Seven-Membered Vibsane-Type Diterpenes with a 5,10-*cis* Relationship from *Viburnum awabuki*

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New five seven-membered vibsane-type diterpenes named 5-*epi*-vibsanin C, 5-*epi*-vibsanin H, 5-*epi*-vibsanin K, 18-*O*-methyl-5-*epi*-vibsanin K and 5-*epi*-vibsanin E have been isolated from the leaves of *Viburnum awabuki* (Caplifoliaceae). Their structures have been elucidated by analyses of spectroscopic data and comparison of their spectral data with those of the previously known seven-membered vibsane-type diterpenes. The occurrence of these seven-membered vibsane-type diterpenes with a *cis* relationship on the C-5 and C-10 positions in nature have been predicted by conformational analysis of vibsanin B, an eleven-membered vibsane-type diterpene. Vibsanin C, 5-*epi*-vibsanin C and 5-*epi*-vibsanin H exhibited moderate cytotoxic activities on KB cells.

Key words *Viburnum awabuki*; Caplifoliaceae; 5-*epi*-vibsanin; seven-membered vibsane-type diterpene; cytotoxicity

Viburnum awabuki (Caplifoliaceae) has elaborated a number of rarely occurring vibsane-type diterpenes, which can be subdivided into three types of eleven-membered, seven-membered and rearranged ones.[1,2] In the preceding paper,[3] we demonstrated that an eleven-membered vibsane-type diterpene, vibsanin B (**11**), exists in solution as two conformational isomers, CT and BC, which can transform to seven-membered derivatives, vibsanin C (**6**) and its 5-epimer (**6a**) by thermal Cope rearrangement, respectively, as shown in Fig. 1. This result suggests the occurrence of natural 5-epimers corresponding to the previously reported seven-membered vibsanins C (**6**), H (**7**), K (**8**), and 18-*O*-methylvibsanin K (**9**) and vibanin E (**10**) with a *trans* relationship on the C-5 and C-10 positions.[4,5] Herein, we report the isolation and structure of five anticipated isomers, 5-*epi*-vibsanin C (**1**), 5-*epi*-vibsanin H (**2**), 5-*epi*-vibsanin K (**3**) and 18-*O*-methyl-5-*epi*-vibsanin K (**4**) and 5-*epi*-vibsanin E (**5**) from the methanol extract of the leaves of *Viburnum awabuki.*

Compound **1** had the molecular formula $C_{25}H_{36}O_5$ established by high resolution (HR)-FAB-MS (*m/z* 439.2436 $[M+Na]^+$). Its IR spectrum showed absorptions attributable to a hydroxy group (3501 cm^{-1}) and three carbonyl groups (1728, 1707, 1668 cm^{-1}). The ^1H- and ^{13}C-NMR data (Tables 1, 2) of **1** showed the presence of six tertiary methyl groups [δ_H 0.67, 1.36, 1.63, 1.70, 1.74 and 2.01 (each s)], an oxymethylene [δ_H 4.21 (d, J=13.2 Hz), 4.30 (d, J=13.2 Hz); δ_C 64.2], three trisubstituted olefins (δ_H 5.17, δ_C 124.9, 131.4; δ_H 5.62, δ_C 115.0, 160.1; δ_H 6.13, δ_C 138.6, 143.9) and a disubstituted olefin [δ_H 5.33 (dd, J=12.5, 11.7 Hz), 7.38 (d, J=12.5 Hz); δ_C 111.7, 137.7]. These spectral data were very similar to those of vibsanin C (**6**), which was a typical seven-membered vibsane-type diterpene isolated from the title plant. In fact, analyses of two-dimensional (2D) NMR spectra such as quantum filtered-correlated spectroscopy (DQF-COSY), heteronuclear multiple quantum coherence (HMQC) and heteronuclear multiple bond correla-

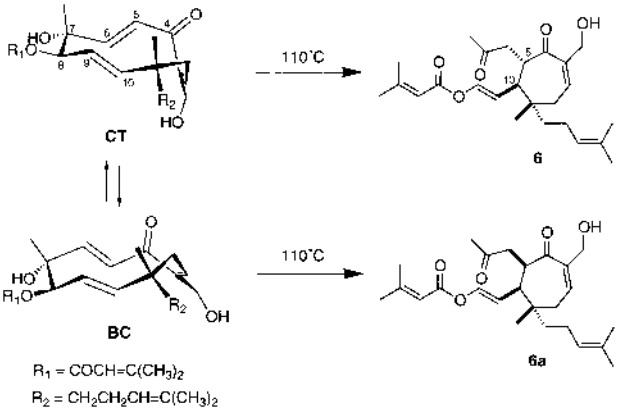

Fig. 1. Two Conformers, CT and BC, of Vibsanin B (**11**) Transformed to Vibsanin C (**6**) and Its Epimer **6a**

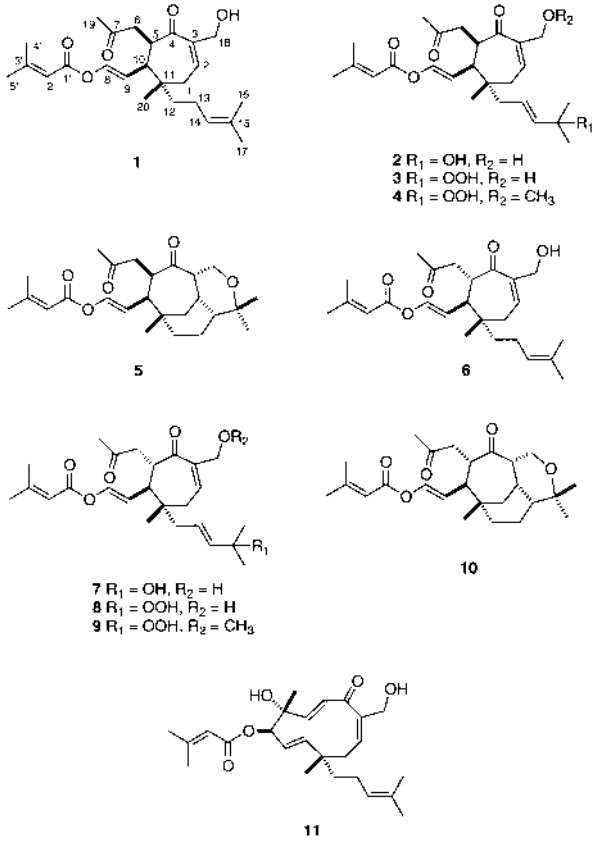

Chart 1. Vibsane-Type Diterpenes from the Leaves of *Viburnum awabuki*

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tion (HMBC) for **1** gave the same planar structure as **6**. In a comparison of ^{1}H-NMR spectra between **1** and **6**, however, the H-5 signal of **1** shifted up to δ_H 3.52 lower than the H-5 (δ_H 2.90) of **6** and also had a vicinal H-5/H-10 coupling constant (4.4 Hz) smaller that that (12.2 Hz) of **6**, suggesting that **1** was an epimer of **6** with regard to the C-5 position. This was substantiated by 2D-nuclear Overhauser enhancement and exchange spectroscopy (NOESY) as shown in Fig. 2. Thus, the cross-peaks between H-10 (δ_H 2.01) and H-5 (δ_H 3.52) enabled the substiuents on C-5 and C-10 to take a *cis* relationship. The circular dichroism (CD) spectrum of **1** showed a positive Cotton [$\Delta\varepsilon$ (249 nm) +3.7] effect, thereby indicating 5*R*, 10*R* and 11*S* configurations.[4] Additionally, **1** was identical in all respects with **6a** generated from vibsanin B (**11**) by the thermal Cope-rearrangement (Fig. 1).[3] Thus the structure of **1** was determined to be 5-*epi*-vibsanin C.

The molecular formula of compound **2** was determined to be $C_{25}H_{36}O_6$ on the basis of HR-FAB-MS (*m/z* 455.2417 $[M+Na]^+$). The presence of hydroxy groups and carbonyl groups were again indicated by an IR spectrum (3492, 1726, 1715, 1660 cm^{-1}). The ^{1}H- and ^{13}C-NMR (Tables 1, 2) of **2** were very similar to those of **1**, except for the C-12—C-17 side chain containing a disubstituted olefin [δ_H 5.60 (ddd, J=15.1, 7.5, 7.2 Hz), 5.68 (d, J=15.1 Hz); δ_C 121.7, 142.8]. These spectral data suggested that the structure of **2** was closely related to those of vibsanin H (**7**)[4] with a *trans* relationship on the C-5 and C-10 positions. Extensive analysis of 2D-NMR indicated the presence of a 4-hydroxy-4-methyl-2-heptenyl unit as a C-12—C-17 side chain which was the same as that of **7**. In the HMBC of **2** (Fig. 3), the observation of a cross peak between the CH_3-20 (δ_H 0.64) and C-12 (δ_C 45.8) signals indicated that the side chain was linked to the C-11 position on the 7-membered ring. Further analyses of HMBC resulted in the formation of the same planar structure as **7**, which was previously isolated from *V. awabuki*.[4] A NOESY experiment and a small $J_{5,10}$ value (4.0 Hz) of **2** indicated that the units on C-5 and C-10 had *cis* arranged in the same manner as that of **1**. In addition, the CD spectrum of **2** [$\Delta\varepsilon$ (245 nm) +3.9] showed a positive Cotton effect, indicating the same absolute configuration as **1**. Thus, **2** was named 5-*epi*-vibsanin H.

The ^{1}H- and ^{13}C-NMR data (Tables 1, 2) of compound **3** were also very similar to those of **2** except for the presence

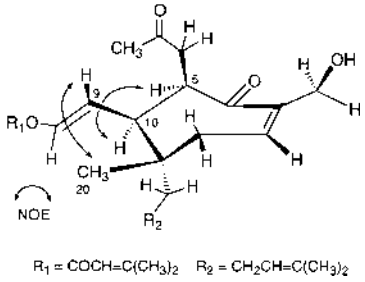

Fig. 2. 2D NOESY of **1**

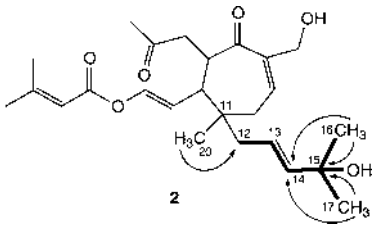

Fig. 3. HMBC Correlation of **2** between Protons (Tail) and Carbons (Head) Denoted by Arrows

Table 1. ^{1}H-NMR Data (δ/ppm) of **1**—**5**[a]

Proton	**1**[b]	**2**[c]	**3**[c]	**4**[c]	**5**[b]
1	1.92 (dd, 16.1, 7.6)	1.78 (dd, 15.8, 7.5)	1.78 (dd, 16.6, 8.1)	1.87 (dd, 16.8, 7.7)	0.99 (dd, 14.6, 4.3)
	2.01 (dd, 16.1, 5.4)	2.19 (dd, 15.8, 4.8)	2.12 (dd, 16.6, 4.6)	2.21 (dd, 16.8, 5.2)	1.52 (dd, 14.6, 2.5)
2	6.13 (dd, 7.6, 5.4)	6.16 (dd, 7.5, 4.8)	6.13 (dd, 8.1, 4.6)	6.48 (dd, 7.7, 5.2)	1.97 (ddd, 7.1, 4.3, 2.5)
3					2.21 (ddd, 7.1, 4.3, 2.5)
5	3.52 (ddd, 9.3, 4.6, 4.4)	3.50 (ddd, 8.8, 4.4, 4.0)	3.49 (ddd, 8.2, 5.1, 3.9)	3.57 (ddd, 9.1, 5.2, 3.8)	4.16 (ddd, 7.4, 5.8, 3.6)
6	1.83 (dd, 17.8, 4.6)	1.89 (dd, 17.6, 4.4)	1.97 (dd, 17.8, 5.1)	2.03 (dd, 17.8, 5.2)	1.95 (dd, 18.1, 5.2)
	3.05 (dd, 17.8, 9.3)	2.98 (dd, 17.6, 8.8)	2.93 (dd, 17.8, 8.2)	2.96 (dd, 17.8, 9.1)	2.99 (dd, 18.1, 7.4)
8	7.38 (d, 12.5)	7.35 (d, 12.5)	7.38 (d, 12.1)	7.39 (d, 12.4)	7.31 (d, 12.4)
9	5.33 (dd, 12.5, 11.7)	5.31 (dd, 12.5, 12.5)	5.28 (dd, 12.1, 12.1)	5.32 (dd, 12.4, 11.8)	5.25 (dd, 12.4, 11.8)
10	2.01 (dd, 11.7, 4.4)	2.12 (dd, 12.5, 4.0)	2.20 (dd, 12.1, 3.9)	2.24 (dd, 11.8, 3.8)	1.78 (dd, 11.8, 3.6)
12	1.31 (m)	1.93 (dd, 13.2, 7.2)	1.90 (dd, 13.5, 5.6)	1.92 (dd, 13.7, 6.9)	1.28 (m)
	1.46 (m)	1.99 (dd, 13.2, 7.5)	1.99 (dd, 13.5, 7.6)	2.08 (dd, 13.7, 8.0)	1.81 (m)
13	1.92 (2H, m)	5.60 (ddd, 15.1, 7.5, 7.2)	5.59 (ddd, 15.9, 7.6, 5.6)	5.61 (ddd, 15.7, 8.0, 6.9)	1.48 (ddd, 14.6, 6.6, 6.6)
					2.04 (m)
14	5.17 (t, 7.2)	5.68 (d, 15.1)	5.68 (d, 15.9)	5.69 (d, 15.7)	0.90 (m)
16	1.63 (3H, s)	1.28 (3H, s)	1.30 (3H, s)	1.30 (3H, s)	1.03 (3H, s)
17	1.70 (3H, s)	1.26 (3H, s)	1.32 (3H, s)	1.33 (3H, s)	1.06 (3H, s)
18	4.21 (d, 13.2)	4.20 (d, 13.4)	4.18 (d, 12.1)	4.15 (d, 13.7)	3.71 (dd, 12.1, 5.8)
	4.30 (d, 13.2)	4.29 (d, 13.4)	4.27 (d, 12.1)	4.20 (d, 13.7)	4.73 (dd, 12.1, 3.0)
19	1.74 (3H, s)	1.75 (3H, s)	1.74 (3H, s)	1.76 (3H, s)	1.70 (3H, s)
20	0.67 (3H, s)	0.64 (3H, s)	0.68 (3H, s)	0.70 (3H, s)	0.80 (3H, s)
2′	5.62 (qq, 1.2, 1.2)	5.62 (br s)	5.60 (br s)	5.59 (qq, 1.4, 1.4)	5.67 (qq, 1.1, 1.1)
4′	2.01 (3H, d, 1.2)	2.03 (3H, s)	2.00 (3H, s)	2.01 (3H, d, 1.4)	2.06 (3H, d, 1.1)
5′	1.36 (3H, d, 1.2)	1.34 (3H, s)	1.33 (3H, s)	1.34 (3H, d, 1.4)	1.36 (3H, d, 1.1)
15-OOH			7.92 (s)	7.97 (s)	
OCH_3				3.13 (3H, s)	

a) Figures in parentheses denote *J* values (Hz). *b*) 600 MHz in C_6D_6. *c*) 400 MHz in C_6D_6.

Table 2. ^{13}C-NMR Data (δ/ppm) of **1**,[a] **2**,[b] **3**,[b] **4**,[b] and **5**[a]

C	1	2	3	4	5
1	38.7	39.1	39.1	39.0	38.3
2	138.6	141.2	139.3	138.9	29.1
3	143.9	142.9	143.5	141.4	53.6
4	203.7	203.9	203.3	202.1	212.6
5	48.3	48.5	48.7	48.2	48.5
6	44.3	44.1	43.9	43.9	45.3
7	205.7	207.7	207.1	206.2	205.6
8	137.7	137.5	138.1	137.0	137.7
9	111.7	111.1	111.7	111.9	111.8
10	47.7	46.9	46.6	46.1	50.7
11	42.7	41.2	41.1	41.0	33.9
12	40.5	45.8	45.9	45.1	38.9
13	22.7	121.7	125.3	126.0	25.2
14	124.9	142.8	139.2	139.7	40.8
15	131.4	70.7	81.4	81.6	73.6
16	17.7	29.9	24.5	25.8	24.8
17	25.8	29.8	24.7	24.5	26.6
18	64.2	64.9	64.2	72.2	64.0
19	29.7	30.5	30.3	29.1	29.8
20	24.6	25.1	25.2	25.0	34.0
1′	163.2	163.3	163.3	163.3	163.3
2′	115.0	114.6	114.9	114.9	115.1
3′	160.1	160.6	160.3	160.1	160.0
4′	20.2	20.6	20.3	20.2	20.3
5′	27.0	27.7	27.0	27.0	27.0
OCH_3				56.3	

a) 150 MHz in C_6D_6. *b*) 100 MHz in C_6D_6.

of a hydroperoxy proton signal (δ 7.92, s) and a low-field shifted quaternary carbon (δ_C 81.4). Analysis of 2D-NMR of **3** showed the same planar structure as vibsanin K (**8**). The molecular formula of $C_{25}H_{36}O_7$ (*m/z* 471.2388 $[M+Na]^+$) for **3**, however, suggested the presence of one oxygen atom more than that of **2**. Moreover, a KI-starch test of **3** showed a positive result.[6] These data implied the presence of a hydroperoxy group on C-15 or C18 in the molecule of **3**. The hydroperoxy group was verified to be located on the C-15 position on the basis of the C-15 quaternary carbon signal appearing abnormally downfield at δ_C 81.4 (**2**; δ_C 70.6).[7] The stereochemistry of **3**, including the absolute configuration, was established to be the same as **2** on the basis of the 2D-NOESY and the CD spectrum [$\Delta\varepsilon$ (248 nm) +3.1]. Accordingly, the structure of **3** was determined to be 5-*epi*-vibsanin K.

Compound **4** had the molecular formula $C_{26}H_{38}O_7$ (*m/z* 485.2537 $[M+Na]^+$), and its spectral data indicated the presence of a hydroperoxy group (δ_H 7.98, δ_C 81.6) at the C-15 position. The NMR data (Tables 1, 2) of **4** were very similar to those of **3** except for the presence of a methoxy group (δ_H 3.13; δ_C 56.3) and a δ_C value difference of C-18 (**4**; δ_C 72.2, **3**; δ_C 64.2). These spectral data disclosed that the hydroxyl group on the C-18 position in 5-*epi*-vibsanin K (**3**) was replaced by a methoxy group in **4**. The relative configuration of **4** was elucidated on the basis of 2D-NOESY, and the absolute configuration of **4** was assigned as the same as that of **3** due to the same positive Cotton effect observed at 251 nm. Accordingly, **4** was represented as 18-*O*-methyl-5-*epi*-vibsanin K.

The IR spectrum of compound **5** displayed absorptions (1730, 1715, 1695 cm^{-1}) due to three carbonyl groups but the absence of a hydroxy group. The NMR data (Tables 1, 2) of **5** indicated the presence of a β, β-dimethylacryl enol ester, but were not similar to the other parts of seven membered vibsanins **1**—**4** discussed above, in particular, lacking two double bonds existing on the C-2 position and the C-12 prenly unit of the former. This type of structure is usually observed in a tricyclic vibsanin E (**10**) previously reported.[4,8] In fact, the molecular formula $C_{25}H_{36}O_5$ determined by HR-FAB-MS revealed seven degrees of unsaturation, indicating that **5** was a tricyclic seven-membered vibsanin. Moreover, the ^{1}H-NMR data of **5** was found to be similar to those of vibsanin E (**10**) except for the H-5 (**5**: δ_H 4.16, $J_{5,10}$=3.6 Hz; **10**: δ_H 3.06, $J_{5,10}$=11.5 Hz), thereby suggesting that **5** was a C-5 epimer of **10**. Additionally, a *cis* relationship on the C-5 and C-10 substiuents was confirmed by the observation of NOE between H-5 and H-10 in the NOESY. Thus, **5** was named 5-*epi*-vibsanin E.

5-*epi*-Vibsanin C (**1**) and 5-*epi*-vibsanin H (**2**) exhibited moderate cytotoxic activities on KB cells (IC_{50} 10.7, 45.5 μM), whereas vibsanin C (**6**) showed a similar degree of cytotoxic activity (IC_{50} 11.3 μM), assuming that the stereochemistry with regard to the C-5 position did not play an important role in these activities.

In conclusion, we were able to isolate the five seven-membered vibsane-type diterpenes with a *cis* relationship on the C-5 and C-10 positions for the first time, and thereby supported our proposed biogenesis of seven-membered vibsane derived from eleven-membered vibsanins *via* a Cope-type rearrangement.[9]

Experimental

Optical rotations were measured on a Jasco DIP-1000. UV spectra were recorded on a Hitachi 340 spectrophotometer. IR spectra were measured on a Jasco FT-IR 5300. ^{1}H- and ^{13}C-NMR spectra were obtained at 400 or 600 MHz (^{1}H-NMR) and 100.16 or 150 MHz (^{13}C-NMR) using JEOL GX-400 or Varian Unity 600 instruments. Chemical shift values were expressed in δ (ppm) downfield from tetramethylsilane as an internal standard. The MS were recorded on a JEOL AX-500 instrument. CD spectra were recorded in EtOH on a JASCO-J-500. Silica gel (Merck, 70—230 mesh and Wakogel C-300) and octadecylsilica gel (Cosmosil ^{75}C18-OPN) were used for column chromatography. Precoated silica gel 60 F_{254} and RP-8 F254 plates were used for analytical thin-layer chromatographies, and spots were visualized by UV (254 nm) light and 2% $CeSO_4$ in H_2SO_4 after heating.

Extraction and Purification Leaves of *V. awabuki* were collected in Tokushima, Japan, and a voucher specimen has been deposited in the herbarium of our institute. The dried and powdered leaves of *V. awabuki* (1.5 kg) were immersed in MeOH at room temperature for 1 month. The MeOH extract was evaporated *in vacuo* to give a gummy extract (500 g). This extract (95 g), mixed with silica gel (Merck, 70—230 mesh, 100 g) in MeOH, was dried under reduced pressure. The obtained solids were pulverized, packed into a glass column, and eluted in order with *n*-hexane (2 l), *n*-hexane–EtOAc (7 : 3, 2 l), *n*-hexane–EtOAc (1 : 1, 2 l), EtOAc (2 l), EtOAc–MeOH (8 : 2, 2 l), and MeOH (4 l) to give 6 fractions (1—6). Fraction 4 (13 g) was purified by repeated silica gel column chromatography (C-300, 1. $CHCl_3$: MeOH=30 : 1; 2. *n*-hexane : EtOAc=7 : 3) to give fractions 12—15. Fraction 15 (300 mg) was subjected to reverse-phase chromatography using Cosmosil ^{75}C18-OPN, then eluted with MeOH–H_2O (7 : 3) to give fractions 16—18. Fraction 18 (40 mg) was rechromatographed on silica gel (Merck, 230—400 mesh, 5 g) with *n*-hexane–acetone (3 : 1) to give 5-*epi*-vibsanin C (**1**) (2.1 mg) and 18-*O*-methyl-5-*epi*-vibsanin K (**4**) (1.3 mg). Fraction 17 (123 mg) was purified by HPLC [Cosmosil ^{5}C18-AR, i.d. 10×250 mm; MeOH–H_2O (13 : 7; 2 ml/min)] to afford 5-*epi*-vibsanin H (**2**) (15.6 mg). Fraction 3 (12 g) was rechromatographed on silica gel (C-300, 120 g) with *n*-hexane–EtOAc (1 : 1) to give fractions 19—21. Fraction 19 (63 mg) was purified by HPLC [Cosmosil ^{5}C18-AR, i.d. 10×280 mm; MeOH–H_2O (2.5 : 1.2; 2 ml/min)] to give 5-*epi*-vibsanin K (**3**) (4.1 mg) and 5-*epi*-vibsanin E (**5**) (8.5 mg).

5-*epi*-Vibsanin C (**1**): $[\alpha]_D^{24}$ +38.6° (*c*=0.59, $CHCl_3$); CD $\Delta\varepsilon$ (249 nm) +3.7; FAB-MS *m/z* (rel. int. %): 439 $[M+Na]^+$, 154 (100); HR-FAB-MS:

Found 439.2436, Calcd 439.2461 for $C_{25}H_{36}O_5Na$; UV λ_{max} (EtOH) nm (ε): 233 (21400); IR (film) cm^{-1}: 3501 (OH), 1728, 1707, 1668 (C=O), 1645 (C=C); ^1H- and ^{13}C-NMR: Tables 1 and 2.

5-*epi*-Vibsanin H (**2**): $[\alpha]_D^{21}$ +49.2° (c=0.41, $CHCl_3$); CD $\Delta\varepsilon$ (245 nm) +3.9; FAB-MS *m*/*z* (rel. int. %): 455 $[M+Na]^+$, 115 (100); HR-FAB-MS: Found 455.2417, Calcd 455.2409 for $C_{25}H_{36}O_6Na$; UV λ_{max} (EtOH) nm (ε): 220 (30300); IR (film) cm^{-1}: 3492 (OH), 1726, 1715, 1660 (C=O), 1645 (C=C); ^1H- and ^{13}C-NMR: Tables 1 and 2.

5-*epi*-Vibsanin K (**3**): $[\alpha]_D^{21}$ +52.4° (c=0.20, $CHCl_3$); CD $\Delta\varepsilon$ (248 nm) +3.1; FAB-MS *m*/*z* (rel. int.%): 471 $[M+Na]^+$, 154 (100); HR-FAB-MS: Found 471.2388, Calcd 471.2359 for $C_{25}H_{36}O_7Na$; UV λ_{max} (EtOH) nm (ε): 225 (21400); IR (film) cm^{-1}: 3414 (OOH), 1730, 1712, 1657 (C=O), 1647 (C=C); ^1H- and ^{13}C-NMR: Tables 1 and 2.

18-*O*-Methyl-5-*epi*-vibsanin K (**4**): $[\alpha]_D^{21}$ +11.9° (c=0.12, $CHCl_3$); CD $\Delta\varepsilon$ (251 nm) +2.5; FAB-MS *m*/*z* (rel. int. %): 485 $[M+Na]^+$, 154 (100); HR-FAB-MS: Found 485.2537, Calcd 485.2516 for $C_{26}H_{38}O_7Na$; UV λ_{max} (EtOH) nm (ε): 230 (26100); IR (film) cm^{-1}: 3412 (OOH), 1715, 1710, 1660 (C=O), 1651 (C=C); ^1H- and ^{13}C-NMR: Tables 1 and 2.

5-*epi*-Vibsanin E (**5**): $[\alpha]_D^{21}$ −34.7° (c=0.21, $CHCl_3$); CD $\Delta\varepsilon$ (288 nm) −5.2; HR-FAB-MS: Found 439.2482 $[M+Na]^+$, Calcd 439.2461 for $C_{25}H_{36}O_5Na$; UV λ_{max} (EtOH) nm (ε): 238 (11400); IR (film) cm^{-1}: 1730, 1715, 1695 (C=O), 1645 (C=C); ^1H- and ^{13}C-NMR: Tables 1 and 2.

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References and Notes

1) Kawazu K., *Agiric. Biol. Chem*., **44**, 1367—1372 (1980).
2) Fukuyama Y., Minami H., Takeuchi K., Kodama M., Kawazu K., *Tetrahedron Lett*., **37**, 6767—6770 (1996).
3) Fukuyama Y., Minami H., Takaoka S., Kodama M., Kawazu K., Nemoto H., *Tetrahedron Lett*., **38**, 1435—1438 (1997).
4) Minami H., Anzaki S., Kubo M., Kodama M., Kawazu K., Fukuyama Y., *Chem. Pharm. Bull*., **46**, 1194—1198 (1998).
5) Fukuyama Y., Minami H., Kagawa M., Kodama M., Kawazu K., *J. Nat. Prod*., **62**, 337—339, (1999).
6) *a*) Krebs K. G., Heuser D., Wimmer H., "Thin Layer Chromatgraphy: A Laboratory Handbook," 2nd Ed., Springer, Berlin, 1969, p. 881; *b*) Hashidoko Y., Tahara S., Mizutani J., *Phytochemistry*, **28**, 425—430 (1989).
7) *a*) Kitagawa I., Cui Z., Son B. W., Kobayashi M., Kyogoku Y., *Chem. Pharm. Bull*., **35**, 124—135 (1987); *b*) Casteel D. A., *Natural Product Reports*, **9**, 289—312 (1992); *c*) Casteel D. A., *ibid*., **16**, 55—73 (1999).
8) Fukuyama K., Katsube Y., Kawazu K., *J. Chem. Soc. Perkin 2*, **1980**, 1701—1703.
9) It should be noted that compound **1** could not be converted from its *trans* one **6** by exposure to silica gel overnight.