

## Xanthone and Benzophenone Glycosides from the Stems of *Cratoxylum formosum* ssp. *pruniflorum*

Ying-hui DUAN,<sup>a,#</sup> Yi DAI,<sup>b,c,#</sup> Guang-hui WANG,<sup>d</sup> Hai-feng CHEN,<sup>d</sup> Hao GAO,<sup>b,c</sup> Jie-bo CHEN,<sup>e</sup>  
Xin-sheng YAO,<sup>\*,a,b,c</sup> and Xiao-kun ZHANG<sup>\*,d,e</sup>

<sup>a</sup> College of Traditional Chinese Materia Medica, Shenyang Pharmaceutical University; Shenyang 110016, China;

<sup>b</sup> Institute of Traditional Chinese Medicine & Natural Products, College of Pharmacy, Jinan University; <sup>c</sup> Guangdong Province Key Laboratory of Pharmacodynamic Constituents of TCM and New Drugs Research, Jinan University;

Guangzhou 510632, China; <sup>d</sup> Institute for Biomedical Research, Xiamen University; Xiamen 361005, China; and <sup>e</sup> Sanford-Burnham Medical Research Institute, Cancer Center; La Jolla, California 92037, U.S.A.

Received September 4, 2010; accepted October 26, 2010; published online November 30, 2010

Two new xanthone glycosides, namely *pruniflorosides* A and B (**1**, **2**), a new benzophenone glycoside, *prunifloroside* C (**3**), and a new xanthone, *pruniflorone* S (**4**) were isolated from the stems of *Cratoxylum formosum* ssp. *pruniflorum*, along with six known xanthones (**5**–**10**). Their structures were determined on the basis of extensive spectroscopic analysis. In addition, their retinoid X receptor  $\alpha$  (RXR $\alpha$ ) transcriptional activities were evaluated *in vitro*.

**Key words** *Cratoxylum formosum*; xanthone; retinoid X receptor  $\alpha$  transcriptional activity

Retinoid X receptors (RXRs) are ligand-controlled transcriptional factors which are members of the nuclear receptor superfamily.<sup>1,2</sup> RXRs play an important role in many diverse physiologic processes, including embryogenesis, calcium homeostasis, and lipid and glucose metabolism due to their functions as heterodimers with other nuclear receptors, such as retinoic acid receptor, thyroid hormone receptors, peroxisome proliferator-activated receptors and a number of orphan receptors.<sup>3,4</sup> Our previous investigation on searching for RXR $\alpha$  transcription inhibitory constituents from *Cratoxylum formosum* ssp. *pruniflorum* led to the isolation of six new xanthones and nineteen known ones.<sup>5</sup> Further research of this plant revealed two new xanthone glycosides, *pruniflorosides* A and B (**1**, **2**), a new benzophenone glycoside, *prunifloroside* C (**3**), and a new xanthone, *pruniflorone* S (**4**), along with six known xanthones (**5**–**10**). Their structures were established on the basis of extensive spectroscopic analysis, and their RXR $\alpha$  transcriptional activities were evaluated *in vitro*.

### Results and Discussion

Compound **1**, obtained as a yellow powder, gave a molecu-

lar formula of C<sub>21</sub>H<sub>22</sub>O<sub>11</sub> by high resolution-electron spray ionization (HR-ESI)-MS. It was suggested the presence of a xanthone skeleton from UV absorption bands at 211, 238, and 266 nm,<sup>6</sup> and the IR spectrum showed absorption bands for hydroxyl (3385 cm<sup>-1</sup>), carbonyl (1648 cm<sup>-1</sup>) and aromatic rings (1488 cm<sup>-1</sup>). The <sup>1</sup>H-NMR data of **1** (Table 1) exhibited a 1,2,4-trisubstituted benzene ring [ $\delta$  7.68 (1H, d, *J*=2.7 Hz, H-8), 7.55 (1H, d, *J*=9.1 Hz, H-5), and 7.51 (1H, dd, *J*=9.1, 2.7 Hz, H-6)], a pentasubstituted benzene ring [ $\delta$  7.12 (1H, s, H-3)], and two methoxy groups at  $\delta$  3.81 and 3.72 (3H, each, s), along with an anomeric proton signal at  $\delta$  4.93 (1H, d, *J*=7.2 Hz, H-1'). The aromatic proton signals at  $\delta$  7.68 was assigned as H-8, according to the significant deshielding shift arising from anisotropic effect of carbonyl group.<sup>7,8</sup> It was further confirmed by the heteronuclear multiple bond connectivity (HMBC) correlation between H-8 and C-9 ( $\delta$  175.1). The aromatic proton signals at  $\delta$  7.55 and 7.51 were then assigned as H-5 and H-6, respectively. In the rotating frame Overhauser enhancement spectroscopy (ROESY) spectrum (Fig. 1), the anomeric proton signal at  $\delta$  4.93 (H-1') correlated with H-8 and H-6, suggesting that the monosaccharide moiety was located at C-7 ( $\delta$  153.5). This

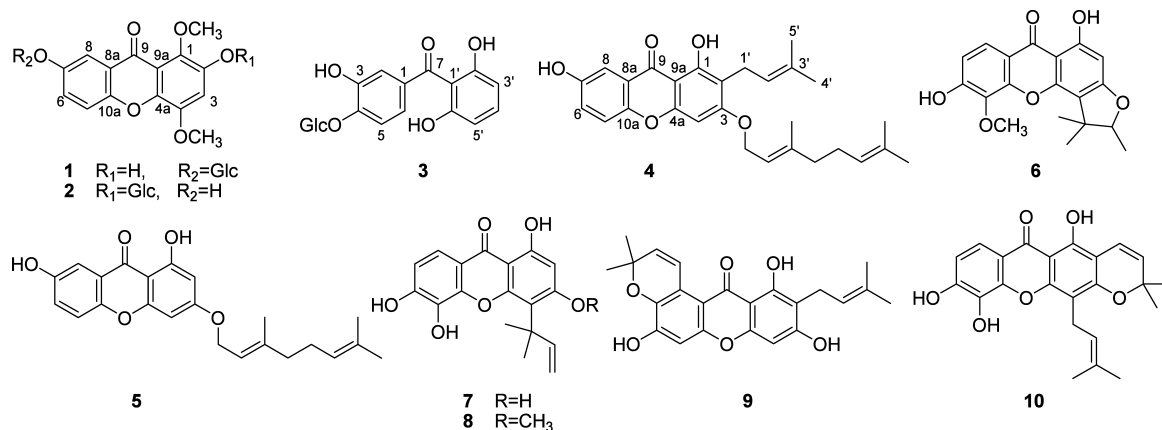


Chart 1. Structures of Compounds **1**–**10**

Table 1. NMR Data for Compounds 1 and 2 in DMSO-*d*<sub>6</sub>

No.	Compound 1		Compound 2	
	$\delta_C$	$\delta_H$	$\delta_C$	$\delta_H$
1	139.1 s		140.9 s	
2	142.5 s		142.1 s	
3	107.2 d	7.12 s	108.5 d	7.47 s
4	148.1 s		147.7 s	
4a	138.6 s		140.5 s	
5	119.0 d	7.55 d (9.1)	119.1 d	7.46 d (9.0)
6	125.0 d	7.51 dd (9.1, 2.7)	124.1 d	7.26 dd (9.0, 3.0)
7	153.5 s		153.8 s	
8	110.7 d	7.68 d (2.7)	108.4 d	7.40 d (3.0)
8a	121.8 s		122.0 s	
9	175.1 s		175.1 s	
9a	116.0 s		115.9 s	
10a	149.9 s		148.1 s	
1'	101.3 d	4.93 d (7.2)	101.2 d	5.06 d (6.8)
2'	73.2 d	3.28 o <sup>a)</sup>	73.3 d	3.40 m
3'	77.1 d	3.35 o <sup>a)</sup>	77.4 d	3.41 m
4'	69.5 d	3.21 m	70.0 d	3.16 t (9.0)
5'	76.4 d	3.30 o <sup>a)</sup>	76.8 d	3.32 m
6'	60.6 t	3.71 m	60.8 t	3.73 o <sup>a)</sup>
		3.51 m		3.44 m
1-OCH <sub>3</sub>	60.9 q	3.72 s	60.9 q	3.75 s
4-OCH <sub>3</sub>	56.4 q	3.81 s	56.6 q	3.86 s

a) "o" refers to peaks overlapped with other signals.

was confirmed by the HMBC correlation of H-1'/C-7. Acid hydrolysis and gas chromatographic analysis showed the presence of a glucose residue, and the absolute configuration of the glucose was demonstrated to be D configuration using the method of Hara *et al.* with slight modification.<sup>9,10</sup> The aromatic singlet signal at  $\delta$  7.12 was assigned as H-3 due to its HMBC correlations with four *O*-linked aromatic carbon signals at  $\delta$  148.1 (C-4), 142.5 (C-2), 139.1 (C-1), 138.6 (C-4a). The methoxy group at  $\delta$  56.4/3.81 was located at C-4 ( $\delta$  148.1) according to the ROESY correlation with H-3. In the <sup>13</sup>C-NMR spectrum, the obvious downfield shift of the other methoxy group at  $\delta$  60.9/3.72 suggested that both of the *ortho*-positions of this methoxy group are substituted.<sup>11,12</sup> In addition, no ROESY correlation was observed between the methoxy group and H-3. Therefore, the carbon signal at  $\delta$  139.1, which has an HMBC correlation with the methoxy group at  $\delta$  60.9/3.72, was assigned as C-1. Thus, the structure of **1** was elucidated as 2-hydroxy-1,4-dimethoxy-7-*O*- $\beta$ -D-glucopyranosylxanthone, namely prunifloroside A.

Compound **2** was obtained as a brownish powder with a molecular formula of C<sub>21</sub>H<sub>22</sub>O<sub>11</sub> established by HR-ESI-MS. The <sup>1</sup>H- and <sup>13</sup>C-NMR data of **2** were similar to those of **1**, except for the linkage of the monosaccharide moiety. When the H-3 ( $\delta$  7.47) was irradiated, the significant nuclear Overhauser effect (NOE) enhancement of the anomeric proton signal at  $\delta$  5.06 (H-1') was observed, suggesting the monosaccharide moiety to be located at C-2 ( $\delta$  142.1). This was further confirmed by the HMBC correlation of H-1'/C-2. Thus, the structure of **2** (prunifloroside B) was elucidated as 7-hydroxy-1,4-dimethoxy-2-*O*- $\beta$ -D-glucopyranosylxanthone.

Compound **3** was obtained as a brownish gum. Its molecular formula was established as C<sub>19</sub>H<sub>20</sub>O<sub>10</sub> by HR-ESI-MS. The <sup>1</sup>H-NMR data of **3** showed a 1,2,4-trisubstituted benzene ring [ $\delta$  7.33 (1H, d, *J*=2.0 Hz, H-2), 7.30 (1H, dd, *J*=8.4, 2.0 Hz, H-6) and 7.19 (1H, d, *J*=8.4 Hz, H-5)], a 1,2,3-

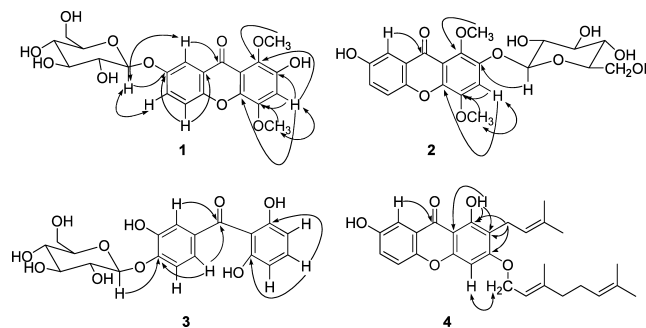


Fig. 1. Key HMBC (→) and ROESY (↔) Correlations of 1—4

trisubstituted benzene ring [ $\delta$  7.09 (1H, t, *J*=8.2 Hz, H-4') and 6.37 (2H, d, *J*=8.2 Hz, H-3', 5')], and an anomeric proton signal at  $\delta$  4.92 (1H, d, *J*=7.3 Hz, H-1'). The <sup>13</sup>C-NMR and distortionless enhancement by polarization transfer (DEPT)135 spectra of **3** showed 19 carbon signals, including one carbonyl carbon signal, twelve aromatic carbon signals, and six carbon signals in the sugar region. The carbonyl group appeared at  $\delta$  198.3 (C-7), which was the characteristic of the carbonyl group of a benzophenone derivative.<sup>13,14</sup> The aromatic proton signals at  $\delta$  7.33 and 7.30 were assigned as H-2 and H-6, respectively, based on their HMBC correlations with the carbonyl carbon (C-7) (Fig. 1). The aromatic proton signal at  $\delta$  7.19 was then assigned as H-5. The *O*-linked aromatic carbon signal at  $\delta$  151.0 was assigned as C-4, due to its HMBC correlations with H-2 and H-6. The HMBC correlation of H-1'/C-4 indicated that the monosaccharide moiety was located at C-4. Hydrolyzed with 5% hydrochloric acid, compound **3** yielded D-glucose identified by gas chromatographic on comparison of the retention time of the derivative with those of authentic.<sup>9,10</sup> Furthermore, the remaining six aromatic carbon signals at  $\delta$  157.6×2, 132.5, 107.9×2 and 116.2 indicated the presence of a symmetrical benzene ring. The two *O*-linked aromatic carbon signals at  $\delta$  157.6×2 were then assigned as C-2', 6', due to their HMBC correlations with H-4' ( $\delta$  7.09). Thus, the structure of **3** (prunifloroside C) was identified as 4-*O*- $\beta$ -D-glucopyranosyl-2',3,6'-trihydroxybenzophenone.

Compound **4**, obtained as a yellow powder, had a molecular formula of C<sub>28</sub>H<sub>32</sub>O<sub>5</sub> established by HR-ESI-MS. The <sup>1</sup>H- and <sup>13</sup>C-NMR data of **4** were similar to those of cochinchinone G (**5**)<sup>15</sup> but showed one more prenyl group signals at  $\delta$  22.0/3.35 (2H, d, *J*=7.2 Hz, H-1'), 123.2/5.23 (1H, t, *J*=7.2 Hz, H-2'), 131.6 (C-3'), 25.8/1.64 (3H, s, H-4') and 18.0/1.78 (3H, s, H-5'). The prenyl group was located at C-2 based on the HMBC correlations of H-1'/C-1 (160.2), C-2 (112.2), and C-3 (164.7) (Fig. 1). Thus, the structure of **4** (pruniflorone S) was determined as 1,7-dihydroxy-2-prenyl-3-geranyloxyxanthone.

Other known compounds were identified as cochinchinone G (**5**),<sup>15</sup> 5-*O*-methyl-2-deprenylrheediaxanthone B (**6**),<sup>16</sup> isocudraniaxanthone A (**7**),<sup>17</sup> isocudraniaxanthone B (**8**),<sup>17</sup> garcinone B (**9**),<sup>18</sup> xanthone V<sub>1</sub> (**10**),<sup>19</sup> by comparison of their physical and spectroscopic data with those reported previously.

The effects on RXR $\alpha$  transcriptional activity of the compounds isolated were evaluated by reporter gene assays, except for compound **4**. CV-1 cells were transiently transfected

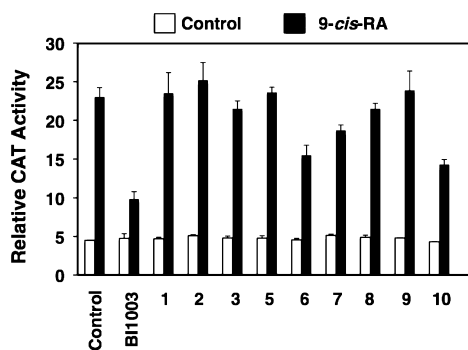


Fig. 2. Effects of Compounds **1** and **3**, **5**–**10** ( $10 \mu\text{M}$ ) on the Transcriptional Activities of RXR $\alpha$

CV-1 cells transfected with TREpal-tk-CAT and RXR $\alpha$  expression vector were treated with  $10 \mu\text{M}$  indicated compound together with or without  $10^{-7} \text{M}$  9-*cis*-RA. Reporter activities were measured and normalized. For comparison, the effect of BII1003 ( $1 \mu\text{M}$ ) was shown.

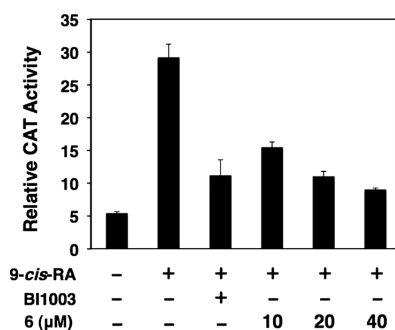


Fig. 3. Effects of Compound **6** on the Transcriptional Activities of RXR $\alpha$

CV-1 cells transfected with TREpal-tk-CAT and RXR $\alpha$  expression vector were treated with the indicated concentrations of compound **6** in the presence of  $10^{-7} \text{M}$  9-*cis*-RA. Reporter activities were measured and normalized. For comparison, the effect of BII1003 ( $1 \mu\text{M}$ ) was shown.

with the TREpal-tk-chloramphenicol acetyltransferase (CAT) reporter, which is known to be activated by RXR $\alpha$  homodimers, and the RXR $\alpha$  expression vector. Cells were then treated with RXR $\alpha$  ligand 9-*cis*-RA in the presence of the indicated compounds and the CAT reporter activities were determined. Consistent with previous results,<sup>20</sup> treatment of cells with 9-*cis*-RA strongly induced the reporter transcription, which was inhibited by cotreatment with BII1003, a known RXR $\alpha$  antagonist.<sup>21</sup> Comparing to the effect of BII1003 ( $1 \mu\text{M}$ ), Compounds **3**, **6**, **7** and **10** ( $10 \mu\text{M}$ ) showed various degrees of effects on the transcriptional activity of RXR $\alpha$  (Fig. 2). Among them, compound **6** possessed concentration-dependent activities (Fig. 3).

## Experimental

**General Procedures** UV spectra were measured on a JASCO V-550 UV/vis spectrophotometer in MeOH. IR spectra were acquired by JASCO FT/IR-480 plus spectrometer. 1D- and 2D-NMR spectra were measured with a Bruker AV-400 spectrometer (400 MHz for  $^1\text{H}$ , 100 MHz for  $^{13}\text{C}$ ). ESI-MS spectra were recorded on a Finnigan LCQ Advantage MAX mass spectrometer. HR-ESI-MS data were determined by an Agilent 6210 LC/MSD time-of-flight (TOF) mass spectrometer. Analytical high-performance liquid chromatography (HPLC) was performed on a Dionex HPLC system equipped with a Dionex P-680 quaternary pump, a PDA-100 autosampling system using a reversed-phase  $\text{C}_{18}$  column (4.6 $\times$ 250 mm, 5  $\mu\text{m}$ , Welch XB-C<sub>18</sub>). Open column chromatography (CC) was performed using silica gel (200–300 mesh, Qingdao Haiyang Chemical Goup Corp., Qingdao, China), ODS (50  $\mu\text{m}$ , YMC), Hw-40 (Tosoh) and Sephadex LH-20 (Pharmacia). Thin-layer chromatography (TLC) was performed using precoated silica gel plates (silica gel GF<sub>254</sub>, 1 mm, Yantai).

**Plant Material** The plant material was collected in Jinghong City, Yunnan Province of P. R. China in August 2008, and identified as stems of *Craetoxylum formosum* (JACK) DYER ssp. *pruniflorum* (KURZ) GOGEL.<sup>5</sup>

**Extraction and Isolation** The dried stems of *C. formosum* (5.0 kg) were extracted with 60% (v/v) EtOH–H<sub>2</sub>O. The extract (600.0 g) was isolated by Diaion HP-20 column to yield three fractions (A to C). Fraction C (90% EtOH–H<sub>2</sub>O eluent, 117.0 g) was then subjected to a silica gel column to give eight subfractions (C1 to C8).<sup>5</sup> Subfraction C3 (95 : 5 cyclohexane–EtOAc eluent, 15.0 g) was further separated by Sephadex LH-20 eluted with  $\text{CHCl}_3$ – $\text{CH}_3\text{OH}$  (1 : 1, v/v), to give eight fine fractions (C3A–C3H). Fine fraction C3H was subjected to ODS CC eluted with  $\text{CH}_3\text{OH}$  to give **4** (2.7 mg). Fine fraction C4E ( $\text{CHCl}_3$  eluent) was submitted to silica gel CC, eluted with  $\text{CHCl}_3$  to give **8** (11.7 mg). Fine fraction C4F ( $\text{CHCl}_3$  eluent) was purified by Sephadex LH-20, eluted with  $\text{CHCl}_3$ – $\text{CH}_3\text{OH}$  (4 : 1, v/v), and then subjected to silica gel CC eluted with  $\text{CHCl}_3$ – $\text{CH}_3\text{OH}$  (100 : 1, v/v) to afford **10** (20.9 mg). Fine subfraction C6D6 (8 : 2 eluent, v/v) was subjected to silica gel CC using  $\text{CHCl}_3$ – $\text{CH}_3\text{OH}$  (100 : 0 and 100 : 1, v/v) as mobile phase to give **9** (25.5 mg) and **5** (26.5 mg). Fine subfraction C6D7 (8 : 2 eluent, v/v) was subjected to Sephadex LH-20 CC eluted with  $\text{CHCl}_3$ – $\text{CH}_3\text{OH}$  (4 : 1, v/v) to give **7** (25.0 mg). Fine subfraction C6D8 (EtOAc eluent) was purified by octadecylsilane (ODS) CC eluted with  $\text{CH}_3\text{OH}$ – $\text{H}_2\text{O}$  (8 : 2, v/v) to afford **6** (14.7 mg).

Fraction B (40% EtOH–H<sub>2</sub>O eluent, 150.0 g) was subjected to ODS CC eluted with  $\text{CH}_3\text{OH}$ – $\text{H}_2\text{O}$  in gradient to yield three subfractions (B1–B3). Subfraction B2 (30%  $\text{CH}_3\text{OH}$ – $\text{H}_2\text{O}$  eluent) was further separated by Sephadex LH-20 eluted with  $\text{CH}_3\text{OH}$ – $\text{H}_2\text{O}$  in gradient to give eight fine fractions (B2A–B2H). Fine fraction B2C (30%  $\text{CH}_3\text{OH}$ – $\text{H}_2\text{O}$  eluent) was purified by Hw-40, eluted with  $\text{CH}_3\text{OH}$ – $\text{H}_2\text{O}$  (1 : 9, v/v), and then subjected to ODS CC, eluted with  $\text{CH}_3\text{OH}$ – $\text{H}_2\text{O}$  (1 : 9, v/v) to afford **3** (17.5 mg). Fine fraction B2E (50%  $\text{CH}_3\text{OH}$ – $\text{H}_2\text{O}$  eluent) was subjected to ODS CC, eluted with  $\text{CH}_3\text{OH}$ – $\text{H}_2\text{O}$  (5 : 5, v/v) to give **1** (13.7 mg), and then purified by Hw-40, using  $\text{CH}_3\text{OH}$ – $\text{H}_2\text{O}$  (8 : 2, v/v) as mobile phase to yield **2** (12.5 mg).

Prunifloroside A (**1**): Yellow powder, UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 211 (4.03), 238 (4.00), 266 (4.12) nm; IR (KBr)  $\nu_{\text{max}}$  3385, 2925, 1648, 1488, 1301, 1226, 835, 797  $\text{cm}^{-1}$ ;  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR data (see Table 1); ESI-MS (positive)  $m/z$ : 473 [ $\text{M}+\text{Na}$ ] $^+$ , 923 [ $2\text{M}+\text{Na}$ ] $^+$ , ESI-MS (negative)  $m/z$ : 449 [ $\text{M}-\text{H}$ ] $^-$ , 899 [ $2\text{M}-\text{H}$ ] $^-$ ; HR-ESI-MS  $m/z$  473.1069 [ $\text{M}+\text{Na}$ ] $^+$  (Calcd for  $\text{C}_{21}\text{H}_{22}\text{NaO}_{11}$ , 473.1054).

Prunifloroside B (**2**): Brownish powder, UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 208 (4.04), 243 (4.22), 266 (4.20) nm; IR (KBr)  $\nu_{\text{max}}$  3380, 2930, 1636, 1487, 1301, 1233, 831, 791  $\text{cm}^{-1}$ ;  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR data (see Table 1); ESI-MS (positive)  $m/z$ : 473 [ $\text{M}+\text{Na}$ ] $^+$ , 923 [ $2\text{M}+\text{Na}$ ] $^+$ , ESI-MS (negative)  $m/z$ : 449 [ $\text{M}-\text{H}$ ] $^-$ , 899 [ $2\text{M}-\text{H}$ ] $^-$ ; HR-ESI-MS  $m/z$  473.1071 [ $\text{M}+\text{Na}$ ] $^+$  (Calcd for  $\text{C}_{21}\text{H}_{22}\text{NaO}_{11}$ , 473.1054).

Prunifloroside C (**3**): Brownish gum, UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 213 (4.38), 225 (4.37), 273 (4.16), 311 (3.97) nm; IR (KBr)  $\nu_{\text{max}}$  3361, 1648, 1611, 1463, 1283, 1072, 799  $\text{cm}^{-1}$ ;  $^1\text{H}$ -NMR (MeOH- $d_4$ , 400 MHz)  $\delta$ : 7.33 (1H, d,  $J=2.0$  Hz, H-2), 7.30 (1H, dd,  $J=8.4$ , 2.0 Hz, H-6), 7.19 (1H, d,  $J=8.4$  Hz, H-5), 7.09 (1H, t,  $J=8.2$  Hz, H-4'), 6.37 (2H, d,  $J=8.2$  Hz, H-3', 5'), 4.92 (1H, d,  $J=7.3$  Hz, H-1''), 3.89 (1H, dd,  $J=12.1$ , 2.0 Hz, H-6'a), 3.70 (1H, dd,  $J=12.1$ , 5.2 Hz, H-6'b), 3.51 (1H, m, H-2''), 3.49 (1H, m, H-5''), 3.46 (1H, m, H-3''), 3.43 (1H, m, H-4'');  $^{13}\text{C}$ -NMR (MeOH- $d_4$ , 100 MHz)  $\delta$ : 198.3 s (C-7), 157.6 $\times$ 2 s (C-2', 6'), 151.0 s (C-4), 147.8 s (C-3), 135.0 s (C-1), 132.5 d (C-4'), 123.8 d (C-6), 117.8 d (C-2), 116.8 d (C-5), 116.2 s (C-1'), 107.9 $\times$ 2 d (C-3', 5'), 103.0 s (C-1''), 78.4 d (C-3''), 77.5 d (C-5''), 74.8 d (C-2''), 71.3 d (C-4''), 62.4 t (C-6''); ESI-MS (positive)  $m/z$ : 431 [ $\text{M}+\text{Na}$ ] $^+$ , 839 [ $2\text{M}+\text{Na}$ ] $^+$ , ESI-MS (negative)  $m/z$ : 407 [ $\text{M}-\text{H}$ ] $^-$ , 815 [ $2\text{M}-\text{H}$ ] $^-$ ; HR-ESI-MS  $m/z$  431.0945 [ $\text{M}+\text{Na}$ ] $^+$  (Calcd for  $\text{C}_{19}\text{H}_{20}\text{NaO}_{10}$ , 431.0949).

Pruniflorone S (**4**): Yellow powder, UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 205 (4.58), 237 (4.60), 259 (4.72), 308 (4.34), 374 (3.96) nm; IR (KBr)  $\nu_{\text{max}}$  3382, 2922, 1678, 1611, 1488, 1105, 820  $\text{cm}^{-1}$ ;  $^1\text{H}$ -NMR (acetone- $d_6$ , 400 MHz)  $\delta$ : 13.12 (1H, s, 1-OH), 7.59 (1H, d,  $J=2.6$  Hz, H-8), 7.45 (1H, d,  $J=8.9$  Hz, H-5), 7.36 (1H, dd,  $J=8.9$ , 2.6 Hz, H-6), 6.62 (1H, s, H-4), 5.56 (1H, t,  $J=6.5$  Hz, H-2''), 5.23 (1H, t,  $J=7.2$  Hz, H-2'), 5.12 (1H, t,  $J=6.7$  Hz, H-6''), 4.77 (2H, d,  $J=6.5$  Hz, H-1''), 3.35 (1H, d,  $J=7.2$  Hz, H-1'), 2.14 (2H, m, H-5''), 2.11 (2H, m, H-4''), 1.81 (3H, s, H-9''), 1.78 (3H, s, H-5'), 1.64 (6H, s, H-4', 8''), 1.60 (3H, s, H-10'');  $^{13}\text{C}$ -NMR (acetone- $d_6$ , 100 MHz)  $\delta$ : 181.3 s (C-9), 164.7 s (C-3), 160.2 s (C-1), 157.2 s (C-4a), 154.8 s (C-7), 150.7 s (C-10a), 142.4 s (C-3''), 132.1 s (C-7'), 131.6 s (C-3'), 125.1 d (C-6), 124.6 d (C-6''), 123.2 d (C-2'), 121.9 s (C-8a), 120.0 d (C-2''), 119.7 d (C-5), 112.2 s (C-2), 109.2 d (C-8), 103.8 s (C-9a), 91.6 d (C-4), 65.5 t (C-1''), 40.1 t (C-4''), 27.0 t (C-5''), 25.9 q (C-8''), 25.8 q (C-4'), 22.0 t (C-1'), 18.0 q (C-5'), 17.7 q (C-10''), 16.7 q (C-9''); ESI-MS (positive)  $m/z$ : 471 [ $\text{M}+\text{Na}$ ] $^+$ , 919 [ $2\text{M}+\text{Na}$ ] $^+$ , ESI-MS (negative)  $m/z$ : 447 [ $\text{M}-\text{H}$ ] $^-$ , 895 [ $2\text{M}-\text{H}$ ] $^-$ ; HR-ESI-

MS  $m/z$  449.2333  $[M+H]^+$  (Calcd for  $C_{28}H_{33}O_5$ , 449.2323).

**Cell Culture and Reporter Gene Assay** The bioassay was carried out according to the procedure reported in the previous paper.<sup>5)</sup>

**Acknowledgements** We thank Jing-yun Cui (Xishuangbanna Tropical Botanic Garden of Chinese Academy of Sciences) for collecting the plant material. We are grateful to Hui-nan Zhao and Rong Ding for measuring the HR-ESI-MS and NMR data. This work was supported by Grants from the National Natural Science Foundation of China (NSFC-30873146).

#### References

- 1) Altucci L., Leibowitz M. D., Ogilvie K. M., De Lera A. R., Gronemeyer H., *Nat. Rev. Drug Discov.*, **6**, 793—810 (2007).
- 2) De Lera A. R., Bourguet W., Altucci L., Gronemeyer H., *Nat. Rev. Drug Discov.*, **6**, 811—820 (2007).
- 3) Moore J. T., Collins J. L., Pearce K. H., *ChemMedChem*, **1**, 504—523 (2006).
- 4) Freemantle S. J., Spinella M. J., Dmitrovsky E., *Oncogene*, **22**, 7305—7315 (2003).
- 5) Duan Y. H., Dai Y., Wang G. H., Zhang X., Chen H. F., Chen J. B., Yao X. S., Zhang X. K., *J. Nat. Prod.*, **73**, 1283—1287 (2010).
- 6) Boonnak N., Karalai C., Chantrapromma S., Ponglimanont C., Fun H. K., Kanjana-Opas A., Chantrapromma K., Kato S., *Tetrahedron*, **65**, 3003—3013 (2009).
- 7) Boonsri S., Karalai C., Ponglimanont C., Kanjana-Opas A., Chantrapromma K., *Phytochemistry*, **67**, 723—727 (2006).
- 8) Mahabusarakam M., Nuangnaowarat W., Taylor W. C., *Phytochemistry*, **67**, 470—474 (2006).
- 9) Dai Y., Zhou G. X., Kurihara H., Ye W. C., Yao X. S., *Chem. Pharm. Bull.*, **56**, 439—442 (2008).
- 10) Hara S., Okabe H., Mihashi K., *Chem. Pharm. Bull.*, **35**, 501—507 (1987).
- 11) Inuma M., Tosa H., Ito T., Tanaka T., Madulid D. A., *Phytochemistry*, **42**, 1195—1198 (1996).
- 12) Silva A. M. S., Pinto D. C. G. A., *Curr. Med. Chem.*, **12**, 2481—2497 (2005).
- 13) Ferrari J., Terreaux C., Sahpaz S., Msonthi J. D., Wolfender J. L., Hostettmann K., *Phytochemistry*, **54**, 883—889 (2000).
- 14) Yu H. Y., Jin S. L., Zhang X., Liu Y., Ou Y. F., Wang N. L., Yao X. S., *Chin. Chem. Lett.*, **20**, 459—461 (2009).
- 15) Mahabusarakam W., Rattanaburi S., Phongpaichit S., Kanjana-Opas A., *Phytochemistry Lett.*, **1**, 211—214 (2008).
- 16) Rath G., Potierat O., Mavi S., Hostettmann K., *Phytochemistry*, **43**, 513—520 (1996).
- 17) Kobayashi M., Mahmud T., Yoshioka N., Shibuya H., Kitagawa I., *Chem. Pharm. Bull.*, **45**, 1615—1619 (1997).
- 18) Sen A. K., Sarkar K. K., Mazumder P. C., Banerji N., Uusvuori R., Hase T. A., *Phytochemistry*, **21**, 1747—1750 (1982).
- 19) Botta B., Delle Monache G., Delle Monache F., Marini B. G. B., Menichini F., *Phytochemistry*, **25**, 1217—1219 (1986).
- 20) Zhang X. K., Lehmann J., Hoffmann B., Dawson M. I., Cameron J., Graupner G., Hermann T., Tran P., Pfahl M., *Nature (London)*, **358**, 587—591 (1992).
- 21) Lu J. Y., Dawson M. I., Hu Q. Y., Xia Z. B., Dambacher J. D., Ye M., Zhang X. K., Li E., *Magn. Reson. Chem.*, **47**, 1071—1080 (2009).