A Method for Obtaining Defined End Groups of Polymethacrylates Prepared by the RAFT Process during Aminolysis

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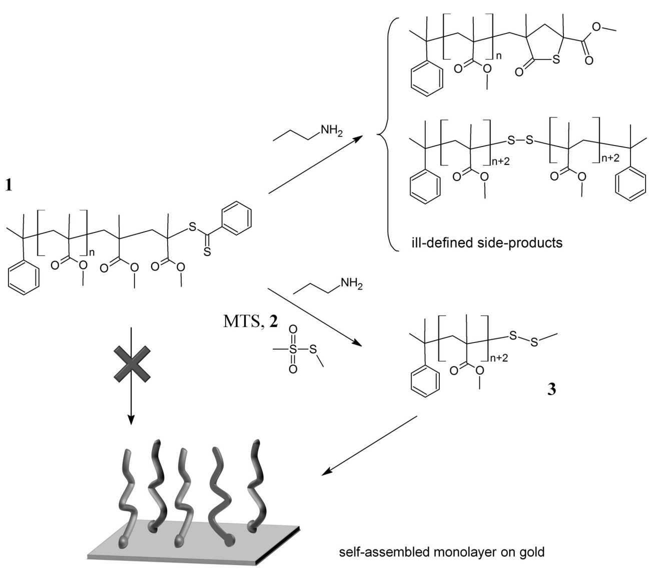
Reversible addition–fragmentation chain transfer (RAFT) polymerization[1] is a very versatile controlled radical polymerization technique. The use of thiocarbonylthio chain transfer agents (CTAs) yields polymers terminated with a dithioester, which is sensitive toward radicals, nucleophiles, temperature, and reducing agents. Thus, many postpolymerization methods may be employed to modify this dithioester end group. By thermolysis or reduction[2,3] the dithioester group may be removed, whereas treatment with an excess of a diazo compound allows for the introduction of functional end groups.[4,5] Very popular is the aminolysis of the dithioester end group; however, the products of this procedure depend very much on the chemical structure of the polymer. Polystyrene derivatives and poly[(meth)acrylamides] yield terminal thiols (or symmetrical disulfides if oxygen is present).[6–12] These end groups are particularly interesting for producing self-assembled monolayers (SAMs) on gold surfaces[13,14] which find applications in biochemistry,[15–17] catalysis,[18,19] nanotechnology,[20] and microelectronics.[21–24] Further, thiol-terminated polystyrene,[25] polystyrene derivatives,[6] and several poly[(meth)acrylamides][6–8] have been used to encapsulate gold nanocrystals, and thiol-terminated poly[(meth)acrylamides] have been used for end-group modifications[9,10] and fluorescent labeling.[11,12] Poly[(meth)acrylates], however, suffer from the great drawback that the aminolysis affords the desired terminal thiol only in low yields.[26–28] It has been reported that reduced polymers with an H end group, a double molecular weight material even in the absence of oxygen,[26,27] and other ill-defined products[26] are produced. Quantitative analysis of a thiol end group such as with Ellman's reagent[9] is only rarely presented. Xu et al.[28] investigated the aminolysis of polymethacrylates in the absence of oxygen in greater detail, providing evidence that the resulting polymer bears a terminal thiolactone, which is obtained by backbiting of an initially formed thiol into the penultimate monomer unit. Although being a defined polymer end group, this thiolactone cannot be employed for conjugation or for surface modifications, very much in contrast to a thiol end group. Also, the native dithioester end groups have been investigated for adsorbing onto a gold surface by Duwez et al.;[29] however, they could only obtain a grafting density of 0.013 chains/nm^2, which is very low compared to the literature values for terminal thiols grafted to gold nanoparticles such as 0.94 chains/nm^2 for polystyrene[30] or 1.8–3.6 chains/nm^2 for poly[*N*-isopropylacrylamide].[8]

In this Communication we investigate the effect of methyl methanethiosulfonate (MTS, **2**) during the aminolysis reaction of polymethacrylates that have been prepared by RAFT polymerization with the goal of producing a defined polymethacrylate end group capable of producing a dense SAM on a gold surface. MTS reacts quickly and selectively with thiols to yield the respective methyl disulfides. Amines increase the hydrolyzation rate but do not attack the sulfur atoms themselves. Thus, methanethiosulfonates have found intensive use in selective[31] labeling of cysteine groups for the determination of structure and function of ion channel,[32] receptor,[33] and membrane[34] proteins. We expect thiols that are released by aminolysis from the polymer dithioester end group also to react with MTS and to prefer this reaction over the competing reactions of thiolactone formation and oxidation to symmetrical polymer–polymer disulfides by oxygen.

Scheme 1. Overview of Aminolysis Products of PMMA



As a model compound we synthesized a short poly(methyl methacrylate) (PMMA) (**1**) ($M_n = 3900$ g/mol, $M_w/M_n = 1.08$) using cumyl dithiobenzoate as chain transfer agent.[35] First, we subjected it to 10 equiv of *n*-propylamine in THF in the presence of oxygen.[36] After 3.5 h the pink color had vanished, and a gel permeation chromatography (GPC) analysis showed a bimodal product distribution (see Figure 1a,b), probably composed of a thiolactone and a polymer–polymer disulfide caused by oxygen

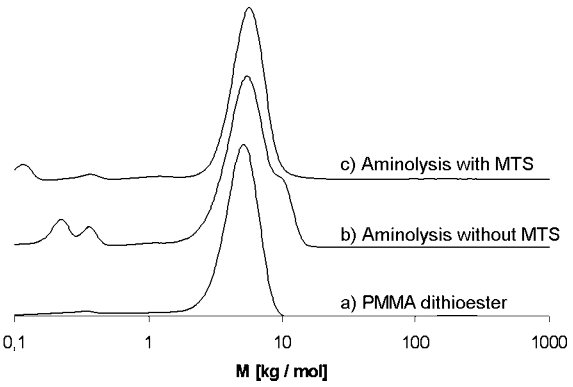


Figure 1. Gel permeation chromatograms of PMMA (a) with dithioester end group (**1**), (b) aminolyzed with 10 equiv of *n*-propylamine without inert atmosphere, and (c) aminolyzed with 10 equiv of *n*-propylamine after addition of 20 equiv of MTS without inert atmosphere (**3**).

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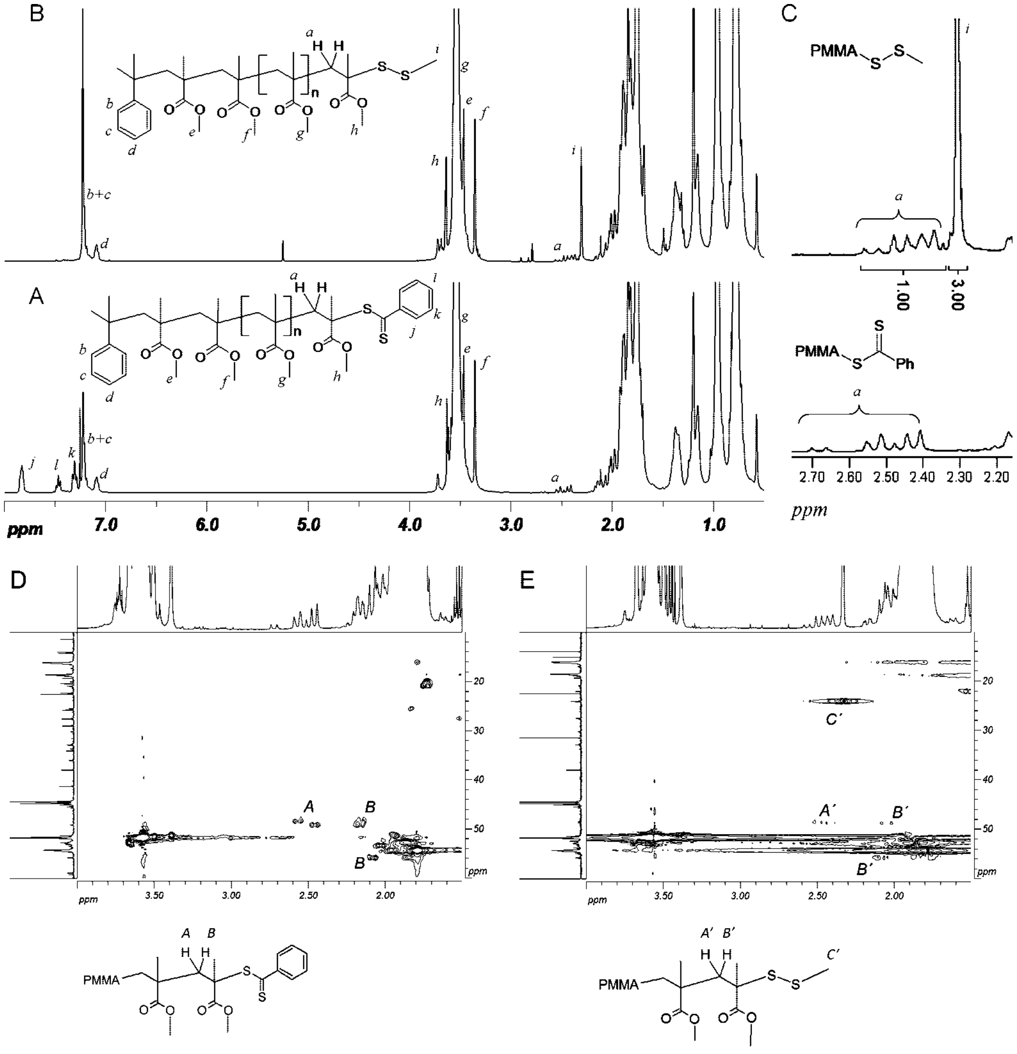

Figure 2. 400 MHz ^{1}H NMR spectra (CDCl$_3$, internal signal at 7.24 ppm used as reference) of (A) the starting PMMA with dithioester end group (**1**) and (B) the product of aminolysis with MTS (**3**). Part C is an enlarged region showing the single proton denoted *a* and the methyl end group with integrals. HSQC spectra of polymer **1** (D) and polymer **3** (E) show the shift of the methylene protons denoted *A* and *B* and the appearance of the distinct signal of the terminal methyl group.

oxidation (see upper part of Scheme 1). A polystyrene with M_n = 1170 g/mol aminolyzed under the same conditions completely transformed into the double molecular weight material,[35] suggesting that the oxygen concentration was sufficient for complete disulfide formation. An aminolysis of PMMA was repeated under the same conditions, except that 20 equiv of MTS was added.[37] The resulting polymer (**3**) was then analyzed by GPC, UV−vis spectroscopy, and NMR. The GPC peak of **3** (Figure 1c) had the same shape and position as the signal of the starting PMMA (**1**) (Figure 1a). No peak of double molecular weight was found, suggesting that thiols formed by aminolysis found a more preferable reaction pathway than being oxidized although oxygen was present. The pink dithioester color had vanished from the MTS aminolysis reaction after 3.5 h, and the precipitated polymer was colorless. UV−vis measurements showed that the characteristic dithioester absorbance peak centered at 302 nm had completely vanished for the polymer that was treated with amine and MTS.[35] ^{1}H, ^{13}C, and HSQC-NMR spectra were measured of both the reactant (**1**) and the product (**3**) polymers and are shown in Figure 2. The ^{1}H NMR spectrum of **1** (Figure 2A) showed exactly the same signals as discussed in detail in the literature,[28] and we could attribute the peaks accordingly. Both end groups were clearly visible in the ^{1}H NMR. The aromatic signals of the cumyl α-group, (denoted *b*, *c*, *d*) appeared in the spectra of both polymer **1** and polymer **3** (see parts A and B of Figure 2, respectively), whereas the three distinct signals of the dithiobenzoate *ω*-end-group (labeled *j*, *k*, *l*) vanished completely after amine/MTS treatment. Most interesting was a single methylene proton signal of the ultimate monomer unit (denoted *a* in Figure 2), which gave rise to a set of signals at 2.40−2.70 ppm well detached from the rest of the methylene group resonances. All signals of this proton were shifted upfield to 2.35−2.58 ppm due to the end-group conversion. The terminal methyl group of polymer **3** (denoted *i* in Figure 2B) gave rise to a broad singlet positioned at 2.31 ppm. By comparison of the integrals of the single backbone hydrogen (1 H) and the terminal methyl group (3 H), a quantitative end-group conversion can be assumed within the accuracy of the NMR evaluation (Figure 2C). Further evidence of the complete transformation could be obtained from ^{13}C and HSQC NMR measurements. The latter are shown in Figure 2D (polymer **1**) and Figure 2E (polymer **3**). The shift of the ultimate methylene group protons *A* and *B* through the MTS/amine reaction can be seen as well as the appearance of the SSCH$_3$ group signal. For reference, interpreted ^{13}C NMR spectra of both polymers are given in the Supporting Information.

Organic disulfides are very stable in air, toward water, toward nucleophiles, and bind strongly to gold surfaces forming the

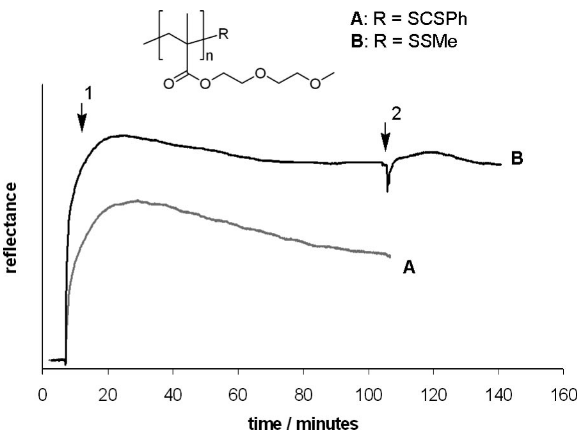

Figure 3. Reflectance vs time from SPR measurements of the starting poly[diethylene glycol monomethyl ether methacrylate] (PDEGMA) with dithioester end group (curve A) and of PDEGMA with methyl disulfide end group (curve B). Both samples were measured in 0.1 mg/mL ethanol solution. Position 1 marks the injection of solutions into the cell. Layer thicknesses before position 2 were 1.93 nm (A) and 3.23 nm (B). At position 2 the surface was washed with pure ethanol; after washing the self-assembled PDEGMA-$SSCH_3$ film had a thickness of 3.22 nm. Layer thicknesses were calculated using $\varepsilon_{\text{real}} = 2.25$ for all organic layers.

SAMs as the corresponding thiols.[38] We expected that the methyl disulfide-terminated polymer would show a stronger affinity toward gold surfaces and would therefore result in better SAMs than the dithioester-terminated polymers. We compared the self-assembly of polymers that differed only by their end group (dithioester vs methyl disulfide) on a gold surface by surface plasmon resonance (SPR) measurements. PMMAs **1** and **3** were measured in 0.1 mg/mL ethyl acetate solution. We also prepared a set of poly(ethylene glycol monomethyl ether methacrylate) (PDEGMA)[39] ($M_n = 5900$ g/mol, $M_w/M_n = 1.09$) exhibiting dithioester and methyl disulfide termini[35] and compared their self-assembly behavior on gold surfaces by SPR using ethanol as solvent. The results are shown in Figure 3. After an initial overshoot, which was probably caused by chains adsorbing onto the surface and then rearranging into a denser, more ordered packing, the $SSCH_3$-terminated PDEGMA reached a reflectance plateau, implying that a stable SAM had been formed. Washing with pure solvent could not remove the adsorbed polymers. The dithioester-terminated polymer also adsorbed onto the gold surface; however, after an overshoot the reflectance showed a steady decrease, suggesting that the polymer desorbed from the surface again and no dense SAM was formed.[29] Similar results were obtained for PMMAs **1** and **3**.[35] SAMs from asymmetric disulfides are known to phase separate upon annealing by S−S bond cleavage,[40] and we therefore analyzed both PDEGMA-$SSCH_3$ and PMMA-$SSCH_3$ covered surfaces by AFM before and after annealing them at 100 °C for 8 h. The measurements revealed a smooth polymer coverage and no influence of annealing for both PMMA and PDEGMA.[35] It is likely that only PMMA-sulfyl groups remained attached to the gold surface with methyl thiols or methyl disulfides being desorbing into the solution again, similar to the results discussed for asymmetric disulfides in the literature,[38] thus producing the same monolayer that would have been obtained from a theoretical PMMA-SH. We also used the disulfide-terminated PMMA to prepare polymer encapsulated gold nanoparticles using a two-phase reduction of auric acid in the presence of PMMA-$SSCH_3$,[41] resulting in particles of 5 ± 2 nm diameter, which were characterized by UV−vis and TEM.[35]

In conclusion, we presented a simple modification of the aminolysis of polymethacrylates prepared by the RAFT process overcoming the problems of thiolactone and side product formation. The method uses the high reactivity of methyl methanethiosulfonate toward thiols, thus favoring methyl disulfide formation even in the presence of oxygen. The transformed disulfide end group showed a higher affinity toward a gold surface than the dithioester end group and could successfully be employed for encapsulation of gold nanoparticles. This method enables polymethacrylates to be grafted onto metal surfaces and also opens new routes to end-group functionalization of RAFT polymers.

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Supporting Information Available: Experimental details for the synthesis of PMMA, PDEGMA, and polystyrene with dithioester termini, GPC analysis of polystyrene aminolysis with and without MTS, UV−vis data following the disappearance of the dithioester absorbance with amine/MTS treatment, ^{13}C NMR spectra of PMMA with SCSPh and $SSCH_3$ end groups, SPR data of PMMA with $SSCH_3$ and SCSPh end groups adsorbing onto a gold surface, AFM images of PMMA-$SSCH_3$ and PDEGMA-$SSCH_3$ covered surfaces before and after annealing and experimental details, and UV−vis absorbance and TEM images of gold nanoparticles obtained from PMMA-$SSCH_3$. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Chiefari, J.; Chong, Y. K.; Ercole, F.; Krstina, J.; Jeffery, J.; Le, T. P. T.; Mayadunne, R. T. A.; Meijs, G. F.; Moad, C. L.; Moad, G.; Rizzardo, E.; Thang, S. H. *Macromolecules* **1998**, *31*, 5559.

(2) Postma, A.; Davis, T. P.; Evans, R. A.; Li, G.; Moad, G.; O'Shea, M. S. *Macromolecules* **2006**, *39*, 5293–5306.

(3) Moad, G.; Chong, Y. K.; Postma, A.; Rizzardo, E.; Thang, S. H. *Polymer* **2005**, *46*, 8458–8468.

(4) Perrier, S.; Takolpuckdee, P.; Mars, C. A. *Macromolecules* **2005**, *38*, 2033–2036.

(5) Roth, P. J.; Wiss, K.; Zentel, R.; Theato, P. *Macromolecules*, accepted.

(6) Lowe, A. B.; Sumerlin, B. S.; Donovan, M. S.; McCormick, C. L. *J. Am. Chem. Soc.* **2002**, *124*, 11562–11563.

(7) Zhu, M.-Q.; Wang, L.-Q.; Exarhos, G. J.; Li, A. D. Q. *J. Am. Chem. Soc.* **2004**, *126*, 2656–2657.

(8) Shan, J.; Nuopponen, M.; Jiang, H.; Kauppinen, E.; Tenhu, H. *Macromolecules* **2003**, *36*, 4526–4533.

(9) Qiu, X.-P.; Winnik, F. M. *Macromol. Rapid Commun.* **2006**, *27*, 1648–1653.

(10) Li, M.; De, P.; Gondi, S. R.; Sumerlin, B. S. *J. Polym. Sci., Part A* **2008**, *46*, 5093–5100.

(11) York, A. W.; Scales, C. W.; Huang, F.; McCormick, C. L. *Biomacromolecules* **2007**, *8*, 2337–2341.

(12) Scales, C. W.; Convertine, A. J.; McCormick, C. L. *Biomacromolecules* **2006**, *7*, 1389–1392.

(13) Sumerlin, B. S.; Lowe, A. B.; Stroud, P. A.; Zhang, P.; Urban, M. W.; McCormick, C. L. *Langmuir* **2003**, *19*, 5559–5562.

(14) Ulman, A. *Chem. Rev.* **1996**, *96*, 1533.

(15) de la Fuente, J.; Barrientos, A. G.; Rojas, T. C.; Canada, J.; Fernandez, A.; Penades, S. *Angew. Chem., Int. Ed.* **2001**, *40*, 2257.

(16) Cao, Y.-W.; Jin, R.; Mirkin, C. A. *J. Am. Chem. Soc.* **2001**, *123*, 7961.

(17) Li, Z.; Jin, R.; Mirkin, C. A.; Letsinger, R. L. *Nucleic Acids Res.* **2002**, *30*, 1558.

(18) Zhao, M.; Crooks, R. M. *Angew. Chem., Int. Ed.* **1999**, *38*, 364.

(19) Zhao, M.; Crooks, R. M. *Adv. Mater.* **1999**, *11*, 217.

(20) Love, J. C.; Estroff, L. A.; Kriebel, J. K.; Nuzzo, R. G.; Whitesides, G. M. *Chem. Rev.* **2005**, *105*, 1103–1169.

(21) Miller, C.; Cuendet, P.; Grätzel, M. *J. Phys. Chem.* **1991**, *95*, 877–886.

(22) Kim, T.; Crooks, R. M.; Tsen, M.; Sun, L. *J. Am. Chem. Soc.* **1995**, *117*, 3963–3967.

(23) Osifchin, R. G.; Andres, R. P.; Henderson, J. I.; Kubiak, C. P.; Dominey, R. N. *Nanotechnology* **1996**, *7*, 412.

(24) Sato, T.; Ahmed, H.; Brown, D.; Johnson, B. F. G. *Appl. Phys.* **1997**, *82*, 696.

(25) Corbierre, M. K.; Cameron, N. S.; Sutton, M.; Mochrie, S. G. J.; Lurio, L. B.; Rühm, A.; Lennox, R. B. *J. Am. Chem. Soc.* **2001**, *123*, 10411–10412.

(26) Lima, V.; Jiang, X.; Brokken-Zijp, J.; Schoenmakers, P. J.; Klumperman, B.; Van der Linde, R. *J. Polym. Sci., Part A* **2005**, *43*, 959–973.

(27) Patton, D. L.; Mulling, M.; Fulghum, T.; Advincula, R. C. *Macromolecules* **2005**, *38*, 8597–8602.

(28) Xu, J.; He, J.; Fan, D.; Wang, X.; Yang, Y. *Macromolecules* **2006**, *39*, 8616–8624.

(29) Duwez, A.-S.; Guillet, P.; Colard, C.; Gohy, J.-F.; Fustin, C.-A. *Macromolecules* **2006**, *39*, 2729–2731.

(30) Corbierre, M. K.; Cameron, N. S.; Lennox, R. B. *Langmuir* **2004**, *20*, 2867–2073.

(31) Smith, D. J.; Maggio, E. T.; Kenyon, G. L. *Biochemistry* **1975**, *14*, 766–771.

(32) Akabas, M. H.; Stauffer, D. A.; Xu, M.; Karlin, A. *Science* **1992**, *258*, 307–310.

(33) (a) Xu, M.; Akabas, M. H. *J. Gen. Physiol.* **1996**, *107*, 195–205. (b) Kuner, T.; Wollmuth, L. P.; Karlin, A.; Seeburg, P.; Sakmann, B. *Neuron* **1996**, *17*, 343–352. (c) Ramirez-Latorre, J.; Yu, C. R.; Qu, X.; Perin, F.; Karlin, A.; Role, L. *Nature (London)* **1996**, *380*, 347–351.

(34) Chen, J.-G.; Liu-Chen, S. G.; Rudnick, G. *Biochemistry* **1997**, *36*, 1479–1486.

(35) See Supporting Information for details.

(36) To a 6 mM solution of 3.9K PMMA-dithioester (**1**) in THF 10 equiv of *n*-propylamine was added, and the mixture was stirred at room temperature for 3.5 h. No inert atmosphere was used. The polymer was precipitated from methanol several times to completely remove low molecular weight substances.

(37) To a 6 mM solution of 3.9K cumyl-PMMA-dithioester (**1**) in THF 20 equiv of MTS (**2**) was added and after 1 min 10 equiv of *n*-propylamine was added, and the mixture was stirred at room temperature for 3.5 h. No inert atmosphere was used. The polymer was precipitated from methanol several times to completely remove low molecular weight substances.

(38) Heister, K.; Allara, D. L.; Bahnk, K.; Frey, S.; Zharnikov, M.; Grunze, M. *Langmuir* **1999**, *15*, 5440–5443.

(39) Lutz, J.-F. *J. Polym. Sci., Part A* **2008**, *46*, 3459–3470.

(40) Ishida, T.; Yamamoto, S.; Mizutani, W.; Motomatsu, M.; Tokumoto, H.; Hokari, H.; Azehara, H.; Fujihira, M. *Langmuir* **1997**, *13*, 3261–3265.

(41) Roth, P. J.; Theato, P. *Chem. Mater.* **2008**, *20*, 1614–1621.

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