Graft Copolymers by a Combination of ATRP and Two Different Consecutive Click Reactions

Nicolay V. Tsarevsky, Sidi A. Bencherif, and Krzysztof Matyjaszewski*

Department of Chemistry, Carnegie Mellon University, 4400 Fifth Avenue, Pittsburgh, Pennsylvania 15213

Received March 22, 2007; Revised Manuscript Received April 23, 2007

ABSTRACT: The epoxide ring in glycidyl butyrate (model compound) and in well-defined copolymers of glycidyl methacrylate (<40 mol %) and methyl methacrylate prepared by ATRP was efficiently opened with sodium azide in the presence of ammonium chloride in DMF at 50 °C. This click-type reaction led to the formation of the corresponding 1-hydroxy-2-azido compounds in high yields. The prepared azide-containing copolymers were functionalized in a second click reaction, the room temperature CuBr/*N,N,N′,N″,N″*-pentamethyldiethylenetriamine-catalyzed 1,3-dipolar cycloaddition, of poly(ethylene oxide) methyl ether pentynoate to yield loosely grafted polymeric brushes with hydrophilic PEO side chains.

Introduction

A vast array of technologies and industries use polymeric materials and constantly demand the development of novel synthetic methods that allow control over the composition, molecular weight, and molecular structure as well as the number and placement of functional groups in these materials. During the past decade, the number and the applications of such synthetic techniques, collectively termed macromolecular engineering,[1] have grown almost explosively. Living polymerizations[2−11] and especially controlled radical polymerization (CRP)[7,12−16] methods have become immensely popular due to the latter's relatively simple experimental setup and applicability to a large number of monomers. The most important CRP methods include atom transfer radical polymerization (ATRP),[17−19] stable free radical (mostly nitroxide) mediated polymerization,[20] and degenerative transfer polymerization,[21,22] particularly reversible addition−fragmentation chain transfer (RAFT)[23−26] polymerization. ATRP has been successfully employed in the synthesis of various homopolymers as well as random, segmented, and gradient copolymers.[27] It enables the controlled synthesis of functional (co)polymers,[28] copolymers with complex molecular architectures,[29,30] and composite materials[31] and has already found industrial applications.[32]

The combination of the mentioned synthetic methods with high-yield chemical transformations is a powerful strategy in the preparation of functional materials. Click reactions[33] include a wide variety of transformations characterized by high yields, selectivity, and the absence of side products other than simple molecules such as water, carbon dioxide, etc. These reactions can be carried out in numerous solvents and are tolerant to various impurities, which makes them particularly attractive. The ring-opening of epoxides in the presence of nucleophiles is an example of click functionalization that has found many applications in organic synthesis.[34,35] The cycloaddition reactions of a 1,3-dipole to a dipolarophile is another reaction of wide synthetic utility.[36] The 1,3-dipolar azide−nitrile cycloaddition[37] has been used in the synthesis of well-defined polymeric tetrazoles.[38] The 1,3-dipolar azide−alkyne cycloaddition originally described by Huisgen[39−41] has become increasingly

important since it was demonstrated that it is regioselective (yielding 1,4-disubstituted 1,2,3-triazoles) and can be conducted at ambient temperature in the presence of Cu[I]-based catalysts.[42,43] Some mechanistic aspects[44−46] of this reaction have been studied due to its significance, and it has already been employed successfully in materials science.[47] The synthesis of a plethora of telechelic[48−52] or backbone-functionalized[53,54] polymers as well as more complex structures such as cross-linked nanoparticles and micelles,[55,56] dendrimers,[57,58] segmented copolymers,[59,60] cyclic polymers,[61] star[62−64] and brush[65,66] copolymers, networks,[67] and many others has been demonstrated.

The development of methods for the synthesis of well-defined polymers containing multiple alkyne or azide groups is very desirable. The direct ATRP of an azide-functionalized monomer, 3-azidopropyl methacrylate, and the efficient functionalization of the corresponding polymers in the presence of monosubstituted alkynes has been described.[53] However, the monomer has to be synthesized in two steps, and its purification by distillation is challenging because of its thermal and shock sensitivity. Herein, we report the much safer and very efficient introduction of azide groups in copolymers prepared by the ATRP of the relatively easy to handle, stable, and commercially available monomer glycidyl methacrylate (GMA) via opening of the oxirane rings in the presence of sodium azide. This click reaction was followed by a second one, namely the Cu[I]-catalyzed cycloaddition of a polymeric alkyne, poly(ethylene oxide) methyl ether 4-pentynoate (MePEO-P), to the azide groups in the copolymers, resulting in the formation of loosely grafted copolymers, i.e., with side chains separated by at least one backbone monomer unit.

Experimental Section

Materials. The monomers, methyl methacrylate (MMA, 99%) and GMA (97%), were obtained from Aldrich. The polymerization inhibitor was removed by passing the monomers through a column filled with basic (MMA) or neutral (GMA) alumina prior to use. 4-Pentynoic acid (98%) was purchased from GFS Chemicals. All other reagents (the highest purity available) and solvents were purchased from Aldrich. The liquid reagents used in the ATRP and CuBr-catalyzed click reactions (*N,N,N′,N″,N‴,N‴*-hexamethyltriethylenetetramine (HMTETA), *N,N,N′,N″,N″*-pentamethyldiethylenetriamine (PMDETA), ethyl 2-bromoisobutyrate (EBiB), and dimethylformamide (DMF)) were deoxygenated prior to use by purging with nitrogen for several hours.

* Corresponding author: Tel 412-268-3209; e-mail km3b@andrew.cmu.edu.

Analyses. Monomer conversions were determined by gas chromatography (GC) with a Shimadzu GC-14A gas chromatograph equipped with a flame ionization detector and using a capillary column (CEC-Wax, 30 m × 0.53 mm × 1.0 μm, Chrom Expert Co.). The ^{1}H NMR spectra (in CDCl$_3$ or DMF-d_7 with tetramethylsilane as the reference) were recorded on a Bruker instrument operating at 300 MHz. IR spectra of the polymers (films deposited on KBr plates from acetone solutions) were recorded on ATI Mattson Infinity Series FTIR spectrometer. The MALDI-TOF MS was performed on a PerSeptive Biosystems Voyager STR in reflectron mode. The MADLI matrix, 2,5-dihydroxybenzoic acid (50 mg), and the polymers (poly(ethylene oxide) methyl ether (MePEO-OH) or its ester with 4-pentynoic acid (MePEO-P), 5 mg) were dissolved in tetrahydrofuran (THF, 1 mL). Sodium trifluoroacetate solution in THF (0.5 mg/mL) was used as the cationizing reagent. The two solutions were mixed in a 1:1 (v/v) ratio. Each spectrum was the sum of 100 discrete laser shots; no smoothing or background subtraction was performed. The estimated expanded uncertainty reported for molecular weight moments arises from the choice of baseline and laser power (5%). Molecular weights were determined by size exclusion chromatography (SEC) using 50 mM solution of LiBr in DMF (flow rate 1 mL/min, 50 °C) or THF (1 mL/min, 30 °C) as the eluent, with a series of three Styragel columns (10^5, 10^3, and 100 Å; Polymer Standard Services) and a Waters 2410 differential refractometer as the detector. Calibration based on polyMMA standards was used with toluene or diphenyl ether as the elution volume marker. The polymer solutions were not filtered through columns filled with alumina but only through a 0.2 μm PTFE filter prior to the analysis. The extent of the click grafting reactions was determined by analysis of the area ratio of the SEC signals of MePEO-P and a nonreactive (dihydroxy-terminated) PEO used as internal standard. Since the signals of MePEO-P and the standard partially overlapped, peak fitting followed by integration was employed in the calculations.

Synthetic Procedures. Copolymerization of GMA and MMA under ATRP Conditions. MMA (9.6 mL, 0.09 mol), acetone (10 mL), and diphenyl ether (internal standard for determination of monomer conversion by GC, 0.5 mL) were mixed in a Schlenk flask, and the solution was degassed by six freeze−pump−thaw cycles. The mixture was then frozen, the flask was backfilled with nitrogen, and a mixture of CuBr (0.0287 g, 0.2 mmol) and CuBr$_2$ (0.0113 g, 0.05 mmol) was quickly added. The flask was closed with a glass stopper, and while the monomer−solvent mixture was still frozen, the flask was evacuated and backfilled with nitrogen several times. Deoxygenated HMTETA (68 μL, 0.0576 g, 0.25 mmol) was then injected through the side arm of the flask, and the mixture was heated to 50 °C. The comonomer, GMA (1.3 mL, 0.01 mol), was added after the formation of the copper complex in order to avoid reaction of the epoxide with free amine (HMTETA). Finally, the nitrogen-purged initiator, EBiB (73 μL, 0.5 mmol; targeted DP$_n$ = 200) was injected, and the reaction was carried out at 50 °C for 290 min. The conversions of MMA and GMA were 72% and 82%, respectively. The polymer was precipitated in ether and analyzed by SEC: M_n = 20 200 g/mol, M_w/M_n = 1.24. The product contained 15 mol % of GMA units (determined by ^{1}H NMR in CDCl$_3$) and is labeled poly(GMA-*co*-MMA)15 in this text. Another reaction was carried out using a different monomer feed composition, namely 0.07 mol of MMA (7.54 mL) and 0.03 mol of GMA (3.97 mL), with the amounts of all other reagents being the same. After 280 min the conversions of MMA and GMA were 73% and 89%, respectively. The polymer was purified as described above and analyzed by SEC (M_n = 20 400 g/mol, M_w/M_n = 1.44) and ^{1}H NMR spectroscopy (36 mol % of GMA units); it is labeled poly(GMA-*co*-MMA)36.

Reaction of (R)-(−)-Glycidyl Butyrate with Sodium Azide. In each of three separate vials equipped with a magnetic stir bar, sodium azide (0.0195 g, 0.3 mmol) and ammonium chloride (0.0161 g, 0.3 mmol) were mixed with DMF-d_7 (1 mL), and (R)-(−)-glycidyl butyrate (14 μL, 0.1 mmol) was added. The reactions were carried out at 50 °C. After a certain reaction time (1, 3, or 9 h), the vial was opened, and the mixture was filtered through a 0.2 μm

PTFE filter, tetramethylsilane was added, and the reaction extent was determined by ^{1}H NMR spectroscopy. The ring-opening reaction was complete within 9 h.

Reaction of Poly(GMA-*co*-MMA) with Sodium Azide and Ammonium Chloride. Copolymer of GMA and MMA (3.12 mmol of epoxide groups, i.e., 2.22 g of the copolymer with 15 mol % of GMA units or 1.00 g of the copolymer with 36 mol % of GMA units) was dissolved in DMF (20 mL). Sodium azide (0.609 g, 9.37 mmol) and ammonium chloride (0.501 g, 9.37 mmol) were added to this solution, and the mixture was stirred at 50 °C for 26 h. The polymers containing 2-hydroxy-3-azidopropyl methacrylate (HAZPMA) units were precipitated in water, washed on the filter with water, and dried. No cross-linking or branching was detected by SEC. The signals of the epoxide protons in the ^{1}H NMR spectrum disappeared completely, indicating the efficiency of the azidation procedure. The IR spectra of the two copolymers contained an absorption peak at 2104 cm^{-1} corresponding to the vibration frequency of the azide group. The two copolymers are named poly-(HAZPMA-*co*-MMA)15 and poly(HAZPMA-*co*-MMA)36 in this work; the number indicates the molar fraction of HAZPMA units.

Synthesis of Poly(ethylene oxide) Monomethyl Ether Pentynoate (MePEO-P). MePEO-OH of M_n = 2000 g/mol (20 g, 10 mmol) was dissolved in dichloromethane (60 mL). A solution of 4-pentynoic acid (1.18 g, 12 mmol) in dichloromethane (10 mL) was added, and the solution was cooled in an ice−water bath. A solution of dicyclohexylcarbodiimide (2.27 g, 13.2 mmol in 20 mL of dichloromethane) was added upon stirring followed by a solution of 4-(dimethylamino)pyridine (0.5 g in 10 mL of dichloromethane). The reaction mixture was kept in the ice−water bath for 10 min and was stirred overnight at room temperature. The precipitated dicyclohexylcarbamide was filtered off and washed with 50 mL of dichloromethane on the filter. The solution was precipitated into a large excess of cold diethyl ether and cooled in a refrigerator at −18 °C for 20 min. The product was then filtered and dried in a vacuum oven overnight at 40 °C. The yield was 92%. The ester was analyzed by ^{1}H NMR spectroscopy (CDCl$_3$, δ, in ppm): 4.24 (t, 2H, CH$_2$OOC), 3.62 (m, 168H, OCH$_2$CH$_2$O), 3.30 (s, 3H, CH$_3$O), 2.56 (m, 2H, OOCCH$_2$), and 2.48 (m, 2H, CH$_2$C≡), and 1.96 (t, 1H, C≡CH). The MALDI-TOF MS spectrum indicated that the esterification of the alcohol was complete. The spectrum of the starting material consisted of a single series of peaks corresponding to oligomers with one methyl and one hydroxy end groups cationized with Na$^+$ and separated by m/z = 44 (ethylene oxide unit). The molecular weight was determined as M_n = 1947 g/mol; M_w/M_n = 1.02. The spectrum of the product also consisted of one set of peaks corresponding to oligomers cationized with Na$^+$ and capped with one methyl and one pentynoyloxy group at each end; M_n = 2008 g/mol and M_w/M_n = 1.02.

Click Grafting of PEO Chains onto Azide-Containing Polymeric Backbones. The azide-containing polymers described above (poly(HAZPMA-*co*-MMA)15 and -36 derived from poly(GMA-*co*-MMA)15 and -36, respectively) were reacted with MePEO-P in the presence of CuBr or CuBr/PMDETA in DMF. The copolymer poly(AZHPMA-*co*-MMA)15 (0.089 g, 0.125 mmol of azide groups), MePEO-P (0.25 g, 0.125 mmol of alkyne groups), CuBr (0.0036 g, 0.025 mmol; 20 mol % relative to alkyne and azide groups), poly(ethylene oxide) of M_n = 1000 g/mol (internal standard for determination of conversion, 0.1 g), and a magnetic stir bar were placed in a round-bottom flask. The flask was then closed with a rubber septum and evacuated and backfilled with nitrogen several times. To this mixture, deoxygenated DMF (2 mL) was added with a nitrogen-purged syringe, and the reaction was carried out at room temperature for 1 h. In another experiment, deoxygenated PMDETA (5.2 μL, 0.025 mmol) was added just prior to the addition of DMF. The experiments with the two catalysts were also carried out with the copolymer poly(HAZPMA-*co*-MMA)36 with 36 mol % of azide groups (0.040 g, corresponding to the same concentration of azide groups (0.125 mmol in 2 mL)). Experiments with twice higher amount of CuBr/PMDETA, all other conditions being constant, were carried out as well. Additionally, experiments were conducted in which the amount of polymeric alkyne was
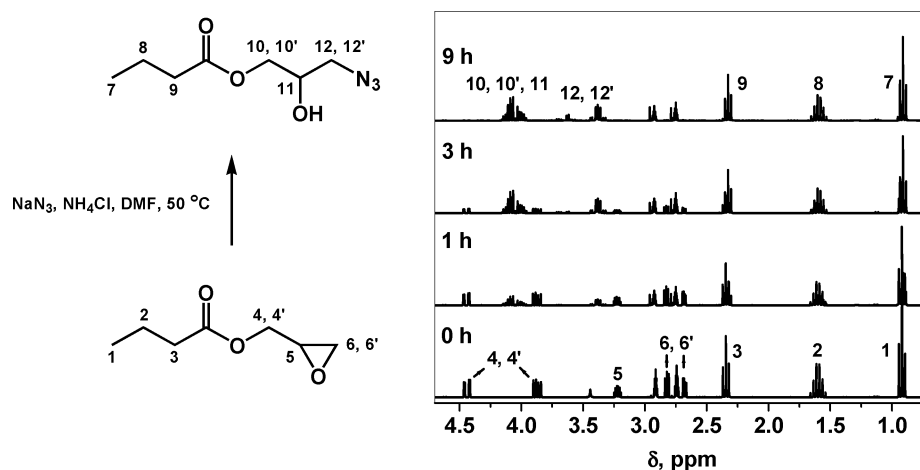
Figure 1. Evolution of ^{1}H NMR spectra with time in the reaction of glycidyl butyrate with NaN$_3$ (3 equiv) and NH$_4$Cl (3 equiv) in DMF-d_7 at 50 °C. The numbering of the hydrogen atoms used for the NMR peak assignment is shown in the reaction scheme on the left.

doubled, and the catalyst was CuBr/PMDETA (20 mol % relative to azide groups).

Results and Discussion

The synthesis of polymers containing azide groups is challenging, mostly due to complications in the synthesis and purification of azide-containing monomers, arising from their thermal instability. Therefore, alternative routes to azide-containing polymers from more stable precursors are desirable. One potential route to polymeric azides is the reaction of polymers containing epoxide groups with sodium azide. The opening of the oxirane ring by an azide anion is a reaction that has found numerous applications in the preparation of β-amino alcohols (after reduction of the azide group) and other synthetically useful molecules[68] (for an early example, see ref 69; later studies concentrated on developing stereoselective ring-opening reactions[70−72]). It was shown that when the reaction was carried out in aqueous solutions, hydroxide ions were produced that could participate in side reactions, and to minimize them, the addition of protic or Lewis acids to the azide−epoxide mixture was recommended.[73] The reaction was also extended to non-aqueous solvents in which sodium azide was employed in combination with various acidic compounds, such as ammonium chloride,[74] magnesium,[74] and lithium salts[71,74,75] as well as acidic solid supports[76] (zeolites, alumina, or silica gels).

Before the azidation of polymers containing epoxide groups was attempted, a model reaction of glycidyl ester (glycidyl butyrate) with sodium azide (3 equiv) in the presence of ammonium chloride (3 equiv) in DMF-d_7 was carried out at 50 °C. During the opening of the oxirane ring, an alkoxide anion is formed, and the role of ammonium chloride was to protonate it. The salts were not completely soluble in the reaction mixture at these conditions. The reaction was monitored by ^{1}H NMR spectroscopy, as shown in Figure 1. The signals at 4.44 and 3.87 ppm (the two protons from CO$_2$CH$_2$), 3.22 ppm (CH−O from the epoxide ring), and 2.82 and 2.68 ppm (CH$_2$−O from the ring) of the starting material disappeared completely within 9 h, indicating the efficient opening of the epoxide ring by the azide anion. New peaks were formed at 3.92−4.20 ppm (CO$_2$CH$_2$ and C*H*−OH) and 3.60 and 3.40 ppm (CH$_2$N$_3$). The results indicate that the azide anion attacked exclusively the less substituted carbon atom of the epoxide ring. This result is in accordance with previous studies.[74]

The ring-opening reaction was then used to prepare polymers with azide groups from the GMA copolymers. The CRP of glycidyl group-containing monomers is well-documented in the

Table 1. Copolymers of MMA and GMA and the Products of Their Azidation

	poly(GMA-*co*-MMA)		poly(HAZPMA-*co*-MMA)
no.	GMA contents (NMR)	M_n, g/mol $(M_w/M_n)^a$	M_n, g/mol $(M_w/M_n)^a$
1	15 mol % (20 wt %)	20 200 (1.34)	24 200 (1.26)
2	36 mol % (44 wt %)	20 400 (1.44)	23 900 (1.45)

^{a} SEC in THF as the eluent and polyMMA-based calibration.

literature. Examples include the ATRP[77,78] and the nitroxide-mediated polymerization of glycidyl acrylate[79] as well as the ATRP[80−85] and RAFT[86] of GMA. In this work, copolymerization of GMA and MMA using two different monomer feed compositions (10 and 30 mol % of GMA) were carried out in acetone at 50 °C with HMTETA as the ligand for the ATRP catalyst and EBiB as the initiator. It was important to preform the catalyst and then add GMA to the reaction mixture in order to avoid reaction of the free amine (uncomplexed ligand) with the epoxide groups from the monomer that could lead to branching or even cross-linking during the polymerization. The monomer conversions were higher than 70% after ca. 4.5 h. The copolymers were precipitated in ether, dried, and characterized by SEC, ^{1}H NMR, and IR spectroscopy. The results are summarized in Table 1, the ^{1}H NMR spectra are presented in Figure 2a,c, and the IR spectra are shown in Figure 3a,c. The molecular weights were close to the theoretical values based on monomer conversion. The molecular weight distribution of the copolymer containing larger fraction of GMA units was broader than that of the GMA-poorer copolymer but was still monomodal. On the basis of the NMR analysis, the GMA contents of the two copolymers was slightly higher than the monomer feed composition—15 and 36 mol % in the copolymers prepared from monomer mixtures containing 10 and 30 mol % of GMA. The two copolymers are labeled poly(GMA-*co*-MMA)15 and poly(GMA-*co*-MMA)36, respectively, where the number indicates the mole fraction of GMA units.

The ring-opening of the oxirane ring of the two copolymers was carried out at conditions similar to those of the model reaction described above (3 equiv of both sodium azide and ammonium chloride relative to azide groups, DMF, 50 °C) but for longer time (26 h). The reaction is presented in Scheme 1. At the end of the reaction, the copolymers were precipitated in water, washed with water, dried, and analyzed by SEC (Table 1) as well as ^{1}H NMR and IR spectroscopy (Figures 2b,d and 3b,d). The molecular weight distributions of the reaction products were monomodal (SEC traces are shown in Figure 4);
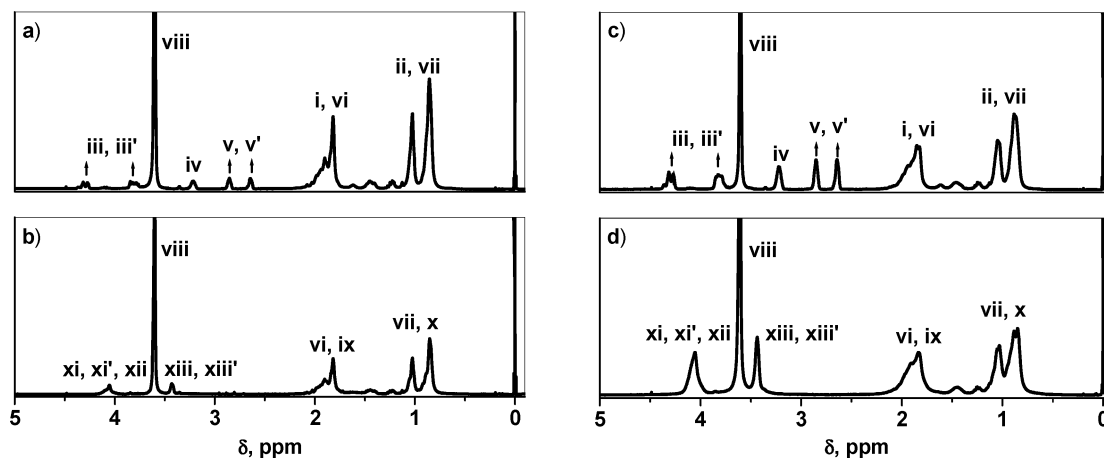
Figure 2. ^{1}H NMR spectra of poly(GMA-*co*-MMA)15 (a), its azidation product, poly(HAZPMA-*co*-MMA)15 (b), poly(GMA-*co*-MMA)36 (c), and its azidation product poly(HAZPMA-*co*-MMA)36 (d).

Figure 3. IR spectra of poly(GMA-*co*-MMA)15 (a), its azidation product, poly(HAZPMA-*co*-MMA)15 (b), poly(GMA-*co*-MMA)36 (c), and its azidation product poly(HAZPMA-*co*-MMA)36 (d).
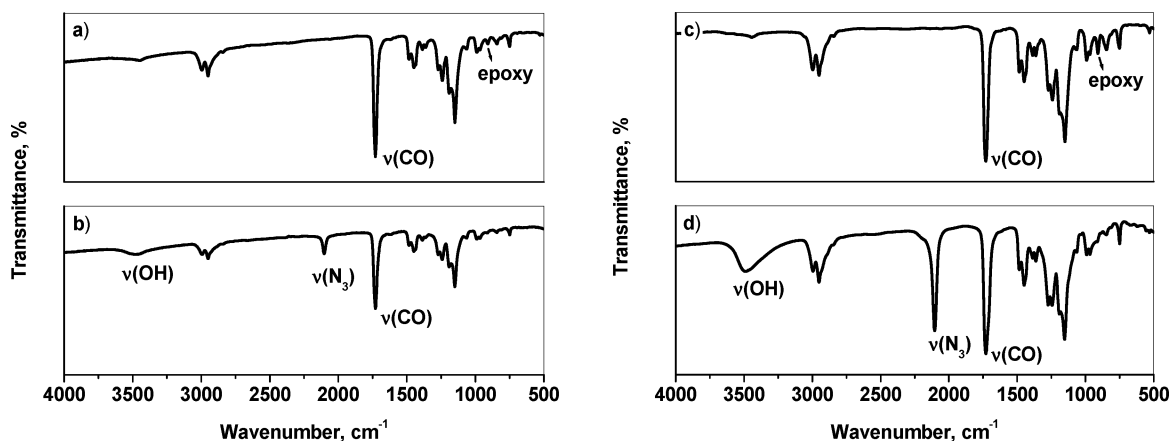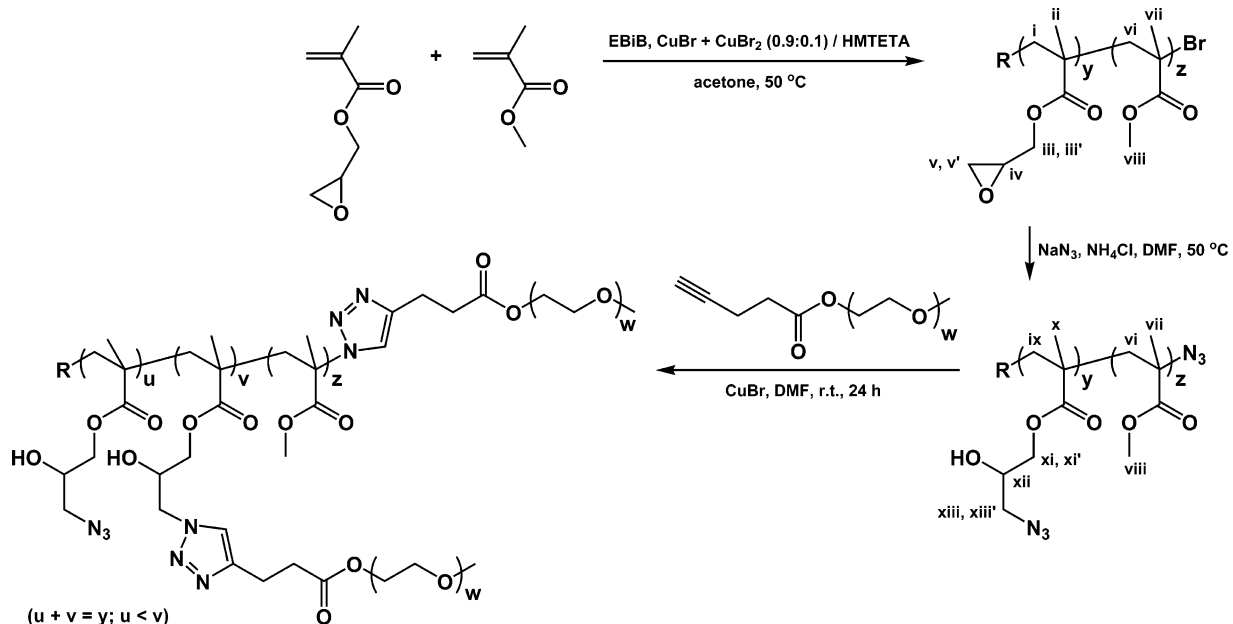
Scheme 1. Copolymerization of GMA and MMA, Ring-Opening of the Epoxide Ring in the Presence of Azide, and Synthesis of Brush Copolymer by a "Grafting Onto" Click Technique

consequently, no branching had taken place during the azidation. Such branching could have resulted from the reaction of alkoxide anion formed during the ring-opening of an epoxide group. The weak acid present in the system (ammonium chloride) apparently protonated rapidly these anions. The

halogen end groups in the copolymers were most likely also converted to azide during the reaction with sodium azide.[87]

The NMR spectra of the starting copolymers and the products of the ring-opening azidation are presented in Figure 2. The spectral characteristics of homo- and copolymers of GMA have
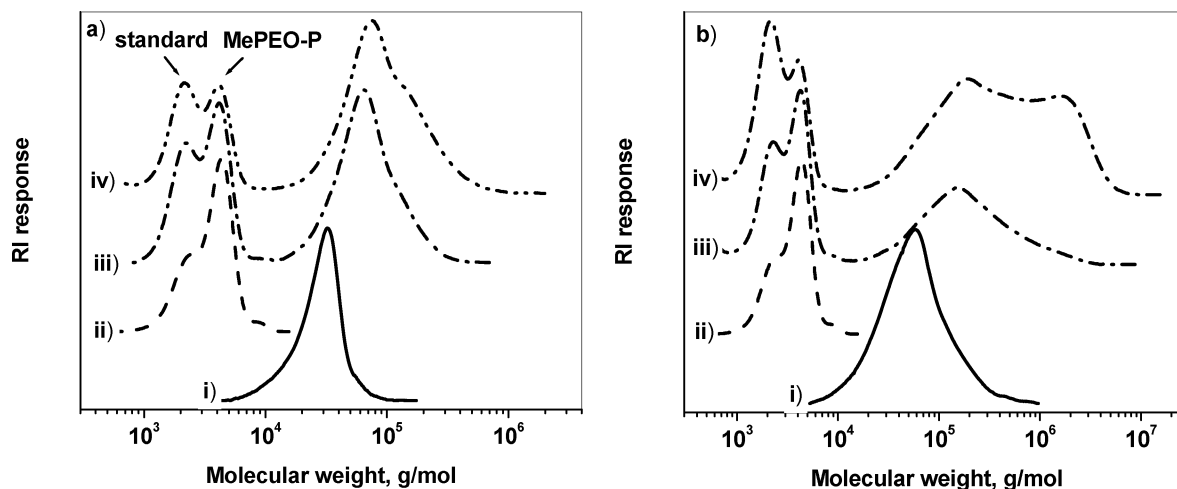
Figure 4. SEC traces of azide-containing polymers (i), mixture of MePEO-P (higher molecular weight) + PEO standard (lower molecular weight) (ii), and the molecular brushes obtained in a click coupling experiment after 1 h in reactions using polymers with alkyne and azide groups (both at 62.5 mM in DMF) with 20 mol % of CuBr (iii) or CuBr/PMDETA (iv) at room temperature. The azide precursors were poly(HAZPMA-*co*-MMA)15 (a) and poly(HAZPMA-*co*-MMA)36 (b).

been studied in detail,[88−90] and the peak assignments shown in Scheme 1 and Figure 2a,c are based on these studies. The peaks belonging to the protons from the epoxide ring at 3.22 ppm (CH from the cycle) and 2.85 and 2.64 ppm (the two protons from the ring CH_2 group) disappeared completely after the reaction with azide, indicating the high efficiency of ring opening. New peaks were observed (Figure 2b,d) at 3.9−4.2 ppm (CO_2CH_2 and CH−OH) and 3.3−3.5 ppm (CH_2N_3), similar to these observed in the model reaction with glycidyl butyrate.

In the IR spectra of the reaction products (Figure 3b,d), a strong absorbance was observed at 2104 cm^{-1} related to the valence vibration of the azide group. The peak at 909 cm^{-1} in the spectra of the starting copolymers, attributed to the epoxide ring,[88,90] was not observed in the spectra of the products. As expected from the copolymer compositions based on NMR analysis of the starting materials, the ratio of the peaks belonging to the azide group (2104 cm^{-1}) and the carbonyl moiety (1729 cm^{-1}) of the azide-containing copolymer derived from poly-(GMA-*co*-MMA)36 (36 mol % of GMA units) was about twice higher than the ratio of the same peaks of the copolymer derived from the copolymer with lower (15 mol %) GMA contents. In the spectra of the products, a broad peak at ca. 3500 cm^{-1} (ν_{OH}) was also seen.

All results presented above clearly demonstrate the very efficient azidation of the epoxide ring-containing copolymers. The prepared azides were used as backbones for a Cu^I-catalyzed click "grafting onto" reaction with a polymeric alkyne, MePEO-P, in DMF. The reactions were carried out at ambient temperature for 1 h with either CuBr or the complex of CuBr with PMDETA as the catalyst (20 mol % relative to azide and alkyne groups). The latter has been shown to be one of the most efficient catalysts in azide−alkyne cycloadditions.[45] During the relatively short reaction time of 1 h, a significant part of the starting MePEO-P was consumed. With the less active catalyst, CuBr, 36 and 44% of the polymeric alkyne had reacted with the polymers poly(HAZPMA-*co*-MMA)15 and poly(HAZPMA-*co*-MMA)36, respectively. When the more active catalyst CuBr/PMDETA was used at the same concentration, the conversions of MePEO-P after 1 h reached 59 and 75% with the two respective backbone polymers. Higher conversion of the alkyne and azide groups was not reached even if the CuBr/PMDETA catalyst concentration was increased 2-fold or after longer

reaction times. In these experiments, the molar amounts of alkyne and azide groups were equal. Additional reactions were carried out in which the ratio of polymeric alkyne (MePEO-P) to azide was increased 2-fold, and the catalyst, CuBr/PMDETA, was used at 20 mol % relative to azide groups. The conversion of azide to triazole groups did not increase compared to the experiments with an alkyne:azide ratio of 1:1. The inability of all azide groups in the HAZPMA−MMA copolymers to participate in the 1,3-dipolar cycloaddition reaction can be attributed to steric hindrance, which increases with the number of attached grafts. Relatively low efficiency is typical in grafting-onto-type preparations of polymer brushes. The results presented here are in accordance with recent data, demonstrating the moderate efficiency of click grafting of PEO chains onto azide-functionalized poly(ε-caprolactonce) backbones, in which the azide groups were separated by several monomer units.[65,66] The efficiency of grafting of a polymer onto polymeric backbones should depend upon several factors including the spatial separation between reactive groups on the backbone and the dimensions of the grafted polymer.

The SEC traces of the starting materials and the polymeric brushes obtained after 1 h in reactions carried out in DMF (62.5 mM azide and alkyne groups) at room temperature with 20 mol % of catalyst relative to the reacting groups are presented in Figure 4. The bimodality in the SEC traces of the graft copolymers, especially pronounced in these derived from the azide-rich poly(HAZPMA-*co*-MMA)36 and at high conversion, was possibly due to the presence of a very small, under the detection limit of MALDI-TOF, amount of dialkyne-terminated PEO in the polymeric pentynoate ester.

Conclusions

Epoxides react with sodium azide in the presence of ammonium chloride to yield the corresponding 1-hydroxy-2-azido compounds. This click reaction was applied to the preparation of copolymers with multiple azide groups derived from well-defined copolymers of MMA and GMA (<40 mol %) prepared by ATRP. The opening of the oxirane ring was very efficient, both in a low molecular weight model compound, glycidyl butyrate, and in the copolymers, as revealed by NMR analysis. The method is a convenient alternative to the synthesis of azide-functionalized polymers by the direct polymerization of monomers with azide groups that are difficult to synthesize and purify

and are explosive. The prepared copolymers were used in a second click reaction (1,3-dipolar cycloaddition) with poly-(ethylene oxide) monomethyl ether pentynoate, catalyzed by CuBr or CuBr/PMDETA, the latter catalyst showing the higher activity. This "grafting onto" approach resulted in the formation of polymeric brushes with hydrophilic PEO side chains with moderate grafting density.

References and Notes

(1) Matyjaszewski, K. *Prog. Polym. Sci.* **2005**, *30*, 858.
(2) Smid, J.; Van Beylen, M.; Hogen-Esch, T. E. *Prog. Polym. Sci.* **2006**, *31*, 1041.
(3) Hadjichristidis, N.; Iatrou, H.; Pitsikalis, M.; Mays, J. *Prog. Polym. Sci.* **2006**, *31*, 1068.
(4) Yagci, Y.; Tasdelen, M. A. *Prog. Polym. Sci.* **2006**, *31*, 1133.
(5) Bielawski, C. W.; Grubbs, R. H. *Prog. Polym. Sci.* **2007**, *32*, 1.
(6) Domski, G. J.; Rose, J. M.; Coates, G. W.; Bolig, A. D.; Brookhart, M. *Prog. Polym. Sci.* **2007**, *32*, 30.
(7) Braunecker, W. A.; Matyjaszewski, K. *Prog. Polym. Sci.* **2007**, *32*, 93.
(8) Yokozawa, T.; Yokoyama, A. *Prog. Polym. Sci.* **2007**, *32*, 147.
(9) Baskaran, D.; Mueller, A. H. E. *Prog. Polym. Sci.* **2007**, *32*, 173.
(10) Goethals, E. J.; Du Prez, F. *Prog. Polym. Sci.* **2007**, *32*, 220.
(11) Penczek, S.; Cypryk, M.; Duda, A.; Kubisa, P.; Slomkowski, S. *Prog. Polym. Sci.* **2007**, *32*, 247.
(12) Matyjaszewski, K., Ed. *Controlled Radical Polymerization; ACS Symp. Ser. 685*; American Chemical Society: Washington, DC, 1998.
(13) Matyjaszewski, K., Ed. *Controlled/Living Radical Polymerization. Progress in ATRP, NMP, and RAFT*; ACS Symp. Ser. 768; American Chemical Society: Washington, DC, 2000.
(14) Matyjaszewski, K.; Davis, T. P., Eds. *Handbook of Radical Polymerization*; Wiley: Hoboken, NJ, 2002.
(15) Matyjaszewski, K., Ed. *Advances in Controlled / Living Radical Polymerization*; ACS Symp. Ser. 854; American Chemical Society: Washington, DC, 2003.
(16) Matyjaszewski, K., Ed. *Controlled/Living Radical Polymerization. From Synthesis to Materials*; ACS Symp. Ser. 944; American Chemical Society: Washington, DC, 2006.
(17) Wang, J.-S.; Matyjaszewski, K. *J. Am. Chem. Soc.* **1995**, *117*, 5614.
(18) Matyjaszewski, K.; Xia, J. *Chem. Rev.* **2001**, *101*, 2921.
(19) Kamigaito, M.; Ando, T.; Sawamoto, M. *Chem. Rev.* **2001**, *101*, 3689.
(20) Hawker, C. J.; Bosman, A. W.; Harth, E. *Chem. Rev.* **2001**, *101*, 3661.
(21) Matyjaszewski, K.; Gaynor, S.; Wang, J.-S. *Macromolecules* **1995**, *28*, 2093.
(22) David, G.; Boyer, C.; Tonnar, J.; Ameduri, B.; Lacroix-Desmazes, P.; Boutevin, B. *Chem. Rev.* **2006**, *106*, 3936.
(23) Moad, G.; Chiefari, J.; Chong, Y. K.; Krstina, J.; Mayadunne, R. T. A.; Postma, A.; Rizzardo, E.; Thang, S. H. *Polym. Int.* **2000**, *49*, 993.
(24) Barner-Kowollik, C.; Davis, T. P.; Heuts, J. P. A.; Stenzel, M. H.; Vana, P.; Whittaker, M. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 365.
(25) Perrier, S.; Takolpuckdee, P. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 5347.
(26) Moad, G.; Rizzardo, E.; Thang, S. H. *Aust. J. Chem.* **2005**, *58*, 379.
(27) Davis, K. A.; Matyjaszewski, K. *Adv. Polym. Sci.* **2002**, *159*, 1.
(28) Coessens, V.; Pintauer, T.; Matyjaszewski, K. *Prog. Polym. Sci.* **2001**, *26*, 337.
(29) Pyun, J.; Kowalewski, T.; Matyjaszewski, K. *Macromol. Rapid Commun.* **2003**, *24*, 1043.
(30) Matyjaszewski, K. *Polym. Int.* **2003**, *52*, 1559.
(31) Pyun, J.; Matyjaszewski, K. *Chem. Mater.* **2001**, *13*, 3436.
(32) Matyjaszewski, K.; Spanswick, J. *Mater. Today* **2005**, *8*, 26.
(33) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004.
(34) Parker, R. E.; Isaacs, N. S. *Chem. Rev.* **1959**, *59*, 737.
(35) Gorzynski Smith, J. *Synthesis* **1984**, 1984.
(36) Gothelf, K. V.; Jorgensen, K. A. *Chem. Rev.* **1998**, *98*, 863.
(37) Himo, F.; Demko, Z. P.; Noodleman, L.; Sharpless, K. B. *J. Am. Chem. Soc.* **2003**, *125*, 9983.
(38) Tsarevsky, N. V.; Bernaerts, K. V.; Dufour, B.; Du Prez, F. E.; Matyjaszewski, K. *Macromolecules* **2004**, *37*, 9308.
(39) Huisgen, R. *Proc. Chem. Soc.* **1961**, 357.
(40) Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 633.

(41) Huisgen, R. *1,3-Dipolar Cycloaddition Chemistry*; Wiley: New York, 1984; Vol. 1.
(42) Tornoe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057.
(43) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596.
(44) Rodionov, V. O.; Fokin, V. V.; Finn, M. G. *Angew. Chem., Int. Ed.* **2005**, *44*, 2.
(45) Golas, P. L.; Tsarevsky, N. V.; Sumerlin, B. S.; Matyjaszewski, K. *Macromolecules* **2006**, *39*, 6451.
(46) Bock, V. D.; Hiemstra, H.; van Maarseveen, J. H. *Eur. J. Org. Chem.* **2006**, 51.
(47) Binder, W. H.; Sachsenhofer, R. *Macromol. Rapid Commun.* **2007**, *28*, 15.
(48) Tsarevsky, N. V.; Sumerlin, B. S.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 3558.
(49) Lutz, J.-F.; Boerner, H. G.; Weichenhan, K. *Macromol. Rapid Commun.* **2005**, *26*, 514.
(50) Lutz, J.-F.; Boerner, H. G.; Weichenhan, K. *Macromolecules* **2006**, *39*, 6376.
(51) Vogt, A. P.; Sumerlin, B. S. *Macromolecules* **2006**, *39*, 5286.
(52) Gondi, S. R.; Vogt, A. P.; Sumerlin, B. S. *Macromolecules* **2007**, *40*, 474.
(53) Sumerlin, B. S.; Tsarevsky, N. V.; Louche, G.; Lee, R. Y.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 7540.
(54) Ladmiral, V.; Mantovani, G.; Clarkson, G. J.; Cauet, S.; Irwin, J. L.; Haddleton, D. M. *J. Am. Chem. Soc.* **2006**, *128*, 4823.
(55) Joralemon, M. J.; O'Reilly, R. K.; Hawker, C. J.; Wooley, K. L. *J. Am. Chem. Soc.* **2005**, *127*, 16892.
(56) O'Reilly, R. K.; Joralemon, M. J.; Hawker, C. J.; Wooley, K. L. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 5203.
(57) Wu, P.; Feldman, A. K.; Nugent, A. K.; Hawker, C. J.; Scheel, A.; Voit, B.; Pyun, J.; Frechet, J. M. J.; Sharpless, K. B.; Fokin, V. V. *Angew. Chem., Int. Ed.* **2004**, *43*, 3928.
(58) Joralemon, M. J.; O'Reilly, R. K.; Matson, J. B.; Nugent, A. K.; Hawker, C. J.; Wooley, K. L. *Macromolecules* **2005**, *38*, 5436.
(59) Opsteen, J. A.; van Hest, J. C. M. *Chem. Commun.* **2005**, 57.
(60) Mantovani, G.; Ladmiral, V.; Tao, L.; Haddleton, D. M. *Chem. Commun.* **2005**, 2089.
(61) Laurent, B. A.; Grayson, S. M. *J. Am. Chem. Soc.* **2006**, *128*, 4238.
(62) Gao, H.; Matyjaszewski, K. *Macromolecules* **2006**, *39*, 4960.
(63) Whittaker, M. R.; Urbani, C. N.; Monteiro, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 11360.
(64) Altintas, O.; Hizal, G.; Tunca, U. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 5699.
(65) Riva, R.; Schmeits, S.; Jerome, C.; Jerome, R.; Lecomte, P. *Macromolecules* **2007**, *40*, 796.
(66) Li, H.; Riva, R.; Jerome, R.; Lecomte, P. *Macromolecules* **2007**, *40*, 824.
(67) Johnson, J. A.; Lewis, D. R.; Diaz, D. D.; Finn, M. G.; Koberstein, J. T.; Turro, N. J. *J. Am. Chem. Soc.* **2006**, *128*, 6564.
(68) Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, *88*, 351.
(69) VanderWerf, C. A.; Hrisler, R. Y.; McEwen, W. E. *J. Am. Chem. Soc.* **1954**, *76*, 1231.
(70) Saito, S.; Takahashi, N.; Ishikawa, T.; Moriwake, T. *Tetrahedron Lett.* **1991**, *32*, 667.
(71) Guy, A.; Doussot, J.; Ferroud, C.; Garreau, R.; Godefroy-Falguieres, A. *Synthesis* **1992**, 821.
(72) Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *J. Org. Chem.* **1999**, *64*, 6094.
(73) Ingham, J. D.; Petty, W. L.; Nichols, j., P. L. *J. Org. Chem.* **1956**, *12*, 373.
(74) Chini, M.; Crotti, P.; Macchia, F. *Tetrahedron Lett.* **1990**, *31*, 5641.
(75) Guy, A.; Dubuffet, T.; Doussot, J.; Godefroy-Falguieres, A. *Synlett* **1991**, 403.
(76) Onaka, M.; Sugita, K.; Izumi, Y. *J. Org. Chem.* **1989**, *54*, 1116.
(77) Matyjaszewski, K.; Coca, S.; Jasieczek, C. B. *Macromol. Chem. Phys.* **1997**, *198*, 4011.
(78) Tsarevsky, N. V.; Sarbu, T.; Goebelt, B.; Matyjaszewski, K. *Macromolecules* **2002**, *35*, 6142.
(79) Benoit, D.; Chaplinski, V.; Braslau, R.; Hawker, C. J. *J. Am. Chem. Soc.* **1999**, *121*, 3904.
(80) Krishnan, R.; Srinivasan, K. S. V. *Macromolecules* **2003**, *36*, 1769.
(81) Krishnan, R.; Srinivasan, K. S. V. *Macromolecules* **2004**, *37*, 3614.
(82) Camero, P. F.; de la Fuente, J. L.; Madruga, E. L.; Fernandez-Garcia, M. *Macromol. Chem. Phys.* **2004**, *205*, 2221.
(83) Dayananda, K.; Dhamodharan, R. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 902.

(84) Li, G.; Zhu, X.; Zhu, J.; Cheng, Z.; Zhang, W. *Polymer* **2005**, *46*, 12716.

(85) De La Fuente, J. L.; Canamero, P. F.; Fernandez-Garcia, M. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 1807.

(86) Zhu, J.; Di, Z.; Zhu, X.; Chen, G. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 2558.

(87) Coessens, V.; Matyjaszewski, K. *J. Macromol. Sci., Pure Appl. Chem.* **1999**, *A36*, 667.

(88) Iwakura, Y.; Toda, F.; Ito, T.; Aoshima, K. *Makromol. Chem.* **1967**, *104*, 26.

(89) Hunter, T. C.; Price, G. J. *Polymer* **1994**, *35*, 3530.

(90) Espinosa, M. H.; del Toro, P. J. O.; Silva, D. Z. *Polymer* **2001**, *42*, 3393.