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**Salleh, WMNHW, On, S, Ahmad, F, Sirat, HM, Taher, M, Sarker, SD and Nahar, L (2019) A new xanthone and a new benzophenone from the roots of *Garcinia hombroniana*. *Phytochemistry Letters*, 35. pp. 216-219. ISSN 1874-3900**

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1 **A new xanthone and a new benzophenone from the roots of *Garcinia hombroniana***

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34 **ABSTRACT**

35 In this study, the roots of *Garcinia hombroniana* were chemically investigated, in which novel  
36 derivatives of xanthone and benzophenone, known as garcihomxanthone (1) and  
37 garcihombrianone (2), respectively, together with garceduxanthone (3), cheffouxanthone (4),  
38 norathyriol (5), and 2,3',4,5'-tetrahydroxy-6-methoxybenzophenone (6) were isolated.. The  
39 structures of these compounds were elucidated by extensive spectroscopic techniques and  
40 evaluated based on references with previous literature data.

41

42 *Keywords:*

43 *Garcinia hombroniana*

44 Clusiaceae

45 Xanthone

46 Benzophenone

47 Garcihomxanthone

48 Garcihombrianone

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## 67 1. Introduction

68 The genus *Garcinia* (Clusiaceae) is distributed in tropical and subtropical countries of  
69 South East Asia, West and East Africa as well as in Central and South America. It comprises  
70 over 400 species in Asia, in which 49 species have been identified in Malaysia (Whitmore,  
71 1973; Li et al., 1990). The chemical analyses of *Garcinia* species revealed the presence of  
72 bioactive molecules such as xanthenes, benzophenones, biflavonoids, and triterpenoids  
73 (Muriithi et al., 2016; Thepthong et al., 2017; Salleh et al., 2017; Abdullah et al., 2018; Ibrahim  
74 et al., 2018;), which were previously shown to possess antioxidant as well as antibacterial,  
75 antimalarial, anti-inflammatory, and cytotoxic activities (Seruji et al., 2013; Oluwatosin et al.,  
76 2014; Dzoyem et al., 2015; Pailee et al., 2017; Tian et al., 2017).

77 *Garcinia hombroniana* Pierre is a small evergreen tree commonly known as ‘*seashore*  
78 *mangosteen*’, which is native to the tropical rainforests in Southeast Asian countries such as  
79 Vietnam, Cambodia, Malaysia and Thailand (Lim, 2012). The root is widely used in folk  
80 medicine as an anti-infective agent after birth and to relieve itchiness. Besides, the ethanolic  
81 extracts of this species have been shown to exhibit cytotoxicity, antitrypanosomal,  
82 antioxidation and antiplatelet aggregation activities (Saputri and Jantan, 2012; Dyary et al.,  
83 2015; Jamila et al., 2017). Although phytochemical analyses were performed on the pericarp,  
84 leaves, and twigs of *G. hombroniana* yielding compounds such as lanostanes,  
85 friedolanostanes, xanthenes, biflavonoids and triterpenes (Klaiklay et al., 2013; Jamila et al.,  
86 2014a, 2014b, 2016), no phytochemical investigation has ever been performed on the roots of  
87 the *G. hombroniana*. Thus, as a continuation of the phytochemical studies on this species (On  
88 et al., 2017; Salleh et al., 2017), we now report on the isolation and identification of novel  
89 derivatives of xanthone and benzophenone, known as garcihomxanthone (**1**) and  
90 garcihombrianone (**2**), (**Figure 1**), respectively, from the roots of *G. hombroniana*.

91

## 92 2. Results and discussion

93 Compound **1** was obtained as yellow needles and the HREIMS spectrum revealed a  
94 molecular ion peak at  $m/z$  342.2212 (calculated as  $m/z$  342.2215) with the molecular formula  
95 deduced as  $C_{19}H_{18}O_6$ . The IR spectrum showed the presence of absorption bands at  $3297\text{ cm}^{-1}$ ,  
96  $1627\text{ cm}^{-1}$ ,  $1603\text{ cm}^{-1}$ ,  $1583\text{ cm}^{-1}$ , and  $1552\text{ cm}^{-1}$  assigned to hydroxyl, carbonyl group,  
97 conjugated double bonds, and aromatic functional groups, respectively. The NMR spectral  
98 data for compound **1** are listed in **Table 1**. The  $^1\text{H}$  NMR spectrum exhibited signals  
99 characteristic for the 1,1-dimethylprop-2-enyl group, which was represented by a singlet of

100 six protons at  $\delta_{\text{H}}$  1.61 assigned to methyl groups, H-4' and H-5'. In addition, mutually coupled  
101 vinylic protons were observed as two doublets of doublets at  $\delta_{\text{H}}$  5.10 ( $J = 10.8$  and  $1.2$  Hz) and  
102  $\delta_{\text{H}}$  5.29 ( $J = 17.6$  and  $1.2$  Hz) assigned to H-3' $\alpha$  and H-3' $\beta$ , respectively. Similarly, another  
103 doublet of doublets signal of one proton was observed at  $\delta_{\text{H}}$  7.03 ( $J = 17.6$  and  $10.4$  Hz) and  
104 assigned to H-2', while a singlet signal at  $\delta_{\text{H}}$  6.40 was assigned to the aromatic proton of H-2.  
105 The spectrum also revealed the presence of a methoxy group which was indicated by a singlet  
106 at  $\delta_{\text{H}}$  3.89. Besides, an AB pattern was observed with  $J$  values of  $8.5$  Hz at  $\delta_{\text{H}}$  6.70 and 6.71,  
107 respectively, which were assigned to *ortho*-coupled aromatic protons, H-6 and H-5. Two  
108 singlets with one proton each resonated at  $\delta_{\text{H}}$  7.12 and 7.28 and were assigned to two hydroxyl  
109 groups at C-7 and C-3, respectively. The deshielded singlet signal at  $\delta_{\text{H}}$  10.75 was attributed  
110 to the chelated hydroxyl group, 1-OH. The COSY spectrum of compound **1** supported the  
111 couplings between the protons in the structure. The signal of H-2' at  $\delta_{\text{H}}$  7.03 was coupled with  
112 H-3' $\alpha$  ( $\delta_{\text{H}}$  5.10) and H-3' $\beta$  ( $\delta_{\text{H}}$  5.24). The presence of cross-peaks validated the assignments  
113 between H-5 ( $\delta_{\text{H}}$  6.71) and H-6 ( $\delta_{\text{H}}$  6.70) as *ortho*-coupled protons. The  $^{13}\text{C}$  NMR and DEPT  
114 spectra revealed eighteen peaks attributable to nineteen carbons in the structure. These peaks  
115 were characterised as a carbonyl, three methyl, one methylene, four methine, and ten  
116 quaternary carbons. The HMQC spectrum further confirmed the direct attachment between  
117 the protons and carbons as indicated by the cross-peaks between H-4'/H-5' ( $\delta_{\text{H}}$  1.61) with C-  
118 4'/C-5' ( $\delta_{\text{C}}$  26.3), H-3' $\alpha$ /H-3' $\beta$  ( $\delta_{\text{H}}$  5.10/5.29) with C-3' ( $\delta_{\text{C}}$  103.7), H-2' ( $\delta_{\text{H}}$  7.03) with C-2' ( $\delta_{\text{C}}$   
119 155.5), H-2 ( $\delta_{\text{H}}$  6.40) with C-2 ( $\delta_{\text{C}}$  97.6), H-5 ( $\delta_{\text{H}}$  6.71) with C-5 ( $\delta_{\text{C}}$  111.6), and H-6 ( $\delta_{\text{H}}$  6.70)  
120 with C-6 ( $\delta_{\text{C}}$  110.8). The HMBC spectrum supported the correlation between the protons and  
121 carbons, in which the side chain 1,1-dimethylprop-2-enyl was substituted at C-4 by exhibiting  
122 long-range correlations between H-4' and H-5' with C-4 ( $\delta_{\text{C}}$  119.3). Additionally, both methyl  
123 protons, H-4' and H-5', showed a correlation with C-2' ( $\delta_{\text{C}}$  155.5), while the aromatic proton,  
124 H-2 ( $\delta_{\text{H}}$  6.40), showed long-range correlations with C-9a ( $\delta_{\text{C}}$  99.5) and C-4 ( $\delta_{\text{C}}$  119.3). The  
125 placement of the methoxy group was also confirmed by the correlation of its proton ( $\delta_{\text{H}}$  3.89)  
126 with C-8 ( $\delta_{\text{C}}$  165.4). Likewise, the aromatic proton, H-6 ( $\delta_{\text{H}}$  6.70) showed correlations with  
127 C-10a ( $\delta_{\text{C}}$  142.9) and C-8 ( $\delta_{\text{C}}$  165.4), whereas H-5 ( $\delta_{\text{H}}$  6.71) was correlated with C-7 ( $\delta_{\text{C}}$  137.3)  
128 and C-8a ( $\delta_{\text{C}}$  135.7). A summary of these correlations is shown in **Figure 2**. Based on the data  
129 obtained from the detailed spectral analyses, compound **1** was determined as a new derivative  
130 of xanthone, identified as 1,3,7-trihydroxy-4-(1,1-dimethylprop-2-enyl)-8-methoxyxanthone,  
131 and given the trivial name, garcihomxanthone.

132 Compound **2** was also obtained as yellow needles and its molecular formula, C<sub>20</sub>H<sub>14</sub>O<sub>8</sub>,  
133 was determined from the HREIMS spectrum, which revealed a corresponding molecular ion  
134 peak at  $m/z$  382.1258 (calculated as  $m/z$  382.1254). The IR spectrum exhibited the presence of  
135 hydroxyl, carbonyl, and aromatic functional groups at 3250 cm<sup>-1</sup>, 1676 cm<sup>-1</sup>, 1579 cm<sup>-1</sup>, and  
136 1470 cm<sup>-1</sup>, respectively. The NMR spectral data of compound **2** are tabulated in **Table 2**. The  
137 <sup>1</sup>H NMR spectrum showed two singlets integrated for each proton at  $\delta_H$  5.97 and 5.98, which  
138 were assigned to H-6 and H-3, respectively. Signals representing the symmetrical resorcinol  
139 in the system were observed as an A<sub>2</sub>B spin system at  $\delta_H$  6.60 (d,  $J$  = 2.4 Hz) and  $\delta_H$  6.48 (t,  $J$   
140 = 2.4 Hz) which were assigned to H-2'/H-6' and H-4', respectively. The spectrum also  
141 displayed the presence of an ABX coupling system as indicated by signals representing a  
142 doublet of doublets at  $\delta_H$  7.17 ( $J$  = 8.0 and 2.4 Hz, H-6'') as well as a doublet at  $\delta_H$  6.86 ( $J$  =  
143 8.0 Hz, H-5'') and  $\delta_H$  7.25 ( $J$  = 2.4 Hz, H-2''). In addition, three broad singlets with two protons  
144 each, were resonated at  $\delta_H$  8.62, 10.14, and 10.42, respectively, and assigned to six hydroxyl  
145 groups at C-4''/C-3'', C-3'/C-5', and C-5/C-2. The COSY spectrum supported the couplings  
146 between the protons in the structure. The signal observed for H-4' at  $\delta_H$  6.48 was coupled with  
147 H-2'/H-6' ( $\delta_H$  6.60), while the signal of the proton, H-5'' ( $\delta_H$  6.86), showed a cross-peak with  
148 H-6'' ( $\delta_H$  7.17) which was also found to be coupled with H-2'' ( $\delta_H$  7.25). Analysis of the <sup>13</sup>C  
149 NMR, DEPT and HMQC spectra revealed the presence of eight methine carbons which  
150 resonated at  $\delta_C$  95.0 (C-3), 105.2 (C-4'), 106.4 (C-2'/C-6'), 114.1 (C-5''), 116.2 (C-2''), and  
151 122.5 (C-6''), ten quaternary carbons at  $\delta_C$  132.9 (C-1'), 144.2 (C-3''), 149.1 (C-4''), 143.7 (C-  
152 1'), 158.0 (C-3'/C-5'), 161.8 (C-1), 162.8 (C-4), 163.5 (C-5), and 164.4 (C-2), and two  
153 carbonyl groups at  $\delta_C$  197.0 and 198.7. Moreover, the HMBC spectrum showed long-range  
154 correlations between H-6 ( $\delta_H$  5.97) with C-4 ( $\delta_C$  162.8) and C-2 ( $\delta_C$  164.4), while H-3 ( $\delta_H$   
155 5.98) displayed correlations with C-1 ( $\delta_C$  161.8) and C-5 ( $\delta_C$  163.5). Cross-peaks were also  
156 observed between H-4' ( $\delta_H$  6.48) with C-2' ( $\delta_C$  106.4) and H-2'/H-6' ( $\delta_H$  6.60) with carbonyl  
157 carbon ( $\delta_C$  198.7) and the neighbouring carbons. Besides, correlations were observed between  
158 H-5'' ( $\delta_H$  6.86) with C-1'' ( $\delta_C$  132.9) and C-3'' ( $\delta_C$  144.2), while H-6'' ( $\delta_H$  7.17) showed cross-  
159 peaks with carbonyl carbon ( $\delta_C$  197.0), C-4'' ( $\delta_C$  149.1), and C-2'' ( $\delta_C$  116.2). In addition, H-  
160 2'' ( $\delta_H$  7.25) showed correlations with carbonyl carbon ( $\delta_C$  197.0) and C-4'' ( $\delta_C$  149.1). The  
161 HMBC connectivities are summarised in **Figure 2**. Based on the data obtained in this study,  
162 the structure of compound **2** was established as [4-(3',5'-dihydroxybenzoyl)-2,5-dihydroxy-  
163 phenyl]-(3'',4''-dihydroxyphenyl)methanone, and given the trivial name, garcihombrianone.

164 In addition to the these new compounds, several other known compounds including  
165 garceduxanthone (**3**) (Zakaria et al., 2006), cheffouxanthone (**4**) (Vanessa et al., 2012),  
166 norathyriol (**5**) (Chappell, 1995) and 2,3',4,5'-tetrahydroxy-6-methoxybenzophenone (**6**) (Ran  
167 et al., 2004) were identified based on the comparison of their spectroscopic data with  
168 respective published data. Based on the NMR data, the purity of all the isolated compounds  
169 was well over 90%.

170

### 171 **3. Experimental**

#### 172 *3.1. General experimental procedures*

173 Mass spectra measurements were performed on a Agilent Technologies 6530 accurate-  
174 mass e-TOF LC/MS, with a ZORBAX Eclipse XDB-C18 rapid resolution HT (4.6 mm×50  
175 mm×1.8 mm column) and electron impact ionization set at 70 eV. The UV spectra were  
176 recorded using a Shimadzu UV 1601PC spectrophotometer. Melting points were determined  
177 using a Leica Gallen III hot-stage melting point apparatus and were reported uncorrected. The  
178 IR spectra were recorded on a Perkin-Elmer 1600 FTIR spectrophotometer. The 1D and 2D  
179 NMR spectra were recorded in deuterated acetone-d<sub>6</sub> on a Bruker Avance 400 MHz  
180 spectrometer, in which chemical shifts ( $\delta$ ) were reported in ppm on  $\delta$  scale and the coupling  
181 constants ( $J$ ) were measured in Hz. Merck silica gels were used for vacuum liquid  
182 chromatography (VLC) (230-400 mesh) and column chromatography (CC) (70-230 mesh).  
183 Thin-layer chromatography (TLC) aluminium sheets pre-coated with silica gel 60 F<sub>254</sub> (0.2  
184 mm thickness) were used to detect and monitor components present in the crude samples or  
185 fractions. The TLC plates were sprayed with 5% H<sub>2</sub>SO<sub>4</sub> and 1% vanillin in MeOH, and heated  
186 at 120°C for 5 min, prior to the visualisation of spots under UV light (254 and 366 nm). All  
187 solvents were of analytical grade.

188

#### 189 *3.2. Plant material*

190 The roots of *Garcinia hombroniana* Pierre was collected from Kuantan, Pahang,  
191 Malaysia in November 2009. The species was identified by Muhammad Taher from the  
192 International Islamic University Malaysia (IIUM) and the voucher specimen (MT20)  
193 deposited at the Herbarium of Kulliyah of Pharmacy, IIUM.

194

#### 195 *3.3. Extraction and isolation*

196 The dried and powdered roots of *G. hombroniana* (200 g) were sequentially extracted  
197 using Soxhlet extraction for 18 hours with *n*-hexane (2.5 L) and acetone (2.5 L) at room  
198 temperature. The extracts were concentrated under reduced pressure to produce *n*-hexane (3.12  
199 g) (GHRH) and acetone (4.86 g) (GHRA) extracts, which were observed as a gummy dark  
200 brown liquid. The *n*-hexane extract (GHRH, 3.12 g) was subjected to silica gel VLC (*n*-  
201 hexane: CHCl<sub>3</sub>: EtOAc), in which nine fractions were obtained. Each fraction was subjected  
202 to TLC analysis. Fractions with similar patterns observed on TLC were combined to produce  
203 four major fractions: GHRH1 (0.15 g), GHRH2 (0.35 g), GHRH3 (0.17 g), and GHRH4 (0.43  
204 g). Fraction GHRH2 (0.35 g), and GHRH4 (0.43 g) were further subjected to silica gel CC  
205 (150 g; *n*-hexane: CHCl<sub>3</sub>) to produce garceduxanthone (**3**) (5.6 mg) (yellow spot; R<sub>f</sub> 0.32; *n*-  
206 hexane: EtOAc, 6:4) and cheffouxanthone (**4**) (6.7 mg) (orange spot; R<sub>f</sub> 0.40; *n*-hexane:  
207 EtOAc, 4:6), respectively, which were both obtained as yellow needles. The acetone extract  
208 of the roots of *G. hombroniana* was subjected to silica gel VLC (200 g, *n*-hexane: CHCl<sub>3</sub>:  
209 EtOAc), in which eight fractions were obtained and subjected to TLC analysis. Similarly, as  
210 performed for *n*-hexane extracts, fractions with similar patterns on the TLC plate were  
211 combined to produce four major fractions: GHRA1 (0.21 g), GHRA2 (0.25 g), GHRA3 (0.35  
212 g), and GHRA4 (0.57 g). Fraction GHRA3 (0.35 g) was subjected to silica gel CC (*n*-  
213 hexane:CHCl<sub>3</sub>) to produce norathyriol (**5**) (4.2 mg) (yellow spot; R<sub>f</sub> 0.50; *n*-hexane: EtOAc,  
214 3:7), which was obtained as yellow needles, while fraction GHRA2 (0.25 g) was subjected to  
215 silica gel CC (150 g, *n*-hexane:CHCl<sub>3</sub>) to produce 2,3',4,5'-tetrahydroxy-6-  
216 methoxybenzophenone (**6**) (7.4 mg) (orange spot; R<sub>f</sub> 0.45; *n*-hexane: EtOAc, 4:6), which was  
217 obtained as pale yellow needles. Fractions GHRA4 (0.57 g) and GHRA1 (0.21 g) were  
218 subjected to silica gel CC (150 g, *n*-hexane: CHCl<sub>3</sub>) to produce compound (**1**) (5.7 mg) and  
219 compound (**2**) (5.3 mg), respectively, which were obtained as yellow needles.

220 Garcihomxanthone (**1**): yellow needles, m.p 152-154°C; R<sub>f</sub> 0.52 (yellow spot; *n*-hexane:  
221 EtOAc, 6:4); IR (KBr): 3297, 1627, 1603, 1583, 1552 cm<sup>-1</sup>; UV<sub>max</sub> (MeOH) nm (log ε) 220  
222 (4.50), 258 (5.70), 275 (4.15), 342 (2.14); HREIMS *m/z* 342.2212 (calculated 342.2215 for  
223 C<sub>19</sub>H<sub>18</sub>O<sub>6</sub>); <sup>1</sup>H NMR (CD<sub>3</sub>COCD<sub>3</sub>, 400 MHz) and <sup>13</sup>C NMR (CD<sub>3</sub>COCD<sub>3</sub>, 100 MHz) data see  
224 **Table 1**.

225 Garcihombrianone (**2**): yellow needles, m.p 170-174°C; R<sub>f</sub> 0.25 (yellow spot *n*-hexane:  
226 EtOAc, 4:6); IR (KBr): 3250, 1676, 1579, 1470 cm<sup>-1</sup>; UV<sub>max</sub> (MeOH) nm (log ε) 220 (3.75),  
227 230 (4.12), 304 (4.35); HREIMS *m/z* 382.1258 (calculated 382.1254 for C<sub>20</sub>H<sub>14</sub>O<sub>8</sub>); <sup>1</sup>H NMR  
228 (CD<sub>3</sub>COCD<sub>3</sub>, 400 MHz) and <sup>13</sup>C NMR (CD<sub>3</sub>COCD<sub>3</sub>, 100 MHz) data see **Table 2**.



229

#### 230 **4. Conclusion**

231 In the present study, the isolation and chemical characterization of a new xanthone (**1**)  
232 and a new benzophenone (**2**) from the roots of *G. hombroniana* were achieved. The structures  
233 of these isolates were accomplished using comprehensive spectroscopic means. Various  
234 xanthenes and benzophenones have previously been reported from other *Garcinia* species,  
235 and the current findings expand and reinforce the existence of chemical diversity in the genus  
236 *Garcinia*. The presence of xanthenes and benzophenones in the genus *Garcinia* might have  
237 some chemotaxonomic implications.

238

#### 239 **Appendix A. Supplementary data**

240 Supplementary data including 1D/2D NMR, IR, and MS for compound (**1-2**) are available as  
241 supporting information.

242

#### 243 **Acknowledgements**

244 The authors thank the Research University Grant (GUP) for financial support under vote  
245 Q.J130000.2526.03H93 and the Faculty of Science, Universiti Teknologi Malaysia for  
246 research facilities. L Nahar gratefully acknowledges the financial support of the European  
247 Regional Development Fund - Project ENOCH (No. CZ.02.1.01/0.0/0.0/16\_019/0000868)

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328 **Table 1.**  
329 NMR spectral data of compound **1**

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331 **Table 2.**  
332 NMR spectral data of compound **2**

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334 **Figure 1.** Chemical structures of the isolated compounds (**1-6**)

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336 **Figure 2.** Selected HMBC correlations of compounds (**1-2**)

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361 **Table 1**  
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No.	$\delta_{\text{H}}$ (m, <i>J</i> in Hz)	$\delta_{\text{C}}$
1	-	164.0
2	6.40 (s)	97.6
3	-	137.9
4	-	119.3
4a	-	158.6
5	6.70 (d, 8.5)	111.6
6	6.71 (d, 8.5)	110.8
7	-	137.3
8	-	165.4
8a	-	135.7
9	-	168.6
9a	-	99.5
10a	-	142.9
1'	-	41.6
2'	7.03 (dd, 17.6, 10.4)	155.5
3' $\alpha$	5.10 (dd, 10.8, 1.2)	103.7
3' $\beta$	5.29 (dd, 17.6, 1.2)	
4'	1.61 (s)	26.3
5'	1.61 (s)	26.3
1-OH	10.75 (s)	-
3-OH	7.28 (s)	-
7-OH	7.12 (s)	-
8-OCH <sub>3</sub>	3.89 (s)	55.6

<sup>1</sup>H (400 MHz) and <sup>13</sup>C (100 MHz) in CD<sub>3</sub>COCD<sub>3</sub>

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382 **Table 2**  
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No.	$\delta_{\text{H}}$ (m, <i>J</i> in Hz)	$\delta_{\text{C}}$
1	-	161.8
2	-	164.4
3	5.98 (s)	95.0
4	-	162.8
5	-	163.5
6	5.97 (s)	95.0
1'	-	143.7
2'	6.60 (d, 2.4)	106.4
3'	-	158.0
4'	6.48 (t, 2.4)	105.2
5'	-	158.0
6'	6.60 (d, 2.4)	106.4
1''	-	132.9
2''	7.25 (d, 2.4)	116.2
3''	-	144.2
4''	-	149.1
5''	6.86 (d, 8.0)	114.1
6''	7.17 (dd, 8.0, 2.4)	122.5
C=O	-	197.0
C=O	-	198.7
3,6-OH	10.42 (br s)	-
3',5'-OH	10.14 (br s)	-
4'',5''-OH	8.62 (br s)	-

384  $^1\text{H}$  (400 MHz) and  $^{13}\text{C}$  (100 MHz) in  $\text{CD}_3\text{COCD}_3$

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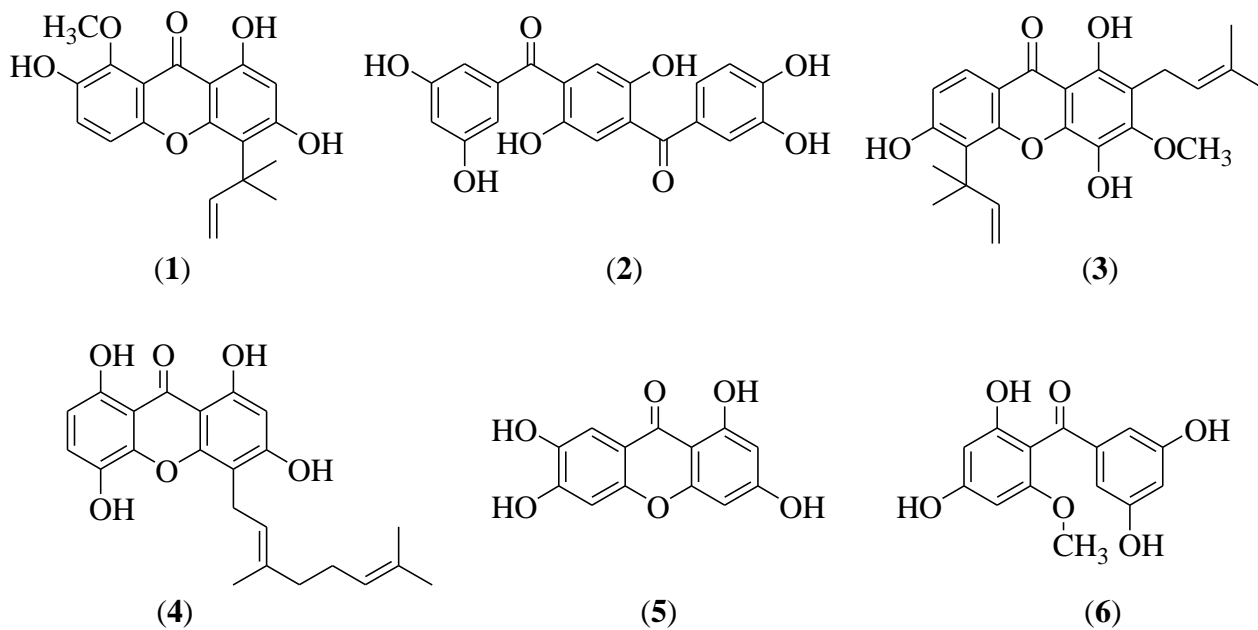
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397 **Figure 1.**

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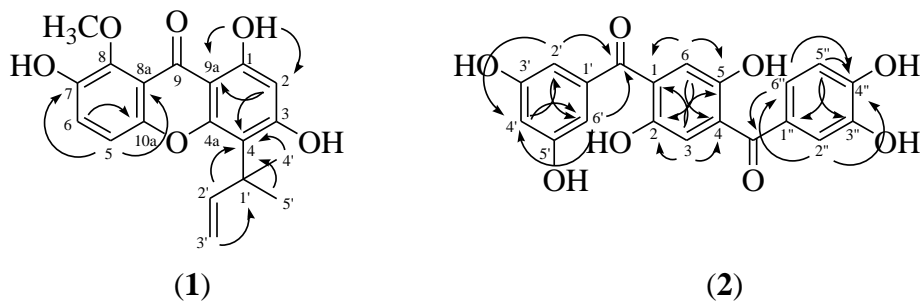
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403 **Figure 2.**

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