Sesqui- and Diterpenoids from the Japanese Liverwort *Jungermannia infusca*

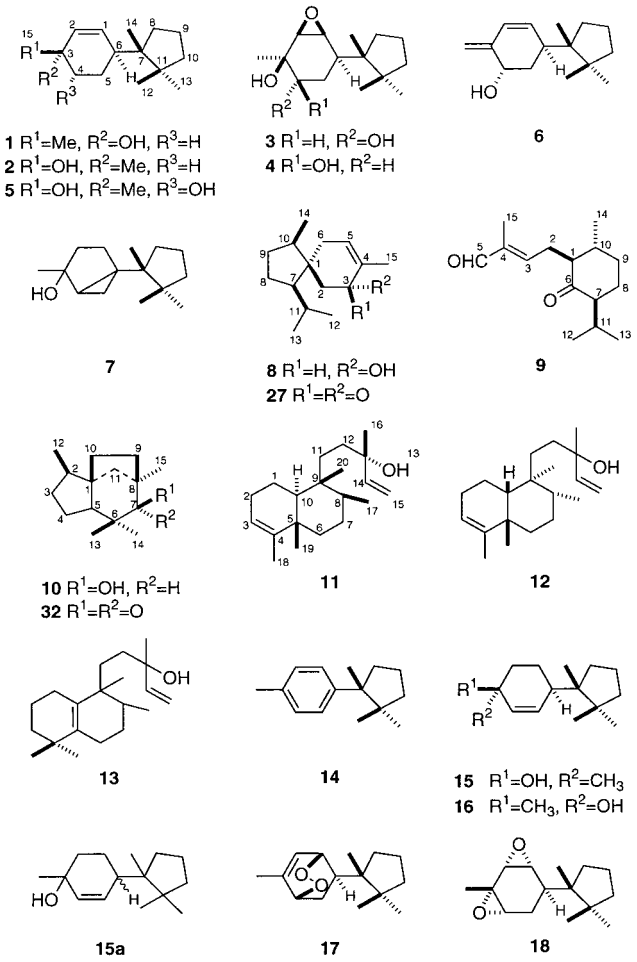
Fumihiro Nagashima,* Makoto Suzuki, Shigeru Takaoka, and Yoshinori Asakawa

Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Yamashiro-cho, Tokushima 770-8514, Japan

Received April 30, 2001

Seven new cuparane-type (**1**−**7**), one new acorane-type (**8**), one new monocyclic-type (**9**), and one new prelacinane-type (**10**) sesquiterpenoid as well as two new clerodane-type (**11**, **12**) and one new halimane-type (**13**) diterpenoid were isolated from the Japanese liverwort *Jungermannia infusca*, together with 12 known cuparane- (**14**−**21**) and aromadendrane-type (**22**) sesquiterpenoids and labdane- (**23**) and *ent*-kaurane-type (**24**) diterpenoids. The structures for **1**−**13** were determined using extensive NMR techniques and by chemical degradation and X-ray crystallographic analysis.

Liverworts are small plants, and their taxonomic identification is quite difficult. As they are a rich source of unique terpenoids and aromatic compounds, these substances may be useful as chemosystematic specific and generic markers. Pinguisane- and sacculatane-type terpenoids as well as bis(bibenzyls) have been repeatedly isolated from liverworts, while they are never found in higher plants.[1,2] Many species belonging to the family Jungermanniaceae (Hepaticae) contain diterpenoids of the clerodane-, labdane-, pimarane-, verrucosane-, and *ent*-kaurane-type as major constituents.[1−3] Particularly, Japanese and Taiwanese collections of the species *Jungermannia infusca* (Mitt.) Steph. (Jungermanniaceae) have yielded diterpenoids, sesquiterpenoids, and aromatic compounds as the main components.[3,4] The distribution of the above-mentioned substances has been shown to be dependent on the plant collection location, and therefore four chemotypes have been established.[5] Recently, we reported the constituents of *J. infusca* collected in Hyogo, Japan, which contains *ent*-kaurane-type diterpenoids as main components.[6] We report herein the results of the chemical investigation of *J. infusca* collected in Tokushima, Japan. An ether extract yielded the new cuparanes **1**−**7**, the new acorane **8**, the new monocyclic sesquiterpenoid **9**, the new prelacinane **10**, the new clerodanes **11** and **12**, and the new halimane **13**, in addition to 12 known sesqui- and diterpenoids (**14**−**24**).



Results and Discussion

Thirteen new sesqui- and diterpenoids **1**−**13** were isolated from the ether extract of *J. infusca* by repeated column chromatography and preparative HPLC, together with the 10 known sesquiterpenoids (+)-cuparene (**14**),[7] neocuprenenol (**15a**),[8] (+)-cuprenenol (**16**),[9] (1*S*,4*R*)-peroxycupar-2-ene (**17**),[6,10] *epi*-cuparadiepoxide (**18**),[8] rosulantol (**19**),[9] microbiotol (**20**),[11] (+)-3,6-peroxycupar-1-ene (**21a**, **21b**),[5] and *ent*-viridiflorol (**22**),[12] as well as two diterpenoids, (13*S*)-hydroxy-8,14-labdadiene (**23**)[13] and *ent*-15α-hydroxykaurene (**24**).[14] The known compounds were identified by comparison of their spectral data with those of authentic samples and/or reference data.

Spectral features of compounds **1** and **2**, which were named infuscols A and B, were similar. The FABMS of both compounds exhibited sodiated molecular ions at *m*/*z* 245 $[M + Na]^+$. The IR spectrum of each compound showed the presence of a hydroxy group. The ^{1}H NMR spectra (Table 1) of **1** and **2** indicated the presence of two olefinic protons (**1**, δ 5.50, 5.60; **2**, δ 5.53, 5.64) and four tertiary methyls (**1**, δ 0.75, 0.95, 0.98, 1.27; **2**, δ 0.72, 0.84, 0.95, 1.25). In the ^{13}C NMR spectrum (Table 2) of both compounds, 15 carbons were evident, and their DEPT spectra indicated the presence of two sp^2 (**1**, δ 131.7, 135.1; **2**, δ 134.0, 135.0) and one quaternary carbon (**1**, δ 69.7; **2**, δ 66.5) bearing a hydroxyl group, together with four methyls, five methylenes, a methine, and two quaternary carbons. The above spectral data of **1** and **2** were similar to those of the cuparane-type sesquiterpenoids **15**−**20**, suggesting that they are based on the same carbon skeleton. The detailed analysis of their ^{1}H−^{1}H COSY, HMQC, and HMBC spectra (Table 3) led to the structures of **1** and **2** as depicted. To clarify the relative stereochemistry of **1**, a *m*-chloro-

* To whom correspondence should be addressed. Tel: +81-88-622-9611. Fax: +81-88-655-3051. E-mail: fnaga@ph.bunri-u.ac.jp.

10.1021/np010223i CCC: $20.00
Published on Web 09/14/2001

Table 1. ^{1}H NMR Data of **1**−**4** (400 MHz, $CDCl_3$)[a]

position	**1**	**2**[b,c]	**3**	**4**[b]
1	5.50 dt (10.6, 1.8)	5.53 ddd (10.2, 1.9, 1.4)	3.33 dd (4.0, 1.1)	3.30 d like (3.8)
2	5.60 ddd (10.6, 2.6, 1.8)	5.64 ddd (10.2, 2.5, 1.9)	2.92 dd (4.0, 1.1)	2.98 d (3.8)
4	1.54−1.76 m	1.35 ddd (13.2, 13.2, 4.7) α	3.57 br s	3.14 ddd (11.8, 10.4, 3.8)
	1.82−1.91 m	1.80 dddd (13.2, 3.6, 3.6, 1.9) *β*		
5	1.48 m	1.55−1.61 2H, m	1.57−1.69 m	1.34 q (12.1)
	1.82−1.91 m		1.71−1.87 m	1.61−1.68 m
6	2.25 m	2.01 tt (8.0, 8.0, 2.5)	2.31 br dd (10.3, 6.2)	2.02 br dd (11.8, 3.8)
8	1.54−1.76 2H, m	1.49−1.54 m	1.71−1.87 2H, m	1.76−1.78 2H, m
		1.55−1.61 m		
9	1.54−1.76 2H, m	1.49−1.54 2H, m	1.57−1.69 2H, m	1.61−1.68 2H, m
10	1.35 ddd (11.7, 11.7, 8.4)	1.31 m, α	1.38 br q like α	1.41 dd (12.6, 6.3)
	1.54−1.76 m	1.66 m, *β*	1.76 m *β*	1.74 dd (12.6, 9.6)
12	0.98 s	0.95 s	1.00 s	1.00 s
13	0.95 s	0.84 s	0.97 s	0.96 s
14	0.75 s	0.72 s	0.97 s	0.96 s
15	1.27 s	1.25 s	1.37 s	1.40 d (0.5)
OH			2.58 s	2.44 d (10.4)
				2.50 s

[a] *J* values (in Hz) in parentheses. [b] Measured by 600 MHz. [c] Measured in C_6D_6.

Table 2. ^{13}C NMR Data of **1**−**10**, **20**, and **25** (100 MHz, $CDCl_3$)

carbon	**1**	**2**[a]	**3**	**4**[b]	**5**	**6**[b]	**7**	**8**	**9**[a,b]	**10**[b]	**20**[a]	**25**
1	131.7	134.0	58.4	59.3	134.4	135.3	27.8	46.3	57.1	53.2	11.5	60.1
2	135.1	135.0	56.2	57.0	131.4	126.4	37.6	34.3	26.2	39.0	32.5	60.3
3	69.7	66.5	68.2	67.8	68.8	144.6	80.2	69.3	152.2	31.2	78.6	70.1
4	38.8	38.1	72.3	73.3	73.6	69.9	33.0	135.1	139.7	21.5	37.2	33.7
5	23.7	21.8	23.8	25.5	27.6	31.5	14.0	124.6	194.0	58.3	28.1	22.8
6	44.0	45.0	35.6	42.3	38.7	38.4	34.6	38.1	210.2	38.0	33.3	41.4
7	47.5	48.1	47.7	47.9	47.4	47.2	46.4	57.0	56.4	85.6	46.8	47.1
8	39.5	40.1	39.4	39.4	39.5	39.6	34.5	26.2	28.8	45.4	34.8	39.4
9	19.1	19.9	19.1	19.1	19.1	19.1	19.4	30.7	34.6	29.3	19.7	19.2
10	42.1	42.9	41.6	41.7	42.1	42.3	41.1	46.2	40.0	22.7	41.5	41.9
11	43.8	44.4	44.1	44.1	43.9	43.8	44.7	29.1	26.6	49.4	44.7	44.0
12	25.0	25.6	25.3	25.0	25.1	25.1	26.2	22.0	18.9	14.3	26.3	24.8
13	24.4	24.9	24.9	24.7	24.5	24.3	25.0	23.7	21.4	16.0	25.3	24.3
14	17.4	18.3	18.5	18.8	17.8	17.9	21.8	16.4	20.6	33.3	21.5	18.1
15	28.0	30.7	22.6	24.4	24.8	113.0	24.8	19.0	9.3	24.8	28.5	22.7

[a] Measured in C_6D_6. [b] Measured by 150 MHz.

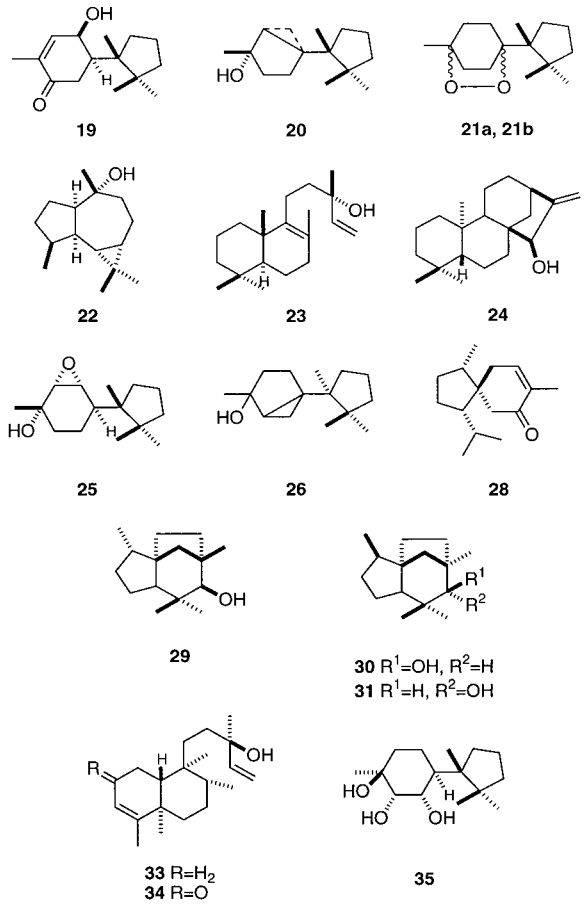
Table 3. HMBC Correlations of **1**, **2**, **9**, **10**, and **12**

1		**2**		**9**		**10**		**12**	
H	C	H	C	H	C	H	C	H	C
1	3, 5, 6, 7	1	3, 5, 6, 7	1	3, 6, 10	3	1, 5	1	2, 5, 9, 10
2	3, 4, 6, 15	2	3, 4, 6	2	1, 3, 4, 6, 10	9	7, 8	3	1, 5, 18
4	2, 3, 5, 6	4	2, 3, 5, 6, 15	3	1, 2, 5, 15	10	1, 2, 5, 9	6	5, 7, 8, 19
6	1, 2, 5, 7, 8, 14	5	1, 3, 4, 6	5	3, 4, 15	11	9, 10	10	1, 2, 4, 5, 9, 20
10	8, 9, 13	6	1, 2, 5, 7, 14	11	6, 7, 8, 12, 13	12	1, 2, 3	14	12, 13, 16
12	7, 10, 11, 13	10	7, 8, 13	12	7, 11, 13	13	5, 6, 14	15	13, 14
13	7, 10, 11, 12	12	7, 10, 11, 13	13	7, 11, 12	14	6, 7, 13	16	12, 13, 14
14	6, 7, 8, 11	13	7, 10, 11, 12	15	3, 4, 5	15	7, 8, 9	17	7, 8, 9
15	2, 3, 4	14	6, 7, 8, 11					18	3, 4, 5
		15	2, 3, 4					19	4, 8, 10
								20	8, 9, 10, 11

perbenzoic acid (*m*-CPBA) oxidation was carried out to give the epoxide **25**. X-ray crystallographic analysis of **25** was performed and gave the corresponding ORTEP drawing as shown in Figure 1. Accordingly, the tertiary hydroxyl group at C-3 is α-oriented. Thus, the structure of infuscol A (**1**) was established as 3α-hydroxycupar-1-ene, and that of infuscol B (**2**) as 3*β*-hydroxycupar-1-ene, based on the phase-sensitive NOESY spectrum of **2** (Figure 2).

The molecular formula $C_{15}H_{26}O_3$ (observed *m*/*z* 254.1859) from the HREIMS of infuscol C (**3**) indicated three degrees of unsaturation. Its IR spectrum showed the presence of a hydroxy group. The ^{1}H NMR spectrum (Table 1) of **3** confirmed three methine protons (*δ* 2.92 dd, 3.33 dd, 3.57 br s) connected to oxygen atoms and four tertiary methyls. Fifteen carbon signals were present in the ^{13}C NMR spectrum (Table 2), and its DEPT spectrum showed three methines (*δ* 56.2, 58.4, 72.3) bearing oxygen atoms, one quaternary carbon (*δ* 68.2) bearing an oxygen atom, four methyls, four methylenes, a methine, and two quaternary carbons. This spectral evidence suggested that **3** is a tricyclic sesquiterpenoid bearing secondary and tertiary hydroxy groups and one epoxide. Analysis of its ^{1}H−^{1}H COSY, HMQC, and HMBC spectra (Figure 3) led to the structure of **3** as depicted. As the phase-sensitive NOESY spectrum of **3** did not provide clear information on its stereochemistry, X-ray crystallographic analysis was carried out and an ORTEP structure is shown in Figure 4. Accordingly, the structure of infuscol C (**3**) was established as 1*β*,2*β*-epoxycupara-3*β*,4α-diol.

As the IR and ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) of **4**, $C_{15}H_{26}O_3$ (observed *m*/*z* 254.1877 $[M]^+$), closely resembled those of **3**, the structure of **4** was presumed to



be a cuparene-type sesquiterpenoid with secondary and tertiary hydroxy groups and one epoxide. The detailed analysis of the $^1H-^1H$ COSY, HMQC, and HMBC NMR spectra suggested the same gross structure for **4** as that of compound **3**. Furthermore, the orientation of the hydroxy group at C-4 was confirmed to be β with an equatorial conformation, in agreement with the observed coupling constants (ddd, J = 11.8, 10.4, 3.8 Hz). The above spectral data suggested that compound **4** is the C-4 epimer of **3**. The phase-sensitive NOESY spectrum of **4** showed NOEs between (i) H-6 and H-1, H-4α, (ii) H-15 and H-2, H-4α, (iii) H-2 and H-1, and (iv) H-14 and H-5β, respectively. Thus, the structure of infuscol D (**4**) was established as 1β,2β-epoxycupara-3β,4β-diol.

The LCMS of infuscol E (**5**) displayed a sodiated molecular ion at m/z 261 $[M + Na]^+$, and its IR spectrum showed the presence of a hydroxy group. The ^1H and ^{13}C NMR spectra (Tables 2 and 4) indicated a disubstituted double bond (δ_H 5.64 ddd, 5.75 ddd; δ_C 131.4, 134.4 each d), a methine (δ_H 3.78 br s; δ_C 73.6) connecting a hydroxy group, and one quaternary carbon (δ_C 68.8) connecting a hydroxy group, as well as four tertiary methyls, four methylenes, three methines, and two quaternary carbons. Since the above spectral data were similar to those of compounds **1**, **2**, **15**, and **16**, the structure of **5** was presumed to be a cuparane-type sesquiterpenoid with secondary and tertiary hydroxy groups. The detailed analysis of $^1H-^1H$ COSY, HMQC, and HMBC (Figure 5) spectra of **5** led to the determination that this compound is a 3,4-dihydroxy-1-cuparene derivative. The signal of H-4 was observed as a broad singlet in the ^1H NMR spectrum, so therefore the orientation of the hydroxy group at C-4 must be axial. The phase-sensitive NOESY spectrum of **5** showed NOEs between (i) H-1 and H-6, H-8α, H-8β, (ii) H-6 and H-5α, H-8α, H-13, (iii) H-12 and H-5α, H-5β, H-13, H-14, (iv) H-14 and H-4β, H-5β, H-8β, H-10β, and (v) H-4 and H-5α, H-5β, H-15, respectively. Thus, infuscol E (**5**) was elucidated as 3β,4α-dihydroxy-1-cuparene.

The IR spectrum of **6** showed the presence of a hydroxy group, and its molecular formula was determined to be

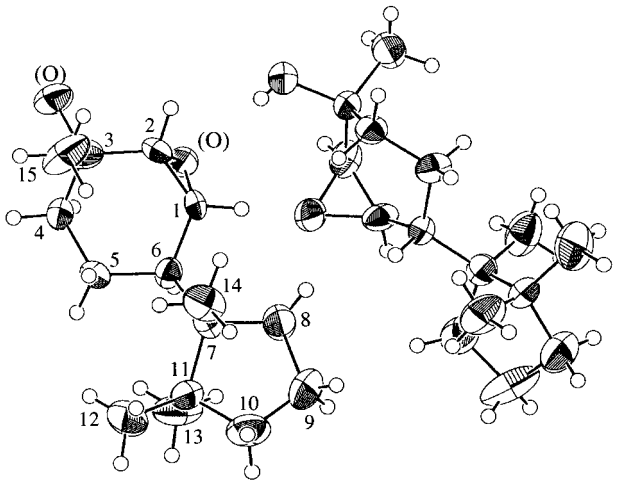


Figure 1. ORTEP drawing of **25**. Anisotropic ellipsoids are represented by a 50% probability level.

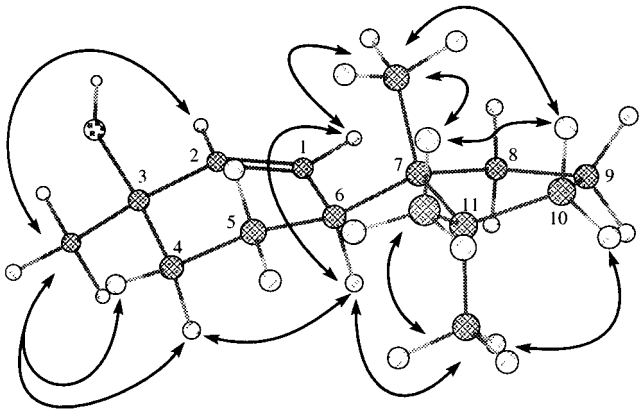


Figure 2. NOE correlations of **2**.

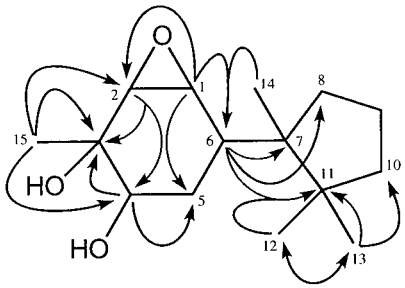


Figure 3. Long-range $^1H-^{13}C$ correlations of **3**.

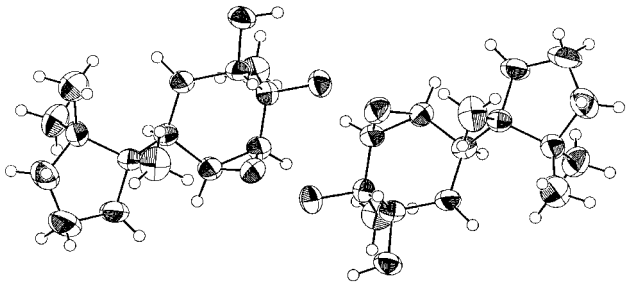


Figure 4. ORTEP drawing of **3**. Anisotropic ellipsoids are represented by a 50% probability level.

Table 4. ^{1}H NMR Data of **5**−**7** and **20** (600 MHz, $CDCl_3$)[a]

position	5	6	7[b]	20[b,c]
1	5.75 ddd (10.4, 2.5, 1.4)	5.81 dd (10.2, 1.4)	1.62−1.70 m α 2.12 ddd (12.8, 12.8, 8.8, 1.8) β	0.46 dd (4.8, 3.3) 0.69−0.78 m
2	5.64 ddd (10.4, 2.7, 1.6)	6.13 dd like (10.2, 3.0)	1.31 m 1.47−1.62 m	0.69−0.78 m
4	3.78 br s	4.41 s like	0.88−0.93 m	1.22 br t like 1.31−1.42 m
5	1.90 dddd (13.7, 6.3, 5.2, 1.1) α 1.96 ddd (13.7, 9.3, 2.7) β	2.13 dddd (13.5, 3.8, 3.8, 1.4) α 1.56 ddd (13.7, 11.0, 2.7) β	0.20 dd (5.5, 3.7) α 0.97 m β	1.44−1.53 m 1.68 br q like
6	2.45 ddd (10.4, 6.3, 2.7)	2.64 br d like		
8	1.79 br q like α 1.69 ddd (12.6, 9.3, 3.6) β	1.83 br q like α 1.75 ddd (13.2, 9.2, 4.1) β	0.88−0.93 m 1.47−1.61 m	0.69−0.78 m 1.31−1.42 m
9	1.57−1.65 m	1.60−1.68 m	1.47−1.61 m 1.62−1.70 m	1.44−1.53 2H, m
10	1.38 ddd (12.4, 8.8, 3.6) α 1.72 br q like β	1.39 ddd (12.1, 8.8, 3.0) α 1.72 br t like β	1.38 m 1.62−1.70 m	1.31−1.42 m 1.59 br q like
12	1.02 s	1.00 s	0.96 s	0.94 s
13	0.98 s	1.01 s	1.00 s	0.95 s
14	0.80 s	0.78 s	1.06 s	0.86 s
15	1.33 s	4.92 s 5.01 s	1.30 s	1.27 s

[a] *J* values (in Hz) in parentheses. [b] Measured by 400 MHz. [c] Measured in C_6D_6.

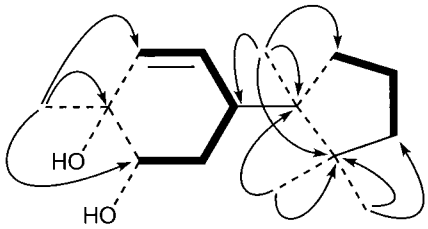


Figure 5. ^{1}H−^{1}H correlations (bold line) and long-range ^{1}H−^{13}C correlations (arrows) of **5**.

$C_{15}H_{24}O$ (observed *m*/*z* 220.1798) by HREIMS. The ^{1}H and ^{13}C NMR spectra (Tables 2 and 4) of **6** confirmed the presence of an exomethylene (δ_H 4.92 s, 5.01 s; δ_C 113.0 t, 144.6 s) and a disubstituted double bond (δ_H 6.13 ddd, 5.81 dd; δ_C 126.4 d, 135.3 d), a methine (δ_H 4.41 s like; δ_C 69.9) bearing a hydroxy group, three tertiary methyls, four methylenes, a methine, and two quaternary carbons. The above spectral data of **6** were similar to those of compounds **1**−**5**, indicating that it is a cuparane-type sesquiterpenoid. A detailed analysis of the ^{1}H−^{1}H COSY, HMQC, and HMBC spectra led to the structure of **6** being determined as 4-hydroxycupar-1,3(15)-diene. Moreover, the relative stereochemistry was clarified by the phase-sensitive NOESY spectrum as shown in Figure 6. Thus, the structure of **6** was established as (+)-*δ*-cuprenen-4α-ol.

The HREIMS spectrum of **7** showed the molecular formula $C_{15}H_{26}O$ (observed *m*/*z* 222.1968 $[M]^+$). Its physicochemical data were identical to that of cyclopropanecuparenol (**26**) isolated from *Marchantia polymorpha*[15] except for the optical rotation (**7**, $[\alpha]_D$ +15.0° *c* 1.15; **26**,[15] $[\alpha]_D$ −14.3° *c* 4.19). Therefore, compound **7** should be the enantiomer of cyclopropanecuparenol (**26**). A complete assignment of the ^{13}C NMR spectrum (Table 2) of **7** was accomplished by interpretation of the ^{1}H−^{1}H COSY, HMQC, and HMBC spectra. It remains to ascertain the stereochemistry of the cyclopropane ring.

The ^{1}H NMR spectrum (Table 5) of **8** indicated the presence of one olefinic proton (*δ* 5.46 m), a methine proton (*δ* 4.29 br s) on a carbon bearing a hydroxy group, one tertiary methyl, and three secondary methyls. The ^{13}C NMR (Table 2) and DEPT spectra of **8** displayed a methine (*δ* 69.3) bearing the hydroxy group, a trisubstituted double bond (*δ* 124.6 d, 135.1 s), four methyls, four methylenes, three methines, and a quaternary carbon. The IR spectrum showed a hydroxy group, and its molecular formula was

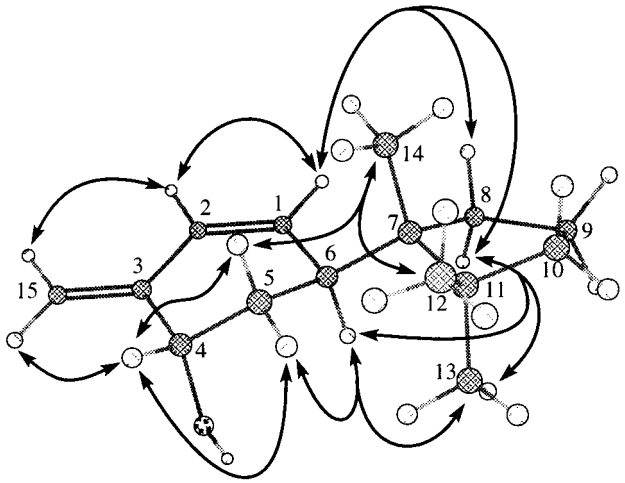


Figure 6. NOE correlations of **6**.

established as $C_{15}H_{26}O$ by the HREIMS, indicating a bicyclic sesquiterpenoid. The above evidence and the ^{1}H−^{1}H COSY, HMQC, and HMBC spectra (Figure 7) of **8** suggested an acorane-type sesquiterpenoid bearing a secondary hydroxy group at C-3. The relative stereochemistry was clarified by the phase-sensitive NOESY spectrum as shown in Figure 8. Additionally, analysis of the ^{1}H and ^{13}C NMR spectra of the enone **27** derived from **8** by oxidation resulted in a product completely identical to (−)-acorenone (**28**), for which the absolute structure has been reported previously,[16,17] but the sign of the optical rotation of **27** ($[\alpha]_D$ +35.1° *c* 1.13) was opposite that of **28**[16] ($[\alpha]_D$ −22.0° *c* 0.05). Thus, the absolute configuration of **27** was elucidated as (1*R*,7*R*,10*R*)-4-acoren-3-one, and that of **8** was established as (+)-(3*R*)-hydroxy-4-acorene.

The molecular formula $C_{15}H_{24}O_2$ (observed *m*/*z* 236.1772 $[M]^+$) of secoinfuscanal (**9**) was determined by HREIMS, suggesting four degrees of unsaturation, and its IR spectrum exhibited a carbonyl group peak. The ^{1}H NMR spectrum (Table 5) of **9** showed a formyl proton (*δ* 9.29 s), an olefinic proton (*δ* 6.21 t), and an olefinic and three secondary methyl protons (*δ* 1.76, 0.65, 0.85, 0.89 each s). Its ^{13}C NMR (Table 2) and DEPT spectra displayed two carbonyl carbons (*δ* 194.0 d, 210.2 s), two trisubstituted olefinic carbons (*δ* 139.7 s, 152.2 d), and signals due to four methyls, three methylenes, and four methines. The above spectral evidence suggested the structure for **9** of a mono-

Table 5. ^{1}H NMR Data of **8**, **9**, and **10** (600 MHz, $CDCl_3$)[a]

position	**8**	**9**[b]	**10**
1		1.57 ddd (11.0, 7.7, 3.3)	
2	1.43 dd (13.2, 9.9)	2.15−2.20 m	1.72 m
	1.99 ddd (13.2, 6.3, 1.9)	2.39 quint. (7.7)	
3	4.29 br s	6.21 t like (7.3)	1.84 m α
			1.13 m *β*
4			1.48−1.56 2H, m
5	5.46 m	9.29 s	1.48−1.56 m
6	1.69−1.74 m		
	2.31 d sext. (18.1, 2.7)		
7	1.27 m	1.65−1.69 m	3.24 s
8	1.30−1.41 m	0.94−1.05 m	
	1.69−1.74 m	1.65−1.69 m	
9	1.30−1.41 m	0.94−1.05 m	1.17 m α
	1.62−1.68 m	1.40 dt like (10.4, 3.0)	1.81 m *β*
10	1.62−1.68 m	1.13 m	1.42 ddd (13.5, 13.5, 3.8) α
			1.31 dddd (13.5, 9.1, 4.4, 2.2) *β*
11	1.62−1.68 m	2.15−2.20 m	1.50 d (11.0) α
			0.93 dt (11.0, 2.2) *β*
12	0.87 d (6.6)	0.85 d (6.9)	0.83 d (6.9)
13	0.95 d (6.6)	0.89 d (6.6)	0.92 s
14	0.93 d (6.9)	0.65 d (6.3)	1.02 s
15	1.75 sext. (1.6)	1.76 d (0.8)	1.06 s

[a] *J* values (in Hz) in parentheses. [b] Measured in C_6D_6.

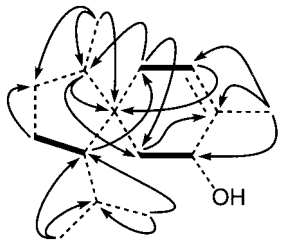


Figure 7. ^{1}H−^{1}H correlations (bold line) and long-range ^{1}H−^{13}C correlations (arrows) of **8**.

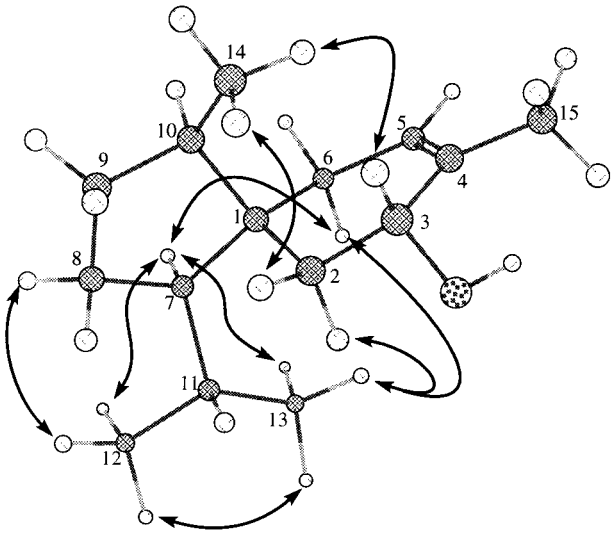


Figure 8. NOE correlations of **8**.

cyclic sesquiterpenoid bearing an aldehyde and a ketone. Its ^{1}H−^{1}H COSY and HMQC spectra indicated the presence of two partial segments: (i) $-CH_2-CH_2-CH(CH_3)-CH-CH_2-CH=$ and (ii) $CH_3-CH-CH_3$. To connect each segment, the analysis of the HMBC spectrum (Table 3) was carried out. Accordingly, compound **9** was assigned as a 5,6-*seco*-cadinane-type sesquiterpenoid bearing a formyl group at C-5 and a ketone at C-6. The phase-sensitive NOESY spectrum of **9** showed NOEs between (i) H-1 and H-7, H-9α, H-14, (ii) H-5 and H-3, (iii) H-14 and H-9α, H-9*β*, and (iv) H-15 and H-2, respectively. Accordingly, an *E* configuration was evident for the $\Delta^{3,4}$ double bond, and the secondary methyl at C-10 and the isopropyl group at C-7 were assigned as being *trans*-oriented. The CD spectrum of **9** indicated first positive (296 nm) and second positive (254 nm) Cotton effects. The absolute structure of secoinfuscanal was determined as shown in formula **9** by the application of the back octant rule of the first positive Cotton effect (296 nm) resulting from the C-6 ketone.[18]

The ^{1}H NMR spectrum (Table 5) of **10** showed a methine proton (*δ* 3.24 s) on the carbon bearing an oxygen atom, a secondary methyl (*δ* 0.83 d), and three tertiary methyl protons (*δ* 0.92, 1.02, 1.06 each s). The IR spectrum displayed a hydroxy group, and its molecular formula $C_{15}H_{26}O$ (observed *m*/*z* 222.1993 $[M]^+$) was established by HREIMS, indicating three degrees of unsaturation. The ^{13}C NMR spectrum (Table 2) showed 15 carbons, and its DEPT spectrum confirmed a methine (*δ* 85.6) bearing the hydroxy group, four methyls, five methylenes, two methines, and three quaternary carbons. The ^{1}H−^{1}H COSY spectrum of **10** indicated the presence of three partial segments: (i) $CH_3-CH-CH_2-CH_2-$, (ii) $-CH_2-CH_2-$, and (iii) $-CH_2-$. Moreover, the analysis of HMQC and HMBC spectra (Table 3) suggested that its gross structure was similar to the tricyclic sesquiterpenoids prelacinan-7-ol (**29**),[19] (−)-7*β*-hydroxy-2,6,8-tetramethyltricyclo[6.2.1.01,5]undecane (**30**),[20] and sesquithurifenol (**31**).[21] However, the ^{1}H and ^{13}C NMR spectra of **10** were not identical to any of the corresponding spectra of **29**−**31**. Therefore, the phase-sensitive NOESY spectrum was run in C_5D_5N (Figure 9) and the relative stereochemistry of **10** established. To determine the absolute configuration of **10**, its oxidation by pyridinium chlorochromate (PCC) was carried out to give a ketone **32** (*m*/*z* 220 $[M]^+$), with a carbonyl absorption at 1700 cm^{-1} in the IR spectrum. The CD spectrum of **32** indicated a negative Cotton effect (299 nm). Accordingly, the absolute structure of **32** was clarified as shown, applying the back octant rule.[18] Thus, the absolute configuration of **10** was established as *ent*-prelacinan-7*S*-ol.

The ^{1}H and ^{13}C NMR spectra of **11** were identical with those of (−)-kolavelool (**33**),[22,23] and this compound has also been isolated from *J. infusca*, collected in Kochi, Japan.[24] However, their optical rotations had opposite signs (**11**, $[\alpha]_D$ +59.1°; **33**,[22] $[\alpha]_D$ −40.4°). The chiral HPLC of **33** from Kochi and **11** showed that they were optically pure. To confirm the absolute configuration of **33**, its oxidation by

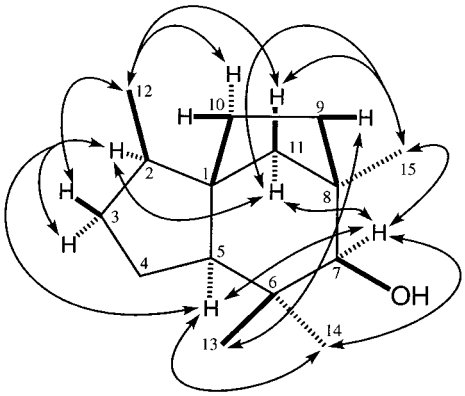


Figure 9. NOE correlations of **10**.

tert-butyl hydroperoxide (*t*-BuOOH)/PDC was carried out to yield the enone **34**. The spectral data of **34** and its X-ray crystallographic analysis were in complete agreement with those of (−)-13-*epi*-2-oxo-kolavelool (**34**), for which the absolute configuration has already been established by CD spectral, ORD spectral, and X-ray crystallographic analysis, when isolated from *Aristolochia chamissonis*.[25] Accordingly, the absolute configuration of (−)-kolavelool was determined as 5*R*, 8*R*, 9*S*, 10*R*, and 13*R*, as shown in formula **33**. Thus, the absolute configuration of *ent*-kolavelool (**11**) was established as *ent*-(13*S*)-hydroxy-3,14-clerodadiene.

The IR spectrum of **12** displayed a hydroxy group, and its molecular formula $C_{20}H_{34}O$ (observed *m*/*z* 290.2583 $[M]^+$) was determined by HREIMS. The ^1H NMR spectrum (Table 6) of **12** indicated four olefinic protons (*δ* 5.27 br s, 5.07 dd, 5.21 dd, 5.91 dd) corresponding to a trisubstituted double bond and a vinyl proton, and an olefinic methyl (*δ* 1.67), a secondary methyl, and three tertiary methyls. The ^{13}C NMR (Table 6) and DEPT spectra showed four olefinic carbons (*δ* 111.8 t, 145.3 d, 123.2 d, 139.9 s) for a vinyl group and a trisubstituted double bond, and a quaternary carbon (*δ* 73.5) bearing the hydroxy group, as well as five methyls, six methylenes, two methines, and two quaternary carbons. A detailed analysis of the $^1H-^1H$ COSY, HMQC, and HMBC (Table 3) spectra of **12** led to the same planar structure as compound **11**. However, the ^{13}C NMR spectrum of **12** was not in agreement with that of **11**. The C-19 signal (*δ* 33.1) in the ^{13}C NMR spectrum of **12** was deshielded with respect to the corresponding signal (*δ* 20.0) in the ^{13}C NMR spectrum of **11**, suggesting a *cis*-clerodane-type diterpenoid skeleton for **12**. The phase-sensitive NOESY spectrum of **12** showed NOEs between (i) H-19 and H-10, (ii) H-10 and H-1α, H-1*β*, and (iii) H-20 and H-2α, H-3, H-17. Thus, the structure of **12** was established as *cis*-3,14-clerodadien-13-ol. However, the stereochemistry at C-13 and absolute configuration of **12** remain to be determined.

The IR spectrum of **13**, which has the molecular formula $C_{20}H_{34}O$ (observed *m*/*z* 290.2583 $[M]^+$), displayed hydroxy group absorption. Its ^1H NMR spectrum (Table 6) showed three vinyl protons (*δ* 5.05, 5.20, 5.90), a secondary methyl (*δ* 0.82), and four tertiary methyls (*δ* 0.81, 0.95, 0.97, 1.27). The ^{13}C NMR (Table 6) and DEPT spectra showed two olefinic carbons (*δ* 132.3, 136.9) in a tetrasubstituted double bond, a quaternary carbon (*δ* 73.4) bearing an oxygen atom, two vinyl carbons (*δ* 111.6 t, 145.3 d), together with five methyls, seven methylenes, one methine, and three quaternary carbons. Subsequently, the detailed analysis of the $^1H-^1H$ COSY, HMQC, and HMBC spectra (Figure 10) indicated that compound **13** is a halimane-type diterpenoid with a hydroxy group at C-13 and $\Delta^{5,10}$ and $\Delta^{14,15}$ double bonds. However, the phase-sensitive NOESY spectrum of **13** did not provide clear information on the stereochemistry. Thus, the gross structure of **13** was determined as 5(10),14-halimadien-13-ol.

The ^1H and ^{13}C NMR spectra of **15** were identical with those of neocuprenenol (**15a**) isolated from *Jungermannia hattoriana*.[8] However, the stereochemistry of **15a** has not

Table 6. ^1H (600 MHz) and ^{13}C (150 MHz) NMR Data of **12** and **13** ($CDCl_3$)

	12		**13**	
position	^{13}C	^1H	^{13}C	^1H
1	17.7	1.75 br dd (13.2, 7.4)[a]	25.7	1.75 m
		2.01 m		1.91−2.00 m
2	24.1	1.95 m	20.0	1.51 m
		2.11 m		1.54−1.62 m
3	123.2	5.27 br s	40.0	1.28−1.40 m
				1.41−1.47 m
4	139.9		34.5	
5	36.9		136.9	
6	37.8	1.04 ddd (13.5, 13.5, 4.1)	25.2	1.90−2.00 2H, m
		1.99 dt (13.5, 3.3)		
7	28.8	1.17 q like	27.2	1.28−1.40 m
		1.20−1.28 m		1.41−1.47 m
8	37.3	1.36−1.45 m	33.5	1.54−1.62 m
9	39.9		40.2	
10	44.6	1.32 d (6.0)	132.3	
11	31.6	1.20−1.28 m	30.0	1.28−1.40 2H, m
		1.47 ddd (10.4, 10.4, 4.4)		
12	35.2	1.36−1.45 m	36.5	1.19 ddd (12.6, 12.6, 3.8)
				1.41−1.47 m
13	73.5		73.4	
14	145.3	5.91 dd (17.3, 10.7)	145.3	5.90 dd (17.3, 10.7)
15	111.8	5.07 dd (10.7, 1.1)	111.6	5.05 dd (10.7, 1.4)
		5.21 dd (17.3, 1.1)		5.20 dd (17.3, 1.4)
16	27.7	1.30 s	27.6	1.27 s
17	15.9	0.75 d (6.9)	16.1	0.82 d (6.9)
18	19.8	1.67 q like (1.9)	29.2[b]	0.95 s[b]
19	33.1	1.03 s	27.7[b]	0.97 s[b]
20	17.4	0.81 s	21.3	0.81 s

[a] *J* values (in Hz) in parentheses. [b] May be interchanged in each vertical column.

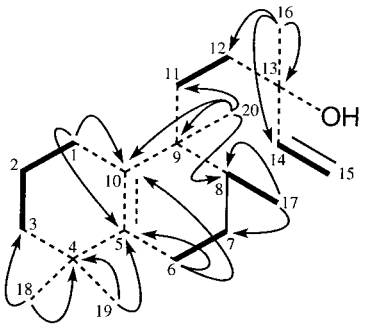


Figure 10. $^1H-^1H$ correlations (bold line) and long-range $^1H-^{13}C$ correlations (arrows) of **13**.

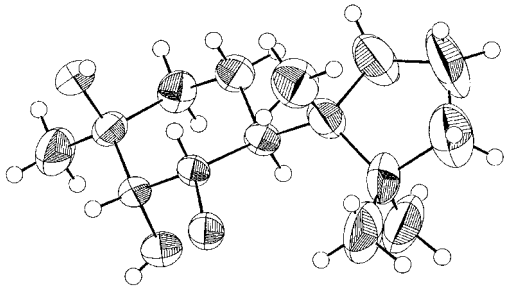


Figure 11. ORTEP drawing of **35**. Anisotropic ellipsoids are represented by a 50% probability level. The drawing shows one of four molecules in the unit cell.

been clarified previously. To determine its relative stereochemistry, the oxidation of **15** by AD-mix α was carried out to give the triol **35** (*m*/*z* 256 $[M]^+$). Suitable crystals were obtained so that X-ray crystallographic analysis could be performed (the ORTEP drawing is shown in Figure 11). Accordingly, the hydroxy group at C-3 of **15** clearly has a *β*-orientation and, consequently, is the epimer of (+)-cuprenenol (**16**).[9] Thus, compound **15a** should be renamed (+)-3-*epi*-cuprenenol, as drawn in the formula **15**, which was already reported as a reaction product.[9]

The absolute configurations of the new cuparane-type compounds **1**−**7** remain to be determined unambiguously. However, their absolute configurations are presumed to be the same as those of compounds **14**−**19**.

It is apparent that there are at least four chemotypes of *J. infusca*,[3−6] in which the following classes of compounds predominate: (i) kaurane-type, (ii) labdane- and clerodane-type, (iii) bis(bibenzyl)-type, and (iv) cuparane- and labdane-type. As the present acquisition contains cuparane-type sesquiterpenoids and clerodane- and labdane-type diterpenoids as the main components, it should be included in the fourth chemotype. Species belonging to the same genus of liverworts occasionally produce normal and enantiomeric terpenoids, and sometimes, the same species from different locations produces both enantiomers.[1−3] The present sample of *J. infusca* contained (+)-kolavelool (**11**) as the main component, while *J. infusca* collected in Kochi, Japan, contained (−)-kolavelool (**33**).[24] This is an interesting observation in relation to the biosynthesis of diterpenoids in *Jungermannia* species.

Experimental Section

General Experimental Procedures. Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. The specific rotations were measured on a JASCO DIP-1000 polarimeter with $CHCl_3$ as a solvent. The UV spectra were obtained on a Hitachi U-3000 spectrophotometer in MeOH solution. The CD spectra were recorded on a JASCO J-725 spectrometer in MeOH solution. IR spectra were measured on a JASCO FT/IR-5300 spectrophotometer by the diffuse reflectance method. All NMR spectra were recorded on a Varian Unity 200, a Varian Gemini 200 (200 MHz), a JEOL JNM GX400 (400 MHz), a JEOL Eclipse 400 (400 MHz), or a Varian Unity 600 (600 MHz) spectrometer, in $CDCl_3$, C_6D_6, or C_5D_5N as the solvent, with TMS (^1H NMR), δ 73.03 ($CHCl_3$, ^{13}C NMR), δ 128.00 (C_6H_6, ^{13}C NMR), and δ 149.83 (C_5H_5N, ^{13}C NMR) as internal references. The mass spectra including high-resolution mass spectra were recorded on a JEOL JMS AX-500 spectrometer (EIMS, CIMS, FABMS) or Hewlett-Packard HP-1100 instrument (LCMS). X-ray reflection data were collected with a Mac Science MXC18 diffractometer or a DIP Image diffractometer using Mo Kα radiation ($\lambda = 0.71073$ Å). Preparative HPLC was performed by a JASCO pump system. Column chromatography was carried out on silica gel 60 (0.2−0.5 mm, 0.04−0.063 mm, Merck), reversed-phase silica gel (Cosmosil 75 C_{18}−OPN, Nacalai Tesque), and Sephadex LH-20 (Amersham Pharmacia Biotech, CH_2Cl_2−MeOH, 1:1). Preparative medium-pressure liquid chromatography (MPLC) was performed with a Work-21 pump (Lab-Quatec Co., Ltd.) and carried out by Lobar column chromatography (Merck). TLC and preparative TLC were carried out on silica gel 60 F254 plates (Merck) and visualized by spraying with Godin reagent[26] followed by heating at 120 °C.

Plant Material. *Jungermannia infusca* (Mitt.) Steph. was collected in Wajiki-cho, Tokushima, Japan, in June 1996 and identified by Prof. M. Mizutani (The Hattori Botanical Laboratory, Miyazaki, Japan). A voucher specimen (N9660801) has been deposited at the Faculty of Pharmaceutical Sciences, Tokushima Bunri University.

Extraction and Isolation. The crude extract (6.3 g) extracted with Et_2O was divided into eight fractions by column chromatography on silica gel using a *n*-hexanes−EtOAc gradient. Fraction 1 was chromatographed on SiO_2 (*n*-hexanes−Et_2O, 97:3) impregnated with 10% $AgNO_3$ to give (+)-cuparene (**1**, 230 mg). Fraction 2 was chromatographed on SiO_2 (*n*-hexanes−EtOAc, 19:1) and divided into five fractions. Preparative medium-pressure liquid chromatography (MPLC) (Si gel 60, *n*-hexanes−EtOAc, 9:1) and reversed-phase SiO_2 (CH_3CN) of fraction 2-1 gave (1*S*,4*R*)-peroxycupar-2-ene (**17**, 51 mg) and (+)-3,6-peroxycupar-1-ene (**21a** and **21b**, 51 mg). Fraction 2-3 was chromatographed on reversed-phase SiO_2 (CH_3CN) to give *ent*-prelacinan-7*S*-ol (**10**, 46 mg) and a diterpene mixture. The mixture was purified to give 5(10),14-halimadien-13-ol (**13**, 5 mg) and *ent*-kauren-15α-ol (**24**, 3 mg) by preparative HPLC (ODS, CH_3CN). Preparative MPLC (RP-8, CH_3CN) of fraction 2-4 gave 8,14-labdadien-13*S*-ol (**23**, 92 mg) and a diterpene mixture. *cis*-3,14-Clerodadien-13-ol (**12**, 11 mg) was purified by preparative HPLC (Nucleosil 50-5, *n*-hexanes−Et_2O, 9:1; ODS, CH_3CN) of the diterpene mixture.

Fraction 3 was chromatographed on Sephadex LH-20 and SiO_2 (*n*-hexanes−EtOAc, 9:1) and divided into five fractions. Secoinfuscanal (**9**, 16 mg) and (+)-kolavelool (**11**, 243 mg) were purified by preparative MPLC (Si gel 60, *n*-hexanes−Et_2O, 17:3; CN, CH_3CN) and preparative HPLC (5-ODS-H, CH_3CN) of fraction 3-2. Fraction 3-3 was chromatographed by preparative MPLC (RP-18, CH_3CN) and preparative HPLC (Nucleosil 50-5, *n*-hexanes−EtOAc or *n*-hexanes−Et_2O; ODS, CH_3CN) to give (+)-(3*R*)-hydroxy-4-acorene (**8**, 9 mg) and *ent*-viridiflorol (**22**, 22 mg). Chromatography on reversed-phase SiO_2 (CH_3CN) and preparative HPLC (Nucleosil 50-5, *n*-hexanes−EtOAc, 9:1) of fraction 3-4 gave infuscol B (**2**, 62 mg), *ent*-cyclopropanecuparenol (**7**, 13 mg), and (+)-3-*epi*-cuprenenol (**15**, 8 mg). Fraction 3-5 was rechromatographed by preparative MPLC (CN, *n*-hexanes−Et_2O, 19:1) and preparative HPLC (5-ODS-H, CH_3CN) to yield (+)-*δ*-cuprenen-4α-ol (**6**, 10 mg).

Fraction 4 was chromatographed on Sephadex LH-20 and SiO_2 (*n*-hexanes−EtOAc, 17:3) and divided into seven fractions. *epi*-Cuparadiepoxide (**18**, 38 mg) was purified by preparative MPLC (RP-18, CH_3CN) and preparative HPLC (5-ODS-H, CH_3CN) of fraction 4-3. Preparative MPLC (RP-18, CH_3CN) and preparative HPLC (Nucleosil 50-5, *n*-hexanes−

EtOAc, 4:1) of fraction 4-4 gave (+)-cuprenenol (**16**, 20 mg) and infuscol A (**1**, 88 mg).

Fraction 5 was rechromatographed on Sephadex LH-20 and preparative MPLC (Si gel 60, *n*-hexanes−EtOAc; Diol, CH_2Cl_2−EtOAc) to yield rosulantol (**19**, 84 mg) and microbiotol (**20**, 16 mg).

Repeated chromatography by preparative MPLC and preparative HPLC of fraction 6 gave infuscol D (**4**, 1 mg) and infuscol E (**5**, 13 mg). Infuscol C (**3**, 7 mg) was purified by chromatography on Sephadex LH-20, SiO_2, and MPLC (RP-18, CH_3CN) of fraction 7.

Infuscol A (1): colorless needles (from *n*-hexane); mp 73−75 °C; $[\alpha]^{23}_D$ −6.7° (*c* 1.06); FTIR ν_{max} 3304 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; positive FABMS *m/z* 245 [M + Na]$^+$, *m/z* 261 [M + K]$^+$; EIMS *m/z* 204 [M − H_2O]$^+$ (49), 189 (10), 161 (18), 145 (39), 132 (100), 119 (92), 93 (39), 77 (17), 69 (71), 55 (40), 40 (25); HREIMS *m/z* 204.1890 [M − H_2O]$^+$ (calcd for $C_{15}H_{24}$, 204.1878).

Infuscol B (2): colorless oil; $[\alpha]^{19}_D$ +35.7° (*c* 1.11); FTIR ν_{max} 3315 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78 (3H, s, H-14), 0.96 (3H, s, H-13), 1.01 (3H, s, H-12), 1.26 (3H, s, H-15), 1.37 (1H, ddd, *J* = 12.1, 8.8, 3.3 Hz, H-10α), 1.49 (1H, ddd, *J* = 14.0, 14.0, 2.7 Hz, H-4α), 1.55 (1H, m, H-5*β*), 1.58−1.65 (2H, m, H-8, H-9), 1.66−1.76 (3H, m, H-8, H-9, H-10*β*), 1.77 (1H, m, H-5α), 1.83 (1H, d quit. like, *J* = 12.9, 1.9 Hz, H-4*β*), 2.15 (1H, m, H-6), 5.65 (1H, dt, *J* = 10.2, 1.4 Hz, H-1), 5.67 (1H, dt, *J* = 10.2, 1.9 Hz, H-2); ^{13}C NMR (50 MHz, $CDCl_3$) δ 133.5 (C-1), 134.4 (C-2), 66.6 (C-3), 37.7 (C-4), 20.9 (C-5), 44.3 (C-6), 47.4 (C-7), 39.4 (C-8), 19.1 (C-9), 42.2 (C-10), 43.8 (C-11), 25.0 (C-12), 24.3 (C-13), 17.7 (C-14), 29.7 (C-15); FABMS *m/z* 245 [M + Na]$^+$, 261 [M + K]$^+$; EIMS *m/z* 204 [M − H_2O]$^+$ (57), 189 (8), 161 (11), 134 (22), 111 (98), 91 (100), 77 (62), 69 (77), 55 (80), 41 (85); HREIMS *m/z* 204.1852 [M − H_2O]$^+$ (calcd for $C_{15}H_{24}$, 204.1878).

Infuscol C (3): colorless needles (from *n*-hexane); mp 140−142 °C; $[\alpha]^{21}_D$ +3.7° (*c* 0.71); FTIR ν_{max} 3395 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; EIMS *m/z* 254 [M]$^+$ (2), 236 (10), 218 (80), 200 (21), 175 (29), 136 (95), 121 (53), 111 (68), 95 (87), 82 (53), 69 (100), 55 (71), 43 (95); HREIMS *m/z* 254.1859 [M]$^+$ (calcd for $C_{15}H_{26}O_3$, 254.1882).

Crystal Data for 3. Data collection: MXC (MAC Science). Cell refinement: MXC (MAC Science). Data reduction: *CRYSTAN*. Program used to solve structure: *CRYSTAN SIR92*. Refinement: full matrix least-squares. Diffractometer: Mac Science MXC18. $C_{15}H_{26}O_3$, MW = 254, triclinic, space group P_1, *a* = 6.310(9) Å, *b* = 7.355(11) Å, *c* = 17.378(36) Å, α = 80.572998(0)°, *β* = 89.844002(70)°, *γ* = 64.16799 (80)°, *V* = 713.900024 (0) Å^3, *Z* = 2, Mo Kα radiation, *λ* = 0.71073 Å, *θ* = 1−20°, *μ* = 0.75 mm^{-1}, 1780 reflections, 328 parameters; only coordinates of H atoms were refined, *R* = 0.071, R_w = 0.103, *S* = 1.508.

Infuscol D (4): amorphous; $[\alpha]^{20}_D$ +34.4° (*c* 0.43); FTIR ν_{max} 3393 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; EIMS *m/z* 254 [M]$^+$ (5), 236 (18), 218 (8), 193 (10), 175 (23), 163 (9), 137 (14), 125 (25), 111 (50), 95 (41), 87 (100), 69 (62), 55 (35), 43 (50); HREIMS *m/z* 254.1877 [M]$^+$ (calcd for $C_{15}H_{26}O_3$, 254.1882).

Infuscol E (5): amorphous; $[\alpha]^{20}_D$ +10.5° (*c* 0.97); FTIR ν_{max} 3368 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 4; LCMS (ES-API) *m/z* 261 [M + Na]$^+$; EIMS *m/z* 238 [M]$^+$ (2), 202 (16), 167 (11), 149 (29), 132 (46), 111 (100), 95 (36), 81 (18), 69 (91), 55 (60); HREIMS *m/z* 238.1925 [M]$^+$ (calcd for $C_{15}H_{26}O_2$, 238.1932).

(+)-*δ*-Cuprenen-4α-ol (6): colorless oil; $[\alpha]^{19}_D$ +88.7° (*c* 1.18); FTIR ν_{max} 3350 cm^{-1}; UV (EtOH) λ_{max} (log ϵ) 233 nm (4.05) (*c* 1.6 × 10^{-4}); ^{1}H and ^{13}C NMR data, see Tables 4 and 2; EIMS *m/z* 220 [M]$^+$ (2), 202 (48), 187 (9), 159 (10), 145 (43), 132 (100), 111 (54), 91 (28), 77 (9), 69 (31), 55 (17), 41 (10); HREIMS *m/z* 220.1798 [M]$^+$ (calcd for $C_{15}H_{24}O$, 220.1827).

***ent*-Cyclopropanecuparenol (7):** amorphous; $[\alpha]^{19}_D$ +15.0° (*c* 1.15); FTIR ν_{max} 3383 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 4 and 2; ^{1}H NMR (C_5D_5N, 600 MHz) δ 1.79 (1H, dd, *J* = 13.5, 8.8 Hz, H-1α), 2.37 (1H, dddd, *J* = 12.1, 12.1, 8.5, 1.6 Hz, H-1*β*), 1.34−1.39 (2H, m, H-2, H-10), 1.61−1.67 (2H, m, H-2, H-10), 1.15 (1H, ddd, *J* = 8.5, 4.1, 1.1 Hz, H-4), 0.23 (1H, dd, *J* = 5.8, 4.4 Hz, H-5α), 0.95 (1H, ddd, *J* = 7.4, 5.5, 1.4 Hz, H-5*β*), 0.92 (1H, m, H-8), 1.49−1.56 (3H, m, H-8, H-9), 1.00 (3H, s, H-12), 1.02 (3H, s, H-13), 1.22 (3H, s, H-14), 1.51 (3H, s, H-15); EIMS *m/z* 222 [M]$^+$ (2), 204 (40), 189 (21), 161 (24), 133 (31), 111 (100), 94 (68), 79 (26), 69 (82), 55 (43), 41 (26); HREIMS *m/z* 222.1968 [M]$^+$ (calcd for $C_{15}H_{26}O$, 222.1984).

(+)-(3*R*)-Hydroxy-4-acorene (8): amorphous; $[\alpha]^{19}_D$ +12.6° (*c* 0.76); FTIR ν_{max} 3312 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 5; CIMS (CH_4) *m/z* 222 [M]$^+$; EIMS *m/z* 222 [M]$^+$ (2), 204 (23), 189 (7), 159 (100), 144 (7), 119 (82), 105 (56), 91 (19), 77 (8), 55 (12), 44 (21); HREIMS *m/z* 222.1980 [M]$^+$ (calcd for $C_{15}H_{26}O$, 222.1984).

Secoinfuscanal (9): colorless oil; $[\alpha]^{19}_D$ −28.0° (*c* 2.03); FTIR ν_{max} 1680, 1641 cm^{-1}; UV (EtOH) λ_{max} (log ϵ) 230 nm (3.90) (*c* 2.36 × 10^{-5}); CD (EtOH) $\Delta\epsilon_{296nm}$ +0.82, $\Delta\epsilon_{254nm}$ +0.48 (*c* 2.3 × 10^{-5}); ^{1}H and ^{13}C NMR data, see Tables 2 and 5; EIMS *m/z* 236 [M]$^+$ (40), 193 (37), 175 (17), 165 (100), 147 (51), 123 (35), 109 (48), 95 (64), 84 (57), 69 (46), 55 (67), 41 (72); HREIMS *m/z* 236.1772 [M]$^+$ (calcd for $C_{15}H_{24}O_2$, 236.1777).

(−)-*ent*-Prelacinan-7*S*-ol (10): amorphous; $[\alpha]^{19}_D$ −4.9° (*c* 4.19); FTIR ν_{max} 3450 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 5; ^{1}H NMR (C_5D_5N, 400 MHz) δ 1.71 (1H, m, H-2), 1.15 (1H, m, H-3*β*), 1.84 (1H, m, H-3α), 1.50−1.61 (3H, m, H-4, H-4, H-5), 3.43 (1H, d, *J* = 1.6 Hz, H-7), 1.22 (1H, m, H-9α), 2.22 (1H, dddd, *J* = 13.7, 8.8, 4.9, 2.2 Hz, H-9*β*), 1.37 (1H, m, H-10α), 1.41 (1H, m, H-10*β*), 0.93 (1H, dt, *J* = 10.7, 2.2 Hz, H-11α), 1.53 (1H, d, *J* = 10.7 Hz, H-11*β*), 0.85 (3H, d, *J* = 6.9 Hz, H-12), 1.20 (3H, s, H-13), 1.19 (3H, s, H-14), 1.29 (3H, s, H-15); ^{13}C NMR (C_5D_5N, 150 MHz) δ 53.5 (C-1), 39.3 (C-2), 31.6 (C-3), 21.9 (C-4), 58.7 (C-5), 38.7 (C-6), 84.6 (C-7), 46.0 (C-8), 30.0 (C-9), 23.2 (C-10), 49.8 (C-11), 14.6 (C-12), 16.9 (C-13), 33.9 (C-14), 25.8 (C-15); EIMS *m/z* 222 [M]$^+$ (94), 207 (22), 191 (100), 179 (29), 166 (24), 149 (17), 135 (35), 121 (81), 108 (85), 95 (48), 81 (54), 69 (34), 55 (26), 43 (29), 32 (35); HREIMS *m/z* 222.1993 [M]$^+$ (calcd for $C_{15}H_{26}O$, 222.1984).

(+)-Kolavelool (11): colorless oil; $[\alpha]^{18}_D$ +59.1° *c* 0.68 (**33**: $^{22}[\alpha]_D$ −40.4°); ^{1}H and ^{13}C NMR, identical with authentic compound **33**;[22−24] CIMS (CH_4) *m/z* 291 [M − H_2O]$^+$; EIMS *m/z* 272 [M − H_2O]$^+$ (8), 257 (14), 189 (44), 175 (16), 147 (13), 135 (18), 121 (36), 107 (56), 95 (100), 81 (36), 69 (26), 55 (33), 40 (27); HREIMS *m/z* 272.2503 [M − H_2O]$^+$ (calcd for $C_{20}H_{32}$, 272.2504).

***cis*-3,14-Clerodadien-13-ol (12):** colorless oil; $[\alpha]^{19}_D$ −24.2° (*c* 1.00); FTIR ν_{max} 3391 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 6; EIMS *m/z* 290 [M]$^+$ (4), 272 (8), 229 (5), 204 (8), 191 (76), 175 (18), 161 (13), 135 (28), 121 (46), 107 (65), 95 (100), 81 (34), 67 (24), 55 (27), 41 (27); HREIMS *m/z* 290.2583 [M]$^+$ (calcd for $C_{20}H_{34}O$, 290.2609).

5(10),14-Halimadien-13-ol (13): colorless oil; $[\alpha]^{19}_D$ −124.1° (*c* 1.37); FTIR ν_{max} 3391 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 6; EIMS *m/z* 290 [M]$^+$ (1), 272 (2), 252 (2), 191 (100), 175 (8), 149 (7), 135 (13), 109 (11), 95 (13), 81 (8), 69 (13), 55 (9), 41 (8); HREIMS *m/z* 290.2617 [M]$^+$ (calcd for $C_{20}H_{34}O$, 290.2610).

Oxidation of 1. A solution of **1** (31.2 mg) and *m*-CPBA (60 mg) in CH_2Cl_2 (2 mL) was stirred for 3 h at room temperature. The reaction mixture was washed into 10% sodium thiosulfate, 5% sodium hydrogen carbonate, and saturated NaCl to give the epoxide **25** (34 mg).

1α,2α-Epoxycupar-3α-ol (25): colorless needles (from *n*-hexane); mp 86−88 °C; $[\alpha]^{22}_D$ +20.5° (*c* 0.86); FTIR ν_{max} 3375 cm^{-1}; ^{1}H NMR δ 3.18 (1H, dd, *J* = 4.0, 1.5 Hz, H-1), 2.97 (1H, d, *J* = 4.0 Hz, H-2), 1.50 (2H, m, H-4), 1.26 (1H, m, H-5), 1.54−1.74 (4H, m, H-5, H-9, H-9, H-10), 1.94 (1H, dd, *J* = 11.7, 6.6 Hz, H-6), 1.77 (1H, ddd, *J* = 13.2, 9.2, 4.4 Hz, H-8), 1.87 (1H, m, H-8), 1.36 (1H, m, H-10), 0.96 (3H, s, H-12), 0.94 (3H, s, H-13), 0.89 (3H, s, H-14), 1.32 (3H, s, H-15); ^{13}C NMR data, see Table 2; EIMS *m/z* 238 [M]$^+$ (2), 220 (8), 177 (23), 149 (21), 137 (41), 109 (100), 95 (56), 81 (51), 69 (76), 55 (59), 43 (90); HREIMS *m/z* 238.1926 [M]$^+$ (calcd for $C_{15}H_{26}O_2$, 238.1933).

Crystal Data for 25. Data collection: MXC (MAC science). Cell refinement: MXC (MAC science). Data reduction: MaXus. Program used to solve structure: maXus *SIR92*. Program used to refine structure: maXus. $C_{15}H_{26}O_2$, MW = 238, orthorhombic, space group $P2_12_12_1$, *a* = 20.136(5) Å, *b* = 21.347(5) Å, *c* = 6.694(2) Å, *V* = 2877.300049 (1) Å^3, *Z* = 8, Mo Kα radiation,

$\lambda = 0.71073$ Å, $\theta = 1-20°$, $\mu = 0.7$ mm^{-1}, 1437 reflections, 313 parameters; only coordinates of H atoms were refined, $R = 0.055$, $R_w = 0.066$, $S = 2.091$.

Oxidation of 8. To a solution of **8** (3.9 mg) in dry CH_2Cl_2 (1.5 mL) was added pyridinium dichromate (PDC, 5 mg), and the mixture was stirred for 4 h at room temperature. Workup as usual gave the ketone **27** (2.3 mg). The spectral data of **27** were completely identical with those of (−)-acorenone (**28**)[16,17] except for the optical rotation (**27**, $[\alpha]_D$ +35.1° *c* 1.13; **28**,[16] $[\alpha]_D$ −22.0 *c* 0.05, $CHCl_3$).

Oxidation of 10. To a solution of **10** (20 mg) in dry CH_2Cl_2 (2 mL) was added PCC (10 mg), and the reaction mixture was stirred for 12 h at room temperature. Workup as usual gave a reaction mixture, which was chromatographed on SiO_2 (*n*-hexanes−EtOAc, 9:1) to yield a ketone **32** (16.3 mg).

***ent*-Prelacinan-7-one (32):** colorless oil; $[\alpha]^{19}_D$ −66.0° (*c* 4.81); FTIR ν_{max} 1700 cm^{-1}; CD (EtOH) $\Delta\epsilon_{299}$ −1.27 (*c* 9.1 × 10^{-4}, EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (3H, d, J = 6.6 Hz, H-12), 1.08 (3H, s, H-14), 1.10 (3H, s, H-15), 1.12 (3H, s, H-13), 1.26 (1H, m), 1.30 (1H, dt, J = 11.4, 1.8 Hz), 1.51−1.67 (4H, m), 1.68−1.89 (4H, m), 1.84 (1H, m), 1.94 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.3 (C-1), 38.8 (C-2), 31.1 (C-3), 21.4 (C-4), 59.2 (C-5), 45.9 (C-6), 220.0 (C-7), 52.9 (C-8), 35.3 (C-9), 22.0 (C-10), 46.8 (C-11), 14.3 (C-12), 21.6 (C-13), 29.3 (C-14), 24.6 (C-15); EIMS *m/z* 220 $[M]^+$ (45), 205 (8), 192 (73), 177 (13), 159 (5), 147 (39), 135 (21), 121 (100), 108 (57), 93 (20), 81 (66), 69 (21), 55 (18), 41 (18); HREIMS *m/z* 220.1830 $[M]^+$ (calcd for $C_{15}H_{24}O$, 220.1827).

Oxidation of 15. AD-mix-α (100 mg) and methansulfonamide (10 mg) were added to the mixed solvent of *t*-BuOH (10 mL) and H_2O (1 mL), and the mixture was cooled to 0 °C with stirring. Compound **15** (8 mg) was added, and stirring was carried out at 0 °C for 14 days. Sodium sulfite (100 mg) was added, and the mixture extracted with EtOAc. The EtOAc layer was washed with 2 N KOH and saturated NaCl and dried over anhydrous magnesium sulfate. The crude product was purified by silica gel column chromatography (*n*-hexane−EtOAc, 1:1) to give the triol **35** (2 mg).

(+)-Cupara-3*β*,4α,5α-triol (35): colorless needles (from *n*-hexane); mp 136−138 °C; $[\alpha]^{19}_D$ +10.9° (*c* 0.47); FTIR ν_{max} 3380 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (3H, s, H-14), 0.97 (3H, s, H-13), 1.11 (3H, s, H-12), 1.31 (3H, s, H-15), 1.39−1.49 (4H, m), 1.50−1.55 (3H, m), 1.68 (1H, dd, J = 13.7, 4.4 Hz), 1.71−1.84 (3H, m), 2.34 (1H, OH), 3.51 (1H, br s, H-4), 3.93 (1H, m, H-5); EIMS *m/z* 256 $[M]^+$ (2), 238 (28), 220 (16), 209 (20), 191 (8), 177 (16), 162 (26), 137 (16), 127 (25), 111 (75), 95 (69), 82 (97), 69 (100), 55 (62), 43 (65); HREIMS *m/z* 256.2046 $[M]^+$ (calcd for $C_{15}H_{28}O_3$, 256.2038).

Crystal Data for 35. Data collection: DIP Image plate. Data reduction: maXus *SIR92*. Program used to solve structure: maXus. Program used to refine structure: maXus. DIP Image plate diffractometer. $C_{15}H_{28}O_3$, MW = 256, monoclinic, space group $P2_1$, $a = 11.787$ Å, $b = 23.145$ Å, $c = 12.277$ Å, $\beta = 112.591003°$, $V = 3092.399902$ Å^3, $Z = 8$, Mo Kα radiation, $\lambda = 0.71073$ Å, $\theta = 1-20°$, $\mu = 0.74$ mm^{-1}, 3274 reflections, 672 parameters; only coordinates of H atoms were refined, $R = 0.069$, $R_w = 0.144$, $S = 2.403$.

Allylic Oxidation of 33. To a solution of **33** (20 mg) in benzene (3 mL) was added Celite (150 mg), PDC (60 mg), and *tert*-butyl hydroperoxide (0.02 mL), and the reaction mixture was stirred for 15 min at 0 °C and then for 6 h at room temperature. The reaction mixture was filtered and chromatographed on silica gel (*n*-hexanes−EtOAc, 3:2) to yield the ketone **34** (12 mg), the spectral data of which were completely identical with published data.[23]

Acknowledgment. We thank Dr. M. Mizutani (Hattori Botanical Laboratory, Miyazaki, Japan) for the identification of the species. We also thank Professor Lucia M. X. Lopes (Universidade Estadual Paulista-UNESP, Araraquara, Brazil) for kindly providing ^{1}H and ^{13}C NMR spectra of compound **34**. Thanks are also due to Dr. M. Tanaka (TBU) and Miss Y. Okamoto (TBU) for measurements of 600 MHz NMR spectra and mass spectra.

References and Notes

(1) Asakawa, Y. In *Progress in the Chemistry of Organic Natural Products*; Herz W., Grisebach H., Kirby G. W., Eds.; Springer: Vienna, 1982; Vol. 42, pp 1−285.
(2) Asakawa, Y. In *Progress in the Chemistry of Organic Natural Products*; Herz W., Kirby G. W., Moore R. E., Steglich W., Tamm Ch., Eds.; Springer: Vienna, 1995; Vol. 65, pp 1−618.
(3) Nagashima, F.; Asakawa, Y. In *Recent Research Developments in Phytochemistry*; Pandalai S. G., Ed.; Research Signpost: Trivandrum, India, 1998; Vol. 2, Part II, pp 327−382.
(4) Wu, C.-L.; Lin, H.-R. *Phytochemistry* **1997**, *44*, 101−105.
(5) Nagashima, F.; Suzuki, M.; Takaoka, S.; Asakawa, Y. *Tetrahedron* **1999**, *55*, 9117−9132.
(6) Nagashima, F.; Suzuki, M.; Asakawa, Y. *Phytochemistry* **2001**, *56*, 807−810.
(7) Enzell, C.; Erdtman, H. *Tetrahedron* **1958**, *4*, 361−368.
(8) Nagashima, F.; Tanaka, S.; Takaoka, S.; Asakawa, Y. *Phytochemistry* **1997**, *45*, 353−363.
(9) Matsuo, A.; Terada, I.; Nakayama, M.; Hayashi, S. *Tetrahedron Lett.* **1977**, *43*, 3821−3824.
(10) Nagashima, F.; Suzuki, M.; Takaoka, S.; Asakawa, Y. *Chem. Pharm. Bull.* **1998**, *46*, 1184−1185.
(11) Tkachev, A. V.; Shakirov, M. M.; Raldugin, V. A. *J. Nat. Prod.* **1991**, *54*, 849−853.
(12) Konecny, K.; Streibl, M.; Vasicková, S.; Budesinsky, M.; Saman, D.; Ubik, K.; Herout, V. *Collect. Czech. Chem. Commun.* **1985**, *50*, 80−93.
(13) Bigley, D. B.; Rogers, N. A. J.; Barltrop, J. A. *J. Chem. Soc.* **1960**, 4613−4627.
(14) Matsuo, A.; Kodama, J.; Nakayama, M.; Hayashi, S. *Phytochemistry* **1977**, *16*, 489−490.
(15) Toyota, M. Chemical Constituents of *Marchantia polymorpha*, *Riccardia multifida* and *Plagiochila* genus (Hepaticae). Ph.D. Thesis, Tokushima Bunri University, Tokushima, Japan, 1987.
(16) Huang, Q.; Tezuka, Y.; Hatanaka, Y.; Kikuchi, T.; Nishi, A.; Tubaki, K. *Chem. Pharm. Bull.* **1995**, *43*, 1035−1038.
(17) Baldwin, S. W.; Fredericks, J. E. *Tetrahedron Lett.* **1982**, *23*, 1235−1238.
(18) Moffitt, W.; Woodward, W. B.; Moscowitz, A.; Klyne, W.; Djerassi, C. *J. Am. Chem. Soc.* **1961**, *63*, 4013−4018.
(19) Fukushi, Y.; Yajima, C.; Mizutani, J. *Tetrahedron Lett.* **1994**, *35*, 8809−8812.
(20) Selvakumar, N.; Subba, G. S. R. *J. Chem. Soc., Chem. Commun.* **1994**, 1303−1304.
(21) Barrero, A. F.; Enrique, A.-M.; Lara, A. *Tetrahedron Lett.* **1996**, *37*, 3757−3760.
(22) Misra, R.; Sukh, D. *Tetrahedron Lett.* **1968**, *22*, 2685−2686.
(23) Misra, R.; Pandey, R. C.; Sukh, D. *Tetrahedron* **1979**, *35*, 985−987.
(24) Nagashima, F.; Tamada, A.; Fujii, N.; Asakawa, Y. *Phytochemistry* **1997**, *46*, 1203−1208.
(25) Bomm, M. D.; Zuherman-Schpector, J.; Lopes, L. M. X. *Phytochemistry* **1999**, *50*, 455−461.
(26) Godin, P. *Nature* **1955**, *174*, 134.

NP010223I