methylindole hydrochloride in 5 ml of absolute alcohol, and the mixture was refluxed for 3 h. It was then cooled and filtered to give 0.1 g (30%) of diindolo[2,3-b;3',2'-e]pyridine (VII) with mp 290°C (from benzene) (mp 288-290°C [4]). The filtrate was evaporated, absolute ether was added to the residue, and the mixture was filtered to give 0.045 g (9%) of hydrochloride III.

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VINYLOGOUS ANHYDRO BASES OF PYRIDYLINDOLES

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The reaction of quaternary salts of pyridylindoles, the heterocyclic rings in which are separated by an ethylene grouping, with alkali was investigated. It was established that 2-(3-indolylvinyl)pyridinium and -quinolinium salts are converted to stable colored anhydro bases in a methanol solution of alkali.

The reaction of quaternary salts of pyridylindoles with alkali leads to stable colored anhydro bases [1, 2]. The anhydro bases of pyridylindoles proved to be extremely reactive compounds and extremely interesting subjects for diverse physicochemical studies.

In the present research we investigated the reaction of quaternary salts of pyridylindoles, the heterocyclic rings of which are separated by a vinyl grouping, with alkali. The possibility of the synthesis of anhydro bases from 2-(3-indolylvinyl)pyridine methiodide is mentioned in the literature [3], but no information regarding the reactivity and physicochemical properties of this compound is available. However, the study of the similarly constructed quaternary salts of sterically hindered p-hydroxystyrylpyridines in alkaline media has been limited to only their acid–base transformations [4].

2-(3-Indolylvinyl)pyridinium salts (I, II) are converted to the deeply colored anhydro bases (III, IV) in a methanol solution of alkali. The presence of a powerful chromophore in the form of a system of conjugated bonds makes their color considerably deeper as compared with the anhydro bases of pyridylindoles (407 and 530-550 nm, respectively) (see next page for scheme). Only deprotonation occurs when quaternary salts I and II are treated with alkali. The products of possible competitive dealkylation of the pyridine ring cannot be detected in even trace amounts. The same pattern was also observed in the synthesis of anhydro bases from quaternary salts of pyridylindoles [1, 2]. Quantum-chemical calculations [by the Pariser–Parr–Pople (PPP) method] show that the highest positive π-electron charge is concentrated on the indole nitrogen atom, which also determines the direction of nucleophilic attack by the hydroxide ion on the N–H group of the indole ring [1]. The presence of a vinyl grouping separating the heterocyclic rings does not change the electron balance of the cation or consequently, the direction of attack by the hydroxide ion. 2-(3-Indolylvinyl)quinoline methiodide (V) — a vinylog of 2-(3-indolyl)quinoline, the behavior of which under alkaline conditions differs somewhat from the behavior of V — reacts similarly with hydroxide ion. In fact, a small amount of dealkylation product is also formed along with the anhydro base in the reaction of 2-(3-indolyl)quinoline with alkali [2].

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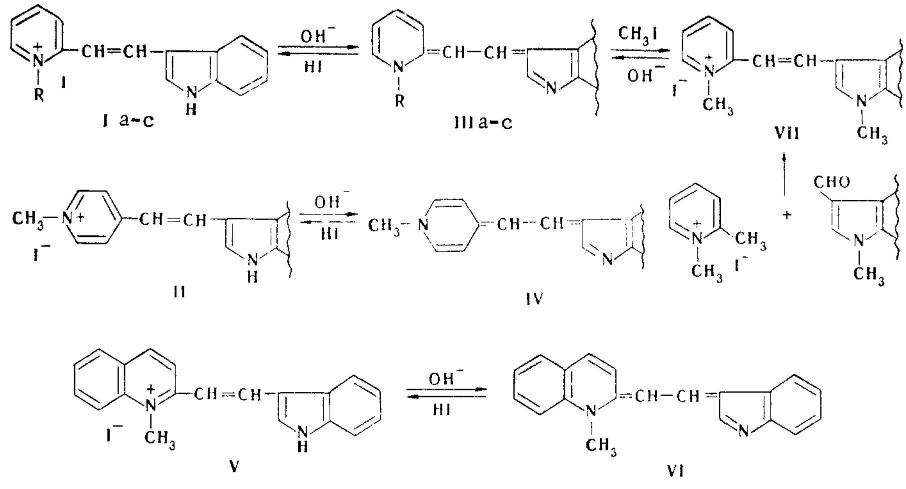
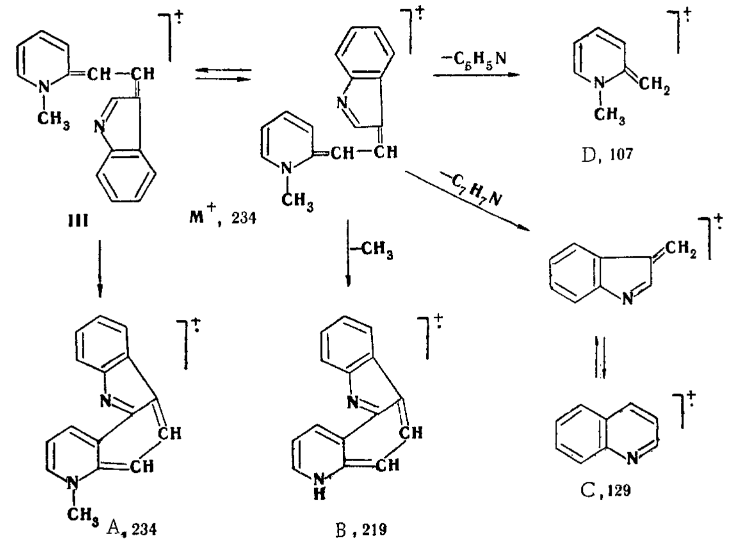


I, III a R = CH$_3$; b R = C$_6$H$_{13}$; c R = C$_{12}$H$_{25}$

The IR spectra of III, IV, and VI contain a series of intense absorption bands at 1610-1660 cm^{-1}, which belong to the stretching vibrations of C=C and C=N bonds. A molecular-ion peak (M$^+$) with m/e 234, which corresponds to the value calculated for C$_{16}$H$_{14}$N$_2$ [the isotope correction found for the (M + 1)$^+$ ion peak is 18.4 (the calculated value is 18.27)], is recorded in the mass spectrum of III. Conjugation between the hetaryl rings ensures high stability of the molecule with respect to electron impact (W$_M$ 24.3). The first acts in the fragmentation entail dehydrogenation of M$^+$. This can be due only to the formation of a new ring (the detachment of a teriary hydrogen atom involves β cleavage and leads to expansion of the pyridine ring to an azatropylium ring). The realization of the indicated processes suggests that M$^+$ has an S-cis-configuration; this is confirmed by detachment of a methyl group from M$^+$ (the elimination of a CH$_3$ group is not characteristic for N-methyl-substituted hetaryls [5]). Ions with cyclic forms (A and B) are formed in both cases; this is reflected in the appearance of rather intense peaks of doubly charged ions. Ordinary β cleavage relative to the heterocyclic rings in M$^+$ ensures the recording of fragment ions that have a quinoline structure and the structure of the corresponding pyridine residue. In this case cleavage of the central C—C bond is accompanied by migration of a hydrogen atom. A similar phenomenon was observed in the case of polymethine dyes [6] and sulfeneamide derivatives of benzothiazole [7]. The detachment of an HCN particle that is typical for N-heterocyclic compounds is realized from ions A and B. The observed fragmentation processes completely confirm the structure of III:



All of the synthesized anhydro bases are converted to the starting quaternary salts when alcohol solutions of them are treated with hydriodic acid, i.e., they undergo protonation at the indolenine nitrogen atom. With respect to their properties, III, IV, and VI were found

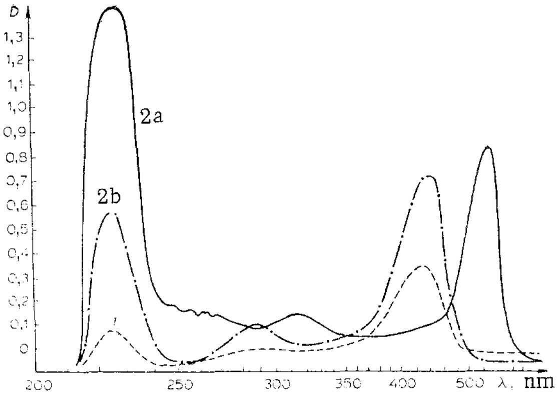


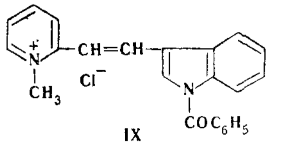
Fig. 1. UV spectra: 1) 1-methyl-2-(3-indolylvinyl)-pyridinium iodide; 2) 1-methyl-2-(2-indolenylidene-3-ethylidene)-1,2-dihydropyridine; a) in 0.01 N methanolic KOH; b) in water.

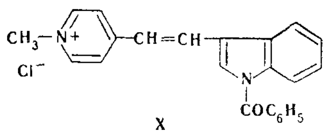
to be very similar to the anhydro bases of pyridylindoles. Their basicities are characterized by pK_a values of 10.00 to 11.17, i.e., they are very strong bases, like the previously described substances [1, 2]. They are hydrated extremely readily in aqueous solutions (when they are dissolved in water or in aqueous alcohol, the violet color of the anhydro bases changes to the bright-yellow color characteristic for the starting quaternary salts).

The hydroxide ion can probably form a covalent bond with the pyridine ring, thereby forming a pseudobase; however, the ionic form evidently predominates in polar solvents. Similar behavior of anhydro bases in aqueous solutions was noted previously [8]. The UV spectra of aqueous solutions of anhydro bases III, IV, and VI, which are completely similar to the spectra of the starting quaternary salts, also constitute evidence in favor of this. We were able to record the spectra of III, IV, and VI only in alkaline media (an aqueous alcohol solution of KOH). They are characterized by a long-wave absorption band with a maximum at 530-550 nm (Fig. 1). This is ~100 nm higher as compared with the quaternized structures. In the determination of the pK_a values of the anhydro bases by a potentiometric method the second sharp pH change on the titration curve from pK_a 6.00 to 7.80 corresponds to their hydrated forms. The first pH changes corresponds to the anhydro bases (pK_a 10.00-11.17). A comparison of the pK_a values of the anhydro bases shows that the character of the substituent attached to the pyridine nitrogen atom has virtually no effect on the basicity, whereas annellation of the benzene ring with the pyridine ring in VI reduces the basicity by approximately one unit. When the concentration of the solution to be titrated is decreased by one order of magnitude, one of the inflections, which corresponds to the anhydro base, vanishes, and only its hydrated form exists in solution.

Like protonation, the alkylation of anhydro bases Ia and II takes place at the indolenine nitrogen atom, and this leads to the formation of (1-methyl-3-indolylvinyl)pyridinium salts, viz., 1-methyl-2- (VII) and 1-methyl-4-(1-methyl-3-indolylvinyl)pyridinium (VIII) iodides, respectively.

The benzoylation of anhydro bases Ia and II proceeds similarly — benzoyl derivatives involving the indolenine nitrogen atom (IX and X, respectively) are formed.


IX


X

The ease of alkylation and acylation of the indolenine nitrogen atom in such systems opens up the possibility for the preparation of an entire set of indole nitrogen atom-substituted indolylvinylpyridinium salts.

One might have assumed that detachment of a proton from the α-carbon atom of the vinyl bridge would be possible as a result of the action of alkali on a quaternary salt of the VII type. However, when salt VIII was treated with an alcohol solution of alkali, only dealkylation to give anhydro base III occurred. It is important that of the two possible dealkylation

TABLE 1. Indolylvinylpyridine Derivatives

Compound	mp, °C (methanol)	pK_a	Found, %			Empirical formula	Calculated, %			Yield, %
			C	H	N		C	H	N	
IIIb	84—86	10,70	82,6	7,5	9,5	$C_{21}H_{24}N_2$	82,9	7,9	9,2	66
IIIc	99—100	11,17	83,2	9,1	7,1	$C_{27}H_{36}N_2$	83,5	9,3	7,2	57
IV	203—204	11,12	82,0	6,3	12,3	$C_{16}H_{14}N_2$	82,1	6,0	12,0	93
VI	128—130	10,00	84,8	5,9	9,8	$C_{20}H_{16}N_2$	84,5	5,6	9,9	44
VIII	252—253	—	54,3	4,3	7,2	$C_{17}H_{17}IN_2$	54,2	4,6	7,4	57
IX	256—258	—	73,4	5,0	7,3	$C_{23}H_{19}N_2OCl$	73,7	5,1	7,5	91
X	261—262	—	73,6	5,3	7,2	$C_{23}H_{19}N_2OCl$	73,7	5,1	7,5	85

variants (dealkylation of the pyridine or indole ring), only the second possibility was realized. This is evidently associated with localization of the high positive π-electron charge on the indole ring nitrogen atom as compared with the pyridine ring nitrogen atom.

EXPERIMENTAL

The IR spectra of chloroform solutions and mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The UV spectra of solutions of the compounds in methanol, water, 10% HCl, and 10% KOH were recorded with a Specord UV-Vis spectrophotometer. The mass spectra were obtained with a Varian MAT-311 spectrometer at an accelerating voltage of 3 kV, a cathode emission current of 300 mA, an ionizing voltage of 75 eV, and an ion-source temperature of 250-300°C. The potentiometric determination of the pK_a values of the bases was carried out with a pH-340 apparatus by titration of solutions of them in aqueous methanol (c 10^{-2} and 10^{-3} mole/liter; the methanol content was 10%) with a 0.1 N solution of HCl. The pK_a value was assumed to be equal to the pH at the half-neutralization point.

1-Methyl-2-(2-indolenylidene-3-ethylidene)-1,2-dihydropyridine (IIIa). A 5-g (0.014 mole) sample of 1-methyl-2-(3-indolylvinyl)pyridinium iodide was heated in 10 ml of a saturated methanol solution of KOH until it dissolved completely, and the solution was then refluxed for 1-2 min. It was then cooled, and the precipitated crystals were removed by filtration and recrystallized from methanol to give 3.1 g (93%) of a product with mp 175-175.5°C. IV spectrum, λ_{max} (log ε): 227 (5.60), 310 (3.67), and 530 nm (4.50). IR spectrum, ν: 1610 (C=C); 1660 cm^{-1} (C=N). Mass spectrum, m/e: 235 (18.4); 234 (100.0); 233 (44.9); 232 (24.0); 231 (16.8); 220 (16.3); 219 (60.2); 218 (22.2); 206 (7.1); 192 (7.0); 191 (12.4); 129 (33.6); 128 (15.8); 117.5 (3.30); 117 (18.6); 116.5 (11.0); 115.5 (4.0); 109.5 (14.6); 109 (8.8); 107 (25.8); 106 (13.3); 102 (6.5); 93 (5.6); 92 (10.1); 91 (6.3); 80 (10.4) 79 (12.4); 78 (10.3). Found: C 82.1; H 6.3; N 12.3%. $C_{16}H_{14}N_2$. Calculated: C 82.0; H 6.0; N 12.0%.

Other anhydro bases, the principal characteristics of which are presented in Table 1, were similarly obtained.

1-Methyl-2-(1-methyl-3-indolylvinyl)pyridinium Iodide (VII). A) A mixture of 0.7 g (3 mmole) of 1-methyl-2-(2-indolenylidene-3-ethylidene)-1,2-dihydropyridine and 0.4 g (3 mmole) of methyl iodide in 10 ml of methanol was refluxed for 10 min, and the resulting precipitate was removed by filtration and recrystallized from methanol to give 0.7 g (62%) of a product with mp 264-265°C. UV spectrum, λ_{max} (log ε): 225 (3.94), 290 (3.15), and 438 nm (4.10). Found: C 54.1; H 4.4; I 33.5; N 7.2%. $C_{17}H_{17}IN_2$. Calculated: C 54.3; H 4.5; I 33.8; N 7.4%.

B) A mixture of 2.34 g (0.01 mole) of α-picoline methiodide, 1.59 g (0.01 mole) of 1-methyl-3-formylindole, and 1 ml of piperidine in 20 ml of ethanol was refluxed for 30-40 min, and the resulting precipitate was removed by filtration and recrystallized from ethanol to give 3.0 g (80%) of a product with mp 264-265°C. No melting-point depression was observed for a mixture of this product with a sample of the product obtained by method A.

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EFFECT OF AZA SUBSTITUTION ON THE FORMATION OF ANHYDRO BASES OF QUINOLYLINDOLES

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The reaction of quaternary salts of 3-(2-quinoxalinyl)indoles with hydroxylamine was investigated. It was established that the presence of a second pyridine nitrogen atom in the ring increases the positive π-electron charge on the nitrogen atom of the quinoxaline ring and, as a consequence of this, markedly increases the contribution of dealkylation.

The NH group of indole is deprotonated by the action of quaternary salts of 3-pyridylindoles, and stable anhydro bases of pyridylindoles are formed [1]. As a result of annellation of the pyridine ring, two competitive processes, viz., deprotonation of the NH group and dealkylation of the pyridine nitrogen atom, take place in the reaction of quaternary salts of benzopyridylindoles with alkali [2]. The ratio of the products of these processes cannot be explained by steric factors, and the direction of the reaction is primarily due to the distribution of the changes of the corresponding cations [2].

Since the introduction of a nitrogen atom into the molecule changes the electron density distribution and may change the ratio of the yields of these competitive processes, it seems of interest to investigate the effect of aza substitution in 3-(2'-quinolyl)indole methiodide (I) on the direction of the reaction of the quaternary salt with hydroxide ion; as in [3], in the quantum-chemical calculations we will describe the effect of aza substitution within the framework of the bonded variant of perturbation theory in the self-consistent-field (SCF) MO LCAO method.

Since the ratio of the indicated competitive processes is determined by the difference in the π-electron charges on the nitrogen atoms in the indole and pyridine rings [2], the effect of aza substitution on the direction of this reaction in the I cation can be described within the framework of the approach being developed here by the difference in the atom—atom mutual polarizabilities, viz., $\pi_{i1}-\pi_{i1'}$, where i is the position at which substitution takes place. The 1 position corresponds to the indole nitrogen atom, while the 1' position corresponds to the quinoline nitrogen atom. The results of calculation of these indexes are presented in Table 1, from which it is apparent that the greatest change in the magnitude of the π-electron charge on the nitrogen atom in the quinoline fragment of the molecule is produced by aza substitution of the $C_{4'}$ atom; the charge on the nitrogen atom in the indole ring remains virtually unchanged. The π-electron positive charge on the nitrogen atom in the quinoline ring decreases in the case of aza substitution of the carbon atoms in the 6, 5, 3, and 6' positions, whereas the charge on the nitrogen atom in the indole ring increases or remains unchanged. The increase in the charge on the nitrogen atom in the quinoline ring in the case of aza substitution of the C_2 atom is compensated by a pronounced increase in the charge on the nitrogen atom in the indole ring. It follows from Table 1 that the degree of dealkylation

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