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NOTE

A New Biphenyl from the Fruits of *Schisandra lancifolia* and Its Cytotoxicity

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A new biphenyl *i.e.*, lancibiphenyl A (**1**) was isolated from the fruits of *Schisandra lancifolia*. The structure of **1** was elucidated by spectroscopic methods including extensive 1D- and 2D-NMR techniques. Compound **1** was evaluated for its cytotoxicity and it exhibited moderate cytotoxicity against A549 and PC3 cell with IC_{50} values of 6.4 and 5.7 μM, respectively.

Keywords: Biphenyl, *Schisandra lancifolia*, Cytotoxicity.

The fruits of *Schisandra* plants are used as herb medicine as the treat of sedative and tonic agents[1,2]. Previous studies[3-5] have shown that the plants of this genus are rich in lignans and triperpenoids, which have been found to possess some beneficial activities. *Schisandra lancifolia* belongs to the genus *Schisandra* of the family *Schisandraceae*. It is a climbing plant mainly distributed in Yunnan, Sichuan and Shanxi Province in mainland China[6]. In previous studies, some new dibenzocyclooctadiene lignans were isolated from the fruits of *S. lancifolia* from of Erlang Mountain area of Sichuan Province[7]. In our continuing efforts to identify bioactive natural products from the medicinal plants of the *Schisandraceae*, a chemical investigation on the fruits of *S. lancifolia* from Lijiang Country, Yunnan Province was carried out. As a result, a new biphenyl (**1**) was separated from this plant and the cytotoxicity of **1** was evaluated. In this paper, the structure elucidation and biological activities of the compound are discussed.

General procedures: Optical rotations were measured in a Horiba SEPA-300 polarimeter. UV spectra were obtained on a Shimadzu UV-2401A spectrophotometer and CD spectra were measured on a JASCO J-810 spectropolarimeter. A Tenor 27 spectrophotometer was used for scanning IR spectra (KBr pellets). 1D- and 2D- NMR spectra were recorded on a DRX-500 spectrometer with TMS as internal standard. Chemical shifts (δ) are expressed in ppm with reference to TMS. HRESIMS was performed on an API QSTAR spectrometer or a VG Autospec-3000 spectrometer. Preparative HPLC was performed on a Shimadzu LC-8A liquid chromatograph equipped with Zorbax PrepHT GF (21.2 mm × 25 cm, 7 μm) column or Venusil MP C_{18} (20 mm × 25 cm, 5 μm) column. Column chromatography was performed using Si gel (200-300 mesh, Qing-dao Marine Chemical, Inc., Qingdao, People's Republic of China), Lichroprep RP-18 gel (40-63 μm, Merck, Darmstadt, Germany), Sephadex LH-20 (Sigma-Aldrich Corp. -St Louis, USA), or MCI gel (75-150 μm, Mitsubishi Chemical Corporation, Tokyo, Japan). Column fractions were monitored by TLC and the spots were visualized by heating the plates after spraying with 5 % H_2SO_4 in EtOH.

The fruits of *S. lancifolia* were collected in Lijiang Country of Yunnan Province, People's Republic of China, in September 2011. The identification of the plant material was verified by Prof. Xi-Wen Li of Kunming Institute of Botany, Chinese Academy of Sciences. A voucher specimen (KIB 11-9-58) has been deposited in our Laboratory.

Extraction and isolation: The air-dried and powdered fruits of *S. lancifolia* (2.2 kg) were extracted four times with 70 % $(CH_3)_2CO$ (4 × 3 L) at room temperature and filtered, with the filtrate evaporated under the reduced pressure and partitioned with EtOAc (3 × 1 L). The EtOAc partition (152 g) was applied to silica gel (200-300 mesh) column chromatography, eluting with a $CHCl_3$-Me_2CO gradient system (20:1, 9:1, 8:2, 7:3, 6:4, 5:5), to give five fractions, A-E. The further separation of fraction D (7:3, 18.6 g) by silica gel column chromatography, eluted with petroleum ether-acetone and semi-preparative HPLC (40 % MeOH-H_2O, flow rate 12 mL/min) to give **1** (15.2 mg).

Lancibiphenyl A (1): White powder; UV (MeOH) λ_{max} (log ε): 210 (4.18), 282 (3.75), 332 (3.08) nm; IR (KBr, ν_{max}, cm^{-1}) 3418, 2914, 1718, 1605, 1538, 1425, 1386, 1325, 1259, 1168, 1074, 867, 748; ^1H and ^{13}C NMR: see Table-1; ESIMS

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	133.6 s	-	5′	116.7 d	6.97, d, *J* = 8.6
2, 6	104.7 d	6.65 s	6′	134.6 d	6.97, dd, *J* = 8.6, 2.0
3, 5	148.9 s	-	7′	168.2 s	-
4	134.5 s	-	3-OMe	56.1 q	3.86 s
1′	133.0 s	-	7′-OMe	52.2 q	4.12 s
2′	135.6 d	7.88, d, *J* = 2.2	4-OH	11.8 s	-
3′	118.3 s	-	4′-OH	12.2 s	-
4′	155.6 s	-		-	-

(positive ion mode): *m/z* 327 $[M + Na]^+$; HRESIMS (positive ion mode): *m/z* 327.0839 $[M + Na]^+$ (calcd $C_{16}H_{16}NaO_6$ for 327.0845).

The fruits of *S. lancifolia* were extracted with 70 % acetone. The extract produced was subjected repeatedly to column chromatography on silica gel, Sephadex LH-20, RP-18 and RP-HPLC, to afford the new biphenyl, lancibiphenyl A. Its structure was shown in Fig. 1 and its ^{1}H and ^{13}C NMR spectroscopic data were listed in Table-1.

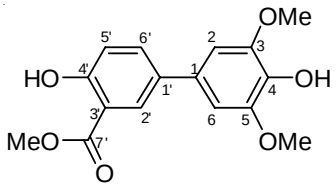

Fig. 1. Structure of compound **1**

Compound **1** was obtained as yellow gum and was assigned the molecular formula of $C_{16}H_{16}O_6$, by HRESIMS at *m/z* 327.0839 $[M + Na]^+$ (calcd *m/z* 327.0845). The ^{1}H and ^{13}C NMR spectrum showed signals characteristic of one 1,3,4,5-tetrasubstituted benzene [δ_C 133.6 s, 104.7 d (2C), 148.9 s (2C), 134.5 s; δ_H 6.65 s], 2.0 Hz), one 1,3,4-trisubstituted benzene [δ_C 133.0 s, 135.6 d, 118.3 s, 155.6 s, 116.7 d, 134.6 d; δ_H 7.88 d *J* = 2.2, 6.97 d *J* = 8.6, 6.97 dd *J* = 8.6, 2.0], one methoxycarbonyl group (δ_C 168.2, 52.2; δ_H 4.12 s), one singlet signal of two identical methoxyl groups (δ_C 56.1 q; δ_H 3.86 s) and two phenolic hydroxyl groups (δ_H 11.8 s, 12.2 s). Strong absorption bands accounting for hydroxy (3418 cm^{-1}), carbonyl (1718) and aromatic groups (1605, 1538, 1425 cm^{-1}) could be observed in its IR spectrum. The UV absorptions at 210, 282 and 330 also suggested the presence of a conjugated aromatic ring system. The HMBC correlations (Fig. 2) of H-2,6 (δ_H 6.65) with C-1' (δ_C 133.0) and of H-2' (δ_H 7.88) and H-6' (δ_H 6.97) with C-1 (133.6) suggested that compounds **1** should be a biphenyl derivative[8]. In the HMBC experiment, the methoxy protons affected the signal of two equivalent aromatic protons (H-2 and H-6), suggesting that two identical methoxyl groups were located at C-3 and C-5 (δ_C 148.9) of the tetrasubstituted benzene ring. HMBC cross-peaks between H-2,6 with C-3,4 and C-5 also confirmed their location. The methoxycarbonyl group at C-6 was supported by HMBC correlations of H-2' with the ester carbonyl carbon (δ_C 168.2) and no correlation was observed between H-5' and the ester carbonyl. Tow phenolic hydroxy groups located at C-4 and C-4' were supported by the HMBC correlations of one phenolic hydroxy proton

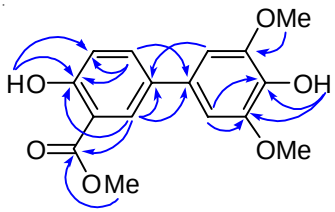

Fig. 2. Selected HMBC ( ) correlation of **1**

signal (δ_H 11.8) with C-4 (δ_C 134.5) and C-3,5 (δ_C 148.9); and of another phenolic hydroxy proton signal (δ_H 12.2) with C-3' (δ_C 118.3), C-4' (δ_C 155.6) and C-5' (δ_C 116.7), respectively.

Compound **1** was tested for its cytotoxicity against five human tumor cell lines (NB4, A549, SHSY5Y, PC3 and MCF7) using the MTT method as reported previously[9]. The cytotoxicity tests for compound was performed against NB4, A549, SHSY5Y, PC3 and MCF7 tumor cell lines by MTT-assay with paclitaxel as the positive control. The results shown that compound **1** exhibited moderate cytotoxicity against A549 and PC3 cell with IC_{50} values of 6.4 and 5.7 μM, respectively.

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