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ARTICLE *in* JOURNAL OF NATURAL PRODUCTS · JULY 2009

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Chemical Constituents from the Aerial Parts of *Artemisia minor*

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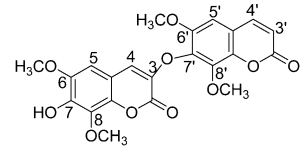
Received October 14, 2008

Four new compounds including three bicoumarins, arteminorins A−C (**1**−**3**), and one neolignan, arteminorin D (**4**), together with 31 known ones were isolated from the aerial parts of *Artemisia minor*. Their structures were established on the basis of spectroscopic data and comparison with those of the related known compounds. Ethyl caffeate (**27**) showed in vitro cytotoxicity against the HepG2 cancer cell line. Arteminorin C (**3**) and luteolin (**19**) showed inhibitory activity on xanthine oxidase (XOD), and caffeic acid (**28**) exhibited inhibitory activity on protein tyrosine phosphatase 1B (PTP1B).

The genus *Artemisia* (Compositae family) comprises approximately 300 species widely distributed in Europe, North America, Asia, and South Africa, with about 200 species occurring in China.[1] Many *Artemisia* species are popular Chinese traditional medicinal plants, and they are frequently used for the treatment of dysmenorrhea, amenorrhea, hepatitis, inflammation, bruising, jaundice, hemostasia, malaria, and cancer.[2] Studies on the chemical components of *Artemisia* species have led to the identification of numerous compounds, such as acetylenic monoterpenes, sesquiterpenes, sesquiterpene-monoterpene lactones, triterpenes, coumarin monoterpene ethers, coumarins, and flavones.[3−11] However, there is no previous report on the chemical constituents of *Artemisia minor* Jacq. ex Bess.

A. minor plants grow uniquely on the Qinghai-Tibet Plateau of China. It has long been used as a substitute for the traditional Tibetan medicine *A. sieversiana* for the treatment of fever, rheumatism, dysentery, scabies, and bruising.[1] Our research led to the isolation and characterization of three new bicoumarins (**1**−**3**), one new neolignan (**4**), and 31 known compounds, which were identified as *β*-sitosterol (**5**), daucosterol (**6**), umbelliferone (**7**), isofraxidin (**8**), scopoletin (**9**), fraxidin (**10**), mandshurin (**11**), fraxin-8-*O*-*β*-D-glucopyranoside (**12**), euoniside (**13**), scopolin (**14**), 5,8-dihydroxy-7,4′-dimethoxyflavone (**15**), syringin (**16**), chryseoriol (**17**), tricin (**18**), luteolin (**19**), acacetin (**20**), apigenin (**21**), 5,7-dihydroxy-3,6,4′-trimethoxyflavone (**22**), tectorigenin (**23**), eicosyl/docosyl-*p*-coumarate (**24**), isoferulic acid (**25**), ferulaldehyde (**26**), ethyl caffeate (**27**), caffeic acid (**28**), (−)-syringaresinol (**29**), (+)-diasyringaresinol (**30**), *p*-hydroxybenzoic acid (**31**), *p*-methylbenzaldehyde (**32**), cleomiscosin C (**33**), cleomiscosin A or B (**34**), and biisofraxidin (**35**) (Supporting Information). We report herein the isolation and structural elucidation of the four new compounds and the results of the bioactivity screening of all the isolated compounds.

Compound **1** was obtained as a white, amorphous powder. It gave pseudomolecular ion peaks at *m*/*z* 443 $[M + H]^+$ and 465 $[M + Na]^+$ in ESIMS. Its molecular formula was tentatively assigned as $C_{22}H_{18}O_{10}$ by HRESIMS at *m*/*z* 465.0786 $[M + Na]^+$ (calcd 465.0792). The IR spectrum of **1** displayed absorptions for hydroxy (3442 cm^{-1}), α,*β*-unsaturated lactone (1723 cm^{-1}), and phenyl (1634, 1572, and 1465 cm^{-1}) functionalities. The ^1H NMR spectrum of **1** exhibited signals at *δ* 6.53 (d, $J = 9.6$ Hz) and 8.07 (d, $J = 9.6$ Hz), which are characteristic of a coumarin skeleton.[12] Apart from the carbon signals due to four methoxy groups (*δ* 62.1, 61.2, 57.0, and 56.4), there remain 16 aromatic carbons and two lactone carbons at *δ* 156.4 and 159.8 in the ^{13}C NMR spectrum, suggesting



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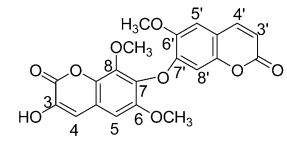

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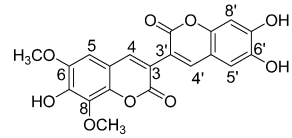

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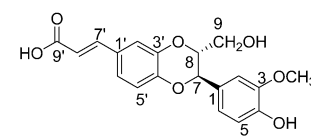

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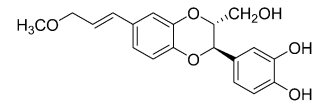

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that **1** possesses a bicoumarin skeleton.[12] The doublets at *δ* 8.07 and 6.53 in the ^1H NMR spectrum were assigned to H-4′ and H-3′, respectively. A cross-peak between H-4′ and H-5′ (*δ* 7.33) in the NOESY experiment (Figure 1) was observed. In addition, the HMBC spectrum (Table 1) showed a cross-peak between H-5′ and C-4′; the NOESY spectrum showed a cross-peak between H-5′ and the methoxy protons at *δ* 3.82, indicating that this methoxy group was attached to C-6′ (*δ* 149.1). The HMBC correlation between H-5′ and C-7′ (*δ* 138.6), as well as the correlation between the methoxy protons (*δ* 3.89) and C-8′ (*δ* 140.5), indicated that this methoxy group was attached to C-8′. The chemical shift of C-7′ suggested that this carbon was also oxygenated.[12] Therefore, C-7′ was determined as the attaching site for the other coumarin moiety. In addition, the ^{13}C NMR data of this moiety were similar to those of isofraxidin.[13] Thus, a 6,7,8-trisubstituted coumarin moiety was identified in **1**.

The structure of the other coumarin moiety was deduced as 3,6,7,8-tetrasubstituted as follows: H-4 (*δ* 7.08) and H-5 (*δ* 6.92) showed a correlation in the NOESY experiment. Accordingly, cross-peaks between H-4 and C-5 (*δ* 104.1) and between H-5 and C-4 (*δ* 119.7) were evident in the HMBC experiment. The correlation between H-5 and the methoxy protons (*δ* 3.74) in the NOESY spectrum indicated that this methoxy group was attached to C-6 (*δ* 146.6), which was further supported by the long-range correlation between this methoxy protons and C-6 in the HMBC spectrum. The long-range correlation between H-5 and C-7 (*δ* 139.5) and the correlation between the hydroxy proton (*δ* 9.60) and C-8 (*δ* 135.2) in the HMBC experiment indicated that the hydroxy group was located at C-7. The HMBC correlation between the remaining

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10.1021/np800643n CCC: $40.75
Published on Web 05/28/2009

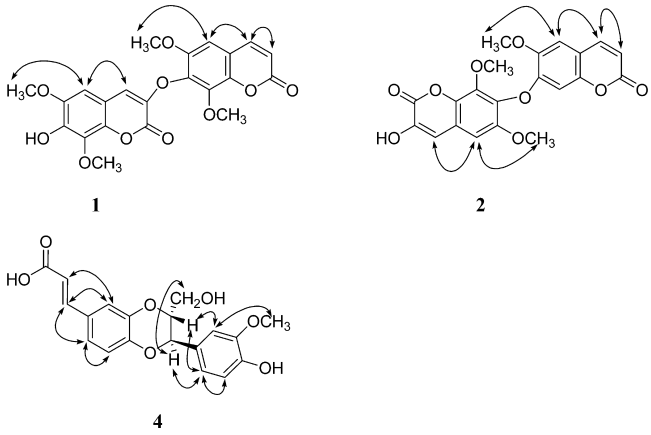

Figure 1. Key NOESY correlations of compounds **1**, **2**, and **4**.

methoxy group (δ 3.86) and C-8 suggested that this methoxy was linked to C-8. The lack of long-range correlations between the methoxy groups in the NOESY spectrum also supports these assignments.

The connection of the two coumarin moieties was done by a comparison of the NMR data of **1** with those of rutamontin,[14] giving rise to the connectivity of C-3 to C-7′ through an ether bond. The ESIMS/MS (Figure 2) of **1** showed a predominant daughter ion peak at *m/z* 221 deriving from fission of the C-3−O bond, together with the ion peaks at *m/z* 207 and 237 formed from fission of the C-7′−O bond, and the ion peaks at *m/z* 428 and 412 formed from loss of CH_3 and OCH_3 groups, respectively. Therefore, the structure of **1** was established as 7-hydroxy-6,8-dimethoxy-3-(6′,8′-dimethoxy-7′-coumarinyloxy)coumarin and named arteminorin A.

Compound **2** was obtained as colorless needles. It gave pseudomolecular ion peaks at *m/z* 413 $[M + H]^+$ in the positive mode ESIMS and *m/z* 411 $[M - H]^-$ in the negative mode ESIMS. The molecular formula $C_{21}H_{16}O_9$ was tentatively determined by HRESIMS (*m/z* 413.0866 $[M + H]^+$, calcd 413.0867). The IR and ^1H and ^{13}C NMR data of compound **2** were similar to those of **1**. One coumarin moiety was determined as 6′-methoxy-7′-substituted based on analysis of the NMR data and comparison of its ^{13}C NMR data with those of scopoletin.[13] The other coumarin unit was assigned to be 3-hydroxy-6,8-dimethoxy-7-substituted as that in **1** by analysis

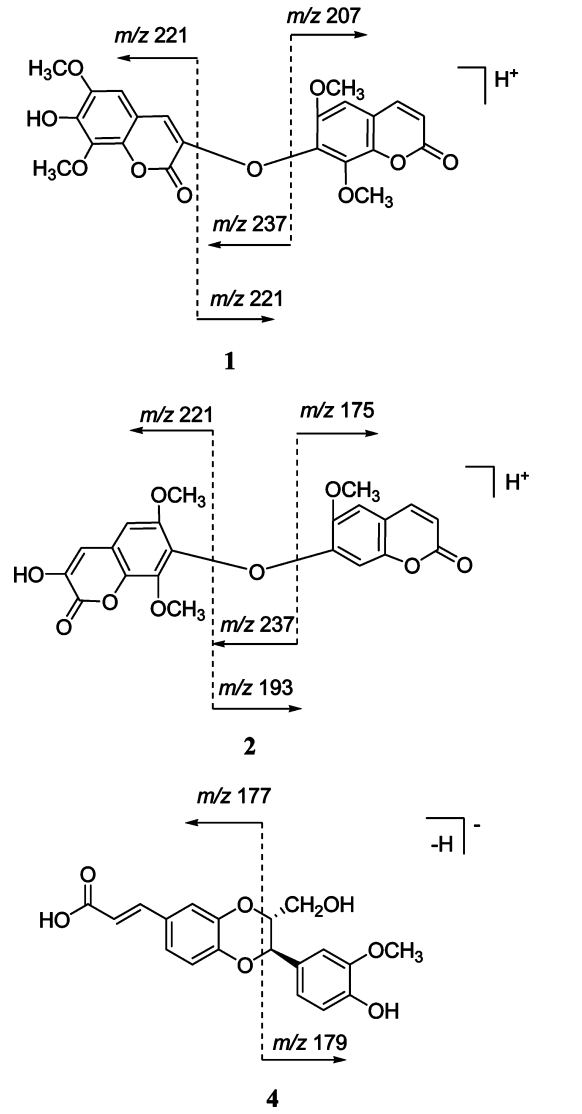

Figure 2. Proposed fragmentation pathways and characteristic ions of compounds **1**, **2**, and **4**.

Table 1. NMR Data of Compounds **1**, **2**, and **3** (DMSO-d_6, δ in ppm, *J* in Hz)

	1			**2**			**3**		
position	δ_H	δ_C	HMBC	δ_H	δ_C	HMBC	δ_H	δ_C	HMBC
2		156.4			156.7			159.7	
3		140.1			137.7			118.4	
4	7.08, s	119.7	2, 3, 5, 9	7.60, s	128.0	2, 3, 5	8.24, s	143.7	2, 3′, 5,9
5	6.92, s	104.1	4, 7, 9	6.99, s	104.5	4, 6, 7, 9	7.10, s	105.1	
6		146.6			146.5			146.4	4, 6, 7, 9
7		139.5			143.2			144.8	
8		135.2			135.2			135.0	
9		142.4			140.9			142.9	
10		110.3			115.1			110.7	
2′		159.8			160.6			160.2	
3′	6.53, d (9.6)	116.4	2′, 10′	6.42, d, (9.6)	110.5	2′, 10′		117.6	
4′	8.07, d (9.6)	144.8	2′, 5′, 9	8.03, d, (9.6)	144.4	2′, 5′, 9′	8.21, s	143.5	2′, 3, 5′, 9′
5′	7.33, s	106.1	4′, 6′, 7′, 9′	7.49, s	111.3	4′, 6′, 7′, 9′	7.04, s	112.9	4′, 6′, 7′, 9′
6′		149.1			146.9			143.7	
7′		138.6			148.4			151.5	
8′		140.5		7.27, s	106.7	10′	6.80, s	102.8	6′, 7′, 9′, 10′
9′		142.3			148.9			148.6	
10′		117.1			115.1			111.3	
6-OCH_3	3.74, s	56.4	6	3.80, s	56.6	6	3.85, s	56.7	6
8-OCH_3	3.86, s	61.2	8	3.87, s	61.2	8	3.87, s	61.3	8
6′-OCH_3	3.82, s	57.0	6′	3.87, s	56.8	6′			
8′-OCH_3	3.89, s	62.1	8′						
3−OH						2, 3			

of its HMBC (Table 1) and NOESY (Figure 1) spectra. Compared with compound **1**, the resonance of C-3 shifted upfield by 2.4 ppm, and C-7 shifted downfield by 3.7 ppm in **2**, indicating that the two coumarin moieties of **2** were connected at C-7 and C-7′ via an oxygen bridge, which was further supported by ESIMS/MS experiment (Figure 2) of **2**. The daughter ion peaks at *m/z* 221 and 193 were derived from fission of the C-7−O bond, *m/z* 175 and 237 were derived from fission of the C-7′−O bond, and *m/z* 398 and 382 were derived from loss of CH_3 and OCH_3 groups, respectively. Therefore, compound **2** was elucidated as 3-hydroxy-6,8-dimethoxy-7-(6′-methoxy-7′-coumarinyloxy)coumarin and named arteminorin B.

Compound **3** was isolated as a yellow, amorphous powder. The ESIMS experiment showed pseudomolecular ion peaks at *m/z* 421 $[M + Na]^+$ and *m/z* 819 $[2M + Na]^+$. The molecular formula was tentatively determined as $C_{20}H_{14}O_9$ by HRESIMS (*m/z* 421.0512 $[M + Na]^+$, calcd 421.0530). The IR and NMR data of **3** (Table 1) resembled those of **1**, and further spectroscopic analysis revealed that **3** was a bicoumarin in which the two courmarin fragments were connected through a C−C bond. One coumarin moiety was determined as 7-hydroxy-6,8-dimethoxy-3-substituted by a comparison of ^{13}C NMR data of **3** with those of 3,3′-biisofraxidin,[15] a known compound isolated from the same plant. This moiety was further backed by the correlations in the HMBC spectrum of **3** (Table 1). Another moiety was confirmed as 6′,7′-dihydroxy-3′-substituted by HMBC correlations as below. The HMBC spectrum of **3** showed correlations of H-4′ (δ 8.21, s) with C-2′ (δ 160.2), C-5′ (δ 112.9), and C-9′ (δ 148.6), indicating that this isolated proton was attached to C-4′ (δ 143.5). The absent adjacent proton to H-4′ (s) suggested C-3′ (δ 117.6) was substituted. Cross-peaks between H-5′ (δ 7.04, s) and C-4′ (δ 143.5) and C-7′ (δ 151.5) as well as between H-8′ (δ 6.80, s) and C-10′ (δ 111.3) and C-6′ (δ 143.7) indicated that C-6′ and C-7′ were oxygenated. In addition, the HMBC spectrum showed the key correlations of H-4 (δ 8.24, s) with C-3′ (δ 117.6) and H-4′ with C-3 (δ 118.4), indicating that these two coumarin units were linked at C-3 and C-3′ via a carbon−carbon bond. Thus, compound **3** was determined as 7,6′,7′-trihydroxy-6,8-dimethoxy-3,3′-bicoumarin and named arteminorin C.

Compound **4** was obtained as a white, amorphous powder, with $[\alpha]^{25}_D$ −4.46. Pseudomolecular ion peaks at *m/z* 381 $[M + Na]^+$ (positive ion mode) and 357 $[M - H]^-$ (negative ion mode) were found in the ESIMS. The molecular formula of **4** was tentatively determined as $C_{19}H_{18}O_7$ by HRESIMS (*m/z* 381.0945 $[M + Na]^+$, calcd 381.0945). The structure of **4** was similar to that of 9′-methylamericanol A (**36**)[16] by comparison of their NMR data (Table 2). The ^1H and ^{13}C NMR spectra of **4** (Table 2) indicated that there is a carboxy group (δ 12.19 and 168.2) in **4** instead of a methoxymethylene group as in **36**. The resonance of C-8′ (δ 115.8) shifted upfield by 8.9 ppm compared to that in **36**, indicating that the carboxy group was linked to C-8′, which was supported by the correlation between H-7′ (δ 7.50) and C-9′ (δ 168.2) in the HMBC spectrum (Table 2). A correlation between methoxy protons (δ 3.77) and C-3 (δ 148.1) in the HMBC spectrum indicated that the methoxy group was linked to C-3. In addition, the ESIMS/MS (Figure 2) of **4** showed predominant daughter ion peaks at *m/z* 177 and 179 deriving from fission of both C-7−O and C-8−O bonds, together with an ion peak at *m/z* 313 formed from loss of a CO_2 group and ion peaks at *m/z* 342 and 326 formed from loss of CH_3 and OCH_3 groups, respectively. Therefore, compound **4** was determined as 3-methoxy-8′-carboxy-7′-en-3′,8-epoxy-7,4′-oxyneoligna-4,9-diol and named arteminorin D.

The relative configuration of **4** was elucidated from coupling constants and correlations observed in the NOESY spectrum as shown in Figure 1. A large coupling constant between H-7 and H-8 (J = 7.8 Hz) indicated that the two protons were in a *trans*-configuration,[17] which was consistent with the correlation between H-7 and H-9_b in the NOESY spectrum.

Table 2. NMR Data of Compound **4** (DMSO-d_6, δ in ppm, J in Hz)

position	δ_H	δ_C	HMBC
1		127.7	
2	7.01, d (1.6)	112.3	4, 6, 7
3		148.1	
4		147.6	
5	6.80, d (8.0)	115.8	1, 3
6	6.85, dd (8.0, 1.6)	121.0	2, 4, 7
7	4.95, d (7.8)	76.6	1, 2, 6, 8
8	4.19, m	78.4	
9	3.33, br d (10.9), 3.54, br d (12.2)	60.6	7, 8
1′		128.2	
2′	7.28, d (1.8)	116.9	4′, 6′, 7′
3′		144.2	
4′		146.1	
5′	6.94, d (8.3)	117.7	1′, 3′
6′	7.20, dd (8.3, 1.8)	122.1	2′, 4′, 7′
7′	7.50, d (15.8)	143.9	2′, 6′, 9′
8′	6.36, d (15.9)	115.8	1′
9′		168.2	
OCH_3	3.77, s	56.2	3

Table 3. Bioactivities of Compounds **3**, **19**, **27**, and **28**

	compounds				positive controls[a]		
bioactivities	**3**	**19**	**27**	**28**	A	B	C
anticancer activity (HepG2) GI_{50} (μM)	no	no	17.21	no	0.059		
XOD inhibition activity IC_{50} (μM)	7.71	11.54	no	no		0.18	
PTP1B inhibition activity IC_{50} (μM)	no	no	no	3.06			27.56

[a] A−C represent taxol, allopourinol, and soduim orthorandate, respectively, which were applied as the positive controls.

In vitro cytotoxicity of all 35 compounds isolated from *A. minor* was examined with HepG2 cells, a cancer cell line. The inhibitory effects on the activity of XOD and PTP1B enzymes of these compounds were also tested.[18−22] As summarized in Table 3, compound **27** was cytotoxic to HepG2 cells. Compounds **3** and **19** showed inhibition to the activity of XOD, while compound **28** had an inhibitory effect on the activity of PTP1B.

Experimental Section

General Experimental Procedures. Melting points were measured on XRC-1 apparatus and are uncorrected. Optical rotations were measured on a PE-341 polarimeter. IR spectra were recorded on a Perkin-Elmer 1725X FT spectrometer with KBr pellets. NMR spectra were recorded on a Bruker AV-600 MHz spectrometer using TMS as internal standard. HRESIMS were measured on a Bruker BioTOF Q spectrometer. ESIMS and ESIMS/MS were measured on a Finnigan LCQ^{DECA} spectrometer. Silica gel (200−300 mesh, Qingdao Marine Chemical Group Co.), MCI (Mitsubishi Chemical Co.), ODS (Cosmosil 75 C_{18}-OPN), and Sephadex LH-20 (Pharmacia) were employed for column chromatography. TLC was carried out using silica gel 60 (>230 mesh, Qingdao Marine Chemical Group Co.) and GF_{254} plates precoated with silica gel 60. Spots on TLC were visually observed under UV light and/or by spraying with anisaldehyde-H_2SO_4 reagent followed by heating.

Plant Material. The plant was collected at Lhasa, in Tibet, China, and identified by Professor Suolang Gesang. A voucher specimen (2007-0418) was deposited in the Herbarium of Chengdu Institute of Biology, Chinese Academy of Sciences.

Extraction and Isolation. A powdered sample from dry aerial parts of *A. minor* (10 kg) was extracted with 90% EtOH at room temperature. The concentrated extract (1.4 kg) was suspended in H_2O and then partitioned with petroleum ether, $CHCl_3$, and *n*-BuOH. The petroleum ether extract (200 g) was chromatographed on an MCI gel column eluted with MeOH−H_2O (9:1) and then was subjected to silica gel column

chromatography (CC) eluted with petroleum ether−acetone (8:1) to obtain compound **22** (20 mg). The $CHCl_3$ extract (250 g) was subjected to silica gel CC eluted with a petroleum ether−acetone gradient (from 10:1 to 0:1) to give seven fractions, A−G. Fraction A was subjected to silica gel CC eluted with petroleum ether−acetone (from 10:1 to 0:1) to obtain compounds **5** (10 mg) and **24** (100 mg). Fraction B was filtered to yield compound **7** (13 g), and the mother liquid was subjected to silica gel CC eluted with a petroleum ether−acetone gradient system (from 1:0 to 0:1) to yield compounds **32** (200 mg) and **15** (80 mg). Fraction C was filtered, the filter cake was applied to a Sephadex LH-20 column (eluted with $CHCl_3$−MeOH, 1:1) to produce compounds **8** (770 mg) and **9** (140 mg), and the mother liquid was chromatographed over a Sephadex LH-20 column (eluted with $CHCl_3$−MeOH, 1:1) to obtain fractions C1−C4. Fraction C2 was applied to a Sephadex LH-20 column (eluted with $CHCl_3$−MeOH, 1:1) again, followed by silica gel CC eluted with a $CHCl_3$−acetone gradient system (from 1:0 to 0:1) to yield compounds **30** (7 mg), **6** (10 mg), **18** (50 mg), **21** (10 mg), **27** (310 mg), **20** (82 mg), **17** (80 mg), **10** (30 mg), **23** (20 mg), **31** (8 mg), **25** (10 mg), **19** (10 mg), and **28** (15 mg). Fraction D was filtered to obtain compound **35** (100 mg), and the mother liquid was subjected to silica gel CC eluted with a gradient of $CHCl_3$−acetone and was then applied to ODS reversed-phase silica gel eluted with MeOH−H_2O (with the MeOH amount from 60 wt % to 100 wt %) to obtain compounds **29** (230 mg), **1** (50 mg), **2** (10 mg), **33** (8 mg), **34** (10 mg), **4** (10 mg), and **3** (400 mg). Fractions E and F were filtered to isolate compounds **11** (10 mg) and **12** (25 mg), respectively. The *n*-BuOH (560 g) extract was subjected to silica gel CC eluted with a gradient of $CHCl_3$−MeOH to yield compounds **26** (15 mg), **16** (25 mg), **13** (20 mg), and **14** (10 mg).

Bioassays. In vitro cytotoxicity of these isolated compounds was tested with HepG2 cells, a cancer cell line, while the inhibitory effects on the enzyme activity were determined with XOD and PTP1B. The general experimental procedures of these bioassays have been described in previous detailed studies.[18−22]

Arteminorin A (1): white, amorphous powder; IR (KBr) ν_{max} 3442, 1723, 1634, 1572, 1465 cm^{-1}; ^1H and ^{13}C NMR data (Table 1); ESIMS *m/z* 443 $[M + H]^+$, 465 $[M + Na]^+$; HRESIMS *m/z* 465.0786 $[M + Na]^+$ (calcd for $C_{22}H_{18}O_{10}Na^+$, 465.0792); ESIMS/MS *m/z* 428 $[M + H - CH_3]^+$, 425 $[M + H - H_2O]^+$, 412 $[M + H - OCH_3]^+$, 237 $[M + H - C_{11}H_{10}O_4]^+$, 221 $[M + H - C_{11}H_{10}O_5]^+$, 207 $[M + H - C_{11}H_8O_6]^+$.

Arteminorin B (2): colorless needles (MeOH); mp 150−151 °C; IR (KBr) ν_{max} 3434, 1721, 1631, 1501, 1461 cm^{-1}; ^1H and ^{13}C NMR data (Table 1); ESIMS *m/z* 413 $[M + H]^+$, 411 $[M - H]^-$; HRESIMS *m/z* 413.0866 $[M + H]^+$ (calcd for $C_{21}H_{16}O_9Na^+$, 413.0867); ESIMS/MS *m/z* 398 $[M + H - CH_3]^+$, 395 $[M + H - H_2O]^+$, 382 $[M + H - OCH_3]^+$, 237 $[M + H - C_{10}H_8O_3]^+$, 221 $[M + H - C_{10}H_8O_4]^+$, 193 $[M + H - C_{11}H_8O_5]^+$, 175 $[M + H - C_{11}H_{10}O_6]^+$.

Arteminorin C (3): yellow, amorphous powder; IR (KBr) ν_{max} 3434, 1721, 1630, 1570, 1464 cm^{-1}; ^1H and ^{13}C NMR data (Table 1); ESIMS *m/z* 421 $[M + Na]^+$, 819 $[2M + Na]^+$; HRESIMS *m/z* 421.0512 $[M + Na]^+$ (calcd for $C_{20}H_{14}O_9Na^+$, 421.0530).

Arteminorin D (4): white, amorphous powder; $[\alpha]^{25}_D$ −4.46 (*c* 1.12, MeOH); IR (KBr) ν_{max} 3438, 2978, 1612, 1505, 1265, 1125, 1048 cm^{-1}; ^1H and ^{13}C NMR data (Table 2); ESIMS *m/z* 381 $[M + Na]^+$ and 357 $[M - H]^-$; HRESIMS (*m/z* 381.0945 $[M + Na]^+$ (calcd for $C_{19}H_{18}O_7Na$, 381.0945); ESIMS/MS *m/z* 342 $[M - H - CH_3]^-$, 339 $[M - H - H_2O]^-$, 326 $[M - H - OCH_3]^-$, 313 $[M - H - CO_2]^-$, 179 $[M - H - C_9H_6O_4]^-$, 177 $[M - H - C_{10}H_{12}O_3]^-$.

Acknowledgment. This work was supported by a grant from the National Natural Sciences Foundation of China (No. 30572254).

Supporting Information Available: The ^1H and ^{13}C NMR, HMBC, and NOESY spectra for compounds **1**−**4**, and the structures of the known compounds (**5**−**35**) are available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Wu, Z. Y. *Flora Xizangica*; Science Press: Beijing, 1985; Vol. 4, pp 742−751.
(2) Zhang, H. Y.; Zhang, Z. Y. *Handbook of Chinese Traditional Medicine Resources*; Science Press: Beijing, 1994; pp 1248−1258.
(3) Yoshimasa, N.; Yoshimi, O.; Akira, M.; Suratwadee, J.; Hajime, O. *J. Agric. Food Chem.* **1998**, *46*, 5031–5036.
(4) Kim, K. S.; Lee, S.; Shin, J. S.; Shim, S. H.; Kim, B. K. *Fitoterapia* **2002**, *73*, 266–268.
(5) Lee, S. H.; Kim, M. J.; Bok, S. H.; Lee, H.; Kwon, B. M. *J. Org. Chem.* **1998**, *63*, 7111–7113.
(6) Kwak, J. H.; Lee, K. B.; Schmitz, F. J. *J. Nat. Prod.* **2001**, *64*, 1081–1083.
(7) Lee, S. H.; Kim, H. K.; Kang, H. M.; Seo, J. M.; Son, K. H.; Lee, H. S.; Kwon, B. H. *J. Org. Chem.* **2002**, *67*, 7670–7675.
(8) Wu, T. S.; Tsang, Z. J.; Wu, P. L.; Lin, F. W.; Li, C. Y.; Teng, C. M.; Lee, K. H. *Bioorg. Med. Chem.* **2001**, *9*, 77–83.
(9) Kwak, J. H.; Lee, K. B.; Schmitz, F. J. *J. Nat. Prod.* **2001**, *64*, 1081–1083.
(10) Kim, J. H.; Kim, H. K.; Jeon, S. B.; Son, K. H.; Kim, E. H.; Kang, S. K.; Sung, N. D.; Kwon, B. M. *Tetrahedron Lett.* **2002**, *43*, 6205–6208.
(11) Ahmed, A. A.; Safaa, A. E. M.; Mohamed, A. E. S.; Hoda, F. A. G.; Joe, K.; George, S.; Kent, D.; Paul, W. P. W. *J. Nat. Prod.* **2004**, *67*, 1705–1710.
(12) Xiao, C. H.; Yang, S. S., Hong, X. K. *Chemistry of Traditional Chinese Medicine*; Shanghai Scientific & Technical Publishers: Shanghai, 2000; p 235.
(13) Barbera, O.; Marco, J. A.; Juan, F. S.; Parareda, J. S. *Phytochemistry* **1986**, *25*, 2357–2360.
(14) Kabbouche, Z.; Benkiki, N.; Seguin, E.; Breneau, C. *Fitoterapia* **2003**, *74*, 194–196.
(15) Wang, F.; Yuan, S. T.; Zhu, D. N. *Chin. J. Nat. Med.* **2007**, *5*, 174–178.
(16) Zhao, P. J.; Shen, Y. M. *Chin. Chem. Lett.* **2004**, *15*, 921–924.
(17) Kunar, S.; Ray, A. B.; Konno, C.; Oshima, Y.; Hikino, H. *Phytochemistry* **1998**, *27*, 636–638.
(18) Skehan, P.; Storing, R.; Scudiero, D.; Monk, A.; Mcmahon, J.; Visica, D. *J. Natl. Cancer Inst.* **1990**, *82*, 1107–1112.
(19) Rubinstein, L. V.; Shoemaker, R. H.; Paul, K. D.; Tosini, S.; Skehan, P.; Scudiero, D. A. *J. Natl. Cancer Inst.* **1990**, *82*, 1113–1118.
(20) Takayuki, S.; Ayano, H.; Takumi, W.; Takashi, Y.; Izumi, T.; Kazuo, U. *J. Biol. Chem.* **2001**, *276*, 27511–27518.
(21) Sukirti, K.; Gopabandhu, J.; Kulbhushan, T.; Anup, K. M. *BMC Biochem.* **2007**, *8*, 8.
(22) Tamta, H.; Kalra, S.; Anand, G. C. S.; Mukhopadhyay, A. K. *J. Biol. Phys. Chem.* **2005**, *5*, 89–99.

NP800643N