Synthesis of Reactive Telechelic Polymers Based on Pentafluorophenyl Esters

Peter J. Roth, Kerstin T. Wiss, Rudolf Zentel, and Patrick Theato*

Institute of Organic Chemistry, University of Mainz, Duesbergweg 10-14, 55099 Mainz, Germany

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ABSTRACT: A diazo initiator and a chain transfer agent (CTA), both containing a pentafluorophenyl (PFP) activated ester, were synthesized. In a RAFT polymerization using the functionalized chain transfer agent (PFP-CTA), methyl methacrylate (MMA), diethylene glycol monomethyl ether methacrylate (DEGMA), poly(ethylene glycol) monomethyl ether methacrylate (PEGMA), and lauryl methacrylate (LMA) could successfully be polymerized into homopolymers and diblock copolymers with good control over molecular weight, very high conversions, and narrow molecular weight distributions. Polymers derived from the PFP−CTA possessed an activated ester at the α-end of the polymer chain, which could be reacted with amines with high conversions. The terminal ω-dithioester group of each polymer chain could quantitatively be removed by treating the polymer with an excess of AIBN, leaving the α-PFP ester functionality intact. Accordingly, the pentafluorophenyl ester diazo compound could successfully be employed to functionalize RAFT polymers with a PFP ester at their ω-end. As a consequence, functionalization of both end groups was possible and led to telechelic polymers, exhibiting an active ester at both ends of the polymer chain. As an example, a high molecular weight PMMA was prepared by polycondensation with ethylenediamine.

Introduction

Polymers carrying reactive functional groups have been receiving an increasing amount of attention. Postmodifications of reactive polymers with a large variety of reagents have been carried out leading to smart materials with adjustable LCSTs[1] or multidentate ligands for the encapsulation of quantum dots,[2,3] titania nanorods,[4] and other inorganic nanoparticles.[5−7] Such hybrid materials are interesting in material development and in optoelectronic research. Also, reactive polymers may be employed for surface modifications.[8] Monomers containing reactive sites such as activated esters,[9−11] acetals,[12,13] azides,[14] oxazolones,[15] acid azides,[16] or protected acetylenes[17] may be converted by free radical or controlled radical polymerization techniques into polymers or block copolymers containing a high number of chemically addressable groups.

A synthetically different challenge is the introduction of functional end groups into a polymer, which was synthesized by a radical polymerization. The linear chain of this polymer then acts as a spacer between the α- and ω-end groups of that specific polymer chain. Polymers with one functional end group may be used for bioconjugates,[18−21] precursors for diblock copolymers,[22] or for synthesizing polymer brushes on surfaces by a grafting-to technique.[23,24] A variety of methods to obtain end-group-functionalized polymers by nitroxide-mediated polymerization (NMP),[25] atom transfer radical polymerization (ATPR),[26−32] or reversible addition−fragmentation chain transfer polymerization (RAFT)[18−22,33−38] have been reported. Telechelic polymers, i.e., polymers that feature the same functional group at both chain ends, are of interest as precursors for multiblock copolymers or as cross-linkers in polymer networks. Synthetic strategies to produce hydroxy,[39] carboxylic acid,[36,39] thiol,[40−42] or amine[43] carrying telechelic polymers have been published.

The RAFT polymerization[44] uses a dithioester chain transfer agent (CTA) and thus results in polymer chains that carry a CTA residue on their α-end and a dithioester at their ω-terminus. These dithioesters are very promising for a subsequent polymer end-group functionalization. A large number of differently functionalized CTAs have been reported. Bathfield et al.[18] performed a dihyclohexylcarbodiimide (DCC) coupling of 2-(phenylthiocarbonylthio)propanoic acid with *N*-hydroxysuccinimide (NHS) and used the resulting NHS-activated CTA for biofunctionalization prior to polymerization of *N*-acryloylmorpholine. These authors also used the activated CTA successfully for the polymerization of *N*-acryloylmorpholine without amidation of the activated ester and also reported the synthesis of a different NHS activated CTA derived from azobis(4-cyanovaleric acid) which was coupled with DCC/NHS. Zheng and Pan[45] synthesized the same CTA by DCC/NHS coupling of 4-phenylthiocarbonylthio-4-cyanovaleric acid and used it as a precursor for the synthesis of polymeric stars carrying 8 or 16 dithioesters groups. An acid chloride precursor trithiocarbonate was presented by Jesberger et al. and was used for the synthesis of a multifunctional RAFT agent.[46]

Common postmodification reactions of the ω-dithioester are aminolysis,[35,38,47] thermolysis, or reduction with borohydride or stannane.[35,38] Perrier et al.[36] presented a method to recycle the chain transfer agent by reacting the polymer obtained from a RAFT polymerization with an excess of AIBN. Thereby, radicals cleave the bond between the ultimate repeating unit and the sulfur atom and saturate both emerging radicals with a cyanopropyl radical.

Herein, we describe the synthesis of a new chain transfer agent, pentafluorophenyl-[4-(phenylthiocarbonylthio)-4-cyanovalerate], via esterification of azobis(4-cyanovaleric acid). While sharing a similar reactivity toward amines as the known NHS esters,[48] pentafluorophenyl (PFP) esters have the advantage of being easily analyzed by ^{19}F NMR spectroscopy. The PFP-activated CTA was employed for the controlled polymerization of methyl methacrylate (MMA), diethylene glycol monomethyl ether methacrylate (DEGMA), poly(ethylene glycol) monomethyl ether methacrylate (PEGMA), lauryl methacrylate (LMA) and *N*-isopropylmethacrylamide (NIPMA) yielding polymers and block copolymers with one chemically addressable PFP end group. By using bis(pentafluorophenyl)azobis-(4-cyanovalerate), the dithioester end groups were be completely removed and replaced with an PFP-activated residue yielding

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* Corresponding author: e-mail theato@uni-mainz.de; phone +49-6131-3926256, Fax +49-6131-3924778.

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reactive telechelic polymers with PFP activated esters at both ends.

Experimental Section

Materials. All reagents were purchased from Acros, Aldrich, or Fluka and used as received unless stated otherwise. Tetrahydrofuran (THF) was distilled from sodium/potassium. Carbon disulfide was distilled from potassium permanganate. Dichloromethane was distilled from phosphor pentoxide. Dioxane was distilled from sodium. The monomers methyl methacrylate (MMA), diethylene glycol monomethyl ether methacrylate (DEGMA), poly(ethylene glycol) monomethyl ether methacrylate (PEGMA), and lauryl methacrylate (LMA) were distilled from calcium hydride.

Dithiobenzoic Acid. This compound was synthesized in analogy to a literature procedure.[49] Briefly, 9.3 mL of dry THF and 7.5 mL of a 2 M phenylmagnesium bromide solution in THF (15 mmol) were heated to 40 °C in a nitrogen atmosphere. 2.06 g (27 mmol) of carbon disulfide was then slowly injected through a septum. After stirring for 45 min at 45 °C it was poured onto a mixture of 110 g of ice and 50 mL of concentrated hydrochloric acid. The violet mixture was then extracted several times with diethyl ether; the organic phases were combined and dried over magnesium sulfate. After evaporation of the solvent 2.10 g (91%) of a violet liquid of characteristic odor was obtained.

Dithiobenzoic Acid Disulfide. 2.07 g (16.33 mmol) of iodine was dissolved in 40 mL of diethyl ether, and 2.10 g (13.61 mmol) of dithiobenzoic acid was added. The mixture was stirred overnight and was then washed with an aqueous solution of sodium carbonate and subsequently with an aqueous solution of sodium sulfite to eliminate the excess of iodine. The organic phase was dried with magnesium sulfate, and the solvent was removed. After drying in high vacuum, the product became a red solid (1.12 g, 54%) with almost no smell.

Bis(pentafluorophenyl)azobis(4-cyanovalerate) (PFP-ACV, 1). 10.0 g (35.7 mmol) of azobis(4-cyanovaleric acid), 15.8 g (85.8 mmol) of pentafluorophenol, 29.1 g (271.3 mmol) of 2,6-lutidine, and 207 mL of dry dichloromethane were combined in a round-bottom flask equipped with a stir bar and a septum in an argon atmosphere. The mixture was cooled to 0 °C, and 22.5 g (107.1 mmol) of trifluoroacetic anhydride was added dropwise through the septum. The reaction was allowed to warm to room temperature overnight. The mixture was then extracted three times with 100 mL of water each, reaching neutral pH after the third extraction. The organic phase was dried over magnesium sulfate and the solvent removed in light vacuum at 30 °C. The raw product was dissolved in dichloromethane and precipitated into cold hexane to remove remaining lutidine. After two consecutive precipitations from dichloromethane into hexane, 12.9 g (59%) of product was obtained which was pure as confirmed by NMR and IR spectroscopy. ^{1}H NMR, 300 MHz, $CDCl_3$: $\delta = 3.00-2.48$ (m, 8 H, CH_2), 1.78, 1.73 (2 s (cis, trans), 6 H, CH_3). ^{13}C NMR, $CDCl_3$: $\delta = 167.5$ (OCO), 142.6, 141.4, 139.5, 138.1 136.2 (weak, CF), 117.0 (CN), 71.7 (CCN), 32.7 ($OCO-CH_2-CH_2$), 28.3 ($OCO-CH_2$); 23.9 (CH_3). ^{19}F NMR, $CDCl_3$, 376 MHz: $\delta = -152.88$ (d, 4 F, $J = 15$ Hz), -157.56 (t, 2 F, $J = 21$ Hz), -162.20 Hz (t, 4 F, $J = 19$ Hz). IR: 2929 cm^{-1} (w, CH), 1766 cm^{-1} (s, C=O), 1517 cm^{-1} (s, PFP), 1398 cm^{-1} (m), 1292 cm^{-1} (m), 1097 cm^{-1} (s), 987 cm^{-1} (s, PFP), 908 cm^{-1} (m).

Pentafluorophenyl-(4-phenylthiocarbonylthio-4-cyanovalerate) (PFP-CTA, 2). 2.17 g (7.08 mmol) of dithiobenzoic acid disulfide, 6.50 g (10.61 mmol) of bis(pentafluorophenyl)azobis(4-cyanovalerate) (**1**), and 40 mL of ethyl acetate were combined in a round-bottom flask with stir bar and condenser. Argon was bubbled through the mixture for 20 min, and the top of the condenser was equipped with a balloon filled with argon to ensure the absence of oxygen. The mixture was refluxed for 16 h. The solvent was removed, and the residue was purified by column chromatography with chloroform as eluent. 5.49 g (87%) of spectroscopically clean product was obtained. ^{1}H NMR, 300 MHz, $CDCl_3$: $\delta = 7.91$ (d, 2 H, $J = 7.8$ Hz, *o*-Ar), 7.57 (t, 1 H, $J = 7.5$ Hz *p*-Ar), 7.39 (t, 2 H, $J = 7.8$ Hz, *m*-Ar), 3.08−3.01 (m, 2 H, $O{=}C-CH_2$), 2.80−2.70 (m, 1 H, $O{=}CH_2-CHH$), 2.59−2.49 (m, 1 H, $O{=}CH_2-CHH$), 1.97 (s, 3 H, CH_3). ^{13}C NMR, $CDCl_3$: $\delta = 219.7$ (SCS), 167.8 (OCO) 144.3 (*ipso*-C_6H_5), 142.7, 139.4, 136.3, 134.4 (weak, CF), 133.2 (*para*-C_6H_5), 128.6 (*meta*-C_6H_5), 126.7 (*ortho*-C_6H_5), 118.2 (CN), 45.5 (CCN), 32.9 ($OCO-CH_2-CH_2$), 29.1 ($OCO-CH_2$); 24.2 (CH_3). ^{19}F NMR, $CDCl_3$, 376 MHz: $\delta = -152.88$ (d, 2 F, $J = 19$ Hz), -157.69 (t, 1 F, $J = 23$ Hz), -162.28 Hz (t, 2 F, $J = 21$ Hz). IR: 2927 cm^{-1} (w, CH), 1785 cm^{-1} (s, C=O), 1516 cm^{-1} (s, PFP), 1445 cm^{-1} (w), 1101 cm^{-1} (s), 990 cm^{-1} (s, PFP), 866 cm^{-1} (m), 761 cm^{-1} (m), 686 cm^{-1} (m). Elem. Anal.: theor C 51.23, H 2.72, N 3.14, S 14.4; found C 50.76, H 2.59, N 3.02, S 14.31.

4-Nitro-7-piperazin-1-yl-2,1,3-benzoxadiazole (NBD-Amine). This compound was synthesized according to a literature procedure.[50]

Diethylene Glycol Monomethyl Ether Methacrylate (DEGMA Synth). This monomer is commercially available but contains traces of a cross-linker leading to high molecular weight shoulders. Synthesis of the monomer led to a higher purity. Diethylene glycol monomethyl ether (Fluka, >99%) was subjected to a column chromatography using ethyl acetate/isopropanol 2:1 as eluent. 6 g (50 mmol) of purified diethylene glycol monomethyl ether, 5.30 g (52.5 mmol) of triethylamine, and 150 mL of dry dichloromethane were combined in a round-bottom flask equipped with a stir bar and a septum. After cooling the mixture to 0 °C, 5.75 g (55 mmol) of methacryloyl chloride was added dropwise, and the reaction allowed to warm to room temperature overnight. The reaction was then washed several times with water, the organic phase dried, and the solvent evaporated. The crude product was distilled over calcium hydride. To ensure a high purity, only the middle fraction of the distillation (boiling point 57−60 °C at 9.7×10^{-2} mbar; 2.8 g, 30%) was used for polymerization.

***N*-Isopropylmethacrylamide (NIPMA).** In a round-bottom flask 85 mL of dry dichloromethane, 9.65 mL (112.7 mmol) of isopropylamine, and 16.63 mL (118.3 mmol) of triethylamine were combined in an argon atmosphere, and the mixture was cooled to 0 °C. 12 mL (124 mmol) of methacryloyl chloride was then added dropwise. The reaction was allowed to warm to room temperature overnight. Precipitated ammonium salts were removed by suction filtration, and the filtrate was extracted with water several times. The organic phase was dried and the solvent evaporated to give 13 g (91%) of crude product, which was recrystallized from hexane yielding 8.7 g (61%) of pure monomer.

General RAFT Polymerization Procedure. All RAFT polymerizations followed the same general procedure. An example is given: 4 mL (21.68 mmol) of commercial diethylene glycol monomethyl ether methacrylate distilled over calcium hydride, 483 mg (1.08 mmol) of PFP-CTA (**2**), 44.4 mg (270.9 mmol) of AIBN, and 6 mL of freshly distilled dioxane were combined in a Schlenk flask. The mixture was degassed by three freeze−pump−thaw cycles and the flask refilled with argon. It was then heated in a stirred oil bath set to 75 °C for 13 h. The polymer was precipitated from diethyl ether/hexane and dried in vacuum. The yield was almost quantitative. For diblock copolymers, a RAFT polymer was used as a macro-CTA instead of the PFP-CTA. Molecular weights and polydispersities are given in Table 1.

PMMA Polymerized in the Presence of Cumyl Dithiobenzoate. The chain transfer agent was synthesized according to a literature procedure.[47] 1.6 mL (15 mmol) of methyl methacrylate, 88.2 mg (0.32 mmol) of cumyl dithiobenzoate, and 12.8 mg (0.078 mmol) of AIBN were added to a Schlenk tube, and oxygen was exchanged with nitrogen by five freeze−pump−thaw cycles. The polymerization was carried out at 75 °C for 21 h. The polymer was purified by precipitation into methanol from THF for three times to yield 1.39 g (88%) of cumyl-PMMA-dithioester. M_n(GPC) = 8.9K; PDI (GPC) = 1.10.

General Procedure for Reaction of PFP-Polymer with NBD-Amine. In a typically experiment, 2 μmol of PFP end-functionalized PMMA was dissolved in 5 mL of dioxane, and a solution of 10 μmol of NDB-amine in 3 mL of dioxane was added. The mixture

Table 1. List of Polymers and Diblock Copolymers Derived from the PFP Functionalized Chain Transfer Agent

entry	first monomer	M_n[h] [g/mol]	PDI[h]	second monomer	M_n [g/mol] diblock	PDI diblock
1	DEGMA[a] com[b]	4K	1.12			
2	DEGMA com	5.5K	1.09	PEGMA	25K	1.31
3	DEGMA com	8K	1.14	NIPMA	9K	1.11
4	DEGMA com	9K	1.14			
5	DEGMA com	10K	1.18	LMA	16K	1.18
				MMA	20K	1.19
6	DEGMA com	25K	1.34			
7	DEGMA synth[c]	2.8K	1.08	NIPMA	3.4K	1.09
8	DEGMA synth	21K	1.12	NIPMA	22K	1.10
9	DEGMA synth	41K	1.19	NIPMA	43K	1.16
10	PEGMA[d]	25K	1.18			
11	NIPMA[e]	3.0K	1.17			
12	LMA[f]	8K	1.06	PEGMA	20K	1.14
13	LMA	22K	1.06			
14	MMA[g]	3.6K	1.08	PEGMA	15K	1.18
15	MMA	14.8K	1.18			

[a] Diethylene glycol monomethyl ether methacrylate. [b] Commercially avaiable monomer containing trace amounts of a cross-linker. [c] Synthetic monomer made from purified diethylene glycol monomethyl ether. [d] Poly(ethylene glycol) monomethyl ether methacrylate. NMR analysis showed that each monomer contained about 4 ethylene glycol units. [e] *N*-Isopropylmethacrylamide. [f] Lauryl methacrylate. [g] Methyl methacrylate. [h] Molecular weights (given in g/mol) and PDIs were determined by GPC analysis.

was stirred for 1 day at 50 °C. After concentrating the solution by removing most of the solvent, the polymer was precipitated from methanol several times until the methanol remained colorless. The absence of unreacted dye was confirmed by GPC using a UV−vis detector set to 475 nm.

General Procedure for Dithioester Removal. In a typical run, a polymer containing a dithioester end group and 20 equiv of the diazo compound (AIBN or PFP-ACV **1**) were dissolved in dry dioxane. 12 mL of dioxane was used for 10 mmol of diazo component. The mixture was heated to 80 °C for 2.5 h. Then the polymer was precipitated three times in methanol (PMMA) or diethyl ether/hexane (1:1) (poly[ethylene glycol methacrylate]). A ^{1}H NMR spectrum showed no remaining residues of the azo compound.

A sample of α-PFP-PDEGMA after AIBN treatment was analyzed by ^{19}F NMR: CDCl$_3$, 376 MHz, $\delta = -153.01$ (m, 2 F), -157.92 (m, 1 F), -162.38 Hz (m, 2 F).

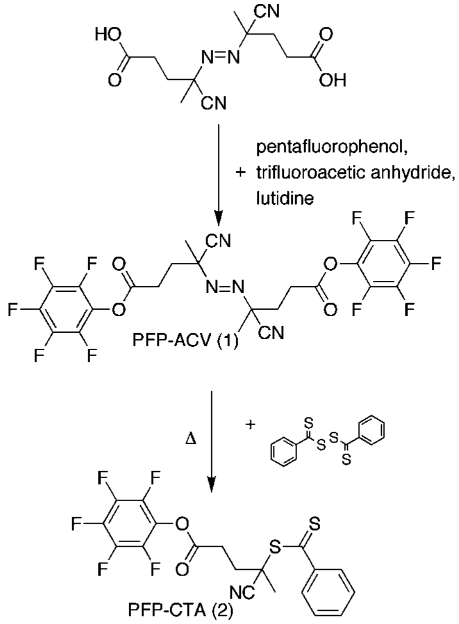
Treating α-cumyl-PMMA with PFP-ACV (**1**) yielded α-cumyl-PMMA-ω-PFP, which was analyzed by ^{19}F NMR: CDCl$_3$, 376 MHz, $\delta = -153.02$ (m, 2 F), -157.68 (m, 1 F), -162.39 Hz (m, 2 F).

Formation of Multiblock PMMA. Telechelic PMMA, exhibiting PFP end groups, was synthesized by reacting α-PFP−PMMA with an excess of PFP−ACV as described above. To ensure an accurate 1:1 ratio of amines and active esters in the polycondensation reaction with ethylenediamine, first a sample of telechelic PMMA was reacted with an excess of ethylenediamine to give telechelic PMMA exhibiting amine end groups: 150 mg of 14.8K g/mol PFP−PMMA−PFP was dissolved in 1 mL of THF and 100 equiv of diethylamine was quickly added. The mixture was stirred overnight at 40 °C, and then the polymer was precipitated three times in methanol and dried in vacuum. 20 mg of telechelic NH$_2$-PMMA-NH$_2$ and 20.2 mg of telechelic PFP-PMMA-PFP (Scheme 2C) were dissolved in 0.6 mL of THF, and a drop of triethylamine was added. The mixture was stirred overnight at 40 °C. A longer reaction time did not increase the conversion; oligo-PMMA was obtained in quantitative yield, M_n(GPC) = 70K g/mol, PDI (GPC) = 1.44.

Results and Discussion

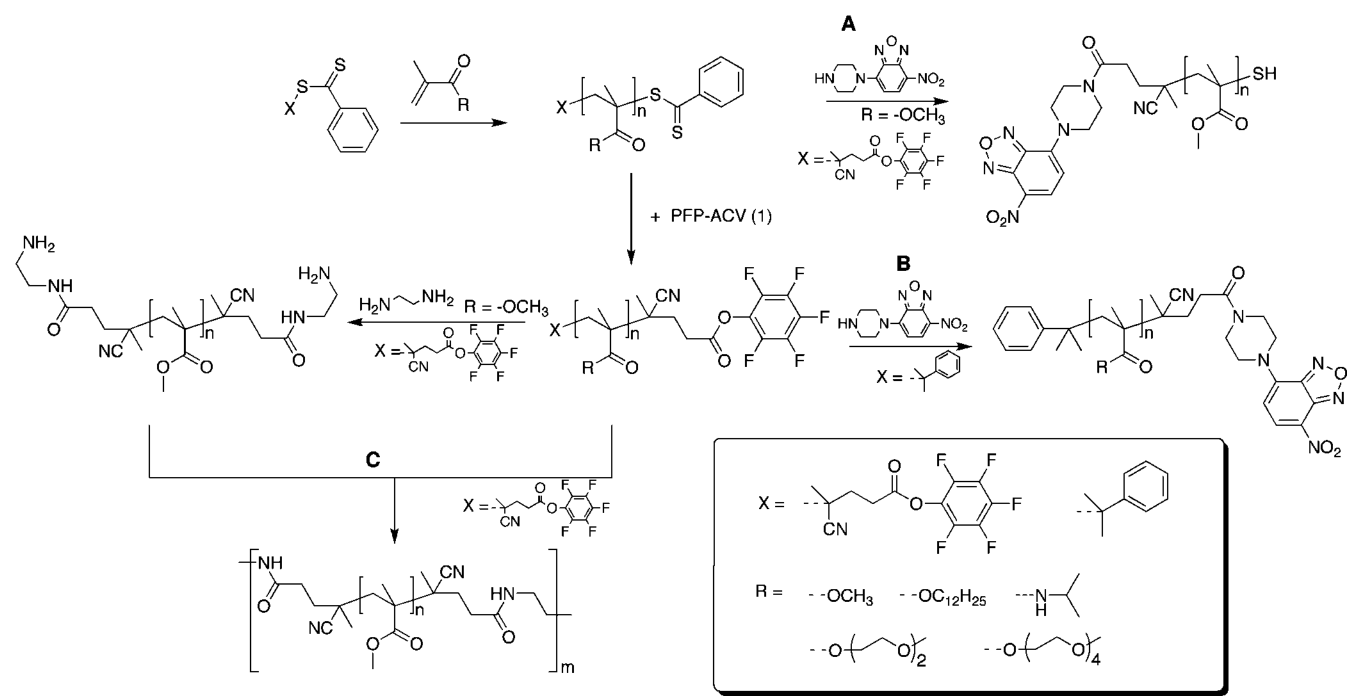
The scope of the present study is to prepare telechelic polymers that possess an activated ester at both end groups. In order to reach this goal, we combined several individual techniques that had recently been presented to prepare either α-end-group-functionalized polymers[18,45,46] or ω-end-group-functionalized polymers[36] synthesized by a radical polymerization technique. As our former investigations had shown, the pentafluorophenyl ester is a very versatile and reactive functionality,[10] and we favored it as the activated ester of choice for the present study. Accordingly, a pentafluorophenyl ester azo initiator was synthesized first. In a second step, this azo initiator was converted into a pentafluorophenyl ester-functionalized chain transfer agent, which should be capable to control a reversible addition−fragmentation chain transfer (RAFT) polymerization. Scheme 2 shows the roles of both of these two new compounds for the preparation of telechelic active ester polymers.

Scheme 1. Synthesis of a Pentafluorophenyl (PFP) Active Ester Functionalized Diazo Initiator (1) in a One-Step Reaction and Conversion into a PFP-Functionalized Chain Transfer Agent (2)



Synthesis of a Pentafluorophenyl Ester Azo Initiator. In contrast to the common methods of synthesizing a PFP ester by either activation of the acid with DCC or by a two-step reaction via an acid chloride, we investigated a one-step reaction to synthesize bis(pentafluorophenyl) azobis(4-cyanovalerate) (PFP−ACV, **1**) from azobis(4-cyanovaleric acid) (ACVA) using trifluoroacetic anhydride (TFAA) to activate the acid (Scheme 1). TFAA is known to react with pentafluorophenol under mild conditions to give pentafluorophenyl trifluoroacetate, which is a commercial, effective, one-step reagent to create PFP esters,[51] although expensive. TFAA also reacts with carboxylic acids under mild conditions[52] to form a mixed anhydride, which is susceptible to alcoholysis. Thus, a reaction composed of a carboxylic acid, TFAA, and pentafluorophenol yielded the desired PFP ester under mild conditions. In the experiment we added 2,6-lutidine to scavenge the trifluoroacetic acid generated during the reaction. After stirring the components overnight at room temperature, pure PFP−ACV (**1**) could be obtained by simple precipitation into cold hexane. The yield was moderate (59%); however, the product was pure and did not contain any monofunctionalized azo-compound side product as could be seen from ^{1}H NMR, ^{19}F NMR, and the bands of IR spectroscopic data (see Supporting Information). The acid precursor showed a prominent O−H band above 3000 cm^{-1} and a carbonyl absorption at 1702 cm^{-1}, while the ester product was lacking the O−H band, only exhibiting a weak C−H band just below 3000 cm^{-1}; the carbonyl peak had completely shifted to 1785 cm^{-1}, indicating the presence of an active ester, and the product

Scheme 2. Overview of Reactions Described in Detail in the Text



spectrum also contained the characteristic aromatic peaks also to be seen in a spectrum of pentafluorophenol centered at 1500 and 990 cm^{-1}.

Synthesis of a Pentafluorophenyl Ester-Functionalized Chain Transfer Agent. From PFP−ACV (**1**), a PFP-functionalized chain transfer agent PFP−CTA (**2**) was synthesized via radical reaction with dithiobenzoic acid disulfide (Scheme 1). After reaction at 77 °C for 16 h the PFP−CTA (**2**) was obtained in 87% yield after purification by column chromatography. This synthesis is well established for the diazo acid derivative ACVA, and we were able to apply it with equally good results for our modified azo initiator PFP−ACV.

Synthesis of Polymers with a PFP Ester at the α-Position. PFP−CTA could successfully be used to polymerize various methacrylates, such as MMA, DEGMA, PEGMA, and LMA, under RAFT polymerization conditions. The RAFT polymerization of *N*-isopropylmethacrylamide (NIPMA) resulted in a very low yield and low molecular weight polymer. Polymerizations of methacrylates, however, proceeded with a very accurate control over the molecular weight, near quantitative monomer conversions, and narrow molecular weight distributions. Table 1 lists polymers and block copolymers derived from PFP-CTA (**2**). In the case of DEGMA, both the monomer available from Aldrich and a homemade monomer were used. The commercial monomer seemed to contain trace amounts of a cross-linker, presumably diethylene glycol dimethacrylate, which caused polymers to have a slight shoulder toward higher molecular weights, and thus broader molecular weight distributions such as $M_w/M_n = 1.34$ at 25K g/mol (Table 1, entries 1−6) were obtained. However, polymerization of the homemade monomer synthesized from carefully purified diethylenglycol monomethyl ether yielded high molecular weight polymers with considerably smaller molecular weight distributions, such as $M_w/M_n = 1.19$ at 41K g/mol (Table 1, entries 7−9).

Polymers derived from PFP-CTA (**2**) carried an activated ester at their α-group, which could be shown by ^{19}F NMR (Figure 1, graph c). In order to address the terminal activated ester, a sample of PFP−PMMA (Table 1, entry 15) was reacted with 4-nitro-7-piperazin-1-yl-2,1,3-benzoxadiazole (an amine-functionalized NBD) (Scheme 2A). The obtained polymer was intensely orange colored, and a GPC measurement with the UV−vis detector set to the absorption maximum of the NBD dye (475 nm) indicated that the polymer was colored and that any excess of dye had successfully been removed from the sample by several precipitation steps (Figure 2). As the amine-functionalized dye was employed in excess, the ω-end group of the polymer was converted into a thiol[35,38] or a thiolactone by backbiting.[47] The GPC curve of the dye-functionalized PMMA was very slightly shifted toward higher molecular weights; however, no peak of twice the molecular weight was observed, indicating that no disulfide coupling had occurred under these conditions.

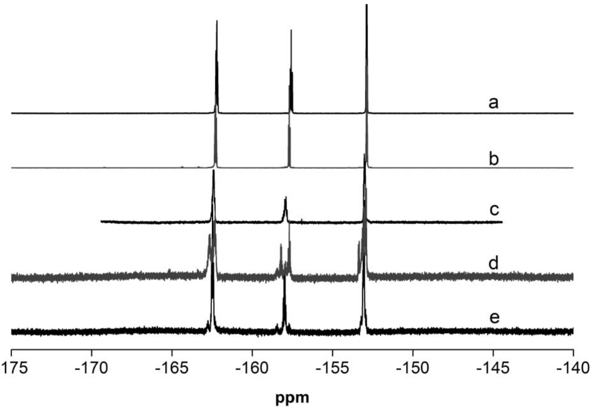


Figure 1. ^{19}F NMR spectra of (a) pentafluorophenyl ester-functionalized azo initiator PFP−ACV (**1**), (b) pentafluorophenyl ester-functionalized chain transfer agent PFP−CTA (**2**), (c) α-pentafluorophenyl ester-functionalized poly(diethylene glycol monomethyl ether methacrylate) derived from PFP−CTA after dithioester removal with AIBN, (d) ω-pentafluorophenyl ester-functionalized PMMA obtained by reacting the dithioester terminated polymer with an excess of PFP−ACV, and (e) telechelic α,ω-pentafluorophenyl ester-functionalized PMMA obtained from combining the use of the modified CTA (**2**) and end-group exchange with an excess of **1**.

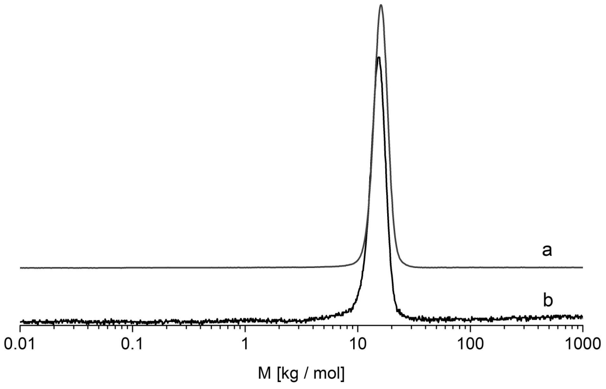


Figure 2. Reaction of an α-PFP ester-functionalized polymer with a functional dye: gel permeation chromatograms of α-pentafluorophenyl ester-functionalized PMMA (Table 1, entry 15) (line b) and after reaction with NBD-amine (Scheme 2, route A) (line a). For the measurement of the NBD-functionalized polymer, the UV−vis detector was set to the absorption maximum of the dye, indicating that no free dye at low molecular weight elution was present.

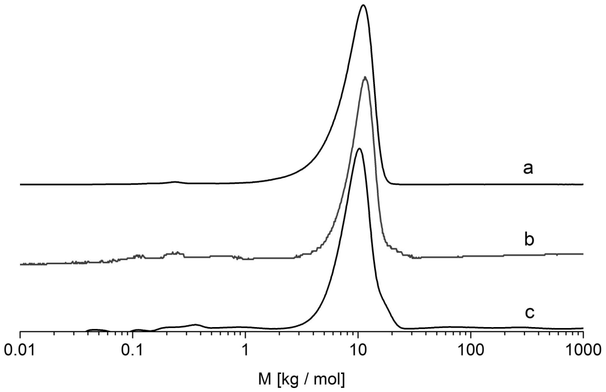


Figure 3. Reaction of α-cumyl, ω-dithioester PMMA with an excess of PFP−ACV (**1**) and functionalization with a functional dye (Scheme 2, route B): gel permeation chromatograms of (a) α-cumyl, ω-pentafluorophenyl ester PMMA, (c) after removal of the dithioester by replacing it with PFP-cyanovalerate, and (b) after reaction with NBD-amine. For this measurement, the UV−vis detector was set to the absorption maximum of the dye, indicating that no free dye at low molecular weight elution was present.

The molecular weight of the employed polymer was determined by two methods: first, by GPC analysis using a light scattering detector and the known value for d*n*/d*c* of 0.085 mL/g for PMMA and, second, by end group analysis. The absorbance of the dithioester end group of PFP−PMMA (Table 1, entry 15) was measured and compared with a calibration curve of the concentration dependent absorbance of PFP−CTA (see Supporting Information). From the GPC/light scattering measurement a molecular weight of 14.8K g/mol could be calculated, whereas the dithioester end-group analysis resulted in a molecular weight of 14.4 ± 0.7K g/mol. The difference of these values being less than 3% indicates that nearly all the polymer chains carried the dithioester end group, and thus, analysis of its absorbance is a valid approach for determination of the molecular weight.

In order to analyze the conversion of the PFP end group with amine-functionalized NBD, the absorbance of the NBD-functionalized PMMA was measured and compared with a calibration curve of the concentration-dependent absorbance of NBD-amine (see Supporting Information). In combination with the molecular weight, a conversion of the PFP ester end group of 83.6% (using GPC/light scattering data) and 81.4 ± 4.0% (using dithioester absorbance data) could be calculated. These values are in very good agreement with end-group conversion presented in the literature; for example, a conversion of 80.1 ± 2.6% for a cysteamine end-capped polymer that had been reacted with an activated ester dye was reported.[19] It should be noted that the nonquantitative conversion may result from (i) PFP esters not being present at the α-end-group, for instance by polymer chains that had been initiated by AIBN, (ii) alcoholysis/hydrolysis of the PFP esters during precipitation or storage, or (iii) an incomplete reaction with the chromophore due to a small concentration of the polymer end groups.

Synthesis of Polymers with a PFP Ester at the ω-Position. To introduce a pentafluorophenyl ester end group at the ω-position, the dithioester end group had to be exchanged in a reaction described in detail by Perrier et al.[36] Similar to the conditions reported there, we treated the dithioester-terminated polymer (PFP−PMMA, Table 1,entry 15) in a first model reaction with 20 equiv of AIBN, resulting in a quantitative replacement of the dithioester by a cyanopropyl group originating from AIBN. The GPC traces of the resulting polymers did not differ from those of the dithioester containing polymers, demonstrating that no polymer−polymer radical coupling had occurred. However, if the temperature exceeded 80 °C during the reaction, then a higher molecular weight shoulder at twice the molecular weight was found, probably caused by the high concentration of radicals during the reaction. The PFP ester at the α-end group was not harmed by this treatment, as the ester is stable toward radicals and elevated temperature in the absence of nucleophiles. Clearly, the ^{19}F NMR spectra of polymers obtained after the exchange reaction still showed the typical PFP ester signals (Figure 1, graph c). This shows that an exchange reaction of RAFT polymers, and we next investigated the use of the PFP-functionalized azo initiator PFP-ACV (**1**) during the end-group exchange reaction. For this, a sample of PMMA was polymerized with cumyl dithiobenzoate, resulting in a polymer terminated in a dithioester but not containing any fluorine. This cumyl-PMMA dithioester was reacted with 20 equiv of PFP−ACV (**1**) at 80 °C for 2.5 h, and the resulting polymer PMMA-ω-PFP was precipitated 3 times into methanol to remove any low molecular weight side products (see Scheme 2). The UV−vis spectrum of PMMA-ω-PFP showed that the absorbance of the dithioester centered at 302 nm had vanished, suggesting a complete removal of the dithioester end group and complete replacement with the PFP ester carrying residue as was shown for exchange reactions with other diazo compounds by Perrier et al.[36] (see Supporting Information). GPC traces recorded before and after the treatment with PFP−ACV did not show any differences showing that no side reactions had occurred that have an influence on the molecular weight or the molecular weight distribution (see Figure 3, curves a and c). A ^{19}F NMR spectrum taken of the product showed three distinct peaks that are typical for a PFP ester, indicating that the PMMA had been functionalized with a pentafluorophenyl active ester at its ω-position (see Figure 1d). Reacting the polymer with NBD-amine yielded a colored PMMA, and a GPC trace was recorded using a UV−vis detector set to 475 nm, the absorbance maximum of the NBD dye (Figure 3, curve b). This measurement clearly showed that the polymer had been functionalized with the dye, as there is a strong signal of the detector and the unmodified polymer has no absorbance at this wavelength. It can also be seen that all unreacted dye had successfully been removed by precipitation for there is no low molecular weight signal of the UV−vis detector.

Synthesis of Telechelic Polymers. The experiments described above showed that we could incorporate pentafluorophenyl esters at either the α-position of a polymer chain utilizing a pentafluorophenyl ester functionalized chain transfer agent or

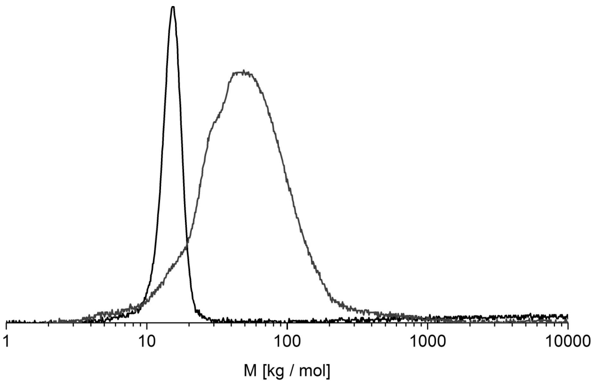


Figure 4. Reaction of telechelic PFP−PMMA−PFP with a diamine to form multiblock homopolymers: gel permeation chromatograms of a single PMMA building block (curve a) and of the multiblock homopolymer obtained from reacting α-PFP, *ω*-PFP PMMA with ethylenediamine (Scheme 2, route C) (curve b). The molecular weight and PDI of the precursor PMMA are 14.8K g/mol and 1.18, whereas the multiblock homopolymer has an average weight of 70K g/mol with a PDI of 1.44.

at the *ω*-terminus of a polymer chain by treating a polymer containing a dithioester with a pentafluorophenyl ester functionalized azo compound. The latter reaction progresses via a radical mechanism and is thus independent of the nature of the α-group of the polymer chain. We therefore took advantage of the pentafluorophenyl ester functionalized azo compound and the pentafluorphenyl ester functionalized chain transfer agent in one synthesis and prepared a telechelic polymer containing pentafluorphenyl esters at both its α- and *ω*-ends (see Scheme 2). For this purpose, PFP−PMMA (Table 1, entry 15) with a molecular weight of 14.8K g/mol was reacted with a 20-fold excess of PFP-ACV (**1**) to yield the polymer PFP−PMMA−PFP. The quantitative removal of the dithioester was again monitored by the disappearance of the absorption band at 302 nm. GPC traces showed only a very slight shift toward higher molecular weights of the telechelic polymer PFP−PMMA−PFP in respect to the precursor polymer PFP−PMMA. The ^{19}F NMR spectrum of PFP−PMMA−PFP showed three peaks (see Figure 1, graph e). The difference of the chemical environment of the α-end group and the *ω*-end group (tail vs head connection to monomers) was not sufficient to result in separate signals.

Polycondensation of Telechelic Polymers. One of the many uses of telechelic polymers is that they can be used in polycondensation reactions yielding multiblock polymers. As an example, we used the telechelic polymer PFP−PMMA−PFP to prepare a multiblock homopolymer with ethylenediamine (see Scheme 2, route C). In such a polycondensation reaction the exact 1:1 ratio of reactive groups is essential to achieve a high conversion. For this reason, the telechelic polymer PFP−PMMA−PFP was first reacted with an excess of ethylenediamine, yielding the telechelic polymer NH_2−PMMA−NH_2 featuring amine groups at the α-position and the *ω*-position of the polymer chain. This polymeric diamine was then allowed to react with the telechelic polymer PFP−PMMA−PFP overnight at 40 °C. A longer reaction time did not result in an increase of the conversion. The resulting multiblock homo-PMMA was analyzed by GPC (Figure 4). Line a represents the precursor PMMA with a molecular weight of 14.8K g/mol, whereas line b is the signal of the product of the polycondensation of the PFP−PMMA−PFP with the respective polymeric diamine, with a resulting molecular weight of 70K g/mol. The multiblock homopolymer still contained some homopolymer chains, probably due to a small fraction of precursor PMMA, which did not exhibit a pentafluorophenyl ester at both α- and *ω*-positions. Further, a shoulder at double molecular weight can be seen. The main peak however comprises molecular weights up to over 100K g/mol, implying that the PMMA chains consisted of at least six or more single building blocks. This is only possible if α,*ω*-difunctional polymer chains had been present in the polycondensation reaction. The overall conversion of the polycondensation is probably limited due to several reasons: (i) a very low concentration of reactive groups with proceeding reaction, (ii) a low mobility of the larger chains, and (iii) an imprecise 1:1 ratio of reactive groups. Compared to other synthetic routes that had been reported on the formation of multiblock homopolymers, our method yields very high molecular weight multiblock homopolymers. For example, You et al.[42] reported multiblock homopolymers by oxidative coupling of different telechelic polymers featuring thiol groups at the α- and *ω*-position of the polymer chain. Their multiblock homopolymers consisted of 7−13 single building blocks, which were of much lower molecular weight (2.5K to 3.5K g/mol).

Considering main applications of telechelic polymers such as formation of multiblocks and use as cross-linkers, our PFP-functionalized polymers are very promising compared to existing hydroxy, carboxylic acid, or thiol terminated polymers as they may be addressed under mild conditions with high conversions and also have the great advantage of being easily characterized with ^{19}F NMR spectroscopy.

Conclusion

A simple synthesis of a pentafluorophenyl (PFP)-functionalized azo initiator, bis(pentafluorophenyl) azobis(4-cyanovalerate), by way of a one-step esterification with trifluoroacetic anhydride as activating agent was described. From this compound, a PFP-functionalized chain transfer agent (CTA) was synthesized, which could polymerize methacrylates effectively producing polymers carrying one active ester per chain. The use of PFP esters has the advantage of elegant analysis trough ^{19}F NMR spectra, which could show that the α-PFP ester is not harmed by removal of the dithioester by treatment with an excess of azo initiator. By using the PFP-functionalized azo compound, we were able to incorporate active esters at the *ω*-terminus of RAFT polymers, thus allowing active ester functionalization at either the α-end of methacrylate polymers or at the *ω*-end or at both ends of a polymer chain together to give telechelic PFP esters. Both the α and the *ω* PFP esters could be addressed with a secondary amine with high conversion. Telechelic PMMA could successfully be employed in a polycondensation with ethylenediamine. As PFP esters may also be conjugated with a manifold variety of compounds of arbitrary molecular weight ranging from inorganic compounds to biologically active molecules, these procedures broaden the possibilities of modern polymer architecture and the development of novel functionalized materials.

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Supporting Information Available: IR spectroscopic data following the synthesis of PFP−ACV, a UV−vis absorbance calibration curve of the CTA dithioester and absorption measurements of PMMA-dithioester for calculation of the molecular weight, determination of NBD conversion through a UV−vis absorption calibration curve and UV−vis data showing the complete removal of the dithioester end group by exchange reaction with PFP−ACV. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Metz, N.; Theato, P. *Eur. Polym. J.* **2007**, *43*, 1202–1209.
(2) Potapova, I.; Mruk, R.; Prehl, S.; Zentel, R.; Basché, T.; Mews, A. *J. Am. Chem. Soc.* **2003**, *125*, 320–321.
(3) Potapova, I.; Mruk, R.; Hübner, C.; Zentel, R.; Basché, T.; Mews, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 2437–2440.
(4) Tahir, M. N.; Eberhardt, M.; Theato, P.; Faiβ, S.; Janshoff, A.; Gorelik, T.; Kolb, U.; Tremel, W. *Angew. Chem.* **2006**, *118*, 922–926.
(5) Muhammad Nawaz Tahir, M. N.; Zink, N.; Eberhardt, M.; Therese, H. A.; Ute Kolb, Theato, P.; Tremel, W. *Angew. Chem.* **2006**, *118*, 4927–4933.
(6) Meuer, S.; Braun, L.; Zentel, R. *Chem. Commun.*, in press.
(7) Zorn, M.; Meuer, S.; Tahir, M. N.; Khalavka, Y.; Sönnichsen, C.; Tremel, W.; Zentel, R. L. *Mater. Chem.* **2008**, *18*, 3050–3058.
(8) Kessler, D.; Metz, N.; Theato, P. *Macromol. Symp.* **2007**, *254*, 34–41.
(9) Batz, H.-G.; Franzmann, G.; Ringsdorf, H. *Angew. Chem.* **1972**, *24*, 1189–1190.
(10) Eberhardt, M.; Theato, P. *Macromol. Rapid Commun.* **2005**, *26*, 1488–1493.
(11) Nilles, K.; Theato, P. *Eur. Polym. J.* **2007**, *43*, 2901–2912.
(12) Li, R. C.; Broyer, R. M.; Maynard, H. D. *J. Polym. Sci., Part A* **2006**, *44*, 5504–5013.
(13) Schulz, R. C. *Angew. Chem., Int. Ed.* **1964**, *3*, 416–423.
(14) Sumerlin, B. S.; Tsarevsky, N. V.; Louche, G.; Lee, R. Y.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 7540.
(15) Fournier, D.; Pascual, S.; Fontaine, L. *Macromolecules* **2004**, *37*, 330.
(16) Klinger, D.; Chang, J. Y.; Theato, P. *Macromol. Rapid Commun.* **2007**, *28*, 718–724.
(17) Fleischmann, S.; Messerschmidt, M.; Voit, B.; Hawker, C. *Polym. Prepr.* **2006**, *47*, 546–547.
(18) Bathfied, M.; D'Agosto, F.; Spitz, R.; Charreye, M.-T-; Delair, T. *J. Am. Chem. Soc.* **2006**, *128*, 2546–2547.
(19) York, A. W.; Scales, C. W.; Huang, F.; McCormick, C. L. *Biomacromolecules* **2007**, *8*, 2337–2341.
(20) You, Y.-Z.; Oupicky, D. *Biomacromolecules* **2007**, *8*, 98–105.
(21) Li, M.; De, P.; Gondi, S. R.; Sumerlin, B. S. *Macromol. Rapid Commun.* **2008**, *29*, 1172–1176.
(22) Li, M.; De, P.; Gondi, S. R.; Sumerlin, B. S. *J. Polym. Sci., Part A* **2008**, *46*, 5093–5100.
(23) Shan, J.; Tenhu, H. *Chem. Commun.* **2007**, 4580–4598.
(24) Roth, P.; Theato, P. *Chem. Mater.* **2008**, *20*, 1614–1621.
(25) Hawker, C. J.; Hedrick, J. L.; Malmström, E. E.; Trollsas, M.; Mecerreyes, D.; Moineau, G.; Dubois, P.; Jerome, R. *Macromolecules* **1998**, *31*, 213–219.
(26) Kopping, J. T.; Tolstyka, Z. P.; Maynard, H. D. *Macromolecules* **2007**, *40*, 8593–8599.
(27) Lutz, J.-F.; Börner, H. G.; Weichenhan, K. *Macromolecules* **2006**, *39*, 6376–6383.
(28) Opsteen, J. A.; van Hest, J. C. M. *Chem. Commun.* **2005**, 57–59.
(29) Matyjaszewski, K.; Nakagawa, Y.; Gaynor, S. G. *Macromol. Rapid Commun.* **1997**, *18*, 1057–1064.
(30) Postma, A.; Davis, T. P.; Moad, G.; O'Shea, M. S. *React. Funct. Polym.* **2006**, *66*, 137–147.
(31) Deng, G.; Chen, Y. *Macromolecules* **2004**, *37*, 18–26.
(32) Mantovani, G.; Lecolley, F.; Tao, L.; Haddleton, D. M.; Clerx, J.; Cornelissen, J. J. L. M.; Velonia, K. *J. Am. Chem. Soc.* **2005**, *127*, 2966–2973.
(33) Lai, J. T.; Filla, D.; Shea, R. *Macromolecules* **2002**, *35*, 6754–6756.
(34) Qiu, X.-P.; Winnik, F. M. *Macromol. Rapid Commun.* **2006**, *27*, 1648–1653.
(35) Postma, A.; Davis, T. P.; Evans, R. A.; Li, G.; Moad, G.; O'Shea, M. S. *Macromolecules* **2006**, *39*, 5293–5306.
(36) Perrier, S.; Takolpuckdee, P.; Mars, C. A. *Macromolecules* **2005**, *38*, 2033–2036.
(37) Chen, M.; Ghiggino, K. P.; Mau, A. W. H.; Rizzardo, E.; Thang, S. H.; Wilson, G. J. *Chem. Commun.* **2002**, 2276–2277.
(38) Moad, G.; Chong, Y. K.; Postma, A.; Rizzardo, E.; Thang, S. H. *Polymer* **2005**, *46*, 8458–8468.
(39) 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.
(40) Gemici, H.; Legge, T. M.; Whittaker, M.; Monteiro, M. J.; Perrier, S. *J. Polym. Sci., Part A* **2007**, *45*, 2334–2340.
(41) Patton, D. L.; Mullings, T. F.; Advincula, R. C. *Macromolecules* **2005**, *38*, 8597–8602.
(42) You, Y.-Z.; Manickam, D. S.; Zhou, Q.-H.; Oupicky, D. *Biomacromolecules* **2007**, *8*, 2038–2044.
(43) Morita, T.; Maughon, B.; Bielawski, C.; Grubbs, R. *Macromolecules* **2000**, *33*, 6621.
(44) 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.
(45) Zheng, Q.; Pan, C.-Y. *Macromolecules* **2005**, *38*, 6841–6848.
(46) Jesberger, M.; Barner, L.; Stenzel, M. H.; Malmström, E.; Davis, T. P.; Barner-Kowollik, C. *J. Polym. Sci A* **2003**, *41*, 3847–3861.
(47) Xu, J.; He, J.; Fan, D.; Wang, X.; Yang, Y. *Macromolecules* **2006**, *39*, 8616–8624.
(48) Eberhardt, M.; Mruk, R.; Zentel, R.; Theato, P. *Eur. Polym. J.* **2005**, *41*, 1569–1575.
(49) Yordanov, N. D.; Ganeva, E.; Gochev, G. *Z. Anorg. Allg. Chem.* **1995**, *621*, 699–703.
(50) Nudelman, R.; Ardon, O.; Hadar, Y.; Chen, Y.; Libman, J.; Shanzer, A. *J. Med. Chem.* **1998**, *41*, 1671–1678.
(51) Green, M.; Berman, J. *Tetrahedron Lett.* **1990**, *31*, 5851–5852.
(52) Grayson, D. H.; Roycroft, E. D. *J. Chem. Soc., Chem. Commun.* **1992**, *18*, 1296–1297.

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