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New C_{19}-Diterpenoid Alkaloids from the Roots of *Delphinium potaninii* var. *jiufengshanense*

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From the roots of *Delphinium potaninii* var. *jiufengshanense*, two new lycoctonine-type C_{19}-diterpenoid alkaloids called jiufengdine (1) and jiufengtine (4) have been isolated. The structures of the new alkaloids (1, 4) were established by 1D and 2D NMR spectra.

Key words *Delphinium potaninii* var. *jiufengshanense*; C_{19}-diterpenoid alkaloid; jiufengdine; jiufengtine

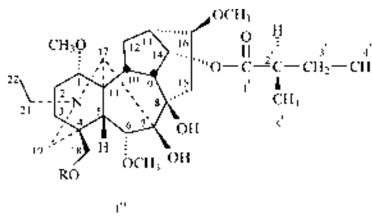
The plants *Delphinium potaninii* W. T. WANG and its variety *D. potaninii* var. *jiufengshanense* W. J. ZHANG *et* G. H. CHEN[1)] grow in Sichuan province, China. Their roots are used as a folk medicine for rheumatism and neuralgia. Our investigations showed that these two plants contain mainly lycoctonine-type alkaloids.[2—7)] In a continuing search for new active alkaloids two new C_{19}-diterpenoid alkaloids, jiufengdine (**1**) and jiufengtine (**4**), were isolated from the roots of *D. potaninii* var. *jiufengshanense*. We report here the isolation and structures of these new alkaloids.

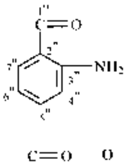
Results and Discussion

Jiufengdine (**1**) was isolated as an amorphous powder, $[\alpha]_D$ +63.8° (c=0.5, $CHCl_3$). The compound was assigned to the molecular formula $C_{36}H_{52}N_2O_9$ by HR-FAB-MS (*m/z* 656.3670 $[M^+]$). Its ^{1}H- and ^{13}C-NMR showed the presence of an *N*-ethyl [δ_H 1.06 (3H, t, J=7.2 Hz), 2.82, 2.93 (each 1H, m); δ_C 51.0 t, 14.0 q], three methoxyl (δ_H 3.26, 3.29, 3.37, each 3H, s; δ_C 55.7 q, 55.8 q, 58.0 q), an isopentanoyl [δ_H 1.15 (3H, d, J=7.2 Hz), 0.90 (3H, t, J=7.2 Hz), 2.36 (1H, m); δ_C see Table 1], and an anthranoyl [δ_H 6.67, 6.67, 7.29, each 1H, m, 7.79 (1H, dd, J=8.2, 1.6 Hz); δ_C see Table 1] groups. Along with the above-mentioned signals, the ^{13}C-NMR spectrum displayed 7 carbon signals (δ_C 68.5 t, 75.3 d, 77.0 s, 82.2 d, 83.9 d, 88.4 s, 90.7 d) attributing to oxygenated cartons. The spectral characteristics of jiufengdine (**1**) are indicative of a lycoctonine-type C_{19}-diterpenoid alkaloid.[8,9)] Since a proton-triplet at δ 4.79 (J=5.0 Hz) was attributable to 14β-H, this is true in many C_{19}-diterpenoid alkaloids bearing an ester group at C-14,[8,9)] especially in the presence of long-range ^{1}H–^{13}C correlations HMBC of the 14-H with the carbonyl carbon (δ 176.8) in the isopentanoate moiety, indicating the presence of the 14-isopentanoyl group. Similarly, the remaining anthranoyl group could be located at C-18 due to the ^{1}H–^{13}C long-range correlations (HMBC) between H_2-18 (δ_H 4.10, 4.15) and the anthranoyl carbonyl carbon (δ_C 167.7). Compared with elanine (**2**),[10)] the ^{1}H-NMR spectrum of jiufengdine (**1**) gave an additional NH_2 group. Except for those differences, the ^{13}C-NMR data (Table 1) of (**1**) and elanine (**2**) are very similar, thus leading to the structure of jiufengdine as **1**. Meanwhile, the stereochemistry of C-2′ in **1** could be deduced temporarily as *S* only based on comparison of the ^{13}C-NMR data with glaucedine (**3**).[11)]

Assignments of ^{1}H- and ^{13}C-NMR data were made by careful analysis of the spectra, including ^{1}H–^{1}H COSY, HMQC and HMBC, in meanwhile, also leading to suggestion of revision of the assignments (Table 1) for C-5, C-9, C-10, and C-13 of the ^{13}C-NMR spectrum of elanine (**2**).

Jiufengtine (**4**), $[\alpha]_D$ +46.0° (c=0.5, $CHCl_3$), was isolated as an amorphous powder. Its molecular formula ($C_{30}H_{42}N_2O_8$) was derived from HR-FAB-MS (*m/z* 558.2906, $[M^+]$). The NMR spectra of **4** revealed the presence of four methoxyls (δ_H 3.31, 3.34, 3.37, 3.42; δ_C 55.7, 56.2, 57.7, 58.0), and an anthranoyl [δ_H 6.64, 6.69, 7.29, 7.76 (each 1H); δ_C see Table 2] group. Compound **4** was considered to be a lycoctonine-type alkaloid by comparison of the NMR properities with many known C_{19}-diterpenoid alkaloids.[8,9)] The 1H-triplet signal at δ 3.62 (J=4.8 Hz) could be assigned to 14β-H based on comparison with many alkaloids bearing a methoxyl at C-14.[8,9)] The NMR spectra of compound **4** lacked an *N*-ethyl group when compared with anthranoyl-lycoctonine (**5**).[12)] Except for this point, the ^{1}H-NMR spectra of the two alkaloids are very similar. Comparison of the ^{13}C-NMR data of **4** and **5** led to the structure of jiufengtine as **4**, an *N*-deethyl derivative of anthranoyl-lycoctonine (**5**) and revision of the assignments (Table 2) for C-5, C-9, C-10, C-13 of the ^{13}C-NMR spectrum of **4**. In addition, as compared with **5**, the ^{13}C-NMR spectrum of **4** clearly showed changes in the chemical shifts of C-1, C-2, C-3, C-5, C-7, C-10, C-17, and C-19 caused by *N*-deethylation, as in *N*-deethyldelphatine.[13)]



1 R=


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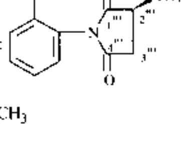
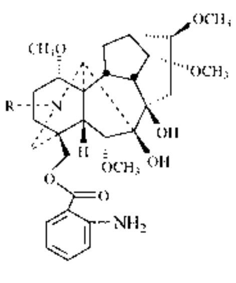


3 R=CH_3



4 R=H
5 R=Et

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Table 1. NMR Data of Jiufengdine (**1**), Elanine (**2**) and Glaucedine (**3**) (CDCl$_3$)

No.	**1**				**2**[10]	**3**[11]
	δ_H (J=Hz)	^{1}H COSY	δ_C	HMBC (H→C)	δ_C	δ_C
1	3.01 dd (9.6, 6.8)	H-2α, H-2β	83.9 d	C-17, 1-OCH$_3$	83.8	84.3
2	2.08 m (α)	H-1, H-3α, H-3β	26.0 t	—	26.1	26.2
	2.16 m (β)	H-1, H-3α, H-3β		C-4		
3	1.72 m (β)	H-2α, H-2β	32.2 t		32.0	32.4
	1.79 m (α)	H-2α, H-2β		C-19		
4	—	—	37.7 s	—	37.6	37.1
5	1.74 m	H-6	51.5 d	C-4, C-6, C-7, C-10, C-17	49.9[a]/43.1[b]	43.2
6	3.91 s	H-5	90.7 d	C-4, C-7, C-8, C-11, 6-OCH$_3$	90.6	90.5
7	—	—	88.4 s	—	88.3	88.4
8	—	—	77.0 s	—	77.3	
9	3.15 dd (6.8, 4.8)	H-10, H-14	43.1 d	C-8, C-10, C-12, C-13, C-14, C-15	43.1[a]/49.9[b]	51.1
10	2.04 m	H-9	45.7 d	C-8, C-17	45.6[a]/37.6[b]	38.1
11	—	—	49.0 s	—	49.0	49.6
12	1.89 m (β)	H-12α	28.2 t	C-9, C-11, C-16	28.2	28.3
	2.46 m (α)	H-12β		C-11, C-14, C-15		
13	2.42 m	H-14	37.6 d	C-9, C-11, C-16	37.6[a]/45.6[b]	45.7
14	4.79 t (5.0)	H-9, H-13	75.3 d	C-8, C-16, C-1″	75.4	75.6
15	1.59 dd (15.2, 6.4) (β)	H-15α, H-16	33.7 t	C-7, C-8, C-16	33.7	33.8
	2.64 dd (15.2, 9.2) (β)	H-15β, H-16		C-7, C-8, C-9, C-13, C-16		
16	3.26 (hidden)	H-15α, H-15β	82.2 d	C-12, C-14, 16-OCH$_3$	82.2	82.3
17	2.96 d (1.0)	—	64.4 d	C-5, C-6, C-11, C-19	64.6	64.8
18	4.10 d (11.2)	H-18 (4.15)	68.5 t	C-3, C-5, C-19, C-7′	69.4	78.1
	4.15 d (11.2)	H-18 (4.10)		C-3, C-5, C-19, C-7′		
19	2.43 (hidden)	H-19 (2.73)	52.4 t	C-18	52.3	52.8
	2.73 d (11.6)	H-19 (2.43)		C-5, C-17		
21	2.82 m	H-21 (2.93), H-22	51.0 t	C-22	51.1	48.9
	2.93 m	H-21 (2.82), H-22		C-22		
22	1.06 t (7.2)	H-21	14.0 q	C-21	14.1	14.2
1-OCH$_3$	3.26 s	—	55.7 q	C-1	55.9	55.8
6-OCH$_3$	3.37 s	—	58.0 q	C-6	58.2	57.4
16-OCH$_3$	3.29 s	—	55.8 q	C-16	55.9	55.8
18-OCH$_3$	—	—	—	—	—	59.0
1′	—	—	176.8 s	—	176.9	176.9
2′	2.36 m	H-5′	41.2 d	C-1′, C-3′, C-4′, C-5′	41.2	41.3
3′	1.48 m	H-4′	26.2 t	C-1′, C-2′, C-4′, C-5′	26.3	26.2
	1.76 m	H-4′		C-1′, C-2′, C-4′, C-5′		
4′	0.90 t (7.2)	H-3′ (1.48) H-3′ (1.76)	11.5 q	C-2′, C-3′, C-5′	11.6	11.6
5′	1.15 d (7.2)	H-2′	16.1 q	C-1′, C-2′, C-3′	16.2	16.2
1″	—	—	167.7 s	—	164.1	
2″	—	—	110.3 s	—	127.0	
3″	—	—	150.7 s	—	133.1	
4″	6.67 br d (8.4)	H-5″	116.7 d	C-6″	130.1	
5″	7.29 td (8.4, 1.2)	H-4″, H-6″	134.3 d	C-3″, C-7″	131.0	
6″	6.67 td (8.2, 1.2)	H-5″, H-7″	116.3 d	C-4″	133.7	
7″	7.79 dd (8.2, 1.6)	H-6″, H-5″	130.6 d	C-1″, C-3″, C-4″	129.5	
1‴					179.8	
2‴					35.2	
3‴					37.0	
4‴					175.8	
5‴					16.4	
NH$_2$	5.73 br s					

a) The revised data. b) The original data.

Experimental

General Experimental Procedures Optical rotations were measured in a 1.0 dm tube with a PE-341 polarimeter at 20±1 °C. ^{1}H- and ^{13}C-NMR spectra were acquired on a Varian INOVA-400/54 spectrometer in CDCl$_3$ with TMS as internal standard; EI-MS and HR-FAB-MS were obtained with a VG AUTO-spec 3000 mass spectrometer; TLC was performed on silica gel GF$_{254}$ percolated plates, sprayed with a modified Dragendorff's reagent for detection; column chromatography was performed using silica gel H; chromatographic separation on a Chromatotron was carried out on rotors coated with 1 mm thick layers of silica gel H and 0.5% CMC. All the silica gel GF$_{254}$ and silica gel H used in the experiments was purchased from the Qindno Sea Chemical Factory, China.

Plant Material The dry roots of *Delphinium potaninii* var. *jiufengshanense* were collected on Mt. Jiufeng, Sichuan, China. A voucher specimen (No. 980812) was deposited in the West China College of Pharmacy, Sichuan University, China.

Extraction and Isolation The total alkaloid (38 g) was obtained from the roots (8.7 kg) of *Delphinium potaninii* var. *jiufengshanense* using an ion exchange resin method[14] as described previously.[8] The total alkaloid (38 g) was chromatographed on a silica gel H column eluting with CHCl$_3$–MeOH (98.5 : 1.5) gave fractions A (600 mg), B (620 mg), C (807 mg), D (278 mg) and E (3.4 g). Fraction D was separated on a silica gel H column eluting

Table 2. NMR Data of Jiufengtine (**4**) and Anthranoyl-lycoctonine (**5**) ($CDCl_3$)

No.	**4**				**5**
	δ_H (J=Hz)	^{1}H COSY	δ_C	HMBC (H→C)	δ_C
1	3.25 m	H-2α	82.3 d	C-3	84.0
2	1.77 m (α)	H-1, H-2α	24.0 t	C-3	26.0
	2.01 m (β)	H-1, H-3β		C-4, C-11	
3	1.81 m		28.3 t		32.3
4	—	—	37.0 s	—	37.6
5	1.95 br s	H-6	47.2 d	C-1, C-4, C-6, C-7, C-18, C-19	50.4[a]/43.3[b]
6	4.01 br s	H-5	90.4 d	C-4, C-7, C-8, C-11, C-17	91.0
7	—	—	83.9 s	—	88.6
8	—	—	77.6 s	—	77.6
9	3.09 dd (6.8, 4.8)	H-10, H-14	43.5 d	C-8, C-12, C-13, C-15	43.3[a]/50.4[b]
10	2.04 m	H-9	44.5 d	C-8, C-17	46.2[a]/38.3[b]
11	—	—	48.8 s	—	
12	1.78 m		29.2 t		28.8
13	2.37 dd (6.8, 4.8)	H-14	38.4 d	C-9, C-11, C-16	38.3[a]/46.2[b]
14	3.62 t (4.8)	H-9, H-13	84.1 d	C-8, C-16	84.0
15	1.75 m (β)	H-15α, H-16	33.3 t	C-7, C-8	33.7
	2.66 dd (14.8, 8.8) (α)	H-15β, H-16		C-7, C-8, C-9, C-13, C-16	
16	3.22 m	H-15α, H-15β	82.2 d	C-12, C-14	82.6
17	3.05 d (2)	—	60.8 d	C-5, C-6, C-19	64.6
18	4.11 d (11.2)		68.2 t	C-3, C-4, C-5, C-7	68.7
	4.15 d (11.2)				
19	2.85 d (13.2)	H-19 (2.95)	48.4 t	C-3, C-4, C-5, C-18	52.6
	2.95 d (13.2)	H-19 (2.85)			
1-OMe	3.31 s	—	55.7 q	C-1	55.8
6-OMe	3.37 s	—	57.7 q	C-6	57.9
14-OMe	3.42 s	—	58.0 q	C-14	58.0
16-OMe	3.34 s	—	56.2 q	C-16	56.3
1″	—	—	167.6 s	—	167.9
2″	—	—	109.9 s	—	110.4
3″	—	—	150.8 s	—	150.9
4″	6.69 br d (8.4)	H-5″	116.8 d	C-2″, C-6″	116.9
5″	7.29 td (8.0, 1.2)	H-4″, H-6″	134.4 d	C-3″, C-7″	134.4
6″	6.64 td (8.4, 1.2)	H-5″, H-7″	116.2 d	C-2″, C-4″	116.4
7″	7.76 dd (8.0, 1.6)	H-6″, H-5″	130.5 d	C-1″, C-3″, C-5″	130.8

a) The revised data. *b*) The original data.

with $CHCl_3$–MeOH (99 : 1) to afford other fractions. Further chromatography of fraction D-1 (120 mg) over silica gel H eluting with $CHCl_3$–MeOH (98 : 2) produced compound **4** (50 mg). Fraction E (3.4 g) was subjected to column chromatography over silica gel H (petroleum–acetone, 10 : 1). A portion of fraction E-1 (140 mg) was chromatographed over silica gel H ($CHCl_3$–MeOH, 98 : 2) to afford compound **1** (12 mg).

Jiufengdine (**1**): White amorphous powder; $[\alpha]_D$ +63.8° (c=0.5, $CHCl_3$); ^{1}H (400 MHz)- and ^{13}C (100 MHz)-NMR see Table 1; EI-MS *m*/*z* (%) 656 (M^+, 20), 641 (32), 625 (100), 571 (10), 120 (69); HR-FAB-MS *m*/*z* 656.3670 (Calcd for $C_{36}H_{52}N_2O_9$, 656.3672).

Jiufengtine (**4**): White amorphous powder; $[\alpha]_D$ +46.0° (c=0.5, $CHCl_3$); ^{1}H (400 MHz)- and ^{13}C (100 MHz)-NMR see Table 2; EI-MS *m*/*z* (%) 558 (M^+, 10), 543 (45), 527 (75), 438 (8), 120 (100); HR-FAB-MS *m*/*z* 558.2906 (Calcd for $C_{30}H_{42}N_2O_8$, 558.2911).

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