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THREE NEW MEXICANOLIDES FROM THE STEM BARK OF *SWIETENIA MAHOGANI* JACQ.

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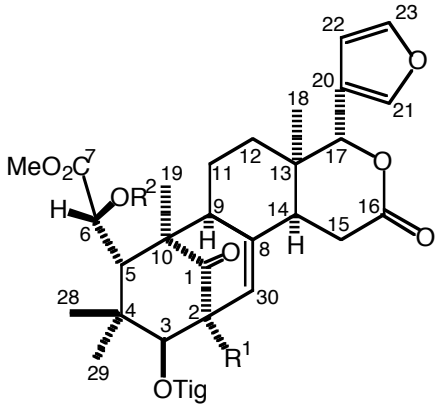
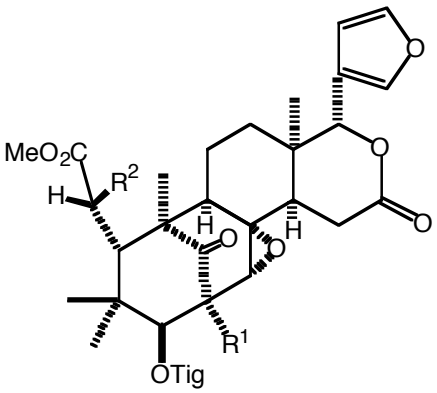
Abstract—Three new mexicanolide-type limonoids were isolated together with two known mexicanolides, 2-hydroxyswietenin and swietemahonin G, from the ether extract of the stem bark of *Swietenia mahogani* JACQ. (Meliaceae). The structure of these compounds was elucidated by spectroscopic means and their biological activities were also tested.

Meliaceae plants are attracting considerable interest, because of their significant biological activities. We have reported many limonoid antifeedants from several Meliaceae plants,[1-3] recently new type mexicanolides and novel rearranged phragmalin compounds from *Khaya senegalensis*.[4-6] *Swietenia mahogani* JACQ. is a large meliaceous mahogany closely related to the African genus *Khaya* and one of the most popular traditional medicines in Africa. The decoction of the bark of these mahoganies is extensively used as febrifuge, which could be associated with its use as an antimalarial drug.[7] Ever since two ring B opened limonoids of methyl angolensate and its 6-*O*-acetate were isolated,[8] many mexicanolides of rings B,D-seco compound having a bicyclo[3,3,1]-ring system have been reported from *S. mahogani*.[9-11]

During our study on limonoid antifeedants from Meliaceae plants, we have found out the extract of the



1: R^1 = OH, R^2 = Ac
4: R^1 = OH, R^2 = H
6: R^1 = H, R^2 =OH



2: R^1 = OH, R^2 = H **8**: R^1 = H, R^2 = OH
3: R^1 = OH, R^2 = OAc **9**: R^1 = OAc, R^2 = OAc
5: R^1 = OH, R^2 = OH **10**: R^1 = OH, R^2 = OBz
7: R^1 = H, R^2 = H **11**: R^1 = OBz, R^2 = OBz

stem bark of *S. mahogany* collected at Alexandria, Egypt, to have potent antifeedant activity against *Spodoptera* insects. Then, we studied the limonoid constituents of the ether and methanol extract, and isolated three new mexicanolide-type limonoids, 6-*O*-acetyl-2-hydroxyswietenin (**1**), 2-hydroxyswietemahonolide (**2**) and 6-*O*-acetylswietemahonin G (**3**) together with two known mexicanolides, 2-hydroxyswietenin (**4**)[9] and swietemahonin G (**5**),[11] as insect antifeedants. Herein we report the structure elucidation of new mexicanolides (**1**-**3**) and antifeedant and antiviral activities of the isolated compounds (**1**-**5**) against *Spodoptera littoralis* (Boisduval) and HIV-1 replication.

The ether extract (3 g) of the stem bark was divided into eight fractions by droplet counter-current chromatography (DCCC) with ascending mode and each of the fractions was purified by reverse-phase HPLC to give two known mexicanolide-type limonoids, (**4**, 3 mg) and (**5**, 7 mg), which were identified by comparing their NMR spectra with those of authentic samples. On the other hand, a methylene chloride soluble part (4 g) of the methanol extract was chromatographed on SiO_2, followed by reverse-phase HPLC to give three new mexicanolides (**1**, 1.5 mg), (**2**, 1.5 mg) and (**3**, 2.5 mg).

Compound (**1**) was isolated as amorphous powder, $[\alpha]_D$ = -45°, and it was shown to have the molecular formula $C_{34}H_{42}O_{11}$ (14 degrees of unsaturation) by accurate MS measurement (HRFAB-MS: m/z 627.2783 $[M+1]^+$; Δ -2.2 mmu) and ^{13}C NMR spectral data. The UV maximum at 214 nm and the IR absorption at 3500-3300 and 1750-1710 cm^{-1} showed the presence of carbon-carbon double bond and hydroxyl and several types of carbonyl groups. From the ^1H and ^{13}C NMR spectral data (Table 1), it was evident that eight of the elements of unsaturation were present as double bonds: four carbon-carbon (one

furan ring) and five CO (as one ketone and four esters). Thus, the molecule is pentacyclic. The ^{1}H NMR spectrum showed the presence of a β-furyl moiety (δ 6.45, 7.44 and 7.71, each 1H) and each one of tigloyl (δ 1.74, 3H, dq, *J* = 7.0 and 1.4 Hz, 1.83, 3H, br s, and 6.92, 1H, qq, *J* = 1.4 and 7.0 Hz) and acetyl (δ 2.20) groups. The presence of methoxy (esteric: δ 3.73) and hydroxyl (δ 4.07) groups was also observed.

From decouplings and the subsequent 2D NMR spectral studies using the ^{1}H-^{1}H COSY, HMQC, HMBC and NOE spectra, it was strongly suggested that **1** was a mexicanolide. Thus, the H-6 methine proton at δ 5.58 coupling with the H-5 broad singlet at δ 3.62 showed a HMBC correlation with the C-7 ester carbonyl at δ 171.3. The presence of this ester moiety and a characteristic low-field singlet at δ 5.56 due to H-17 and the absence of one tertiary methyl signal at 8β (30) in the basic limonoid skeleton strongly suggested that **1** was a mexicanolide-type rings B,D-seco limonoid.

The NMR spectral data of **1** were very similar to those of 2-hydroxyswietenin (**4**), reported from the same species,[9] except for the change of one hydroxyl group at C-6 in **4** to an acetate group in **1**. The presence of a trisubstituted C-8/C-30 double bond in **1** was elucidated by HMBC correlations of the H-3 and 9 signals at δ 4.78 and 2.29 with the C-30 signal at δ 129.5d and the H-14 and 15β signals at δ 2.23 and 2.80 with the C-8 signal at δ 136.9, and a remarkable NOE correlation between the olefinic H-30 signal at δ 5.32 and the H-15β signal. An allylic coupling between the H-9 and H-30 signals also supported the presence of the C-8/C-30 double bond. The tigloyloxy group was also assigned to C-3 by a HMBC correlation of the H-3 signal with the tigloyl carbonyl carbon signal at δ 167.4s.

The structure of **1** as 6-*O*-acetyl-2-hydroxyswietenin including the stereochemistry appears to fully explain the NMR spectral data by consideration of a molecular model and the NOESY spectrum. Significant NOE correlations (Figure 1) between the H-11β signal at δ 2.19 and the H-5 and 17 signals, the H-9 signal and the 10-Me (19) signal at δ 1.28, the H-14 signal and the 13-Me (18) signal at δ 1.04 clarified relative stereochemistry of these protons in the dicyclo[3.3.1]nonane ring system. As the absolute structure of swietenin (**6**) isolated from the same species[10] has been determined by X-Ray analysis,[12] the configulation at C-6 in **1** was assumed as the same *R*.

Compound (**2**) was isolated as amoulphous powder, $C_{32}H_{40}O_{10}$ (13 unsaturations), $[\alpha]_D$ = -35°. The UV and IR spectra showed similar absorptions to those of **1**. The ^{1}H and ^{13}C NMR (Table 1) spectra showed that **2** was a mexicanolide similar to **1** except for the lack of a carbon-carbon double bond and one

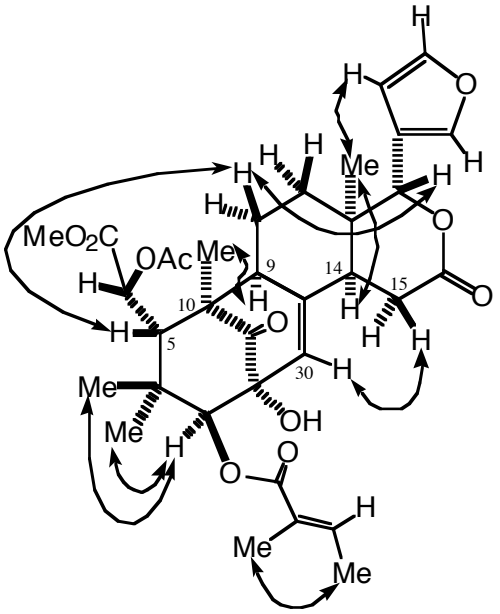


Figure 1. Significant NOE correlations in **1**.

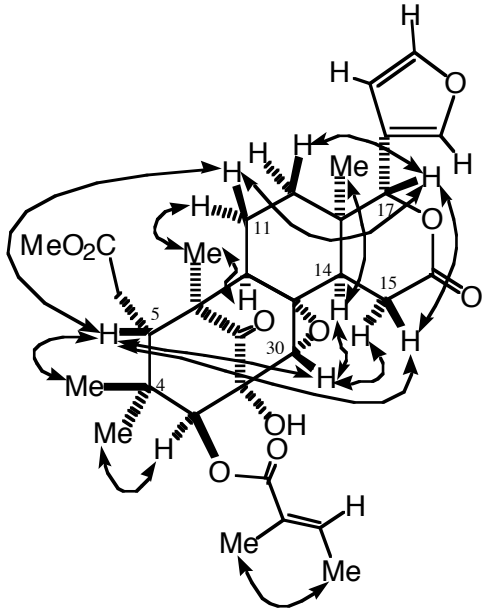


Figure 2. Significant NOE correlations in **2**.

hydroxyl group and the presence of a trisubstituted epoxide group at δ 63.2s and 67.4d. Compound (**2**) being a 6-dehydroxyl derivative of **5** was evident from the change of the 6-methine signal at δ 5.58 in **5** to methylene signals at δ 2.33 (1H, dd, J = 16.9 and 2.1 Hz) and 2.37 (1H, dd, J = 16.9 and 9.3 Hz). The presence of a C-8α/C-30α epoxide group was elucidated by HMBC correlations of the H-9, 11α, 14 and 15β signals at δ 1.89, 1.81, 1.61 and 3.49 with the C-8 signal at δ 63.2, the H-9 and H-3 signals at δ 5.14 with the C-30 signal at δ 67.4 and the H-30 signal at δ 3.50 with the C-1, 2, 3 and 8 signals at δ 213.1, 78.4, 84.8 and 63.2, respectively, and by remarkable NOEs between the H-30 signal and the H-14 and 15α signals. The tigloyloxy group was also assigned to C-3 by a HMBC correlation of the H-3 signal at δ 5.14 with the tigloyl carbonyl carbon signal at δ 166.9s. These information indicated **2** to be the 6-dehydroxyl derivative of swietemahononine G (**5**), 2-hydroxyswietemahonolide.

However, several proton signals in **2** showed considerable shifts from those of **5**; H-3: δ 5.14. H-12α: δ 1.22, H-12β: δ 1.99, H-15β: δ 3.49 in **2**. H-3: δ 4.94. H-12α: δ 1.42, H-12β: δ 2.16, H-15β: δ 3.11 in **5**. As similar chemical shift changes have been observed in swietemahonolide (**7**) and swietemahonin E (**8**),[11] they may be accounted for by a conformational change based on the dissolution of a seven-membered hydrogen bonding between the 6-OH and 1-carbonyl groups in **5** and **8**. This conformation change was revealed from that new distinct NOE correlations (Figure 2) were observed in the NOESY spectrum of **2** between the H-30 and H-14 signals and between the H-5 signal and the H-30 and 4β-Me signals in addition to between the H-30 and H-15α signals and the H-5 and 15β signals observed in **5**.

On the other hand, the NOE between the H-11β and H-15β signals in **5** was not observed in **2**.

Compound (**3**), $C_{34}H_{42}O_{12}$; $[\alpha]_D$ = -61°, showed similar ^1H and ^{13}C NMR spectra to those of **2** including the presence of one C-8α/C-30α epoxide groupexcept for the addition of one acetoxy group in **3**. Significant NOE correlations were also observed between the H-30 signal and the H-14 and 15α signals, as well as in **2**. The structure (**3**) derived from the downfield shift of the 6-methine proton signal to δ 5.50, was elucidated by acetyla-tion of **5** with Ac_2O in pyridine to give 6-*O*-acetylswietemahonin G (**3**).

Acetylation of **5** in the presence of *p*-dimethylaminopyridine gave the 2,6-diacetate (**9**). Similarly *p*-bromobenzoylation of **5** on addition of *p*-dimethylaminopyridine gave the 2-mono (**10**) and 2,6-dibenzoate (**11**). The CD spectrum of **10** showed an absorption due to π-π* transition of benzoate at 243 nm (Δε – 0.44: λmax 247 nm) along with the absorption at 290 nm (Δε – 0.27) by n-π* transition of the 1-keto group, but the dibenzoate (**11**) exhibited a positive split CD at 236 (Δε - 0.36) and 252 nm (Δε + 0.59) based on the interaction of two benzoate π–π* transition (Figure 3), which accounted well for the stereochemistry of C-6 to be *R*,[13] because the preferential conformation (Figure 4) of **11** was derived from the H-6 singlet at δ 5.85 referring to the dihedral angle of H-5/H-6 to be *ca* 90°, a significant low field shift of the 4α-Me to δ 1.49 from δ 1.03 in **3** and strong NOE correlations of the H-6 signal with the 10-Me (19) and H-11β signals.

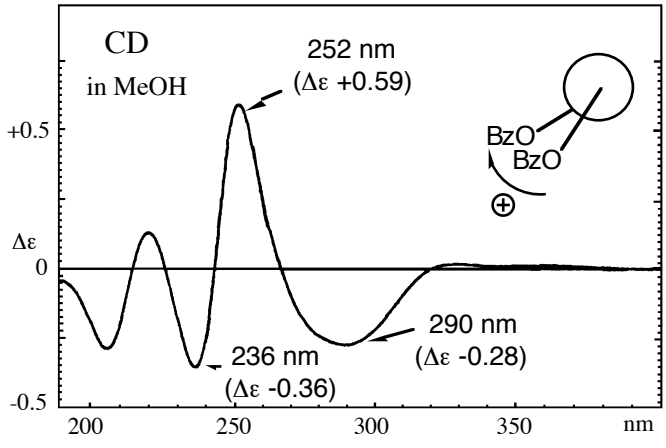


Figure 3. CD spectrum of **11**.

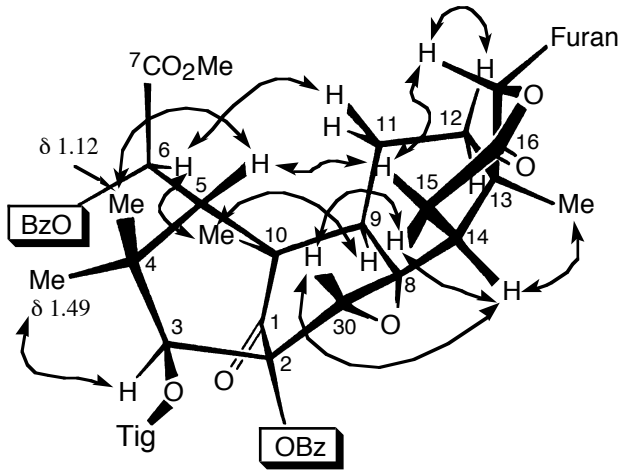


Figure 4. NOEs and preferential conformation of **11**.

Antifeedant activity of **1**-**5** was tested using a conventional leaf disk method[14] against third instar larvae of *Spodoptera littoralis* (Boisduval), and all of the compounds showed considerable activities. Most potent was swietemahonin G (**5**), which was active at 300 ppm, with 50 ppm corresponding to a

Table 1. ^{1}H and ^{13}C NMR spectral data of mexicanolides (**1**-**3**).

no	**1**		**2**		**3**	
	H	C	H	C	H	C
1		214.4 s		213.1 s		212.3 s
2		77.2 s		78.4 d		78.3 d
3	4.78 s	85.7 d	5.14 s	84.8 d	5.01 s	85.9 d
4		39.7 s		40.1 s		40.6 s
5	3.62 br s	44.5 d	3.23 dd (9.3, 2.1)	42.3 d	3.47 br s	45.1 d
6	5.58 br s	76.7 d	2.33 dd (16.9, 2.1)	32.9 t	5.50 br s	72.0 d
			2.37 dd (16.9, 9.3)			
7		171.3 s		174.0 s		171.1 s
8		136.9 s		63.2 s		62.8 s
9	2.29 br dd (13.0, 4.5)	57.3 d	1.89 dd (13.0, 3.2)	55.2 d	1.95 m	55.0 d
10		49.4 s		49.1 s		49.2 s
11α	1.81 m	20.9 t	1.81 m	19.4 t	1.95 m	19.8 t
β	2.19 m		1.86 dt (3.1, 13.0)		1.94 m	
12α	1.44 dt (4.1, 13.9)	34.3 t	1.22 ddd(14.5, 13.0, 3.2)	33.2 t	1.27 m	32.8 t
β	1.75 br dt (13.9, 3.8)		1.99 dt (14.6, 3.1)		2.08 dt (14.8, 3.2)	
13		36.6 s		36.2 s		35.8 s
14	2.23 br d (5.9)	44.9 d	1.61 dd (13.5, 5.3)	45.2 d	1.59 dd (12.8, 6.2)	44.2 s
15α	2.84 dd (19.0, 5.9)	29.4 t	2.83 dd (16.4, 5.3)	33.5 t	2.78 dd (16.8, 6.2)	32.9 t
β	2.80 dd (19.0, 1.5)		3.49 dd (16.2, 13.5)		3.29 dd (16.8, 12.8)	
16		168.6 s		171.3 s		171.1 s
17	5.56 s	72.5 d	5.18 s	78.9 d	5.13 s	79.7 d
18	1.04 s	21.3 q	1.00 s	26.3 q	1.02 s	26.4 q
19	1.28 s	15.4 q	1.17 s	16.1 q	1.19 s	16.0 q
20		120.9 s		120.2 s		120.5 s
21	7.71 br s	141.5 d	7.51 br s	141.0 d	7.47 br s	141.1 d
22	6.45 br d (1.0)	109.5 d	6.44 br s	110.2 d	6.40 br s	110.1 d
23	7.44 t (1.5)	143.4 d	7.43 br t (1.5)	143.2 d	7.43 t (1.7)	143.5 d
28	0.95 s	22.2 q	0.79 s	22.0 q	0.95 s	22.1 q
29	1.10 s	21.9 q	0.81 s	20.5 q	1.07 s	22.5 q
30	5.32 br s	129.5 d	3.50 s	67.4 d	3.38 s	67.3 d
7-OMe	3.73 s	53.2 q	3.74 s	52.4 q	3.82 s	53.4 q
2-OH	4.07 br s		4.00 br s		4.00 br s	
6-OAc	2.20 s	20.8 q			2.19 s	20.7 q
		169.9 s				169.9 s
Tig						
1’		167.4 s		166.9 s		167.0 s
2’		127.6 s		127.8 s		128.0 s
3’	6.92 qq (7.0, 1.4)	139.9 d	7.03 qq (7.1, 1.3)	139.7 d	7.01 qq (7.1, 1.2)	139.9 d
4’	1.74 dq (7.0, 1.4)	14.5 q	1.92 br dq (7.1, 1.2)	14.7 q	1.95 br d (7.1)	14.5 q
2’-Me	1.83 br s	11.7 q	1.96 br quint (1.3)	12.6 q	1.96 br s	12.4 q

^{1}H and ^{13}C spectra were measured in $CDCl_3$ at 600 and 150 MHz, respectively.
Chemical shifts are expressed in ppm and *J* values in parentheses are in Hz.

concentration of *ca.* 1 μg/leaf cm^2. 2-Hydroxyswietemahonolide (**2**) and 6-*O*-acetylswietemahonin G (**3**) were active at 500 ppm. Two swietenins of **1** and **4** were not active at 750 ppm. These activities are weaker than those of well-known limonoid antifeedants (10-50 ppm) such as the azadirachtins[15] from *Melia azadirachta* indica and meliacarpinins[16] from *Melia azedarach* Linn., but comparable to those of the second compounds, trichilin-type limonoids[2] from *Tolichilia roka* and *M. azedarach*. and rearranged phragmalins[4-6] from *K. senegalensis*. Antiviral activity against HIV-1 replication was also tested on the inhibition of virus-induced cytopathicity in MT-4 cells,[17] but they showed no activity at 100 μg/mL.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were measured at 600 and 150 MHz at 27° C in $CDCl_3$ on a JEOL FX-600 spectrometer. IR (KBr) and UV (MeOH) spectra were recorded on JASCO FT/IR 5300 and Shimadzu UV-210A spectrophotometers. Optical and CD spectra were measured in MeOH at 22° using JASCO DIP-370S and JASCO J-720 spectropolarimeters. HPLC was performed on Waters μBondapak C_{18} column by using 35-45% H_2O-MeOH and 50-55% H_2O-MeCN as solvents. Kieselgel $60F_{254}$ plates (0.2 mm thick, Merck) were used for prep TLC.

Plant material. The stem bark was collected in April 2001 at Alexandria in Egypt.

Extraction and isolation. The dried stem bark (1 kg) was extracted with successive, each 3 L of hexane, ether, acetone and MeOH to give the extracts of 6, 13, 58 and 100 g, respectively. i) The ether extract (3 g) was fractionated by DCCC in ascending mode with CH_2Cl_2-MeOH-H_2O (= 5:8:4) solvent system to give five limonoid fractions of 70 mg, 100 mg, 400 mg, 180 mg and 65 mg. The second fraction was roughly purified through HPLC with 35% H_2O-MeOH as the solvent and then purified with HPLC using 55% H_2O-MeCN to give **4** (3 mg). In the same manner, **5** (7 mg) was isolated from the forth fraction. ii) The CH_2Cl_2 soluble part (4 g) of the MeOH extract was fractionated by chromatography on SiO_2 with CH_2Cl_2, 1%, 2%, 5% and 20% MeOH-CH_2Cl_2, and MeOH. The 5% MeOH-CH_2Cl_2 fraction (500 mg) was separated into two limonoid parts of 1 (28 mg) and 2 (10 mg) by HPLC using 35% H_2O-MeOH. Fraction 1 was purified by HPLC using 50% H_2O-MeCN to give **2** (1.5 mg) and **3** (2.5 mg). From fraction 2, **1** (1.5 mg) was isolated by using HPLC with 40% H_2O-MeOH.

6-*O*-Acetyl-2-hydroxyswietenin (1). White amorphous powder; $C_{34}H_{42}O_{11}$; HRFAB-MS m/z:

627.2783 $[M+1]^+$, Δ –1.9 mmu.; $[\alpha]_D$= -45° (c 0.08); UV λ_{max} nm (ε): 214 (12,000). IR ν_{max} cm^{-1}: 3500-3300, 1750-1710, 1221, 1126 and 729; ^1H and ^{13}C NMR: Table 1.

2-Hydroxyswietemahonolide (2). White amorphous powder; $C_{32}H_{40}O_{10}$; HRFAB-MS m/z: 585.2690 $[M+1]^+$, Δ –1.0 mmu.; $[\alpha]_D$= -35° (c 0.075); UV λ_{max} nm (ε): 215 (12,000); IR ν_{max} cm^{-1}: 3500-3300, 1760(sh), 1730, 1710 (sh), 1261, 1126, 1074, 1028 and 733; ^1H and ^{13}C NMR: Table 1.

6-*O*-Acetylswietemahonin G (3). A white amorphous powder; $C_{34}H_{42}O_{12}$; HRFAB-MS m/z: 643.2730 $[M+1]^+$, Δ –0.2 mmu.; $[\alpha]_D$= -61° (c 0.12); UV λ_{max} nm (ε): 215 (13,000); IR ν_{max} cm^{-1}: 3500-3300, 1760 (sh), 1738, 1710 (sh), 1219, 1124, 1080, 1028, 875 and 763; CD: $\Delta\varepsilon_{220}$ –0.13, $\Delta\varepsilon_{230}$ +0.03, $\Delta\varepsilon_{291}$ –0.19 (n-π* of ketone); ^1H and ^{13}C NMR: Table 1.

Acetylation of swietemahonin G (5). i) Acetylation of **5** (2 mg) with Ac_2O (0.2 mL) in pyridine (1 mL) at rt gave **3** (1.4 mg). ii) Acetylation of **5** (3 mg) with Ac_2O (0.2 mL) and *p*-(2,6-dimethylamino)pyridine (DMAP: 5 mg) in pyridine (2 mL) at rt gave the diacatate (**9**: 1.9 mg). **9**: $C_{36}H_{44}O_{13}$; FAB-MS m/z: 685 $[M+1]^+$: CD: $\Delta\varepsilon_{227}$ +0.13, $\Delta\varepsilon_{291}$ –0.46; ^1H NMR ($CDCl_3$): δ 0.97 (3H, s, 4β-Me), 1.01 (3H, s, 13-Me), 1.18 (3H, s, 4α-Me), 1.29 (3H, s, 10-Me), 1.26 (1H, m, H-12α), 1.55 (1H, dd, J = 13.9 and 5.5 Hz, H-14), 1.91 (1H, m, H-9), 1.85-1.96 (2H, m, H-11α and H-11β), 1.95 (3H, br d, J = 7.1 Hz, 3'-Me), 1.96 (3H, br s, 2'-Me), 2.07 (1H, dt, J = 15.0 and 3.6 Hz, H-12β), 2.18 and 2.19 (each 3H, s, Ac), 2.80 (1H, dd, J = 16.2 and 5.5 Hz, H-15α), 3.45 (1H, dd, J = 16.2 and 13.9 Hz, H-15β), 3.42 (1H, br s, H-5), 3.53 (1H, s, H-30), 3.82 (3H, s, OMe), 5.10 (1H, s, H-17), 5.51 (1H, br s, H-6), 5.74 (1H, s, H-3), 6.41 (1H, br d, J = 1.5 Hz, H-22), 7.00 (1H, qq, J = 7.1 and 1.5 Hz, H-3'), 7.43 (1H, t, J = 1.5 Hz, H-23), 7.46 (1H, br s, H-21).

Benzoylation of swietemahonin G (5). Treatment of **5** (5 mg) with *p*-brombenzoyl chloride (10 mg) and DMAP (8 mg) in pyridine (2 mL) at rt for 48 h gave **10** (3.2 mg) and **11** (1.9 mg). **10**: $C_{39}H_{43}O_{12}Br$; FAB-MS m/z: 783, 785 $[M+1]^+$; UV λ_{max} nm (ε): 247 (16,000); CD: $\Delta\varepsilon_{215}$ –0.18, $\Delta\varepsilon_{243}$ –0.44 (π-π* of benzoate), $\Delta\varepsilon_{260}$ +0.06, $\Delta\varepsilon_{290}$ –0.27 (n-π* of ketone); ^1H NMR ($CDCl_3$): δ 1.03 (3H, s, 13-Me), 1.06 (3H, s, 4β-Me), 1.16 (3H, s, 4α-Me), 1.19 (3H, s, 10-Me), 1.30 (1H, m, H-12α), 1.61 (1H, dd, J= 12.8 and 6.5 Hz, H-14), 1.94 (3H, dq, J = 7.2 and 1.1 Hz, 3'-Me), 1.9-2.05 (2H, m, H_2-11), 1.98 (3H, br s, 2'-Me), 2.00 (1H, m, H-9), 2.11 (1H, br d, J = 15.0 Hz, H-12β), 2.81 (1H, dd, J = 16.9 and 6.5 Hz, H-15α), 3.33

(1H, dd, J = 16.9 and 12.8 Hz, H-15β), 3.40 (1H, s, H-30), 3.61 (1H, br s, H-5), 3.82 (3H, s, OMe), 4.01 (1H, s, OH), 5.06 (1H, s, H-3), 5.16 (1H, s, H-17), 5.82 (1H, s, H-6), 6.42 (1H, br d, J = 1.5 Hz, H-22), 7.04 (1H, qq, J = 7.2 and 1.5 Hz, H-3'), 7.44 (1H, t, J = 1.5 Hz, H-23), 7.49 (1H, br s, H-21), 7.66 (2H, br d, J = 8.8 Hz, H-4" and 6"), 7.89 (2H, br d, J = 8.8 Hz, H-3" and 7"). **11**: $C_{46}H_{46}O_{13}Br_2$; FAB-MS m/z: 967 $[M+1]^+$; UV λ_{max} nm (ε): 246 (28,000); CD: $\Delta\varepsilon_{206}$ –0.29, $\Delta\varepsilon_{220}$ +0.14, $\Delta\varepsilon_{236}$ –0.36 (π-π* of benzoate), $\Delta\varepsilon_{252}$ +0.59 (π-π* of benzoate), $\Delta\varepsilon_{290}$ –0.28 (n-π* of ketone); ^{1}H NMR ($CDCl_3$): δ 1.05 (3H, s, 13-Me), 1.12 (3H, s, 4β-Me), 1.21 (3H, s, 10-Me), 1.29 (1H, m, H-12α), 1.49 (3H, s, 4α-Me), 1.63 (1H, dd, J = 13.8 and 6.2 Hz, H-14), 1.96 (3H, br s, 2'-Me), 1.97 (3H, br d, J = 6.7 Hz, 3'-Me), 1.97 (1H, m, H-11α), 2.01 (1H, m, H-9), 2.02 (1H, m, H-11β), 2.13 (1H, br d, J = 15.0 Hz, H-12β), 2.89 (1H, dd, J = 16.7 and 13.8 Hz, H-15α), 3.53 (1H, dd, J = 16.7 and 6.2 Hz, H-15β), 3.64 (1H, s, H-5), 3.74 (1H, s, H-30), 3.82 (3H, s, OMe), 5.15 (1H, s, H-17), 5.85 (1H, s, H-6), 5.96 (1H, s, H-3), 6.43 (1H, br s, H-22), 7.05 (1H, m, H-3'), 7.45 (1H, br t, J = 1.6 Hz, H-23), 7.49 (1H, br s, H-21), 7.56 and 7.67 (each 2H, br d, J = 8.5 Hz, H-4" and 6"), 7.91 and 7.92 (each 2H, br d, J= 8.5 Hz, H-3" and 7"); ^{13}C NMR: δ 12.6 (q, 2'-Me), 14.7 (q, C-4'), 16.3 (q, C-19), 20.9 (t, C-11), 22.8 (q, C-28), 24.2 (q, C-29), 26.8 (q, C-18), 33.0 (t, C-12), 33.5 (t, C-15), 36.1 (s, C-13), 44.9 (d, C-14), 45.4 (d, C-5), 50.7 (s, C-4), 50.7 (s, C-10), 53,6 (q, OMe), 55.3 (d, C-9), 62.7 (s, C-8), 65.6 (d, C-30), 73.0 (d, C-6), 79.4 (d, C-17), 80.8 (d, C-3), 86.2 (s, C-2), 110.1 (d, C-22), 121.0 (s, C-20), 126.6 (s, C-2'), 127.5 (s, 2 x C-2"), 128.7 and 129.3 (each s, C-5"), 131.4, 131.6 (each d, 2 x C-3" and 7"), 131.7 and 132.3 (each d, 2 x C-4" and 6"), 140.0 (d, C-3'), 140.5 (d, C-23), 143.4 (d, C-21), 164.0 and 165.3 (each s, C-1"), 166.5 (s, C-1'), 169.9 (s, C-7), 171.0 (s, C-16), 203.7 (s, C-1).

Antifeedant test. The antifeeding potential of the isolated compounds was assessed by presenting them, on leaf disks of a Chinese cabbage, to the third-instar larvae of *Spodoptera littoralis* (Boisduval), and visually comparing the treated and untreated disks eaten by the larvae. The feeding assay terminated after the larvae had eaten approximately 50% of one of the disks. This choice test was done at 300, 500 and 1000 ppm concentrations.

Antiviral assays. The inhibitory activity on HIV-1-induced cytopathic effect in MT-4 cell was measured by the method reported previously.[15] Cytotoxicity of the compounds was also evaluated in parallel with their anti-HIV-1 activity.

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