Reanal, and 3-, 5-, 6-, and 8-quinolinecarboxylic acids and 8-methyl-5-quinolinecarboxylic acid were prepared by literature methods. The properties of (IIa-g) and (IIIa-g) are given in Tables 1-3.

1,2,3,4-Tetrahydroquinolinecarboxylic Acids (IIa-g). To a solution of 0.05 mole of the acid (Ia-g) in 50 ml of 10% aqueous sodium hydroxide was added in small portions with stirring over 1 h, 8 g of Raney alloy, and the mixture stirred for 1 h at 20°C. The solid was filtered off and washed with hot water, and 5% hydrogen chloride in ethanol added to the filtrate to pH 2-3 (universal indicator). It was then extracted with chloroform, the organic layer dried over magnesium sulfate, and the solvent removed to give the acids (IIa-g), which were crystallized from aqueous ethanol for analysis. The compounds were homogeneous on TLC. The acids (IIa-g) were used without purification to obtain the esters (IIIa-g).

Ethyl Esters of 1,2,3,4-Tetrahydroquinolinecarboxylic Acids (IIIa-g). A solution of 0.02 mole of the acid (IIa-g) in a mixture of 10 ml of absolute ethanol, 5 ml of conc. sulfuric acid, and 3 ml of 30% hydrogen peroxide was heated at 120°C (in a bath) for 30-40 min. The mixture was then poured into 50 ml of water, 25% ammonia added to pH 6-7, extracted with chloroform, and the organic layer washed with 3% sodium bicarbonate and water, dried over magnesium sulfate, and the solvent removed to give the ethyl esters (IIIa-g).

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

12.* AROMATIZATION OF 1-SUBSTITUTED-2-(INDOL-3-YL)-1,2-DIHYDROQUINOLINES WITH 1,3,5-TRINITROBENZENE

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UDC 547.546'759.2'832.5'543.87

As the electron-acceptor properties of the N-substituents in 1-R-2-(indol-3-yl)-1,2-dihydroquinolines decrease, their ability to undergo heterolysis of the internuclear C—C bond to give ion pairs of 1-R-quinolinium cations and indole anions decreases. Reaction of these ion pairs with 1,3,5-trinitrobenzene gives salts of 1-R-quinolinium cations and the 1-(indol-3-yl)-2,4,6-trinitrocyclohexadiene anion. With undissociated dihydroquinolines, aromatization under similar conditions gives salts of 1-R-2(indol-3-yl)quinolinium cations and the 1,1-dihydro-2,4,6-trinitrocyclohexadiene anion.

In polar solvents, some C-substituted dihydroaromatic compounds dissociate to a heteroaromatic cation and the substituent as an anion [2], displaying dual reactivity on aromatiza-

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*For Communication 11, see [1].

Dnepropetrovsk Institute of Structural Engineering, Dnepropetrovsk 320600. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 80-84, January, 1988. Original article submitted May 11, 1986.

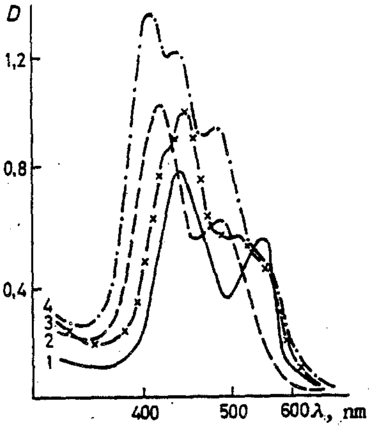
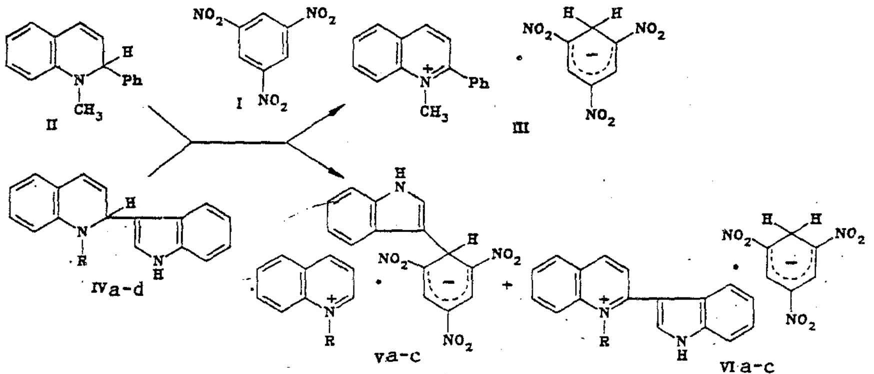


Fig. 1. UV Spectra (in acetonitrile): 1) 1-methyl-2-phenylquinolinium 1,1-dihydro-2,4,6-trinitrocyclohexadienate; 2) 1-benzylquinolinium 1-(indol-3-yl)-2,4,6-trinitrocyclohexadienate; 3), 4) reaction mixture of 1-ethyl-2-(indol-3-yl)-1,2-dihydroquinoline and 1,3,5-trinitrobenzene in ether (3) and acetonitrile (4).

tion. On reaction with compounds in which the electron-donor properties exceed the oxidative properties, for instance triphenylcarbenium perchlorate, loss of the substituent occurs with the formation of unsubstituted heteroaromatic cations with simultaneous alkylation of the aromatizing agent (so-called nucleophilic alkylation [3]). Aromatization of compounds which are more active oxidants and have low electrophilic properties, such as 2,2,6,6-tetramethyl-1-oxopiperidinium perchlorate, results in cleavage of the hydride-labile hydrogen atom, usually by a one-electron mechanism [4], with retention of the geminal substituent, even when in solution the dihydroheteroaromatic compounds are present almost completely in the ionic form [2]. The aromatization products formed in this reaction therefore serve as a measure of the ratio of oxidative to electrophilic properties in the aromatizing agents. In addition, as we have found, it is possible to select aromatizing agents which possess sufficiently great electrophilic properties, and are capable of aromatizing dihydro compounds by an ionic mechanism both with removal of the substituents, if the latter are dissociated in solution, and with hydride ion transfer if present in the covalent form. In such a case, it should be possible to measure dissociation, particularly in cases in which it is not possible to use electrochemical methods, since in solution close ion pairs of the heteroaromatic cations and organic anions are formed, which do not contribute to the electrical conductivity of their solutions [2].

Such an aromatizing agent is 1,3,5-trinitrobenzene (I). Trinitrobenzene is known to be a good dehydroaromatizing agent for many dihydroheteroaromatic compounds [5-7]. The writers consider that in these cases the ionic mechanism of transfer of the hydride-labile hydrogen is involved. It was natural to assume that in the dissociated forms of dihydroaromatic compounds, aromatization with 1,3,5-trinitrobenzene would proceed with transfer of the substituent and formation of salts of the heteroaromatic cations and the substituted σ-complexes.

It was in fact found that reaction of (I) in acetonitrile with 1-methyl-2-phenyl-1,2-dihydroquinoline (II), dissociation of which with cleavage of a phenyl anion is known to be impossible, transfer of the hydride ion of the salt of the 1-methyl-2-phenylquinolinium cation with the hydride σ-complex of trinitrobenzene (III) occurs, as described for 2-phenyl-benzimidazoline [7]. Under similar conditions, 1-methyl-2-(indol-3-yl)-1,2-dihydroquinoline (IVa), which, as we have previously shown, dissociates to the indole anion and 1-methylquinolinium cation, forms the salt of the 1-methylquinolinium cation and the anionic indole σ-complex of trinitrobenzene (Va), which we have previously obtained by a different route [8]:



IV–VI a $R=CH_3$; b $R=C_2H_5$; c $R=CH_2C_6H_5$; d $R=COC_6H_5$

TABLE 1. UV Spectra of Dihydroquinolines (IVa-d) and the Corresponding Starting Cations

Compound	λ_{max}, nm ($\varepsilon \cdot 10^{-4}$)		
	dihydroquinoline		starting cation, in acetonitrile
	in acetonitrile	in ether	
IVa	216 (4,3), 233 (3,1), 278 (1,3), 288 (1,2), 312 (0 9)	216 (3,7), 231 (2,4), 278 (1,1), 288 (0,9)	205 (3,3), 233 (7,0), 312 (2,1)
IVb	219 (2,3), 238 (2,5), 314 (0,5)	219 (4,0), 278 (0,9), 288 (0,7)	238 (1,8), 314 (0,4)
IVc	219 (4,2), 238 (3,9), 314 (0,7)	219 (4,2), 278 (0,9), 288 (0,6)	238 (3,5), 314 (0,6)
IVd	216 (7,2), 232 (5,4), 272 (3,1), 288 (2,5)	216 (6,9), 232 (5,4), 272 (3,1), 288 (2,4)	225 (3,1), 255 (2,8), 290 (1,0), 333 (0,6)

TABLE 2. Properties of Compounds Obtained

Compound	mp, °C	IR spectrum, cm^{-1} (in KBr)	Found, %			Empirical formula	Calculated, %			Yield, %
			C	H	N		C	H	N	
III	126—127	1520, 1200 (NO_2)	60,7	4,4	12,7	$C_{22}H_{18}N_4O_6$	60,8	4,2	12,9	74
Va	160	1468, 1245, 1207 (NO_2), 3460 (NH)	59,8	3,6	14,6	$C_{24}H_{19}N_5O_6$	60,8	4,0	14,8	77
Vb	142—144	1507, 1120 (NO_2), 3445 (NH)	61,6	4,7	14,9	$C_{25}H_{21}N_5O_6$	61,6	4,3	14,4	52
Vc	135—137	1515, 1200 (NO_2), 3450 (NH)	65,1	4,4	12,9	$C_{30}H_{23}N_5O_6$	65,6	4,2	12,8	55
VIc	60 (decomp)	1500, 1225 (NO_2), 3400 (NH)	65,3	4,5	12,3	$C_{30}H_{23}N_5O_6$	65,6	4,2	12,8	23

*From acetonitrile–ether.

It was of interest to examine the aromatizing effects of 1,3,5-trinitrobenzene on some 1-R-2-(indol-3-yl)-1,2,dihydroquinolines (IVa-d), while reducing their ability to dissociate by adding quinolinium salts to the acetonitrile solution (the similar-ion effect), and to increase the electron-acceptor properties of the substituent at the nitrogen heteroatom of the dihydroquinoline ring.

Examination of the UV spectra of (IVa-d) in acetonitrile (Table 1) showed that depending on the electron-acceptor properties of the substituent, the compounds (IV) are present in solution either in the ionic (IVa) or the covalent form (IVd), but usually both forms are present (IVb, c). In ether, the spectra of (IVa-d) are similar to that of (IVd) in acetonitrile. No absorption was present corresponding to the quinolinium cations (Table 1), showing that (IVa-d) were present in the covalent form (in making the assignments, previous data were taken into account [2]).

Accordingly, treatment of (IVb, c) with 1,3,5-trinitrobenzene in acetonitrile gave, in contrast to the reaction with (IVa), a mixture of salts (Vb, c) and (VIb, c). The dihydroquinoline (IVd) did not react, probably as a result of the inadequate hydride lability of the α-hydrogen in consequence of the strong electron-acceptor effect of the benzoyl substituent.

In ether, (IVa) with 1,3,5-trinitrobenzene gave the salt of (Va) with the indole complex, (Ib) gave the salt of (VIb) with the hydride σ-complex of trinitrobenzene (although the UV spectrum indicated contamination by the salt of (Vb), and (IVc) with (I) gave only the salt (VIc) (Fig. 1). Similarly, only salt (VIc) was obtained on reacting (I) with dihydroquinoline (IVc) with the addition of 1-benzylquinolinium chloride to suppress the dissociation of (IVc). 1,3,5-Trinitrobenzene is, therefore, a very sensitive reagent for the estimation of dissociated forms of dihydroquinolines (IVa-d).

In the UV spectra of the salts (V) in acetonitrile, four characteristic absorption bands are seen, two of which (233 and 312 nm) are attributed to absorption by the 1-substituted quinolinium cations [2], and the other two (434 and 532 nm), with a ratio of extinction coefficients of 2:1, correspond to absorption of the indole σ-complex of trinitrobenzene [8]. In the IR spectra of these salts, the strongest absorption, as in all the known σ-complexes of trinitrobenzene [7], is assigned to symmetrical (1468) and asymmetrical (1245 and 1207 cm^{-1}) stretching vibrations of the nitro group. The quinolinium cation is characterized by a number of bands at 1580, 1520, 1230, 1160, 800, and 700 cm^{-1}. The presence of the indole moiety in the anions of salts (V) is shown by the PMR spectral data. It would be expected that the position and intensity of the signal for the proton at the sp^3-hybridized carbon atom in the PMR spectra of salts of the indole (V) and hydride complexes (III) and (VI) would be very different. For example, in (III) and (VI) the signal for the geminal protons of integral intensity 2H should appear at 3.60-3.90 ppm [9], whereas in the anionic σ-complexes with a substituent at the geminal node the signal for the methine proton appears at lower field (6.20-5.00 ppm) [10]. In fact, the PMR spectrum of (Va) shows a multiplet of intensity 1H at 6.48 ppm, confirming the presence of a substituent at the geminal node of the anion. In addition to this signal, the spectrum contains multiplet signals for the 3-H and 5-H protons at 8.48 ppm, the indole ring, and the quinolinium cation.

When dissociation of dihydroaromatic compounds takes place, therefore, reaction with 1,3,5-trinitrobenzene gives salts of substituted anionic σ-complexes (V), whereas when no dissociation occurs, hydride complexes of (VI) are formed, thus allowing 1,3,5-trinitrobenzene, in conjunction with the spectral data, to be used as a test for the dissociation of dihydroheteroaromatic compounds in solution. The presence of electron-acceptor substituents at the nitrogen heteroatom in the dihydro-compounds reduces their tendency to dissociate.

EXPERIMENTAL

UV spectra were recorded on a Specord UV-VIS spectrophotometer, and IR spectra on a Specord IR-75 in KBr disks. PMR spectra were obtained on a Tesla BS-467 spectrometer (60 MHz).

Compound (IVa) has been reported [2]. The constants and yields of the salts obtained are given in Table 2.

1-Ethyl-2-(indol-3-yl)-1,2-dihydroquinoline (IVb). A mixture of 1.43 g (5 mmole) of 1-ethylquinolinium bromide, 0.59 g (5 mmole) of indole in 10 ml of aqueous acetonitrile (1:1), and 0.5 ml of 10 N NaOH was stirred for 1 h. Water (50 ml) was added, the mixture cooled to 0°C, and the resulting oil extracted with ether, dried over magnesium sulfate, and the solvent removed to give (IVb) as an oil which decomposed on crystallization. Yield 0.48 g (35%). Found: C 83.0; H 6.6; N 10.1%. $C_{19}H_{18}N_2$. Calculated: C 83.2; H 6.6; N 10.2%.

1-Benzyl-2-(indol-3-yl)-1,2-dihydroquinoline (IVc) was obtained similarly. Yield 0.47 g (28%). Found: C 85.4; H 5.9; N 8.5%. $C_{24}H_{20}N_2$. Calculated: C 85.7; H 6.0; N 8.3%.

1-Methylquinolinium 1-(Indol-3-yl)-2,4,6-trinitrocyclohexadienate (Va). To a solution of 0.21 g (1 mmole) of 1,3,5-trinitrobenzene in 5 ml of dry acetonitrile was added 0.26 g (1 mmole) of the dihydroquinoline (IVa), and the mixture stirred for 5 h. The deep red solid which separated was filtered off and recrystallized from ether—acetonitrile to give 0.33 g (77%) of product, mp 160°C. PMR spectrum (DMSO-D$_6$): 4.73 (3H, s, CH$_3$), 6.48 (1H, m, 1-H), 9.58 (1H, s, NH), 8.48 (2H, m, 3-H, 5-H), 7.03-7.61 (5H, m, indole ring), 7.33-9.32 ppm (7H, m, quinoline ring).

Compounds (Vb) and (Vc) were obtained similarly by repeated crystallization from ether—acetonitrile.

1-Benzyl-2-(indol-3-yl)quinolinium 1,1-Dihydro-2,4,6-trinitrocyclohexadienate (VIc). To a solution of 0.21 g (1 mmole) of 1,3,5-trinitrobenzene in 10 ml of dichloromethane was added 3.9 g (15 mmole) of 1-benzylquinolinium chloride and 0.34 g (1 mmole) of the dihydroquinoline (IVc) in 10 ml of ether, and the mixture stirred for 5 h. The solid which separated was recrystallized from ether—acetonitrile to give 1.9 g (50%) of product, mp 60°C (decomp.). UV spectrum (in acetonitrile), λ_{max}, nm ($\varepsilon \cdot 10^{-4}$): 476 (6.3), 588 (3.8). Found: C 65.3; H 4.5; N 12.3%. $C_{30}H_{25}N_5O_6$. Calculated: C 65.5; H 4.2; N 12.8%.

1-Methyl-2-phenylquinolinium 1,1-Dihydro-2,4,6-trinitrocyclohexadienate (III). To a solution of 0.42 g (2 mmole) of 1,3,5-trinitrobenzene in 5 ml of acetonitrile was added under argon a solution of 0.44 g (2 mmole) of 1-methyl-2-phenyl-1,2-dihydroquinoline (II) in 5 ml of acetonitrile. After 5 h, the mixture was poured into ether, and the solid filtered off to give 0.64 g (74%) of product.

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2-ARYLAMINO-3-CYANO-5,6,7,8-TETRAHYDROQUINOLINES AND 2-SUBSTITUTED 1-ARYL-6,7,8,9-TETRAHYDROPYRIMIDO[4,5-b]-QUINOLIN-4-ONES DERIVED THEREFROM

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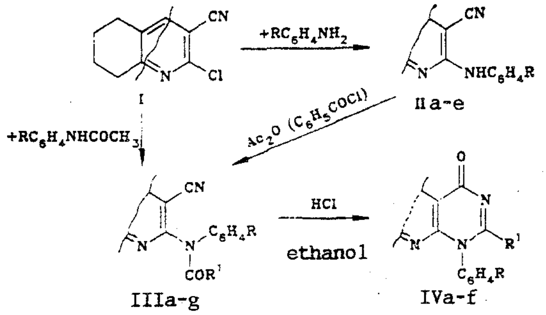
UDC 547.831'.4'832'859.2.07:542.953

Reaction of 2-chloro-3-cyano-5,6,7,8-tetrahydroquinoline with arylamines gives 2-arylamino-3-cyano-5,6,7,8-tetrahydroquinolines, which on reaction with acetic anhydride or benzoyl chloride are converted into the N-acyl derivatives, and on further treatment with hydrogen chloride in anhydrous ethanol, into 2-substituted 1-aryl-6,7,8,9-tetrahydropyrimido[4,5-b]quinolin-4-ones.

6,7,8,9-Tetrahydropyrimido[4,5-b]quinolines are not known. We have shown that the related 1-aryl-7-methyl-4-oxopyrido[2,3-d]pyrimidines are obtained in high yields on cyclizing N-acyl-2-arylamino-6-methylnicotinonitriles [1]. In order to examine the possibility of synthesizing 6,7,8,9-tetrahydropyrimido[4,5-b]quinolin-4-ones in a similar way, the 2-arylamino-3-cyano-5,6,7,8-tetrahydroquinolines (IIa-e) (Table 1) were obtained. The latter compounds are of interest as starting materials for the synthesis of naphthyridines [2], and as synthons in the preparation of potentially biologically active quinolines [3].

The nitriles (IIa-e) were obtained in 60-95% yields by heating (180°C) a mixture of equimolar amounts of 2-chloro-3-cyano-5,6,7,8-tetrahydroquinoline and the arylamine for 4 h. Attempts to carry out the reaction in boiling butanol for 6 h were unsuccessful. When the reaction was carried out in butanol with the arylamine hydrochloride rather than the aryl-



II—IVa $R=H$, b $R=p\text{-}CH_3$, c $R=o\text{-}CH_3$, d $R=m\text{-}CH_3$, e $R=p\text{-}CH_3O$, IIIf, IVf $R=H$, IIIg $R=p\text{-}C_2H_5O$; III, IV a-e $R^1=CH_3$; f $R^1=C_6H_5$; IIIg $R^1=CH_3$

Perm State Institute of Pharmacy, Perm 614600. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 85-87, January, 1988. Original article submitted August 6, 1986.