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REACTIVITIES OF HETEROCYCLIC COMPOUNDS IN NITRATION.

6.* IONIZATION CONSTANTS OF 2-ANILINOPYRIDINES

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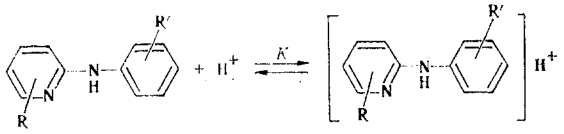
The pK_a values of 2-anilinopyridines with electron-acceptor substituents in the 3 and 5 positions of the pyridine ring and in the 2, 4, and 6 positions of the benzene ring determined by spectrophotometry range from 2.4 to −6.4. The sensitivity to the introduction of nitro groups in the pyridine ring is considerably higher than the sensitivity to introduction in the benzene ring in the case of both isomeric dinitro and tri- and tetranitro derivatives of 2-anilinopyridines.

N-Phenyl-2-aminopyridine derivatives that contain substituents with different chemical natures are convenient models for the study of the effect of the structure on the basicities and reactivities of the rings in electrophilic nitration. Data on the effect of the structure on the basicities of mononuclear pyridine derivatives are available in the literature [2]. However, the basicities of polynuclear pyridine-containing compounds have not yet been studied systematically.

In the present research we studied the effect of the number of nitro groups and their position on the equilibrium constant of reaction (1) in water.



(1)

$R = (NO_2)_n$, Br, Cl, I; $n = 0, 1, 2$; $R' = (NO_2)_m$; $m = 0, 1, 2, 3$

We found that the ionization of these compounds as the sulfuric acid concentration is increased is accompanied by appreciable changes in the UV spectra. The spectral characteristics of the neutral forms and conjugate acids of 2-(N-arylamino)pyridines are presented in Table 1. Their spectra were identified by a generally accepted method [3]. The results show that ionization of the compounds gives rise to a hypsochromic shift of the absorption maximum (Figs. 1 and 2). The protonation of 2-(N-arylamino)pyridines is described by the Hammett acidity function. Thus the dependence of the logarithm of the indicator ratio (log $I = \log [BH^+]/[B]$ on acidity function H_0 is expressed by a straight line. The slopes of these lines (m) are close to unity, and the investigated compounds are consequently Hammett bases. The analytical wavelengths and m and pK_a values for the investigated 2-(N-arylamino) pyridines are presented in Table 1. The pK_a values were calculated by means of expression (2):

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*See [1] for Communication 5.

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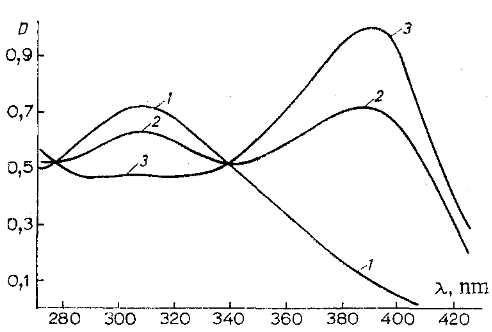


Fig. 1

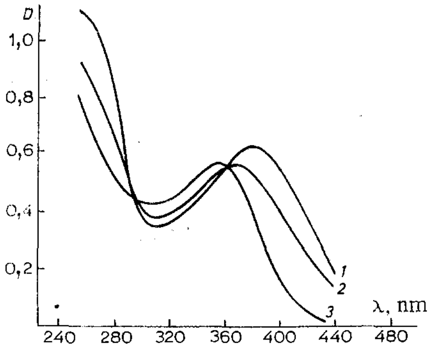


Fig. 2

Fig. 1. UV spectrum of 2-(N-picrylamino)-5-nitropyridine: 1) in 50% H_2SO_4; 2) in 30% H_2SO_4; 3) in 10% H_2SO_4; (c = $5 \cdot 10^{-5}$ mole-liter^{-1}).

Fig. 2. UV spectrum of 2-(N-picrylamino)pyridine: 1) in 0.002% H_2SO_4; 2) in 0.13% H_2SO_4; 3) in 10% H_2SO_4 (c = $4.89 \cdot 10^{-5}$ mole-liter^{-1}).

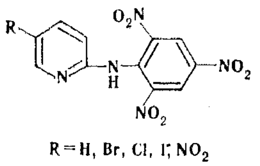
$$pK_a = \lg I + m \cdot H_0 \tag{2}$$

The ionization ratios were calculated from Eq. (3):

$$I = \frac{[BH^+]}{[B]} = \frac{\varepsilon_B - \varepsilon}{\varepsilon - \varepsilon_{BH^+}} \tag{3}$$

It is apparent from Table 1 that the basicities of 2-(N-arylamino)pyridines depend markedly on the number of nitro groups in the molecule. The difference between the most basic 2-(N-dinitrophenylamino)pyridine and 2-(N-picrylamino)-3,5-dinitropyridine is almost nine pK_a units. The pK_a of the latter compound (Table 1) is close to that of 2-bromo-4,6-dinitroaniline (−6.68 [4]).

It is interesting that the sensitivity to the introduction of nitro groups in the pyridine ring of 2-(N-arylamino)pyridines is higher than the sensitivity to the introduction of nitro groups in the phenyl ring. The indicated dependence is manifested in the case of both isomeric dinitro (I and II) and trinitro (III and IV) and tetranitro (VIII-X) derivatives. This can be explained by the fact that the protonation center in 2-(N-arylamino)pyridines is the ring nitrogen atom. The existence of a satisfactory correlation of the pK_a values of 2-(N-arylamino)pyridines with the σ_m substituent constants in the series shown below confirms the correctness of this assumption:



R=H, Br, Cl, I; NO_2

The equation of the regression line calculated by the method of least squares has the form

$$pK_a = -4.16 \cdot \sigma_m + 0.97;\ n = 5;\ r = 0.982;\ s = 0.14$$

The absence of correlation of the basicity constants with the σ_p substituent constants indicates that the protonation center is in the meta position relative to the substituent.

It is apparent from the data in Table 1 that a nitro group introduced into the 3 position of the pyridine ring decreases the basicity of the compound by a greater amount than a nitro group introduced into the 5 position. Thus a comparison of the pK_a values of the isomeric

TABLE 1. Spectral Characteristics of N-Phenyl-2-aminopyridines (Water, 20°C) and Data on the Protonation of 2-(N-Phenylamino)pyridines in Sulfuric Acid at 20°C

Compound	R	R′	Neutral molecule		Protonated molecule		λ_{anal}, nm	m	pK_a
			λ_{max}, nm	lg ε_{max}	λ_{max}, nm	lg ε_{max}			
I	H	2′,4′-$(NO_2)_2$	365	4,255	360	4,220	365	1,05	2,4±0,1
II	3,5-$(NO_2)_2$	H	345	4,127	306	4,114	390	0,99	−2,04±0,05
III	3,5-$(NO_2)_2$	4′-NO_2	366	4,280	301	4,250	364	1,0	−3,30±0,05
IV	H	2′,4′,6′-$(NO_2)_3$	380	4,110	357	4,064	400	1,0	1,06±0,04
V	5-Br	2′,4′,6′-$(NO_2)_3$	385	4,060	364	4,130	410	1,06	−0,87±0,07
VI	5-Cl	2′,4′,6′-$(NO_2)_3$	380	4,120	361	4,070	410	1,03	−0,80±0,06
VII	5-I	2′,4′,6′-$(NO_2)_3$	367	4,233	356	4,086	410	1,03	−0,55±0,08
VIII	5-NO_2	2′,4′,6′-$(NO_2)_3$	390	4,302	312	4,107	390	1,02	−1,87±0,06
IX	3-(NO_2)	2′,4′,6′-$(NO_2)_3$	385	3,970	342	3,941	390	1,0	−2,97±0,07
X	3,5-$(NO_2)_2$	2′,4′-$(NO_2)_2$	385	4,380	335	4,150	385	0,98	−4,89±0,07
XI	3,5-$(NO_2)_2$	2′,4′,6′-$(NO_2)_3$	380	4,280	280	4,270	380	1,06	−6,41±0,06

TABLE 2. Properties of the Substituted 2-(N-Phenylamino)pyridines

Compound	Substance and cited method of preparation	mp, °C	Recrystallization solvent
I	2-(N-Dinitrophenylamino)pyridine	155	Ethanol
II	2-(N-Phenylamino)-3,5-dinitropyridine [9]	149	Ethanol—acetone
III	2-[N-(4-Nitrophenylamino)]-3,5-dinitropyridine [9]	202—203	Ethanol
IV	2-(N-Picrylamino)pyridine [7]	134	Ethanol
V	2-(N-Picrylamino)-5-bromopyridine [1]	173—174	Methanol—acetic acid
VI	2-(N-Picrylamino)-5-chloropyridine [1]	165—165,5	Methanol—acetic acid
VIII	2-(N-Picrylamino)-5-nitropyridine [10]	166—168	Ethanol—acetone
IX	2-(N-Picrylamino)-3-nitropyridine [10]	188	Ethanol—acetone
X	2-(N-Dinitrophenylamino)-3,5-dinitropyridine	173	Ethanol—acetone
XI	2-(N-Picrylamino)-3,5-dinitropyridine [7]	205—206	Ethanol—acetic acid

3-nitro- (IX) and 5-nitro-2-(N-picrylamino)pyridines (VIII) shows that the difference in their basicities is 1.1 pK_a units. The reason for this phenomenon evidently consists in the special orientation of the nitropyridine and trinitrophenyl rings in the 2-(N-picrylamino)-3-nitropyridine molecule. The presence in both rings of nitro groups in the ortho positions relative to the amino group leads to disruption of the coplanarity of the molecule due to the steric effects of the substituents. Evidence for this is also provided by the literature data [5] on the three-dimensional structures of nitrodiphenylamines, which are structural analogs of nitro-2-(N-phenylamino)pyridines. The effect of the —NH—Pic fragment on the basicity of the endocyclic nitrogen atom is decreased as a result of rotation of the rings about the N—Ar and N—Py bonds. The pronounced effect of an o-nitro group also on the acidities of nitrodiphenylamines is similarly explained [6].

EXPERIMENTAL

Except for aminopyridines I and X, the subjects of the investigation were synthesized by known methods. Compound I was obtained by condensation of 2,4-dinitrochlorobenzene with 2-aminopyridine by a method similar to that proposed in [7] for the synthesis of 2-(N-picrylamino)pyridine.

2-(N-Dinitrophenylamino)-3,5-dinitropyridine (X). A 0.56-g sample of powdered KOH was sprinkled with stirring into a solution of 1.83 g (0.01 mole) of 2,4-dinitroaniline in 20 ml of dry DMF. After 15 min, 2.03 g (0.01 mole) of 2-chloro-3,5-dinitropyridine was added, and the resulting mixture was maintained at room temperature for 10 days, during which time the dark-red solution became appreciably lighter. At the end of this period the mixture was poured into 100 ml of water, and 2-3 ml of hydrochloric acid was added. The precipitate was removed by filtration and washed with water, alcohol, and ether to give 2.5 g (71%) of a product with mp 173°C (from acetic acid) (Mp 171-172°C [8]).

The substances were recrystallized no less than two to three times and dried in vacuo. The purity of the samples was monitored by TLC on Silufol UV-254 plates in a mixture of toluene and chloroform (1:1). The melting points of the prepared samples and the solvents used for recrystallization are indicated in Table 2.

The sulfuric acid solutions were prepared by dilution of 96% H_2SO_4 (chemically pure) with distilled water. The sulfuric acid concentration was determined with an accuracy of ±0.1% by titration with 0.1 N KOH solution. The basicities were measured with an SF-4 spectrophotometer with a thermostatted block. The concentration of the compound was $5\cdot10^{-5}$ mole/liter. The extinction coefficients ±3-4 H_0 units away from the half-protonation point were taken as the ε_B and ε_{BH^+} values. The analytical wavelength was selected near the absorption maximum of the neutral molecule, at which point the optical densities of both particles differ as much as possible from one another. The acidity functions were taken from the data in [11].

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REACTIVITIES OF HETEROCYCLIC COMPOUNDS IN NITRATION.

7.* EXPERIMENTAL AND THEORETICAL STUDY OF THE REACTIVITIES OF PYRIDINES

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The relationship between the rates of nitration of pyridines and the calculated [by the CNDO/2 (complete neglect of differential overlap) method] indexes of aromatic electrophilic substitution was investigated. The possibility of the use of two-center components of the localization energies for the theoretical description of the reactivities of pyridines in nitration is demonstrated. The rates of nitration of a number of previously uninvestigated pyridines are predicted.

A significant amount of experimental data on the reactivities of pyridine compounds with respect to nitration has been accumulated thus far [2-4]. Some kinetic data on the re-

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*See [1] for Communication 6.

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