Structures of New Sesquiterpenoids from Farfarae Flos[1)]

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Received December 20, 2000; accepted February 7, 2001

Two new bisabolane-type sesquiterpenoids, (3*R*,4*R*,6*S*)-3,4-epoxybisabola-7(14),10-dien-2-one and (1*R*,3*R*, 4*R*,5*S*,6*S*)-1-acetoxy-8-angeloyloxy-3,4-epoxy-5-hydroxybisabola-7(14),10-dien-2-one, and a new oplopane-type sesquiterpenoid, 14(*R*)-hydroxy-7β-isovaleroyloxyoplop-8(10)-en-2-one, were isolated from Farfarae Flos along with three known compounds. The structures of these compounds were elucidated on the basis of spectroscopic evidence.

Key words Farfarae Flos; *Tussilago farfara*; sesquiterpenoid

The flower buds of *Tussilago farfara* L. (Compositae), called "Farfarae Flos," have been widely used for the treatment of coughs, bronchitis and asthmatic disorders in China.[2)] In previous papers, we reported the isolation and structural elucidation of the essential oil components,[3)] phenolic compounds,[4)] sesquiterpenoids[1,5)] and triterpenoids[6)] from the plant. Here, we report the isolation and structural elucidation of two new bisabolane-type sesquiterpenoids, (3*R*,4*R*,6*S*)-3,4-epoxybisabola-7(14),10-dien-2-one (**1**) and (1*R*,3*R*,4*R*,5*S*,6*S*)-1-acetoxy-8-angeloyloxy-3,4-epoxy-5-hydroxybisabola-7(14),10-dien-2-one (**2**), and a new oplopane-type sesquiterpenoid, 14(*R*)-hydroxy-7β-isovaleroyloxyoplop-8(10)-en-2-one (**3**), as well as three known compounds, (−)-cryptomerion (**4**),[7)] (−)-spathulenol (**5**)[8)] and hydroxytremetone (**6**).[9)] This is the first report of the isolation of **4**—**6** from Farfarae Flos. Extraction and isolation were carried out as described in the Experimental section.

Compound **1** was isolated as a colorless oil, $[\alpha]_D$ −23.2°. The molecular formula was determined to be $C_{15}H_{22}O_2$ by high-resolution (HR)-MS, indicating five degrees of unsaturation. The IR spectrum showed the presence of a carbonyl group (1713 cm^{-1}). The ^{1}H- (Table 1) and ^{13}C-NMR spectra (Table 2), obtained with the aid of a ^{1}H–^{1}H shift correlation spectroscopy (^{1}H–^{1}H COSY), ^{1}H-detected heteronuclear multiple quantum coherence (HMQC) and distorsionless enhancement by polarization transfer (DEPT) spectra, showed signals due to a tertiary methyl group [δ_H 1.41 (3H, H_3-15); δ_C 14.9 (C-15)], two olefinic methyl groups [δ_H 1.60 (3H, H_3-13), 1.68 (3H, H_3-12); δ_C 17.8 (C-13), 25.7 (C-12)], four methylenes [δ_H 2.00 (2H, H_2-8), 2.01 (1H, H-5α), 2.10 (2H, H_2-9), 2.16 (1H, H-1β), 2.21 (1H, H-5β), 2.82 (1H, H-1α); δ_C 26.5 (C-9), 29.7 (C-5), 33.8 (C-8), 40.9 (C-1)], a methine [δ_H 2.58 (1H, H-6); δ_C 43.9 (C-6)], an exomethylene [δ_H 4.80 (1H, H-14a), 4.81 (1H, H-14b); δ_C 109.5 (C-14), 150.3 (C-7)], a trisubstituted double bond [δ_H 5.08 (1H, H-10); δ_C 123.6 (C-10), 132.1 (C-11)] and a carbonyl carbon [δ_C 208.4 (C-2)]. The presence of a trisubstituted epoxide was inferred from the chemical shifts[10)] [δ_H 3.45 (1H, H-4); δ_C 59.4 (C-3), 64.9 (C-4)] and the unsaturation degree. Detailed analysis of the ^{1}H–^{1}H COSY spectrum of **1** implied connectivities for H_2-1–H-6, H-4–H-5β, H_2-5–H-6, H_2-8–H_2-9 and H_2-9–H-10 (Fig. 1). Interpretation of the ^{1}H-detected heteronuclear multiple bond connectivity (HMBC) spectrum revealed correlations from H_2-1 to C-2; H_3-12 and H_3-13 to C-10 and C-11; and H_3-15 to C-2, C-3 and C-4 (Fig. 1). Therefore, the planar structure of **1** was deduced to be 3,4-epoxybisabola-7(14),

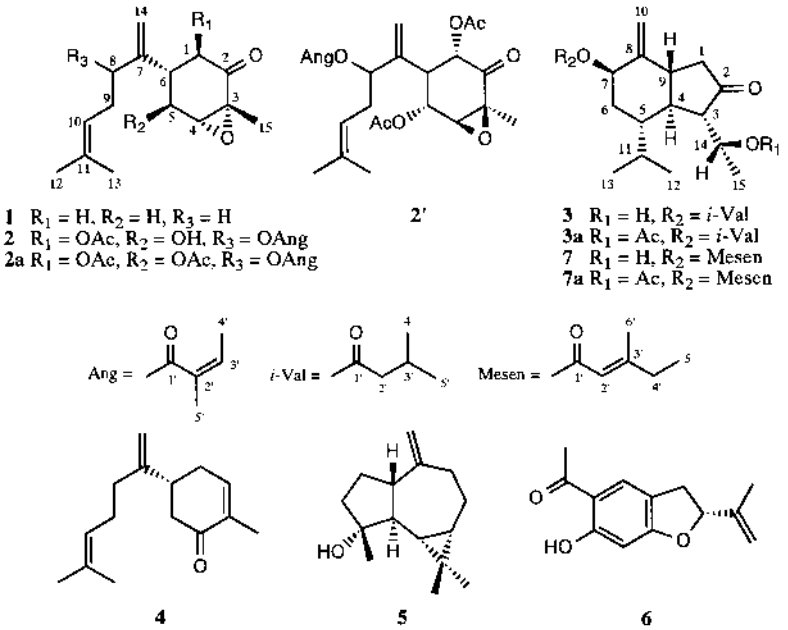

Chart 1

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Table 1. ^{1}H-NMR Chemical Shifts of Compounds **1**, **2**, **2a**, **2′**,[13] **3** and **7**[5] (400 MHz, $CDCl_3$)[a]

Proton	**1**[b]	**2**	**2a**	**2′**	**3**[b]	**7**
1	α 2.82 (1H, dd, 13.9, 12.8) β 2.16 (1H, ddd, 12.8, 2.6, 1.8)	5.68 (1H, d, 13.7)	5.68 (1H, d, 12.7)	5.68 (1H, d, 12.77)		
3					2.50 (1H, dd, 11.0, 3.7)	2.50 (1H, dd, 11.0, 4.0)
4	3.45 (1H, d, 4.4)	3.51 (1H, s)	3.40 (1H, s)	3.40 (1H, s)	1.39 (1H, m)	1.39 (1H, m)
5	α 2.01 (1H, dd, 15.4, 11.7) β 2.21 (1H, dddd, 15.4, 6.2, 4.4, 1.8)	4.25 (1H, d, 8.5)	5.35 (1H, d, 8.8)	5.35 (1H, d, 8.67)	1.91 (1H, m)	1.98 (1H, m)
6	2.58 (1H, dddd, 13.9, 11.7, 6.2, 2.6)	2.56 (1H, d, 13.7, 8.5)	2.87 (1H, dd, 12.7, 8.8)	2.87 (1H, dd, 12.77, 8.67)		
7					5.57 (1H, dd, 3.3, 2.9)	5.58 (1H, t, 2.9)
8	2.00 (2H, m)	4.72 (1H, dd, 8.8, 2.7)	5.23 (1H, dd, 7.1, 3.2)	5.23 (1H, dd, 7.78, 4.32)		
9	2.10 (2H, m)	a 2.18 (1H, m) b 2.52 (1H, m)	2.33 (2H, m)	2.33 (2H, m)	2.61 (1H, m)	2.64 (1H, m)
10	5.08 (1H, tq, 7.0, 1.1)	5.13 (1H, tq, 7.1, 1.0)	5.04 (1H, tq, 7.3, 1.0)	5.04 (1H, br t, 7.22)	a 4.79 (1H, d, 1.5) b 5.13 (1H, s)	a 4.79 (1H, d, 1.1) b 5.15 (1H, s)
11					2.01 (1H, m)	2.02 (1H, m)
12	1.68 (3H, d, 1.1)	1.70 (3H, d, 1.0)	1.68 (3H, d, 1.0)	1.68 (3H, br s)	0.95 (3H, d, 6.6)	0.95 (3H, d, 6.6)
13	1.60 (3H, s)	1.64 (3H, s)	1.62 (3H, s)	1.62 (3H, br s)	0.73 (3H, d, 7.0)	0.73 (3H, d, 6.9)
14	a 4.80 (1H, s) b 4.81 (1H, s)	a 5.08 (1H, s) b 5.20 (1H, d, 0.7)	a 5.24 (1H, s) b 5.33 (1H, s)	a 5.24 (1H, s) b 5.33 (1H, s)	4.05 (1H, m)	4.06 (1H, m)
15	1.41 (3H, s)	1.48 (3H, s)	1.48 (3H, s)	1.48 (3H, s)	1.19 (3H, d, 6.6)	1.19 (3H, d, 6.2)
2′					2.19 (2H, m)	5.65 (1H, q, 1.1)
3′		6.20 (1H, qq, 7.3, 1.5)	6.08 (1H, qq, 7.1, 1.5)	6.08 (1H, qq, 7.11, 1.59)	2.08 (1H, m)	
4′		2.00 (3H, dq, 7.3, 1.5)	1.97 (3H, dq, 7.1, 1.5)	1.97 (3H, dq, 7.11, 1.49)	0.95 (3H, d, 6.6)	
5′		1.91 (3H, dq, 1.5, 1.5)	1.88 (3H, dq, 1.5, 1.5)	1.89 (3H, dq, 1.59, 1.49)	0.95 (3H, d, 6.6)	1.08 (3H, t, 7.5)
6′						2.15 (3H, d, 1.1)
1-$COCH_3$		2.09 (3H, s)	2.06 (3H, s)	2.06 (3H, s)		
5-$COCH_3$			2.15 (3H, s)	2.15 (3H, s)		

a) Chemical shifts are in δ-values from internal tetramethylsilane (TMS) and are followed by multiplicities and *J*-values (in Hz). *b*) Measured at 600 MHz.

Table 2. ^{13}C-NMR Chemical Shifts of Compounds **1**, **2**, **2a**, **2′**,[13] **3** and **7**[5] (100 MHz, $CDCl_3$)

Carbon	**1**	**2**	**2a**	**2′**	**3**[a]	**7**
1	40.9	71.4	72.5	72.9	42.4	42.2
2	208.4	200.3	199.5	199.9	221.2	221.4
3	59.4	61.4	61.4	61.8	60.1	60.2
4	64.9	68.2	65.7	66.1	49.2	49.3
5	29.7	73.7	72.6	73.0	44.2	44.2
6	43.9	54.0	48.5	48.9	31.1	31.3
7	150.3	148.2	145.8	146.1	73.7	73.0
8	33.8	78.4	74.9	75.3	145.7	146.0
9	26.5	31.8	31.9	32.3	42.7	42.6
10	123.6	119.1	119.0	119.4	110.3	110.1
11	132.1	134.8	134.5	134.9	28.3	28.3
12	25.7	25.8	25.7	26.1	21.4	21.4
13	17.8	18.0	18.0	18.4	15.3	15.3
14	109.5	110.8	114.1	114.4	68.4	68.5
15	14.9	14.7	14.4	14.8	18.9	18.9
1′		168.9	166.5	166.9	172.1	165.9
2′		127.2	127.8	128.2	43.9	114.6
3′		140.6	138.5	139.0	26.0	162.1
4′		15.9	15.7	16.1	22.3[c]	33.8
5′		20.4[b]	20.6	21.0	22.4[c]	11.9
6′						18.9
1-CO<u>C</u>H_3		20.4[b]	20.3	20.7		
1-<u>C</u>OCH_3		169.5	169.5	169.9		
5-CO<u>C</u>H_3			20.8	21.2		
5-<u>C</u>OCH_3			170.0	170.4		

a) Measured at 150 MHz. *b*) Signals overlapped. *c*) Assignments may be interchangeable.

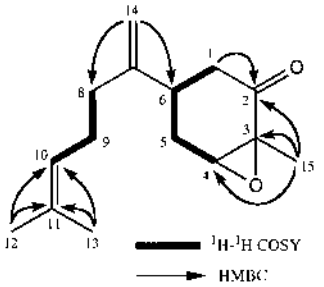

Fig. 1. ^{1}H–^{1}H COSY and HMBC Correlations for **1**

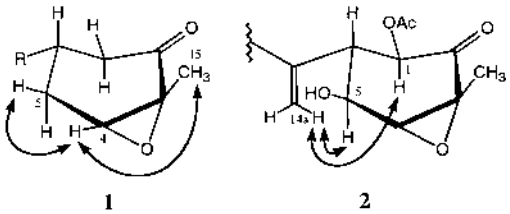

Fig. 2. NOEs Detected for Compounds **1** and **2**

10-dien-2-one. The relative stereochemistry of **1** was determined as follows. The coupling pattern and the constants for H-6 (dddd, $J_{1\alpha,6}$=13.9 Hz, $J_{5\alpha,6}$=11.7 Hz, $J_{5\beta,6}$=6.2 Hz, $J_{1\beta,6}$=2.6 Hz) suggested that H-1α and H-6, and H-5α and H-6 were diaxially related and the side chain at C-6 was α-equatorially oriented. The epoxide ring at C-3–C-4 must have been α-oriented because of the small coupling constant of H-4 with H-5β ($J_{4,5\beta}$=4.4 Hz).[11] It was mentioned that the coupling constant of H-4 with H-5α was almost zero so their dihedral angle must be about 90° which results from the 3α,4α-epoxide ring.[11] The configuration of the epoxide was supported by the nuclear Overhauser effect correlation spectroscopy (NOESY) cross peaks between H-4 and H-5β; and

H-4 and H_3-15 (Fig. 2). The absolute stereochemistry of **1** was determined by a circular dichroism (CD) spectrum. The empirical reversed octant rule can be applied to elucidate the absolute configuration of an epoxy-ketone ring system.[12] The CD spectrum of **1** showed a positive Cotton effect by the C-2 carbonyl group at 302.0 nm ($\Delta\varepsilon=+1.05$), indicating that the absolute configurations at C-3, C-4 and C-6 were *R*, *R* and *S*, respectively. On the basis of the above data, the structure of **1** was determined to be (3*R*,4*R*,6*S*)-3,4-epoxybisabola-7(14),10-dien-2-one.

Compound **2** was isolated as a colorless oil, $[\alpha]_D$ −32.0°. The molecular formula was determined to be $C_{22}H_{30}O_7$ by HR-MS. The IR spectrum showed the presence of a hydroxyl group (3419 cm^{-1}), an α,β-unsaturated ester (1734, 1647 cm^{-1}) and a carbonyl group (1698 cm^{-1}). The ^{1}H- and ^{13}C-NMR spectra of **2** were similar to those of **1** except for the appearance of three oxygenated methine signals at C-1, C-5 and C-8 [δ_H 4.25 (1H, H-5), 4.72 (1H, H-8), 5.68 (1H, H-1); δ_C 71.4 (C-1), 73.7 (C-5), 78.4 (C-8)] instead of the methylene signals at C-1, C-5 and C-8 in **1**. Furthermore, the signals ascribable to an acetyl group [δ_H 2.09 (3H); δ_C 20.4, 169.5] and an angeloyl group [δ_H 1.91 (3H, H_3-5′), 2.00 (3H, H_3-4′), 6.20 (1H, H-3′); δ_C 15.9 (C-4′), 20.4 (C-5′), 127.2 (C-2′), 140.6 (C-3′), 168.9 (C-1′)][1] were also observed in the ^{1}H- and ^{13}C-NMR spectra of **2**. In the HMBC spectrum, a cross peak was observed between the H-1 at δ_H 5.68 and the carbonyl carbon in the acetyl group at δ_C 169.5, suggesting that the acetoxyl group was located at C-1. On acetylation, **2** gave a diacetate (**2a**), whose ^{1}H-NMR spectrum showed a downfield shifted oxymethine proton assignable to H-5 at δ_H 5.35. Thus, the hydroxyl group was located at C-5. By considering the chemical shift of H-8 (δ_H 4.72), the linking position of the angeloyl group was deduced to be the C-8 oxygen. The coupling pattern and the constants for H-1α (d, $J_{1\alpha,6}$=13.7 Hz) and H-5α (d, $J_{5\alpha,6}$=8.5 Hz) suggested that the acetoxyl group at C-1 and the hydroxyl group at C-5 each had β configurations, respectively, which were supported by the NOESY cross peaks between H-1α and H-14a; and H-5α and H-14a (Fig. 2). The absolute stereochemistry of **2** was determined by the CD spectrum, in which a positive Cotton effect by the C-2 carbonyl group was shown at 296.0 nm ($\Delta\varepsilon=+0.91$). Application of the reversed octant rule[12] to **2** suggested that the absolute configurations at C-1, C-3, C-4, C-5 and C-6 were *R*, *R*, *R*, *S* and *S*, respectively. The stereochemistry at C-8 could not be established. Accordingly, the structure of **2** was determined to be (1*R*,3*R*,4*R*,5*S*,6*S*)-1-acetoxy-8-angeloyloxy-3,4-epoxy-5-hydroxybisabola-7(14),10-dien-2-one.

The sign of the optical rotation, ^{1}H- and ^{13}C-NMR spectra of **2a** were identical with those of 1α,5α-diacetoxy-8-angeloyloxy-3β,4β-epoxybisabola-7(14),10-dien-2-one (**2′**), recently isolated from the flower buds of *T. farfara*, as an inhibitor of nitric oxide synthesis in lipopolysaccharide-activated macrophages.[13] Thus, the absolute configuration of **2′** was deduced to be **2a**.

Compound **3** was isolated as a colorless oil, $[\alpha]_D$ −57.6°. The molecular formula was determined to be $C_{20}H_{32}O_4$ by HR-MS. The IR spectrum showed the presence of hydroxyl (3511 cm^{-1}) and carbonyl (1726 cm^{-1}) groups. The ^{1}H- and ^{13}C-NMR spectra were similar to those of 14(*R*)-hydroxy-7β-(4-methylsenecioyloxy)oplop-8(10)-en-2-one (**7**),[5] except for the presence of an isovaleroyl group [δ_H 0.95 (6H, H_3-4′, H_3-5′), 2.08 (1H, H-3′), 2.19 (2H, H-2′); δ_C 22.3, 22.4 (each C-4′, C-5′), 26.0 (C-3′), 43.9 (C-2′), 172.1 (C-1′)][14] in place of the 4-methylsenecioyl group in **7**. In the HMBC spectrum, a cross peak was observed between the H-7 at δ_H 5.57 and the C-1′ at δ_C 172.1, confirming that the isovaleroyl group was attached to the oxygen at C-7. On acetylation, **3** gave a monoacetate (**3a**), whose ^{1}H-NMR spectrum showed a downfield shifted oxymethine proton assignable to H-14 at δ_H 5.10. The chemical shift value, coupling pattern and constants for H-14 (qd, $J_{14,15}$=6.6 Hz, $J_{3,14}$=3.3 Hz) in **3a** were in accord with those of tussilagone (**7a**), whose relative stereochemistry has been established by the X-ray diffraction method,[15] confirming the relative configuration at C-14 as *R**. The CD spectrum of **3a** showed a negative Cotton effect by the C-2 carbonyl group at 303.0 nm ($\Delta\varepsilon=-2.37$) as observed in tussilagone (**7a**),[15] indicating that the absolute configuration at C-14 was *R*. On the basis of this evidence, the structure of **3** was determined to be 14(*R*)-hydroxy-7β-isovaleroyloxyoplop-8(10)-en-2-one. Compound **3** is the first example of the isolation of an oplopane derivative with an isovaleroyl group at the C-7 position from Farfarae Flos.

Experimental

General Procedures Optical rotations were determined with a JASCO DIP-360 digital polarimeter. CD spectra were performed on a JASCO J-720 spectropolarimeter. IR spectra were recorded with a Perkin-Elmer FT-IR 1725X infrared spectrophotometer and UV spectra with a Beckman DU-64 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded with JEOL JNM-LA 600 (600 and 150 MHz, respectively) and JEOL JNM-LA 400 (400 and 100 MHz, respectively) spectrometers. Chemical shifts are given on a δ (ppm) scale with TMS as an internal standard (s, singlet; br s, broad singlet; d, doublet; dd, double doublet; ddd, double double doublet; dddd, double double double doublet; q, quartet; tq, triplet quartet; dq, double quartet; qd, quartet doublet; qq, quartet quartet; m, multiplet). The HR-MS were recorded on a JEOL JMS-DX 303 mass spectrometer. Column chromatography was carried out on Kieselgel 60 (Merck; 230—400 mesh). Preparative HPLC was carried out on a Tosoh HPLC system (pump, CCPD; detector, RI-8010) using a TSK gel ODS-120T (7.8 mm i.d.×30 cm) column (Tosoh). Preparative GC was carried out on a Shimadzu GC-7A gas chromatograph.

Plant Material The dried flower buds of *Tussilago farfara*, "Farfarae Flos," were purchased from Tochimoto Tenkaido Co., Ltd., Osaka, Japan in 1990.

Extraction and Isolation The dried flower buds of *T. farfara* (5.0 kg) were extracted with Et_2O at room temperature for one week. The Et_2O extract was subjected to steam distillation to give an essential oil (7.7 g) and residue (64.5 g). The essential oil (7.7 g) was separated to neutral oil (7.0 g) and acidic oil (0.7 g). The neutral oil (7.0 g) was placed on a silica gel column and developed with *n*-hexane, benzene and Et_2O to afford *n*-hexane elution part (4.5 g), benzene elution part (1.3 g) and Et_2O elution part (1.2 g). The benzene elution part (1.3 g) was purified by preparative GC [column, 10% silicone SE-30 on Chromosorb W (AW) (60—80 mesh) 3 mm i.d.× 3 m; column temp., 80—230 °C (3 °C/min); carrier gas, He; flow rate, 45 ml/min; detector, TCD] to give **1** (1.5 mg), **4** (1.3 mg) and **6** (1.1 mg). The Et_2O elution part (1.2 g) was purified by preparative GC [column, 3% silicone SE-52 on Chromosorb W (AW) (60—80 mesh) 3 mm i.d.×2 m; column temp., 150 °C; carrier gas, He; flow rate, 45 ml/min; detector, TCD] to give **5** (29.1 mg).

A part of the residue of steam distillation (23.5 g) was placed on a silica gel column and developed with *n*-hexane–AcOEt (4 : 1—1 : 4), AcOEt and MeOH to afford 19 fractions (frs. 1—19). Fraction 8 was separated by preparative HPLC [MeOH–H_2O (4 : 1); flow rate, 1.2 ml/min; column temperature, 40 °C] to give a mixture of **2** and **3**. The mixture of **2** and **3** was purified by preparative HPLC [MeOH–H_2O (3 : 2); flow rate, 2.0 ml/min; column temperature, 40 °C] to give **2** (3.9 mg) and **3** (2.5 mg).

(3*R*,4*R*,6*S*)-3,4-Epoxybisabola-7(14),10-dien-2-one (**1**): Colorless oil. $[\alpha]_D^{22}$ −23.2° (c=0.2, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 1713. UV λ_{max} (MeOH) nm (log ε): 202 (3.9). CD ($c=1.27\times10^{-4}$, MeOH) $\Delta\varepsilon$ (nm): +1.05 (302.0), −6.63 (206.5). HR-MS *m/z*: 234.1646 (M^+, Calcd for $C_{15}H_{22}O_2$;

234.1620). ^{1}H-NMR (600 MHz, $CDCl_3$): see Table 1. ^{13}C-NMR (100 MHz, $CDCl_3$): see Table 2.

(1*R*,3*R*,4*R*,5*S*,6*S*)-1-Acetoxy-8-angeloyloxy-3,4-epoxy-5-hydroxybisabola-7(14),10-dien-2-one (**2**): Colorless oil. $[\alpha]_D^{23}$ −32.0° (c=0.4, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3419, 1734, 1698, 1647. UV λ_{max} (MeOH) nm (log ε): 217 (4.0). CD (c=8.90×10^{-5}, MeOH) $\Delta\varepsilon$ (nm): +0.91 (296.0), −4.69 (214.5). HR-MS m/z: 406.1964 (M^+, Calcd for $C_{22}H_{30}O_7$; 406.1991). ^{1}H-NMR (400 MHz, $CDCl_3$): see Table 1. ^{13}C-NMR (100 MHz, $CDCl_3$): see Table 2.

Acetylation of 2 Compound **2** (3.7 mg) was treated overnight with 0.5 ml of acetic anhydride and 0.5 ml of pyridine. The products were purified by HPLC [MeOH–H_2O (4 : 1); flow rate, 1.2 ml/min; column temperature, 40 °C], giving **2a** (2.6 mg).

(1*R*,3*R*,4*R*,5*S*,6*S*)-1,5-Diacetoxy-8-angeloyloxy-3,4-epoxybisabola-7(14),10-dien-2-one (**2a**): Colorless oil. $[\alpha]_D^{22}$ +3.86° (c=0.3, $CHCl_3$) [lit.,[13] $[\alpha]_D$ +4.64° (c=0.22, $CHCl_3$)]. IR ν_{max} ($CHCl_3$) cm^{-1}: 1738, 1650. UV λ_{max} (MeOH) nm (log ε): 219 (4.0). HR-MS m/z: 448.2078 (M^+, Calcd for $C_{24}H_{32}O_8$; 448.2098). ^{1}H-NMR (400 MHz, $CDCl_3$): see Table 1. ^{13}C-NMR (100 MHz, $CDCl_3$): see Table 2.

14(*R*)-Hydroxy-7β-isovaleroyloxyoplop-8(10)-en-2-one (**3**): Colorless oil. $[\alpha]_D^{19}$ −57.6° (c=0.2, $CHCl_3$). IR ν_{max} ($CHCl_3$) cm^{-1}: 3511, 1726. HR-MS m/z: 336.2283 (M^+, Calcd for $C_{20}H_{32}O_4$; 336.2301). ^{1}H-NMR (600 MHz, $CDCl_3$): see Table 1. ^{13}C-NMR (150 MHz, $CDCl_3$): see Table 2.

Acetylation of 3 Compound **3** (2.3 mg) was treated overnight with 0.5 ml of acetic anhydride and 0.5 ml of pyridine. The products were purified by HPLC [MeOH–H_2O (4 : 1); flow rate, 1.2 ml/min; column temperature, 40 °C], giving **3a** (1.8 mg).

14(*R*)-Acetoxy-7β-isovaleroyloxyoplop-8(10)-en-2-one (**3a**): Colorless oil. $[\alpha]_D^{22}$ −39.8° (c=0.2, $CHCl_3$). CD (c=1.38×10^{-4}, MeOH) $\Delta\varepsilon$ (nm): −2.37 (303.0). HR-MS m/z: 378.2409 (M^+, Calcd for $C_{22}H_{34}O_5$; 378.2406). ^{1}H-NMR (600 MHz, $CDCl_3$) δ: 0.77 (3H, d, J=6.6 Hz, H_3-13), 0.94 (6H, d, J=6.6 Hz, H_3-4′, H_3-5′), 0.97 (3H, d, J=7.0 Hz, H_3-12), 1.22 (3H, d, J=6.6 Hz, H_3-15), 2.11 (3H, s, $COCH_3$), 2.30 (1H, m, H-11), 2.39 (1H, dd, J=16.5, 5.9 Hz, H-1β), 2.50 (1H, dd, J=11.0, 3.3 Hz, H-3), 2.55 (1H, m, H-9), 4.78 (1H, d, J=1.1 Hz, H-10a), 5.10 (1H, qd, J=6.6, 3.3 Hz, H-14), 5.12 (1H, s, H-10b), 5.56 (1H, dd, J=2.9, 2.9 Hz, H-7).

The sign of optical rotation and spectral data of **4**, **5** and **6** were identical with those of the reported values.

(−)-Cryptomerion (**4**): $[\alpha]_D^{23}$ −31.4° (c=0.1, $CHCl_3$) [lit.,[7] $[\alpha]_D^{29}$ −37° (c=2.65, $CHCl_3$)].

(−)-Spathulenol (**5**): $[\alpha]_D^{26}$ −2.9° (c=1.3, $CHCl_3$) [lit.,[8] $[\alpha]_D^{20}$ −7.5° (c=1.48, $CHCl_3$)].

Hydroxytremetone (**6**): $[\alpha]_D^{20}$ −26.8° (c=0.1, MeOH) [lit.,[9a] $[\alpha]_D^{24}$ −50.7° (EtOH)].

Acknowledgments We are grateful to Mrs. S. Sato and T. Matsuki of this university for measurement of the mass and NMR spectra.

References and Notes

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