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TETRAHEDRON

Prenylated Benzophenone Derivatives from Caribbean *Clusia* species (Guttiferae). Plukenetiones B-G and Xerophenone A.

Geneive E. Henry,[a] Helen Jacobs,[a*†] C. M. Sean Carrington,[b] Stewart McLean[c] and William F. Reynolds[c*]

[a]*Department of Chemistry, University of the West Indies, Mona, Kingston 7, Jamaica.*
[b]*Department of Chemical and Biological Sciences, University of the West Indies, Cave Hill, Barbados.*
[c]*Department of Chemistry, University of Toronto, Toronto, Canada.*

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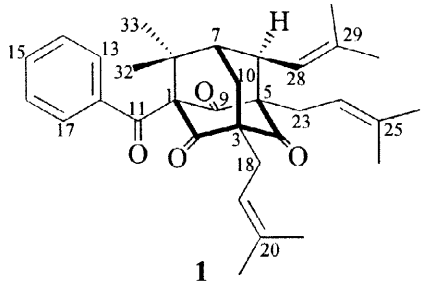
Abstract: Six new prenylated benzophenone derivatives plukenetiones B-G (**2-7**) have been isolated from the fruits of the Barbadian plant *Clusia plukenetii*. These structures were elucidated by the use of 2D NMR spectroscopic methods. The regiochemistry of xerophenone A from *Clusia portlandiana* has been revised.

Keywords: *cage compounds; peroxide; pyrans; tautomerism.*

INTRODUCTION

As part of our phytochemical survey of the Caribbean Guttiferae [1,2] we have examined extracts of *Clusia plukenetii*, an endemic plant of the Lesser Antilles which occurs commonly in Barbados [3]. In a preliminary communication we described the unusual adamantyl ketone, plukenetione A (**1**) [2] isolated from the fruit of this plant. Plukenetione A (**1**) exemplifies an unprecedented variation in the mode of cyclization of the putative precursor to the prenylated 2,4,6-trihydroxybenzophenone derivatives [4,5]. This structurally diverse group of compounds, of mixed shikimate, acetate and isoprenoid biogenesis, is confined to the Guttiferae. Both the simple and complex derivatives have been the subject of recent attention owing to their biological activity [4,6,7].



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†Fax: (876)977-1835, E-mail: hjacobs@uwimona.edu.jm

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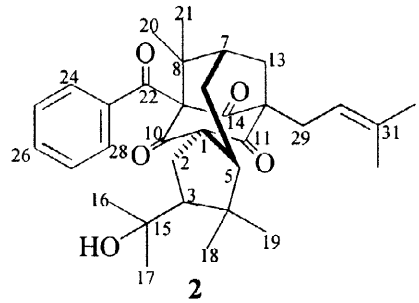
This report describes the structures of plukenetiones B-G (**2-7**), further metabolites of the fruit of *C. plukenetii,* and corrects the previously assigned stereochemistry of xerophenone A isolated from *C. portlandiana* [1].

RESULTS AND DISCUSSION

Plukenetione B (**2**), a colourless oil, was assigned the molecular formula $C_{33}H_{42}O_5$ on the basis of HREIMS. The base peak at *m/z* 105 in the LREIMS and NMR resonances attributable to a phenyl group (Table1) suggested an unsubstituted benzoyl moiety. This, in conjunction with the molecular formula, indicated a trioxygenated benzophenone-derived skeleton incorporating four five-carbon units as observed for plukenetione A (**1**) [2].

One isoprenoid unit was identified from the NMR data as the 2-methylbut-2-enyl group (C-29-C-33) attached to a quaternary centre, δ_C 68.9. The IR spectrum displayed absorptions at 3565 cm^{-1}, due to one hydroxyl group, and at 1732, 1702, 1699 and 1683 cm^{-1} for four carbonyl groups. Additional evidence for the four ketones was the presence of resonances at δ 192.5, 204.1, 204.8 and 206.5 in the ^{13}C NMR spectrum. The foregoing data accounts for nine of the thirteen required degrees of unsaturation. The absence of further signals for sp^2 carbons suggested that the remaining three isoprenoid units formed a tetracyclic moiety.



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The structure of the tetracycle and the location of the attached groups were determined by a combination of ^1H-^1H COSY, HSQC and HMBC data (Table 1). This was complicated somewhat by overlap of two pairs of carbon signals, in addition to those of the phenyl group. A peak at δ 134.8 indicating quaternary sp^2 carbon was eventually assigned to C-23 and C-31. The signal for sp^3 methine carbon at δ 57.6 showed direct correlations to hydrogens at δ 2.10 (dd, 7.8, 11.7) and δ 2.52 (dd, 13.0, 18.0). The intensity of this ^{13}C signal and the absence of correlation between the associated ^1H shifts in the COSY spectrum revealed that it represented two methine carbons, subsequently assigned as C-3 and C-5. Incremental addition of C_6D_6 to the original $CDCl_3$ solution optimized the resolution of the ^1H signals at 25%C_6D_6-$CDCl_3$. The overlapping carbon signals did not resolve in this solvent mixture.

In the HMBC spectrum, the methyl groups at C-18 and C-19 were shown to be geminal on the quaternary carbon designated C-4 (δ 44. 9). This was flanked by the two methine carbons C-3 and C-5, demonstrated by the C-18→H-3, C-19→H-5 and C-4→H-3, H-5 cross-peaks,

Table 1

NMR Data for Plukenetione B (2)

Pos.	^{13}C	^{1}H $CDCl_3$	^{1}H (J, Hz) 25% $C_6D_6/CDCl_3$	^{1}H-^{1}H COSY	HMBC[a]
1	73.2				2, 3, 5, 6
2	33.2	2.20 (dd, 7.1, 13.1)[b]	2.17 (dd, 13.0,18.0)	2,3	
		2.48 (t, 12.1)[b]	2.50 (t, 13.0)		
3	57.6	2.52 (dd, 7.5, 12.5)[b]	2.48 (dd, 13.0,18.0)	2	2, 16, 17, 18,19
4	44.9				2, 3, 5, 6 (1.48), 18, 19
5	57.6	2.10 (t, 8.8)[b]	2.05 (dd, 7.8, 11.7)	6	6, 7, 18, 19
6	28.6	1.63	1.48 (dd, 3.5, 8.1)	5,6,7	5, 7, 13
		2.30	2.12 (m)	5,6,7	
7	43.8	2.13	1.89 (m)	6,13	13, 20, 21
8	50.9				6, 7, 13, 20, 21
9	80.8				7, 20, 21
10	204.1				2, 5
11	206.5				2, 5, 13, 29
12	68.9				7, 13, 29
13	42.6	β1.89	1.73 (d ,14.3)	7, 13	6, 7, 29
		α2.52 (dd, 6.0, 14.9)[b]	2.38 (dd, 7.8, 14.3)		
14	204.8				13, 29
15	73.4				2, 16, 17
16	30.2	1.33	1.28 (s)		17
17	30.1	1.38	1.20 (s)		16
18	28.4	0.93	0.87 (s)		3, 19
19	27.2	1.23	1.16 (s)		5, 18
20	25.2	1.46	1.41 (s)		21
21	22.8	1.41	1.35 (s)		20
22	192.5				24, 28
23	134.8				25, 27
24, 28	128.9	7.11 (dd, 1.1, 8.9)	7.11[c]	25,26, 27	24, 26, 28
25, 27	128.0	7.29 (dd , 7.2, 8.9)	7.29[c]	24,26, 28	25, 27
26	132.1	7.40 (dt ,7.2)	7.40[c]	24,25, 27,28	24, 28
29	29.5	2.55	2.56 (d, 5.1)	30	13, 30
30	119.0	5.07 (t, 7.0)	5.07[c]	29,32, 33	29, 32
31	134.8				29, 32, 33
32	26.1	1.68	1.67 (s)	30	30, 33
33	18.1	1.66	1.65 (s)	30	30, 32

[a] ^{1}H correlating with ^{13}C resonance. [b] Values from coupled HSQC spectra.

[c] J values in 25% C_6D_6-$CDCl_3$ were not determined.

while ^{1}H-^{1}H COSY established the protonated sequence H_2-2—H-3. A quaternary carbon at δ 73.2, C-1, presumably vicinal to two carbonyl groups, displayed HMBC correlations to the above mentioned methylene and methine protons, i.e. C-1→H_2-2, H-3, H-5, establishing the cyclopentane moiety. A deshielded quaternary sp^3 carbon, C-15, δ 73.4, assumed to be oxygen-substituted and showing cross-peaks to two geminally correlated methyl groups and to the protons at C-2, was placed at position 3 of the cyclopentane.

The expected correlations were observed between C-10, C-11, the carbonyl carbons flanking C-1, and the cyclopentanoid H_2-2 and H-5. No further cross peaks to C-10 were observed, suggesting full substitution at the remaining α and three β positions. C-11 was demonstrated to be vicinal to the quaternary position bearing the isopentenyl group by the C-11→H_2-29 peak. C-11 also displayed cross-peaks to both protons at C-13. This H_2-13 group, from the ^{1}H-^{1}H COSY data, was one end of the linear protonated four-carbon fragment H_2-13—H-7—H_2-6—H-5, the second terminus of which formed part of the cyclopentane ring. This analysis establishes the sequence C-11—C-12—C-13—C-7—C-6—C-5.

The quaternary carbon C-12, δ 68.9, attached to the isopentenyl side chain, was vicinal to the C-11 carbonyl as already shown; the deshielded position suggested a second vicinal carbonyl group, C-14, δ 204.8, placement of which was corroborated by the C-14→H-29, H-13 HMBC peaks.

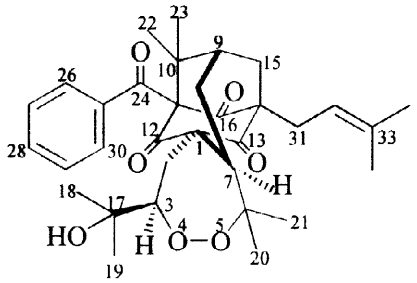
Completion of the tetracycle required assignment of two quaternary sp^3 carbons, one highly deshielded, δ 80.8, and the second, δ 50.9 substituted with two correlated methyl groups, C-20 and C-21. The first, from its position, and by analogy with plukenetione A (**1**) [2], was vicinal to three carbonyl groups; this position, C-9, is the point of attachment of the benzoyl group to the cyclohexane trione and closes the acetate-derived six-membered ring. C-9 was shown to be vicinal to the *gem*-dimethyl substituted quaternary carbon at δ 50.9 (C-8) by the C-9→H_3-20, H_3-21 peaks while the C-8→H_2-6, H-7, H_2-13 peaks provided corroboration for placement of C-8.

There was a notably strong correlation in the HMBC spectrum between the C-11 carbonyl and H-13α (δ 2.38) suggesting an *anti* relationship between H-13α and C-11. Similarly H-13β (δ 1.73) showed a strong correlation to the C-14 carbonyl and a weak correlation to the C-11 carbonyl, indicating that H-13β and C-14 are *anti*.

Plukenetione B contains a tetracyclo[5.3.3.1.^{9,12}0^{1,5}]tetradecane-10,11,14-trione moiety, which is being observed for the first time among the prenylated benzophenones.

Plukenetione C (**3**) was obtained as a colourless oil. The HREIMS gave a molecular formula of $C_{33}H_{42}O_7$, containing two oxygens more than **2**. Careful analysis of the IR, NMR and mass spectral data of **3** revealed several similarities with plukenetione B (**2**). There was

clear evidence for the unsubstituted benzoyl group (*m/z* 105), one hydroxyl group (3579-3375 cm^{-1}), four carbonyls (1732, 1704, 1698 and 1682 cm^{-1}) and one 2-methylbut-2-enyl group.



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The salient differences between the NMR data for **3** (Table 2) and **2** were in the signals for the moiety spiro-fused to C-1. Within this portion of the molecule the methine carbon bearing the hydroxyisopropyl group was now bonded to oxygen (δ_C 88.8, δ_H 4.58, dd, 2.7, 10.8) as was the quaternary carbon with the *gem*-dimethyl groups (δ_C 88.5). On the basis of the molecular formula these carbons were linked through a peroxide bridge to provide structure **3**. The strong peak at *m/z* 518 $[M-32]^{+\cdot}$ in the EIMS due to the loss of O_2 also provided persuasive evidence for the presence of this peroxide [8]. The possibility of the alternative linkage between C-6 and C-17 via a peroxy group, with the tertiary hydroxyl located at C-3 was also considered. However this was rejected on the basis of the carbon shift observed for C-17 (δ 73.1) which is typical of quaternary centres with a hydroxyl and two methyl groups and compares very well with that observed for the similar position in **2**, (δ 73.4). The relative stereochemistry shown for H-3 and H-7 was based on a strong nOe association observed between these signals, suggesting that they are on the same face of the molecule.

Plukenetione C (**3**), contains a 4,5-dioxatetracyclo[7.3.3.$1^{11,14}0^{1,7}$]hexadecane-12,13,16-trione moiety. This is the first report of a peroxide among the prenylated benzophenones. For formal reasons the numbering differs from that of the closely related plukenetione B (**2**). A plausible biogenetic pathway to **3** involves the formation of an allylic hydroperoxide at the incipient C-6 via an ene reaction of singlet oxygen [9] with the precursor methylbutenyl group consisting of C-8, C-7, C-6, C-20, C-21. Spiro-fusion af C-7 to C-1, with concomitant ketonization of the precursor C-12 enol, epoxidation of a precursor C-3—C-17 double bond and cyclization of the hydroperoxide onto the methine C-3 of the epoxide would result in the hydroxyisopropyl cyclic peroxide shown [10].

Plukenetione D (**4a**) and plukenetione E (**5a**) were present in $CDCl_3$ solution as a tautomeric pair in a ratio 1:1, which made assignments for each tautomer difficult. The mixture was acetylated to afford the regioisomeric pair plukenetione D acetate (**4b**) and plukenetione E acetate (**5b**), separable by chromatography as colourless oils. The molecular formula of each isomeric acetate was determined to be $C_{35}H_{44}O_5$ by HREIMS. The base peak for each was observed at *m/z* 105 which is consistent with structures derived from 2,4,6-

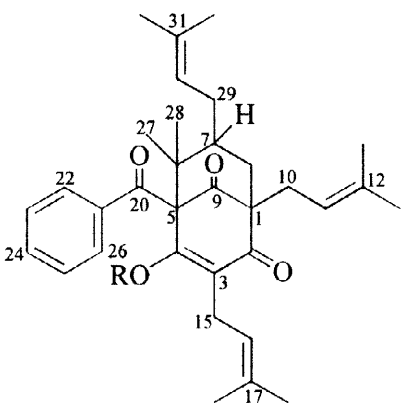
Table 2
NMR Data for Plukenetione C (3) in $CDCl_3$

Pos.	^{13}C	^{1}H (J, Hz)	^{1}H-^{1}H COSY	HMBC[a]
1	66.5			2, 7
2	31.1	1.54 (m)	2, 3	3
		3.54 (dd, 10.8, 16.0)	2, 3	
3	88.8	4.58 (dd, 2.7, 10.8)	2	2, 18, 19
6	88.5			7, 20, 21
7	42.5	2.78 (dd, 7.0, 14.0)	8	20, 21
8	31.4	1.52 (m)	7, 9	7, 15
		2.42 (m)	7, 9	
9	44.4	2.10 (m)	8, 15 (2.58)	15, 22, 23
10	50.3			15 (1.88), 22, 23
11	82.9			22, 23
12	208.0			2 (3.54), 7
13	205.1			7, 15, 31
14	68.5			15, 31
15	41.6	β1.88 (d ,14.0)	15	31
		α2.58 (dd ,7.0, 14.0)	9, 15	
16	204.4			15 (1.88), 31
17	73.1			18, 19
18	25.9	1.08 (s)		19
19	24.9	1.14 (s)		18
20	28.2	1.30 (s)		7, 21
21	17.8	1.09 (s)		7, 20
22	24.9	1.49 (s)		23
23	22.7	1.37 (s)		22
24	192.1			26, 30
25	135.3			27, 29
26, 30	128.8	7.16 (d, 8.0)	27, 28, 29	26, 28, 30
27, 29	128.0	7.29 (dd, 8.0)	26, 28, 30	27, 29
28	132.4	7.41 (d, 8.1)	26, 27, 29, 30	26, 30
31	29.7	2.60 (d,7.0)	32	
32	118.8	5.10 (t, 8.1)		31, 35
33	135.3			31, 35
34	26.1	1.70 (s)		
35	18.2	1.69 (s)		

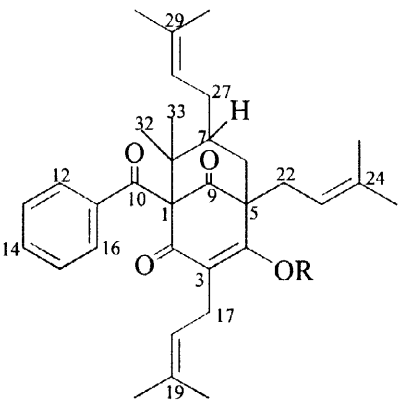
[a] ^{1}H correlating with ^{13}C resonance.

trihydroxybenzophenone. The NMR data indicated the presence of three isopentenyl groups. The IR spectrum of **4b** exhibited absorption bands due to the carbonyl of an enol ester (1783 cm^{-1}) and three ketones (1730, 1700 cm^{-1} and 1674 cm^{-1}). Similar IR bands were observed for **5b** (1774, 1729, 1697 and 1659 cm^{-1}). The foregoing data accounts for twelve of the requisite fourteen double bond equivalents which suggested that the isomers contain a bicyclic system.

The bicyclo[3.3.1]nonane structures of **4b** and **5b** and the location of the functionalities and ligands were deduced from the NMR data (Table 3). This skeleton is the most frequently encountered among the bridged bicyclic prenylated benzophenone derivatives of the Guttiferae [6].



4a R = H
4b R = CH_3CO



5a R = H
5b R = CH_3CO

HMBC connectivities enabled differentiation between the two isomers. For **4b** there were cross peaks between the carbonyl group at C-2 (δ 197.5) and the protons at C-8, C-10 and C-15, while the enol carbon C-4 (δ 158.8) showed correlations only to the C-15 protons. For **5b** the enol carbon C-4 (δ 163.3) showed correlations to the C-6, C-17 and C-22 protons, while the carbonyl at C-2 (δ 194.2) showed correlations only to the C-17 protons.

Plukenetione D and plukenetione E are a new tautomeric pair of prenylated benzophenone derivatives based on the bicyclo[3.3.1]nonane-2,4,9-trione system. Plukenetione D is closely related to nemorosonone, isolated from *Clusia nemorosa* [11], differing only in the position of the *gem*-dimethyl group on the bicyclononane.

The regioisomeric pair plukenetione F (**6**) and plukenetione G (**7**) were isolated as yellow oils. The molecular formula of each was determined to be $C_{33}H_{40}O_4$ by HREIMS, requiring fourteen degrees of unsaturation. The NMR data (Table 4) provided evidence for an unsubstituted benzoyl group, a 2,2-dimethyl-2H-pyran moiety, three carbonyls and two isopentenyl groups. The absence of further evidence of unsaturation suggested that the

Table 3

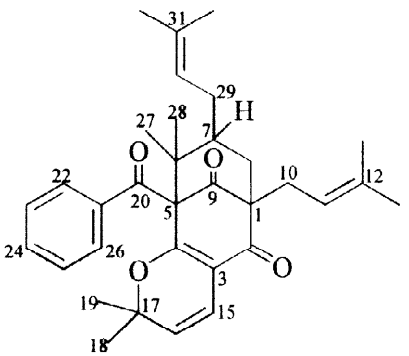
NMR Data of Plukenetione D acetate (**4b**) and Plukenetione E acetate (**5b**) in $CDCl_3$

Pos.	^{13}C (**4**)	^{1}H (J, Hz) (**4**)	Pos.	^{13}C (**5**)	^{1}H (J Hz) (**5**)
1	64.3		1	77.7	
2	197.5		2	194.2	
3	130.9		3	132.8	
4	158.8		4	163.3	
5	71.8		5	55.9	
6	50.0		6	37.4	2.16 (dd, 7.5,14.5) 2.40 (d,14.5)
7	48.3	1.46 (m)	7	48.0	1.52 (m)
8	42.1	2.11 (m) 2.22 (dd,1.5, 13,3)	8	50.2	
9	208.5		9	206.7	
10	30.3	2.47 (dd, 8.8,15.5) 2.62 (dd, 8.8,15.5)	10	193.0	
11	119.0	4.95 (t, 7.3)	11	136.4	
12	135.1		12, 16	128.4	7.49 (dd,1.0, 8.3)
13	26.1	1.65 (s)	13, 15	128.1	7.27 (dd, 7.6, 8.3)
14	18.2	1.67 (s)	14	132.1	7.40 (dt, 7.5)
15	24.9	2.82 (dd, 8.8,15.5) 3.22 (dd, 8.8,15.5)	17	24.3	2.84 (dd, 7.7,14.5) 3.02 (dd, 7.7, 14.5)
16	118.4	4.83 (m)	18	118.2	4.92 (dt,1.2, 6.4)
17	134.2		19	133.8	
18	25.8	1.62 (s)	20	25.7	1.57 (s)
19	17.7	1.52 (s)	21	17.9	1.57 (s)
20	193.2		22	30.4	2.45 (dd, 7.0, 15.5) 2.51 (dd, 7.0, 15.5)
21	137.0		23	119.2	5.16 (dt, 1.0, 6.2)
22, 26	129.0	7.58 (dd,1.4, 8.3)	24	134.1	
23, 25	127.7	7.26 (dd, 7.6, 8.3)	25	26.0	1.71 (s)
24	132.2	7.44 (dt, 1.4, 7.6)	26	18.0	1.65 (s)
27	27.1	1.33 (s)	27	29.9	2.14 (m)
28	23.3	1.48 (s)	28	125.2	5.02 (dt, 1.4, 7.1)
29	29.7	2.10 (m) 2.34 (d,15.5)	29	131.9	
30	124.6	4.83 (m)	30	25.8	1.69 (s)
31	132.9		31	17.7	1.56 (s)
32	25.8	1.67 (s)	32	26.6	1.36 (s)
33	17.9	1.54 (s)	33	22.0	1.44 (s)
$CH_3\underline{C}O$	164.1		$CH_3\underline{C}O$	166.7	
$\underline{C}H_3CO$	20.9	1.93 (s)	$\underline{C}H_3CO$	20.6	2.26 (s)

[a] ^{1}H correlating with ^{13}C resonance.

molecules contained two further rings. Comparison of the spectra with those of **4b** and **5b** suggested similar bicyclo[3.3.1]nonane moieties. The position of the 2,2-dimethyl-2H-pyran ring in each regioisomer was determined from the HMBC spectra.

For **6**, cross peaks were observed between the carbonyl carbon at C-2 (δ 192.0) and the protons at C-8 and C-10. The quaternary carbon C-4 (δ 168.2), ascribed to an enol ether, showed connectivity only to the vinylic hydrogen H-15. For **7**, C-4 (δ 170.9) displayed correlations to protons at C-6, C-17 and C-22. The unusually high field signal observed for the C-19 methyl hydrogens (δ 0.54) for plukenetione F (**6**) may be due to shielding effects from the unsubstituted phenyl group. This effect is absent in plukenetione G (**7**).



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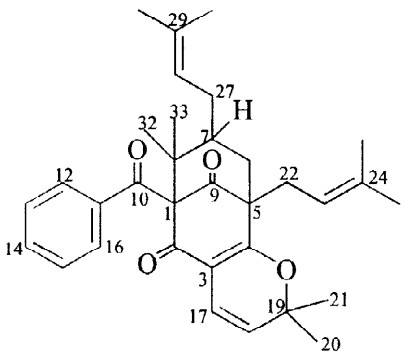

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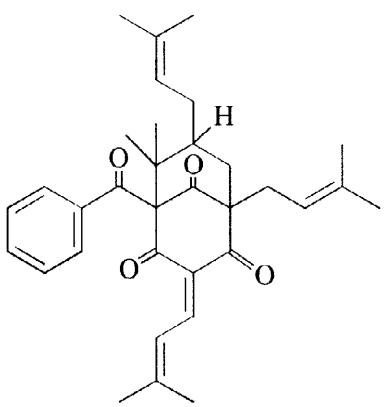
Plukenetione F and plukenetione G were well resolved by TLC in several solvent systems but when separated the individual regioisomers equilibrated, over a period of about twelve hours, to a mixture of **6** and **7**. The isomers were therefore sufficiently stable in solution for the structures to be determined promptly after separation. Although no special precautions were taken, e.g. use of acid free glassware, this equilibration appeared to be spontaneous and is likely to entail the quinone-methide intermediate **7a**.

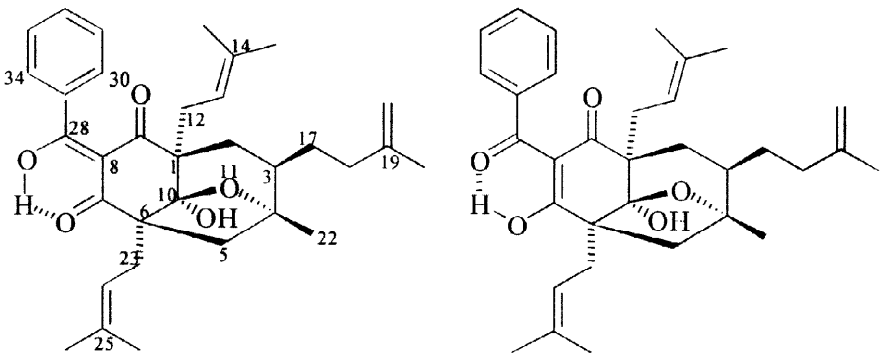


7a

Table 4
NMR Data of Plukenetiones F and G (**6** and **7**) in $CDCl_3$

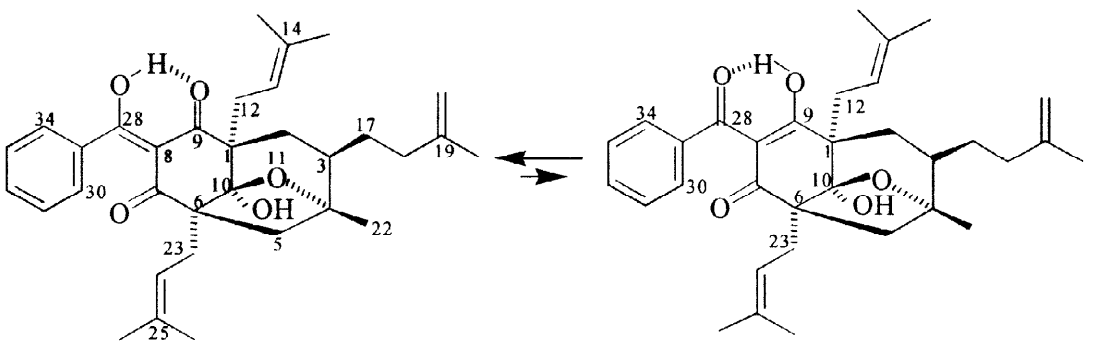
Pos.	^{13}C (**6**)	^{1}H (J, Hz) (**6**)	Pos.	^{13}C (**7**)	^{1}H (J, Hz) (**7**)
1	63.8		1	77.7	
2	192.0		2	192.0	
3	112.5		3	113.9	
4	168.2		4	170.9	
5	70.8		5	55.9	
6	50.0		6	39.6	2.16 (dd, 7.5, 15.0)
					2.26 (d, 15.0)
7	48.5	1.50 (m)	7	48.2	1.52 (m)
8	40.9	2.10 (m)	8	50.0	
		2.19 (dd, 7.3, 13.4)			
9	207.5		9	206.8	
10	30.0	2.51 (dd, 7.3, 14.0)	10	193.2	
		2.59 (dd, 7.3, 14.0)			
11	119.5	5.07 (t, 6.9)	11	136.6	
12	134.5		12, 16	128.2	7.56 (d, 8.0)
13	26.0	1.68 (s)	13, 15	127.9	7.27 (dd, 8.0, 8.0)
14	18.2	1.70 (s)	14	132.0	7.40 (t, 8.0)
15	114.8	6.46 (d, 10.0)	17	115.7	6.44 (d, 10.0)
16	124.0	5.24 (d, 10.0)	18	124.2	5.41 (d, 10.0)
17	83.4		19	82.5	
18	30.4	1.39 (s)	20	29.2	1.55 (s)
19	28.3	0.54 (s)	21	28.4	1.43 (s)
20	193.2		22	30.2	2.51 (d, 7.5)
21	136.8		23	119.7	5.03 (t, 8.3)
22,26	128.5	7.62 (d, 6.9)	24	133.9	
23,25	128.0	7.29 (dd, 6.9, 8.6)	25	26.1	1.67 (s)
24	132.2	7.43 (t, 8.6)	26	18.2	1.68 (s)
27	27.3	1.40 (s)	27	29.9	1.98 (m)
28	23.5	1.52 (s)	28	125.1	4.95 (t, 8.3)
29	29.7	2.11 (m)	29	132.2	
		2.30 (m)			
30	124.8	4.86 (t, 6.9)	30	26.0	1.67 (s)
31	132.8		31	18.2	1.55 (s)
32	25.8	1.67 (s)	32	26.8	1.34 (s)
33	18.0	1.51 (s)	33	22.5	1.47 (s)

Xerophenones A and B, a tautomeric pair of prenylated benzophenone derivatives containing the 11-oxatricyclo[4.3.1.1^{4,10}]undecane-7,9-dione system, isolated from *C. portlandiana*, were assigned structures **8** (major tautomer in $CDCl_3$, 80%) and **9** (minor tautomer in $CDCl_3$, 20%) with the proviso that the C-8—C-28 double bond isomer **10a** was a



8 **9**

possible structure for the major tautomer [1]. The main reason for choosing structure **8** as the major tautomer was that the interconversion of **8** and **9** would require less rearrangement than interconversion of **10a** and **9**.



10a **10b**

The enolic protons of the xerophenone tautomeric mixture have extremely low field signals (δ 17.29, 17.83) (Table 5). These fall in the range predicted for low barrier hydrogen bonds which have been claimed to be responsible for the efficiency of enzyme catalysis [12-14]. The current debate over low barrier hydrogen bonds [15,16] prompted us to re-examine the structures of the xerophenone tautomers.

The occurrence of two enolic signals in the ^{1}H NMR spectrum of this tautomeric pair indicates a double well potential due to a slow tautomeric equilibrium. If the tautomeric equilibrium involves structures **8** and **9**, this would conclusively confirm that low field OH shifts are not diagnostic of low barrier hydrogen bonds [17]. However, careful analysis of the

Table 5
NMR Data for Xerophenones A and B (**10a** and **9**) in $CDCl_3$

Pos.	^{13}C (**10a**)	^{1}H (J, Hz) (**10a**)	HMBC[a] (**10a**)	^{13}C[b] (**9**)	^{1}H[b] (**9**)
1	52.6		2, 12	54.7	
2	37.8	β1.10 dd (12.0,14.5)			
		α1.98 dd (5.0, 14.0)			
3	39.7	1.62 m	2α, 5α, 5β, 17, 22		
4	82.4		2α, 22	82.1	
5	40.5	α1.78 m	22, 23	41.9	2.33 d
		β2.16 d (14.0)			2.74
6	60.7		OH, 5β, 23		
7	199.7		5β, 23	197.6	
8	110.1		enol H	109.6	
9	203.6		12, enol H		
10	104.7		OH, 2α, 5β, 22	104.8	
12	27.4	2.63 m	2β		
		2.90 dd (8.6, 15.6)			
13	121.4	5.64 dd (7.1, 8.0)	12, 15, 16	122.0	
14	136.6		12, 15, 16	137.5	
15	26.2	1.77 s			
16	18.2	1.78 s	13, 15		
17	28.0	0.90 m			
		1.50 m			
18	35.0	1.80 m	20, 21	35.0	
		1.95 m			
19	144.9		21		
20	110.5	4.61 s	18, 21	110.5	4.64 s
		4.69 s			4.71 s
21	22.3	1.65 s	18, 20	22.2	
22	24.7	1.33 s	5α	24.7	1.39 s
23	34.7	2.49 dd (6.2, 14.6)	5β	34.7	
		2.62 m			
24	120.0	5.42 dd (6.3, 7.4)	23, 26	120.5	
25	135.2		26, 27	135.4	
26	26.2	1.77 s	24		
27	18.1	1.70 s	24		
28	191.9		30, 34, enol H	199.7	
29	135.0		31, 33, enol H	135.2	
30,34	128.3	7.48 d (7.3)	30, 32, 34	128.5	7.44
31,33	127.9	7.38 dd (7.3,7.3)	31, 33	127.7	7.42
32	131.9	7.50 d (7.3)	30, 34	132.0	7.53
OH		4.19 s			4.12 s
Enol H		17.83 s			17.29 s

[a] ^{1}H correlating with ^{13}C resonance.
[b] Resonances not given overlapped with those of **9**.

nOe associations and HMBC connectivities in the benzoyl portion of the major tautomer of the xerophenone mixture has necessitated revision of the structure from **8** to **10a**. Irradiation of the enolic proton gave a weak nOe of H-12 while irradiation of the *ortho* protons gave a similarly weak nOe of H-23. These are approximately 1.0% in each case but would not be expected for structure **8**. A cross-section through the enolic OH in the HMBC spectrum showed cross-peaks not only to C-8, C-28 and C-29, but also to C-9. We are unable to conclude whether this indicates a single well potential with partial bonding of the hydrogen to the oxygens at C-9 and C-28 or to a rapid tautomeric equilibrium (double well potential) between **10a** and **10b**. The stronger intensity of the OH→C-8 peak is consistent with either possibility as OH→C-8 is a 3-bond pathway in each case. A third explanation is that the structure is **10a** and the OH→C-9 cross-peak is due either to a four-bond or a "through space" coupling. The absence of an enolic OH→C-1 cross-peak fits the latter explanation and structure **10a**. The assignment of structure **9** to the minor tautomer remains unchanged.

EXPERIMENTAL

General Experimental

Melting points were determined on a Thomas-Hoover melting point apparatus. Ultraviolet (UV) spectra were recorded on a Perkin Elmer UV/VIS/NIR Lambda 19 spectrophotometer. Infrared spectra were recorded on a FT-IR SPECTRUM 1000 spectrometer with NaCl discs or as KBr pellets. Mass spectral data (EI) were determined at an ionizing voltage of 70 eV on a Micromass 70-250S spectrometer. Optical rotations were measured using a Perkin-Elmer model 241MC or 243B polarimeter using a 1 cm or 10 cm cell. NMR data were recorded on a Varian UNITY-500 spectrometer equipped with a 5 mm inverse detection probe with deuterochloroform ($CDCl_3$) as solvent and tetramethylsilane (TMS) as internal standard. Column chromatography was performed using Whatman silica gel (60Å 230-400 mesh). Analytical thin layer chromatographic (TLC) analyses were carried out using Whatman polyester or aluminium backed plates precoated with silica gel UV_{254} (0.25 mm).

Plant material

Fruit of *Clusia plukenetii* Urban were collected at St. Thomas in Barbados in April 1996. Aerial parts of *C. portlandiana* Howard & Proctor were collected in Ecclesdown, Portland, Jamaica in June 1994. Voucher specimens of both species were deposited in the herbarium, UWI, Mona, Jamaica; a specimen of *C. plukenetii* is also lodged in the herbarium, UWI, Cave Hill, Barbados.

Isolation of Compounds 2-7

Dried, ground fruits of *C. plukenetii* (1 kg) were exhaustively extracted by cold percolation with hexanes. Evaporation of the hexanes *in vacuo* gave a viscous reddish-brown oil (262 g, 26.2%), a portion of which (19.7 g) was chromatographed using a Me_2CO-hexane gradient. The fraction eluted with 5% Me_2CO-hexane was subjected to repeated column chromatography using Me_2CO-hexanes mixtures and finally 10% EtOAc-hexanes to afford plukenetione B (**2**) (8.3 mg) and plukenetione C (**3**) (15 mg) as colourless oils.

A second portion of the hexane extract (21.6 g) was chromatographed using a Me_2CO-hexanes gradient (5-15%). The fraction eluted with 10% Me_2CO-hexanes was further chromatographed using 4% Me_2CO-hexanes to afford a mixture (1.56 g) which was acetylated using Ac_2O/pyridine to afford a brown oil (1.53 g) which was chromatographed with 5% EtOAc-hexane as eluent to afford plukenetione D acetate (**4**) (31 mg) and plukenetione E acetate (**5**) (153 mg) as colourless oils.

The fraction eluted with 5% Me_2CO-hexanes was subjected to repeated column chromatography to afford a yellow oil (167 mg). A portion of the oil was dissolved in EtOH (3 mL), and the EtOH solution was treated with an excess of 2,4-dinitrophenylhydrazine. After concentration the resulting orange solid was chromatographed with 1.5% EtOAc-hexanes to afford a yellow oil, plukenetione F (**6**) (3 mg), which was not the 2,4-dinitrophenylhydrazone derivative.

The fraction eluted with 15% Me_2CO-hexanes was chromatographed with 10% EtOAc-hexanes to afford a yellow semi-solid, which was further purified by gravity column chromatography with 3% EtOAc-hexanes to afford a yellow oil, plukenetione G (**7**) (1.6 mg).

Plukenetione B (2): colourless oil; $[\alpha]_D$ +17.2° (c 0.029, $CHCl_3$); UV (EtOH), λ_{max} nm (log ε): 246 (3.82); IR ν_{max} cm^{-1} (KBr): 3565, 1732, 1702, 1699, 1683; ^1H NMR (500 MHz), ^{13}C NMR (125 MHz): Table 1; EIMS *m/z* (rel. int.): 518 $[M]^{+\cdot}$ (4), 503 (11), 490 (9), 472 (9), 457 (11), 431 (7), 413 (6), 363 (8), 309 (8), 105 (100), 77 (37), 69 (21), 59 (35); HREIMS: 518.3023 $[M]^{+\cdot}$, (calcd. for $C_{33}H_{42}O_5$, 518.3032).

Plukenetione C (3): colourless oil; $[\alpha]_D$ +65.9° (c 0.13, $CHCl_3$); UV (EtOH), λ_{max} nm (log ε): 246 (3.98); IR ν_{max} cm^{-1} (NaCl): 3579-3375, 1732, 1702, 1698, 1682; ^1H NMR (500 MHz), ^{13}C NMR (125 MHz): Table 2; EIMS *m/z* (rel. int.): 550 $[M]^{+\cdot}$ (1), 518 (6), 417 (6), 381 (26), 365 (9), 309 (8), 105 (100), 77 (42), 69 (27), 59 (55); HREIMS: 550.2907 $[M]^{+\cdot}$, (calcd. for $C_{33}H_{42}O_7$, 550.2930).

Plukenetione D acetate (4b): colourless oil; $[\alpha]_D$ +34.5° (c 0.029, $CHCl_3$); UV (EtOH), λ_{max} nm (log ε): 250 (4.29); IR ν_{max} cm^{-1} (NaCl): 1783, 1730, 1700; ^1H NMR (500 MHz), ^{13}C NMR (125 MHz): Table 3; HMBC correlations (C#→H#) 1→8,10,11, 2→8,10,15, 3→15, 4→15,

5→27,28, 6→8,27,28, 7→8,27,28,29, 8→10,29, 9→8,10, 11→10,13,14, 12→10,13,14, 14→11, 16→15,18,19, 17→15,18,19, 18→16, 19→16, 20→22,26, 21→23,25, 22,26→22,24,26, 23,25→23,25, 24→22,26, 27→28, 28→27, 29→8, 30→29,32, 31→29,32,33, 32→30, 33→30,32; EIMS *m/z* (rel. int.): 544 $[M]^{+\cdot}$ (2), 502 (20), 433 (50), 365 (23), 309 (95), 295 (26), 105 (100), 77 (36), 69 (54); HREIMS: 544.3179 $[M]^{+\cdot}$, (calcd. for $C_{35}H_{44}O_5$, 544.3189).

Plukenetione E acetate (5b): colourless oil; $[\alpha]_D$ -37.6° (c 0.117, $CHCl_3$); UV (EtOH), λ_{max} nm (log ε): 245 (4.16); IR ν_{max} cm^{-1} (KBr): 1774, 1729, 1697; ^1H NMR (500 MHz), ^{13}C NMR (125 MHz): Table 3; HMBC correlations (C#→H#) 1→7,32,33, 2→17, 3→17, 4→6,17,22, 5→6,7,22,23, 6→7,22, 7→6,28,32,33, 8→6,7,32,33, 9→6,22, 10→12,16, 11→13,15, 12,16→12,14,16, 13,15→13,15, 14→12,16, 17→18, 18→17,20,21, 19→17,20,21, 20→18, 21→18, 22→23, 23→22,25,26, 24→22,25,26, 25→23,26, 26→23, 27→6,7,28, 28→7,30,31, 29→30,31, 30→28, 31→28, 32→33, 33→32; EIMS *m/z* (rel. int.): 544 $[M]^{+\cdot}$ (2), 501 (1), 475 (19), 433 (10), 351 (46), 309 (100), 295 (26), 105 (97), 77 (30), 69 (35); HREIMS: 544.3177 $[M]^{+\cdot}$, (calcd. for $C_{35}H_{44}O_5$, 544.3189).

Plukenetione F (6): yellow oil, $[\alpha]_D$ -53.6° (c 0.028, $CHCl_3$); UV (EtOH), λ_{max} nm (log ε): 247 (3.98), 324 (3.32); IR ν_{max} cm^{-1} (KBr): 1723, 1704, 1652; ^1H NMR (500 MHz), ^{13}C NMR (125 MHz): Table 4; HMBC correlations (C#→H#) 1→8,10, 2→8,10, 3→16, 4→15, 5→27,28, 6→8,27,28, 7→8,27,28, 9→8,10, 12→10,13, 14→11,13, 16→18,19, 17→15,16,18,19, 18→19, 19→18, 20→22,26, 21→23,25, 22,26→22,24,26, 23,25→23,25, 24→22,26, 27→28, 28→27, 29→8, 30→32,33, 31→29, 32→30,33, 33→30,32; EIMS *m/z* (rel. int.): 500 $[M]^{+\cdot}$ (44), 500 (12), 485 (8), 472 (10), 432 (37), 417 (68), 363 (27), 349 (14), 309 (48), 293 (28), 105 (100), 77 (39), 69 (36); HREIMS: 500.2929 $[M]^{+\cdot}$, (calcd. for $C_{33}H_{40}O_4$, 500.2927).

Plukenetione G (7): yellow oil; UV (EtOH), λ_{max} nm (log ε): 247 (4.17), 324 (3.59); IR ν_{max} cm^{-1} (KBr): 1723, 1700, 1648; ^1H NMR (500 MHz), ^{13}C NMR (125 MHz): Table 4; HMBC correlations (C#→H#) 1→32,33, 3→18, 4→6,17,22, 5→6,22, 6→22,27, 7→6,27,32,33, 8→6,7,32,33, 9→6,22, 10→12,16, 12,16→12,14,16, 14→12,16, 18→20,21, 19→17,18,20,21, 20→21, 21→20, 23→22,26, 24→22,25,26, 25→23,26, 26→23,25, 27→6, 28→27,30,31, 29→27,30,31, 30→28,30, 31→28,30, 32→33, 33→32; EIMS *m/z* (rel. int.): 500 $[M]^{+\cdot}$ (44), 500 (4), 485 (4), 432 (19), 417 (38), 363 (18), 309 (35), 293 (24) 149 (24), 105 (100), 77 (32), 69 (45); HREIMS: 500.2947 $[M]^{+\cdot}$, (calcd. for $C_{33}H_{40}O_4$, 500.2927).

Isolation of Compounds 10a and 9

Dried ground leaves and twigs of *C. portlandiana* (630 g) were exhaustively extracted by cold percolation with hexanes. Evaporation of the extract gave a yellow-brown gum (14 g, 2.2%) which was chromatographed using a Me_2CO-hexanes gradient. The fraction eluted with

40% Me_2CO-hexanes was subjected to repeated chromatography, again using Me_2CO-hexanes mixtures. Combination of fractions eluting with 5% Me_2CO-hexane gave a solid which was recrystallized from hexanes to afford the xerophenone tautomeric mixture **10a** and **9**, (13 mg).

Xerophenone A and B (10a and 9): white needles, mp 172-173°; $[\alpha]_D$ -36.4° (Me_2CO, c 0.055); UV (MeOH), λ_{max} nm (log ε): 296 (5.10), 243 (4.98), 201 (5.30); IR ν_{max} cm^{-1} (KBr): 3500-3100, 1648, 1635; ^1H NMR (500 MHz), ^{13}C NMR (125 MHz): Table 5; EIMS *m/z* (rel. int.): 518 $[M]^{+\cdot}$ (44), 500 (13), 450 (6), 431 (6), 413 (9), 381 (6), 353 (7), 311 (17), 295 (6), 255 (10), 198 (8), 177 (6), 147(6), 105 (100), 95 (17), 77 (21), 69 (47); HREIMS: 518.3033 $[M]^{+\cdot}$, (calcd. for $C_{33}H_{42}O_5$, 518.3032).

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