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Spirovibsanin A, an unprecedented vibsane-type 18-norditerpene from *Viburnum awabuki*

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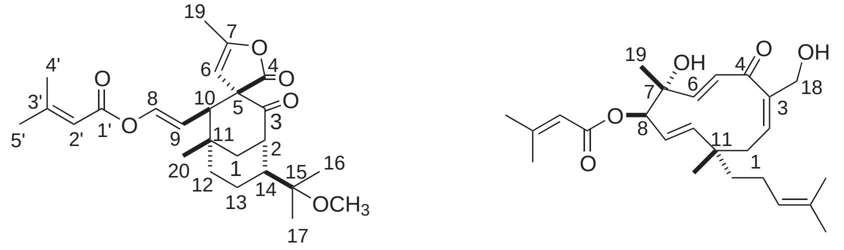
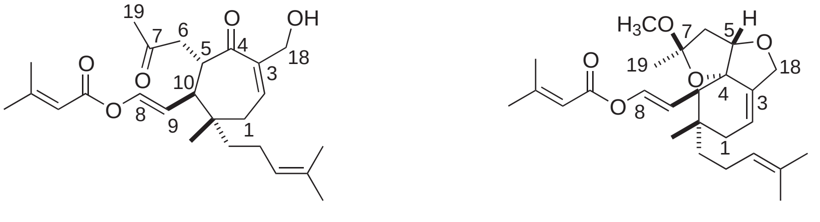
Abstract—Spirovibsanin A, isolated from *Viburnum awabuki*, has been demonstrated to be an unprecedented vibsane-type 18-norditerpene consisting of a unique bicyclo[3.3.1] nonanespiro-γ-lactone framework by a combination of 2D NMR data and conformational analysis using MacroModel. © 2001 Elsevier Science Ltd. All rights reserved.

Vibsane-type diterpenes are quite rare natural products and their occurrence has been limited to *Viburnum awabuki* and *V. odoratissimum* .[1–6] The carbon skeletons of vibsane-type diterpenes can be further divided into three subtypes such as 11-membered ring, 7-membered ring, and a rearranged type which vibsanin B (**2**), vibsanin C (**3**)[1,8] and neovibasnin A (**4**)[7] are representative of. We have already succeeded in converting vibsanin B (**2**) to vibsanin C (**3**) and neovibasnin A (**4**), respectively, by thermal and photochemical reactions.[7,8] However, vibsane-type diterpene which is unable to categorize to the above three subtypes has not been



Spirovibsanin A (**1**)

Vibsanin B (**2**)



Vibsanin C (**3**)

Neovibsanin A (**4**)

Figure 1. Structures of spirovibsanin A (**1**) and three type of vibsane-type diterpens **2**–**4**.

Keywords: *Viburnum awabuki*; vibsane-type 18-norditerpene; spirovibsanin A; structure elucidation.

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Table 1. ^{13}C (150 MHz) and ^{1}H (600 MHz) NMR data of **1** in C_6D_6

C	^{13}C	^{1}H	C	^{13}C	^{1}H
1	28.2	1.62 (brd, 13.7) 2.98 (dd, 13.7, 4.7)	11	33.2	
2	43.5	2.94 (d, 4.7)	12	38.2	0.65(m) 1.25 (m)
3	210.3		13	19.6	1.20 (m) 1.29 (m)
4	172.9		14	50.4	2.32 (dd, 11.0, 7.4)
5	68.1		15	76.8	
6	107.7	4.61 (q, 1.4)	16	22.9	0.94 (s)
7	152.6		17	22.5	0.94 (s)
8	137.7	7.44 (d, 12.4)	18		
9	110.4	5.90 (dd, 12.4, 11.3)	19	13.2	1.49 (d, 1.4)
10	54.3	1.96 (d, 11.3)	20	26.2	0.75 (s)
1′	163.1		4′	20.2	1.99 (d, 1.4)
2′	115.1	5.51 (qq, 1.4, 1.4)	5′	27.0	1.32 (d, 1.4)
3′	159.8		OCH_3	48.8	3.02 (s)

found in nature, or even in the chemical reactions of vibsanin B (**2**).[3]

Our continuing studies on the methanol extract of the leaves of *Viburnum awbuki* have resulted in the first isolation of a vibsane-type 18-norditerpene **1**, named spirovibsanin A, which belongs to none of the three subtypes. Herein, we report the structure elucidation of **1** which features a unique bicyclo[3.3.1]nonane spiro-γ-lactone structure.

Spirovibsanin A (**1**)[9] (Fig. 1) has the molecular formula, $C_{25}H_{34}O_6$, established by HR-FABMS. Its IR spectrum showed the presence of two carbonyl groups (1730, 1710 cm^{-1}), and a γ-lactone ring (1780 cm^{-1}). The ^{1}H NMR data of **1** showed the signals due to a methoxy group (δ_H 3.02), a β,β-dimethyl acrylate group [δ_H 1.32 (d, $J=1.4$ Hz), 1.99 (d, $J=1.4$ Hz), 5.51 (qq, $J=1.4$, 1.4 Hz)], a trisubstituted olefinic proton [δ_H 4.61 (q, $J=1.4$ Hz)], two disubstituted olefinic protons [δ_H 5.90 (dd, $J=12.4$, 11.3 Hz), 7.44 (d, $J=12.4$ Hz)], and four tertiary methyl groups (δ_H 0.75, 0.94, 0.94, 1.49) (Table 1). However, no signal corresponding to the oxymethylene at the C-18 position which commonly exists in vibsane-type diterpenes[6] has been found to be missing in the ^{1}H NMR spectrum. The molecular formula indicated that the carbon number for **1** was one less than that of normal vibsane-type diterpenes. These spectral data of **1** failed to refer to those of the previously known vibsane-type diterpenes.

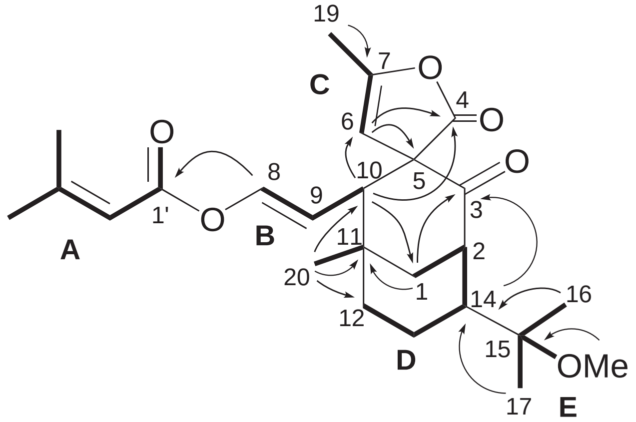

Figure 2. Connectivities established by 2D NMR (600 MHz) of **1**. Bold line: partial units infered from COSYand HMQC; Arrows: HMBC correlation between the proton (tail) and carbons (head).

Extensive analyses of 2 D ^{1}H–^{1}H COSY and HMQC gave the five partial structures **A**–**E** as shown in Fig. 2 and five quaternary carbons (δ_C 33.2, 68.1, 76.8, 172.9, 210.3). In order to determine the connectivity between these five partial structures **A**–**E** and five quaternary carbons, HMBC experiments were carried out (Fig. 2). The HMBC correlation of H-8 to C-1′ linked as usual the β,β-dimethylacrylate group **A** to C-8 in the partial unit **B**. The 2-methoxy isopropyl part **E** bonded to C-14 in the partial unit **D** on the basis of the correlation of CH_3-16 and CH_3-17 to the C-14 methine resonated at δ_C 50.4. Additionally, the CH_3-20 signal (δ_H 0.75) had cross peaks to C-12 and C-10, and the C-11 quaternary carbon (δ_C 33.2), to the latter of which the H-1 resonance in turn showed the HMBC correlation, indicating the bond formation of C-1, C-12, C-10 and C-20 through C-11.

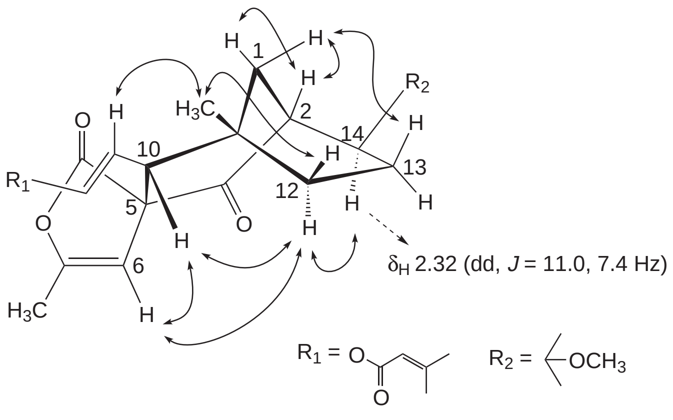

Figure 3. NOESY correlations of **1**.

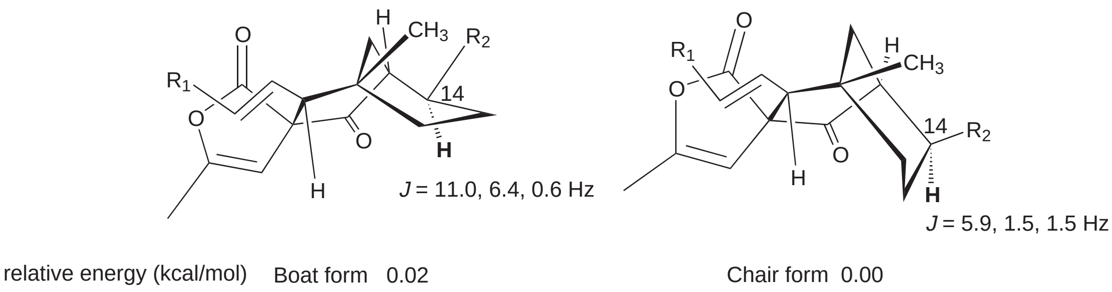

Figure 4. Boat and chair conformations obtained by conformational searches using MacroModel and calculated *J* values for H-14 in each conformation.

The presence of the HMBC correlation from the carbonyl carbon resonated at δ_C 210.3 to H-14 and H-1 turned out to be the carbonyl function connected to C-2 in the unit **D**. Moreover, the HMBC correlations of H-6 to the C-4 carbonyl (δ_C 172.9) and another C-5 quaternary carbon (δ_C 68.1) as well as of H-10 to C-6 and C-4, respectively, led to the formation of a γ-lactone ring containing C-5 and the unit **C**. Although the remaining connectivity between C-5 and the C-3 carbonyl failed to be confirmed by HMBC experiments,[10] considering 8 degrees of unsaturation, **1** should consist of a tricyclic carbon skeleton. As results, this allowed us to connect C-5 to C-3 and C-10, thereby resulting in the construction of bicyclo[3.3.1]nonane framework having a spiro-γ-lactone ring fused on the C-5 position. Thus, the above spectral data gave the planar structure **1**.

The relative stereochemistry of **1** was elucidated by nuclear overhouser exchange spectroscopy (NOESY) as shown in Fig. 3. Namely, H-10 and H-6 showed cross peaks to H-12α, respectively, indicating that the carbonyl of spirolactone took the *exo* orientation. The observation of cross peaks from H-1β to H-13β as well as from H-12α to H-14α in addition to the large coupling constant (11.0 Hz) for H-14 suggests that the cyclohexane ring adopts a boat conformation with a pseudoequatorial 2-methoxy isopropyl group at the C-14 position. Conformational searches of **1** using MacroModel (v. 6.0) provided both chair and boat conformers for global minimum structure as shown in Fig. 4. However, the observed *J* values (11.0, 7.4 Hz) was comparable with the calculated coupling constants (11.0, 6.4 Hz) for H-14 in the boat form, but is not consistent with those (5.9, 1.5 Hz) in the chair form. Hence, on the basis of the above data, the structure of spirovibsanin A was elucidated as **1**.

It should be emphasized that spirovibsanin A (**1**) is the first example of vibsane-type 18-norditerpene and consists of a unique bicyclo[3.3.1]nonanespiro-γ-lactone structure. This type of natural products has not been documented so far. It is of great significance that plausible procedure for biosynthesis of **1** will be investigated and biological activity of **1** will be evaluated.

Acknowledgements

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9. Spirovibsanin A (**1**): $[\alpha]_D^{22}$ +87.6 (*c* 0.12, $CHCl_3$); IR: 1710, 1730, 1782 (C=O), 1644 (C=C) cm^{-1}; UV nm: 228 (ε 14600); FABMS: *m*/*z* 453 $[M+Na]^+$, 469 $[M+K]^+$; HR-FABMS: found 453.2226. Calcd 453.2253 for $C_{25}H_{34}O_6Na$.
10. The absence of HMBC correlations of H-6 and H-10 to C-3 is rationalized presumably due to the fact that the three bonded C-H coupling is calculated to be $^3J_{CH}$ = 1.2 Hz based on the dihedral angles (70°) between C(10)-H and C-3, and C(6)-H and C-3.[11]
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