Bioactive Xanthones from the Stems of Cratoxylum formosum ssp pruniflorum

ARTICLE *in* JOURNAL OF NATURAL PRODUCTS · JULY 2010

Impact Factor: 3.8 · DOI: 10.1021/np1001797 · Source: PubMed

Bioactive Xanthones from the Stems of *Cratoxylum formosum* ssp. *pruniflorum*

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Received March 15, 2010

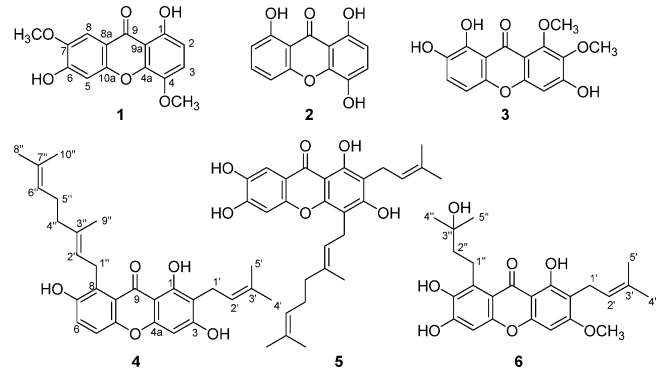
Six new compounds, pruniflorones M−R (**1**−**6**), together with 19 known compounds (**7**−**25**) were isolated from the stems of *Cratoxylum formosum* ssp. *pruniflorum*. The structures of the new compounds were established on the basis of extensive spectroscopic data interpretation. In addition, their RXRα transcriptional activities were evaluated using an in vitro assay.

Retinoid X receptors (RXRs) are members of the nuclear receptor superfamily, which function as transcriptional factors to positively or negatively regulate gene expression.[1] RXRs play an important role in many diverse physiologic processes, including embryogenesis, calcium homeostasis, and lipid and glucose metabolism. This is due to their ability to heterodimerize with a number of nuclear receptors, such as retinoic acid receptor, vitamin D_3 receptor, thyroid hormone receptors, peroxisome proliferator-activated receptors, and a number of orphan receptors.[2−4] Therefore, there has been tremendous interest in identifying agents that regulate RXR activities. *Cratoxylum formosum* ssp. *pruniflorum* belongs to the family Clusiaceae, which is distributed widely in several Southeast Asian countries.[5] This plant is known locally as "Kuding Tea" in southwest mainland China and has been used as a folk medicine for the treatment of fever, coughs, ulcers, and diarrhea.[6] Previous chemical investigations on this species have revealed a series of xanthones and anthraquinones.[7,8] Some of these compounds possess various bioactivities, such as antimalarial,[9] antibacterial,[7,8] and cytotoxic effects.[7,9] The present investigation on the stems of *C. formosum* ssp. *pruniflorum* led to the isolation of six new xanthones, pruniflorones M−R (**1**−**6**), and 19 known xanthones (**7**−**25**). The compounds isolated were investigated for their effects on RXRα transcriptional activities using an in vitro bioassay.

Results and Discussion

A 60% EtOH extract of the stems of *C. formosum* ssp. *pruniflorum* was subjected to column chromatography to yield six new compounds (**1**−**6**). All of these gave characteristic UV absorption bands in the range 226−269 and 312−379 nm, typical of a xanthone chromophore.[7,10] Their IR spectra also showed characteristic conjugated carbonyl and hydroxy groups in the range 1618−1650 and 3200−3435 cm^{-1}, respectively.

Compound **1** was obtained as a yellow powder. Its molecular formula was established as $C_{15}H_{12}O_6$ by HRESIMS. The ^1H NMR data of **1** (Table 1) showed signals for *ortho*-coupled aromatic protons at δ 7.40 (1H, d, J = 8.8 Hz, H-3) and 6.69 (1H, d, J = 8.8 Hz, H-2), two aromatic protons at δ 7.47 (1H, s, H-8) and 6.97 (1H, s, H-5), two methoxy groups at δ 3.90 (3H, s) and 3.88 (3H, s), and a hydrogen-bonded hydroxy group at δ 12.06 (1H, s, OH-1). The *ortho*-coupled aromatic protons at δ 6.69 and 7.40 were assigned to H-2 and H-3, respectively, due to the HMBC correlation between the hydrogen-bonded hydroxy group at δ 12.06 (OH-1) and an aromatic carbon at δ 108.0 (C-2) (Figure 1). The singlet signal at δ 7.47 was assigned to H-8, according to the significant deshielding shift arising from the anisotropic effect of the carbonyl group.[11,12] The H-8 assignment was confirmed by the HMBC correlation between H-8 and C-9 (180.0). In the ROESY spectrum, the methoxy groups at δ 3.88 (3H, s) and 3.90 (3H, s) correlated with H-3 and H-8, respectively, suggesting these two methoxy groups to be located at C-4 (139.6) and C-7 (146.5). The two oxygenated aromatic carbon signals at δ 152.3 and 155.6 were then assigned to C-6 and C-10a, due to their HMBC correlations with H-8. Furthermore, the remaining aromatic proton at δ 6.97 was located at C-5 (102.8), according to the HMBC correlations of H-5/C-7, C-8a (111.7), C-6, and C-10a. Thus, compound **1** was proposed as 1,6-dihydroxy-4,7-dimethoxyxanthone, and the trivial name pruniflorone M was assigned to this substance.



Compound **2**, a brownish, amporphous powder, gave a molecular formula of $C_{13}H_8O_5$ by HREIMS. The ^1H NMR spectrum of **2** (Table 1) revealed the presence of three hydroxy groups [δ 11.78, 11.00, and 9.73 (1H each, s, OH-8, OH-1, and OH-4)] and *ortho*-coupled aromatic protons [δ 7.31, 6.67 (1H each, d, J = 8.8 Hz, H-3 and H-2)], in addition to a 1,2,3-trisubstituted benzene ring [δ 7.75 (1H, t, J = 8.4 Hz, H-6), 7.06 (1H, d, J = 8.4 Hz, H-5), and 6.83 (1H, d, J = 8.4 Hz, H-7)]. In the ^{13}C NMR spectrum, the carbonyl carbon was observed at δ 185.6, a significant downfield shift of about 5 ppm, compared to that of compound **1**, which indicated that **2** is a 1,8-dihydroxyxanthone derivative.[13] The *ortho*-coupled aromatic protons at δ 6.67 and 7.31 were assigned to H-2

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10.1021/np1001797
Published on Web 07/07/2010

Table 1. ^{1}H and ^{13}C NMR Data for Compounds **1**−**3** (400 MHz for ^{1}H NMR)

	compound **1**[a]		compound **2**[a]		compound **3**[b]	
position	δ_C, mult	δ_H (J in Hz)	δ_C, mult	δ_H (J in Hz)	δ_C, mult	δ_H (J in Hz)
1	153.2, C		151.8, C		154.4, C	
2	108.0, CH	6.69, d, (8.8)	109.4, CH	6.67, d (8.8)	139.5, C	
3	119.4, CH	7.40, d (8.8)	124.3, CH	7.31, d (8.8)	155.8,[c] C	
4	139.6, C		137.4, C		99.9, CH	6.73, s
4a	144.8, C		143.6, C		158.8,[c] C	
5	102.8, CH	6.97, s	107.4, CH	7.06, d (8.4)	105.9, CH	6.79, d (8.8)
6	152.3,[c] C		138.0, CH	7.75, t (8.4)	123.3, CH	7.24, d (8.8)
7	146.5, C		110.4, CH	6.83, d (8.4)	141.0, C	
8	104.5, CH	7.47, s	160.4, C		148.9, C	
8a	111.7, C		107.5, C		109.5, C	
9	180.0, C		185.6, C		182.3, C	
9a	108.1, C		107.9, C		108.9, C	
10a	155.6,[c] C		155.8, C		149.1, C	
OCH_3-1					62.1, CH_3	3.97, s
OCH_3-2					61.6, CH_3	3.90, s
OCH_3-4	56.7, CH_3	3.88, s				
OCH_3-7	55.9, CH_3	3.90, s				
OH-1		12.06, s		11.00, s		
OH-4				9.73, s		
OH-8				11.78, s		13.26, s

[a] Measured in DMSO-d_6. [b] Measured in acetone-d_6. [c] Signals may be interchanged in each column.

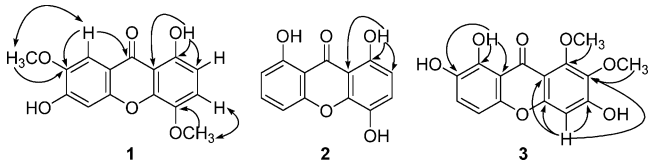

Figure 1. Key HMBC (→) and ROESY (↔) correlations of **1**−**3**.

and H-3, respectively, on the basis of the HMBC correlation between the hydrogen-bonded hydroxy group at δ 11.00 (OH-1) and an aromatic carbon at δ 109.4 (C-2) (Figure 1). Therefore, compound **2** (pruniflorone N) was assigned as 1,4,8-trihydroxyxanthone.

Compound **3**, obtained as a yellow, amporphous powder, gave a molecular formula of $C_{15}H_{12}O_7$ by analysis of the HRESIMS data. The ^{1}H NMR data of **3** (Table 1) showed one hydrogen-bonded hydroxy signal at δ 13.26 (1H, s, OH-8), two *ortho*-coupled aromatic signals at δ 7.24 and 6.79 (1H, each, d, J = 8.8 Hz, H-6 and H-5), and an aromatic signal at δ 6.73 (1H, s, H-4), in addition to two methoxy signals at δ 3.97 and 3.90 (3H each, s). The aromatic carbon signals at δ 148.9, 141.0, and 109.5 were assigned to C-8, C-7, and C-8a, due to their HMBC correlations with the hydroxy group at δ 13.26 (OH-8) (Figure 1). The *ortho*-coupled aromatic protons at δ 7.24 and 6.79 were then assigned to H-6 and H-5, on the basis of the HMBC correlations of H-6/C-8 and C-7. The aromatic carbon signal at δ 149.1 was assigned to C-10a, as a result of its HMBC correlation with H-6. The remaining six aromatic carbon signals at δ 158.8, 155.8, 154.4, 139.5, 108.9, and 99.9 were assigned to the other benzene ring of **3**. The quaternary carbon signal at δ 154.4, which correlated with the methoxy group at δ 3.97 in the HMBC spectrum, was attached to the benzene ring *para* to the aromatic proton at δ 6.73, which gave the HMBC correlations with the quaternary carbon signals at δ 158.8, 155.8, 139.5, and 108.9. The aromatic proton at δ 6.73 was assigned to H-4 when the chemical shift was taken into account.[11,12] Furthermore, the methoxy carbon signal appeared at δ 61.6, suggesting that both of the *ortho*-positions of this methoxy group are substituted.[5,13] Therefore, the carbon signal at 139.5, with a HMBC correlation with the methoxy group at δ 61.6/3.90, was assigned to C-2. Thus, compound **3** (pruniflorone O) was elucidated as 1,2-dimethoxy-3,7,8-trihydroxyxanthone.

Compound **4** was obtained as a reddish-brown gum with a molecular formula of $C_{28}H_{32}O_5$, on the basis of its HRESIMS data. The ^{1}H NMR data of **4** (Table 2) exhibited signals of a hydrogen-bonded hydroxy group at δ 13.65 (1H, s, OH-1), two *ortho*-coupled aromatic signals at δ 7.13 and 7.08 (1H each, d, J = 8.8 Hz, H-6 and H-5), and an aromatic signal at δ 6.22 (1H, s, H-4). Furthermore, the proton signals at δ 3.41 (2H, d, J = 7.0 Hz, H-1′), 5.29 (1H, t, J = 7.0 Hz, H-2′), 1.74 (3H, s, H-4′), and 1.83 (3H, s, H-5′) suggested the presence of a prenyl moiety in the structure of **4**.[12] In addition, the presence of a geranyl side chain was indicated as a series of proton signals observed at δ 4.24 (2H, d, J = 6.6 Hz, H-1″), 5.27 (1H, t, J = 6.6 Hz, H-2″), 2.06 (2H, m, H-4″), 2.09 (2H, m, H-5″), 5.04 (1H, t, J = 6.4 Hz, H-6″), 1.64 (3H, s, H-8″), 1.86 (3H, s, H-9″), and 1.57 (3H, s, H-10″). The prenyl moiety was placed at C-2 on the basis of the HMBC correlations of H-1′/C-1 (160.4), C-2 (108.9), and C-3 (161.9). The geranyl unit was located at the *peri*-position to the carbonyl group (C-8), according to the downfield shift of H-1″ at δ 4.24.[10,14] This was confirmed by the HMBC correlations of H-1″/C-7 (150.9), C-8 (127.3), and C-8a (118.3) (Figure 2). Therefore, the structure of **4** (pruniflorone P) was determined as 1,3,7-trihydroxy-2-prenyl-8-geranylxanthone.

Compound **5**, a pale yellow, amporphous powder, gave a molecular formula of $C_{28}H_{32}O_6$, as established by HRESIMS. The ^{1}H and ^{13}C NMR data of **5** (Table 2) were similar to those of cudratricusxanthone E (**19**),[15] except that a geranyl group in **5** replaced the prenyl group in the latter compound. The geranyl group was located at C-4 (106.5) using the HMBC correlations of H-1″/C-3 (160.2), C-4, and C-4a (154.0) (Figure 2). Thus, the structure of **5** (pruniflorone Q) was elucidated as 1,3,6,7-tetrahydroxy-2-prenyl-4-geranylxanthone.

Compound **6** was afforded as a yellow, amporphous powder, with the molecular formula $C_{24}H_{28}O_7$ established by HRESIMS. The ^{1}H and ^{13}C NMR data of **6** (Table 2) were similar to those of dulcisxanthone B (**17**),[16] except for the appearance of a 3-hydroxy-3-methylbutyl moiety at δ 3.48 (2H, t, J = 7.2 Hz, H-1″), 1.88 (2H, t, J = 7.2 Hz, H-2″), and 1.30 (6H, s, H-4″ and H-5″) instead of the prenyl group presented in dulcisxanthone B. Similarly, the linkage of the 3-hydroxy-3-methylbutyl group was located at C-8 by the HMBC correlations of H-1″/C-7 (141.4), C-8 (131.1), and C-8a (112.0) (Figure 2). Thus, the structure of **6** (pruniflorone R) was determined as 1,6,7-trihydroxy-2-prenyl-3-methoxy-8-(3-hydroxy-3-methylbutyl)xanthone.

Several known compounds were identified as 1,7-dihydroxy-8-methoxyxanthone (**7**),[17] 1,6-dihydroxy-7,8-dimethoxyxanthone (**8**),[18] 1,7-dihydroxyxanthone (**9**),[19] 1,6-dihydroxy-5-methoxyxanthone (**10**),[20] 1,4,7-trihydroxy-8-methoxyxanthone (**11**),[5] 1,4,7-

Table 2. ^{1}H and ^{13}C NMR Data for Compounds **4**−**6** (400 MHz for ^{1}H NMR)

	compound **4**[a]		compound **5**[b]		compound **6**[b]	
position	δ_C, mult	δ_H (J in Hz)	δ_C, mult	δ_H (J in Hz)	δ_C, mult	δ_H (J in Hz)
1	160.4, C		158.8, C		160.5, C	
2	108.9, C		110.5, C		111.5, C	
3	161.9, C		160.2, C		164.4, C	
4	93.0, CH	6.22, s	106.5, C		89.3, CH	6.46, s
4a	155.0, C		154.0, C		156.2, C	
5	116.4, CH	7.08, d (8.8)	103.4, CH	6.97, s	101.1, CH	6.80, s
6	123.9, CH	7.13, d (8.8)	152.6,[c] C		153.4,[c] C	
7	150.9, C		143.8, C		141.4, C	
8	127.3, C		109.2, CH	7.56, s	131.1, C	
8a	118.3, C		113.7, C		112.0, C	
9	183.2, C		180.8, C		183.1, C	
9a	103.8, C		103.3, C		104.3, C	
10a	151.7, C		153.9,[c] C		154.0,[c] C	
1′	21.4, CH_2	3.41, d (7.0)	22.1, CH_2	3.43, d (7.0)	21.9, CH_2	3.31, d (7.2)
2′	121.6, CH	5.29, t (7.0)	123.2, CH	5.24, t (7.0)	123.4, CH	5.21, t (7.2)
3′	134.4, C		132.3, C		131.4, C	
4′	25.6, CH_3	1.74, s	25.8, CH_3	1.66, s	25.8, CH_3	1.64, s
5′	17.8, CH_3	1.83, s	17.9, CH_3	1.79, s	17.8, CH_3	1.78, s
1″	25.7, CH_2	4.24, d (6.6)	22.4, CH_2	3.57, d (7.0)	22.5, CH_2	3.48, t (7.2)
2″	121.7, CH	5.27, t (6.6)	123.2, CH	5.24, t (7.0)	44.1, CH_2	1.88, t (7.2)
3″	138.1, C		135.9, C		71.2, C	
4″	39.7, CH_2	2.06, m	40.3, CH_2	1.99, m	29.6, CH_3	1.30, s
5″	26.4, CH_2	2.09, m	27.2, CH_2	2.06, m	29.6, CH_3	1.30, s
6″	123.9, CH	5.04, t (6.4)	124.9, CH	5.02, t (6.6)		
7″	131.8, C		131.6, C			
8″	25.5, CH_3	1.64, s	25.7, CH_3	1.52, s		
9″	16.3, CH_3	1.86, s	16.4, CH_3	1.90, s		
10″	17.6, CH_3	1.57, s	17.6, CH_3	1.50, s		
OCH_3-3					56.4, CH_3	3.96, s
OH-1		13.65, s		13.47, s		13.75, s

[a] Measured in $CDCl_3$. [b] Measured in acetone-d_6. [c] Signals may be interchanged in each column.

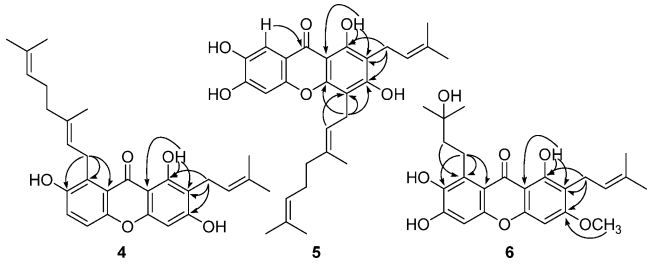

Figure 2. Key HMBC (→) correlations of **4**−**6**.

trihydroxyxanthone (**12**),[5] 1,3,6-trihydroxy-5-methoxyxanthone (**13**),[21] 1,5-dihydroxy-6-methoxyxanthone (**14**),[22] 1,7-dihydroxy-4-methoxyxanthone (**15**),[17] 1,3,6-trihydroxy-7-methoxyxanthone (**16**),[23] dulcisxanthone B (**17**),[16] 1,3,7-trihydroxy-2,4-diprenylxanthone (**18**),[24] cudratricusxanthone E (**19**),[15] 1,3,5-trihydroxy-4-geranylxanthone (**20**),[25] γ-mangostin (**21**),[26] cochinchinone A (**22**),[12] 1,3,7-trihydroxy-2-prenylxanthone (**23**),[27] cochinchinone B (**24**),[12] and α-mangostin (**25**),[26] by comparison of their physical and spectroscopic data with those reported previously. Compounds **15**, **22**, and **24** were isolated from the stems of *C. formosum* ssp. *pruniflorum* for the first time. In addition, compounds **8**, **9**, **16**, **19**, **20**, and **23** have not been isolated from the genus *Cratoxylum* previously.

The isolated compounds (**2**−**25**) were evaluated for their effects on RXRα transcriptional activity using a reporter gene assay. CV-1 cells were transiently transfected with the TREpal-tk-CAT reporter, which is known to be activated by RXRα homodimers, and the RXRα expression vector. Cells were then treated with RXRα ligand 9-*cis*-RA in the presence of the indicated compounds, and the CAT reporter activities were determined. Consistent with previous results,[28] treatment of cells with 9-*cis*-RA strongly induced the reporter transcription, which was inhibited by co-treatment with BI1003, a known RXRα antagonist.[29] Comparing with the effect of BI1003 (1 μM), compounds **5**−**7**, **11**, **15**−**17**, **19**, and **24** (10 μM) showed transcriptional-inhibitory activities of RXRα to various degrees. Among them, compounds **6**, **7**, and **11** exhibited concentration-dependent activities. These compounds are currently being evaluated for their effects on RXR-mediated growth inhibition and apoptosis induction in cancer cells as well as RXR-dependent regulation of gene expression.

Experimental Section

General Experimental Procedures. UV spectra were measured on a JASCO V-550 UV/vis spectrophotometer. IR spectra were recorded on a JASCO FTIR-400 spectrometer. 1D and 2D NMR spectra were recorded on a Bruker AV-400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C). ESIMS data were recorded on a Finnigan LCQ Advantage MAX mass spectrometer. HRESIMS data were determined by an Agilent 6210 LC/MSD TOF mass spectrometer. Open column chromatography (CC) was performed using silica gel (200−300 mesh, Qingdao Haiyang Chemical Goup Corp., Qingdao, People's Republic of China), ODS (50 μm, YMC), and Sephadex LH-20 (Pharmacia). Thin-layer chromatography (TLC) was performed using precoated silica gel plates (silica gel GF_{254}, 1 mm, Yantai).

Plant Material. The plant material was collected in Jinghong City, Yunnan Province, People's Republic of China in August 2008 and was identified as the stems of *Cratoxylum formosum* (Jack) Dyer ssp. *pruniflorum* (Kurz) Gogel by Jing-yun Cui, Xishuangbanna Tropical Botanic Garden of the Chinese Academy of Sciences. A voucher specimen (20080911) was deposited in the Institute of Traditional Chinese Medicine and Natural Products, Jinan University, Guangzhou, China.

Extraction and Isolation. The chopped, dried stems of *C. formosum* (5.0 kg) were refluxed with 40 L of 60% (v/v) EtOH−H_2O twice, for two hours each time. After filtration, the filtrate was concentrated under reduced pressure to yield a brownish extract (675.0 g). The extract (600.0 g) was then separated over a Diaion HP-20 column, using EtOH−H_2O as mobile phase, to give three fractions (A−C). Fraction C (90% EtOH−H_2O eluent, 117.0 g) was chromatographed over silica gel eluted with cyclohexane−EtOAc in a gradient to yield eight fractions (C1−C8). Fraction C4 (9:1 cyclohexane−EtOAc as eluent, 4.0 g) was further separated over Sephadex LH-20 eluted with cyclohexane−$CHCl_3$ (1:1), $CHCl_3$, and $CHCl_3$−CH_3OH (1:1), succes-

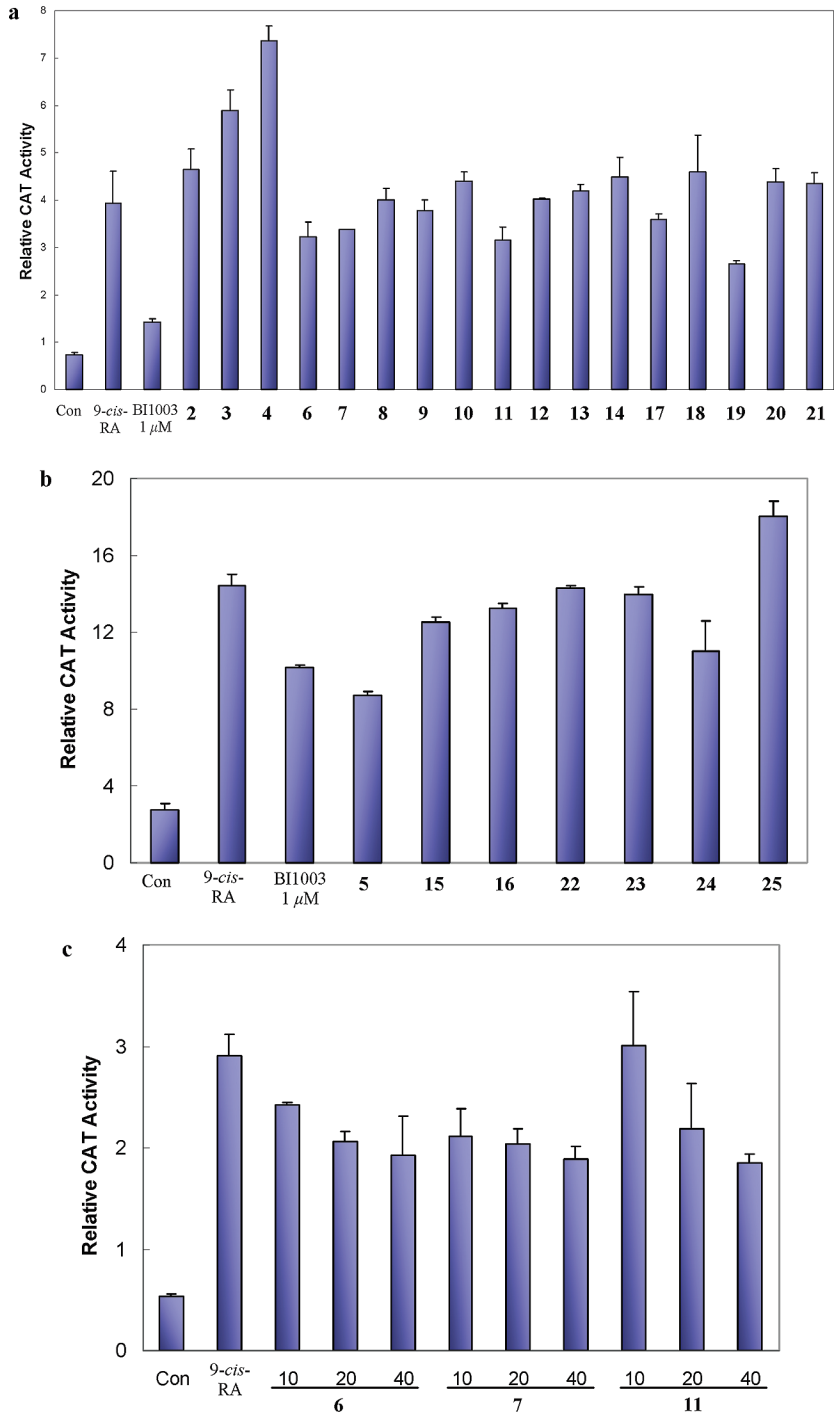

Figure 3. Effects of compounds **2**−**25** (10 μM) on the transcriptional activities of RXRα (a and b), effects of compounds **6**, **7**, and **11** (10, 20, and 40 μM) on the transcriptional activities of RXRα (c).

sively, to give eight subfractions (C4A−C4H). Subfraction C4B ($CHCl_3$ eluent) was submitted to silica gel CC, eluted with cyclohexane−acetone (9:1), to give **8** (12.8 mg) and **11** (13.3 mg). Subfraction C4C ($CHCl_3$ eluent) was purified over Sephadex LH-20 eluted with $CHCl_3$−CH_3OH (4:1), yielding **2** (14.2 mg) and **24** (15.5 mg). Subfraction C4D ($CHCl_3$ eluent) was subjected to silica gel CC, eluted with $CHCl_3$−CH_3OH (50:1), to afford **23** (42.5 mg). After purification with repeated silica gel CC, eluted with $CHCl_3$ and $CHCl_3$−CH_3OH (100:1), subfractions C4E and C4F ($CHCl_3$ eluents) yielded **4** (15.8 mg), **5** (27.5 mg), **7** (15.0 mg), **1** (13.6 mg), **6** (10.3 mg), **9** (20.9 mg), **10** (11.7 mg), and **14** (15.3 mg). Subfraction C4G [$CHCl_3$−CH_3OH (1:1) as eluent] was subjected to Sephadex LH-20 CC, eluted with $CHCl_3$−CH_3OH (3:2), to give **12** (9.5 mg) and **3** (11.6 mg). Compound **13** (11.6 mg) was recrystallized in $CHCl_3$−CH_3OH (4:1) from subfraction C4H [$CHCl_3$−CH_3OH (1:1) as eluent].

Fraction C6 (8:2 cyclohexane−EtOAc as eluent; 8.0 g) was further separated by passage over Sephadex LH-20, eluted with $CHCl_3$−CH_3OH (4:1), to give four subfractions (C6A−C6D). Subfraction C6D was applied to silica gel CC eluted with cyclohexane−EtOAc in gradient to afford eight subfractions (C6D1−C6D8). Subfraction C6D2 (9:1 cyclohexane−EtOAc) was subjected to silica gel CC, using $CHCl_3$−CH_3OH (50:1 and 20:1) as mobile phase, to give **22** (9.3 mg) and **20** (45.0 mg). Compound **16** (14.7 mg) was recrystallized in $CHCl_3$−CH_3OH (4:1) from subfraction C6D3 (9:1 cyclohexane−EtOAc). Subfraction C6D4 (8:2 cyclohexane−EtOAc) was subjected to Sephadex LH-20 CC, eluted with $CHCl_3$−CH_3OH (4:1), to give **17** (180.0 mg) and **21** (16.5 mg). Subfraction C6D6 (8:2 cyclohexane−EtOAc) was purified by silica gel CC, eluted with $CHCl_3$ and $CHCl_3$−CH_3OH (100:1), to give **18** (26.4 mg) and **19** (25.0 mg). Subfraction C6D7 (8:2 cyclohexane−EtOAc) was subjected to Sephadex LH-20 CC, eluted

with $CHCl_3-CH_3OH$ (3:2), to yield **15** (9.4 mg). Subfraction C6D8 (EtOAc eluent) was purified by ODS CC, eluted with CH_3OH-H_2O (8:2), to afford **25** (37.2 mg).

Pruniflorone M (1): yellow, amorphous powder; UV (MeOH) λ_{max} (log ε) 205 (4.31), 228 (4.25), 255 (4.23), 281 (4.09), 379 (3.82) nm; IR (KBr) ν_{max} 3202, 1650, 1605, 1480, 1293, 797 cm^{-1}; ^1H and ^{13}C NMR data (see Table 1); HRESIQTOFMS *m/z* 287.0551 $[M - H]^-$ (calcd for $C_{15}H_{11}O_6$, 287.0561).

Pruniflorone N (2): brownish, amorphous powder; UV (MeOH) λ_{max} (log ε) 205 (4.40), 226 (4.22), 299 (4.25), 312 (4.29) nm; IR (KBr) ν_{max} 3424, 1629, 1502, 1237, 1064, 818 cm^{-1}; ^1H and ^{13}C NMR data (see Table 1); HRESIQTOFMS *m/z* 243.0302 $[M - H]^-$ (calcd for $C_{13}H_7O_5$, 243.0299).

Pruniflorone O (3): yellow, amorphous powder; UV (MeOH) λ_{max} (log ε) 205 (4.78), 238 (4.50), 269 (4.41), 281 (4.09), 309 (4.23), 372 (4.23) nm; IR (KBr) ν_{max} 3435, 1619, 1473, 1293, 1081, 782 cm^{-1}; ^1H and ^{13}C NMR data (see Table 1); HRESIQTOFMS *m/z* 303.0509 $[M - H]^-$ (calcd for $C_{15}H_{11}O_7$, 303.0510).

Pruniflorone P (4): reddish-brown gum; UV (MeOH) λ_{max} (log ε) 205 (4.55), 241 (4.54), 265 (4.48), 316 (4.24), 379 (3.77) nm; IR (KBr) ν_{max} 3414, 2923, 1645, 1458, 1167, 820 cm^{-1}; ^1H and ^{13}C NMR data (see Table 2); HRESIQTOFMS *m/z* 447.2184 $[M - H]^-$ (calcd for $C_{28}H_{31}O_5$, 447.2177).

Pruniflorone Q (5): pale yellow, amorphous powder; UV (MeOH) λ_{max} (log ε) 206 (4.73), 235 (4.57), 263 (4.59), 321 (4.34), 374 (4.15) nm; IR (KBr) ν_{max} 3349, 2914, 1618, 1481, 1292, 808 cm^{-1}; ^1H and ^{13}C NMR data (see Table 2); HRESIQTOFMS *m/z* 463.2132 $[M - H]^-$ (calcd for $C_{28}H_{31}O_6$, 463.2126).

Pruniflorone R (6): yellow, amorphous powder; UV (MeOH) λ_{max} (log ε) 206 (4.56), 243 (4.51), 261 (4.51), 318 (4.30), 340 (4.02), 361 (4.02) nm; IR (KBr) ν_{max} 3374, 2969, 2926, 1648, 1579, 1285, 1113, 825 cm^{-1}; ^1H and ^{13}C NMR data (see Table 2); HRESIQTOFMS *m/z* 427.1748 $[M - H]^-$ (calcd for $C_{24}H_{27}O_7$, 427.1762).

Cell Culture and Reporter Gene Assay. CV-1 green monkey kidney cells were grown in DME medium supplemented with 10% fetal bovine serum (FBS). The expression vectors for RXRα and reporter TREpal-tk-CAT have been described previously.[28] For reporter assays, CV-1 cells were seeded at 5×10^4 cells/well in 24-well plates. Cells were transfected with 50 ng of TREpal-tk-CAT plasmid, 20 ng of β-galactosidase expression vector (pCH 110; Amersham), and 20 ng of RXRα expression vectors for receptors using Lipofectamine 2000 (Invitrogen). Cells were treated with compound for 20 h. CAT activity was normalized with β-galactosidase activity for transfection efficiency.

Acknowledgment. We thank J.-y. Cui (Xishuangbanna Tropical Botanic Garden of the Chinese Academy of Sciences) for collecting the plant material. We are grateful to H.-n. Zhao and Z.-q. Mu for measuring the HRESIMS and NMR data. This work was supported by grants from the National Natural Science Foundation of China (NSFC-30873146).

Supporting Information Available: NMR spectra of compounds **1**−**6**. Structures of compounds **7**−**25**. This information is available free of charge via the Internet at http://pubs.acs.org.

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NP1001797