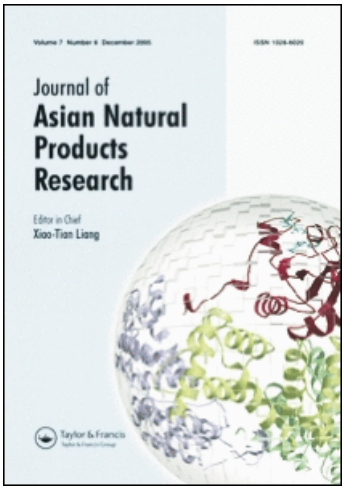

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FIVE NEW NORDITERPENOID ALKALOIDS FROM *ACONITUM SINOMONTANUM*

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From the roots of *Aconitum sinomontanum*, five new norditerpenoid alkaloids, sinomontanitines **A** (**1**) and **B** (**2**), sinomontanines **A** (**3**), **B** (**4**) and **C** (**5**), were isolated together with the known alkaloids lappaconitine (**6**) and ranaconitine (**7**). The structures of the new alkaloids were determined by spectral analysis.

Keywords: *Aconitum sinomontanum*; Ranunculaceae; Norditerpenoid alkaloid; Sinomontanitine **A**; Sinomontanitine **B**; Sinomontanine **A**; Sinomontanine **B**; Sinomontanine **C**

INTRODUCTION

Aconitum sinomontanum Nakai, an endemic plant of China, was collected in South part of Gansu province, and is prescribed in folk-lore medicine for bruises and injuries [1]. Now, it mainly is useful for the extraction of lappaconitine, which is used clinically in the treatment of analgesis in China. An earlier physiochemical work on *Aconitum sinomontanum* reported that two norditerpenoid alkaloids lappaconitine and ranaconitine, as well as lycaconitic acid monomethyl ester were isolated [2]. In continuation of studies on this plant, we have isolated five new norditerpenoid alkaloids, sinomontanitines **A** (**1**) and **B** (**2**), sinomontanines **A** (**3**), **B** (**4**) and **C** (**5**), together with lappaconitine (**6**) [3] and ranaconitine (**7**) [4], from the roots of

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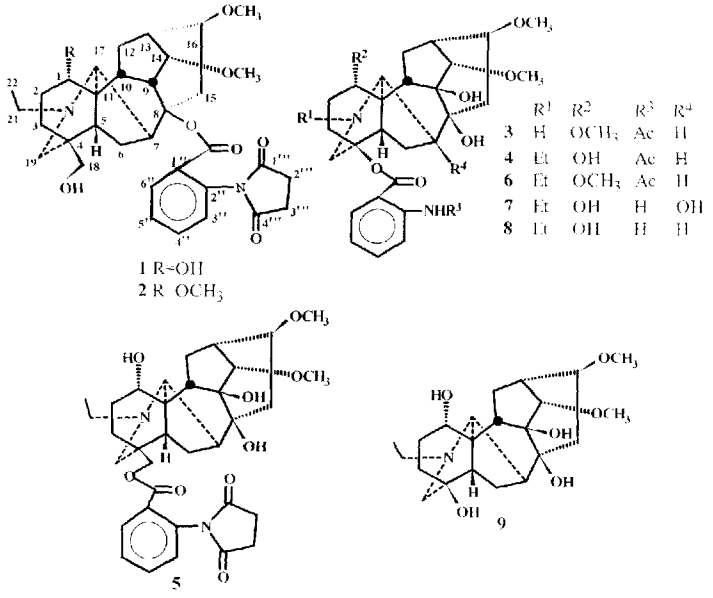
Aconitum sinomontanum. The structures of the new alkaloids were determined by spectral analysis.



RESULTS AND DISCUSSION

The new norditerpenoid alkaloids exhibites characteritsic signals in their NMR [5, 6] and MS spectra [7]. Their molecular formulae were determined by their MS, ^{1}H- and ^{13}C-NMR spectra.

Sinomontanitine **A** (**1**), $C_{35}H_{44}N_2O_9$, is an aconitine-type norditerpenoid alkaloid as inferred from its ^{1}H- and ^{13}C-NMR spectra (Tab. I). The NMR spectra of sinomontanitine **A** (**1**) gave signals at δ_H 1.14 (3H, t, $J = 7.2$ Hz), δ_C 48.3 t and 12.9 q, for the *N*-ethyl group, δ_H 3.27 (3H, s) and δ_C 56.0 q, for the methoxyl group, δ_H 2.06 (3H, s), δ_C 170.4 s and 21.2 q, for the acetyl group, and δ_H 7.27 (1H, d, $J = 7.6$ Hz), 7.69 (1H, t, $J = 7.6$ Hz), 7.54 (1H, t, $J = 7.6$ Hz), 8.06 (1H, d, $J = 6.4$ Hz), 2.92, 2.95 (each 2H, ABq, $J = 6.8$ Hz H-2'' / 3'' (α) or H-2'' / 3'' (β)); δ_H 164.3 s (O=CO), 126.9 s (C-1'), 132.6 s (C-2'), 129.1 d (C-3'), 133.6 d (C-4'), 129.4 d (C-5'), 131.2 d (C-6'), 176.5 s (C-1'', 4''), 28.8 t (C-2'', 3''), for an *N*-acetyl anthranoyl group. The 1H signal at δ_H 3.78 (br.s, $W_{1/2} = 5.4$ Hz) and the 2H signals at δ_H 3.89, 4.09 (ABq, $J = 10.8$ Hz), which correlated with the carbon signals at δ 71.8 d and 70.2 t.

TABLE I NMR data of compounds **1** and **2** (^{1}H : 400 MHz; ^{13}C : 100 MHz)

	1			**2**
Carbon	δ_C	δ_H	*HMBC* (*H*→*C*)	^{13}C
1	71.8 d	3.78(br.s, $W1/2 = 5.4$)		85.3 d
2	29.5 t	1.61 m (β) 2.08 m (α)	C-3, C-10 C-4	26.0 t
3	26.4 t	1.60 m (β) 1.84 m (α)	C-1,C-2, C-4, C-18	32.5 t
4	36.6 s	–	–	37.9 s
5	41.2 d	1.86 m	C-10, C-11, C-17	46.2 d
6	25.1 t	1.68 m (β) 2.13 m (α)	C-5, C-8, C-11	25.1 t
7	45.4 d	2.10 m	C-8,C-9,C-11,C-17	45.8 d
8	74.6 s	–	–	73.6 s
9	44.6 d	2.26 m	C-8, C-10, C-12, C-13, C-14	45.2 d
10	43.1 d	1.94 m	C-8,C-9,C-11,C-12,C-17	44.7 d
11	48.9 s		–	48.7 s
12	28.9 t	1.73 m (β) 2.13 m (α)	C-11, C-13, C-14, C-16	28.3 t
13	36.5 d	2.65 dd (7.4, 4.8)	C-9, C-10, C-14, C-16	35.3 d
14	76.9 d	4.86 t (4.8)	C-8, C-9, C-13, C-16 CO-CH_3	76.8 d
15	42.5 t	2.28 m (β) 1.88 m (α)	C-7, C-8, C-9, C-16	41.4 t
16	81.9 d	3.27 m	C-8, C-9, C-16'	81.6 d
17	63.2 d	2.78 s	C-5, C-6, C-19	62.0 d
18	70.2 t	3.89, 4.09 (ABq, 10.8)	C-3, C-4, C-5, C-19	70.6 t
19	56.1 t	2.16, 2.41 (ABq, 10.8)	C-3, C-4, C-18, C-20	52.6 t
NCH_2CH_3	48.3 t	2.54 m	C-21	49.3 t
NCH_2CH_3	12.9 q	1.14 t (7.2)		13.5 q
1'	-	-	–	56.3 q
16'	56.0 q	3.27 s	C-16	56.1 q
$COCH_3$	170.4 s	–	–	170.8 s
$COCH_3$	21.2 q	2.06 s	$CO-CH_3$	21.4 q
COO	164.3 s	–	–	164.2 s
1"	126.9 s	–	–	127.1 s
2"	132.6 s	–	–	132.7 s
3"	129.1 d	7.27 d (7.6)	C-1", C-5"	129.6 d
4"	133.6 d	7.69 t (7.6)	C-4", C-6"	133.5 d
5"	129.4 d	7.54 t (7.6)	C-1", C-3"	129.4 d
6"	131.2 d	8.06 d (6.4)	C-14", CO-Ar	131.3 d
1"', 4"'	176.5 s	–	–	176.7 s
2"', 3"'	28.5 t	2.92, 2.95 (ABq, 6.8)	C-2"', C-3"' C-1"', C-4"'	28.8 t

respectively, in the HMQC spectrum, indicated that sinomontanitine **A** (**1**) had one secondary and one primary hydroxyl groups. They may be located at C-1 and C-18, respectively, because of the three-bond connectivity of their geminal protons (δ_H 3.78 and δ_H 3.89, 4.09) with the C-3, C-10 and C-3, C-5,

respectively, observed in the HMBC spectrum (Tab. I). The HMBC spectrum of **1** showed three-bond connectivity between the methoxyl (δ_H 3.27, s; HMQC δ_C 56.0 q) and the C-16(δ_C 81.9 d), suggesting the presence of 16-OMe group. The remaining work of structural elucidation of sinomontanitine **A** (**1**) is of assignments for both acetyl and anisoyl groups. The acetyl group may be located at C-14 due to the correlation of the H-14β with the carbonyl carbon signal (δ_C 171.4 s) of the OAc group in the HMBC spectrum (Tab. I). The ^{13}C NMR spectrum of sinomontanitine **A** (**1**) exhibited only one signal (δ_C 74.6 s) of the oxygenated quaternary carbon, which was assigned to C-8 because of its two- and three-bond connectivities with the H-14β and H_2-15α, β resonances showed in the HMBC spectrum, indicating that the anthranoyl group may be assigned at C-8.

The ^1H NMR spectrum of sinomontanitine **B** (**2**), $C_{36}H_{46}N_2O_9$, showed the presence of an *N*-ethyl group (δ 1.06, 3H, t, $J = 7$ Hz), two aliphatic methoxyls (δ 3.26 and 3.32, each 3H, s), an acetyl group (δ 2.04, 3H, s) and an *N*-acetyl anthranoyl group (δ 7.23–8.10, 4H, m; 2.92, 2.94, each 2H, ABq, $J = 6.8$ Hz). The NMR and MS spectral data of **2** indicated that it had an additional methoxyl group but lacked a primary hydroxyl group when compared with **1**. A comparison of the ^{13}C NMR data of the ring *A* between **1** and **2** showed clearly difference among the C-1, C-2, C-3, C-5, C-17 and C-19 probably due to the different conformation for the ring *A* [8, 9]. This leds to deduce that the extra methoxyl group of **2** was located at C-1 position. Thus the structure of **2** was determined as sinomontanitine **B** (**2**).

The ^1H NMR spectrum of sinomontanine **A** (**3**), $C_{30}H_{40}N_2O_8$, showed the presence of three aliphatic methoxyl groups (δ 3.27, 6H; 3.38, 3H, s), an *N*-acetyl anthranoyl group (δ_H 6.9–8.7, 4H, m; δ_H 11.0, 1H, br.s, disappeared with D_2O; δ 2.20, 3H, s) and lacked an *N*-ethyl group when compared with lappaconitine (**6**) [3]. Except for this point, the ^1H NMR spectra of the both alkaloids are very similar. Comparison of the ^{13}C NMR data of **3** and **6** led to the structure of sinomontanine **A** as **3**, which is an *N*-deethyl derivative of lappaconitine (**6**). In addition, as compared with **6**, the ^{13}C NMR spectrum of **3** showed clearly changes of the chemical shifts of C-1, C-2, C-3, C-4, C-5, C-7, C-17 and C-19 caused by *N*-deethylation, as in *N*-deethyl aconitine [10].

The ^1H NMR spectrum of sinomontanine **B** (**4**), $C_{31}H_{42}N_2O_8$, displayed the presence of an *N*-acetyl anthranoyl group (δ 7.03–7.92, 4H, m; δ 2.25, 3H, s; δ 11.07, 1H, s, disappeared with D_2O). Its NMR and MS spectra showed that it had an extra *N*-ethyl group but lacked a methoxyl group when compared with sinomontanine **A** (**3**). The NMR data of **4** and

4-anthranoyl lappaconidine (**7**) [11] are very similar except for those of the aromatic moiety, thus leading to the structure of sinomontanine **B** as **4**.

The ^{1}H NMR spectrum of sinomontanine **C** (**5**), $C_{34}H_{44}N_2O_9$, gave signals at δ 1.12 (3H, t, $J=7.1$ Hz) for an *N*-ethyl group, δ 3.30 and 3.33 (each 3H, s) for two methoxyl groups, and δ 7.21 ~ 8.07 (4H, m), δ 2.93, 2.95 (each 2H, ABq, $J=6.8$ Hz) for a 2-(butaneimide) benzoyl group. Its ^{13}C NMR spectra (Tab. II) also showed the presence of one secondary and two tertiary hydroxyl groups. As compared with lappaconidine (**9**) [3], the ^{13}C NMR spectrum of sinomontanine **C** (**5**) gave an additional oxymethylene signal at δ 70.4 t attributable to C-18 ester group, and the NMR spectra of both alkaloids are very similar except for the signals of the aromatic ester moieties. Thus the structure of **5** was confirmed as sinomontanine **C**.

TABLE II ^{13}C NMR data of compounds **3**, **4**, **5**, **6**, **7** and **8** (50 MHz)

Carbon	**3**	**4**	**5**	**6**	**7**	**8**
1	82.2 d	71.9 d	72.1 d	84.0	72.2	72.0
2	24.4 t	29.7 t	29.3 t	26.0	29.6	29.7
3	30.0 t	30.2 t	27.0 t	31.7	33.2	30.3
4	83.2 s	82.6 s	36.6 s	84.5	70.4	81.0
5	52.1 d	48.2 d	40.9 d	48.3	48.0	48.2
6	26.3 t	27.1 t	26.3 t	26.6	27.2	27.1
7	44.2 d	47.0 d	45.9 d	47.7	46.7	46.4
8	76.0 s	76.0 s	75.9 s	75.3	76.0	75.9
9	78.0 s	77.3 s	77.2 s	78.4	77.3	77.2
10	49.0 d	43.7 d	48.6 d	49.7	48.2	43.9
11	51.0 s	50.1 s	49.2 s	50.8	50.1	50.0
12	23.7 t	23.5 t	23.5 t	24.0	22.9	23.5
13	36.6 d	36.1 d	36.1 d	36.1	36.2	36.1
14	90.0 d	90.1 d	90.2 d	89.9	90.1	90.1
15	44.2 t	45.1 t	44.7 t	44.6	44.8	44.8
16	82.4 d	82.7 d	82.7 d	82.7	82.7	82.7
17	57.1 d	63.0 d	63.5 d	61.3	62.8	63.0
18			70.4 t	–	–	–
19	50.6 t	57.8 t	56.5 t	55.3	60.3	57.9
NCH_2CH_3	–	48.2 t	48.3 t	48.9	46.4	48.1
NCH_2CH_3		13.0 q	12.8 q	13.4	12.9	12.9
1'	55.8 q	–	–	56.4	–	–
14'	57.8 q	57.9 q	57.8 q	57.7	57.8	57.8
16'	56.1 q	56.2 q	56.1 q	55.9	56.1	56.1
O=CO	167.2 s	167.1 s	164.4 s	167.2		166.9
1''	115.4 s	115.5 s	127.1 s	115.6	–	151.3
2''	141.6 s	141.7 s	132.6 s	141.4	–	150.5
3''	120.1 d	120.2 d	129.7 d	120.0	–	116.6
4''	134.4 d	134.5 d	133.01 d	134.2	–	133.9
5''	122.2 d	122.7 d	139.3 d	122.2	–	116.0
1''', 4'''	–	–		176.5	–	–
2''', 3'''	–	–	–	28.7	–	–
$NHCOCH_3$	168.5 s	169.0 s	–	168.9	–	–
$NHCOCH_3$	25.6 q	25.5 q		25.5	–	–

EXPERIMENTAL

General Experimental Procedures

IR spectra were measured on a Nicolet 200 SXV spectrometer. Optical rotations were measured on a Perkin-Elmer 241 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were measured in $CDCl_3$, with TMS as internal standard, on a Bruker AC-E 200 and Varian INOVA 400/54 spectrometer. MS data were recorded by VG Autospec 3000 instrument. Silica gel (GF_{254} and H, Qingdao Sea Chemical Factory, China) were used for TLC (S_1: $CHCl_3$–MeOH, 9 : 1; S_2: Et_2O–CH_3COCH_3, 8 : 2). Chromatotron and column chromatography. Spots on chromatograms were detected with Dragendorff's reagent.

Plant Material

Plants were collected in South of Gansu province, China, and authen-ticated by Professor Xian-Wu Kong, Ganshu Teaching University, where a voucher specimen has been deposited.

Extraction and Isolation

The total alkaloids (76 g) obtained from the roots (5 kg) of *Aconitum sinomontanum*, which was provided by Lanzhou Pharmaceutical Company, were dissolved in ether (150 ml) and filtered to give the soluble and insoluble parts I (30 g) and II (46 g), respectively. CC of part II (19 g) using $CHCl_3$–MeOH (100 : 1) gave fractions *A* (3.3 g), *B* (6.1 g) and *C* (2.17 g). Fraction *B* was treated with 5% HCl and filtered. The acid solution was basified with NH_4OH to pH 8 and extracted with $CHCl_3$ to give the residue (3.4 g), which was chromatographed on a Chromatotron eluting with Et_2O–Me_2CO (95 : 5) → cyclohexane–acetone (2 : 1) containing 1‰ ethylamine to afford sinomontanitine **A** (**1**) (30 mg). CC of fraction *C* using $CHCl_3$–MeOH (100 : 1→90 : 10) gave fractions *D* (380 mg), *E* (660 mg) and *F* (190 mg). Fraction *D* was chromatographed on a Chromatotron eluting with $CHCl_3$–MeOH (98 : 2→95 : 5) to give lappaconitine (**6**) (15 mg) and ranaconitine (**7**) (120 mg). Fraction *E* was repeatly chromatographed on a Chromatotron eluting with cyclohexane–acetone (1 : 1) containing 3‰ ethylamine to afford sinomontanine **B** (**4**) (20 mg) and sinomontanine **C** (**5**) (30 mg). Fraction *F* was chromatographed on a Chromatotron eluting with cyclohexane–acetone (2 : 1) to give sinomontanitine **B** (**2**) (30 mg) and

sinomontanine **A** (**3**) (50 mg). Separation and identification (TLC, MS, m.p., ^{1}H- and ^{13}C-NMR) of two known alkaloids lappaconitine and ranaconitine were carried out.

Sinomontanitine A (1)

White amorphous foam, $[\alpha]_D$ +24.2 (c 1.0, $CHCl_3$); IR_{max}^{KBr} cm^{-1} 3464, 1717, 1453, 1257, 1086, 759; EIMS *m/z*: 636 $[M]^+$ (10), 621 $[M—CH_3]^+$ (29), 619 $[M—OH]^+$ (100), 603 (22), 400 (35), 202 (53); ^{1}H and ^{13}C-NMR: see Table I.

Sinomontantine B (2)

White amorphous powder, $[\alpha]_D$ +1.0 (c 0.5, $CHCl_3$); IR_{max}^{KBr} cm^{-1} 3360, 1727, 1588, 1527, 1449, 1250, 1089, 757; EIMS *m/z*: 651 $[M+1]^+$ (15), 618 $[M—COCH_3—H]^+$ (100); ^{1}H-NMR (200 MHz): δ 1.06 (3H, t, $J=7.1$ Hz, $N-CH_2CH_3$), 2.04 (3H, s, OAc), 3.21. 3.26, 3.32 (each 3H, s, $3 \times OCH_3$), 3.85, 4.02 (each 1H, ABq, $J=10.8$ Hz, H_2-18), 7.23–8.10 (4H, m, aromatic protons), 2.92, 2.94 [each 2H, ABq, $J=6.8$ Hz, H-2''/3'' (α) or H-2''/3'' (β)]; ^{13}C-NMR (50 MHz): see Table I.

Sinomontanine B (3)

White amorphous powder, $[\alpha]_D$+31.2 (c 0.5, $CHCl_3$); IR_{max}^{KBr} cm^{-1} 3411, 1680, 1660, 1588, 1525, 1448, 1268, 1087, 758; CIMS *m/z*: 557 $[M+1]^+$ (8), 525 $[M—OCH_3]^+$ (3), 378 (31) 360 (42), 180 (100). 162 (74), 138 (33), 120 (74); ^{1}H NMR (200 MHz): δ 2.20 (3H, s, $NHCOCH_3$), 3.27 (6H, s, $2 \times OCH_3$), 3.38 (3H, s, OCH_3), 6.90~8.70 (4H, m, aromatic protons), 11.0 (1H, br.s, disappeared with D_2O, NH); ^{13}C-NMR (50 MHz): see Table II.

Sinomontanine B (4)

White amorphous powder, $[\alpha]_D$ +37.1 (c 1.0, $CHCl_3$); IR_{max}^{KBr} cm^{-1} 3490, 1700, 1682, 1588, 1525, 1448, 1267, 1087, 757; EIMS *m/z*: 570 $[M]^+$ (9), 569 $[M-1]^+$ (64), 553 $[M—OH]^+$ (23), 376 (100); ^{1}H-NMR (200 MHz): δ 1.14 (3H, t, $J=7.1$ Hz, N-CH_2CH_3), 2.25 (2.23) (3H, s, $COCH_3$), 3.33 (3.32), 3.36 (each 3H, s, $2 \times OCH_3$), 7.03 (1H, t, $J=7.2$ Hz, H-4'), 7.69 (1H, d, $J=8.3$ Hz, H-6'), 7.92 (1H, d, $J=7.9$ Hz, H-3'), (1H, t, $J=$ H-5'). 11.07 (1H, s, disappeared with D_2O, NH); ^{13}C-NMR (50 MHz): see Table II.

Sinomontanine B (5)

White amorphous powder $[\alpha]_D$ +21.8 (c 0.5, $CHCl_3$); IR_{max}^{KBr} cm^{-1} 3400, 3291, 1714, 1630, 1600, 1495, 1454, 1389, 1264, 1187, 1085, 759; EIMS *m/z*: 624 $[M]^+$ (4), 607 $[M—OH]^+$ (23), 591 (5), 404 (11), 388 (14), 350 (12), 219 (11), 202 (ArCO, 38), 119 (51), 83 (93), 57 (77), 41 (100); ^{1}H-NMR (200 MHz): δ 1.12 (3H, t, J = 7.1 Hz, NCH_2CH_3), 3.30, 3.33 (each 3H, s, 2 × OCH_3), 4.84 (1H, d, J = 4.8 Hz, H-14β), 7.21–8.07 (4H, m, aromatic protons); ^{13}C NMR (50 MHz): see Table II.

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