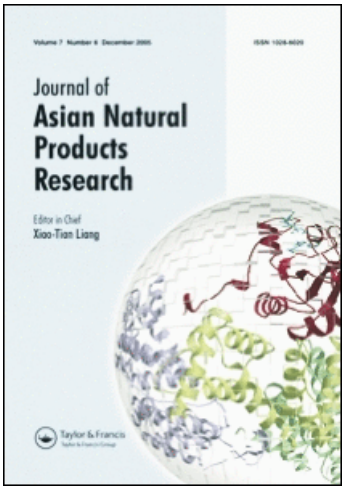

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Coumarins from *Coriaria nepalensis*

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Two new coumarins (**1**) and (**2**), along with seven known coumarins **3**–**9**, were isolated from the leaves and stems of *Coriaria nepalensis* Wall. The two new compounds were established as 7-hydroxy-6-methoxy-3,8-bis(3-methyl-2-butenyl) coumarin (**1**) and 7-hydroxy-6-methoxy-3-(3-methyl-2-butenyl) coumarin (**2**), on the basis of 1D and 2D NMR techniques. The known compounds **3**, **6**–**9** were isolated from this plant for the first time.

Keywords: *Coriaria nepalensis*; Coriariaceae; Coumarins; 7-Hydroxy-6-methoxy-3,8-bis(3-methyl-2-butenyl) coumarin; 7-Hydroxy-6-methoxy-3-(3-methyl-2-butenyl) coumarin

1. Introduction

The genus *Coriaria* belonging to the family Coriariaceae have been reported to contain sesquiterpene lactones [1–5], tannins [6–8], triterpenoids [9], and coumarins [4]. As a member of Coriariaceae, *Coriaria nepalensis* Wall is widely distributed in most parts of Yunnan Province. In our investigation on the chemical constituents from *C. nepalensis*, nine coumarins, including two new ones, were separated from the leaves and stems of this plant.

2. Results and discussion

7-Hydroxy-6-methoxy-3,8-bis(3-methyl-2-butenyl) coumarin (**1**) was isolated as yellow powder. Its molecular formula was analysed as $C_{20}H_{24}O_4$ from its EIMS, ^{1}H NMR and ^{13}C NMR data, and confirmed by HRESI-MS (*m/z* 329.1754 $[M + H]^+$). Besides two isopentenyl and one methoxy substituent, the ^{1}H NMR and ^{13}C NMR spectra (table 1) showed characterised signals for a coumarin skeleton. Two downfield singlets (δ_H 7.30 s, 6.67 s) in the ^{1}H NMR (table 1) spectrum of **1** suggested that compound **1** was a tetrasubstituted coumarin. Thus, the remaining substitute should be a hydroxyl group due to its molecular formula.

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Table 1. ^{1}H NMR and ^{13}C NMR data of **1** and **2** (in $CDCl_3$).

No.	*1*		*2*	
	δ_H *(mult.)*	δ_C *(mult.)*	δ_H *(mult.)*	δ_C (mult.)
2		162.5 (s)		162.4 (s)
3		125.3 (s)		125.4 (s)
4	7.30 (s)	138.5 (d)	7.31 (s)	138.1 (d)
5	6.67 (s)	104.7 (d)	6.85 (s)	107.1 (d)
6		143.6 (s)		143.9 (s)
7		146.2 (s)		148.7 (s)
8		115.8 (s)	6.78 (s)	102.7 (d)
9		147.1 (s)		148.5 (s)
10		111.9 (s)		112.1 (s)
1′	3.20 (d, 7.2 Hz)	28.7 (t)	3.17 (d, 7.2 Hz)	28.5 (t)
2′	5.27 (m)	119.7 (d)	5.26 (m)	119.4 (d)
3′		135.2 (s)		135.3 (s)
4′	1.78 (s)	17.9 (q)	1.76 (s)	17.7 (q)
5′	1.67 (s)	25.8 (q)	1.64 (s)	25.3 (q)
OCH_3	3.89 (s)	56.2 (q)	3.90 (s)	56.3 (q)
OH	6.07 (s)			
1″	3.54 (d, 7.2 Hz)	22.2 (t)		
2″	5.27 (m)	120.9 (d)		
3″		132.9 (s)		
4″	1.82 (s)	17.8 (q)		
5″	1.65 (s)	25.8 (q)		

The ^{1}H NMR signals at δ_H 3.20 (2H, d, $J = 7.2$ Hz), 5.27 (1H, m), 1.78 (3H, s) and 1.67 (3H, s) were attributable to one isopentenyl based on the HMBC (see figure 1) correlations of H-1′ with C-2′ and C-3′, H-4′ and H-5′ with C-2′ and C-3′; while another group of ^{1}H NMR signals at δ_H 3.54 (2H, d, $J = 7.2$ Hz), 5.27 (1H, m), 1.82 (3H, s), and 1.65 (3H, s) were assignable to another isopentenyl due to similar HMBC interactions.

The HMBC correlations (see figure 1) of H-1′ with C-2 (δ_C 162.5), C-3 (δ_C 125.3) and C-4 (δ_C 138.5) suggested an isopentenyl at C-3, while another isopentenyl was linked to the C-8 position of the coumarin skeleton due to the HMBC interactions observed between H-1″ and C-7 (δ_C 146.2), C-8 (δ_C 115.8) and C-9 (δ_C 147.1). The connectivity of methoxyl to C-6 was

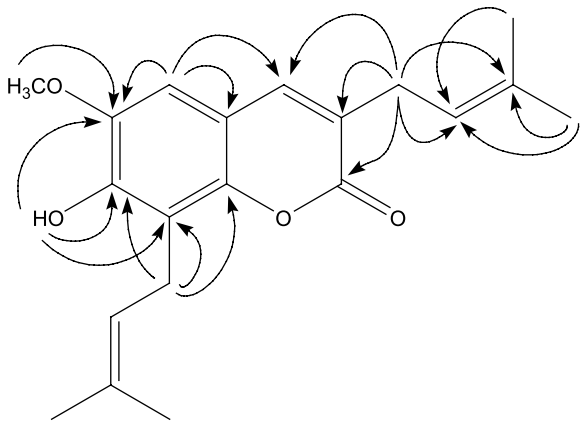

Figure 1. Selected HMBC correlations for **1**.

established via HMBC correlation between δ_H 3.89 (3H, s, OMe) and C-6, which was further confirmed by ROESY correlation (see figure 2) between δ_H 3.89 (3H, s, OMe) and H-5. Hydroxylation at the C-7 position was determined because of the correlations of the hydroxyl proton (δ_H 6.07, 1H, s) with C-6, C-7, C-8 in the HMBC spectrum of **1**. The HMBC correlations of H-4 (δ_H 7.30, s) with C-2, C-5, C-9, C-10, C-1′ and H-5 (δ_H 6.67, s) with C-4, C-6, C-7, C-10 further supported the above inferences. Thus, the structure of **1** was elucidated as 7-hydroxy-6-methoxy-3,8-bis (3-methyl-2-butenyl) coumarin.

7-Hydroxy-6-methoxy-3-(3-methyl-2-butenyl) coumarin (**2**), yellow powder, was assigned a molecular formula of $C_{15}H_{16}O_4$ from its molecular ion peak at *m/z* $[M]^+$260 in the EI-MS as well as analysis of NMR data, and further confirmed by HRESI-MS (*m/z* 261.1124 $[M + H]^+$). The ^{13}C NMR spectrum (see table 1) indicated a coumarin skeleton and a methoxyl (δ_C 56.3, q), an isopentenyl due to a set of carbon signals at δ_C 28.5 (t), 119.4 (d), 135.3 (s), 25.3 (q), 17.7 (q). Three singlets at δ_H 7.31 (1H, s), 6.85 (1H, s), 6.78 (1H, s) in the ^1H NMR spectra (see table 1) of **2** suggested that compound **2** was a trisubstituted coumarin. Therefore, the remained substitute in the structure of **2** should be a hydroxyl group based on its molecular formula. The isopentenyl was attached to C-3 due to the HMBC (see figure 3) correlations observed between H-1′ and C-2 (δ_C 162.4, s), and C-3 (δ_C 125.4, s), H-4 (δ_H 7.31, s) and C-1′ (δ_C 28.5, t), C-2 (δ_C 125.4, s), C-5 (δ_C 107.1, d), C-9 (δ_C 148.5, s), C-10 (δ_C 112.1, s). The HMBC correlations between δ_H 3.90 (3H, s, OMe) and C-6 (δ_C 143.9, s) suggested a methoxyl substitution at the C-6 position, and further confirmed by correlations of 6-methoxyl with H-5 in ROESY spectral (see figure 4). The hydroxylation of the C-7 position was elucidated from its downfield chemical shifts at δ_C 148.7 relative to normal coumarin skeleton, and HMBC interactions of H-5 (δ_H 6.85, s) with C-4 (δ_C 138.1, d), C-6 (δ_C 143.9, s), C-7 (δ_C 148.7, s), of H-8 (δ_H 6.78, s) with C-6 (δ_C 143.9, s), C-7 (δ_C 148.7, s) and C-10 (δ_C 112.1, s). Thus, compound **2** was elucidated as 7-hydroxy-6-methoxy-3-(3-methyl-2-butenyl) coumarin.

Seven known coumarins were identified as marmesin (**3**) [10], braylin (**4**) [4], norbraylin (**5**) [4], scopoletin (**6**) [11], 7-hydroxy coumarin (**7**) [12], 7-hydroxy-6-(3-methyl-2-butenyl) coumarin (**8**) [13], and 7-hydroxy-3-(3-methyl-2-butenyl) coumarin (**9**) [14], respectively, by comparison of their spectral data with those reported in the literature. Compounds **3**, **6**–**9** were isolated from this plant for the first time.

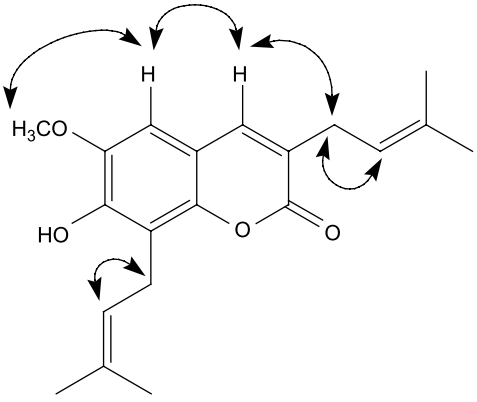

Figure 2. Key REOSY correlations for **1**.

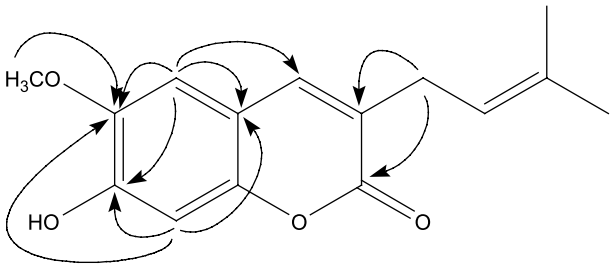

Figure 3. Selected HMBC correlations for **2**.

3. Experimental

3.1 General experimental procedures

Melting points were measured on an XRC-1 micromelting apparatus and are uncorrected. IR and UV spectra were obtained on a Bio-Rad FTS-135 infrared spectrometer with KBr pellets and a Shimadzu double-beam 210A spectrometer in MeOH, respectively. MS spectra were performed on a VG Autospec-3000 spectrometer of 70 eV. ^{1}H, ^{13}C and 2D NMR were recorded on a Bruker AM-400 and DRX-500 spectrometers with TMS as internal standard. The silica gel for TLC and column chromatography was obtained from Qingdao Marine Chemical Inc., China.

3.2 Plant material

The leaves and stems of *Coriaria nepalensis* were collected in the Kunming region of Yunnan Province, China, in August 2002, and were identified by Professor Zhong-Wen Lin. The voucher specimen (KIB 2002-08-22 Lin) has been deposited in the Laboratory of Phytochemistry, Kunming Institute of Botany, Chinese Academy of Sciences.

3.3 Extraction and isolation

Dried and powdered leaves and stems (7 kg) of *C. nepalensis* were extracted with 95% ethanol (3 × 25 l) at room temperature and filtered. The filtrate was concentrated *in vacuo* and partitioned with petroleum ether, chloroform and EtOAc. The chloroform extract was evaporated to afford 106 g of residue, which was chromatographed on a silica gel column eluting with a petroleum ether/acetone (1:0–0:1) gradient system to furnish fractions 1–9.

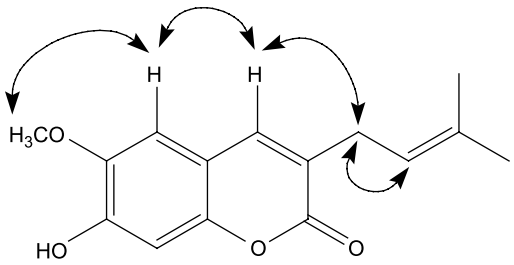

Figure 4. Key REOSY correlations for **2**.

The fractions were combined by monitoring with TLC. Fraction 1 was subjected to column chromatography over MCI-gel CHP-20P (MeOH/H_2O, 9:1) and silica gel ($CHCl_3$/i-PrOH, 30:1) to afford **1** (20 mg) and **3** (15 mg). Fraction 2 was purified by repeated column chromatography over silica gel developing with $CHCl_3$/MeOH (40:1) and over MCI-gel CHP-20P (MeOH/H_2O, 9:1) to yield **2** (22 mg). Fraction 3 was subjected to column chromatography over silica gel and RP-18 eluting with $CHCl_3$/EtOAc (9:1), cyclohexane/i-PrOH (9:1), and MeOH/H_2O to give **4** (9 mg) and **5** (13 mg). Fraction 5 was subjected to column chromatography over MCI-gel CHP-20P (MeOH/H_2O, 9:1) and purified by Sephadex LH-20 (MeOH) to afford **6** (20 mg). Fraction 6 was purified by column chromatography on MCI-gel CHP-20P (MeOH/H_2O, 9:1) and Sephadex LH-20 (MeOH), then subjected to column chromatography on silica gel eluting with petroleum ether/EtOAc (3:1) to yield **7** (17 mg). Fraction 8 was subjected to column chromatography on MCI-gel CHP 20P (MeOH/H_2O, 9:1), Sephadex LH-20 (MeOH) and silica gel ($CHCl_3$/i-PrOH, 20:1) to give **8** (9 mg) and **9** (9 mg).

3.3.1 7-Hydroxy-6-methoxy-3,8-bis (3-methyl-2-butenyl) coumarin (1). Yellow powder, UV (MeOH) λ_{max} (log ε) (nm): 210 (4.65), 347 (4.13); IR (KBr) ν_{max} (cm^{-1}): 3471, 2923, 2856, 1706, 1591, 1461, 1294, 1063, 933, 913, 854, 833, 786, 762; ^{1}H NMR and ^{13}C NMR: see table 1; EIMS (70 eV) *m/z* (rel. int. %): 328 (M^+, 100), 311 (8), 273 (98), 257 (29), 217 (62), 189 (28), 108 (21); HRESI-MS *m/z*: 329.1754 $[M + H]^+$ (calcd for $C_{20}H_{25}O_4$: 329.1752).

3.3.2 7-Hydroxy-6-methoxy-3-(3-methyl-2-butenyl) coumarin (2). Yellow powder, $C_{15}H_{16}O_4$, UV (MeOH) λ_{max} (log ε) (nm): 207 (4.42), 344 (4.06); IR (KBr) ν_{max} (cm^{-1}): 3432, 2971, 2931, 2854, 1701, 1619, 1580, 1509, 1463, 1452, 1405, 1376, 1269, 1145, 1021; ^{1}H NMR and ^{13}C NMR: see table 1; EI-MS (70 eV) *m/z* (rel. int. %): 260 (M^+, 77), 245 (29), 217 (36), 205 (100); HRESI-MS *m/z*: 261.1124 $[M + H]^+$ (calcd for $C_{15}H_{16}O_4$: 261.1126);

3.3.3 Marmesin (3). Light yellow needles, $C_{14}H_{14}O_4$, mp 188–189°C; $[\alpha]_D^{16.6}$: 0 ($CHCl_3$, *c* 0.23); UV ($CHCl_3$): λ_{max} (log ε) = 336 nm (0.61); EI-MS (70 eV) *m/z* (rel. int. %): 246 (M^+, 39), 213 (21), 188 (65), 187 (100), 175 (12), 160 (28), 131 (21). ^{1}H NMR (400 MHz, $CDCl_3$): 6.71 (1H, d, J = 9.4 Hz, H-3), 8.08 (1H, d, J = 9.4 Hz, H-4), 7.72 (1H, s, H-5), 7.23 (1H, s, H-8), 5.24 (1H, t, J = 8.6 Hz, H-2′), 3.71 (2H, m, H-3′), 1.87, 1.74 (each 3H, s, 2 × CH_3).

3.3.4 Braylin (4). White needles, $C_{15}H_{14}O_4$, mp 144–146°C; EI-MS (*m/z*, rel. %): 258 (M^+, 32), 243 (M^+-CH_3, 100), 228 (23), 215 (10), 200 (14).

3.3.5 Norbraylin (5). White needles, $C_{14}H_{12}O_4$, mp 140–141°C; EI-MS (*m/z*, rel %): 244 (M^+, 96), 230 (47), 229 (69), 228 (100), 201 (64).

3.3.6 Scopoletin (6). Light yellow needles, $C_{10}H_8O_4$, mp 205–206°C; EI-MS (*m/z*, rel. %): 192 (M^+, 100), 177 (70), 164 (38), 149 (64), 121 (29), 69 (30).

3.3.7 7-Hydroxy coumarin (7). White needles, $C_9H_6O_3$, mp 226–227°C; EI-MS (*m/z*, rel. %): 162 (M^+, 100), 134 (91), 105 (20), 78 (20).

3.3.8 7-Hydroxy-6-(3-methyl-2-butenyl) coumarin (8). Light yellow needles, $C_{14}H_{14}O_3$, mp 134–135°C; FAB^+ (*m/z*, rel. %): 231 ($[M + 1]^+$, 100), 175 (26).

3.3.9 7-Hydroxy-3-(3-methyl-2-butenyl) coumarin (9). Light yellow needles, $C_{14}H_{14}O_3$, mp 122–123.5°C; FAB^+ (*m/z*, rel. %): 231 ($[M + 1]^+$, 100).

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