Asian Journal of Chemistry; Vol. 26, No. 9 (2014), 2621-2623

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2014.15763

A New Phenolic Compound from the Stems of Flue-Cured Tobacco and Its Anti-Tobacco Mosaic Virus Activity

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Received: 14 May 2013; *Accepted*: 17 August 2013; *Published online*: 28 April 2014; AJC-15082

A new phenolic compound, (*E*)-7-(3,7-dimethylocta-2,6-dienyl)-4-methoxybenzofuran-2(3*H*)-one (1), was isolated from the stems of flue-cured tobacco (a variety of *Nicotiana tabacum* L). Its structure was elucidated by spectroscopic methods, including extensive 1D and 2D NMR techniques. Compound **1** was tested for its anti-tobacco mosaic virus (anti-TMV) activity and it shows potential anti-tobacco mosaic virus activity with inhibition rates of 12.5 %.

Keywords: Phenolic compound, Flue-cured tobacco, Anti-tobacco mosaic virus activity.

INTRODUCTION

Nicotiana tabacum L. is a perennial herbaceous plant. It is found only in cultivation, where it is the most commonly grown of all plants in the *nicotiana* genus and its leaves are commercially grown in many countries to be processed into tobacco[1,2]. In addition to being used in cigarette industry, *N. tabacum* is also used as insecticide, anesthetic, diaphoretic, sedative and emetic agents in Chinese folklore medicine because of it containing many useful chemical compounds[1,3-5]. In previous work, a number of bioactive compounds, such as terpenoids[6-8], alkaloids[9,10], lignans[11,12], flavonoid[13], phenyl-propanoids[14] and the homologous, were isolated from this plant. The stems and roots of *N. tabacum* are big amount of by-product in tobacco planting and are normally used as organic fertilizer. The multipurpose utilization of the stems and roots of *N. tabacum* is an interesting topical and receives more and more attentions[15-17]. With the aims of search for bioactive metabolites from this plant, the investigation on the chemical constituents of the steams of flue-cured tobacco (a variety of *Nicotiana tabacum* L) was carried out. As a result, a new phenolic compound (**1**) (Fig. 1) was isolated. In addition, the anti-tobacco mosaic virus (anti-TMV) activity of **1** was evaluated. This article deals with the isolation, structural elucidation and biological activities of this new compound.

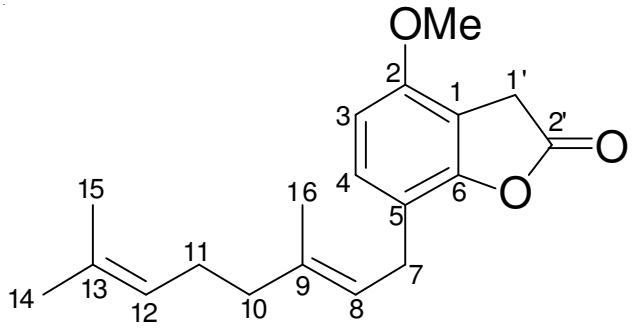

Fig. 1. Structure of new phenolic compound

EXPERIMENTAL

UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. 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. ^{1}H, ^{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 μm), Qingdao Marine Chemical Inc., China). Preparative HPLC was used an Agilent 1100 HPLC equipped with ZORBAX-C18 (21.2 mm × 250 mm, 7.0 μm) column and DAD detector.

The stems of flue-cured tobacco were collected in Yuxi 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 University of Nationalities).

Extraction and isolation: The air-dried and powdered stems of tobacco stems (2.2 kg) were extracted 4 times with 90 % methanol (4 × 5 L) at room temperature and filtered to

yield a filtrate. The crude extract (85.2 g) was applied to silica gel (200 - 300 mesh) column chromatography, eluting with a chloroform-acetone system (20:1, 9:1, 8:2, 7:3, 6:4, 5:5), to give six fractions A-F. The further purification of fraction A (20:1, 22.4 g) by silica gel column chromatography, eluted with petroleum ether-acetone (9:1, 8:2, 7:3, 6:4, 5:5), yielded mixtures A1-A5. Fraction A2 (8:2, 1.65 g) was subjected to preparative HPLC (75 % MeOH-H_2O, flow rate 12 mL/min) to yield compound **1** (14.3 mg).

(*E*)-7-(3,7-dimethylocta-2,6-dienyl)-4-methoxybenzofuran-2(3*H*)-one: Obtained as a white amorphous powder; UV (MeOH), λ_{max} (log ε) 278 (3.98), 210 (4.30) nm; IR (KBr, λ_{max}, cm^{-1}) 3028, 2965, 2918, 1768, 1602, 1536, 1449, 1150, 1105, 894; ^1H NMR and ^{13}C NMR data (C_5D_5N, 500 MHz and 125 MHz, respectively), (Table-1); ESIMS (positive ion mode), *m/z* 323 $[M + Na]^+$; HRESIMS (positive ion mode), *m/z* 323.1628 $[M + Na]^+$ (calcd. 323.1623 for $C_{19}H_{24}O_3Na$).

RESULTS AND DISCUSSION

Compound **1** was obtained as white amorphous powder. Its molecular formula was determined as $C_{19}H_{24}O_3Na$ by HRESIMS, *m/z* 323.1628 $[M + Na]^+$ (calcd. 323.1623), corresponding to 8 degrees of unsaturation. Its ^1H and ^{13}C NMR spectral data (Table-1) showed signals to 24 hydrogens and 19 carbons, respectively, corresponding to one aromatic ring (δ_C 115.6 s, 155.4 s, 112.7 d, 129.0 d, 128.6 s, 135.8 s) with two aromatic protons (6.82 (d) *J* = 8.8, 7.26 (d) *J* = 8.8), one geranyl moiety[18] (δ_C 28.2 t, 121.6 d, 138.2 s, 33.6 t, 26.0 t, 124.6 d, 131.2 s, 25.2 q, 18.2 q, 16.8 q; δ_H 3.22 (d) *J* = 7.2, 5.26 (t) *J* = 7.2, 2.22 m, 2.18 m, 5.06 m, 1.62 s, 1.50 s, 1.68 s), a furan-2(3*H*)-one[18] (39.2 t, 175.0 s; 3.58 s) and a methoxy group (δ_C 56.2 q; δ_H 3.81 s). Strong absorption bands accounting for carbonyl (1768 cm^{-1}) and aromatic group (1602, 1536, 1449 cm^{-1}) could be observed in its IR spectrum. The UV spectrum of **1** showed absorption maxima at 278 and 210 nm also confirmed the existence of the aromatic function. The HMBC correlations (Fig. 2) of H-7 (δ_H 3.22) with C-4 (δ_C 129.0), C-5 (δ_C 128.6) and C-6 (δ_C 135.8), of H-4 (δ_H 7.26) with C-7 (δ_C 28.2) suggested the geranyl moiety was attached to C-1. The long-range correlation of the methoxy proton signal (δ_H 3.81) with C-2 (δ_C 155.4) clearly indicated that the methoxy group located at C-2. The HMBC correlations of H-1' (δ_H 3.58) with C-1 (δ_C 115.6), C-2 (δ_C 155.4), C-6 (δ_C 135.8) and the carbonyl carbon (δ_C 175.0) indicated that the furan-2(3*H*)-one should be fused at C-1 and C-6. The protons signals (δ_H 6.82 (d) *J* = 8.8, 7.26 (d) J = 8.8) also supported the substituents position on the aromatic ring. Thus, the structure of **1** was established as (*E*)-7-(3,7-dimethylocta-2,6-dienyl)-4-methoxybenzofuran-2(3*H*)-one.

TABLE-1
^1H NMR AND ^{13}C NMR DATA OF COMPOUND **1**
(C_5D_5N, δ, ppm, *J* (Hz)

No.	δ_C (mult.)	δ_H (mult, *J*, Hz)	No.	δ_C (mult.)	δ_H (mult, *J*, Hz)
1	115.6 s		11	26.0 t	2.18, m
2	155.4 s		12	124.6 d	5.06, m
3	112.7 d	6.82, d, *J* = 8.8	13	131.2 s	
4	129.0 d	7.26, d, *J* = 8.8	14	25.2 q	1.62, s
5	128.6 s		15	18.2 q	1.50, s
6	135.8 s		16	16.8 q	1.68, s
7	28.2 t	3.22, d, *J* = 7.2	1′	39.2 t	3.58, s
8	121.6 d	5.26, t, *J* = 7.2	2′	175.0 s	10.8 brs
9	138.2 s		2-OMe	56.2 q	3.81 s
10	33.6 t	2.22, m			

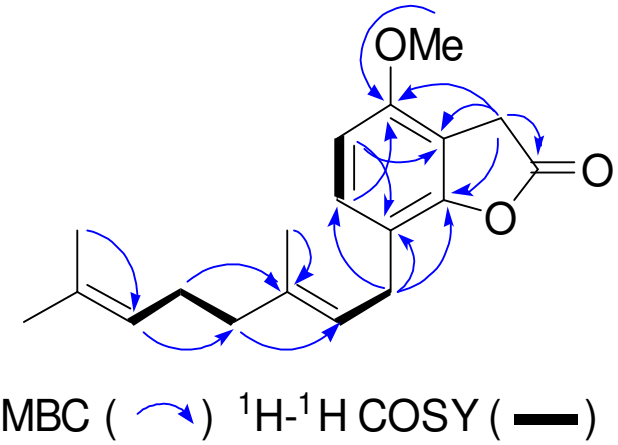

Fig. 2. Key HMBC and ^1H-^1H COSY correlations of **1**

Since certain of the phenolic compounds exhibit potential anti-TMV activity[19-21], compounds **1** was tested for it anti-tobacco mosaic virus activity. The anti-TMV activities were tested using the half-leaf method[21]. Ningnanmycin (2 % water solution), a commercial product for plant disease in China, was used as a positive control. The results showed that compound **1** exhibited inhibition rates of 12.5 %.

ACKNOWLEDGEMENTS

This project was supported financially by the Basic Research Foundation of Yunnan Tobacco Industry Co. Ltd (2012JC01), the National Natural Science Foundation of China (No. 31360081), the Excellent Scientific and Technological Team of Yunnan High School (2010CI08).

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