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THE STRUCTURE OF ALKALOID A FROM DELPHINIUM BICOLOR NUTT

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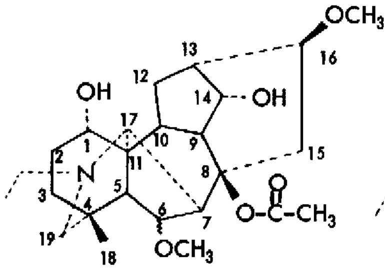
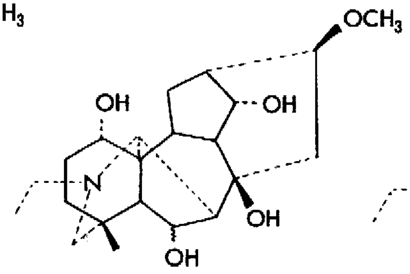
Recently Jones and Benn reported the isolation of two new alkaloids A and B in very small amounts from Delphinium bicolor Nutt.[1,2] Structures 1 and 2, respectively, were assigned to these alkaloids mainly on the basis of the correlation with the carbon-13 nmr spectra of a variety of model Delphinium alkaloids, e.g., deoxylycoctonine and isotalatizidine.[3] Because these new alkaloids are more closely related to neoline-type systems, we undertook the correlation of the carbon-13 nmr spectra of A and B with those of neoline 4 and its derivatives.

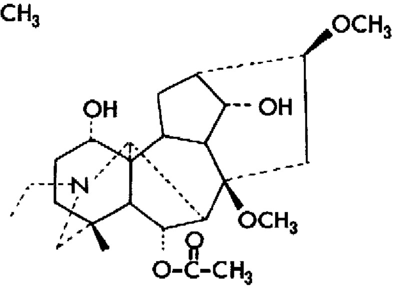
A recent investigation of carbon-13 nmr spectra of more than 50 Aconitium and Delphinium alkaloids and derivatives in our laboratory[5,6] provides a foundation for unambiguous assignment of all carbon resonances for alkaloids A and B. Our examination of the ^{13}C nmr spectra of alkaloids A and B leads us to assign structure 3 to alkaloid A on the basis of arguments presented below. We have also revised the ^{13}C chemical shifts assignments for alkaloid B.



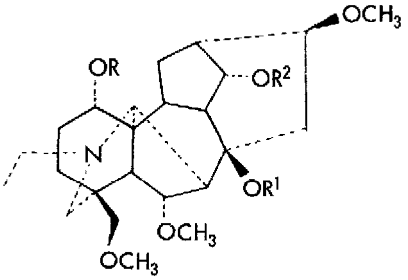
1

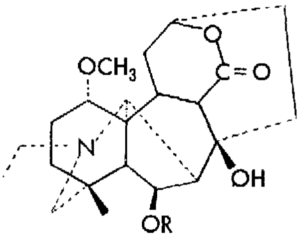


2 Alkaloid B



3 Alkaloid A





4 R = -H, R^1 = -H, R^2 = -H
5 R = -H, R^1 = -COCH$_3$, R^2 = -H
6 R = -H, R^1 = -COCH$_3$, R^2 = -COCH$_3$
7 R = -CH$_3$, R^1 = -CH$_3$, R^2 = -CH$_3$

8 R = -H
9 R = -COCH$_3$

Structure 1 for alkaloid A was based on the results of a study of the pyrolysis of this alkaloid in glycerol. The formation of acetic acid during pyrolysis was monitored by the ^{1}H nmr spectrum as per the published procedure.[7] In the case of the pyrolysis of jesaconitine[7], the generation of acetic acid during pyrolysis may be monitored easily by the ^{1}H nmr spectrum because the C-8 acetyl group in jesaconitine absorbs at δ 1.54 and the formation of acetic acid during pyrolysis can be detected by appearance of new absorption between δ 2.0 and δ 2.10 in the ^{1}H nmr spectrum. However, in the case of the pyrolysis of alkaloid A, detection of the formation of acetic acid is difficult because the acetyl group in alkaloid A absorbs at δ 2.10. Because of this situation the results of the pyrolysis study of alkaloid A do not prove the presence of an acetyl group at C-8.

Because the position of acetyl group in alkaloid A was in doubt, we decided to investigate its structure by comparison of its ^{13}C nmr spectrum with that of other closely related alkaloids. Comparison of the carbon-13 chemical shifts of alkaloids A and B was made with known alkaloids, neoline 4[8], 8-acetyl-neoline 5, delphisine 6[9], trimethoxy neoline 7, heteratisine 8[10] and 6-acetyl heteratisine 9 (Table 1). The unambiguous assignments of the ^{13}C chemical shifts in alkaloids 2 to 9 were made by extensive correlation with other known diterpene alkaloids and their derivatives,[5,6] and by using conventional techniques,[11,12] chemical-shift theory and direct analysis of non-protonated carbon centers.

The comparison of ^{13}C chemical shifts of the acetyl group and the acetyl-group-containing carbons in alkaloid A was made with closely related compounds 5 and 6. In all acetyl groups in diterpene alkaloids, secondary and tertiary acetyl groups can be distinguished easily by a difference of ~1 ppm in their carbon-13 chemical shifts. In secondary acetyl groups, the ^{13}C chemical shift of carbonyl and methyl occur at ~169 ppm and ~22 ppm, respectively. In the case of a tertiary acetyl group, carbonyl and methyl chemical shifts occur at ~170 ppm and ~21 ppm, respectively (Table 1). From this observation we concluded that a secondary acetyl group is present and a tertiary acetyl group is absent at C-8 position in alkaloid A. This result was confirmed by comparison of the C-8 chemical shift in alkaloid A with those of 8-acetyl neoline 5

Table 1. Carbon-13 Chemical Shifts and Assignments for the Alkaloid A, Alkaloid B, Neoline-type Bases and Heteratisine-type Bases[a].

Carbon	1[b]	2[b]	2	3	4	5	6	7[c]	8	9
1	72.6	72.9	72.9	72.6	72.3	72.0	72.1	85.4	83.5	82.2
2	31.6**	32.2**	29.7	29.7	29.5†	29.5†	29.5†	26.3	26.9	26.7
3	37.8**	42.4**	32.2	31.6	29.9†	29.9†	30.1†	35.2	36.8	36.4
4	32.8	32.8	32.8	32.8	38.2	38.2	38.1	39.0	34.7	34.7
5	42.3**	44.4**	46.1	42.3	44.9	46.1	44.1	48.4	50.9	49.7
6	72.3	72.0	72.0	72.3	83.3	84.1	84.2	84.1†	72.9	74.0
7	44.4	50.2	54.8	48.0	52.3	48.2	48.3	48.4	49.3	48.6
8	79.9	76.0	76.0	79.9*	74.3	85.4	85.8	78.3	75.4	75.3
9	48.0**	54.8**	50.2	44.4	48.3	44.0	43.3	45.6	57.8	57.4
10	44.4**	46.1**	40.0	40.0	40.7	40.8	38.5	38.1	42.8	42.8
11	48.9	48.4	48.4	48.9	49.6	49.9	49.8	50.9	49.3	49.7
12	30.6**	29.7**	29.7	30.6	29.8†	29.5†	29.5†	30.2	33.1	35.7
13	40.0	40.0	44.4	44.4	44.3	44.0	43.3	46.1	75.8	75.8
14	75.9	76.0	76.0	75.9	75.9	75.0	75.5	83.6†	176.0	173.8
15	29.7**	29.7**	42.4	37.8	42.7	38.4	38.5	34.7	29.1†	28.9†
16	83.3	82.4	82.4	83.3	82.3	82.4	82.7	83.6†	29.2†	29.4†
17	65.5	64.9	64.9	65.5	63.6	63.0	62.7	60.8	62.2	62.4
18	27.3	27.4	27.4	27.3	80.3	79.8	79.8	80.4	26.2	25.9
19	61.6	61.8	61.8	61.6	57.2	56.8	56.8	54.3	58.3	54.8
N-CH$_2$	48.3	48.4	48.4	48.3	48.2	48.4	48.0	48.9	49.0	48.7
CH$_3$	12.9	13.0	13.0	12.9	13.0	12.7	12.9	13.4	13.5	13.4
1'	-	-	-	-	-	-	-	56.3	55.2	55.5
6'	52.8	-	-	-	57.8	58.1	58.0	57.6	-	-
16'	56.4	56.3	56.3	56.4	56.3	56.6	56.5	56.1	-	-
18'	-	-	-	-	59.1	59.1	59.0	59.1	-	-
-C=O	-	-	-	-	-	169.9	169.3	-	-	-
	170.9	-	-	170.9	-	-	170.4	-	-	170.8
CH$_3$	-	-	-	-	-	22.5	22.2	-	-	
	21.5	-	-	21.5	-	-	21.1	-	-	21.7

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[a] In ppm downfield to TMS, solvent deuterochloroform. [b] Jones's and Benn's assignments for alkaloids A and B. [c] Chemical shifts of methoxyls at C-8 and C-14 occur at 48.0 and 58.5 ppm, respectively. † Values within any vertical column may be interchanged. * Chemical shift of methoxyl at C-8 occurs at 52.8 ppm.
**tentative assignment.

and delphisine 6. In 8-acetyl neoline 5 and delphisine 6, the C-8 chemical shift occur as a singlet at 85.4 ppm and 85.8 ppm, respectively. In alkaloid A, there is no singlet in the region of 85 ppm. Comparison of ^{13}C chemical shifts of methoxyl and methoxyl-containing carbons in alkaloids 2 to 7 is noteworthy. The ^{13}C chemical shift of methoxyl at C-6 occurs between 57.8 ppm and 58.0 ppm in all known diterpene alkaloids[5], while in alkaloid A there is no chemical shift at ~ 58 ppm, indicating the absence of a 6-methoxyl group. The ^{13}C chemical shifts at 52.8 ppm (quartet) and 79.9 ppm (singlet) are in good agreement with the presence of a methoxyl group at C-8 position in alkaloid A. From these results we conclude that an acetyl group is present at C-6. That the acetyl group is in the α-configuration is indicated by comparison with the ^{13}C chemical shifts of heteratisine 8 and 6-acetyl heteratisine 9.[13]

On the basis of arguments and data presented here, we assign structure 3 to alkaloid A. We have also revised the ^{13}C chemical shift assignments of alkaloids A and B.

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References and Notes

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13. Carbon-13 spectra were taken at 25.03 MHz in the Fourier mode using a JEOL-PFT-100 spectrometer in conjuction with a EC-100-20K memory computer. Samples were dissolved in $CDCl_3$ containing TMS as an internal standard. Concentrations were about 0.3 ~ 0.9 M.