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# Vibsanin O, a novel diterpenoid from *Viburnum awabuki*

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**Abstract**—Vibsanin O, isolated from the leaves and twigs of *Viburnum awabuki*, is an unprecedented bicyclic diterpenoid. The structures of vibsanin O was established by extensive analysis of spectroscopic data.


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 (Caplifoliaceae) 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 a novel cytotoxic diterpenoid, vibsanin O (**1**) (novel carbon skeleton).

Visanin O (**1**), obtained as amorphous solids $[\alpha]_D^{25}$ +36° (*c* 0.3, $CHCl_3$), has the molecular formula $C_{25}H_{34}O_7$ [$MNa^+$, *m*/*z* 469.2183 (Δ −3 mmu)] established by HR-FAB-MS and $^{13}C$ NMR data (Table 1), indicating 9 degrees of unsaturation. The IR spectrum of **1** shows absorptions due to hydroxyl (3440 $cm^{-1}$) and carbonyl (1755, 1730, 1715, and 1670 $cm^{-1}$) groups. The $^1H$ and $^{13}C$ NMR data of **1** exhibited the presence of six tertiary methyl groups [$\delta_H$ 0.84, 1.26, 1.27, 1.94, 2.07, and 2.20] (Table 1). In addition, the $^{13}C$ and HSQC spectra indicated distinct resonances due to a conjugated ester carbonyl at $\delta_C$ 163.3, a conjugated ketone at $\delta_C$ 203.7, a conjugated carboxylic carbonyl at $\delta_C$ 175.0, two trisubstituted olefins ($\delta_H$ 6.57, $\delta_C$ 132.7 and 135.4, and $\delta_H$ 5.67, $\delta_C$ 114.6 and 160.6), one disubstituted olefin ($\delta_H$ 6.99, 4.94, $\delta_C$ 137.1 and 113.1), three methylenes ($\delta_C$ 35.7, 35.8, and 48.4), and two $sp^3$ quaternary carbons including one oxygenated carbon ($\delta_C$ 34.9, 77.5).

**Table 1.** $^1H$ and $^{13}C$ NMR data of **1** (300 and 75 MHz, respectively, in $CDCl_3$) ($\delta$ in ppm relative to TMS)

| Pos. | $\delta_H$[a] | $\delta_C$[a] |
|---|---|---|
| 1 | 2.87m | 31.6 |
| 2 | 6.57 d (2.4)[b] | 132.7 |
| 3 | | 135.4 |
| 4 | | 203.7 |
| 5 | 3.33 m | 43.7 |
| 6 | 2.70 dd (17.4, 4.5), 2.90 dd (17.4, 6.9) | 48.4 |
| 7 | | 204.7 |
| 8 | 6.99 d (12.3) | 137.1 |
| 9 | 4.94 dd (12.3, 11.1) | 113.1 |
| 10 | 3.71 t (11.1) | 40.6 |
| 11 | | 34.9 |
| 12 | 1.39 m, 2.05 m | 35.8 |
| 13 | 1.09 m, 1.77 m | 35.7 |
| 14 | 1.60 m | 40.4 |
| 15 | | 77.5 |
| 16 | 1.26 s | 25.3 |
| 17 | 1.27 s | 25.6 |
| 18 | | 175.0 |
| 19 | 2.07 s | 30.2 |
| 20 | 0.84 s | 23.9 |
| 1′ | | 163.3 |
| 2′ | 5.67 br s | 114.6 |
| 3′ | | 160.6 |
| 4′ | 2.20 s | 20.6 |
| 5′ | 1.94 s | 27.7 |

[a] Assigned by DEPT, COSY, HSQC, and HMBC experiments.
[b] Coupling constant in Hz in parentheses.

Detailed analysis of the COSY and HSQC of **1** gave three partial structures (Fig. 1 in boldface). The double bond in the **b** part should take *E*-geometry due to the coupling constant ($J$ = 12.3 Hz). The presence of the partial structure **a** which corresponded to a β,β-dimethylacryl group was additionally supported by the observa-

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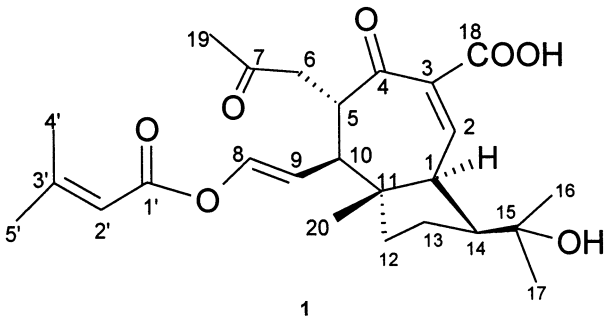
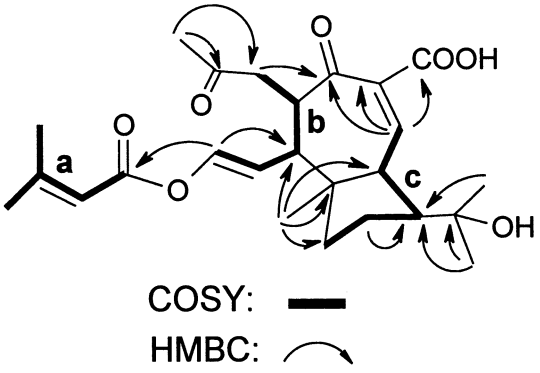



1




COSY:

HMBC:

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

tion of the prominent fragment ion peak at $m/z$ 83 in the MS.

The HMBC experiment was used to assemble the skeletal fragments through quaternary carbons and heteroatoms. Thus, these substructures were connected through HMBC correlations between the protons H-8 ($\delta_H$ 6.99) and the carbons C-1′ ($\delta_C$ 163.3) and C-10 ($\delta_C$ 40.6), between the protons $H_3$-19 ($\delta_H$ 2.07) and the carbons C-7 ($\delta_C$ 204.7), and C-6 ($\delta_C$ 48.4), between the protons $H_2$-6 ($\delta_H$ 2.70, 2.90) and the carbon C-4 ($\delta_C$ 203.7), between the methyl protons $H_3$-20 ($\delta_H$ 0.84) and carbons C-1 ($\delta_C$ 31.6), C-10 ($\delta_C$ 40.6), C-11 ($\delta_C$ 34.9), and C-12 ($\delta_C$ 35.8), between the protons $H_3$-16/17 ($\delta_H$ 1.26, 1.27) and the carbons C-15 ($\delta_C$ 77.5) and C-14 ($\delta_C$ 40.4), and between the proton H-2 ($\delta_H$ 6.57) and carbons C-3 ($\delta_C$ 135.4), C-4 ($\delta_C$ 203.7), and C-18 ($\delta_C$ 175.0). These relationships are represented in Figure 1. All these data allowed us to identify compound **1** as a new diterpenoid with novel carbon skeleton.

With the gross structure of **1** in hand, the relative stereochemistry of compound **1** was deduced from NOESY correlations (Fig. 2), and by comparison of its spectroscopic data to those of vibsanin analogues.[1–12] NOESY correlations from H-5 to H-9/$H_3$-20 and from H-9 to $H_3$-20 suggested that H-5, Me-20, and C-10 side chain are on the same face of the 7-membered ring. NOESY correlations from $H_3$-20 to H-5/H-12β, H-1 to H-12α/H-14 established the stereochemistry of the 5-membered ring. Vibsanin O (**1**) exhibited cytotoxicity against P-388 cell with $ED_{50}$ of 3.68 μg/mL.

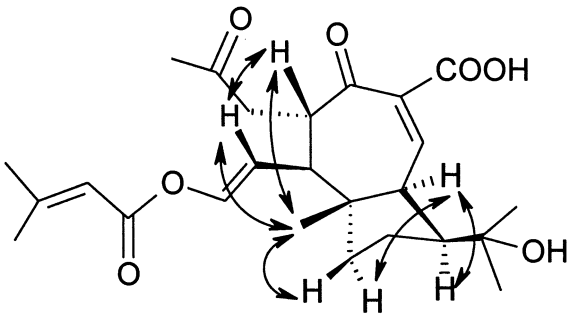



**Figure 2.** Selected NOESY correlations of **1**.

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