New Route to Synthesis of Cyclic Polystyrenes Using Controlled Free Radical Polymerization

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ABSTRACT: The synthesis of heterotelechelic polystyrene chains containing α-hydroxy-ω-carboxy end groups and their intramolecular cyclization are described. The controlled free radical polymerization of styrene was carried out using 4,4′-azobis(4-cyanovaleric acid) as the initiator and 4-hydroxy-TEMPO as the terminator, to generate difunctional macromolecules with molar masses in the range 1−10 kg mol^{-1}. The cyclization reaction is clearly evidenced by infrared spectrometry and size exclusion chromatography (SEC). In addition, matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry and liquid chromatography at the exclusion−adsorption transition point (LC PEAT) analyses were successfully applied. The yield of low molar mass (1 kg mol^{-1}) macrocycles was close to 95%. For higher molar masses, polycondensate byproducts and nonfunctionalized chains due to styrene thermal initiation reduce the cyclization efficiency.

Introduction

Cyclic polymers have attracted considerable attention because of their special properties that result from the topological constraints inherent in their architecture. Synthesis of well-defined macrocyclic polymers has been reported by several research groups.[1,2] Two main techniques are generally used for synthesizing cyclic polymers. One consists of bimolecular cyclization between a living α,ω-dicarbanionic polymer and a difunctional electrophile compound under extreme dilution. This method has been used to prepare cyclic polystyrenes[3−8] by coupling a living polystyryl dianion with difunctional electrophile such as dibromo-*p*-xylene, dichlorodimethylsilane, and 1,3-bis(1-phenylethylenyl)benzene. The other strategy is based on the intramolecular cyclization of a linear α,ω-heterodifunctional polymer and is called "unimolecular cyclization". Deffieux et al.[9−11] prepared α-styrenyl-ω-acetal heterodifunctional poly(chloroethyl vinyl ether) and polystyrene by living polymerizations and closed the ring in the presence of a Lewis acid. Kubo et al.[12,13] prepared cyclic polystyrene using α-carboxyl-ω-amino heterodifunctional linear precursor. The cyclization was carried out using 1-methyl-2-chloropyridinium iodide as the coupling agent. Mizawa et al.[14] described the synthesis of heterotelechelic poly(methyl methacrylate) containing α-maleimide-ω-dienyl end groups and its intramolecular cyclization via a Diels−Alder reaction. Traditionally, such well-defined structures are only available from living techniques such as anionic polymerization which requires highy-purity conditions (reactants and solvent purifications and use of high-vacuum techniques). In the past decade, a number of systems based on reversible termination of growing radicals have been reported[15−17] in order to control the free radical polymerization process. Nitroxide-mediated living radical polymerization[18,19] is the most extensively studied system and enables polymers with well-controlled structures such as block[20] or random[21] copolymers, end-functionalized,[22] multistar,[23] and hyperbranched[23] polymers to be synthesized under mild conditions and without the need for stringent purification of chemicals and protection of the functional groups.

This paper reports the synthesis of heterotelechelic polystyrene chains using controlled free radical polymerization via functional initiator and nitroxide and its cyclization by intramolecular esterification reaction. The latter reaction is followed by infrared spectrometry, and the products are characterized by several techniques such as SEC, liquid chromatography at the exclusion−adsorption transition point (LC PEAT), and MALDI-TOF mass spectrometry.

Experimental Section

Materials. Styrene (Aldrich, 99%) was distilled from CaH_2 under reduced pressure. Dichloromethane (CH_2Cl_2, SDS, 99.9%) was distilled from CaH_2 and triethylamine (Acros, 99%) from BaO under a nitrogen atmosphere. Other reagents, *N*,*N*-dimethylformamide (DMF, Acros, 99.5%), 4-hydroxy-2,2,6,6-tetramethylpiperidinyloxyl (4-hydroxy-TEMPO, Acros, >97%), 4,4′-azobis(4-cyanovaleric acid) (Acros, 97%), and 2-chloro-1-methylpyridinium iodide (Acros, 97%), were used as received.

Synthesis of Linear Polystyrene Chains. A mixture of 4,4′-azobis(4-cyanovaleric acid) (280 mg, 1 mmol), 4-hydroxy-TEMPO (224 mg, 1.3 mmol), styrene (20 mL, 174 mmol), and DMF (0.5 mL) was degassed for 15 min under nitrogen and then heated at 125 °C under nitrogen for 5h20. The viscous reaction mixture was then dissolved in CH_2Cl_2, precipitated into methanol, and dried to obtain 10.5 g of the desired polymer as a white solid (M_n = 9000 g mol^{-1}, PDI = 1.2, conversion 59%, sample PS4).

Cyclization Reaction. The α-hydroxy-ω-carboxyl heterodifunctional polystyrene (300 mg, M_n = 1 kg mol^{-1}, $M_{plinear}$ = 1400 g mol^{-1}, sample PS1) was dissolved in freshly distilled CH_2Cl_2 (50 mL), poured in a dropping funnel, and added dropwise (over 4 h) to a large volume of CH_2Cl_2 (150 mL) containing 2-chloro-1-methylpyridinium iodide (383 mg, 1.5 mmol) and triethylamine (303 mg, 3 mmol) maintained at reflux under rapid stirring. After the addition was complete, the system was allowed to react for an additional 12 h at 40 °C. Then, the mixture was concentrated to 50 mL, washed with dilute aqueous hydrochloric acid, dried over anhydrous sulfate magnesium, and placed under reduced atmosphere to remove the solvent. The residue was charged on a silica gel column using ethyl acetate an eluent. The first band was collected to give PS as a white solid (200 mg, $M_{pcyclic}$ = 980 g mol^{-1}, $\langle G \rangle = M_{pcyclic}/M_{plinear}$ = 0.71, polycondensates: <5%).

Size Exclusion Chromatography (Refractive Index and Viscometry Detectors). SEC was performed using a

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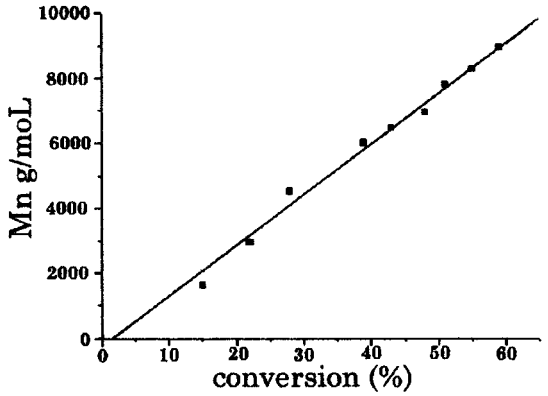


Figure 1. M_n vs conversion for polymerization of styrene at 125 °C; [initiator] = 4.8×10^{-2} mol L^{-1}, [nitroxide]/[initiator] = 1.3.

Waters apparatus working at 30 °C with tetrahydrofuran eluent at a flow rate of 1 mL min^{-1} and equipped with three columns Shodex (exclusion limit: 2×10^4, 4×10^5, and 4×10^6 g mol^{-1}). Differential refractive index (Viscotek) and viscometry (Viscotek DM 400) detectors were used, and molar masses were determined from a calibration curve based on linear polystyrene standards.

Infrared Characterization. Infrared spectra were recorded on IRFT 45 Bruker spectrometer. A solution of polystyrene in CH_2Cl_2 was deposited on a NaCl pellet, and the polymer was analyzed after evaporation of the solvent.

HPLC Equipment. LC PEAT experiments were carried out on a modular HPLC system constituted of a Varian 9002 model pump. An ultraviolet spectrophotometric detector (Jasco UV-975) working at 261 nm was used.

Analytical Chromatography. The flow rate was 1 mL min^{-1} at 25 °C. A Nucleosil silica column, dimension 250 × 4.6 mm, filled with particles of 5 μm size and porosity of 100 Å was used. The eluent was THF/hexane (48/52 wt %)

Semipreparative Chromatography. The flow rate was 15 mL min^{-1} at 25 °C. A Kromasil silica column, dimension 250 × 20 mm, was used filled with particles of 5 μm size and porosity of 100 Å. The eluent was THF/hexane (50.5/49.5 wt %).

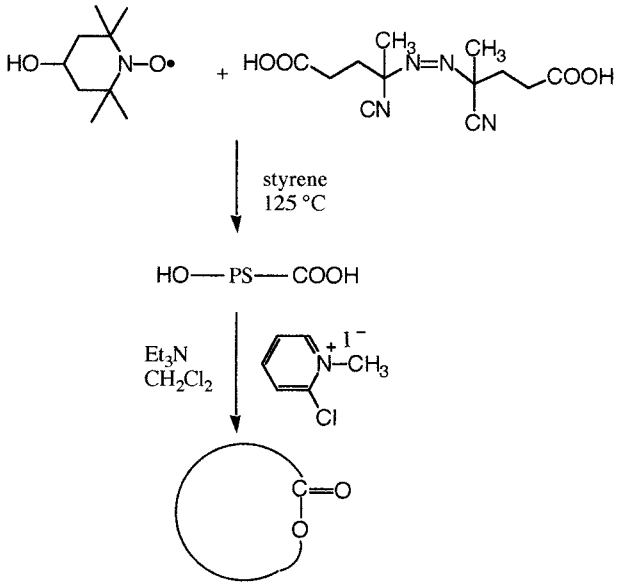
MALDI-TOF Mass Spectrometry. MALDI-TOF mass spectrometry was performed using a PerSeptive Biosystems Voyager Elite time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm), a delayed extraction, and a reflector. The MALDI mass spectra represent averages over 256 laser shots. This instrument operated at an accelerating potential of 20 kV in both linear and reflector modes.

The polymer solutions (2−5 g L^{-1}) were prepared in THF. The matrix 2,5-dihydroxybenzoic acid was dissolved in THF (15 g L^{-1}). The polymer solution (10 μL) was mixed with 50 μL of the matrix solution. A 1 μL portion of the final solution was deposited onto the sample target and allowed to dry in air at room temperature. Internal standards (peptides or porphyrin derivatives) were used to calibrate the mass scale using the two-point calibration software 3.07.1 from PerSeptive Biosystems.

Results and Discussion

Synthesis of α-Hydroxy-ω-carboxyl Heterodifunctional Polystyrenes. Linear heterodifunctional polystyrenes were obtained in one step by nitroxide-mediated "living" radical polymerization. The polymerization was initiated by the 4,4′-azobis(4-cyanovaleric acid) and controlled by the 4-hydroxy-TEMPO. To solubilize the initiator in styrene, the polymerization was performed in the presence of 5 wt % of DMF at 125 °C. The [nitroxide]/[initiator] ratio was equal to 1.3. A linear increase of molar mass with monomer conversion (Figure 1) was observed, showing the lack of chain transfer. A linear increase of $\ln(M_0/M)$ with conversion

Scheme 1. General Pathway for Synthesis of Cyclic Polystyrenes



is also observed. These two observations together with low polydispersity index (around 1.2) show the "living" nature of the polymerization. To obtain samples with molar masses ranging from 1 to 10 kg mol^{-1}, several polymerizations were performed using the same conditions and stopped at different times.

The advantage of this method is that the linear precursor was obtained in only one step by controlled radical polymerization without chemical purification (only O_2 elimination) vs the usual multisteps procedure by ionic polymerization.

Cyclization Reactions. Cyclization by end-to-end coupling was performed in a completely separate stage by esterification. The equimolar reaction of carboxylic acids and alcohols with 1-methyl-2-halopyridinium salt in the presence of two equimolar amounts of tri-*n*-butylamine previously afforded the corresponding carboxylic ester in good yield.[12,13,24] Scheme 1 shows the general pathway used here for the synthesis of macrocycles.

To reduce the concentration of active groups, the solution of linear polystyrene was added dropwise to a volume of CH_2Cl_2 containing the condensing agent (2-chloro-1-methylpyridinium iodide) and triethylamine. This procedure should favor intramolecular reaction cyclization over intermolecular reactions (polycondensation). The reaction between the polymer end groups was followed by infrared spectrometry (disappearance of absorbance of C═O band (acid) at 1713 cm^{-1} and the appearance of a new band C═O (ester) at 1731 cm^{-1}) as shown in Figure 2.

The cyclization was further confirmed by the reduction of the hydrodynamic volume as shown by the increase of the SEC elution volume. Table 1 summarizes the main features of the linear and cyclic polystyrene samples.

The SEC curves of the lowest molar mass (PS 1, M_n = 1 kg mol^{-1}) linear precursor and corresponding product obtained after cyclization without any fractionation procedure are shown in Figure 3. The ratio $\langle G \rangle$ of the apparent peak molar mass of cyclic and linear polystyrene is equal to 0.71, which is now considered as a proof of the efficiency of cyclization reaction instead of viscosimetric measurements.[2]

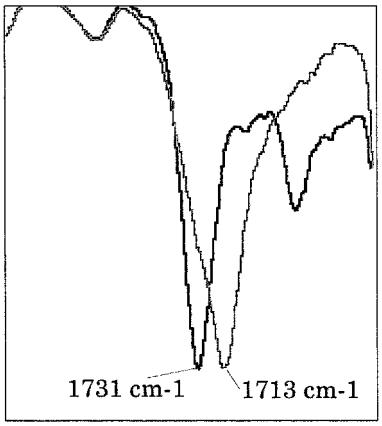


Figure 2. IR spectra of linear precursor (acid band, 1713 cm^{-1}) and cyclization product (ester band, 1731 cm^{-1}).

Table 1. SEC Data for Linear and Macrocyclic Polystyrenes

samle	$M_{nlinear}$ (kg mol^{-1})	$\langle G \rangle^a$	% higher molar mass products[b]
PS1	1	0.71	<5
PS2	3.3	0.89	16
PS3	4	0.9	17
PS4	9	0.9	37

[a] $\langle G \rangle = M_{plinear}/M_{pcyclic}$. [b] % higher molar mass products obtained by deconvolution of chromatograms.

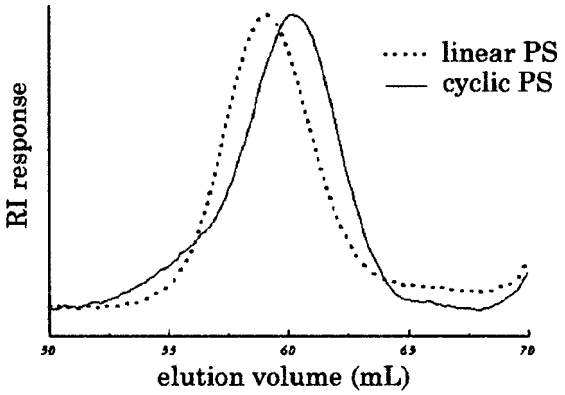


Figure 3. SEC chromatograms of linear polystyrene (sample PS1, M_n = 1 kg mol^{-1}) and its crude cyclization product.

Furthermore, as can be seen in the SEC chromatogram, polycondensates are formed in very small proportions (only a small shoulder in the high molar mass region). The yield of macrocyclic polystyrenes is as high as 95%. In addition, the cyclization reaction was also confirmed by MALDI-TOF mass spectrometry by analysis of the linear precursor and cyclization product. It was previously demonstrated[25] that the best conditions for the analysis of polystyrene chains containing a TEMPO-based alkoxyamine end group used 2,5-dihydroxybenzoic acid as the matrix without added salt; a protonation of the alkoxyamine functionality occurs. The MALDI spectra of linear precursor and cyclization product are presented in Figure 4. The spacing between the peaks is 104 g, corresponding to the molar mass of the styrene unit.

Both spectra present a major distribution, the calculated and the experimental mass numbers being in very good agreement (Table 2). The MALDI spectrum of the linear precursor corresponds to the proposed chemical structure (HOOC−(styrene)$_n$−OH, H^+) and that of cyclization product to (−OC−(styrene)$_n$−O−, H^+). The

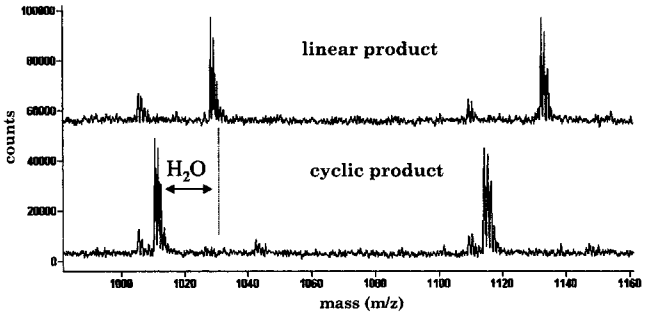


Figure 4. MALDI-TOF spectra of linear precursor and cyclization product (sample PS 1, M_n = 1 kg mol^{-1}).

Table 2. MALDI-TOF Experimental and Theorical Molar Masses of Protonated Polystyrenes

av molar mass peak for exptl series	assumed structure	calcd molar mass peak av
1028.4	HO−(styrene)$_n$−COOH, H^+	1028.4
1010.4	O−(styrene)$_n$−CO, H^+	1010.5

cyclization reaction is supported by the gap of 18 g (elimination of H_2O during esterification reaction) between these two series. The minor distribution present on the two spectra is attributed to thermally self-initiated chains[25,26] and controlled with 4-hydroxy-TEMPO.

For polystyrene samples with higher molar masses (PS2 to PS4), the ratio $\langle G \rangle$ increases (equal to 0.9), indicating the presence of noncyclized chains. Since the reaction involving the acid function is quantitative, there must be non- and/or monofunctionalized chains due to the thermally initiated autopolymerization of styrene[27] for longer reaction times. These chains are formed according to the Mayo mechanism which involves a reaction between a Diels−Alder styrene dimer and a molecule of styrene,[26] leading to the initiating radicals. These thermally self-initiated chains can be formed by irreversible termination (essentially combination in the case of styrene) and by reversible termination (reaction with 4-hydroxy-TEMPO). This effect in combination with the influence of molar mass (formation of polycondensates byproducts) reduces the efficiency of the cyclization reaction. To obtain further information about the composition of linear and cyclic products, the samples were analyzed by LC PEAT.

Liquid Chromatography at the Exclusion−Adsorption Transition Point (LC PEAT) Characterizations. At the critical point of adsorption, the molar mass distribution does not contribute to retention and behaves chromatographically "invisible". Separation is directed by the heterogeneities of polymeric chains including functional end groups,[28] molecular composition,[29] and architecture.[30] Gorbunov et al.[31] have studied the theoritical aspect of separation of linear and cyclic products with the same chemical structure. In their study, the macrocycles are eluted later than linear analogues. The critical conditions for polystyrene were previously reported[32] using a silica stationary phase and a mixture of THF/hexane (48/52 wt %) as eluent. The retention time of polystyrene standard in these conditions is 3.46 min. In the case of eluent containing more than 48% THF, the retention time decreases with increasing polystyrene molar mass, indicating the exclusion mode. For eluents containing less than 48% THF, the retention time increases with increasing molar mass according to an adsorption mode. Between these

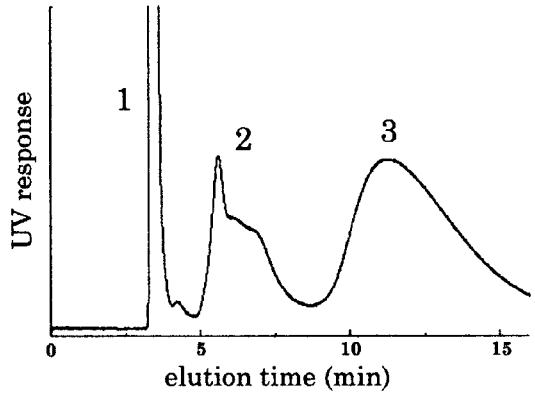


Figure 5. Critical chromatogram of linear precursor (sample PS3, $M_n = 4$ kg mol^{-1}).

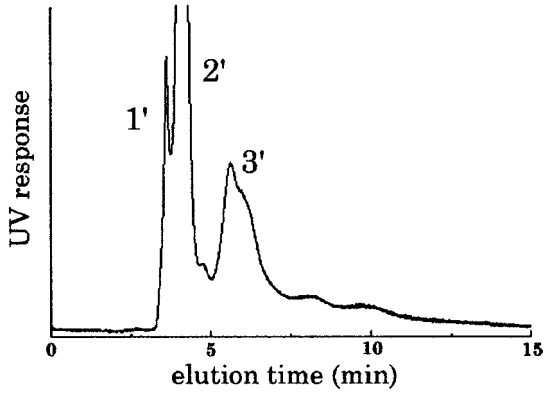


Figure 6. Critical chromatogram of crude cyclization product (sample PS3, $M_n = 4$ kg mol^{-1}).

two modes, for 48/52 wt % THF/hexane, the polystyrene standards elute at the same time whatever their molar masses, in accordance with the "critical conditions". Liquid chromatography at PTEA can thus yield interesting information on composition (functionality) and architecture of polymer samples.

The "critical chromatogram" of the linear polystyrene PS3 exhibiting a molar mass of 4 kg mol^{-1} is shown in Figure 5. As can be observed, several elution regions are present.

The first peak ((1), 3.46 min) corresponds to nonfunctionalized polystyrene chains as the retention time is similar to that of the polystyrene standard used for calibration. These chains are attributed to thermally self-initiated styrene polymerization which cannot be avoided at high temperature (125 °C).

The medium elution time products ((2), 5−9 min) can be compared with previous analyses using the same conditions on monofunctional chain[33] (polystyrene functionalized with hydroxyl groups). These products probably arise from styrene thermal initiation and contain 4-hydroxy-TEMPO chain ends.

The higher elution time products ((3), 9−16 min) correspond to the expected α-hydroxy-ω-carboxyl polystyrene chains. The high polarity of the carboxylic groups yields strong interactions with the silica surface and leads to the formation of large peaks.

The crude cyclization product was then analyzed using the same conditions. The critical chromatogram is shown in Figure 6.

The first peak obtained at 3.46 min ((1′)) is attributed to the residual linear nonfunctionalized chains unable

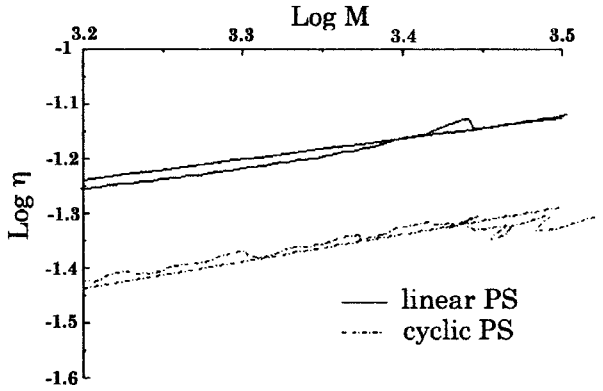


Figure 7. Intrinsic viscosities of linear and of cyclic polystyrenes as a function of molar mass.

to lead to cyclic material. The major product ((2′), 4 min) corresponds to the cyclized polymer chains since the ester function is less polar than the hydroxyl and acidic functions; this product makes few interactions with silica column and is eluted close to the nonfunctionalized chains. The last peak ((3′), 5−7 min) can be attributed to monofunctionalized chains and polycondensate byproducts. The major peak present in the linear precursor analysis ((3), 9−16 min) has disappeared, which confirms its former assignment. LC PEAT separates products according to their functionalities and architecture. In our study, cyclic products are eluted earlier than linear ones in opposition with the theoretical study of Gorbunov[31] due to polarity effects (different chemical functionality between linear and cyclic products).

To further confirm this, the two major peaks corresponding to the linear difunctional precursor ((3), 9−16 min) and cyclic product ((2′), 4 min) were fractionated using a semipreparative column. The viscosimetry of these two fractions was then measured by SEC (viscosimetry detector) in THF at 30 °C. Figure 7 shows the Mark−Houwink plot (log[η] vs log M). There are straight parallel lines and the ratio g' of the intrinsic viscosity of the macrocycles to that of the linear precursor with the same molar mass ($g' = [\eta]_C/[\eta]_L$) is close to 0.65, which is similar to previous results[34] and confirms the isolation of pure cyclic polystyrenes.

Further works on the synthesis of a linear precursor without thermal initiation (use of an alkoxyamine cleavable at lower temperature) and on the application of this method to other monomers are under investigation.

Conclusion

For the first time, macrocyclic polystyrenes with controlled dimensions and narrow distribution have been obtained using "living" radical polymerization. The advantage of this method is that the linear precursor is prepared in one step via nitroxide-mediated free radical polymerization with very simple experimental conditions compared to ionic processes (purification, high-vacuum techniques). The unimolecular cyclization was performed by esterification reaction. These products were accurately analyzed, using different analytical techniques. For a low molar mass precursor, macrocycles can be prepared quantitatively (95%). For higher molar masses, the yield decreases due to additional styrene thermal initiation at 125 °C. Despite its drawbacks, this simple method is as efficient as the traditional technique using anionic polymerization.

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