AN INVESTIGATION BY THE NMR METHOD OF THE STRUCTURE OF THE ALKALOID SOPHORINE FROM *Sophora alopecuroides*

F. G. Kamaev, S. Kuchkarov,
Yu. K. Kushmuradov, and Kh. A. Aslanov

UDC 547.944/945

A new base — sophorine, with mp 59-60°C, $[\alpha]_D^{23} - 18.9°$ (c 0.98; ethanol) — has been isolated from the epigeal part of the plant *Sophora alopecuroides* L. Its IR spectrum and the nature of its mass spectrometric composition have permitted sophorine to be assigned to the quinolizidine alkaloids. The ^{13}C NMR spectrum has shown the presence of 19 carbon atoms. The analysis of several of the carbon signals has confirmed the results of IR and mass spectroscopy. Additional details of the structure of sophorine have been obtained from its PMR spectrum.

The alkaloid-rich plant *Sophora alopecuroides* L. (family Leguminosae) is considered to be included among the well-studied plants. Nevertheless, recently several new alkaloids have been isolated from it: neosophoramine, allylaloperine, 3-hydroxysophoridine, dehydrosophoridine, etc. [1-5]. We have continued the study of the composition of the total alkaloids of this plant. From the mother liquor after the separation of the combined bases we have isolated a new compound we have called sophorine (base 8) with mp 59-60°C $[\alpha]_D^{23} - 18.9°$ (c 0.98; ethanol) having a molecular weight of 338 (mass spectrometrically) [6]. The nature of the mass-spectrometric decomposition permits sophorine to be assigned to the lupinine alkaloids [7], and the 100% intensity of the ions with m/z 138^+ indicates the presence of a trans-quinolizidine fragment. A trans-quinolizidine system is also confirmed by a Bohlmann band (2675-2945 cm^{-1}) in the IR spectrum of the base. Absorption in the 1605 and 1683 cm^{-1} regions relates to a secondary amide group. Thus, the information available (high molecular weight, presence of a N—H—CO group) indicate that sophorine does not belong to the derivatives of matrine, sparteine, cytisine or aloperine traditionally isolated from this plant.

The NMR spectrum of sophorine on ^{13}C nuclei at the natural concentration of this isotope is shown in Fig. 1, from which the presence of 19 carbon atoms in the molecule can be seen. The chemical shifts of the signals of the carbon atoms and their splitting in double-resonance experiments with a strong out-of-resonance irradiation of the protons are given in Table 1. The two weakest signals belong to ketone groups present in ester and/or amide groupings [8]. Two close signals (56.4 and 56.1 ppm) are characteristic for trans-quinolizidine derivatives (the α-carbon atoms C_2 and C_{10}) [9, 10]. The signals of two tertiary carbons at 64.9 and 41.4 ppm (doublets on partial decoupling) are analogous to those of the C_6 and C_7 carbons in lupinine derivatives [9]. The analysis of some of the carbon signals confirms the results of mass and IR spectroscopy showing that sophorine is a lupinine derivative.

It is important to note that the spectra on ^{13}C nuclei with incomplete decoupling shows the absence of other tertiary and quaternary carbons in the skeleton of the molecule. Consequently, the sophorine molecule consists of the bicyclic system of lupinine with a long linear substituent. From the value of its chemical shift and its multiplicity [8], the signal at 63.7 ppm belongs to a $-OCH_2$ group apparently forming part of an ester grouping. The signal at 41.0 ppm must be assigned to a carbon atom present in the α position to an amide nitrogen. The absence of a second similar signal in the same region indicates that the third bond of this nitrogen atom is not attached to a carbon atom. From the IR spectra it may be concluded that the molecule contains an amide proton. A signal at 13.2 ppm belongs to a terminal methyl group. The signals of the other carbon atoms relate to ordinary $C-CH_2-C$ methylene fragments.

Thus, from an analysis of the chemical shifts and multiplicities of the signals it is possible to suggest the following composition: To a quinolizidine nucleus (C_9H_{16}) is at-

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V. I. Lenin Tashkent State University. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 604-608, September-October, 1981. Original article submitted February 27, 1981.

0009-3130/81/1705-0439$07.50

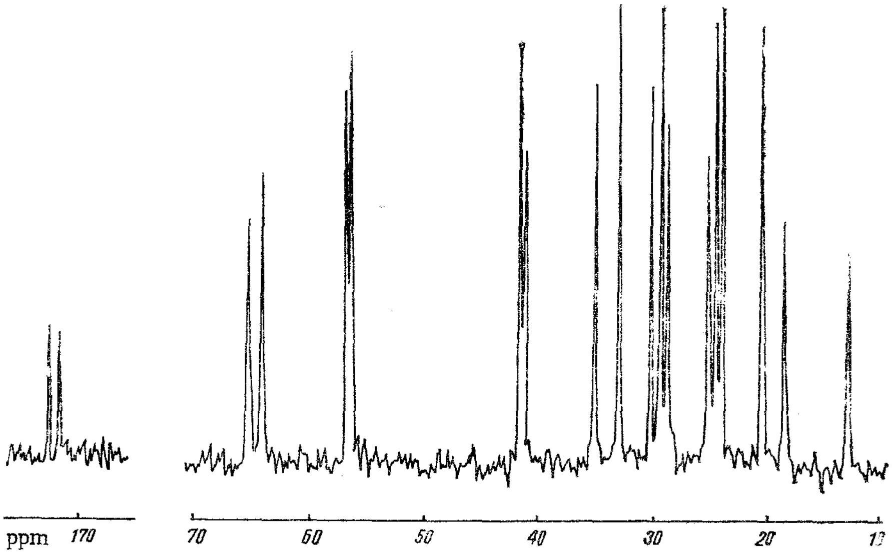


Fig. 1. ^{13}C NMR spectrum of sophorine.

tached a linear substituent containing $-CH_2-NH-CO$, $-CH_2COO$, five $-CH_2-$, and one $-CH_3$ groups. The empirical formula of sophorine established in this way, $C_{19}H_{34}N_2O_3$, has a molecular weight coinciding with that determined mass spectrometrically [6] — 338.

Additional details of the structure of sophorine can be obtained from its PMR spectra (Fig. 2). A triplet at 6.06 ppm with broad components and with an intensity that falls when D_2O is added relates to an amide $-NH$ proton. On its irradiation (total resonance), the two-proton signal in the 2.9-3.4 ppm region forms the AB part of the ABX system. The chemical shifts and multiplicities of these signals indicate that the substituent contains the fragment $-CH-CH_2-NH-CO$.

The PMR spectra of lupinine and its derivatives usually contain at 3.7 ppm a complex multiplet of the protons of a $-CH_2O-R$ substituent at C_7 [11], but this is absent from the sophorine spectrum. Consequently, the fragment found on the basis of double resonance can be considered to be the beginning of the substituent at C_7. A two-proton doublet at 3.95 ppm relates to the methylene protons in an oxygen fragment $-CH_2CH_2-O-CO-$. A two-proton signal in the 2.5-2.8 ppm region is characteristic for the H_{2e} and H_{10e} protons of a trans-quinolizidine system [11]. An unsymmetrical triplet at 1.89 ppm of the terminal methyl group has well-defined components the intensities of which are distorted by second-order effects. The nature of the triplet and a comparison with the spectra of the model compounds permit the assumption that there is a butyl or propyl radical at the end of the substituent, separated from the remainder of the molecule by an ester group.

On the basis of the experimental facts, structure (I) may be suggested for sophorine.

Taking biogenetic considerations connected with the structure of the skeleton of the matrine and sparteine alkaloids into account, the structure of the sophorine molecule can be refined as (II). Apparently, sophorine is a precursor of the matrine and sparteine alkaloids.

We give below the values of the ^{13}C chemical shifts of the carbon atoms in the NMR spectrum of sophorine and their multiplicities with incomplete decoupling from ^1H nuclei (δ scale; s — singlet; d — doublet; t — triplet; q — quartet):

172,7	s	56,1	t	30.2	t	24.1	t
171,8	s	41.4	d	29.4	t	20,6	t
64,9	d	41,0	t	28 8	t	18,7	t
63,7	t	34.9	t	25.2	t	13,2	q
56,4	t	33.0	t	24.6	t		

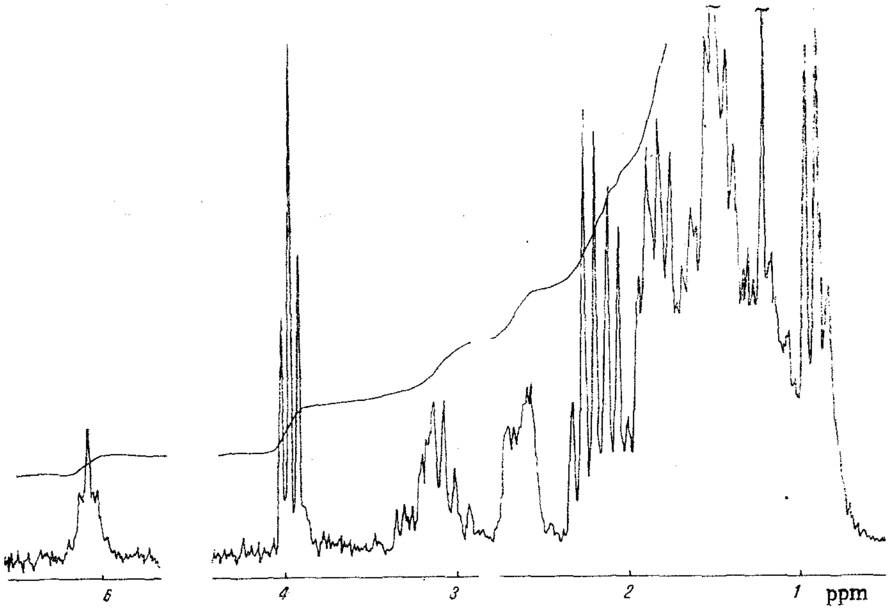
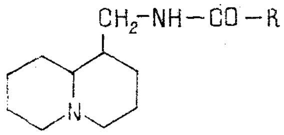


Fig. 2. PMR spectrum of sophorine.



I

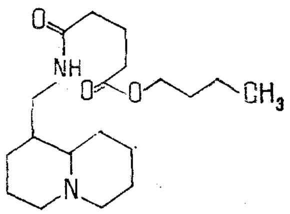
R = $-(CH_2)_3-COO-(CH_2)_3-CH_3$

or

R = $-(CH_2)_4-COO-(CH_2)_2-CH_3$

or

R = $-(CH_2)_2-COO-(CH_2)_4-CH_3$



II

NMR spectra were recorded on a Varian XL-100 spectrometer. The resonance frequency for protons was 100 MHz and for ^{13}C nuclei it was 25.1 MHz. The chemical shifts are given in parts per million relative to TMS. The solvents used were chloroform (^{13}C) and carbon tetrachloride (^{1}H).

SUMMARY

A new base, sophorine, has been isolated from the epigeal part of *Sophora alopecuroides* L. A detailed study of the ^{13}C NMR and PMR spectra has permitted a most probable structure to be suggested for it.

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NMR INVESTIGATION OF ALKALOIDS.

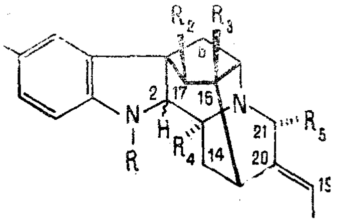
II.* DETERMINATION OF THE CONFIGURATIONS OF THE C_{17} and C_2 ASYMMETRIC CENTERS IN INDOLINE ALKALOIDS OF THE AJMALINE TYPE BY THE DOUBLE PROTON RESONANCE METHOD†

M. R. Yagudaev

UDC 547.944.1.92

By the method of double proton resonance, in the alkaloids of the ajmaline type, ajmaline, majoridine, herbamine, quebrachidine (vincarine), vincamajine, and vincamedine a long-range stereospecific interaction through four σ-bonds between the $H_{6\alpha}$ and $H_{17\alpha}$ protons of about 1 Hz has been found and in compounds with C_2-βH and C_{17}-αH (ajmaline, majoridine), the $H_{2\beta}$ and $H_{17\alpha}$ protons exhibit a NOE of the order of 10%. These facts can be used successfully in determining the orientation of the hydrogen atoms and the corresponding configurations of C_{17} and C_2 asymmetric centers in such systems.

To determine the orientation of the H_{17} hydrogen atom and the corresponding configuration of the C_{17} asymmetric center in indoline alkaloids of the ajmaline type (I-VI) use is made of chemical methods [3, 4] and also of PMR spectroscopic characteristics (CSs and SSCCs) [3, 5-7]. In the present communication we give the results of the use of double-proton resonance methods — collapse and the intramolecular nuclear Overhauser effect (NOE) — to determine the configurations of the C_{17} and C_2 asymmetric centers in alkaloids of the ajmaline type (I-VI) (Table 1).



I. Ajmaline $R = R_3 = R_4 = H$, $R_1 = CH_3$, $R_2 = R_5 = OH$, 19,20 dihydro C_2–βH.
II. Majoridine $R = OCH_3$, $R_1 = CH_3$, $R_2 = OAc$, $R_3 = R_4 = R_5 = H$, C_2–βH.
III. Herbamine $R = R_5 = H$, $R_1 = CH_3$, $R_2 = R_4 = OH$, $R_3 = COOCH_3$, C_2–αH.
IV. Quebrachidine (vincarine [8]): $R = R_1 = R_5 = H$, $R_2 = OH$, $R_3 = COOCH_3$, C_2–αH.
V. Vincamajine $R = R_4 = R_5 = H$, $R_1 = CH_3$, $R_2 = OH$, $R_3 = COOCH_3$, C_2–αH.
VI. Vincamedine. $R = R_4 = R_5 = H$, $R_1 = CH_3$, $R_2 = OAc$ $R_3 = COOCH_3$, C_2–βH.

When the hydrogen atom at C_{16} in the alkaloids of the type under consideration is substituted and the hydrogen at C_{17} is β-oriented, the configuration of the C_{17} center can be established unambiguously from the value of the vicinal spin coupling constant of the $H_{17\beta}$ and $H_{16\beta}$ protons, since under these conditions, as can be seen from models, the dihedral angle between the $H_\beta - C_{17} - C_{16} - H_\beta$ protons is approximately 0 and, consequently, in accord-

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*For Communication I, see [1].
†Delivered at an All-Union Conference on Modern Advances in High-Resolution NMR spectroscopy, Tashkent, September, 1975 [2].

Institute of the Chemistry of Plant Substances of the Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 608-613, September-October, 1981. Original article submitted March 11, 1981.

0009-3130/81/1705-0442$07.50