New Diterpenoids from *Viburnum awabuki*

Ali A. H. El-Gamal,[†,‡] Shang-Kwei Wang,[§] and Chang-Yih Duh*[,†]

Department of Marine Resources, National Sun Yat-sen University, Kaohsiung, Taiwan, Republic of China, and Department of Microbiology, Kaohsiung Medical University, Kaohsiung, Taiwan, Republic of China

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Eight new vibsane-type diterpenoids, vibsanins P−W (**1**−**8**), were isolated from the methanol extracts of the leaves and twigs of *Viburnum awabuki*. The structures were elucidated by 1D and 2D NMR spectral analysis, and their cytotoxicity against selected cancer cells was measured in vitro.

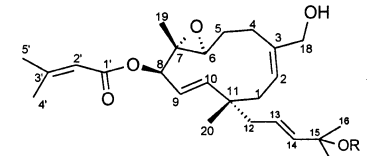
The plants of genus *Viburnum* are rich in diterpenoids.[1−12] As part of our search for bioactive substances from marine and terrestrial organisms, the leaves and twigs of *Viburnum awabuki* K. Koch (Caprifoliaceae) were studied because MeOH extracts showed significant cytotoxicity to A549 (human lung adenocarcinoma), HT-29 (human colon adenocarcinoma), and P-388 (mouse lymphocytic leukemia) cell cultures as determined by standard procedures.[13,14] Bioassay-guided fractionation resulted in the isolation of eight new vibsane-type diterpenoids, vibsanins P−W (**1**−**8**).

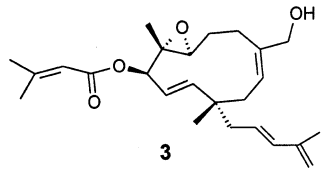
Results and Discussion

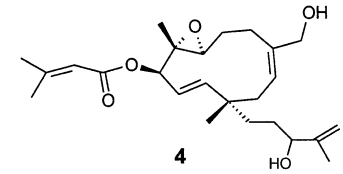
The molecular formula of vibsanin P (**1**) was established as $C_{25}H_{38}O_5$ from HREIMS, ^{13}C NMR, and DEPT spectra. Its IR spectrum indicated the presence of hydroxyl and α,β-unsaturated ester groups. The ^1H NMR spectrum (Table 1) exhibited six methyl singlets (δ 1.08, 1.25, 1.26, 1.43, 1.88, 2.12), an oxymethylene [δ 4.01 (d, J = 12.9 Hz), 4.10 (d, J = 12.9 Hz)], two oxymethines [δ 2.76 (dd, J = 12.0, 2.4 Hz), 5.07 (d, J = 9.9 Hz)], and six olefinic protons [5.31 (dd, J = 15.9, 9.9 Hz), 5.55 (dd, J = 9.3, 7.2 Hz), 5.56 (m), 5.65 (d, J = 16.5 Hz), 5.69 (br s), 5.82 (d, J = 15.9 Hz)]. Detailed analysis of the COSY and HSQC spectra of **1** gave six partial structures (Figure 1 in boldface). The double bond in the **b** part should have *E*-geometry due to the coupling constant (J = 15.9 Hz). The partial strcture **a** corresponding to a β,β-dimethylacryl group was additionally supported by observation of the prominent fragment ion peak at *m*/*z* 83 in the MS.

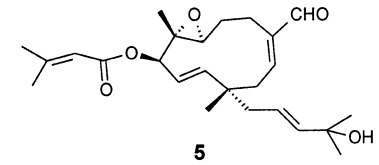
These substructures were connected through HMBC correlations between proton H-8 (δ_H 5.07) and carbons C-1′ (δ_C 165.7) and C-7 (δ_C 61.2), between protons H_3-19 (δ_H 1.43) and carbons C-7 (δ_C 61.2) and C-6 (δ_C 63.1), between proton H-6 (δ_H 2.76) and carbons C-5 (δ_C 26.3) and C-7 (δ_C 61.2), between methyl protons H_3-20 (δ_H 1.08) and carbons C-1 (δ_C 41.7), C-10 (δ_C 146.5), C-11 (δ_C 40.1), and C-12 (δ_C 41.4), between the protons H_3-16/17 (δ_H 1.26, 1.25) and carbons C-15 (δ_C 70.4) and C-14 (δ_C 144.4), between H_2-18 (δ_H 4.01, 4.10) and carbons C-2 (δ_C 120.5) and C-4 (δ_C 23.8), and between H-1 (δ_H 1.95) and carbons C-3 (δ_C 142.0) and C-12 (δ_C 41.4). Thus, the above spectral data indicated the planar structure **1** as shown in Figure 1.

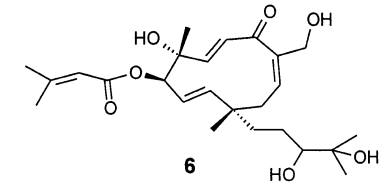
The relative stereochemistry of **1** was deduced from a 2D NOESY experiment (Figure 2), which indicated that Me-19, Me-20, H-6, and H-9 were on the β-face of the 11-membered ring, while H-8, H-10, and the epoxy ring at C-6/C-7 were on the α-face of the 11-membered ring.

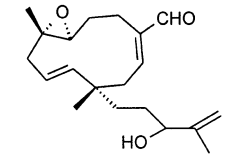


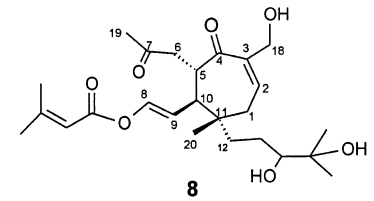












* To whom correspondence should be addressed. Tel: 886-7-525-2000, ext. 5036. Fax: 886-7-525-5020. E-mail: yihduh@mail.nsysu.edu.tw.
† National Sun Yat-sen University.
‡ On leave from Faculty of Pharmacy, Mansoura University, Egypt.
§ Kaohsiung Medical University.

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Table 1. ^{1}H NMR Data of **1**−**8**

H	**1**[a]	**2**[a]	**3**[b]	**4**[a]	**5**[a]	**6**[b]	**7**[b]	**8**[a]
1	1.95 m 2.15 m	2.02 m 2.16 m	1.97 m 2.14 m	1.98 m 2.18 m	2.35 m 2.41 m	1.93 m 2.09 m	2.35 m 2.52 m	1.90 m 2.35 m
2	5.55 dd (9.3, 7.2)	5.44 dd (9.3, 7.2)	5.56 m	5.55 dd (9.3, 7.2)	6.59 t (8.4)	6.04 dd (13.0, 4.0)	6.59 m	6.57 dd (8.7, 5.4)
4	2.12 m 2.25 m	2.11 m 2.26 m	2.13 m 2.26 m	2.11 m 2.22 m	1.90 m 2.59 m	2.12 m 2.25 m	2.42 m	
5	1.17 m 2.36 m	1.16 m 2.38 m	1.26 m 1.90 m	1.16 m 2.35 m	1.89 m 2.60 m	6.08 d (16.2)	2.21 m	3.02 m
6	2.76 dd (12.0, 2.4)	2.78 dd (11.4, 2.4)	2.78 dd (11.5, 2.0)	2.78 dd (11.7, 2.4)	2.78 dd (11.7, 2.4)	6.57 d (16.2)	2.73 d (10.0)	2.68 dd (12.3, 2.1) 2.96 dd (12.3, 2.1)
8	5.07 d (9.9)	5.17 d (9.9)	5.17 d (10.0)	5.14 d (9.9)	5.00 d (9.9)	5.34 d (9.0)	2.07 m	6.96 d (12.3)
9	5.31 dd (15.9, 9.9)	5.40 dd (15.9, 9.9)	5.40 dd (16.0, 10.0)	5.38 dd (15.9, 9.9)	5.32 dd (15.3, 9.9)	5.17 dd (16.0, 9.0)	5.31 dd (15.9, 9.9)	5.17 dd (12.3, 11.7)
10	5.82 d (15.9)	5.86 d (15.9)	5.88 d (16.0)	5.86 d (15.9)	5.74 d (15.3)	5.74 d (16.0)	5.82 d (15.9)	2.19 m
12	1.99 m 2.25 m	2.05 m 2.26 m	2.02 m 2.26 m	1.47 m	1.16 m 2.29 m	1.76 m	1.26 m 1.32 m	1.21 m 1.56 m
13	5.56 m	5.56 m	5.55 m	1.46 m	5.56 m	1.16 m	1.44 m 1.57 m	1.20 m 1.14 m
14	5.65 d (16.5)	5.45 m	6.15 d (16.0)	4.00 m	5.72 d (15.6)	3.39 d (9.0)	4.05 t (5.5)	3.22 d (9.0)
16	1.25 s	1.22 s	4.87 s	4.80 s 4.92 s	1.27 s	1.15 s	4.95 s 4.96 s	1.14 s
17	1.26 s	1.22 s	1.80 s	1.70 s	1.28 s	1.20 s	1.73 s	1.17 s
18	4.01 d (12.9) 4.10 d (12.9)	4.03 d (12.9) 4.12 d (12.9)	4.04 d (12.5) 4.11 d (12.5)	4.01 d (12.6) 4.07 d (12.6)	9.42 s	4.21 d (12.5) 4.42 d (12.5)	9.41 s	4.16 d (12.9) 4.29 d (12.9)
19	1.43 s	1.43 s	1.44 s	1.44 s	1.41 s	1.40 s	1.38 s	2.13 s
20	1.08 s	1.07 s	1.06 s	1.09 s	1.19 s	1.03 s	1.18 s	0.89 s
2′	5.69 br s	5.70 br s	5.71 br s	5.71 br s	5.68 br s	5.79 br s		5.67 br s
4′	2.12 s	2.15 s	2.18 s	2.13 s	2.12 s	2.19 s		2.18 s
5′	1.88 s	1.90 s	1.90 s	1.89 s	1.89 s	1.94 s		1.93 s
OMe		3.09 s						

[a] Recorded in $CDCl_3$ at 300 MHz. [b] Recorded in $CDCl_3$ at 500 MHz.

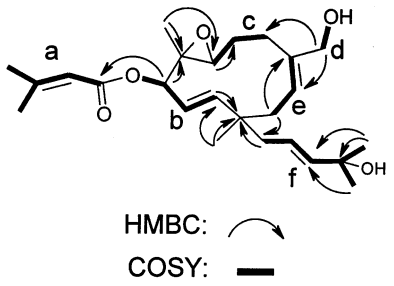

Figure 1. COSY and HMBC correlations of **1**.

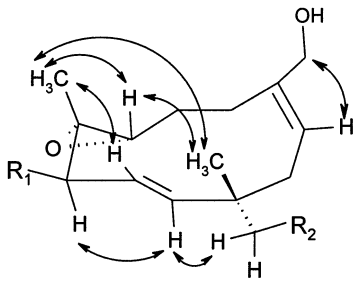

Figure 2. NOESY correlations of **1**−**4**.

NOESY correlation between H-2 and H_2-18 indicated the double bond in the substructure **d** had *Z*-geometry. From the aforementioned data, vibsanin P was formulated as **1**.

The molecular formula of vibsanin Q (**2**) proved to be $C_{26}H_{40}O_5$ from HREIMS, ^{13}C NMR, and DEPT spectra. Its IR spectrum showed the presence of hydroxyl and α,β-unsaturated ester groups. The ^{1}H and ^{13}C NMR spectral data (Tables 1 and 2) resembled those of **1** except that the tertiary hydroxyl at C-15 was replaced by a methoxyl group (δ_H 3.09). HMBC correlations from OCH_3 (δ_C 75.0) to C-15 clearly positioned the methoxyl group at C-15. The assigned relative stereochemistry of **2** was the same as that of **1**.

Table 2. ^{13}C NMR Spectral Data (δ) of **1**−**8** in $CDCl_3$

	1[a]	**2**[a]	**3**[b]	**4**[a]	**5**[a]	**6**[b]	**7**[b]	**8**[a]
1	41.7	41.1	40.7	42.3	42.4	45.0	43.4	36.3
2	120.5	120.5	120.6	120.8	149.6	129.3	147.1	138.9
3	142.0	142.0	142.1	141.8	146.0	142.8	141.7	142.2
4	23.8	23.3	23.2	23.2	25.9	202.2	26.5	205.6
5	26.3	26.4	27.4	26.4	25.9	128.8	26.5	48.3
6	63.1	63.1	63.0	63.1	62.6	154.3	62.9	44.1
7	61.2	61.3	61.2	61.3	61.1	74.1	60.8	208.1
8	78.5	77.7	77.8	78.1	78.4	81.9	39.1	137.4
9	122.9	121.4	121.2	121.1	122.1	123.3	122.7	112.9
10	146.5	146.2	146.2	147.9	145.0	145.8	141.9	46.1
11	40.1	40.0	40.2	39.5	41.1	40.5	40.5	40.1
12	41.4	41.9	42.1	30.1	42.4	35.6	30.0	37.2
13	120.9	126.3	126.6	35.0	122.1	26.3	29.7	26.2
14	144.4	138.2	135.5	75.5	142.2	78.6	76.2	79.1
15	70.4	75.0	141.9	147.2	70.4	73.3	147.4	73.1
16	29.2	25.8	114.7	110.5	29.2	23.1	111.3	24.3
17	29.8	26.1	18.7	18.0	29.9	26.3	17.7	24.3
18	66.0	66.1	66.0	66.2	195.0	65.0	195.2	63.6
19	17.8	17.7	17.7	17.7	17.7	18.4	23.2	31.0
20	23.3	23.6	23.5	23.2	22.9	22.8	23.6	23.8
1′	165.7	165.2	165.2	165.5	165.6	168.7		163.1
2′	116.1	116.0	116.0	116.1	116.0	115.3		114.6
3′	157.3	157.2	154.3	157.2	157.5	159.5		160.6
4′	20.4	20.2	20.2	20.3	20.4	20.5		20.6
5′	27.5	27.4	26.3	27.5	27.5	27.6		27.7
OMe		50.3						

[a] Recorded in $CDCl_3$ at 75 MHz (assigned by DEPT, COSY, HSQC, and HMBC experiments). [b] Recorded in $CDCl_3$ at 125 MHz (assigned by DEPT, COSY, HSQC, and HMBC experiments).

The molecular formula of vibsanin R (**3**) was deduced to be $C_{25}H_{36}O_4$ from HRFABMS, ^{13}C NMR, and DEPT spectra. Its IR spectrum showed the presence of hydroxyl and α,β-unsaturated ester groups. The ^{1}H and ^{13}C NMR spectral

data (Tables 1 and 2) were similar to those of **1** except that the tertiary hydroxyl at C-15 was dehydrated to form a conjugated diene at C-13 and C-15. The conjugated diene at C-13 and C-15 was confirmed by HMBC correlations from H_2-16 to C-17 and from H_3-17 to C-14/C-15. NOESY correlations between H-14 and H-17 established the geometry between C-13 and C-17. The relative stereochemistry of the 11-membered ring of **3** was assigned to be the same as that of **1**.

Vibsanin S (**4**) had a molecular formula of $C_{25}H_{38}O_5$ as indicated by HREIMS, ^{13}C NMR, and DEPT spectra, and the IR spectrum indicated the presence of hydroxyl and α,β-unsaturated ester groups. The ^1H and ^{13}C NMR spectral data (Tables 1 and 2) were analogous to those of **1** except that the side chain at C-11 was replaced by that of visbanin G.[2] The side chain was confirmed by HMBC correlations from H-17 to C-14/C-15/C-16. The relative stereochemistry of the 11-membered ring of **3** was the same as that of **1**.

Vibsanin T (**5**) had a molecular formula of $C_{25}H_{36}O_5$ as determined by HREIMS, ^{13}C NMR, and DEPT spectra, and the IR spectrum showed the presence of hydroxyl and α,β-unsaturated carbonyl groups. The ^1H and ^{13}C NMR spectral data (Tables 1 and 2) resembled those of **1** except that the hydroxymethyl at C-3 was replaced by an aldehyde group (δ_H 9.42 s, δ_C195.0). HMBC correlations from H-18 to C-2 /C-4 clearly positioned the aldehyde group at C-3. The assigned relative stereochemistry of the 11-membered ring of **5** was the same as that of **1**.

Vibsanin U (**6**) had a molecular formula of $C_{25}H_{38}O_7$ as established by HREIMS, ^{13}C NMR, and DEPT spectra. Its IR spectrum showed the presence of hydroxyl and α,β-unsaturated ester absorption groups. The ^1H NMR spectrum (Table 1) exhibited six methyl singlets (δ 1.03, 1.15, 1.20, 1.40, 1.94, 2.19), an oxymethylene (δ 4.21, 4.42), two oxymethines (δ 3.39, 5.34), and six olefinic protons (δ 5.17, 5.74, 5.79, 6.04, 6.08, 6.57). These data resembled the ^1H NMR data of the 11-membered ring system and the β,β-dimethyl acryl substituent at C-8 of vibsanin B, isolated previously from *V. odoratissimum*.[1,11] The COSY spectrum, which showed correlations between H-6/H-5, H-8/H-9, H-9/H-10, and H-1/H-2, supported the presence of an 11-membered ring in **1** as in vibsanin B. Comparison of the ^{13}C NMR data (Table 2) and HMQC of **6** with those of vibsanin B showed that the two compounds are identical except that the double bond at C-14 was replaced by two hydroxyl groups. HMBC correlations from H-16/H-17 to C-15/C-14 confirmed this assignment. The relative stereochemistry of **6** was deduced from a 2D NOESY experiment, which showed cross-peaks (H_3-19/H-5, H_3-19/H-5, H-9/H_3-20, H-8/H-10, H-8/H-6, H-6/H-10) indicating that Me-19, Me-20, H-5, and H-9 were on the β-face of the 11-membered ring, while H-8, H-10, and H-6 were on the α-face of the 11-membered ring.

HRFABMS, ^{13}C NMR, and DEPT spectra revealed vibsanin V (**7**) to have a molecular formula of $C_{20}H_{30}O_3$. Its IR spectrum showed the presence of hydroxyl and α,β-unsaturated carbonyl groups. The ^1H and ^{13}C NMR spectral data (Tables 1 and 2) resembled those of 14-hydroxyvibsanin F[5] except that the hydroxymethyl at C-3 was replaced by an aldehyde group (δ_H 9.41 s, δ_C 195.2). HMBC correlations (Figure 3) from H-18 to C-2 /C-4 clearly positioned the aldehyde group at C-3. The relative stereochemistry of **7** was deduced from a 2D NOESY experiment, which indicated that Me-19, Me-20, H-6, and H-9 were on the

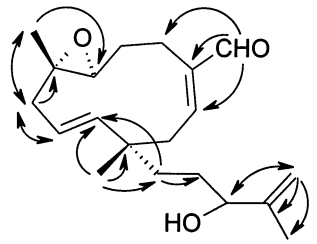

Figure 3. HMBC correlations of **7**.

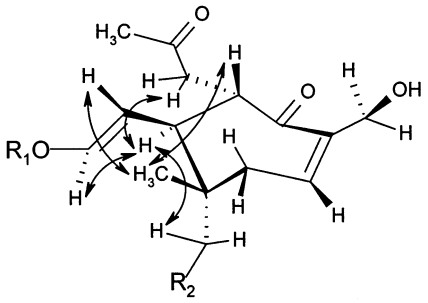

Figure 4. NOESY correlations of **8**.

β-face of the 11-membered ring, while H-8, H-10, and the epoxy ring at C-8 were on the α-face of the 11-membered ring.

Vibsanin W (**8**) was shown to have the molecular formula of $C_{25}H_{38}O_7$ by HRFABMS, ^{13}C NMR, and DEPT spectra. Its IR spectrum showed the presence of hydroxyl and α,β-unsaturated carbonyl groups. The ^1H and ^{13}C NMR data (Tables 1 and 2) of **8** showed the presence of six tertiary methyl groups [δ_H 0.89, 1.14, 1.17, 1.93, 2.13, 2.18], an oxymethylene [δ_H 4.16 (d, J = 12.9 Hz), 4.29 (d, J = 12.9 Hz), δ_C 63.6], an oxymethine [δ_H 3.22 (d, J = 9.0 Hz), δ_C 79.1], two trisubstituted olefins [δ_H 5.67, δ_C 114.6, 160.6; δ_H 6.96, δ_C 138.9, 142.2], and a disubstituted olefin [δ_H 5.17 (dd, J = 12.3, 11.7 Hz), 6.96 (d, J = 12.3 Hz), δ_C 112.9, 137.4]. These spectral features indicated that **8** was a typical seven-membered vibsane-type diterpene. The ^1H and ^{13}C NMR spectral data were very similar to those of vibsanin C[1,2,11] except that the double bond at C-14 was replaced by two hydroxyl groups. HMBC correlations from H-16/H-17 to C-15 /C-14 confirmed this assignment. The relative stereochemistry of **8** was deduced from a 2D NOESY experiment (Figure 4), which indicated that Me-20, H-5, and the β,β-dimethylacryl group were on the β-face of the seven-membered ring.

Compounds **1** and **8** exhibited significant cytotoxicity against P-388 cells with ED_{50} values of 2.25 and 2.18 μg/mL, respectively, and compounds **2**−**7** were moderately cytotoxic (ED_{50} < 10.0 μg/mL). For comparison, compounds **1** and **8** were also moderately cytotoxic against A549 cells (ED_{50} 4.62 and 5.60 μg/mL, respectively) and against HT-29 cells (ED_{50} 9.97 and 8.15 μg/mL, respectively).

Experimental Section

General Experimental Procedures. Melting points were determined using a Yanagimoto micromelting point apparatus and are reported uncorrected. Optical rotations were determined on a JASCO DIP-181 polarimeter. UV spectra were obtained on a Shimadzu UV-160A spectrophotometer, and IR spectra were recorded on a Hitachi 26-30 spectrophotometer. The NMR spectra were recorded on a Varian Inova 500 or a Bruker Avance 300 spectrometer. The chemical shifts are given in δ (ppm) and coupling constants in Hz. EIMS spectra were obtained with a JEOL JMS-SX/SX 102A mass spectrometer at 70 eV. Si gel 60 (Merck, 230−400 mesh) was used for column

chromatography; precoated Si gel plates (Merck, Kieselgel 60 F_{254}, 0.25 mm) were used for TLC analysis.

Plant Material. The leaves and twigs of *V. awabuki* were collected at Hen-Chung, Pin-tong County, Taiwan, in October 1990. A voucher specimen, HS-032, was deposited in the Department of Marine Resources, National Sun Yat-sen University, Taiwan.

Extraction and Isolation. The dried leaves and twigs (4.40 kg) of *V. awabuki* were extracted with MeOH (10 L × 3). After removal of solvent in vacuo, the residue (196 g) was chromatographed over Si gel 60 using $CHCl_3$ and $CHCl_3$−MeOH mixtures as eluting solvents. Elution by $CHCl_3$−MeOH (98:2) afforded fractions containing **1**−**8**. Compounds **1** and **2** were further purified by Si gel column chromatography, by eluting with *n*-hexane−acetone (75:25), and a RP-18 HPLC column by eluting with MeOH−H_2O (40:60). Compounds **3** and **4** were further purified by Si gel column chromatography, by eluting with *n*-hexane−acetone (70:30), and a RP-18 HPLC column by eluting with MeOH−H_2O (43:57). Compound **5** was further purified by Si gel column chromatography, by eluting with *n*-hexane−acetone (75:25), and a RP-18 HPLC column by using MeOH−H_2O (42:58). Compounds **6** and **7** were further purified by Si gel column chromatography, by eluting with *n*-hexane−acetone (80:20), and a RP-18 HPLC column by eluting with MeOH−H_2O (45:55). Compound **8** was further purified by Si gel column chromatography, by eluting with *n*-hexane−acetone (55:45), and a RP-18 HPLC column by using MeOH−H_2O (50:50).

Vibsanin P (1): colorless amorphous solid (6 mg); $[\alpha]^{25}_D$ +24° (*c* 0.3, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 237 (3.74) nm; IR (KBr) ν_{max} 3420, 1720, 1670 cm^{-1}; ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; EIMS *m*/*z* 418 $[M]^+$ (8), 400 (2), 384 (2), 319 (28), 135 (23), 109 (30), 83 (100); HREIMS *m*/*z* 418.2706 (calcd for $C_{25}H_{38}O_5$, 418.2709).

Vibsanin Q (2): colorless amorphous solid (5 mg); $[\alpha]^{25}_D$ +23° (*c* 0.4, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 238 (3.89) nm; IR (KBr) ν_{max} 3450, 1715, 1668 cm^{-1}; ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; EIMS *m*/*z* 432 $[M]^+$ (9), 319 (5), 135 (26), 109 (48), 83 (100); HREIMS *m*/*z* 432.2869 (calcd for $C_{26}H_{40}O_5$, 432.2865).

Vibsanin R (3): colorless amorphous solid (1 mg); $[\alpha]^{25}_D$ +43° (*c* 0.5, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 237 (3.78) nm; IR (KBr) ν_{max} 3460, 1718, 1665 cm^{-1}; ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; HRFABMS *m*/*z* 423.2512 (calcd for $C_{25}H_{36}O_4$-Na, 423.2502).

Vibsanin S (4): oil (8 mg); $[\alpha]^{25}_D$ +25° (*c* 0.3, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 240 (3.68) nm; IR (KBr) ν_{max} 3460, 1715, 1660 cm^{-1}; ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; EIMS *m*/*z* 418 $[M]^+$ (8), 400 (1), 384 (2), 109 (58), 83 (100); HREIMS *m*/*z* 418.2701 (calcd for $C_{25}H_{38}O_5$, 418.2709).

Vibsanin T (5): oil (12 mg); $[\alpha]^{25}_D$ +46° (*c* 0.4, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 239 (3.78) nm; IR (KBr) ν_{max} 3415, 1720, 1670 cm^{-1}; ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; EIMS *m*/*z* 416 $[M]^+$ (5), 401 (1), 217 (20), 109 (15), 83 (100); HREIMS *m*/*z* 416.2559 (calcd for $C_{25}H_{36}O_5$, 416.2553).

Vibsanin U (6): gum (1 mg); $[\alpha]^{25}_D$ +21° (*c* 0.6, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 241 (3.90) nm; IR (KBr) ν_{max} 3415, 1715, 1665 cm^{-1}; ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; HRFABMS *m*/*z* 473.2512 (calcd for $C_{25}H_{38}O_7Na$, 473.2505).

Vibsanin V (7): colorless amorphous solid (2 mg); $[\alpha]^{25}_D$ +30° (*c* 0.5, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 233 (3.66) nm; IR (KBr) ν_{max} 3445, 1720 cm^{-1}; ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; HRFABMS *m*/*z* 341.2094 (calcd for $C_{20}H_{30}O_3$ Na, 341.2085).

Vibsanin W (8): colorless amorphous solid (4 mg); $[\alpha]^{25}_D$ +16° (*c* 0.3, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 244 (3.96) nm; IR (KBr) ν_{max} 3500, 1745, 1722, 1672 cm^{-1}; ^1H NMR, see Table 1; ^{13}C NMR, see Table 2; HREIMS *m*/*z* 473.2512 (calcd for $C_{25}H_{38}O_7$ Na, 473.2505).

Cytotoxicity Testing. P-388 cells were kindly supplied by J. M. Pezzuto, Department of Medicinal Chemistry and Molecular Pharmacology, Purdue University; A549 and HT-29 were purchased from the American Type Culture Collection. Cytotoxic assays were carried out according to the procedure described previously.[14]

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