New Vibsane Diterpenes and Lupane Triterpenes from *Viburnum odoratissimum*

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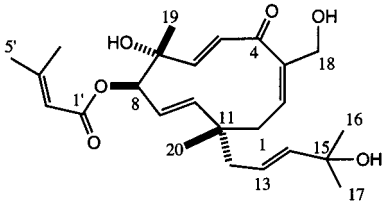
Bioassay-directed fractionation of the methanolic extract of the leaves and flowers of *Viburnum odoratissimum* resulted in the isolation of two new diterpenes, vibsanol A (**1**) and vibsanol B (**2**), together with two new triterpenoids, 6*β*-hydroxylup-20(29)-en-3-oxo-27,28-dioic acid (**3**) and 6α-hydroxylup-20-(29)-en-3-oxo-27,28-dioic acid (**4**). In addition, the known terpenoids vibsanins B and E, and 6α-hydroxylup-20(29)-en-3-oxo-28-oic acid, were also isolated. The structures of the new compounds were established by chemical and spectroscopic means. Vibsanol A (**1**) and compound **3** exhibited significant cytotoxicity against human gastric (NUGC) tumor cells.

The plant *Viburnum odoratissimum* Ker. (Caprifoliaceae) is very rich in diterpenoids of the vibsane type.[1] It has been reported that vibsanin A possesses piscicidal activity, whereas vibsanins B and C exhibit plant growth regulatory and cytotoxic activities.[2] As part of our continuing research on biologically active natural compounds,[3−5] we have undertaken the chemical examination of *V. odoratissimum*. The MeOH extract of the plant material furnished seven compounds after extensive chromatography, including vibsanins B and E, 6α-hydroxylup-20(29)-en-3-oxo-28-oic acid, along with two new diterpenoids of the vibsanine type, which were named vibsanol A (**1**) and vibsanol B (**2**), and two new triterpenoids, 6*β*-hydroxylup-20(29)-en-3-oxo-27,28-dioic acid (**3**) and 6α-hydroxylup-20-(29)-en-3-oxo-27,28-dioic acid (**4**).

Fractionation of the EtOAc-soluble portion of the MeOH extract of the plant by silica gel column chromatography afforded seven compounds, vibsanin B (0.0055%), vibsanin E (0.005%), vibsanol A (**1**, 0.0055%), vibsanol B (**2**, 0.0036%), 6*β*-hydroxylup-20(29)-en-3-oxo-27,28-dioic acid (**3**, 0.009%), 6α-hydroxylup-20(29)-en-3-oxo-27,28-dioic acid (**4**, 0.0055%), and 6α-hydroxylup-20(29)-en-3-oxo-28-oic acid. The structures of the known compounds were confirmed by comparing their spectral data with literature values.[6]

The molecular formula of vibsanol A (**1**), [α] +5.6° ($CHCl_3$), was established as $C_{25}H_{36}O_6$ from EIMS, FABMS, and HRFABMS. Its IR spectrum showed the presence of hydroxyl, unsaturated ester, and carbonyl absorption groups. The ^{1}H NMR spectrum (Table 1) exhibited six methyl singlets, an oxymethylene (*δ* 4.21, 4.40), an oxymethine (*δ* 5.38), and eight olefinic protons (*δ* 5.98, 6.08, 6.67, 5.18, 5.59, 5.51, 5.56, 5.73). These spectral data resembled the ^{1}H 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*.[2] The COSY spectrum, which showed correlations between H-5/H-6, 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 1) and HMQC of **1** with those of vibsanin B showed that the two compounds are identical except for the nature of the side chain. The ^{1}H NMR spectrum coupled with HMQC and HMBC spectra of **1** showed the presence of a broad singlet at δ_H 5.56 (δ_C 141.7, C-14) and a multiplet centered at δ_H 5.51 (δ_C 122.0, C-13) of a disubstituted olefinic double bond. Two methyl singlets appeared at *δ* 1.26 and 1.29 connected to a carbon bearing a hydroxyl group (*δ* 70.6, C-15) and a methylene group (*δ* 40.9, C-12) adjacent to an olefinic carbon and appearing as multiplets at *δ* 2.31 and 2.05 for the side chain at C-11. A search of the literature indicated that the ^{1}H and ^{13}C



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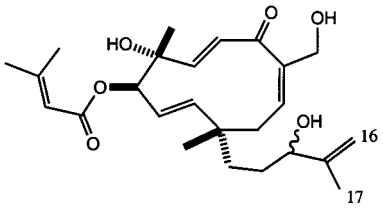

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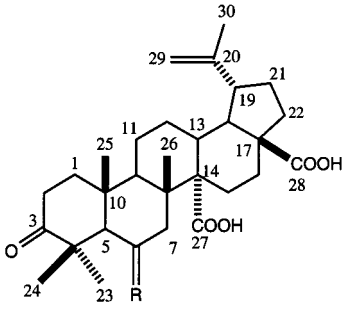

3 R = α-H, β-OH
4 R = α-OH, β-H
5 R = O
6 R = α-OAc, β-H

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Table 1. ^{1}H ($CDCl_3$, 300 MHz) and ^{13}C NMR (75 MHz) Data of **1** and **2**

position	**1**		**2**	
1	2.03 m, 1.82 m	43.5 t	2.03 m, 1.82 m	44.7 t
2	5.98 dd (12, 3.3)	128.9 d	5.93 dd (12, 3.3)	129.1 d
3		142.9 s		142.8 s
4		202.4 s		202.4 s
5	6.08 d (15.9)	128.6 d	6.10 d (16.0)	128.5 d
6	6.67 d (15.9)	154.9 d	6.62 d (16.0)	154.6 d
7		74.1 s		74.1 s
8	5.38 d (9.0)	81.5 d	5.33 d (9.0)	81.7 d
9	5.18 dd (16, 9)	123.2 d	5.13 dd (16, 9)	123.6 d
10	5.59 d (16.0)	145.2 d	5.70 d (16.0)	145.5 d
11		40.6 s		40.3 s
12	2.31 m, 2.05 m	40.9 t	1.21 m	34.3 t
13	5.51 m	122.0 d	1.41 m	30.3 t
14	5.56 br s	141.7 d	4.02 t (4.0)	76.1 d
15		70.6 s		147.2 s
16	1.29 s	29.6 q	4.86 s, 4.93 s	111.3 t
17	1.26 s	29.7 q	1.72 s	17.7 q
18	4.21 d (12.4)	64.8 t	4.21 d (13.2)	64.9 t
	4.40 d (12.4)		4.45 d (13.2)	
19	1.39 s	23.2 q	1.39 s	22.9 q
20	1.00 s	22.6 q	1.02 s	22.4 q
1		167.1 s		167.3 s
2′	5.73 br s	115.3 d	5.72 br s	115.2 d
3		159.5 s		159.5 s
4′	2.19 s	20.5 q	2.22 s	20.5 q
5′	1.95 s	27.6 q	1.97 s	27.6 q

[a] Assignments made using HMQC and HMBC techniques. [b] Coupling constants in Hz are in parentheses.

NMR values of the side chain at C-11 of vibsanin H, isolated from *V. awabuki*,[2] were almost identical to those of **1**, suggesting the similar nature of the side chain. This was further supported by COSY (H-12/H-13 and H-13/H-14) and HMBC correlations (H-12/C-11, C-13; H-13/C-11, C-12, C-14; H-14/C-13, C-15; H-16 and H-17/C-15, H-10/C-11; H-1/C-11; and H-12/C-11). The relative stereochemistries of the hydroxyl at C-7, the *β*,*β*-dimethyl acryl group at C-8, and the two methyl groups at C-7 and C-11 were assigned as α, *β*, *β*, and *β*, respectively, the same as those of vibsanin B, based on the almost identical coupling constants in the ^{1}H NMR spectra and ^{13}C NMR chemical shifts for C-7, C-8, C-19, and C-20.[7]

The molecular formula of vibsanol B (**2**), [α] +17.4° ($CHCl_3$), was established as $C_{25}H_{36}O_6$ from the EI, FABMS, and HRFABMS, the same as vibsanol A. The IR spectrum showed the presence of hydroxyl, unsaturated ester, and carbonyl groups, as in vibsanol A. Compound **2** also showed significant fragments at *m*/*z* 414, 396, and 378 in its EIMS, similar to vibsanol A (**1**), which indicated the presence of three hydroxyl groups in its structure. Its ^{1}H NMR spectrum was also very similar to that of vibsanol A (**1**). The ^{1}H and ^{13}C NMR data, in addition to the HMQC spectra of **2**, permitted the assignment of the olefinic carbons C-9, C-10 (*δ* 123.6 and 145.5), C-5, C-6 (*δ* 128.5 and 154.6), C-2, C-3 (*δ* 129.1 and 142.8), and C-2′, C-3′ (*δ* 115.2 and 159.5). The signals of C-18 (*δ* 64.9), C-8 (*δ* 81.7), C-19 (*δ* 22.9), C-20 (*δ* 22.4), C-4′ (*δ* 20.5), and C-5′ (*δ* 27.6), for a *β*,*β*-dimethyl acryl functional group and the 11-membered ring system in **2** were also assigned. However, the carbon chemical shifts from C-12 to C-17 and their proton data (*δ* 4.02, 4.86, and 4.93) in the side chain of **2** varied from those in **1**. Furthermore, the COSY (H-12/H-13 and H-13/H-14) and HMBC (H-12/C-11, C-13, C-14 and H-13/C-12, C-14; H-14/C-13, C-15; H-17/C-15 and H-16/C-15, C-14) correlations confirmed the side chain at C-11 in **2**. A close comparison of the ^{13}C NMR values of **2** and vibsanin G, isolated from *Viburnum awabuki*, suggested the similar nature of their side chains.[2] The relative stereochemistry of the hydroxyl at C-7, the *β*,*β*-dimethyl acryl group at C-8, and the two methyl groups at C-19 and C-20 for **2** was also assigned as α, *β*, *β*, and *β*, respectively, since both **1** and **2** exhibited almost identical ^{13}C NMR values at C-7, C-8, C-19, and C-20. However, the stereochemistry at C-14 in **2** remained unassigned.

Table 2. ^{1}H NMR Data ($CDCl_3$, 300 MHz) for Compounds **3**−**5**[a]

position	**3**	**4**	**5**
1	1.70 m, 1.25 m	1.70 m, 1.22 m	1.70 m, 1.20 m
2	2.82 ddd	2.84 ddd	2.77 ddd
	(6.1, 8.1, 6.1)	(6.1, 8.1, 6.1)	(6.1, 8.1, 6.1)
2	2.32 m	2.30 m	2.30 m
5	1.62 d (7.0)	1.60 d (7.0)	2.43 s
6	4.49 br s	3.91 td (9.5, 4.2)	
7	1.60 m, 1.25 m	1.60 m, 1.35 m	2.37 m, 2.02 m
9	1.42 m	1.42 m	1.61 m
11	1.53 m	1.50 m	1.54 m
12	1.70 m, 1.05 m	1.73 m, 1.05 m	1.82 m, 1.05 m
13	2.35 m	2.31 m	2.35 m
15	1.68 m, 1.18 m	1.68 m, 1.18 m	1.68 m, 1.18 m
16	1.62 m, 1.38 m	1.62 m, 1.36 m	1.62 m, 1.39 m
18	1.67 m	1.67 m	1.65 m
19	3.04 td (12, 4.5)	3.01 td (10.5, 4.5)	3.01 td (12, 4.5)
21	1.92 m, 1.62 m	2.00 m, 1.62 m	1.93 m, 1.62 m
22	2.00 m, 1.52 m	2.08 m, 1.46 m	2.00 m, 1.52 m
23	1.16 s	1.16 s	1.13 s
24	1.23 s	1.27 s	1.23 s
25	1.35 s	1.39 s	1.37 s
26	0.93 s	0.95 s	1.01 s
29	4.76 s	4.73 s	4.76 s
	4.63 s	4.61 s	4.63 s
30	1.71 s	1.71 s	1.70 s

[a] Assignment made using HMQC and HMBC techniques.

The molecular formula of **3**, [α] −17.5° ($CHCl_3$), was deduced as $C_{30}H_{44}O_6$ from the EIMS and HREIMS data. The IR spectrum showed the presence of hydroxyl and carbonyl functional groups in the molecule. Its ^{1}H and ^{13}C NMR spectral data (Tables 2 and 3) resembled those reported for 6*β*-hydroxylup-20(29)-en-3-on-28-oic acid isolated earlier from *V. awabuki*.[8] The presence of an extra acid carbonyl group at *δ* 179.5 coupled with the mass fragment at *m*/*z* 410 $[M - 2COOH]^+$ suggested that the methyl group at C-27 in 6*β*-hydroxylup-20(29)-en-3-on-28-oic acid was oxidized to a carboxylic acid in **3**. This was supported further from the HMBC correlations H-13/C-14, C-27, C-12, C-18 and H-15/C-14, C-27, C-16. A NOESY spectrum showed a correlation between the methyl group at C-23 and the broad singlet at *δ* 4.49 and supported the *β*-orientation of the hydroxyl group at C-6.

Compound **4**, [α] +70.6° ($CHCl_3$), is an isomer of **3**, and its molecular formula was derived from HREIMS. The IR spectrum showed the presence of hydroxyl and carbonyl functional groups, the same as in **3**. Its ^{1}H NMR spectrum showed the presence of two singlets (*δ* 4.73, 4.61, H-29), a doublet of triplets (H-6), and four methyl singlets, similar to the ^{1}H NMR data of **3**. Instead of the broad singlet at *δ* 4.49 for H-6α observed for **3**, compound **4** showed a triplet of doublets at *δ* 3.91 (1H, J = 4.2, 9.5 Hz). Comparison of the ^{1}H and ^{13}C NMR data of **4** with **3** and 6α-hydroxylup-20(29)-en-3-oxo-28-oic acid suggested the presence of a 6α-hydroxy group in **4**.[8] This was further confirmed by the NOESY spectrum, which showed a correlation of the C-24 methyl, which was in the *β*-orientation, with the *β*-proton at C-6. Oxidation of **3** and **4**, respectively, with CrO_3/pyridine furnished the same dione, lup-20(29)-en-3,6-dioxo-27, 28-dioic acid (**5**), confirming that the two compounds are epimers. The structure of compound **5**, which is a new lupane derivative, has been established on the basis of IR, ^{1}H and ^{13}C NMR, HMQC, HMBC, and EIMS data. How-

Table 3. ^{13}C NMR Data ($CDCl_3$, 75 MHz) of Compounds **3**−**5**[a]

carbon	3	4	5
1	39.8 t	39.5 t	41.0 t
2	34.4 t	33.0 t	33.6 t
3	216.7 s	219.4 s	214.6 s
4	42.6 s	42.3 s	42.8 s
5	56.6 d	58.5 d	65.2 d
6	69.6 d	67.8 d	211.7 d
7	41.8 t	44.3 t	51.9 t
8	37.2 s	38.3 s	38.0 s
9	50.6 d	48.9 d	50.5 d
10	33.9 s	32.0 s	31.9 s
11	21.1 t	21.6 t	21.6 t
12	24.9 t	25.2 t	24.9 t
13	36.8 d	37.6 d	38.0 d
14	56.3 s	56.3 s	56.0 s
15	24.6 t	25.2 t	24.6 t
16	23.7 t	23.2 t	24.1 t
17	56.3 s	56.3 s	56.0 s
18	49.2 d	48.7 d	49.2 d
19	46.8 d	47.1 d	46.7 d
20	150.2 s	150.1 s	150.0 s
21	30.4 t	30.4 t	30.4 t
22	37.2 t	36.7 t	36.8 t
23	25.4 q	25.2 q	24.9 q
24	21.1 q	19.5 q	21.4 q
25	17.1 q	16.6 q	16.4 q
26	16.9 q	17.6 q	16.9 q
27	179.5 s	179.5 s	177.5 s
28	182.0 s	181.7 s	179.3 s
29	109.5 t	109.8 t	110.0 t
30	19.3 q	19.3 q	19.2 q

[a] Assignments made using DEPT, HMQC, and HMBC techniques.

ever, it was found that acetylation of **3** with Ac_2O/pyridine at room temperature was not successful, whereas **4** furnished a monoacetate, 6α-acetoxylup-20(29)-en-3-oxo-27,-28-dioic acid (**6**), indicating that the 6α-hydroxyl group undergoes acetylation more easily than its 6β-epimer.

Preliminary biological study revealed that compounds **1** and **3** showed significant cytotoxicity (15% and 20% percentage of cell growth, respectively) at concentrations of 10 μM, whereas compounds **2** and **4** were inactive (>50%).

Experimental Section

General Experimental Procedures. Optical rotations were recorded on a JASCO DIP-1000 polarimeter. IR and UV spectra were measured on a Hitachi T-2001 and a Hitachi U-3210 spectrophotometer, respectively. The NMR experiments were recorded either 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 were recorded on a VG Quattro 5022 mass spectrometer.

Plant Material. The leaves and flowers of *Viburnum odoratissimum* were collected in Hen-Chung, Ping-tong County, Taiwan, in November 1999. A voucher specimen (TPG8-1) was deposited in the Institute of Marine Resources, National Sun Yat-sen University.

Extraction and Isolation. The leaves and flowers of *V. odoratissimum* (2.2 kg) were dried at room temperature and powdered. The powdered material was extracted three times with MeOH at room temperature. The combined MeOH extract was concentrated, and the residue was diluted with water (600 mL). The aqueous suspension was then extracted with EtOAc three times (600 mL each time). The EtOAc layer was concentrated to give a residue (40 g), which on flash chromatography with *n*-hexane/$CHCl_3$ and $CHCl_3$/MeOH mixtures, furnished 13 fractions (A−M). A cytotoxic bioassay revealed that fractions H−M were significantly active against NUGC cells (1−4% at 50 μM). Fraction K (3.84 g) on chromatography over silica gel furnished vibsanin B (12 mg) and **4** (12 mg). Fraction J (2.22 g), when chromatographed over silica gel with $CHCl_3$ and $CHCl_3$/MeOH solvent mixtures, followed by recrystallization from *n*-hexane/$CHCl_3$, furnished **3** (20 mg). Fraction L (2.58 g) on chromatography over silica gel with the solvent mixture $CHCl_3$/MeOH followed by reversed-phase HPLC (UV: 200 nm, LiChrosorb RP-C_{18} column, MeOH/H_2O, 70:30) yielded vibsanin E (11 mg) and vibsanols A (**1**, 12 mg) and B (**2**, 8 mg).

Vibsanol A (**1**): colorless oil; $[\alpha]^{26}_D$ +5.6° (*c* 0.05, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 238 (3.72) nm; IR ($CHCl_3$) ν_{max} 3430, 1719, 1651, 1531, 1442, 1342, 1214, 1149, 1010, 964, 775 cm^{-1}; ^1H and ^{13}C NMR, see Table 1; FABMS *m/z* 432 $[M]^+$, 455 $[M + Na]^+$; EIMS (70 eV) *m/z* 432 ($[M]^+$, 0.5), 414 ($[M - H_2O]^+$, 1.5), 396 ($[M - 2H_2O]^+$, 2), 378 ($[M - 3H_2O]^+$, 2), 315 ($[M - H_2O - C_6H_{11}O]^+$, 2), 215 (3), 83 (100); HRFABMS *m/z* $[M + Na]^+$ 455.2407 ($C_{25}H_{36}O_6Na$ requires 455.2409).

Vibsanol B (**2**): colorless oil; $[\alpha]^{26}_D$ +17.4° (*c* 0.05, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 244 (3.56) nm; IR ($CHCl_3$) ν_{max} 3436, 1712, 1645, 1535, 1440, 1332, 1204, 1145, 1016, 962, 773 cm^{-1}; ^1H and ^{13}C NMR, see Table 1; FABMS *m/z* 455 $[M + Na]^+$; EIMS (70 eV) *m/z* 432 ($[M]^+$, 1), 414 ($[M - H_2O]^+$, 1), 396 ($[M - 2H_2O]^+$, 2), 378 ($[M - 3H_2O]^+$, 1), 315 ($[M - H_2O - C_6H_{11}O]^+$, 4), 297 ($[M - 2H_2O - C_6H_{11}O]^+$, 13), 215 (6), 83 (100); HRFABMS *m/z* $[M + Na]^+$ 455.2409 ($C_{25}H_{36}O_6Na$ requires 455.2409).

6β-Hydroxylup-20(29)-en-3-oxo-27,28-dioic acid (**3**): amorphous powder; $[\alpha]^{26}_D$ −17.5° (*c* 0.05, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3530, 1703, 1540, 1465, 1385, 1110, 995 cm^{-1}; ^1H NMR, see Table 2; ^{13}C NMR, see Table 3; EIMS (70 eV) *m/z* 500 ($[M]^+$, 1), 482 ($[M - H_2O]^+$, 1.3), 455 ($[M - COOH]^+$, 1.4), 437 ($[M - H_2O - COOH]^+$, 1), 410 ($[M - 2COOH]^+$, 2), 392 ($[M - H_2O - 2COOH]^+$, 2), 248 (14), 203 (24), 189 (28), 107 (68); HREIMS *m/z* $[M]^+$ 500.3125 ($C_{30}H_{44}O_6$ requires 500.3139).

6α-Hydroxylup-20(29)-en-3-oxo-27,28-dioic acid (**4**): amorphous powder; $[\alpha]^{26}_D$ +70.6° (*c* 0.05, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3480, 1695, 1524, 1462, 1381, 1108, 990 cm^{-1}; ^1H NMR, see Table 2; ^{13}C NMR, see Table 3; EIMS (70 eV) *m/z* 500 ($[M]^+$, 1), 482 ($[M - H_2O]^+$, 1), 437 ($[M - H_2O - COOH]^+$, 2), 392 ($[M - H_2O - 2COOH]^+$, 1), 248 (22), 203 (27), 189 (23), 107 (40); HREIMS *m/z* $[M]^+$ 500.3129 ($C_{30}H_{44}O_6$ requires 500.3139).

Oxidation of 6β-Hydroxylup-20(29)-en-3-oxo-27,28-dioic Acid (**3**). To a solution of CrO_3 (25 mg) in a mixture of CH_2Cl_2 (1.0 mL) and pyridine (0.05 mL) was added **3** (5 mg), and the mixture was stirred for 1 h at room temperature. The reaction mixture was filtered over Celite, the filtrate was concentrated, and the residue obtained was chromatographed over a silica gel column, yielding 2.5 mg of lup-20(29)-en-3,6-dione-27,28-dioic acid (**5**) as an amorphous powder: $[\alpha]^{26}_D$ +16.4° (*c* 0.05, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3450, 1692, 1537, 1463, 1375, 1114, 992 cm^{-1}; ^1H NMR, see Table 2; ^{13}C NMR, see Table 3; EIMS (70 eV) *m/z* 498 ($[M]^+$, 1), 483 ($[M - CH_3]^+$, 1.4), 481 ($[M - OH]^+$, 0.5), 468 ($[M - 2CH_3]^+$, 15), 453 ($[M - COOH]^+$, 5), 423 ($[M - 2CH_3 - COOH]^+$, 8), 408 ($[M - 2COOH]^+$, 3), 368 (6), 248 (45), 189 (71), 147 (32), 119 (50), 83 (93), 55 (100).

Oxidation of 6α-Hydroxylup-20(29)-en-3-oxo-27,28-dioic Acid (**4**). Compound **4** (3 mg) was oxidized as above, and the product obtained (1.2 mg) was found identical with **5** (^1H NMR and TLC).

Acetylation of 6α-Hydroxylup-20(29)-en-3-oxo-27, 28-dioic Acid (**4**). Acetylation of **4** (3 mg) with Ac_2O/pyridine (1:1, 3 mL, room temperature for 6 h) furnished, after the usual workup, **6** (2.1 mg) as a solid: $[\alpha]^{26}_D$ +45.2° (*c* 0.05, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3450, 1735 (acetate carbonyl), 1703, 1470, 1372, 1109, 988 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20, 1.68 (2H, m, H-1), 2.79 (1H, ddd, J = 6.1, 8.1,6.1, H-2β), 2.30 (1H, m, H-2α), 1.72 (1H, m, H-5), 5.05 (1H, td, J = 4.2, 9.5 Hz, H-6β), 1.38, 1.64 (2H, m, H-7), 1.44 (1H, m, H-9), 1.52 (2H, m, H-11), 1.05, 1.71 (2H, m, H-12), 2.27 (1H, m, H-13), 1.18, 1.70 (2H, m, H-15), 1.40, 1.68 (2H, m, H-16), 1.67 (1H, m, H-18), 3.01 (1H, td, J = 4.5, 12, H-19β), 1.60, 2.02 (2H, m, H-21), 1.48, 2.04 (2H, m, H-22), 1.08 (3H, s, H-23), 1.27 (3H, s, H-24), 1.39 (3H, s, H-25), 0.93 (3H, s, H-26), 4.63, 4.75 (each 1H, s, H-29), 1.70 (3H, s, H-30), 2.05 (3H, s, OAc); EIMS (70 eV) *m/z* 542 ($[M]^+$, 1), 528 ($[M - H_2O]^+$, 2), 512 ($M - 2CH_3$, 3), 497 ($[M - COOH]^+$,

2), 467 ([M − 2CH_3 − COOH]$^+$, 2), 452 ([M − 2CH_3 − AcOH]$^+$, 10), 437 (9), 391 (5), 248 (49), 189 (51), 147 (42), 119 (75), 83 (46), 55 (70).

Cytotoxicity Assay. The cytotoxicity of compounds **1**−**4** against NUGC (gastric tumor) cells was assayed by the 5-(3-carboxymethoxyphenyl)-2-(4,5-dimethylthiazoyl)-3-(4-sulfophenyl)tetrazolium salt (MTS) colorimetric method to measure the mitochondrial NADPH dehydrogenase activity as previously described.[9−11] The percent survival rates of NUGC cells at a concentration of 10 μM of each test compound compared to the untreated cells in the MTS assay are given in the text. Antinomycin D (5 μM) was used as a positive control (0−2%).

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