STUDIES ON THE ALKALOIDS FROM *ACONITUM BARBETUM* VAR. HISPIDUM LEDEB.

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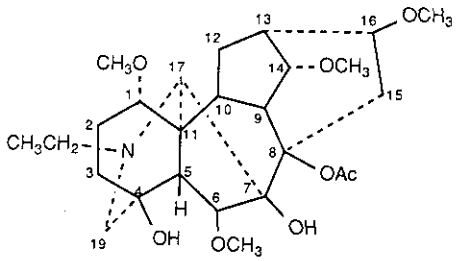
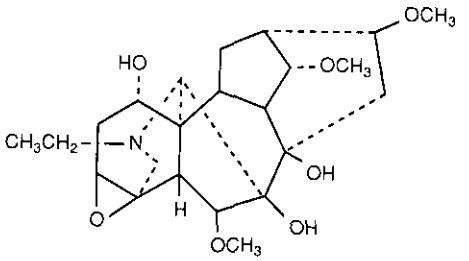
Abstract —— A new C_{19}-diterpenoid alkaloid, hispaconitine (1) and four known alkaloids, tuguaconitine (2), delsoline (3), 14-acetyldelcosine (4) and delcosine (5), have been isolated from the roots of *Aconitum barbetum* var. hispidum Ledeb. The structure of hispaconitine (1) was determined by 2D-nmr spectroscopic analyses.

From ancient times the roots of *Aconitum* plants have been used for treatment of rheumatism and neuralgia. As a part of our program to investigate the constituents of Chinese *Aconitum* species, *Aconitum barbetum* var. hispidum Ledeb. collected in Shan Xi (陕西) province of China has been investigated. From the alcohol extracts of the roots of this plant, we isolated a new C_{19}-diterpenoid alkaloid, hispaconitine (1), along with four known alkaloids, tuguaconitine[1] (2), delsoline[2] (3), 14-acetyldelcosine[2] (4) and delcosine[2] (5). In this communication, we report here the structural elucidation of hispaconitine (1) by 2D-nmr spectroscopic means and the revised assignments of the ^{13}C chemical shifts of C-5 and C-10 in tuguaconitine (2).

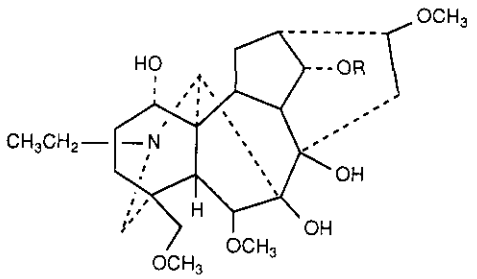
Hispaconitine (1): mp 185-187 ℃, $[\alpha]_D$ +43.4° (c 1.29, $CHCl_3$), ^1H-nmr (400 MHz, pyridine-d5, δ): 1.10 (3H, t, J=7.0 Hz), 1.98 (3H, s, $COCH_3$), 2.04 (1H, br s, H-5), 2.47 (1H, br t, J=4.4 Hz, H-13), 2.57 (1H, dd, J=4.4, 13.8 Hz, H-12), 2.72 (1H, br d, J=9.5 Hz, H-3), 2.92 (1H, dd, J=7.3, 9.9 Hz, H-1), 3.20, 3.24, 3.32,



1: hispaconitine



2: tuguaconitine



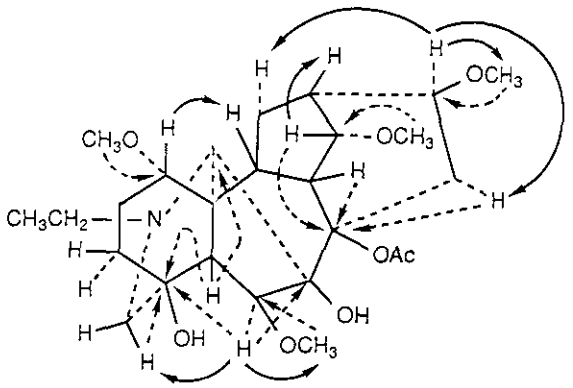
3: R = CH_3, delsoline
4: R = Ac, 14-acetyldelcosine
5: R = H, delcosine

3.47 (3H each, s, OCH_3 X 4), 3.68 (1H, t, J=4.4 Hz, H-14), 3.84 (1H, d, J=11.7 Hz, H-19), 4.25 (1H, br s, H-6), 4.36 (br s, OH), 5.52 (br s, OH). The high resolution ms (M^+ 495.2817, calcd 495.2832) indicated the molecular formula, $C_{26}H_{41}NO_8$. The ir spectrum of 1 exhibited hydroxyl (3450, 3600 cm^{-1}) and ester (1730 cm^{-1}) absorptions. Treatment of 1 with acetic anhydride-pyridine at room temperature did not give any acetylated compound, thereby suggesting the absence of primary or secondary hydroxyl groups. The ^{1}H-nmr spectrum of 1 indicated the presence of an N-$CH_2\underline{CH_3}$ (δ 1.10), an acetyl group (δ 1.98) and four methoxyls (δ 3.20, 3.24, 3.32, 3.47). These spectral data and the molecular formula suggested that the compound 1 should be a C_{19}-diterpene alkaloid. A triplet signal at δ 3.68 (J=4.4 Hz) characteristic to CH_3O-C(14)-β $\underline{H}$ and a broad singlet signal at δ 4.25 (1H) assignable to $CH_3OC(6)$-α $\underline{H}$ were observed in its ^{1}H-nmr spectrum. The ^{13}C-nmr spectrum of 1 also showed two $\underline{C}H$ signals characteristic to $CH_3O\underline{C}(14)$ (δ 84.5) and $CH_3O\underline{C}(6)$(δ 90.9) in all lycoctonine-type alkaloids bearing oxygen substituents at C-6, 7 and 8 positions.[2] One of the other two methoxyl groups was deduced to be situated at C-16 position from the consideration of biogenesis. The failure of acetylation of 1 and a strong peak (m/z 464, M^+-OCH_3,

Table 1
The ^{13}C-nmr data (100 MHz, δ) *for hispaconitine (1) in pyridine-d5 and tuguaconitine (2) in* $CDCl_3$.

	compound		
carbon	1	2	2*
1	83.2	77.9	77.9
2	27.2	31.6	31.5
3	31.6	58.6	58.5
4	81.4	58.7	58.6
5	54.9	48.7	43.2
6	90.9	90.3	90.2
7	89.4	89.4	89.4
8	77.9	78.5	78.5
9	44.0	43.3	48.7
10	46.2	42.7	37.9
11	51.0	53.9	53.9
12	28.9	30.7	30.7
13	38.8	37.9	42.6
14	84.5	84.3	84.2
15	34.5	33.3	33.3
16	83.6	82.8	82.7
17	64.5	67.0	67.0
18	-	-	-
19	56.0	54.3	54.2
N-CH_2	50.8	50.0	49.9
CH_3	14.2	14.0	13.9
6-OCH_3	58.3	58.8	58.8
14-OCH_3	57.5	57.7	57.5
16-OCH_3	56.1	56.3	56.3
1-OCH_3	55.7		
O-CO	169.9		
CH_3	22.0		

* reported data for tuguaconitine



selected data of observed nOe (⟶)
and ^{1}H-^{13}C long range correlation (⇢)
for hispaconitine (1)

70%) in its ms spectrum suggested that the remaining methoxyl group should be situated at C-1.[3] The compound (1) exhibited a fragment ion at m/z 435 ($M-CH_3COOH$)$^+$ as the base peak in its ms spectrum. Easy elimination of acetoxyl group under ms measurement conditions indicated that an acetoxyl group should be attached at C-8 position.[4] From consideration of the empirical formula and the nmr data of 1, the remaining oxygen function should be two tertiary hydroxyl groups and they might be connected at C-4 and C-7, because both the signals due to H-5 and H-6 were appeared as broad singlets, respectively in the ^{1}H-nmr spectrum. The chemical shifts of C-4 (δ 81.4) and C-7 (δ 89.4) also indicated the presence of hydroxyl groups on these two carbons. Further confirmation of the structure and the stereochemistry of 1 were made by the analysis of its 13C-^{1}H long range COSY spectrum and the results of nOe experiments on the

compound (1).

The compound (2) {mp 200-201 ℃, $[\alpha]_D$ +77.3° (c 0.50, $CHCl_3$)} was identical with tuguaconitine in comparison of its spectral data with those described in the literature.[1] The ^{13}C-nmr chemical shifts of 2 were almost identical with the reported values, but some of the assignments should be revised. The signals at δ 43.2 and 37.9 have been assignd to C-5 and C-10, respectively by Chung et al. However, the ^1H-^1H COSY, ^1H-^{13}C COSY and ^1H-^{13}C long range COSY spectrum of 2 indicated that the assignments for C-5 and C-10 described in the literature should be reviced to C-9 and C-13, respectively (Table 1).

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Received, 18th October, 1989