Practical Chain-End Reduction of Polymers Obtained with ATRP


A practical and user-friendly strategy for the chain-end reduction of halogen terminated polymers that employs hydrogen gas and heterogeneous catalysis (palladium on carbon) is reported. Quantitative dehalogenation of a wide variety of monomer families (polystyrenes, polyacrylates, and polymethacrylates) with either chlorine or bromine chain-ends is observed. The utility of this chain-end reduction is further highlighted by mild reaction conditions, simple purification, and compatibility with a wide range of solvents.

1. Introduction

Modern reversible deactivation radical polymerization (RDRP) techniques have enabled the preparation of well-defined, functional polymers by nonexperts without the need for rigorous experimental setups. Atom transfer radical polymerization (ATRP)\(^1\textsuperscript{–3}\) and copper(0)-mediated RDRP\(^4\textsuperscript{–7}\) stand out as powerful synthetic variants of RDRP due to the large number of compatible monomers and initiators available. A consequence of these mechanisms is the presence of a halide chain-end, which not only permits reinitiation of the polymer leading to block copolymers, but also serves as a valuable functional handle for postpolymerization modification with nucleophiles such as azides and thiols.\(^8\textsuperscript{–11}\) While useful synthetically, the inherent reactivity of these halide chain-ends is often an undesirable feature from a performance and properties perspective for the final materials.\(^12,13\) Studies by the Bibiao, Hawker, and Barner–Kowollik groups have demonstrated the deleterious effect of bromine chain-ends in a range of polystyrene samples under thermal and thermomechanical stress due to the generation of HCl/HBr through elimination.\(^14\textsuperscript{–17}\) Additionally, even small changes to the nature of the chain-end groups (i.e., oxidation or hydrolysis over time) have been shown to have significant impacts on properties as well as polymer self-assembly.\(^18\textsuperscript{–21}\)

To resolve the issue of undesired chain-end reactivity, Matyjaszewski and Coessens reported the dehalogenation of bromide terminated polymers in 1999 using tributyltin hydride and a radical initiator (Scheme 1A).\(^22\) This protocol forms Sn-based radicals that react with the terminal alkyl halides to form carbon-centered radicals. These chain-end radicals can then react with tributyltin hydride to give the hydrogen terminated chain-end and regenerate...
a tributyltin radical that continues the radical chain process. Since the publication of this method, it has been the primary tool used by polymer chemists for the conversion of halogen chain-ends into more inert hydrogen atoms. While effective, this method has a number of disadvantages, such as the use of undesirable tributyltin hydride, the need to exclude oxygen, and the formation of chain–chain coupled polymers as by-products. Additional methods for chain-end removal of ATRP polymers have been reported.[23,24] However, these approaches typically involve the reaction of chain-end radicals with other hydrogen donors, such as excess N,N,N′,N″,N‴-pentamethyldiethylenetriamine (PMDETA) ligand[13] or cumene,[15] and have not been readily adopted. Further methods involve the reduction of the bromides using zinc metal in acetic acid[25] and transfer hydrogenation with homogeneous ruthenium complexes,[26] the latter requiring forcing conditions and expensive catalysts. Recently, a photochemically driven and spatially resolved reduction protocol was developed by our group, however, the process is limited by the use of a noncommercial photocatalyst and specific solvents.[16,27]

In contrast to these methods, a commonly employed reaction in small molecule organic chemistry is the reduction of halogen containing organic molecules with hydrogen in the presence of a noble metal heterogeneous catalyst, such as palladium on carbon (Pd/C).[28–30] These reactions have a number of advantages over the tin-based methodologies including the tolerance of a wide range of solvents, less need for moisture exclusion, and the use of hydrogen gas as an ideal stoichiometric reductant. Importantly, the products are frequently obtained in quantitative yields after simple filtration. The heterogeneous catalysts employed in the dehalogenation reactions have been shown to be recoverable[31,32] and the process scaled to multiton levels[33] Given the mild and high yielding nature of these reactions, we were interested if the robustness and generality of this approach could be extended to the clean and selective reduction of halogen chain-ends of polymers prepared using ATRP and copper (0)-mediated RDRP techniques.

2. Experimental Section

2.1. Materials and Characterization

All materials were purchased from Sigma-Aldrich and used as received unless otherwise noted. Palladium on carbon (10 wt%) was purchased from Strem Chemicals Inc. All solvents were purchased from Fischer Scientific and used as received, with the exception of tetrahydrofuran (THF), which was passed through activated alumina columns. Polymer samples were prepared using ATRP[34] (PTBA-Br, PS-Br, PS-Cl), organic photo-ATRP[35] (pMMA-Br), or photoinduced Cu(II)-mediated radical polymerization[36] (PMA-Br) following literature methods.

Nuclear magnetic resonance spectra were recorded on a Bruker 500 MHz or a Varian 600 MHz instrument. All 1H-NMR experiments are reported in δ units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26 ppm) in the deuterated solvent, unless otherwise stated. Gel permeation chromatography (GPC) was performed on a Waters 2695 separation module with a Waters 2414 refractive index detector in chloroform with 0.25% triethylamine (TEA). Number average molecular weights (Mn) and weight average molecular weights (Mw) were calculated relative to linear polystyrene standards for calculation of Mw/Mn. A Micromass QTOF Quadrupole/Time-of-Flight Tandem mass spectrometer was used for mass analysis of polystyrene (PS) samples using field desorption mass spectroscopy (FD-MS). Matrix-Assisted Laser Desorption Ionization time of flight mass spectrometry (MALDI-ToF-MS) was conducted using a Bruker Microflex LRF MALDI-ToF mass spectrometer, equipped with a 60 Hz nitrogen laser at 337 nm. Solutions in tetrahydrofuran with dithranol as the matrix (saturated solution, 10.0 µL) sodium trifluoroacetate as the cationization agent (1.0 mg mL⁻¹, 2.0 µL) and the sample (1.0 mg mL⁻¹, 10.0 µL) were mixed, and 0.7 µL of the mixture was applied to the sample plate.
applied to the target plate. Spectra were recorded in reflectron mode for poly(methyl acrylate) (PMA) samples.

### 2.2. Hydrogenation of Polymer Chain-End

Representative procedure for chain-end hydrogenation:

- **Bromine terminated polystyrene (PS-Br)**
  \( M_n = 1500 \text{ g mol}^{-1}, \quad M_w/M_n = 1.17 \) (300 mg, 0.16 mmol) was added to a 20 mL green cap vial equipped with a stir bar and septum. The polymer was dissolved in THF (7.9 mL) and TEA (110 µL) was added followed by palladium on carbon (17 mg of 10 wt% Pd/C). The vial was capped and the reaction mixture was bubbled with H2 using a balloon connected to a needle with needle outlet (21 gauge) for 15 min. The balloon needle was then moved from the solution to the headspace, and the vent needle was removed. The reaction mixture was vigorously stirred for 4 h under a hydrogen atmosphere. The reaction mixture was then purged with argon to evacuate hydrogen gas and the reaction mixture was filtered through a pad of Celite. This mixture was concentrated in vacuo and precipitated into methanol (80 mL) to give PS-H as a white powder \( M_n = 1600 \text{ g mol}^{-1}, \quad M_w/M_n = 1.18 \). Alternative workup procedures involve extraction with aqueous HCl (1M) after Celite filtration or layering Celite with acidic alumina in order to remove the triethylamine (and corresponding salt).

- **Note:** Celite should not be filtered to dryness due to a fire hazard from ignition of the palladium on carbon; water should be added to the Celite afterward to quench active Pd/C.

### 3. Results and Discussion

To initially test this approach, bromine-terminated poly(methyl acrylate) (PMA-Br) \( (M_n, 1100, D: 1.10, \text{Scheme 1B}) \) was prepared using copper(II) bromide-mediated photopolymerization\(^{36}\) and subjected to heterogeneous...
hydrogenation reaction conditions with Pd/C (Table 1, entry 1). Significantly, the reaction was operationally straightforward to setup. PMA-Br was dissolved in THF and followed by the addition of a catalytic amount of Pd/C. The resulting solution was bubbled with hydrogen gas from a balloon for 10 min, followed by rapid stirring under the hydrogen atmosphere at room temperature. The reaction was easily monitored with ¹H-NMR by following the disappearance of the proton alpha to the terminal bromide at 4.5 ppm (black circle, Figure 1A) and the terminal methyl ester at 3.7 ppm (black triangle). Smaller changes in the ¹H-NMR are also noted in the 2–3 ppm range due to the electron withdrawing influence of the bromide on more distal protons. The reaction proceeded rapidly and quantitatively, with no chain-end protons observable for the bromine-terminated starting polymer after 1 h. Despite the absence of starting material signals by ¹H-NMR, this reaction and all future reactions were performed for a total of 4 h to ensure full reduction of the halide. Triethylamine was added to the reaction mixture to scavenge hydrobromic acid that is formed as a by-product. In the absence of base, the reaction does not go to completion, which is consistent with reports that hydrobromic acid poisons heterogeneous catalysts such as Pd/C. Other amine bases were also briefly explored. Diisopropylethylamine performed identically to TEA, though pyridine was less effective and incomplete conversion was observed (Figure S3, Supporting Information).

Further characterization reinforced the observation of complete and quantitative conversion of the bromo group to a hydrogen chain-end. MALDI-ToF-MS of both the starting PMA-Br and the product PMA-H (Figure 2A) shows only one set of periodic peaks. In each spectrum, the peaks are separated by 86 mass-to-charge units correlating to the molecular mass of a methyl acrylate repeat unit. Additionally, the observed mass values for each peak in the PMA-Br series are identical to the calculated molecular weight for poly(methyl acrylate) initiated with ethyl α-bromoisobutyrate. As shown in an expanded portion of the MALDI spectra (Figure 2B), an m/z = 1077.3 corresponds to the sodium salt of the decamer of PMA-Br. An analogous set of peaks are present for PMA-H, but they do not have the isotopic splitting and are offset by 78 mass-to-charge units, which corresponds to the loss of a bromine and addition of a hydrogen. Again, the m/z = 999.4 is fully consistent with the sodium salt of the PMA-H decamer. GPC showed no observable change in the chromatogram (Mₙ 1100, D: 1.14) with the PMA-Br and PMA-H traces being fully superimposable (Figure 3). This highlights the absence of any chain–chain coupling or crosslinking reactions taking place during this dehalogenation reaction, which has been observed in classical radical dehalogenation methods.

Encouraged by the initial results with PMA-Br, the scope of this method was extended to encompass a range of monomer families. Acrylates (Scheme 1B) were prepared by a variety of methods (traditional ATRP, metal-free photo-ATRP,[35] Cu(II)-photomediated polymerization,[36] and Cu(0)-RDRP[37]). Using unaltered hydrogenation conditions, the reaction proved to be very general with respect to polymer type, size, and architecture (Table 1). To evaluate a more hindered acrylate monomer, various poly(tert-butyl acrylate) (PTBA-Br) samples were subjected to the hydrogenation conditions. Two different molecular weights (Mₙ 1400 and 6800; DP 9
and 50, respectively) were tested (entries 2 and 3), along with a more architecturally complex six-arm PTBA star polymer (StarPTBA-Br; entry 4). Additionally, poly(methyl methacrylate) PMMA-Br was prepared and hydrogenated (entry 5). This example is particularly notable, since the bromide is on a fully substituted quaternary carbon center. In all of these cases, the polymers were fully converted to the respective dehalogenated polymers as judged by 1H-NMR and mass spectrometric analysis, with no significant change to the molecular weight or molecular weight dispersity (Figures S4–S12, Supporting Information).

Ubiquitous bromide terminated polystyrene (Table 1, entry 6) derivatives were then prepared and their compatibility with the above hydrogenation process evaluated. Once again, without need to modify the standard reaction conditions, the PS-Br was fully converted to the reduced PS-H. These results were confirmed through 1H-NMR chain-end analysis (Figure 4) and FD-MS (Figure S15, Supporting Information) with GPC analysis clearly showing no chain–chain coupling (Figure S16, Supporting Information). In addition to PS-Br, a chloride-terminated polystyrene (PS-Cl, entry 7) was also examined as a starting material. Alkyl chlorides are generally less reactive in general than alkyl bromides, making the PS-Cl sample a more challenging substrate for the methodology. Despite the reduced reactivity of the carbon–chlorine bond, the H2Pd/C catalytic system was able to fully reduce the polymer chain-end to the corresponding hydrogen under identical conditions and reaction times (Figures S17 and S18, Supporting Information).

In an effort to test the limits of this methodology in terms of practicality and scope, reaction parameters were modified with respect to catalyst loading, concentration, catalyst type, and solvent. First, a larger scale experiment was performed with the more difficult to reduce PS-Cl in which the Pd/C catalyst loading was lowered and the hydrogenation was performed under more concentrated conditions (Scheme 2). Specifically, 3 g of PS-Cl in 12 mL of THF (0.05 M) was hydrogenated with 6.5 mg of Pd/C catalyst (1 mol%) and a reaction time of 4 h. Once again, full conversion of the chloride chain-end to a hydrogen atom occurred with no evidence of side reactions. This suggests that large scale reactions are viable with significant minimization of solvent and catalyst use.

Examination of other palladium catalysts suggests that heterogeneous conditions may be preferable to homogeneous precatalysts. Switching to, Adam’s Catalyst (PtO2), provided similar results to Pd/C for the conversion of PMA-Br to PMA-H in THF (Figure S19, Supporting Information).

Figure 3. GPC traces before and after hydrogenation of PMA-Br are superimposable.

Figure 4. 1H-NMR A) before and B) after hydrogenation of PS-Br highlighting the loss of the diagnostic proton associated with the halogen chain-end.
In contrast, the use of bis(dibenzylideneacetone)palladium(0), Pd(dba)$_2$, as a homogeneous precatalyst results in broadening of the molecular weight dispersity as evidenced by GPC analysis of the resulting PMA-H, suggesting that chain coupling occurs during the homogeneous process. Given the established success of many different heterogeneous catalysts for dehalogenation in small molecule chemistry, it is likely that a wide range of catalysts would also be successful for polymer chain-end reduction. In a final set of experiments, a variety of common solvents were explored for the reduction (Scheme 3). This is particularly important since the solubility profiles of polymeric materials can be a limiting factor during post-polymerization modification. Dehalogenation of PS-Br and PTBA-Br in ethyl acetate and methanol resulted in complete conversion with identical results to the standard conditions in THF (Scheme 3). Given the utility of copper mediated-derived polymers in aqueous systems, water was also examined as a reaction medium.$^{[7,38]}$ To demonstrate this broad utility, PTBA-Br was deprotected with trifluoroacetic acid (TFA) to give water-soluble poly(acrylic acid) (PAA-Br) derivatives that could be quantitatively hydrogenated in water to give PAA-H. Significantly, the same PAA-H product could also be obtained through initial debromination of the PTBA-Br starting material followed by deprotection of the PTBA-H with TFA to give PAA-H. Further characterization of PAA-H was performed on the PMA-H derivative after methylation with trimethylsilyl diazomethane. GPC analysis displayed the expected change in molecular weight compared to the starting PTBA-Br with low dispersity being maintained ($M_n$, 1100, $D$: 1.10 (Figures S20–S22, Supporting Information)). This further highlights the broad applicability of this method to polymer families with widely varied solubility and functionalization profiles.

4. Conclusions

A practical and operationally straightforward protocol for the conversion of bromo- and chloro-chain-ends to inert hydrogen end groups in a range of ATRP-derived polymers is presented. This method offers a number of advantages over existing systems including increased versatility, the use of hydrogen gas as the stoichiometric reductant at balloon pressures, facile reaction setup and purification, fast reaction times, and broad solvent scope. Synthetically, the process is amenable to large scale manufacturing and serves as a practical alternative to currently employed dehalogenation methods.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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