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STRUCTURES OF AJACUSINE AND AJADINE, TWO NEW C_{19}-DITERPENOID ALKALOIDS FROM DELPHINIUM AJACIS L.[1]

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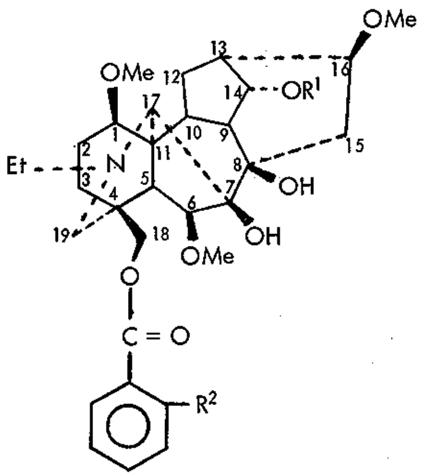
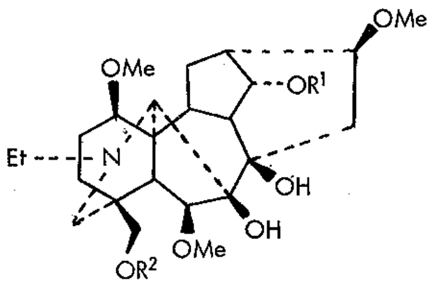
The complete structures of two new diterpenoid alkaloids, ajacusine (1) and ajadine (2), have been established by physico—chemical methods.

In continuation of our efforts to elucidate the structures of complex diterpenoid alkaloids[2,3] we carried out a careful reexamination of the seeds of Delphinium ajacis L. In addition to several previously reported alkaloids,[4,5] we have isolated and identified several other C_{19}-diterpenoid alkaloids from this source. In this paper, we wish to report the structures of two new alkaloids, ajacusine (1) and ajadine (2), of complex and unusual structure.

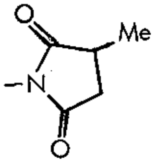
The new alkaloids were isolated from the ethanol (85%) extract of the seeds by a combination of gradient pH separation, thin layer, and column chromatographic techniques. Ajacusine, $C_{43}H_{52}N_2O_{11}$, crystallized from CH_2Cl_2-hexane, mp 158-161° (d), $[\alpha]_D^{24}$ + 65.2° (c 0.98, abs. EtOH), and showed ir absorption (Nujol) at 3475 (OH), 1715, 1705, 1695 (carbonyl), 1605 (aromatic) and 1087 (ether) cm^{-1}. The ^1H nmr ($CDCl_3$, PFT100) spectrum of ajacusine indicates the presence of an $N-CH_2-C\underline{H}_3$ (3H, t) at δ 1.07 and 3 aliphatic methoxy groups at δ 3.27, 3.29 and 3.32 ppm. The spectrum also shows a doublet of doublets at δ 5.03 ppm which is typical of a C-14β-proton. A group of signals appearing in the region δ 7.22 - 8.16 ppm are indicative of the aromatic protons of benzoyl and anthranoyl groups.

The ^{13}C nmr spectrum of ajacusine was particularly revealing. The chemical shifts of the 43-carbons in the molecule have been assigned on the basis of noise decoupled spectra, direct analysis of non-protonated carbons, single-frequency off-resonance



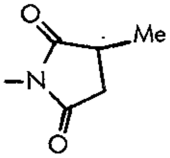


1 R^1 = Bz; R^2 =



2 R^1 = Ac; R^2 = -NHCOMe

3 R^1 = Me; R^2 =



4 R^1 = Me; R^2 = -NHCOMe

5 R^1 = H; R^2 = H

6 R^1 = H; R^2 = Me

7 R^1 = Me; R^2 = H

8 R^1 = Bz; R^2 = Me

decoupling (SFORD), and by direct comparison[2] with the ^{13}C nmr spectrum of methyllycaconitine (3). The ^{13}C nmr spectrum of ajacusine closely resembles that of methyllycaconitine, except that the former exhibits additional signals at 167.0, 132.5, 129.9 and 128.3 ppm (benzoate carbons). The presence of a benzoyl group in ajacusine at C-14 was confirmed by comparison (Table 1) of the observed resonances in (1) with those of synthetic 14-benzoylbrowniine (8).

Ajacusine, on saponification with 5% methanolic KOH at room temperature afforded the known aminoalcohol (5). The structure of 5 was confirmed by comparison of its ^{13}C nmr spectrum with those of browniine (6) and lycoctonine (7). The signals at 75.3 and 67.6 ppm in compound 5 unambiguously show the presence of hydroxy groups at C-14 and C-18 respectively.

Ajadine, $C_{35}H_{48}N_2O_{10}$, crystallized from acetone-hexane, mp 134-136° (d), $[\alpha]_D + 43.9^\circ$ (c 1.0, abs. EtOH), and showed ir bands (Nujol) at 3465 (OH), 1733, 1700, 1685 (carbonyls), 1600 (aromatic) and 1080 (ether) cm^{-1}. The ^1H nmr ($CDCl_3$, PFT100) spectrum of ajadine exhibits signals at δ 1.07 (3H, t, $N\text{-}CH_2\text{-}C\underline{H}_3$), 2.07 (3H, s, $OCOC\underline{H}_3$), 2.24 (3H, s, $NHCOC\underline{H}_3$), 3.28, 3.34, 3.38 (each 3H, s, $-OC\underline{H}_3$), 4.77 (1H, d of d, 14β $\underline{H}$), 7.13, 7.59, 7.97, 8.72 (aromatic protons) and 11.0 (broad s, $N\underline{H}COCH_3$) ppm. The ^{13}C nmr spectrum of ajadine exhibits signals corresponding to 35 carbons in the molecule. The spectrum closely resembles that of ajacine (4) with the addition of a quartet at 21.5 ppm and a singlet at 172.1 ppm. These signals in ajadine must be attributed to an acetyl group at C-14.

Although the esters of lycoctonine are well known in nature, ajacusine and ajadine are esters of an aminoalcohol (5), which has been encountered only rarely in nature.

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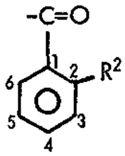
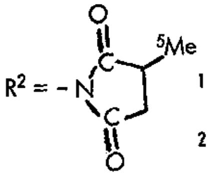
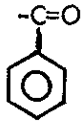
Table 1. Carbon-13 Chemical Shifts and Assignments for Ajacusine, Ajadine and Related Alkaloids[a]

Carbon	1	8	2	5
1	84.0	84.2	83.7	85.1
2	26.0	25.9	26.0	25.3
3	32.1	32.0	32.2	31.6
4	37.6	38.1	37.6	38.8
5	43.1	43.1	42.6	45.1
6	90.6	90.2	90.7	90.1
7	88.5	88.3	88.4	89.0
8	77.3	77.5	77.4	76.3
9	50.0	51.3	50.1	49.5
10	37.6	37.6	38.1	36.5
11	48.9	49.2	49.0	48.2
12	28.1	28.3	28.1	27.5
13	45.7	45.5	45.7	46.1
14	75.9	76.0	75.9	75.3
15	34.0	34.0	33.7	33.1
16	82.1	82.2	82.4	81.8
17	64.5	64.8	64.5	65.4
18	69.4	77.9	69.6	67.6
19	52.2	52.9	52.2	52.8
N-CH_2	51.1	51.3	51.1	51.3
CH_3	14.1	14.0	14.1	14.2
1'	55.9	55.9	55.8	56.0
6'	58.1	57.4	58.1	58.1
16'	56.1	56.1	56.3	56.5
18'	-	59.1	-	-

Table 1 - continued

Carbon		1	8	2	5
		164.1	-	168.1	-
	1	127.0	-	114.5	-
	2	133.1	-	141.8	-
	3	129.4	-	120.6[b]	-
	4	133.7	-	135.1[c]	-
	5	130.9	-	122.7[b]	-
	6	129.9	-	130.3[c]	-
	1	179.8	-	-	-
	2	37.0	-	-	-
	3	35.3	-	-	-
	4	175.8	-	-	-
	5	16.4	-	-	-
$R^2 = NHC{=}O$		-	-	169.2	-
Me		-	-	25.5	-
		167.0	167.0	-	-
		132.5	132.5	-	-
		129.9	129.9	-	-
		128.3	128.3	-	-
-C=O		-	-	172.1	-
CH_3		-	-	21.5	-

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[a] In ppm downfield to TMS; Solvent deuterochloroform.

[b, c] Values within any vertical column are interchangeable.

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