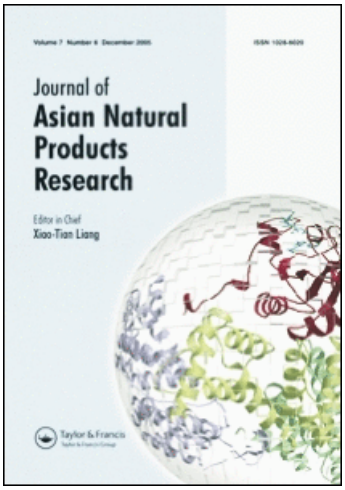

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New Norditerpenoid Alkaloids from the Roots of *Aconitum Geniculatum*

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NEW NORDITERPENOID ALKALOIDS FROM THE ROOTS OF *ACONITUM GENICULATUM*

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Four new norditerpenoid alkaloids, geniculatines A (**1**), B (**4**), C (**7**) and D (**8**), were isolated from the roots of *Aconitum geniculatum* Fletcher, and their structures were elucidated by spectral methods.

Keywords: *Aconitum geniculatum*; *Ranunculaceae*; Norditerpenoid alkaloid; Geniculatine A; Geniculatine B; Geniculatine C; Geniculatine D

INTRODUCTION

Aconitum geniculatum Fletcher, native to China, grows in northeast part of Yunnan province. Hao *et al.* [1] reported seven norditerpenoid alkaloids, yunnaconitine, crassicauline A, vilmorrianine C, talatisamine, chasmanine, 8-deacetylyunnaconitine and geniconitine isolated from this plant. In our continuing investigation of *Aconitum geniculatum*, the known norditerpenoid alkaloids, yunnaconitine, foresaconitine, vilmorrianines A and C, austroconitine B, 8-acetyl-14-benzoylneoline, indaconitine, 8-acetyl-14-benzoylchasmanine, 14-acetylsachaconitine, sachaconitine, karacoline, cammaconine, talatisamine, isotalatizidine and chasmanine [2], as well as four new norditerpenoid alkaloids, geniculatines A (**1**), B (**4**), C (**7**), and D (**8**)

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were isolated. In this paper we report the structure determination of these new alkaloids.

RESULTS AND DISCUSSION

The molecular formulae of the new alkaloids, geniculatine A (**1**), $C_{34}H_{47}NO_9$, B (**4**), $C_{33}H_{47}NO_9$, C (**7**), $C_{34}H_{47}NO_9$, and D (**8**), $C_{32}H_{45}NO_8$, were determined from their EI mass, ^{1}H- and ^{13}C-NMR spectra. Their ^{1}H-and ^{13}C-NMR spectra showed characteristic signals of the aconitine-type norditerpenoid alkaloids [3, 4].

The NMR spectrum of geniculatine A (**1**) exhibited the presence of an *N*-ethyl group (δ_H 1.14, 3H, t, $J = 7.2$ Hz; δ_C 48.2 t and 12.8 q), three methoxyl groups (δ_H 3.17, 3.30 and 3.37, each 3H, s; δ_C 56.6 q, 57.9 q and 59.1 q), an acetyl group (δ_H 1.42, 3H, s; δ_C 169.7 s and 21.6 q) and an anisoyl group (δ_H 3.84, 3H, s; 6.90 and 7.89, each 2H, AA′BB′ system, d, $J = 8.8$ Hz); δ_C 165.1 s (COO), 122.5 s (C-1′), 131.6 d (C-2′, 6′), 113.6 d (C-3′, 5′), 163.3 s (C-4′), 55.3 q (4′-OCH_3). The ^{1}H NMR spectrum of geniculatine A (**1**) also gave a signal at δ_H 5.04 (^{1}H, t, $J = 5.0$ Hz), attributable to the H-14β [3, 4]. Its ^{1}H NMR spectrum displayed the 3H singlet at δ 1.42 and the 1H triplet ($J = 5.0$ Hz) at δ 5.04, suggesting the presence of the 8-OAc and 14-OAs moiety [4–6]. Comparison of the ^{1}H- and ^{13}C-NMR spectra of geniculatine A (**1**) with those of 8-acetyl-14-benzoyl neoline (**2**) [3] (Tab. I) clearly indicated that the new alkaloid is derivative of **2** possessing an anisoyl group at C-14α instead of a benzoyl group. Treatment of **1** with 10% NaOH methanol solution gave neoline (**3**) [3].

The NMR spectrum of geniculatine B (**4**) gave signals at δ_H 1.15 (3H, t, $J = 6.8$ Hz), δ_C 48.2 t and 12.9 q for an *N*-ethyl group, δ_H 3.26, 3.31 and 3.31 (each 3H, s); δ_C 56.0 q, 57.9 q and 59.1 q for three methoxyl groups, and δ_H 3.91 (6H, s), 6.87, 7.62 (each 1H, d, $J = 8.4$ Hz), 7.56 (1H, s), δ_C 165.8 s (COO), 122.5 s (C-1′), 112.0 d (C-2′), 148.5 d (C-3′), 152.9 s (C-4′), 110.3 d (C-5′), 123.5 d (C-6′), 55.8 q (3′-OCH_3), 56.1 q (4′-OCH_3) for a veratroyl group. In its ^{1}H NMR spectrum, the 1H triplet ($J = 4.6$ Hz) at δ 5.15 was assigned as the H-14β [3]. Compared with 14-benzoyl neoline (**5**) [4], their ^{13}C NMR data (Tab. I) are very similar, except for the ester groups. Hydrolysis of geniculatine B (**4**) with 10% NaOH methanol solution afforded neoline (**3**) [3].

The NMR spectrum of geniculatine C (**7**) showed the presence of an *N*-ethyl group (δ_H 1.13, 3H, t, $J = 7.2$ Hz; δ_C 48.4 t and 12.7 q), two aliphatic

TABLE I ^{13}C NMR data of compounds **1**, **2** [3], **4**, **5** [7], **7** and **8**

Carbon no.	**1**	**2**	**4**	**5**	**7**	**8**
1	72.0	72.2	72.0	72.0	71.9	85.7
2	29.3	29.5	29.3	29.3	26.5	25.4
3	29.9	30.1	30.8	29.9	29.6	31.8
4	38.0	38.9	38.0	38.1	37.0	38.2
5	44.1	44.4	44.3	44.4	41.2	45.8
6	83.7	84.0	83.3	83.3	24.8	24.9
7	47.9	48.2	53.1	52.9	43.1	45.6
8	85.7	85.9	74.7	74.8	86.3	72.7
9	43.2	43.5	45.8	46.0	41.2	46.8
10	42.9	43.2*	43.6	43.6	40.5	45.8
11	49.6	49.9	49.7	49.6	48.8	48.7
12	29.3	29.5	29.5	29.5	29.0	27.6
13	38.8	38.2*	37.6	37.4	39.0	37.5
14	75.4	75.7	76.7	76.9	75.8	75.4
15	38.6	38.9	42.5	42.5	38.4	38.4
16	82.7	82.8	81.9	81.9	82.8	82.0
17	62.9	63.0	63.2	63.3	63.2	62.6
18	79.8	79.9	80.0	80.0	78.6	70.1
19	56.6	56.9	56.8	56.9	56.3	52.9
NCH_2CH_3	48.2	48.3	48.2	48.2	48.4	49.4
NCH_2CH_3	12.8	13.0	12.9	13.0	12.7	13.4
1α-OCH_3	–	–	–	–	–	56.4
6α-OCH_3	57.9	57.9	57.9	57.9	–	–
16β-OCH_3	56.6	56.6	56.0	56.0	56.6	56.3
18-OCH_3	59.1	59.1	59.1	59.1	59.3	–
O=C	165.1	166.0	165.8	166.0	164.7	166.2
1′	122.5	130.3	122.5	130.1	123.2	122.6
2′	131.6	129.7	112.0	129.5	111.4	112.2
3′	113.6	128.4	148.5	128.4	148.5	148.6
4′	163.3	133.0	152.9	132.9	152.9	152.9
5′	113.6	128.4	110.3	128.4	110.1	110.2
6′	131.6	129.7	123.5	129.5	123.2	123.3
3′-OCH_3	–	–	55.8	–	55.8	55.9
4′-OCH_3	55.3	–	56.1	–	55.9	55.9
O=C–CH_3	169.7	169.6	–	–	171.2	–
O=C–CH_3	21.6	21.6	–	–	21.5	–

* Assignments in Ref. [3] may be interchangeable.

methoxyl groups (δ_H 3.23, 3.33, each 3H, s; δ_C 56.6 q, 59.3 q), the acetyl group (δ_H 1.77, 3H, s; δ_C 171.2 s, 21.5 q), and a veratroyl group (δ_H 6.85, 1H, t, $J = 8.4$ Hz; 7.44, 1H, d, $J = 1.8$ Hz; 7.57, 1H, dd, $J = 8.4$, 1.8 Hz; 3.90, 3.91, each 3H, s; δ_C 164.7 s (COO), 123.2 s (C-1′), 111.4 d (C-2′), 148.5 s (C-3′), 152.9 s (C-4′), 110.1 d (C-5′), 123.2 d (C-6′), 55.8 q (3′-OCH_3), 55.9 q (4′-OCH_3). Only one secondary hydroxyl group in **7** was located at C-1 due to the chemical shifts of the C-4 (δ_C 37.0 s) and C-11 (δ_C 48.8 s) (Tab. I) [3, 4]. Assignments of two aliphatic methoxyl groups at C-16 and C-18 were carried out mainly based on biogenesis [3, 4] and the triplet signal at δ_C 78.6

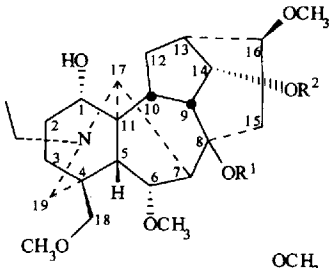
(Tab. I) attributable to C-18. The key point for structural elucidation of geniculatine C (**7**) was the location of two ester groups. Because the ^{1}H NMR spectrum of **7** exhibited the 1H triplet ($J=4.6$ Hz) at δ_C 4.79, attributable to the H-14β, one of two ester groups is probably at C-14. The remaining ester group was located at C-8 due to the presence of the downshifted signal at δ_C 86.3 s. Finally, a substitution relationship of the 8-OVr and 14-OAc groups, as in ezochasmacontine (**6**) [3], was determined owing to the absence of the signal at about δ_H 1.3 for the 8-OAc group.

The NMR spectrum of geniculatine D (**8**) showed signals at δ_H 1.07 (3H, t, $J=6.6$ Hz); δ_C 49.4 t and 13.4 q for an *N*-ethyl group, δ_H 3.27, 3.34 (each 3H, s), δ_C 56.3 q, 56.4 q for two aliphatic methoxyl groups, δ_H 6.88 (1H, d, $J=8.4$ Hz), 7.52 (1H, br.s), 7.63 (1H, dd, $J=8.4$, 1.6 Hz), 3.93 (6H, s); δ_C 166.2 s (COO), 122.6 s (C-1′), 112.2 d (C-2′), 148.6 s (C-3′), 152.9 s (C-4′), 110.2 d (C-5′), 123.3 d (C-6′), 55.9 q (3′-OCH_3), 55.9 q (4′-OCH_3) for the veratroyl group. The 1H triplet ($J=4.6$ Hz) at δ_H 4.84 in the ^{1}H NMR spectrum of **8** was assigned to the H-14β, indicating that it had a veratroyl group at C-14. Two aliphatic methoxyl groups at C-1 and C-16 were located on basis of a characteristic fragment ion peak at *m/z* 540 (M-31, 100) in the MS spectrum of **8** [6] and the biogenetical consideration for the norditerpenoid alkaloids [3, 4], respectively. Only one primary hydroxyl group should be located at C-18 due to the triplet signal at δ_C 70.1 (Tab. I). In addition, according to the biogenetical relationship of the norditerpenoid alkaloids [3, 4], the remaining tertiary hydroxyl group also was assigned at C-8 (δ_C 72.7 s) (Tab. I). Thus, the structure of geniculatine D was deduced as **8**.

EXPERIMENTAL SECTION

General Experimental Procedures

The IR were recorded on Perkin-Elmer 983 spectrophotometer. The OR were taken on a Perkin-Elmer 241 polarimeter. The EIMS were measured on a VG Auto spec 3000 instrument, 70 eV. The ^{1}H- and ^{13}C-NMR spectra were recorded on Bruker AC-E 200 spectrometer with TMS as internal standard. Silica gel GF_{254} and H (Qingdao Sea Chemical Factory, China) were used for TLC, Chromatodron and CC, respectively. Spots on TLC plates were detected under UV light (254 nm) and with modified Dragendorff's reagent.



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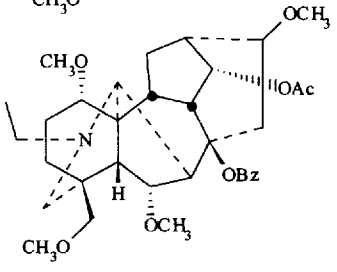
2	Ac	Bz
3	H	H
4	H	Vr
5	H	Bz



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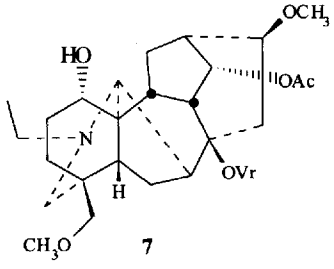

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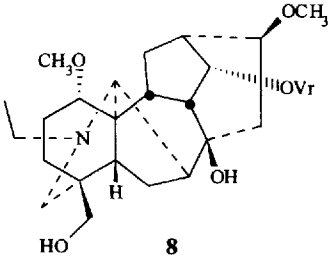

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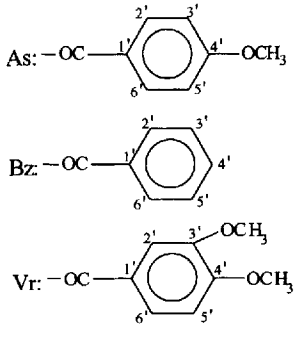

Plant Material

Plants were collected in Huize county of Yunnan province, China, at an altitude 3200 m, and authenticated by Professor Wu, Kunming Institute of Botany, Chinese Academy of Sciences, where a voucher specimen has been deposited.

Extraction and Isolation of Alkaloids

The total alkaloids (96.0 g), which were obtained from the air-dried roots (13 kg) of this plant by using an ion exchange method [2, 7], were divided into four parts: A (pH 1 : 12.5 g), B (pH 5 : 3.0 g), C (pH 7.5 : 39.0 g) and D (pH 12 : 3.0 g), by pH gradient separation.

CC of part A using $CHCl_3$–MeOH (98 : 2) led to fractions A (0.8 g), which was chromatographed on a Chromatodron eluting with ether–petroleum (3 : 1) to give geniculatine A (**1**) (34 mg) and geniculatine C (**7**) (20 mg). CC of part **B** using hexane–acetone (9 : 1) containing 0.5% diethylamine afforded fractions C (0.6 g), D (65 mg) and geniculatine D (**8**) (48 mg). CC of fractions D using $CHCl_3$–MeOH (98 : 2) gave geniculatine B (**4**) (35 mg). Separation and identification (TLC, MS, ^{1}H-and ^{13}C-NMR) of all of the known alkaloids see Ref. [2].

Geniculatine A (1) White amorphous substance, $[\alpha]_D + 19.3$ (*c* 0.5, $CHCl_3$). EIMS *m/z* (%): 613 (M^+, 3), 596 (M–OH, 8), 554 (M–OAc, 6), 135 (OAs, 15), 57 (100). ^{1}H NMR: δ 1.14 (3H, t, $J = 7.2$ Hz, NCH_2CH_3), 1.42 (3H, s, OAc), 3.17, 3.30, 3.37, 3.84 (each 3H, s, $4 \times OCH_3$), 4.04 (1H, d, $J = 5.4$ Hz, H-6β), 5.04 (1H, t, $J = 5.0$ Hz, H-14β), 6.90, 7.98 (each 2H, AA′BB′ system, d, $J = 8.8$ Hz, H–Ar). ^{13}C NMR: Table I.

Geniculatine B (4) White amorphous substance, $[\alpha]_D + 27.0$ (*c* 0.5, $CHCl_3$). IR $\lambda_{max}^{KBr}cm^{-1}$: 3460 (OH), 1720 (COO), 1284. EIMS *m/z* (%): 601 (M^+, 13), 584 (M–OH, 39), 165 (28), 43 (100). ^{1}H NMR: δ 1.15 (3H, t, $J = 6.8$ Hz, NCH_2CH_3), 3.26, 3.31, 3.31 (each 3H, s, $3 \times OCH_3$), 3.91 (6H, s, two aromatic methoxyl groups), 5.15 (1H, t, $J = 4.6$ Hz, H-14β), 7.56 (1H, s, H-2′), 6.87, 7.62 (each 1H, ABq, $J = 8.4$ Hz, H-5′ and H-6′). ^{13}C NMR: Table I.

Geniculatine C (7) White amorphous substance, $[\alpha]_D + 50.0$ (*c* 0.70, $CHCl_3$). IR $\lambda_{max}^{KBr}cm^{-1}$: 3470, 1745, 1716, 1280, 1120. EIMS *m/z* (%): 613 (M^+, 4), 596 (M–OH, 81), 554 (M–OAc, 4), 135 (OAs, 18), 43 (100). ^{1}H NMR: δ 1.13 (3H, t, $J = 7.2$ Hz, NCH_2CH_3), 1.77 (3H, s, OAc), 3.23, 3.33 (each 3H, s, $2 \times OCH_3$), 3.90, 3.91 (each 3H, s, two aromatic methoxyl groups), 4.79 (1H, t, $J = 4.6$ Hz, H-14β), 7.44 (1H, d, $J = 1.8$ Hz, H-2′), 6.85, 7.57 (each 1H, ABq, $J = 8.4$ Hz, H-5′ and H-6′). ^{13}C NMR: Table I.

Geniculatine D (8) White amorphous substance, $[\alpha]_D + 7.30$ (*c* 0.6, $CHCl_3$). IR $\lambda_{max}^{KBr}cm^{-1}$: 3464, 1745, 1720, 1280, EIMS *m/z* (%): 571(M^-, 6), 540 (M–OCH_3, 100), 492 (20). ^{1}H NMR: δ1.07 (3H, t, $J = 6.6$ Hz, NCH_2CH_3), 3.27, 3.34 (each 3H, s, $2 \times OCH_3$), 3.93 (6H, s, two aromatic methoxyl groups), 4.84 (1H, t, $J = 4.5$ Hz, H-14β), 7.52 (1H, d, $J = 1.6$ Hz, H-2′), 6.88, 7.63 (each 1H, ABq, $J = 8.4$ Hz, H-5′ and H-6′). ^{13}C NMR: Table I.

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