NMR INVESTIGATION OF ALKALOIDS.

IV. ^{13}C NMR SPECTRA AND STRUCTURES OF NORFLUOROCURARINE, AKUAMMICINE, VINCANIDINE, AND VINERVININE

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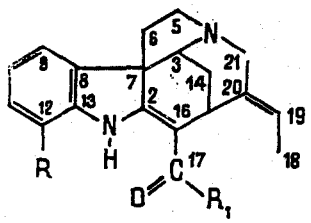
On the basis of the results of a comparative analysis of the ^{13}C NMR spectra of α-methyleneindoline alkaloids with the akuammicine nucleus, an assignment has been made of the carbon signals, and the structures of vincanidine and vinervinine with the substituents OH and OCH_3 at C_{12} of the aromatic nucleus established previously with the aid of PMR have been confirmed unambiguously.

The structures of α-methyleneindole alkaloids with the akuammicine nucleus – vincanidine, vincanicine, vinervine, and vinervinine – were previously [2] established on the basis of an analysis of their PMR spectra. It appeared of interest to study the structures of these alkaloids with the aid of ^{13}C NMR spectroscopy, since the ^{13}C chemical shifts (CSs) of the carbons of an aromatic ring change in accordance with the positions of the substituents. The literature contains practically no information on the ^{13}C NMR spectra of alkaloids of the akuammine nucleus (III), with the exception of the ^{13}C CSs of the C_9, C_{10}, C_{11}, and C_{12} aromatic carbon atoms of (III) itself and of the alkaloids alstovine [3], with a reduced C_{19}–C_{20} bond, and 16-isoretuline [4], which is a dihydroindole derivative.

We give the results of a study of the ^{13}C NMR spectra of norfluorocurarine (vincanine) (I), vincanidine (II), akuammacine (III), and vinervinine (IV).



I $R=R_1=H$, norfluorocurarine (vincanine)

II $R=OH$, $R_1=H$, vincanidine

III $R=H$, $R_1=OCH_3$, akuammicine

IV $R=R_1=OCH_3$, vinervinine

The spectral characteristics are given in Table 1 and in Fig. 1. The assignment of the ^{13}C signals of compounds (I-IV) was based on an experiment with the complete decoupling of C–H interactions and by a comparison of the ^{13}C CSs of (I-IV) with literature reports of the ^{13}C NMR spectra of alkaloids containing an α-methyleneindole nucleus [5, 6], and also with the ^{13}C NMR spectra of model compounds – o-methoxyphenol [7] and o-anisidine taking into account the α, β, and γ contributions of the OH and OCH_3 groups to the CSs of the aromatic carbon atoms. In the spectra of the α-methyleneindoline alkaloids (I)-(IV) in the 109-188 ppm region the signals clearly appear of ^{13}C sp^2 carbons: C_2, C_8, C_{13}, and C_{20} as singlets, and C_9, C_{10}, C_{11}, C_{12} (in (I) and (III) and C_{19} as doublets in the off-resonance spectrum, the H–C=O signal of the aldehyde carbon in (I) and (II) naturally appearing in the form of a doublet and the C=O signal of the ester group in (III) and (IV)

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TABLE 1. ^{13}C Chemical Shifts and Assignments of the Signals of the Carbon Atoms of α-Methyleneindoline Alkaloids with the Akuammicine Nucleus (I-IV)

Carbon atoms and multiplicities	Norfluorocurarine (vincanine) (I), $CDCl_3$	Vincanidine (II), Py-d_5	Akuammicine (III), $CDCl_3$	Vinervinine (VI), $CDCl_3$
C_2s	168,7	169,4	167,5*	167,7*
C_3d	62,7	62,5	61,7	62 0
C_5t	56 4	56,9	56,1	56,2
C_6t	46,2	47,2	46,1	46,2
C_7s	58,3	59,8	57,4	58,5
C_8s	136 9	141,0	136,8	138,0
C_9d	121,7	115,9	120,4	113,2
C_{10}d	120,7	123,5	120,3	121,5
C_{11}d	127,6	112,7	127,4	110,3
C_{12}	110,2d	143,7s	109,1d	144 3s
C_{13}s	142.9	131,8	135,8	132,5
C_{14}t	30,8	31,2	30,8	31,0
C_{15}d	31,2	31,4	29,6	30,0
C_{16}s	111,1	112,2	101,1	101,6
C_{17}=O	183,2d	187,9d	167,7s*	167,8s*
18—CH_3q	12,7	13,0	13,1	12,7
C_{19}d	120,2	120,0	120,0	120,3
C_{20}s	139,6	139,4	139,2	139,3
C_{21}t	56,6	57,1	56,8	57,0
$COOCH_3$q	—	—	50,6	50,8
Ar—OCH_3q	—	—	—	55,5

*The assignment of the C_2 and C_{17} signals in (III) and (IV) is ambiguous.

in the form of a singlet. The CSs of the carbon atom of the aldehyde groups of norfluorocurarine (I) and of vincanidine (II) are close to the CS of the C=O group of acrolein [2]. As was to be expected, the signal of the C_{12} aromatic carbon atom, bearing a OH group in (II) and a OCH_3 group in (IV) has a singlet nature in the off-resonance spectrum. The values of the CSs of the ^{13}C sp^2 carbons C_9, C_{10}, C_{11}, and C_{12} of akuammicine (III) coincide to within an accuracy of 0.2 ppm with the literature figures [3], and the CSs of the C_2 and C_{16} carbon atoms of (III) and of vinervinine (IV) are close to those of tabersonine and of vincadifformine [5]. At the same time, in the ^{13}C NMR spectra the signals of the C_{19} and C_{20} carbon atoms of the ethylidene double bond are shifted downfield by 2-3 ppm as compared with the same signals of the dihydroindole alkaloids of the type of ajmaline with C_2—αH [1, 9].

In the 62.7-12.7 ppm region of the spectra of the alkaloids studied, the signals of sp^3 carbon atoms appear in numbers and multiplicities corresponding accurately to structures (I)-(IV) (Table 1). A comparison of the CSs of the quaternary C_7 carbon atom of alkaloids of the ajmaline type [1, 9] and of alkaloids of the oxindole series [10] with those of compounds (I-IV) showed their closeness. The assignment of the signals of the C_6, C_{14}, and C_{21} carbon atoms in (I-IV) was made on the basis of a comparison with such alkaloids of the vincadifformine [5] and ajmaline [1, 9] series. The CSs of the C_6 carbon atoms in alkaloid (I-IV) and those of the vincadifformine series practically coincide. The CSs of the C_{14} and C_{21} carbon atoms of the alkaloids (I-IV) and those of the ajmaline type [1, 9] are also close.

The carbon atoms of the methyl groups of Ar—OCH_3, $COOCH_3$, and C=C—CH_3 differ sharply, and their CSs correspond to the standard values [11].

In a determination of the positions of the OH and OCH_3 substituents in the aromatic ring of vincanidine (II) and in that of vinervine (IV), the most characteristic criterion is the fact that these substituents, being electron donors, lead to a substantial screening of the carbon atoms located in the ortho and para positions to them. An analysis of literature information on the ^{13}C NMR spectra of model hydroxy- and methoxy-substituted phenols [7], o-anisidine, the α-methyleneindoline alkaloid alstovine [3], and those given in Table 1 shows that the OH and OCH_3 substituents in the aromatic ring make the following contributions (increments) to the ^{13}C CSs of the neighboring carbon atoms: α = +34 ± 15 ppm, ortho = −15 ± 2.5 ppm; para = −7 ± 1 ppm; meta = +2 ± 0.5 ppm, and we have observed that the magnitudes of these contributions depend on the degree of substitution of the carbon atoms. Since the C_{12} carbon atom in indoline and α-methyleneindoline alkaloids is the most highly screened through the donor influence of the N_a atom its signal is observed in a weak field relative

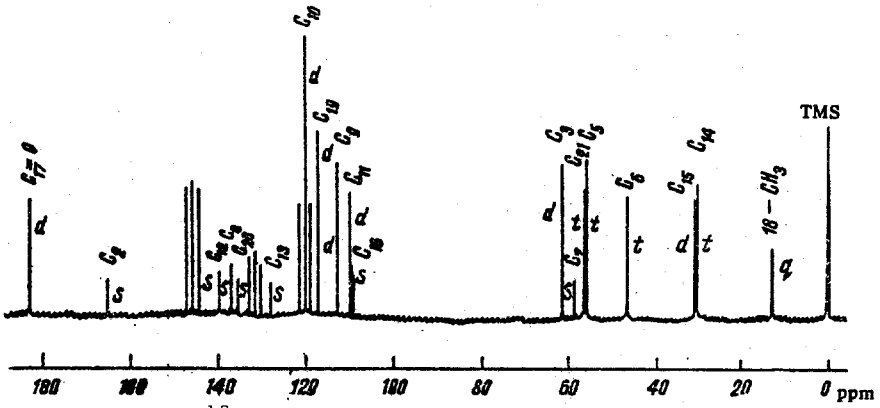

Fig. 1. ^{13}C NMR spectrum of vincanidine in Py-d_5.

to the other carbon atoms of the aromatic ring (see Table 1). In the ^{13}C NMR spectrum of (I) and (III), the differences in the CSs of the C_{11} and C_{12} carbon atoms amount to 17.4 and 18.3 ppm, respectively (see Table 1). Taking into account the α and β contributions of the OH substituent in (II) and the OCH_3 substituent in (IV) to the CSs of the carbon atoms to which they are attached and of the ortho carbon atom of the aromatic ring permits the position of the OH group in vincanidine and the OCH_3 group in vinervine to be determined unambiguously as C_{12}. These characteristics of the ^{13}C NMR spectra agree completely with the analogous conclusions drawn previously on the structures of the alkaloids vincanidine, vincanicine, vinervine, and vinervinine drawn previously on the basis of an analysis of the PMR spectra.

EXPERIMENTAL

The ^{13}C NMR spectra of the alkaloids (I-IV) were obtained on Varian CFT-20 and XL-100-15 and Bruker WM-250 spectrometers in $CDCl_3$, O — TMS ($\delta_{TMS} = \delta_{CDCl_3} + 76.91$ ppm) and in Py-d_5, O — TMS, in the pulsed regime with subsequent Fourier transformation under the conditions of complete and incomplete off-resonance decoupling of C—H interactions.

SUMMARY

On the basis of the results of a comparative study of the ^{13}C NMR spectra of α-methyleneindoline alkaloids with the akuammicine nucleus, an assignment of the signals of the carbon atoms has been made and the structures of vincanidine and vinervinine established previously by analysis of PMR spectra have been unambiguously confirmed.

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