TWO NEW DITERPENOID ALKALOIDS FROM *DELPHINIUM VESTITUM* WALL.

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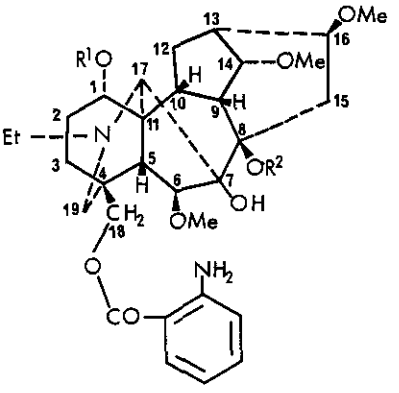
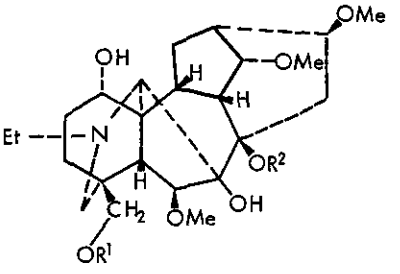
Abstract - The isolation and structure determination of two C_{19}-diterpenoid alkaloids, delvestine (1) and delvestidine (7) from *Delphinium vestitum* Wall. are described. The structures were based on spectroscopic data and correlation with compounds of known structures.

Delphinium vestitum Wall. (Family Ranunculaceae) grows in Western Himalayas and inner Tibetan valleys at elevations of 10,000-12,000 ft and is reported to be poisonous to goats.[1] An earlier investigation reported the isolation from the roots, of two weak bases one of which on saponification gave lycoctonine.[2] In continuation of our interest in the diterpenoid alkaloids of the genus *Delphinium*[3], we have investigated the aerial parts of *D. vestitum* and wish to report the isolation and structure elucidation of two new C_{19}-diterpenoid alkaloids designated as *delvestine and delvestidine.*

From the 85% ethanol extract of the plant, by a combination of cation exchange, vacuum liquid chromatography and centrifugally accelerated radial tlc ("Chromatotron"[4]) we isolated *delvestine*, mp 185-187°C, $[\alpha]_D^{27}$ +18.6° (c, 0.8, $CHCl_3$), $C_{32}H_{46}N_2O_8$ (Found: C, 65.58; H, 7.93; N, 4.75. $C_{32}H_{46}N_2O_8$ requires: C, 65.51; H, 7.90; N, 4.77%). The alkaloid showed ir (nujol) bands at 3460, 3364 (OH, NH_2), 1690 (ester carbonyl), 1615, 1590 (aromatic) cm^{-1}. The aromatic protons (^{1}H-NMR) δ 6.52 (2H), 7.3 (1H), 7.9 (1H) and the low field signals (110-168 ppm) in the ^{13}C nmr spectrum indicated that the alkaloid contains an aromatic ring. Since delvestine contains two nitrogen atoms, the aromatic part appears to be an anthranoyl group (δ 5.74, 2H, $N\underline{H}_2$, exch. with D_2O). The ethyl group (2C) (δ 1.11, 3H, $NCH_2C\underline{H}_3$), four methoxyls (4C), δ 3.35, 3.38, each 3H; 3.37, 6H) and the anthranoyl group (7C) add to thirteen carbon atoms. The alkaloid therefore belongs to the C_{19}-diterpenoid class and the anthranoyl moiety is esterified at the C(18)-*methylene* (δ 4.2, dd, J = 9Hz, $COOC\underline{H}_2$) as in the case of some alkaloids in this group.[5] Of the eight oxygen functions of delvestine, four are present as methoxyl groups, two are part of an ester and the remaining two must be present as hydroxyl groups. The presence of an ether function can be discounted from the molecular formula and the number of rings of C_{19}-diterpenoid alkaloids. Normal oxygen functions at C(1), C(8) and C(14), and a methoxyl group at C(16) can be assumed to be present in delvestine. The ^{13}C-NMR spectrum showed 30 signals corresponding to 32 carbon atoms of the molecule (Table 1) and the SFORD spectrum indicated four quaternary carbons appearing at 91.1, 82.0, 49.1 and 36.6 ppm. The singlets at 49.1 and 36.6 ppm belong to C(11) and C(4) respectively. The other two singlets at 91.1 and 82.0 should be ascribed to carbons bearing an oxygen atom.[6] These positions could be C(7), C(8), C(9) or

C(10). A hydroxyl group at C(10) is expected to have an α-effect on C(11) shifting the signal downfield to around 53-54 ppm. Alkaloids having a hydroxyl group at C(9), e.g. ranaconitine and lappaconitine, exhibit a singlet around 78.6 ppm.[7] These data indicate that the oxygen functions should be located at C(7) and C(8), leading to a lycoctonine type of alkaloid. Oxygen functions at C(3), C(13) and C(15), present only in the aconitine type, can therefore be discounted. The singlets at 91.1 and 82.0 ppm should be assigned to C(7) carrying a hydroxyl group and C(8) bearing a methoxyl group, respectively.[3] Downfield from 65 ppm, doublets appear at 91.1, 84.1, 83.1 and 72.2 ppm due to carbons carrying an oxygen function. The signal at 91.1 ppm can only be attributed to C(6) carrying a methoxyl group as no other carbon having an oxygen function is expected to appear this low field. The remaining methoxyl group should be located at C(1) or C(14). Most of the alkaloids bearing a hydroxyl group at C(14) exhibit a signal at ~ 74-77 ppm and those at C(1) appear around 72-73 ppm. The doublet at 72.7 ppm can thus be assigned to C(1) bearing a hydroxyl group, and delvestine can be tentatively formulated as (1).





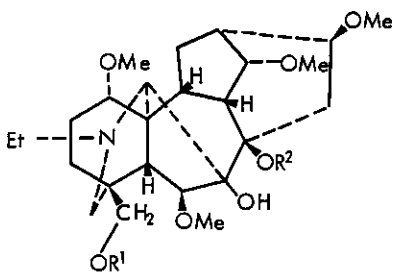
1: R^1 = H; R^2 = Me Delvestine
2: R^1 = Me; R^2 = H

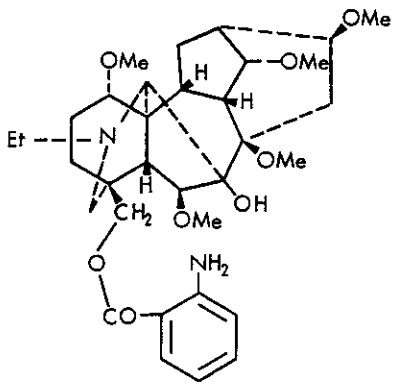
3: R^1 = R^2 = Me
4: R^1 = H; R^2 = Me
5: R^1 = R^2 = H Gigactonine

In order to confirm the structure proposed (**1**), delvestine was hydrolysed with 5% methanolic KOH at 20° to give the amino alcohol (**4**) which on heating with aqueous sulfuric acid afforded (**5**), mp 190-192°C. This compound was found to be identical with gigactonine[10,11] by comparison of its tlc, mixed mp, IR and ^{13}C-NMR spectrum. As the structure of gigactonine was established by its conversion to delsoline which was in turn correlated with delcosine (X-ray structure),[12] the structure and stereochemistry of delvestine remain confirmed as in **1**.

Delvestidine, $C_{33}H_{48}N_2O_8$, (Found: C, 66.04; H, 8.06; N, 4.63. $C_{33}H_{48}N_2O_8$ requires: C, 65.98; H, 8.05; N, 4.66%) was obtained as a homogeneous amorphous alkaloid, $[\alpha]_D^{26}$ +22.1° (c, 0.515,

$CHCl_3$), from the less polar fractions during separation on the "Chromatotron". The infrared spectrum (nujol) showed ν_{max} 3480, 3365 (OH, NH_2), 1692 (ester carbonyl), 1615, 1590 (aromatic) cm^{-1}. The ^{1}H-NMR spectrum indicated the presence of five aliphatic methoxyl singlets, δ 3.18 (3H), 3.3, 2.4 (each 6H), a primary amine δ 5.63 (br, 2H) and four aromatic protons δ 6.43 (2H) 7.17 (1H) and 7.73 (1H). Delvestidine contains a methoxyl group instead of the hydroxyl of delvestine and its ^{13}C-NMR spectrum closely resembled that of deltatsine dimethyl ether (**6**)[3b] (see Table 1). Delvestidine was tentatively formulated as (7) on the basis of this data.





6: $R^1 = R^2 = Me$

8: $R^1 = R^2 = H$

7 Delvestidine

The structure of delvestidine was confirmed by correlation with anthranoyllycoctonine (**2**) and lycoctonine (**8**). Demethylation of delvestidine with 3M sulfuric acid afforded a compound which was shown to be identical with anthranayllycoctonine (**2**) in its ^{13}C-NMR spectrum. Saponification of this product with 5% methanolic potassium hydroxide gave lycoctonine (**8**), identified by comparison of the IR and ^{13}C-NMR spectra. A comparison of the ^{13}C-chemical shifts and assignments of delvestine **1**, anthranoyllycoctonine **2**[8], deltatsine-14-methyl ether **3**, gigactonine **5**[10], deltatsine dimethyl ether **6**, lycoctonine **8**, and delvestidine **7**, is given in Table 1.

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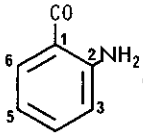
We wish to thank Dr. S. Sakai for an authentic sample of gigactonine.

Table 1. Carbon-13 chemical shifts[+] and assignments for delvestine (1), anthranoyllycoctonine (2), deltatsine-14-methylether (3), gigactonine (5), deltatsine dimethyl ether (6), lycoctonine (8) and delvestidine (7).

Carbons	1	2	3	5	6	8	7
C(1)	72.2 (d)	84.0 b	72.3	72.7	82.9	84.3 b	83.4 b
C(2)	26.9 (t)	26.2	27.0	29.4	25.6	26.2	25.6
C(3)	29.5 b (t)	32.2	29.7	30.5	31.7	31.8	31.9
C(4)	36.6 (s)	37.5	37.2	38.2	38.1	38.7	37.7
C(5)	39.0 (d)	43.2	39.0	44.7	40.6	43.4	40.5
C(6)	91.1 (d)	90.9	91.2	90.6	91.4	90.8	91.3
C(7)	91.1 (s)	88.5	91.2	87.8	89.7	88.6	90.1
C(8)	82.0 (s)	77.6	82.1	78.5	80.6	77.6	80.7
C(9)	49.1 (d)	50.3	49.1	43.4	52.0	49.9	51.9
C(10)	44.8 (d)	46.1 a	44.9	44.0	46.7	46.3 a	46.6
C(11)	49.1 (s)	49.1	49.1	49.4	47.4	49.0	47.5
C(12)	29.3 b (t)	28.7	29.4	26.7	27.9	28.8	27.9
C(13)	36.7 (d)	38.2 a	36.7	37.8	38.0	38.3 a	37.9
C(14)	84.1 (d)	83.9 b	84.0	84.6	83.5	84.1 b	83.0 b
C(15)	30.1 (t)	33.6	30.2	33.5	28.1	33.8	28.0
C(16)	83.1 (d)	82.6	83.2	83.0	83.2	82.7	82.8
C(17)	65.8 (d)	64.5	66.1	66.1	66.7	64.8	66.2
C(18)	69.0 (t)	68.6	78.8	66.8	79.4	68.0	69.5
C(19)	57.3 (t)	52.4	57.6	57.3	54.3	52.8	53.3
N-CH_2	50.3 (t)	51.0	50.4	50.4	51.9	51.1	51.8
CH_3	13.7 (q)	14.1	13.7	13.6	15.0	14.1	14.8
C(1)'	-	55.8	-	-	55.5	55.7	55.6
C(6)'	59.8 (q)	57.8	59.5	57.7	59.5	57.8	59.8
C(8)'	50.8 (q)	-	50.8	-	53.5	-	54.3
C(14)'	57.6 (q)	58.0	57.6	57.7	57.6	58.0	57.6
C(16)'	56.3 (q)	56.3	56.4	56.4	56.3	56.3	56.4
C(18)'	-	-	59.5	-	-	-	-
CO	167.9 (s)	167.8	-		-	-	167.9
 (1)	110.4 (s)	110.3	-		-	-	110.7
(2)	150.9 (d)	150.8	-		-	-	150.6
(3)	116.9 d (d)	116.8 d	-		-		116.7 d
(4)	134.4 c (d)	134.3 c	-		-		134.1 c
(5)	116.4 d (d)	116.2 d	-		-		116.3 d
(6)	130.8 c (d)	130.7 c	-		-		131.0 c

+ In ppm downfield from TMS. Spectra were taken in $CDCl_3$.

a These assignments from literature values[8] have been reversed for reasons given earlier[9].

b,c,d The assignments in any vertical column may be interchanged.

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