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REACTIVITIES OF HETEROCYCLIC COMPOUNDS IN NITRATION. 5.* KINETICS OF NITRATION OF 5-SUBSTITUTED 2-PICRYLAMINOPYRIDINES

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The kinetics of nitration of 5-bromo-, 5-chloro-, and 5-nitro-2-picrylaminopyridines in 80-96% sulfuric acid were studied by a spectrophotometric method. The kinetic parameters of nitration were calculated. The UV spectra of the neutral and protonated forms in aqueous sulfuric acid solutions were identified. It was established that the indicated compounds are nitrated in the protonated form. The relative (as compared with benzene) rates of nitration were calculated.

The kinetics of nitration of polynuclear pyridine-containing compounds have not yet been studied systematically. The literature contains only a report regarding the study of the reactivity of 2-picrylaminopyridine [1]. In the present research we investigated the kinetics of the nitration of 5-nitro-, 5-chloro-, and 5-bromo-substituted 2-picrylaminopyridines in sulfuric acid.

3-Nitro derivatives are formed in close-to-quantitative yields in the nitration of nitro-, chloro-, and bromo-substituted 2-picrylaminopyridines with a 15-20-fold excess of concentrated nitric acid in 95% sulfuric acid (H_2SO_4:HNO = 90:10) at 40-70°C:

R Cl, Br, NO$_2$

The nitration of the iodo derivative at 60°C terminates with the formation of 5-nitro-2-picrylaminopyridine when an equimolar amount of HNO_3 is used and with the formation of 3,5-dinitro-2-picrylaminopyridine when a 15-20-fold excess of HNO_3 is used. This constitutes evidence for a reaction that proceeds in accordance with the scheme (see scheme after Table 2 at top of next page):

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*See [1] for communication 4.

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TABLE 1. Constants of 2-Picrylaminopyridine Derivatives

Compound	R^1	R^2	mp., °C	pK_a, 25° C	Found, %			Empirical formula	Calc., %			Yield, %
					C	H	N		C	H	N	
I	Br	H	173--174	−0,87±0,07	34,2	1,4	18,2	$C_{11}H_6BrN_5O_6$	34,38	1,30	18,23	93
II	Cl	H	165—165,5	−0,80±0,06	39,1	1,8	20,1	$C_{11}H_6ClN_5O_6$	39,90	1,47	20,60	91,5
III	NO_2	H	167—168	−1,87±0,06	38,1	1,9	23,9	$C_{11}H_6N_6O_8$	37,70	1,71	24,00	90,1
IV	I	H	185—186	−0,55±0,08	30,2	1,2	16,3	$C_{11}H_6IN_5O_6$	30,63	1,16	16,24	94
V	Br	NO_2	202—203	—	30,1	1,1	19,7	$C_{11}H_5BrN_6O_8$	30,17	1,16	19,58	95
VI	Cl	NO_2	193	—	34,3	1,2	21,7	$C_{11}H_5ClN_6O_8$	34,33	1,30	21,85	94
VII*	NO_2	NO_2	204—205	—								93,5

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*The reaction product was described in [4].

TABLE 2. Spectral Characteristics of 2-Picrylaminopyridine Derivatives

Compound	Solvent	Form*	λ_{max}, nm	lg ε
5-Bromo-2-picrylaminopyridine	75,5% H_2SO_4	CA	364	4,13
	6,0% H_2SO_4	NM	385	4,06
	Dioxane	NM	382,5	4,00
5-Chloro-2-picrylaminopyridine	75,5% H_2SO_4	CA	361	4,07
	6,0% H_2SO_4	NM	380,5	4,12
	Dioxane	NM	383	4,10
5-Nitro-2-picrylaminopyridine	75,5% H_2SO_4	CA	312	4,11
	15,0% H_2SO_4	NM	390	4,30
	Dioxane	NM	385	4,28

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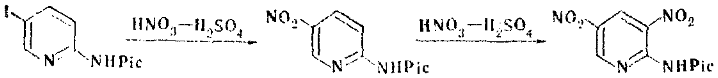
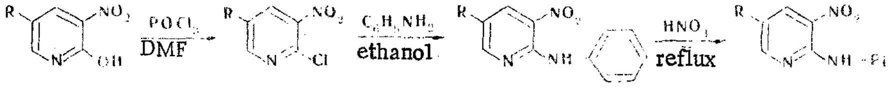
*Abbreviations: CA is the conjugate acid, and NM is the neutral molecule.



The constants of the starting compounds and the products of nitration are presented in Table 1. The compositions and structures of the compounds obtained were confirmed by the results of elementary analysis and the IR spectroscopic data. The position of the entering nitro group in the 5-chloro- and 5-bromo-3-nitro-2-picrylaminopyridines was proved by alternative synthesis from the known 5-chloro-3-nitro-2-anilinopyridine [2] and 5-bromo-3-nitro-2-hydroxypyridine [3] via the scheme



R Br, Cl

The product of nitration of 5-nitro-2-picrylaminopyridine, viz., 3,5-dinitro-2-picrylaminopyridine, was described by Coburn [4].

In order to study the kinetics of nitration it was necessary to ascertain the behavior of the compounds to be nitrated in the reaction medium. The establishment of the possibility of their protonation in aqueous sulfuric acid solutions was carried out by UV spectroscopy, which made it possible to establish the transition from the neutral molecule to the protonated compound from the shift of the absorption maxima. The spectra of the neutral molecules and the conjugate acids of the investigated compounds are presented in Table 2. Protonation leads to the disappearance of the n–π* transition due to bonding of the unshared pair of electrons of the nitrogen atom with a proton; this is expressed in the shift of the long-wave maximum to the shorter-wave region and in the decrease in its intensity. Experiments showed that 2-picrylaminopyridines also readily undergo protonation in sulfuric acid solutions with concentrations greater than 50% and that the presence of a neutral molecule is not recorded in the UV spectrum of even the most acidic representative, viz., 5-nitro-2-picrylaminopyridine. Their basicities determined by a spectrophotometric method are presented in Table 1.

The kinetics of nitration of the compounds were studied in 80-96% H_2SO_4 by a UV spec-

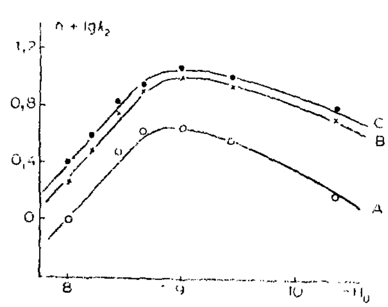


Fig. 1

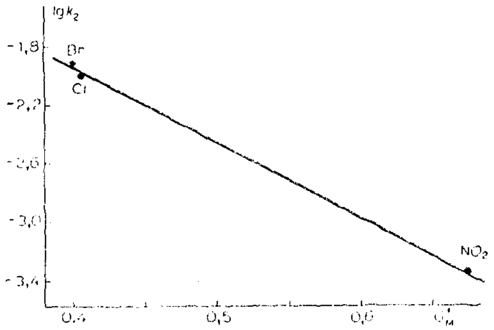


Fig. 2

Fig. 1. Dependence of the rate of nitration of 5-substituted 2-picrylaminopyridine on the acidity of the medium at 64.6°C: A) 5-R = NO_2, n = 4; B) 5-R = Br, n = 3; C) 5-R = Cl, n = 3.

Fig. 2. Dependence of the rates of nitration of 5-substituted 2-picrylaminopyridines in 90.4% H_2SO_4 on the substituents.

trophotometric method in the presence of a 40-80-fold excess of nitric acid. The first-order rate constant was calculated from the change in the concentration of the compound undergoing nitration and was converted to a second-order rate constant by division by the nitric acid concentration. The results of the kinetic studies are presented in Tables 3 and 4. An analysis of the data shows that the dependence of log k_2 on the acidity of the medium is a linearly increasing function up to 90% sulfuric acid, after which the rate of nitration decreases. A similar dependence has also been observed for other compounds that are nitrated

TABLE 3. Rate Constants (k_2) for the Nitration of 5-Substituted 2-Picrylaminopyridine* in Sulfuric Acid at 64.6°C

H_2SO_4 concn., mass %	$-H_0$†	$k_2 \cdot 10^3$, liters•mole^{-1}/sec^{-1}, for		
		5-bromo	5-chloro	5-nitro
96	10,36	5,2±0,5	6,1±0,4	0,17±0,5
92,7	9,43	8,5±0,5	9,6±0,3	0,35±0,4
90,4	8,99	10,0±0,4	12,0±0,3	0,44±0,3
88,2	8,65	7,9±0,5	8,5±0,5	0,41±0,4
86,8	8,42	5,5±0,3	6,6±0,3	0,29±0,4
85,5	8,21	3,0±0,4	3,9±0,4	0,15±0,5
83,2	7,99	1,9±0,5	2,6±0,5	0,097±0,5

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*The concentration of the substrate was 10^{-2} mole/liter.

†The H_0 values were taken from [5].

TABLE 4. Activation Parameters for the Nitration of 2-Picrylaminopyridine Derivatives in 90.4% Sulfuric Acid

R in comp. undergoing nitration	Temp., °C	$k_2 \cdot 10^3$, liters•mole^{-1}/sec^{-1}	ΔE, kcal•mole^{-1}	lg A	ΔS, eu
Br	70	15,0±0,6	15,5	8,0	−24,2
	80	28,0±0,5			
	93	61,0±0,5			
Cl	40	2,9±0,4	13,9	6,3	−31,9
	50	6,7±0,5			
	60	10,0±0,5			
	70	18,0±0,3			
NO_2	60	0,17±0,4	15,0	6,3	−31,7
	70	0,62±0,3			
	75	0,92±0,4			
	80	1,61±0,5			

TABLE 5. Relative Reactivities of 2-Picrylaminopyridines at 64.6°C in 85.5% H_2SO_4

Compound	k_2, kcal•mole^{-1}• sec^{-1}	k_{rel}
5-Bromo-2-picrylaminopyridine	0,0030	$0{,}32 \cdot 10^{-9}$
5-Chloro-2-picrylaminopyridine	0,0039	$0{,}42 \cdot 10^{-9}$
5-Nitro-2-picrylaminopyridine	0,00015	$0{,}16 \cdot 10^{-10}$
Benzene*	$9{,}26 \cdot 10^{6}$	1

*Calculated from the results in [8].

in the conjugated acid form [1, 6]. The activation parameters for the nitration of 2-picrylaminopyridines confirm this fact. The entropies of activation of less than —20 eu are characteristic for reactions between two positively charged particles. The data from kinetic measurements provide evidence for nitration of 5-substituted 2-picrylaminopyridines in sulfuric acid in the protonated form. This affects the reactivities as follows: the rate constants of the investigated 2-picrylaminopyridine derivatives are smaller by a factor of 10^9 to 10^{10} than in the case of benzene (Table 5). The polar effect of substituents, which is satisfactorily described by the σ_M^+ substituent constants (Fig. 2), has a significantly smaller effect on the reaction rate (Fig. 2).

EXPERIMENTAL

The 5-bromo- and 5-chloro-2-aminopyridines used in the experiments were pure-grade or analytically pure-grade reagents. The 5-iodo-2-aminopyridine and 5-nitro-2-picrylaminopyridine were obtained by the method in [1, 9].

5-R-2-Picrylaminopyridines (R = Br, Cl, and I). A mixture of 0.1 mole of 5-R-2-aminopyridine and 0.05 mole of picryl chloride in 180-200 ml of ethanol was refluxed for 3 h, after which it was cooled, and the precipitated crystals (85-88% yield) were removed by filtration. Partial evaporation of the alcohol mother liquor yielded an additional portion of the product, which was recrystallized from acetic acid—methanol (1:1) (Table 1).

5-R-3-Nitro-2-picrylaminopyridines (R = Br, Cl, and NO_2). A 0.05-mole sample of 5-R-2-picrylaminopyridine was dissolved in 250 ml of 95% H_2SO_4, and the resulting solution was treated with 37 mg of 98% HNO_3. The mixture was stirred at 60°C for 1.5 h, after which it was poured over ice. The precipitate was removed by filtration, washed with water, dried, and purified by recrystallization from acetic acid—methanol (2:1) (Table 1).

In the case of the iodo derivative nitration takes place with the liberation of iodine (the solution becomes darker). Workup gave 3,5-dinitro-2-picrylaminopyridine, with mp 204-205°C (mp 204-205°C [4]), in 90% yield. The IR and UV spectra were identical to the spectra of an authentic sample of 3,5-dinitro-2-picrylaminopyridine.

Chlorination of 2-Hydroxy-3-nitro-5-R-pyridines (R = Cl, Br). A 0.03-mole sample of 5-bromo- [3] and 5-chloro-3-nitro-2-hydroxypyridine [10] was dissolved in 30 ml of dry dimethylformamide (DMF), and 20 ml of phosphorus oxychloride was added dropwise at 20°C to the solution. The mixture was heated at 80°C for 5 h, after which it was cooled and poured over ice. The resulting precipitate was removed by filtration, washed repeatedly with water, and dried. The chlorination products were identified in the form of the 2-anilino derivatives.

2-Anilino-3-nitro-5-R-pyridines (R = Cl, Br). A 0.01-mole sample of the chloro derivative and 0.01 mole of aniline were heated in dry DMF at 50°C for 5 h, after which the mixture was diluted with water. Workup gave red needles of 2-anilino-3-nitro-5-chloropyridine (85%) with mp 85°C (from isopropyl alcohol) (mp 85-85.5°C [2]). 2-Anilino-3-nitro-5-bromopyridine (75%), with mp 91-92°C (from isopropyl alcohol), was obtained in the form of acicular crystals. Found: C 44.8; H 2.7; N 14.3%. $C_{11}H_8BrN_3O_2$. Calculated C 44.9; H 2.72; N 14.29%.

Nitration of 2-Anilino-3-nitro-5-R-pyridines (R = Cl, Br). A 0.5-g sample of the anilino derivative was dissolved in 20 ml of cooled (to 0°C) concentrated HNO_3, and the solution was gradually heated to the boiling point and was then refluxed for 20 min. Dilution with cold water yielded 3-nitro-5-R-2-picrylaminopyridines. The melting points, data from thin-layer chromatography (TLC), and mixed-melting-point determinations demonstrated that the products were identical to the substances obtained by nitration of 2-picrylamino-5-chloro- and -5-bromopyridines.

The nitration of the anilino derivatives in a sulfuric acid—nitric acid mixture at 60°C led to the same results.

The substances and reagents for the spectral and kinetic studies were purified until they had constant melting points. Their purity was verified by TLC, which was carried out on silica gel under standard conditions on Silufol UV-254 plates in chloroform. The dried (to constant weight) substances were stored over a drying agent ($CaCl_2$). Sulfuric acid of the analytically pure-grade category was used without additional purification. The dioxane was purified by the method in [11].

The recording of the UV spectra and the kinetic measurements were realized with an SF-4 spectrophotometer. The nitrating mixture was prepared by dissolving weighed samples of KNO_3 in sulfuric acid. The percentage composition of the H_2SO_4 was determined by alkalimetric titration; the accuracy in the determination was ±0.1%.

Method for the Study of the Kinetics of Nitration. A 10-ml sample of the nitrating mixture of the required concentration was placed in a test tube equipped with a ground glass stopper and thermostatted. A 1-ml sample of a concentrated solution of the substrate (0.05 mole-liter^{-1}) in sulfuric acid of the same concentration was added. Under these conditions the concentration of the substrate in the sulfuric acid—nitric acid mixture was $5 \cdot 10^{-3}$ mole-liter^{-1}. The change in the concentration was monitored by the selection of aliquot samples from the reaction medium, 150-fold dilution of them with 50% H_2SO_4, and subsequent measurement of the optical densities at the absorption maxima of the nitration products. The rate constants were determined graphically by the method in [12]. The average values of three parallel experiments are presented in Table 3.

The basicities of the 5-substituted 2-picrylaminopyridines were measured by spectrophotometry [13].

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