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Antifeedant Rings B and D Opened Limonoids from *Khaya senegalensis*

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Three new rings B and D opened limonoids, two mexicanolides named khayanone (**1**) and 2-hydroxyseneganolide (**2**) and one rearranged phragmalin limonoid of 1-*O*-acetylkhayanolide A (**3**), were isolated together with six known B,D-seco compounds from the acetone extract of the stem bark of *Khaya senegalensis*. Structures of new compounds were elucidated by spectroscopic means, and the absolute stereochemistry of **1** was established by CD study of the dibenzoate derivative. The insect antifeedant and antiviral activities of the new compounds were also determined.

Khaya senegalensis (Desr.) A. Juss. (Meliaceae) is a large tree native to the sub-Sahara savannah from Senegal to Uganda[1] and a source of popular traditional medicine in Africa. The bark is extensively used as febrifuge for malarial fever.[2] This genus is an African mahogany closely related to the South American genus *Swietenia*. *Swietenia* and *Khaya* are the main sources of rings B and D opened limonoids such as mexicanolides[3] having a bicyclo[3.3.1] ring system. Several types of the B,D-seco limonoids containing mexicanolides and A-ring-bridged phragmalin limonoids and several rearranged compounds have been reported from *K. senegalensis*.[4−6]

During our study on limonoid antifeedants from Meliaceae plants,[7−9] we found the ether extract of the stem bark of *K. senegalensis* collected at Alexandria, Egypt, to have antifeedant activity against *Spodoptera littoralis* (Boisduval). Recently, we reported the isolation of two mexicanolide-type limonoids, seneganolide (**4**)[10] and khayalactol,[11] four rearranged phragmalin limonoids, khayanolides A (**5**), B, and C[12,13] and 1-*O*-acetylkhayanolide B,[11] and some known compounds from the ether extract. Preliminary separation of compounds from the acetone extract of *K. senegalensis* by droplet countercurrent chromatography (DCCC), followed by HPLC separation, yielded three new antifeedant limonoids **1**−**3** and six known compounds. In this paper, we report the isolation, structure elucidation, and antifeedant and antiviral activities of compounds **1**−**3**.

Results and Discussion

Khayanone (**1**) was isolated as colorless prisms, and its molecular formula was established as $C_{27}H_{34}O_9$ (11 unsaturations) by accurate HRFABMS and NMR data. The UV (211 nm) and IR (3650−3200, 1745−1705, 1635, and 875 cm^{-1}) data indicated the presence of carbon−carbon double bond, hydroxyl, keto, and ester carbonyl groups. From the ^1H and ^{13}C NMR data, it was evident that six of the elements of unsaturation were present as double bonds: two carbon−carbon double bonds (as a furan ring) and four CO (as two ketones and two esters). A β-furyl moiety and one methoxycarbonyl group were also apparent from the spectra.

All protons directly bonded to carbon atoms were first assigned by the HMQC spectrum, and $^1H-^1H$ COSY and $^1H-^{13}C$ long-range HMBC studies indicated **1** to be a

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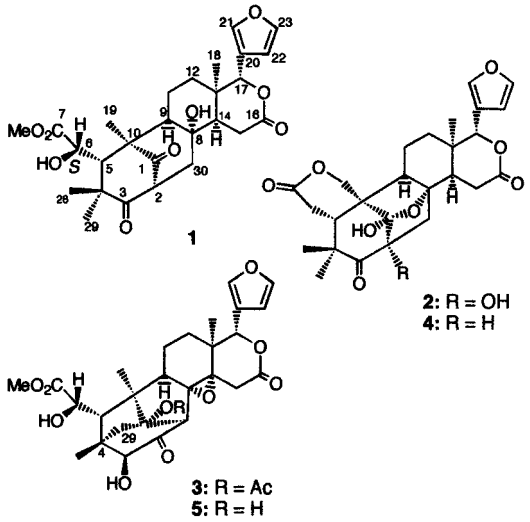

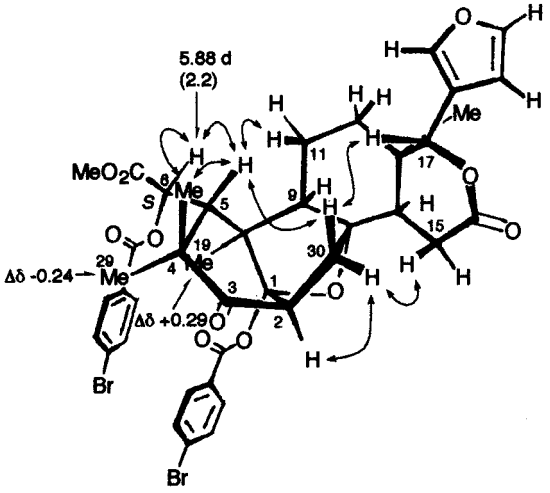

Figure 1. Selected NOEs in **8** and significant ^{1}H NMR data.

mexicanolide. A broad singlet (H-6) at δ 4.43 coupled to a broad singlet (H-5) at δ 2.78, a characteristic H-17 singlet at δ 5.50, and the absence of a Me signal due to 8β (C-30) in the basic limonoid skeleton strongly suggested that **1** was a limonoid with rings B and D opened. From the HMBC spectrum, the H-5 signal was correlated with C-28, C-29, C-10, C-3, and C-1, and a methine proton (H-2) at δ 3.16 (d), coupled to one of the 30-methylene protons at δ 2.33, was correlated with C-1, C-3, C-4, and C-10. Further, H-9 at δ 1.87 (br dd) and Me-19 at δ 1.36 showed correlations with C-8 and C-10, and C-1, C-5, and C-9, respectively. These findings clearly characterized the first molecular fragment, the left-hand bicyclo decane ring system including Me-19, 28, and 29 in the molecule. H-9 also showed correlations with C-11 and C-12. Another methine proton (H-14) at δ 1.73 (dd) coupling with methylene protons (H_2-15) at δ 2.82 and 2.75 showed HMBC correlations with C-8, C-13, C-17, C-18, and C-30. These correlations characterized the second fragment of the molecule, C-8−C-17, of the C and D rings in the limonoid skeleton.

Relative stereochemistry of the dicyclo[3.3.1^{2,10}]decane ring in **1** was elucidated by decoupling and NOE studies. Irradiation of the H-30α signal at δ 2.33 coalesced the H-9 signal to a sharp double doublet. This W-type long-range coupling and NOEs between H-9 and Me-19 and between H-5 and H-11β clarified the stereochemistry of the dicyclodecane system. NOEs between H-9 and H-14 and between H-14 and Me-18 clarified the *cis*-fusion of the rings C/D. The correlation of H-30β with H-12b and H-17 also clarified the ring C to be a skew boat form.

Identification of the stereochemistry of C-6 was first attempted using a modified Mosher's method,[14] but esterification of **1** with (*R*)- and (*S*)-MTPA chlorides gave unexpected 1-mono- (**6**) and 1,6-diMTPA esters (**7**), respectively, instead of the desired 6-MTPA esters (Scheme 1). The lactol formation was suggested from the presence of an acetal carbon assigned to C-1 by HMBC correlations: **6**, δ 111.9; **7**, δ 111.7. This is based on a ketone/lactol equilibrium of khayanone that exists primarily in the keto-form **1** as shown in Scheme 1. *p*-Bromobenzoylation of **1** gave the 1,6-dibenzoate (**8**) in high yield. The preferential conformation of **8** was assigned from the significant NOEs and the considerable high and low field shifts of 4α- (29) and 10-Me (19) in comparison with those in **1** (Figure 1). This dibenzoate (**8**) exhibited a negative split CD at 233 ($\Delta\epsilon$ +1.1) and 256 nm ($\Delta\epsilon$ −1.4) based on the interaction of a benzoate π−π* transition, which revealed the stereochemistry of C-6 to be *S*.[15,16] The structure of khayanone was therefore identified as methyl 6*S*-6,8α-dihydroxy-1,3-dioxo[3.3.1^{2,10}]dicyclomeliac-7-oate (**1**).

The seneganolide-type C-19 oxygenated 1,8-ketal structure of compound **2**, $C_{26}H_{30}O_9$, was suggested from comparison of the spectral data with those of seneganolide (**4**).[10] The ^{1}H and ^{13}C NMR spectra (Table 1) were similar to those of **4** except for the presence of an additional hydroxyl group. In particular, the presence of an acetal carbon signal at δ 111.2 and oxygenated 19-methylene signals at δ 4.25 and 4.54 (each d, J = 12.0 Hz) strongly suggested that **2** had the same ring structure as **4**. A significant downfield shift for the C-2 signal to δ 89.2 in **2** from δ 53.8 in **4** determined the position of the hydroxyl at C-2. Although several proton and carbon signals showed considerable shifts from those of **4**, they were assigned to the structure

Scheme 1. Equilibrium of Khayanone (**1**) and Reaction with (*R*),(*S*)-MTPA-Cl and *p*-Br-benzoyl Chloride

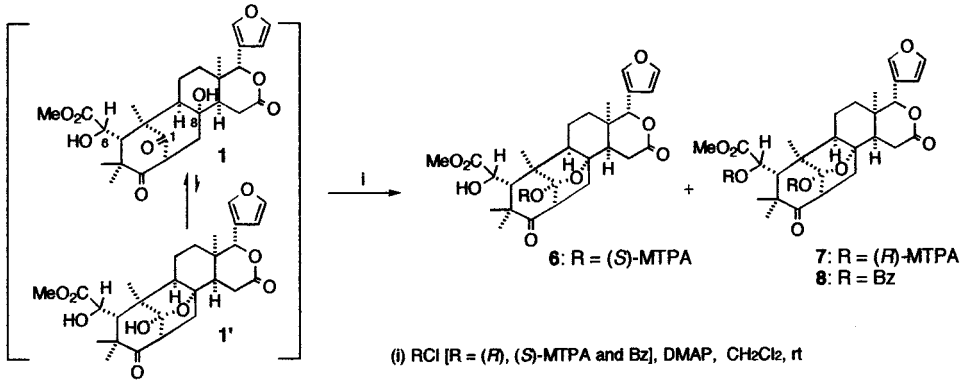

Table 1. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR Spectral Data of Compounds **1**, **2**, and **3**[a]

	1		**2**		**3**	
C no.	δ_H (mult.)	δ_C (mult.)	δ_H (mult.)	δ_C (mult.)	δ_H (mult.)	δ_C (mult.)
1		212.1 (s)		111.2 (s)		90.6 (s)
2	3.16 (d, 9.3)	54.3 (d)		89.6 (s)		209.8 (s)
3		213.6 (s)		204.7 (s)	3.97 (s)	85.2 (d)
4		50.3 (s)		44.9 (s)		44.1 (s)
5	2.78 (br s)	46.3 (d)	2.45 (dd, 9.2, 7.6)	42.5 (d)	1.72 (d, 4.4)	43.7 (d)
6α	4.43 (br s)	71.0 (d)	2.69 (dd, 14.9, 9.2)	29.4 (t)	4.35 (dd, 5.4, 4.4)	72.2 (d)
β			2.53 (dd, 14.9, 7.6)			
7		175.3 (s)		172.3 (s)		174.7 (s)
8		73.8 (s)		79.0 (s)		75.2 (s)
9	1.87 (dd, 13.1, 4.9)	61.8 (d)	2.05 (dd, 11.5, 4.9)	57.2 (d)	1.99 (dd, 13.5, 5.2)	54.4 (d)
10		50.3 (s)		51.1 (s)		58.8 (s)
11α	1.21 (br dt, 13.1, 3.2)	22.8 (t)	1.91 (dq, 13.6, 5.5)	19.0 (t)	1.20 (m)	18.9 (t)
β	1.80 (m)		1.57 (m)		1.06 (ddd, 15.4, 13.9, 3.0)	
12α	1.72 (m)	35.1 (t)	1.42 (ddd, 14.4, 8.3, 6.1)	32.9 (t)	1.20 (m)	31.3 (t)
β	1.25 (m)		1.65 (dt, 14.4, 5.5)		1.48 (ddd, 13.4, 3.8, 3.0)	
13		35.6 (s)		37.0 (s)		36.3 (s)
14	1.73 (dd, 7.6, 2.0)	51.7 (d)	2.17 (dd, 7.3, 5.5)	49.5 (d)		63.9 (s)
15α	2.82 (dd, 19.0, 2.0))	27.0 (t)	2.76 (dd, 18.0, 7.3)	27.9 (t)	3.07 (d, 18.8)	36.3 (t)
β	2.75 (dd, 19.0, 7.6))		2.66 (dd, 18.0, 5.5)		2.51 (d, 18.8)	
16		169.9 (s)		169.4 (s)		169.4 (s)
17	5.59 (s)	76.7 (d)	5.07 (s)	78.6 (d)	5.49 (s)	76.8 (d)
18	1.00 (s)	23.7 (q)	1.07 (s)	23.4 (q)	1.10 (s)	16.1 (q)
19α	1.36 (s)	24.5 (q)	4.54 (d, 11.8)	73.3 (t)	1.37 (s)	18.3 (q)
β			4.25 (d, 11.8)			
20		121.0 (s)		120.6 s		120.4 (s)
21	7.45 (br s)	141.2 (d)	7.40 (br s)	141.0 d	7.45 (br s)	141.1 (d)
22	6.36 (m)	110.0 (d)	6.34 (dd, 1.7, 0.7)	109.9 d	6.41 (br)	109.9 (d)
23	7.42 (br t, 1.7)	143.2 (d)	7.41 (t, 1.7)	143.2 d	7.44 (t, 1.7)	143.3 (d)
28	1.26 (s)	23.9 (q)	0.89 (s)	25.2 q	1.40 (s)	18.8 (q)
29$_{Pro-R}$	1.29 (s)	24.5 (q)	1.11 (s)	19.3 q	2.24 (d, 12.5)	40.6 (t)
$_{Pro-S}$					2.92 (d, 12.5)	
30α	2.33 (ddt, 14.9, 9.5, 2.0)	39.5 (t)	2.75 (s)	40.3 t	3.53 (s)	57.6 (d)
β	3.01 (d, 14.9)		2.75 (s)			
OMe	3.85 (s)	53.3 (q)			3.78 (s)	52.6 (q)
6-OH	2.95 (br s)				2.56 (d, 5.4)	
OH	2.78 (br)		1.60 (br), 4.68 (br)		3.59 (s)	
OAc					2.11 (s)	21.7 (q)
						170.0 (s)

[a] Measured in $CDCl_3$. Chemical shift valuues are in ppm from TMS, and *J* values (in Hz) are presented in parentheses.

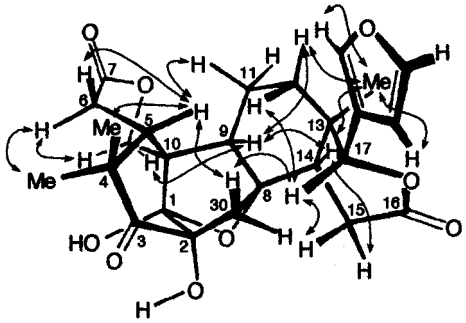

Figure 2. Selected NOE correlations in **2**.

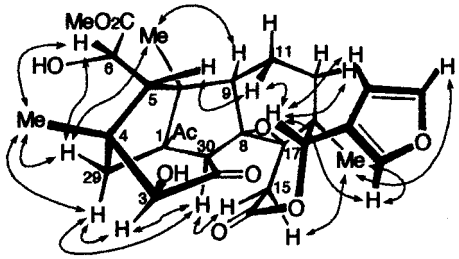

Figure 3. Significant NOE correlations in **3**.

by considering conformational change primarily based on the formation of a five-membered hydrogen bond between the 2-OH and 3-carbonyl groups. The relative stereochemistry of **2** derived from the NOE correlations (Figure 2) was also accounted for by a consideration of the conformation change. Thus, **2** was characterized as 2-hydroxyseneganolide.

The rearranged phragmalin structure of compound **3**, $C_{29}H_{34}O_{11}$, was also suggested from the spectral data. 2D NMR studies and NOE measurements (Figure 3) indicated that **3** was a rearranged phragmalin limonoid like khayanolide A (**5**).[12] The ^{1}H and ^{13}C NMR spectra were similar to those of **5** except for the presence of an additional acetyl group. When compared with the NMR of **5**, significant differences observed in **3** were upfield shifts for C-29 ($\Delta\delta$ −3.6 ppm) and C-30 ($\Delta\delta$ −3.4 ppm) together with a downfield shift for C-1 ($\Delta\delta$ +4.3 ppm), which placed the acetoxy at C-1. A W-type long-range coupling between H-9 and H-30 and NOEs between H-30 and H-5, H-17, and H-15*β* and between H-14 and H-9 and 10-Me (19) elucidated the same relative stereochemistry of six chiral centers at C-8, 9, 13, 14, 17, and 30 with **5**.

Antifeedant activity of **1**−**3** was tested with a conventional leaf disk method against third instar larvae of *Spodoptera littoralis* (Boisduval).[17] The most potent was **3**, which was active at 100 ppm, with 50 ppm corresponding to a concentration of ca. 1 μg/leaf·cm^2. Compounds **1** and **2** were active at 300 and 200 ppm, respectively. These activities are weaker than that of well-known limonoid antifeedants (10−50 ppm) such as the azadirachtins and meliacarpinins.[18,19] Antiviral activity against HIV-1 replication was also tested on the inhibition of virus-induced cytopathicity in MT-4 cells,[20] but **1**−**3** showed no activity at 100 μg/mL.

Experimental Section

General Experimental Procedures. ^{1}H and ^{13}C NMR spectra were measured at 500 and 125 MHz at 40 °C on a JEOL FX-500 spectrometer. IR and UV spectra were recorded on JASCO FT/IR 5300 and Shimazu UV-210A spectrophotometers. Specific rotations and CD spectra were measured using JASCO DIP-370S and JASCO J-720 spectropolarimeters. HPLC was performed on a Waters μBondapak C_{18} column.

Plant Material. The stem bark was collected in January 1999 at Alexandria, Egypt, and identified by Mr. Ahmed Moharib of Alexandria University. A voucher specimen is deposited in the Faculty of Agriculture, Alexandria University.

Extraction and Isolation. After extraction with hexane, followed by ether, the dried stem bark (910 g) was extracted with acetone (3 L) to yield 19 g of material. The acetone extract was fractionated by DCCC using CH_2Cl_2−MeOH−H_2O (5:5:3 v/v) in ascending mode to give five limonoid fractions of 149, 319, 108, 117, and 321 mg. The first fraction was purified through HPLC with 35−55% H_2O−MeOH as the solvent to give khayanolide B (39 mg), and from the second fraction, compound **5** (138 mg) was purified with the same solvent. The third fraction was purified with 35−50% H_2O−MeOH to give **3** (7 mg) and 1-*O*-acetylkhayanolide B (24 mg). Compound **1** (44 mg) and compounds **2** (5.5 mg) and **5** (34 mg) were purified with 40−50% H_2O−MeOH, respectively, from the fourth and fifth fractions.

Khayanone (1): colorless prisms from AcOEt, mp 170−171 °C; $[\alpha]_D$ +2.6° (*c* 0.85, MeOH); IR (KBr) ν_{max} 3650−3200, 1740, 1705, 1635, and 875 cm^{-1}; UV (MeOH) λ_{max} 211 (log ϵ = 3.5) nm; CD (MeOH) $\Delta\epsilon_{215}$ +1.4 (π−π* of furan), $\Delta\epsilon_{260}$ −1.3, and $\Delta\epsilon_{300}$ −1.2 (n−π* of C=O); ^{1}H NMR and ^{13}C NMR, see Table 1; HRFABMS *m*/*z* 503.2270 [M + H]$^+$ (calcd for $C_{27}H_{35}O_9$, 503.2280).

2-Hydroxyseneganolide (2): white amorphous powder; $[\alpha]_D$ +61° (*c* 0.28, MeOH); IR (KBr) ν_{max} 3640−3200, 1750−1700, 1637, and 875 cm^{-1}; UV (MeOH) λ_{max} 211 (log ϵ = 3.7) nm; CD (MeOH) $\Delta\epsilon_{292}$ +0.9 (n−π* of C=O); ^{1}H NMR and ^{13}C NMR, see Table 1; HRFABMS *m*/*z* 487.1990 [M + H]$^+$ (calcd for $C_{27}H_{35}O_9$, 487.1968).

1-*O*-Acetylkhayanolide A (3): white amorphous powder; $[\alpha]_D$ +59° (*c* 0.35, MeOH); $C_{29}H_{34}O_{11}$; IR (KBr) ν_{max} 3650−3200, 1760−1705, 1640, 1618, 1030, and 875 cm^{-1}; UV (MeOH) λ_{max} 211 (log ϵ = 3.6) nm; ^{1}H NMR and ^{13}C NMR, see Table 1; HRFABMS *m*/*z* 559.2179 [M + H]$^+$ (calcd for $C_{29}H_{35}O_{11}$, 559.2179).

(*R*)-MTPA Ester (7) of Khayanone (1). To a solution of khayanone (**1**, 3.0 mg), triethylamine (20 μL), and (dimethylamino)pyridine (DMAP, 1 mg) was added (*S*)-MTPA chloride prepared from (*R*)-MTPA acid (44.8 mg) and oxalyl chloride (80 μL), and the reaction mixture was stirred at 25 °C for 38 h. The reaction mixture was applied to a small silica column and eluted with AcOEt to give a crude product, which was purified by preparative TLC using hexane−AcOEt (1:1) as solvent to give the diMTPA ester (**7**, 4.2 mg). Compound **7**: ^{1}H NMR ($CDCl_3$) δ 0.58 (3H, s, CH_3-29), 1.01 (3H, s, CH_3-18), 1.06 (3H, s, CH_3-19), 1.18 (3H, s, CH_3-28), 1.23 (1H, m, H-11β), 1.26 (1H, m, H-12β), 1.48 (1H, m, H-9), 1.56 (1H, m, H-11α), 1.67 (1H, dd, *J* = 11.5, 2.4 Hz, H-12α), 1.84 (1H, dd, *J* = 13.2, 6.6 Hz, H-30β), 2.22 (1H, dd, *J* = 7.4, 2.0 Hz, H-14), 2.31 (1H, dt, *J* = 1.7, 13.2 Hz, H-30α), 2.50 (1H, d, *J* = 3.0 Hz, H-5), 2.83 (1H, dd, *J* = 19.4, 7.5 Hz, H-15α), 2.89 (1H, dd, *J* = 19.5, 1.9 Hz, H-15β), 3.40, 3.62 (each 3H, s, 2′-OCH_3), 3.76 (3H, s, CO_2CH_3), 3.89 (1H, dd, *J* = 13.3, 6.5 Hz, H-2), 5.10 (1H, s, H-17), 5.28 (1H, d, *J* = 3.0 Hz, H-6), 6.28 (1H, br d, H-22), 7.28 (1H, br s, H-21), 7.41 (1H, t, *J* = 1.7 Hz, H-23), 7.36−7.43 (8H, m, H-4′, 5′, 7′, and 8′), 7.57−7.60 (2H, m, H-6′); ^{13}C NMR ($CDCl_3$) δ 19.5 (t, C-11), 20.0 (q, C-29), 22.6 (q, C-18), 23.0 (q, C-19), 24.5 (q, C-28), 27.6 (t, C-15), 31.4 (t, C-30), 35.1 (t, C-12), 35.4 (s, C-13), 44.8 (d, C-14), 47.4 (s, C-4), 46.9 (s, C-10), 47.4 (s, C-4), 47.5 (d, C-5), 49.2 (d, C-2), 52.6 (q, CO_2*Me*), 55.4, 55.8 (each q, 2′-OMe), 62.6 (d, C-9), 74.1 (d, C-6), 77.5 (d, C-17), 82.3 (s, C-8), 84.3, 85.6 (each s, C-2′), 109.8 (d, C-22), 111.7 (s, C-1), 120.9 (s, C-20), 123.3, 124.7 (each q, 2′-CF_3), 127.3, 127,6 (each d, C-6′), 128.5, 128.6 (each d, C-4′, C-8′), 129.0, 130.0 (each d, C-5′, C-7′), 131.4, 131.5 (each s, C-3′), 140.9 (d, C-21), 143.1 (d, C-23), 162.9, 166.3 (each s, C-1′), 168.9 (s, C-16), 169.2 (s, C-7), 210.6 (s, C-3); (−) HRFABMS *m*/*z* 933.2911 [M − H]$^-$ (calcd for $C_{47}H_{47}O_{13}F_6$, 933.2921).

(*S*)-MTPA Ester (6) of Khayanone (1). To a solution of khayanone (**1**, 8.0 mg), DMAP (7.5 mg), and triethylamine (31 μL) in 0.5 mL of CH_2Cl_2 was added (*R*)-MTPA chloride (5.6 mL), and the mixture was stirred at 25 °C for 72 h. The reaction product was subjected to preparative TLC with hexane−AcOEt (3:7) as solvent to give a crude product, which was purified through HPLC with a normal-phase column using 0.5% MeOH−CH_2Cl_2 as solvent to give the (*S*)-MTPA ester (**6**, 1 mg). Compound **6**: ^{1}H NMR ($CDCl_3$) δ 0.49 (3H, s, CH_3-29), 0.97 (3H, s, CH_3-18), 1.06 (3H, s, CH_3-28), 1.27 (3H, s, CH_3-19), 1.27 (1H, m, H-11β), 1.28 (1H, m, H-12β), 1.65 (1H, m, H-9), 1.70 (1H, m, H-11α), 1.74 (1H, m, H-12α), 1.89 (1H, dd, *J* = 12.8, Hz, H-30β), 2.19 (1H, dd, *J* = 7.3, Hz, H-14), 2.25 (1H, br, 6-OH), 2.26 (1H, d, *J* = 3.9 Hz, H-5), 2.35 (1H, dt, *J* = 2.0, 13.3 Hz, H-30α), 2.77 (1H, dd, *J* = 18.8, 7.6 Hz, H-15α), 2.84 (1H, dd, *J* = 18.8, Hz, H-15β), 3.57 (3H, s, 2′-OCH_3), 3.70 (3H, s, CO_2CH_3), 3.89 (1H, dd, *J* = 13.3, 5.6 Hz, H-2), 4.36 (1H, br s, H-6), 5.11 (1H, s, H-17), 6.28 (1H, br d, *J* = 1.5 Hz, H-22), 7.28−7.30 (5H, m, H-4′- H-8′), 7.33 (1H, t, *J* = 1.7 Hz, H-23), 7.34 (1H, br s, H-21); ^{13}C NMR ($CDCl_3$) δ 20.5 (t, C-11), 20.3 (q, C-29), 23.1 (q, C-18), 23.3 (q, C-19), 24.7 (q, C-28), 27.9 (t, C-15), 32.7 (t, C-30), 34.6 (t, C-12), 36.1 (s, C-13), 45.0 (s, C-14), 46.8 (s, C-4), 47.4 (s, C-10), 47.4 (s, C-4), 47.5 (d, C-5), 48.3 (d, C-2), 52.7 (q, CO_2*Me*), 56.1 (q, 2′-OMe), 62.3 (s, C-9), 70.9 (d, C-6), 78.0 (d, C-17), 82.4 (s, C-8), 84.6 (s, C-2′), 110.0 (d, C-22), 111.9 (s, C-1), 121.0 (s, C-20), 123.0 (q, 2′-CF_3), 128.5 (d, C-4′, C-8′), 128.7 (d, C-5′, C-7′), 128.9 (d, C-6′), 131.9 (s, C-3′), 140.9 (d, C-21), 143.1 (d, C-23), 163.5 (s, C-1′), 169.4 (s, C-16), 175.3 (s, C-7), 211.8 (s, C-3); HRFABMS *m*/*z* 719.2650 [M + H]$^+$ (calcd for $C_{37}H_{42}O_{11}F_3$, 719.2679).

Benzoylation of Khayanone (1). Khayanone (**1**, 5.0 mg) was treated with *p*-bromobenzoyl chloride (10 mg), DMAP (8 mg), and triethylamine (40 μL) in CH_2Cl_2 (0.5 mL) at room temperature for 48 h. The reaction product was purified by preparative TLC using ether−hexane (1:1) to give the 1,6-dibenzoate (**8**, 5.6 mg). Compound **8**: UV (MeOH) λ_{max} 207 (log ϵ = 4.4) and 247 (log ϵ = 4.6) nm; ^{1}H NMR ($CDCl_3$) δ 0.97 (3H, s, CH_3-18), 1.05 (3H, s, CH_3-29), 1.24 (1H, m, H-12β), 1.29 (1H, m, H-11β), 1.34 (3H, s, CH_3-28), 1.65 (3H, s, CH_3-19), 1.72 (1H, m, H-12α), 1.75 (1H, m, H-9), 1.75 (1H, m, H-11α), 1.99 (1H, dd, *J* = 12.9, 5.1 Hz, H-30β), 2.20 (1H, dd, *J* = 7.3, 3.4 Hz, H-14), 2.48 (1H, br t, *J* = 13.4 Hz, H-30α), 2.70 (1H, d, *J* = 2.2 Hz, H-5), 2.76 (1H, dd, *J* = 18.7, 7.5 Hz, H-15α), 2.85 (1H, dd, *J* = 18.7, 3.4 Hz, H-15β), 3.73 (3H, s, CO_2CH_3), 4.19 (1H, dd, *J* = 13.7, 5.1 Hz, H-2), 5.14 (1H, s, H-17), 5.88 (1H, d, *J* = 2.2 Hz, H-6), 6.24 (1H, m, H-22), 7.30 (1H, br s, H-21), 7.32 (1H, t, *J* = 1.7 Hz, H-23), 7.45, 7.57 (each 2H, br d, *J* = 8.8 Hz, H-4′, H-6′), 7.78, 7.86 (each 2H, br d, *J* = 8.8 Hz, H-3′, H-7′); ^{13}C NMR ($CDCl_3$) δ 20.3 (t, C-11), 21.1 (q, C-29), 23.3 (q, C-18), 24.7 (q, C-19), 25.1 (q, C-28), 27.8 (t, C-15), 33.4 (t, C-30), 34.6 (t, C-12), 36.2 (s, C-13), 45.2 (d, C-14), 46.7 (d, C-5), 47.3 (s, C-10), 47.7 (d, C-2), 47.9 (s, C-4), 52.9 (q, CO_2*Me*), 62.4 (d, C-9), 72.5 (d, C-6), 78.1 (d, C-17), 82.1 (s, C-8), 109.9 (d, C-22), 110.0 (s, C-1), 121.0 (s, C-20), 128.2 and 128.9 (each s, C-2′), 129.1, 129.2 (each s, C-5′), 131.2, 131.2 (each d, C-3′, C-7′), 132.1, 132.3 (each d, C-4′, C-6′), 140.9 (d, C-21), 143.1 (d, C-23), 162.5, 165.3 (each s, C-1′), 169.4 (s, C-16), 170.2 (s, C-7), 211.7 (s, C-3); (−)FABMS *m*/*z* 867 and 869 [M − H]$^+$ (calcd for $C_{41}H_{42}O_{12}Br_2$, 868 and 870).

Antifeedant Test. The feeding bioassay was carried out by the conventional leaf disk method,[17] cutting out a 2 cm leaf disk of Chinese cabbage. Each of these disks was dipped for 2 s in an acetone soution of the sample, 5 treated disks were arranged with another 5 control disks (immersed for 2 s in acetone only) concentrically in a Petri dish, 10 third-instar larvae of *Spodoptera littoralis* were placed in the center, and the score for the treated and untreated leaves eaten by the larvae in 2−12 h was evaluated at appropriate intervals. This choice test was done at 100, 200, 300, 500, and 1000 ppm concentrations to determine minimum inhibitory concentration for each of the compounds.

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