New Diterpenoid Alkaloids from *Aconitum liangshanicum*

by **Zhong-Tang Zhang**, **Xiao-Yu Liu**, **Dong-Lin Chen***, and **Feng-Peng Wang**

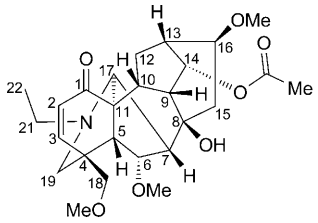
Department of Chemistry of Medicinal Natural Products, West China College of Pharmacy, Sichuan University, No. 17, Duan 3, Renmin Nan Road, Chengdu 610041, P. R. China (phone/fax: +86-28-5501368; e-mail: chendl@scu.edu.cn)

One new C_{19}-diterpenoid alkaloid, named liangshantine (**1**), and three new C_{20}-diterpenoid alkaloids, liangshansines A – C (**2** – **4**, resp.), as well as eight known compounds, were isolated from the roots of *Aconitum liangshanicum*. The structures of these new alkaloids were elucidated by spectroscopic methods.

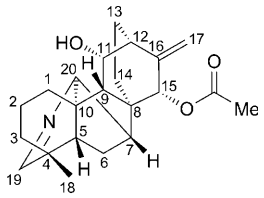
Introduction. – Diterpenoid alkaloids, with intriguing chemistry and various bioactivities, constitute a large and complicated group of terpenoid alkaloids [1]. A large number of diterpenoid alkaloids have been isolated from species of genera *Aconitum* and *Delphinium*, and are structurally classified as C_{18}-, C_{19}-, and C_{20}-diterpenpoid alkaloids [2].

The genus *Aconitum*, which comprises *ca.* 400 species, is well-known to comprise poisonous and medicinal plants, more than a half of them growing in China [3]. As a part of our continuing phytochemical investigations on this genus [4 – 6], we have now studied the roots of *Aconitum liangshanicum* W. T. WANG [7], which is native to the southwest area of Sichuan province in China. Consequently, four new diterpenoid alkaloids, including one new C_{19}-diterpeniod alkaloid, named liangshantine (**1**), and three new C_{20}-diterpenoid alkaloids, liangshansines A – C (**2** – **4**, resp.), were obtained. In addition, eight known compounds were also isolated and identified as bullatine B [8], bullatine C [8], denudatine [9], jynosine [10], kirinine A [11], kirinine B [12], lepenine [13], and tongolinine [14]. In this article, we report the isolation and structure determination of the new alkaloids **1** – **4**.

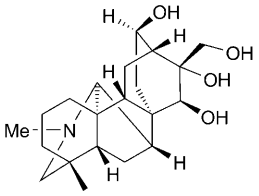
Results and Discussion. – Liangshantine (**1**), an amorphous powder, has the molecular formula $C_{26}H_{37}NO_7$, as determined by the *pseudo*-molecular ion peak in the HR-ESI-MS experiment (calc. for $[M + H]^+$: 476.2648; found: 476.2642). The IR spectrum indicated the presence of an OH group (3503 cm^{-1}), a C=O group (1740 cm^{-1}), and a C=C bond (1673 cm^{-1}). The ^{1}H-NMR spectrum (*Table 1*) showed the presence of a typical EtN group (δ(H) 0.98 (*t*, *J* = 7.2, 3 H) and 2.39 – 2.45 (*m*, 2 H), three MeO groups (δ(H) 3.26, 3.27, 3.38 (3*s*)), an AcO group (δ(H) 2.07 (*s*)), and a characteristic disubstituted C=C bond (δ(H) 6.22, 6.50 (2*d*, *J* = 10.4)). The ^{13}C-NMR and DEPT data (*Table 1*) of **1** demonstrated the presence of five Me, five CH_2, eleven CH, and five quaternary C-atoms. The above-mentioned data revealed that compound **1** was an aconitine-type C_{19}-diterpenoid alkaloid [15]. The three MeO groups could be



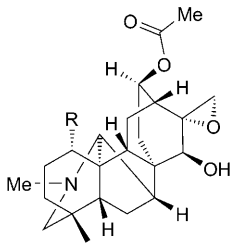
1



2



3



4 R = H
5 R = OH

Table 1. *^{1}H- and ^{13}C-NMR Data of* **1**. In $CDCl_3$; δ in ppm, J in Hz.

	δ(H)	δ(C)		δ(H)	δ(C)
C(1)	–	200.6 (*s*)	H–C(14)	4.90 (*t*, J = 4.8)	76.8 (*d*)
H–C(2)	6.22 (*d*, J = 10.4)	131.7 (*d*)	CH_2(15)	1.97–2.02 (*m*, H_a)	42.3 (*t*)
H–C(3)	6.50 (*d*, J = 10.4)	147.7 (*d*)		2.39–2.45 (*m*, H_b)	
C(4)	–	49.4 (*s*)	H–C(16)	3.18 (*t*, J = 8.0)	81.9 (*d*)
H–C(5)	3.05 (*d*, J = 6.4)	48.6 (*d*)	H–C(17)	2.46–2.50 (*m*)	60.7 (*d*)
H–C(6)	4.20 (*d*, J = 6.8)	81.8 (*d*)	CH_2(18)	3.89, 3.84 (*AB*, J = 8.4)	72.0 (*t*)
H–C(7)	2.22–2.24 (*m*)	53.5 (*d*)	CH_2(19)	2.46–2.50 (*m*, H_a),	51.3 (*t*)
C(8)	–	74.6 (*s*)		2.66–2.70 (*m*, H_b)	
H–C(9)	2.22–2.24 (*m*)	40.9 (*d*)	CH_2(21)	2.39–2.45 (*m*)	48.5 (*t*)
H–C(10)	2.66–2.70 (*m*)	36.4 (*d*)	Me(22)	0.98 (*t*, J = 7.2)	12.9 (*q*)
C(11)	–	50.9 (*s*)	*Me*O–C(6)	3.38 (*s*)	57.9 (*q*)
CH_2(12)	1.33–1.38 (*m*, H_a),	31.1 (*t*)	*Ac*O–C(14)	2.07 (*s*)	170.0 (*s*), 20.8 (*q*)
	2.39–2.45 (*m*, H_b)		*Me*O–C(16)	3.26 (*s*)	56.0 (*q*)
H–C(13)	2.39–2.45 (*m*)	45.7 (*d*)	*Me*O–C(18)	3.27 (*s*)	59.0 (*q*)

located at C(6), C(16), and C(18), respectively, according to their HMBCs (*Fig. 1*). The AcO group was placed at C(14), due to the HMBCs from H–C(14) to C(8), C(10), C(16), and the C=O C-atom of the AcO group. The HMBCs observed from H–C(16), H–C(6), H–C(14), and H–C(9) to the quaternary C(8) (δ(C) 74.6, *s*) suggested that the OH group was attached to C(8). In addition, a rare α,β-unsaturated ketone was determined according to the two characteristic H-atoms at δ(H) 6.22, 6.50 (*d*, J = 10.4, each 1 H), together with the C-atom signals at δ(C) 131.7 (*d*), δ(C) 147.7 (*d*), and δ(C) 200.6 (*s*). The HMBCs between H–C(3)/C(1), H–C(3)/C(5), H–C(3)/

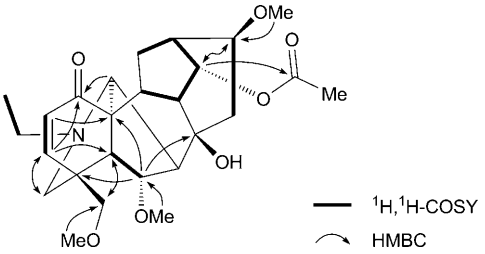


Fig. 1. *Key ^{1}H,^{1}H-COSY correlations and HMBCs of liangshantine* (**1**)

C(19), H−C(17)/C(1), and H−C(2)/C(11), demonstrated that the C=O group is located at C(1), and the C=C bond between C(2) and C(3). The above evidence strongly suggested the structure of liangshantine as depicted in **1**. The relative configuration of **1** was confirmed by comparing it with the known compound bullatine C (=(1α,6α,14α,16β)-14-(acetyloxy)-20-ethyl-6,16,18-trimethoxyaconitane-1,8-diol) [8]. Hence, the structure of **1** was established as (6α,14α,16β)-14-(acetyloxy)-20-ethyl-8-hydroxy-6,16,18-trimethoxyaconit-2-en-1-one.

Liangshansine A (**2**) was obtained as a white powder. The molecular formula was established as $C_{22}H_{29}NO_3$, derived from the HR-ESI-MS spectrum (calc. for $[M+H]^+$: 356.2226; found: 356.2213). The ^{13}C-NMR (DEPT) data (*Table 2*) indicated five quaternary C-atoms, and eight CH, seven CH_2, and two Me groups. Coupled with the ^{1}H-NMR spectrum, a typical exocyclic C=C bond (δ(H) 5.01, 4.94, *s*, each 1 H), a C=N azomethine (δ(H) 7.17, *s*), and an AcO group (δ(H) 2.16, *s*, 3 H) were found. It was evident that compound **2** was a denudatine-type C_{20}-diterpenoid alkaloid [2]. The HMBCs (*Fig. 2*) from H−C(15) to C(9), C(7), C(12), C(17), and the C=O C-atom of AcO indicated that the AcO group was attached to C(15). The OH group should be positioned at C(11) because of the correlations observed between H−C(11) and C(16), C(8), C(10), and C(13). The correlations from H−C(19) to C(3), C(5), and C(18) showed that the C=N bond was assigned between N and C(19). The coupling constant between H−C(11) with H_β−C(9) (J = 9.2 Hz) indicated a 1,2-diaxial relationship, implying that HO−C(11) was α-oriented. The correlations between H−C(15) and H_β−C(9) in the NOESY experiment revealed that AcO−C(15) was in α-orientation. Accordingly, the structure of liangshansine A was established as (11α,15α)-15-(acetyloxy)-11-hydroxydenudat-16-ene.

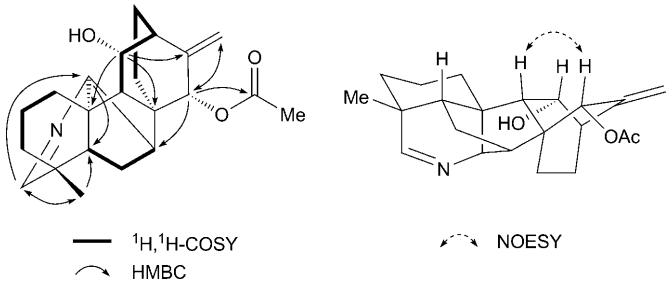


Fig. 2. *Key ^{1}H,^{1}H-COSY, HMBC, and NOESY correlations of liangshansine A* (**2**)

Table 2. *^{1}H- and ^{13}C-NMR Data of Compounds* **2**–**4**. In $CDCl_3$; δ in ppm, J in Hz.

	2		**3**		**4**	
	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)
CH_2(1)	26.4 (*t*)	0.80–0.89 (*m*)	23.9 (*t*)	0.96 (*t*, J = 12.8)	26.3 (*t*)	1.12–1.32 (*m*, H_a), 1.59–1.60 (*m*, H_b)
CH_2(2)	20.3 (*t*)	0.80–0.89 (*m*)	21.6 (*t*)	1.31–1.39 (*m*)	20.5 (*t*)	1.40–1.47 (*m*, H_a), 2.23–2.29 (*m*, H_b)
CH_2(3)	34.5 (*t*)	1.39–1.49 (*m*, H_a), 1.18–1.25 (*m*, H_b)	41.2 (*t*)	1.52–1.56 (*m*, H_a), 1.21–1.22 (*m*, H_b)	39.9 (*t*)	1.40–1.47 (*m*, H_a), 1.81–1.86 (*m*, H_b)
C(4)	44.1 (*s*)	–	35.2 (*s*)	–	34.0 (*s*)	–
H–C(5)	48.7 (*d*)	1.29–1.34 (*m*)	53.8 (*d*)	1.10–1.15 (*m*)	51.9 (*d*)	1.12–1.32 (*m*)
CH_2(6)	24.6 (*t*)	1.29–1.34 (*m*)	23.8 (*t*)	1.18–1.22 (*m*, H_a), 2.66–2.70 (*m*, H_b)	23.1 (*t*)	1.12–1.32 (*m*, H_a), 2.61–2.66 (*m*, H_b)
H–C(7)	47.6 (*d*)	2.09–2.11 (*m*)	43.5 (*d*)	2.07–2.08 (*m*)	41.9 (*d*)	1.81–1.86 (*m*)
C(8)	44.7 (*s*)	–	44.4 (*s*)	–	43.3 (*s*)	–
H–C(9)	57.2 (*d*)	1.34 (*d*, J = 9.2)	40.6 (*d*)	1.63–1.70 (*m*)	43.9 (*d*)	2.23–2.29 (*m*)
C(10)	45.0 (*s*)	–	46.2 (*s*)	–	45.0 (*s*)	–
H–C(11) or CH_2(11)	71.4 (*d*)	3.81 (*d*, J = 9.2)	27.4 (*t*)	1.31–1.39 (*m*, H_α), 1.77–1.83 (*m*, H_β)	22.8 (*t*)	1.28–1.32 (*m*, H_α), 1.73–1.78 (*m*, H_β)
H–C(12)	46.6 (*d*)	2.22–2.27 (*m*)	40.1 (*d*)	1.85–1.88 (*m*)	38.7 (*d*)	1.73–1.78 (*m*)
CH_2(13) or H–C(13)	23.6 (*t*)	1.53–1.64 (*m*, H_a), 1.71–1.79 (*m*, H_b)	72.2 (*d*)	3.94 (br. *d*, J = 10.0)	71.5 (*d*)	4.82 (*dd*, J = 9.2, 2.8)
CH_2(14)	27.3 (*t*)	1.39–1.49 (*m*, H_α), 1.98–2.04 (*m*, H_β)	41.9 (*t*)	1.18–1.22 (*m*, H_α), 2.37–2.46 (*m*, H_β)	36.4 (*t*)	1.36–1.38 (*m*, H_α), 2.39–2.47 (*m*, H_β)
H–C(15)	77.1 (*d*)	5.44 (*s*)	88.1 (*d*)	4.09 (*s*)	76.9 (*d*)	4.18 (*s*)
C(16)	147.3 (*s*)	–	82.9 (*s*)	–	64.5 (*s*)	–
CH_2(17)	110.2 (*t*)	5.01 (*s*), 4.94 (*s*)	67.4 (*t*)	4.05 (*AB*, J = 11.2, H_a), 3.54 (*AB*, J = 11.2, H_b)	45.5 (*t*)	3.12 (*AB*, J = 5.2, H_a), 2.44 (*AB*, J = 5.2, H_b)
Me(18)	21.4 (*q*)	0.99 (*s*)	27.0 (*q*)	0.70 (*s*)	26.3 (*q*)	0.71 (*s*)
H–C(19) or CH_2(19)	169.9 (*d*)	7.17 (*s*)	60.7 (*t*)	2.30–2.34 (*m*, H_a), 2.40 (hidden, H_b)	59.4 (*t*)	2.16–2.20 (*m*, H_a), 2.39–2.47 (*m*, H_b)
H–C(20)	71.7 (*d*)	4.29 (*s*)	74.5 (*d*)	3.13 (*s*)	72.8 (*d*)	3.20 (br. *s*)
MeN			44.4 (*q*)	2.24 (*s*)	41.8 (*q*)	2.44 (*s*)
*Ac*O–C(13)					170.8 (*s*), 21.3 (*q*)	2.06 (*s*)
*Ac*O–C(15)	170.6 (*s*), 21.7 (*q*)	2.16 (*s*)				

Liangshansine B (**3**), with a molecular formula $C_{21}H_{33}NO_4$ (according to the HR-ESI-MS (calc. for $[M + H]^+$: 364.2488; found: 364.2477)), was obtained as colorless crystals. The NMR spectra (*Table 2*) showed 21 C-atoms, which consisted of four quaternary C-atoms, eight CH_2 groups, including one O-bearing CH_2 (δ(C) 67.4 (*t*)), seven CH, and two Me groups including a characteristic MeN (δ(C) 44.4 (*q*)). According to the above-mentioned data, it was concluded that compound **3** was a denudatine-type C_{20}-diterpenoid alkaloid [2]. Four OH groups are present in this molecule based on the NMR data and HR-ESI-MS spectrum, two of which are connected to C(16) (δ(C) 82.9 (*s*)) and C(17) (δ(C) 67.4 (*t*)), while the two additional OH groups are located at C(13) (δ(C) 72.2 (*d*)) and C(15) (δ(C) 88.1 (*d*)), respectively. All the evidence was detailed in the HMBCs shown in *Fig. 3*. The relative configuration of liangshansine B was deduced from the NOESY spectrum (*Fig. 3*). The NOESY correlations observed, H–C(9)/H_a–C(17), H–C(13)/H_α–C(11), and H–C(15)/H–C(14), revealed that H–C(13) and H–C(15) are α-oriented, and also HO–C(16) must be α. Therefore, the structure of **3** was elucidated as (13β,15β,16α)-13,15,16,17-tetrahydroxy-21-methyldenudatane.

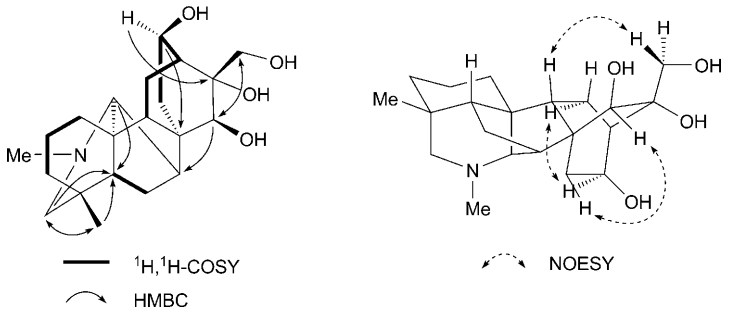


Fig. 3. *Key ^{1}H,^{1}H-COSY, HMBC, and NOESY correlations of liangshansine B* (**3**)

Liangshansine C (**4**) was isolated as a white powder, whose molecular formula was established as $C_{23}H_{33}NO_4$ by the HR-ESI-MS data (calc. for $[M + H]^+$: 388.2488; found: 388.2489). Compound **4** exhibited characteristic NMR features of a denudatine-type C_{20}-diterpenoid alkaloid [2] bearing five quaternary C-atoms, seven CH, eight CH_2, and three Me groups (*Table 2*). Selected ^{1}H- and ^{13}C-NMR resonances of **4** indicated the characteristic pattern of an epoxy group (δ(H) 3.12, 2.44 (*AB*, $J = 5.2$); δ(C) 64.5 (*s*), 45.5 (*t*)) instead of a typical exocyclic C=C bond in C_{20}-diterpenoid alkaloids. Comparison of the NMR data of **4** with those of gomandonine-3-*O*-acetate (**5**) [16] revealed that they were structurally similar, except for the presence of an additional OH group in the latter. The constitutional formula of **4** was further verified by the analyses of the HMBC and ^{1}H,^{1}H-COSY spectra (*Fig. 4*). The relative configuration was supported by the NOESY data shown in *Fig. 4*. The 16,17-epoxy group was assigned α-orientation, since the epoxy moiety exhibited nearly identical NMR data to those of two known alkaloids bearing a 16,17-epoxy segment, yesoxine [17] and gomandonine [18], whose structures were unambiguously determined by X-ray crystallography. Thus, the structure of **4** was deduced as (13β,15β,16α)-13-acetyoxy-

15-hydroxy-21-methyl-16,17-epoxydenudatane, and was given the trivial name liangshansine C.

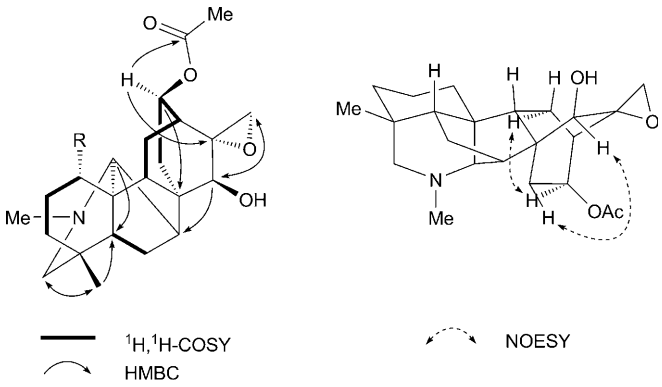


Fig. 4. *Key ^{1}H,^{1}H-COSY, HMBC, and NOESY correlations of liangshansine C* (**4**)

This research work was financially supported by the *National Natural Science Foundation of China* (No. 30672526 and No. 30873147).

Experimental Part

General. Silica gel *H* (*Qingdao Haiyang Chemical Group Co.*, P. R. China) were used for column chromatography (CC) and TLC, resp.; the spots were detected by the use of *Dragendorff*'s reagent. Optical rotations: *Perkin-Elmer 341* polarimeter. IR Spectra: *Nicolet FT-IR 200SXY* spectrophotometer; KBr pellets; in cm^{-1}. ^{1}H- and ^{13}C-NMR spectra: *Varian INOVA400/45* and *Bruker Advance600* spectrometer; in $CDCl_3$ with TMS as internal standard, δ in ppm. HR-MS: *VG Auto Spec3000* mass spectrometer.

Plant Material. Aconitum liangshanicum was collected in the Liangshan Mountains of Sichuan Province, China. The plant was authenticated by *W.-J. Zhang* of the Pengzhou County Center of Disease Prevention and Control. A specimen of this plant was deposited with the herbarium of the West China College of Pharmacy, Sichuan University.

Extraction and Isolation. Air-dried roots of *A. liangshanicum* (5.0 kg) were powdered and percolated with 0.05 mol/l HCl (75 l). The filtrate was alkalized to pH > 10 with 10% aq. $NH_3 \cdot H_2O$ and was extracted with AcOEt until the aq. phase contained no more alkaloids. Evaporation of AcOEt gave the crude alkaloids (25.0 g), which were chromatographed on SiO_2 (200 g) columns (petroleum ether (PE)/acetone 10:1 to 0:1) to give fractions *I* (2.1 g), *II* (3.6 g), *III* (3.1 g), *IV* (0.92 g), *V* (2.2 g), *VI* (1.1 g), and *VII* (3.0 g). Repeated separation of *Frs. I*, *III*, and *VI* over SiO_2 by CC (PE/acetone/Et_2NH 100:7:1 to 100:20:1) afforded **1** (50 mg), **2** (40 mg), and **3** (30 mg). The *Fr. II* was further purified by repeated CC (SiO_2; $CHCl_3$/MeOH 200:1) to furnish **4** (25 mg).

Liangshantine (*=(6α,14α,16β)-20-Ethyl-8-hydroxy-6,16-dimethoxy-4-(methoxymethyl)-1-oxoaconit-2-en-14-yl Acetate*; **1**). Amorphous powder. $[\alpha]_D^{20} = +118.5$ ($c = 0.6$, $CHCl_3$). IR (KBr): 3503, 2932, 1740, 1673, 1455, 1370, 1241, 1096. ^{1}H- (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$): *Table 1*. HR-ESI-MS: 476.2642 ($[M+H]^+$, $C_{26}H_{38}NO_7^+$; calc. 476.2648).

Liangshansine A (*=(7β,11α,15α)-11-Hydroxy-4-methyl-7,20-cycloatida-16,19-dien-15-yl Acetate*; **2**). White powder. $[\alpha]_D^{20} = +23.6$ ($c = 0.25$, $CHCl_3$). IR (KBr): 3392, 2925, 1739, 1651, 1458, 1372, 1235, 1058. ^{1}H- (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$): *Table 2*. HR-ESI-MS: 356.2213 ($[M+H]^+$, $C_{22}H_{30}NO_3^+$; calc. 356.2226).

Liangshansine B (=*(7β,13*R,*15β)-4,21-Dimethyl-7,20-cycloatidane-13,15,16,17-tetrol*; **3**). Colorless crystals. $[\alpha]_D^{20} = -79.0$ ($c = 0.3$, MeOH). IR (KBr): 3380, 2925, 1456, 1068. ^{1}H- (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$): *Table 2*. HR-ESI-MS: 364.2477 ($[M+H]^+$, $C_{21}H_{34}NO_4^+$; calc. 364.2488).

Liangshansine C (=*(5*R,*9*S,*10*R,*11*S,*12*R,*13*R,*15*S,*16*R,*18*R*)-11-Hydroxy-5,7-dimethylspiro[7-aza-hexacyclo[7.6.2.2^{10,13}.0^{1,8}.0^{5,16}.0^{10,15}]nonadecane-12,2′-oxiran]-18-yl Acetate*; **4**) White powder. $[\alpha]_D^{20} = -73.7$ ($c = 0.3$, $CHCl_3$). IR (KBr): 3416, 2931, 1730, 1645, 1457, 1375, 1251. ^{1}H- (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$): *Table 2*. HR-ESI-MS: 388.2489 ($[M+H]^+$, $C_{23}H_{34}NO_4^+$; calc. 388.2488).

REFERENCES

[1] Atta-ur-Rahman, M. I. Choudhary, *Nat. Prod. Rep.* **1999**, *16*, 619.
[2] F.-P. Wang, X.-T. Liang, in 'The Alkaloids: Chemistry and Biology', Ed. G. A. Cordell, Elsevier Science, New York, 2002, Vol. 59, p. 1.
[3] P.-G. Xiao, F.-P. Wang, F. Gao, L.-P. Yan, D.-L. Chen, Y. Liu, *Acta Phytotaxon. Sin.* **2006**, *44*, 1.
[4] H. Yan, D.-L. Chen, X.-X. Jian, F.-P. Wang, *Helv. Chim. Acta* **2007**, *90*, 1133.
[5] F. Gao, Q.-H. Chen, F.-P. Wang, *J. Nat. Prod.* **2007**, *70*, 876.
[6] L. Lin, D.-L. Chen, X.-Y. Liu, Q.-H. Chen, F.-P. Wang, C.-Y. Yang, *Nat. Prod. Commun.* **2009**, *4*, 897.
[7] H. Takayama, F.-E. Wu, H. Eda, K. Oda, N. Aimi, S. I. Sakai, *Chem. Pharm. Bull.* **1991**, *39*, 1644.
[8] D. Uhrin, B. Proksa, J. Zhamiansan, *Planta Med.* **1991**, *57*, 390.
[9] D. H. Chen, W. L. Sung, *Acta Pharm. Sin.* **1981**, *16*, 748.
[10] H. Takayama, A. Tokita, M. Ito, S. Sakai, F. Kurosaki, T. Okamoto, *J. Pharm. Soc. Japan* **1982**, *102*, 245.
[11] F. Feng, J.-H. Liu, *J. Chin. Pharm. Sci.* **1997**, *6*, 17.
[12] L. He, Y.-Z. Chen, L.-S. Ding, B.-G. Li, *Chin. Chem. Lett.* **1996**, *7*, 557.
[13] S. W. Pelletier, Z. Djarmati, *J. Am. Chem. Soc.* **1976**, *98*, 2626.
[14] F. Feng, J.-H. Liu, S.-X. Zhao, *Phytochemistry* **1998**, *49*, 2557.
[15] S. W. Pelletier, N. V. Mody, B. S. Joshi, L. C. Schramm, in 'Alkaloids: Chemical and Biological Perspectives', Ed. S. W. Pelletier, Wiley, New York, 1984, Vol. 2, p. 205.
[16] P. Kutathaivel, M. H. Benn, *Phytochemistry* **1988**, *27*, 3998.
[17] H. Bando, K. Wada, T. Amiya, K. Kobayashi, Y. Fujimoto, T. Sakurai, *Heterocycles* **1987**, *26*, 2623.
[18] S. Sakai, T. Okazaki, K. Yamaguchi, H. Takayama, N. Aimi, *Chem. Pharm. Bull.* **1987**, *35*, 2615.

Received October 26, 2009