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NOTE

A New Biphenyl from *Garcinia oligantha* and Its Cytotoxicity

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A new biphenyl *i.e.*, 3-methoxy-5-methoxycarbonyl-4-hydroxy-biphenyl (**1**) was isolated from the stems of *Garcinia oligantha*. Its structure was elucidated by spectroscopic methods, including extensive 1D- and 2D- NMR. This biphenyl was tested for its cytotoxicity against five human tumor cell lines (NB4, A549, SHSY5Y, PC3 and MCF7) and it showed modest cytotoxicity against SHSY5Y, A549 and MCF7 cell with IC_{50} values of 7.1, 6.2 and 4.8 μM, respectively.

Keywords: *Garcinia oligantha*, Biphenyl, Cytotoxicity.

Garcinia is a plant genus of the family Clusiaceae native to Asia, Australia, tropical and southern Africa and Polynesia[1]. This genus is known to be a rich source of polyisoprenylated benzophenones and xanthones. Up to now, series of active components extracted from this genus displayed clear apoptosis-inducing effect against different cancer cells such as HeLa[2-4].

In our previous studies, some apoptotic compounds were isolated from the stems of *Garcinia oligantha*[5]. Continuing the efforts to discover bioactive metabolites from local plants, we now reinvestigated the chemical constituents of the *G. oligantha* growing in Xishuangbanna Prefecture, leading to the isolation of a new biphenyl. The structure of this new biphenyl was determined by means of spectroscopic methods including 1D and 2D NMR techniques and this compound exhibited modest cytotoxicity against SHSY5Y, A549 and MCF7 cell with IC_{50} values of 7.1, 6.2 and 4.8 μM, respectively.

IR spectra were obtained in KBr disc on a Bio-Rad Wininfmred spectrophotometer. ESI-MS were measured on a VG Auto Spec-3000 MS spectrometer. ^1H, ^{13}C and 2D NMR spectra were recorded on Bruker DRX-500 instrument with TMS as internal standard. Column chromatography was performed on silica gel (200-300 mesh), or on silica gel H (10-40 mm, Qingdao Marine Chemical Inc., China). Second separation was used an Agilent 1100 HPLC equipped with ZORBAX-C_{18} (21.2 mm × 250 mm, 7.0 μm) column and DAD detector.

The stems of *Garcinia oligantha* were collected in Xishuangbanna Prefecture, Yunnan Province, People's Republic of China, in September 2011. The identification of the plant material was verified by Prof. Chen Y. J. (Yunnan Nationalities University). A voucher specimen (YNNI 11-9-38) has been deposited in our laboratory.

Extraction and isolation: The air-dried and powdered stems of *G. oligantha* (2.2 kg) were extracted four times with 70 % methanol (4 × 5 L) at room temperature and filtered. The crude extract (105 g) was applied to silica gel (200-300 mesh) column chromatography, eluting with a chloroform-acetone gradient system (20:1, 9:1, 8:2, 7:3, 6:4, 5:5), to give six fractions A-F. The further separation of fraction D (7:3, 5.2 g) by silica gel column chromatography, eluted with chloroform-methanol (9:1, 8:2, 7:3, 6:4, 1:1), yielded mixtures D1-D5. Fraction D2 (8:2, 0.86 g) was subjected to preparative HPLC (42 % methanol, flow rate 12 mL/min) to give the new biphenyl (12.8 mg).

3-Methoxy-5-methoxycarbonyl-4-hydroxy-biphenyl (1): White powder; UV (MeOH) λ_{max} (log ε): 210 (4.22), 285 (3.68), 326 (3.15) nm; IR (KBr, ν_{max}, cm^{-1}): 3406, 2927, 1722, 1606, 1542, 1428, 1389, 1320, 1237, 1165, 1062, 865, 728; ^1H and ^{13}C NMR: Table-1; ESIMS (positive ion mode): *m/z* 281 $[M + Na]^+$; HRESIMS (positive ion mode): *m/z* 281.072 $[M + Na]^+$ (calcd $C_{15}H_{14}O_4Na$ for 281.079).

A 70 % aq. methanol extract prepared from the stems of *G. oligantha* was subjected repeatedly to column chromatography on Si gel, Sephadex LH-20, RP-18 and preparative

TABLE-1
^{1}H NMR AND ^{13}C NMR DATA OF COMPOUND **1** (IN C_5ND_5; 500 AND 125 MHz)

No.	δ_C (m)	δ_H (m, J, Hz)	No.	δ_C (m)	δ_H (m, J, Hz)
1	122.5 s	-	1′	140.6 s	-
2	115.8 d	6.97 d (2.2)	2′, 6′	127.5 d	7.58 dd (8.0, 1.8)
3	151.6 s	-	3′, 5′	129.2 d	7.46 td (8.0, 1.8)
4	149.7 s	-	4′	128.3 d	7.35 tt (8.0, 1.8)
5	118.2 s	-	5-OMe	56.3 q	3.82 s
6	125.8 d	7.62 d (2.2)	7-OMe	52.6 q	4.15 s
7′	169.2 s	-	4-OH	-	12.26 s

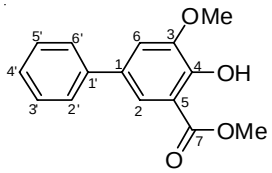

Fig. 1. Structure of **1**

HPLC to afford the new biphenyl. Its structure was as shown in Fig. 1 and its ^{1}H and ^{13}C NMR data was listed in Table-1.

Compound **1** was obtained as white powder and was assigned the molecular formula of $C_{15}H_{14}O_4$, by HRESIMS at *m/z* 281.072 [M + Na]$^+$ (calcd *m/z* 281.079). The ^{1}H and ^{13}C NMR spectrum showed signals characteristic of one 1,3,4,5-tetrasubstituted benzene [δ_C 122.5 s, 115.8 d, 151.6 s, 149.7 s, 118.2 s, 125.8 d; δ_H 6.97 d (2.2) and 7.62 d (2.2), one 1-monosubstituted benzene [δ_C 140.6 s, 127.5 d (2C), 129.2 d (2C), 128.3 d; δ_H 7.58 dd 2H (8.0, 1.8), 7.46 td 2H (8.0, 1.8) and 7.35 tt (8.0, 1.8)], one methoxycarbonyl group (δ_C 169.2, 52.6; δ_H 4.15 s)[6], one methoxyl groups (δ_C 56.3 q; δ_H 3.82 s) and one phenolic hydroxyl group (δ_H 12.26 s). Strong absorption bands accounting for hydroxyl (3406 cm^{-1}), carbonyl (1722) and aromatic groups (1606, 1542, 1428 cm^{-1}) could be observed in its IR spectrum. The UV absorptions at 210, 285 and 326 also suggested the presence of a conjugated aromatic ring system. The HMBC correlations (Fig. 2) of H-2',6' (δ_H 7.58) with C-1 (δ_C 122.5) and of H-2 (δ_H 6.97) and H-6 (δ_H 7.62) with C-1' (δ_C 140.6) suggested that compound **1** should be a biphenyl derivative[7,8]. In the HMBC experiment, the methoxycarbonyl group at C-5 was supported by HMBC correlations (Fig. 2) of H-6 (δ_H 7.62) with the ester carbonyl carbon (δ_C 169.2) and no correlation was observed between H-2 (δ_H 6.97) and the ester carbonyl. The HMBC correlation of methoxy proton (δ_H 3.82) and C-3 (δ_C 151.6) suggesting that the methoxyl group was located at C-3. The phenolic hydroxyl groups located at C-4 was supported by the HMBC correlations of the phenolic hydroxyl proton signal (δ_H 12.26) with C-3 (δ_C 151.6), C-4 (δ_C 149.7) and C-5 (δ_C 118.2). Thus, the structure of **1** was determined as 3-methoxy-5-methoxycarbonyl-4-hydroxy-biphenyl.

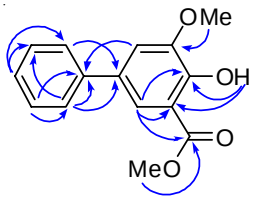

Fig. 2. Selected HMBC (⌒) correlation of **1**

Since certain of the compounds form Garcinia genus exhibit potential cytotoxicity[5,9,10]. The new biphenyl was tested for its cytotoxicity against five human tumor cell lines (NB4, A549, PC3 and MCF7) using the MTT method as reported previously[11]. Taxol was used as the positive control. The results shown that the new biphenyl exhibited modest cytotoxicity against SHSY5Y, A549 and MCF7 cell with IC_{50} values of 7.1, 6.2 and 4.8 μM, respectively.

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REFERENCES

1. D. Obolskiy, I. Pischel, N. Siriwatanametanon and M. Heinrich, *Phytother. Res.*, **23**, 1047 (2009).
2. X.M. Gao, T. Yu, F. Lai, Y. Zhou, X. Liu, C.F. Qiao, J.Z. Song, S.L. Chen, K.Q. Luo and H.X. Xu, *Bioorg. Med. Chem.*, **18**, 4957 (2010).
3. X.-M. Gao, T. Yu, F.S.F. Lai, J.-X. Pu, C.-F. Qiao, Y. Zhou, X. Liu, J.-Z. Song, K.Q. Luo and H.-X. Xu, *Tetrahedron Lett.*, **51**, 2442 (2010).
4. X. Liu, T. Yu, X.M. Gao, Y. Zhou, C.F. Qiao, Y. Peng, S.L. Chen, K.Q. Luo and H.X. Xu, J. Nat. Prod., **73**, 1355 (2010).
5. X.M. Gao, T. Yu, M.Z. Cui, J.X. Pu, X. Du, Q. Han, Q. Hu, T.-C. Liu, K.Q. Luo and H.-X. Xu, *Bioorg. Med. Chem.*, **22**, 2350 (2012).
6. H.Y. Yang, Y.H. Gao, D.Y. Niu, L.Y. Yang, X.M. Gao, G. Du and Q.F. Hu, *Fitoterapia*, **91**, 189 (2013).
7. V. Rukachaisirikul, K. Tadpetch, A. Watthanaphanit, N. Saengsanae and S. Phongpaichit, *J. Nat. Prod.*, **68**, 1218 (2005).
8. K.H. Kim, S.U. Choi, S.K. Ha, S.Y. Kim and K.R. Lee, *J. Nat. Prod.*, **72**, 2061 (2009).
9. X.-M. Gao, M.-Z. Cui, T. Yu, Q.-F. Hu, J.-X. Pu, X. Du, T.-C. Liu and K.Q. Luo, *Helv. Chim. Acta*, **96**, 494 (2013).
10. Q. Hu, X. Gao, D. Niu, X. Li, Y. Qin, Z. Yang, G. Zhao, Z. Yang and Z. Chen, *Heterocycles*, **87**, 1127 (2013).
11. X.M. Gao, R.R. Wang, D.Y. Niu, C.Y. Meng, L.M. Yang, Y.T. Zheng, G.Y. Yang, Q.F. Hu, H.D. Sun and W.L. Xiao, *J. Nat. Prod.*, **76**, 1052 (2013).