Studies on Nepalese Crude Drugs. XXIII.[1] On the Diterpenoid Constituents of the Aerial Parts of *Scutellaria grossa* WALL.

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From the aerial parts of *Scutellaria grossa*, a new neoclerodane diterpene named scutegrossin A has been isolated together with five known neoclerodane diterpenes, jodrellin B, scutecolumnin A, scutalsin, scutecyprol B and scutalbin B.

The structure of a new compound has been determined by spectroscopic and chemical methods as (11*S*,13*S*,16*S*,19*R*)-6α-*O*-acetyl-19-*O*-[(*E*)-2-methyl-2-butenoyl]-2α,19; 4α,18; 11,16; 15,16-tetraepoxy-14-neoclerodene-6,19-diol.

In addition, the absolute stereochemistry of 2-methylbutanoyl group of scutecolumnin A and scutalbin B has been ascertained to be the *S* form.

Key words *Scutellaria grossa*; neoclerodane diterpene; scutegrossin A; Lamiaceae

In a previous paper,[2] we reported the structural identification of twelve flavonoids and three iridoids isolated from the leaves of *Scutellaria grossa*. In the course of our studies on Nepalese crude drugs[1] and on the constituents of *Scutellaria* species,[3] we have subsequently investigated the dried aerial parts of *Scutellaria grossa*. This paper deals with the isolation and structural elucidation of the neoclerodane-type diterpenoids from this plant.

Repeated chromatography of the acetone extract of the material gave a new compound named scutegrossin A together with five known compounds, as described in the experimental section.

Compound **1** was identified as jodrellin B based on the spectral and physical data.[4]

Scutegrossin A (**2**) was obtained as a white powder and was presumed to be a compound related to **1** from its spectral features. Its molecular formula was determined as $C_{27}H_{36}O_8$ based on high resolution (HR) electron impact (EI) MS and ^{13}C-NMR spectral data. ^{1}H- and ^{13}C-NMR spectra for **2** showed quite similar signal patterns to those for **1** except for the presence of the signals due to a tigloyl group instead of a 2-methylpropanoyl group in **1** (Tables 1, 2). The tigloyl group was suggested to be connected to the oxygen at C-19 position because the H-19 signal of **2** was observed at 0.13 ppm lower field than that of **1**, whereas the H-6 signal remained almost unchanged. This was confirmed based on the ^{1}H detected heteronuclear multiple bond connectivity (HMBC) spectral data: a ^{1}H–^{13}C long-range correlation was observed between the H-19 (δ 7.22) and C-1′ (δ 166.3) as well as between the H-6 (δ 4.93) and a carbonyl carbon in an acetyl group (δ 169.6). All the ^{1}H and ^{13}C signals were firmly assigned based on the ^{1}H–^{1}H shift correlation (COSY), ^{1}H–^{13}C COSY and HMBC spectral data.

The relative stereochemistry at the C-19 position was determined as the *R** configuration based on the difference nuclear Overhauser effect (NOE) spectral data: irradiation at the H-19 strongly enhanced the signal intensity of the H_3-20.

The absolute stereochemistry of **2** was confirmed by the fact that **2**, on partial hydrolysis with 23% AcOH in tetrahydrofuran (THF)–H_2O, gave 19-*O*-deacetyljodrellin A (**7**), whose absolute stereochemistry was reported earlier.[5]

Consequently, the structure of scutegrossin A (**2**) was concluded to be (11*S*,13*S*,16*S*,19*R*)-6α-*O*-acetyl-19-*O*-[(*E*)-2-methyl-2-butenoyl]-2α,19; 4α,18; 11,16; 15,16-tetraepoxy-14-neoclerodene-6,19-diol.

Compound **3** was suggested to be identical with scutecolumnin A[6] from its spectral features. However, the absolute stereochemistry of the 2-methylbutanoyl group as well as the clerodane skeletone of scutecolumnin A has not been elucidated.

Compound **3** was hydrolyzed with an alkali and then treated with (*R*)-(+)-α-phenylethylamine to give (2*S*)-*N*-

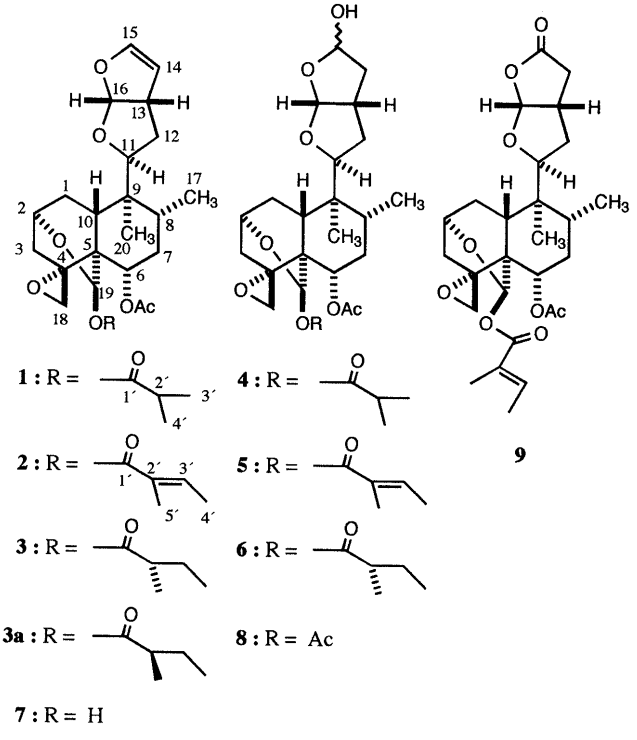

Chart 1

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(1*R*-phenylethyl)-2-methylbutanamide, which was identified as a synthesized authentic specimen by means of capillary GLC. From this result the absolute configuration of 2-methylbutanoyl group proved to be the 2*S* form.

In order to confirm the structure including the absolute stereochemistry, 2*S*- and a mixture of 2*S*- and 2*R*-methylbutanoyl derivatives of **7** were synthesized. Compound **3** agreed with 2*S*-methylbutanoyl derivative. In addition, it was found that **3** and its 2′-epimer (**3a**) were clearly distinguishable from each other by comparisons of ^{1}H- and ^{13}C-NMR spectra.

On the basis of these findings, the structure of **3** was concluded to be (11*S*,13*S*,16*S*,19*R*)-6α-*O*-acetyl-19-*O*-(2*S*-methylbutanoyl)-2α,19; 4α,18; 11,16; 15,16-tetraepoxy-14-neoclerodene-6,19-diol.

Compound **4** was deduced to be identical with scutalsin isolated from *Scutellaria altissima*[7] from comparisons of its NMR spectral data with those of **1** and 14-hydro-15-hydroxyjodrellin A (**8**).[5]

Compound **5** was deduced to be (11*S**,13*S**,16*S**,19*R**)-6α-*O*-acetyl-19-*O*-[(*E*)-2-methyl-2-butenoyl]-2α,19; 4α,-18; 11,16; 15,16-tetraepoxyneoclerodane-6,15,19-triol from comparisons of its NMR spectral data with those of **2** and **4**. That is, **5** should be identical with scutecyprol B, however, none of the spectral or physical data are given in the literature.[8] Thus, **5** was subjected to oxidation with chromium trioxide to yield the lactone derivative (**9**), which was identified as the 15-oxo derivative of scutecyprol B.[8]

Consequently, **5** is identical with scutecyprol B.

Compound **6** was easily assigned as (11*S**,13*S**,16*S**,19*R**)-6α-*O*-acetyl-19-*O*-(2*S**-methylbutanoyl)-2α,19;-4α,18; 11,16; 15,16-tetraepoxyneoclerodane-6,15,19-triol by comparisons of its spectral data (MS, IR, UV, NMR) with those of **3**, **3a** and **5**. Although the absolute configuration of **6** has not been confirmed, it is probably the same as **3** from a biogenetic point of view.

Compound **6** is presumably identical with scutalbin B isolated from *Scutellaria albida*.[7] However, the absolute stereochemistry of its 2-methylbutanoyl group has not been elucidated.

As described above, the diterpenoid constituents from the aerial parts of *Scutellaria grossa* were examined and a new neoclerodane diterpene, scutegrossin A (**2**) was isolated and characterized. Five known ones [**1** (jodrellin B), **3** (scutecolumnin A), **4** (scutalsin), **5** (scutecyprol B), **6** (scutalbin B)] were also isolated and the absolute configuration of the 2-methylbutanoyl part of **3** and **6** has been determined. Although compound **5** has proved to be identical with scutecyprol B, its isolation and characterization are the first example because it was separated as the 15-oxo derivative.[8]

Experimental

General Procedures Unless otherwise stated, the following instruments and conditions were used. Optical rotation was recorded in EtOH on a JASCO DIP-370 digital polarimeter. IR spectra were recorded in KBr disks on a Hitachi 270-30 IR spectrophotometer and the data are given in cm^{-1}. UV spectra were recorded in EtOH on a Shimadzu UV-3000 recording spectrophotometer and peaks are given in λ_{max} nm (log ε). NMR spectra were recorded in pyridine-d_5 on a JEOL GSX-400 spectrometer (^{1}H-NMR at 400 MHz, ^{13}C-NMR at 100 MHz) using a

Table 1. ^{13}C-NMR Spectral Data for Compounds **1**—**6**, **3a** and **9** (100 MHz, Pyridine-d_5)

C No.	**1**	**2**	**3**	**3a**[a]	**4**[b]		**5**[b]		**6**[b]		**9**
					15β form	15α form	15β form	15α form	15β form	15α form	
1	28.6	28.7	28.7		(28.6	28.7)	(28.7	28.8)	28.7	28.7	28.5
2	67.7	67.7	67.7		67.7	67.7	67.7	67.7	67.7	67.7	67.1
3	37.1	37.2	37.1		(37.1	37.2)	37.2	37.2	(37.1	37.2)	36.8
4	60.8	61.0	60.8		(60.8	60.9)	61.0	61.0	(60.8	60.9)	60.5
5	41.9	42.1	41.9		41.9	41.9	42.2	42.2	41.9	41.9	41.6
6	68.6	68.5	68.7		(68.7	68.8)	(68.6	68.7)	(68.7	68.9)	68.1
7	33.5	33.6	33.5		33.6	33.6	33.7	33.7	33.6	33.6	33.5[c]
8	35.9	36.0	35.9		35.8	35.8	35.8	35.8	35.8	35.8	35.3
9	41.1	41.2	41.2		41.3	41.3	41.3	41.3	41.3	41.3	41.2
10	41.6	41.4	41.6		41.5	41.5	41.4	41.4	41.5	41.5	41.0
11	86.0	86.0	86.0		84.3	84.9	84.3	84.9	84.3	84.9	85.0
12	32.3	32.3	32.3		33.3	33.9	33.3	33.9	33.3	33.9	33.1[c]
13	46.2	46.2	46.2		40.7	41.4	40.7	41.4	40.7	41.4	37.8
14	102.6	102.6	102.6		39.9	40.7	39.9	40.7	39.8	40.7	35.3
15	147.1	147.1	147.1		99.4	98.7	99.4	98.7	99.4	98.7	175.1
16	108.6	108.6	108.6		107.9	109.8	107.9	109.8	107.9	109.8	107.1
17	16.6	16.5	16.6		16.6	16.6	16.6	16.6	16.7	16.7	16.8
18	50.0	50.1	50.1		50.0	50.0	50.1	50.1	50.1	50.1	50.0
19	91.9	91.9	91.9		92.0	92.0	92.0	92.0	(91.9	92.0)	91.3
20	14.2	14.2	14.3		(14.2	14.3)	14.2	14.2	(14.2	14.3)	13.8
$CH_3\underline{C}O$	169.6	169.6	169.7	169.7	169.6	169.6	169.6	169.6	169.7	169.7	170.0
$\underline{C}H_3CO$	21.4	21.1	21.5	21.4	21.4	21.4	21.1	21.1	21.5	21.5	20.9
1′	175.4	166.3	175.0	175.0	175.4	175.4	166.4	166.4	175.0	175.0	166.3
2′	34.6	129.5	41.6	40.9	34.6	34.6	129.5	129.5	41.6	41.6	128.8
3′	19.1	138.5	26.3	27.0	19.1	19.1	138.5	138.5	26.3	26.3	138.6
4′	18.6	12.1	11.8	11.4	18.6	18.6	12.1	12.1	11.8	11.8	11.9
5′	—	14.3	16.6	15.7	—	—	14.3	14.3	16.6	16.6	14.5

a) Data are taken from a ^{13}C-NMR spectrum of a mixture of **3** and **3a**. Chemical shifts of C-1—C-20 are almost the same as **3**. *b*) Assignments in parentheses are not strict; they are merely estimated based on a signal intensity because the 15β form/15α form ratios are 6/5—4/3. *c*) May be reversed.

Table 2. ^{1}H-NMR Spectral Data for Compounds **1**—**3** and **3a** (400 MHz, Pyridine-d_5)[a]

H No.	1	2	3	3a[b]
1α	2.35 m	2.39 m	2.35 m	
1β	1.57 dd (11.4, 14.3)	1.60 dd (11.4, 14.3)	1.57 m	
2	4.17 m	4.19 m	4.17 m	
3α	2.63 br d (14.3)	2.66 br d (14.3)	2.63 br d (13.9)	
3β	1.81 dd (2.6, 14.3)	1.83 dd (2.6, 14.3)	1.81 dd (2.6, 13.9)	
6	4.93 dd (4.4, 11.7)	4.93 dd (4.4, 11.7)	4.95 dd (4.4, 11.7)	
7α	1.71 br q (12.5)	1.73 br q (12.5)	1.70 br q (12.5)	
7β	1.41 td (4.4, 12.5)	1.42 ddd (3.3, 4.4, 12.8)	1.41 ddd (3.3, 4.4, 13.2)	
8	1.53 m	1.51 ddd (3.3, 6.6, 12.5)	1.53 m	
10	2.15 dd (4.0, 11.4)	2.16 dd (4.0, 11.4)	2.15 dd (4.0, 11.4)	
11	4.04 dd (4.4, 11.7)	4.06 dd (4.4, 11.7)	4.04 dd (4.8, 11.7)	
12α	1.61 dd (4.4, 12.1)	1.61 dd (4.4, 11.7)	1.61 dd (4.4, 12.5)	
12β	1.81 dt (8.1, 12.1)	1.81 dt (8.4, 11.7)	1.81 dt (8.4, 12.1)	
13	3.49 m	3.49 m	3.49 m	
14	4.85 t (2.6)	4.85 t (2.2)	4.85 t (2.6)	
15	6.68 dd (2.2, 2.6)	6.68 dd (2.2, 2.6)	6.69 dd (2.2, 2.6)	
16	6.17 d (6.2)	6.17 d (6.2)	6.17 d (6.2)	
17	0.73 d (6.6)	0.73 d (6.6)	0.73 d (6.6)	
18A	2.42 d (4.4)	2.45 d (4.4)	2.42 d (4.4)	
18B	3.13 d (4.4)	3.17 d (4.4)	3.14 d (4.4)	
19	7.09 s	7.22 s	7.09 s	7.11 s
20	1.14 s	1.17 s	1.15 s	1.17 s
CH_3CO	2.05 s	1.92 s	2.07 s	1.95 s
2′	2.69 septet (7.0)	—	2.52 sextet (7.0)	2.60 m
3′	1.29 d (7.0)	7.35 br q (7.0)	1.93, 1.54 each d-quintet (14.0, 7.0)	1.85 m[c]
4′	1.27 d (7.0)	1.66 br d (7.0)	0.96 t (7.0)	0.96 t (7.0)
5′	—	1.98 br s	1.29 d (7.0)	1.26 d (7.0)

a) Coupling constants (J) in Hz are given in parentheses. b) Data are taken from a ^{1}H-NMR spectrum of a mixture of **3** and **3a**. Chemical shifts of H_2-1—H_3-17 and H_2-18 are almost the same as **3**. c) Overlapped.

residual signal (β-CH) of the solvent as an internal standard (δ_C 123.5, δ_H 7.20), and chemical shifts are given in δ (ppm). When $CDCl_3$ was employed, tetramethylsilane was used as an internal standard. EI-MS and FAB-MS (positive ion mode; matrix, magic bullet) spectra were recorded on a JEOL JMS-SX-102A mass spectrometer and major peaks are indicated as m/z (%). For TLC, pre-coated silica gel $60F_{254}$ plates (Merck) were used and spots were detected by spraying with dil. H_2SO_4 followed by heating. HPLC was performed on a Shimadzu LC-10AS pump system with a refractive index detector, Model RI-2 (Japan Analytical Industrial Co., Ltd.). GLC was performed on a Shimadzu GC-6AM instrument with a flame ionization detector, using a fused silica WCOT column with Carbowax 20M (Shinwa Kako Co., 0.2 mm i.d. × 25 m): column temperature, 178 °C; injection temperature, 250 °C; carrier gas, He; inlet press, 1.0 kg/cm^2; make-up gas flow rate, 60 ml/min.

Isolation The plant material of *Scutellaria grossa* was collected at Kalopani, Dhaulagiri Zone in Nepal, in September, 1986, and a voucher specimen is deposited at the Herbarium of the Faculty of Pharmaceutical Sciences, Hokuriku University, Kanazawa, Japan. The dried aerial parts (1 kg) were extracted with boiling acetone (5 l × 3). The acetone extract was concentrated under reduced pressure. The residue (93 g) was chromatographed on silica gel (solv., benzene : AcOEt = 1 : 0 → 0 : 1) to give six fractions (fr. 1—6, in the order of elution). Fraction 2 (4.1 g) was treated with hexane–acetone (8 : 1) and precipitates deposited were filtered off. The hexane–acetone soluble part was chromatographed on silica gel (solv., hexane : acetone = 8 : 1) to give a diterpenoid mixture. The mixture was subjected to HPLC separation [column, YMC packed column D-SIL-5 S-5 120 Å SIL (20 mm i.d. × 250 mm); solv., benzene : AcOEt = 10 : 1] to give **1** (54 mg) and a mixture of **2** and **3** (120 mg). The mixture of **2** and **3** was separated with HPLC (column, the same as above; solv., hexane : acetone = 8 : 1) to give **2** (70 mg) and **3** (9 mg). Fraction 5 (2.4 g) was chromatographed on silica gel (solv., benzene : AcOEt = 10 : 1 → 0 : 1) and then purified with medium pressure liquid chromatography (solv., benzene : acetone = 4 : 1) to give a diterpenoid mixture. It was separated with HPLC [column, YMC packed column D-ODS-5 S-5 120 Å ODS (20 mm i.d. × 250 mm); solv., 65% MeOH] to give **4** (133 mg), **5** (97 mg) and **6** (37 mg).

Compound 1 White powder (from hexane–ether), $[\alpha]_D^{31}$ −12.4° (c = 0.791), $[\alpha]_D^{31}$ −17.7° (c = 0.807, $CHCl_3$). ^{13}C-NMR: Table 1. ^{1}H-NMR: Table 2. Spectral and physical data are compatible with jodrellin B.[4]

Scutegrossin A (2) {(11*S*,13*S*,16*S*,19*R*)-6α-*O*-Acetyl-19-*O*-[(*E*)-2-methyl-2-butenoyl]-2α,19; 4α,18; 11,16; 15,16-tetraepoxy-14-neoclerodene-6,19-diol} White powder (from hexane–acetone). $[\alpha]_D^{32}$ +8.8° (c = 0.228). IR: 2984, 1738, 1704, 1652, 1620, 1372, 1274, 1236, 1194, 1142, 1012. UV: 222 (3.80). ^{13}C-NMR: Table 1. ^{1}H-NMR: Table 2. EI-MS: 488 (M^+, 0.8), 428 (0.8), 405 [$(M-C_5H_7O)^+$, 13], 389 [$(M-C_5H_7O_2)^+$, 92], 218 (25), 111 (61), 83 (100). HR-EI-MS m/z: 488.2408 (M^+) (Calcd for $C_{27}H_{36}O_8$: 488.2410).

Partial Hydrolysis of 2 To a solution of **2** (8 mg) in a mixture of THF (1.6 ml) and water (0.4 ml) was added AcOH (0.6 ml) and the solution 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. After removal of the solvent, the residue was chromatographed on silica gel (solv., benzene : AcOEt = 3 : 1) to give **7** (3 mg) and unchanged **2** (3 mg). Compound **7** was identified as 19-*O*-deacetyljodrellin A by direct comparison with an authentic sample.[5]

Compound 3 [(11*S*,13*S*,16*S*,19*R*)-6α-*O*-Acetyl-19-*O*-(2*S*-methylbutanoyl)-2α,19; 4α,18; 11,16; 15,16-tetraepoxy-14-neoclerodene-6,19-diol] Colorless oil, $[\alpha]_D^{31}$ −12.8° (c = 0.296), $[\alpha]_D^{30}$ −18.4° (c = 0.287, $CHCl_3$). IR ($CHCl_3$ soln.): 2976, 2944, 1728, 1620, 1466, 1376, 1256, 1140, 1082, 1008. UV: 211 (3.52), 266 (1.92). ^{13}C-NMR: Table 1. ^{1}H-NMR: Table 2. EI-MS: 490 (M^+, 3), 405 [$(M-C_5H_9O)^+$, 6], 389 [$(M-C_5H_9O_2)^+$, 100], 218 (35), 172 (30), 111 (78). HR-EI-MS: 490.2565 (M^+) (Calcd for $C_{27}H_{38}O_8$: 490.2567).

Synthesis of (2*S*)- and (2*RS*)-*N*-(1*R*-Phenylethyl)-2-methylbutanamide To a solution of (*S*)-(+)-2-methylbutanoic acid (Aldrich®, 31 mg) in CH_2Cl_2 (1.5 ml) was added successively dicyclohexylcarbodiimide (74 mg), 4-dimethylaminopyridine (8 mg) and (*R*)-(+)-α-phenylethyl amine (Tokyo Kasei Kogyo Co., Ltd., 45 mg) at 0 °C and the reaction mixture was stirred at room temperature for 3 h. After filtration, the filtrate was diluted with CH_2Cl_2 and then washed successively with 1 N HCl, 1 N NaOH and brine. The organic layer was dried over anhyd. Na_2SO_4 and then concentrated. The residue was chromatographed on silica gel (solv., hexane : aetone = 3 : 1) to give (2*S*)-*N*-(1*R*-phenylethyl)-2-methylbutanamide (43 mg). In the same

manner, (2*RS*)-*N*-(1*R*-phenylethyl)-2-methylbutanamide (85 mg) was prepared from (*RS*)-(±)-2-methylbutanoic acid (Aldrich®, 58 mg) and (*R*)-(+)-α-phenylethyl amine (59 mg).

(2*S*)-*N*-(1*R*-Phenylethyl)-2-methylbutanamide: Colorless needles (from ether), mp 104—105 °C. ^{1}H-NMR ($CDCl_3$): 0.92 (3H, t, J=7.3 Hz), 1.12 (3H, d, J=7.0 Hz), 1.50 (3H, d, J=7.0 Hz), 1.44, 1.68 (each 1H, double quintet, J=13.6, 7.3 Hz), 2.08 (1H, sextet, J=7.0 Hz), 5.16 (1H, quintet, J=7.0 Hz), 5.63 (1H, br s), 7.25—7.35 (5H, m). ^{13}C-NMR ($CDCl_3$): 11.9, 17.5, 21.7, 27.4, 43.3, 48.4, 126.2 (×2), 127.3, 128.7 (×2), 143.3, 175.4. Retention time on GLC: 30.9 min.

(2*RS*)-*N*-(1*R*-Phenylethyl)-2-methylbutanamide: ^{1}H- and ^{13}C-NMR ($CDCl_3$) signals due to the 2*S* form are the same as described above. ^{1}H-NMR ($CDCl_3$) signals due to the 2*R* form: 0.85 (3H, t, J=7.3 Hz), 1.14 (3H, d, J=7.0 Hz), 1.49 (3H, d, J=7.0 Hz), 1.41, 1.65 (each 1H, double quintet, J=13.6, 7.3 Hz), 2.09 (1H, sextet, J=7.0 Hz), 5.15 (1H, quintet, J=7.0 Hz), 7.25—7.35 (5H, m). ^{13}C-NMR ($CDCl_3$) signals due to the 2*R* form: 11.9, 17.5, 21.6, 27.4, 43.3, 48.4, 126.2 (×2), 127.2, 128.6 (×2), 143.3, 175.5. Retention times on GLC: 30.1 min (2*R* form), 30.9 min (2*S* form).

Alkaline Hydrolysis of 3 Followed by Amidation with (*R*)-(+)-α-Phenylethylamine A solution of **3** (2 mg) in a mixture of 1 N NaOH (0.6 ml) and THF (0.75 ml) was vigorously stirred at 60 °C for 8 h. After cooling, the reaction mixture was diluted with H_2O and extracted with $CHCl_3$. Aqueous layer was acidified with 1 N HCl and extracted with $CHCl_3$. The $CHCl_3$ layer was dried over anhyd. Na_2SO_4 and then concentrated to dryness to give a residue (0.3 mg). To a solution of the residue in CH_2Cl_2 (1 ml) were added dicyclohexylcarbodiimide (1.7 mg), 4-dimethylaminopyridine (0.6 mg) and (*R*)-(+)-α-phenylethyl amine (0.8 mg) at 0 °C. The reaction mixture was allowed to stand at room temperature for 2 h, diluted with CH_2Cl_2 (10 ml) and poured into ice water. After being washed successively with 1 N HCl, 1 N NaOH and brine, the CH_2Cl_2 layer was dried over anhyd. Na_2SO_4 and concentrated. The residue was dissolved in MeOH and analyzed by GLC, which revealed the presence of (2*S*)-*N*-(1*R*-phenylethyl)-2-methylbutanamide (t_R 30.9 min).

Synthesis of 3 and 3a from 7 i) To a solution of **7** (21 mg) and (*S*)-(+)-2-methylbutanoic acid (6 mg) in benzene (12 ml) was added molecular sieve 5 A° (1 g) and the solution was refluxed for 1 h. After filtration, the residue was washed with CH_2Cl_2. The washings and filtrate were combined and washed successively with 1 N NaOH and brine. The organic phase was dried over anhyd. Na_2SO_4 and concentrated to give a residue, which was chromatographed on silica gel (solv., benzene: AcOEt = 4 : 1 → 1 : 1) to give a product (5 mg) together with unchanged **7** (4 mg). ^{1}H- and ^{13}C-NMR spectra and optical rotation of the product coincided with those of **3**.

ii) In the same manner, **7** (20 mg) was treated with (*RS*)-(+)-2-methylbutanoic acid (6 mg) to give a mixture of **3** and **3a** (4 mg). ^{1}H- and ^{13}C-NMR signals due to **3a** are described in Tables 2 and 1, respectively.

Compound 4 [(11*S,13*S**,16*S**,19*R**)-6α-*O*-Acetyl-19-*O*-(2-methylpropanoyl)-2α,19; 4α,18; 11,16; 15,16-tetraepoxyneoclerodane-6,15,19-triol]** White powder (from hexane–acetone), $[\alpha]_D^{25}$ +8.3° (c=0.805), IR ($CHCl_3$ soln.): 3016, 2980, 1730, 1456, 1376, 1256, 1158, 1082, 1022. ^{1}H-NMR signals due to 15*R** form: 0.78 (3H, d, J=6.6 Hz, H_3-17), 1.17 (3H, s, H_3-20), 1.27, 1.29 (each 3H, d, J=7.0 Hz, H_3-3′, H_3-4′), 2.05 (3H, s, Ac), 2.41, 3.14 (each 1H, d, J=4.4 Hz, H_2-18), 4.10 (1H, dd, J=4.8, 11.7 Hz, H-11), 4.15 (1H, m, H-2), *ca.* 4.9 (overlapped with water, H-6), 6.05 (1H, m, H-15), 6.13 (1H, d, J=5.1 Hz, H-16), 7.11 (1H, s, H-19). ^{1}H-NMR signals due to 15*S** form: 0.82 (3H, d, J=6.6 Hz, H_3-17), 1.15 (3H, s, H_3-20), 1.27, 1.29 (each 3H, d, J=7.0 Hz, H_3-3′, H_3-4′), 2.05 (3H, s, Ac), 2.36, 3.13 (each 1H, d, J=4.4 Hz, H_2-18), 4.15 (1H, m, H-2), 4.85 (1H, dd, J=5.9, 11.0 Hz, H-11), *ca.* 4.9 (overlapped with water, H-6), 5.82 (1H, d, J=5.1 Hz, H-15), 6.01 (1H, d, J=5.5 Hz, H-16), 7.11 (1H, s, H-19). ^{13}C-NMR: Table 1. FAB-MS: 517 [(M+Na)$^+$, 48], 407 [(M−$C_4H_7O_2$)$^+$, 90], 219 (28), 173 (49), 119 (100), 111 (79), 85 (75). *Anal.* Calcd. for $C_{26}H_{38}O_9$: C, 63.13; H, 7.75. Found: C, 63.34; H, 8.02.

Compound 5 {(11*S,13*S**,16*S**,19*R**)-6α-*O*-Acetyl-19-*O*-[(*E*)-2-methyl-2-butenoyl]-2α,19; 4α,18; 11,16; 15,16-tetraepoxyneoclerodane-6,15,19-triol}** White powder (from hexane–acetone), $[\alpha]_D^{26}$ +32.8° (c=0.569), IR ($CHCl_3$ soln.): 3016, 2976, 1730 (sh), 1710, 1252, 1142, 1084, 1020. UV: 228 (2.33). ^{1}H-NMR signals due to 15*R** form: 0.77 (3H, d, J=6.6 Hz, H_3-17), 1.17 (3H, s, H_3-20), 1.66 (3H, m, H_3-4′), 1.93 (3H, s, Ac), 1.98 m (3H, m, H_3-5′), 2.44, 3.17 (or 3.16) (each 1H, d, J=4.8 Hz, H_2-18), 2.63 (1H, m, H-3α), 3.12 (1H, m, H-13), 4.12 (1H, dd, J=4.8, 11.4 Hz, H-11), 4.17 (1H, m, H-2), 4.94 (1H, dd, J=4.8, 12.1 Hz, H-6), 5.82 (1H, br d, J=5.5 Hz, H-15), 6.01 (1H, d, J=5.5 Hz, H-16), 7.24 (1H, s, H-19), 7.35 (1H, m, H-3′), 8.22 (1H, br s, 15-OH). ^{1}H-NMR signals due to 15*S** form: 0.81 (3H, d, J=6.6 Hz, H_3-17), 1.19 (3H, s, H_3-20), 1.66 (3H, m, H_3-4′), 1.92 (3H, s, Ac), 1.98 m (3H, H_3-5′), 2.78 (1H, m, H-13), 4.17 (1H, m, H-2), 4.86 (1H, dd, J=5.9, 11.0 Hz, H-11), 4.94 (1H, dd, J=4.8, 12.1 Hz, H-6), 6.06 (1H, br d, J=3 Hz, H-15), 6.13 (1H, d, J=5.5 Hz, H-16), 7.24 (1H, s, H-19), 7.35 (1H, m, H-3′), 8.26 (1H, br s, 15-OH). ^{13}C-NMR: Table 1. FAB-MS: 529 [(M+Na)$^+$, 30], 407 [(M−C_5H_7O)$^+$, 48], 371 (22), 177 (30), 119 (100), 111 (43), 103 (46), 85 (72), 83 (92). *Anal.* Calcd for $C_{27}H_{38}O_9 \cdot 1/2H_2O$: C, 62.88; H, 7.63. Found: C, 62.81; H, 7.68.

Oxidation of 5 To a solution of **5** (30 mg) in pyridine (2 ml) was added chromium trioxide (100 mg) and the reaction mixture was allowed to stand at room temperature for 20 h. After being diluted with H_2O (10 ml), the reaction mixture was extracted with ether. The ether extract was washed with H_2O and concentrated to give a residue, which was chromatographed on silica gel (solv., benzene: AcOEt = 10 : 1 → 1 : 1) to give the lactone derivative (**9**, 17 mg). Compound **9**: colorless needles (from ether–acetone), mp 237—239 °C, $[\alpha]_D^{28}$ +15.5° (c=0.177, $CHCl_3$). ^{13}C-NMR: Table 1. The ^{1}H-NMR spectrum and optical rotation of **9** coincided with those of the 15-oxo derivative of scutecyprol B.[8]

Compound 6 [(11*S,13*S**,16*S**,19*R**)-6α-*O*-Acetyl-19-*O*-(2*S**-methylbutanoyl)-2α,19; 4α,18; 11,16; 15,16-tetraepoxyneoclerodane-6,15,19-triol]** White powder (from hexane–acetone), $[\alpha]_D^{26}$ +3.1° (c=0.382), IR ($CHCl_3$ soln.): 3016, 2980, 1730, 1466, 1376, 1256, 1152, 1082, 1022. UV: 217 (1.61). ^{1}H-NMR signals due to 15*R** form: 0.78 (3H, d, J=6.6 Hz, H_3-17), 0.96 (3H, t, J=7.3 Hz, H_3-4′), 1.17 (3H, s, H_3-20), 1.29 (3H, d, J=7.3 Hz, H_3-5′), 2.08 (3H, s, Ac), 2.41, 3.15 (each 1H, d, J=4.4 Hz, H_2-18), 4.10 (1H, dd, J=4.8, 11.4 Hz, H-11), 4.15 (1H, m, H-2), *ca.* 4.9 (overlapped with H_2O, H-6), 6.06 (1H, br s, H-15), 6.13 (1H, d, J=5.5 Hz, H-16), 7.11 (1H, s, H-19). ^{1}H-NMR signals due to 15*S** form: 0.82 (3H, d, J=6.2 Hz, H_3-17), 0.95 (3H, t, J=7.3 Hz, H_3-4′), 1.15 (3H, s, H_3-20), 1.29 (3H, d, J=7.3 Hz, H_3-5′), 2.07 (3H, s, Ac), 2.36, 3.14 (each 1H, d, J=4.4 Hz, H_2-18), 4.15 (1H, m, H-2), 4.85 (1H, dd, J=5.9, 11.0 Hz, H-11), *ca.* 4.9 (overlapped with H_2O, H-6), 5.82 (1H, br d, J=5.1 Hz, H-15), 6.01 (1H, d, J=5.5 Hz, H-16), 7.11 (1H, s, H-19). ^{13}C-NMR: Table 1. FAB-MS: 531 [(M+Na)$^+$, 30], 407 [(M−$C_5H_9O_2$)$^+$, 44], 371 (26), 195 (28), 177 (34), 119 (100), 111 (31), 103 (41), 85 (64). HR-FAB-MS: 531.2571 [(M+Na)$^+$] (Calcd for $C_{27}H_{40}NaO_9$: 531.2570).

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References and Notes

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