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Norditerpenoid Alkaloids from the Roots of *Aconitum hemsleyanum* Pritz. *var*. *Pengzhouense*

Chong Sheng PENG, Feng Peng WANG*, Xi Xian JIAN

Department of Chemistry of Medicinal Natural Products, West China College of Pharmacy, Sichuan University, Chengdu 610041

Abstract: In continuation of our studies on *Aconitum hemsleyanum* Pritz. var. p*engzhouense*, two new norditerpenoid alkaloids, pengshenines A (**1**) and B (**2**), have been isolated from the roots of the plants and their structures were elucidated by 1D- and 2D-NMR.

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Abstract: In continuation of our studies on *Aconitum hemsleyanum* Pritz. var. p*engzhouense*, two new norditerpenoid alkaloids, pengshenines A (**1**) and B (**2**), have been isolated from the roots of the plants and their structures were elucidated by 1D- and 2D-NMR.

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Aconitum hemsleyanum Pritz var. *pengzhouense* G. J. Zhang *et al.* G. H. Chen native to China distributes only in Longmen mountain, Sichuan province[1]. In the previous work, we have isolated the norditerpenoid alkaloids, 1-epicrassicaudine, indaconitine, crassicaudine, 13-dehydroxylindaconitine, talatisamine, ezochasmanine, 6-epiforsticine, franchetine, 14-debenzoylfranchetine, chasmanine, 8-deacetylsungpaconitine, 13-dehydroxylludaconitine from the plant[2,3]. Continuation of our studies on the alkaloids of *Aconitum hemsleyanum* Pritz *var*. *pengzhouense* led to the isolation of two new norditerpenoid alkaloids named pengshenines A (**1**) and B (**2**). The new alkaloids, whose molecular formulae were determined by their MS, ^{1}H- and ^{13}C-NMR spectra, revealed distinctive signals of the norditerpenoid alkaloids in their NMR spectra[4,5].

Pengshenine A (**1**)[6], mp 189-191°C $C_{24}H_{37}NO_6$, was isolated as colorless rhombic crystals. The NMR spectrum of **1** gave characteristic signals at δ_H 1.02 (t, 3H, J = 7.1 Hz), δ_C 45.7 t and 14.3 q for an *N*-ethyl group; δ_H 3.25, 3.27, and 3.35 (s, each 3H), δ_C 56.4 q, 56.7 q and 59.3 q for three methoxyl groups, and δ_H 4.71(dd, 1H, J = 4.4, 2.8 Hz) and 4.35 (s, 1H), δ_C 78.9 d and 92.1 d for an *N*, *O*-mixed acetyl moiety. Its NMR spectra also showed the connectivity of the signal at δ_H 4.05 (t, 1H, J = 4.5 Hz) with that at δ_C 74.9 d (HMQC), and observation of the signal at δ_C 70.1 s, indicated that pengshenine A (**1**) had one secondary and one tertiary hydroxyl groups.

* E-mail: wfp@wcums.edu.cn

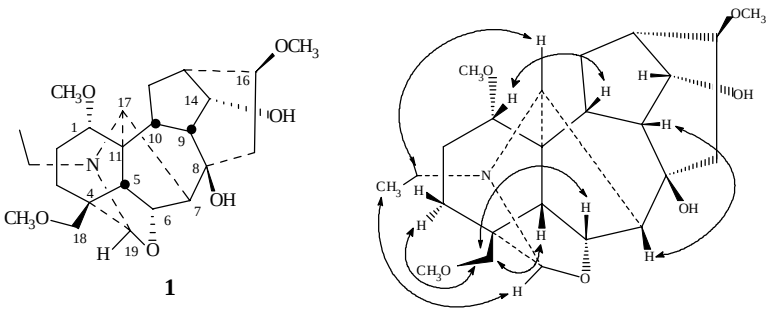
The methoxyl groups at C-1 and C-18 were assigned due to showing a distinctive fragment peak at *m/z* 404 (M-31)[7] and the correlation of the H_2-18 [δ_H 2.95, 3.20 (ABq, each 1H, J = 8.8 Hz)] with C-18 (δ_C 80.0 t) in the HMQC spectrum of **1**. The remained methoxyl group may be located at C-16 because of the presence of the connectivity between 16-OCH_3 (δ_H 3.33, 3H, s) and C-16 (δ_C 82.1 d). The ^{1}H NMR spectrum (**Table 1**) exhibited a signal at δ 4.05 (t, 1H, J = 4.5 Hz), attributable to the proton attached to C-14, suggesting the presence of the secondary hydroxyl group at C-14. The tertiary hydroxyl group was assigned at C-8 owing to the two- and three-bond connectivities of C-8 (δ 70.1 s) with the H-7 (δ_H 2.29, 1H, brs), H-9 (δ_H 1.84, 1H, m), 10-H (δ_H 1.62, 1H, m), H-14 (δ_H 4.05, 1H, t, J = 4.6 Hz), and H-16 (δ_H 3.45, 1H, m) in the HMBC spectrum of **1** (**Table 1**).

Table 1 NMR data of pengshenine A (**1**) (^{1}H: 400MHz; ^{13}C: 100MHz)

Carbon	δ_C	δ_H	HMBC (H→C)
1	86.8 d	3.19 m (hidden)	C (1'), C (10'), C (11), C (17)
2	24.9 t	1.82 m (β)	C (1), C (11), C (3), C (4),
		2.34 m (α)	C (1), C (3)
3	25.9 t	1.50 m (β)	C (3), C (1), C (18), C (19)
		2.04 m (α)	C (1), C (2), C (5), C (10)
4	45.5 s	—	—
5	51.4 d	1.90 d (4.4)	C (4), C (11), C (17), C (18), C (19)
6	78.9 d	4.70 dd (4.4, 2.8)	C (17)
7	53.0 d	2.29 brs (W1/2 = 2.0)	C (5), C (6), C (8), C (17), C (9), C (15)
8	70.1 s	—	—
9	46.5 d	1.84 m	C (8), C (10), C (11), C (14)
10	45.5 d	1.62 m	C (1), C (8), C (9), C (17)
11	47.3 s	—	—
12	27.4 t	1.46 m (β)	C (11), C (13), C (14), C (16)
		1.84 m (α)	C (10), C (11), C (14)
13	36.8 d	2.38 m	C (1), C (12)
14	74.9 d	4.05 dd (4.9, 2.6)	C (8), C (9), C (13), C (16)
15	34.3 t	1.98 m (β)	C (8), C (9), C (13), C (16)
		2.08 m (α)	C (7), C (8), C (16)
16	82.1 d	3.45 m	C (13), C (14), C (8)
17	63.2 d	3.35 s	C (5), C (19)
18	80.0 t	2.95 (β)	C (3), C (4), C (5), C (19), C (18')
		3.20 ABq (8, 8) (α)	C (4), C (5), C (18')
19	92.1 d	4.35 s	C (4), C (5), C (6), C (17)
21	45.7 t	2.54 m (β)	C (17), C (19), NCH_2CH_3
		2.82 m (α)	C (17), C (19), NCH_2CH_3
22	14.3 q	1.02 t (7.2)	NCH_2
1'	56.4 q	3.25 s	C (1)
16'	56.7 q	3.33 s	C (16)
18'	59.3 q	3.27 s	C (18)
8-OH		3.74 s	C (7), C (8)
14-OH	—	5.35 d (5.2)	C (14), C (13)

Attention was then focused on the location of the *N*, *O*-mixed acetyl moiety. The H-19 signal at δ_H 4.35 (s, 1H), (δ_C 92.1 d) gave: (a) spatial correlations with the H_2-18 at δ_H 2.95 and 3.20 (ABq, each 1H, J = 8.8 Hz) (δ_C 80.0 t) in the NOESY spectra of **1**(**Figure l**); (b) two- and three-bond connectivities with C-4 (δ_C 45.5 s), C-5 (δ_C 51.4 d), C-6 (δ_C 78.9 d), and C-17 (δ_C 63.2 d) (**Table l**). In addition, the chemical shift of C-4 in ^{13}C NMR spectrum of **1** (**Table 1**) was shifted downfield due to a shielding effect of the oxygenated substitution at C-19 and the H-6 at δ_H 4.71 (dd, 1H, J = 4.4, 2.8 Hz) correlated with C-17 (δ_C 63.2 d) in the HMBC spectrum of **1**. In fact, treatment of 6-epiforsticine (**3**)[8] with $KMnO_4$ or $K_3Fe(CN)_6$ at room temperature for 15 min or 4 h, respectively, gave compound **1**. These observations indicated that there was an *N*, *O*-mixed acetal belonging to the C (6) α-*O*-C(19)-*N* moiety in **1**. Thus, the structure of pengshenine A was elucidated as **1**. This is a first naturally-occurring norditerpenoid alkaloid with an C (6)-*O*-C (19)-*N* mixed acetal moiety.

Figure 1 Key NOESY correlation for **1**



1

Pengshenine B (**2**)[9], $C_{22}H_{33}NO_5$, was isolated as an amorphous substance. The NMR spectrum (**Table 2**) of **2** gave the distinctive signals at δ_H 3.20, 3.32 and 3.34 (s, each 3H), δ_C 56.0 q, 56.5 q, and 59.6 q for three methoxyl groups and δ_H 7.27 (s, 1H), δ_C 165.3 d for an imine group. The presence of the connectivity of the signal at δ_H 4.10 (brs, 1H) with that at δ_C 75.3 d (HMQC) and observation of the signal at δ_C 72.7 s indicated that it had one secondary and one tertiary hydroxyl groups. The absence of *N*-Et and the presence of a *N* = C (19)-H moiety in **2** suggested that it was an imine-containing alkaloid, like bulleyanitine A[10]. Observation of an intense fragment ion peak at *m/z* 360 (M-31) in the MS of **2** showed the presence of the 1α-OCH_3[7], in addition to consideration of the chemical shifts of the signals at δ_H 3.20 (m, 1H, H-1β) and δ_C 84.7 d (C-1) (HMQC). The 18-OCH_3 group may be assigned easily due to the signals at δ_H.

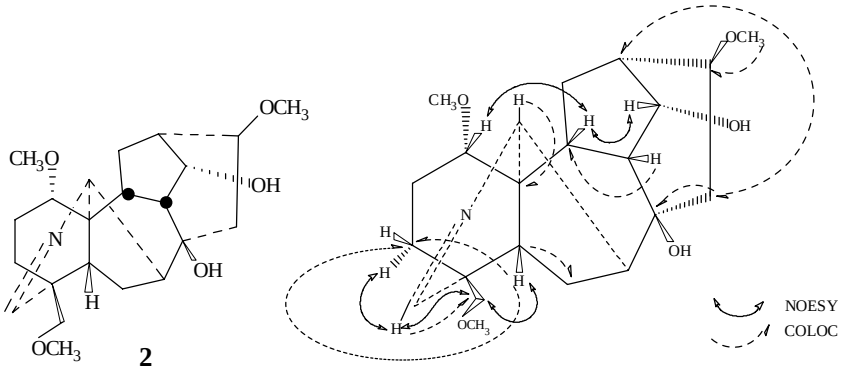
3.08, 3.35 (ABq, each 1H, J = 8.0 Hz) and δ_C 75.5 t (HMQC), contributing to H_2-18 and C (18), respectively. The correlation between H-16α at δ_H 3.44 (m, 1H) and H_2-15 at δ_H 2.04 (m, 1H) and 2.58 (dd, 1H, J = 17.5, 8.4 Hz) in the ^{1}H-^{1}H COSY spectrum of **2** indicated the presence of 16β-OCH_3. The ^{1}H NMR spectrum showed a signal at δ_H 4.10 (t, 1H, J = 4.6 Hz) attributable to H-14β geminal to a hydroxyl group. The signal at δ_C 72.7 belonging to C-8 exhibited connectivities with the H_2-15 at δ_H 2.04 (m, 1H)

and 2.58 (dd, 1H, *J* = 17.5, 8.4 Hz) (COLOC) (**Figure 2**), indicating that **2** had an 8-OH group. Thus, the structure of pengshenine B (**2**) was assigned as **2**.

Table 2 NMR data of pengshenine B (**2**) ($CDCl_3$, C ^{1}H: 400 MHz; ^{13}C: 100 MHz)

Carbon	δ_C	δ_H	Carbon	δ_C	δ_H
1	84.7 d	3.14 m	13	37.2 d	2.36 brs (W1/2 = 16.8)
2	25.5 t	1.28 m (β), 1.92 m (α)	14	75.3 d	4.10 brs (W1/2 = 4.6)
3	27.8 t	1.33 m (β), 1.68 m (hidden) (α)	15	37.5 t	2.04 m (β)
4	47.6 s	—			2.58 dd (17.5, 8.4) β
5	52.3 d	2.08 d (5.6)	16	81.9 d	3.44 m
6	25.6 t	1.42 m (β), 1.94 m (hidden) (α)	17	62.7 d	4.08 s (β)
7	42.6 d	1.65 m (hidden)	18	75.5 d	3.08 ABq (8.0) (β)
8	72.7 s	—			3.35 (hidden) (α)
9	46.1 d	2.14 dd (4.8, 4.4)	19	165.3 d	7.27 s
10	46.2 d	1.69 m	1'	56.5 q	3.34 s
11	50.4 s	—	16'	56.0 q	3.20 s
12	27.1 t	1.66 m (β), 1.80 m (α)	18'	59.5 q	3.32 s

Figure 2 Key NOESY and COLOC correlation for **2**



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6. Pengshenine A **1**: A colorless needle crystals, $[\alpha]_D$ +26 (c 0.5, $CHCl_3$); IR (cm^{-1} KBr): 3521 (OH), 3382, 2935, 1102, 1070, 894; EIMS: *m/z* (%): 435 (M^+, 18), 420 (M-15, 45), 405 (58), 404 (M-31, 100), 392 (20), 367 (61), 91 (18).
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9. Pengshenine B (**2**). White amorphous substance, $[\alpha]_D$ +22.8 (c 0.5, $CHCl_3$); IR (cm^{-1} KBr): 3448 (OH), 1459, 1068; EIMS *m/z* (%): 391 (M^+, 20), 360 (M-31, 19).
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