ACS Macro Letters
Letter
pubs.acs.org/macroletters

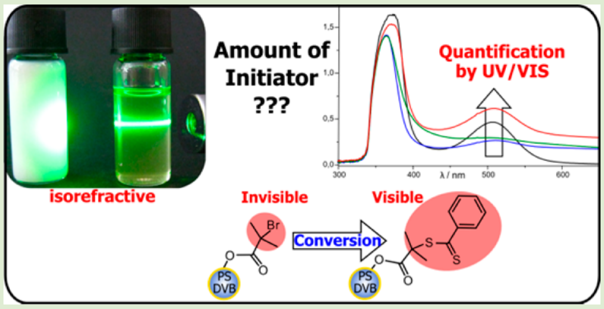
Convenient Quantification of Accessible Surface-Attached ATRP Initiators and RAFT Chain Transfer Agents on Cross-Linked Polystyrene Nanoparticles

Markus Mazurowski, Markus Gallei,* and Matthias Rehahn

Ernst-Berl Institute for Chemical Engineering and Macromolecular Science, Darmstadt University of Technology, Petersenstraße 22, D-64287 Darmstadt, Germany

Supporting Information

ABSTRACT: The exact quantification of surface-attached initiators for grafting-from radical polymerization on micro- and nanoparticles is still a challenging task. Here we demonstrate that, by combining UV/vis spectroscopy and an efficient derivatization protocol, the originally nearly invisible ATRP initiators and RAFT chain transfer agent entities can be quantified easily and precisely. Application of an isorefractive dispersion medium for the nanoparticles moreover provides reliable information about the amount of chemically really "accessible" surface-grafted initiators, that is, those that are not hidden in the particle's shell interior. To qualify the developed procedure further, nanoparticles of different grafting densities were generated, and the values determined afterward for the initiator concentration were in good agreement with expectations.



In recent years, nanoparticles attract more and more attention due to their high potential in applications ranging from material sciences to medicine such as electronics, biomedical, pharmaceutical, optics, and catalysis.[1−9] Surface-modification of both inorganic and organic particles leads to tunable spheres with core/shell structures that allow, for example, improvement of established materials as well as development of basically new systems.[10,11] Since the pioneering work of Prucker and Rühe,[12,13] who grafted silica nanoparticles with polystyrene (PS) by a free radical process, many further methodologies came up for so-called surface-initiated polymerization strategies. The "grafting from" approach has the main advantage over the "grafting onto" method in generating remarkably higher grafting densities of surface-anchored polymer chains on the solid substrate.[14−18] All above controlled radical polymerization strategies such as atom transfer radical polymerization (ATRP) and the reversible addition−fragmentation chain transfer (RAFT) processes seem to be the most promising routes for decorating particles with high grafting densities resulting in polymer brushes.[14,16,19−25] By these methods, surfaces of particles have furthermore been modified with stimuli-responsive polymers leading to so-called "smart surfaces".[10,26,27] Especially the surface-grafting of cross-linked polymeric microspheres leads to very interesting materials with a wide range of potential applications.[9,28−30] Recently, Barner-Kowollik et al. highlighted scope and limitations in polymeric microparticle science.[31]

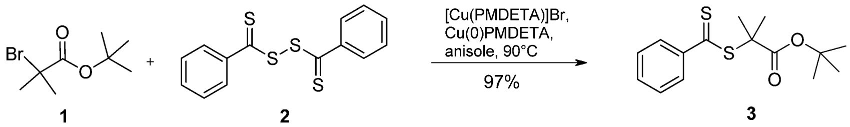
Crucial information for all mentioned methods is the number of surface-attached initiator molecules whose amount plays an important role regarding the polymerization mechanism itself, which was carefully investigated by Vancso et al.[32] For silica nanoparticles Prucker and Rühe,[12,13] and Böttcher et al.[33] reported that TGA is a reliable method to determine the amount of surface-attached initiator. Other analytical tools for an estimation are based on elemental analysis,[17,34,35] attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR),[36] X-ray photoelectron spectroscopy (XPS),[37] solid-state NMR,[38] or calorimetric methods.[37,39] For functional groups such as acids or bases attached to the particle surface also potentiometry and conductometry are applicable.[40] More sensitive and emerging are methods based on colorimetry and fluorometry.[41,42] Benefits in that direction and direct comparison with before mentioned analytical tools were carried out by Resch-Genger et al.[43,44]

Knowing the amount of functional groups on the particle surface however does not necessarily mean to know the amount of so-called "accessible" initiator for a polymerization. Initiators may be somehow hidden in an inner part of the functional shell of the particles and are therefore not available for surface-initiated polymerization strategies especially in the case of high grafting densities. It should be emphasized that the term "accessibility" of initiator sites intrinsically cannot be defined precisely but depends strongly on the size of the approaching molecules (substrate) and the molecular and local environment. Among others, pore sizes and swelling capability of the particle surface are crucial parameters.[43]

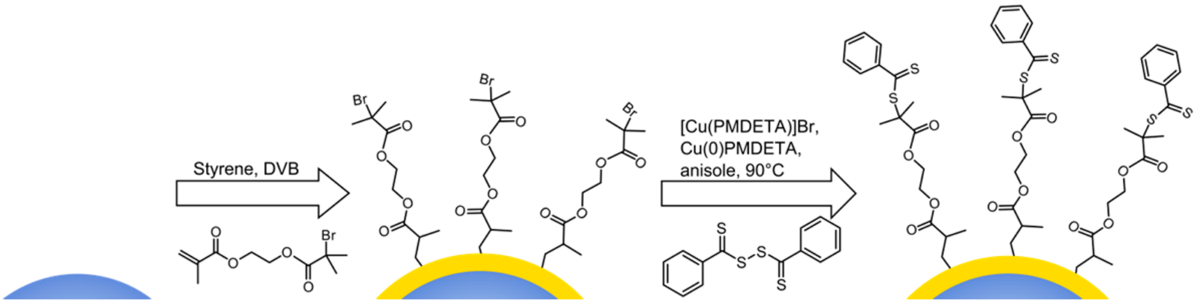
Received: October 9, 2012
Accepted: November 6, 2012
Published: November 9, 2012

dx.doi.org/10.1021/mz300523y | *ACS Macro Lett.* 2012, 1, 1362−1366

Scheme 1. Model Reaction for the Conversion of ATRP-Initiator 1 into Chromophore 3 in Approximately Quantitative Yield



Scheme 2. Functionalization of Cross-Linked PS Nanoparticles with ATRP Initiator and Conversion into Surface-Attached Chromophore



Herein, we report a convenient experimental verification of the areal densities for chemically accessible ATRP initiator functionalities on cross-linked PS microsphere surfaces without use of sophisticated laboratory equipment. Different amounts of surface-attached ATRP initiators were quantitatively converted into functional groups, which have remarkably higher UV/vis absorption. The amount of converted ATRP initiators can be precisely determined using UV/vis spectroscopy in an isorefractive solvent for PS microspheres so that no undesirable particle scattering takes place. This method seems to be a general, feasible and fast tool for surface initiator quantification, and to the best of our knowledge, this route has not been reported before.

It is known that commonly used ATRP initiators like alkylhalides can be quantitatively converted into the corresponding RAFT termini when treated with bis(thiobenzoyl) disulfide (BTBD) in the presence of ATRP-active copper complexes.[45] Boyes et al. reported that even for ATRP initiators and ATRP chain ends anchored to silicon wafers this conversion into the corresponding RAFT termini is a powerful tool for, for example, the synthesis of homo- and block copolymers.[46,47] Matyjaszewski et al. reported an even higher efficiency for the ATRP initiator conversion into a RAFT reagent.[45] Exchange of ATRP by RAFT initiator functionalities, however, seemed not only useful for chain-growth via sequential monomer addition protocols, but also may offer a new opportunity to convert the spectroscopically nearly ‘invisible’ bromide or chloride ATRP functionalities into much better UV/vis-detectable RAFT moieties. Thus, we first valuated this concept by means of the model reaction of 2-(2-bromoisobutyryloxy)ethyl methacrylate **1** as ATRP-inimer with BTBD **2** (Scheme 1). The conversion indeed led to chain-transfer agent **3** in essentially quantitative yield (97%) when carried out in homogeneous solution. Therefore, the ATRP-inimer was synthesized as described elsewhere,[48] and BTBD **2** was easily obtained following the reaction sequence described by Sanderson et al.[49]

After finding appropriate conditions for nearly quantitative conversion of initiator functionality **1** into chromophore **3**, the efforts have been expanded to organic particle surface functionalization. Cross-linked PS nanoparticles were synthesized via seeded emulsion polymerization leading to narrowly distributed particles with an average diameter of 50 and 93 nm, respectively. Bare particles were functionalized with ATRP-inimer **4** (Scheme 2), which could be obtained by esterification with hydroxyethyl methacrylate (HEMA) according to literature.[48]

Four different grafting densities were generated for the ATRP-inimer on the PS nanoparticle shell by a modified protocol of the method reported by Morbidelli et al.[15] After completed PS seed latex synthesis, a mixture of the ATRP-inimer, divinylbenzene and styrene were added. This method allows selective variation of the surface-attached ATRP initiator grafting density by varying the initiator to styrene ratio. The initiator density can be calculated from the initiator concentration, c_{ini}, the average diameter of the particle, d_{particle}, the density of the particle core, $\rho(\text{PS})$, and the Avogadro constant, N_A, by using eq 1:

$$\sigma\left(\frac{N}{A(\text{particle})}\right) = \frac{c_{\text{ini}} \cdot N_A \cdot \rho(\text{PS}) \cdot d_{\text{particle}}}{6}\ (\text{nm}^{-2}) \qquad (1)$$

Initiator concentration, c_{ini}, indicates the molar amount of initiator in relation to the weight amount of the PS particles. The amount of ATRP initiator, N, per particle shell area, A, was chosen to be in a range where either mushroom-like polymers, semidiluted polymers, or polymer brushes should be obtained in a standard surface-initiated ATRP protocol.[19,50] Additionally, a quite high concentration of initiator in the particle shell was generated in a fourth sample to identify the upper density limit of accessible initiator molecules by conversion with BTBD **2**. Hence, calculated grafting densities were realized in the range of 0.30 to 2.51 nm^{-2} and were directly compared with the experimental values obtained by the method described in the following (Table 1).

TEM images of the purified functionalized particles (Figure 1, right) clearly indicate the newly formed shells, which tend to form agglomerates in the course of the drying process of the samples, in contrast to the bare PS particles (Figure 1, left).

In the next step, four samples of ATRP initiator functionalized PS nanoparticles were converted with BTBD **2** to quantify the respective grafting density that can be realized by the chemically “accessible” initiator moieties (Scheme 2). Thus, the particles were treated with equimolar amounts of BTBD **2**,

Table 1. Comparison of the Amount of Initiator on the Particles with Chromophore Amount on the Particle Surface

entry	d_{particle} (nm)	c_{ini} (mmol g^{-1})	c_{chromo} (mmol g^{-1})	calculated initiator density (nm^{-2})	chromophore density (nm^{-2})
PS1	50	0.186	0.220	1.05	1.14
PS2	50	0.393	0.365	2.51	1.93
PS3	95	0.110	0.120	1.18	1.21
PS4	95	0.030	0.030	0.31	0.34

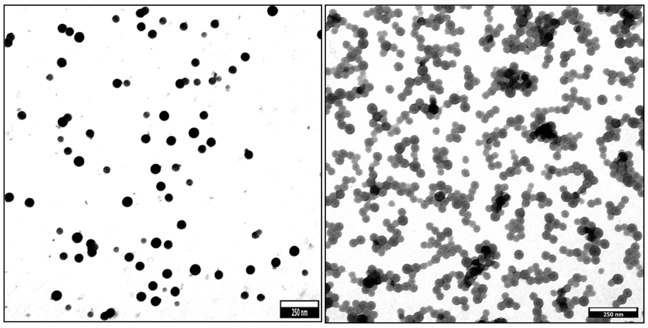


Figure 1. TEM image of the bare PS particle sample via the drop-cast method of their water dispersion on carbon-coated copper grids (left) and TEM image of ATRP-inimer functionalized particles drop-casted in the same way from their toluene dispersion (right).

assuming 100% accessibility of surface-attached initiators under ATRP conditions to ensure as quantitative conversion as possible. After repeated dispersing of the particles in THF followed by ultracentrifugation and precipitation in methanol, the concentration of chromophore groups immobilized on the particle surface was determined using UV/vis spectroscopy. For these measurements an isorefractive dispersion medium was needed, which allows UV/vis absorption measurements in the heterogeneous systems free of interfering particle scattering. When 2-ethylnaphthalene was used as the dispersion medium, which is isorefractive with the PS cores, the dispersion appeared without any haze (Figure 2).[51] In dependency of the amount of surface-attached BTBD, the dispersion appears gradually pink. Of course, after conversion, these newly generated functionalities can also be used for surface-initiated RAFT polymerization of, for example, styrene or methyl methacrylate from the particles.

Figure 2. Dispersion of PS nanoparticles with surface-attached chromophore BTBD in THF (left) and the same particles as clear dispersion in isorefractive 2-ethylnaphthalene (right) illustrated with a commercial green laser pointer.

The recorded UV/vis absorption spectra indicated lack of any particle scattering induced by mesoscalic heterogeneity of the systems. For quantification of the converted initiator functionalities we determined the molar extinction coefficient, ε, of model chromophore **2** in homogeneous solution of 2-ethylnaphthalene (Figure S2 in Supporting Information). Based on this value, a very precise quantification of the concentration of surface-attached functional groups proved to be possible for the particle dispersions as well. Corresponding UV/vis spectra are illustrated in Figure 3.

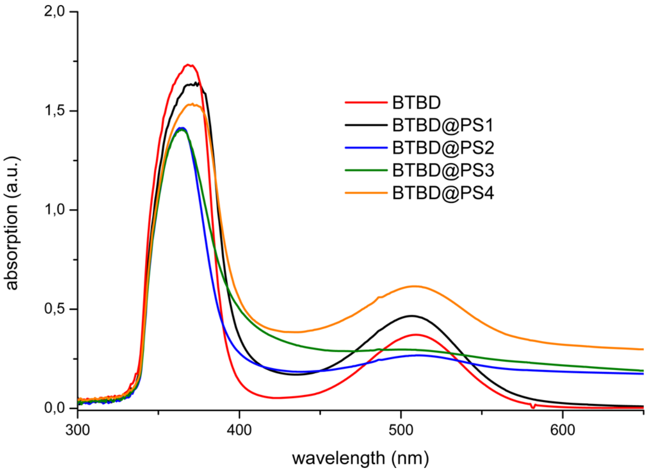


Figure 3. UV/vis-spectra of chromophore BTBD, **2**, and of different chromophore-labeled PS nanoparticles in 2-ethylnaphthalene.

By assuming identical values of the molar extinction coefficient in solution and for the surface-anchored chromophore, the chromophore concentration, c_{chromo}, can easily be obtained. The molar amount of chromophore per weight amount of particles can be determined by the absorbance, E, of chromophore-bearing particles from dispersion with a known mass concentration, c_w, by using eq 2, where d_{cuv} is defined as the thickness of the cuvette used:

$$c_{\text{chromo}} = \frac{E}{\varepsilon \cdot d_{\text{cuv}} \cdot c_w} \ (\text{mol g}^{-1}) \tag{2}$$

It was found that the density of chemically accessible ATRP initiator groups on the nanoparticle surface was in very good agreement with calculated values for the amount of initiator for three synthesized samples. The results are summarized and directly compared in Table 1. There the theoretically calculated amount of ATRP initiator is given as "calculated initiator density" and the experimentally determined amount of surface-attached BTBD as "chromophore density".

The thus obtained theoretical and experimental values of the grafting densities are in a very good agreement, thereby underlining the excellent reliability of the methodology. Nevertheless, a significant gap between the calculated initiator density and the value determinated using UV/vis spectroscopy is evident for sample PS2, the sample with highest content of ATRP initiator in the shell. The "missing" amount, which seems to be somehow "inaccessible" for BTBD conversion, is assumed to be hidden within the surface shell. Moreover, it can be assumed that these "hidden" ATRP initiator entities will not react in surface-initiated ATRP. The value of the grafting density of about 1.93 nm^{-2} can thus be considered as an upper limit for initiation of a monomer with comparable hydrodynamic volume as BTBD on the surface of particles with 50 nm average diameter. Thus, the information about initiator densities obtained from the above functionalization approach should be even more relevant for estimating the "true" grafting density than just an overall determination of bromine groups estimated by, for example, elemental analysis or rather inaccurate TGA measurements.

In conclusion, a novel and convenient method for quantification of surface-attached initiators on organic particles for ATRP and/or RAFT processes has been developed. Narrowly distributed cross-linked polystyrene nanoparticles have been used as model systems. They have been synthesized via seeded emulsion polymerization and functionalized with four different amounts of surface-immobilized ATRP initiators. The only weakly UV/vis light absorbing ATRP initiator molecules were quantitatively converted into remarkably better absorbing RAFT chromophores. By using an isorefractive solvent for PS microspheres and measuring the absorbance we could successfully quantify the amount of chemically accessible surface-attached RAFT initiators, which is supposed to be the true value for surface-attached initiators really active in controlled polymerization reactions. We envisage that the method developed here is applicable to many other particle/initiator systems and delivers precise results fast and easily. This method can be furthermore utilized to quantify precisely the amount of UV/vis-detectable polymers attached to surfaces.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Additional data, general experimental data, instrumentation setup, description for conversion of the ATRP-initiator (model reaction), ^{1}H NMR and ^{13}C NMR of converted ATRP-initiator (Figure S1), synthesis of PS latexes, description for immobilization of ATRP-inimer on PS particles surface (Table S1), description for conversion of surface-attached ATRP-initiator, UV/vis spectra of BTBD **2** in 2-ethylnaphthalene, and determination of molar extinction coefficient (Figure S2). This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: m.gallei@mc.tu-darmstadt.de.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

M.G. wants to thank the Landesoffensive zur Entwicklung Wissenschaftlich-ökonomischer Exzellenz (LOEWE Soft Control) for financial support of this work. M.M. wants to thank the Deutsche Forschungsgemeinschaft DFG-SPP 1369 (Interfaces and Interphases) for financial support.

■ REFERENCES

(1) Chaudhuri, R.; Paria, S. *Chem. Rev.* **2012**, *112*, 2373.
(2) Caruso, F. *Adv. Mater.* **2001**, *13*, 11.
(3) Ohno, K. *Polym. Chem.* **2010**, *1*, 1545.
(4) Giannelis, E. P. *Appl. Organometal. Chem.* **1998**, *12*, 675.
(5) Jankiewicz, B. J.; Jamiola, D.; Choma, J.; Jaroniec, M. *Adv. Colloid Interface Sci.* **2012**, *170*, 28.
(6) Alexandre, M.; Dubois, P. *Mater. Sci. Eng.* **2000**, *28*, 1.
(7) Yamanaka, J.; Murai, M.; Iwayama, Y.; Yonese, M.; Ito, K.; Sawada, T. *J. Am. Chem. Soc.* **2004**, *126*, 7156.
(8) Bockstaller, M. R.; Thomas, E. L. *J. Phys. Chem. B* **2003**, *107*, 10017.
(9) Ishizu, K.; Amir, I.; Okamoto, N.; Uchida, S.; Ozawa, M.; Chen, H. *J. Colloid Interface Sci.* **2011**, *353*, 69.
(10) Ballauff, M. *Macromol. Chem. Phys.* **2003**, *204*, 220.
(11) Ho, K. M.; Li, W. Y.; Wong, C. H.; Li, P. *Colloid Polym. Sci.* **2010**, *288*, 1503.
(12) Prucker, O.; Rühe, J. *Macromolecules* **1998**, *31*, 602.
(13) Prucker, O.; Rühe, J. *Macromolecules* **1998**, *14*, 6893.
(14) Barbey, R.; Lavanant, L.; Paripovic, D.; Schüwer, N.; Sugnaux, C.; Tugulu, S.; Klok, H.-A. *Chem. Rev.* **2009**, *109*, 5437.
(15) Mittal, V.; Matsko, N. B.; Butte, A.; Morbidelli, M. *Polymer* **2007**, *48*, 2806.
(16) Ye, P.; Dong, H.; Zhong, M.; Matyjaszewski, K. *Macromolecules* **2011**, *44*, 2253.
(17) Chakkalakal, G. L.; Alexandre, M.; Abetz, C.; Boschetti-de-Fierro, A.; Abetz, V. *Macromol. Chem. Phys.* **2012**, *213*, 513.
(18) Haase, A.; Hesse, P.; Brommer, L.; Jacobs, O.; Abetz, C.; Handge, U. A.; Boschetti-de-Fierro, A.; Abetz, V. *Macromol. Mater. Eng.* **2012**, DOI: 10.1002/mame.201200041.
(19) Brittain, W. J.; Minko, S. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 3505.
(20) Matyjaszewski, K.; Tsarevsky, N. V. *Nat. Chem.* **2009**, *1*, 276.
(21) Boyes, S. G.; Brittain, W. J.; Weng, X.; Cheng, S. Z. D. *Macromolecules* **2002**, *35*, 4960.
(22) D'Agosto, F.; Charreyre, M.; Pichot, C.; Gilbert, R. G. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 1188.
(23) You, Y.-Z.; Hong, C.-Y.; Pan, C.-Y.; Wang, P.-H. *Adv. Mater.* **2004**, *16*, 1953.
(24) Min, K.; Gao, H.; Yoon, J. A.; Wu, W.; Kowalewski, T.; Matyjaszewski, K. *Macromolecules* **2009**, *42*, 1597.
(25) Maillard, D.; Kumar, S. K.; Rungta, A.; Benicewicz, B. C.; Prud'homme, R. E. *Nano Lett.* **2011**, *11*, 4569.
(26) Ballauff, M.; Lu, Y. *Polymer* **2007**, *48*, 1815.
(27) Ni, C.; Wang, W.; Zhu, C.; Huang, B.; Yao, B. *Soft Mater.* **2010**, *8*, 14.
(28) Zheng, G.; Stöver, H. D. H. *Macromolecules* **2002**, *35*, 6828.
(29) Barner, L. *Adv. Mater.* **2009**, *21*, 2547.
(30) Bayramoglu, G.; Karagoz, B.; Altintas, B.; Arica, M. Y.; Bicak, N. *Bioprocess. Biosyst. Eng.* **2011**, *34*, 735.
(31) Goldmann, A. S.; Barner, L.; Kaupp, M.; Vogt, A. P.; Barner-Kowollik, C. *Prog. Polym. Sci.* **2012**, *37*, 975.
(32) Benetti, E. M.; Reimhult, E.; Bruin, J. d.; Zapotoczny, S.; Textor, M.; Vancso, G. J. *Macromolecules* **2009**, *42*, 1640.
(33) Böttcher, H.; Hallensleben, M. L.; Nuß, S.; Wurm, H. *Polym. Bull.* **2000**, *44*, 223.
(34) Nordborg, A.; Lim, F.; Shchukarev, A.; Irgum, K. *J. Sep. Sci.* **2008**, *31*, 2143.
(35) Kaupp, M.; Vogt, A. P.; Natterodt, J. C.; Trouillet, V.; Gruendling, T.; Hofe, T.; Barner, L.; Barner-Kowollik, C. *Polym. Chem.* **2012**, *3*, 2605.
(36) Nebhani, L.; Sinnwell, S.; Inglis, A. J.; Stenzel, M. H.; Barner-Kowollik, C.; Barner, L. *Macromol. Rapid Commun.* **2008**, *29*, 1431.
(37) Goldmann, A. S.; Walther, A.; Nebhani, L.; Joso, R.; Ernst, D.; Loos, K.; Barner-Kowollik, C.; Barner, L.; Müller, A. H. E. *Macromolecules* **2009**, *42*, 3707.
(38) Gaborieau, M.; Nebhani, L.; Graf, R.; Barner, L.; Barner-Kowollik, C. *Macromolecules* **2010**, *43*, 3868.
(39) Barish, J. A.; Goddard, J. M. *J. Appl. Polym. Sci.* **2011**, *120*, 2863.
(40) Hoare, T.; Pelton, R. *Langmuir* **2004**, *20*, 2123.
(41) Rödiger, S.; Ruhland, M.; Schmidt, C.; Schröder, C.; Grossmann, K.; Böhm, A.; Nitschke, J.; Berger, I.; Schimke, I.; Schierack, P. *Anal. Chem.* **2011**, *83*, 3379.
(42) Hennig, A.; Hoffmann, A.; Borcherding, H.; Thiele, T.; Schedler, U.; Resch-Genger, U. *Anal. Chem.* **2011**, *83*, 4970.
(43) Hennig, A.; Borcherding, H.; Jaeger, C.; Hatami, S.; Würth, C.; Hoffmann, A.; Hoffmann, K.; Thiele, T.; Schedler, U.; Resch-Genger, U. *J. Am. Chem. Soc.* **2012**, *134*, 8268.

(44) Hennig, A.; Hoffmann, A.; Borcherding, H.; Thiele, T.; Schedler, U.; Resch-Genger, U. *Chem. Commun.* **2011**, *47*, 7842.
(45) Kwak, Y.; Nicolay, R.; Matyjaszewski, K. *Macromolecules* **2009**, *42*, 3738.
(46) Rowe-Konopacki, M. D.; Boyes, S. G. *Macromolecules* **2007**, *40*, 879.
(47) Rowe, M. D.; Hammer, B. A. G.; Boyes, S. G. *Macromolecules* **2008**, *41*, 4147.
(48) Matyjaszewski, K.; Gaynor, S. G.; Kulfan, A.; Podwika, M. *Macromolecules* **1997**, *30*, 5192.
(49) Vosloo, J. J.; Wet-Roos, D. D.; Tonge, M. P.; Sanderson, R. D. *Macromolecules* **2002**, *35*, 4894.
(50) Zhao, B.; Brittain, W. J. *Prog. Polym. Sci.* **2000**, *25*, 677.
(51) Eckert, T.; Bartsch, E. *Phys. Rev. Lett.* **2002**, *89*, 125701.