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A 2-ACYLCYCLOHEXANE-1,3-DIONE FROM *VIROLA OLEIFERA*

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Key Word Index—*Virola oleifera*; Myristicaceae; leaves; polyketide; oleiferinone; 3,6β-dihydroxy-2-(13-phenyltridecanoyl)-2-cyclohexen-1-one; 2-acylarylcyclohexane-1,3-dione.

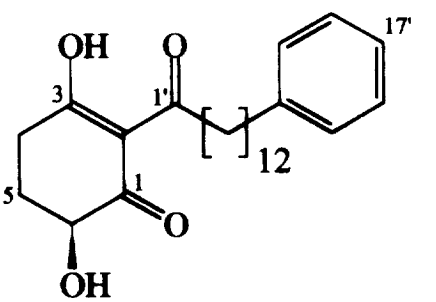
Abstract—A novel arylalkanone derivative, oleiferinone, has been isolated from the chlorophyll-free hexane fraction of the 95% ethanol extract from leaves of *Virola oleifera*. Its structure was deduced as 3,6β-dihydroxy-2-(13-phenyltridecanoyl)-2-cyclohexen-1-one, on the basis of the NMR techniques. © 1997 Elsevier Science Ltd

INTRODUCTION

Virola oleifera, ucuúba-branca, is endemic to the Atlantic Forest in the south-eastern region of Brazil and has been used in traditional 'caiçara' medicine in order to relieve gastric-intestinal disorders, as a wound-healing anti-inflammatory, and to stimulate memory and cerebral intelligence [1]. Previous chemical investigations of leaves from this species have shown the presence of lignan-7-ols, oleiferins A–C, a lignan-7-one (oleiferin-D), a 2,7′-cyclolignan-7-ol (oleiferin-E), besides the known compounds, galbacin, (+)-aristolignin and (+)-eupomatenoid-8 [2], two 7,7′-cyclolignans, verrucosin and galbulin, and otobafenol in the arils, and otobain, methyl-austrobailignan-6 and arylalkanones in the kernels [3]. In other studies [4], the absolute configurations for oleiferins A–C were established from acid-catalysed Friedel–Crafts-type cyclization and comparison of the spectral data, and optical rotations for known 2,7′-cyclolignans. Herein, we now report on the isolation and characterization of an arylalkanone, oleiferinone (**1**), from the chlorophyll-free hexane fraction of the 95% ethanol extract from the leaves of *V. oleifera*.

RESULTS AND DISCUSSION

The chlorophyll-free hexane fraction of the 95% ethanol extract from the leaves was separated by vacuum liquid chromatography [5]. After continuous preparative TLC separation, compound **1** was isolated as a pale amorphous yellow solid, mp 59.5–60°. It had a molecular formula of $C_{25}H_{36}O_4$ ([M]$^+$ at *m/z* 400), as determined by EI mass spectrometry, and its IR



1

spectrum contained absorptions due to hydroxyl groups at 3420 cm^{-1}, conjugated carbonyl (1665 cm^{-1}) and a conjugated chelated carbonyl group at 1546 cm^{-1}; its long-chain nature was revealed by the presence of bands at 2918, 2847, 1465 and 724 cm^{-1}. The UV spectrum exhibited maxima at 233 and 271 nm (log ε 4.08 and 4.14, respectively), indicating the presence of the cyclic polyketone group, 'β-triketone'. Adding base caused enhancement of the peak at 271 nm and disappearance of the peak at 233 nm, similar to those of acylcyclohexane-1,3-diones [6]. The ^{13}C NMR decoupled spectrum (Table 1) showed 25 lines in agreement with the molecular formula. DEPT pulse sequences allowed the determination of the hydrogenation pattern of each carbon, revealing five unsaturated non-hydrogenated carbons, including enol and two keto carbonyls [δ 195.0, 197.2 and 205.7], five unsaturated and one saturated methine, and 14 saturated methylenes. The ^{1}H NMR spectrum contained the signal of a H-bonded hydroxyl proton at exceptionally large downfield shift [δ 18.30 (1H, *sl*, OH-3)], consistent with the proposed six-membered ring structure [7], signals of an unsubstituted phenyl group [δ 7.02–7.20 (5H, *m*)], benzylic methylene signals [δ

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Table 1. ^1H and ^{13}C NMR assignments for compound **1**

C	^{13}C	HETCOR	COSY*
1	197.2	—	
2	110.0	—	
3	195.0	—	
4	31.0	2.74	
5	27.1	1.75	
		2.32	
6	71.3	3.95	
1′	205.7	—	
2′	39.9	2.90	
		3.03	
3′	24.4	1.60	
4′–11′	29.1, 29.2(2), 29.3, 29.4(3), 29.5	1.26	
12′	31.3	1.60	
13′	35.9	2.56	
14′	142.2	—	
15′, 19′	128.1	7.02–7.20	
16′, 18′	128.2		
17′	125.5		
OH-3	—	18.30	
OH-6	—	3.71	

* Observed ^1H-^1H correlations are connected by arrows.

2.56 (*t*, $J = 7.9$ Hz, H-13′)], α-methylene signals of a ketone [δ 2.90 (1H, *ddd*, $J = 6.5$, 8.5 and 16 Hz, H-2′a), δ 3.03 (1H, *ddd*, $J = 6.5$, 8.5 and 16 Hz, H-2′b)], signals of homobenzylic methylene and β-methylene protons of ketone [δ 1.60 (4H, *m*, H-3′ and H-12′)], and signals of alkyl polymethylene chain [δ 1.26 (16H, *sl*, H-4′–H-11′)]. Additionally, the substructure $\cdot CH_2 \cdot CH_2 \cdot CH(OH) \cdot$ incorporating a β-triketone system was established through a homonuclear COSY spectrum. The methylene signal at δ 2.74 (2H, *m*, H-4) was coupled with the diastereotopic protons at δ 2.32 (1H, *m*, H-5α) and δ 1.75 (1H, *ddt*, $J = 11$, 13 and 14 Hz, H-5β), which itself was coupled with the oxygenated methine signal at δ 3.95 (1H, *dd*, $J = 5.5$ and 13 Hz, H-6α), indicating that the isolated compound has the 2-acylcyclohexane-1,3-dione system [8]. ^{13}C-^1H HETCOR and further ^1H-^1H COSY correlations allowed assignments of the carbon resonance and the connectivity between the above-mentioned partial substructure (Table 1). Interestingly, the spin-system of H-2′a/b in **1** displayed two distinct signals (δ 2.90 and δ 3.03), indicating that free rotation of the side-chain is hindered, as a consequence of a hydrogen bond between the enolic proton and the carbonyl group. However, no direct evidence for the alternative positions of the enolic double bond is available. The relative stereochemistry of compound **1** was determined by the ^1H NMR spectrum. The large coupling constant ($J = 13$ Hz) between H-5 axial and H-6 indicates that OH-6 is equatorial. The EI mass spectrum was in agreement with the structure proposed from the ^1H and ^{13}C analyses. It exhibited the $[C{=}C(OH)CH_2CH_2CH(OH)COCOCH_2CH_2]^+$ fragment at *m/z* 183, accompanied by characteristic base peak at *m/z* 91. Hence, based on the accumulated evidence, the structure of oleiferinone, **1**, was elucidated as 3,6β-dihydroxy-2-(13-phenyltridecanoyl)-2-acylcyclohexen-1-one. While acyl- and acylaryl-resorcinols or phloroglucinols-type arylalkanones are well known in various species of *Virola*, *Knema* and *Myristica* [9, 10], compound **1** is distinguished by a 2-acylarylcyclohexane-1,3-dione system, which has been rarely reported in plants [11]. However, 2-acylcyclohexane-1,3-diones have been isolated from the larval mandibular glands of some Lepidoptera [12] and have a wide range of activity as kairomones [13]. Similar synthetic compounds have been described as insecticidal, fungicidal and possessing antibiotic properties [14].

EXPERIMENTAL

General. Mp: uncorr. ^1H and ^{13}C NMR: 300 and 75.5 MHz, respectively, using TMS as int. standard. IR: KBr pellet. EIMS: 70 eV.

Plant material. Leaves of *V. oleifera* (Schott) A. C. Smith were collected by Dr Gentil Gody (Reserva Florestal Atlântica, Ubatuba, SP, Brazil) in May 1990, and authenticated by Dr Jorge Tamashiro (Departamento de Botânica, Universidade Estadual de Campinas-UNICAMP, Campinas, SP, Brazil). A voucher specimen is deposited in the Herbarium of Unicamp.

Isolation. In order to eliminate chlorophylls and other colouring matter, air-dried powdered leaves were extracted with 95% EtOH. The deep green leaf extract (24 g) was dissolved in MeOH and H_2O was added in order to reach a 7:3 ratio. The resulting soln was filtered off over a layer of prewashed Celite. Hexane was used to partition the MeOH–H_2O soln, yielding a yellowish fr. The chlorophyll-free hexane fr. (2.7 g) was fractionated by vacuum LC [5] over silica gel H (40 μm) using hexane and hexane–EtOAc mixts of increasing polarity, to yield **1** (6 mg).

3,6β-Dihydroxy-2(13-phenyltridecanoyl)-2-cyclohexen-1-one (**1**). Pale amorphous yellow solid, mp 59.5–60° (hexane). IR ν_{max} cm^{-1}: 3420, 2918, 2847, 1665, 1546, 1465, 1404, 1114, 755, 724, 704. UV λ_{max}^{MeOH} nm (log ε): 233 (4.08), 271 (4.14); +NaOH: 265 (4.2). ^1H NMR (300 MHz, CCl_4) δ: 1.26 (16H, *sl*, H-4′–H-11′), 1.60 (4H, *m*, H-3′ and H-12′), 1.75 (1H, *ddt*, $J = 11$, 13 and 14 Hz, H-5β), 2.32 (1H, *m*, H-5α), 2.56 (2H, *t*, $J = 7.9$ Hz, H-13′), 2.74 (2H, *m*, H-4), 2.90 (1H, *ddd*, $J = 6.5$, 8.5 and 16 Hz, H-2′a), 3.03 (1H, *ddd*, $J = 6.5$, 8.5 and 16 Hz, H-2′b), 3.71 (1H, *sl*, OH-6), 3.95 (1H, *dd*, $J = 5.5$ and 13 Hz, H-6α), 7.02–7.20 (5H, *m*, Ar-H), 18.30 (1H, *s*, OH-3). ^{13}C NMR (75.5 MHz, CCl_4): Table 1. EIMS *m/z* (rel. int.): 400 $[M]^+$ (30), 183 (40), 91 (100), 69 (30), 55 (60).

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REFERENCES

1. Rodrigues, W. A., *Acta Amazonica*, 1980, **10**, 5.
2. Fernandes, A. M. A. P., Barata, L. E. S. and Ferri, P. H., *Phytochemistry*, 1993, **32**, 1567.
3. Sartorelli, P. and Kato, M. J., *19th Annual Meeting of Sociedade Brasileira de Química*, Poços de Caldas, Brazil, Abstract PN-010, 1996.
4. Fernandes, A. M. A. P., Barata, L. E. S. and Ferri, P. H., *Phytochemistry*, 1994, **36**, 533.
5. Coll, J. C. and Bowden, B. F., *Journal of Natural Products*, 1986, **49**, 934.
6. Mudd, A., *Journal of the Chemical Society, Chemical Communications*, 1978, 1075.
7. Forsen, S., Merenyi, F. and Nilsson. M., *Acta Chemica Scandinavica*, 1964, **18**, 1208.
8. Mudd, A., *Journal of the Chemical Society, Perkin Transaction* 1, 1981, 2357.
9. Paulino Filho, H. F., Ph.D. Thesis. USP, São Paulo, Brazil, 1985.
10. Gonzalez, M. J. T. G., DeOliveira, C. J. C., Fernandes, J. O., Kijjoa, A. and Herz, W., *Phytochemistry*, 1996, **43**, 1333.
11. Kato, M. J., Lopes, L. M. X., Paulino Filho, H. P., Yoshida, M. and Gottlieb, O. R., *Phytochemistry*, 1985, **24**, 533.
12. Mudd, A., *Journal of the Chemical Society, Perkin Transactions* 1, 1983, 2161.
13. Mudd, A. and Corbet, S. A., *Journal of Chemical Ecology*, 1982, **8**, 843.
14. Ando, M., Tashiro, M., Sato, M. and Iwataki, M., *Jap. P.* 125738 (*Chem. Abstr.* **87**, 5499a).