NOTE

A New Xanthone from the Stems of *Garcinia oligantha* and their Anti-tobacco Mosaic Virus Activity

YANLIN MENG¹, YUCHUN YANG¹, YING QIN¹, CONGFANG XIA¹, YANQING YE¹, QIUFEN HU¹ and YINKE LI^{1,2,*}

¹Key Laboratory of Chemistry in Ethnic Medicinal Resources, State Ethnic Affairs Commission and Ministry of Education, Yunnan University of Nationalities, Kunming 650031, P.R. China

²College of Resource and Environment, Yuxi Normal University, Yuxi 653100, P.R. China

*Corresponding author: E-mail: linkli609@126.com

Received: 4 October 2013;

Accepted: 17 April 2014;

Published online: 16 September 2014;

AJC-15988

For more bioactive compounds, phytochemical investigations of the methanol extract of the stems of *Garcinia oligantha* resulted in the isolation of a new xanthone, (S)-1,8-dihydroxy-4-(1-hydroxy-3-oxobutyl)-3-methoxy-9H-xanthen-9-one (**1**). Structural elucidation of **1** was performed by spectral methods. Compound **1** showed anti-tobacco mosaic virus (anti-TMV) activities with inhibition rates of 15.2 %.

Keywords: Xanthone, *Garcinia oligantha*, Anti-tobacco mosaic virus activity.

Genus *Garcinia* (Guttiferae family) is known to be a rich source of polyisoprenylated benzophenones and xanthones^{1,2}. It has been widely used as a traditional Chinese medicine for treating toothache, sore mouth, and scald³. In our continuing efforts to finding more bioactive compounds from *Garcinia* species, we explored the chemical constituents of *G. oligantha*, a shrub 1-3 m tall, which is distributed in 200-1200 m dense forests in the district of Xishuangbanna Prefecture Yunnan province, People's Republic of China. The present studies on chemical constituents of the methanol extract of the dried stems of *G. oligantha* afforded a new xanthones, (S)-1,8-dihydroxy-4-(1-hydroxy-3-oxobutyl)-3-methoxy-9H-xanthen-9-one (**1**) (Fig. 1). In this paper, we describe the isolation, structure elucidation, and anti-tobacco mosaic virus (anti-TMV) activities of this compound.

Optical rotations were measured by a JASCO DIP-1000 polarimeter. Ultraviolet absorption spectra were recorded using

a Perkin-Elmer Lambda L14 spectrometer. A Perkin Elmer spectrum 100 FT-IR spectrometer was used for scanning IR spectroscopy. The ¹D and ²D NMR spectra were recorded on a Bruker AV-400 spectrometer with TMS as the internal standard. Chemical shifts (δ) were expressed in ppm with reference to the solvent signals. HRMS were obtained using a nano LC-MS/MS system, with a nano Acquity ultra-performance liquid chromatography (UPLC) module and a quadrupole time-of-flight (Q-TOF) spectrometer equipped with a nanoelectrospray ion source (Waters, Milford, MA) and connected to a lock-mass apparatus to perform a real-time calibration correction. Column chromatography was performed with silica gel (200-300 mesh, Qingdao Marine Chemical, Inc.), Sephadex LH-20 (Pharmacia), and reversed-phase C₁₈ silica gel (250 mesh, Merck). Precoated TLC sheets of silica gel 60 GF₂₅₄ were used. An Agilent 1200 series equipped with an Alltima C₁₈ column (4.6 × 250 mm) was used for HPLC analysis, and semipreparative and preparative Alltima C₁₈ columns or Zorbax SB-C₁₈ columns (9.4 × 250 and 22 × 250 mm) were used in sample preparation. Spots were visualized by heating silica gel plates sprayed with 10 % H₂SO₄ in EtOH.

The stems of *Garcinia oligantha* were collected in October 2012 from the district of Xishuangbanna Prefecture Yunnan Province in China. The plant was identified by Rong-Jing Zhang. A voucher specimen (YNNI 12-9-27) has been deposited at the Key Laboratory of Ethnic Medicine Resource Chemistry (Yunnan University of Nationalities), State Ethnic Affairs Commission & Ministry of Education.

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

Extraction and isolation: An methanol extract prepared from the stems of *Garcinia oligantha* (2.5 kg) was decolorized by MCI and chromatographed on a silica gel column eluting with hexane/acetone (1:0, 4:1, 2:1, 1:1, and 0:1) to afford five fractions A-E. Further separation of fraction B (11.5 g) on silica gel, eluted with petroleum ether-acetone (9:1-1:2), yielded fractions B1-B7. Fraction B2 (2.65 g) was subjected to silica gel column chromatography using petroleum ether-acetone followed by semipreparative HPLC (72 % MeOH-H₂O, flow rate 3 mL/min) to give **1** (8.6 mg).

(S)-1,8-Dihydroxy-4-(1-hydroxy-3-oxobutyl)-3-methoxy-9H-xanthen-9-one (1): Obtained as a yellow gum; [α]_D^{22.5} -45.6 (c 0.25, MeOH); UV (MeOH) λ_{max} (log ϵ) 210 (4.18), 244 (3.72), 302 (3.75) nm; CD (MeOH, c 0.25) $\Delta\epsilon_{215} + 1.26$, $\Delta\epsilon_{235} - 5.96$, $\Delta\epsilon_{274} + 0.38$, $\Delta\epsilon_{320} - 0.98$; IR (KBr ν_{max} , cm⁻¹) 3421, 3065, 2870, 2802, 1708, 1646, 1602, 1565, 1470, 1351, 1166, 1062, 878, 765; ESIMS m/z (positive ion mode) 367 [M + Na]⁺; HRESIMS (positive ion mode) m/z 367.0790 [M + Na]⁺ (calcd C₁₈H₁₆NaO₇ for 367.0794).

Compounds (**1**) was isolated as a yellow gum, and its molecular formula was determined as C₁₈H₁₆NaO₇ through HRESI-MS analysis (pseudomolecular ion [M + Na]⁺ at m/z 367.0790). Its UV spectrum showed the maximum absorption at 302, 244, and 210 nm. Strong absorption bands accounting for hydroxy (3421 cm⁻¹), carbonyl (1708, 1646 cm⁻¹), and aromatic groups (1602, 1565, 1470 cm⁻¹) could also be observed in its IR spectrum. The ¹H- and ¹³C NMR spectrum (Table-1) displayed signals for all 18 carbons and 16 protons, including a xanthenes skeleton⁴ (C-1-C-9, C-4a, C-8a-C-10a; H-2, H-5-H-7), a methoxy groups (δ_{C} 55.9 q, δ_{H} 3.82 s), a 1-hydroxy-3-oxobutyl moiety⁵ [δ_{C} 63.7 d, 51.2 t, 205.4 s, 31.2 q; δ_{H} 5.18 dd (8.8, 3.2), 2.82 dd (15.4, 3.2), 2.46 dd (15.4, 8.8), 2.18 s], and two phenolic hydroxyl group (δ_{H} 12.24 s and 13.05 s). The HMBC correlation (Fig. 2) of the methoxy proton signal (δ_{H} 3.82) with C-3 (δ_{C} 161.2) showed this methoxy group was located at C-3. The long-range correlations of H-1' (δ_{H} 5.18) to C-3 (δ_{C} 161.2), C-4 (δ_{C} 110.3) and C-4a (δ_{C} 156.4), of H₂-2' (δ_{H} 2.82 and 2.46) to C-4 (δ_{C} 110.3) were observed in **1**. This led us to conclude that the 1-hydroxy-3-oxobutyl moiety was located on C-4. Finally, HMBC correlations between the hydroxy proton (δ_{H} 12.24) and C-1 (δ_{C} 162.5), C-2 (δ_{C} 97.4), and C-9a (δ_{C} 105.7), as well as those between the other hydroxy proton (δ_{H} 13.05) and C-7 (δ_{C} 108.2), C-8 (δ_{C} 162.9), and C-8a (δ_{C} 107.5), led to the assignment of the phenolic groups at C-1 and C-8. The typical proton signals of ring A [δ_{H} 6.85 d (8.3), 7.42 t (8.3), 6.65 d (8.3)] and ring B (δ_{H} 6.47 s) also supported that **1** should be a 1,3,4,8-tetrasubstituted xanthone⁴. To determine the absolute configuration of **1**, the circular dichroism (CD) analysis was employed. The experimental CD spectrum of **1** exhibited a positive Cotton effect at 215 nm and a negative Cotton effect near 235 nm. The Cotton effects, optical rotation, and coupling constant values of **1** were in excellent agreement with these of known compound⁵, (1'S)-7-hydroxy-3-(1'-hydroxy-3'-butanoyl) chromone-5-carboxylic acid. Therefore, compound **1** was assigned as (S)-1,8-dihydroxy-4-(1-hydroxy-3-oxobutyl)-3-methoxy-9H-xanthen-9-one.

Since certain chromones exhibit potential anti-TMV activities^{4,6,7}, compounds **1** was tested for it anti-TMV activity. The inhibitory activities of compound **1** against TMV repli-

TABLE-1
¹H AND ¹³C NMR DATA OF COMPOUND **1**
(δ in ppm, in C₅D₅N, 500 AND 125 MHz)

No.	δ_{C} (m)	δ_{H} (m, J, Hz)
1	162.5 s	-
2	97.4 d	6.47 s
3	161.2 s	-
4	110.3 s	-
5	112.5 d	6.85 d (8.3)
6	135.7 d	7.42 t (8.3)
7	108.2 d	6.65 d (8.3)
8	162.9 s	-
9	183.1 s	-
4a	156.4 s	-
8a	107.5 s	-
9a	105.7 s	-
10a	159.0 s	-
1'	63.7 d	5.18 dd (8.8, 3.2)
2'	51.2 t	2.82 dd (15.4, 3.2); 2.46 dd (15.4, 8.8)
3'	205.4 s	-
4'	31.2 q	2.18 s
3-OMe	55.9 q	3.82 s
Ar-OH-1	-	12.24 s
Ar-OH-8	-	13.05 s

Fig. 2. Key HMBC ($\curvearrowright$) correlations of **1**

cation were tested using the half-leaf method⁶. Ningnanmycin, a commercial biochemical pesticide against virus diseases on tomato, pepper, melons, tobacco, and many other crops with high efficiency, was used as a positive control. The result showed that compound **1** exhibited inhibition rates of 15.2 %.

ACKNOWLEDGEMENTS

This research was supported by the National Natural Science Foundation of China (No. 21362044), the Basic Research Foundation of Yunnan Tobacco Industry Co. Ltd (2012JC01), 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).

REFERENCES

1. X.M. Gao, T. Yu, F. Lai, Y. Zhou, X. Liu, C.F. Qiao, J.Z. Song, S.L. Chen, K.Q. Luo and H.X. Xu, *Bioorg. Med. Chem.*, **18**, 4957 (2010).
2. Q. Hu, X. Gao, D. Niu, X. Li, Y. Qin, Z. Yang, G. Zhao, Z. Yang and Z. Chen, *Heterocycles*, **87**, 1127 (2013).
3. A. Libman, S. Bouamanivong, B. Southavong, K. Sydara and D.D. Soejarto, *J. Ethnopharmacol.*, **106**, 303 (2006).
4. Y.P. Wu, W. Zhao, Z.Y. Xia, G.H. Kong, X.P. Lu, Q.F. Hu and X.-M. Gao, *Phytochem. Lett.*, **6**, 629 (2013).
5. M. Gan, Y. Liu, Y. Bai, Y. Guan, L. Li, R. Gao, W. He, X. You, Y. Li, L. Yu and C.L. Xiao, *J. Nat. Prod.*, **76**, 1719 (2013).
6. Q.F. Hu, B. Zhou, J.-M. Huang, X.-M. Gao, L.-D. Shu, G.-Y. Yang and C.-T. Che, *J. Nat. Prod.*, **76**, 292 (2013).
7. Q.F. Hu, B. Zhou, X.M. Gao, L.Y. Yang, L.D. Shu, Y.Q. Shen, G.P. Li, C.T. Che and G.Y. Yang, *J. Nat. Prod.*, **75**, 1909 (2012).