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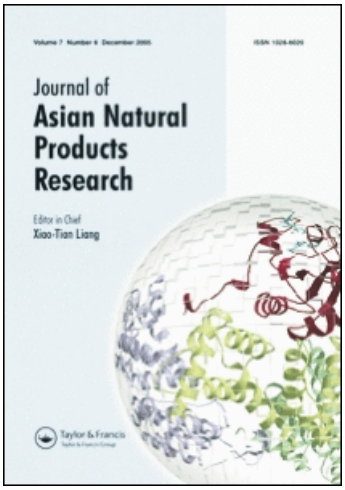

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Two novel isosteroid alkaloids from *Fritillaria monatha*

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Two novel isosteroid alkaloids from *Fritillaria monatha*

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Two new isosteroid alkaloids, *N*-methyl-22,26-imino-13,22-oxido-5α,20α-jervine-3β-ol-6-one, pengbeimine B (**1**) and *N*-methyl-22,26-imino-13,22-oxido-5α,20β-jervine-3β-ol-6-one, pengbeimine D (**2**) were isolated from the fresh bulbs of *Fritillaria monatha* Migo. Their structures were determined by spectral methods, and were proved by X-ray diffraction.

Keywords: *Fritillaria monatha*; Isosteroid alkaloid; Pengbeimine B; Pengbeimine D

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1. Introduction

Fritillaria monatha Migo is a new plant of the genus *Fritillaria* in Jiangxi Province of China. Only one paper reported the isolation and identification of the chemical constituents from its bulbs, while some new constituents were obtained from other plants of the same genus, such as fritillahupehin [1]. Our investigation on the *F. monatha* Migo led to the isolation of two new compounds, *N*-methyl-22,26-imino-13,22-oxido-5α,20α-jervine-3β-ol-6-one, pengbeimine B (**1**) and *N*-methyl-22,26-imino-13,22-oxido-5α,20β-jervine-3β-ol-6-one, pengbeimine D (**2**). Here we report the isolation and structure elucidation.

2. Results and discussion

Compound **1** was obtained as colourless sheet crystals (MeOH). The molecular formula of **1** was deduced to be $C_{28}H_{45}NO_3$ according to the HREI-MS ($M^+ = m/z$ 443.3391) measurement. The IR spectrum of **1** gave the characteristic absorptions at 3400 cm^{-1} (OH), 1701 cm^{-1} (C═O). In EI-MS, fragment ion peaks at *m/z* 138, 125, 124, 114, 110, indicated that **1** had the skeleton of jervine alkaloid [2]. In ^1H NMR, signals at δ 0.76 (3H, s), 0.86 (3H, d, $J = 6.5$ Hz), 1.03 (3H, s), 1.07 (3H, d, $J = 7.0$ Hz) and 2.21 (3H, s) suggested five methyl groups, one of them connecting with nitrogen. The chemical shift at δ 3.60 was the signal

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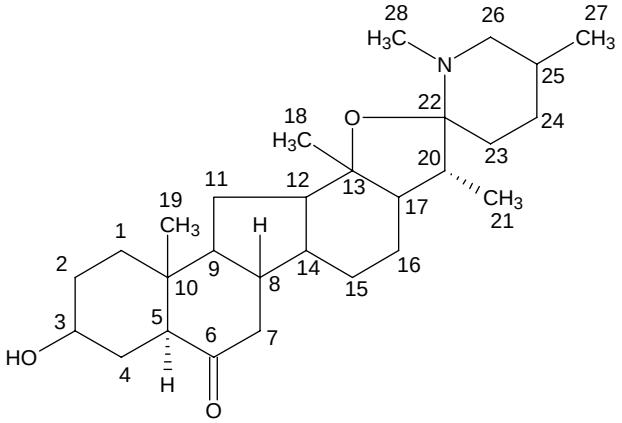
of a methine proton having a hydroxyl group. Comparing the NMR data with those of the analogue peimisine [3], the hydroxyl group in **1** was pointed at C-3. According to the $W_{1/2}$ value (24 Hz) of H-3, the hydroxyl group of C-3 should be located in β orientation [4]. The ^{13}C NMR spectrum of **1** showed the presence of one carbonyl carbon (δ 211.1, C-6) and two special signals at δ 96.9 and 81.7 were suggested to the oxygenated carbon. In HMBC spectrum, there were long-range correlations between C-13 (δ 81.7) with H-14 (δ 2.42), H-12 (δ 1.98), H-18 (δ 1.03), and C-22 (δ 96.9) with H-28 (δ 2.21), H-23 (δ 1.85), H-21 (δ 1.07). These suggested that C-13 and C-22 were connected with oxygen composing oxygen-ring. Combined with the X-ray diffraction (figure 2), the structure of **1** was determined as *N*-methyl-22,26-imino-13,22-oxido-5α,20α-jervine-3β-ol-6-one, named pengbeimine B (figure 1).

Compound **2** was obtained as colourless nubbly crystal (EtOH). The molecular formula of **2** was deduced to be $C_{28}H_{45}NO_3$ by the HREI-MS analysis ($M^+ = m/z$ 443.3356). The IR spectrum gave the characteristic absorptions at 3423 cm^{-1} (OH), 1702 cm^{-1} (C═O). In EI-MS, fragment ion peaks at *m*/*z* 138, 125, 124, 114, 110 indicated that **2** had the skeleton of jervine alkaloid [2]. In ^1H NMR, signals at δ 0.62 (3H, s), 0.79 (3H, d, $J = 6.5$ Hz), 0.99 (3H, d, $J = 7.0$ Hz), 1.02 (3H, s) and 2.08 (3H, s) suggested five methyl groups, one of them



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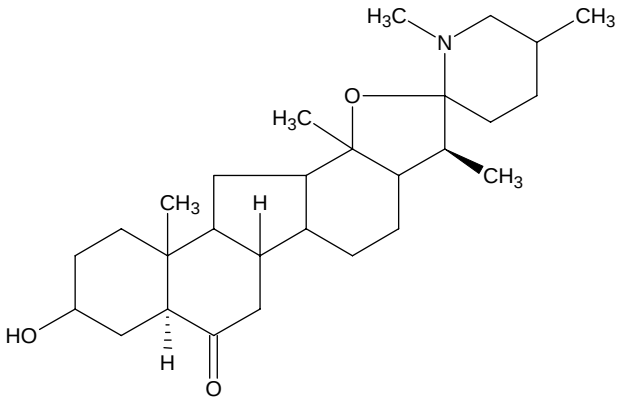

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Figure 1. Structures of **1** and **2**.

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connecting with nitrogen; signal at δ 3.34 (1H, m) suggested the presence of a hydroxyl group. Comparing the ^{1}H NMR and ^{13}C NMR data of compound **1**, the chemical shifts of **1** and **2** were similar, except for C-17, C-20, C-21 and C-22. These data indicated **1** and **2** were isomers. Combined with the X-ray diffraction (figure 2), the structure of **2** was established to be *N*-methyl-22,26-imino-13,22-oxido-5α,20β-jervine-3β-ol-6-one, named pengbeimine D.

3. Experimental

3.1 General experimental procedures

All melting points were determined on a X-4A micro-melting point apparatus and are uncorrected. IR spectra were recorded with a Nicolet Impact 400 spectrometer. ^{1}H NMR, ^{13}C NMR, and HMBC were recorded on AN Innova 500 instrument. EI-MS spectra were recorded on Ultima-Tof. X-ray diffraction was recorded with DIP-2030K apparatus. Silica gel (200–300 mesh; Qingdao Marine Chemical Plant) was used for column chromatography.

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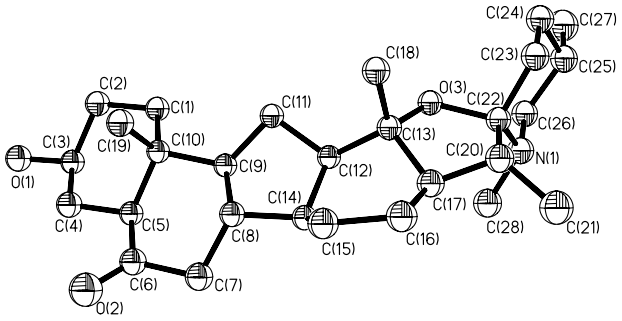
3.2 Plant material

The bulbs of *Fritillaria monatha* Migo were collected in Jiujiang region of Jiangxi Province of China, and identified by Professor Cui-Sheng Fan. A voucher specimen (20030508) is deposited in the Herbarium of Jiangxi University of Traditional Chinese Medicine.



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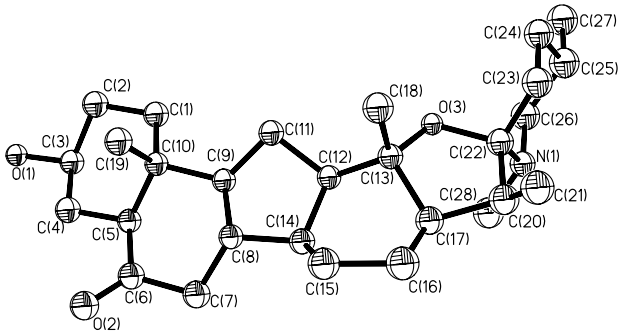

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Figure 2. Perspective view of compounds **1** and **2**.

3.3 Extraction and isolation

Fresh bulbs of *F. monatha* Migo (90 kg) were soaked with 95% EtOH at room temperature. The filtered extract was concentrated *in vacuo* at 60°C. The concentrated EtOH extract was dissolved in 2% HCl aqueous solution. The solution was extracted with chloroform, obtained extract A. The pH of the aqueous solution was readjusted with NH_4OH to 9 and extracted with chloroform, obtaining extract B. The extract A (50 g) was separated by column chromatography on silica gel using a gradient mixture of $CHCl_3$/MeOH as eluting solvent. **1** (46 mg) was obtained in $CHCl_3$/MeOH (5:5). The extract B (80 g) was separated by column chromatography on silica gel using a gradient mixture of C_6H_{12}/EtOAc/ $(Et)_2NH$ (6:4:1) as eluting solvent to give four fractions. Fraction 4 afforded **2** (400 mg).

3.3.1 Pengbeimine B (1). It was obtained as colourless sheet crystal, mp 275–276°C. HREI-MS *m/z* 443.3391 [M^+] (calcd for $C_{28}H_{45}NO_3$, 443.3399). EI-MS *m/z*: 443, 428, 400, 208, 153, 139, 128, 125, 124, 110. IR (KBr) cm^{-1}: 3400, 1701. ^{1}H NMR and ^{13}C NMR data: see table 1.

X-ray diffraction: The crystal belongs to monoclinic with space group $P2_1$, the unit cell parameters being as follows: $a = 7.379$ (1), $b = 10.615$ (1), $c = 16.494$ (1) nm, $\beta = 85.83$ (1)°, $V = 1288.5$ (2) nm, $Z = 2$. All of the measurements were made on an MAC DIT-2030K diffractometer with graphite monochromated MoKα. The data were collected at room

Table 1. ^{1}H-NMR and ^{13}C-NMR spectral data† of **1** and **2**.

	1 *(in $CDCl_3$)*		***2*** *(in DMSO-d_6)*	
No.	δ_C	δ_H	δ_C	δ_H
1	37.7t	1.70 (m, 1H), 1.36 (m, 1H)	36.8t	1.58 (m, 1H), 1.28 (m, 1H)
2	21.4t	1.68 (m, 1H), 1.18 (m, 1H)	21.7t	1.56 (m, 1H), 1.18 (m, 1H)
3	71.2d	3.60 (m, 1H)	68.9d	3.34 (m, 1H)
4	40.2t	1.74 (m, 1H), 1.54 (m, 1H)	39.8t	1.64 (m, 1H), 1.38 (m, 1H)
5	56.5d	2.19 (s, 1H)	55.1d	2.00 (s, 1H)
6	211.1s	–	210.5s	–
7	47.1t	2.50 (m, 1H), 2.10 (m, 1H)	46.0t	2.50 (m, 1H), 2.10 (m, 1H)
8	47.5d	1.84 (m, 1H)	46.7d	1.75 (m, 1H)
9	55.9d	1.62 (m, 1H)	54.4d	1.54 (m, 1H)
10	37.7s	–	37.3s	–
11	29.7t	1.51 (m, 1H), 1.32 (m, 1H)	29.8t	1.36 (m, 1H), 1.26 (m, 1H)
12	42.2d	1.98 (s, 1H)	41.6d	2.14 (s, 1H)
13	81.7s	–	82.4s	–
14	50.5d	2.42 (m, 1H)	48.2d	2.26 (m, 1H)
15	25.4t	1.84 (m, 1H), 1.28 (m, 1H)	24.6t	1.77 (m, 1H), 1.22 (m, 1H)
16	24.8t	1.82 (m, 1H), 1.24 (m, 1H)	24.3t	1.76 (m, 1H), 1.20 (m, 1H)
17	49.3d	1.48 (m, 1H)	37.7d	1.64 (m, 1H)
18	21.0q	1.03 (s, 3H)	19.4q	1.02 (s, 3H)
19	12.7q	0.76 (s, 3H)	12.2q	0.62 (s, 3H)
20	42.6d	2.00 (s, 1H)	39.6d	1.97 (s, 1H)
21	11.6q	1.07 (d, 3H, $J = 7.0$ Hz)	13.2q	0.99 (d, 3H, $J = 7.0$ Hz)
22	96.9s	–	98.3s	–
23	30.8t	1.85 (m, 1H), 1.44 (m, 1H)	30.4t	1.78 (m, 1H), 1.32 (m, 1H)
24	30.2t	1.94 (m, 1H), 1.48 (m, 1H)	29.8t	1.94 (m, 1H), 1.34 (m, 1H)
25	50.3d	2.38 (m, 1H)	50.9d	2.26 (m, 1H)
26	60.5t	2.44 (m, 1H), 2.26 (m, 1H)	59.0t	2.32 (m, 1H), 2.19 (m, 1H)
27	19.5q	0.86 (d, 3H, $J = 6.5$ Hz)	19.4q	0.79 (d, 3H, $J = 6.5$ Hz)
28	40.5q	2.21 (s, 3H)	40.0q	2.08 (s, 3H)

† Assignments based upon HMQC and HMBC experiments.

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temperature by using the $\omega - 2\theta$ scan technique to a maximum 2θ value of 50.0°. A total of 2619 unique reflections were collected. The final cycle of full-matrix least-square refinements was based on 2105 observed reflections $[|F|^2 \geq 3\sigma|F|^2]$ and $R_f = 0.068$, $R_w = 0.066$ ($w = 1/\sigma|F|^2$).

3.3.2 Pengbeimine D (2). It was obtained as colourless nubbly crystal, mp 259–261°C. HREI-MS *m/z* 443.3356 [M^+] (calcd. for $C_{28}H_{45}NO_3$, 443.3399). EI-MS *m/z*: 443, 428, 400, 208, 153, 139, 128, 125, 124, 110. IR (KBr) cm^{-1}: 3423, 1702. ^1H NMR and ^{13}C NMR data: see table 1.

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