is dissolved in 95% alcohol and the solution is brought up to the mark with ethanol. Portions (0.1, 0.2, 0.4, 0.6, 0.8, and 1 ml) of the solution obtained are transferred into 10ml volumetric flasks, and into each flask 95% ethanol is added up to a total volume of 2 ml. Then, 5 ml of an ammoniacal buffer solution are added, and the volume of the solution is brought up to the mark with distilled water. The solutions are placed in turn into a polarographic cell, and the procedure is carried out as described above. A calibration graph is constructed by plotting concentrations of I in the polarographic solution (in g/ml) on the abscissa and the corresponding wave heights (in nm) on the ordinate.

When constructing the calibration graph, compound I which has been purified by reprecipitation from its solution in methylene chloride by CCl₄ (at a 1:10 ratio of solvents) is used. The melting point of a pure sample of I is 123-124°C and the content of the principal substance is 100%.

<u>Preparation of Ammoniacal Buffer Solution.</u> A 13.5-g portion of NH₄Cl (cp) is placed in a 250-ml volumetric flask, 87 ml of 25% NH₃ are added, and the solution is brought up to the mark with distilled water.

<u>Dipicolindiamide (III)</u>. A solution of 3 g of I in 10 ml of concentrated H_2SO_4 is heated for 3 h at 100°C. It is then cooled and poured into 50 ml of water. The white crystalline precipitate is filtered and washed with water, alcohol, and ether. Yield, 3.23 g (84%) of diamide III, mp 305-306°C (dec) [2].

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STUDY OF CERTAIN STRUCTURAL FEATURES AND PROPERTIES

OF 8-HYDROXYQUINOLINE DERIVATIVES

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The structural features and properties of 8-hydroxyquinoline derivatives must be studied for increasing the quality and yield of the intermediate and end products in the production of medicinal preparations of the quinoline series (nitroxoline, enteroseptol, quinosol, etc.). At present, the results are known of several investigations on the structure and properties of 8-hydroxyquinoline (I) and its derivatives in solution by the methods of fluorescent analysis, and UV and PMR spectroscopy [2, 4, 13, 15, 17, 18]. The UV spectra of these compounds were studied in the greatest detail. In their short-wavelength region, up to five absorption bands that appear in protic and aprotic solvents were detected and assigned [4, 15]. The UV absorption spectra of the aqueous solutions in the visible region, the PMR spectra, and the behavioral features of derivatives of I in the gaseous phase in their interaction with electrons have been less studied.

In the present work, we used the analysis of UV, PMR, and dissociative resonance electron capture (DREC) mass spectra to describe the not-yet-discussed structural features of the nitro (nitroso) derivatives of I, and the individual aspects of their reactivity in solutions

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<u></u>	1	1	UV spectra	DRE	C mass spectra
pound	рКа1	pKa ₂	$\lambda (\log \varepsilon),$ nm	m/z (process)	peak intensity, % (position of maximum, eV)
Ĩ	5,13	9,89	215 (3,92) 242 (4,54) 215 (2,25)	145 M-• 144 [MH]	7,0(0) 86.7 (0.4), 91.6 (1.8)
Ħ	2,88	6,02	207 (4,03) 240 (4,24)	190 M-* 189 [M—H]-	100 (0.05) 0.2 (1.5), 0.7 (3.3), 0.06 (7.0)
111	1,94	5,81	356 (3,76) 450 (4,45) 215 (4,19) 280 (4,13) 364 (3,63)	160 [M—NO]- 144 [M—NO ₂]- 190 M-• 173 [M—OH]- 172 (M—H ₂ O]-•	4,2 (1,5), 1,9 (2,5) 2,0 (1,5), 2,7 (2,8), 2,4 (3,6) 100 (0,05) 33 (0,5), 19,5 (2,7) 20,9 (0,05), 18,0 (0,3), 1,2 (2,5)
IV	-1,75	4,75	440 (3,86) 285 (4,07) 388 (3,31)	218 [M—OH]- 205 [M—NO]-	100,0 (0,2), 24,0 (1,0), 21,0 (2,2 9,4 (0,2), 0,7 (1,0), 0,3 (2,2)
v	2,46	7,52	430 (4,28) 240 (3,96) 383 (4 11)	174 M•	100 (0 5)
٧I	3,68	10,45	337 (3,98) 430 (4,11) 316 (3,02) 330 (3,52) 388 (3,31)	173 [M—H]- 144 [M—NO]- 179 M-• 178 [M—H]-	100 (0,5) 0,4 (1,5), 0,4 (2,7), 0,8 (4,1) 3,0 (1,7), 1,8 (2,8) 100 (0,3) 7,9 (2,0), 8,0 (5,7), 5,6 (7,8)
VII	4,75		241 (4,60) 310 (3,49)	144 [M-Cl]- 143 [M-H-Cl]- 158 [M-H]- 144 [M-CH ₃]- 143 [M-CH ₃ -H]-• 128 [M-CH ₃ -H]-•	7,7 (7,1) 37,0 (3,3), 18,0 (4,4) 11,5 (8,0) 100,0 (4,7) 4,0 (8,5) 23.0 (8,2)
VIII	3,55		237 (4,40) 348 (3,93)	204 M ^{-•} 189 [MCH ₃ O] ⁻	100,0 (0,1) 100,0 (0,1) 100,0 (0,4), 42 (1,6), 35 (3,0) 0.2 (0,2) + 0 (5,3) + 0.7 (8,5)
IX	4,13	•••	244 (5,02) 320 (3,12)	193 M-• 193 M-• 178 [MCH ₃] 162 [MCH ₃ O]- 158 [MCl]-	12,5 (0,3) 100 (3,3), 73 (4,7) 30,0 (8,3) 7,0 (5,7), 13,5 (7,0)

TABLE 1. Ionization Constants (pKa_1 and pKa_2) and Characteristics of UV and DREC Mass Spectra of Compounds I-IX

and in the gaseous phase are discussed. We were first to study the DREC mass spectra of I and its substituted analogs.

The results of a previous investigation of fluorescence spectra of alkaline solution of 5-nitro-8-hydroquinoline (II) showed that the high-intensity band in the 450 nm region can be explained by the formation of an anionic form [18]. However, studies on the electronic structure of derivatives of I, carried out using quantum-chemical calculation methods, showed that it could possibly be assumed that the presence of an absorption band in this region may also be due to a zwitterionic form [4].

We studied the long-wavelength region of the UV absorption spectra of solutions of I, II, 7-nitro- (III), 5,7-dinitro- (IV), 5-nitroso- (V), and 5-chloro-8-hydroxyquinoline (VI), and also 8-methoxyquinoline (VII) and 5-nitro- (VIII) and 5-chloro-8-methoxyquinoline (IX). We also determined the acid-base characteristics of these compounds (the pKa₁ and pKa₂ values, see Table 1) by the UV spectroscopy method. The joint examination of the UV spectra of nitro derivatives II-V and model analogs of I, VI-IX was carried out for the first time.

In the UV spectra of aqueous solutions of compounds II-V (nitro and nitroso compounds) an intense absorption band is observed in the 430-450 nm region (see Table 1), whose extinction increases linearly (for example, for II) from 4566 to 31,105 with increase in pH from 3.0 to 12.0. However, this fact cannot be explained by the formation of the zwitterionic form, since the isoelectric point for ampholytes II, III, and V lies within this pH range, and hence, under these conditions, the concentration of the zwitterionic form cannot change linearly as a function of the pH values. Also at pH 10.0-12.0, compounds I-VI should be completely deprotonated, i.e., they should be present in the solution in the anionic form. However, no absorption appears in the long-wavelength region of the spectra of I and its chlorosubstituted analog (VI). We believed that to explain the spectra in the long-wavelengths region, not only the possible formation of the anionic form, but also the effect of the substituent in the 5(7) position should be taken into account. The characteristic features of the in-



Fig. 1. Dependences of chemical shifts of signals of absorption (δ) of quinoline ring protons on trifluoroacetic acid concentration C. Unfilled circles - compound II; circles with dots - compound VIII.

fluence of the substituents are particularly noticeable in the values of the ionization constants pKa_1 (protonation) and pKa_2 (deprotonation) (see Table 1).

In fact, the results presented in Table 1 show a noticeable tendency for a decrease in pKa_1 and pKa_2 values with increase in the acceptor capacity of the substituents at the 5 position. The decrease in pKa_1 and pKa_2 values in the I-II-IV series and on transition from VII to VIII can be explained by increase in the inductive effect at the side of the substituent. Decrease in the corresponding values of pKa on transition from VI to V is most probably due to the conjugation effect.

We believe that since the intensity of the absorption band at 450 nm changes symbatically and reversibly with change in the pH of the medium, this band can be explained by the presence of $p-\pi$ conjugation [7]. The formation of an anion in the presence of a nitro (nitroso) group at the para {ortho} positions with respect to the negatively charged oxygen atom, probably greatly favors increase in the contribution of the AO of oxygen to the π -MO (due to the M-effect of the NO₂ group), and this leads to an increase in the energy of the π -orbital, and hence to the appearance of an intense absorption in the long-wavelength region of the spectrum.

The presence of the $p-\pi$ conjugation in the nitro derivatives of I also explains certain regularities that we observed in the DREC mass spectra. For compounds VII-IX (the methoxy derivatives), peaks of $[M - CH_3]$ are observed which are due to the formation of anion A. The low energy of the appearance of anion A under the conditions of DREC by the molecules of VII-IX (see Table 1) may indicate that its structure should be analogous to the structure of an anion formed by hydroxy derivatives in an alkaline solution.



The value of the energy (E) of the captured electrons at which the maximum yield of the $[M - CH_3]$ ions is observed decreases in the series VII \rightarrow XI \rightarrow VIII (replacement of H by Cl and NO₂ at the 5 position): $E = 4.7 \rightarrow 3.3 \rightarrow 0.4$ eV. This indicates a considerable decrease in the strength of the O-CH₃ bond and its dependence on the substituent. In this case, we can unequivocally assume that only the conjugation effect can cause an appreciable decrease in the electron density on the O-CH₃ bond in compound VIII, and hence a ready splitting off of the CH₃ group. Table 1 also shows other very characteristic fragments observed in the decrease in the decrease of compounds I-IX.

The marked acceptor properties of the nitro group during $p-\pi$ -conjugation favor localization of the negative charge on this group. This, in particular, is indicated by the results of the quantum-chemical calculations of the structure of nitrophenols [5, 16], from which it follows that the nitro group at the 5 and 7 positions can play the role of a proton acceptor.

We studied the influence of the intermolecular hydrogen bond on the spectral and chemical properties of the nitro derivatives of I by the PMR method, using the example of compounds II and VIII. The results of the investigation are shown in Fig. 1 in the form of a dependence of the chemical shifts of the signals of proton absorption at positions 2, 3, 4, 6, and 7 of the quinoline ring of these compounds on the CF₃COOH concentration in hexadeuteroacetone solution. The signals of the proton absorption of the compounds studied were assigned according to the data in [13].

The values of the acid concentrations corresponding to the inflection points (in the 0.1-15 moles/liter region) indicate that the heterocyclic nitrogen atom in compound II is more basic than in derivative VIII (see Fig. 1). However, in aqueous solutions, the nitrogen atom in compound VIII is more basic (see the pK values for compounds II and VIII in Table 1). This difference in basicity of analogs II and VIII can probably be explained by the formation of different associates in the hexadeuteroacetone solutions.

The change in the values of the chemical shifts of signals of proton absorption of derivative VIII in the initial acid concentration region is probably the result of the formation of an associate due to an intermolecular hydrogen bond of type:



The possible formation of such a bond has already been shown in the investigation of the acid-base equilibria in nitrobenzene solutions [3, 6].

A similar regularity was not observed for the protons of compound II, which may indicate the formation of associates due to hydrogen bonds between two molecules of the dissolved compound.



The formation of these dimeric structures was observed in the study of formation of hydrogen bonds by p-substituted phenols [10]. The formation of an intramolecular hydrogen bond is characteristic of compounds III and IV, which agrees with the results of the investigation of the hydrogen bond in o-nitrophenol [11].

In the DREC mass spectra of compounds III and IV, high-intensity peaks were observed, which are due to the formation of the (M - OH) ions (see Table 1). It is probable that the presence of the intramolecular hydrogen bond leads to an energetically favorable splitting off of the hydroxyl radical and the formation of an anion with an orthoquinoid structure.



If we assume that the nitro group at position 5 (7) forms a bond with a proton, the structure of compound II can be represented in the form of a pseudoacid. Such a possibility has already been discussed within the bounds of the tautomerism of 5-nitroso-8-hydroxyquinoline (compound V) [14].



It is therefore most probable that the quinoid structure (B) will give an appreciable contribution to the structure of the anionic form of compounds II-V. For example, in pnitrophenol, the electronic low-energy transitions were explained by the contribution of the quinoid structure [8].

The possible formation of such a structure also in the gaseous phase is confirmed by the low intensity of the peak of the (M - H) ion (the hydroxyl group hydrogen) in the spectra of the nitro (nitroso) derivatives II and V. The splitting off of hydrogen from the stable quinoid structure is energetically unfavorable, and the maximal peak in the spectra of these compounds corresponds to the negative molecular ion M° . In contrast, in the spectrum of I, the peak with the principal intensity corresponds to the $(M - H)^{\circ}$ ion (see Table 1). By using a deutero tracer, it was found that, in particular, the hydroxyl group hydrogen atom participates in this dissociation that proceeds at low energies (E = 0.2-5.5 eV) of the captured electrons.

The reaction of pseudoacid B with an alkali should lead to the formation of an aci-salt. We isolated a bright-orange product (X) from an alkaline solution of compound II. The UV spectra of compound X and compound II in an alkaline solution coincide. The most characteristic feature of the IR spectrum of compound X in mineral oil is the absence of an absorption band characteristic of the OH group vibration, and a shift in the absorption band corresponding to the asymmetric vibration of the NO₂ group. The absence of absorption in the OH group vibrations region agrees with the fact that compound X should be present in a deprotonated state. The shift of $v_{NO_2}^{ac}$ from 1500 to 1520 cm⁻¹ on transition from compound II to compound X may be due to the interaction of the asymmetric vibration of the NO₂ group with the M - NO₂ vibration (M = Na, K). These data show that the structure of compound X can exhibit certain properties characteristic of an aci-salt.

From the data obtained, pH = 4.5 was determined as optimal for the isolation of nitroxoline, and methods for its purification have been developed via an alkali salt, and of identification of impurities (compounds IV and V) by UV and DREC mass spectrometry. The following conclusions can be drawn from these investigations.

The structural features and reactivity of 5- and 7-nitro and nitroso derivatives of I are due to the presence of p-m-conjugation between the substituent and the ring.

The shift in the electronic density of the nitro (nitroso) group as a result of conjugation may lead to the formation of hydrogen-bonded associates in concentrated acidic and neutral solutions of 5-nitro-8-hydroxyquinoline, and of aci-salts in alkaline solutions.

EXPERIMENTAL

Before their spectra were taken, compounds I, V, and VI, which are commercial products, were recrystallized twice from acetone and were thoroughly dried. As compound II, a Pharmacopoeia grade sample from the production of nitroxoline was used. Compounds III and IV were synthesized by methods described in [12, 13]. Their physical constants (melting points, UV and PMR spectra) agree with those described in the literature. Ethers VII-IX were obtained by methylation of the corresponding 8-hydroxyquinolines by the methyl ester of benzenesulfonic acid in an aqueous solution of NaOH. Their purity was controlled mass spectrometrically (electron impact) on a Varian-MAT-112 apparatus (USA) and by PMR spectra, which were run on a Tesla BS-467 spectrometer (60 MHz, CzechSSR).

The UV spectra were obtained on a Perkin-Elmer apparatus, model 402 (USA); the PMR spectra of compounds I-IX, in a deuteroacetone solution on a Tesla BS-467 spectrometer, using HMDS as internal standard. The concentration of the compounds studied in solution was 0.1 mole/liter. The IR spectra were run on a Perkin-Elmer apparatus, model 577 (USA) in mineral oil. The pKa values were determined by a known method [1]. The DREC mass spectra were run on a MKh-1303 mass spectrometer (USSR), modified for recording negative ions [9].

The alkali salt of compound II was isolated as follows: Compound II was added, with stirring, to 50 ml of distilled water heated to 90-95°C (pH 10.0) up to saturation. The hot solution was then filtered and cooled. When cool, bright-orange crystals precipitated. At the end of crystallization, the precipitate was filtered, and washed with water and acetone.

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ELECTROCATALYTIC SYNTHESIS OF 3,4-DIMETHOXYPHENYLETHYLAMINE

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One of the stages in the synthesis of papaverine is the reduction of 3,4-dimethoxyphenylacetonitrile (I) to 3,4-dimethoxyphenylethylamine (II). At present, II is obtained industrially by hydrogenation of I in an autoclave on a Raney nickel catalyst in a nonaqueous medium [3]. The catalyst loses its activity because of adsorption of reaction products, and this leads to a decrease in the rate of reduction of I.

We proposed a new method for the preparation of II by electrocatalytic hydrogenation of I in an alcoholic-alkaline medium using skeletal ferromagnetic catalysts [1]. With this method, II could be obtained under mild conditions (at a temperature of 40°C and at atmospheric pressure) in a yield of 96-98%, calculated for the base compound, and the catalyst could be repeatedly used.

The studies were carried out in a thermostated electrochemical cell with separation of the cathode and anode space by an ion-exchange diaphragm MK-40. A layer of skeletal coating was deposited on the cathode from a first class conductor; it was held in the reaction zone by the magnetic field of a permanent magnet. A platinum gauze, submerged in a 20% alkali solution, was used as the anode. To the cathode space, 2-5% aqueous and alcoholic solutions of alkali were added. The electrosynthesis was carried out at a given current intensity, which was regulated by a VSA-5A-K rectifier.

The hydrogenation kinetics of the nitrile was studied in the electrolysis: the influence of the concentration of the nitrile to be reduced, amounts and nature of the catalyst, current density, and temperature on the rate of hydrogen absorption.

The skeletal catalysts were prepared by leaching out Ni-Al and Co-Al alloys in which the content of the active metal was 50% of the weight of the alloy.

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