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Synthesis of Degradable Miktoarm Star Copolymers via Atom Transfer Radical Polymerization

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ABSTRACT: Both nondegradable and degradable miktoarm star copolymers were synthesized via ATRP using the "in−out" method. The synthesis consisted of three steps: synthesis of a linear macroinitiator (MI) using the first monomer, a core-forming reaction with a divinyl compound, and then further chain extension with the second monomer. Various characterization methods, including GPC, NMR, and GC, were used to analyze the initial star polymers and to identify the optimal experimental conditions for the synthesis of the multifunctional star initiators and the miktoarm star copolymers. During the synthesis of miktoarm star copolymers, both interstar and intrastar arm−arm couplings were observed. The initiating efficiency of the alkyl bromide sites in the core of the star polymers was determined by analysis of the linear block copolymers, obtained after cleavage of the degradable star and miktoarm star copolymers. The results confirmed that the initiation efficiency was reduced by the highly cross-linked star core. In the case of degradable miktoarm star copolymers, only 19% of the total Br functionality incorporated into the first star copolymer initiated the polymerization of the second monomer.

Introduction

Star polymers consist of several linear polymer chains connected at one point.[1] Their compact structure and globular shape predetermine their unique properties, such as low solution viscosity, and enable potential applications, including use as drug carriers.[2] Star polymers can be divided into two structural categories: homoarm and miktoarm star polymers. In the former case, the arms are identical in chemical composition, while in the latter case, two or more than two different types of arms build the star molecule. Typically, star polymers are prepared by anionic polymerization because it allows one to control the arm size and size distribution. Drawbacks of this method include stringent reaction conditions, such as high sensitivity to CO_2 and moisture.

In contrast, free radical polymerization is more tolerant to protic impurities and is capable of polymerizing a vast variety of vinyl monomers. However, because of slow initiation and fast radical−radical termination reactions, the resulting materials are polydisperse, and the control over molecular weight and functionality is very difficult. However, recently developed controlled/"living" radical polymerization (CRP) processes allow for the synthesis of well-designed (co)polymers.[3−8] All CRP methods are based on establishing a dynamic equilibrium between a low concentration of active propagating chains and a large number of dormant chains, which are unable to propagate or terminate but can be reactivated. Thus, the fraction of chains that undergo radical−radical termination is reduced, and the radical polymerization system attains a "living" character. One of the most efficient and popular CRP methods is atom transfer radical polymerization (ATRP),[7,9,10] which allows for the synthesis of (co)polymers with predetermined degree of polymerization, narrow molecular weight distribution (low polydispersity, M_w/M_n),[11] high functionality,[12] and desired microstructure.[13−16]

CRP permits the synthesis of star polymers by one of three methods: "core-first",[17−21] "arm-first",[22−24] or their combination.[25,26] The combination of "core-first" and "arm-first" methods is particularly useful in the synthesis of miktoarm star copolymers.[1,19] The procedure involves the synthesis of the first type of polymer chain polyA, which can be used as a macroinitiator (MI) in a subsequent cross-linking reaction using a divinyl compound to produce a $(\text{polyA})_n$−polyX star polymer, where polyX represents the core of the star polymer and n is the number of polyA arms. Because of the "living" nature of the CRP, the initiating sites are preserved in the core of the star polymer (i.e., alkyl halide groups in ATRP), and the star polymer can be used as a multifunctional initiator in the chain extension reaction with a different monomer, B, to yield a miktoarm star copolymer, $(\text{polyA})_n$−polyX−$(\text{polyB})_m$. This combination method for synthesizing miktoarm star copolymers was termed the "in−out" method.[1,25]

One important challenge in the synthesis of miktoarm star copolymers using this method is to determine the initiation efficiency for the chain extension reactions with the second monomer, B, i.e., the percent of initiating sites that actually initiated the polymerization of B. Because of the high cross-linking density in the star core, it can be envisioned that not all of the dormant sites would be efficiently activated in a chain extension reaction. Thus, evaluation of initiation efficiency becomes a significant challenge because the presence of a highly cross-linked core hinders the accurate analysis of star polymers using NMR or GPC.

The strategy proposed here is to degrade the star polymers into the constituent linear polymer chains. Through analysis of the cleaved linear chains by standard techniques, it should be possible to determine the initiation efficiency in the second chain extension reaction. Decomposition of a star polymer requires a degradable cross-linker used in the formation of the star. It is well-known that the disulfide group can be easily cleaved in the presence of various reducing agents,[27,28]

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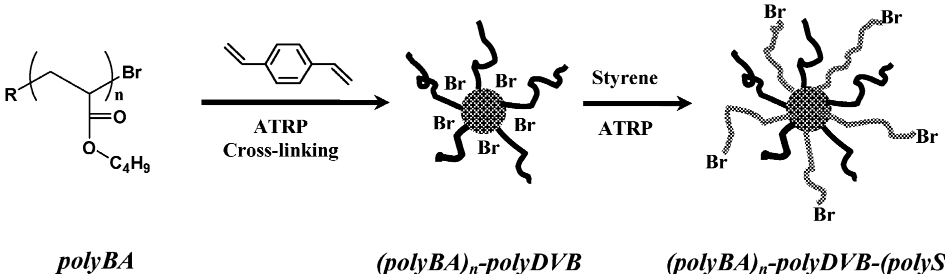
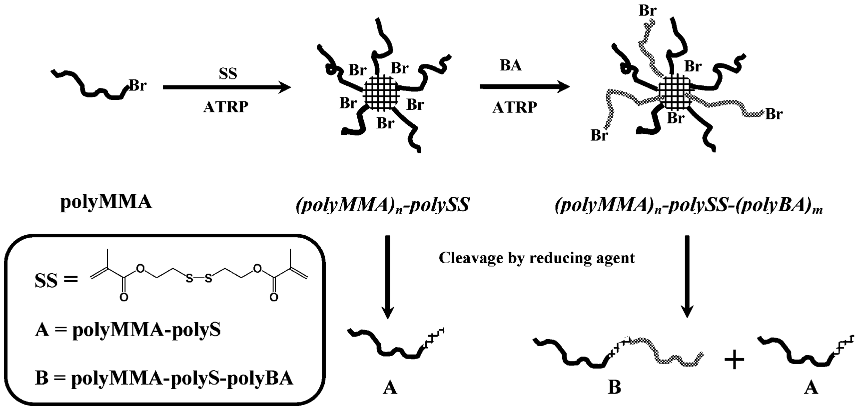
Scheme 1. Scheme of the Synthetic Procedure of (PolyBA)$_n$−PolyDVB−(PolySt)$_m$ Miktoarm Star Copolymers



Scheme 2. Proposed Synthetic Procedure of (PolyMMA)$_n$−PolySS−(PolyBA)$_m$ Miktoarm Star Copolymers and Their Cleavage by a Reducing Agent



such as thiols[29] and phosphines.[30,31] Both initiators and monomers containing disulfide groups were successfully used in ATRP for the preparation of reversibly degradable polymeric materials via a redox process,[32,33] for cleavage of polymers attached to gold surfaces,[34] and for polymers useful in protein modification.[35] Introducing the disulfide group into a divinyl compound should provide a cross-linker with the needed degradability.

This article reports the syntheses of both nondegradable and degradable miktoarm star copolymers via ATRP using the "in−out" method. Two different cross-linkers were used in the synthetic procedures, as shown in Scheme 1 and Scheme 2. For the synthesis of nondegradable miktoarm star copolymers (Scheme 1), ATRP was used to produce a poly(n-butyl acrylate) (polyBA) MI with narrow molecular weight distribution (MWD) and high degree of Br functionality. This was accomplished by employing ethyl 2-bromopropionate (EBrP) as initiator and CuBr/N,N,N',N'',N''-pentamethyldiethylenetriamine (PMDETA) as catalyst. Using ATRP, this polyBA MI was then chain extended, cross-linked with divinylbenzene (DVB) to form nondegradable (polyBA)$_n$−polyDVB star polymers by the "arm-first" method. Finally, polymerization of a second monomer, styrene, initiated by the active alkyl halide initiating sites remaining within the core of the star, formed polystyrene chains (polySt) and thereby a (polyBA)$_n$−polyDVB−(polySt)$_m$ miktoarm star copolymer.

Degradable miktoarm star copolymers were synthesized using a similar strategy: a poly(methyl methacrylate) MI was prepared employing ethyl 2-bromoisobutyrate (EBiB) as initiator and CuBr/2,2′-bipyridine (bpy) as catalyst followed by chain extension with a divinyl monomer containing an internal degradable disulfide link, bis(2-methacryloyloxyethyl) disulfide (SS), producing degradable star polymers. Subsequent polymerization of the second monomer, BA, resulted in a degradable (polyMMA)$_n$−polySS−(polyBA)$_m$ miktoarm star copolymer. The initiating efficiency of the alkyl halide sites within the core of the (polyMMA)$_n$−polySS star polymer in the chain extension with BA was evaluated by GPC and NMR analysis of the linear block copolymers formed when the star and miktoarm star copolymers were cleaved by a reducing agent, tributylphosphine (Bu_3P).

Experimental Section

Materials. Styrene (St, 99%, Aldrich), n-butyl acrylate (BA, 99%, Aldrich), methyl methacrylate (MMA, 99%, Aldrich), and divinylbenzene (DVB, 99%, Aldrich) were purified by passing the neat liquid through a column filled with basic alumina to remove the inhibitor. CuBr (98%, Acros) was purified using a modified literature procedure,[36] namely washing with glacial acetic acid followed by filtration and rinsing with 2-propanol. All other reagents—bis(2-hydroxyethyl) disulfide (99%, TCI), methacryloyl chloride (98%, Aldrich), pyridine, ethyl 2-bromopropionate (EBrP), ethyl 2-bromoisobutyrate (EBiB), N,N,N',N'',N''-pentamethyldiethylenetriamine (PMDETA), 2,2′-bipyridine (bpy), tributylphosphine (Bu_3P), and $CuBr_2$—and all solvents were used as received without further purification.

Synthesis of the Disulfide Cross-Link Agent Bis(2-methacryloyloxyethyl) Disulfide (SS). A clean, dry round-bottom flask containing 200 mL of methylene chloride (dried overnight with $MgSO_4$) was cooled to 0 °C in an ice−water bath. The solvent was purged with N_2 for 30 min before pyridine (15.8 mL, 0.195 mol) and bis(2-hydroxyethyl) disulfide (10.00 g, 0.065 mol) were added. The heterogeneous mixture was magnetically stirred for 10 min before dropwise addition of methacryloyl chloride (18.8 mL, 0.195 mol) over a period of 30 min. The flask was then removed from the ice−water bath, and the reaction was allowed to proceed for 24 h at room temperature. During the reaction, the initially heterogeneous mixture slowly turned into a yellowish solution. The methylene chloride solution was washed successively with 300 mL of 1 M HCl, 300 mL of 1 M NaOH, and 300 mL of deionized water and was then dried over anhydrous $MgSO_4$ overnight. After removing the solvent via rotary evaporation, the product was dissolved in 200 mL of ethyl ether and passed through a column filled with anhydrous Na_2CO_3 and basic alumina (two bands, 30/70 by volume). The absorbent was washed with 50 mL of ethyl ether, and the final product was obtained after removing the ethyl ether from the combined filtrate. The yield of SS cross-linker was 11.9 g (63%), and the monomer structure was verified by ^{1}H NMR spectroscopy (δ, $CDCl_3$ as solvent): 4.40 ppm (t, 2H, CH_2S), 2.95 ppm (t, 2H, CH_2O), 6.12 ppm (s, 1H, $CH_2{=}C(CH_3)$), 5.57 ppm (s, 1H, $CH_2{=}C(CH_3)$), and 1.94 ppm (s, 3H, $CH_2{=}C(CH_3)$). On the basis of the NMR and IR spectral analysis, the final product contained no unreacted methacrylic acid.

Synthesis of PolyBA MI by ATRP. A clean and dry Schlenk flask was charged with BA (24 mL, 0.167 mol), PMDETA (0.291 mL, 1.4 mmol), and DMF (4.0 mL). The flask was degassed by five freeze−pump−thaw cycles. During the final cycle the flask was filled with nitrogen and CuBr (0.200 g, 1.4 mmol) was quickly added to the frozen mixture. Special care was not taken to avoid moisture condensation. The flask was sealed with a glass stopper and then evacuated and backfilled with nitrogen five times before it was immersed in an oil bath at 60 °C. Finally, the N_2-purged initiator EBrP (0.181 mL, 1.4 mmol) was injected into the reaction system, via a syringe, through the sidearm of the Schlenk flask. At timed intervals, samples were withdrawn via a N_2-purged syringe fitted with stainless steel needle and diluted with THF. The samples were used to measure the monomer conversion and polymer molecular weights by GC and GPC, respectively. The reaction was stopped after 1.5 h, at about 60% BA conversion, via exposure to air and dilution with THF. The solution was filtered through a column filled with neutral alumina to remove the copper complex before the polymer was precipitated by addition to a methanol/water mixture (1/1 by volume). The precipitant was dried under vacuum at 60 °C for 2 days. The polyBA MI had $M_n = 9000$ g/mol and $M_w/M_n = 1.12$.

Synthesis of (PolyBA)$_n$−PolyDVB Star Polymer Using PolyBA as MI. PolyBA MI (1.0 g, 111 μmol), DVB (0.237 mL, 1.67 mmol), PMDETA (23.2 μL, 111 μmol), and anisole (4.0 mL) were charged to a Schlenk flask. The flask was degassed by five freeze−pump−thaw cycles and filled with nitrogen. CuBr (15.9 mg, 111 μmol) was quickly added to the frozen mixture. The flask was sealed with a glass stopper and then evacuated and backfilled with nitrogen five times before being immersed in a 110 °C oil bath. At timed intervals, samples for GC and GPC analysis were withdrawn via syringe. After 20 h (ca. 86% DVB conversion by GC), the reaction mixture was exposed to air and diluted with THF. The solution was filtered through a column filled with neutral alumina to remove the copper complex before the polymer was precipitated in a methanol/water mixture (1/1 by volume). Finally, the polymer product was dried under vacuum at 60 °C for 2 days.

Synthesis of (PolyBA)$_n$−PolyDVB−(PolySt)$_m$ Miktoarm Star Copolymer Using (PolyBA)$_n$−PolyDVB Star Polymer as a Multifunctional MI. The synthesis and postpurification procedures for the (polyBA)$_n$−polyDVB−(polySt)$_m$ miktoarm star copolymers were similar to those of (polyBA)$_n$−polyDVB star polymers. Assuming there was no loss for Br functionality during the synthesis of the star MI, the number of initiating sites per star molecule would be the same as the number of arms per star. A typical reaction mixture composition was (polyBA)$_n$−polyDVB star MI (0.233 g, 21.8 μmol of alkyl bromide initiating sites), St (1 mL, 8.7 mmol), PMDETA (9.1 μL, 43.6 μmol), DMF (3 mL), CuBr (5.6 mg, 39.0 μmol), and $CuBr_2$ (1.0 mg, 4.5 μmol). The reaction was conducted at 110 °C. Samples for GC and GPC measurements were periodically withdrawn, and the reaction was stopped after 21.5 h at approximately 14% St conversion.

Synthesis of PolyMMA MI by ATRP. The synthetic procedure for the preparation of polyMMA MI was similar to that for the polyBA MI. MMA (20 mL, 0.187 mol) was polymerized using EBiB (0.274 mL, 1.87 mmol) as the initiator and CuBr (0.134 g, 0.93 mmol)/bpy (0.292 g, 1.87 mmol) as the catalyst. The reaction was carried out at 50 °C in acetone (12.0 mL), containing 0.8 mL of anisole as internal standard for GC analysis. At timed intervals, samples were withdrawn for GC measurement of MMA conversion. After removal of acetone by evaporation, the sample was dissolved in THF for measurement of molecular weight using GPC. The reaction was stopped at 60% MMA conversion after 2 h by exposure to air and dilution with acetone. Polymers were purified via filtration through a column filled with neutral alumina before precipitation in hexane. The final product was dried under vacuum at 60 °C for 2 days. $M_n = 8800$ g/mol, $M_w/M_n = 1.40$.

Synthesis of (PolyMMA)$_n$−PolySS Star Polymer Using PolyMMA as MI. The synthetic procedure of (polyMMA)$_n$−polySS star polymers was similar to that of (polyBA)$_n$−polyDVB star polymers. With polyMMA of $M_n = 8800$ g/mol (1.0 g, 114 μmol) as MI, degradable cross-linker SS (1.15 g, 3.97 mmol) was polymerized with CuBr (16.3 mg, 114 μmol)/bpy (35.5 mg, 227 μmol) as catalyst in acetone (8.0 mL) containing 0.4 mL of anisole. The reaction temperature was 50 °C. At timed intervals, samples were withdrawn for the analysis of SS conversion and polymer molecular weight via ^{1}H NMR and GPC, respectively. After 10 h, the reaction was stopped at about 64% conversion of SS by exposure to air and dilution with acetone. The solution was filtered through a column filled with neutral alumina, and the final star copolymer was obtained after precipitation into hexane and drying under vacuum at 60 °C for 2 days.

Synthesis of (PolyMMA)$_n$−PolySS−(PolyBA)$_m$ Miktoarm Star Copolymer Using (PolyMMA)$_n$−PolySS Star Polymer as MI. The synthetic procedure of (polyMMA)$_n$−polySS-(polyBA)$_m$ miktoarm star copolymers was similar to that employed for the (polyBA)$_n$−polyDVB−(polySt)$_m$ miktoarm star copolymers. The polymerization was carried out at 60 °C using (polyMMA)$_n$−polySS star MI (0.38 g, 24.8 μmol of −Br initiating sites), BA (1.61 mL, 11.2 mmol), PMDETA (10.4 μL, 49.8 μmol), CuBr (6.4 mg, 44.6 μmol), $CuBr_2$ (1.1 mg, 4.92 μmol), and DMF (4 mL) as reactants. The reaction was stopped after 20 h by exposure to air and dilution with THF, ca. 25% BA conversion. To purify the polymer, the copper complex was removed by filtration through a column filled with neutral Al_2O_3, and then the polymer was precipitated in hexane and dried under vacuum at 60 °C for 2 days.

Cleavage of Star Polymers and Miktoarm Star Copolymers with Disulfide Core by Reducing Agent. In a typical procedure, 0.1 g of the star polymer or 0.05 g of the miktoarm star copolymer was mixed with 5 mL of 0.08 M Bu_3P in THF. The solution was stirred magnetically at room temperature. Samples were periodically withdrawn to determine the molecular weights of the product of the reductive cleavage using GPC.

Characterization. Monomer conversions were determined from the concentration of the unreacted monomer in the samples periodically removed from the reactions using a Shimadzu GC-14A gas chromatograph, equipped with a capillary column (DB-Wax, 30 m × 0.54 mm × 0.5 μm, J&W Scientific). The conversion of SS was measured using ^{1}H NMR (with $CDCl_3$ as the solvent). In both techniques, DMF or anisole was used as an internal standard for the calculation of monomer conversion. The molecular weights and MWD of the samples were measured by GPC (Polymer Standards Services (PSS) columns (guard, 10^5, 10^3, and 10^2 Å), with THF eluent at 35 °C, flow rate = 1.00 mL/min, and differential refractive index (RI) detector (Waters, 2410)). Toluene was the internal standard; the apparent molecular weights were determined with a calibration based on linear polySt or polyMMA standards using WinGPC 6.0 software from PSS. The detectors employed to measure the absolute molecular weights were a RI detector (Wyatt Technology, Optilab REX) and a multiangle laser light scattering (MALLS) detector (Wyatt Technology, DAWN EOS) with the light wavelength at 690 nm. The same RI detector was used to determine the refractive index increment (dn/dc) of the star and miktoarm star samples in THF at 35 °C with the light wavelength at 690 nm. Absolute molecular weights were determined using ASTRA software from Wyatt Technology. NMR spectra of the polymer solutions in $CDCl_3$ or THF-d_8 were collected on Bruker Avance 300 MHz spectrometer at 27 °C.

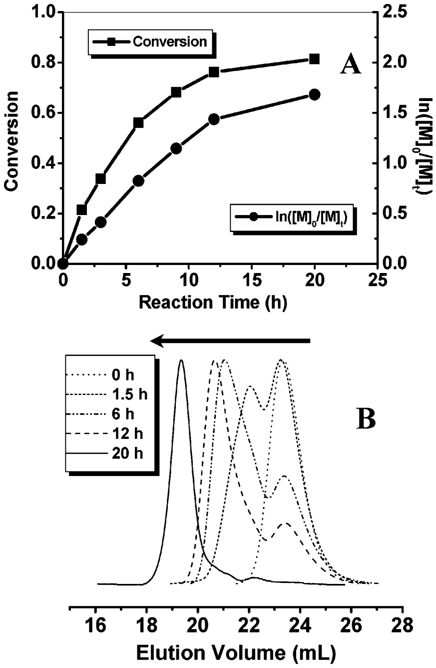


Figure 1. Dependence of DVB conversion and ln([M]$_0$/[M]) on reaction time (A) and GPC traces (B) during the synthesis of (polyBA)$_n$–polyDVB star polymers. Experimental conditions: [DVB]/15 = [polyBA-Br] = [CuBr] = [PMDETA] = 0.018 M in anisole at 110 °C. GPC conditions: RI detector, linear polySt as standard.

Results and Discussion

Synthesis of (PolyBA)$_n$–PolyDVB–(PolySt)$_m$ Miktoarm Star Copolymers by ATRP. Generally, three steps are needed to synthesize (polyA)$_n$–polyX–(polyB)$_m$ miktoarm star copolymers using ATRP via the "in–out" method. First, a highly functionalized mono-Br-terminated linear polymer, polyA, is synthesized via ATRP. Then, a divinyl compound (X) is employed to chain extend and cross-link the polyA MI into (polyA)$_n$–polyX star polymer. Finally, polymer chains of a second monomer, polyB, are grown from the alkyl halide initiating sites located in the core of (polyA)$_n$–polyX star polymer to produce the desired (polyA)$_n$–polyX–(polyB)$_m$ miktoarm star copolymer. DVB was selected as the cross-linker for the synthesis of nondegradable miktoarm star copolymers with polyBA and polySt arms (Scheme 1) because the chain extension from polyBA to DVB is easily accomplished in ATRP and the chemical structure of DVB is similar to the subsequent monomer, St. In other words, the initiation efficiency in the two chain extension steps is expected to be sufficiently high.[37]

Synthesis of (PolyBA)$_n$–PolyDVB Star Polymers. Linear polyBA chains (M_n = 9000 g/mol, M_w/M_n = 1.12) were synthesized via ATRP by employing EBrP as initiator and CuBr/PMDETA as catalyst at 60 °C. With this polyBA polymer as MI, a ratio of [DVB]/[polyBA-Br]/[CuBr]/[PMDETA] = 15/1/1/1 (Figure 1A) was employed for the synthesis of the (polyBA)$_n$–polyDVB star polymer, and a semilogarithmic kinetic plot was linear up to ca. 60% DVB conversion. A possible reason for the curvature at higher DVB conversion was that some alkyl bromide initiating sites inside the highly cross-linked polyDVB core became less accessible and less likely to be activated and react with DVB. The GPC curves in Figure 1B indicate that as the conversion of DVB increased, the amount of polyBA chains incorporated into the star polymers increased, which was confirmed by the decreasing RI signal corresponding to the unreacted linear polyBA MI. After a 20 h reaction period nearly all the MI molecules were incorporated into the star polymers, and the peak representing unreacted linear polyBA chains became undetectable. The GPC elution volume of the product, (polyBA)$_n$–polyDVB star polymers, gradually decreased due to the increasing hydrodynamic volume and star formation.

Polymers with a complex structure, such as stars or brush-like polymers, have a more compact structure than the corresponding linear polymers of the same molecular weight. Therefore, when a mass-sensitive detector (e.g., RI detector) is used in GPC measurements, the apparent molecular weight values determined with a calibration based on linear polymer standards are smaller than the true molecular weight.[39] A more advanced and accurate technique is to measure the molecular weights of star polymers using light scattering techniques. A MALLS detector was used in conjunction with GPC for this purpose. The absolute molecular weights of (polyBA)$_n$–polyDVB star polymers were calculated with the assumption that all of the star polymers (Table 1, entries 2–8) had the same dn/dc value (0.072 ± 0.003 mL/g), which was equal to the measured dn/dc for the (polyBA)$_n$–polyDVB star polymer in Table 1, entry 5. Because of the similarity of repeating unit structure, it is assumed that the dn/dc of the polyDVB segment is equal to that of polySt homopolymer (0.195 mL/g).[38] However, the actual measured dn/dc value of the star polymer was closer to that for polyBA homopolymers in THF (0.065 mL/g)[38] because the weight fraction of polyBA arms in the star polymer (e.g., 85 wt % for Table 1, entry 5) was dominant. Therefore, the (polyBA)$_n$–polyDVB star polymers listed in Table 1 should have the dn/dc values close to 0.072 ± 0.003 mL/g. The peak molecular weights (M_p) of the star polymers were obtained when the [DVB]/[polyBA-Br] ratio was 15/1. Although the M_p values using either RI detector or MALLS detector increased with DVB conversion, their ratio ($M_{p,MALLS}/M_{p,RI}$) also changed gradually. As a general trend, this ratio increases as the star polymer becomes more compact. When the DVB conversion reached ca. 86%, after 20 h reaction, the molecular weight of (polyBA)$_n$–polyDVB star polymers obtained from the MALLS detector was more than 3 times larger than that determined from the RI detector (Table 1, entry 5). The number-average value of the number of arms per star molecule (N_{arm}) was calculated using the following equation:

$$N_{arm} = \frac{M_{p,star} \times arm_{wt\%}}{M_{p,polyBA}} = \frac{M_{p,star}}{M_{p,polyBA} + M_{DVB} \times conv_{DVB} \times [DVB]/[polyBA\text{-}Br]} \qquad (1)$$

where $M_{p,star}$ and $M_{p,polyBA}$ are the peak molecular weights of (polyBA)$_n$–polyDVB star and polyBA MI from GPC-MALLS measurement; $arm_{wt\%}$ is the weight fraction of polyBA arm in the star polymer, M_{DVB} is the molecular weight of DVB, and [DVB]/[polyBA-Br] is the molar ratio of the added DVB to polyBA before polymerization. The conversion of DVB ($conv_{DVB}$) was determined using GC. The results listed in Table 1 (entries 1–5) show that the number-average arm number per star increased with DVB conversion and reached 25

Table 1. Synthesis of (PolyBA)$_n$−PolyDVB Star Polymers at Various Ratio of [DVB]/[PolyBA-Br][a]

entry	[DVB]/[polyBA-Br]	time (h)	conv[b]	$M_{p,RI}$[c] (g/mol)	$M_{p,MALLS}$[e] (g/mol)	M_w/M_n[e]	$M_{p,MALLS}/M_{p,RI}$	N_{arm}[f]
1	15	0	0	9 000[d]	9 500	1.03		
2	15	1.5	0.214	27 600	44 000	2.60	1.59	4.4
3	15	6	0.561	60 400	106 000	3.25	1.75	10.0
4	15	12	0.762	82 100	202 500	2.05	2.47	18.4
5	15	20	0.862	92 300	279 300	1.37	3.03	25.0
6	5	20	0.960	64 900	107 200	2.89	1.65	10.6
7	10	20	0.907	112 100	236 200	1.54	2.11	22.1
8	40	20	0.702	173 400	835 000	1.89	4.82	63.5

[a] Experimental conditions: [polyBA-Br] = [CuBr] = [PMDETA] = 0.018 M in anisole at 110 °C. [b] Conversion of DVB, determined by GC measurement. [c] GPC in THF with RI detector, calibration with linear polySt as standard. [d] Number-average molecular weight from GPC-RI measurement. [e] GPC in THF with MALLS detector, dn/dc (polyBA) = 0.065 mL/g,[38] dn/dc (entries 2−8) = 0.072 ± 0.003 mL/g. [f] Number-average value of the number of arms per star molecule (N_{arm}) was calculated from eq 1.

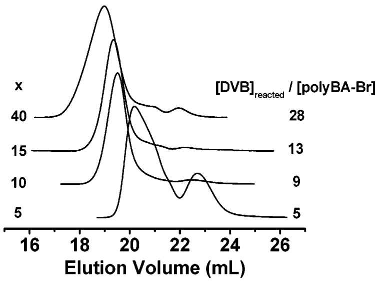


Figure 2. Effect of the molar ratio of DVB to polyBA MI on the synthesis of (polyBA)$_n$−polyDVB star polymers. Experimental conditions: [DVB]/x = [polyBA-Br] = [CuBr] = [PMDETA] = 0.018 M in anisole at 110 °C, reaction time 20 h. GPC conditions: RI detector, linear polySt as standard.

arms per star when the DVB conversion was ca. 86%. The molar ratios of [DVB]/[polyBA-Br] were varied in order to study the influence of the amount DVB added to the reaction on the yield of the star polymer and the average arm number per star. The results are shown in Figure 2. As the amount of DVB added to the reaction increased, the size of star polymers also increased, which is confirmed not only by the larger hydrodynamic volume of the reaction product but also by the increased number of arm per star molecule (Table 1, entries 5−8). Figure 2 shows that some unreacted polyBA MI remained even at high DVB conversion when the molar ratio of [DVB]/[polyBA-Br] was 5/1; however, when this ratio was 15/1 or 10/1, the presence of unreacted MI at high DVB conversion was nearly undetectable. Although the polyBA chains were "living", which will be demonstrated later, not all of them could be incorporated into the star molecules. A detailed examination of Figure 2 reveals that the low molecular weight species in the case of [DVB]/[polyBA-Br] = 40/1 eluted earlier than those in the case of 5/1. A plausible explanation is that in the case of 40/1 the small peak corresponding to low molecular weight polymer represented star with only several arms. These small stars could be formed at high amount of DVB, which did not favor the formation of a single population of highly organized star macromolecules. Figure 2 demonstrates that at a mole ratio of [DVB]/[polyBA-Br] = 15/1 the amount of unreacted polyBA MI was the lowest and the obtained star polymers had a relatively narrow MWD (M_w/M_n = 1.37) characterized by GPC-MALLS and symmetric GPC elution curve. Furthermore, the calculated number-average arm number per star was sufficiently high (25) for further synthesis of (polyBA)$_n$−polyDVB−(polySt)$_m$ miktoarm star copolymers. Thus, the star polymer in entry 5 of Table 1 was used as multifunctional star MI for further chain extension reactions.

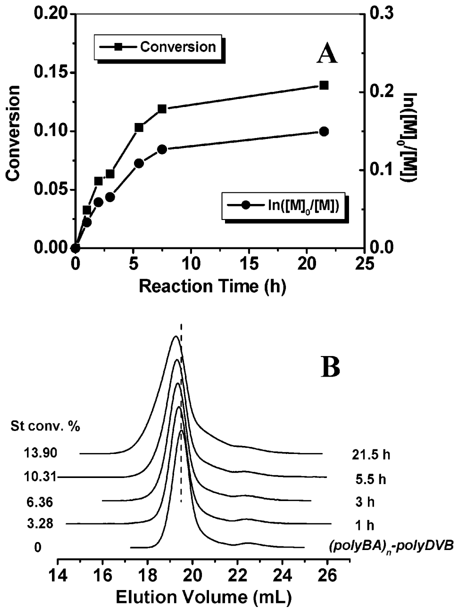


Figure 3. Dependence of St conversion and ln([M]$_0$/[M]) on reaction time (A) and GPC traces (B) during the synthesis of (polyBA)$_n$−polyDVB−(polySt)$_m$ miktoarm star copolymers. Experimental conditions: [St]/400 = [initiating sites]/1 = [CuBr]/1.8 = [CuBr$_2$]/0.2 = [PMDETA]/2 = 0.005 M, 110 °C in DMF. GPC conditions: RI detector, linear polySt as standard.

Synthesis of (PolyBA)$_n$−PolyDVB−(PolySt)$_m$ Miktoarm Star Copolymers. Since the alkyl halide initiating sites in the core of (polyBA)$_n$−polyDVB star polymers were still "living", the ATRP of St from these sites produced (polyBA)$_n$−polyDVB−(polySt)$_m$ miktoarm star copolymers. Figure 3A shows that the conversion of St reached 14% after 21.5 h reaction. The curvature of the semilogarithmic kinetic plot could be due to intrastar arm−arm radical coupling, which is a likely process due to the close distance between two active initiating sites in one star molecule. The obtained miktoarm star copolymer had a larger hydrodynamic volume than the parent star MI, (polyBA)$_n$−polyDVB. In Figure 3B, the peak elution volume (V_p) of the miktoarm star copolymers decreased from 19.51 mL for the star MI to 19.27 mL after 21.5 h polymerization of St. Correspondingly, the absolute molecular weights of the miktoarm star copolymers increased from 2.79 × 10^5 to 4.44 × 10^5 g/mol (determined from GPC-MALLS), in which the dn/dc value of (polyBA)$_n$−polyDVB−(polySt)$_m$ miktoarm star copolymer was measured as 0.091 ± 0.003 mL/g.

NMR was used to determine the chemical composition of the (polyBA)$_n$−polyDVB star and (polyBA)$_n$−poly-

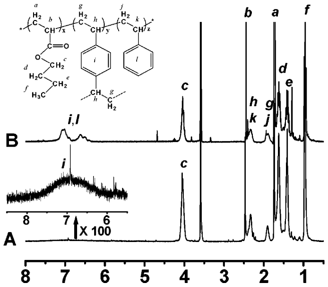


Figure 4. ^{1}H NMR spectra of (polyBA)$_n$−polyDVB star polymer (A) and (polyBA)$_n$−polyDVB−(polySt)$_m$ miktoarm star copolymers (B). NMR conditions: 27 °C, THF-d_8 as solvent.

DVB−(polySt)$_m$ miktoarm star copolymers (Figure 4). Comparing the peak area of *c* (CH_2CH_2O from BA unit) and *i, j* (phenyl protons from St and DVB units), the molar ratio of BA and DVB units in (polyBA)$_n$−polyDVB star polymers was 1.00/0.10, and the molar ratio of BA, DVB, and St units in the miktoarm star copolymer was 1.00/0.10/0.50. It should be noted that since the star polymer contained a highly cross-linked polyDVB core, the integration of peak area of polyDVB in Figure 4A was not very accurate. The phenyl protons from polyDVB core showed a weak and broad peak in NMR spectrum due to the partial immobilization of the cross-linked polyDVB in the star core.[40] The amplified plot (×100) is shown in Figure 4. Such an error is inevitable for the NMR analysis of cross-linked polymers or microgels, particularly since an alternative method, GC measurement, showed that the conversion of DVB was 86.2% during the synthesis of (polyBA)$_n$−polyDVB star polymer. Combining this GC result with the molecular weight of polyBA MI ($M_n = 9000$ g/mol), the molar ratio of BA and DVB in the star was 1.00/0.18, which confirmed that NMR measurement underestimated the polyDVB content in the star and miktoarm star copolymers.

Since the average number of arms per star molecule was relatively large (25), it was reasonable to expect that some of the alkyl bromide sites in the core of (polyBA)$_n$−polyDVB star would not be accessible. Therefore, during the synthesis of (polyBA)$_n$−polyDVB-(polySt)$_m$ miktoarm star copolymers, not all the initiating sites have the chance to initiate the polymerization of St. To study the initiation efficiency of these alkyl bromide sites during the extension of second linear polymer chains, it is necessary to degrade the miktoarm star product into the constituent linear chains and analyze the cleaved linear chains using standard techniques, such as NMR and GPC. Accordingly, a miktoarm star copolymer with a chemically degradable core was synthesized.

Synthesis of (PolyMMA)$_n$−PolySS−(PolyBA)$_m$ Miktoarm Star Copolymers by ATRP. A degradable divinyl cross-linker (SS) was synthesized and used to prepare (polyMMA)$_n$−polySS−(polyBA)$_m$ miktoarm star copolymers, as illustrated in Scheme 2. Initially, polyMMA MI was synthesized by ATRP with EBiB as the initiator and CuBr/bpy as the catalyst. The produced linear polyMMA ($M_n = 8800$ g/mol, $M_w/M_n = 1.40$) was then used as MI to initiate the ATRP of SS cross-linker and formed (polyMMA)$_n$−polySS star polymers.

Synthesis of (PolyMMA)$_n$−PolySS Star Polymers. Figure 5 shows the dependence of SS conversion on reaction time for this reaction as well as the evolution of GPC traces of the produced star polymer with increasing SS conversion. It should be noted that the SS conversion determined by NMR reflected the consumption of the vinyl bond in the SS cross-linker, not SS monomer itself. Since each SS monomer contains two vinyl bonds, the SS conversion measured by NMR could be underestimated, although some unreacted vinyl bonds from SS monomer, located in the cross-linked core of (polyMMA)$_n$−polySS star polymer, could be undetectable by NMR measurement. The conversion of SS reached ca. 65% after 10 h reaction. The semilogarithmic kinetic plot deviated from linearity when SS conversion was above 30%. A possible explanation is that the embedded alkyl bromide initiating sites in the highly cross-linked star core became less likely to react with SS monomer, as discussed above. GPC results in Figure 5B indicate that, with the increase of SS conversion, more polyMMA linear chains were incorporated into the star polymer, and at ca. 65% SS conversion, 20% polyMMA MI remained unreacted. These residual MI chains were expected to be a mixture of "living" polyMMA and inactive polyMMA chains, and this conjecture will be confirmed later. The absolute molecular weight ($M_{p,MALLS}$) of the (polyMMA)$_n$−polySS star polymer was determined by GPC-MALLS measurement under the assumption that its d*n*/d*c* value is the same as that of polyMMA homopolymer (0.088 mL/g).[38] Such an assumption was supported by the fact that both polySS and polyMMA had the similar repeating unit structure, and the core segment contributed less to the d*n*/d*c* value of the star copolymer, as discussed above. The obtained $M_{p,MALLS}$ value of the (polyMMA)$_n$−polySS star polymer was much larger than the $M_{p,RI}$ value (Table 2, entries 1−4). As the star polymer became more compact (i.e., at higher SS conversion), the ratio of $M_{p,MALLS}/M_{p,RI}$ increased. Calculated from eq 1, the number-average arm number per (polyMMA)$_n$−polySS star molecule increased gradually with the consumption of SS and finally reached 46.8 arms per star on average (Table 2, entry 4). The optimal ratio of [SS], [polyMMA-Br], and [CuBr] (35/1/1) was obtained from a

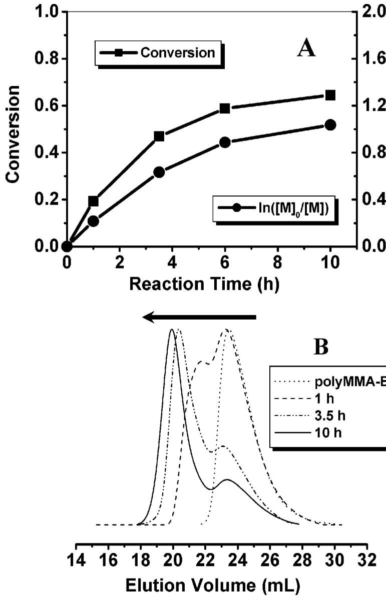


Figure 5. Dependence of SS conversion and ln([M]$_0$/[M]) on reaction time (A) and GPC traces (B) during the synthesis of (polyMMA)$_n$−polySS star polymers. Experimental conditions: [SS]/35 = [polyMMA-Br] = [CuBr] = [bpy]/2 = 0.011 M in acetone at 50 °C. GPC conditions: RI detector, linear polyMMA as standard.

Table 2. Synthesis of (PolyMMA)$_n$−PolySS Star Polymers via ATRP[a]

entry	[SS]/[CuBr/bpy$_2$]/[polyMMA-Br]	time (h)	conv[b]	$M_{p,RI}$ (g/mol)[c]	$M_{p,MALLS}$ (g/mol)[e]	M_w/M_n[e]	$M_{p,MALLS}/M_{p,RI}$	N_{arm}[f]
1	35/1/1	0	0	8 800[d]	12 600	1.19		
2	35/1/1	1	0.194	40 600	124 600	3.57	3.07	8.6
3	35/1/1	3.5	0.469	107 800	369 600	7.95	3.43	21.3
4	35/1/1	10	0.645	153 100	896 300	5.55	5.85	46.8
5	20/1.5/1	10	0.743	81 600	317 800	6.90	3.89	18.8
6	35/1.8/1	10	0.557	94 300	533 900	4.38	5.66	29.2

[a] Experimental conditions: [polyMMA-Br] = 0.011 M in acetone at 50 °C. [b] Conversion of SS, determined by ^{1}H NMR. [c] GPC in THF with RI detector, calibration with linear polyMMA as standard. [d] Number-average molecular weight from GPC-RI measurement. [e] GPC in THF with MALLS detector, d*n*/d*c* = 0.088 mL/g.[38] [f] Number-average value of the number of arms per star molecule (N_{arm}) was calculated from eq 1.

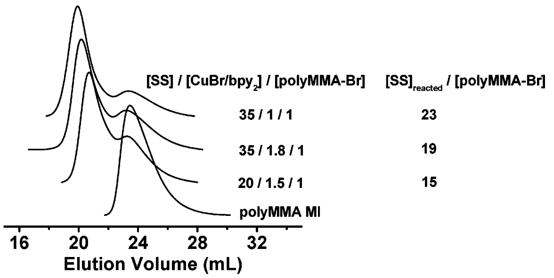


Figure 6. Effects of the molar ratio of SS and CuBr/bpy$_2$ to polyMMA MI during the synthesis of (polyMMA)$_n$−polySS star polymer. Experimental conditions: [polyMMA-Br] = 0.011 M in acetone at 50 °C, reaction time 10 h. GPC conditions: RI detector, linear polyMMA as standard.

detailed study of the influence of the molar ratio of these reactants on the yield of the (polyMMA)$_n$−polySS star polymers. Figure 6 shows the GPC results of three reactions carried out at various molar ratios of [SS]/[polyMMA-Br]/[CuBr]. After 10 h reaction, the amount of unreacted polyMMA MI was the lowest when the ratio was 35/1/1. Table 2 (entries 4−6) shows that the star polymers in entry 4 obtained under the above condition had more arms per star (N_{arm} = 46.8) and more compact structure ($M_{p,MALLS}/M_{p,RI}$ = 5.85) than the other synthesized star polymers.

Cleavage of (PolyMMA)$_n$−PolySS Star Polymers by Reducing Agent. Before chain extension with the second monomer, BA, from the core of the (polyMMA)$_n$−polySS star polymer, it was important to examine its degradability. The efficiency of the reductive cleavage was crucial not only for the further studies of the initiation efficiency of the alkyl halide sites in the star core but also of interest due to the potential application of the star polymers as degradable carriers for drugs or bioactive compounds. The (polyMMA)$_n$−polySS star polymer was completely cleaved into linear chains within 1 h after mixing with 5 mL of 0.08 M Bu_3P solution in THF, as recorded in Figure 7. Similar high cleavage efficiency was reported in the case of degradable gels with disulfide cross-linker.[33] The product of the reductive degradation had a single GPC elution peak, which represented a polymer with higher molecular weight than the starting polyMMA MI. This indicated that the cleaved product was not the initial polyMMA MI homopolymer, but a polyMMA-*b*-polyS block copolymer, where S represents the $CH_2{-}C(CH_3)(COOCH_2CH_2SH)$ unit. Based on NMR and GPC results, the chemical composition of the above linear block copolymer was MMA_{88}-*b*-S_{36}. Since one SS monomer contains two S subunits, the molar ratio of MMA and SS units in the (polyMMA)$_n$−polySS star molecule was 88/18, which agrees well with the ratio (88/23), determined by the SS conversion measurement.

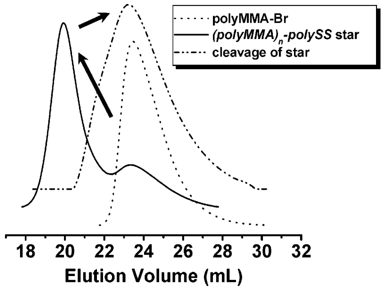


Figure 7. Cleavage of (polyMMA)$_n$−polySS star polymers by reducing agent, Bu_3P, experimental condition: 0.1 g of star polymer in 5 mL of 0.08 M Bu_3P THF solution, room temperature, 1 h. GPC conditions: RI detector, linear polyMMA as standard.

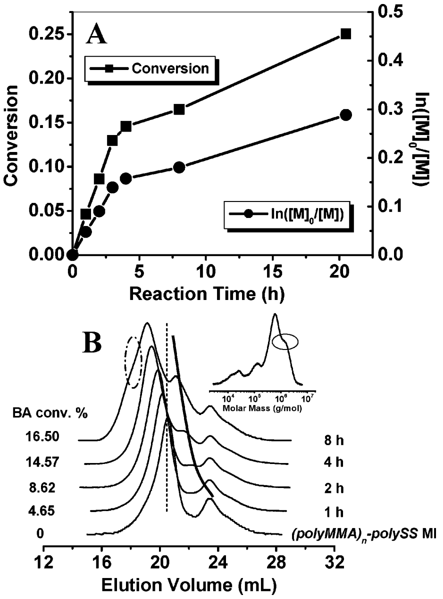


Figure 8. Dependence of BA conversion and ln([M]$_0$/[M]) on reaction time (A), GPC traces (B) during the synthesis of (polyMMA)$_n$−polySS−(polyBA)$_m$ miktoarm star copolymers (B inset is the GPC-MALLS curve of the products after 8 h reaction). Experimental conditions: [BA]/450 = [initiating sites]/1 = [CuBr]/1.8 = [CuBr$_2$]/0.2 = [PMDETA]/2 = 0.004 M in DMF at 60 °C. GPC conditions: RI detector, linear polyMMA as standard.

Synthesis of (PolyMMA)$_n$−PolySS−(PolyBA)$_m$ Miktoarm Star Copolymers. Further chain extension with BA, forming polyBA chains, from the "living" alkyl bromide sites in the core of the (polyMMA)$_n$−polySS star polymer (Figure 8A) demonstrates that ln([M]$_0$/[M]) increased linearly during the first 5 h of reaction time and after that curvature was observed. Since tens of initiating sites were situated in the core of each (poly-

MMA)$_n$−polySS star, the adjacent growing radicals in one star molecule became rather easy to terminate by coupling, leading to a decrease of the number of living chains. Actually, not only intrastar but also interstar radical−radical coupling reactions should be considered. The latter coupling produces some large star aggregates.[25] Some interstar coupling was observed by GPC measurement during the synthesis of (polyMMA)$_n$−polySS−(polyBA)$_m$ miktoarm star copolymers, and the results are shown in Figure 8B. In addition to the decreasing elution volume of miktoarm star copolymers with the increase reaction time, after 8 h of reaction a small shoulder (marked with a circle in Figure 8B) appeared at higher molecular weight, which represents star aggregates formed by interstar coupling. To verify this interstar coupling peak, GPC-MALLS measurement was performed for the miktoarm stars after 8 h reaction. Since MALLS detector is very sensitive to high molecular weight species, the interstar coupling peak became more evident (circle in Figure 8B, inset). This interstar coupling became more significant at higher BA conversion. After reacting for 20 h, when the BA conversion reached 25%, the interstar coupling was so significant that the solution of miktoarm star copolymers could no longer be filtered through a 0.2 μm PTFE filter, indicating the formation of gel. Figure 8B provides more details on the reaction. For example, it indicates the formation of a linear block copolymer, polyMMA-*b*-polyBA, from the free polyMMA existing in the star polymer, which is marked by a solid line in Figure 8B (i.e., the relative area of polyMMA linear polymer dropped from 27.2% to 21.2% after 8 h of reaction). Such a result verified that some fraction of the unreacted polyMMA linear chains remaining after the synthesis of (polyMMA)$_n$−polySS star were still “living” and could initiate the polymerization of a second monomer, producing a linear block copolymer, polyMMA-*b*-polyBA. However, some polyMMA chains were “inactive”, due to a loss of Br functionality, most likely in a radical disproportionation reaction.

Cleavage of (PolyMMA)$_n$−PolySS−(PolyBA)$_m$ Miktoarm Star Copolymers by Reducing Agent. Because the structure of (polyMMA)$_n$−polySS−(polyBA)$_m$ miktoarm star copolymer was more compact than that of the parent (polyMMA)$_n$−polySS star MI, the degradable disulfide-containing core was more “shielded” by the crowded arms. It was expected that their cleavage by reducing agent would be slower. Indeed, when comparing the fast cleavage of (polyMMA)$_n$−polySS star polymers in a 0.08 M Bu_3P THF solution, to the rate of cleavage of the (polyMMA)$_n$−polySS−(polyBA)$_m$ miktoarm star, the latter was much slower and less efficient. The miktoarm star copolymers obtained after 4 h of BA polymerization needed 40 h for complete cleavage. The degradation of the more compact miktoarm star copolymers, obtained at higher BA conversion, was even slower, and the GPC curve of the product was polymodal, confirming star−star coupling and gel formation during the polymerization of BA.

Figure 9A shows the GPC results from analysis of the product obtained after cleaving (polyMMA)$_n$−polySS−(polyBA)$_m$ miktoarm star copolymers. Two elution peaks can be seen: one corresponded to the same molecular weight as the cleaved product from (polyMMA)$_n$−polySS star polymer (marked by solid line); the other peak had a higher molecular weight, perhaps representing a triblock copolymer, polyMMA-*b*-polyS-*b*-polyBA, whose molecular weight was a little bit larger that the polyMMA-*b*-polyBA linear block copolymer in the miktoarm star copolymer system, formed during the polymerization of BA with free polyMMA as MI (marked by dashed line). These results indicate that the cleaved product from (polyMMA)$_n$−polySS−(polyBA)$_m$ miktoarm star copolymers was the mixture of two types of linear chains: polyMMA-*b*-polyS-*b*-polyBA and polyMMA-*b*-polyS block chains, which confirmed that not all the alkyl bromide sites in (polyMMA)$_n$−polySS core initiated the polymerization of BA.

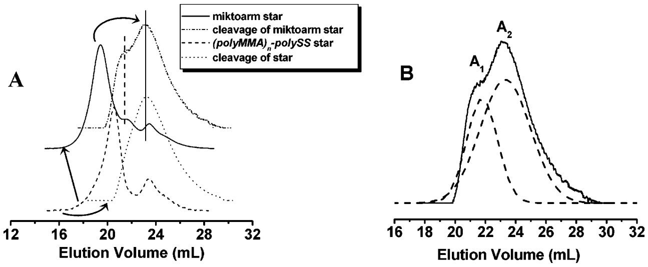


Figure 9. GPC traces (A) and deconvolution curves (B) of the product from the cleavage of (polyMMA)$_n$−polySS−(polyBA)$_m$ miktoarm star copolymers by reducing agent, Bu_3P. Experimental conditions: 0.05 g of miktoarm star copolymer in 5 mL of 0.08 M Bu_3P THF solution, room temperature. GPC conditions: RI detector, linear polyMMA as standard.

Evaluation of the Initiation Efficiency of Br Sites in (PolyMMA)$_n$−PolySS Star. To quantify the initiation efficiency of alkyl bromide sites in the multifunctional star initiators during the polymerization of BA, it is essential to know the molar ratio of chain-extended polyMMA-*b*-polyS-*b*-polyBA and unreacted polyMMA-*b*-polyS copolymers after cleavage. We neglected the contributions of “dead” polyMMA and free polyMMA-*b*-polyBA chains to the GPC curve of the cleaved product from miktoarm star. The two peaks deconvoluted in Figure 9B represent the polyMMA-*b*-polyS-*b*-polyBA (A_1) and polyMMA-*b*-polyS (A_2) block copolymers. They had an area ratio of 1/2 (A_1/A_2). When linear polyMMA were employed as standard for GPC calibration, the M_p values of these two block copolymers were 5.09×10^4 and 2.00×10^4 g/mol, respectively. The weight fractions of BA units and (MMA + S) units in polyMMA-*b*-polyS-*b*-polyBA triblock copolymer were 0.607 (w_{BA}) and 0.393 ($w_{M\&S}$). The d*n*/d*c* values of polyMMA and polyBA homopolymers at 35 °C in THF were 0.088 and 0.065 mL/g, respectively.[38] Assuming polyS segment has the same d*n*/d*c* value as polyMMA, as discussed above, the d*n*/d*c* value of polyMMA-*b*-polyS-*b*-polyBA triblock copolymer, $(dn/dc)_{block}$, was calculated to be 0.074 mL/g using the following equation.[41]

$$\left(\frac{dn}{dc}\right)_{block} = \left(\frac{dn}{dc}\right)_{BA} \times w_{BA} + \left(\frac{dn}{dc}\right)_{M\&S} \times w_{M\&S} \qquad (2)$$

In eq 2, $(dn/dc)_{BA}$ and $(dn/dc)_{M\&S}$ are the d*n*/d*c* values of polyBA and polyMMA-*b*-polyS chains. Because the intensity of RI signal is proportional to the d*n*/d*c* value and weight concentration of the polymer solute, using eq 3,[41] the molar ratio of polyMMA-*b*-polyS-*b*-polyBA and polyMMA-*b*-polyS block chains was calculated to be 0.23:1. This means that only 19% of the total alkyl bromide sites from the (polyMMA)$_n$−polySS star polymers initiated the polyBA chains. In eq 3

$$\frac{A_1}{A_2} = \frac{\left(\frac{\mathrm{d}n}{\mathrm{d}c}\right)_1 \times M_{p1} \times x_1}{\left(\frac{\mathrm{d}n}{\mathrm{d}c}\right)_2 \times M_{p2} \times x_2} \tag{3}$$

$(\mathrm{d}n/\mathrm{d}c)_1$, $M_{\mathrm{p}1}$, and x_1 are the refractive index increment, M_{p} value from GPC analysis, and molar fraction of polyMMA-*b*-polyS-*b*-polyBA block copolymer, and $(\mathrm{d}n/\mathrm{d}c)_2$, $M_{\mathrm{p}2}$, and x_2 are the refractive index increment, M_{p} value, and molar fraction of polyMMA-*b*-polyS block copolymer.

To calculate the chemical composition of (polyMMA)$_n$−polySS−(polyBA)$_m$ miktoarm star copolymers, ^{1}H NMR analysis of the cleaved linear block copolymers from star and miktoarm star copolymers (Figure 10) should provide a more accurate result because of the removal of the cross-linked core. The molar ratio of MMA and SS units in the (polyMMA)$_n$−polySS star molecule was 1.00/0.20, as discussed above. Combining this result with integrating the area of peaks *c* (C*H*$_3$O from MMA unit) and *f, j* (C*H*$_2$O from both SS and BA units), the calculated molar ratio of MMA, SS, and BA units in (polyMMA)$_n$−polySS−(polyBA)$_m$ miktoarm star copolymers was 1.00/0.20/0.84.

The molecular weight of linear polyMMA MI was 8800 g/mol (degree of polymerization (DP) = 88), and there were an average of 47 arms in the (polyMMA)$_n$−polySS star polymer. If every alkyl bromide site could initiate the polymerization of BA, the average chemical composition of (polyMMA)$_n$−polySS−(polyBA)$_m$ miktoarm star copolymers should be (polyMMA)$_{88\times47}$−polySS$_{18\times47}$−(polyBA)$_{74\times47}$, where the subscript number is the DP of each arm multiplied with the arm number per miktoarm star, and for polySS core, the product of 18 × 47 is the average number of SS units. However, through GPC analysis of the product obtained from the cleavage reaction of miktoarm star copolymers, it was determined that only 19% of the alkyl bromide sites actually initiated the chain extension of polyBA, which means that the real chemical composition of the obtained miktoarm star was (polyMMA)$_{88\times47}$−polySS$_{18\times47}$−(polyBA)$_{389\times9}$. The average arm number of polyBA chain per miktoarm star was 9, rather than 47. Consequently, the DP of each polyBA arm in the miktoarm star copolymer was 389, rather than 74. Although this result is based on the relative (apparent) molecular weights using linear polyMMA as GPC standard, it does qualitatively illustrate the incomplete initiation of the alkyl bromide sites in the core of (polyMMA)$_n$−polySS multifunctional initiators. This can be due to both highly congested macroinitiator-core structure and incompatibility between polyMMA and new polyBA chains.

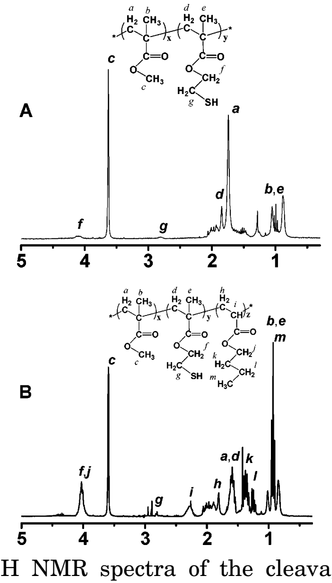


Figure 10. ^{1}H NMR spectra of the cleavage products of (polyMMA)$_n$−polySS star polymers (A) and (polyMMA)$_n$−polySS−(polyBA)$_m$ miktoarm star copolymers (B), NMR condition: 27 °C, CDCl$_3$ as solvent.

Conclusion

Two miktoarm star copolymers, (polyBA)$_n$−polyDVB−(polySt)$_m$ and (polyMMA)$_n$−polySS−(polyBA)$_m$, were successfully synthesized using ATRP via the “in−out” method. Linear polyBA and polyMMA macroinitiators were chain extended, cross-linked by reaction with divinylbenzene (DVB) or bis(2-methacryloyloxyethyl) disulfide (SS), to form nondegradable and degradable star polymers. The preserved alkyl bromide sites in the star molecules were reactivated to polymerize a second monomer in a “grafting from” reaction to form miktoarm star copolymers. Various reaction parameters, especially the molar ratio of linear macroinitiator (MI), cross-linker, and catalyst, were studied to select the optimal experimental conditions for the synthesis of the multifunctional star initiators. During the synthesis of miktoarm star copolymers through the polymerization of the second monomer, both interstar and intrastar couplings were observed. The initiation efficiency of the alkyl bromide sites in the core of star molecules during the extension of the second polymer chains was studied by cleavage of the degradable miktoarm star copolymers using a reducing agent, tributylphosphine, forming linear block copolymers. GPC and NMR analysis of these linear copolymers indicated that the compact nature of the core affected the initiation efficiency of these alkyl bromide sites and caused slower polymerization and incomplete initiation. In the case of (polyMMA)$_n$−polySS−(polyBA)$_m$ miktoarm star system, semiquantitative results indicate that only 19% of the total Br functionality sites initiated the polymerization of BA, leading to the following average molecular structure of the miktoarm star copolymer: (polyMMA)$_{88\times47}$−polySS$_{18\times47}$−(polyBA)$_{389\times9}$.

These results provide deeper insight into the synthesis of star and miktoarm star copolymers and also into other controlled/“living” radical polymerization systems with sterically confined environments around the tethered initiating sites.

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