Iridoids and Sesquiterpenoids from the Roots of *Valeriana officinalis*

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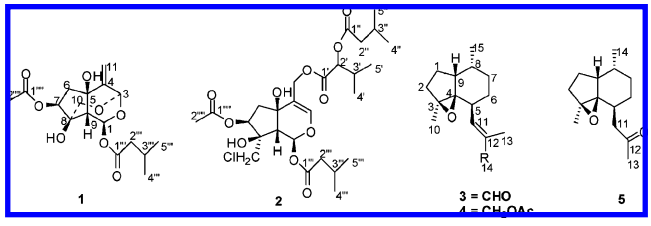
Received June 4, 2009

Two new iridoids, volvaltrates A and B (**1** and **2**), and three new sesquiterpenoids, *E*-(−)-3*β*,4*β*-epoxyvalerenal (**3**), *E*-(−)-3*β*,4*β*-epoxyvalerenyl acetate (**4**), and mononorvalerenone (**5**), together with five known iridoids and two known sesquiterpenoids were isolated from the roots of *Valeriana officinalis*. The structures and relative configurations of **1**−**5** were elucidated by spectroscopic evidence. Compound **1** was an unusual iridoid with an oxygen bridge connecting C-3 and C-10, forming a cage-like structure, and compound **5** was a mononorsesquiterpenoid.

The genus *Valeriana* (Valerianaceae) comprises about 200 species and is widely distributed throughout the world.[1] Valerian is an herb native to Europe and Asia and has been used in mild sedatives and tranquilizers for centuries.[2] Previous phytochemical investigations on this genus revealed the presence of iridoids, sesquiterpenoids, flavone glycosides, ligans, and alkaloids.[3−8] *Valeriana officinalis* is the official species used in Europe and is commonly referred to as valerian. Valerian is known for its pharmacological properties, including sedative, anxiolytic, antidepressant, and antispasmodic activities.[9−12] A recent report has also revealed the anti-HIV activity of valtrate as a new rev-transport inhibitor.[13] *V. officinalis* is still an object of research aimed at establishing the chemical and pharmacological basis of the activity demonstrated in previous studies.[14]

Our phytochemical investigation of the roots of *V. officinalis* has led to the isolation of two new iridoids (**1** and **2**) and three new sesquiterpenoids (**3**, **4**, and **5**), together with seven known compounds. The known compounds were identified as IVHD-valtrate,[15] 1,5-dihydroxy-3,8-epoxyvalechlorine,[16] valeteriotriate B,[17] jatamanvaltrate B,[18] jatamanvaltrate C,[18] valerenic acid,[4] and acetoxyvalerenic acid[4] by comparison of their spectroscopic data with those reported in the literature.



Compound **1** was isolated as a colorless oil. Its molecular formula was determined to be $C_{17}H_{24}O_8$, with six degrees of unsaturation, by HRESIMS (*m/z* 379.1362 $[M + Na]^+$). The IR spectrum indicated the presence of OH (3448 cm^{-1}), carbonyl (1737 cm^{-1}), and double-bond (1626 cm^{-1}) groups. The ^1H NMR spectrum of compound **1** showed three methyl [δ_H 2.17 (3H, s), 0.95 (3H, d, J = 6.5 Hz), 0.94 (3H, d, J = 6.5 Hz)] and two terminal olefinic protons [δ_H 5.39 and δ_H 5.15 (each 1H, s)]. The ^{13}C NMR and DEPT data (Table 1) revealed the presence of three methyl, four methylene, five methine, and five quaternary carbons. Comparison of the 1D NMR and 2D NMR data with compounds reported in the literature[16] suggested that **1** had a skeleton similar to that of 1,5-dihydroxy-3,8-epoxyvalechlorine A, with an exocylic olefinic bond at C-4 (δ_C 149.9), an acetate group linked to C-7 (δ_C 79.0), and an additional isovalerate moiety. The isovalerate group was attached to C-1 on the basis of a comparison of 1D NMR data with those reported.[16−20] The oxygen bridge between C-3 (δ_C 96.3) and C-10 (δ_C 66.7) in compound **1** was different from that of 1,5-dihydroxy-3,8-epoxyvalechlorine A, which was established by the key HMBC correlations from H-3 (δ_H 5.41), H-7 (δ_H 4.95), and H-9 (δ_H 2.67) to C-10, and H-10 (δ_H 4.00, 3.67) to C-9 (δ_C 57.3), C-8 (δ_C 79.4), and C-3 (δ_C 96.3) as shown in Figure 1. HMBC correlations from H-7 (δ_H 4.95) to C-1‴ (δ_C 170.9) and H-11 (δ_H 5.15) to C-3 and $^1H-^1H$ COSY cross-peaks of H-6/H-7 and H-1/H-9 further supported this presumption. Finally, the two oxygenated groups were adjacent to C-5 (δ_C 74.4) and C-8 (δ_C 79.4) as established by 1D and 2D NMR analyses.

The relative configuration of **1** was elucidated by a ROESY experiment and by comparison of the NMR data with those reported for valepotriates. Comparing NMR data indicated that the 5-OH and H-9 were both *β*-oriented.[3,16−20] H-1should be α-oriented since all the naturally occurring valepotriates exhibit α-orientation.[3,16−20] The key ROESY correlations of H-10b/H-1 and H-10a/H-7, as shown in the molecular model (Figure 2), indicated *β*-orientation of 8-OH and α-orientation of H-7. No correlations were observed between H-7 and H-9 and between H-9 and H-10. The α-orientation of C-10 was confirmed by NOEs between H-1/H-10b and between H-7/H-10a in 1D NOE experiments. Thus, the structure of **1** was determined, and it was named volvatrate A.

Compound **2** possessed a molecular formula of $C_{27}H_{41}O_{11}Cl$ as established by HRESIMS (*m/z* 599.2243 $[M + Na]^+$). The IR spectrum had absorption bands at 3447 cm^{-1}(OH), 1742 cm^{-1} (C═O), and 1638 cm^{-1} (C═C). The ^1H and ^{13}C NMR spectra (Table 1) had signals that were characteristic of valepotriates.[3,16−20] The signals at δ_H 6.56 and δ_C 89.3 were assigned to H-1 and C-1 attached to two oxygen atoms. The two olefinic carbons at δ_C 144.7 (CH) and 112.8 (qC) were assigned to C-3 and C-4 as in usual iridoid compounds. Comparison of the NMR data (Table 1) with jatamanvaltrate B showed that compound **2** had a similar skeleton, except for a downfield shift of δ_C 49.7 (C-10, $\Delta = -17.6$ ppm),[17] which suggested that C-10 was connected with a polar atom.[19] The presence of a chlorine atom was confirmed by HRESIMS and the appearance of a $[M + Na + 2]^+$ ion peak at 601 due to the chlorine isotopes present in the ESI mass spectrum. Further analysis of its ^1H and ^{13}C NMR data and comparison with those of the reported valpotriates indicated the presence of an acetate, an isovalerate group, and an isovaleroyloxyisovaleryl moiety in the molecule.[3,16−20] The correlations from H-2′ (δ_H 4.77) to C-1″ (δ_C 173.2) and C-1′ (δ_C 169.9) in the HMBC spectrum supported the presence of an isovaleroyloxyisovaleryl moiety in **2**. Attachments of acyloxy

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10.1021/np9003382 CCC: $40.75
Published on Web 08/19/2009

Table 1. NMR Data[a] for Volvatrate A (**1**) and Volvatrate B (**2**) in $CDCl_3$

	volvatrate A (**1**)		volvatrate B (**2**)	
position	δ_C, mult	δ_H (J in Hz)	δ_C, mult	δ_H (J in Hz)
1	91.2, CH	6.56, d (2.2)	89.3, CH	6.56, s
3	96.3, CH	5.41, s	144.7, CH	6.60, s
4	149.9, qC		112.8, qC	
5	74.4, qC		70.1, qC	
6a (β-H)	47.1, CH_2	2.28, d (16.0)	40.7, CH_2	2.07, m
6b (α-H)		2.60, dd (16.0, 6.6)		2.60, dd (13.6, 6.1)
7	79.0, CH	4.95, t (6.4)	79.7, CH	4.97, t (7.0)
8	79.4, qC		70.1, qC	
9	57.3, CH	2.67, s	54.1, CH	2.71, s
10a	66.7, CH_2	3.67, 1H, AB, (12.3)	49.7, CH_2	3.67, 1H, AB (11.5)
10b		4.00, 1H, AB, (12.3)		3.73, 1H, AB (11.5)
11a	110.5, CH_2	5.15, s	61.9, CH_2	4.67, 1H, AB (12.4)
11b		5.39, s		4.90, 1H, AB (12.4)
1′			169.9, qC	
2′			76.7, CH	4.77, d (4.8)
3′			29.8, CH	2.22, m
4′			17.3, CH_3	1.00, d (6.6)
5′			18.6, CH_3	0.99, d (6.6)
1″			173.2, qC	
2″			43.0,[e] CH_2	2.24,[i] m
3″			25.6,[h] CH	2.07,[j] m
4″			22.3,[f] CH_3	0.96,[k] d, (6.6)
5″			22.3,[f] CH_3	0.96,[k] s, (6.6)
1‴	170.9,[b−k] qC		170.7,[g] qC	
2‴	43.3, CH_2	2.19, m	43.0,[e] CH_2	2.24,[i] m
3‴	25.7, CH	2.05, m	25.7,[h] CH	2.07,[j] m
4‴	22.3,[c] CH_3	0.96,[d] d (6.5)	22.4,[f] CH_3	0.95,[k] d, (6.6)
5‴	22.3,[c] CH_3	0.94,[d] d (6.5)	22.4,[f] CH_3	0.95,[k] d, (6.6)
1⁗	170.9,[b−k] qC		170.6,[g] qC	
2⁗	21.1, CH_3	2.17, s	20.8, CH_3	2.09, s

[a] ^{1}H NMR at 500 MHz, ^{13}C NMR at 125 MHz, and multiplicities inferred from DEPT and HSQC experiments. [b−k] Assignments bearing the same superscript may be interchanged in each column.

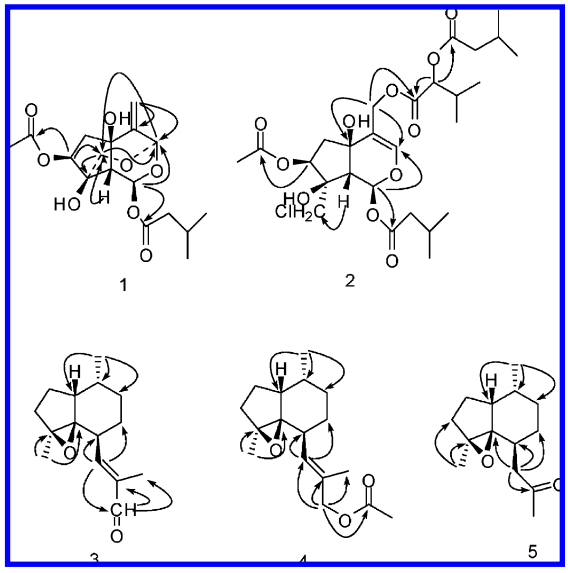

Figure 1. Key HMBC correlations for **1**−**5**.

substituents to the iridoid nucleus were assigned by the HMBC correlations as shown in Figure 1. The isovalerate group was attached to C-1 by the HMBC correlation from H-1 (δ_H 6.56) to C-1‴ (δ_C 170.7). The acetate group linked to C-7 and the isovaleroyloxyisovaleryl moiety to C-11 were established by the HMBC correlations from H-7 (δ_H 4.97) to C-1⁗ (δ_C 170.6) and from H-11 (δ_H 4.90, 4.67) to C-1′ (δ_C 169.9), respectively. The relative configurations of **2** at C-1, C-5, C-7, C-8, and C-9 were the same as those in compound **1**, which were determined by the key ROESY correlations of H-1/H-10 and H-10/H-7 as shown in Figure 2. Thus, the structure of compound **2** was established, and it was named volvatrate B.

Compounds **3**, **4**, and **5** were obtained as colorless oils from the petroleum ether extract. The molecular formula of **3** was deduced as $C_{15}H_{22}O_2$ by HRESIMS (m/z 257.1524 $[M + Na]^+$). The ^{13}C NMR and DEPT spectra of **3** (Table 2) showed a total of 15 carbon signals, including three methyl, four methlene, five methine, and three quaternary carbons, indicating a valerenane sesquiterpenoid skeleton, often reported in this plant.[4] The IR spectrum revealed the presence of a conjugated group consisting of an aldehyde function (1688 cm^{-1}) and a double bond (1640 cm^{-1}), which was confirmed by the HMBC correlation from H-14 (δ_H 9.45) to C-11 (δ_C 153.7) and C-12 (δ_C 140.2). Comparison of the NMR spectroscopic data with those reported for valerenal[4] indicated that **3** had a structure similar to that of valerenal, except for upfield shifts of C-3 (δ_C 70.4) and C-4 (δ_C 71.2) in **3**. This suggested that the double bond between C-3 and C-4 in valerenal was a 3,4-epoxy analogue in **3**, similar to that in (−)-3β,4β-epoxyvalerenic acid.[21] HMBC correlations (Figure 1) from H-10 (δ_H 1.43) to C-3 and C-4 confirmed the 3,4-epoxy group in **3**. The HMBC correlations from H-11 (δ_H 6.87) to C-4, C-5 (δ_C 34.7), C-6 (δ_C 24.3), and C-14 (δ_C 195.4) and correlations from H-5 (δ_H 2.76) to C-11 and C-12 indicated that the α,β-unsaturated aldehyde function was attached to C-5 as in valerenal. The relative configuration of **3** was elucidated by the ROESY experiment and comparison with other naturally occurring valerenane sesquiterpenoids possessing a β-orientation of H-9 and H-8 and an α-orientation of H-5.[4,21] The orientations were further confirmed by ROESY correlations of H-8/H-9 and H-9/H-11 (Figure 2). The ROESY correlations of H-5 with H-10 established the α-orientation of 10-CH_3, and H-11 with H-14 (δ_H 9.45) indicated the E configuration of the double bond between C-11 and C-12. The specific rotation was negative ($[\alpha]^{20}_D$ −83.3, c 0.25, MeOH). Therefore, compound **3** was determined to be E-(−)-3β,4β-epoxyvalerenal.

The molecular formula of compound **4** was determined as $C_{17}H_{26}O_3$ by HRESIMS. The IR spectrum indicated the presence of a carbonyl (1740 cm^{-1}) and a double bond (1628 cm^{-1}). The

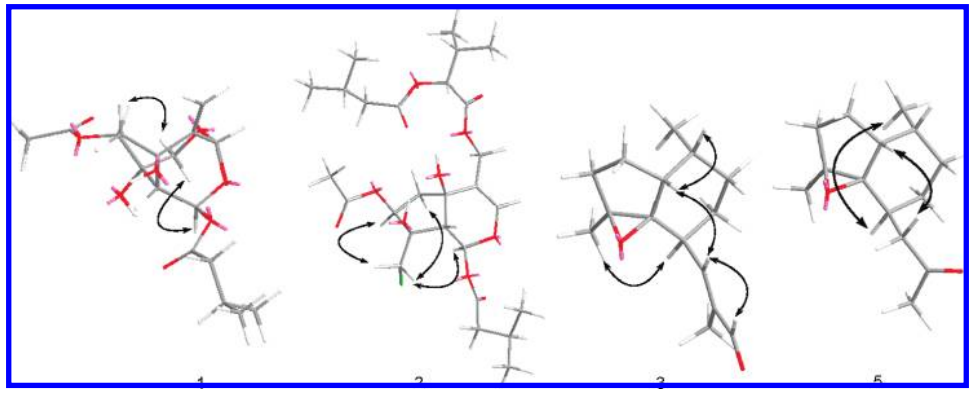

Figure 2. Key ROESY correlations for **1**−**3** and **5**.

Table 2. NMR Data[a] for Compounds **3**−**5** in $CDCl_3$

	compound **3**		compound **4**		compound **5**	
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)
1a	23.9, CH_2	1.35, m	23.9, CH_2	1.27, m	23.9, CH_2	1.49, m
1b		1.60, m		1.59, m		1.76, m
2a	32.7, CH_2	1.63, m	32.9, CH_2	1.62, m	32.8, CH_2	1.60, m
2b		1.86, m		1.84, m		1.82, m
3	70.4, qC		70.3, qC		71.8, qC	
4	71.2, qC		72.1, qC		72.0, qC	
5	34.7, CH	2.76, m	33.3, CH	2.50, m	30.4, CH	1.25, m
6a	24.3, CH_2	1.64, m	24.9, CH_2	1.53, m	23.6, CH_2	1.27, m
6b		1.96, m		1.83, m		1.53, m
7a	27.5, CH_2	1.45, m	27.1, CH_2	1.36, m	26.6, CH_2	1.33, m
7b		1.80, m		1.79, m		1.68, m
8	32.7, CH	2.09, m	32.9, CH	2.06, m	32.7, CH	1.99, m
9	41.0, CH	2.45, t, (7.5)	40.9, CH	2.36, t (7.4)	40.9, CH	2.25, m
10	15.2, CH_3	1.43, s	5.2, CH_3	1.40, s	15.0, CH_3	1.38, s
11	153.7, CH	6.87, d (9.4)	129.2,CH	5.89, d (9.2)	43.7, CH_2	2.70, d, (7.0)
12	140.2, qC		131.3, qC		208.3, qC	
13	9.5, CH_3	1.77, s	14.3, CH_3	1.67, s	30.1, CH_3	2.16, s
14	195.4, CH	9.45, s	70.3, CH_2	4.49, dd (15.6, 12.2)	13.8, CH_3	0.81, d, (7.3)
15	13.8, CH_3	0.89, d (7.3)	14.0, CH_3	0.85, d, (7.2)		
16			171.0, qC			
17			21.0, CH_3	2.07, s		

[a] ^{1}H NMR at 400 MHz, ^{13}C NMR at 100 MHz, and multiplicities inferred from DEPT and HSQC experiments.

^{13}C NMR and DEPT spectra of **4** (Table 2) indicated that the molecule contained four methyl, five methlene, four methine, and four quaternary carbons. The ^{1}H NMR spectrum showed four methyl groups (δ_H 1.40, 1.67, 0.85, 2.07) and an olefinic methine (δ_H 5.89). The ^{1}H and ^{13}C NMR spectra of **4** were similar to those of **3** except that the aldehydic function (δ_C 195.4) in **3** was replaced by a $-CH_2OOCCH_3$ (δ_C 70.3, 171.0, 21.0) group in **4**, which was confirmed by the HMBC correlations from H-14 (δ_H 4.49) to C-16 (δ_C 171.0), C-11 (δ_C 129.2), C-12 (δ_C 131.3), and C-13 (δ_C 14.3). The relative configuration of **4** was consistent with that of **3**. ROESY correlation of H-11 (δ_H 5.89) with H-14 (δ_H 4.49) established the *E* configuration of the double bond at C-11 and C-12. The optical activity of **4** was negative; thus, compound **4** was identified as *E*-(−)-3β,4β-epoxyvalerenyl acetate.

Compound **5** had the molecular formula $C_{14}H_{22}O_2$, by HRESIMS, with 4 degrees of unsaturation. The ^{13}C NMR and DEPT spectra (Table 2) showed only14 carbon signals in accordance with the HRESIMS, including three methyl, five methylene, three methine, and three quaternary carbons. The NMR spectra of **5** were similar to those of **3** and **4** except that the side chain at C-5 only had three carbons in **5**. The five methylene signals were assigned to C-1, C-2, C-6, C-7, and C-11, respectively, and the two quaternary carbon signals were assigned to C-3 and C-4 by comparison of the 1D NMR and 2D NMR spectra with those of **3** and **4**. The appearance of a quaternary carbon at δ_C 208.3 (C-12) revealed the presence of a ketonic carbonyl in the molecule, which was confirmed by the IR absorption at 1714 cm^{-1}. HMBC correlations from H-13 (δ_H 2.16) to C-12 and C-11 (δ_C 43.7) and from H-11 (δ_H 2.70) to C-12, C-4 (δ_C 72.0), C-5 (δ_C 30.4), and C-6 (δ_C 22.6) indicated that there was a $-CH_2COCH_3$ group attached to C-5. The two methyl groups were attached to C-3 and C-8, respectively, which was established by the HMBC correlations from H-10 (δ_H 1.38) to C-3 and C-2 (δ_C 32.8) and from H-14 (δ_H 0.81) to C-7 (δ_C 26.6), C-8 (δ_C 32.7), and C-9 (δ_C 40.9). H−H COSY correlations of H-1/H-2, H-6/H-7, H-8/H-9, H-9/H-1, and H-8/H-14 confirmed the carbon linkages in the molecule. The relative configuration of **5** was also consistent with **3** and **4**, which was supported by a ROESY experiment. The ROESY correlations of H-9/H-11 and H-5/H-14 verified the α-orientation of H-5 and β-orientation of H-8 as shown in Figure 2. The 10-CH_3 was determined to be α-oriented by comparison of the NMR data with compounds **3**, **4**, and (−)-3β,4β-epoxyvalerenic acid.[21] Thus, the structure of **5** was assigned, and it was named mononorvalerenone.

Experimental Section

General Experimental Procedures. Optical rotations were taken on a Horiba SEAP-300 polarimeter. UV spectra were obtained on a Hitachi UV 210A spectrophotometer. IR spectra were measured with a Bio-Rad FTS-135 spectrometer with KBr pellets. Mass spectra were obtained on a VG Auto Spec-3000 mass spectrometer (VG, Manchester, England). 1D and 2D NMR spectra were recorded on a Bruker AM-400 or a DRX-500 NMR spectrometer (Karlsruhe, Germany). Semi-preparative HPLC were performed on an Agilent 1100 liquid chromatograph with a Zorbax SB-C18 (9.4 mm × 25 cm) column. Column chromatography was performed either on silica gel (200−300 mesh,

Qindao Marine Chemical Inc., Qingdao, People's Republic of China) or RP-18 gel (LiChroprep, 40−63 μm, Merck, Darmstadt, Germany). Sephadex LH-20 for chromatography was purchased from Amersham Biosciences. Fractions were monitored by TLC, and spots were visualized by heating silica gel plates sprayed with 10% H_2SO_4 in EtOH.

Plant Material. The plant, cultivated from the seeds of *V. officinalis* (purchased from Germany) at Songhuaba in Kunming, Yunnan Province, P. R.China, in March 2007, was collected in January 2008 and identified as *V. officinalis* Linn. by Prof. Hu-Biao Chen, School of Pharmaceutical Sciences, Peking University, P. R. China. A voucher specimen (KIB-XC0701) was preserved at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, the Chinese Academy of Sciences, P. R. China.

Extraction and Isolation. Dried root powder of *V. officinalis* (5 kg) was extracted with 95% EtOH at room temperature to give a residue (1 kg) after removal of solvent under reduced pressure. The EtOH extract was suspended in H_2O (3 L) and then partitioned successively with petroleum ether (3 × 2 L), EtOAc (3 × 2 L), and *n*-BuOH (3 × 2 L). The petroleum ether extract (106 g) was subjected to silica gel column chromatography (CC) eluted with petroleum ether−acetone (from 100:1 to 1:1) to afford fractions A−H. Fraction B (15 g) was subjected to CC over silica gel (200−300 mesh) eluted with petroleum ether−EtOAc (from 50:1 to 1:1) to give four fractions, Ba−Bd. Valerenic acid (387 mg) was crystallized from a Me_2CO solution of fraction Ba. Fraction Bb was chromatographed over a Sephadex LH-20 column, using $CHCl_3$−MeOH (1:1) as solvent, and then purified by semipreparative HPLC (CH_3CN-H_2O, 40:60) to yield **3** (5 mg), **4** (8 mg), and **5** (5 mg). Fraction C (5 g) was subjected to CC over silica gel eluted with petroleum ether−EtOAc (10:1 to 1:1) to afford three fractions, Ca−Cc. Fraction Ca was chromatographed over an RP-18 column eluted with a MeOH−H_2O gradient system (60%−100%) to afford acetoxyvalerenic acid (50 mg). The EtOAc extract (80 g) was subjected to CC over silica gel eluted with petroleum ether−EtOAc (from 50:1 to 1:1) to give six fractions, Fr1−Fr6. Fraction 3 was chromatographed over silica gel eluted with petroleum ether−EtOAc (from 10:1 to 1:1) to afford four fractions, Fr3a−Fr3d. Fr3a was purified over a Sephadex LH-20 column eluted with $CHCl_3$−MeOH (1:1) to obtain IVHD-valtrate (180 mg). Fr3b was purified by a RP-18 column eluted with a MeOH−H_2O gradient system (50%−100%) and repeated chromatography over silica gel using petroleum ether−EtOAc (5:1 to 1:1) and then chromatographed over a Sephadex LH-20 column eluted with $CHCl_3$−MeOH (1:1) and purified by semipreparative HPLC (CH_3CN-H_2O, 35:65) to afford **1** (3 mg), **2** (7 mg), 1,5-dihydroxy-3,8-epoxyvalechlorine (38 mg), valeteriotriate B (8 mg), jatamanvaltrate B (6 mg), and jatamanvaltrate C (12 mg).

Volvatrate A (1): colorless oil; $[\alpha]^{20}_D$ −34.9 (*c* 0.18, CH_3OH); IR (KBr) ν_{max} 3448, 2961, 2874, 1737, 1626, 1374, 1248, 1104 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) data, see Table 1; ESIMS *m/z* 379 $[M + Na]^+$; HRESIMS *m/z* 379.1362 $[M + Na]^+$ (calcd for $C_{17}H_{24}O_8Na$, 379.1368).

Volvatrate B (2): colorless oil; $[\alpha]^{20}_D$ −72.3 (*c* 0.30, $CHCl_3$); IR (KBr) ν_{max} 3447, 2965, 2926, 1742, 1638, 1374, 1242 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) data, see Table 1; positive ESIMS *m/z* 599 $[M + Na]^+$; HRESIMS *m/z* 599.2243 $[M + Na]^+$ (calcd for $C_{27}H_{41}O_{11}ClNa$, 599.2235).

***E*-(−)-3*β*,4*β*-Epoxyvalerenal (3):** colorless oil; $[\alpha]^{20}_D$ −83.3 (*c* 0.25, MeOH); IR (KBr) ν_{max} 2931, 1688, 1640, 1422, 1107 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) data, see Table 2; positive ESIMS *m/z* 257 $[M + Na]^+$; HRESIMS *m/z* 257.1524 $[M + Na]^+$ (calcd for $C_{15}H_{22}O_2Na$, 257.1517).

***E*-(−)-3*β*,4*β*-Epoxyvalerenyl acetate (4):** colorless oil; $[\alpha]^{20}_D$ −52.63 (*c* 0.19, MeOH); IR (KBr) ν_{max} 3070, 2929, 1740, 1628, 1456, 1379, 1290, 1235, 1047, 1024, 959 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) data, see Table 2; positive ESIMS *m/z* 301 $[M + Na]^+$; HRESIMS *m/z* 301.1773 (calcd for $C_{17}H_{26}O_3Na$ 301.1779).

Mononorvalerenone (5): colorless oil; $[\alpha]^{20}_D$ −39.29 (*c* 0.28. MeOH); IR (KBr) ν_{max} 2926, 2861, 1714, 1454, 1385, 1284, 1084 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) data, see Table 2; positive ESIMS *m/z* 245 $[M + Na]^+$; HRESIMS *m/z* 245.1511 (calcd for $C_{17}H_{26}O_3Na$ 245.1517).

Acknowledgment. This work was supported by the fund (P2008-ZZ22) of State Key Laboratory of Phytochemistry and Plant Resources in West China and Natural Science Foundation of Yunnan (2008CD159). The authors thank Dr. X.-H. Cai for initial proofreading of the document and the members of the analytical group of the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, for the spectral measurements.

Supporting Information Available: 1D and 2D NMR spectra of compounds **1**−**5**. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Houghton, P. J. *J. Ethnopharmacol.* **1988**, *22*, 121–142.
(2) Yager, J.; Siegfreid, S. L.; DiMattero, T. L. *Am. J. Psych.* **1999**, *156*, 1432–1438.
(3) Tang, Y. P.; Liu, X.; Yu, B. *J. Nat. Prod.* **2002**, *6*, 1949–1952.
(4) Bos, R.; Hendriks, H.; Bruins, A. P.; Kloosterman, J.; Sipma, G. *Phytochemistry* **1985**, *25*, 133–135.
(5) Ming, D. S.; Yu, D. Q.; Yang, Y. Y.; He, C. M. *Tetrahedron Lett.* **1997**, *38*, 5205–5208.
(6) Kurt, T.; Kerstin, W. *Tetrahedron Lett.* **1966**, *7*, 445–448.
(7) Piccinelli, A. L.; Arana, S.; Caceres, A.; Roberta, E. B.; Raffaella, S.; Luca, R. *J. Nat. Prod.* **2004**, *67*, 1135–1140.
(8) Tang, Y. P.; Liu, X.; Yu, B. *J. Asian Nat. Prod. Res.* **2003**, *5*, 257–261.
(9) Leathwood, P. D.; Chauffard, F.; Heck, E.; Munoz-Box, R. *Pharmacol., Biochem. Behav.* **1982**, *17*, 65–71.
(10) Morazzoni, P.; Bombardelli, E. *Fitoterapia* **1995**, *66*, 99–112.
(11) Miguel, H.; Feistelb; Hartwig, S.; Romanus, L.; Mirjam, H.; Hilke, W. *Phytomedicine* **2008**, *15*, 2–15.
(12) Hazelhoff, B.; Smith, D.; Malingre, T. M. *Arch. Int. Pharmacodyn.* **1982**, *257*, 274–287.
(13) Murakami, N.; Ye, Y.; Kawanishi, M.; Aoki, S.; Kudo, N.; Yoshida, M.; Nakayama, E.; Shiodac, T.; Kobayashia, M. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 2807–2810.
(14) Clara, C.; Rita, D. P.; Stefania, S.; Annalisa, P.; Francesco, O. *J. Ethnopharmacol.* **2007**, *112*, 361–367.
(15) Mikhova, B. P.; Handjieva, N. V.; Popov, S. S.; Spassov, S. L. *J. Nat. Prod.* **1987**, *50*, 1141–1145.
(16) Wang, R.; Xiao, D.; Bian, Y. H.; Zhang, X. Y.; Li, B. J.; Ding, L. S.; Peng, S. L. *J. Nat. Prod.* **2008**, *71*, 1254–1257.
(17) Yu, L. L.; Huang, R.; Han, C. R.; Lv, Y. P.; Zhao, Y.; Chen, Y. G. *Helv. Chim. Acta* **2005**, *88*, 1059–1061.
(18) Lin, S.; Shen, Y. H.; Li, H. L.; Yang, X. W.; Chen, T.; Lu, L. H.; Huang, Z. S.; Liu, R. H.; Xu, X. K.; Zhang, W. D.; Wang, H. *J. Nat. Prod.* **2009**, *72*, 650–655.
(19) Yang, X. P.; Yuan, C. S.; Jia, Z. J. *Chin. Chem. Lett.* **2006**, *17*, 337–340.
(20) Yu, L. L.; Han, C. R.; Huang, R.; Lv, Y. P.; Gui, S H.; Chen, Y. G. *Pharmazie* **2006**, *61*, 486–488.
(21) Pharmaratne, H. R.; Nanayakkara, N. P.; Khan, I. K. *Planta Med.* **2002**, *15*, 661–662.

NP9003382