2-(1-Hydroxyethyl)-5-methylindole-3-carboxylic Acid (Va). In one portion, 0.2 g (2.7 mmole) of sodium tetrahydroborate was added to a solution of 1.09 g (5 mmole) of 2-acetyl-5-methylindole-3-carboxylic acid in 25 ml of DMFA, and the mixture was stirred for 30 min. Then it was poured into water, impurities were removed by extraction with ether, the aqueous solution was acidified with 5% sulfuric acid, the oil that separated out was extracted with ether (14 × 100 ml), the extract was dried with anhydrous sodium sulfate and was evaporated, and the residue was crystallized from a mixture of benzene and acetone. Yield 0.76 g (69%), mp 189-190°C. Found, %: C 66.0, H 6.2, H 6.2. $C_{12}H_{11}NO_3$. Calculated, %: C 65.7, H 6.0, N 6.4.

5-Bromo-2-(1-hydroxyethyl)indole-3-carboxylic Acid (Vd). This was obtained in a similar manner to (Va). Yield 75%, mp 243°C. Found, % C 46.8, H 3.6, N 4.8, Br 28.0. $C_{11}H_{10}BrNO_3$. Calculated, % C 46.5, H 3.5, N 4.9, Br 28.1.

5-Chloro-2-(1-hydroxyethyl)indole-3-carboxylic Acid (Ve). This was obtained by a similar procedure. Yield 67%, mp 203°C. Found, %: C 55.4, H 4.4, N 5.7, Cl 15.0. $C_{11}H_{10}ClNO_3$. Calculated, %: C 55.1, H 4.2, N 5.8, Cl 14.8.

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THE DUAL REACTIVITY OF 1,2-DISUBSTITUTED DIHYDRO-N-HETEROAROMATIC SYSTEMS.

5.* A CASE OF AN UNUSUALLY EASY HETEROLYSIS OF THE INTERNUCLEAR BOND IN 2-(INDOL-3-YL)-1-METHYL-1,2-DIHYDROQUINOLINE AND ITS ANALOGS†

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UDC 547.751.831.832.833.541.573

The reaction of the 1-methylquinolinium cation with the indole anion has given a crystalline adduct of saltlike structure forming an ion pair in polar solvents and 2-(indol-3-yl)-1-methyl-1,2-dihydroquinoline in nonpolar solvents.

The aromatization of substituted dihydroheteroaromatic compounds takes place with the loss of the hydride-mobile hydrogen atom or of a substituent in the form of a carbanion as the result of the heterolysis of C—H or C—C bonds under the action of electrophiles. An alternative is a stepwise process of the one-electron oxidation of the dihydro derivatives to the corresponding radical cations with the subsequent splitting out of hydrogen or a substituent in the form of a radical [3-5]. Other mechanisms of bimolecular aromatization reactions are also widely discussed [1, 3-5]. A hypothesis has recently been put forward of the possibility of monomolecular aromatization reactions if, in polar solvents, they are preceded by a heterolytic dissociation of dihydroheteroatomic compounds with the formation of ion pairs [5]. This apparently explains the appearance of spontaneous aromatization and also of transhetarylation reactions [6], the nucleophilic alkylation of dihydroheteroaromatic compounds [7], and other reactions [5]. Examples of such dissociation are known. For instance, in

*For communication 4, see [1].
†For a preliminary communication on this, see [2].

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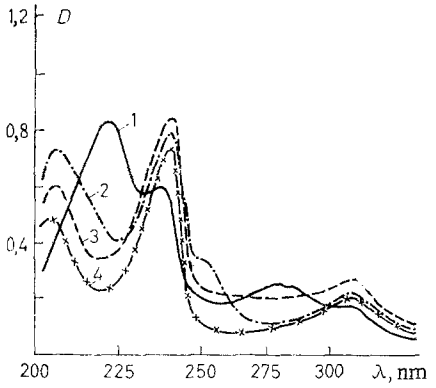


Fig. 1

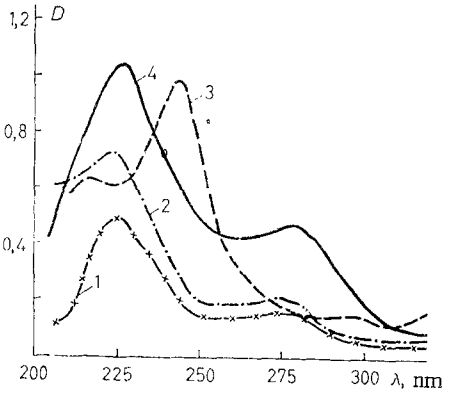


Fig. 2

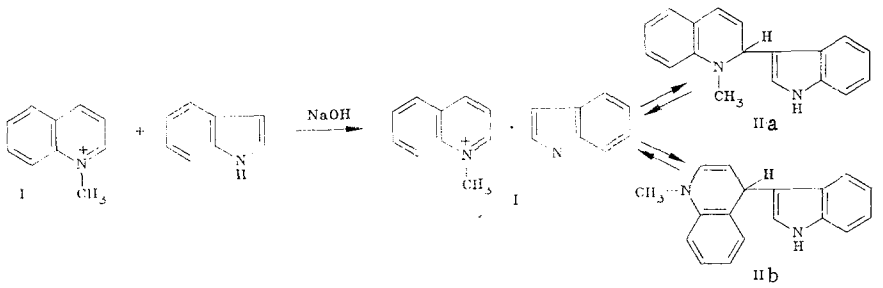
Fig. 1. UV spectra (in CH_3CN): 1) 2-(indol-3-yl)-1-methyl-1,2-dihydro quinoline; 2) 1-methylquinolinium iodide; 3) 1-methylquinolinium 1-acetonyl-2,4,6-trinitrocyclohexadienate; 4) 1-methylquinolinium perchlorate.

Fig. 2. UV spectra: 1) 2-(indol-3-yl)-1-methyl-1,2-dihydroquinoline in heptane (1) and in ether (2); 3) 1-methyl-2-phenyl-1,2-dihydroquinoline in CH_3CN; 4) 1-benzoyl-2-(indol-3-yl)-1,2-dihydroquinoline in CH_3CN.

polar solvents 2-trichloromethyl-1-dichlorobenzyl-1,2-dihydropyridine forms an ion pair with a pyridinium cation and a trichloromethyl anion [8].

The heterolysis of dihydroaromatic compounds is a reaction that is the reverse of nucleophilic addition to heteroatomic cations. In accordance with this, in our opinion, dissociation should be facilitated for N-alkyl derivatives and be hindered for N-acyl derivatives. For example, the reduction potentials, $E_{1/2}$, for N-acyl cations are $-(0.4-0.5)$ V [9], and for N-alkyl cations $E_{1/2}$ $-(0.8-1.0)$ V [10]. The influence of the nature of N-substituents on the electrophilicity of cations is discussed in our previous papers [11, 12].

To confirm these hypotheses we have studied the structures and reactions of the products of nucleophilic addition of the indole anion to the N-methylpyridinium, -quinolinium, and -isoquinolium cations and have compared them with the corresponding compounds obtained in reactions with N-acyl cations. It is known that the reaction of quinoline methiodide with indole in methanol in the presence of sodium methanolate leads to 2-(indol-3-yl)quinoline methiodide [13], probably formed as the result of the aromatization of the intermediate product of nucleophilic addition under the action of an excess of quinolinium cation, as frequently takes place in hetarylation reactions [12]. On the reaction of quinoline methiodide with indole in the presence of alkali we succeed in isolating an addition product in the form of the individual crystalline compound (I):



According to its IR spectrum (in KBr tablets), compound (I) in the solid state consisted of a salt of the 1-methylquinolinium cation and the indole anion. All the characteristic bands of the quinolinium cation were observed in the IR spectrum in the 1580, 1520, 1230, 1160, 800, and 770 cm^{-1} regions (as in the spectrum of quinoline methiodide) and the band of the stretching vibrations νNH in the 3400-3500 cm^{-1} region was absent. In a polar solvent (acetonitrile) the IR spectrum scarcely changed, since compound (I) was present in the form of an ion pair or as free ions. The UV spectrum contained the characteristic absorption bands of the 1-methylquinolinium cation (233 and 312 nm) (Fig. 1), like the spectra of salts of the

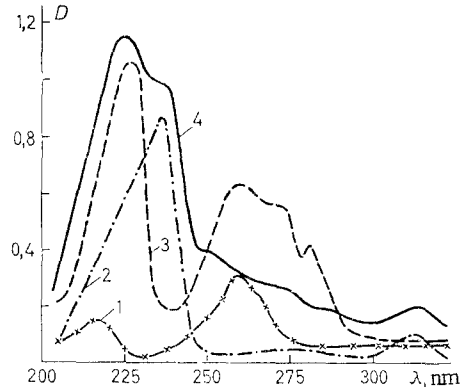
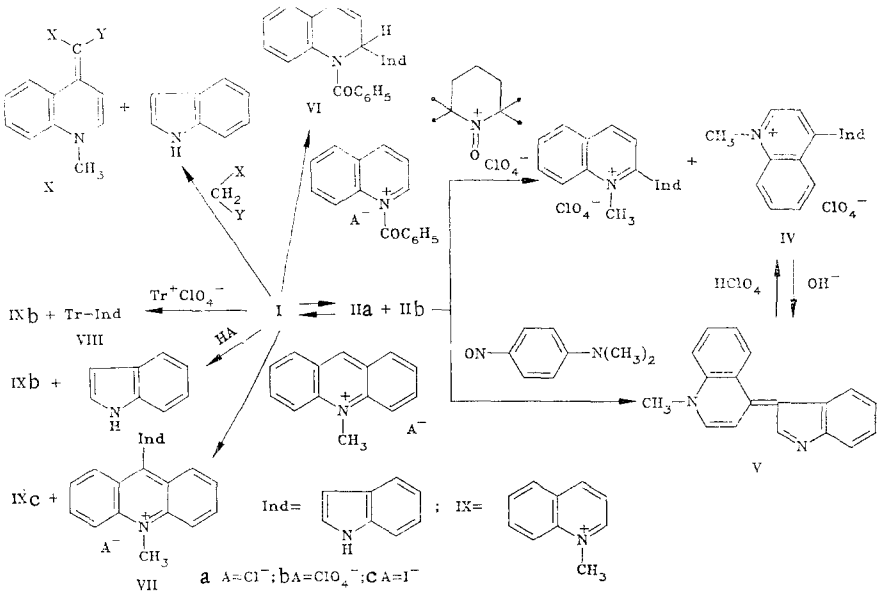


Fig. 3. UV spectra (in CH_3CN): 1) 1-methylpyridinium perchlorate; 2) N-methylisoquinolinium perchlorate; 3) 2-(indol-3-yl)-1-methyl-1,2-dihydropyridine; 4) 1-(1-indol-3-yl)-2-methyl-1,2-dihydroisoquinoline.

1-methylquinolinium cation with inorganic (ClO_4^-, I^-) and organic (Yanovskii's anionic σ-complex) anions. In nonpolar solvents (heptane, ether) these bands in the UV spectrum disappeared and the spectrum became similar to those of 1-benzoyl-2-(indol-3-yl)-1,2-dihydroquinoline and 1-methyl-2-phenyl-1,2-dihydroquinoline (Fig. 2). In nonpolar solvents such as toluene, the νNH band of indole appeared in the IR spectrum in the 3450 cm^{-1} region, which showed the formation of the covalent form (IIa) or (IIb). The existence of an equilibrium of the ionic and covalent forms (I) $\rightleftarrows$ (II) in solutions was also confirmed by an investigation of the electrochemical behavior of the adduct (I) with the aid of a rotating platinum disk electrode with a ring. In acetonitrile, compound (I) was reduced at the potential $E_{1/2}$ = −0.84 V, like the 1-methylquinolinium cation, and was oxidized at $E_{1/2}$ = +0.82 V — approximately the same potential as that at which 1-methyl-2-phenyl-1,2-dihydroquinoline is oxidized ($E_{1/2}$ = +0.70 V). The ratio of the ionic (I) and covalent (II) forms in acetonitrile was approximation 1:10.

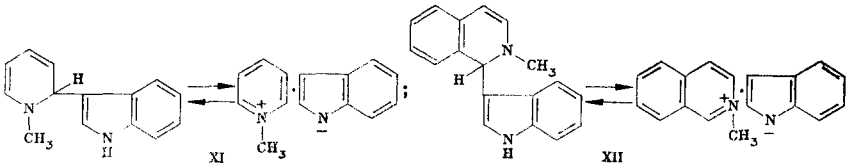
The presence of both forms (I) and (II) in acetonitrile solution was confirmed by many reactions. Thus, mineral acids decomposed compound (I) to indole and salts of 1-methylquinolinium with the anions of the acid used. Various CH acids the pK_a values of which were higher than pK_a of indole, and also alcohols, amines, and other proton-donating compounds decomposed the adduct (I) into indole and a new derivative of the quinolinium cation, either of the ionic form of type (I) or the covalent form of type (II) (so-called transhetarylation reaction [5]). The organic cations triphenylcarbenium, acylium, 1-methylacridinium, N-benzoylquinolinium, N-benzoylisoquinolinium, aryldiazonium, and others, formed with adduct (I) the 1-methylquinolinium cation and the corresponding β-substituted indole derivative (so-called nucleophilic alkylation reaction [7]). It must be mentioned that adduct (I) is active in these reactions and is similar to an indole Grignard reagent, so that it may find use in the preparative chemistry of indole for introducing electrophilic agents into the indole nucleus. The presence of the covalent form (II) in solutions was evidenced by many reactions.



Thus, in the reaction with 2,2,6,6-tetramethyl-1-oxo-tetramethylpiperidinium perchlorate, as a result of the aromatization of form (II) we obtained 2- and 4-(indol-3-yl)-1-methylquinolinium perchlorates (III) and (IV), and with p-nitrosodimethylaniline we obtained the anhydrobase (V), the reaction which with $HClO_4$ formed the salt (IV).

The structures of compounds (III-X) were shown by comparison with authentic samples of known structure.

The reaction of pyridine and isoquinoline methiodides with the indole anion under similar conditions likewise formed saltlike adducts but we were unable to isolate them in the form of crystalline compound. The UV spectra in acetonitrile (Fig. 3) showed not only the absorption bands of the cations (233 and 331 nm for 1-methylisoquinolinium and 265 and 259 nm for 1-methylpyridinium) and of the indole anion (223 and 288 nm) but also those of the covalent forms of a substituted 1,2-dihydropyridine (XI) and a dihydroisoquinoline (XII):



The corresponding N-acyl derivatives of indolyldihyropyridine, quinoline, and isoquinoline are extremely stable [14] and do not reveal the presence of ions in solutions in acetonitrile and other solvents with a high ionizing capacity.

As was found, the degree of electrolytic dissociation of the adducts (I), (XI), and (XII) in acetonitrile determined with the aid of a measurement of the electrical conductivities of the solutions of these compounds was vanishingly small, the specific electrical conductivities of the solutions and of the pure solvent being approximately the same ($\sigma_{solution}$ $5.03 \cdot 10^{-7}$, $\sigma_{acetonitrile}$ $1.77 \cdot 10^{-7}$ $\Omega \cdot cm^{-1}$).

Thus, the N-methylpyridinium, -quinolinium, and -isoquinolinium cations, unlike the corresponding N-acyl cations, form with the indole cation ion pairs that change in nonpolar solvents into the covalent 1,2-dihydro derivatives, which are the more stable the more pronounced are the electrophilic properties that the corresponding heteroaromatic cation possesses, and the electrophilicity of the cations can be increased not only by the introduction of electron-accepting substituents into the nucleus, which is sometimes very complicated, but also by their addition to the heteroatom.

EXPERIMENTAL

IR spectra were taken on a Specord 75 IR spectrometer in toluene and acetonitrile and in KBr tablets, and electronic spectra on a Specord UV-vis instrument. The construction and characteristics of the rotating platinum electrode with a ring and the method of recording the voltamperograms and calculating the number of electrons transferred has been described by Subbotin et al. [15]. The electrical conductivity of a solution of 2-(indol-3-yl)-1-methyl-1,2-dihydroquinoline was measured at a constant current in a measuring cell with plane-parallel electrodes and a protecting ring.

2-(Indol-3-yl)-1-methyl-1,2-dihydroquinoline (I, II). To 1.36 g (5 mmole) of 1-methylquinolinium iodide in 10 ml of water–acetonitrile (1:1) were added 0.59 g (5 mmole) of indole and 0.5 ml of 10 N NaOH. After 30 min, the precipitate was filtered off and it was washed with dry acetonitrile and with ether. The yield was 1.1 g (85%), mp 140-142°C (decomp.). Found, %: C 82.7, H 6.3, N 10.8. Calculated, %: C 83.1, H 6.3, N 10.8.

Reaction of Adduct (I) with Perchloric Acid. A solution of 0.26 g (1 mmole) of the adduct (I) in chloroform was treated with 0.15 ml of 55% perchloric acid, and then with 50 ml of ether and the resulting precipitate was filtered off. The yield of 1-methylquinolinium perchlorate (IXb) was 0.23 g (97%), mp 120-121°C (from ethanol) [10]. When the filtrate was evaporated, 0.11 g (98%) of indole was obtained.

Reaction of Adduct (I) with Triphenylmethyl Perchlorate. A solution of 0.85 g (2.5 mmole) of triphenylmethyl perchlorate in 5 ml of acetonitrile was treated with 0.65 g (2.5 mmole) of the adduct (I) in 3 ml of methylene chloride. After 1 h, the mixture was poured into 50 ml of ether and the precipitate was filtered off. The yield of 1-methylquinolinium

perchlorate (IXb) was 0.6 g (100%), mp 120-121°C (from ethanol). The filtrate was evaporated, giving 0.6 g (66%) of (indol-3-yl)triphenylmethane, mp 210-211°C (from n-butanol) [16].

Interaction of Adduct (I) with N-Benzoylisoquinolinium Chloride. To a solution of N-benzoylisoquinolinium chloride obtained from 0.39 g (3 mmole) of isoquinoline and 0.21 g (1.5 mmole) of benzoyl chloride [14] was added 0.39 g (1.5 mmole) of the adduct (I). After 1 h, the reaction mixture was poured into water and the precipitate was filtered off. The yield of N-benzoyl-1-(indol-3-yl)-1,2-dihydroisoquinoline was 0.45 g (90%), mp 228°C (from propanol) [13]. The aqueous solution was evaporated and the residue was washed with ether, to give 1-methylquinolinium chloride. Yield 0.2 g (84%), mp 125-126°C (from ethanol) [17].

Similarly, a N-benzoylquinolinium salt and the adduct (I) gave N-benzoyl-2-(indol-3-yl)-1,2-dihydroquinoline (VI) with a yield of 0.1 g (20%); mp 200-201°C (from propanol) [13].

Interaction of Adduct (I) with N-Methylacridinium Iodide. A solution of 0.64 g (2 mmole) of N-methylacridinium iodide in 3 ml of acetonitrile was treated with 0.26 g (1 mmole) of the adduct (I). After 3 h, the precipitate that had formed was filtered off. This gave 0.35 g (80%) of 9-(indol-3-yl)-N-methylacridinium iodide with mp 279°C (from acetonitrile) [7].

Reaction of Adduct (I) with Cyanoacetic Ester. A solution of 0.26 g (1 mmole) of the adduct (I) in 5 ml of cyanoacetic ester was boiled for 5 h. After the excess of cyanoacetic ester had been distilled off, 50 ml of ether was added. The precipitate was filtered off to give 0.06 g (23%) of 4-(α-carboxy-α-cyanomethylene)-1-methyl-1,4-dihydroquinoline, mp 180-181 °C from ethanol [18].

Reaction of 2,2,6,6-Tetramethyl-1-oxopiperidinium Perchlorate with Adduct (I). A solution of 0.38 g (1.5 mmole) of the oxo ammonium salt in 5 ml of dry acetonitrile was treated with 0.26 g (1 mmole) of the adduct (I). After 30 min, the reaction mixture was poured into 50 ml of ether and the precipitate was filtered off. This gave 0.33 g (93%) of a mixture of 2(4)-(indol-3-yl)-1-methylquinolinium perchlorates.

4-(Indol-3-ylidene)-1-methyl-1,4-dihydroquinoline (V). A solution of 0.26 g (1 mmole) of the adduct (I) in ethanol was treated with 0.08 mg (0.5 mmole) of p-nitrosodimethylaniline and 0.1 ml of 10 N NaOH. After 15 min, the reaction mixture was poured into water and the resulting mixture was cooled to 0°C. The yield of product was 0.24 g (94%), mp 176-178°C (acetonitrile–ether). Found, %: C 83.6, H 5.1, N 10.6. Calculated, %: C 83.7, H 5.4, N 10.8.

4-(Indol-3-yl)-1-methylquinolinium Perchlorate (IV). A solution of 0.26 g (1 mmole) of the dihydroquinoline (V) in 5 ml of acetonitrile was treated with 0.1 ml of 55% perchloric acid. The resulting precipitate was filtered off. Yield 0.32 g (90%), mp 310°C (from acetonitrile). Found, %: C 60.0, H 4.0, N 7.7. Calculated, %: C 60.2, H 4.1, N 7.8.

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PYRROLOINDOLES.

11.* ELECTROPHILIC SUBSTITUTION IN THE 1H,7H-PYRROLO[3,2-f]INDOLE SERIES

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UDC 547.759,5:541.63:543.422.25'4'6

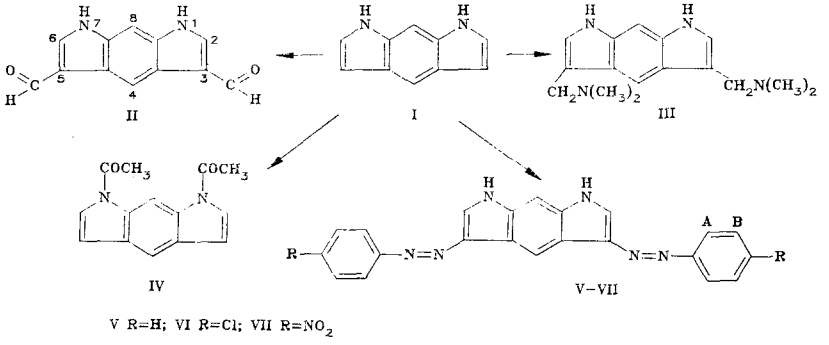
It has been shown with the aid of quantum-chemical calculation by the CNDO/2 method that the reaction centers of electrophilic attack in the molecule of 1H,7H-pyrrolo[3,2-f]indole are positions 3 and 5. These results are in agreement with those of studies of electrophilic substitution reactions.

Electrophilic substitution reactions of the 1H,7H-pyrrolo[3,2-f]indole (I) which we synthesized previously [2] have been investigated. The Vilsmeier, Mannich, azo-coupling, and acetylation reactions have been performed.

In order to determine the main reaction centers in electrophilic substitution reactions in the heterocycle (I), a quantum-chemical calculation of its molecule has been made by the SCF MO method in the CNDO/2 approximation [3] for a planar structure and the geometric parameters of the indole ring [4]. The results of the quantum-chemical calculations are presented in Fig. 1 in the form of a molecular diagram (the total electron densities are shown with the π-electron densities in parentheses).

It can be seen from the molecular diagram of the pyrroloindole (I) that the nature of the electron density distribution of the indole ring is retained in its molecule. The greatest electron densities, both the total (σ + π) and the π-electron densities, are concentrated in the β positions of the pyrrole nuclei. Consequently, in electrophilic substitution the process should take place at positions 3 and 5.

The formylation of the pyrroloindole (I) using the Vilsmeier complex [5] in a ratio of 1:3 led to 3,5-diformyl-1H,7H-pyrrolo[3,2-f]indole (II). When compound (I) was aminomethylated in acetonitrile with the crystalline Mannich reagent at room temperature, 3,5-bisdimethyl-



*For communication 10, see [1].

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