Asian Journal of Chemistry; Vol. 26, No. 8 (2014), 2411-2413

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2014.16082

A New Cytotoxic Stilbenoid from *Arundina graminifolia*

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Received: 22 July 2013; *Accepted*: 2 December 2013; *Published online*: 15 April 2014; AJC-15037

A new stilbenoid, gramniphenol K (**1**) was isolated from *Arundina graminifolia*. Its structure was elucidated by spectroscopic methods including extensive 1D- and 2D-NMR techniques. The cytotoxicity of gramniphenol K was evaluated against five human tumor cell lines, and it showed cytotoxicity against A549, SHSY5Y and MCF7 cells with IC_{50} values of 6.2, 7.5 and 4.7 μM, respectively.

Keywords: *Arundina graminifolia*, Stilbenoid, Structure elucidation, Cytotoxicity.

INTRODUCTION

Arundina graminifolia (bamboo orchid) is a terrestrial multiperennial orchid[1]. It has been widely used for clearing heat, detoxicating and dissipating blood stasis by Dai people lived in Xishuangbanna, Yunnan province of China[2]. Previous phytochemical studies of *A. graminifolia* have shown the presence of stilbenoids[3], dibenzyls[4], phenanthrenes[5,6] and other phenolic compounds[7,8]. In our previous studies, some new phenolic compounds possessing anti-tobacco mosaic virus (anti-TMV) and anti-HIV-1 properties were isolated from *A. gramnifolia* grown in the Xishuangbanna and Honghe Prefecture[7,8]. Motivated by a search for new bioactive metabolites from local plants, our group has reinvestigated the chemical constituents of the whole plant of *A. graminifolia* growing in the Honghe Prefecture, Yunnan province, which led to the isolation and characterization of a new stilbenoid gramniphenol K (**1**). This paper deals with the isolation, structural characterization of this new compound and its cytotoxicity was evaluated against five human tumor cell lines.

EXPERIMENTAL

UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. A Tenor 27 spectrophotometer was used for scanning IR spectroscopy with KBr pellets. 1D and 2D NMR spectra were recorded on a DRX-500 NMR spectrometer with TMS as internal standard. Unless otherwise specified, chemical shifts (δ) are expressed in ppm with reference to the solvent signals. HRESIMS was performed on a VG Autospec-3000 spectrometer. Semipreparative HPLC was performed on a Shimadzu LC-8A preparative liquid chromatograph with Zorbax PrepHT GF (21.2 mm × 25 cm) or Venusil MP C_{18} (20 mm × 25 cm) columns. Column chromatography was performed using silica 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) and MCI gel (75-150 μm, Mitsubishi Chemical Corporation, Tokyo, Japan). The fractions were monitored by TLC and spots were visualized by heating silica gel plates sprayed with 5 % H_2SO_4 in EtOH.

The whole plant of *A. graminifolia* was collected in Honghe Prefecture, Yunnan province, People's Republic of China, in September 2011. The identification of the plant material was verified by Dr. Chen Y. J., Yunnan University of Nationalities. A voucher specimen (YNNU 2011-9-41) has been deposited in our laboratory.

Extraction and isolation: The air-dried and powdered *A. graminifolia* (0.8 kg) were extracted four times with 70 % aqueous acetone (4 × 1.5 L) at room temperature and filtered. The filtrate was evaporated under reduced pressure and the crude extract (22.6 g) was decolorized by MCI. The 90 % methanol part (14.5 g) was chromatographed on a silica gel column eluting with a $CHCl_3$-MeOH gradient system (20:1, 9:1, 8:2, 7:3, 6:4, 5:5), to give six fractions A-F. Further separation of fraction C (8:2, 22.6 g) by silica gel column chromatography, eluted with petroleum ether-acetone (9:1-1:2), yielded mixtures C1-C7. Fraction C3 (7:3, 0.87 g) was subjected to silica gel column chromatography using petroleum ether-acetone and semi-preparative HPLC (55 % MeOH-H_2O, flow rate 12 mL/min) to give gramniphenol K (1) (8.62 mg).

Gramniphenol K: Yellow gum; UV (MeOH), λ_{max} (log ε) 316 (3.76), 238 (4. 02), 210 (4.38); IR (KBr, ν_{max}, cm^{-1}): 3408, 3025, 2962, 2877, 1610, 1582, 1520, 1453, 1424, 1397, 1180, 1156, 1128, 1075, 852. ^1H and ^{13}C NMR data ($CDCl_3$, 500 MHz and 125 MHz, respectively) (Table-1). ESIMS (positive ion mode), *m/z* 323 $[M + Na]^+$; HRESIMS (positive ion mode), *m/z* 323.0890 $[M + Na]^+$ (Calcd. 323.0895 for $C_{17}H_{16}NaO_5$).

RESULTS AND DISCUSSION

The whole plants of *A. graminifolia* was extracted with 70 % aqueous acetone. The extract was subjected repeatedly to column chromatography and semi-preparative RP-HPLC separation to afford compound **1**. Its structure was shown in Fig. 1 and its ^1H and ^{13}C NMR data were listed in Table-1.

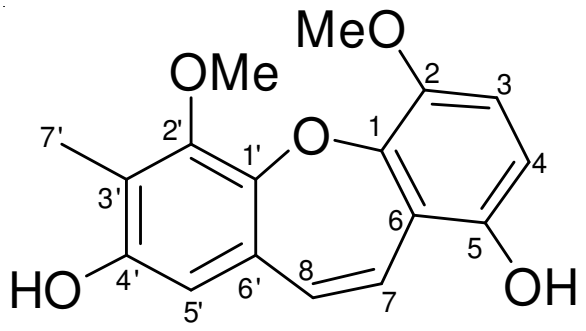

Fig. 1. Structures of new diphenylethylene

TABLE-1
^1H AND ^{13}C NMR DATA OF COMPOUND **1**
(δ IN ppm, DATA OBTAINED IN $CDCl_3$)

No.	δ_C (m)	δ_H (m, J, Hz	No.	δ_C (m)	δ_H (m, J, Hz)
1	143.6 s		3′	116.7 d	
2	145.3 s		4′	149.7 s	
3	114.2 d	6.76 d (8.8)	5′	104.3 d	6.53 s
4	107.8 d	6.65 d (8.8)	6′	127.5 s	
5	148.6 s		7′	11.2 q	2.15 s
6	120.2 s		2-OMe	55.8 q	3.81 s
7	126.4 d	7.04 d (11.6	2′-OMe	61.2 q	3.85 s
8	130.3 d	6.75 d (11.6	5-Ar-OH		10.58 brs
1′	136.0 s		4′-Ar-OH		10.72 brs
2′	154.4 s				

Compound **1** was obtained as a yellow gum. Its HRESIMS in the positive mode revealed a peak at *m/z* 323.0890 $[M + Na]^+$ indicative of the molecular formula of $C_{17}H_{16}NaO_5$, corresponding to 10 degrees of unsaturation. Its UV spectrum showed the maximum absorption at 316, 238 and 210 nm and its IR spectrum also exhibited the presence of hydroxy group (3408 cm^{-1}) and aromatic ring (1610, 1582, 1520, 1453 cm^{-1}). Its ^1H, ^{13}C and DEPT NMR spectra (Table-1) showed signals for 18 carbons and 18 hydrogen atoms, corresponding to the following functional groups: 1,2,5,6-Tetrasubstituted benzene [C-1 to C-6; δ_C 143.6, 145.3, 114.2, 107.8, 148.6 and 120.2; δ_H 6.76 d (J = 8.8) and 6.65 d (J = 8.8)], 1',2',3',4',6'-pentsubstituted benzene (C-1' to C-6'; δ_C 136, 154.4, 116.7, 149.7, 104.3, 127.5; δ_H 6.53 s), a pair of double bond [CH-7 and CH-8; δ_C 126.4 and 130.3; δ_C 7.04 d (J = 11.6) and 6.75 d (J = 11.6)], a methyl (δ_C 11.2, δ_H 2.15 s), two methoxyl groups (δ_C 55.8 q and 61.2 q; δ_H 3.81 s, 3.85 s) and two phenolic hydroxyl groups (δ_H 10.58 brs, 10.72 brs). Detailed analysis the functional groups suggested that compound **1** should be an dibenz[b,f]oxepin derivatives[9]. The general features of the ^1H and ^{13}C NMR spectra of compound **1** resembled to those of bauhiniastatin D[9], except that the disappearance of an aromatic proton and the appearance of a methoxy group signal (δ_C 55.8; δ_H 3.81) in **1**. In HMBC spectrum, the long-range correlations (Fig. 2) of methyl signal (δ_H 2.15) to C-2' (δ_C 154.4), C-3' (δ_C 116.7) and C-4' (δ_C 149.7) were observed in **1**. This led us to conclude that the methyl was located on C-3'. The HMBC correlations of two methoxy protons (δ_H 3.80, 3.87) with C-2 (δ_C 145.3) and C-2' (δ_C 154.4) revealed that two methoxy groups should be located at C-2 and C-2'. The HMBC correlations between the phenolic hydroxy proton (δ_H 11.58) and C-4 (δ_C 107.8), C-5 (δ_C 148.6) and C-6 (δ_C 120.2), as well as those between the other hydroxy proton (δ_H 10.72) and C-3' (δ_C 116.7), C-4' (δ_C 149.7) and C-5' (δ_C 104.3), led to the assignment of two phenolic hydroxyl groups at C-5 and C-4'. The above evidence led to oxepin structure **1** for gramniphenol K.

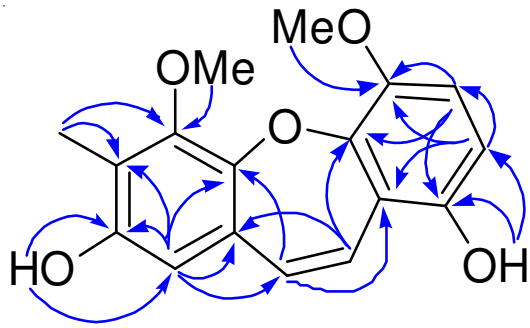

Fig. 2. Selected HMBC (↷) correlations of **1**

Since some of the stilbenoids from Orchidaceae exhibit potential cytotoxicity[9-12], compound **1** were tested for their cytotoxicity against five human tumor cell lines (NB4, A549, SHSY5Y, PC3 and MCF7) using the MTT method as reported previously[13]. Paclitaxel was used as the positive control. Compound **1** showed cytotoxicity against A549, SHSY5Y and MCF7cells with IC_{50} values of 6.2, 7.5 and 4.7 μM, respectively.

ACKNOWLEDGEMENTS

This research was supported by the National Natural Science Foundation of China (No. 21032085), the excellent Scientific and Technological Team of Yunnan High School (2010CI08), the Yunnan University of Nationalities Green Chemistry and Functional Materials Research for Provincial Innovation Team (2011HC008) and Open Research Fund Program of Key Laboratory of Ethnic Medicine Resource Chemistry (Yunnan University of Nationalities) (2010XY08).

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