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SESQUITERPENOIDS FROM THE LIVERWORTS *BAZZANIA TRILOBATA* AND *PORELLA CANARIENSIS*

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Key Word Index—*Bazzania trilobata*; *Porella canariensis*; Lepidoziaceae; Porellaceae; Hepaticae; (1*R*,4*R*)-*cis*-5-hydroxycalamenene; aromadendranes; drimanes; pinguisanes; cadinanes; gymnomitrane; bazzanane; myltaylane; sesquiterpenoid; chemosystematics.

Abstract—A new myltaylane-type sesquiterpene alcohol and nine known sesquiterpenoids were isolated from *Bazzania trilobata*. The absolute stereostructure of (1*S*,4*S*)-*cis*-5-hydroxycalamenene was revised to be (1*R*,4*R*)-*cis*-5-hydroxycalamenene by the X-ray crystallographic analysis of its *p*-bromobenzoate derivative. Four previously known sesquiterpenoids were isolated from *Porella canariensis*, together with an artefact of a pinguisane-type sesquiterpene lactone. Their structures were determined by the use of extensive NMR techniques.

INTRODUCTION

We are continuing to study the chemical constituents of the liverworts and in the search for biologically active substances [1, 2]. *Bazzania trilobata*, belonging to the Lepidoziaceae, contains the various sesquiterpenoids [1, 2]. On the other hand, the *Porella* species were classified into two types, one of which contains the pungent sesquiterpene dialdehyde and the other containing non-pungent substances such as pinguisane-, aromadendrane-, drimane-, africane-type sesquiterpenoids and sacculatane- and kaurane-type diterpenoids [1, 2]. Reinvestigation of the chemical constituents of French *Bazzania trilobata* resulted in the isolation of a new myltaylane-type sesquiterpene alcohol (**9**). *Porella canariensis* collected in the Canary Islands was analysed and four known sesquiterpenoids (**10**–**13**) were isolated together with a pinguisane-type sesquiterpene artefact (**14**). Here we report the distribution of sesquiterpenoids in *B. trilobata* and *P. canariensis* and their chemosystematics. We have also revised the absolute configuration of (1*R*,4*R*)-*cis*-5-hydroxycalamenene (**8**) [3] following the X-ray crystallographic analysis of its *p*-bromobenzoate derivative (**17**).

RESULTS AND DISCUSSION

The CC on silica gel, Sephadex LH-20 and preparative HPLC of the ether extract of *Bazzania trilobata* resulted in the isolation of eight known compounds, β-bazzanene (**1**) [4], gymnomitrol (**2**) [5, 6], *ent*-viridiflorol (**3**) [7], drimenol (**4**) [8], (1*R*,4*R*)-calamenene (**5**) [9], *cis*-8-hydroxycalamenene (**6**) [10], 7,10-peroxycadina-5-ene (**7**) [11] and (1*R*,4*R*)-*cis*-5-hydroxycalamenene (**8**) [3, 12], and a new myltaylane-type sesquiterpene alcohol (**9**). The structures of known compounds were identified by comparison of the spectral data of authentic samples and reference data.

Most of the sesquiterpenoids isolated from the liverworts are the enantiomers to those found in higher plants, although there are some exceptions, such as drimane-, germacrane- and guaiane-type sesquiterpenoids [1, 2]. Thus, in the case of liverwort chemistry, it is very important to confirm the absolute configuration at C-1 and C-4 and substitution mode of the benzene and cyclohexane rings in calamenane-type sesquiterpenoids, many of which have also been found in higher plants. The spectral data of **8** ($[\alpha]_D$ −15.0°, *c* 4.67) were identical with those of 5-hydroxycalamenene (**15**) ($[\alpha]_D$ −8.4°, *c* 2.98) [3, 12]. The absolute structure of **15** was elucidated by its CD spectrum [3]. However, the sign of the specific rotation ($[\alpha]_D$ +33.4°) of *cis*-calamenene (**5**) isolated from the same species was identical to that of (1*R*,4*R*)-calamenene (**5**) ($[\alpha]_D$ +43.0°) [9] whose absolute structure was determined by X-ray crystallographic analysis of (1*R*,4*R*)-7-hydroxycalamenene (**16**) [9] which was converted to (1*R*,4*R*)-calamenene (**5**). As the presence of both enantiomers of **5** and **15** in the same plant is not common, we carried out an X-ray crystallographic analysis of the *p*-bromobenzoate **17** produced from **8** in order to clarify its absolute configuration. The final residuals of **17** were *R*; R_w 0.034;

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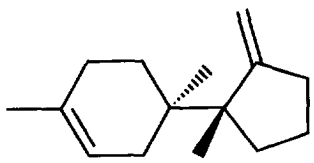

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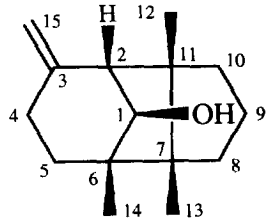

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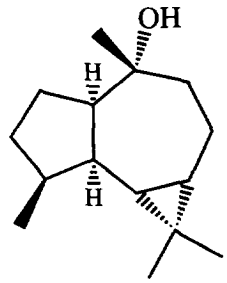

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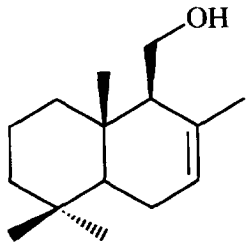

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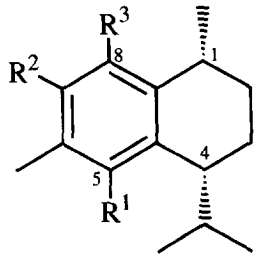
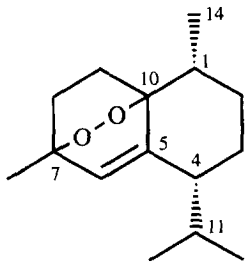


5 : $R^1=R^2=R^3=H$
6 : $R^1=R^2=H$, $R^3=OH$
8 : $R^1=OH$, $R^2=R^3=H$
16 : $R^1=R^3=H$, $R^2=OH$
17 : $R^1=OCOC_6H_4Br$-*p*, $R^2=R^3=H$



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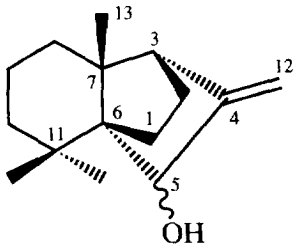

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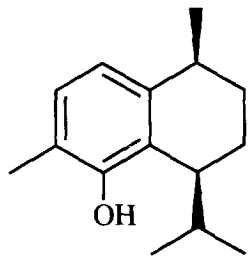

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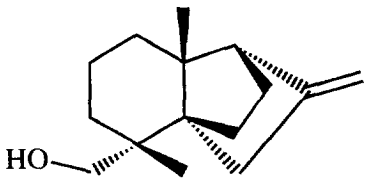

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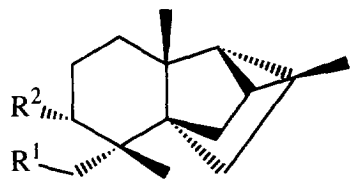


19 R^1=OH, R^2=H
20 R^1=H, R^2=OH

0.045 (alternative chirality, 0.043; 0.059) and its absolute structure is depicted in Fig. 1. Thus, the absolute structure of **8** was revised to (1*R*,4*R*)-*cis*-5-hydroxycalamenene. As far as we are aware, this is the second example of the determination of the absolute stereochemistry of a calamenane-type compound by X-ray crystallographic analysis [9].

The IR and ^{1}H NMR spectra of **9** ($C_{15}H_{24}O$, anal. 220.1832) showed the presence of a hydroxyl group (3450 cm^{-1}), three tertiary methyls (δ 0.95, 0.97, 1.06

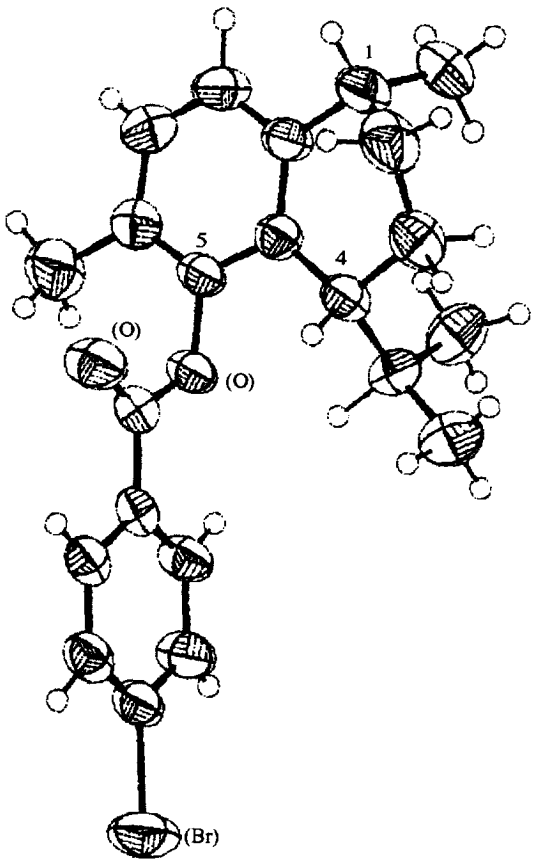


Fig. 1. ORTEP drawing of compound **17**.

each *s*), a methine proton with a hydroxyl group (δ 4.65 1H, *br s*) and *exo*-methylenic protons (δ 4.88, 4.93 each 1H, *s*). The ^{13}C NMR spectrum (Table 1) displayed 15 carbon atoms: three methyls, five methylenes, one methine and three quaternary carbon atoms, one methine carbon with a hydroxyl group and *exo*-methylenic carbons. From the above spectral data, compound **9** was indicated to be a tricyclic sesquiterpene alcohol. In order to establish the whole structure of **9**, $^{1}H-^{1}H$, $^{13}C-^{1}H$ COSYs and HMBC spectra were measured. In the HMBC spectrum (Table 2), the highest methyl signal, at δ 0.95, was correlated with the second highest methyl at δ 0.97, and these two methyls were correlated with a methylene and two quaternary carbons, respectively. The third methyl at δ 1.06 was correlated with a methylene, a methine and two quaternary carbons. Furthermore, the detailed analysis of each cross-peak showed the gross structure of **9** to be myltayl-4(12)-en-5-ol. Although the stereochemistry of **9** remains to be clarified because of the tiny amount of compound available and its instability, the tentative stereochemistry of **9** was deduced by the consideration of the presence of the similar myltaylane- (**18**) and cyclomyltaylane-type sesquiterpenes (**19**, **20**), which have been isolated from the liverworts *Mylia taylorii* [13, 14], *Bazzania japonica* [15] and *B. tridens* [16] and their absolute configurations established by X-ray crystallographic analysis and CD spectra.

The methanol extract of *Porella canariensis* gave a pinguisane-type sesquiterpene **14** as artefact and four known sesquiterpenoids, *ent*-cyclocolorenone (**10**) [17], cinnamolide (**11**) [18], *cis*-dihydrocinnamolide (**12**) [18, 19] and isodrimeniol (**13**) [20, 21] whose structures were determined by their spectral and physical data in comparision with authentic samples.

The IR and NMR spectra of **14** ($C_{17}H_{24}O_5$, anal. 308.1621) indicated the presence of a carbomethoxy group (1720 cm^{-1}; δ_H 3.78 *s*; δ_C 169.9 or 170.2) and a γ-lactone ring (1770 cm^{-1}; δ_C 169.9 or 170.2), a secondary methyl (δ 0.92 3H, *d*), two tertiary methyls (δ 0.69, 0.91 each 3H, *s*) and a methoxyl group (δ 3.15 3H, *s*) together with an isolated methine (δ 3.55 1H, *d*),

Table 1. ^{13}C NMR data of compounds **2**, **7**, **9**, **12**, **13** and **14** (100 MHz, $CDCl_3$)

C	**2**	**7**	**9**	**12**	**13**	**14**
1	91.8	30.6	18.0	40.4	39.8	36.1
2	62.7	26.7	28.3	18.0	18.5	28.1
3	151.3	19.3	55.8	41.9	42.4	33.5
4	28.3	39.4	159.3	32.8	32.9	47.7
5	37.2	148.5	75.2	51.4	49.8	163.2
6	47.6	126.3	56.5	18.4	23.7	106.9
7	54.4	75.3	47.3	22.3	117.1	41.1
8	37.0	30.0	29.8	37.4	136.4	53.8
9	27.2	21.9	19.0	49.9	61.5	47.1
10	38.5	79.3	36.9	35.3	33.4	118.9
11	55.4	27.5	33.8	67.6	99.4	169.9*
12	28.8	16.9*	104.4	179.1	69.0	18.4
13	24.8	21.4*	20.5	21.9	21.5	14.9
14	19.8	15.4	23.7*	33.5	33.1	16.6
15	109.0	22.0	30.1*	14.4	14.0	170.2*
OMe						50.5
COOMe						52.0

*Assignments may be interchangeable in vertical columns.

Table 2. Long-range $^{13}C-^{1}H$ correlations by the HMBC spectrum of compound **9**

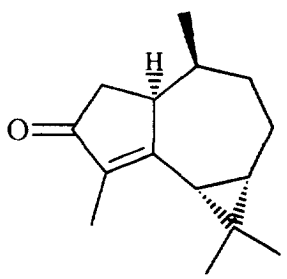
H	[C]
1	3, 5, 7
2	1, 4, 6
3	1, 5, 6
12	3, 5
13	3, 6, 7, 8
14	6, 10, 11, 15
15	6, 10, 11, 14

Table 3. Long-range $^{13}C-^{1}H$ correlations by the HMBC spectrum of compound **14**

H	[C]
3β	4, 8, 14
4	5, 8, 10, 14, 15
7α	1, 5, 6, 8, 9
7β	1, 6, 9, 12
10	6, 11
12	1, 7, 8, 9
13	1, 2, 8
14	3, 4, 8, 9

an isolated methylene (δ 1.46, 2.37 each 1H, *d*) and a trisubstituted olefinic proton (δ 6.34 1H, *d*). The ^{13}C NMR spectrum (Table 1) showed 15 carbon atoms: five methyls, three methylenes, two methines and two quaternary carbons, along with a trisubstituted olefinic carbon and a hemiacetal quaternary carbon (δ 106.9 *s*). The $^{1}H-^{1}H$ and $^{13}C-^{1}H$ COSYs of **14** indicated the structure of a pinguisane-type sesquiterpene. Furthermore, the detailed analysis of the HMBC spectrum (Table 3) revealed that the structure of **14** was a pinguisane-type sesquiterpene lactone with a methoxyl group at C-6 and a carbomethoxyl group at C-10. The stereochemistry of **14** was clarified by the difference NOE spectrum. Thus, the stereostructure of **14** was elucidated to be 4β-carbomethoxy-6α-methoxypinguis-6,11-olide. As the plant material was extracted with methanol, it seems that compound **14** was an artefact the same as **21** and **22** which have already been obtained from the liverwort *Trocholejeunea sandvicensis* as artefacts [22].

The complete assignments of the ^{13}C NMR in **2**, **12** and **13** were carried out and their data are summarized in Table 1. The isolation of calamenene-, gymnomitrane- and aromadendrane-type sesquiterpenoids has already been reported from European *Bazzania trilobata* [12, 23, 24], therefore, no geographical race of *B. trilobata* was observed. The chemical constituents of *Porella* species have already been reported and six chemotypes of *Porella* species are known [1, 2]. *P. canariensis* contained *ent*-cyclocolorenone (**10**) as a main component and the drimane- and pinguisane-types as minor components, indicating that this species belongs to the chemotype I (aromadendrane-, drimane-, pinguisane-type) of the *Porella* species [1, 2].



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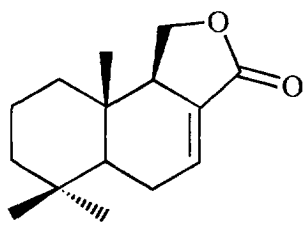

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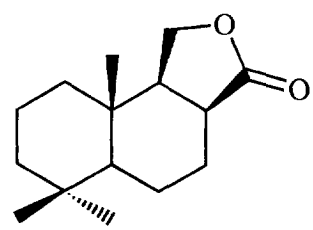

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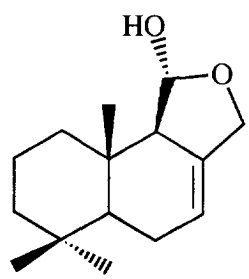

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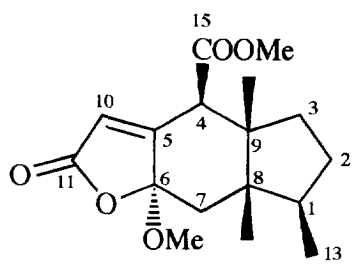

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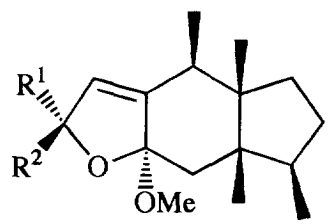

21 : R^1=H, R^2=OMe
22 : R^1=OMe, R^2=H

EXPERIMENTAL

The solvents used for spectral measurements were TMS-$CDCl_3$ [^{1}H- (400 MHz) and ^{13}C (100 and 50 MHz) NMR]; $CHCl_3$ ($[\alpha]_D$); UV and CD (MeOH). TLC was carried out as previously reported [25].

Plant material. Porella canariensis (Web.) Bryhn was collected by S. H. in the Canary Islands, in March, 1992. *Bazzania trilobata* (L.) S. Gray was collected by Y. A. in Vosges, France, in Oct. 1994. The voucher specimen was deposited at the Institute of Pharmacognosy, Tokushima Bunri University.

Extraction and isolation. The Et_2O extract (5.4 g) of *B. trilobata* was divided into nine fractions by CC silica gel using *n*-hexane–EtOAc gradient. Fr. 2 was subjected to rechromatography on silica gel (*n*-hexane) and prep. TLC (*n*-hexane) impregnated 10% $AgNO_3$ to give β-bazzanene (**1**) (2 mg) [3] and (1*R*,4*R*)-calamenene (**5**) (3 mg) [8], respectively. Fr. 4 was subjected to chromatography on Sephadex LH-20 (CH_2Cl_2) and silica gel (*n*-hexane–Et_2O 19:1) to divide into A-C fractions. Fr. A was subjected to rechromatography on silica gel (CH_2Cl_2) and prep. HPLC (Nucleosil 50-5, *n*-hexane–AcOEt 9:1, *n*-hexane–Et_2O 19:1) to give gymnomitrol (**2**) (34 mg) [4, 5], 7,10-peroxycadina-5-ene (**7**) (3 mg) [10] and myltayl-4(12)-en-5-ol (**9**) (3 mg).

Myltayl-4(12)-en-5-ol (**9**). $[\alpha]_D$ −35.0° (*c* 0.24); HR-EIMS: found 220.1832 $C_{15}H_{24}O$ requires 220.1827; FTIR ν_{max} cm^{-1}: 3450 (OH); ^{1}H NMR: δ 1.46–1.71 (2H, *m*, H-1 and 9), 1.87 (1H, *m*, H-1), 1.18–1.41 (6H, *m*, H-2, 8, 9 and 10), 1.96 (1H, *m*, H-2), 2.12 (1H, *d*, J = 4.4 Hz, H-3), 4.65 (1H, *br s*, H-5), 4.88 (1H, *s*, H-12), 4.93 (1H, *s*, H-12), 1.06 (3H, *s*, H-13), 0.97 (3H, *s*, H-14), 0.95 (3H, *s*, H-15); ^{13}C NMR: Table 1; EIMS *m/z* (rel. int.): 220 $[M]^+$ (100), 205 (57), 187 (38), 177 (20), 163 (39), 149 (43), 133 (40), 123 (89), 107 (63), 95 (74), 91 (56), 81 (58), 69 (48), 55 (46), 41 (67).

The CC on Sephadex LH-20 (MeOH) and MPLC (DIOL, *n*-hexane–Et_2O 19:1) of fr. B gave (1*R*-4*R*)-*cis*-5-hydroxycalamenene (**8**) (61 mg) ($[\alpha]_D$ +33.4°, *c* 0.39) [11, 12]. Fr. C was rechromatographed on Sephadex LH-20 (MeOH) and prep. TLC (CH_2Cl_2–Et_2O 19:1) to give *cis*-8-hydroxycalamenene (**6**) (11 mg) [9].

Benzoylation of compound **8**. To compound **8** (26 mg) in pyridine (2 ml) was added *p*-bromobenzoylchloride (10 mg) and 4-dimethylaminopyridine (3 mg) and the mixture stirred overnight at room temp. Work up as usual gave a mixture which was chromatographed on silica gel (*n*-hexane–Et_2O 19:1) to afford *p*-bromobenzoate **17** (10 mg) which was recrystallized from *n*-hexane: $[\alpha]_D$ −124.0° (*c* 0.08); HR-EIMS: found 400.1033 $C_{22}H_{25}O_2Br$ require 400.1038; FTIR ν_{max} cm^{-1}: 1750 (COO), 1280, 1180, 1100; UV λ_{max} nm (log ε): 247 (4.40), 207 (4.37) (*c* 0.69×10^{-4}); ^{1}H NMR: δ 0.84, 0.90 (each 3H, *d*, J = 6.8 Hz, H-12 or 13), 1.33 (3H, *d*, J = 6.8 Hz, H-14), 1.53–1.58 (3H, *m*), 1.75–1.87 (2H, *m*), 2.01 (1H, *m*, H-1), 2.11 (3H, *s*, H-15), 2.93 (1H, *m*, H-11), 7.07, 7.09 (each 1H, *d*, J = 7.8 Hz, H-7 or 8), 7.68, 8.09 (each 2H, *d*, J = 8.8 Hz); EIMS *m/z* (rel. int.): 402, 400 $[M]^+$ (2), 359 (77), 217 (2), 183 (100), 155 (15), 145 (5), 104 (7), 91 (5), 76 (9), 41 (3); CD: $\Delta\varepsilon_{265}$ −0.48, $\Delta\varepsilon_{230}$ +0.35, $\Delta\varepsilon_{210}$ −2.41 (*c* 0.69×10^{-4}).

Crystal data. $C_{22}H_{25}O_2Br$, M_r = 401, tetragonal, $P4_32_12$ (#96), a = 10.349 (2), b = 10.349 (4), c = 36.712 (2) Å, V = 3932 (2) Å^3, Z = 8, D_{obs} = 1.30 g/cm^3, D_{calc} = 1.35 g/cm^3, Cu K_α radiation, λ = 1.54178, μ = 27.29 cm^{-1}, $F(000)$ = 1664, R_{int} = 0.00, R = 0.034, R_w = 0.045. Diffraction measurements were made on a Mac Science MXC18 diffractometer using Cu K_α radiation. Of 2025 reflections, 1958 were unique. The structure was solved by direct methods using MONTECALRO-MULTAN and refined by full-matrix least-squares. The function $\Sigma w(|F_O|^2 - |F_C|^2)^2$ was minimized, where $w = 1.0/[(\sigma|F_O|^2 + 0.0000|F_O|^2]$. The reflection used 1904 and the number of variables was 311. Final R = 0.034, R_w = 0.045, S = 1.58 (alternative chirality: R = 0.043, R_w = 0.059).

Air dried *P. canariensis* (287 g) was extracted with MeOH and the crude extract (4.8 g) was divided into eight fractions by silica gel CC (*n*-hexane–EtOAc gradient). Fr. 6 was subjected to rechromatography on Sephadex LH-20 (CH_2Cl_2–MeOH 1:1) and silica gel (CH_2Cl_2–Et_2O 49:1) to give *ent*-cyclocolorenone (**10**) [13] (1.2 g) and a mixture of sesquiterpene fractions, recrystallization of which gave a cinnamolide (**11**) [14] (124 mg) and mother liquor. The mother liquor was purified by prep. HPLC (NUCLEOSIL 50-5, CH_2Cl_2–Et_2O 19:1 or *n*-hexane–Et_2O 7:2) to give *cis*-dihydrocinnamolide (**12**) [14, 15] (44 mg) and 4β-carbomethoxy-6α-methoxypinguis-6,11-olide (**14**) (9 mg): $[\alpha]_D$ −156.7° (*c* 0.81); HR-EIMS: found 308.1621 $C_{17}H_{24}O_5$ requires 308.1623; FTIR ν_{max} cm^{-1}: 1770, 1720 (C=O); UV λ_{max} nm (log ε): 212 (3.27) (*c* 3.5×10^{-4}); ^{1}H NMR: δ 2.72 (1H, *m*, H-1), 1.95–2.06 (2H, *m*, H-2α and H-3α), 1.31 (1H, *q*-like, H-2β), 1.54 (1H, *m*, H-3β), 3.55 (1H, *d*, J = 1.5 Hz, H-4), 2.37 (1H, *d*, J = 15.1 Hz, H-7α), 1.46 (1H, *d*, J = 15.1 Hz, H-7β), 6.34 (1H, *d*, J = 1.5 Hz, H-10), 0.69 (3H, *s*, H-12), 0.92 (3H, *s*, H-13), 0.91 (3H, *s*, H-14), 3.15 (3H, *s*, OMe), 3.78 (3H, *s*, COOMe); ^{13}C NMR: Table 1; EIMS *m/z* (rel. int.): 308 $[M]^+$ (3), 276 (24), 248 (9), 233 (5), 217 (15), 189 (7), 156 (15), 123 (6), 109 (100), 95 (6), 81 (5), 67 (6), 55 (5), 41 (7); CD: $\Delta\varepsilon_{220}$ −2.98 (*c* 3.5×10^{-4}).

Fr. 7 was rechromatographed on Sephadex LH-20, silica gel and finally prep. HPLC (NUCLEOSIL 50-5, CH_2Cl_2–Et_2O 19:1) to give isodrimeniol (**13**) (16 mg) [16, 17].

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REFERENCES

1. Asakawa, Y. (1982) in *Progress in the Chemistry of Organic Natural Products* (Herz, W., Grisebach, H. and Kirby, G. W., eds), Vol. 42, p. 1. Springer, Wien.
2. Asakawa, Y. (1995) in *Progress in the Chemistry of Organic Natural Products* (Herz, W., Kirby, G. W., Moore, R. E., Steglich, W. and Tamm, Ch., eds), Vol. 65, p. 1. Springer, Wien.
3. Huneck, S., Jänicke, S., Meinunger, L., Snatzke, G., Connolly, J. D. and Asakawa, Y. (1984) *J. Hattori, Bot. Lab.* **57**, 784.
4. Matsuo, A. and Hayashi, S. (1977) *J. Chem. Soc., Chem. Commun.* 566.
5. Connolly, J. D., Harding, A. E. and Thornton, I. M. S. (1972) *J. Chem. Soc., Chem. Commun.* 1320.
6. Connolly, J. D., Harding, A. E. and Thornton, I. M. S. (1974) *J. Chem. Soc., Perkin Trans. I* 2487.
7. Faure, R., Ramanoelina, A. R. P., Pakotonirainy, O., Bianchini, P. and Gaydou, E. M. (1991) *Magn. Reson. Chem.* **29**, 969.
8. Toyota, M. and Asakawa, Y. (1988) *Phytochemistry* **27**, 2155.
9. Croft, K. D., Ghisalberti, E. L., Hocart, C. H., Jefferies, P. R., Raston, C. L. and White, A. H. (1978) *J. Chem. Soc., Perkin Trans. I* 1267.
10. Tanaka, J., Nobutani, K. and Adachi, K. (1988) *Nippon Kagaku Kaishi* **7**, 1065.
11. Buchanan, M. S. (1993) PhD thesis, University of Glasgow.
12. Tanaka, J. and Adachi, K. (1990) *Bull. Chem. Soc. Jpn.* **63**, 272.
13. Takaoka, D., Matsuo, A., Kuramoto, J., Nakayama, M. and Hayashi, S. (1985) *J. Chem. Soc., Chem. Commun.* 482.
14. Takaoka, D., Tani, H. and Matsuo, A. (1988) *J. Chem. Res. (S)* 130.
15. Asakawa, Y., Toyota, M., Ueda, A., Tori, M. and Fukazawa, Y. (1991) *Phytochemistry* **30**, 3037.
16. Wu, C.-L. and Chang, S.-J. (1992) *Phytochemistry* **31**, 2150.
17. Asakawa, Y. and Tori, M. (1993) in *The Atlas of 400 MHz NMR Spectra of Natural Products*, p. 66. Hirokawa Pub. Co., Japan.
18. Canonica, L., Corbell, A., Gariboldi, P., Jommi, G. and Krepinsky, J. (1969) *Tetrahedron* **25**, 3895.
19. Canonica, L., Corbell, A., Jommi, G., Krepinsky, J., Ferrari, G. and Casagrande, C. (1967) *Tetrahedron Letters* **23**, 2137.
20. Asakawa, Y. and Takemoto, T. (1979) *Experientia* **35**, 1420.
21. Hollinshead, D. H., Howell, S. C., Ley, S. U., Mahon, M., Ratdiffe, N. M. and Worthington, P. A. (1983) *J. Chem. Soc., Perkin Trans. I* 1579.
22. Tori, M., Arbiyanti, H., Taira, Z. and Asakawa, Y. (1993) *Phytochemistry* **32**, 335.
23. Toyota, M., Asakawa, Y. and Takemoto, T. (1981) *Phytochemistry* **20**, 2359.
24. Konecny, K., Streibl, M., Vasickova, S., Budensinsky, M., Saman, D., Ubik, K. and Herout, V. (1985) *Collect. Czech. Chem. Commun.* **50**, 80.
25. Asakawa, Y., Tori, M., Takikawa, K., Krishnamurty, H. G. and Kar, S. K. (1987) *Phytochemistry* **26**, 1811.