Diterpenoids and Aromatic Compounds from the Three New Zealand Liverworts *Jamesoniella kirkii*, *Balantiopsis rosea*, and *Radula* Species

Fumihiro NAGASHIMA,* Yoshiyuki KUBA, and Yoshinori ASAKAWA

Faculty of Pharmaceutical Sciences, Tokushima Bunri University; Yamashiro-cho, Tokushima 770–8514, Japan.
Received January 5, 2006; accepted March 9, 2006

Three new aromatics were isolated from the New Zealand liverwort *Balantiopsis rosea*. A new bibenzyl was isolated from an unidentified *Radula* species, together with known bibenzyls. *Jamesoniella kirkii* yielded three known *ent*-isopimarane and two *ent*-kaurane diterpenoids. Their structures were confirmed by NMR techniques, chemical reaction, and X-ray crystallographic analysis.

Key words liverwort; *Balantiopsis rosea*; *Jamesoniella kirkii*; *Radula* species; aromatic; diterpenoid

We are currently studying the chemical constituents of liverworts as a part of a search for novel chemical components and biologically active substances in bryophytes.[1,2] Liverworts are distributed widely throughout the world, including the Antarctic. The southern hemisphere has more numerous endemic liverwort genera than the northern hemisphere including Japan.[3] Therefore we focused on the chemical constituents of southern hemispheric liverworts and reported on the secondary metabolites of some New Zealand liverworts.[4—7] Here, we report on the isolation and structural elucidation of new aromatic compounds and known diterpenoids as well as bibenzyl derivatives from three New Zealand liverworts, *Balantiopsis rosea* BERGGREN, *Jamesoniella kirkii* STEPH., and an unidentified *Radula* species.

The known *ent*-kauranes **1**—**3** and *ent*-isopimarane diterpenoids **4** and **5** were isolated from *J. kirkii*. The new bibenzyl **6** was isolated from an unidentified *Radula* species as well as the two known bibenzyls **7** and **8**. Three new aromatics **10**—**12** were isolated from *B. rosea*. The structural elucidation of the isolated compounds was established by spectroscopic analysis, chemical reaction, and X-ray crystallographic analysis.

The fractionation of the ether extract of *J. kirkii* resulted in the isolation of three *ent*-kaurenes, *ent*-16-kauren-19-oic acid (**1**),[8] *ent*-methyl-16-kauren-19-oate (**2**),[8] and *ent*-16-kauren-19-ol (**3**),[9] and two *ent*-isopimaranes, oblongifolic acid (**4**)[10] and *ent*-isopimara-7(8),15-dien-19-ol (**5**).[11] Their spectral data were identical to those of reference compounds. The stereochemistry of oblongifolic acid (**4**) was established in X-ray crystallographic analysis (data not shown).

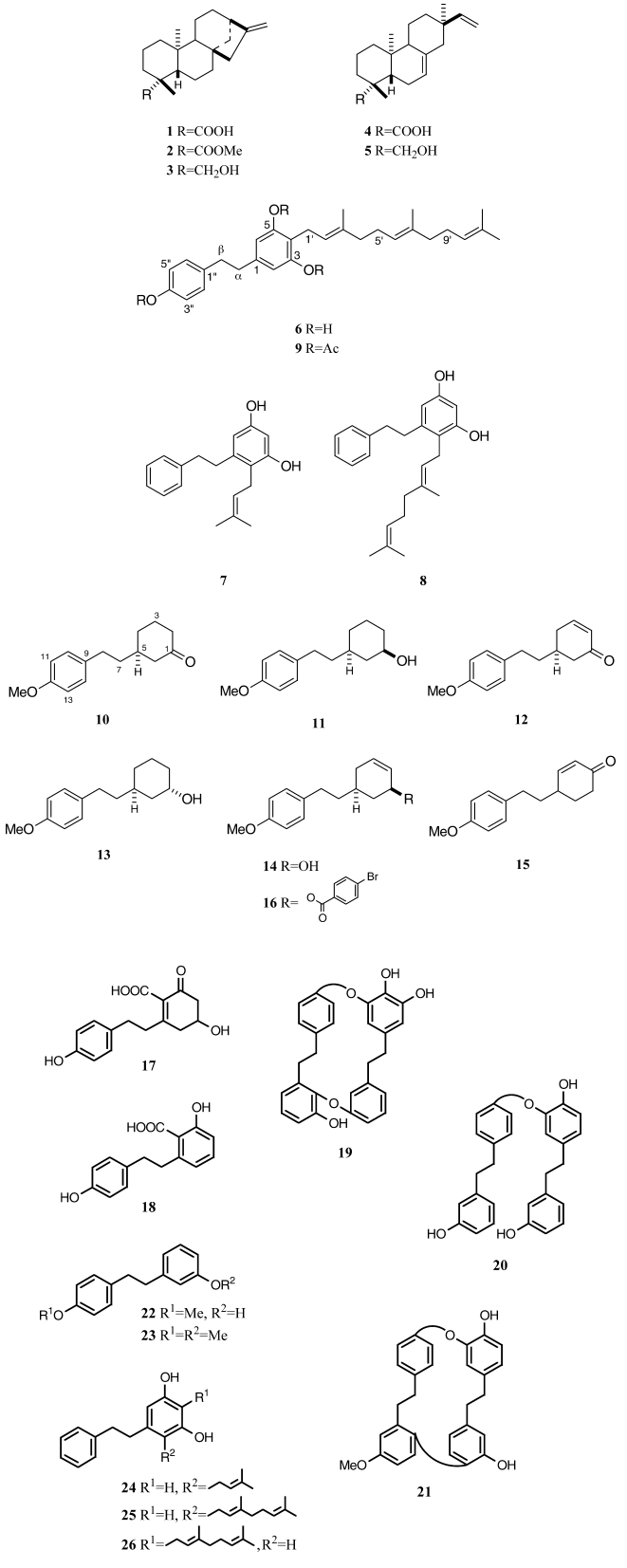
The new bibenzyl **6** and two known bibenzyls, 3,5-dihydroxy-2-(3-methyl-2-butenyl)bibenzyl (**7**)[12] and 2-geranyl-3,5-dihydroxybibenzyl (**8**),[12] were isolated from the ether extract of an unidentified *Radula* species by repeated column chromatography and preparative HPLC. The structures of known bibenzyls were established by the comparison with those of reference data.

The IR spectrum of **6** showed the presence of a hydroxyl group (3400 cm^{-1}). Its ^{1}H-NMR spectrum confirmed the presence of four olefinic methyls (δ 1.59, 1.60, 1.67, 1.82 each 3H, s), disubstituted (δ 7.04, 6.75 each 2H, d) and tetrasubstituted (δ 6.24 2H, s) aromatic protons, and three olefinic protons (δ 5.27, 5.08, 5.09). The ^{1}H-NMR spectrum of **6** was similar to those of bibenzyls **7** and **8**, indicating that the structure of **6** was also bibenzyl with an isoprene unit (Table 1). The ^{13}C-NMR spectrum of **6** displayed 25 carbons and its distortionless enhancement by polarization transfer (DEPT) spectra confirmed the presence of four methyls, seven methylenes, nine olefinic methines, and nine olefinic quaternary carbons. Electron-impact mass spectrometry (EI-MS) showed the molecular ion at *m*/*z* 434 $[M]^+$ and the molecular formula $C_{29}H_{38}O_3$ was confirmed by its high-resolution EI-MS (HR-EI-MS). The acetylation of **6** gave a triacetate **9**, which showed three acetyl signals (δ 2.28 6H, 2.29 3H, each s) in ^{1}H-NMR. Thus the above spectral evidence showed that compound **6** is a bibenzyl with three aromatic hydroxyl groups with a farnesyl group. The analysis of the ^{1}H–^{1}H correlated spectroscopy (^{1}H–^{1}H COSY) and the heteronuclear multiple-bond correlation (HMBC) spectra shown in Fig. 1 clarified that the structure of **6** is 3,5,4′-trihydroxy bibenzyl. Moreover, the NOESY spectrum shown in Fig. 2 verified that the geometry of the two double bonds at C2′–C3′ and C6′–C7′ was the *trans* form. Thus the structure of **6** was established to be 3,5,4′-trihydroxy-4-(3,7,11-trimethyl-2,6,10-dodecatrienyl)bibenzyl.

The fractionation of the ether extract of *B. rosea* resulted in the isolation of three new aromatic compounds **10**—**12**. The IR spectrum of **10** showed the presence of a carbonyl group (1721 cm^{-1}), and its HR-EI-MS spectrum confirmed the molecular ion peak at *m*/*z* 232.1460 ($C_{15}H_{20}O_2$ Calcd for 232.1463). The ^{1}H-NMR (Table 2) displayed A_2B_2 aromatic protons (δ 6.82, 7.07 each d) and a methoxy group (δ 3.77 s), indicating the presence of a *para*-substituted benzene ring. The ^{13}C-NMR (Table 3) spectrum showed a ketone carbonyl carbon (δ 211.7), four aromatic methines (δ 129.1, 113.8 each ×2), two aromatic quaternary carbons (δ 134.0, 157.8), one methoxy carbon (δ 55.3), six methylenes, and one methine. The above results indicate that **10** is a bicyclic compound. On basis of ^{1}H–^{1}H COSY, HMBC, and NOESY spectra (Fig. 3) the structure of **10** was established to be 5-*p*-(methoxyphenylethyl)cyclohexan-1-one.

The ^{1}H- and ^{13}C-NMR spectra (Tables 2, 3) of **11** showed the presence of a methine (δ_H 3.56 dddd; δ_C 70.8) bearing a hydroxy group and *para*-substituted aromatic protons [δ_H 7.08, 6.82 each d; δ_C 129.2 (×2), 113.7 (×2) each CH, 134.8, 157.6 each C]. The IR spectrum indicated the presence of a hydroxy group (3365 cm^{-1}) and its HR-EI-MS showed the molecular formula to be $C_{15}H_{22}O_2$ (Calcd for 234.4620). The analyses of ^{1}H–^{1}H COSY and HMBC spectra

* To whom correspondence should be addressed. e-mail: fnaga@ph.bunri-u.ac.jp



of **11** showed that the structure was 5-*p*-(methoxyphenylethyl)cyclohexan-1-ol, with spectral data identical to those of one of the cyclohexanol derivatives **11** and **13** prepared from **10** with lithium aluminum hydride ($LiAlH_4$) reduction. The NOESY spectrum of **11** showed NOEs between i) H-1 and H-2α, H-5α, H-6α, ii) H-2β and H-4β, H-6β, and iii) H-5α and H-3α, H-6α. Furthermore, the relative stereochemistry of **11** was confirmed by X-ray crystallographic analysis, as shown in Fig. 4. Thus the stereostructure of **11** was established to be 5-*p*-(methoxyphenylethyl)cyclohexan-1β-ol.

Table 1. ^{1}H- (600 MHz) and ^{13}C- (100 MHz) NMR Data of **6** ($CDCl_3$)

	^{13}C	^{1}H		^{13}C	^{1}H
1	141.6		10′	124.4	5.09 m
2, 6	108.4	6.24 2H, s	11′	131.3	
3, 5	154.9		12′	17.7	1.60 s
4	111.0		13′	25.7	1.67 s
1′	22.3	3.40 2H, d (7.1)*a)*	14′	16.1	1.82 s
2′	121.6	5.27 t (7.1)	15′	16.3	1.59 s
3′	139.1		α	37.7	2.72 d (10.2)
4′	39.68*b)*	2.02—2.08 m			2.73 d (9.1)
		2.09—2.14 m	β	36.6	2.79 d (9.1)
5′	26.4	2.02—2.08 m			2.80 d (10.1)
		2.09—2.14 m	1″	134.1	
6′	123.6	5.08 m	2″, 6″	129.5	7.04 2H, d (8.5)
7′	135.6		3″, 5″	115.2	6.75 2H, d (8.5)
8′	39.72*b)*	1.98 2H, m	4″	153.7	
9′	26.7	2.02—2.08 2H, m			

a) Coupling constants (*J* in Hz) are given in parentheses. *b*) Assignments may be interchangeable.

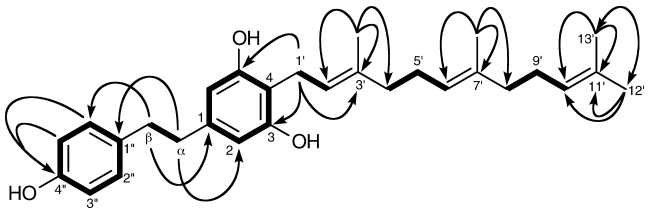


Fig. 1. ^{1}H–^{1}H (Bold Line) and Long-Range ^{1}H–^{13}C (Arrows) Correlations of **6**

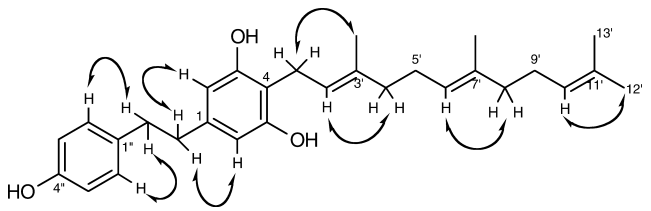


Fig. 2. NOE Correlations of **6**

The CD spectrum of **10** showed first negative (293 nm) and second positive (223 nm) Cotton effects (Fig. 3).[13] Thus the absolute configuration of **10** and **11** was established as shown in Fig. 3.

The ^{1}H- and ^{13}C-NMR spectra (Tables 2, 3) of **12** resembled those of compounds **10** and **11** except for the presence of a disubstituted olefinic group (δ_H 6.01 d, 6.96 ddd; δ_C 129.8, 149.7 each CH), indicating that **12** possessed a *p*-(methoxyphenylethyl)cyclohexane skeleton. The IR spectrum confirmed the presence of an unsaturated carbonyl group (1683 cm^{-1}) and its HR-EI-MS spectrum showed the molecular formula to be $C_{15}H_{18}O_2$ (Calcd for 230.1307). Furthermore, the reduction of **12** gave a monoalcohol **14** (*m*/*z* 232 $[M]^+$) in which the presence of the methine (δ_H 4.29 m; δ_C 68.1) bearing a hydroxy group was confirmed by ^{1}H- and ^{13}C-NMR spectra (Tables 2, 3). Moreover, the ^{1}H- and ^{13}C-NMR data of **12** were not identical to those of 4-*p*-(methoxyphenylethyl)cyclohex-2-en-1-one (**15**) isolated from

Table 2. ^{1}H-NMR of **10**—**12** and **14** (600 MHz, $CDCl_3$)

H	10	11	12	14
1		3.56 dddd (11.8, 11.8, 4.4, 4.4)		4.29 m
2	2.35 br d (13.7)[a] α	1.96 br d (11.8) α	6.01 d (9.9)	5.67 br d (8.8)
	2.25 dddd (13.7, 12.4, 6.3, 1.4) β	1.14 m β		
3	1.63 m	1.25 ddddd (13.2, 13.2, 13.2, 3.6, 3.6) α	6.96 ddd (9.9, 5.8, 2.5)	5.76 m
	2.01—2.06 m	1.77 d quint. (13.2, 3.3) β		
4	1.93 br d (13.5) α	1.72 br d (12.9) α	2.47 dd (14.6, 5.8)	2.13 m
	1.37 m β	0.83 dddd (13.2, 13.2, 13.2, 3.8) β	2.08 m	1.70 m
5	1.79 m	1.34 m	2.12 m	1.66 m
6	2.46 dddd (13.7, 3.8, 1.9, 1.9) α	2.05 br d (11.8) α	2.58 m	2.15 m α
	2.01—2.06 m β	0.92 q (11.8) β	2.15 q (13.5)	1.17 ddd (12.1, 12.1, 10.2) β
7	1.59 m	1.48—1.58 2H m	1.65—1.72 2H m	1.60 2H m
	1.65 m			
8	2.57 2H t (8.2)	2.57 2H t (8.2)	2.61 2H m	2.60 2H t (8.0)
10, 14	7.07 d (8.8)	7.08 d (8.5)	7.08 d (8.5)	7.09 2H d (8.8)
11, 13	6.82 d (8.8)	6.82 d (8.5)	6.83 d (8.5)	6.83 2H d (8.8)
O$\underline{CH_3}$	3.77 s	3.79 s	3.78 s	3.79 s

a) Coupling constants (*J* in Hz) are given in parentheses.

Table 3. ^{13}C-NMR of **10**—**14** (100 MHz, $CDCl_3$)

C	10	11	12	13	14
1	211.7	70.8	199.7	66.9	68.1
2	41.5	35.8	129.8	33.4	131.2
3	25.2	24.1	149.7	20.0	128.6
4	31.2	32.0	32.2	32.1	31.8
5	38.4	35.9	34.5	31.3	32.5
6	48.0	42.5	44.3	39.7	39.5
7	38.6	39.1	37.7	38.6	38.6
8	32.0	32.2	31.8	32.4	32.0
9	134.0	134.8	133.7	135.0	134.5
10, 14	129.1	129.2	129.1	129.2	129.2
11, 13	113.8	113.7	113.9	113.7	113.8
12	157.8	157.6	157.9	157.6	157.7
O$\underline{CH_3}$	55.3	55.3	55.2	55.3	55.3

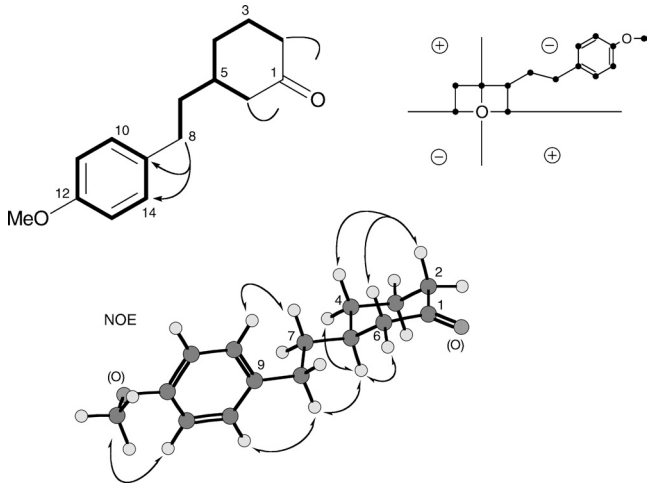


Fig. 3. ^{1}H–^{1}H (Bold Line), Long-Range ^{1}H–^{13}C (Arrows), NOE (Half Arrows) Correlations, and the Octant Diagram of **10**

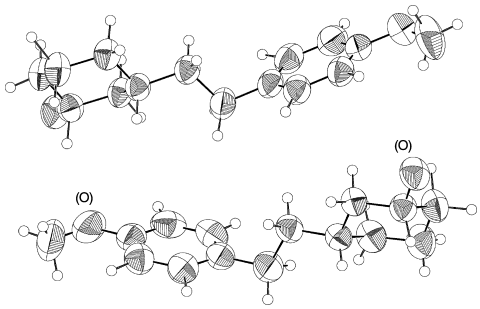


Fig. 4. ORTEP Drawing of **11**

Anisotropic ellipsoids are represented by a 50% probability level.

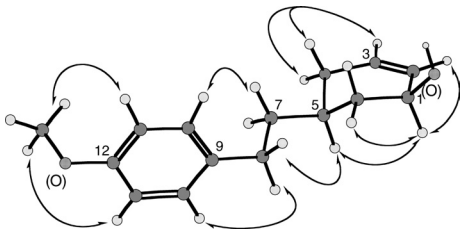


Fig. 5. NOE Correlations of **14**

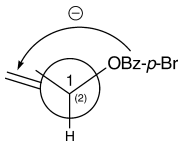


Fig. 6. Sign of the Cotton Effect of *p*-Bromobenzoate Derivative **16**

Plagiochila longispina.[14] Successive ^{1}H–^{1}H COSY, HMQC, and HMBC spectral analyses of **12** led to the structure of 5-*p*-(methoxyphenylethyl)cyclohex-2-en-1-one. The stereochemistry of **12** was clarified by analysis of the NOESY spectrum of monoalcohol **14**, as shown in Fig. 5. To determine of the absolute configuration of **12**, *p*-bromobenzoate **16** was prepared from **14**. The CD spectrum of **16** showed a negative Cotton effect (242 nm). Application of the allyl benzoate rule[15] clearly established the absolute configuration of **12** as shown in Fig. 6.

Previously, the chemical constituents of *B. rosea* were analyzed by our group, and sulfur-containing acrylates, phthalide, and methyl benzoate were isolated.[16] Sulfur-containing acrylate was not found in the present species, although, the phenylethyl compounds **10**—**12** were the first isolated from liverworts. Two similar *p*-substituted phenylethyl cyclo-

hexane derivatives **15** and **17** were previously isolated from the liverwort *Plagiochila longispina*[14] and suspension-cultured cells of *Marchantia polymorpha*,[17] respectively. The latter compound has been suggested to be a plausible precursor of lunularic acid (**18**), a ubiquitous bibenzyl of liverworts,[2] from which cyclic bisbibenzyls **19**—**21** were biosynthesized.[18,19] Although the present *B. rosea* contains neither bibenzyls nor cyclic bisbibenzyls, the new *p*-methoxyphenylethyl cyclohexane derivatives **10**—**12** may be probable precursors of decarboxylic bibenzyls **22** and **23** or cyclic bisbibenzyls **19**—**21** that were found in the liverworts *Frullania*, *Plagiochila*, and *Radula* species,[2] although the biosynthetic mechanism remains to be clarified. Furthermore, phenyl bibenzyls **6** and **24**—**26** might originate from these bibenzyl derivatives.

There has been no description of the chemical components of *J. kirkii* thus far. This is the first report of the isolation of *ent*-kaurane and *ent*-isopimarane diterpenoids from *J. kirkii*. While various bisbibenzyls have been found in *Radula* species,[20] this is the first isolation of farnesyl bibenzyl **6** from *Radula* species.

Experimental

General Methods Melting points was measured on a Yanagimoto micromelting point apparatus without correction. Optical rotations were measured on a Jasco DIP-1000 polarimeter. IR spectra were recorded on a Shimadzu FTIR 8400S infrared spectrophotometer. UV spectra were recorded on a Shimadzu UV-1650PC UV-visible spectrophotometer. CD spectra were run on a Jasco J-725 spectropolarimeter. The ^{1}H- and ^{13}C-NMR spectra were measured with Varian Unity-600 (^{1}H, 600 MHz; ^{13}C, 150 MHz) and Jeol Eclipse-400 (^{1}H, 400 MHz; ^{13}C, 100 MHz) instruments. Chemical shift values are expressed in δ (ppm) downfield from tetramethylsilane as an internal standard (^{1}H-NMR), and in δ 77.03 (ppm) from $CDCl_3$ as a standard (^{13}C-NMR). Mass spectra were obtained on a JEOL Mstation JMS 700 instrument. X-Ray crystallographic analysis was carried out on a Mac Science DIP-2020 instrument. TLC was performed using Silica gel 60F_{254} plates (Merck). Column chromatography was performed on Silica-gel 60 (Merck, 230—400, 35—70 mesh) and Sephadex LH-20 (Amersham Pharmacia Biotech, sol. CH_2Cl_2–MeOH 1 : 1). TLC spots were visualized under UV (254 nm) light and by spraying with Godin reagent[21] and 30% H_2SO_4, followed by heating.

Plant Material *B. rosea* Berggren (NZ-156) was collected in Hasst, New Zealand, and an unidentified *J. kirkii* Steph. (NZ-201) and *Radula* species (NZ-204) in Jackson River, New Zealand, and identified by J. E. Braggins (University of Auckland, New Zealand). A voucher specimen was deposited in the Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Japan.

Extraction and Isolation The ether extract (1.9 g) of *J. kirkii* was divided into eight fractions by column chromatography (CC) on silica gel using an *n*-hexane–EtOAc gradient (*n*-hexane alone, 19 : 1, 9 : 1, 4 : 1, 7 : 3, 1 : 1, EtOAc alone; each 300 ml) solvent system. *ent*-Methyl-16-kauren-19-oate (**2**, 13.2 mg) was isolated from fraction (fr.) 1 on column chromatography with Sephadex LH-20 and preparative HPLC (Chemcosorb 5Si-U, *n*-hexane–EtOAc 49 : 1). Fr. 3 was rechromatographed on Sephadex LH-20, silica gel, and Lobar (Diol, *n*-hexane–EtOAc 17 : 3) to give *ent*-16-kauren-19-oic acid (**1**, 96.1 mg) and oblongifolic acid (**4**, 50.9 mg). *ent*-16-Kauren-19-ol (**3**, 17.6 mg) and *ent*-isopimara-7(8),15-dien-19-ol (**5**, 34.5 mg) were purified on column chromatography with Sephadex LH-20, Lobar (Diol, *n*-hexane–EtOAc 9 : 1), and preparative HPLC (Cosmosil 5SL-II, *n*-hexane–EtOAc 9 : 1) of fr. 4.

The ether extract (220 mg) of *Radula* sp. was divided into three fractions on column chromatography with Sephadex LH-20. Fr. 3 was rechromatographed on silica gel (CH_2Cl_2–Et_2O 49 : 1, 19 : 1, 9 : 1) and divided into six subfractions. 3,5,4′-Trihydroxy-4-(3,7,11-trimethyl-2,6,10-dodecatrienyl)bibenzyl (**6**, 3.5 mg) and 2-geranyl-3,5-dihydroxybibenzyl (**8**, 6.3 mg) were purified on preparative HPLC (Chemcosorb 5Si-U, CH_2Cl_2–Et_2O 19 : 1) of fr. 3 and 4. Preparative HPLC (Chemcosorb 5Si-U, CH_2Cl_2–Et_2O 19 : 1) of fr. 3-5 gave 3,5-dihydroxy-2-(3-methyl-2-butenyl)bibenzyl (**7**, 6.3 mg).

The ether extract (750 mg) of *B. rosea* was divided into five fractions on column chromatography with silica gel using an *n*-hexane–EtOAc gradient solvent system (*n*-hexane alone, 19 : 1, 9 : 1, 4 : 1, 7 : 3, 1 : 1, EtOAc alone; each 200 ml). Fr. 3 was rechromatographed on Sephadex LH-20 and silica gel to yield 5-*p*-(methoxyphenylethyl)cyclohexan-1-one (**10**, 170.9 mg). 5-*p*-(Methoxyphenylethyl)cyclohex-2-en-1-one (**12**, 193.3 mg) was purified on column chromatography with Sephadex LH-20 and silica gel of fr. 4. Fr. 5 was rechromatographed on Sephadex LH-20 and silica gel and finally purified on preparative TLC (CH_2Cl_2–EtOAc 4 : 1) to give 5-*p*-(methoxyphenylethyl)cyclohexan-1β-ol (**11**, 2.9 mg).

3,5,4′-Trihydroxy-4-(3,7,11-trimethyl-2,6,10-dodecatrienyl)bibenzyl (**6**): FT-IR cm^{-1}: 3400, 1605, 1440, 1231. UV λ_{max} (EtOH) nm (log ε): 279 (2.60), 229 (3.49) (c=1.18×10^{-4}). ^{1}H- and ^{13}C-NMR: see Table 1. HR-EI-MS *m/z*: 434.2832 (Calcd for $C_{29}H_{38}O_3$: 434.2821). EI-MS *m/z* (int.): 434 [M]$^+$ (15), 365 (2), 352 (3), 298 (7), 297 (12), 281 (30), 243 (50), 191 (16), 175 (16), 137 (20), 121 (17), 107 (100), 81 (14), 69 (38), 44 (95).

5-*p*-(Methoxyphenylethyl)cyclohexan-1-one (**10**): $[\alpha]_D^{17}$ −10.5° (c=0.17). FT-IR cm^{-1}: 1721. UV λ_{max} (EtOH) nm (log ε): 285 (3.26), 278 (3.33), 225 (4.35) (c=9.70×10^{-5}). CD (EtOH): $\Delta\varepsilon_{293}$ −1.25, $\Delta\varepsilon_{223}$ +0.64 (c=1.46×10^{-4}). ^{1}H- and ^{13}C-NMR: see Tables 2 and 3. HR-EI-MS *m/z*: 232.1460 (Calcd for $C_{15}H_{20}O_2$: 232.1463). EI-MS *m/z* (int.): 232 [M]$^+$ (58), 214 (6), 171 (2), 134 (6), 121 (100), 97 (57), 91 (8), 77 (7), 41 (5).

5-*p*-(Methoxyphenylethyl)cyclohexan-1β-ol (**11**): Colorless crystals, mp 64—66 °C. $[\alpha]_D^{17}$ −10.2° (c=1.32). FT-IR cm^{-1}: 3365. UV λ_{max} (EtOH) nm (log ε): 284 (1.98), 277 (2.03), 223 (2.51) (c=2.74×10^{-4}). ^{1}H- and ^{13}C-NMR: see Tables 2 and 3. HR-EI-MS *m/z*: 234.1626 (Calcd for $C_{15}H_{22}O_2$: 234.1620). EI-MS *m/z* (int.): 234 [M]$^+$ (61), 216 (16), 173 (6), 159 (3), 147 (6), 134 (74), 121 (100), 108 (22), 91 (10), 77 (9), 65 (3), 55 (3), 41 (4). Crystal data: orthorhombic, $P2_122_1$, a=9.739(3) Å, b=10.181(4) Å, c=28.214(13) Å, α=90.0°, β=90.0°, γ=90.0°, V=2797.5(2) Å^3, Z=8, Mo$K\alpha$ radiation, λ=0.71073, DIP image plate, refinement on F^2, fullmatrix least-squares refinement, R(gt)=0.0573, wR(gt)=0.1623, S(ref)=1.091, 4317 reflections, 308 parameters, only coordinates of H atoms refined, cell refinement, Scalepack (HKL); data reduction, maXus; program used to refine structure, *SHELXL*-97.

5-*p*-(Methoxyphenylethyl)cyclohex-2-en-1-one (**12**): $[\alpha]_D^{20}$ +18.5° (c=0.56). FT-IR cm^{-1}: 1683. UV λ_{max} (EtOH) nm (log ε): 285 (3.27), 278 (3.33), 225 (4.08) (c=1.48×10^{-4}). CD (EtOH): $\Delta\varepsilon_{312}$ −0.21, $\Delta\varepsilon_{233}$ −2.71, $\Delta\varepsilon_{221}$ +1.53 (c=1.48×10^{-4}). ^{1}H- and ^{13}C-NMR: see Tables 2 and 3. HR-EI-MS *m/z*: 230.1308 (Calcd for $C_{15}H_{18}O_2$: 230.1307). EI-MS *m/z* (int.): 230 [M]$^+$ (49), 201 (2), 172 (4), 160 (6), 147 (4), 134 (15), 121 (100), 110 (75), 95 (86), 91 (15), 77 (18), 65 (8), 53 (3), 41 (8).

Acetylation of 6 To compound **6** (5 mg) was added pyridine (1 ml) and Ac_2O (1 ml), the mixture was kept at room temperature overnight, and then worked up as usual to give the triacetate **9** (1.8 mg).

3,5,4′-Triacetoxy-4-(3,7,11-trimethyl-2,6,10-dodecatrienyl)bibenzyl (**9**): FT-IR cm^{-1}: 1738, 1726, 1238. ^{1}H-NMR (400 MHz, $CDCl_3$): δ: 1.58 (3H, s), 1.59 (3H, s), 1.67 (3H, s), 1.72 (3H, s), 1.93—2.06 (8H, m), 2.28 (6H, s), 2.29 (3H, s), 2.84—2.91 (4H, m), 3.15 (2H, d, J=6.6 Hz), 4.98—5.06 (2H, m), 5.08 (1H, t, J=7.0 Hz), 6.79 (2H, s), 6.99 (2H, d, J=8.8 Hz), 7.17 (2H, d, J=8.8 Hz). EI-MS *m/z* (int.): 560 [M]$^+$ (21), 517 (10), 476 (7), 407 (6), 393 (12), 380 (11), 365 (15), 351 (15), 339 (39), 323 (32), 285 (88), 243 (10), 191 (31), 189 (13), 149 (20), 136 (39), 121 (37), 107 (100), 95 (22), 81 (34), 69 (58), 57 (31), 43 (42).

Reduction of 10 To a suspension of $LiAlH_4$ (24 mg) in dry Et_2O (2 ml) was added compound **10** (21.2 mg) in dry Et_2O (2 ml) and the mixture was stirred for 1 h at room temperature. Work-up as usual gave a mixture that was purified by preparative HPLC (Chemcosorb 5Si-U *n*-hexane–EtOAc 4 : 1) to give a monoalcohol (**11**, 13.4 mg) and its epimer (**13**, 3.8 mg). The spectral data of **11** were completely identical to those of natural **11**.

5-*p*-(Methoxyphenylethyl)cyclohexan-1α-ol (**13**): $[\alpha]_D^{17}$ −10.9° (c=0.16). FT-IR cm^{-1}: 3320. UV λ_{max} (EtOH) nm (log ε): 285 (3.63), 278 (3.70), 224 (4.41) (c=5.56×10^{-5}). ^{1}H-NMR (400 MHz, $CDCl_3$): δ: 7.09 (2H, d, J=8.4 Hz, H-10, 14), 6.82 (2H, d, J=8.4 Hz, H-11, 13), 4.07 (1H, br s, H-1), 3.79 (3H, s, –O<u>CH</u>$_3$), 2.57 (1H, dd, J=7.3, 2.2 Hz, H-8), 2.55 (1H, dd, J=7.3, 1.8 Hz, H-8′), 1.69—1.79 (3H, m, H-4, 5, 6), 1.62—1.68 (2H, m, H-2, 3), 1.46—1.60 (4H, m, H-2, 3, 7), 1.30 (1H, like t, J=10.6 Hz, H-6), 1.02 (1H, m, H-4). ^{13}C-NMR: see Table 3. HR-EI-MS *m/z*: 234.1619 (Calcd for $C_{15}H_{22}O_2$: 234.1620). EI-MS *m/z* (int.): 234 [M]$^+$ (52), 216 (1), 147 (1), 134 (5), 121 (100), 108 (6), 91 (4), 83 (7), 77 (4), 41 (2).

Reduction of 12 To a suspension of $LiAlH_4$ (20 mg) in dry Et_2O (2 ml) was added compound **12** (17.1 mg) in dry Et_2O and the mixture was stirred for 1 h at room temperature. Work-up as usual gave a mixture that was purified with preparative HPLC (Chemcosorb 5Si-U *n*-hexane–EtOAc 4 : 1) to

give a monoalcohol (**14**, 13.9 mg).

5-*p*-(Methoxyphenylethyl)cyclohex-2-en-1β-ol (**14**): Amorphous, $[\alpha]_D^{19}$ +3.3° (c=1.40). FT-IR cm^{-1}: 3323. UV λ_{max} (EtOH) nm (log ε): 285 (3.27), 278 (3.34), 224 (4.10) (c=1.29×10^{-4}). ^{1}H- and ^{13}C-NMR: see Tables 2 and 3. HR-EI-MS *m/z*: 232.1463 (Calcd for $C_{15}H_{20}O_2$: 232.1464). EI-MS *m/z* (int.): 232 $[M]^+$ (19), 214 (16), 185 (3), 160 (22), 134 (88), 121 (100), 110 (56), 91 (11), 78 (11), 41 (4).

Esterification of 14 To a suspension of **14** (16.2 mg) in pyridine (1 ml) and CH_2Cl_2 (1 ml) was added *p*-bromobenzoylchloride (51 mg) and *p*-dimethylaminopyridine (DMAP, 8 mg) and the mixture was stirred for overnight at room temperature. The reaction mixture was filtered and purified on silica gel column chromatography to yield the benzoate derivative **16** (6.7 mg): $[\alpha]_D^{22}$ −94.1° (c=0.53). FT-IR cm^{-1}: 1715. UV λ_{max} (EtOH) nm (log ε): 284 (2.65), 275 (2.77), 245 (3.66), 229 (3.58) (c=2.14×10^{-4}). CD (EtOH): $\Delta\varepsilon_{242}$ −2.38 (c=2.14×10^{-4}). ^{1}H-NMR (600 MHz, $CDCl_3$): δ: 5.61 (1H, br s, H-1), 5.71 (1H, d, J=10.2 Hz, H-2), 5.91 (H, m, H-3), 1.81 (1H, m, H-4), 2.23 (1H, m, H-4), 1.80 (1H, m, H-5), 2.28 (1H, m, H-6α), 1.46 (1H, q, J=12.1 Hz, H-6β), 1.64 (2H, m, H-7), 2.61 (2H, t, J=8.0 Hz, H-8), 7.09 (2H, d, J=8.8 Hz, H-10, 14), 6.83 (2H, d, J=8.8 Hz, H-11, 13), 3.79 (3H, s, –O<u>CH</u>$_3$), 7.57 (2H, d, J=8.8 Hz), 7.90 (2H, d, J=8.8 Hz). HR-EI-MS *m/z*: 414.0828 (Calcd for $C_{22}H_{23}O_3Br$: 414.0830). EI-MS *m/z* (int.): 416 $[M+2]^+$ (5), 414 $[M]^+$ (5), 214 (25), 202 (12), 200 (12), 185 (24), 183 (24), 160 (15), 134 (94), 121 (100), 110 (56), 91 (13), 79 (16), 77 (14), 43 (7).

Acknowledgments We thank Dr. S. Takaoka, Dr. M. Tanaka, and Miss Y. Okamoto (Tokushima Bunri University) for measurements of X-ray crystallographic analysis, NMR, and mass spectra. Thanks are also due to Prof. J. E. Braggins (Auckland University, New Zealand) for the identification of the species. We are grateful to Miss T. Yamaguchi and Miss A. Mabuchi for their experimental assistance. This work was supported by a Grant-in-Aid for Scientific Research (A) (No. 11309012) from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

References

1) Asakawa Y., "Progress in the Chemistry of Organic Natural Products," Vol. 42, ed. by Herz W., Grisebach H., Kirby G. W., Springer, Vienna, 1982, pp. 1—285.
2) Asakawa Y., "Progress in the Chemistry of Organic Natural Products," Vol. 65, ed. by Herz W., Grisebach H., Kirby G. W., Moore R. E., Steglich W., Tamm Ch., Springer, Vienna, 1995, pp. 1—562.
3) Allison K. W., Child J., "The Liverworts of New Zealand," University of Otago Press, Dunedin, 1975, pp. 1—300.
4) Nagashima F., Murakami M., Takaoka S., Asakawa Y., *Chem. Pharm. Bull.*, **52**, 949—952 (2004).
5) Toyota M., Omatsu I., Braggins J., Asakawa Y., *Chem. Pharm. Bull.*, **52**, 481—484 (2004).
6) Asakawa Y., Toyota M., von Konrat M., Braggins J. E., *Phytochemistry*, **62**, 439—452 (2003).
7) Toyota M., Shimamura T., Ishii H., Renner M., Braggins J., Asakawa Y., *Chem. Pharm. Bull.*, **50**, 1390—1392 (2002).
8) Pyrek J. St., *Tetrahedron*, **26**, 5029—5032 (1970).
9) Piozzi F., Passannanti S., Paternostro M., Sprio V., *Phytochemistry*, **10**, 1164—1166 (1971).
10) Aiyar V. N., Seshadri T. R., *Tetrahedron*, **26**, 5275—5279 (1970).
11) Aiyar V. N., Seshadri T. R., *Indian J. Chem.*, **9**, 613—614 (1971).
12) Asakawa Y., Kondo K., Tori M., Hashimoto T., Ogawa S., *Phytochemistry*, **30**, 219—234 (1991).
13) Moffitt W., Woodward R. B., Moscowitz A., Klyne W., Djerassi C., *J. Am. Chem. Soc.*, **83**, 4013—4018 (1961).
14) Siegel U., Mues R., Dönig R., Eicher T., *Phytochemistry*, **30**, 3643—3646 (1991).
15) Nina C. G., Koji N., Victor S. M., Sharpless K. B., *J. Am. Chem. Soc.*, **104**, 3115—3116 (1982).
16) Asakawa Y., Takikawa K., Tori M., Campbell E. O., *Phytochemistry*, **25**, 2543—2546 (1986).
17) Ohta Y., Abe S., Komura H., Kobayashi M., *J. Am. Chem. Soc.*, **105**, 4480—4481 (1983).
18) Friederich S., Maier U. H., D.-Neumann B., Asakawa Y., Zenk M. H., *Phytochemistry*, **50**, 589—598 (1999).
19) Friederich S., Rueffer M., Asakawa Y., Zenk M. H., *Phytochemistry*, **52**, 1195—1202 (1999).
20) Scher J. M., Zapp J., Schmidt A., Becker H., *Phytochemistry*, **64**, 791—796 (2003).
21) Godin P., *Nature* (London), **174**, 134 (1954).