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INFLUENCE OF SOLVENTS ON THE PARAMETERS OF THE NMR SPECTRA OF *Vinca* ALKALOIDS. V

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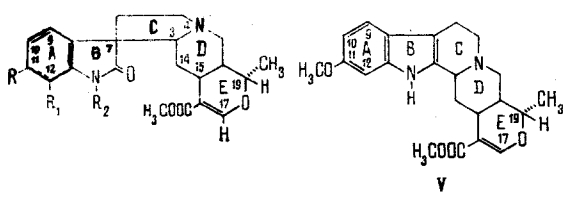
Continuing a study of the influence of solvents on the parameters of the NMR spectra of alkaloids [1], we give the results for a number of hydroxyindole bases belonging to the allo series (majdine (I), isomajdine (II), and N-acetylvinerine (III), and the epiallo series (vineridine (IV)). In addition, for the purpose of comparing results and checking our conclusions concerning the influence of solvents on the parameters of the PMR spectra of alkaloids of the hydroxyindole series we have studied the indole alkaloid reserpinine (V). The stereochemistry and absolute configurations of bases (I-V) have been established previously [2, 3].



V

I. $R = R_1 = OCH_3$, $R_2 =$ $= H$, 7R, 3S, 4R
II. $R = R_1 = OCH_3$, $R_2 =$ $= H$, 7S, 3S, 4R
III. $R = OCH_3$, $R_1 = H$, $R_2 = Ac$, 7S, 3S, 4R
IV. $R = OCH_3$, $R_1 = R_2 =$ $= H$, 7S, 3R, 4S

Influence of Aromatic Solvents on the Chemical Shifts (CSs) of the Bases (I-IV). As can be seen from Tables 1-4, the CSs of the $C_{19}-CH_3$ protons in benzene for majdine, isomajdine, and N-acetylvinerine shift upfield by +0.18 ppm, and in vineridine by +0.36 ppm. The signal of the H_{19} proton in alkaloids (I-III) undergoes an appreciable paramagnetic shift, while in the base (IV) this signal is shifted upfield. It has been established previously [4] that the difference in the CSs of $C_{19}-CH_3$ and H_{19} in solutions of $CDCl_3$ in the alkaloids of the allo and epiallo series are due mainly to the descreening influence on them of the unshared electron pair (UEP) of the N_4 nitrogen atom. It is known that the benzene molecule, in the main, strives to place itself as far as possible from the negatively-charged part of the molecule [5, 6]. As can be seen from Dreiding stereomodels, in the allo alkaloids the protons at the C_{19} carbon atom are located between the unshared electron pairs of the N_4 and O_{18} atoms and, obviously, the latter prevent the interaction of C_6D_6 with this part of the molecule. In the epiallo bases, the UEP of the N_4 atom is α-oriented and the approach of the molecules of the benzene solvent to the protons at C_{19} is facilitated. In view of this, the values of $\Delta^{C_6D_6}_{CDCl_3}$ for $C_{19}-CH_3$ differ in magnitude while for H_{19} the sign is different. Consequently, differences in the configuration of the N_4 center of the compounds investigated not only cause changes in the CSs of the protons mentioned above but are also the cause of the different influences of benzene on the CSs of these groups.

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TABLE 1. Chemical Shifts of the Protons of Majdine in Various Solvents and Their Relative Differences $\Delta = \delta_{CDCl_3} - \delta_{solvent}$

Solvent	19-CH_3	CO_2CH_3	11-OCH_3	12-OCH_3	H_{19}	H_{10}	H_9	H_{17}
$CDCl_3$	1,39	3,62	3,89	3,89	4,55	6,56	6,86	7,48
CCl_4	1,39	3,56	3,83	3,83	4,51	6,40	6,74	7,38
	0,00	+0,06	+0,06	+0,06	+0,04	+0,16	+0,12	+0,10
CS_2	1,39	3,47	3,74	3,80	4,42	6,41	6,71	7,31
	0,00	+0,15	+0,15	+0,09	+0,13	+0,15	+0,15	+0,17
CD_3CN	1,36	3,57	3,79	3,86	4,40	6,67	6,97	7,49
	+0,03	+0,05	+0,10	+0,03	+0,15	−0,11	−0,11	−0,01
CD_3OD	1,38	3,60	3,81	3,86	4,46	6,66	6,94	7,51
	+0,01	+0,02	+0,08	+0,03	+0,09	−0,10	−0,08	−0,03
$(CD_3)_2CO$	1,36	3,57	3,79	3,86	4,49	6,64	6,97	7,47
	+0,03	+0,05	+0,10	+0,03	+0,06	−0,08	−0,11	+0,01
DMF	1,38	3,59	3,78	3,88	4,43	6,70	7,07	7,54
	+0,01	+0,03	+0,11	+0,01	+0,12	−0,14	−0,21	−0,06
TFA	1,61	3,82	4,02	4,09	4,22	6,95	7,26	7,81
	−0,21	−0,20	−0,13	−0,20	+0,33	−0,39	−0,40	−0,33
C_5D_5N	1,31	3,46	3,79	3,86	4,77	6,64	7,01	7,66
	+0,08	+0,16	+0,10	+0,03	−0,22	−0,08	−0,15	−0,18
C_6D_6	1,20	3,26	3,37	3,63	4,72	6,24	6,64	7,63
	+0,19	+0,36	+0,52	+0,26	−0,17	+0,32	+0,22	−0,15

TABLE 2. Chemical Shifts of the Protons of Isomajdine in Various Solvents and Their Relative Differences $\Delta = \delta_{CDCl_3} - \delta_{solvent}$

Solvent	19-CH_3	CO_2CH_3	11-OCH_3	12-OCH_3	H_{19}	H_{10}	H_9	H^a_{14}	H_{17}
$CDCl_3$	1,37	3,58	3,78	3,81	4,30	6,47	6,86	0,78	7,40
TFA	1,58	3,81	4,01	4,08	4,44	6,89	7,35	1,70	7,81
	−0,21	−0,23	−0,23	−0,27	−0,14	−0,42	−0,59	−0,92	−0,41
C_5D_5N	1,42	3,49	3,76	3,86	4,60	6,66	7,18	1,35	7,60
	−0,05	+0,08	+0,02	+0,05	−0,30	−0,19	−0,32	−0,57	−0,20
C_6D_6	1,23	3,28	3,31	3,68	4,50	6,66	7,18	1,22	7,59
	+0,14	+0,30	+0,47	+0,13	−0,20	−0,19	−0,32	−0,44	−0,19

TABLE 3. Chemical Shifts of the Protons of N-Acetylvinerine in Various Solvents and Their Relative Differences $\Delta = \delta_{CDCl_3} - \delta_{solvent}$

Solvent	19-CH_3	N-C(=O)-CH_3	CO_2CH_3	11-OCH_3	H_{19}	H_{12}	H_{10}	H_9	H_{17}	H^a_{14}
$CDCl_3$	1,41	2,70	3,63	3,84	4,30	7,88	6,74	7,22	7,41	0,89
CCl_4	1,39	2,64	3,56	3,82	4,26	7,80	6,53	7,11	7,28	0,78
	+0,02	+0,06	+0,07	+0,02	+0,04	+0,08	+0,21	+0,11	+0,13	+0,11
CD_3CN	1,38	2,60	3,55	3,79	4,32	7,77	6,77	7,29	7,40	0,76
	+0,03	+0,10	+0,08	+0,05	−0,02	+0,11	−0,03	−0,07	+0,01	+0,13
CD_3OD	1,41	2,64	3,60	3,82	4,33	7,81	6,79	7,35	7,45	0,72
	0,00	+0,06	+0,03	+0,02	−0,03	+0,07	−0,05	−0,13	−0,04	+0,17
$(CD_3)_2CO$	1,40	2,64	3,55	3,82	4 35	7,81	6,78	7,32	7,36	0,89
	+0,01	+0,06	+0,08	+0,02	−0,05	+0,07	−0 04	−0,10	+0,05	0,00
DMF	1,42	2,66	3,58	3,81	*	7,79	6,86	7,36	7,43	0,82
	−0,01	+0,04	+0,05	+0,01		+0,09	−0,12	−0,14	−0,02	+0,07
DMSO	1,38	2,61	3,54	3,77	4,19	7,72	6,82	7,26	7,41	0,74
	+0,03	+0,09	+0,09	+0,07	+0,11	+0,16	−0,08	−0,04	0,00	+0,15
TFA	1,59	2,90	3,82	4,02	4,52	8,07	7,05	7,57	7,78	†
	−0,18	−0,20	−0,19	−0,18	−0,22	−0,19	−0,31	−0,35	−0,37	
C_5D_5N	1,39	2,61	3,49	3,70	4,49	8,19	6,86	7,40	7,58	1,15
	+0,02	+0,09	+0,14	+0,14	−0,19	−0,31	−0,12	−0,18	−0,17	−0,26
C_6D_6	1,20	2,36	3,26	3 36	4,37	8,27	6,64	*	7,55	1,13
	+0,21	+0,34	+0,37	+0,48	−0,07	−0,39	−0,10		−0,14	−0,24

*Masked by signal of the solvent.

†Superposition of the signals of two protons.

The methoxycarbonyl group (CO_2CH_3) in vineridine undergoes a diamagnetic shift by +0.19 ppm as a result of the action of C_6D_6 (see Tables 1-4). In bases (I-III) in benzene as solvent the CO_2CH_3 signal shifts upfield by +0.30-0.37 ppm. In the alkaloid (IV), the CO_2CH_3 group is located fairly close to the aromatic ring A, which, as a consequence of interaction with the π currents of the benzene solvent, has a considerable influence on the stereochemistry of the substance+solvent complexes formed. This probably leads to the situation that the molecules of the solvent, being located in the direction away from ring A, have only a small influence on

TABLE 4. Chemical Shifts of the Protons of Vineridine in Various Solvents and Their Relative Differences $\Delta = \delta_{CDCl_3} - \delta_{solvent}$

Solvent	19-CH_3	CO_2CH_3	11-OCH_3	H_{19}	H_{18}	H_{10}	H_9	H_{17}
$CDCl_3$	1,25	3,43	3,80	4,21	6,57	6,52	7,01	7,34
CCl_4	1,22	3,36	3,70	4,16	6,53	6,38	6,91	7,25
	+0,03	+0,07	+0,10	+0,05	+0,04	+0,14	+0,10	+0,09
CD_3CN	1,20	3,38	3,77	4,22	6,50	6,55	7,03	7,34
	+0,05	+0,05	+0,03	−0,01	+0,07	−0,03	−0,02	0,00
CD_3OD	1,23	3,39	3,78	4,22	6,49	6,55	7,02	7,33
	+0,02	+0,04	+0,02	−0,01	+0,08	+0,03	0,01	+0,01
$(CD_3)_2CO$	1,23	3,37	3,77	4,25	6,55	6,50	7,05	7,32
	+0,02	+0,06	+0,03	−0,04	+0,02	+0,02	−0,04	+0,02
DMF	1,24	3,42	3,79	*	6,52	6,56	7,11	7,38
	+0,01	+0,01	+0,01		+0,05	−0,04	−0,10	−0,04
DMSO	1,19	3,32	3,73	4,24	6,38	6,47	7,01	7,32
	+0,06	+0,11	+0,07	−0,03	+0,19	+0,05	0,00	+0,02
TFA	1,42	3,72	4,01	4,46	6,99	6,92	7,30	7,76
	−0,17	−0,29	−0,21	−0,25	−0,42	−0,40	−0,29	−0,42
C_5D_5N	1,10	3,44	3,67	4,18	6,70	6,66	7,14	7,58
	+0,15	−0,01	+0,13	+0,03	−0,13	−0,14	−0,13	−0,24
C_6D_6	0,89	3,24	3,36	3,91	6,58	6,46	6,75	7,52
	+0,36	+0,19	+0,44	+0,30	−0,01	+0,06	+0,26	0,18

*Masked by the signal of the solvent.

the CS of the CO_2CH_3 group $\Delta = +0.19$ ppm). In bases (I-III), this group is located at a considerable distance from ring A, and therefore undergoes a greater influence of the molecules of C_6D_6 as the solvent (see Tables 1-3).

For the correct assignment of the signals of the CO_2CH_3 groups which, in benzene solutions, because of the closeness of their CSs, can easily be taken as the signals relating to the 11-OCH_3 or 12-OCH_3 group, we additionally investigated bases (I-IV), making use of experiments on the observation of the intramolecular nuclear Overhauser effect (NOE). In base (III) in C_5D_5N with saturation of 11-OCH_3 signal with $\nu_2 = 367$ Hz, the one-proton doublet with δ 6.86 ppm relating to H_{10} becomes more intense. This shows that the singlet (3 H) with δ 3.70 ppm relates to the 11-OCH_3 group and the singlet with δ 3.49 ppm to the CO_2CH_3 group. In vineridine, as a result of the saturation of the 11-OCH_3 signal with $\nu_2 = 367$ Hz, the intensity of the H_{12} signal (δ 6.70 ppm) increases by 12%, while the intensity of the H^9 signal does not change. Consequently, the 3.67 ppm signal relates to the 11-OCH_3 group and the singlet with δ 3.44 ppm to the CO_2CH_3 group. It has also been found by the NOE method in majdine and isomajdine the CSs of the 11-OCH_3 groups in C_5D_5N solution are 3.79 and 3.76 ppm, respectively. The CSs of the 12-OCH_3 and CO_2CH_3 groups were determined by diluting the substances in $CDCl_3$ with pyridine.

It is obvious that the values of $\Delta^{C_6D_6}_{CDCl_3}$ found for the protons considered – $C_{19}-CH_3$, CO_2CH_3, and H_{19} – may be regarded as criteria for distinguishing and identifying the hydroxyindole alkaloids of the allo and epi-allo series.

The further analysis of the figures of Tables 1-4 shows that the methyl protons of the 11-OCH_3 group on the aromatic nucleus in bases (I-IV) undergo approximately the same diamagnetic influence of benzene (Δ = +0.44 to +0.52 ppm). Some scatter of the values of Δ is natural, since the substances studied have definite structural differences. At the same time, the influence of benzene on the CSs of the 12-OCH_3 groups in bases (I) and (II) is +0.26 and +0.13 ppm, respectively. It is likely that the specific value of Δ, averaging +0.48 ppm, is characteristic only for the 11-OCH_3 protons, which may serve as an additional fact permitting the arrangement of the latter in the aromatic nucleus of the hydroxyindole alkaloids to be determined.

The signal of the H_{17} olefinic proton in alkaloids (I-IV) in C_6D_6 as solvent shifts downfield by approximately 0.15 ppm, which is obviously explained by the fact that this proton comes into a descreening plane of the solvent molecule.

On considering the influence of benzene on the CSs of the H_9, H_{10}, and H_{12} aromatic protons, we took into account the fact that various factors will influence the formation of complexes of the solvent in the aromatic part of the molecule in alkaloids (I-IV). In the first place, an appreciable influence on the CS of the H_9 aromatic proton is exerted by the UEP of the N_4 nitrogen atom, which makes a definite contribution to the arrangement of the solvent molecules. In the second place, the different numbers of methoxy groups in the aromatic nucleus of the compounds investigated must have an effect, causing changes in the π-electron density on the ring carbon atoms at different degrees of interaction with benzene. Furthermore, the presence in alkaloid (IV) of a N-acetyl group also affects the interaction of the solvent and the substance in the region of ring A.

The action of the combination of these factors leads to the situation that the values of Δ for the individual aromatic protons in C_6D_6 do not coincide for these alkaloids. In all cases (see Tables 1-4), pyridine causes paramagnetic shifts of the signals of these protons.

The next important conclusion was made in a detailed analysis of the influence of various solvents on the CSs and SSCCs of the aromatic protons of vineridine. The one-proton signal at 6.57 ppm was previously assigned to the H_{17} proton. In $CDCl_3$ solution it appears in the form of a singlet, since its multiplicity is masked by the signal of the H_{10} proton, the CS of which is 6.52 ppm. However, in benzene solution the H_{10} and H_{12} aromatic protons become nonequivalent. As a result of this, the CSs and SSCCs differ distinctly. From the SSCC value J = 2.2 Hz, corresponding to the meta constant, of the signal of the proton with δ 6.57 ppm we have concluded that this signal relates to H_{12}. Consequently, the one-proton signal in the 7.34 ppm region with an SSCC of 2.0 Hz belongs to the H_{17} olefinic proton. It has been established by the double-resonance method that the doublet splitting of the H_{17} olefinic proton is due to long-range (allyl) coupling with H_{15} and, in view of the stereospecificity of the allyl SSCC, is characteristic only for the epiallo alkaloids [4]. An analogous conclusion has been made for a number of other polar solvents.

Influence of Polar Solvents. Analysis of Tables 1-4 showed that the influence of polar solvents, with the exception of TFA, on the CSs of the protons of the compounds investigated is basically slight. The results that we have obtained on the influence of polar solvents on the CSs of the protons of the hydroxyindole alkaloids shows that the signals of all the methyl radicals of the $C_{19}-CH_3$, CO_2CH_3, and OCH_3 groups are shifted upfield. The value of Δ in individual cases for the protons of these groups reaches 0.11 ppm. Consequently, the H_9, H_{10}, and H_{12} aromatic protons undergo paramagnetic shifts.

It is desirable to consider the influence of TFA in more detail, since it causes considerable shifts of all the signals of the protons and in individual cases the values of Δ may be characteristic. Thus, on analyzing the figures of Tables 1-4 it can be seen that the signals of the $C_{19}-CH_3$, CO_2CH_3, 11-OCH_3, and 12-OCH_3 groups and that of the methyl radical in the acetyl group of the alkaloid (III) undergo paramagnetic shifts averaging 0.24 ppm. The H_7 proton undergoes a considerable downfield shift (from −3.0 to −0.42 ppm). This shift in acid solution may be a consequence of several factors; the formation of π complexes between the double bond and the solvent [7], the effects of protonation, the effect of the reaction field of the medium, the formation of oxonium salts, and specific interactions which can take place in this part of the molecule.

The signals of the protons of the aromatic ring in alkaloids (I-IV) in TFA solution are located in a weaker field than in other solvents. A comparison of the values of Δ for the individual proton in each alkaloid shows that there is no clear dependence of the change in the CS on the configuration of the molecules investigated. The decisive factor of the changes in the CSs of the protons that have been found is probably effects of conjugation, as a result of which the degrees of protonation by acid of the individual parts of the molecule are different. Furthermore, the reaction field of the medium, TFA, introduces additional changes into the CS values of the aromatic protons.

It is known that on being heated in acetic acid solution the hydroxyindole alkaloids isomerize at the C_7 and C_3 centers [8, 9]. Thus, for example, majdine isomerizes to form isomajdine and epimajdine [10]. On analyzing the NMR spectra of majdine and isomajdine in TFA solution it can be seen that the signal of the H^a_{14} proton shifts downfield by approximately 0.90 ppm. This shift is difficult to explain solely by the action of the reaction field of the medium or by the effects of the protonation of the N_4 nitrogen atom, all the more since this proton is located in the β position to the nitrogen. It has been established that the H_{19} signal appears in the allo bases in the form of a sextet with $J_{H_{19}H_{20}} = 9.0$-11.0 Hz, and in the epiallo alkaloids, because of the conversion of ring D from one chair conformation to another, it has the form of a quartet with $J_{H_{19}H_{20}} = 1.5$-2.0 Hz [4]. In the NMR spectrum of the allo base of majdine in TFA, the signal of the H_{19} proton appears in the form of a quartet and shifts upfield by 0.33 ppm, although because of the superposition of the signals of the other protons it is difficult to determine the SSCC value for H_{19} and H_{20}.

Thus, the paramagnetic shift of the H^a_{14} signal by 0.90 ppm and the transformation of the signal of the H_{19} proton from a sextet to a quartet with a simultaneous downfield shift by 0.33 ppm in TFA as solvent is a consequence of the isomerization of majdine at C_7 and C_3. Analogous changes in the NMR spectra of the bases (II)-(IV) in TFA solution also show their isomerization.

Influence of Solvents on the Parameters of the NMR Spectra of Reserpinine. This indole alkaloid belongs to the pentacyclic heteroyohimbine series and has complete analogy in the structure and stereochemistry of rings D and E with bases (I-IV). Furthermore, the position of the methoxy substituent of the aromatic nucleus in (V) coincides with that for (III) and (IV).

TABLE 5. Chemical Shifts of the Protons of Reserpinine in Various Solvents and Their Relative Differences $\Delta = \delta_{CDCl_3} - \delta_{solvent}$

Solvent	19-CH_3	CO_2CH_3	11-OCH_3	H_{19}	H_{12}	H_{10}	H_9	H_{17}
$CDCl_3$	1,39	3,76	3,82	4,49	6,79	6,70	7,31	7,57
CCl_4	1,36	3,73	3,77	4,47	6,60	6,60	7,17	7,49
	+0,03	+0,03	+0,05	+0,02	+0,19	+0,10	+0,14	+0,08
CD_3CN	1,40	3,72	3,80	4,40	6,83	6,65	7,25	7,56
	−0,01	+0,04	+0,02	+0,09	−0,04	+0,05	+0,06	+0,01
CD_3OD	1,40	3,77	3,80	4,55	6,84	6,63	7,26	7,60
	−0,01	−0,01	+0,02	−0,06	−0,05	+0,07	−0,05	−0,03
$(CD_3)_2CO$	1,37	3,70	3,76	4,47	6,85	6,63	7,23	7,49
	+0,02	+0,06	+0,06	+0,02	−0,06	+0,07	+0,08	+0,08
DMF	1,39	3,72	3,79	*	6,89	6,65	7,27	7,54
	0,00	+0,04	+0,03		−0,10	+0,05	+0,04	+0,03
DMSO	1,38	3,70	3,74	4,40	6,76	6,58	7,20	7,53
	+0,01	+0,06	+0,08	+0,09	+0,03	+0,12	+0,11	+0,04
TFA	1,57	3,96	4,10	4,57	7,15	6,97	7,45	7,86
	−0,18	−0,20	−0,28	−0,08	−0,36	−0,27	−0,14	−0,19
C_5D_5N	1,36	3,58	3,74	4,58	7,15	7,00	7,54	7,67
	+0,03	+0,18	+0,08	−0,09	−0,36	−0,30	−0,23	−0,10
C_6D_6	1,20	3,55	3,61	4,43	6,70	6,94	7,36	7,70
	+0,19	+0,21	+0,21	+0,06	+0,09	−0,24	−0,05	−0,13

*Masked by a signal of the solvent.

Analysis of the results obtained (Table 5) shows that the protons of the C_{19} methyl group undergo a diamagnetic shift in C_6D_6 solution by 0.19 ppm, as in the case of bases (I-III). This value of Δ is not unexpected. As already mentioned, the influence of benzene on the CSs of the protons in this part of the molecule depends on the closeness of the UEP of the N_4 nitrogen atom to the center of the methyl radical at C_{19}. In the hydroxyindole alkaloids of the allo series, this mutual arrangement of the UPE of N_4 and $C_{19}-CH_3$ affects complex-formation with the solvent and leads to only slight changes in the CSs of the methyl group. The value of $\Delta^{C_6D_6}_{CDCl_3}$ of the $C_{19}-CH_3$ group in reserpinine can be explained similarly. The magnitude of the change in the H_{19} CS under the action of benzene in (V) is intermediate between ΔH_{19} in the allo and in the epiallo hydroxyindole bases (see Tables 1-5). The differences in the values of $\Delta^{C_6D_6}_{CDCl_3}$ for H_{19} in alkaloids (I-IV) and (V) are obviously due to the structural features of these alkaloids. Thus, for example, a lactam group in the hydroxyindole bases has an influence both on the H_{19} CS and on the stereospecificity of the formation of complexes with benzene. It follows from Table 5 that the CO_2CH_3 signal in C_6D_6 as solvent is shifted upfield by $\Delta = +0.21$ ppm. Such a value of Δ corresponds to the changes in the CS of the carboxymethyl group in base (IV) and is comparable with those for (I-III). On analyzing the figures in Tables 1-5, we also found that the value of $\Delta^{C_6D_6}_{CDCl_3} = -0.16$ ppm for H_{17} is characteristic for the alkaloids investigated.

The facts given enable us to consider that the value of Δ that we have found for $C_{19}-CH_3$, CO_2CH_3, H_{19}, and H_{17} in benzene solutions are characteristic for the hydroxyindole alkaloids and can be used in structural and stereochemical investigations of the bases of this series.

On comparing the values of $\Delta^{C_6D_6}_{CDCl_3}$ for the 11-OCH_3 group in bases (I-V) it can be seen that the methoxy group in reserpinine undergoes a diamagnetic shift of +0.21 ppm which differs considerably from the corresponding values of Δ in the hydroxyindole alkaloids. The conjugation of the aromatic ring with the pyrrole ring leads to a definite redistribution of the π-electron densities on the carbon atoms of ring A of reserpinine which differ from the π-electron densities in the hydroxyindole bases (I-IV). As a result, the interaction of benzene with this part of the molecule must differ in the indole alkaloids from what it is in the hydroxyindole alkaloids. In view of this, differences are observed in the Δ values not only for 11-OCH_3 but also for the protons of the aromatic nucleus. Pyridine shifts the signals of the H_9, H_{10}, H_{12}, and H_{17} aromatic protons of reserpinine downfield, as in the case of the hydroxyindole bases, but no numerical coincidence of the values of Δ is observed. A common qualitative generalization for the hydroxyindole alkaloids (I-IV) and the indole alkaloid (V) investigated in pyridine solution is the observed diamagnetic shifts of the signals of the methyl protons in the paramagnetic shifts of those of the methine protons.

The influence of polar solvents, with the exception of TFA, on the CSs of the protons of reserpinine is slight and has a somewhat chaotic nature, and therefore at the present time it is difficult to give any recommendations whatever for using polar solvents in investigations of the structure of the alkaloids of the indole series. The change in the CSs of the function groups of reserpinine in acid are comparable with the corresponding values of Δ found for the alkaloids of the hydroxyindole series (I-IV).

A consideration of the values of the SSCCs of the protons in alkaloids (I-V) that have been obtained has shown that, with the exception of solutions in TFA, the conformations of the compounds investigated do not change.

SUMMARY

On the basis of the results of a study of the influence of various solvents on the parameters of the NMR spectra of some hydroxyindole alkaloids, the following characteristic values of Δ for the protons have been found:

a) $\Delta^{C_6D_6}_{CDCl_3}$ for $C_{19}-CH_3$ in the allo bases is +0.18 ppm; b) in the epiallo bases it is +0.36 ppm; c) $\Delta^{C_6D_6}_{CDCl_3}$ for CO_2CH_3 in the allo bases is +0.30 to +0.37 ppm; d) in the epiallo bases it is +0.19 ppm; and e) $\Delta^{C_6D_6}_{CDCl_3}$ for the 11-OCH_3 group in the hydroxyindoles is +0.44 to +0.52 ppm.

It has been established that in the epiallo bases benzene causes a diamagnetic shift, and in the allo bases a paramagnetic shift, of the H_{19} signal. It is possible to perform a stereochemical identification of the hydroxyindole alkaloids on the basis of the value of $\Delta^{C_6D_6}_{CDCl_3}$ for $C_{19}-CH_3$, CO_2CH_3, and H_{19} protons.

Analysis of the signals of the aromatic protons of vineridine in C_6D_6 solution and in a number of other solvents has permitted their assignments to be refined and a long-range (allyl) coupling of the H_{17} and H_{15} protons with an SSCC of 2.0 Hz that is characteristic of the epiallo alkaloids to be found. It has been shown that the change in the CSs of the protons of rings D and E of the hydroxyindole alkaloids and the indole alkaloid reserpinine as a result of the influence of various solvents mainly has a symbatic nature. The invariability of the SSCCs of the protons in the solvents investigated with the exception of solutions in TFA, shows that the conformations of rings C, D, and E in them do not change. The changes in the CSs and SSCCs of the protons in the alkaloids investigated in TFA are an indication of the isomerization of these compounds in the acid.

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