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Synthesis of Cyclic (Co)polymers by Atom Transfer Radical Cross-Coupling and Ring Expansion by Nitroxide-Mediated Polymerization

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ABSTRACT: A novel approach to prepare cyclic polymers via a combination of atom transfer radical polymerization (ATRP) and atom transfer radical cross-coupling (ATRC) is presented. A functional ATRP initiator possessing an alkoxyamine group was synthesized and used to prepare well-defined linear telechelic α-nitroxy,ω-bromo homo- and block copolymers via ATRP and subsequent thermal deprotection of the α-terminal nitroxide function. Cyclization reactions were achieved by intramolecular ATRC under high dilution. Ring expansion of a cyclic polystyrene alkoxyamine prepared by ATRC was conducted via nitroxide-mediated polymerization (NMP) of styrene and yielded a mixture of linear and cyclic polycondensates. This result is discussed in detail and explained by the persistent radical effect (PRE), thermal initiation, and the occurrence of radical crossover reactions during chain extension via NMP.

Introduction

Cyclic polymers are fascinating materials for physicists and theoreticians.[1,2] The absence of chain-ends imposes a topological restriction that results in a variety of physical properties that significantly distinguish macrocycles from their linear counterparts. For example, it has been shown that cyclic polymers have smaller hydrodynamic volumes and are less viscous than their linear analogues.[1,2] In addition, rheological studies of cyclic polymers, which cannot reptate in the conventional sense, due to a lack of chain-ends, could help improving the current understanding of the fundamentals of polymer chain dynamics.[3−5]

However, the synthesis of well-defined cyclic polymers is still a challenge in polymer science.[1,2] Cyclic polymers can be obtained in several different ways. Macrocycles can be directly recovered, as a more or less important fraction, in polymer systems exposed to ring−chain equilibria, or they can be synthesized using either ring expansion or ring closure of linear chains by end-to-end coupling.

Only few reports describe the formation of large rings by direct insertion of a monomer into a reactive cyclic precursor.[2] Although very attractive, this approach requires use of polymerization processes in which chain transfer and exchange reactions between active species are absent. One of the most striking examples of macrocycles synthesis by monomer insertion is the ring expansion of a cyclic carbene ruthenium complex by ring-opening metathesis polymerization (ROMP).[6−8]

The simplest and most appropriate methods for the synthesis of cyclic polymers, with controlled size and narrow molecular weight distribution (MWD), are based on the end-to-end chain coupling of α,ω-hetero-difunctional linear chains in highly dilute reaction conditions.[2] This approach offers several significant advantages over other approaches as it may be used both for polymers having in-chain reactive functions and for systems with no labile linkages in their backbone, such as saturated carbon−carbon bonds polymers. Since the macrocycle is directly obtained from the linear parent by ring closing, and the size of linking unit is negligible, this approach provides linear and cyclic structures with same molar mass. Moreover, the use of living polymerization techniques for the preparation of the linear precursors allows control of the molecular weight with narrow MWD. This is of special importance for direct comparison of the properties of materials consisting of linear or cyclic chains.

Such an approach has been applied to controlled radical polymerization (CRP).[9] A strategy to prepare macrocycles via the combination of atom transfer radical polymerization (ATRP)[10−13] and click chemistry[14−16] was recently reported.[17] Linear PSt precursors were prepared by ATRP of St, using propargyl 2-bromoisobutyrate, as an initiator, followed by nucleophilic substitution of the terminal bromine atom by an azido group.[18] The cyclization reaction was conducted under high dilution conditions, with Cu^{I}/L complexes as catalyst. The functionalization and the cyclization were essentially quantitative, eliminating the need for purification. This approach was subsequently extended to the synthesis of cyclic poly(*N*-isopropylacrylamide)[19] (PNIPAM) and cyclic poly(methyl acrylate)-*b*-polystyrene (PMA-*b*-PSt) block copolymers.[20] However, in the latter case, the alkyne moiety of the ATRP initiator had to be protected with a trimethylsilyl group, which added an additional deprotection step to the synthesis. Recently, reversible addition−fragmentation chain transfer (RAFT) polymerization[21,22] and nitroxide-mediated radical polymerization (NMP)[23,24] were also combined with Huisgen 1,3-dipolar cycloaddition reaction to prepare cyclic PNIPAM[25] and PSt.[26−28]

Click reactions are perfectly suited for the preparation of cyclic polymers, due to the near-quantitative yields and high selectivity, even in the presence of other functional groups. However, the synthesis of cyclic polymers via a combination of CRP and azide−alkyne click coupling always requires one or two post-polymerization functionalization steps in order to introduce the reactive chain-end groups. Therefore, the search for a synthetic route that would lead to well-defined cyclic polymers in high

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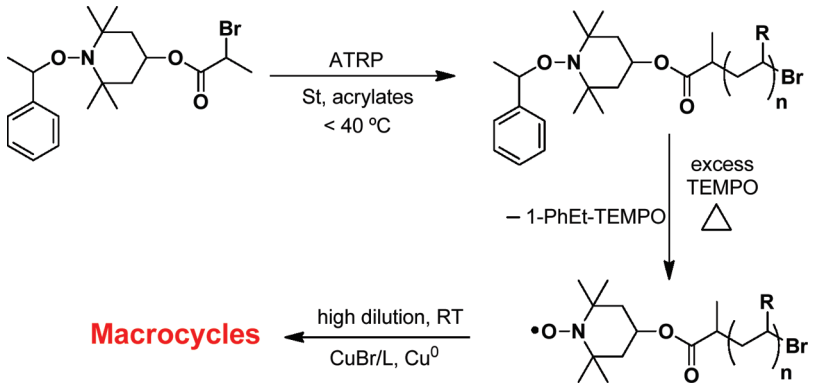
Scheme 1. Synthesis of Cyclic Polymers via a Combination of ATRP and ATRC



yields, without postpolymerization functionalization, or with a single, simple, deprotection step before the cyclization, is still ongoing.

In the present work, we introduce a novel approach to prepare cyclic polymers via a combination of ATRP and atom transfer radical cross-coupling (ATRC)[29,30] (Scheme 1). Linear telechelic α-nitroxy-ω-bromo precursors were prepared via ATRP at relatively low temperature, using an initiator bearing an alkoxyamine group, followed by thermal deprotection of the nitroxide function. Cyclization reactions were subsequently achieved by intramolecular ATRC, under high dilution conditions. Well-defined cyclic PMA, PSt, and cyclic PMA-*b*-PSt block copolymer were prepared using this approach.

Experimental Section

Materials. Methyl acrylate (MA, 99%) and styrene (St, 99%) were purchased from Aldrich and purified by passing through a column filled with basic alumina to remove inhibitors or antioxidants. Dichloromethane was distilled from calcium hydride. 4-Hydroxy-TEMPO was received from NOVA Molecular Technologies Inc. Tris(2-pyridylmethyl)amine (TPMA) was purchased from ATRP Solutions. All other reagents, including (1-bromoethyl)benzene, 2-bromopropionyl bromide, Cu^0 powder (75 μm), CuBr, $CuBr_2$, *N,N,N′,N″,N″*-pentamethyldiethylenetriamine (PMDETA), pyridine, and 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO), and solvents were purchased from Aldrich with the highest purity available and used as received without further purification.

Analyses. NMR spectra were recorded on a Bruker instrument operating at 300 MHz. Monomer conversions were determined by ^{1}H NMR. MW and MWD were determined by size exclusion chromatography (SEC). The SEC analysis was conducted with a Waters 515 pump and Waters 410 differential refractometer using Polymer Standards Services (PSS) columns (Styrogel 10^5, 10^3, and 10^2 Å) in THF as eluent at 35 °C and at a flow rate of 1 mL/min. The apparent MW ($M_{n,SEC}$ and $M_{w,SEC}$) and M_w/M_n values were determined with a calibration based on polystyrene (PSt) standards. Mass spectral data were acquired using a PerSeptive Voyager STR MS matrix-assisted laser desorption ionization (MALDI) time-of-flight (TOF) mass spectrometer using the reflection positive ion mode. Dithranol was used as the matrix, and silver trifluoroacetate as the cation source. The relaxation delay was set to 450 ns, with an acceleration voltage of 20 kV.

Synthesis of the 1-Phenylethylhydroxy-TEMPO Alkoxyamine (1-(1-Phenylethoxy)-2,2,6,6-tetramethylpiperidin-4-ol), 3. A Schlenk flask was charged with hydroxy-TEMPO (7.89 g, 45.8 mmol), copper powder (11.6 g, 183 mmol), copper bromide (52.5 mg, 0.366 mmol), and 50 mL of anisole. The solution was degassed by bubbling with nitrogen for 30 min, and then PMDETA (76.6 μL, 0.366 mmol) was added. After 5 min, (1-bromoethyl)benzene (5 mL, 36.6 mmol) was added, and the solution was then heated to 40 °C for 18 h. The solution was filtered and concentrated under vacuum. The crude product was purified by column chromatography eluting with hexane/ethyl acetate (95/5 gradually increasing to 5/5) to afford 8.15 g (yield = 80.2%) of a white solid. ^{1}H NMR ($CDCl_3$) δ: 7.38−7.00 (m, 5H), 4.80 (q, 1H, J = 5.54 Hz), 4.05−3.88 (m, 1H), 1.87 (td, 1H, J_d = 10.2 Hz, J_t = 3.2 Hz), 1.74 (td, 1H, J_d = 10.3 Hz, J_t = 3.2 Hz), 1.58−1.39 (m, 2H), 1.52 (d, 3H, J = 5.63 Hz), 1.36 (s, 3H), 1.25 (s, 3H), 1.11 (s, 3H), 0.71 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 145.60, 128.19, 127.08, 126.80, 83.44, 63.47, 60.35, 60.14, 49.07, 48.97, 34.60, 34.28, 23.49, 21.40.

Synthesis of the 2-Bromopropionate Alkoxyamine, 4. 1-Phenylethylhydroxy-TEMPO alkoxyamine (**3**) (3 g, 10.8 mmol) and pyridine (1.26 mL, 15.5 mmol) were dissolved in dry dichloromethane (17.5 mL). The reaction mixture was cooled in an ice−water bath, and a solution of 2-bromopropionyl bromide (1.42 mL, 13.5 mmol) in dry dichloromethane (7.5 mL) was slowly added while stirring. The mixture was stirred in the cooling bath for 1 h and then at room temperature for 16 h. The excess 2-bromo-2-methylpropionyl bromide was neutralized with 0.2 mL of water, and the reaction mixture was then poured into a solution of hydrochloric acid (100 mL, 0.3 M). The organic layer was washed with a solution of sodium hydroxide (100 mL, 0.3 M), dried over magnesium sulfate, and concentrated under vacuum. The product was purified by flash column chromatography on basic alumina using THF as solvent to afford 4.460 g (quantitative yield) of yellow oil. ^{1}H NMR ($CDCl_3$) δ: 7.37−7.17 (m, 5H), 5.11−4.96 (m, 1H), 4.78 (q, 1H, J = 5.58 Hz), 4.31 (q, 1H, J = 5.74 Hz), 1.97−1.83 (m, 2H), 1.80 (d, 3H, J = 5.78 Hz), 1.70−1.54 (m, 2H), 1.49 (d, 3H, J = 5.48 Hz), 1.35 (s, 3H), 1.27 (s, 3H), 1.13 (s, 3H), 0.68 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 169.97, 145.41; 128.23, 127.18, 126.84, 83.55, 68.86, 60.08, 44.38, 44.15, 40.58, 34.50, 34.19, 23.37, 21.70, 21.24.

General Procedure for the ATRP of MA and St with the 2-Bromopropionate Alkoxyamine 4 or a PMA Macroinitiator. In a typical experiment, CuBr (71.7 mg, 0.5 mmol) and $CuBr_2$ (11.2 mg, 0.05 mmol) were charged to a flask. The flask was deoxygenated by purging with N_2 for 30 min. Deoxygenated acetone (3.25 mL) and PMDETA (115 μL, 0.55 mmol) were added. After 5 min, deoxygenated methyl acrylate (6.5 mL, 72 mmol) and 2-bromopropionate alkoxyamine, **4** (412 mg, 1 mmol), were added. An initial sample was taken, and then the flask was placed in an oil bath thermostated at 40 °C for 20.5 h. The polymerization was stopped via exposure to air and dilution in THF (M_n = 2620, M_w/M_n = 1.09, conversion = 38.0%).

General Procedure for the Synthesis of α-Nitroxy-ω-Bromo PMA, PSt, and PMA-*b*-PSt. In a typical experiment, TEMPO (6.25 g, 40 mmol), α-aminooxy-ω-bromo PMA (1.05 g, 0.4 mmol, M_n = 2620, M_w/M_n = 1.09), and anisole (15 mL) were charged to a 25 mL Schlenk flask and bubbled with nitrogen for 30 min. The flask was then placed in an oil bath thermostated at 120 °C for 3 h. The polymer was purified by precipitation into isopropanol cooled with dry ice (M_n = 2540; M_w/M_n = 1.06).

Scheme 2. Synthesis of the 2-Bromopropionate Alkoxyamine Initiator, 4

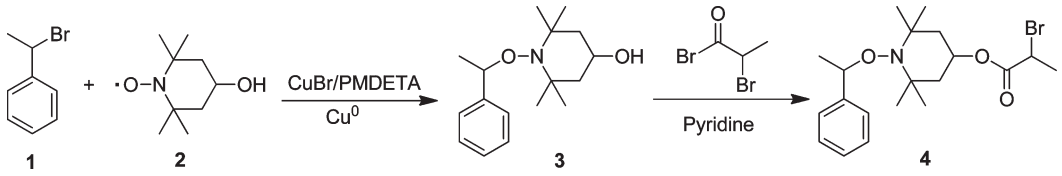


Table 1. ATRP of MA and St with the 2-Bromopropionate Alkoxyamine 4 and Synthesis of α-Nitroxy-ω-bromo and Cyclic (Co)polymers

entry	M/I/CuBr/$CuBr_2$/L	conv (%)	$M_{n,th}$	$M_{n,SEC}$; M_w/M_n	$M_{n,SEC}$; M_w/M_n after deprotection	$M_{n,SEC}$; M_w/M_n after cyclization
1[a]	72/1/0.5/0.05/0.55	38	2790	2620; 1.09	2540; 1.06	1850; 1.07
2[b]	131/1/0.75/0.25/1	18.8	2990	3200; 1.10	3030; 1.09	2580; 1.24
3[c]	262/1/0.75/0.25/1	4.8	3930	3670; 1.07	3530; 1.07	2900; 1.12

[a] M/I/L = MA/**4**/PMDETA, MA/acetone = 2/1 v/v, 40 °C, 20.5 h. [b] M/I/L = St/**4**/TPMA, St/anisole = 2/1 v/v, 40 °C, 220 min. [c] M/I/L = St/PMA (from entry 1)/TPMA, St/anisole/acetone = 2/2/1 v/v/v, 40 °C, 360 min.

General Procedure for the Synthesis of Cyclic PMA, PSt, and PMA-*b*-PSt. In a typical experiment, CuBr (28.7 mg, 0.2 mmol), TPMA (58.1 mg, 0.2 mmol), and Cu^0 (31.8 mg, 0.5 mmol) were charged to a flask. The flask was deoxygenated by purging with N_2 for 30 min, and then deoxygenated acetone (30 mL) was introduced. The contents of the flask were stirred for 15 min, and then a solution of α-nitroxy-ω-bromo PMA (2,540, 50.8 mg, 0.02 mmol) in 20 mL of deoxygenated acetone was introduced over a period of 30 h. The solution was subsequently stirred for 5 h at RT. The solution was passed through a neutral alumina column to remove the copper catalyst and concentrated under vacuum, and the resulting polymer was analyzed by SEC without any additional treatment (M_n = 1850; M_w/M_n = 1.07).

General Procedure for the Ring Expansion of Cyclic PSt by NMP of St. In a typical experiment, cyclic PSt (22 mg, 0.01 mmol, M_n = 2200, M_w/M_n = 1.24) and deoxygenated St (0.6 mL, 5.24 mmol) were charged in a deoxygenated flask. The flask was placed in an oil bath thermostated at 125 °C for 10 h. The polymerization was stopped via immersion in an ice bath.

Results and Discussion

Synthesis of the 2-Bromopropionate Alkoxyamine Initiator, 4. An ATRP initiator carrying alkoxyamine and bromoester groups was prepared in two steps (Scheme 2). The first step was the synthesis of the 1-phenylethylhydroxy-TEMPO alkoxyamine (1-(1-phenyl-ethoxy)-2,2,6,6-tetramethylpiperidin-4-ol), **3**, in 80.2% yield, by an ATRC reaction between (2-bromoethyl)benzene, **1**, and 4-hydroxy-TEMPO, **2**. The 2-bromopropionate alkoxyamine, **4**, was obtained, in quantitative yield by condensation of **3** with 2-bromopropionyl bromide.

Synthesis of Cyclic PMA. The conditions for the ATRP of MA with the 2-bromopropionate alkoxyamine **4** were chosen to limit, as much as possible, termination events between propagating radicals, since any such reactions would affect the chain-end functionality of polymer chains. Therefore, 10% of Cu^{II}/L deactivator was initially introduced to limit the concentration of propagating radicals by shifting the ATRP equilibrium toward the dormant species and reducing the concentration of radicals in the system. In addition, to suppress the homolytic cleavage of the terminal alkoxyamine bond, a low reaction temperature (40 °C) was used, and the polymerization was stopped at relatively low conversion (38%) (Table 1).

The ATRP of MA, initiated by the 2-bromopropionate alkoxyamine **4**, was conducted in 33% acetone solution (v/v) at 40 °C with a ratio $[MA]_0/[\mathbf{4}]_0/[CuBr]_0/[CuBr_2]_0/[PMDETA]_0$ = 72/1/0.5/0.05/0.55 (Table 1). After 20.5 h, a well-defined PMA, with M_n = 2620 ($M_{n,th}$ = 2790) and M_w/M_n = 1.09, was obtained (Figure 1).

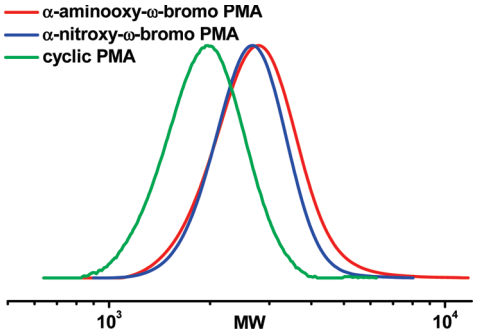


Figure 1. SEC traces of the α-aminooxy-ω-bromo PMA, the α-nitroxy-ω-bromo PMA obtained after deprotection of the alkoxyamine function, and the final cyclic PMA.

Deprotection of the nitroxide function was achieved by heating the α-aminooxy-ω-bromo PMA in anisole ([PMA] = 26.7 mmol/L), at 120 °C for 3 h, in the presence of 100 equiv of TEMPO. The deprotected PMA (M_n = 2540 and M_w/M_n = 1.06) was recovered by precipitation into cold (dry ice) isopropanol (Figure 1). The fact that deprotection of the nitroxide function had occurred was confirmed by MALDI-TOF analysis. A loss of mass 107.7 g/mol, corresponding to the terminal phenylethyl group plus a proton, was observed going from the α-aminooxy-ω-bromo PMA population to the α-nitroxy-ω-bromo PMA population (Figure 2). The isotopic pattern of the bromine atom could not be observed in the spectra, indicating that the bromine chain-end of the polymers was cleaved during the ionization process.

The telechelic PMA was subsequently cyclized by ATRC at RT under nitrogen atmosphere and high dilution conditions. A 20 mL deoxygenated solution of α-nitroxy-ω-bromo PMA (n = 0.02 mmol, M_n = 2540, M_w/M_n = 1.06) in acetone was introduced over a period of 30 h (0.67 mL/h) into a 30 mL deoxygenated solution of acetone containing 0.2 mmol of CuBr/TPMA complex and 0.5 mmol of Cu^0. After completion of the addition of the α-nitroxy-ω-bromo PMA solution, the resulting reaction mixture was stirred for an additional 5 h at RT. The SEC analysis of the polymer after reaction showed a decrease of the apparent molecular weight (M_n = 1850; M_w/M_n = 1.07) (Figure 1).

The ratio of the apparent molecular weights of the macrocyclic PMA and of its α-nitroxy-ω-bromo linear precursor is 0.73, in excellent agreement with the literature.[31,32] This result confirms the cyclic nature of the polymer obtained by intramolecular ATRC of the α-nitroxy-ω-bromo PMA, under high dilution conditions. Furthermore, the SEC trace

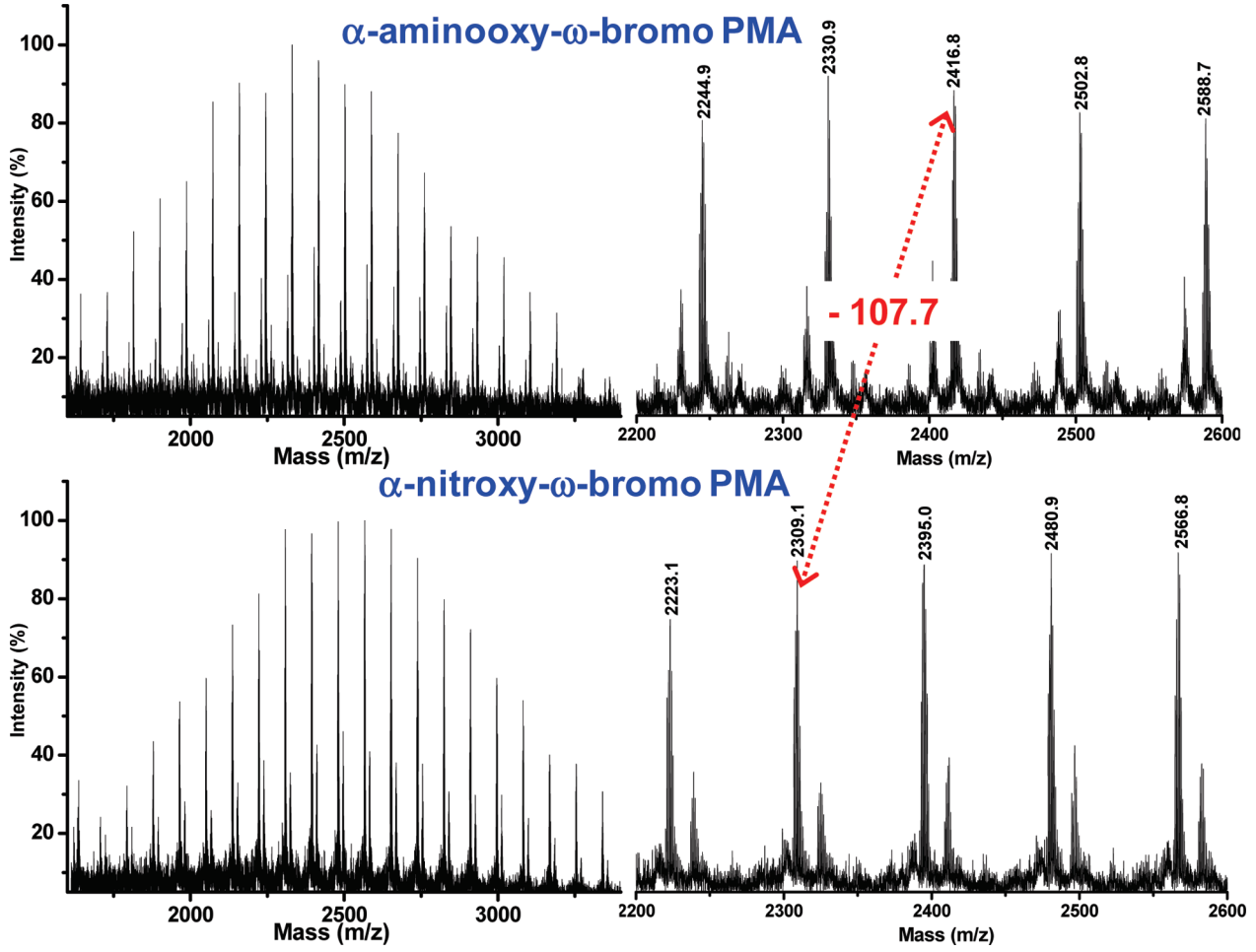


Figure 2. MALDI-TOF spectra of the α-aminooxy-*ω*-bromo PMA (top) and of the α-nitroxy,*ω*-bromo PMA (bottom) obtained after deprotection of the alkoxyamine.

of the final polymer does not show any tailing toward high molecular weight, indicating an essentially quantitative yield of the cyclic polymer via intramolecular process.

Synthesis of Cyclic PSt. The conditions for the ATRP of St were also selected to limit, as much as possible, termination events between propagating radicals (Table 1).

The ATRP of St, initiated by the 2-bromopropionate alkoxyamine **4**, yielded a well-defined PSt, with $M_n = 3200$ ($M_{nth} = 2990$) and $M_w/M_n = 1.10$ (Table 1 and Figure 3).

Deprotection of the nitroxide function was achieved by heating the α-aminooxy-*ω*-bromopolystyrene in anisole at 120 °C for 3 h, in the presence of 100 equiv of TEMPO. The deprotected PSt ($M_n = 3030$ and $M_w/M_n = 1.09$) was purified by three successive precipitations into cold (dry ice) isopropanol (Table 1).

The telechelic PSt was subsequently cyclized by ATRC at RT under nitrogen atmosphere and high dilution conditions. The SEC analyses of the polymers after reaction demonstrate a decrease of the apparent molecular weight, with $M_n = 2580$ ($M_w/M_n = 1.24$) (Table 1). The SEC trace of the final PSt shows the presence of higher molecular weight polymer, indicating that some intermolecular coupling occurred during the cyclization (estimated to be ~5% by deconvolution of the SEC trace) (Figure 3). The occurrence of intermolecular coupling under these conditions could indicate that the linear precursor was not perfectly functionalized. Chain-end functionality defects could result from the partial homolytic cleavage of the terminal C−Br bond during the deprotection of the α-aminooxy-*ω*-bromopolystyrene at 120 °C.

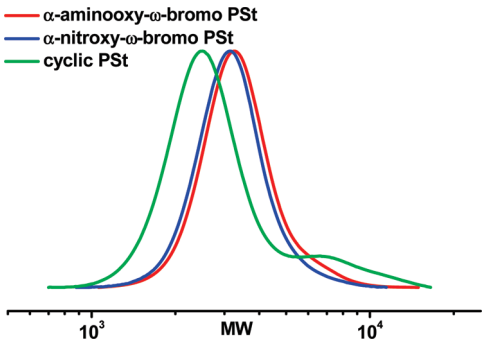


Figure 3. SEC traces of the α-aminooxy-*ω*-bromo PSt, the α-nitroxy-*ω*-bromo PSt obtained after deprotection of the alkoxyamine function, and the final cyclic PSt.

However, the ratio of the apparent molecular weights of the final PSt and of the α-nitroxy-*ω*-bromo linear precursor is 0.85, demonstrating that most of the final polymer chains were the product of intramolecular cyclization.[31,32]

Synthesis of Cyclic PMA-*b*-PSt. Diblock copolymers demonstrate a unique ability to self-assemble into complex nanoscale morphologies in bulk (e.g., lamellae, hexagonally packed cylinders, bicontinuous gyroids, and body-centered-cubic arrays of spheres) or in solution (e.g., micelle, vesicle, tube).[2,33−36] Cyclic block copolymers could self-assemble in new morphologies in solution or in bulk due to their unique topology.[2,36]

Cyclic PMA-*b*-PSt block copolymers were prepared in order to exemplify the wide range of cyclic polymers accessible via this new approach. A linear α-aminooxy-ω-bromo PMA (entry 1, Table 1), prepared with the 2-bromopropionate alkoxyamine **4**, was chain extended by ATRP of St to yield a well-defined PMA-*b*-PSt, with M_n = 3930 ($M_{n,th}$ = 3670) and M_w/M_n = 1.07 (entry 3, Table 1). The SEC chromatogram of the linear PMA-*b*-PSt block copolymer did not present any shoulder toward low molecular weight, indicating high initiation efficiency for the block extension from the PMA macroinitiator (MI) (Figure 4). Deprotection and cyclization of the resulting α-nitroxy-ω-bromo PMA-*b*-PSt copolymer were conducted under the same conditions as described for the homopolymers. The apparent MW of the cyclic block copolymer (M_n = 2900; M_w/M_n = 1.12) was significantly lower (M_n = 3530; M_w/M_n = 1.07) than that of its linear α-nitroxy-ω-bromo PMA-*b*-PSt precursor, confirming the efficient cyclization (Figure 4 and entry 3, Table 1). The SEC trace of the final PMA-*b*-PSt copolymer shows the presence of higher MW copolymer, indicating that a small fraction of the copolymer underwent intermolecular coupling during the cyclization reaction (estimated to be less than 2% by deconvolution of the SEC trace) (Figure 4).

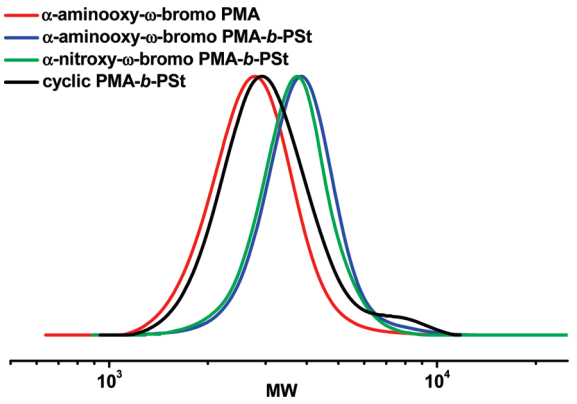


Figure 4. SEC traces of the α-aminooxy-ω-bromo PMA, the α-aminooxy-ω-bromo PMA-*b*-PSt, the α-nitroxy-ω-bromo PMA-*b*-PSt obtained after deprotection of the alkoxyamine function, and the final cyclic PMA-*b*-PSt.

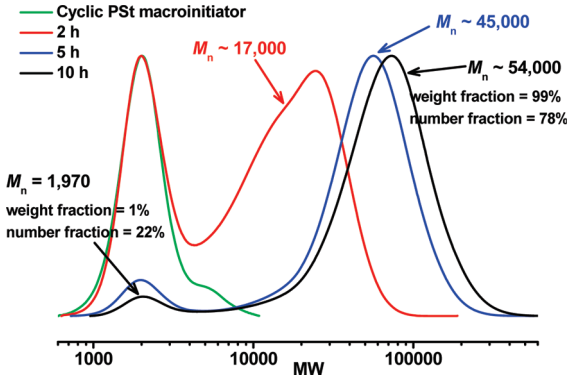


Figure 5. Evolution of SEC traces during the NMP of St with a cyclic PSt MI. Conditions: St/MI = 525, bulk, 125 °C, 10 h.

Ring Expansion of Cyclic PSt. The direct synthesis of well-defined cyclic polymers from cyclic initiators is an attractive route to cyclic polymers as it eliminates the need to prepare linear precursors. However, this approach requires cyclic initiators and polymerization processes in which chain transfer and exchange reactions between active species are absent. There have been only three reports in the literature regarding the synthesis of macrocycles by ring expansion of cyclic alkoxyamines.[28,37,38] These reports indicated difficulty associated with the preparation of well-defined macrocycles by NMP from cyclic alkoxyamines. Therefore, we were interested in conducting further studies on this process using macrocyclic alkoxyamines prepared by ATRC.

A macrocyclic polystyrene alkoxyamine (M_n = 2200; M_w/M_n = 1.24) was used as macroinitiator for the NMP of St. The polymerization was conducted in bulk over 10 h at 125 °C with an initial ratio [St]/[MI] = 525 (Figure 5 and Table 2). SEC analyses of the reaction medium during the NMP of St from the macrocyclic polystyrene alkoxyamine revealed the existence of two populations (Figure 5). A high MW population corresponding to a mixture of cyclic and linear polystyrene chains, with approximately three to four alkoxyamine functions per chain on average (Table 2). The high MW population peak shifts toward higher MW as the reaction progressed (Figure 5 and Table 2). In contrast, the peak corresponding to a low MW population does not shift as the reaction progressed and its relative intensity decreases with time (Figure 5 and Table 2). The low MW population corresponds to monocyclic PSt and to dead chains. Deconvolution of the final SEC curve (Figure 5, 10 h) indicates that the low and high MW populations represent approximately 22% and 78% of the total number of chains, respectively. This corresponds to a weight fraction of 1% for the low MW population and 99% for the high MW population.

These results are in good agreement with previous literature reports and confirm the challenges for ring expansion of cyclic (macro)alkoxyamines.[28,37,38]

Three phenomena, namely the PRE,[39,40] radical crossover reactions,[24,41] and styrene thermal self-initiation,[42,43] are responsible for the fact that ring expansion of (macro)cyclic alkoxyamine did not yield well-defined (mono)macrocycles but a mixture of cyclic and linear polyadducts. While styrene thermal self-initiation is specific to styrene, the PRE and radical crossover reaction are inherent to any NMP systems.

The persistent radical effect in NMP describes the variation of concentrations of growing (transient) and persistent (nitroxyl) radicals involved in this polymerization process.[39,40,44] At the early stages, a (small) fraction of the growing radicals R$^\bullet$ formed by dissociation of the unimolecular cyclic macroinitiator undergo radical−radical coupling. This leads, in the present case, to terminated PSt ($^\bullet$Y—RR—Y$^\bullet$ species) and loss of two growing radicals, R$^\bullet$ (Scheme 3). However, by its nature, the persistent radical, Y$^\bullet$, does not undergo coupling,

Table 2. Ring Expansion of Cyclic PSt by NMP of St[a]

time (h)	conv (%)	ln([M]$_0$/[M]$_t$)	$M_{n,th}$[b]	$M_{n,th\ cyclic}$[c]	$M_{n,SEC(low\ MW\ population)}$	$M_{n,SEC(high\ MW\ population)}$	$M_{n,SEC(high\ MW\ population)}/M_{n,th}$	$M_{n,SEC(high\ MW\ population)}/M_{n,th\ cyclic}$
0	0	0	2 200	1 650				
2	6.5	0.0673	5 750	4 310	1950	17 000	2.96	3.94
5	20.9	0.234	13 600	10 200	1920	45 000	3.30	4.41
10	31.5	0.378	19 400	14 500	1970	54 300	2.80	3.73

[a] [St]$_0$/[MI]$_0$ = 525, bulk, 125 °C, 10 h. [b] $M_{n,th}$ = [St]$_0$/[MI]$_0$ × 104.15 × conv + 2200; no correction made regarding the cyclic nature of the polymers. [c] $M_{n,th\ cyclic}$ corresponds to the theoretical apparent M_n that would be observed by SEC assuming a cyclic topology: $M_{n,th\ cyclic} = M_{n,th} \times 0.75$.

and its overall concentration should continuously increase. This increase of [Y•] is self-controlling since a higher concentration leads to more efficient formation of the dormant alkoxyamines R−Y and a decrease in the amount of radical−radical coupling (Scheme 3). Therefore, the persistent radical effect, which is a key feature to the nature of control in a NMP, breaks the stoichiometric balance between growing and persistent radicals (needed for preservation of cyclic structures).

The equilibrium concentration of propagating radicals can be easily calculated from the rate of polymerization (eq 1). This concentration was found to be equal to 4.55×10^{-9} mol/L, using a propagation rate constant of 2310 L mol^{-1} s^{-1} (pre-exponential factor of $10^{7.63}$ L mol s^{-1} and activation energy of 32.5 kJ mol^{-1})[45,46] for styrene at 125 °C.

$$R_p = \frac{-d[M]}{dt} = k_p[R^\bullet][M] \Rightarrow \ln\left(\frac{[M]_0}{[M]}\right) = k_p[R^\bullet]t \Rightarrow [R^\bullet] = \frac{\ln\left(\frac{[M]_0}{[M]}\right)}{k_p t} = 4.55 \times 10^{-9}\ \text{mol/L} \quad (1)$$

Knowing the concentration of propagating radicals at the equilibrium, one can estimate the concentration of chains that underwent termination after the equilibrium was reached (eq 2).

$$R_t = \frac{-d[R^\bullet]}{dt} = \frac{d[P]}{dt} = 2k_t[R^\bullet]^2 \Rightarrow [P] = 2k_t[R^\bullet]^2 t = 5.96 \times 10^{-4}\ \text{mol/L} \quad (2)$$

Taking a rate constant of termination of $\sim 4 \times 10^8$ L mol^{-1} s^{-1} for styrene at 125 °C,[47] the estimated concentration of dead chains after 10 h should be 5.96×10^{-4} mol/L, i.e., ~3.6% of the initial MI concentration. This would indicate that only a small fraction of chains were lost through irreversible termination after the equilibrium was reached.

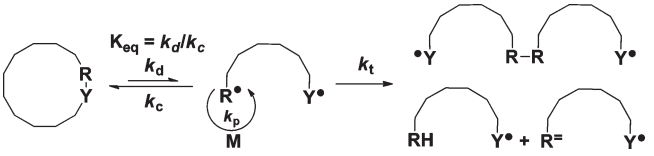
However, such a calculation does not take into account the fact that styrene undergoes spontaneous thermal polymerization at high temperatures.[42,43] It has been shown, for the bulk polymerization of styrene at 125 °C in the presence of the PSt-TEMPO adduct, that the rate of polymerization is independent of the adduct concentration and is equal to the rate of thermal polymerization.[46,48−50] The proposed kinetic scheme assumes a stationary state with respect to both [R•] and [Y•], with a concentration of R• determined by the equality of the rate of thermal initiation and that of R•−R• biradical termination.[46,49−51] Under the conditions used in our study for the ring expansion of cyclic PSt, i.e., 10 h in bulk at 125 °C, the concentration of radicals generated during the course of the reaction could be as much as 5 mM, that is, ~30% of the initial concentration of cyclic PSt.[52]

The unbalanced stoichiometry between growing and persistent radicals, resulting from the PRE (Scheme 4a), and the generation of new chains by thermal initiation (Scheme 4b) both shift the topology of polymer chains from purely cyclic to a mixture of linear and cyclic polymers (Scheme 4).

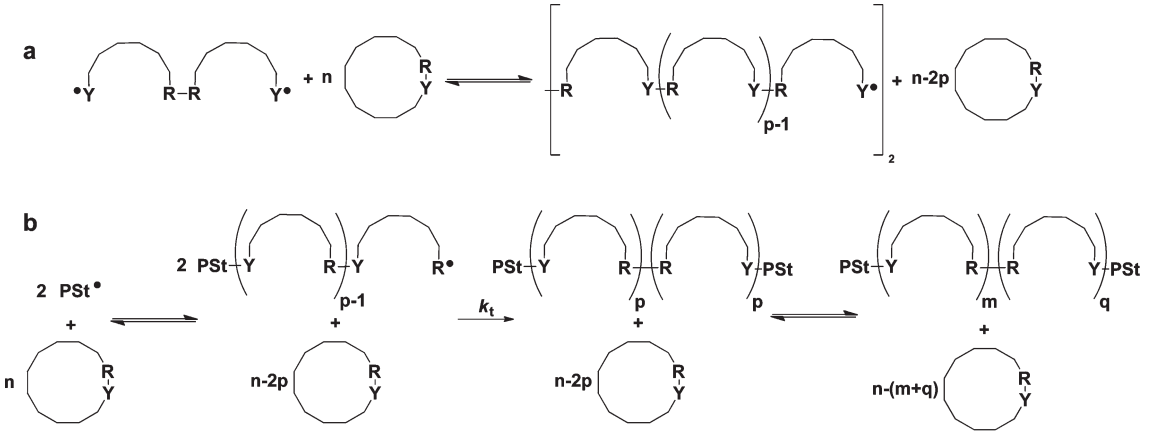
This topological change also reflects radical crossover reactions[41] taking place during NMP. Radical crossover corresponds to the recombination of a growing radical R^1 with a persistent radical Y^2 generated from the homolytic cleavage of two distinct alkoxyamines R^1−Y^1 and R^2−Y^2. For example, it has been reported that the NMP of St at 125 °C, using a 1:1 mixture of unfunctionalized alkoxyamine, **5**, and dihydroxy alkoxyamine, **6**, yielded a mixture of polystyrene macromolecules where all four possible products (**7**, **8**, **9**, and **10**) were present in an approximately statistical ratio (Scheme 5).[41] It was concluded from these results that persistent nitroxide radicals are free to diffuse out of the reaction cage during NMP and that statistical exchange of the chain ends should occur even at an early stage of the polymerization.

Crossover reactions between growing and persistent radicals are incompatible with the formation of well-defined macrocycles. These exchange reactions will lead to the formation of different populations that could still present a cyclic topology but will contain different number of alkoxyamine functions per chain (Scheme 6). Such reshuffling reactions will occur even if the stoichiometric balance between growing and persistent radicals is preserved. In addition, in the presence of persistent radicals and/or thermal

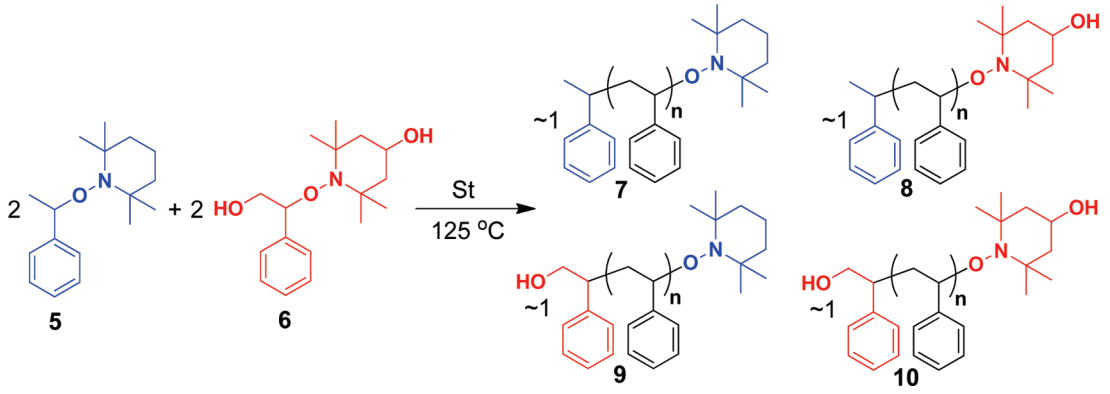
Scheme 3. General Scheme for NMP from Cyclic Alkoxyamines



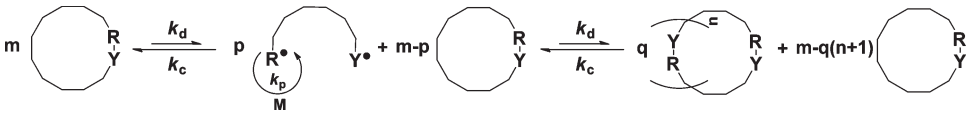
Scheme 4. Equilibrium between Linear and Cyclic Polymer Chains during NMP with Cyclic Alkoxyamines



Scheme 5. Radical Crossover during NMP of St from a 1:1 Mixture of Unfunctionalized and Dihydroxy Alkoxyamines[41]



Scheme 6. Population Redistribution via Radical Crossover during NMP with Cyclic Alkoxyamines



initiation, crossover reactions will convert part of the cyclic polymers into linear polyadducts (Scheme 4).

Conclusion

A novel approach to prepare cyclic polymers via a combination of ATRP and ATRC was developed. A functional ATRP initiator carrying an alkoxyamine group was synthesized in two steps with an overall yield of 80%. This initiator was successfully employed to prepared well-defined linear telechelic α-nitroxy,ω-bromo homo- and block copolymers via ATRP of MA or St and subsequent thermal deprotection of the terminal nitroxide function. Cyclization reactions were achieved by intramolecular ATRC, under high dilution conditions. Well-defined, low MW cyclic PMA, PSt as well as cyclic PMA-*b*-PSt block copolymers were prepared using this approach. This approach requires a minimal number of high yield steps to prepare well-defined macrocycles by radical means. The ring expansion of a cyclic polystyrene alkoxyamine prepared by ATRC was conducted via NMP of St and resulted in the formation of a mixture of products, comprising cyclic and linear polymers with an average of three to four alkoxyamine functions per chain. The presence of linear polymer chains reflects the nonstoichiometric balance between growing and persistent radicals, caused by the PRE, as well as the generation of new chains by thermal initiation. Radical crossover amplifies these phenomena and also leads to the formation of cyclic polycondensates during NMP. Therefore, ring expansion of cyclic (macro)alkoxyamines by NMP does not appear to be a suitable approach, by nature, for the preparation of well-defined macrocycles.

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