Iridoids and Lignans from *Valeriana jatamansi*

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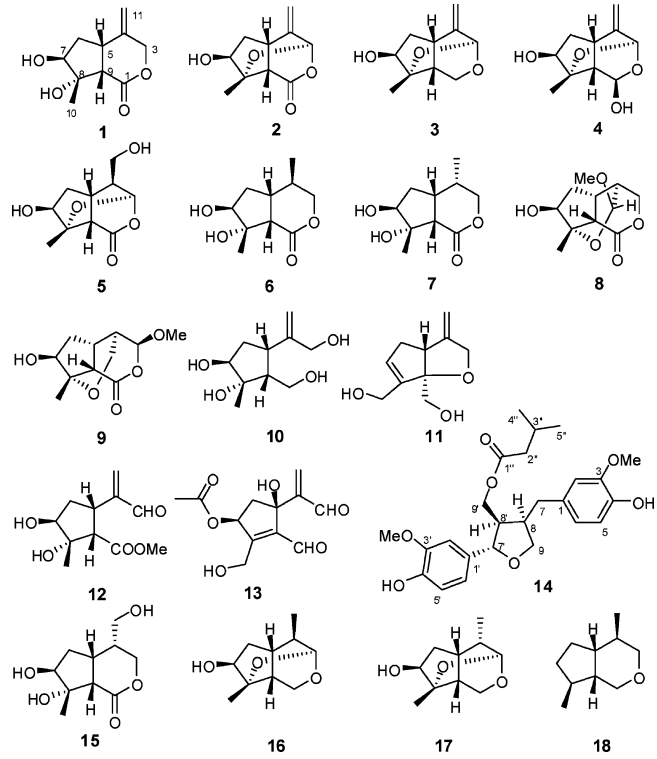
Received December 8, 2009

Thirteen new iridoids including seven iridolactones, jatamanins A−M (**1**−**13**), and a new lignan, (+)-9′-isovaleroxylariciresinol (**14**), together with seven known iridoids and 13 lignans were obtained from whole plants of *Valeriana jatamansi*. Structures of the new compounds were determined by spectroscopic and crystallographic methods, and the absolute configuration of compound **1** was assigned by application of the modified Mosher method. Jatamanins H (**8**) and I (**9**) are iridolactones with an unusual C-8−C-11 oxygen bridge, forming a cage-like structure. (+)-9′-Isovaleroxylariciresinol (**14**) showed significant in vitro cytotoxicity against PC-3M and HCT-8 cell lines, with IC_{50} values of 8.1 and 5.3 μM, respectively.

Chemical investigations of *Valeriana* species have mainly focused on low-polarity components, leading to the isolation of two major groups of constituents: essential oil sesquiterpenes and valepotriates.[1−9] The latter, ester iridoids typical of the family Valerianaceae, are responsible for sedative, cytotoxic, antitumor, and antifugal activities.[10] In previous work we isolated 13 new and nine known valepotriates from the EtOAc-soluble fraction of an ethanolic extract of *Valeriana jatamansi* (Valerianaceae) whole plants. Many of these compounds exhibited cytotoxicity against the metastatic prostate cancer (PC-3M) cell line, with IC_{50} values ranging from 1.4 to 6.3 μM.[11] As part of our ongoing efforts to systematically study the chemical and biological diversity of this plant, we herein report the isolation and structure assignments of 13 new iridoids, jatamanins A−M (**1**−**13**), a new lignan, (+)-9′-isovaleroxylariciresinol (**14**), seven known iridoids, and 13 known lignans from fractions of the EtOAc portion having intermediate polarity. Jatamanins H (**8**) and I (**9**) represent the first iridolactones with an unusual C-8−C-11 oxygen bridge, forming a cage-like structure. Cytotoxicity results are also reported in this paper.



Results and Discussion

Jatamanin A (**1**) was isolated as colorless crystals that analyzed for the molecular formula $C_{10}H_{14}O_4$ by HRESIMS. This formula suggested 4 units of unsaturation in the molecule and was consistent with the ^{1}H and ^{13}C NMR data. The IR spectrum showed broad absorption for multiple OH groups (3564 cm^{-1}) and a lactone carbonyl (1710 cm^{-1}) functionality. Analysis of the ^{1}H and ^{13}C NMR spectroscopic data (Tables 1 and 2) indicated signals for one terminal double bond [δ_H 5.08, 5.02 (each 1H, s, H_2-11); δ_C 145.4 (C-4) and 113.2 (C-11)], two methylenes [δ_H 5.04 (1H, d, J = 11.4 Hz, H-3a), 4.38 (1H, dd, J = 11.4, 1.2 Hz, H-3b), 2.18 ddd (1H, J = 13.2, 9.6, 2.4 Hz, H-6α), 2.01 (1H, dd, J = 13.2, 4.8 Hz, H-6β); δ_C 70.6 (C-3) and 41.4 (C-6)], three methines [δ_H 3.35 (dd, J = 10.8, 9.6 Hz, H-5), 3.85 (brs, H-7), 2.99 (d, J = 10.8 Hz, H-9); δ_C 41.3 (C-5), 81.5 (C-7), and 53.7 (C-9)], a methyl singlet [δ_H 1.51 (Me-8); δ_C 22.8 (C-10)], and one oxygenated quaternary carbon at δ_C 86.4 (C-5). These data and the presence of two aliphatic OH protons (δ_H 4.11 and 4.08) and a lactone carbonyl (δ_C 172.1) led to the preliminary conclusion that **1** was an iridolactone containing two rings and two OH groups.[12] Analysis of 2D COSY correlations showed the presence of a spin system involving the protons at C-9, C-5, C-6, C-7, and OH-7. Further analysis of 2D NMR HSQC and HMBC data allowed assignment of all proton and carbon signals. Key HMBC correlations from H_2-11 to C-3 and C-5, from Me-8 to C-8, C-7, and C-9, and from both H-5 and H_2-3 to C-1 established the planar structure of **1**. An X-ray diffraction experiment was then undertaken, which confirmed the structure and provided the relative configuration of **1**. An ORTEP drawing, with the atom-numbering scheme indicated, is shown in Figure 1. Finally, the absolute configuration of compound **1** was established by application of the modified Mosher method. *R*- and *S*-Mosher esters of the OH at C-7 were prepared. Subsequent NMR analysis of the $\Delta\delta$ values for the two MTPA esters assigned the

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10.1021/np900795c
Published on Web 02/12/2010

Table 1. ^{1}H NMR Data (δ) for Compounds **1**−**13** and **15**−**18**[a]

position	**1** (Me_2CO-d_6)	**2** (Me_2CO-d_6)	**3** (Me_2CO-d_6)	**4** (Me_2CO-d_6)	**5** (Me_2CO-d_6)	**6** (Me_2CO-d_6)	**7** (Me_2CO-d_6)	**8** (Me_2CO-d_6)
1			4.08 dd (9.6, 2.4) 3.90 d (9.6)	5.43 dd (4.8, 3.6)				
3	5.04 d (11.4) 4.38 dd (11.4, 1.2)	5.73 s	4.84 s	4.92 s	5.57 d (2.4)	4.20 dd (10.8, 11.4) 3.82 brd (10.8)	4.24 dd (10.8, 3.0) 3.87 dd (10.8, 8.4)	4.39 dd (11.4, 2.4) 4.36 dd (11.4, 1.8)
4					1.98 m	2.18 m	1.74 m	2.03 m
5	3.35 dd (10.8, 9.6)	3.19 dd (6.0, 4.8)	2.97 dd (6.6, 5.4)	3.13 dd (6.6, 4.8)	2.23 dd (7.2, 4.8)	2.81 m	2.31 m	2.79 ddd (7.2, 4.8, 3.0)
6α	2.18 ddd (13.2, 9.6, 2.4)	2.27 dd (13.8, 7.2)	2.03 dd (13.2, 6.6)	2.02 dd (13.2, 6.6)	2.32 dd (13.8. 7.2)	2.06 ddd (12.6, 7.8, 3.6)	1.94 ddd (10.8, 7.8, 2.4)	2.72 dd (14.4, 6.6)
6β	2.01 dd (13.2, 4.8)	1.99 ddd (13.8, 6.0, 4.8)	1.86 ddd (13.2, 7.2, 3.6)	1.83 ddd (13.2, 7.8, 4.8)	1.79 ddd (13.8, 6.0, 4.8)	1.63 dd (12.6, 7.2)	1.92 ddd (10.8, 8.4, 2.4)	1.61 ddd (14.4, 7.2, 3.0)
7	3.85 brs	3.97 dd (7.2, 4.8)	3.74 dd (7.2, 2.8)	3.79 m	4.01 m	3.82 brs	3.75 brs	4.11 m
9	2.99 d (10.8)	2.85 d (4.8)	2.05 d (5.4)	2.22 dd (4.8, 3.6)	2.68 d (4.8)	2.87 d (10.8)	2.86 d (10.8)	2.74 brd (6.6)
10	1.51 s	1.31 s	1.41 s	1.32 s	1.25 s	1.49 s	1.52 s	1.28 s
11	5.08 s 5.02 s	5.17 s 5.05 s	4.79 s 4.77 s	4.77 s 4.68 s	3.40 s	0.87 d (6.6)	0.95 d (6.6)	4.67 s
OMe								3.32 s

position	**9** (Me_2CO-d_6)	**10** (MeOD)	**11** (Me_2CO-d_6)	**12** (Me_2CO-d_6)	**13** (Me_2CO-d_6)[b]	**15** (Me_2CO-d_6)	**16** ($CDCl_3$)	**17** ($CDCl_3$)	**18** (Me_2CO-d_6)
1		3.66 dd (10.8, 6.0) 3.58 dd (10.8, 7.2)	3.66 d (4.8) 3.61 d (4.8)		10.09 s		4.16 dd (9.6, 3.0) 4.13 d (9.6)	4.08 d (2.4)	3.69 dd (11.4, 4.8) 3.47 dd (11.4, 2.4)
3	5.21 s	4.02 s	4.34 d (4.8) 4.13 d (4.8)	9.50 s	9.57 s	4.46 dd (10.8, 3.0) 4.12 dd (10.8, 6.6)	4.44 s	4.63 d (3.0)	4.32 dd (10.8, 11.4) 4.09 dd (10.8, 3.6)
4	1.75 m					1.76 m	2.28 m	1.65 m	2.26 m
5	2.97 ddd (7.8, 4.8, 4.2)	3.06 dd (10.2, 9.6)	3.11 d (7.8)	3.69 dd (10.2, 9.6)		2.52 m	2.45 m	1.97 m	2.36 m
6α	2.33 dd (14.4, 7.2)	2.19 ddd (13.2, 9.6, 4.8)	2.73 dd (10.2, 7.8)	2.30 ddd (13.2, 9.6, 4.5)	2.69 dd (14.4, 7.8)	1.98 ddd (12.6, 9.6, 3.6)	2.35 dd (13.8, 7.2)	2.10 dd (13.8, 7.8)	2.03 m
6β	1.80 ddd (14.4, 7.8, 3.0)	1.72 ddd (13.2, 4.8, 1.8)	2.24 d (10.2)	1.87 dd (13.2, 8.4)	1.88 dd (14.4, 4.8)	1.91 dd (12.6, 7.8)	1.36 ddd (13.8, 6.0, 3.0)	1.63 ddd (13.8, 7.2, 3.6)	1.27 m
7	4.01 d (7.2)	3.80 dd (4.8, 4.8)	5.78 brs	3.98 brs	5.97 dd (7.8, 4.8)	3.75 d (3.6)	3.76 dd (7.2, 3.0)	3.88 dd (7.8, 3.6)	1.85 m, 1.13 m
8									1.67 m
9	2.42 d (4.8)	2.19 ddd (10.2, 7.2, 6.0)		3.22 d (10.2)		2.83 d (10.8)	1.92 dd (4.2, 3.0)	1.82 dd (3.0, 2.4)	2.39 m
10	1.18 s	1.34 s	4.11 s	1.38 s	4.79 dt (13.2, 4.8) 4.52 dt (13.2, 4.8)	1.48 s	1.38 s	1.39 s	1.13 d (7.2)
11	3.88 dd (12.6, 4.2) 3.75 d (12.6)	5.22 s 5.03 s	4.98 s 4.94 s	6.46 s 6.18 s	6.84 s 6.31 s	3.58 dd (10.8, 5.4) 3.43 d (10.8)	0.90 d (7.2)	1.04 d (7.2)	1.13 d (7.2)
OMe	3.48 s			3.50 s					

[a] ^{1}H NMR data (δ) were measured on a 600 MHz NMR instrument. Proton coupling constants (J) in Hz are given in parentheses. The assignments are based on DEPT, ^{1}H−^{1}H COSY, NOESY, HSQC, and HMBC experiments. [b] Data of the acetoxy group at C-7 of **13**: δ 2.09 (3H, s, H_3-2′).

Table 2. ^{13}C NMR Data (δ) for Compounds **1**−**6**, **8**−**13**, and **15**−**18**[a]

position	**1**[b]	**2**[b]	**3**[b]	**4**[b]	**5**[b]	**6**[b]	**8**[b]	**9**[b]	**10**[d]	**11**[b]	**12**[b]	**13**[b,e]	**15**[b]	**16**[c]	**17**[c]	**18**[b]
1	172.1	171.4	61.0	91.1	171.9	172.4	170.5	170.5	61.0	66.2	174.6	190.3	172.3	60.3	59.6	57.6
3	70.6	99.1	93.8	94.8	98.2	70.3	73.5	107.0	67.5	71.8	195.4	192.9	67.6	95.2	93.7	69.6
4	145.4	147.5	152.0	152.5	49.9	39.2	38.9	37.9	150.5	156.8	153.6	152.5	41.4	36.3	43.6	39.1
5	41.3	39.3	42.0	37.5	35.7	32.0	36.3	33.4	41.5	49.7	36.3	81.0	34.9	36.9	39.9	39.7
6	41.4	44.5	43.7	44.3	43.9	34.0	39.1	39.4	38.8	40.0	39.8	45.7	37.9	33.5	42.9	33.1
7	81.5	78.2	79.3	80.0	78.7	81.0	77.2	76.4	81.0	130.7	80.2	75.7	79.2	79.1	79.5	35.3
8	86.4	87.6	83.1	83.3	87.5	85.5	88.0	87.0	83.5	145.1	83.3	158.2	84.0	81.9	81.3	44.3
9	53.7	50.7	43.8	45.6	51.7	53.0	58.7	50.0	51.3	100.5	51.9	140.2	49.2	38.9	38.2	49.5
10	22.8	20.6	19.0	19.8	20.8	22.9	20.1	19.9	23.5	59.1	23.3	57.5	21.5	18.5	18.3	20.5
11	113.2	111.3	106.8	106.0	62.9	13.8	103.8	63.7	122.3	104.9	135.8	134.6	61.3	13.5	17.9	16.0
OMe							56.0	56.8			56.0					

[a] ^{13}C NMR data (δ) were measured at 150 MHz. The assignments were based on DEPT, ^{1}H−^{1}H COSY, HSQC, and HMBC experiments. [b] ^{13}C NMR data (δ) were measured in Me_2CO-d_6. [c] ^{13}C NMR data (δ) were measured in $CDCl_3$. [d] ^{13}C NMR data (δ) were measured in MeOD. [e] Data of the acetoxy group at C-7 of **13**: δ 169.5 (C-1′), 19.7 (C-2′).

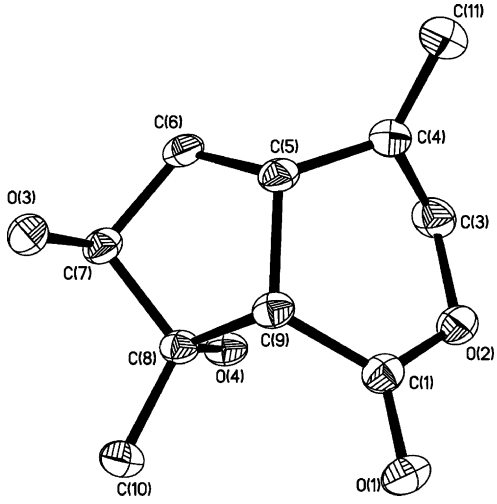
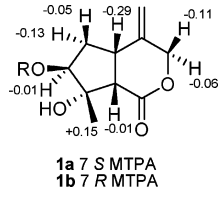


Figure 1. ORTEP drawing of jatamanin A (**1**).



1a 7 *S* MTPA
1b 7 *R* MTPA

Figure 2. Delta values ($\Delta\delta_{S-R}$) for 7*S* (**1a**) and 7*R* (**1b**) esters. $\Delta\delta$ values are expressed in ppm.

absolute configuration at C-7 as *S* (Figure 2). On the basis of these data, the structure of jatamanin A (**1**) was defined as (5*S*,7*S*,8*S*,9*S*)-7,8-dihydroxy-$\Delta^{4,11}$-dihyronepetalactone.

Jatamanin B (**2**) analyzed for $C_{10}H_{12}O_4$ by HRESIMS, a formula indicating one more unit of unsaturation than that of **1**. The ^{1}H and ^{13}C NMR data of this compound closely resembled those of **1** except for the presence of a hemiketal methine [δ_H 5.73 (s, H-3); δ_C 99.1 (C-3)] instead of an oxymethylene in **1**. These data suggested that an oxo bridge connecting C-3 and C-8 was present in **2**.[13] Supporting this assignment was a strong HMBC correlation observed between H-3 and C-8. This oxo bridge must be α-oriented on the basis of analysis of the molecular model and the observed NOESY correlations that were analogous to those of **1**. Because of biogenetic considerations, the absolute configurations at C-5, C-7, C-8, and C-9 of **2** were assumed to be identical to those of **1**. Therefore, jatamanin B (**2**) was assigned as (3*R*,5*S*,7*S*,8*S*,9*S*)-3,8-epoxy-7-hydroxy-$\Delta^{4,11}$-dihyronepetalactone.

Jatamanin C (**3**) gave a molecular formula of $C_{10}H_{14}O_3$, as indicated by HRESIMS. The ^{1}H and ^{13}C NMR data of **3** were similar to those of **2** except that the lactone carbonyl signal of **2** was replaced by an oxymethylene [δ_H 4.08 (1H, dd, J = 9.6, 2.4 Hz, H-1a) and 3.90 (1H, d, J = 9.6 Hz, H-1b); δ_C 61.0 (C-1)]. 2D COSY correlations from the oxymethylene protons H_2-1 to the methine proton H-9, in addition to the COSY correlation from H-9 to H-5, confirmed the position of the oxymethylene. The position was also consistent with observed correlations in the HMBC NMR spectrum of **3**. Thus, the structure of jatamanin C (**3**) was elucidated as (3*S*,5*S*,7*S*,8*S*,9*S*)-3,8-epoxy-7-hydroxy-$\Delta^{4,11}$-dihyronepetane.

The ^{1}H and ^{13}C NMR spectroscopic data of jatamanin D (**4**) suggested that **4** had the same carbon skeleton as **3**, but that it possessed an OH group at C-1. These observations, coupled with analysis of the 2D HSQC and HMBC NMR spectra, disclosed that **4** was a HO-1 derivative of **3**. NOESY correlation of H-1 with H_3-10 for **4** was identical to that of 1,5-dihydroxy-3,8-epoxyvalechlorine and rupesin E, two related iridoids isolated from the same plant.[13] These observations indicated that these compounds have the same relative configuration at C-1. Thus, jatamanin D (**4**) was determined to be (1*S*,3*R*,5*S*,7*S*,8*S*,9*S*)-3,8-epoxy-1,7-dihydroxy-$\Delta^{4,11}$-dihyronepetane.

Jatamanin E (**5**) had the molecular formula $C_{10}H_{14}O_5$. The ^{1}H and ^{13}C NMR data showed signals similar to those of **2**, but also revealed that the signals attributed to the terminal double bond at C-4−C-11 of **2** were absent. Instead, signals assignable to an oxymethylene and a methine appeared at δ_H 3.40 (2H, brs, H_2-11) and 1.98 (1H, m, H-4), and δ_C 62.9 (C-11) and 49.9 (C-4), respectively. In the ^{1}H NMR spectrum of **5** there were two exchangeable OH protons at δ_H 4.65 (d, J = 5.4 Hz, OH-7) and 3.95 (brs, OH-11). These data suggested that **5** was an analogue of **2** by addition of H_2O to the double bond, and the structure was supported by 2D COSY, HSQC, and HMBC experiments. The relative configuration of H-4 was determined by the NOESY correlations of H-4 with H-6α, and H-5 with H-9, H-6β, and H_2-11. Accordingly, the structure of jatamanin E (**5**) was identified as (3*R*,4*S*,5*R*,7*S*,8*S*,9*S*)-3,8-epoxy-7,11-dihydroxydihyronepetalactone.

Jatamanin F (**6**) and a minor metabolite, jatamanin G (**7**), had the same molecular formula and exhibited NMR spectroscopic features similar to those of **1**. The main difference was the presence of a terminal methyl doublet and a methine multiplet and lack of a terminal double bond in both the ^{1}H NMR spectra of **7** and **8**. In the ^{1}H NMR spectrum of **6**, the splitting patterns of H_2-3 and the chemical shifts of H-4, H_2-3, H-5, and Me-4 are obviously different than those of **7**. The coupling split analyses of **6** indicated that H-3ax appeared clearly as a double doublet with two large coupling constants (10.8 and 11.4 Hz), and H-3eq was a doublet with a coupling constant of 10.8 Hz. These coupling patterns demonstrated that H-4 in **6** was in a quasi-axial position. This assignment was also supported by the NOESY correlations of H-4 with H-6α, and H-5 with H-9, H-6β, and H_3-11. In the case of **7**, however, a quasi-equatorial position of H-4 was established by the small coupling constants, $J_{H4,H3ax}$ = 3.0 Hz and $J_{H4,H3ex}$ = 8.4 Hz. These data and biogenetic considerations suggested that **6** and **7** were a pair of C-4 diastereomers. Hence, the structures of jatamanins F (**6**) and

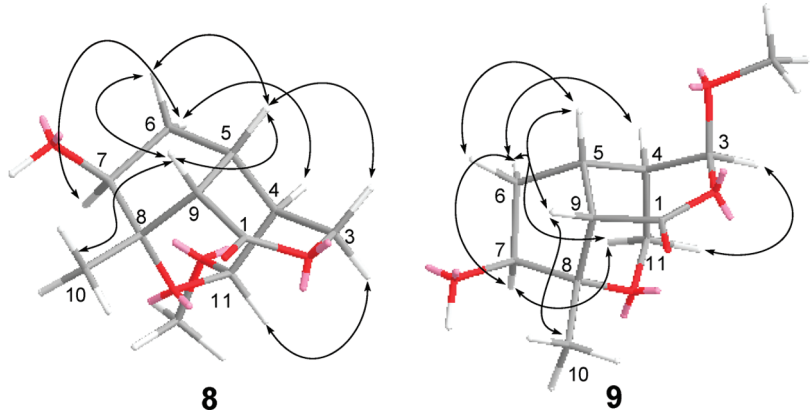


Figure 3. Key NOESY correlations for compounds **8** and **9**.

G (**7**) were characterized as (4*R*,5*R*,7*S*,8*S*,9*S*)-7,8-dihydroxydihyronepetalactone and (4*S*,5*R*,7*S*,8*S*,9*S*)-7,8-dihydroxydihyronepetalactone, respectively.

Jatamanins H (**8**) and I (**9**) were obtained as an inseparable mixture of two related compounds in a near 1:1 ratio, as determined by the doubling of signals in the ^{1}H and ^{13}C NMR spectra. Exhaustive efforts to separate this mixture were unsuccessful using the normal-phase and reversed-phase HPLC techniques. The structural elucidation of both compounds from the mixture was possible due to the well-separated signals observed in the ^{1}H and ^{13}C NMR spectra (see Supporting Information). On the basis of NMR and HRESIMS data, the two compounds were also assigned as iridolactones closely related to compound **5** with three rings and an additional OCH_3 group. After assignment of all protons to their directly attached carbon atoms via 2D HSQC, the 2D COSY correlations were observed from H_2-3→H-4→H-5→H_2-6 and from H-4→H-11 in **8**, suggesting that the C-8−C-3 oxo bridge in **5** was replaced in **8** by a C-8−C-11 oxo bridge. Key HMBC correlations between H-11 and C-8, between H_2-3 and C-1, and between OCH_3 protons and C-11 also served to construct this oxo bridge and confirmed the location of the OCH_3 group at C-11 in **8**. Like jatamanin H (**8**), jatamanin I (**9**) was shown to possess the C-8−C-11 oxo bridge by interpretation of the 2D COSY and HMBC spectra. Unlike **8**, however, compound **9** was confirmed by HMBC NMR data to contain a OCH_3 group at C-3.

The relative configuration of compounds **8** and **9** was elucidated by NOESY NMR experiments (Figure 3). NOESY correlations of H-9 with H-5 and Me-8, and H-5 with H-6β, indicated that **8** and **9** had the same configuration as **5** at C-5, C-7, C-8, and C-9, thereby confirming the α-orientation of the C-8−C-11 oxo bridge. As expected, the protons at C-11 showed NOESY correlations with H-3α in **8**, and with H-7 and H-6α in **9**, in full support of this assignment. The presence of a NOESY correlation between H-11 and H-3α in **8** also revealed that these protons, opposite of MeO-11, were spatially close, whereas in **9**, the MeO-3 was determined to be β-oriented on the basis of a NOESY correlation of H-11b with H-3. Thus, the structures of jatamanins H (**8**) and I (**9**) were confirmed as (4*S*,5*R*,7*S*,8*S*,9*S*,11*R*)-8,11-epoxy-7-hydroxy-11-methoxydihyronepetalactone and (3*S*,4*R*,5*R*,7*S*,8*S*,9*S*)-8,11-epoxy-7-hydroxy-3-methoxydihyronepetalactone, respectively.

The molecular formula of jatamanin J (**10**) was established as $C_{10}H_{18}O_4$ by HRESIMS, 20 mass units more than **3**. The ^{1}H and ^{13}C NMR spectra of **10** were generally similar to those observed for **3**. In the ^{13}C NMR spectrum of **3**, the hemiketal methine signal for C-3 (δ_C 93.8) was replaced in **10** by an oxymethylene at δ_C 67.5, indicating the absence of a C-8−C-3 oxo bridge in **10**. However, the formula of **10** possessed two fewer units of unsaturation than compound **3**, implying that **10** was a monocyclic iridoid ring-opened via the ether bond to form hydroxymethyl groups at C-1 and C-3, respectively. This was supported by the absence of HMBC correlations between H_2-3 and C-1 and/or between H_2-1 and C-3 in the HMBC spectrum of **10**. Comparisons of the NOESY NMR data for **10** with those from **3** allowed the relative configurations at C-5, C-7, C-8, and C-9 to be identically assigned. Therefore, the structure of jatamanin J (**10**) was determined as (5*S*,7*S*,8*S*,9*R*)-7,8-dihyroxy-$\Delta^{4,11}$-dihyronepeta-1,3-diol.

The molecular formula of jatamanin K (**11**) was found to be $C_{10}H_{14}O_3$ on the basis of HRESIMS. The ^{1}H, ^{13}C, and DEPT NMR spectra for **11** (Tables 1 and 2) revealed the presence of a nonoxygenated methine, one nonoxygenated and three oxygenated methylenes, an oxygenated quaternary carbon, a terminal double bond, and a trisubstituted double bond, all of which suggested a molecule of iridoid origin. The remaining two degrees of unsaturation required by the molecular formula indicated that **11** was still a bicyclic iridoid. Analysis of the 2D COSY NMR experiment permitted the establishment of two spin systems corresponding to the C-3/C-4/C-11 and C-11/C-4/C-5/C-6/C-7/C-8/C-10 portions of **11**. Interpretation of 2D HSQC and HMBC experiments allowed all of the protons and carbons to be assigned. As in the other metabolites, numerous HMBC correlations were observed, but those between H_2-10 and C-9, between H_2-1 and C-9 and C-5, between H_2-11 and C-4, C-3, and C-5, and between H_2-3 and C-9 clearly established connection of the two spin systems and allowed the full structure of compound **11** to be assigned. No NOE correlation between H-5β and H_2-1 was observed, thus requiring α-orientation for H_2-1. From the above data and on biogenetic grounds, the structure of jatamanin K (**11**) was established as (5*R*,9*R*)-3,9-epoxy-10-hydroxy-$\Delta^{4,11,7,8}$-dihyronepeta-1-ol.

Jatamanin L (**12**) was formulated as $C_{11}H_{16}O_5$ from the HRESIMS, and the ^{1}H and ^{13}C NMR spectra of **12** (Tables 1 and 2) were very similar to those of **11**. However, the data for **12** contained signals for a conjugated aldehyde and a methyl ester group in place of the signals for two oxymethylenes (C-1 and C-3, respectively) observed in the spectra of **11**. The ester carbonyl carbon was assigned to C-1 on the basis of HMBC correlations from the ester carbonyl (δ_C 174.0) to H-5, H-9, and the *O*-methyl protons, leaving the conjugated aldehyde carbonyl to be assigned as C-3. Further, the chemical shifts H_2-11(δ 6.46. and 6.18), along with HMBC correlations of the aldehyde proton with C-4, C-5, and C-11, were in full agreement with this assignment. The structure of **12** was consequently established as shown.

HRESIMS analysis of jatamanin M (**13**) indicated that it had the molecular formula $C_{12}H_{14}O_6$. The ^{1}H and ^{13}C NMR data contained signals for two aldehyde groups, an oxygenated methine, one nonoxygenated and one oxygenated methylene, an oxygenated quaternary carbon, a terminal double bond, a tetrasubstituted double bond, an acetyl moiety, and two aliphatic OH groups (δ 4.53 and 4.63). When compared with the NMR data of **12**, it was concluded

that one conjugated aldehyde was at C-3, C-4, and C-11, while another conjugated aldehyde was located at C-1, C-9, and C-8. The hydoxymethyl was assigned to C-10. These assignments were confirmed by the HMBC correlations between aldehyde H-3 and C-4, C-11, and C-5, between aldehyde H-1 and C-8, C-9, and C-5, between H_2-10 and C-8 and C-9, and between the OH proton triplet at δ_H 4.53 (t, $J = 4.8$ Hz, OH-10) and C-10. The remaining aliphatic OH proton (δ 4.63) showed HMBC correlations to the oxygenated quaternary carbon (C-5), C-6, and C-4, placing this OH group at C-5. Finally, the acetoxy group was connected to C-7 to complete the structure assignment for **13** on the basis of on a strong HMBC correlation between H-7 and the ester carbonyl carbon at δ_C 169.5. In the NOESY spectrum, NOE correlations of OH-5 with H-6β, and H-7 with H-6α, indicated that OH-5 was β-oriented and that H-7 was α-oriented. Thus, the structure of jatamanin M (**13**) was elucidated as (5*S*,7*S*)-7-acetoxy-5,10-dihyroxy-$\Delta^{8,9}$-dolichodial.

Compound **14** was isolated as a colorless oil, which analyzed for $C_{25}H_{32}O_7$ by HRESIMS. The IR spectrum gave an absorption peak at 1736 cm^{-1} indicative of an ester carbonyl. The ^1H and ^{13}C NMR spectra of **14** closely resembled those of the co-occurring lignan lariciresinol,[14] except that a set of signals characteristic of an isovaleryl group appeared, and H_2-9′ was shifted significantly downfield. The HMBC spectrum revealed a correlation between H_2-9′ and the ester carbonyl carbon at δ_C 173.6. Compound **14** is thus the 9′-*O*-isovaleryl derivative of lariciresinol, and (+)-9′-isovaleroxylariciresinol is proposed as the trivial name.

Compound **15** had a molecular formula $C_{10}H_{16}O_5$ on the basis of its ESIMS and NMR data. Comparison with NMR data from the literature indicated that the structure of compound **15** was identical to that of longiflorone.[15] However, the relative configuration of longiflorone had not been reported. Like **7**, the small coupling constants between H-4 and H-3ax ($J = 3.0$ Hz) and between H-4 and H-3ex ($J = 6.6$ Hz) indicated that H-4 was quasi-equatorial. The NOESY correlations of H-4 with H-5 and H-6β, H-6α with H_2-11, H-5 with H-9 and H-6β, and H-7 with H-6α were also consistent with this and established the configuration of **15**.

During the isolation process we also obtained another pair of C-4 diastereomers of iridoids, (3*S*,4*R*,5*S*,7*S*,8*S*,9*S*)-3,8-epoxy-7-hydroxy-4,8-dimethylperhydrocyclopenta[*c*]pyran (**16**) and (3*S*,4*S*,5*S*,-7*S*,8*S*,9*S*)-3,8-ethoxy-7-dihydroxy-4,8-dimethylperhydrocyclopenta-[*c*]pyran (**17**), and a related irdoid, 4,7-dimethyloctahydrocyclopenta[*c*]pyran (**18**). No NMR spectroscopic data for these compounds had been reported, although **16**, **17**, and **18** had been described as synthetic products in a German patent and earlier literature, respectively.[16,17] Therefore, compounds **16**−**18** were obtained as natural products for the first time, and their ^1H and ^{13}C NMR data assigned by interpretation of their 2D NMR spectra are included in this report.

The other known compounds were identified by comparison of spectroscopic data with those reported in the literature as 4-hydroxy-8-methoxy-3-methyl-10-methylene-2,9-dioxatricyclo(4,3,1,$0^{3,7}$)-decane,[18] patriscabrol,[12] rupesin E,[19] lariciresinol,[14] pinsepiol,[20] (+)-1-hydroxypinoresinol, (+)-acetoxypinoresinol,[21] (+)-medioresinol,[22] (+)-monomethylpinoresinol,[23] (+)-syringaresinol, (+)-pinoresinol,[21] (+)-5′-hydroxypinoresinol,[24] (+)-cyclo-olivil,[21] (−)-massoniresinol,[25] 4,4′,9,7′-tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan,[26] and (−)-berchemol.[27]

Cytotoxic activity evaluation of the isolated iridoids and compound **14** in a panel of four human tumor cell lines, lung adenocarcinoma (A549), metastatic prostate cancer (PC-3M), colon cancer (HCT-8), and hepatoma (Bel7402), revealed that only the lignan (+)-9′-isovaleroxylariciresinol (**14**) showed selective cytotoxicity against PC-3M and HCT-8 cell lines, with IC_{50} values of 8.1 and 5.3 μM, respectively. All of the other compounds tested were considered to be noncytotoxic.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Perkin-Elmer 341 polarimeter. IR and UV spectra were recorded on Bruker Vector-22 and Shimadzu UV-2550 UV−visible spectrophotometers, respectively. NMR spectra were obtained on a Bruker Avance 600 MHz NMR spectrometer in Me_2CO-d_6, MeOD, or $CDCl_3$ with TMS as an internal standard. ESIMS and HRESIMS were acquired on an Agilent LC/MSD Trap XCT and a Q-TOF micro mass spectrometer (Waters, Milford, MA), respectively. Column chromatography (CC) was performed using silica gel (100−200 mesh, and 10−40 μm; Huiyou Silica Gel Development Co. Ltd., Yantai, People's Republic of China) and Sephadex LH-20 (40−70 μm; Amersham Pharmacia Biotech AB, Uppsala, Sweden). Semipreparative HPLC was conducted on an ODS column (Kromasil, 5 μm, 300 × 10 mm) using a PDA UV detector at 208 nm. Preparative TLC (0.4−0.5 mm) was carried out on precoated silica gel GF_{254} plates (Yantai). Zones were visualized under UV light (254 nm) or by spraying with 10% H_2SO_4 followed by heating.

Plant Material. Whole plants of *V. jatamansi* were collected in Gaopo, Guizhou Province, People's Republic of China, in July 2007, and identified by Prof. Shun-zhi He, Guiyang University of Traditional Chinese Medicine. A herbarium specimen was deposited in the School of Pharmacy, Second Military Medical University, People's Republic of China (herbarium no. 2007-08-16).

Extraction and Isolation. The air-dried whole plants of *V. jatamansi* (8.5 kg) were powdered and extracted with 11.0 L of 95% EtOH at room temperature for 3 × 48 h. The combined extracts were evaporated under reduced pressure. The residue was suspended in H_2O (1500 mL) and then partitioned with EtOAc (5 × 1000 mL). The EtOAc fraction (420 g) was chromatographed over silica gel (1500 g), eluting with increasing amounts of Me_2CO (0−100%) in petroleum ether, to afford 10 fractions (F_1−F_{10}) based on TLC analysis. Fractions F_7−F_{10} were separated by CC over Sephadex LH-20 using $CHCl_3$−MeOH (1:1) as eluent to give corresponding subfractions. The first and second subfractions of F_7 were purified by preparative TLC developed with $CHCl_3$−MeOH (20:1) to give **13** (3.5 mg) and **14** (32.3 mg), respectively. The second subfraction of F_8 was fractionated by reversed-phase C-18 silica flash chromatography eluting with a step gradient from 20% to 80% MeOH in H_2O. The 40% MeOH−H_2O fraction was separated by preparative TLC developed with $CHCl_3$−MeOH (10:1) to obtain **5** (7.8 mg). The second subfraction of F_9 was subjected to chromatography on silica gel, eluting with $CHCl_3$−Me_2CO (8:1), to give **3** (5.5 mg) and **4** (2.1 mg). Using the same procedure as described above for the isolation of **5**, the third subfraction of F_9 yielded **2** and a mixture of **8** and **9**, which could not be separated by normal-phase HPLC techniques. The fourth subfraction of F_9 was isolated after reversed-phase C-18 silica flash chromatography eluting with a step gradient from 10% to 60% MeOH in H_2O and then reversed-phase preparative HPLC (RP_{18}, 5 μm, 208 nm, MeCN−H_2O, 15:85) to give **6** (12.3 mg) and **7** (0.3 mg). The first subfraction of F_{10} was purified using the same method, but eluting the HPLC system with 18% H_2O−MeCN, to afford **11** (18.1 mg) and **12** (4.2 mg). White crystals of **1** were obtained upon slow evaporation of the Me_2CO solution of the second subfraction of F_{10}. The fourth subfraction of F_{10} was separated by preparative HPLC (RP_{18}, 5 μm, 208 nm, MeCN−H_2O, 12:88) to give **10** (11.3 mg).

Jatamanin A (1): colorless crystals, mp 177−178 °C; $[\alpha]^{20}_D$ +139.0 (*c* 0.20, MeOH); IR (KBr) ν_{max} 3564, 3464, 2972, 2863, 1710, 1647, 1432, 1372, 1233, 1100 cm^{-1}; ^1H NMR (Me_2CO-d_6, 600 MHz) and ^{13}C NMR (Me_2CO-d_6, 150 MHz) data, see Tables 1 and 2; positive-mode ESIMS *m/z* 221 $[M + Na]^+$; negative-mode ESIMS *m/z* 233 $[M + {}^{35}Cl]^-$; HRESIMS *m/z* 221.0786 $[M + Na]^+$ (calcd for $C_{10}H_{14}O_4Na$, 221.0790).

Jatamanin B (2): colorless solid; $[\alpha]^{20}_D$ +111.3 (*c* 0.91, MeOH); IR (KBr) ν_{max} 3564, 2970, 2863, 1708, 1641, 1472, 1375, 1232, 1088 cm^{-1}; ^1H NMR (Me_2CO-d_6, 600 MHz) and ^{13}C NMR (Me_2CO-d_6, 150 MHz) data, see Tables 1 and 2; positive-mode ESIMS *m/z* 219 $[M + Na]^+$; negative-mode ESIMS *m/z* 231 $[M + {}^{35}Cl]^-$; HRESIMS *m/z* 219.0641 $[M + Na]^+$ (calcd for $C_{10}H_{12}O_4Na$, 219.0633).

Jatamanin C (3): colorless solid; $[\alpha]^{20}_D$ +102.5 (*c* 0.18, MeOH); IR (KBr) ν_{max} 3552, 2967, 2862, 1637, 1463, 1361, 1246, 1096 cm^{-1}; ^1H NMR (Me_2CO-d_6, 600 MHz) and ^{13}C NMR (Me_2CO-d_6, 150 MHz) data, see Tables 1 and 2; positive-mode ESIMS *m/z* 205 $[M + Na]^+$;

negative-mode ESIMS *m/z* 217 $[M + {}^{35}Cl]^-$; HRESIMS *m/z* 205.0835 $[M + Na]^+$ (calcd for $C_{10}H_{14}O_3Na$, 205.0841).

Jatamanin D (4): colorless solid; $[\alpha]^{20}_D$ +89.3 (*c* 0.10, MeOH); IR (KBr) ν_{max} 3564, 3540, 2968, 2860, 1640, 1465, 1363, 1238, 1101 cm^{-1}; ^1H NMR (Me_2CO-d_6, 600 MHz) and ^{13}C NMR (Me_2CO-d_6, 150 MHz) data, see Tables 1 and 2; positive-mode ESIMS *m/z* 221 $[M + Na]^+$; negative-mode ESIMS *m/z* 233 $[M + {}^{35}Cl]^-$; HRESIMS *m/z* 221.0782 $[M + Na]^+$ (calcd for $C_{10}H_{14}O_4Na$, 221.0790).

Jatamanin E (5): colorless solid; $[\alpha]^{20}_D$ +108.0 (*c* 0.26, MeOH); IR (KBr) ν_{max} 3564, 3422, 2968, 2859, 1708, 1366, 1228, 1096 cm^{-1}; ^1H NMR (Me_2CO-d_6, 600 MHz) and ^{13}C NMR (Me_2CO-d_6, 150 MHz) data, see Tables 1 and 2; positive-mode ESIMS *m/z* 237 $[M + Na]^+$; negative-mode ESIMS *m/z* 249 $[M + {}^{35}Cl]^-$; HRESIMS *m/z* 237.0736 $[M + Na]^+$ (calcd for $C_{10}H_{14}O_5Na$, 237.0739).

Jatamanin F (6): colorless solid; $[\alpha]^{20}_D$ +96.5 (*c* 0.12, MeOH); IR (KBr) ν_{max} 3564, 2973, 2861, 1711, 1370, 1235, 1087 cm^{-1}; ^1H and ^{13}C NMR (Me_2CO-d_6, 600 MHz), see Tables 1 and 2; positive-mode ESIMS *m/z* 223 $[M + Na]^+$; negative-mode ESIMS *m/z* 235 $[M + {}^{35}Cl]^-$; HRESIMS *m/z* 223.0941 $[M + Na]^+$ (calcd for $C_{10}H_{16}O_4Na$, 223.0946).

Jatamanin G (7): colorless solid; $[\alpha]^{20}_D$ +54.5 (*c* 0.06, MeOH); IR (KBr) ν_{max} 3560, 2975, 2861, 1713, 1238, 1083 cm^{-1}; ^1H NMR (Me_2CO-d_6, 600 MHz), see Table 1; positive-mode ESIMS *m/z* 223 $[M + Na]^+$; negative-mode ESIMS *m/z* 235 $[M + {}^{35}Cl]^-$; HRESIMS *m/z* 223.0939 $[M + Na]^+$ (calcd for $C_{10}H_{16}O_4Na$, 223.0946).

Jatamanins H (8) and I (9): colorless solid; ^1H NMR (Me_2CO-d_6, 600 MHz) and ^{13}C NMR (Me_2CO-d_6, 150 MHz) data, see Tables 1 and 2; positive-mode ESIMS *m/z* 251 $[M + Na]^+$; negative-mode ESIMS *m/z* 263 $[M + {}^{35}Cl]^-$; HRESIMS *m/z* 251.0893 $[M + Na]^+$ (calcd for $C_{11}H_{16}O_5Na$, 251.0895).

Jatamanin J (10): colorless solid; $[\alpha]^{20}_D$ +87.0 (*c* 0.36, MeOH); IR (KBr) ν_{max} 3552, 3542, 2971, 2862, 1647, 1468, 1363, 1245, 1098 cm^{-1}; ^1H NMR (MeOD, 600 MHz) and ^{13}C NMR (MeOD, 150 MHz) data, see Tables 1 and 2; positive-mode ESIMS *m/z* 225 $[M + Na]^+$; negative-mode ESIMS *m/z* 237 $[M + {}^{35}Cl]^-$; HRESIMS *m/z* 225.1102 $[M + Na]^+$ (calcd for $C_{10}H_{18}O_4Na$, 225.1103).

Jatamanin K (11): colorless solid; $[\alpha]^{20}_D$ +56.8 (*c* 0.16, MeOH); IR (KBr) ν_{max} 3546, 2967, 2857, 1642, 1446, 1329, 1230, 1086 cm^{-1}; ^1H NMR (Me_2CO-d_6, 600 MHz) and ^{13}C NMR (Me_2CO-d_6, 150 MHz) data, see Tables 1 and 2; positive-mode ESIMS *m/z* 205 $[M + Na]^+$; negative-mode ESIMS *m/z* 217 $[M + {}^{35}Cl]^-$; HRESIMS *m/z* 205.0834 $[M + Na]^+$ (calcd for $C_{10}H_{14}O_3Na$, 205.0841).

Jatamanin L (12): colorless solid; $[\alpha]^{20}_D$ +92.0 (*c* 0.28, MeOH); IR (KBr) ν_{max} 3542, 2970, 2857, 1692, 1646, 1447, 1330, 1236, 1069 cm^{-1}; ^1H NMR (Me_2CO-d_6, 600 MHz) and ^{13}C NMR (Me_2CO-d_6, 150 MHz) data, see Tables 1 and 2; positive-mode ESIMS *m/z* 251 $[M + Na]^+$; negative-mode ESIMS *m/z* 263 $[M + {}^{35}Cl]^-$; HRESIMS *m/z* 251.0890 $[M + Na]^+$ (calcd for $C_{11}H_{16}O_5Na$, 251.0895).

Jatamanin M (13): colorless oil; $[\alpha]^{20}_D$ −98.5 (*c* 0.13, MeOH); IR (KBr) ν_{max} 3463, 2970, 2863, 1738, 1684, 1468, 1372, 1233, 1077 cm^{-1}; ^1H NMR (Me_2CO-d_6, 600 MHz) and ^{13}C NMR (Me_2CO-d_6, 150 MHz) data, see Tables 1 and 2; positive-mode ESIMS *m/z* 277 $[M + Na]^+$; negative-mode ESIMS *m/z* 289 $[M + {}^{35}Cl]^-$; HRESIMS *m/z* 277.0707 $[M + Na]^+$ (calcd for $C_{12}H_{14}O_6Na$, 277.0688).

(+)-9′-Isovaleryllariciresinol (14): colorless oil; $[\alpha]^{20}_D$ +23.2 (*c* 0.22, MeOH); IR (KBr) ν_{max} 3435, 1736, 1604, 1516, 1464 cm^{-1}; ^1H NMR (Me_2CO-d_6, 600 MHz) δ 6.86 (1H, d, J = 2.4 Hz, H-2), 6.79 (1H, d, J = 8.4 Hz, H-5), 6.81 (1H, dd, J = 8.4, 2.4 Hz, H-6), 2.87 (1H, dd, J = 13.2, 4.8 Hz, H-7), 2.78 (1H, m, H-8), 4.02 (1H, dd, J = 8.4, 6.6 Hz, H-9a), 3.72 (1H, dd, J = 8.4, 6.6 Hz, H-9b), 6.97 (1H, d, J = 1.8 Hz, H-2′), 6.75 (1H, d, J = 7.8 Hz, H-5′), 6.69 (1H, dd, J = 7.8, 1.8 Hz, H-6′), 4.75 (1H, d, J = 6.6 Hz, H-7′), 2.53 (1H, m, H-8′), 4.39 (1H, dd, J = 11.4, 6.6 Hz, H-9′a), 4.19 (1H, dd, J = 11.4, 7.2 Hz, H-9′b), 2.19 (2H, m, H_2-2″), 2.05 (1H, m, H-3″), 0.95 (6H, d, J = 6.6 Hz, H_3-4″/ H_3-5″); ^{13}C NMR (Me_2CO-d_6, 150 MHz) δ 133.5 (C, C-1), 113.8 (CH, C-2), 148.9 (C, C-3), 146.4 (C, C-4), 116.1 (CH, C-5), 122.5 (CH, C-6), 34.3 (CH_2, C-7), 44.1 (CH, C-8), 73.7 (CH_2, C-9), 136.2 (C, C-1′), 111.1 (CH, C-2′), 148.9 (C, C-3′), 147.4 (C, C-4′), 116.4 (CH, C-5′), 120.2 (CH, C-6′), 84.4 (CH, C-7′), 51.2 (CH, C-8′), 63.6 (CH_2, C-9′), 173.6 (C, C-1″), 44.4 (CH_2, C-2″), 26.9 (CH, C-3″), 23.2 (CH_3, C-4″/C-5″); positive-mode ESIMS *m/z* 467 $[M + Na]^+$; negative-mode ESIMS *m/z* 443 $[M - H]^-$; HRESIMS *m/z* 467.2058 $[M + Na]^+$ (calcd for $C_{25}H_{32}O_7Na$, 467.2046).

Longiflorone (15): colorless solid; $[\alpha]^{20}_D$ +68.3 (*c* 0.32, MeOH); IR (KBr) ν_{max} 3562, 3400, 2952, 2860, 1706, 1372, 1233, 1092 cm^{-1}; ^1H NMR (Me_2CO-d_6, 600 MHz) and ^{13}C NMR (Me_2CO-d_6, 150 MHz) data, see Tables 1 and 2; positive-mode ESIMS *m/z* 239 $[M + Na]^+$; negative-mode ESIMS *m/z* 215 $[M - H]^-$.

X-ray Crystallographic Analysis of Jatamanin A (1). A plate crystal of **1** (0.25 × 0.20 × 0.18 mm) was orthorhombic (space group $P2_12_12_1$) with cell dimensions a = 5.957(14) Å, b = 13.28(3) Å, c = 7.662(17) Å. Data were collected on a Bruker SMART CCD diffractometer with Mo Kα radiation (λ = 0.71073 Å) from a normal focus sealed tube. In total, 2385 frames were collected with the detector set in different positions of 2θ. Each frame covered 0.20° in ω. Of the 1835 reflections collected with 3.07° ≤ 2θ ≤ 24.99°, 1835 were independent (R_{int} = 0.0406). This represents 99.2% of the unique data to the maximum value of 2θ. The structure was solved using the SHELXTL package.[28] The full-matrix least-squares (on F^2) of 162 variables gave values of the conventional crystallographic residuals R_1 = 0.0595 (wR_2 = 0.1501) for 1835 observed data with $I > 2\sigma(I)$ and R_1 = 0.0606 (wR_2 = 0.1517) for all data. Crystallographic data for jatamanin A (**1**) have been deposited with the Cambridge Crystallographic Data Centre (deposition number CCDC 757165). Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB21EZ, UK [fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk].

Preparation of Mosher Esters of Jatamanin A (1). One crystal of dimethylaminopyridine (DMAP) was added to 2.0 mg (0.01 mmol) of compound **1**. One milliliter of freshly distilled pyridine was added to this mixture, and the mixture was stirred at RT for 30 min. Next, 6 μL of (*R*)-MTPA chloride (0.03 mmol) was added. The resultant reaction mixture was stirred at RT for 90 min under N_2. The solutions were diluted with water and extracted with ethyl acetate. After removal of solvents under vacuum, the residue was purified by preparative TLC, developing with $CHCl_3$−MeOH (20:1), to afford *S*-MTPA ester **1a** (0.5 mg). The identical procedure was carried out to obtain the *R*-MTPA ester **1b** (0.4 mg) with *S*-MTPA chloride.

7-(*S*-MTPA) Ester of Jatamanin A (1a): ^1H NMR (Me_2CO-d_6, 600 MHz) δ 5.01 (1H, d, J = 11.4 Hz, H-3a), 4.35 (1H, d, J = 11.4 Hz, H-3b), 2.86 (1H, dd, J = 10.8, 9.6 Hz, H-5), 2.30 (1H, ddd, J = 13.2, 9.6, 3.0 Hz, H-6α), 2.25 (1H, dd, (J = 13.2, 4.8 Hz, H-6β), 5.45 (1H, brs, H-7), 2.83 (1H, d, J = 10.8 Hz, H-9), 1.19 (3H, s, H_3-10), 4.99 (1H, s, H-11a), 4.90 (1H, s, H-11b). positive-mode ESIMS *m/z* 437 $[M + Na]^+$; negative-mode ESIMS *m/z* 413 $[M - H]^-$.

7-(*R*-MTPA) Ester of Jatamanin A (1b): ^1H NMR (Me_2CO-d_6, 600 MHz) δ 5.12 (1H, d, J = 11.4 Hz, H-3a), 4.43 (1H, d, J = 11.4 Hz, H-3b), 3.15 (1H, dd, J = 10.8, 9.6 Hz, H-5), 2.43 (1H, ddd, J = 13.2, 9.6, 3.6 Hz, H-6α), 2.30 (1H, dd, J = 13.2, 4.8 Hz, H-6β), 5.46 (1H, brs, H-7), 2.84 (1H, d, J = 10.8 Hz, H-9), 1.04 (3H, s, H_3-10), 5.03 (1H, s, H-11a), 4.97 (1H, s, H-11b); positive-mode ESIMS *m/z* 437 $[M + Na]^+$; negative-mode ESIMS 413 $[M - H]^-$.

Cytotoxicity Assays. Cytotoxic activity was determined against four human cancer cell lines, A549, PC-3M, HCT-8, and Bel7402, obtained from the American Type Culture Collection (ATCC, Rockville, MD). Cells were seeded in 96-well plates at a cell density of 3000 per well and were treated 24 h later with various concentrations of the isolated iridoids and compound **14**. After 24 h of incubation, MTT was added to all wells. Plates were incubated for another 24 h, and cell viability was measured by observing absorbance at 570 nm on a SpectraMax[190] microplate reader (Molecular Devices, USA).[29,30] IC_{50} values were calculated using Microsoft Excel software. Paclitaxel was used as a positive control.

Acknowledgment. We acknowledge the Pharmaceutical Analysis Center of the Second Military Medical University, Shanghai, for measuring the IR and NMR spectra. We also thank the Shanghai Institute of Materia Medica, Chinese Academy of Sciences, for the optical rotation determinations. The work was supported by Changjiang Scholars and Innovative Research Team in University (PCSIRT), NCET Foundation, NSFC (30725045), National 863 Program (2006AA02Z338), and Shanghai Leading Academic Discipline Project (B906), and in part by the Scientific Foundation of Shanghai, China (07DZ19728, 06DZ19717, 06DZ19005).

Supporting Information Available: 1D and 2D NMR spectra of compounds **1**, **2**, and **8/9**. 1D NMR spectra of compounds **3**−**7** and **10**−**14**. X-ray crystallographic data of compound **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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NP900795C