APPLICATIONS OF ^{1}H AND ^{13}C NMR SPECTROSCOPY IN STRUCTURAL INVESTIGATIONS OF Vinca INDOLE ALKALOIDS

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This review considers the laws connecting the parameters of the ^{1}H and ^{13}C NMR spectra with the structure of the substances and the use of these laws for solving structural and stereochemical problems of the Vinca indole alkaloids and other compounds of closely related structure. For each type of alkaloids, characteristic features of the PMR and ^{13}C NMR spectra are given that permit the structures of similar bases to be established and their stereochemical identification to be performed.

This review considers the laws connecting the parameters of the ^{1}H and ^{13}C NMR spectra with the structures of compounds, and the use of these laws for solving problems of the structure and stereochemistry of the Vinca indole alkaloids. At the present time, more than 120 alkaloids have been isolated from plants of the genus Vinca (family Apocynaceae) [1, 2], these including in their structure nuclei of dihydroindole (indoline) (I-VIII), α-methyleneindoline (X-XII), indole (XIII-XXI), oxindole (XXII-XXVII), and indolenine (3H-indole) (XXVIII). Previous reviews [3-5, 188, 189] have discussed some features of the PMR and ^{13}C NMR spectra of a number of indole alkaloids, and a handbook [148] gives the ^{13}C chemical shifts of these alkaloids from the literature, up to 1979.

In generalizing and establishing correlations of the parameters of the spectra with structures, we make use of the published PMR and ^{13}C NMR characteristics of related alkaloids in the indole series isolated from sources other than Vinca plants, as well.

PMR Spectra. On the basis of literature descriptions of the PMR spectra of model bases – dihydroindoles [6-9], indoles [57-59], oxindoles [99], and alkaloids derived from them of the indoline [6, 10-45], indole [60-97], and oxindole [110-117] series, and also α-methyleneindoline (79-90) [13, 21, 37, 44-56], and indolenine [124-129, 103, 130-132] alkaloids – in the determination of the positions of substituents (OCH_3 and OH) in the benzene ring we have found diagnostic values of the chemical shifts and spin-spin coupling constants of the aromatic protons, the generalized values and signals of which are given in Fig. 1. No account has been taken of the CSs of the aromatic protons of N-acetyl derivatives of indoles [7-9, 13], oxindoles [100, 102, 105a, 106] and acetylnorharmine [90].

On comparing these results, the following relations of the parameters of PMR spectra with structure were found (Fig. 1):

1. In the dihydroindoles and the indoline alkaloids substituted at C-10 or C-11 of the benzene ring, the three aromatic protons give a pattern corresponding to a spin system of the ABX type; in the case of the C-10 derivatives, the signal of the X proton having a meta-coupling constant (2-2.5 Hz) is observed in the weak field, and in the case of the C-11 derivatives the signal of X with an ortho-coupling constant (8-8.5 Hz) is observed. This can be used as a criterion to distinguish C-10-substituted indolines from the corresponding C-11-substituted compounds. Indolines substituted in the C-12 or C-9 position differ from those substituted at C-10 and C-11. The position of the OCH_3 groups in vincaricine and vincarinine was corrected on this basis [162], which involved the necessity for reconsidering the structure of vincovine [42].

2. The pattern of signals of three aromatic protons of the substituted α-methyleneindoline and oxindole alkaloids is analogous to that for the indoline derivatives.

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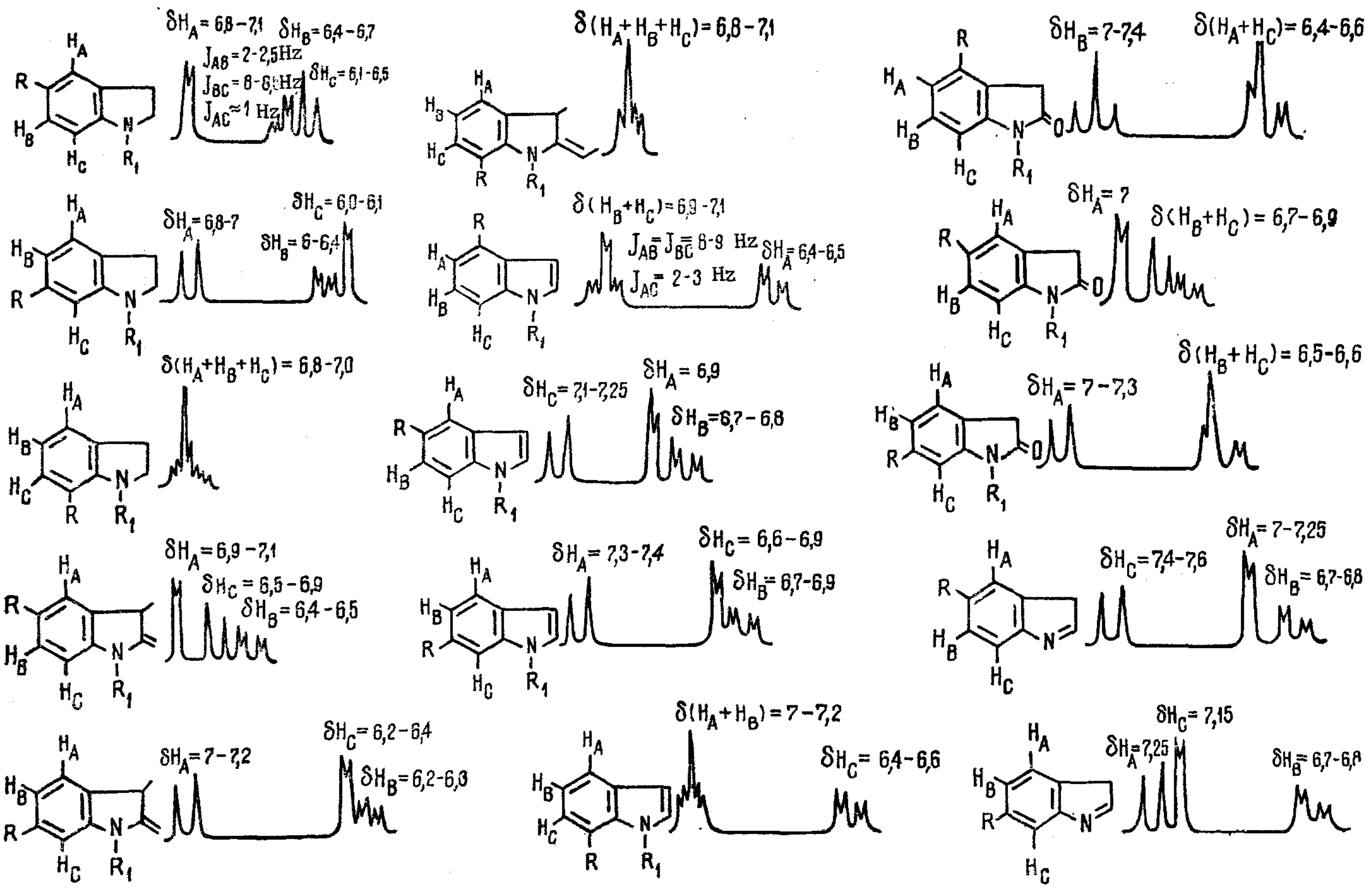


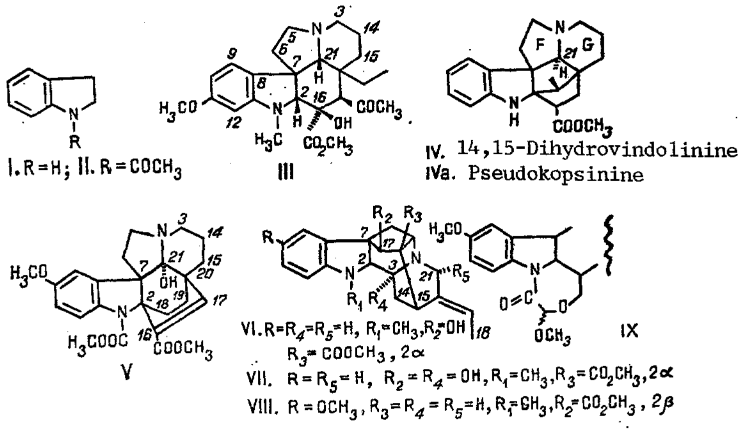
Fig. 1

3. In the C-9- and C-12-substituted indoles, three protons appear in the form of a multiplet of the ABC type, and in the C-10 and C-11 substituted indoles the same protons form complex ABX systems differing only by their position. However, these differences in the CSs are insufficient for an unambiguous deduction of the position of the substituents at C-10 or C-11.

4. The C-10-substituted indolenines have approximately the same ABX pattern as the corresponding indoles, with the difference that, in the former, the signal of the X proton with an ortho-coupling constant is appreciably shifted downfield. The C-10- and C-11-substituted indolenines likewise differ by the CSs of the protons having ortho- and meta-coupling constants

To establish the positions of substituents in the benzene rings of dihydroindoles [7-9] and the indole [13, 20, 21] and oxindole [20, 100, 102, 105, 106] alkaloids another important criterion relating to the paramagnetic shift Δδ = 0.7-1.8 ppm of the H-terminal aromatic pro-

Scheme 1


I. R=H; II. R=COCH$_3$

III

IV. 14,15-Dihydrovindolinine

IVa. Pseudokopsinine

V

VI. R=R$_4$=R$_5$=H, R$_1$=CH$_3$, R$_2$=OH, R$_3$= COOCH$_3$, 2α

VII. R=R$_5$=H, R$_2$=R$_4$=OH, R$_1$=CH$_3$, R$_3$=CO$_2$CH$_3$, 2α

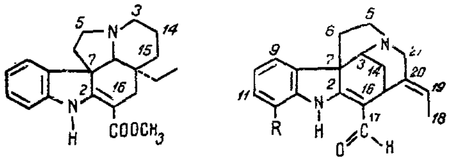
VIII. R=OCH$_3$, R$_3$=R$_4$=R$_5$=H, R$_1$=CH$_3$, R$_2$=CO$_2$CH$_3$, 2β

IX

ton in the acetylation of N$_a$–H in them has been found. It has been shown that in the N$_a$-acetylindolines [8, 9] and oxindoles [100, 102, 105] the C=O of the N$_a$-acetyl group is locate in the plane of the aromatic ring predominantly in the endo conformation and a substantial contribution (more than 2/3) to the descreening of the H-12 proton is made by the electric field of the C=O of this group [105].

In actual fact, in the 10-methoxy-substituted indoline alkaloid rindline (IX) [45] with a N–C=O group fixed in the endo conformation, the H-12 signal is shifted downfield to 8.08 ppm, i.e., the relative paramagnetic shift of H-12 as the result of the influence of the C=O group on it amounts to 1.3-1.4 ppm as compared with other 10-methoxy-substituted indolines [9, 25, 162].

Scheme 2



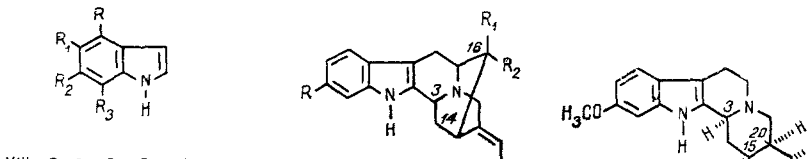
X XI R=H; XII R=OH

The position of the OCH$_3$ group in the benzene ring of 2,16-dihydrovinervinine [21], ciliaphylline, stipulatine [101, 102], vinerine (XXIV), and vineridine (XXV) has been determined with the aid of this criterion [105, 106]. In addition, we have proposed for the first time an effective method for establishing the position of substituting groups in the aromatic ring of N$_a$-methylindoline and N$_a$-methylindole alkaloids by measuring the intramolecular nuclear Overhauser effect (NOE) [71].

On the double irradiation of the signals of the N–CH$_3$ protons of majoridine (VIII) and of N$_a$-methyl-O-acetyllochnerine, the integral intensity of the H-12 signal increased by 18 and 13%, respectively [71]. By using this NOE method, Lewin et al. determined the position of the OCH$_3$ group in the benzene ring of each of a number of new indoline and indole alkaloids [25]. The positions of the aromatic OCH$_3$ groups of majdine (XXVII) and of isomajdine were shown similarly [113].

It must be mentioned that the method of measuring NOEs has been used successfully not only in determining the positions of substituents, but also for elucidating structural and stereochemical features of alkaloids of the indole series [23, 139, 141-143]. Thus, the cis-linkage of rings B and C and the cisoid arrangement of N–CH$_3$ and C$_8$–H in the alkaloids physostigmine [141] and geneserine [142], the geometry of the C-18 methyl of the ethylidene bond of gardnutine [143] and dehydrovoachalotine [139] and the orientation of the H-2 and H-17 protons in indoline alkaloids of the ajmaline type [23] have been established by the NOE method

Scheme 3



XIII. R = R$_1$ = R$_2$ = R$_3$ = H

XIV. R = OCH$_3$, R$_1$ = R$_2$ = R$_3$ = H

XV. R$_1$ = OCH$_3$, R = R$_2$ = R$_3$ = H

XVI. R = R$_1$ = R$_3$ = H; R$_2$ = OCH$_3$

XVII. R = R$_1$ = R$_2$ = H, R$_3$ = OCH$_3$

XVIII. R = OCH$_3$, R$_1$ = CH$_2$OH, R$_2$ = H

XIX. R = R$_1$ = H, R$_2$ = CH$_2$OH

XX. R = H, R$_1$ = COOCH$_3$, R$_2$ = CH$_2$OH

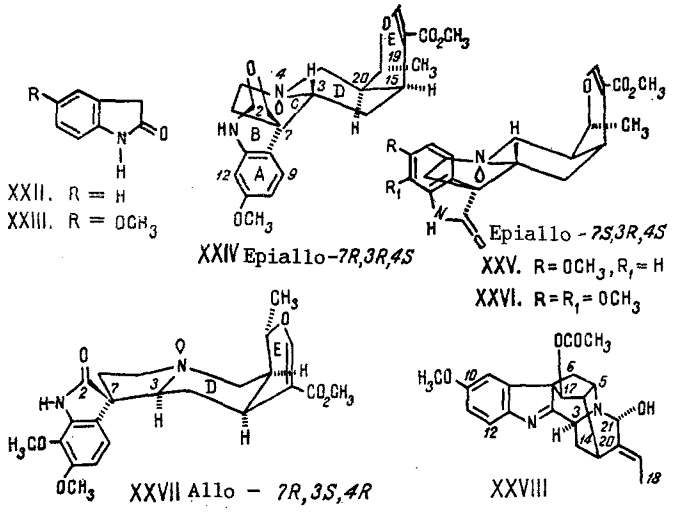
XXI

In addition to NOEs, other methods of double proton-proton resonance have been used in the assignment of the signals of the protons in the solution of structural questions – total [20, 23, 24, 46, 81, 105, 106, 142, 140, 183] and INDOR [20, 23, 140]. By the double-resonance method we have found a stereospecific long-range spin-spin interaction between four σ-bonds by a W-type pathway between the H$_\alpha$-6 and H$_\alpha$-17 protons of about 1 Hz in alkaloids of the type of ajmaline (VI) [23] and vomilenine (XXVIII) [132] which can be used to establish the orientation of a substituent at C-17 in them and also a long-range (allyl) σ–π interaction between Hα-15 and H-17 with $^4J \approx 2$ Hz, which is characteristic for the epiallo pentacyclic oxindole alkaloids [106] and enables them to be distinguished from the corresponding allo stereomers. This is due to the stereochemical difference between rings D and E in the two series, in which a simultaneous change in the configuration of the C-3 and C-7 centers leads to the conversion of the piperidine (D) and dihydropyran (E) rings from a chair conformation (D) and a half-chair conformation (E) into others during which a reorientation of C_{15}—H_e from equatorial to axial and the opposite reorientation of C_{20}—H_a takes place [106, 108, 111]. Another consequence of this is a substantial change in the H—C_{19}—C_{20}—H dihedral angles from 80° (epiallo) to 170° (allo), leading to a considerable difference in the SSCCs of the H-19 and H-20 protons, which are 1.5 and 11 Hz [106, 108, 111], while the CS of the H_a-14 proton in them also changes appreciably [106].

On passing to an analysis of the CSs of the H-3, H-9, H-19, and NH protons, it must be observed in the first place that in the various alkaloids of the indole series a substantial contribution to them is made by the magnetic anisotropy (σ_χ) and the electric field (σ_E) of the unshared electron pair (UEP) of the N_b nitrogen atom, while σ_χ and σ_E of the benzene ring and the C—OH bond also affect the CSs of the 18-CH_3, $COOCH_3$, and H-21 protons. It has been found that in the indole alkaloids of the heteroyohimbine series with the cisoid arrangement of H-3 and the UEP of the N_b atom, the H-3 signal is observed in a weaker field (in the range of 3.8-4.5 ppm) than in the case of their transoid orientation (3.2-3.5 ppm) [81, 137, 138]. Thus, in 3-isoajmalicine [81] and raufloridine [82] H-3 resonates at 4.45 and 4.50 ppm, respectively, while in ajmalicine, tetrahydroalstonine and rauniticine the chemical shift of H-3 is 3.42-3.48 ppm [81].

The orientation of H-3 with respect to UEP of N_b may affect not only the CS but also the value of its SSCC with the neighboring H-14 protons. In the case of the cisoid arrangement of the UEP of N_b and H_3, the latter gives a quartet with two small SSCCs, ae (3-5 Hz) and ee (2-5 Hz), and in the case of the transoid relationship H-3 has one large SSCC, aa (12 Hz), and one small one, ee (3-5 Hz) [81, 137].

Scheme 4



In the indole and oxindole pentacyclic allo alkaloids (XXVII) [81, 105-121, 135], the CSs of the 18-CH_3 protons (δ 1.38-1.45) and of H-19 (δ 4.35-4.45) are shifted downfield by 0.15-0.20 ppm as compared with those of the normal series (δ 1.18 and 1.22 and 4.18-4.20 ppm, respectively) [81, 122, 135] and those of the epiallo series (XXIV, XXV) [105—111], with an exception [81], which is due mainly to the descreening influence of the UEP of N_b on these protons in the allo alkaloids in analogy with the methyl-substituted quinolizidines [135].

The CSs of the signals of the H-9 protons in the oxindole alkaloids with the anti arrangement of the N—C=O group and the UEP of N_4 are found 0.2 and 0.3 downfield as compared with those with the syn arrangement of these groups, obviously because of the influence of the UEP of N_4 in the former. Furthermore, the CSs of the signals of the NH protons measured under identical conditions in the spectra of the epiallo-A alkaloids (XXIV) are shifted upfield by 0.8 ppm in comparison with those of the epiallo-B alkaloids (XXV), which can also be explained by the influence of the UEP of N_4 on the lactam C=O group [105, 106]. The diamagnetic screening of the benzene ring is responsible for the upfield shift to 0.67 ppm of the signal of the 18-CH_3 protons in aspidospermine (14) [14] and its analogs [6, 14-16, 181], and also for the upfield shift by 0.2-0.3 ppm of the signal of the $COOCH_3$ methyl group in the epiallo-A oxindole alkaloids (XXIV) [105 - 109, 111] as compared with the epiallo-B alkaloids (XXV) [106, 108].

It has been found that the nonequivalence of the C_{21}—H_2 protons of the alkaloids herbamine and herbadine is connected with the influence on them of the σ_χ and σ_E contributions of the C_3—O bond and of the $2p_z$ UEP of the O atom [23], and this has shown the erroneousness of the ideas of authors [24] who have considered that the nonequivalence of these protons was due to the β configuration of C-2 in these bases. We are the first to have established the substantial diamagnetic shift of 4 ppm of the CS of the NH proton on the hydrogenation of the double bond in the α position to the N_a atom of the α-methyleneindoline and oxindole alkaloids, which permits their differentiation [133, 134]. On the basis of the results of a study of the influence of solvents on the CSs and SSCCs of the protons of the alkaloids under consideration, characteristic increments of the solvent shifts of various protons have been found [184] which have permitted the mutual positions of the OCH_3 and OH groups of the new oxindole base vinerinine to be determined [117].

^{13}C NMR Spectra. In addition to PMR, beginning from 1969-1970, due to the creation and introduction of pulsed Fourier NMR spectrometers, the method of NMR on ^{13}C nuclei in their natural concentration has been used extremely successfully in the solution of problems of the structure of natural substances, especially alkaloids [144-149]. Many questions connected with the elucidation of features of the structure and stereochemistry of alkaloids of the indole series have been answered with the aid of ^{13}C NMR [148-182, 185, 186]. The values of the SCs and the assignment of the signals of the carbon atoms for various model indole derivatives and indole alkaloids are given in Table 1.

An analysis of the literature figures for the CSs of the carbon atoms of the benzene rings of the alkaloids under consideration (Table 1) shows that they differ distinctly from one another, and the introduction of the donor substituents OCH_3 and OH in various positions of the ring leads to substantial and characteristic changes of the values of the CSs of C-1 and of the ortho-, meta-, and para-carbon atoms [189], the increments for these being given in Table 2.

It must be mentioned that the assignment of the C-4 and C-5 carbons of 7-methoxyindole (Table 1, XVII) in [167] was made incorrectly: they must be interchanged [182]. The slight difference for OCH_3 as compared with OH is obviously due to the effect of the methylation of the phenolic hydroxyl [187]. Furthermore, we have observed that the magnitude of the increment of a substituent depends on the degree of substitution of the ortho-, meta-, and para-carbons of the benzene ring. By using the OCH_3 increments in the ^{13}C NMR spectra, Chatterjee et al. established the structure of the indoline alkaloide rauflexine and thereby refined the structure of reflexine [161]. Likewise, on the basis of the results of an analysis of the ^{13}C NMR spectra we reconsidered the structure of vincaricine and vincarinine [162] and confirmed the positions of the OH and OCH_3 substituents in the benzene rings of vincanidine (XII) and vinervinine [165].

A consideration of the figures in Table 1 shows that many alkaloids containing no substituent in the benzene ring can be distinguished by the CS of the C-13 carbon, since it is characteristic for each type of alkaloid, having values of 148.7-155.3 ppm in indolines, 142.9-144.1 ppm in α-methyleneindolines, 135.7-137.8 ppm in indoles, and 154.9-156.6 ppm in indolenines, while in the oxindoles the interval of changes in the C-13 CS (140.7-143.8) is close to that for the α-methyleneindoline alkaloids. However, the oxindole alkaloids can be identified, in addition, from their exhibiting a signal of the carbon of the lactam C=O group. At the same time, in alkaloids having a C_{19}=C_{20} ethylidene double bond the C-20 signal resonates between 136.4 and 141 ppm, i.e., its position almost coincides with that of the C-13 signals of indoles and oxindoles, which leads to ambiguity in their assignment.

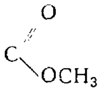
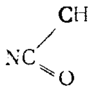
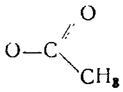
By analyzing their ^{13}C NMR spectra, we have established the structures of two new indolenine alkaloids and have reconsidered the structures of two known alkaloids from Vinca erecta [177]. It must be mentioned that in Table 1, of the ^{13}C CSs of the bases (III) and (V) in [177] a misprint occurred and in actual fact in the spectrum of (III) the CS of the C-12 carbon has a value of 108.4 ppm and that of C-18 in (V) a value of 13.6 ppm.

TABLE 1. ^{13}C Chemical Shifts (δ, ppm, 0–TMS, $CDCl_3$) and Assignments of the Signals of the Carbon Atoms of Some Alkaloids of the Indole Series

Carbon atom	I[37,150]	II[150]	III[151]	IV[152]	IVa[154]	V[156]	VI[161]	VII[162]	VIII[161]
2	47,1	48 6	83,2	80 6	79,9	71.2	74,4	80,8	79,6
3	29,7	27,8	50.9	55,0	55,5	43;5	52.7	85.0	49,3
5			51,9	48,1	47,3	47,5	61,1	62,9	55,9
6			43,9	37,3	34,6	36,9	35,0	34,6	36,1
7			52,6	60,3	60.0		56,5	57.6	53,6
8	129,1	131,4	124,9	140.1	135,0		129.7	129,4	133.3
9	124,4	123,4	122,4	123.6	125.3	116,2	124,2	124.1	110,0
10	118,3	124,5	104,5	121,1	121,8		118,5	118,9	153,0
11	127,1	127,3	161,1	127.2	128.1	112,9	127,6	128,4	111,1
12	109,2	116.7	95,5	112,7	112,0	110,4	108,4	108.9	109.6
13	151,6	142,9	153,6	149,5	148 3		153,8	154,1	147.8
14			123,9	20,7	19,1	29,9	21,4	29,5	29.4
15			130,2	31 2	33,2	16,4	29.6	32,4	27,8
16			42,8	40,2	40,0		59,6	59,0	50.1
17			76,2	29,0	24 8	143,7	73,9	74,1	79.1
18			7,5	7,5	6.8	29,6	12,3	12,7	12.8
19			30,6	51,0	51,6	25,0	116,1	115,7	114,3
20				44.5	42,6	42,6	135,6	136,5	139.3
21			67,0	78,8	72,1	91,9	54,7	48,4	55,2
O			170,4	175,5	173,4	167,1	172.8	172,6	
$C{\diagdown}OCH_3$			51,9	52.0	52,1	52,5	51,1	51,4	
O			171,7						169,9
$OC{\diagdown}CH_3$			20,8			56,1			21,2
Ar—OCH_3			55,1						55,5
O		168.5							
$NC{\diagdown}CH_3$		24,0							
N—CH_3			38,0				33,8	35,8	35,1
C=O									
O						157,4			
$NC{\diagdown}OCH_3$						52,2			

Carbon atom	X[151]	XI [165]	XII [165]	XIII [182]	XIV [167, 182]	XV [167]	XVI [167]	XVII [167. 182]	XVIII [170]	XIX*	XX*	XXI [169]
2	167.8	168.7	169.4	124,8	125,7	124,3	123,2	123,6	138,3	140 2	139,6	133,1
3	51,7	62,7	62.4	102,2	100,9	101 6	102,4	102,8	50 5	51,0	51,3	59.8
5	50,7	56.4	56.9						53,0	55,6	58.7	52.9
6	45,3	46,2	47,2						23.4	27,7	25,1	20,8
7	55 5	58,3	59.8						106.0	104.2	106.0	107,2
8	138.0	136,9	141,0	128.4	128,1	127.7	122.3	126,9		128,5	127,9	121 1
9	121,0	121,7	115.9	120,9	153,4	111,6	121,2	113 5	118,8	118,2	118,2	117,2
10	120.5	120,7	123.5	121,5	101,9	153,1	110 0	120,2	108,7	121,0	121,0	109,1
11	127,4	127,6	112,7	119,9	111,2	101,8	156,5	102.1	156,3	119.0	119,0	155,5
12	109,3	110 2	143,7	111,4	112.0	111,9	94.8	146,7	95,8	111,6	111,6	[illegible]4,3
13	143.4	142,9	131,8	135,7	131 2	130,3	136.6	129,6	137,9	137,5	137,8	136.7
14	22,2	30,8	31.2						27,9	34,1	29,7	33,7
15	32,9	31.2	31,4						27.3	28 3	30,0	37,9
16	92.8	111,1	112.2						43,6	45,2	52,5	106,4
17	25.6	188,2	187,9						60,5	64,5	68.8	154,7
18	7,3	12,7	13 0						13,5	12,9	13,3	17,4
19	29.3	120.2	120.0						112,6	111.9	115,9	71,1
20	38,2	139,6	139,4						142,3	137,5	139,8	30,8
21	72,7	56,6	57,1						56,9	56,4		55,3
O	169,2										174,0	165,4
$C{\diagdown}OCH_3$	50,9										50,7	49,1
Ar—OCH_3					55,7	55,5	55.3	55,4	55,6			55,2

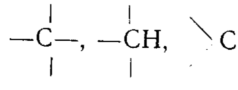
TABLE 1 (continued)

Carbon atom	XXII [172, 173]	XXIII [172]	XXIV [176]	XXV [174]	XXVI*	XXVII [174]	XXVIII*
2	178,6	176.3	182,0	182,5	180,3	180 8	179,8
3	36,3	36.3	67,2	70,1	70,1	74,0	54,6
5			53,2	53 2	53,2	53,3	52,6
6			34,8	34,2	34,5	33,7	36,5
7			56,0	55,3	55.8	55 9	64,7
8	125.4	127.2	125,4	125,0	126,3	126,5	137,1
9	124,4	109.4	125,3	123,0	117.8	117,8	110,8
10	122 2	154,7	106,8	107,6	105,8	106,1	157,9
11	127,9	112.3	159 6	159,8	152,3	152,2	112.8
12	110,0	111,6	96,6	96,7	134,0	133,9	121,1
13	142,9	137.1	141,5	142,2	132,4	132,5	149.8
14			27,0	26,2	26,2	29 3	26 5
15			24,8	25,1	25 0	30,8	28,6
16			104.9	105,4	105,0	109,1	49,1
17			153.5	153,5	153,3	154.9	77,1
18			18.4	18,5	18,7	18,6	13,0
19			74,5	74,6	74 7	72,0	11,9
20			36,8	36,5	36,4	38,1	123.6
21			53,7	54,6	54,6	54.6	82,4
			167,3 50,7	167,3 50,3	167,4 50,5	167,4 50,6	
Ar—OCH_3		55.5	55,3	55,3	55,9 60,7	56,2 60,5	55,6
							169,9
							20,9

*Author's previously unpublished results.

TABLE 2

Alkaloid	Substituent	C_1	ortho	meta	para
Indolines	OCH_3	+35,5±2,0	−13.9±2.7	+0,5±1.0	−7,8±1,5
α-Methylene-indolines	OCH_3	+34,0±1,5	−14,1±1,7	+1,4±0,7	−7.2±0,2
	OH	+33,0±0,5	−15.0±2,0	+3,0±0,5	−6,0±0.5
Indoles	OCH_3	+35.0±1.6	−14,6±4.8	+0.9±1,2	−7,0±2.5
	OH	+31.6±0 6	−12,5±2,8	−0,5±0,4	−5.0±0,4
Oxindoles	OCH_3	+32.3±0,5	−14,7±1,5	+1,5±0.3	−7,7±1,5
Indolenines	OCH_3	+32±0.5	−14,5±1,2	−2±1.5	−6,0±1,2
	OH	+31±1,8	−13 ±4,2	−4±3,5	−6,0±1,2

In the case of the indolenine bases, the C-2 signal of the azomethine bond is located in the 179.8-187.7 ppm region (Table 1), while the same signal of a C=C bond in the α-methyleneindoline alkaloids has a CS of 165.4-169.4 ppm, coinciding in magnitude with the CS of the acetyl C=C group. On analyzing the link between the CSs of the sp^3-carbon atoms with the structure and stereochemical features of the alkaloids under consideration, the dominating role in this question of the α-, β-, γ-, and δ-contributions of the various bonds and groups to the values of the CSs of the corresponding carbon atoms must be noted [144-149, 151, 152]. Here, extremely valuable assistance for the assignment of the signals of the  $-\overset{|}{\underset{|}{C}}-$, $-\overset{|}{\underset{|}{C}}H$, $\diagdown CH_2$ and $-CH_3$ carbon atoms is provided by the method of incomplete, off-resonance, decoupling of C–H interactions [144, 149].

The range of values of the CSs of the sp^3 carbons in the alkaloids under study amounts to 6.0-107.1 ppm (Table 1). As literature figures and Table 1 show, the CSs of the carbon atoms of the methyls of Ar-OCH_3 groups (54.2-56.8 ppm), $COOCH_3$ groups (49.1-51.6 ppm), $NCOCH_3$ groups (23.0-26.6 ppm), $OCOCH_3$ groups (20.5-21.2 ppm), and NCH_3 groups (30-38 ppm) differ appreciably from one another and are easily recognized. The CSs of the C-2, C-3, C-5, and C-21 carbon atoms, linked to the N_a or N_b atoms vary within the range of 47.0-83.2 ppm. Where carbon is bound to two heteroatoms, N_a and O, the C-2 CS shifts downfield to 107.1 ppm, as is observed in the spectrum of picraline [74]. At the same time, the CS of the C-5 atom of picraline, which is similarly bound to the N_b and O atoms, amounts to 87.1 ppm. This difference in the α-contributions of N and O to the magnitude of the CS of the C-2 and C-5 atoms is obviously due to the degree of substitution of these carbon atoms. In actual fact, we have established that the values of the α-, β-, and γ-contributions of CH_3 and OH to the CSs of the corresponding carbon atoms of the indoline alkaloids do depend on the degree of their substitution. For example, when the C-2 carbon is tertiary, the replacement of the hydrogen atom of NH by CH_3 leads to its descreening by +4.5-5.1 ppm, i.e., the β-contribution of an NCH_3 methyl group to the CS of the C-2 atom amounts to approximately 5 ppm.

Thus, in herbamine the β-contribution of CH_3 as compared with herbadine, containing no NCH_3 group, amounts to +4.5 ppm and in vincamajine as compared with quebrachedine, correspondingly, it is +5.1 ppm [162]. At the same time, when C-2 is quaternary (compare vindolinine and its NCH_3 derivative [152]), this increment is only +3 ppm.

A similar pattern is observed in model substituted pyrroles [149]. Furthermore, we have shown that the α-, β-, and γ-contributions of the 3α-OH group of herbadine and herbamine depend substantially on its orientation with respect to the corresponding carbon atoms at the degrees of their substitution. On this basis we have reconsidered the incorrect stereochemistry that was previously proposed for them [162].

In the indole alkaloids, the interpretation of the CSs of the C-15 and C-21 carbon atoms located adjacent to an ethylidene double bond with allowance for the γ-effect of the C-18 methyl has enabled the E configuration of the double bond to be confirmed [170]. It has been shown that in compounds with the E configuration, i.e., when C-18 is present in the cis position with respect to C-15, the signal of the latter is found in a stronger field than the analogous C-15 signal when it is trans-oriented with respect to C-18 (Z configuration) [170].

Table 1 shows that a change in the configuration of the C-7 spiro center in the pentacyclic oxindole epiallo alkaloids leads to a downfield shift of the C-3 signal by 2.9 ppm, while the signal of C-7 atom itself shifts upfield by 0.7 ppm [174]. It must be mentioned that we made the assignment of the C-3 and C-19 signals of vinerine (XXIV) from general considerations [174] and then confirmed them by the experimental method of selective decoupling from the H-19 protons (4.16 ppm).

The change in the configuration at C-7 from R to S in the epiallo bases causes an upfield shift of C-9 in the aromtic ring by 1.7 ppm, apparently as a result of the influence of the UEP of N_4 on C-9 in vinerine (XXIV) [194]. On passing from the epiallo to the allo compounds, a substantial change in the CSs of the carbon atoms of rings D and E can be observed which is connected with a change in their conformations. The greatest downfield shift of $\Delta\delta$, 7.0 ppm, is experienced by the C-3 signal, and this can be used as a test characteristic for the recognition and stereochemical identification of the epiallo-7(R) and allo-7(R) oxindole alkaloids [174]. It was shown that the closeness of the N_4UEP in the allo bases causes a characteristic upfield shift by 2.5 ppm of the C-19 signal relative to the epiallo series due to the γ-effect of the N_4 atom [174, 180].

Similarly to what was found for model and natural tetracyclic oxindoles [149], in the allo pentacyclic oxindole alkaloids indications of differences in the CSs of the C-3, C-7, and C-9 atoms according to the configuration of the C-7 atom that are characteristic for them have been found [174]. The correlations of the ^{13}C CSs with the conformations and configurations of the oxindole alkaloids that have been found may be useful for answering stereochemical questions for new bases of this series.

Thus, the results of an analysis of the PMR and ^{13}C NMR spectra show that the complex application of the correlations found between the spectral parameters and structures of alkaloids of the indole series may serve as an extremely effective and reliable basis for establishing their structures and stereochemistry.

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POLYSACCHARIDES OF *Polygonatum*.

VII. A GLUCOFRUCTAN FROM *P. sewerzowii*

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A glucofructan has been isolated from the rhizomes of *Polygonatum sewerzowii* Bunge and has been called pseverin. According to its chemical and spectral characteristics, pseverin is a polysaccharide containing both inulin, 2 → 1, and leven, 2 → 6, glycosidic bonds. The problem of the correlation between the molecular structure of a glucofructan and its supermolecular organization has been considered. X-radiographic and electron-microscope studies have been made of pseverin and its acetate. It has been established that on precipitating from solution pseverin forms globular particles which aggregate to give elongated necklace-like formations. Fine lamellar structures are characteristic for the acetate.

We have previously reported the isolation of water-soluble polysaccharides from the rhizomes of *Polygonatum sewerzowii* Ragel [1]. After the water-soluble polysaccharide (WSPS) had been precipitated with ethanol from the aqueous ethanolic filtrate, we obtained the combine polysaccharides with a yield of 17.6% on the air-dry raw material. The polysaccharides were dialyzed against distilled water. The dialysate was found to contain glucose, fructose, sucrose, and fructooligosaccharides. The undialyzed part remaining within the membrane was evaporated to a syrup and, by trituration with acetone, was converted into a powder. A hydrolysate of the latter was found by PC (system 1, revealing agents 1 and 2) to contain glucose and fructose. Consequently, this polysaccharide was a glucofructan; it has been called pseverin. A determination of the amounts of monosaccharides in the polysaccharide by the Bertrand–Kolthoff method [2] showed that it contained 96% of fructose and 4% of glucose.

Pseverin is a white amorphous powder readily soluble in water, $[\alpha]_D^{22}$ 30° (c 0.4; water). On gel filtration through Sephadex G-50, pseverin proved to be homogeneous. Its IR spectrum contained absorption bands at 820 and 940 cm^{-1}, which are characteristic for glucofructans of the inulin type and at 860 cm^{-1}, which are characteristic for levan. Consequently, pseverin contains 2 → 1 and 2 → 6 bonds.

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