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AFRICANE-AND SANTALANE-TYPE SESQUITERPENOIDS FROM THE LIVERWORT *PORELLA CAESPITANS* VAR. *SETIGERA*

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Key Word Index—*Porella caespitans* var. *setigera*; Porellaceae; Jungermanniales; Hepaticae; sesquiterpenoids; africane- and santalane-type.

Abstract—The structures of two new africane- and a new santalane-type sesquiterpene alcohols, isolated from the ethyl acetate extract of the liverwort *Porella caespitans* var. *setigera*, have been established by chemical and spectral means. This is the first report of the isolation of these skeleton types of sesquiterpenoids from liverworts.

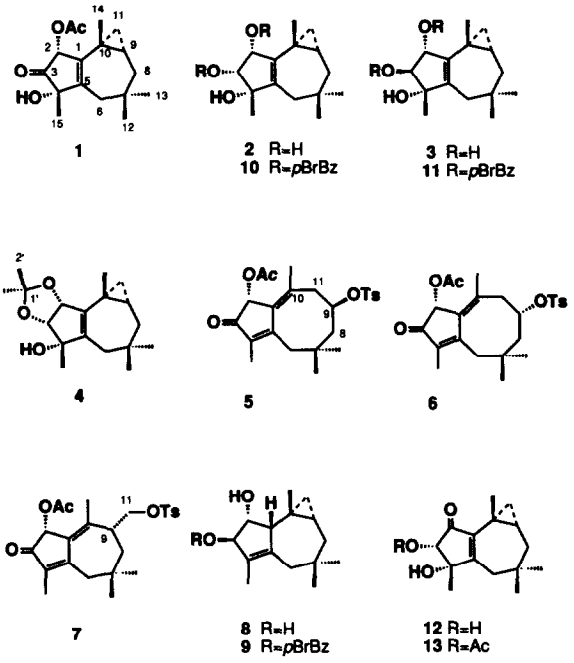
INTRODUCTION

The epiphytic liverwort, *Porella caespitans* var. *setigera* belonging to the Jungermanniales grows on trunks of deciduous plants or rock. The liverworts, including the Jungermanniales, are rich sources of terpenoids with a variety of carbon skeletons [1]. Our previous phytochemical investigation of the Porellaceae has led to the isolation of pinguisane-, aromadendrane-, drimane-, cyclopropanopseudoguaiane- and aristolane-type sesqui- and sacculatane- and labdane-type diterpenoids [1–10]. The liverworts occasionally produce their own peculiar constituents: the sacculatane- and the pinguisane-type terpenoids have not been found in higher plants, fungi or marine organisms. Chemosystematic studies of this family have been reported in previous papers [2–9]. We now report on the isolation and the structural elucidation of three new sesquiterpenoids from *P. caespitans* var. *setigera*, two of the africane-type and one of the santalane type.

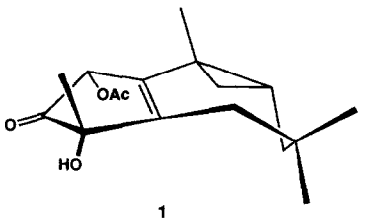
RESULTS AND DISCUSSION

The ethyl acetate extract of *P. caespitans* var. *setigera* was chromatographed on silica gel and Sephadex LH-20 to give three new sesquiterpene alcohols **1**, **12** and **14**, in addition to perrottetianal A and (+)-aristolone [4, 5].

The mass spectrum of **1** gave a molecular ion peak at *m/z* 292. Its IR spectrum indicated the presence of a hydroxyl group (3550 cm^{-1}), a carbonyl group (1765 cm^{-1}) and an acetyl group (1740, 1240 cm^{-1}). The ^1H NMR spectrum (Table 1) had signals for three protons on a cyclopropane ring, five tertiary methyl groups, and a methine group bearing an oxygen. The ^{13}C NMR spectrum (Table 2) of **1** displayed 17 carbons: five methyls, three methylenes, a methine, an oxygenated methine, an oxygenated quaternary carbon, two sp^2 quaternary carbons, two sp^3 quaternary carbons and two carbonyl carbons. The INEPT spectra indicated the presence of 23 protons. The ^1H NMR spectrum further showed the presence of an exchangeable hydroxyl proton at δ2.95 (*s*) which disappeared upon addition of D_2O. Hence, the molecular formula of **1** was found to be $C_{17}H_{24}O_4$,



confirming six degrees of unsaturation. The above spectral data revealed that **1** is a tricyclic compound. The ^1H NMR data, including the COSY spectrum, spin–spin ^1H decoupling and difference NOE experiments (Table 3) were used to deduce the structural units of compound **1**. Irradiation at δ0.86 (H-9) of the cyclopropane ring proton which showed the presence of the NOE between a tertiary methyl group (at δ1.14, H-14), led to an AB system of the non-equivalent methylene proton signals [δ0.79 (H-8) and δ1.81 (H-8′)] and to a doublet of the cyclopropane ring protons (δ0.27 and 0.58) (unit C), respectively. Irradiation at δ5.81 (1H, *d*, J=2.9 Hz) caused one of the nonequivalent methylene proton signals (δ2.38, *d*, J=14.7, 2.9 Hz, H-6) to collapse to a sharp doublet (J=14.7 Hz), indicating the presence of the long



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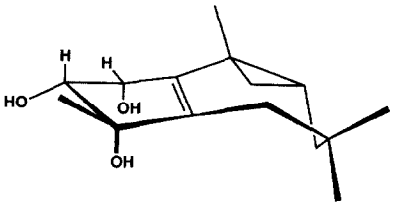

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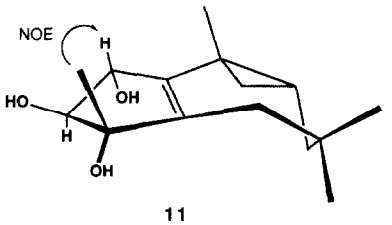

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range coupling between the oxygenated proton (unit F) and δ2.38 (unit A). the ^1H–^{13}C and ^1H–^{13}C long range COSY (Table 4) analyses were used to assemble the segments of the partial structures of **1**. The carbonyl carbon correlated between a proton of a tertiary methyl group (δ1.32, H-15) which was correlated with an oxygenated quaternary carbon (δ76.17, C-4), and with a sp^2 quaternary carbon (δ144.73, C-5) thus suggesting that the units B, E and D must be connected. Correlation between a methylene proton (δ2.06, 2.38, H-6, 6') (unit A) and a quaternary carbon (δ30.99, C-7), methylene carbon (δ43.01, C-8) (unit C), sp^2 quaternary carbon (δ144.73, C-5) (unit B) and two tertiary methyl carbons (δ22.29, 30.93, C-12, 13) were observed. This indicated two methyl groups on a quaternary carbon (unit C) bearing unit A which was connected with a sp^2 carbon (unit B). The presence of the cross peaks between the sp^2 carbon (δ137.03, C-1) (unit B) and the proton signals of the tertiary methyl group (H-14) and a cyclopropane ring (H-11) (unit C) in the long range ^1H–^{13}C COSY spectrum of **1**, indicated that unit C must be linked to unit B. The remaining unit F, including the acetyl group must be attached to the carbonyl carbon and the sp^2 carbon (unit B), because the cross peaks were observed between the acetyl carbonyl carbon (δ170.12) and a methine proton signal (δ5.81, H-2) (unit F) and between two sp^2 carbons and the methine proton (unit F). The above spectral data are consistent with the planar structure of **1** which possesses the africane-type sesquiterpene skeleton. Further confirmation of the structure was provided by chemical transformation of **1**. The presence of the carbonyl groups were confirmed by reduction of **1** with lithium aluminium hydride ($LiAlH_4$), giving a triol **2** and its epimer **3**. The absorption bands of a ketone and an acetyl group in the IR spectrum of **1** were absent in those of **2** and **3**. The stereochemistry of C-2 and C-3 of the triol **2** was confirmed to be the *cis*-configuration, because an acetonide **4** was formed by treatment of **2** with dry $CuSO_4$ in acetone and the NOEs were observed as shown in Table 3. Dehydration of **1** with *p*-toluenesulphonic acid gave three rearranged compounds **5**–**7**, whose ^1H NMR spectra exhibited no signals for the cyclopropane ring. However, a vinyl methyl group and an oxygenated methine proton were observed. Whereas the absorption of a hydroxyl group was missing in the IR spectra of **5**–**7**, the presence of a conjugated carbonyl group, a sulphonyl ester group and an aromatic ring was confirmed. The $LiAlH_4$ reduction of **5** afforded a diol **8**, whose ^1H NMR (Table 1) spectrum showed the presence of the cyclopropane ring. However, the sulphonyl ester group was absent. The above chemical and spectral evidence further supported the planar structure of **1**. The stereochemistry of **1** was deduced from difference NOE experiments (Table 3). The NOEs were observed between (i) H-15 and H-2, (ii) H-14 and H-2 and (iii) H-14 and H-9, indicating that the methyl groups on C-10 and C-4 were β-oriented and the acetyl group had the α-configuration as shown. Finally, the absolute configuration of **1** was elucidated by means of difference NOE experiments and CD [11, 12] of the *p*-bromobenzoates **10** and **11** prepared from **2** and **3** by benzoylation with *p*-bromobenzoyl chloride. The difference NOEs of compound **10** were observed as described in Table 5. Accordingly, the conformation of compound **10** was deduced as shown. On the other hand, the difference NOE (Table 5) experiments of **11** suggested that the conformation should be as shown. There had been a small difference between the conformation of **10** and **11** on the five-membered ring, so that the NOE of **10** was not observed between H-15 and H-2. The negative Cotton effect ($\Delta\varepsilon_{244\,nm}$-8.7) of **10**, revealed a 2*R*-configuration. Further support for this assignment was available from the negative Cotton effect ($\Delta\varepsilon_{253\,nm}-53$) of **11**. The above data completely defined the absolute stereostructure of the novel sesquiterpene alcohol as **1**.

The structure of **12** was deduced by acetylation, reduction and its spectral data. The EI mass spectrum of **12** gave a molecular ion peak at *m/z* 250 and its HRMS showed *M*,250.1565. Thus the molecular formula was confirmed as $C_{15}H_{22}O_3$. The IR and ^1H NMR spectral data of **12** closely resembled those of **1**, except for the missing of an acetyl group. Acetylation of **12** with acetic anhydride and pyridine gave the monoacetate **13**. $LiAlH_4$ reduction of compound **12** gave a triol whose spectral data were identical to those of **2**. Accordingly, the structure of **12** was formulated as shown.

The africane-type sesquiterpenoid is quite rare in nature, although it has been isolated from the marine invertebrate, *Lemnalia africana* (Octocorallia) [13] and from the root of *Senecio oxyriifolius* (Compositae) [14]. This is the first isolation of africane-type sesquiterpenoids from liverworts. The previous work suggested that the carbon skeleton of **1** originated from humulene by cyclization [13, 15].

The EI mass spectrum of **14** gave a molecular ion peak at *m/z* 238 and its HRMS measurement showed the molecular formula as $C_{15}H_{26}O_2$, confirming three degrees of unsaturation. Its IR and the ^1H NMR spectra indicated the presence of four tertiary methyl groups, a cyclopropane ring and a secondary hydroxyl group (3380 cm^{-1}). The ^{13}C NMR spectrum (Table 2) contained 15 carbons, including two signals due to an oxygenated sp^3 carbon (δ73.19, 79.41). However, no signals

Table 1. ^{1}H NMR spectral data for compounds **1**, **5**, **6**, **8**, **9** and **12**

H	1	5[a]	6[a]	7	12[b]	H	8	9
2	5.81 *d* (2.9)	5.36 (*s*)	5.65 (*s*)	5.57 (*s*)			2.90 *br d* (6)	3.04 *br d* (7)
3					4.16 *s*	2	4.33 *br t* (6)	4.59 *br t* (7)
6α	2.06 *d* (14.7)	2.54 *d* (13.7)	2.54 *d* (14.1)	2.53 *d* (13.2)	2.40 *d* (15)	3	4.22 *br d* (6)	5.68 *br d* (7)
6β	2.38 *dd* (14.7, 2.9)	2.60 *d* (13.7)	2.66 *d* (14.1)	2.31 *d* (13.2)	2.54 *d* (15)	6α	2.20 *d* (13.7)	2.31 *d* (14.2)
8α	0.79 *t* (13.2)	1.33 *dd* (16.1, 4.4)	1.42 *dd* (13.7, 3.9)	1.50 *br d* (14.2)	0.67 *dd* (11, 14)	6β	1.81 *br d* (13.7)	1.85 *d* (14.2)
8β	1.81 *dd* (13.2, 4.4)	1.82 *dd* (16.1, 11.2)	1.73 *dd* (13.7, 11.7)	1.62 *dd* (14.2, 8.8)	1.83 *dd* (5, 14)	8α	1.10 *dd* (14.6, 9.3)	1.13 *dd* (14.6, 9)
9	0.86 *dddd* (13.2, 4.4) 4.4, 7.3)	4.89 *dddd* (11.23, 3.42, 3.42, 3.42)	4.98 *dddd* (11.7, 3.9) 3.9, 3.9)	2.85 *br s*	0.85 *m*	8β	1.65 *dd* (14.6, 6.3)	1.74 *dd* (14.6, 7)
11α	0.27 *t* (4.4)	2.48 *br d* (14.1)	2.50 *br d* (15.6)	4.15 *dd* (9.3, 5.4)	0.22 *t* (4.4)	9	0.64 *dddd* (9.3, 6.3, 4.9, 3.4)	0.69 *dddd* (9, 7, 5, 4)
11β	0.58 *dd* (7.3, 4.4)	3.29 *br d* (14.1, 3.4)	3.25 *dd* (15.6, 3.9)	4.19 *dd* (9.3, 4.4)	0.72 *dd* (4.4, 8)	11α	0.69 *dd* (8.8, 4.9)	0.73 *dd* (9, 5)
12 (Me)	1.12 *s*	0.89 *s*	0.87 *s*	0.94 *s*	1.18 *s*	11β	0.47 *dd* (8.8, 3.4)	0.57 *dd* (9, 4)
13 (Me)	0.89 *s*	1.03 *s*	1.06 *s*	1.03 *s*	0.95 *s*	12 (Me)	1.11 *s*	1.17 *s*
14 (Me)	1.14 *s*	1.89 *s*	1.87 *s*	1.76 *s*	1.15 *s*	13 (Me)	0.91 *s*	0.97 *s*
15 (Me)	1.32 *s*	1.79 *s*	1.79 *s*	1.79 *s*	1.30 *s*	14 (Me)	1.18 *s*	1.21 *s*
OAc (Me)	2.13 *s*	2.11 *s*	2.11 *s*	2.12 *s*		15 (Me)	1.66 *s*	1.64 *s*
OTs		2.46 *s*	2.46 *s*	2.46 *s*		OH	2.60 *br s*	
		7.36 *d* (8.3)	7.36 *d* (8.3)	7.37 *d* (8.3)				
		7.80 *d* (8.3)	7.80 *d* (8.3)	7.80 *d* (8.3)				
OH	2.95 *s*					aromatic		7.60 *d* (8.3) 7.92 *d* (8.3)

Assignments were confirmed by ^{1}H-^{1}H COSY spectrum and difference NOE experiments.
J (Hz) in parentheses.
[a]The stereochemistry of C-9 was tentatively assigned.
[b]Measured in chloroform-*d* + acetone-d_6 (1:1).

Table 2. ^{13}C NMR spectral data for compounds **1**, **12**, **14** and **15**

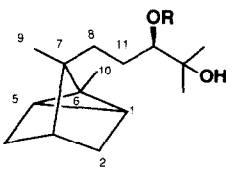
C	1*	12†‡	14*	15‡
1	137.03	139.24	19.37	19.44
2	72.77	203.48	30.87	30.64
3	212.02	82.54	38.02	38.11
4	76.17	78.40	31.31	31.00
5	144.73	173.68	19.37	19.47
6	36.24	37.83	27.23	27.26
7	30.99	31.88	45.67	45.67
8	43.01	43.65	31.42	31.42
9	18.21	18.63	17.35	17.38
10	17.16	15.53	10.59	10.59
11	18.61	19.29	26.64	26.77
12	22.29	22.80	79.41	80.73
13	30.93	31.59	73.19	72.51
14	28.87	29.61	23.02	24.62
15	22.81	23.15	26.41	25.00
OAc	20.32			21.05
	170.12			171.30

*Assignments were confirmed by ^{1}H-^{13}C and long range ^{1}H-^{13}C COSY spectra.

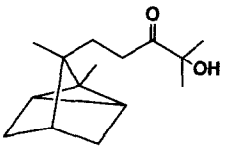
†Measured in chloroform-d + acetone-d_6 (1:1).

‡Assignments were made by comparison with compound **1** or **14**.

due to a sp^2 carbon and a carbonyl group were observed at the downfield region in the ^{13}C NMR spectrum. Furthermore, the IR spectrum of **14** showed no absorption band of a carbonyl group. The above spectral evidence indicated **14** must be a tricyclic diol. Acetylation of **14** with acetic anhydride–pyridine gave an acetate **15** which still showed hydroxyl absorption bands (3590, 3450 cm^{-1}) in the IR spectrum. This strongly suggested that a tertiary hydroxyl group must be present in the molecule. A base peak at m/z 59 $[-CMe_2OH]^+$ in the EI mass spectrum of **14** provided further evidence for the presence of a tertiary hydroxyl group. Oxidation of **14** with pyridinium chlorochromate (PCC) gave the keto-



14 R=H
15 R=Ac



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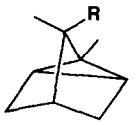
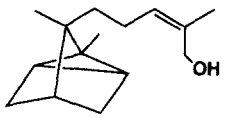


17 R=$(CH_2)_2CHO$
18 R=CH_3
20 R=$(CH_2)_3OH$



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alcohol **16**, and an aldehyde **17** as major products, whose ^{13}C NMR spectral data showed 12 carbons. The ^{1}H NMR spectrum of **17** had a doublet signal due to an aldehyde (δ9.78, t, J=2.2 Hz), confirming the presence of a 1,2-glycol system as the partial structure $-CH_2CH(OH)-C(CH_3)_2OH$ in **14**. The remaining partial structure, including a cyclopropane ring and two tertiary methyl groups was assembled by the ^{1}H–^{13}C and long range ^{1}H–^{13}C COSY analyses (Table 4) of **14**. This indicated that the partial structure was quite similar to that of tricyclene (**18**) and α-santalol (**19**). Actually, the ^{13}C NMR spectrum of **14** closely resembled that of **18** and α-santalol (**19**). The above evidence led to the conclusion that the structure of **14** only differed from α-santalol (**19**) by the presence of a vicinal diol in the side chain. Further confirmation of the structure of **14** was provided by chemical transformations. Oxidation of the commercially available (+)-α-santalol (**19**) with potassium permanganate gave tricycloekasantalal [16, 17], whose spectral data were identical to those of **17** derived from **14**. $LiAlH_4$ reduction of **17** yielded the alcohol **20**, $[\alpha]_D$–9, whose

Table 3. The NOE correlations of compounds **1**, **4**, **8** and **9**

1		4		8		9	
Irradiated ^{1}H	Observed ^{1}H	Irradiated ^{1}H	Observed ^{1}H	Irradiated ^{1}H	Observed ^{1}H	Irradiated ^{1}H	Observed ^{1}H
13 (δ0.89)	8β	2′ (δ1.39)	3	13 (δ0.91)	6α	13 (δ0.97)	8α
	OH						8β
12 (δ1.12)	8β	15 (δ1.23)	3	12 (δ1.11)	9	12 (δ1.17)	6β
	6β				6β		9
					1		
14 (δ1.14)	11β	14 and 12	2	14 (δ1.18)	1	14 (δ1.21)	11β
	9	(δ1.07)	6β		11		9
	6β		9		9		1
	2		11β				
15 (δ1.32)	2	13 (δ0.87)	6α	15 (δ1.66)	3	15 (δ1.64)	3
	OH						6α
				1 (δ2.90)	2	1 (δ3.04)	2
					6β		
				3 (δ4.22)	2	2 (δ4.59)	1
						3 (δ5.68)	2

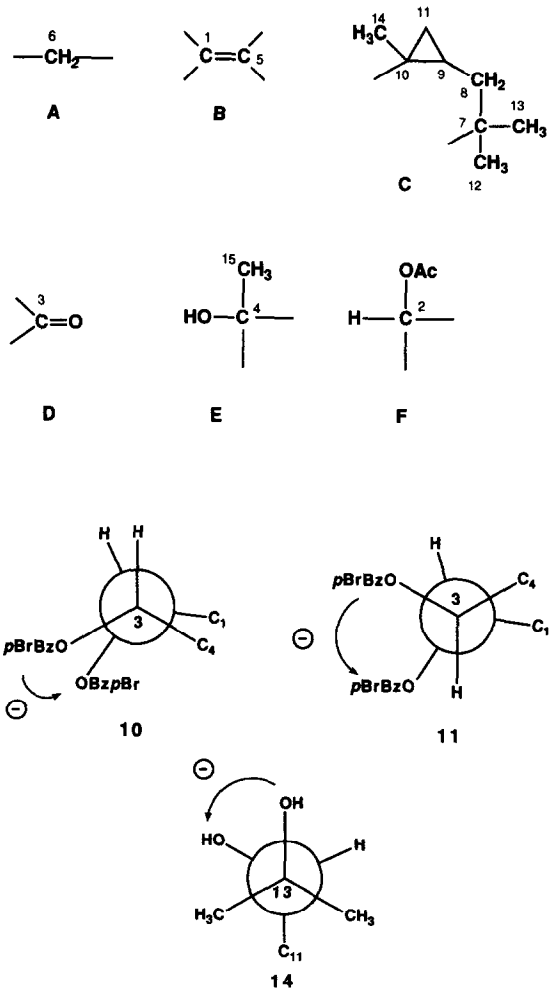

Table 4. The long range ^{1}H–^{13}C coupling correlations of compounds **1** and **14**

	1		**14**
^{13}C	^{1}H	^{13}C	^{1}H
1	11α, β, 14, 6α, β	1, 5	10, 2*, 4*, 3
3	15	3	9, 2*, 4*, 8
4	15*, 6α, β	6	9, 10*, 3
5	15, 6α, β*	7	9*, 10, 8*
6	8β*, 12, 13	9	8, 8′
7	12*, 13*, 6α*, β*, 8*	10	1, 5
8	11α, 13, 14, 6α, β	12	14, 15
9	11α*, 14, 8β*	13	12*, 14, 15
10	11α*, 14*, 8β	14	15
11	9*, 8α	15	14
12	13, 8α, β, 6α, β		
13	12, 8α, β, 6α, β		

*$^{2}J_{CCH}$ coupling.

spectral data were in agreement with those of tricycloeksantalol, $[\alpha]_D$–10 [17] which was prepared from (+)-α-santalol (**19**). Finally the stereochemistry at C-12 was determined by means of the diol complexation method [18, 19]. The CD spectrum ($\Delta\varepsilon_{342}$-0.03 in CCl_4 employing $Eu(FOD)_3$ as the complexing agent) of **14** revealed a 12*R*-configuration as shown. Accordingly, the absolute stereostructure of the novel santalane-type sesquiterpene alcohol was elucidated as **14**. The distribution of the santalane-type sesquiterpenoids in nature is very rare. Previously, β-santalene was detected in the liverwort, *Plagiochila yokogurensis* by GC-MS [1]. This is the first isolation of the α-santalane-type sesquiterpenoid from liverworts.

Table 5. The NOE correlations of compounds **10**–**12**

10		**11**		**12**	
Irradiated ^{1}H	Observed ^{1}H	Irradiated ^{1}H	Observed ^{1}H	Irradiated ^{1}H	Observed ^{1}H
15 (δ1.38)	6α	15 (δ1.21)	2	13 (δ0.95)	12
	3		6α		8α
			OH		8β
					6α
14 and 12	2	14 (δ1.12)	2	14 (δ1.15)	11β
(δ1.14)	6β		6β		9
	9		11β		6β
	11β		9		
12 (δ1.05)*	9*				
	6β*				
	6α*				
13 (δ0.98)	6α	12 (δ1.11)	9	12 (δ1.18)	9
	8β		8β		13
			6β		8β
					6β
		13 (δ0.97)	8β	15 (δ1.30)	6α
			6α		3
			OH		

*Observed in benzene-d_6.

EXPERIMENTAL

General. TLC was carried out on silica gel. Detection was with 30% H_2SO_4. Mps: uncorr.

Plant material. Porella caespitans var. *setigera* (Steph.) Hatt. (963 g) was collected in Momijigawa, Nakagun, Tokushima in April 1989 by Y. A. and identified by Dr. M. Mizutani and Y. A. The voucher specimen is deposited in the Institute of Pharmacognosy, Tokushima Bunri University.

Spectral data. UV spectra were measured in EtOH. NMR spectra were recorded at 100 MHz for ^{13}C and 400 MHz for ^{1}H. EIMS were measured at 70 eV.

Extraction and isolation. Porella caespitans var. *setigera* was dried for 1 week, ground mechanically and then extracted with EtOAc for 1 month. The EtOAc extract (26.3 g) was chromatographed on silica gel using a *n*-hexane–EtOAc gradient, giving 7 frs (I–VII). Fraction IV (4.2 g) was rechromatographed on TSK-Gel Toyopearl using MeOH to give a mixt. The mixt. was further sepd by CC on silica gel using a *n*-hexane–EtOAc gradient to give perrottetianal A (7 mg) [4], aristolone (10 mg) [5] and **1** (1.41 g). fraction VI (8.8 g) was rechromatographed on Sephadex LH-20 using $CHCl_3$–MeOH (1:1), giving a mixt. which was further sepd by CC on silica gel using a *n*-hexane–EtOAc gradient to give **14** (1.2 g) and **12** (15 mg). Compound **1**: needles, mp 96–98°, $[\alpha]_D$-141 ($CHCl_3$; *c* 0.63), UV λ_{max} nm (log ε): 235 (4.15), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 1765, 1740, 1640, 1465, 1450, 1370, 1240, 1090, 1020, 980, EIMS *m/z* (rel. int.): 292 $[M]^+$ (0.3), 232 (49), 217 (23), 204 (37), 189 (47), 161 (65), 147 (25), 133 (23), 119 (29), 105 (32), 91 (23), 86 (36), 84 (50), 43 (100). Compound **12**: mp 194–195° C, UV λ_{max} nm (log ε): 245 (4.29), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400, 1705, 1625, 1450, 1375, 1365, 1080, 965. HRMS: found 250.1565 $C_{15}H_{22}O_3$ requires 250.1569; EIMS *m/z* (rel. int.): 250 $[M]^+$ (100), 235 (35), 233 (49), 232 (43), 221 (82), 217 (60), 207 (44), 194 (30), 189 (55), 177 (38), 176 (37), 175 (44), 161 (38), 147 (31), 133 (41), 119 (30), 105 (34), 91 (33). Compound **14**: mp 87–90°, $[\alpha]_D$–27 ($CHCl_3$, *c* 1.02), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3380, 1465, 1385, 1320, 1200, 1170, 1090, 935, 850, 785. ^{1}H NMR ($CDCl_3$): δ0.82, 1.02, 1.16 and 1.21 (each 3H, *s*), 0.85 (2H, *s*, H-1, 5). 1.04 and 1.08 (each 1H, *d*, *J* = 11 Hz, H-2, 4), 1.24 (3H, *m*, H-8), 1.40 (1H, *m*, H-11), 1.47 (1H, *m*, H-8′), 1.62 (1H, *m*, H-2, 4). HRMS: found 238.1922 $C_{15}H_{26}O_2$ requires 238.1911; EIMS *m/z* (rel. int.): 238 $[M]^+$ (20), 220 (5), 205 (3), 180 (7), 134 (15), 123 (73), 121 (71), 105 (21), 93 (65), 79 (17), 71 (14), 59 (100). CD: $\Delta\varepsilon_{342\,nm}$ −0.033 [employing 5.19×10^{-3} M Eu(FOD)$_3$, CCl_4, *c* 0.0052].

Reduction of compound **1** *with* $LiAlH_4$. Compound **1** (250 mg) in dry Et_2O (5 ml) was added dropwise to a suspension of $LiAlH_4$ (150 mg) in dry Et_2O (10 ml) and stirred at room temp. for 1 hr. Usual work-up afforded an oil, which was purified by CC on silica gel using *n*-hexane–EtOAc (1:1) to give triols **2** (113 mg) and **3** (110 mg). Triol **2**, needles, mp 47–50°, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3520, 3400, 1450, 1380, 1370, 1130, 1090, 1080, 950, 890. EIMS *m/z* (rel. int.): 252 $[M]^+$ (46), 234 (52), 219 (100), 217 (37), 201 (34), 192 (30), 191 (95),179 (55), 177 (30), 176 (32), 175 (37), 173 (47), 163 (44), 161 (63), 149 (44), 145 (36), 135 (54), 121 (32), 107 (37), 105 (32), 91 (39). Triol **3**, needles, mp. 66–67° C, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3370, 1450, 1380, 1370, 1120, 1070, 990. EIMS *m/z* (rel. int.): 252 $[M]^+$ (72), 237 (31), 234 (46), 219 (88), 217 (35), 216 (59), 201 (89), 191 (100), 179 (73), 177 (39), 176 (35), 175 (40), 173 (51), 163 (49), 161 (74), 160 (40), 159 (46), 149 (45), 145 (69), 135 (67), 121 (32), 107 (35), 91 (32).

Treatment of compound **2** *with dry* $CuSO_4$ *in* Me_2CO. A mixt. of **2** (12 mg) and an excess of dry $CuSO_4$ in dry Me_2CO was refluxed for 2 hr. The reaction mixt. was filtered through a short column packed with celite and gave after removal of the solvent, an oil which was purified by prep. TLC using *n*-hexane–EtOAc (4:1) to yield **4** (4 mg). Compound **4**: oil, ^{1}H NMR ($CDCl_3$): δ0.56 (1H, *t*, *J* = 4.4 Hz, H-11α), 0.58 (1H, *dd*, *J* = 4.4, 8 Hz, H-11β), 0.76 (1H, *m*), 0.79 (1H, *br t*, *J* = 15 Hz, H-8α), 0.87, 1.23, 1.39 and 1.41 (each 1H, *s*, H-13, H-15, H-2′ and H-3′), 1.07 (6H, *s*, H-12 and H-14), 1.55 (1H, *br s*, OH), 1.80 (1H, *br d*, *J* = 15 Hz, H-8β), 1.90 (1H, *d*, *J* = 15 Hz, H-6α), 2.17 (1H, *br d*, *J* = 15 Hz, H-6β), 4.34 (1H, *d*, *J* = 6 Hz, H-3), 5.08 (1H, *dd*, *J* = 1.5, 6 Hz, H-2), ^{13}C NMR ($CDCl_3$): δ23.16, 25.50, 26.50, 28.00, 29.09 and 31.67 (Me), 18.85, 36.40 and 43.94 (CH_2), 18.39, 82.07 and 83.19 (CH), 17.39, 30.87, 78.58, 111.87, 134.50 and 142.73 (C) EIMS *m/z* (rel. int.): 292 $[M]^+$ (60), 234 (34), 219 (90), 217 (60), 191 (100), 177 (34), 173 (37), 161 (43), 149 (34), 135 (36).

Reduction of compound **5** *with* $LiAlH_4$. Compound **5** (53 mg) in dry Et_2O (3 ml) was added dropwise to a suspension of $LiAlH_4$ (50 mg) in dry Et_2O (3 ml) and stirred at room temp. for 1 hr. After CC on silica gel using a *n*-hexane–EtOAc gradient, diol **8** (12 mg) was obtained compound **8**: ^{13}C NMR ($CDCl_3$): 12.09, 16.98, 18.14, 21.81, 29.26, 29.69, 32.25, 33.63, 40.72, 41.01, 55.32, 72.43, 78.43, 132.59, 138.20.

Dehydration of compound **1**. The mixt. of **1** (100 mg) and *p*-TsOH (10 mg) in C_6H_6 (8 ml) was refluxed for 5 min and filtered through a short column packed with silica gel. Removal of the solvent gave an oil which was purified by prep. HPLC to give **5** (53.4 mg), **6** (4.6 mg) and **7** (9.5 mg). Compound **5**: oil, IR ν_{max}^{Film} cm^{-1}: 1743, 1710, 1590, 1370, 1230, 1180, 910. ^{13}C NMR ($CDCl_3$): δ8.80, 20.50, 21.60, 25.65, 28.26 and 31.42 (Me), 38.87, 39.43 and 40.84 (CH_2), 72.10, 79.82, 127.61 (×2) and 129.81 (×2) (CH), 33.88, 131.31, 134.19, 135.20, 138.32, 144.74 and 163.55 (C), 169.61 and 200.28 (C=O). EIMS *m/z* (rel. int.): 446 $[M]^+$ (2), 386 (25), 274 (15), 232 (70), 214 (87), 199 (52), 189 (20), 171 (34), 158 (22), 143 (16), 119 (18), 105 (21), 91 (93), 43 (100). Compound **6**: oil, IR ν_{max}^{Film} cm^{-1}: 1740, 1700, 1590, 1370, 1180, 910. ^{13}C NMR ($CDCl_3$): δ8.74, 20.58, 21.69, 25.24, 28.52 and 31.34 (Me), δ38.16, 39.75 and 41.69 (CH_2), 71.11, 79.32, 127.67 (×2) and 129.81 (×2) (CH), 33.66, 131.98, 134.13, 135.06, 138.84, 144.90 and 163.61 (C), 169.65 and 200.28 (C=O). EIMS *m/z* (rel. int.): 446 $[M]^+$ (1), 386 (10), 274 (34), 232 (100), 214 (65), 199 (40), 189 (19), 176 (24), 158 (17), 145 (11), 119 (15), 105 (15), 91 (80), 43 (88). Compound **7**: oil, IR ν_{max}^{Film} cm^{-1}: 1740, 1700, 1600, 1390, 1230, 1180, 1100, 960, 910, 840. ^{13}C NMR ($CDCl_3$): δ8.31, 18.80, 20.56, 21.67, 29.23 and 29.90 (CH_3), 41.16, 46.32 and 72.20 (CH_2), 38.89, 72.51, 127.93 (×2) and 129.94 (×2) (CH), 33.62, 132.97, 135.42, 136.59, 138.72, 145.06, 164.78 and 169.80 (C), 199.71 (C=O). EIMS *m/z* (rel. int.): 446 $[M]^+$ (1), 386 (32), 274 (13), 232 (71), 214 (100), 199 (64), 171 (38), 158 (21), 145 (15), 105 (18), 91 (91), 43 (74).

Benzoylation of compounds **2**, **3** *and* **8**. To a soln of **2**, **3** and **8** (100, 100 and 12 mg) in pyridine (8, 8 and 3 ml) was added *p*-bromobenzoyl chloride (150, 150 and 30 mg) and the mixts were left overnight at room temp. Usual work-up and prep. HPLC to give the benzoate **9** (8 mg). The dibenzoats **10** (98 mg) and **11** (95 mg) were obtained after CC on silica gel using a *n*-hexane–EtOAc gradient. Compound **9**: oil, ^{1}H NMR data and NOE correlations are shown in Tables 3 and 1. ^{13}C NMR ($CDCl_3$): δ12.32, 16.91, 18.04, 21.99, 29.00, 29.22, 33.06, 33.19, 41.24, 41.31, 55.29, 71.51, 81.08, 128.11, 129.29, 129.84, 131.14 (×2), 131.83 (×2), 141.51, 165.75. Compound **10**: needles, mp 133–135°, UV λ_{max}^{MeOH} nm (log ε): 245 (4.90), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3570, 1720, 1590, 1480, 1400, 1270, 1170, 1110, 1100, 1065, 1010, 840, CD: $\Delta\varepsilon_{244\,nm}$ −8.7 (MeOH; *c* 0.0004). Compound **11**: needles, mp. 139–140°, UV λ_{max}^{MeOH} nm (log ε): 247 (4.91), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1715, 1590, 1485, 1400, 1290, 1265, 1175, 1110, 1100, 1070, 1010, 845. CD $\Delta\varepsilon_{253\,nm}$ −53.0 (MeOH; *c* 0.0003).

Acetylation of compound **12**. A mixture of **12** (5 mg), Ac_2O (1 ml) and dry pyridine (1 ml) was left overnight at room temp. after the usual work-up, the acetate **13** (3 mg) was obtained by prep. TLC using *n*-hexane–EtOAc (4:1). Compound **13**: ^{1}H NMR ($CDCl_3$): δ0.97, 1.18, 1.16 and 1.21 (each, 3H, *s*), 0.29

(1H, *t*, $J=4.4$ Hz, H-11α), 0.64 (1H, *dd*, $J=10$, 14 Hz, H-8α), 0.88 (1H, *dd*, $J=4.4$, 7.3 Hz, H-11β), 0.85 (1H, *m*, H-9), 1.87 (1H, *dd*, $J=4.4$, 14 Hz, H-8β), 2.38 (1H, *d*, $J=14$ Hz, H-6α), 2.55 (1H, *d*, $J=14$ Hz, H-6β), 4.98 (1H, *s*).

Oxidation of compound **14** *with pyridinium chlorochromate (PCC).* To PCC (100 mg) in CH_2Cl_2 (5 ml) was added **14** (50 mg) in CH_2Cl_2 (2 ml) and the mixt. stirred overnight at room temp. The resulting mixt. was filtered and gave after removal of the solvent, a residue that was purified by CC on silica gel using a *n*-hexane–EtOAc gradient to yield **16** (2 mg) and **17** (28 mg). Compound **16**: oil, ^{1}H NMR (90 MHz, $CDCl_3$): δ0.83, 1.03 (each 3H, *s*), 0.89 (2H, *s*), 1.39 (6H, *s*), 1.50–1.70 (4H, *m*), 2.38–2.55 (2H, *m*), 3.83 (1H, *s*, OH). Compound **17**: ^{1}H NMR ($CDCl_3$): δ0.82 and 1.04 (each 3H, *s*), 0.88 (2H, *s*), 1.06 (1H, *br d*, $J=11$ Hz, H-4), 1.09 (1H, *br d*, $J=11$ Hz, H-2), 1.48–1.64 (5H, *m*), 2.34–2.38 (2H, *m*), 9.78 (1H, *t*, $J=2.2$ Hz). ^{13}C NMR ($CDCl_3$): δ10.58, 17.30, 19.41, 19.67, 26.32, 27.29, 30.92, 31.42, 38.17, 39.89, 45.47, 202.97. EIMS *m/z* (rel. int.): 178 $[M]^+$ (4), 121 (42), 119 (22), 105 (21), 93 (100), 91, (34), 79 (26), 77, (22), 73 (47).

Oxidation of (+)-α-*santalol* (**19**). $KMnO_4$ (800 mg) in H_2O (20 ml) was added dropwise to a soln of **19** (1 g) in EtOH (30 ml) at 0° and the mixt. was stirred for 1 hr. After removal of the solvent, H_2O (3 ml) was added and the soln extracted with Et_2O. The organic layer was washed with H_2O, dried over Na_2SO_4 and **17** (89 mg) obtained after CC on silica gel using a *n*-hexane–EtOAc gradient.

Reduction of compounds **17** *and* **12** *with* $LiAlH_4$. compounds **17** (32 mg) and **12** (5 mg) in dry Et_2O (**17**; 3 ml, **12**; 2 ml) were added dropwise to a suspension of $LiAlH_4$ (**17**; 80 mg, **12**; 20 mg) in dry Et_2O (5 ml) and the mixt. stirred at room temp. for 30 min. Usual work-up afforded an oil, which was purified by CC on silica gel using a *n*-hexane–EtOAc gradient to give an alcohol **21** (30 mg) from **17** and a mixt. containing **2** from **12** which was further purified by prep. HPLC to yield the triol **2** (3 mg). Compound **21**: oil, $[\alpha]_D$ −9 ($CHCl_3$; *c* 1.5, from **14**), −10 ($CHCl_3$; *c* 1.1, from (+)-α-santalol (**20**)), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3420, 1450, 1370, 1290, 1050, 1000, 850. ^{1}H NMR ($CDCl_3$): δ0.82 (H-9), 1.01 (H-10) (each 3H, *s*), 0.84 (2H, *s*, H-1, 5), 1.03, 1.06 (each 1H, *br d*, $J=12$ Hz, H-2, 4), 1.15 (1H, *ddd*, $J=6$, 13, 13 Hz, H-8′), 1.25 (1H, *ddd*, $J=5$, 13, 13 Hz, H-8), 1.50 (2H, *m*), 1.55 (1H, *br s*), 1.58 (1H, *br d*, $J=12$ Hz, H-2), 1.61 (1H, *br d*, $J=12$ Hz, H-4), 1.65 (1H, *br s*, OH), 3.61 (1H, *t*, $J=7$ Hz, H-12). ^{13}C NMR ($CDCl_3$): δ10.65 and 17.51 (CH_3), 28.05, 30.25, 30.96, 31.46 and 63.92 (CH_2), 19.50, 19.62 and 38.23 (CH), 27.35 and 45.61 (C).

Acetylation of compound **14**. A mixture of **14** (50 mg), Ac_2O (2 ml) and dry pyridine (2 ml) was left overnight at room temp. The usual work-up afforded the acetate **15** (40 mg). Compound **15**: oil, $[\alpha]_D$ −12 ($CHCl_3$; *c* 1.94), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590, 3450, 1730, 1460, 1375, 1250, 1060, 1035, 1020, 950. ^{1}H NMR ($CDCl_3$): δ0.79, 0.98, 1.19, 1.20 and 2.12 (each 3H, *s*), 0.83 (2H, *s*), 1.05 (2H, *t*, $J=11$ Hz), 1.15 (*m*), 1.85 (*br s*, OH), 4.72 (1H, *dd*, $J=9$, 3 Hz). EIMS *m/z* (rel. int.): 280 $[M]^+$ (8), 222 (11), 162 (12), 147 (11), 134 (15), 133 (18), 122 (13), 121 (87), 120 (17), 119 (31), 109 (10), 107 (30), 106 (18), 105 (35), 95 (15), 94 (27), 93 (100), 92 (22), 91 (44), 81 (15), 79 (35), 77 (27), 71 (12), 69 (11), 67 (16), 65 (10), 59 (56).

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