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A highly rearranged tetraprenylxanthonoid from *Garcinia gaudichaudii* (Guttiferae)

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Abstract—Gaudispirolactone (**1**), a novel degraded and rearranged tetraprenylated xanthone isolated from the bark of *Garcinia gaudichaudii*, has the unique hexacyclic dioxospirotrione structure. © 2001 Published by Elsevier Science Ltd.

Garcinia gaudichaudii Planch et Triana from Borneo is a local medicinal plant, the juice from the leaves being used by the natives to rub on cuts and minor wounds.[1] We have found that the bark provides an array of xanthonoid compounds which are surprisingly different from the leaves of the plant.[2,3] Gaudispirolactone (**1**) was isolated together with another new compound, 7-isoprenylmorellic acid (**2**), and other known compounds.[4]

Gaudispirolactone (**1**) was obtained as a yellow oil, $[\alpha]_D^{29.7}$+64 (*c* 1.5, $CHCl_3$). The molecular formula of $C_{32}H_{34}O_8$ (ESIMS, *m*/*z* 569.2134, $[M+Na]^+$) approximated that for a tetraprenylxanthonoid, but the IR absorptions of the carbonyl groups (1735, 1689 and 1646 cm^{-1}) and the NMR data of **1** (Table 1) did not indicate much similarity to the caged structure of gaudichaudiones or gaudichaudiic acids previously isolated from the leaves of the plant.[5] However, **1** exhibited NMR signals showing the presence of the B and C rings of prenylated xanthonoids, e.g. (a) a pair of doublets at δ_H 5.53 and 6.60 (d, $J=9.9$ Hz) together with two methyl groups at δ 1.43 and 1.45 accounted for a dimethylpyran ring system, (b) a chelated phenolic proton at δ_H 12.04, and (c) a vinylic proton at δ_H 5.22 (t, $J=7.2$ Hz) and corresponding ^{13}C data for all these features. The spectra also showed a clear absence of a non-conjugated ketone, but the presence of a ketal carbon (δ_C 109.6) was noteworthy. With only 32 carbons in the structure instead of the usual 33 carbons for a tetraprenylxanthonoid, **1** was likely to have lost a carbonyl carbon in the degradation and rearrangement of a tricyclo-4-oxa[4.3.1.0^{3,7}]decane precursor which was a prominent structural feature of gaudichaudiic acids and morellic acids.

The presence of a lactone carbonyl carbon (δ_C 162.6, C-15) and the HMBC connectivities between the Me-16 at δ_H 1.74 and carbon signals at δ_C 162.6 (C-15), 128.1 (C-14), and 134.9 (C-13), and the vinylic proton H-13 at δ_H 6.26 with the ketal carbon at δ_C 109.6 (C-11) indicated **1** had a partial structure of a six-membered α,β-unsaturated lactone (Fig. 1). The remaining part of the core ring structure was deduced from the following HMBC correlations. (a) The methylene protons at δ_H 2.59 and 2.77 (H-6α and H-6β) correlated with quaternary carbons at δ_C 196.2 (C-7), 87.8 (C-10a) and a methine carbon at δ_C 51.7 (C-5); (b) the vinylic proton at δ_H 6.80 (H-8) correlated with quaternary carbons at δ_C 87.8 (C-10a) and 184.4 (C-9); (c) the methine proton at δ_H 3.24 (H-5) correlated with C-10a; (d) the chelated hydroxyl proton at δ_H 12.04 correlated with the aromatic carbons at δ_C 156.7 (C-1), 103.6 (C-2), and 102.8 (C-9a). In addition to the main skeleton, other readily identifiable pendant residues were the isoprenyl group substituted at C-4, which was deduced from HMBC correlations H-25/C-3,4,4a,26,27, and the dimethylpyran ring fused to the C ring of the xanthonoid, which was deduced from the HMBC correlations H-20/C-1,3,22; H-21/C-2,22 and the ROESY correlation 1-OH/H-20.

The relative stereochemistry of **1** was supported from the postulated biosynthesis (Fig. 3) and confirmed by 2D ROESY spectra (Fig. 1 and Table 1). The key ROESY correlations were between H-18 and H-12α, H-12β, which indicated Me-18 and C-12 were on the same side of the five-membered ring. The Me-18 was

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Keywords: gaudispirolactone; xanthonoid; *Garcinia gaudichaudii*; cytotoxic.

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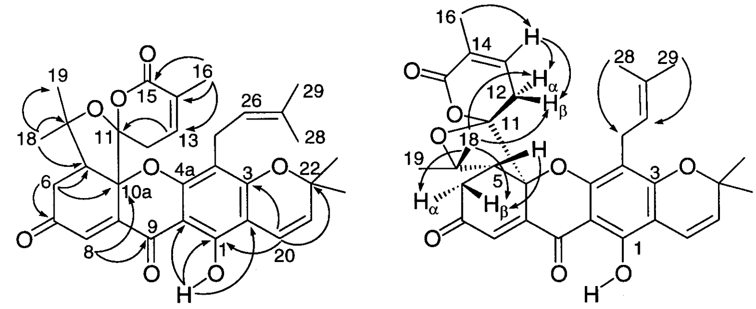
Table 1. NMR data for gaudispirolactone (**1**)[a]

#	^{1}H NMR	^{13}C NMR	HMBC	COSY	ROESY
1	12.04, s (-OH)	156.7	1, 2, 9a		20
2		103.6			
3		162.3			
4		109.9			
4a		156.9			
5	3.24, t, J=6.5 Hz	51.7	6, 7, 10a, 19	6α, 6β	6β
6	α: 2.59, dd, J=16.9, 6.5 Hz	36.8	5, 7, 10a, 17	5, 6β	18
	β: 2.77, dd, J=16.9, 6.5 Hz		5, 7, 10a, 17	5, 6α	5, 18
7		196.2			
8	6.80, s	131.6	9, 10a		
8a		145.5			
9		184.4			
9a		102.8			
10a		87.8			
11		109.6			
12	A: 2.65, d, br, J=17.4 Hz	33.8		12B, 13	13
	B: 2.54, d, br, J=17.4 Hz			12A, 13	13
13	6.26, s, br	134.9	11, 14	12A, 12B, 16	12A, 12B, 16
14		128.1			
15		162.6			
16	1.74, d, J=1.5 Hz	16.6	13, 14, 15	13	13
17		84.4			
18	1.20, s	25.7	5, 17, 19		6α, 6β, 12A, 12B
19	1.71, s	30.5	5, 17, 18		
20	6.60, d, J=9.9 Hz	115.0	1, 3, 22	21	1-OH, 21
21	5.53, d, J=9.9 Hz	126.7	2, 22	20	20, 23, 24
22		79.1			
23	1.43, s	28.5	21, 22, 24		20
24	1.45, s	28.6	21, 22, 23		20
25	3.26, d, J=7.2 Hz	21.6	3, 4, 4a, 26, 27	26	26, 28
26	5.22, t, J=7.2 Hz	121.9	28, 29	25	25, 29
27		131.7			
28	1.76, s	18.0	26, 27, 29		25
29	1.67, s	25.7	26, 27, 28		26

[a] Recorded in $CDCl_3$ at 500 MHz (^{1}H NMR) and 125 MHz (^{13}C NMR).



HMBC ROESY

Figure 1. Selected HMBC AND ROESY correlations of gaudispirolactone (**1**).

assigned as β because it showed correlations with H-6α and H-6β while H-5 showed only one correlation with H-6β. Thus the structure of **1** was depicted as shown in Fig. 1.

7-Isoprenylmorellic acid (**2**)[6] was isolated as a yellow oil, $[\alpha]_D^{29.7}$–191.5 (c 3.4, $CHCl_3$). A molecular formula of $C_{38}H_{44}O_8$ (ESIMS, m/z 629.3098, $[M+H]^+$) indicated a pentaprenylxanthonoid. ^{1}H and ^{13}C data showed resonances for the skeleton of gaudichaudiic and morellic acids. Extensive analyses of 1D (^{1}H, ^{13}C) and 2D

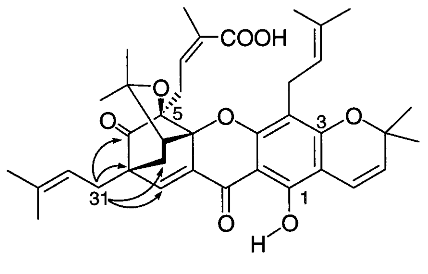


Figure 2. Selected HMBC correlations of 7-isoprenylmorellic acid (**2**).

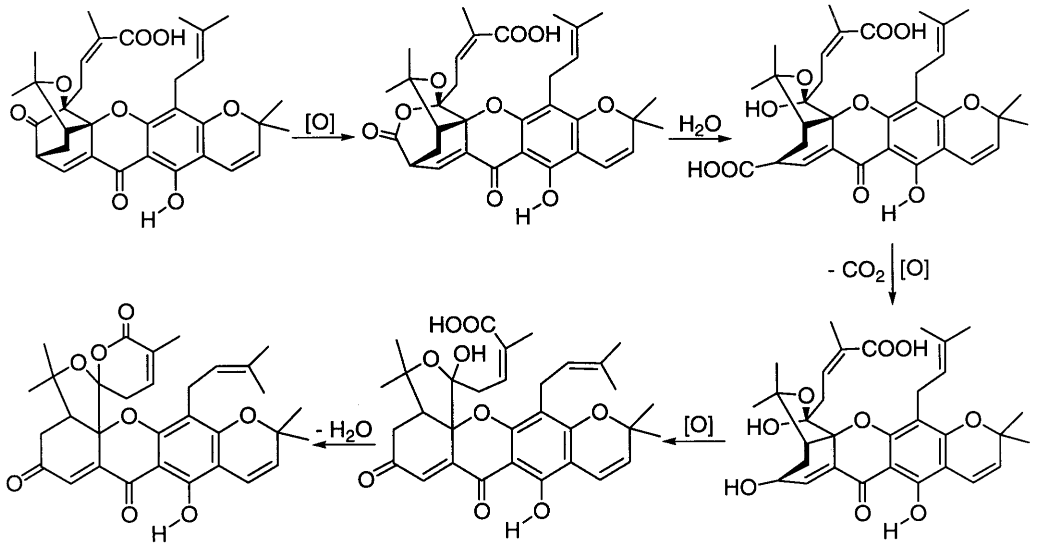


Figure 3. Postulated biosynthesis pathway for gaudispirolactone (**1**).

(^{1}H-^{1}H COSY, HMQC, and HMBC) NMR spectra of **2** showed that it was a 7-prenylated derivative of morellic acid.[5] The structure of **2** shown in Fig. 2, was supported by the presence of HMBC cross peaks between the methine protons H-31 at δ_H 2.44 and 2.61 and the carbons at δ_C 204.1 (C-6), 53.3 (C-7), 30.9 (C-11) 139.2 (C-8).

It is reasonable to assume that **1** was a degraded derivative of the tricyclo-4-oxa[4.3.1.0^{3,7}]decane skeleton comprising gaudichaudiones and gaudichaudiic acids furnished by this plant. A plausible biosynthetic route involving morellic acid, which is the major natural product from the bark, is given in Fig. 3.

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4. Other compounds isolated: morellic acid (0.03%), isomorellin (0.0005%), isomoreollin (0.0003%), isomorellinol (0.0003%), gaudichaudiic acid E (0.001%), isomorellic acid (0.001%).
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6. NMR data of **2**. ^{1}H NMR: δ 12.98 (1H, s, OH), 7.32 (1H, s, H-8), 6.58 (1H, d, J=9.9 Hz, H-21), 6.07 (1H, t, J=7.3 Hz, H-17), 5.48 (1H, d, J=9.9 Hz, H-22), 5.22 (1H, t, J=7.3 Hz, H-32), 5.05 (1H, t, J=6.1 Hz, H-27), 3.33 (1H, m, H-26α), 3.17 (1H, m, H-26β), 2.95 (1H, m, H-16α), 2.87 (1H, m, H-16β), 2.61 (1H, m, H-31α), 2.57 (1H, d, J=9.2 Hz, H-12), 2.44 (1H, m, H-31β), 1.75 (6H, s, H-35 and H-30), 1.75 (3H, s, H-19), 1.71 (3H, s, H-34), 1.69 (3H, s, H-15), 1.65 (3H, s, H-29), 1.45 (3H, s, H-25), 1.41 (3H, s, H-24), 1.24 (3H, s, H-14). ^{13}C NMR: δ 204.1 (C-6), 179.0 (C-9), 169.0 (C-20), 161.2 (C-3), 157.7 (C-4a), 157.3 (C-1), 139.2 (C-8), 136.8 (C-33), 135.9 (C-17), 133.0 (C-8a), 131.5 (C-28), 128.0 (C-18), 126.1 (C-22), 122.1 (C-27), 118.2 (C-32), 115.4 (C-21), 108.1 (C-4), 103.1 (C-2), 100.6 (C-9a), 90.6 (C-5a), 84.2 (C-5), 84.1 (C-13), 78.6 (C-23), 53.3 (C-7), 50.5 (C-12), 30.9 (C-11), 29.9 (C-15), 29.4 (C-16), 28.8 (C-14), 28.7 (C-31), 28.5 (C-25), 28.3 (C-24), 25.9 (C-35), 25.7 (C-29), 21.6 (C-26), 20.8 (C-19),18.1 (C-30).