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3,7-DIDEACETYL-6α-HYDROXYKHIVORIN, A NEW LIMONOID FROM *KHAYA SENEGALENSIS (*MELIACEAE)

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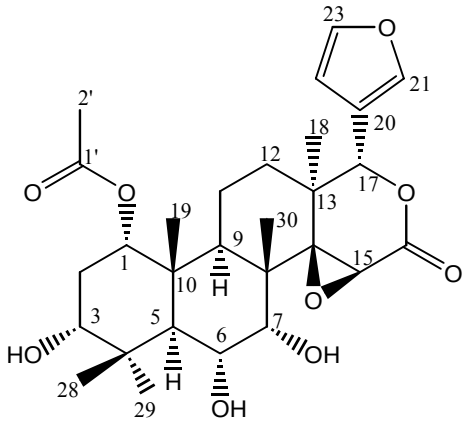
ABSTRACT. A new limonoid, 3,7-dideacetyl-6α-hydroxykhivorin, together with khivorin, 3-deacetylkhivorin, 7-deacetoxy-3-deacetyl-7-oxokhivorin, and 6-deoxydestigloylswietenine acetate have been isolated from the seeds of *Khaya senegalensis*. Their structures were established by analysis of the high-field NMR and MS data.

KEYWORDS: *Khaya senegalensis,* Limonoids, 3,7-Dideacetyl-6α-hydroxykhivorin, 7-Deacetoxy-3-deacetyl-7-oxokhivorin, 3-Deacetylkhivorin, 6-Deoxydestigloylswietenine acetate

INTRODUCTION

Khaya senegalensis (Desr.) A. Juss. is a large tree native to the sub-Saharan savannah from Senegal to Uganda and a source of popular traditional medicine in Africa [1]. The decoction of the stem bark is extensively used as a febrifuge, which could be associated with its use as an antimalarial drug [2]. In continuation of our investigations on Cameroonian medicinal plants [3], we have isolated from the seed of *Khaya senegalensis* a new tetranortriterpenoid, 3,7-dideacetyl-6α-hydroxykhivorin (**1**), together with khivorin (**2**) [4], 3-deacetylkhivorin (**3**) [5], 7-deacetoxy-3-deacetyl-7-oxokhivorin (**4**) [6], and 6-deoxydestigloylswietenine acetate (**5**) [7].



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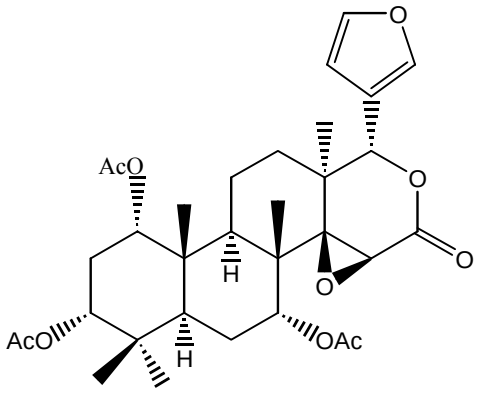

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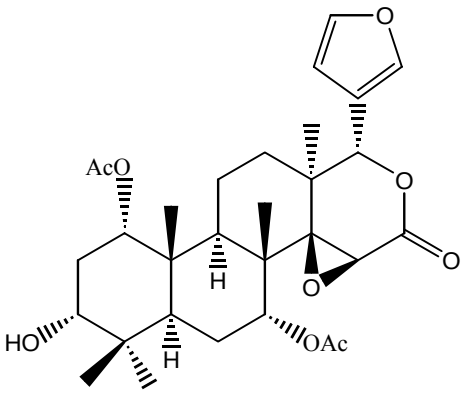

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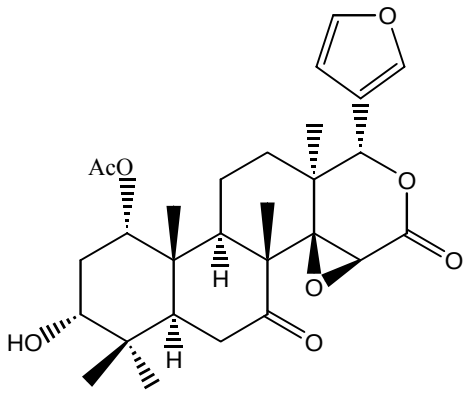

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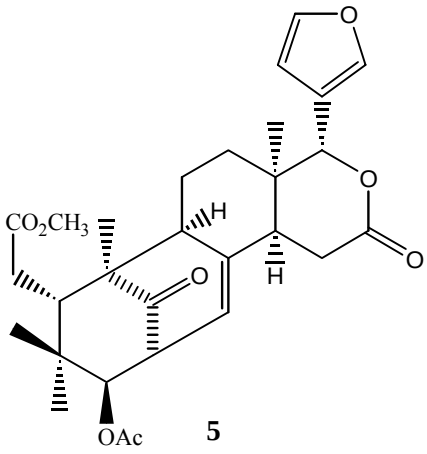

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RESULTS AND DISCUSSION

Compound **1** was obtained from hexane:EtOAc (9:1) as colourless crystals, m.p. 144-145 °C, $[\alpha]_D^{22}$ + 9° (*c* 0.19, $CHCl_3$). The molecular formula $C_{28}H_{38}O_9$ was deduced from its ^{13}C NMR spectra and HRESIMS (*m/z* 519.3671 $[M + H]^+$). Its IR spectrum showed absorption bands at ν_{max} 3436 cm^{-1} (sharp), 1729 cm^{-1} and 875 cm^{-1}, characteristic of hydroxyl, carbonyl and furan moieties [8], respectively. The ^{13}C NMR (Table 1) and associated DEPT spectra of **1** revealed twenty-eight carbons signals, comprising six methyl, three methylene, eleven methine (including six oxygenated and three olefinic carbons) and eight fully substituted carbon signals (including three oxygenated and one olefinic). The ^1H NMR spectrum showed signals characteristic of a furan ring at δ 6.32 (1H, d, *J* = 0.5 Hz), 7.39 (2H, br s). Further examination of the ^1H and ^{13}C NMR spectra confirmed the presence of a β-substituted furan ring and suggested a khivorin skeleton [9]. This was evident in the HMBC spectrum where correlations were observed between the signals of H-15 (3.88, s) and C-16 (168.1 C), whereas the H-17 (5.58, s) resonance was correlated with those of C-13 (38.9, C), and C-14 (69.8, C) indicating the 14,15-

epoxylactone-substitution pattern of khivorin derivatives. The ^{1}H NMR data of **1** were very similar to those reported for 3,7-dideacetylkhivorin [10] except for the presence of an additional hydroxy group [δ 4.11, dd, *J* = 10.9, 4.2; 69.6 (CH)].

A strongly coupled system observed in the ^{1}H NMR and COSY spectra, comprising H-9 (δ 2.79, dd, *J* = 12.5, 5.7 Hz), 2H-11 (δ 1.28/1.56, m) and 2H-12 (δ 1.40/1.67, m), excluded any substitution at these positions. Correlations in the COSY spectrum to both H-5 (δ 2.38, d, *J* = 10.9) and H-7 (δ 3.35 br s), suggested that the additional group be placed at position 6. The complete analysis of COSY, HMQC, and HMBC spectra confirmed structure **1** as a new limonoid derivative, 3,7-dideacetyl-6α-hydroxykhivorin.

The relative stereochemistry at C-1, C-3, C-7 and C-17 and the ring junctions were assumed from biogenetic analogy with **2**. The NOESY data (Figure 1) is consistent with these assignments and also confirms the stereochemistry of the new hydroxy group at C-6 as α.

Table 1. NMR spectra data of compound **1** ($CDCl_3$, δ in ppm).

No C	δ C	δ H	HMBC (H → C)
1	74.4, CH	4.74, t (3.2)	C-1’
2	28.3, CH_2	2.28, dt (15.9, 3.2)	C-3, C-5
		1.93, dt (15.9, 3.2)	
3	77.2, CH	3.36, br s	
4	38.0, C		
5	40.9, CH	2.38, d (10.9)	C-6, C-8, C-9
6	69.6, CH	4.11, dd (10.9, 4.2)	
7	75.9, CH	3.35, br s	C-5, C-6, C-8, C-9, C-14, C-30
8	43.2, C		
9	35.0, CH	2.79, dd (2.5, 5.7)	C-10, C-11
10	42.0, C		
11	14.8, CH_2	1.28, m	
		1.56, m	
12	26.7, CH_2	1.40, m	
		1.67, m	
13	38.9, C		
14	69.8, C		
15	57.2, C	3.88, s	C-14, C-16
16	168.1, C		
17	78.7, CH	5.58, s	C-12, C-13, C-14, C-18
18	17.7, CH_3	1.23, s	C-13, C-17
19	17.9, CH_3	1.01, s	C-5, C-9, C-10
20	120.8, C		
21	143.0, CH	7.39, br s	
22	110.0, CH	6.32, d (0.5)	
23	141.1, CH	7.39, br s	C-20, C-22
28	22.5, CH_3	1.06, s	C-29, C-4
29	31.4, CH_3	1.30, s	C-4, C-5, C-28
30	18.8, CH_3	1.04, s	
1’	169.6, C		
2’	21.4, CH_3	2.06, s	

NMR spectra were acquired on a BRUKER DPX-500 spectrometer in $CDCl_3$, 500 MHz for ^{1}H and 125 MHz for ^{13}C.

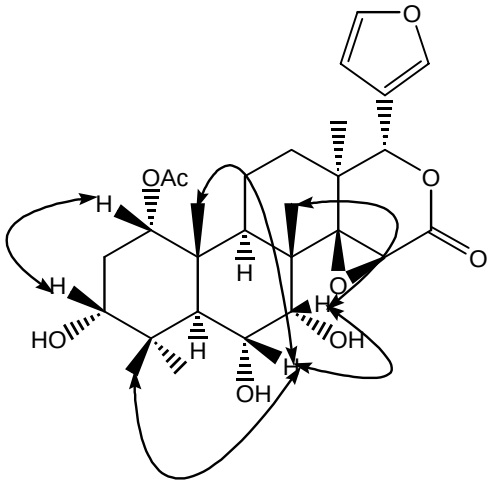

Figure 1. Significant NOESY correlations of **1**.

EXPERIMENTAL

General. Melting points were recorded with a Reichert microscope and are uncorrected. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) were recorded in $CDCl_3$, using a Bruker ARX500 spectrometer with an inverse 5 mm probe equipped with a shielded gradient coil. The solvent signals (7.26 and 77.0 ppm, respectively) were used as reference, while the coupling constants (J) are given in Hz. COSY, HMQC, and HMBC experiments were performed with gradient enhancements using shaped gradient pulses, and for the 2D heteronuclear correlation spectroscopy the refocusing delays were optimized for $^{1}J_{CH}$ = 145 Hz and $^{2}J_{CH}$ = 10 Hz. The raw data were transformed and the spectra were evaluated with the standard Bruker UXNMR software (re.941001). ESIMS were recorded by Bruker Biopex FTMS. Column chromatography was carried out using Merck silica gel $60F_{254}$ (230-400 mesh) and TLC on silica gel GF-254 precoated plates. Detection was accomplished by spraying with 50 % H_2SO_4 followed by heating.

Plant material. The seeds of *Khaya senegalensis* (Desr.) A. Juss. were collected in Ngaoundere, Adamaoua province of Cameroon, in June 2001. Mezili Paul, a botanist, identified the plant material. Voucher specimen PM0102/01 is deposited at the University of Dschang, Cameroon**.**

Extraction and isolation. The air-dried and powdered plant material (4 kg) was macerated in a mixture of CH_2Cl_2-MeOH (1:1) for 24 h. Removal of the solvent *in vacuo* in a rotary evaporator provided an organic extract (200 g). The resultant extract was then subjected to open column chromatography using hexane-EtOAc mixtures as eluent. Fractions of 500 mL were collected and regrouped on the basis of their TLC profiles. The combined fractions eluted with hexane-EtOAc (4:6) (500 mg) revealed the presence of at least three limonoids (Ehrlich's reagent). Further purification of this fraction by column chromatography with a gradient of acetone in CH_2Cl_2 afforded 3,7-dideacetyl-6α-hydroxykhivorin (**1**) (20 mg), 7-deacetoxy-3-dideacetyl-7-oxokhivorin (**4**) (30 mg) and 3-deacetylkhivorin (**3**) (100 mg). The combined fractions eluted with hexane-EtOAc (6:4) (1 g) were further purified by repeated column chromatography to yield khivorin (**2**) (200 mg) and 6-deoxydestigloylswietenine acetate (**5**) (90 mg).

3,7-Dideacetyl-6α-hydroxykhivorin (**1**). Colourless crystals; m.p. 144-145 °C; $[\alpha]_D^{22}$ + 9° (*c* 0.19, $CHCl_3$); IR ν_{max} (cm^{-1}) 3436, 1729, 875; ^1H and ^{13}C NMR see Table1. HRESIMS *m/z:* 519.3671$[M + H]^+$ (calcd. for $[C_{28}H_{38}O_9H]^+$ 519.3673).

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