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NOTE

A New Biphenyl from *Nicotiana tabacum* and its Anti-tobacco Mosaic Virus Activity

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A new biphenyl, tababiphenyl F (**1**) was isolated from the leaves of *Nicotiana tabacum*. Its structure was established on the basis of extensive spectroscopic analyses. Compound **1** was also tested for its anti-tobacco mosaic virus (anti-TMV) activity and its exhibited notable anti-tobacco mosaic virus activity with inhibition rate of 22.6 %.

Keywords: ***Nicotiana tabacum,*** **Biphenyl, Tababiphenyl F, Anti-tobacco mosaic virus activity.**

Nicotiana tabacum, tobacco, is a stout herbaceous plant in the Solanaceae (nightshade family) and now cultivated worldwide as the primary commercial source of tobacco, which is smoked or chewed as a drug for its mild stimulant effects[1,2]. In addition, *N. tabacum* is also used as insecticides, anesthetics, diaphoretics, sedatives and emetic agents in Chinese folklore medicines because of its containing many useful chemical compounds[1,3]. Previous investigation of this species led to the discovery of a number of new compounds by our groups, which were found to be shown various bioactivities, such as anti-HIV-1, anti-tobacco mosaic virus and cytotoxicity[4-9]. In continuing efforts to utilize *N. tabacum* and identify bioactive natural products, the phytochemical investigation of the leaves of Honghua Dajinyuan (a variety of *N. tabacum*) led to the isolation of a new biphenyls (**1**). This paper deals with the isolation, structural elucidation and anti-tobacco mosaic virus activity of this new compound.

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 DRX-500 spectrometers with TMS as internal standard. Unless otherwise specified, chemical shifts (δ) were expressed in ppm with reference to the solvent signals. HRESIMS was performed on an API QSTAR time-of-flight spectrometer, or a VG Autospec-3000 spectrometer, respectively. Preparative HPLC was performed on a Shimadzu LC-8A preparative liquid chromatograph with a ZORBAX PrepHT GF (21.2 mm × 25 cm, 7 μm) column or a Venusil MP C_{18} (20 mm × 25 cm, 5 μm) column. Column chromatography was performed with Si gel (200-300 mesh, Qing-dao Marine Chemical, Inc., Qingdao, 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 Si gel plates sprayed with 5 % H_2SO_4 in EtOH.

The variety of *Nicotiana tabacum* L studied is Honghuadajinyuan. Its leaves were collected from Wenshan County, Yunnan Province, P.R. China, in September 2012.

Extraction and isolation: The plant material of *N. tabacum* (1.5 kg) was ground and exhaustively extracted with Me_2CO-H_2O (v/v = 7:3, 3 × 5 L) at room temperature. The solvent was evaporated *in vacuo* and the crude extract was dissolved in H_2O and partitioned with EtOAc. The EtOAc portion (48.2 g) was chromatographed on a silica gel column (200-300 mesh, 15 × 120 cm, 0.8 kg), eluting with a $CHCl_3$-MeOH gradient system (20:1, 9:1, 8:2, 7:3, 6:4, 5:5 and 0:1), to give seven fractions A-G. Fraction C (8:2, 5.2 g) was decolorized by MCI gel (8 × 50 cm) firstly and then further separation of fraction C by silica gel column chromatography (200-300 mesh, 8 × 50 cm), eluted with $CHCl_3$/$(CH_3)_2CO$ (9:1-2:1), yielded mixtures C1-C6. C3 (0.65 g) were repeatedly chromatographed on silica gel (a, 200-300 mesh, 3 × 35 cm, petroleum ether-Me_2CO, 12:1, 9:1, 6:1 and 2:1, each 0.5 L; b, 200-300 mesh, 1.5 × 35 cm, $CHCl_3$-Me_2CO, 30:1, 20:1, 15:1, 10:1, each 0.2 L) and semi-preparative HPLC (38 % MeOH-H_2O, flow rate 12 mL/min) to yield **1** (11.8 mg).

Tababiphenyl F (**1**): $C_{13}H_{10}O_3$, white powder; UV (MeOH) λ_{max} (log ε): 215 (4.08), 269 (3.75), 315 (293) nm; IR (KBr,

ν_{max}, cm^{-1}): 3372, 2915, 2854, 1716, 1606, 1524, 1446, 1383, 1328, 1252, 1168, 1050, 874, 768; ^1H NMR and ^{13}C NMR ($CDCl_3$, 500 and 125 MHz) (Table-1); Negative ESIMS *m/z* 251 $[M-H]^-$; Negative HRESIMS *m/z* 213.0546 $[M-H]^-$ (calcd $C_{13}H_9O_3$ for 213.0552).

TABLE-1
^1H NMR AND ^{13}C NMR DATA OF COMPOUNDS **1**
(IN $CDCl_3$, 400 AND 100 MHz)

No.	δ_C	δ_H (m, *J*, Hz)	No.	δ_C	δ_H (m, *J*, Hz
1	129.2 s		1'	132.4 s	
2	155.5 s		2',6'	131.2 d	7.60 (d) 8.8
3	115.2 d	6.82 (d) 1.8	3',5'	116.8 d	6.87 (d) 8.8
4	137.9 s		4'	157.7 s	
5	122.4 d	7.11 (dd) 1.8, 8.2	Ar-OH-2		10.06 s
6	127.0 d	7.46 (d) 8.2	Ar-OH-2		10.35 s
7	191.8 d	9.76 s			

Anti-tobacco mosaic virus assay: The anti-tobacco mosaic virus activities were tested using the half-leaf method[10,11]. Ningnanmycin (2 % water solution), a commercial product for plant disease in China, was used as a positive control.

Powdered leaves and stems of *N. tabacum* were extracted with 70 % aqueous acetone. The filtrate was concentrated and partitioned between H_2O and EtOAc. The EtOAc fraction was dried under reduced pressure and then submitted to silica gel, MCI, RP-18 gel column chromatography (CC) and semi-preparative HPLC to yield compound **1**. The structure of compound **1** was shown in Fig. 1 and the ^1H NMR and ^{13}C NMR spectroscopic data of compound **1** are listed in Table-1. Tababiphenyl F (**1**) was obtained as white powder and assigned a molecular formula of $C_{13}H_{10}O_3$ as supported by the HRESIMS (*m/z* 213.0546 [*M*-H]$^-$), corresponding to nine degrees of unsaturation. Strong absorption bands accounting for hydroxy (3372 cm^{-1}) and aromatic groups (1606, 1524 and 1446 cm^{-1}) were observed in the IR spectrum. The ^1H NMR data (Table-1) exhibited signals for one AA'BB'-aromatic system at δ_H 7.60 (2H, d, *J* = 8.8 Hz, H-2',6'), 6.87 (2H dd, *J* = 8.8 Hz, H-3',5'), one ABX-aromatic system at δ_H 6.82 (1H, d, *J* = 1.8 Hz, H-3), 7.46 (1H d, *J* = 8.2 Hz, H-6), 7.11 (1H, dd, *J* = 1.8, 8.2 Hz, H-5), one aldehyde signal at δ_H 9.76 (1H, s) and two hydroxy groups at δ_H 10.07, 10.35 (1H, s) (Table-1). The ^{13}C NMR and DEPT spectra exhibited fourteen carbon signals, including twelve sp^2 carbons (seven methines and five quaternary carbons) indicative of the presence of two benzene rings and one aldehyde carbon (Table-1). Analyses of ^1H–^1H COSY, HSQC, HMBC and ROESY spectra suggested that it had a biphenyl skeleton. Two groups were deduced to be located at C-2 and C-4' by the HMBC correlations from 2-OH to C-2 and 4'-OH to C-4' (Fig. 2) and ^1H–^1H COSY correlations (H-2'/H-3' and H-5'/H-6'). The HMBC correlations of H-6 with C-1 and C-1' and of H-2' with C-1 and C-1' revealed that the two benzene rings joined together through the band between C-1 and C-1'. The HMBC correlations from H-7 to C-3, C-4 and C-5 and the ^1H–^1H COSY correlation between H-5 and H-6 indicated that the aldehyde group was attached to C-4. Thus, the structure of compound **4** was established.

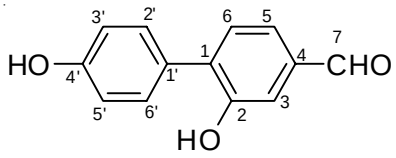

Fig. 1. Structure of compound **1**

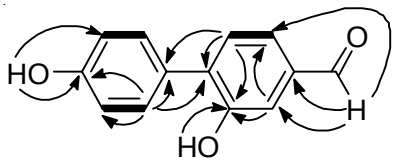

Fig. 2. Key HMBC (H↷C) and ^1H–^1H COSY (▬) correlations of compound **1**

Compound **1** was tested for its anti-tobacco mosaic virus activities. The inhibitory activities of compound **1** against tobacco mosaic virus replication were tested using the half-leaf method[10,11]. Ningnanmycin (inhibition rate of 27.4 %), a commercial product for plant disease in China, was used as a positive control. The results showed that compound **1** exhibited notable anti-tobacco mosaic virus activity with inhibition rate of 22.6 %.

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