Controlled Synthesis of Single-chain Nanoparticles Under Various Atom Transfer Radical Coupling Conditions

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Introduction

Atom-transfer radical coupling (ATRC) is a promising synthetic route to single-chain nanoparticles (SCNP) and other specialized macromolecules; however, limitations in our current understanding of the key design parameters and ideal reaction conditions remain a barrier to the widespread implementation of this technique. To address these concerns, we have systematically examined the formation of SCNP by ATRC, varying the chemistry of the cross-linkable unit, length of the parent polymer, and ligand for the copper catalyst.

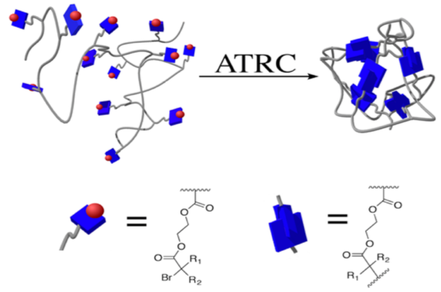

Figure 1. Illustration of SCNP formation using ATRC though pendent monomer units.

Experimental Design

Scheme 1. Copolymerization of MeBrema or PhBrema with Methyl Methacrylate followed by ATRC nanoparticle formation.

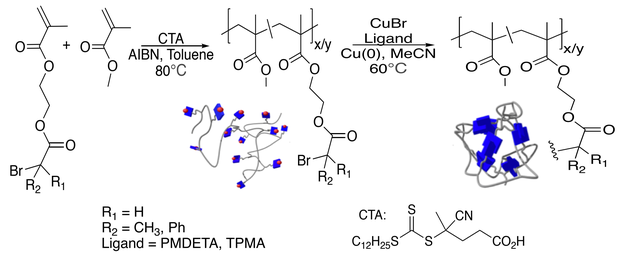

Table 1. Mebrema polymer target characteristics during synthesis.

MeBrema Polymer	Target Molecular Weight (kDa)	Target MeBrema Incorporation	Target MMA Incorporation
1	10,000	25%	75%
2	20,000	25%	75%
3	30,000	25%	75%
4	40,000	25%	75%

Table 2. Phbrema polymer target characteristics during synthesis.

PhBrema Polymer	Target Molecular Weight (kDa)	Target PhBrema Incorporation	Target MMA Incorporation
1	10,000	25%	75%
2	20,000	25%	75%
3	30,000	25%	75%
4	40,000	25%	75%

Characterization of SCNP

An increase in retention time is expected for a nanoparticle because smaller objects take a more torturous path through the GPC chamber. Therefore, the shift in longer retention times of the two desired SCNP, compared to the parent polymer, confirms that the collapses were successful. The nanoparticle collapsed using a TPMA ligand has a small shoulder peak, which is most likely the nanoparticle trace, while the taller, more prominent peak is remaining ligand.

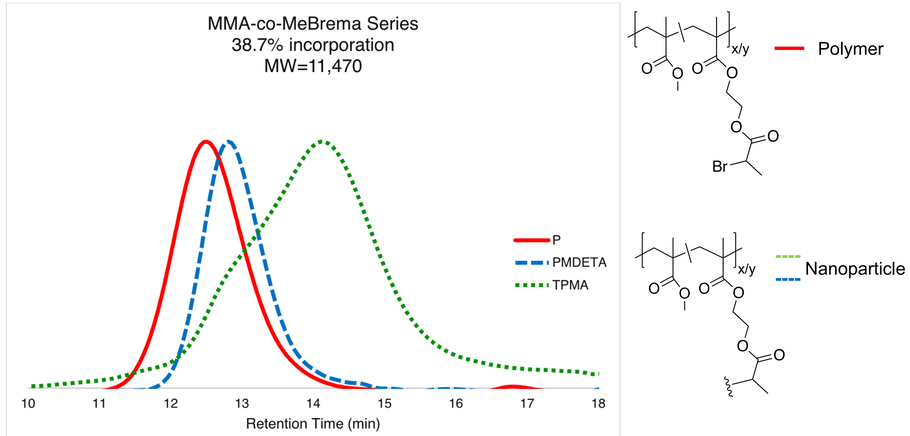

Figure 2: Effect on retention time of collapsing a MeBrema polymer with two different ligands via ATRC.

The characteristic peaks for the parent copolymer, MeBrema, is observed in the H^1 NMR spectrum. As the polymer is collapsed into a nanoparticle, two shift changes occur as the bromine is removed to open a crosslinking site. The ATRC reaction changes the environment of protons, A and E, causing them to shift up-field where you can see the A' and E' peaks grow in the SCNP spectra.

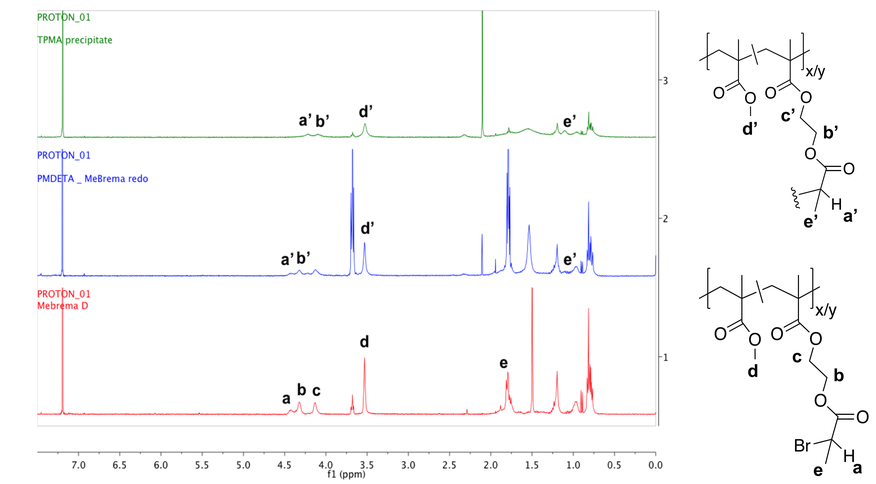

Figure 3: H NMR of MeBrema parent polymer, and two SCNP collapsed with a different ligand via ATRC.

Discussion

Both of the copolymers, MeBrema and PhBrema, were synthesized successfully and tracked by H^1 NMR. The integration of peaks B and C were used to calculate the percent incorporation of MMA to MeBrema and PhBrema. H^1 NMR also shows the two significant peak shifts in protons A and E. During the ATRC process, radical are formed at the bromine-terminated site in order for crosslinking to occur. This change in environment will then affect where those two proton peaks are observed. When comparing the parent copolymer spectrum to the SCNP spectrum, it is clear that these two peaks, now labeled A' and E' have shifted up-field. The GPC MALS also confirms the polymer collapse as both SCNP traces have longer retention times indicating they took a more torturous path through the column. The left shoulder on the TPMA peak is the target compound while the large peak is likely due to excess ligand.

Summary and Future Work

The MeBrema and PhBrema target monomers, polymers, and Single-chain nanoparticles, were all synthesized successfully. The proton NMR and GPC data confirm the polymer formation and collapse into SCNP. A few of the remaining single-chain nanoparticles in the series need to be synthesized and corresponding data must be collected and analyzed.

Other combinations of ligand, solvent, polymer length, and copolymer percent incorporation could be used to further identify the key design parameters and reaction conditions for the ATRC synthetic route to SCNP.

Acknowledgements

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References

1. Hanlon, A. M.; Lyon, C. K.; Berda, E. B.: What is next in single-chain nanoparticles? *Macromolecules* **2016**, *49*, 2-14.
2. Hanlon, A. M.; Chen, R.; Rodriguez, K. J.; Willis, C.; Dickinson, J. G.; Cashman, M.; Berda, E. B. Scalable synthesis of single-chain nanoparticles under mild conditions. *Macromolecules,* **2017**, *50*(7), 2996-3003.