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New thermoresponsive polyester-graft-polyoxazolines based on sulfonyl chloride macroinitiators

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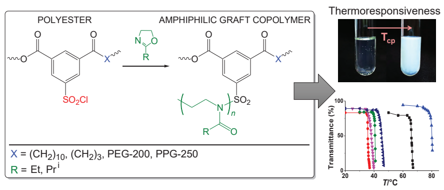
Novel amphiphilic graft copolymers with various polyester backbone and poly(2-alkyl-2-oxazoline) side chains were synthesized using polyester-type macroinitiators with sulfonyl chloride initiating groups. The obtained graft copolymers exhibit thermoresponsive properties in aqueous solutions in a broad temperature interval.



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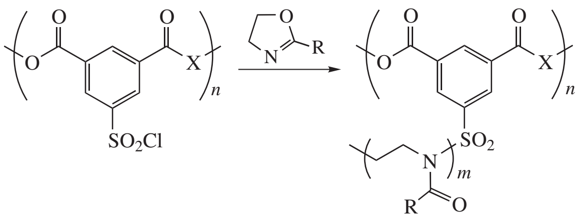
Graft polymers with a long backbone and short side chains with high degree of grafting have a unique ability to maintain their worm-like conformation,[1] since the steric effect prevents the folding of the backbone. Among these polymers, the most interesting are heterostructures where the backbone and side chains are of principally different chemical nature. Such macromolecular structure would promote segregation of the complementary fragments in solution and, as a result, unique supramolecular structures which cannot be obtained for polymers with other architectures are formed.[2–4] Thermoresponsive graft copolymers are of special interest as their hydrophilic-hydrophobic balance enables them to undergo reversible phase transitions in aqueous solutions with temperature growth.[5] Since cylindrical brushes with hydrophilic side chains solubilize different compounds with low molecular weight, such high sensitivity to external impact can be used in biomedical and engineering technologies, for example, in the development of drug delivery systems, sensors and synthesis of nanoparticle templates.[6–8]

A number of synthetic procedures towards polyester-based and polyimide-based graft copolymers with polyacrylate and polyoxazoline side chains are documented.[9–11] Generally, multicenter macroinitiators are obtained by polycondensation method, so the distance between initiating groups is determined by the structure of the main chain of the polycondensation polymer. The present paper reports on the synthesis of novel poly(ester)-graft-poly(2-alkyl-2-oxazolines) using original approach, which was described in detail recently.[12]

Since the reactivities of the carbonyl and sulfonyl chlorides with respect to nucleophiles (*e.g.* amines, alcohols) differ significantly, it is possible to selectively obtain aromatic esters with retained sulfonyl chloride groups.[13] As shown earlier, sulfonyl chlorides are effective initiators of cationic polymerization of 2-alkyl-2-oxazolines, which occurs in the absence of irreversible chain termination and allows one to obtain thermoresponsive homo- and block-copolymers.[14] Thereby, it can be assumed that polycondensation of 5-(chlorosulfonyl)-isophthaloyl dichloride with a diol followed by 2-alkyl-2-oxazoline polymerization will afford amphiphilic polyester-graft-polyoxazolines **1–8** with hydrophilic amide fragments and



1–8

1 X = $(CH_2)_{10}$, R = Et **5** X = PEG-200, R = Et
2 X = $(CH_2)_{10}$, R = Pr^i **6** X = PEG-200, R = Pr^i
3 X = $(CH_2)_3$, R = Et **7** X = PPG-250, R = Et
4 X = $(CH_2)_3$, R = Pr^i **8** X = PPG-250, R = Pr^i

Scheme 1 *Reagents and conditions*: 1,2-dichloroethane, 100 °C, 120 h.

hydrophobic alkyl substutients in grafted poly(2-alkyl-2-oxazoline) chains (Scheme 1). Polyesters with sulfonyl chloride groups were synthesized by the usual procedure of acceptor polycondensation (Online Supplementary Materials, Scheme S1). As co-monomers, diols and oligomeric glycols of various chemical nature were used. Propane-1,3-diol was chosen as a structural unit that provides the highest density of side chain grafting, whereas decane-1,10-diol was chosen for obtaining flexible backbone with lower grafting density. Poly(ethylene glycol), PEG-200, and poly(propylene glycol), PPG-250, were used in order to introduce flexible hydrophilic or hydrophobic spacers of similar length. Molecular weight characteristics of the synthesized macroinitiators are given in Table 1.

Polyester-graft-polyoxazolines **1–8** were synthesized by ring opening cationic polymerization using a series of macroinitiators with sulfonyl chloride initiating groups (see Scheme 1). Polyesters are known to be soluble only in several types of solvents (chlorinated hydrocarbons, fluorinated acetic acids, *m*-cresol), which significantly limits the choice of medium for

Table 1 Molecular weight characteristics of polyester macroinitiators.

Sample	M_w/kDa	$Đ = M_w/M_n$
X = $(CH_2)_{10}$	26	1.7
X = $(CH_2)_3$	16	2.0
X = PEG-200	17	2.4
X = PPG-250	15	2.0

polymerization. Chlorinated hydrocarbons were shown to be close to θ-solvents for alkylene-aromatic macroinitiators at room temperature.[15] Following the upper critical solution temperature (UCST) behavior of such polymer–solvent systems, the thermodynamic quality of the solvent is improved at higher temperatures. In this way, the grafting of polyoxazoline chains was carried out in 1,2-dichloroethane at 100 °C. Nitrogen-based terminating agents are recognized to be the mostly preferred for 2-oxazoline polymerization due to rapid termination on the position 5 of the oxazolinium ring.[16] In this study, pyrrolidine was used as the termination agent.

The structure of the synthesized polymers was verified by NMR spectroscopy (Figure S1, see Online Supplementary Materials). Characteristic signals for the corresponding monomer unit for all the obtained polymers as well as minor signals of the polyester backbone were detected.

To determine the molecular mass characteristics of grafted chains, the polymer samples were subjected to alkaline hydrolysis using the procedure that ensures quantitative cleavage of the polyester chain.[17] In a model experiment, poly(2-ethyl-2-oxazoline) was stable for at least 1 h, therefore it was possible to perform a selective destruction of the main chain of graft copolymer. Molecular weight characteristics of abstracted polyoxazoline moieties and their calculated grafting densities are given in Table 2.

Since poly(2-oxazolines) are amphiphilic polymers, they can perform a 'coil-to-globule' phase transition in aqueous solution.[18,19] Polyoxazoline–water mixtures belong to systems with lower critical solution temperature (LCST).[20] In this way, thermoresponsive properties of the synthesized graft copolymers were studied, and the relationship between the polymer structure and the demonstrated properties was investigated. Cloud points of 1% polymeric solutions were determined with a medium heating rate of 0.5 K min^{-1} as temperatures of 50% decrease in light transmission (Table 2), according to recommendations.[21] The turbidimetric curves are shown in Figure 1. It should be noted that phase transitions were found to be sharp and reversible for all studied samples.

As can be seen, samples **1** and **3** with alkyl polyester backbone and grafted hydrophilic poly(2-ethyl-2-oxazoline) chains possess rather high cloud points due to the good solubility of *N*-propionyl substituents. It was expected that phase transition temperature decreases with the increase in the number of methylene groups in the spacer backbone. On the other hand, samples **5** and **7** with PEG-200 and PPG-250 polyester backbones were not thermoresponsive due to the good solubility of hydrophilic backbone. All samples with poly(2-isopropyl-2-oxazoline) side chains demonstrated thermoresponsive properies. Cloud points of samples with alkyl polyester backbone differed in the same manner as those for poly(2-ethyl-2-oxazoline), whereas for

Table 2 Molecular weight characteristics, grafting density and cloud points of poly(2-alkyl-2-oxazoline) graft copolymers based on 5-sulfoisophthalate macroinitiators.

Sample	Grafted chains		Grafting density	Cloud point/°C
	M_w/kDa	*Đ*		
1	7.3	1.40	0.67	65.8
2	4.3	1.50	0.63	35.7
3	4.4	1.48	0.66	80.0
4	4.1	1.44	0.62	38.1
5	3.0	1.37	0.62	–
6	3.4	1.15	0.65	40.6
7	4.1	1.24	0.65	–
8	2.8	1.14	0.61	45.1

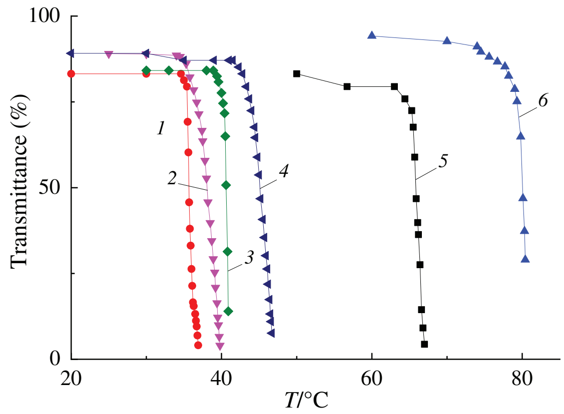


Figure 1 Turbidimetric curves of synthesized graft copolymers: (*1*) sample **2**, (*2*) sample **4**, (*3*) sample **6**, (*4*) sample **8**, (*5*) sample **1**, (*6*) sample **3**.

samples **6** and **8** with PEG-200 and PPG-250 polyester backbones inverted dependence was observed. It is known that the PPG polymeric chain is more hydrophobic than the PEG one due to the additional methyl group in the structure of the former. However, polyether fragments in the backbone of the synthesized graft copolymers are short enough in comparison with polyoxazoline side chains, so the difference in the hydrophobic-hydrophilic balance of PEG and PPG produces small effect on thermoresponsive properies. Obviously, there are some other factors influencing phase transition temperature. One of them is possibly higher rigidity of PPG chain compared with PEG. As a result, the macromolecule of the graft copolymer has more stretched conformation without any entanglement.

In summary, based on polyester macroinitiators with various hydrophilic/hydrophobic balance of the backbone and sulfonyl chloride initiating groups a number of new thermosensitive polyester-graft-polyoxazolines was synthesized. The obtained grafted copolymers perform a reversible 'coil-to-globule' phase transition in aqueous solution in a broad temperature interval from 35 to 80 °C. The new copolymers can be useful for the development of drug delivery systems as well as in other biomedical applications.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2020.11.037.

References

1 S. S. Sheiko, B. S. Sumerlin and K. Matyjaszewski, *Prog. Polym. Sci.*, 2008, **33**, 759.

2 M. Zhang, T. Breiner, H. Mori and A. H. E. Müller, *Polymer*, 2003, **44**, 1449.

3 G. Carrot, J. Hilborn and D. M. Knauss, *Polymer*, 1997, **38**, 6401.

4 S. Y. Yu-Su, S. S. Sheiko, H. Lee, W. Jakubowski, A. Nese, K. Matyjaszewski, D. Anokhin and D. A. Ivanov, *Macromolecules*, 2009, **42**, 9008.

5 I. Muljajew, C. Weber, I. Nischang and U. S. Schubert, *Materials*, 2018, **11**, 528.

6 J.-Z. Du, L.-Y. Tang, W.-J. Song, Y. Shi and J. Wang, *Biomacromolecules*, 2009, **10**, 2169.

7 M. Müllner, J. Yuan, S. Weiss, A. Walther, M. Förtsch, M. Drechsler and A. H. E. Müller, *J. Am. Chem. Soc.*, 2010, **132**, 16587.

8 Z. Zheng, A. Daniel, W. Yu, B. Weber, J. Ling and A. H. E. Müller, *Chem. Mater.*, 2013, **25**, 4585.

9 M. P. Kurlykin, A. E. Bursian and A. V. Tenkovtsev, *Polym. Sci., Ser. B*, 2017, **59**, 157 (*Vysokomol. Soedin., Ser. B*, 2017, **59**, 135).

10 T. K. Meleshko, I. V. Ivanov, A. V. Kashina, N. N. Bogorad, M. A. Simonova, N. V. Zakharova, A. P. Filippov and A. V. Yakimansky, *Polym. Sci., Ser. B*, 2018, **60**, 35 (*Vysokomol. Soedin., Ser. B*, 2018, **60**, 16).

11 I. V. Ivanov, T. K. Meleshko, A. V. Kashina and A. V. Yakimansky, *Russ. Chem. Rev*., 2019, **88**, 1248.

12 A. B. Razina and A. V. Ten'kovtsev, *J. Polym. Sci., Ser. B*, 2019, **61**, 589 (*Vysokomol. Soedin., Ser. B*, 2019, **61**, 363).

13 Yu. A. Moskvichev, A. V. Tarasov, E. M. Alov and N. P. Gerasimov, *Ross. Khim. Zh.*, 2005, **49** (6), 21 (in Russian).

14 A. N. Blokhin, M. P. Kurlykin, A. B. Razina, M. M. Dudkina and A. V. Ten'kovtsev, *Polym. Sci., Ser. B*, 2018, **60**, 421 (*Vysokomol. Soedin., Ser. B*, 2018, **60**, 269).

15 A. A. Kudryavtseva, M. P. Kurlykin, E. B. Tarabukina, A. V. Tenkovtsev and A. P. Filippov, *Int. J. Polym. Anal. Charact*., 2017, **22**, 526.

16 B. Verbraeken, B. D. Monnery, K. Lava and R. Hoogenboom, *Eur. Polym. J.*, 2017, **88**, 451.

17 B. J. Allen, G. M. Elsea, K. P. Keller and H. D. Kinder, *Anal. Chem*., 1977, **49**, 741.

18 A. I. Amirova, A. N. Blokhin, A. B. Razina, A. V. Tenkovtsev and A. P. Filippov, *Mendeleev Commun*., 2019, **29**, 472.

19 A. I. Amirova, T. U. Kirila, A. N. Blokhin, A. B. Razina, A. E. Bursian, A. V. Tenkovtsev and A. P. Filippov, *Mendeleev Commun*., 2020, **30**, 502.

20 C. Weber, R. Hoogenboom and U. S. Schubert, *Prog. Polym. Sci*., 2012, **37**, 686.

21 Q. Zhang, C. Weber, U. S. Schubert and R. Hoogenboom, *Mater. Horiz*., 2017, **4**, 109.

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