



TRITERPENOIDS FROM *OWENIA CEPIODORA*

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(Received 16 March 1998; accepted in revised form March 1998)

Key Word Index—*Owenia cepiodora*; Meliaceae; Melioideae; 28-deoxonimbolide, 24*S*,25-dihydroxytirucall-7-en-3-one; 3-oxo-tirucalla-7,24-dien-21-al; 21,24*R*-epoxy-25-hydroxytirucall-7-en-3-one.

Abstract—The limonoid, 28-deoxonimbolide, and three protolimonoids, 24*S*,25-dihydroxytirucall-7-en-3-one, 3-oxo-tirucalla-7, 24-dien-21-al and 21,24*R*-epoxy-25-hydroxytirucall-7-en-3-one were isolated from the leaves and bark of *Owenia cepiodora*. © 1998 Published by Elsevier Science Ltd. All rights reserved

INTRODUCTION

The Meliaceae family produces a class of compounds called limonoids. Limonoids are tetranortriterpenoids with a β -substituted furan ring at C-17 α . Rings A–D of the triterpenoid skeleton may be oxidized and rearrangements may occur giving different types of limonoids. The type of limonoid produced by a species has been used for taxonomic purposes [1]. *Owenia* is a genus of the Meliaceae found only in Australia and has been placed in the tribe Trichileae of the subfamily Melioideae. Seed of *Owenia acidula* and *Owenia venosa* have been examined previously and have yielded the limonoid 6 α -acetoxyhavanensin acetate and the triterpenoid 3 α -isobutyryl-7 α -deacetylglabretal [2]. Glabretal-type compounds are an interesting by-product of limonoid metabolism and have been isolated from *Aglaia* [3], *Guarea* [4], *Owenia* [2], *Turraea* [3], and *Dysoxylum* [5–7], species. In the classification of Pennington and Styles [8], these genera belong to different tribes of the subfamily Melioideae. However, in spite of the thorough investigation of *Melia* and *Azadirachta* in recent years, glabretal-type compounds have not been found in the Meliaceae tribe of the Melioideae subfamily. The limonoid 6 α -acetoxydeoxyhavanensin is a common limonoid and hence its presence in the *Owenia* examined previously is not of taxonomic significance.

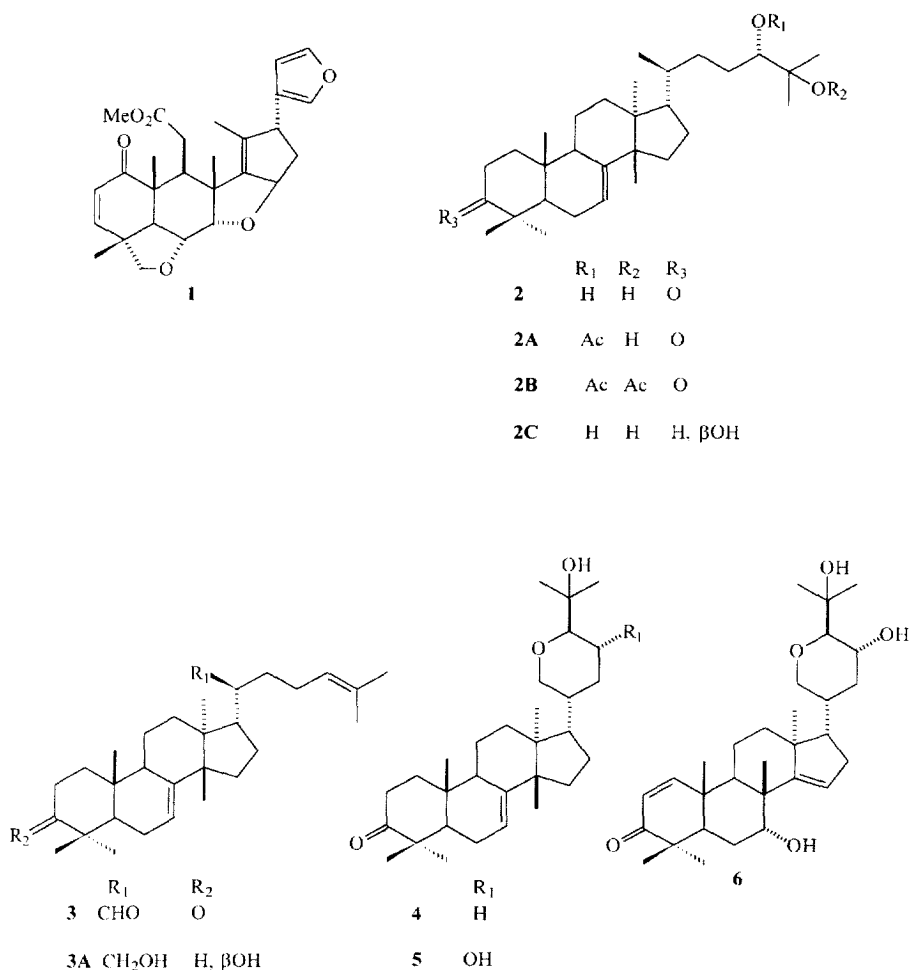
The leaves and bark of *Owenia cepiodora* F. Muell. were investigated in order to determine their chemical composition.

RESULTS AND DISCUSSION

The ring C opened limonoid, 28-deoxonimbolide (**1**) was isolated from the leaves of *Owenia cepiodora*. The compound has been isolated previously from the leaves of *Azadirachta indica* (neem) [9]. *Melia* and *Azadirachta* are very similar chemically and contain ring C-oxidized limonoids of the nimbin class. These compounds were thought to distinguish *Melia* and *Azadirachta* from the rest of the Meliaceae family [1], although one other example of a ring C opened limonoid had been found previously in the *Trichilieae* tribe of which *Owenia* is also a member: the isolation of heudelbolin from *Trichilia heudelotti* [10]. This second report confirms that ring-C opened limonoids are not restricted to *Melia* and *Azadirachta*.

Three triterpenoids were isolated from the hexane extract of the bark of *O. cepiodora*. The first compound was identified as 24*S*,25-dihydroxytirucall-7-en-3-one (**2**). This compound has not been reported previously, although the 3 β -hydroxy derivative (**2C**) has been described [11]. C-3 occurred at δ 216.1 confirming the presence of a ring A ketone, H-7 occurred at δ 5.28 and C-7 and C-8 at δ 117.8 and δ 145.9, respectively. Resonances occurred at δ 73.2 and δ 78.6 in the ^{13}C NMR spectrum and these were assigned to C-25 and C-24, respectively. H-24 occurred at δ 3.32. Standard acetylation of **2** yielded the 24-acetate, (**2A**); forced acetylation of **2** led to the 24,25-diacetate (**2B**), and NaBH₄ reduction yielded the known compound 3 β ,24*S*,25-trihydroxytirucall-7-ene (**2C**). The stereochemistry at C-24 of the 3 β -hydroxy derivative **2C** was determined by the lanthanide complex method of

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Nakanishi *et al.* [12–14]. Complexation [4:1 ratio, substrate: Eu(dpm)₃] of **2C** in dry chloroform provided a CD spectrum $\Delta\epsilon + 4.5$ at 314 nm indicating the C-24 hydroxy group to have the *S*-configuration [11].

The second compound was identified as 3-oxo-tirucalla-7,24-dien-21-al (**3**) and has been isolated previously from *Simarouba amara* [15]. Reduction of the two carbonyl groups with NaBH₄ yielded the 3 β ,21-diol (**3A**) as expected.

The third compound was identified as 21,24R-epoxy-25-hydroxytirucall-7-en-3-one (**4**) and has not been reported previously although the 23 α -hydroxy analogue, bourjotinolone A (**5**) has been isolated from *Flindersia bourjotiana* [16]. Mass spectrometry indicated a molecular formula of C₃₀H₄₈O₃. ¹³C NMR spectra were similar to (**2**), with a keto group at C-3 (δ 216.9) and Δ^7 -double bond (δ 117.9, 145.8). C-24 had been shifted from δ 78.6 in (**2**) to δ 84.3 and C-25 from δ 73.2 to δ 72.1. The C-21 methyl carbon resonance had been replaced by a methylene carbon resonance at δ 70.6. The H₃-21 doublet which occurred at δ 0.85 in (**2**) was replaced by a pair of resonances at δ 4.02 (*d*,

$J = 11.4$ Hz) and δ 3.42 (*dd*, $J = 11.4, 2.4$ Hz). The molecular formula indicated a ring was necessary in the side chain. Thus structure (**4**) is proposed. Acetylation was unsuccessful confirming the absence of a primary hydroxy group at C-21. The ¹H NMR spectrum for bourjotinolone A (**5**) [16] showed H-24 as a doublet at δ 2.9 ($J_{23\beta,24\alpha} = 9.0$ Hz) and the ¹H NMR spectrum for sapelin C (**6**) [17] showed H-24 as a doublet at δ 2.9 ($J_{23\beta,24\alpha} = 10.0$ Hz). In (**4**), H-24 appears as a doublet of doublets signal ($J_{23\beta,24\alpha} = 10.5$ Hz, $J_{23\beta,24\alpha} = 2.4$ Hz) at δ 3.10. These coupling constants suggest the configuration at C-24 of (**4**) to be *R*, as in bourjotinolone A (**5**) and sapelin C (**6**). The ¹³C NMR data for bourjotinolone A (**5**) [18], is given in Table 1 for comparison purposes.

EXPERIMENTAL

Dried leaves (250 g) and bark (121 g) of *Owenia cepiodora* F. Muell. (Voucher Specimen UND.HAM 8) were collected in Rockhampton, Australia. The leaves were crushed and extracted with hexane and CHCl₃. The CHCl₃ extract yielded,

Table 1. ^{13}C NMR data for compounds (2), (3), (4) and (5) (75 MHz, CDCl_3)

Carbon	(2)	(3)	(4)	(5)
1	38.5 t	38.3 t	38.5 t	38.6 t
2	34.9 t	34.8 t	34.9 t	35.0 t
3	216.0 s	216.7 s	216.9 s	216.8 s
4	47.8 s	47.8 s	47.8 s	47.9 s
5	53.1 d	55.2 d	52.3 d	52.4 d
6	24.3 t	24.3 t	24.3 t	24.4 t
7	117.8 d	118.3 d	17.9 d	118.1 d
8	145.9 s	145.2 s	45.8 s	145.7 s
9	52.3 d	52.2 d	48.4 d	48.5 d
10	34.9 s	35.0 s	35.0 s	35.1 s
11	18.2 t	17.7 t	18.2 t	18.2 t
12	32.9 t	31.9 t	32.9 t	33.0 t
13	43.4 s	43.3 s	43.1 s	43.3 s
14	51.1 s	50.9 s	51.3 s	51.3 s
15	34.0 t	33.6 t	33.9 t	34.0 t
16	28.2* t	29.2 t	27.2 t	27.4 t
17	48.4 d	48.2 d	43.2 d	44.8 d
18	21.5 q	21.5 q	21.6 q	21.6 q
19	12.7 q	12.7 q	12.7 q	12.8 q
20	35.9 d	48.2 d	35.6 d	37.5 d
21	18.2 q	205.8 d	70.6 t	70.1 t
22	28.4* t	26.9* t	27.0 t	36.5 t
23	33.6 t	25.9* t	21.2 t	64.6 d
24	78.6 d	123.5 d	84.3 d	86.5 d
25	73.2 s	132.5 s	72.1 s	74.2 s
26	24.5 q	17.8 q	24.5 q	24.0 q
27	26.5 q	24.5 q	25.8 q	28.5 q
28	23.1 q	25.6 q	23.5 q	24.6 q
29	21.9 q	22.8 q	22.4 q	22.3 q
30	27.4 q	27.2 q	27.5 q	27.5 q

* Values for the same compound may be interchanged.

after repeated CC over silica gel (Merck 9385), the limonoid 28-deoxonimbolide (1). The hexane extract of the ground bark afforded three triterpenoids, 24*S*,25-dihydroxytirucall-7-en-3-one (2), 3-oxo-tirucalla-7,24-dien-21-al (3) and 21,24*R*-epoxy-25-hydroxytirucall-7-en-3-one (4). The structures of the compounds were determined using 2D NMR and MS techniques. ^1H NMR spectra were recorded using a Varian Gemini 300 NMR spectrometer in CDCl_3 . ^{13}C NMR data for (2), (3), and (4) are given in Table 1.

28-Deoxonimbolide (1) $\text{C}_{27}\text{H}_{32}\text{O}_6$ (found 452.2178, requires 452.2181). The structure was confirmed by comparison of physical data against literature values [9].

24*S*,25-Dihydroxytirucall-7-en-3-one (2) (616 mg), HRMS m/z 458.3746 ($\text{C}_{30}\text{H}_{50}\text{O}_3$ requires 458.3760). ^1H NMR (300 MHz, CDCl_3): δ 0.78 (3H, s), 0.85 (3H, d, $J = 6.0$ Hz, H_3-21), 0.97 (6H, s, $2 \times \text{CH}_3$), 1.02 (3H, s), 1.08 (3H, s), 1.14 (3H, s), 1.19 (3H, s), 2.73 (1H, td, $J = 5.7, 15.4$ Hz, H-2ax), 3.32 (1H, m, H-24), 5.28 (1H, m H-7). IR $\lambda_{\text{max}}^{\text{NaCl}}$ cm^{-1} : 3450, 1700.

Acetylation of (2) with Ac_2O /pyridine yielded 24-acetoxy-tirucall-7-en-25-ol-3-one (2A). ^1H NMR: δ 0.78 (3H, s), 0.84 (3H, d, $J = 6.0$ Hz, H_3-21), 0.98 (6H, s), 1.02 (3H, s), 1.09 (3H, s), 1.17 (6H, s), 2.09 (3H, s OAc), 2.73 (1H, td, $J = 5.4, 14.4$ Hz, H-2ax), 4.77 (1H, dd, $J = 2.7, 10.2$ Hz, H-24), 5.28 (1H, m H-7).

Acetylation of 2 with Ac_2O /pyridine/dimethylaminopyridine yielded 24*S*,25-diacetoxy-tirucall-7-en-3-one (2B). ^1H NMR: δ 0.78 (3H, s), 0.84 (3H, d, $J = 6.0$ Hz, H_3-21), 0.98 (3H, s), 1.02 (3H, s), 1.09 (3H, s), 1.23 (3H, s), 1.42 (3H, s), 1.46 (3H, s), 1.94 (3H, s, OAc), 2.09 (3H, s, OAc), 2.73 (1H, td, $J = 6.6, 14.4$ Hz, H-2ax), 5.10 (1H, dd, $J = 2.7, 9.9$ Hz, H-24), 5.30 (1H, m, H-7).

Reduction of 2 with NaBH_4 yielded 3 β ,24*S*,25-trihydroxy-tirucall-7-ene (2C). ^1H NMR. δ 0.72 (3H, s, H_3-19), 0.80 (3H, s, H_3-18), 0.84 (3H, s, H_3-30), 0.86 (3H, d, $J = 6.0$ Hz, H_3-21), 0.95 (6H, s H_3-29 , H_3-28), 1.14 (3H, s, H_3-26), 1.20 (3H, s, H_3-27), 3.25 (1H, dd, $J = 4.5, 10.8$ Hz, H-24), 3.33 (1H, m, H-3x, $W_{1/2} = 12.0$ Hz).

3-Oxo-tirucalla-7,24-dien-21-al (3) (678 mg), HRMS M^+ at m/z 438.3487 ($\text{C}_{30}\text{H}_{46}\text{O}_2$ requires 438.3498). ^1H NMR: δ 0.81 (3H, s), 0.97 (3H, s), 0.99 (3H, s), 1.02 (3H, s), 1.08 (3H, s), 1.54 (3H, s), 1.65 (3H, s), 2.71 (1H, td, $J = 6.3, 14.4$ Hz, H-2ax), 5.05 (1H, m H-24), 5.30 (1H, m, H-7), 9.47 (1H, d, H-21, $J = 5.4$ Hz). IR $\lambda_{\text{max}}^{\text{NaCl}}$ cm^{-1} : 1730, 1680.

Reduction of 3 with NaBH_4 yielded 3 β ,21-dihydroxy-tirucalla-7,24-diene (3A), mp 136–138 $^\circ$ (lit. 138–139 $^\circ$ [12]). ^1H NMR: δ 0.72 (3H, s), 0.81 (3H, s), 0.84 (3H, s), 0.95 (3H, s), 0.97 (3H, s), 1.60 (3H, s), 1.69 (3H, s), 3.22 (1H, dd, H-3x, $J = 4.5, 10.8$ Hz), 3.58 (1H, dd, $J = 4.8, 11.1$ Hz, H-21a), 3.71 (1H, dd, $J = 3.0, 11.1$ Hz, H-21b), 5.08 (1H, m, H-24), 5.25 (1H, m, H-7).

21,24*R*-Epoxy-25-hydroxytirucall-7-en-3-one (4) (1.0 g), HRMS M^+ at m/z 456.3609 ($\text{C}_{30}\text{H}_{48}\text{O}_3$ requires 456.3603). ^1H NMR: δ 0.77 (3H, s), 0.98 (3H, s), 1.02 (3H, s), 1.03 (3H, s), 1.09 (3H, s), 1.13 (6H, s), 2.73 (1H, td, $J = 6.6, 14.4$ Hz, H-2ax), 3.10 (1H, dd, $J = 2.4, 10.5$ Hz, H-24), 3.43 (1H, dd, $J = 2.4, 11.4$ Hz, H-21a), 4.02 (1H, d, $J = 11.4$ Hz, H-21b), 5.29 (1H, m, H-7). IR $\lambda_{\text{max}}^{\text{NaCl}}$ cm^{-1} : 3420, 1700.

Acknowledgements—We are grateful to Mrs J. King for providing the plant material and the University of Natal Research Fund for funding this project. MK and HAM were funded by Foundation for Research Development post graduate bursaries. We thank Dr P Boshoff of the Cape Technikon for mass spectral data.

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