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Two New Norditerpenoid Alkaloids of *Aconitum nagarum*

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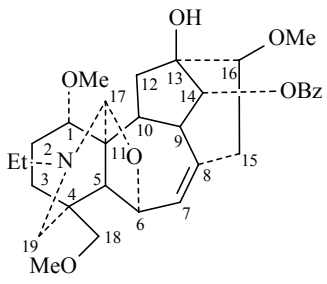
Abstract: Two new norditerpenoid alkaloids were isolated from the roots of *Aconitum nagarum*. Their structures were elucidated as 13-hydroxyfranchetine **1** and 10-dehydroxyflavaconitine **2**, respectively, by 1D and 2D NMR experiments.

Keywords: *Aconitum nagarum*, norditerpenoid alkaloid, 13-hydroxyfranchetine, 10-dehydroxy-flavaconitine.

Aconitum nagarum Stapf is mainly distributed in Yunnan province of China. Its roots can release pain and dispel dampness. They have been used as a folk medicine in China for the treatment of cold limbs in syncope, epigastric pain, vomiting and diarrhea[1]. The chemical constituents of this plant have been investigated[1-4]. For the further investigation, two new norditerpenoid alkaloids 13-hydroxyfranchetine **1** and 10-dehydroxyflavaconitine **2** were isolated from the ethanol extract of the roots of this plant. In this paper, we report their structural elucidation.

Compound **1** is a white amorphous powder, m.p. 97-98℃, $[\alpha]_D^{25}$–120 (*c* 0.1, $CHCl_3$). The HR-ESIMS of **1** indicated a protonated molecular ion peak at *m/z* 540.2971 $[M+H]^+$ requiring a molecular formula $C_{31}H_{41}NO_7$. The IR spectrum (3734, 2929, 1713cm^{-1}) exhibited the presence of hydroxyl and benzoyl groups. Compound **1** showed the distinct NMR (**Table 1**) features of a franchetine-type norditerpenoid alkaloid skeleton[5],



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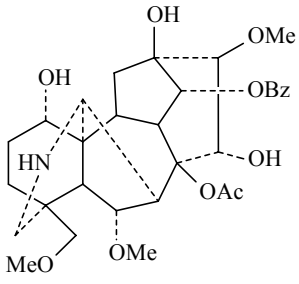

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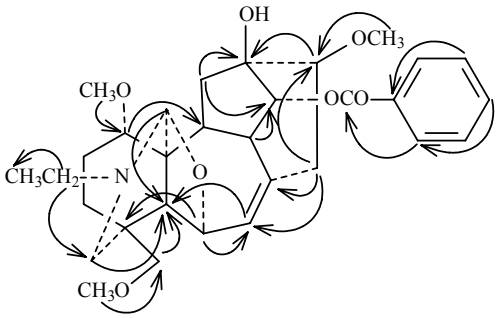
Figure 1 The key HMBC correlations for **1**



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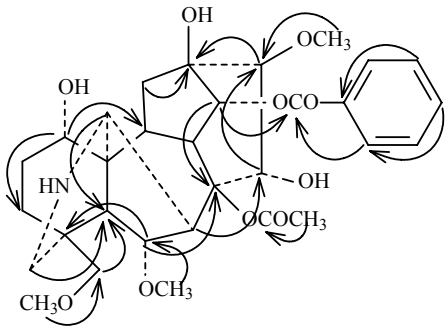
bearing an N-ethyl (δ_H 1.01, t, 3H, *J*=7 Hz), three methoxyl groups (δ_H 3.47, 3.37, 3.28, s, each 3H), a benzoyl group [δ_H 8.07 (d, 2H, *J*=8 Hz), 7.57 (t, 1H, *J*=8 Hz), 7.45 (t, 2H, *J*=8 Hz)] and a tertiary hydroxyl group (δ_C 77.3 s) as well as a N,O-mixed acetal moiety [δ_H 4.37 (s, 1H), 4.40 (d, 1H, *J*=6 Hz); δ_C 92.5 d, 74.7 d]. In the HMBC spectrum (**Figure 1**) of **1**, the long-range correlations between methoxyl signals at δ_H 3.37 (s), 3.47 (s), 3.28 (s) and carbonic signals at δ_C 86.3 (d), 86.0 (d), 79.1 (t), respectively, indicated three methoxyl at C-1, C-16 and C-18. Also, a hydroxyl group was located at C-13 due to correlations between C-13 and H-12, H-15 and H-16 in HMBC. Observations of the correlations between H_2-15/C-7 and H_2-15/C-8 supported a double bond between C-7 and C-8. A broad singlet at δ_H 5.06 was attributed to H-14β, indicating the presence of an ester group at C-14[5]. Finally, the comparison of 1D and 2D NMR data of **1** with those of franchetine[5] confirmed the structure of 13-hydroxy-franchetine **1**.

Compound **2** is a white powder, m.p. 130-132℃, $[\alpha]_D^{25}$ +48 (*c* 0.1, $CHCl_3$). The molecular formula $C_{31}H_{41}NO_{10}$ of **2** was derived from its HR-ESIMS (*m/z* 588.2837 $[M+H]^+$). Its IR spectrum showed distinctive signals at 3494 and 1722 cm^{-1} for hydroxyl and acetyl groups, respectively. Compound **2** exhibited characteristic NMR (**Table 1**) spectral features of an aconitine-type norditerpenoid alkaloid[6] bearing three methoxyl groups (δ_H 3.78 s, 3.33 s, 3.19 s), an acetyl group (δ_H 1.42 s; δ_C 172.4 s, 21.3 q), a benzoyl group (δ_H 8.04 d, 7.59 d, 7.47 t) and two hydroxyl groups (δ_C 74.0 s, 78.9 d). Among them, three methoxyl groups could be located at C-6, C-16 and C-18, respectively, on the basis of the presence of the correlations between OMe-6 (δ_H 3.19) and C-6 (δ_C 83.4, d), OMe-16 (δ_H 3.78) and C-16 (δ_C 89.6, d), OMe-18 (δ_H 3.33) and C-18 (δ_C 79.8, t) in HMBC spectrum (**Figure 2**). In ^1H NMR spectrum, the methoxyl signal at lower field (δ_H 3.78, OMe-16) indicated the presence of two hydroxyl groups at C-13 and C-15[7]. Also, the acetyl signal at higher field (δ_H 1.42) and a doublet (*J*=5 Hz) at δ_H 4.91 (H-14β) suggested the acetyl and benzoyl groups were located at C-8 and C-14 respectively[8]. Comparison of ^1H and ^{13}C NMR data of **2** with those of flavaconitine[9] showed that two structures looked very similar, but no hydroxyl group at C-10 for **2**. So the structure of **2** was determined as 10-dehydroxyflavaconitine.

Table 1 ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) for **1** and **2** (in $CDCl_3$, δ_{ppm}, J_{Hz})

No.	**1**		**2**	
	δ_H	δ_C	δ_H	δ_C
1	3.36 (m)	86.3 (d)	3.70 (br s)	72.0 (d)
2	2.41, 1.95 (each m)	24.3 (t)	1.65, 1.55 (each m)	30.2 (t)
3	1.76 (dd, *J*=14,3)	32.7 (t)	1.89, 1.68 (each m)	29.0 (t)
	1.55 (m)			
4		37.3 (s)		38.4 (s)
5	2.25 (s)	47.3 (d)	2.31 (br s)	44.1 (d)
6	4.40 (d, *J*=6)	74.7 (d)	4.00 (d, *J*=6)	83.4 (d)
7	5.76 (d, *J*=6)	129.1 (d)	2.73 (br s)	50.7 (d)
8		135.7 (s)		91.6 (s)
9	3.20 (br s)	44.0 (d)	2.82 (dd, *J*=7,5)	43.1 (d)
10	2.66 (m)	47.0 (d)	2.15 (m)	39.6 (d)
11		50.5 (s)		48.7 (s)
12	2.12 (t, *J*=11), 2.01 (m)	38.9 (t)	2.32, 2.21 (each m)	36.2 (t)
13		77.3 (s)		74.0 (s)
14	5.06 (br s)	83.5 (d)	4.91 (d, *J*=5)	79.1 (d)
15	3.90 (dd, *J*=12,8)	39.0 (t)	4.51 (d, *J*=5)	78.9 (d)
	2.64 (m)			
16	3.35 (m)	86.0 (d)	3.43 (d, *J*=5)	89.6 (d)
17	4.37 (s)	92.5 (d)	3.07 (br s)	57.6 (d)
18	3.15, 3.04 (each d, *J*=9)	79.1 (t)	3.57, 3.11 (each d, *J*=8)	79.8 (t)
19	2.44, 2.04 (each m)	52.1 (t)	3.27 (d, *J*=11), 2.30 (m)	49.2 (t)
NH			3.96 (br s)	
NCH_2CH_3	2.60, 2.41 (each m)	49.1 (t)		
NCH_2CH_3	1.01 (t, *J*=7)	13.1 (q)		
OMe-1	3.37 (s)	57.1 (q)		
OMe-6			3.19 (s)	58.1 (q)
OMe-16	3.47 (s)	58.0 (q)	3.78 (s)	61.4 (q)
OMe-18	3.28 (s)	59.4 (q)	3.33 (s)	59.1 (q)
Bz-CO		166.7 (s)		165.9 (s)
1'		130.3 (s)		129.7 (s)
2',6'	8.07 (d, *J*=8)	129.8 (d)	8.04 (d, *J*=7)	129.6 (d)
3',5'	7.45 (t, *J*=8)	128.4 (d)	7.47 (t, *J*=7)	128.6 (d)
4'	7.57 (t, *J*=8)	133.0 (d)	7.59 (t, *J*=7)	133.3 (d)
$COCH_3$				172.4 (s)
$COCH_3$			1.42 (s)	21.3 (q)

Figure 2 The key HMBC correlations for **2**



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