polyphosphoric acid. The reaction mixture was stirred at 20°C for 2 h, after which it was heated to 90°C. The heater was removed, and the mixture was allowed to cool spontaneously to 40°C. The reaction mass was poured over ice (~1200 g), and the resulting mixture was neutralized with ammonium hydroxide. The precipitate was removed by filtration, washed with water, air dried, and recrystallized from methanol to give 2 g (59%) of XI with mp 178-180°C (from methanol). IR spectrum: 1715, 1680 cm^{-1} (C=O). UV spectrum, λ_{max} (log ε): 238 (4.34) and 302 nm (3.90). PMR spectrum ($CDCl_3$): 2.17 (s, $COCH_3$), 2.55 (s, CH_3), 3.30 (s, 2H-C_4), 7.94 (s, H-C_2), 7.36, 8.18, 8.58 ppm (3m, aromatic ring protons). Found: C 65.8; H 5.1; N 16.6%; M^+ 255. $C_{14}H_{13}N_3O_2$. Calculated: C 65.9; H 5.1; N 16.5%; M 255.

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PYRROLOINDOLES.

5.* ACETYLATION OF 1H,6H-PYRROLO[2,3-e]INDOLE BY MEANS OF THE VILSMEIER–HAACK REACTION

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The Vilsmeier–Haack reaction with 1H,6H-pyrrolo[2,3-e]indole with the participation of dimethylacetamide was studied. 3-Acetyl, 8-acetyl, 2-acetyl, and 3,8-diacetyl derivatives (with great preponderance of the 3-acetyl derivative) were obtained. The formation of a 2-substituted product does not have an analogy in the chemistry of indole. On the basis of data from the IR and PMR spectra it was established that an intramolecular hydrogen bond between 1-H and the C=O group in the 8 position exists in the 8-acetylpyrroloindole molecule. This bond also affects the mass-spectral fragmentation of the 8-acetyl derivative.

The aim of the present research was to determine the positions of the centers of electrophilic attack in the 1H,6H-pyrrolo[2,3-e]indole (I) molecule by means of the Vilsmeier–Haack reaction.

We have previously reported [2] that Vilsmeier formylation of 1H,6H-pyrrolo[2,3-e]indole gives its 3,8-diformyl derivative. In the present research we studied acetylation. The interest in this reaction is due to the fact that the complex based on dimethylacetamide (DMAA) and phosphorus oxychloride reacts only with sufficiently highly nucleophilic substances. Some indole-containing polycyclic systems virtually do not react with it [3], while the degree of reaction of indole is only 22% at 85°C [4].

The acetylation of 1H,6H-pyrrolo[2,3-e]indole was carried out in analogy with the acetylation of indole [4]. Four compounds that differed with respect to their R_f values and melting points but were similar in that their IR spectra contained bands of a C=O bond at 1620-1660 cm^{-1} were isolated from the reaction products. The structures of acetylpyrroloindoles II-V were established on the basis of data from the PMR, IR, UV, and mass spectra. The principal

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*See [1] for communication 4.

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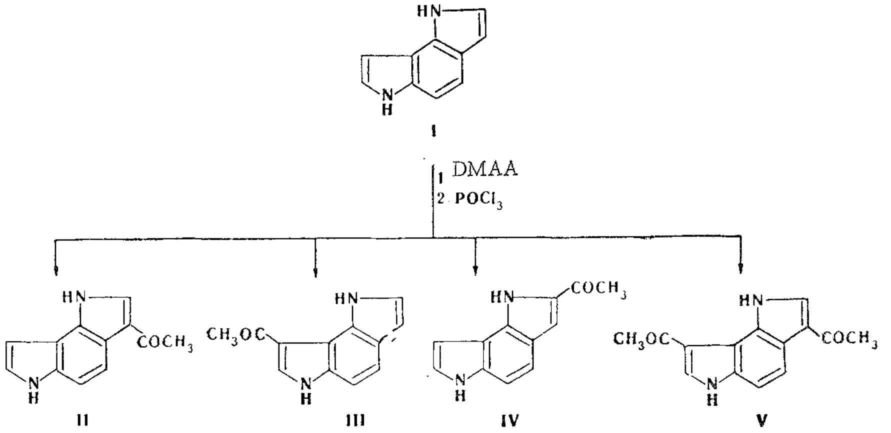
TABLE 1. Absorption Bands of the NH and C=O Groups of I-V

Compound	NH	C=O	Solvent
1H,6H-Pyrrolo[2,3-e]indole (I)	3375, 3495,	—	Chloroform
	3375, 3435	—	Mineral oil
3-Acetyl-1H,6H-pyrrolo[2,3-e]indole (II)	3325	1620	Mineral oil
8-Acetyl-1H,6H-pyrrolo[2,3-e]indole (III)	3300, 3405	1635	Chloroform
2-Acetyl-1H,6H-pyrrolo[2,3-e]indole (IV)	3330, 3430	1620	Mineral oil
3,8-Diacetyl-1H,6H-pyrrolo[2,3-e]indole (V)	3370	1645	Mineral oil

reaction product is 3-acetyl-1H,6H-pyrrolo[2,3-e]indole (II). During monitoring of the reaction by thin-layer chromatography (TLC) it was observed that 3-acetyl derivative II is formed at room temperature immediately after mixing the starting compounds. 8-Acetyl- (III) and 2-acetyl-1H,6H-pyrrolo[2,3-e]indole (IV) are formed when the reaction mixture is heated, while 3,8-diacetyl-1H,6H-pyrrolo[2,3-e]indole (V) is formed after a certain time. The overall yield of the reaction products is ~40%.



The formation of 2-acetylpyrroloindole IV may be the result of migration of an acetyl group during the reaction from the 3 position to the 2 position; rearrangement of the substituent from the 3 position to the 2 position [5] and from the 2 position to the 3 position [6] have been described. However, a genuine sample of 3-acetylpyrroloindole (II) remains unchanged under the reaction conditions; IV is consequently formed by direct substitution.

Data from the IR spectra of II-V are presented in Table 1. It is apparent from Table 1 that the absorption bands of the NH group for the acetylpyrroloindoles obtained appear at lower frequencies as compared with unsubstituted pyrroloindole.

The spectra of dilute solutions of 8-acetylpyrroloindole (III) contain two absorption bands of NH groups at 3300 and 3405 cm^{-1}, in contrast to the spectra of unsubstituted pyrroloindole I and its 3-acetyl derivative II (Table 1). This can be explained by the existence in III of an intramolecular hydrogen bond (IMHB) between the NH and C=O groups. We were unable to detect this sort of IMHB in 3,8-diacetyl-1H,6H-pyrrolo[2,3-e]indole (V) because of its slight solubility in inert solvents.

The introduction of acetyl groups in the pyrroloindole molecule gives rise to an increase in the intensities of the absorption maxima in the UV spectra and a bathochromic shift to the long-wave region of the spectrum; the latter is due to π—π^* polar transitions. The spectrum of 2-acetylpyrroloindole IV is characterized by a larger bathochromic shift as compared with the 3- and 8-substituted derivatives (Fig. 1).

The assignment of the signals in the PMR spectra of the acetylpyrroloindoles was accomplished by comparison with the spectrum of the starting heterocycle on the basis of disappearance of the signals and the spin—spin coupling constants (SSCC) of the corresponding protons.

The assignment of the lines in the PMR spectra also made it possible to observe different rates of deuteration of the protons of the NH groups in D_6-acetone. The rate of deuterium exchange is higher, the greater the acidity of the indicated protons, which depends on the position of the electron-acceptor substituents (Table 2).

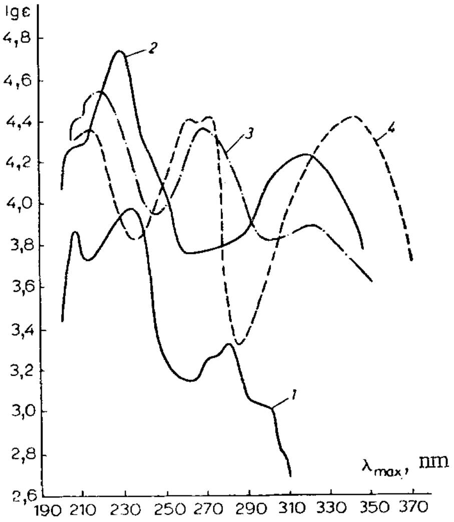


Fig. 1. UV spectra: 1) 1H,6H-pyrrolo[2,3-e]indole (I); 2) 3-acetyl-1H,6H-pyrrolo[2,3-e]indole (II); 3) 8-acetyl-1H,6H-pyrrolo-[2,3-e]indole (III); 4) 2-acetyl-1H,6H-pyrrolo[2,3-e]indole (IV).

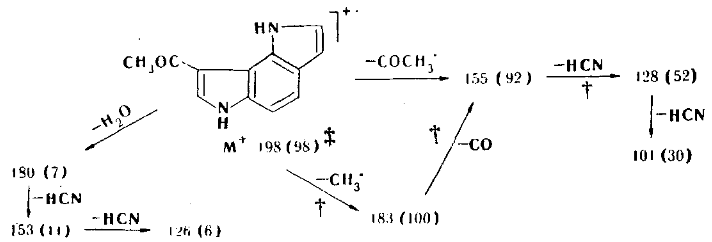
It follows from the PMR spectral data that the introduction of electron-acceptor substituents decreases the electron density primarily on the closest carbon atoms, which corresponds to the weak-field chemical shift of the corresponding protons.

In contrast to the spectra of unsubstituted pyrroloindole I and its 3-acetyl derivative II, differences between the chemical shifts of the protons of the NH groups are not observed in the PMR spectrum of 8-acetylpyrroloindole III (Table 2). This is probably due to the effect of the electron-acceptor substituent on 6-H, as well as to the participation of 1-H in an IMHB with the C=O group in the 8 position*; the latter conclusion is in agreement with data from the IR spectra of III (Table 1).

The molecular masses of II-IV found by mass spectroscopy are in agreement with the calculated values, and the character of the subsequent fragmentation does not contradict the proposed structures.

The character of the fragmentation of monoacetylpyrroloindoles II-IV under the influence of electron impact is common to all of the isomers [for example, see the fragmentation of 8-acetyl-1H,6H-pyrrolo[2,3-e]indole (III)].

The molecular ions (M^+) eliminate the CH_3 group bonded to the carbonyl carbon atom to give $[M - CH_3]^+$ fragment ions with mass 183, after which a molecule of CO is eliminated, and pyrroloindolyl cations with mass 155 are formed. This fragment ion is also formed by detachment of a $COCH_3$ group directly from M^+, which is characteristic for the fragmentation of unsymmetrical ketones [8].



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*One must also take into account the effect of the solvent.

†Metastable transitions.

‡These are the m/z values (relative intensities of the ion peaks in percent relative to the maximum ion peak).

TABLE 2. Chemical Shifts and Spin–Spin Coupling Constants in the PMR Spectra of I-V in d_6-Acetone

Compound	δ, ppm									*J*, Hz
	1-H	2-H	3-H	4-H	5-H	6-H	7-H	8-H	$COCH_3$	
I	10,3, br s	7,10, dd	6,46, dd	7,30, dd	7,12, dd	10,1, br s	7,18, dd	6,66, m	—	$J_{1,2}=2{,}4$; $J_{1,3}=2{,}1$; $J_{1,4}=0{,}8$; $J_{2,3}=3{,}0$; $J_{4,5}=8{,}9$; $J_{5,8}=0{,}7$; $J_{6,7}=2{,}5$; $J_{6,8}=2{,}2$; $J_{7,8}=3{,}0$
II	11,2, br s	8,04, d	—	8,12, br d	7,32, dd	10,5, br s	7,31, dd	6,74, dd	2,47, s	$J_{1,2}=3{,}0$; $J_{4,5}=8{,}8$; $J_{6,8}=1{,}9$; $J_{7,8}=2{,}9$; $J_{5,8}=0{,}8$; $J_{6,7}=2{,}0$
III	10,9, br s	7,30, dd	6,54, dd	7,46, br d	7,17, d	10,9, br s	8,16, d	—	2,56, s	$J_{1,2}=2{,}4$; $J_{2,3}=3{,}0$; $J_{1,3}=2{,}4$; $J_{4,5}=8{,}5$; $J_{6,7}=3{,}1$
IV	11,0, br s	—	7,34, d	7,38, br d	7,23, dd	10,5, br s	7,27, dd	6,97, m	2,49, s	$J_{1,3}=2{,}0$; $J_{4,5}=8{,}9$; $J_{5,8}=0{,}6$; $J_{6,8}=2{,}0$; $J_{7,8}=2{,}9$; $J_{6,7}=2{,}5$
V*	11,3†, br s	8,16, d	—	8,26, br d	7,37, d	11,3†, br s	8,26, d	—	2,50, s 2,58, s	$J_{1,2}=2{,}9$; $J_{4,5}=8{,}8$; $J_{6,7}=3{,}1$

*At 45°C.

†The 1-H and 6-H protons show up in the form of one broad signal ($\Delta H^{1}/_{2}$ = 30 Hz), and this made it impossible to determine the chemical shift of each of them.

In contrast to other isomers, the mass spectrum of 8-acetyl-1H,6H-pyrrolo[2,3-e]indole (III) contains a peak of $[M - 18]^+$ ions, which most likely corresponds to the loss of an H_2O molecule from M^+; this latter is possibly realized by a skeletal rearrangement of M^+. This fragmentation pathway is characterized by fragment ions with m/z values of 180, 153, 126.

The subsequent steps in the fragmentation of isomers II-IV are similar to those in the fragmentation of pyrroloindole I [9] with successive detachment of two HCN molecules or CN radicals.

A difference in the mass spectra of isomers II-IV is observed with respect to the stability of the molecular ions with respect to electron impact (the W_M values), as well as with respect to the relative intensities of the peaks of the common fragment ions (Table 3).

A comparison of the W_M values of II-IV shows that the 2 isomer has higher stability to electron impact than the 3 and 8 isomers, in agreement with the literature data on the mass spectra of 2- and 3-acetylindoles [7].

It is apparent from Table 3 that the stabilities of the $ArCO^+$ ($[M - CH_3]^+$) ions are higher in the case of the 3 isomer than in the case of the 2 isomer. This difference is also observed in the spectra of 2- and 3-acylindoles [7]; this is explained by additional stabilization of the $ArCO^+$ fragment ion in the case of the 3 isomer by direct p–π conjugation of the nitrogen atom with the carbonyl group. This sort of conjugation is less favorable in the case of the 2 isomer, since it involves disruption of the aromatic system of the benzene ring.

However, the large difference between the mass-spectral data for 3- and 8-acetylpyrroloindoles is surprising (Table 3). As compared with the 3 isomer, the molecular ion of the 8 isomer has higher stability with respect to electron impact, whereas the reverse is observed for the stabilities of the $ArCO^+$ ions. In our opinion, this is due to the existence of an IMHB in the 8-acetyl-1H,6H-pyrrolo[2,3-e]indole (III) molecule between the NH and C=O groups, which evidently may increase the stability of M^+ with respect to electron impact and, in addition, may destabilize the positive charge on the oxygen atom of the carbonyl group in the $ArCO^+$ ion.

It is apparent from Table 3 that the 8 isomer is the most stable isomer of the 2-, 3-, and 8-pyrroloindolyl cations. This is evidently associated with additional stabilization of the positive charge on the C_8 atom by the π electrons of the spatially close adjacent pyrrole ring.

Thus, in contrast to formylation, the acetylation of 1H,6H-pyrrolo[2,3-e]indole by the Vilsmeier method gives a mixture of mono- and disubstituted derivatives with great preponderance of the 3-substituted derivative. This can be explained, on the one hand, by the low electrophilicity of the reagent used, which is insufficient for reaction with the resulting monoacetyl derivatives, viz., aromatic systems with an electron-acceptor substituent [10-12], and, on the other, by the steric effect on the C_8 atom of the adjacent pyrrole ring.

TABLE 3. W_M Values and Relative Intensities of Some Fragment Ions with Respect to the Total Ion Current

Compound	W_M	$ArCo^+$ ($[M-CH_3]^+$)	$[M-COCH_3]^+$
3-Acetylpyrroloindole (II)	4,6	16,9	6,5
8-Acetylpyrroloindole (III)	11,0	11,2	10,3
2-Acetylpyrroloindole (IV)	13,2	14,9	6,3

Substitution in the 2 position in the acetylation of 1H,6H-pyrrolo[2,3-e]indole, which was not noted in the other electrophilic substitution reactions that we investigated [2], is possibly explained by the high temperature of acetylation with the participation of dimethylacetamide. However, attempts to obtain 2-substituted derivatives in other acylation reactions by raising the temperature were unsuccessful.

The formation of a 2-substituted product in the acetylation of 1H,6H-pyrrolo[2,3-e]indole by the Vilsmeier reaction, which does not have an analogy with indole, indicates the increased reactivity of pyrroloindole.

EXPERIMENTAL

Monitoring of the course of the reaction and the purity of the compounds and determination of the R_f values of the synthesized compounds were carried out on Silufol UV-254 plates. The UV spectra of solutions of the compounds in ethanol were recorded with a Specord spectrophotometer. The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer with NaCl and LiF prisms. The mass spectra were recorded with an MKh-1303 spectrometer with direct introduction of the samples into the ion source at an ionizing-electron energy of 50 eV. The PMR spectra were obtained with a Variant CFT-20 spectrometer (f_0 = 80 MHz); the accuracy in the measurement of the chemical shifts and the SSCC did not exceed ±0.01 ppm and ±0.1 Hz, and the internal standard was tetramethylsilane. Chromatography was carried out on silica gel.

Acetylation of 1H,6H-pyrrolo[2,3-e]indole. A 1.1-ml (12 mmole) sample of $POCl_3$ was added dropwise to cooled (to 3°C) dimethylacetamide, and the mixture was stirred at 20°C for 30 min. It was then cooled to 0°C, and a solution of 0.62 g (4 mmole) of I in 10 ml of dimethylacetamide was added slowly. The mixture was maintained at 75-80°C for 45 min, after which it was poured with uninterrupted stirring into 40 ml of water. The aqueous mixture was made alkaline to pH 12 with NaOH solution, and the precipitate was removed by filtration, washed with water until the wash waters were neutral, and dried to give 0.32 g (~40%) of product. The product was chromatographed with a column. The yields of the individual compounds were calculated as a function of the initial amount of the mixture applied to the column.

2-Acetyl-1H,6H-pyrrolo[2,3-e]indole (IV). This compound was eluted with petroleum ether—diethyl ether (5:2). The yield was 0.03 g (9%). The colorless crystals had mp 223-224°C and R_f 0.62 [benzene—ethyl acetate (3:2)]. UV spectrum, λ_{max} (log ε): 215 (4.36), 262 (4.40), 272 (4.42), and 342 nm (4.40). Found: C 73.2; H 5.3; N 14.1%. $C_{12}H_{10}N_2O$. Calculated: C 72.7; H 5.1; N 14.1%. Mass spectrum, m/z (%*): 198 (13.2), 183 (14.9), 155 (6.3), 128 (8.0), and 101 (2.3).

8-Acetyl-1H,6H-pyrrolo[2,3-e]indole (III). This compound was eluted with petroleum ether—diethyl ether (2:1). The yield was 0.06 g (195). The colorless crystals had mp 214.5-215.5°C and R_f 0.54 [benzene—ethyl acetate (3:2)]. UV spectrum, λ_{max} (log ε): 207 (4.40) shoulder, 220 (4.54), 269 (4.36), and 323 nm (3.89). Found: C 73.1; H 5.3; N 14.1%. $C_{12}H_{10}N_2O$. Calculated: C 72.7; H 5.1; N 14.1%.

3-Acetyl-1H,6H-pyrrolo[2,3-e]indole (II). This compound was eluted with petroleum ether—diethyl ether (3:5). The yield was 0.11 g (34%). The light-yellow crystals had mp 270-272°C (dec.) and R_f 0.44 [benzene—ethyl acetate (3:4)]. UV spectrum, λ_{max} (log ε): 205 (4.28) shoulder, 229 (4.74), and 317 nm (4.23). Found: C 72.5; H 5.2; N 14.2%. $C_{12}H_{10}N_2O$. Calculated: C 72.7; H 5.1; N 14.1%. Mass spectrum, m/z (%): 198 (4.6), 183 (16.9), 155 (6.5), 128 (4.3), and 101 (6.9).

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*Relative intensities in percent relative to the total ion current.

3,8-Diacetyl-1H,6H-pyrrolo[2,3-e]indole (V). This compound was eluted with petroleum ether–diethyl ether (3:5). The yield was 0.02 g (6%). The colorless crystals had mp 240-241°C and R_f 0.69 (ethyl acetate). Found: C 70.2; H 4.6; N 11.9%. $C_{14}H_{12}N_2O_2$. Calculated: C 70.0; H 5.0; N 11.7%.

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