

Rearranged Vibsane-Type Diterpenes from *Viburnum awabuki* and Photochemical Reaction of Vibsanin B

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Nine new diterpenes, neovibsanin D (1), 7-*epi*-neovibsanin D (2), 15-*O*-methylneovibsanin F (3), 14-*epi*-15-*O*-methylneovibsanin F (4), 15-*O*-methyl-18-oxoneovibsanin F (5), 2-*O*-methylneovibsanin H (6), 2-*O*-methylneovibsanin I (7), neovibsanin G (8), and 14-*epi*-neovibsanin G (9), were isolated from a methanol extract of the leaves of *Viburnum awabuki*. Their structures were elucidated to be uniquely rearranged vibsane-type diterpenes by spectroscopic analyses and comparison of NMR data with those of previously reported vibsane-type diterpenes. In addition, irradiation of vibsanin B (12) in methanol with a high-pressure Hg lamp led to the direct formation of neovibsanins A (14) and B (15). These results gave a clue to understanding of the biogenetic interconversion of 11-membered vibsanins into neovibsanins.

Key words vibsane-type diterpene; neovibsanin; *Viburnum awabuki*; Caprifoliaceae; photochemical reaction

Vibsane-type diterpenes can be regarded as quite rare natural products because they occur exclusively in *Viburnum* species such as *V. awabuki*^{1–11} and *V. odoratissimum*.^{12–15} The carbon skeletons of vibsane-type diterpenes consist of three structural subtypes, *i.e.*, 11- and 7-membered ring compounds, and rearranged type (neovibsanin-type) such as vibsanins B (12) and C (13),^{1,3} and neovibsanin A (14),² respectively. Among these three subtypes, neovibsanin-type

diterpenes occupy a particular position in the vibsane-type natural products, owing to their unprecedented skeleton as well as intriguing biological activities.¹⁶ We have already established the chemical conversion of vibsanin B (12) to neovibsanin skeletons,^{2,3} but have not succeeded in determining conditions suitable for the provision of any intact neovibsanins. Thus, our continuing interests in chemical and biological profiles of vibsane-type diterpenes have resulted in

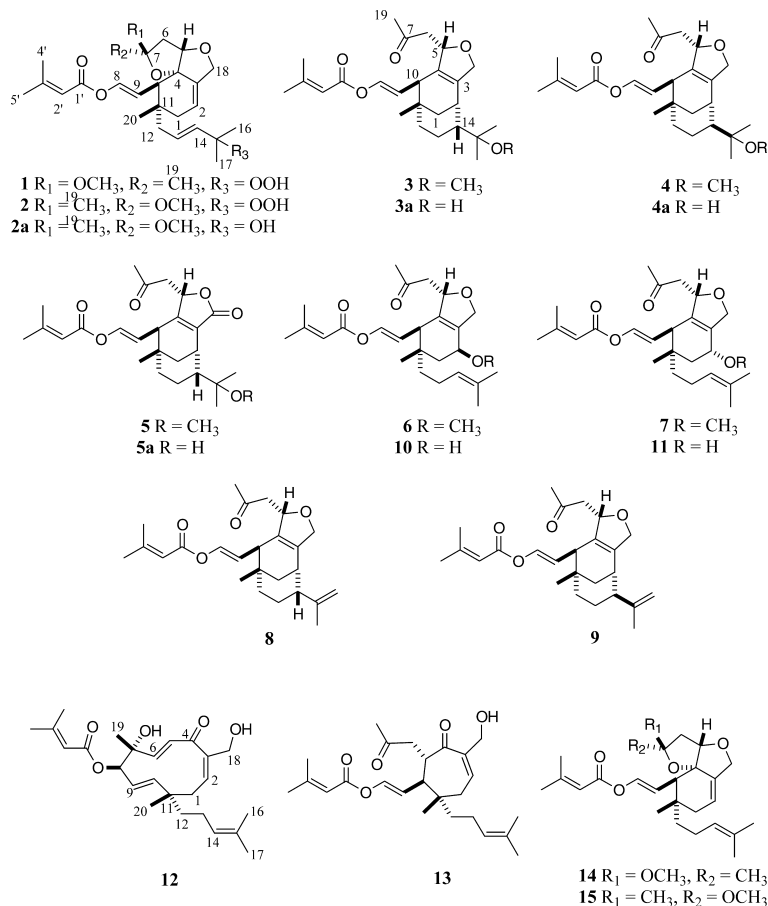


Fig. 1. Vibsanin-Type Diterpenes from *Viburnum awabuki*

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the isolation of nine new neovibsanane-type diterpenes **1**–**9** from a methanol extract of the leaves of *Viburnum awabuki*, as well as the successful interconversion of vibsanin B (**12**) to neovibsanins A (**14**) and B (**15**) by photochemical reaction. Herein, we report the structure elucidation of **1**–**9** and the detailed photochemical reaction of **12**.

Results and Discussion

Compounds **1** and **2** had the same molecular formula, $C_{26}H_{38}O_7$, as established by the high-resolution (HR)-FAB-MS at m/z 485.2512 $[M+Na]^+$. Their NMR data (Table 1) were not only very similar to each other but also resembled those of neovibsanins A (**14**) and/or B (**15**)²⁾ except for the data of a C-12–C-17 side chain. Routine analyses of 1H – 1H shift correlated spectroscopy (COSY), 1H -detected heteronuclear correlation through multiple quantum coherence (HMQC) and 1H -detected heteronuclear multiple-bond correlation (HMBC) spectra of **1** and **2** implied that both compounds were congeners of neovibsanins A and/or B bearing an *E* double bond [δ 5.86 (ddd, $J=15.6, 8.8, 6.4$ Hz, H-13), 5.59 (d, $J=15.6$ Hz, H-14)] at the C-13 position, and a hydroperoxyl group at the C-15 position, the presence of which was supported by a low-field C-15 quaternary carbon signal resonated at δ 81.7 and a positive KI-starch test. Reduction of this hydroperoxyl group in **2** with triphenylphosphine gave rise to **2a** (δ 70.3 for C-15), the spectral data of which were consistent with those of the compound derived from neovibsanin B (**15**) by a photosensitized oxida-

tion, followed by reduction with triphenylphosphine.⁸⁾ These results indicated that **2** was neovibsanin B with a hydroperoxyl group at the C-15 position, whereas **1** was the 15-hydroperoxyl congener of neovibsanin A. These assignments were supported by nuclear Overhauser effect (NOE) correlations between H-10 and H₃-19 for **1**, and H-10 and OCH₃ for **2** in the nuclear Overhauser effect spectroscopy (NOESY) spectra. Accordingly, the structure of **1**, named neovibsanin D, was determined as shown in Fig. 1, whereas **2** was assigned as a stereoisomer of **1** with regard to C-7, and thus designated 7-*epi*-neovibsanin D.

15-*O*-Methylneovibsanin F (**3**)¹⁷⁾ had the molecular formula $C_{26}H_{38}O_5$, as established by HR-FAB-MS. The NMR (Table 2) and physical data of **3** showed the presence of a methoxy group [δ_H 2.82 (3H, s); δ_C 48.6], three tertiary methyl groups [δ 0.81 (H-20), 0.84 (H-16), and 0.88 (H-17)], a disubstituted double bond with an *E* geometry [δ 5.19 (dd, $J=12.4, 11.0$ Hz, H-9), 7.43 (d, $J=12.4$ Hz, H-8); δ 114.9 (C-9), 136.1 (C-8)], an oxymethylene [δ_H 4.42 (br ddd, $J=11.5, 3.3, 3.3$ Hz, H-18), 4.95 (ddd, $J=11.5, 4.9, 3.0$ Hz, H-18), δ_C 77.3 (C-18)] having long-range couplings with H-2 at δ 2.38 (dddd, $J=3.3, 3.2, 3.0, 2.5$ Hz) and H-5 at δ 5.26 (dddd, $J=7.3, 4.9, 3.8, 3.3$ Hz), a methyl ketone [1725 cm^{-1} ; δ 2.03 (C-19); δ 206.6 (C-7)], as well as a β,β -dimethyl acrylate group (partial unit **A**) as most vibsanane-type diterpenes have. Analyses of COSY and HMQC spectra provided the partial structures **B** and **C** as depicted in Fig. 2. These spectral data suggested that **3** was a neovibsanane-type

Table 1. 1H -NMR (600 MHz) and ^{13}C -NMR (150 MHz) Data^{a,b)} for Compounds **1**, **2** and **2a** in C_6D_6

Position	1		2		2a	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1	1.58 dd (18.6, 3.0) 1.93 dd (18.6, 2.1)	33.4	1.67 dd (18.6, 3.7) 1.84 d (18.6, 2.1)	36.0	1.68 dd (15.8, 3.5) 1.86 dd (15.8, 2.0)	36.5
2	5.23 ddd (3.0, 2.3, 2.1)	120.4	5.33 ddd (3.7, 2.2, 2.1)	120.9	5.33 ddd (3.5, 2.2, 2.0)	120.3
3		137.8		138.2		138.0
4		91.6		91.6		91.6
5	4.49 d (4.4)	87.5	4.63 d (5.6)	86.4	4.65 d (5.8)	86.4
6	2.30 dd (12.5, 4.4) 2.22 d (12.5)	45.1	1.70 dd (14.2, 5.6) 2.44 d (14.2)	46.6	1.70 dd (14.0, 5.8) 2.45 dd (14.0)	46.6
7		110.9		109.6		108.9
8	7.50 d (12.5)	137.5	7.47 d (12.5)	138.0	7.49 d (12.4)	138.3
9	5.12 dd (12.5, 11.7)	112.6	5.22 dd (12.5, 11.5)	112.7	5.24 dd (12.4, 11.5)	112.7
10	2.69 dd (11.7)	48.2	2.37 d (11.5)	48.5	2.36 d (11.5)	48.6
11		35.7		36.5		36.0
12	2.41 dd (13.7, 8.8) 2.83 dd (13.7, 6.4)	42.2	2.09 dd (13.7, 8.8) 2.65 dd (13.7, 5.9)	43.9	2.10 dd (13.1, 8.8) 2.63 dd (13.1, 6.3)	43.6
13	5.86 ddd (15.6, 8.8, 6.4)	128.5	5.86 ddd (15.9, 8.8, 5.9)	127.9	5.80 ddd (15.7, 8.8, 6.3)	123.9
14	5.59 d (15.6)	137.3	5.63 d (15.9)	137.3	5.60 d (15.7)	141.8
15		81.7		81.7		70.3
16	1.28 s	24.8	1.30 s	24.7	1.22 s	30.3
17	1.29 s	24.8	1.32 s	24.8	1.23 s	30.2
18	4.16 d (11.0) 4.54 dd (11.0, 2.3)	70.0	4.17 d (10.4) 7.79 dd (10.4, 2.2)	70.5	4.18 d (10.2) 4.82 dd (10.2, 2.2)	70.5
19	1.44 s	23.8	1.35 s	23.3	1.36 s	25.4
20	0.90 s	26.1	0.88 s	25.5	0.89 s	27.0
1'		163.2		163.3		163.1
2'	5.66 qq (1.2, 1.2)	115.1	5.67 qq (1.2, 1.2)	115.1	5.68 qq (1.4, 1.1)	115.1
3'		159.6		160.0		159.8
4'	2.03 d (1.2)	20.2	2.04 d (1.2)	20.3	2.05 d (1.1)	20.3
5'	1.36 d (1.2)	27.0	1.39 d (1.2)	27.0	1.38 d (1.4)	27.0
OCH ₃	3.19 s	50.0	3.12 s	48.9	3.14 s	48.9
OOH	7.11 s		7.10 s			

a) Coupling constants (J) in parentheses in Hz. b) Assignment made by COSY, DEPT, HMQC, and HMBC spectra.

diterpene having no acetal ring like neovibsanin I (**11**).⁶⁾

As the HMBC of **3** is summarized in Fig. 2, a methoxy, H₃-17, and H₃-16 signals showed correlations to the quaternary C-15 resonated at δ 75.1 indicating the presence of a

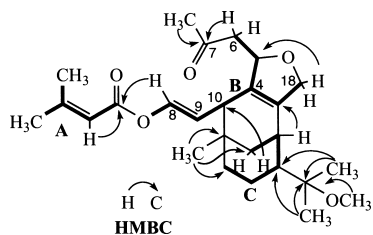


Fig. 2. HMBC of 15-*O*-Methylneovibsanin F (**3**)

2-methoxyisopropyl unit, which was proved to be bonded to C-14 in unit C on the basis of a HMBC correlation between H₃-16 and/or H₃-17 and C-14. The H-5 and H-8 signal showed a cross peak to the C-7 carbonyl resonance in unit B and the C-1' ester carbonyl signal at δ 163.2 in unit A, respectively, indicating that the methyl ketone function bonded to C-6 and unit A linked to C-8 *via* an ester bond. Moreover, one (δ 4.95) of the H₂-18 signals showed an HMBC correlation with C-5 at δ 83.9. In addition to this HMBC data, long-range couplings between H-5 and H-18 and low-field chemical shifts observed for C-5 and C-18 allowed an ether bond to be put together between C-5 and C-18 in unit B. From the additional HMBC correlations of H₃-20 to C-1 at δ 40.1, C-12 at δ 43.3, and a quaternary car-

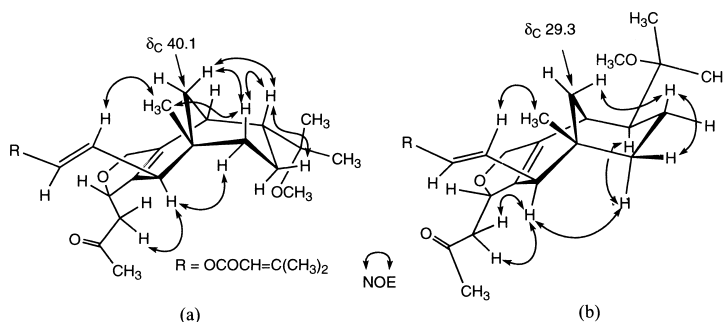


Fig. 3. NOESY Correlations for **3** (a) and **4** (b)

Table 2. ¹H-NMR (600 MHz) and ¹³C-NMR (150 MHz) Data^{a,b)} for Compounds **3**–**5** in C₆D₆

Position	3		4		5	
	δ_{H}	δ_{C}	δ_{H}	δ_{C}	δ_{H}	δ_{C}
1	1.00 dd (12.4, 2.5) 1.48 dd (12.4, 3.2)	40.1	1.21 m 1.21 m	29.3	0.95 dd (12.6, 2.5) 1.12 dd (12.6, 3.0)	38.8
2	2.38 dddd (3.3, 3.2, 3.0, 2.5)	30.1	2.22 br s	28.3	2.95 dd (3.0, 2.5)	28.5
3		136.1		141.5		130.6
4		137.0		133.3		162.2
5	5.26 dddd (7.3, 4.9, 3.8, 3.3)	83.9	5.27 dddd (8.0, 5.2, 4.1, 3.3)	82.9	5.04 dd (8.2, 3.8)	77.6
6	2.51 dd (14.0, 7.3) 2.60 dd (14.0, 3.8)	48.7	2.31 dd (14.3, 8.0) 2.38 dd (14.3, 4.1)	48.4	2.25 dd (15.4, 3.8) 2.34 dd (15.4, 8.2)	45.8
7		206.6		206.6		203.1
8	7.43 d (12.4)	136.1	7.47 d (12.4)	137.5	7.30 d (12.4)	136.7
9	5.19 dd (12.4, 11.0)	114.9	5.33 dd (12.4, 9.6)	113.0	4.83 dd (12.4, 11.4)	113.6
10	2.41 d (11.0)	42.9	2.10 d (9.6, 2.5)	44.8	2.33 d (11.4)	43.5
11		32.9		32.3		32.9
12	1.12 ddd (13.2, 13.2, 4.6) 1.55 dddd (13.2, 3.0, 2.5, 2.2)	43.3	1.24 m 1.39 m	35.8	1.04 ddd (14.4, 14.4, 4.5) 1.22 m	42.8
13	1.42 dddd (12.6, 4.6, 3.0, 2.5) 1.66 dddd (13.2, 12.6, 12.4, 2.2)	20.7	1.23 m 1.29 m	19.9	1.37 m 1.50 m	19.2
14	1.13 dd (12.4, 3.0)	51.3	1.27 m	45.6	1.15 m	51.0
15		75.1		76.9		75.4
16	0.84 s	23.8	0.86 s	21.0	1.42 s	22.8
17	0.88 s	29.1	0.86 s	22.3	1.03 s	23.6
18	4.95 ddd (11.5, 4.9, 3.0) 4.42 ddd (11.5, 3.3, 3.3)	77.3	4.44 dd (12.1, 3.3) 4.69 dd (12.1, 5.2)	75.1		171.1
19	2.03 s	30.7	1.95 s	30.4	1.75 s	30.4
20	0.81 s	29.7	0.87 s	27.8	0.69 s	29.0
1'		163.1		163.4		163.3
2'	5.63 qq (1.4, 1.4)	115.3	5.65 qq (1.4, 1.4)	115.2	5.64 qq (1.4, 1.4)	114.9
3'		159.4		159.6		160.3
4'	2.03 d (1.4)	20.2	2.04 d (1.4)	20.2	2.03 d (1.4)	20.3
5'	1.35 d (1.4)	27.0	1.36 d (1.4)	27.0	1.37 d (1.4)	27.0
OCH ₃	2.82 s	48.6	2.92 s	48.7	3.01 s	48.7

a) Coupling constants (*J*) in parentheses in Hz. b) Assignment made by COSY, DEPT, HMQC, and HMBC spectra.

bon C-11 at δ 32.9, unit **C** led to the formation of a cyclohexane ring including the C-11 quaternary carbon. Finally, another cyclohexane ring was obtained by the HMBC correlations of H-1 and H-2 to C-10 at δ 42.9 and C-3 at δ 136.1 in unit **B**. These HMBC data culminated in the plane structural proposal of **3** with a bicyclo[3.3.1]nonane ring. The relative stereochemistry of **3** was elucidated by NOESY experiments as summarized in Fig. 3a. According to the NOESY correlations of H-1 α to H-14 β and H-12 β , and the large J values (12.4 Hz) of H-13 α and H-14 β , a cyclohexane ring adopts a chair conformation with an α and equatorial 2-methoxy isopropyl group at the C-14 position. The other NOESY correlations, as shown in Fig. 3a, supported the relative configurations on C-5 and C-10. Hence, on the basis of the above spectral data, the structure of 15-*O*-methylneovibsanin **F** was represented as **3**.

The spectral data of 14-*epi*-15-*O*-methylneovibsanin **F** (**4**)¹⁷ were very similar to those of **3**. Routine analyses of 2D NMR spectra for **4** gave the same plane structure as that of **3**. This result suggests that **4** is a stereoisomer of **3** with regard to C-14. The relative stereochemistry of **4** was defined as taking the same stereogenic centers as those of **3** except for C-14 by the NOESY experiments summarized in Fig. 3b. The observation of cross peaks between H-1 α and H-13 β as well as H-12 α and H-10/H-14 α suggested that in the case of **4** the cyclohexane ring adopts a boat conformation with a pseudoequatorial 2-methoxy isopropyl group at the C-14 position. Additionally, this was supported by the fact that the chemical shift of C-1 shifted to a significantly high-field by *ca.* 10 ppm as compared with that of **3**, presumably because of a steric effect between C-1 and C-13 which exists only in the boat conformation. Thus, the structure of **4** was elucidated as 14-*epi*-15-*O*-methylneovibsanin **F**.

15-*O*-Methyl-18-oxoneovibsanin **F** (**5**)¹⁷ was assigned the molecular formula of C₂₆H₃₆O₆, as established by HR-FAB-MS. The IR spectrum displayed absorption at 1757 cm⁻¹ characteristic of a 5-membered lactone ring, and the NMR data (Table 2) was very similar to those of **3** except for the absence of H₂-18 oxymethylene and the presence of an additional ester carbonyl at δ_C 171.1. This means that the C-18 oxymethylene occurring in most vibsane-type diterpenes is oxidized to a carbonyl function. Intensive analyses of ¹H-¹H COSY and HMQC for **5** gave the same partial structures **A**—**D** as **1**—**3**, in addition to a different unit **E** having no hydrogen as shown in Fig. 4a. The partial unit **E** contains a newly appeared carbonyl group (C-18) and a tetrasubstituted double bond that resonated at δ_C 130.6 (C-3) and 162.2 (C-4), and thus C-18 and C-4 signals had a HMBC correlation with H-5 and one of the H₂-6 signals in unit **D** bearing a methyl ketone moiety, respectively. Consequently, the partial unit **E** turned out to be an α,β -unsaturated γ -lactone ring with unit **D** at the γ -position. The other HMBC correlations, as shown by arrows in Fig. 4a, led us to propose the plane structure **5**. As shown in Fig. 4b, the relative configuration of **5** was elucidated by NOESY to be identical with that of **3**. On the basis of the above spectral data, the structure of 15-*O*-methyl-18-oxoneovibsanin **F** was represented as **5**.

2-*O*-Methylneovibsanin **H** (**6**) and 2-*O*-methylneovibsanin **I** (**7**) had the same molecular formula C₂₆H₃₈O₅, as determined by HR-FAB-MS at m/z 453.2595 [M+Na]⁺ and their ¹³C-NMR data (Table 3). The ¹³C-NMR data of **6** and **7**

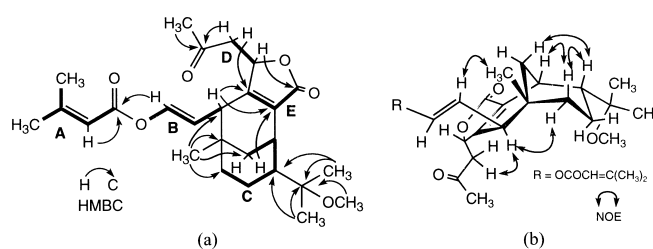


Fig. 4. HMBC (a) and NOESY (b) Correlations of **5**

Table 3. ¹H-NMR (600 MHz) and ¹³C-NMR (150 MHz) Data^{a,b} for Compounds **6** and **7** in C₆D₆

Position	6		7	
	δ_H	δ_C	δ_H	δ_C
1	1.50 dd (13.0, 8.7) 1.62 dd (13.0, 6.2)	36.2	1.49 dd (12.9, 4.9) 1.72 dd (12.9, 5.5)	38.1
2	3.72 dd (8.7, 6.2)	72.6	3.60 br dddd (5.5, 4.9, 2.2, 2.2)	72.9
3		133.8		137.2
4		137.5		175.4
5	5.22 m	83.1	5.25 dddd (8.5, 5.4, 3.3, 2.2)	83.7
6	2.31 dd (14.3, 7.7) 2.41 dd (14.3, 4.1)	48.1	2.36 dd (14.6, 8.5) 2.49 dd (14.6, 3.3)	47.9
7		205.0		205.0
8	7.50 d (12.4)	137.7	7.45 d (12.6)	138.6
9	5.28 dd (12.4, 11.0)	113.0	5.18 dd (12.6, 10.7)	111.3
10	2.34 d (11.0)	41.6	2.56 d (10.7)	41.9
11		37.8		38.1
12	1.27 br dd (10.2, 7.1)	39.0	1.48 ddd (16.8, 11.5, 5.2)	40.8
	1.32 br dd (10.2, 6.9)		1.40 ddd (16.8, 11.5, 5.2)	
13	1.98 m (2H)	23.0	1.94 dddd (19.2, 11.5, 5.2, 7.1) 2.04 dddd (19.2, 11.5, 5.2, 5.1)	22.8
14	5.24 t (7.4)	125.3	5.20 ddqq (7.1, 5.1, 0.8, 0.5)	125.5
15		131.0		131.0
16	1.69 s	25.6	1.61 d (0.5)	25.8
17	1.61 s	17.7	1.67 d (0.8)	17.8
18	4.57 br d (12.1) 4.97 br d (12.1)	75.0	4.56 ddd (11.8, 3.3, 2.2) 4.97 ddd (11.8, 5.4, 2.2)	74.8
19	1.89 s	30.2	1.89 s	30.7
20	0.84 s	24.6	0.69 s	21.1
1'		163.2		163.1
2'	5.60 qq (1.1, 1.1)	115.1	5.61 qq (1.4, 1.1)	115.1
3'		159.7		160.0
4'	2.02 d (1.1)	20.2	2.00 d (1.1)	20.2
5'	1.35 d (1.1)	27.0	1.34 d (1.4)	27.0
OCH ₃	3.02 s	56.0	3.02 s	56.1

a) Coupling constants (J) in parentheses in Hz. b) Assignment made by COSY, DEPT, HMQC, and HMBC spectra.

showed the presence of a ketone (δ 205.0 for **6** and **7**) and a conjugated ester (δ 163.2 for **6**; δ 163.1 for **7**). The NMR data (Table 3) of **6** and **7** were similar to those of neovibsanin **H** (**10**) and neovibsanin **I** (**11**) except for the presence of a methoxyl group (δ_H 3.02, δ_C 56.0 for **6**; δ_H 3.02, δ_C 56.1 for **7**). These spectral data disclosed that the C-2 hydroxyl group existing in **10** and **11** was methylated, respectively, in the cases of **6** and **7**. The methoxyl proton signal showed a HMBC correlation with the C-2 oxy-carbon resonating at

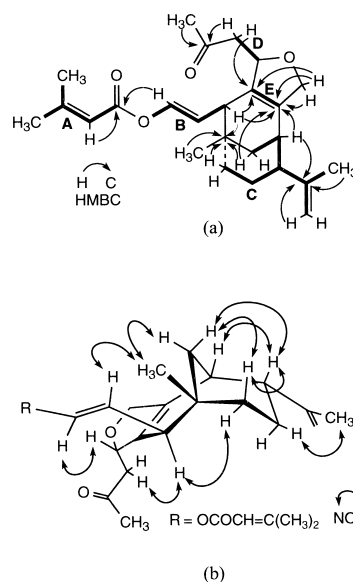
Table 4. $^1\text{H-NMR}$ (600 MHz) and $^{13}\text{C-NMR}$ (150 MHz) Data^{a,b} for Compounds **8** and **9** in C_6D_6

Position	8		9	
	δ_{H}	δ_{C}	δ_{H}	δ_{C}
1	1.02 dd (12.4, 2.5)	38.3	1.29 dd (12.9, 2.2)	30.4
	1.46 dd (12.4, 3.0)		1.18 dd (12.9, 3.0)	
2	2.34 m	32.6	2.24 m	30.9
3		137.2		137.5
4		134.8		136.4
5	5.24 dddd (7.1, 5.5, 4.1, 2.7)	83.9	5.30 ddd (7.2, 5.5, 3.8)	83.6
	2.41 dd (14.0, 7.1)		2.37 dd (14.3, 7.2)	
6	2.55 dd (14.0, 4.1)	48.5	2.45 dd (14.3, 3.8)	48.4
7		205.8		205.3
8	7.41 d (12.6)	136.3	7.39 d (12.4)	136.5
9	5.17 dd (12.6, 10.7)	114.3	5.22 dd (12.4, 10.2)	114.0
10	2.73 ddd (10.7, 3.0, 2.7)	49.1	2.23 dd (10.2, 2.6)	42.7
11		32.9		33.0
12	1.12 ddd (13.7, 13.5, 4.7)	42.3	1.46 ddd (13.5, 13.5, 5.5)	37.6
	1.51 ddd (13.7, 3.3, 3.3)		1.22 br d (13.5)	
13	1.40 m	23.5	1.65 m	22.1
	1.69 m		1.60 m	
14	1.70 m	45.0	1.81 m	40.1
15		147.9		146.1
16	1.53 s	22.5	1.57 s	22.6
17	4.70 s (2H)	110.1	4.89 br s	111.3
			4.92 br s	
18	4.11 ddd (12.1, 5.5, 3.0)	77.0	4.32 br d (12.0)	74.9
	4.30 ddd (12.1, 2.7, 2.7)		4.44 ddd (12.0, 5.5, 2.6)	
19	1.96 s	30.9	1.96 s	30.4
20	0.79 s	29.5	0.77 s	29.7
1'		163.3		163.3
2'	5.63 qq (1.4, 1.1)	115.2	5.64 qq (1.4, 1.1)	115.2
3'		159.6		159.7
4'	2.03 d (1.1)	20.2	2.03 d (1.1)	20.3
5'	1.35 d (1.4)	27.0	1.36 d (1.4)	27.0

a) Coupling constants (J) in parentheses in Hz. b) Assignment made by COSY, DEPT, HMQC, and HMBC spectra.

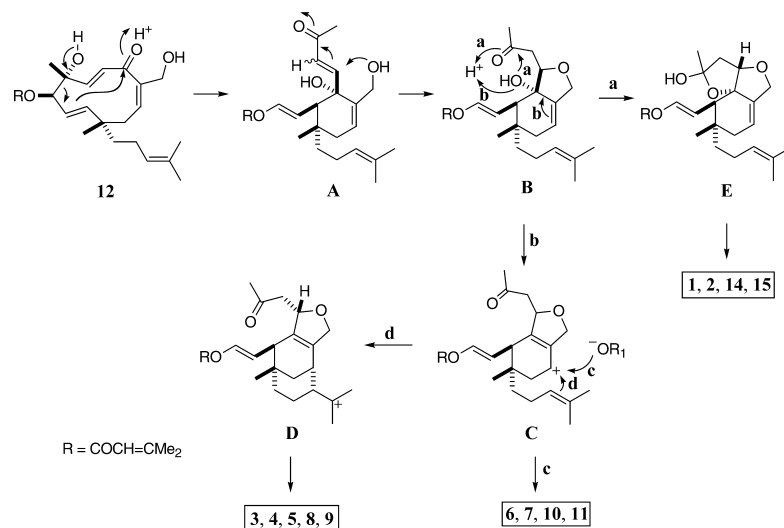
δ 72.6 for **6** and 72.9 for **7**. Consequently, **6** and **7** have the same plane structure. The relative configuration of **6** and **7** was assigned to be the same as that of neovibsanin H (**10**) and neovibsanin I (**11**), respectively, by analysis of NOESY (data not shown).

Neovibsanin G (**8**) had the molecular formula $\text{C}_{25}\text{H}_{34}\text{O}_4$, as established by HR-FAB-MS. The ^1H - and ^{13}C -NMR spectral (Table 4) and physical data of **8** showed the presence of a tertiary methyl group (δ_{H} 0.79, δ_{C} 29.5), a β,β -dimethylacrylate group (1728 cm^{-1}) which commonly exists in the vibsane-type diterpenes, a disubstituted *E*-olefin [δ 5.17 (dd, $J=12.6, 10.7\text{ Hz}$, H-9), 7.41 (d, $J=12.6\text{ Hz}$, H-8); δ 114.3 (C-8), 136.3 (C-9)], an oxymethylene [δ 4.11 (ddd, $J=12.1, 5.5, 3.0\text{ Hz}$, H-18), 4.30 (ddd, $J=12.1, 2.7, 2.7\text{ Hz}$, H-18); δ 77.0 (C-18)] which showed long-range couplings with H-5 at δ 5.24 (dddd, $J=7.1, 5.5, 4.1, 2.7\text{ Hz}$) and H-10 at δ 2.73 (ddd, $J=10.7, 3.0, 2.7\text{ Hz}$), an exomethylene [δ 4.70 (2H, s, H-17), δ 110.1 (C-17)], a tetrasubstituted double bond [δ 134.8 (C-4), 137.2 (C-3)], and a ketone function [1720 cm^{-1} ; δ 205.8 (C-7)]. These spectral data for **8** were similar to those of compound **3** except for the presence of the

Fig. 5. HMBC (a) and NOESY (b) Correlations of **8**

exo-methylene unit. This implied that the C-15 methoxyl group existing in **3** is eliminated to give the exo-methylene. The analysis of ^1H - ^1H COSY and HMQC of **8** provided a new partial structure **C**, in addition to the other partial structures **A**, **B**, **D** and **E**, which were involved in the structure of **3** as shown in Fig. 5a. In order to determine the connectivity between these five partial structures and six quaternary carbons (C-3, C-4, C-7, C-11, C-15, C-1'), HMBC experiments were carried out. The HMBC correlations of H-2 and H-1 to C-3 showed that C-2 connected to the C-3 carbon of the tetrasubstituted double bond **E**. The quaternary carbon C-11 showed HMBC correlations with H-1, H-12, and H₃-20 signals, and also H-10 had a correlation with C-11, thereby the quaternary carbon C-11 being bonded to C-1, C-12, C-10, and C-20. The other HMBC correlations as shown in Fig. 5a allowed us to propose the plane structure **8** consisting of a bicyclo[3.3.1]nonane framework with units **C** and **E** being fused together at C-2 and C-11, and C-5 and C-18, respectively. The relative stereochemistry of **8** was elucidated on the basis of NOESY correlations as shown in Fig. 5b. Namely, H-9 and H-10 showed cross-peaks to H₃-20, and to H-6 and H-12, respectively, indicating that 20-Me and an enol ester moiety attached on C-10 took β -configurations. In the NOESY spectrum, cross-peaks were observed between H-14 at δ 1.70 and H-1 α at δ 1.46, and H-12 β at δ 1.12, accounting for an equatorial and α configuration of an isopropenyl group at C-14. Hence, on the basis of the above data, the structure of neovibsanin G was elucidated as **8**.

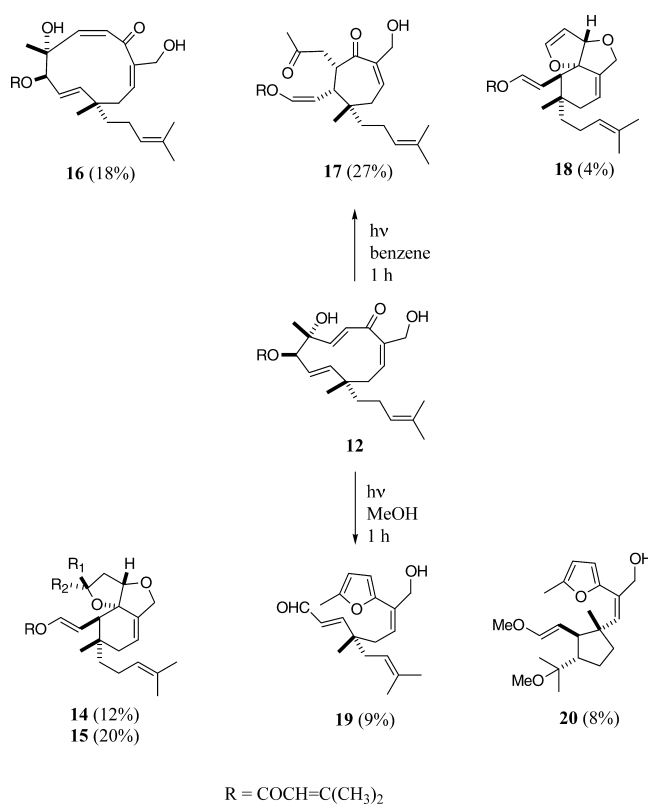
Compound **9** had the same molecular formula as **8**, and its physical and spectral data were very similar to those of **8**. Analysis of 2D NMR data for **9** gave the same plane structure as **8**. These spectral data suggest that **9** is a stereoisomer of **8** at the C-14 or C-5 position. In order to define the relative stereochemistry of **9**, 2D-NOESY experiments were carried out, and most correlations were identical with those of **8** except for H-1 α at δ 1.18, which had a cross-peak to H₃-16 at δ 1.57 but not to H-14. This means that **9** bears a β -oriented isopropenyl group at the C-14 position. Thus compound **9** was an epimer with regard to C-14 in **8** and assigned

Chart 1. Plausible Biosynthetic Pathway to Neovibsanins from Vibsantin B (**12**)

as 14-*epi*-neovibsanin G.

In the present study, we isolated nine new rearranged vibsane-type diterpenes **1**–**9** from the leaves of *V. awabuki*. In addition to 7-membered and 11-membered ring-types, rearranged types are not only regarded as characteristic components of some *Viburnum* species but also provide a unique framework for a variety of diterpenoids. However, biogenetic correlation between these three subtypes of vibsane-type diterpenes remains an elusive problem. In a previous paper,³ we showed that heating a toluene solution of vibsantin B (**12**) brought about an oxy-Cope rearrangement, giving rise to a 7-membered ring-type, vibsantin C (**13**), but not to neovibsanins at all. Although no chemical proof is available, vibsantin B (**12**) is presumably involved in the biosynthesis of the neovibsanins. Herein, we propose a possible biosynthetic pathway to neovibsanins **1**–**15**, as outlined in Chart 1. Namely, protonation of the C-4 carbonyl would cause a cyclization from the Δ^{10} double bond, which would trigger a retro-aldol reaction to afford a basic neovibsanin-skeleton **A**. The C-18 hydroxyl group would undergo a 1,4-addition to yield **B**. In the case of route a, a hemiacetal **E** would be formed, then leading to **1**, **2**, **14**, and **15**. Likewise, route b would give an intermediate allyl cation **C** followed by dehydration, which would be not only trapped by some nucleophiles such as water to afford **6**, **7**, **10**, and **11** (route c) but also would cause a cationic cyclization to give **D**, then leading to **3**, **4**, **5**, **8**, and **9** (route d).

We earlier reported the preparation of 7-membered vibsane-type diterpenes from vibsantin B (**12**) by heating its toluene solution.³ The stereospecific outcome for the generation of vibsantin C (**13**) and its 6-epimer can be rationalized by comparison of the stable conformations of **12** suitable for an oxy-Cope rearrangement. However, no reaction postulated in Chart 1 took place even on heating under acidic or basic conditions. Surprisingly, irradiation of **12** in benzene for 1 h with a high-pressure mercury lamp produced **18** with neovibsanin-framework in 4% yield together with (5*Z*)-10-*epi*-vibsantin B (**16**) and (8*Z*)-vibsantin C (**17**) in 18% and 27% yield, respectively.² It should be noted that these products **16**–**18** have never been found as natural products.¹⁸ This encouraged us to examine photochemical conditions for conversion

Chart 2. Photochemical Reaction of Vibsantin B (**12**)

of **12** to naturally occurring neovibsanins. After several trials, we found that irradiation of **12** in MeOH for 1 h directly yielded neovibsanins A (**14**) and B (**15**) in 12% and 20% yield, respectively, along with **19** and **20**¹⁸ as minor products (Chart 2).

A hydrogen abstraction mechanism of the hydroxyl group at the C-7 position is most likely to be involved in the initial transformation to **A** as shown in Chart 1. If this is intramolecular, the distance between the C-4 carbonyl and the C-7 OH plays a crucial role in this OH hydrogen abstraction. The MM2 calculations for (5*Z*)-vibsantin B and vibsantin B, in which the C12–C17 side chain was replaced with a *t*-butyl

group, were performed using MacroModel[®],¹⁹ providing the most stable conformers **12a** and **12b** for each molecule as shown in Fig. 6, respectively. In the case of **12a**, this distance is 1.65 Å, whereas **12b** has a distance of 4.98 Å. This result reasonably explains why a facile [1,7] hydrogen shift from the OH group at C-7 to the carbonyl at C-4 occurs in **12a**, but not in **12b**. Namely, vibsantin B (**12**) first isomerizes photochemically to (5*Z*)-form **16**, which subsequently not only causes a [1,7] hydrogen shift, followed by retro-aldol and subsequent cyclization, to afford neovibsantins, but also undergoes an oxy-Cope rearrangement to give a 7-membered (8*Z*)-vibsantin C (**17**) through the conformer **12a**. Thus, the photochemical reaction of **12** throws light on a biosynthetic pathway leading to neovibsantins.

Finally, Chart 3 shows that the generations of **19** and **20** are rationalized reasonably on the basis of a series of retro-Michael reactions and cationic cyclizations triggered by the methanolysis of a β,β -dimethylacryl ester group.

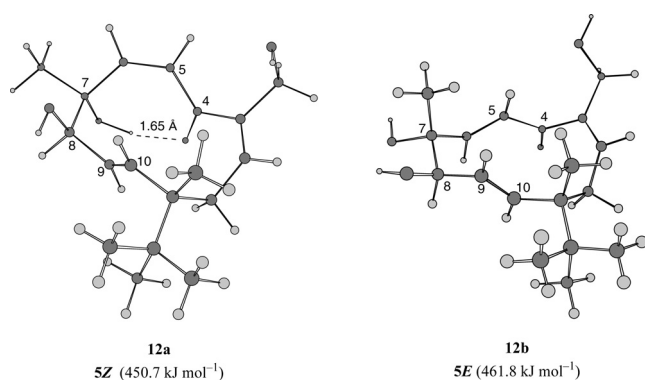


Fig. 6. The Most Stable Conformers **12a** (5*Z*) and **12b** (5*E*) for (5*Z*)-Vibsantin B and Vibsantin B, Respectively, Obtained by MM2 Calculation

Experimental

Optical rotations were measured with a JASCO DIP-1000 digital polarimeter. UV spectra were recorded on a Shimadzu UV-300 or Hitachi-U-3000 spectrophotometer. IR spectra were recorded on a JASCO FT-IR 5300 or FT-IR 410 infrared spectrophotometer. 1D and 2D NMR spectra were recorded on a Varian Unity 600. MS were recorded on a JEOL AX-500 instrument. Silica gel (Merck, 70–230, 230–400 mesh, Wacogel C-300, Cosmosil 75C₁₈-OPN) was used for column chromatography. Sephadex LH-20 was used for gel filtration chromatography. Precoated silica gel 60F₂₅₄ and RP-8 F₂₅₄ plates were used for analytical or preparative thin-layer chromatography, and spots were visualized by UV (254 nm) light and 2% CeSO₄ in H₂SO₄ after heating.

Plant Material The leaves of *Viburnum awabuki* K. KOCH were collected in Tokushima city in September 1999. A voucher sample has been preserved in the Institute of Pharmacognosy, Tokushima Bunri University.

Extraction and Isolation Air-dried and powdered leaves (15 kg) of *V. awabuki* were immersed in MeOH at room temperature for 30 d. The MeOH extract was concentrated *in vacuo* to give a gummy extract (500 g). The MeOH extract was mixed with silica gel [Merck silica gel 70–230 mesh (600 g)] and then MeOH was removed under reduced pressure. The obtained solids were pulverized, packed into a glass column, and eluted in order with CH₂Cl₂ (2 l), CH₂Cl₂-EtOAc (9:1, 2 l), CH₂Cl₂-EtOAc (3:2, 2 l), CH₂Cl₂-EtOAc (2:3, 2 l), EtOAc (2 l), EtOAc-MeOH (9:1, 2 l), EtOAc-MeOH (3:2, 2 l), EtOAc-MeOH (1:1, 2 l), and MeOH (2 l) to give fractions 1–9.

Fraction 3 (4.8 g) was divided by silica gel column chromatography eluted with hexane-EtOAc (7:3) to give fractions 10–13. Fraction 12 was purified by silica gel chromatography with CHCl₃-EtOAc (5:1), and then finally purified by HPLC [Cosmosil 5C₁₈-AR, i.d. 10×250 mm; MeOH-CH₃CN-H₂O (8:0.5:1.5; 2.0 ml/min); det. 254 nm] to give neovibsantin G (**8**) (6.3 mg) and 14-*epi*-neovibsantin G (**9**) (3.8 mg). Fraction 13 was purified by silica gel chromatography with hexane-EtOAc (3:1), and then finally purified by HPLC [Cosmosil 5C₁₈-AR, i.d. 10×250 mm; CH₃CN-H₂O (4:1; 2.0 ml/min); det. 254 nm] to give 15-*O*-methylneovibsantin F (**3**) (1.5 mg), and 14-*epi*-15-*O*-methylneovibsantin F (**4**) (5.4 mg), 15-*O*-methyl-18-oxoneovibsantin F (**5**) (1.7 mg). Fraction 10 was purified by a combination of LH-20 (MeOH) and silica gel chromatography with hexane-EtOAc (3:1), and then finally purified by column chromatography with MeOH-H₂O (7:3) to give neovibsantin D (**1**) (6.0 mg) and 7-*epi*-neovibsantin D (**2**) (2.3 mg). Fraction 11 was subjected to silica gel column chromatography eluted with hexane-EtOAc (2:1), and finally purified by silica gel column chromatography eluted with CHCl₃-EtOAc (4:1) to give 2-*O*-methylneovibsantin H (**6**) (3.0 mg) and 2-*O*-methylneovibsantin I (**7**) (7.0 mg).

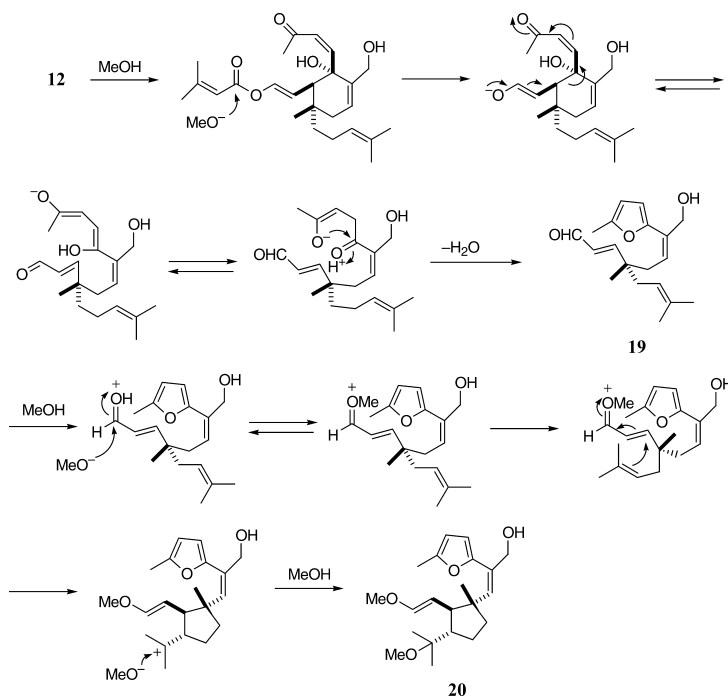


Chart 3. Mechanism for the Formations of **19** and **20**

Neovibsanin D (**1**): Colorless paste; $[\alpha]_D^{23} -66.1^\circ$ ($c=0.30$, CHCl_3); UV (EtOH) λ_{max} (EtOH) nm: 225 (ϵ 15900); IR (film) ν_{max} cm^{-1} : 3360 (OOH), 1645 (C=O); FAB-MS m/z 485 $[\text{M}+\text{Na}]^+$; HR-FAB-MS m/z : 485.2512 $[\text{M}+\text{Na}]^+$ (Calcd for $\text{C}_{26}\text{H}_{38}\text{O}_5\text{Na}$: 485.2515); ^1H - and ^{13}C -NMR: Table 1.

7-*epi*-Neovibsanin D (**2**): Colorless paste; $[\alpha]_D^{23} +24.2^\circ$ ($c=0.70$, CHCl_3); UV (EtOH) λ_{max} nm: 225 (ϵ 15200); IR (film) ν_{max} cm^{-1} : 3366 (OOH), 1645 (C=O); FAB-MS m/z 485 $[\text{M}+\text{Na}]^+$; HR-FAB-MS m/z : 485.2527 $[\text{M}+\text{Na}]^+$ (Calcd for $\text{C}_{26}\text{H}_{38}\text{O}_5\text{Na}$: 485.2515); ^1H - and ^{13}C -NMR: Table 1.

15-*O*-Methylneovibsanin F (**3**): Colorless paste; $[\alpha]_D^{23} +75.5^\circ$ ($c=0.12$, CHCl_3); UV (EtOH) λ_{max} nm: 225 (ϵ 18400); IR (film) ν_{max} cm^{-1} : 1725 (C=O), 1642 (C=C); FAB-MS m/z 453 $[\text{M}+\text{Na}]^+$, 469 $[\text{M}+\text{K}]^+$; HR-FAB-MS m/z : 453.2581 $[\text{M}+\text{Na}]^+$ (Calcd for $\text{C}_{26}\text{H}_{38}\text{O}_5\text{Na}$: 453.2617); ^1H - and ^{13}C -NMR: Table 1.

14-*epi*-15-*O*-Methylneovibsanin F (**4**): Colorless paste; $[\alpha]_D^{23} +65.9^\circ$ ($c=0.14$, CHCl_3); UV (EtOH) λ_{max} nm: 224 (ϵ 8700); IR (film) ν_{max} cm^{-1} : 1724 (C=O), 1641 (C=C); FAB-MS m/z 453 $[\text{M}+\text{Na}]^+$, 469 $[\text{M}+\text{K}]^+$; HR-FAB-MS m/z : 453.2661 $[\text{M}+\text{Na}]^+$, (Calcd for $\text{C}_{26}\text{H}_{38}\text{O}_5\text{Na}$: 453.2617); ^1H - and ^{13}C -NMR: Table 2.

15-*O*-Methyl-18-oxoneovibsanin F (**5**): Colorless paste; $[\alpha]_D^{23} +155.9^\circ$ ($c=0.08$, EtOH); UV (EtOH) λ_{max} nm: 231 (ϵ 35800); IR (film) ν_{max} cm^{-1} : 1757, 1725 (C=O), 1643 (C=C); FAB-MS m/z 467 $[\text{M}+\text{Na}]^+$; HR-FAB-MS m/z 467.2429 $[\text{M}+\text{Na}]^+$ (Calcd for $\text{C}_{26}\text{H}_{36}\text{O}_6\text{Na}$: 467.2448); ^1H - and ^{13}C -NMR: Table 2.

2-*O*-Methylneovibsanin H (**6**): Colorless oil; $[\alpha]_D^{23} +320.0^\circ$ ($c=0.22$, EtOH); UV (EtOH) λ_{max} nm: 225 (ϵ 51700); IR (film) ν_{max} cm^{-1} : 1729 (C=O), 1644 (C=C); FAB-MS m/z 453 $[\text{M}+\text{Na}]^+$; HR-FAB-MS m/z 453.2595 $[\text{M}+\text{Na}]^+$ (Calcd for $\text{C}_{26}\text{H}_{38}\text{O}_5\text{Na}$: 453.2618); ^1H - and ^{13}C -NMR: Table 3.

2-*O*-Methylneovibsanin I (**7**): Colorless paste; $[\alpha]_D^{23} +51.5^\circ$ ($c=0.28$, CHCl_3); IR (film) ν_{max} cm^{-1} : 1728 (C=O), 1645 (C=C); UV (EtOH) λ_{max} nm: 225 (ϵ 18400); FAB-MS m/z 453 $[\text{M}+\text{Na}]^+$, 469 $[\text{M}+\text{K}]^+$; HR-FAB-MS m/z 453.2628 $[\text{M}+\text{Na}]^+$ (Calcd for $\text{C}_{26}\text{H}_{38}\text{O}_5\text{Na}$: 453.2618); ^1H - and ^{13}C -NMR: Table 3.

Neovibsanin G (**8**): Colorless paste; $[\alpha]_D^{23} +96.2^\circ$ ($c=0.32$, EtOH); UV (EtOH) λ_{max} nm: 231 (ϵ 13100); IR (film) ν_{max} cm^{-1} : 1726, 1720 (C=O), 1644 (C=C); FAB-MS m/z 421 $[\text{M}+\text{Na}]^+$; HR-FAB-MS m/z 421.2337 $[\text{M}+\text{Na}]^+$ (Calcd for $\text{C}_{25}\text{H}_{34}\text{O}_4\text{Na}$: 421.2354); ^1H - and ^{13}C -NMR: Table 4.

14-*epi*-Neovibsanin G (**9**): Colorless paste; $[\alpha]_D^{23} +136.2^\circ$ ($c=0.09$, EtOH); UV (EtOH) λ_{max} nm: 233 (ϵ 13000); IR (film) ν_{max} cm^{-1} : 1728, 1720 (C=O), 1645 (C=C); FAB-MS m/z 421 $[\text{M}+\text{Na}]^+$; HR-FAB-MS m/z 421.2346 $[\text{M}+\text{Na}]^+$ (Calcd for $\text{C}_{25}\text{H}_{34}\text{O}_4\text{Na}$: 421.2354); ^1H - and ^{13}C -NMR: Table 4.

Reduction of 7-*epi*-Neovibsanin D (2**)** A mixture of **2** (2.0 mg) and triphenylphosphine (0.8 mg) in benzene (1 ml) was stirred at room temperature for 24 h. Removal of solvent left the residue, which was purified by preparative TLC [hexane-EtOAc (19:1)] to give **2a** (1.7 mg), the spectral data of which were identical with those of the compound derived from neovibsanin B (**15**) by a photo-sensitized oxidation, and then reduction of the formed hydroperoxyl group with triphenylphosphine.⁸⁾ ^1H - and ^{13}C -NMR for **2a**: Table 1.

Photochemical Reaction of Vibsanin B (12**) in Benzene** A solution of **12** (50 mg, 0.12 mmol) in benzene (2 ml) was irradiated for 1 h with a high-pressure mercury lamp. The reaction solution was condensed under reduced pressure to the residue, which was purified by HPLC [Cosmosil 5C₁₈-AR, i.d. 10×250 mm; MeOH-CH₃CN-H₂O (3:1:1; 2.0 ml/min); det. 254 nm] to give **16** (9.0 mg, 18%), **17** (14.0 mg, 27%), and **18** (2.0 mg, 4%).

(5*Z*)-Vibsanin B (**16**): Colorless oil; FAB-MS m/z 439 $[\text{M}+\text{Na}]^+$; HR-FAB-MS m/z 439.2460 $[\text{M}+\text{Na}]^+$ (Calcd for $\text{C}_{25}\text{H}_{36}\text{O}_5\text{Na}$: 439.2461); ^1H -NMR (200 MHz, C₆D₆) δ : 0.95 (3H, s, H₃-20), 1.24 (2H, m, H-12), 1.29 (3H, s, H₃-19), 1.55 (3H, s, H₃-17), 1.70 (3H, s, H₃-16), 1.88 (2H, m, H-13), 1.97 (3H, s, H₃-5'), 2.02 (2H, m, H-1), 2.18 (3H, H₃-4'), 4.07 (1H, d, $J=11.2$ Hz, H-18), 4.41 (1H, d, $J=11.2$ Hz, H-18), 5.03 (1H, m, H-14), 5.11 (1H, dd, $J=15.7$, 8.0 Hz, H-9), 5.21 (1H, d, $J=8.0$ Hz, H-8), 5.41 (1H, d, $J=15.1$ Hz, H-10), 5.74 (1H, m, H-2'), 5.78 (1H, d, $J=6.9$ Hz, H-5), 5.99 (1H, br d, $J=12.8$ Hz, H-2), 6.05 (1H, d, $J=6.9$ Hz, H-6).

(8*Z*)-10-*epi*-Vibsanin B (**17**): Colorless oil; $[\alpha]_D^{23} +62.7^\circ$ ($c=0.15$, CHCl_3); UV (EtOH) λ_{max} nm: 228 (ϵ 21500); IR (film) ν_{max} cm^{-1} : 3449 (OH), 1732, 1720 (C=O), 1647 (C=C); FAB-MS m/z 439 $[\text{M}+\text{Na}]^+$, 154; HR-FAB-MS m/z : 439.2485 $[\text{M}+\text{Na}]^+$ (Calcd for $\text{C}_{25}\text{H}_{36}\text{O}_5\text{Na}$: 439.2461); ^1H -NMR (400 MHz, C₆D₆) δ : 1.07 (3H, s, H₃-20), 1.13 (1H, ddd, $J=13.5$, 13.5, 4.9 Hz, H-12), 1.21 (1H, ddd, $J=13.5$, 11.5, 4.4 Hz, H-12), 1.37 (3H, d, $J=1.1$ Hz, H-5'), 1.54 (3H, s, H₃-16), 1.62 (3H, s, H₃-17), 1.73 (3H, s, H₃-19), 1.83 (1H, m, H-13), 1.91 (1H, m, H-13), 1.92 (2H, d, $J=6.0$ Hz, H-1),

2.12 (1H, dd, $J=18.1$, 5.4 Hz, H-6), 2.20 (3H, d, $J=1.1$ Hz, H₃-4'), 2.95 (1H, dd, $J=11.5$, 4.1 Hz, H-10), 3.04 (1H, dd, $J=18.1$, 7.7 Hz, H-6), 3.58 (1H, ddd, $J=7.7$, 5.4, 4.1 Hz, H-5), 4.22 (1H, d, $J=13.2$ Hz, H-18), 4.28 (1H, d, $J=13.2$ Hz, H-18), 4.45 (1H, dd, $J=11.5$, 6.6 Hz, H-9), 5.11 (1H, t, $J=7.0$ Hz, H-14), 5.64 (1H, qq, $J=1.1$, 1.1 Hz, H-2'), 6.10 (1H, t, $J=6.0$ Hz, H-2), 7.34 (1H, d, $J=6.6$ Hz, H-8); ^{13}C -NMR (100 MHz, C₆D₆) δ : 17.5 (C-16), 20.3 (C-4'), 23.0 (C-13), 25.8 (C-17), 26.2 (C-20), 27.0 (C-5'), 29.7 (C-19), 35.8 (C-1), 39.3 (C-12), 40.4 (C-11), 43.6 (C-10), 44.8 (C-6), 47.9 (C-5), 64.7 (C-18), 110.6 (C-9), 114.8 (C-2'), 125.0 (C-14), 131.2 (C-15), 136.9 (C-8), 137.8 (C-2), 143.4 (C-3), 160.4 (C-3'), 162.7 (C-1'), 203.9 (C-4), 205.9 (C-7).

Compound **18** with Neovibsanin Skeleton: Colorless oil; $[\alpha]_D^{23} -11.2^\circ$ ($c=0.31$, CHCl_3); UV (EtOH) λ_{max} nm: 216 (ϵ 25000); IR (film) ν_{max} cm^{-1} : 1728 (C=O), 1644 (C=C); EI-MS m/z 398 $[\text{M}]^+$, 154; HR-EI-MS m/z 398.2437 $[\text{M}]^+$ (Calcd for $\text{C}_{25}\text{H}_{34}\text{O}_4$: 398.2417); ^1H -NMR (600 MHz, C₆D₆) δ : 0.90 (3H, s, H₃-20), 1.12 (1H, ddd, $J=13.4$, 12.2, 4.9 Hz, H-12), 1.36 (3H, d, $J=1.2$ Hz, H₃-5'), 1.61 (3H, s, H₃-19), 1.62 (3H, s, H₃-16), 1.71 (3H, s, H₃-17), 1.72 (2H, d, $J=2.7$ Hz, H-1), 2.01 (1H, m, H₃-13), 2.03 (3H, d, $J=1.2$ Hz, H₃-4'), 2.10 (1H, m, H-13), 2.25 (1H, ddd, $J=13.4$, 10.0, 5.0 Hz, H-12), 2.47 (1H, d, $J=11.2$ Hz, H-10), 4.08 (1H, d, $J=10.3$ Hz, H-18), 4.25 (1H, dd, $J=10.3$, 2.0 Hz, H-18), 4.63 (1H, d, $J=1.2$ Hz, H-6), 5.27 (1H, dd, $J=12.5$, 11.2 Hz, H-9), 5.28 (1H, m, H-14), 5.32 (1H, dt, $J=2.7$, 2.0 Hz, H-2), 5.30 (1H, d, $J=1.2$ Hz, H-5), 5.62 (1H, qq, $J=1.2$, 1.2 Hz, H-2'), 7.47 (1H, d, $J=12.5$ Hz, H-8).

Photochemical Reaction of Vibsanin B (12**) in Methanol** A solution of **12** (50 mg, 0.12 mmol) in MeOH (2 ml) was irradiated for 1 h with a high-pressure mercury lamp. The reaction solution was condensed under reduced pressure to the residue, which was purified by HPLC [Cosmosil 5C₁₈-AR, i.d. 10×250 mm; MeOH-CH₃CN-H₂O (3:1:1; 2.0 ml/min); det. 254 nm] to give **14** (6.0 mg, 12%), **15** (10 mg, 20%), **19** (1.9 mg, 9%), and **20** (1.7 mg, 8%). Compounds **15** and **16** were identical in all respects with neovibsanins A and B, respectively.

8-Hydroxy-4-methyl-4-(3-methylbut-2-enyl)-7-(5-methylfuran-2-yl)-octa-2,6-dienal (**19**): Colorless oil; $[\alpha]_D^{23} -16.3^\circ$ ($c=0.20$, CHCl_3); EI-MS m/z 316 $[\text{M}]^+$; HR-EI-MS m/z : 316.2023 $[\text{M}]^+$ (Calcd for $\text{C}_{20}\text{H}_{30}\text{O}_3$: 316.2038); UV (EtOH) λ_{max} nm: 249 (ϵ 7100); IR (film) ν_{max} cm^{-1} : 3424 (OH), 1688 (C=C); ^1H -NMR (600 MHz, C₆D₆) δ : 0.83 (3H, s, H₃-20), 1.30 (1H, ddd, $J=10.2$, 6.6, 3.6 Hz, H-12), 1.31 (1H, ddd, $J=10.2$, 6.0, 3.0 Hz, H-12), 1.47 (3H, d, $J=0.5$ Hz, H₃-16), 1.52 (3H, d, $J=1.1$ Hz, H₃-17), 1.76 (1H, dddd, $J=15.9$, 7.1, 6.0, 3.6 Hz, H-13), 1.82 (1H, dddd, $J=15.7$, 7.1, 6.6, 3.0 Hz, H-13), 1.98 (3H, d, $J=0.5$ Hz, H₃-19), 2.45 (1H, br dd, $J=15.7$, 6.9 Hz, H-1), 2.54 (1H, br dd, $J=15.7$, 7.7 Hz, H-1), 4.17 (2H, br s, H-18), 5.05 (1H, ddq, $J=7.1$, 7.1, 1.1, 0.5 Hz, H-14), 5.46 (1H, br dd, $J=7.7$, 6.9 Hz, H-2), 5.80 (1H, dq, $J=3.3$, 0.5 Hz, H-6), 6.04 (1H, dd, $J=15.9$, 7.4 Hz, H-9), 6.19 (1H, br d, $J=3.3$ Hz, H-5), 6.26 (1H, d, $J=15.9$ Hz, H-10), 9.36 (1H, d, $J=7.4$ Hz, H-8); ^{13}C -NMR (150 MHz, C₆D₆) δ : 13.4 (C-19), 17.6 (C-16), 22.5 (C-20), 23.2 (C-13), 25.8 (C-17), 39.2 (C-1), 40.5 (C-12), 40.9 (C-11), 65.5 (C-18), 107.4 (C-6), 110.4 (C-5), 127.6 (C-2), 127.8 (C-14), 131.4 (C-15), 131.6 (C-3), 151.3 (C-4), 151.4 (C-7), 164.9 (C-10), 192.9 (C-8).

3-[3-(1-Methoxy-1-methylethyl)-2-(2-methoxyvinyl)-1-methylcyclopropyl]-2-(5-methylfuran-2-yl)-prop-2-en-1-ol (**20**): Colorless oil; $[\alpha]_D^{23} -24.2^\circ$ ($c=0.35$, CHCl_3); EI-MS m/z 362 $[\text{M}]^+$; HR-EI-MS m/z : 362.2549 $[\text{M}]^+$ (Calcd for $\text{C}_{22}\text{H}_{34}\text{O}_4$: 362.2457); UV (EtOH) λ_{max} nm: 242 (δ 1000); IR (film) λ_{max} cm^{-1} : 3418 (OH); ^1H -NMR (600 MHz, C₆D₆) δ : 0.87 (3H, s, H₃-20), 1.08 (3H, s, H₃-16), 1.09 (3H, s, H₃-17), 1.48 (1H, ddd, $J=12.1$, 7.7, 3.3 Hz, H-12), 1.58 (1H, ddd, $J=12.1$, 9.6, 3.8 Hz, H-12), 1.73 (1H, dddd, $J=13.5$, 9.9, 9.6, 7.7 Hz, H-13), 1.79 (1H, dddd, $J=13.5$, 6.0, 3.8, 3.0 Hz, H-13), 1.94 (1H, ddd, $J=9.9$, 9.9, 6.0 Hz, H-14), 2.13 (1H, dd, $J=10.2$, 9.9 Hz, H-10), 2.33 (1H, dd, $J=15.1$, 6.9 Hz, H-1), 2.79 (1H, dd, $J=15.1$, 8.2 Hz, H-1), 3.04 (3H, s, C15-OCH₃), 3.20 (3H, s, C8-OCH₃), 4.32 (2H, br s, H-18), 4.54 (1H, dd, $J=12.6$, 10.2 Hz, H-9), 5.78 (1H, $J=8.2$, 6.9 Hz, H-2), 5.81 (1H, dq, $J=3.3$, 0.5 Hz, H-6), 6.20 (1H, d, $J=12.6$ Hz, H-8), 6.30 (1H, d, $J=3.3$ Hz, H-5); ^{13}C -NMR (150 MHz, C₆D₆) δ : 13.4 (C-19), 21.0 (C-20), 23.1 (C-17), 24.4 (C-16), 25.1 (C-13), 37.7 (C-12), 40.2 (C-1), 46.9 (C-11), 48.8 (OCH₃-15), 49.7 (C-10), 52.8 (C-14), 55.6 (OCH₃-8), 66.2 (C-18), 76.8 (C-15), 105.8 (C-9), 107.3 (C-6), 110.1 (C-5), 126.2 (C-2), 130.8 (C-3), 147.7 (C-8), 151.0 (C-7), 151.9 (C-4).

Acknowledgements We wish to thank Prof. Kazuyoshi Kawazu for his valuable comments and encouragement, and Dr. Masami Tanaka and Miss Yasuko Okamoto (TBU) for measuring NMR and Mass spectra. This work was supported by a Grant-in Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

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- 16) Neovibsanins A (**14**) and B (**15**) show weak cytotoxicity against KB cell with IC_{50} 30.0 μ M and 32.9 μ M, respectively. More interestingly, they have neurite outgrowth promoting activity at 0.01 μ M in the primary cultured rat cortical neurons.²⁰ Their detailed biological activities will be reported elsewhere.
- 17) Recently we isolated new compounds **3a**, **4a**, and **5a** from a methanol extract of the leaves of *Viburnum suspensum*, and termed them neovibsanin F, 14-*epi*-neovibsanin F, and 18-*oxo*-neovibsanin F, respectively. Their detailed structures will be reported in due course. In this paper, we wish to retain these interim names for **3a**, **4a**, and **5a**.
- 18) New compounds **16**—**20** were fully characterized by extensive analysis of 2D NMR data.
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