Pergamon

0031-9422(94)00589-3

Phytochemistry, Vol. 38, No. 1, pp. 233–236, 1995

0031-9422/95 $9.50 + 0.00

THREE PRENYLATED PHENOLIC BENZOPHENONES FROM *GARCINIA MYRTIFOLIA*

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(*Received in revised form* 29 *June* 1994)

Key Word Index—*Garcinia myrtifolia*; Clusiaceae; bark; myrtiaphenones; prenylated benzophenones; vismiaphenone C; eupha-8,24-dien-3β-ol; friedelin.

Abstract—The bark of *Garcinia myrtifolia* contains three biogenetically related prenylated phenolic benzophenones, two of which are new natural products. These two are: myrtiaphenone-A which has been identified as 6-hydroxy-2,4-dimethoxy-3,5-bis(3-methyl-2-butenyl)benzophenone and myrtiaphenone-B which is 2,2-dimethyl-8-benzoyl-7-hydroxy-5-methoxy-6-(3-methyl-2-butenyl)benzopyran. The third benzophenone compound has been identified as vismiaphenone-C. It also contains two triterpenes: eupha-8,24-dien-3β-ol and friedelin.

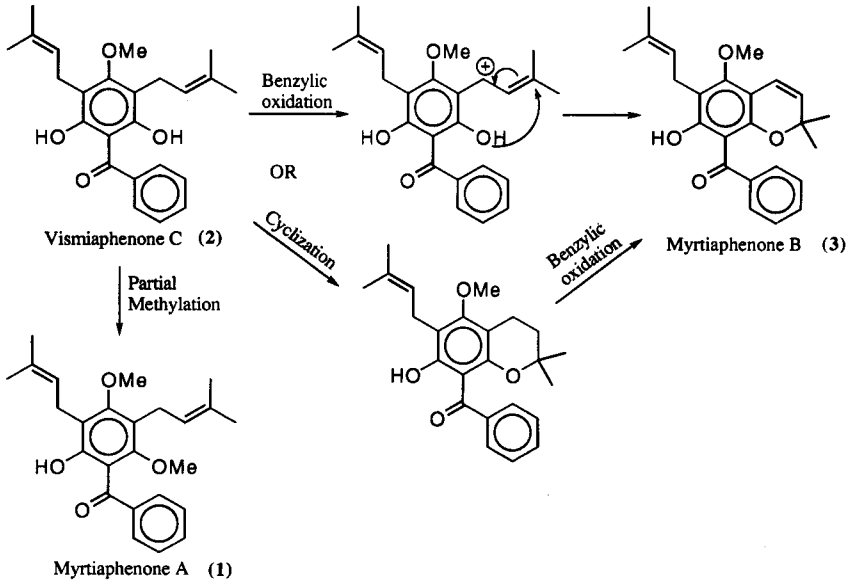
INTRODUCTION

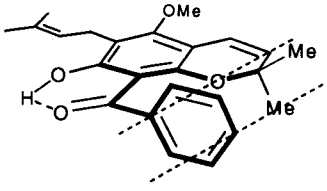
Garcinia myrtifolia of the family Clusiaceae (Guttiferae) [1] is a moderately common tree on the Fijian main islands of Viti Levu and Kadavu. It is a useful timber tree which is locally referred to as laubu. No phytochemical studies have hitherto been undertaken on *G. myrtifolia*, though several plant species of the genus *Garcinia* have yielded novel biflavanones [2–6], phenols [7–9] and xanthones [10]. In this paper, we report the results of our phytochemical investigation of *G. myrtifolia*.

RESULTS AND DISCUSSION

The bark of *Garcinia myrtifolia* was extracted with *n*-hexane and chloroform. The extracts were found to be chemically identical by TLC analysis. Upon separation by vacuum liquid chromatography followed by prep. TLC (elution with 2% ethyl acetate–hexane), the extracts were found to contain five natural products in the following order of polarity: phenols G1 (major and minor components), triterpene T1, phenol G2 and triterpene T2. The major and minor components of G1 could not be separated despite attempts at repurification using a chromatotron (10% ethyl acetate–hexane). Nevertheless, each of their individual signals in the ^{1}H and ^{13}C NMR were well-separated and resolved (with the exception of the phenyl proton signals). The ^{1}H NMR chemical shifts of every signal of the major component of G1 were identical with those reported in the literature for the synthetic compound [11] (the phenolic signal at δ10.92 was, however, not reported). All other signals, which were smaller in intensity, could thus be assigned to the minor component of G1. The low resolution mass spectrum, although obtained on the mixture, displayed the expected masses for the two proposed structures. The expected fragments for both proposed structures were also observed (cf. Figs 1 and 2 and the following discussion). We were thus able to unambiguously characterize the two phenols of G1, myrtiaphenone A and B, and the phenol G2 as follows.

Myrtiaphenone–A (**1**) was assigned a formula $C_{25}H_{30}O_4$ ([M]$^+$ 394) from its mass spectrum and exact mass. The ^{1}H NMR spectrum showed the presence of two -OMe groups, a hydrogen-bonded phenolic -OH group (δ10.92 ppm), two isoprenyl groups and two well-resolved triplet of heptets for CH_2–CH=$C(Me)_2$, and a monosubstituted phenyl ring. The ^{13}C NMR spectrum showed the presence of a carbonyl at δ199.7. The other resonances are reported in Table 1. Myrtiaphenone-A has a methoxy group at C-2, whereas the known vismiaphenone-C (*vide infra*) has a hydroxy group at C-2. Replacing the methoxy group in **1** by the hydroxyl group in **3** should change the chemical shifts of the C-1 to C-6 carbons by calculated values of +1.6, −4.5, +1.6, +0.4, −1.3, and +0.4, respectively [12]. The observed differences in chemical shifts for those carbons are in good agreement with the calculated values (+1.3, −2.0, +2.2, 0.0, −1.0 and +3.4, respectively). All other resonances are within 1 ppm of each other which is consistent with a simple substitution of the hydroxyl for the methoxy group. Comparison of the mass spectra of **1** and **3** was also useful in characterizing the former. Compounds **1** and **3** gave a fragment at *m/z* 363 corresponding to the loss of a methoxy or hydroxyl group, respectively, at C-2. The loss of Me (15 amu) and OMe (31 amu) was more prominent in **1** since it possesses two methoxy groups,





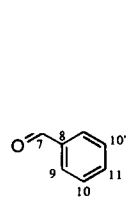
whereas the loss of OH (17 amu) was more prominent in **3** because it has two hydroxyl groups. The benzophenone moiety in each compound was easily identified from the intense peaks at *m/z* 105 and 77. Based on the above data, the structure of 6-hydroxy-2,4-dimethoxy-3,5-diprenylbenzophenone (**1**) was assigned to myrtiaphenone-A. It is a new natural product, although it has been synthesized previously [11]. Myrtiaphenone-A may be biosynthetically derived from vismiaphenone-C (Fig. 1).

Myrtiaphenone B (**2**) is a prenylated benzophenone and was assigned the formula $C_{24}H_{26}O_4$ ($[M]^+$ 378) based on its mass spectrum and exact mass measurements. The ^1H NMR spectrum showed the presence of one -OMe group, a hydrogen-bonded phenolic -OH group at δ12.04, one isoprenyl group, one doublet of multiplets for CH_2–CH = C(Me), one triplet of heptets for CH_2–CH = C(Me), and a monosubstituted phenyl ring. The chromene ring was apparent from the resonances at δ6.40 and 5.32 (each $J = 10$ Hz) and the *gem*-dimethyl group at δ0.97. Such a *gem*-dimethyl group generally resonates at $\sim \delta$1.4–1.5. This discrepancy could be due to the hydrogen bond between the phenolic proton and the ketone of the benzophenone moiety which forces the monosubstituted phenyl ring to adopt a perpendicular orientation to the chromene ring (cf. Fig. 2). This, in effect, puts the methyl groups in the shielding zone of the phenyl ring, this shifting their resonances to higher field. The ^{13}C NMR spectrum showed the presence of a carbonyl at δ200.8. The other resonances are reported in Table 1 and

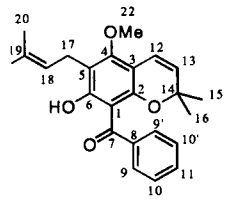
Table 1. ^{13}C–^1H NMR resonances for **1**–**3**

C	1	2	3
1	106.4	107.9	107.7
2	159.4	158.1	157.4
3	111.5	119.2	113.7
4	162.9	162.1	162.9
5	114.7	120.3	113.7
6	154.0	160.6	157.4
7	199.7	200.8	199.1
8	139.6	142.4	140.3
9-9′	129.2	127.6	128.3
10-10′	127.7	127.3	128.2
11	132.2	130.4	132.1
12	23.1	126.1	22.9
13	122.7	116.9	122.4
14	131.2	77.1	133.2
15	17.9	27.3	17.9
16	25.7	27.3	25.7
17	23.1	22.2	22.9
18	123.8	123.8	122.4
19	132.0	131.6	133.2
20	17.9	17.9	17.9
21	25.7	25.8	25.7
22	61.5	62.0	61.5
23	62.6	—	—

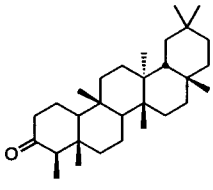
were consistent with the presence of the 2,2-dimethyl chromene ring and isoprenyl group. Directly comparing the carbon resonances in the substituted benzene ring between **1** and **2** was not useful because of the cyclic ether structure. This structure influences chemical shifts in a way not presently predictable. However, the similarities in chemical shifts and the signals for hydrogen-bonded phenols in both structures suggest a substitution pattern for **2** that is similar to **1**. The benzophenone moiety was apparent from the integration of the phenyl hydrogen



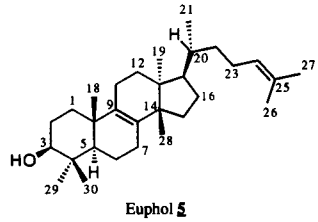
Myrtiaphenone A **1** R=Me
Vismiaphenone C **3** R=H



Myrtiaphenone B **2**



Friedelin **4**



Euphol **5**

signals in the proton NMR. There was clearly only one isoprenyl group since only one olefinic signal integrating for one proton and only one methylene signal integrating for two protons were found in the ^{1}H NMR. The proton signals at δ6.40 and 5.32 shared a J constant of 10 Hz which is typical of a *cis* double bond and the singlet at δ0.97 integrating for six protons had to be two chemically equivalent methyl groups. The ^{13}C NMR spectrum correlated all of these observations and the signals for each group can be found in Table 1. The mass spectral fragmentation pattern for **2** was similar to **1** and **2**. An intense peak at m/z 363 $[M-Me]^+$ is indicative of the *gem*-dimethyl group of the chromene ring. Based on the above discussion, the structure of 2,2-dimethyl-8-benzoyl-7-hydroxy-5-methoxy-6-(3-methyl-2-butenyl) benzopyran (**2**) was assigned to myrtiaphenone-B. From a biosynthetic point of view, myrtiaphenone-B could be formed from vismiaphenone-C via a cyclization between a hydroxyl and isoprenyl group (Fig. 1).

Vismiaphenone-C (**3**): The phenol G2 has been shown to be identical with vismiaphenone-C(**3**) from comparison of the ^{1}H NMR data with those reported in the literature [13]. It had a molecular formula of $C_{24}H_{28}O_4$ ($[M]^+$ 380). The ^{1}H NMR spectrum and integration showed the presence of two symmetrically positioned prenyl groups. All resonances were consistent with the reported values [13]. The ^{13}C NMR spectrum showed the presence of a carbonyl at δ199.1. Other resonances are reported in Table 1.

The triterpene T1 was identified as friedelin (**4**) from its IR, MS, ^{1}H and ^{13}C NMR data [14]. The triterpene T2 was identified as eupha-8,24-dien-3β-ol (euphadienol, **5**) by comparison of its ^{1}H, ^{13}C NMR, IR and mass spectra with those found in the literature [15] [$C_{30}H_{50}O$ ($[M]^+$ 426]. We have recorded the 2D ^{13}C–^{1}H CORRELATED spectra of the latter compound and the correlation is shown in Table 2. Since the carbon signals have all been assigned previously by comparison with related triterpenes [15], it was possible to assign all of the methyl singlets in the ^{1}H NMR spectrum (Table 2). This may prove useful for further characterization of related compounds.

EXPERIMENTAL

The bark of *Garcinia myrtifolia* was collected in Suva, Fiji and the voucher specimens have been lodged at the South Pacific Regional Herbarium in Suva, Fiji. The bark (1 kg) on separate extractions with hexane and CH_2Cl_2 yielded 5 and 10 g of extracts, respectively. Both extracts appeared to have the same set of compounds when examined on TLC. Vacuum liquid chromatographic sepns using 2% EtOAc–hexanes yielded G1 (0.08%) as a gum, G2 (0.16%, mp 58–60°), T1 (0.02%, mp 259–261°, lit. 268° [16]) as a white powder, and T2 (0.06%, mp 118–120°, lit. 119–120°, [17]) as needles.

Flash CC was performed using Merck silica gel Kieselgel 60 from EM Science, particle size 230–400 mesh ASTM). Mps: uncorr.

Myrtiaphenone-A. ^{1}H NMR (360 MHz, $CDCl_3$): δ10.92 (*s*, 1H), 7.85–7.70 (*m*, 2H), 7.52–7.21 (*m*, 3H), 5.26 (*tm*, 1H, J = 6.9 Hz), 5.11 (*dm*, 1H, J = 6.9 Hz), 3.76 (*s*, 3H), 3.36 (*dm*, 2H, J = 6.9 Hz), 3.23 (*dm*, 2H, J = 6.9 Hz), 3.19 (*s*, 3H), 1.78 (*d*, 6H, J = 1.2 Hz), 1.70 (*d*, 6H, J = 1.2 Hz); ^{13}C NMR (90 MHz, $CDCl_3$): δ199.7 (*s*), 162.9 (*s*), 159.4 (*s*), 154.0 (*s*), 139.6 (*s*), 132.2 (*d*), 132.0 (*s*), 131.2 (*s*), 129.2 (*d*), 127.7 (*d*), 123.8 (*d*), 122.7 (*d*), 120.3 (*s*), 119.2 (*s*), 106.4 (*s*), 62.6 (*q*), 61.5 (*q*), 25.7 (*q*), 25.7 (*q*), 23.1 (*t*), 23.1 (*t*), 17.9 (*q*), 17.9 (*q*), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500–3300 (*b*), 3100–3000 (*m*), 3000–2800 (*m*), 2392 (*w*), 2296 (*w*), 2232 (*w*), 1608 (*s*), 1456 (*m*), 1416 (*s*), 1328 (*s*), 1145 (*s*); EIMS (probe) 70 eV,

Table 2. ^{13}C–^{1}H NMR correlations of euphol (**5**)

C	^{13}C	^{1}H
1	35.2	1.75 *m*
2	27.6	2.2 *m*
3	79.0	3.21 *dd*
5	50.9	1.5 *m*
6	18.9	1.35, 1.7 *m*
7	27.9	0.9, 1.1 *m*
11	21.5	2.2 *m*
12	28.1	1.0, 1.3 *m*
15	30.9	1.65, 1.67 *m*
16	29.7	1.15 *m*
17	49.6	1.5 *m*
18	20.1	0.93 *s*
19	15.5	0.77 *s*
20	35.8	1.43 *m*
21	18.9	0.82 *s*
22, 23	35.4, 24.7	—
24	125.2	5.07 *bt*
26	17.6	1.58 *bs*
27	25.7	1.66 *d*
28	24.4	0.84 *s*
29	28.0	0.98 *s*
30	15.6	0.73 *s*

m/z: (rel. int.): 394 $[M]^+$ (90), 379 $[M-15]^+$ (40), 363 $[M-31]^+$(100), 339 $[M-55]^+$(50), 323 (86), 105 $[PhCO]^+$ (70), 77 $[Ph]^+$ (38). Exact mass (calcd for $C_{25}H_{30}O_4$): 394.2144 found: 394.2166.

Myrtiaphenone-B. ^{1}H NMR (360 MHz, $CDCl_3$): δ12.04 (*s*, 1H), 7.85–7.70 (*m*, 2H), 7.52–7.21 (*m*, 3H), 6.40 (*d*, 1H, J = 10.0 Hz), 5.32 (*d*, 1H, J = 10.0 Hz), 5.23 (*tm*, 1H, J = 6.9 Hz), 3.76 (*s*, 3H), 3.31 (*dm*, 2H, J = 6.9 Hz), 1.70 (*d*, 3H, J = 1.2 Hz), 1.68 (*d*, 3H, J = 1.2 Hz), 0.97 (*s*, 6H); ^{13}C NMR (90 MHz, $CDCl_3$): δ200.8 (*s*), 162.1 (*s*), 160.6 (*s*), 158.1 (*s*), 142.4 (*s*), 131.6 (*s*), 130.4 (*d*), 127.3 (*d*), 127.6 (*d*), 126.1 (*d*), 123.8 (*d*), 116.9 (*d*), 114.7 (*s*), 111.5 (*d*), 107.9 (*s*), 77.1 (*s*), 62.0 (*q*), 27.3 (*q*), 27.3 (*q*), 25.8 (*q*), 22.2 (*t*), 17.9 (*q*); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500–3300 (*b*), 3100–3000 (*m*), 3000–2800 (*m*), 2392 (*w*), 2296 (*w*), 2232 (*w*), 1608 (*s*), 1456 (*m*), 1416 (*s*), 1328 (*s*), 1145 (*s*); EIMS (probe) 70 eV, *m/z*: (rel. int.): 378 $[M]^+$ (30), 363 (100), 307 (20), 323 (86), 105 (70), 77 (38). Exact mass (calcd for $C_{24}H_{26}O_4$): 378.1831, found: 378.1854.

Vismiaphenone-C: ^{1}H NMR (360 MHz, $CDCl_3$): δ8.52 (*s*, 2H), 7.7–7.6 (*m*, 2H), 7.55–7.4 (*m*, 3H), 5.18 (*tm*, 2H, J = 6.9 Hz), 3.74 (*s*, 3H), 3.32 (*dm*, 4H, J = 6.9 Hz), 1.75 (*d*, 6H, J = 1.2 Hz), 1.68 (*d*, 6H, J = 1.2 Hz), ^{13}C NMR (90 MHz, $CDCl_3$):δ199.1 (*s*), 162.9 (*s*), 157.4 (*s*), 140.3 (*s*), 133.2 (*s*), 132.1 (*d*), 128.3 (*d*), 128.2 (*d*), 122.4 (*d*), 113.7 (*s*), 107.7 (*s*), 61.5 (*s*), 25.7 (*q*), 22.9 (*t*), 17.9 (*q*), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3528 (*m*), 3500–3000 (*b*), 3100–3000 (*m*), 3000–2800 (*m*), 2392 (*w*), 2296 (*w*), 2232 (*w*), 1616 (*s*), 1440 (*m*), 1320 (*s*), 1112 (*s*); EIMS (probe) 70 eV, *m/z*: (rel. int.): 380 $[M]^+$ (90), 365 $[M-15]^+$(8), 363 $[M-17]^+$(20), 325 $[M-55]^+$(50), 309 (100), 105 $[Ph-CO]^+$ (90), 77 $[Ph]^+$ (50). Exact mass (calcd for $C_{24}H_{28}O_4$): 380.1988, found: 380.2023.

Acknowledgements—The authors are grateful to the University of Victoria for financial support and for an Asia-Pacific travel grant to J. L. One of us (J. L.) wishes to acknowledge financial support provided by the University of the South Pacific.

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