

# Synergistic Effect of 1-Butyl-3-methylimidazolium Hexafluorophosphate and DMSO in the SARA ATRP at Room Temperature Affording Very Fast Reactions and Polymers with Very Low Dispersity

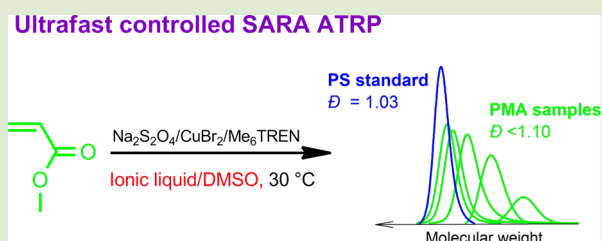
Joana P. Mendes,<sup>†</sup> Fábio Branco,<sup>†</sup> Carlos M. R. Abreu,<sup>†</sup> Patrícia V. Mendonça,<sup>†</sup> Anatoliy V. Popov,<sup>‡</sup> Tamaz Guliyashvili,<sup>\*†</sup> Arménio C. Serra,<sup>†</sup> and Jorge F. J. Coelho<sup>\*†</sup>

<sup>†</sup>CEMUC, Department of Chemical Engineering, University of Coimbra, 3030-790 Coimbra, Portugal

<sup>‡</sup>Department of Radiology, University of Pennsylvania, Philadelphia, Pennsylvania 19104, United States

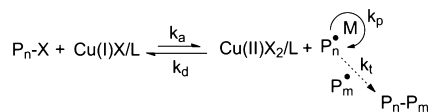
## S Supporting Information

**ABSTRACT:** An unusual synergistic effect between 1-butyl-3-methylimidazolium hexafluorophosphate (BMIM-PF<sub>6</sub>) and dimethyl sulfoxide (DMSO) mixtures is reported for the supplemental activator and reducing agent transfer radical polymerization (SARA ATRP) of methyl acrylate (MA) using a catalytic system composed by sodium dithionite (Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub>) and CuBr<sub>2</sub>/Me<sub>6</sub>TREN (Me<sub>6</sub>TREN: tris[2-(dimethylamino)ethyl]amine) at room temperature. To the best of our knowledge, the use of ionic liquids (IL) has never been reported for the SARA ATRP. The kinetic data obtained for a broad range of target molecular weights revealed very fast polymerization rates, low dispersity values ( $\bar{D} < 1.05$ ) and well-defined chain-end functionalities.



Atom transfer radical polymerization (ATRP) is one the most efficient, versatile and robust reversible deactivation radical polymerization (RDRP) techniques.<sup>1</sup> This method allows the synthesis of polymers having a vast range of specific functionalities with controlled molecular weight, architecture, and topology.<sup>2</sup> ATRP is based on the use of a transition metal complex, which mediates a fast equilibrium between dormant and active species (Scheme 1).

### Scheme 1. General Mechanism of ATRP



Several transition metal complexes in combination with different ligands (typically nitrogen-based ligands) have been employed in ATRP,<sup>3</sup> with Cu-based being the most used ones.<sup>4</sup> Aiming to reduce the amount of metal complexes required to control the polymerizations, new ATRP variations were proposed, such as activators regenerated by electron transfer (ARGET) ATRP using inorganic or organic reducing agents,<sup>5,6</sup> supplemental activator and reducing agent (SARA) ATRP involving the use of zerovalent transition metals<sup>3,5,7–9</sup> or inorganic sulfites;<sup>10–12</sup> initiators for continuous activator regeneration (ICAR) ATRP employing conventional thermal radical initiators; and electrochemically mediated ATRP (*e*-ATRP) that uses electrical current for the reduction process.<sup>13</sup>

The use of reducing agents allows the continuous regeneration of Cu(I) species during the polymerization, lowering the amount of catalyst to ppm levels. Ionic liquids (IL) are a class of green solvents<sup>14–16</sup> that present important advantages over several conventional and harmful organic solvents. Among those, one can stress the possibility of tailoring the properties of the IL by varying the structure of both cation and anion, excellent solubility of polar substrates, low volatility, recyclability and compatibility with various organic compounds. Since the pioneer works of Haddleton,<sup>17</sup> Kubisa<sup>18</sup> and Matyjaszewski,<sup>19</sup> several reports have been published using IL as solvents for ATRP.<sup>16,20–23</sup> The results revealed interesting features of these green solvents related to simplified separation of the polymer from the catalyst,<sup>17,19</sup> controlled reactions in the absence of ligand, and reduction of side reactions and catalytic effects.<sup>20</sup>

Here, we report the synergistic effect of dimethyl sulfoxide (DMSO) and 1-butyl-3-methylimidazolium hexafluorophosphate (BMIM-PF<sub>6</sub>) in the SARA ATRP of methyl acrylate (MA) catalyzed by Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub> and small amounts of CuBr<sub>2</sub>/Me<sub>6</sub>TREN (Me<sub>6</sub>TREN: tris[2-(dimethylamino)ethyl]amine) deactivator complex at room temperature.

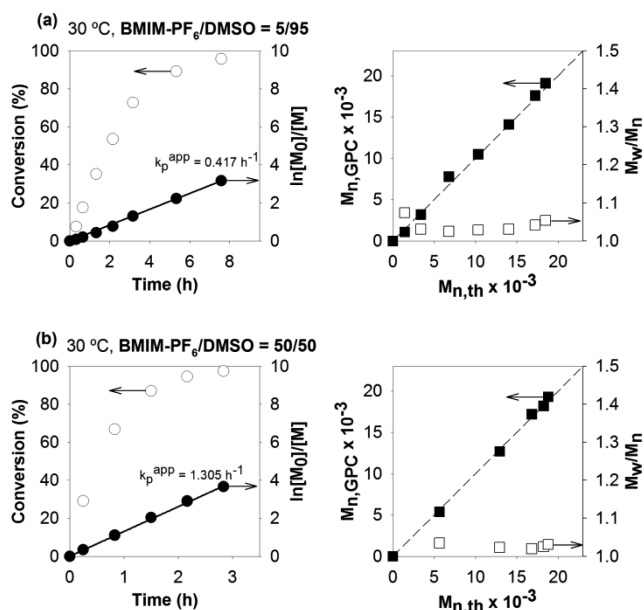
Preliminary experiments were performed using only BMIM-PF<sub>6</sub> as solvent for the MA polymerization, but no polymer was

Received: April 18, 2014

Accepted: May 23, 2014

Published: May 27, 2014

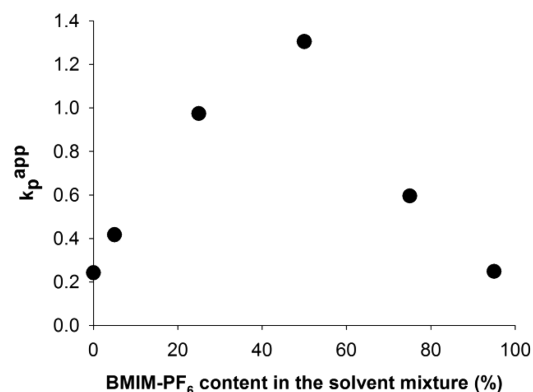
formed. This result can be justified based on the partial solubilization of the  $\text{CuBr}_2/\text{Me}_6\text{TREN}$  complex and, most importantly, to the complete insolubility of the SARA agent ( $\text{Na}_2\text{S}_2\text{O}_4$ ) in the  $\text{BMIM-PF}_6$ , preventing the formation of  $\text{Cu(I)}$  activator species. With the introduction of DMSO as a cosolvent a controlled polymerization was observed. The kinetic plots of SARA ATRP carried out at room temperature in  $\text{BMIM-PF}_6/\text{DMSO}$  (ratio 5/95 and 50/50) catalyzed by  $\text{Na}_2\text{S}_2\text{O}_4/\text{CuBr}_2/\text{Me}_6\text{TREN}$  are presented in Figure 1a,b and



**Figure 1.** Kinetic plots of conversion and  $\ln[M]_0/[M]$  vs time and plots of number-average molecular weights ( $M_{n,\text{GPC}}$ ) and  $\bar{D}$  ( $M_w/M_n$ ) vs theoretical number-average molecular weights ( $M_{n,\text{th}}$ ) for the SARA ATRP of MA catalyzed by  $\text{Na}_2\text{S}_2\text{O}_4/\text{CuBr}_2/\text{Me}_6\text{TREN}$  in (a)  $\text{BMIM-PF}_6/\text{DMSO} = 5/95$  and (b)  $\text{BMIM-PF}_6/\text{DMSO} = 50/50$ . Conditions:  $[\text{MA}]_0/[\text{solvent}] = 2/1$  (v/v);  $[\text{MA}]_0/[\text{EBiB}]_0/[\text{Na}_2\text{S}_2\text{O}_4]_0/[\text{CuBr}_2]_0/[\text{Me}_6\text{TREN}]_0 = 222/1/1/0.1/0.1$  (molar);  $T = 30^\circ\text{C}$ .

Table 1 (entries 2 and 4), respectively. The rate of polymerization (Figure 1) was first-order with respect to the concentration of monomer and the final conversion was close to 100%. The theoretical molecular weights were in very close agreement with  $M_{n,\text{GPC}}$  for the full range of monomer conversions, which indicates a quantitative initiation and an excellent control during the entire course of the polymerization (Figure S1). Interesting, for a  $\text{BMIM-PF}_6/\text{DMSO}$  ratio of 50/50 (Figure 1b, Table 1, entry 4), the kinetic data allowed us to

draw the same conclusions as the ones obtained for a ratio of 5/95. However, the reaction rate was 3× faster for the ratio 50/50 (6× faster than that obtained for pure DMSO, Table 1, entry 1). In order to determine the optimal ratio  $\text{BMIM-PF}_6/\text{DMSO}$  to afford fast polymerization while maintaining the living characteristics of the system, different ratios were investigated (Figure 2, Figure S2, Table 1, entries 1–6). Regardless the



**Figure 2.**  $k_p^{\text{app}}$  values of the SARA ATRP of MA catalyzed by  $\text{Na}_2\text{S}_2\text{O}_4/\text{CuBr}_2/\text{Me}_6\text{TREN}$  in  $\text{BMIM-PF}_6/\text{DMSO}$  mixtures for different contents of  $\text{BMIM-PF}_6$  in the reaction mixture. Conditions:  $[\text{MA}]_0/[\text{solvent}] = 2/1$  (v/v);  $[\text{MA}]_0/[\text{EBiB}]_0/[\text{Na}_2\text{S}_2\text{O}_4]_0/[\text{CuBr}_2]_0/[\text{Me}_6\text{TREN}]_0 = 222/1/1/0.1/0.1$  (molar);  $T = 30^\circ\text{C}$ .

solvent ratio studied the control over the SARA ATRP of MA was perfect ( $\bar{D}$  always below 1.07). Indeed, the only observed difference was the overall polymerization rate, which as referred above was faster for the ratio  $\text{DMSO}/\text{IL} = 50/50$ . It is interesting to note that this ratio represents an optimum value for the mixture, which suggests that there is a synergistic effect between the two solvents (Figure 2).

Considering the perfect miscibility of the  $\text{BMIM-PF}_6$  and DMSO for the different mixtures, it is believed that the polarity values of the mixture may play an important role in the kinetics of the polymerization. In this regard, it was reported that mixtures of  $\text{BMIM-PF}_6$  and tetraethylene glycol (TEG) exhibit unusual synergistic solvent effect, particularly a remarkable “hyperpolarity” for the mixture. In the presence of solvatochromic probes, as  $E_T(33)$ , polarity of the medium is always higher in the mixtures than in pure solvents reaching a maximum value for equimolar mixtures of the two solvents.<sup>24</sup>

Using this analogy, absorbance spectra of Reichardt’s dye (30) were collected in  $\text{BMIM-PF}_6/\text{DMSO}$  (Figure S3) mixtures, showing that value of  $E_T(30)$  for the different mixtures exceeds the value predicted by the simple mixture

**Table 1.** Kinetic Data for the SARA ATRP of MA in  $\text{BMIM-PF}_6/\text{DMSO}$  Mixtures<sup>a</sup>

entry	$\text{BMIM-PF}_6/\text{DMSO}$ ratio	targeted DP	$k_p^{\text{app}}$ ( $\text{h}^{-1}$ )	time (h)	conv. <sup>b</sup> (%)	$M_{n,\text{th}} \times 10^{-3b}$	$M_{n,\text{GPC}} \times 10^{-3b}$	$\bar{D}$
1	0/100	222	0.242	14	97	18.7	20.7	1.04
2	5/95	222	0.417	7.5	96	18.5	19.1	1.05
3	25/75	222	0.974	3.6	97	18.7	20.20	1.04
4	50/50	222	1.305	2.8	98	18.8	19.3	1.03
5	75/25	222	0.595	5.9	97	18.7	19.5	1.03
6	95/5	222	0.248	10.5	93	17.9	19.1	1.07
7	50/50	100	1.588	1.7	93	8.20	8.30	1.04
8	50/50	1100	0.053	23	58	56.1	51.2	1.04

<sup>a</sup>Conditions:  $[\text{MA}]_0/[\text{solvent}] = 2/1$  (v/v);  $[\text{MA}]_0/[\text{EBiB}]_0/[\text{Na}_2\text{S}_2\text{O}_4]_0/[\text{CuBr}_2]_0/[\text{Me}_6\text{TREN}]_0 = 222/1/1/0.1/0.1$ ;  $T = 30^\circ\text{C}$ . <sup>b</sup>Maximum monomer conversion obtained in the reaction.

indicating that some synergistic effect occurs. On the other hand, the kinetic data using tetrabutylammonium hexafluorophosphate (TBAPF<sub>6</sub>) was determined in order to evaluate if the previous results were due to the BMIM-PF<sub>6</sub> structure, or if the speed up effect could be mainly due to the anion (PF<sub>6</sub>). When the ratio TBAPF<sub>6</sub>/DMSO 6/94 (Figure S4) was used, the obtained  $k_p^{app}$  was 0.295 h<sup>-1</sup>, which is higher than using pure DMSO, but much lower than the value obtained for a mixture BMIM-PF<sub>6</sub>/DMSO 5/95.

The effect of the target molecular weight on the control over the polymerization is a critical parameter that should be evaluated, since it could lead to possible solubility issues of the polymer in the reaction mixture. Therefore, different targeted degrees of polymerization (DP) were investigated for the SARA ATRP of MA (Figure S5, Table 1, entries 4, 7, and 8) using a BMIM-PF<sub>6</sub>/DMSO ratio of 50/50. As expected, the polymerization rate was higher for lower DP values due to the higher number of growing radicals. It is worthwhile to mention that even for the highest DP = 1100, the PMA dispersity values remained very low ( $\bar{D} = 1.04$ ). Additionally, a 4-arm initiator was used to evaluate the potential of the polymerization method in the synthesis of 4-arm star PMA (Figure S6). The results obtained regarding the kinetic data were similar to the ones described for the monofunctional initiator (Figure S7). Again, the final dispersity obtained for the star-shaped PMA was very low ( $\bar{D} = 1.04$ ). On this matter, it should be mentioned that the GPC apparatus used is equipped with multidetectors (light scattering, viscosimeter and refractive index), which allows a very accurate determination of the molecular weights, without the use of common calibration curves.<sup>25</sup> Table 1 summarizes the kinetic data obtained for the SARA ATRP of MA in the presence of Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub>/CuBr<sub>2</sub>/Me<sub>6</sub>TREN in BMIM-PF<sub>6</sub>/DMSO mixtures at 30 °C. Independently of the BMIM-PF<sub>6</sub>/DMSO ratio used, the polymer architecture or the target molecular weight, the reported system allowed the synthesis of well-defined PMA at room temperature with very low dispersity ( $\bar{D} < 1.1$ ) below the reported values using the same IL.<sup>18</sup> The efficiency of initiation was always close 100%.

The level of control obtained under the different polymerization conditions investigated should be a direct consequence of three main aspects: high propagation rates; absence of side reactions, and fast reduction of Cu(II) species to Cu(I). On this matter, the use of IL is known to decrease the activation energy involved in the propagation steps due to high polarity.<sup>26</sup> The increase in the rate of polymerization was postulated based on a complex formation between the growing radicals and the IL.<sup>27</sup> The hypothesis was later confirmed by showing that when chiral IL were used more isotactic sequences were formed.<sup>21</sup> In contrast, the termination rate decreases<sup>18</sup> due to higher viscosity limiting the diffusion of radicals.<sup>26</sup> In order to evaluate the viscosity of the solvent mixture BMIM-PF<sub>6</sub>/DMSO, rheology tests were carried out (Figure S8). Indeed, it was observed that there was no relevant variation of the viscosity up to a ratio 50/50. However, for higher contents of BMIM-PF<sub>6</sub>, the increase of the viscosity was found exponential. These results show that the observed maximum rate of polymerization ( $k_p^{app}$ ) at 50/50 vol % composition of BMIM-PF<sub>6</sub>/DMSO cannot be simply explained solely based on viscosity changes and, hence, the  $k_p/k_t$  value increase. We believe that while IL favors  $k_p/k_t$  increase (well-known fact), the role of DMSO seems to be more complex. Besides the influence on the reduction rate of Cu(II) to Cu(I) (highest rate observed for

ratio 50/50, see Figure S9), the DMSO may also have an important role on the mechanism involving the radical generation. The data presented in this work suggests that the ideal balance of the different factors described is observed for a ratio 50/50. The clear understanding of the full mechanism requires additional studies.

The “living” nature of the PMA-Br synthesized by the reported method was confirmed by doing a chain extension experiment (Figure S10), showing the complete movement of the macroinitiator GPC ( $M_{n,GPC} = 6.9 \times 10^3$ ,  $\bar{D} = 1.05$ ) trace toward high molecular weight fractions. The chemical structure of the PMA-Br ( $M_{n,GPC} = 6.9 \times 10^3$ ,  $\bar{D} = 1.05$ ) synthesized by SARA ATRP in BMIM-PF<sub>6</sub>/DMSO = 50/50 was analyzed by and MALDI-TOF (Figures S11 and S12) and <sup>1</sup>H NMR spectroscopy (Figure S13). The results confirmed the expected structure and a high degree of chain-end functionality (92%).

In conclusion, a synergistic effect of BMIM-PF<sub>6</sub>/DMSO in the SARA ATRP of MA using Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub>/CuBr<sub>2</sub>/Me<sub>6</sub>TREN as the catalytic system is reported. The polymerization system allowed very fast polymerizations for a broad range of targeted molecular weights leading to polymers with very low dispersity values ( $\bar{D} < 1.1$ ).

## ■ ASSOCIATED CONTENT

### 📄 Supporting Information

Materials, techniques, procedures, kinetic data, PMA <sup>1</sup>H NMR spectrum, and MALDI-TOF data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

## ■ AUTHOR INFORMATION

### Corresponding Authors

\*E-mail: [tamazguliashvili@yahoo.com](mailto:tamazguliashvili@yahoo.com).

\*E-mail: [jcoelho@eq.uc.pt](mailto:jcoelho@eq.uc.pt).

### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

P.V.M. acknowledges FCT-MCTES for her Ph.D. scholarship (SFRH/BD/69152/2010). C.M.R.A. acknowledges FCT-MCTES for his Ph.D. scholarship (SFRH/BD/88528/2012). The authors acknowledge FCT-MCTES for funding (PTDC/EQU-EPR/098662/2008 and PTDC/EQU-EPR/114354/2009). The MALDI-TOF-MS data were obtained by Dr. Manuel Marcos Garcia and Dr. Paula Alvarez Chaver at Unidad de Espectrometria de Masas do Servicio de Determinación Estructural, Proteómica y Genómica, Centro de Apoyo Científico y Tecnológico a la Investigación (CACTI, University of Vigo, Spain). The <sup>1</sup>H NMR data were obtained at the Nuclear Magnetic Resonance Laboratory of the Coimbra Chemistry Centre (<http://www.nmrcc.uc.pt>), University of Coimbra, supported in part by Grant REEQ/481/QUI/2006 from FCT, POCI-2010 and FEDER, Portugal. A.V.P.'s research reported in this publication was supported by the National Center for Advancing Translational Sciences of the National Institutes of Health under Award No. UL1TR000003.

## ■ REFERENCES

- (1) Matyjaszewski, K. *Macromolecules* **2012**, *45* (10), 4015–4039.
- (2) Ouchi, M.; Terashima, T.; Sawamoto, M. *Chem. Rev.* **2009**, *109* (11), 4963–5050.
- (3) Mendonca, P. V.; Serra, A. C.; Coelho, J. F. J.; Popov, A. V.; Guliashvili, T. *Eur. Polym. J.* **2011**, *47* (7), 1460–1466.

- (4) Guliashvili, T.; Mendonça, P. V.; Serra, A. C.; Popov, A. V.; Coelho, J. F. J. *Chem.—Eur. J.* **2012**, *18* (15), 4607–4612.
- (5) Zhang, Y.; Wang, Y.; Matyjaszewski, K. *Macromolecules* **2011**, *44* (4), 683–685.
- (6) Jakubowski, W.; Min, K.; Matyjaszewski, K. *Macromolecules* **2005**, *39* (1), 39–45.
- (7) Abreu, C. M. R.; Mendonca, P. V.; Serra, A. C.; Coelho, J. F. J.; Popov, A. V.; Guliashvili, T. *Macromol. Chem. Phys.* **2012**, *213* (16), 1677–1687.
- (8) Cordeiro, R. A.; Rocha, N.; Mendes, J. P.; Matyjaszewski, K.; Guliashvili, T.; Serra, A. C.; Coelho, J. F. J. *Polym. Chem.* **2013**, *4* (10), 3088–3097.
- (9) Rocha, N.; Mendonca, P. V.; Mendes, J. P.; Simoes, P. N.; Popov, A. V.; Guliashvili, T.; Serra, A. C.; Coelho, J. F. J. *Macromol. Chem. Phys.* **2013**, *214* (1), 76–84.
- (10) Abreu, C. M. R.; Mendonca, P. V.; Serra, A. C.; Popov, A. V.; Matyjaszewski, K.; Guliashvili, T.; Coelho, J. F. J. *ACS Macro Lett.* **2012**, *1* (11), 1308–1311.
- (11) Abreu, C. M. R.; Serra, A. C.; Popov, A. V.; Matyjaszewski, K.; Guliashvili, T.; Coelho, J. F. J. *Polym. Chem.* **2013**, *4* (23), 5629–5636.
- (12) Gois, J. R.; Rocha, N.; Popov, A.; Guliashvili, T.; Matyjaszewski, K.; Serra, A. C.; Coelho, J. *Polym. Chem.* **2014**, *5* (12), 3919–3928.
- (13) Magenau, A. J. D.; Strandwitz, N. C.; Gennaro, A.; Matyjaszewski, K. *Science* **2011**, *332* (6025), 81–84.
- (14) G. Huddleston, J.; D. Rogers, R. *Chem. Commun.* **1998**, *16*, 1765–1766.
- (15) Wheeler, C.; West, K. N.; Liotta, C. L.; Eckert, C. A. *Chem. Commun.* **2001**, *10*, 887–888.
- (16) Erdmenger, T.; Guerrero-Sanchez, C.; Vitz, J.; Hoogenboom, R.; Schubert, U. S. *Chem. Soc. Rev.* **2010**, *39* (8), 3317–3333.
- (17) Carmichael, A. J.; Haddleton, D. M.; Bon, S. A. F.; Seddon, K. R. *Chem. Commun.* **2000**, *14*, 1237–1238.
- (18) Biedroń, T.; Kubisa, P. *Macromol. Rapid Commun.* **2001**, *22* (15), 1237–1242.
- (19) Sarbu, T.; Matyjaszewski, K. *Macromol. Chem. Phys.* **2001**, *202* (17), 3379–3391.
- (20) Percec, V.; Grigoras, C. J. *Polym. Sci., Part A: Polym. Chem.* **2005**, *43* (22), 5609–5619.
- (21) Biedroń, T.; Kubisa, P. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43* (15), 3454–3459.
- (22) Ma, H.; Wan, X.; Chen, X.; Zhou, Q.-F. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41* (1), 143–151.
- (23) Biedroń, T.; Kubisa, P. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40* (16), 2799–2809.
- (24) Sarkar, A.; Trivedi, S.; Baker, G. A.; Pandey, S. J. *Phys. Chem. B* **2008**, *112* (47), 14927–14936.
- (25) Coelho, J. F. J.; Gonçalves, P. M. F. O.; Miranda, D.; Gil, M. H. *Eur. Polym. J.* **2006**, *42* (4), 751–763.
- (26) Harrisson, S.; Mackenzie, S. R.; Haddleton, D. M. *Macromolecules* **2003**, *36* (14), 5072–5075.
- (27) Harrisson, S.; Mackenzie, S. R.; Haddleton, D. M. *Chem. Commun.* **2002**, *23*, 2850–2851.