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## DITERPENOID ALKALOIDS FROM *ACONITUM RACEMULOSUM* FRANCH VAR. *PENGZHOUENSE*

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A new diterpenoid alkaloid, racemulotine (**1**), was isolated from the whole plants of *Aconitum racemulosum* Franch var. *pengzhouense*, and its structure was elucidated by 1D- and 2D-NMR spectra.

**Keywords:** *Aconitum racemulosum* Franch var. *pengzhouense*; *Ranunculaceae*; Diterpenoid alkaloid; Racemulotine

### INTRODUCTION

New species plant *Aconitum racemulosum* Franch var. *pengzhouense* Zhang and Chen (*Ranunculaceae*) [1] native to China was collected at elevation of 1500–2200 m in Peng county of Sichuan Province, China. To our knowledge, no chemical work on this plant has been carried out before. In the course of our research in *Aconitum* species, many of which are used in the traditional folk medicines of China, from the whole plant of *Aconitum racemulosum* Franch var. *pengzhouense*, we have isolated a diterpenoid alkaloid, racemulotine (**1**), together with 6 known alkaloids, isotalatizidine, nevadene, virescine, 14-acetylvirescine, anthranoyllycoctonine and atisinum hydrochloride [2]. In this paper, we report structural elucidation of new alkaloid (**1**).

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## RESULTS AND DISCUSSION

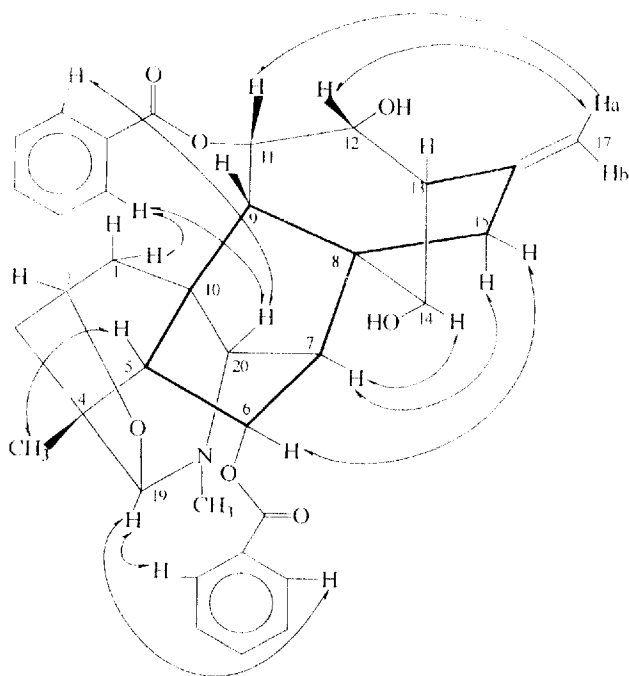
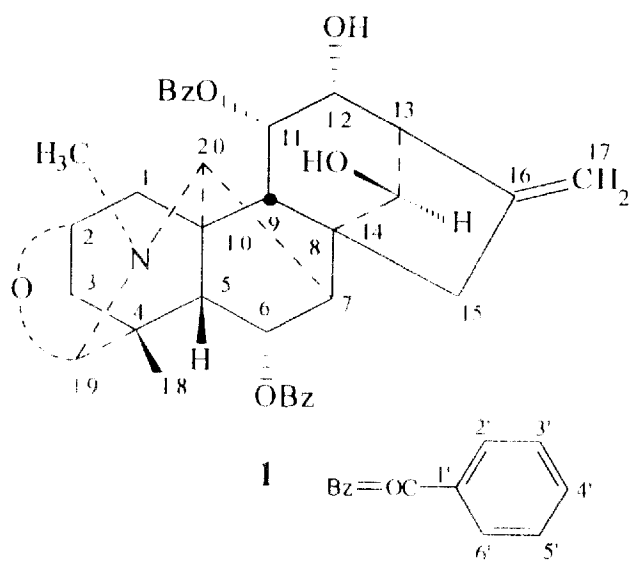
Racemulotine (**1**) was isolated as an amorphous powder and its molecular formula  $C_{35}H_{35}NO_7$  was confirmed by NMR and MS spectra. The NMR and IR spectra of **1** showed signals at  $\delta_H$  2.97 (3H, s),  $\delta_C$  35.3 q for the *N*-methyl group,  $\delta_H$  1.07 (3H, s),  $\delta_C$  21.1 q for the angular methyl group,  $\delta_H$  4.85, 4.97 (each 1H, br.s),  $\delta_C$  148.2 s and 109.3 t for an exocyclic methylene group,  $\delta_H$  6.94–7.66 (10H, m),  $\delta_C$  164.1 s (164.1 s), 142.7 s (142.7 s), 127.5 d (127.8 d), 129.0 d (128.5 d) and 132.4 d (132.7 d); 1710, 1601, 1581, 1450, 1276 and  $710\text{ cm}^{-1}$  for two benzoyl groups, and  $\delta_H$  5.45 (1H, s),  $\delta_C$  102.4 d;  $\delta_H$  5.56 (1H, br.s,  $W_{1/2}=6.0\text{ Hz}$ ),  $\delta_C$  67.5 d for the *N,O*-mixed acetal [C(2)–O–C(19)–N] moiety, which was assigned because of the presence of the three-bond correlations of the H-18 ( $\delta$  1.07, 3H, s) and the H-2 ( $\delta$  5.56, 1H, br.s,  $W_{1/2}=6.0\text{ Hz}$ ) with the C-19 at  $\delta_C$  102.4 d in the HMBC spectrum of **1**. The correlations of the signals at  $\delta_H$  4.36 (1H, d,  $J=9.2\text{ Hz}$ ) and  $\delta_H$  3.71 (1H, br.s) with that at  $\delta_C$  72.5 d and  $\delta_C$  72.5 d, respectively, in the HMQC spectrum of **1** indicated that racemulotine (**1**) had two secondary hydroxyl groups. The analysis of the spectral data of **1** mentioned above led to the experimental formula  $C_{20}H_{22}(NCH_3 \times 1 - OOC - C_6H_5 \times 2 - HO \times 2 - O \times 1)$ , in addition to the biogenetical consideration, suggesting that racemulotine (**1**) was a diterpenoid alkaloid. The new base racemulotine (**1**) belongs to the napelline-type diterpenoid alkaloids instead of the others, e.g., the atisines, hetidines, hetisines, vatchines and anopterines because of possessing 7 unsaturated degrees for the skeletal system and three distinctive quarternary carbon signals at  $\delta_C$  39.5 (C-4), 50.3 (C-8) and 48.3 (C-10) in the  $^{13}\text{C}$ -NMR spectrum of **1** [3].

The key points of structural elucidation of **1** are determination of location of two benzoyl and two hydroxyl groups, attributable at C-1, C-3, C-6, C-11, C-12, C-14 and C-15. The  $^1\text{H}$ – $^1\text{H}$  COSY spectrum of racemulotine (**1**) revealed scalar connectivities of the H-2 $\beta$  ( $\delta$  5.56, br.s) and the H-17 ( $\delta$  4.88 and 4.97, each 1H, br.s) with the H-1 $\alpha$  ( $\delta$  3.48, d,  $J=16.8\text{ Hz}$ ), H-1 $\beta$  ( $\delta$  2.18, dd,  $J=17.2, 5.2\text{ Hz}$ ), H-3 $\alpha$  ( $\delta$  1.99, d,  $J=16.2\text{ Hz}$ ), H-3 $\beta$  ( $\delta$  1.76, dd,  $J=16.2, 4.4\text{ Hz}$ ) and the H-15 $\alpha$  ( $\delta$  2.19, br.d,  $J=17.2\text{ Hz}$ ), H-15 $\beta$  ( $\delta$  2.47, br.d,  $J=18.0\text{ Hz}$ ) (Tab. I), respectively, thus ruling out the substitutions at C-1, C-3 and C-15. This implied that four oxygenated functionalities in **1** were located at C-6, C-11, C-12 and C-14. Two secondary benzoyl groups ( $\delta_C$  65.8 d and 72.5 d) in **1** may be assigned as the 6 $\alpha$ - and 11 $\alpha$ -patterns due to spatial correlations between the H-19 ( $\delta_H$  5.45, s;  $\delta_C$  102.4 d) and H-2''/6'' ( $\delta_H$  7.36, dd,  $J=8.4, 1.2\text{ Hz}$ ;  $\delta_C$  127.5 d), the H-1 $\alpha$  ( $\delta_H$  3.48, d,  $J=16.8\text{ Hz}$ ;  $\delta_C$  30.4 t) and H-2''/6'' ( $\delta_H$  7.66, dd,  $J=8.4, 1.2\text{ Hz}$ ;  $\delta_C$  127.8 d), in the

TABLE I NMR data of compound 1 ( $^1\text{H}$ : 400 MHz,  $^{13}\text{C}$ : 100 MHz;  $\text{CDCl}_3$ )

Carbon	$\delta_{\text{C}}$	$\delta_{\text{H}}$
1	30.4 t	2.18 dd (17.2, 5.2) ( $\beta$ ) 3.48 d (16.8) ( $\alpha$ )
2	67.5 d	5.56 br.s ( $W/2 = 6.0$ )
3	34.7 t	1.76 dd (16.2, 4.4) ( $\beta$ ) 1.99 d (16.2) ( $\alpha$ )
4	39.5 s	—
5	55.1 d	2.39 br.s
6	65.8 d	4.00 m ( $W/2 = 8.0$ ) ( $\beta$ )
7	56.8 d	2.39 s
8	50.3 s	—
9	49.1 d	2.57 d (2.8)
10	48.3 s	—
11	73.8 d	5.31 dt (10.2, 2.0)
12	72.5 d	4.36 d (9.2)
13	44.0 d	3.13 dd (9.8, 1.8)
14	72.5 d	3.71 s
15	28.7 t	2.19 br.d (17.2) ( $\alpha$ ) 2.74 br.d (18.0) ( $\beta$ )
16	142.8 s	—
17	109.3 t	4.85 br.s (a), 4.97 br.s (b)
18	21.1 q	1.07 s
19	102.4 d	5.45 s
20	68.2 d	3.71 br.s
<i>N</i> -CH <sub>3</sub>	35.3 q	2.97 s
6-COO	164.1 s	—
1''	142.7 s	—
2'/6'	127.5 d	7.36 dd (8.4, 1.2)
3'/5'	129.0 d	7.25 t (7.6)
4'	132.4 d	7.44 ddt (7.6, 7.6, 1.2)
11-COO	164.1 s	—
1'	142.7 s	—
2'/6'	127.8 d	7.66 dd (8.4, 1.2)
3'/5'	128.5 d	6.94 t (7.6)
4'	132.7 d	7.19 ddt (7.6, 7.6, 1.2)

NOESY spectrum (Tab. I). Determination of the 12 $\alpha$ -hydroxyl group in **1** was inferred from observation of spatial connectivity between the H<sub>a</sub>-17 ( $\delta_{\text{H}}$  4.85, br.s;  $\delta_{\text{C}}$  109.3 t) and H-12 ( $\delta_{\text{H}}$  4.36, d,  $J = 9.2$  Hz;  $\delta_{\text{C}}$  72.5 d) in the NOESY spectrum and coupling constant ( $J = 9.2$  Hz) between the H-11 and H-12 in the  $^1\text{H}$  NMR spectrum. On the other hand, the H-14 $\alpha$  ( $\delta_{\text{H}}$  3.71, s;  $\delta_{\text{C}}$  72.5 d, MHQC) signals, which is part of the ring D, gave correlations with the H-7 ( $\delta_{\text{H}}$  2.39, s;  $\delta_{\text{C}}$  56.8 d) in the NOESY spectrum and the H-7 and H-9 ( $\delta_{\text{H}}$  2.57, d,  $J = 2.8$  Hz;  $\delta_{\text{C}}$  49.1 d) in the HMBC spectrum, respectively (Figs. 1 and 2). These observations indicated there was a secondary hydroxyl group at C-14 $\alpha$  in racemulotine (**1**). Thus, the structure of racemulotine was elucidated as **1**.



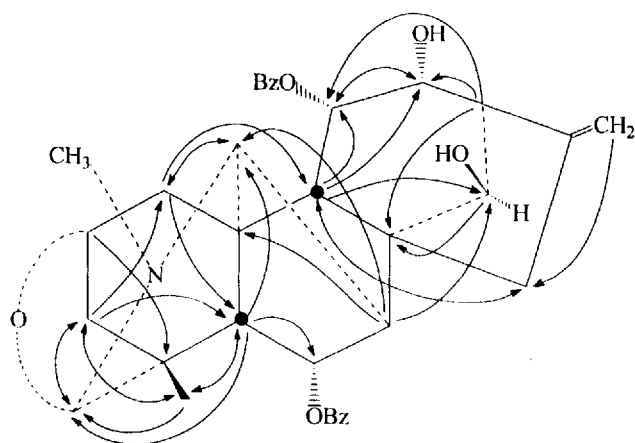


FIGURE 2 Key HMBC (H to C) correlations for **1**.

## EXPERIMENTAL SECTION

### General Experimental Procedures

IR spectra were measured on Nicolet 200 SXV spectrometer. Optical rotations were measured on Perkin-Elmer 241 polarimeter,  $\text{CHCl}_3$ , 1 cm cell. FABMS data were recorded by VG Auto spec 3000 instruments.  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR were measured on a Varian INOVA-400/54 spectrometers,  $\text{CDCl}_3$  and TMS as internal standard. Silica gel (GF<sub>254</sub> and H) (Qindao Sea Chemical Factory, China) were used for TLC (S<sub>1</sub>:  $\text{CHCl}_3$ -MeOH, 9:1; S<sub>2</sub>:  $\text{Et}_2\text{O}$ - $\text{CH}_3\text{COCH}_3$ , 85:15), Chromatodron and column chromatography. Spots on chromatograms were detected with modified Dragendorff's reagent. A polyvinyl sulphonic ion exchange resin (H-form, cross linking 1 × 3, Nankai University Chemical Factory, China) was used in the extraction of total alkaloids.

### Plant Material

Plants were collected in Peng county of Sichuan province, China, and authenticated by Professor W. T. Wang, Institute of Botany, Chinese Academy of Sciences, where a voucher specimen has been deposited.

### Extraction and Isolation

According to the literature method [4], 4.0 kg of dried powdered whole plants of *Aconitum racemulosum* Franch var. *pengzhouense* were percolated

with 0.2% HCl until 50 L were collected. A column of 9 kg wet resin (dry weight 0.9 kg) was used to treat the percolates. After exchange, the resin was washed repeatedly on a suction filter with deionized water, spread out and air dried overnight. The resin, now weighing 1.1 kg, was well mixed with 1800 ml of 10% ammonia water and continuously extracted in a specially designed extractor [4] with several portions of ether (total amount: 2500 ml) under reflux until a negative detection to modified Dragendorff's reagent. White powder (18.6 g) of the crude alkaloids I from the ethereal extracts were collected by evaporation of ether on reduced pressure.

Using a pH gradient method, the crude alkaloids I (18 g) was separated in four parts, part A (pH 2, 1.7 g), part B (pH 7, 5.7 g), part C (pH 9, 9.5 g) and part D (pH 11, 910 mg). Part A was chromatographed successively on silica gel column and a Chromatodron, respectively, eluting with  $\text{CHCl}_3$ -MeOH (93:7  $\rightarrow$  95:5) containing 1% diethylamine to give racemulotine (**1**) (11 mg). Separation and identification (TLC, MS,  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR) of all of the known alkaloids besides **5** were described in Ref. [2].

**Racemulotine (1)** White amorphous powder,  $[\alpha]_{\text{D}}^{17} -34.4$  (c 0.2,  $\text{CHCl}_3$ );  $\text{IR}_{\text{max}}^{\text{KBr}} \text{ cm}^{-1}$ : 3410, 3066, 1710, 1601, 1581, 1456, 1276, 710; FABMS:  $m/z$  (%) 584 (100,  $\text{M} + 1$ ), 564 (41), 344 (19), 330 (23), 105 (56), 77 (19);  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR, see Table I.

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