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NOVEL BIBENZYL DERIVATIVES AND ENT-CUPARENE-TYPE SESQUITERPENOIDS FROM *RADULA* SPECIES*

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Key Word Index—*Radula buccinifera*; *R. complanata*; *R. japonica*; *R. oyamensis*; *R. perrottetii*; *R. tokiensis*; *R. variabilis*; Radulaceae; Jungermanniales; Hepaticae; prenyl bibenzyls; dihydro-oxepin skeleton; perrottetins; radulanins; radulanolide; ent-cuparene-type sesquiterpenoids; antibiotics; chemosystematics; allergy.

Abstract—Four novel prenyl bibenzyls, perrottetin A–D were isolated from the liverwort *Radula perrottetii* together with a new sesquiterpene phenol, ent-2, 3-dihydroxycuparene and a prenyl dihydrochalcone, and their structures were determined by spectral methods and chemical transformations. Further investigation of the French species *R. complanata* resulted in the isolation of four new bibenzyls, 3, 4′-dimethoxybibenzyl, 3, 5-dihydroxy-4-(2, 3-epoxy-3-methylbutyl)bibenzyl, radulanin H and radulanolide. *R. buccinifera* was chemically close to *R. complanata*. The composition of bibenzyls found in *R. perrottetii* and *R. oyamensis* were different from that of the other *Radula* species referred to in the section *Radula*. Some prenyl bibenzyls showed antimicrobial activity against *Streptococcus aureus* (20 μg/ml). The allergenic activity of *R. complanata* is due to (+)-frullanolide from the liverwort *Frullania dilatata* which is intermingled in *R. complanata*.

INTRODUCTION

Most liverworts produce mono-, sesqui- and diterpenoids, and lipophilic aromatic compounds which often show interesting biological activity, such as allergenic contact dermatitis, antifeedant, anticancer and plant growth regulatory activity [1]. These substances are also valuable in chemosystematic studies of the Hepaticae [2–17]. *Radula* Dum. is an isolated genus in the Jungermanniales. These species contain large oil bodies, usually one per cell and have the basic chromosome number of $n = 8$. *Radula* is composed of 14 sections and 350 species. Yamada [18] recognized 61 taxa of *Radula* growing in Asia. Lopès [19] reported that European *R. complanata* caused allergenic contact dermatitis, and it produced 3-methoxybibenzyl (**1**) as the major component [20, 21], along with various prenyl bibenzyls. Recently, we reported the structural determination of new prenyl bibenzyls isolated from three Japanese *Radula* species [22–24].

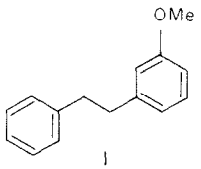
As part of our systematic investigation of the biologically active substances of the Hepaticae, we have studied the chemical constituents of the three *Radula* species, *R. buccinifera* (Hook. f. et Tayl.) Tayl., *R. oyamensis* Steph. and *R. perrottetii* Gott. and the previously investigated *R. complamata* (L.) Dum. The present paper reports the isolation and structural elucidation of eight novel prenyl bibenzyl derivatives and a new ent-cuparene-type sesquiterpene phenol.

RESULTS AND DISCUSSION

Air-dried and ground material of *R. perrottetii* and *R. complanata* were extracted with diethyl ether and then methanol. Each crude extract from *R. perrottetii* was combined and then directly chromatographed on Si gel or Sephadex LH-20, followed by purification on TLC to afford four new prenyl bibenzyls, perrottetin A (**9**), perrottetin B (**11**), perrottetin C (**13**) and perrottetin D (**18**), a prenyl dihydrochalcone (**31**) and a new sesquiterpene phenol, ent-2, 3-dihydroxycuparene (**43**), the previously known bibenzyl (**5**), ent-cuparene (**44**) and two unidentified bibenzyls, named perrottetin E and perrottetin F. The same treatment of the crude extracts from *R. complanata* resulted in the isolation of four novel bibenzyl derivatives, lunularin dimethyl ether (3, 4′-dimethoxybibenzyl) (**3**), 3, 5-dihydroxy-4-(2, 3-epoxy-3-methylbutyl)bibenzyl (**7**), radulanin H (**25**) and radulanolide (**30**).

Two further *Radula* species, *R. buccinifera* collected in Australia and *R. oyamensis* in Japan were analysed by GC/MS equipped with a computer, since only limited amounts of fresh material were available. The mass spectra obtained by GC/MS were identified by direct comparison with those of authentic samples. *R. buccinifera* contained the previously known bibenzyls (**1**, **3** and **5**), radulanin A (**21**) and radulanin C (**22**). *R. oyamensis* produced the new bibenzyls (**33–37**) whose structures were assigned by analyses of the mass spectra obtained (see Experimental).

*Part 12 in the series "Chemosystematics of the Bryophytes". For Part 11, see (1982) *Phytochemistry* **21**, 2471.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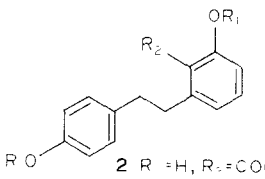
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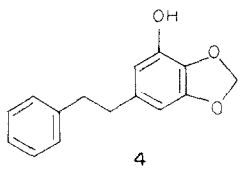
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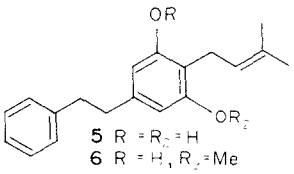
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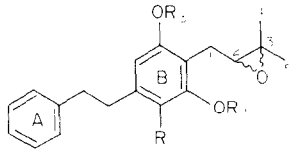
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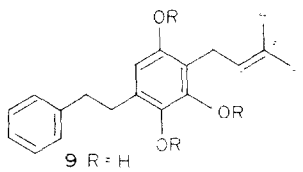
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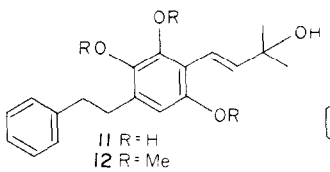
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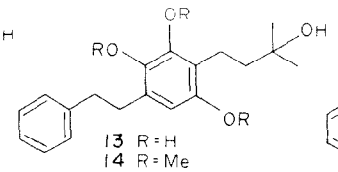
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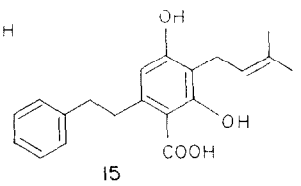
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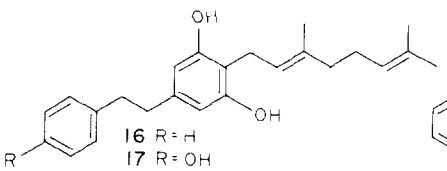
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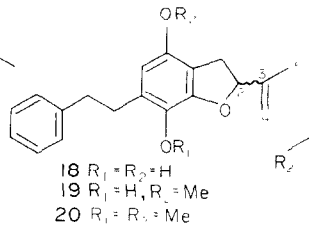
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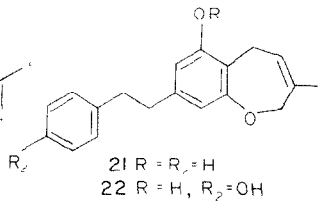
20 R$_1$ = R$_2$ = Me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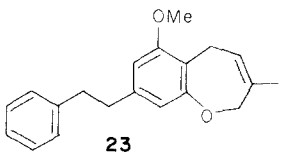
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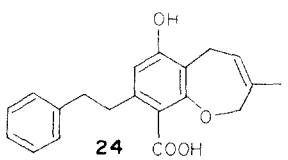
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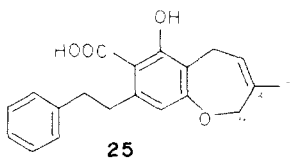
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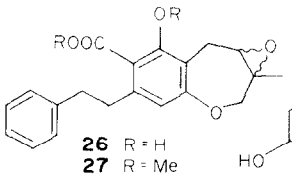
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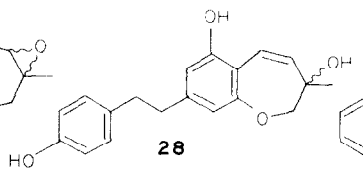
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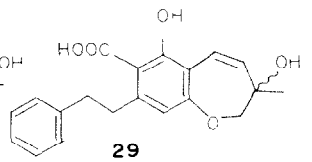
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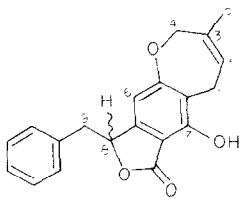
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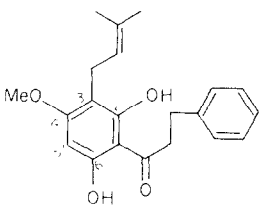
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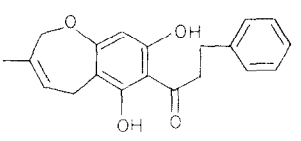
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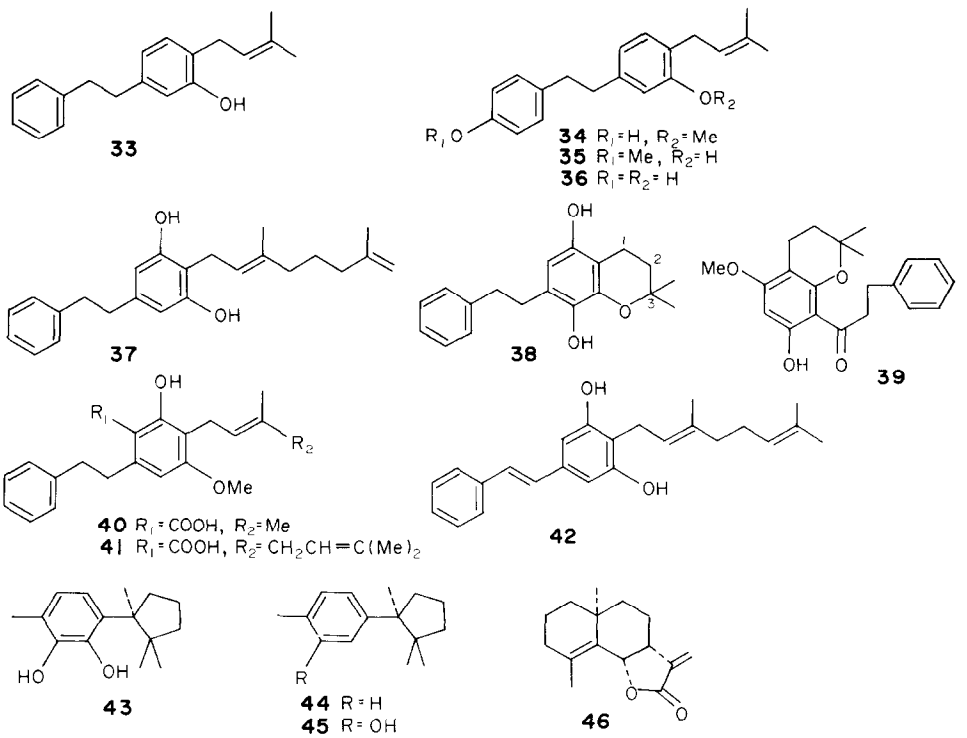

Perrottetin A (2, 3, 5-*trihydroxy*-4-(3-*methyl*-2-*butenyl*)*bibenzyl*)

The major component (**9**), mp 99–100°, $C_{19}H_{22}O_3$ (M^+ 298), isolated from *R. perrottetii* showed the presence of a hydroxyl group (3420 cm^{-1}), and an aromatic ring (1600, 1510, 1505 cm^{-1}). The presence of an unsubstituted benzyl group was confirmed by the singlet signal of ^1H NMR at δ 7.13 (5H, *s*) and the fragment ion at *m/z* 91 (57%). The ^1H NMR spectrum (Table 1) of **9** also contained the signals of a dimethylallyl group [δ 1.63, 1.70 (each 3H), 3.25 (2H, *br d*, $J = 6$ Hz), 5.05 (1H, *br t*, $J = 6$ Hz)], one aromatic proton (δ 6.28, *s*) and four equivalent methylene protons (δ 2.70, *s*). Methylation of **9** with methyl iodide gave a trimethyl ether (**10**), $C_{22}H_{28}O_3$ [M^+ 340; δ 3.77, 3.84, 3.89 (each 3H, *s*)], which on oxidation with *m*-chloroperbenzoic acid (*m*-CPBA) gave a monoepoxide (**8**), $C_{22}H_{28}O_4$ (M^+ 356). This showed that **9** contains three phenolic hydroxyl groups. Treatment of **9** with hydrochloric acid–acetic acid afforded a 2, 2-dimethylchromane (**38**), mp 132–133°; $C_{19}H_{22}O_3$ [M^+ 298, δ 1.28 (6H, *s*)], indicating a phenolic hydroxyl group *ortho* to the isoprene chain. The above chemical and spectral data were identical to those of the co-occurring 3, 5-dihydroxy-4-(3-methyl-2-butenyl)bibenzyl (**5**) [22], except for the presence of an additional phenolic hydroxyl group in **9**. The structure of perrottetin A is therefore 2, 3, 5-trihydroxy-4-dimethylallylbibenzyl. NOE experiments on the trimethyl ether (**10**) showed 10% increase of the intensity of the signal of the aromatic proton, after irradiation of the singlet signal of the benzylic methylenes. Thus, the structure of perrottetin A is established to be **9**.

Perrottetin B and perrottetin C

The polar fraction of *R. perrottetii* was composed of the viscous bibenzyl mixtures lacking methoxyl groups. The two bibenzyls, perrottetin B (**11**) [2, 3, 5 - trihydroxy - 4 - (3 - hydroxy - 3 - methyl - 1 - butenyl)bibenzyl] and perrottetin C (**13**) [2, 3, 5 - trihydroxy - 4 - (3 - hydroxy - 3 - methylbutyl)bibenzyl] were isolated as the methyl ethers, after methylation with methyl iodide, followed by purification on TLC. The methylated perrottetin B (**12**), $C_{22}H_{28}O_4$ (M^+ 356), displayed the presence of a benzylic group [δ 7.22 (5H, *s*)], two equivalent methylenes [δ 2.87 (4H, *s*)], attributable to characteristic benzylic methylenes, one proton (δ 6.42, *s*) in an aromatic ring, three methoxy groups [δ 3.77, 3.78, 3.85 (each 3H, *s*)], a dimethylcarbinol group [δ 1.42 (6H, *s*)] and *trans*-ethylenic protons [δ 6.15, 6.52 (each 1H, *d*, $J = 16$ Hz)]. Hydrogenation of **12** in the presence of PtO_2 afforded a dihydro derivative [$C_{22}H_{30}O_4$ (M^+ 358); 3600–3300 cm^{-1}; δ 1.28 (6H, *s*)], whose spectral data and chromatographic behavior were identical to those of perrottetin C trimethyl ether (**14**). Treatment of **14** with *p*-TsOH, followed by purification on TLC gave a dehydrated bibenzyl, whose spectral data were in good agreement with those of perrottetin A trimethyl ether (**10**). Thus the structures of the methylated perrottetin B and C were established as **12** and **14**; hence the original prenyl bibenzyls are formulated as **11** and **13**, respectively.

Perrottetin D

The minor component (**18**), $C_{19}H_{20}O_3$ (M^+ 296), isolated from *R. perrottetii*, displayed the presence of an unsubstituted benzylic group [δ 7.08 (5H, *s*); *m/z*

Table 1. ^{1}H NMR data* of the new

Compounds	3	7	9	10	12
Ar(A-ring)	6.38–7.42 (*m*)	7.23 (*s*)	7.13 (*s*)	7.20 (*s*)	7.22 (*s*)
Ar(B-ring)	6.90 (*d*, *J* = 9 Hz)	6.18 (*d*, *J* = 2 Hz)	6.28 (*s*)	6.42 (*s*)	6.42 (*s*)
	7.20 (*d*, *J* = 9 Hz)	6.27 (*d*, *J* = 2 Hz)			
Ar–$(CH_2)_2$–Ar	2.78 (*s*)	2.80 (*s*)	2.70 (*s*)	2.85 (*s*)	2.87 (*s*)
Ar–CH_2–CH–O–	—	—	—	—	—
Ar–$(CH_2)_2$CO–	—	—	—	—	—
Isoprene unit					
H-1	—	3.63–3.87 (*m*)	3.25 (*br d*, *J* = 6 Hz)	3.30 (*d*, *J* = 6 Hz)	6.52 (*d*, *J* = 16 Hz)
H-2	—	2.60 (*m*)	5.05 (*br t*, *J* = 6 Hz)	5.05 (*br t*, *J* = 6 Hz)	6.15 (*d*, *J* = 16 Hz)
H-4	—	1.25 (*s*)	1.63 (*br s*)	1.68 (*br s*)	1.42 (*s*)
H-5	—	1.30 (*s*)	1.70 (*br s*)	1.75 (*br s*)	
Ar–OH	—	—	6.10 (*br s*)	—	—
Ar–OMe	3.68 (*s*)	—	—	3.77 (*s*)	3.77 (*s*)
	3.72 (*s*)	—	—	3.84 (*s*)	3.78 (*s*)
				3.89 (*s*)	3.85 (*s*)

*Chemical shifts in δ values.
†The signals of three benzylic methylenes were overlapped.

91 (83%)], hydroxyl group (3420 cm^{-1}), four equivalent methylene protons [δ 2.70 (4H, *s*)], characteristic of benzylic methylenes, one proton [δ 6.27 (1H, *s*)] on the aromatic ring, a vinylic methyl group [δ 1.65 (3H, *s*)] and an exocyclic methylene group [δ 4.80, 4.97 (each 1H, *br s*)]. Methylation of **18** with methyl iodide gave a dimethyl ether (**20**), together with a monomethyl ether (**19**), showing that one of the three oxygen atoms of **18** might be an ether link. The ^{1}H NMR spectrum (Table 1) of **18** also showed the presence of additional benzylic methylene protons coupled with a proton on a carbon bearing an ether oxygen, whose assignment was confirmed by spin decoupling experiments. Thus perrottetin D is represented by structure **18**, except for the configuration of a isopropenyl group. Perrottetin D may be biogenetically formed from the co-occurring perrottetin A by the cyclization of a dimethylallyl group with a phenolic hydroxyl group.

2′ - 6′ - Dihydroxy - 3′ - (3 - methyl - 2 - butenyl) - 4′ - methoxydihydrochalcone (**31**)

A minor component (**31**), $C_{21}H_{24}O_4$ (M$^+$ 340), isolated from *R. perrottetii* showed the presence of a conjugated carbonyl group (1650 cm^{-1}), a chelated hydroxyl group [δ 11.35 (1H, *s*)], a free hydroxyl group [δ 6.05 (1H, *br s*) disappearing on addition of D_2O], a dimethylallyl group, one aromatic proton, an unsubstituted benzene ring, one methoxyl group and two methylenes located between a benzene ring and a carbonyl group, indicating the presence of a 6′-hydroxydihydrochalcone with an unsubstituted benzene ring. The arrangement of the unchelated hydroxyl group, the methoxyl group and the dimethylallyl group was confirmed by acid treatment of **31** to give a 2, 2-dimethylchromane (**39**), [mp 111–113°; $C_{21}H_{24}O_4$ (M$^+$ 340); δ 1.29 (6H, *s*)], indicating that the hydroxyl group (C-2′) is *ortho* to the isoprene chain (C-3′). The UV spectrum of **31** showed the absorption bands at 267.5 and 310 nm and no bathochromic shift occurred upon addition of sodium acetate, indicating that the methoxyl group is located at C-5′ or C-4′. Thus structure **31** can be advanced for what is a new isoprenylated dihydrochalcone. The related dihydrochalcone (**32**) with a dihydro-oxepin skeleton has been isolated from *R. variabilis* [23].

Lunularin dimethyl ether

3, 4′-Dimethoxy-bibenzyl (**3**), [$C_{16}H_{18}O_2$ (M$^+$ 242)], was obtained from *R. complanata* as an oil. The ^{1}H NMR spectrum (Table 1) exhibited the presence of two methoxyl groups, two equivalent benzylic methylenes, four aromatic protons and four protons on *para*-substituted benzene rings. On the basis of the ^{1}H NMR spectrum and the fragment ion at *m/z* 121 (100%, $C_7H_7OMe^+$), its structure could be assigned as **3**. In fact, spectral and chromatographic data of **3** are identical to those of authentic lunularin dimethyl ether.

3, 5-Dihydroxy-4-(2, 3-epoxy-3-methylbutyl)bibenzyl

The spectral data of compound **7**, $C_{19}H_{22}O_3$ (M$^+$ 298), isolated from *R. complanata* were similar to those of the co-occurring isoprenyl bibenzyl (**5**). The analysis of the fragment ions at *m/z* 91 (50%) and *m/z* 227 [M − 71]$^+$ (100%) and ^{1}H NMR spectrum (Table 1) suggested that **7** might be the epoxide of **5**. Treatment of **5** with *m*-CPBA afforded a monoepoxide whose spectral data were identical to those of the natural epoxide (**7**). Thus, the structure of the natural epoxide was formulated as **7**, in which the configuration of the epoxide remains to be clarified.

Radulanin H

From the most polar fraction of the crude extract of *R. complanata*, the acidic bibenzyl (**25**), mp 122–

)ibenzyls and their derivatives

14	18	20	25	30	31
7.15 (*s*)	7.08 (*s*)	7.15 (*s*)	7.15 (*s*)	7.22 (*s*)	7.20 (*s*)
6.37 (*s*)	6.27 (*s*)	6.15 (*s*)	6.40 (*s*)	6.36 (*d*, J = 0.8 Hz)	6.30 (*s*)
2.83 (*s*)	2.70 (*s*)	2.78 (*s*)†	2.98 (*m*)	—	—
—	—	—	—	3.11 (*dd*, J = 14.2, 6.2 Hz)	
—	—	—	—	3.23 (*dd*, J = 14.2, 7.0 Hz)	—
—	—	—	—	5.62 (*ddd*, J = 7.0, 6.2, 0.8 Hz)	2.63–3.17 (*m*)
2.53 (*m*)	2.77 (*d*, J = 8 Hz)	2.78†	3.53 (*br s*)	3.44 (*br dq*, J = 5.6, 1.3 Hz)	3.32 (*br d*, J = 6 Hz)
1.80 (*m*)	5.06 (*t*, J = 8 Hz)	5.10 (*t*, J = 8 Hz)	5.68 (*br t*, J = 7 Hz)	5.64 (*br t*, J = 5.6 Hz)	5.05 (*m*)
	4.80 (*br s*)	4.83 (*br s*)	4.47 (*br s*)	4.45 (*m*)	1.70 (*br s*)
1.28 (*s*)	4.97 (*br s*)	5.00 (*br s*)			
	1.65 (*br s*)	1.70 (*br s*)	1.62 (*br s*)	1.57 (*s*)	1.75 (*br s*)
—	5.90 (*br s*)	—	—	7.88 (*s*)	6.05 (*br s*)
					11.35 (*s*)
3.75 (*s*)	—	3.77 (*s*)	—	—	3.93 (*s*)
3.82 (*s*)	—	3.92 (*s*)	—	—	—
3.85 (*s*)					

123°; $C_{20}H_{20}O_4$ (M^+ 324), was obtained as colorless crystals, together with the previously known acidic bibenzyl (**29**). The presence of the chelated carboxylic acid was confirmed by the intense IR absorption band at 1640 cm^{-1}. The ^1H NMR spectrum (Table 1) contained the signals of an unsubstituted benzylic group, one aromatic proton and two benzylic methylenes. The presence of the dihydro-oxepin skeleton of **25** was also confirmed by the ^1H NMR signals assignable to a vinylic proton, a vinylic methyl, one methylene located between a double bond and an aromatic ring, and one methylene between an ether and a double bond. The above spectral data coupled with the molecular formula suggest that **25** is the acidic bibenzyl with a cyclic isoprene unit which could be formed from the co-occurring acidic isoprenyl bibenzyl (**15**). Further evidence for structure **25** for the new bibenzyl was obtained as follows. Methylation of **25** gave a methyl ester, which on oxidation with *m*-CPBA afforded a monoepoxide whose spectral data were identical to those of the methyl ester (**27**) prepared from the co-occurring acidic bibenzyl (**26**) [21].

Radulanolide

The new bibenzyl (**30**), mp 103–104°; $C_{20}H_{18}O_4$ (M^+ 322), was obtained from *R. complanata* as needles. The UV and IR spectra showed the presence of a hydroxyl group (3450 cm^{-1}) and aromatic ring (1610, 1495 cm^{-1}; UV λ_{max} nm: 216, 250. The ^1H NMR spectrum (Table 1) of **30** showed the presence of one unsubstituted benzene ring, one proton on an aromatic ring, one benzylic methylene [δ 3.23 (1H, *dd*, J = 14.2, 7.0 Hz), 3.11 (1H, *dd*, J = 14.2, 6.2 Hz)] coupled with one methine [δ 5.62 (1H, *ddd*, J = 7.0, 6.2, 0.8 Hz)] bearing an ether oxygen, one chelated hydroxyl group [δ 7.88 (1H, *s*)] and a cyclic isoprene unit, a vinylic methyl, a vinylic proton, one methylene located between double bond and benzene ring, and an additional methylene between an ether oxygen and a double bond. The above spectral evidence coupled with the molecular formula indicated the presence of a γ- or δ-lactone in radulanolide. The presence of a 7-hydroxyphthalide group was confirmed by the intense IR absorption band at 1735 cm^{-1} in a chloroform solution of **30** [25]. As unchelated phthalides and chelated- or unchelated dihydroisocoumarins show the characteristic IR bands listed in Table 2, their partial structures could not be present in radulanolide (**30**). From the above evidence, the structure of radulanolide might be formulated as **30**. This structure was further supported by the ^1H NMR spectrum (400 MHz) and spin decoupling experiments. Irradiation of a double double doublet signal at δ 5.62 (H-8) caused the broad doublet at δ 6.36 (H-6) to collapse to a singlet (41% increase in intensity). Irradiation of the signal at δ 7.22 (5H on A-ring) showed a 21% increase in intensity of two double doublet signals at δ 3.11 and 3.23 (H-9) and the signal at δ 5.62 (H-8) was unchanged. Thus, the radulanolide was represented as **30**, except for the stereochemistry of H-8.

Ent-2,3-*dihydroxycuparene*

A new sesquiterpene phenol (**43**), mp 124–125°, $C_{15}H_{22}O_2$ (M^+ 234), was obtained from *R. perrottetii* as a minor component, together with the previously known ent-cuparene (**44**). The spectral data showed the presence of a hydroxyl group (3600, 3500 cm^{-1}), an aromatic group (1620, 1600, 1505 cm^{-1}), three tertiary methyl groups (δ 0.75, 1.17, 1.40) and one methyl (δ 2.20) on a benzene ring. The presence of the *ortho* protons on the benzene ring was confirmed by two doublet signals at δ 6.82 (1H, *d*, J = 8 Hz) and δ 6.48 (1H, *d*, J = 8 Hz). The above spectral data resembled those of cuparene (**44**) and 2-hydroxy-

Table 2. IR absorption bands of lactone carbonyl group of phthalides and isocoumarins

	OH-bonded CO	Non-OH-bonded CO
Phthalides	1734–1738 cm^{-1} [25]	1754–1764 cm^{-1} [25] 1763 [26]
Isocoumarins	1661 [28] 1645 [29] 1650 [30]	1715 [27] 1690 [30]

cuparene (**45**), indicating that **43** might be a cuparene-type sesquiterpene with *ortho* hydroxyl groups. Further confirmation of the *ortho* position of two hydroxyl groups was obtained by the bathochromic shift (+9 nm) of the UV maximum (λ_{max} 277 nm) of **43**, after addition of boric acid. Thus, the structure of the new cuparene-type sesquiterpene phenol can be represented by **43**. The fragment ions at *m/z* 151 $[C_9H_{11}O_2]^+$ (100) and *m/z* 164 $[C_{10}H_{12}O_2]^+$ (80) [32] of **43** further supported the above structure. The absolute configuration of **43** was established by the negative optical rotation and its co-occurrence with (−)-cuparene (**44**) [24, 31].

Table 3 summarizes the distribution of the bibenzyl derivatives and cuparene-type sesquiterpenoids found in those *Radula* species analysed so far. All the species produce bibenzyl derivatives. *R. buccinifera*, *R. complanata*, *R. japonica*, *R. tokiensis* and *R. variabilis* commonly elaborate radulanin A (**21**) and radulanin C (**22**) with a seven-membered heterocyclic ring and the latter four species all produce radulanin E (**24**). Among radulanin-producing species, *R. buccinifera* is chemically rather similar to *R. complanata*, since the two species commonly elaborate 3-methoxybibenzyl (**1**), lunulatin dimethyl ether (**3**) and 3,5-dihydroxy-4-(3-methyl-2-butenyl)-bibenzyl (**5**). *R. buccinifera*, *R. complanata*, *R. japonica*, *R. tokiensis* and *R. variabilis* are referred to the section *Radula* (subgenus *Radula*, series *Radula*) [18]. The above chemical results agree with the morphological classification of *Radula* species (section *Radula*). *R. perrottetii* and *R. oyamensis* are chemically different from the species of the section *Radula*. *R. perrottetii* is also quite distinct from *R. oyamensis*. The former species mainly produces 2, 3, 5-trihydroxy-4-(3-methyl-2-butenyl)bibenzyl (perrottetin A) (**9**), and its derivatives (**11**, **13**, and **18**) and the latter elaborates 3-hydroxy-4-(3-methyl-2-butenyl)bibenzyl (**33**) as the major component. Thus, *R. perrottetii* contains more oxygenated bibenzyls and *R. oyamensis* more reduced bibenzyls, when compared with the prenyl bibenzyls found in the species of *Radula* section. Morphologically, *R. perrottetii* is referred to in the section *Cladoradula* (subgenus *Cladoradula*). The above chemical data also support the morphological classification of *R. perrottetii*; *R. oyamensis* belonging to the section *Radula* is referred to the series *Saccatae*, but not to the series *Radula*. This morphological separation from the section *Radula* species is also supported by the chemical difference between *R. oyamensis* and the other species in section *Radula* (series *Radula*).

We have now analysed more than 250 species of the liverworts; the presence of bibenzyl derivatives with a prenyl group or a dihydro-oxepin skeleton has only been noted in *Radula* species. Thus, these benzyls are significant chemosystematic markers for the Radulaceae (Jungermanniales). It is interesting that similar bibenzyls (**40–42**) to the bibenzyl (**16**) found in *Radula* species have been isolated from Composiate [32] and Leguminosae [33, 34].

Lopès [19] reported that *R. complanata* caused allergenic contact dermatitis. During the course of the investigation of the allergenic nature of *R. complanata*, we isolated (+)-frullanolide (**46**), a potent allergenic agent from the crude extract of *R. complanata*. The sesquiterpene lactone (**46**) is the major component of the liverwort *Frullania dilatata* [35, 36]. European *R. complanata* grows on some birch trees often with *F. dilatata*. Careful examination under the binocular microscope of *R. complanata* collected in France showed that a small piece of *F. dilatata* was mixed with *R. complanata*. Thus, (+)-frullanolide (**46**) isolated from *R. complanata* originated from *F. dilatata* and *Radula* species do not in fact have allergenic properties.

Recently, Mitscher *et al.* [33] reported that the bibenzyl derivatives (**40**, **41**) isolated from Leguminosae and a decarboxylated product (**6**) of **40** showed antimicrobial activity against *Streptoccocus aureus* (3–6.25 μg/ml). The naturally occurring bibenzyls (**5**, **9**, **10**) and chemically modified bibenzyls (**20**, **38**) were tested against 12 species of micro-organisms. The prenyl bibenzyls (**5**, **9**, **10**) showed antimicrobial activity against *S. aureus* (20–30 μg/ml). The other compounds did not show significant activity against the micro-organisms tested.

Lunularic acid (**2**), which is promoter of dormancy and plant growth inhibitor [37] is widely distributed in the liverworts [38, 39]. The leaves of some *Radula* species fall away easily from their stems during collection, on washing with water or on air-drying. It is assumed that this phenomenon may be caused by some endogeneous acidic bibenzyl derivatives such as (**15**, **25**, **26**, **29**) which are structurally close to lunularic acid (**2**).

EXPERIMENTAL

The solvents used for spectral determination were TMS–$CDCl_3$ [^{1}H NMR (60, 90, 400 MHz], $CHCl_3$ ($[\alpha]_D$ and IR) unless otherwise stated, 95% EtOH (UV). GC/MS, EI/MS (DI), TLC and GC were carried out as indicated earlier [13, 23].

Plant materials. R. buccinifera (Hook. f. et Tayl.) Tayl., *R. complanata* (L.) Dum., *R. oyamensis* Steph. and *R. perrottetii* Gott. identified by Dr. K. Yamada were deposited

Table 3. Bibenzyl derivatives and sesquiterpenoids of some *Radula* species

Species	Compounds detected: Bibenzyls																												Sesquiterpenoids		
	1	**3**	**4**	**5**	**6**	**7**	**9**	**11**	**13**	**15**	**16**	**17**	**18**	**21**	**22**	**23**	**24**	**25**	**26**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**43**	**44**	**45**
Radula buccinifera	+*	+	—	+*	—	—	—	—	—	—	—	—	—	+	+	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	+	—
R. complanata [20, 21]	+*	+	—	+	+	+	—	—	—	+	+	—	—	+	+	—	+	+	+	—	—	+	—	—	—	—	—	—	—	—	+	—
R. japonica [24]	—	—	—	—	—	—	—	—	—	—	—	—	—	+*	+	—	+	—	—	—	—	—	—	—	—	—	—	—	—	—	+	+
R. oyamensis	—	—	—	—	+	—	—	—	—	+	—	—	—	—	—	—	—	—	—	—	—	—	—	—	+*	+	+	+	+	—	+	—
R. perrottetii	—	—	—	+	—	—	+*	+	+	—	—	—	+	—	—	—	—	—	—	—	—	—	+	—	—	—	—	—	—	+	+	—
R. tokiensis [24]	—	—	—	—	+	—	—	—	—	—	+	—	—	+*	+	+	+	—	—	—	—	—	—	—	—	—	—	—	—	—	+	+
R. variabilis [22, 23]	—	—	+†	—	—	—	—	—	—	—	+*	+	—	+	+	—	+	—	—	+	+	—	—	+	—	—	—	—	—	—	—	—

*The major component.

†Unpublished result in ref. [23].

1: 3-Methoxybibenzyl; **3**: lunularin dimethyl ether; **4**: 3-hydroxy-4, 5-methylenedioxybibenzyl; **5**: 3, 5-dihydroxy-4-(3-methyl-2-butenyl)bibenzyl; **6**: 3-hydroxy-5-methoxy-4-(3-methyl-2-butenyl)bibenzyl; **7**: 3, 5-dihydroxy-4-(2, 3-epoxy-3-methylbutyl)bibenzyl; **9**: perrottetin A; **11**: perrottetin B; **13**: perrottetin C; **15**: 2-carboxy-3, 5-dihydroxy-4-(3-methyl-2-butenyl)bibenzyl; **16**: 3, 5-dihydroxy-4-(3, 7-dimethyl-2, 6-octadienyl)bibenzyl; **17**: 3, 5, 4′-trihydroxy-4-(3, 7-dimethyl-2, 6-octadienyl)bibenzyl; **18**: perrottetin D; **21**: radulanin A; **22**: radulanin C; **23**: radulanin B; **24**: radulanin E; **25**: radulanin H; **26**: radulanin F; **28**: radulanin D; **29**: radulanin G; **30**: radulanolide; **31**: 2′, 6′-dihydroxy-3′-(3-methyl-2-butenyl)-4′-methoxydihydrochalcone; **32**: variabilin; **33**: 3-hydroxy-4-(3-methyl-2-butenyl)bibenzyl; **34**: 3-hydroxy-4-(3-methyl-2-butenyl)-4′-methoxybibenzyl; **35**: 3-methoxy-4-(3-methyl-2-butenyl)-4′-hydroxybibenzyl; **36**: 3-hydroxy-4-isopropenylbibenzyl; **37**: 3, 5-dihydroxy-4-(3, 7-dimethyl-3, 7-octadienyl)bibenzyl; **43**: ent-2, 3-dihydroxycuparene; **44**: ent-cuparene; **45**: ent-2-hydroxycuparene.

in the Herbarium of the Institute of Pharmacognosy, Tokushima Bunri University. The plant materials were collected in the following locations and months. *R. buccinifera*: Blue Mountain, New South Wales, Australia, Aug. 1981; *R. complanata*: Dordogne, France, Apr. 1978; *R. oyamensis*: Ise-shi, Mie, Japan, Dec. 1980; and *R. perrottetii*: Kito, Nakagun, Tokushima, Japan, Sept. 1980.

Extraction and isolation. Powdered, air-dried material (1 g) was extracted with Et_2O (20 ml) for 10 days. The green extracts were filtered through a short glass column packed with Si gel. The filtrates after solvent removal were monitored by TLC and GC, and then directly analysed by GC/MS equipped with a computer. The components obtained by GC/MS were identified by direct comparison of the mass spectra with those of authentic samples. The remaining materials were also extracted with Et_2O for 2 months and then re-extracted with MeOH for 1 month. The crude extracts from *R. perrottetii* were combined and the viscous oil (5.54 g) was directly chromatographed on Si gel using a C_6H_6–EtOAc gradient and then divided into six fractions. The first fraction (C_6H_6 100%) gave sesquiterpenes (450 mg) from which (−)-cuparene (**44**) (30 mg) was isolated by prep. GC. The second fraction (C_6H_6–EtOAc, 19:1) (400 mg) was rechromatographed on Sephadex LH-20 using $CHCl_3$–MeOH (1:1) and divided into two fractions. The first fraction was purified by prep. TLC to afford ent-2, 3-dihydroxycuparene (**43**) (9 mg) and an unidentified bibenzyl (1.3 mg) [M^+ 238, *m/z* 147 (100%)]. Compound **43**: mp 124–125°; $[\alpha]_D$ −20.9° (*c* 2.4); UV λ_{max} nm (log ϵ): 209.5 (4.13), 277 (3.07); UV λ_{max}^{+H,BO^-} nm (log ϵ): 210.5 (4.20), 286 (3.23); IR ν_{max} cm^{-1}: 3600, 3500 (OH), 1620, 1505, 1455 (aromatic ring), 1370, 1360 (gem-dimethyl), 1290, 1140; ^1H NMR δ: 0.75, 1.17, 1.40, 2.20 (each 3H, *s*), 5.50 (2H, OH), 6.48, 6.82 (each, 1H, *d*, *J* = 8 Hz); MS *m/z* (rel. int.) 234 $[M]^+$ ($C_{15}H_{22}O_2$), (56), 164 $[C_{10}H_{12}O_2]^+$ (80), 152 $[C_9H_{11}O_2]^+$ (51), 151 $[C_9H_{11}O_2]^+$ (100), 147 (36), 137 (28). The second fraction was rechromatographed on Si gel using C_6H_6 to give a prenyldihydrochalcone (**31**) (25 mg). UV λ_{max} nm (log ϵ): 217.5 (4.66), 267.5 (4.15), 310 (3.86); UV λ_{max}^{+NaOAc} nm: no bathchromic shift; IR ν_{max} cm^{-1}: 3400 (OH), 1650 (OH-bonded CO), 1600, 1495 (aromatic ring), 1320, 1255, 1030, 750, 695; MS *m/z* (rel. int.): 340 $[M]^+$ ($C_{21}H_{24}O_4$) (43), 308 $[M-MeOH]^+$ (43), 280 $[M-MeOH-CO]^+$ (72), 265 (100), 253 (43), 252 (33), 217 (39), 189 (57), 175 (64), 174 (54), 91 $[C_7H_7]^+$ (99).

The third fraction (C_6H_6–EtOAc, 9:1) (1.93 g) was rechromatographed on Sephadex LH-20 ($CHCl_3$–MeOH, 1:1) and divided into two fractions. The first fraction was further chromatographed on Si gel ($CHCl_3$–MeOH, 49:1) to give perrottetin D (**18**) (400 mg) and 3, 5-dihydroxy-4-(3-methyl-2-butenyl)bibenzyl (**5**) (320 mg) [21]. Perrottetin D (**18**): UV λ_{max} nm (log ϵ): 216 (4.71), 275 (3.61); IR ν_{max}^{liquid} cm^{-1}: 3420 (OH), 1610, 1520, 1490 (aromatic ring), 1038, 750, 700; MS *m/z* (rel. int.): 296 $[M]^+$ ($C_{19}H_{20}O_3$) (91), 281 $[M-15]^+$ (49), 205 $[M-C_7H_7]^+$ (100), 191 (28), 187 (47), 177 (27), 163 (38), 159 (36), 91 (83). From the second fraction perrottetin A (**9**) (380 mg) was obtained as colorless needles, mp 99–100°; UV λ_{max} nm (log ϵ): 211 (4.22), 268 (2.91); IR ν_{max} cm^{-1}: 3420 (OH), 1600, 1510, 1505 (aromatic ring), 1077, 750, 695; MS *m/z* (rel. int.): 298 $[M]^+$ ($C_{19}H_{22}O_3$) (35), 281 $[M-17]^+$ (6), 207 $[M-91]^+$ (100), 165 (39), 91 (57).

The fourth fraction (C_6H_6–EtOAc, 4:1) was rechromatographed on Sephadex LH-20 ($CHCl_3$–MeOH, 1:1) to give perrottetin A (350 mg) and unidentified bibenzyl, named perrottetin E (M^+ 426) (87 mg). The same fraction (390 mg) was methylated with MeI in the presence of dry K_2CO_3 and the crude product was chromatographed on Si gel (*n*-hexane–EtOAc gradient) to give perrottetin A trimethyl ether (**10**) (220 mg), perrottetin E trimethyl ether (70 mg) and perrottetin B trimethyl ether (**12**) (4.7 mg). The compound (**12**): UV λ_{max} nm (log ϵ): 219 (4.34), 257.5 (3.94); IR ν_{max} cm^{-1}: 3600–3300 (OH), 1595, 1490 (aromatic ring), 1405, 1320, 1235, 1195, 1127; MS *m/z* (rel. int.): 356 $[M]^+$ ($C_{22}H_{28}O_4$) (20), 338 $[M-18]^+$ (29), 283 (11), 265 $[M-91]^+$ (6), 248 $[M-18-91]^+$ (34), 233 $[M-32-91]^+$ (100), 216 (60), 207 (31), 202 (32), 192 (48), 105 (47), 91 (66), 59 (21), 43 (23).

The fifth fraction (C_6H_6–EtOAc, 1:1) (300 mg) and the sixth fraction (2:3) (610 mg) were methylated with MeI, respectively. The two methylated products were monitored on TLC, combined and then chromatographed on Si gel (C_6H_6–EtOAc gradient) to give perrottetin C trimethyl ether (**14**) (54 mg) and an additional unidentified bibenzyl named perrottetin F tetramethyl ether (M^+ 498) (132 mg). Compound **14**: UV λ_{max} nm (log ϵ): 215.5 (4.11), 230 sh (3.88), 275 (3.08); IR ν_{max} cm^{-1}: 3600–3300 (OH), 1600, 1580, 1495, 1405, 1320, 1235, 1195, 1115, 1065, 1045, 985, 910, 835, 745, 695; MS *m/z* (rel. int.): 358 $[M]^+$ ($C_{22}H_{30}O_4$) (63), 340 $[M-18]^+$ (5), 299 (4), 285 $[M-18-55]^+$ (41), 249 $[M-91]^+$ (100), 196 (13), 181 (22), 151 (12), 105 (14), 91 (56), 59 (16).

The crude extract (35.03 g) of *R. complanata* was chromatographed on Si gel (*n*-hexane–EtOAc gradient) and divided into six fractions. The first fraction (*n*-hexane 100%) (1.10 g) contained sesquiterpene mixtures in which cuparene (**44**) was detected by GC/MS. The second fraction (*n*-hexane–EtOAc, 19:1–9:1) (7.74 g) was rechromatographed on Si gel impregnated with $AgNO_3$ (*n*-hexane–EtOAc gradient) to afford 3-methoxybibenzyl (**1**) (3.60 g) [20, 21], 3, 4′-dimethoxybibenzyl (**3**) (120 mg) and fatty acid methyl esters (90 mg). The compound (**3**): UV λ_{max} nm (log ϵ): 206 (4.15), 225 sh (3.96), 274 (3.22), 279 (3.21); IR ν_{max} cm^{-1}: 1595, 1510, 1240, 1140, 1145, 1032, 688; MS *m/z* (rel. int.): 242 $[M]^+$ ($C_{16}H_{18}O_2$) (3.5), 151 (31), 121 (100), 91 (16). ^1H NMR spectrum (Table 1) and the above spectral data were in good agreement with those of the authentic lunularin dimethyl ether (**3**). The third fraction (*n*-hexane–EtOAc, 17:3–7:3) (7.24 g) was rechromatographed on Sephadex LH-20 ($CHCl_3$–MeOH, 1:1) and divided into five fractions. From the second fraction phytosterol (750 mg) was obtained. The third fraction (2.00 g) was rechromatographed on Si gel (*n*-hexane–EtOAc gradient) to give (+)-frullanolide (**46**) (31 mg) [35, 36], radulanolide (**30**) (15 mg) and phytol (45 mg). Compound **30**: mp 103–104°; UV λ_{max} nm (log ϵ): 216 (4.50), 250 (3.91), 300 (3.58); IR ν_{max} cm^{-1}: 3450 (OH), 1735 (γ-lactone), 1635 (C=C), 1610, 1495, 1335, 1240, 1130, 1080, 695; high MS *m/z* (rel. int.): 322 $[M]^+$ ($C_{20}H_{18}O_4$) (found 322.1180, calc. 322.1205, 21), 247 (13), 231 $[M-91]^+$ ($C_{13}H_{11}O_4$) (found 231.0642, calc. 231.0657, 100), 189 (8), 160 (5), 115 (6), 91 (34), 65 (14), 39 (16).

The fourth fraction (*n*-hexane–EtOAc, 3:2–2:3) (11.29 g) was rechromatographed on Sephadex LH-20 ($CHCl_3$–MeOH, 1:1) and divided into four fractions. The second fraction (2.91 g) was rechromatographed on Sephadex LH-20 (MeOH) to give a prenyl bibenzyl (**16**) (185 mg) [23] and a new acidic bibenzyl, radulanin H (**25**) (350 mg), mp 122–123°; UV λ_{max} nm (log ϵ): 220 (4.48), 260 (3.84), 310 (3.65); IR ν_{max} cm^{-1}: 3600, 3500 (OH), 1640 (OH-bonded COOH), 1615, 1580, 1500, 1260, 1175, 700; MS *m/z* (rel. int.): 324 $[M]^+$ ($C_{20}H_{20}O_4$) (9), 306 $[M-18]^+$ (11), 280 $[M-CO_2]^+$ (52), 265 (59), 189 (55), 174 (33), 121 (30), 105 (16), 91 (100). The third fraction (2.86 g) was rechromatographed on Sephadex LH-20 ($CHCl_3$–MeOH, 1:1), followed by purification on TLC to afford a new epoxybibenzyl (**7**) (6 mg), together with the previously known bibenzyl (**5**) (112 mg) and **15** (38 mg) [21].

Compound **7**: UV λ_{max} nm (log ϵ): 209 (4.26), 227.5 sh (3.84), 280 (3.34); IR ν_{max} cm^{-1}: 3600, 3350 (OH), 1620, 1600, 1490, 1385, 1370, 1132, 1062, 1010, 845, 695; MS *m/z* (rel. int.): 298 $[M]^+$ ($C_{19}H_{22}O_3$) (71), 227 $[M-C_4H_7O]^+$ (100), 149 (23), 91 (58), 59 (25).

The crude extract from *R. buccinifera* showed the presence of three major and eight minor peaks on GC. The MS and retention times of the major peaks were identical to those of the authentic bibenzyls (**1**, **5** and **21**). Among the minor components, the bibenzyls (**3** and **22**) and cuparene (**44**) were identified through agreement of the MS and retention times with those of the authentic samples.

The crude extract of *R. oyamensis* was also analysed by GC and GC/MS and 13 bibenzyls and cuparene (**44**) were detected. Among the bibenzyls, the previously known compounds (**6**, **16**) were confirmed through the identity of the MS and retention times with authentic samples. The other bibenzyls (**33–37**) were assigned by the following molecular ion and the fragment ions, and by comparison of the MS of the authentic or co-occurring bibnezyls. The major component (**33**): MS *m/z* (rel. int.): 266 $[M]^+$ ($C_{19}H_{22}O$) (52), 211 $[M-C_4H_7]^+$ (30), 175 $[M-91]^+$ (100), 90 (90). (**34**): 296 $[M]^+$ ($C_{20}H_{24}O_2$) (88), 241 $[M-C_4H_7]^+$ (8), 189 $[M-107]^+$ (76), 107 (100). (**35**): 296 $[M]^+$ ($C_{20}H_{24}O_2$) (80), 241 $[M-C_4H_7]^+$ (9), 175 $[M-121]^+$ (100). (**36**): 282 $[M]^+$ ($C_{19}H_{22}O_2$) (29), 277 $[M-C_4H_7]^+$ (5), 175 $[M-107]^+$ (25), 107 (100). (**37**): 350 $[M]^+$ ($C_{24}H_{30}O_2$) (100), 265 (56), 259 $[M-91]^+$ (30), 227 $[M-C_9H_{15}]^+$ (75), 91 (59), 55 $[C_4H_7]^+$ (20). The retention times of the bibenzyls (**16**, **37**) were close and their fragmentation patterns of MS were identical except for the relative intensity of each fragment ion. The terminal isopropenyl group of **37** was assigned by the presence of the fragment ion at *m/z* 55.

Methylation of **9**. Compound **9** (70 mg) in Me_2CO was treated with MeI (1 ml) K_2CO_3 for 12 hr. Work-up as usual gave the trimethyl ether (**10**) (72 mg). UV λ_{max} nm (log ϵ): 214 (4.39), 230 sh (4.06), 277.5 (3.16); IR ν_{max} cm^{-1}: 1600, 1495, 1405, 1240, 1195, 1120, 1065, 1040, 750, 695; MS *m/z* (rel. int.): 340 $[M]^+$ ($C_{22}H_{28}O_3$) (56), 249 $[M-91]^+$ (100), 218 (21), 207 (20), 192 (18), 91 (18).

Epoxidation of **10**. To compound **10** (18 mg) in CH_2Cl_2 (1 ml) was added *m*-CPBA (20 mg) and stirred for 30 min at 0°. Work-up as usual gave the epoxide (**8**). UV λ_{max} nm (log ϵ): 213.5 (4.44), 230 sh (3.87), 280 (2.96); IR ν_{max} cm^{-1}: 1600, 1580, 1495, 1435, 1410, 1375, 1320, 1240, 1190, 1120, 1065, 1050, 990, 915, 695; ^1H NMR δ: 1.30, 1.40 (each 3H, *s*), 2.79 (3H *m*), 2.90 (4H, *s*), 3.80, 3.87, 3.90 (3H, *s*), 6.47 (1H, *s*), 7.27 (5H, *s*); MS *m/z* (rel. int.): 356 $[M]^+$ ($C_{22}H_{28}O_4$) (36), 285 $[M-71]^+$ (100), 265 $[M-91]^+$ (33), 207 (42), 195 (53), 181 (26), 91 (52), 71 (11), 43 (24).

Cyclization of **9**. Compound **9** (93 mg) in HOAc (4.3 ml) and conc. HCl (0.1 ml) was heated at 120–125° for 1 hr. Work-up gave the 2, 2-dimethylchromane derivative (**38**) (80 mg), mp 132–133°; UV λ_{max} nm (log ϵ): 217.5 (4.36), 275 (2.96); IR ν_{max} cm^{-1}: 3560 (OH), 1615, 1500, 1368, 1295, 1180, 1120, 1090, 1045, 695; ^1H NMR δ: 1.28 (6H, *s*), 1.70, 2.47 (each 2H, *t*, $J = 6$ Hz), 2.75 (4H, *s*), 5.47 (2H, *br s*, OH), 6.40 (1H, *s*), 7.17 (5H, *s*); MS *m/z* (rel. int.): 298 $[M]^+$ ($C_{19}H_{22}O_3$) (40), 227 (37), 207 $[M-91]^+$ (100), 91 (52).

Hydrogenation of **12**. Compound **12** (4 mg) in EtOAc was hydrogenated in the presence of PtO_2 to give the crude product, purified by prep. TLC to afford the dihydro-derivative (3.2 mg) which was identical to the natural perrottetin C trimethyl ether (**14**) in all respects.

Dehydration of **14**. The bibenzyl (**14**) (27 mg) obtained by the methylation of the extract of *R. perrottetii* was dissolved in C_6H_6 and treated with *p*-TsOH for 30 min at 85°. Work-up gave the dehydrated product, purified by prep. TLC to give a pure compound (20 mg) whose chromatographic behavior and spectral data were in good agreement with those of perrottetin A trimethyl ether (**10**).

Methylation of **18**. Compound **18** (197 mg) in dry Me_2CO was methylated with MeI (2 ml). The reaction mixture showed two spots on TLC and two methylated compounds, **19** (71 mg) and **20** (56 mg) were isolated by prep. TLC. **19**: UV λ_{max} nm (log ϵ): 219 (4.18), 282.5 (3.19); IR ν_{max} cm^{-1}: 3500, 3450 (OH), 1600, 1510, 1440, 1050, 750, 700; ^1H NMR δ: 1.73 (3H, *s*), 2.78 (2H, *m*), 2.85 (4H, *s*), 3.98 (3H, *s*), 4.88, 5.03 (each 1H, *br s*), 5.16 (1H, *t*, $J = 8$ Hz), 5.60 (1H, *br s*, OH), 6.35 (1H, *s*), 7.22 (5H, *s*); MS *m/z* (rel. int.): 310 $[M]^+$ ($C_{20}H_{22}O_3$) (42), 295 $[M-15]^+$ (7), 220 (14), 219 $[M-91]^+$ (100), 91 (17). (**20**); UV λ_{max} nm (log ϵ): 215.5 (4.35), 235 sh (3.85), 282 (3.03); IR ν_{max} cm^{-1}: 1620, 1600, 1505, 1230, 1115, 740, 700; ^1H NMR δ: 1.70 (3H, *s*), 2.78 (4H, *s*), 2.87 (2H, *m*), 3.77, 3.92 (each 3H, *s*), 4.83, 5.00 (each 1H, *br s*), 5.10 (1H, *t*, $J = 8$ Hz), 6.15 (1H, *s*), 7.15 (5H, *s*); MS *m/z* (rel. int.): 324 $[M]^+$, ($C_{21}H_{24}O_3$) (34), 234 (14), 233 $[M-91]^+$, 91 (13).

Cyclization of **31**. Compound **31** (10 mg) was treated in the same manner as described in the cyclization of **9** to give a 2, 2-dimethylchromane derivative (**39**) (6.6 mg), mp 111–113° UV λ_{max} nm (log ϵ): 210 (4.16), 267.5 (3.66), 310 (3.39); IR ν_{max} cm^{-1}: 1650 (OH bonded CO), 1600, 1580, 1435, 1300, 1245, 1155, 1120, 960, 850, 660; ^1H NMR δ: 1.29 (6H, *s*), 1.80 (2H, *t*, $J = 6$ Hz), 2.6–3.1 (6H, *m*), 3.92 (3H, *s*), 6.29 (1H, *s*), 7.20 (5H, *s*), 11.08 (1H, *s*, chelated OH); MS *m/z* (rel. int.): 340 $[M]^+$ ($C_{21}H_{24}O_4$) (52), 309 $[M-31]^+$ (34), 308 $[M-32]^+$ (100), 253 (69), 217 (25), 91 (73), 69 (20).

Methylation and epoxidation of **25**. Compound **25** (57 mg) in Me_2CO was methylated with MeI. The crude methylated product (52 mg) was treated with *m*-CPBA (42 mg). Work-up gave a viscous oil, purified by prep. TLC to afford the monoepoxide (43 mg), whose spectral data were identical to those of the methyl ester (**27**) of the co-occurring acidic bibenzyl (**26**) [21].

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