

STUDIES IN THE FIELD OF CHEMISTRY OF NITRO COMPOUNDS (TO 100TH BIRTHDAY ANNIVERSARY OF S. S. NOVIKOV)

Nitration Kinetics of 6-Hydroxy-2-methylpyrimidin-4(3*H*)-one and 2-Methoxy-2-methylimidazolidine-4,5-dione

A. A. Kushtaev, A. V. D'yakonov, N. V. Yudin, and V. L. Zbarskii

Mendeleev Russian University of Chemical Engineering, Moscow, Russia

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Abstract—Possibility of synthesizing sulfo- and aminomethyl derivatives of 4-isononylphenol (**I**) was examined and the anticorrosion activity of the compounds obtained was determined.

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Derivatives of hydroxypyrimidines and imidazoles, widely used in syntheses of biologically active compounds and medicinal preparations [1], have been attracting researchers' attention in recent years as starting products in obtaining energetic materials. Therefore, of indubitable interest is analysis of the kinetics and mechanism of reactions yielding 1,1-diamino-2,2-dinitroethylene (DADNE, FOX-7), a promising insensitive explosive [2]. In this communication, we report on a study of the nitration kinetics of 6-hydroxy-2-methylpyrimidin-4(3*H*)-one (**I**) and 2-methoxy-2-methylimidazolidine-4,5-dione (**II**), which are starting products in synthesis of DADNE with sulfuric-nitric acid mixtures (SNAMs).

EXPERIMENTAL

We studied the nitration kinetics by the spectrophotometric method on a Specord M-40 UV spectrophotometer. The nitration was performed with sulfuric-nitric acid mixtures in a thermostated cell. Analyses were made by the sampling method, with the reaction in the samples terminated by a 100-fold (by volume) dilution with water. The optical density was determined in 1.6–1.8% sulfuric acid solutions. Under the experimental conditions, the concentration of the compound being nitrated was $(0.4\text{--}0.7) \times 10^{-2}$ M, which is 150–500 times lower than that of nitric acid.

We used known procedures to synthesize the starting compounds **I** [3] and **II** [4] and their nitro derivatives, 6-hydroxy-2-methyl-5-nitropyrimidin-4(3*H*)-one (**III**)

[5], 2-(dinitromethylene)-5,5-dinitropyrimidine-4,6-(1*H*,3*H*,5*H*)-dione (**IV**) [5], 2-(dinitromethylene)imidazolidine-4,5-dione (**V**) [4], and DADNE [5]. The structure and purity were confirmed by IR and PMR spectroscopic data. The IR and PMR spectra were measured with FTIR Avatar 360 and Bruker AM 300 instruments, respectively. An HPLC analysis was made on an Agilent 1100 instrument [Hipersil ODS 2×100 mm column in the gradient mode; acetonitrile : buffer solution (0.2 M NaClO₄, 0.005 M HClO₄) : water as eluent at 10 : 20 : 70 to 40 : 20 : 20 ratio in 5 min and further to 75 : 20 : 5 by 10th minute; diode array as detector; analytical wavelength 350 nm].

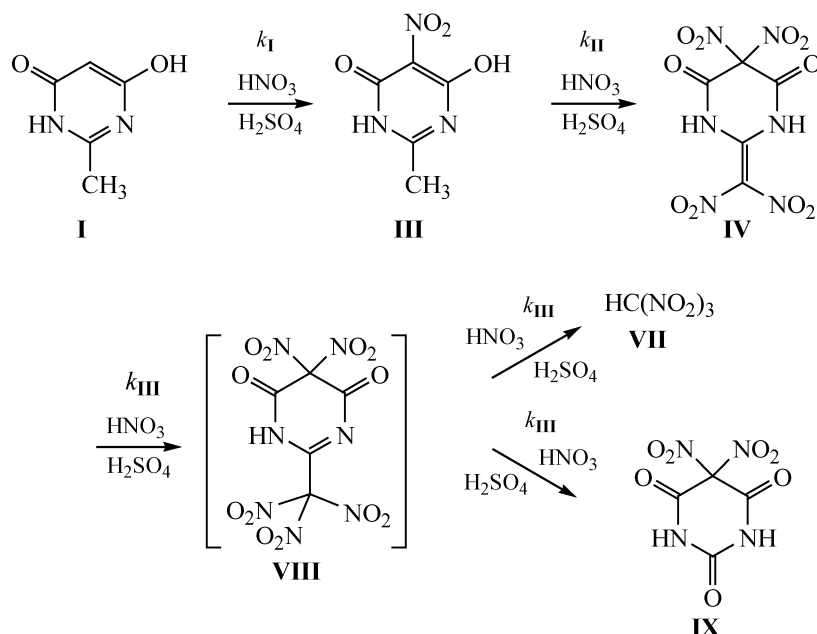
To perform qualitative and quantitative analyses of the reaction masses, UV spectral characteristics of compounds **I–V**, dinitromethane (**VI**), trinitromethane (**VII**), and DADNE were determined in a 1.8% sulfuric acid solution. The results obtained are listed in Table 1.

Compounds **II** and **VI** show no absorption at 250–500 nm, compound **V** is unstable in the 1.8% sulfuric acid solution and its concentration was found from that

Table 1. Absorption peaks (λ) and molar extinction coefficients $\log \epsilon$ of the components present in the reaction masses in nitration

Parameter	Compound					
	I	III	IV	VII	DADNE	
λ , nm	252	324	336	352	278	348
$\log \epsilon$	4.07	3.80	4.32	4.07	3.78	4.05

Scheme 1.



of DADNE upon complete hydrolysis, with allowance for the yield.

The content of the components in the reaction mixture in nitration was determined using the Lambert–Burger–Beer law and the principle of additivity of optical densities. To improve the calculation accuracy, we used full spectra in a tabulated form in the wavelength range 250–500 nm. The system of equations we obtained was solved numerically.

Nitration kinetics of 6-hydroxy-2-methylpyrimidin-4(3H)-one. Preliminary experiments on nitration of **I** demonstrated the process does not end with synthesis of **IV**. This compound is comparatively rapidly converted to give a mixture of products, one of which was identified as trinitromethane. Based on these results and published data on nitration of 2-methyl-1,3,5-triazine-4,6-dione and 5-alkyl-substituted derivatives of compound **I** [6], we suggested that 5,5-dinitro-2-(trinitromethyl)pyrimidine-4,6-(1H,5H)-dione (**VIII**) is formed from **IV** in the reaction mixture and decomposes in the nitrating mixture, with trinitromethane eliminated and 5,5-dinitrobarbituric acid (**IX**) formed (Scheme 1).

Indeed, on keeping **IV** in an SNAM, compound **IX** is precipitated, which was isolated by washing with trifluoroacetic acid in 60% yield; in the case of nitration of **IV** in 99% HNO₃, followed by evaporation of the

acid, the yield of **IX** is nearly quantitative. Compound **IX** was identified by comparison with a known sample obtained in accordance with the recommendations of [7], by IR spectroscopy, and using the hydrolysis product, dinitroacetylurea **X**, by IR spectroscopy and HPLC. The fact that **IX** is isolated from the reaction mixture without dilution with water indicates that the elimination of the nitrophorm from compound **VIII** occurs directly in a sulfuric acid medium at a high rate, which makes impossible accumulation of the product of further nitration of **IV**.

The nearly complete absence of other processes is confirmed by quantitative analysis of reaction masses by HPLC and UV spectrophotometry. Compounds **VII** and **IX** are formed almost synchronously, with their yield being nearly quantitative. Only upon a long keeping time (>10 h), the amount of **VII** starts to decrease which is due to its nitration to tetranitromethane. The rate of tetranitromethane formation is in good agreement with the data reported in [8].

No intermediates containing two or three nitro groups were recorded. The chromatograms of reaction mass samples taken at different conversions show only **III**, **VI**, **VII**, DADNE, **X**, and insignificant amounts of tetranitromethane. The percentage of the peak areas of unidentified compounds, relative to the total are of peaks in the chromatograms, is insignificant.

A processing of the spectral data obtained in kinetic experiments in 78–96% sulfuric acid confirmed that only the compounds mentioned above are present.

The nitration kinetics of **I** was studied in a large excess of nitric acid. At concentrations of the starting sulfuric acid in the range 78–98%, the data obtained are well described by equations for systems of two or three successive first-order reactions.

If the concentration of the starting compound in nitration of **I** and **III** is varied within the range $(0.3\text{--}0.9) \times 10^{-2}$ M, the rate constants remain unchanged, which points to the first order of the reaction with respect to the compound being nitrated.

The reaction orders with respect to nitric acid vary between the process stages observed. Figure 1 shows log–log dependences of the rate constants on the nitric acid concentration.

As follows from Fig. 1, the reaction is first-order for the first and third stages and approaches 2.5 for the second stage. Presumably, the fractional order appears because of the occurrence of three successive reactions in a single observed stage in the absence of a pronounced leading reaction.

It should be noted that the reaction in which DADNE is synthesized has a complicated multistage nature and the transformation chain comprises, in addition to the nitration proper, rearrangements to give various tautomeric forms of pyrimidine derivatives including

those of the keto-enol and methyl-methylene types. The rate of these latter processes and the positions of the equilibria can strongly affect the nitration kinetics.

Taking into account the reaction orders obtained, we calculated the rate constants by the formula

$$k_i = k_i^{\text{eff}}/[\text{HNO}_3]^n,$$

where k_i is the rate constant of i th stage; k_i^{eff} , effective rate constant of i th stage; $[\text{HNO}_3]$, concentration of nitric acid; and n , formal reaction order with respect to nitric acid. The data obtained are shown in Fig. 2.

The rate constant k_{II} was calculated from the consumption of **III** or formation of **IV**; the values obtained well coincided which confirms the adequacy of the calculation. Further processing was made using the average value. The constant k_{III} was determined from the formation of the nitrophorm and dinitroacetylurea, with the value obtained verified against the consumption of **IV**; the resulting values were also averaged.

The mononitration rate constant k_{I} is, on average, 10 times the rate constant k_{II} of **IV** formation, and k_{III} is three times smaller than k_{II} . As the sulfuric acid concentration increases, k_{II} and k_{III} grow somewhat faster than k_{I} . The dependences show maxima in the H_2SO_4 concentration range 88–92%, characteristic of the Martensen maximum [9]. The overall yield of the reaction products in 78–98% sulfuric acid is $95 \pm 2\%$.

At sulfuric acid concentrations lower than 78% in SNAM, the rate of **IV** formation becomes negligible. Simultaneously, the convergence in calculating the composition of the reaction products from UV spectroscopic data becomes poorer, which may be due to

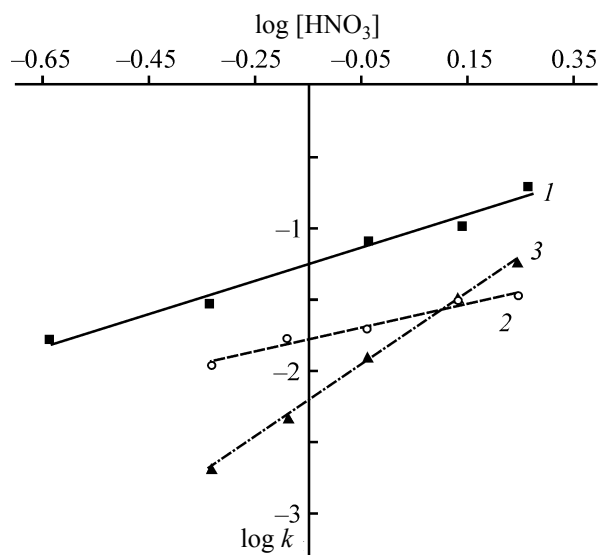


Fig. 1. Formal reaction orders of the first, second, and third stages of nitration of **I** with respect to nitric acid at 25°C. (1) $\log k_{\text{I}}^{\text{eff}}$, (2) $\log k_{\text{II}}^{\text{eff}}$, and (3) $\log k_{\text{III}}^{\text{eff}}$.

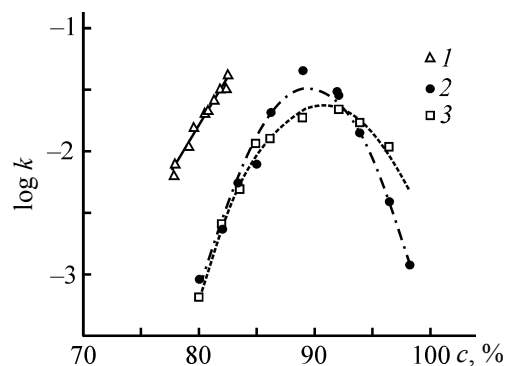


Fig. 2. Dependences of the rate constants of the first, second, and third stages of nitration of **I** on the sulfuric acid concentration c , calculated by taking into account the reaction orders.

appearance of intermediates or by-products in samples in significant amounts. Indeed, a chromatographic analysis demonstrated the presence of unidentified compounds. These deviations may be due to the capacity of substituted pyrimidines and, in particular, hydroxy derivatives, for nitrosation in an acid medium to give 5-nitrosopyrimidines [10]. It was suggested that the electrophilic agent changed in this region: this may be the nitrosonium ion instead of the nitronium ion. To verify this hypothesis, we studied the nitration of **III** in an SNAM with addition of sodium nitrite. Preliminarily, with an SNAMs prepared using freshly distilled anhydrous HNO_3 with or without addition of urea, we found that they contain no nitrogen oxides, i.e., the effect of urea on the process kinetics is a minimum. The data obtained are listed in Table 2.

It can be seen in Table 2 that, at an H_2SO_4 concentration lower than 74.7%, the overall nitration rate is determined by the nitrosation reaction. Simultaneously, on passing from 72 to 76.5% sulfuric acid, the reaction rate decreases, which may be due to a lower concentration of the free form of **I**.

According to [11], compound **I** is a weak base with $\text{p}K_b$ 0.21 for the monoprotection reaction, i.e., the transition to the salt form occurs even in a 5–10% aqueous sulfuric acid solution. Data on the subsequent protonation stages are lacking, and, therefore, we spectrophotometrically studied the behavior of **I** in sulfuric acid solutions with concentrations of 0.09 to 94% and in water. It was found that the absorption peak at 252 nm ($\log \varepsilon = 4.09$) corresponded to the free form, and peaks at 242 nm ($\log \varepsilon = 3.93$) and 247 nm ($\log \varepsilon = 4.08$) correspond to mono- and diprotonated forms. The Firordt equation was used to calculate the concentrations of the components

Table 2. Rate constants of the reaction of nitration of **I** to **III** with SNAM at 25°C. $[\text{HNO}_3] = \text{const} = 0.46 \text{ M}$

Run series no.	$k_{\text{eff}} \times 10^2, \text{ min}^{-1}$, at indicated H_2SO_4 concentration, %							
	72.0	74.7	76.5	78.1	79.1	80.9	81.3	82.0
1 ^a	0.22	0.20	—	0.31	—	—	—	1.75
2 ^b	0.20	0.20	—	0.42	—	—	—	1.65
3 ^c	7.42	3.92	0.50	0.34	0.51	0.99	1.19	1.56

^a Nitrating mixtures based on freshly distilled nitric acid.

^b Nitrating systems based on freshly distilled nitric acid, with addition of urea, $[\text{CH}_4\text{N}_2\text{O}] = 9.6 \times 10^{-3} \text{ M}$.

^c Nitrating systems with addition of nitrogen oxides, $[\text{N}_2\text{O}_3] = 2.8 \times 10^{-3} \text{ M}$.

of the mixture, and the Yates–McClelland equation, to find the basicity constants for both protonation stages to be $\text{p}K_b$ 0.24 at $m = 1.06$ (half-protonation point in 4.5% H_2SO_4) and $\text{p}K_b$ 2.248 at $m = 0.41$ (half-protonation point in 71.5% H_2SO_4) on the H_0 acidity scale. In the first stage of protonation, compound **I** behaves as a Hammett base which is indicated by the coefficient $m \approx 1$. In the second stage of protonation, the observed value of the coefficient m means that it is necessary to use the acidity function HA [12]. It should be noted that solutions of **I** are stable for at least 24 h in the entire range of sulfuric acid concentrations.

In 72–76% H_2SO_4 , mono- and diprotonated forms of **I** are present. Taking into account the low concentration of the free form of **I**, we could assume that protonated forms are involved in the nitration reactions, and, therefore, we considered all the possible variants of the process: via free (**B**), protonated (BH^+), and diprotonated (BH_2^{2+}) forms.

For this purpose, we calculated by the formulas

$$[\text{B}] = [\text{B}_0]/(1 + k_1 k_2 \text{H}_1^+ \text{H}_2^+ + \text{H}_1^+ k_1),$$

$$[\text{BH}^+] = [\text{B}_0]/\{1 + k_2 \text{H}_2^+ + [1/(k_1 \text{H}_1^+)]\},$$

$$[\text{BH}_2^{2+}] = [\text{B}_0](1 - [\text{B}] - [\text{BH}^+]),$$

where $[\text{B}_0]$ is the initial concentration of **I** in the reaction mixture; $[\text{B}]$, $[\text{BH}^+]$, and $[\text{BH}_2^{2+}]$, concentrations of free and mono- and diprotonated forms of **I** in the reaction mixture, respectively; $k_1 = 10^{\text{p}K_{b1}}$ and $k_2 = 10^{\text{p}K_{b2}}$, equilibrium constants of the first and second stages of protonation of **I**, respectively; $\text{H}_1^+ = 10^{m_1 \text{H}_0}$; $\text{H}_2^+ = 10^{m_2 \text{H}_0}$; and H_0 , value of the acidity function; and m_1 and m_2 , slope ratios, the concentrations of all the components. Then, using the effective rate constants and taking into account the degrees of conversion of nitric acid to the nitronium ion [13], we found the true second-order constants. As can be seen in Fig. 3, the constant is the same in the entire range of sulfuric acid concentrations only in the case of nitration of a free base. A good convergence of constants calculated for the free base is also observed for the rate of **III** formation with nitrous acid involved. In this case the concentration of the active agent was taken to be equal to the concentration of nitrous acid, because its degree of ionization is close to 100% in sulfuric acid of the concentrations used [9]. The constants were calculated

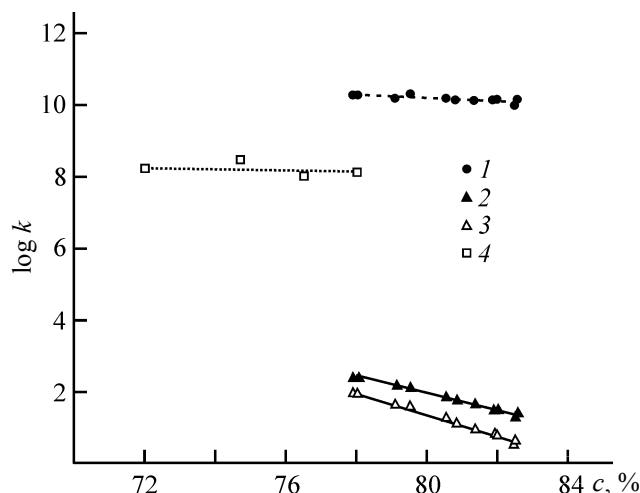


Fig. 3. Dependence of the true second-order rate constants of nitration of **I** on the sulfuric acid concentration c . Calculation of k_I^{eff} for nitration of (1) free, (2) monoprotonated, and (3) diprotonated forms; (4) calculation of k_{III} for nitration of the free form, with nitrous acid involved.

by the formula

$$k_I^{\text{eff}}[\text{I}]\text{NO}_2^+/\text{NO}^+ = k_I^{\text{eff}}/([\text{I}][\text{N}]),$$

where k_I^{eff} is the effective rate constant of nitration of **I** to **III**; $[\text{I}]$, concentration of the corresponding form (B, BH^+ , BH_2^{2+}) of **I**; $[\text{N}]$, concentration of the electrophilic agent (NO_2^+ , key role of nitric acid; NO^+ , key role of nitrous acid).

The resulting values of the nitrosation rate constants are two orders of magnitude lower than the nitration rate constants. At the same time, the absolute values of the nitration rates of the free form of **I** exceed those of anisole and toluene [14], which results from the presence of several activating groups in the molecule.

In determining the constants k_{II} and k_{III} , it seemed impossible, because of the lack of data on the leading stage of the process and $\text{p}K_b$ values for intermediate compounds (except **III**), to take into account the decrease in the activity of the substrate because of its protonation. Figure 4 shows how the nitration rate constants depend on the acidity function, $\text{HR} + \log a_w$. At sulfuric acid concentrations in the range from 80 to 90%, the dependences are linear; however, the slope ratios are substantially lower than those in nitration of aromatic compounds (Fig. 4 shows nitration constants for nitrobenzene [14] and *p*-chloronitrobenzene [14]) and are 0.38 for k_{II} and 0.43 for k_{III} . Figure 5 shows data on the nitration rates of 2,4-DNT [15], nitrobenzene [14],

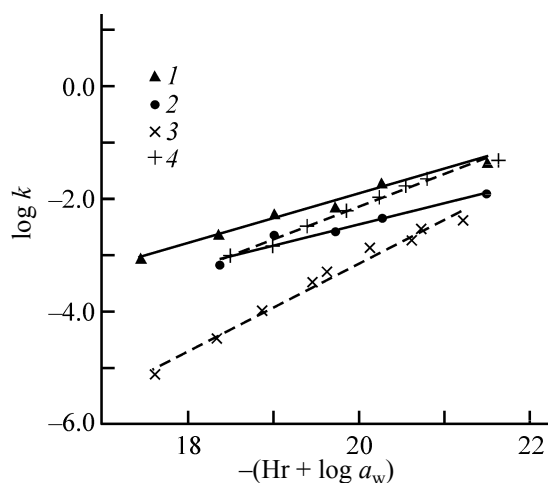


Fig. 4. Nitration rate constants (1) k_{II} , (2) k_{III} , (3) of *p*-chloronitrobenzene, and (4) of nitrobenzene in the H_2SO_4 concentration range 80–90%.

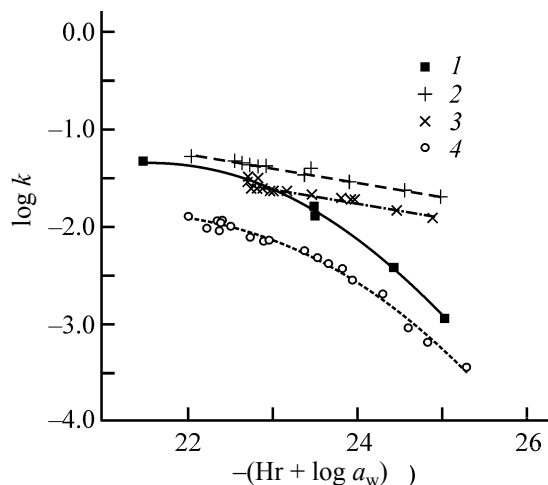
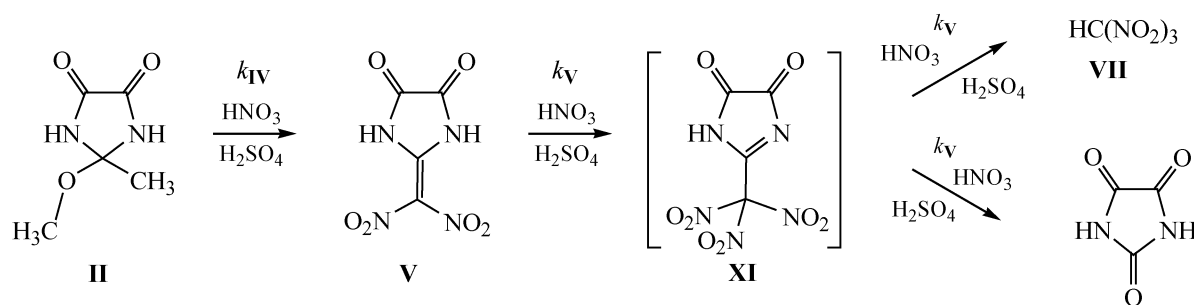


Fig. 5. Nitration rate constants (1) k_{II} of **I**, (2) of nitrobenzene, (3) of 2,4-dinitrotoluene, and (4) of trinitromethane at H_2SO_4 concentrations exceeding 90%.

and nitrophorm [8]. It can be seen that, in the case of nitration of **III** and **IV**, the dependence differs from that for nitration of aromatic compounds, with its slope ratio being substantially smaller than unity. At sulfuric acid concentrations exceeding 90%, the shape of the curve is similar to that for nitration of nitrophorm.

This coincidence indicates that the rate-determining stage of the process in nitration of **III** is the reaction of introduction of a nitro group into the side chain. Taking into account the concentration of the nitronium ion also fails to yield the true rate constant of the process: its monotonic decrease is observed, which cannot be attributed to a decrease in the activity of the nitronium

Scheme 2.



ion at sulfuric acid concentrations exceeding 90%. A similar situation is observed in nitration of aliphatic nitro compounds: nitrophorm, dinitroacetonitrile, and 1,1,1,2,2-pentanitroethane. In this case, the parameters of the Arrhenius equation for k_I – k_V well correspond to the electrophilic nitration and values of the pre-exponential factors point to a bimolecular type of the reaction (Table 3).

Nitration kinetics of 2-methyl-2-methoxyimidazolidine-4,5-dione. Nitration of **II** with SNAM occurs similarly to that of **I**. 2-(Dinitromethylene)imidazolidine-4,5-dione is supposedly transformed to 2-(trinitromethyl)-imidazolidine-4,5-dione-1-ene, which is hydrolyzed in the reaction mixture to give trinitromethane and parabanic acid **XIII** (Scheme 2).

Nitration of **II** with nitric acid in the course of 24 h, followed by filtration and washing of the product with trifluoroacetic acid, yielded parabanic acid in quantitative

yield. Its structure was confirmed by the identity of its IR spectrum with that described previously. Trinitromethane was isolated as a sodium salt by neutralization of the acid mixture, followed by extraction with isobutanol.

Immediately before performing kinetic experiments on nitration, we studied the stability of **II** in 0.5–95% solutions of sulfuric acid and in water. It was found that compound **II** is stable in water and H_2SO_4 solutions with concentrations of 0.5–15 and 80–95%. In 20–80% solutions of sulfuric acid, compound **II** is unstable. In 87–95% sulfuric acid, compound **II** exists in the protonated form, which confirms the reversibility of this reaction.

Based on data on the stability of **II**, we studied its

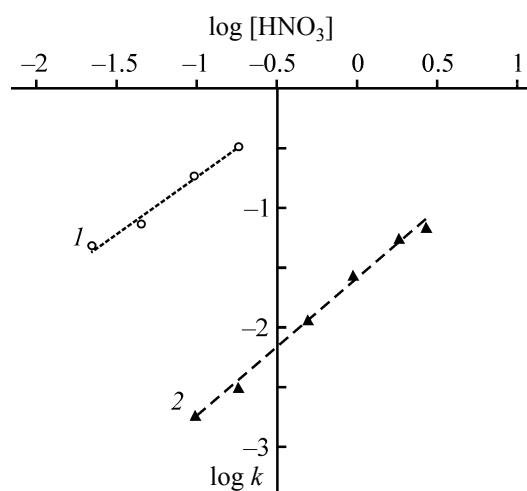


Fig. 6. Dependence of the effective rate constants of the first and second stages of nitration of **II** on the HNO_3 concentration in 95% H_2SO_4 at 25°C. (1) $\log k_{IV}^{eff}$ and (2) $\log k_V^{eff}$.

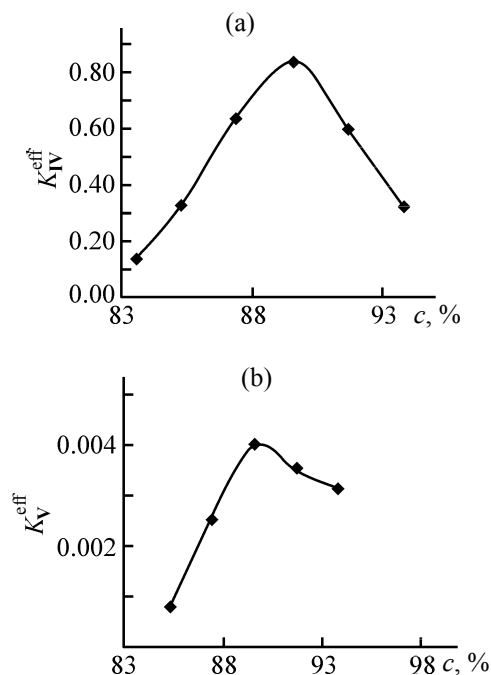


Fig. 7. Dependence of the effective rate constants of nitration of **II** on the sulfuric acid concentration at 25°C. $[HNO_3] = 0.18$ M. Stage: (a) first and (b) second.

Table 3. Activation energies and pre-exponential factors of the reactions of nitration of **I–V** (according to Schemes 1, 2)

Parameter	k_I	k_{II}	k_{III}	k_{IV}	k_V
E_{acts} , kJ	91.8 ± 2.6	78.6 ± 5.7	65.5 ± 7.6	59.6 ± 4.0	90.0 ± 4.3
log A	14.1 ± 0.5	11.9 ± 1.0	9.8 ± 1.3	9.9 ± 0.7	13.2 ± 0.8

nitration kinetics in an SNAM based on 80–95% sulfuric acid.

As in the case of nitration of **I**, no mononitration product was found. In chromatograms of reaction mass samples taken at different conversions, we observed only DADNE, **XI**, and **VII**. The areas of peaks of unidentified compounds constitute an insignificant percent of the total area of peaks in the chromatograms. The total yield of reaction products in 85–95% sulfuric acid is $95 \pm 2\%$.

Experiments in SNAMs based on 95% sulfuric acid at a variable concentration of nitric acid (0.02–2.56 M) made it possible to determine the formal order of the first and second stages of nitration of **II** with respect to nitric acid (Fig. 6). It can be seen in Fig. 6 that the reaction is first-order in both cases. Hence, a conclusion can be made that introduction of the first nitro group into the molecule of compound **II** is the rate-determining stage of the process.

Figure 7 shows how the rate constants of the first and second stages of nitration of **II** depend on the sulfuric acid concentration. These dependences are similar to those in nitration of **I**, both have maxima at about 90% sulfuric acid; however, in the given case, the rate of the first stage exceeds that of the second stage by approximately a factor of 20. The slope ratios in the dependence of the rate constants on the function $-(\text{HR} + \log a_w)$ are small (0.36).

CONCLUSIONS

(1) Nitration of **I** and **II** with sulfuric-nitric acid mixtures is a complex multistage process whose rate depends on the acidity of the medium, nitric acid concentration, and a number of other factors.

(2) Substitution at the methyl group is the rate-determining stage in nitration of **III** and **II**.

(3) Data on the nitration kinetics of **I** and **II** can find use in development of an effective technology for

synthesis of 1,1-diamino-2,2-dinitroethylene.

(4) Nitrous acid affects the nitration rate of **I**, which can be used in selective synthesis of 5-nitro derivatives of substituted pyrimidines.

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