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New Acorane- and Cuparane-type Sesqui- and New Labdane- and *seco*-Labdane-type Diterpenoids from the Japanese Liverwort *Jungermannia infusca* (Mitt.) Steph.

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Abstracts: A new acorane- and five new cuparane-type sesqui- and two new labdane- and two new *seco*-labdane-type diterpenoids have been isolated from the Japanese liverwort *Jungermannia infusca* (Mitt.) Steph., together with previously known sesqui- and diterpenoids. Their structures were determined by extensive NMR techniques, chemical degradation and X-ray crystallographic analysis.

INTRODUCTION

As part of search for novel chemical compounds and biologically active substances of bryophytes, we are continuing to study the chemical constituents of liverworts (Hepaticae).[1,2] The liverworts have cellular oil bodies, which contain many terpenoids and aromatic compounds. Generally almost all liverworts are small, particularly the *Jungermannia* species are morphologically very complex, so that their identification is quite difficult. The *Jungermannia* species are especially rich source of diterpenoids such as *ent*-kaurane-, labdane-, clerodane-, pimarane- and trachylobane-types.[3] It is known that they are generally classified in three chemo-types; kaurane-, clerodane-labdane- and bisbibenzyl-groups, of *Jungermannia infusca* (Mitt.) Steph.[3,4] We reinvestigated the chemical constituents of *J. infusca* collected in Tochigi Pref., Japan, in order to confirm the presence of the different chemo-type of this species. Here, we report the isolation and structural determination of a new acorane-, five new cuparane-type sesquiterpenoids, and two new labdane- and two new *seco*-labdane-type diterpenoids, together with previously known cuparane- and thujopsane-type sesquiterpenoids, and labdane-type diterpenoids.[5]

RESULTS AND DISCUSSION

Ten new terpenoids, five cuparanes **1** – **4b**, an acorane **5**, two labdanes **6** and **7**, and two 8,9-*seco*-labdanes **8** and **9**, have been isolated from the ether extract of *J. infusca* by the column chromatography

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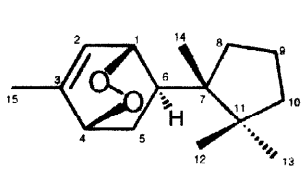

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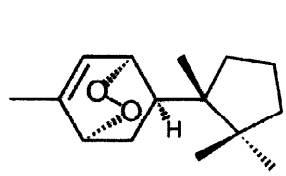

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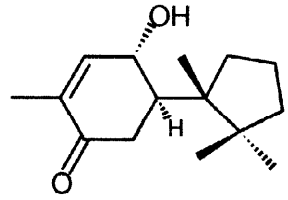

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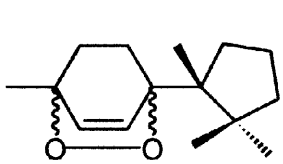

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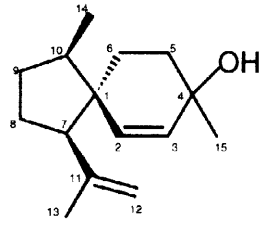

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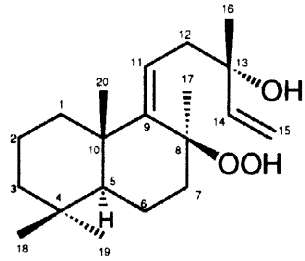

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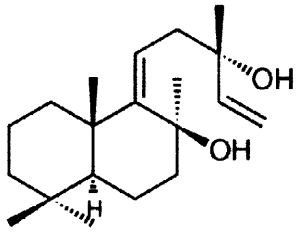

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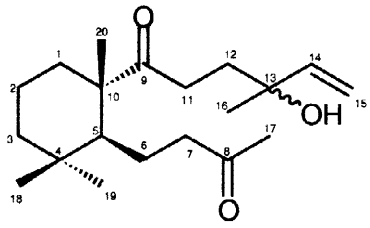

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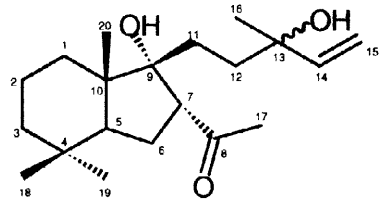

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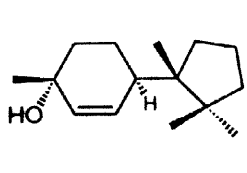
on silica gel, Sephadex® LH-20, Lobar® and preparative HPLC (ODS). Additionally, eight previously known sesqui- and diterpenoids, (+)-cuprenenol (**10**),[6] rosulantol (**11**),[6] cuparadiepoxide (**12**),[7] *epi*-cuparadiepoxide (**13**),[7] thujopsane-7β-ol (**14**),[8] (+)-(9*R**,13*S**)-dihydroxy-8(17),14-labdadiene (**15**),[6] 13-*epi*-sclareol (**16**)[9] and (13*S*)-hydroxy-8,14-labdadiene (**17**),[10] were isolated. Their structures were elucidated by the analysis of extensive NMR techniques, chemical degradation and X-ray crystallographic analysis.

In the previously report, the optical rotation of **14** have not been mentioned.[8b,8c] Compound **14** from this species was showed the negative value ($[\alpha]_D$ −5.5°). On the other hand, that of *ent*-thujopsan-7β-ol (**18**) isolated from *Marchantia polymorpha* has been reported to be $[\alpha]_D$ 0°.[8a] To confirm the absolute structure of **14**, dehydration of **14** was carried out and gave a hydrocarbon. Its ^{1}H NMR spectrum was completely identical with that of thujopsene (**19**).[8a] The optical rotation of the synthetic thujopsene (**19**) ($[\alpha]_D$ −121.8°) was the same as natural **19** ($[\alpha]_D$ −103.9°),[11] indicating that the structure of **14** was the antipode of **18**.[8a] Thus the structure of **14** was clarified to be thujopsan-7β-ol.

The molecular formula of compound **1**[5] was determined to be $C_{15}H_{24}O_2$ by HREIMS. The presence



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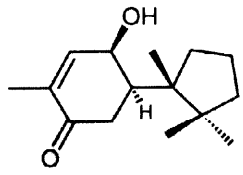

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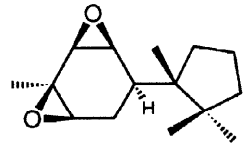

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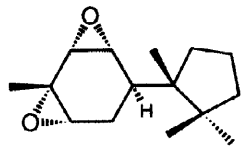

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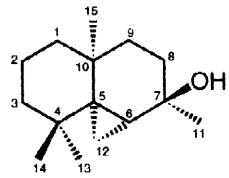

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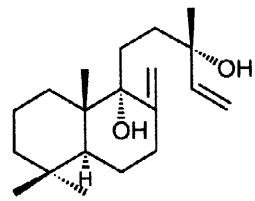

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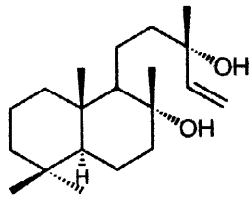

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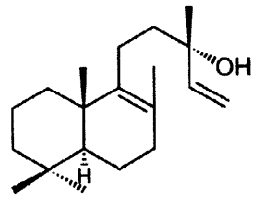

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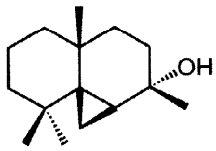

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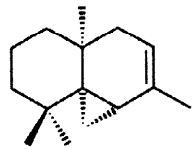

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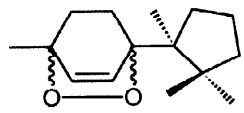
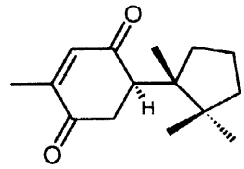


20a, 20b



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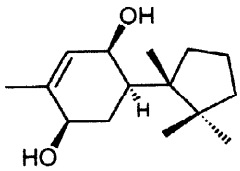

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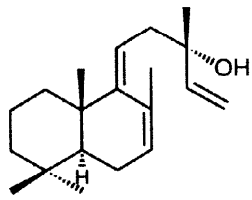

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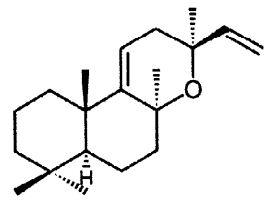

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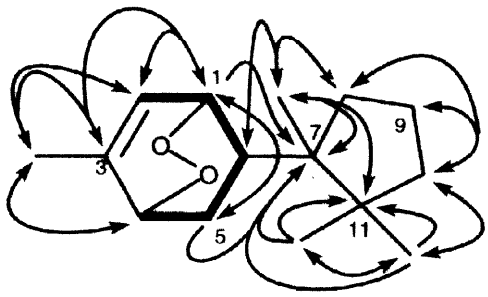

Figure 1. HMBC correlations (by arrows) and spin-spin ^{1}H decoupling (by bold line) of **1**.

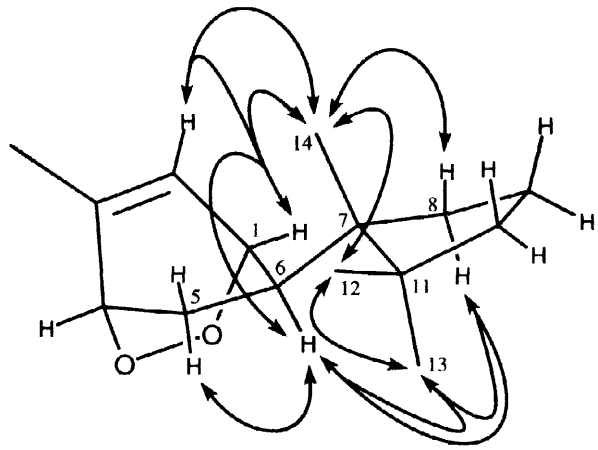

Figure 2. NOE correlations of **2** by the phase sensitive NOESY spectrum.

of a hydroxyl or a carboxyl group has not been confirmed by the IR spectrum, indicating that **1** showed the presence of peroxy group. TLC spraying reagents containing iron (II) thiocyanate or dimethyl-*p*-phenylenediamine dihydrochloride also visualized the detection of peroxy group.[12] The analysis of spin-spin ^{1}H decoupling, ^{13}C-^{1}H COSY, HMBC spectra (Figure 1) and difference NOE experiments revealed that structure of **1** might be a peroxycuparane-type sesquiterpenoid. Furthermore the correct stereochemistry of **1** was established as 1*S**,4*R**-peroxycupar-2-ene by X-ray crystallographic analysis.[5] The ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) of **2**[5] with $C_{15}H_{24}O_2$ resembled those of **1**. Therefore, the structure of **2** was supported to be diastereomer of **1** by the detailed analysis of ^{1}H-^{1}H and ^{13}C-^{1}H COSYs, and HMBC spectra. Subsequently phase sensitive NOESY experiment (Figure 2) was carried out and NOEs were observed between (i) H-14 and H-1, H-2, H-5β, H-8β, H-12, (ii) H-12 and H-5α, H-5β, H-13, (iii) H-13 and H-5α, H-6, H-8α, H-12, and (iv) H-6 and H-1, H-5α. From the above results, the structure of **2** was established to be 1*R**,4*S**-peroxycupar-2-ene, the 1,4-stereoisomer of **1**. To determine the absolute configuration of **1** and **2**, oxidation of **11**,[6] whose absolute configuration has been known, with pyridinium dichromate (PDC) gave a diketone **21** which was identical with **21** obtained from **1** by samarium diiodide (SmI_2) reduction and PDC oxidation. The absolute configurations at C-6 and C-7 of **21** were clarified to be *R* and *S*, respectively. Thus the absolute structures of **1** and **2** were established to be 1*S*,4*R*-peroxycupar-2-ene and 1*R*,4*S*-peroxycupar-2-ene, respectively.

The molecular formula of **3** was established as $C_{15}H_{24}O_2$ by HREIMS. The IR spectrum showed the presence of a hydroxyl (3414 cm^{-1}) and an unsaturated carbonyl group (1649 cm^{-1}). The ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) of **3** were similar to those of rosulantol (**11**).[6] This assumption was confirmed by ^{1}H-^{1}H COSY, HMQC and HMBC spectra, indicating that **3** might possess 1-hydroxy-2-cuparen-4-one structure. Analysis of NOESY spectrum showed that **3** was supported to be C-1 epimer of **11**, and subsequently X-ray crystallographic analysis revealed the stereostructure of **3** as shown in Figure 3.

Table 1. ^{1}H NMR data of **1 – 3, 5, 14** and **21** (600 MHz, $CDCl_3$).

H	1*	2	3	5	14‡	21
1	4.47 d (6.3)†	4.44 ddd (6.3, 2.5, 1.6)	4.48 br. t		0.27 dd (10.7, 5.8) α	
					-0.09 1H, t (5.8) β	
2	6.37 dt (6.4, 2.0)	6.20 d quit. (6.3, 1.9)	6.61 six. (1.4)	5.52 d (10.4)	1.20 dd (10.4, 6.4)	6.57 q (1.4)
3				5.72 d (10.4)		
4	4.41 br s	4.46 m			1.23 dt (13.5, 4.4)	
					1.54 ddd (13.5, 11.3, 6.4)	
5	1.54 ddd (12.2, 11.2, 2.5) α	2.31 ddd (13.7, 9.1, 4.9) α	2.75 dd (15.9, 3.3) α	1.66 m	0.85 2H, m	2.97 2H, d (6.9)
	2.13 ddd (12.2, 5.4, 3.4) β	1.35 m, β	2.27 dd (15.9, 12.6) β	1.69-1.84 m		
6	1.58 m	2.50 ddd (9.1, 6.9, 2.7)	2.21 ddd (12.6, 8.5, 3.8)	1.60 m		3.03 t (6.9)
				1.69-1.84 m		
7				2.34 dd (11.8, 8.5)		
8	1.60 - 1.70 2H, m	1.82 like br q, α	1.97 br. q like, α	1.69-1.84 2H, m	1.14 m	1.85 m, α
		1.49 ddd (12.1, 9.1, 3.0) β	1.78 ddd like, β		1.68 ddd (12.9, 12.9, 3.8)	1.80 m, β
9	1.60 - 1.70 2H, m	1.58 m	1.56 - 1.63 2H, m	1.89 m, α	1.47 m	1.53 - 1.64 2H, m
		1.64 m		1.40 m, β	1.73 m	
10	1.35 m, α	1.36 m, α	1.37 ddd (12.4, 9.1, 3.8) α	1.69-1.84 m	1.28 ddd (12.3, 12.3, 4.7)	1.39 ddd (12.6, 9.1, 3.6) α
	1.78 m, β	1.67 m, β	1.66 m, β		1.41 dddd (13.2, 4.7, 4.7, 1.6)	1.67 ddd like, β
12	0.98 3H, s	0.86 3H, s	1.05 3H, s	4.74 s like	0.96 3H, s	1.06 3H, s
				4.81 s like		
13	0.82 3H, s	0.99 3H, s	0.95 3H, s	1.68 3H, s like	0.55 3H, s	0.95 3H, s
14	1.16 3H, s	0.60 3H, s	0.92 3H, s	0.86 3H, d (6.9)	1.01 3H, s	0.89 3H, s
15	1.93 3H, d (2.0)	1.94 3H, d (1.6)	1.77 3H, t (1.9)	1.24 3H, s	1.15 3H, d (0.5)	1.97 3H, d (1.4)

* Measured by 400 MHz. † J values in Hz (in the parentheses). ‡ Measured in C_6D_6.

Oxidation of **3** gave a diketone, the spectral data of that were identical with those of **21**. On the basis of the above results, the absolute structure of **3** was established to be *epi*-rosulantol.

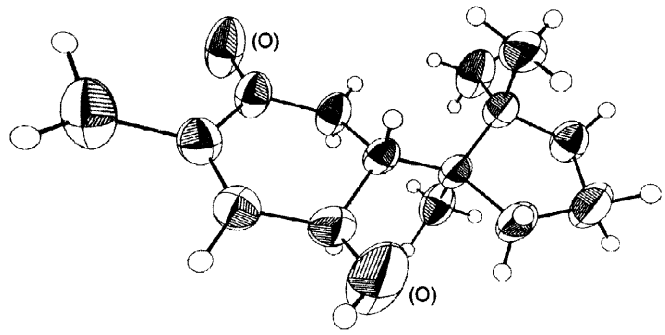

Figure 3. ORTEP drawing of *epi*-rosulantol (**3**).

The spectral data of new compounds of **4a** and **4b** were completely identical with those of 3,6-peroxo-cupar-1-ene (**20a** and **20b**) isolated from *Nardia scalaris*,[13] except for optical rotation (see experiment). Therefore, the structures of **4a** and **4b** were established to be *ent*-3,6-peroxo-cupar-1-ene and its diastereomer, respectively.

The EIMS spectrum of compound **5** indicated *m/z* 220 (M^+) and its molecular formula was decided to be $C_{15}H_{24}O$ by HREIMS. The ^{13}C NMR (Table 2) and IR spectra confirmed the presence of a tertiary hydroxyl group (δ_C 68.3 s; IR ν_{max} 3410 cm^{-1}). The ^1H NMR (Table 1) and DEPT spectra also showed the presence of an *exo*-methylene (δ_C 112.8 t, 146.8 s; δ_H 4.74, 4.81 each s like) and a disubstituted double bond (δ_C 130.7, 134.6 each d; δ_H 5.52, 5.72 each d), along with three methyls, four methylenes, two methines and two quaternary carbons. HMBC (Figure. 4), HMQC and ^1H-^1H COSY spectra clarified that **5** possessed the acorane-type skeleton. The NOESY spectrum, which observed NOEs between (i) H-2 and H-9β, H-14, (ii) H-14 and H-9α, H-9β, and (iii) H-7 and H-6, confirmed the stereochemistry. Thus the structure of **5** was 2,11-acoradien-4-ol. However, the stereochemistry of the hydroxyl group at C-4 remained to be clarified.

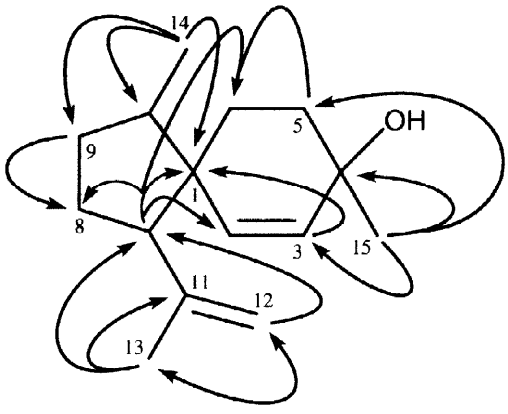

Figure 4. HMBC correlations of **5**.

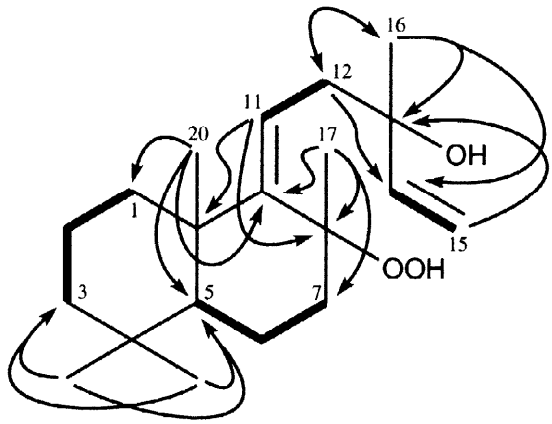

Figure 5. ^1H-^1H correlations (by bold lines) and HMBC correlations (by arrows) of **6**.

Table 2. ^{13}C NMR data of **1** – **9**, **14**, **21**, **23** and **24** (150 MHz, $CDCl_3$).

C	**1***	**2**	**3**	**4a**	**4b**	**5**	**6†**	**7***	**8**	**9**	**14†**	**21‡**	**23†**	**24†**
1	75.7	74.6	69.3	135.5	134.5	48.8	41.4	41.1	37.2	31.4	9.7	198.9	38.8	39.7
2	127.4	124.8	148.8	134.0	134.9	130.7	19.7	19.3	18.2	19.4	32.4	149.1	19.7	19.3
3	139.4	139.8	134.6	73.5	73.6	134.6	42.5	42.1	41.1	41.1	68.8	140.1	42.7	42.4
4	75.3	76.2	200.0	30.0	29.5	68.3	34.3	34.1	34.3	33.1	34.6	200.6	33.8	33.8
5	23.3	27.1	38.8	24.6	26.0	35.6	44.8	44.1	47.7	51.3	35.9	38.6	48.7	44.5
6	41.1	41.5	51.2	83.2	82.3	30.3	18.1	18.3	22.2	26.7	32.9	54.9	25.4	18.1
7	47.2	45.7	47.2	50.3	49.9	60.4	29.1	36.5	45.6	54.5	32.0	47.5	§	33.1
8	39.2	39.1	41.0	34.8	34.2	27.2	84.6	72.8	209.2	215.8	36.9	40.4	131.6	74.6
9	19.3	19.2	19.6	19.8	19.4	30.1	154.5	158.9	218.2	85.0	19.1	19.3	150.7	157.5
10	40.8	40.6	41.7	42.1	42.1	45.4	40.9	40.7	53.2	49.1	40.3	41.4	39.4	39.0
11	44.5	44.4	45.0	45.4	45.0	146.8	119.4	119.3	32.5	31.0	33.5	44.8	116.6	114.6
12	24.6	24.6	25.3	28.2	28.1	112.8	39.7	41.0	35.7	36.4	27.5	25.1	42.3	35.4
13	25.4	25.4	24.3	26.2	25.9	21.3	74.2	73.0	72.6	73.0	29.4	24.8	73.3	74.1
14	17.7	19.0	18.0	21.7	21.4	15.7	144.3	144.8	144.4	144.9	29.1	18.5	145.6	146.4
15	18.7	18.3	15.0	21.4	21.4	29.0	112.3	112.0	112.2	111.9	29.6	15.8	111.8	112.1
16							30.3	29.4	28.8	28.6			28.1	30.8
17							27.2	30.8	29.9	31.5			25.3	29.4
18							21.5	21.2	22.5	20.9			22.1	21.3
19							32.7	32.6	33.4	33.4			32.8	32.8
20							24.5	25.4	17.3	16.2			20.6	25.6

* Measured by 100 MHz. † Measured in C_6D_6. ‡ Tentative assigns. § Overlapped in solvent signal.

The ^{1}H and ^{13}C/DEPT spectra (Tables 2 and 3) of **6** confirmed the presence of a trisubstituted double bond (δ_C 119.4 d, 154.5 s; δ_H 5.47 dd) and a vinyl group (δ_C 112.3 t, 144.3 d; δ_H 4.97, 5.01, 5.64 each dd), together with five methyls, six methylenes, a methine and two quaternary carbons. In addition, the IR and DEPT spectra indicated the presence of two oxygen-bearing quaternary carbons (δ_C 74.2, 84.6 each s) one of which was substituted by a hydroxyl group. The presence of the peroxy group in **6** was suggested by the spraying reagents on TLC plate as indicated previously. The FABMS spectra showed a quasi-molecular ion at *m/z* 345 $[M+Na]^+$ and/or *m/z* 361 $[M+K]^+$, therefore, the molecular formula of **6** was established to be $C_{20}H_{34}O_3$ (MW 322). The structure of **6** was clarified to be a labdane-type diterpenoid with a hydroperoxyl and tertiary hydroxyl group by the 2D NMR experiments (Figure 5). In the NOESY spectrum, the NOEs were observed between (i) H-18 and H-19, H-20, (ii) H-5 and H-17, (iii) H-11 and H-1α, H-1β, and (iv) H-12 and H-17. Accordingly, the geometry of 9,11-double bond was supported to be *Z*. Thus, the structure of **6** revealed to be 8-hydroperoxy-13-hydroxy-9(11),14-labdadiene.

The IR and ^{13}C/DEPT (Table 2) spectra of **7** showed the presence of two tertiary hydroxyl group (δ_C 72.8, 73.0 each s, 3325 cm^{-1}). The ^{1}H NMR spectrum (Table 3) confirmed the presence of a trisubstituted olefinic proton, vinyl protons and five methyls. The ^{1}H and ^{13}C NMR spectra of **7** resembled those of **6**, indicating that **7** possessed the labdane skeleton. The analysis of 2D COSY experiments clarified that structure of **7** was 8,13-dihydroxy-9(11),14-labdadiene. To obtain further confirmation of the stereochemistry of **7**, X-ray crystallographic analysis was carried out. The ORTEP drawing was shown in Figure 6. In addition, the spectral data of **7** were completely identical with those of diol derived from **6** by reduction. Accordingly, the structures of **6** and **7** were (8*S**)-hydroperoxy-(13*S**)-hydroxy-9(11),14-labdadiene and (8*S**,13*S**)-dihydroxy-9(11),14-labdadiene, respectively. When compound **7** in $CDCl_3$ solution was allowed to stand overnight, dehydration reaction occurred to give **23** and **24**. The structures of **23** and **24** were decided to be (13*S**)-hydroxy-7,9(11),14-labdatriene and (8*S**,13*S**)-epoxy-9(11),14-

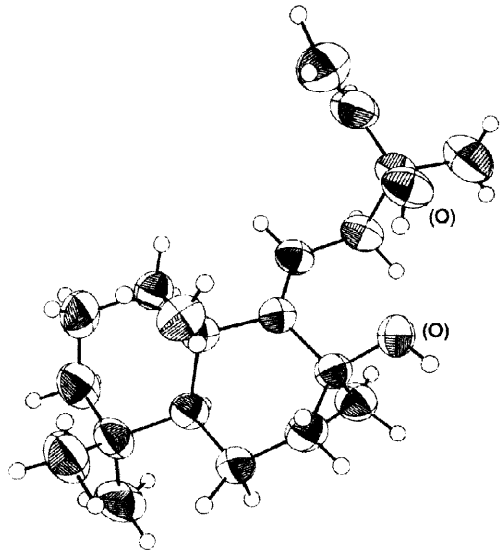

Figure 6. ORTEP drawing of (8*S**,13*S**)-dihydroxy-9(11),14-labdadiene (**7**).

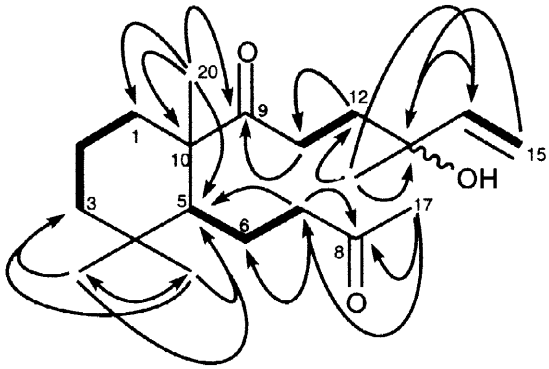

Figure 7. ^{1}H-^{1}H correlations (by bold lines) and HMBC correlations (by arrows) of **8**.

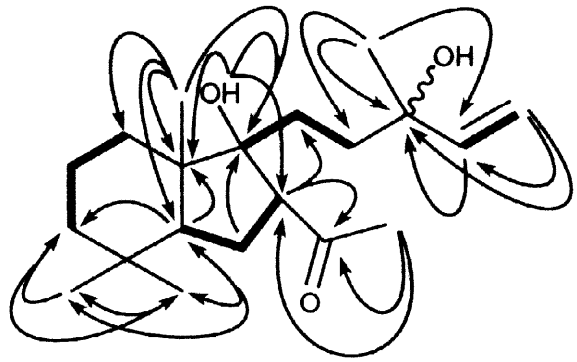

Figure 8. ^{1}H-^{1}H correlations (by bold lines) and HMBC correlations (by arrows) of **9**.

labdadiene by the 2D NMR experiments.

The IR and ^{13}C NMR (Table 2) spectra of secoinfuscadione (**8**)[5] indicated the presence of a tertiary hydroxyl (δ_C 72.6 s, IR ν_{max} 3476 cm^{-1}) and two ketone carbons (δ_C 209.2, 218.2 each s, IR ν_{max} 1701 cm^{-1}). The EIMS spectrum showed as a dehydration peak at *m/z* 304 and its molecular formula was indicated $C_{20}H_{32}O_2$ by HREIMS. The DEPT spectra showed the presence of five methyls, seven methylenes, a methine and two quaternary carbons, along with a quaternary carbon with a hydroxyl group, two olefinic and two ketone carbons. Thus the molecular formula of **8** was determined as $C_{20}H_{34}O_3$, indicating that **8** was a monocyclic diterpenoid. Successively, the analysis of ^{1}H-^{1}H and ^{13}C-^{1}H COSYs, HMBC (Table 3, Figure 7) and NOESY spectra established that structure of **8** was 8,9-dioxo-*seco*-13-hydroxylabd-14-ene.

The CIMS of infuscadiol (**9**) showed a quasi-molecular ion at *m/z* 323 $[M+H]^+$. The IR and ^{13}C/DEPT spectra observed the presence of a ketone (δ_C 215.8 s, IR ν_{max} 1690 cm^{-1}) and two tertiary hydroxyl group (δ_C 73.0, 85.0 each s, IR ν_{max} 3450 cm^{-1}). Additionally the ^{13}C NMR spectrum (Table 2) displayed 20 carbons and its DEPT spectra indicated the presence of five methyls, five methylenes, a methine, two quaternary carbons and a vinyl carbon. The ^{1}H NMR spectrum (Table 3) showed the presence of five methyls one of which was an acetyl group (δ_H 2.23 s), a vinyl proton (δ_H 5.06, 5.20, 5.86 each, dd) and an OH proton (δ_H 4.95 s) exchangeable with D_2O. Therefore, the molecular formula of **9** was established to be $C_{20}H_{34}O_3$, indicating that **9** was a bicyclic diterpenoid. The structure of the rearranged labdane-type skeleton for **9** was clarified by means of ^{1}H-^{1}H COSY, HMQC and HMBC spectra (Figure 8). Its stereochemistry was clarified by NOESY spectrum in $CDCl_3$, in which NOEs were observed between (i) H-7 and H-6β, H-20, (ii) H-18 and H-3β, H-19, H-20, (iii) H-19 and H-3α, H-5, (iv) H-5 and H-3α, and (v) H-5 and C_9-OH, respectively. Furthermore, in NOESY spectrum with C_5D_5N the NOEs were observed between NOEs (i) H-7 and H-6β, H-11, H-20, (ii) H-20 and H-11, H-18, (iii) H-5α and H-3α, H-19. Thus, the structure of **9** was established as the rearranged labdane-type diterpenoid formed by intramolecular aldol condensation[14] of **8**.

Table 3. ^{1}H NMR data of **6 – 9**, **23** and **24** (600 MHz).

H	6*	7‡§	8‡	9‡	23*	24*
1	1.25 ddd (13.7, 13.7, 4.7)†	1.14 m	1.39 m	1.34 dt (12.9, 3.3)	1.46-1.53 m	1.16 ddd (13.7, 13.7, 4.1) α
	1.92 br d	1.87 d like (11.4)	1.47 m	1.57-1.69 m	1.77 br t like	1.84 m, β
2	1.43 d quit. (14.0, 3.6)	1.44-1.79 2H, m	1.49 m	1.51-1.60 2H, m	1.46-1.53 m	1.38 m, α
	1.51-1.67 m		1.56 tt. like		1.56 m	1.53 tt (13.7, 13.7, 3.3) β
3	1.04 ddd (13.2, 13.2, 2.8) α	1.07 ddd (13.5, 13.5, 4.0)	1.41 m	1.11 ddd (13.2, 13.2, 4.9) α	1.10 ddd (13.5, 13.5, 3.3)	1.04 ddd (13.7, 13.7, 3.8) α
	1.34 d six., *J*=13.2, 1.4) β	1.39 br d like	1.16 - 1.23 m	1.40 dt (13.2, 3.6) β	1.33 m	1.33 dddd (13.7, 3.3, 3.3, 1.6) β
5	1.15 dd (11.5, 8.2 Hz	1.21 dd (11.4, 8.4)	1.72 t (4.7)	2.07 dd (12.6, 8.0)	1.36 dd (11.0, 5.8)	1.30 dd (11.8, 8.0)
6	1.51-1.67 2H, m	1.44-1.79 2H, m	1.16 - 1.23 m	1.57-1.69 m, α	1.91 br t	1.58 m, α
			1.61 m	1.86 q (12.6) β	2.06 m	1.42 m, β
7	1.51-1.67 m	1.44-1.79 m	2.39 tt (17.5, 5.5)	2.87 dd (12.6, 4.9)	5.49 br s	1.83 dd (13.2, 9.6) α
	2.98 t like	2.02 q (10.9)	2.44 tt (17.3, 5.5)			2.08 q like, β
11	5.47 dd (12.5, 4.1)	5.34 dd (10.6, 6.2)	2.56 ddd (18.1, 7.7, 6.9)	1.57-1.69 2H, m	5.45 t (7.4)	5.48 dd (8.5, 3.0)
			2.61 ddd (18.1, 7.7, 6.3)			
12	1.82 dd (14.0, 4.1)	2.23 dd (13.9, 6.2)	1.73 ddd (14.6, 7.7, 6.3)	1.51-1.60 m	2.47 dd (15.4, 8.0)	2.20 dd (15.7, 3.0) α
	3.56 dd (14.0, 12.4)	3.12 dd (13.9, 10.6)	1.82 ddd (14.6, 8.0, 6.9)	1.57-1.69 m	2.59 dd (15.4, 6.3)	2.04 dd (15.7, 8.5) β
14	5.64 dd (17.3, 10.7)	5.90 dd (17.2, 10.9)	5.83 dd (17.3, 10.7)	5.86 dd (17.3, 10.7)	5.83 dd (17.3, 10.7)	5.70 dd (17.0, 10.4)
15	4.97 dd (10.7, 1.4)	5.07 dd (10.9, 1.8)	5.07 dd (10.7, 1.4)	5.06 dd (10.7, 1.4)	4.99 dd (10.7, 1.6)	4.98 dd (10.4, 2.2)
	5.01 dd (17.3, 1.4)	5.19 dd (17.2, 1.8)	5.23 dd (17.3, 1.4)	5.20 dd (17.3, 1.4)	5.25 dd (17.3, 1.6)	5.26 dd (17.0, 2.2)
16	1.01 3H, s	1.32 3H, s	1.29 3H, s	1.26 3H, s	1.18 3H, s	1.36 3H, s
17	1.39 3H, d (0.8)	1.43 3H, s	2.09 3H, s	2.23 3H, s	2.03 3H, s	1.40 d (0.8)
18	0.86 3H, s	0.91 3H, s	0.92 3H, s	0.89 3H, s	0.85 3H, s	0.85 3H, s
19	0.79 3H, s	0.82 3H, s	0.91 3H,s	0.87 3H, s	0.76 3H, s	0.78 3H, s
20	1.28 3H, d (0.8)	1.15 3H, s	1.22 3H, s	0.85 3H, s	1.02 3H, s	1.10 3H, d (0.8)
OH				4.95 s		
OOH	10.51br s like					

* Measured in C_6D_6. † J values in Hz (in the parentheses). ‡ Measured in $CDCl_3$. § Measured by 400 MHz.

Some *J. infusca* collected in different locations contain kaurane-type glucoside, kaurane-, clerodane- and labdane-type diterpenoids, and bis(bibenzyl) type aromatic compounds as main components.[3] As the present species contains mainly cuparane-type sesquiterpenoids and labdane-type diterpenoids, this is the new chemo-type of *J. infusca*.

The diterpenoids with 8,9-*seco*-labdane- and rearranged labdane-type skeletons have been found in the higher plants, *Gypothamnium pinifolium* (Gochnatiinae)[14] and *Galeopsis angustifolia* (Labiatae).[15] These skeletons are rare in Nature and first report from liverworts.

EXPERIMENTAL

Mps are uncorr. The IR spectra were measured with a JASCO FT/IR-5300 spectrophotometer by the diffuse reflectance method. The ^1H and ^{13}C NMR spectra were recorded on a Varian Unity 200, a Varian Gemini 200 (200 MHz), a JEOL JNM GX400, 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 δ149.83 (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. 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. The specific rotations were measured by a JASCO DIP-1000 polarimeter with $CHCl_3$ as a solvent. X-ray reflection data were collected with a Mac Science MXC18 diffractometer using MoKα radiation (λ=0.71073 Å). Preparative HPLC was performed by JASCO pump system. Column chromatography (CC) was carried out on silica gel 60 (0.2-0.5 mm, 0.04-0.063 mm, Merck), cosmosil 75C_{18}-OPN (Nakarai Tesque) and Sephadex® LH-20 (Pharmacia). TLC and preparative TLC were carried out on silica gel 60 F254 plate (Merck) and visualized by spraying Godin reagent[16] followed by heating at 120 °C.

Extraction and isolation. *Jungermannia infusca* (Mitt.) Steph. was collected in Tochigi, Japan 1995. The voucher specimen was deposited at the Faculty of Pharmaceutical Sciences, Tokushima Bunri University. The ground material of *J. infusca* (547 g) was extracted with Et_2O for one month. The crude extract (5.0g) was divided into eight fractions by CC on silica gel using *n*-hexane-EtOAc gradient. Fr. 3 was rechromatographed on Sephadex® LH-20 (50% CH_2Cl_2/MeOH), Lobar® (Si 60, 10% Et_2O/*n*-hexane) and finally preparative HPLC (Chemcosorb 5-ODS-H, 100% CH_3CN) to give 1*S*,4*R*-peroxycupar-2-ene (**1**) (84 mg). CC on Sephadex® LH-20, reverse phase silica gel (100% CH_3CN), Lobar® (Si 60, 5% EtOAc/*n*-hexane) and prep. HPLC (Chemcosorb 5-ODS-H, 100% CH_3CN; Chemcosorb 5CN-U, 10% Et_2O/*n*-hexane) of Fr. 4 gave **1** (52 mg), 1*R*,4*S*-peroxycupar-2-ene (**2**) (6 mg), (13*S*)-hydroxy-8,14-labdadiene (**17**)[9] (134 mg) and a mixture of sesquiterpenoids which was further purified by prep. chiral HPLC (Chiralcel OD-H, *n*-hexane, DAICEL) to give *ent*-3,6-peroxo-cupar-1-ene (**4a**) (3 mg) and *ent*-3,6-peroxo-cupar-1-ene (**4b**) (5 mg). Fr. 5 and 6 were rechromatographed on Sephadex® LH-20, silica gel,

Lobar® (RP-18, 100% CH_3CN) and prep. HPLC (Chemcosorb 5-ODS-H, 100% CH_3CN) to yield 2,11-acoradien-4-ol (**5**) (2 mg), (8*S**)-hydroperoxy-(13*S**)-hydroxy-9(11),14-labdadiene (**6**) (72 mg), secoinfuscadione (**8**) (20 mg), cuparadiepoxide (**12**)[6] (20 mg), *epi*-cuparadiepoxide (**13**)[6] (36 mg) and thujopsane-7β-ol (**14**)[7] (2 mg). CC on Sephadex® LH-20 and silica gel of Fr. 7 gave (+)-cuprenenol (**10**)[6] (230 mg), rosulantol (**11**)[6] (59 mg) and (+)-(9*R**,13*S**)-dihydroxy-8(17),14-labdadiene (**15**)[5] (43 mg). *epi*-Rosulantol (**3**) (4 mg), (8*S**,13*S**)-dihydroxy-9(11),14-labdadiene (**7**) (9 mg), infuscadiol (**9**) (5 mg) and 13-*epi*-sclareol (**16**)[9] (74 mg) were isolated by CC on Sephadex® LH-20, silica gel, Lobar® (Si 60 or RP-18) of Fr. 8. Compound **9** was finally purified by prep. TLC (Diol, 20% EtOAc/CH_2Cl_2). Compounds **3** and **7** were further recrystallized from *n*-hexane, respectively. Compound **7** in $CDCl_3$ solution was converted into a dehydrated mixture when it was kept in NMR tube overnight. The mixture was purified by prep. TLC (20% EtOAc/ *n*-hexane) to give (13*S**)-hydroxy-7,9(11),14-labdatriene (**23**) (4 mg) and (8*S**,13*S**)-epoxy-9(11),14-labdadiene (**24**) (4 mg).

1*S*,4*R*-Peroxycupar-2-ene (**1**): Crystal; mp. 77-78°C (from *n*-pentane); $[\alpha]_D^{23}$ +28.9° (*c* 5.33); IR ν_{max} 1465, 1445, 1380, 1370, 620 cm^{-1}; HREIMS obs. *m/z* 236.1786 $C_{15}H_{24}O_2$ requires 236.1777; ^1H and ^{13}C NMR: Tables 1 and 2; EIMS *m/z* (int.) 236 $[M]^+$ (8), 204 (7), 135 (13), 123 (21), 111 (71), 95 (59), 81 (37), 69 (100), 55 (51), 41 (42).

1*R*,4*S*-Peroxycupar-2-ene (**2**): Oil; $[\alpha]_D^{19}$ +136.2° (*c* 2.46); IR ν_{max} 1658, 1460, 1379, 1215, 1111 cm^{-1}; HREIMS obs. *m/z* 236.1770 $C_{15}H_{24}O_2$ requires 236.1776; ^1H and ^{13}C NMR: Tables 1 and 2; EIMS *m/z* (int.) 236 $[M]^+$ (1), 204 (15), 135 (6), 123 (12), 111 (100), 94 (46), 81 (23), 69 (76), 55 (38), 41 (33).

***epi*-Rosulantol** (**3**): Crystal; mp. 139-140°C (from *n*-hexane); $[\alpha]_D^{20}$ +155.4° (*c* 0.66); IR ν_{max} 3414, 1649 cm^{-1}; HREIMS obs. *m/z* 236.1775 $C_{15}H_{24}O_2$ requires 236.1776; UV λ_{max} (log ε) 234nm (3.54) (*c* 3.0×10^{-4}); CD $\Delta\varepsilon_{241\ nm}$ +7.40, $\Delta\varepsilon_{208\ nm}$ −7.32 (*c* 3.0×10^{-4}); ^1H and ^{13}C NMR: Tables 1 and 2; EIMS *m/z* (int.) 236 $[M]^+$ (40), 218 (5), 151 (23), 125 (27), 109 (21), 98 (100), 81 (9), 69 (30), 55 (19), 41 (19), 32 (8); *Crystal data*: Recrystallized from *n*-hexane; Monoclinic, space group $P2_1$, *a*=7.218 (0) Å, *b*=7.802 (0) Å, *c*=11.943 (0) Å, *β*=95.111 (0)°, *V*=669.900(0) $Å^3$, *Z*=2; *Dx*=1.530 Mg m^{-3}, μ=0.705 mm^{-1}, The structure was solved by direct methods using *CRYSTAN SHELX86* and refined by full matrix least-squares; Refinement on *F*, R=0.056, *wR*=0.051, *S*=0.507.

***ent*-3,6-Peroxo-cupar-1-ene** (**4a**): Oil; $[\alpha]_D^{20}$ +61.2° (*c* 0.58: ref.[13] −14.2°, $CHCl_3$); HREIMS obs. *m/z* 236.1810 $C_{15}H_{24}O_2$ requires 236.1777; ^1H NMR (600 MHz, $CDCl_3$): δ 6.72 (1H, d, *J*=8.8 Hz, H-1), 6.32 (1H, d, *J*=8.8 Hz, H-2), 1.45-1.47 (2H, m, H-4 and 5), 2.02 (1H, m, H-4), 2.41 (1H, m, H-5), 1.39-1.44 (2H, m, H-8 and 10), 2.19 (1H, ddd, *J*=13.2, 9.9, 7.4 Hz, H-8), 1.60-1.73 (3H, m, H-9 and 10), 1.12 (3H, s, H-12), 1.05 (3H, s, H-13), 1.08 (3H, d, *J*=0.5 Hz, H-14), 1.36 (3H, s, H-15); ^{13}C NMR: Table 2; EIMS *m/z* (int.) 236 $[M]^+$ (10), 218 (32), 204 (64), 202 (50), 189 (12), 175 (14), 161 (22), 145 (47), 132

(100), 119 (61), 105 (34), 95 (61), 79 (19), 69 (31), 55 (27), 41 (33). The spectral data except for the optical rotation were in accordance with those of reference data.[13]

***ent*-3,6-Peroxo-cupar-1-ene (4b)**: Oil; $[\alpha]_D^{20}$ +75.0° (*c* 2.29: ref.[13] –12.9°, $CHCl_3$); HREIMS obs. *m/z* 236.1754 $C_{15}H_{24}O_2$ requires 236.1776; ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.80 (1H, d, *J*=8.8 Hz, H-1), 6.35 (1H, d, *J*=8.8 Hz, H-2), 1.50 (1H, dd, *J*=12.6, 2.5 Hz, H-4), 2.02 (1H, ddd, *J*=12.6, 10.2, 3.8 Hz, H-4), 1.53 (1H, dd, *J*=12.1, 3.6 Hz, H-5), 2.28 (1H, ddd like, H-5), 1.47 (1H, m, H-8), 2.25 (1H, t like, H-8), 1.55-1.68 (2H, m, H-9), 1.42 (1H, ddd, *J*=12.9, 9.1, 4.1 Hz, H-10), 1.71 (1H, q like, H-10), 1.07 (3H, s, H-12), 1.06 (3H, s, H-13), 1.04 (3H, d, *J*=0.5 Hz, H-14), 1.36 (3H, s, H-15); ^{13}C NMR: Table 2; EIMS *m/z* (int.) 236 $[M]^+$ (7), 218 (26), 204 (61), 202 (50), 189 (8), 187 (9), 175 (9), 161 (21), 145 (46), 132 (100), 119 (60), 105 (31), 95 (51), 77 (15), 69 (22), 55 (22), 41 (26). The spectral data except for the optical rotation were identical with those of reference data.[13]

2,11-Acoradien-4-ol (5): Oil; $[\alpha]_D$ 0° (*c* 0.1); IR ν_{max} 3410 cm^{-1}; HREIMS: obs. *m/z* 220.1826 $C_{15}H_{24}O$ requires 220.1827; ^{1}H and ^{13}C NMR: Tables 1 and 2. EIMS *m/z* (int.) 220 $[M]^+$ (22), 205 (13), 177 (16), 159 (13), 149 (52), 123 (29), 109 (48), 95 (100), 81 (42), 69 (51), 55 (37), 43 (38).

(8*S)-Hydroperoxy-(13*S**)-hydroxy-9(11),14-labdadiene (6)**: Oil; $[\alpha]_D^{24}$ –4.6° (*c* 5.97); IR ν_{max} 3250 cm^{-1}; HREIMS obs. *m/z* 304.2378 $[M-H_2O]^+$ $C_{20}H_{32}O_2$ requires 304.2354; FABMS *m/z* 345 $[M+Na]^+$, 361 $[M+K]^+$; ^{1}H and ^{13}C NMR: Tables 2 and 3; EIMS *m/z* (int.) 304 $[M-H_2O]^+$ (11), 286 (33), 243 (12), 191 (17), 177 (26), 161 (32), 147 (41), 119 (70), 109 (60), 95 (68), 81 (68), 69 (70), 55(77), 43 (100), 32 (42).

(8*S,13*S**)-Dihydroxy-9(11),14-labdadiene (7)**: Crystal; mp. 113-115°C (from *n*-hexane); $[\alpha]_D^{19}$ –36.6° (*c* 3.64); IR ν_{max} 3325 cm^{-1}; HREIMS obs. *m/z* 288.2462 $[M-H_2O]^+$ $C_{20}H_{32}O$ requires 288.2453; ^{1}H and ^{13}C NMR: Tables 2 and 3; EIMS *m/z* (int.) 288 $[M-H_2O]^+$ (8), 270 (100), 255 (51), 241 (8), 218 (50), 203 (33), 185 (27), 145 (27), 133 (23), 119 (36), 105 (16), 91 (15), 69 (11), 55 (13), 41 (11), 32 (7). *Crystal data*: Recrystallized from *n*-hexane; Monoclinic; space group *C*2; *a*=24.057(0) Å, *b*=7.496 (0) Å, *c*=12.770 (0) Å, β=119.843 (0)°; *V*=1997.6 (0) $Å^3$; *Z*=4; *Dx*=1.530Mg m^{-3}; μ=0.592 mm^{-1}; The structure was solved by direct methods using *CRYSTAN SIR92* and refined by full matrix least-squares; Refinement on *F*; R=0.062; *wR*=0.076; *S*=1.785.

Secoinfuscadione (8): Oil; $[\alpha]_D^{22}$ –3.2° (*c* 2.99); IR ν_{max} 3476, 1701 cm^{-1}; HREIMS obs. *m/z* 304.2420 $C_{20}H_{32}O_2$ requires 304.2403; ^{1}H and ^{13}C NMR: Tables 2 and 3; EIMS *m/z* (int.) 304 $[M-H_2O]^+$ (10), 196 (43), 177 (100), 163 (15), 137 (34), 127 (50), 109 (38), 95 (32), 81 (43), 69 (47), 55 (17), 43 (50).

Infuscadiol (9): Oil; $[\alpha]_D^{22}$ –7.8° (*c* 1.88); IR ν_{max} 3450, 1690 cm^{-1}; CIMS (CH_4) *m/z* 323 $[M+H]^+$; ^1H and ^{13}C NMR: Tables 2 and 3; ^1H NMR (600 MHz, C_5D_5N): δ 1.52 (1H, dt like, H-1), 1.97-2.05 (3H, m, H-1, 6 and 12), 1.47 (1H, m, H-2), 1.60 (1H, m, H-2), 1.07 (1H, ddd, *J*=13.5, 13.5, 3.8 Hz, H-3α), 1.35 (1H, dt, *J*=13.5, 3.8 Hz, H-3β), 2.29 (1H, dd, *J*=13.5, 7.4 Hz, H-5), 1.64 (1H, q, *J*=12.6 Hz, H-6), 3.04 (1H, dd, *J*=11.3, 3.8 Hz, H-7), 2.06-2.15 (2H, m, H-11 and 12), 2.37 (1H, ddd, *J*=13.2, 13.2, 2.5 Hz, H-11), 6.16 (1H, dd, *J*=17.3, 10.7 Hz, H-14), 5.17 (1H, dd, *J*=10.7, 1.9 Hz, H-15), 5.58 (1H, dd, *J*=17.3, 1.9 Hz, H-15), 1.48 (3H, s, H-16), 2.28(3H, s, H-17), 0.87 (3H, s, H-18), 0.88 (3H, s, H-19), 0.92 (3H, s, H-20), 5.67 (1H, s, OH); EIMS *m/z* (int.): 304 $[M-H_2O]^+$ (11), 289 (23), 251 (18), 236 (9), 205 (17), 193 (12), 179 (39), 161 (19), 137 (38), 123 (26), 109 (39), 95 (37), 81(56), 69 (53), 55 (35), 43 (100).

(13*S)-Hydroxy-7,9(11),14-labdatriene (23)**: Oil; $[\alpha]_D^{22}$ –283.1° (*c* 1.19, benzene); IR ν_{max} 1452, 1388, 1369, 1072 cm^{-1}; HREIMS obs. *m/z* 288.2456 $C_{20}H_{32}O$ requires 288.2453; ^1H and ^{13}C NMR: Tables 2 and 3; EIMS *m/z* (int.) 288 $[M]^+$ (8), 218 (100), 203 (33), 189 (14), 175 (22), 161 (40), 147 (52), 133 (56), 105 (51), 91 (44), 81 (35), 71 (78), 55 (51), 41 (51), 32 (15).

(8*S,13*S**)-Epoxy-9(11),14-labdadiene (24)**: Oil; $[\alpha]_D^{22}$ –34.6° (*c* 1.34, benzene); IR ν_{max} 3377, 1460, 1370 cm^{-1}; HRMS obs. *m/z* 288.2450 $C_{20}H_{32}O$ requires 288.2453; ^1H and ^{13}C NMR: Tables 2 and 3; EIMS *m/z* (int.): 288 $[M]^+$ (18), 273 (100), 218 (34), 193 (23), 177 (12), 163 (55), 150 (45), 135 (68), 121 (26), 107 (34), 95 (25), 81 (43), 69 (33), 55 (33), 43 (26).

Preparation of diketone 21 from 1. To a solution of **1** (10 mg) in THF (1 ml) was added dropwise 0.1 M solution of SmI_2 in THF (1 ml) at room temp. under argon. After stirred for 30 min., tc the mixture was added satd. aq. Rochelle salt and Et_2O, and stirred for 15 min., then extracted with Et_2O. The extract was treated with brine, dried ($MgSO_4$) and chromatographed on silica gel (*n*-hexane/EtOAc gradient) to give a diol **22** (7.5 mg): amorphous; $[\alpha]_D^{21}$ –84.1° (*c* 0.28, MeOH); IR ν_{max} 3293, 1470, 1373, 1296 cm^{-1}; ^1H NMR(400 MHz, C_5D_5N): δ 0.95 (3H, s), 1.01 (3H, s), 1.34 (3H, s), 1.45 (1H, m), 1.54-1.71 (3H, m), 1.77 (1H, br d), 1.98 (1H, m), 2.06 (3H, s), 2.09 (1H, m), 2.31-2.42 (2H, m), 4.41 (1H, m), 5.90 (1H, m); ^{13}C NMR (100 MHz, C_5D_5N): δ 19.2, 20.1, 26.6, 26.7 (*q*), 20.0, 31.8, 37.0, 41.6 (*t*), 42.7, 68.1, 71.6, 128.1 (*d*), 45.4, 48.0, 141.0 (*s*); EIMS *m/z* (int.): 238 $[M]^+$ (1), 220 (3), 202 (10), 187 (2), 159 (3), 145 (9), 132 (22), 111 (100), 100 (28), 95 (16), 81 (10), 69 (65), 55 (25), 41 (10), 32 (54).
To solution of diol **22** in dry DMF (2 ml) was added pyridinium dichromate (PDC, 10 mg) and stirred at room temp. for 1.5 h The mixturc was filtrated with short pad column and extracted with Et_2O, then dried ($MgSO_4$). The resulting mixture was purified by CC on silica gel and reverse phase prep. TLC to give diketone (2 mg) whose spectral data were agreement with those of diketone **21** derived from **11**.

Oxidation of 3. To solution of **3** (3 mg) in dry CH_2Cl_2 (2 ml) was added PDC (5 mg) and stirred at room temp. After 4 h, the mixture was filtrated and chromatographed on silica gel to yield diketone (1 mg), the ^1H NMR spectral data of which and the sign of optical rotation were identical with those of

diketone **21** derived from **11**.

Reduction of 6. To a suspension of $LiAlH_4$ (5mg) in dry Et_2O was added compound **6** (12.5 mg) in dry Et_2O and stirred for 30 min at room temp. Work-up as usual gave a resulting mixture., which was chromatographed on Lobar® (Si 60, 30% EtOAc/*n*-hexane) to give diol (5.8 mg), the spectral data of which were completely identical with those of **7** from this species.

Oxidation of 11. To solution of **11** (10 mg) in dry CH_2Cl_2 (2 ml) was added PDC (10 mg) and stirred at room temp. After 1 h, the mixture was filtrated and chromatographed on silica gel to yield diketone **21** (2 mg): Oil; $[\alpha]_D^{21}$ +115.3° (*c* 1.00); IR ν_{max} 1685, 1470, 1375 cm^{-1}; ^1H and ^{13}C NMR: Tables 1 and 2; EIMS *m/z* (int.) 234 $[M]^+$ (27), 219 (5), 191 (7), 177 (8), 164 (20), 151 (49), 135 (11), 124 (100), 109 (26), 95 (36), 81 (8), 68 (15), 55 (14), 41 (14), 32 (7).

Dehydration of 14. *p*-Toluenesulfonic acid (1.7 mg) was added to **14** (2 mg) in dry benzene (2 ml) and solution stirred 1.5 h at room temp. The mixture was quenched with aq. $NaHCO_3$, extracted with Et_2O, then dried ($MgSO_4$). Evaporation of the solvent yielded a hydrocarbon (2 mg) whose spectral data were identical to those of (-)-thujopsene (**19**)[11] (natural $[\alpha]_D$ –121.8°, *c* 1.01; ref.[11] $[\alpha]_D$ –103.9°, *c* 1.02).

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