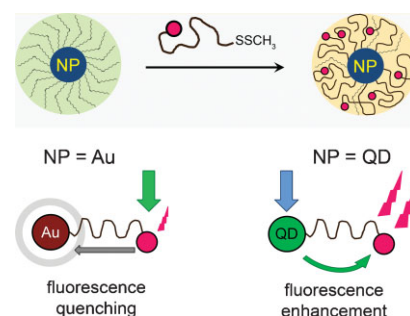


Hetero-Telechelic Dye-Labeled Polymer for Nanoparticle Decoration^a

Peter J. Roth, Ki-Se Kim, Su Hak Bae, Byeong-Hyeok Sohn, Patrick Theato,*
Rudolf Zentel*

The synthesis of poly(methyl methacrylate) (PMMA) exhibiting one fluorescent dye (Texas Red) and one methyl disulfide end group is described. It is shown that the latter end group enabled the exchange of both oleic amine on gold nanoparticles (AuNP) and of oleic acid on CdSe/ZnS quantum dots (QD), allowing for a phase transfer of both types of nanoparticles (NP) from hexane into dimethylformamide due to the solubility provided by the PMMA chains. For AuNP, a fluorescence quenching of the dye was found due to fluorescence resonance energy transfer (FRET) from the dye to the AuNP, while QDs caused a fluorescence enhancement by FRET from the QD to the attached dyes. Due to the hetero-telechelic geometry of the polymer, the separation between NP and dye is governed by the end-to-end distance of the polymer.



Introduction

Polymers are promising materials for nanoparticle (NP) surface modifications, as hybrid materials combining the solubility, processability, and functionality of the polymeric shells and the unique optical and electrical properties inherent to metal or semiconductor NP can be obtained.^[1,2] Gold NPs (AuNP) have an intense plasmon oscillation. Electronic excitation energy from a nearby molecule can be transferred to a AuNP, resulting for instance in the

fluorescence quenching of chromophores.^[3–5] Semiconductor NP [quantum dots (QD)] are used as biolabels^[2,6] and as energy donors in biological^[7] and optoelectronic^[8] research because of their high quantum yields, high photostability, and their narrow fine-tunable emission spectra. For both types of NP, there is a strong dependency of the energy transfer efficiency on the distance between NP and chromophore.^[4,9] Thus, there is a high scientific interest in fine-tuning this distance,^[10–14] both to gain further insights into transfer mechanisms deviating from the r^{-6} distance dependence^[5,15] and for applications such as (bio-) sensors^[16] or optical memory.^[17] Specific distances between dyes and a NP have especially been realized through DNA and protein spacers of a known size, requiring however, an elaborate micro-scale multistep synthesis, as the biomolecules need to be tailored with a fluorescent dye and need to have an appropriate binding site for NP attachment.^[6,7,11] Polymeric ligands have the advantages of functionalities such as anchor groups capable of coordinating to a NP surface, fluorescent dyes, or residues providing solubility being easily introduced along the backbone of a reactive polymer and of being available on a multi-gram scale.^[18,19] However, the average NP dye

P. J. Roth, P. Theato, R. Zentel
Institute of Organic Chemistry, University of Mainz,
Duesbergweg 10-14, 55099 Mainz, Germany
Fax: (+49) 6131 3924778; E-mail: theato@uni-mainz.de;
zentel@uni-mainz.de

P. J. Roth, K.-S. Kim, S. H. Bae, B.-H. Sohn
Department of Chemistry, NANO Systems Institute, Seoul
National University, 151-747 Korea

^a Supporting information for this article is available at the bottom of the article's abstract page, which can be accessed from the journal's homepage at <http://www.mrc-journal.de>, or from the author.

distance is ill-defined as both the dyes and the anchor groups are statistically distributed along each polymer chain. A straightforward polymer architecture giving rise to a well-defined NP dye distance would be a hetero-telechelic polymer with an anchor group at one end and a fluorescent dye at the other, with the polymer chain in between acting as a spacer with a known end-to-end distance.

Herein, we present the synthesis of such a polymer by reversible addition fragmentation chain transfer (RAFT) polymerization combining two recent methods for end group functionalization. RAFT polymerization produces polymers with a dithioester or trithiocarbonate ω -end group.^[20] Aminolysis of this group may yield a terminal thiol, capable of coordinating to a gold surface; however, side reactions occur with poly[(meth)acrylates].^[21] It was recently shown that addition of methyl methanethiosulfonate (MTS) to an aminolysis produces defined methyl disulfide end groups also on poly[(meth)acrylates]. The $\text{SS}-\text{CH}_3$ terminated polymers were well capable of attaching to a planar gold surface and could also stabilize AuNP.^[22] For the present purpose, the use of MTS for ω -end group modification was combined with an activated pentafluorophenyl (PFP) ester α -end group,^[23] to produce a poly[methyl methacrylate] (PMMA) carrying the fluorescent dye Texas Red (TR) and a $\text{SS}-\text{CH}_3$ moiety as end group, in a one pot reaction. Apart from presenting a simple but

effective route to hetero-telechelic polymers, we further exploit the use of terminal $\text{SS}-\text{CH}_3$ groups in tethering fluorescent dyes to both metal and semiconductor NP through ligand exchange and observing the effects of each type of NP onto the dye.

Experimental Part

Oleic Acid Stabilized CdSe/ZnS Quantum Dots (3b)

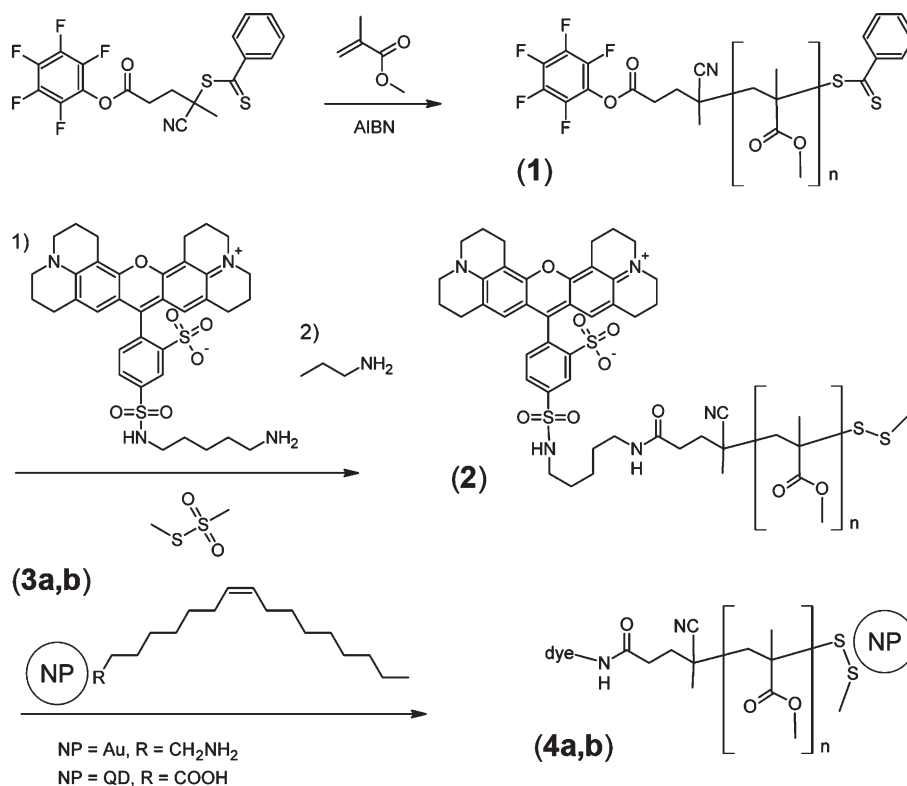
Oleic Acid stabilized CdSe/ZnS quantum dots with an emission maximum of 534 nm were courteously provided by Professor K. Char and coworkers (SNU, Korea).^[24]

α -Pentafluorophenyl, ω -Dithioester Poly(methyl methacrylate) (1)

α -Pentafluorophenyl, ω -dithioester poly(methyl methacrylate) was synthesized as previously reported.^[23] \overline{M}_n [(Gel permeation chromatography (GPC))] = 9 800 g · mol⁻¹, PDI (GPC) = 1.14.

α -Texas Red, ω -Methyl Disulfide Poly(methyl methacrylate) (2)

α -Pentafluorophenyl, ω -dithioester poly(methyl methacrylate) **1** [25.5 mg (2.6 μmol)] was dissolved in 50 μL of dry chloroform and



Scheme 1. RAFT polymerization of methyl methacrylate using a PFP activated ester functionalized chain transfer agent, synthesis of α -PFP, ω -methyl disulfide poly(methyl methacrylate) and its use in modifying OA-AuNP or OA-QD through ligand exchange.

300 μL of dry DMF. MTS [4.92 μL (52 μmol)] was added, followed by 1.477 mg (2.1 μmol) of TR Cadaverine and 1.32 μL (9.5 μmol) of triethylamine. The mixture was stirred at 35 $^{\circ}\text{C}$ for 16 h and 2.14 μL (26 μmol) of *n*-propylamine was then added. Stirring was continued at room temperature for 24 h. The polymer was precipitated into cold methanol three times and removed by centrifugation each time. After drying, 18.7 mg (73%) of a dark violet solid was obtained. UV-Vis: $\lambda_{\text{max}} = 580 \text{ nm}$; \overline{M}_n (GPC) = 12 200 $\text{g} \cdot \text{mol}^{-1}$; PDI = 1.13; amount of dye labeling: 74% (for details, please see Supporting Information).

For synthesis of oleyl amine stabilized AuNPs (OA-Au, **3a**); modification of AuNPs **3a** with polymer **2** (Au-TR, **4a**) and modification of QD **3b** with polymer **2** (QD-TR, **4b**) (please see Supporting Information).

Results and Discussion

The synthesis of the α , ω functionalized polymer **2** is outlined in Scheme 1. RAFT polymerization employing a PFP functionalized chain transfer agent afforded the α -PFP, ω -dithioester PMMA **1**. As the PFP ester reacts faster with amines than the dithioester, after the addition of an excess of MTS, 0.81 equiv. of TR Cadaverine was added first. As several polymer chains would be attached to each NP, it was not necessary that every single chain be dye-functionalized, thus less than 1 equiv. of TR was used and a functionality of 74% was obtained. After 16 h, an excess of *n*-propylamine was added in order to aminolyze both the remaining PFP esters and to set free the terminal thiols on the other end group which could then react with the MTS reagent. GPC using a UV-Vis detector set to the absorbance maximum of the dye (580 nm) showed that the dye had been attached to the polymer and that repeated precipitation had successfully removed any loose dye (Figure 1a). The apparent molecular weight of polymer **2** was higher than expected from polymer **1**, because of a modified coil conformation in the presence of the two new end groups.^[22] The polydispersity of polymer **2** did, however, not increase and no peak nor shoulder of double molecular weight appeared, indicating that no side reactions such as formation of polymer-polymer disulfides had occurred. The ability of the polymer to coordinate to a gold surface was confirmed by a surface plasmon resonance (SPR) measurement, indicating that the methyl disulfide had also successfully been introduced into the polymer (Figure 1b). The end-to-end distance of TR-PMMA-SSMe **2** was calculated to be 7.1 nm (for details, please see Supporting Information).

As phosphine oxides usually bind very strongly to the QD surface, we employed QD stabilized with oleic acid (OA-QD) ($6.2 \pm 1.0 \text{ nm}$ diameter) which allowed for an easier ligand substitution with thiols or disulfides.^[24] In order to also facilitate ligand exchange on AuNP, those stabilized with oleic amine (OA-Au) ($3.9 \pm 0.8 \text{ nm}$ diameter) were chosen over thiol stabilized AuNP. The NP modification is outlined

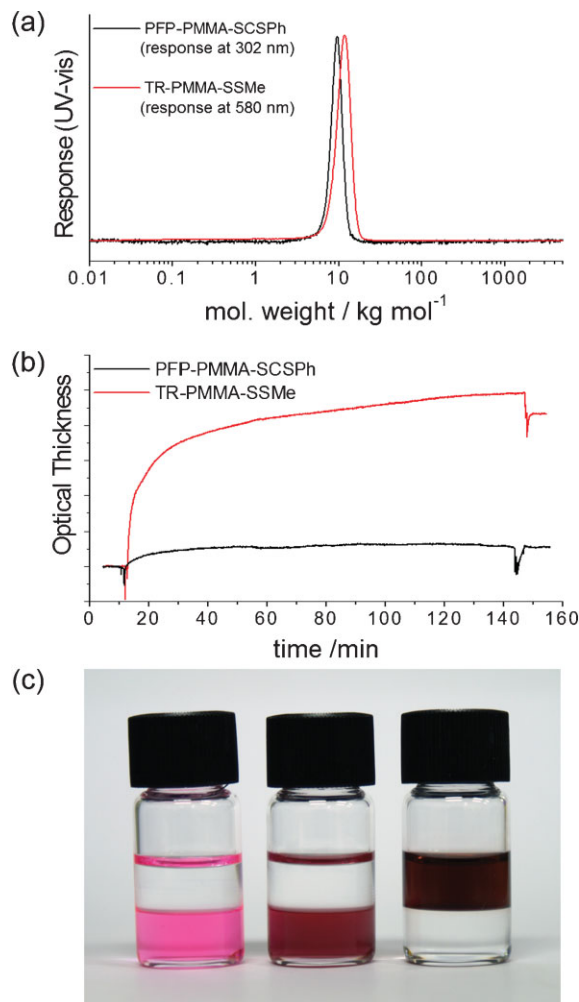


Figure 1. (a) Gel permeation chromatograms of the starting polymer **1** (black curve), recorded with a UV-Vis detector set to 302 nm (maximum absorbance of dithioester end group) and of the product polymer **2** (red curve, UV-Vis detector at 580 nm; absorbance maximum of dye end group). As the polymer itself has no absorbance at this wavelength, this data suggests that the dye is attached to the polymer and that any (low molecular weight), loose dye was successfully removed. (b) SPR measurements of polymers **1** (black line) and **2** (red line). Whereas the dithioester terminated polymer showed only a light nonspecific adsorption corresponding to a thickness of 0.47 nm, the methyl disulfide terminated polymer examined under the same conditions could build up a stable self-assembled monolayer of 3.68 nm thickness. Measurements were performed in ethyl acetate with a concentration of 0.4 $\text{mg} \cdot \text{mL}^{-1}$ and a refractive index of 1.5 was assumed for both polymers. (c) Photograph of two-phase mixtures of hexane (upper phase) and DMF (lower phase). The vials contain: TR-PMMA-SSMe **2** (left), hybrid Au-PMMA-TR **4a** with DMF soluble AuNP (middle), and OA-AuNP **3a** soluble in hexane (right).

in Scheme 1. Briefly, polymer **2** and either OA-Au **3a** or OA-QD **3b** were combined in a good solvent (toluene or chloroform), stirred overnight, and evaporated to dryness. For workup, a two-phase system consisting of hexane and

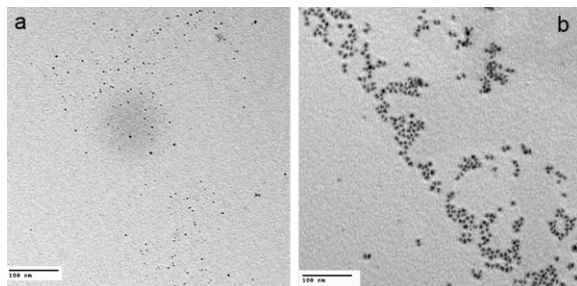


Figure 2. TEM images of (a) DMF soluble AuNP decorated with the dye labeled polymer **2** and (b) DMF soluble QD decorated with the dye labeled polymer **2**. Scale bars: 100 nm.

DMF was employed for both types of NP. While both OA-Au and OA-QD are soluble in hexane, polymer **2** is not. It could transfer the NP into DMF as seen from the color of the DMF phases (see Figure 1c and Supporting Information). Also, TEM images showed the presence of nonaggregated, nonripened NP in both DMF phases, accounting for a successful ligand exchange with the terminal methyl disulfide groups (Figure 2). Both NP dispersions could be passed through a 200 nm filter without product loss, indicating that no large agglomerates were present. In addition to the polymer functionalized NPs, which were transferred into the DMF phase, in both the case of AuNP and of QD, two side products were found. Trace amounts of NP remained in the hexane phases. Here, none or only an insufficient ligand exchange had taken place. Also, in both cases some material became insoluble in both phases and precipitated. Here, a partial ligand exchange could be assumed that provided solubility in neither phase. For AuNP, 32% of total Au was lost to these side reactions, while 10% of QD were not included in the hybrid material. As not all NP could be sufficiently functionalized with polymer, it could be assumed that the polymer was the limiting reagent and that the amount of dye not connected to a NP in the products was low.

The hybrid materials were further characterized by UV-Vis and fluorescence spectroscopy. Au-PMMA-TR **4a** showed an absorbance matching a calculated sum of 100% of the starting polymer **2** and 68% of OA-Au **3a** fed into the reaction, proposing the composition of **4a** (Figure 3b). In addition, a light band broadening of the dye caused by the near metal sphere occurred. The photoluminescence measurements shown in Figure 3c were measured (i) directly after mixing polymer **2** and OA-Au **3a** together in toluene, and (ii) from purified **4a** after re-dispersion into toluene. This last sample (ii) con-

tained the same amount of dye but only 68% of AuNP. The emission from TR in **4a** was decreased by a factor of 1.75 compared to the emission before the reaction. When the lower AuNP absorbance, which allowed for a higher dye excitation in sample **4a**, was taken into account, an emission decrease by a factor of 2.22 could be estimated (for details, please see Supporting Information). This suggested that fluorescence resonance energy transfer (FRET) from the dye molecules to the AuNP was occurring, as was expected concerning the polymer dimensions (Figure 3a). It also showed that the polymer was indeed attached to the AuNP, as otherwise there would have been no influence of the NP on the dye. For QD-TR **4b**, three samples of PMMA-TR **2**, OA-QD **3b**, and QD-TR **4b**, having the same dye and QD concentrations were prepared. The absorbances are shown in Figure 3e. Due to the influence of the NP core and the different local environment, the dye experienced a blue-shift. Exciting the three samples at 400 nm gave rise to the emission plots shown in Figure 3f. The expected effects were found (Figure 3d): The emission of the dye was increased by about factor of 2.5. On the other hand, QD emission in the hybrid material was decreased drastically, as energy was transferred nonradiatively. Again, the influence of the QD on the dye showed that the polymer was attached to the QD, tethering the chromophores to their surface. From the spectroscopic data, an average distance between QD and dyes could be estimated to be 6.4 nm, following the Förster formalism (for details, please see Supporting Information). This value is in good agreement with the end-to-end distance of the polymer as obtained by light scattering (7.1 nm) and

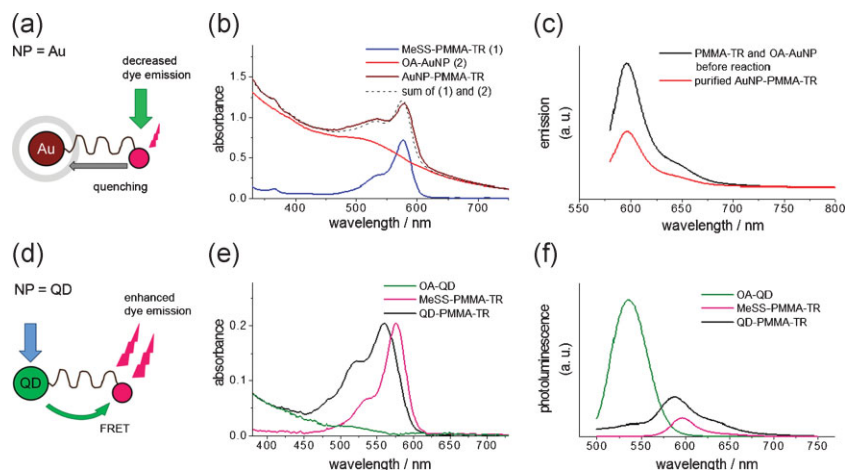


Figure 3. (a) Scheme illustrating the effect of the nearby Au core on the emission of the dye. (b) UV-Vis absorbance of polymer **2**, OA-AuNP **3a**, Au-TR **4a**, and the calculated sum of the former two curves. (c) Photoluminescence (excitation at 560 nm) of OA-AuNP **3a** mixed together with polymer **2** (before ligand exchange) and Au-TR **4a** after reaction, purification, and re-dispersion into toluene. (d) Scheme illustrating the effect of the nearby QD on the emission of the dye. (e) UV-Vis absorbance of samples of polymer **2**, OA-QD **3b** and QD-TR **4b** with the same dye and QD concentrations. (f) Photoluminescence (excitation at 400 nm) of the same samples as in figure (d).

suggested that the polymer coils were spacing the dyes from the NP surface. Dispersions of the composites were stable for several months without aggregation or precipitation occurring.

Conclusion

A simple one-pot synthesis of a hetero-telechelic polymer with fluorescent dye and methyl disulfide end groups was described. Each part of this product fulfilled a certain job; while the methyl disulfide end group enabled the attachment onto planar gold, AuNP or semiconductor NP, the dye at the other end group could be used to probe local electronic effects caused by the NP. In addition, the polymer chain kept its end groups at a known distance and provided solubility of the encapsulated NP. Although the surface chemistry and the workup for both types of NP proceeded very similarly, the physical effects of the different cores on the dye molecules were quite contrary. While the dyes acted as energy donors for a nearby AuNP, the same core-shell configuration using QD gave the dyes the role of energy acceptor. The architectural setup allows creating hybrid materials with a tunable distance between NP and dyes, as it depends on the polymer end-to-end distance which may easily be determined using conventional methods. Taking into account, that “smart” polymers may change their end-to-end distance on demand through external stimuli, more sophisticated setups become thinkable; experiments are in progress and will be published soon.

Acknowledgements: The authors gratefully acknowledge financial support from the *International Research and Training Group* (IRTG 1404) funded by the *DFG*. The authors thank *Kookheon Char* and *Wan Ki Bae* for providing the quantum dots and *Karl Fischer* for help with end-to-end distance calculation.

Received: April 16, 2009; Revised: May 8, 2009; Accepted: May 11, 2009; DOI: 10.1002/marc.200900254

Keywords: end group; fluorescence resonance energy transfer (FRET); nanoparticles; polymer; reversible addition fragmentation chain transfer (RAFT)

- [1] X. Zhao, X. Ding, Z. Zheng, Y. Peng, C. Tian, J. Wang, X. Long, *Huaxue Jinzhan* **2005**, *17*, 847.
- [2] A. F. E. Hezinger, J. Teßmar, A. Göpferich, *Eur. J. Pharm. Biopharm.* **2008**, *68*, 138.
- [3] E. Dulkeith, A. C. Morteani, T. Niedereichholz, T. A. Klar, J. Feldmann, S. A. Levi, F. C. J. M. van Veggel, D. N. Reinhoudt, M. Möller, D. I. Gittins, *Phys. Rev. Lett.* **2002**, *89*, 203002.
- [4] K. E. Sapsford, L. Berti, I. L. Medintz, *Angew. Chem., Int. Ed.* **2006**, *45*, 4562.
- [5] C. S. Yun, A. Javier, T. Jennings, M. Fisher, S. Hira, S. Peterson, B. Hopkins, N. O. Reich, G. F. Strouse, *J. Am. Chem. Soc.* **2005**, *127*, 3115.
- [6] I. L. Medintz, H. Tetsuo, H. T. Uyeda, E. R. Goldmann, H. Mattoussi, *Nat. Mater.* **2005**, *4*, 435.
- [7] A. R. Clapp, I. L. Medintz, H. Mattoussi, *Chem. Phys. Chem.* **2006**, *7*, 47.
- [8] W. U. Huynh, J. J. Dittmer, A. P. Alivisatos, *Science* **2002**, *295*, 2425.
- [9] J. R. Lakowicz, *Anal. Biochem.* **2005**, *337*, 171.
- [10] S. Saini, G. Srinivas, B. Bagchi, *J. Phys. Chem. B* **2009**, *113*, 1817.
- [11] E. Dulkeith, M. Ringler, T. A. Klar, J. Feldmann, A. M. Javier, W. J. Parak, *Nano Lett.* **2005**, *5*, 585.
- [12] S. H. Bae, S. I. Yoo, W. K. Bae, S. Lee, J.-K. Lee, B.-H. Sohn, *Chem. Mater.* **2008**, *20*, 4185.
- [13] G. Schneider, G. Decher, N. Nerambourg, R. Praho, M. H. V. Werts, M. Blanchard-Desce, *Nano Lett.* **2006**, *6*, 530.
- [14] H. Imahori, Y. Kashiwagi, Y. Endo, T. Hanada, Y. Nishimura, I. Yamazaki, Y. Araki, O. Ito, S. Fukuzumi, *Langmuir* **2004**, *20*, 73.
- [15] S. Bhowmick, S. Saini, V. B. Shenoy, B. Bagchi, *J. Chem. Phys.* **2006**, *125*, 181102.
- [16] D. J. Maxwell, J. R. Taylor, S. M. Nie, *J. Am. Chem. Soc.* **2002**, *124*, 9606.
- [17] X. Li, J. W. M. Chon, R. A. Evans, M. Gu, *Appl. Phys. Lett.* **2008**, *92*, 063309.
- [18] I. Potapova, R. Mruk, C. Hübner, R. Zentel, T. Basché, A. Mews, *Angew. Chem., Int. Ed.* **2005**, *44*, 2437.
- [19] M. T. Fernández-Argüelles, A. Yakovlev, R. A. Sperling, C. Luccardini, S. Gaillard, A. Sanz Medel, J.-M. Mallet, J.-C. Brochon, A. Feltz, M. Oheim, W. J. Parak, *Nano Lett.* **2007**, *7*, 2613.
- [20] J. Chiefari, Y. K. Chong, F. Ercole, J. Krstina, J. Jeffery, T. P. T. Le, R. T. A. Mayadunne, G. F. Meijs, C. L. Moad, G. Moad, E. Rizzardo, S. H. Thang, *Macromolecules* **1998**, *31*, 5559.
- [21] J. Xu, J. He, D. Fan, X. Wang, Y. Yang, *Macromolecules* **2006**, *39*, 8616.
- [22] [22a] P. J. Roth, D. Kessler, R. Zentel, P. Theato, *Macromolecules* **2008**, *41*, 8316; [22b] P. J. Roth, D. Kessler, R. Zentel, P. Theato, *J. Polym. Sci. A* **2009**, *47*, 3118.
- [23] P. J. Roth, K. T. Wiss, R. Zentel, P. Theato, *Macromolecules*, **2008**, *41*, 8513.
- [24] W. K. Bae, K. Char, H. Hur, S. Lee, *Chem. Mater.* **2008**, *20*, 531.