Regular Article

Megastigmane Glucosides and Megastigmanes from the Leaves of *Meliosma lepidota* ssp. *squamulata*

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From the leaves of *Meliosma lepidota* ssp. *squamulata*, megastigmane glucosides with *spiro*-structures and megastigmanes were isolated. Their structures were determined by X-ray crystallographic analyses and spectroscopic investigation. The absolute structures of the megastigmanes were determined by the modified Mosher's method.

Key words *Meliosma lepidota* ssp. *squamulata*; Sabiaceae; megastigmane glucoside; megastigmane

Meliosma lepidota Blume ssp. *squamulata* (Hance) Beusekom (syn. *M. squamulata* Hance) is a tall evergreen tree belonging to the family Sabiaceae. However, the International Plant Names Index currently classifies *Meliosma* species in the Meliosmaceae.[1] Whereas the latest taxonomic publication observes the classical taxon Sabiaceae.[2] The Sabiaceae comprises about one hundred species in five major genera, and *M. lepidota* ssp. *squamulata* grows wild in the Amami Islands, the Okinawa Islands, Taiwan and Southern China.[3] This plant is also known as a feeding plant for the larvae of a butterfly, *Dichorragia nesimachus*.[4] There has been no report on the constituents of the title plant and its medicinal use is also uncertain. This paper deals with isolation work on the plant.

Results and Discussion

Chromatographic isolation work on the 1-butyl alcohol (BuOH)-soluble fraction of a methanol (MeOH) extract of the title plant afforded five new megastigmane glucosides, named melionosides A–E (**1**–**5**), and two megastigmanes, named meliosma-ionols A (**6**) and B (**7**), as well as four known megastigmane glucosides, scorospiroside (**8**),[5] citroside A (**9**),[6] dihydrosyringin (**10**),[7] and (*Z*)-hex-3-en-1-ol *β*-D-glucopyranoside (**11**)[8] (Fig. 1). The structures of the new compounds were mainly elucidated by NMR spectroscopic investigation. X-Ray crystallographic analysis was performed for melionoside A (**1**), and the modified Mosher's method was applied for determination of the absolute stereochemistry of meliosma-ionols (**6**, **7**). Those of known glucosides were identified by comparison of their spectroscopic data with those reported in the literature.

Melionoside A (**1**), $[\alpha]_D^{25}$ −36.3, was isolated as colorless needles and its elemental composition was determined to be $C_{19}H_{34}O_9$ by high-resolution (HR)-electrospray ionization (ESI)-MS. The IR spectrum showed a strong absorption band at 3433 cm^{-1} attributable to stretching signals for hydroxy groups. The ^{1}H-NMR spectrum exhibited three singlet methyl (δ_H 1.07, 1.16 and 1.19), one doublet methyl (δ_H 1.20), three oxymethine proton (δ_H 3.38, 3.88 and 4.10), and one anomeric proton (δ_H 4.29) resonance. The ^{13}C-NMR exhibited six signals assignable as those of the glucopyranose moiety, and the remaining 13 signals comprised those of four methyls, three methylenes, three oxymethines, two oxygenated tertiary carbons and one quaternary carbon (Table 1). From the above evidence, **1** was expected to be a megastigmane glucoside and due to three degrees of unsaturation, the aglycone must have a bicyclic system. The ^{1}H–^{1}H correlation spectroscopic (COSY) spectrum indicated the presence of two proton–proton sequences, –C(2)H–C(3)H–C(4)H_2– and –C(7)$_2$–C(8)$_2$–C(9)H–C(10)H_3, and diagnostic heteronulear multiple bond correlation (HMBC) spectroscopy (Fig. 2) suggested a planar structure of **1**, as shown in Fig. 1, and the position of sugar attachment to be the hydroxy group at the 2-position. However, the crucial HMBC correlation from H-9 (δ_H 4.10) and C-6 (δ_C 92.9), which supports the presence of a *spiro*-ring was, not observed (Fig. 2). Accordingly, **1** was subjected to X-ray crystallographic analysis and Fig. 3 shows an ORTEP drawing of it. The absolute structure of the aglycone was confirmed by HPLC analysis of the glucose, which was found to be of the D-series. Therefore, the structure of melionoside A (**1**) was elucidated to be (2*R*,3*R*,5*R*,6*R*,9*R*)-2,3,5-trihydroxy-megastigman-6,9-epoxide 2-*O*-*β*-D-glucopyranoside, as shown in Fig. 1.

Melionoside B (**2**), $[\alpha]_D^{24}$ −25.3, was isolated as an amorphous powder and its elemental composition was the same as that of melionoside A (**1**). The ^{13}C-NMR spectrum exhibited the same functional groups as those of **1**, and the coupling pattern of the protons on the six membered-ring was essentially the same that of **1**. Since other NMR spectroscopic data showed good similarity to those of **1**, melionoside B (**2**) was expected to be an isomeric compound of **1** as to the 6-position and/or 9-position. A phase-sensitive (PS) nuclear Overhauser exchange spectroscopy (NOESY) correlation, *i.e.*, between H-7b (δ_H 1.98) and H_3-12 (δ_H 1.08) (Fig. 4b), as was also seen for **1** (Fig. 4a), which suggested the configuration at the 6-position was the same as that of **1**, and that between H-9 and H_3-11 enabled assignment of the absolute configuration at

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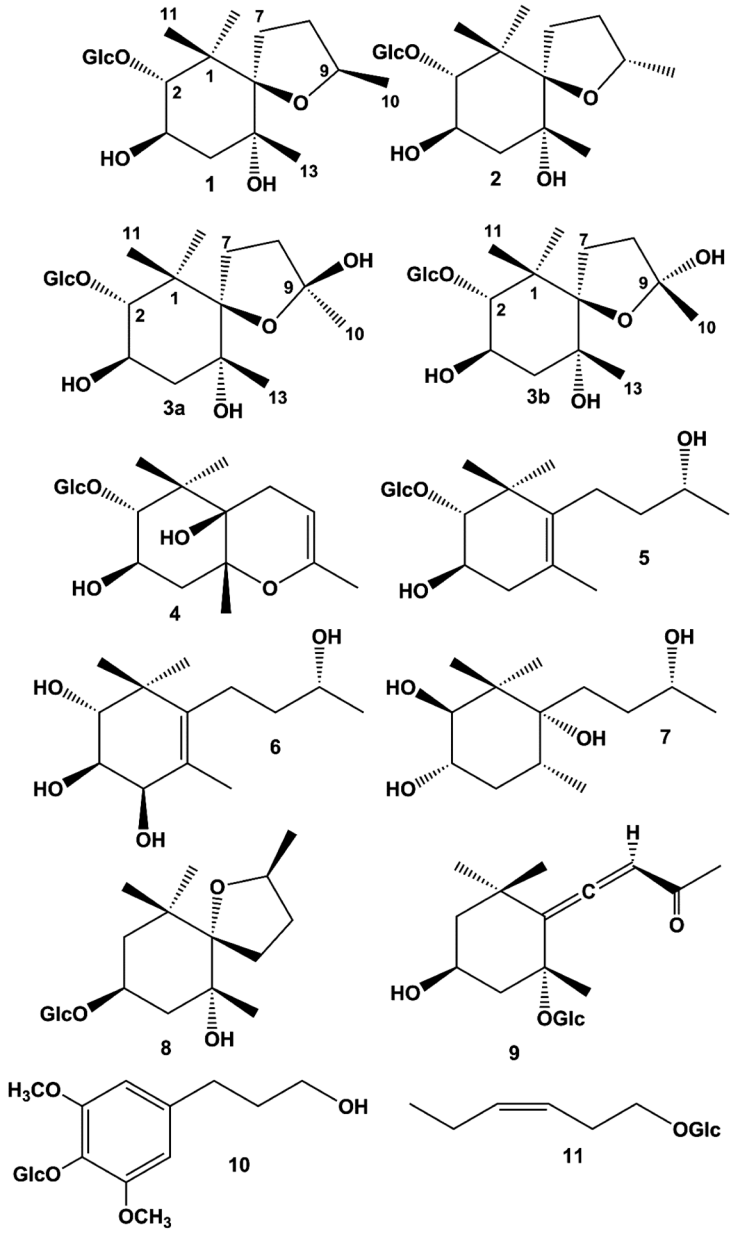

Fig. 1. Structures of Compounds Isolated

the 9-position as *S*, which is the opposite to that of **1** (Fig. 3). Therefore, the structure of melionoside B (**2**) was established to be (2*R*,3*R*,5*R*,6*R*,9*S*)-2,3,5-trihydroxymegastiman-6,9-epoxide 2-*O*-*β*-D-glucopyranoside, as shown in Fig. 1.

Melionoside C (**3**), $[\alpha]_D^{27}$ −13.3, was isolated as an amorphous powder and its elemental composition was determined to be $C_{19}H_{34}O_{10}$. Melionoside C (**3**) was first isolated by HPLC as two peaks, which were, however, found to be interconvertible. The NMR spectra revealed that the two closely related compounds existed as minor (**3a**) and major (**b**) isomers in a ratio of approximately 1 : 2 in CD_3OD as well as in pyridine-d_5. NMR spectra also revealed that the two isomers possessed glucopyranose as a sugar component, and the functionalities of the aglycone moieties were similar to those of **1** and **2**, except for the presence of ketal carbons (δ_C 107.8 and 107.3) and the absence of one oxygenated methine carbon. The degrees of unsaturation also suggested that the aglycone moieties comprised bicyclic ring systems. The hydrogen atoms of the three hydroxy groups at the C-3, C-5 and C-9 positions were assigned in the ^{1}H-NMR spectrum for pyridine-d_5, and HMBC correlations between 9-OH (δ_H 7.14) and C-8 (δ_C 40.8) and C-9 (δ_C 107.2), and H_3-10 (δ_H 1.82) and C-8 and C-9 together with the COSY relationship between H_2-7 and H_2-8 clearly demonstrated that the ketal carbon was at the 9-position (**3a**), such correlations being found in **3b**, and PS-NOESY correlations between H_3-10 (δ_H 1.81) and H_3-13 (δ_H 1.47) in **3a** and 9-OH (δ_H 7.00) and H_3-13 (δ_H 1.47) in **3b** substantiated that the minor isomer had the 9*S* configuration and the major one the 9*R* configuration (Fig. 5). Therefore, the structure of **3** was depicted as a mixture of two interconvertible isomers, **3a** (minor) and **b** (major), as shown in Fig. 1.

Melionoside D (**4**), $[\alpha]_D^{27}$ −11.8, was isolated as an amorphous powder and its elemental composition was determined to be $C_{19}H_{32}O_9$. A total of 19 signals was observed in the ^{13}C-NMR spectrum, six of which were assignable as those of a glucopyranose unit. The remaining 13 carbons com-

Table 1. ^{13}C-NMR Spectroscopic Data for Melionosides A–E (**1**–**5**), and Meliosma-Ionols A and B (**6** and **7**) (150 MHz, CD_3OD)

C	1	2	3a	3b	4	5	6	7
1	46.0	47.7	47.3 (46.9)[a)]	46.0 (46.7)[a)]	46.6 (46.7)[a)]	44.0	43.5	46.3
2	91.3	92.4	91.5 (91.5)	92.0 (92.9)	90.8 (91.9)	92.5	74.9	79.2
3	67.8	67.8	67.9 (67.2)	67.8 (67.0)	67.2 (66.7)	67.5	71.0	71.7
4	44.2	43.4	44.2 (45.3)	43.3 (44.4)	41.7 (42.5)	40.8[c)]	73.5	38.1
5	77.3	76.3	76.7 (75.8)	76.8 (75.9)	80.3 (80.4)	124.4	127.4	35.4
6	92.9	92.6	95.1 (94.4)	95.2 (94.5)	73.8 (73.4)	137.9	143.0	78.0
7	28.7	29.0	27.7 (27.7)	27.4 (27.4)	30.6 (30.9)	25.8	26.3	33.9
8	36.0	36.2	40.8 (40.8)	40.2 (40.2)	97.6 (97.5)	40.7[c)]	40.0	35.6
9	78.2	78.8	107.8 (107.2)	107.3 (106.8)	149.6 (149.2)	69.1	69.1	69.9
10	21.2	21.1	28.3 (29.0)	28.0 (28.9)	19.9 (20.5)	23.3	23.3	23.7
11	23.7	23.7	24.0 (24.2)	24.8 (25.0)	22.4[b)](23.0)	22.9	20.8	17.7
12	19.9	19.2	20.0 (20.5)	19.8 (20.5)	17.8 (18.2)	25.6	26.0	21.4
13	27.6	27.7	28.5 (29.3)	28.2 (28.4)	22.5[b)](23.1)	19.6	18.2	16.4
1′	105.9	106.1	106.0 (106.5)	105.9 (106.5)	106.1 (106.9)	106.2		
2′	75.5	75.6	75.6 (75.7)	75.5 (75.6)	75.5 (76.0)	75.5		
3′	78.1	78.3	78.2 (78.7)	78.2 (78.7)	78.2 (79.1)	78.2[d)]		
4′	71.4	71.5	71.4 (71.5)	71.4 (71.6)	71.4 (71.9)	71.4		
5′	78.0	78.1	78.1 (78.3)	78.1 (78.5)	78.2 (78.8)	78.1[d)]		
6′	62.4	62.5	62.4 (62.4)	62.5 (62.6)	62.5 (62.9)	62.5		

a) Data for pyridine-d_5. *b*)–*d*) Interchangeable.

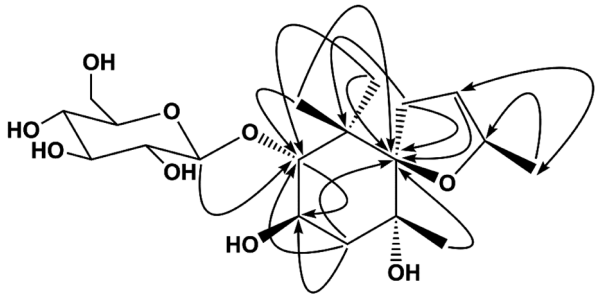

Fig. 2. Diagnostic HMBC Correlations of **1**

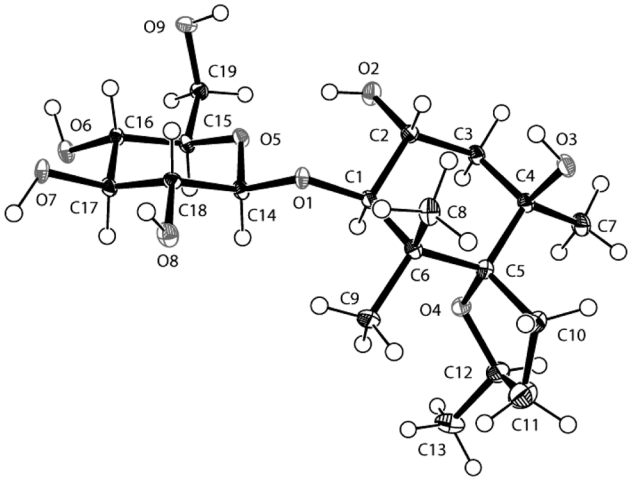

Fig. 3. Computer Generated ORTEP Drawing of **1**

The structure has crystallographic numbering.

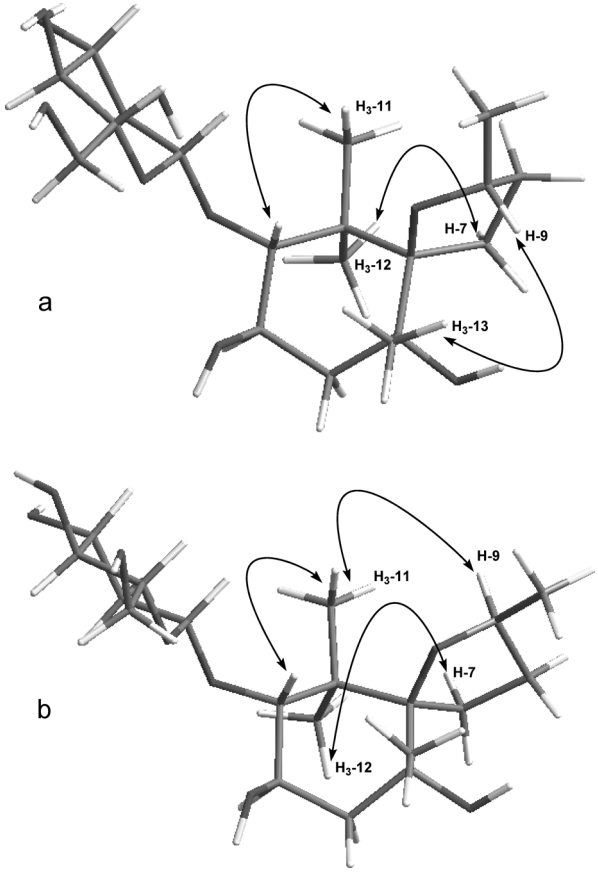

Fig. 4. PS-NOESY Correlations of **1** (a) and **2** (b)

prised those of four methyls, two methylenes, two oxygenated methines, two oxygenated tertiary carbons, one quaternary carbon and a trisubstituted double bond representing a magastigmane skeleton, and three degrees of unsaturation in the aglycone indicated a bicyclic system. One of the double bond carbons was highly deshielded (δ_C 149.6) and was implied to carry an electronegative substituent. The above mentioned functionalities indicated a structure formed on dehydration between 9-OH and H-8 of **3a** or **b**, and placed a double bond

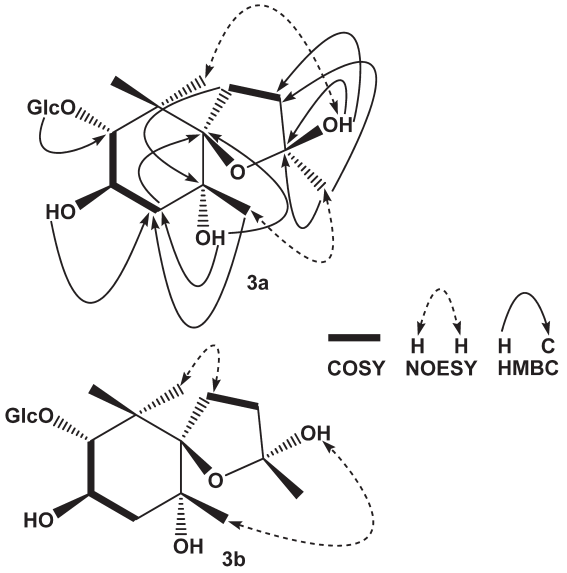

Fig. 5. Two-Dimensional Correlations of **3a** and **3b**

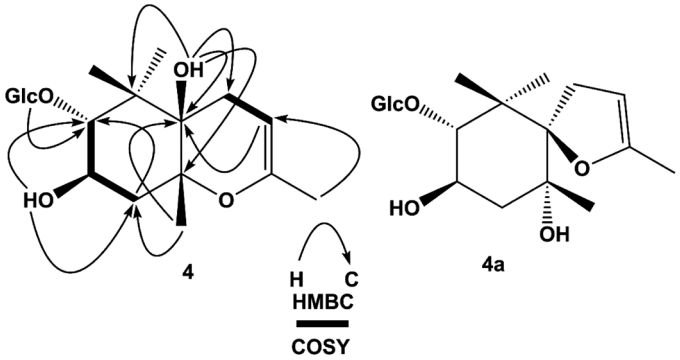

Fig. 6. COSY and HMBC Correlations for **4**

between C-8 and C-9, giving probable compound **4a** in Fig. 6. However, some HMBC correlations in pyridine-d_5 did not support this structure. In pyridine-d_5, two hydrogens on the hydroxy groups appeared at δ_H 5.33 and 6.11, the former being assigned to 3-OH from HMBC correlations with C-2 and C-4. The latter showed correlation cross peaks with C-1 and C-7, which should not be observed in the case of **4a** (Fig. 6). Therefore, the structure of **4** must be depicted as a bicyclic 4a,5,6,7,8,8a-hexahydro-*4H*-chromene system, instead of a spiro skeleton (**4a**). The PS-NOESY correlation between 6-OH and H-2ax placed 6-OH and H-2ax on the same side (Fig. 6). Therefore, the structure of **4** is as shown in Fig. 1.

Melionoside E (**5**), $[\alpha]_D^{22}$ −60.0, was isolated as an amorphous powder and its elemental composition was determined to be $C_{19}H_{32}O_9$. The ^{13}C-NMR spectrum exhibited 19 signals, six of which were assigned to those of a glucopyranose unit. The remaining 13 signals comprised those of four methyls, three oxymethines and one tetrasubstituted double bond, indicating a megastigmane skeleton. The COSY spectrum indicated the presence of two carbon sequences, such as –C(2)H–C(3)H–C(4)H_2– and –C(7)H_2–C(8)H_2–C(9)H–C(10)H_3, and the HMBC correlations shown in Fig. 7 connected these sequences and the double bond to establish the structure of **5**. The coupling constants

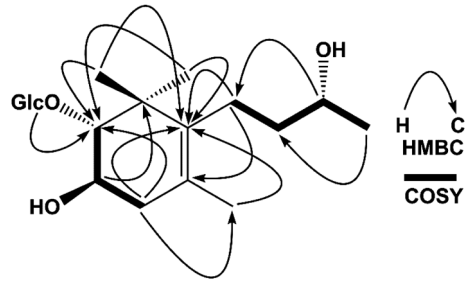

Fig. 7. COSY and HMBC Correlations for **5**

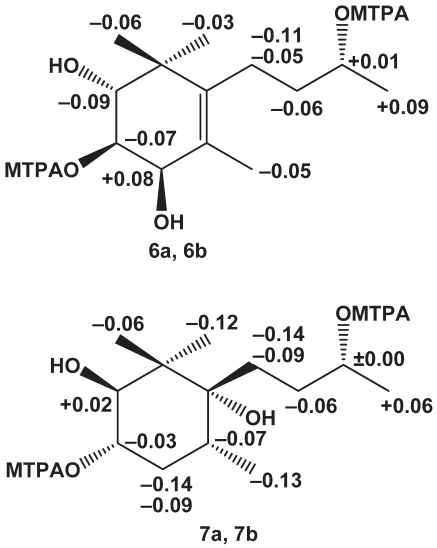

Fig. 8. Results with Modified Mosher's Method for **6** and **7**

between H-2 and H-3 (J=10.0 Hz) indicated these protons were in a diaxial orientation and to examine the absolute structure of the aglycone, **5** was enzymatically hydrolyzed to give **5a**. The aglycone **5a** was found to be a known compound, isolated from *Acer trucatum*[9] and NMR spectroscopically identical. Since the stereochemistry of the side chain remained uncertain,[10] the absolute structure of **5a** was examined by the modified Mosher's method[11] and it proved to be exactly the same compound as that isolated from *A. trucatum* (data not shown). Glucopyranose was analayzed by HPLC to be of the D-series and the mode of linkage was determined to be β from the coupling constant (J=7.6 Hz) of the anomeric proton. Therefore, the structure of melionoside E (**5**) was elucidated to be (2*R*,3*R*,9*R*)-2,3,9-trihydroxymegastigman-5-ene 2-*O*-β-D-glucopyranoside, as shown in Fig. 1.

Meliosma-ionol A (**6**), $[\alpha]_D^{22}$ −118, was isolated as a colorless syrup and its elemental composition was determined to be $C_{13}H_{24}O_4$. NMR spectroscopic data indicated that **6** was a non-glycosidic compound and 13 signals observed in the ^{13}C-NMR spectrum comprised those of four methyls, two methylenes, four oxymethines, one quaternary carbon and a tetrasubstituted double bond. The COSY spectrum indicated that three oxymethines were connected in a series manner, and two methylenes, one oxygenated methine and terminal methyl were found to form another sequence. HMBC correlations gave a megastigmane skeleton using these sequences together with the remaining three methyls and the double bond.

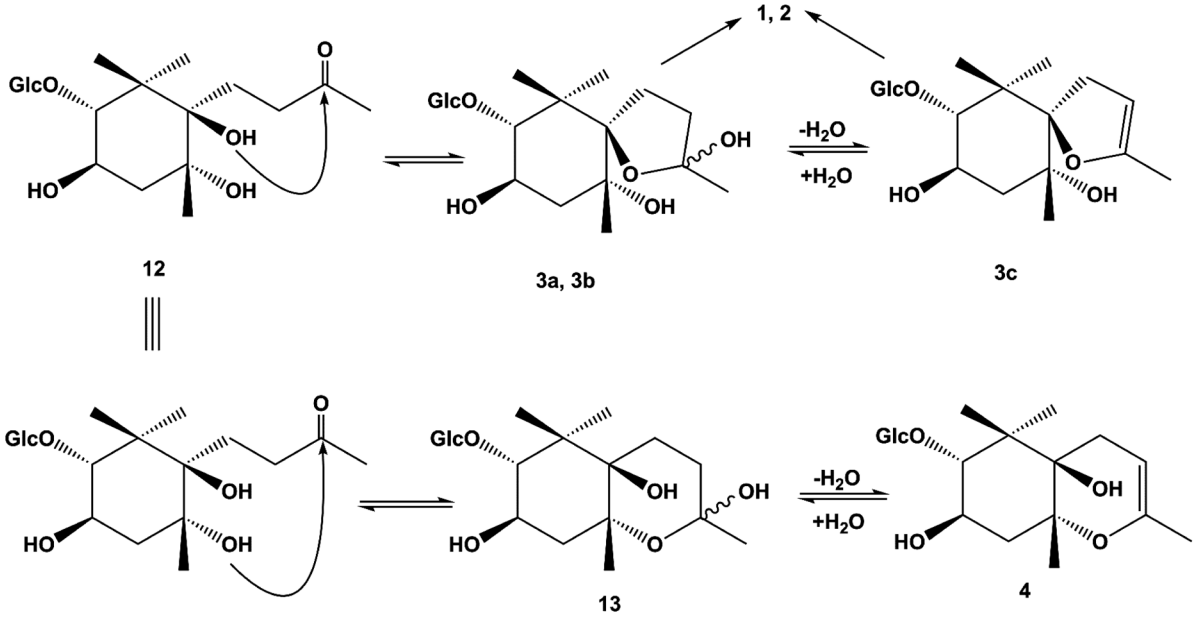

Fig. 9. Possible Relationship of Compounds **1**–**4**

The coupling constant (J=11.2 Hz) of H-2 indicated H-2 and H-3 were in *trans* diaxial positions, and from that (J=4.2 Hz) between H-3 and H-4, H-4 was in an equatorial orientation. Finally, the modified Mosher's method[11] (Fig. 8) was applied to **6** to establish its structure to be (2*R*,3*R*,4*R*,9*R*)-2,3,4,9-tetrahydroxymegastigman-5-ene, as shown in Fig. 1.

Meliosma-ionol B (**7**), $[\alpha]_D^{22}$ −0.45, was isolated as a colorless syrup and its elemental composition was determined to be $C_{13}H_{26}O_4$. NMR spectroscopic data indicated that **7** was also a megastigmane derivative with two singlet methyls, two doublet methyls, three methylenes and four hydroxy groups. The COSY spectrum established two proton sequences, C(2)H to C(13)H_3 and C(7)H_2 to C(10)H_3, which were connected through a quaternary carbon, C-1, and an oxygenated tertiary one, C-6, as shown in Fig. 1. The coupling constant (J=9.8 Hz) of H-2 indicated that H-2 and H-3 were in a *trans* diaxial geometry, and those of H-5 (J=12.6, 6.8, 4.2 Hz) with H-4 placed the C-13 methyl group in an equatorial position. From the PS-NOESY correlations, H-3 (δ_H 3.50) and H-5 (δ_H 1.98), H-5 and H_3-11 (δ_H 0.86), and H_2-7 (δ_H 1.64 and 1.67) and H_3-11, H-3, H-5, the side chain and H_3-11 were expected to be on the same face. Finally, the modified Mosher's method[11] (Fig. 8) established the absolute structure of **7** to be (2*S*,3*S*,5*R*,6*R*,9*R*)-2,3,6-trihydroxymegastigmane, as shown in Fig. 1.

From the leaves of *M. lepidota* ssp. *squamulata*, five new megastigmane glucoside, named melionosides A–E (**1**–**5**), and meliosma-ionols A (**6**) and B (**7**) were isolated, along with four known compounds. The structure of **1** was confirmed by X-ray crystallographic analyses. Melionoside C (**3**) was obtained as a mixture of interconvertible isomers, **3a** and **b**, their rate of conversion being fairly rapid, probably on an hour-time scale. The biosynthetic precursor of **3a** and **b** must be the 9-keto derivative, **12**, in Fig. 9. The ring closure between the 6-OH group and the ketone group forms a megastigmane glucoside possessing a *spiro*-structure at the 6-position and an interconvertible hemiketal at the 9-position. The alternative ring closure, between the 5-OH group and the ketone gives with a hemiketalic six-membered oxyrane derivative, **13**, which ends up as **4** through elimination of a water molecule. A dehydrated compound (**3c**) derived from **3a** and **c** may exist in the extract, although its isolation has not been successful so far. The formation of melionoside D (**4**) seems to be reversible, since after a week or so slight amounts of **3a** and **b** were found in the NMR sample solution of **4**, residual water molecules probably being picked up in pyridine-d_5. Due to the instability of **3a**, **b** and **4**, their absolute stereochemistries were not examined. However, since melionosides A and B (**1**, **2**) may be derivatives of **3a**, **b** or **c**, and the ^{13}C-NMR spectral data for the ring regions of melionosides A–D (**1**–**4**) exhibited close resemblance, they probably have the same absolute configurations.

Experimental

General Experimental Procedure Melting points were measured with a Yanagimoto micromelting point apparatus and are uncorrected. Optical rotations were measured on a JASCO P-1030 polarimeter and IR spectra on a Horiba FT-710 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were taken on a JEOL α-400 or Brucker Avance III 600 spectrometer at 400 MHz or 600 MHz, and 100 MHz or 150 MHz, respectively, with tetramethylsilane as an internal standard. Positive-ion HR-MS were taken with an Applied Biosystem QSTAR XL system ESI (Nano Spray)-MS.

A highly-porous synthetic resin (Diaion HP-20) was purchased from Mitsubishi Kagaku (Tokyo, Japan). Silica gel CC and reversed-phase [octadecylsilanized silica gel (ODS)] open CC were performed on silica gel 60 (Merck, Darmstadt, Germany) and Cosmosil 75C_{18}-OPN (Nacalai Tesque, Kyoto, Japan), respectively. The droplet counter-current chromatograph (DCCC) (Tokyo Rikakikai, Tokyo, Japan) was equipped with 500 glass columns (Φ=2 mm, L=40 cm), the lower and upper layers of a solvent mixture of $CHCl_3$–MeOH–H_2O–*n*-PrOH (9 : 12 : 8 : 2) being used as the stationary and mobile phases, respectively. Five-gram fractions were collected and numbered according to their order of elution with the mobile phase. HPLC was performed on an ODS column (Inertsil; GL Science, Tokyo, Japan), and the eluate was monitored

with a UV detector at 254 nm and a refractive index monitor. β-Glucosidase from almond, and (*R*)- and (*S*)-α-methoxy-α-trifluoromethylphenyl acetic acids (MTPA) were purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan).

Plant Material Leaves of *M. lepidota* ssp. *squamulata* were collected in Kunigami-gun, Okinawa, Japan, in July 2006, and a voucher specimen was deposited in the Herbarium of Pharmaceutical Sciences, Graduate School of Biomedical Sciences, Hiroshima University (06-MLS-Okinawa-0703).

Extraction and Separation Leaves of *M. lepidota* spp. *squamulata* (8.80 kg) were extracted three times with MeOH (4.5 L×3) at room temperature for one week and then concentrated to 3 L *in vacuo*. The concentrated extract was washed with *n*-hexane (3 L, 41.0 g), and then the MeOH layer was concentrated to a gummy mass. The latter was suspended in water (3 L) and then extracted with EtOAc (3 L) to give 104 g of an EtOAc-soluble fraction. The aqueous layer was extracted with 1-BuOH (3 L) to give a 1-BuOH-soluble fraction (125 g), and the remaining water-layer was concentrated to furnish 198 g of a water-soluble fraction.

The 1-BuOH-soluble fraction (124 g) was subjected to Diaion HP-20 CC (*Φ*=60 mm, *L*=46 cm), using H_2O–MeOH (4 : 1, 4 L), (3 : 2, 4 L), (2 : 3, 4 L), and (1 : 4, 4 L), and MeOH (4 L), 1 L-fractions being collected. The residue (18.0 g) in fractions 4–7 was subjected to silica gel (450 g) CC with increasing amounts of MeOH in $CHCl_3$ [$CHCl_3$ (6 L), and $CHCl_3$–MeOH (49 : 1, 3 L), (24 : 1, 3 L), (23 : 2, 3 L), (9 : 1, 3 L), (17 : 3, 3 L), (4 : 1, 3 L), (3 : 1, 3 L) and (7 : 3, 3 L)], 500-mL fractions being collected. The residue (706 mg) in fractions 34–38 was subjected to ODS CC [*Φ*=40 mm, *L*=25 cm, linear gradient: MeOH–H_2O (1 : 9, 2 L) → (9 : 1, 2 L), 10 g-fractions being collected] to give a residue (141 mg) in fractions 96–108 which was then purified by DCCC to give a residue (52.6 mg) in fractions 43–49. Final purification by HPLC (ODS, *Φ*=10 mm, *L*=25 cm; H_2O–MeOH, 3 : 2; flow rate: 2.8 mL/min) gave **6** (35.0 mg) and **7** (7.6 mg) from the peaks at 16 min and 18 min, respectively.

The residue (1.75 g) in fractions 39–43 obtained on silica gel CC was separated by ODS CC [*Φ*=40 mm, *L*=25 cm, linear gradient: MeOH–H_2O (1 : 9, 1 L) → (1 : 1, 1 L), and then (1 : 1, 1 L) → (9 : 1, 1 L), 10 g-fractions being collected] to give 318 mg of **9** in fractions 82–92. The residue (84.3 mg) in fractions 53–69 was separated by DCCC to give a residue (35.8 mg) in fractions 10–36, which was finally purified by HPLC [Cosmosil Cholester (Nakalai Tesque), *Φ*=10 mm, *L*=25 cm; H_2O–MeOH, 7 : 3; flow rate: 2.8 mL/min] to yield **3** (6.6 mg) from the peaks at 13 min and 16 min, and **4** (2.8 mg) from the peak at 47 min. The residue (41.3 mg) in fractions 76–79 was purified by DCCC to give 7.7 mg of **10** in fractions 32–38. The residue (80.6 mg) in fractions 107–112 was purified by DCCC to give 20.2 mg of **1** in fractions 25–27 as a crystalline state. The residue (101 mg) in fractions 113–121 was purified by DCCC to give 9.5 mg of **11** in fractions 53–60. The residue (111 mg) in fractions 122–131 was subjected to DCCC and then the residue (40.2 mg) in fractions 33–39 was purified by HPLC (*Φ*=6 mm, *L*=25 cm; H_2O–MeOH, 13 : 7; flow rate: 1.6 mL/min) to give 5.9 mg of **2** from the peak at 20 min. The residue (86.1 mg) in fractions 144–156 was separated by DCCC to give a residue (56.3 mg) in fractions 39–45, which was the purified by HPLC (ODS, *Φ*=10 mm, *L*=25 cm; H_2O–MeOH, 20 : 7; flow rate: 2.8 mL/min) to afford 26.3 mg of **5** from the peak at 28 min. The residue (86.1 mg) in fractions 157–175 was purified by DCCC to give 16.9 mg of **8** in fractions 53–60.

Melionoside A (**1**)

Colorless needles; mp 223–225°C; $[\alpha]_D^{25}$ −36.3 (*c*=0.51, MeOH); IR ν_{max} (KBr) cm^{-1}: 3433, 2974, 2925, 2882, 1647, 1073, 1037, 1018; ^{1}H-NMR (600 MHz, CD_3OD) *δ*: 4.29 (1H, d, *J*=7.7 Hz, H-1′), 4.10 (1H, dqd, *J*=12.1, 11.9, 5.9 Hz, H-9), 3.88 (1H, ddd, *J*=11.5, 9.5, 5.3 Hz, H-3), 3.87 (1H, dd, *J*=11.7, 2.0 Hz, H-6′a), 3.68 (1H, dd, *J*=11.7, 4.9 Hz, H-6′b), 3.38 (1H, d, *J*=9.5 Hz, H-2), 3.33–3.40 (3H, m, H-3′, 4′ and 5′), 3.28 (1H, dd, *J*=8.9, 7.7 Hz, H-2′), 2.10 (1H, ddd, *J*=10.4, 10.3, 9.9 Hz, H-7a), 2.05 (1H, dddd, *J*=12.1, 10.4, 10.3, 1.6 Hz, H-8a), 1.95 (1H, ddd, *J*=10.3, 10.2. 1.6 Hz, H-7b), 1.89 (1H, dd, *J*=13.3, 5.3 Hz, H-4a), 1.83 (1H, dd, *J*=13.3, 11.5 Hz, H-4b), 1.48 (1H, dddd, *J*=11.9, 10.3, 10.2, 9.9 Hz, H-8b), 1.20 (3H, d, *J*=5.9 Hz, H_3-10), 1.19 (3H, s, H_3-12), 1.16 (3H, s, H_3-13), 1.07 (3H, s, H_3-11); ^{13}C-NMR (150 MHz, CD_3OD): Table 1; HR-ESI-MS (positive-ion mode) *m/z*: 429.2089 $[M+Na]^+$ (Calcd for $C_{19}H_{34}O_9Na$: 429.2095).

Melionoside B (**2**)

Colorless needles; mp 220–222°C; $[\alpha]_D^{24}$ −25.3 (*c*=0.39, MeOH); IR ν_{max} (film) cm^{-1}: 3396, 2973, 2929, 2882, 1649, 1078, 1032, 1008; ^{1}H-NMR (600 MHz, CD_3OD) *δ*: 4.32 (1H, d, *J*=7.8 Hz, H-1′), 4.10 (1H, ddq, *J*=11.3, 10.9, 5.9 Hz, H-9), 3.88 (1H, ddd, *J*=10.5, 9.5, 6.1 Hz, H-3), 3.86 (1H, dd, *J*=11.9, 1.3 Hz, H-6′a), 3.68 (1H, dd, *J*=11.9, 5.2 Hz, H-6′b), 3.46 (1H, d, *J*=9.5 Hz, H-2), 3.33–3.40 (3H, m, H-3′, 4′ and 5′), 3.27 (1H, dd, *J*=9.0, 7.8 Hz, H-2′), 2.11 (1H, ddd, *J*=9.7, 9.5, 3.3 Hz, H-7a), 1.98 (1H, ddd, *J*=9.5, 9.5, 8.9 Hz, H-7b), 1.97 (1H, dddd, *J*=10.9, 10.7, 9.7, 9.5 Hz, H-8a), 1.77 (1H, dd, *J*=13.1, 6.1 Hz, H-4a), 1.76 (1H, dd, *J*=13.1, 10.5 Hz, H-4b), 1.47 (1H, br ddd, *J*=11.3, 10.7, 8.9 Hz, H-8b), 1.19 (1H, d, *J*=5.9 Hz, H_3-10), 1.13 (3H, s, H_3-13), 1.11 (3H, s, H_3-11), 1.08 (3H, s, H_3-12); ^{13}C-NMR (150 MHz, CD_3OD): Table 1; HR-ESI-MS (positive-ion mode) *m/z*: 429.2094 $[M+Na]^+$ (Calcd for $C_{19}H_{34}O_9Na$: 429.2095).

Melionoside C (**3**)

Amorphous powder, $[\alpha]_D^{27}$ −13.3 (*c*=0.26, MeOH); IR ν_{max} (film) cm^{-1}: 3374, 2979, 2941, 1587, 1483, 1376, 1159, 1076, 1029, 996; **3a**: ^{1}H-NMR (600 MHz, CD_3OD) *δ*: 4.28 (1H, d, *J*=7.9 Hz, H-1′), 3.89 (1H, m, H-3), 3.37 (1H, m, H-2), 3.86 (1H, dd, *J*=12.0, 2.1 Hz, H-6′a), 3.68 (1H, dd, *J*=12.0, 5.5 Hz, H-6′b), 3.27 (1H, m, H-2′), 3.34–3.33 (3H, m, H-3′, 4′ and 5′), 2.26 (1H, m, H-7a), 2.00 (3H, m, H-7b, 8a and 8b), 1.85 (1H, m, H-4a), 1.79 (1H, m, H-4b), 1.51 (3H, s, H_3-10), 1.34 (3H, s, H_3-13), 1.17 (3H, s, H_3-12), 1.10 (3H, s, H_3-11); (600 MHz, pyridine-d_5) *δ*: 7.14 (1H, brs, 9-OH), 5.86 (1H, brs, 5-OH), 5.36 (1H, brs, 3-OH), 5.02 (1H, overlapped with H_2O signal, H-1′), 4.60 (1H, m, H-3), 4.51 (1H, dd, *J*=11.7, 2.6 Hz, H-6′a), 4.36 (1H, m, H-6′b), 4.28 (1H, dd, *J*=9.1, 9.1 Hz, H-4′), 4.23 (1H, dd, *J*=9.1, 8.7 Hz, H-3′), 4.13 (1H, m, H-2′), 4.10 (1H, d, *J*=10.2 Hz, H-2), 4.00 (1H, ddd, *J*=9.1, 5.7, 2.6 Hz, H-5′), 2.75 (1H, m, H-7a), 2.50 (1H, m, H-4a), 2.49 (1H, m, H-4b), 2.34 (1H, m, H-8a), 2.25 (1H, m, H-7b), 2.15 (1H, m, H-8b), 1.92 (3H, s, H_3-13), 1.82 (3H, s, H_3-10), 1.77 (3H, s, H_3-12), 1.67 (3H, s, H_3-11); ^{13}C-NMR (150 MHz, CD_3OD and pyridine-d_5): Table 1; **3b**: ^{1}H-NMR (600 MHz, CD_3OD) *δ*: 4.31 (1H, d, *J*=7.9 Hz, H-1′), 3.89 (1H, m, H-3), 3.86 (1H, dd, *J*=12.0, 2.1 Hz, H-6′a), 3.68 (1H, dd, *J*=12.0, 5.5 Hz, H-6′b), 3.38 (1H, m, H-2), 3.34–3.33 (3H, m, H-3′, 4′ and 5′), 3.27 (1H, m, H-2′),

2.13 (2H, m, H_2-7), 1.93 (2H, m, H_2-8), 1.77 (2H, m, H_2-4), 1.49 (3H, s, H_3-13), 1.24 (3H, s, H_3-11), 1.15 (3H, s, H_3-10), 1.12 (3H, s, H_3-12); (600 MHz, pyridine-d_5) δ: 7.00 (1H, brs, 9-OH), 5.97 (1H, brs, 5-OH), 5.24 (1H, brs, 3-OH), 4.84 (1H, d, J=7.9 Hz, H-1′), 4.67 (1H, m, H-3), 4.58 (1H, dd, J=11.7, 2.6 Hz, H-6′a), 4.36 (1H, m, H-6′b), 4.24 (1H, dd, J=9.4, 9.1 Hz, H-4′), 4.15 (1H, dd, J=9.1, 8.7 Hz, H-3′), 4.10 (1H, m, H-2′), 4.07 (1H, d, J=9.4 Hz, H-2), 3.91 (1H, ddd, J=9.4, 5.7, 2.6 Hz, H-5′), 2.57 (1H, m, H-7a), 2.55 (1H, m, H-7b), 2.44 (1H, m, H-4a), 2.42 (1H, m, H-4b), 2.27 (1H, m, H-8a), 2.13 (1H, m, H-8b), 2.00 (3H, s, H_3-11), 1.81 (3H, s, H_3-10), 1.72 (3H, s, H_3-12), 1.47 (3H, s, H_3-13); ^{13}C-NMR (150 MHz, CD_3OD and pyridine-d_5): Table 1; HR-ESI-MS (positive-ion mode) m/z: 445.2044 $[M+Na]^+$ (Calcd for $C_{19}H_{34}O_{10}Na$: 445.2044).

Melionoside D (**4**)

Amorphous powder, $[\alpha]_D^{27}$ −11.8 (c=0.13, MeOH); IR ν_{max} (film) cm^{-1}: 3382, 2980, 2927, 1587, 1379, 1328, 1159, 1052, 1029, 1014; ^{1}H-NMR (600 MHz, CD_3OD) δ: 4.47 (1H, ddq, J=4.9, 2.3, 1.1 Hz, H-8), 4.29 (1H, d, J=7.8 Hz, H-1′), 3.87 (1H, dd, J=11.7, 2.3 Hz, H-6′a), 3.85 (1H, ddd, J=13.6, 9.8, 5.3 Hz, H-3), 3.68 (1H, dd, J=11.7, 5.1 Hz, H-6′b), 3.50 (1H, d, J=9.8 Hz, H-2), 3.20–3.38 (3H, m, H-3′, 4′ and 5′), 3.26 (1H, dd, J=9.1, 7.8 Hz, H-2′), 2.33 (1H, ddq, J=17.1, 4.9, 1.3 Hz, H-7a), 1.99 (1H, dd, J=11.7, 5.3 Hz, H-4a), 1.91 (1H, ddq, J=17.1, 2.3, 2.3 Hz, H-7b), 1.85 (1H, dd, J=13.6, 11.7 Hz, H-4b), 1.61 (3H, ddd, J=2.3, 1.3, 1.1 Hz, H_3-10), 1.23 (3H, s, H_3-11), 1.16 (3H, s, H_3-12), 1.00 (3H, s, H_3-13); (600 MHz, pyridine-d_5) δ: 6.11 (1H, brs, 6-OH), 5.33 (1H, brs, 3-OH), 4.97 (1H, overlapped with H_2O signal, H-1′), 4.55 (1H, m, H-8), 4.54 (1H, m, H-6′a), 4.51 (1H, ddd, J=10.2, 9.6, 6.0 Hz, H-3), 4.36 (1H, dd, J=11.3, 5.2 Hz, H-6′b), 4.27 (1H, d, J=9.6 Hz, H-2), 4.25 (1H, dd, J=9.4, 9.1 Hz, H-4′), 4.21 (1H, dd, J=9.1, 8.7 Hz, H-3′), 4.11 (1H, m, H-2′), 3.97 (1H, ddd, J=9.4, 5.2, 2.3 Hz, H-5′), 2.57 (1H, br dd, 17.3, 3.6 Hz, H-7a), 2.54 (1H, dd, 13.6, 6.0 Hz, H-4a), 2.51 (1H, dd, J=13.6, 10.2 Hz, H-4b), 2.28 (1H, ddq, J=17.3, 2.3, 1.9 Hz, H-7b), 1.79 (3H, s, H_3-11), 1.70 (3H, brs, H_3-10), 1.53 (3H, s, H_3-13), 1.45 (3H, s, H_3-12); ^{13}C-NMR (150 MHz, CD_3OD and pyridine-d_5): Table 1; HR-ESI-MS (positive-ion mode) m/z: 427.1939 $[M+Na]^+$ (Calcd for $C_{19}H_{32}O_9Na$: 427.1936).

Melionoside E (**5**)

Amorphous powder, $[\alpha]_D^{22}$ −60.0 (c=0.58, MeOH); IR ν_{max} (film) cm^{-1}: 3335, 2967, 1650, 1557, 1512, 1456, 1160, 1078, 1035, 996; ^{1}H-NMR (600 MHz, CD_3OD) δ: 4.35 (1H, d, J=7.6 Hz, H-1′), 3.87 (1H, dd, J=12.1, 1.7 Hz, H-6′a), 3.79 (1H, ddd, J=10.0, 9.7, 6.8 Hz, H-3), 3.71 (1H, m, H-9), 3.68 (1H, m, H-6′b), 3.36 (2H, m, H-3′ and 5′), 3.34 (1H, m, H-4′), 3.29 (1H, m, H-2′), 3.27 (1H, d, J=10.0 Hz, H-2), 2.34 (1H, dd, J=17.0, 6.8 Hz, H-4a), 2.23 (1H, m, H-7a), 2.05 (1H, dd, J=17.0, 9.7 Hz, H-4b), 1.63 (3H, s, H_3-13), 1.22 (3H, s, H_3-12), 1.91 (1H, ddd, J=15.1, 10.2, 6.8 Hz, H-7b), 1.50 (2H, m, H_2-8), 1.17 (3H, d, J=6.4 Hz, H_3-10), 1.03 (3H, s, H_3-11); ^{13}C-NMR (150 MHz, CD_3OD): Table 1; HR-ESI-MS (positive-ion mode) m/z: 413.2140 $[M+Na]^+$ (Calcd for $C_{19}H_{32}O_9Na$: 413.2146).

Meliosma-ionol A (**6**)

Colorless syrup, $[\alpha]_D^{22}$ −118 (c=0.58, MeOH); IR ν_{max} (film) cm^{-1}: 3386, 2969, 1651, 1512, 1457, 1118, 1083, 1038, 963; ^{1}H-NMR (600 MHz, CD_3OD) δ: 3.87 (1H, d, J=4.2 Hz, H-4), 3.73 (1H, qdd, J=6.4, 6.1, 6.1 Hz, H-9) 3.53 (1H, dd, J=11.2, 4.2 Hz, H-3), 3.48 (1H, d, J=11.2 Hz, H-2), 2.25 (1H, ddd, J=13.2, 12.1, 5.7 Hz, H-7a), 1.96 (1H, ddd, J=13.2, 12.5, 5.3 Hz, H-7b), 1.56 (1H, m, H-8a), 1.51 (1H, m, H-8b), 1.77 (3H, s, H_3-13), 1.17 (3H, d, J=6.4 Hz, H_3-10), 1.13 (3H, s, H_3-12), 0.94 (3H, s, H_3-11); ^{13}C-NMR (150 MHz, CD_3OD): Table 1; HR-ESI-MS (positive-ion mode) m/z: 267.15670 $[M+Na]^+$ (Calcd for $C_{13}H_{24}O_4Na$: 267.1567).

Meliosma-ionol B (**7**)

Colorless syrup, $[\alpha]_D^{22}$ −0.45 (c=0.44, MeOH); IR ν_{max} (film) cm^{-1}: 3368, 2970, 1650, 1458, 1373, 1108, 1048, 1012, 967; ^{1}H-NMR (600 MHz, CD_3OD) δ: 3.56 (1H, tq, J=6.8, 6.0 Hz, H-9), 3.50 (1H, ddd, J=11.7, 9.8, 5.3 Hz, H-3), 3.41 (1H, d, J=9.8 Hz, H-2), 1.98 (1H, dqd, J=12.6, 6.8, 4.2 Hz, H-5), 1.70 (1H, ddd, J=12.8, 5.3, 4.2 Hz, H-4a), 1.67 (1H, dt, J=16.0, 7.8 Hz, H-7a), 1.64 (1H, dt, J=16.0, 7.8 Hz, H-7b), 1.54 (2H, dd, J=7.8, 6.8 Hz, H_2-8), 1.50 (1H, ddd, J=12.8, 12.6, 11.7 Hz, H-4b), 1.16 (3H, d, J=6.0 Hz, H_3-10), 1.05 (3H, s, H_3-12), 0.93 (3H, d, J=6.8 Hz, H_3-13), 0.86 (3H, s, H_3-11); ^{13}C-NMR (100 MHz, CD_3OD): Table 1; HR-ESI-MS (positive-ion mode) m/z: 267.1722 $[M+Na]^+$ (Calcd for $C_{13}H_{26}O_4Na$: 267.1723).

Sugar Analysis About 500 μg each of melionosides A–E (**1–5**) was hydrolyzed with 1 M HCl (0.1 mL) at 90°C for 2 h. The reaction mixtures were partitioned with an equal amount of EtOAc (0.1 mL), and the water layers were analyzed with a chiral detector (JASCO OR-2090*plus*) on an amino column [Asahipak NH_2P-5 4E; CH_3CN–H_2O, 4 : 1; flow rate 1 mL/min]. Melionosides A–E (**1–5**) each gave a peak for D-glucose at the retention time of 13.7 min with a positive optical rotation sign. The peak was identified by co-chromatography with authentic D-glucose.

X-Ray Analysis of Melionoside A (1) A suitable crystal (0.42 mm×0.07 mm×0.05 mm) was used for analysis. The data were measured using a Bruker SMART 1000 CCD diffractometer, using Mo$K\alpha$ graphite-monochromated radiation (λ=0.71073 Å). The structure was solved by a direct method using the program SHELXTL-97.[12] The refinement and all further calculations were carried out using SHELXTL-97. The absorption correction was carried out utilizing the SADABS routine.[13] The H atoms were included at calculated positions and treated as riding atoms using the SHELXTL default parameters. Figure 3 was drawn with ORTEP32.[14] Crystal data: $C_{19}H_{34}O_9$, M=406.46 g mol^{-1}, monoclinic, $C2$, a=22.469(5) Å, b=6.3195(13) Å, c=14.461(3) Å, β=102.844(3)°, V=2002.0(7) Å^3, T=90 K, Z=4, D_c=1.349 g cm^{-3}, μ(Mo$K\alpha$)=0.106 mm^{-1}, F(000)=880, 6056 reflections were measured in the range of 2θ<56.66°, 3851 being unique and used in all calculations. The final goodness-of-fit on F^2 was 1.066, and the final R indices were R_1=0.0459 based on $I>2\sigma(I)$, and wR_2=0.1411 with all data. The largest differences between the peak and the hole were 0.733 and −0.337 eÅ^{-3}, respectively. The CCDC deposit contains supplementary crystallographic data (No. 1033761) These data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223 336 033; or e-mail: deposit@ccdc.cam.ac.uk.

Enzymatic Hydrolysis 5 to 5a Melionoside E (**5**: 5.1 mg) was hydrolyzed with 5 mg of β-glucosidase in 1 mL of acetate buffer (pH 5.0, 20 mM) at 37°C for 11 h. The reaction mixture was subjected to silica gel CC (Φ=2.5 cm, L=20 cm) with increasing amounts of MeOH in $CHCl_3$ [$CHCl_3$ (200 mL), and $CHCl_3$–MeOH (19 : 1, 100 mL), (9 : 1, 100 mL), (17 : 3, 100 mL), (4 : 1, 100 mL), (3 : 1, 100 mL), and (7 : 3, 100 mL)] and MeOH

(200 mL), 5-g fractions being collected. **5a** (2.3 mg) was obtained in fractions 114–119 and D-glucose in the MeOH eluate. **5a:** Colorless syrup, $[\alpha]_D^{21}$ −78.7 (c=0.15, $CHCl_3$), {$[\alpha]_D^{25}$ −66.3 (c=0.056, $CHCl_3$)}[9]; ^{1}H-NMR (600 MHz, $CDCl_3$) δ: 3.81 (1H, m, H-9), 3.77 (1H, ddd, J=9.8, 9.8, 6.4 Hz, H-3), 3.27 (1H, d, J=9.8 Hz, H-2), 2.33 (1H, dd, J=16.6, 6.4 Hz, H-4a), 2.22 (1H, m, H-7a), 2.06 (1H, dd, J=16.6, 9.8 Hz, H-4b), 1.91 (1H, m, H-7b), 1.63 (3H, s, H_3-13), 1.52 (2H, m, H_2-8), 1.22 (3H, d, J=6.1 Hz, H_3-10), 1.13 (3H, s, H_3-11), 0.93 (3H, s, H_3-12); ^{13}C-NMR (150 MHz, $CDCl_3$): essentially identical data with those reported in ref. 9; ^{1}H-NMR (600 MHz, CD_3OD) δ: 3.70 (1H, dq, J=6.5, 6.2 Hz, H-9), 3.67 (1H, ddd, J=10.1, 9.9, 6.5 Hz, H-3), 3.15 (1H, d, J=10.1 Hz, H-2), 2.27 (1H, dd, J=16.9, 6.5 Hz, H-4a), 2.22 (1H, m, H-7a), 2.01 (1H, dd, J=16.9, 9.9 Hz, H-4b), 1.91 (1H, ddd, J=15.1, 10.2, 6.8 Hz, H-7b), 1.62 (3H, s, H_3-13), 1.50 (2H, m, H_2-8), 1.17 (3H, d, J=6.2 Hz, H_3-10), 1.11 (3H, s, H_3-12), 0.93 (3H, s, H_3-11); ^{13}C-NMR (150 MHz, CD_3OD) δ: 138.3 (C-6), 124.5 (C-5), 81.1 (C-2), 69.2 (C-9), 68.7 (C-3), 43.2 (C-1), 41.3 (C-4), 40.7 (C-8), 26.9 (C-12), 26.05 (C-7), 23.3 (C-10), 22.0 (C-11), 19.7 (C-13).

Preparation of (*R*)- and (*S*)-MTPA Diesters (5b and c) from 5a A solution of **5a** (0.7 mg) in 1 mL of dehydrated CH_2Cl_2 was reacted with (*R*)-MTPA (11.1 mg) in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC) (11.1 mg) and *N*,*N*′-dimethyl-4-aminopyridine (4-DMAP) (10.0 mg), and then the mixture was occasionally stirred at 37°C for 12 h. After the addition of 1 mL of CH_2Cl_2, the solution was washed with H_2O (1 mL), 1 M HCl (1 mL), $NaHCO_3$-saturated H_2O (1 mL), and then brine (1 mL), successively. The organic layer was dried over Na_2SO_4 and then evaporated under reduced pressure. The residue was purified on a preparative TLC [silica gel (0.25 mm thickness), being applied for 9 cm, developed with $CHCl_3$–$(CH_3)_2CO$ (19 : 1) for 9 cm, and then eluted with $CHCl_3$–MeOH (5 : 1)] to furnish an ester, **5b** (0.1 mg). Through a similar procedure, **5c** (0.4 mg) was prepared from **5b** (0.7 mg) using (*S*)-MTPA (13.0 mg), EDC (10.5 mg), and 4-DMAP (15.7 mg). **5b**: Amorphous powder, ^{1}H-NMR (600 MHz, $CDCl_3$) δ: 7.40–7.57 (10H, aromatic protons), 5.15 (1H, m, H-3), 5.13 (1H, m, H-9), 3.57 (3H, s, $-OCH_3$), 3.51 (3H, s, $-OCH_3$), 3.51 (1H, m, H-2), 2.46 (1H, dd, J=16.7, 6.9 Hz, H-4a), 2.34 (1H, m, H-7a), 2.14 (1H, m, H-a), 2.08 (1H, m, H-7b), 1.93 (1H, m, H-8a), 1.65 (1H, m, H-8b), 1.54 (3H, s, H_3-13), 1.30 (3H, d, J=6.1 Hz, H_3-10), 1.09 (3H, s, H_3-11), 0.99 (3H, s, H_3-12); HR-ESI-MS (positive-ion mode) m/z: 684.2413 $[M+Na]^+$ (Calcd for $C_{33}H_{38}O_7F_6Na$: 683.2414). **5c**: Amorphous powder, ^{1}H-NMR (600 MHz, $CDCl_3$) δ: 7.26–7.55 (1H, aromatic protons), 5.15 (1H, m, H-9), 5.12 (1H, m, H-3), 3.58 (3H, s, $-OCH_3$), 3.45 (3H, m, $-OCH_3$), 2.50 (1H, dd, J=16.7, 6.1 Hz, H-4a), 2.32 (1H, m, H-7a), 2.16 (1H, m, H-4b), 2.02 (1H, m, H-7b), 1.84 (1H, m, H-8a), 1.62 (1H, m, H-8b), 1.49 (3H, s, H_3-13), 1.38 (3H, d, J=6.1 Hz, H_3-10), 1.02 (3H, s, H_3-11), 0.94 (3H, s, H_3-12); HR-ESI-MS (positive-ion mode) m/z: 684.2412 $[M+Na]^+$ (Calcd for $C_{33}H_{38}O_7F_6Na$: 683.2414).

Preparation of (*R*)- and (*S*)-MTPA Diesters (6a and b) from 6 Using a similar procedure to that used for the preparation of **5b** and **c** from **5a**, **6a** (0.3 mg) and **b** (0.4 mg) were prepared from **6** (0.4 mg each) by use of the respective amounts of (*R*)- and (*S*)-MTPA (10.0 mg and 10.0 mg), EDC (10.0 mg and 10.0 mg), and DMAP (10.0 mg and 10.0 mg). **6a**: Amorphous powder, ^{1}H-NMR (600 MHz, $CDCl_3$) δ: 7.39–7.61 (10H, aromatic protons), 5.15 (1H, m, H-9), 5.10 (1H, m, H-3), 4.09 (1H, m, H-4), 3.84 (1H, m, H-2), 3.50 (6H, s, $-OCH_3\times2$), 1.96 (1H, m, H-7a), 1.70 (2H, m, H_2-8), 1.68 (3H, s, H_3-13), 1.67 (1H, m, H-7b), 1.29 (3H, d, J=6.1 Hz, H_3-10), 1.12 (3H, s, H_3-11), 1.00 (3H, s, H_3-12); HR-ESI-MS (positive-ion mode) m/z: 699.2365 $[M+Na]^+$ (Calcd for $C_{33}H_{38}O_8F_6Na$: 699.2363). **6b**: Amorphous powder, ^{1}H-NMR (600 MHz, $CDCl_3$) δ: 7.39–7.62 (10H, aromatic protons), 5.15 (1H, m, H-9), 5.03 (1H, m, H-3), 4.17 (1H, m, H-4), 3.75 (1H, m, H-2), 3.50 (6H, s, –OCH3×2), 1.85 (1H, m, H-7a), 1.64 (2H, m, H_2-8), 1.63 (3H, s, H_3-13), 1.62 (1H, m, H-7b), 1.38 (3H, d, J=6.1 Hz, H_3-10), 1.06 (3H, s, H_3-11), 0.97 (3H, s, H_3-12); HR-ESI-MS (positive-ion mode) m/z: 699.2366 $[M+Na]^+$ (Calcd for $C_{33}H_{38}O_8F_6Na$: 699.2363).

Preparation of (*R*)- and (*S*)-MTPA Diesters (7a and b) from 7 Using a similar procedure to that used for the preparation of **6a** and **b** from **6**, **7a** (0.8 mg) and **b** (0.3 mg) were prepared from **7** (0.6 mg each) by use of the respective amounts of (*R*)- and (*S*)-MTPA (19.5 mg and 25.4 mg), EDC (11.4 mg and 9.0 mg), and DMAP (15.7 mg and 15.4 mg). **7a**: Amorphous powder, ^{1}H-NMR (600 MHz, $CDCl_3$) δ: 7.40–7.55 (10H, aromatic protons), 5.07 (1H, m, H-9), 4.99 (1H, ddd, J=11.7, 9.8, 5.3 Hz, H-3), 3.69 (1H, dd, J=9.8, 4.2 Hz, H-2), 3.58 (3H, s, $-OCH_3$), 3.50 (3H, s, $-OCH_3$), 1.98 (1H, m, H-5), 1.85 (1H, m, H-4a), 1.70 (2H, m, H_2-8), 1.64 (1H, m, H-4b), 1.63 (1H, m, H-7a), 1.57 (1H, m, H-7b), 1.30 (3H, d, J=6.2 Hz, H_3-10), 1.09 (3H, s, H_3-11), 0.90 (3H, s, H_3-12), 0.88 (3H, s, H_3-13); HR-ESI-MS (positive-ion mode) m/z: 701.2518 $[M+Na]^+$ (Calcd for $C_{33}H_{40}O_8F_6Na$: 701.2520). **7b**: Amorphous powder; ^{1}H-NMR (600 MHz, $CDCl_3$) δ: 7.40–7.55 (10H, aromatic protons), 5.07 (1H, m, H-9), 4.96 (1H, ddd, J=11.7, 10.2, 5.3 Hz, H-3), 3.71 (1H, dd, J=10.2, 5.7 Hz, H-2), 3.58 (3H, s, $-OCH_3$), 3.55 (3H, s, $-OCH_3$), 1.91 (1H, m, H-5), 1.76 (1H, m, H-4a), 1.74 (1H, m, H-7a), 1.64 (2H, m, H_2-8), 1.50 (1H, m, H-4b), 1.47 (1H, m, H-7b), 1.36 (3H, d, J=6.2 Hz, H_3-10), 1.06 (3H, s, H_3-12), 0.97 (3H, s, H_3-11), 0.75 (3H, s, H_3-13); HR-ESI-MS (positive-ion mode) m/z: 701.2520 $[M+Na]^+$ (Calcd for $C_{33}H_{38}O_8F_6Na$: 701.2520).

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Conflict of Interest The authors declare no conflict of interest.

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