

Use of micromixers to control the molecular weight distribution in continuous two-stage nitroxide-mediated copolymerizations

Carine Rosenfeld^a, Christophe Serra^{a,*}, Cyril Brochon^a,
Volker Hessel^b, Georges Hadziioannou^a

^a Laboratoire d'Ingénierie des Polymères pour les Hautes Technologies (LIPHT) – CNRS UMR 7165,
École Européenne de Chimie Polymères et Matériaux (ECPM), 25 rue Becquerel, F-67087 Strasbourg, France

^b Institut für Mikrotechnik Mainz GmbH, Carl-Zeiss-Str.18-20, D-55129 Mainz, Germany

Abstract

The synthesis of poly(*n*-butyl acrylate)-*block*-poly(styrene) copolymers by nitroxide-mediated radical polymerization (NMRP) in two serial continuous microtube reactors have been performed. The influence of the micromixer used to mix the first block with the second monomer, either an interdigital multilamination micromixer or a T-junction, on the control of the polymerization reaction as well as the copolymerization temperature was investigated. Results were compared with those obtained in a macroscale batch reactor. The main advantage of interdigital micromixers is their ability to achieve an efficient and intimate mixing between a viscous (first block) and a liquid (comonomer) fluid due to the small film thicknesses of the lamellae. In all experiments, the microtube reactors coupled with a multilamination micromixer give the narrowest molecular weight distributions, which implies that the control of the copolymerization reaction is improved.

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1. Introduction

During the last 20 years, new polymerization techniques so called controlled/'living' polymerizations permit to synthesize well-defined macromolecular architectures [1] (block, graft or multifunctional copolymers with various reactive pendant and terminal functions). These techniques allow controlling predetermined molecular weights and molecular weight distributions. In particular, nitroxide-mediated radical polymerization (NMRP) can be applied to a wide range of monomers [2] (styrene, acrylates, acrylamides, acrylonitrile, 1,3-dienes. . .) in presence of acyclic nitroxides such as 2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide (TIPNO) or *N*-*tert*-butyl-*N*-(1-diethyl phosphono-2,2-dimethylpropyl) nitroxide (DEPN also well known as SG1), which terminates reversibly the growing chains (Scheme 1). Copolymerization reactions are usually carried out in macroscale batch [3,4] or semi-batch [5] reactors.

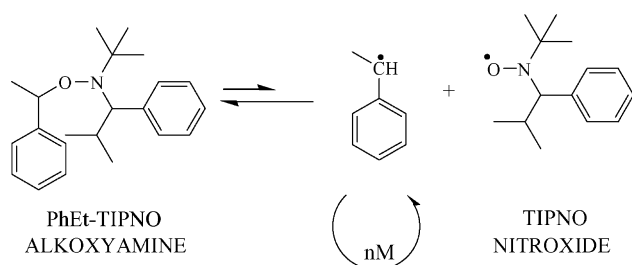
The use of microfluidic devices are now widely used in chemical engineering [6] but these microsystems only begin to be implemented within the framework of polymerization processes

[7]. So far, very few references are available on the synthesis of block copolymers in microfluidic devices. Shen and Zhu [8] have successfully synthesized methacrylate-based block copolymers in packed column reactors of 4 mm inner diameter (ID) stainless steel tubing containing silica-supported ATRP (Atom Transfer Radical Polymerization) catalyst in a continuous way. More recently, Wu et al. [9] have prepared some poly(ethylene oxide)-*block*-2-hydroxypropyl methacrylate) (PEO-*b*-PHPMA) block copolymers also by ATRP, on a microchip using a PEO macroinitiator.

The main advantage using microstructured micromixers is their ability to put in contact two fluids achieving a rapid and efficient mixing. In addition, homogenization of the reaction medium is also considerably improved due to the small film thickness, typically smaller than 100 μm , which implies a better diffusional mass transport in the time scale of the polymerization reaction.

In this paper, nitroxide-mediated block copolymerizations (NMBC) of *n*-butyl acrylate (BA) and styrene (S) in two serial continuous microtube reactors are studied and compared to a macroscale batch reactor. The two-stage copolymerizations are carried out without any intermediate purification step. For the continuous process, the viscous poly(*n*-butyl acrylate) (PBA) first block and the liquid comonomer, i.e. styrene, are mixed

* Corresponding author. Tel.: +33 390 242 718; fax: +33 390 242 716.
E-mail address: SerraC@ecpm.u-strasbg.fr (C. Serra).



Scheme 1. Activation–deactivation equilibrium in TIPNO-mediated radical polymerization.

through an interdigital multilamination micromixer or a basic T-junction prior to enter in the second microtube reactor. The influence of the process, either batch mode or continuous mode with a multilamination or a bilamination micromixer, and the copolymerization temperature are investigated. It is expected that by increasing the contact area in the multilamination micromixer, the overall distribution of the copolymers will be narrower.

2. Materials and procedure

2.1. Materials

n-Butyl acrylate, styrene and acetic anhydride were purchased from Aldrich. Monomers were passed through a basic alumina column to remove inhibitor. Toluene and

acetic anhydride were used as received. The nitroxide TIPNO and the unimolecular alkoxyamine initiator 2,2,5-trimethyl-3-(1-phenylethoxy)-4-phenyl-3-azahexane (PhEt-TIPNO in Scheme 1) were prepared using the procedures, respectively, developed by Benoit et al. [3] and Matyjaszewski et al. [10].

2.2. Microfluidic setup

Continuous two-stage NMBC were carried out in two serial 900 μm ID stainless steel tube reactors (μR1 and μR2). The setup is shown in Fig. 1. It is composed of a pressure sensor (Swagelok PTU Series UHP Transducer) and a temperature controller. The system is kept under a minimum pressure of 20 bars so that all components remain liquid by means of a back pressure cartridge (Upchurch BPR 300). Temperature and pressure data were collected through Labview[®] software. The polymerization solutions were injected in the microtubes with two 307 SC HPLC Gilson piston pumps. Microtube reactors were heated with heater collars.

Two micromixers were used as depicted in Fig. 2: (a) High Pressure Interdigital Multilamination Micromixer (HPIMM) provided by the IMM Company (Mainz, Germany) [11] and (b) a basic 1/16" T-junction (TJ) purchased from Swagelok (Paris, France). The HPIMM laminates both inlet flows (PBA solution + styrene) into 15 lamellae of 20 μm thickness for each flow. These lamellae are arranged in staggered rows and confined in the half-moon shaped focusing section (Fig. 2a).

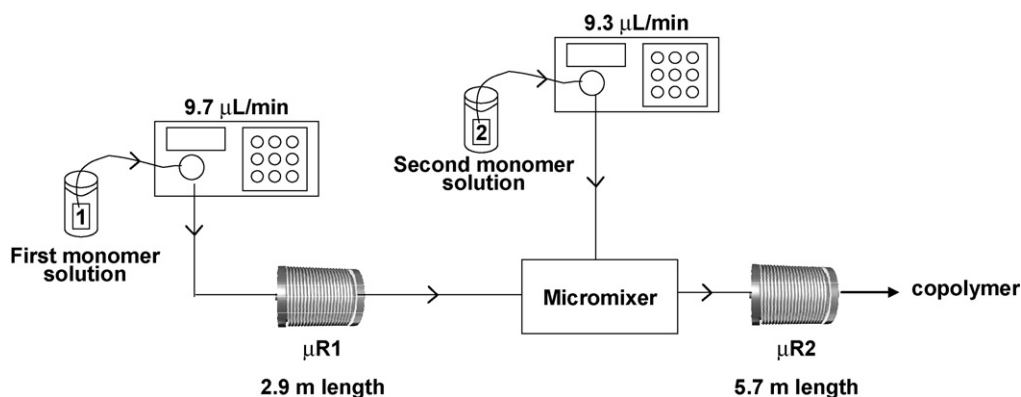


Fig. 1. Continuous microfluidic setup for the two-stage NMBC.

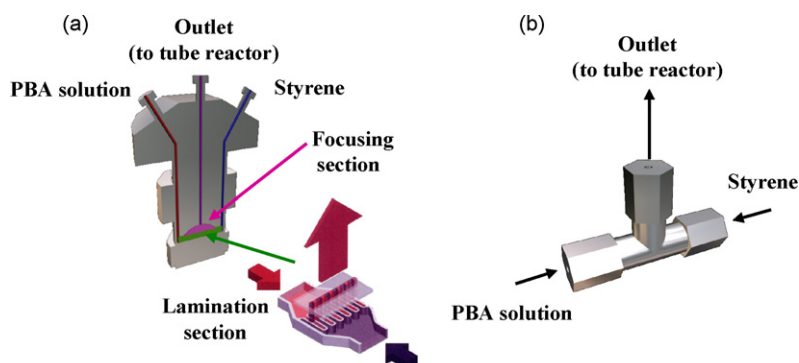


Fig. 2. Microfluidic devices considered: (a) High Pressure Interdigital Multilamination Micromixer (courtesy of IMM) and (b) T-junction.

With this micromixer the contact area between the two fluids is greatly increased by the multilamination (ML) of each flow as compared to the TJ micromixer [12,13] which can be considered as a bilamination mixer (BL) with two streams of 450 μm width.

2.3. Characterizations

Monomer conversions were determined by nuclear magnetic resonance (NMR) (Bruker 300 Ultrashield Trade Mark 300 MHz) using deuterated chloroform (CDCl_3) as solvent and the internal solvent peak as the reference. Size exclusion chromatography (SEC) measurements were performed in tetrahydrofuran (THF) on a PL-gel 5 μm mixed-C, a 5 μm 100 \AA and a 5 μm Guard columns in a Shimadzu LC-10AD liquid chromatograph equipped with a Shimadzu RID-10A refractive index detector. Molecular weights are reported in polystyrene equivalents.

2.4. General procedures

2.4.1. Microtube reactor (μR process)

Polymerization solution containing 75 vol.% *n*-butyl acrylate, 25 vol.% toluene, the unimolecular alkoxyamine initiator, 5 mol% nitroxide (TIPNO) and two molar equivalents of acetic anhydride with respect to the alkoxyamine are firstly degassed with nitrogen for 30 min at room temperature. Then they are pumped through the first microtube reactor ($\mu\text{R}1$) with a flow rate of 9.7 $\mu\text{L}/\text{min}$ so that the residence time is 190 min. The temperature of that reactor is kept constant and equal to 140 $^\circ\text{C}$. The flow coming out of this first microtube reactor is then mixed with the pure styrene either with the HPIMM (μR -ML process) or with the TJ (μR -BL process). Then the resulting mixed solution flows through the second microtube reactor ($\mu\text{R}2$) heated at 120, 125 or 130 $^\circ\text{C}$. The liquid comonomer is pumped with a flow rate of 9.3 $\mu\text{L}/\text{min}$ so that the overall residence time in the second microtube reactor is 190 min. After at least three residence times, i.e. when the steady state is reached, 2 g samples were collected at the exit of each microtube reactor for analysis.

2.4.2. Batch reactor (BR process)

In a Schlenk flask, 2 g of the same initial first block solution was degassed with nitrogen by three freeze-pump-thaw cycles and the flask was sealed and placed in an oil bath at 140 $^\circ\text{C}$ to start the reaction. After 190 min, the polymerization is stopped by cooling with cold water. For the block copolymerization, the second monomer is directly added into the Schlenk flask and the same procedure is used to degas. The flask was again sealed and placed in an oil bath at 120, 125 or 130 $^\circ\text{C}$ to copolymerize for another 190 min. After the reaction time, the polymerization is stopped by cooling and the polymer is collected for analysis.

In both cases, the conversions were determined by ^1H NMR. The polymers were dried at 50 $^\circ\text{C}$ under vacuum and were analyzed by SEC without further purification.

Table 1

Synthesis of poly(*n*-butyl acrylate) at 140 $^\circ\text{C}$ in microtube and batch reactors in presence of acetic anhydride

Experiment	Reactor	x^a (%)	$M_{n,\text{th}}^b$ (g/mol)	M_n^c (g/mol)	PDI ^d
1a	μR	90	32800	26600	1.44
1b	BR	95	34800	29700	1.80

^a Monomer conversion.

^b Theoretical M_n were given in function of the conversion, x , according to: $[\text{BA}]_0/[\text{PhEt-TIPNO}]_0 \times M_{\text{BA}} \times x + M_{\text{PhEt-TIPNO}}$ where $M_{\text{PhEt-TIPNO}}$ and M_{BA} are, respectively, the molecular weight of the alkoxyamine and the *n*-butyl acrylate.

^c SEC results in PS equivalents.

^d Polydispersity index.

3. Results and discussion

3.1. *n*-Butyl acrylate homopolymerization

The results are summarized in Table 1. These are used as a reference for the polymerization of the first block at 140 $^\circ\text{C}$ in microtube and batch reactors.

In order to avoid gradient segment as much as possible into the copolymers, one needs to polymerize at least 90% of the monomer. The first block PBA has been prepared in presence of two equivalents of acetic anhydride. This reagent is known to be a rate-accelerating agent in NMRP [14]. It allows reaching higher monomer conversions faster. Due to a higher surface to volume ratio, we showed that the heat released by the acrylate polymerization reaction is more efficiently removed from the microtube reactor than from the batch reactor [15]. As a consequence, the polydispersity index of the PBA is much lower (1.44) in the microtube reactor than in the batch reactor (1.80). This difference in the PDI values between those two processes already shows that using microtube reactor leads to a very good control over the polymerization, which will necessarily echo on the copolymerization results.

3.2. Two-stage block copolymerization

3.2.1. Influence of the process

Block copolymerizations were carried out in batch (BR) and in microtube reactors (μR) with two different mixers: either a multilamination (ML) or bilamination (BL) micromixer. The results for the second stage reaction (copolymerization) carried out at 125 $^\circ\text{C}$ are presented in Table 2.

Table 2

Synthesis of PBA-*b*-PS block copolymers at 125 $^\circ\text{C}$ in microtube and batch reactors

Experiment	1st block	Process	x_{BA}^a (%)	x_{S}^a (%)	M_n^b (g/mol)	PDI
2	1a	μR -ML	96	50	36600	1.40
3	1a	μR -BL	99	36	26600	1.73
4	1b	BR	99	50	33600	1.74

^a Monomer conversions, respectively, of *n*-butyl acrylate and styrene measured by ^1H NMR.

^b SEC results in PS equivalents.

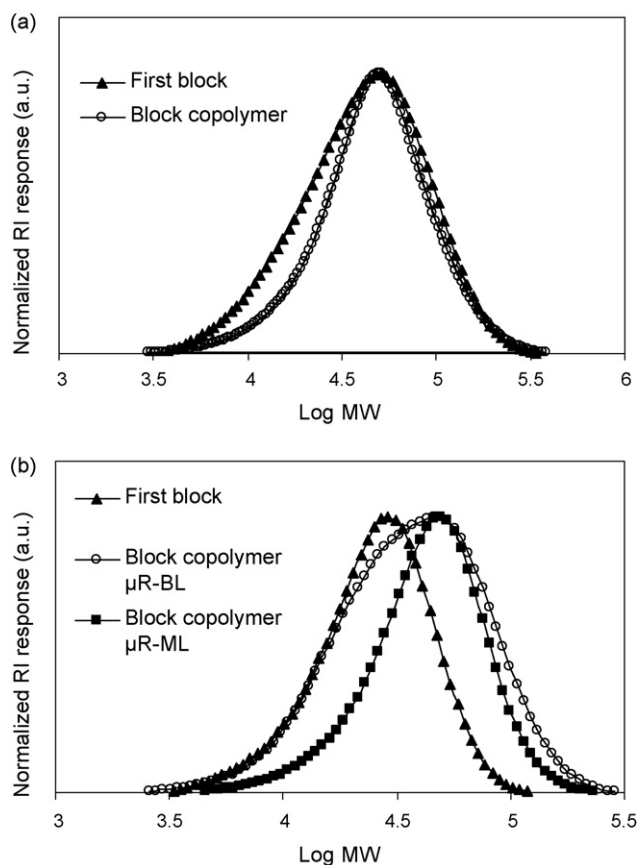


Fig. 3. Evolution of the molecular weight distribution of the first block PBA and the block copolymer PBA-*b*-PS synthesized (a) in batch and (b) in microtube reactors.

In batch reactor, styrene conversion reaches 50% (experiment 4 in Table 2). Moreover, it can be seen that the copolymer synthesized in this system has roughly the same molecular weight than that of the first block PBA (33600 g/mol (Table 2) as compared to 29700 g/mol (Table 1)). On the other hand, the polydispersity index is slightly decreasing from 1.80 for the first block (Table 1) to 1.74 (Table 2) for the copolymer. One can also observe that the normalized RI response of the copolymer exhibits no shift towards higher molecular weights (see right part of the chromatogram in Fig. 3a). This means that the longest PBA chains produced at the first polymerization stage are no longer living, probably resulting from a termination by combination. As a consequence, these chains cannot incorporate the comonomer. Furthermore, the shift on the left part of the block copolymer curve indicates that the smallest TIPNO-terminated PBA chains have been extended by few styrene units. Thus, the results obtained for the BR process illustrate that the mixing is not efficient and therefore that the control of the copolymerization reaction is quite low.

In microtube reactors, the rate-incorporation of styrene is higher with the HPIMM than with the TJ (experiments 2 and 3 in Table 2). Moreover, number-average molecular weight of the copolymer synthesized in the microtube reactor with the HPIMM (36,600 g/mol) matches with the incorporation of 5% of butyl acrylate and 50% of styrene in the first block PBA

(26,600 g/mol). This gives evidences that conversely to the batch reactor one obtains a copolymer. It is worthwhile to note that the distribution of that copolymer is getting narrower as the lamination increases, down to 1.40 for the multilamination micromixer compared to 1.73 for the bilamination micromixer. Indeed, for the later, the film thickness of each fluid (450 μm) put in contact is too large so that a good mixing through diffusional transport can be fully achieved in the copolymerization time-scale (τ_2). Only a fraction of the styrene and the first PBA block can react, mainly at the interface between the two fluids. This is confirmed by the SEC distribution curve which exhibits a shoulder (see Fig. 3b) meaning that TIPNO-terminated PBA chains are still present in the medium along with copolymer chains.

The mixing is therefore much better with the HPIMM and helps to improve the control over the copolymer synthesis.

3.2.2. Influence of the copolymerization temperature

After the first polymerization step, only few percents of BA monomer are left, which are diluted twice with styrene just before the copolymerization step. Thus, since the *n*-butyl acrylate concentration is very low (0.24 and 0.13 mol/L, respectively, in the continuous and batch reactors), the BA polymerization rate is getting slower and as a consequence the conversion does not change very much (about 5%) from the homopolymerization, whatever the copolymerization temperature and the process used (Fig. 4a). On the other hand, the increase of the copolymerization temperature enhances the styrene conversion for all processes (Fig. 4b). Indeed, polymerization rate increases as each rate coefficient follows its own Arrhenius law.

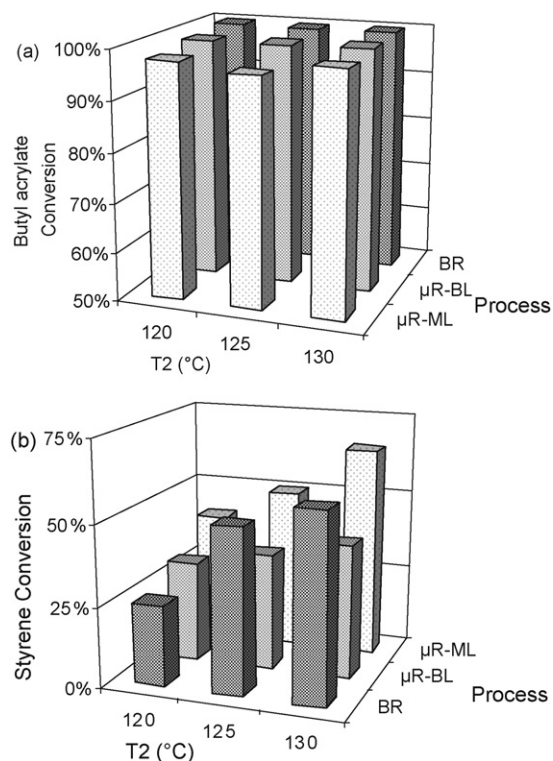


Fig. 4. Influence of copolymerization temperature and process on the overall conversion of (a) *n*-butyl acrylate and (b) styrene.

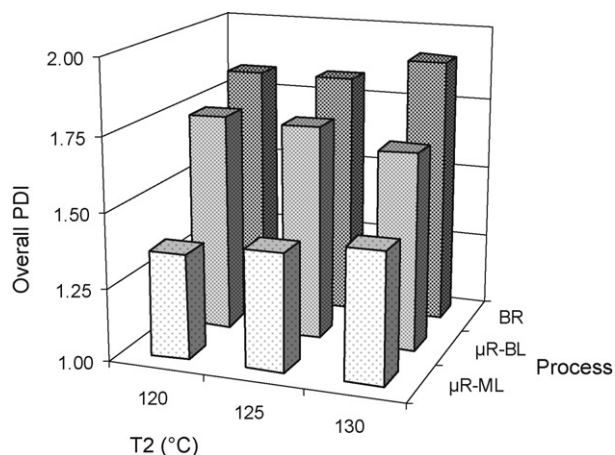


Fig. 5. Influence of copolymerization temperature and process on the overall copolymer polydispersity index.

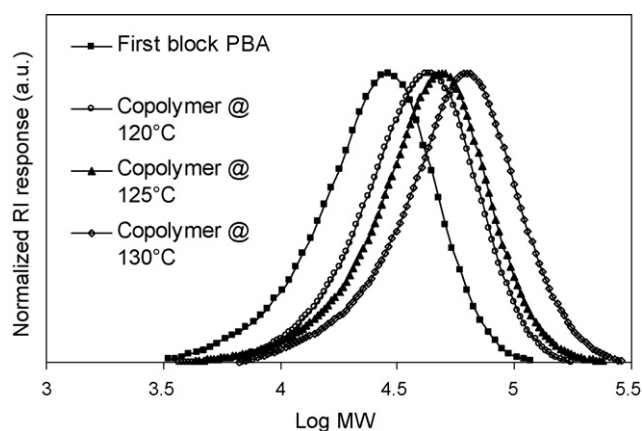


Fig. 6. Evolution of the number molecular weight distribution of the first block PBA and the block copolymer PBA-*b*-PS synthesized in microtube reactors with the multilamination micromixer (HPIMM).

In the microtube reactor coupled with the T-junction, the control over the polymerization is slightly improved with the increasing temperature, as the polydispersity indices go down from 1.74 to 1.67. Since the mixing is poor (low contact area), a temperature increase improves the diffusional transport by reducing the medium viscosity.

With the multilamination micromixer, the polydispersity index increases with temperature but only of 3% every 5 °C from 1.36 at 120 °C to 1.44 at 130 °C. This increase of the PDI values can be attributed to the activation/deactivation equilibrium in NMRP which is shifted to the active species when the temperature is getting higher. Since the monomer conversion increases, the shift in the SEC distribution curves to higher molecular weights is coherent as shown in Figs. 5 and 6. In this configuration, the very efficient mixing would permit to increase the copolymerization temperature to achieve higher comonomer conversion while keeping very narrow distributions.

4. Conclusion

Continuous two-stage nitroxide-mediated block copolymerization of *n*-butyl acrylate and styrene in two serial 900 μm

inner diameter stainless steel tube reactors has been demonstrated for the first time. For the continuous process, two different micromixers, either a multilamination micromixer or a bilamination micromixer, as well as different copolymerization temperatures have been investigated. The use of microfluidic devices, i.e. microtube reactors along with an interdigital multilamination micromixer, can significantly reduce the polydispersity index of the copolymer synthesized (1.36 at 120 °C) as compared to a macroscale batch reactor (1.83 at 120 °C). This improved control over the polymerization reaction is quite important for the synthesis of poly(*n*-butyl acrylate)-*block*-polystyrene copolymers since the highest exothermic monomer benefits from the advantages not only of the microtube reactor, i.e. a high surface to volume ratio to remove the heat released by the polymerization reaction, but also of the microstructured micromixer, i.e. the small film thicknesses of the lamellae to enhance the mixing between the viscous poly(*n*-butyl acrylate) and the liquid styrene. The use of a multilamination micromixer as compared to a bilamination micromixer allows on one hand to increase the comonomer incorporation rate into the copolymer chains and on the other hand to notably reduce the overall molecular weight distribution. This results directly from the increasing contact area as the lamination increases.

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References

- [1] K. Matyjaszewski, *Prog. Polym. Sci.* 30 (2005) 858–875.
- [2] C.J. Hawker, A.W. Bosman, E. Harth, *Chem. Rev.* 101 (2001) 3661–3688.
- [3] D. Benoit, V. Chaplinski, R. Braslau, C.J. Hawker, *J. Am. Chem. Soc.* 121 (1999) 3904–3920.
- [4] S. Robin, Y. Gnanou, *Macromol. Symp.* 165 (2001) 43–53.
- [5] Y. Wang, R.A. Hutchinson, M.F. Cunningham, *Macromol. Mater. Eng.* 290 (2005) 230–241.
- [6] K. Jähnisch, V. Hessel, H. Löwe, M. Baerns, *Angew. Chem. Int.* 43 (2004) 406–446.
- [7] V. Hessel, C. Serra, H. Löwe, G. Hadziioannou, *Chem. Ing. Tech.* 77 (2005) 1693–1714.
- [8] Y. Shen, S. Zhu, *AIChE J.* 48 (2002) 2609–2619.
- [9] T. Wu, Y. Mei, C. Xu, H.C.M. Byrd, K.L. Beers, *Macromol. Rapid Commun.* 26 (2005) 1037–1042.
- [10] K. Matyjaszewski, B.E. Woodworth, X. Zhang, S.G. Gaynor, Z. Metzner, *Macromolecules* 31 (1998) 5955–5957.
- [11] W. Ehrfeld, K. Golbig, V. Hessel, H. Löwe, T. Richter, *Ind. Eng. Chem. Res.* 38 (1999) 1075–1082.
- [12] A.E. Kamholz, B.H. Weigl, B.A. Finlayson, P. Yager, *Anal. Chem.* 71 (1999) 5340–5347.
- [13] D. Gobby, P. Angeli, A. Gavriilidis, *J. Micromech. Microeng.* 11 (2001) 126–132.
- [14] E. Malmström, R.D. Miller, C.J. Hawker, *Tetrahedron* 53 (1997) 15225–15236.
- [15] C. Rosenfeld, C. Serra, C. Brochon, G. Hadziioannou, *Chem. Eng. Sci.* 62 (2007) 5245–5250.