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OCCURRENCE OF EPIJUVABIONE-TYPE SESQUITERPENOIDS IN *ABIES SACHALINENSIS*

ATSUSHI NUMATA,* KENZO KAWAI, CHIKA TAKAHASHI and TAMIE MIYAMOTO

Osaka University of Pharmaceutical Sciences, 2-10-65 Kawai, Matsubara, Osaka 580, Japan

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Key Word Index—*Abies sachalinensis*; Pinaceae; wood; epijuvabione analogue; sesquiterpenoid.

Abstract—The wood of *Abies sachalinensis* from the Taisetsu mountain range of Japan afforded, in addition to 10 known compounds, seven new epijuvabione-type sesquiterpenoids, (+)-4′-dehydro-oxoepijuvabione, (−)-4′-dehydro-oxojuvabione, epijuvabienol ether, 5′-hydroxyepijuvabione, *ar*-dihydroxyepijuvabione, 3′-dehydroepijuvabi-5′-ol and 3′-isodihydroepitodomatuic acid. Their stereostructures were elucidated by chemical and spectral evidence.

INTRODUCTION

A number of studies on the wood of coniferous species such as *Abies, Pseudotsuga* and *Cedrus* have shown the occurrence of (+)-juvabione (4*R*,1′*R*) and several other insect juvenile hormone analogues [1–3]. Previously, we reported the isolation and identification of some epijuvabione-type sesquiterpenoids from the wood of *Abies sachalinensis* (FR. SCHM.) MAST. grown in the southern base of the Taisetsu mountain range in Hokkaido, Japan [1]. Further investigation on the same wood has led to the isolation of seven new epijuvabione-type sesquiterpenoids as well as 10 known compounds.

RESULTS AND DISCUSSION

The acetone extract of the wood was purified by Sephadex LH-20 and silica gel CC and HPLC to afford the new sesquiterpenoids, (+)-4′-dehydro-oxoepijuvabione (**1**), (−)-4′-dehydro-oxojuvabione (**2**), epijuvabienol ether (**3**), 5′-hydroxyepijuvabione (**4**), *ar*-dihydroxyepijuvabione (**5**), 3′-dehydroepijuvabi-5′-ol (**6**) and 3′-isodihydroepitodomatuic acid (**7**), together with the known epijuvabiol (**8**) [4], isoepijuvabiol (**9**) [4], epitodomatuic acid (**10**) [2], 4′-dehydroepitodomatuic acid (**11**) [2], (+)-pinoresinol (**12**) [5–7], (+)-epipinoresinol (**13**) [6,7], manool (**14**) [4,8–10], coniferyl aldehyde (**15**) [11], vanillin (**16**) and sitosterol (**17**). Compounds **10** and **11**, previously reported as syrup [2], were isolated as crystals in this case. Compounds **16** and **17** were identified by direct comparison with authentic samples, while **8**, **9** and **12**–**15** were identified by comparison of their physical and spectral data with those already published [4, 6, 7, 9–11]. Compounds **10** and **11** were identified by deriving epijuvabione (**18**) [1] and 4′-dehydroepijuvabione (**19**) [1], respectively, from them. This is the first isolation of **8**–**11**, **13**–**15** and **17** from the *A. sachalinensis* wood.

(+)-4′-Dehydro-oxoepijuvabione (**1**) analysed for $C_{16}H_{22}O_4$ by HR-EI mass spectrometry ([M]$^+$ at *m/z* 278.1514). Its UV and IR spectra demonstrated the presence of an α,β-unsaturated ester, a conjugated ketone and a double bond (see Experimental). The ^{1}H NMR spectrum of **1** is indicative of the dehydrojuvabione skeleton with signals corresponding to one methyl ester, two trisubstituted double bonds, one *sec*-methyl and two allylic methyl groups (Table 1). Cross comparison of the ^{13}C NMR spectra of **1** and (+)-4′-dehydroepijuvabione (**19**) revealed that one of the methylene groups in **19** was replaced by a conjugated ketone function in **1** (Table 2). The EI mass spectrum of **1** exhibited fragments at *m/z* 154 and 125, corresponding to ions *a* and *b*, respectively, together with the fragments at *m/z* 223 (*c*), 195 (*d*), 181 (*e*) and 83 (*f*). In addition, the proton and carbon signals of the C-4 methine appeared shifted downfield relative to **19** (Tables 1 and 2) [ref. 1 for ^{1}H NMR data of **19**] and the coupling pattern (*ddd*) of the H-4 methine proton implied the absence of the H-3 methylene protons in **1**. The above evidence demonstrated the existence of the ketone function at C-3 in **1**. The coupling constants (J = 10.5 and 4.8 Hz) between H-4 and both H-5β and H-5α showed the side-chain moiety at C-4 to be attached in an equatorial manner. The allylic oxidation of **19** with chromium trioxide–acetic anhydride [12] afforded a 3-oxo derivative, identical with **1** in all respects examined, including the ORD and CD spectra. This evidence led to assignment of stereostructure **1** with the 4*S*,1′*S*-configuration for (+)-4′-dehydro-oxoepijuvabione.

(−)-4′-Dehydro-oxojuvabione (**2**) has the same molecular formula as that of **1** as deduced from HR-EI mass spectrometry. The general features of the UV, IR, NMR and mass spectra of **2** closely resembled those of **1**. In the ^{13}C NMR spectrum of **2** (Table 2), however, the C-5 and C-1′ signals exhibited a greater chemical shift difference relative to **1**. In addition, in the ^{1}H NMR spectrum of **2** (Table 1), the coupling constants between H-4 and both H-5β and H-5α were almost identical to those of **1**, indicating that the side-chain moiety at C-4 was also attached in an equatorial manner, whereas the coupling constant (J = 11.0 Hz) between H-4 and H-1′ was larger than that (J = 8.5 Hz) of **1**. Based on this evidence, **2** was assumed to be an epimer of **1** at C-1′, namely, a 3-oxo derivative of 4′-dehydrojuvabione. In order to confirm

*Author to whom correspondence should be addressed.

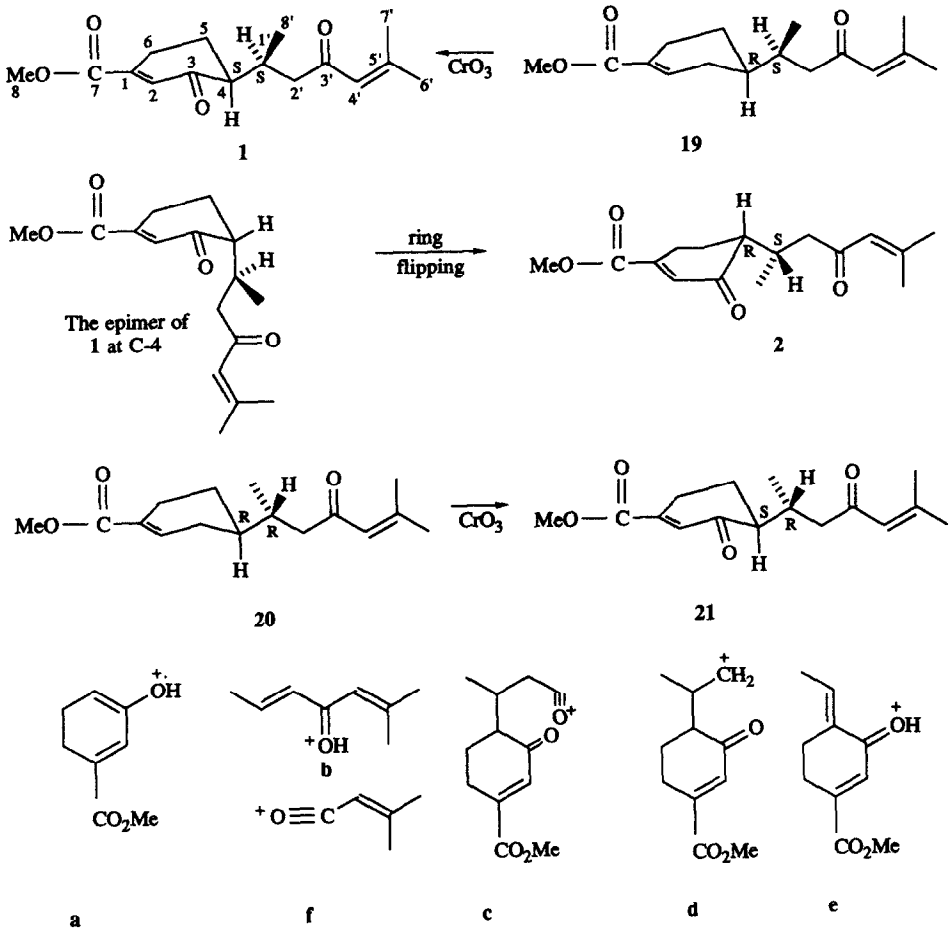
Table 1. ^{1}H NMR spectral data of compounds 1–7 (300 MHz, $CDCl_3$, TMS as int. standard)*

	1		2		3		4		5		6		7	
H	δ	J(Hz)	δ	J(Hz)	δ	J(Hz)	δ	J(Hz)	δ	J(Hz)	δ	J(Hz)	δ	J(Hz)
2	6.70 *dd*	2.8 (6α)† 1.2 (6β)	6.70 *dd*	2.6 (6β) 1.3 (6α)	6.92 *br s*		6.95 *m*				6.97 *m*		7.11 *br s*	
3α							2.12 *m*		6.75 *s*		2.15 *m*		2.10 *m*	
β					4.20 *ddd*	9.8 (4) 3.8 (6α) 1.9 (2, 6 β)	1.96 *m*				1.87 *m*		1.99 *m*	
4	2.34 *ddd*	10.5 (5β) 8.5 (1′) 4.8 (5α)	2.29 *td*	11.0 (5α, 1′) 4.8 (5β)	1.71 *m*		1.45 *ttd*	12.0 (3β, 5β) 5.0 (3α, 5α) 2.8 (1′)			1.48 *m*			
5α	2.11 *dtd*	13.0 (5β) 4.8 (4, 6α) 3.6 (6β)	1.84 *m*		1.79 *m*		1.77 *dtd*	12.0 (5β) 5.0 (4, 6α) 2.5 (6β)			1.81 *dtd*	12.8 (5β) 5.1 (4, 6α) 2.5 (6β)		
β	1.84 *dtd*	13.0 (5α) 10.5 (4, 6α) 4.8 (6β)	2.07 *dq*	14.0 (5α) 4.8 (4, 6α, 6β)	1.44 *tdd*	12.8 (4, 5α) 11.2 (6α) 6.1 (6 β)	1.24 *qd*	12.0 (4,5α, 6α) 5.2 (6β)			1.30 *m*			
6α	2.53 *dddd*	19.3 (6β) 10.5 (5β) 4.8 (5α) 2.8 (2)	2.75 *dtd*	19.2 (6β) 4.8 (5α, 5β) 1.3 (2)	2.30 *m*		2.09 *m*		7.37 *s*		2.20 *m*		2.09 *m*	
β	2.78 *dddd*	19.3 (6α) 4.8 (5β) 3.6 (5α) 1.2 (2)	2.52 *dddd*	19.2 (6α) 9.6 (5α) 4.8 (5β) 2.6 (2)	2.47 *ddq*	16.7 (6α) 6.1 (5β) 1.9 (2, 3, 5α)	2.48 *br d*	17.5 (6α)			2.44 *br d*	18.1 (6α)	2.48 *br d*	17.2 (6α)
8	3.83 *s*		3.82 *s*		3.73 *s*		3.73 *s*		3.91 *s*		3.73 *s*			

1′	2.62 *m*		2.75 *m*		2.22 *quin. d*	7.0 (4,8′) 5.1 (2′)	2.05 *m*		3.58 *dqd*	9.5 (2′ B) 7.1 (8′) 4.0 (2′A)	1.48 *m*			
2′A	2.25 *dd*	15.1 (2′B) 6.9 (1′)	2.37 *dd*	15.5 (2′B) 7.5 (1′)	4.56 *d*	5.1 (1′)	2.24 *dd*	16.2 (2′B) 9.1 (1′)	2.74 *dd*	18.4 (2′B) 4.0 (1′)	1.90 *m*		1.49 *dt*	13.8 (2′B) 6.0 (1′, 3′)
B	2.57 *dd*	15.1 (2′A) 5.0 (1′)	2.42 *dd*	15.5 (2′A) 6.4 (1′)			2.50 *dd*	16.2 (2′A) 4.6 (1′)	2.84 *dd*	18.4 (2′A) 9.5 (1′)	2.13 *m*		1.36 *m*	
3′											5.56 *dd*	15.0 (4′) 6.0 (2′)	3.76 *br s*	
4′A	6.12 *sept.*	1.3 (6′, 7′)	6.08 *sept.*	1.3 (6′, 7′)	1.86 *m*		2.59 *d*	17.0 (4′B)	2.19 *dd*	15.1 (4′B) 6.8 (5′)	5.63 *dd*	15.0 (3′) 2.0 (2′)		
B							2.62 *d*	17.0 (4′A)	2.25 *dd*	15.1 (4′A) 7.5 (5′)				
5′					1.83 *m*				2.04 *m*					
6′	1.89 *d*	1.3 (4′)	1.88 *d*	1.3 (4′)	0.88 *d*	6.4 (5′)	1.25 *s*		0.81 *d*	6.8 (5′)	1.31 *s*		0.93 *d*	6.6 (5′)
7′	2.14 *d*	1.3 (4′)	2.13 *d*	1.3 (4′)	0.87 *d*	6.4 (5′)	1.25 *s*		0.81 *d*	6.8 (5′)	1.31 *s*		0.92 *d*	6.6 (5′)
8′	0.95 *d*	7.6 (1′)	0.88 *d*	7.0 (1′)	0.88 *d*	7.0 (1′)	0.90 *d*	6.8 (1′)	1.27 *d*	7.1 (1′)	0.86 *d*	6.4 (1′)	0.90 *d*	6.5 (1′)
OH									10.26 7.15					

*Signal assignments were based on ^{1}H–^{1}H COSY spectra and ^{1}H-homonuclear decoupling.

†Figures in parentheses indicate a proton coupling with that in question.



the structure and stereochemistry, natural (+)-4′-dehydrojuvabione (**20**) was treated with chromium trioxide–acetic anhydride to afford an allylic oxidation product (**21**). The UV, IR, NMR and mass spectral properties of the synthetic material (**21**) were identical to those of **2**. However, the ORD and CD curves of **21** were opposite to those of **2**. Thus, **2** was established as the enantiomer (4*R*,1′*S*) of (+)-4′-dehydro-oxojuvabione (**21**). This compound (**2**) corresponds to the C-4 epimer of **1** having the side chain in a more thermodynamically stable equatorial orientation. Thus, **2** may be described as an epijuvabione-type compound rather than a juvabione-type one.

Epijuvabienol ether (**3**) has the molecular formula $C_{16}H_{24}O_3$, as deduced from HR-EI mass spectrometry ($[M]^+$ at *m/z* 264.1730). Its UV and IR spectra showed the presence of an α,β-unsaturated ester and a double bond. The ^1H and ^{13}C NMR spectra of **3** (Tables 1 and 2) revealed the presence of one methyl ester, two trisubstituted double bonds and three groups each of *sec*-methyl, methylene and methine, and the absence of a ketone function. Based on the chemical shift values of the ^{13}C NMR spectrum, one carbon each of the methine group and the double bond appeared to be linked to an oxygen function. In addition, the absence of a hydroxyl group, as indicated by the IR spectrum, suggested the presence of an enol ether in **3**. A close inspection of the proton coupling relationship (Table 1) by ^1H–^1H COSY and ^1H-homonuclear decoupling technique revealed partial structures representing C2-C4 (C5-C6)-C1′ (C8′)-C2′ and C4′-C5′ (C6′)-C7′ (isobutyl). Thus, the planar structure of epijuvabienol ether was assigned as **3**, which had the ether linkage between C-3 and C-3′. The coupling constant ($J = 9.8$ Hz) between H-3 and H-4 showed these protons to be diaxial, and the coupling constant ($J = 7.0$ Hz) between H-4 and H-1′ suggested an equatorial orientation for H-1′. Furthermore, this compound was treated with chromium trioxide in acetic acid to afford (+)-oxoepijuvabione (**22**) previously reported [1]. This evidence allowed assignment of the 3*S*,4*S*,1′*R*-stereoconfiguration for **3**.

The molecular formula of 5′-hydroxyepijuvabione (**4**) was suggested to be $C_{16}H_{26}O_4$ based on a $[M+1]^+$ peak at *m/z* 283 in the CI mass spectrum and a $[M-H_2O]^+$ peak at *m/z* 264.1731 in HR-EI mass spectrum. The general features of the UV, IR, ^1H and ^{13}C NMR spectra of **4** closely resembled those of epijuvabione (**18**) [1] except that the H-6′ and H-7′ methyl proton signals appeared as a singlet whilst there was a quaternary sp^3-carbon signal bearing an oxygen function and an IR absorption band due to a hydroxyl group. Treatment of **4** with Ac_2O gave 4′-dehydroepijuvabione (**19**). The above evidence led to assignment of stereostructure **4** (4*R*,1′*S*) for 5′-hydroxyepijuvabione.

ar-Dihydroxyepijuvabione (**5**) analysed for $C_{16}H_{22}O_5$ by HR-EI mass spectrometry ($[M]^+$ at *m/z* 294.1472),

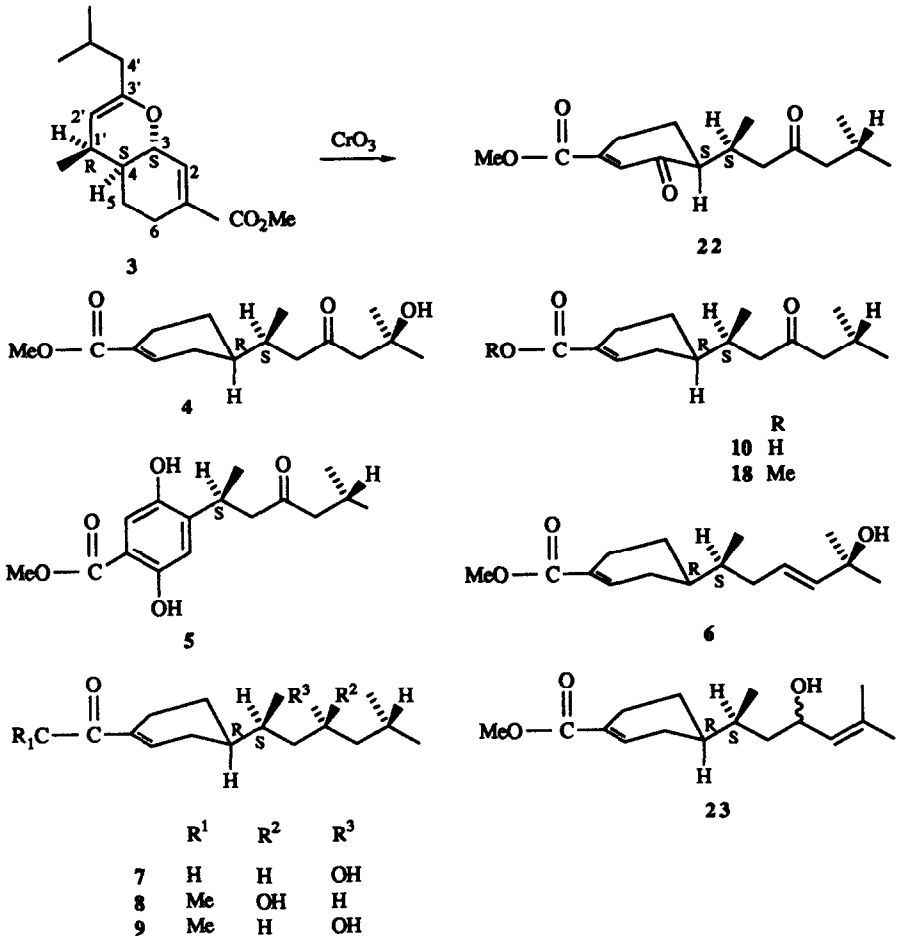


Table 2. ^{13}C NMR spectral data of compounds **1**–**7** and **19** (75.4 MHz, $CDCl_3$, δ-values, TMS as int. standard)*

C	1	2	3	4	5	6	7	19
1	147.7 (q)†	147.7 (q)	131.9 (q)	130.3 (q)	110.8 (q)	130.0 (q)	129.9 (q)	130.2 (q)
2	133.6 (t)	133.4 (t)	138.6 (t)	139.0 (t)	155.9 (q)	139.5 (t)	142.3 (t)	139.4 (t)
3	201.2 (q)	201.2 (q)	70.3 (t)	28.5 (s)	114.6 (t)	28.3 (s)	27.7 (s)	28.5 (s)
4	51.2 (t)	50.4 (t)	37.3 (t)	37.7 (t)	143.2 (q)	37.2 (t)	36.9 (t)	37.7 (t)
5	24.7 (s)	23.0 (s)	23.1 (s)	26.1 (s)	146.0 (q)	26.3 (s)	26.4 (s)	26.2 (s)
6	24.9 (s)	24.4 (s)	25.1 (s)	24.9 (s)	118.0 (t)	25.0 (s)	24.8 (s)	25.0 (s)
7	167.0 (q)	167.0 (q)	167.5 (q)	167.8 (q)	170.2 (q)	168.0 (q)	172.4 (q)	167.9 (q)
8	52.6 (p)	52.6 (p)	51.7 (p)	51.5 (p)	52.2 (p)	51.5 (p)		51.5 (p)
1′	28.8 (t)	27.5 (t)	29.2 (t)	32.9 (t)	26.4 (t)	37.2 (t)	33.7 (t)	33.5 (t)
2′	48.3 (s)	48.8 (s)	104.2 (t)	49.1 (s)	51.6 (s)	36.9 (s)	42.7 (s)	49.0 (s)
3′	200.4 (q)	200.0 (q)	152.6 (q)	212.8 (q)	213.1 (q)	125.6 (t)	68.4 (t)	200.8 (q)
4′	123.9 (t)	123.7 (t)	43.5 (s)	53.6 (s)	52.9 (s)	139.7 (t)	46.9 (s)	124.1 (t)
5′	155.4 (q)	155.8 (q)	26.0 (t)	69.7 (q)	24.8 (t)	70.2 (q)	24.6 (t)	155.2 (q)
6′	27.7 (p)	27.7 (p)	22.4 (p)	29.4 (p)	22.3 (p)	29.9 (p)	23.7 (p)	27.7 (p)
7′	20.7 (p)	20.8 (p)	22.3 (p)	29.4 (p)	22.5 (p)	29.9 (p)	21.9 (p)	20.7 (p)
8′	16.8 (p)	16.7 (p)	17.5 (p)	16.4 (p)	20.9 (p)	15.7 (p)	16.1 (p)	16.4 (p)

*Signal assignments were based on ^1H–^{13}C HETCOR spectra.

†Letters p, s, t and q, in parentheses indicate, respectively, primary, secondary, tertiary and quarternary carbons, assigned by DEPT.

and its UV spectrum showed the presence of an aromatic ring. This compound exhibited IR absorption bands, characteristic of a hydroxyl, a ketone, a hydrogen-bonded α,β-unsaturated ester and an aromatic ring. The ^1H NMR spectrum of **5** (Table 1) revealed the presence of a 1,2,4,5-tetrasubstituted benzene ring, one methyl ester and two phenolic hydroxyl groups, one of which formed hydrogen bonds to an adjacent carbonyl group of ester

as deduced from the chemical shift value (δ10.26). This evidence suggested the presence of either methyl 4-alkyl-2,5-dihydroxybenzoate or methyl 5-alkyl-2,4-dihydroxybenzoate moiety. The chemical shift values (δ7.37 and 6.75) of the aromatic protons supported the former moiety because at least one of these signals should appear at higher field in the latter moiety [13]. The presence of the 1,5-dimethyl-3-oxohexyl substituent was established from the remaining ^{1}H NMR data, the ^{13}C NMR signal of a ketone function (Table 2) and the EI mass spectral fragment ion at *m/z* 85, corresponding to $^+O{\equiv}C{-}CH_2CH(Me)_2$. The above evidence led to assignment of planar structure **5** for *ar*-dihydroxyepijuvabione. In view of the absolute stereochemistry of *ar*-todomatuic acid [14] and *ar*-pseudotsugonal [15], it is certain that **5** possesses the *S* configuration at C-1′ since it has a positive optical rotation.

3′-Dehydroepijuvabi-5′-ol (**6**) analysed for $C_{16}H_{26}O_3$ by HR-EI mass spectrometry ($[M]^+$ at *m/z* 266.1872). The general features of the NMR spectra of **6** (Tables 1 and 2) closely resembled those of 5′-hydroxyepijuvabione (**4**) except that the carbon signal of the ketone function in the side chain of **4** was missing from **6** and instead the proton and carbon signals due to *E*-disubstituted double bond (J = 15 Hz) were observed in **6**. In addition, the proton coupling relationship in the side chain led to assignment of structure **6** for 3′-dehydroepijuvabi-5′-ol. The 4*R*, 1′*S* configuration of this compound was determined by the fact that it was derived from 4′-dehydroepijuvabione (**19**) by the following reaction. Reduction of **19** with $NaBH_4$ afforded a 3′-hydroxy compound (**23**), which was converted by silicic acid column chromatography into **6**. This compound could be an artefact of the isolation procedure.

The molecular formula of 3′-isodihydroepitodomatuic acid (**7**) was suggested to be $C_{15}H_{26}O_3$ on the basis of a $[M+H]^+$ peak at *m/z* 255 in CI mass spectrum and a $[M-H_2O]^+$ peak at *m/z* 236 in EI mass spectrum. Its IR spectrum indicated an absorption band due to an α,β-unsaturated carboxylic acid. The ^{1}H NMR spectrum of **7** exhibited signals corresponding to three *sec*-methyl groups, a proton geminal to a hydroxyl group and an olefinic proton β to a conjugated carboxyl group (Table 1). The presence of these functional groups was supported by the ^{13}C NMR spectrum (Table 2). Treatment of **7** with diazomethane afforded a methyl ester derivative, identical with isoepijuvabiol (**9**). This evidence allowed assignment of stereostructure **7** with the 4*R*, 1′*S*, 3′*R*-configuration for 3′-isodihydroepitodomatuic acid.

EXPERIMENTAL

General. HPLC was carried out on a Waters ALC-200 instrument equipped with a differential refractometer (R-401) and a Shim-pack PREP-SIL column or a Shim-pack PREP-ODS column (each, 25 cm × 20 mm i.d.). Spectral measurements were carried out with the instruments described in the previous paper [1].

Plant material. The *Abies sachalinensis* tree was collected from the southern base of Mt Upepesanke located at Shikaoi-cho, Kato-gun, in Hokkaido, Japan during September 1989 and identified by Dr G. Murata, Department of Botany, Faculty of Science, Kyoto University, and Drs J. Samejima and K. Takahashi, Hokkaido Research Center, Forestry and Forest Products Research Institute. A voucher specimen (Numata No. 2) is deposited at the Herbarium of Kyoto University.

Extraction and isolation. As reported previously [1], the Me_2CO extract (79 g) from the debarked whole wood (2.73 kg) was passed through a Sephadex LH-20 column with Me_2CO–CH_2Cl_2 (1:1) to afford 7 fractions [Fr. 1 (2.9 g), Fr. 2 (5.0 g), Fr. 3 (19 g), Fr. 4 (4.3 g), Fr. 5 (4.3 g), Fr. 6 (1.5 g), Fr. 7 (4.9 g)]. Fr. 3 (14 g) was chromatographed on silica gel with a gradient of CH_2Cl_2–MeOH as the eluent. The CH_2Cl_2–MeOH (99.5:0.5) eluate (1.3 g) was further repeatedly chromatographed on silica gel with a gradient of C_6H_6–EtOAc as the eluent and finally the C_6H_6–EtOAc (97.5:2.5) eluate afforded **17** (2 mg). The CH_2Cl_2–MeOH (99:1) eluate (634 mg) from silica gel CC of Fr. 3 was subjected to HPLC [SIL, C_6H_6–EtOAc (85:15)], affording Fr. 8 (35 mg), Fr. 9 (18 mg), Fr. 10 (26 mg) and **4** (20 mg). Fr. 8 yielded **1** (4 mg) and **2** (4 mg) after another series of HPLC separations by SIL [C_6H_6–EtOAc (95:5)] followed by ODS [MeOH–H_2O (8:1)]. Fr. 9 afforded **8** (70 mg) and **9** (5 mg) after purification by HPLC [SIL, C_6H_6–EtOAc (85:15)]. Fr. 10 was subjected to HPLC [SIL, CH_2Cl_2–Me_2CO (97:3)] to afford **6** (5 mg). Fr. 4 was chromatographed on silica gel with C_6H_6 as the eluent. The first and second fractions afforded, respectively, **3** (40 mg) and **14** (9 mg) after purification by HPLC [ODS, MeOH]. Fr. 5 was repeatedly chromatographed on silica gel with a gradient of C_6H_6–EtOAc as the eluent and the final separation of the C_6H_6–EtOAc (99:1) eluate by HPLC [SIL, C_6H_6–EtOAc (92:8)] afforded **5** (5 mg). Fr. 6 was subjected to CC on silica gel and eluted with a gradient of C_6H_6–EtOAc. The C_6H_6–EtOAc (99:1) eluate (47 mg) yielded **16** (18 mg) after purification by HPLC [ODS, MeOH]. The C_6H_6–EtOAc (95:5) eluate was collected as 3 fractions [Fr. 11 (756 mg), Fr. 12 (112 mg) and Fr. 13 (74 mg)]. Fr. 11 yielded **15** (10 mg), **11** (69 mg) and **10** (10 mg) after purification by repeated HPLC [ODS, MeOH]. Fr. 12 and Fr. 13 were purified by HPLC (ODS) using MeOH and MeOH–H_2O (6:4) as the eluents, respectively, to afford **13** (7 mg). and **12** (8 mg). Fr. 7 was repeatedly chromatographed on silica gel with a gradient of C_6H_6–EtOAc as the eluent and finally the C_6H_6–EtOAc (94:6) eluate gave **7** (30 mg).

Methyl 4(S)-[1(S), 5-*dimethyl*-3-*oxo*-4-*hexenyl*]-3-*oxo*-1-*cyclohexene*-1-*carboxylate* [(+)-4′-*dehydro-oxoepijuvabione*] (**1**). Pale yellow oil, $[\alpha]_D^{19}$ +72.7° (EtOH; *c* 0.33). UV λ_{max}^{EtOH} nm (log ε): 238 (4.67). IR ν_{max}^{film} cm^{-1}: 1724 (CO_2R), 1681 (C=C–C=O), 1642, 1620 (C=C). EIMS *m/z* (rel. int): 278 $[M]^+$ (11), 223 [ion *c*] (1), 195 [ion *d*] (4), 181 [ion *e*] (33), 154 [ion *a*] (1), 125 [ion *b*] (21), 83 [ion *f*] (100). HR-EIMS *m/z*: 278.1514 $[M]^+$ ($C_{16}H_{22}O_4$ requires: 278.1516), 223.0976 [ion *c*] ($C_{12}H_{15}O_4$ requires: 223.0969), 195.1021 [ion *d*] ($C_{11}H_{15}O_3$ requires: 195.1020), 181.0867 [ion *e*] ($C_{10}H_{13}O_3$ requires: 181.0864), 154.0632 [ion *a*] ($C_8H_{10}O_3$ requires: 154.0629), 125.0961 [ion *b*] ($C_8H_{13}O$ requires: 125.0965), 83.0497 [ion *f*] (C_5H_7O requires: 83.0497). ORD λ_{ext}^{EtOH} nm [*c* 0.33] (ϕ): 450 (+431.5), 396 (+704.5), 388 (+633.8), 366 (+532.7), 300 (+1298.0), 280 (+2832.0). CD λ_{ext}^{EtOH} nm [*c* 4.31×10^{-4} M] (θ): 436(0), 404 (+630.5), 393 (+996.7), 385 (+964.3), 375 (+1043.1), 364 (+927.2), 345 (+964.3), 330 (+1029.2), 320 (+973.5), 291 (+551.7), 265 (+5841.1).

Preparation of **1** *from* **19**. A soln of **19** (10 mg) in C_6H_6 (2 ml) was treated with a soln of CrO_3 (22 mg), Ac_2O (10 ml) and glacial HOAc (5 ml) in C_6H_6 (5 ml), according to the procedure previously reported [1], to afford the oxidation product (**1**, 3.5 mg) as pale yellow oil besides **19** (4 mg). This product was identical with the natural product (**1**) in all respects examined, including ORD and CD spectra.

Methyl 4(R)-[1(S),5-*dimethyl*-3-*oxo*-4-*hexenyl*]-3-*oxo*-1-*cyclohexene*-1-*carboxylate* [(−)-4′-*dehydrooxojuvabione*] (**2**). Pale yellow oil, $[\alpha]_D^{17}$ −34.3° (EtOH; *c* 0.32). UV λ_{max}^{EtOH} nm (log ε): 238 (4.70). IR ν_{max}^{film} cm^{-1}: 1724 (CO_2R), 1681 (C=C–C=O), 1642,

1620 (C=C). EIMS *m/z* (rel. int.): 278 $[M]^+$ (11), 223 [ion *c*] (1), 195 [ion *d*] (4), 181 [ion *e*] (35), 154 [ion *a*] (6), 125 [ion *b*] (27), 83 [ion *f*] (100). HR-EIMS *m/z*: 278.1522 $[M]^+$ ($C_{16}H_{22}O_4$ requires: 278.1516), 223.0957 [ion *c*] ($C_{12}H_{15}O_4$ requires: 223.0969), 195.1022 [ion *d*] ($C_{11}H_{15}O_3$ requires: 195.1020), 181.0858 [ion *e*] ($C_{10}H_{13}O_3$ requires: 181.0864), 154.0635 [ion *a*] ($C_8H_{10}O_3$ requires: 154.0629), 125.0969 [ion *b*] ($C_8H_{13}O$ requires: 125.0965), 83.0501 [ion *f*] (C_5H_7O requires: 83.0497). ORD λ_{ext}^{EtOH} nm [*c* 0.32] (ϕ): 450 (−321.5), 416 (−635.9), 402 (−515.8), 398 (−549.3), 383 (0), 379 (+33.6), 376 (+28.3), 363 (+362.1), 355 (+162.5), 350 (+134.2), 346 (0), 320 (−998.0), 294 (−1582.2). CD λ_{ext}^{EtOH} nm [$c\ 3.6\times10^{-4}$ M] (θ): 440 (0), 412 (−678.7), 393 (−1324.5), 383 (−1051.4), 374 (−984.7), 363 (0), 355 (+322.7), 340 (+778.8), 317 (0), 289 (−1929.2), 250 (−3404.6).

Preparation of methyl 4(S)-[1(R),5-*dimethyl*-3-*oxo*-4-*hexenyl*]-3-*oxo*-1-*cyclohexene*-1-*carboxylate* [(+)-4′-*dehydrooxojuvabione*] (**21**) from **20**. A soln of **20** (8 mg) in C_6H_6 (2 ml) was treated with a soln of CrO_3 (20 mg), Ac_2O (10 ml) and glacial HOAc (4 ml) in C_6H_6 (5 ml) to afford, in addition to **20** (4 mg), the oxidation product (**21**, 3 mg) as pale yellow oil, $[\alpha]_D^{20}$ +32.2° (EtOH; *c* 0.3). Its UV, IR and NMR spectra were in accord with those of **2**, but the ORD and CD curves were opposite to those of **2**.

Methyl 2-*isobutyl*-4 (R)-*methyl*-4*a* (S), 5,6,8*a* (S)-*tetrahydro*-4H-1-*benzopyran*-7-*carboxylate* (*epijuvabienol ether*) (**3**). Pale yellow oil, $[\alpha]_D^{28}$ +121° (EtOH; *c* 0.87). UV λ_{max}^{EtOH} nm (log ε): 215 (3.77). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1710 (CO_2R), 1665, 1650 (C=C). EIMS *m/z* (rel. int): 264 $[M]^+$ (62), 249 (47), 232 (32), 179 (31), 164 (32), 138 (50), 137 (100), 127 (28), 105 (45), 85 (37), 79 (41). HR-EIMS *m/z*: 264.1724 $[M]^+$ ($C_{16}H_{24}O_3$ requires: 264.1719), 137.0599 ($C_8H_9O_2$ requires: 137.0601). ORD λ_{ext}^{EtOH} nm [*c* 0.89] (ϕ): 500 (+485.8), 410 (+838.1), 355 (+1220.7). CD λ_{ext}^{EtOH} nm [$c\ 3.79\times10^{-4}$ M] (θ): 315 (0), 289 (+422.7), 273 (+317.0), 256 (+700.1), 245 (0), 235 (−3830.5).

Oxidation of **3**. A soln of **3** (9 mg) in C_6H_6 (1 ml) was treated with a soln of CrO_3 (10 mg), Ac_2O (2.5 ml) and glacial HOAc (5 ml) in C_6H_6 (5 ml) as mentioned above to afford the oily substance (5 mg). It was purified by HPLC with C_6H_6–EtOAc (95:5) as the eluent to give (+)-oxoepijuvabione (**22**, 2.8 mg) as pale yellow oil. It was identical with an authentic sample in all respects.

Methyl 4(R)-[5-*hydroxy*-1(S),5-*dimethyl*-3-*oxohexyl*]-1-*cyclohexene*-1-*carboxylate* (5′-*hydroxyepijuvabione*) (**4**). Pale yellow oil, $[\alpha]_D^{23}$ +54° (EtOH; *c* 0.9). UV ν_{max}^{EtOH} nm (log ε): 219 (3.79). IR ν_{max}^{film} cm^{-1}: 3330 (OH), 1700 (CO_2R, C=O), 1642 (C=C). CIMS *m/z*: 283 $[M+1]^+$. EIMS *m/z* (rel. int.): 264 $[M-H_2O]^+$ (2), 209 (1), 166 (26), 139 (31), 137 (17), 134 (100), 107 (36), 83 (10), 79 (12). HR-EIMS *m/z*: 264.1725 $[M-H_2O]^+$ ($C_{16}H_{24}O_3$ requires: 264.1719), 134.0731 ($C_9H_{10}O$ requires: 134.0733). ORD λ_{ext}^{EtOH} nm [*c* 0.9] (ϕ): 450 (+394.4), 308 (+1896.3), 282 (+1116.6). CD λ_{ext}^{EtOH} nm [$c\ 6.01\times10^{-4}$ M] (θ): 290 (+995.9), 267 (+639.1), 252 (+747), 233 (+3236.8).

Methyl 2,5-*dihydroxy*-4-[1 (S), 5-*dimethyl*-3-*oxohexyl*] *benzoate* (ar-*dihydroxyepijuvabione*) (**5**). Pale yellow oil, $[\alpha]_D^{23}$ +66.7° (EtOH; *c* 0.27). UV λ_{max}^{EtOH} nm (log ε): 223 (3.75), 250 (3.40). IR ν_{max}^{film} cm^{-1}: 3391 (OH), 1705 (C=O), 1679 (C=C-CO_2R), 1626, 1586 (ar. C–C). EIMS *m/z* (rel. int.): 294 $[M]^+$ (94), 262 $[M-MeOH]^+$ (100), 195 (76), 162 (58), 135 (32), 85 $[O\equiv CCH_2CH(Me)_2]^+$ (32). HR-EIMS *m/z*: 294.1466 $[M]^+$ ($C_{16}H_{22}O_5$ requires: 294.1461), 85.0653 (C_5H_9O requires: 85.0653). ORD λ_{ext}^{EtOH} nm [*c* 0.27] (ϕ): 450 (+152.6), 390 (+228.9), 380 (0), 280 (−610.4). CD λ_{ext}^{EtOH} nm [$c\ 3.74\times10^{-4}$ M] (θ): 360 (0), 314 (+187.2), 309 (+133.7), 282 (+468), 255 (0), 249 (−574.9), 246 (0), 240 (−374.4).

Methyl 4(R)-[5-*hydroxy*-1(S),5-*dimethyl*-3-*hexenyl*]-1-*cyclohexene*-1-*carboxylate* (3′-*dehydroepijuvabi*-5′-*ol*) (**6**). Pale yellow oil, $[\alpha]_D^{28}$ +64° (EtOH; *c* 0.2). UV ν_{max}^{EtOH} nm (log ε): 219 (4.00). IR ν_{max}^{film} cm^{-1}: 3450 (OH), 1705 (CO_2R), 1645 (C=C). EIMS *m/z* (rel. int.): 266 $[M]^+$ (1.4). HR-EIMS *m/z*: 266.1877 $[M]^+$ ($C_{16}H_{26}O_3$ requires: 266.1881).

Preparation of **6** *from* **19**. A soln of **19** (7 mg) and $NaBH_4$ (15 mg) in MeOH (1 ml) was kept at room temp. for 3 hr. The mixture was diluted with H_2O and extracted with CH_2Cl_2. Concn of the CH_2Cl_2 layer gave the hydroxy ester (**23**, 7 mg) as pale yellow oil. The ester (**23**) was subjected to CC on silicic acid with a gradient of C_6H_6–EtOAc. The C_6H_6–EtOAc (9:1) eluate yielded **6** (3.5 mg).

3′-*Isodihydroepitodomatuic acid* (**7**). Needles, mp 90–93° (MeCN), $[\alpha]_D^{23}$ +111.1° (EtOH; *c* 0.09). UV λ_{max}^{EtOH} nm (log ε): 218 (3.96). IR ν_{max}^{KBr} cm^{-1}: 3360 (OH), 3325–2400, 1686 (C=C-CO_2H), 1647 (C=C). CIMS *m/z* (rel. int.): 255 $[M+H]^+$ (24). EIMS *m/z* (rel. int.): 236 $[M-H_2O]^+$ (3.3). Methylation of **7** (5.2 mg) with CH_2N_2 afforded isoepijuvabiol (**9**, 5 mg), identical with an authentic sample as judged by direct comparison.

Epijuvabiol (**8**). Pale yellow oil, $[\alpha]_D^{22}$ +46.6° (EtOH; *c* 0.32). UV λ_{max}^{EtOH} nm (log ε): 219 (4.38). IR ν_{max}^{film} cm^{-1}: 3445 (OH), 1716 (CO_2R), 1651 (C=C). EIMS *m/z* (rel. int.):268 $[M]^+$ (1.6). ^1H NMR (300 MHz, $CDCl_3$): δ0.91 (3H, *d*, *J* = 6.7 Hz, H-8′), 0.93 (6H, *d*, *J* = 6.8 Hz, H-6′, H-7′), 3.72 (3H, *s*, H-8), 3.76 (1H, *m*, H-3′), 6.98 (1H, *m*, H-2). ORD λ_{ext}^{EtOH} nm [*c* 0.32] (ϕ): 450 (+253.4), 350 (+567.6), 300 (+115.0), 250 (+1588.0). CD λ_{ext}^{EtOH} nm [$c\ 7.46\times10^{-4}$ M] (θ): 290 (0), 248 (+254.8), 245 (+871.7), 216 (+3164.8). Its ^{13}C NMR spectrum was in accord with the published data [4].

Isoepijuvabiol (**9**). Pale yellow oil, $[\alpha]_D^{22}$ +90.3° (EtOH; *c* 0.29). UV λ_{max}^{EtOH} nm (log ε): 219 (4.35). IR ν_{max}^{film} cm^{-1}: 3445 (OH), 1716 (CO_2R), 1651 (C=C). EIMS *m/z* (rel. int.): 268 $[M]^+$ (1.4). ^1H NMR ($CDCl_3$): δ0.90 (3H, *d*, *J* = 6.5 Hz, H-8′), 0.92 (3H, *d*, *J* = 6.7 Hz, H-7′), 0.94 (3H, *d*, *J* = 6.7 Hz, H-6′), 3.73 (3H, *s*, H-8), 3.75 (1H, *m*, H-3′), 6.98 (1H, *m*, H-2). ORD λ_{ext}^{EtOH} nm [*c* 0.29] (ϕ): 450 (+428.4), 350 (+782.3), 300 (+1378.3), 260 (+3315.3). Its ^{13}C NMR spectrum was in accord with the published data [4].

Epitodomatuic acid (**10**). Needles, mp 58–59° (MeCN), $[\alpha]_D^{23}$ +95.7° (EtOH; *c* 0.35). UV λ_{max}^{EtOH} nm (log ε): 218 (3.99). IR ν_{max}^{KBr} cm^{-1}: 3325–2400, 1683 (C=C-CO_2H), 1705 (C=O), 1645 (C=C). EIMS *m/z* (rel. int.): 252 (1.2). ^1H NMR ($CDCl_3$): δ0.88 (3H, *d*, *J* = 6.6 Hz, H-8′), 0.91 (3H, *d*, *J* = 6.6 Hz, H-7′), 0.92 (3H, *d*, *J* = 6.6 Hz, H-6′), 1.24 (1H, *qd*, *J* = 12.5, 5.2 Hz, H-5β), 1.45 (1H, *ttd*, *J* = 12.5, 5.0, 2.9 Hz, H-4), 1.79 (1H, *dtd*, *J* = 12.5, 5.0, 2.5 Hz, H-5α), 1.94 (1H, *m*, H-3β), 2.03 (1H, *m*, H-1′),2.13 (1H, *nonuplet*, *J* = 6.6 Hz, H-5′), 2.14 (1H, *m*, H-6α), 2.18 (1H, *m*, H-3α), 2.19 (1H, *dd*, *J* = 15.9, 7.0 Hz, H-2′A), 2.28 (2H, *d*, *J* = 6.6 Hz, H-4′), 2.44 (1H, *dd*, *J* = 15.9, 4.5 Hz, H-2′B), 2.48 (1H, *br d*, *J* = 17.0 Hz, H-6β), 7.10 (1H, *m*, H-2). Its ^{13}C NMR spectrum was in accord with the published data [2]. Treatment of **10** (5 mg) with CH_2N_2 afforded epijuvabione (**18**, 4 mg), identical with an authentic sample as judged by direct comparison.

4′-*Dehydroepitodomatuic acid* (**11**). Needles, mp 75–78° (MeCN), $[\alpha]_D^{23}$ +139.6° (EtOH; *c* 0.28). UV λ_{max}^{EtOH} nm (log ε): 227 (4.01). IR ν_{max}^{KBr} cm^{-1}: 3325–2400, 1670 (C=C-CO_2H), 1710 (C=O), 1645, 1615 (C=C). ^1H NMR ($CDCl_3$): δ0.90 (3H, *d*, *J* = 6.6 Hz, H-8′), 1.26 (1H, *qd*, *J* = 12.5, 5.2 Hz, H-5β), 1.48 (1H, *ttd*, *J* = 12.5, 5.0, 2.5 Hz, H-4), 1.79 (1H, *dtd*, *J* = 12.5, 5.0, 2.5 Hz, H-5α), 1.89 (3H, *d*, *J* = 1.1 Hz, H-7′), 1.95 (1H, *m*, H-3β), 2.01 (1H, *m*, H-1′), 2.14 (3H, *d*, *J* = 1.1 Hz, H-6′), 2.14 (1H, *m*, H-6α), 2.18 (1H, *m*, H-3α), 2.22 (1H, *dd*, *J* = 15.4, 8.9 Hz, H-2′A), 2.45 (1H, *br d*, *J* = 16.9 Hz, H-6β), 2.49 (1H, *dd*, *J* = 15.4, 4.7 Hz, H-2′B), 6.07 (1H, *sept.*, *J* = 1.1 Hz, H-4′), 7.11 (1H, *m*, H-2). Its ^{13}C NMR spectrum was in accord with the published data [2]. Treatment of **11** (4.2 mg) with CH_2N_2 afforded 4′-dehydroepijuvabione (**19**, 4 mg), identical to an authentic sample as judged by direct comparison.

(+)-*Pinoresinol* (**12**). Needles, mp 123–124° (MeOH), $[\alpha]_D^{19}$ +163.2° (EtOH; *c* 0.19). EIMS *m/z* (rel. int.): 358 $[M]^+$ (13), 205 (7), 152 (45), 151 (100). HR-EIMS *m/z*: 358.1410 $[M]^+$ ($C_{20}H_{22}O_6$ requires: 358.1414). ^{1}H NMR ($CDCl_3$): δ3.10 (2H, *m*, H-1, H-5), 3.87 (2H, *dd*, *J* = 9.2, 3.8 Hz, H-4ax, H-8ax), 3.91 (6H, *s*, OMe-3′, OMe-3″), 4.25 (2H, *dd*, *J* = 9.2, 7.0 Hz, H-4eq, H-8eq), 4.74 (2H, *d*, *J* = 4.6 Hz, H-2, H-6), 5.63 (2H, *s*, OH-4′, OH-4″), 6.82 (2H, *dd*, *J* = 8.5, 2.2 Hz, H-6′, H-6″), 6.90 (2H, *d*, *J* = 8.5 Hz, H-5′, H-5″), 6.91 (2H, *d*, *J* = 2.2 Hz, H-2′, H-2″). Its ^{13}C NMR spectrum was in accord with the published data [6].

(+)-*Epipinoresinol* (**13**). Needles, mp 135–136° (MeOH), $[\alpha]_D^{19}$ +86.2° (EtOH; *c* 0.39). EIMS *m/z* (rel. int.): 358 $[M]^+$ (69), 205 (18), 152 (33), 151 (100). HR-EIMS *m/z*: 358.1412 $[M]^+$ ($C_{20}H_{22}O_6$ requires: 358.1414). ^{1}H NMR ($CDCl_3$): δ2.92 (1H, *m*, H-5), 3.31 (2H, *m*, H-1, H-4), 3.80–3.88 (2H, *m*, H-4, H-8), 3.90, 3.92 (3H each, *s*, OMe-3′, OMe-3″), 4.13 (1H, *br d*, *J* = 9.2 Hz, H-8), 4.43 (1H, *d*, *J* = 7.1 Hz, H-6), 4.86 (1H, *d*, *J* = 5.4 Hz, H-2), 5.58, 5.61 (1H each, *s*, OH-4′, OH-4″), 6.78 (1H, *dd*, *J* = 8.3, 2.0 Hz, H-6″ or H-6′), 6.84 (1H, *dd*, *J* = 8.3, 2.2 Hz, H-6′ or H-6″), 6.89 (2H, *d*, *J* = 8.3 Hz, H-5′, H-5″), 6.91 (1H, *d*, *J* = 2.2 Hz, H-2′ or H-2″), 6.95 (1H, *d*, *J* = 2.0 Hz, H-2″ or H-2′). Its ^{13}C NMR spectrum was in accord with the published data [6].

Manool (**14**). Needles, mp 53–54° (MeOH), $[\alpha]_D^{22}$ +14.6° (EtOH; *c* 0.33). EIMS *m/z* (*rel. int.*): 272 $[M-H_2O]^+$ (27). ^{1}H NMR ($CDCl_3$): δ0.68 (3H, *s*, H-20), 0.80 (3H, *s*, H-19), 0.87 (3H, *s*, H-18), 1.27 (3H, *s*, H-16), 4.81, 4.51 (1H each, *br s*, H-17), 5.05 (1H, *dd*, *J* = 11.1, 2.0 Hz, H-15), 5.20 (1H, *dd*, *J* = 17.0, 2.0 Hz, H-15), 5.92 (1H, *dd*, *J* = 17.0, 11.1 Hz, H-14). Its ^{13}C NMR spectrum was in accord with the published data [10].

Coniferyl aldehyde (**15**). Yellow oil, EIMS *m/z* (rel. int.): 178 $[M]^+$ (100). Its spectral data were in accord with the published values [11].

Vanillin (**16**). Needles, mp 80–82° (MeOH–H_2O). EIMS *m/z* (rel. int.): 152 $[M]^+$ (100). It was identified by direct comparison with an authentic sample.

Sitosterol (**17**). Needles, mp 140–141° (MeOH). EIMS *m/z*: 414 $[M]^+$. It was identified by direct comparison with an authentic sample.

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