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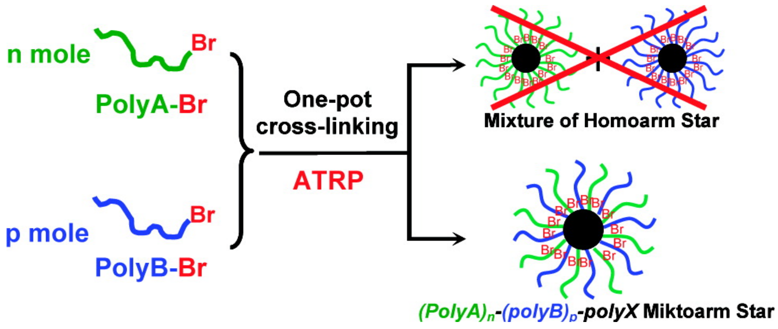

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Arm-First Method As a Simple and General Method for Synthesis of Miktoarm Star Copolymers

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Abstract: Miktoarm star copolymers containing two or more arm species were synthesized by atom transfer radical polymerization using a simple and general "arm-first" method, that is, one-pot cross-linking a mixture of different linear macroinitiator (MI) species by a divinyl cross-linker, such as divinylbenzene. Using linear MIs with a high degree of bromine chain-end functionality, including polyacrylate, polystyrene, polymethacrylate and poly(ethylene oxide), resulted in high-yield star polymers (>90%). Characterized by liquid adsorption chromatography techniques, which separated star polymers on the basis of the chemical composition of arms, the obtained star product was proved to be miktoarm star copolymers containing two or more arm species in one molecule, instead of mixture of different homoarm star polymers. Within our investigation, the molar ratios of the arms in the miktoarm star copolymers were always in agreement with the composition of the initial MI mixture, indicating the powerful capacity of this arm-first method for synthesis of miktoarm star copolymers with potentially any molar ratios and species of the arms. By using a mixture containing five types of linear MIs with different chemical compositions, miktoarm star copolymers containing five kinds of arms were synthesized for the first time, which significantly expanded the methodologies for synthesis of miktoarm star copolymers by living polymerization techniques.

Introduction

Miktoarm (or heteroarm) star copolymers, which contain two or more arm species connecting to one central core, have attracted considerable attention because of their branched architectures, globular shapes, and segmented block structures.[1,2] The different chemical compositions of the arms in miktoarm star molecules lead to their interesting microphase separations in bulk,[3−5] in solution,[6] and at different interfaces.[7] The segregated compartments in the aggregates, such as micelles, could in turn provide distinct chemical environments to store various kinds of drug molecules, fragrance compounds, and gene therapy agents.[8−10]

Until recently, most of the miktoarm star copolymers were synthesized by the living anionic polymerization method.[11,12] However, the development of controlled/"living" radical polymerization (CRP)[13−15] techniques in the past decade is changing this situation rapidly because of the broad variety of applicable monomers and benign experimental conditions in CRPs, for example, atom transfer radical polymerization (ATRP),[16−18] nitroxide mediated polymerization (NMP),[19,20] and reversible addition−fragmentation chain transfer (RAFT) polymerization.[21,22]

By using CRP techniques, miktoarm star copolymers can be synthesized by several strategies. The first one involves the use of a multifunctional miktoinitiator ("core-first" method) by combining various CRP techniques with other living polymerization methods, especially the ring-opening polymerization (ROP) technique.[23−27] The miktoinitiator usually contains two

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or more than two kinds of initiating sites with different initiation mechanisms. Different types of arms grow sequentially from the corresponding initiating sites via polymerization of various monomer species by using different polymerization methods. Therefore, the numbers and species of the arms in the miktoarm star copolymer are determined by the numbers and species of the initiating sites in the miktoinitiator. Chain-end modification of preformed macroinitiator (MI) is an alternative strategy for synthesis of miktoinitiators.[28−31] A branching point containing multiple initiating sites is introduced into the chain-end of linear polymer, which is subsequently used as a MI for polymerization of another monomer to grow the second kind of arms from the branching point. However, the synthesis of multifunctional miktoinitiators and the essential protection/deprotection steps of different initiating sites during polymerization are usually complicated and inefficient.

In a second method, miktoarm star copolymers are synthesized by chain-end coupling reactions between reactive linear chains and multifunctional coupling agents. In such a case, selecting an organic coupling reaction with fast kinetics and high efficiency is crucial to obtain a high coupling yield. Recently, the Cu(I)-catalyzed 1,3-dipolar cycloaddition reactions between an azide and an alkyne, that is, “click reactions”,[32] have emerged as a powerful method for synthesis and functionalization of polymers with complex architectures.[33−36] Several groups have used the “click reactions” to synthesize star[37−40] and miktoarm star copolymers.[41,42]

The third method, “in−out” method,[43−46] is also important for synthesis of miktoarm star copolymers containing two kinds of arms with different chemical compositions and multiple arm numbers since the tedious synthesis of multifunctional miktoinitiator and/or coupling agents is largely avoided. A multifunctional star polymer, synthesized by arm-first method,[47−52] is used as MI to initiate the polymerization of another monomer and form a miktoarm star copolymer. Therefore, the word “in” refers to the arm-first method for formation of the star MI and the word “out” represents the subsequent growth of the second generation of arms from the multifunctional star core. Because of the congested environment around the cross-linked core in the star MI, not all of the initiating sites participated in the formation of the second generation of arms and the initiation efficiency (IE) of the star MI was less than 100%.[45,46] In other words, the number of the second generation of arms is always lower than the number of the first generation of arms in the miktoarm star copolymers. To obtain a miktoarm star copolymer with potentially any molar ratio of the two kinds of arms, an easier and more general method is needed.[53]

In this paper, we report the synthesis of high-yield miktoarm star copolymers containing two or more arm species with various arm numbers and ratios, merely by using the arm-first method. Comparing to the previous in−out method, miktoarm star copolymers were synthesized here by using a mixture of linear MIs with similar reactivity but different chemical compositions and molar ratios to initiate the polymerization of a divinyl cross-linker, such as divinylbenzene (DVB). Thus, the obtained miktoarm star copolymers are formulated as $(\text{polyA})_n$-$(\text{polyB})_p$-polyX, where polyX represents the cross-linked core of the miktoarm star copolymer; n and p are the average numbers of polyA and polyB arms per miktoarm star molecule, respectively. ATRP was used as an illustrative method for synthesis of various kinds of miktoarm star copolymers although the same synthetic strategy can be easily applied to other CRP techniques.[54] The species and initial molar ratios of the MIs directly determined the species and molar ratios of the arms in the final miktoarm star copolymers. Characterization of star products by various techniques, including GPC, ^{1}H NMR spectroscopy, and liquid adsorption chromatography techniques, proved that the star polymer was a miktoarm star copolymer containing two or more arm species in one molecule, instead of mixture of different homoarm star polymers.

Results and Discussion

Miktoarm star copolymers synthesized by the in−out method have an intrinsic problem, the low IE of star MI, which results in an unequal number of two kinds of arms in the miktoarm star copolymers. Furthermore, it is strategically impossible to synthesize a miktoarm star copolymer containing more than two kinds of arms by using the in−out method. Both problems motivated us to develop new and easier methodology for synthesis of miktoarm star copolymers with various molar ratios and species of the arms connecting to one star core.

Several types of linear MIs with different chemical compositions and molecular weights were synthesized by either ATRP of the corresponding monomers, such as, poly(*n*-butyl acrylate) (polyBA-Br), poly(methyl acrylate) (polyMA-Br), poly(*tert*-butyl acrylate) (poly*t*BA-Br), polystyrene (polySt-Br), and poly(methyl methacrylate) (polyMMA-Br) or chain-end esterification

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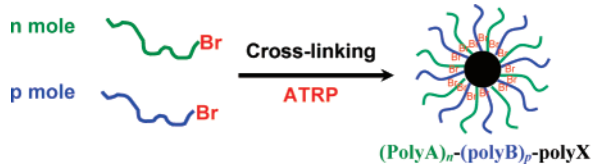
Table 1. Summary of Used Linear MIs

entry	linear MI[a]	$M_{n,NMR}$ (kg/mol)[b]	DP[b]	$M_{n,GPC}$ (kg/mol)[c]	M_w/M_n[c]
MI-1	PolyBA-Br	9.87	76	9.40	1.10
MI-2	PolyMA-Br	6.10	69	6.20	1.07
MI-3	PolyMA-Br	2.10	22	2.05	1.08
MI-4	Poly*t*BA-Br	5.87	44	6.04	1.08
MI-5	PolySt-Br	8.32	78	8.10	1.10
MI-6	PolyMMA-Br	6.63	64	6.48	1.17
MI-7	PEO-Br	5.02	110	5.20	1.04

[a] Detailed synthetic procedures for all MIs are described in the Supporting Information. [b] Number-average molecular weight and degree of polymerization (DP) determined by ^{1}H NMR at 27 °C with $CDCl_3$ as solvent. [c] Number-average molecular weight and polydispersity measured by GPC in THF with RI detector; calibration with linear polyMMA as standard for polyMMA-Br and PEO-Br MIs and linear polySt as standard for the others.

Scheme 1. Synthesis of Miktoarm Star Copolymers by Cross-Linking Two Kinds of Linear MIs via the Arm-First Method



of poly(ethylene glycol) monomethyl ether (PEO-OH) to form PEO-Br. All polymer chains had narrow molecular weight distribution (MWD, low M_w/M_n) and the relevant information is summarized in Table 1. Simply cross-linking a mixture of two or more than two types of linear MIs by DVB produced high-yield (>90%) miktoarm star copolymers with the arm ratio determined by the initial molar ratio of the used MIs (Scheme 1).

Synthesis of Miktoarm Star Copolymers via Equimolar Cross-Linking of Two MIs. As the first example to illustrate the capacity of the arm-first method for synthesis of miktoarm stars copolymers, an equimolar mixture of polyBA-Br and polyMA-Br MIs (MI-1 and MI-2 in Table 1) was cross-linked by using DVB as cross-linker and CuBr/*N*,*N*,*N*′,*N*′′,*N*′′-pentamethyldiethylenetriamine (PMDETA) as catalyst.

Before the polymerization, the system is a mixture of two kinds of linear MIs, whose GPC curve showed two peaks (dashed lines in Figure 1B). During the cross-linking reaction, the semilogarithmic kinetic plot is linear (Figure 1A), indicating a constant concentration of radicals. The conversion of DVB reached 98% at 20 h. The GPC curves in Figure 1B indicate that as the conversion of DVB increased, the amount of MIs incorporated into the star polymers increased, which was confirmed by the decreasing RI signal corresponding to the unreacted linear MIs and a increasing GPC peak at higher molecular-weight direction. After 20 h, the area percentage of the star polymer peak in the GPC curve was around 93%, according to the multipeak splitting of the GPC curve at 20 h using Gaussian function. Based on the DVB conversions and the d*n*/d*c* values of different polymeric segments in THF at 35 °C, for example, polyDVB (0.180 mL/g, the value of linear polySt), polyBA (0.069 mL/g), and polyMA (0.069 mL/g),[55] ca. 89 wt % of the linear MIs were incorporated into the star format (a detailed calculation is described in the Supporting Information). Since the initial weight ratio of polyBA-Br and polyMA-Br MIs was 0.61/0.39 (molar ratio $f_{MI-1}/f_{MI-2} = 0.50/0.50$, entry M12−55, Table 2), incorporation of 89 wt % of MIs into star product indicates that the obtained star product contained both linear arms.

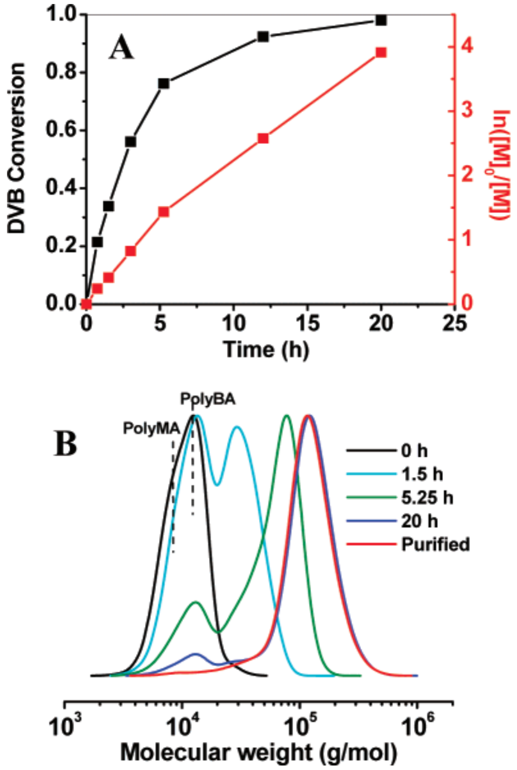


Figure 1. (A) Dependence of DVB conversion and ln([M]$_0$/[M]) on reaction time and (B) the GPC traces during the synthesis of (polyBA)$_n$-(polyMA)$_p$-polyDVB miktoarm star copolymers (M12−55, Table 2). Experimental conditions: [polyBA-Br (MI-1)]$_0$/[polyMA-Br (MI-2)]$_0$/[DVB]$_0$/[CuBr]$_0$/[PMDETA]$_0$ = 0.5/0.5/12/0.8/0.8, [polyBA-Br] = 0.015 M, 110 °C in anisole for 20 h; linear polySt standards for THF GPC calibration.

After precipitation of the star product into cold methanol to remove the unreacted linear chains (Figure 1B), the purified star polymers were analyzed by ^{1}H NMR spectroscopy (Figure 2). The proton peaks from polyBA and polyMA arms are clearly observed. While the phenyl proton peaks from polyDVB core between 6.0 and 7.5 ppm are too broad to be detected because of the restricted rotation of the highly cross-linked polyDVB core.[45] On the basis of the integration of proton peaks (H_c from polyBA arm and H_g from polyMA arm) and the degree of polymerization (DP) of these two arms ($DP_{polyBA\ (MI-1)} = 76$, $DP_{polyMA\ (MI-2)} = 69$ in Table 1), the molar fraction of polyBA and polyMA arms in the final star polymer was around $n_1/n_2 = 0.52/0.48$, which is close to their initial 0.50/0.50 molar ratio in the MI mixture (M12−55, Table 2). The results from GPC and NMR analyses indicate that both MIs were successfully incorporated into the star molecules, although the final star product could be either a miktoarm star copolymer containing two kinds of arms in one molecule or a mixture of two homoarm star molecules.

It is seen in Figure 3A that the GPC curve of the star product M12−55 significantly overlapped with those of (polyBA)$_n$-polyDVB (S1, Table 2) and (polyMA)$_n$-polyDVB (S2, Table 2) homoarm star polymers, which were synthesized under similar conditions to M12−55 with molar ratio of [MI]$_0$/[DVB]$_0$

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Table 2. Synthesis of Star and Miktoarm Star Copolymers by Arm-First Method[a]

entries[b]	f_{MI-1}	f_{MI-2}	A_{star}[c]	$M_{w,RI}$ (kg/mol)[d]	$M_{w,MALLS}$ (kg/mol)[e]	M_w/M_n[d]	n_1/n_2[f]	N_{arm} per star[g]	N_{arm_1} per star[g]	N_{arm_2} per star[g]
S1	1.00	0	0.93	169	606	1.36		54	54	0
S2	0	1.00	0.91	130	583	1.48		73	0	73
M12−91	0.90	0.10	0.95	167	605	1.37	0.87/0.13	57	49	8
M12−73	0.70	0.30	0.93	142	468	1.37	0.68/0.32	46	32	14
M12−55	0.50	0.50	0.93	129	465	1.39	0.52/0.48	49	25	24
M12−37	0.30	0.70	0.93	130	448	1.34	0.34/0.66	50	17	33
M12−19	0.10	0.90	0.92	121	434	1.39	0.12/0.88	52	6	46

[a] Synthesis of $(\text{polyBA})_n$-$(\text{polyMA})_p$-polyDVB miktoarm star copolymers by cross-linking two kinds of linear MIs: polyBA-Br (MI-1) and polyMA-Br (MI-2). Experimental conditions: $[\text{MI-1}]_0/[\text{MI-2}]_0/[\text{DVB}]_0/[\text{CuBr}]_0/[\text{PMDETA}]_0 = f_{MI-1}/f_{MI-2}/12/0.8/0.8$, 110 °C in anisole for 20 h. [b] In "Mxy-$\alpha\beta$", "M" represents "miktoarm star", "x" and "y" represent the corresponding linear MIs listed in Table 1 with feed ratio as α/β ($=f_{MI-1}/f_{MI-2}$), respectively. [c] Area fraction of star or miktoarm star polymers, determined by the multipeak splitting of the GPC curve using Gaussian function. [d] Weight-average molecular weight and polydispersity, measured by THF GPC with RI detector; calibration with linear polySt as standard. [e] Weight-average molecular weight, measured by THF GPC with MALLS detector. [f] Average molar fraction of arm 1 and arm 2 in the miktoarm star copolymers, determined by ^{1}H NMR, 27 °C, $CDCl_3$ as solvent. [g] Number-average value of the number of arms per star or miktoarm star molecule (N_{arm}) was calculated based on eq S1 in the Supporting Information. $N_{arm1} = N_{arm} \times n_1$; $N_{arm2} = N_{arm} \times n_2$.

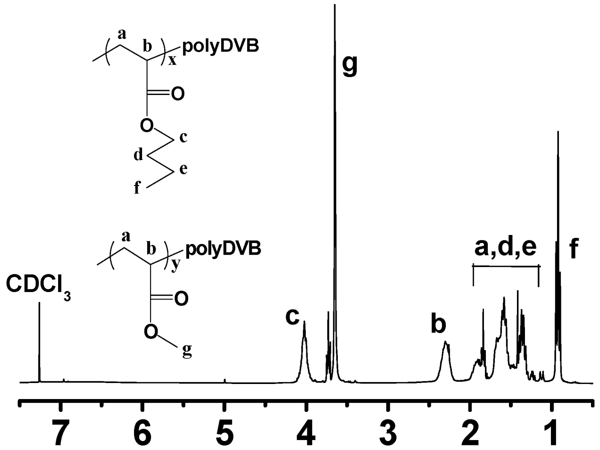

Figure 2. ^{1}H NMR spectrum of the purified $(\text{polyBA})_n$-$(\text{polyMA})_p$-polyDVB miktoarm star copolymers synthesized by ATRP cross-linking equimolar polyBA-Br (MI-1) and polyMA-Br (MI-2) MIs (M12−55, Table 2). NMR condition: 27 °C, $CDCl_3$ as solvent.

= 1/12. Therefore, we could not exclude the possibility that the elution peak of the purified star product in Figure 1B represented a mixture of two homoarm star polymers because polymers are separated in GPC only according to their hydrodynamic volume or molecular weight. In other words, GPC alone cannot differentiate two kinds of stars with similar size but different chemical compositions. To determine the distribution of the two kinds of arms in the miktoarm star copolymers, a liquid chromatography technique, which separates polymers on the basis of their chemical compositions, should be employed. The purified star polymer was characterized by the liquid chromatography under the critical conditions (LCCC) of polyMA homopolymer, under which the elution volume of polyMA-containing copolymers is solely determined by the molecular weight of other polymeric segments.[56,57] By using normal phase silica columns as stationary phase and 2-butanone/cyclohexane mixtures (86/14 by volume) as eluent, the polyMA segment becomes chromatographically "invisible" and the elution behavior of the polyBA and polyDVB segments is in the size exclusion mode.[57] In other words, the copolymer containing more polyBA arms elutes earlier.

Under the LCCC of polyMA homopolymer, the peak elution volume of $(\text{polyMA})_n$-polyDVB homoarm star polymers was $V_e = 4.96$ mL, lower than that of the polyMA-Br linear MI ($V_e = 5.38$ mL) owing to the existence of a polyDVB core in the star polymers. In contrast, the elution volume of $(\text{polyBA})_n$-polyDVB homoarm star polymers was $V_e = 3.01$ mL. If the star product of M12−55 were a mixture of $(\text{polyMA})_n$-polyDVB and $(\text{polyBA})_n$-polyDVB homoarm star polymers, its chromatogram under the LCCC should show two elution peaks around 4.96 mL and 3.01 mL, respectively. If the product were a $(\text{polyBA})_n$-$(\text{polyMA})_p$-polyDVB miktoarm star copolymer containing two kinds of arms in one molecule with a homogeneous distribution, it should show one elution peak located between 4.96 and 3.01 mL. The result in Figure 3B clearly indicates that the star product of M12−55 only showed one elution peak with $V_e = 3.37$ mL. The absence of elution peaks at ca. 4.96 and 3.01 mL indicates that the star product of M12−55 was a $(\text{polyBA})_n$-$(\text{polyMA})_p$-polyDVB miktoarm star copolymer instead of mixture of two homoarm stars. The elution volume of the miktoarm star copolymer was larger than that of $(\text{polyBA})_n$-polyDVB homoarm star, because the number of polyBA arms in the miktoarm star copolymer was smaller than that in the $(\text{polyBA})_n$-polyDVB homoarm star polymer. At the same time, the polyMA arms in the miktoarm star copolymer did not influence its elution behavior, as discussed above. The absolute molecular weight of the miktoarm star copolymer M12−55 was $M_{w,MALLS} = 465$ kg/mol, determined by THF GPC with a multi-angle laser light scattering (MALLS) detector. On the basis of the weight fraction of incorporated linear MIs into the miktoarm star, the total average arm number per miktoarm star molecule in M12−55 is ca. $N_{arm} = 49$, in which 25 arms are polyBA and 24 arms are polyMA (detailed calculation is described in the Supporting Information).

Synthesis of $(\text{PolyBA})_n$-$(\text{polyMA})_p$-polyDVB Miktoarm Star Copolymers with Various Molar Ratios of the Two Kinds of Arms. One advantage of this new arm-first method is that we can easily synthesize miktoarm star copolymers with potentially any molar ratio of the two kinds of arms by tuning the initial molar ratio of the two MIs. Table 2 summarizes the results of a series of $(\text{polyBA})_n$-$(\text{polyMA})_p$-polyDVB miktoarm star copolymers with various molar ratios of polyBA and polyMA arms. By simply changing the initial molar ratio of polyBA-Br to polyMA-Br MIs from 0.90/0.10 (M12−91 in Table 2) to 0.10/0.90 (M12−19 in Table 2), miktoarm star

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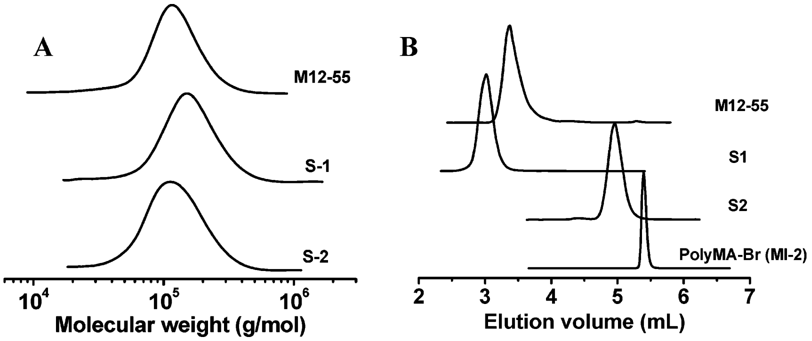

Figure 3. (A) GPC traces and (B) LCCC chromatograms of (polyBA)$_n$-polyDVB (S1), (polyMA)$_n$-polyDVB (S2) homoarm stars and *(polyBA)$_n$*-(polyMA)$_p$-polyDVB (M12−55) miktoarm star copolymers. LCCC conditions for polyMA homopolymers: two sets of silica columns with pore size of 100 and 300 Å, respectively, mobile phase as 2-butanone/cyclohexane (86/14 by volume) with flow rate as 0.5 mL/min at 32 °C.

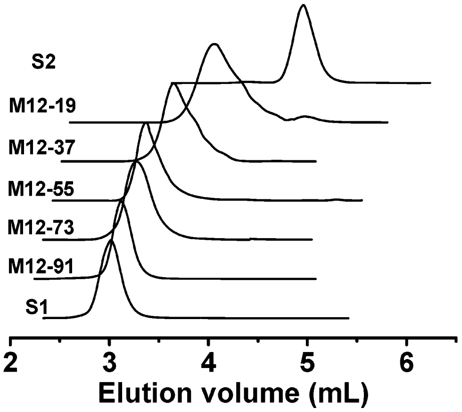

Figure 4. LCCC chromatograms of (polyBA)$_n$-polyDVB stars (S1), (polyMA)$_n$-polyDVB stars (S2) and (polyBA)$_n$-*(polyMA)$_p$*-polyDVB miktoarm stars with various molar ratios of polyBA (MI-1) and polyMA (MI-2) arms ($f_{\mathrm{MI-1}}/f_{\mathrm{MI-2}}$ = 0.90/0.10, 0.70/0.30, 0.50/0.50, 0.30/0.70, and 0.10/0.90, M12−91 to M12−19 in Table 2); the same LCCC conditions as those in Figure 3.

copolymers with different arm compositions were obtained. The average number of arms per miktoarm star molecule was around 50 when the molar ratio of the two kinds of MIs ($f_{\mathrm{MI-1}}/f_{\mathrm{MI-2}}$) varied from 0.90/0.10 to 0.10/0.90, similar to that of the (polyBA)$_n$-polyDVB homoarm star polymer ($N_{\mathrm{arm}} = 54$). However, the molecular weights of the miktoarm star copolymers decreased with the increase of the molar fraction of polyMA-Br MI in the MI mixture, since the molecular weight of polyMA-Br arm (MI-2, $M_{\mathrm{n,NMR}} = 6.10$ kg/mol) was smaller than that of polyBA-Br arm (MI-1, $M_{\mathrm{n,NMR}} = 9.87$ kg/mol).

Under the LCCC, these miktoarm star copolymers had different elution volumes. In Figure 4, the miktoarm star copolymers with initially higher molar ratio of polyBA-Br to polyMA-Br, such as M12−91, have a smaller elution volume than miktoarm stars obtained from lower molar ratio of the two MIs, indicating the initial composition of linear MIs directly determined the arm composition of the miktoarm star product. Such a result is consistent with the results from ^{1}H NMR analysis, which indicate that the arm composition in the purified miktoarm star product (n_1/n_2) was always in agreement with the initial composition of the two MIs ($f_{\mathrm{MI-1}}/f_{\mathrm{MI-2}}$, Table 2).

It is found in Figure 4 that when the average number of polyBA arms (N_{arm1}) in one miktoarm star copolymer decreased, the elution peak of the miktoarm star copolymers under LCCC analysis became broader, although their $M_{\mathrm{w}}/M_{\mathrm{n}}$ values from GPC measurements remained similar. It is worth noting that the miktoarm star copolymer synthesized by this arm-first method is comparable to a multi-segmented block copolymer containing different numbers of polyBA and polyMA blocks, although the miktoarm star copolymer has a more compact structure compared to its linear analogue. Since the average molecular weight of one polyBA arm was ca. $M_{\mathrm{n,NMR}} = 9.87$ kg/mol (DP = 76), the cumulative MWD of polyBA segments in the miktoarm star copolymers became broader when the N_{arm1} decreased, especially to a single digit, such as M12−19 ($N_{\mathrm{arm1}} = 6$). A small peak with $V_{\mathrm{e}} = 4.98$ mL was detected in the elution chromatogram of M12−19, indicating that there was a small amount of (polyMA)$_n$-polyDVB homoarm star polymers (<5% by area) existing in the miktoarm star product. This phenomenon is reasonable because the probability (fraction) of a star molecule containing zero polyBA arms increased with the decrease of the average number of polyBA arms per miktoarm star molecule (N_{arm1}).

(PolyBA)$_n$-(polyMA)$_p$-polyDVB miktoarm star copolymers were also synthesized by using MIs with different molecular weights. PolyMA-Br MI with low molecular weight (MI-3, $M_{\mathrm{n,NMR}} = 2.10$ kg/mol) and polyBA-Br MI with high molecular weight (MI-1, $M_{\mathrm{n,NMR}} = 9.87$ kg/mol) were mixed together with equimolar ratio for cross-linking reactions. The obtained miktoarm star copolymers (M13−55 in Table 3) had high star yield ($A_{\mathrm{star}} = 0.94$) and high molecular weight ($M_{\mathrm{w,MALLS}} = 447$ kg/mol). The molar ratio of the incorporated two arm species was $n_1/n_3 = 0.46/0.54$, in agreement with the initial molar ratio of the two MIs in the mixture.

Synthesis of Various Miktoarm Star Copolymers Containing Two Kinds of Arms with Different Chemical Compositions. By changing the initial molar ratio of the two MIs, such as polyBA-Br and polyMA-Br, miktoarm star copolymers with various arm numbers and compositions were synthesized via cross-linking two MIs in a one-pot reaction. To illustrate the versatility of this facile method, various miktoarm star copolymers containing two types of arms with different chemical compositions and molecular weights were synthesized via ATRP by using series of combinations of linear MIs with equal moles, including polyBA-Br, polyMA-Br, poly*t*BA-Br, polySt-Br, polyMMA-Br, and PEO-Br. Table 3 summarizes the results of the obtained miktoarm star copolymers, including (polyBA)$_n$-(polytBA)$_p$-polyDVB, (polyBA)$_n$-(polySt)$_p$-polyDVB, (polyBA)$_n$-(polyMMA)$_p$-polyDVB and (polyBA)$_n$*-(PEO)$_p$*-polyDVB. The purified miktoarm star copolymers were obtained by precipitation of the product into cold methanol to remove the unreacted linear chains. The GPC curves during each polymerization are shown in the Supporting Information

Table 3. Synthesis of Miktoarm Star Copolymers by Cross-Linking Various MIs[a]

entries[b]	arm compositions	A_{star}[c]	$M_{w,RI}$ (kg/mol)[d]	$M_{w,MALLS}$ (kg/mol)[e]	M_w/M_n[d]	n_x/n_y[f]	N_{arm} per star[g]	N_{arm-x} per star[g]	N_{arm-y} per star[g]
M13−55	(PolyBA)$_n$-(polyMA)$_p$-	0.94	114	447	1.43	0.46/0.54	63	29	34
M14−55	(PolyBA)$_n$-(polytBA)$_p$-	0.93	119	334	1.37	0.51/0.49	35	18	17
M15−55	(PolyBA)$_n$-(polySt)$_p$-	0.87	206	898	1.48	0.56/0.44	84	47	37
M16−55	(PolyBA)$_n$-(polyMMA)$_p$-	0.86	150	532	1.46	0.52/0.48	53	28	25
M17−55	(PolyBA)$_n$-(PEO)$_p$-	0.89	103	483	1.39	0.47/0.53	52	24	28

[a] Synthesis of (polyA)$_n$-(polyB)$_p$-polyDVB miktoarm star polymers by cross-linking two kinds of linear MIs with equal moles. Experimental conditions: $[\text{MI-x}]_0/[\text{MI-y}]_0/[\text{DVB}]_0/[\text{CuBr}]_0/[\text{PMDETA}]_0 = 0.5/0.5/12/0.8/0.8$, 110 °C in anisole for 20 h. [b] In "Mxy-$\alpha\beta$", "M" represents "miktoarm star", "x" and "y" represent the corresponding linear MIs listed in Table 1 with feed ratio as α/β ($=f_{\text{MI-x}}/f_{\text{MI-y}}$), respectively. [c] Area fraction of star or miktoarm star polymers, determined by the multipeak splitting of the GPC curve using Gaussian function. [d] Weight-average molecular weight and polydispersity, measured by THF GPC with RI detector; calibration with linear polySt as standard. [e] Weight-average molecular weight, measured by THF GPC with MALLS detector. [f] Average molar fraction of arm x and arm y in the miktoarm star copolymers, determined by ^{1}H NMR, 27 °C, $CDCl_3$ as solvent. [g] Number-average value of the number of arms per star or miktoarm star molecule (N_{arm}) was calculated based on eq S1 in the Supporting Information. $N_{arm-x} = N_{arm} \times n_x$; $N_{arm-y} = N_{arm} \times n_y$.

(Figures S2, S3, S4, and S5). Table 3 shows that the molecular weights of the miktoarm star copolymers depend on the arm composition. The molecular weight can be influenced by several parameters, including the molecular weight and reactivity of the linear MI, the incorporation rates of the two kinds of MIs, and their relative molar ratio in the initial mixture.[52,58]

For (polyBA)$_n$-(polytBA)$_p$-polyDVB and (polyBA)$_n$-(polySt)$_p$-polyDVB miktoarm star copolymers, because of the similar polarity of polyBA polymers to poly*t*BA and polySt polymers, separation of the miktoarm star copolymers, that is, M14−55, M15−55, on the basis of their chemical composition is difficult. However, ^{1}H NMR analyses of the purified miktoarm star copolymers indicate that the molar ratio of the two kinds of arms in the final star products is very close to that of the initial composition of MI mixture. Since reaction solvent anisole is a good solvent for all of these linear MIs and the activity of these MIs under ATRP conditions is similar, it is reasonable to expect that the obtained star product was a miktoarm star copolymer.

When linear MIs with different activity are used, the synthesis of miktoarm star copolymers by using this simple arm-first method could be a challenge, owing to the different incorporation rates of the two MIs. The activity of polymethacrylate chain-end is much higher than that of polyacrylate.[59−62] To explore the feasibility of the incorporation of polymethacrylate and polyacrylate arms into one miktoarm star molecule, polyMMA-Br linear MI with $M_{n,NMR} = 6.63$ kg/mol (MI-6 in Table 1) was mixed with equimolar amount of polyBA-Br MI (MI-1 in Table 1) to prepare (polyBA)$_n$-(polyMMA)$_p$-polyDVB miktoarm star copolymers. The LCCC for polyMMA homopolymers was used to differentiate the miktoarm star copolymers from the homoarm star polymers based on the chemical composition of the arms. The critical conditions for polyMMA were established by using silica columns as stationary phase and 2-butanone/cyclohexane mixtures (74/26 by volume) as eluent, in which the polyMMA segment in the block copolymer became chromatographically "invisible". Under the LCCC analysis (Figure 5), the chromatogram of the miktoarm star product showed one elution peak at $V_e = 3.72$ mL. The location of this peak was different from those of (polyBA)$_n$-polyDVB ($V_e = 3.24$ mL) and (polyMMA)$_n$-polyDVB ($V_e = 4.63$ mL) homoarm star polymers, indicating that the star product by cross-linking equimolar polyBA-Br MI and polyMMA-Br MI was a miktoarm star copolymer containing two arm species in one star molecule.

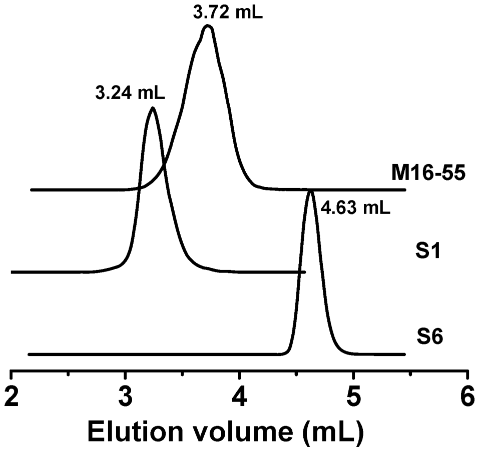

Figure 5. LCCC chromatograms of (polyBA)$_n$-polyDVB (S1), (polyMMA)$_n$-polyDVB (S6) homoarm stars, and (polyBA)$_n$-(polyMMA)$_p$-polyDVB (M16−55, Table 3) miktoarm star copolymers. The homoarm star S6 was synthesized at 110 °C with the initial ratio of reagents as $[\text{polyMMA-Br (MI-6)}]_0/[\text{DVB}]_0/[\text{CuBr}]_0/[\text{PMDETA}]_0 = 1/12/0.8/0.8$ ($[\text{polyMMA-Br}]_0 = 0.016$ M in anisole). LCCC conditions for polyMMA homopolymers: two sets of silica columns with pore size of 100 and 300 Å, respectively, mobile phase as 2-butanone/cyclohexane (74/26 by volume) with flow rate as 0.5 mL/min at 32 °C.

Another kind of interesting linear polymer is PEO, whose water-solubility and biocompatibility provide it many potential applications. PEO-Br linear MI with a 2-bromoisobutyrate chain-end functionality ($M_{n,NMR} = 5.02$ kg/mol, MI-7) was mixed with polyBA-Br (MI-1) with equimolar ratio for synthesis of (polyBA)$_n$-(PEO)$_p$-polyDVB miktoarm star copolymers. ^{1}H NMR result indicates that the fraction ratio of the incorporated polyBA and PEO arms in the star product ($n_1/n_7 = 0.47/0.53$) was close to the initial molar ratio of the two MIs (M17−55, Table 3). Gradient polymer elution chromatography (GPEC) was applied to analyze the star polymer on the basis of their chemical composition. The preliminary result (Figure S6 in the Supporting Information) indicates that there was no (PEO)$_n$-polyDVB homoarm star polymers in the final star product, suggesting the obtained star polymer was a (polyBA)$_n$-(PEO)$_p$-polyDVB miktoarm star copolymer.

Synthesis of Miktoarm Star Copolymers Containing Five Types of Arms with Different Chemical Compositions. Till now, all of the miktoarm star copolymers synthesized by the

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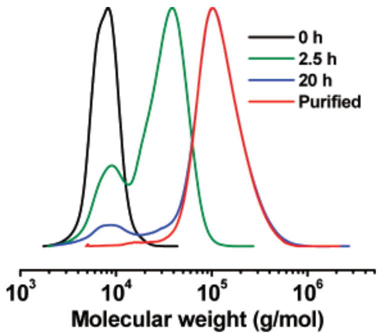

Figure 6. GPC traces of (polyBA)$_l$-(polyMA)$_m$-(polytBA)$_n$-(polySt)$_o$-(PEO)$_p$-polyDVB miktoarm star copolymers synthesized by cross-linking five kinds of linear MIs. Experimental conditions: [polyBA-Br]$_0$/[polyMA-Br]$_0$/[poly*t*BA-Br]$_0$/[polySt-Br]$_0$/[PEO-Br]$_0$/[DVB]$_0$/[CuBr]$_0$/[PMDETA]$_0$ = 0.2/0.2/0.2/0.2/0.2/12/0.8/0.8, [polyBA-Br] = 0.007 M, 110 °C in anisole; linear polySt standards for GPC calibration.

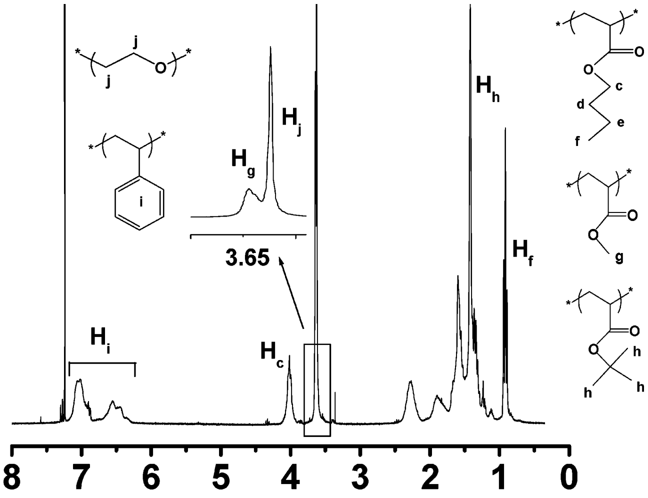

Figure 7. ^{1}H NMR spectrum of the purified (polyBA)$_l$-(polyMA)$_m$-(polytBA)$_n$-(polySt)$_o$-(PEO)$_p$-polyDVB miktoarm star copolymers containing five types of arms with different chemical compositions. NMR condition: 27 °C, $CDCl_3$ as solvent.

in−out method contain only two kinds of arms, because of the inherent restriction of this method. Therefore, no report has been published on synthesis of miktoarm star copolymers containing more than two kinds of arms with different chemical compositions based on the in−out method. In order to show the versatility and simplicity of this new arm-first method for synthesis of miktoarm star copolymers, five kinds of linear MIs with different chemical compositions, polyBA-Br, polyMA-Br, poly*t*BA-Br, polySt-Br, and PEO-Br, were simply mixed together in equimolar amounts. By using DVB as cross-linker, miktoarm star copolymers, (polyBA)$_l$-(polyMA)$_m$-(polytBA)$_n$-(polySt)$_o$-(PEO)$_p$-polyDVB, containing five kinds of arms in one star molecule were synthesized. The reaction was stopped at 20 h, and the GPC trace in Figure 6 indicates that the final star yield was ca. 90% by area. By precipitation into cold methanol, purified star polymers without the contaminant of unreacted linear chains were obtained, whose apparent molecular weight and the absolute molecular weight of the miktoarm star copolymers were $M_{w,RI}$ = 138 kg/mol and $M_{w,MALLS}$ = 521 kg/mol, respectively.

The NMR spectrum in Figure 7 indicates that all five types of arms are present in the purified star copolymers. The proton peaks from polyBA (H_c, H_f) and polySt arms (H_i) are distinguished completely from other signals, although the proton peak of polyMA arms (H_g) overlapped with that from PEO arms (H_j) and the proton peak from poly*t*BA arms (H_h) overlapped with the proton peaks from polyBA arms (H_e). Integration of these peaks indicates that the area ratio of peaks $H_c/H_g/H_h/H_i/H_j$ equals to 1.00/1.13/3.14/2.98/2.37. On the basis of the DP of each linear MI, the average molar fraction of each arm in the miktoarm star copolymer is 0.20, 0.17, 0.24, 0.23, and 016 for polyBA, polyMA, poly*t*BA, polySt, and PEO arms, respectively, although the partially overlapped peaks hampered the accuracy of the corresponding integration. Such a result clearly indicates that the arm composition of the finally obtained miktoarm star copolymers is predetermined by the initial molar ratios of the linear MIs. Within the scale of our investigation, the arm species incorporated into the miktoarm star molecules included PEO, polyacrylate, polymethacrylate, and polystyrene. By changing the initial molar ratios of linear MIs with different chemical compositions, miktoarm star copolymers with more than two kinds of arms and various arm compositions were easily synthesized by simply cross-linking the mixture of linear MIs.

Conclusions

Miktoarm star copolymers containing two or more arm species with various arm numbers and molar ratios were successfully synthesized by a simple and general arm-first method, that is, one-pot cross-linking the mixture of different linear MIs by a divinyl cross-linker, such as DVB. Different from previous in−out method, the arm-first method can yield miktoarm star copolymers with potentially any molar ratios and species of the arms by simply changing the molar ratios of the linear MIs. The used linear MIs included polyBA, polyMA, polytBA, polySt, polyMMA, and PEO, and the star polymers were obtained in high yield (>90%). Characterization of the star products by LCCC or GPEC techniques proved that the obtained star polymers were miktoarm star copolymer containing two or more arm species in one molecule, instead of a mixture of different homoarm star polymers. The molar ratios of the arms in the miktoarm star copolymers were always in agreement with the composition of the initial MI mixture. By using a similar method, miktoarm star copolymers containing five kinds of arms with different chemical compositions were synthesized for the first time by cross-linking a mixture of five different MI species. These results indicate that the one-pot arm-first method is a general and simple method for synthesis of miktoarm star copolymers.

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Supporting Information Available: Procedures for preparation and analysis of various kinds of star and miktoarm star copolymers, their GPC plots, LCCC chromatograms, and GPEC chromatograms. This material is available free of charge via the Internet at http://pubs.acs.org.

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