
17	16.5	16.8	16.7	16.9	16.5	16.9	16.7	16.9	16.9	16.6	16.6	16.9	16.9
18	50.0	49.2	49.5	50.3	50.1	49.6	49.6	49.6	49.6	50.1	50.1	49.5	49.5
19	91.9	93.4	93.0	93.3	204.3	99.0	99.1	99.1	99.0	92.0	92.0	93.0	93.1
20	14.3	13.9	14.2	14.6	15.6	14.2	14.6	14.2	14.3	14.2	14.3	14.2	14.3
Ac	169.8	168.7	169.8	170.0	169.8	169.9	169.9	169.9	169.9	169.8	169.8	169.7	169.7
	169.5									169.5	169.5		
	21.8	20.8	21.5	21.1	21.1	21.5	21.5	21.5	21.5	21.8	21.8	21.5	21.5
	21.3									21.4	21.4		
EtO						63.4	63.3	63.3	63.3				
						63.0	62.9						
						16.0	16.0	16.0	16.0				
						15.4	15.4						

a) Assignments of **7** and **8** were confirmed based on ^{1}H–^{1}H, ^{1}H–^{13}C and ^{1}H–^{13}C long-range COSY spectral data. *b*) Measured in pyridine-d_5. *c*) Measured in benzene-d_6. *d*) May overlap with some other signal.

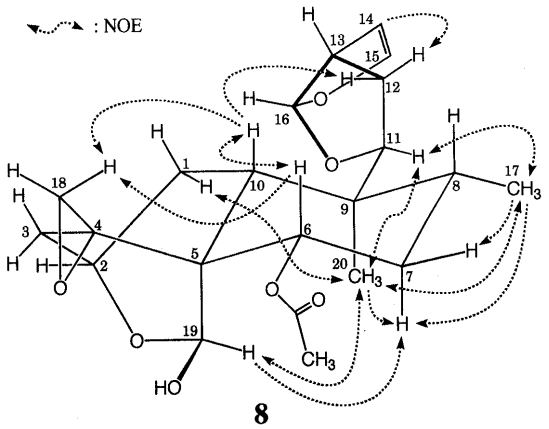


Fig. 1. NOEs Observed in the Difference NOE Spectra of **8**

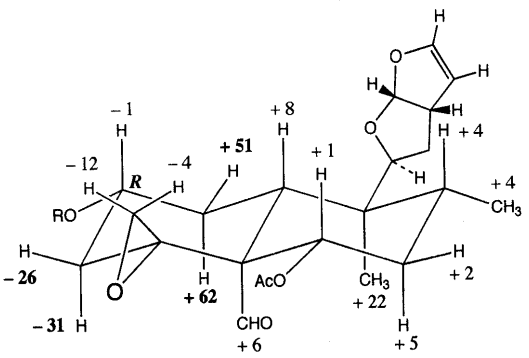


Fig. 2. Chemical Shift Differences between **8***S* and **8***R*

$\Delta\delta$ values ($\Delta\delta = \delta_S - \delta_R$) are shown in Hz (400 MHz, pyridine-d_5). **8***S*, R = *S*-(−)-MTPA; **8***R*, R = *R*-(+)-MTPA; **8**A, R = Ac.

From these data, the structure of **6** was determined to be (6α)-19-*O*-acetyl-4,18 : 11,16 : 15,16-triepoxyneoclerodane-6,15,19-triol (14-hydro-15-hydroxy-6-*O*-deacetylclerodin).

Compound **8** was obtained as a white powder and showed absorption bands of hydroxy (3492 cm^{-1}) and carbonyl (1732, 1704 cm^{-1}) groups in its IR spectrum. Its molecular formula was determined as $C_{22}H_{30}O_7$ from elemental analysis, EIMS and ^{13}C-NMR spectral data. The ^{1}H- and ^{13}C-NMR spectra in benzene-d_6 were very similar to those of **7** (jodrellin A) (Table 2) except for the presence of signals corresponding to only one acetyl group, suggesting that **8** was a monodeacetate of **7**. The molecular formula was also consistent with this assumption. The acetoxy group is linked with C-6, because the H-19 signal of **8** (δ 5.82) was shifted upfield by 1.3 ppm compared with that of **7** (δ 7.15), whereas the H-6 signal remained almost unchanged. Consequently, compound **8** is 19-*O*-deacetyljodrellin A. This was confirmed by partial deacetylation of **7** with 23% AcOH in THF–H_2O which gave **8**. The stereochemistry at the C-19 position was determined as the 19*S** configuration by an NOE experiment, in which NOE was observed between H-19 and H_3-20. In addition, the proposed 11*S** configuration in jodrellin A[5] was confirmed based on the result of the NOE experiment on **8**: NOEs were observed between H-11/H_3-17 and H_3-20, and H-10/H-12 (Fig. 1). This result implies that a tetrahydro-furofuran ring in **8** does not rotate freely but exists in a relatively fixed conformation with respect to a decaline ring.

Compound **8** was subjected to acetylation using acetic anhydride and pyridine in order to convert it into **7**. However, **7** was not produced but **8**A was instead. The ^{1}H-NMR spectrum of **8**A showed a signal assignable to H-2 at 5.06 ppm as a tripletriplet (J = 12.1, 5.1 Hz) together with those due to an aldehyde (δ_H 10.46, s) and two acetyls (δ_H 2.04, 1.96, each s), indicating that **8**A was a 2α-acetoxy-5-formyl derivative in which an A ring existed in the chair form.

The absolute configuration of **8** was determined by the advanced Mosher method[11] which involved treating it with (−)-methoxy(trifluoromethyl)phenylacetyl (MTPA) chloride in pyridine to give a 2-*O*-(*S*)-(−)-MTPA ester (**8***S*). A 2-*O*-(*R*)-(+)-MTPA ester (**8***R*) was prepared in the same manner. The $\Delta\delta$ value (δ_S–δ_R) of each proton is shown in Fig. 2 and these data, especially, the $\Delta\delta$ values of H-1β (+51), H-1α (+62), H-3β (−26) and H-3α (−31 Hz), indicate the absolute configuration at the C-2 position to be *R*. Accordingly, the stereochemistry of the decalin part of **8** is 2*R*, 4*S*, 5*R*, 6*S*, 8*R*, 9*S*, 10*R* and 19*S*.

The NMR spectra of **8** in benzene-d_6 showed signals due to only one component, but in pyridine-d_5, signals due to three components existing in equilibrium (**8a** : **8b** : **8c** = 5 : 3 : 1) were observed. The major component **8a** was deduced to have the 19*S* configuration based on the result of an NOE experiment, in which an NOE was observed between H-19 and H_3-20. Component **8b** was deduced to have the 19*R* configuration based on the chemical shift of its H_3-20 signal (δ 1.65) and **8c** to have a 2-hydroxy-5-formyl moiety based on the aldehyde proton signal observed at δ 10.46. The assignment of most of these proton signals was based on signal magnitude and ^{1}H–^{1}H and ^{1}H–^{13}C COSY spectral data.

Compound **9** was obtained as a white powder and the molecular formula was determined as $C_{26}H_{40}O_8$ from elemental analysis, EIMS and ^{13}C-NMR data. It was also deduced to have the neoclerodane skeleton based on its ^{1}H- and ^{13}C-NMR spectra. Compound **9** has a furofuran ring moiety which was shown to be the same as **3** by ^{1}H- and ^{13}C-NMR spectral data (Tables 1 and 2). The ^{13}C signals assignable to the decaline part of **9** were similar to those of **7**. However, the NMR spectra of **9** showed the presence of one acetoxy and one ethoxy group in the decaline part, while **7** possessed two acetyl groups. In **9**, the C-19 signal was observed downfield (δ 99.0) and the H-19 signal upfield (δ 5.44) compared with **7** ($\delta_{C\text{-}19}$ 91.9, $\delta_{H\text{-}19}$ 7.15), indicating that an ethoxy group was present at the C-19 position. The configuration at the C-19 position was determined as β by an NOE experiment: a significant NOE between H-19 and H_3-20 was observed.

Based on these data, the structure of **9** was concluded to be 6α-*O*-acetyl-15β,19β-di-*O*-ethyl-2,19 : 4,18 : 11,16 : 15,16-tetraepoxyneoclerodane-6,15,19-triol.

Compound **10** was obtained as colorless prisms, mp 188—190 °C, $C_{26}H_{40}O_8$, and was shown to possess an analogous structure to **9** by NMR spectral data. ^{1}H and ^{13}C signals due to decaline and furofuran ring moieties were almost the same as **9** and **4**, respectively (Tables 1 and 2). These data indicated that **10** was a C_{15}-epimer of **9**.

Compounds **11** and **12** were both equilibrium mixtures,

just like **5**, based on their ^{1}H- and ^{13}C-NMR spectra. However, they differed from each other in the functional group attached to the C-19. The structure of their furofuran part was considered to be the same as **5** because the ^{13}C signals assignable to C-11—C-16 corresponded to those of **5**. The ^{1}H and ^{13}C signals due to the decaline moiety of **11** and **12** were almost the same as **9** and **7**, respectively.

Based on these findings, the structures of **11** and **12** were concluded to be 6α-*O*-acetyl-19β-*O*-ethyl- and 6α,19-di-*O*-acetyl-2,19 : 4,18 : 11,16 : 15,16-tetraepoxyneoclerodane-6,15,19-triol, respectively.

As described above, the constituents of the aerial part of *Scutellaria discolor* were examined and eight new neoclerodane diterpenoids (**3**, **4**, **6**, **8**, **9**, **10**, **11** and **12**) were isolated together with five known neoclerodane diterpenoids (**1**, **2**, **5**, **7** and **13**) and four known triterpenoids (**14**—**17**). Among these, compounds **3**, **4**, **9**, **10** and **11**, which have an ethoxy functional group, are considered to be artifacts formed in the course of extraction and/or separation using ethanol, although analogous compounds possessing a C_{15}-ethoxy group were isolated as natural products from *Ajuga iva*[12] and *A. chamaepityes*.[13]

Experimental

General Procedures Unless otherwise stated, the following instruments and conditions were used. Melting points were determined on a Yanagimoto micro melting-point apparatus and are uncorrected. UV spectra were recorded in EtOH on a Shimadzu dual-wavelength/double-beam recording spectrophotometer UV-3000 and peaks are given in λ_{max} nm (log ε). IR spectra were recorded in KBr disks on a Hitachi 270-30 infrared spectrophotometer and the data are given in cm^{-1}. NMR spectra were recorded in pyridine-d_5 on a JEOL GSX-400 spectrometer (^{1}H-NMR at 400 MHz and ^{13}C-NMR at 100 MHz), and the chemical shifts are given in δ (ppm). EI-MS spectra were recorded on a JEOL JMS-DX-300 mass spectrometer and major peaks are indicated as *m/z* (%). Optical rotation was recorded in EtOH on a JASCO DIP-370 digital polarimeter. For TLC, Merck pre-coated Kieselgel 60F_{254} plates were used and spots were detected by spraying with dil. H_2SO_4 followed by heating. Analytical HPLC was performed on a YMC-PACKed column R-ODS-5 S-5 120 Å (4.6 mm i.d. × 250 mm): flow rate, 0.8 ml/min; detection, UV 210 nm; column temperature, 35 °C. Preparative HPLC was performed on a YMC-PACKed column D-ODS-5 S-5 120 Å (20 mm i.d. × 250 mm): flow rate, 8 ml/min; column temperature, ambient; detection, UV 210 nm.

Isolation Dried aerial parts of *Scutellaria discolor* (4.3 kg) were extracted three times with EtOH at room temperature. The EtOH extract was concentrated under reduced pressure and the residue was treated with EtOH (2.5 l). After filtration, the solvent was evaporated to yield a residue (166 g), which was suspended in water and extracted with ether. The ether–water insoluble part (6 g) was chromatographed on silica gel eluting with benzene–AcOEt (2 : 1→1 : 1) to give chrysin (1.1 g),[2] **1** (0.2 g) and **7** (1.3 g). The ether layer was concentrated to dryness and the residue (117 g) was treated with hexane. The hexane-soluble part (54 g) was chromatographed on silica gel eluting with benzene–AcOEt (1 : 0→0 : 1) to give four fractions, fr. 1—4, in the order of elution. Fraction **1** was rechromatographed on silica gel eluting with hexane–benzene (10 : 1) to give **14** (80 mg). Fraction 2 was rechromatographed on silica gel eluting with hexane–acetone (4 : 1) to give **15** (90 mg) and a mixture of **16** and **17** (320 mg). Fraction 3 was rechromatographed on silica gel eluting with benzene–AcOEt (2 : 1→1 : 1) to give a mixture of **3** and **4** (4 g), a part of which was separated by preparative HPLC (solv., 50% EtOH) to give **3** and **4**. Fraction 4 was recrystallized from acetone to give **5a** (2 g).

The hexane-insoluble part of the ether extract was treated with benzene. The benzene-soluble part (40 g) was chromatographed on silica gel eluting with benzene–AcOEt (1 : 0→0 : 1) to give five fractions, fr. 5—9. An EtOH solution of fr. 5 was poured into 50% EtOH to give a precipitate, which was recrystallized from EtOH–ether to give **1** (1.5 g). The resulting filtrate was chromatographed on an ODS column (solv., 50% EtOH) and then rechromatographed on silica gel (solv., benzene : AcOEt = 3 : 1→1 : 2) to give **1** (1.2 g), **5** (0.85 g) and a mixture of **3** and **4** (2.8 g). Fraction 6 was chromatographed on silica gel (solv., benzene : AcOEt = 9 : 1→1 : 2) and then rechromatographed on silica gel (solv., benzene : acetone = 6 : 1→1 : 1) to give **7** (200 mg), **2** (170 mg), **8** (270 mg) and **5** (2.4 g). Fractions 7, 8 and 9 were separately chromatographed on silica gel (solv., hexane : acetone = 3 : 1→0 : 1). A mixture of **9** and **10** (250 mg) was obtained from fr. 7 together with **5** (1.9 g) and a mixture of **3** and **4** (600 mg). The mixture of **9** and **10** was subjected to preparative HPLC (solv., 50% EtOH) to give **9** and **10** separately. Compounds **11** (160 mg), **6** (200 mg) and **12** (180 mg) were obtained from fr. 8 and **13** (2 g) from fr. 9.

Identification of Compounds 1, 2, 13, 14 and 15 Compounds **1** [colorless needles from ether–EtOH, mp 162—164 °C, $[\alpha]_D^{28}$ −42.8° (c = 0.360)], **2** [colorless prisms from ether, mp 170—172 °C, $[\alpha]_D^{32}$ −12.8° (c = 0.407)], **13** [colorless prisms from acetone–benzene, mp 133—138 °C, $[\alpha]_D^{26}$ −10.8° (c = 0.512)], **14** and **15** were identified as clerodin,[3] dihydroclerodin-I,[4] scutaltisin,[6] squalene[7] and 24-methylenecycloartanol,[8] respectively, by comparison of their spectral and physical data with those in the literature.

Identification of Compounds 16 and 17 Compounds **16** and **17** were discriminated by analytical HPLC (solv., 90% MeOH) [**16** (3-epioleanolic acid), t_R 11.6 min; **17** (3-epiursolic acid), t_R 11.9 min]. The ^{1}H- and ^{13}C-NMR spectra of a mixture of **16** and **17** were consistent with a mixture of 3-epioleanolic acid and 3-epiursolic acid.

^{1}H-NMR signals due to **16** ($CDCl_3$): 5.27 (1H, br t, J = 3.3 Hz, H-12), 3.40 (1H, br s, H-3), 2.81 (1H, dd, J = 13.9, 4.7 Hz, H-18), 1.13 (3H, s), 0.94 (3H, s), 0.92 (6H, s), 0.89 (3H, s), 0.82 (3H, s), 0.74 (3H, s) (*tert*-CH_3 × 7). ^{13}C-NMR signals due to **16** ($CDCl_3$): 184.0 (C-28), 143.6 (C-13), 122.7 (C-12), 76.2 (C-3), 48.9 (C-5), 47.4 (C-9), 46.5 (C-17), 45.9 (C-19), 41.6 (C-14), 40.9 (C-18), 39.4 (C-8), 37.3 (C-4), 37.2 (C-10), 33.8 (C-21), 33.1 (C-29), 32.5 (C-1 and C-22), 32.8 (C-7), 30.7 (C-20), 28.3 (C-23), 27.6 (C-15), 25.2 (C-2), 23.6 (C-30), 23.3 (C-16), 22.9 (C-11), 22.2 (C-24), 26.1 (C-27), 18.2 (C-6), 17.2 (C-26), 15.1 (C-25). ^{1}H-NMR signals due to **17** ($CDCl_3$): 5.24 (1H, br t, J = 3.3 Hz, H-12), 3.40 (1H, br s, H-3), 2.17 (1H, d, J = 10.6 Hz, H-18), 1.09 (3H, s), 0.94 (3H, s), 0.93 (3H, s), *ca.* 0.93 (overlapped, H_3-30), 0.85 (3H, d, J = 6.6 Hz, H_3-29), 0.82 (3H, s), 0.77 (3H, s) (*tert*-CH_3 × 5). ^{13}C-NMR signals due to **17** ($CDCl_3$): 183.7 (C-28), 137.9 (C-13), 125.9 (C-12), 76.2 (C-3), 52.5 (C-18), 49.0 (C-5), 47.9 (C-17), 47.3 (C-9), 42.0 (C-14), 39.6 (C-8), 39.0 (C-19), 38.8 (C-20), 36.7 (C-22), 37.3 (C-4), 37.1 (C-10), 33.0 (C-1), 32.8 (C-7), 30.6 (C-21), 28.3 (C-23), 27.9 (C-15), 25.2 (C-2), 24.1 (C-16), 23.8 (C-27), 23.2 (C-11), 22.3 (C-24), 21.2 (C-30), 18.2 (C-6), 17.1 (C-29), 17.0 (C-26), 15.3 (C-25).

Compound 3 (15β-Ethoxy-14-hydroclerodin) White powder (from EtOH–hexane), $[\alpha]_D^{27}$ −56.9° (c = 0.371). *Anal.* Calcd for $C_{26}H_{40}O_8$: C, 64.96; H, 8.39. Found: C, 64.80; H, 8.39. UV: 208 (2.25). IR: 2984, 2940, 2880, 1730, 1450, 1374, 1252, 1188, 1112. ^{1}H-NMR: 5.84 (1H, d, J = 5.5 Hz, H-16), 5.32 (1H, br d, J = 4.0 Hz, H-15), 4.92 (1H, dd, J = 11.7, 4.8 Hz, H-6), 5.17, 4.45 (each 1H, d, J = 12.1 Hz, H_2-19), 4.09 (1H, dd, J = 11.7, 4.4 Hz, H-11), 3.76, 3.40 (each 1H, dq, J = 9.5, 7.0 Hz, OC$\underline{H}_2$CH$_3$), 3.14 (1H, dd, J = 4.0, 2.2 Hz, H-18), 2.99 (1H, m, H-13), 2.21 (1H, d, J = 4.0 Hz, H′-18), 2.15, 2.03 (each 3H, s, Ac × 2), 1.12 (3H, t, J = 7.0 Hz, OCH$_2$C$\underline{H}_3$), 0.94 (3H, s, H_3-20), 0.72 (3H, d, J = 6.2 Hz, H_3-17). ^{13}C-NMR: See Table 1. EIMS: 480 (M^+, 0.2), 435 (2), 349 (3), 323 (3), 286 (5), 264 (6), 221 (8), 204 (28), 175 (20), 157 (40), 111 (100).

Compound 4 (15α-Ethoxy-14-hydroclerodin) Colorless prisms (from ether), mp 152-154 °C, $[\alpha]_D^{28}$ +40.6° (c = 0.286). *Anal.* Calcd for $C_{26}H_{40}O_8$: C, 64.96; H, 8.39. Found: C, 64.96; H, 8.36. UV: 209 (2.13). IR: 2988, 2948, 1738, 1390, 1374, 1258, 1232, 1102, 1032, 1000. ^{1}H-NMR: 5.90 (1H, d, J = 5.5 Hz, H-16), 5.08 (1H, d, J = 5.5 Hz, H-15), 5.19, 4.49 (each 1H, d, J = 12.1 Hz, H_2-19), 4.95 (1H, overlapped with H_2O, H-6), 4.55 (1H, dd, J = 11.4, 5.5 Hz, H-11), 3.80, 3.39 (each 1H, dq, J = 9.5, 7.0 Hz, OC$\underline{H}_2$CH$_3$), 3.15 (1H, dd, J = 4.0, 2.2 Hz, H-18), 2.73 (1H, m, H-13), 2.21 (1H, d, J = 4.0 Hz, H′-18), 2.16, 2.05 (each 3H, s, Ac × 2), 1.16 (3H, t, J = 7.0 Hz, OCH$_2$C$\underline{H}_3$), 0.99 (3H, s, H_3-20), 0.84 (3H, d, J = 6.6 Hz, H_3-17). ^{13}C-NMR: See Table 1. EIMS: 480 (M^+, 0.2), 435 (2), 349 (2), 323 (2), 286 (3), 264 (3), 221 (4), 204 (16), 157 (40), 111 (100).

Conversion of 1 to a Mixture of 3 and 4 A solution of **1** (10 mg) in 50% AcOH–EtOH (3 ml) was allowed to stand at room temperature for 1 d. The reaction mixture was diluted with $CHCl_3$ and then washed successively with 1 N NaOH and brine. The organic layer was dried over

anhyd. Na_2SO_4 and concentrated. The residue was chromatographed on silica gel (solv., benzene : acetone = 4 : 1) to give a product (10 mg) whose ^{1}H- and ^{13}C-NMR spectra were consistent with a mixture of **3** and **4** (ratios of **3** : **4** = 6 : 5 as determined by ^{1}H-NMR signal magnitude).

Compound 5 (14-Hydro-15-hydroxyclerodin) Compound **5a**: colorless prisms (from acetone), mp 188—191 °C. IR: 3432, 2948, 2880, 1734, 1714, 1374, 1236, 1112. EIMS: 434 [$(M-H_2O)^+$, 8], 349 (8), 323 (12), 286 (15), 264 (18), 221 (24), 204 (100), 175 (57), 173 (56), 111 (89). ^{13}C-NMR: see Table 1. ^{1}H-NMR: 8.19 (1H, d, J = 4.0 Hz, 15-OH), 6.12 (1H, d, J = 5.5 Hz, H-16), 6.04 (1H, m, H-15), 5.18, 4.47 (each 1H, d, J = 12.1 Hz, H_2-19), 4.95 (1H, dd, J = 11.7, 4.4 Hz, H-6), 4.16 (1H, dd, J = 11.7, 4.4 Hz, H-11), 3.16 (1H, m, H-13), 3.15 (1H, dd, J = 4.4, 2.2 Hz, H-18), 2.21 (1H, d, J = 4.4 Hz, H′-18), 2.15, 2.04 (each 3H, s, Ac × 2), 0.97 (3H, s, H_3-20), 0.74 (3H, d, J = 6.2 Hz, H_3-17). ^{1}H-NMR signals due to **5b** in a equilibrium solution: 8.23 (1H, br d, J = 1.5 Hz, 15-OH), 5.98 (1H, d, J = 5.5 Hz, H-16), 5.80 (1H, dd, J = 4.8, 2.6 Hz, H-15), 5.18, 4.48 (each 1H, d, J = 12.1 Hz, H_2-19), 4.95 (1H, dd, J = 11.7, 4.4 Hz, H-6), 4.93 (1H, overlapped with H-6 and H_2O, H-11), 2.80 (1H, m, H-13), 2.21 (1H, d, J = 4.4 Hz, H-18), 2.15, 2.03 (each 3H, s, Ac × 2), 0.95 (3H, s, H_3-20), 0.82 (3H, d, J = 6.6 Hz, H_3-17).

Conversion of 1 to 5 To a solution of **1** (10 mg) in THF (1 ml) and water (1 ml) was added AcOH (2 ml). The reaction mixture was stirred at room temperature for 24 h and then diluted with $CHCl_3$. The organic layer was washed successively with 1 N NaOH and brine, dried over anhyd. Na_2SO_4 and concentrated to give a residue. This was chromatographed on silica gel (solv., benzene : acetone = 2 : 1) to give a product (12 mg) which was identified as **5** by NMR (ratios of **5a** : **5b** = 6 : 5 as determined by ^{1}H-NMR signal magnitude).

Compound 6 (14-Hydro-15-hydroxy-6-*O*-deacetylclerodin) White powder (from CH_2Cl_2–hexane), $[\alpha]_D^{26}$ +16.3° (c = 0.233). *Anal.* Calcd for $C_{22}H_{34}O_7$: C, 64.35; H, 8.35. Found: C, 64.67; H, 8.39. UV: 210 (2.20). IR: 3488, 2952, 1738, 1372, 1236, 1104, 1014. EIMS: 392 [$(M-H_2O)^+$, 6], 374 [$(M-2H_2O)^+$, 23], 301 (42), 281 (13), 263 (25), 204 (50), 203 (79), 175 (72), 111 (94), 55 (100). ^{13}C-NMR: see Table 1. ^{1}H-NMR signals due to **6a**: 8.19 (1H, br s, 15-OH), 6.10 (1H, d, J = 5.5 Hz, H-16), 6.03 (1H, m, H-15), 5.03, 4.64 (each 1H, d, J = 12.1 Hz, H_2-19), 4.15 (1H, dd, J = 11.7, 4.4 Hz, H-11), 3.84 (1H, br s, 6-OH), 3.69 (1H, dd, J = 10.6, 5.1 Hz, H-6), 3.31 (1H, d, J = 3.7 Hz, H-18), 3.14 (1H, m, H-13), 2.43 (1H, d, J = 3.7 Hz, H′-18), 2.06 (3H, s, Ac), 0.95 (3H, s, H_3-20), 0.77 (3H, d, J = 7.0 Hz, H_3-17). ^{1}H-NMR signals due to **6b**: 8.23 (1H, br s, 15-OH), 5.96 (1H, d, J = 5.1 Hz, H-16), 5.80 (1H, d, J = 5.1 Hz, H-15), 5.03, 4.66 (each 1H, d, J = 12.1 Hz, H_2-19), 4.94 (1H, overlapped with H_2O, H-11), 3.81 (1H, br s, 6-OH), 3.69 (1H, dd, J = 10.6, 5.1 Hz, H-6), 3.31 (1H, d, J = 3.7 Hz, H-18), 2.78 (1H, m, H-13), 2.43 (1H, d, J = 3.7 Hz, H′-18), 2.06 (3H, s, Ac), 0.94 (3H, s, H_3-20), 0.85 (3H, d, J = 6.6 Hz, H_3-17).

Compound 8 (19-*O*-Deacetyljodrellin A) White powder (from EtOH–hexane), $[\alpha]_D^{28}$ −53.0° (c = 0.491). *Anal.* Calcd for $C_{22}H_{30}O_7$: C, 64.99; H, 7.44. Found: C, 64.88; H, 7.26. UV: 215 (3.28). IR: 3492, 2964, 1732, 1704, 1618, 1376, 1270, 1140. ^{1}H-NMR (benzene-d_6): 6.26 (1H, t, J = 2.6 Hz, H-15), 5.87 (1H, d, J = 6.2 Hz, H-16), 5.82 (1H, s, H-19), 4.72 (1H, dd, J = 12.1, 4.8 Hz, H-6), 4.44 (1H, t, J = 2.6 Hz, H-14), 3.93 (1H, m, H-2), 3.85 (1H, dd, J = 11.7, 4.4 Hz, H-11), 3.70 (1H, br d, J = 1.1 Hz, 19-OH), 3.01 (1H, m, H-13), 2.79 (1H, dt, J = 13.9, 2.6 Hz, H-3α), 2.70, 1.90 (each 1H, d, J = 4.4 Hz, H_2-18), 2.12 (1H, dtd, J = 14.2, 4.6, 2.8 Hz, H-1α), 1.71 (1H, dd, J = 11.4, 4.8 Hz, H-10), 1.67 (3H, s, Ac), 1.34 (1H, td, J = 12.0, 8.5 Hz, H-12β), 1.33 (1H, m, H-7α), 1.27 (1H, dd, J = 13.9, 2.6 Hz, H-3β), 1.26 (2H, m, H-7β, H-8), 1.16 (1H, dd, J = 12.0, 4.4 Hz, H-12α), 1.15 (1H, dd, J = 14.2, 11.4 Hz, H-1β), 0.96 (3H, s, H_3-20), 0.58 (3H, d, J = 5.9 Hz, H_3-17). ^{13}C-NMR: See Table 2. EIMS: 405 [$(M-1)^+$, 2], 347 (8), 300 (12), 274 (10), 235 (12), 219 (28), 190 (48), 173 (44), 159 (41), 145 (33), 133 (26), 119 (37), 111 (100).

^{1}H-NMR signals due to **8a**: 6.68 (1H, t, J = 2.7 Hz, H-15), 6.49 (1H, d, J = 2.9 Hz, 19-OH), 6.20 (1H, d, J = 6.2 Hz, H-16), 6.09 (1H, d, J = 2.9 Hz, H-19), 5.00 (1H, dd, J = 12.1, 4.4 Hz, H-6), 4.87 (overlapped, H-14), 4.19 (overlapped, H-2), 4.09 (1H, dd, J = 11.7, 4.8 Hz, H-11), 3.52 (1H, m, H-13), 3.11, 2.36 (each 1H, d, J = 4.4 Hz, H_2-18), 2.93 (1H, dt, J = 13.9, 2.0 Hz, H-3α), 2.37 (1H, m, H-1α), 2.11 (1H, dd, J = 11.4, 4.4 Hz, H-10), 2.08 (3H, s, Ac), 1.85 (1H, td, J = 11.7, 8.4 Hz, H-12β), 1.74 (1H, dd, J = 13.9, 2.9 Hz, H-3β), 1.73 (1H, br q, J = 12.5 Hz, H-7α), 1.64 (1H, dd, J = 11.7, 4.8 Hz, H-12α), 1.58 (1H, dd, J = 13.9, 11.4 Hz, H-1β), 1.55 (1H, m, H-8), 1.47 (1H, ddd, J = 12.8, 4.4, 3.3 Hz, H-7β), 1.17 (3H, s, H_3-20), 0.78 (3H, d, J = 6.6 Hz, H_3-17). ^{1}H-NMR signals due to **8b**: 8.84 (1H, d, J = 4.4 Hz, 19-OH), 6.67 (1H, t, J = 2.7 Hz, H-15), 6.22 (1H, d, J = 6.2 Hz, H-16), 6.15 (1H, d, J = 4.4 Hz, H-19), 5.09 (1H, dd, J = 11.7, 5.1 Hz, H-6), 4.87 (overlapped, H-14), 4.20 (overlapped, H-2), 4.18 (overlapped, H-11), 3.47 (overlapped, H-13), 3.46, 2.53 (each 1H, d, J = 4.0 Hz, H_2-18), 2.59 (1H, br q, J = 12.1 Hz, H-7α), 2.56 (overlapped, H-1α), 2.24 (1H, t, J = 10.0 Hz, H-10), 2.06 (overlapped, H_2-3), 1.95 (3H, s, Ac), 1.94 (overlapped, H-12β), 1.93 (overlapped, H-1β), 1.65 (overlapped, H-12α), 1.65 (3H, s, H_3-20), 1.51 (overlapped, H-8), 1.38 (1H, ddd, J = 12.3, 5.1, 2.6 Hz, H-7β), 0.87 (3H, d, J = 6.6 Hz, H_3-17). ^{1}H-NMR signals due to **8c**: 10.46 (1H, s, H-19), 6.61 (1H, br t, J = 2.4 Hz, H-15), 5.98 (1H, d, J = 6.2 Hz, H-16), 5.12 (overlapped, H-6), 4.82 (1H, br t, J = 2.4 Hz, H-14), 4.20 (overlapped, H-2), 4.16 (overlapped, H-11), 3.18 (1H, dd, J = 4.4, 2.0 Hz, H-18), 2.44 (1H, d, J = 4.4 Hz, H′-18), 2.04 (3H, s, Ac), 1.08 (3H, s, H_3-20), 0.75 (3H, d, J = 6.6 Hz, H_3-17).

Partial Deacetylation of 7 Twenty-six mg of **7**, in a mixture of THF (1.6 ml), water (0.4 ml) and AcOH (0.6 ml), was allowed to stand at room temperature overnight. The reaction mixture was diluted with $CHCl_3$ and then washed successively with 1 N NaOH and brine. The organic layer was dried over anhyd. Na_2SO_4. After removal of the solvent, a residue was obtained which was chromatographed on silica gel (solv., benzene : AcOEt = 2 : 1) to give **8** (17 mg).

Acetylation of 8 Compound **8** (10 mg) was acetylated with acetic anhydride and pyridine in the usual way to give **8**A as a white powder (10 mg). IR: 2976, 1740, 1734, 1618, 1376, 1238, 1088. ^{1}H-NMR: 10.46 (1H, s, H-19), 6.63 (1H, t, J = 2.6 Hz, H-15), 6.18 (1H, d, J = 6.2 Hz, H-16), 5.12 (1H, dd, J = 12.1, 5.1 Hz, H-6), 5.06 (1H, tt, J = 12.1, 5.1 Hz, H-2), 4.82 (1H, t, J = 2.6 Hz, H-14), 4.22 (1H, dd, J = 11.7, 4.8 Hz, H-11), 3.54 (1H, m, H-13), 3.19 (1H, dd, J = 4.4, 2.2 Hz, H-18), 3.05 (1H, dt, J = 2.6, 12.1 Hz, H-3α), 2.96 (1H, m, H-1β), 2.43 (1H, d, J = 4.4 Hz, H′-18), 2.04, 1.96 (each 3H, s, Ac × 2), 1.83 (1H, br q, J = 12.8 Hz, H-7α), 1.54 (1H, m, H-8), 1.07 (3H, s, H_3-20), 0.76 (3H, d, J = 6.6 Hz, H_3-17). ^{13}C-NMR: 204.2 (C-19), 147.1 (C-15), 108.3 (C-16), 102.5 (C-14), 85.0 (C-11), 72.1 (C-6), 71.1 (C-2), 61.9 (C-4), 55.1 (C-5), 50.2 (C-18), 46.5 (C-13), 45.6 (C-10), 40.7 (C-9), 38.7 (C-3), 36.0 (C-8), 34.2 (C-7), 31.6 (C-12), 28.9 (C-1), 16.2 (C-17), 15.6 (C-20), 170.3, 169.7, 21.1 (× 2) (Ac × 2). EIMS: 448 (M^+, 84), 419 (4), 388 (4), 359 (4), 321 (45), 299 (20), 218 (57), 172 (100), 111 (58).

S*-(−)- and *R*-(+)-MTPA Esterification of 8** To a solution of **8** (7.8 mg) in pyridine (1 ml) was added (−)-MTPA chloride (5 μl) and the mixture was allowed to stand at room temperature for 1 h. The reaction mixture was diluted with $CHCl_3$ and then washed successively with 1 N HCl, 1 N NaOH and brine. The $CHCl_3$ layer was dried over anhyd. Na_2SO_4. After concentration, the residue was chromatographed on silica gel (solv., hexane : acetone = 3 : 1) to give **8S* (8.7 mg) as a white powder. In the same manner as for **8***S*, **8***R* (10 mg) was obtained from **8** (7.3 mg) as a white powder.

Compound **8***S*: IR: 2936, 1746, 1620, 1456, 1378. ^{1}H-NMR: 10.42 (1H, s, H-19), 7.77—7.72 (2H, m, phenyl part), 7.42—7.36 (3H, m, phenyl part), 6.65 (1H, t, J = 2.6 Hz, H-15), 6.21 (1H, d, J = 6.2 Hz, H-16), 5.43 (1H, m, H-2), 5.14 (1H, dd, J = 12.1, 4.8 Hz, H-6), 4.83 (1H, t, J = 2.6 Hz, H-14), 4.24 (1H, dd, J = 11.7, 4.4 Hz, H-11), 3.59 (3H, s, OCH_3), 3.58 (1H, m, H-13), 3.21 (1H, dd, J = 4.0, 2.2 Hz, H-18), 3.12 (1H, dt, J = 1.7, 11.9 Hz, H-3α), 3.11 (1H, dd, J = 12.1, 1.7 Hz, H-1β), 2.49 (1H, d, J = 4.0 Hz, H′-18), 2.11 (1H, br s, H-10), 2.11 (1H, m, H-1α), 2.03 (3H, s, Ac), 2.00 (1H, dt, J = 8.4, 12.1 Hz, H-12β), 1.83 (1H, br q, J = 13.2 Hz, H-7α), 1.75 (1H, dd, J = 12.1, 5.1 Hz, H-12α), 1.74 (1H, m, H-3β), 1.65 (1H, ddd, J = 13.6, 4.8, 3.3 Hz, H-7β), 1.56 (1H, m, H-8), 1.04 (3H, s, H_3-20), 0.77 (3H, d, J = 6.6 Hz, H_3-17). ^{13}C-NMR: 204.0 (C-19), 147.1 (C-15), 108.3 (C-16), 102.6 (C-14), 85.1 (C-11), 73.9 (C-2), 72.1 (C-6), 61.8 (C-4), 54.9 (C-5), 50.3 (C-18), 46.6 (C-13), 45.6 (C-10), 40.8 (C-9), 38.3 (C-3), 35.9 (C-8), 34.2 (C-7), 31.6 (C-12), 28.7 (C-1), 16.1 (C-17), 15.7 (C-20), 169.8, 21.1 (Ac), 166.4, 132.8, 127.8, 128.9, 130.2, 55.5 (MTPA part). EIMS: 623 [$(M+1)^+$, 23], 622 (M^+, 76), 562 (4), 495 (22), 189 (100), 172 (29), 111 (27).

Compound **8***R*: IR: 2956, 1754, 1620, 1455, 1370, 1242, 1170, 1014. ^{1}H-NMR: 10.41 (1H, s, H-19), 7.75 (2H, m, phenyl part), 7.44—7.35 (3H, m, phenyl part), 6.66 (1H, t, J = 2.6 Hz, H-15), 6.23 (1H, d, J = 6.2 Hz, H-16), 5.43 (1H, m, H-2), 5.14 (1H, dd, J = 12.1, 5.1 Hz, H-6), 4.85 (1H, t, J = 2.6 Hz, H-14), 4.21 (1H, dd, J = 12.1, 4.4 Hz, H-11), 3.60 (1H, m, H-13), 3.57 (3H, s, OCH_3), 3.22 (1H, dd, J = 3.7, 2.2 Hz, H-18), 3.20 (1H, dt, J = 2.2, 11.7 Hz, H-3α), 2.98 (1H, dt, J = 12.5, 2.2 Hz, H-1β), 2.52 (1H, d, J = 3.7 Hz, H′-18), 2.09 (1H, br d, J = 12.8 Hz, H-10), 2.04 (3H, s, Ac), 1.98 (1H, dt, J = 4.0, 12.1 Hz, H-1α), 1.95 (1H, dt, J = 8.4, 12.5 Hz, H-12β), 1.82 (1H, br q, J = 13.2 Hz, H-7α), 1.81 (1H, ddd, J = 11.7, 8.4, 2.2 Hz, H-3β), 1.74 (1H, dd, J = 12.5, 4.4 Hz, H-12α), 1.64

(1H, ddd, J=13.6, 5.1, 3.3 Hz, H-7β), 1.55 (1H, m, H-8), 0.98 (3H, s, H_3-20), 0.76 (3H, d, J=6.6 Hz, H_3-17). ^{13}C-NMR: 204.0 (C-19), 147.2 (C-15), 108.3 (C-16), 102.6 (C-14), 85.0 (C-11), 73.7 (C-2), 72.1 (C-6), 61.8 (C-4), 54.8 (C-5), 50.3 (C-18), 46.6 (C-13), 45.5 (C-10), 40.8 (C-9), 38.5 (C-3), 35.9 (C-8), 34.2 (C-7), 31.6 (C-12), 28.4 (C-1), 16.1 (C-17), 15.6 (C-20), 169.8, 21.1 (Ac), 166.3, 132.8, 127.8, 128.9, 130.2, 55.6 (MTPA part). EIMS: 622 (M^+, 34), 562 (4), 495 (10), 189 (100), 172 (26), 111 (42).

Compound 9 (6α-*O*-Acetyl-15β,19β-di-*O*-ethyl-2,19 : 4,18 : 11,16 : 15,16-tetraepoxyneoclerodane-6,15,19-triol) White powder (from CH_2Cl_2), $[\alpha]_D^{26}$ −38.7° (c=0.158). *Anal.* Calcd for $C_{26}H_{40}O_8$: C, 64.96; H, 8.39. Found: C, 65.11; H 8.50. UV: 211 (2.02). IR: 2976, 1732, 1372, 1252, 1102. ^{1}H-NMR: 5.94 (1H, d, J=5.5 Hz, H-16), 5.44 (1H, s, H-19), 5.37 (1H, br d, J=4.0 Hz, H-15), 4.91 (1H, dd, J=12.1, 4.8 Hz, H-6), 4.10 (1H, m, H-2), 4.09 (1H, dd, J=11.4, 4.8 Hz, H-11), 4.03, 3.67 (each 1H, dq, J=9.5, 7.0 Hz, 19-OC$\underline{H}_2$CH$_3$), 3.81, 3.44 (each 1H, dq, J=9.5, 7.0 Hz, 15-OCH_2CH$_3$), 3.07, 2.29 (each 1H, d, J=4.8 Hz, H_2-18), 3.00 (1H, m, H-13), 2.73 (1H, br d, J=13.9 Hz, H-3α), 2.41 (1H, m, H-1α), 2.22 (1H, ddd, J=13.4, 9.5, 1.5 Hz, H-14β), 2.12 (3H, s, Ac), 2.07 (1H, dd, J=11.4, 4.4 Hz, H-10), 1.82 (1H, ddd, J=12.5, 11.4, 8.4 Hz, H-12β), 1.79 (1H, m, H-14α), 1.71 (1H, q, J=12.5 Hz, H-7α), 1.65 (1H, dd, J=13.9, 2.6 Hz, H-3β), 1.58 (1H, dd, J=13.9, 11.4 Hz, H-1β), 1.56 (1H, m, H-8), 1.48 (1H, dd, J=12.5, 4.8 Hz, H-12α), 1.44 (1H, ddd, J=12.5, 4.4, 3.3 Hz, H-7β), 1.28 (3H, t, J=7.0 Hz, 19-OCH$_2$C$\underline{H}_3$), 1.18 (3H, s, H_3-20), 1.14 (3H, t, J=7.0 Hz, 15-OCH$_2$C$\underline{H}_3$), 0.84 (3H, d, J=6.6 Hz, H_3-17). ^{13}C-NMR: See Table 2. EIMS: 480 (M^+, 0.2), 435 (12), 374 (5), 300 (5), 218 (10), 190 (35), 172 (17), 161 (21), 157 (40), 111 (100).

Compound 10 (6α-*O*-Acetyl-15α,19β-di-*O*-ethyl-2,19 : 4,18 : 11,16 : 15,16-tetraepoxyneoclerodane-6,15,19-triol) Colorless prisms (from EtOH–ether), mp 188—190 °C, $[\alpha]_D^{25}$ + 55.5° (c=0.198). *Anal.* Calcd for $C_{26}H_{40}O_8$: C, 64.96; H, 8.39. Found: C, 65.13; H 8.51. UV: 206 (1.96). IR: 2932, 1726, 1368, 1260, 1098, 1068, 1022. ^{1}H-NMR: 5.96 (1H, d, J=5.5 Hz, H-16), 5.47 (1H, s, H-19), 5.10 (1H, d, J=5.5 Hz, H-15), 4.92 (1H, overlapped with H_2O, H-6), 4.54 (1H, dd, J=10.6, 5.9 Hz, H-11), 4.13 (1H, m, H-2), 4.03, 3.67 (each 1H, dq, J=9.5, 7.0 Hz, 19-OC$\underline{H}_2$CH$_3$), 3.83, 3.40 (each 1H, dq, J=9.5, 7.0 Hz, 15-OC$\underline{H}_2$CH$_3$), 3.08, 2.28 (each 1H, d, J=4.8 Hz, H_2-18), 2.74 (1H, m, H-3α), 2.12 (3H, s, Ac), 2.10 (1H, dd, J=11.4, 4.4 Hz, H-10), 1.75 (1H, q, J=12.5 Hz, H-7α), 1.67 (1H, dd, J=13.9, 3.9 Hz, H-3β), 1.61 (1H, dd, J=14.7, 11.4 Hz, H-1β), 1.55 (1H, m, H-8), 1.44 (1H, ddd, J=12.5, 4.4, 3.3 Hz, H-7β), 1.28 (3H, t, J=7.0 Hz, 19-OCH$_2$C$\underline{H}_3$), 1.26 (3H, s, H_3-20), 1.18 (3H, t, J=7.0 Hz, 15-OCH$_2$C$\underline{H}_3$), 0.91 (3H, d, J=6.6 Hz, H_3-17). ^{13}C-NMR: See Table 2. EIMS: 479 [$(M-1)^+$, 0.7], 450 (1.2), 434 (10), 374 (4), 218 (8), 190 (24), 172 (16), 157 (47), 111 (100).

Compound 11 (6α-*O*-Acetyl-19β-*O*-ethyl-2,19 : 4,18 : 11,16 : 15,16-tetraepoxyneoclerodane-6,15,19-triol) White powder (from CH_2Cl_2–hexane), $[\alpha]_D^{25}$ +2.6° (c=0.118). *Anal.* Calcd for $C_{24}H_{36}O_8$: C, 63.68; H, 8.02. Found: C, 63.99; H, 8.21. UV: 206 (2.19). IR: 3420, 2956, 1732, 1374, 1252, 1098, 1022. EIMS: 434 [$(M-H_2O)^+$, 3], 406 (6), 389 (10), 300 (11), 218 (18), 190 (100), 189 (44), 172 (34), 161 (46), 111 (83). ^{13}C-NMR: See Table 2. ^{1}H-NMR signals due to **11a**: 6.15 (1H, d, J=5.5 Hz, H-16), 6.06 (1H, dd, J=4.8, 2.2 Hz, H-15), 5.43 (1H, s, H-19), 4.92 (1H, dd, J=11.8, 4.4 Hz, H-6), 4.14 (1H, dd, J=11.4, 4.8 Hz, H-11), 4.08 (1H, m, H-2), 4.02, 3.67 (each 1H, dq, J=9.5, 7.0 Hz, OC$\underline{H}_2$CH$_3$), 3.14 (1H, m, H-13), 3.06, 2.23 (each 1H, d, J=4.8 Hz, H_2-18), 2.11 (3H, s, Ac), 1.27 (3H, t, J=7.0 Hz, OCH$_2$C$\underline{H}_3$), 1.19 (3H, s, H_3-20), 0.85 (3H, d, J=6.6 Hz, H_3-17). ^{1}H-NMR signals due to **11b**: 6.02 (1H, d, J=5.5 Hz, H-16), 5.82 (1H, d, J=5.5 Hz, H-15), 5.43 (1H, s, H-19), 4.92 (1H, dd, J=11.8, 4.4 Hz, H-6), 4.88 (1H, dd, J=11.0, 6.2 Hz, H-11), 4.08 (1H, m, H-2), 4.03, 3.66 (each 1H, dq, J=9.5, 7.0 Hz, OC$\underline{H}_2$CH$_3$), 3.06, 2.28 (each 1H, d, J=4.8 Hz, H_2-18), 2.80 (1H, m, H-13), 2.11 (3H, s, Ac), 1.27 (3H, t, J=7.0 Hz, OCH$_2$C$\underline{H}_3$), 1.17 (3H, s, H_3-20), 0.88 (3H, d, J=6.2 Hz, H_3-17).

Compound 12 (6α,19-Di-*O*-acetyl-2,19 : 4,18 : 11,16 : 15,16-tetraepoxyneoclerodane-6,15,19-triol) Colorless prisms (from acetone), mp 222—224 °C, $[\alpha]_D^{26}$ −2.3° (c=0.318). *Anal.* Calcd for $C_{24}H_{34}O_9$: C, 61.77; H, 7.35. Found: C, 61.58; H, 7.20. UV: 210 (2.06). IR: 3496, 2960, 1732, 1436, 1380, 1262, 1084, 1018. EIMS: 448 [$(M-H_2O)^+$, 2], 406 (10), 388 (13), 346 (9), 300 (8), 278 (28), 218 (94), 190 (44), 172 (62), 159 (47), 145 (35), 111 (100). ^{13}C-NMR: See Table 2. ^{1}H-NMR signals due to **12a**: 8.21 (1H, br d, J=1.8 Hz, 15-OH), 7.16 (1H, s, H-19), 6.13 (1H, d, J=5.5 Hz, H-16), 6.06 (1H, m, H-15), 4.93 (1H, dd, J=11.0, 4.8 Hz, H-6), 4.16 (1H, m, H-2), 4.11 (1H, dd, J=11.4 , 4.8 Hz, H-11), 3.13 (1H, m, H-13), 3.13, 2.40 (each 1H, d, J=4.8 Hz, H_2-18), 2.15, 2.04 (each 3H, s, Ac × 2), 1.18 (3H, s, H_3-20), 0.78 (3H, d, J=6.6 Hz, H_3-17). ^{1}H-NMR signals due to **12b**: 8.25 (1H, d, J=4.0 Hz, 15-OH), 7.16 (1H, s, H-19), 6.01 (1H, d, J=5.5 Hz, H-16), 5.82 (1H, dd, J=4.4, 2.6 Hz, H-15), 4.93 (1H, dd, J=11.0, 4.8 Hz, H-6), 4.85 (1H, dd, J=10.6, 5.9 Hz, H-11), 4.16 (1H, m, H-2), 3.12, 2.35 (each 1H, d, J=4.8 Hz, H_2-18), 2.78 (1H, m, H-13), 2.15, 2.03 (each 3H, s, Ac × 2), 1.17 (3H, s, H_3-20), 0.82 (3H, d, J=6.6 Hz, H_3-17).

Acknowledgements We are grateful to members of the analytical center of this university for elemental analyses and EI-MS measurements.

References

1) Part XX: Miyaichi Y., Tomimori T., *Planta Med.*, **61**, 584 (1995).
2) Tomimori T., Miyaichi Y., Imoto Y., Kizu H., Namba T., *Chem. Pharm. Bull.*, **36**, 3654—3658 (1988).
3) Barton D. H. R., Cheung H. T., Cross A. D., Jackman L. M., Martin-Smith M., *J. Chem. Soc.*, **1961**, 5061—5073; Lin Y. L., Kuo Y. H., Chen Y. L., *Chem. Pharm. Bull.*, **37**, 2191—2193 (1989).
4) Hosozawa S., Kato N., Munakata K., *Phytochemistry*, **12**, 1833—1834 (1973).
5) Anderson J. C., Blaney W. M., Cole M. D., Fellows L. L., Ley S. V., Sheppard R. N., Simmonds M. S. J., *Tetrahedron Lett.*, **30**, 4737—4740 (1989).
6) Malakov P. Y., Papanov G. Y., Boneva I. M., *Phytochemistry*, **41**, 855—857 (1996).
7) Jautelat M., Grutzner J. B., Roberts J. D., *Proc. Natl. Acad. Sci.*, **65**, 288—292 (1970).
8) Yoshida K., Hirose Y., Imai Y., Kondo T., *Agric. Biol. Chem.*, **53**, 1901—1912 (1989).
9) Huneck S., *Tetrahedron*, **19**, 479—482 (1963); Ishiura A., Kizu H., Tomimori T., *Shoyakugaku Zasshi*, **47**, 287—290 (1993).
10) Mukherjee K. S., Bhattacharya M. K., Ghosh P. K., *Phytochemistry*, **21**, 2416—2417 (1982).
11) Ohtani I., Kusumi T., Kashman Y., Kakisawa H., *J. Org. Chem.*, **56**, 1296—1298 (1991).
12) Camps F., Coll J., Cortel A., *Chem. Lett.*, **1982**, 1053—1056.
13) Camps F., Coll J., Dargallo O., *Phytochemistry*, **23**, 2577—2579 (1984).