Phytochemistry Letters 11 (2015) 24–27

Contents lists available at ScienceDirect

Phytochemistry Letters

journal homepage: www.elsevier.com/locate/phytol

Biphenyl derivatives from the twigs of *Garcinia bracteata* and their biological activities

Yinke Li [a,c], Zhengyin Wang [c], Xianxue Wu [a], Yuchun Yang [b], Ying Qin [b], Congfang Xia [b], Yanlin Meng [b], Ming Li [a], Xue-Mei Gao [b], Qiufen Hu [b,*]

[a] College of Resource and Environment, Yuxi Normal University, Yuxi 653100, PR China
[b] Key Laboratory of Chemistry in Ethnic Medicinal Resources, State Ethnic Affairs Commission & Ministry of Education, Yunnan University of Nationalities, Kunming 650031, PR China
[c] College of Resources and Environment, Southwest University, Chongqing 400716, PR China

ARTICLE INFO

Article history:
Received 4 August 2014
Received in revised form 9 November 2014
Accepted 14 November 2014
Available online 25 November 2014

Keywords:
Biphenyl derivatives
Garcinia bracteata
Anti-tobacco mosaic virus activity
Cytotoxicity

ABSTRACT

Three new biphenyl derivatives, bractebiphenyls A–C (**1**–**3**), along with five known biphenyl derivatives (**4**–**8**) were isolated from the acetone extract of the twigs of *Garcinia bracteata*. Their structures were elucidated by spectroscopic methods, including extensive 1D and 2D NMR techniques. The anti-tobacco mosaic virus (anti-TMV) activities of **1**–**8** were evaluated. Compound **3** showed high anti-TMV activities with inhibition rates of 28.4%, which is close to that of Ningnanmycin (30.2%). Compounds **1**–**3**, **6** and **8** were also tested for their cytotoxicities against five human tumor cell lines (NB4, A549, SHSY5Y, PC3, and MCF7), and **3** showed high cytotoxicities against A549 and PC3 cell with IC_{50} values of 3.6 and 2.7 μM, respectively.

1. Introduction

The genus *Garcinia* (Clusiaceae) is commonly distributed in tropical and subtropical countries of South East Asia, West and East Africa, and Central and South America. This genus is known to produce xanthones and benzophenones [Gao et al., 2010; Liu et al., 2010; Ritthiwigrom et al., 2013; Wu et al., 2013a,b], and many of these compounds show interesting biological activities including anti-microbial, anti-HIV and anti-oxidant activities.

The *Garcinia bracteata*, a plant of genus *Garcinia*, is distributed in the south of Yunnan and Guangxi Province of China [Li et al., 2007]. In previous, some xanthones and benzophenones were isolated from this plant [Hu et al., 2013a; Na et al., 2010; Niu et al., 2012; Thoison et al., 2000, 2005], and these compounds exhibited various activities. Motivated by a search for new bioactive metabolites from genus Garcinia, the chemical constituents of the twigs of *G. bracteata* were reinvestigated by our group. As a result, three new (**1**–**3**) and five known (**4**–**8**) biphenyl derivatives were isolated. This paper deals with the isolation and structural characterization of these compounds, their anti-tobacco mosaic virus (anti-TMV) activities, and their cytotoxicities against five human tumor cell lines (NB4, A549, SHSY5Y, PC3, and MCF7).

2. Results and discussion

The twigs of *G. bracteata* were extracted with 70% aqueous acetone. The extract was subjected repeatedly to column to column chromatography on silic gel, sephadex LH-20, RP-18 and preparative HPLC to afford compounds **1–8**, including three new biphenyl derivatives, bractebiphenyls A–C (**1**–**3**), together with five known biphenyl derivatives, doitungbiphenyl A (**4**) [Siridechakorn et al., 2014], doitungbiphenyl B (**5**) [Siridechakorn et al., 2014], 2,2-dimethyl-3,5-dihydroxy-7-(4-hydroxyphenyl) chromane (**6**) [Ribeiro et al., 2011], oblongifoliagarcinine A (**7**) [Wu et al., 2008], and schomburgbiphenyl (**8**) [Mungmeea et al., 2013]. The structures of the compounds **1–8** were shown in Fig. 1, and the ^1H and ^{13}C NMR data of **1–3** were listed in Table 1.

Bractebiphenyl A (**1**) was obtained as a pale yellow gum. Its molecular formula, $C_{18}H_{20}O_5$, was deduced from its HR-EI-MS data, which show a molecular ion peak at *m/z* 339.1202 $[M+Na]^+$ (calcd. 339.1208). Its UV spectrum reveals maximal absorption bands at 210, 231, 265, and its IR spectrum indicated the presence of hydroxyl group at 3435 cm^{-1}. The ^1H NMR and ^{13}C NMR spectra of **1** (Table 1) display a 1,2,3,4,5-pentasubstituted aromatic ring

* Corresponding author. Tel.: +86 871 5913043.
E-mail addresses: huqiufena@aliyun.com, mingli@yxnu.net (Q. Hu).

http://dx.doi.org/10.1016/j.phytol.2014.11.003
1874-3900/

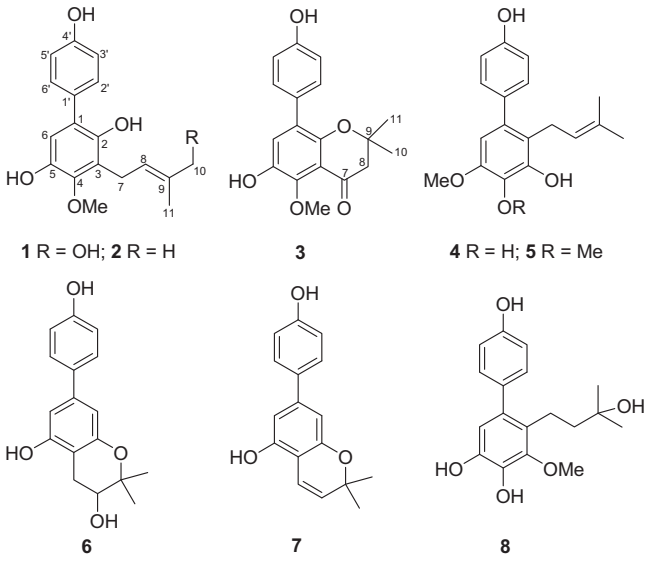

Fig. 1. The structures of compounds **1**–**8**.

(δ_C 134.6 s, 145.0 s, 124.7 s, 147.9 s, 138.4 s, 113.8 d; δ_H 6.44 s), a 1,4-disubstituted aromatic ring (δ_C 134.3 s, 131.6 d (2C), 115.6 d (2C), 156.9 s; δ_H 7.05 (d) 8.5, 6.80 (d) 8.5), a 4-hydroxy-3-methylbutyl group (δ_C 26.8 t, 127.2 d, 134.7 s, 68.9 t, 13.7 q; δ_H 3.24 d (6.8), 5.37 t (6.8), 3.85 s, 1.49 s) [Asano et al., 1996], and a methoxy group (δ_C 60.7 q, δ_H 3.81 s). The HMBC correlations of H-6 (δ_H 6.44 s) with C-1′ (δ_C 134.3 s), and of H-2′,6′ (δ_H 7.05) with C-1 (δ_C 134.6) indicated **1** should be processed a biphenyl skeleton [Siridechakorn et al., 2014]. The 4-hydroxy-3-methylbutyl group was placed on C-3 because the methylene protons H-7 (δ_H 3.24) showed HMBC correlations (Fig. 2) with C-2 (δ_C 145.0), C-3 (δ_C 124.7), and C-4 (δ_C 147.9); whereas the methoxy group (δ_H 6.44) was placed at C-4 (δ_C 147.9) because of its HMBC correlation with C-4. In addition, three phenolic group should be located at C-2, C-5, and C-4′ to support the 1,2,3,4,5-pentasubstituted aromatic ring and 1,4-disubstituted aromatic ring in **1**. The geometry of the prenyl side-chain double bond was determined to be *E* by the chemical shift of the methyl carbon (δ_C 13.7) [Asano et al., 1996]. This was distinguished from the *Z* form [Zhang et al., 2012] by the

Table 1
^{1}H and ^{13}C NMR data for compounds **1–3** (in C_5DOD_3, 100 and 400 MHz).

No.	**1**		**2**		**3**	
	δ_C	δ_H (m, *J*, Hz)	δ_C	δ_H (m, *J*, Hz)	δ_C	δ_H (m, *J*, Hz)
1	134.6 s		134.8 s		119.3 s	
2	145.0 s		144.4 s		146.1 s	
3	124.7 s		124.4 s		110.6 s	
4	147.9 s		148.0 s		151.8 s	
5	138.4 s		138.8 s		138.5 s	
6	113.8 d	6.44 s	113.1 d	6.47 s	118.2 d	6.71 s
7	26.8 t	3.24 d (6.8)	27.8 t	3.08 d (6.6)	192.1 s	
8	127.2 d	5.37 t (6.8)	123.5 d	5.29 t (6.6)	48.0 t	2.54 d (11.1)
9	134.7 s		132.1 s		79.0 s	
10	68.9 t	3.85 s	17.5 q	1.55 s	26.3 q	1.55 q
11	13.7 q	1.49 s	25.9 q	1.74 s	26.3 q	1.55 q
1′	134.3 s		134.1 s		133.0 s	
2′,6′	131.6 d	7.05 (d) 8.5	131.4 d	7.08 (d) 8.5	131.4 d	7.07 (d) 8.5
3′,5′	115.6 d	6.80 (d) 8.5	115.7 d	6.83 (d) 8.5	115.9 d	6.81 (d) 8.5
4′	156.9 s		157.1 s		157.3 s	
4-OMe	60.7 q	3.81 s	61.0 q	3.84 s	61.1 q	3.83 s

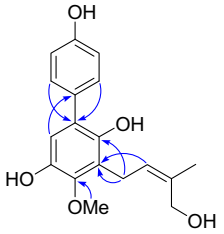

Fig. 2. Selected HMBC (–) correlations of **1**.

methyl signal (δ_C 20–22 ppm) of the *Z* form because it would appear more low-field by the decreasing γ-effect. The structure of **1** was therefore, assigned.

Compounds **2** and **3** were obtained as yellow gum. Compound **2** was assigned the molecular formula $C_{18}H_{20}O_4$ by HRESIMS at *m/z* 323.1254 $[M+Na]^+$. The ^{1}H and ^{13}C NMR spectra of **2** (Table 1) were very similar to those of **1**. The major differences due to an oxidation methylene group (δ_C 68.9 t, δ_H 3.85 s) in **1** was replaced by a methyl group (δ_C 25.9 q; δ_H 1.74 q) in **2**. These changes indicated the 4-hydroxy-3-methylbutyl group was replaced by a prenyl group. The precise subsituents position aslo conducted by further analysis of it HMBC correlations. The structure of bractebiphenyl B **(2)** is therefore determined.

The ^{1}H and ^{13}C NMR data of **3** was also very similar to these of **1**. The major difference resulted from the appearance of a dimethyl-2,3-dihydropyran-4-one moiety [Hu et al., 2013b] [δ_C 192.1 s, 48.0 t, 79.0 s, 26.3 q (2C); δ_H 2.52, 2.55 s (2H), 1.55 s, (6H)] and disappearance of 4-hydroxy-3-methylbutyl group in **3**. The HMBC correlation of the methoxy protons (δ_H 3.83) with C-4 (δ_C 147.9) indicated that this methoxy group located at C-4. Since the methoxy group at C-4 was determined, the Long-range HMBC correlations of H-8 [δ_H 2.54 d (11.1)] to C-3 (δ_C 110.6), C-9 (δ_C 79.0), and C-10,11 (δ_C 26.3) indicated that the isoamyl ketone moiety was attached to the aromatic ring at positions of C-2 and C-3, to form a dimethyl-2,3-dihydropyran-4-one moiety. Two phenolic group should be located at C-5, and C-4′ to support the 1,2,3,4,5-pentasubstituted aromatic ring and 1,4-disubstituted aromatic ring in **3**. Compound **3** was thus defined as shown, and given the the trivail name of bractebiphenyl C.

Compounds **1–8** were tested for their anti-TMV activities. The anti-TMV activities were tested using the half-leaf method [Hu et al., 2013c]. Ningnanmycin (a commercial product for plant disease in China), was used as a positive control. Their antiviral inhibition rates at the concentration of 20 μM are listed in Table 2. The results showed that compound **3** had high anti-TMV activities with inhibition rates of 28.4%, which is close to that of Ningnanmycin (30.2%). Compounds **1**, **2**, **4**–**8** also showed modest anti-TMV activities with inhibition rates in the range of 15.5–21.5%, respectively.

The cytotoxicities of compounds **1**–**3**, **6** and **8** were tested using a previously reported procedure [Hu et al., 2013b]. The cytotoxic abilities against NB4, A549, SHSY5Y, PC3, and MCF7 tumor cell lines by MTT-assay (with taxol as the positive control) are shown in Table 3. The results revealed that compound **3** showed high

Table 2
TMV infection inhibition activities of compounds **1**–**8**.

Compounds	Inhibition rates (%)	Compounds	Inhibition rates (%)
1	15.5 ± 2.3	**6**	19.5 ± 2.9
2	18.2 ± 2.7	**7**	21.0 ± 2.5
3	28.4 ± 2.5	**8**	16.7 ± 2.6
4	15.8 ± 2.0	Ningnamycin	30.2 ± 3.3
5	21.5 ± 2.4		

All results are expressed as mean ± SD (standard deviations); $n = 3$ for all groups.