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ENT-KAURANE-TYPE DITERPENOIDS FROM THE LIVERWORT *JUNGERMANNIA EXSERTIFOLIA* SSP. *CORDIFOLIA*

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Key Word Index—*Jungermannia exsertifolia* ssp. *cordifolia*; Jungermanniaceae; liverwort; secoexsertifolins A, B; exsertifolins A, B, C, D, E, F, G, H; nardiin; 6,7-seco-*ent*-kaurane; bis-*ent*-kaurane; *ent*-kaurane; diterpenoid; X-ray analysis

Abstract—A new bis-*ent*-kaurane-type, exsertifolin A, two new 6,7-seco-*ent*-kaurane-type, secoexsertifolins A and B, and seven new *ent*-kaurane-type diterpenoids, exsertifolins B, C, D, E, F, G and H, were isolated from the French liverwort *Jungermannia exsertifolia* Steph. ssp. *cordifolia* (Dum.) Va'ňa, together with the previously known seven *ent*-kaurane-type diterpenoids. These structures were determined by means of extensive NMR techniques, chemical degradation and X-ray crystallographic analysis.

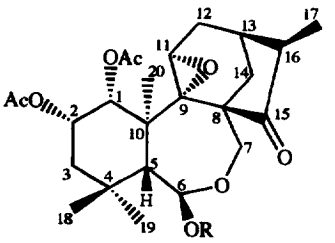
INTRODUCTION

As part of a chemosystematic study combined with a search for biologically active substances, we are continuing to study the chemical constituents of liverworts. *Jungermannia* species containing *Jungermannia exsertifolia* ssp. *cordifolia* are rich sources of diterpenoids of the *ent*-kaurane-, clerodane-, pimarane-, and labdane-type [1, 2]. Generally, the *Jungermannia* species are morphologically small, therefore, the identification of each species is quite difficult. Previously, we reported on the isolation of trachylobane-type diterpernoids from English *J. exsertifolia* ssp. *cordifolia* [3]. We reinvestigated the chemical constituents of *J. exsertifolia* ssp. *cordifolia* collected in France and found that this species produced a new bis-*ent*-kaurane- and 6,7-seco-*ent*-kaurane-type diterpenoids [4]. In this paper, we report on the isolation and characterization of the structures of two new 6,7-seco-*ent*-kaurane-type (**1**, **2**), a new bis-*ent*-kaurane-type (**3**), seven new *ent*-kaurane-type (**4**–**10**) and seven previously known *ent*-kaurane-type diterpenoids (**11**–**17**).

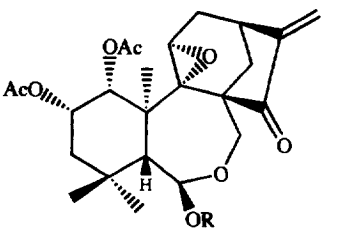
RESULTS AND DISCUSSION

CC of the ether extract of *J. exsertifolia* ssp. *cordifolia* yielded two new 6,7-seco-*ent*-kaurane-type, secoexsertifolins A (**1**) and B (**2**) [4], a bis-*ent*-kaurane-type, exsertifolin A (**3**) [4], and seven new *ent*-kaurane-type diterpenoids, exsertifolins B (**4**), C (**5**), D (**6**), E (**7**), F (**8**), G (**9**) and H (**10**), together with previously known seven *ent*-kaurane-type diterpenoids, *ent*-11α-hydroxykauren-15-one (**11**) [5, 6], *ent*-11α-hydroxy-16-kauren-15α-yl acetate (**12**) [5, 6], (16*R*)-*ent*-11α-hydroxykauran-15-one (**13**) [5, 6], *ent*-16-kauren-11α,15α-diol (**14**) [5, 6], *ent*-16-kauren-15α-ol (**15**) [7], *ent*-16-kauren-15-one (**16**) [7] and nardiin (**17**) [8]. The spectral data of known compounds **11**–**17** were identical with those of authentic samples.

The EI-mass spectrum of **1** [4] showed *m/z* 450 $[M]^+$ and the degree of unsaturation was confirmed to be eight from the molecular formula $C_{24}H_{34}O_8$ (analyt. 450.2261) determined by HRMS. The IR and ^{13}C NMR spectra showed the presence of a ketone carbonyl (δ216.8 *s*), two acetoxyl groups (1740, 1250 cm^{-1}; δ_C20.8, 20.9 each *q*, 169.1, 170.6 each *s*), and a hemiacetal hydroxyl group (3450 cm^{-1}; δ_C96.3 *d*) which was further confirmed by the formation of a triacetate (**18**) (δ_H1.93, 2.06 and 2.13 each 3H, *s*) by acetylation with Ac_2O-pyridine. The ^1H NMR spectrum (Table 1) of **1** indicated the presence of a secondary methyl, three tertiary methyls, two acetoxyl methyls and two methine protons (δ_H4.87 *dd*, 5.04 *ddd*) each bearing an acetoxyl group, and an additional methine proton (δ_H5.24 *dd*) bearing an hydroxyl group and isolated methylenic protons (δ_H3.17, 4.69 each *d*). The ^{13}C NMR spectrum (Table 2) of **1** showed 24 carbons and its DEPT spectrum indicated the presence of six methyls, three methylenes, three methines, three quaternary carbons together with two methine carbons (δ_C 66.7, 75.7) each bearing an acetoxyl group, an oxygen-bearing methylene (δ_C 61.8) and a hemiacetal carbon. In addition, an oxygen-bearing methine (δ_C 50.3) and quaternary (δ_C 65.9) carbons which are assignable to epoxide carbons were observed. From the above data, compound **1** was suggested to be a pentacyclic diterpene diacetate with one hemiacetal, one epoxide and one oxo group. The ^1H–^1H and ^{13}C–^1H COSY spectra of **1** indicated the presence of four partial structures as shown in Fig. 1. The connectivities of these partial structures were established by HMBC spectroscopy as shown in Table 3. In the



1 R=H
18 R=Ac



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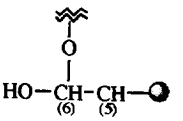
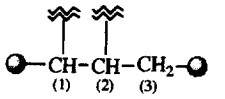


A



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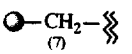

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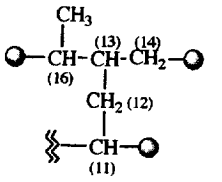
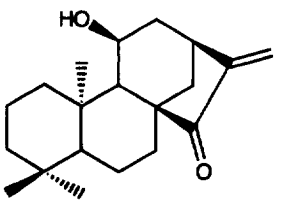


D

Fig. 1. Partial structures of 1.



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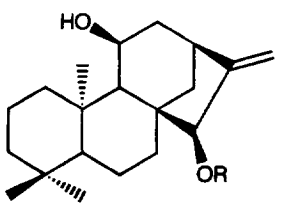
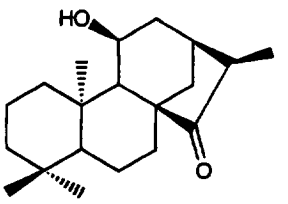


12 R=Ac
14 R=H



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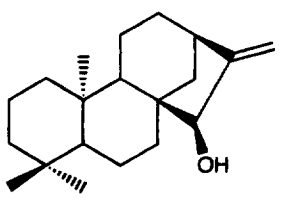

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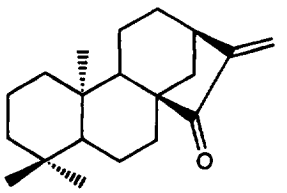

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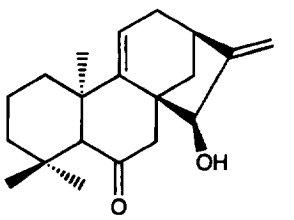


17

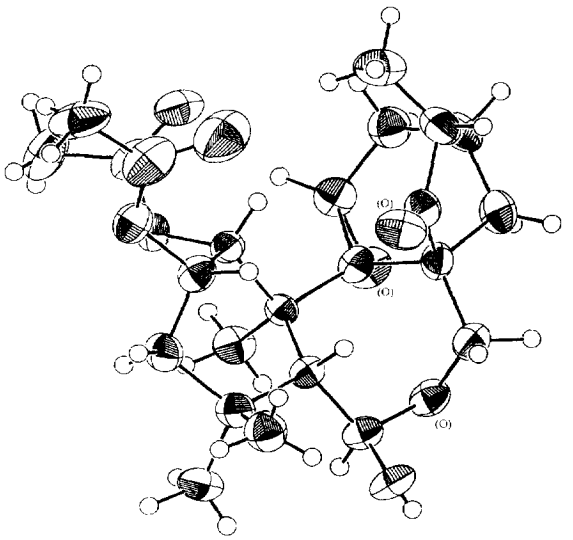
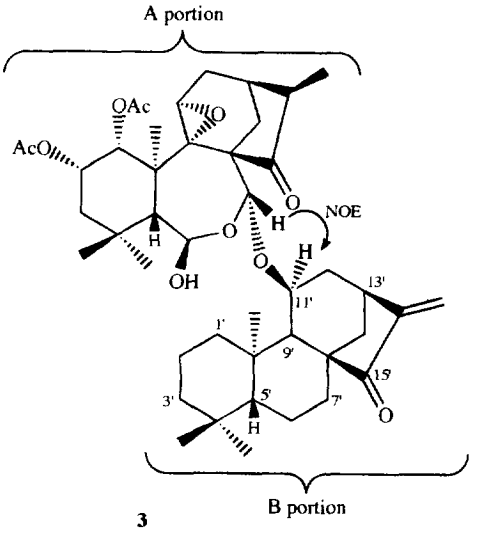


Fig. 2. ORTEP Drawing of **1**.



3

Fig. 3.

HMBC spectrum, isolated methylene protons (segment C in Fig. 1) were correlated with a methine carbon of the hemiacetal. Thus, the structure of **1** was shown to be that of a 6,7-seco-kaurane-type diterpenoid with two acetoxyl groups at C-1 and 2, a hydroxyl group at C-6 and C-9/C-11 epoxide. The stereochemistry of **1** was clarified by the difference NOE spectrum in which NOEs were observed between (i) H-20 and H-6, (ii) H-20 and H-11, (iii) H-19 and H-20, (iv) H-19 and H-6, (v) H-18 and H-5, and (vi) H-18 and H-2, respectively. However, the stereochemistry of the acetoxyl group at C-1 and the C-9/C-11 epoxide could not be clarified, therefore, an X-ray crystallographic analysis of **1** was carried out. The ORTEP drawing is shown in Fig. 2. Thus, the relative stereostructure of secoexsertifolin A, a 6,7-seco-kaurane-type diterpenoid, is as shown in **1**.

The IR spectrum of compound **2**, $C_{24}H_{32}O_8$, *m/z* 448.2096 $[M]^+$, showed the presence of two acetoxyl (1740, 1250 cm^{-1}; δ_H 1.90, 2.03 each 3H, *s*) and an oxo (1720 cm^{-1}; δ_C 202.9) and a hydroxyl group (3450 cm^{-1}) which was confirmed by the formation of the triacetate **19** (δ_H 1.91, 2.03 and 2.15 each 3H, *s*). The ^1H and ^{13}C NMR spectra (Tables 1 and 2) of **2** were very similar to those of **1** except for the presence of an *exo*-methylene group (δ_H 5.57, 6.34 each *s*, δ_C 121.5 *t*, 147.8 *s*) in place of the secondary methyl group, indicating that **2** was probably the C-17 dehydro derivative of **1**. Hydrogenation of **2** gave a dihydro derivative the spectral data of which were completely identical with those of secoexsertifolin A (**1**). Thus, the structure of secoexsertifolin B was established to be **2**.

The ^{13}C NMR (Table 4) and IR spectra of **3** showed the presence of a hydroxyl (3500 cm^{-1}), two oxo carbonyl (1730 cm^{-1}; δ 209.5, 217.2 each *s*) and two acetoxyl (1740, 1250 cm^{-1}; δ 20.9 (×2) *q*, 169.1, 170.4 each *s*) groups. The FAB-mass spectrometry of **3** showed the quasi-molecular ion at *m/z* 773 $[M + Na]^+$, therefore, the M_r of **3** was 750. The ^1H and ^{13}C NMR spectra (Table 4) established the presence of two hemiacetal methine carbons (δ_H 5.23 *dd*, 5.44 *s*; δ_C 93.3, 95.1), two oxygen-bearing methines (δ_H 2.51–2.57 *m*, 3.89 *br s*; δ_C 50.9, 70.9), quaternary (δ_C 65.4) carbons and *exo*-methylenic carbons (δ_H 5.13, 5.69 each *s*; δ_C 112.8 *t*, 149.8 *s*), along with a secondary methyl, six tertiary methyls, ten methylenes, six methines and six quaternary carbons. The above spectral evidence and FAB-mass spectrometry showed that molecular formula of **3** was $C_{44}H_{62}O_{10}$. Moreover, the ^1H and ^{13}C NMR spectra closely resembled those of secoexsertifolin A (**1**) and *ent*-11α-hydroxykauren-15-one (**11**) [5, 6] isolated from the present species. Therefore, the structure of **3** was that of a bis-kaurane-type diterpenoid composed of **1** and **11**. In order to clarify the above assumption, a detailed analysis of the ^{13}C–^1H COSY and HMBC spectra of **3** was carried out. The HMBC spectrum of **3** indicated the correlation between the hemiacetal proton at δ 5.44 (H-7) of the A portion and the methine carbon at δ 70.9 (C-11′) of the B portion as shown in Fig. 3. Moreover, NOEs were observed between the hemiacetal proton H-7 and the methine proton H-11′ as shown in Fig. 3. On the basis of the above spectra data, compound **3** was almost certainly a bis-kaurane linked by an ether bond between C-7 in portion A and C-11′ in portion B. Conclusive evidence of the stereostructure of **3** was given by X-ray crystallographic analysis. The ORTEP drawing is shown in Fig. 3. Thus, the stereostructure of exsertifolin A, bis-kaurane-type diterpenoid, is as shown in **3**.

EIMS of **4** showed the molecular ion at *m/z* 374 $[M]^+$ and by HRMS gave the molecular formula $C_{22}H_{30}O_5$. The IR and ^{13}C NMR spectra indicated the presence of a secondary hydroxyl (3550 cm^{-1}; δ_H 4.50 *br t*; δ_C 66.7 *d*), an oxo carbonyl (1720 cm^{-1}; δ_C 206.5) and an acetoxyl group (1720, 1240 cm^{-1}; δ_H 1.96 *s*; δ_C 21.3 *q*, 169.7 *s*). The resistance of **4** to acetylation indicated that the secondary hydroxyl group might be *axial*. The ^1H and ^{13}C NMR spectra (Tables 1 and 2) showed the presence of a methine

Table 1. ^{1}H NMR data of compounds **1**, **2** and **4–6** (400 MHz, in $CDCl_3$)

H	1	2	4	5	6
1	4.87 *dd*, *J* = 4.9, 2.0 Hz	4.96 *d*, *J* = 2.0 Hz	4.64 *dd*, *J* = 8.8, 4.9 Hz	4.57 *dd*, *J* = 7.8, 5.4 Hz	4.90 *d*, *J* = 4.9 Hz
2	5.04 *ddd*, *J* = 13.2, 4.9, 2.4 Hz	4.93 *m*	1.46–1.71 *m*	1.48–1.59 *m*	5.15 *ddd*, *J* = 10.7, 5.9, 3.9 Hz
			1.72–1.79 *m*	1.84–1.96 *m*	
3	1.25 *dt*, *J* = 13.2, 4.9, 2.4 Hz	1.26 *br d*	1.33–1.41 *m*	1.39 *m*	1.51 *dd*, *J* = 13.7, 2.9 Hz
	1.86 *t*, *J* = 12.2 Hz	1.82–1.93 *m*	1.46–1.71 *m*	1.48–1.59 *m*	1.86–1.95 *m*
5	2.78 *d*, *J* = 9.8 Hz	2.64 *d*, *J* = 9.8 Hz	1.80 *br s*	1.84–1.96 *m*	2.12 *s*
6	5.24 *dd*, *J* = 9.3, 2.9 Hz	5.25 *dd*, *J* = 9.8, 2.9 Hz	4.50 *br t*	4.45 *br t*	4.43 *br t*
7	3.17 *d*, *J* = 13.2 Hz	3.18 *d*, *J* = 13.2 Hz	1.46–1.71 *m*	1.48–1.59 *m*	1.56 *br d*
	4.69 *d*, *J* = 13.2 Hz	4.80 *d*, *J* = 13.2 Hz	2.41 *dd*, *J* = 14.6, 6.3 Hz	2.28 *dd*, *J* = 15.1, 6.8 Hz	2.28 *dd*, *J* = 15.1, 6.4 Hz
11	2.64 *br s*	2.75 *d*, *J* = 4.9 Hz	3.37 *dd*, *J* = 4.9, 1.5 Hz	3.33 *dd*, *J* = 4.4, 1.6 Hz	2.98 *dd*, *J* = 4.4, 1.5 Hz
12	1.93 2H, *m*	1.82–1.93 *m*	1.72–1.79 *m*	1.84–1.96 *m*	1.86–1.95 *m*
		2.22 *dd*, *J* = 15.1, 5.4 Hz	2.34 *dd*, *J* = 14.7, 4.9 Hz	2.08 *dd*, *J* = 15.6, 5.4 Hz	2.02 *m*
13	2.17 *br q*	2.71 *br t*	2.69 *br t*	2.15 *br q*	2.17 *br q*
14	1.37 *ddd*, *J* = 12.2, 4.9, 1.5 Hz	1.42 *m*	1.33–1.41 *m*	1.35 *m*	1.39 *ddd*, *J* = 11.2, 5.3, 2.0 Hz
	2.54 *d*, *J* = 12.2 Hz	2.39 *d*, *J* = 12.2 Hz	2.21 *d*, *J* = 11.7 Hz	2.32 *d*, *J* = 11.2 Hz	2.32 *d*, *J* = 11.2 Hz
16	2.34 quit. *J* = 7.3 Hz			2.30 *m*	2.33 *m*
17	1.32 3H, *d*, *J* = 7.3 Hz	5.57 *s*	5.41 *s*	1.08 *d*, *J* = 7.3 Hz	1.20 *d*, *J* = 7.3 Hz
		6.34 *s*	6.11 *s*		
18	1.41 3H, *s*	1.41 3H, *s*	1.06 3H, *s*	1.04 3H, *s*	1.15 3H, *s*
19	1.13 3H, *s*	1.14 3H, *s*	1.16 3H, *s*	1.16 3H, *s*	1.23 3H, *s*
20	0.88 3H, *s*	0.89 3H, *s*	1.12 3H, *s*	1.14 3H, *s*	1.21 3H, *s*
OAc	1.92 3H, *s*	1.90 3H, *s*	1.96 3H, *s*	2.00 3H, *s*	1.96 3H, *s*
	2.06 3H, *s*	2.03 3H, *s*			2.04 3H, *s*
OH	2.49 *br s*	2.45 *d*, *J* = 2.9 Hz			

Table 2. ^{13}C NMR data of compounds **1**, **2**, **4**–**10** and **17** (100 MHz, in $CDCl_3$)

C	1	2	4	5	6	7	8*	9	10*	17†
1	75.7	74.6	76.8	77.3	73.6	73.5	78.3	42.6	41.5	43.0
2	66.7	66.8	26.3	26.1	67.4	68.0	25.5	19.4	19.4	18.7
3	38.5	38.7	38.8	38.1	39.2	40.7	38.7	44.8	45.2	47.4
4	33.0	33.0	33.4	33.3	33.0	33.0	32.5	34.5	34.6	32.5
5	44.1	44.3	50.3	49.7	46.5	47.7	46.0	48.1	49.0	60.4
6	96.3	96.1	66.7	66.7	66.0	66.0	17.5	66.5	67.4	211.2
7	61.8	60.7	39.2	39.9	39.7	38.9	26.8	36.8	41.9	39.9
8	56.2	56.5	49.9	49.4	49.0	49.6	51.3	50.0	44.7	45.2
9	65.9	67.1	62.7	61.1	62.0	63.3	65.6	150.8	153.7	151.1
10	46.1	46.3	42.4	42.2	42.1	42.3	43.5	38.9	38.2	39.8
11	50.3	50.5	52.3	52.2	51.5	51.7	52.9	119.1	117.4	118.3
12	23.3	31.1	31.8	24.2	23.9	31.6	32.2	36.4	39.2	38.8
13	31.1	32.8	33.3	31.1	31.5	33.4	33.7	36.5	38.0	38.0
14	39.4	37.5	36.5	38.7	38.4	36.3	35.7	39.6	40.8	39.8
15	216.8	202.8	206.5	220.1	220.1	206.5	207.7	202.7	86.7	87.9
16	47.7	147.8	148.5	46.6	46.9	148.2	149.5	151.3	161.9	161.0
17	11.2	121.5	119.4	12.1	11.9	119.9	117.6	116.2	108.0	108.6
18	32.8	32.9	33.0	32.8	32.1	32.6	33.0	32.5	32.7	33.5
19	25.4	25.3	24.0	24.3	25.7	25.4	22.2	25.4	25.0	21.7
20	15.5	14.8	14.1	14.8	16.5	15.5	12.0	27.0	27.5	27.2
OAc	20.8	20.8	21.3	21.6	20.9	20.8	21.5			
	20.9	20.9	169.7	169.9	21.0	21.0	170.3			
	169.1	169.2			169.5	169.6				
	170.6	170.3			170.2	169.8				

* Measured by 150 MHz.
† Tentative assign and measured by 50 MHz.

Table 3. Long-range ^{13}C–^{1}H correlations by the HMBC spectrum of **1**

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

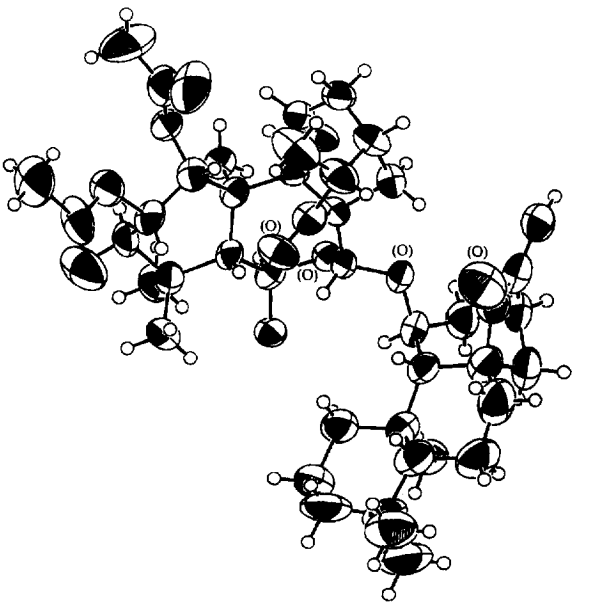


Fig. 4. ORTEP drawing of **3**.

(δ_H 4.64 *dd*; δ_C 76.8) bearing an acetoxyl group, a methine (δ_H 3.37 *dd*; δ_C 52.3) and quaternary carbons (δ_C 62.7) of an epoxide and an *exo*-methylene (δ_H 5.41, 6.11 each *s*; δ_C 119.4 *t*, 148.5 *s*) together with three tertiary methyls, five methylenes, two methines and three quaternary carbons. As these spectral data were similar to those of compounds **1** and **2**, this led to the structure of **4** being that of a kaurane-type diterpenoid with an epoxide. The ^{1}H–^{1}H, ^{13}C–^{1}H COSYs and HMBC spectra of **4** clarified its relative structure. In the HMBC spectrum, the *exo*-methylene protons (H_2-17) were correlated with a ketone carbonyl (C-15), a quaternary carbon (C-16) and a methine carbon (C-13). A methine proton (H-13) was correlated with a methine carbon (C-11) of the epoxide

Table 4. ^1H and ^{13}C NMR data of exsertifolin A (3) (400 MHz, in $CDCl_3$)

	C	H		C	H
1	75.1	4.86 *br d*	1′	40.1	*
					2.16 *br d*
2	66.7	5.02 *br d*	2′	18.3†	*
3	38.6	*	3′	41.4	*
4	33.3		4′	33.3	
5	45.6	2.51–2.57 *m*	5′	54.9	*
6	95.1	5.23 *dd*, J = 9.8, 3.4 Hz	6′	18.4†	*
7	93.3	5.44 *s*	7′	33.7	*
8	61.4		8′	50.7	
9	65.4		9′	61.8	
10	46.6		10′	38.3	
11	50.9	2.51–2.57 *m*	11′	70.9	3.89 *br s*
12	22.9	*	12′	39.7	2.01 2H, *m*
13	31.9	2.24 *m*	13′	36.8	2.95 *br s*
14	29.4	*	14′	36.8	*
					2.36 *d*, J = 11.7 Hz
15	217.2		15′	209.5	
16	47.2	2.51–2.57 *m*	16′	149.8	
17	10.7	1.28 3H, *d*, J = 7.3 Hz	17′	112.8	5.13 *s*
					5.69 *s*
18	32.7	1.35 3H, *s*	18′	33.4	0.91 3H, *s*
19	25.0	1.10 3H, *s*	19′	21.8	0.81 3H, *s*
20	15.7	0.84 3H, *s*	20′	18.0	1.00 3H, *s*
OAc	20.9	1.91 3H, *s*			
	20.9	2.03 3H, *s*			
	169.1				
	170.4				
OH		2.78 *d*, J = 3.4 Hz			

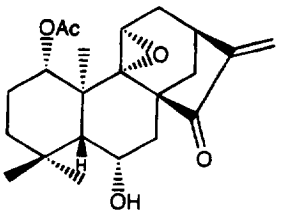
*Overlapped signals at δ 0.82–1.07 (3H), 1.13–1.48 (7H), 1.58–1.72 (5H) and 1.79–1.90 (5H).

† May be interchanged.

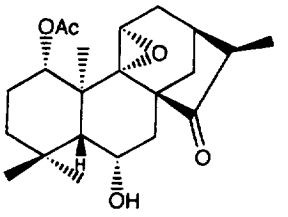
group, a quaternary carbon (C-8), a ketone carbonyl (C-15) and two *exo*-methylenic carbons (C-16 and 17). The most high-field tertiary methyl (H-18) was correlated with a methyl (C-19), a methylene (C-3), a methine (C-5) and a quaternary carbon (C-4), and second high-field tertiary methyl (H-20) was correlated with a methine (C-1) bearing the acetoxyl group, a methine carbon (C-5), a quaternary (C-10) and an oxygen-bearing quaternary carbon (C-9), respectively. Successively, the detailed analysis of each cross-peak indicated the presence of a C-9/C-11 epoxide, an acetoxyl group at C-1 and a hydroxyl group at C-6. The stereochemistry of **4** was confirmed by the difference NOE, in which the NOEs were observed between (i) H-18 and H-5, (ii) H-18 and H-6, (iii) H-20 and H-11, (iv) H-5 and H-1, (v) H-5 and H-6, respectively. The stereochemistry of the hydroxyl group at C-6 and an acetoxyl group at C-2 was *axial* and an additional acetoxyl group at C-1 was *equatorial*. From the above spectral evidence, the structure of exsertifolin B was established to be that of the C-9/C-11 epoxide **4**.

The IR, ^1H and ^{13}C NMR (Tables 1 and 2) spectra of **5**, $C_{22}H_{32}O_5$, *m/z* 376.2254 $[M]^+$, resembled those of **4**, except for the presence of a secondary methyl group in place of the *exo*-methylene in **4** indicating that compound **5** was the C-16/C-17 dihydro derivative of **4**. Hydrogenation of **4** in the presence of Pd-C gave only one dihydro derivative, the spectral data of which were completely identical with those of **5**. Furthermore, its relative stereochemistry was established by X-ray crystallographic analysis (Fig. 5).

The IR, ^1H and ^{13}C NMR data (Tables 1, 2 and 5) of compounds **6**, $C_{24}H_{34}O_7$, *m/z* 434.2287 $[M]^+$, and **7**, $C_{24}H_{32}O_7$, *m/z* 432.2111 $[M]^+$, were similar to those of exsertifolins B (**4**) and C (**5**) indicating that the structures of **6** and **7** were based on a kaurane-type diterpenoid [5–7] with a C-9/C-11 epoxide group. Acetylation of **6** with Ac_2O-pyridine did not proceed as seen in exsertifolin B (**4**). Oxidation of **6** and **7** by pyridinium dichromate (PDC) gave the diketones **20** ($C_{24}H_{32}O_7$, *m/z* 432.2145, δ_C 207.9, 219.6, each *s*) and **21** (*m/z* 430, δ_C 206.2, 207.5, each *s*), respectively. The ^1H and ^{13}C NMR spectra (Tables 1, 2 and 5) of **6** were similar to those of **7** except for the presence of an *exo*-methylene group (δ_H 5.45, 6.16 each *s*; δ_C 119.9 *t*, 148.2 *s*) in place of the secondary methyl group (δ_H 1.20 *d*; δ_C 11.9), suggesting that the structure of **6** was that of the dihydro derivative of **7**. This presumption was confirmed by hydrogenation of **7** to furnish a dihydro derivative whose spectral data were completely identical with those of **6**.



4



5

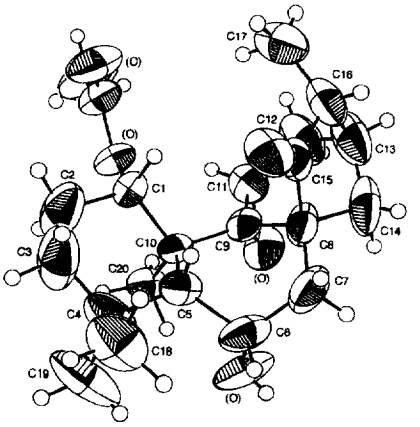
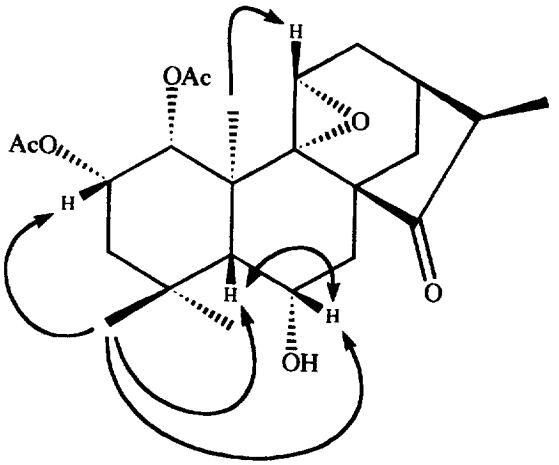
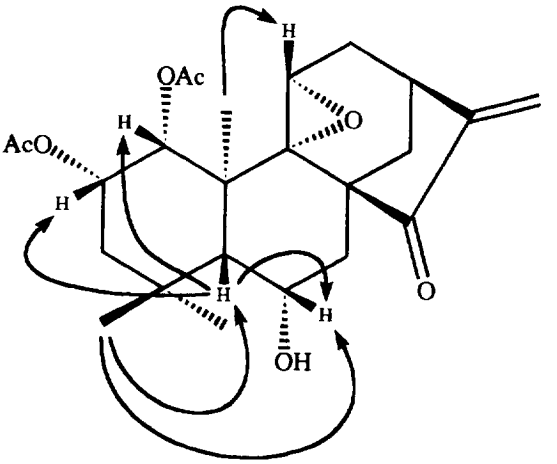


Fig. 5. ORTEP drawing of 5.



6



7

Fig. 6. NOEs observed in the difference NOE spectrum of 6 and 7 in C_6D_6.

The stereochemistries of **6** and **7** were confirmed by the difference NOE spectra as shown in Fig. 6. Furthermore, X-ray crystallographic analysis of **7** was carried out and gave the ORTEP drawing shown in Fig. 7. From the above spectral evidence and X-ray analysis, the stereostructures of exsertifolins D and E are as depicted in **6** and **7**, respectively.

HRMS of **8** gave the molecular formula $C_{22}H_{30}O_4$, *m/z* 358.2173 $[M]^+$. The IR and ^{13}CNMR spectra showed the presence of a ketone carbonyl (1720 cm^{-1}; δ207.7 *s*) and an acetoxyl group (1740, 1260 cm^{-1}; δ21.5 *q*, 170.3 *s*). The ^1H and ^{13}CNMR spectra (Tables 5 and 2) of **8** closely resembled those of compound **4** except for the absence of the hydroxyl group indicating that **8** was deoxy **4**. The structure of exsertifolin F was further established by detailed analysis of the ^1H–^1HCOSY, HSQC, HMBC (Fig. 8) and NOESY (Fig. 9) spectra.

The IR spectrum of **9**, $C_{20}H_{28}O_2$ *m/z* 300.2072 $[M]^+$, showed the presence of a hydroxyl (3500 cm^{-1}) and

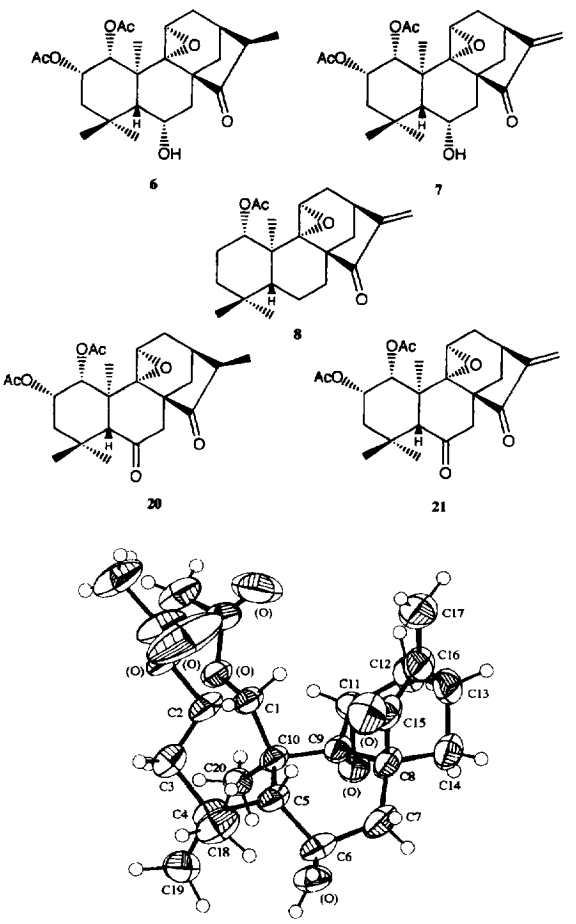


Fig. 7. ORTEP drawing of 7.

a ketone (1720 cm^{-1}; δ_C 202.7). The ^{13}C and ^1H NMR spectra (Tables 2 and 5) of **9** were similar to those of nardiin (**17**) [8] isolated from the present species, suggesting that **9** was a kaurane-type diterpenoid with a C-9/C-11 double bond. The ^1H–^1H COSY spectrum of **9** showed the presence of two partial structures, (i) –CH(5)–CH(OH)(6)–CH_2(7)– and (ii) –C=CH(11)–CH_2(12)–CH(13)–CH_2(14)–. Thus, the structure of **9** was clarified to be 6-hydroxy-9(11), 16-kauradien-15-one. The stereochemistry of the hydroxyl group at C-6 was established to be *axial* by the difference NOE spectrum in which NOEs were observed between (i) H-18 and H-6, (ii) H-18 and H-5, and (iii) H-19 and H-18 and 20. On oxidation of **9**, a diketone derivative **22** ($C_{20}H_{26}O_2$, *m/z* 298.1949; 1720, 1700 cm^{-1}; δ_C 201.7, 209.4 each *s*) was obtained. Its spectral data were in good agreement with those of an oxidation product of nardiin (**17**) [8]. Thus, the absolute structure of exsertifolin G was elucidated to be *ent*-6β-hydroxy-9(11),16-kauradien-15-one (**9**).

The IR, ^1H (Table 5) and ^{13}C NMR (Table 2) spectra of **10**, $C_{20}H_{30}O_2$, *m/z* 302.2256 $[M]^+$, indicated the presence of two secondary hydroxyl groups (3440 cm^{-1}; δ_H 4.08 *br d*, 4.59 *br q*; δ_C67.4, 86.7 each *t*), and *exo*-methylene group (δ_H 5.06 *d*, 5.10 *s*; δ_C 108.0 *t*, 161.9 *s*) and trisubstituted olefinic carbons (δ117.4 *d*, 153.7 *s*). The spectral data of **10** were closely related to those of exsertifolin G (**9**) except for the absence of a ketone group suggesting that compound **10** was the C-15 dihydro derivative of **9**. This assumption was confirmed by detailed analysis of the ^1H–^1H COSY, HMQC and HMBC spectra. The stereochemistry of **10** was clarified by the NOESY spectrum in which NOEs were observed between (i) H-6 and H-5β, 7β and 18, and (ii) H-15 and H-7β and 14β. The spectral data of the diketone obtained from **10** by oxidation using PDC were completely identical with those of **22** derived from **9**. The above chemical and spectral evidences established that the absolute structure of exsertifolin H to be *ent*-9(11),16-kauradien-6β,15α-diol (**10**).

The CD spectrum of **9** and **22** showed positive ($\Delta\varepsilon_{348}$ + 1.00 in **9** and $\Delta\varepsilon_{340}$ + 2.30 in **22**) and negative ($\Delta\varepsilon_{265}$ – 1.04, $\Delta\varepsilon_{235}$ – 0.90 in **9** and $\Delta\varepsilon_{262}$ – 2.79 in **22**) Cotton effects. By contrast, that of nardiin (**17**) [8] showed the negative ($\Delta\varepsilon_{292}$ – 6.9) and positive ($\Delta\varepsilon_{218}$ + 12.7) Cotton effects as seen in compounds **11**, **13** and **16** [5–8] isolated from present species. The CD spectra of compounds **1**, **2** and **4**–**8** showed the positive (first) and negative (second) Cotton effects (see Experimental) seen in compounds **9** and **22**, respectively. The influence of the C-9/C-11 double bond may be one of the reasons why the Cotton effect shows the opposite signs. In view of the presence of *ent*-kauran-type compounds **11**–**17** in the present species and the CD spectra of compounds **9** and **22**, the structures of secoexsertifolin A (**1**), B (**2**) and exsertifolin A (**3**), B (**4**), C (**5**), D (**6**), E (**7**) and F (**8**) were suggested to be 6,7-seco-*ent*-1β,2β-diacetoxy-9β, 11β-epoxy-6α-hydroxy-kaur-15-one, 6,7-seco-*ent*-1β,2β-diacetoxy-9β,11β-epoxy-6α-hydroxy-16-kauren-15-one, bis-6,7-seco-*ent*-1β,2β-diacetoxy-9β,11β-epoxy-6α-hydroxy-16α-kauran-15-one,*ent*-16-kauren-15-one-7α,11′β-ether, *ent*-1β-acetoxy-6β-hydroxy-9β,11β-epoxy-16-kauren-15-one, *ent*-1β-acetoxy-6β-hydroxy-9β, 11β-epoxy-kaur-15-one, *ent*-1β,2β-diacetoxy-6β-hydroxy-9β,11β-epoxy-16-kauren-15-one and *ent*-1β,2β-diacetoxy-6β-hydroxy-9β,11β-epoxy-kaur-15-one, respectively.

This is the first example of the isolation of the 6,7-seco-9,11-epoxy-*ent*-kaurane-type and 9,11-epoxy-*ent*-kaurane-type diterpenoids from liverworts. The isolation of bis-*ent*-kaurane-type diterpenoids is the third report from liverworts [9, 10]. Previously, we reported that English *J. exsertifolia* ssp. *cordifolia* produced trachylobane-type diterpenoid [3]. However, the present species does not contain trachylobane-type diterpenoids. It is considered that there are at least two chemotypes of European *J. exsertifolia* ssp. *cordifolia*.

EXPERIMENTAL

Mps: uncorr. The solvents used for spectral measurements were TMS–$CDCl_3$ [^1H–(600, 400 and 200 MHz) and ^{13}C (120, 100 and 50 MHz) NMR]; $CHCl_3$ ($[\alpha]_D$); UV and CD (MeOH). TLC was carried out as previously reported [11].

Plant material. J. exsertifolia Steph. ssp. *cordifolia* (Dum.) Vana. was collected in the Vosges Mountains,

Table 5. ^{1}H NMR data of compounds **7–10** (400 MHz, in $CDCl_3$)

H	7	8*	9	10*
1	4.87 *d*, J = 5.4 Hz	4.60 *dd*, J = 13.3, 4.9 Hz	0.95–1.17 *m*	1.11–1.22 *m*
			1.87 *br d*	1.91 *m*
2	5.14 *like quit.*	1.52 *m*	1.41 *m*	1.45 *m*
		1.71 *m*	1.60 *m*	1.65 *m*
3	1.53–1.60 *m*	1.41 2H, *m*	0.95–1.17 *m*	1.11–1.22 *m*
	1.87 *m*		1.26 *m*	1.29 *m*
5	1.97 *m*	1.89–1.95 *m*	1.53 *d*, J = 5.4 Hz	1.89 *d*, J = 6.3 Hz
6	4.50 *br t*	1.47 *m*	4.96 *br q*	4.59 *br q*
		1.89–1.95 *m*		
7	1.53–1.60 *m*	1.62 *m*	1.78 *dd*, J = 14.2, 7.3 Hz	1.96 *dd*, J = 13.9, 8.8 Hz
	2.42 *dd*, J = 15.1, 6.4 Hz	1.89–1.95 *m*	2.34 *dd*, J = 14.2, 9.3 Hz	2.13 *dd*, J = 13.9, 9.0 Hz
11	3.13 *d*, J = 4.4 Hz	3.17 *dd*, J = 4.2, 1.2 Hz	5.52 *t*, J = 3.4 Hz	5.44 *t*, J = 3.4 Hz
12	1.80 *m*	1.76 *m*	2.15 *br d*	2.03 *br d*
	2.30 *dd*, J = 15.1, 5.4 Hz	2.26 *dd*, J = 14.9, 5.6 Hz	2.65 *ddd*, J = 17.6, 4.4, 2.9 Hz	2.48 *ddd*, J = 17.3, 4.6, 2.9 Hz
13	2.71 *br t*	2.67 *t*, J = 5.4 Hz	2.99 *br s*	2.72 *br s*
14	2.21 *d*, J = 11.7 Hz	2.16 *d*, J = 12.0 Hz	1.66 *d*, J = 10.7 Hz	1.50 *d*, J = 11.2 Hz
	1.39 *ddd*, J = 12.2, 5.9, 2.0 Hz	1.27 *m*	1.74 *dd*, J = 10.7, 4.4 Hz	1.63 *m*
15				4.08 *br d*
17	5.45 *s*	5.34 *t*, J = 1.0 Hz	5.44 *s*	5.06 *d*, J = 2.4 Hz
	6.16 *s*	6.04 *s*	5.90 *s*	5.10 *s*
18	1.15 3H, *s*	1.01 3H, *s*	1.13 3H, *s*	1.10 3H, *s*
19	1.27 3H, *s*	0.91 3H, *s*	1.29 3H, *s*	1.28 3H, *s*
20	1.24 3H, *s*	0.97 3H, *s*	1.37 3H, *s*	1.31 3H, *s*
OAc	1.98 3H, *s*	1.99 3H, *s*		
	1.99 3H, *s*			

* Measured by 600 MHz.

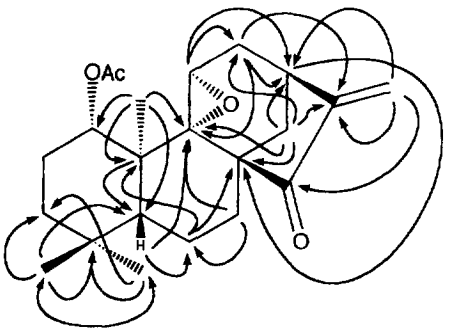


Fig. 8. ^{1}H–^{13}C long-range correlations observed in the HMBC spectrum of **8**.

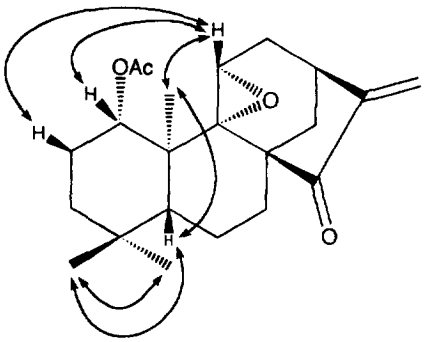
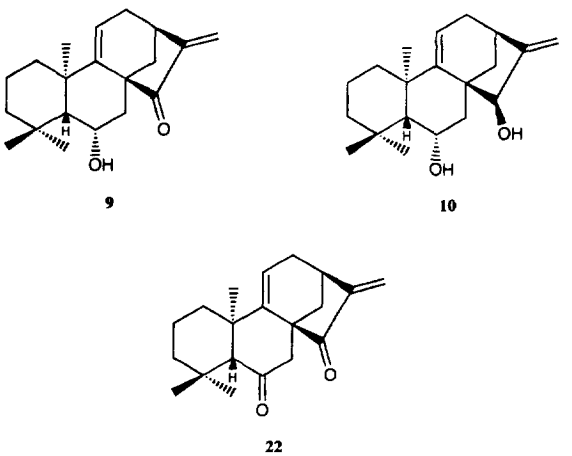


Fig. 9. NOEs observed in the NOESY spectrum of **8**.



France, in April, 1993 and identified by Prof. J. P. Frahm. The voucher specimen is deposited at the Institute of Pharmacognosy, Tokushima Bunri University.

Extraction and isolation. The dry material (161 g) of *J. exsertifolia* ssp. *cordifolia* was ground and extracted with Et_2O for four weeks. The crude extract (4.2 g) was divided into 6 frs by CC on silica gel using an *n*-hexane–EtOAc gradient. Fr. 1 was rechromatographed on Sephadex LH-20 (CH_2Cl_2–MeOH, 1:1) and silica gel and finally purified on prep. HPLC (NUCLEOSIL 50-5, *n*-hexane–Et_2O; 9:1 and 4:1) to give *ent*-15α-hydroxykaurene (**15**) (7 mg) [7] and *ent*-kauren-15-one (**16**) (10 mg) [7]. Fr. 2 gave a nardiin (**17**) (11 mg) [8] on rechromatography on silical gel (*n*-hexane–EtOAc, 9:1). The spectral data of **15**, **16** and **17** were identical with those of authentic samples. Fr. 3 was rechromatographed on Sephadex LH-20 and silica gel to give exsertifolin G (**9**) (14 mg), H (**10**) (3 mg) and a mixture of diterpene frs which were purified on prep. TLC (CH_2Cl_2–Et_2O, 9:1) to give exsertifolin F (**8**) (5 mg).

Exsertifolin F (**8**). $[\alpha]_D$ +103.0° (*c* 0.49); HREI-MS: found 358.2173 $C_{22}H_{30}O_4$ requires 358.2144; UV λ_{max} nm (log ε): 231 (3.67) (*c* 3.2×10^{-4}); FTIR ν_{max} cm^{-1}: 1720 (C=O), 1740, 1260 (OAc); ^{13}C and ^{1}H NMR: Tables 2 and 5; EIMS *m/z* (rel. int.): 358 $[M]^+$(100), 298 (69), 283 (96), 267 (14), 259 (26), 239 (16), 229 (24), 205 (37), 187 (33), 161 (32), 147 (31), 121 (41), 105 (41), 91 (55), 81 (35), 69 (21), 55 (32), 43 (68); CD: $\Delta\varepsilon_{330}$ + 0.19, $\Delta\varepsilon_{240}$ − 1.42 (*c* 3.2×10^{-4}).

Exsertifolin G (**9**). Mp. 108–110°; $[\alpha]_D$ +115.2° (*c* 1.38); HREIMS: found 300.2072 $C_{20}H_{28}O_2$ requires 300.2090; UV λ_{max} nm (log ε): 231 (3.42), 211 (3.40) (*c* 3.3×10^{-4}); FTIR ν_{max} cm^{-1}: 3500 (OH), 1720 (C=O); ^{13}C and ^{1}H NMR: Tables 2 and 5; EIMS *m/z* (rel. int.): 300 $[M]^+$ (40), 285 (19), 267 (100), 251 (1), 239 (11), 226 (37), 205 (20), 197 (42), 187 (96), 173 (17), 161 (9), 145 (13), 129 (12), 105 (12), 95 (12), 91 (17), 79 (9), 69 (23), 55 (15), 41 (17); CD: $\Delta\varepsilon_{348}$ + 1.00, $\Delta\varepsilon_{265}$ − 1.04, $\Delta\varepsilon_{235}$ − 0.90 (*c* 3.2×10^{-4}).

Exsertifolin H (**10**). Mp.: 181–183°; $[\alpha]_D$ + 56.5° (*c* 0.31); HREIMS: found 302.2256 $C_{20}H_{30}O_2$ requires 302.2245; FTIR ν_{max} cm^{-1}: 3440 (OH); ^{1}H and ^{13}C NMR: Tables 5 and 2; EIMS *m/z* (rel. int.): 302 $[M]^+$ (33), 287 (32), 296 (100), 251 (29), 241 (9), 227 (6), 215 (11), 199 (16), 189 (10), 173 (12), 157 (11), 145 (12), 131 (14), 119 (12), 105 (15), 91 (18), 81 (11), 69 (22), 55 (15), 41 (17), 32 (20).

Fr. 4 was rechromatographed on Sephadex LH-20 (CH_2Cl_2–MeOH, 1:1) and silica gel (CH_2Cl_2–Et_2O gradient) to give fractions A–E. Fr. B on prep. HPLC (NUCLEOSIL 50-5, CH_2Cl_2–Et_2O, 4:1) a *ent*-11α-hydroxykaurene-11α, 15α-diol (**12**) (90 mg) [5, 6]. Prep. HPLC (NUCLEOSIL 50-5, CH_2Cl_2–Et_2O, 4:1) of fr. D gave (16*R*)-*ent*-11α-hydroxykauran-15-one (**13**) (32 mg) [5, 6] and *ent*-kaurane-11α, 15α-diol (**14**) (30 mg) [5, 6]. The spectral data of **12**–**14** were identical with those of authentic samples. Fr. 5 was divided into fractions A and B by CC on Sephadex LH-20 (CH_2Cl_2–MeOH, 1:1). Fr. A was rechromatographed on silica gel (CH_2Cl_2–Et_2O, 2:1) to give fractions A-1 and A-2. Fr. A-1 was rechromatographed on Sephadex LH-20 (MeOH) and prep. TLC (CH_2Cl_2–Et_2O, 2:1) to give exsertifolin A (**3**) (17 mg). Fr. B was chromatographed on silica gel (CH_2Cl_2–Et_2O, 95:5) to give *ent*-11α-hydroxykauren-15-one (**11**) (208 mg) [5, 6] and a mixture of diterpene fractions which was further chromatographed on prep. HPLC (NUCLEOSIL 50-5, *n*-hexane–EtOAc, 7:3) to give exsertifolins B (**4**) (31 mg) and C (**5**) (12 mg).

Exsertifolin A (**3**). Mp: 198–200°; $[\alpha]_D$ − 67.6° (*c* 1.69); FAB-MS: *m/z* 773 $[M + Na]^+$ (*m*-nitrobenzyl alcohol), *m/z* 789 $[M + K]^+$ (*m*-nitrobenzyl alcohol + KCl); UV

Table 6. Summary of crystallographic data of **1**, **3**, **5** and **7**

	1	3	5	7
Chemical formula	$C_{24}H_{34}O_8$	$C_{44}H_{62}O_{10}$	$C_{22}H_{32}O_5$	$C_{24}H_{22}O_7$
fw	450	750	376	422
Crystal system	Orthorhombic	Monoclinic	Orthorhombic	Orthorhombic
Space group	$P2_12_12_1$ (#19)	$P2_1$ (#4)	$P2_12_12_1$ (#19)	$P2_12_12_1$ (#19)
a, Å	12.856 (2)	16.411 (5)	13.977 (4)	8.854 (5)
b, Å	17.531 (4)	10.500 (4)	19.650 (5)	30.05 (2)
c, Å	10.173 (2)	14.292 (5)	7.686 (3)	8.574 (6)
β, degrees		112.69 (2)		
V, A^{-3}	2292.8 (8)	2272 (1)	2111 (1)	2281 (2)
Z	4	2	4	4
Dcalc, g/cm^3	1.30	1.10	1.18	1.23
Diffractometer	Mac Science MXC 18	Mac Science MXC 18	Mac Science MXC 18	Mac Science MXC 18
Radiation	Cu Kα $\lambda = 1.54178$	Cu Kα $\lambda = 1.54178$	Cu Kα $\lambda = 1.54178$	Cu Kα $\lambda = 1.54178$
Total reflections	2266	4176	1992	2236
Unique reflections	2174	3959	1909	2144
Rint	0.00	0.08	0.00	0.00
F(000)	968	811	815	888
Linear absorption, cm^{-1} (Cu Kα)	7.15	5.874	5.88	6.70
Maximum $\sin\theta/\lambda$	0.583	0.581	0.582	0.580
Total reflections used	2132	3376	1992	2113
No. variables	401	572	335	386
R	0.051	0.1170	0.068	0.044
Rw	0.072	0.1104	0.067	0.063

λ_{max} nm (log ε): 234 (3.73) (c 5.7×10^{-4}); FTIR ν_{max} cm^{-1}: 3500 (OH), 1740, 1250 (OAc), 1730 (C=O); ^{1}H and ^{13}C NMR: Table 4; EIMS *m/z* (rel. int.): 732 $[M^+ - H_2O]^+$ (1), 406 (5), 378 (9), 329 (7), 287 (86), 235 (43), 217 (28), 164 (74), 123 (55), 95 (50), 81 (40), 69 (56), 55 (43), 43 (100); CD: $\Delta\varepsilon_{360} - 0.08$, $\Delta\varepsilon_{330} - 0.13$, $\Delta\varepsilon_{295} + 1.70$, $\Delta\varepsilon_{245} - 2.30$ (c 5.7×10^{-4}).

X-ray crystallographic analysis. Compound **3** was recrystallized from *n*-hexane–Et_2O. The X-ray analysis was carried out on a Mac Science MXC 18 diffractometer with Cu Kα radiation ($\lambda = 1.54178$). The structure was solved by direct methods using SHELXS-86 and refined by block-matrix least-squares. The weighting function used was $w = 1$ for the function of $\Sigma w(|F_o|^2 - |F_c|^2)^2$ to be minimized. Crystal data and other information are summarized in Table 6.

Exsertifolin B (**4**). Amorphous; $[\alpha]_D + 62.1°$ (c 2.43); HREI-MS: found 374.2087 $C_{22}H_{30}O_5$ requires 374.2094; UV λ_{max} nm (log ε): 231 (3.51) (c 2.7×10^{-4}); FTIR ν_{max} cm^{-1}: 3550 (OH), 1720, 1240 (C=O, OAc); ^{1}H and ^{13}C NMR: Tables 1 and 2; EIMS *m/z* (rel. int.): 374 $[M]^+$ (100), 314 (10), 275 (35), 253 (10), 233 (27), 215 (25), 203 (19), 175 (16), 121 (26), 107 (17), 91 (19), 81 (26), 69 (14), 55 (18), 43 (53); CD: $\Delta\varepsilon_{340} + 0.31$, $\Delta\varepsilon_{245} - 1.01$ (c 2.7×10^{-4}).

Exsertifolin C (**5**). Mp. 172–173°, $[\alpha]_D + 97.2°$ (c 1.02); HREI-MS: found 376.2254; $C_{22}H_{32}O_5$ requires 376.2250; FTIR ν_{max} cm^{-1}: 3550 (OH), 1720 (C=O), 1740 (*sh*), 1240 (OAc); ^{1}H and ^{13}C NMR: Tables 1 and 2; EIMS *m/z* (rel. int.): 376 $[M]^+$ (100), 316 (13), 301 (22), 275 (30), 255 (8), 235 (27), 217 (19), 203 (12), 193 (18), 159 (17), 147 (14), 121 (26), 109 (28), 95 (17), 81 (30), 69 (14), 55 (20), 43 (43); CD: $\Delta\varepsilon_{295} + 1.37$, $\Delta\varepsilon_{215} - 1.52$ (c 6.4×10^{-4}).

X-ray crystallographic analysis. Compound **4** was recrystallized from *n*-hexane–Et_2O. The X-ray analysis was carried out on a Mac Science MXC 18 diffractometer with Cu Kα radiation ($\lambda = 1.54178$). The structure was solved by direct methods using MONTE-CARLO-MULTAN and refined by full-matrix least-squares. The weighting function used was $w = 1.0/[(\sigma|F_o|^2 + 0.0000|F_o|^2]$ for the function of $\Sigma w(|F_o|^2 - |F_c|^2)^2$ to be minimized. Crystal data and other information are summarized in Table 6.

Fr. 6 was rechromatographed on Sephadex LH-20 (CH_2Cl_2–MeOH, 1:1) and silica gel (CH_2Cl_2–Et_2O gradient) to give fractions A–D. Fr. B on prep. HPLC (NUCLEOSIL 50-5, *n*-hexane–Et_2O, 4:1) gave exsertifolins D (**6**) (44 mg) and E (7) (64 mg). Rechromatography on prep. HPLC (NUCLEOSIL 50-5, *n*-hexane–EtOAc, 1:1) of fr. C gave secoexsertifolins A (**1**) (26 mg) and B (**2**) (10 mg).

Secoexsertifolin A (**1**). Mp. 218–219°; $[\alpha]_D - 40.7°$ (c 1.95); HREI-MS: found 450.2261 $C_{24}H_{34}O_8$ requires 450.2254; FTIR ν_{max} cm^{-1}: 3450 (OH), 1740, 1250 (C=O, OAc); ^{1}H and ^{13}C NMR: Tables 1 and 2; EI-MS *m/z* (rel. int.): 450 $[M]^+$ (24), 432 (17), 417 (9), 390 (1), 357 (1), 348 (1), 330 (10), 315 (1), 297 (13), 284 (8), 219 (14), 181 (22), 163 (16), 122 (41), 107 (27), 97 (24), 79 (18), 55 (22), 43 (100); CD: $\Delta\varepsilon_{290} + 1.86$ (c 3.3×10^{-4}).

X-ray crystallographic analysis. Compound **1** was recrystallized from *n*-hexane–Et_2O. The X-ray analysis was carried out as reported for compound **4**. Crystal data and other information are summarized in Table 6.

Secoexsertifolin B (**2**). Mp. 217–218°; $[\alpha]_D$ − 25.8° (*c* 1.00); HREI-MS: found 448.2096 $C_{24}H_{32}O_8$ requires 448.2097; FTIR ν_{max} cm^{-1}: 3450 (OH), 1740, 1250 (OAc), 1720 (C=O); UV λ_{max} nm (log ε): 230 (3.62) (*c* 6.0×10^{-4}); ^1H and ^{13}C NMR: Tables 1 and 2; EI-MS *m/z* (rel. int.): 448 $[M]^+$ (16), 430 (21), 415 (10), 388 (1), 328 (15), 313 (1), 295 (17), 277 (22), 267 (11), 235 (33), 203 (17), 189 (22), 161 (18), 133 (22), 121 (30), 107 (21), 97 (29), 83 (15), 69 (15), 55 (16), 43 (100); CD: $\Delta\varepsilon_{390}$ + 0.42 (*c* 6.0×10^{-4}).

Exsertifolin D (**6**). Mp. 213–215°; $[\alpha]_D$ + 40.3° (*c* 1.81); HREI-MS: found 434.2287 $C_{24}H_{34}O_7$ requires 434.2305; FTIR ν_{max} cm^{-1}: 3500 (OH), 1740, 1230 (OAc), 1720 (C=O); ^1H and ^{13}C NMR: Tables 1 and 2, δ_H (C_6D_6, 400 MHz) 5.22 (1H, *d*, *J* = 5.4 Hz, H-1), 5.53 (1H, *m*, H-2), 1.44 (1H, *dd*, *J* = 13.2, 3.4 Hz, H-3), 1.78–1.87 (2H, *m*, H-3 and H-16), 2.34 (1H, *brs*, H-5), 4.15 (1H, *brt*, H-6), 1.26 (1H, *d*, *J* = 14.7 Hz, H-7), 2.10 (1H, *dd*, *J* = 15.1, 6.3 Hz, H-7), 2.96 (1H, *d*, *J* = 2.9 Hz, H-11), 1.54 (1H, *m*, H-12), 1.62–1.75 (2H, *m*, H-12 and H-13), 0.92 (1H, *ddd*, *J* = 11.7, 4.9, 1.5 Hz, H-14), 2.19 (1H, *d*, *J* = 11.7 Hz, H-14), 1.20 (3H, *d*, *J* = 7.8 Hz, H-17), 1.09 (3H, *s*, H-18), 1.22 (3H, *s*, H-19), 1.48 (3H, *s*, H-20), 1.59 and 1.72 (3H, *s*, OAc); EI-MS *m/z* (rel. int.): 434 $[M]^+$ (100), 406 (1), 374 (13), 332 (13), 314 (17), 299 (10), 275 (21), 257 (11), 233 (24), 217 (20), 193 (12), 159 (15), 121 (24), 109 (25), 97 (30), 91 (13), 69 (12), 55 (19), 43 (95); CD: $\Delta\varepsilon_{298}$ + 0.85, $\Delta\varepsilon_{218}$ − 0.76 (*c* 6.8×10^{-4}).

Exsertifolin E (**7**). Mp. 197–198°; $[\alpha]_D$ + 50.1° (*c* 1.03); HREI-MS: found 432.2111 $C_{24}H_{32}O_7$ requires 432.2149; FTIR ν_{max} cm^{-1}: 3450 (OH), 1740, 1240 (OAc), 1720 (C=O); UV λ_{max} nm (log ε): 231 (3.61) (*c* 3.0×10^{-4}); ^{13}C and ^1H NMR: Tables 2 and 5, δ_H(C_6D_6, 400 MHz) 5.19 (1H, *d*, *J* = 5.4 Hz, H-1), 5.47 (1H, *m*, H-2), 1.40 (1H, *dd*, *J* = 13.7, 3.9 Hz, H-3), 1.73 (1H, *m*, H-3), 2.21 (1H, *brs*, H-5), 4.26 (1H, *t*, *J* = 5.4 Hz, H-6), 1.28 (1H, *d*, *J* = 14.7 Hz, H-7), 2.28 (1H, *dd*, *J* = 14.7, 6.4 Hz, H-7), 3.10 (1H, *dd*, *J* = 4.4, 1.5 Hz, H-11), 1.48 (1H, *m*, H-12), 1.94 (1H, *dd*, *J* = 15.1, 5.4 Hz, H-12), 2.10 (1H, *brt*, H-13), 0.95 (1H, *ddd*, *J* = 11.7, 5.4, 2.0 Hz, H-14), 2.06 (1H, *d*, *J* = 11.7 Hz, H-14), 4.95 and 6.18 (each 1H, *s*, H-17), 1.06 (3H, *s*, H-18), 1.27 (3H, *s*, H-19), 1.52 (3H, *s*, H-20), 1.60 and 1.69 (3H, *s*, OAc); EI-MS *m/z* (rel. int.): 432 $[M]^+$ (85), 391 (1), 372 (12), 330 (16), 312 (25), 297 (16), 275 (27), 255 (13), 233 (28), 215 (35), 201 (21), 189 (16), 173 (24), 159 (20), 135 (19), 121 (32), 107 (22), 97 (31), 83 (15), 69 (15), 55 (18), 43 (100); CD: $\Delta\varepsilon_{338}$ + 0.29, $\Delta\varepsilon_{244}$ − 1.39 (*c* 3.0×10^{-4}).

X-ray crystallographic analysis. Compound **7** was recrystallized from *n*-hexane–Et_2O. The X-ray analysis was carried out as indicated for compound **4**. Crystal data and other information are summarized in Table 6.

Acetylation of **1**. Compound **1** (12 mg) in Ac_2O (1 ml) and pyridine (1 ml) was kept overnight at room temp. Usual work up including prep TLC gave a triacetate **18** (2 mg): $[\alpha]_D$ − 63.2° (*c* 0.86); HREI-MS: found 492.2344 $C_{26}H_{36}O_9$ requires 492.2359; FTIR ν_{max} cm^{-1}: 1750, 1260, 1240 (C=O, OAc); ^1H NMR (400 MHz): δ4.90 (1H, *dd*, *J* = 4.9, 2.0 Hz, H-1), 5.04 (1H, *dddd*, *J* = 13.7, 13.7, 4.9, 2.9 Hz, H-2), 1.24 (1H, *m*, H-3), 1.84–1.96 (4H, *m*, H-3, H-12 (2H) and H-14), 3.07 (1H, *d*, *J* = 10.3 Hz, H-5), 6.15 (1H, *d*, *J* = 10.3 Hz, H-6), 3.28 (1H, *d*, *J* = 13.2 Hz, H-7), 4.55 (1H, *d*, *J* = 13.2 Hz, H-7), 2.63 (1H, *d*, *J* = 3.4 Hz, H-11), 2.17 (1H, *br q*, H-13), 2.56 (1H, *d*, *J* = 12.2 Hz, H-14), 2.34 (1H, *quit.*, *J* = 7.3 Hz, H-16), 1.33 (3H, *d*, *J* = 7.8 Hz, H-17), 1.37 (3H, *s*, H-18), 0.96 (3H, *s*, H-19), 0.93 (3H, *s*, H-20), 1.93, 2.06, 2.13 (each 3H, *s*, OAc); EI-MS *m/z* (rel. int.): 492 $[M]^+$ (0.2), 432 (23), 417 (7), 373 (11), 330 (19), 297 (12), 276 (13), 261 (8), 235 (100), 219 (19), 205 (10), 192 (37), 121 (15), 109 (25), 97 (19), 79 (12), 55 (12), 43 (74).

Acetylation of **2**. Acetylation of compound **2** (9 mg) in the same manner as described above afforded a triacetate mixture which was chromatographed on prep. TLC to give triacetate **19** (2 mg): $[\alpha]_D$ − 58.7° (*c* 0.90); HREI-MS: found 490.2234 $C_{26}H_{34}O_9$ requires 492.2203; FTIR ν_{max} cm^{-1}: 1750, 1260, 1240 (C=O, OAc); ^1H NMR (400 MHz): δ4.97 (1H, *m*, H-1), 4.94 (1H, *m*, H-2), 1.28–1.43 (2H, *m*, H-3 and H-14), 1.82–1.97 (2H, *m*, H-3 and H-12), 2.93 (1H, *d*, *J* = 9.8 Hz, H-5), 6.17 (1H, *d*, *J* = 10.3 Hz, H-6), 3.28 (1H, *d*, *J* = 13.2 Hz, H-7), 4.66 (1H, *d*, *J* = 13.2 Hz, H-7), 2.74 (1H, *d*, *J* = 4.4 Hz, H-11), 2.23 (1H, *dd*, *J* = 15.1, 4.9 Hz, H-12), 2.72 (1H, *br q*, H-13), 2.40 (1H, *d*, *J* = 11.7 Hz, H-14), 2.34 (1H, *quit.*, *J* = 7.3 Hz, H-16), 5.59 (1H, *s*, H-17), 6.35 (1H, *s*, H-17), 1.36 (3H, *s*, H-18), 0.98 (3H, *s*, H-19), 0.94 (3H, *s*, H-20), 1.91, 2.03, 2.15 (each 3H, *s*, OAc); EI-MS *m/z* (rel. int.): 490 $[M]^+$ (0.1), 430 (22), 415 (8), 388 (6), 371 (14), 355 (1), 342 (7), 328 (28), 311 (20), 295 (12), 274 (14), 259 (10), 233 (100), 217 (22), 203 (12), 190 (39), 133 (13), 97 (18), 79 (12), 55 (13), 43 (87); CD: $\Delta\varepsilon_{325}$ + 0.14, $\Delta\varepsilon_{237}$ − 0.52, $\Delta\varepsilon_{215}$ + 1.01 (*c* 3.7×10^{-4}).

Catalytic hydrogenation of **2**. Compound **2** (5 mg) in EtOH (4 ml) was hydrogenated in the presence of 10% Pd-C for 30 min. Usual work up gave a dihydro compound (4.5 mg) whose spectral data were completely identical with those of secoexsertifolin A (**1**).

Catalytic hydrogenation of **4**. Hydrogenation of compound **4** (7 mg) in the same manner as described above afforded a dihydro compound (6.6 mg) whose spectral data were completely identical with those of exsertifolin C (**5**).

Catalytic hydrogenation of **7**. Hydrogenation of compound **7** (20 mg) in the same manner as described above afforded a dihydro compound (20 mg) whose spectral data were completely identical with those of exsertifolin D (**6**).

Oxidation of **6**. To compound **6** (20 mg) in CH_2Cl_2 (5 ml) was added PDC (10 mg) and the mixture stirred for 3 hr at room temp. Usual work-up afforded a diketone, **20** (15 mg): $[\alpha]_D$ + 17.0° (*c* 2.00); HREI-MS: found 432.2145 $C_{24}H_{32}O_7$ requires 432.2148; FITR ν_{max} cm^{-1}: 1720, 1260 (C=O, OAc); ^1H NMR (400 MHz): δ4.77 (1H, *d*, *J* = 4.4 Hz, H-1), 5.31 (1H, *dd*, *J* = 7.8, 3.9 Hz, H-2), 1.57 (1H, *dd*, *J* = 15.1, 3.4 Hz, H-3), 1.67 (1H, *dd*, *J* = 15.1, 3.4 Hz, H-3), 3.74 (1H, *s*, H-5), 2.34 (1H, *d*, *J* = 21.5 Hz, H-7), 2.49 (1H, *d*, *J* = 18.6 Hz, H-7), 3.25

(1H, *d*, J = 2.9 Hz, H-11), 1.95 (1H, *m*, H-12), 2.04 (1H, *m*, H-12), 2.20 (1H, *br q*, H-13), 1.36 (1H, *ddd*, J = 12.2, 4.9, 1.5 Hz, H-14), 2.31–2.44 (2H, *m*, H-17 and H-16), 1.16 (3H, *d*, J = H-17), 1.46 (3H, *s*, H-18), 1.17, 1.20 (each 3H, *s*, H-19 or H-20), 2.00, 2.03 (each 3H, *s*, OAc); ^{13}C NMR: δ12.2, 15.7, 21.1 (×2), 23.5, 33.0 (each *q*), 24.7, 36.6, 42.8, 43.6 (each *t*), 31.0, 47.6, 54.3, 58.0, 69.1, 75.3 (each *d*), 32.2, 51.7, 64.3, 77.2, 170.0, 170.1, 207.9, 219.6 (each *s*); EI-MS *m/z* (rel. int.): 432 $[M]^+$ (73), 404 (12), 372 (12), 344 (1), 330 (45), 316 (19), 297 (43), 284 (12), 273 (95), 233 (24), 203 (33), 189 (10), 175 (18), 159 (24), 149 (14), 137 (17), 109 (27), 97 (18), 91 (12), 83 (23), 69 (12), 55 (20), 43 (100); CD: $\Delta\varepsilon_{298}$ − 2.85, $\Delta\varepsilon_{212}$ − 3.61 (c 4.8 × 10^{-4}).

Oxidation of **7**. To compound **7** (20 mg) in CH_2Cl_2 (5 ml) was added PDC (10 mg) and the mixture stirred for 3 hr at room temp. Usual work-up gave a diketone, **21** (20 mg): $[\alpha]_D$ + 15.7° (c 1.55); FTIR ν_{max} cm^{-1}: 1760, 1260 (OAc), 1740 (C=O); ^{1}H NMR (200 MHz): δ1.19, 1.23 (each 3H, *s*, H-19 or H-20), 1.46 (3H, *s*, H-2), 1.98, 2.02 (each 3H, *s*, OAc), 2.37, 2.56 (each 1H, *d*, J = 18.4 Hz, H-7), 2.77 (1H, *br t*, H-13), 3.28 (1H, *dd*, J = 4.0, 1.1 Hz, H-11), 3.50 (1H, *s*, H-5), 4.80 (1H, *d*, J = 4.2 Hz, H-1), 5.30 (1H, *dd*, J = 3.6 Hz, H-2), 5.46, 6.12 (each 1H, *s*, H-17); ^{13}C NMR ($CDCl_3$, 50 MHz); δ15.5, 15.7, 21.1 (×2), 23.4, 31.0, 32.1, 32.2, 33.1, 33.5, 34.5, 43.0, 43.1, 43.6, 54.3, 58.1, 69.1, 77.2, 119.4, 148.5, 170.0, 170.1, 206.2, 207.5; EI-MS *m/z* (rel. int.): 430 $[M]^+$ (53), 404 (1), 370 (12), 355 (13), 328 (34), 313 (34), 295 (33), 271 (69), 255 (17), 231 (22), 215 (10), 201 (22), 159 (16), 149 (9), 137 (16), 109 (15), 97 (15), 83 (21), 69 (11), 55 (15), 43 (100).

Oxidation of **9**. To compound **9** (7 mg) in CH_2Cl_2 (2 ml) was added PDC (10 mg) and the mixture stirred for 30 min at room temp. Usual work-up furnished a diketone, **22** (6 mg): $[\alpha]_D$ + 37.3° (c 0.67); HREI-MS: found 298.1949 $C_{20}H_{26}O_2$ requires 298.1932; FTIR ν_{max} cm^{-1}: 1720, 1700 (C=O); UV λ_{max} nm (log ε): 230 (3.77), 211 (3.69), (c 3.2 × 10^{-4}); ^{1}H NMR (400 MHz): δ1.10 (1H, *m*), 1.13 (3H, *s*), 1.18 (6H, *s*), 1.25–1.34 (2H, *m*), 1.47 (1H, *m*), 1.55 (1H, *m*), 1.74–1.78 (2H, *m*), 1.98 (1H, *br d*), 2.22 (1H, *br d*), 2.42 (1H, *d*, J = 19.1 Hz), 2.54 (1H, *d*, J = 19.1 Hz), 2.60 (1H, *s*), 2.69 (1H, *ddd*, J = 17.6, 4.4, 2.9 Hz), 3.05 (1H, *br s*), 5.53 (1H, *s*), 5.63 (1H, *t*, J = 3.4 Hz), 5.99 (1H, *s*); ^{13}C NMR ($CDCl_3$, 100 MHz): δ18.7, 21.8, 26.8, 32.6, 33.1, 36.0, 36.2, 38.3, 40.2, 40.3, 41.7, 42.7, 49.7, 58.6, 117.4, 119.9, 147.8, 201.7, 209.4; EI-MS *m/z* (rel. int.): 298 $[M]^+$ (18), 283 (100), 265 (1), 241 (1), 227 (12), 213 (21), 203 (6), 187 (7), 173 (4), 159 (5), 146 (13), 129 (4), 117 (4), 105 (4), 91 (7), 83 (6), 69 (6), 55 (6), 41 (5); CD: $\Delta\varepsilon_{340}$ + 2.30, $\Delta\varepsilon_{262}$ − 2.79 (c 6.2 × 10^{-4}).

Oxidation of **10**. To compound **10** (3 mg) in CH_2Cl_2 (2 ml) was added PDC (10 mg) and the mixture stirred for 30 min at room temp. Usual work-up gave a diketone (2 mg) whose spectral data were identical with those of **22**.

Oxidation of **17**. To compound **17** (7 mg) in CH_2Cl_2 (2 ml) was added PDC (10 mg) and the mixture stirred for 30 min at room temp. Work-up as usual afforded a diketone (6 mg) whose spectral data were identical with those of **22**.

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