Pergamon

Tetrahedron Letters, Vol. 37, No. 48, pp. 8663-8666, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)02004-7

Plukenetione A. An Unusual Adamantyl Ketone from *Clusia plukenetii* (Guttiferae)

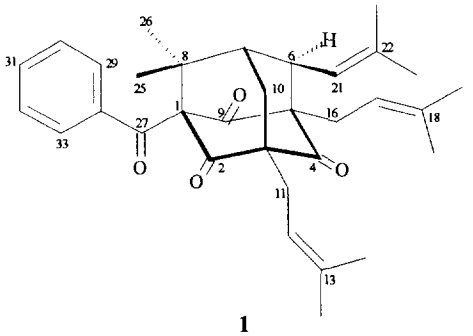
Geneive E. Henry and Helen Jacobs*
Department of Chemistry, University of the West Indies, Mona, Kingston 7, Jamaica

C.M. Sean Carrington
Department of Chemical and Biological Sciences, University of the West Indies, Cave Hill, Barbados

Stewart McLean and William F. Reynolds*
Department of Chemistry, University of Toronto, Toronto, Canada, M5S 1A1

Abstract: The structure of plukenetione A from *Clusia plukenetii* Urban has been shown by spectroscopic methods to be 1-benzoyl-8,8-dimethyl-3,5-bis(3-methyl-2-butenyl)-6-(2-methylpropenyl)tricyclo[3.3.1.1^{3,7}]decane-2,4,9-trione.

Guttiferous plants produce a series of 2,4,6-trihydroxybenzophenone derivatives of mixed shikimate and acetate biogenesis.[1] The acetate-derived trihydroxy aromatic ring is usually chromenylated or otherwise prenylated.[1,2] In a few cases, all from the subfamily Clusioideae, this ring is non-aromatic and C_5/C_{10} alkylation has resulted in the formation of complex bridged bicyclic or tricyclic systems.[1,3] Both the simple and complex compounds display a wide range of biological activity,[1,4] making the family an attractive target for phytochemical study. In this context we have examined extracts of *Clusia plukenetii*, a plant endemic to the Lesser Antilles and which occurs commonly in Barbados.[5]



1

Fractionation of the hexane extract of the fruit[6] afforded plukenetione A **1** (0.012%) as a colorless amorphous solid with the following physicochemical and spectral characteristics: $[\alpha]_D$ +1° (c. 0.77, $CHCl_3$); IR (film) υ_{max} 1742, 1703, 1699, 1685 cm^{-1}; UV (EtOH) λ_{max} (log ε) 246 (3.85), 206 (4.15) nm; HRMS [$M^{+\cdot}$] 500.2934, calcd. for $C_{33}H_{40}O_4$, 500.2927; ^{1}H and ^{13}C NMR, Table 1.

The molecular formula, and evidence from the NMR (Table 1) and mass spectrum (m/z 77, base peak at m/z 105) for an unsubstituted phenyl ketone, indicated that **1** is a trihydroxybenzophenone derivative incorporating four five-carbon units. It was also apparent that the tri-oxygenated ring is non-aromatic, with

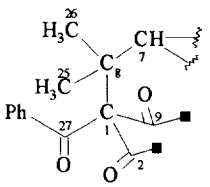
Table 1. NMR Data for Plukenetione A (1)[a]

Carbon	δC[b]	δH[b c d]	HMBC[e]
1	82.13		25, 26
2	202.21		10, 11
3	68.66		10, 11
4	203.28		6, 10, 11
5	71.88		6, 16, 17, 21
6	51.57	3.63 (9.3, 2.7, 2.5)	10, 16, 21
7	48.74	1.58[f]	6, 10, 25, 26
8	54.96		10, 25, 26
9	201.81		16
10	40.53	2.45 (13.7, 2.7, 2.7)	6, 11
		2.47 (13.7, 2.7)	
11	27.67	2.52 (7.3)	
12	118.44	5.19 (7.3, 1.5)	11, 14, 15, 16
13	134.94		11, 12, 14, 15
14	25.98	1.70	12, 15
15	18.05	1.67	12
16	26.45	2.39 (7.1)	
17	118.33	5.08 (7.1, 1.4)	19
18	134.61		16, 19, 20
19	25.98	1.64	20
20	17.95	1.57	21
21	119.49	5.00 (9.3, 1.4)	6, 23, 24
22	137.02		6, 23, 24
23	26.09	1.75	
24	17.86	1.59	21, 23
25	22.90	1.45	26
26	23.26	1.54	25
27	193.24		29, 33
28	134.87		30, 32
29, 33	129.11	7.18 (8.3)	29, 31, 33
30, 32	127.85	7.27 (8.3, 8.3)	32, 30
31	132.26	7.41 (8.3)	29, 33

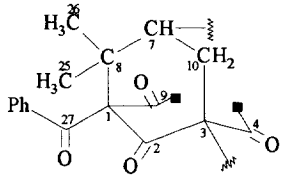
[a]recorded for a $CDCl_3$ solution of 1 on a Varian UNITY-500 spectrometer equipped with a 5mm inverse detection probe; [b]chemical shifts in ppm from TMS; [c]J_{HH} in brackets; [d]direct ^1H-^{13}C connectivities established by HMQC; [e]protons correlating with carbon resonance; [f]H-H couplings obscured by overlap with CH_3 singlets.

three ketones tetrasubstituted at all α positions. These conclusions are based on ^{13}C NMR signals for three nonconjugated carbonyls (δ 203.28. 202.21, 201.81) and the absence of a ^{1}H NMR peak (even in a spectral window of 20 ppm) attributable to a hydrogen-bonded enolic proton, a common feature in these systems.[3b] In addition to the phenyl ketone, other readily identifiable pendant residues were: (a) the gem-dimethyl group (C-25 and C-26) correlating by HMBC to each other and to C-8 on the main skeleton; (b) two 3-methyl-2-butenyl groups (C-11 to C-15 and C-16 to C-20) both linked to the basic skeleton at quaternary positions; (c) the 2-methylpropenyl group (C-21 to C-24);

The structure of the tricyclic core of the molecule was determined by tracing the connectivities shown in the HMBC spectra. Starting with the gem-dimethyl at C-8, cross peaks were observed between protons of both methyl groups and: (a) the quaternary carbon signal at δ 82.13 (C-1) which, from its deshielded position, had to be flanked by three carbonyl groups (shown as C-2, C-9 and C-27); (b) the methine carbon at δ 48.74 (C-7) establishing the structure of the fragment **2**.



2



3

Cross peaks between the quaternary carbon bearing the gem-dimethyl group, C-8 (δ 54.96), and the methylene protons at δ 2.45 and 2.47 necessitated their being in a 3-bond relationship, attached to C-10. Correlation of these protons with the quaternary carbon signal at δ 68.66 (C-3, α to two carbonyls, C-2 and C-4) and with the two carbonyls established C-10 as the sixth carbon in the ring comprised of carbons 3, 2, 1, 8, 7 and 10 on the left hand side of the tricycle and led to the formulation of fragment **3**.

The methine proton at δ 3.63 which correlated with signals for two already assigned core carbons C-7 and C-10, one carbonyl (δ 203.28) and the α carbon at δ 71.88 was placed at the position designated C-6 in **1**. The latter two carbons were assigned to positions 4 and 5, as shown, on the biogenetically based assumption that they are respectively three and two bonds away from the proton. This completed the structure of the tricycle.

Proof that the three protonated carbons in the core of **1** are contiguous was provided by the ^{1}H-^{1}H COSY spectrum which showed correlations between H-6 (δ 3.63) and H-7 (δ 1.58) and between H-7 and the H-10 methylene protons (δ 2.45, 2.47). In addition, H-6 shows a 4-bond W-coupling (J = 2.7 Hz) to the C-10 (δ 2.45) proton.

The 3-methyl-2-butenyl groups were assigned to positions 3 and 5; each allylic methylene group showed an HMBC cross peak to one bis-α carbon, CH_2-11 (δ 2.52) to C-3 (δ 68.66) and CH_2-16 (δ 2.39) to C-5 (δ 71.88). CH_2-16 also displays a strong nOe interaction with H-6. This C-6 methine proton is directly coupled (J = 9.3 Hz) to the C-21 vinyl proton, making C-6 the point of attachment of the 2-methylpropenyl group.

The stereochemistry at H-6 was determined by: (a) the W-coupling to H-10; (b) the observation of a strong H-6/C-4 HMBC peak and a very weak H-6/C-9 peak indicating an *anti* arrangement of C-4 and H-6; (c) an nOe interaction of H-6 with the C-26 methyl protons (a similar interaction was observed between the C-25 methyl and the W-coupled C-10 proton, further confirming the geminal methyl assignments).

Plukenetione A **1** is almost symmetric. Carbons 4, 7, 8, 1, 27, 28 and 31 lie in a plane about which the symmetry is perturbed only by the 2-methylpropenyl group at C-6; the corresponding position on the opposite side of this plane is occupied by the C-10 methylene group. This symmetry provides a rationale for the small specific rotation. Also of interest in this regard is the magnetic equivalence of the individual protons of the methylene pairs at C-11 (δ 2.52) and C-16 (δ 2.39).

Plukenetione A **1** is biogenetically derivable from the proposed precursor of the bridged polyisoprenylated benzophenone derivatives from Guttiferae.[1,7] It shows a number of structural features not encountered previously in the series. To our knowledge this is the first report of an adamantyl derivative as a plant metabolite.

Acknowledgements: We thank Mr. Wesley Taylor for assistance with plant collection. Financial support from the University of the West Indies Board for Postgraduate Studies, the Canada-UWI Institutional Strengthening Project and the Natural Sciences and Engineering Research Council of Canada is gratefully acknowledged.

References and Notes

1. Bennett, G.J.; Lee, H-H. *Phytochem.* **1989**, *28*, 967-998.
2. Martinez Olivares, E.; Gonzalez Gonzalez, J.; Delle Monache, F. *Phytochem.* **1994**, *33*, 473-475.
3. (a) Delle Monache, F.; Delle Monache, G.; Gacs-Baitz, E. *Phytochem.* **1991**, *30*, 2003-2005. (b) Henry, G.E.; Jacobs, H.; McLean, S.; Reynolds, W.F.; Yang, J-P. *Tetrahedron Lett.* **1995**, *36*, 4575-4578.
4. (a) Gustafson, K.R.; Blunt, J.W.; Munro, M.H.G.; Fuller, R.W.; McKee, T.C.; Cardinella, J.H.II; McMahon, J.B.; Cragg, G.M.; Boyd, M.R. *Tetrahedron* **1992**, *48*, 10093-10102. (b) Iinuma, M.; Tosa, H.; Tanaka, T.; Kanamaru, S.; Asai, F.; Kobayashi, Y.; Miyauchi, K.; Shimano, R. *Biol. Pharm. Bull.* **1996**, *19*, 311-314.
5. Carrington, S. *Wild Plants of Barbados*; Macmillan: London. 1993; pp. 69-70.
6. Collected in St. Thomas, Barbados, April 1996; specimens are deposited in the herbaria at the University of the West Indies, Mona and Cave Hill campuses, voucher #'s 33,674 and SC1781.
7. Delle Monache, F.; Delle Monache G.; Pinherio, R.M.; Radics, L. *Phytochem.* **1988**, *27*, 2305-2308.

(*Received in USA* 16 *September* 1996; *accepted* 7 *October* 1996)