Synthesis of Multiarm Star Poly(glycerol)-*block*-Poly(2-hydroxyethyl methacrylate)

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Well-defined multiarm star block copolymers poly(glycerol)-*b*-poly(2-hydroxyethyl methacrylate) (PG-*b*-PHEMA) with an average of 56, 66, and 90 PHEMA arms, respectively, have been prepared by atom transfer radical polymerization (ATRP) of HEMA in methanol by a *core-first* strategy. The hyperbranched macroinitiators employed were prepared on the basis of well-defined hyperbranched polyglycerol by esterification with 2-bromoisobutyryl bromide. Polydispersites M_w/M_n of the new multiarm stars were in the range of 1.11−1.82. Unexpectedly, with the combination of CuCl/$CuBr_2$/2,2′-bipyridyl as catalyst, the polymerization conversion can be driven to maximum values of 79%. The control of CuCl catalyst concentration is also very important to achieve high conversion and narrow polydispersity. The absolute M_n values of the obtained multiarm star polymers were in good agreement with the calculated ones, and the highest M_n values of the multiarm star copolymer is around 10^6 g/mol. Kinetic analysis shows that an induction period exists in the polymerization of HEMA. After this induction period, a linear dependence of ln ($[M]_0/[M]_t$) on time was observed. Due to the star architecture, the viscosity of the obtained multiarm star PHEMA is much lower than that of linear PHEMA.

Introduction

Multiarm star polymers are attractive materials due to their unusual bulk and solution properties.[1] Two major strategies have been employed for their preparation: (1) the *core-first* approach, living polymerization on the basis of a multifunctional initiator core, and (2) the *arm-first* approach, quenching of living polymers with a multifunctional coupling agent or linking reactions of living polymers with a small amount of bifunctional vinyl compounds. Among these strategies, polymerization with a multifunctional initiator and quenching of living polymers with a multifunctional coupling agent lead to star polymers with predetermined numbers of arms. In contrast, linking reactions of living polymers with a small amount of bifunctional vinyl compounds afford star polymers with a random distribution of arms per macromolecule.

Since well-defined star polymers cannot be prepared by means of conventional free radical polymerization, a large variety of star polymers has been synthesized by ionic polymerization procedures.[2] However, these approaches are only applicable for a limited number of monomers and are sensitive to impurities. During the past couple of years, several procedures for the controlled or "living" radical polymerization have been developed and employed to prepare polymers with complex macromolecular architectures.[3] Among these methods, atom transfer radical polymerization (ATRP)[4] is of considerable efficiency. Indeed, well-defined star polymers with several arms (arm number ≤ 10) have been reported in a number of papers, by use of a core-first strategy[5] via the ATRP approach. For the preparation of star polymers with a larger number of arms (arm numbers >10) via ATRP, both arm-first[6] and core-first strategies[7] have been exploited; however, the materials obtained by arm-first strategies were usually less defined than those by the core-first strategy.

Dendrimers,[7a−e,8] hyperbranched polymers,[7h−k,9] and cyclodextrins[7f,10] are attractive (macro)initiators for the preparation of multiarm star polymers by the core-first strategy. Cyclodextrins possess well-defined structures and exact, multiple functionality. However, cyclodexdrins are normally limited to α-, *β*-, and *γ*-cyclodextrin with 18, 21 and 24 hydroxyl groups, respectively. As far as dendrimers are concerned, their synthesis is time-consuming, which currently limits the practical use to laboratory scale. Thus, hyperbranched polymers prepared from AB_m-type monomers in a one-step process have gained increasing interest.[11] Hyperbranched polymers with narrow polydispersity and predictable molecular weight require special preparation procedures, such as hyperbranched polyglycerol (PG) with narrow polydispersity (M_w/M_n < 1.5, mostly <1.3), which is obtained via ring-opening multibranching polymerization (ROMBP) under slow monomer addition conditions.[12] Solubility and flexibility of these hyperbranched polyether polyols can be tailored by the attachment of oligo(propylene oxide) segments,[9a] leaving the functionality unchanged. Based on these initiator cores, poly(ethylene oxide) stars with up to 55 PEO chains and low polydispersity (M_w/M_n < 1.5) have been prepared[9b] as well as poly(*ϵ*-caprolactone)[9d] multiarm star polymers.

Even though dendrimers and hyperbranched polymers with high functionalities are available, to date the arm numbers of most of the well-defined multiarm star polymers obtained via ATRP are usually below 30,[7a−h] since intermolecular radical−radical coupling reaction becomes a serious problem with increasing arm number, leading to gel formation or high polydispersity polymers.[7d] Modified hyperbranched polyglycerols as dendritic macroinitiators have been used in our group to initiate methyl acrylate (MA) polymerization under ATRP condition, resulting in star copolymers with polyether core and

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Table 1. Preparation of 56-Arm Star PHEMA Based on $P(G_{66}In_{56})$ Macroinitiator[a]

entry	[M]:[I]:[CuCl]	[CuCl] (10^2 M)	[$CuBr_2$] (10^3 M)	V_r[b]	time (min)	conv (%)	$M_{n(SEC)}$[c] ($\times 10^{-4}$)	M_w/M_n[c]	$M_{n(calc)}$[d] ($\times 10^{-4}$)
$P(G_{66}In_{56})$							0.36	1.64	1.32
1	50:1:0.4	3.2	0	1[e]	10	gel			
2	50:1:0.4	3.2	0	1	7200	22			
3	50:1:0.6	4.8	0	1	42	50.3	10.0	1.43	25.5
4	50:1:0.6	4.8	0	1	60	63.1	11.8	1.80	31.7
5	50:1:0.4	4.3	0	2	20	45.3	9.27	1.60	23.1
6	50:1:0.8	8.6	0	2	10	gel			
7	50:1:0.4	4.3	4.3	2	36	34.9	8.14	1.21	18.1
8	50:1:0.4	4.3	4.3	2	60	60.5	11.5	1.30	30.5
9	50:1:0.4	4.3	4.3	2	92	78.9	14.0	1.36	39.3
10	50:1:0.4	4.3	8.6	2	60	56.0	11.3	1.28	28.3
11[f]	50:1:0.4	4.3	4.3	2	90	64.8	microgel		
12	100:1:0.4	2.1	2.1	2	3600	24.9			
13[g]	50:1:0.4	4.3	4.3	2	73	53.1	10.4	1.49	26.9
14[g]	100:1:0.8	4.3	4.3	2	75	44.8	15.2	1.34	44.5

[a] Polymerization conditions: L = 2,2′-bipyridyl; I is the initiating site of polyglycerol; [CuCl]:[L] = 1:2; polymerization was conducted at room temperature. [b] V_r is the volume ratio of HEMA to methanol. [c] $M_{n(SEC)}$ and M_w/M_n were obtained from the acetylated polymers in $CHCl_3$. [d] $M_{n(calc)} = [M]/[I] \times M$ (acetylated monomer) $\times$ conversion $\times$ number of initiating sites per macroinitiator + $M_{n(initiator)}$. [e] Solvent mixture of water and methanol (v/v =1:1). [f] CuBr was used instead of CuCl. [g] $CuCl_2$ was used instead of $CuBr_2$.

45−55 PMA arms.[7i] However, to avoid gelation, the polymerization conversion had to be limited to below 35% and well-defined multiarm star polymers could be obtained only when the conversion was below 20%. Gao et al.[7j,k] have employed modified hyperbranched polyoxetane polyols as ATRP macroinitiators with average 27 and 58 initiating sites for the ATRP of 2-hydroxyethyl methacrylate (HEMA) in the mixed solvent of ethyl methyl ketone and 2-propanol (70/30 v/v) with the CuBr/PMDETA catalyst system at 50 °C. If the ratio of catalyst to initiating sites was fixed at 0.1:1 and the concentrations of monomer and reaction temperature were changed, the obtained multiarm star copolymers had a polydispersity in the range of 1.38−1.65 at low polymerization conversion. When the ratio of catalyst to initiating sites was enhanced to 0.5, the polymerization conversion could be increased, but the polydispersity of the obtained multiarm star block copolymers was relatively broad: 1.52−2.75 and 1.81−2.81 for average 27- and 58-arm star copolymers, respectively. Thus, to date, it remains a challenge to prepare well-defined multiarm star polymers via controlled radical polymerization to satisfy both aspects simultaneously;, that is, to obtain well-defined star polymers with more than 30 arms *and* high polymerization conversion.

HEMA is an important functional monomer, and PHEMA represents a major component in contact lenses, drug delivery, and biocompatible hydrogels used for a variety of applications.[13] Armes and co-workers[14] recently reported that ATRP of HEMA is both efficient and well-controlled in either 50:50 methanol/water mixtures or pure methanol at room temperature. In this paper we report the ATRP of HEMA initiated by hyperbranched polyglycerol-based macroinitiators, leading to well-defined multiarm star block copolymers PG-*b*-PHEMA with arm numbers in the range of 56−90. After optimization of the polymerization conditions, the polymerization conversion could be driven to maximum values of 79%. Since both PHEMA and PG are biocompatible polymers, the obtained multiarm copolymers with a large number of hydroxyl groups are promising with respect to biomedical application.

Experimental Section

Materials. CuCl (99.99%), $CuBr_2$ (99+%), $CuCl_2$ (99%), and 2,2′-bipyridyl (bpy, 99+%), were used as received from Acros. CuBr (98%, Acros) was purified as described in the literature.[15] 2-Hydroxyethyl methacrylate (HEMA, Acros, 98%) was purified by washing an aqueous solution of 25 vol % monomer with hexanes (8 × 200 mL), salting the monomer out of the aqueous phase by addition of NaCl, and subsequent drying over Na_2SO_4. The monomer was passed through a column of basic alumina and distilled under reduced pressure. Pyridine was dried over KOH and distilled under argon. 2-Bromoisobutyryl bromide (98%) was used as received from Aldrich. Methanol was used as received.

PG_{66} (M_n = 4800 g/mol, M_w/M_n = 1.5) and PG_{90} (M_n = 6600 g/mol, M_w/M_n = 1.7) were prepared as reported previously[11] and dried under vacuum.

Characterization. ^1H and ^{13}C NMR spectra were recorded on a Bruker ARX 300 spectrometer, operated at 300 and 75.4 MHz, respectively, and the chemical shifts are given in parts per million (ppm). Molecular weight distributions were determined by means of size exclusion chromatography (SEC) on a Knauer microgel set A22 at 30 °C, with $CHCl_3$ as eluent and linear polystyrene standards for calibration. Absolute molecular weights were measured in tetrahydrofuran (THF) on a Gonotec Membrane Osmomat 090. Viscosity was measured by Lauda Processor-Viscosity-System 2.52a.

Syntheses of Macroinitiators for ATRP. Three macroinitiators, $P(G_{66}In_{56})$, $P(G_{66}In_{66})$, and $P(G_{90}In_{90})$, for ATRP were prepared as reported previously by esterification of hyperbranched PG_{66} or PG_{90} with 2-bromoisobutyryl bromide.[7i]

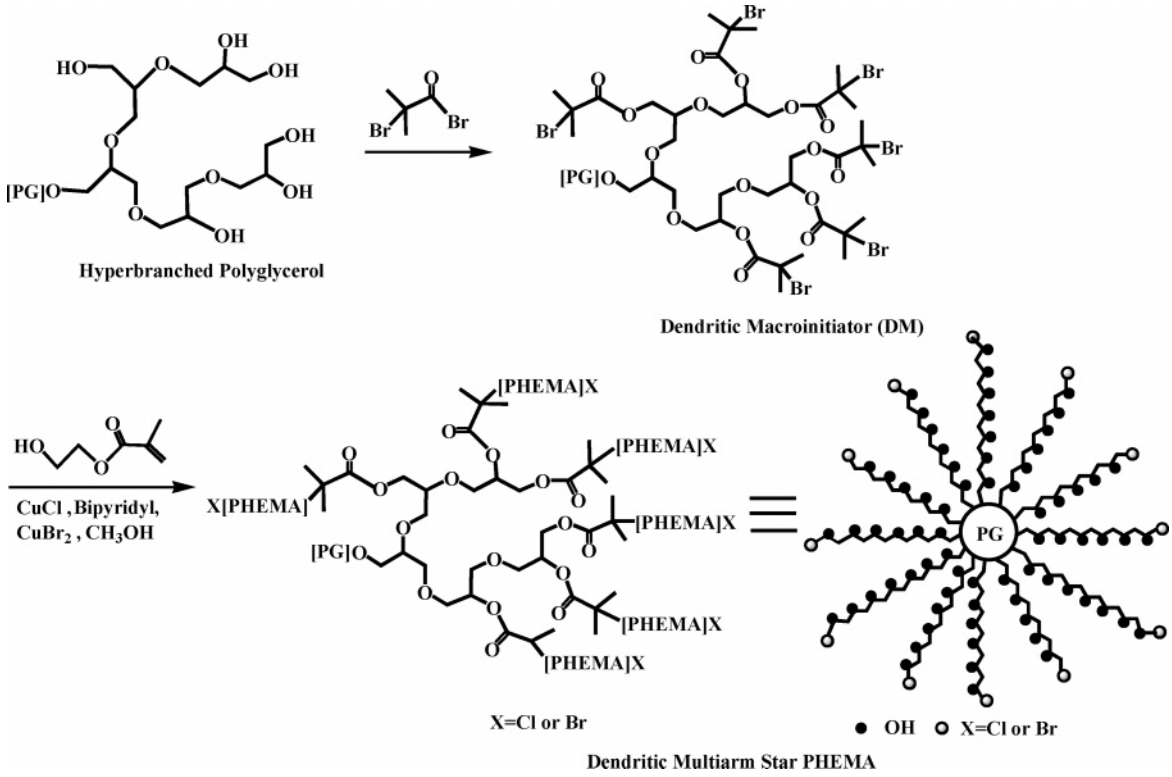
(A) $P(G_{66}In_{56})$. Initiator functionality is 85% (with respect to the number of hydroxy groups of PG), which is calculated from the ^1H NMR spectrum. Thus, the number of initiating sites (In) per polymer is 56. ^1H NMR ($CDCl_3$): δ = 5.15−5.0, 4.64−3.14, and 1.92. ^{13}C NMR ($CDCl_3$): δ = 171, 79, 74.5−64, 55.5, and 30.5. $M_{n(SEC)} = 3.6 \times 10^3$, $M_{n(NMR)} = 1.32 \times 10^4$, $M_w/M_n = 1.64$.

(B) $P(G_{66}In_{66})$. Initiator functionality is 100% (with respect to the number of hydroxy groups of PG), which is calculated from the ^1H NMR spectrum, so the number of initiating sites (In) per polymer is 66. ^1H NMR ($CDCl_3$): δ = 5.15−5.0, 4.64−3.14, and 1.92. ^{13}C NMR ($CDCl_3$): δ = 171, 79, 74.5−64, 55.5, and 30.5. $M_{n(SEC)} = 4.3 \times 10^3$, $M_{n(NMR)} = 1.46 \times 10^4$, $M_w/M_n = 1.49$.

(C) $P(G_{90}In_{90})$. Initiator functionality is 100% (with respect to the number of hydroxy groups of PG), which is calculated from the ^1H NMR spectrum, so the number of initiating sites (In) per polymer is 90. ^1H NMR ($CDCl_3$): δ = 5.15−5.0, 4.64−3.14, and 1.92. ^{13}C NMR ($CDCl_3$): δ = 171, 79, 74.5−64, 55.5, and 30.5. $M_{n(SEC)} = 5.2 \times 10^3$, $M_{n(NMR)} = 2.00 \times 10^4$, $M_w/M_n = 1.71$.

Synthesis of PG-*block*-PHEMA Multiarm Star Copolymer. The synthesis is exemplified for entries 7−9 of Table 1. The above-described initiator $P(G_{66}In_{56})$ (0.16 g, 0.012 mmol, 0.66 mmol of Br atoms), 4 mL of HEMA (4.32 g, 0.033 mol, 50 equiv to the initiating sites), 2

Scheme 1: Synthesis of Multiarm Star PHEMA



mL of methanol, 0.0832 g of 2,2′-bipyridyl (0.53 mmol, 0.8 equiv to the initiating sites), and 0.0059 g of $CuBr_2$ (0.026 mmol, 0.04 equiv to the initiating sites) were placed in a flask and freeze−pump−thaw degassed three times. Then 0.0256 g of CuCl (0.26 mmol, 0.4 equiv to the initiating sites) was introduced into the solution mixture under argon, and polymerization started immediately. Samples were taken after certain time intervals with a syringe, then diluted with deuterated methanol and subsequently analyzed by ^{1}H NMR spectroscopy, from which the polymerization conversion was obtained. The residual reaction mixture was diluted with methanol and passed through a silica gel column to remove copper ions. Precipitation in diethyl ether and drying at 40 °C under vacuum produced a white powder polymer, which was soluble in methanol, *N*,*N*-dimethylformamide (DMF), and dimethyl sulfoxide (DMSO). ^{1}H NMR(CD_3OD): δ = 4.85, 4.04, 3.78, and 2.18−0.67. ^{13}C NMR(CD_3OD): δ = 179.5, 178.6, 67.7, 60.6, 55.1, 46.1, 19.7, and 17.7.

Esterification of PG-*block*-PHEMA Multiarm Star Copolymer with Acetic Anhydride. Copolymer (0.2 g) was mixed with 5 mL of acetic anhydride, and the solution was refluxed for 4 h. Most of the unreacted acetic anhydride was distilled under vacuum. The residues were dissolved in 20 mL of chloroform. The solution was washed with 10% Na_2CO_3 aqueous solution three times and then washed with deionized water until pH = 7. The solution was dried over anhydrous sodium sulfate. After solvent evaporation, the obtained acetylated polymers were placed in a vacuum oven for 24 h. ^{1}H NMR ($CDCl_3$): δ = 4.26, 4.15, 2.09, 2.03−1.68, 1.03, and 0.87.

Results and Discussion

Hyperbranched polyglycerol samples PG_{66} (M_n = 4800 g/mol, M_w/M_n = 1.5) and PG_{90} (M_n = 6600 g/mol, M_w/M_n = 1.7) were prepared by anionic polymerization of glycidol in the presence of trimethylolpropane, (TMP, 2-ethyl-2-(hydroxymethyl)-1, 3-propanediol) as initiator core according to previously published procedures.[12] Subsequently, the hydroxyl groups of PG were esterified by 2-bromoisobutyryl bromide to generate macroinitiators for ATRP, as previously described.[7h] Three macroinitiators with average 56, 66, and 90 initiating sites for ATRP, respectively, have been prepared, namely, $P(G_{66}In_{56})$, $P(G_{66}In_{66})$, and $P(G_{90}In_{90})$, which were used in the ATRP of HEMA to prepare the well-defined multiarm star PHEMA as shown in Scheme 1.

To date the synthesis of linear PHEMA by ATRP has been attempted in bulk,[14,16] extremely polar solvents, such as DMF, DMSO, hexamethylphosphoric triamide (HMPA),[16] and methanol,[14] or solvent mixtures, such as methyl ethyl ketone (MEK) with 1-propanol (70/30 v/v)[16] and water with methanol (1:1 v/v).[14] The best results were obtained when methanol or the mixture of water with methanol (1:1 v/v) was chosen as solvent. On the basis of these results, ATRP of HEMA with the PG-based macroinitiators was first conducted at room temperature with the complex of CuCl/2,2-bipyridyl as catalyst system in a water/methanol mixture (1:1 v/v); however, in this case the polymerization rate was found to be very high. Even with low concentration of CuCl (the ratio of CuCl to initiating sites was 0.4), gelation occurred within 10 min (entry 1 in Table 1). Thus, in all subsequent experiments, polymerizations were conducted in methanol only. Under these conditions, the rate of polymerization can be slowed and soluble materials are obtained.

On the other hand, in previous works no attention has been paid to the concentration of Cu(I) catalyst during the synthesis of linear PHEMA by ATRP in methanol.[14] However, we found that control of the Cu(I) concentration was crucial in the synthesis of multiarm star PHEMA. In fact, when the concentration of Cu(I) catalyst was around 4.3×10^{-2} M, a monomer conversion around 50% was obtained within 2 h. Meanwhile, the presence of considerably higher amounts of Cu(I) catalyst resulted in rapid gel formation (entry 6 in Table 1). When a lower amount of Cu(I) catalyst was used, the polymerization rate became very low (entries 2 and 12 in Table 1).

When CuBr was used as a catalyst, the monomer conversion reached 64.8% (entry 11 in Table 1); however, the resulting polymer obtained in solution could not be filtered for SEC

Table 2. Preparation of 66-Arm Star PHEMA Based on $P(G_{66}In_{66})$ Macroinitiator[a]

entry	[M]:[I]:[CuCl]	time (min)	conv (%)	$M_{n(SEC)}$[b] ($\times10^{-4}$)	M_w/M_n[b]	$M_{n(calc)}$[c] ($\times10^{-4}$)	$M_{n(abs)}$ ($\times10^{-4}$)
$P(G_{66}In_{66})$				0.43	1.49	1.46	
1	50:1:0.4	15	3.8	2.55	1.25	3.64	3.75[d]
2	50:1:0.4	30	9.8	2.71	1.23	7.05	7.22,[d] 7.19[e]
3	50:1:0.4	45	18.2	4.50	1.14	11.8	13.6,[d] 11.5[e]
4	50:1:0.4	60	29.3	6.17	1.21	18.1	16.5[e]
5	50:1:0.4	75	37.2	7.40	1.13	22.6	22.5[e]
6	50:1:0.4	90	46.8	8.97	1.11	28.1	26.5[e]
7	100:1:0.8	110	47.3	14.0	1.38	55.2	54.5[e]
8	200:1:1.6	540	47.1	26.5	1.82	108.5	

[a] Polymerization conditions: L = 2,2′-bipyridyl; I is the initiating site of polyglycerol; $[CuCl] = 4.3 \times 10^{-2}$ M; $[CuBr_2] = 4.3 \times 10^{-3}$ M; V(HEMA):$V(CH_3OH)$ = 2:1; [CuCl]:[L] = 1:2; polymerization was conducted at room temperature. [b] $M_{n(SEC)}$ and M_w/M_n were obtained from the acetylated polymers in $CHCl_3$. [c] $M_{n(calc)}$ = [M]/[I] × M (acetylated monomer) × conversion × number of initiating sites per macroinitiator + $M_{n(initiator)}$. [d] Measured by ^{1}H NMR (acetylated polymers). [e] Measured by membrane osmometry (acetylated polymers).

Table 3. Preparation of 90-Arm Star PHEMA Based on $P(G_{90}In_{90})$ Macroinitiator[a]

entry	[M]:[I]:[CuCl]	$[CuBr_2]$ (10^3 M)	time (min)	conv (%)	$M_{n(SEC)}$[b] ($\times10^{-4}$)	M_w/M_n[b]	$M_{n(calc)}$[c] ($\times10^{-4}$)
$P(G_{90}In_{90})$					0.52	1.71	2.0
1	50:1:0.4	6.5	60	37.2	8.42	1.80	30.8
2	50:1:0.4	8.6	70	35.1	6.71	1.33	29.3

[a] Polymerization conditions: L = 2,2′-bipyridyl; I is the initiating site of polyglycerol; $[CuCl] = 4.3 \times 10^{-2}$ M; V(HEMA):$V(CH_3OH)$ = 2:1; [CuCl]:[L] = 1:2; polymerization was conducted at room temperature. [b] $M_{n(SEC)}$ and M_w/M_n were obtained from the acetylated polymers in $CHCl_3$. [c] $M_{n(calc)}$ = [M]/[I] × M (acetylated monomer) × conversion × number of initiating sites per macroinitiator + $M_{n(initiator)}$.

characterization, indicating microgel formation. Under the same polymerization conditions the monomer conversion with CuCl as catalyst was found to be 78.9% (entry 9 in Table 1), and nevertheless no microgel was formed. This is explained by the higher stability of C−Cl bonds, leading to considerably lower radical concentration.[17]

It is not necessary to add extra deactivating agent CuX_2 (X = Cl or Br) for the synthesis of well-defined linear PHEMA;[14] however, to obtain well-defined multiarm star polymers, additional deactivating agent CuX_2 must be introduced into the reaction in order to suppress the radical coupling side reaction.[18] The M_w/M_n values of the obtained 56- and 66-arm star PHEMA could be controlled in the range of 1.11−1.36, when the feed ratio of HEMA to initiating sites is 50:1 and 10 mol % $CuBr_2$ (relative to CuCl) was added (entries 7−10 in Table 1 and 1−6 in Table 2). Without $CuBr_2$, the M_w/M_n values of the star polymers were in the range of 1.43−1.80 (entries 3−5 in Table 1). To obtain well-defined 90-arm star PHEMA, more $CuBr_2$ was required (Table 3). Furthermore, when $CuCl_2$ was used instead of $CuBr_2$, the polydispersity values of the obtained polymers were higher than those with $CuBr_2$ (entries 8, 9, and 13 in Table 1).

Kinetics of the Polymerization. Figure 1 shows kinetic data for the ATRP of HEMA in methanol with $P(G_{66}In_{66})$ as macroinitiator. Clearly, there is an induction period at the beginning of the polymerization. We ascribe this to the limited solubility of the macroinitiator in the reaction mixture and the low number of propagating sites in the early stages of the reaction. When a certain fraction of the potential initiating sites of the macroinitiators has initiated polymerization of HEMA, the solubility of the macroinitiators with short PHEMA arms in the polymerization solution increases. After the induction period, the polymerization solution becomes fully homogeneous. To monitor the homogeneity of the polymerization, samples of the solution were taken after the induction time and checked with respect to homogeneity. No insoluble residue was found, indicating homogeneity of the polymerization after the induction period. From Figure 1 it is obvious that after the induction period a linear dependence of ln ($[M]_0/[M]_t$) on time occurred, indicating a constant number of propagating species throughout the reaction. The molecular weights increase linearly with conversion, and the molecular weight distributions are fairly narrow (M_w/M_n < 1.3) (Figure 2), demonstrating that the polymerizations are controlled.

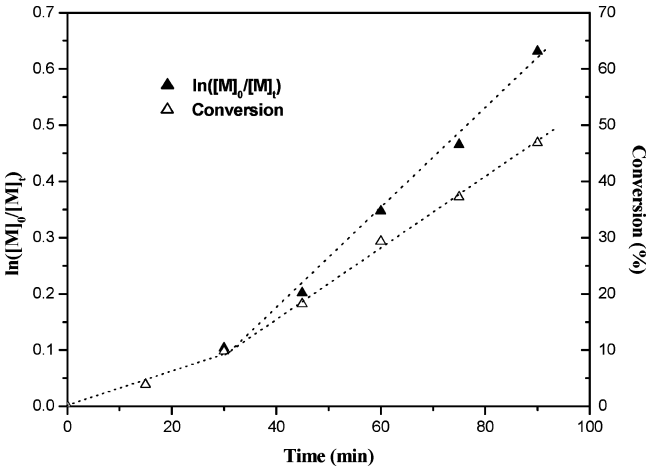


Figure 1. Dependence of ln ($[M]_0/[M]_t$) and monomer conversion on time for the polymerization of HEMA in methanol with hyperbranched $P(G_{66}In_{66})$ as macroinitiator at room temperature. [M]:[I]:[CuCl]:$[CuBr_2]$:[L] = 50:1:0.4:0.04:0.88; V_{HEMA}/V_{CH3OH} = 2.

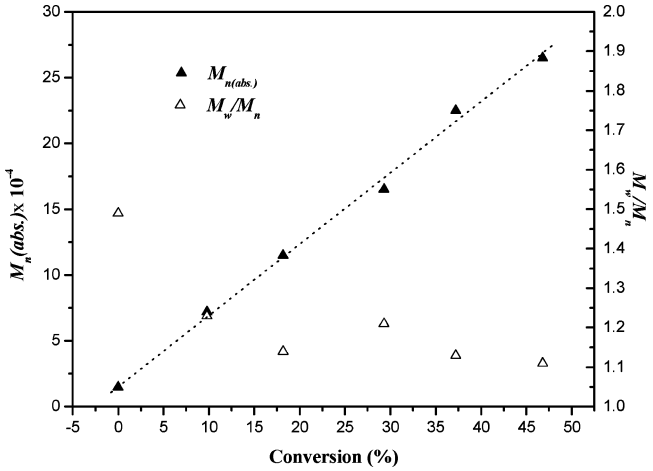


Figure 2. Dependence of molecular weight, $M_{n(abs)}$, and molecular weight distribution, M_w/M_n, on monomer conversion for the polymerization of HEMA in methanol with hyperbranched $P(G_{66}In_{66})$ as macroinitiator at room temperature. [M]:[I]:[CuCl]:$[CuBr_2]$:[L] = 50:1:0.4:0.04:0.88; V_{HEMA}/V_{CH3OH} = 2.

Characterization of the Star Polymers by NMR Spectroscopy. The obtained multiarm star copolymers before and after peracetylation by acetic anhydride were characterized by ^{1}H NMR as shown in Figure 3, panels B and C, respectively. Figure 3A shows the ^{1}H NMR spectrum of a macroinitiator, in which the signals of hyperbranched polyglycerol located in the region of 3.14−5.15 ppm can be divided into three parts. The resonances in the region of 5.0−5.15 ppm are assigned as the methine protons of the end groups, and those shifted between 4.57 and 4.0 ppm are due to methylene protons of end groups, while the inner methine and methylene protons appear at 3.14−4.0 ppm. The signals of inner methine and methylene protons are considerably more intense than the other two parts. The

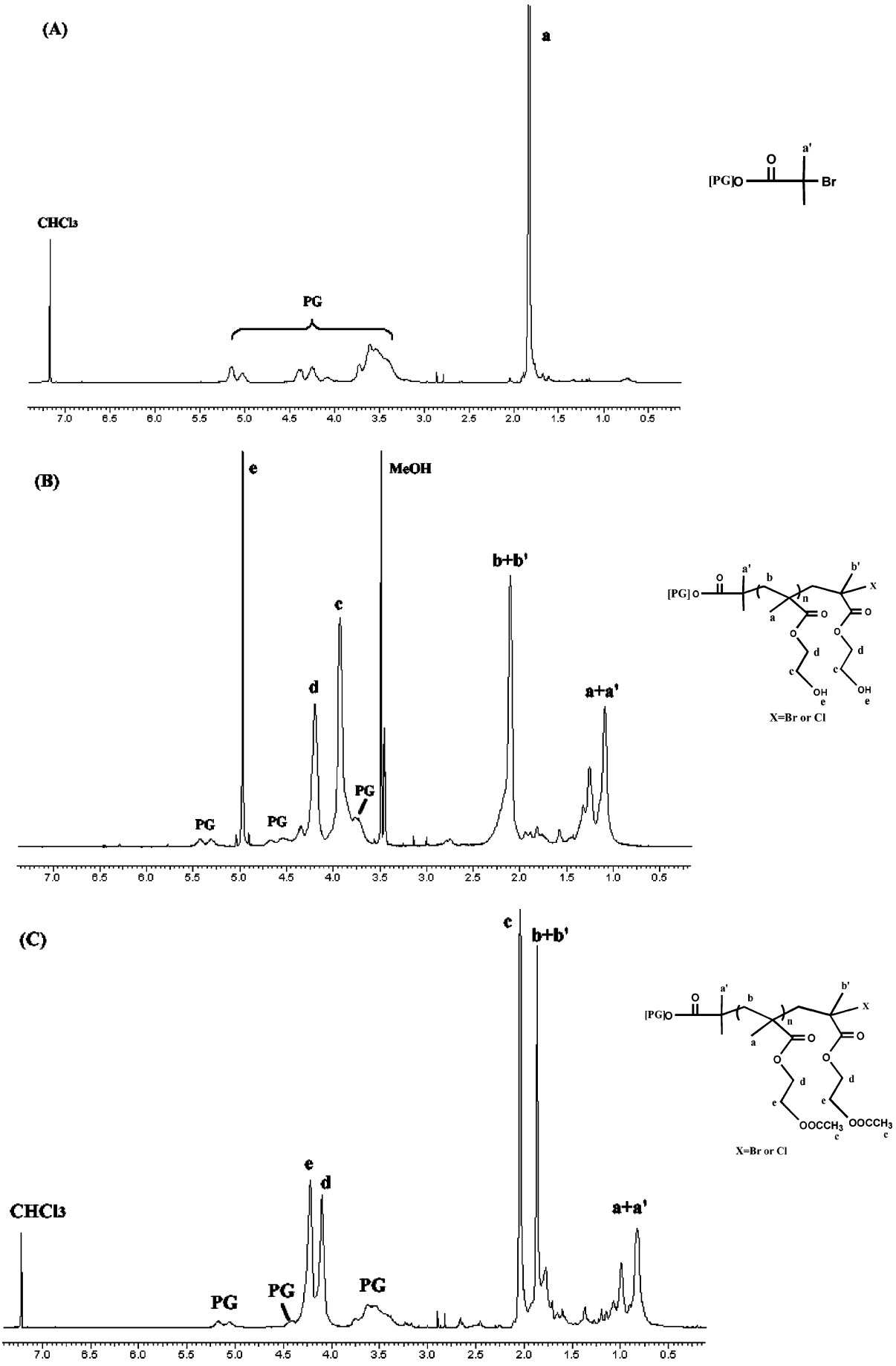


Figure 3. ^{1}H NMR spectra of (A) macroinitiator P($G_{66}In_{66}$) in $CDCl_3$, (B) multiarm star PG-*b*-PHEMA in CD_3OD (entry 1 in Table 2), and (C) acetylated multiarm star PG-*b*-PHEMA in $CDCl_3$.

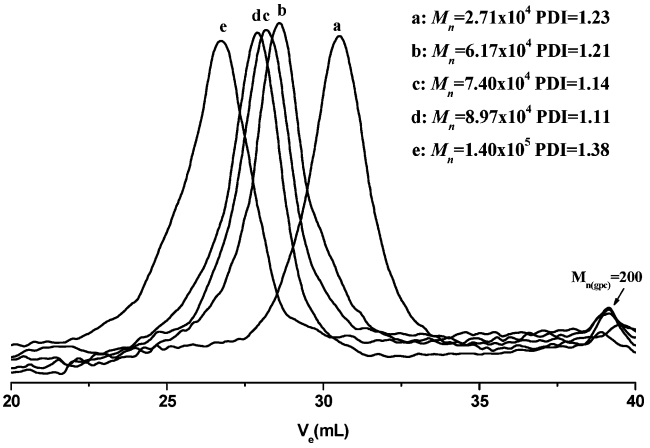


Figure 4. SEC curves of acetylated 66-arm PG-*b*-PHEMA star copolymers.

methine protons of end groups lead to the weakest signals. When Figure 3 panels A and B are compared, it is clear that the peaks from the PHEMA arms partially overlap with the strong signals of the PG core. However, in the ^{1}H NMR spectrum of the acetylated polymer (Figure 3C), the peaks from the PHEMA arms only overlap with the weak signals of methylene protons of the end groups of PG. Thus, it is more accurate to calculate the absolute molecular weight of the polymers from the ^{1}H NMR spectra of the acetylated polymers. Calculation of the absolute molecular weight of polymers from the ^{1}H NMR spectra is only accurate for the low molecular weight materials, such as the polymers presented in entries 1 and 2 of Table 2, because the signals of the PG core are very weak and thus cannot be discerned in the ^{1}H NMR spectra of high molecular weight materials.

Characterization by SEC and Membrane Osmometry. All polymer samples have been analyzed by SEC. When DMF was used as eluent, part of the polymer peak was out of the calibration range due to strong aggregation. To prevent aggregation, the hydroxyl groups of polymers were fully acetylated with an excess of acetic anhydride. Complete conversion was achieved, as demonstrated by the ^{1}H NMR spectra. The modified polymers were then characterized by SEC in the presence of chloroform, and the molecular weights of the polymers were in the range of calibration, as shown in Figure 4. Since the star polymers were acetylated at 110 °C by acetic anhydride, transesterification is a possible side reaction. In this case, the ester groups linking the core of the multiarm star polymers with the PHEMA arms would be cleaved. However, except for the signal caused by residual acetylated monomer, no further distribution modes pointing to such a degradation reaction can be observed (Figure 4). In addition, if this kind of transesterification reaction occurred to a considerable extent, the polydispersity of the polymers obtained should increase. This is not observed, as demonstrated in Tables 1−3 and Figure 4. Thus, we conclude that transesterification with the core ester groups does not occur to a significant extent during the acetylating reaction, and the results obtained from acetylated polymers actually reflect distribution modes of the unmodified polymers.

Since M_n values determined by SEC with polystyrene standards give only relative M_n values, some samples have also been studied by membrane osmometry in order to determine absolute values of M_n. From Table 2 and Figure 5, it becomes clear that the M_n values of the polymers obtained are in good agreement with the calculated values of M_n, demonstrating that the polymerization was well-controlled.

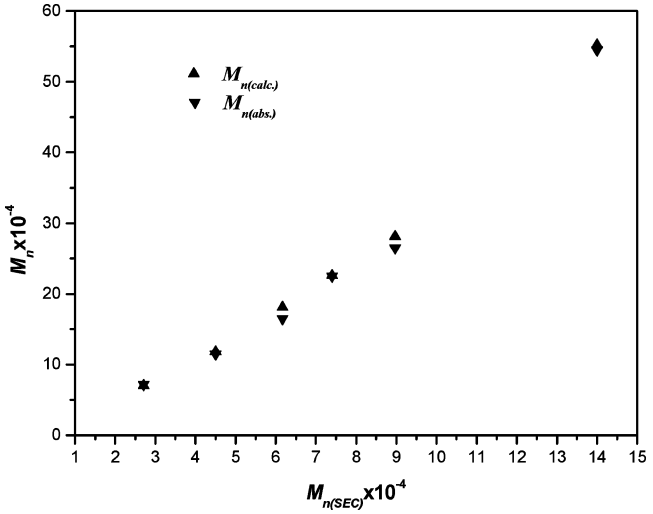


Figure 5. Relationship between $M_{n(SEC)}$, $M_{n(calc)}$, and $M_{n(abs)}$ for the peracetylated multiarm star PG-*b*-PHEMA.

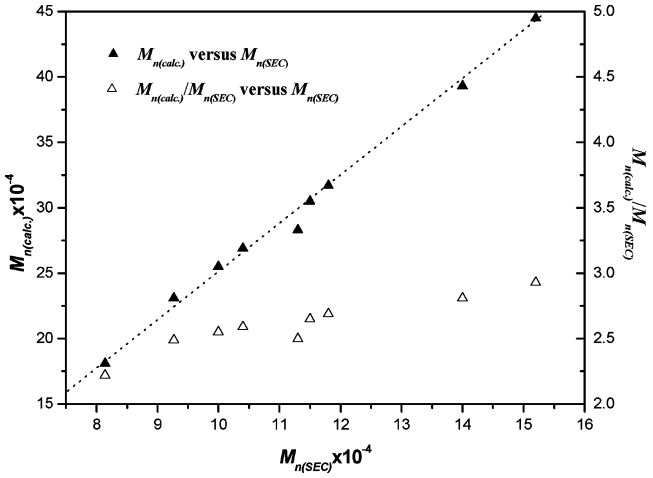


Figure 6. Relationship between $M_{n(SEC)}$ and $M_{n(calc)}$ for the 56-arm star PG-*b*-PHEMA prepared from the hyperbranched macroinitiator P(G_{66}In$_{56}$).

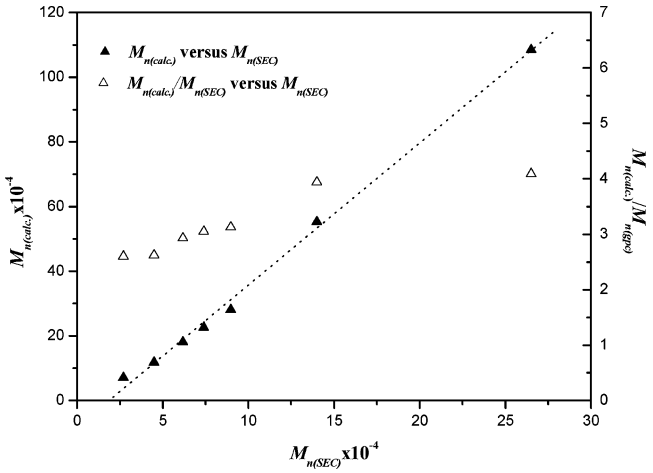


Figure 7. Relationship between $M_{n(SEC)}$ and $M_{n(calc)}$ for the 66-arm star PG-*b*-PHEMA prepared from the hyperbranched macroinitiator P(G_{66}In$_{66}$).

From Figures 6 and 7 it can be seen that M_n values determined by SEC are considerably smaller than the calculated data, which points to the expected compact structure of the multiarm stars. In addition, the calculated M_n values exhibit a linear correlation with the data obtained by SEC. However, the ratio of the

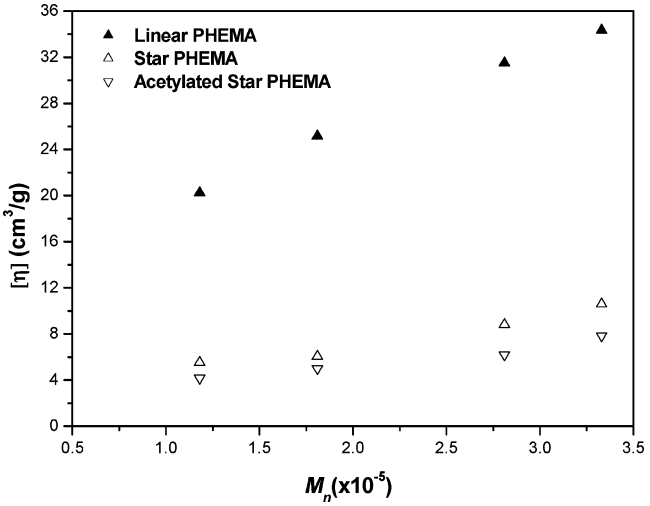


Figure 8. Comparison of the viscosity at 30 °C of (▲) linear PHEMA in methanol,[19] (△) 66-arm star PHEMA in methanol, and (▽) acetylated 66-arm star PHEMA in THF.

calculated M_n values to those determined by SEC was not constant. With an increase of M_n values, the ratio also increases, indicating that SEC is not so sensitive to the molecular weight change of multiarm star polymers, since the M_n determined bySEC was obtained from the hydrodynamic volumes of the polymers. Comparison of Figure 6 with Figure 7 implies that the more arms the polymer has, the larger the ratio of the calculated M_n values to those determined by SEC is for the multiarm star polymers with the same M_n value.

Viscosity Measurements. The viscosity of the obtained average 66-arm star PHEMA before and after acetylation was measured at 30 °C. The values of K and α for linear PHEMA in methanol at 30 °C have already been reported ($K = 5.24 \times 10^{-2}$ mL/g, $\alpha = 0.51$);[19] thus, the viscosity of linear PHEMA with the same molecular weight as multiarm star PHEMA could be calculated according to the known Mark−Houwink equation $M = K[\eta]^{\alpha}$. From Figure 8 it can be seen that the viscosity of 66-arm star PHEMA is much lower than that of linear PHEMA with the same molecular weight. The viscosity increases with molecular weight; however, this trend is not so significant as that for linear PHEMA. The viscosity of 66-arm star PHEMA after acetylation was measured with THF as solvent, which is a little lower than that before acetylation. Because of the relatively low viscosity and high concentration of hydroxyl groups per macromolecule, the multiarm star PHEMA is expected to be useful for biomedical application.

Conclusions

A convenient method for the preparation of well-defined multiarm star copolymers with an average of 56, 66, and 90 PHEMA arms (M_w/M_n as low as 1.1) and hyperbranched polyglycerol as core has been developed: Well-defined hyperbranched polyglycerols were esterified with 2-bromoisobutyryl bromide and subsequently used as macroinitiators for the ATRP of HEMA in methanol. With the CuCl/$CuBr_2$/2,2′-bipyridyl catalyst system, the polymerization conversion could be driven to 79% in the absence of gelation. The control of CuCl catalyst concentration is very important to obtain high conversion and narrow polydispersity. Absolute M_n values of the polymers were similar to the calculated values. In addition, we have developed a strategy to realize higher molecular weight with M_n around 10^6 g/mol. The viscosity of the obtained multiarm star PHEMA is much lower than that of linear PHEMA.

Since the new multiarm star copolymers possess a large number of hydroxyl groups and consist of biocompatible monomer units (i.e., glycerol and HEMA), the materials are promising with respect to biomedical application.

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