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Synthesis and hydrodynamic properties of star poly(2-alkyl-2-oxazolines) and poly(2-alkyl-2-oxazines) based on sulfochlorinated calix[4]arene initiator

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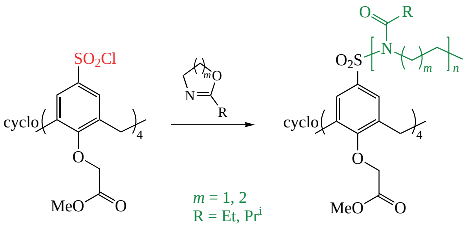
New four-arm star poly(2-alkyl-2-oxazolines) and poly(2-alkyl-2-oxazines) were synthesized using sulfochlorinated calix[4]arene derivative as a multifunctional initiator. Their characteristics were investigated by gel permeation chromatography, light scattering and viscometry. The polymer stars obtained were shown to have well-defined architecture and high intramolecular density.



$Đ$ = 1.17–1.25
R = 2.9–3.2 nm
Four-arm structure

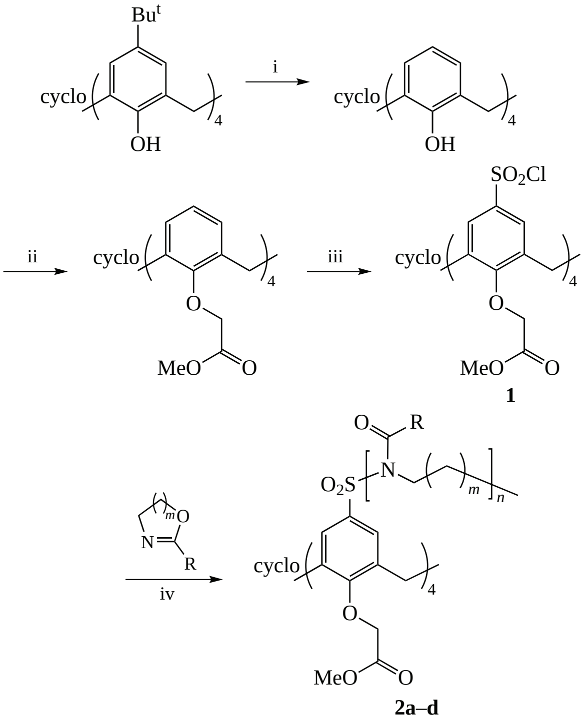
Keywords: cationic polymerization, ring-opening polymerization, polyoxazoline, polyoxazine, star polymer, calixarene, sulfonyl chloride.

Cationic ring-opening polymerization (CROP) of 2-alkyl-2-oxazolines and 2-alkyl-2-oxazines allows easy preparation of block copolymers, molecular brushes and star polymers. The resulting amphiphilic *N*-acylated poly(ethyleneimines) or poly(propyleneimines), which are known as poly(2-alkyl-2-oxazolines) (PAlOx) or poly(2-alkyl-2-oxazines) (PAlOz), exhibit thermoresponsibility in aqueous media.[1] This property as well as biocompatibility of PAlOx and PAlOz can be applied for the preparation of 'smart' materials, in particular for various biomedical applications.

Compounds of different nature were successfully used as core precursors for the polymerization of oxazolines and oxazines including multifunctional initiators.[2] In this way, the application of calixarene-based initiators for CROP is of special interest due to their perfect complexation properties.[3] Calix[*n*]arenes are cyclic oligomers, which can be easily prepared by the template phenol–formaldehyde condensation.[4] Calix[*n*]arenes exhibit 'guest–host' interactions with low molecular weight organic compounds and transition metal ions.[5] Their low toxicity allows one to use them in living systems, however, due to hydrophobic nature of calixarene fragments, they are poorly soluble in water. In this work, a new approach to amphiphilic star PAlOx and PAlOz is considered which suggests the use of sulfochlorinated calix[4]arene derivative **1** as a multifunctional initiator. The application of sulfonyl chlorides as initiators for the CROP was thoroughly studied and reported in our papers.[6]

Tetrafunctional initiator **1** was synthesized from commercially available *tert*-butylcalix[4]arene according to the known technique (Scheme 1).[7] In the first stage, *tert*-butyl groups were removed from the upper rim of the macrocycle to increase the yield of the final sulfonyl chloride. Ester groups were introduced into the lower rim to reduce O-nucleophilicity and improve the solubility of the macrocycle. Finally, sulfonyl chloride initiating groups were introduced into the upper rim by treatment with chlorosulfonic acid. The structure of resulting initiator **1** was confirmed by ^{1}H NMR spectroscopy and elemental analysis (see Online Supplementary Materials, Figure S1).

To establish the applicability of initiator **1** for the star polymer synthesis, the kinetics of 2-ethyl-2-oxazoline polymerization was investigated. The polymerization was carried out at 100 °C in sulfolane as a perfect solvent for calixarene derivatives and oxazoline polymerization.[8] The initiator-to-monomer molar ratio was chosen to be equal to 1 : 120. Quantitative analysis was carried out by ^{1}H NMR spectroscopy. The monomer conversion



a $m = 1$, R = Et **c** $m = 2$, R = Et
b $m = 1$, R = Pr^i **d** $m = 2$, R = Pr^i

Scheme 1 *Reagents and conditions*: i, PhOH, AlCl$_3$, PhMe; ii, ClCH$_2$CO$_2$Me, K$_2$CO$_3$, MeCN; iii, ClSO$_3$H, CHCl$_3$, 50 °C, 20 min; iv, sulfolane, 100 °C, 24–96 h.

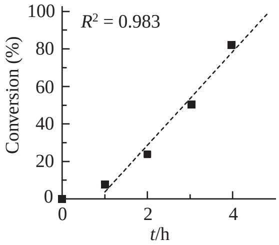


Figure 1 Monomer conversion *vs.* time for 2-ethyl-2-oxazoline polymerization using calix[4]arene-based tetrafunctional initiator **1**.

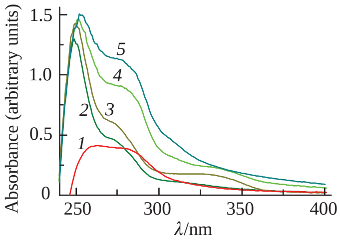


Figure 2 UV-VIS spectra of ethanol solutions of (*1*) initiator **1** as well as polymers (*2*) **2a**, (*3*) **2b**, (*4*) **2c** and (*5*) **2d** at concentration of 0.005 g cm^{-3}.

was calculated from the integral intensity for the oxazoline protons at 4.20 ppm using the signal of the sulfolane protons at 3.00 ppm as an internal standard (see Online Supplementary Materials, Figure S2). Figure 1 shows the dependence of the monomer conversion on the polymerization time.

An induction period was detected, which was possibly caused by steric hidrances taking place at the initial stage of the polymerization. Nevertheless, the subsequent linear dependence of the monomer conversion on time allows us to conclude that the polymerization proceeds in a controlled manner and there is no irreversible chain termination.

Using initiator **1**, a series of four-armed stars with calix[4]-arene core was synthesized, namely poly(2-ethyl-2-oxazoline) **2a**, poly(2-isopropyl-2-oxazoline) **2b**, poly(2-ethyl-2-oxazine) **2c** and poly(2-isopropyl-2-oxazine) **2d** (see Scheme 1). Using ^{1}H NMR and UV-VIS spectroscopy, the four-arm structure of the obtained polymers was confirmed (Figure S3) and their molar masses were determined (Table 1). Numerical average molar masses of arms M_arm were calculated based on the integral intensities ratio of calix[4]arene methylene bridge signals at 4.1 ppm *vs.* side alkyl substituents in the polymeric chains (2.41 + 2.32, 2.87 + 2.64, 2.32 and 2.72 ppm for polymers **2a**, **2b**, **2c** and **2d**, respectively). The signals of calix[4]arene aromatic protons, however, were not visible in the ^{1}H NMR spectra, which was explained by the long relaxation times of these fragments.[9] The obtained M_arm values are shown in Table 1. Using them and the molecular weight of calix[4]arene initiator, the numerical average molar masses of star-shaped polymers M_star were calculated.

UV-Vis spectra of ethanol solutions of polymer samples **2a–d** contain the characteristic absorption of aromatic fragments in the range of 260–290 nm, which confirms the presence of calix[4]arene core in their structure (Figure 2). The intensive absorption band with the maximum of 248–250 nm can be attributed to amide groups while the hyperchromic effect correlates with the hydrocarbon fragments content of the polymer.[10]

To determine molar mass distribution of star polymers **2a–d**, they were explored using gel permeation chromatography (GPC) (Figure S4). All the samples are characterized by a monomodal molecular weight distribution. The thus determined dispersions *Đ* of the polymer samples are collected in Table 1.

Static and dynamic light scattering as well as viscosity measurements were used for the determination of molar masses and hydrodynamic characteristics of polymers **2a–d** (see Online Supplementary Materials). The dynamic light scattering confirms the monomodal distribution obtained by GPC (Figures S4 and S5). It can be seen from Table 1 that the M_star values, taking into account the type of averaging, are in good agreement with the M_w values obtained by the light scattering method. This fact, together with the data obtained by GPC and dynamic light scattering, confirms that during the synthesis mainly four-armed star-shaped macromolecules are formed.

Table 1 Molecular weight characteristics of star polymers **2a**–**d**.

Sample	M_arm/ Da	M_star/ Da	M_w/Da	*Đ*	R_h/nm	L_arm/nm	[η]/ cm^3 g^{-1}
2a	2100	9500	11500 ± 300	1.17	3.1 ± 0.3	10.2 ± 0.4	6.6 ± 0.5
2b	2490	11000	15500 ± 400	1.25	2.9 ± 0.3	12.2 ± 0.4	9.9 ± 0.4
2c	2300	10200	11650 ± 600	1.18	3.0 ± 0.3	9.1 ± 0.5	5.4 ± 0.4
2d	2400	10800	11600 ± 300	1.21	3.2 ± 0.3	8.0 ± 0.4	7.0 ± 0.3

Using the M_w values, the arm lengths L_arm were calculated (see Table 1). For all the polymers, the L_arm values are much longer than the hydrodynamic radii of their macromolecules. Taking into account this fact and the obtained low values of intrinsic viscosity [η] (Figure S7), it can be concluded that the molecules of stars **2a–d** have high intramolecular density and the arms are strongly folded. The results obtained allow us to deduce the possibility of practical application of sulfochlorinated derivatives of calix[n]arenes in the synthesis of star-shaped poly(2-alkyl-2-oxazolines) and poly(2-alkyl-2-oxazines) with a well-defined architecture and specified characteristics.

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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.2022.03.031.

References

1 (*a*) O. Sedlacek, B. D. Monnery, S. K. Filippov, R. Hoogenboom and M. Hruby, *Macromol. Rapid Commun.*, 2012, **33**, 1648; (*b*) Z. Varanaraja, J. Kim and C. R. Becer, *Eur. Polym. J.*, 2021, **147**, 110299.

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

3 (*a*) I. R. Knyazeva, T. P. Gerasimova, I. E. Kolesnikov, V. V. Syakaev, S. A. Katsyuba and A. R. Burilov, *Mendeleev Commun.*, 2020, **30**, 650; (*b*) A. M. Kulakova and M. G. Khrenova, *Mendeleev Commun.*, 2021, **31**, 185; (*c*) A. E. Putkov, A. N. Vasiliev, Ya. V. Zubavichus, Yu. A. Teterin, K. E. Ivanov, A. L. Trigub, V. V. Kovalev and I. M. Vatsouro, *Mendeleev Commun.*, 2021, **31**, 188.

4 C. D. Gutsche and R. Muthukrishnan, *J. Org. Chem.*, 1978, **43**, 4905.

5 (*a*) S. Shinkai, S. Mori, H. Koreishi, T. Tsubaki and O. Manabe, *J. Am. Chem. Soc.*, 1986, **108**, 2409; (*b*) A. V. Tenkovtsev, M. M. Dudkina, L. I. Scherbinskaya, V. Aseyev and H. Tenhu, *Polymer*, 2010, **51**, 3108; (*c*) 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.

6 (*a*) 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); (*b*) A. N. Blokhin, A. B. Razina, M. P. Kurlykin, A. V. Kashina and A. V. Tenkovtsev, *Mendeleev Commun.*, 2020, **30**, 799.

7 V. Percec, T. K. Bera, B. B. De, Y. Sanai, J. Smith, M. N. Holerca, B. Barboiu, R. B. Grubbs and J. M. J. Fréchet, *J. Org. Chem.*, 2001, **66**, 2104.

8 M. Vergaelen, B. Verbraeken, B. D. Monnery and R. Hoogenboom, *ACS Macro Lett.*, 2015, **4**, 825.

9 G. W. Nederbragt and C. A. Reilly, *J. Chem. Phys.*, 1956, **24**, 1110.

10 (*a*) J. K. Young, W. H. Graham, D. J. Beard and R. P. Hicks, *Biopolymers*, 1992, **32**, 1061; (*b*) N. K. Sharma, M. Singh and A. Bhattarai, *RSC Adv.*, 2016, **6**, 90607.

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