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TETRANORTRITERPENES FROM *MELIA VOLKENSII*

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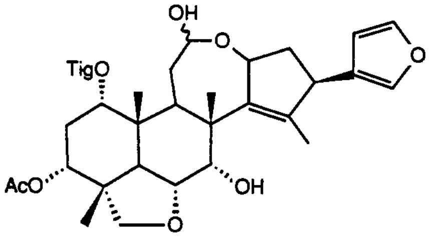
ABSTRACT.—Three new tetranortriterpenes, 1-cinnamoyltrichilinin [**4**], 1-tigloyltrichilinin [**5**], and 1-acetyltrichilinin [**6**], in addition to the known ohchinin-3-acetate [**3**], have been isolated from the fruit of *Melia volkensii*. Their structures have been established by spectroscopic methods. They are probable biosynthetic precursors of the salannin type limonoids.

Melia volkensii Gürke (Meliaceae) is a tree found in the dry areas of East Africa. A tea prepared from the bark is used in local folk medicine for pain, and it is said to be poisonous in an overdose (1). Extracts of the seed kernels have been reported to have potent antifeedant activity against nymphs and adults of the desert locust, *Schistocerca gregaria* (2). Recently (3), we reported the isolation and structure of a new insect antifeedant, volkensin [**1**], together with the known salannin [**2**] (4) as the major limonoids of *M. volkensii*. Further investigation of *M. volkensii* fruit extracts has now led to the isolation of three new tetranortriterpenes designated as 1-cinnamoyltrichilinin [**4**], 1-tigloyltrichilinin [**5**], 1-acetyltrichilinin [**6**], and the known ohchinin-3-acetate [**3**] (5). These three new limonoids belong to the uncommon class of tetranortriterpenes bearing C-ring oxidation at C-12 alone and appear to be biosynthetic precursors of volken-



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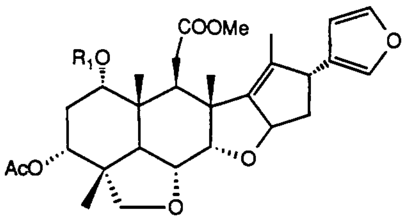
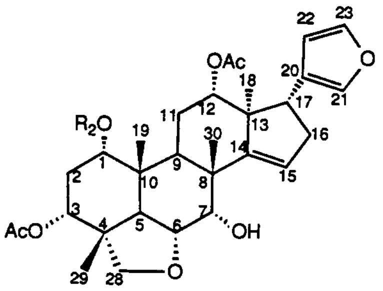
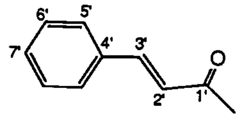


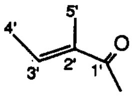
2 R_1=tiglate
3 R_1=cinnamate

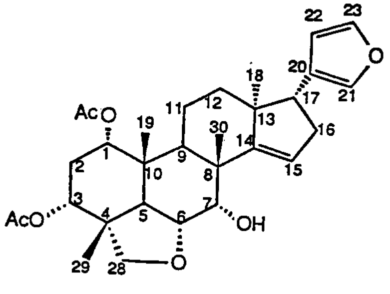


4 R_2=



5 R_2=





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6 R_2=Ac
7 R_2=H

sin [**1**] and salannin [**2**]. The structure elucidation of **3**–**6** was carried out by spectroscopic techniques.

RESULTS AND DISCUSSION

Spectroscopic evidence (Tables 1 and 2) indicated that compounds **4**, **5**, and **6** are all closely related to the vilasinin class (6). All have a β-substituted furan ring, four quaternary methyls, and a hydroxyl group. The three new compounds have a similar substitution pattern, differing only in the C-1 substituent. Compound **3** was shown by identity with published values (5) of the ^{1}H- and ^{13}C-nmr spectra, mass spectrum, ir spectrum, and melting point to be ohchinin-3-acetate [**3**].

Comparison of the ^{1}H-nmr and ^{13}C-nmr absorption of **4**, **5**, and **6** with those reported for trichilinin [**7**] (7) allowed us to place **4**, **5**, and **6** in the structural class with **7**. ^{1}H-^{1}H COSY experiments allowed us to establish coupling of H-2αβ to H-1 and H-3, H-6 to H-5 and H-7, H-16αβ to H-15 and H-17, H-9 to H-11αβ, and H-22 to H-21 and H-23. We also observed long range coupling between H-28αβ and 29-Me. The magnitude of the coupling constants of H-1 and H-3 to H-2 (in all three new com-

TABLE 1. ^{1}H-nmr Data of Compounds **4**–**7**.

Proton	Compound			
	4	**5**	**6**	**7**[a]
1	4.71 dd (2.7,3.6)	4.67 dd (3.0,3.4)	4.61 dd (2.6,3.6)	3.45 br
2	2.24 m	2.18 m	2.16 m	1.98 td (2.5,16.5) 2.30 td (3,16.5)
3	4.96 dd (2.7,3.6)	4.91 dd (3.0,3.4)	4.93 dd (2.6,3.6)	5.09 dd (2.5,3)
5	2.84 d (12.0)	2.76 d (12.0)	2.66 d (12.0)	2.42 d (12)
6	4.21 dd (3.0,12.0)	4.18 dd (3.0,12.0)	4.16 dd (3.0,12.0)	4.16 dd (3,12)
7	4.25 d (3.0)	4.22 d (3.0)	4.19 d (3.0)	4.21 d (3)
9	2.92 m	2.80 dd (7.7,12.8)	2.80 dd (7.0,12.0)	2.88 dd (8,17)
11α	1.20 m	1.07 m	1.05 m	1.49 m
11β	2.18 m	2.10 m	2.10 m	2.18 m
12β	5.07 dd (9.0,7.0)	5.06 dd (9.0,7.0)	5.09 dd (10.0,6.6)	5.07 dd (7,9)
15	5.72 dd (1.5,3.0)	5.70 dd (1.8,3.3)	5.71 dd (1.5,3.5)	5.70 dd (1.5,3)
16αβ	2.50 m	2.51 m	2.53 m	2.58 ddd (1.5,11,16) 2.47 ddd (3,8,16)
17	2.99 m	3.03 dd (8.4,10.4)	3.05 dd (9.0,11.0)	3.04 dd (8,11)
18	0.97 s	0.95 s	1.07 s	1.12 s
19	1.05 s	1.03 s	0.99 s	0.94 s
21	7.26 m	7.21 m	7.23 m	7.23 dd (1.2,1.5)
22	6.19 m	6.25 m	6.26 m	6.28 dd (1.2,2)
23	7.17 m	7.34 m	7.35 m	7.35 dd (1.5,2)
28α	3.68 d (7.6)	3.61 br s	3.60 br s	3.45 br d (7.5)
28β	3.62 d (7.6)	—	—	3.59 d (7.5)
29	1.24 s	1.22 s	1.20 s	1.19 br s
30	1.14 s	1.12 s	1.12 s	1.12 s
C-12 Ac	1.86 br s	1.89 s	1.92 s	1.91 s
C-3 Ac	1.86 br s	1.91 s	2.04 br s	2.13 s
C-1 Ac	—	—	2.04 br s	
2′	6.40 d (15.9)	—	—	
3′	7.76 d (15.9)	6.97 qq (7.0,1.4)	—	
4′	—	1.76 dq (7.0,1.4)	—	
5′	7.37–7.51	1.84 dq (1.4,1.4)	—	
6′	7.37–7.51	—	—	
7′	7.37–7.51	—	—	

[a] Data for compound 7 are from Nakatani *et al.* (7).

TABLE 2. ^{13}C-nmr Data of Compounds **4**–**7**.

Carbon	Compound			
	4	**5**	**6**	**7**[a]
1	72.58	72.48	72.52	71.8
2	27.27	27.44	27.50	30.1
3	71.68	71.77	71.64	74.0
4	42.32	42.39	42.24	42.5
5	39.63	39.62	39.56	38.9
6	72.22	71.89	72.17	72.5
7	73.99	73.96	73.90	78.0
8	45.30	45.42	45.19	45.3
9	34.38	34.36	34.33	34.8
10	39.36	39.50	38.95	40.2
11	24.29	24.26	24.40	36.8
12	77.12	77.23	77.03	77.8
13	51.44	51.39	51.41	51.7
14	157.23	157.42	156.63	157.6
15	122.74	122.71	122.91	122.6
16	36.62	36.66	36.58	36.8
17	50.35	50.40	50.33	50.3
18	26.77	26.88	26.62	27.1
19	15.24	15.31	15.24	15.5
20	124.41	124.53	124.32	124.6
21	140.19	140.31	140.11	140.2
22	111.57	111.74	111.52	111.8
23	142.01	142.05	141.97	142.0
Ac (CO) . . .	170.14	170.20	169.80	169.6
Ac (CO) . . .	170.77	170.83	170.00	171.0
Ac (CO) . . .	—	—	170.61	—
Ac (Me) . . .	21.18	20.86	21.28	21.3
Ac (Me) . . .	21.03	21.32	21.21	21.2
Ac (Me) . . .	—	—	21.04	—
1′	165.43	166.00	—	—
2′	118.01	128.73	—	—
3′	145.48	137.93	—	—
4′	134.07	11.91	—	—
5′	128.00	14.40	—	—
6′	129.03	—	—	—
7′	130.53	—	—	—
28	77.93	78.08	77.93	73.6
29	19.58	19.72	19.49	19.1
30	15.24	15.31	15.74	15.6

[a] Data for compound **7** are from Nakanishi *et al.* (7).

pounds) is about 3 Hz, establishing these protons to be equatorial as is generally the case in related limonoids. The very close correspondence of ^{1}H chemical shifts at position 3 for **4**, **5**, and **6** with those observed for salannin [**2**] (4,8), ohchinin-3-acetate [**3**], 1,3-diacetylvilasinin [**8**] (6), and related compounds is consistent with placement of the acetate at C-3 instead of C-1 in all the three new compounds. Also, the signal for the methyl protons of the C-12 acetate, which normally appear at 1.92 ppm as in the case of mzikonone (9) and trichilinin [**7**] (7), is observed to shift upfield from 1.92 ppm in 1-acetyltrichilinin to 1.86 ppm in 1-cinnamoyltrichilinin. This observation would reasonably be expected due to the shielding effect of a substituent at C-1. It is also noted that the ^{1}H chemical shift of the 3-acetate moves upfield from 2.04 ppm through 1.91 ppm to 1.86 ppm as the substituent at C-1 changes from an acetate through a tiglate to a cinnamate. This is consistent with the 1,3 diaxial relationship of the 1-acyloxy substituent. These observations confirm the placement of the cinnamate and tiglate at C-1 in **4** and **5**, respectively. Carbon and proton chemical shifts at C-7 demonstrated this to be the location of the OH, while the H-7–H-6 coupling constant ($J=3$ Hz) in the three new compounds established the 7-OH to be in the α position.

Stereochemical assignments were further verified with NOESY techniques. For 1-cinnamoyltrichilinin [**4**], correlations were observed between the 29-Me and H-2β, H-3β, H-6β, and H-28β; the 30-Me correlated with H-6β, H-7β, H-12β, and H-15. The 19-Me correlated with H-1β, H-2β, H-6β, and the H-11β. The 18-Me correlated with H-9, H-21, and H-22. The correlations between 30-Me, H-12β, and H-17, as well as between H-21, H-22, H-23, and the acetate methyl confirmed α-stereochemistry for both the furan and the C-12 acetate.

In assigning ^{13}C absorptions (Table 2), APT techniques were used to differentiate methyls, methylenes, methines, and quaternary carbons. HETCOR and COSY techniques were used to correlate ^{13}C and ^{1}H shift assignments. In addition, ^{13}C and ^{1}H shifts reported by Nakatani *et al.* for **7** (7) and related limonoids were useful in making assignments for **4**, **5**, and **6**.

Biogenetically, compounds **4**, **5**, and **6** could be derived from vilasinin by C-12 oxidation and appropriate substitution at C-1, C-3, C-7, and C-12. The isolation of volkensin [**1**], salannin [**2**], and ohchinin-3-acetate [**3**] in the same fruit extract supports the recently proposed biogenetic link between these compounds and salannin type limonoids (10).

EXPERIMENTAL

General experimental procedures.—Melting points were determined on a Fisher hot-stage apparatus and are uncorrected. Ir spectra were recorded on a Perkin-Elmer 283 spectrometer. ^{1}H- and ^{13}C-nmr spectra were obtained on a Varian XL-200 and a GE GN-500 NMR spectrometer. Low resolution mass spectra were recorded on an HP-5985 mass spectrometer operating at 70ev. High resolution mass spectra were obtained on a VG-70E system at the Auburn University Mass Spectrometry Facility by Dr. George Goodloe.

Extraction.—Ripening fruit of *M. volkensii* was collected in November 1983, in Tsavo Park, Kenya. A voucher specimen of the leaves is deposited in the University of Nairobi herbarium. Crushed whole fruit (7.9 kg) was allowed to stand 2 weeks in 8 liters of MeOH. The extract was decanted and the residual pulp similarly extracted a second time. The combined extracts were evaporated under vacuum and the residue partitioned between $CHCl_3$ and H_2O. After drying over Na_2SO_4, the $CHCl_3$ layer was evaporated under vacuum to yield 64 g of a brown oil.

Isolation and identification.—A portion of the oil (10.8 g) was carefully chromatographed on Si gel (70–130 mesh, Merck) using a hexane-Me_2CO (4:1)/Me_2CO gradient. The four limonoids eluted in the order ohchinin-3-acetate [**3**], 1-cinnamoyltrichilinin [**4**], 1-tigloyltrichilinin [**5**], and 1-acetyltrichilinin [**6**].

Compound **4** was crystallized from Me_2CO/hexane to give a white microcrystalline solid: hrms $[M]^+$ 658.3170, calcd for $C_{39}H_{46}O_9$, 658.3143; mp 134–136°; ir (KBr) cm^{-1} 3480 (OH), 1730, 1710 (C=O), 1640 (C=C), 1240 (C-O), 870 (furan); ^{1}H-nmr see Table 1; ^{13}C-nmr see Table 2.

Compound **5** was crystallized from Me_2CO/hexane to give white crystals: hrms $[M]^+$ 610.3128 calcd for $C_{35}H_{46}O_9$, 610.3143; mp 168–170°; ir (KBr) cm^{-1} 3480 (OH), 1740, 1710 (C=O), 1650 (C+C), 1250 (C-O), 875 (furan); ^{1}H-nmr see Table 1; ^{13}C-nmr see Table 2.

Compound **6** was purified further by preparative tlc using EtOAc-$CHCl_3$ (3:7) to give a white solid which was recrystallized from Me_2CO/hexane: hrms $[M]^+$ 570.2840, calcd for $C_{32}H_{42}O_9$, 570.2830; mp 114–116°; ir (KBr) cm^{-1} 3480 (OH), 1740 (C=O), 1250 (C-O), 880 (furan); ^{1}H-nmr see Table 1; ^{13}C-nmr see Table 2.

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