Limonoids and Triterpenoids from *Khaya senegalensis*

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Received January 7, 2010

Seven new limonoids (**1**−**7**), named khayalenoids C−I, three new triterpenoids (**8**−**10**), named senegalenes A−C, and eight known limonoids have been isolated from stems of *Khaya senegalensis*. The structures of these compounds were elucidated on the basis of spectroscopic analyses.

Biological activities of limonoids from plants of the family Meliaceae have attracted considerable interest.[1] The genus *Khaya* is the main source of African mahogany,[2] and there are eight *Khaya* species that grow in tropical regions.[3] *Khaya senegalensis* (Desr.) A. Juss. (Meliaceae) has been used traditionally in Africa for treatment of malaria.[4] Previous chemical investigations on this plant have afforded a series of rings B, D-*seco* limonoids.[5] Some limonoids have exhibited antifungal, antimalarial,[6] antifeedant,[5c] antiprotozoal,[5e] and/or antiviral[5b] activities. Two novel limonoids were recently isolated from the stems of *K. senegalensis*.[7] In continuation of our studies we now report the isolation of seven additional new limonoids (**1**−**7**), three new triterpenoids (**8**−**10**), and eight known limonoids from this plant. We present herein details of the isolation and structural elucidation of the new compounds.

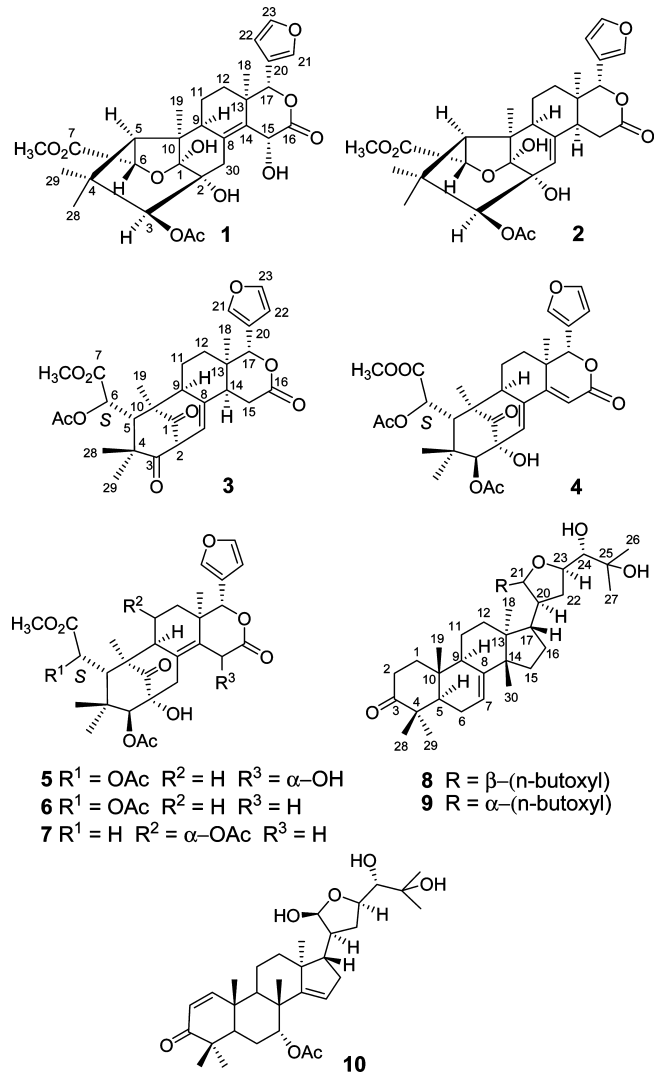
Results and Discussion

Compound **1** had the molecular formula $C_{29}H_{36}O_{11}$ with 12 degrees of unsaturation, as determined by HREIMS. The IR spectrum revealed the presence of OH (3444 cm^{-1}) and carbonyl (1743 cm^{-1}) groups. The ^1H NMR spectrum (Table 1) indicated the presence of four tertiary methyl signals (δ_H 0.91, 1.13, 1.18, 1.18), an acetyl (δ 2.17, 3H, s), a methoxy (δ 3.79, 3H, s), and signals typical of a β-substituted furan ring [δ 7.46 (t, J = 0.8 Hz), 6.42 (t, J = 1.0 Hz), 7.42 (t, J = 1.8 Hz)]. The ^{13}C NMR spectrum (Table 1) resolved 29 carbon resonances comprising six methyl, three methylene, nine methine (three olefinic), and 11 quaternary carbons (three ester carbonyls, three olefinic ones) as categorized by DEPT experiments. The aforementioned spectroscopic data and functionalities suggested that **1** was a limonoid featuring a pentacyclic core.

Detailed analyses of 1D and 2D NMR spectra revealed that **1** shared high structural similarity to khayalenoid B,[7] and the only difference was that **1** possessed one more OH group, which was assigned to C-15 (δ_C 66.5) by the key HMBC correlations (Figure 1a) from H-15 to C-8, C-13, C-14, and C-16. The relative configuration of **1** was mainly assigned by the ROESY spectrum (Figure 1b). The OH at C-15 was α-oriented, as indicated by the chemical shifts of H-15 at δ_H 4.98 and C-15 at δ_C 66.5, which were very similar to those of swietmanin F, bearing a 15α-OH (H-15 at δ_H 5.02, C-15 at δ_C 65.7).[8] The structure of **1** was thus assigned as shown.

Compound **2** had the same molecular formula as khayalenoid B (by HREIMS), suggesting that they are likely stereoisomers. Analysis of 1D and 2D NMR spectra of **2** indicated that its structure was closely related to that of khayalenoid B,[7] with the only difference being a $\Delta^{8(30)}$ double bond in **2** instead of the $\Delta^{8(14)}$ double bond of khayalenoid B. This conclusion was confirmed by the HMBC correlations of H-3/C-30 (δ_C 123.6), H_2-15/C-8 (δ_C 140.5), and H-30/C-1 (δ_C 105.5) and C-8 (δ_C 140.5). The α-orientation of H-14 of **2** was indicated by the ROESY correlations from H-14 to H-9 and H_3-18.

Compound **3**, a white amorphous powder, had the molecular formula $C_{29}H_{34}O_9$ (HREIMS). IR absorptions revealed the presence of OH (3438 cm^{-1}) and carbonyl (1739 cm^{-1}) groups. Four tertiary methyl signals (δ_H 1.30, 1.16, 1.13, 1.06), an acetyl (δ_H 2.18, 3H, s), a methoxy (δ_H 3.70, 3H, s), and a β-substituted furan ring [δ_H 7.61 (s), 6.40 (d, J = 1.7 Hz), 7.41 (t, J = 1.7 Hz)] were readily identified from the ^1H NMR spectrum (Table 1). All 29 carbons in the molecule were resolved and classified



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10.1021/np1000158
Published on Web 03/11/2010

Table 1. ^{1}H and ^{13}C NMR Data of **1**−**3** (in $CDCl_3$)[a]

	1		**2**		**3**	
position	δ_H (mult, *J*, Hz)	δ_C	δ_H (mult, *J*, Hz)	δ_C	δ_H (mult, *J*, Hz)	δ_C
1		105.8		105.5		210.8
2		77.1		77.6	3.66 (ddd, 7.2, 5.1, 1.5)	61.3
3	5.01 (s)	80.8	5.05 (s)	80.6		204.1
4		37.9		37.4		49.0
5	2.46 (s)	56.3	2.51 (s)	57.8	3.39 (s)	44.2
6	4.61 (s)	76.4	4.61 (s)	76.8	5.64 (s)	72.3
7		172.9		172.8		170.6
8		138.3		140.5		138.9
9	2.58 (dd, 10.0, 6.2)	39.2	2.41 (m)	49.5	2.45 (dd, 12.8, 4.0)	57.5
10		48.1		46.4		51.0
11α	2.13 (m)	20.4	1.88 (m)	20.8	2.31 (m)	20.4
11*β*	1.65 (m)		2.40 (m)		1.85 (m)	
12α	1.40 (dd, 9.9, 4.7, 2H)	28.2	1.73 (m)	29.2	1.78 (ddd, 17.6, 11.2, 3.3)	34.2
12*β*			1.85 (m)		1.45 (ddd, 17.6, 14.0, 4.1)	
13		39.6		39.0		36.6
14		127.9	1.46 (m)	46.4	2.15 (dd, 6.1, 2.3)	45.0
15α	4.98 (s)	66.5	2.93 (dd, 15.2, 10.5, 2H)	35.0	2.93 (dd, 19.0, 6.1)	29.4
15*β*					2.87 (dd, 19.0, 2.3)	
16		170.5		169.8		168.9
17	5.64 (s)	79.4	5.36 (s)	78.2	5.46 (s)	77.2
18	0.91 (3H, s)	14.4	1.06 (3H, s)	22.1	1.06 (3H, s)	21.7
19	1.18 (3H, s)	22.7	1.22 (3H, s)	22.3	1.30 (3H, s)	15.5
20		119.9		121.0		120.5
21	7.46 (t, 0.8)	141.1	7.42 (s)	140.4	7.61 (s)	141.3
22	6.42 (t, 1.0)	110.1	6.34 (d, 1.0)	109.5	6.40 (d, 1.7)	109.4
23	7.42 (t, 1.8)	143.0	7.35 (s)	143.2	7.41 (t, 1.7)	143.1
28	1.18 (3H, s)	24.1	1.11 (3H, s)	23.9	1.16 (3H, s)	20.5
29	1.13 (3H, s)	30.0	1.34 (3H, s)	29.9	1.13 (3H, s)	21.3
30α	3.16, d (17.0)	31.5	5.33 (s)	123.6	5.74 (dd, 7.2, 2.1)	122.1
30*β*	2.42, d (17.0)					
3-OAc		171.6		172.3		
	2.17 (3H, s)	20.8	2.14 (3H, s)	20.9		
6-OAc						169.5
					2.18 (3H, s)	20.9
7-OMe	3.79 (3H, s)	52.7	3.79 (3H, s)	52.5	3.70 (3H, s)	53.5

[a] Recorded at 400 or 100 MHz for ^{1}H and ^{13}C, respectively.

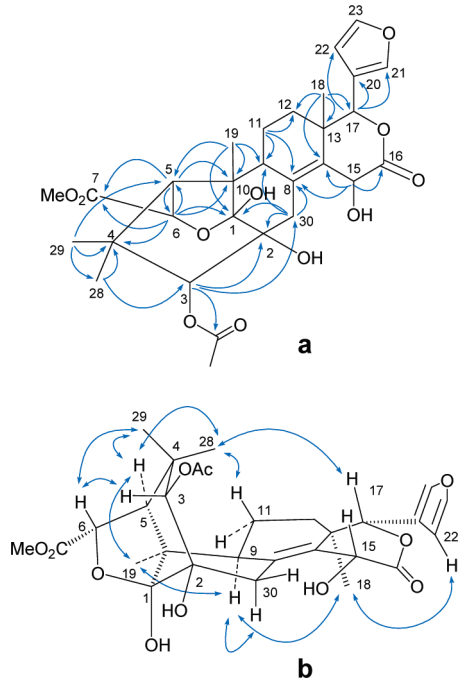

Figure 1. (a) Key HMBC correlations (H→C) of **1**. (b) Selected ROESY correlations (H↔H) of **1**.

by the ^{13}C NMR spectrum (Table 1) with DEPT experiments as six methyl, three methylene, 10 methine, and 10 quaternary carbons. This analysis suggested that compound **3** was also a limonoid. The NMR data of **3** showed many similarities to those of swietenine acetate in the limonoid core,[9] the large change of chemical shift at C-3 (δ_C 204.1), and some small changes at its adjacent atoms, indicating that a keto group was located at C-3 of **3** instead of a tigloxyl group. This assignment was verified by 2D NMR spectra (Supporting Information, S12, S13), and the structure of **3** was thus assigned as depicted.

Compound **4** possessed the molecular formula $C_{31}H_{36}O_{11}$ by HREIMS. The IR absorptions implied the presence of OH (3459 cm^{-1}) and carbonyl (1739 cm^{-1}) groups. The ^{1}H NMR spectrum of **4** (Table 2) revealed the existence of four tertiary methyls (δ_H 1.28, 1.07, 1.05, 0.87), two acetyls (δ_H 2.22, 2.18, each 3H, s), a methoxy group (δ_H 3.74, 3H, s), and a *β*-substituted furan ring [δ_H 7.52 (d, J = 0.7), 6.48 (t, J = 1.1 Hz), 7.44 (t, J = 1.6 Hz)]. The ^{13}C NMR (Table 2) and DEPT spectra of **4** showed 31 carbon resonances comprising seven methyl, two methylene, 10 methine (five olefinics), and 12 quaternary carbons (five carbonyls, three olefinic ones).

Extensive analysis of 1D and 2D NMR spectra revealed that the structure of compound **4** was very similar to that of swietmanin H,[8] except for the presence of an additional acetoxy group at C-6. This was verified by HMBC correlations (Figure 2a) from H-5 to C-6 and C-7 and from H-6 to C-5 and C-7 and, in particular, the HMBC correlation between H-6 and the ester carbonyl at δ_C 170.2 of the acetoxy group at C-6. The relative configuration of **4** was elucidated, on the basis of the ROESY spectrum (Figure 2b), to be identical to that of swietmanin H in the limonoid core, and the newly formed stereocenter of C-6 was tentatively assigned an *S*-configuration by comparing the NMR data of the side chain at C-5 with those of khayanolide A,[5c] which was assigned to have a 6*S*-configuration by X-ray diffraction and CD analysis. The structure of **4** was assigned accordingly.

Table 2. ^{1}H and ^{13}C NMR Data of **5**−**7** (in $CDCl_3$)[a]

	4	**5**		**6**		**7**	
position	δ_H (mult, *J*, Hz)	δ_C	δ_H (mult, *J*, Hz)	δ_C	δ_H (mult, *J*, Hz)	δ_C	δ_H (mult, *J*, Hz)	δ_C
1		211.4		216.1		216.5		216.0
2		77.4		78.2		77.9		78.3
3	4.86 (s)	86.6	4.96 (s)	86.6	4.95 (s)	86.6	5.08 (s)	85.6
4		39.9		39.4		39.4		38.9
5	3.32 (s)	43.8	3.36 (s)	44.4	3.31 (s)	44.3	3.03 (dd, 10.8, 1.3)	40.7
6a	5.41 (s)	71.9	5.44 (s)	72.6	5.46 (s)	72.7	2.42 (dd, 16.8, 10.8)	32.9
6b							2.28 (dd, 16.8, 1.3)	
7		170.5		171.4		171.1		174.0
8		134.6		132.4		125.6		123.0
9	2.27 (ddd, 13.0, 5.3, 2.8)	55.1	2.10 (m)	52.0	2.07 (m)	52.8	2.05 (brs)	57.2
10		53.0		52.9		52.4		51.5
11α	1.88 (m)	22.2	1.93 (m)	18.3	1.91 (m)	18.6	5.32 (dd, 5.2, 3.8)	66.9
11*β*	1.54 (ddd, 17.8, 13.0, 5.3)		1.81 (m)		1.76 (m)			
12α	2.03 (ddd, 6.8, 4.3, 2.6)	33.1	1.81 (m)	28.2	1.82 (m)	29.3	1.90 (dd, 15.0, 3.8)	34.4
12*β*	1.23 (m)		1.11 (m)		1.17 (m)		1.49 (dd, 15.0, 5.2)	
13		37.5		39.0		38.3		37.3
14		160.2		136.5		133.6		133.2
15α	6.28 (s)	113.7	5.13 (s)	65.7	3.77 (d, 19.8)	33.5	3.89 (d, 21.2)	33.0
15*β*					3.51 (dt, 19.8, 2.4)		3.51 (dt, 21.2, 2.8)	
16		164.6		174.2		169.3		169.1
17	5.14 (s)	79.6	5.52 (s)	81.2	5.59 (s)	80.7	5.62 (s)	80.4
18	1.05 (3H, s)	22.4	1.03 (s, 3H)	16.5	1.05 (3H, s)	16.7	1.20 (3H, s)	18.6
19	1.28 (3H, s)	15.2	1.27 (s, 3H)	17.0	1.26 (3H, s)	18.0	1.33 (3H, s)	17.0
20		119.9		120.1		120.4		120.1
21	7.52 (d, 0.7)	141.5	7.58 (s)	141.9	7.53 (t, 0.7)	141.6	7.60 (s)	141.9
22	6.48 (t, 1.1)	110.1	6.49 (s)	109.8	6.46 (dd, 1.8, 0.7)	109.8	6.49 (d, 1.6)	109.8
23	7.44 (t, 1.6)	143.2	7.43 (s)	143.0	7.43 (t, 1.8)	143.0	7.40 (t, 1.6)	143.0
28	0.87 (3H, s)	21.3	1.03 (s, 3H)	22.5	1.03 (3H, s)	22.6	0.76 (3H, s)	19.8
29	1.07 (3H, s)	23.0	0.83 (s, 3H)	22.6	0.83 (3H, s)	22.6	0.72 (3H, s)	22.6
30α	6.29 (d, 2.8)	133.1	3.60 (d, 15.8)	45.1	3.20 (d, 14.1)	44.4	3.25 (d, 14.3)	43.5
30*β*			1.95 (d, 15.8)		1.76 (dd, 14.1, 2.4)		1.75 (brd, 14.3)	
3-OAc		169.9		169.5		169.8		169.8
	2.22 (3H, s)	20.7	2.18 (s, 3H)	20.9	2.18 (3H, s)	21.0	2.19 (3H, s)	21.2
6(11)-		169.6		169.7		169.6		169.6
OAc	2.18 (3H, s)	20.9	2.16 (s, 3H)	21.2	2.18 (3H, s)	21.2	1.97 (3H, s)	21.2
7-OMe	3.74 (3H, s)	53.1	3.76 (s, 3H)	53.3	3.75 (3H, s)	53.2	3.71 (3H, s)	52.3

[a] Recorded at 400 or 100 MHz for ^{1}H and ^{13}C, respectively.

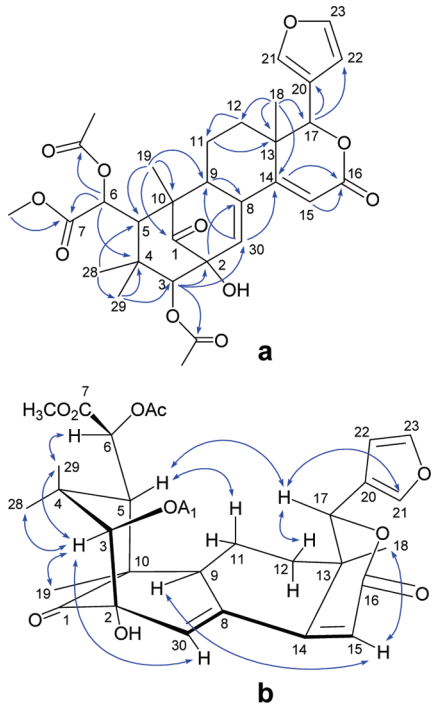

Figure 2. (a) Key HMBC correlations (H→C) of **4**. (b) Selected ROESY correlations (H↔H) of **4**.

Compound **5** had a molecular formula of $C_{31}H_{38}O_{12}$ as assigned by HREIMS. Analysis of ^{1}H and ^{13}C NMR (Table 2) spectra of **5** suggested that its structure was closely related to swietmanin F,[8] with the only difference being the presence of an OAc at C-6, which was confirmed by the HMBC correlations of H-5/C-6 and C-7, and H-6/C-5 and C-7, as well as the correlation between H-6 and the ester carbonyl at δ_C 169.7 of C-6-OAc. The relative configuration of **5** was the same as in swietmanin F in the limonoid core, as established by the ROESY spectrum (Supporting Information, S20). The 6*S*-configuration of **5** was proposed on the same basis as in compound **4**.

Compound **6**, a white, amorphous powder, had the molecular formula $C_{31}H_{38}O_{11}$. Analysis of its ^{1}H and ^{13}C NMR spectra (Table 2) indicated that **6** was a structural analogue of **5**, the only difference being the absence of the 15-OH in **6**. This was verified by two downfield proton signals of CH_2-15 at δ 3.77 (d, 19.8), 3.51 (dt, 19.8, 2.4), which showed HMBC correlations with C-8, C-13, C-14, and C-16. The relative configuration of **6** was tentatively assigned by comparing the NMR data with those of **5**, and the structure of **6** was therefore established as shown.

Compound **7** had the same molecular formula as **6**, as determined by HREIMS. Its ^{1}H and ^{13}C NMR spectra (Table 2) showed many similarities to those of compounds **5** and **6**, suggesting that they were limonoid analogues. An acetoxy group was attached to C-11 of **7**, as indicated by HMBC correlations (Figure 3a) from H-9 and H-12 to C-11 at δ_C 66.9 and especially the HMBC correlation between H-11 and the ester carbonyl (δ_C 169.6) of C-11-OAc. The ROESY correlations (Figure 3b) of H-11/H-5, H-11/H_2-12, and H-11/H-17 showed that H-11 was *β*-oriented.

The IR spectrum of compound **8** ($C_{34}H_{56}O_5$) indicated the presence of OH (3473 cm^{-1}) and carbonyl (1706 cm^{-1}) groups.

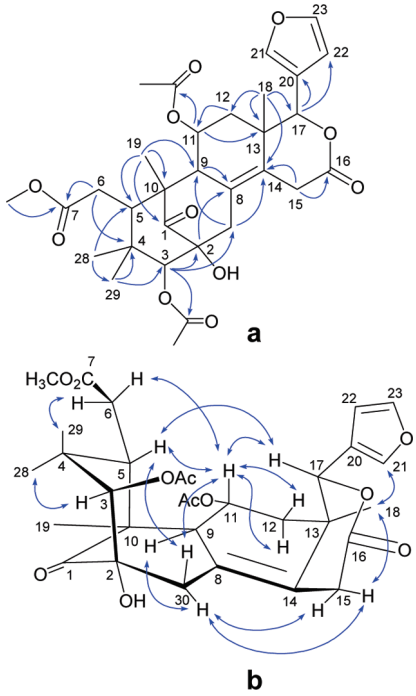

Figure 3. (a) Key HMBC correlations (H→C) of **7**. (b) Selected ROESY correlations (H↔H) of **7**.

The ^{1}H NMR spectrum (Table 3) showed seven tertiary methyl signals (δ_H 0.83, 1.02, 1.25, 1.25, 1.03, 1.12, and 1.05), a *n*-butoxy group, and an olefinic proton resonance at δ_H 5.32. The ^{13}C NMR spectrum (Table 3) showed 34 carbon resonances, which were assigned by DEPT and HSQC experiments as eight methyl, a trisubstituted double bond, 11 methylene, seven sp^3 methine, five sp^3 quaternary carbons, and a keto carbonyl (δ_C 216.8). Comparison of its NMR data with those of toonaciliatin K[10] indicated that they were analogues of tirucallane-type triterpenoids and that the only difference was the C-21 attachment. The *n*-butoxy group was linked to C-21 of **8** by the key HMBC correlation (Figure 4a) between H$_2$-1′ and C-21. The ROESY (Figure 4b) experiment revealed that the relative configuration of the tetracyclic core of **8** was identical to that of toonaciliatin K. The chemical shifts from C-20 to C-27 and coupling constants of protons in the side chain of **8** were highly compatible with those of toonaciliatin K, suggesting that the *n*-butoxy was β-oriented and H-23 and OH-24 were α-oriented, which was verified by the ROESY correlations of H$_3$-18/H-21, H-21/H-12α, H$_3$-18/H-20, and H-20/H-23 (Supporting Information, S31).

Compound **9** had the same molecular formula as **8**. Analysis of NMR spectra (Table 3) showed that **9** was likely the C-21 epimer of **8**. The C-21 carbon resonance of **9** was obviously downfield shifted ($\Delta\delta$ 4.2) as compared to that of **8**, suggesting that the *n*-butoxy at C-21 of **9** was α-oriented. In consequence, the C-17 and C-22 carbon resonances of **9** were also downfield shifted ca. $\Delta\delta$ 4.3 and 3.4, respectively, due largely to the absence of the γ-gauche effects from the *n*-butoxy as compared with **8**.

Compound **10** gave the molecular formula $C_{32}H_{48}O_7$. Its IR spectrum indicated the presence of OH (3554 cm^{-1}) and carbonyl (1704 cm^{-1}) groups. The ^{1}H NMR spectrum (Table 3) indicated the presences of seven tertiary methyl signals (δ_H 1.01, 1.18, 1.27, 1.29, 1.07, 1.07, 1.18), an acetyl (δ_H 2.18, 3H, s), and a *cis*-double bond [δ_H 7.18, (d, J = 10.2 Hz); 5.86, (d, J = 10.2 Hz)]. The ^{13}C NMR with DEPT experiments revealed the presence of eight methyl, a trisubstituted double bond (δ_C 159.0 and 119.0), a disubstituted double bond (δ_C 158.2 and 125.4), five methylene, eight sp^3 methine, and seven quaternary carbons (including two carbonyls). These data suggested that compound **10** was also an apotirucallane-type triterpenoid. Analysis of the NMR data of **10** revealed that its structure was closely related to that of piscidinol G,[11] and the only difference was the presence of an C-7-OAc in **10** instead of C-7-OH in piscidinol G. The structure of **10** was thus established and confirmed by 2D NMR spectra (Supporting Information, S38).

The seven new limonoids (**1**−**7**) were named khayalenoids C−I, and the three new triterpenoids (**8**−**10**) were named senegalenes A−C, respectively. Eight known limonoids were also isolated and were identified as 2,6-dihydroxyfissinolide,[5e] 2-hydroxyfissinolide,[12] 3-*O*-acetylswietenolide,[9] fissinolide,[5e] 3,6-di-*O*-acetylswietenolide,[13] khayanone,[5b] swietmanin F,[8] and swietmanin H,[8] by comparison of their spectroscopic data with those reported.

Experimental Section

General Experimental Procedures. IR spectra were recorded on a Perkin-Elmer 577 spectrometer with a KBr disk. UV spectra were measured on a Shimadzu UV-2550 UV−visible spectrophotometer. Specific rotations were made on a Perkin-Elmer 341 polarimeter at room temperature. NMR spectra were measured on a Bruker AM-400 spectrometer with TMS as internal standard. EIMS (70 eV) and ESIMS were carried out on a Finnigan MAT 95 mass spectrometer and an Esquire 3000plus LC-MS instrument, respectively. Semipreparative HPLC was performed on a Waters 515 pump equipped with a Waters 2487 UV detector (254 nm) and a YMC-Pack ODS-A column (250 × 10 mm, S-5 μm, 12 nm). All solvents used were of analytical grade (Shanghai Chemical Plant, Shanghai, People's Republic of China). Silica gel (300−400 mesh), C18 reverse-phased silica gel (150−200 mesh, Merck), Sephadex LH-20 gel (Amersham Biosciences), and MCI gel (CHP20P, 75−150 μM, Mitsubishi Chemical Industries Ltd.) were used for column chromatography, and precoated silica gel GF254 plates (Qingdao Marine Chemical Plant, Qingdao, People's Republic of China) were used for TLC.

Plant Material. Stems of *K. senegalensis* were collected from Hainan Province of China and were identified by Professor Shi-Man Huang. A voucher specimen has been deposited in the Shanghai Institute of Materia Medica, Chinese Academy of Sciences (accession number: KS-2005-1Y).

Extraction and Isolation. The air-dried powder of *K. senegalensis* plant material (6.0 kg) was extracted with 95% EtOH three times at room temperature (each 10 L), and the crude was partitioned between H$_2$O and EtOAc. The EtOAc-soluble fraction (220 g) was subjected to a column of MCI gel eluted with methanol in water (MeOH/H$_2$O, 30:70 to 90:10) to give five fractions, A−E. Fraction A was separated over a column of silica gel and eluted with CHCl$_3$/MeOH (50:1 to 5:1) to obtain fractions A1−A4. Fraction A1 was chromatographed over silica gel eluted with petroleum ether/acetone (5:1 to 2:1) to give six subfractions, A1a−A1f. Fraction A1c was purified over a column of RP-18 silica gel (MeOH/H$_2$O, 60:40) to give 2-hydroxyfissinolide (35 mg) and 3-*O*-acetylswietenolide (20 mg). Fraction A1d was chromatographed over a column of RP-18 silica gel (MeOH/H$_2$O, 60:40) to afford four fractions, A1d1−A1d4. Fraction A1d2 was purified by silica gel CC eluted with CHCl$_3$/MeOH (40:1) to yield 2,6-dihydroxyfissinolide (22 mg). Fraction A1d3 was separated by semipreparative HPLC (MeOH/H$_2$O, 70:30, 3 mL/min) to obtain **5** (10 mg), swietmanin H (5 mg), and **4** (10 mg). Fraction A2 was subjected to silica gel CC eluted with petroleum ether/EtOAc (2:1 to 1:1) to obtain five fractions, A2a−A2e. Fraction A2a was chromatographed over a column of Sephadex LH-20 eluted with MeOH to give swietmanin F (8 mg). Fraction A2d was purified by a column of RP-18 silica gel eluted with MeOH/H$_2$O (45:55 to 65:35; v/v) to yield khayanone (170 mg), **1** (12 mg), and **2** (8 mg). Fraction C was chromatographed over silica gel eluted with petroleum ether/acetone (8:1 to 1:2; v/v) to give four subfractions, C1−C4. Fraction C1 was separated by semipreparative HPLC (MeOH/H$_2$O, 95:5, 3 mL/min) to give **8** (7 mg), **9** (8 mg), and **10** (20 mg). Fraction C2 was purified by silica gel CC eluted with petroleum ether/EtOAc (3:1) to obtain fissinolide (22 mg). Fraction C3 was separated by semipreparative HPLC (MeOH/H$_2$O, 70:30, 3 mL/min) to give 3,6-di-*O*-acetylswietenolide (8 mg), **3** (10 mg), **6** (10 mg), and **7** (12 mg).

Khayalenoid C (1): white, amorphous powder; $[\alpha]^{20}_D$ −45 (*c* 0.060, CHCl$_3$); IR (KBr) ν_{max} 3444, 2952, 1743, 1238, 1026, 601 cm^{-1}; for

Table 3. ^{1}H and ^{13}C NMR Data of **8**−**10** (in $CDCl_3$)[a]

	8		**9**		**10**	
position	δ_H (mult, *J*, Hz)	δ_C	δ_H (mult, *J*, Hz)	δ_C	δ_H (mult, *J*, Hz)	δ_C
1α	1.46 (m)	38.5	1.45 (m)	38.5	7.18 (d, 10.2)	158.2
1*β*	1.99 (m)		2.00 (m)			
2α	2.24 (dt, 14.5, 3.3)	34.9	2.24 (dt, 14.6, 3.5)	34.9	5.86 (d, 10.2)	125.4
2*β*	2.76 (td, 14.5, 5.6)		2.76 (td, 14.6, 5.5)			
3		216.8		NB		204.6
4		47.9		47.8		44.1
5	1.72 (dd, 9.4, 7.8)	52.4	1.72 (m)	52.4	2.19 (m)	46.2
6	2.10 (2H, m)	24.4	2.10 (2H, m)	24.4	1.95 (m); 1.80 (m)	23.8
7	5.32 (dd, 6.3, 3.0)	118.1	5.32 (dd, 6.3, 3.1)	118.1	5.24 (brs)	74.5
8		145.6		145.6		42.7
9	2.32 (m)	48.3	2.33 (m)	48.3	2.25 (m)	38.4
10		35.1		35.1		40.6
11α	1.59 (m)	17.7	1.58 (m)	17.8	2.00 (m)	16.5
11*β*					1.78 (m)	
12α	1.56 (m)	31.7	1.50 (m)	31.7	1.71 (m)	33.5
12*β*	1.93 (m)		1.75 (m)		1.90 (m)	
13		43.4		43.7		46.3
14		50.7		51.0		159.0
15	1.53 (2H, m)	34.2	1.53 (2H, m)	33.8	5.29 (d, 2.6)	119.0
16α	1.34 (m)	27.2	1.36 (m)	27.5	2.13 (m)	35.1
16*β*	1.88 (m)		1.95 (m)		2.02 (m)	
17	1.97 (m)	46.1	1.98 (m)	50.4	1.97 (m)	52.9
18	0.83 (3H, s)	23.2	0.86 (3H, s)	22.6	1.01 (3H, s)	20.5
19	1.02 (3H, s)	12.7	1.01 (3H, s)	12.7	1.18 (3H, s)	18.9
20	2.08 (m)	44.8	2.18 (m)	47.8	2.15 (m)	44.9
21	4.78 (d, 3.0)	103.6	4.87 (d, 3.5)	107.8	5.31 (d, 3.7)	96.8
22	1.90 (2H, m)	31.0	1.95 (m); 1.75 (m)	34.4	2.01 (m); 1.90 (m)	30.0
23	4.40 (m)	78.6	4.23 (ddd, 10.4, 4.7, 1.5)	76.6	4.51 (t, 8.0)	78.6
24	3.17 (brs)	76.7	3.24 (brs)	75.5	3.17 (brs)	74.9
25		72.9		73.1		73.6
26	1.25 (3H, s)	26.3	1.28 (3H, s)	26.4	1.27 (3H, s)	26.7
27	1.25 (3H, s)	26.2	1.26 (3H, s)	26.4	1.29 (3H, s)	26.8
28	1.03 (3H, s)	24.5	1.01 (3H, s)	24.5	1.07 (3H, s)	21.3
29	1.12 (3H, s)	21.5	1.12 (3H, s)	21.5	1.07 (3H, s)	27.0
30	1.05 (3H, s)	27.4	1.04 (3H, s)	27.3	1.18 (3H, s)	27.3
21-(*n*-butoxyl)					7-OAc	
1′	3.68 (m); 3.31 (m)	67.9	3.62 (m); 3.35 (m)	68.2		170.1
2′	1.34 (2H, m)	31.8	1.35 (2H, m)	32.0	1.90 (3H, s)	21.1
3′	1.38 (2H, m)	19.4	1.38 (2H, m)	19.4		
4′	0.93 (t, 7.3)	13.9	0.92 (t, 7.3)	13.8		

[a] Recorded at 400 or 100 MHz for ^{1}H and ^{13}C, respectively; NB: not observed.

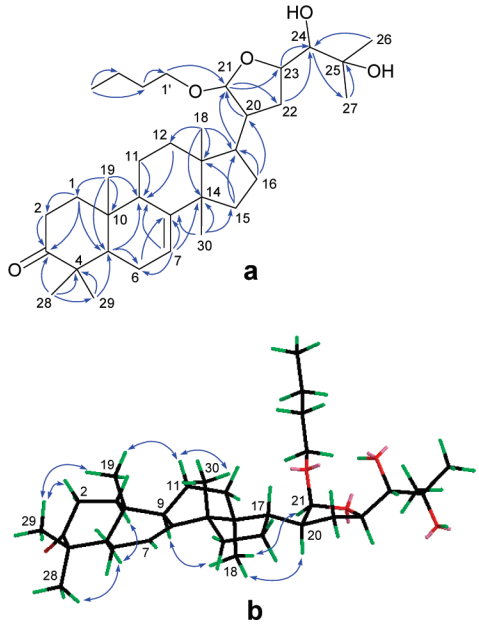

Figure 4. (a) Key HMBC correlations (H→C) of **8**. (b) Selected ROESY correlations (H↔H) of **8**.

^{1}H NMR and ^{13}C NMR data, see Table 1; ESIMS *m/z* 583.3 [M + Na]$^+$, 1143.5 [2 M + Na]$^+$, 605.3 [M + HCOO]$^-$; HREIMS *m/z* 560.2240 [M]$^+$ (calcd for $C_{29}H_{36}O_{11}$ 560.2258).

Khayalenoid D (2): white, amorphous powder; $[\alpha]^{20}_D$ −25 (*c* 0.105, $CHCl_3$); IR (KBr) ν_{max} 3446, 2950, 1739, 1234, 1028, 601 cm^{-1}; for ^{1}H NMR and ^{13}C NMR data, see Table 1; ESIMS *m/z* 567.3 [M + Na]$^+$, 1111.5 [2 M + Na]$^+$, 589.8 [M + HCOO]$^-$, 1087.8 [2 M − H]$^-$; EIMS *m/z* 544 [M]$^+$ (56), 484 (23), 409 (27), 395 (15), 375 (27), 183 (26), 134 (41), 95 (100); HREIMS *m/z* 544.2303 [M]$^+$ (calcd for $C_{29}H_{36}O_{10}$ 544.2308).

Khayalenoid E (3): white, amorphous powder; $[\alpha]^{20}_D$ −551 (*c* 0.100, $CHCl_3$); IR (KBr) ν_{max} 3438, 2971, 2950, 1739, 1386, 1292, 1218, 1035, 603 cm^{-1}; for ^{1}H NMR and ^{13}C NMR data, see Table 1; ESIMS *m/z* 549.2 [M + Na]$^+$, 1075.5 [2 M + Na]$^+$, 525.6 [M − H]$^-$; EIMS *m/z* 526 [M]$^+$ (43), 484 (76), 425 (8), 313 (11), 253 (53), 175 (22), 134 (100), 95 (67); HREIMS *m/z* 526.2186 [M]$^+$ (calcd for $C_{29}H_{34}O_9$ 526.2203).

Khayalenoid F (4): white, amorphous powder; $[\alpha]^{20}_D$ +720 (*c* 0.150, $CHCl_3$); IR (KBr) ν_{max} 3459, 2952, 1739, 1222, 1029, 759 cm^{-1}; for ^{1}H NMR and ^{13}C NMR data, see Table 2; ESIMS *m/z* 585.3 [M + H]$^+$, 1191.5 [2 M + Na]$^+$, 629.2 [M + HCOO]$^-$; EIMS *m/z* 584 [M]$^+$ (65), 542 (19), 496 (18), 327 (66), 271 (26), 254 (100), 183 (27), 147 (100), 95 (25); HREIMS *m/z* 584.2255 [M]$^+$ (calcd. for $C_{31}H_{36}O_{11}$ 584.2258).

Khayalenoid G (5): white, amorphous powder; $[\alpha]^{20}_D$ −85 (*c* 0.060, $CHCl_3$); IR (KBr) ν_{max} 3463, 2954, 1735, 1217, 1024, 756 cm^{-1}; for ^{1}H NMR and ^{13}C NMR data, see Table 2; ESIMS *m/z* 603.3 [M + H]$^+$, 1227.7 [2 M + Na]$^+$, 601.3 [M − H]$^-$; EIMS *m/z* 602 [M]$^+$ (6), 524 (8), 460 (41), 418 (28), 343 (88), 287 (70), 269 (100), 223 (86), 195 (54), 135 (74), 95 (59); HREIMS *m/z* 602.2351 [M]$^+$ (calcd for $C_{31}H_{38}O_{12}$ 602.2363).

Khayalenoid H (6): white, amorphous powder; $[\alpha]^{20}_D$ −209 (*c* 0.175, $CHCl_3$); IR (KBr) ν_{max} 3450, 2952, 1741, 1220, 1026 cm^{-1}; for ^{1}H NMR and ^{13}C NMR data, see Table 2; EIMS *m/z* 586 [M]$^+$ (5),

568 (5), 490 (100), 462 (57), 430 (41), 402 (24), 342 (15), 247 (29), 223 (41), 189 (38), 95 (22); HREIMS *m/z* 586.2428 $[M]^+$ (calcd for $C_{31}H_{38}O_{12}$ 586.2414).

Khayalenoid I (7): white, amorphous powder; $[\alpha]^{20}_D$ −113 (*c* 0.100, $CHCl_3$); IR (KBr) ν_{max} 3446, 2971, 1733, 1238, 1026 cm^{-1}; for ^1H NMR and ^{13}C NMR data, see Table 2; EIMS *m/z* 586 $[M]^+$ (1), 568 (1), 490 (40), 402 (9), 370 (28), 342 (100), 324 (42), 196 (28), 118 (18), 95 (16); HREIMS *m/z* 586.2397 $[M]^+$ (calcd. for $C_{31}H_{38}O_{12}$ 586.2414).

Senegalene A (8): white, amorphous powder; $[\alpha]^{20}_D$ 0 (*c* 0.100, $CHCl_3$); IR (KBr) ν_{max} 3473, 3357, 2950, 2919, 2860, 1706, 1386, 1132, 1031 cm^{-1}; for ^1H NMR and ^{13}C NMR data, see Table 3; ESIMS *m/z* 567.4 $[M + Na]^+$; EIMS *m/z* 544 $[M]^+$ (0.1), 468 (53), 455 (100), 412 (53), 397 (27), 365 (26), 297 (31), 126 (30), 95 (15); HREIMS *m/z* 544.4133 $[M]^+$ (calcd. for $C_{34}H_{56}O_5$ 544.4128).

Senegalene B (9): white, amorphous powder; $[\alpha]^{20}_D$ −155 (*c* 0.100, $CHCl_3$); IR (KBr) ν_{max} 3554, 3515, 2968, 2869, 1704, 1386, 1107, 977 cm^{-1}; for ^1H NMR and ^{13}C NMR data, see Table 3; ESIMS *m/z* 567.5 $[M + Na]^+$, 1111.9 $[2\ M + Na]^+$; EIMS *m/z* 544 $[M]^+$ (0.2), 468 (18), 455 (100), 412 (18), 383 (25), 365 (25), 297 (19), 126 (14), 95 (8); HREIMS *m/z* 544.4145 $[M]^+$ (calcd. for $C_{34}H_{56}O_5$ 544.4128).

Senegalene C (10): white, amorphous powder; $[\alpha]^{20}_D$ −26 (*c* 0.100, $CHCl_3$); IR (KBr) ν_{max} 3434, 2973, 2937, 1733, 1670, 1380, 1249, 1029, 754 cm^{-1}; for ^1H NMR and ^{13}C NMR data, see Table 3; EIMS *m/z* 526 $[M - H_2O]^+$ (42), 466 (19), 451 (14), 368 (100), 308 (46), 293 (19), 150 (36), 93 (18); HREIMS *m/z* 526.3287 $[M - H_2O]^+$ (calcd for $C_{32}H_{46}O_6$ 526.3294).

Acknowledgment. Financial support from the Key Project of National Natural Science Foundation (Grant No. 30630072; 30721005) and National Science & Technology Major Project "Key New Drug Creation and Manufacturing Program" (Grant No. 2009ZX09301-001) of the People's Republic of China is gratefully acknowledged. We thank Prof. S.-M. Huang of Department of Biology, Hainan University, for the identification of this plant material.

Supporting Information Available: IR, MS, $^1H/^{13}C$ NMR, and 2D NMR spectra of compounds **1**−**10** are available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Brandt, G. E. L.; Schmidt, M. D.; Prisinzano, T. E.; Blagg, B. S. J. *J. Med. Chem.* **2008**, *51*, 6495–6502. (b) Roy, A.; Saraf, S. *Biol. Pharm. Bull.* **2006**, *29*, 191–201. (c) Mulholland, D. A.; Parel, B.; Coombes, P. H. *Curr. Org. Chem* **2000**, *4*, 1011–1054. (d) Champagne, D. E.; Koul, O.; Isman, M. B.; Scudder, G. G. E.; Towers, G. H. N. *Phytochemistry* **1992**, *31*, 377–394. (e) Akhila, A.; Rani, K. In *Progress in the Chemistry of Organic Natural Products*; Herz, W., Falk, H., Kirby, G. W., Moore, R. E., Eds.; Springer: Vienna, 1999; Vol. 78, pp 47−149. (f) Corey, E. J.; Reid, J. G.; Myers, A. G.; Hahl, R. W. *J. Am. Chem. Soc.* **1987**, *109*, 918–919.

(2) Adesida, G. A.; Adesogan, E. K.; Okorie, D. A.; Taylor, D. A. H.; Styles, B. T. *Phytochemistry* **1971**, *10*, 1845–1853.

(3) Chen, S. K., Chen, B. Y., Li, H. *The Flora Reipublicae Popularis Sinicae (Zhongguo Zhiwu Zhi)*; Science Press: Beijing, 1997; Vol. 43 (3), p 46.

(4) Dalziel, J. M. *The Useful Plants of West Tropical Africa*; The Crown Agents For The Colonies: London, 1937; p 325.

(5) (a) Nakatani, M.; Abdelgaleil, S. A. M.; Kassem, S. M. I.; Takezaki, K.; Okamura, H.; Iwagawa, T.; Doe, M. *J. Nat. Prod.* **2002**, *65*, 1219–1221. (b) Nakatani, M.; Abdelgaleil, S. A. M.; Kurawaki, J.; Okamura, H.; Iwagawa, T.; Doe, M. *J. Nat. Prod.* **2001**, *64*, 1261–1265. (c) Abdelgaleil, S. A. M.; Okamura, H.; Iwagawa, T.; Sato, A.; Miyahara, I.; Doe, M.; Nakatani, M. *Tetrahedron* **2001**, *57*, 119–126. (d) Nakatani, M.; Abdelgaleil, S. A. M.; Okamura, H.; Iwagawa, T.; Sato, A.; Doe, M. *Tetrahedron Lett.* **2000**, *41*, 6473–6477. (e) Khalid, S. A.; Friedrichsen, G. M.; Kharazmi, A.; Theander, T. G.; Olsen, C. E.; Christensen, S. B. *Phytochemistry* **1998**, *49*, 1769–1772. (f) Govindachari, T. R.; Krishna kumari, G. N. *Phytochemistry* **1998**, *47*, 1423–1425. (g) Olmo, L. R. V.; Silva, M. F.; das G. F. da, Rodrigues; Fo., E.; Vieira, P. C.; Fernandes, J. B.; Pinheiro, A. L.; Vilela, E. F. *Phytochemistry* **1997**, *44*, 1157–1161. (h) Olmo, L. R. V.; Silva, M. F.; das G. F. da Rodrigues Fo., E.; Vieira, P. C.; Fernandes, J. B.; Marsaioli, A. J.; Pinheiro, A. L.; Vilela, E. F. *Phytochemistry* **1996**, *42*, 831–837.

(6) (a) Abdelgaleil, S. A. M.; Iwagawa, T.; Doe, M.; Nakatani, M. *Fitoterapia* **2004**, *75*, 566–572. (b) Abdelgaleil, S. A. M.; Hashinaga, F.; Nakatani, M. *Pest Manag. Sci.* **2005**, *61*, 186–190. (c) Roy, A.; Saraf, S. *Biol. Pharm. Bull.* **2006**, *29*, 191–201.

(7) Yuan, T.; Yang, S. P.; Zhang, C. R.; Zhang, S.; Yue, J. M. *Org. Lett.* **2009**, *11*, 617–620.

(8) Lin, B. D.; Yuan, T.; Zhang, C. R.; Dong, L.; Zhang, B.; Wu, Y.; Yue, J. M. *J. Nat. Prod.* **2009**, *72*, 2084–2090.

(9) Kadota, S.; Marpaung, L.; Kikuchi, T.; Ekimoto, H. *Chem. Pharm. Bull.* **1990**, *38*, 639–651.

(10) Chen, H. D.; Yang, S. P.; Wu, Y.; Dong, L.; Yue, J. M. *J. Nat. Prod.* **2009**, *72*, 685–689.

(11) Balakrishna, K.; Sukumar, E.; Connolly, J. D. *Nat. Prod. Sci.* **2003**, *9*, 192–194.

(12) Mulholland, D. A.; Taylor, D. A. H. *Phytochemistry* **1992**, *31*, 4163–4166.

(13) Mootoo, B. S.; Ali, A.; Motilal, R.; Pingal, R.; Ramlal, A.; Khan, A.; Reynolds, W. F.; McLean, S. *J. Nat. Prod.* **1999**, *62*, 1514–1517.

NP1000158