4384 *Macromolecules* **2009**, *42*, 4384–4387
DOI: 10.1021/ma900551a

Macromolecules
COMMUNICATION TO THE EDITOR

Microflow System Controlled Anionic Polymerization of Alkyl Methacrylates

Aiichiro Nagaki, Yutaka Tomida, Atsuo Miyazaki, and Jun-ichi Yoshida*

Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Nishikyo-ku, Kyoto 615-8510, Japan

Received March 13, 2009
Revised Manuscript Received June 1, 2009

Synthesis of poly(alkyl methacrylate)s with well-defined structures has received significant research interests from both academic and industrial polymer chemists.[1] Nowadays, poly(alkyl methacrylate)s are utilized as versatile materials such as plastics, adhesives and elastomers containing a number of different reactive functions. In general, these commercially available methacrylate polymers are prepared by radical polymerization processes. Recent development in living radical polymerization method offers great promise,[2] and a number of methods using a capping agent have been developed such as degeneration or exchange chain transfer, atom transfer radical polymerization, nitroxide-mediated radical polymerization, and reversible addition−fragmentation chain transfer polymerization.[3]

In contrast, living anionic polymerization of alkyl methacrylates does not need a capping agent.[4] Therefore, living anionic polymerization is very fast compared to living radical polymerization. Living anionic polymerization also provides easy access to tailor-made macromolecules, such as graft, block, star, α,ω-difunctional polymers and macromonomers.[5] However, in a conventional macrobatch reactor, living anionic polymerization of alkyl methacrylates should be carried out at low temperatures such as −78 °C to obtain polymers of narrow molecular weight distribution.[6] The requirement of such low temperatures causes severe limitations in the use of this highly useful polymerization technology in industry.

Recently, polymerization in microflow systems[7−9] has attracted a great deal of attention,[10] and extensive studies on radical[11] and cationic polymerization[12] of vinyl monomers have been reported. However, to the best of our knowledge, only a few reports on the use of microflow systems for anionic polymerization have been published.[13] Thus, we initiated our project on living anionic polymerization of alkyl methacrylates, and herein we report the results of this study.

Various initiators having different counterions such as Li^+, Na^+, K^+, and Cs^+ are developed for anionic polymerization of methyl methacrylate (MMA). Among them, Li^+ is very popular. In a macrobatch system, organolithium-initiated living anionic polymerization of MMA should be carried out at low temperatures such as −78 °C.[14] It is necessary to use an additive such as $LiClO_4$ and *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) to accomplish the polymerization at higher temperatures such as −20 and −40 °C.[15] However, these additives contaminate the product polymers and decrease the polymerization rate.

We reexamined the polymerization of MMA in a macrobatch reactor in the absence of an additive at various temperatures (0, −28, −48, −78 °C). A solution of MMA in tetrahydrofuran (THF) (0.50 M, 6.0 mL) was added to a solution of 1,1-diphenylhexyllithium in THF/hexane (99/1 v/v) (0.050 M, 2.0 mL) in a 20 mL flask. The reaction mixture was stirred for t min ($t = 1$, temperature = 0, −28, and −48 °C; $t = 5$, temperature = −78 °C), and the polymerization was quenched with methanol (0.33 M in THF, 3.0 mL). As shown in Table 1, the number-average molecular weight (M_n) was greater than the theoretical value, presumably because of insufficient temperature control of the macrobatch reactor. It is also important to note that the molecular-weight distribution of the obtained polymers was not very narrow even at −48 °C. The ratio of the weight-average molecular weight (M_w) and the M_n was 1.44. A further increase in the temperature caused an increase in the M_w/M_n. This phenomenon is well-known for conventional macrobatch polymerization.[14]

Next, we examined the anionic polymerization of MMA using a microflow system composed of two T-shaped micromixers (**M1** and **M2**) and two microtube reactors (**R1** and **R2**: inner diameter (ϕ) = 1000 μm, length (L) = 50 cm) (Table 2). A solution of MMA in THF (0.50 M) and a solution of 1,1-diphenylhexyllithium in THF/hexane (99/1 v/v) (0.050 M) were mixed using **M1**, and the resulting solution was introduced to **R1**, where the polymerization took place. The polymerization was quenched by adding methanol using **M2**. The results obtained with varying the temperature (T: 24, 0, −28, −48, and −78 °C), the inner diameter of micromixer **M1**, the flow rate of the solutions of MMA and 1,1-diphenylhexyllithium, and the residence time in **R1** are summarized in Table 2.

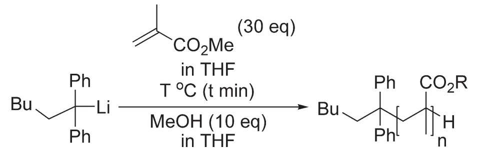
The polymerization at 24, 0, −28, and −48 °C was complete within the residence time of 11.8 s to give polymers in quantitative yields. The molecular-weight distribution was narrow even at temperatures higher than −28 °C (entries 1−9). Extremely fast heat transfer of the microflow system seems to be responsible for preventing decomposition of the reactive polymer chain end. Polymerization at higher temperatures such as 24 and 0 °C resulted in a slight increase in the M_w/M_n presumably because of decomposition of the reactive polymer chain end (entries 3, 6). At 24 °C, a decrease in the residence time causes a decrease in the M_w/M_n (entries 1−3). Therefore, short residence times in microflow systems also seem to be responsible for preventing decomposition of the reactive polymer chain end.

The M_w/M_n of the polymer obtained at −48 and −78 °C was also large presumably because of slow initiation (entries 10−13). These results show that precise control of the reaction temperature is very important to control the molecular-weight distribution in the microflow system. The M_w/M_n also strongly depended on the flow rate. In fact, the M_w/M_n increased with a decrease in the flow rate (entries 9, 14−17). This is presumably because mixing speed decreased with a decrease in the flow rate, which is well-known in the literature.[16] The M_w/M_n also depended on the inner diameter of micromixer **M1**. The use of **M1** with 500 or 1000 μm inner diameter resulted in lower controllability (entries 9, 18, 19). This is because of the decrease in the mixing speed caused by an increase in the diffusion path in the microstructure. Thus, the present results indicate that extremely fast mixing as well as precise temperature control is responsible for the observed excellent controllability of molecular-weight distribution in the microflow system. Moreover, M_n can also be controlled by changing the concentration of the initiator solution (entries 9, 20, 21). Higher monomer/initiator ratio led to the formation of the polymers of higher M_n (entry 20: M_n = 7,100; entry 21: M_n = 11,000). Further increase in the

---

*Corresponding author.

Table 1. Anionic Polymerization of Methyl Methacrylate in a Conventional Macrobatch Reactor[a]



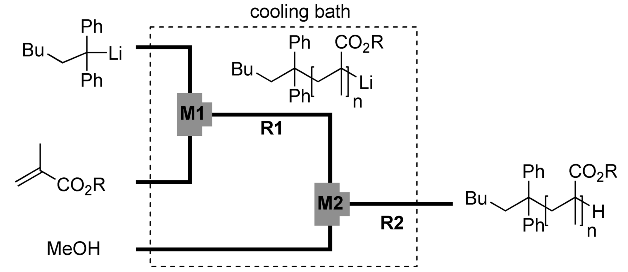
temperature (°C)	reaction time (min)	convn (%)	M_n[b]	M_w/M_n[b]
0	1	97	5400	1.80
−28	1	100	5100	1.60
−48	1	100	5300	1.44
−78	5	100	5400	1.32

[a] A solution of methyl methacrylate in THF (tetrahydrofuran) (0.50 M, 6.0 mL) was added to a solution of 1,1-diphenylhexyllithium in THF/hexane (99/1 v/v) (0.050 M, 2.0 mL) in a 20 mL flask. After the reaction was stirred for *t* min, the polymerization was quenched with methanol (0.33 M in THF, 3.0 mL). [b] Polymers were analyzed with size-exclusion chromatography calibrated with polystyrene.

monomer/initiator ratio will hopefully give rise to higher M_n. Polymerization reactions of other alkyl methacrylates were also examined using the microflow system. Thus, *n*-butyl methacrylate (BuMA) and *tert*-butyl methacrylate (Bu^tMA) underwent the polymerization in a highly controlled manner to give the polymers of narrow molecular-weight distribution at 0 or 24 °C (entries 22−27). Presumably the bulkiness of the alkyl group seems to suppress side reactions such as the attack of propagating enolate on the carbonyl group.[17] These results indicate that microflow systems open a new possibility of living anionic polymerization of alkyl methacrylates.

It is important to characterize the reactive carbanionic polymer chain end because its livingness leads to the production of end functionalized polymers and block copolymers. Thus, the following experiments were carried out at −28 °C (MMA), 0 °C (BuMA), and 24 °C (Bu^tMA) to verify the living nature of the polymer chain end. Thus, using the microflow system shown in Figure 1, a solution of *an alkyl methacrylate* in THF (0.50 M, flow rate: 3.0 mL/min) and that of 1,1-diphenylhexyllithium in THF/hexane (99/1 v/v) (0.050 M, flow rate: 1.0 mL/min) were introduced to micromixer **M1**, and the polymerization was carried out

Table 2. Microflow System Controlled Anionic Polymerization of Alkyl Methacrylates[a]



entry	alkyl methacrylate[b]	bath temperature (°C)	inner diameter of **M1** (μm)	flow rate of methacrylates (mL/min)	flow rate of 1,1-diphenylhexyllithium (mL/min)	residence time in **R1** (s)	[M]/[I]	convn (%)	M_n[c]	M_w/M_n[c]
1	MMA	24	250	6.0	2.0	0.736	30	81	3200	1.35
2	MMA	24	250	6.0	2.0	2.95	30	95	3700	1.41
3	MMA	24	250	6.0	2.0	11.8	30	99	4000	1.44
4	MMA	0	250	6.0	2.0	0.736	30	76	3000	1.25
5	MMA	0	250	6.0	2.0	2.95	30	98	3600	1.25
6	MMA	0	250	6.0	2.0	11.8	30	99	3600	1.27
7	MMA	−28	250	6.0	2.0	0.736	30	39	1600	1.22
8	MMA	−28	250	6.0	2.0	2.95	30	89	3000	1.17
9	MMA	−28	250	6.0	2.0	11.8	30	99	3400	1.16
10	MMA	−48	250	6.0	2.0	2.95	30	96	3400	1.20
11	MMA	−48	250	6.0	2.0	11.8	30	100	3900	1.19
12	MMA	−78	250	6.0	2.0	11.8	30	58	2600	1.31
13	MMA	−78	250	6.0	2.0	23.6	30	74	3300	1.30
14	MMA	−28	250	9.0	3.0	11.8	30	100	3600	1.15
15	MMA	−28	250	3.0	1.0	11.8	30	100	3700	1.17
16	MMA	−28	250	1.5	0.50	11.8	30	100	3700	1.44
17	MMA	−28	250	0.75	0.25	11.8	30	78	3200	2.04
18	MMA	−28	500	6.0	2.0	11.8	30	100	3600	1.21
19	MMA	−28	1000	6.0	2.0	11.8	30	100	3600	1.32
20[d]	MMA	−28	250	6.0	2.0	11.8	50	100	7100	1.19
21[e]	MMA	−28	250	6.0	2.0	11.8	75	97	11000	1.24
22	BuMA	24	250	6.0	2.0	11.8	30	100	6000	1.32
23	BuMA	0	250	6.0	2.0	11.8	30	100	5700	1.24
24	BuMA	−28	250	6.0	2.0	11.8	30	100	5500	1.30
25	Bu^tMA	24	250	6.0	2.0	11.8	30	99	6600	1.12
26	Bu^tMA	0	250	6.0	2.0	11.8	30	100	6900	1.16
27	Bu^tMA	−28	250	6.0	2.0	11.8	30	89	7000	1.40

[a] A solution of an alkyl methacrylate in THF (tetrahydrofuran) (0.50 M) and a solution of 1,1-diphenylhexyllithium in THF/hexane (99/1 v/v) (0.050 M) were reacted in the microflow system. A resulting solution was quenched with a solution of methanol (0.33 M in THF, 3.0 mL/min) in microflow system. [b] Alkyl methacrylate: MMA (methyl methacrylate), BuMA (*n*-butyl methacrylate), or Bu^tMA (*tert*-butyl methacrylate). [c] Polymers were analyzed with size-exclusion chromatography calibrated with polystyrene. [d] The concentration of 1,1-diphenylhexyllithium in THF/hexane (99/1 v/v) was 0.030 M. [e] The concentration of 1,1-diphenylhexyllithium in THF/*n*-hexane (99/1 v/v) was 0.020 M.

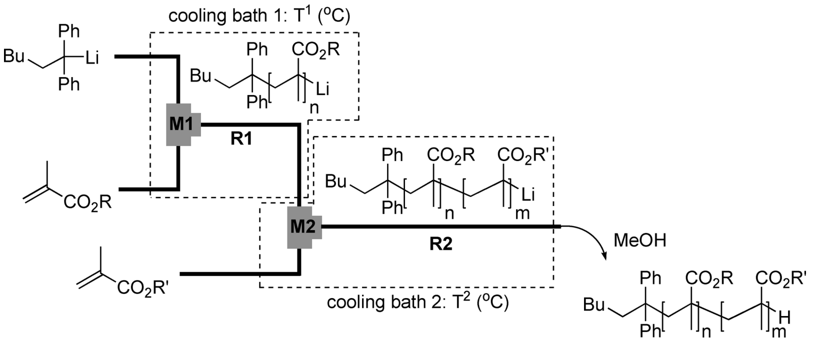


Figure 1. Schematic diagram of the microflow system for the synthesis of block copolymers, flow rate of a solution of alkyl methacrylates (first monomer) in THF (0.50 M): 3.0 mL/min, flow rate of a solution of 1,1-diphenylhexyllithium in THF/hexane (99/1 v/v) (0.050 M): 1.0 mL/min, flow rate of a solution of alkyl methacrylates (second monomer) in THF (0.50 M): 3.0 mL/min, **M1**, **M2**: T-shaped micromixer. **R1**, **R2**: microtube reactor. Temperature of cooling bath in polymerization: −28 °C (MMA), 0 °C (BuMA), 24 °C (Bu^{t}MA).

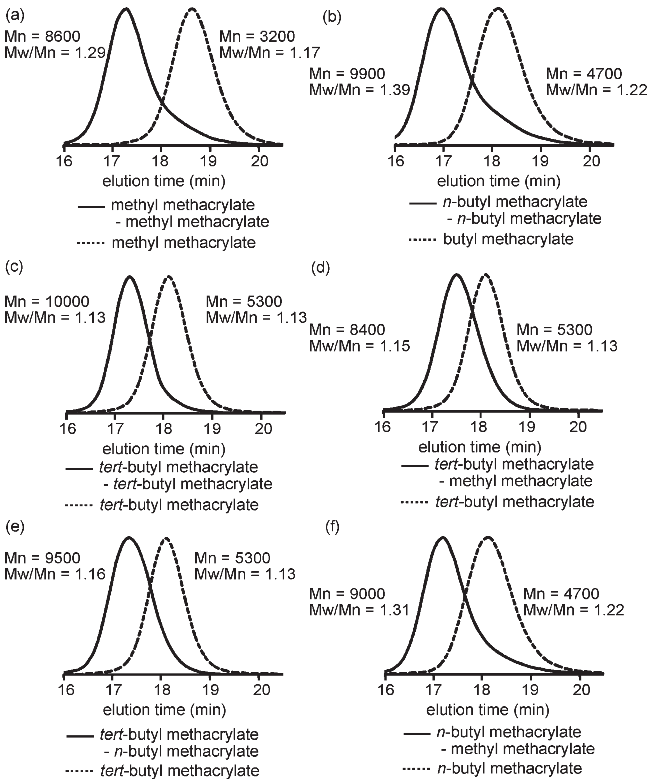


Figure 2. Size exclusion chromatography traces of block copolymers obtained in the microflow system: (a) methyl methacrylate−methyl methacrylate, (b) *n*-butyl methacrylate−*n*-butyl methacrylate, (c) *tert*-butyl methacrylate−*tert*-butyl methacrylate, (d) *tert*-butyl methacrylate−methyl methacrylate, (e) *tert*-butyl methacrylate−*n*-butyl methacrylate, and (f) *n*-butyl methacrylate−methyl methacrylate.

in microtube reactor **R1** (MMA, $\phi = 1000\ \mu$m, $L = 25$ cm; BuMA, $\phi = 1000\ \mu$m, $L = 7.0$ cm; Bu^{t}MA, $\phi = 1000\ \mu$m, $L = 100$ cm). Immediately after the polymerization, a solution of the same monomer in THF (0.50 M, flow rate: 3.0 mL/min) was introduced to micromixer **M2**, which was connected to microtube reactor **R2** ($\phi = 1000\ \mu$m, $L = 50$ or 200 cm) where the second polymerization took place. As shown in Figure 2, parts a, b, and c, the M_n increased by the addition of the second monomer solution, but the molecular-weight distribution stayed very narrow. These facts show that the polymer chain end is really living within the residence time (2.95 s (MMA) or 0.825 s (BuMA) or 11.8 s (Bu^{t}MA)) in the microflow system.

Based on the livingness of the polymer chain end, we synthesized structurally defined block copolymers composed of two different monomers using the microflow system (Figure 1). After polymerization of an alkyl methacrylate in **R1**, a solution of a different alkyl methacrylate in THF (0.50 M, flow rate: 3.0 mL/min) was introduced to **M2**. A polymer of higher M_n was obtained with narrow molecular-weight distribution (Figure 2, parts d, e, and f), indicating that the present method serves as an effective method for synthesis of block copolymers.

In conclusion, we have found that living anionic polymerization of alkyl methacrylates initiated by 1,1-diphenylhexyllithium can be conducted in microflow systems. Polymers of narrow molecular-weight distribution were obtained at −28 °C − room temperature (24 °C) by virtue of fast mixing and residence time control. Block polymerization has also been achieved by sequential use of two monomers in the microflow system. The observations illustrated here open a new possibility of living anionic polymerization for synthesis of structurally well-defined polymers and copolymers having various functions in both laboratory synthesis and industrial production.

Acknowledgment. This work was partially supported by the Grant-in-Aid for Scientific Research and NEDO projects.

Supporting Information Available: Text giving experimental procedures and spectroscopic data of compounds, schemes showing the polymerizations, tables showing polymerization data, and figures showing the block polymerization plots and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Jagur-Grodzinski, J. *Living and controlled polymerization: synthesis, characterization, and properties of the respective polymers and copolymers*; NOVA: New York, 2006.

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

(3) (a) Kamigaito, M.; Ando, T.; Sawamoto, M. *Chem. Rev.* **2001**, *101*, 3689–3746. (b) Matyjaszewski, K.; Xia, J. *Chem. Rev.* **2001**, *101*, 2921–2990. (c) Hawker, C. J.; Bosman, A. W.; Harth, E. *Chem. Rev.* **2001**, *101*, 3661–3688. (d) Yamago, S. *J.Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 1–12.

(4) (a) Hsieh, H. L.; Quirk, R. P. *Anionic polymerization: principles and practical applications*; Marcel Dekker: New York, 1996. (b) Jagur-grodzinski, J. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 2116–2133. (c) Smid, J. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 2101–2107. (d) Hirao, A.; Loykulnant, S.; Ishizone, T. *Prog. Polym. Sci.* **2002**, 27, 1399–1471.

(5) Hadjichristidis, N.; Pitsikalis, M.; Pispas, S.; Iatrou, H. *Chem. Rev.* **2001**, *101*, 3747−3792 and references therein.

(6) (a) Zune, C.; Jérôme, R. *Prog. Polym. Sci.* **1999**, *24*, 631–664. (b) Baskaran, D. *Prog. Polym. Sci.* **2003**, *28*, 521–581.

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

(8) (a) Jähnisch, K.; Hessel, V.; Löwe, H.; Baerns, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 406–446. (b) Doku, G. N.; Verboom, W.; Reinhoudt, D. N.; van den Berg, A. *Tetrahedron* **2005**, *61*, 2733–2742. (c) Watts, P.; Haswell, S. J. *Chem. Soc. Rev.* **2005**, *34*, 235–246. (d) Geyer, K.; Codee, J. D. C.; Seeberger, P. H. *Chem.—Eur. J.* **2006**, *12*, 8434–8442. (e) deMello, A. J. *Nature* **2006**, *442*, 394–402. (f) Song, H.; Chen, D. L.; Ismagilov, R. F. *Angew. Chem., Int. Ed.* **2006**, *45*, 7336–7356. (g) Kobayashi, J.; Mori, Y.; Kobayashi, S. *Chem. Asian J.* **2006**, *1*, 22–35. (h) Mason, B. P.; Price, K. E.; Steinbacher, J. L.; Bogdan, A. R.; McQuade, D. T. *Chem. Rev.* **2007**, *107*, 2300–2318. (i) Ahmed-Omer, B.; Brandtand, J. C.; Wirth, T. *Org. Biomol. Chem.* **2007**, *5*, 733–740. (j) Fukuyama, T.; Rahman, M. T.; Sato, M.; Ryu, I. *Synlett* **2008**, 151–163. (k) Yoshida, J.; Nagaki, A.; Yamada, T. *Chem.—Eur. J.* **2008**, *14*, 7450–7459.

(9) Recent examples: (a) Nagaki, A.; Togai, M.; Suga, S.; Aoki, N.; Mae, K.; Yoshida, J. *J. Am. Chem. Soc.* **2005**, *127*, 11666–11675. (b) He, P.; Watts, P.; Marken, F.; Haswell, S. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 4146–4149. (c) Uozumi, Y.; Yamada, Y.; Beppu, T.; Fukuyama, N.; Ueno, M.; Kitamori, T. *J. Am. Chem. Soc.* **2006**, *128*, 15994–15995. (d) Tanaka, K.; Motomatsu, S.; Koyama, K.; Tanaka, S.; Fukase, K. *Org. Lett.* **2007**, *9*, 299–302. (e) Usutani, H.; Tomida, Y.; Nagaki, A.; Okamoto, H.; Nokami, T.; Yoshida, J. *J. Am. Chem. Soc.* **2007**, *129*, 3046–3047. (f) Sahoo, H. R.; Kralj, J. G.; Jensen, K. F. *Angew. Chem., Int. Ed.* **2007**, *46*, 5704–5708. (g) Hornung, C. H.; Mackley, M. R.; Baxendale, I. R.; Ley, S. V. *Org. Process Res. Dev.* **2007**, *11*, 399–405. (h) Nagaki, A.; Takabayashi, N.; Tomida, Y.; Yoshida, J. *Org. Lett.* **2008**, *18*, 3937–3940. (i) Fukuyama, T.; Kobayashi, M.; Rahman, M. T.; Kamata, N.; Ryu, I. *Org. Lett.* **2008**, *10*, 533–536. (j) Nagaki, A.; Kim, H.; Yoshida, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 7833–7836. (k) Nagaki, A.; Takizawa, E.; Yoshida, J. *J. Am. Chem. Soc.* **2009**, *131*, 1654–1655.

(10) (a) Steinbacher, J. L.; Mcquade, D. T. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, *44*, 6505–6533. (b) Hessel, V.; Serra, C.; Löwe, H.; Hadziioannou, G. *Chem. Ing. Tech.* **2005**, *77*, 1693−1714 and references therein.

(11) For radical polymerization using the microflow reactor: (a) Wu, T.; Mei, Y.; Cabral, J. T.; Xu, C.; Beers, K. L. *J. Am. Chem. Soc.* **2004**, *126*, 9880–9881. (b) Russum, J. P.; Jones, C. W.; Schork, F. J. *Macromol. Rapid Commun.* **2004**, *25*, 1064–1068. (c) Serra, C.; Sary, N.; Schlatter, G.; Hadziioannou, G.; Hessel, V. *Lab Chip* **2005**, *5*, 966–973. (d) Enright, T. E.; Cunningham, M. F.; Keoshkerian, B. *Macromol. Rapid Commun.* **2005**, *26*, 221–225. (e) Xu, C.; Wu, T.; Drain, C. M.; Batteas, J. D.; Beers, K. L. *Macromolecules* **2005**, *38*, 6–8. (f) Iwasaki, T.; Kawano, N.; Yoshida, J. *Org. Process Res. Dev.* **2006**, *10*, 1126–1131. (g) Rosenfeld, C.; Serra, C.; Brochon, C.; Hadziioannou, G. *Chem. Eng. Sci.* **2007**, *62*, 5245–5250.

(12) For cationic polymerization using the microflow reactor: (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.

(13) (a) Nagaki, A.; Tomida, Y.; Yoshida, J. *Macromolecules* **2008**, *41*, 6322–6330. (b) Wurm, F.; Wilms, D.; Klos, J.; Löwe, H.; Frey, H. *Macromol. Chem. Phys.* **2008**, *209*, 1106–1114.

(14) (a) Baskaran, D. *Prog. Polym. Sci.* **2003**, *28*, 521–581. (b) Zune, C.; Jérme, R. *Prog. Polym. Sci.* **1999**, *24*, 631–664.

(15) (a) Baskaran, D.; Sivaram, S. *Macromolecules* **1997**, *30*, 1550–1555. (b) Baskaran, D.; Müller, A. H. E. *Macromolecules* **1999**, *32*, 1356–1361. (c) Varshney, S. K.; Jérme, R.; Bayard, P.; Jacobs, C.; Fayt, R.; Teyssi, P. *Macromolecules* **1992**, *25*, 4457–4463. (d) Baskaran, D.; Chakrapani, S.; Sivaram, S. *Macromolecules* **1995**, *28*, 7315–7317.

(16) Ehrfeld, W.; Golbig, K.; Hessel, V.; Löwe, H.; Richter, T. *Ind. Eng. Chem. Res.* **1999**, *38*, 1075–1082.

(17) Zhang, H.; Ishikawa, H.; Ohata, M.; Kazama, T.; Isono, Y.; Fujimoto, T. *Polymer* **1992**, *33*, 828–833.