ХИМИЯ

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THE STUDIES OF MECHANISM AND KINETICS OF 2-ETHYL-2-OXAZOLINE POLYMERIZATION INITIATED BY METHANESULFONYL HALIDES*

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Model compounds (methanesulfonyl halides) were used to illustrate the possibility of initiating cationic polymerization of 2-oxazolines by acyl halides of sulfonic acids. Kinetics of 2-ethyl-2-oxazoline polymerization was studied; rate constants of chain growth were determined for the case of initiating polymerization by methanesulfonyl chloride (in the 80–110°C temperature range) and for the case of initiating polymerization by methanesulfonyl bromide (in the 70–100°C temperature range); the values of activation energy for these processes were calculated. The obtained kinetic dependences indicate slow initiation followed by rapid chain growth. Experimental data shows that the polymerization of 2-ethyl-2-oxazoline initiated by methanesulfonyl halides proceeds mostly via an ionic species both for chloride and bromide. Refs 17. Figs 4. Table 1.

Keywords: oxazoline cationic polymerization, polymerization kinetics, methanesulfonyl halides, 2-ethyl-2-oxazoline, polyoxazolines.

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ИССЛЕДОВАНИЕ МЕХАНИЗМА И КИНЕТИКИ ПОЛИМЕРИЗАЦИИ 2-ЭТИЛ-2-ОКСАЗОЛИНА, ИНИЦИИРУЕМОЙ МЕТАНСУЛЬФОНИЛГАЛОГЕНИДАМИ

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На примере модельных соединений — метансульфонилгалогенидов показана возможность инициирования катионной полимеризации 2-оксазолинов галогенангидридами сульфокислот. В рамках исследования кинетики полимеризации 2-этил-2-оксазолина определены константы скорости роста цепи при инициировании полимеризации метансульфонилхлоридом при температурах 80, 90, 100, 110°C, и метансульфонилбромидом при температурах 70, 80, 90, 100°C, а также рассчитаны величины энергий активации процессов. Полученные кинетические зависимости свидетельствуют о медленном инициировании полимеризации с последующим быстрым ростом цепи. Экспериментальным путём показано, что полимеризация

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2-этил-2-оксазолина, инициируемая метансульфонилгалогенидами, протекает преимущественно по механизму живых цепей, а не по механизму «обрыв—реинициирование». Установление влияния избыточной концентрации галогенид ионов на скорость полимеризации позволило оценить относительный вклад двух возможных механизмов. Библиогр. 17 назв. Ил. 4. Табл. 1.

Ключевые слова: катионная полимеризация с раскрытием цикла, кинетика полимеризации, оксазолины, 2-этил-2-оксазолин, метансульфонилгалогениды, полиоксазолины.

Introduction. 2-Oxazolines belong to the class of cyclic imino ethers. They polymerize easily under the action of cationic initiators with opening ring and the formation of *N*-acylated polyethylene imines. The possibility of 2-oxazoline polymerization was revealed in the mid-1960s [1–4]. Living mechanism of 2-oxazoline polymerization allows controlling molecular masses of the obtained polymers, and easily preparing block-copolymers with different end groups (when using initiators and chain terminating agents with various chemical structures). Biocompatibility of polyoxazolines (which are structural isomers of peptides) provides a possibility of using these polymers for various biomedical purposes as analogs of polyethylene oxides [5].

Cationic polymerization of 2-oxazolines can be initiated by various compounds, such as Brønsted acids [6], Lewis acids [2, 4], alkyl halides [7], iodine [8]. Polymerization initiated by acyl halides of sulfonic acids (particularly, alkyl sulfonyl halides) is of special interest, since it is known that sulfonyl halide group can be easily introduced into various compounds.

Capability of alkyl sulfonyl halides for initiating 2-oxazoline polymerization may be used in developing new functional materials (e. g., amphiphilic polymers based on sulfochlorinated polyethylene).

Therefore, the purpose of this work was establishing mechanism and the main kinetic parameters of 2-ethyl-2-oxazoline polymerization initiated by model compounds (methanesulfonyl halides).

Results and discussion. Two mechanisms have been suggested for describing 2-oxazoline polymerization (see scheme on Fig. 1).

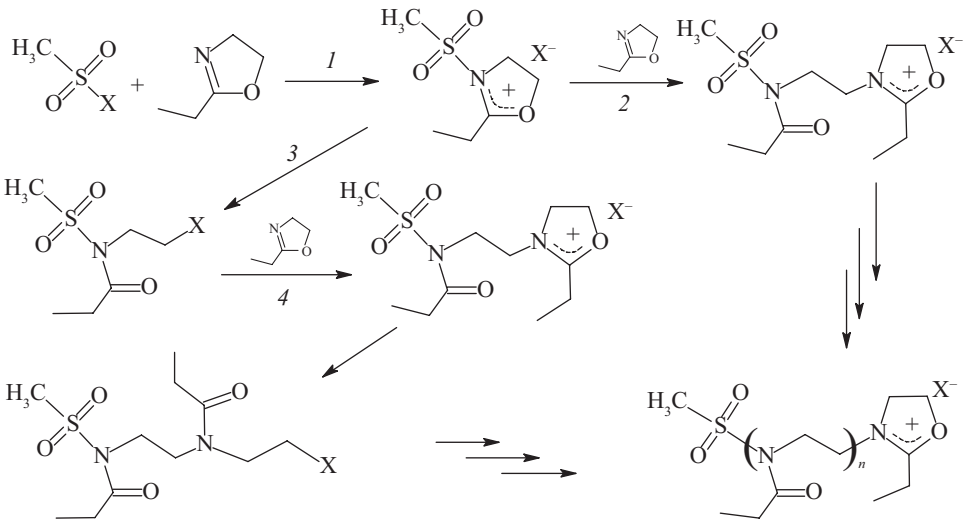


Fig. 1. Mechanism of 2-ethyl-2-oxazoline polymerization initiated by methanesulfonyl halides: *1* — initiation; *2* — chain growth (living mechanism); *3* — reversible chain termination (reaction with a counterion); *4* — re-initiation of polymerization by an alkyl halide group; X = F, Cl, Br, I

In the initiation stage, oxazolinium cation is formed; in the first case, this cation interacts with a monomer molecule, thus leading to oxazoline ring opening and retaining of active ionic site. In the absence of irreversible chain termination, chain growth proceeds according to the living mechanism. In the second case, reversible termination involving counterion occurs followed by reinitiation of polymerization by a covalent type active site (the so-called termination-reinitiation mechanism).

In order to reveal the reaction mechanism, we studied kinetics of 2-ethyl-2-oxazoline polymerization in tetrachloroethane solutions; the polymerization was initiated by methanesulfonyl chloride (MesCl) and methanesulfonyl bromide (MesBr). The initiator/monomer ratio was 1 : 30, and the initial concentration of the monomer was 6 mol/L. Quantitative analysis was performed using the NMR data obtained for the reaction mixture samples in the initial stages of polymerization. Monomer conversion was determined using the decrease in intensity of the signal attributed to protons of methylene group $-O-CH_2-$ of oxazoline heterocycle (4.21 ppm, triplet) with respect to the signal of internal standard (tetrachloroethane solvent, 5.96 ppm, singlet). As the reaction proceeds, broadened signal of methylene protons of $N-CH_2-CH_2-N$ polymer fragments appears in NMR spectra (3.37 ppm, triplet).

Rate constants of chain growth initiated by methanesulfonyl chloride (mesyl chloride) were obtained at temperatures of 80, 90, 100 and 110°C and were equal to $1.31 \cdot 10^{-4}$, $1.93 \times \times 10^{-4}$, $6.94 \cdot 10^{-4}$ and $25.5 \cdot 10^{-4}$ $L \cdot mol^{-1} \cdot s^{-1}$ respectively. As seen from Fig. 2, logarithmic dependences of inverse monomer conversion on time are not linear, this indicating increase in the amount of reactive sites with time. This phenomenon is presumably related to slow initiation.

In this case, reaction kinetics can be analyzed with the use of Eq. (∗), which takes into account the initiation stage [9],

$$\log \frac{[M_0]}{[M]} = [I_0] \left(k_P t + \frac{k_P}{k_I} e^{-k_I t} - \frac{k_P}{k_I} \right), \qquad (*)$$

where $[M_0]$ is the initial concentration of the monomer; $[I_0]$ is the initial concentration of the initiator; k_I is the initiation rate constant; k_P is the chain growth rate constant; t is the time.

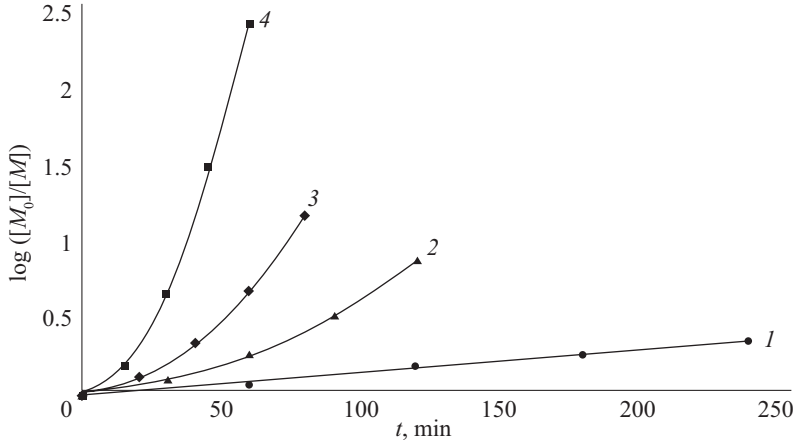


Fig. 2. Dependence of logarithm of inverse 2-ethyl-2-oxazoline conversion on time: *1* — 80°C; *2* — 90°C; *3* — 100°C; *4* — 110°C; monomer concentration is 6 mol/L, methanesulfonyl chloride (MesCl) concentration is 0.2 mol/L

The suggested kinetic equation is applicable only for the case when the initiation stage exhibits first-order kinetics with respect to initiator. In order to reveal the reaction order, polymerization was carried out at other $[M_0]/[I_0]$ ratios (1 : 15, 1 : 20 and 1 : 40), and at a temperature of 100°C. The obtained data were used to plot dependence of inverse monomer conversion logarithm vs. initiator concentration; this dependence was close to linear ($Y = 0.109[I_0] + 0.063$; $R = 0.998$), this indicating first-order kinetics with respect to initiator.

The rate constants of chain growth for the case of initiating polymerization by methanesulfonyl bromide were obtained at 70, 80, 90, and 100°C and were equal to $2.67 \cdot 10^{-4}$, $6.07 \cdot 10^{-4}$, $10.0 \cdot 10^{-4}$ and $18.1 \cdot 10^{-4}$ L·mol^{-1}·s^{-1} (100°C) respectively.

As can be seen in Fig. 3, using methanesulfonyl bromide as an initiator does not lead to qualitative changes in kinetic curves, though it causes increase in the values of rate constants of chain growth.

The obtained kinetic curves do not help reveal the chain growth mechanism, since the reactions proceeding via the living chain mechanism and the termination-reinitiation mechanism (pseudo-living process) demonstrate equivalent kinetics. The true mechanism may be discovered after comparison between kinetics of 2-ethyl-2-oxazoline polymerization initiated by methanesulfonyl chloride and *N*-(2-chloroethyl)-*N*-methanesulfonyl propionamide (theoretically, the primary product of interaction between methanesulfonyl chloride and 2-ethyl-2-oxazoline); synthesis of this compound was described earlier [10]. Following the Flory principle of equal reactivity for all active sites independently of their molecular masses, it might be expected that in the case of polymerization proceeding according to the termination-reinitiation mechanism, kinetic dependences should be similar.

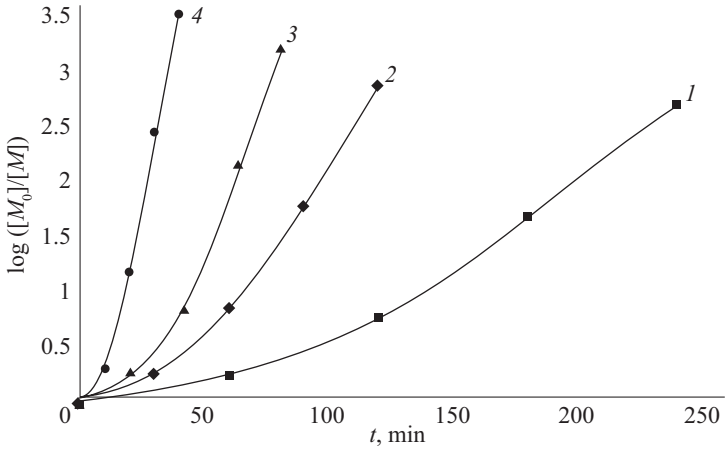


Fig. 3. Time dependence of logarithm of inverse 2-ethyl-2-oxazoline conversion: *1* — 70°C; *2* — 80°C; *3* — 90°C; *4* — 100°C; monomer concentration is 6 mol/L, methanesulfonyl bromide (MesBr) concentration is 0.2 mol/L, solvent is tetrachloroethane

However, the kinetic dependences obtained for these two initiators are different. The chain growth rate constant for the case of *N*-(2-chloroethyl)-*N*-methanesulfonyl propionamide was $5.6 \cdot 10^{-5}$ L·mol^{-1}·s^{-1} (100°C), i. e., an order of magnitude lower than that for the case of methanesulfonyl chloride ($6.9 \cdot 10^{-4}$ L·mol^{-1}·s^{-1}). Therefore, we can conclude that the polymerization initiated by methanesulfonyl chloride proceeds mainly according to the living chain mechanism.

The choice between parallel polymerization reactions proceeding via pseudo-living and living mechanisms can be made also using the method of competitive reactions. When an excess of counterions is added to the reaction mixture in the case of the living mechanism, increase in counterion concentration will lead to increase in reversible termination rate and, therefore, has an influence on the total chain growth rate. At the same time, in the case of the living mechanism, the excess of counterions should not influence reaction kinetics. In our experiments, benzyltributylammonium chloride (which is inert to monomer and easily dissolves in the reaction medium) was used as a source of additional chlorine ions.

The analysis of experimental data has demonstrated that adding the amount of benzyltributylammonium chloride equivalent to that of methanesulfonyl chloride leads to decrease in the reaction rate constant by a factor of 27, i. e. from $6.9 \cdot 10^{-4}$ to $2.5 \cdot 10^{-5}$ $L \cdot mol^{-1} \cdot s^{-1}$. It is known that chain growth on ionic active sites proceeds at a significantly higher rate than that on covalent active sites [11, 12]. Therefore, it can be presumed that 2-ethyl-2-oxazoline polymerization initiated by methanesulfonyl chloride proceeds mainly via the living chain mechanism.

Time dependences of logarithm of inverse monomer conversion in the cases of various initiators (the reaction temperature was 100°C)

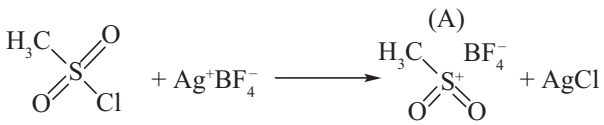
Initiator	Time, min			
	20	40	60	80
1	0.078	0.241	0.468	0.804
2	0.008	0.011	0.073	0.145
3	0.002	0.023	0.048	0.093
4	0.294	1.175	2.442	3.499
5	0.103	0.448	1.019	1.815

1 — MesCl (0.2 mol/L); *2* — *N*-(2-chloroethyl)-*N*-methanesulfonyl propionamide (0.2 mol/L); *3* — MesCl (0.2 mol/L) in the presence of 0.2 mol/L of benzyltributylammonium chloride; *4* — MesBr (0.2 mol/L); *5* — MesBr (0.2 mol/L) in the presence of 0.2 mol/L hexadecyltrimethylammonium bromide.

Similar experiments were carried out in order to study kinetics of 2-ethyl-2-oxazoline polymerization initiated by methanesulfonyl bromide in the presence of hexadecyltrimethylammonium bromide.

Adding the amount of hexadecyltrimethylammonium bromide equivalent to that of the initiator leads to decrease in the reaction rate constant only by a factor of 1.6 (from $1.81 \times \times 10^{-3}$ to $1.14 \cdot 10^{-3}$ $L \cdot mol^{-1} \cdot s^{-1}$). These data indicate that the polymerization initiated by methanesulfonyl bromide can be considered "living" to a lesser degree than the process initiated by methanesulfonyl chloride.

The series of experiments described above was aimed at suppressing the reaction which proceeds according to the living chain mechanism. Besides, we have conducted a qualitative experiment with the purpose of creating conditions for the pure living mechanism without termination. This experiment was carried out in the presence of silver tetrafluoroborate as a co-initiator. In this case, the formation of an intermediate compound (A) is highly probable according to the reaction scheme given below. Since the BF_4^- ion is not nucleophilic, termination involving this counterion is unlikely.



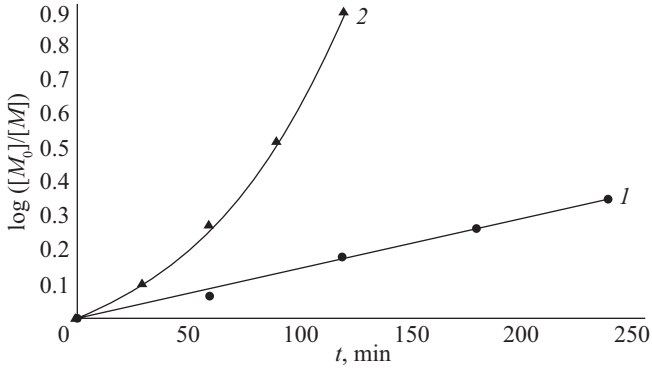


Fig. 4. Time dependence of logarithm of inverse 2-ethyl-2-oxazoline conversion: *1* — initiation by MesCl; *2* — initiation by MesCl in the presence of silver tetrafluoroborate; MesCl concentration was 0.2 mol/L, monomer concentration was 6 mol/L, reaction temperature was 80°C

Fig. 4 presents the time dependence of logarithm of inverse 2-ethyl-2-oxazoline conversion in the case of polymerization initiated by methanesulfonyl chloride in the presence of $AgBF_4$. As can be seen form the plot, polymerization rate increases in the presence of $AgBF_4$; this leads to the conclusion that chain termination has a considerable influence on the total reaction rate.

Analysis of temperature dependences of chain growth rate constants allowed us to determine activation energies of these processes, which were equal to 114 ± 9 kJ/mol in the case of methanesulfonyl chloride ($\ln k_p = 29.6 - 13700/T$; $R = 0.987$) and 67 ± 4 kJ/mol in the case of methanesulfonyl bromide ($\ln k_p = 15.1 - 7990/T$; $R = 0.996$). Differences in activation energies indicate the influence of counterion on the transition state; this influence may be explained by differences in basicity of the corresponding anions (Cl^- and Br^-). The obtained values were close to activation energies of 2-ethyl-2-oxazoline polymerization initiated by other compounds [13, 14].

Conclusions. Model compounds (methanesulfonyl halides) were used to demonstrate possibility of using alkyl sulfonyl halides for initiating cationic polymerization of 2-oxazolines. The main kinetic parameters of the process were determined; it was established that in the selected conditions, polymerization proceeds mainly according to the living chain mechanism.

Experimental. 1,1,2,2-Tetrachloroethane (Aldrich) was distilled over P_2O_5. 2-Ethyl-2-oxazoline (Aldrich) was left to stand over calcium hydride and then distilled. Methanesulfonyl chloride (Aldrich) was distilled in vacuum. Methanesulfonyl bromide was synthesized according to the method described elsewhere [15]. Benzyltributylammonium chloride, silver tetrafluoroborate (Aldrich) and hexadecyltrimethylammonium bromide were dehydrated by azeotropic distillation of water-benzene mixture. *N*-(2-chloroethyl)-*N*-methanesulfonyl propionamide was synthesized according to the technique described earlier [10].

NMR spectra of solutions of samples in deuterated chloroform were taken using a Bruker AVANCE instrument (400 MHz); tetrachloroethane was used as an internal standard.

Methanesulfonyl bromide. 6.2 g (0.045 mol) of hemisulfate of S-methylisothiourea obtained by the method described earlier [16] and 100 mL of water were placed into a flask equipped with magnetic stirrer, dropping funnel and thermometer. The solution was cooled down to 0–5°C in an ice-water bath, and 57 g (0.36 mol) of bromine was added during one hour at intense stirring and at the above-mentioned temperature. After all bromine was

added, the solution was left at stirring for 5 hours at a temperature lower than 5°C. The product was extracted with 70 mL of dichloromethane. Excess bromine was removed by 10% solution of sodium hydrocarbonate. The extract was washed with water and dried over calcined magnesium sulfate. The solvent was removed by distillation, and the residue was distilled under vacuum. The yield was 1.88 g (27%). The following parameters were measured: b. p. 95°C (15 mm Hg), $n_D^{20} = 1.5090$ (literature data: b. p. 75°C (15 mm Hg), $n_D^{20} = 1.5080$ [17]). ^{1}H NMR signal: 3.83 ppm singlet (H_3C-), ^{13}C NMR signal: 57.08 ppm singlet (H_3C-).

***N*-(2-chloroethyl)-*N*-methanesulfonyl propionamide.** 2.5 mL (30 mmol) of methanesulfonyl chloride dissolved in 3 mL dichloromethane was placed into a 50 mL flat-bottom flask equipped with stirrer and dropping funnel. 3 mL (30 mmol) of 2-ethyl-2-oxazoline dissolved in 6 mL of dichloromethane was placed into a dropping funnel. This solution was added to reaction mixture at stirring for 30 min; after all oxazoline was added, the reaction mixture was stirred for 2 hrs. The mixture was left to stand for 7 days at room temperature. Then the solvent was distilled under vacuum, and the residue was recrystallized from acetone. The yield was 5.8 g (89%). The following parameters were measured: m. p. 56°C (literature data: m. p. 55–58°C [10]). ^{1}H NMR signals: 1.20 ppm triplet (H_3C-), 2.71 ppm quadruplet ($-CH_2-C{=}O$), 3.33 ppm singlet (H_3C-SO_2-), 3.74 ppm triplet ($N-CH_2-$), 4.08 ppm triplet ($-CH_2-Cl$).

Determination of chain growth rate constants. 0.45 g (4.5 mmol) of 2-ethyl-2-oxazoline, 0.45 g of tetrachloroethane, the calculated amount of the initiator (initiator : monomer ratio was 1 : 30) were placed into a glass tube. The sample was heated at several temperatures, and spectra were taken at certain intervals; the solvent was used as an internal standard for quantitative analysis.

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