THE STRUCTURE OF CODONOPSINE

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The structure of 3, 4-dihydroxy-1, 2-dimethyl-5-veratrylpyrrolidine has previously been proposed for codonopsine [1].

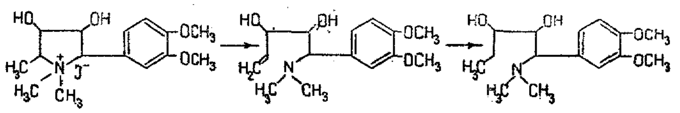
The NMR spectrum of codonopsine, taken on a JNM-4H-100/100 MHz spectrometer has signals from the protons of N—CH_3 (singlet, τ 7.94), CH—CH_3 (doublet, τ 8.84), two methoxyl (singlet, τ 6.38; 6.48), and two hydroxyl groups (singlet, τ 6.74). The aromatic protons appear in the τ 3.18 region (3H, multiplet).

The NMR spectrum of the diacetyl derivative shows signals from two ester methoxyls (singlet, τ 7.99, 8.10).

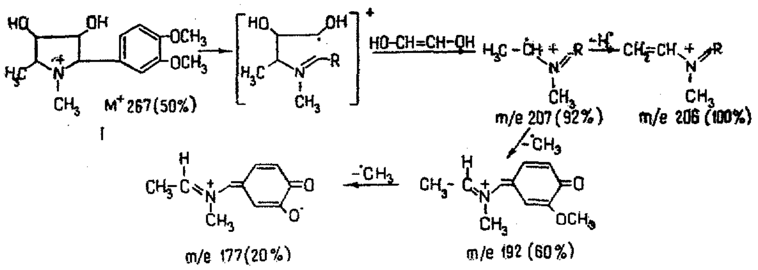
In the spectrum of the 1-des-base obtained after the first stage of Hofmann degradation there is no signal from a CH—CH_3 group; in the spectrum of its dihydro derivative there is a signal in the τ 9.13 region in the form of a three-proton triplet which must be ascribed to an ethyl group. Consequently, in the first stage of Hofmann degradation the $C_{(1)}$—N bond ruptures with the formation of a double bond in the side chain. This shows the presence in codonopsine of a CH—CH_3 group in the α-position with respect to the nitrogen.

From these results and the equivalence of the hydroxyl groups in the NMR spectrum it follows that they are in the 3, 4-positions of the pyrrolidone nucleus.

What has been said above permits the structure of the des-base to be shown in the following way:



In the NMR spectrum of the dihydrogenated nitrogen-free base obtained after the second stage of Hofmann degradation there is no absorption in the region of olefinic protons. Here the formation of an epoxide bridge apparently takes place, this being characteristic for alkaloids having an OH group in the τ-position with respect to nitrogen [3]. On further hydrogenation, two atoms of hydrogen are absorbed, being consumed in the opening of the epoxide bridge.



Codonopsine is oxidized by periodic acid on prolonged shaking (6 hr) to a dialdehyde, codonopsidinal (mol. wt. 265). We have isolated its 2, 4-dinitrophenylhydrazone with mp 136–138° C. The formation of codonopsidinal also shows that the hydroxyl groups are vicinal.

The mass spectra of codonopsine and the tetrahydrogenated nitrogen-free substance obtained from it agree with the structural formulas suggested for them. The spectrum of the base has ions with m/e 267 (M^+), 207, 206, and 192, the formation of which is analogous to the fragmentation of the pyrrolidine alkaloids [2] and is confirmed by the presence of the corresponding metastable peaks in the spectrum.

R EFERENCES

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