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Synthesis of Multisegmented Degradable Polymers by Atom Transfer Radical Cross-Coupling

Renaud Nicolaÿ,[†,‡] Lucien Marx,[‡] Patrick Hémery,[‡] and Krzysztof Matyjaszewski*,[†]

Department of Chemistry, Carnegie Mellon University, 4400 Fifth Avenue, Pittsburgh, Pennsylvania 15213, and Laboratoire de Chimie des Polymères, UMR 7610, Université Pierre et Marie Curie-Paris 6, 4 Place Jussieu, 75252 Paris Cedex 05, France

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ABSTRACT: Multisegmented degradable polymers were successfully synthesized via atom transfer radical cross-coupling of α,ω-dihalogenated polymers prepared by atom transfer radical polymerization with dinitroxides. High molecular weight polymers ($M_n > 100\,000$ g mol^{-1}) with more than 10 cleavable units in the main chain were prepared. These multisegmented polymers were chemically and thermally degraded. Chemical degradation, via basic hydrolysis or disulfide reduction, as well as thermal degradation, by heating in the presence or in the absence of free nitroxides, led to low molecular weight polymers with relatively low polydispersity (2100 g mol^{-1} $\leq M_n \leq$ 15 100 g mol^{-1}; $1.08 \leq M_w/M_n \leq 1.46$).

Introduction

Multisegmented polymers are composed of successive polymer blocks that can exhibit quite different properties. For instance, soft and hard incompatible blocks,[1] hydrophilic and hydrophobic blocks,[2] or crystallizable and noncrystallizable blocks[3] have been linked together. Because of these unusual features, materials with new morphologies[4] and new or improved properties[5,6] may be obtained. Potential applications for these materials include surfactants, thermoplastic elastomers, compatibilizers for polymer blends, and pressure-sensitive adhesives.[7,8] Ongoing research, however, has shown the complexity of creating multisegmented polymers with low polydispersity blocks. Current techniques to create such multisegmented polymers include nitroxide-mediated polymerization,[9,10] reversible addition fragmentation chain transfer,[11−15] and atom transfer radical polymerization (ATRP).[16,17] Degradable multisegmented polymers would extend the scope of potential applications of multisegmented polymers to green chemistry and drug delivery.[18,19] In this paper, a novel one-pot synthesis to prepare degradable multisegmented polymers via atom transfer radical cross-coupling (ATRC) between dihalogenated polymers obtained by ATRP[20−22] and dinitroxide compounds is presented. This approach does not require postpolymerization functionalization or difficult organic synthesis, as it takes advantage of the common catalyst used for both processes, i.e., ATRP and ATRC. This strategy allows introducing various functionalities into the polymer backbone and preparing high molecular weight polymers ($M_n > 100\,000$ g mol^{-1}) with more than 10 cleavable units in the main chain. These multiblock polymers can be completely degraded under thermal, redox, or solvolytic conditions to yield low polydispersity polymers.

Experimental Section

Materials. Styrene (99%, Aldrich) and *tert*-butyl acrylate (*t*BA, 98%, Aldrich) were purified by passing the monomers through a column filled with basic alumina to remove the inhibitor. CuBr (98%, Acros) was purified using a modified literature procedure.[23] Dichloromethane was distilled from calcium hydride, and THF was distilled from sodium benzophenone. 4-Hydroxy-TEMPO was received from NOVA Molecular Technologies Inc. All other reagents, namely, adipoyl chloride, $CuBr_2$, *N*,*N*′-dicyclohexylcarbodiimide (DCC), dimethyl 2,6-dibromoheptanedioate (DMDBHD), 4-(dimethylamino)pyridine (DMAP), 3,3′-dithiodipropionic acid, *N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine (PMDETA), pyridine, 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO), tri(*n*-butyl)phosphine (*n*-Bu_3P), and solvents, were purchased from Aldrich with the highest purity and used as received without further purification.

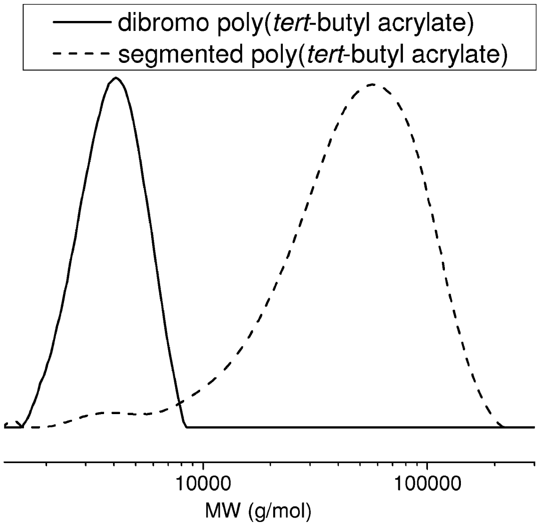

Figure 1. SEC traces of α,ω-dibromo poly(*tert*-butyl acrylate) (M_n = 3680 g mol^{-1}, PDI = 1.13) synthesized by ATRP and the resulting segmented poly(*tert*-butyl acrylate) (M_n = 27 710 g mol^{-1}, PDI = 1.92).

Analyses. NMR spectra were recorded on a Bruker instrument operating at 300 MHz. Monomer conversions were determined on a Shimadzu GC 14-A gas chromatograph equipped with a flame ionization detector using a J&W Scientific 30 m WAX Megabore column and anisole as the internal standard. Molecular weight and polydispersity were determined by size exclusion chromatography (SEC). The SEC analysis was conducted with a Waters 515 pump and Waters 410 differential refractometer using PSS columns (Styrogel) with THF as the eluent at 35 °C and at a flow rate of 1 mL/min. Linear polystyrene standards were used for calibration.

Synthetic Procedures. Synthesis of Di[4-(2,2,6,6-tetramethylpiperidine 1-oxyl)] Adipate, 1. A 250 mL oven-dried flask

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* To whom correspondence should be addressed. E-mail: km3b@andrew.cmu.edu. Phone: 412-268-3209.

[†] Carnegie Mellon University.

[‡] Université Pierre et Marie Curie-Paris 6.

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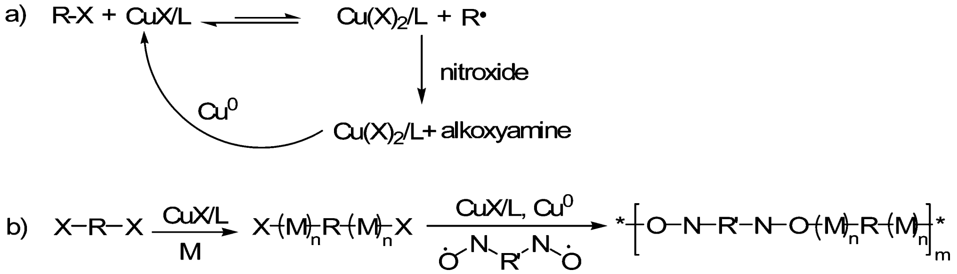
Scheme 1. (a) Atom Transfer Radical Cross-Coupling Mechanism and (b) Synthesis of Multisegmented Degradable Polymers by ATRC



equipped with a dropping funnel was charged with 4-hydroxy-TEMPO (10.335 g, 60 mmol) and purged with nitrogen for 30 min. Anhydrous dichloromethane (70 mL) and pyridine (4.850 mL, 60 mmol) were then charged, and the flask was placed in an ice bath. After 10 min, a solution of adipoyl chloride (2.917 mL, 20 mmol) in 15 mL of anhydrous dichloromethane was added dropwise. The mixture was stirred for 1 h at 0 °C and then for 12 h at room temperature. The solution was then washed several times with acidic water (pH ~ 4). The organic phase was dried over magnesium sulfate and concentrated by rotary evaporation. The raw product was then purified by flash chromatography eluting with cyclohexane/ethyl acetate (8/2, gradually increasing to 5/5) to afford 8.376 g (yield = 92.1%) of red solid. ^{1}H NMR (300 MHz, $CDCl_3$, in the presence of pentafluorophenyl hydrazine) δ: 5.10−4.93 (m, 2H), 2.33−2.19 (m, 4H), 1.94−1.81 (m, 4H), 1.69−1.49 (m, 8H), 1.33, 1.20, 1.18, 1.14 (each br s, 24H). ^{13}C NMR (75.5 MHz, $CDCl_3$, in the presence of pentafluorophenyl hydrazine) δ: 171.01, 66.61, 59.82, 43.77, 34.23, 31.61, 24.46, and 20.65.

Synthesis of Bis[2-(4-oxy-2,2,6,6-tetramethylpiperidine 1-oxyl)ethyl] Disulfide, 2. A 250 mL oven-dried flask containing 3,3′-dithiodipropionic acid (6.308 g, 30 mmol), 4-hydroxy-TEMPO (15.502 g, 90 mmol), dicyclohexylcarbodiimide (18.570 g, 90 mmol), and 4-(dimethylamino)pyridine (2.2 g, 18 mmol) was purged with nitrogen. Anhydrous THF (50 mL) was then charged, and the mixture was stirred for 12 h at room temperature. The white precipitate that formed was discarded by filtration through a Buchner funnel and the solvent was removed by rotary evaporation to give a red oil, which was then purified by flash chromatography eluting with cyclohexane/ethyl acetate (8/2, gradually increasing to 5/5) to afford 15.01 g (yield = 96.5%) of red solid. ^{1}H NMR (300 MHz, $CDCl_3$, in the presence of pentafluorophenyl hydrazine) δ: 5.06 (m, 2H), 3.20−2.77 (m, 4H), 2.73−2.49 (m, 4H), 2.03−1.46 (m, 8H), 1.28, 1.24, 1.19, 1.18 (each br s, 24H). ^{13}C NMR (75.5 MHz, $CDCl_3$, in the presence of pentafluorophenyl hydrazine) δ: 171.35, 67.37, 59.56, 43.83, 34.42, 31.77, and 20.55.

Synthesis of α,ω-Dibromo Polymers. A 50 mL Schlenk flask was charged with CuBr (64.5 mg, 4.5×10^{-4} mol) and $CuBr_2$ (11.2 mg, 5×10^{-5} mol) and purged with N_2 for 30 min. Deoxygenated anisole (9.5 mL) and PMDETA (104.5 μL, 5×10^{-4} mol) were added followed by the addition of deoxygenated styrene (18.5 mL, 161.5×10^{-3} mol). A sample was taken for ulterior conversion monitoring, and dimethyl 2,6-dibromoheptanedioate (109 μL, 5×10^{-4} mol) was finally added. The flask was placed in an oil bath thermostated at 90 °C for 3 h 45 min. The monomer conversion was 17.9%. The flask was then removed from the oil bath, and the solution was diluted in tetrahydrofuran and purified by passing through a neutral alumina column. The solvent and monomer were then removed under vacuum at 45 °C. The polymer was precipitated in cold methanol and analyzed by SEC: $M_n = 6250$ g mol^{-1}, $M_w/M_n = 1.11$.

The same procedure was applied to ATRP of *tert*-butyl acrylate both in bulk and in 25% acetone solution.[24]

ATRC between α,ω-Dibromo Polymer and Dinitroxide. Dinitroxide **1** (177.7 mg, 3.9×10^{-4} mol), dibromo poly(*tert*-butyl acrylate) (1.541 g, 4.19×10^{-4} mol, $M_n = 3{,}680$ g mol^{-1}, PDI = 1.13), $Cu(OTf)_2$ (36.2 mg, 1×10^{-4} mol), Cu^0 (76.2 mg, 1.2×10^{-3} mol), and anisole (5 mL) were charged in a 10 mL Schlenk flask and bubbled with nitrogen for 45 min. PMDETA (20.9 μL, 1×10^{-4} mol) was then added, and the flask was placed in an oil bath thermostated at 80 °C for 22 h 30 min. The flask was then removed from the oil bath, and the solution was diluted in tetrahydrofuran and purified by passing through a neutral alumina column. The solvent and monomer were then removed under vacuum at 45 °C. The polymer was analyzed by SEC: $M_n = 27\,710$ g mol^{-1}, $M_w/M_n = 1.92$, DP = 7.

One-Pot Synthesis of Multisegmented Degradable Polymers. CuBr (3.6×10^{-3} g, 2.5×10^{-5} mol) was charged in a 10 mL Schlenk flask and, after 30 min under nitrogen atmosphere, deoxygenated *tert*-butyl acrylate (3 mL, 20.48×10^{-3} mol), PMDETA (5.2 μL, $2{,}5 \times 10^{-5}$ mol), deoxygenated acetone (1 mL), and deoxygenated anisole (0.5 mL) were added. The solution turned light green as the complex formation occurred. A sample was removed to measure the initial monomer/internal standard ratio to determine afterward the conversion. DMDBHD (21.76×10^{-3} μL, 1×10^{-4} mol) was then added, and the flask was placed in an oil bath thermostated at 60 °C for 5 h. Dinitroxide **1** (45.4×10^{-3} g, 1×10^{-4} mol), CuBr ($28{,}7 \times 10^{-3}$ g, 2×10^{-4} mol), Cu^0 ($63{,}5 \times 10^{-3}$ g, 1×10^{-3} mol), and PMDETA (41.8 μL, 2×10^{-4} mol) were then added to the reaction medium. The reaction was stopped after 4 h at 60 °C. The flask was then removed from the oil bath, and the solution was diluted in tetrahydrofuran and purified by passing through a neutral alumina column. The solvent and monomer were then removed under vacuum at 45 °C. The polymer was analyzed by SEC: after 5 h of ATRP conversion = 31.36%, $M_n = 8500$ g/mol, $M_w/M_n = 1.28$, and after 4 h of ATRC $M_n = 108\,150$ g mol^{-1}, $M_w/M_n = 1.86$, DP = 12.3.

Thermal Degradation of Segmented Polymers in the Presence of TEMPO. TEMPO (187.2 mg, 1.2×10^{-3} mol), multisegmented polystyrene (89.2 mg, 1×10^{-5} mol, $M_n = 8920$ g mol^{-1}, PDI = 2.07), and anisole (5 mL) were charged in a 10 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 analyzed by SEC: $M_n = 3850$ g mol^{-1}, $M_w/M_n = 1.12$.

Thermal Degradation of Segmented Polymers in the Absence of TEMPO. Multisegmented polystyrene (89.2 mg, 1×10^{-5} mol, $M_n = 8{,}920$ g mol^{-1}, PDI = 2.07) and anisole (5 mL) were charged in a 10 mL Schlenk flask and bubbled with nitrogen for 30 min. The flask was then placed in an oil bath thermostated at 120 °C for 100 h. The polymer was analyzed by SEC: $M_n = 3780$ g mol^{-1}, $M_w/M_n = 1.18$.

Degradation of Segmented Polymers by Basic Hydrolysis. Multisegmented polystyrene (108 mg, 1×10^{-5} mol, $M_n = 10\,820$ g mol^{-1}, PDI = 1.88) and KOH (2.5 g, 44.5×10^{-3} mol) were dissolved in a mixture of methanol (10 mL) and tetrahydrofuran (30 mL), and the solution was refluxed for 22 h. The polymer was analyzed by SEC: $M_n = 3630$ g mol^{-1}, $M_w/M_n = 1.16$.

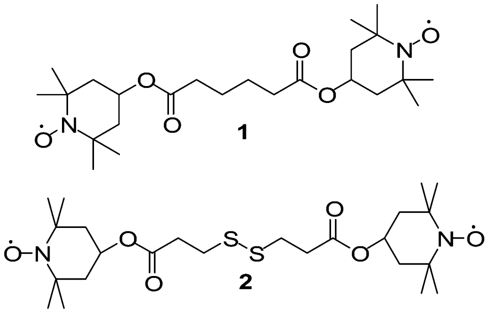
Degradation of Segmented Polymers by Reduction of Disulfide Bond. Disulfide-containing multisegmented polystyrene (40 mg, 1.7×10^{-6} mol, $M_n = 23\,570$ g mol^{-1}, PDI = 2.30) was dissolved in 2 mL of DMF, and 0.05 mL of *n*-Bu_3P was added. The solution was stirred at room temperature overnight (16 h), and the polymer was analyzed by SEC: $M_n = 6610$ g mol^{-1}, $M_w/M_n = 1.11$.

Table 1. ATRC of Poly(*tert*-butyl acrylate) in Bulk or with 25% of Acetone

		0 h	1 h	2 h	4 h
bulk[a]	M_n (g/mol)	6180	65 255	157 340	211 960
	PDI	1.34	1.71	1.49	1.84
	DP	1	10.08	24.30	32.74
25% acetone[b]	M_n (g/mol)	8500	105 690	110 270	108 150
	PDI	1.28	1.74	1.67	1.86
	DP	1	12.02	12.54	12.30

[a] ATRP: $[tBA]_0/[DMDBHD]_0/[CuBr]_0/[PMDETA]_0 = 300/1/0.5/0.5$, 3 h at 60 °C. ATRC: $[DMDBHD]_0/[dinitroxide]_0/[CuBr]_0/[PMDETA]_0/[Cu]_0 = 1/1/2/2/10$, 4 h at 60 °C. [b] ATRP: $[tBA]_0/[DMDBHD]_0/[CuBr]_0/[PMDETA]_0 = 200/1/0.25/0.25$, $[tBA]_0/[acetone]_0 = 3/1$, 5 h at 60 °C. ATRC: $[DMDBHD]_0/[dinitroxide]_0/[CuBr]_0/[PMDETA]_0/[Cu]_0 = 1/1/2/2/10$, 4 h at 60 °C.

Scheme 2. Dinitroxide, 1, and Disulfide−Dinitroxide, 2



Results and Discussion

Synthesis of Multisegmented Degradable Polymers. The synthesis of segmented degradable polymers involves the preparation of dihalogenated telechelic polymers by ATRP[20−22] and their subsequent coupling with dinitroxide by ATRC[25] (Scheme 1). By using of ATRP to synthesize telechelic polymers and block polymers, it is possible to prepare a wide range of multisegmented polymers and block copolymers.

The preparation of multisegmented polymers by ATRC also provides an attractive method to introduce various functions into the main chain of polymers via the dinitroxide moiety. The preparation of multisegmented polymers by ATRC also provides an attractive method to introduce various functions into the main chain of polymers via the dinitroxide moiety. These functions may be degradable, such as disulfide, or can be light responsive, such as azobenzene[26−28] and spiroxazine,[29,30] depending on the applications targeted for the material (Scheme 2). Cis−trans isomerization of azobenzene results in large changes in the size and polarity of the unit while spiroxazine can undergo reversible isomerization between the hydrophobic spiropyran and the hydrophilic merocyanine.

Multisegmented polystyrene and poly(*tert*-butyl acrylate) were prepared in two steps. Telechelic α,ω-dibromo polymers were synthesized by ATRP, isolated, and then coupled with dinitroxide **1** or **2** in the presence of an excess of Cu^0 to reduce the Cu^{II} formed during the ATRC step-growth process (Scheme 1). For example, with 83.7 mmol L^{-1} of poly(*tert*-butyl acrylate) (M_n = 3,680 g mol^{-1}, PDI = 1.13), 78.2 mmol L^{-1} of dinitroxide **1**, 20 mmol L^{-1} of Cu^{II} triflate/PMDETA complex, and 0.24 mol L^{-1} of Cu^0, segmented poly(*tert*-butyl acrylate) with a degree of polymerization (DP) of 7 (M_n = 27 710 g mol^{-1}, PDI = 1.92) was obtained after a reaction time of 22 h 30 min at 80 °C (Figure 1). In the case of polystyrene, a lower DP was always observed for the ATRC step-growth process. For example, with 12.5 mmol L^{-1} of α,ω-dibromo polystyrene (M_n = 6250 g mol^{-1}, PDI = 1.11), 12.5 mmol L^{-1} of dinitroxide **2**, 2.5×10^{-1} mmol L^{-1} of Cu^IBr/PMDETA complex, and 0.5 mol L^{-1} of Cu^0, segmented polystyrene with a DP of 3.6 (M_n = 23 570 g mol^{-1}, PDI=2.3) was obtained after a reaction time of 30 h at 45 °C.

Table 2. Evolution of Conversion and Molecular Weight during ATRC of Poly(*tert*-butyl acrylate) in Bulk

time of ATRC[a] (min)	0[b]	30	60	90	120
conversion (%)	12.2	15.9	18.4	24.4	39.6
M_n (g mol^{-1})	4500	24 800	72 600	97 000	114 900

[a] ATRP: $[tBA]_0/[DMDBHD]_0/[CuBr]_0/[PMDETA]_0 = 300/1/0.5/0.5$, 3 h at 60 °C. ATRC: $[DMDBHD]_0/[dinitroxide]_0/[CuBr]_0/[PMDETA]_0/[Cu]_0 = 1/1/2/2/10$, 2 h at 60 °C. [b]after 3 h of ATRP of *tert*-butyl acrylate

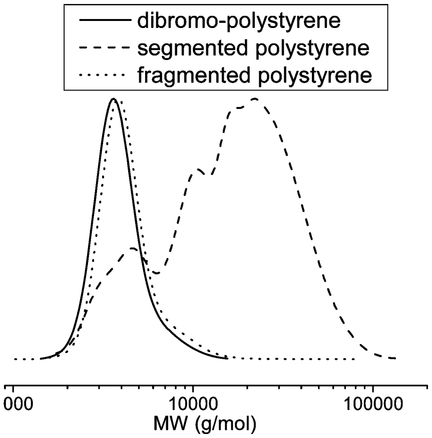


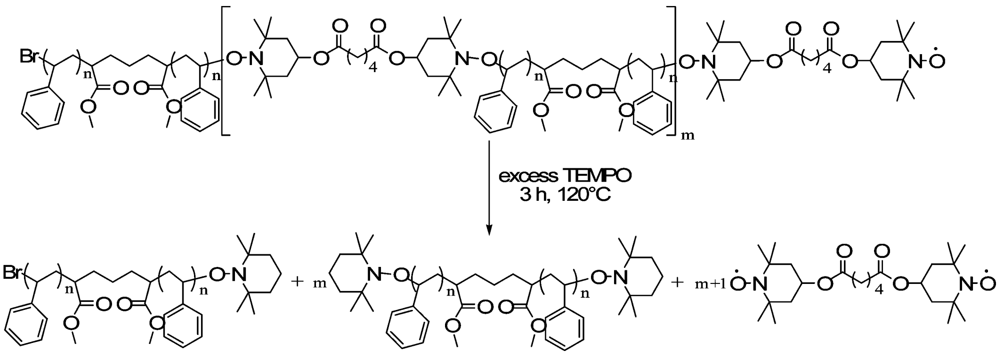
Figure 2. SEC chromatograms of the starting α,ω-dibromo polystyrene (M_n = 3570 g mol^{-1}, PDI = 1.10), the resulting segmented polystyrene (M_n = 8920 g mol^{-1}, PDI = 2.07), and the polystyrene thermally fragmented (M_n = 3850 g mol^{-1}, PDI = 1.12) at 120 °C for 3 h in the presence of excess TEMPO.

Table 3. M_n and PDI of Segmented and Fragmented Poly(*tert*-butyl acrylate) Obtained by One-Pot ATRC

		α,ω-dibromo poly(*t*BA)	segmented poly(*t*BA)	fragmented poly(*t*BA)
ATRC in bulk	M_n (g mol^{-1})	8980	119 850	15 130
	PDI	1.46	1.93	1.46
ATRC in 25% acetone	M_n (g mol^{-1})	1900	11 900	2130
	PDI	1.06	1.82	1.08

The lower DP observed for the ATRC process in the case of polystyrene compared to poly(*tert*-butyl acrylate) can be attributed to termination by the macroradicals coupling as well as loss of chain-end functionality by β-H elimination.[31] The loss of functionality in styrene ATRP is predominantly due to β-H elimination reactions catalyzed by the Cu^{II} deactivator. Bimolecular coupling termination also occurs, but mostly at low monomer conversions (conversion < 40%).[32] Quantification of the chain-end functionality of polystyrene by ^1H NMR during normal ATRP showed that at high conversions (conversion >90%), despite of low polydipersity ($M_w/M_n \sim 1.2$), polystyrene has a low bromine end functionality ($f \sim 35\%$). It has also been reported that by using Cu^0/Cu^I as a catalytic system the coupling of bromo-terminated polystyrene is faster (more than 95% of polymeric chains were found to be reacted after 3 h) than the coupling of poly(methyl acrylate), due to a larger ATRP equilibrium constant for PS−Br and, consequently, higher radical concentration.[33] Loss of chain-end functionality as well as termination by macroradicals coupling during both ATRP and ATRC processes affect the stoichiometric ratio, *r*, between the bromine end groups and the nitroxide functions. The stoichiometric ratio is a key parameter in step-growth polymerization, as DP equals $(1 + r)/(1 - r)$ at full conversion. Finally, the lower DP of the final segmented polymers may also be explained by the higher dissociation constant between the styryl

Scheme 3. Thermal Degradation of Segmented Polymers in the Presence of TEMPO



unit and TEMPO (5.2×10^{-4} s^{-1} at 120 °C)[34] compared to that of acrylate−TEMPO (3.4×10^{-5} s^{-1} at 120 °C),[34] which makes the main chain less stable during the step-growth process with polystyrene.

In order to better control the stoichiometry between bromine end groups and nitroxide functions, a one-pot process was used for the synthesis of multisegmented degradable polymers. In this process, when the polymer reaches the desired molecular weight, all reagents needed for the ATRC reaction are introduced in the reaction medium. Two systems were studied for the polymerization of *tert*-butyl acrylate: bulk and 25 vol % acetone solution (Table 1).

The use of a one-pot process yielded segmented polymers with higher DP. One major difference can be noted between the two systems. The molecular weight of the segmented polymer synthesized in bulk increased during the whole reaction, while the molecular weight of the polymer synthesized in 25% of acetone solution remained constant.

This observation prompted us to follow the conversion in monomer during the ATRC process. The conversion did not change during the ATRC process in 25% acetone solution; however, it increased during the ATRC process in bulk (Table 2). These two phenomena can be correlated to the differences in the solubility of the catalyst in bulk versus in 25% acetone solution. It is known that increasing the polarity of the solvent can affect the solubility of the ATRP catalyst.[35−37] CuBr/PMDETA catalyst system is heterogeneous in bulk *t*BA monomer unlike the analogous methyl acrylate system.[38] It was shown that the use of 25% acetone or 25% DMF for the ATRP of *t*BA resulted in a better controlled reaction through higher solubility of the Cu^{II} deactivator species.[39] In the first stage of the ATRC process, the amount of nitroxide present in the solution is large enough to prevent the polymerization of *t*BA. However, the nitroxide concentration decreases rapidly as the cross-coupling reaction takes place. In addition, the mobility of the remaining nitroxide moieties is also decreased, because they are, at this stage of the reaction, at the chain end of the macromolecules. In the case of 25% acetone solution, the Cu^{II} complex present in solution prevents the monomer addition, while in bulk system a much lower concentration of the soluble Cu^{II} complex does not allow efficient deactivation of the propagating radicals.

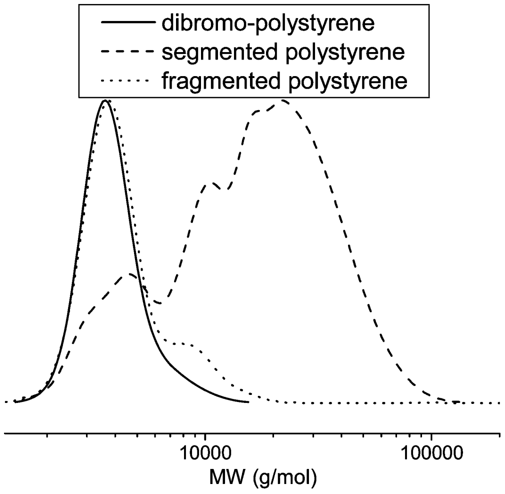
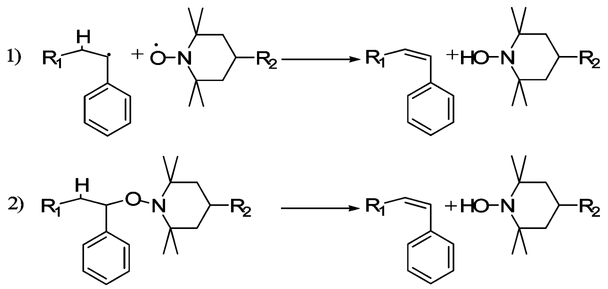


Figure 3. SEC chromatograms of the starting α,*ω*-dibromo polystyrene (M_n = 3570 g mol^{-1}, PDI = 1.10), the resulting segmented polystyrene (M_n = 8920 g mol^{-1}, PDI = 2.07), and the polystyrene thermally fragmented (M_n = 3780 g mol^{-1}, PDI = 1.18) at 120 °C for 100 h in the absence of nitroxide.

Scheme 4. *β*-Hydrogen Atom Transfer Mechanism



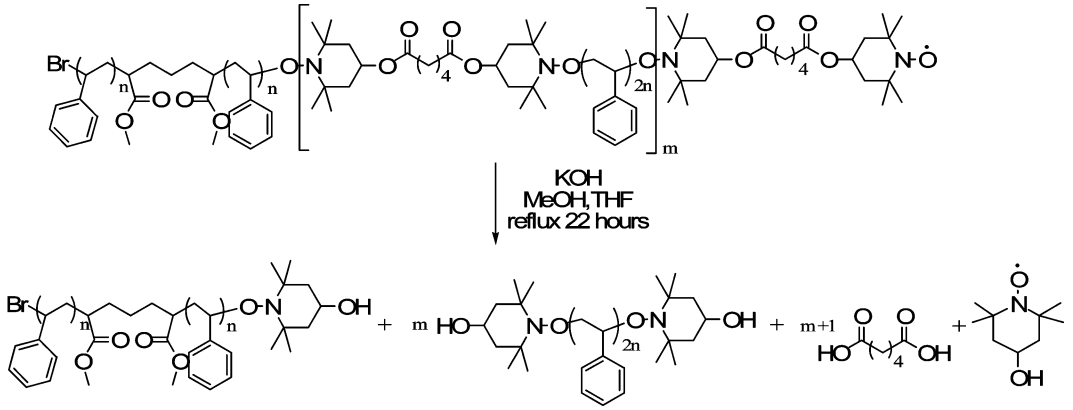
Thermal Fragmentation of Multisegmented Polymers. The multisegmented polymers formed by coupling dinitroxide and α,*ω*-dihalogenated polymers can be degraded through several processes, depending on the function incorporated in the dinitroxide moiety.

The multisegmented polymers were degraded thermally employing the presence of thermolabile alkoxyamine bonds in the main chain (Scheme 3).

Thermal degradation was achieved by heating the multisegmented polymers in the presence of an excess of TEMPO for 3 h at 120 °C (in the case of segmented polystyrene) or at 130 °C (in the case of segmented poly(*tert*-butyl acrylate). For instance, the degradation of multisegmented polystyrene of molecular weight 8920 g mol^{-1}, obtained from α,*ω*-dibromo polystyrene with a molecular weight of 3570 g mol^{-1} and a PDI of 1.10, yielded a low PDI polymer with the same molecular weight as that of the starting dibromo polystyrene (M_n = 3850 g mol^{-1}; PDI = 1.12) (Figure 2).

Multisegmented poly(*tert*-butyl acrylate) obtained using a one-pot process either in bulk or in 25% acetone solution was similarly degraded. In the case of multisegmented poly(*tert*-butyl acrylate) prepared using 25% acetone solution, the molecular weight of the fragmented polymer was essentially the same as that of the starting α,*ω*-dibromo poly(*tert*-butyl acrylate) when the chain-end modification from bromine to TEMPO moiety was taken into account. On the contrary, the

Scheme 5. Fragmentation of Segmented Polymers by Basic Hydrolysis



fragmented polymer obtained from multisegmented poly(*tert*-butyl acrylate) prepared in bulk showed a significantly higher molecular weight while still presenting a relatively low PDI (Table 3). These results are in good agreement with the observed limited monomer conversion during the one-pot ATRC process of poly(*tert*-butyl acrylate) in 25% acetone solution compared to that of the bulk system. The successful degradation of the segmented polymers, obtained either in one-pot process or in two steps and both in bulk and in 25% acetone solution, confirms that in every case the step-growth process occurs predominantly by radical cross-coupling of α,ω-dihalogenated polymers with dinitroxides rather than by polymeric radical coupling. Polymers obtained by macroradical coupling cannot be degraded thermally or by disulfide reduction, as there is no cleavable function in the polymer chains. Furthermore, if some polymeric radical coupling could occur during the step-growth process, polymers with polymodal distribution should be formed after thermal degradation in the presence of excess nitroxide. However, monomodal polymers with relatively low polydispersity were recovered in every case after thermal degradation in the presence of excess nitroxide.

The mass redistibution of the segmented polymer, when heated alone in solution at 120 °C, was also studied. This process did not yield a monomodal Bernoullian distribution, but led, after 100 h at 120 °C, to the initial polystyrene unit ($M_n = 3780$ g mol^{-1}, PDI = 1.18 vs starting polystyrene $M_n = 3570$ g mol^{-1}, PDI = 1.10) with a small amount of coupling product. This can be seen as the tail in the SEC chromatogram (Figure 3).

In the latter case, we assume that the degradation is due to radical coupling (10% from Figure 3), to radical disproportionation, and to β-hydrogen atom transfer from the styryl moiety to the nitroxide radical. β-Hydrogen atom transfer can occur by a radical cross-disproportionation (reaction 1) or by a nonradical alkene elimination (reaction 2)[40] (Scheme 4) and leads to polymer chains with a terminal double bond (a macromonomer) and hydroxylamines. In this degradation process, the dormant alkoxyamine species are in equilibrium with the active carbon radicals and free nitroxide. In the first stage of the degradation, terminations by radical coupling or radical disproportionation will increase the concentration of free nitroxide, leading to the so-called persistent radical effect.[41] In the second stage, β-hydrogen atom transfer from the styryl moiety to the nitroxide radical will be the predominant reaction, as the concentration in free nitroxide will remain constant (or slightly increase) while every termination act will decrease the concentration of dormant alkoxyamine species and, thus, the probability of termination by radical coupling or disproportionation.

Chemical Degradation of Multisegmented Polymers. The multisegmented polymers can also be degraded by basic hydrolysis of the ester groups in the dinitroxide (Scheme 5).

Chemical degradation was achieved by refluxing the multisegmented polymers for 22 h in a solution of potassium hydroxide in 3/1 mixture of tetrahydrofuran and methanol. The dissociation rate constant of styryl−TEMPO alkoxyamine was calculated as $k_d = 6.97 \times 10^{-7}$ s^{-1} at 65 °C from the Arrhenius equation (using $A = 2.6 \times 10^{14}$ s^{-1} and $E_a = 133$ kJ mol^{-1}).[34] As a result, less than 5% of the alkoxyamine moieties is expected to dissociate during basic hydrolysis; therefore, thermal degradation can be neglected under these conditions. The degradation of multisegmented polystyrene of molecular weight 10 825 g mol^{-1}, obtained from α,ω-dibromo polystyrene with a molecular weight of 3570 g mol^{-1} and a PDI of 1.10, yielded a low PDI polymer with the same molecular weight as that of the initial dibromo polystyrene ($M_n = 3630$ g mol^{-1}, PDI = 1.16) (Figure 4).

The disulfide moiety in multisegmented polymers prepared using bis[2-(4-oxy-2,2,6,6-tetramethylpiperidine 1-oxyl)ethyl] disulfide, **2**, can be cleaved in the presence of reducing agents,[42−46] nucleophiles, electrophiles,[47,48] or photochemically.[49,50] Since the redox potential of the disulfide (R_1−S−S−R_2)/thiol couple depends on the nature of substitutents R_1 and R_2 as well as the reaction medium composition (solvent polarity, pH, etc.),[43,51] disulfide-containing dinitroxide can be designed to degrade at a sufficient rate only under certain conditions. In this study, n-Bu$_3$P was used to reduce the disulfide

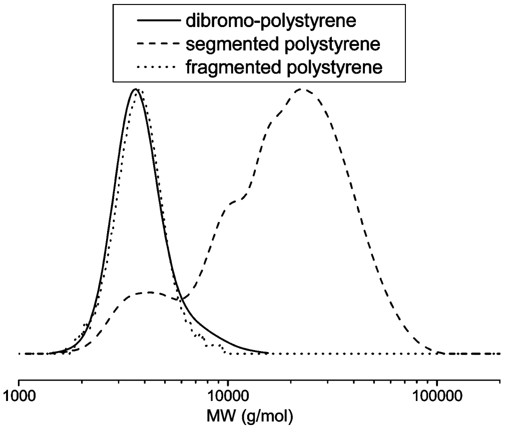
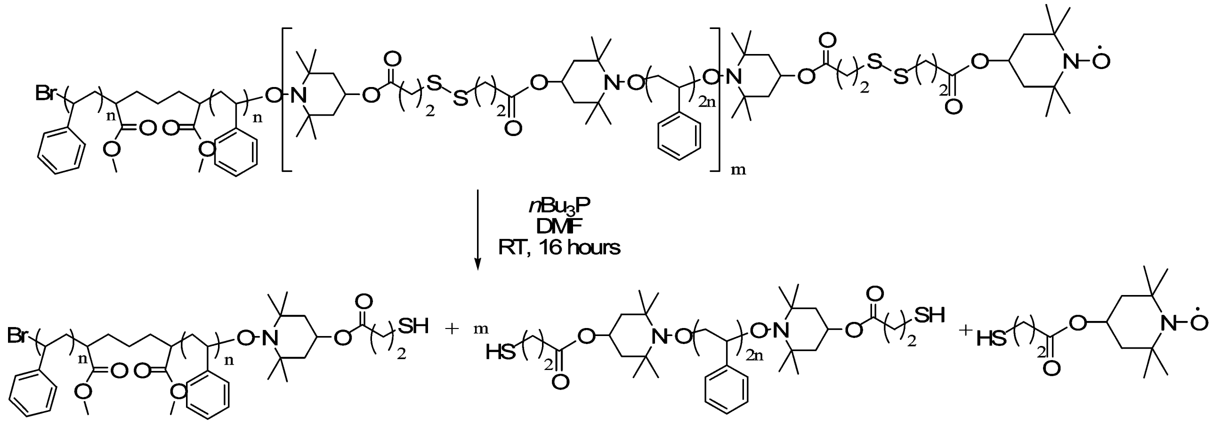


Figure 4. SEC traces of the starting α,ω-dibromo polystyrene ($M_n = 3570$ g mol^{-1}, PDI = 1.10), the resulting segmented polystyrene ($M_n = 10\,825$ g mol^{-1}, PDI = 1.88), and the polystyrene fragmented by basic hydrolysis ($M_n = 3630$ g mol^{-1}, PDI = 1.16) at 65 °C for 22 h in the presence of KOH.

Scheme 6. Fragmentation of Segmented Polymers by Reduction of Disulfide Bond



group to thiols (Scheme 6). Phosphines, such as Ph_3P[52] and especially n-Bu_3P, in the presence of water (or moisture) reduce the disulfide group significantly more efficiently than dithiothreitol.[45]

The degradation of the multisegmented polystyrene with molecular weight 23 570 g mol^{-1}, obtained from α,ω-dibromo polystyrene with a molecular weight of 6250 g mol^{-1} and a PDI of 1.11, yielded a low PDI polymer ($M_n = 6610$ g mol^{-1}, PDI = 1.11) after 16 h at room temperature (Figure 5).

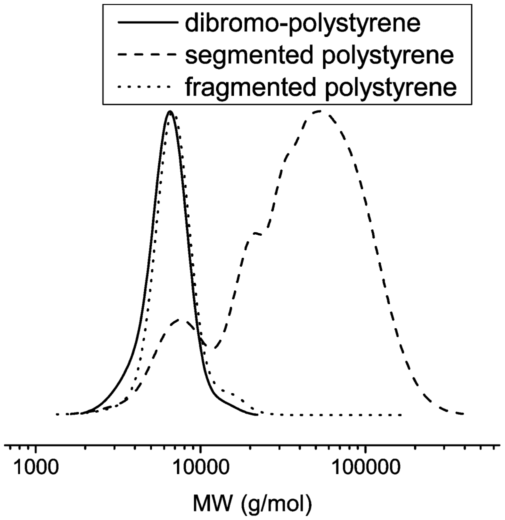


Figure 5. SEC traces of the starting α,ω-dibromo polystyrene (M_n = 6250 g mol^{-1}, PDI = 1.11), the resulting segmented polystyrene (M_n = 23 570 g mol^{-1}, PDI = 2.30), and the polystyrene fragmented by disulfide reduction (M_n = 6610 g mol^{-1}, PDI = 1.11) at room temperature for 16 h in the presence of n-Bu_3P.

Conclusion

A new one-pot strategy to prepare degradable multisegmented polymers via ATRC has been described. High molecular weight multisegmented degradable polymers ($M_n > 100\,000$ g mol^{-1}) with more than 10 cleavable units in the main chain were obtained by cross-coupling of α,ω-dihalogenated polymers prepared by ATRP with dinitroxides. This process offers an efficient way to introduce various functions in the main chain of polymers. The ability of the multisegmented polymers to be degraded by basic hydrolysis, by disulfide reduction to thiols, or by heating in the presence and absence of nitroxide has been demonstrated. Polymers with relatively low polydispersity were recovered in every case.

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