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Three new compounds from the bark of *Antiaris toxicaria*

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ABSTRACT

Three new compounds, namely (+)-pranferol (**1**), antiarone M (**2**), and anticerol A (**3**), together with 9 known compounds, were obtained from the bark of *Antiaris toxicaria*. Their chemical structures were elucidated on the basis of spectroscopic methods including UV, IR, (HR) ESI–MS, ^{1}H, ^{13}C NMR, HSQC, ^{1}H-^{1}H COSY, HMBC and X-ray crystallographic technique. The absolute configurations of compounds **1** and **2** were determined by modified mosher method and CD spectrum.

1. Introduction

Antiaris toxicaria (Pers.) Lesh. (Moraceae), also known as "upas tree", is widely distributed throughout over tropic rain forest. Previous chemical investigations of this species have revealed that it was rich in cardiac glycosides, especially from its latex (Liu et al., 2013; Que et al., 2010) and seed (Zuo et al., 2013). Apart from the cardiac glycosides, prenylflavanones (Hano et al., 1990a,b; Hano et al., 1991; Que et al., 2009), phenylpropanoid and lignan derivatives (Jiang et al., 2009), and coumarin derivatives (Shi et al., 2014) were other kinds of components discovered from this plant, which exhibited anti-osteoporosis (Jiang et al., 2009) and antibacterial activities (Que et al., 2009).

In our search for anticancer agents from this plant, about 50 cardiac glycosides were isolated from the stem, latex, and bark of *A. toxicaria* by using bioassay and chemical guided fractionation (Jiang et al., 2008; Li et al., 2014; Liu et al., 2013). Herein, we reported the isolation and structural elucidation of three new (**1–3**) (Fig. 1) and 9 known compounds from the bark of *A. toxicaria*.

2. Results and discussion

Compound **1** was obtained as white amorphous powder. The HR–ESI–MS showed quasimolecular ion at *m/z* 289.1079 $[M+H]^{+}$ (calcd. for 289.1076), indicating the molecular formula of $C_{16}H_{16}O_5$ and accounting for 9 degrees of unsaturation. The IR spectrum of **1** displayed prominent absorption maxima at 3454, 1698, and 1628 cm^{-1}, indicating the presence of hydroxyl group (s), α,β-unsaturated lactone, conjugated carbonyl functionality. The UV absorptions at 204, 219, 249, 265, and 309 nm suggested that it was a coumarin derivative (Scott, 1964). The ^{1}H and ^{13}C NMR signals for **1** were assigned using 1D and 2D NMR experiments (Table 1). The ^{1}H NMR spectrum of **1** showed characteristic signals of psoralen (also known as furocoumarin) (Wulff et al., 1988) for two AB type system protons both at δ 6.31 (1H, d, *J* = 9.8 Hz, H-3), 8.32 (1H, d, *J* = 9.8 Hz, H-4) and δ 7.28 (1H, d, overlap, *J* = 2.5 Hz, H-9), 7.87 (1H, d, *J* = 2.5 Hz, H-10) as well as one aromatic proton at δ 7.28 (1H, s, overlap, H-8). In the ^{1}H-^{1}H COSY spectrum of **1**, successive correlations of protons at δ 4.68 (2H, m, H-1′), 4.06 (1H, m, H-2′), 2.10 (1H, m, H-3′), 1.14 (3H, d, *J* = 6.8 Hz, H-4′), and 1.20 (3H, d, *J* = 6.8 Hz, H-5′) revealed the presence of an 1,2-dioxyisopentyl group in the structure of **1**. Comparison of the ^{1}H and ^{13}C NMR data of **1** with that of (−)-pranferol revealed that they had the same planar structures (Kuznetsova et al., 1966; Shi et al., 2013). Key ^{1}H-^{1}H COSY and HMBC correlations (Fig. 2) together with X-ray Crystallographic analysis confirmed the deduction mentioned above (Fig. 3). Interestingly, the directions of specific rotation for

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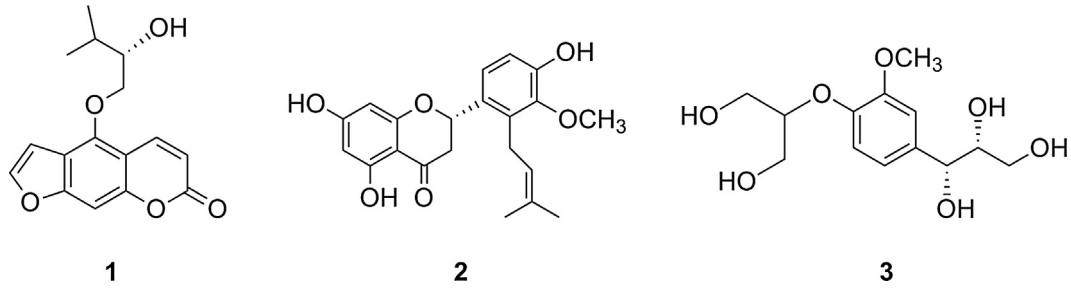

Fig. 1. Chemical structures of compounds 1–3.

Table 1
^{13}C and ^{1}H NMR spectral data of compounds **1–3** (δ in ppm, J in Hz).

No.	**1**[a] (pyridine-d_5)		**2**[a] (pyridine-d_5)		No.	**3**[b] (CH_3OH-d_4)	
	δ_C	δ_H	δ_C	δ_H		δ_C	δ_H
2	161.2	–	77.2	5.87, dd (13.2, 2.7)	1	138.2	–
3	113.2	6.31, d (9.8)	43.5	3.37, dd (17.2, 13.2) 2.93, dd (17.2, 2.7)	2	112.5	7.08, d (2.0)
4	140.1	8.32, d (9.8)	197.3	–	3	151.9	–
4a	107.8	–	103.2	–	4	148.3	–
5	150.9	–	165.6	–	5	118.7	7.06, d (8.0)
6	114.6	–	97.7	6.50, d (2.1)	6	120.7	6.91, dd (8.0, 2.0)
7	158.9	–	169.0	–	7	75.2	4.58, d (6.2)
8	94.4	7.28, s	96.5	6.42, d (2.1)	8	77.6	3.67, m
8a	153.7	–	164.7	–	9	64.4	3.51, m/3.40, m
9	106.2	7.28, d (2.5)			1′	83.2	4.21, m
10	146.0	7.87, d (2.5)			2′	62.2	3.76, m
1′	77.3	4.68, m	129.1	–	3′	62.2	3.76, m
2′	75.1	4.06, m	135.1	–	3-OMe	56.7	3.86, s
3′	32.0	2.10, m	147.5	–			
4′	20.0	1.14, d (6.8)	152.6	–			
5′	18.3	1.20, d (6.8)	116.2	7.25, d (8.5)			
6′			123.8	7.47, d (8.5)			
7′			26.0	3.78, m			
8′			124.7	5.32, t (6.6)			
9′			131.8	–			
10′			26.1	1.61, s			
11′			18.3	1.71, s			
3′-OMe			60.8	3.94, s			

The assignments of ^{1}H and ^{13}C NMR signals are based on HSQC, ^{1}H-^{1}H COSY, and HMBC experiments.
[a] ^{1}H for 400 MHz and ^{13}C for 100 MHz.
[b] ^{1}H for 500 MHz and ^{13}C for 125 MHz.

compound **1** and (−)-pranferol were opposite, which indicated that they were enantiomers (Kuznetsova et al., 1966). The absolute configuration of C-2′ for **1** was determined to be S configuration by the modified mosher method (Fig. 4). Thus, the structure of **1** was elucidated as 5-[(2S)-2-hydroxy-3-methylbutyloxy)]-psoralen named (+)-pranferol.

Compound **2** was obtained as white amorphous powder. The HR–ESI–MS showed quasimolecular ion at m/z 371.1496 $[M+H]^+$ (calcd. for 371.1495), indicating the molecular formula of $C_{21}H_{22}O_6$ and accounting for 11 degrees of unsaturation. The IR spectrum showed absorption bands at 3446 cm^{-1} and 1639 cm^{-1}, indicating the existence of hydroxyl group and conjugated carbonyl functionality. The UV spectrum exhibited the maxima absorption at 205, 228, 289 and 331 nm, suggesting that it was a flavonoid derivative (Scott, 1964). The ^{1}H and ^{13}C NMR signals for **2** were assigned using 1D and 2D NMR experiments (Table 1). The ^{1}H NMR spectrum of **2** revealed the presence of an 1,2,3,5-tetrasubstituted benzene ring proton signals at δ_H 6.50 (1H, d, J = 2.1 Hz, H-6) and 6.42 (1H, d, J = 2.1 Hz, H-8), an 1,2,3,4-tetrasubstituted benzene ring proton signals at δ_H 7.25 (1H, d, J = 8.5 Hz, H-5′)

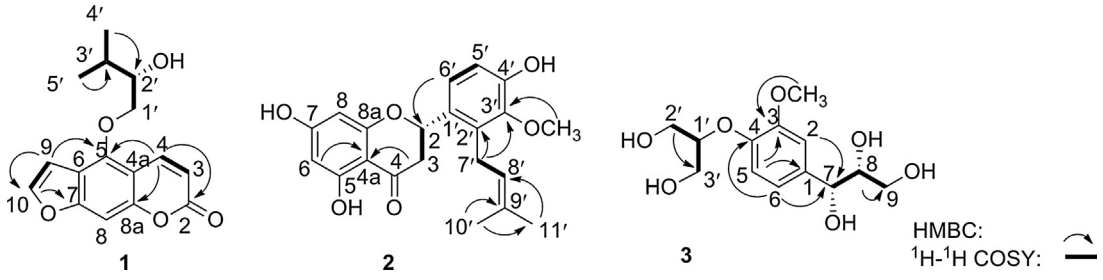

Fig. 2. Key ^{1}H-^{1}H COSY and HMBC correlations of compounds 1–3.