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Two new xanthenes from the stems of *Cratoxylum cochinchinense*

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Two new xanthenes, 6-hydroxy-3,7-dimethoxy-8-(3-methylbut-2-enyl)-6',6'-dimethyl-5'-hydroxy-4',5'-dihydropyrano(2',3':1,2)xanthone (**1**) and 6-hydroxy-3,7-dimethoxy-8-(2-oxo-3-methylbut-3-enyl)-6',6'-dimethyl-5'-hydroxy-4',5'-dihydropyrano(2',3':1,2)xanthone (**2**), have been isolated from the stems of *Cratoxylum cochinchinense* (Lour.) Blume. Their structures were established on the basis of spectroscopic analysis.

Keywords: Guttiferae; *Cratoxylum cochinchinense* (Lour.) Blume; xanthone

1. Introduction

Cratoxylum cochinchinense (Lour.) Blume, called 'Huangniuemu' in the producing area of China, is a shrub belonging to the family Guttiferae [1]. It was used as a traditional medicine for fevers, coughs, diarrhea, itches, ulcers, and abdominal complaints therapy [2]. A series of chemical components including triterpenoids, tocotrienols, flavonoids, and xanthenes have been previously reported from this plant [1–6]. This paper demonstrated the isolation and structure elucidation of two new xanthenes from the 60% ethanol extract of the stems of this plant (Figure 1).

2. Results and discussion

Compound **1** was obtained as brown gum, $[\alpha]_D^{26} +25.2$ ($c = 0.4$, acetone). The HR-TOF-MS showed a quasi-molecular ion at m/z 463.1705 $[M+Na]^+$, and suggested that its molecular formula was $C_{25}H_{28}O_7$. The 1H and ^{13}C NMR spectra of **1** showed the

presence of two methoxyl groups at δ_H 3.87 (3H, s), 3.68 (3H, s) and δ_C 55.9, 59.9, two aromatic methines at δ_H 6.72 (1H, s), 6.53 (1H, s) and δ_C 101.1, 90.2, one conjugated carbonyl at δ_C 174.9, and one prenyl group at δ_H 3.95 (2H, brs), 5.18 (1H, t, $J = 6.5$ Hz), 1.77 (3H, s), 1.62 (3H, s) and δ_C 25.4, 124.4, 129.6, 25.5, 17.9 along with 10 aromatic quaternary carbons (six oxygenated). These data indicated that compound **1** was a xanthone derivative linking two methoxyl groups and a prenyl group. Two methyls at δ_H 1.32 (3H, s), 1.20 (3H, s) and δ_C 25.4, 20.5 connected with an oxygenated quaternary carbon at δ_C 77.6, one oxygenated methine at δ_H 3.65 (1H, m) and δ_C 66.8, and one methylene at δ_H 2.76 (1H, dd, $J = 17.0$, 5.5 Hz), 2.40 (1H, dd, $J = 17.0$, 7.3 Hz) and δ_C 25.9 in the 1H and ^{13}C NMR spectra, as well as one residual unsaturation, were deduced as 6',6'-dimethyl-5'-hydroxy-4',5'-dihydropyran system in **1**. Both protons of the methylene at δ 2.40 (H-4'a) and δ 2.76

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(H-4'b) were correlated with C-1, C-2, and C-3 in the HMBC spectrum of **1**. The HMBC correlation between 3-OCH₃/C-3 indicated that the methoxyl group was located at C-3, thus the dihydropyran ring should be positioned at C-1 and C-2 of the xanthone skeleton. The HMBC correlations between H-1'' at δ 3.95 and C-7, C-8, C-8a suggested that the prenyl group was located at C-8. The chemical shift of H-1'' at δ 3.95, which appeared more downfield than the usual values for this functional group due to the deshielded effect of the carbonyl group, further confirmed the linkage of the prenyl group at C-8 [4,7,8]. The HMBC correlations of 7-OCH₃ and C-7, H-4 and C-2, C-3, C-4a, C-9a, as well as H-5 and C-6, C-7, C-10a, C-8a, indicated that the other methoxyl group was located to C-7 and the two aromatic protons were positioned at C-4 and C-5, respectively. According to the molecular formula and chemical shift, the unassigned hydroxyl group should be located at C-6. Compound **1** was therefore established as 6-hydroxy-3,7-dimethoxy-8-(3-methylbut-2-enyl)-6',6'-dimethyl-5'-hydroxy-4',5'-dihydropyrano(2',3':1,2)xanthone (Figure 2).

Compound **2** was obtained as yellow powder, $[\alpha]_D^{26} +20.5$ ($c = 0.3$, acetone). The molecular formula of C₂₅H₂₆O₈ was established by HR-TOF-MS (m/z 477.1560, $[M+Na]^+$). The ¹H and ¹³C NMR spectra of compound **2** were similar to those of **1**, except for the absence of a prenyl group. In addition, it appeared one conjugated ketonic carbonyl at δ_C 198.8, one sp² quaternary carbon at δ_C 144.5,

one sp² methylene at δ_H 6.16 (1H, brs), 5.85 (1H, brs), δ_C 123.2, one sp³ methylene at δ_H 4.65 (2H, brs), δ_C 36.7, and one methyl at δ_H 1.89 (3H, s), δ_C 17.6. The HMBC correlations of H-5'' and C-2'', C-3'', C-4'' and H-1'' and C-2'', C-7, C-8, C-8a revealed the presence of a 2-oxo-3-methylbut-3-enyl group at C-8 [9] (Figure 2). Thus, compound **2** was deduced as 6-hydroxy-3,7-dimethoxy-8-(2-oxo-3-methylbut-3-enyl)-6',6'-dimethyl-5'-hydroxy-4',5'-dihydropyrano(2',3':1,2)xanthone.

3. Experimental

3.1 General experimental procedures

Optical rotations were measured using a JASCO P-1020 polarimeter. The UV spectra were recorded on a JASCO V-550 UV/Vis spectrometer. The IR spectra were obtained using a JASCO FT/IR-480 plus spectrometer. The NMR spectra were run on a Bruker AVANCE 400 NMR spectrometer (400 MHz for ¹H and 100 MHz for ¹³C). ESI-MS spectra were performed on a Bruker Esquire 2000 mass spectrometer. HR-TOF-MS spectra were measured on a Micromass mass spectrometer. The analytical and preparative HPLC were performed on a Shimadzu Pak with UV-VIS detector using a Shim-pack VP-ODS column (4.6 × 250 mm) and a Shim-pack PREP-ODS column (20 × 250 mm), respectively. Column chromatography was carried out over silica gel H60 (Qingdao Haiyang Chemical Group Corp., Qingdao, China) and ODS (60–80 μ m, YMC) as packing materials. Silica gel G was used for analytical TLC.

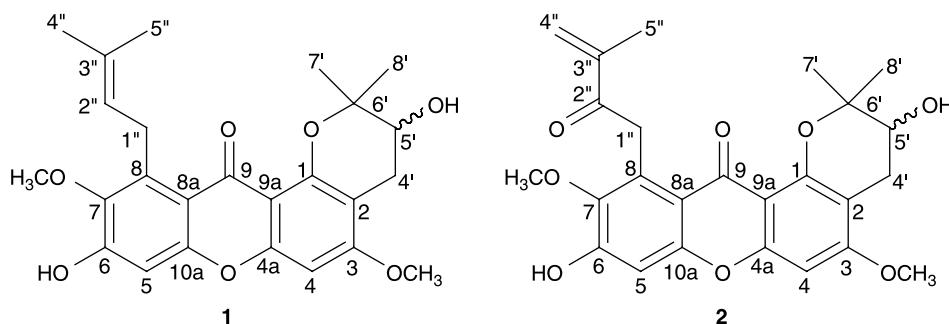
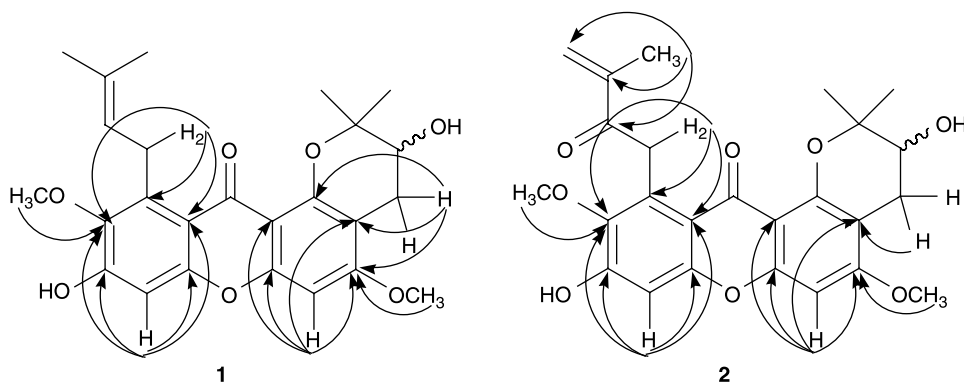


Figure 1. Chemical structures of **1** and **2**.

Figure 2. The important HMBC correlations of **1** and **2**.

3.2 Plant material

The stems of *C. cochinchinense* were collected from Yunnan Province of China in August 2004, and identified by Prof. Hao Zhang, West

China School of Pharmacy, Sichuan University. A voucher specimen (YJSLCC-2004-8) is deposited at the Key Laboratory for Research & Development of New Drugs from Traditional

Table 1. ^1H and ^{13}C NMR spectral data of compounds **1** and **2** (400 MHz for ^1H , in $\text{DMSO}-d_6$).

No.	1		2	
	δ_{H}	δ_{C}	δ_{H}	δ_{C}
1		153.7		153.8
2		104.3		104.3
3		161.0		161.1
4	6.53 (s)	90.2	6.57 (s)	90.4
4a		156.3		156.5
5	6.72 (s)	101.1	6.79 (s)	101.7
6		153.2*		153.0*
7		143.2		143.9
8		136.0		130.2
8a		113.2		112.8
9		174.9		174.6
9a		106.7		106.2
10a		155.1*		155.7*
4'	2.76 (dd, 17.0, 5.5) 2.40 (dd, 17.0, 7.3)	25.9	2.74 (dd, 17.0, 5.5) 2.38 (dd, 17.0, 7.3)	25.9
5'	3.65 (m)	66.8	3.61 (m)	66.7
6'		77.6		77.6
7'	1.32 (s)	25.4	1.28 (s)	25.4
8'	1.20 (s)	20.5	1.16 (s)	20.5
1''	3.95 (brs)	25.4	4.65 (s)	36.7
2''	5.18 (t, 6.5)	124.4		198.8
3''		129.6		144.5
4''	1.62 (s)	25.5	6.16 (s)	123.2
			5.85 (s)	
5''	1.77 (s)	17.9	1.89 (s)	17.6
3-OMe	3.87 (s)	55.9	3.88 (s)	56.0
7-OMe	3.68 (s)	59.9	3.63 (s)	60.1

* Signals may be interchanged within a column.

Chinese Medicine and Natural Products in Shenzhen, China.

3.3 Extraction and isolation

The air-dried stems of *C. cochinchinense* (6.0 kg) were minced finely and then refluxed with 60% EtOH thrice. After evaporation of solvent *in vacuo*, the residue (480.0 g) was suspended in H₂O and partitioned with EtOAc and *n*-BuOH successively. The EtOAc extract (142.5 g) was subjected to column chromatography over silica gel, eluting with cyclohexane/acetone (100:0 → 0:100), to afford 10 fractions. Fraction 3 (14.7 g) was chromatographed on silica gel MPLC by gradient elution with cyclohexane/acetone (15:1 → 0:1) to give 14 subfractions. Subfraction 10 (442 mg) was applied to an ODS column and eluted with MeOH/H₂O (7:3 → 9:1). The fraction eluted with 70% MeOH was further purified by preparative HPLC (70% MeOH) to yield compounds **1** (32.0 mg) and **2** (5.2 mg).

3.3.1 6-Hydroxy-3,7-dimethoxy-8-(3-methylbut-2-enyl)-6',6'-dimethyl-5'-hydroxy-4',5'-dihydropyrano(2',3':1,2)xanthone (**1**)

Brown gum; $[\alpha]_D^{26} + 25.2$ ($c = 0.38$, acetone); UV (CH₃OH) λ_{\max} (log ϵ): 350 (3.76), 313 (4.05), 246 (4.46), 206 (4.20); IR (KBr) ν_{\max} (cm⁻¹): 3380, 1612, 1456; ¹H and ¹³C NMR spectral data: see Table 1; ESI-MS (m/z): 463 [M + Na]⁺, 439 [M - H]⁻; HR-TOF-MS (m/z): 463.1705 [M + Na]⁺ (calcd for C₂₅H₂₈O₇Na, 463.1733).

3.3.2 6-Hydroxy-3,7-dimethoxy-8-(2-oxo-3-methylbut-3-enyl)-6',6'-dimethyl-5'-hydroxy-4',5'-dihydropyrano(2',3':1,2)xanthone (**2**)

Yellow powder; $[\alpha]_D^{26} + 20.5$ ($c = 0.26$, acetone); UV (CH₃OH) λ_{\max} (log ϵ): 337

(3.68), 306 (4.01), 251 (4.20), 243 (4.25), 212 (4.29); IR (KBr) ν_{\max} (cm⁻¹): 2984, 1600, 1463; ¹H and ¹³C NMR spectral data: see Table 1; ESI-MS (m/z): 477 [M + Na]⁺, 453 [M - H]⁻; HR-TOF-MS (m/z): 477.1560 [M + Na]⁺ (calcd for C₂₅H₂₆O₈Na, 477.1525).

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