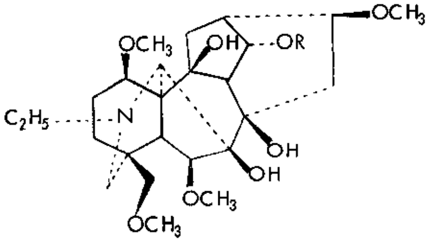
DELCAROLINE, A NOVEL ALKALOID FROM DELPHINIUM CAROLINIANUM WALT.

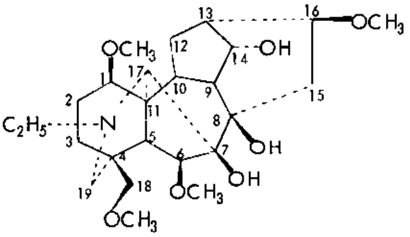
S. William Pelletier*, Naresh V. Mody*, and Ranjit C. Desai
Institute for Natural Products Research and the Department of Chemistry
The University of Georgia, Athens, Georgia 30602, U. S. A.

Abstract: The structure of delcaroline (1), a novel C_{19}-diterpenoid alkaloid isolated from Delphinium carolinianum Walt., has been determined with the aid of proton and carbon-13 NMR spectroscopy. Delcaroline is the first C_{19}-diterpenoid alkaloid bearing a C(10) hydroxyl group in which the C(4) methyl and C(7)-C(8) methylenedioxy groups are absent

In continuation of our efforts to isolate and determine the structures of complex diterpenoid alkaloids from the genus Delphinium, we have examined whole plants of Delphinium carolinianum Walt.[1], a relatively rare plant native to the southeastern United States. In this communication, we report the isolation and structure elucidation of a new C_{19}-diterpenoid alkaloid named delcaroline (1), as well as the isolation of the known alkaloids, browniine (2)[2] and ajaconine (3)[3,4].



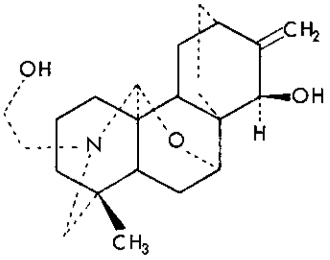
1 R = H Delcaroline
4 R = Ac



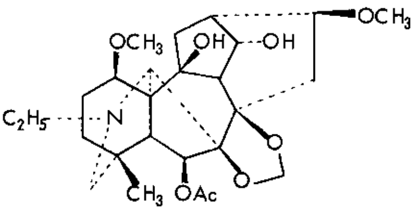
2 Browniine

Delcaroline, the major alkaloid of the 95% ethanolic extract of D. carolinianum, was isolated as an amorphous compound by a combination of pH gradient extraction, thick-layer, and column chromatographic techniques. Delcaroline, $C_{25}H_{41}NO_8$, $[\alpha]_D^{23.5}$ + 49.8° (c 0.49, MeOH), formed a crystalline perchlorate,[5] mp. 160-162°C, when treated with 6% perchloric acid in methanol. The IR spectrum of 1 in nujol showed absorption at 3442 (hydroxyl) and 1083 (ether) cm^{-1}. The 100 MHz proton NMR spectrum of delcaroline in $CDCl_3$ exhibited absorption for an N-CH_2-CH_3 group (3H, t) centered at δ 1.05, four aliphatic methoxy groups (each 3H, s) at δ 3.25, 3.30, 3.35, and 3.42, and a one-proton broad multiplet centered at δ 4.06 for the C(14)-β-proton.

Treatment of delcaroline with acetic anhydride in pyridine at room temperature for 3 days afforded 14-acetyldelcaroline (4) as an amorphous compound. The IR spectrum showed absorption in nujol at 3425 (hydroxyl), 1735 (acetate), and 1085 (ether) cm^{-1}. The 90 MHz proton NMR spectrum of 4 in deuterochloroform indicated the presence of an N-CH_2-$C\underline{H_3}$ group (3H, *t*) centered at δ 1.03, an acetoxy group (3H, *s*) at δ 2.02, two three-proton singlets for two methoxy groups at δ 3.20 and 3.35, a six-proton singlet for two methoxy groups at δ 3.25, and a poorly resolved doublet of doublets centered at δ 5.15 for the C(14)-β-proton. The signal at δ 4.06 in delcaroline (1) is shifted downfield to δ 5.15 in compound 4, an indication that the C(14) hydroxy group of 1 is acetylated.



3 Ajaconine



5 Dictyocarpine

The carbon-13 NMR spectrum of delcaroline (1) showed twenty-five signals corresponding to twenty-five carbon atoms in the molecule. Comparison of the carbon-13 NMR spectrum of delcaroline was made with the spectra of browniine (2)[6], dictyocarpine (5)[7], and other published carbon-13 NMR data for the lycoctonine-type alkaloids.[6] The chemical shifts pattern in delcaroline is very close to that of browniine (2) except for a few changes. The appearance of an extra singlet at 79.9 ppm in the spectrum of delcaroline and the disappearance of a doublet at 36.4 ppm (compared to browniine) afforded evidence for the presence of an additional tertiary hydroxyl group in delcaroline. According to the known substitution patterns in this class of alkaloids, the extra tertiary hydroxyl group in delcaroline can be assigned to one of the three possible sites, viz. C(9), C(10), or C(13). The chemical shift of C(11) in delcaroline appeared at 53.8 ppm - significantly downfield compared with browniine and other lycoctonine-type alkaloids. This observation indicates that the neighbouring C(10) carbon is substituted by a hydroxyl group. The presence of a doublet of doublets centered at δ 5.15 for the C(14)-β-proton in the proton NMR spectrum of 14-acetyldelcaroline (4) confirmed that the C(9) and C(13) carbons are not substituted by a hydroxyl group in delcaroline. All the signals in the carbon-13 NMR spectrum of delcaroline are in agreement with the assigned structure (1).

Biogenetically, delcaroline is an important alkaloid because it is the first example of a C_{19}-diterpenoid alkaloid bearing a C(10) hydroxyl group in which the methyl group at C(4) and the methylenedioxy group between C(7) and C(8) are absent. All the known C(10) hydroxyl group-containing alkaloids[8] possess the C(4) methyl and C(7)-C(8) methylenedioxy groups except karakolidine and demethylene-eldelidine in which the C(4) methyl group is present. Delcaroline thus represents a novel substitution pattern among all the known C_{19}-diterpenoid alkaloids. It is the most highly oxygenated alkaloid of the lycoctonine-type isolated to date. Occurrence of delcaroline with browniine in the same plant indicates that browniine is probably the precursor of delcaroline. We suggest that the presence of the C(4) methyl group and/or the C(7)-C(8) methylenedioxy group is not essential for the occurrence of the C(10) hydroxyl group, and that C(10) hydroxylation probably is taking place at the last stage of the biosynthesis of these alkaloids.

TABLE 1

Carbon-13 Chemical Shifts and Assignments for Delcaroline (1), 14-Acetyldelcaroline (4), Browniine (2), and Dictyocarpine (5)[a,b]

	(1)	(4)	(2)	(5)
C(1)	79.4	78.1	85.2	78.7
C(2)	25.5	26.2	25.5	26.4
C(3)	32.2	32.2	32.5	37.6
C(4)	38.1	38.0	38.4	34.0
C(5)	45 1	45.3	45.1	51.8
C(6)	90.8	91.1	90.1	77.2
C(7)	88.0	87.6	89.1	93.0
C(8)	75.1	75.6	76.3	82.9
C(9)	54.0	54.5	49.6	50.4
C(10)	79.9	81.8	36.4	79.9
C(11)	53.8	52.8	48.2	55.1
C(12)	37.6	38.3	27 5	36.5
C(13)	37.0	38.8	46.1	36.6
C(14)	73.6	74.8	75.3	72.8
C(15)	33.9	34.6	33.1	32.9
C(16)	81.3	82.0	81.7	81.2
C(17)	66.1	65.3	65.4	64.4
C(18)	77.2	77.4	78.0	25.5
C(19)	52.5	52.8	52.7	56.9
N-CH_2	51.3	51.3	51.3	50.4
CH_3	14.3	14.2	14.3	14.0
C(1)'	55.5	55.5	56.0	55.6
C(6)'	57.7	57.6	57.5	-
C(16)'	56.3	56.3	56.5	56.3
C(18)'	59.1	59.1	59.1	-
C = O	-	172.0	-	170.2
CH_3	-	21.6	-	21.8

[a] Chemical shifts in ppm downfield from TMS. The solvent is deuterochloroform.

[b] Carbon-13 NMR spectra were taken at 15.03 MHz in Fourier mode using a JEOL-FX 60 spectrometer.

REFERENCES AND NOTES

1. This plant was collected in Oktibbhea County, Mississippi on May 8, 1977. A voucher specimen (Michael B. Brooks and Sidney McDaniel No. 154) has been deposited in the herbarium of Mississippi State University.
2. M. H. Benn, M. A. M. Cameron, and O. E. Edwards, *Can. J. Chem.*, **41**, 477 (1963).
3. D. Dvornik and O. E. Edwards, *Tetrahedron*, **14**, 54 (1961).
4. *Delphinium carolinianum* contained very small amounts of alkaloids. Thus, 4560 g. of dry plant yielded the following: delcaroline - 1.69 g. (0.037%); ajaconine - 1.50 g. (0.033%) and browniine - 1.185 g. (0.026%).
5. $C_{25}H_{41}NO_8 \cdot HClO_4$ requires: C 51.41; H 7.19; N 2.39%. Found: C 51.21; H 7.20; N 2.36%.
6. S. W. Pelletier, N. V. Mody, R. S. Sawhney, and J. Bhattacharyya, *Heterocycles*, **7**, 327 (1977).
7. S. W. Pelletier, N. V. Mody, and O. D. Dailey, Jr., *Can. J. Chem.*, **58**, 1875 (1980).
8. S. W. Pelletier and N. V. Mody in *The Alkaloids*, Vol. 17, Edited by R. H. F. Manske and R. Rodrigo, Academic Press, New York, 1979, Chapter 1.

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