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Multicenter Polyester Initiators for the Synthesis of Graft Copolymers with Oligo(2-ethyl-2-oxazoline) Side Chains

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Abstract—Multicenter alkylene-aromatic polyester initiators for the cationic polymerization of oxazolines are synthesized via the high-temperature polycondensation of 2-[4-(2-Br-ethyl)]phenylsulfonyl hydroquinone with 4,4'-(alkanoyldioxydibenzoyl)dichlorides. The Kuhn segment values, liquid-crystalline properties, and molecular-mass characteristics of the macroinitiators are determined. It is shown that the obtained polyesters may be used as initiators for the cationic polymerization of 2-ethyl-2-oxazoline. The graft copolymers form aqueous micellar solutions with a narrow particle-size distribution and possess a lower critical solution temperature.

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INTRODUCTION

Polymer brushes belong to the class of copolymers containing long main chains and tightly grafted relatively short side fragments. They possess the unique ability to preserve fully extended macromolecular conformations owing to the steric interactions of side chains, which prevent the folding of main chains [1]. Owing to their rigidity, these cylindrical brushes find ever-growing use for the creation of novel nanostructures that cannot be obtained from conventional linear polymers. In particular, varying the length-to-diameter ratio of cylindrical brushes (from tens to hundreds of nanometers) makes it possible to obtain templates for the synthesis of ordered nano-objects of various morphologies [2].

Unlike conventional polymer micelles, cylindrical brushes consist of single macromolecules. This circumstances allows, for example, unimolecular core–shell micelles to be formed in solution if the side chains are hydrophilic and makes it possible to obtain one-dimensionally ordered organic–inorganic objects in which the core is used to bind inorganic particles, while the shell plays the role of a protective layer preventing intermolecular aggregation [3–6]. The self-organization and aggregation of amphiphilic polymer brushes markedly differ from the solution behavior of linear amphiphilic copolymers. For example, it was shown [7] that the graft copolymer of polyisoprene containing side polystyrene fragments in solvents “good” for polyisoprene form hollow cylinders with lengths of up to 700 nm. In contrast, no folding of cylindrical brushes occurs in their melts, owing to a high grafting density of side chains [8].

At present, one of the most topical directions in the development of nanostructured polymer materials is the design and synthesis of complex associating polymer systems that are able to reversibly change their hydrophilic–hydrophobic balance, depending on external conditions (variation in temperature and pH, irradiation at a certain wavelength), and, as a consequence, complex-formation behavior. As a result, the controlled dissociation or formation of a complex occurs. Among thermosensitive polymer systems, polymers based on poly(*N*-isopropylacrylamide), dimethylaminoethyl acrylates, and oligo(ethylene oxide) have been investigated in sufficient detail, while poly(2-oxazolines) have been studied to a lesser extent [9]. The latter type of polymer is extremely promising for biomedical purposes because poly(*N*-acylethyleneimines) are nontoxic biocompatible polymers with a lower critical solution temperature in water, which makes it possible to control the processes of association of these polymers with low-molecular-mass compounds. Changes in the alkyl group structure in poly(2-alkyl-2-oxazolines) allow the polymer properties to be widely varied in both solution (control over the lower critical solution temperature) and the solid state (formation of nanospheres and nanofibers) [10–12]. Complexes of homopolymers and copolymers of poly(2-alkyloxazolines) with low-molecular - mass compounds and metal ions are used as drug- and DNA-delivery systems [13] and materials for the creation of biocompatible composites [14]. The effects of polymer-chain structure (block, graft, starlike polymers), end groups, and the hydrophilic–hydrophobic balance on the temperature dependence of polymer solubility have been investigated [15, 16]. In these studies, branched polymers in general and graft polymers in particular were shown to be promising matrixes for drug delivery [11]. Note that, in the overwhelming majority of cases, the backbones of comblike polymers are either poly[(meth)acrylic acid] or polystyrene derivatives. No data are available on thermosensitive comblike polymers with poly(2-alkyloxazoline) side chains and backbones with substantially different (e.g., polyester) chemical structures. It may be supposed that the great difference in the thermodynamic affinities of main and side chains for solvents leads to thermosensitive unimolecular micelles and aggregates of unusual morphologies and makes it possible to create a new type of smart macrocyclic receptor able of multicenter binding to organic and inorganic substrates.

It is obvious that the highest grafting regularity of side groups may be provided by the approach known as "grafting from," which implies the synthesis of a macroinitiator with active groups along the polymer chain. The macroinitiators of this type may be synthesized via two alternative approaches: the introduction of initiating groups into a preformed polyester chain or the synthesis of a compound with the initiating functional group followed by its polycondensation with a complementary monomer.

In this study, the structure of a polycondensation monomer containing functional groups that can initiate the cationic polymerization of 2-alkyl-2-oxazolines is suggested and its synthesis and the properties of alkylene-aromatic polyesters involving this structural fragment are described.

EXPERIMENTAL

In this study, 2-[4-(2-Br-ethyl)]phenylsulfonyl hydroquinone (1) [17], 4,4'-alkanedioyldioxydibenzoic acids (2a–2g), and 4,4'-alkanedioyldioxydibenzoyl dichlorides (3a–3g) [18] were obtained according to the known procedures. 2-Ethyl-2-oxazoline, diphenyl oxide, and 1,1,2,2-tetrachloroethane (Aldrich) were dried over calcium hydride and distilled. Procedures for the synthesis of poly(2-[4-(2-Br-ethyl)phenylsulfonyl]-1,4-phenylene-4',4''-adipoyldioxydibenzoate) (4c) and for the polymerization of 2-ethyl-2-oxazoline by macroinitiators of this type are presented below as examples.

Poly(2-[4-(2-Br-ethyl)phenylsulfonyl]-1,4-phenylene-4',4''-adipoyldioxydibenzoate) (4c)

A flask equipped with a stirrer and a gas-supplying tube was charged with **1** (4.23 g, 0.01 mol), **3c** (3.57 g, 0.01 mol), and diphenyl oxide (30 mL). The obtained mixture was purged with dry argon and heated up to 200°C under a flow of gas. The reaction mixture was kept at 200°C for 2 h. The polymer was precipitated with hexane, separated, reprecipitated from chloroform into hexane, and dried to a constant mass. The product yield was 6.5 g (92%).

^{1}H NMR ($CDCl_3$): 1.86 (t, $COCH_2\underline{CH_2}$), 2.68 (t, $CO\underline{CH_2}CH_2$), 3.22 (d, $Ar\underline{CH_2}CH_2Br$), 3.56 (d, $ArCH_2\underline{CH_2}Br$), 7.11–8.43 (m, Ar–H) ppm. $[\eta]$ = 0.24 dL/g ($CHCl_3$, 25°C); $M_w = 23\,000$.

Polymerization of 2-Ethyl-2-oxazoline by the Polyester Initiator

For the polymerization of 2-ethyl-2-oxazoline by the multicenter polyester initiator, a solution of the initiator and the monomer in 1,1,2,2-tetrachloroethane was prepared. The molar ratio between the initiator functional groups and the monomer was 1 : 60. The initiator concentration was 30 wt %. Polymerization was conducted in sealed tubes at a temperature of 150°C for 4 h. After completion of polymerization and removal of volatile compounds, the reaction mixture was diluted with ethanol and dialyzed against water for 48 h. The obtained aqueous solution of the polymer was lyophilized.

Intrinsic-viscosity values $[\eta]$ of polymers were determined in chloroform at 25°C with the use of an Ubbelohde viscometer.

NMR spectra were recorded on a Bruker AC 400 device (400 MHz) for solutions in $CDCl_3$.

Dialysis was performed with the use of dialysis bags (CellaSep, Orange Scientific) with an MWCO of 3500 D.

The values of M_w and the second virial coefficient were determined via static light scattering for chloroform solutions with the use of a Photocor Complex (Photocor Instruments Inc., Russia) setup. As a light source, a He–Ne laser (λ = 632.8 nm) was used at a scattering angle of θ = 90°.

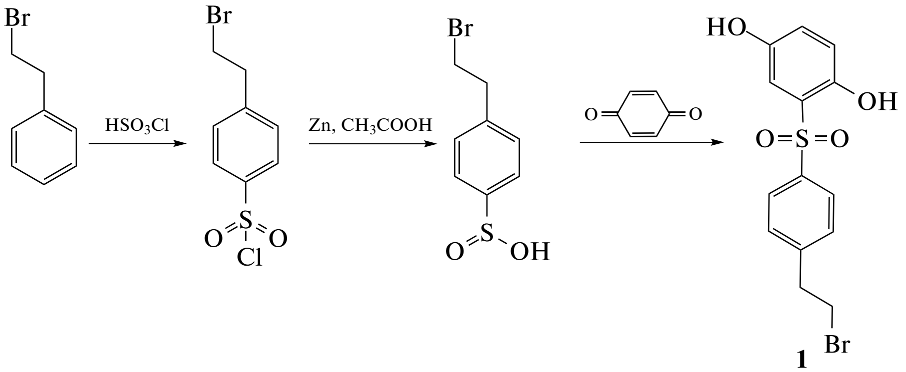
The chromatographic analysis was performed on a Shimadzu LC-20AD chromatograph equipped with a TSKgel G5000HHR column (5 μm, 7.8 mm × 300 mm, Tosoh Bioscience) and a refractometric detector. A solution of LiBr in DMF (0.1 mol/L) at 60°C was used as the mobile phase. Calibration was performed relative to poly(ethylene glycol) standards ($M_w = 6 \times 10^2$–4×10^4).

RESULTS AND DISCUSSION

Synthesis of Multicenter Oligoester Initiators

Compound **1** was used as a polycondensation monomer containing functional groups able to initiate the cationic polymerization of 2-alkyl-2-oxazolines. This choice was determined by the fact that the earlier described alkylene-aromatic polyesters based on 2,5-dioxydiphenylsulfone and 4,4'-(1,10-decamethylenedioxy)dibenzoic acid [19] may be synthesized via acceptor-free polycondensation because the presence of the 2-Br-ethyl group in the target monomer makes the monomer sensitive to tertiary amines and alkalis, thereby precluding the use of conventional acceptor methods for the synthesis of polyesters. In contrast, it may be supposed that the direct nucleophilic substitution of a phenolic hydroxyl for the bromine in the 2-Br-ethyl group has a low probability in the absence of bases.

Compound **1** was synthesized via the Spinner method [17], which includes chlorosulfonation of 2-phenethyl bromide, reduction of the corresponding sulfochloride to sulfinic acid, and addition of the latter to 1,4-benzoquinone under the Michael reaction conditions.



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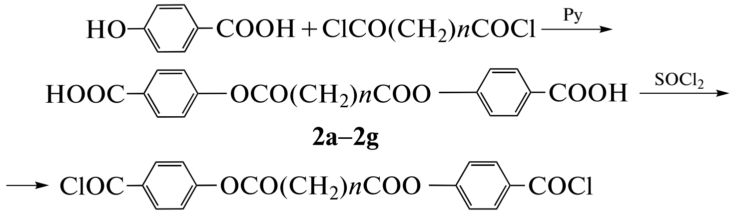
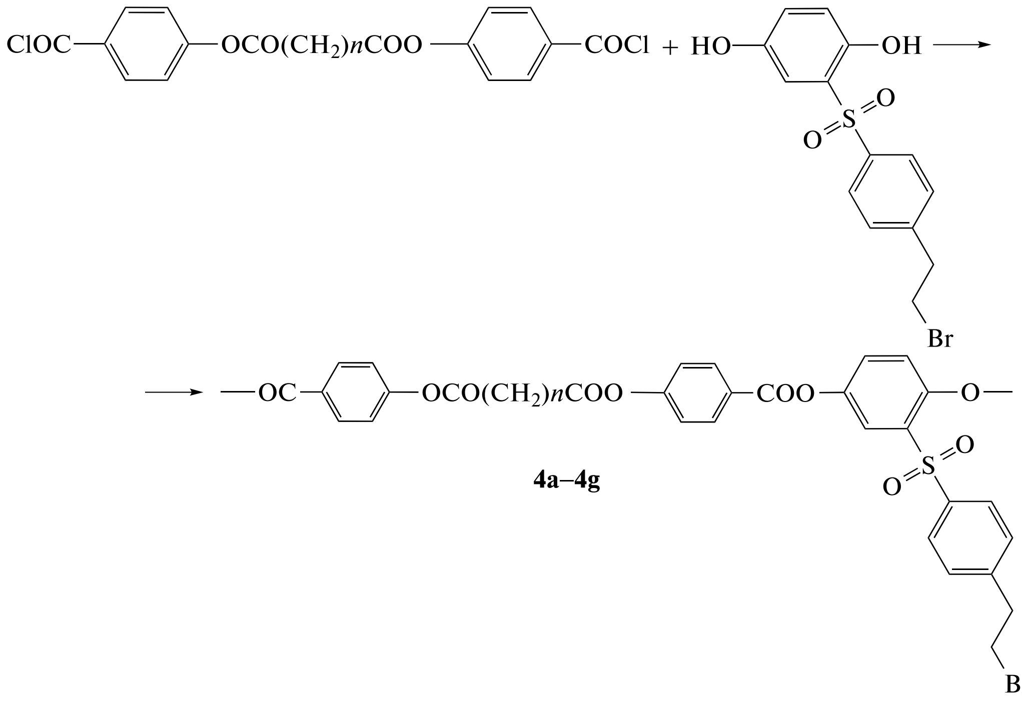
As comonomers, compounds **3a–3g** with an aliphatic spacer length from 2 to 8 methylene groups were chosen. These compounds were synthesized according to the following scheme [20].



2a–2g

3a–3g

Poly-2-([4-(2-Br-ethyl)phenylsulfonyl]-1,4-phenylene-4',4''-alkanedioyldioxydibenzoates (**4a–4g**) were synthesized via high-temperature acceptor-free polycondensation in solution [21].



4a–4g

Poly(2-[4-(2-Br-ethyl)phenylsulfonyl]-1,4-phenylene-4',4''-alkanedioyldioxydibenzoates) (**4a–4g**)

Designation	Intrinsic viscosity in $CHCl_3$ at 25°C, [η], dL/g	$M_w \times 10^{-3}$*	Phase-transition temperatures, °C**	A_2, cm^3/mol***
4a	0.20	18	S-155–LC-200–I	0.06
4b	0.18	17	S-110–LC-115–I	0.04
4c	0.24	23	S-125–LC-205–I	0.06
4d	0.21	20	S-105–LC-125–I	0.05
4e	0.20	19	S-75–LC-145–I	0.06
4f	0.22	20	S-95–LC-110–I	0.05
4g	0.19	18	S-104–LC-150–I	0.04

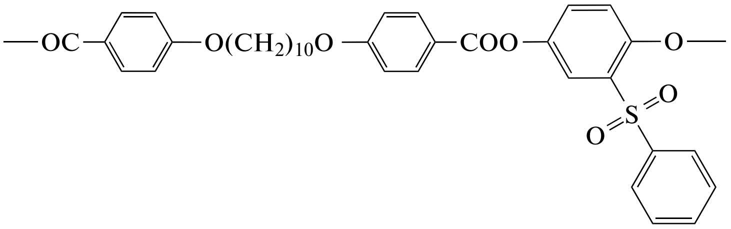
* M_w was determined via the static light-scattering method.

** S is the solid state, LC is the liquid crystal, and I is the isotropic liquid.

*** A_2 is the second virial coefficient for a solution in chloroform at 23°C.

It was found that the optimum polycondensation conditions are as follows: solvent, diphenyloxide; temperature, 200°C; monomer concentration, 25 wt %; and reaction time, 2 h. Properties of the obtained polyesters are listed in the table.

It is interesting that the viscometric and light-scattering data from this study correlate well with similar data available for a structurally analogous polyester, poly(2-phenylsulfonyl-1,4-phenylene-4',4''-decamethylenedioxydibenzoate).



Therefore, the constants in the Mark–Kuhn–Houwink equation ($K = 3.7 \times 10^{-6}$, $a = 1.1$) reported in [22] may be used to estimate the M_η values of the synthesized polymers.

As is seen from the static light-scattering data, chloroform is practically a θ solvent for the considered polymers. For example, Fig. 1 shows the Debye diagram for polymer **4a** ($n = 2$). The fact that the second virial coefficient is close to zero makes it possible to estimate the Kuhn segment length on the basis of the viscometry data and with the use of the Flory–Fox formula as 20–22 Å.

This Kuhn segment value is typical for liquid-crystalline rigid–flexible (RF) polymers [23], and it specifies their ability to exhibit mesomorphism in melts. Indeed, all of the synthesized polymers are thermotropic liquid crystals. Note that the even members of this series form liquid-crystalline phases within a wider temperature range than that for odd members of the series. Polarization–optical observations of melts of the obtained polyesters suggest that they exhibit nematic thermotropic mesomorphism.

Synthesis of Graft Copolymers of 2-Ethyl-2-oxazoline by Polyester Macroinitiators

The task of the next step of this study was to prepare polyester-*graft*-polyoxazoline graft copolymers via

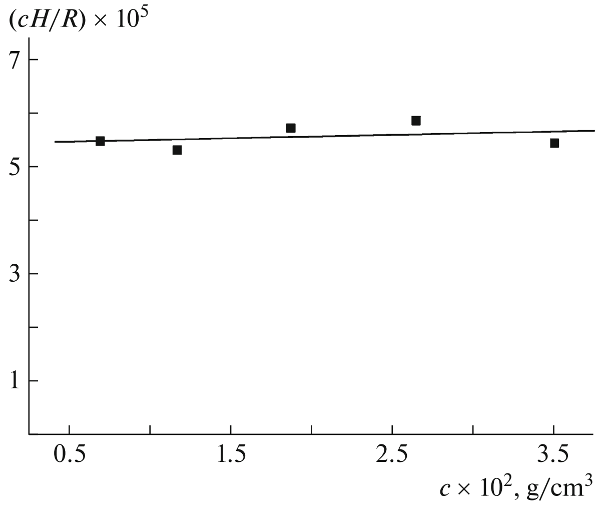


Fig. 1. The Debye diagram for the solution of **4a** ($n = 2$) in chloroform at 23°C.

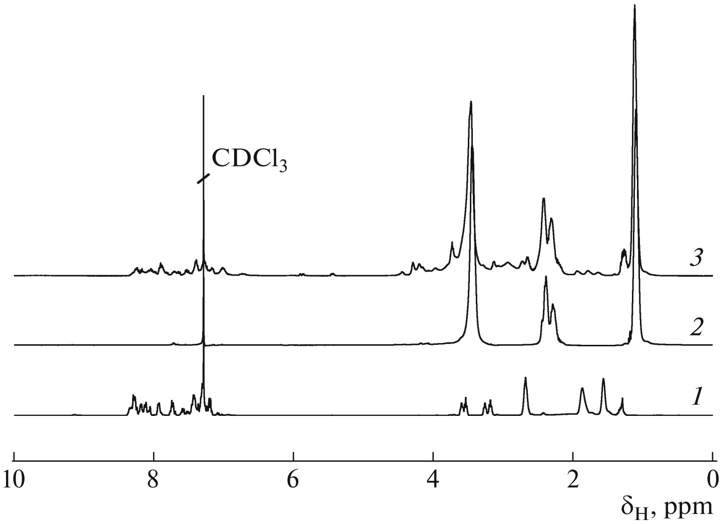
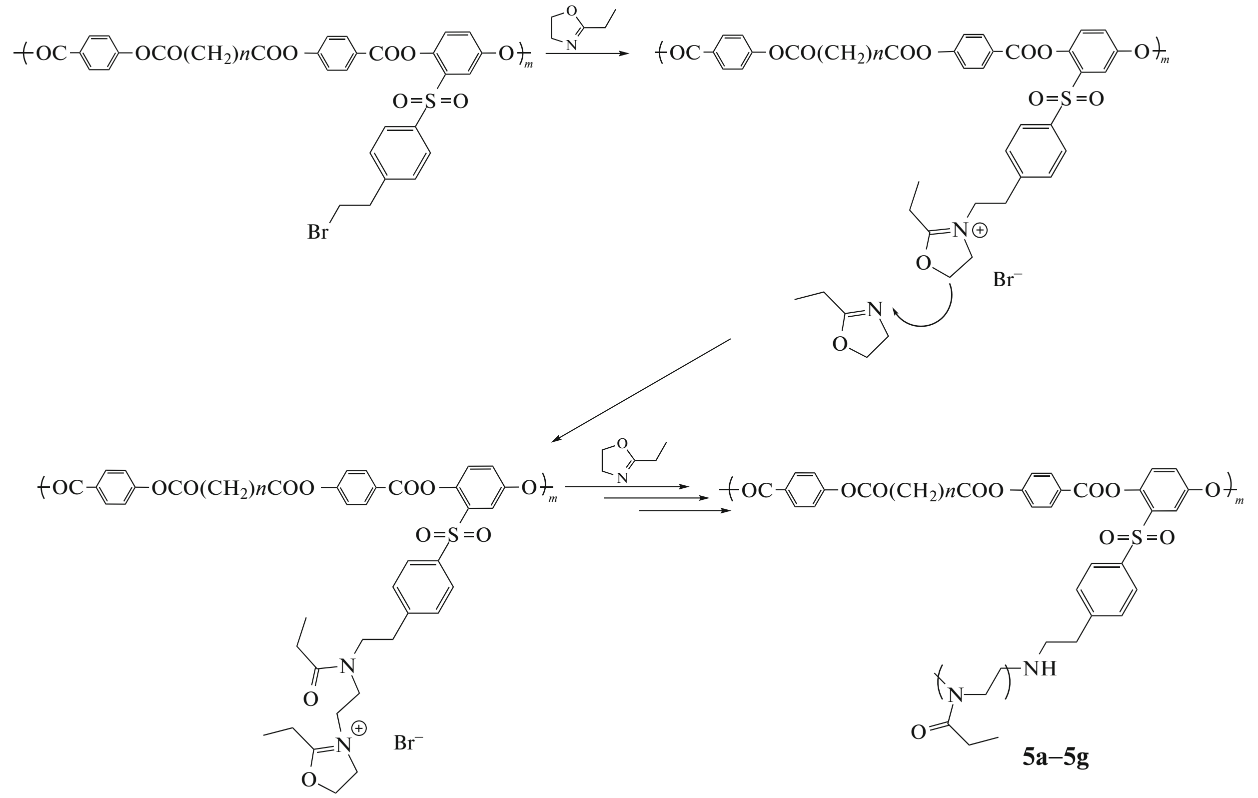


Fig. 2. ^{1}H NMR spectra of (*1*) polymer **4e** (n = 6), (*2*) poly(2-ethyl-2-oxazoline), and (*3*) polymer **5e**.

cationic polymerization. For this method to be successful, it is necessary as a rule to search for optimum conditions of the process for each particular monomer and initiator. In our study, we confined ourselves to the possibility to obtain polyesters with grafted polyoxazoline groups with the use of suggested macroinitiators in accordance with the following scheme.



Alkylene-aromatic polyesters are soluble in a limited number of solvents (chlorinated hydrocarbons, CF_3COOH, *m*-cresol). This circumstance substantially restricts the choice of a medium for polymerization. It is obvious that protic acids are inappropriate for cationic polymerization, while chlorinated hydrocarbons are poor solvents for the synthesized macroinitiators at room temperature. It is well known that

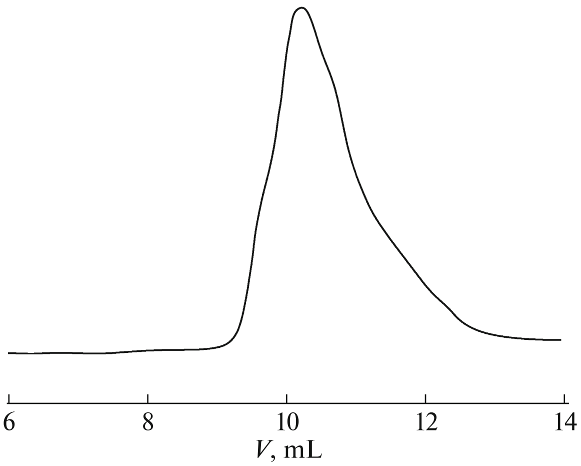


Fig. 3. SEC chromatogram of copolymer **5e**.

polymer-analogous transformations in poor solvents are unable to provide a sufficiently high grafting degree, owing to inaccessibility of a considerable part of the functional groups. As a rule, the thermodynamic quality of a solvent improves with an increase in temperature. Therefore, polyoxazoline side chains were grafted in the medium of tetrachloroethane at 150°C.

A comparison of ^{1}H NMR spectra of the macroinitiator and the graft copolymer (Fig. 2) shows that the signals of both aromatic protons of the backbone and those assigned to poly(2-ethyl-2-oxazoline) side chains are present in the spectrum of the copolymer. Together with the unimodal molecular-mass distribution of the obtained polymer (Fig. 3), these data make it possible to state that the studied sample is a graft copolymer. The quantitative analysis of the NMR data demonstrates that the average length of grafted oligooxazoline chains is 45–47 monomer units. However, the chromatogram for the graft copolymer has an asymmetric pattern. This finding probably is evidence for a somewhat nonuniform distribution of graft oligomers along the backbone.

The obtained samples of the graft copolymers form micellar solutions in water (up to 1 wt %). Note that the size distribution of macromolecular aggregates is unusually narrow (Fig. 4). It may be assumed that this behavior is related to the dual character of water, which serves as a solvent for grafted polyoxazoline chains and as a nonsolvent for the main polyester chain.

Preliminary studies of the thermosensitive properties of the graft copolymers showed (Fig. 5) that the lower critical solution temperature of the obtained copolymer is about 40°C lower than those of linear [24] and starlike [25] analogs. This value is close to the lower critical solution temperature of poly(ω-*n*-hexadecyl-2-ethyloxazoline) [24]. In addition, this finding is evidence that the graft copolymer containing both hydrophobic (polyester) and hydrophilic (polyoxazoline) fragments is formed.

Problems related to optimization of conditions for the synthesis of graft copolymers and precise determination of the grafting density, molecular-mass characteristics, and thermosensitivity of grafted chains are the subject of our further investigations, which are in progress now.

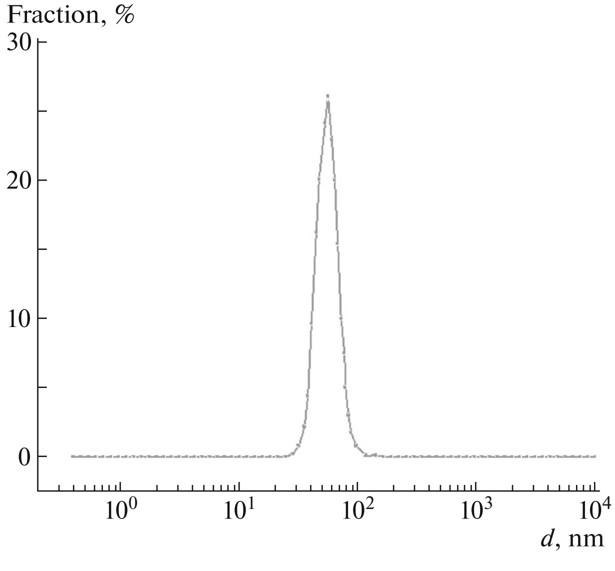


Fig. 4. Particle-size distribution in the aqueous colloid solution (1%) of **5c**.

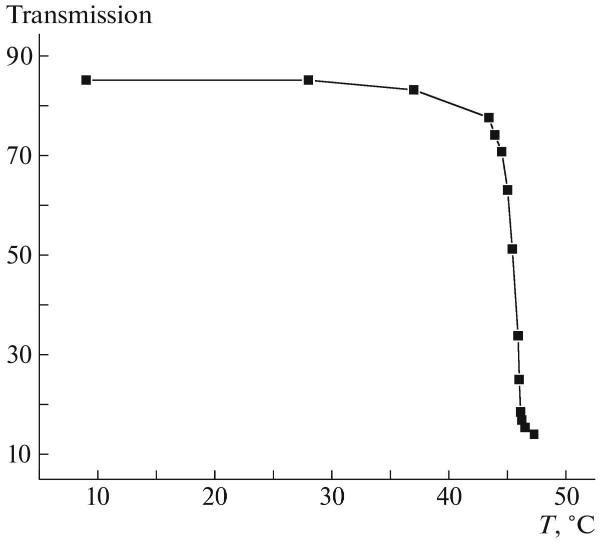


Fig. 5. Temperature dependence of the transmission (λ = 650 nm) of a 1% aqueous solution of **5c**.

CONCLUSIONS

Polymerization–polycondensation polymer brushes consisting of a main polyester chain and poly(2-ethyl-2-oxazoline side chains) have been prepared. A new polycondensation monomer containing functional groups that are able to initiate cationic polymerization of oxazolines has been designed for their synthesis. A method of the polyester macroinitiators of the cationic polymerization of oxazolines has been developed; it makes it possible to synthesize the indicated macroinitiators, which contain initiating groups in each repeating unit of the polymer. It is shown that polymer brushes with poly(2-ethyl-2-oxazoline) side chains and a polyester backbone may be synthesized via ring-opening cationic polymerization. A substantial difference in the affinities of main and side chains of these polymers for solvents helps to vary their conformational compositions with the thermodynamic quality of the medium, and this circumstance in turn makes it possible to control the morphologies of the films based on these polymers.

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