ATRANES

XLII.* KINETICS OF THE HYDROLYSIS OF 1-ALKOXY- AND 1-ARYLOXYSILATRANES.

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The hydrolysis of silatranes of the $RO\overset{\downarrow}{Si}(OCH_2CH_2)_3\overset{|}{N}$: type (R = alkyl, aryl) in the presence of HCl at 25°C is described by a second-order kinetic equation. The correlation dependence of the log k values on the σ^*_{OR} values makes it possible to divide the investigated compounds into two reaction series – 1-alkoxy- and 1-aryloxysilatranes. An investigation of the potentiometric curves and the change in the acid functions of the media during the hydrolysis of the silatranes made it possible to propose a scheme for the mechanism of this reaction. The linear dependence of the v values on [HCl] provides evidence that noncatylic hydrolysis of the silatranes practically does not occur under the investigated conditions. A salt effect is not manifested during the hydrolysis of the silatranes (at KCl concentrations from 0.05 to 0.25 mole/liter). The toxicity of the 1-aryloxysilatranes is basically reduced as their rate of hydrolytic cleavage increases.

We have previously made a preliminary study of the kinetics of the hydrolysis of silatranes of the $X\overset{\downarrow}{Si}(OCH_2CH_2)_3\overset{|}{N}$ type [2]. In this study, the rate of hydrolysis was determined from the accumulation of the reaction products by titration with hydrochloric acid. However, we subsequently became convinced that this method does not make it possible to obtain sufficiently accurate kinetic data.

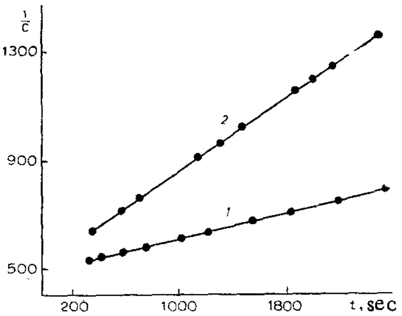

Fig. 1. Dependence of the 1/c values on the time for the hydrolysis of $ROSi(OCH_2CH_2)_3N$: 1) $R = (CH_3)_3C$, $r = 0.997$, and $s_0 = 0.005$; 2) $R = C_6H_5$, $r = 0.998$, and $s_0 = 0.002$.

In the present research we studied the kinetics of hydrolysis of 12 1-organoxysilatranes with the general formula $RO\overset{\downarrow}{Si}(OCH_2CH_2)_3N$ (R = alkyl or aryl) by means of polarography. Our goal was to determine the effect of the nature of substituent R on the rate of hydrolysis and also to establish how the pH of the medium is reflected in the free energy of activation of the reaction (the rate of hydrolysis). Finally, we proposed to ascertain whether there is a relationship between the rate of hydrolysis of 1-aryloxysilatranes and their toxicity.

The silatranes were hydrolyzed in dilute aqueous solutions at 25° in the presence of HCl and KCl. Under these conditions, the hydrolysis process is made up of a number of parallel-successive reactions and is satisfactorily described by a second-order equation [3] (Fig. 1). The rate constants that we obtained for the hydrolysis of the silatrane (k) and their mean-square deviations, the σ^*_{OR} val-

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*See [1] for communication XLI.

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TABLE 1. Rate Constants for the Hydrolysis of Silatranes

$ROSi(OCH_2CH_2)_3N$

Compound	R	k_2^{25}, liter · mole^{-1} · sec^{-1}	σ^*_{OR}	LD_{50}, mg/kg
1	C_2H_5	0,37±0,01	1,37	
2	n-C_3H_7	0,40±0,01	1,34	
3	i-C_3H_7	0,51±0,01	1,26	
4	t-C_4H_9	0,12±0,02	1,15	
5	t-$C_4H_9CH_2$	0,47±0,01	1,28	
6	C_6H_5	0,33±0,01	2,38	200
7	2-$CH_3C_6H_4$	0,38±0,01	2,19	1200
8	3-$CH_3C_6H_4$	0,35±0,01	2,31	708
9	4-$CH_3C_6H_4$	0,36±0,01	2,23	710
10	4-$CH_3OC_6H_4$	0,37±0,01	2,22	345
11	4-ClC_6H_4	0,39±0,02	2,11	565
12	$C_6H_5CH_2$	0,57±0,02	1,37	2250

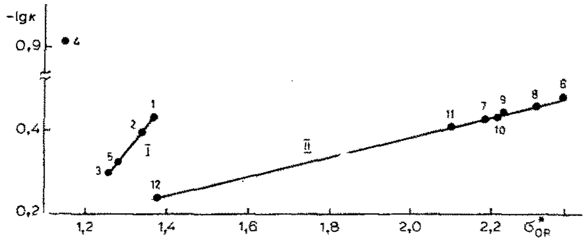


Fig. 2. Relationship between the log k and σ^*_{OR} values for the following reaction series: I) R=alkyl, log k = 1.29–1.26 σ^*_{OR}, s_0 = 0.006; II) R=aryl, log k = 0.07–0.23 σ^*_{OR}, s_0 = 0.005 (the numbering of the points corresponds to the numbers presented in Table 1).

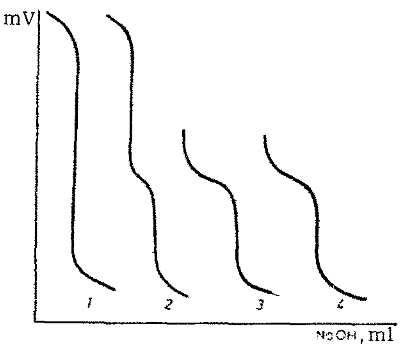


Fig. 3. Potentiometric titration curves for $5 \cdot 10^{-3}$ M HCl and a $5 \cdot 10^{-3}$ M solution of 1-ethoxysilatrane: 1) immediately after mixing; 2) 7 min after mixing; 3) 7 min after mixing with the addition of $5 \cdot 10^{-3}$ mole/liter of triethanolamine; 4) artificial mixture of $5 \cdot 10^{-3}$ mole/liter of HCl and $5 \cdot 10^{-3}$ mole/liter of triethanolamine.

ues of the corresponding OR groups [4], and the average lethal doses (LD_{50}) of the 1-aryloxysilatranes are presented in Table 1.

The quantitative evaluation of the k value from the nature of substituent OR was accomplished on the basis of the Taft equation [5]

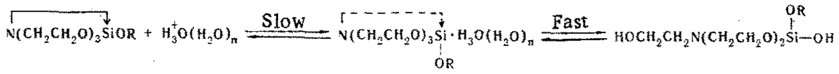
$$\lg k = \lg k_0 + \rho^* \sigma^*_{OR},$$

where σ^*_{OR} is the induction constant of substituent OR, and ρ^* is the reaction constant.

All of the investigated compounds are divided into two reaction series (Fig. 2). The first series includes the 1-alkoxysilatranes, whereas the second series includes 1-aryloxysilatranes and 1-benzyloxysilatrane. In series I, where $\rho^* = -1.26$ (R = C_2H_5, n-C_3H_7, iso-C_3H_7, tert-C_4H_9, and tert-$C_4H_9CH_2$), and series II (R = C_6H_5, 2-$CH_3C_6H_4$, 3-$CH_3C_6H_4$, 4-$CH_3C_6H_4$, 4-$CH_3OC_6H_4$, 4-ClC_6H_4, and $C_6H_5CH_2$), where $\rho^* = -0.23$, the rate of hydrolysis falls as induction constants σ^*_{OR} of substituent OR increases. The negative ρ^* values indicate the formation in the transition state of a positive charge at the reaction center. The log k value for 1-tert-butoxysilatrane deviates markedly from the correlation line of I (its rate of hydrolysis proved to be much lower than the expected value). This should apparently be ascribed to the large steric effect of the substituent.

A study of the PMR spectra [6] and dipole moments [7] of 1-alkoxy- and 1-aryloxysilatranes showed that the oxygen atoms in the silatrane system of the molecule are the most basic atoms. Data on the kinetics of hydrolysis [2] confirm that the endocyclic Si–O–C bonds in 1-alkoxysilatranes are the first to undergo hydrolysis.

The linear relationship between rate of hydrolysis (v) and the pH of the medium (Table 2) shows that electrophilic attack on the reaction center by the hydronium ion is the rate-determining step for the given reaction series of compounds:



$$N(CH_2CH_2O)_3SiOR + \overset{+}{H_3}O(H_2O)_n \xrightleftharpoons{\text{Slow}} N(CH_2CH_2O)_3\underset{\substack{|\\OR}}{Si} \cdot H_3O(H_2O)_n \xrightleftharpoons{\text{Fast}} HOCH_2CH_2N(CH_2CH_2O)_2\overset{\substack{OR\\|}}{Si}{-}OH$$

TABLE 2. Change in the Rate of Hydrolysis of Silatranes $ROSi(OCH_2CH_2)_3N$ As a Function of the pH and HCl Concentration

HCl concn., mmole/liter	pH*	$v \cdot 10^{-6}$, mole/liter$^{-1} \cdot$ sec^{-1}	
		R=t-C_4H_9	R=C_6H_5
1,0	3,06	0,18±0,02	0,64±0,05
1,5	2,88	0,30±0,01	1,02±0,02
2,0	2,75	0,45±0,03	1,32±0,04
2,5	2,66	0,65±0,02	1,60±0,02
3,0	2,58	0,72±0,01	2,04±0,03
3,5	2,51	0,91±0,02	
4,0	2,45	1,12±0,03	
5,5	2,31	1,32±0,04	3,52±0,01
6,0	2,27		3,96±0,03

* The pH value was determined from the equation pH = 1.009 log [HCl] − 0.031 ($r = 0.999$, $s_0 = 0.001$) calculated on the basis of the experimental data [8].

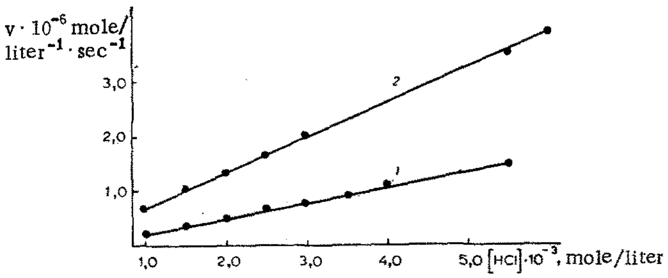


Fig. 4. Dependence of the rate of hydrolysis of $ROSi(OCH_2CH_2)_3N$ on the HCl concentration: 1) R = $(CH_3)_3C$, $v_0 = -0.06 \cdot 10^{-6}$, $\rho^* = 0.27$, $r = 0.99$, and $s_0 = 0.02$; 2) R = C_6H_5, $v_0 = 0.02 \cdot 10^{-6}$, $\rho^* = 0.65$, $r = 0.99$, and $s_0 = 0.01$.

The subsequent steps of cleavage of the Si−O−C bonds in the disrupted silatrane framework of the molecule proceed very rapidly with the formation of triethanolamine hydrochloride as the final product of the hydrolysis. The potentiometric titration curves provide evidence for this (Fig. 3).*

When the composition of the solvent is constant, the rate of hydrolysis increases in proportion to the increase in the HCl concentration (Table 2). The satisfactory linear relationship between the v values and [HCl] is illustrated in Fig. 4. The correlation parameters show that the lines intersect with the axis of ordinates near their origin ($v \approx 0$). Consequently, noncatalytic hydrolysis (in the absence of HCl) has practically no effect on the rate constants under the investigated conditions.

Small amounts (0.05-0.25 mole/liter) of KCl (used as the background) do not have an appreciable effect on the rate of hydrolysis of the silatranes, i.e., a salt effect is not observed.

The toxicity of the 1-aryloxysilatranes is definitely related to their stability in the organism. Table 1 shows that an increase in the rate of hydrolysis of the 1-aryloxysilatranes leads to a decrease in their toxicity. This indicates that the 1-aryloxysilatranes themselves rather than the products of their hydrolytic disintegration primarily display a toxic effect. This is also attested to by the satisfactory linear relationship between the average lethal dose (LD_{50}) and log k: $\log k = 0.50 - 1.05 \cdot 10^{-4}\ LD_{50}$ ($r = 0.91$, $s_0 = 0.02$).

EXPERIMENTAL

The kinetics of the hydrolysis of the 1-alkoxy- and 1-aryloxysilatranes were investigated in aqueous solutions in the presence of HCl and KCl (KCl was used as the background) at 25 ± 0.02°. The initial concentration of the silatranes was $2 \cdot 10^{-3}$ mole/liter, and the HCl concentration varied from $1 \cdot 10^{-3}$ to $6 \cdot 10^{-3}$ mole/liter. A weighed sample of the test substance was placed in a flask with a ground glass stopper. An

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* The authors thank S. V. Ponomareva for performing the potentiometric titrations.

HCl solution containing 0.05 mole/liter of KCl was prepared in another flask. Both flasks were thermostatted for 30 min, after which their contents were mixed, and the mixture was shaken vigorously until the silatrane had dissolved completely. The resulting solution was transferred to a thermostatted electrolytic cell of an Lp-60 polarograph, by means of which the decrease in the HCl concentration with time was measured.

The reaction order was established graphically (Fig. 1), and the rate constants (k) were calculated with a BÉSMA-4 computer from the equation for a second-order reaction:

$$(c_{A_0}-c_{B_0})kt=\ln\frac{c_{A_0}}{c_{B_0}}-\ln\frac{c_{A_t}}{c_{B_t}}.$$

The rate of hydrolysis (v) was calculated from the expression

$$v=k[c_{A_0}][c_{B_0}],$$

where c_{A_0} and c_{B_0} are the starting concentrations of the silatrane and HCl, respectively.

An LP-58 potentiometer was used for the titration; the electrodes were a calomel electrode saturated with a methanol solution of KCl and a glass electrode. The titrant was 0.1 N NaOH.

The toxicity was determined with 160 mongrel white mice weighing 18-20 g. All of the preparations were injected intraperitoneally in water-based emulsions. The LD_{50} values were calculated by the Kerber method [9].

LITERATURE CITED

1. M. G. Voronkov, V. M. D'yakov, G. A. Samsonova, Yu. A. Lukina, and N. M. Kudyakov, Izv. Akad. Nauk SSSR, Ser. Khim., 2794 (1974).
2. M. G. Voronkov and G. I. Zelchan, Khim. Geterotsikl. Soedin., 450 (1969).
3. S. Benson, Foundations of Chemical Kinetics, McGraw-Hill (1960).
4. Chemist's Handbook [in Russian], Vol. 3, Khimiya, Leningrad (1964), p. 955.
5. V. A. Palm, Fundamentals of the Quantitative Theory of Organic Reactions [in Russian], Khimiya, Leningrad (1967).
6. G. I. Zelchan, Master's Dissertation, Riga (1967).
7. V. A. Chetverikova, V. A. Kogan, G. I. Zelchan, M. G. Voronkov, and O. A. Osipov, Khim. Geterotsikl. Soedin., 446 (1969).
8. Experimental Methods of Chemical Kinetics [in Russian], Vysshaya Shkola, Moscow (1971), p. 31.
9. M. L. Belen'kii, Elements of the Quantitative Evaluation of Pharmacological Effects [in Russian], Leningrad (1963), p. 23.