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Two New Prenylated Xanthones from the Bark of *Garcinia xanthochymus*

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Extensive phytochemical studies have shown that *Garcinia* species are rich in a variey of oxygenated and prenylated xanthones.[1] Xanthone are class of polyphenolics that exhibit well-documented pharmacological properties, such as antioxidative, antileukaemic, antitumour, antiulcer, antimicrobial, antihepatotoxic, and CNS depressant activities,[2] mainly due to their oxygenated heterocyclic nature and diversity of functional groups.[3] The leaves, seeds, fruits, twig bark, and wood of *G. xanthochymus* were previously reported to contain benzophenones,[4] flavonoids,[5] triterpenes[6] and xanthones.[7] As a continuation of our efforts to purse the active natural products from *G. xanthochymus*, two new xanthones (**1**) and (**2**), together with 12 known xanthones were isolated by repeated column chromatography from the EtOAc fraction of the ethanolic extract of *G. xanthochymus* gathered in Yunnan province of China. The structures of twelve known compounds **3**-**14** were elucidated as subelliptenone H (**3**),[8] ananixanthone (**4**),[9] pyranojacareubin (**5**),[10] rheediaxanthone A (**6**),[11] toxyloxanthone (**7**),[12] 6-deoxyisojacareubin (**8**),[13] atroviridin (**9**),[14] 6-deoxyjacareubin (**10**),[15] 1-*O*-methylsymphoxanthone (**11**),[16] 1-*O*-methylglobuxanthone (**12**),[17] globuxanthone (**13**),[18] and garciniaxanthone H (**14**)[19] by interpreting the NMR spectroscopic data and comparing those data with the published values. In this paper, we reported the isolation and structural elucidation of two new xanthones (**1**) and (**2**) using spectroscopic evidence.

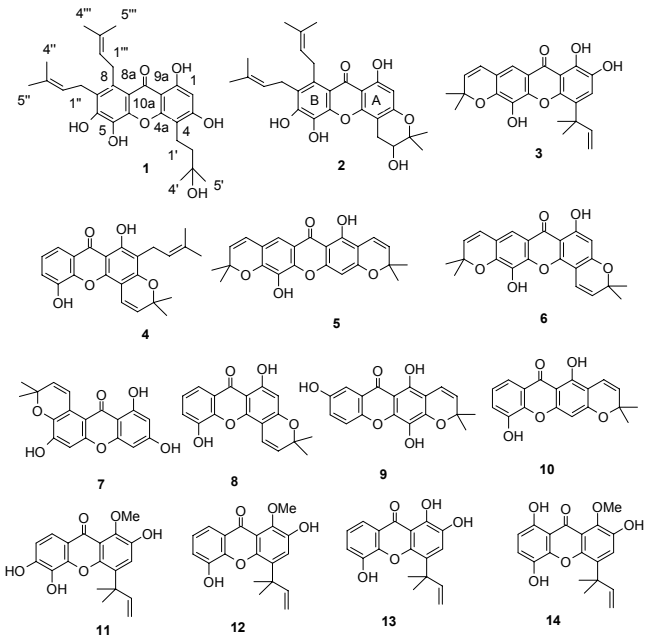

Figure 1. The structures of compounds **1**-**14**.

Compound **1** was obtained as a yellow powder, and its molecular formula was assigned as $C_{28}H_{34}O_7$ by the molecular ion peak at *m*/*z* 482.2301 in the HREIMS. Its UV absorptions at 230, 265, and 346 nm suggested a xanthone skeleton as its base structure. The ^{1}H NMR spectrum of **1** revealed the presence of a hydrogen-bonded hydroxyl group [δ_H 13.41 (1H, s)], one aromatic proton [δ_H 6.27 (1H, s)], two 3-methyl-2-butenyl groups [δ_H 3.46 (2H, d, J = 6.3 Hz), 5.09 (1H, br s), 1.79 (3H, s), 1.67 (3H, s), 4.11 (2H, d, J = 5.7 Hz), 5.09 (1H, br s), 1.79 (3H, s), and 1.67 (3H, s)], and a 3-hydroxy-3-methylbutyl group [δ_H 2.98 (2H, m), 1.79 (2H, m), and 1.33 (6H, s)]. The ^{13}C NMR spectrum showed 28 carbon signals, including 6 methyl, 4 methylene, 3 methine and 15 quaternary carbons by analysis of the DEPT spectra. The NMR data of **1** was similar to those of 1,3,5,6-tetrahydroxy-4,7,8-tri(3-methyl-2-butenyl)xanthone,[7a] a xanthone isolated from the same plant except that a 3-methyl-2-butenyl group of the latter was replaced in **1** by 3-hydroxy-3-methylbutyl group. The substituents on the xanthone skeleton were determined on the basis of the HMBC spectral analysis (Fig. 2). The locations of the two 3-methyl-2-butenyl groups were placed at the C-7 and C-8 positions by the HMBC correlations of H_2-1''/C-6 (δ_C 149.4), C-7 (δ_C 125.6), and C-8 (δ_C 134.2) and H_2-1'''/C-7 (δ_C 125.6), C-8 (δ_C 134.2), and C-8a (δ_C 111.4). The remaining 3-hydroxy-3-methylbutyl group was located at C-4 based on the HMBC correlations of H_2-1'/C-3 (δ_C 162.1), C-4 (δ_C 107.3), and C-4a (δ_C 154.3). Therefore, the structure

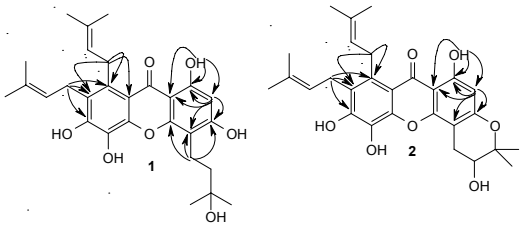

Figure 2. Significant HMBC correlations of compounds **1** and **2**.

of **1** was established to be 1, 3, 5, 6-tetrahydroxy-4-(3-hydroxy-3-methylbutyl)-7,8-di-(3-methyl-2-butenyl) xanthone.

Compound **2** was obtained as a yellow powder. The molecular formula was determined as $C_{28}H_{32}O_7$ (*m/z* 480.2147) by HREIMS. Comparing its ^{13}C NMR and DEPT data with those of **1**, it was found that compound **2** had almost the same chemical shifts as those of **1**, except for one 2,2-dimethyl-3-hydroxydihydropyran ring carbon signals at δ_c 29.3 (t), 68.6 (d), 79.2 (s), 20.7 (q), and 25.5 (q) in **2** instead of 3-hydroxy-3-methylbutyl carbon signals at δ_c 16.9 (t), 42.3 (t), 71.4 (s), and 28.9 (q) in **1**. These facts suggested that 2,2-dimethyl-3-hydroxydihydropyran ring in the structure of **2** replaced 3-hydroxy-3-methylbutyl group found in **1**. The HMBC correlations between H_2-1"/C-6 (δ_C 150.6), C-7 (δ_C 125.9), and C-8 (δ_C 135.1) and H_2-1'"/C-7 (δ_C 125.9), C-8 (δ_C 135.1), and C-8a (δ_C 111.8) suggested that two prenyl groups were located at C-7 and C-8, respectively. The position of 2,2-dimethyl-3-hydroxydihydropyran ring was determined as follow. In the ^{13}C-NMR spectrum, the aromatic carbons with an oxygen function were observed at δ_c 161.7, 160.2, and 154.3, which suggested the presence of a 1,3,5-trioxygenated benzene ring in partial structure A. The HMBC of H-2 [δ_H 6.09 (1H, s)] showed correlations to C-9a, C-1, an oxygenated aromatic carbon (δ_C 160.2) and a substituted aromatic carbon (δ_C 98.7). Thus, the carbon signals at δ_C 160.2 and δ_C 98.7 were assigned to C-3 and C-4, respectively. The 2,2-dimethyl-3-hydroxydihydropyran ring should be fused at C-3 and C-4 of the xanthone nucleus with an ether linkage at C-3. Therefore, **2** was assigned as 3,4-dihydro-3,6,7,11-tetrahydroxy-8,9-di-(3-methyl-2-butenyl)-2,2-dimethyl-pyrano-[2,3-c] xanthone.

Compounds **1** and **2** were evaluated for their antimicrobial activities in broth microdilution bioassay.[20] Compound **2** displayed moderate activity against *Candida tropicalis* with MICs 8.13 μM using nystatin as a positive control (MIC = 0.53 μM). Compound **1** was inactive against tested fungi.

Experimental Section

Reagent and equipment. Thin-layer chromatography (TLC): Pre-coated silica gel *GF$_{254}$* plates (*Qingdao Haiyang Chemical Co., Ltd.*, P. R. China). Column Chromatography (CC): Silica gel (200 - 300 mesh; *Qingdao Haiyang Chemical Co., Ltd.*, P. R. China) and C_{18} reversed-phase silica gel (YMC *CO., LTD.*, Japan). UV spectral: SP-2102UVPC spectrometer using MeOH as the solvent. ^{1}H- and ^{13}C-NMR spectral: *Bruker-AM-400* instrument (Bruker company, Massachusetts, USA); δ in ppm rel. to $SiMe_4$ as internal standard (= 0 ppm), *J* in Hz. EI-MS: *Finnigan -MAT-95* mass spectrometer (Finnigan company; UK) (70 ev); in *m/z* (rel. %).

Plant material. The bark of *G. xanthochymus* was collected from Xishuangbanna Prefecture, Yunnan Province, P. R. China and identified by Xishuangbanna Prefecture National Medicine Research Institute. The voucher specimen (06061201) was deposited with the Herbarium of College of Pharmacy, South Central University for Nationalities.

Extraction and isolation. The powdered bark of *G. xanthochymus* (6.5 kg) was extracted with 95% EtOH and then successively partitioned with petroleum ether (P.E.) (3.0 L × 3), EtOAc (3.0 L × 3), and *n*-BuOH (3.0 L × 3). The combined extract of EtOAc (590 g) was chromatographed on silica gel with P.E-Me_2CO (9:1, 8:2, 7:3, 1:1, 3:7, and 0:1, *v/v*) to give thirteen fractions (fr.1 - fr.13). After repeated silica gel (cyclohexane-Me_2CO, 95:1→0:1 gradient system) and RP-18 (MeOH-H_2O, 8:2) column chromatography, Fr. 5 (10.7 g) afforded compounds **4** (4.5 mg), **5** (0.5 mg), **6** (0.8 mg), **8** (1.0 mg) and **10** (3.6 mg). Fr.6 (17.0 g) was separated on a silica column (toluene/Me_2CO 95:5→3:7 gradient system), and then purified by chromatography on a silica gel ($CHCl_3$-MeOH, 1:0→1:1 gradient system) and RP-18 (MeOH-H_2O, 8:2) to yield compounds **1** (10.0 mg), **3** (4.2 mg), **7** (2.6 mg), **12** (0.9 mg), **13** (4.3 mg), and **14** (3.8 mg), respectively. Fr.7 (33.8 g) was extensively separated over a silica column (toluene/Me_2CO 95:5→3:7 gradient system) and RP-18 (MeOH-H_2O, 3:7→7:3 gradient system) to afford compounds **2** (7.5 mg) and **9** (0.4 mg). Fr. 9 (10.8 g) was also subjected to silica gel with a gradient elution (toluene-Me_2CO, 9:1→3:7 gradient system) and RP-18 (MeOH-H_2O, 3:7→7:3 gradient system) to afford compounds **11** (2.7 mg).

Table 1. ^{1}H and ^{13}C NMR data of compounds **1-2** in acetone-d_6[a]

	1		**2**	
	δ_H[b]	δ_C[c]	δ_H[b]	δ_C[c]
1		161.7 (qC)		161.7 (qC)
2	6.27 (1H, s)	97.8 (CH)	6.09 (1H, s)	99.1 (CH)
3		162.1 (qC)		160.2 (qC)
4		107.3 (qC)		98.7 (qC)
4a		154.3 (qC)		154.3 (qC)
5		130.2 (qC)		130.2 (qC)
10a		145.9 (qC)		147.0 (qC)
6		149.4 (qC)		150.6 (qC)
7		125.6 (qC)		125.9 (qC)
8		134.2 (qC)		135.1 (qC)
8a		111.4 (qC)		111.8 (qC)
9		183.2 (qC)		183.1 (qC)
9a		103.6 (qC)		104.0 (qC)
1'	2.98 (2H, m)	16.9 (CH_2)	1.26 (2H, m)	29.3 (CH_2)
2'	1.79 (2H, m)	42.3 (CH_2)	3.88 (1H, br s)	68.6 (CH)
3'		71.4 (qC)		79.2 (qC)
4'	1.33 (3H, s)	28.9 (CH_3)	1.31 (3H, s)	20.7 (CH_3)
5'	1.33 (3H, s)	28.9 (CH_3)	1.40 (3H, s)	25.5 (CH_3)
1"	3.46 (2H, d , *J* = 6.3)	24.9 (CH_2)	3.47 (2H, d , *J* = 7.2)	25.0 (CH_2)
2"	5.09 (1H, br s)	125.2 (CH)	5.09 (1H, br s)	123.5 (CH)
3"		130.6 (qC)		131.6 (qC)
4"	1.79 (3H, s)	17.8 (CH_3)	1.79 (3H, s)	17.8 (CH_3)
5"	1.67 (3H, s)	25.5 (CH_3)	1.67 (3H, s)	25.5 (CH_3)
1'"	4.11d (2H, d , *J* = 5.7)	28.6 (CH_2)	4.12 (2H, d , *J* = 7.2)	28.7 (CH_2)
2'"	5.09 (1H, br s)	123.6(CH)	5.09 (1H, br s)	125.1(CH)
3'"		131.5 (qC)		130.3 (qC)
4'"	1.67 (3H, s)	25.5 (CH_3)	1.67 (3H, s)	25.5 (CH_3)
5'"	1.79 (3H, s)	18.0 (CH_3)	1.79 (3H, s)	18.0 (CH_3)
1-OH	13.41 (1H, s)		13.50 (1H, s)	

[a]Chemical shifts (δ) in ppm; Coupling constant (*J*) in Hz. [b]Measured in 400 MHz in Me_2CO-d_6. [c]Measured in 100 MHz in Me_2CO-d_6.

1,3,5,6-Tetrahydroxy-4-(3-hydroxy-3-methylbutyl)-7,8-di-(3-methyl-2-butenyl) xanthone (1): Yellow amorphous powder; UV λ_{max} (MeOH) nm (log ε): 230 (3.54), 265 (3.53), 346 (3.62); For ^{1}H NMR and ^{13}C NMR (in Me_2CO-d_6) spectroscopic data, see Table 1; EIMS (70 eV) *m*/*z* (%): 482 (M^+, 10), 464(16), 421(60), 409(100), 385(44), 365(68), 353(76), 323(24); HREIMS *m*/*z* 482.2301 (calcd. for $C_{28}H_{34}O_7$, 482.2305).

3,4-Dihydro-3,6,7,11-tetrahydroxy-8,9-di-(3-methyl-2-butenyl)-2,2-dimethyl-pyrano-[2,3-c] xanthone (2): Yellow amorphous powder; UV λ_{max} (MeOH) nm (log ε): 230 (3.52), 265 (3.25), 349 (3.63); For ^{1}H NMR and ^{13}C NMR (in Me_2CO-d_6) spectroscopic data, see Table 1; EIMS (70 eV) *m*/*z* (%): 480 (M^+, 20), 462(4), 437(64), 409(36), 383(100), 74(56); HREIMS *m*/*z* 480.2147 (calcd. for $C_{28}H_{32}O_7$, 480.2148).

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