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Limonoid derivatives from *Astrotrichilia voamatata*

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Abstract

The stem bark of *Astrotrichilia voamatata* (Meliaceae) has yielded the novel limonoids voamatins C and D. These compounds represent a new type of pentanortriterpenoid and are unique in containing a ring A cyclic ether.

Keywords: Meliaceae; *Astrotrichilia voamatata*; Limonoids; Voamatin C; Voamatin D

1. Introduction

In continuation of our investigations into the chemistry of the Meliaceae of Madagascar, the stem bark of *Astrotrichilia voamatata* Leroy was investigated. *Astrotrichilia asterotricha*, also from Madagascar, has yielded dammaranes (Mulholland, Nair & Taylor, 1994) and the complex limonoid, astrotrichilin (Mulholland, Nair & Taylor, 1996). Two trijugin-type limonoids, voamatins A and B have been isolated previously as crystalline compounds from *A. voamatata* (Mulholland, Randrianarivelojosia & Schwikkard, 1999). In this investigation, the residual mother liquor, after filtration of voamatins A and B, yielded voamatins C and D.

2. Results and discussion

HRMS of voamatin C gave a molecular ion at *m/z* 726.4062 indicating a molecular formula of $C_{41}H_{58}O_{11}$. A peak at *m/z* 698.4033 ($C_{40}H_{58}O_{10}$) indicated the loss of a CO fragment and a peak at *m/z* 498 $[M\text{-}228]^+$ indicated the loss of a palmitate ester. Attempts at acetylating the compound (Ac_2O/py) were unsuccessful indicating no primary or secondary hydroxy groups.

The ^{1}H-NMR spectrum of voamatin C indicated that it was a limonoid of the ekebergolactone type. Resonances ascribable to protons in the β-substituted furanyl ring occurred at δ 7.49 (H-21), 7.46 (H-23) and δ 6.35 (H-22). Ring D was oxidised to a C-16 lactone, with H-17 occurring as a sharp singlet at δ 6.23 and 2H-15 occurring as a pair of doublets at δ 2.92 and δ 2.75 (*J* 17.5 Hz) which were not further coupled. The COSY spectrum showed coupled resonances at δ 4.09, δ 5.29 and δ 5.29 ascribable to H-1, H-2 and H-3, respectively, and indicated the presence of esters at C-2 and C-3. The ^{1}H-NMR spectrum confirmed that the one ester present was a palmitate and the second was an acetate. The H-2 and H-3 protons were distinguishable when the spectrum was re-run in $CDCl_3$ containing a few drops of C_6D_6 ($\Delta\delta = 0.03$ ppm = 15 Hz). These signals exhibited correlations with the two ester carbonyls in the HMBC experiment. The one at 169.64 ppm showed $^3J_{H-C}$ correlations with the acetate methyl protons and H-2; the second at 173.91 ppm was correlated with the protons of the palmitate (H-2″)

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Table 1
NMR data for voamatin C ($CDCl_3$, 500 MHz, *J* in brackets) [values in square brackets indicate spectra run in $CDCl_3$ + C_6D_6]

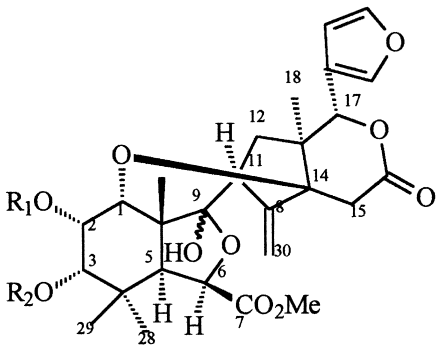
	^{1}H	^{13}C	HMBC (C → H)	ROESY
1	4.09 *s*	88.17	2, 3, 19	2, 15β, 19, 30A
2	5.29 *m* [5.38 *dd* (3.0, 1.6)]	67.65	1, 3	
3	5.29 *m* [5.41 *d* (3.0)]	77.22	1, 28, 29	
4	–	77.95	5, 28, 29	–
5	3.62 *s*	80.17	1, 6, 19	19, 28
6	9.75 *s*	200.13	5	–
8	–	145.89	11, 12α, 12β, 15α, 30A, 30B	–
9	–	211.43	5, 12α, 12β, 19, 30A, 30B	–
10	–	65.61	5, 19	–
11	3.52 *dd* (9.9, 3.1)	52.74	12α, 12β, 30A, 30B	12α, 12β, 18, 30A
12α	2.03 *dd* (9.9, 13.2)	38.95	18	11, 18
12β	2.20 *dd* (3.1, 13.2)			11, 17
13	–	44.58	12α, 12β, 15β, 18, 17	–
14	–	88.17	1, 12α, 15α, 15β, 18, 30	–
15α	2.75 *d* (17.5)	32.02	–	18, 30B
15β	2.92 *d* (17.5)			1, 30B
16	–	168.00	15α, 15β	–
17	6.23 *s*	78.76	18	12β, 2″
18	0.82 *s*	18.24	12α, 12β, 17	12α, 15α
19	1.45 *s*	21.57	1, 5	1, 5, 30A, 30B
20	–	121.72	17, 21, 22, 23	–
21	7.49 *brs*	139.66	17, 22, 23	17
22	6.35 *d* (1.6)	108.20	17, 21	12β
23	7.46 *d* (1.6)	143.59	21, 22	22
28α	1.38 *s*	24.83		1, 5
29β	1.24 *s*	26.25	4	
30A	5.53	115.17	11	11, 19
30B	5.39			1, 15α
Acetate 1′	–	169.82	2, 3, 2′	
Acetate 2′	2.13 *s*	20.80		
Palmitate 1″	–	174.08	2, 3, 2″	
Palmitate 2″	2.35 *dt* (15.8, 7.80)	33.36		
	2.50 *ddd* (15.8, 8.6, 6.8)			
Palmitate 3″	1.58 *m*	25.06		
Palmitate 4–13″	1.2–1.5	29.2–31.8		
Palmitate 14″	0.90 *t* (6.8)	14.08		

and H-3. Ring B was opened to give a 8,30-double bond, C-8 and C-30 occurring at δ 145.89 and δ 115.17, respectively, in the ^{13}C-NMR spectrum. The non-equivalent H-30 protons occurred as singlets at δ 5.53 and δ 5.39 in the ^{1}H-NMR spectrum. The expected carbomethoxy group at C-7 and H-5α/2H-6 coupled system was, however, not present. An aldehyde group was present and the aldehyde group proton resonance at δ 9.75 was coupled to a resonance at δ 3.62 which was not further coupled and whose related carbon shift occurred at δ 80.17. A further fully substituted carbon atom resonated at δ 77.95. The HMBC spectrum showed that the aldehyde group occurred at C-6, the resonance at δ 80.17 was due to C-5 and the resonance at δ 77.95 was due to C-4. An oxygen atom was placed between C-4 and C-5 to account for the downfield carbon shifts.

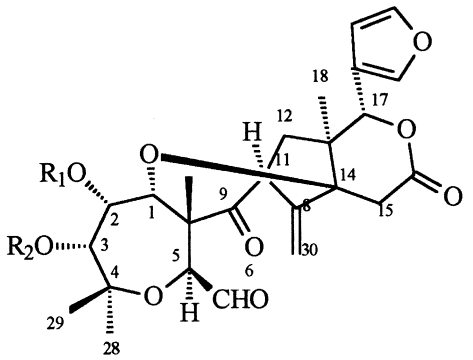
The H-11 resonance occurred as a double-doublet at δ 3.52 and was coupled to two H-12 protons and long range coupled to the H-30 protons. The absence of coupling to H-9 suggested a contracted ring C as in voamatins A and B. Thus the ketonic carbonyl carbon resonance occurring at 211.43 ppm was assigned to C-9. This resonance showed long-range correlations with H-12 and H-30 ($^4J_{H-C}$) of ring C and with H-5 and the 3H-19 protons of ring A. The molecular formula indicated that another ring was necessary so the ekebergolactone 1,14-oxide bridge was proposed. This was supported by a HMBC correlation between C-14 and H-1. The stereochemistry at the chiral centres was established by a ROESY experiment and agrees with X-ray results found previously for *Ekebergia* compounds (Kehrli, Taylor & Niven, 1990). The Logic for Structure Determination (LSD) Program (Nuzillard & Massiot, 1991) was used to confirm the structure of voamatin C. In this program, all HMBC correlations are taken into account and the program indicated that only one structure was compatible with this data. Thus structure C was assigned to voamatin C. The insertion of an oxygen atom between C-4 and C-5, and loss of

C-7 in a ring B-opened limonoid has not been described previously.

The ^{1}H-NMR data for voamatin D was very similar to that of voamatin C but the palmityl ester at C-3α was replaced with a cinnamate. Mass spectrometry indicated a molecular formula of $C_{36}H_{38}O_{11}$ and showed the typical loss of fragments of 131 and 148 confirming the presence of the cinnamate ester. Resonances ascribable to a *trans*-cinnamate ester were present in the NMR spectra for this compound (Table 2).



		R_1	R_2
A	9α-OH	H	Cinn
B	9β-OH	H	Cinn



		R_1	R_2
C	Ac		Palmityl
D	Ac		Cinn

3. Experimental

Bark of *Astrotrichilia voamatata* Leroy was collected from Feverive East, Madagascar by M. Randrianarivelojosia and identified by comparison against specimens at the Parc de Botanique et de Zoologie de Tsimbazaza. Voucher specimens are deposited at the University of Antananarivo (008-MJ-M.Dul).

Dried, milled bark (1 kg) was extracted successively with hexane, methylene chloride and methanol in a soxhlet apparatus. A white crystalline mixture of voamatins A and B precipitated out of the methylene chloride extract and was filtered off. Separation of the mother liquor by means of column chromatography over silica gel (Merck 9385) yielded voamatins C and D.

NMR spectra were recorded in $CDCl_3$ on a Varian 300 MHz NMR spectrometer in Durban and on a Bruker 500 MHz NMR spectrometer in Reims. ^{1}H- and ^{13}C-NMR data of voamatins C and D are given in Tables 1 and 2. HRMS and EIMS were recorded at the Cape Technikon on Kratos HRMS 9/50 and Finnigan 1020 GC MS instruments. IR spectra were recorded on a Nicolet Impact 400D instrument.

Voamatin C, (**C**) (20 mg), amorphous, HRMS M^+ at m/z 726.4062 ($C_{41}H_{58}O_{11}$ requires 726.4054), EIMS m/z 726 [M^+], 698, 670, 603, 498, 455, 410, 383, 220, 211, 134. IR ν_{max} (NaCl) (cm^{-1}): 2925, 2853, 1740, 1472, 1387, 1232, 1165, 1106, 1025.

Voamatin D, (**D**) (6 mg), amorphous, HRMS M^+ at m/z 646.2420 ($C_{36}H_{38}O_{11}$ requires 646.2414, EIMS m/z 646 [M^+], 586 [M–CH_3COOH], 615, 498.

Table 2
NMR data for Voamatin D (300 MHz, $CDCl_3$, J in parenthesis)

	^{1}H	^{13}C		^{1}H	^{13}C
1	4.10 *bs*	82.19	19	1.46 *s*	21.61
2	5.30 *m*[b]	67.84	20	–	121.97
3	5.30 *m*[b]	77.22	21	7.45 *s*	139.95
4	–	78.18	22	6.37 *s*	108.38
5	3.62 *s*	80.31	23	7.39 *s*	143.76
6	9.73 *s*	200.15	28	1.37 *s*	24.87
8	–	145.99	29	1.23 *s*	26.30
9	–	211.48	30A and B	5.50 *s*, 5.35 *s*	115.15
10	–	65.80	Acetate 1′	–	167.53[a]
11	3.4 *dd* (9.9, 3.1)	52.92	Acetate 2′	2.11 *s*	20.90
12α	2.02 *dd* (9.9, 13.2)	39.02	Cinnamate 1″	–	169.99
12β	2.20 *dd* (3.1, 13.2)				
13	–	44.73	Cinnamate 2″	7.64 *d* (15.8)	146.44
14	–	88.29	Cinnamate 3″	6.54 *d* (15.8)	117.02
15α	2.71 *d* (17.5)	32.12	Ph	–	134.47
15β	2.90 *d* (17.5)				
16	–	167.22[a]		7.2 *m* (1H)	130.17
17	6.34 *s*	78.77		7.2 *m* (2H)	128.57
18	0.79 *s*	18.29		7.4 *m* (2H)	128.43

[a] Resonances may be interchanged.
[b] Resonances superimposed.

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