Magnetite Nanoparticles for the Preparation of Ultrapure RAFT Polymers

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Introduction. Controlled/"living" radical polymerization (CRP) produces well-defined polymers by free radical reactions.[1] Although CRP methods primarily produce "living" chains, termination and transfer reactions that produce "dead" chains cannot be avoided. These dead chains cannot produce diblock copolymers, or be modified, and therefore exist as a contaminant in CRP reactions. They are usually chemically and physically similar to living chains, making separation difficult. This can be problematic when living polymers of high purity and functionality are required.

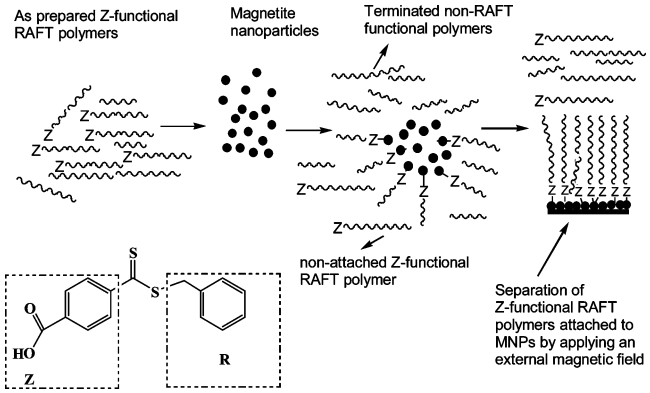
Living chains have been separated from side products of CRP reactions anchoring growing polymer chains to a solid substrate.[2,3] Most previous grafting studies (e.g., refs 4−10) have involved attachment by a nonliving chain end, which does not selectively attach living chains and/or involve difficult extraction/separation processes. Magnetic nanoparticles (MNPs) have previously been used in biomedical separation techniques (e.g., refs 11−13) but have not been used for the separation of living polymers.

Colloidally stable dispersions of very small MNPs each containing only a single magnetic domain have no net magnetism in the absence of a magnetic field, but the MNPs will be attracted to an external magnet. This allows convenient separation of the MNPs from the remainder of the mixture, with much higher efficiency than processes such as sedimentation or ultracentrifugation. Polymers containing groups capable of strong attraction to the MNP surfaces can be separated with the MNPs.

The reversible addition−fragmentation chain transfer (RAFT) process[14] uses a RAFT agent to rapidly transfer radical activity and chain dormancy between growing (living) chains in an otherwise conventional free radical polymerization reaction (and thus also produces dead chains). Living chains (and any (normally small) fraction of cross-terminated chains) contain the RAFT group, whereas the dead chains do not. RAFT agents contain activating (Z) and leaving (R) groups. In this study, a functional moiety that is strongly attracted to MNP surfaces was incorporated into the Z group of the RAFT agent (see Scheme 1). Thus, the living chains were strongly attracted to MNP surfaces, whereas dead chains were not.

This method is only effective when the functional moiety is part of the Z group; in the case of an R-functional RAFT agent, dead chains (which also usually contain at least one R group) will also be attracted to the MNP surfaces, thus invalidating the procedure. By analogy, such functional polymers produced by any CRP method require the functional moiety to be on the living chains for selective attraction of living chains to the MNP surfaces. Thus, of the commonly used CRP methods, only the RAFT(/MADIX) and nitroxide-mediated polymerization (NMP) techniques are likely to be efficient for this extraction method, since ATRP and degenerative transfer techniques do not involve groups that are strongly attracted to MNPs exclusively on the living chains. NMP is at this stage considered to be less versatile than the RAFT technique.

Scheme 1. Separation of Z-Functional RAFT Agents by Attachment to Magnetic Nanoparticles in the Presence of an External Magnetic Field



In this study, MNPs and the application of a strong external magnetic field are used to separate living chains from dead chains previously prepared by the RAFT process, by using Z-functional RAFT agents that are strongly attracted to the MNP surface. The resulting extracted polymer chains are of much higher purity and functionality than the "as-prepared" polymer chains that have not undergone the extraction process. This allows access to higher purity RAFT functional polymers based on the wide range of monomers available to the RAFT process.

Experimental Section. The materials used are described in Supporting Information.

RAFT Agent Synthesis. The synthesis of benzyl-(4-carboxydithiobenzoate) **(1)**, which contains the carboxylate moiety in its Z group (which is strongly attracted to the MNP surface), is described in the Supporting Information.

Preparation of the Magnetite Nanoparticles. Magnetite nanoparticles (of formula Fe_3O_4, average diameter = 10 nm) were prepared by a coprecipitation method.[15] Other methods (e.g., refs 16−18) exist for the preparation of MNPs, but the method used here is convenient and inexpensive and allows large quantities of well-defined and very small MNPs to be produced in high yield.

The as-prepared MNPs are colloidally unstable in organic solvents and thus were sterically stabilized by coating with oleic acid (in dichloromethane). The resulting colloidally stable MNP dispersions were used for the extraction procedures. Details of the synthesis and stabilization of the MNPs are available in the Supporting Information.

Polymerization. A typical polymerization to produce "as-prepared" polystyrene is as follows: a solution of styrene (25.0 g, 240 mmol), RAFT agent **(1)** (0.10 g, 0.34 mmol), and azobis(isobutyronitrile) (AIBN) (0.007 g, 0.04 mmol) in tetrahydrofuran (THF) (70 mL) was flushed with nitrogen, then sealed, and heated to 70 °C for 7 h, before the reaction was stopped by removing the heat and opening to the atmosphere. The "as-prepared" polystyrene was dried, characterized, and used in the extractions. In this example, conversion was 1.6%, and the "as-prepared" polymer had $\bar{M}_n$ = 4170 and PDI = 1.20.

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Extraction Process. The extraction process is depicted in Scheme 1 and is described in greater detail in the Supporting Information. The polymer containing the RAFT groups was separated from the remaining chains by mixing a dichloromethane solution of the as-prepared polymer chains with an MNP dispersion. The Z groups of the RAFT-functional polymer exchanged (and competed for the surface, since the Z group and the oleic acid have similar acid functionality (although the carboxyl group is attached to a stabilizing aromatic ring on the RAFT agent)) with the oleic acid on the MNP surface. A significant fraction of the RAFT-functional chains attached to the MNP surfaces and provide additional steric stabilization.

A strong, external magnetic field was applied to the MNP dispersion, which attracted the MNPs and any attached chains to the magnet, thus separating the MNPs from the remaining solution. The remaining solution (the unextracted solution) was decanted, and the remaining (unextracted) polymer was collected and dried. The MNP dispersion was mixed with a 32% HCl solution, which dissolved the MNPs. The organic phase containing the oleic acid and the polymer was extracted and dried to give the extracted polymer. The final extracted and unextracted polymers were characterized and used for polymer chain extension studies.

Chain Extension. The extracted and unextracted polymers were tested for living behavior by chain extension. A sample of each polymer was dissolved in styrene and heated to 100 °C for ca. 12 h. The resulting polymers were evaluated for chain extension efficiency.

Size Exclusion Chromatographic Analysis. The size exclusion chromatography (SEC) setup and calibration are described in the Supporting Information.

Comparison of the UV and differential refractive index (DRI) data is a powerful diagnostic tool. The UV detector detects (approximately) one chromophore per polymer chain for the RAFT-capped polymers, whereas the DRI detector observes one unit of signal per monomer unit in each polymer chain. Thus, for a valid approximate comparison of the UV and DRI data, the UV data were multiplied by M at each point in the UV chromatograms. These corrected UV data were used for all UV/DRI comparisons.

Results and Discussion. A polymer produced with a low initiator concentration was extracted by the above procedure. The DRI and UV SEC traces of the as-prepared (the unmodified polymer initially synthesized), extracted (the polymer that has been purified by the attachment to MNPs and extraction process), and unextracted (the polymer that remained in solution after the extraction process) polymers are shown in Figure 1. The comparison (Figure 1d) of the polymers shows distinct differences in the molar mass distributions (including $\bar{M}_n$) and UV signal at 320 nm (which is dominated by absorption by the RAFT functionality (plus a very weak contribution from the aromatic rings of each styrene unit)). The PDIs of the unextracted polymer and the as-prepared polymer were the highest (1.20, $\bar{M}_n$ = 2900, 4170), and the extracted polymer had a significantly lower PDI (1.13, $\bar{M}_n$ = 4730). For as-prepared polymers of higher PDI, the order of PDIs was unextracted polymer > as-prepared polymer > extracted polymer, as expected for the separation of living (low PDI) from dead (high PDI) chains. Dead chains are formed throughout the reaction (indicating the termination history of the reaction) and are mostly of lower M than the living chains. This is illustrated by the comparison of extracted and unextracted distributions. Dead chains lack RAFT functionality and absorb little radiation at 320 nm, as observed from the smaller UV signal than the DRI signal in the low M tail. In the case of the extracted polymer (Figure 1c), there is minimal deviation between the DRI and UV data, implying that the extracted polymer consists almost entirely of RAFT-functional chains and contains little or no dead chains.

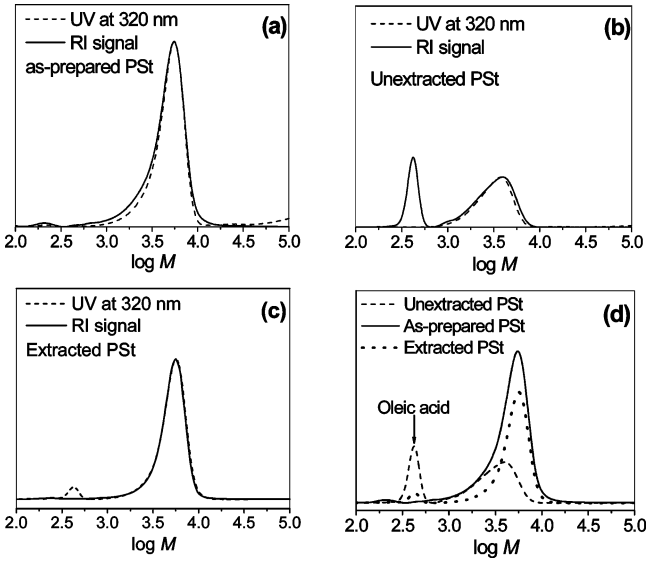

Figure 1. Differential refractive index and corrected UV (320 nm) size exclusion chromatograph traces of polystyrene (PSt) polymers produced with **1**: (a) as-prepared polymer, (b) polymer remaining in the solution after extraction, (c) purified polymer extracted with the magnetic nanoparticles, (d) comparison of (a)−(c).

Thus, the extracted polymer is apparently almost 100% RAFT functional and should undergo almost complete reinitiation for chain extension. The unextracted polymer (Figure 1b) apparently partly contains RAFT functional groups and thus should partially chain extend.

The RAFT functional chains in the unextracted polymer probably result from the ligand exchange process in the extraction step, which does not attach all RAFT functional chains to the MNP surface, thus leaving unattached RAFT chains to be decanted with the unextracted solution. This is consistent with the amount of polymer extracted, which was 75% by weight and 65% by number of chains, although only about 5% dead chains are expected here. Thus, a substantial fraction of living chains are in the unextracted polymer. These chains could be removed from this fraction by further extractions with MNPs, if desired.

Figure 2 shows the SEC results of the extension tests. The insets magnify the region where the initial polymer was found, to demonstrate the fraction of chains that did not reinitiate. The extracted polymer in Figure 2a apparently underwent almost complete reinitiation, since there is no measurable initial polymer remaining, which would correspond to dead chains. Thus, the separation process is extremely efficient in terms of removing dead chains. The PDI of 1.84 ($\bar{M}_n$ = 212 000) is rather (but understandably) high here due to the very high target molar mass (ca. 500 000) resulting in less control, but still good living behavior.

The extension data for the unextracted polymer show a significant fraction of high M polymer that apparently contains some RAFT groups, as expected. A large fraction of the chains were not reactivated (Figure 2b); these (apparently up to about 30%) show almost no UV signal, indicating absence of the RAFT functionality. The PDI of 1.80 ($\bar{M}_n$ = 224 000) is similar to that of the chain extended extracted polymer in this case, due to the high target M being the dominant factor controlling the PDI here.

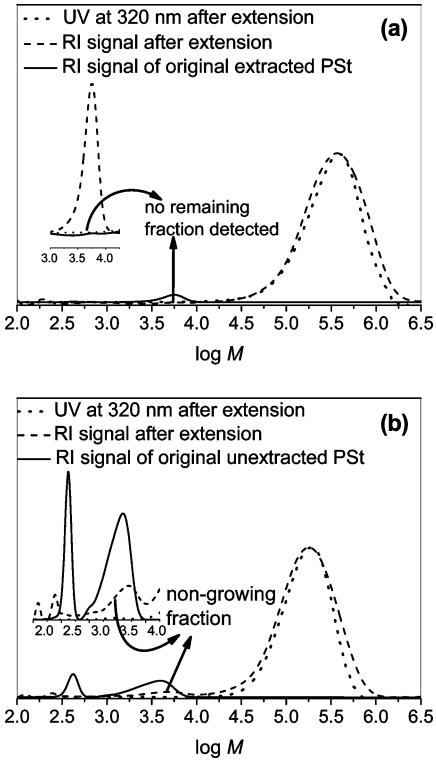

Figure 2. Differential refractive index and corrected UV (320 nm) size exclusion chromatograph traces of polystyrene (PSt) chain extended polymers initially produced from **1**: (a) using the purified polymer extracted with magnetic nanoparticles; (b) using the polymer remaining in the solution after extraction.

Further samples were prepared under similar conditions, but using a high initiator concentration (using 8.5 g of styrene (82 mmol), 0.042 g of AIBN (0.26 mmol), 0.15 g of RAFT agent **(1)** (0.52 mmol) at 70 °C for 4.5 h), and successfully extracted. These accentuated the separation of living chains from dead chains and showed apparent cross-termination side products. The mechanistic and diagnostic implications of this will be discussed in a forthcoming publication, as will this extraction process at the end of each polymerization stage in the formation of purer diblock (or multiblock) copolymers. Promising work is in this regard is in progress.

Dithiobenzoates were used here, which undergo extensive retardation and apparent cross-termination reactions. The apparent cross-termination products are presumably dead chains, and if this is the case, the extracted product is not completely living. Trithiocarbonates induce less retardation and form lower intermediate radical concentrations, which should minimize any cross-termination; studies using trithiocarbonates show promising initial results.

Improvements to this technique are under investigation, such as the use of Z groups that form stronger attachments (e.g., phosphates) to the MNPs and the use of trithiocarbonates.

Conclusions. MNPs were used to separate living chains from dead chains prepared by the RAFT process using Z-functional RAFT agents with very high efficiency. Separated living chains showed apparently 100% RAFT functionality, a lower PDI than the as-prepared polymer, and no detectable dead chains. Chain extension of the separated living chains showed no measurable deviation from 100% extension efficiency, whereas the remaining chains showed poor extension efficiency.

This is, to our knowledge, the first efficient postpolymerization separation method of living from dead chains formed in a homogeneous medium by CRP. Since this method incorporates the RAFT process, it can produce a broad range of ultrahigh-purity diblock copolymers.

Although the results here were for styrene-based polymers, initial results for the attachment to MNPs and extraction have been successful for homo- and copolymers based on other monomers, and it is expected that this process will be applicable for a wide range of polymers.

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Supporting Information Available: Further detail on the syntheses and experimental techniques. This material is available free of charge via the Internet at http://pubs.acs.org.

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