

Chemical Evaluation of *Betula* Species in Japan. II.¹⁾ Constituents of *Betula platyphylla* var. *japonica*

Hiroyuki FUCHINO, Soh KONISHI, Tetsuya SATOH, Akiko YAGI, Kohei SAITSU, Tatsuya TATSUMI, and Nobutoshi TANAKA*

Faculty of Pharmaceutical Sciences, Science University of Tokyo, Funakawara-machi, Ichigaya, Shinjuku-ku, Tokyo 162, Japan. Received December 5, 1995; accepted January 27, 1996

The constituents of *Betula platyphylla* var. *japonica* were identified as follows: Fresh leaves: 12-*O*-acetyl-3-*O*-malonylbetulafolienetriol, 12-*O*-acetyl-3-*O*-malonylbetulafolienetriol oxide I (= papyriferic acid), 12-*O*-acetyl-betulafolienediolone, hydroxyhopanone, caryophyllene oxide, kaempferol 3-*O*-(4-*O*-acetyl)- α -L-rhamnopyranoside*, quercetin 3-*O*-(4-*O*-acetyl)- α -L-rhamnopyranoside. Outer bark: betulin, lupeol, betulinic acid, betulone, betulin 3-*O*-caffeate, oleanolic acid, oleanolic acid 3-*O*-acetate. Inner bark: (–)-catechin, (–)-catechin 7-*O*- β -D-xylopyranoside, rhododendrin (= betuloside), aceroside VII, aceroside VIII, 1,7-bis[4-hydroxyphenyl]-3-hepten-5-one, 2-hydroxy-1,7-bis[4-hydroxyphenyl]-3-hepten-5-one*, acrogenin E, (3*R*)-3,5'-dihydroxy-4'-methoxy-3',4''-oxo-1,7-diphenyl-1-heptene*, 7 α -hydroxy- β -sitosterol, 7 β -hydroxy- β -sitosterol. Root bark: dammarediol II 3-*O*-*p*-coumarate*, dammarediol II 3-*O*-caffeate, ocotillol II 3-*O*-caffeate*, stigmast-4-ene-3-one. Spikes: caryophyllene oxide, (–)-rhododendrol (= betuligenol), 12-*O*-acetylbetulafolienetriol. The compounds with an asterisk are new.

Key words *Betula platyphylla* var. *japonica*; dammarane; lupane; diarylheptanoid; caryophyllene oxide; flavonoid

In the previous paper, we reported the constituents of *Betula ermanii* CHAM.¹⁾ For comparison, a detailed chemical examination of *B. platyphylla* SUKATCHEV var. *japonica* (MIQ.) HARA, Shirakanba in Japanese, was made. Several reports had already revealed the presence of the following compounds: betulafolienetriol (**1a**), betulafolienetriol oxide I (**2a**), dammar-24-ene-12 β ,20(*S*)-diol-3-one (**3a**), hydroxyhopanone (**4**),²⁾ 3 α ,12 β ,20(*S*),24-tetrahydroxydammar-25-ene and 3 α ,12 β ,20(*S*),25-tetrahydroxydammar-23-ene³⁾ from the nonsaponifiable fraction of the ether extracts of the leaves; betulin (**8**), lupeol (**9**), betulin 3-*O*-caffeate (**12**), betulinic acid 3-*O*-caffeate,

oleanolic acid (**13**), oleanolic acid 3-*O*-acetate (**14**), β -sitosterol, several long-chain hydrocarbons⁴⁾ and several antifungal phenolics⁵⁾ from the outer bark; salidoside, rhododendrin (= betuloside) (**17**) and platyphylloside⁶⁾ from the inner bark; ocotillol II, 3-epi-ocotillol II, sinapic acid, apigenin, hydroxyhopanone and betulafolienetriol oxide I (**2a**) from the pollen grains.⁷⁾ The examination was carried out referring to these reports, and herein the result is described.

Constituents of Fresh Leaves From the MeOH extract of fresh leaves collected in June, acylated dammarane-type triterpenes, 12-*O*-acetyl-3-*O*-malonylbetulafolienetriol

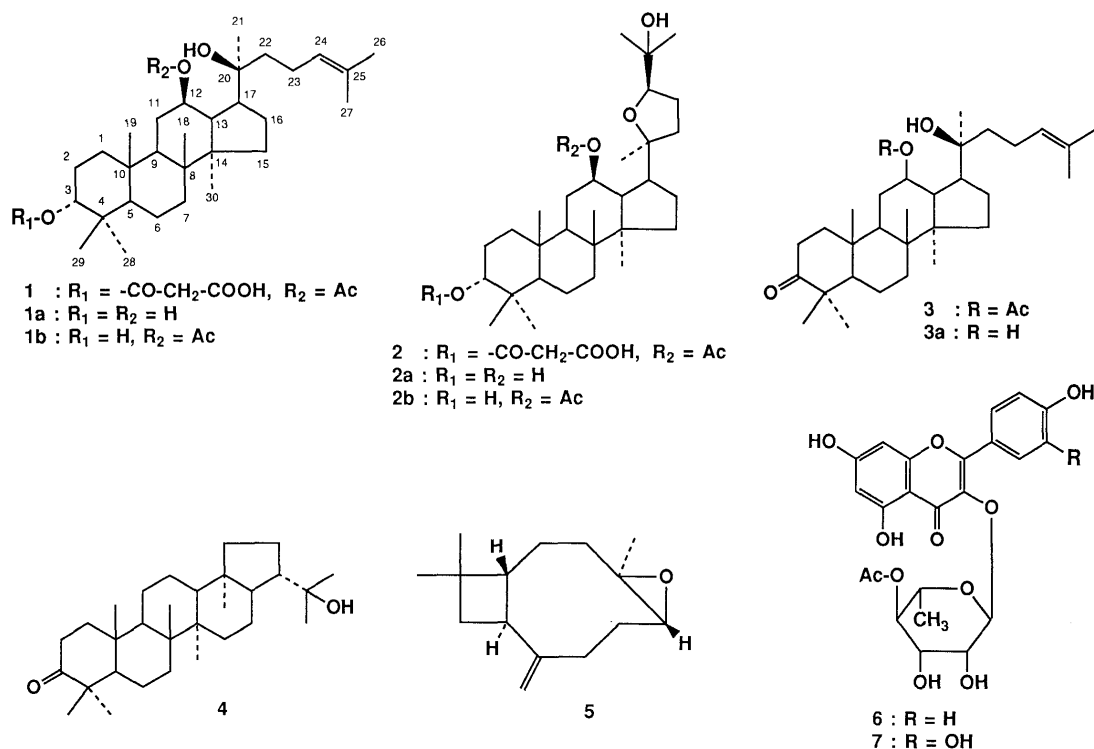


Chart 1. Constituents of Leaves

* To whom correspondence should be addressed.

(1),⁸⁾ 12-*O*-acetyl-3-*O*-malonylbetulafolienetriol oxide I (2)⁹⁾ and 12-*O*-acetylbetulafolienediolone (3)¹⁰⁾ were isolated together with hydroxyhopanone (4),²⁾ caryophyllene oxide (5),¹¹⁾ quercetin 3-*O*-(4-*O*-acetyl)- α -L-rhamnopyranoside (7)¹²⁾ and a new flavonol glycoside 6. Their structures were confirmed by comparison of the physical properties and spectral data with those previously reported (see Experimental).

The new flavonol glycoside 6, a pale yellow amorphous powder, $[\alpha]_D -138^\circ$ ($c=1.0$, MeOH), was formulated as $C_{23}H_{22}O_{11}$ by high resolution fast atom bombardment mass spectrum (HR-FAB-MS). Its 1H - and ^{13}C -NMR data were similar to those of 7 except for the B-ring signals which were characteristic of a *p*-hydroxyphenyl group (see Experimental). On alkaline methanolysis, 6 gave afzelin; thus, the structure was determined to be kaempferol 3-*O*-(4-*O*-acetyl)- α -L-rhamnopyranoside.

Compounds 1, 2 and 3 are the original forms of the previously reported compounds, 1a, 2a and 3a, respectively.²⁾ Compound 2 has been isolated from *B. papyrifera* subsp. *humilis*,^{9a)} *B. nana* subsp. *exilis*^{9b)} and *B. pendula*^{9c)} and named papyriferic acid. This compound is known as a herbivore-deterrent of the juvenile twigs of these birches. Confirming the role of this compound, the leaves collected in August contained neither 2, 1 nor 3.

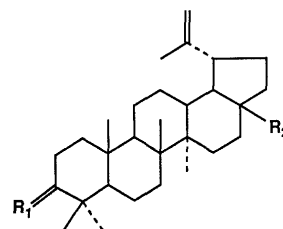
Caryophyllene oxide (5) is responsible for a noticeable and pleasant odor of the leaves.

Constituents of Outer Bark From the dried outer bark, 12% of betulin (8) was obtained together with lupeol (9),⁴⁾ betulinic acid (10),¹³⁾ betulone (11),¹⁴⁾ betulin 3-*O*-caffeate (12),⁴⁾ oleanolic acid (13),⁴⁾ oleanolic acid 3-*O*-acetate (14).⁴⁾ All the compounds have already been reported. A large amount of betulin causes the characteristic white color of the outer bark.¹⁵⁾

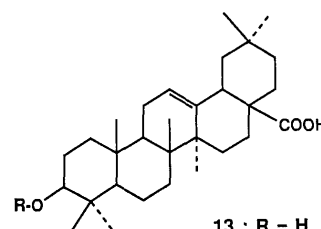
Constituents of Inner Bark From the dried inner bark collected in June, (–)-catechin (15),¹⁾ (–)-catechin 7-*O*- β -D-xylopyranoside (16),¹⁾ rhododendrin (=betuloside) (17),⁶⁾ aceroside VII (18),¹⁶⁾ aceroside VIII (19),¹⁶⁾ 1,7-

bis[4-hydroxyphenyl]-3-hepten-5-one (20),¹⁷⁾ acerogenin E (22),¹⁸⁾ 7 β -hydroxy- β -sitosterol (24),¹⁹⁾ 7 α -hydroxy- β -sitosterol (25)¹⁹⁾ and two new diarylheptanoids, 21 and 23, were isolated.

Compound 21 was found to have a molecular formula with one more oxygen atom than 20, $C_{19}H_{20}O_4$, from the HR-EI-MS. The 1H - and ^{13}C -NMR data of 21 are similar to those of 20 and revealed its structure as 1,7-bis[4-hydroxyphenyl]-3-hepten-5-one with one more hydroxyl group. The position of the hydroxyl group was easily determined to be at C-2 based on the coupling of the carbonyl proton (δ 4.39, ddt, $J=5.2, 1.5, 6.7$ Hz) with the

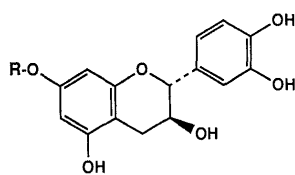


- 8 : $R_1 = \beta\text{-OH}, \alpha\text{-H}; R_2 = \text{CH}_2\text{OH}$
 9 : $R_1 = \beta\text{-OH}, \alpha\text{-H}; R_2 = \text{CH}_3$
 10 : $R_1 = \beta\text{-OH}, \alpha\text{-H}; R_2 = \text{COOH}$
 11 : $R_1 = \text{O}; R_2 = \text{CH}_2\text{OH}$
 12 : $R_1 = \beta\text{-caffeoyloxy}, \alpha\text{-H}; R_2 = \text{CH}_2\text{OH}$

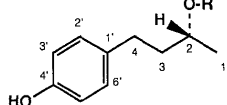


- 13 : $R = \text{H}$
 14 : $R = \text{Ac}$

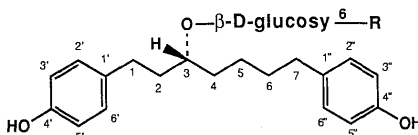
Chart 2. Constituents of Outer Bark



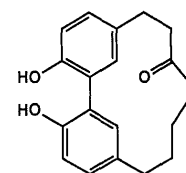
- 15 : $R = \text{H}$
 16 : $R = \beta\text{-D-xylosyl}$



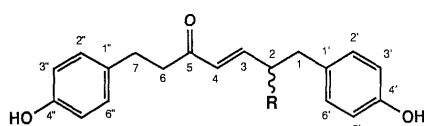
- 17 : $R = \beta\text{-D-glucosyl}$
 17a : $R = \text{H}$



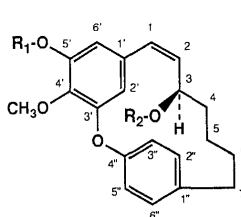
- 18 : $R = \text{H}$
 19 : $R = \beta\text{-D-apiosyl}$



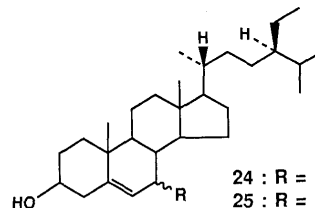
22



- 20 : $R = \text{H}$
 21 : $R = \text{OH}$



- 23 : $R_1 = R_2 = \text{H}$
 23a : $R_1 = \text{CH}_3, R_2 = \text{H}$
 23b : $R_1 = \text{CH}_3, R_2 = (S)\text{-MTPA}$
 23c : $R_1 = \text{CH}_3, R_2 = (R)\text{-MTPA}$



- 24 : $R = \text{OH}$
 25 : $R = \text{OH}$

Chart 3. Constituents of Inner Bark

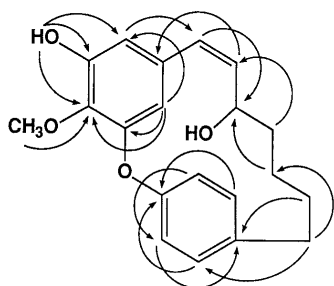


Fig. 1. Diagnostic Correlations Observed in the Long-Range ^{13}C - ^1H COSY of **23**

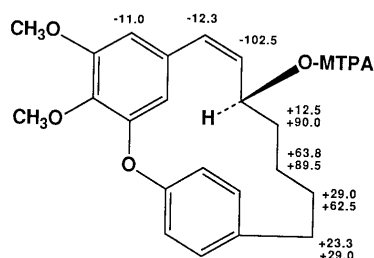


Fig. 2. Chemical Shift Differences, $\Delta\delta(\delta\text{S}-\delta\text{R})$, for the (*R*)-MTPA Ester (**23b**) and (*S*)-MTPA Ester (**23c**) in Hertz at 500 MHz

olefinic proton at C-3 (δ 6.81, dd, J = 15.9, 5.2 Hz) in the ^1H -NMR. The ^1H - ^1H and long range ^{13}C - ^1H COSY which indicated a correlation between H-2 and C-1' also confirmed the structure. As **21** showed no optical rotation, it may be a racemate resulting from enolization.

Compound **23**, a colorless crystalline powder, mp 186–187 °C from a mixture of EtOAc and *n*-hexane, $[\alpha]_{\text{D}} + 79^\circ$ (c = 1.0, CHCl_3), was formulated as $\text{C}_{20}\text{H}_{22}\text{O}_4$ from the HR-EI-MS. The ^1H -NMR spectrum showed the presence of a 3,4,5-trisubstituted phenyl group [6.38 (1H, d, J = 2.1 Hz), 5.17 (1H, d, J = 2.1 Hz)], a 4-substituted phenyl group which is restricted free rotation [7.33 (1H, dd, J = 8.2, 2.1 Hz), 7.30 (1H, dd, J = 8.2, 2.1 Hz), 7.12 (1H, dd, J = 8.2, 2.4 Hz), 7.01 (1H, dd, J = 8.2, 2.4 Hz)], an aromatic methoxy group [4.11 (3H, s)], a *cis*-substituted double bond [6.11 (1H, d, J = 11.3 Hz), 5.30 (1H, dd, J = 11.3, 8.6 Hz)] and a secondary hydroxy group [3.95 (1H, ddd, J = 11.3, 8.6, 3.1 Hz)]. By the ^1H - ^1H and long-range ^{13}C - ^1H COSY and the nuclear Overhauser effect correlation spectroscopy (NOESY), the structure of **23** was determined as 3,5'-dihydroxy-4'-methoxy-3',4'-oxo-1,7-diphenyl-1-heptene (Fig. 1). The absolute configuration at C-3 was confirmed by application of the modified Mosher method.²⁰⁾ After methylation of the phenolic hydroxy group at C-5' (**23a**), (–)-(*S*)- α -methoxy- α -(trifluoromethyl)phenylacetic (MTPA) ester (**23b**) and (+)-(*R*)-MTPA ester (**23c**) were prepared. As shown in Fig. 2, the signals due to the protons at C-1, C-2, C-2' and C-6' in the (–)-(*S*)-MTPA ester (**23b**) were observed at higher field in the ^1H -NMR spectrum than those in the (+)-(*R*)-MTPA ester (**23c**), while the signals due to the protons at C-4, C-5, C-6 and C-7 in **23b** were observed at lower field than those in **23c**. Thus, the absolute configuration at C-3 was determined as *R*.

Constituents of Root Bark From the dried root bark collected in June, two new acylated triterpenes, **26** and **28**, were isolated together with dammarendiol II 3-*O*-caffeate

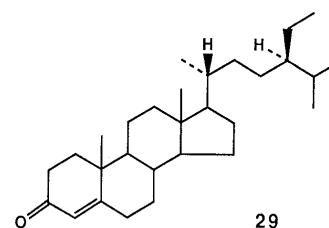
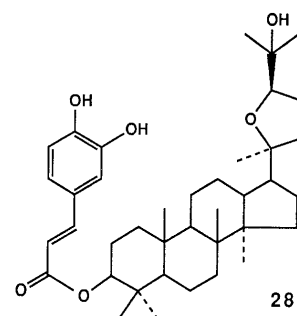
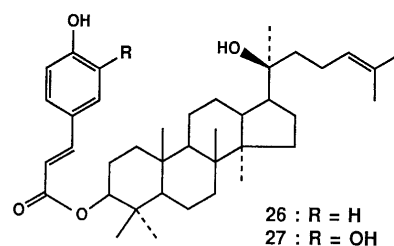


Chart 4. Constituents of Root Bark

(**27**)¹⁾ and stigmaster-4-ene-3-one (**29**).¹⁹⁾

Compound **26**, a colorless amorphous powder, $[\alpha]_{\text{D}} - 16^\circ$ (c = 0.5, MeOH), gave the molecular formula, $\text{C}_{39}\text{H}_{58}\text{O}_4$, which is one oxygen atom less than that of **27**, in the HR-FAB-MS. The ^1H - and ^{13}C -NMR spectra of **26** were similar to those of **27** except that the signals of the caffeoyl group of **27** were substituted by those of a *p*-coumaroyl group in **26**. On alkaline methanolysis, **26** gave dammarendiol II and methyl *p*-coumarate. Thus, the structure of **26** was determined as dammarendiol II 3-*O*-*p*-coumarate.

Compound **28**, a colorless crystalline powder from EtOAc, mp 222–224 °C, $[\alpha]_{\text{D}} - 10^\circ$ (c = 0.5, MeOH), gave the molecular formula, $\text{C}_{39}\text{H}_{58}\text{O}_6$, which was one oxygen atom more than that of **27**, in the HR-FAB-MS. In the ^1H - and ^{13}C -NMR spectra, **28** showed the presence of a caffeoyl group and a dammarane-type triterpene having the side chain as that of betulafolienetriol oxide I. On alkaline methanolysis, **28** gave methyl caffeate and a triterpene which was identified as ocotillol II by comparison of its physical properties and spectral data. Thus, the structure of **28** was determined as ocotillol II 3-*O*-caffeate.

It is remarkable that the dammarane-type triterpenes are present in both leaves and root bark, but not in stem bark. Those in leaves have 3 α - and 12 β -hydroxyl groups and those in root bark have 3 β -hydroxyl group and lack 12-hydroxyl group.

Constituents of Spikes From the fresh spikes collected in August, 12-*O*-acetylbetulafolienetriol (**1b**),^{8,21} caryophyllene oxide (**5**) and (–)-rhododendrol (=betuligenol) (**17a**)¹¹ were isolated. Their structures were determined by comparison of their physical properties and spectral data with those of authentic samples or those reported.

Concerning the stereochemistry of (–)-rhododendrol (**17a**), two groups have reported opposite conclusions. Inoue *et al.* concluded (*S*) for (+)-rhododendrol by comparison of the optical rotation with those of the related compounds and application of Brewster's rule,²² while Klischies & Zenk as (*S*) for (–)-rhododendrol as a result of a tritium labelled experiment.²³

In this study, we applied the glucosylation shift rule in ¹³C-NMR spectroscopy.²⁴ In case of the β-D-glucopyranoside of a secondary alcohol, rotation around the glucosidic bond is rather restricted and a conformation where an anomeric proton and a *sec*-carbinol proton are *syn* to each other is predominant.²⁵ This causes unequal β-D-glucosylation shifts of the β-carbons. Thus, the β-carbons of aglycones situated on the same side as the C-2-hydroxyl group of the glucosyl are more shielded (–3.6—–4.4 ppm) than those on the opposite side (–1.8—–2.7 ppm) in the ¹³C-NMR spectra in C₅D₅N. When compared with rhododendrin (**17**), (–)-rhododendrol (**17a**) showed β-D-glucosylation shifts of –3.7 ppm for C-1 and –1.5 ppm for C-3 in CD₃OD solution. Furthermore, β-D-glucosylation shifts of –1.4 ppm for C-1 and –2.4 ppm for C-3 in CD₃OD solution can be estimated for (+)-rhododendrol from the reported ¹³C-NMR data for (+)-rhododendrin (=epirhododendrin).²⁶ The results indicated (*R*)-configuration at C-2 for (–)-rhododendrol (**17a**) and (*S*) for (+)-rhododendrol.

Spikes contain a dammarane-type triterpene (**1b**) even in August when leaves lose this type of compounds. It seems that the compound plays a role of antifeedant in spikes which are very important organs for the plant.

In this study, thirty-one compounds including five which were new, **6**, **21**, **23**, **26** and **28**, were isolated, and, the following remarkable distinction between *B. platyphylla* var. *japonica* and *B. ermanii* was revealed.

1) The dammarane-type triterpenes in leaves of *B. platyphylla* var. *japonica* have 3α- and 12β-hydroxyl groups and form malonates, while those of *B. ermanii* have 3β- and 11α-hydroxyl groups and form glucosides.

2) The lignans in inner bark of *B. ermanii* are replaced by diarylheptanoids in that of *B. platyphylla* var. *japonica*.

3) The content of betulin in outer bark of *B. ermanii* is less than half of that in *B. platyphylla* var. *japonica*.

A more detailed report of the comparative studies among *Betula* species will be presented in the near future.

Experimental

The instruments, materials and experimental conditions were the same as described in Part 1 of this series.¹⁾

Isolation. Leaves Fresh leaves (1.8 kg) collected in June at Iizuna Highland, Nagano Prefecture, were extracted with MeOH (20 l) at room temperature for 2 weeks. The extract and then MeOH (10 l) were passed over activated charcoal (130 g) packed in a column of 7 cm diameter. The resulting solution was concentrated to a syrup under reduced pressure. The syrup was chromatographed on silica gel using CHCl₃ and MeOH. Each fraction was rechromatographed on silica gel using *n*-hexane and EtOAc and/or on Sephadex LH-20 using 90% MeOH to

yield **1** (141 mg), **2** (35 mg), **3** (66 mg), **4** (12 mg), **5** (52 mg), **6** (33 mg) and **7** (22 mg).

Outer Bark Outer bark (460 g) of a tree aged 32 years and collected in June at Iizuna Highland was extracted twice with CHCl₃ (3 l) under reflux for 3 h. The extracts were concentrated to 700 ml and EtOH (1 l) was added. Crystallized crude betulin was filtered off and recrystallized from EtOH to obtain 56 g of betulin (**8**). The filtrates were combined and chromatographed on silica gel using *n*-hexane–CHCl₃, *n*-hexane–EtOAc and CHCl₃–EtOAc as eluents to obtain **9** (1.4 g), **10** (210 mg), **11** (140 mg), **12** (255 mg), **13** (470 mg) and **14** (80 mg). All the compounds were identified by direct comparison with their authentic samples.

Inner Bark Air-dried inner bark (2 kg) was extracted twice with MeOH (4 l) under reflux for 6 h. The extracts were concentrated to a syrup under reduced pressure. The syrup was extracted with Et₂O (2 l). The Et₂O soluble compounds were chromatographed on silica gel using CHCl₃–MeOH and *n*-hexane–EtOAc, and on Sephadex LH-20 using MeOH to obtain **20** (220 mg), **21** (7 mg), **22** (33 mg), **23** (36 mg) and a mixture of **24** and **25**. The mixture was chromatographed on silica gel impregnated with 20% AgNO₃ using CHCl₃ to obtain **24** (7 mg) and **25** (6 mg). The Et₂O insoluble compounds were chromatographed on silica gel using CHCl₃–MeOH and on Sephadex LH-20 using 80% MeOH to obtain **15** (210 mg), **16** (70 mg), **19** (65 mg) and a mixture of **17** and **18**. The mixture was subjected to droplet counter current chromatography using CHCl₃–MeOH–H₂O (4 : 4 : 3) to obtain **17** (35 mg) and **18** (15 mg).

Root Bark Air-dried root bark (360 g) was extracted three times with MeOH (1.5 l) under reflux for 6 h. The extracts were concentrated and partitioned with CHCl₃ (1 l), MeOH (1 l) and H₂O (750 ml). The upper layer was concentrated to a syrup and chromatographed on silica gel using CHCl₃–MeOH and *n*-hexane–EtOAc to obtain **26** (10 mg), **27** (42 mg) and **28** (108 mg). The lower layer was concentrated to a syrup and chromatographed on silica gel using *n*-hexane–EtOAc to obtain **29** (6 mg).

Spikes Fresh spikes (1.3 kg) collected in August at Iizuna highland were extracted with MeOH (10 l) at room temperature for 4 weeks. The extract and MeOH (5 l) were passed over activated charcoal (80 g). The resulting solution was concentrated to a syrup, and partitioned with CHCl₃ (500 ml), MeOH (500 ml) and H₂O (350 ml). The upper layer was chromatographed on silica gel using CHCl₃–MeOH and on Sephadex LH-20 using 90% MeOH to yield **17a** (56 mg). The lower layer was chromatographed on silica gel using *n*-hexane–EtOAc and benzene, and on ODS using MeOH to obtain **1b** (12 mg) and **5** (8 mg).

12-*O*-Acetyl-3-*O*-malonylbetulafolienetriol (1**)** A colorless amorphous powder, [α]_D²⁰ (+2°) (*c* = 1.0, CHCl₃). ¹H-NMR (C₅D₅N) δ: 0.77 (3H, s), 0.80 (3H, s), 0.85 (3H, s), 0.96 (3H, s), 1.03 (3H, s), 1.37 (3H, s), 1.69 (3H, s), 1.72 (3H, s), 2.22 (3H, s), 3.84 (2H, s), 4.93 (1H, br s), 5.19 (1H, dt, *J* = 5.5, 10.7 Hz), 5.39 (1H, t, *J* = 7.3 Hz). ¹³C-NMR (CDCl₃) δ: 34.4 (C-1), 22.6 (C-2), 80.2 (C-3), 37.1 (C-4), 50.6 (C-5), 18.0 (C-6), 34.0 (C-7), 40.0 (C-8), 49.8 (C-9), 36.8 (C-10), 28.1 (C-11), 76.9 (C-12), 44.8 (C-13), 52.9 (C-14), 31.5 (C-15), 27.2 (C-16), 52.8 (C-17), 16.1 (C-18), 15.6 (C-19), 73.9 (C-20), 26.1 (C-21), 36.1 (C-22), 22.2 (C-23), 125.1 (C-24), 131.4 (C-25), 25.8 (C-26), 17.7 (C-27), 27.9 (C-28), 21.6 (C-29), 17.5 (C-30), 21.6 (CH₃–CO), 169.9 (CH₃–CO), 41.8 (CO–CH₂–CO), 166.0 (CO–CH₂–CO), 167.2 (CO–CH₂–CO). FAB-MS (positive mode) *m/z*: 571 [M + H – H₂O]⁺, 511 [M + H – H₂O – AcOH]⁺.

12-*O*-Acetylbetulafolienetriol (1b**)** A colorless amorphous powder, [α]_D²⁰ (+2°) (*c* = 1.0, MeOH). ¹H-NMR (CDCl₃) δ: 0.77 (3H, s), 0.80 (3H, s), 0.87 (3H, s), 0.89 (3H, s), 0.94 (3H, s), 1.07 (3H, s), 1.57 (3H, s), 1.64 (3H, s), 1.98 (3H, s), 3.33 (1H, t, *J* = 2.8 Hz), 4.67 (1H, dt, *J* = 5.1, 11.4 Hz), 5.09 (1H, t, *J* = 6.9 Hz). ¹³C-NMR (CDCl₃) δ: 33.9 (C-1), 25.8 (C-2), 76.5 (C-3), 38.0 (C-4), 49.9 (C-5), 18.6 (C-6), 35.0 (C-7), 40.4 (C-8), 50.3 (C-9), 37.7 (C-10), 31.6 (C-11), 77.6 (C-12), 45.3 (C-13), 53.3 (C-14), 28.8 (C-15), 27.6 (C-16), 53.3 (C-17), 16.5 (C-18), 16.0 (C-19), 74.2 (C-20), 26.6 (C-21), 36.5 (C-22), 22.7 (C-23), 125.6 (C-24), 131.8 (C-25), 26.2 (C-26), 18.1 (C-27), 28.6 (C-28), 22.5 (C-29), 17.8 (C-30), 170.1 (CH₃CO), 22.0 (CH₃CO). EI-MS *m/z*: 502 (M⁺), 484.

12-*O*-Acetyl-3-*O*-malonylbetulafolienetriol Oxide I (= Papyriferic Acid, **2)** A colorless amorphous powder, [α]_D²⁰ –12° (*c* = 0.38, CHCl₃). ¹H-NMR (CDCl₃) δ: 0.85, 0.86, 0.88, 0.96, 0.98, 1.10, 1.17, 1.19, 2.01 (each 3H, s), 3.45 (2H, s), 3.65 (1H, dd, *J* = 8.2, 6.4 Hz), 4.70 (1H, br s), 4.82 (1H, td, *J* = 10.7, 5.2 Hz). ¹³C-NMR (CDCl₃) δ: 33.9 (C-1), 22.6 (C-2), 80.3 (C-3), 36.8 (C-4), 50.6 (C-5), 18.0 (C-6), 34.3 (C-7), 39.8 (C-8), 49.6 (C-9), 37.0 (C-10), 28.2 (C-11), 75.7 (C-12), 46.2 (C-13), 52.3 (C-14), 31.3 (C-15), 26.8 (C-16), 50.4 (C-17), 15.5 (C-18), 15.9 (C-19), 85.8 (C-20), 22.3 (C-21), 38.7 (C-22), 26.1 (C-23), 83.3 (C-24), 71.2 (C-25), 27.4 (C-26),

24.1 (C-27), 27.9 (C-28), 21.8 (C-29), 17.7 (C-30), 169.2 (HOOCC₂CO), 40.9 (HOOCC₂CO), 167.1 (HOOCC₂CO), 21.5 (CH₃C=O), 170.8 (CH₃C=O). FAB-MS (negative mode) *m/z*: 603 [M-H]⁻.

12-O-Acetylbutulofolienolone (3) A colorless amorphous powder, $[\alpha]_D^{25} + 25^\circ$ (*c*=1.0, CHCl₃). ¹H-NMR (CDCl₃) δ: 0.94 (3H, s), 0.97 (3H, s), 1.04 (3H, s), 1.05 (3H, s), 1.09 (3H, s), 1.14 (3H, s), 1.64 (3H, brs), 1.71 (3H, brs), 2.05 (3H, s), 4.74 (1H, dt, *J*=10.7, 6.1 Hz), 5.16 (1H, t, *J*=7.0 Hz). ¹³C-NMR (CDCl₃) δ: 39.5 (C-1), 33.8 (C-2), 217.5 (C-3), 47.2 (C-4), 55.0 (C-5), 19.6 (C-6), 33.8 (C-7), 39.6 (C-8), 49.3 (C-9), 36.8 (C-10), 28.6 (C-11), 76.3 (C-12), 45.0 (C-13), 52.7 (C-14), 31.4 (C-15), 27.1 (C-16), 52.9 (C-17), 16.0 (C-18), 15.2 (C-19), 73.6 (C-20), 26.2 (C-21), 36.1 (C-22), 22.2 (C-23), 125.2 (C-24), 131.3 (C-25), 25.7 (C-26), 17.7 (C-27), 26.8 (C-28), 20.9 (C-29), 17.2 (C-30), 21.5 (CH₃CO), 169.6 (CH₃CO). EI-MS *m/z*: 500 (M⁺), 482, 440.

Hydroxyhopanone (4) Colorless needles from MeOH, mp 247–252 °C, $[\alpha]_D^{25} + 54^\circ$ (*c*=0.5, CHCl₃). ¹H-NMR (CDCl₃) δ: 0.76 (3H, s), 0.92 (3H, s), 0.96 (3H, s), 1.00 (3H, s), 1.02 (3H, s), 1.07 (3H, s), 1.18 (3H, s), 1.20 (3H, s). ¹³C-NMR (CDCl₃) δ: 39.6 (C-1), 34.2 (C-2), 218.8 (C-3), 47.4 (C-4), 54.9 (C-5), 19.8 (C-6), 32.6 (C-7), 41.7 (C-8), 49.7 (C-9), 36.9 (C-10), 21.6 (C-11), 24.1 (C-12), 50.0 (C-13), 41.9 (C-14), 34.4 (C-15), 21.9 (C-16), 53.9 (C-17), 44.1 (C-18), 41.3 (C-19), 26.6 (C-20), 51.1 (C-21), 74.1 (C-22), 26.6 (C-23), 21.1 (C-24), 15.7 (C-25), 16.5 (C-26), 16.9 (C-27), 16.2 (C-28), 28.7 (C-29), 30.7 (C-30). EI-MS *m/z*: 442 (M⁺), 424, 409, 384, 236, 189, 149.

Caryophyllene Oxide (5) Colorless oil, $[\alpha]_D^{25} - 40^\circ$ (*c*=1.0, CHCl₃). ¹H-NMR (CDCl₃) δ: 0.99 (3H, s), 1.01 (3H, s), 1.20 (3H, s), 2.88 (1H, dd, *J*=10.4, 4.0 Hz), 4.86 (1H, brs), 4.97 (1H, brs). ¹³C-NMR (CDCl₃) δ: 50.7 (C-1), 27.2 (C-2), 39.1 (C-3), 59.8 (C-4), 63.7 (C-5), 30.2 (C-6), 29.8 (C-7), 151.8 (C-8), 48.7 (C-9), 39.7 (C-10), 34.0 (C-11), 29.9 (C-12), 21.6 (C-13), 112.7 (C-14), 17.0 (C-15). EI-MS *m/z*: 220 (M⁺), 205, 187, 177.

Kaempferol 3-O-(4-O-Acetyl)-α-L-rhamnopyranoside (6) A yellow amorphous powder, $[\alpha]_D^{25} - 138^\circ$ (*c*=1.0, MeOH). UV $\lambda_{\max}^{\text{MeOH}}$ nm (log *ε*): 342 (4.04), 262 (4.30). ¹H-NMR (DMSO-*d*₆) δ: 0.70 (3H, d, *J*=6.3 Hz), 2.00 (3H, s), 3.26 (1H, dq, *J*=9.9, 5.9 Hz), 3.70 (1H, dd, *J*=9.9, 3.0 Hz), 4.03 (1H, dd, *J*=3.0, 1.0 Hz), 4.70 (1H, t, *J*=9.9 Hz), 5.29 (1H, d, *J*=1.0 Hz), 6.23 (1H, d, *J*=1.0 Hz), 6.43 (1H, d, *J*=1.0 Hz), 6.95 (2H, d, *J*=8.6 Hz), 7.74 (2H, d, *J*=8.6 Hz), 12.58 (1H, s). ¹³C-NMR (DMSO-*d*₆) δ: 156.6 (C-2), 134.0 (C-3), 177.6 (C-4), 160.2 (C-5), 98.8 (C-6), 164.4 (C-7), 93.8 (C-8), 157.4 (C-9), 104.1 (C-10), 120.3 (C-1'), 130.6 (C-2', 6'), 115.3 (C-3', 5'), 161.3 (C-4'), 101.4 (C-1''), 69.9 (C-2''), 67.9 (C-3''), 73.1 (C-4''), 67.8 (C-5''), 17.1 (C-6''), 169.9 and 20.9 (Ac). HR-FAB-MS (negative mode) *m/z*: 473.106 [M-H]⁻. Calcd for C₂₃H₂₁O₁₁: 473.108. On alkaline methanolysis, **6** gave afzelin which was identified by direct comparison with an authentic sample.

Quercetin 3-O-(4-O-Acetyl)-α-L-rhamnopyranoside (7) A yellow crystalline powder, mp 171–176 °C, $[\alpha]_D^{25} - 158^\circ$ (*c*=1.0, MeOH). IR ν_{\max}^{KBr} cm⁻¹: 3400, 1719, 1644, 1559, 1495, 1437, 1349, 1293, 1255, 1194, 1160, 950. UV $\lambda_{\max}^{\text{MeOH}}$ nm (log *ε*): 348 (4.21), 256 (4.35). ¹H-NMR (DMSO-*d*₆) δ: 0.73 (3H, d, *J*=6.3 Hz), 2.01 (3H, s), 3.40 (1H, dq, *J*=9.9, 6.3 Hz), 3.75 (1H, dd, *J*=9.9, 3.0 Hz), 4.04 (1H, dd, *J*=3.0, 1.0 Hz), 4.72 (1H, t, *J*=9.9 Hz), 5.24 (1H, d, *J*=1.0 Hz), 6.22 (1H, d, *J*=2.0 Hz), 6.40 (1H, d, *J*=2.0 Hz), 6.91 (1H, d, *J*=8.3 Hz), 7.24 (1H, dd, *J*=8.3, 2.0 Hz), 7.30 (1H, d, *J*=2.0 Hz), 12.61 (1H, s). ¹³C-NMR (DMSO-*d*₆) δ: 156.5 (C-2), 134.0 (C-3), 177.6 (C-4), 161.3 (C-5), 98.9 (C-6), 164.6 (C-7), 93.7 (C-8), 157.5 (C-9), 104.0 (C-10), 121.0 (C-1'), 115.5 (C-2'), 145.3 (C-3'), 148.6 (C-4'), 115.8 (C-5'), 120.6 (C-6'), 101.5 (C-1''), 70.0 (C-2''), 67.9 (C-3''), 73.2 (C-4''), 67.9 (C-5''), 17.1 (C-6''), 170.0 and 20.9 (Ac). HR-FAB-MS (negative mode) *m/z*: 489.105 [M-H]⁻. Calcd for C₂₃H₂₁O₁₂: 489.103.

Rhododendrin (=Betuloside) (17) Colorless needles from MeOH–H₂O, mp 191–193 °C, $[\alpha]_D^{25} - 48^\circ$ (*c*=1.0, MeOH). IR ν_{\max}^{KBr} cm⁻¹: 3350, 2915, 1611, 1507, 1444, 1377, 1248, 1166, 1103, 1057, 1026, 826, 612. UV $\lambda_{\max}^{\text{MeOH}}$ nm (log *ε*): 278 (3.43). ¹H-NMR (CD₃OD) δ: 1.19 (3H, d, *J*=6.1 Hz), 4.32 (1H, d, *J*=7.9 Hz), 6.67 (2H, d, *J*=10.2 Hz), 7.02 (2H, d, *J*=10.2 Hz). ¹³C-NMR (CD₃OD) δ: 19.9 (C-1), 74.9 (C-2), 40.9 (C-3), 31.7 (C-4), 134.4 (C-1'), 130.2 (C-2', 6'), 115.9 (C-3', 5'), 156.0 (C-4'), 102.0 (Glc-1), 75.0 (Glc-2), 78.0 (Glc-3), 71.6 (Glc-4), 77.6 (Glc-5), 62.7 (Glc-6). HR-FAB-MS *m/z*: 328.151 [M⁺], Calcd for C₁₆H₂₄O₇: 328.152. On acid hydrolysis with 3% HCl, **17** gave (–)-rhododendrol and D-glucose, $[\alpha]_D^{25} + 50^\circ$ (*c*=1.0, H₂O).

(–)-Rhododendrol (=Betuligenol) (17a) A colorless amorphous powder, $[\alpha]_D^{25} - 16^\circ$ (*c*=1.0, MeOH). UV $\lambda_{\max}^{\text{MeOH}}$ nm (log *ε*): 276 (3.76). ¹H-NMR (CD₃OD) δ: 1.17 (3H, d, *J*=6.3 Hz), 1.65 (2H, m), 2.58 (2H,

m), 3.76 (1H, m), 6.68 (2H, d, *J*=8.4 Hz), 7.00 (2H, d, *J*=8.4 Hz). ¹³C-NMR (CD₃OD) δ: 23.6 (C-1), 67.9 (C-2), 42.4 (C-3), 32.3 (C-4), 134.4 (C-1'), 130.3 (C-2', 6'), 116.1 (C-3', 5'), 156.3 (C-4'). EI-MS *m/z*: 166 (M⁺), 148, 133, 107, 77.

Aceroside VII (18) A colorless amorphous powder, $[\alpha]_D^{25} - 30^\circ$ (*c*=1.0, MeOH). UV $\lambda_{\max}^{\text{MeOH}}$ nm (log *ε*): 279 (3.56). ¹H-NMR (C₅D₅N) δ: 1.5–2.9 (12H), 3.98 (1H, ddd, *J*=9.2, 5.2, 2.4 Hz), 4.96 (1H, d, *J*=7.6 Hz), 7.17 (4H, d, *J*=8.5 Hz), 7.19 (2H, d, *J*=8.5 Hz), 7.32 (2H, d, *J*=8.5 Hz). ¹³C-NMR (C₅D₅N) δ: 31.1 (C-1), 37.7 (C-2), 78.5 (C-3), 34.4 (C-4), 25.0 (C-5), 32.5 (C-6), 35.3 (C-7), 133.6 (C-1' or 1''), 133.4 (C-1' or 1''), 130.1 (C-2', 6' or 2'', 6''), 129.8 (C-2', 6' or 2'', 6''), 116.1 (C-4', 4''), 103.6 (Glc-1), 75.4 (Glc-2), 78.6 (Glc-3), 71.8 (Glc-4), 78.2 (Glc-5), 63.0 (Glc-6). FAB-MS *m/z*: 463 [M+H]⁺, 375, 301, 283, 185, 145, 137, 107.

Aceroside VIII (19) A colorless amorphous powder, $[\alpha]_D^{25} - 48^\circ$ (*c*=1.0, MeOH). UV $\lambda_{\max}^{\text{MeOH}}$ nm (log *ε*): 279 (3.81). ¹H-NMR (C₅D₅N) δ: 1.4–3.1 (12H), 4.90 (1H, d, *J*=7.6 Hz), 5.81 (1H, d, *J*=2.4 Hz), 7.17 (4H, d, *J*=8.5 Hz), 7.23 (2H, d, *J*=8.5 Hz), 7.32 (2H, d, *J*=8.5 Hz). ¹³C-NMR (C₅D₅N) δ: 31.2 (C-1), 37.8 (C-2), 78.5 (C-3), 34.6 (C-4), 25.0 (C-5), 32.5 (C-6), 35.2 (C-7), 133.8 (C-1' or 1''), 133.4 (C-1' or 1''), 130.1 (C-2', 6' or 2'', 6''), 129.8 (C-2', 6' or 2'', 6''), 116.1 (C-3', 5' or 3'', 5''), 116.0 (C-3', 5' or 3'', 5''), 156.8 (C-4' or 4''), 156.7 (C-4' or 4''), 103.5 (Glc-1), 75.2 (Glc-2), 78.6 (Glc-3), 71.6 (Glc-4), 76.8 (Glc-5), 68.6 (Glc-6), 111.0 (Api-1), 77.8 (Api-2), 80.4 (Api-3), 74.9 (Api-4), 65.6 (Api-5). FAB-MS *m/z*: 595 [M+H]⁺, 300, 283, 185, 133, 107.

1,7-Bis[4-hydroxyphenyl]-3-hepten-5-one (20) A colorless oil. UV $\lambda_{\max}^{\text{MeOH}}$ nm (log *ε*): 225 (4.20), 278 (3.67). ¹H-NMR (CDCl₃–CD₃OD, 1:1) δ: 2.49 (2H, t, *J*=7.3 Hz), 2.67 (2H, t, *J*=7.3 Hz), 2.80 (4H, s), 6.07 (1H, brd, *J*=16.2 Hz), 6.74 (4H, d, *J*=7.3 Hz), 6.85 (1H, dt, *J*=16.2, 7.3 Hz), 6.99 (4H, d, *J*=7.3 Hz). ¹³C-NMR (C₅D₅N) δ: 34.7 (C-1), 33.8 (C-2), 146.5 (C-3), 131.1 (C-4), 199.2 (C-5), 42.2 (C-6), 29.7 (C-7), 131.7 and 132.2 (C-1' and 1''), 129.9 and 130.0 (C-2', 6' and 2'', 6''), 116.3 (C-3', 5', 3'', 5''), 157.3 and 157.2 (C-4' and 4''). HR-EI-MS *m/z*: 296.142, Calcd for C₁₉H₂₀O₃: 296.141.

2-Hydroxy-1,7-bis[4-hydroxyphenyl]-3-hepten-5-one (21) A colorless oil. UV $\lambda_{\max}^{\text{MeOH}}$ nm (log *ε*): 224 (4.16), 278 (3.64). ¹H-NMR (CD₃OD) δ: 2.7–2.8 (6H), 4.39 (1H, tdd, *J*=6.7, 5.2, 1.5 Hz), 6.18 (1H, dd, *J*=15.9, 1.5 Hz), 6.68 (2H, d, *J*=8.6 Hz), 6.70 (2H, d, *J*=8.6 Hz), 6.81 (1H, dd, *J*=15.9, 5.2 Hz), 6.84 (2H, d, *J*=8.6 Hz), 7.02 (2H, d, *J*=8.6 Hz). ¹³C-NMR (CD₃OD) δ: 40.1 (C-1), 73.3 (C-2), 150.5 (C-3), 131.6 (C-4), 202.7 (C-5), 43.5 (C-6), 30.6 (C-7), 129.7 and 133.2 (C-1' and 1''), 129.3 and 130.3 (C-2', 6' and 2'', 6''), 116.1 and 116.2 (C-3', 5' and 3'', 5''), 156.1 and 156.7 (C-4' and 4''). HR-EI-MS *m/z*: 312.137, Calcd for C₁₉H₂₀O₄: 312.136.

(3R)-3,5'-Dihydroxy-4'-methoxy-3',4'-oxo-1,7-diphenyl-1-heptene (23) A colorless crystalline powder from *n*-hexane–EtOAc, mp 186–187 °C, $[\alpha]_D^{25} + 79^\circ$ (*c*=1.0, CHCl₃). IR ν_{\max}^{KBr} cm⁻¹: 3300, 3010, 2940, 2860, 1574, 1500, 1425, 1400, 1350, 1250, 1208, 1170, 1130, 1100, 1035, 1012, 995, 920, 865, 830, 770. UV $\lambda_{\max}^{\text{MeOH}}$ nm (log *ε*): 223 (4.39), 258 (3.95). ¹H-NMR (CDCl₃) δ: 2.43 (1H, td, *J*=12.8, 5.5 Hz, H-7), 3.02 (1H, ddd, *J*=12.8, 4.9, 2.8 Hz, H-7), 3.95 (1H, ddd, *J*=11.3, 8.6, 3.1 Hz, H-3), 4.11 (3H, s, CH₃O–), 5.17 (1H, d, *J*=2.1 Hz, H-2'), 5.30 (1H, dd, *J*=11.3, 8.6 Hz, H-2), 6.11 (1H, d, *J*=11.3 Hz, H-1), 6.38 (1H, d, *J*=2.1 Hz, H-6'), 7.01 (1H, dd, *J*=8.2, 2.4 Hz, H-3'' or 5''), 7.12 (1H, dd, *J*=8.2, 2.4 Hz, H-3'' or 5''), 7.30 (1H, dd, *J*=8.2, 2.1 Hz, H-2'' or 6''), 7.33 (1H, dd, *J*=8.2, 2.1 Hz, H-2'' or 6''). ¹³C-NMR (CDCl₃) δ: 127.8 (C-1), 135.3 (C-2), 69.1 (C-3), 37.5 (C-4), 22.0 (C-5), 28.8 (C-6), 35.6 (C-7), 132.1 (C-1'), 109.0 (C-2'), 153.5 (C-3'), 134.5 (C-4'), 149.3 (C-5'), 108.8 (C-6'), 139.2 (C-1''), 130.1 (C-2'' or 6''), 123.9 (C-3'' or 5''), 154.1 (C-4''), 122.3 (C-3'' or 5''), 132.7 (C-2'' or 6''), 61.4 (CH₃O–). HR-EI-MS *m/z*: 326.152, Calcd for C₂₀H₂₂O₄: 326.152.

Methylation of 23 A solution of CH₂N₂ in ether (9 ml) was added to a solution of **23** (22 mg) in MeOH and the mixture was allowed to stand at room temperature for 12 h. Then the reaction mixture was concentrated *in vacuo* and the residue was crystallized (AcOEt–*n*-hexane) to afford **23a** (15 mg) as a colorless crystalline powder.

Compound 23a A colorless crystalline powder, mp 132–135 °C, $[\alpha]_D^{25} + 141^\circ$ (*c*=1.0, CHCl₃). UV $\lambda_{\max}^{\text{MeOH}}$ nm (log *ε*): 222 (4.40), 261 (4.07). ¹H-NMR (CDCl₃) δ: 2.43 (1H, td, *J*=12.8, 5.2 Hz, H-7), 3.02 (1H, ddd, *J*=12.8, 4.6, 2.8 Hz, H-7), 3.85 (3H, s, CH₃O–), 4.03 (3H, s, CH₃O–), 5.27 (1H, d, *J*=2.1 Hz, H-2'), 5.32 (1H, dd, *J*=11.9, 8.3 Hz, H-2), 6.16 (1H, d, *J*=11.9 Hz, H-1), 6.33 (1H, d, *J*=2.1 Hz, H-6'), 7.01 (1H, dd, *J*=8.2, 2.4 Hz, H-3'' or 5''), 7.13 (1H, dd, *J*=8.2, 2.4 Hz, H-2'' or 6''), 7.29 (1H, dd, *J*=8.2, 2.1 Hz, H-2'' or 6''), 7.33 (1H, dd, *J*=8.2, 2.1 Hz,

H-3" or 5"). $^{13}\text{C-NMR}$ (CDCl_3) δ : 127.8 (C-1), 135.4 (C-2), 69.1 (C-3), 37.5 (C-4), 22.0 (C-5), 28.8 (C-6), 35.6 (C-7), 131.6 (C-1'), 109.8 (C-2' or 6'), 153.5 (C-3'), 137.0 (C-4'), 154.6 (C-5'), 106.0 (C-2' or 6'), 139.0 (C-1'), 130.1 (C-2" or 6"), 124.0 (C-3" or 5"), 154.5 (C-4'), 122.4 (C-3" or 5"), 132.6 (C-2" or 6"), 61.3 ($\text{CH}_3\text{O}-$), 56.2 ($\text{CH}_3\text{O}-$). HR-EI-MS m/z : 340.166 [M^+], Calcd for $\text{C}_{21}\text{H}_{24}\text{O}_4$: 340.167.

MTPA Ester of 23a (S) or (R)-MTPA chloride (6 mg) was added to a solution of **23a** (7 mg) in dry pyridine (1 ml) and the mixture was stirred at room temperature for 15 h. The reaction mixture was then poured into water and extracted with CHCl_3 and the extract was concentrated *in vacuo*. The residue was purified by preparative thin-layer chromatography (TLC) to give **23b** or **23c** as a colorless oil.

(S)-MTPA Ester (23b) A colorless oil, $[\alpha]_{\text{D}} -21^\circ$ ($c=2.3$, CHCl_3). IR $\nu_{\text{max}}^{\text{CHCl}_3 \text{ soln.}}$ cm^{-1} : 3010, 2920, 1740, 1572, 1495, 1445, 1090, 992. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 222 (4.40), 263 (4.02). $^1\text{H-NMR}$ (CDCl_3) δ : 0.31–0.38 (1H, m, H-4), 0.88–0.98 (1H, m, H-5), 1.13–1.23 (1H, m, H-6), 1.50–1.60 (1H, m, H-4), 1.62–1.73 (1H, m, H-5), 2.00–2.08 (1H, m, H-6), 2.41 (1H, td, $J=12.8$, 5.2 Hz, H-7), 3.02 (1H, ddd, $J=12.8$, 4.9, 2.1 Hz, H-7), 3.52 (3H, s, MTPA- OCH_3), 3.87 (3H, s, 5'- OCH_3), 4.05 (3H, s, 4'- OCH_3), 5.05 (1H, dd, $J=11.9$, 8.6 Hz, H-2), 5.18 (1H, ddd, $J=11.6$, 8.6, 3.1 Hz, H-3), 5.27 (1H, d, $J=2.1$ Hz, H-2'), 6.25 (1H, d, $J=11.9$ Hz, H-1), 6.38 (1H, d, $J=2.1$ Hz, H-6'), 7.12 (1H, dd, $J=8.2$, 2.1 Hz), 7.15 (1H, dd, $J=8.2$, 2.1 Hz), 7.28–7.34 (2H), 7.37–7.41 (3H), 7.44–7.47 (2H). HR-EI-MS m/z : 556.207 [M^+], Calcd for $\text{C}_{31}\text{F}_3\text{H}_{31}\text{O}_6$: 556.207.

(R)-MTPA Ester (23c) A colorless oil, $[\alpha]_{\text{D}} +93^\circ$ ($c=0.3$, CHCl_3). IR $\nu_{\text{max}}^{\text{CHCl}_3 \text{ soln.}}$ cm^{-1} : 3010, 2920, 2850, 1740, 1572, 1495, 1445, 1415, 1390, 1322, 1232, 1090, 992, 855. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 222 (4.48), 263 (4.04). $^1\text{H-NMR}$ (CDCl_3) δ : 0.38–0.46 (1H, m, H-4), 0.77–0.85 (1H, m, H-5), 1.08–1.17 (1H, m, H-6), 1.32–1.42 (1H, m, H-4), 1.46–1.55 (1H, m, H-5), 1.87–1.95 (1H, m, H-6), 2.37 (1H, td, $J=12.8$, 5.2 Hz, H-7), 2.96 (1H, ddd, $J=12.8$, 4.9, 2.7 Hz, H-7), 3.49 (3H, s, MTPA- OCH_3), 3.86 (3H, s, 5'- OCH_3), 4.05 (3H, s, 4'- OCH_3), 5.26 (1H, dd, $J=11.9$, 8.5 Hz, H-2), 5.26–5.32 (1H, m, H-3), 5.29 (1H, d, $J=2.1$ Hz, H-2'), 6.28 (1H, d, $J=11.9$ Hz, H-1), 6.36 (1H, d, $J=2.1$ Hz, H-6'), 7.11 (1H, dd, $J=8.0$, 2.1 Hz), 7.14 (1H, dd, $J=8.0$, 2.1 Hz), 7.27–7.31 (2H), 7.37–7.42 (3H), 7.48–7.52 (2H). HR-EI-MS m/z : 556.206, Calcd for $\text{C}_{31}\text{F}_3\text{H}_{31}\text{O}_6$: 556.207.

Dammarenediol II 3-O-*p*-Coumarate (26) A colorless amorphous powder, $[\alpha]_{\text{D}} -16^\circ$ ($c=0.5$, MeOH). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 329 (4.23). $^1\text{H-NMR}$ (CDCl_3) δ : 0.889, 0.893, 0.90, 0.93, 0.97, 1.15, 1.63, 1.69 (each 3H, s), 4.62 (1H, dd, $J=10.7$, 4.9 Hz), 5.12 (1H, brt, $J=7.0$ Hz), 6.30 (1H, d, $J=15.9$ Hz), 6.84 (2H, d, $J=8.9$ Hz), 7.43 (2H, d, $J=8.9$ Hz), 7.61 (1H, d, $J=15.9$ Hz). $^{13}\text{C-NMR}$ (CDCl_3) δ : 38.8 (C-1), 23.8 (C-2), 80.9 (C-3), 38.2 (C-4), 56.0 (C-5), 18.2 (C-6), 35.2 (C-7), 40.4 (C-8), 50.6 (C-9), 37.1 (C-10), 21.6 (C-11), 27.5 (C-12), 42.3 (C-13), 50.3 (C-14), 31.2 (C-15), 24.8 (C-16), 49.8 (C-17), 15.5 (C-18), 16.3 (C-19), 75.6 (C-20), 25.4 (C-21), 40.5 (C-22), 22.6 (C-23), 124.7 (C-24), 131.7 (C-25), 25.7 (C-26), 17.7 (C-27), 28.0 (C-28), 16.7 (C-29), 16.5 (C-30), 127.3 (C-1'), 129.9 (C-2', 6'), 115.9 (C-3', 5'), 157.7 (C-4'), 144.0 (C-7), 116.3 (C-8'), 167.3 (C-9'). HR-EI-MS m/z : 590.435, Calcd for $\text{C}_{39}\text{H}_{58}\text{O}_4$: 590.433. On alkaline methanolysis, **26** gave dammarenediol II and methyl *p*-coumarate. Dammarenediol II: $[\alpha]_{\text{D}} +15^\circ$ ($c=0.2$, CHCl_3). $^{13}\text{C-NMR}$ (CDCl_3) δ : 39.0 (C-1), 27.4 (C-2), 79.0 (C-3), 39.0 (C-4), 55.8 (C-5), 18.3 (C-6), 35.2 (C-7), 40.3 (C-8), 50.6 (C-9), 37.1 (C-10), 21.5 (C-11), 27.5 (C-12), 42.3 (C-13), 50.3 (C-14), 31.2 (C-15), 24.8 (C-16), 49.8 (C-17), 15.5 (C-18), 16.2 (C-19), 75.4 (C-20), 25.4 (C-21), 40.5 (C-22), 22.5 (C-23), 124.7 (C-24), 131.6 (C-25), 25.7 (C-26), 17.7 (C-27), 28.0 (C-28), 15.3 (C-29), 16.4 (C-30). The $^{13}\text{C-NMR}$ data were identical with those reported.²⁷⁾

Ocotillol II 3-O-Caffeate (28) A colorless crystalline powder from EtOAc, mp 222–224°C. $[\alpha]_{\text{D}} -10^\circ$ ($c=0.5$, MeOH). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3450, 1705, 1178. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 329 (4.31). $^1\text{H-NMR}$ (CDCl_3) δ : 0.85, 0.87, 0.88, 0.91, 0.95, 1.14, 1.15, 1.24 (each 3H, s), 4.59 (1H, dd, $J=9.0$, 7.0 Hz), 6.25 (1H, d, $J=16$ Hz), 6.87 (1H, d, $J=8$ Hz), 6.99 (1H, dd, $J=8.5$, 1.5 Hz), 7.10 (1H, d, $J=1.5$ Hz), 7.56 (1H, d, $J=16$ Hz). $^{13}\text{C-NMR}$ (CDCl_3) δ : 38.7 (C-1), 23.8 (C-2), 81.1 (C-3), 38.1 (C-4), 56.0 (C-5), 18.2 (C-6), 35.2 (C-7), 40.4 (C-8), 50.7 (C-9), 37.1 (C-10), 21.6 (C-11), 25.8 (C-12), 43.0 (C-13), 50.1 (C-14), 31.5 (C-15), 27.5 (C-16), 49.4 (C-17), 15.4 (C-18), 16.3 (C-19), 86.7 (C-20), 23.8 (C-21), 35.4 (C-22),

26.2 (C-23), 83.2 (C-24), 72.1 (C-25), 24.1 (C-26), 27.5 (C-27), 28.0 (C-28), 16.7 (C-29), 16.5 (C-30), 127.3 (C-1'), 129.9 (C-2', 6'), 115.9 (C-3', 5'), 157.7 (C-4'), 144.0 (C-7), 116.3 (C-8'), 167.3 (C-9'). HR-EI-MS m/z : 622.423, Calcd for $\text{C}_{39}\text{H}_{58}\text{O}_6$: 622.423. On alkaline methanolysis, **28** gave ocotillol II and methyl caffeate. Ocotillol II: $[\alpha]_{\text{D}} +28^\circ$ ($c=0.5$, CHCl_3). $^{13}\text{C-NMR}$ (CDCl_3) δ : 39.1 (C-1), 27.4 (C-2), 79.0 (C-3), 39.0 (C-4), 55.9 (C-5), 18.3 (C-6), 35.3 (C-7), 40.4 (C-8), 50.8 (C-9), 37.2 (C-10), 21.6 (C-11), 25.7 (C-12), 43.0 (C-13), 50.0 (C-14), 31.5 (C-15), 27.4 (C-16), 49.5 (C-17), 15.4 (C-18), 16.2 (C-19), 86.4 (C-20), 23.5 (C-21), 35.7 (C-22), 26.1 (C-23), 83.3 (C-24), 71.5 (C-25), 24.3 (C-26), 27.5 (C-27), 28.0 (C-28), 15.3 (C-29), 16.5 (C-30). The $^{13}\text{C-NMR}$ data were identical with those previously reported.²⁸⁾

References and Notes

- 1) Part I: Fuchino H., Satoh T., Tanaka N., *Chem. Pharm. Bull.*, **43**, 1937–1942 (1995).
- 2) Nagai M., Tanaka N., Tanaka O., Ichikawa S., *Chem. Pharm. Bull.*, **21**, 2061–2065 (1973).
- 3) Ikekawa N., Ohta A., Seki M., Takahashi A., *Phytochemistry*, **11**, 3037–3040 (1972).
- 4) Ohara S., Yatagai M., Hayashi Y., *Mokuzai Gakkaishi*, **32**, 266–273 (1986).
- 5) Yokota M., Zenda H., Kosuge T., Yamamoto T., Torigoe Y., *Yakugaku Zasshi*, **98**, 1607–1612 (1978).
- 6) Terazawa M., Koga T., Okuyama H., Miyake M., *Mokuzai Gakkaishi*, **30**, 391–403 (1984).
- 7) Ohmoto T., Nikaido T., Ikuse M., *Chem. Pharm. Bull.*, **26**, 1437–1442 (1978).
- 8) Rickling B., Glombitza K.-W., *Planta Med.*, **59**, 76–79 (1993).
- 9) a) Reichardt P. B., *J. Org. Chem.*, **46**, 4576–4578 (1981); b) Reichardt P. B., Green T. P., Chang S., *Phytochemistry*, **26**, 855–856 (1987); c) Taipale H. T., Vepsäläinen J., Laatikainen R., Reichardt P. B., Lapinjoki S. P., *Phytochemistry*, **34**, 755–758 (1993).
- 10) Williams D. E., Sinclair A. R. E., Andersen R. J., *Phytochemistry*, **31**, 2321–2324 (1992).
- 11) Groweiss A., Kashman Y., *Tetrahedron*, **39**, 3385–3396 (1983).
- 12) Tanaka N., Murakami T., Saiki Y., Chen C.-M., *Chem. Pharm. Bull.*, **26**, 3580–3582 (1978).
- 13) Hejnov K., Jarolin V., Sorm F., *Collection Czech. Chem. Commun.*, **30**, 1009–1015 (1965).
- 14) Cole B. J. W., Bentley M. D., Hua Y., *Holzforchung*, **45**, 265–268 (1991).
- 15) The content of betulin in the outer bark of *B. ermanii*, which is pale white, is below 5%.¹⁾
- 16) Nagai M., Kenmochi N., Fujita M., Furukawa N., Inoue T., *Chem. Pharm. Bull.*, **34**, 1056–1060 (1986).
- 17) Nomura M., Tokoroyama T., Kubota T., *Phytochemistry*, **20**, 1097–1104 (1981).
- 18) Nagumo S., Kaji N., Inoue T., Nagai M., *Chem. Pharm. Bull.*, **41**, 1255–1257 (1993).
- 19) Greca M. D., Monaco P., Previtera L., *J. Nat. Prod.*, **53**, 1430–1435 (1990).
- 20) Ohtani I., Kusumi T., Kashman Y., Kakisawa H., *J. Am. Chem. Soc.*, **113**, 4092–4096 (1991).
- 21) Asakawa J., Kasai R., Tanaka O., *Tetrahedron*, **33**, 1935–1939 (1977).
- 22) Inoue T., Ishidate Y., Fujita M., Kubo M., Fukushima M., Nagai M., *Yakugaku Zasshi*, **98**, 41–46 (1978).
- 23) Klischies M., Zenk M. H., *Phytochemistry*, **17**, 1281–1284 (1978).
- 24) Kasai R., Suzuo M., Asakawa J., Tanaka O., *Tetrahedron Lett.*, **1977**, 175–178; Tori K., Seo S., Yoshimura Y., Arita H., Tomita Y., *ibid.*, **1977**, 179–182.
- 25) Lemieux R. U., Koto S., *Tetrahedron*, **30**, 1933–1944 (1974).
- 26) Pan H., Lundgren L. N., *Phytochemistry*, **36**, 79–83 (1994).
- 27) Tori M., Matsuda R., Sono M., Asakawa Y., *Magnetic Resonance Chemistry*, **26**, 581–590 (1988).
- 28) Tanaka R., Masuda K., Matsunaga S., *Phytochemistry*, **32**, 472–474 (1993).