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TETRANORTRITERPENOIDS FROM *KHAYA SENEGALENSIS*

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Key Word Index—*Khaya senegalensis*; Meliaceae; Tetranortriterpenoids; Mexicanolide; Khivorin; Prep. HPLC.

Abstract—Preparative HPLC of an ethanol extract of seeds of *Khaya senegalensis* yielded three new tetranortriterpenoids of the mexicanolide type. These compounds were identified as 2-hydroxymexicanolide, 6-deoxydestigloylswietenine and 2,3-dihydroxy-3-deoxymexicanolide. In addition, mexicanolide, 3β-hydroxy-3-deoxymexicanolide, 3β-hydroxy-3-deoxycarapin, 6-hydroxy methyl angolensate, 3-acetyl-7-keto khivorin, 3-deacetyl khivorin and 3,7-dideacetyl khivorin were also isolated. © 1998 Elsevier Science Ltd. All rights reserved

INTRODUCTION

Taylor and co-workers[1, 2] have investigated extensively the genus *Khaya* A. Juss (Meliaceae) which is the main source of African mahagony. Three structural types of tetranortriterpenoids are encountered in this genus: khivorin, a D-seco compound, mexicanolide and methyl angolensate which are B-seco compounds. From *K. senegalensis*, the most distinctive species of the genus *Khaya*, fifteen compounds belonging to the above mentioned types have been isolated from various parts of the tree [3]. In a recent publication [4] three new tetranortriterpenoids were reported which are again mexicanolide derivatives.

Extensive biological work has been carried out on C-seco-tetranortriterpenoids of the type of azadirachtin [5, 6] but, very little work has been done on B-seco-tetranortriterpenoids. It was found that nymania-3, a B-seco compound [7] isolated in this laboratory [8] from *Dysoxylum malabaricum* was a very potent insect antifeedant. Since *K. senegalensis* is a good source of B-seco compounds, it was decided to isolate various compounds present in this source and examine their biological activities. Mexicanolide was the principal compound isolated from the 30–40% hexane–ethyl acetate eluent in VLC (0.6%). The more polar compounds isolated from the ethyl acetate eluate were conveniently separated by prep. HPLC. Nine compounds were isolated of which three were new [9].

RESULTS AND DISCUSSION

The three new compounds were assigned structures on the basis of extensive spectral analysis. Compound **1**, $C_{27}H_{32}O_8$ (HRMS), showed IR peaks at 3688, 3566 cm^{-1} (OH), 1732 cm^{-1} (CO) and 875 cm^{-1} (furan). The ^1H NMR spectrum (Table 1) indicated four tertiary methyls (δ 0.85, 1.0, 1.3), a β-substituted furan ring (δ 7.6, 7.43 and 6.51) and a carbomethoxy group (δ 3.75, *s*, 3H). The ^{13}C NMR spectrum (Table 2) showed the presence of two six membered ketones (δ 212.8, 209.6) and a tetra substituted double bond (δ 135.3 *s* and 123.6 *s*). A study of the NMR data of compound **1** indicated a mexicanolide skeleton. The ^{13}C NMR spectrum of compound **1** showed only two CH signals (DEPT 90) in the δ 40–60 region in comparison to mexicanolide. The presence of a singlet at δ 80.3 indicated that one of the CHs in mexicanolide was replaced by —C—OH which was in agreement with the HRMS data. In the ^1H NMR spectrum, the two protons at C-30 appeared as geminally coupled doublets at δ 2.12 and 3.35 (J = 13.3 Hz) showing the absence of a proton at C-2. Consequently the hydroxyl was placed at position C-2 and this was supported by the downfield shift of the β-carbon at C-30 compared to mexicanolide. Hence compound **1** was assigned the structure, 2α-hydroxymexicanolide.

The NMR data of compound **2** also showed a similar skeleton. The ^1H NMR spectrum showed a sharp singlet at δ 3.64 (*s*, 1H) for a C*H*OH which was connected to a carbon at δ 85.5 (*d*) in the HETCOR spectrum. This indicated the presence of a secondary hydroxyl group. This suggested the replacement of a keto group by a hydroxyl group either at C-1 or C-3. The placement of the hydroxyl group at position C-3 was confirmed by COLOC. C-3 showed $^3J_{CH}$ correlation to the gem dimethyl protons at C-4. C-1 at δ 219 showed correlation to the 19-Me. Thus compound **2** was assigned the structure 2α,3β-dihydroxy-3-

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Table 1. ^{1}H NMR spectral data of compounds **1**, **2** and **3** (200 MHz, δ values in $CDCl_3$)

H	1	2	3
2	—	—	3.42 *m*
3		3.64 *s*	3.80*d*(*J* = 9.3 Hz)
5	2.8 *m*	3.16 *dd*(*J* = 3.9, 9.4 Hz)	3.31 *m*
6	2.5 *m*, 2H	2.36 *m*	2.40 *m*
9	2.12 *m*	1.96 *m*	2.21 *m*
11	1.8 *m*	1.81 *m*	1.75 *m*
12	1.8 *m*	1.1 *m*	1.75 *m*
	1.3 *m*	1.05 *m*	1.48 *m*
14	—	—	2.28 *m*
15	3.5 *m*	4.13*d*(*J* = 21.1 Hz)	2.94 *m*
		3.48*d*(*J* = 21.1 Hz)	
17	5.25 *s*	5.59 *s*	5.74 *s*
21	7.60 *s*	7.57 *s*	7.76 *s*
22	6.51 *s*	6.50*d*(*J* = 1.5 Hz)	6.48 *s*
23	7.43*d*(*J* = 1.6 Hz)	7.41*d*(*J* = 1.5 Hz)	7.43*d*(*J* = 1.6 Hz)
30	3.3*d*(*J* = 13.3 Hz)	3.48*d*(*J* = 13.7 Hz)	5.72*d*(*J* = 7.5 Hz)
	2.12*d*(*J* = 13.3 Hz)	1.64*d*(*J* = 13.7 Hz)	
18Me	1.00 *s*	1.05 *s*	1.11 *s*
19Me	1.00 *s*	1.24 *s*	1.15 *s*
28Me	0.85 *s*	0.68 *s*	0.84 *s*
29Me	1.30 *s*	0.83 *s*	0.76 *s*
COOMe	3.75 *s*	3.71 *s*	3.72 *s*

Table 2. ^{13}C NMR spectral data of mexicanolide, compounds **1**, **2** and **3*** (50 MHz. δ values in $CDCl_3$)

	Mexicanolide	1	2	3
C-1	212.8	212.8	219.2	218.3
C-2	57.9	80.3	79.6	51.2
C-3	210.8	209.6	85.5	76.3
C-4	49.3	49.2	39.5	39.7
C-5	40.1	40.1	39.4	40.5
C-6	32.1	32.2	33.2	33.1
C-7	173.5	173.6	174.9	174.2
C-8	133.7	135.3	132.7	138.6
C-9	50.4	50.2	51.4	56.7
C-10	54.2	52.9	52.5	50.1
C-11	18.4	18.5	18.6	20.8
C-12	28.6	28.7	28.4	29.2
C-13	37.9	38.1	38.0	36.8
C-14	125.2	123.6	125.7	45.3
C-15	32.8	32.8	35.3	34.4
C-16	169.7	169.8	171.4	169.9
C-17	80.5	80.7	80.1	77.1
C-18	17.4	17.4	17.4	21.9
C-19	17.9	21.9	16.8	15.6
C-20	120.6	120.4	120.6	120.6
C-21	142.6	141.6	141.6	141.9
C-22	109.8	109.9	110.0	109.6
C-23	141.4	142.8	142.5	142.8
C-28	17.9	17.9	23.6	22.4
C-29	21.9	17.8	19.6	20.5
C-30	36.2	44.2	43.9	123.3
$COOCH_3$	52.0	52.8	52.0	52.2

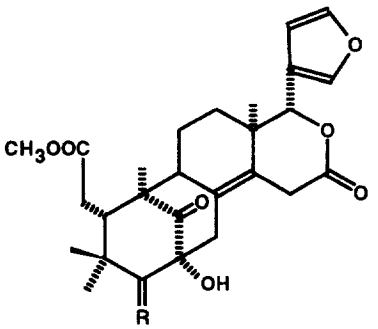
* Assignments were supported by DEPT experiments.

deoxymexicanolide. The 3-acetate of this compound was previously reported from *K. ivorensis* [10].

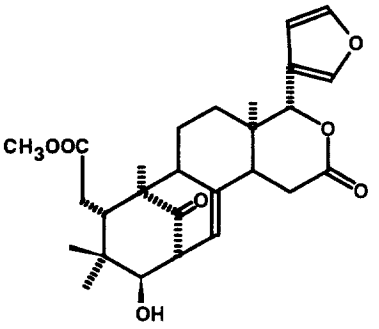
Compound **3** also showed the mexicanolide skeleton but with only one keto group in a six membered ring. The ^{13}C NMR spectrum showed a trisubstituted double bond (δ 136.6 *s* and 123.3 *d*). This was also supported by the presence of an olefinic proton at δ 5.72 (*d*, *J* = 7.5 Hz) in the 1H NMR spectrum. The *J* value suggested a double bond between C-8 and C-30. Thus compound **3** was tentatively given the structure 6-deoxydestigloylswietenine. The 3-tiglate of this compound was previously reported from *Soymida febrifuga* [11].

EXPERIMENTAL

Dried fruits of *Khaya senegalensis* were collected and identified by Dr D. B. Gude (Geneticist, Forest Research Centre, Wada, Pune) and a voucher specimen was deposited by him in the herbarium of Forest Research Centre, Pune, Maharashtra. Dried seeds (1.015 kg) were powdered and extracted with *n*-hexane at room temp. The defatted seed powder was then extracted with EtOH and the residue (74.2 g) after removal of the solvent was suspended in H_2O and extracted with EtOAc. The EtOAc fr after removal of solvent (50 g) was adsorbed on 100 g of 60–120 silica gel and applied to a column of 400 g silica gel (200–400) and eluted rapidly with 10–100% EtOAc in hexane. The frs from 30 and 40% EtOAc in hexane eluate gave a solid which was identified as mexican-



1 R = O
2 R = H, β OH



3

olide. The frs from 50% EtOAc and EtOAc eluent are similar on HPLC except for the variable amounts.

The residue from EtOAc fraction (10.5 g) was subjected to prep. HPLC using MeOH–H_2O (60–40) as eluent in a Shimpack reverse phase prep. column 25 cm × 4.6 mm with a flow rate of 10 ml min^{-1}. Details of the prep. HPLC procedure are presented in another communication [9]. In all, nine compounds were isolated in pure form out of which three were new.

Compound **1**. Yield: 150mg, mp 212°; $[\alpha]_D$ −64° (MeOH; *c* 0.5). UV λ_{max} nm (log ε): 230 (3.27), 280 2.62). IR ν_{max} cm^{-1}: 3688, 3566, 1732, 875. ^1H NMR and ^{13}C NMR: Tables 1 and 2. HRMS $C_{27}H_{32}O_8$ 484.213195 (obs) 484.209718 (cal).

Compound **2**. Yield: 100 mg mp 120° $[\alpha]_D$ +79.54° (MeOH; *c* 0.088). UV λ_{max} nm (log ε): 224 (3.07), 280 (2.82). IR ν_{max} cm^{-1}: 3685, 3560, 1720, 875. ^{1}HNMR and ^{13}C NMR: Tables 1 and 2. HRMS (M + H) $C_{27}H_{35}O_8$ 487.2328 (obs) 487.2332 (cal)

Compound **3**. Yield: 10 mg, mp 198°, ^1H NMR and ^{13}C NMR: Tables 1 and 2. HRMS (M + H) $C_{27}H_{35}O_7$ 471.2360 (obs) 471.2383 (cal).

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