The results of the elementary analysis of all the compounds obtained corresponded to the calculated figures.

SUMMARY

The catalytic hydroamination of d-fenchone by aliphatic nitriles in an apparatus of the flow-through type has been studied. The optimum conditions for the performance of the reaction have been determined. The scheme is suggested for the mechanism of the formation of secondary amines. The absolute configurations of the compounds obtained have been established.

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NMR STUDY OF ALKALOIDS.

V. ^{13}C NMR SPECTRA AND RECONSIDERATION OF THE STRUCTURES OF 11- AND 10-HYDROXYPLEIOCARPAMINES AND THE STRUCTURES OF NEW ALKALOIDS FROM *Vinca erecta*

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UDC 547.944.1

The structures of phenolic alkaloids isolated previously from *Vinca erecta* Rgl. et Schmalh. have been reconsidered on the basis of the results of a study of their ^{13}C NMR spectra, and it has been shown that a base with mp 228-229° has the structure of 11-hydroxystrictamine and an amorphous base of the same composition isomeric with it is 10-hydroxystrictamine. The structures of two new indolenine alkaloids — ercinamine and **ercinaminine** — have been determined from an analysis of ^{13}C NMR spectra, and also on the basis of PMR and IR spectra and chemical transformations.

Previously, on the basis of an analysis of the UV, IR, PMR, and mass spectra, a phenolic base with mp 228-229°C isolated from the plant *Vinca erecta* Rgl. et Schmalh. [1] was ascribed the structure of 11-hydroxypleiocarpamine (I). The pleiocarpamine skeleton in (I) was proposed on the basis of the composition and the absence from its IR and PMR spectra of the signals of N–H and N–CH_3 groups, and also the closeness of its mass-spectrometric fragmentation and that of pleiocarpamine [1]. Then an amorphous base (II) with the same composition as (I) was isolated from the same plant. On the assumption that base (II) also had a pleiocarpamine skeleton and analyzing the chemical shifts of the aromatic protons in the PMR spectra of (I), (II), and other hydroxy- and methoxy-substituted indole alkaloids, we came to the conclusion that (I) was 10-hydroxypleiocarpamine and (II) was 11-hydroxypleiocarpamine [2]. In order to elucidate the skeletons and structures of alkaloids (I) and (II), we have now studied the ^{13}C spectrum of (I) (Fig. 1).

The assignment of the signals of the carbon atoms was made on the basis of the results of an experiment with incomplete decoupling of C–H interactions, i.e., from the multiplicities of the signals in the off-resonance spectrum, and also by comparing the ^{13}C CSs with the ^{13}C CSs given in the literature for alkaloids of similar structure taking the α-, β-, and γ-contributions into account [3, 4]. As can be seen from Fig. 1, in the 100-192 ppm region of the

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Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 483-488, July-August, 1983. Original article submitted May 31, 1982.

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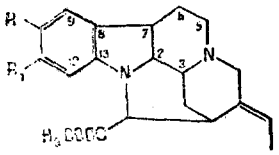
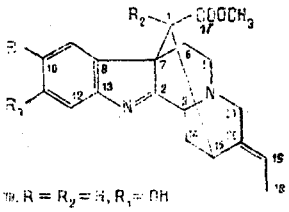




ercinamine

ercinaminine

^{13}C NMR spectrum of (I) there are nine signals relating to sp^2 carbons, one of which corresponds to two carbons (Table 1). In the off-resonance spectrum, five of these signals are represented in the form of singlets, and four in the form of doublets. Taking into account the number of sp^2 carbons and their multiplicities clearly shows the noncorrespondence of the skeleton of (I) to that of pleiocarpamine, since in the ^{13}C NMR spectrum of the latter eleven signals of sp^2 carbons should be observed (eight carbons of the indole nucleus, two carbons of the ethylenic double bond, and one signal of the carbonyl carbon of an ester group at about 170 ppm [3, 4]). At the same time, in the ^{13}C NMR spectrum of (I), judging from the multiplicities of the signals of the sp^2 carbons, there should be four doublets and seven singlets. In addition to this noncorrespondence of the numbers and multiplicities of the signals of the sp^2 carbons of (I) to those of pleiocarpamine, the expected CSs of a number of other carbons in them likewise differ distinctly. In the spectrum of (I) (see Fig. 1 and Table 1), in addition to the signal of the C=O group of $COOCH_3$ at 171.5 ppm a carbon signal is observed in the weak field at 191 ppm in the form of a singlet the presence of which can in no way be explained on the basis of the skeleton of pleiocarpamine. A comparison of the ^{13}C CS of the latter signal with information in the literature shows that it can relate only to the signal of the C_2 carbon, bound by a double bond with the nitrogen atom of the indolamine fragment [5, 6].

The number and multiplicities of the signals of the sp^3 carbons in the ^{13}C NMR spectrum of (I) in the 0-60 ppm region also shows that (I) does not contain the pleiocarpamine skeleton since there should be no signal of a quaternary carbon atom in the form of a singlet in the off-resonance spectrum of the latter, while the spectrum of (I) does have such a signal at 55.3 ppm. This signal obviously relates to the C_7 sp^3 carbon [6]. A subsequent comparative analysis of the number and magnitudes of the CSs and multiplicities of the signals of the sp^2 and sp^3 carbons in the ^{13}C NMR spectrum of (I) showed that it was based on the akuammiline-strictamine skeleton (III) [7, 8] – and not the pleiocarpamine skeleton as was previously assumed [7]. The CSs of the signals of the sp^3 carbons linked with a carbon atom (C_3d, C_5t, C_{21}t) and of the sp^2 carbons of the ethylenic bond (C_{20}s and C_{19}d) in (III), and also of 18-CH_3q are close to those of the indole [9] and dihydroindole [10] alkaloids. The signal of the C_{16}d carbon (III) is observed in a relatively weak field apparently because of the α-contribution (+24 ppm) of the ester C=O group [3].

For an unambiguous choice of the position of the OH substituent in the aromatic ring at C_{10} or C_{11} of substance (III) we started from the contributions (increments) of the OH group to the ^{13}C CSs in the ortho (–13 ± 2 ppm), para (–6 ± 0.5 ppm), and meta (+0.8 ± 0.5 ppm) carbons of benzene [3, 4]. The magnitudes of these contributions of the OH group to the CSs of aromatic carbons of the unsubstituted indolamine nucleus [5, 6] permits us to consider that the alkaloid with mp 228-229°C (I) has the structure of 11-hydroxystrictamine (III), and the isomeric alkaloid with the same composition is 10-hydroxystrictamine (IV).

In a further study of the alkaloids of *Vinca erecta*, we isolated two new bases: an optically active base with mp 238-240°C, composition $C_{21}H_{24}N_2O_4$, M^+ 368, $[\alpha]_D$ + 53°, which we have called ercinamine (V), and an amorphous base with the composition $C_{21}H_{24}N_2O_3$, M^+ 352, which we have called **ercinaminine** (VI). The results of a comparison of the UV, IR, PMR, and mass spectra (see the Experimental part) of bases (V) and (VI) with (III) and (IV) showed that they had a common skeleton. Furthermore, from a comparison of the signals of the aromatic protons of (V) and (VI) it follows that in the 6.6-7.4 ppm region of the PMR spectrum signals of the ABX type appear from three protons for (V) and from four protons for (VI), i.e., ercin-

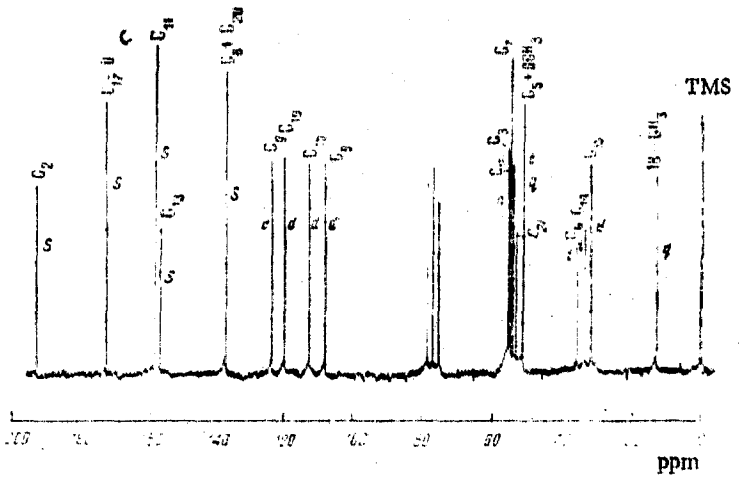


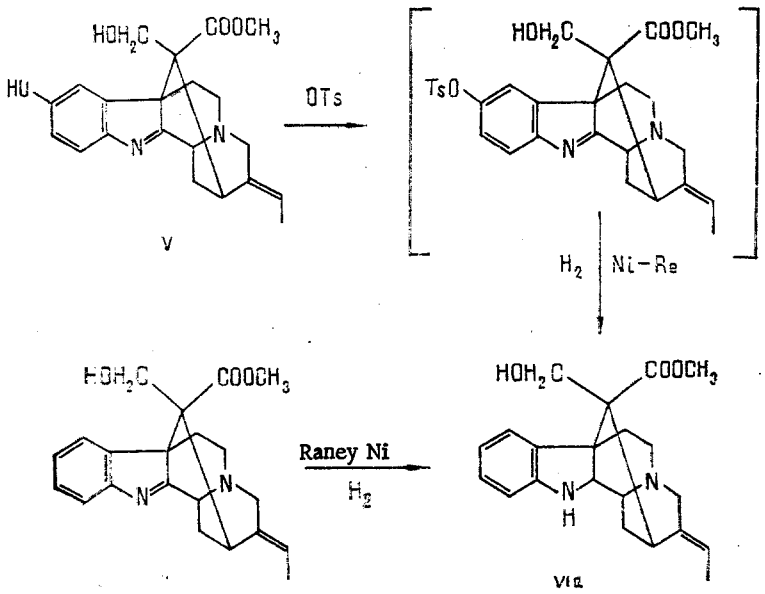
Fig. 1. ^{13}C NMR spectrum of the base (I) in $CDCl_3$.

TABLE 1. ^{13}C Chemical Shifts and Assignments of the Signals of the Carbons of Bases (III) and (V), ppm

Carbon atom and multiplicity	III, $CDCl_3$	V, Py-d,	Carbon atom and multiplicity	III, $CDCl_3$	V, Py-d,
C_2s	191.7	187.7	C_{14}t	33.3	31.2
C_3d	55.6	55.2	C_{15}d	32.2	35.1
C_5t	51.5	52.4	C_{16}	54.6d	61.1s
C_6t	35.8	39.3	C_{17}—Os	171.5	174.0
C_7s	55.3	59.4	OCH_3q	51.5	51.4
C_8s	137.1	147.6	C_{18}—H_3q	12.8	131.6
C_9d	123.8	114.1	C_{19}d	120.2	118.8
C_{10}	113.0d	157.4s	C_{20}s	137.1	141.5
C_{11}	157.5s	115.3d	C_{21}t	53.5	54.4
C_{12}d	168.4	121.7	C_{22}—OH	—	64.0
C_{13}s	136.0	149.2			

amine contains a trisubstituted and **ercinaminine** a disubstituted aromatic ring. The IR spectra of (V) and (VI) in the 700-900 cm^{-1} region characterizing the type of aromatic substitution also confirms this conclusion. Since the mass spectrometric fragmentations of bases (V) and (VI) are similar with ions differing in mass by 16 units, it may be assumed that these two alkaloids differ by an aromatic OH group. The latter hypothesis was confirmed by the tosylation of ercinamine (V) followed by reduction with Raney nickel: A product was obtained with M^+ 354 identical to the product of the Raney nickel reduction of **ercinaminine** (VIa). This gives grounds for considering that **ercinaminine** is a deoxy product of ercinamine (scheme). For a definitive establishment of the structure of ercinamine (V) we studied its ^{13}C NMR spectrum (Fig. 2, Table 1). As can be seen from the table, the number and CSs of the signals of sp^2 carbons and their multiplicities in the off-resonance spectrum of ercinamine (V) agree completely with an indolenine structure for it. (Scheme, top, following page.)

Analysis of the ^{13}C signals of the aromatic carbons of (V) taking into account the ortho-, para-, and meta-contributions of the OH group to the ^{13}C CSs show its position at C_{10}. An important difference between the ^{13}C NMR spectrum of ercinamine (V) and that of (III) is the presence of an additional signal of a sp^3 carbon at 64.0 ppm (t), and also the appearance of two singlet signals of carbons at 59.4 and 61.1 ppm in the spectrum of (V), while in the spectrum of (III) there is only one singlet of the C_7 carbon at 55.3 ppm (see Table 1). It is obvious that the additional triplet signal in the ^{13}C off-resonance spectrum of (V) belongs to the carbon of a CH_2OH group attached to C_{16}, as a result of which the signal of the latter carbon appears in the form of a singlet and its CS is shifted downfield by 6.5 ppm in comparison with that of (III) through the β-contribution of the OH of the hydroxymethyl group [3, 4]. As can be seen from the figures given in Table 1, the CS of the signal of the C_7 sp^3 carbon in (V) is shifted downfield by 4.1 ppm in comparison with (III). This paramagnetic displacement of the signal of C_7 in (V) is apparently due to the specific influence of Py as a solvent associated with the hydroxyl of the hydroxymethyl group. The CSs of the other sp^3 carbons of (III) and (V) differ little.



Thus, an analysis of the ^{13}C NMR spectra of ercinamine establishes its structure as (V). As mentioned above, passage from ercinamine and **ercinaminine** to the same product (VIa) has been performed (see scheme). Consequently, **ercinaminine** has the structure (VI).

EXPERIMENTAL

The ^{13}C NMR spectra of the alkaloids (III) and (V) were obtained on a Varian CFT-20 spectrometer in $CDCl_3$ (III), 0 – TMS ($\delta_{TMS} = \delta_{CDCl_3} + 76.91$ ppm) and in Py-d_5 (V), 0 – TMS, in the pulsed regime followed by Fourier transformation under the **conditions** of complete and incomplete off-resonance decoupling of C–H interactions.

The PMR spectrum were taken on a JNM 4H-100/100 MHz instrument, 0 – HMDS (δ scale), IR spectra on a UR-20 spectrophotometer in KBr tablets, and mass spectra on a MKh-1303 instrument fitted with a system for the direct introduction into the ion source.

Ercinamine (V) formed white crystals with the composition $C_{21}H_{24}NO_4$ readily soluble in ethanol and methanol and sparingly soluble in chloroform, mp 238-240°C, $[\alpha]_D$ + 53° (c 0.15; CH_3OH).

IR spectrum (ν, cm^{-1}): 3400 (OH group); 1732 (ester C=O); 1630 (indolamine C=N); 1590 and 1500 (C=C of an aromatic ring); 760, 795, and 825 (1,2,4-trisubstituted aromatic ring). UV spectrum (ν_{max}^{EtOH}, nm): 226, 283 (log ε 3.95, 3.66). PMR spectrum ($CDCl_3$, ppm): 1.55 (3 H, d, J = 7 Hz, CH_3–CH=); 5.40 (1 H, q, J = 7 Hz, CH_3–CH=); 3.68 (3 H, s, $COOCH_3$); 3.60 (2 H, br.s, $-OCH_2$); **Ar–H:** 7.35 (1 H, d, J = 8 Hz, –12-H); 6.66 (2 H, q, J = 8 and 2 Hz, –11-H);

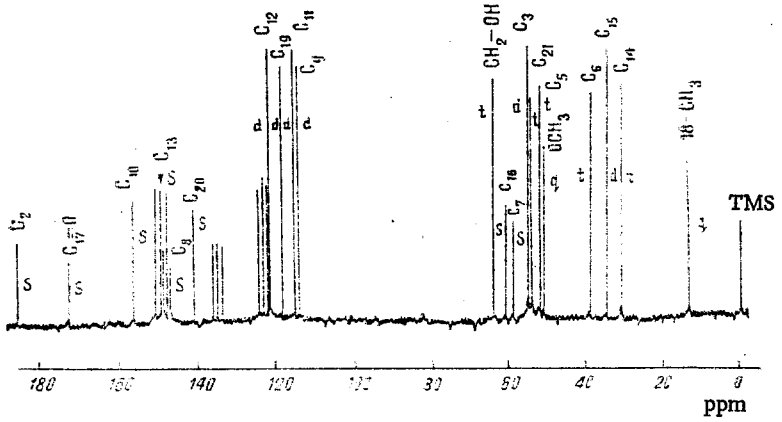


Fig. 2. ^{13}C NMR spectrum of base (V) in Py-d_5.

6.98 (1 H, d, J = 2 Hz, –9-H). Mass spectrum, (m/z, %): 368 (100) $-M^+$, 338 (26), 337 (59), 309 (12), 149 (8), 97 (18), 85 (19).

Ercininamine (VI). This was obtained in the form of an amorphous base with the composition $C_{21}H_{24}N_2O_3$, readily soluble in methanol, chloroform, and acetone, and sparingly soluble in ether. IR spectrum (ν, cm^{-1}): 3400 (OH group); 1730 (ester C=O); 1630 (indolenine C=N); 1600 and 1580 (C=C of an aromatic ring); 760 (1,2-disubstituted aromatic ring). UV spectrum (C_2H_5OH, ν_{max}, nm): 222, 279 (log ε 3.91, 3.64); PMR spectrum ($CDCl_3$, ppm): 1.58 (3 H, d, J = 7 Hz, $\underline{CH_3}$–CH=); 5.40 (1 H, q, J = 7 Hz, =$\underline{CH}$–CH_3); 3.75 (3 H, s, $COOCH_3$); 3.62 (2 H, br. s, –O–CH_2); Ar–H: 7.56-6.65 (4 H, m). Mass spectrum, (m/z, %): 352 (100%) – M^+ 322 (21), 321 (33), 293 (15), 149 (9), 97 (30), 85 (27), 83 (37).

Tosyl Ester of Ercinamine. To 30 mg of ercinamine were added 60 mg of p-toluenesulfonyl chloride and 5 ml of absolute pyridine. The mixture was left for 12 h. After the pyridine had been distilled off, the residue was dissolved in chloroform, and the solution was treated with three 50-ml portions of 4% NaOH solution. The chloroformic residue was filtered, and after the chloroform had been distilled off a yellowish amorphous product was obtained.

Reduction of the Tosyl Ester. A solution of 30 mg of the tosyl ester of ercinamine in 10 ml of methanol was treated with 0.5 g of activated Raney Ni and with heating, a current of hydrogen was passed through it for 2 h. The reaction mixture was filtered and, after the methanol had been distilled off, an amorphous product was obtained which on TLC in the acetone–methanol (4:1) system had R_f 0.6 and gave a lilac-pink coloration with the cerium sulfate reagent.

Reduction of Ercinaminine. A solution of 15 mg of ercininamine in methanol was treated with 0.5 g of activated Raney Ni, and, with heating, a current of hydrogen was passed through it for 2 h. After the end of the reaction, the mixture was filtered and the methanol was distilled off. This gave an amorphous product, $C_{21}H_{26}N_2O_3$, with M^+ 354, 339, 321, 97, 85, 83.

SUMMARY

On the basis of the results of a study of ^{13}C spectra, the structures of phenolic alkaloids previously isolated from *Vinca erecta* have been reconsidered, and it has been shown that a base with mp 228-229°C has the structure of 11-hydroxystrictamine and an amorphous base isomeric with it, of the same composition, is 10-hydroxystrictamine.

2. The structures of two new indolamine alkaloids – ercinamine and ercinaminine – have been established with the aid of analysis of ^{13}C NMR spectra and also PMR and IR spectra and chemical transformations.

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