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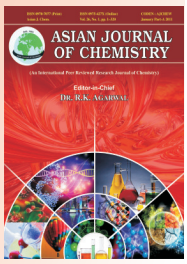

NOTE

A New Cytotoxic Diphenylethylene from *Arundina graminifolia*

JUAN XIA YANG, HUAN WANG, JIE LOU, LIMEI LI, GUI YOU LIU, XUEMEI GAO, QIUFEN HU and YANQING YE*

Key Laboratory of Chemistry in Ethnic Medicinal Resources, State Ethnic Affairs Commission and Ministry of Education, Yunnan University of Nationalities, Kunming 650031, P.R. China

*Corresponding author: E-mail: yey-qing@163.com

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A new diphenylethylene (**1**), gramistilbenoid L was isolated from *Arundina graminifolia*. Its structure was elucidated by spectroscopic methods including extensive ^{1}D- and ^{2}D NMR techniques. Compound **1** was evaluated for its cytotoxicity against five human tumor cell lines and it showed potent cytotoxicity against PC3 and SHSY5Y cells with IC_{50} values of 5.5 and 3.6 μM, respectively.

Keywords: *Arundina graminifolia*, Diphenylethylene, Cytotoxicity.

Arundina graminifolia (bamboo orchid) is a terrestrial multiperennial orchid with reedy stems, forming into large clumps growing to a height between 70 cm and 2 m. This tropical Asiatic genus extends from India, Nepal, Thailand, Malaysia, Singapore, South China to Indonesia and across the Pacific Islands[1]. It has been widely used for clearing heat, detoxicating and dissipating blood stasis by Dai people lived in Xishuangbanna, Yunnan province[2]. Previous phytochemical studies of *A. graminifolia* have shown the presence of stilbenoids[3], bibenzyls[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*[7,8]. Motivated by a search for new bioactive metabolites from local plants, our group has investigated the chemical constituents of the whole plant of *A. graminifolia* growing in the Honghe Prefecture, which led to the isolation and characterization of a new diphenylethylene (**1**). This paper deals with the isolation, structural characterization and cytotoxicity of this new compound.

General. UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. 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.

Plant material: Whole plant of *A. graminifolia* was collected in Honghe Prefecture, Yunnan Province, People's Republic of China, in September 2012. The identification of the plant material was verified by Dr. Yuan. N, of Kunming Institute of Botany, Chinese Academy of Sciences. A voucher specimen (YNNU 2012-9-44) has been deposited in our laboratory.

Extraction and isolation: The air-dried and powdered *A. graminifolia* (2.5 kg) were extracted four times with 70 % aqueous acetone (4 × 5 L) at room temperature and filtered. The filtrate was evaporated under reduced pressure and the crude extract (210 g) was decolourized by MCI. The 90 % methanol part (83.5 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. The further separation of fraction C (8:2, 8.26 g) by silica gel column chromatography, eluted with petroleum ether-acetone (9:1-1:2), yielded mixtures C1-C7. Fraction C3 (7:3, 1.62 g) was subjected to silica gel column chromatography using petroleum ether-acetone and semi-preparative HPLC (40 % MeOH-H_2O, flow rate 12 mL/min) to give **1** (7.6 mg).

TABLE-1
^{1}H AND ^{13}C NMR DATA OF COMPOUNDS **1** (δ IN ppm, 500 AND 125 MHz, IN C_5D_5N)

No.	δ_C (m)	δ_H (m, *J*, Hz)	No.	δ_C (m)	δ_H (m, *J*, Hz)
1	138.6 s		3′,5′	159.4 s	
2,6	105.3 d	6.58 s	4′	102.2 d	6.16 t, *J* = 2.0
3,5	156.8 s	-	7′	126.6 d	7.27 d, *J* = 16.2
4	112.7 s	-	8′	125.5 d	6.94 d, *J* = 16.2
7	22.3 t	2.92 t, *J* = 7.2	Ar-OH-3,5	-	10.86 brs
8	65.6 t	4.48 t, *J* = 7.2	Ar-OH-3′,5′	-	11.35 brs
1′	139.8 s	-	1″	169.4 s	-
2′, 6′	105.9 d	6.48 d, *J* = 2.0	2″	21.5 q	1.96 s

Gramistilbenoid L (1): Orange gum; UV (MeOH) λ_{max} (log ε) 210 (4.15), 240 (2.57), 286 (3.79) nm; IR (KBr, ν_{max}, cm^{-1}): 3420, 2915, 2884, 1687, 1615, 1532, 1450, 1363, 1264, 1038, 875, 774; ^{1}H and ^{13}C NMR data (C_5D_5N, 500 and 125 MHz) (Table-1). Neagative ESIMS *m/z* 329 $[M-H]^-$; neagative HRESIMS *m/z* 329.1029 $[M-H]^-$ (calcd. 329.1025 for $C_{18}H_{17}O_6$).

Whole plants of *A. graminifolia* was extracted with 70 % aqueous acetone. The extract was subjected repeatedly to column chromatography on silica gel, RP-18 and semi-preparative RP-HPLC separation to afford compound **1**. Its structure was shown in Fig. 1 and the ^{1}H and ^{13}C NMR data of the compound **1** were listed in Table-1.

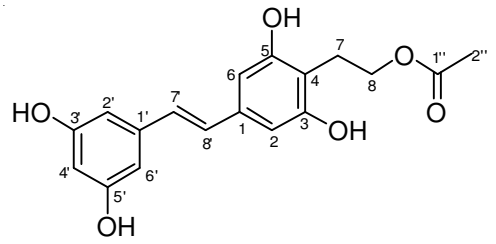

Fig. 1. Structures of compound **1**

Compound **1** was obtained as an orange gum. Its HRESIMS displayed a pseudomolecular ion [M-H]- at *m/z* 329.1029, consistent with the molecular formula $C_{18}H_{18}O_6$. The ^{1}H NMR spectrum of **1** (Table-1) showed resonances for two meta-aromatic protons from one 1,3,4,5-substituted phenyl ring at δ_H 6.58 (s, 2H), three *meta*-coupled aromatic protons at δ_H 6.16 (t, *J* = 2.0 Hz, 1H) and 6.48 (d, *J* = 2.0 Hz, 2H) from one 1,3,5-trisubstituted phenyl ring, as well as a pair of *trans*-olefinic proton, at δ_H 6.94 and 7.27 (d, *J* = 16.2 Hz, 1H each), typical of a trans-stilbene[9]. Two two-proton triplets at δ_H 2.92 and 4.48 with the same coupling constant (*J* = 7.2 Hz) observed suggested the existence a hydroxyethyl group. A singlet at δ_H 1.96 should be an acetoxy group. It ^{13}C NMR data (Table-1) also support the above structural units. The hydroxyethyl group located at C-4 was elucidated on the basis of the HMBC correlations of H-7 (δ_H 2.92) with C-3,5 (δ_C 156.8) and C-4 (δ_C 112.7) and H-8 (δ_H 4.48) with C-4 (δ_C 112.7). The long-range correlations between Ar-OH (δ_H 10.86) and the signal of C-2, C-3, C-4, C-5 and C-6 confirmed two hydroxy groups at C-3 and C-5, respectively. Correlations were also observed between Ar-OH (δ_H 11.35) and the signals of C-2′, C-3′, C-4′, C-5′ and C-6′ suggested that the other two hydroxy groups was attributed to C-3′ and C-5′, respectively. Moreover, the acetoxy group located at C-8 was supported by the HMBC correlation of H-8 (δ_H 4.48) with ester carbonyl (δ_C 169.4). Compound **9** was then elucidated as shown in Fig. 1 and gave the trivial name of gramistilbenoid L.

Since certain of the stilbenoids from orchidaceae exhibit potential cytotoxicity[10-12], 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[13]. Paclitaxel was used as the positive control. The results showed that compound **1** exhibited obvious cytotoxicity against PC3 and SHSY5Y cells with IC_{50} values of 5.5 and 3.6 μM.

ACKNOWLEDGEMENTS

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