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Polyisoprenylated Benzophenones and an Unusual Polyisoprenylated Tetracyclic Xanthone from the Fruits of *Garcinia cambogia*

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In light of the wide range of biological activities of garcinol and with the aim of exploring some of them, we carried out its isolation from the fruits of *Garcinia cambogia* L. (Guttiferae). Surprisingly, the fruits were also found to contain guttiferones I, J, and K, compounds never reported in *G. cambogia*, along with three new compounds, namely, guttiferone M (**1**), guttiferone N (**2**), and the oxidized derivative of guttiferone K (**6**). Oxy-guttiferone K (**6**) is the first example of tetracyclic xanthone derived from the oxidation of a polyisoprenylated benzophenone from natural source. The natural formation of oxy-guttiferone K is in agreement with the previously described cyclization of garcinol by DPPH.

KEYWORDS: Guttiferae; Garcinia cambogia fruits; polyisoprenylated benzophenones; polyisoprenylated tetracyclic xanthone; oxy-guttiferone K

INTRODUCTION

An interest in the potential human health benefits that may be gathered from the consumption of berry fruits is growing more and more. Among berry phytochemicals, recent research progress was made in identifying plant chemicals present in berry fruits and in elucidating the cellular and molecular mechanisms of actions of these compounds. In particular, the *Garcinia* genus is a rich source of molecules exhibiting a wide pharmacological profile. *Garcinia* (Guttiferae) is a large genus of polygamus trees or shrubs commonly found in tropical Asia, Africa, and Polynesia, and consists of 180 species (*1*). *Garcinia cambogia* L. is a small or medium-sized tree whose fruits, surrounded by a succulent aril, contain 31% edible fat (*2*). *G. cambogia* extract has been used traditionally in Indian medicine to treat tumors, ulcers, hemorrhoids, diarrhea, dysentery, fever, open sores, and parasites (*3*). The dried fruit rind is widely used in India for culinary purposes as a condiment for flavoring curries in place of tamarind or lemon. In Ceylon the dried fruit rind is used along with salt in the curing of fish (*1*).

Chemically, xanthones, xanthone derivatives, polyisoprenylated benzophenones, and (−)-hydroxycitric acid have been isolated from various species of *Garcinia* (*4, 5*). (−)-Hydroxycitric acid is present in the pericarp of *G. cambogia* fruit up to 30% by weight and its physiological and biochemical effects have been extensively studied for the unique regulatory effect on fatty acid synthesis, lipogenesis, appetite, and weight loss (*2*). With respect to the biological activity of polyisoprenylated benzophenones, initial investigations dealt with their antibacterial (*6*), anti-HIV (*7*), and cytotoxic effects (*5*). Interestingly, garcinol, a polyisoprenylated benzophenone derivative occurring in *G. cambogia*, has been reported to possess antibiotic and antiulcer activities (*8*), ability to suppress colonic aberrant crypt foci (ACF) formation, ability to inhibit histone acetyltransferases (HATs), which modulate gene expression (*9*), and ability to induce apoptosis through cytocrome *c* release and activation of caspase in human leukemia HL-60 cells (*10*). More recently, studies on garcinol and its three oxidation derivatives (GDPPH-1, GDPHH-2, and isogarcinol) have demonstrated their anti-inflammatory and anticarcinogenic properties (*11, 12*). These compounds are reported to exert their activity by inhibiting NF-κB activation and COX-2 expression, and by decreasing iNOS expression and NO release from LPS-stimulated macrophages, probably via the inhibition of the signal transducer and activator of transcription-1 (STAT-1) (*12, 13*). The remarkable biological activity of garcinol and the possibility that some of the biological properties of garcinol could also be examined on a molecular basis prompted us to carry out its isolation from the fruits of *Garcinia cambogia* (*14*). Therefore, we investigated the diethyl ether extract of the fruit of *G. cambogia*, and here, we report the isolation and structure elucidation of its constituents by spectroscopic methods including 1D-(^{1}H and ^{13}C) and 2D-NMR (DQF-COSY, HSQC, HMBC, ROESY, and HSQC-TOCSY) experiments as well as ESI-MS analysis.

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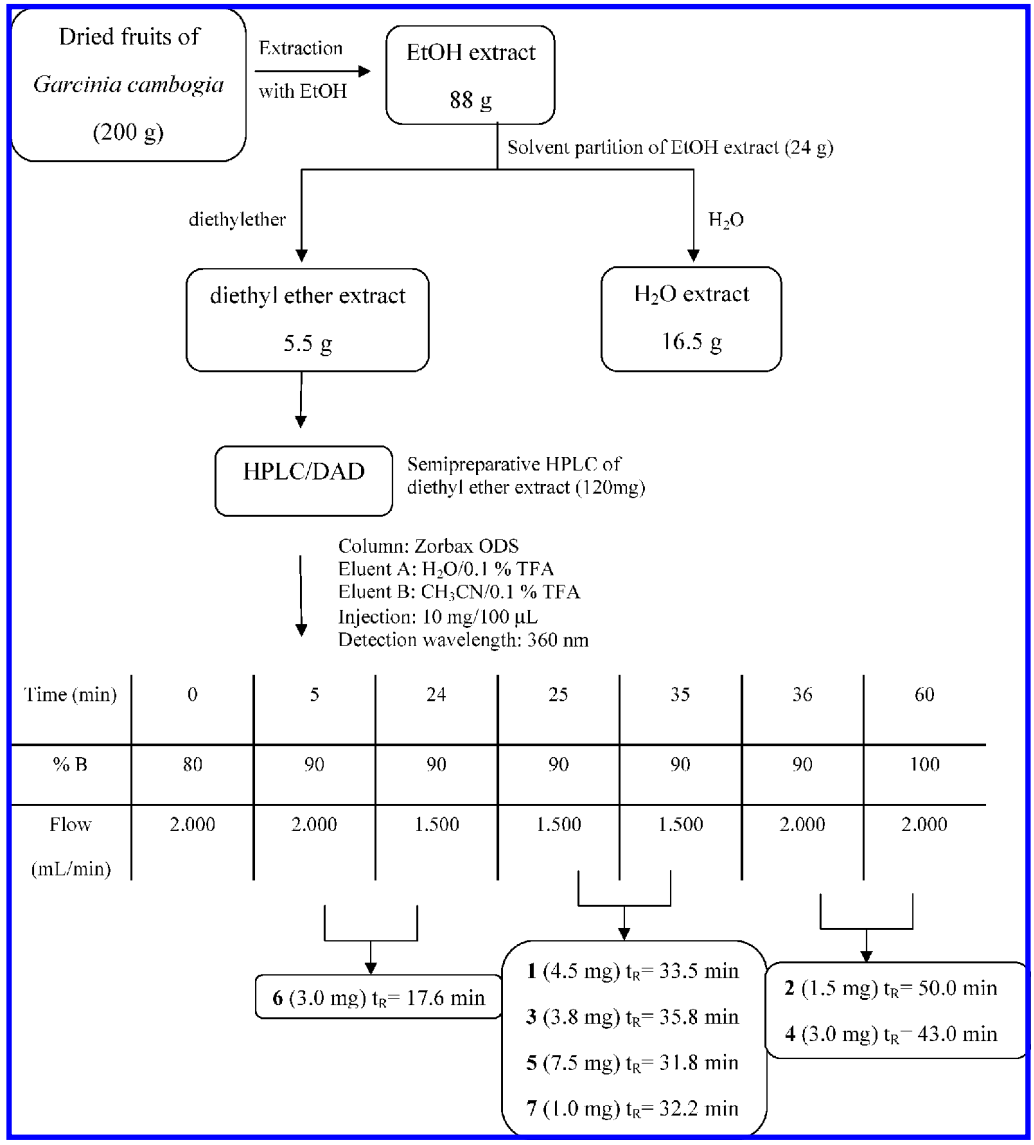
Scheme 1. Flow Chart Describing the Steps from Crude Drug to Isolated Compounds (**1**−**7**)



MATERIALS AND METHODS

Instrumentation. Optical rotations were measured on a JASCO DIP 1000 polarimeter. IR measurements were obtained on a Bruker IFS-48 spectrometer. UV spectra were recorded on a UV-2101PC Shimadzu UV/vis scanning spectrophotometer. NMR experiments were performed on a Bruker DRX-600 spectrometer equipped with a Bruker 5 mm TCI CryoProbe. All spectra were acquired in the phase sensitive mode, and the TPPI method was used for quadrature detection in the ω_1 dimension. The ^{1}H, gCOSY, ROESY, gHSQC, and gHMBC NMR experiments were run under standard conditions at 300 K, dissolving each sample in 500 μL of 99.8% D CD_3OD (Carlo Erba) with 0.1% TFA (^{1}H, δ = 3.34 ppm; ^{13}C, δ = 49.0 ppm). The ROESY spectra were acquired with t_{mix} = 400 ms.

ESI-MS analyses were performed using a ThermoFinnigan LCQ Deca XP Max ion trap mass spectrometer equipped with Xcalibur software. Samples were dissolved in MeOH (Baker) and infused in the ESI source by using a syringe pump; the flow rate was 3 μL/min. The capillary voltage was 43 V, the spray voltage was 5 kV, and the tube lens offset was 30 V. The capillary temperature was 280 °C.

Exact masses were measured by a Voyager DE mass spectrometer (Applied Biosystems, Foster City, CA). Samples were analyzed by matrix assisted laser desorption ionization (MALDI) mass spectrometry. A mixture of analyte solution and α-cyano-4-hydroxycinnamic acid (Sigma, St. Louis, MO) was applied to the metallic sample plate and dried. Mass calibration was performed with the ions from ACTH (fragment 18−39) at 2465.1989 Da and Angiotensin 294 III at 931.5154 Da as internal standards. HPLC separations were carried out on an Agilent 1100 series chromatograph, equipped with a G-1312A binary pump, a G-1328B rheodyne injector, and a G-1365B photodiode array detector using a 25 cm × 9.4 mm i.d. Zorbax ODS semipreparative column (Agilent Technologies, Palo Alto, CA, USA). HPLC grade acetonitrile (CH_3CN), trifluoroacetic acid (TFA), MeOH, and H_2O from J. T. Baker (Baker Mallinckrodt, Phillipsburg, NJ) were used for HPLC and LC-MS. TLC was performed on silica gel F254 (Merck) plates, and reagent grade chemicals (Carlo Erba) were used throughout.

Plant Material. *G. cambogia* L. fruits were collected in Ceylon in April 2006. Samples of *G. cambogia* were identified by Professor Vincenzo De Feo, Dipartimento di Scienze Farmaceutiche, Università di Salerno. A voucher specimen (No. 121) has been deposited in this department.

Extraction and Isolation Procedures. *G. cambogia* L. dried fruits (200 g) were extracted with EtOH (3 × 1.5 L) for 20 days at room temperature (**Scheme 1**). The solvent was removed under reduced pressure to afford 88 g of crude extract. The EtOH extract (24 g) was partitioned with diethyl ether-H_2O (1:1) to afford a dried diethyl ether extract (5.5 g). Part of the diethyl ether extract (120 mg) was chromatographed by semipreparative HPLC/DAD on Zorbax ODS (injections 10 mg/100 μL) using H_2O/0.1% TFA as eluent A and CH_3CN/0.1% TFA as eluent B as mobile phases to afford compounds **1** (4.5 mg, t_R = 33.5 min), **2** (1.5 mg, t_R = 50 min), **3** (3.8 mg, t_R = 35.8 min), **4** (3.0 mg, t_R = 43.0 min), **5** (7.5 mg, t_R = 31.8 min), **6** (3.0 mg, t_R = 17.6 min), and **7** (1.0 mg, t_R = 32.2 min) (**Figure 1**). The

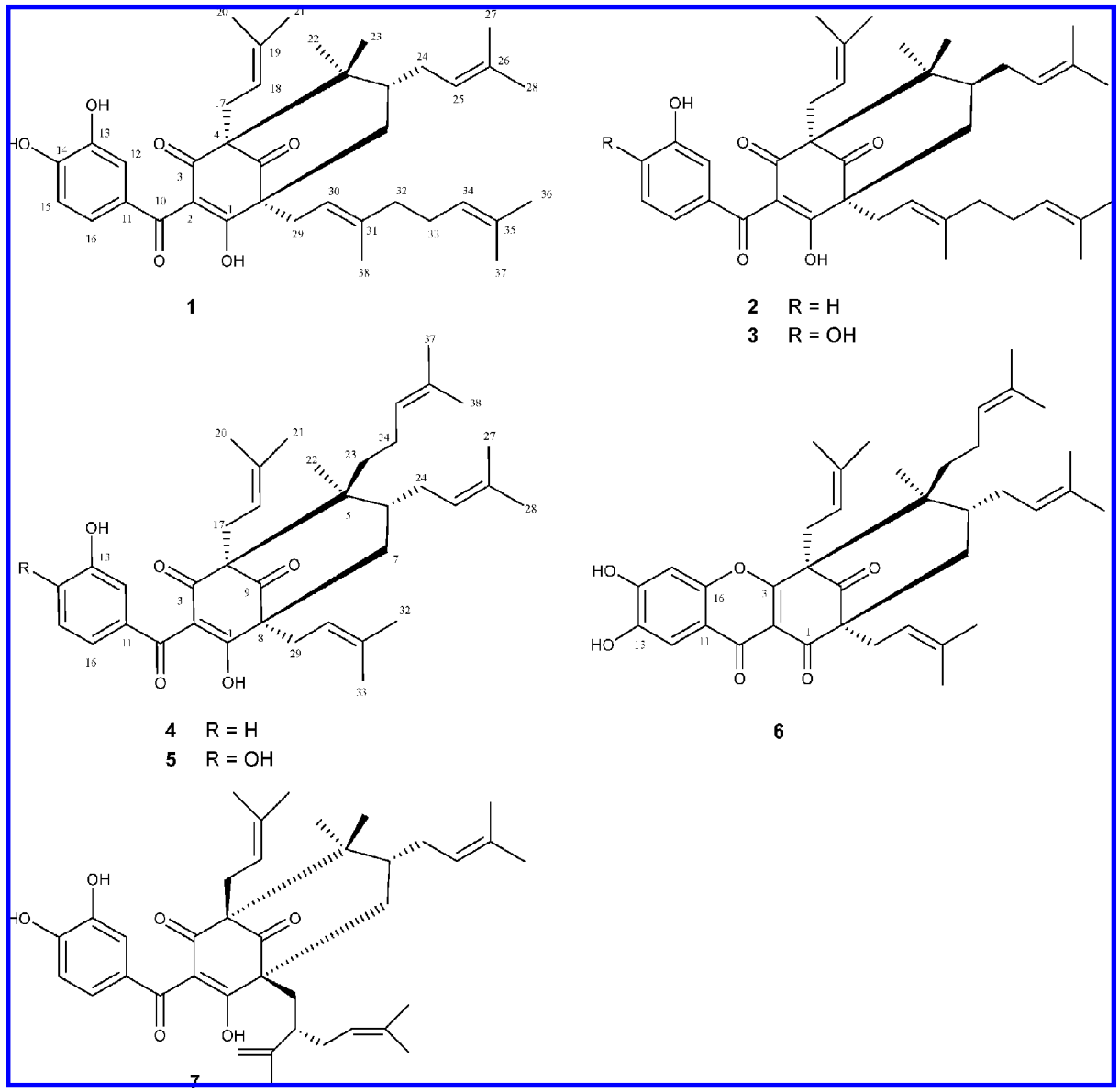


Figure 1. Structures of polyisoprenylated benzophenones (**1**−**5**, **7**) and oxy-guttiferone K (**6**) isolated from *Garcinia cambogia*.

elution program started with a linear gradient of 80% of eluent B to 90% of B in 5 min and remained isocratic for 19 min at a flow rate of 2.000 mL/min, then at 24 min, the flow rate was decreased to 1.500 mL/min while the elution remained isocratic for 12 min. Finally, the flow rate was increased again to a flow rate of 2.000 mL/min, and a linear gradient was performed to 100% B in 24 min. The detection wavelength was 360 nm.

Physical data for guttiferone M (**1**): yellow oil; $[\alpha]_D^{24}$: −29.8 (MeOH; *c* 0.15); IR (KBr) ν_{max} 3425, 2936, 1715, 1641, 1225, 1060 cm^{-1}; UV (MeOH) λ_{max} (log ε) 230 (sh), 280 (3.80), 355 (sh) nm; ^1H NMR (CD_3OD/0.1% TFA, 600 MHz) and ^{13}C NMR (CD_3OD/0.1% TFA, 150 MHz) (**Table 1**). ESI-MS *m/z* 625 $[M + Na]^+$, HR-MALDI-MS *m/z* $[M + Na]^+$ calcd for $C_{38}H_{50}O_6Na$, 625.3609; found, 625.3616.

Physical data for guttiferone N (**2**): yellow oil; $[\alpha]_D^{24}$: −34.5 (MeOH; *c* 0.07); IR (KBr) ν_{max} 3410, 2952, 1725 1650, 1190, 1030 cm^{-1}; UV (MeOH) λ_{max} (log ε) 220 (1.7), 245 (1.6), 293 (1.5) nm; ^1H NMR (CD_3OD/0.1% TFA, 600 MHz) and ^{13}C NMR (CD_3OD/0.1% TFA, 150 MHz) (**Table 1**). ESI-MS *m/z* 609 $[M + Na]^+$; HR-MALDI-MS *m/z* $[M + Na]^+$ calcd for $C_{38}H_{50}O_5Na$, 609.3660; found, 609.3667.

Physical data for oxy-guttiferone K (**6**): yellow oil; $[\alpha]_D^{24}$: +20.9 ($CHCl_3$; *c* 0.1); IR (KBr) ν_{max} 3450, 2966, 2922, 2856, 1732, 1672, 1604, 1494, 1384, 1292, 1267, 1191 cm^{-1}; UV (MeOH) λ_{max} (log ε) 250 (4.0), 285 (sh), 364 (3.6) nm; ^1H NMR (CD_3OD/0.1% TFA, 600 MHz) and ^{13}C NMR (CD_3OD/0.1% TFA, 150 MHz) (**Table 1**). ESI-MS *m/z* 623 $[M + Na]^+$; HR-MALDI-MS *m/z* $[M + Na]^+$ calcd for $C_{38}H_{48}O_6Na$, 623.3452; found, 623.3458.

RESULTS AND DISCUSSIONS

The diethyl ether extract of the fruits of *G. cambogia* submitted to RP-HPLC yielded, together with garcinol (**7**), three known guttiferones I, J, and K (**3**, **4**, and **5**), whose occurrence in *G. cambogia* has been described for the first time here. Furthermore, new polyisoprenylated benzophenones, namely, guttiferone M (**1**) and guttiferone N (**2**), along with the novel oxidized derivative of guttiferone K (**6**), have been identified (**Figure 1**).

The ^1H and ^{13}C NMR spectra of all compounds were recorded in CD_3OD with 0.1% TFA to enhance the rate of the keto−enol interconversion of the β-hydroxy-α,β-unsaturated ketone. The ^1H and ^{13}C NMR data in combination with the IR spectroscopic characteristics and the known phytochemistry of the genus *Garcinia* suggested that these compounds were members of the guttiferone family (*9*).

The ESI-MS spectra of **1** and **3** showed a sodium-containing molecular ion $[M + Na]^+$ at *m/z* 625 and a protonated molecular

Table 1. ^{13}C and ^{1}H NMR Spectroscopic Data of Compounds **1**, **2**, and **6**

	1			**2**			**6**		
position	δ_C	δ_H (J in Hz)	HMBC (H→C)	δ_C	δ_H (J in Hz)	HMBC (H→C)	δ_C	δ_H (J in Hz)	HMBC (H→C)
1	194.0	–		195.4	–		196.5	–	
2	119.5	–		118.4	–		119.8	–	
3	191.2	–		195.4	–		177.6	–	
4	69.3	–		67.6	–		66.2	–	
5	48.0	–		49.1	–		51.4	–	
6	44.0	1.63 m	C5, C7, C22, C23, C24	47.5	1.57, m	C5, C7, C22, C23, C24	39.2	1.79, m	C5, C7, C22, C23
7	43.1	eq. 2.06, m ax. 1.53, t (13.1)	C1, C5, C6, C8, C9, C24, C29	40.6	2.18, m 2.08, m	C1, C5, C6, C8, C9, C24, C29	43.5	2.09 dd (13.5, 3.8) 1.57, m	C1, C5, C6, C8, C9, C24, C29
8	63.4	–		63.0	–		66.2	–	
9	208.8	–		209.0	–		206.4	–	
10	196.5	–		197.5	–		173.9	–	
11	129.6	–		139.6	–		118.0	–	
12	116.9	7.25, d (2.0)	C10, C11, C13, C14, C16	115.8	7.02, br t (2.4)	C16	109.5	7.50, s	C10, C11, C13, C14, C16
13	145.9	–		158.3	–		150.9	–	
14	152.2	–		120.3	7.00, br dt (7.7, 2.4)	C12, C16	154.8	–	
15	114.7	6.70, d (8.3)	C10, C11, C12, C13, C14,	129.4	7.18, t (7.7)	C11, C14	103.9	6.88, s	C10, C11, C13, C14, C16
16	124.8	6.99, dd (8.3, 2.0)	C10, C12, C13, C14	121.0	6.93, br dt (7.7, 1.6)	C12, C14	147.0	–	
17	25.6	2.73, dd (13.3, 8.2) 2.65, m	C4, C5, C9, C18, C19	26.7	2.74, dd (13.7, 8.8) 2.62, m	C4, C5, C9, C18, C19	26.6	3.04, dd (14.1, 8.8) 2.91, dd (14.1, 3.6)	C4, C5, C9, C18, C19
18	120.8	4.94, m	C20, C21	120.2	4.98, m	C20, C21	120.6	4.73, dd (8.8, 3.6)	C17, C20, C21
19	135.4	–		136.0	–		135.2	–	
20	26.1	1.66, s	C17, C18, C19, C21	26.0	1.69, s	C17, C18, C19, C21	26.0	1.53, s	C18, C19, C21
21	18.0	1.72, s	C18, C19, C20	18.1	1.70, s	C18, C19, C20	18.5	1.87, s	C18, C19, C20
22	16.2	0.83, s	C4, C5, C6, C23	27.1	1.06, s	C4, C5, C6, C23	17.2	0.95, s	C4, C5, C6, C23
23	23.6	1.20, s	C4, C5, C6, C22	22.9	1.26, s	C4, C5, C6, C22	37.2	1.99, m 1.62, m	C4, C5, C6, C22
24	28.9	2.17, m 1.76, m	C6, C25, C26	30.0	2.16, m 2.08, m	C6, C25, C26	30.2	2.03, m 1.81, m	C5, C6, C7, C25, C26,
25	123.4	5.04, m	C24, C27, C28	125.3	4.91, m	C24, C27, C28	122.6	4.96, br t (6.8)	C24, C27, C28
26	134.0	–		133.6	–		134.7	–	
27	25.7	1.71, s	C25, C26, C28	26.0	1.69, s	C25, C26, C28	25.7	1.69, s	C25, C26, C28
28	17.7	1.60, s	C25, C26, C27	17.9	1.52, s	C25, C26, C27	18.0	1.59, s	C25, C26, C27
29	30.8	2.55 (2H), d (7.3)	C1, C7, C8, C9, C30, C31,	31.5	2.55 (2H), d (6.8)	C1, C7, C8, C9, C30, C31	31.1	2.57, d (7.3)	C1, C7, C8, C9, C30, C31
30	120.3	5.20, t (7.3)	C29, C32, C38	120.0	5.20, t (6.8)	C29, C32, C38	120.4	5.01, br t (6.8)	C29, C32, C33
31	138.8	–		139.3	–		135.1	–	
32	40.8	2.03 (2H), m	C30, C31, C33	40.9	2.02 (2H), m	C30, C31, C33	25.9	1.64, s	C30, C31, C33
33	27.3	2.09, m 2.03, m	C31, C32, C34, C35	27.5	2.09 (2H), m	C31, C32, C34, C35	17.9	1.73, s	C30, C31, C32
34	125.1	5.10, m	C32, C33, C36, C37	125.0	5.11, m	C32, C33, C36, C37	29.8	1.81, m 1.39, m	C5, C35, C36
35	132.0	–		132.2	–		123.7	4.96, t (6.8)	C34, C37, C38
36	25.7	1.60, s	C34, C35, C37	25.8	1.62, s	C34, C35, C37	133.7	–	
37	17.5	1.57, s	C34, C35, C36	17.7	1.58, s	C34, C35, C36	25.9	1.63, s	C35, C36,C38
38	16.5	1.72, s	C29, C30, C31, C32	16.7	1.71, s	C29, C30, C31, C32	17.5	1.24, s	C35, C36,C37

ion $[M + H]^+$ at m/z 603; in the HR-MALDI-MS spectrum of **1**, a sodium-containing molecular ion $[M + Na]^+$ at m/z 625.3616 suggested the molecular formula $C_{38}H_{50}O_6Na$. For compound **1**, the proton signals at δ 6.99 (dd, $J = 8.3, 2.0$ Hz), δ 6.70 (d, $J = 8.3$ Hz), and δ 7.25 (d, $J = 2.0$ Hz), typical of an aromatic trisubstituted AMX system, together with the two *ortho*-dihydroxy aromatic carbon signals (δ 145.9 and 152.2), and a conjugated carbonyl signal (δ 196.5) suggested the presence of a 3,4-dihydroxybenzoyl group (**Table 1**). Moreover, the ^{13}C NMR spectrum showed signals for a nonconjugated ketone (δ 208.8), two quaternary carbons (δ 69.3 and 63.4), and an enolized 1,3-diketone (δ 194.0, 119.5, and 191.2), which along with quaternary (δ 48.0), methine (δ 44.0), and methylene (δ 43.1) carbons allowed us to identify the bicyclo[3.3.1]nonane ring system typical of the polyisoprenylated benzophenones (*8*). The NMR data of **1** revealed the presence of two tertiary methyl groups (δ_H 1.20/δ_C 23.6 and δ_H 0.83/δ_C 16.2), two prenyl, and one geranyl units (**Table 1**). The positions of the side chains were assigned by the HMBC, HSQC-TOCSY, and ROESY experiments: two isoprenyl units were located at C-4 and C-6, while the geranyl unit was located at C-8. HMBC correlations between the *gem*-dimethyl group (Me-22 δ_H 0.83 and Me-23 δ_H 1.20) and C-4, C-5, and C-6 allowed us to establish its position at C-5.

The ^{1}H and ^{13}C chemical shifts of compound **3** were almost superimposable on those of **1** except for Me-22 (δ_H 1.05/δ_C 27.1), Me-23 (δ_H 1.27/δ_C 23.0), C-6 (δ 47.6), and C-7 (δ 40.4) signals. Furthermore, whereas the large coupling constant of $^3J_{H6-H7ax} = 13.1$ Hz in **1** indicated a diaxial orientation between H6 and H7ax and an equatorial asset of the prenyl group at C-6, the coupling constant of $^3J_{H6-H7ax} = 6.0$ Hz in compound **3** was in agreement with the axial position of the prenyl group at C-6. As reported elsewhere (*9*), the ^{13}C chemical shift values of Me-22ax and C-6, experiencing significant variations upon the inversion of configuration at C-6, were considered diagnostic for the relative configurational assignment of C-6. Thus, when the C-6 isoprenyl group was equatorial we confirmed for compound **1** the carbon resonance of Me-22ax at δ 16.2 and the carbon resonance of C-6 upfield shifted at δ 44.0, whereas, when the C-6 isoprenyl group was axial, we found for compound **3** the expected carbon resonances of Me-22ax and C-6 to be δ 27.1 and δ 47.6, respectively.

The NMR data of compound **3** are also consistent with those of guttiferone I reported by Nilar (*15*). Hence, compound **1** was a diastereomer of guttiferone I (**3**) and was named guttiferone M.

The HR-MALDI-MS spectrum of **2** showed a major ion peak at m/z 609.3667 $[M + Na]^+$, corresponding to the molecular formula $C_{38}H_{50}O_5Na$. The ^{1}H and ^{13}C NMR data (**Table 1**) were superimposable on those of **3**, except for the aromatic protons at δ 7.18 (t, $J = 7.7$ Hz), 7.02 (br t, $J = 2.4$ Hz), 7.00 (br dt, $J = 7.7, 2.4$ Hz), and 6.93 (br dt, $J = 7.7, 1.6$ Hz), which were typical of a 1,3-disubstituted

benzene ring. The HSQC, HMBC, and ROESY experiments confirmed that **2** corresponded to the new 14-deoxyderivative of guttiferone I (**3**), named guttiferone N. In agreement with the above NMR data, the IR spectra of **1** and **2** exihibited absorptions characteristic for derivatives of this class of compounds. In particular, these spectra showed the stretching band of the O−H group at around 3400 cm^{-1}, the stretching band of the C−H group at around 2950 cm^{-1}, the C−C stretching band of a nonconjugated alkene in the range 1680−1640 cm^{-1}, and the absorption frequency of the C═O group at around 1715−1730 cm^{-1}. Furthermore, guttiferones M and N showed UV spectra typical for benzoylphloroglucinols.

Guttiferone J (**4**) and guttiferone K (**5**) were identified by comparison of their ^{1}H and ^{13}C NMR data with those reported in the literature (*16, 17*). Finally, garcinol (**7**) was identified by comparison of its ^{1}H and ^{13}C NMR data with those reported in the literature (*18*).

The HR-MALDI-MS spectrum of **6** showed a major ion peak at *m/z* 623.3458 $[M + Na]^+$, ascribable to the molecular formula $C_{38}H_{48}O_6Na$. The molecular formula suggested 15 degrees of unsaturation, thereby indicating that **6** had one more unsaturation than the above polyisoprenylated skeletons. Unlike previous compounds, the ^{1}H NMR aromatic region contained two unique singlet aromatic proton signals at δ 6.88 and δ 7.50 whose corresponding carbons were assigned by the HSQC experiment at δ 103.9 and at δ 109.5, respectively (**Table 1**). HMBC correlations between the proton signals at δ 6.88 and δ 7.50 to the carbon resonances at δ 147.0, 150.9, 154.8, together with the long-range correlations between the proton signal at δ 6.88 to the carbon resonance at δ 118.0, and between the proton signal at δ 7.50 to the carbon resonance at δ 173.9, allowed us to understand that C-16 was oxygenated. Moreover, HMBC correlations between the carbon resonance at δ 196.5 and the proton resonances of H-7 (δ 2.09 and 1.57) and H-29 (δ 2.57), and between the carbon resonance at δ 177.6 and the proton resonances of H-17 (δ 3.04 and 2.91) allowed the assignments of the signals at δ 196.5 and 177.6 to C-1 and C-3, respectively. Consequently, it was clear that the carbonyl at C-3 was enolized and that the oxygen was attached to C-16. Finally, the NMR data of **6** also revealed the presence of one tertiary methyl group (δ_H 0.95/δ_C 17.2) and four prenyl units, as found in guttiferone K (**5**). As concerning the IR data, together with the frequencies already observed for compounds **1** and **2**, other significant absorptions were present in the IR spectrum of **6**. The frequency at 1605 cm^{-1} was indicative of a C−C stretching of a conjugated alkene, while the frequency values in the 1300−1000 cm^{-1} region (e.g., 1292, 1267, and 1191 cm^{-1}) were attributable to the C−O stretching bond. The UV spectrum exhibited maxima at 250 and 364 nm, characteristic of an oxygenated xanthone skeleton.

Compound **6** could be well explained in terms of a cyclization involving the catechol ring as described in the literature (*11*). With the aim of studying the antioxidant mechanism and the oxidation pathways of garcinol in detail, Sang et al. (*11, 12*) studied the reactions of garcinol with the stable free radical DPPH and with the initiator AIBN. While the reaction of garcinol with DPPH involved the 1,3-diketone and the phenolic ring portions, the reaction of garcinol with the initiator AIBN involved the 1,3-diketone moiety, the two double bonds of the isoprenyl, and the isopropenyl units. Thus, GDPPH-1 and GDPPH-2 were obtained by a reaction initiated by DPPH at the hydroxyl group of C-3 and C-1 of the enolized diketone, respectively, and terminated on the catechol ring, while further minor products, a hydroperoxy derivative and isogarcinol, were obtained by reaction initiated by AIBN at the hydroxyl group of C-3 and C-1 of the enolized diketone and terminated on the isoprenyl and the isopropenyl moieties, respectively. Oxy-guttiferone K differs from guttiferone K in the same way that GDPPH-1 obtained by oxidation with DPPH differs from garcinol. To our knowledge, oxy-guttiferone K is the first example of a tetracyclic xanthone deriving from the oxidation of a polyisoprenylated benzophenone from a natural source, and its occurrence as a natural compound confirms the observation of Sang et al. that the principal sites of antioxidant reactions of polyprenylated benzophenones involve the 1,3-diketone and the phenolic ring.

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