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ARTICLE

Synthesis of Polystyrenes−Poly(alkyl methacrylates) Block Copolymers via Anionic Polymerization Using an Integrated Flow Microreactor System

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ABSTRACT: The polystyrene living polymer end, which was produced by butyllithium initiated anionic polymerization of styrene in a flow microreactor system was found to be effectively trapped with 1,1-diphenylethylene. The resulting organolithium species could be used as a macro initiator for anionic polymerization of alkyl methacrylates to obtain styrene−alkyl methacrylate diblock copolymers using an integrated flow microreactor system. A high level of control of molecular weight was achieved at easily accessible temperatures such as +24 to −28 °C by virtue of the fast mixing, fast heat transfer, and residence time control. Triblock copolymers were also synthesized by sequential introduction of styrene and two different alkyl methacrylates in a similar manner.

Introduction

The synthesis of structurally well-defined functionalized polymers has attracted a great deal of attention.[1] Precise control of molecular weight and molecular weight distribution, selective end-functionalization, and highly controlled block copolymerization are key to synthesize such polymers. Living polymerization[2] enables such control.[3−5] However, development of an alternative method for synthesizing such polymers without deceleration by capping agents has been strongly needed.

Recently, we have proposed the concept of flash chemistry,[6] in which extremely fast reactions are conducted in highly controlled manners using flow microreactor systems.[7−9] Based on the concept, flow-microreactor-system-controlled polymerization has been developed.[10] In the cationic polymerization, excellent molecular weight control and molecular weight distribution control can be achieved without deceleration by the equilibrium between active species and dormant species.[11] Characteristic features of flow microreactors including fast mixing stemming from short diffusion path,[12] fast heat transfer by virtue of high surface-to-volume ratio, and short residence time[13,14] are responsible for the control of the polymerization. In addition, it is noteworthy that the molecular weight of polymers can be controlled by modulating the flow rates of the solutions of an initiator and a monomer to produce libraries of polymers for high-throughput evaluation.

Radical polymerization can also be conducted in flow microreactor systems.[15−17] Although polymers with narrower molecular weight distribution are obtained without deceleration, the polymerization is not living. To achieve living radical polymerization, a capping agent to slow down the polymerization is needed even in flow microreactor systems, presumably because lifetimes of radical growing polymer ends are too short in comparison with typical residence times in flow microreactors.

Anionic polymerization serves as an excellent method for the synthesis of polymers of well-defined end-structures, because the anionic reactive polymer ends are living even in the absence of a capping agent.[4,18] The anionic growing polymer ends (usually organolithium species) can be utilized for end-functionalization reactions with various electrophiles and block copolymerization with another monomer. Recently, it was found that a flow microreactor is effective for accomplishing the controlled anionic polymerization of styrenes or alkyl methacrylates.[19] A high level of control of the molecular weight distribution can be achieved in a flow microreactor under easily accessible conditions such as +24 to −28 °C by virtue of the characteristic features of flow microreactors including fast mixing, fast heat transfer, and precise residence time control.

Another advantage of flow-microreactor-controlled polymerization is easy modulation of flow microreactors to integrate polymerization reactions and/or end functionalization. For example, space integration[20] of polymerization reactions by sequential introduction of different types of monomers using an integrated flow microreactor system leads to the formation of block copolymers, which have received significant research interest from a viewpoint of functional materials based on microphase separation structures.

In this paper we focus on the integration of the anionic polymerization of styrenes and the anionic polymerization of alkyl methacrylates to produce copolymers consisting of blocks having different natures. To the best of our knowledge, block copolymerization of styrenes and alkyl methacrylates using an integrated flow microreactor system has not been reported so far. At first glance, direct integration does not seem to be successful because a polystyrene living polymer end is too reactive and may attack the alkoxycarbonyl group of alkyl methacrylate. To achieve copolymerization, the polystyrene living polymer end needs to be trapped with 1,1-diphenylethylene before subsequent polymerization with an alkyl methacrylate.[21]

Here, we report that the polystyrene living polymer end produced in a flow microreactor system could be effectively trapped with 1,1-diphenylethylene and that copolymerization of styrenes and alkyl methacrylates was successfully achieved using an integrated flow microreactor system. Diblock and triblock copolymers were obtained with a narrow molecular weight distribution under easily accessible conditions.

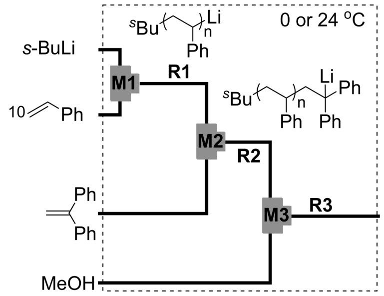

Figure 1. Flow microreactor system for trapping of a polystyrene living polymer end with 1,1-diphenylethylene at 0 or 24 °C. T-shaped micromixer: **M1** (ϕ = 250 μm), **M2** (ϕ = 500 μm), and **M3** (ϕ = 500 μm). Microtube reactor: **R1** (ϕ = 1000 μm, L = 100 cm (9.29 s)), **R2** (ϕ = 1000 μm, L = 3.5 or 6 or 12.5 or 25 or 50 or 100 or 200 cm), and **R3** (ϕ = 1000 μm, L = 200 cm (8.33 s)). Solution: *s*-BuLi 0.050 M in hexane (3.12 mL/min), styrene 0.80 M in THF (tetrahydrofuran) (1.95 mL/min), 1,1-diphenylethylene 0.050 M in THF (3.12 mL/min), and methanol 0.50 M in THF (3.12 mL/min).

Results and Discussion

Trapping of the Polystyrene Living Polymer End with 1,1-Diphenylethylene in a Flow Microreactor System. We first examined the trapping of the polystyrene living polymer end with 1,1-diphenylethylene using an integrated flow microreactor system composed of three T-shaped micromixers and three microtube reactors (Figure 1). A solution of *s*-BuLi (0.050 M in hexane, 3.12 mL/min) and a solution of styrene (0.80 M in THF, 1.95 mL/min, 10 equiv based on *s*-BuLi) were mixed using micromixer **M1**, and the resulting solution was introduced into microtube reactor **R1**, where the polymerization took place. The resulting solution containing the polystyrene living polymer was introduced to micromixer **M2**, where 1,1-diphenylethylene (0.050 M in THF, 3.12 mL/min, 1.0 equiv based on *s*-BuLi) was mixed. The solution was passed through microtube reactor **R2**, where the trapping reaction took place. The resulting solution was quenched with methanol (0.50 M in THF, 3.12 mL/min, 10 equiv based on *s*-BuLi) using micromixer **M3** and microtube reactor **R3**. The whole system was dipped in a cooling bath, the temperature of which was maintained at 0 °C, because this temperature was found to be suitable for conducting polymerization of styrene in a flow microreactor in the previous studies.[19b] The results obtained by varying the residence time in **R2** by changing the length of **R2** are summarized in Table 1. The conversion of 1,1-diphenylethylene increased with an increase in the residence time in **R2** until the residence time reached ca. 1.4 s because of the progress of the trapping reaction. However, further increase in the residence time did not cause a significant increase of the conversion.

In a previous study, it was revealed that the polymerization of styrenes can also be carried out at 24 °C effectively using flow microreactors.[20b] Therefore, we also examined the polymerization of styrene followed by trapping with 1,1-diphenylethylene at 24 °C using the integrated flow microreactor. As shown in Table 1, the trapping was effective even at 24 °C. The conversion of 1,1-diphenylethylene increased with an increase in the residence time in **R2** until the residence time reached ca. 0.7 s. A further increase in the residence time, however, did not cause an appreciable increase in the conversion.

Although it was difficult to obtain quantitative conversion of 1,1-diphenylethylene (a maximum conversion was ca. 80%, presumably because of insufficient initiation of *sec*-BuLi leading to a smaller number of polystyrene living end than the theoretical value), the present data indicate that the polystyrene living end can be effectively trapped with 1,1-diphenylethylene (the residence time greater than ca. 1.4 s at 0 °C, the residence time greater than ca. 0.7 s at 24 °C). Therefore, we conducted the trapping reaction under such conditions to examine the subsequent copolymerization with an alkyl methacrylate in the following studies.

Table 1. Trapping of a Polystyrene Living Polymer End with 1,1-Diphenylethylene in an Integrated Flow Microreactor System[a]

T (°C)	residence time in **R2** (s)	conversion of 1,1-diphenylethylene (%)	conversion of styrene (%)	M_n[b]	M_w/M_n[b]
0	0.201	48	99	1200	1.09
0	0.345	65	99	1200	1.09
0	0.719	72	99	1200	1.08
0	1.44	79	99	1200	1.08
0	2.88	81	99	1200	1.08
0	5.75	81	99	1300	1.10
0	11.5	79	99	1300	1.10
24	0.201	55	quant	1100	1.08
24	0.345	67	quant	1200	1.08
24	0.719	78	quant	1200	1.08
24	1.44	81	quant	1200	1.08
24	2.88	80	quant	1200	1.08
24	5.75	80	quant	1300	1.09
24	11.5	80	quant	1300	1.09

[a] A solution of *s*-BuLi (0.050 M in hexane) and a solution of styrene (0.80 M in THF (tetrahydrofuran), 10 equiv) were reacted to produce a polystyrene living polymer, which was treated with a solution of 1,1-diphenylethylene (0.050 M in THF, 1.0 equiv), and the resulting solution was reacted with methanol (0.50 M in THF, 10 equiv) in an integrated flow microreactor system. [b] Polymers were analyzed with size-exclusion chromatography calibrated with polystyrene.

Synthesis of Styrenes and Alkyl Methacrylates Diblock Copolymers Using an Integrated Flow Microreactor System. Next, we examined the anionic polymerization of an alkyl methacrylate using an in situ generated adduct of the polystyrene living polymer and 1,1-diphenylethylene as a macro initiator. An integrated flow microreactor system composed of three T-shaped micromixers and four microtube reactors was used (Figure 2). It should be noted that the suitable temperature for polymerization of alkyl methacrylates depends on the nature of the monomer. For example, it was found that the best temperature for the polymerization of methyl methacrylate (MMA) is −28 °C, whereas that for *tert*-butyl methacrylate (Bu^tMA) is 24 °C in the previous studies. Therefore, we conducted the polymerization of styrene and trapping with 1,1-diphenylethylene at 0 °C, whereas the polymerization of alkyl methacrylates was carried out at a temperature suitable for the monomer. Thus, we divided the system into two parts and each part was dipped in a different cooling bath.

A solution of *s*-BuLi (0.050 M in hexane) and a solution of styrene (**m1**) (0.80 M in THF) were mixed using micromixer **M1**, and the resulting solution was introduced into microtube reactor **R1**, where the polymerization took place. The resulting solution was passed through micromixer **M2**, and two microtube reactors **R2** and **R3** (residence time: 2.92−4.38 s), where the trapping reaction with 1,1-diphenylethylene (0.050 M in THF) took place. Microtube reactor **R3** was used to change the temperature for the next polymerization. The resulting solution and a solution of alkyl methacrylate (**m2**) (1.2 M in THF) were mixed using micromixer **M3**, and the resulting solution was introduced to microtube reactor **R4**, where the second polymerization took place. Copolymerization was carried out by varying the monomer ratio, which was controlled by varying the flow rates of the solutions.

The block copolymerization of styrene and MMA was carried out at T = −28 °C (entries 1−6). The copolymers of higher molecular weight were obtained by the introduction of MMA as the second monomer, although a small amount of polystyrene homopolymer was produced because the inevitable side reaction of 1,1-diphenylalkyllithium with the ester carbonyl groups (Figure 3a).[4a,22]

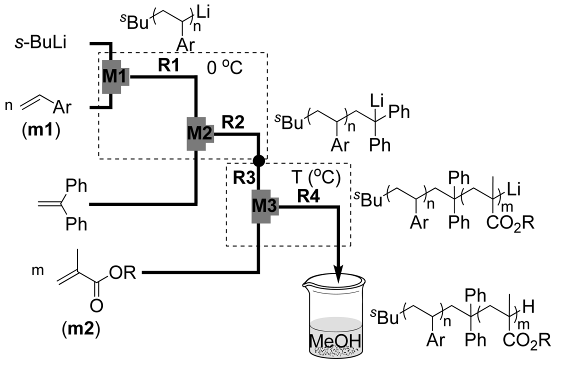

Figure 2. Flow-microreactor-system-controlled block copolymerization of styrenes and alkyl methacrylates. T-shaped micromixer: **M1** (ϕ = 250 μm), **M2** (ϕ = 500 μm), and **M3** (ϕ = 250 μm). Microtube reactor: **R1** (ϕ = 1000 μm, L = 100 cm), **R2** (ϕ = 1000 μm, L = 12.5 cm), **R3** (ϕ = 1000 μm, L = 50 cm), and **R4** (ϕ = 1000 μm, L = 400 cm).

The increase in the amount of MMA caused an increase in the molecular weight (entries 1−3). The increase in the amount of styrene also led to an increase in the molecular weight (entries 3, 5, 6 and entries 2, 4). The block copolymerization of styrene and other alkyl methacrylates, such as *tert*-butyl methacrylate (Bu^{t}MA) and butyl methacrylate (BuMA), was also successfully achieved to produce the corresponding block copolymers with a narrow molecular weight distribution (entries 7−18) (Figure 3b,c).

Moreover, substituted styrenes, such as *p*-dimethylsilylstyrene, can be used as the first monomer (**m1**) for copolymerization with alkyl methacrylates (Table 2, entries 19−21). In this case the first polymerization and the trapping with 1,1-diphenylethylene could also be effectively carried out at 0 °C. The subsequent polymerization reactions with MMA, Bu^{t}MA, and BuMA were successfully achieved at temperatures suitable for the polymerization of the second monomer.

The results show that the combinatorial synthesis of polystyrene−poly(alkyl methacrylate) block copolymers with various molecular weights can be easily achieved using an integrated flow microreactor system. It should be noted that the temperatures for the present copolymerization range from +24 to −28 °C, much higher than those used for macrobatch polymerization.

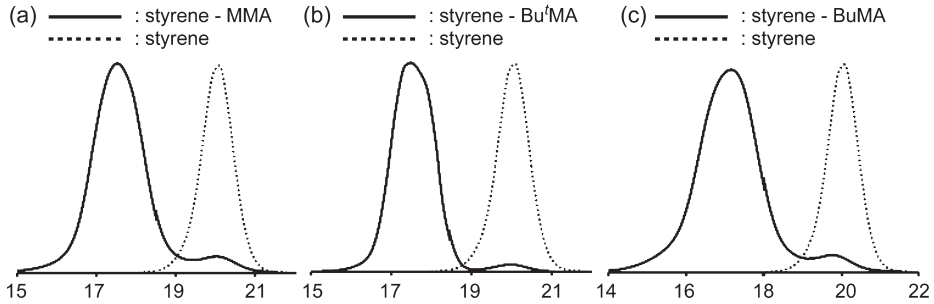

Figure 3. Size exclusion chromatography traces of block copolymerization with styrene and alkyl methacrylates using the integrated flow microreactor system (styrene, 10 equiv based on *s*-BuLi; alkyl methacrylate, 75 equiv based on *s*-BuLi): (a) styrene−MMA; (b) styrene−Bu^{t}MA; (c) styrene−BuMA.

Table 2. Flow-Microreactor-System-Controlled Block Copolymerization of Styrenes and Alkyl Methacrylates[a]

					flow rate of solution (mL/min)					conversion (%)			
entry	monomer1 (**m1**)	monomer2 (**m2**)[b]	[**m1**]/[*s*-BuLi]	[**m2**]/[*s*-BuLi]	*s*-BuLi	**m1**	1,1-diphenyl ethylene	**m2**	T (°C)	**m1**	**m2**	M_n[c]	M_w/M_n[c]
1	styrene	MMA	10	25	3.84	2.40	3.84	4.00	−28	99	99	3900	1.14
2	styrene	MMA	10	50	3.12	1.95	3.12	6.50	−28	quant	99	6500	1.23
3	styrene	MMA	10	75	2.56	1.60	2.56	8.00	−28	quant	99	9000	1.30
4	styrene	MMA	25	50	2.40	3.75	2.40	5.00	−28	quant	99	9100	1.21
5	styrene	MMA	25	75	2.24	3.50	2.24	7.00	−28	quant	99	11500	1.31
6	styrene	MMA	50	75	1.60	5.00	1.60	5.00	−28	quant	96	15600	1.37
7	styrene	Bu^{t}MA	10	25	3.84	2.40	3.84	4.00	24	99	99	5000	1.10
8	styrene	Bu^{t}MA	10	50	3.12	1.95	3.12	6.50	24	quant	quant	7100	1.15
9	styrene	Bu^{t}MA	10	75	2.56	1.60	2.56	8.00	24	quant	quant	9200	1.19
10	styrene	Bu^{t}MA	25	50	2.40	3.75	2.40	5.00	24	quant	quant	8300	1.15
11	styrene	Bu^{t}MA	25	75	2.24	3.50	2.24	7.00	24	quant	quant	10900	1.20
12	styrene	Bu^{t}MA	50	75	1.60	5.00	1.60	5.00	24	quant	quant	12400	1.22
13	styrene	BuMA	10	25	3.84	2.40	3.84	4.00	0	99	99	5100	1.30
14	styrene	BuMA	10	50	3.12	1.95	3.12	6.50	0	99	100	7600	1.48
15	styrene	BuMA	10	75	2.56	1.60	2.56	8.00	0	quant	quant	12200	1.55
16	styrene	BuMA	25	50	2.40	3.75	2.40	5.00	0	quant	quant	8900	1.40
17	styrene	BuMA	25	75	2.24	3.50	2.24	7.00	0	quant	quant	11300	1.56
18	styrene	BuMA	50	75	1.60	5.00	1.60	5.00	0	quant	quant	16900	1.44
19	*p*-Me$_2$HSi− styrene	MMA	10	50	3.12	1.95	3.12	6.50	−28	quant	quant	8100	1.40
20	*p*-Me$_2$HSi− styrene	Bu^{t}MA	10	50	3.12	1.95	3.12	6.50	24	quant	quant	13600	1.18
21	*p*-Me$_2$HSi− styrene	BuMA	10	50	3.12	1.95	3.12	6.50	0	quant	99	12000	1.59

[a] A solution of *s*-BuLi (0.050 M in hexane) and a solution of monomer1 (**m1**) (0.80 M in THF (tetrahydrofuran)) were reacted in the flow microreactor. The resulting solution was trapped with a solution of 1,1-diphenylethylene (0.050 M in THF). The resulting solution was reacted with a solution of monomer2 (**m2**) (1.2 M in THF). [b] Alkyl methacrylate: MMA (methyl methacrylate), Bu^{t}MA (*tert*-butyl methacrylate), BuMA (butyl methacrylate). [c] Polymers of the peak in the region of high molar masses were analyzed with size-exclusion chromatography calibrated with polystyrene.

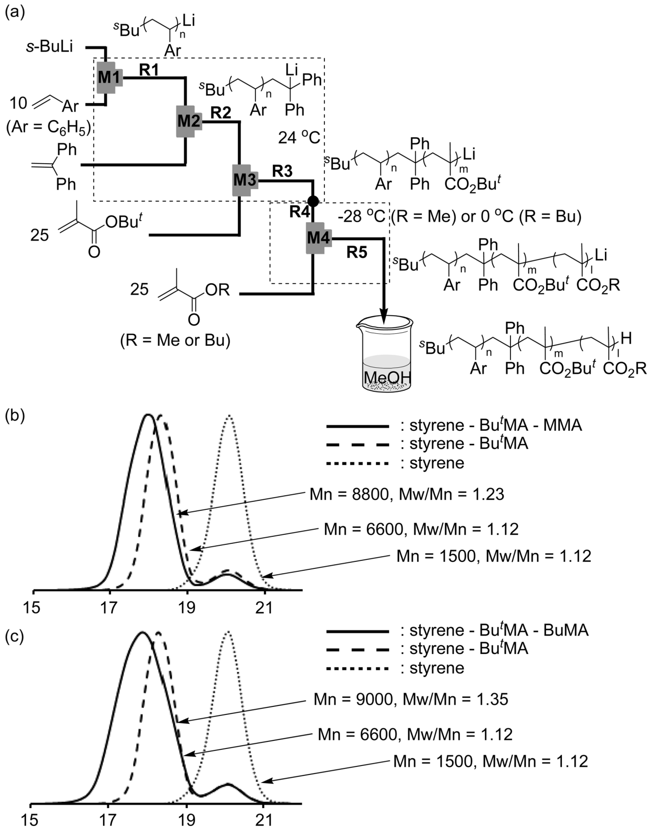

Figure 4. Flow-microreactor-system-controlled block copolymerization of styrene−alkyl methacrylate−alkyl methacrylate. (a) Schematic diagram of the flow microreactor system. T-shaped micromixer: **M1** (ϕ = 250 μm), **M2** (ϕ = 500 μm), **M3** (ϕ = 250 μm), and **M4** (ϕ = 250 μm). Microtube reactor: **R1** (ϕ = 1000 μm, L = 100 cm (9.29 s)), **R2** (ϕ = 1000 μm, L = 50 cm (2.88 s)), **R3** (ϕ = 1000 μm, L = 100 cm (4.12 s)), **R4** (ϕ = 1000 μm, L = 100 cm (4.12 s)), and **R5** (ϕ = 1000 μm, L = 400 cm (12.8 s)). Solution: *s*-BuLi 0.050 M in hexane (3.12 mL/min), styrene 0.80 M in THF (1.95 mL/min), 1,1-diphenylethylene 0.050 M in THF (3.12 mL/min), Bu^{t}MA 1.2 M in THF (3.25 mL/min), and MMA or BuMA 1.2 M in THF (3.25 mL/min). (b) Size exclusion chromatography traces of styrene−Bu^{t}MA−MMA. (c) Size exclusion chromatography traces of styrene−Bu^{t}MA−BuMA.

Synthesis of Styrenes, Alkyl Methacrylates and Alkyl Methacrylates Triblock Copolymers Using an Integrated Flow Microreactor System. Next, we examined the block copolymerization of polystyrene, poly(Bu^{t}MA), and poly(MMA) using an integrated flow microreactor composed of four T-shaped micromixers and five microtube reactors, as shown in Figure 4a. In this case the polymerization of styrene and trapping with 1,1-diphenylethylene was carried out at 24 °C. The subsequent polymerization of Bu^{t}MA was also carried out at 24 °C. Thus, solutions of *s*-BuLi (0.050 M in hexane, 3.12 mL/min) and styrene (0.80 M in THF, 1.95 mL/min, 10 equiv based on *s*-BuLi) were introduced to micromixer **M1** using syringe pumps, and the mixture was introduced into microtube reactor **R1**, in which the first polymerization took place. In the next stage, a solution of 1,1-diphenylethylene (0.050 M in THF, 3.12 mL/min, 1.0 equiv based on *s*-BuLi) was passed through micromixer **M2** and microtube reactor **R2**. In the third stage, a solution of Bu^{t}MA (1.2 M in THF, 3.25 mL/min, 25 equiv based on *s*-BuLi) was introduced to micromixer **M3**. The reaction mixture was introduced to microtube reactor **R3**, where the second polymerization took place. Then, the reaction temperature was changed from +24 to −28 °C using microtube reactor **R4**. In the final stage, a solution of MMA (1.2 M in THF, 3.25 mL/min, 25 equiv based on *s*-BuLi) was introduced to micromixer **M4**. Then, the reaction mixture was introduced to microtube reactor **R5**, where the third polymerization took place. After the product solution was introduced to methanol to quench the polymerization, the reaction mixture was purified by GPC to remove the unchanged homopolymer of lower molecular weight. This sequential polymerization took place effectively with good control of the molecular weight distribution (M_w/M_n = 1.23) (Figure 4b). The molecular weight of the triblock copolymer (M_n = 8800) was higher than that of the polymer obtained without adding the third monomer (M_n = 6600) and the polymer obtained without adding the second and third monomers (M_n = 1500). Moreover, the synthesis of polystyrene−poly(Bu^{t}MA)−poly(BuMA) triblock copolymers was also achieved using this integrated flow microreactor with a good control of the molecular weight distribution, as shown in Figure 4c. In this case the third polymerization was carried out at 0 °C. These results show that flow microreactor systems are effective for the synthesis of polystyrene−poly(alkyl methacrylate)−poly(alkyl methacrylate) triblock copolymers.

Conclusions

We have found that controlled anionic diblock copolymerization of styrene−alkyl methacrylate and triblock copolymerization of styrene−alkyl methacrylate−alkyl methacrylate can be carried out in an integrated flow microreactor system. A high level of control of the molecular weight distribution was achieved easily under accessible conditions because of fast mixing and residence time control. The present observations open up a new possibility in anionic polymerization and synthesis of structurally well-defined block copolymers having various functions.

Experimental Section

General Information. GC analysis was performed on a SHIMADZU GC-2014 gas chromatograph equipped with a flame ionization detector using a fused silica capillary column. Hexane was purchased from Wako, distilled before use, and stored over molecular sieves 4A. Tetrahydrofuran (THF) was purchased from Kanto as a dry solvent and used as obtained. All monomers were distilled twice over CaH_2 before use. 1,1-Diphenylethylene was purchased from Aldrich and distilled before use. *s*-BuLi in cyclohexane/hexane (95:5) (1.03 M) was purchased from Kanto and used as obtained. Stainless steel (SUS304) T-shaped micromixers having inner diameter of 250 and 500 μm were manufactured by Sanko Seiki Co., Inc. Stainless steel (SUS316) microtube reactors having inner diameter of 1000 μm were purchased from GL Sciences. Micromixers and microtube reactors were connected with stainless type fittings (GL Sciences, 1/16 OUW). The flow microreactor system was dipped in a cooling bath to control the temperature. Solutions were introduced to a flow microreactor using syringe pumps, Harvard Model 11, equipped with gastight syringes purchased from SGE.

Molecular Weight and Molecular Weight Distribution. The molecular weight (Mn) and molecular weight distribution (M_w/M_n) were determined in THF at 40 °C with a Shodex GPC-101 equipped with two LF-804 L columns (Shodex) and an RI detector using a polystyrene (polySt) standard sample for calibration.

Trapping of Polystyrene Living Polymer End with 1,1-Diphenylethylene in an Integrated Flow Microreactor System. An integrated flow microreactor system composed of three T-shaped micromixers (**M1**, **M2**, and **M3**) and three microtube reactors (**R1**, **R2**, and **R3**) was used. Microtube precooling units (for **P1**, ϕ = 1000 μm, length = 50 cm; for **P2**, **P3** and **P4**, ϕ = 1000 μm, length = 100 cm) were connected to each inlet of the micromixers. The whole microflow system was dipped in a cooling bath of 0 or 24 °C. A solution of *s*-BuLi (0.050 M in hexane, 3.12 mL/min) and a solution of styrene (0.80 M in THF, 1.95 mL/min) were introduced to **M1** (ϕ = 250 μm) by syringe pumps. The resulting solution was

Table 3. Flow-Microreactor-System Controlled Triblock Copolymerization of Styrene and Alkyl Methacrylates

monomer1 (**m1**)	conversion of **m1** (%)	monomer2 (**m2**)	conversion of **m2** (%)	monomer3 (**m3**)	conversion of **m3** (%)	M_n	M_w/M_n
styrene	99					1500	1.12
styrene	quant	^{t}BuMA	99			6600	1.12
styrene	quant	^{t}BuMA	quant	MMA	quant	8800	1.23
styrene	quant	^{t}BuMA	quant	BuMA	quant	9000	1.35

passed through **R1** (ϕ = 1000 μm, length = 100 cm) and was mixed with 1,1-diphenylethylene (0.050 M in THF, 3.12 mL/min) in **M2** (ϕ = 500 μm). The resulting solution was passed through **R2** (ϕ = 1000 μm, length = 3.5, 6, 12.5, 25, 50, 100, or 200 cm). The resulting solution was quenched with methanol (0.50 M in THF, 3.12 mL/min) using **M3** (ϕ = 500 μm) and **R3** (ϕ = 1000 μm, length = 200 cm). Residence time in **R2** was varied by changing the length of **R2**. The conversions of styrene and 1,1-diphenylethylene were determined by GC. The solvent was removed under reduced pressure to obtain the polymer product and the polymer sample was analyzed with size exclusion chromatography with the calibration using standard polystyrene samples and the results are summarized in Table 1.

Typical Procedure for Synthesis of Polystyrene−Poly(alkyl methacrylate) Diblock Copolymers Using an Integrated Flow Microreactor System. An integrated flow microreactor system composed of three T-shaped micromixers (**M1**, **M2**, and **M3**) and four microtube reactors (**R1**, **R2**, **R3**, and **R4**) was used. Microtube precooling units (for **P1**, ϕ = 1000 μm, length = 50 cm; for **P2**, **P3**, and **P4**, ϕ = 1000 μm, length = 100 cm) were connected to each inlets of the micromixers. **M1**, **R1**, **M2**, and **R2** were dipped in a cooling bath of 0 °C. **R3**, **M3**, and **R4** were dipped in a cooling bath of a different temperature (T °C). **R3** was used to connect **R2** and **M3**. A solution of *s*-BuLi (0.050 M in hexane) and a solution of styrenes (monomer1, **m1**) (0.80 M in THF) were introduced to **M1** (ϕ = 250 μm) by syringe pumps. The resulting solution was passed through **R1** (ϕ = 1000 μm, length = 100 cm, 0 °C) and was mixed with 1,1-diphenylethylene (0.050 M in THF) in **M2** (ϕ = 500 μm). The resulting solution was passed through **R2** (ϕ = 1000 μm, length = 12.5 cm, 0 °C) and **R3** (ϕ = 1000 μm, length = 50 cm, T °C) (residence time in **R2** and **R3**: 2.92−4.38 s) and was mixed with alkyl methacrylates (monomer2, **m2**) (1.2 M in THF) in **M3** (ϕ = 250 μm). The resulting solution was passed through **R4** (ϕ = 1000 μm, length = 400 cm, T °C). After a steady state was reached, the product solution was introduced (30 s) to methanol to quench the polymerization. The polymerization was carried out with varying flow rates of solutions. The conversions of styrenes and alkyl methacrylates were determined by GC. The solvent was removed under reduced pressure to obtain the polymer product and the polymer sample was analyzed with size exclusion chromatography with the calibration using standard polystyrene samples and the results are summarized in Table 2.

Polystyrene−Poly(alkyl methacrylate)−Poly(alkyl methacrylate) Triblock Copolymers Using an Integrated Flow Microreactor System. An integrated flow microreactor system composed of four T-shaped micromixers (**M1**, **M2**, **M3**, and **M4**) and five microtube reactors (**R1**, **R2**, **R3**, **R4**, and **R5**) was used. Microtube precooling units (for **P1**, ϕ = 1000 μm, length = 50 cm; for **P2**, **P3**, **P4**, and **P5**, ϕ = 1000 μm, length = 100 cm) were connected to each inlets of the micromixers. **M1**, **R1**, **M2**, **R2**, **M3**, and **R3** were dipped in a cooling bath of 24 °C. **R4**, **M4**, and **R5** were dipped in a cooling bath of a different temperature (−28 or 0 °C). **R4** was used to connect **R3** and **M4**. A solution of *s*-BuLi (0.050 M in hexane) (flow rate: 3.12 mL/min) and a solution of styrene (**m1**) (0.80 M in THF) (flow rate: 1.95 mL/min) were introduced to **M1** (ϕ = 250 μm) by syringe pumps. The resulting solution was passed through **R1** (ϕ = 1000 μm, length = 100 cm) and was mixed with 1,1-diphenylethylene (0.050 M in THF) (flow rate: 3.12 mL/min) in **M2** (ϕ = 500 μm). The resulting solution was passed through **R2** (ϕ = 1000 μm, length = 50 cm) and was mixed with *tert*-butyl methacrylate (**m2**) (1.2 M in THF) (flow rate: 3.25 mL/min) in **M3** (ϕ = 250 μm). The resulting solution was passed through **R3** (ϕ = 1000 μm, length = 100 cm) and **R4** (ϕ = 1000 μm, length = 100 cm) and was mixed with methyl methacrylate or butyl methacrylate (**m3**) (1.2 M in THF) (flow rate: 3.25 mL/min) in **M4** (ϕ = 250 μm). The resulting solution was passed through **R5** (ϕ = 1000 μm, length = 400 cm). After a steady state was reached, the product solution was introduced (30 s) to methanol to quench the polymerization. The cooling bath was controlled at the appropriate temperature (styrene, 24 °C; MMA, −28 °C; BuMA, 0 °C; Bu^{t}MA, 24 °C). The conversions of styrene, *tert*-butyl methacrylate, and methyl methacrylate or butyl methacrylate were determined by GC. The polymer sample was analyzed with size exclusion chromatography with the calibration using standard polystyrene samples, and the results are summarized in Table 3.

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Supporting Information Available: Experimental procedures and spectroscopic data of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) *Chem. Rev.* **2001**, *101*, issue 12.

(2) Szwarc, M. *Nature* **1956**, *178*, 1168–1169.

(3) Living cationic polymerization: Matyjaszewski, K.; Sawamoto, M. in *Cationic Polymerizations*, Matyjaszewski, K., Ed. Marcel Dekker, New York, 1996.

(4) Living anionic polymerization: (a) Hsieh, H. L.; Quirk, R. P. *Anionic polymerization: principles and practical applications*; Marcel Dekker: New York, 1996. (b) Hong, K.; Uhrig, D.; Mays, J. W. *Current Opinion in Solid State and Material Science* **1999**, *4*, 531–538. (c) Jagur-grodzinski, J. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 2116–2133. (d) Smid, J. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 2101–2107. (e) Hirao, A.; Loykulnant, S.; Ishizone, T. *Prog. Polym. Sci.* **2002**, *27*, 1399–1471. (f) Hadjichristidis, N.; Pitsikalis, M.; Pispas, S.; Iatrou, H. *Chem. Rev.* **2001**, *101*, 3747–3792 and references therein .

(5) Living radical polymerization: (a) Matyjaszewski, K.; Davis, T. P. *Handbook of Radical Polymerization*, 1st ed.; Wiley: New York, 2002. (b) Moad, G.; Solomon, D. H. *The Chemistry of Radical Polymerization*, 2nd ed.; Elsevier: Amsterdam, 2006.

(6) Flash chemistry: (a) Yoshida, J. *Flash Chemistry Fast Organic Synthesis in Microsystems*; Wiley: Chichester, 2008. (b) Yoshida, J. *Chem. Commun.* **2005**, 4509–4516. (c) Yoshida, J.; Nagaki, A.; Yamada, T. *Chem.—Eur. J.* **2008**, *14*, 7450–7459.

(7) (a) Hessel, V.; Hardt, S.; Löwe, H. *Chemical Micro Process Engineering*; Wiely-VCH Verlag: Weinheim, 2004. (b) Wirth, T. *Microreactors in Organic Synthesis and Catalysis*; Wiley-VCH Verlag: Weinheim, 2008. (c) Hessel, V.; Renken, A.; Schouten, J. C.; Yoshida, J. *Micro Process Engineering*; Wiley-VCH Verlag: Weinheim, 2009.

(8) Reviews for microreactor: (a) Fletcher, P. D. I.; Haswell, S. J.; Pombo-Villar, E.; Warrington, B. H.; Watts, P.; Wong, S. Y. F.; Zhang, X. *Tetrahedron* **2002**, *58*, 4735–4757. (b) Jähnisch, K.; Hessel, V.; Löwe, H.; Baerns, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 406–446. (c) Doku, G. N.; Verboom, W.; Reinhoudt, D. N.; van den Berg, A. *Tetrahedron* **2005**, *61*, 2733–2742. (d) Watts, P.; Haswell, S. J. *Chem. Soc. Rev.* **2005**, *34*, 235–246. (e) Geyer, K.; Codee, J. D. C.; Seeberger, P. H. *Chem.—Eur. J.* **2006**, *12*, 8434–8442. (f) deMello, A. J. *Nature* **2006**, *442*, 394–402. (g) Song, H.; Chen, D. L.; Ismagilov, R. F. *Angew. Chem., Int. Ed.* **2006**, *45*, 7336–7356. (h) Kobayashi, J.; Mori, Y.; Kobayashi, S. *Chem. Asian J.* **2006**, *1*, 22–35. (i) Mason, B. P.; Price, K. E.; Steinbacher, J. L.; Bogdan, A. R.; McQuade, D. T. *Chem. Rev.* **2007**, *107*, 2300–2318. (j) Ahmed-Omer, B.; Brandtand, J. C.; Wirth, T.

Org. Biomol. Chem. **2007**, *5*, 733–740. (k) Fukuyama, T.; Rahman, M. T.; Sato, M.; Ryu, I. *Synlett* **2008**, 151–163. (l) McMullen, J. P.; Jensen, K. F. *Annu. Rev. Anal. Chem.* **2010**, *3*, 19–42.

(9) Recent examples: (a) de Bellefon, C.; Tanchoux, N.; Caravieilhes, S.; Grenouillet, P.; Hessel, V. *Angew. Chem., Int. Ed.* **2000**, *39*, 3442–3445. (b) Watts, P.; Wiles, C.; Haswell, S. J.; Pombo-Villar, E.; Styring, P. *Chem. Commun.* **2001**, 990–991. (c) Hisamoto, H.; Saito, T.; Tokeshi, M.; Hibara, A.; Kitamori, T. *Chem. Commun.* **2001**, 2662–2663. (d) Suga, S.; Okajima, M.; Fujiwara, K.; Yoshida, J. *J. Am. Chem. Soc.* **2001**, *123*, 7941–7942. (e) Wiles, C.; Watts, P.; Haswell, S. J.; Pombo-Villar, E. *Chem. Commun.* **2002**, 1034–1035. (f) Fukuyama, T.; Shinmen, M.; Nishitani, S.; Sato, M.; Ryu, I. *Org. Lett.* **2002**, *4*, 1691–1694. (g) Ueno, M.; Hisamoto, H.; Kitamori, T.; Kobayashi, S. *Chem. Commun.* **2003**, 936–937. (h) Garcia-Egido, E.; Spikmans, V.; Wong, S. Y. F.; Warrington, B. H. *Lab Chip* **2003**, *3*, 73–76. (i) Lai, S. M.; Martin-Aranda, R.; Yeung, K. L. *Chem. Commun.* **2003**, 218–219. (j) Mikami, K.; Yamanaka, M.; Islam, M. N.; Kudo, K.; Seino, N.; Shinoda, M. *Tetrahedron Lett.* **2003**, *44*, 7545–7548. (k) Suga, S.; Nagaki, A.; Tsutsui, Y.; Yoshida, J. *Org. Lett.* **2003**, *5*, 945–947. (l) Kobayashi, J.; Mori, Y.; Okamoto, K.; Akiyama, R.; Ueno, M.; Kitamori, T.; Kobayashi, S. *Science* **2004**, *304*, 1305–1308. (m) Horcajada, R.; Okajima, M.; Suga, S.; Yoshida, J. *Chem. Commun.* **2005**, 1303–1305. (n) Ducry, L.; Roberge, D. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 7972–7975. (o) He, P.; Watts, P.; Marken, F.; Haswell, S. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 4146–4149. (p) Uozumi, Y.; Yamada, Y.; Beppu, T.; Fukuyama, N.; Ueno, M.; Kitamori, T. *J. Am. Chem. Soc.* **2006**, *128*, 15994–15995. (q) Tanaka, K.; Motomatsu, S.; Koyama, K.; Tanaka, S.; Fukase, K. *Org. Lett.* **2007**, *9*, 299–302. (r) Ushiogi, Y.; Hase, T.; Iinuma, Y.; Takata, A.; Yoshida, J. *Chem. Commun.* **2007**, 2947–2949. (s) Sahoo, H. R.; Kralj, J. G.; Jensen, K. F. *Angew. Chem., Int. Ed.* **2007**, *46*, 5704–5708. (t) Hornung, C. H.; Mackley, M. R.; Baxendale, I. R.; Ley, S. V. *Org. Process Res. Dev.* **2007**, *11*, 399–405. (u) Fukuyama, T.; Kobayashi, M.; Rahman, M. T.; Kamata, N.; Ryu, I. *Org. Lett.* **2008**, *10*, 533–536.

(10) Reviews on polymerizations using microreactors: (a) Hessel, V.; Serra, C.; Löwe, H.; Hadziioannou, G. *Chemie Ingenieur Technik* **2005**, *77*, 1693–1714. (b) Steinbacher, J. L.; Mcquade, D. T. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 6505–6533and references therein.

(11) Cationic polymerization using microreactors: (a) Nagaki, A.; Kawamura, K.; Suga, S.; Ando, T.; Sawamoto, M.; Yoshida, J. *J. Am. Chem. Soc.* **2004**, *126*, 14702–14703. (b) Iwasaki, T.; Nagaki, A.; Yoshida, J. *Chem. Commun.* **2007**, 1263–1265. (c) Nagaki, A.; Iwasaki, T.; Kawamura, K.; Yamada, D.; Suga, S.; Ando, T.; Sawamoto, M.; Yoshida, J. *Chem. Asian J.* **2008**, *3*, 1558–1567.

(12) (a) Suga, S.; Nagaki, A.; Yoshida, J. *Chem. Commun.* **2003**, 354–355. (b) Nagaki, A.; Togai, M.; Suga, S.; Aoki, N.; Mae, K.; Yoshida, J. *J. Am. Chem. Soc.* **2005**, *127*, 11666–11675. (c) Yoshida, J.; Nagaki, A.; Iwasaki, T.; Suga, S. *Chem. Eng. Technol.* **2005**, *28*, 259–266. (d) Nagaki, A.; Takabayashi, N.; Tomida, Y.; Yoshida, J. *Org. Lett.* **2008**, *18*, 3937–3940. (e) Nagaki, A.; Takabayashi, N.; Tomida, Y.; Yoshida, J. *Beilstein J. Org. Chem.* **2009**, *5*, No16.

(13) Kawaguchi, T.; Miyata, H.; Ataka, K.; Mae, K.; Yoshida, J. *Angew. Chem., Int. Ed.* **2005**, *44*, 2413–2416.

(14) (a) Usutani, H.; Tomida, Y.; Nagaki, A.; Okamoto, H.; Nokami, T.; Yoshida, J. *J. Am. Chem. Soc.* **2007**, *129*, 3046–3047. (b) Nagaki, A.; Tomida, Y.; Usutani, H.; Kim, H.; Takabayashi, N.; Nokami, T.; Okamoto, H.; Yoshida, J. *Chem. Asian J.* **2007**, *2*, 1513–1523. (c) Nagaki, A.; Kim, H.; Yoshida, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 7833–7836. (d) Nagaki, A.; Takizawa, E.; Yoshida, J. *J. Am. Chem. Soc.* **2009**, *131*, 1654–1655. (e) Nagaki, A.; Takizawa, E.; Yoshida, J. *Chem. Lett.* **2009**, *38*, 486–487. (f) Tomida, Y.; Nagaki, A.; Yoshida, J. *Org. Lett.* **2009**, *11*, 3614–3617. (g) Nagaki, A.; Takizawa, E.; Yoshida, J. *Chem. Lett.* **2009**, *38*, 1060–1061. (h) Nagaki, A.; Kim, H.; Yoshida, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 8063–8065. (i) Nagaki, A.; Kim, H.; Matsuo, C.; Yoshida, J. *Org. Biomol. Chem.* **2010**, *8*, 1212–1217.

(15) Living radical polymerization using microreactors: (a) Wu, T.; Mei, Y.; Cabral, J. T.; Xu, C.; Beers, K. L. *J. Am. Chem. Soc.* **2004**, *126*, 9880–9881. (b) Serra, C.; Sary, N.; Schlatter, G.; Hadziioannou, G.; Hessel, V. *Lab Chip* **2005**, *5*, 966–973. (c) Enright, T. E.; Cunningham, M. F.; Keoshkerian, B. *Macromol. Rapid Commun.* **2005**, *26*, 221–225. (d) Russum, J. P.; Jones, C. W.; Schork, F. J. *Ind. Eng. Chem. Res.* **2005**, *44*, 2484–2493. (e) Xu, C.; Wu, T.; Drain, C. M.; Batteas, J. D.; Beers, K. L. *Macromolecules* **2005**, *38*, 6–8. (f) Rosenfeld, C.; Serra, C.; Brochon, C.; Hadziioannou, G. *Chem. Eng. Sci.* **2007**, *62*, 5245–5250. (g) Rosenfeld, C.; Serra, C.; Brochon, C.; Hadziioannou, G. *Lab Chip* **2008**, *8*, 1682–1687. (h) Enright, T. M.; Cunningham, M. F.; Keoshkerian, B. *Macromol. React. Eng.* **2010**, *4*, 186–196.

(16) Control of molecular weights of polymers in radical polymerization by modulating the residence time in the microreactor: (a) Russum, J. P.; Jones, C. W.; Schork, F. J. *Macromol. Rapid Commun.* **2004**, *25*, 1064–1068. (b) Wu, T.; Mei, Y.; Xu, C.; Byrd, H. C. M.; Beers, K. L. *Macromol. Rapid Commun.* **2005**, *26*, 1037–1042.

(17) Radical polymerization using microreactors: (a) Iwasaki, T.; Yoshida, J. *Macromolecules* **2005**, *38*, 1159–1165. (b) Iwasaki, T.; Kawano, N.; Yoshida, J. *Org. Process Res. Dev.* **2006**, *10*, 1126–1131.

(18) Synthesis of polymers of well-defined end-structures by anionic polymerization: (a) Morton, M.; Fetters, L. J. *J. Polym. Sci., Macromol. Rev.* **1967**, *2*, 71–113. (b) French, D. M. *Rubber Chem. Technol.* **1969**, *42*, 71–109. (c) Bi, L.-K.; Fetters, L. J. *Macromolecules* **1976**, *9*, 732–742. (d) Hirao, A.; Hattori, I.; Sasagawa, T.; Yamaguchi, K.; Nakahama, S. *Makromol. Chem.* **1982**, *RC3*, 59–63. (e) Young, R. N.; Quirk, R. P.; Fetters, L. J. *Adv. Polym. Sci.* **1984**, *56*, 1–90. (f) Quirk, R. P.; Yin, J.; Guo, S.-H.; Hu, X.-W.; Summers, G.; Kim, J.; Zhu, L.-F.; Schock, L. E. *Makromol. Chem., Macromol. Symp.* **1990**, *32*, 47–59. (g) Hirao, A.; Nagahama, H.; Ishizone, T.; Nakahama, S. *Macromolecules* **1993**, *26*, 2145–2150. (h) Allgaier, J.; Young, R. N.; Efstratiadis, V.; Hadjichristidis, N. *Macromolecules* **1996**, *29*, 1794–1797. (i) Floudas, G.; Pispas, S.; Hadjichristidis, N.; Pakula, T.; Erukhimovich, I. *Macromolecules* **1996**, *29*, 4142–4154. (j) Avgeropoulos, A.; Hadjichristidis, N. *J. Polym. Sci., Part A: Polym. Chem.* **1997**, *35*, 813–816. (k) Beyer, F. L.; Gido, S. P.; Poulos, Y.; Avgeropoulos, A.; Hadjichristidis, N. *Macromolecules* **1997**, *30*, 2373–2376. (l) Uhrig, D.; Mays, J. W. *Macromolecules* **2002**, *35*, 7182–7190. (m) Zhao, Y.; Higashihara, T.; Sugiyama, K.; Hirao, A. *J. Am. Chem. Soc.* **2005**, *127*, 14158–14159. (n) Schappacher, M.; Deffieux, A. *Macromolecules* **2005**, *38*, 7209–7213. (o) Ji, H.; Sakellariou, G.; Mays, J. W. *Macromolecules* **2007**, *40*, 3461–3467.

(19) Anionic polymerization using microreactors: (a) Wurm, F.; Wilms, D.; Klos, J.; Löwe, H.; Frey, H. *Macromol. Chem. Phys.* **2008**, *209*, 1106–1114. (b) Nagaki, A.; Tomida, Y.; Yoshida, J. *Macromolecules* **2008**, *41*, 6322–6330. (c) Nagaki, A.; Tomida, Y.; Miyazaki, A.; Yoshida, J. *Macromolecules* **2009**, *42*, 4384–4387. (d) Iida, K.; Chastek, T. Q.; Beers, K. L.; Cavicchi, K. A.; Chunc, J.; Fasolka, M. J. *Lab Chip* **2009**, *9*, 339–345.

(20) Suga, S.; Yamada, D.; Yoshida, J. *Chem. Lett.* **2010**, *39*, 404–406.

(21) (a) Freyss, D.; Rempp, P.; Benoit, H. *Polym. Lett.* **1964**, *2*, 217–222. (b) Ramireddy, C.; Tuzar, Z.; Procházka, K.; Webber, S. E.; Munk, P. *Macromolecules* **1992**, *25*, 2541–2545. (c) Kiserow, D.; Chan, J.; Ramireddy, C.; Munk, P.; Webber, S. E. *Macromolecules* **1992**, *25*, 5338–5344. (d) Chan, J.; Fox, S.; Kiserow, D.; Ramireddy, C.; Munk, P.; Webber, S. E. *Macromolecules* **1993**, *26*, 7016–7023. (e) Pitsikalis, M.; Siakali-Kioulafa, E.; Hadjichristidis, N. *Macromolecules* **2000**, *33*, 5460–5469. (f) Weidisch, R.; Michler, G. H.; Arnold, M. *Polymer* **2000**, *41*, 2231–2240. (g) Kim, W.; Han, J.; Ryu, C. Y.; Yang, H. *J. Polym. Sci., Part B: Polym. Phys.* **2006**, *44*, 3612–3620.

(22) (a) Auschra, C.; Stadler, R. *Polym. Bull.* **1993**, *30*, 257–264. (b) Feldthusen, J.; Ivan, B.; Müller, A. H. E. *Macromolecules* **1998**, *31*, 578–585. (c) Matsumoto, K.; Wahnes, C.; Mouri, E.; Matsuoka, H.; Yamaoka, H. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 86–92. (d) Cho, J. C.; Cheng, G.; Feng, D.; Faust, R.; Richard, R.; Schwarz, M.; Chan, K.; Boden, M. *Biomacromolecules* **2006**, *7*, 2997–3007. (e) Feng, D.; Higashihara, T.; Faust, R. *Polymer* **2008**, *49*, 386–393.