Novel Initiators for Atom Transfer Radical and Ring-Opening Polymerization: A New General Method for the Preparation of Thiol-Functional Polymers

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Novel initiators containing a protected thiol moiety have been developed and used for the preparation of thiol functional polymers by either atom transfer radical or ring-opening polymerization of methyl methacrylate (MMA) or ϵ-caprolactone (ϵ-CL), respectively. These novel initiators are based on Sangers reagent (2,4-dinitrofluorobenzene) and produce α-mercapto-functional polymers with controlled molecular weights and narrow polydispersities in only two steps.

The use of thiols is widespread in many areas of chemistry, and the specific interaction of the mercapto group with metals such as gold, silver, and cadmium has expanded the interest of thiols into such areas as materials science, microelectronics, and biotechnology.[1] The progress in these technologies, have increased the demand for well-defined polymers with thiol functionality. Although many synthetic routes for the preparation of organic thiols are well-known, only a few examples have been reported in polymer science.[1b,1h,2,3]

To date, the most controlled procedure for the incorporation of thiol groups in macromolecules at the chain-end or along the polymer backbone is to couple a protected thiol to an existing functionality in the polymer followed by deprotection. Tohayama et al.[3c] reported mercapto-functionalized polystyrene and polyisoprene, prepared by the termination of anionic living polymers with alkyl halides containing protected thiol functionalities. In a similar but milder and more versatile approach, −SH functional polymers have been prepared from hydroxy-functionalized polymers.[3d] This approach utilizes mercapto-acetic acid, where the thiol moiety is protected with 2,4-dinitrofluorobenzene, and produces thiol-functional poly(ϵ-caprolactone) and poly(ethylene oxide). Since the method is very mild and the degree of functionality is almost quantitative (95−100% as determined by a combination of ^{1}H NMR and UV−vis spectroscopy), it is desirable to modify and extend this technique to polymers that do not contain hydroxyl moieties.

Initiators bearing different functionalities as well as protected functional groups have been employed in most polymerization techniques.[4] The advantages of these techniques include quantitative functionality and the ability to produce block copolymers and macromonomers as well as asymmetric telechelics.[4] In this communication, we report the design, synthesis, and polymerization of two novel initiators, containing thiol groups protected with Sangers reagent, amenable toward either ring-opening (ROP) or atom transfer radical (ATRP) polymerization. These two polymerization procedures encompass a large number of available monomers as well as many biodegradable and biocompatible polymers.

The preparation of the two initiators **1** and **2** was accomplished by the slow addition of mercaptoethanol to a solution of 2,4-dinitrofluorobenzene and triethylamine in $CHCl_3$ according to a modified literature procedure (Scheme 1).[5] Recrystallization of the crude product from $CHCl_3$ gave **1**, the ROP initiator, as yellow crystals in high yield (85%).[6] Then, **1** was coupled with 2-bromo-2-methylpropionyl bromide to produce **2**, the ATRP initiator, as yellow crystals after recrystallization from MeOH.[7]

The synthetic approach surveyed for the preparation of poly(ϵ-caprolactone) (PCL) uses $Al(O^iPr)_3$ as the catalyst (Scheme 1).[8] The key feature in such a polymerization is the use of the organometallic compound in catalytic amounts to minimize complexation of aluminum alkoxides.[9] It has been shown that $Al(O^iPr)_3$ undergoes rapid exchange reactions with the dormant alcohol **1** and that the 2-propanol can be selectively removed through an azeotropic distillation, leaving the new alkoxide as the sole initiating species.[4e,9] The aluminum alkoxide functional chain end propagates by a living character and generates a hydroxyl-functional polymer after hydrolysis of the active metal−alkoxide chain end. The ROP carried out at ambient temperature in THF generated polymers with controlled molecular weights and narrow molecular weight distributions (Table 1). Most important, the accurate chain ends were confirmed by ^{1}H NMR spectroscopy; see Figure 1.[3d,10]

ATRP, recently described by Matyjaszewski et al.[11] and Sawamoto[12] et al., was the synthetic approach surveyed for the preparation of thiol-functional poly(methyl methacrylate) (PMMA) using bis(triphenylphosphine) nickel dibromide as the catalyst (Scheme 1).[13] The initiator **2** and the catalyst were weighted into a flame-dried flask, followed by several cycles of evacuation and subsequent purging with argon to remove dissolved oxygen. Finally the purified and degassed MMA monomer was added under argon, and the mixture was heated at 85 °C for 24 h. The polymer was then precipitated into methanol. The number-average molecular weights (M_n), obtained from both ^{1}H NMR integration and size exclusion chromatography (SEC), agreed well with the target molecular weights calculated from the monomer-to-initiator ratio (Table 1).[14] In addition, ^{1}H NMR spectroscopy in combination with the narrow molecular weight distribution as measured by SEC indicates that the requisite end-groups are obtained and that the polymerization is controlled. This is also supported by the fact that the molecular weight is controlled by the ratio of monomer-to-initiator in the initial feed.

The protecting groups of the prepared polymers were removed through an exchange reaction of the protected chain-end with a large excess of mercaptoethanol or 1-propanethiol in the presence of triethylamine (Scheme 2).[3d] The desired thiol-functional polymers were recovered by precipitation into cold methanol or hexane, and the end-groups were confirmed by ^{1}H NMR spectroscopy (Figure 1b).[3d] In no cases could any change of molecular weight (according to ^{1}H NMR) or molecular weight

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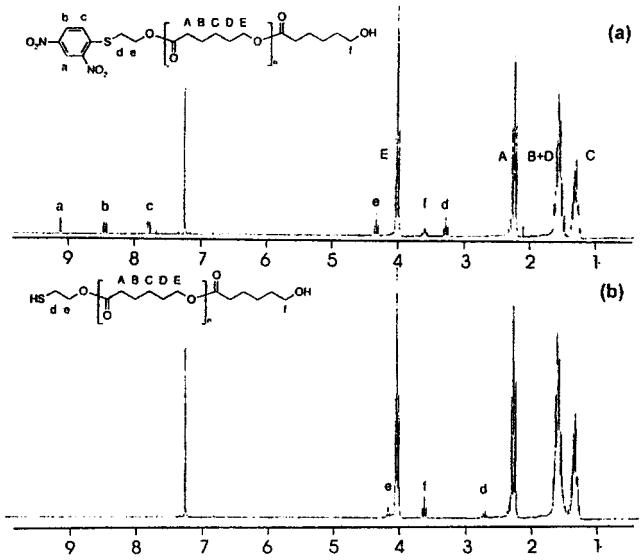
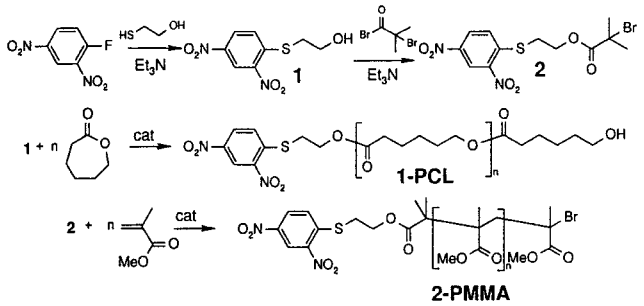


Figure 1. ^{1}H NMR spectra of (a) **1**-PCL and (b) **1**-PCL-SH.

Scheme 1. Synthesis of the Protected Thiol-Functional Polymers



Scheme 2. Synthesis of the Thiol-Functional Polymers

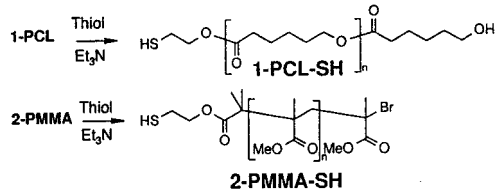


Table 1. Characteristics of the Prepared Polymers

polymer/initiator	target DP	M_n/DP (^{1}H NMR)	M_n (SEC)	M_w/M_n (SEC)
1-PCL/**1**	15	1600/14	2900	1.28
1-PCL-SH/**1**	15	1500/14	4000	1.25
2-PMMA/**2**	30	3800/35	6600	1.28
2-PMMA-SH/**2**	30	3700/35	8300	1.24

distribution (according to SEC) from the deprotection reaction be observed. Figure 2 shows the SEC traces for the PMMA before (**2**-PMMA) and after (**2**-PMMA−SH) deprotection. Although a small shift of the hydrodynamic volume is noticed, no change of the molecular weight distribution is observed.

In conclusion, it has been demonstrated that well-defined thiol-functional polymers can be prepared by the use of easily accessible initiators bearing a protected mercapto moiety. The convenient technique is mild and produces asymmetric telechelic polymers by either ATRP or ROP. Extensions of this useful and simple technique are the grafting and subsequent polymerization of thiol-functional initiators to both gold surfaces and nanoparticles.

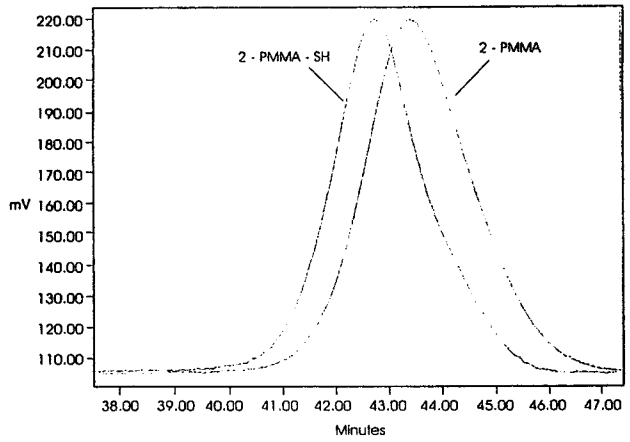


Figure 2. SEC traces of **2**-PMMA and **2**-PMMA-SH.

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(6) *2-(2,4-Dinitrophenylthio)ethanol* **1**: 5.00 g (26.9 mmol) of mercaptoethanol dissolved in $CHCl_3$ (20 mL) was slowly added to a solution of 2.10 g (26.9 mmol) of 2,4-dinitrofluorobenzene and 8.14 g (81.0 mmol) of Et_3N in $CHCl_3$ (30 mL). The reaction was stirred for 15 h at 25 °C before it was extracted twice with HCl (2 M) and H_2O. The organic phase was separated and filtered to yield yellow crystals, which were recrystallized from $CHCl_3$. Yield: 4.8 g (85%). Mp: 100 °C. ^{1}H NMR ($CDCl_3$): δ 1.90 (t, 1H, −O*H*), 3.29 (t, 2H, −SCH_2−), 4.01 (q, 2H, −CH_2OH), 7.64 (d, 1H, −Ar, J_o = 9.0 Hz), 8.35 (dd, 1H, −Ar, J_m = 3.0 Hz, J_o = 9.0 Hz), 9.07

(d, 1H, −Ar, J_m = 3.0 Hz). ^{13}C NMR ($CDCl_3$): δ 35.3, 60.2, 121.8, 127.1, 127.2, 143.9, 146.2, 146.3.

(7) *2-(2,4-Dinitrophenylthio)ethyl 2-bromo-2-methylpropionate* **2**: 0.71 g (3.06 mmol) of 2-bromo-2-methyl propionic acid dissolved in THF (10 mL) was slowly added to a solution of 0.50 g (2.35 mmol) of **1** and 0.71 g (7.02 mmol) of Et_3N in THF (10 mL). The reaction was stirred for 12 h at room temperature before it was extracted twice with HCl (1 M) and H_2O. The organic phase was separated and filtered to yield yellow crystals, which were recrystallized from MeOH. Yield: 0.65 g (77%). Mp: 83−84 °C. ^{1}H NMR ($CDCl_3$): δ 1.92 (s, 6H, −CH_3), 3.36 (t, 2H, −SCH_2−), 4.44 (q, 2H, −CH_2-OCO−), 7.78 (d, 1H, −Ar, J_o = 9.0 Hz), 8.44 (dd, 1H, −Ar, J_m = 3.0 Hz, J_o = 9.0 Hz), 9.07 (d, 1H, −Ar, J_m = 3.0 Hz). ^{13}C NMR ($CDCl_3$): δ 30.3, 30.6, 55.2, 62.5, 121.8, 127.1, 127.5, 144.3, 145.1, 145.3, 171.7.

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