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Kinetics of Hydrolysis of the Geminal Alkoxy-NNO-azoxy Compounds in Sulfuric Acid

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Abstract—The kinetics of hydrolysis of two alkoxy-NNO-azoxy compounds with geminal position of N_2O_2 groups, di(methoxy-NNO-azoxy)methane (**I**) and di(methyl-NON-azoxy)formal (**II**), as well as isomeric geminal nitramine, 2,4-dinitro-2,4-diazapentane (**III**) in 64.16% H_2SO_4 were studied by a manometric method. The relative rates of the hydrolysis at 80°C of compounds **I–III** and methoxy-NNO-azoxymethane (**IV**) were found to be equal to 4.2:77:~50000:1. The limiting stage of hydrolysis of compound **I** is the attack of the nucleophile on the carbon atom of the MeO group of the protonated molecule **I** by S_N2 mechanism. According to the parameters of the Arrhenius equation the hydrolysis of compound **II** proceeds more probably by the S_N1

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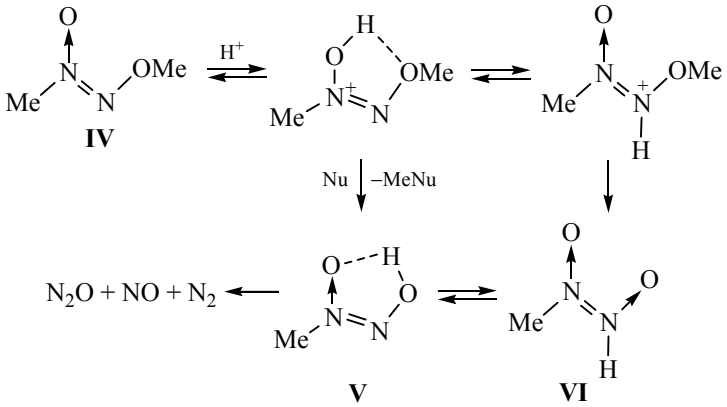
Alkoxy-NNO-azoxy compounds are known since the end of the XIX century [1, 2]. In the last 30 years, some of compounds of this poorly studied class were recognized as biologically active compounds (NO donors, anticancer drugs) [3–5] and components of gas-generating compositions [6]. To optimize the conditions for the synthesis of new compounds of this class it is necessary to estimate their stability to various reagents, particularly to acids and bases. Kinetics and mechanisms of alkaline hydrolysis of the alkoxy-NNO-azoxy compounds in the relation to their structure we have studied earlier [7].

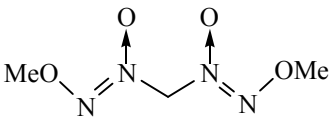
A detailed study of the kinetics and mechanisms of acid hydrolysis of alkoxy-NNO-azoxy compounds we carried out using the first representative of this class of compounds, methoxy-NNO-azoxymethane **IV** [8]. The found dependences of the reaction rate on the concentration of acid and its nature (more precisely, the nature of the strongest nucleophile) and temperature we used to prove the following mechanism of acid hydrolysis of compound **IV**: Its rate-limiting step was the attack of the nucleophile on the carbon atom of the MeO group of the protonated molecule **IV**, and the process was followed by the fast decomposition of the intermediates **V** and/or **VI** [8].

Scheme 1.

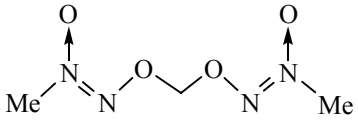


Nu = H_2O, Cl^-, Br^-.

For practical purposes, the azoxy compounds with two azoxy groups, –N(O)=NO–, are often more useful, especially with these groups in the geminal position [2, 5, 6, 9–18]. In this paper we studied manometrically the kinetics of acid hydrolysis of the two bisazoxy compounds with geminal N_2O_2 groups: bis(methoxy-NNO-azoxy)-methane (**I**) and bis(methyl-NON-azoxy)formal distinguished by the position of these groups.



I



II

As the acid 64.16% H_2SO_4 was taken, because just in this medium had the Arrhenius equation parameters for compounds **IV** been measured [8]. The rate of the acid hydrolysis of the azoxy compounds **I** and **II** is satisfactorily described by the kinetic equation for consecutive first order reactions:

$$P = P_0 + P_\infty\{1 - [k_2\exp(-k_1t) - k_1\exp(-k_2t)]/(k_2 - k_1)\}, \quad (1)$$

where k_1 and k_2 are the effective rate constants of pseudo-first order ($k_2 > k_1$), t is time, P_0 is vapor pressure above the acid after heating (2–3 min), $P = (P_0+P_{prod.})$ is the observed pressure, $P_{prod.}$ is the pressure of gaseous products of hydrolysis, and $P_\infty = P_{prod.}$ at $t \to \infty$. The following four parameters were optimized: P_0, P_∞, k_1, and k_2. For $k_2/k_1 > 104$ the curves of the pressure growth were treated with a first-order kinetic equation with the optimization of P_0, P_∞, and k_1. The calculation included the points obtained to the conversion up to 0.8. The value of P_∞ ranged from 300 to 500 Torr. Standard deviation of the calculated and experimental pressure values $s(\Delta P)$ (Table 1) is close to the instrumental error at measuring the pressure. In the cases of slow hydrolysis of azoxy compound **I** at 80°C and 90°C and **II** at 80°C the P_∞ was calculated based on the yield of gaseous products α_∞ at 106°C and 90.1°C, respectively. The results are listed in Table 1.

Table 1. Effective rate constants of hydrolysis reactions of compounds **I**, **II,** and **III** in 64.16% H_2SO_4

Comp. no.	T, °C	k_1, s^{-1}	k_2, s^{-1}	$s(\Delta P)$, Torr[a]	α_∞[b]
I	80	1.00×10^{-6}	2.5×10^{-5}	1.9	2.5
	90	3.20×10^{-6}	[c]	3.9	2.5
	106	1.73×10^{-5}	1.01×10^{-3}	0.7	2.5
	120	9.52×10^{-5}	2.73×10^{-3}	1.1	2.54
	125	1.273×10^{-4}	[c]	0.8	2.59
II	76.1	1.15×10^{-5}	[c]	1.5	2.09
	80	1.87×10^{-5}	1.05×10^{-3}	0.5	2.06
	90.1	7.38×10^{-5}	[c]	0.7	2.06
	98.7	2.15×10^{-4}	[c]	0.8	2.00
	120	2.77×10^{-3}	[c]	1.6	2.2
III	80	$\sim1.2\times10^{-2}$	[c]		

[a] Standard deviation $s(\Delta P) = [(n-1)^{-1}\Sigma (P_{exp} - P_{calc})^2]^{0.5}$. [b] The yield of gaseous products when $t \to \infty$ is: $\alpha_\infty = (P_\infty - P_0)/P_{1\ mol}$, where $P_{1\ mol}$ is the calculated pressure of the equimolar amount of ideal gas.

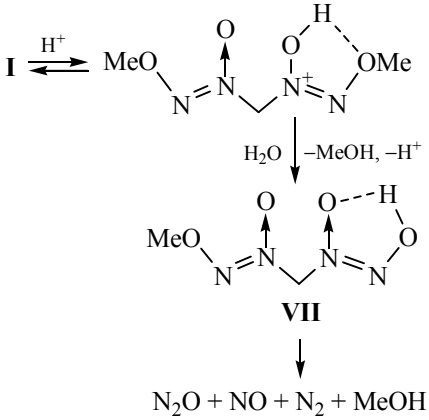
The k_1 plots of compounds **I** and **II** obey satisfactorily the Arrhenius equation (see the figure).

Table 2 lists the parameters of the Arrhenius equation, the relative rate constant at 80°C, and yields of gaseous products at 120°C.

The closeness of the parameters of the Arrhenius equation for compounds **I** and **IV** and the similarity in the composition of gaseous hydrolysis products (N_2O mainly, Table 2) suggest that compound **I** is hydrolyzed according to the same mechanism as has been found for **IV** [8]: S_N2 attack of the H_2O molecule on the C atom of the protonated $CH_3ON{=}N(O)$ group.

Scheme 2 shows the protonation of the azoxy group at the *N*-oxide oxygen atom corresponding to one of two options shown in Scheme 1. In favor of this choice argues the possibility of stabilization due to the intramolecular hydrogen bond similar to the hydrogen bond in hydroxy-NNO-azoxy compounds (*N*-nitroso-

Scheme 2.

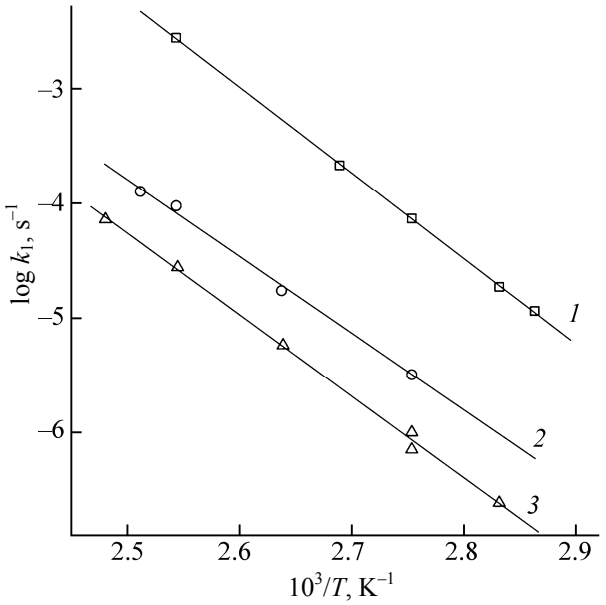


hydroxylamines) [19, 20], as well as the results of X-ray analysis of hydroxymethyl derivatives of the azoxy compounds. In all five structures the electron donor for the proton of CH_2OH group is the *N*-oxide oxygen atom of the azoxy group [18].

In [8] we showed that the azoxy compound **IV** is a very weak base: $pK_{BH^+} \approx -6$, for comparison, for Et_2O $pK_{BH^+} \approx -5.2$ [21], for $MeNO_2$ –11.9 [21]. Compound **I** is obviously even weaker base due to the mutual influence of geminal electron-acceptor $CH_3ON{=}N(O)$ groups. However, the rate of hydrolysis of compound **I** is 4.2 times higher compared with **IV**. This fact can be attributed only to a much higher constant *k* of bimolecular nucleophilic substitution (S_N2) for compound **I** compared with **IV**. The relationship between the constant *k* and the experimental rate constant of pseudo first order reaction k_1 (Table 1) corresponds to Eq. (2) [8, 22]:

$$\log [k_1/\{c(H^+)c(H_2O)\}] = m^{\neq}m^*X_0 + \log (k/K_{BH^+}), \qquad (2)$$

where $X_0 = -H_0 - \log c(H^+)$ is the excess acidity (H_0 is the Hammett acidity function) [23, 24], $m^{\neq}$ and m^* are coefficients. In turn, substantially higher constant *k* for compound **I** is probably due to the fact that the acid **VII** (Scheme 2) is a much more easily leaving group in comparison with the hydroxy-NNO-azoxymethane **V** (Scheme 1) due to electron-withdrawing effect of the geminal $CH_3ON{=}N(O)$ group.



Correspondence of the hydrolysis rate constants k_1 of compounds **II** (*1*), **I** (*2*) and **IV** [8] (*3*) in 64.16% H_2SO_4 to the Arrhenius equation.

The activation energy and, in particular, the value of preexponential term for compound **II** is significantly higher compared with those for azoxy compounds **I** and **IV** (Table 2). This indicates a change in the mechanism from S_N2 to S_N1 in the key step [25]. The S_N1 mechanism is promoted by the mesomeric stabilization of the carbocation **VIII** (Scheme 3).

Scheme 3.

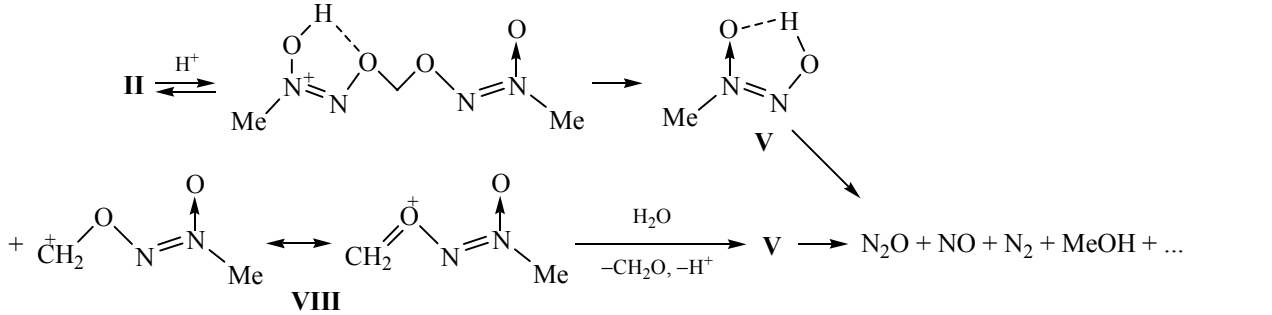
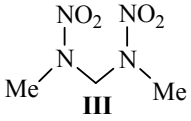


Table 2. Parameters of the Arrhenius equation, relative rate constants (80°C), and yields of gaseous products (120°C) of hydrolysis of compounds **I**, **II**, and **IV** in 64.16% H_2SO_4

Comp. no.	Arrhenius equation parameters			k_1^{rel} 80°C	Yield, %		
	T, °C	log (A/s^{-1})	E_A, kJ mol^{-1}		N_2 + NO	N_2O	CO_2
I	80–125	13.2±1.4	130±10	4.2	0.30	1.43	0.02
II	76–120	16.5±0.7	144±5	77	0.11	1.86	0.02
III	–	–	–	~50000	–	–	–
IV [8]	80–130	13.6±1.4	137±10	1	0.02	0.98	0.01

By the composition of gaseous products of the hydrolysis, compound **II** is closer to **IV** (Table 2). This confirms Scheme 3, which includes the same intermediate **V** as Scheme 1.

Compound **II** is less stable in acid compared to azoxide **I**, but both are by 3–4 orders of magnitude more stable than the nitramine isomer, 2,4-dinitro-2,4-diazapentane **III** (Tables 1 and 2) .

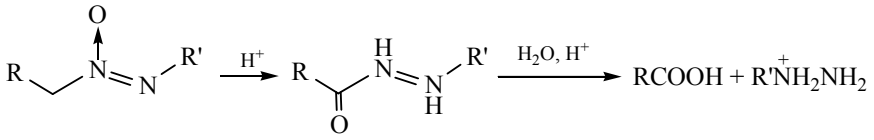


III

The ratio of the hydrolysis rates of compounds **I**, **II**, **III**, and **IV** in 64.2% sulfuric acid at 80°C is 4.2:77:~5.104:1.

The suggested mechanism of acid hydrolysis of the azoxy compounds **I**, **II** and **IV** (Schemes 1–3) that includes the nucleophilic substitution at the carbon atom of alkoxy group in the key step differs fundamentally from the mechanism of hydrolysis of aliphatic azoxy compounds [26], where the substituent at the *N*-oxide nitrogen atom is involved (Scheme 4).

Scheme 4.



Thus, we found that the rate of hydrolysis of compounds **I**, **II**, **III** and **IV** in 64.16% sulfuric acid at 80°C relate as 4.2:77:~5.104:1. The rate limiting step of hydrolysis of compound **I** is the attack of the nucleophile on the methoxy group carbon atom of the protonated molecule **I** in accordance with the S_N2 mechanism. Compound **II** is hydrolyzed along the S_N1 mechanism facilitated by the mesomeric stabilization of the resulting carbocation.

EXPERIMENTAL

Compounds **I–III** were synthesized according to the known methods [9, 11, 27], twice recrystallized and thoroughly dried. The kinetics of hydrolysis was measured manometrically in a glass vessels with a crescent-shaped null manometer (Bourdon vessel) of 140–170 ml volume using 100–200 mg of a weighed substance and 2 ml of acid. To prepare the 64.16% H_2SO_4 solution, the concentrated acid of chemically pure grade was diluted with distilled water. Temperature was maintained within ±0.1°C by water thermostat, for reactions at temperatures above 100°C we used oil thermostat (accuracy ±0.2°C). The gaseous products of hydrolysis were analyzed on a chromatograph LKhM-8MD, detector katharometer, carrier gas helium (100 ml min^{-1}), copper columns (*l* 6 m, *d* 5 mm) with polisorb-1 (0.2–0.3 mm), column temperature 60°C and 35°C.

REFERENCES

1. Behrend, R. and König, E., *Liebigs Ann*., 1891, vol. 263, no. 2, p. 175.
2. Traube, W., *Liebigs Ann*., 1898, vol. 300, no. 1, p. 81.
3. Hrabie, J.A. and Keefer, L.K., *Chem. Rev*., 2002, vol. 102, no. 4, p. 1135.
4. Brand, J., Huhn, T., Groth, U., and Jochims, J.C., *Chem. Eur. J*., 2006, vol. 12, no. 2, p. 499.
5. Granik, V.G. and Grigor'ev, N.B., *Izv. Akad. Nauk, Ser. Khim*., 2002, no. 8, p. 1268 .
6. Zyuzin, I.N. and Lempert, D.B., *Propellants, Explosives, Pyrotechnics*, 2007, vol. 32, no. 1, p. 42.
7. Zyuzin, I.N. and Lempert, D.B., *Zh. Obshch. Khim*., 2010, vol. 80, no. 9, p. 1473.
8. Zyuzin, I.N. and Lempert, D.B., *Kinet. Kat.*, 2011, vol. 52, no. 1, p. 19.
9. Yandovskii, V.N., Dobrodumova, E.Yu., and Tselinskii, I.V., *Zh. Org. Khim*., 1980, vol. 16, no. 5, p. 933.
10. Zyuzin, I.N. and Golovina, N.I., *Izv. Akad. Nauk, Ser. Khim*., 1995, no. 8, p. 1598.
11. Zyuzin, I.N., Nechiporenko, G.N., Golovina, N.I., Trofimova, R.F., and Loginova, M.V., *Izv. Akad. Nauk, Ser. Khim*., 1997, no. 8, p. 1486.
12. Lempert, D.B., Avdonin, V.V., and Nechiporenko, G.N., *Zh. Prikl. Khim*., 1998, vol. 71, no. 1, p. 45.
13. Zyuzin, I.N., Golovina, N.I., Lempert, D.B., Nechiporenko, G.N., and Shilov, G.V., *Izv. Akad. Nauk, Ser. Khim*., 2008, no. 3, p. 619.
14. Zyuzin, I.N. and Lempert, D.B., *Izv. Akad. Nauk, Ser. Khim*., 2009, no. 10, p. 2108.
15. Zyuzin, I.N., *Zh. Pikl. Khim*., 2009, vol. 82, no. 10, p. 1647.
16. Zyuzin, I.N., *Ibid.,* p. 1677.
17. Zyuzin, I.N., Golovina, N.I., and Shilov, G.V., *Zh. Org. Khim*., 2010, vol. 46, no. 7, p. 1086.

18. Zyuzin, I.N., Golovina, N.I., Lempert, D.B., and Shilov, G.V., *Izv. Akad. Nauk, Ser. Khim*., 2010, no. 10, p. 1875.
19. Hickmann, E., Hädicke, E., and Reuther, W., *Tetrahedron Lett*., 1979, vol. 20, no. 26, p. 2457.
20. Hrabie, J.A., Arnold, E.V., Citro, M.L., George, C., and Keefer, L.K., *J. Org. Chem*., 2000, vol. 65, no. 14, p. 5745.
21. Reutov, O.A., Kurts, A.L., and Butin, K.P., *Organicheskaya khimiya. Chast' 1* (Organic Chemistry. Part 1), Moscow: BINOM, Laboratoriya Znanii, 2005, p. 223.
22. Cox, R.A. and Yates, K., *Canad. J. Chem*., 1979, vol. 57, no. 22, p. 2944.
23. Cox, R.A. and Yates, K., *Canad. J. Chem*. 1983, vol. 61, no. 10, p. 2225.
24. Cox, R.A., *Adv. Phys. Org. Chem*., 2000, vol. 35, no. 1, p. 1.
25. Bekker, H., *Introduction to Electronic Theory of Organic Reactions*, Moscow: Mir, 1977, p. 145.
26. Langley, B.W., Lythgoe, B., and Riggs, N.V., *J. Chem. Soc*., 1952, p. 4191.
27. Tartakovskii, V.A., Ermakov, A.S., Sigai, N.V., and Varfolomeeva, O.N., *Izv. Akad. Nauk, Ser. Khim*., 2000, no. 6, p. 1085.