Studies on the Constituents of *Scutellaria* Species. XVIII.[1] Structures of Neoclerodane-Type Diterpenoids from the Whole Herb of *Scutellaria rivularis* WALL.

Haruhisa KIZU,[a] Yoshitaka IMOTO,[a] Tsuyoshi TOMIMORI,*,[a] Tohru KIKUCHI,[b] Shigetoshi KADOTA,*,[b] and Koji TSUBONO[b]

Faculty of Pharmaceutical Sciences, Hokuriku University,[a] Ho-3, Kanagawa-machi, Kanazawa 920–11, Japan and Research Institute for Wakan-Yaku (Oriental Medicines), Toyama Medical and Pharmaceutical University,[b] 2630 Sugitani, Toyama 930–01, Japan. Received July 5, 1996; accepted September 27, 1996

Five neoclerodane-type diterpenoid lactones, scuterivulactones A, B, C_1, C_2 and D, have been isolated (scuterivulactone C_2 was separated as the acetate) from the whole herb of *Scutellaria rivularis* WALL. (Labiaceae), and their structures have been determined based on chemical and physicochemical evidence as follows: scuterivulactone A, (4*S*,11*S*)-11-acetoxy-6α-benzoyloxy-3,4-epoxy-8β-hydroxy-13(14)-neocleroden-15,16-olide; scuterivulactone B, (4*R*,13*R*)-11β-acetoxy-6α-benzoyloxy-8β,13-epoxy-3-oxo-15,16-neoclerodanolide; scuterivulactone C_1, (4*R*,13*R*)-11β-acetoxy-6α-benzoyloxy-3α,4β-dihydroxy-8β,13-epoxy-15,16-neoclerodanolide; scuterivulactone C_2, (4*R,13*S**)-11β-acetoxy-6α-benzoyloxy-3α,4β-dihydroxy-8β,13-epoxy-15,16-neoclerodanolide; and scuterivulactone D, (4*R*)-6α-benzoyloxy-3α,4β-dihydroxy-11,13(14)-neoclerodadien-15,16-olide.**

Key words *Scutellaria rivularis*; neoclerodane diterpene; scuterivulactone (A, B, C_1, C_2, D); Ban Zhi Lian; Labiaceae

In previous papers,[2] we reported the structural identification of 14 flavonoid constituents isolated from the Chinese crude drug "Ban Zhi Lian" (半枝蓮), the whole herb of *Scutellaria rivularis* (Labiaceae). In our further studies on the constituents of this crude drug, five new neoclerodane-type diterpenoid lactones, named scuterivulactones A (**5**), B (**3**), C_1 (**1**), C_2 (**2**, separated as the acetate) and D (**4**), were isolated from the ethereal extract by repeated silica gel column chromatography followed by repeated crystallization as described in the experimental section. Among them, the relative stereochemical structures of **1**, **2** and **4** were determined by means of NMR, MS, IR and UV spectroscopy as described in the previous communications.[3,4] This paper deals with the structural elucidation of scuterivulactones A (**5**) and B (**3**), and full descriptions of C_1 (**1**), C_2 (**2**) and D (**4**), including absolute configuration, are also given.

Scuterivulactone C_1 (**1**) showed absorption bands at 3580 (OH), 1786 (γ-lactone), 1725 sh, 1716 (ester), 1600 and 1580 cm^{-1} (phenyl) in the IR spectrum. The FAB-MS exhibited an ion peak due to $(M+H)^+$ at *m/z* 531, and electron impact-mass spectra (EI-MS) showed fragment ion peaks at *m/z* 512 $[(M-H_2O)^+]$, 494 $[(M-2H_2O)^+]$, 390 $[(M-H_2O-C_6H_5COOH)^+]$, 122 (C_6H_5COOH) and 105 (C_6H_5CO). The molecular formula of **1** was determined to be $C_{29}H_{38}O_9$ based on elemental analysis and

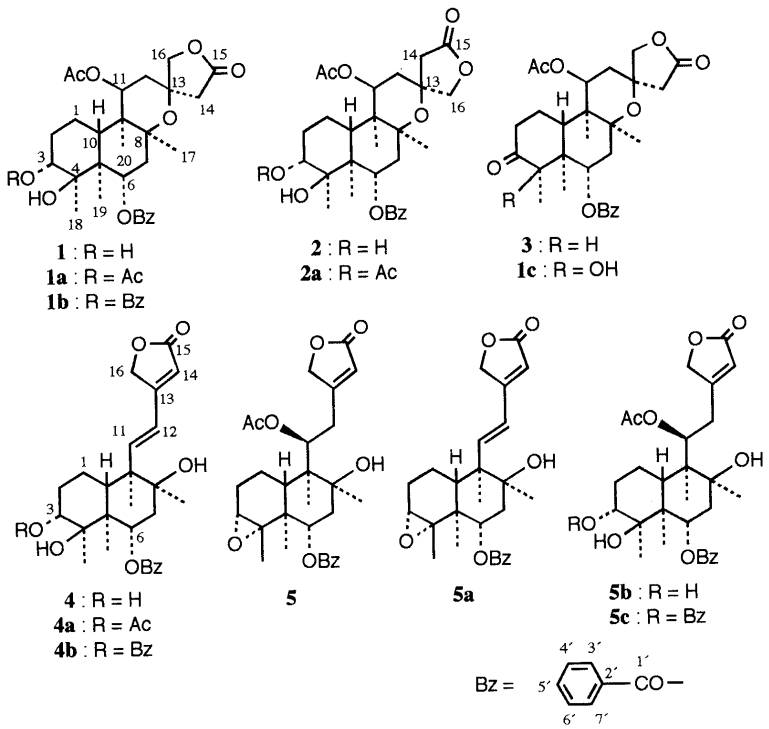


Chart 1

* To whom correspondence should be addressed.

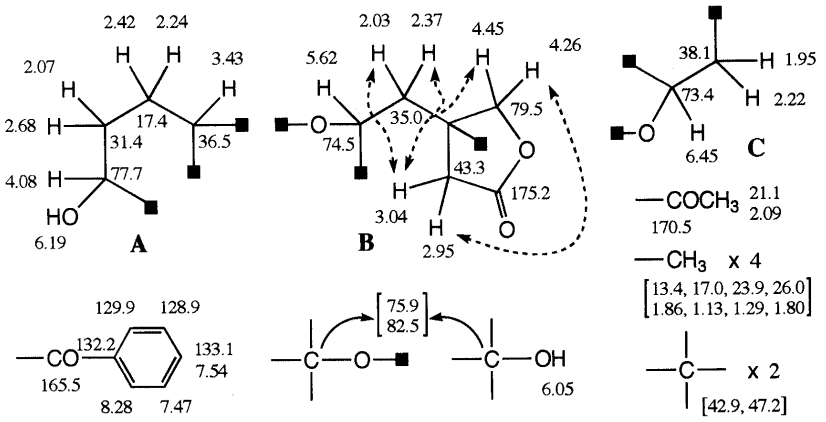


Fig. 1. Partial Structures in **1** (δ Values in Pyridine-d_5)

Long-range correlations observed in ^{1}H–^{1}H COSY are shown by the dotted curved arrows.

the MS and ^{13}C-NMR spectral data. The ^{1}H-NMR, ^{13}C-NMR and ^{1}H–^{1}H correlation spectroscopy (COSY) spectra (in pyridine-d_5 and dimethyl sulfoxide (DMSO)-d_6) suggested the presence of partial structures A, B, and C in addition to an acetyl, a benzoyl, a *tert*-hydroxy (δ_H 6.05 in pyridine-d_5), four *tert*-methyl groups and four quaternary carbons. Each carbon signal, except for the quaternary one, was assigned based on the ^{1}H–^{13}C COSY spectral data (Fig. 1). The sequence of carbon atoms in the molecule was examined based on the 2-D incredible natural abundance double quantum transfer experiment (INADEQUATE) spectral data (in DMSO-d_6), which exhibited correlated peaks of all the coupled ^{13}C–^{13}C pairs except those between the C-2′ (δ_C 130.8) and C-1′ (δ_C 164.4), and between the methyl carbon (δ_C 21.0) and ester-carbonyl carbon (δ_C 169.9) in an acetyl group. The gross planar structure of **1** was deduced from these findings and from the ^{1}H–^{13}C long-range COSY spectrum (in DMSO-d_6), which showed long-range correlations between the carbon at δ 169.9 and the protons at δ 2.05 (CH_3COO) and 5.28 (H-11), the carbon at δ 164.4 (C-1′) and the protons at δ 5.72 (H-6) and 7.92 (H-3′, H-7′), and between the carbon at δ 175.1 (C-15) and the protons at δ 2.74 (H-14A), 2.87 (H-14B), 4.19 (H-16A) and 4.22 (H-16B).

The relative stereochemistry of **1** was determined as follows. In the ^{1}H-NMR spectrum of **1** (in $CDCl_3$), the H-3, H-6, H-10 and H-11 were observed, respectively, as a broad singlet [half-height width (W_h) = 6 Hz], double-doublet (J = 11, 5.5 Hz), broad doublet (J = 13 Hz) and double-doublet (J = 13, 4 Hz), showing that these protons were oriented as equatorial, axial, axial and axial, respectively. In the difference nuclear Overhauser effect (NOE) experiments using the corresponding acetate (**1a**), irradiation at H_3-20 and H_3-18 enhanced the signal intensity of H-11, H_3-17 and H_3-19, and H-3 and H_3-19, respectively, whereas irradiation at H_3-17 and H_3-19 enhanced the signal intensity of H-11, H_2-14 and H_3-20, and H-1α, H_3-18 and H_3-20, respectively. In addition, NOEs were observed between H-6 and H-10, whereas no NOE was observed between H_3-18 and H-6 nor between H_3-18 and H-10. From these findings, the relative stereochemistry of **1** is represented as shown in Chart 1.

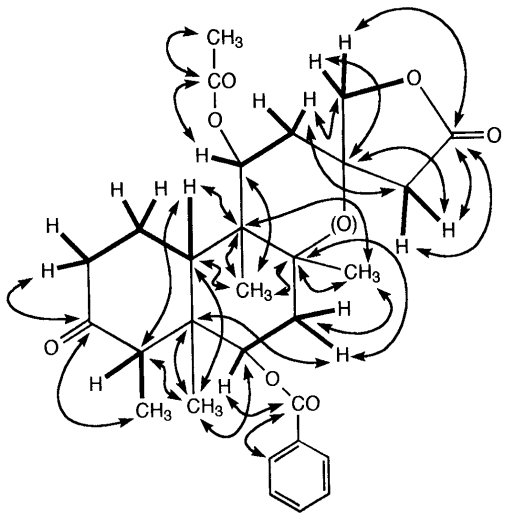
The CD spectral data of the 3-*O*-benzoate (**1b**) of **1** showed a negative first Cotton effect at 235 nm ($\Delta\varepsilon$ = −39.7) and a positive second one at 219 nm ($\Delta\varepsilon$ = +4.6). By applying the exciton chirality rule[5] to this result, *R*-configuration was assigned to the C-3 position of **1**.

Based on these data, the structure of scuterivulactone C_1 (**1**) was concluded to be (4*R*,13*R*)-11β-acetoxy-6α-benzoyloxy-3α,4β-dihydroxy-8β,13-epoxy-15,16-neocleroodanolide.

Scuterivulactone C_2 (**2**) was isolated as an acetate (**2a**) from a mixture of **1** and **2** by normal acetylation followed by HPLC separation. The acetate (**2a**) was considered to be the C-13 epimer of **1a** from comparisons of its ^{1}H- and ^{13}C-NMR spectral data with those of **1a** (Tables 1, 2). This was confirmed by the NOE experiments, in which NOEs were evidently observed between the H_3-17 and H_2-16 as well as between the H_3-17 and H-11.

Consequently, the structure of scuterivulactone C_2 should be represented as formula **2**, except for the absolute configuration.

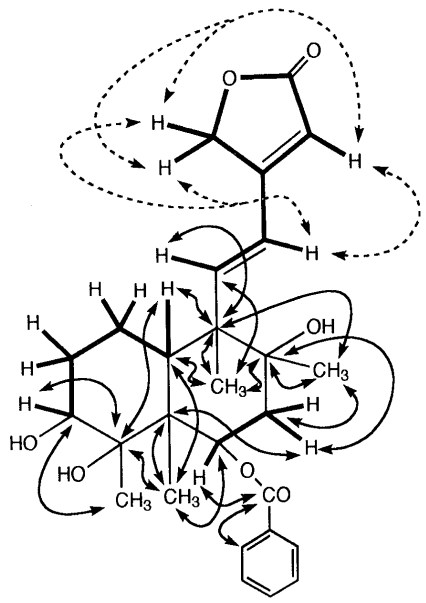
Scuterivulactone B (**3**) showed absorption bands at 1782 (γ-lactone), 1740 sh, 1720 sh, 1710, 1270, 1230 (ester and ketone), 1600 and 1580 cm^{-1} (phenyl) in the IR spectrum. The EI-MS exhibited a molecular ion peak at m/z 512 and fragment ion peaks at m/z 452 [$(M-CH_3COOH)^+$], 390 [$(M-C_6H_5COOH)^+$], 330 [$(M-CH_3COOH-C_6H_5COOH)^+$] and 105 ($C_6H_5CO$), suggesting the presence of an acetyl and a benzoyl group. The molecular formula of **3** was determined to be $C_{29}H_{36}O_8$ based on the EI-MS and ^{13}C-NMR spectral data. The ^{1}H- and ^{13}C-NMR, ^{1}H–^{1}H COSY and ^{1}H–^{13}C COSY spectra suggested the presence of five partial structures in addition to an acetyl, a benzoyl, a keto, three *tert*-methyl and four quaternary carbons (Fig. 2). This sequence was clarified based on ^{1}H–^{13}C long-range COSY spectral data. A carbonyl carbon at δ 210.5 (C-3) was correlated with the methyl protons at δ 0.91 (H_3-18) and a proton at δ 2.40 (H-2β). So, it should be situated at the α- position of both carbons at δ 41.1 (C-2) and 57.7 (C-4). Then, observation of a long-range correlation between the methyl protons at δ 0.91 (H_3-18) and a quaternary carbon at δ 46.4 denoted that the carbon at δ 46.4 (C-5) should be connected to the carbon at δ 57.7 (C-4). In the same manner, observed long-range correlations were examined in detail and the



3

Fig. 2. Gross Planar Structure of **3**

Partial structures deduced from ^{1}H–^{1}H COSY are depicted with bold lines. ^{1}H–^{13}C long-range correlations observed in ^{1}H–^{13}C long-range COSY are shown by curved arrows.



4

Fig. 3. Gross Planar Structure of **4**

Partial structures deduced from ^{1}H–^{1}H COSY are depicted with bold lines. ^{1}H–^{1}H long-range correlations observed in ^{1}H–^{1}H COSY (in pyridine-d_5) are shown by the dotted curved arrows. ^{1}H–^{13}C long-range correlations observed in ^{1}H–^{13}C long-range COSY (in DMSO-d_6) are shown by curved arrows.

results are shown in Fig. 2. The gross planar structure of **3** was deduced from these data.

The relative stereochemistry in **3** was determined from its difference NOE spectra, in which NOEs were observed between H_3-18/H_3-19, H4/H-6 and H-10, H_3-17/H_2-7, H-11, H_2-14 and H_3-20, and H_3-20/H-1α, H-7α, H-11 and H_3-17.

The absolute configuration at the C-5 position of **3** was estimated as *R* based on the CD spectral data ($[\theta]_{280\,nm} = +5200$, $[\theta]_{286\,nm\,sh} = +4950$) by applying the octant rule.[6] This result was supported by the CD spectral data of the 3-keto derivative (**1c**) of **1** ($[\theta]_{280\,nm} = +1980$, $[\theta]_{297\,nm} = 2540$)[7] and 17$\beta$-hydroxy-4$\alpha$-methyl-19-nor-5$\alpha$-androstan-3-one ($[\theta]_{290\,nm} = +4460$).[8]

On the basis of these findings, the structure of scuterivulactone B (**3**) has been assigned as (4*R*,13*R*)-11β-acetoxy-6α-benzoyloxy-8β,13-epoxy-3-oxo-15,16-neoclerodanolide.

The relative stereochemical structure of scuterivulactone B is identical with scutellone B which has been isolated from the same sources and reported by Y. Lin and Y. Kuo[9,10] after we had presented it at the 107th Annual Meeting of the Pharmaceutical Society of Japan.[11] However, their optical rotations [scuterivulactone B, $-19.4°$ ($c = 0.86$, $CHCl_3$); scutellone B, $+54.9°$ ($c = 1.00$, $CHCl_3$)] were different from each other. Scuterivulactone B is expected to be compared with scutellone B directly.

Scuterivulactone D (**4**) showed absorption bands due to hydroxy (3518 cm^{-1}) and carbonyl groups (1747, 1725 sh cm^{-1}). The EI-MS exhibited an M^+ peak at *m/z* 470 and fragment ion peaks at *m/z* 452, 434, 348, 330, 312, 122 and 105, suggesting the presence of a benzoyl group, which was confirmed by the ^{1}H- and ^{13}C-NMR spectral data. The molecular formula of **4** was determined to be $C_{27}H_{34}O_7$ based on EI-MS and ^{13}C-NMR spectral data. The ^{1}H- and ^{13}C-NMR spectra indicated the presence of four *tert*-methyl groups and four quaternary sp^3 carbons in addition to both a di- and tri-substituted double bond. The presence of three partial structures was deduced from ^{1}H–^{1}H COSY spectral data (in pyridine-d_5), and each carbon signal except for the quaternary one was assigned based on the ^{1}H–^{13}C COSY spectral data. The ^{1}H- and ^{13}C-NMR, ^{1}H–^{1}H COSY and ^{1}H–^{13}C COSY spectra were measured in DMSO-d_6 too, and the same results as for in pyridine-d_5 were obtained. In the ^{1}H–^{13}C COSY spectrum in DMSO-d_6, three protons at δ 4.22, 4.39 and 4.46 showed no correlation with any carbon, denoting that these were attributable to the protons of the hydroxy groups.

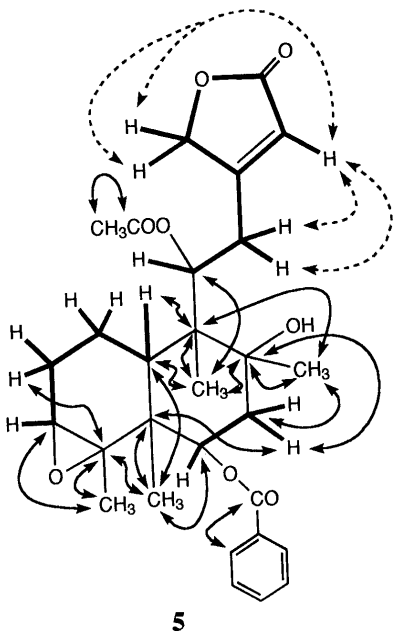
The sequence of the partial structures and functional groups was clarified in the same way as for **3** with the aid of ^{1}H–^{13}C long-range COSY spectral data (in DMSO-d_6) (Fig. 3).

The relative stereochemistry of **4** was determined on the basis of the coupling constant of each proton and the results of NOE experiments (in benzene-d_6) using its 3-*O*-acetate (**4a**): NOEs were observed between H_3-17/H_2-7, H_3-18/H-3 and H_3-19, H_3-19/H-7α, H_3-18 and H_3-20, and H_3-20/H-1α, H-7α, H-11 and H_3-19.

The absolute configuration was determined based on the CD spectral data of its 3-*O*-benzoate (**4b**): a negative Cotton effect ($\Delta\varepsilon = -45.4$) was observed at 232 nm.[5]

These findings led us to conclude that the structure of scuterivulactone D (**4**) should be (4*R*)-6α-benzoyloxy-3α,4β-dihydroxy-11,13(14)-neoclerodadien-15,16-olide.

Scuterivulactone A (**5**) was obtained as colorless prisms and its IR spectrum showed absorption bands at 3416 (hydroxy group), 1782, 1734, 1726, 1638, 1268 and 1238 cm^{-1} (α,β-unsaturated-γ-lactone and ester group). The molecular formula of **5** was determined to be $C_{29}H_{36}O_8$ from the EI-MS (molecular ion at *m/z* 512) and ^{13}C-NMR spectral data. The presence of acetyl and



5

Fig. 4. Gross Planar Structure of **5**

Partial structures deduced from ^{1}H–^{1}H COSY are depicted with bold lines. ^{1}H–^{1}H long-range correlations observed in ^{1}H–^{1}H COSY are shown by the dotted curved arrows. ^{1}H–^{13}C long-range correlations observed in ^{1}H–^{13}C long-range COSY are shown by curved arrows.

benzoyl groups was shown by the EI-MS [*m/z* 452 $(M-60)^+$, 390 $(M-122)^+$] and ^{1}H- and ^{13}C-NMR spectral data. The ^{1}H- and ^{13}C-NMR spectra indicated the presence of four *tert*-methyl groups and four sp^3 quaternary carbons. The presence of a tri-substituted oxirane ring in **5** was suggested from the observation of a set which included a quaternary carbon at δ 66.1 and a methine one at δ 62.9. From these and 2D-NMR spectral data (^{1}H–^{1}H, ^{1}H–^{13}C, and ^{1}H–^{13}C long-range COSY), **5** was deduced to have a 13(14)-cleroden-15,16-olide skeleton possessing 3,4-epoxide, 6,11 (or 8)-diacyl and 8 (or 11)-hydroxy groups (Fig. 4).

Scuterivulactone A (**5**) partly changed to **5a** when its solution in pyridine was left to stand for several days or when its solution in $CHCl_3$ was shaken with 28% ammonia water. In the ^{1}H- and ^{13}C-NMR spectra of **5a**, signals due to an oxymethine at C-11 and a methylene group at the C-12 position of **5** disappeared, and those assignable to di-substituted olefin were observed. In addition, the ^{13}C-NMR spectrum of **5a** was very similar to that of **4** except for the A-ring part, denoting that **5a** was a deacetic acid derivative of **5**. Therefore, in **5**, hydroxy, acetoxy and benzoyloxy groups are connected to the C-8, C-11 and C-6 positions, respectively.

The relative stereochemistry of **5**, including that of the C-11 position, was determined based on difference NOE spectral data, as shown in Fig. 5. It is noted that the C-9 side chain part does not move freely but exists in a relatively fixed conformation with respect to a decaline ring. The absolute configuration was determined as follows. Treatment of **5** with mild acid gave a 3α,4β-diol derivative (**5b**) whose structure was confirmed by ^{1}H-NMR ($J_{2\alpha,3}=2.5$ Hz, $J_{2\beta,3}=3.5$ Hz) and difference NOE spectra: an NOE was observed between H_3-18 and H_3-19. Compound **5b** was subjected to benzoylation to afford the

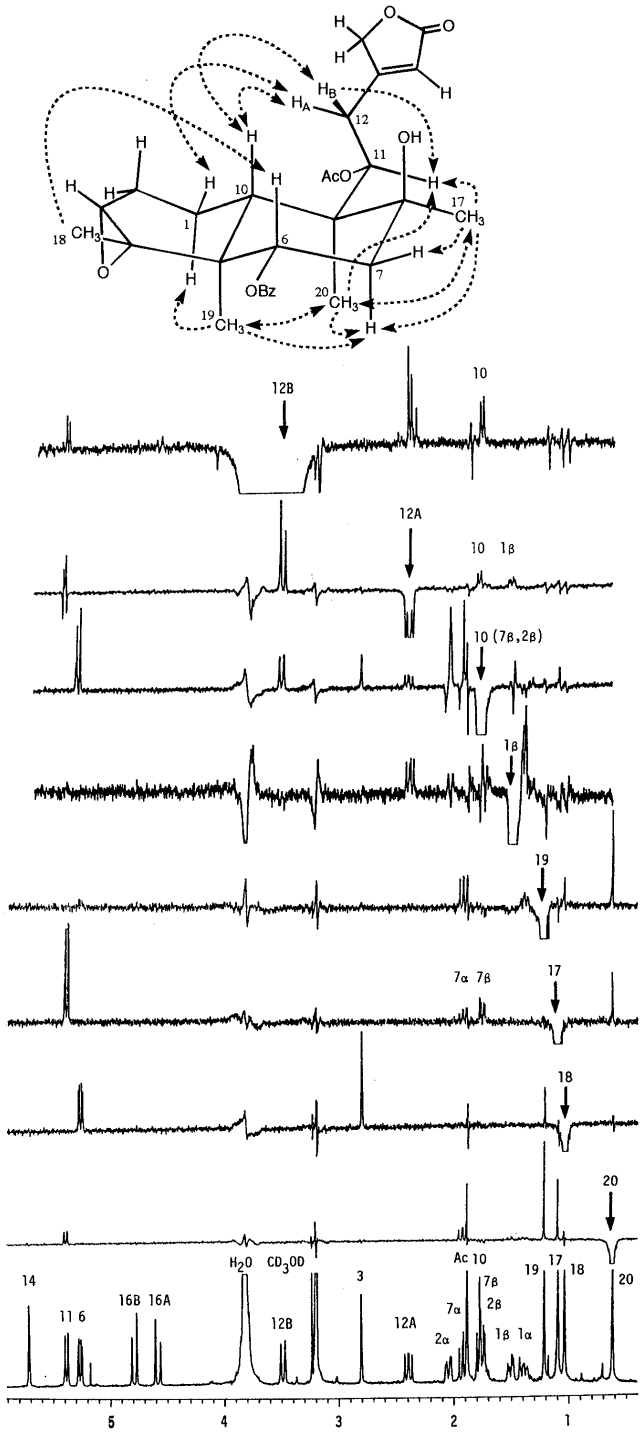


Fig. 5. Normal ^{1}H-NMR and Difference NOE Spectra of Scuterivulactone A (**5**) in $CDCl_3$–CD_3OD (2:1)

An irradiated position is shown by an arrow.

3-*O*-benzoate (**5c**) whose CD spectrum showed a negative first Cotton effect at 236 mn ($\Delta\varepsilon=-21.6$) and a positive second one at 222 nm ($\Delta\varepsilon=+6.2$), denoting that the absolute configuration at the C-3 position of **5c** was *R*.

On the basis of these facts, the structure of scuterivulactone A (**5**) was concluded to be (4*S*,11*S*)-11-acetoxy-6α-benzoyloxy-3,4-epoxy-8β-hydroxy-13(14)-neocleroden-15,16-olide.

Y. Lin and Y. Kuo also investigated the diterpenoid constituents of the whole herb of *Scutellaria rivularis* and reported the structures of nine neoclerodane diterpenoids,

Table 1. ^{13}C-NMR Spectral Data for Scuterivulactones and Their Derivatives (at 100 MHz)

C No.	**1**[a]	**1a**[a]	**2a**[a]	**1b**[a,g]	**1c**[a]	**3**[a]	**4a**[a]	**4b**[a,g]	**5**[b]	**5a**[a]
1	16.2	16.8	16.7	17.0	22.4	23.0	18.3	18.5	16.0	16.9
2	30.1	27.1	27.1	27.3	36.7	41.1	27.4	27.5	26.8	27.7
3	77.5	78.3	78.3	79.1	212.0	210.7	78.4	79.2	62.9	63.1
4	75.6	74.9	74.8	75.3	80.6	57.7	75.4[f]	75.8[f]	66.1	65.7
5	46.5	46.7	46.6	46.6	49.3	46.4	46.1	46.1	42.1	41.8
6	72.0	71.7	71.8	71.9	69.5	75.3	72.8	73.1	74.6	74.5
7	37.9	38.1	37.9	38.1	38.1	38.2	38.0	38.1	39.7	39.2
8	82.1	82.0	81.7	82.1	81.8	82.0	75.5[f]	75.9[f]	75.3	75.5
9	42.3	42.4	43.8	42.5	42.7	42.9	47.9	48.0	47.1	48.1
10	36.3	36.1	36.0	36.1	34.4	43.5	39.6	39.7	41.4	44.2
11	74.0	73.9	73.9	74.0	73.8	73.1	148.9	149.1	75.1	147.6
12	34.9	35.1	34.7	35.1	35.1	35.5	121.5	121.8	32.9	121.9
13	77.1	77.1	77.5	77.3	77.2	77.2	162.4	162.8	169.3	162.1
14	43.0	43.0	42.4	43.1	43.1	42.9	114.5	114.6	116.0	114.8
15	174.9	174.5	173.6	175.0	174.9	174.0	174.1	174.5	174.8	174.0
16	79.4	79.3	77.8	79.5	79.5	79.2	70.8	71.0	73.3	70.6
17	23.8	23.8	24.0	23.9	23.9	24.0	26.5	26.4	25.3	26.4
18	25.1	24.7	24.7	24.8	19.4	9.8	24.4	24.4	21.0	21.2
19	12.6	12.4	12.4	13.0	11.2	10.3	12.4	13.0	13.1	13.5
20	16.9	16.9	16.9	17.0	16.7	16.7	15.6	15.8	16.0	15.7
$CH_3\underline{C}O$	170.5	169.8	169.9	170.7	170.5	170.1	169.9		171.1	
		170.3	170.5							
$\underline{C}H_3CO$	21.3	21.2	21.3	21.4	21.3	21.2	21.4		20.4	
		21.4	21.5							
1′	166.2	166.0	165.9	166.1	165.8	165.4	166.2	166.0	166.2	165.8
(or 1″)				166.3				166.6		
2′	166.2	130.7	130.6	130.7	130.7	130.4	130.5	130.7	130.0	130.5
(or 2″)				130.8				130.7		
3′, 7′	129.6	129.6	129.6	129.8	129.7	129.5	129.6	129.8	129.3	129.6
(or 3″, 7″)				129.8				129.8		
4′, 6′	128.5	128.5	128.5	128.8	128.8	128.5	128.6	128.8	128.4	128.6
(or 4″, 6″)				128.8				128.8		
5′	133.2	133.1	133.2	133.4	133.4	133.2	133.3	133.3	133.3	133.3
(or 5″)				133.4				133.5		

C No.	**5b**[c]	**5c**[a]	**1**[d]	**4**[d]	**5**[d]	**5a**[d]	**1**[e]	**4**[e]	**5**[e]
1	17.7	18.4	17.4	19.0	16.8	17.2	16.1	17.7	15.9
2	29.7	27.1	31.4	31.6	27.5	28.0	29.8	30.1	26.4
3	77.3	79.0	77.7	78.2	62.9	63.1	75.9	76.4	61.9
4	75.4[f]	75.5	75.9	76.1	65.7	65.7	74.5	74.6	65.1
5	46.4	46.6	47.2	46.8	42.8	42.2	45.7	45.1	41.6
6	73.3	72.5	73.4[f]	74.8	75.2[f]	75.6	72.4	73.5	74.2
7	38.8	39.8	38.1	38.7	41.1	39.7	37.1	37.3	39.3
8	75.7[f]	75.5	82.5	74.8	75.6	74.6	81.5	73.8	74.8
9	47.0	47.2	42.9	48.8	47.9	48.8	41.7	47.7	46.7
10	36.8	36.9	36.5	40.4	42.1	44.4	35.2	38.8	41.0
11	75.7	75.3	74.5[f]	151.9	75.8[f]	149.6	73.6	150.8	74.8
12	33.2	33.4	35.0	121.0	33.6	121.8	32.9	120.5	32.4
13	169.6	168.4	77.7	163.8	171.3	163.5	77.3	164.0	170.1
14	116.1	116.7	43.3	113.7	116.3	114.3	42.4	112.6	114.7
15	174.9	174.1	175.2	174.3	174.4	174.7	175.1	173.8	173.4
16	73.5	73.3	79.5	71.0	73.5	70.9	78.5	70.6	73.1
17	26.1	26.8	23.9	26.6	25.8	25.9	23.6	25.6	24.8
18	24.5	24.8	26.0	25.9	21.8	21.4	24.8	24.7	20.9[f]
19	12.2	12.7	13.4	13.4	13.9	13.9	12.4	12.3	13.2
20	16.2	16.6	17.0	15.8	16.4	15.6	16.3	15.3	15.9
$CH_3\underline{C}O$	171.2	170.9	170.5		169.9		169.9		170.7
$\underline{C}H_3CO$	20.7	20.8	21.1		20.7		21.0		20.6[f]
1′	166.7	165.8	165.5	165.7	165.8	165.7	164.4	164.4	164.7
(or 1″)		166.3							
2′	130.5	130.4	132.2	132.4	131.6	131.5	130.8	131.0	130.2
(or 2″)		130.4							
3′, 7′	129.5	129.6	129.9	129.9	129.9	129.9	128.9	128.9	129.0
(or 3″, 7″)		129.7							
4′, 6′	128.4	128.6	128.9	128.9	129.1	129.1	128.6	128.6	128.8
(or 4″, 6″)		128.6							
5′	133.2	133.2	133.1	133.1	133.6	133.5	132.9	132.8	133.4
(or 5″)		133.4							

a) Measured in $CDCl_3$. *b*) Measured in $CDCl_3$–CD_3OD (2:1). *c*) Measured in $CDCl_3$–CD_3OD (7:1). *d*) Measured in pyridine-d_5. *e*) Measured in DMSO-d_6. *f*) May be reversed in each vertical column. *g*) Measured at 25 MHz.

Table 2. ^{1}H-NMR Spectral Data for Scuterivulactones and Their Derivatives[a]

H No.	1[b]	1a[b]	2a[b]	3[b]	4a[b]
1α	1.75 qd (13, 3)	1.62 qd (13, 3)	1.62 qd (13, 3)	1.89 m	1.62 qd (13.5, 4)
1β	*ca.* 2.12	*ca.* 2.13	2.13 br d (13)	2.71 m	*ca.* 1.14
2α	1.66 m	1.68 br d (13)	1.69 br d (13)	2.47 ddd (13.5, 6, 2)	1.66 m
2β	*ca.* 2.12	*ca.* 2.07	*ca.* 2.06	2.40 td (13.5, 7.5)	2.04 tt (13.5, 4)
3	3.53 m (W_h=6)	4.68 m (W_h=6)	4.68 m (W_h=6)	—	4.72 m (W_h=6.5)
4	—	—	—	2.61 q (7)	—
6	5.80 dd (11, 5.5)	5.84 dd (9.5, 7)	5.85 t (8)	5.38 dd (11.5, 5)	5.98 dd (11.5, 5)
7α	1.91 dd (14, 11)	*ca.* 1.90	1.91 d (8)	1.79 dd (14, 11.5)	2.10 dd (14, 11.5)
7β	1.87 dd (14, 5.5)	*ca.*1.90	1.91 d (8)	2.04 dd (14, 5)	1.96 dd (14, 5)
10	2.83 br d (13)	2.87 br d (13)	2.90 br d (13)	2.68 dd (12, 3)	2.62 dd (13.5, 2)
11	5.35 dd (13, 4)	5.36 dd (13, 4)	5.36 dd (13, 4.5)	5.42 dd (13, 4)	6.38 d (17)
12α (12A)	*ca.* 1.88	*ca.* 1.90	2.05 dd (13, 4.5)	2.01 dd (13, 4)	6.40 d (17) (H-12)
12β (12B)	*ca.* 2.12	*ca.* 2.10	*ca.* 2.09	2.14 t (13)	—
14A	2.72 d (17)	2.73 d (17)	2.62 d (17.5)	2.81 d (17)	5.88 t (1.5) (H-14)
14B	2.83 d (17)	2.83 d (17)	3.01 d (17.5)	2.87 d (17)	—
16A	4.21 d (9)	4.22 d (9.5)	4.25 d (9)	4.28 d (9)	4.97 dd (17, 1.5)
16B	4.37 d (9)	4.36 d (9.5)	4.38 d (9)	4.41 d (9)	5.01 dd (17, 1.5)
17	1.30 s	1.31 s	1.25 s	1.36 s	1.09 s
18	1.27 s	1.15 s	1.16 s	0.91 d (7)	1.20 s
19	1.43 s	1.40 s	1.40 s	1.08 s	1.44 s
20	1.02 s	1.03 s	1.03 s	1.03 s	1.15 s
CH_3CO	2.09 s	2.08 s	2.08 s	2.10 s	2.09 s
CH_3CO	—	2.09 s	2.09 s	—	—
3′, 7′	8.01 dd (7.5, 1.5)	8.00 dd (7.5, 1.5)	8.00 dd (7.5, 1.5)	7.98 br d (7.5)	7.99 dd (7.5, 1.5)
4′, 6′	7.44 t (7.5)	7.44 t (7.5)	7.45 t (7.5)	7.44 br t (7.5)	7.44 t (7.5)
5′	7.57 tt (7.5, 1.5)	7.57 tt (7.5, 1.5)	7.57 tt (7.5, 1.5)	7.57 br t (7.5)	7.57 tt (7.5, 1.5)

H No.	5a[b]	5[c]	5b[d]	5c[b]
1α	*ca.* 1.41	1.40 m	1.81 m	1.88 m
1β	1.02 br dd (13.5, 6)	1.51 br dd (14, 5.5)	1.56 br d (14)	1.76 br d (13.5)
2α	2.13 m	2.05 m	1.62 dq (14, 2.5)	1.88 m
2β	1.74 m	1.75 m	2.05 tt (14, 3.5)	2.23 tt (13.5, 3.5)
3	2.90 br s	2.81 br s	3.44 br t (3)	5.04 m (W_h=6)
4	—	—	—	—
6	5.58 dd (10, 6)	5.27 dd (11, 4.5)	5.69 dd (11.5, 4.5)	5.96 dd (12, 4.5)
7α	2.06 m	1.93 dd (14, 11)	2.01 dd (14, 11.5)	2.21 dd (14, 12)
7β	2.06 m	1.76 dd (14, 4.5)	1.68 dd (14, 4.5)	1.84 dd (14, 4.5)
10	1.89 br d (11.5)	1.79 br d (10.5)	2.59 dd (12, 1.5)	2.82 br d (11)
11	6.23 d (17)	5.39 br d (11)	5.48 dd (11, 1.5)	5.61 d (10.5)
12α (12A)	6.40 d (17) (H-12)	3.50 br d (15.5)	3.60 br d (15.5)	3.65 br d (15)
12β (12B)	—	2.40 dd (15.5, 11)	2.56 dd (15.5, 11)	2.63 dd (15, 10.5)
14A	5.91 br s (H-14)	5.72 br s	5.78 br s	5.88 br s
14B	—	—	—	—
16A	4.96 dd (16.5, 1.5)	4.59 dd (18, 1.5)	4.65 dd (17.5, 1.5)	4.69 dd (17, 1.5)
16B	5.03 dd (16.5, 1.5)	4.80 dd (18, 1.5)	4.86 dd (17.5, 1.5)	4.90 dd (17, 15)
17	1.08 s	1.10 s	1.18 s	1.34 s
18	1.21 s	1.05 s	1.20 s	1.29 s
19	1.38 s	1.22 s	1.38 s	1.60 s
20	1.05 s	0.63 s	0.78 s	0.92 s
CH_3CO	—	1.89 s	1.95 s	2.01 s
CH_3CO	—	—	—	—
3′, 7′	8.06 br d (7)	7.89 dd (7.5, 1.5)	7.94 dd (7.5, 1.5)	7.99, 8.08 m
4′, 6′	7.47 br t (7)	7.33 t (7.5)	7.38 t (7.5)	7.43, 7.51 t (7.5)
5′	7.59 br t (7)	7.46 tt (7.5, 1.5)	7.51 tt (7.5, 1.5)	7.56, 7.62 tt (7.5, 1.5)

a) Coupling constants (J) and half-height width (W_h) in Hz are given in parentheses. *b*) Measured in $CDCl_3$. *c*) Measured in $CDCl_3$–CD_3OD (2 : 1). *d*) Measured in $CDCl_3$–CD_3OD (7 : 1).

scutellones A,[12] B,[9,10] C,[13] D,[14] E,[14] F,[13] G,[10,15] H[10] and I.[10] Among these, scutellone A and D should be identical to scuterivulactone C_1 and D, respectively, although the absolute configurations of all of the scutellones have not yet been elucidated.

Experimental

General Procedures All melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. The instruments used in this study were as follows: UV spectra, Shimadzu UV-3000 recording spectrophotometer; IR spectra, Hitachi infrared spectrophotometer 270-30; CD spectra, JASCO J-20A automatic recording spectrophotometer; FAB- (positive mode) and EI-MS spectra, JEOL JMS-DX-300 and JEOL JMS-SX-102A mass spectrometers; NMR spectra, JEOL JNM-FX-100, JEOL GX-400 and JEOL GSX-400 spectrometers (tetramethylsilane was used as an internal standard and chemical shifts are given as δ values); optical rotation, JASCO DIP-4

Table 3. ^{1}H-NMR Spectral Data for Scuterivulactones and Their Derivatives[a)]

H No.	1[b)]	4[b)]	5a[b)]	5[b)]	1[c)]	4[c)]	4a[d)]
1α	2.24 qd (13, 4)	2.24 qd (13, 3)	1.48 m	1.64 m	1.65 qd (13, 2)	1.61 qd (13, 3)	1.56 qd (13, 3.5)
1β	2.42 br d (13)	1.38 br d (13)	1.07 br dd (12.5, 5)	1.79 br dd (14, 5.5)	1.95 br d (13)	0.91 br d (13)	1.06 m
2α	2.07 m	2.03 dq (13.3)	2.06 m	*ca.* 2.15	1.45 br d (13)	1.40 br d (13)	1.76 m
2β	2.68 tt (13, 4)	2.61 tt (13, 3.5)	1.63 m	1.90 br td (13, 5.5)	2.05 m	1.92 tt (13, 3)	2.18 tt (14, 4)
3	4.08 m (W_h=9.5)	4.09 m (W_h=9.5)	2.84 br s	2.93 br s	3.27 m (W_h=10)	3.27 m (W_h=10)	4.91 m (W_h=6.5)
6	6.45 dd (11, 5.5)	6.91 dd (11, 5)	6.11 dd (11, 5)	5.93 dd (9.5, 6)	5.72 dd (11, 6)	5.90 dd (11, 5)	6.23 dd (11.5, 5)
7α	1.95 dd (13.5, 11.5)	2.20 dd (13, 11)	2.12 dd (14, 11)	*ca.* 2.15	1.83 dd (13, 11)	1.85 dd (13, 11)	1.80 dd (14, 11.5)
7β	2.22 dd (13.5, 5)	2.38 dd (13, 5)	2.30 dd (14, 5)	*ca.* 2.15	1.77 dd (13, 6)	1.78 dd (13, 5)	1.93 dd (14, 5)
10	3.43 dd (13, 2)	3.47 dd (13, 2)	2.18 br d (11)	*ca.* 2.15	2.77 br d (13)	2.56 br d (13)	2.79 dd (13, 2)
11	5.62 dd (13, 4)	6.83 d (17)	6.66 d (16.5)	5.91 br d (10.5)	5.28 dd (13, 4)	6.34 d (17)	6.18 d (17)
12α (12A)	2.03 dd (13, 4)	6.51 d (17) (H-12)	6.50 br d (16.5) (H-12)	2.72 dd (15.5, 10.5)	2.03 t (13)	6.41 d (17) (H-12)	5.91 d (17) (H-12)
12β (12B)	2.37 t (13)	—	—	3.88 d (15.5)	1.86 dd (13, 4)	—	—
14A	2.95 d (17)	6.03 br s (H-14)	6.12 br s (H-14)	6.18 br s (H-14)	2.74 d (17)	6.03 br s (H-14)	5.54 br s (H-14)
14B	3.04 d (17)	—	—	—	2.87 d (17)	—	—
16A	4.26 d (9)	4.77 dd (16, 1)	4.90 dd (16.5, 1.5)	4.89 br d (17)	4.19 d (9)	5.12 br s	4.28 dd (16.5, 1)
16B	4.45 d (9)	4.88 dd (16, 1)	5.05 dd (16.5, 1.5)	5.12 br d (17)	4.22 d (9)	5.12 br s	4.46 dd (16.5, 1)
17	1.29 s	1.30 s	1.27 s	1.47 s	1.23 s	0.94 s	0.88 s
18	1.80 s	1.86 s	1.32 s	1.33 s	1.09 s	1.12 s	1.25 s
19	1.86 s	1.94 s	1.55 s	1.53 s	1.34 s	1.34 s	1.43 s
20	1.13 s	1.26 s	1.05 s	0.86 s	0.93 s	1.02 s	0.83 s
CH_3CO	2.09 s	—	—	2.05 s	2.05 s	—	1.74 s
3′, 7′	8.28 dd (7, 1.5)	8.33 dd (7.5, 1)	8.31 dd (7, 1)	8.28 br d (7.5)	7.92 dd (7.5, 1)	7.96 br d (7.5)	8.16 m
4′, 6′	7.47 t (7)	7.49 t (7.5)	7.52 t (7)	7.51 br t (7.5)	7.53 t (7.5)	7.53 t (7.5)	7.13 m
5′	7.54 tt (7, 1.5)	7.55 tt (7.5, 1.5)	7.61 tt (7.1)	7.59 br t (7.5)	7.64 tt (7.5, 1)	7.64 br t (7.5)	7.18 m
3-OH	6.19 d (4.5)	6.20 d (4.5)	—	—	4.49 d (4.5)	4.46 d (4.5)	—
4-OH	6.05 s	6.06 s	—	—	4.30 s	4.22 s	—
8-OH	—	6.29 s	—	—	—	4.39 s	—

a) Coupling constants (J) and half-height width (W_h) in Hz are given in parentheses. *b*) Measured in pyridine-d_5. *c*) Measured in DMSO-d_6. *d*) Measured in benzene-d_6.

digital polarimeter. For column chromatography, Wakogel C-200 was used. TLC was performed on pre-coated Silica gel 60F_{254} plates (Merck) and spots were detected under UV light (254 nm) and by spraying with 10% H_2SO_4, followed by heating.

Extraction and Separation Commercial "Ban Zhi Lian" (半枝蓮, Osaka market, 2 kg), the dried whole herb of *Scutellaria rivularis* (Labiaceae), was extracted three times with hot EtOH. The EtOH extract was concentrated to dryness and a residue was suspended in H_2O and then extracted with ether. The ether extract was concentrated and a residue was partitioned between hexane and 90% MeOH. The lower phase was evaporated and a residue (30 g) was chromatographed over silica gel (2 kg) and eluted with a gradient of $CHCl_3$–MeOH (1 : 0→9 : 1) containing a trace amount of H_2O and AcOH to give fr. 1—7, in the order of elution. Fraction 1 was chromatographed over silica gel with a gradient of hexane–acetone (1 : 0→4 : 1) containing a trace amount of AcOH to give crude **5** along with 7-hydroxy-5,8-dimethoxyflavone.[1a)] Crude **5** was recrystallized from a mixture of $CHCl_3$ and MeOH to give pure **5** (30 mg). Fraction 2 was chromatographed similarly to fr. 1 to give **3** (100 mg) together with wogonin and 5,7-dihydroxy-8,2′-dimethoxyflavone.[1a)] Fraction 4 was subjected to silica gel column chromatography eluted with a gradient of benzene–AcOEt (1 : 0→4 : 1) containing a trace amount of AcOH to give a mixture of **1** and **2** along with 5,2′,6′-trihydroxy-7,8-dimethoxyflavone.[1a)] The mixture of **1** (overwhelmingly major) and **2** (minor) was repeatedly crystallized from MeOH or acetone to give pure **1** (80 mg). The mixture (36 mg) of **1** and **2** obtained from the mother liquor of crystallization was acetylated with pyridine (0.6 ml) and acetic anhydride (0.6 ml) at room temperature for 48 h. After the usual work-up, a product (38 mg) was repeatedly crystallized from a mixture of ether and MeOH to give the pure 3-*O*-acetate (**1a**, 25 mg) of **1**. The mother liquor of crystallization was subjected to HPLC separation [column, TSK-GEL Silica-150 (4.6 mm i.d. × 250 mm); solv., $CHCl_3$–MeOH (199 : 1)] to give the 3-*O*-acetate (**2a**, 3 mg) of **2** together with **1a** (6 mg). Fraction 6 was submitted to repeated crystallization from MeOH to give **4** (100 mg).

Scuterivulactone C_1 (1) Colorless prisms (from acetone), mp 268—272 °C, $[\alpha]_D^{26}$ −7.0° (c=0.5, MeOH). *Anal.* Calcd for $C_{29}H_{38}O_9$: C, 65.64; H, 7.22. Found: C, 65.68; H, 7.15. IR (KBr) cm^{-1}: 3580, 1786, 1725 sh, 1716, 1600, 1580, 1318, 1272, 1256, 1120, 1070, 1026, 982, 710. FAB-MS m/z: 531 $(M+H)^+$. EI-MS m/z: 512 $(M-H_2O)^+$, 494 $(M-2H_2O)^+$, 390 $(M-H_2O-C_6H_5COOH)^+$, 122 (C_6H_5COOH), 102 (C_6H_5CO). ^{1}H-NMR: Tables 2, 3. ^{13}C-NMR: Table 1.

Scuterivulactone C_1 3-*O*-Acetate (1a) Colorless prisms (from MeOH), mp 258—263 °C, $[\alpha]_D^{26}$ −50.6° (c=0.5, $CHCl_3$). IR (KBr) cm^{-1}: 3523, 1783, 1731, 1602, 1584, 1276, 1249, 1040, 1027. FAB-MS m/z: 573 $[(M+H)^+]$. EI-MS m/z: 572 (M^+), 530 $[(M-CH_3CO+H)^+]$, 512 $[(M-CH_3COOH)^+]$, 470 $[(M-CH_3COOH-CH_3CO+H)^+]$, 450 $[(M-C_6H_5COOH)^+]$, 408 $[(M-C_6H_5COOH-CH_3CO+H)^+]$, 390 $[(M-C_6H_5COOH-CH_3COOH)^+]$. HR-EI-MS m/z: 572.2620 (M^+) (Calcd for $C_{31}H_{40}O_{10}$ 572.2622). ^{1}H-NMR: Table 2. ^{13}C-NMR: Table 1.

Scuterivulactone C_1 3-*O*-Benzoate (1b) A solution of **1** (15 mg) in a mixture of pyridine (0.4 ml) and benzoylchloride (0.1 ml) was allowed to stand for 43 h at room temperature. A reaction mixture was poured into ice-water and then extracted with ether. The ether phase was washed successively with 0.1 N HCl, saturated $NaHCO_3$ aq. and water (twice), and then evaporated. The residue was chromatographed over silica gel (2 g) and eluted with $CHCl_3$ to give the 3-*O*-benzoate (**1b**, 17 mg). Compound **1b**, white amorphous powder, $[\alpha]_D^{15}$ −104.3° (c=0.4, MeOH). IR (KBr) cm^{-1}: 3508, 1792, 1742 sh, 1718, 1602, 1580, 1274, 1232, 1102, 1072, 1038, 1026, 712. EI-MS m/z: 634 (M^+), 574 $[(M-CH_3COOH)^+]$, 512 $[(M-C_6H_5COOH)^+]$, 452 $[(M-CH_3CO-OH-C_6H_5COOH)^+]$, 390 $[(M-2C_6H_5COOH)^+]$, 330 $[(M-CH_3-COOH-2C_6H_5COOH)^+]$. HR-EI-MS m/z: 634.2770 (M^+) (Calcd for $C_{36}H_{42}O_{10}$ 634.2778). UV λ_{max} (MeOH) nm (log ε): 202 (4.23), 229 (4.52), 272 (3.35), 280 (3.25). CD ($c=2.88\times10^{-5}$, MeOH) $\Delta\varepsilon$ (nm): 0 (214), +4.6 (219), 0 (223), −39.7 (235), 0 (270). ^{1}H-NMR (100 MHz, $CDCl_3$): 1.08 (3H, s, H_3-20), 1.25 (3H, s, H_3-18), 1.35 (3H, s, H_3-17), 1.59 (3H, s, H_3-19), 2.08 (3H, s, CH_3CO), 2.78 and 2.82 (each 1H, d, J=17 Hz, H_2-14), 2.98 (1H, br d, J=11 Hz, H-10), 4.23 and 4.41 (each 1H, d, J=9.5 Hz, H_2-16), 4.99 (1H, br s, H-3), 5.40 (1H, dd, J=12.5, 4.5 Hz, H-11), 5.93 [1H, t, J=8 Hz (virtual coupling), H-6], 7.3—7.7 (6H) and 7.9—8.1 (4H) (each m, benzoyl part × 2). ^{13}C-NMR: Table 1.

Scuterivulactone C_2 3-*O*-Acetate (2a) White amorphous powder, $[\alpha]_D^{24}$ −31.0° (c=0.6, $CHCl_3$). IR (KBr) cm^{-1}: 3522, 1786, 1731, 1600, 1580, 1278, 1248, 1038, 1027. EI-MS m/z: 572 (M^+), 530 $[(M-CH_3CO+H)^+]$, 512 $[(M-CH_3COOH)^+]$, 470 $[(M-CH_3COOH-CH_3CO+H)^+]$, 450 $[(M-C_6H_5COOH)^+]$, 408 $[(M-C_6H_5COOH-CH_3CO+H)^+]$, 390 $[(M-C_6H_5COOH-CH_3COOH)^+]$. HR-EI-MS m/z: 572.2618 (M^+) (Calcd for $C_{31}H_{40}O_{10}$ 572.2622). ^{1}H-NMR: Table 2.

^{13}C-NMR: Table 1.

Scuterivulactone B (3) Colorless needles (from MeOH), mp 145—147 °C, $[\alpha]_D^9$ −19.4° (c=0.86, $CHCl_3$). *Anal.* Calcd for $C_{29}H_{36}O_8$: C, 67.95; H, 7.08. Found: C, 67.99; H, 7.20. IR(KBr) cm^{-1}: 1780, 1740 sh, 1720 sh, 1710, 1270, 1230, 1110, 1090, 1030, 710. CD ($c=6.92\times10^{-3}$, MeOH) $\Delta\varepsilon$ (nm): −2.9 (220), 0 (243), + 1.58 (280), +1.50 (286 sh), 0 (325). EI-MS m/z: 512 (M^+), 390 [$(M-C_6H_5COOH)^+$], 330 [$(M-CH_3COOH-C_6H_5COOH)^+$], 105 ($C_6H_5CO$). ^{1}H-NMR: Table 2. ^{13}C-NMR: Table 1.

Oxidation of 1 To a solution of **1** (30 mg) in acetone (10 ml) was added Jones reagent (6 drops) at 0 °C with stirring. After 1.5 h, a few drops of 2-propanol were added. The reaction mixture was neutralized with saturated $NaHCO_3$ aq. and extracted with AcOEt. The AcOEt extract was washed with water and dried over anhydrous Na_2SO_4 followed by filtration. The filtrate was evaporated and the residue was chromatographed over silica gel (2 g) and eluted with CH_2Cl_2–MeOH (99 : 1) to give **1c** (21 mg). Compound **1c**, colorless needles (from MeOH), mp 237—240 °C. IR (KBr) cm^{-1}: 3468, 1788, 1776, 1724 sh, 1714, 1602, 1584, 1274, 1256, 1232, 1116, 1100, 1080, 1070, 1036, 720. EI-MS m/z: 528 (M^+), 485 [$(M-CH_3CO)^+$], 406 [$(M-C_6H_5COOH)^+$], 363 [$(M-C_6H_5COOH-CH_3CO)^+$], 346 [$(M-C_6H_5COOH-CH_3COOH)^+$]. HR-EI-MS m/z: 528.2367 (M^+) (Calcd for $C_{29}H_{36}O_9$ 528.2359). CD ($c=6.81\times10^{-3}$, MeOH) $\Delta\varepsilon$ (nm): 0 (240.5), +0.14 (245), +0.10 (254), +0.60 (279.5), +0.77 (297), 0 (340). ^{1}H-MNR (100 MHz, $CDCl_3$): 1.01 (3H, s, H_3-20), 1.10 (3H, s, H_3-19), 1.17 (3H, s, H_3-18), 1.34 (3H, s, H_3-17), 2.09 (3H, s, CH_3CO), 2.81 (2H, m, H_2-14), 3.47 (1H, dd, J=12.5, 2.5 Hz, H-10), 4.24 and 4.44 (each 1H, d, J=9.5 Hz, H_2-16), 5.40 (1H, dd, J=12.5, 4.5 Hz, H-11), 5.85 (1H, dd, J=11, 5.5 Hz , H-6), 7.3—7.6 (3H, m, H-3′, 4′, 5′) , 7.98 (2H, m, H-2′, 6′). ^{13}C-NMR: Table 1.

Scuterivulactone D (4) Colorless needles (from acetone), mp 260—262 °C, $[\alpha]_D^{26}$ +57.5° (c=0.50, MeOH), *Anal.* Calcd for $C_{27}H_{34}O_7$: C, 68.92; H, 7.28. Found: C, 68.89; H, 7.33. IR (KBr) cm^{-1}: 3518, 1782, 1748, 1716, 1692 sh, 1672, 1644, 1318, 1286, 1122, 1054, 716. FAB-MS m/z: 471 [$(M+H)^+$]. EI-MS m/z: 470 (M^+), 452 [$(M-H_2O)^+$], 434 [$(M-2H_2O)^+$], 348 [$(M-C_6H_5COOH)^+$], 330 [$(M-H_2O-C_6H_5COOH)^+$], 312 [$(M-2H_2O-C_6H_5COOH)^+$], 122 (C_6H_5COOH), 105 (C_6H_5CO). UV λ_{max} (MeOH) nm (log ε): 202 (4.08), 236.5 (4.30), 263 (4.44). ^{1}H-NMR: Table 3. ^{13}C-NMR: Table 1.

Scuterivulactone D 3-*O*-Acetate (4a) To a solution of **4** (5.2 mg) in pyridine (0.1 ml) was added acetic anhydride (0.1 ml), and the reaction mixture was left to stand for 41 h at room temperature. After the usual work-up, the product was purified with preparative TLC [solv., $CHCl_3$–MeOH (99 : 7)] to give the acetate (**4a**, 5.4 mg). Compound **4a**, colorless columns (from MeOH), mp 242—244 °C, $[\alpha]_D^{22}$ +21.8° (c= 0.50, $CHCl_3$). IR (KBr) cm^{-1}: 3488, 1782, 1748, 1741, 1718, 1646, 1278, 1250, 1112, 1028, 714. FAB-MS m/z: 513 [$(M+H)^+$]. EI-MS m/z: 390 [$(M-C_6H_5COOH)^+$], 372 [$(M-H_2O-C_6H_5COOH)^+$], 330 [$(M-CH_3COOH-C_6H_5COOH)^+$], 312 [$(M-CH_3COOH-C_6H_5COOH-H_2O)^+$], 105 ($C_6H_5CO$). HR-FAB-MS m/z: 513.2484 [$(M+H)^+$] (Calcd for $C_{29}H_{37}O_8$ 513.2488). ^{1}H-NMR: Table 2. ^{13}C-NMR: Table 1.

Scuterivulactone D 3-*O*-Benzoate (4b) To a solution of **4** (18 mg) in pyridine (0.4 ml) was added benzoylchloride (0.1 ml). The reaction mixture was allowed to stand for 23 h at room temperature and was worked up in the same way as **1b**. The product was purified with a silica gel column [solv., $CHCl_3$–MeOH (99 : 1)] to give the benzoate (**4b**, 11 mg). Compound **4b**, white amorphous powder, $[\alpha]_D^{15}$ +30.8° (c=0.62, MeOH). IR (KBr) cm^{-1}: 3504, 1782, 1750, 1724, 1716, 1644, 1602, 1586, 1278, 1110, 1028, 974, 712. FAB-MS m/z: 575 [$(M+H)^+$]. EI-MS m/z: 574 (M^+), 556 [$(M-H_2O)^+$], 452 [$(M-C_6H_5COOH)^+$], 434 [$(M-H_2O-C_6H_5COOH)^+$], 330 [$(M-2C_6H_5COOH)^+$], 312 [$(M-H_2O-2C_6H_5COOH)^+$], 105 (C_6H_5CO). HR-FAB-MS m/z: 575.2640 [$(M+H)^+$] (Calcd for $C_{34}H_{39}O_8$ 575.2645). UV λ_{max} (MeOH) nm (log ε): 202.5 (4.21), 230.5 (4.52), 261 (4.50). CD ($c=3.72\times10^{-5}$, MeOH) $\Delta\varepsilon$ (nm): −10.3 (214), −45.4 (232), 0 (241), +26.2 (257), 0 (300). ^{1}H-NMR (100 MHz, $CDCl_3$): 1.14 (3H, s, H_3-20), 1.21 (3H, s, H_3-18), 1.30 (3H, s, H_3-17), 1.65 (3H, s, H_3-19), 2.74 (1H, br d, J=11 Hz, H-10), 5.04 (3H, m, H-3 and H_2-16), 5.90 (1H, br s, H-14), 6.07 (1H, dd, J=10.5, 5.5 Hz, H-6), 6.45 (2H, br s, H-11 and H-12), 7.3—7.6 (6H, m), 7.9—8.1 (4H, m) (benzoyl group × 2). ^{13}C-NMR: Table 1.

Scuterivulactone A (5) Colorless needles (from $CHCl_3$–MeOH), mp 250—254 °C, $[\alpha]_D^9$ +5.0° [c=0.20, $CHCl_3$–MeOH (1 : 1)]. *Anal.* Calcd for $C_{29}H_{36}O_8$: C, 67.95; H, 7.08. Found: C, 68.01; H, 7.12. IR (KBr) cm^{-1}: 3416, 3088, 1808, 1782, 1734, 1716, 1638, 1600, 1580, 1268, 1238, 1216, 1112, 1022, 720. EI-MS m/z: 512 (M^+), 484 [$(M-H_2O)^+$], 452 [$(M-CH_3COOH)^+$], 436 [$(M-H_2O-CH_3COOH)^+$], 390 [$(M-C_6H_5COOH)^+$], 372 [$(M-H_2O-C_6H_5COOH)^+$], 330 [$(M-CH_3COOH-C_6H_5COOH)^+$], 312 [$(M-H_2O-CH_3COOH-C_6H_5COOH)^+$]. ^{1}H-NMR: Tables 2, 3. ^{13}C-NMR: Table 1.

Deacetic Acid Derivative (5a) of 5 (i) A solution of **5** (11 mg) in pyridine (3 ml) was allowed to stand for 7 d and then evaporated to dryness under reduced pressure. The residue was chromatographed over silica gel and eluted with a gradient of CH_2Cl_2–ether (1 : 0→3 : 1) to give **5a** (2 mg) together with unchanged **5** (6 mg). (ii) A solution of **5** (6.5 mg) in $CHCl_3$ (10 ml) was shaken with ammonia water (28%) and was allowed to stand for 3 d. A $CHCl_3$ phase was evaporated and the residue was chromatographed similarly to the method described above to give **5a** (3 mg) along with unchanged **5** (2 mg). Compound **5a**, white amorphous powder. IR (KBr) cm^{-1}: 3496, 1782, 1748, 1740, 1728, 1718, 1712, 1644, 1602, 1282, 1118, 1070, 1028, 714. EI-MS m/z: 452 (M^+), 330 [$(M-C_6H_5COOH)^+$], 105 (C_6H_5CO). HR-EI-MS m/z: 452.2191 (M^+) (Calcd for $C_{27}H_{32}O_6$ 452.2199). ^{1}H-NMR: Tables 2, 3. ^{13}C-NMR: Table 1.

Mild Acid-Hydrolysis of 5 A solution of **5** (10 mg) in acetone (20 ml) and 0.1 N H_2SO_4 (0.54 ml) was heated under reflux for 4 h. After cooling, the reaction mixture was neutralized with $BaCO_3$ and centrifuged. The supernatant was evaporated and the residue was chromatographed over silica gel (4 g) and eluted with a gradient of $CHCl_3$–MeOH (1 : 0→24 : 1) to give **5b** (8 mg). Compound **5b**, colorless prisms (from MeOH), mp 250—252 °C. IR (KBr) cm^{-1}: 3592, 3436, 3112, 1812, 1784, 1730, 1646, 1602, 1584, 1250, 1118, 1104, 1052, 1026, 972, 718. FAB-MS m/z: 553 [$(M+Na)^+$]. EI-MS m/z: 530 (M^+), 512 [$(M-H_2O)^+$], 470 [$(M-CH_3COOH)^+$], 452 [$(M-H_2O-CH_3COOH)^+$], 408 [$(M-C_6H_5COOH)^+$], 390 [$(M-H_2O-C_6H_5COOH)^+$], 348 [$(M-CH_3COOH-C_6H_5COOH)^+$], 330 [$(M-H_2O-CH_3COOH-C_6H_5COOH)^+$], 122 ($C_6H_5COOH$), 105 ($C_6H_5CO$). HR-FAB-MS m/z: 553.2407 [$(M+Na)^+$] (Calcd for $C_{29}H_{38}O_9Na$ 553.2413). ^{1}H-NMR: Table 2. ^{13}C-NMR: Table 1.

3-*O*-Benzoate (5c) of 5b To a solution of **5b** (5 mg) in pyridine (0.2 ml) was added benzoyl chloride (0.08 ml). The reaction mixture was allowed to stand for 24 h at room temperature. To the reaction mixture were added CH_2Cl_2 (5 ml) and benzene (10 ml), and precipitates deposited were filtered off. The filtrate was evaporated and the residue was chromatographed over silica gel (5 g) and eluted with a gradient of CH_2Cl_2–MeOH (1 : 0→99 : 7) to give the benzoate (**5c**, 4 mg). Compound **5c**, white amorphous powder. IR (KBr) cm^{-1}: 3504, 1784, 1748, 1724, 1642, 1604, 1586, 1316, 1274, 1244, 1178, 1108, 1026, 970, 714. FAB-MS m/z: 635 [$(M+H)^+$]. EI-MS m/z: 634 (M^+), 574 [$(M-CH_3COOH)^+$], 556 [$(M-H_2O-CH_3COOH)^+$], 512 [$(M-C_6H_5COOH)^+$], 452 [$(M-CH_3COOH-C_6H_5COOH)^+$], 434 [$(M-H_2O-CH_3COOH-C_6H_5COOH)^+$], 330 [$(M-CH_3COOH-2C_6H_5COOH)^+$], 312 [$(M-H_2O-CH_3COOH-2C_6H_5COOH)^+$], 122 ($C_6H_5COOH$), 105 ($C_6H_5CO$). HR-FAB-MS m/z: 635.2870 [$(M+H)^+$] (Calcd for $C_{36}H_{43}O_{10}$ 635.2856). ^{1}H-NMR: Table 2. ^{13}C-NMR: Table 1.

Acknowledgement The authors are grateful to Dr. K. Kuriyama, Shionogi Research Laboratory, for CD measurement (scuterivulactone B and compound **1c**) and for valuable instruction. Thanks are also due to members of the analytical center of this university for MS measurement and elemental analyses. This work was partly supported by a Grant-in-Aid for Scientific Research to T. K. and S. K. (No. 61470147) from the Ministry of Education, Science, Sports and Culture, Japan.

References and Notes

1) Part XVII: Miyaichi Y., Tomimori T., *Natural Medicines*, **49**, 350—353 (1995).
2) *a*) Tomimori T., Miyaichi Y., Imoto Y., Kizu H., *Shoyakugaku Zasshi*, **38**, 249—252 (1984); *b*) *Idem*, *Ibid.*, **40**, 432—433 (1986).
3) Kikuchi T., Tsubono K., Kadota S., Kizu H., Imoto Y., Tomimori T., *Chemistry Lett.*, **1987**, 987—990.
4) Kizu H., Imoto Y., Tomimori T., Tsubono K., Kadota S., Kikuchi T., *Chem. Pharm. Bull.*, **35**, 1656—1659 (1987).
5) Harada N., Nakanishi K., "Circular Dichroic Spectroscopy—an Application for Organic Stereochemistry," Tokyo Kagaku Dojin, Tokyo, 1982.
6) Moffitt W., Woodward R. B., Moscowitz A., Klyne W., Djerassi C., *J. Am. Chem. Soc.*, **83**, 4013—4018 (1961).
7) An α-axial-oriented hydroxy group is known to make a small negative contribution, as well as to induce a red shift in UV

absorption. Djerassi C., Halpern O., Halpern V., Schindler O., Tamm C., *Helv. Chim. Acta*, **41**, 250—274 (1958).
8) Berkoz B., Chavez E. P., Djerassi C., *J. Chem. Soc.*, **1962**, 1323—1329; Kirk D. N., Klyne W., *J. Chem. Soc., Perkin Trans., 1*, **1974**, 1076—1103.
9) Lin Y. L., Kuo Y. H., *Chem. Express*, **3**, 37—40 (1988).
10) Lin Y. L., Kuo Y. H., *Chem. Pharm. Bull.*, **37**, 582—585 (1989).
11) Presented at the 107th Annual Meeting of the Pharmaceutical Society of Japan, Kyoto, April, 1987. Abstract of Papers, p. 327.
12) Lin Y. L., Kuo Y. H., Lee G. H., Peng S. M., *J. Chem. Research(s)*, **1987**, 320—321.
13) Lin Y. L., Kuo Y. H., *Heterocycles*, **27**, 779—783 (1988).
14) Lin Y. L., Kuo Y. H., Cheng M. C., Wang Y., *Chem. Pharm. Bull.*, **36**, 2642—2646 (1988).
15) Kuo Y. H., Lin Y. L., *Chem. Express*, **6**, 343—346 (1988).