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 $5 \cdot 10^{-5}$ 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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TABLE 1. Relative Delocalization Energies and Logarithms of the Rate Constants for the Nitration of Pyridines

Compound	Substrate	Position	$-\log K_2^0$, liter/mole · sec	$\Delta\Delta E$, eV	$\Delta\Delta\tilde{E}$, eV	Q_C
1	3-Hydroxypyridine	2	7,66	0	0	+0,031
2	3-Methoxypyridine	2	8,09	0,30	0,53	+0,033
3	4-Methoxypyridine	5	10,20	0,61	0,52	−0,096
4	2-Methoxy-3-methylpyridine	5	7,98	0,83	0,44	−0,047
5	4-Dimethylaminopyridine	3	2,98	3,59	3,28	−0,076
6	2,6-Dimethoxypyridine	3	4,73	1,79	2,42	−0,157
7	2-Dimethylaminopyridine	5	1,77	4,33	3,84	−0,054

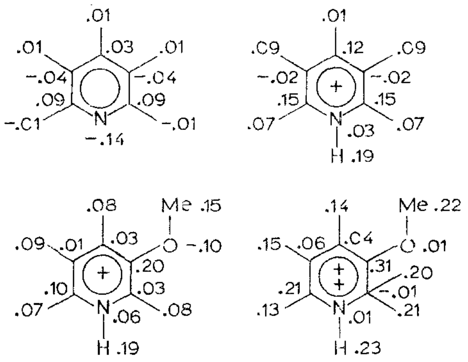
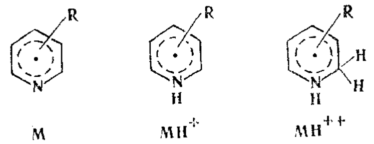


Fig. 1. Diagram of the charge distribution in pyridines.

activities of pyridines have been correlated and are presented in the literature in the form of comparable "standard rate constants" (k_2^0) for nitration [4]. The most typical conditions, corresponding to 75% H_2SO_4 ($H_0 = -6.60$) and 25°C, have been selected as the standard conditions. In this connection it becomes possible to obtain an empirical solution of the problem of the establishment of a quantitative relationship between the structures and reactivities of pyridine compounds with respect to nitration. For example, attempts have been made to establish a correlation of the reactivities with the substituent constants [5, 6]. Calculation of the localization energies within the π approximation [9] was used in [7, 8] for the theoretical description of the reactivities of pyridine compounds.

In the present research we attempted, with allowance for interaction of all of the valence electrons, to describe and predict the reactivities of a number of pyridines with respect to nitration. For compounds of this class we observed a correlation relationship between the localization energies calculated by the CNDO/2 (complete neglect of differential overlap) method and the $\log k_2^0$ values and predicted the reactivities. The experimental $\log k_2^0$ values [4] are compared with the characteristics ($\Delta\Delta E$ and $\Delta\Delta\tilde{E}$) of the localization energies in Table 1.

The standard rate constants correspond to the nitration of protonated substrates [4]. In this connection we adopted the pyridine bases nitrated at the nitrogen atom as substrate MH^+. The doubly protonated MH^{++} structure with a tetrahedral carbon atom and a C—H bond length of 1.47 Å was adopted as a model of the transition σ complex.



The localization energies are the differences between the total energies of the substrate and MH^{++}:

$$\Delta E = E(MH^+) - E(MH^{++});\ \Delta\tilde{E} = \tilde{E}(MH^+) - \tilde{E}(MH^{++}).$$

TABLE 2. Results of the Prediction of the Rate Constants for the Nitration of Pyridine Compounds

No.	Compound	Position	Form	$\Delta\Delta\tilde{E}$, eV	$-\log k_2^0$, liter/mole·sec
1	Pyridine	2	Neutral	3,46	2,32
2	Pyridine	3	"	3,97	1,27
3	Pyridine	4	"	3,47	2,30
4	Pyridine	4	Protonated	−1,36	12,20
5	Pyridine	3	"	−1,51	12,51
6	Pyridine	2	"	−2,36	12,25
7	2,6-Dichloropyridine	3	Neutral	0,10	9,20
8	2-Methoxypyridine	5	Protonated	0,44	8,51

TABLE 3. Experimental Parameters of the Nitration of 2,6-Dichloro and 2-Methoxypyridines in Sulfuric Acid

Compound, position of nitration, temp. (°C)	H_2SO_4 concn., %	$k_2^0\cdot10^4$, liters/mole·sec	$\log k_2^0$, liters/mole·sec
2,6-Dichloropyridine, 3, 120	94,5	0,50±0,08	−9,01
	91,4	1,36±0,12	
	88,4	0,58±0,06	
	85,4	0,18±0,02	
2-Methoxypyridine, 5, 70	95,2	8,3±0,6	−8,68
	89,8	30,9±3,0	
	88,2	34,6±2,4	
	86,1	11,5±1,0	
	84,8	8,5±0,6	

It follows from the data obtained that both characteristics of the localization energy make it possible to quantitatively describe the relative reactivities of pyridines with respect to nitration. The interrelationship between the logarithms of the standard rate constants for nitration and the localization energies is described by the linear expressions (n = 7)

$$-\lg k_2^0 = 8.95 - 1.67\Delta\Delta E;\ r = 0.923 \tag{1}$$

$$-\lg k_2^0 = 9.41 - 2.05\Delta\Delta\tilde{E};\ r = 0.985 \tag{2}$$

The correlation coefficients (r) of expressions (1) and (2) show that the $\Delta\Delta\tilde{E}$ values give the best agreement between the calculated and experimental reactivity parameters. This can be explained by compensation of the contributions to the reactivity of the atomic component and the solvation energy, which are not taken into account in the calculation.

We also used the two-center component of the localization energies ($\Delta\tilde{E}$), which is the difference between the two-center components of the energies [9] of the cation and its σ complex.

A diagram of the charge distribution in the base, the protonated cation, and the doubly protonated σ complex is shown in Fig. 1. As in our previous paper [10], the results of the calculation show that in the protonated structure the positive charge is delocalized over the entire molecule rather than being concentrated on the heteroatom. According to semiempirical calculations, in the pyridinium cation the increase in the positive charge on the nitrogen atom is 0.02 [11], which is close to our results. Charge delocalization stabilizes the protonated cation and its σ complex.

The energies of the individual bonds change during the formation of the σ complex. The changes in the energy of the C—H bond [ΔE(C—H)] at the reaction center are proportional to $\Delta\tilde{E}$ — the overall change in the energies of all of the bonds. Satisfactory correlation between the ΔE(C—H) values and the logarithms of the rate constants for nitration is retained:

$$\lg k_2^0 = 67.89 + 13.98\cdot\Delta E(\text{C—H});\ r = 0.952 \tag{3}$$

Let us discuss the relationship between the charge distribution in the protonated cation (the starting substrate), the site of protonation, and the rate constant. It is apparent from Fig. 1 that the charge on the atom in the protonated complex does not characterize the direction of nitration — charge redistribution and the corresponding resonance stabilization of the σ complex have a greater effect on the change in the total energy. However, with few exceptions, one observes symbatic character between the changes in log k_2^0, ΔΔE, and the effective charge on the carbon atom undergoing nitration (QC) (Table 1). The electrostatic interaction of this charge with the positive charge of the nitronium cation has a definite effect on the magnitude of the rate constant.

We used expression (2) to predict the rates of nitration of uninvestigated pyridines. We examined models that differ with respect to their chemical structures and reactivities (Table 2). The results of calculation of the rates of nitration of pyridine are in agreement with the known facts regarding the extremely low reactivity of pyridine with respect to nitration. Thus the predicted rates of nitration in acidic media, in which pyridine exists in the form of the pyridinium cation, for the 2, 3, and 4 positions, are lower by factors of, respectively, $5.0 \cdot 10^{14}$, $9.1 \cdot 10^{14}$, and $4.5 \cdot 10^{14}$ than the rate of nitration of benzene ($k_2^0 = 2.8184$) [4]. Experiments on the kinetics of nitration of 2,6-dichloro- and 2-methoxypyridines (Table 3) showed that Eq. (2) ensures an accuracy of prediction of the rate constants that is sufficient for practical purposes.

The errors in the prediction of the rate constants for the nitration of 2,6-dichloro- and 2-methoxypyridines did not exceed 40%. The agreement between the predicted and experimental values is satisfactory if one considers the fact that we did not take into account the differences in the solvation energies in our calculations.

EXPERIMENTAL

2,6-Dichloropyridine was obtained by the method in [12], while 2-methoxypyridine was obtained by the method in [13]. Nitration was accomplished by the methods described in [14, 15]. The kinetics of nitration were studied by spectrophotometry in 85-96% sulfuric acid with a 200-fold excess of nitric acid. The first-order rate constants were calculated from the change in the concentration of the compound undergoing nitration and were rescaled to second-order rate constants by division by the nitric acid concentration. The accuracy in the measurements was ±10%. Standardization of the nitration rate constants obtained was realized by the Katritzky method [4]. The results of the experiments are presented in Table 3.

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