C. Bromine (1.0 g, 12.48 mmole) was added at 5-6°C to a solution of VIII (0.2 g, 0.6 mmole) in benzene (20 ml) and held for 3 h. After distillation of the benzene, water (20 ml) and a solution of sodium carbonate (20 ml) were added to pH 10. Extraction with chloroform (3 × 10 ml) and chromatography gave V (0.01 g, 8%).

Bis[4-azafluoren-9-yl] (IX, $C_{24}H_{16}N_2$). A. A solution of III (0.2 g, 0.5 mmole) in absolute ethanol (10 ml) was refluxed with activated zinc dust (0.5 g, 7.6 mmole) for 1 h. Alcohol was distilled off and water (10 ml) and sodium carbonate were added to pH 8. The product was extracted with chloroform (2 × 10 ml) and the extract dried with potassium carbonate. After distillation of chloroform it was crystallized from a mixture of heptane and benzene (13:1) to give IX (0.08 g, 50%) as colorless crystals with mp 283-284°C and Rf 0.6. Found: M^+ 332. Calculated: M 332.

B. V (0.08 g, 0.6 mmole), absolute alcohol (5 ml), and zinc dust (0.2 g, 3 mmole) were refluxed for 3 h to give IX (0.05 g, 93%) with mp 282-284°C.

Refluxing bromide IV with zinc dust in absolute ethanol gave 4-azafluorene (90%) with mp 93-94°C.

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TAUTOMERS OF AZINE DERIVATIVES.

21.* TAUTOMERISM IN 2-(2-HYDROXYARYL)AZINES

S. A. Stekhova, V. V. Lapachev, and V. P. Mamaev

UDC 541.623:547.82'83:543.422.25'6

Tautomerism in 2-(2-hyroxyaryl)azines has been studied using ^{17}O NMR and UV spectroscopy. Consideration has been given to the influence of solvent and structural factors which facilitate the establishment of a tautomeric equilibrium in these compounds.

A study of tautomerism in 2-hydroxyarylazines of the type A ⇆ B (Scheme 1) is of value for an understanding both of the properties of the azine fragment and of tautomerism in compounds of the phenol series. Work on this class of compound is also of practical value in so far as many 2-hydroxyarylazines possess light-stabilizing and complex-forming properties [2, 3].

The ability of 2-hydroxyarylazines to form tautomers with the participation of the ylidene form B has been much discussed in the literature [4-6]. The possibility of realizing the NH form had already been formulated by A. E. Chichibabin in 1918 [4] during a study of the simplest example of the 2-hydroxyarylazines – 2-(2-hydroxyphenyl)pyridine. In the 1970s, R. Abramovich [5, 6], on the basis of IR spectra in KBr, assigned to 2-(2-hydroxy-5-nitrophenyl)pyridine III the zwitterion structure IIIB' which, as can easily be seen, represents an NH type tautomer in the form of its other resonance hybrid. Nevertheless, there are at present no reliable data on tautomerism in 2-hydroxyarylazines in the literature.

*Communication 20, see [1].

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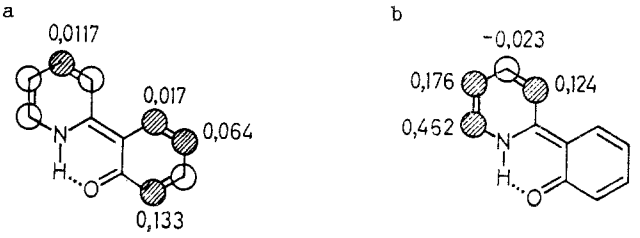
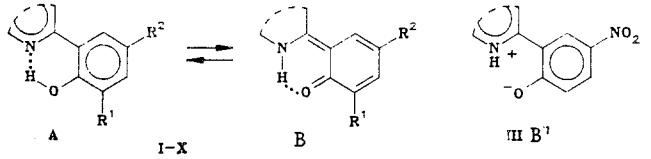


Fig. 1. Maps of differences: a) squares of coefficients on PMO ($c_B^2 - c_A^2$); b) energies of aromatic and quinoid tautomers.

The present work was devoted to a study of tautomerism in hydroxyarylazines, including a scan of tautomeric compounds together with the influence of structural factors which facilitate the equilibrium occurrence of tautomeric forms in solution (preliminary communications, [7, 8]).

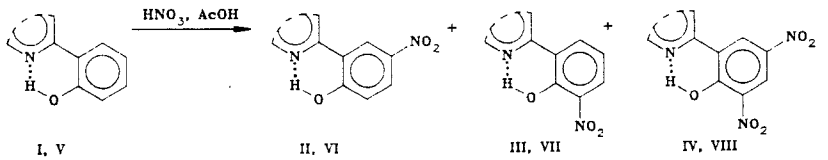
For a purposeful scan of tautomeric compounds we examined the influence of structural factors on the relative stability of the tautomers using the approach of [9], based on the PMO method. The maps of energy differences and squares of coefficients of frontal orbitals necessary for this were calculated by the CNDO/2 method (Fig. 1). In accordance with [9] one of the routes for stabilizing of the "rare" NH form, judging from the map of c^2 differences (Fig. 1a) is the introduction of π-acceptor substituents at the shaded positions on the molecule. From the map of energy differences (Fig. 1b), introduction of a nitrogen atom at the shaded positions must also facilitate this [9]. In addition, taking into consideration the analysis of the effects of annellation carried out previously [1], one would expect additional stabilization of the quinoid form on annellation of the pyridine fragment at the 5-6 bond and of the phenol fragment at the 3-4 bond. It should also be noted that according to results obtained in a study of the influence of the solvent on intrachelate tautomer equilibrium of acylmethylazines [10], polar solvents should facilitate the stabilization of the quinoid tautomer.

The compounds selected for study, on the basis of their preparative accessibility and analysis carried out, were compounds I-X below:



I—IV Het=Py, V—VIII Het=Qui, IX Het=4-Pym; I, V $R^1=R^2=H$; II, VI $R^1=NO_2$, $R^2=H$; III, VII, IX $R^1=H$, $R^2=NO_2$; IV, VIII $R^1=R^2=NO_2$; X, 2,2'-(1-hydroxynaphthyl)quinoline

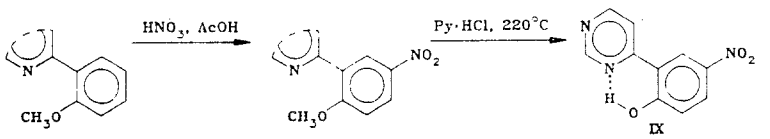
Hydroxyphenylpyridine (I) was prepared by heating 2-(2-methoxyphenyl)pyridine [11] with hydriodic acid in a sealed ampul. The preparation of 2-(2-hydroxyphenyl)quinoline (V) and 2-(2-hydroxynaphthyl)quinoline (X) is decribed in [12]. The nitrophenyl derivatives (II-IV, VI-VIII) were prepared by nitration of the corresponding hydroxyphenylazines by fuming nitric acid in acetic acid solution.



The mixture of 3- and 5- nitro and 3,5-dinitro derivatives was separated by chromatography. Isolation and purification of the nitro derivatives proved to be somewhat laborious and hence a more convenient method was chosen for the preparation of 5-nitro derivatives — nitration of the corresponding o-methoxyphenylazines with subsequent demethylation.

In the nitration of the methoxy derivatives by fuming nitric acid in acetic acid the 5-nitro derivative is almost exclusively formed in high yield [11]. This reaction was also used for identifying the 3- and 5-nitro derivatives in the reaction mixture in the nitration

of 2-(2-hydroxyphenyl)quinoline. 4-(2-Hydroxy-5-nitrophenyl)pyrimidine (IX) was prepared by condensation of o-hydroxyphenyl acetone with tris-(formamido)methane by known methods [13].



Reliable information on the ratio of the tautomers A ⇄ B for compounds I to X can be obtained from their UV and ^{17}O NMR spectra. Comparison of the ^{17}O NMR spectra of 2-(2-hydroxyphenyl)pyridine (I), its nitro derivatives (II, III), and the quinoline (V) with those of phenol and enol chelate compounds studied earlier [14] shows that for compounds I-III and V the A ⇄ B equilibrium is almost completely shifted towards the aromatic form A. The oxygen chemical shift for pyridine (I) and quinoline (V) is found in the range 93-95 ppm which is entirely characteristic for phenol compounds of such a type [15]. A certain downfield shift of the signals for nitrophenylpyridine (III) ($\delta^{17}O$ 119 ppm) evidently occurs as a result of direct conjugation of the hydroxy and nitro groups and is not due to tautomerism involving the NH form (cp [11]). Such a shift of signals can be clearly seen on comparing the ^{17}O NMR spectrum of 2-hydroxyacetophenone ($\delta^{17}O$ 90 ppm [16]) with that of 2-hydroxy-5-nitroacetophenone (XI) ($\delta^{17}O$ 102 ppm – Table 1) which we recorded. In the UV spectra of the pyridine I, its mononitro derivatives II and III, and the quinoline V there are no absorptions characteristic of the NH form in the 350-420 nm region (11) and the long-wave band is found in the 320-350 nm region which is characteristic of the enol form. In moving to an alcohol solvent, the form of the UV spectra of compounds I-III and V is unchanged whereas in DMSO and DMF a long-wave absorption is observed for the mononitro derivatives II and III in the 420 nm region. On acidifying these solutions with a drop of trifluoroacetic acid in the spectrometer cell the long-wave band disappears (Fig. 2). This is evidence that the long-wave absorption arises from ionization of the 3- and 5-nitrophenol derivatives of 2-(2-hydroxyphenyl)pyridine II and III in dipolar aprotic solvents, and is not due to tautomerization. Further support for this is found in the coincidence of the UV spectra of compounds II and III in DMSO and in alcoholic alkali. In order to make a reliable assignment of the long-wave bands either to absorption of the NH tautomer or to the ionized form, a similar verification was carried out for other 2-hydroxyarylazines.

A significant amount of the quinoid tautomer was recorded for the dinitro derivatives of 2-(2-hydroxyphenyl)pyridine (IV) in chloroform. In the UV spectrum, in addition to the absorption of the aromatic tautomer at 280 and 340 nm, in chloroform there was also observed a low-intensity band for the NH form B with λ_{max} 400 nm, broad; this did not disappear on acidification. On addition of the more polar acetonitrile the intensity of this band increased but on addition of hexane it decreased which is in accordance with the effect of polar media on inner-chelate equilibrium of A ⇄ B type [10].

Annelation in the azine part of the molecule as one passes from pyridine I to quinoline V is not sufficient for the realization of the NH tautomer. The introduction of yet another structural factor facilitating the stabilization of the quinoid tautomer, for example, annella-

TABLE 1. Spectra of Compounds I to XII

Compound	^{17}O NMR spectra, δ ppm (in $CHCl_3$)	PMR spectra δ_{OH} ppm (in $CHCl_3$)	UV absorption, λ_{max} nm			
			$CHCl_3$	C_2H_5OH	KBr	DMSO
I	93	14.41	260, 285, 320	255, 290, 320	—	320
II	—	16,34	357	345	345, 450	480
III	119	15,67	280, 327	275, 325	290, 360 br, 410br.	325
IV	—	—	280, 340, 400	280, 350, 410	410	400
V	95	15,26	350	350	350	350
VI	—	17,69	350, 420	350, 425	470br	350, 480
VII	—	16,6	345, 400	350, 410	350, 450	350, 480
VIII	—	16,20	350, 430	350, 420	370, 440	425
IX	118,5	—	325	320, 400	345	—
X	111	—	380	357	400	370
			480 br.	480 br.	480br.	
XI	102	—	—	—	—	—
XII	95	—	—	—	—	—

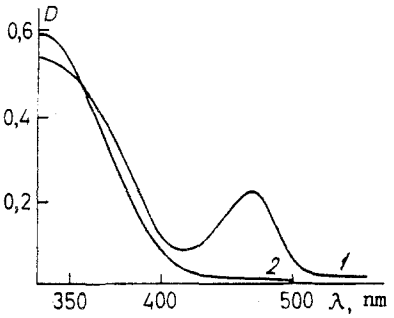


Fig. 2. UV spectra of compound III. I) in DMSO; 2) in DMSO with the addition of trifluoroacetic acid.

tion at bond 3-4 of the phenol ring, leads to the appearance of tautomer B in the mixture. Thus, a small downfield shift of the oxygen signal (111 ppm as against 95 ppm for the model compound XII – Table 1) is evidence in favor of the formation of trace quantities of the NH form. In the UV spectrum in chloroform, it appears as a weak long-wave absorption in the 480 nm region the intensity of which grows in proportion as ethanol is added.

For quinoline derivatives, the introduction of one nitro group into the phenol part of the molecule proves to be sufficient for the observation of tautomer equilibrium. Thus, in the UV spectrum of compounds VI and VII in chloroform an absorption is observed at around 400 and 420 nm, respectively. The intensity of the long-wave absorption, as for the previous compounds, depends on the polarity of the medium; increasing the polarity increases the fraction of the quinoid tautomer.

On moving to the dinitrohydroxyphenyl quinoline (VIII), one observes an intense band in the UV spectrum in the 430 nm region which is evidence of a significant concentration of the ylidene tautomer in the mixture. The intensity of the band increases on passing from chloroform to acetonitrile and alcohol and decreases on the addition of heptane to the solution. In DMSO compounds VI-VIII are ionized.

For the pyrimidine IX in chloroform, ethyl acetate, dichloroethane, and acetic acid the absence of long-wave absorptions in the 320 nm region in the UV spectrum would seem to indicate that the phenol structure IXA is characteristic and this is supported by the ^{17}O NMR spectrum ($\delta_{^{17}O}$ 118.5 ppm). The downfield shift of the signal in comparison with unsubstituted 2-hydroxyphenylazines [12] evidently arises, as for 2-(2-hydroxy-5-nitrophenyl)pyridine (III), from the effect of the nitro group. In alcohol, acetonitrile, and acetone compound IX is ionized.

It should be noted that on passing from solution to the crystalline state the fraction of the NH form increases. Thus, for the mononitrophenyl derivatives of the pyridine series II and III the NH form, unstable in solution, is observed in considerable proportion in the solid state. This can be well seen on comparing the UV spectra in solution and in KBr: in the solid state an intense absorption band appears in the UV spectrum with λ_{max} 420 nm, characteristic for the quinoid tautomer. The increase in the stability of the NH form on passing to the crystalline state is typical also for quinoline derivatives. Although for all the nitro derivatives of the quinoline series V-VIII which we have examined the quinoid tautomer is present also in solution, the fraction thereof increases on passing to the solid state. In so far as the NH form is the more polar, the increase in the fraction of this form in the crystalline state is in good agreement with the usual concept of the preferred crystallization of the more polar form rather than the less polar.

Thus, in the series of 2-hydroxyphenylazines annellation in the azine part and the phenyl fragment, the introduction of acceptor substituents on the phenyl ring, and the introduction of a nitrogen atom into the pyridine ring taken separately do not lead to the appearance of the quinoid form in solution. Nevertheless equilibrium with this form can be partially achieved by a combination of two or more of the factors listed above.

EXPERIMENTAL

The oxygen-17 NMR spectra (on the natural content of the isotope) were recorded on a Bruker CXP-300 instrument (40.67 MHz) at the Institute of Catalysis of the Siberian Branch of the Academy of Sciences of the USSR.

Concentrations of the chloroform solutions were in the range 5-20%, temperature 300 K. Rate of accumulation of ^{17}O NMR spectra, 20-50 Hz, number of accumulations 10^5 to 10^6. Chem-

ical shifts were measured against H_2O as internal standard; a positive sign to a chemical shift corresponds to a downfield shift (deshielding).

2-(2-Hydroxyphenyl)pyridine (I) was prepared by demethylation of 2-(2-methoxyphenyl)pyridine [11]. A solution of 3 g (16 mmole) 2-(2-methoxyphenyl)pyridine [11] in 20 ml hydriodic acid was heated for 5 h at 125°C. The reaction was carried out either in a sealed ampul or under a current of argon. The hydriodic acid was evaporated off in vacuum and the residue treated with ammonia solution to give a weakly alkaline reaction and extracted with chloroform. Yield of pure pyridine I = 2 g (73%), mp 56°C – from[11], mp 56°C (from ethanol).

2-(2-Hydroxy-3-nitrophenyl)pyridine (II) and 2-(2-Hydroxy-5-nitrophenyl)pyridine (III). A solution of 2 g (12 mmole) compound I in 10 ml acetic acid was cooled to 16°C (the fp of acetic acid) and 3 ml nitric acid (d = 1.5) cautiously added dropwise with stirring over a period of 30 min. The reaction mixture was poured into an excess of cooled KOH solution and the precipitate which formed was filtered off. Chromatographic separation of the precipitate on silica gel plates with chloroform as eluent yielded 0.2 g ortho-isomer II, mp 167-168°C (from ethanol) (from [15], mp 167-168°C), and 0.3 g para-isomer III, mp 219-220°C (from ethanol) (from [5] mp 216-217°C).

2-(2-Hydroxy-5-nitrophenyl)pyridine (III). To a solution of 1 g (6 mmole) 2-(2-methoxyphenyl)pyridine in 2 ml glacial acetic acid was added, dropwise with stirring, 3 ml fuming nitric acid and the mixture heated at bp for 0.5 h and then poured into an excess of aqueous KOH solution. The precipitate which formed was filtered off and recrystallized from ethanol to yield 1 g 2-(2-methoxy-5-methoxy-5-nitrophenyl)pyridine, mp 124-125°C, which was subjected to hydrolysis without further purification. Hydrolysis of the methoxy group was effected by a method similar to that of [15]. A mixture of 0.25 g (1 mmole) 2-(2-methoxy-5-nitrophenyl)pyridine was heated for 20 min at 210°C. The flask was cooled, the reaction mixture dissolved in water and the aqueous solution extracted with chloroform. The extract was dried over $MgSO_4$ and the residue recrystallized from alcohol to yield 0.125 g compound II, mp 219-220°C (from [5], mp 216-217°C).

2-(2-Hydroxy-3,5-dinitrophenyl)pyridine (IV $C_{11}H_7N_3O_5$). To a solution of 0.5 g (3 mmole) compound I in 10 ml glacial acetic acid at room temperature was added, with stirring, 3 ml fuming nitric acid (d = 1.5). The mixture was heated at bp under reflux for 30 min, the precipitate filtered off and the mother liquor poured into an excess of KOH solution. The precipitate which formed here was combined with the first precipitate to give 0.2 g compound IV, mp 302-306°C.

2-(2-Hydroxyphenyl)quinoline (V) was prepared by the method of [12], mp 114-115°C (literature 113-114°C).

2-(2-Hydroxy-3-nitrophenyl)quinoline (VI, $C_{15}H_{10}N_2O_3$) was prepared in a similar manner to compound II, mp 160-163°C.

2-(2-Hydroxy-5-nitrophenyl)quinoline (VII, $C_{15}H_{10}N_2O_3$) was prepared in a similar manner to compound III, mp 254-256°C.

2-(2-Hydroxy-3,5-dinitrophenyl)quinoline (VIII, $C_{15}H_9N_3O_5$) was prepared in a similar manner to compound IV, mp 298-300°C.

4-(2-Hydroxy-5-nitrophenyl)pyrimidine (IX) was prepared by the method of [16], mp 229-231°C.

2-(2-Hydroxynaphthyl)quinoline (X) was prepared by the method of [11], mp 162-163°C.

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LACTAM AND AMIDE ACETALS.

56.* SYNTHESIS OF PYRIMIDINES FROM N-CARBAMOYLAMIDINES

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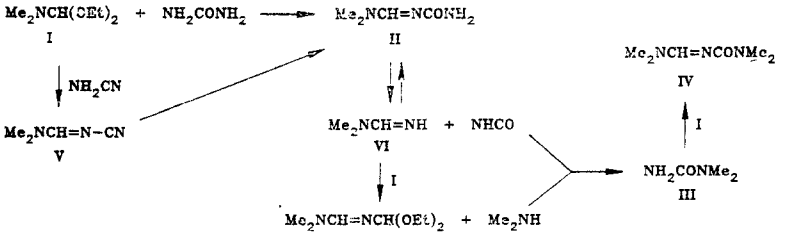
UDC 547.854'421.51'262'495.2.07

N-Carbamoyl-N,N'-dimethylformamidine reacts with ethyl anthranilate to give quinazoline-2,4-dione, and with cyanoacetamide to give 4-amino-5-carbamoylpyrimidin-2-one. The reaction of dimethylacetamide diethyl acetal with urea proceeds via N-carbamoyl-N',N'-dimethylacetamidine with the subsequent formation of 4-dimethylamino-6-methyl-pyrimidin-2-one and 4,6-dimethyl-sym-triazin-2-one

DMF diethylacetal (I) is known to react with urea to give N-carbamoyl-N',N'-dimethylurea (II) [2]. Our attempts to repeat this procedure resulted [2] in the isolation of a compound with a much lower melting point, which according to mass and PMR spectroscopy was a mixture of the amidine (II) and N,N-dimethylurea (III). Separation of (II) from (III) was effected by heating in vacuo, when the dimethylurea sublimed. Comparison of the PMR spectra of the pure (II) and (III) with that of the mixture showed that the ratio of the amidine (II) to the dimethylurea (III) in the mixture was approximately 3:2. The dimethylurea (III) is apparently formed by reversible decomposition of the amidine (II) under the reaction conditions to give N,N-dimethylformamidine and HNCO, as we have previously suggested for the heterocyclization of cyclic amidines [3], as follows:



This reaction pathway is supported by the observation that the mass spectrum of the reaction mixture showed the presence, in addition to compounds (II) and (III), of a compound with M^+ 143, which may be the amidine (IV).

A more suitable preparative method for the N-carbamoylamidine (II) is by reaction of the acetal (I) with cyanamide, followed by acid hydrolysis of the intermediate N-cyanoamide (V). A similar method using lactam acetal has been reported previously by the authors [4]. The unusually facile cleavage of the N-carbamoylamidine (II) to dimethylformamidine (VI) and

*For Communication 55, see [1].

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 0009-3122/90/2601-0070$12.50