ABSOLUTE CONFIGURATION OF VINERINE
AND VINERIDINE

M. R. Yagudaev, V. M. Malikov,
and S. Yu. Yunusov

Previously [1-3], structures (I) and (II), respectively, have been established for the hydroxyindole al-kaloids vinerine and vineridine isolated from the epigeal part of <u>Vinca erecta</u> on the basis of chemical and spectral characteristics, and the hypothesis has been put forward that vineridine, which is a stereoisomer of vinerine, differs from the latter by its configuration at C_3 and, possibly, C_7. The configurations of the asymmetric centers at C_7, C_{19}, and C_{20} in vinerine and vineridine remained undetermined. In addition, the position of the OCH_3 group in the aromatic ring in (I) and (II) was not shown strictly.

In the present paper we give the results of a study of the structure and stereochemistry of the alka-loids vinerine (I), vineridine (II), and N-acetylvinerine (III) obtained by a comparative analysis by the meth-ods of NMR spectroscopy and circular dichroism — CD (Figs. 1, 2, and 3 and Tables 1 and 2). In the assign-ment of the signals of a series of protons in the NMR spectra of (I)-(III) we took into account the contribu-tions from the magnetic anisotropy ($\Delta\delta_\chi$) and the electric field ($\Delta\delta_E$) of the carbonyl and methoxy groups, respectively, in accordance with the McConnell [4] and Buckingham [5] relations, with Zurcher's param-eters for C=O and OH [6]. The value of the anisotropy of the diamagnetic susceptibility of the benzene ring was calculated by the method of Johnson and Bovey [7].

To evaluate the atomic contribution ($\Delta\delta_A$) to the magnetic screening of the aromatic protons at C_9, C_{10}, C_{11}, and C_{12} we calculated the π-electron densities of the charges on these carbon atoms of the frag-ments of the molecules of (I)-(III) by the MO LCAO method in Huckel's approximation,* using the hetero-parameters of Pullman and Pullman [8]. In assigning the signals of the protons, we also used the double resonance method: the collapse method for (I)-(III), and the INDOR and intramolecular nuclear Overhauser effect (NOE) method for (III).

The spectral parameters of compounds (I) and (II) (see Fig. 1a, b, and Tables 1 and 2) show that the free aromatic protons give a spectrum of the AMX type, the chemical shifts (CSs) and constants of which can be determined from the spectrum. However, from the CS and J values of the bases themselves alone, it is impossible to make a choice between the alternative positions 10 and 11 for the OCH_3 group, since in the two cases a similar spectrum of the aromatic protons may be expected. To establish the position of the OCH_3 group in (I) and (II) we used the criterion of the relative CSs of $C_{12}H$ on the acetylation of the N−H groups in them [9-15]. As can be seen from the spectrum of (III) (Fig. 1c) and the data of Table 1, a rela-tively large paramagnetic shift is undergone by the doublet in (I) with $\delta 7.40$ ppm (J = 2.2 Hz) to 7.87 ppm in (III), i.e., $\Delta\delta = \delta_{III} - \delta_I = 0.47$ ppm, which shows the location of the OCH_3 group in (I)-(III) at C_{11}. How-ever, the value of $\Delta\delta = 0.47$ ppm of the relative CSs of (III) and (I) is anomalously low. To explain this an-omaly, we have performed a quantitative calculation of the contributions to the value of $\Delta\delta$ for $C_{12}H$ in (III) which can be represented approximately in the form of the additive sum of the contributions:

$$\Delta\delta = \Delta\delta_A + \Delta\delta_{C=O} + \Delta\delta_{C-CH_3}, \tag{1}$$

where $\Delta\delta_A$ is the atomic contribution due to the charge of the given atom, and $\Delta\delta_{C=O} = \Delta\delta_\chi + \Delta\delta_E$, and $\Delta\delta_{C-CH_3}$ are the contributions caused by the magnetic anisotropy and electric fields of the C=O and C−CH_3 groups.

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* The program for calculation on a type M-20 computer was drawn up and kindly given to us by A. V. Tut-kevich (Institute of Heteroorganic Compounds, Academy of Sciences of the USSR).

TABLE 1. Chemical Shifts (δ, ppm) and Spin–Spin Coupling Constants (J, Hz) of the Protons of Vinerine, Vineridine, and Their Derivatives

Compound	Chemical shifts, ppm								H–N	$\overline{NCOCH_3}$	$\overline{OCOCH_3}$	Constants, Hz				
	H_3	H_5	H_6	HC_8	$Ar-OCH_3$	$\overline{COOCH_3}$	H_{12}	CH_3-C_8				$H_{11}\cdot H_{10}$	$H_{10}\cdot H_9$	$H_9\cdot H_8$	$H_8\cdot H_6$	$H_{19}\cdot CH_3$
Vinerine (I)	7.24 d	6.51 q	7.40 d	4.16	3.77 s	3.59 s	6.47 s	1.20 d	8.90 b.s.	—	—	8.5	2.2	1.5		6.5
Vineridine (II)	6.99 d*	6.51 q	7.37 d	4.22 o	3.77 s	3.40 s	6.5 s	1.24 d	9.60 b.s.	—	—	8.5	2.2	1.5		6.5
N-Acetylvinerine (III)	7.20 d	6.71 q	7.87 d	4.36 s	3.82 s	3.60 s	7.40 s	1.41 d	—	2.66 s	—	8.5	2.2	11.0		6.5
Reduced vinerine (IV)	7.15 d	6.28 q	6.19 d	4.00†	3.71 s	—	6.24 b.s.	1.20 d	3.96 b.s.	—	—	8.5	2.2	†		6.5
N,O-Diacetyl derivative of reduced vinerine (VI)	7.25 d	6.58 q	7.85 d	4.10†	3.79 s	—	6.36 b.s.	1.24 d	—	2.23 s	2.00 s	8.5	2.3	†		6.5

* s — singlet; d — doublet; q — quartet; m — multiplet; b.s. — broadened singlet; o — octet; se — sextet.
† Signals masked by the signal from CH_2-OH.

On calculating the contribution of $\Delta\delta_A$ on the basis of the fact that in aromatic systems a linear relationship is observed between the CS of a proton and the π-electronic charge on the carbon atom to which it is attached q_π [16, 17]: $\Delta\delta_A = K \cdot \Delta q_\pi$, where the coefficient of proportionality $K \approx 10$ ppm per electron. On comparing the calculated values of q_π for the C_{12} atom in (III) and (I) (see Table 2) it can be seen that their difference $\Delta\delta_\pi = +0.010$. Consequently, the contribution $\Delta\delta_A = 0.1$ ppm (downfield).

The value of the contribution $\Delta\delta_{C=O}$ was taken into account for the two possible extreme conformations of the $-CO-CH_3$ group located in the plane of the aromatic rings a and b:

a   b
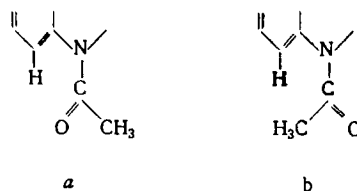
The results of the calculation of the contributions $\Delta\delta_\chi$ and $\Delta\delta_E$ of the C=O group to the CS of the $C_{12}H$ proton (H_{12}) with Zurcher's parameters [6] led to the following values: in conformation $a - \Delta\delta_\chi = +0.423$ ppm, $\Delta\delta_E = 1.474$ ppm, $\Delta\delta_{tot} = 1.897$ ppm; in conformation $b - \Delta\delta_\chi = +0.350$ ppm, $\Delta\delta_E = -0.090$ ppm, $\Delta\delta_{tot} = +0.260$ ppm (downfield). The contribution of the magnetic anisotropy of the $C-CH_3$ group in conformation b to H_{12} with the parameters $\Delta\chi_{C-C} = 5.0 \cdot 10^{-30}$ and $\Delta\chi_{C-H} = 1.5 \cdot 10^{-30}$ cm³ per molecule [34] gives a value of $\Delta\delta \approx -0.20$ ppm (upfield). On the basis of relation (1) the total contribution to the relative CS of the H_{12} proton in (III) in conformation $a - \Delta\delta = 1.997$ ppm, and in conformation b $\Delta\delta = 0.160$ ppm. The agreement of the calculated value of the contribution $\Delta\delta = 1.997$ ppm with the experimental value of $\Delta\delta = 1.77$ ppm for the indoline derivative, with a discrepancy of about 10%, shows that in all the indolines the preferred conformation of the acetyl group is a and an essential contribution (more than 2/3) to the descreening of the H_{12} proton is made by the electric field $(\Delta\delta_E)$ of the C=O group. In N-acetylvinerine the observed value of the relative CS of H_{12}, $\Delta\delta = 0.47$ ppm, cannot be explained by conformation b of the $COCH_3$ group: in this conformation the total contribution to the CS of H_{12} is extremely small (0.16 ppm).

The fact must likewise be taken into account that conformation b for $COCH_3$ in (III) is apparently energetically unfavorable because of a possible electrostatic interaction of the two closely adjacent polar =O groups (lactam and N-acetyl groups). Consequently, in (III) the C=O of the N-acetyl group is apparently above or below the plane of the aromatic ring, i.e., at an angle to H_{12}. This is confirmed by the fact that in N-acetylvinerine no NOE is observed between the sig-
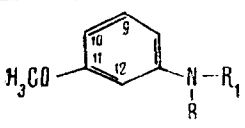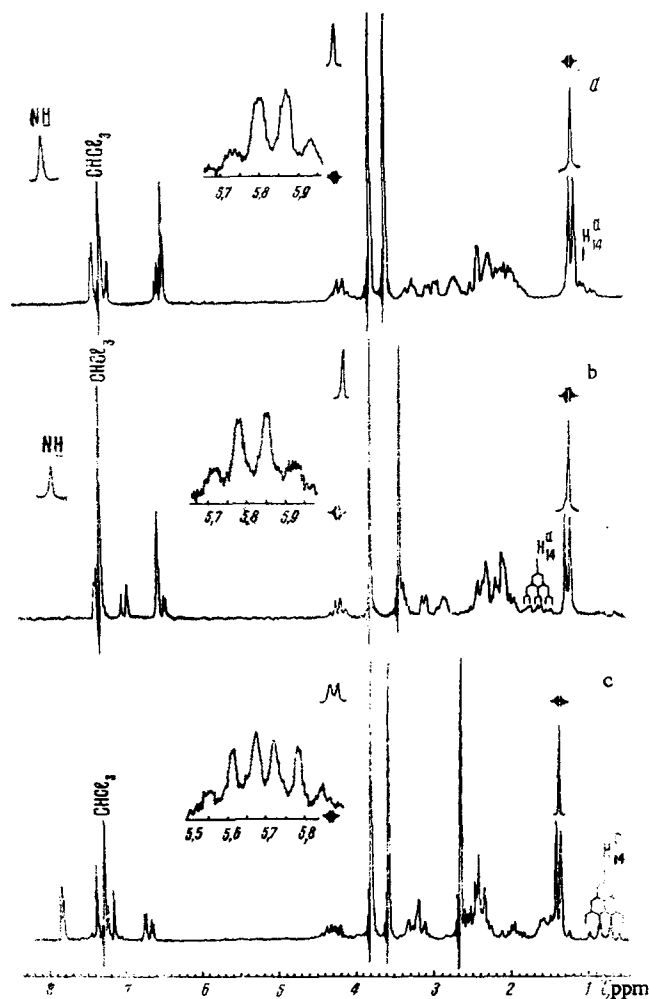
Fig. 1. NMR Spectra of vinerine (a), vineridine (b),
and N-acetylvinerine (c).

TABLE 2. Calculated π-Electronic Charges (q_π) on the Carbon
Atoms of the Chemical Shifts (δ, ppm) of the Protons in the Frag-
ments of the Molecules of the Alkaloids Vinerine and Vineridine
and Their Derivatives

	q_π				δ, ppm		
	C_9	C_{10}	C_{11}	C_{12}	C_9H	$H_{10}H$	$C_{12}H$
R=H; R_1=C=O Vinerine (I) Vineridine (II)	+0,006	−0,100	+0,057	−0,119	7,2	6,51	7,40
R=R_1=C=O					6,99	6,51	7,37
N-acetylvinerine (III)	+0,005	−0,093	+0,057	−0,109	7,20	6,71	7,87
R=H: R_1=CH₂							
Reduced vinerine (IV)	+0,006	−0,111	+0,057	−0,132	7,15	6,28	6,19
N,O-diacetyl derivative of reduced vinerine (V)	+0,006	−0,100	+0,057	−0,119	7,25	6,58	7,85

nals of the $COCH_3$ protons (ν_{irr} = 266 Hz) and the H_{12} doublet (δ 7.87 ppm). If the $COCH_3$ group in (III) were
in conformation b, then, since the distance between the center of CH_3 and H_{12} in this conformation b is ap-
proximately 2.2 Å, on the basis of the known correlation of the value of the NOE with the distances between
the CH_3 group and H [18] a NOE in (III) of not less than 10% should be observed. Thus, we have detected
a considerable NOE between the signals of the $Ar−OCH_3$ group (ν_{irr} = 382 Hz) and the H_{12} doublet (δ 7.87
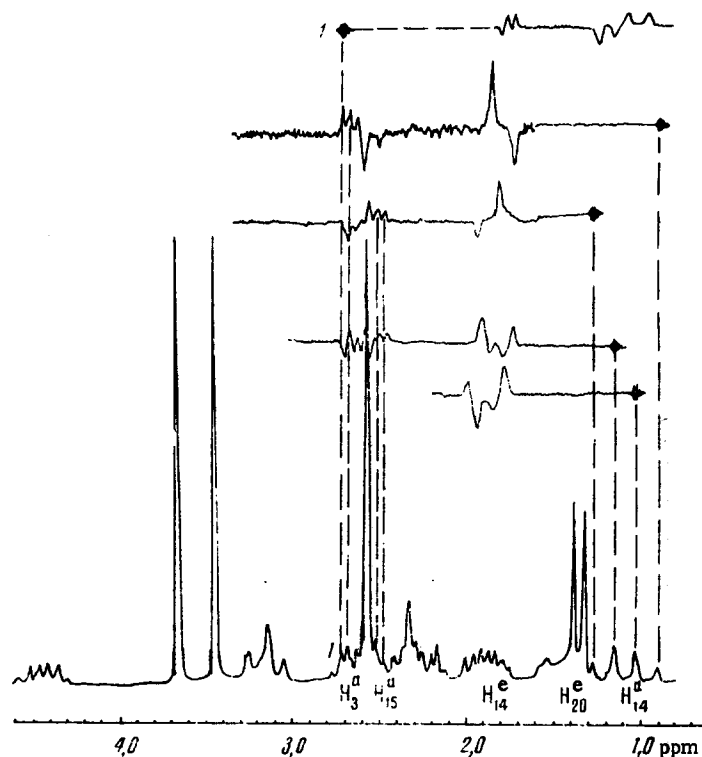ppm), amounting to 25%, and between the $Ar−OCH_3$ group and the quartet (δ 6.71 ppm), amounting to 10%.

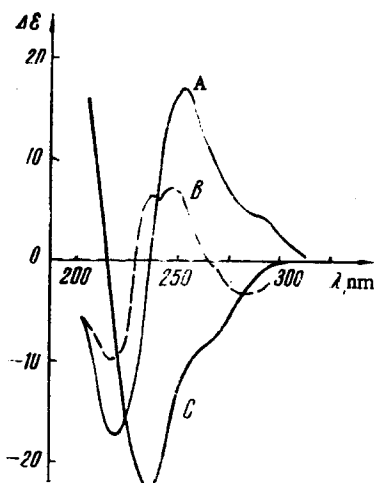Fig. 2. Part of the spectrum of N-acetylvinerine in C_5D_5N.

Fig. 3. Circular dichroism spectra of vinerine (A), vineridine (B), and N-acetylvinerine (C).

On the reduction of the lactam C=O group of vinerine and its acetylation, the value of the relative CS, a doublet with J=2.2 Hz, amounted to 1.66 ppm [see Table 1, compounds (IV) and (V)]. Such a large value of the shift of the signal in (V) definitively confirms the position of the OCH_3 group at C_{11} and shows that on reduction of the lactam carbonyl conformation a becomes the preferred one for the N-acetyl group.

In the CD spectrum of vinerine (see Fig. 3, curve A), the signs of the maxima at λ 293 and 252 nm are positive. This shows that vinerine belongs to the hydroxyindole alkaloids of group B and that the C_7 and C_3 centers have the R configuration with C=O of the lactam group located above the planes of rings C, D, and E [19-21, 23]. In contrast to the CD spectrum of vinerine, in the spectrum of vineridine (see Fig. 3, curve B) the long-wave maximum at 284 nm is negative, i.e., in vineridine the lactam C =O group is below the planes of rings C, D, and E (S configuration of C_7). The signs of the maxima at 250 nm in (I) and (II) coincide. Consequently, the R configuration of the C_3 centers in them does not change. Thus, vinerine and vineridine differ only by the configuration of the spiro center at C_7, i.e., they are spiroisomers.

In the CD spectrum of N-acetylvinerine (see Fig. 3, curve C) the signs of both maxima change, and they are shifted in the short-wave direction as compared with the CD spectrum of vinerine.

Thus, in the acetylation of vinerine with acetic anhydride in pyridine with heating [3], three centers isomerize: those at C_3 and C_7 and that of the N_4 nitrogen atom, where inversion of the unshared pair of electrons (UPE) takes place. This result is in harmony with the previously known [13, 20, 21] properties of the hydroxyindole alkaloids, according to which, on being heated in acetic acid or in pyridine, they all isomerize at C_3 and C_7, and the change at C_3 is accompanied by the inversion of the UPE. The signs of the maxima in the CD spectrum of (III) (see Fig. 3, curve C) provide grounds for assuming for it the 3S and 7S configuration with the C=O of the lactam group located under the C, D, and E planes. On the basis of the NMR figures it may be considered that in vinerine the UPE of the N_4 nitrogen atom exists in the anti orientation

to the C_2-C_7 bond, and in vineridine it is in the syn orientation, since the difference in the CSs of the NCH_3 group in the methiodide of (I) $(\Delta\delta = \delta_{pyridine} - \delta_{formamide})$ (0.66 ppm) is greater than $\Delta\delta$ NCH_3 in (II) (0.47 ppm) [21]. This, in turn, shows the S configuration of N_4 in (I) and (II) and the trans linkage of rings C/D, and not cis as suggested previously [3]. The trans linkage of rings C/D in (I) and (II) also agrees with the fact that in all the hydroxyindole alkaloids studied rings C and D have the trans linkage, which is preferable to the cis linkage because of its thermodynamic stability [20]. It must be mentioned that the curve of the CD spectrum of vineridine (see Fig. 3, curve B) practically coincides with the curve of the CD spectrum of rauvoxinine, the structure of which has been shown by x-ray structural analysis [22], and the CD curve of N-acetylvinerine is close to the CD curve of isocarapanaubine [21]. This, additionally, confirms the configurations of the C_7 and C_3 centers in (I), (II), and (III) and the trans linkage of the C/D rings in them that have been established.

The results of a comparison of the NMR spectra of (I) and (II) (Fig. 1a, b) and the data of Table 1 [(I) and (II)] show that the CS of the H_9 aromatic proton in (I) is shifted downfield by 0.25 ppm relative to the CS of H_9 in (II). On considering spatial models of the Dreiding type of the molecules of (I) and (II) it can be seen that in (I) the UPE of N_4 is fairly close to H_9 (distance measured on a stereomodel ~ 2.2 Å), and in (II) the distance from the UPE to H_9 is ~ 5.2 Å, i.e., 2.4 times greater than in (I). The electric field of the UPE of N_4 apparently exerts a considerable descreening action on H_9 in (I), which leads to a paramagnetic shift of H_9 by 0.25 ppm in relation to the CS of H_9 in (II). Our results agree well with the difference of the CSs of H_9 in the hydroxyindole alkaloids rauvoxine and rauvoxinine [21]. On considering models, it can be seen that the distance between the UPE of N_4 and $C=O$ of the lactam group in (II) is approximately 2.8 Å, and this closeness of the UPE and $C=O$ is apparently responsible for the difference in the basicities and the rates of iodomethylation of vineridine and vinerine [3]. The chemical shifts of the signal of the $N-H$ proton in the NMR spectra of (II) and (I) taken at the same three concentrations (C = 0.125, 0.0625, and 0.0312 M) at room temperature differ by $\Delta\delta = 0.80$ ppm. The paramagnetic shift of $\Delta\delta = 0.80$ ppm of the $N-H$ signal in (II) is apparently connected with additional delocalization of the UPE of the N_1 nitrogen atom through the interaction of $C=O$ and the UPE of N_4, leading to the descreening of the $N-H$ proton in vineridine in comparison with vinerine.

In the NMR spectrum of N-acetylvinerine in $CDCl_3$ and pyridine-d (see Fig. 1c and Fig. 2), in the strongest field there are one-proton quartets with centers at 0.83 and 1.10 ppm, respectively, with the same value of the spin–spin coupling constants (J) between the components of 12 Hz and with intensity ratios of 1:3:3:1. The results of an analysis of the values of J and of the intensities of the components of this quartet (see Fig. 2) shows that it is due to the axial proton at $C_{14}H$, which has $J_{gem} = 12$ Hz with $C_{14}H^e$, and the two equal diaxial vicinal constants are likewise 12 Hz with the C_3H and $C_{15}H$, respectively. It is obvious that the J values of the quartet cannot belong to the signal of the C_6H^a and $C_{20}H^a$ protons, and its assignment to $C_{21}H^a$ or C_5H^a is excluded through the CS and J values and the multiplicity. Thus, the strong-field quartet in the spectrum of (III) (Fig. 2) unambiguously shows that the C_3H and $C_{15}H$ protons are axial.

We obtained additional information on the CSs of the $C_{14}H^e$ and C_3H^a protons and, particularly, the SSCC of $C_{15}H$ and $C_{20}H$ by using the INDOR method on the nondegenerate extreme lines with ν_1 92 Hz and ν_4 128 Hz of the strong-field quartet in the NMR spectrum of N-acetylvinerine (Fig. 2). As the INDOR signals show, the CS of the equatorial $C_{14}H$ proton is 1.83 ppm. The value of the geminal constant corresponding to the distance between signals in different fields in the spectrum of the equatorial H_{14} proton is 12.0 Hz. The chemical shifts of the signals of the C_3H^a and $C_{15}H^a$ protons are, respectively, 2.68 and 2.61 ppm. This assignment was made from the results of a consideration of the INDOR signals in the weak-field lines of the quartet with ν_1 276 and ν_2 272 Hz, from which it follows that the quartet is due to interaction with the signals of $C_{14}H^e$ at 1.77 ppm and $C_{14}H^a$ at 1.10 ppm. At the same time, the INDOR signals for the line with ν 249 Hz of the quartet with its center at 2.61 ppm show that this quartet arises as the result of interaction with three signals: $C_{14}H^e$, $C_{14}H^a$, and $C_{20}H$. In these circumstances, the CS of $C_{20}H$ is 1.44 ppm. As can be seen from Fig. 2, the INDOR signal for line 1 (ν 276 Hz) of the C_3H^a signal is a quartet, from which it follows that the large value (J = 4 Hz) corresponds to the vicinal constant of $C_{14}H^e$ with $C_{15}H^a$ and the small constant (J = 3 Hz) to that of $C_{14}H^e$ with C_3H^a. The INDOR signal of $C_{15}H^a$ is a quartet, the analysis of which shows that the large constant of 12 Hz corresponds to the diaxial vicinal coupling of the $C_{14}H^a$ and $C_{15}H^a$ protons, and the small constant of 4.5 Hz, to the coupling of $C_{15}H^a$ with $C_{20}H$. Consequently, the INDOR spectrum of N-acetylvinerine shows that the $C_{20}-H$ proton is equatorial, since the value of J = 4.5 Hz corresponds to the a–e interaction of $C_{15}H^a$ and $C_{20}H^e$ and shows the cis linkage of rings D/E in (III) and, accordingly, in (I) and (II).

It follows from Wenkert's hypothesis of the α-configuration of the $C_{15}H$ proton of the majority of penta-cyclic indole and hydroxyindole alkaloids [20, 26, 27] that the $C_{20}H$ proton in (I)-(III) also have the α-configuration.

In the NMR spectra of (I) and (II) (Fig. 1a, b) the $C_{14}H^a$ signal is a sextet with centers at 1.07 and 1.60 ppm. The cause of the difference in the CSs of this proton in (II) as compared with (I) and (III) is the considerable descreening influence of the carbonyl group on it. The quantitative calculation of this contribution by Zurcher's method [6] to the CS of the $C_{14}H^a$ proton in (II) is $\Delta\delta = 0.60$ ppm (downfield) which agrees well with the experimental difference of the CS of $C_{14}H^a$ ($\Delta\delta = \delta_{II} - \delta_I = 0.53$ ppm). One of the vicinal constants of the $C_{14}H^a$ sextets in (I) and (II), equal to 5 Hz, corresponds to its interaction with the $C_{15}H$ equatorial proton, since the C_3H is always axial. This circumstance is a consequence of the fact that on isomerization of the C_3 and N_4 centers the conversion of ring D from one chair conformation to the other takes place, and this leads to a change in the orientation of the $C_{15}H$ and $C_{20}H$ protons, i.e., in (I) and (II) $C_{15}H$ is equatorial and $C_{20}H$ is axial, while in (III) $C_{15}H$ is axial and $C_{20}H$ is equatorial in relation to ring D. From a consideration of models of (I) and (II) it can be seen that with a change in the orientation of $C_{20}H$ from axial in (I) and (II) to equatorial in (III) the dihedral angle $H-C_{20}-C_{19}-H$ changes considerably [from 80° in (I) and (II) to 170° in (III)], which is reflected in corresponding changes in the $J_{C_{19} \cdot H_\beta \cdot C_{20}H}$ constants [from 1.5 Hz in (I) and (II) to 11.0 Hz in (III)]. The latter was confirmed by the double resonance spectra of (I)-(III) in which when the $C_{19}-CH_3$ signal was irradiated with $\nu_{H_2} = 120$ and 124 Hz, respectively, in (I) and (II), the $C_{19}H$ octets at 4.16 and 4.22 ppm ($J_{C_{19}H-CH_3} = 6.5$ Hz, $J_{C_{19}H \cdot C_{20}H} \approx 1.5$ Hz) were converted into broadened singlets, and on irradiation of the $C_{19}-CH_3$ signal with $\nu_{H_2} = 141$ Hz in (III) the $C_{19}H$ sextet with $\delta 4.36$ ppm was converted into a doublet with $J = 11.0$ Hz. Thus, the observed changes in the constants of the $C_{19}H \cdot C_{20}H$ protons from 1.5 in (I) and (II) to 11.0 Hz in (III) are due to the conversion of ring D from one chair conformation into the other and are possible in (I)-(III) only with the β-configuration $C_{19}H$ and the α-configuration of $C_{19}CH_3$.

The results of a comparison of the CS of $COOCH_3$ for (II) with those for (I) and (III) (see Fig. 1 and Table 1) show that in (II) it is shifted upfield by 0.19 ppm in comparison with the CS of OCH_3 in (I) and (III). According to Johnson and Bovey [7] the contribution of the anisotropy of the benzene ring to the CS of the $COOCH_3$ signal in (II) is ≈ 0.3 ppm (upfield), i.e., the diamagnetic shift of the OCH_3 protons in (II) is due to the screening of the benzene ring. In the NMR spectra of (I) and (II) (see Fig. 1a, b) the CSs of $C_{17}H$ have anomalously low values of 6.47 and 6.55 ppm, respectively, while in (III) the signals are found in the usual part of the field at 7.40 ppm [21, 28, 30] [it undergoes a considerable paramagnetic shift of 0.93 ppm in comparison with (I)]. To explain the difference in the CSs of $C_{17}H$ in (I), (II), and (III), we calculated the value of the contributions $\Delta\delta_\chi$ and $\Delta\delta_E$ from the $C=O$ and OCH_3 groups to the CS of the $C_{17}H$ proton in the two possible rotomeric forms A and B.


A   B
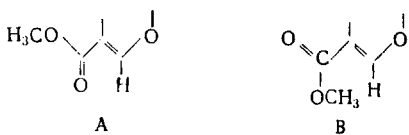
In form A, the total contribution of the $C=O$ and OCH_3 groups to the CS of $C_{17}H$ is 0.30 ppm greater than the contribution in form B. Although this value (0.30 ppm) does not qualitatively explain the anomalous CSs of $C_{17}H$ in (I), (II), and (III), it nevertheless gives grounds for assuming that in (I) and (II) form B is realized and in (III), form A. Apart from this, a considerable contribution to the CS of $C_{17}H$ may be made by an unshared pair of electrons of the oxygen atom of ring E [31]. In the spectra of compound (IV) and (V) (see Table 1) in which the $C=O$ of the methoxycarbonyl group has been reduced, the CS of $C_{17}H$ has a minimum value relative to the other compounds of (I)-(III).

Thus, a combination of the characteristics of the circular dichroism and NMR spectra shows the following absolute configuration for the hydroxyindole alkaloids according to the Cahn-Ingold-Prelog nomenclature [24, 25, 32, 33]: 7R, 3R, 4S, 15S, 19S, 20S for vinerine; 7S, 3R, 4S, 15S, 19S, 20S for vineridine; and 7S, 3S, 4R, 15S, 19S, 20S for N-acetylvinerine. (See scheme on following page.)

EXPERIMENTAL

The CD spectra were obtained on a Roussel-Jouan recording "dichrograph" (CH_3OH), the NMR spectra of (I), (II), and (III) on a JNM-4H-100/100 MHz spectrometer ($CDCl_3$, with TMS as internal standard),

I   II

III
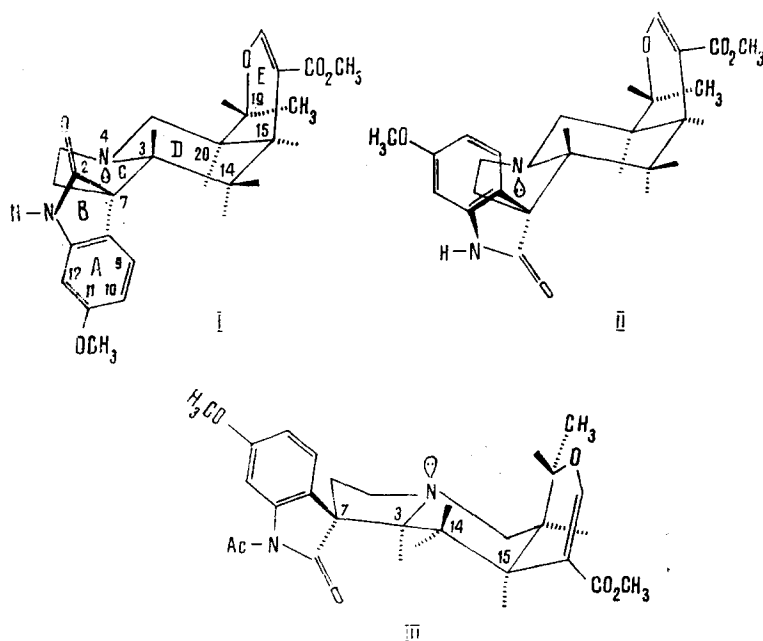
the INDOR spectra on a Varian -HA-100D instrument (deuteropyridine, O − TMS,) and the spectra of the methiodides of (I) and (II) on a JNM-C-60 HL/60 MHz instrument, O − TMS. Distances and angles were measured on stereomodels of the Dreiding type.

Vinerine was reduced with LiAlH$_4$ in absolute ether with heating for 6 h, after which the LiAlH$_4$ was decomposed with ice water and the mixture was made alkaline with sodium bicarbonate and extracted with ether. The ether was distilled off, and treatment of the residue with petroleum ether yielded an amorphous powder. The individuality of the compound was checked by thin-layer chromatography in several solvent systems.

The product of the reduction of vinerine (IV) was acetylated with acetic anhydride in pyridine at room temperature for 12 h. The acetate was isolated by the usual method [3].

SUMMARY

On the basis of an analysis of the circular dichroism and NMR spectra the absolute configuration 7R, 3R, 4S, 15S, 19S, 20S has been established for vinerine; 7S, 3R, 4S, 15S, 19S, 20S for vineridine; and 7S, 3S, 4R, 15S, 19S, 20S for N-acetylvinerine.

LITERATURE CITED

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