

THREE NEW C₁₉-DITERPENOID ALKALOIDS FROM *DELPHINIUM OCCIDENTALE* S. WATS.

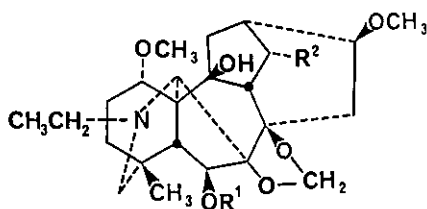
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Abstract - Three new C₁₉-diterpenoid alkaloids have been isolated from *Delphinium occidentale* S. Wats.: *occidentaline* (16), *occidentalidine* (17) and *6-acetyldelpheline* (18). Structures were deduced by spectroscopic methods and chemical correlations. Twelve known C₁₉- and two C₂₀-diterpenoid alkaloids were also isolated.

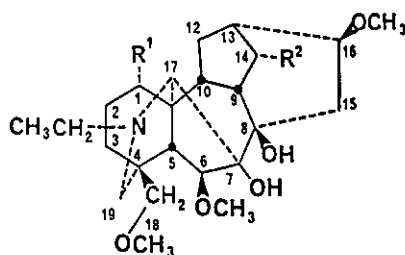
Previous chemical studies of *Delphinium occidentale* S. Wats. revealed the presence of deltaline (1), deltamine (2), dictyocarpine (3), delcosine (4), delsoline (5), delpheline (6) and three unidentified alkaloids.¹⁻³ As part of our continuing study of *Delphinium* species⁴ (Ranunculaceae) which elaborate a variety of diterpenoid alkaloids, we have investigated aerial parts of *D. occidentale* collected from semi-open areas in an aspen tree community on the Logan River drainage in northern Utah. Gradient pH extraction and extensive chromatography, including vacuum liquid chromatography (vlc)⁵ and centrifugally accelerated, radial, thin-layer chromatography (Chromatotron)^{6,7} resulted in the isolation of deltaline (1),^{1,2,8} deltamine (2),^{8,9} dictyocarpine (3),^{10,11} delcosine (4),¹² delpheline (6),^{8,13,14} 14-dehydrodelcosine (7),¹⁵ browniine (8),^{11,16} 14-dehydrobrowniine (9),^{8,17} dictyocarpinine (10),¹⁸ glaucerine (11),¹⁸ glaucenine (12),¹⁸ glaucedine (13),¹⁸ hetisine (14)¹⁹ and hetisinone (15).²⁰ The identity of these alkaloids were determined spectroscopically and by direct comparison with known samples. The three new alkaloids designated as *occidentaline* (16), *occidentalidine* (17) and *6-acetyldelpheline* (18) were isolated in very small amounts.

Occidentaline has a molecular formula C₂₅H₃₉NO₅ (ms) and showed no carbonyl or hydroxyl absorptions (ir). Analysis of the ¹H nmr (CDCl₃) spectrum indicated the following functional groups: methylenedioxy (δ 5.02 and 4.92, each d, J = 0.9 Hz), three methoxys (3.43, 3.33 and 3.26), N-ethyl (1.06, t, J = 7 Hz) and a tertiary methyl (0.78, s). Absence of resonances in the range 3.7 to 4.2 ppm suggested lack of an oxygen substituent at C-6, a fact consistent with the upfield shift (Δ 0.1 ppm) of the C-4 methyl group when compared with those of deltaline (1), delpheline (6) and related alkaloids possessing such substituent.²¹ The triplet at 3.66 ppm (J = 4.5 Hz) was assigned to H-14β bearing a methoxyl group. These facts and the molecular formula which showed one less oxygen when compared with that of delpheline (6) led to the structure 16 for *occidentaline*. To verify the conclusions drawn from the spectral data and to confirm the structure of *occidentaline*, a partial synthesis from delpheline (6) was effected. Thus conversion of 6 to the

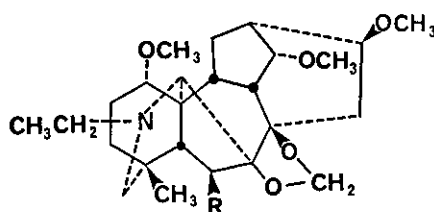


- 1 R¹ = Ac; R² = OCH₃
 2 R¹ = H; R² = OCH₃
 3 R¹ = Ac; R² = OH
 10 R¹ = H; R² = OH
 11 R¹ = Ac; R² = $\text{OC}-\text{CH}(\text{CH}_3)_2$

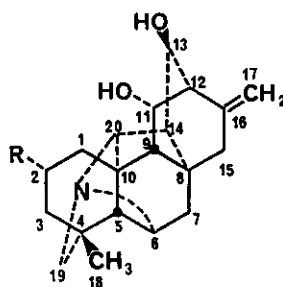
- 12 R¹ = Ac; R² = $\text{OC}-\overset{\text{O}}{\underset{\text{H}}{\text{C}}}-\text{CH}_2\text{CH}_3$



- 4 R¹ = R² = OH
 5 R¹ = OH; R² = OCH₃
 7 R¹ = OH; R² = 0
 8 R¹ = OCH₃; R² = OH
 9 R¹ = OCH₃; R² = 0
 13 R¹ = OCH₃; R² = $\text{OC}-\overset{\text{O}}{\underset{\text{H}}{\text{C}}}-\overset{\text{CH}_3}{\text{C}}-\text{CH}_2\text{CH}_3$
 17 R¹ = OCH₃; R² = $\text{OC}-\overset{\text{O}}{\text{C}}-\text{CH}(\text{CH}_3)_2$



- 6 R = OH
 16 R = H
 18 R = OAc
 19 R = $-\text{OC}-\overset{\text{S}}{\underset{\text{S}}{\text{C}}}-\text{SCH}_3$



- 14 R = OH
 15 R = 0

S-methyl dithiocarbonate 19 and subsequent reduction with tributyltin hydride produced 16, mp 119.5-120.5°C and $[\alpha]_D^{28} -40.5^\circ$ (c 0.64, CHCl₃). The synthetic alkaloid²² showed identical ir (nujol) and ¹H nmr (CDCl₃) spectra with those of the natural substance.

Occidentalidine was admixed with glaucedine (13) and careful chromatography furnished about 2 mg of reasonably pure (90%) sample, molecular formula, C₂₉H₄₇NO₈ (ms). Structure 17 was appar-

ent from the analysis of the ^1H nmr (CDCl_3) spectrum: δ 4.77 (t, $J = 4.5$ Hz, H-14 β), 3.88 (br, H-6 α), 3.41 (s, OMe), 3.30 (s, 2XOMe), 3.25 (s, OMe), 1.17 (d, $J = 6$ Hz, $\text{CH}-(\text{CH}_3)_2$) and 1.04 (t, $J = 7$ Hz, $\text{N}-\text{CH}_2-\text{CH}_3$); comparison of the above shifts with those of glaucedine (13)¹⁸ indicated that they differed only in the nature of the C-14 ester side chain, a result was also suggested by the difference of 14 mass units between the two compounds in their mass spectra. Finally, the structure of occidentalidine was confirmed by acylation of browniine (8) with isobutyryl chloride, which gave a compound identical (^1H nmr and mass spectra) with the natural alkaloid. The synthetic alkaloid melted at 137-140°C and had $[\alpha]_D^{22} +31.3^\circ$ (c 0.32, CHCl_3) and ir (nujol): 3450, 3400 and 1722 cm^{-1} . The ^{13}C nmr data are provided in Table 1.

Table 1. ^{13}C NMR (22.49 MHz, CDCl_3) Spectra of Compounds 17 and 18

Carbon*	17	18	Carbon	17	18
1	84.2	83.3	17	64.7	64.2
2	26.2	26.9	18	78.4	25.4
3	32.4	36.7	19	52.6	56.7
4	38.0	33.8	N-CH ₂	51.1	50.3
5	43.0	55.9	CH ₃	14.1	13.9
6	90.4	78.4	1'	55.7	55.3
7	88.3	91.8	6'	57.2	-
8	77.4	83.3	-OCH ₂ O-	-	93.4
9	49.5	48.2	14'	-	57.6
10	45.6	39.8	16'	55.8	56.1
11	48.8	50.2	18'	58.9	-
12	28.1	27.9	C=O	177.2	-
13	37.7	38.6	CH	34.2	-
14	75.6	81.6	(CH ₃) ₂	18.8	-
15	33.7	33.8			
16	82.2	82.0	C=O		170.0
			CH ₃		21.7

*Multiplicities were determined by a DEPT sequence

The third new alkaloid, mp 120-122°C, and molecular formula $\text{C}_{27}\text{H}_{41}\text{NO}_7$ (ms) was a monoacetate as evidenced by ir (1732 cm^{-1}), ^1H (δ 2.05, 3H, s) and ^{13}C nmr (170, 21.7 ppm) spectra. The location of the acetate group at C-6 was discerned from the downfield proton signal at δ 5.39 (br). This evidence in conjunction with the remaining ^1H nmr signals at δ 4.91, 4.88 (each s, -OCH₂O-), 3.42, 3.32 and 3.25 (each s, OMe), 1.03 (t, $J = 7$ Hz, $\text{N}-\text{CH}_2-\text{CH}_3$) and ^{13}C nmr (Table 1) spectral data established the structure as 6-acetyldelpheline (18). This alkaloid was identical in all respects (ir, ^1H and ^{13}C nmr spectra) with the substances prepared from deoxygenation of deltaline (1)²² and acetylation of delpheline (6). 6-Acetyldelpheline has been prepared previously^{13,14} from delpheline, but never to our knowledge had it been isolated as a natural product.

The literature¹⁸ assignments of ^{13}C nmr shifts for glaucerine (11), glaucenine (12) and glaucedine (13) require comment as a result of the present study. The chemical shifts for C-3 and C-13 need to be reversed in 11 and 12. The following are the correct assignments for 13: C-4 (38.4 ppm), C-9 (49.6), C-10 (45.7), C-11 (48.9), C-13 (37.7) and $\text{N-CH}_2\text{-CH}_3$ (51.1). These changes in assignments are based on a DEPT (distortionless enhancement by polarization transfer) experiment in determining the carbon multiplicities.

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