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THE APPLICATION OF CARBON-13 MAGNETIC RESONANCE TO STRUCTURAL PROBLEMS: TWO NEW DITERPENOID ALKALOIDS FROM *DELPHINIUM BICOLOR* NUTT

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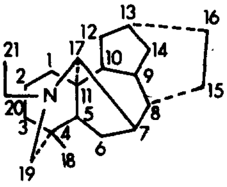
We have examined the utility of the carbon-13 magnetic resonance technique in the area of the diterpenoid alkaloids and wish to report structures for two unknown alkaloids, A and B, which have been isolated in small amounts from *Delphinium bicolor* Nutt. Assignment of the structures relies on evidence from a variety of sources but the ^{13}C studies proved of critical importance in determining the degree and sites of oxygen-substitution in these molecules.

The base A, $[\alpha]_D^{24}$ + 10° ($CHCl_3$), which was not obtained in crystalline form although it yielded a hydroiodide salt m.p. >240° (methanol-ether), had composition $C_{25}H_{39}NO_6$ ($M^{+\cdot}$ calc. 449.2777, found 449.2797 amu). The pmr spectrum[1] indicated the presence of a tertiary methyl (1.04), an N-ethyl (CH_3 at 1.09, J=7Hz), an acetoxyl (2.10), two methoxyls (3.18, 3.46) and *ca*. two hydroxyls (6.90, disappearing on addition of D_2O). Infrared absorptions at 3500, 3150, 1735 and 1238 cm^{-1} also indicated the presence of hydroxyl and acetate functions. The base B, m.p. 190-191°, $[\alpha]_D^{24}$ + 16° ($CHCl_3$), was similarly shown to have the composition $C_{22}H_{35}NO_5$ ($M^{+\cdot}$ calc. 393.2515, found 393.2523 amu), and to contain a tertiary methyl, an N-ethyl, a methoxyl, and hydroxyl groups. Given the nature of *Delphinium* alkaloids,[2] these data suggest that A and B have the part structure **1**. Further, a prominent ion in the mass spectra of A and B at m/e M-17 characterises the location of a hydroxyl at C-1,[3] and we ascribe this the α-hydrogen bonded configuration.[4] Finally, pyrolysis of A in glycerol, monitored by pmr indicated the generation of acetic acid, consistent with the location of an acetoxyl group at C-8.[5]

The ^{13}C chemical shifts determined for solutions of the bases A and B in deuterochloroform[6] are shown in the Figure. Assignment of the resonances to



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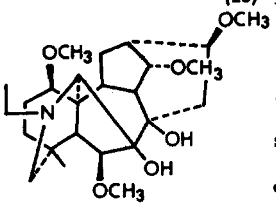

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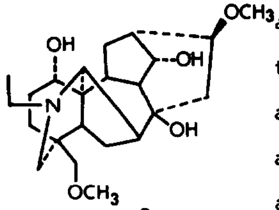

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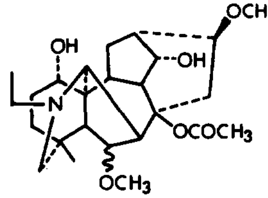

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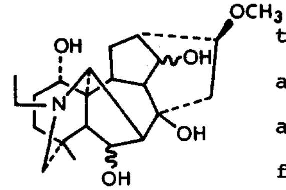

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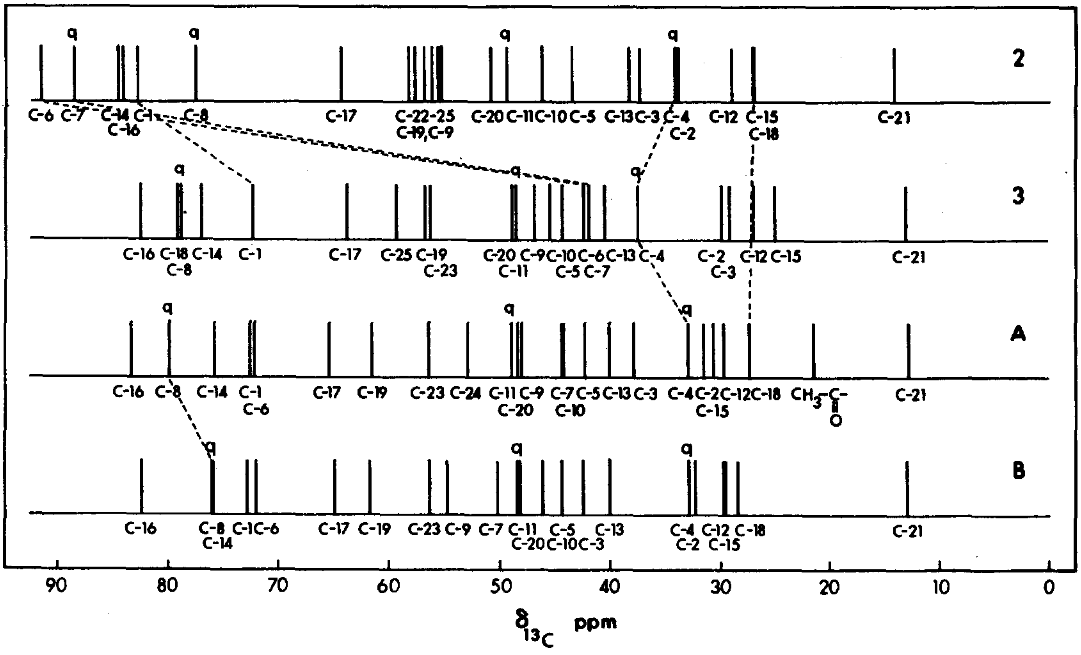
individual carbon atoms was made using conventional techniques, additivity relationships,[7] and from studies of a variety of model *Delphinium* alkaloids.[8] ^{13}C data for the representative model systems deoxylycoctonine (2) and isolatizidine (3) are also shown in the Figure. Given these data we propose the structures 4 and 5 for the bases A and B, respectively.

The pattern of ^{13}C shifts for 2 and 3, shown in the Figure, are typical for this class of compounds. In general, the hetero substituted carbon atoms resonate downfield of 50 ppm, while other carbons are upfield. Groups such as methoxyl (56-61 ppm), acetoxyl (*ca.* 22 and 170 ppm) and N-ethyl (*ca.* 14 and 50 ppm) are easily characterized by their off-resonance spectra and typical shifts.[9] Thus, A and B possess an N-ethyl function, A, an acetoxyl group, and there are 2 and 1 methoxyl groups in A and B, respectively. It is noteworthy that the methoxyl group at C-16 in 3 is the only one common in position to that in 2 and is, therefore, characterized by the shift 56.3 ppm. Both A and B exhibit similar resonances at 56.4 and 56.3 ppm, respectively. Hence, methoxyl substitution at C-16 is indicated in A and B. The second methoxyl group resonance in A is at relatively high field (52.8 ppm) and cannot be readily assigned.

The pattern of quaternary carbon shifts exhibited in 2 is typical for this class of alkaloids. In 3 oxygen substituents at C-6 and C-7 are removed, resulting in upfield shifts of 49.1 and 46.7 ppm, respectively.[9d] The absence of resonances downfield of 84 ppm, in particular for quaternary carbons, in the bases A and B indicate there are no substituents at C-7. Further, the downfield shifts at C-7 in A and B, compared to 3, and the absence of a methine resonance attributable to C-6 at approximately 42 ppm in A and B suggest oxygen substitution at C-6. Consequently, a resonance at 72-76 ppm in A and B is due to C-6. The quaternary center C-11 exhibits negligible shifts (48.8±0.5 ppm) throughout this series indicating close structural resemblance at this site. However, the shift at C-4, which is similar in 2, A and B (33.3±0.8 ppm), contrasts with that in 3 *(37.5 ppm) and indicates a* $C-CH_3$ *group at this site. As a corollary, the resonance* at 26.8-27.5 ppm in 2, A and B is characteristic of the methyl group C-18. *The observed shifts at C-8 in 2 and 3 are more difficult to reconcile. However,* chemical evidence shows that A is substituted by the acetoxyl group at this site. Replacement of this group by hydroxyl in B is indicated by the upfield shift (3.9 ppm)[9a] at this position.

Having established the similarity between the structure of 3 and the bases A and B it is instructive to compare the shifts of several characteristic methine resonances. Thus, the similar shift at C-16 (82.5 to 84.1 ppm) confirms methoxyl substitution at this site in 2, 3, A and B. The upfield shift at C-1 (10.3 ppm) in 3, compared to 2, characterizes the C-1 shift for the C_1-OH carbon (72.5 ppm) and is observed in the bases A (72.6 ppm) and B (73.0 ppm), corroborating the mass spectral evidence for hydroxyl substitution at this site. A similar feature at C-14 indicates that this carbon is substituted by a hydroxyl group in the bases A and B. Further, the absence of structural or substituent changes at C-13 and C-17 in 3, A and B is reflected by the relatively constant shifts, 40.2±0.2 and 64.5±1 ppm, respectively. The methine resonances at 72 ppm in both A and B are assigned to C-6.



The evidence in these cases is less compelling and the assignment is tentative. However, the observed β-substituent effects at C-7 and the absence of gross modification in the general pattern of shifts in **2** or **3** and A and B, in particular, at the alternative sites of oxygen substitution, C-2, C-3, C-12, C-15 and C-19, lend credence to the assignment. Note, for example, the shift at C-3 in **2**, A and B is characteristically at low field for a methyl substituent at C-4 and differs from that in **3** and other alkaloids of this type[8] in which the C-4 substituent is $-CH_2OR$. The absence or an appreciable upfield shift at C-6 in B, compared to A, and the high field methoxyl shift (52.8 ppm) in A might be indicative of a stereochemical modification at this site compared with the model systems. However, in the present study our efforts relate only to gross structural features.

We conclude that the foregoing evidence is compatible with the structures **4** and **5** for the bases A and B, respectively. Base **5** is the desmethyl desacetate of base **4**. These structures are closely related to those of the chasmainine and neoline systems,[2] and are additions to this still poorly represented group of C_{19} diterpenoid alkaloids with the lycoctonine skeleton unoxygenated at C-18.[10]

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