Fabrication of Polymer Nanoparticles *via* Intrachain Ring-Opening Metathesis Polymerization (ROMP)

Sarah J. Benware, Isabelle M. Crawford-Eng, Ruiwen Chen, Erik B. Berda. Department of Chemistry, *University of New Hampshire.*

Introduction

The function of biomolecules is heavily dependent on structure and specific placement of functional groups. The formation of these precise structures is often the result of perfectly controlled polymerizations. Many polymer chemists study fundamentals of these complex natural processes and attempt to synthesize similarly complex and feature-rich macromolecules. To this end, research in the Berda group involves the synthesis of polymers with narrow molecular weight distributions using controlled radical polymerizations. These polymers are designed to incorporate cross-linkable functionalities which may be reacted to form three-dimensional nano-objects. Intramolecular cross-linking induces a collapse observed by the reduction of the hydrodynamic radius of the polymer, producing single-chain nanoparticles (SCNPs) (Fig. 1)[1].

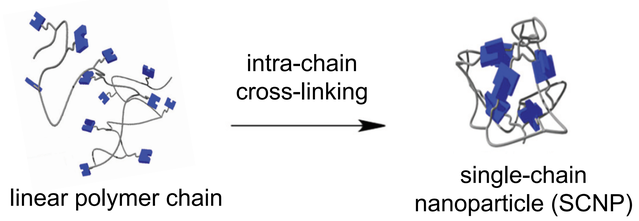
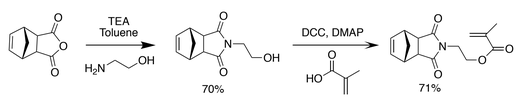


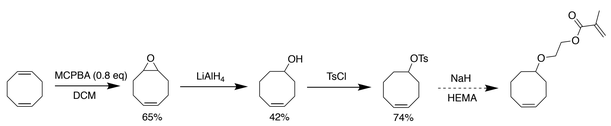
Fig. 1 Linear polymer chains are decorated with functional groups that will promote intra-chain interactions when triggered in dilute solution.

Monomer Synthesis



Scheme 1. Synthetic route to norbornene-imide methacrylate monomer

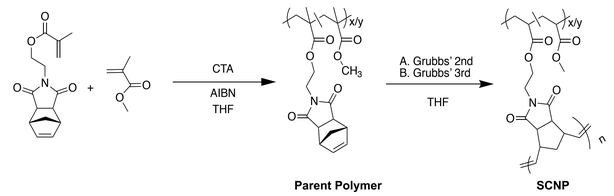
The norbornene imide ethanol was synthesized through the reaction of the cyclic anhydride with 2-aminoethanol and triethyl amine. A dicyclohexylcarbodiimide (DCC) coupling converted the product to NBI-methacrylate, through the use of dimethylamino pyridine (DMAP) and methacrylic acid (Scheme 1).



Scheme 2. Synthetic route to substituted cyclooctene (SCO) methacrylate monomer

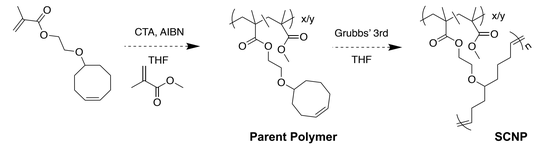
Monoepoxidation of cyclooctadiene was facilitated by *m*-chloroperbenzoic acid. The product underwent reduction by lithium aluminum hydride and subsequent protection of the alcohol through tosylation. Substitution with hydroxyethyl methacryale will form the bifunctional substituted cyclooctene (SCO) methacrylate monomer (Scheme 2).

Synthesis of SCNPs



Scheme 3. Synthetic Route to NBI-methacrylate SCNPs

The random copolymer was synthesized with a target of 20% incorporation of NBI-methacrylate in poly(methyl methacrylate). The resulting copolymer was found to contain 15.9% incorporation by nuclear magnetic resonance (NMR) analysis. The polymer was cross-linked into single-chain nanoparticles (SCNPs) in dilute solution *via* ring-opening metathesis polymerization (ROMP) through the use of Grubbs' 3rd and 2nd generation catalysts (Scheme 3). Intra-chain ROMP of SCO decorated RAFT polymers will also be explored. By confining the SCO monomer to a polymer chain, this work will investigate the minimum effective local concentration of ROMP active pendants (Scheme 4).



Scheme 4. Synthetic Route to SCO-methacrylate SCNPs

Characterization of SCNPs

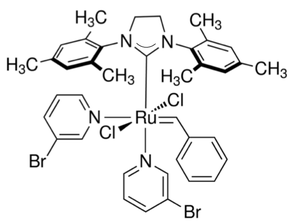


Fig. 2 Grubbs' 3rd generation catalyst

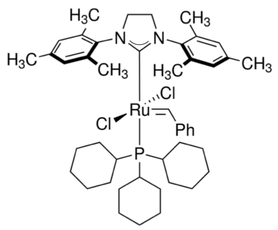


Fig. 3 Grubbs' 2nd generation catalyst

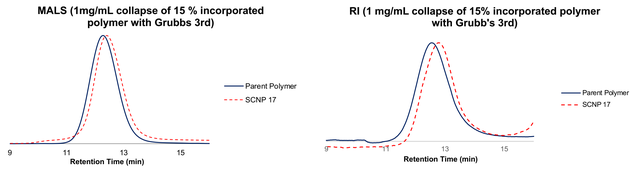


Fig. 4 GPC trace of parent polymer and SCNP formed through Intra-chain ROMP with Grubbs' 3rd generation catalyst (1mg/mL). Multi-angle light scattering (MALS) and Refractive Index (RI) traces are reported. An Increase in retention time from parent polymer to SCNP is observed.

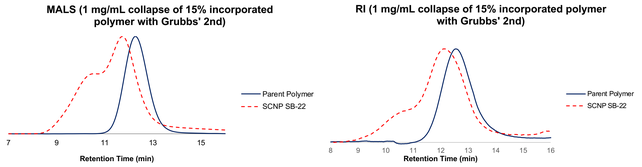


Fig. 5 GPC trace of parent polymer and SCNP formed through Intra-chain ROMP with Grubbs' 2nd generation catalyst (1mg/mL). Multi-angle light scattering (MALS) and Refractive Index (RI) traces are reported. No increase in retention time of the SCNP is observed, coupled with a broad, higher molecular weight distribution.

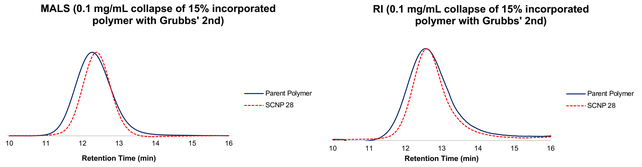


Fig. 6 GPC trace of parent polymer and SCNP formed through Intra-chain ROMP with Grubbs' 2nd generation catalyst (1mg/mL). Multi-angle light scattering (MALS) and Refractive Index (RI) traces are reported. An increase in retention time of the SCNP is observed with no higher molecular weight aggregates.

Characterization continued

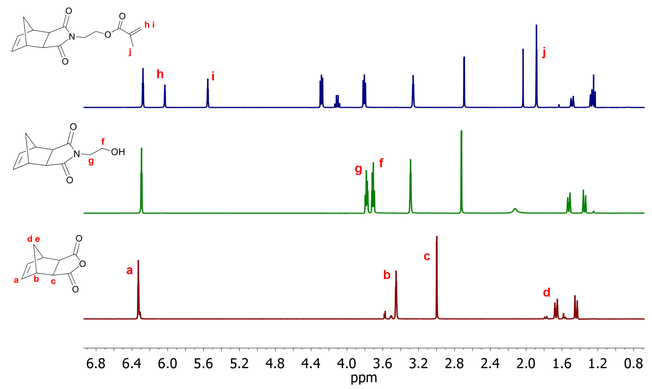


Fig. 7 Stepwise nuclear magnetic resonance analysis

Summary and Conclusions

The results of gel permeation chromatography support the conclusion of the synthesis of SCNPs through the collapse of the parent polymer with Grubbs' 3rd as well as Grubbs' 2nd generation catalyst. The effective reactions were noted by an increase in retention time, suggesting a decrease in the hydrodynamic radius of the particles. Effective intramolecular crosslinking of the 15% incorporated polymer with Grubbs' 3rd was carried out at 1 mg of polymer per mL of solvent, while the Grubbs' 2nd collapse to SCNPs is effective at 0.1 mg/mL. This is likely attributed to the slower initiation time of Grubbs' 2nd, associated with a higher probability of formation of multi-chain aggregates.

Future Work

- Perform collapse experiments with Grubbs' 3rd on 30% incorporated polymer and collapse with both catalysts on 50% incorporated polymer
- Prepare and collapse polymers with varying incorporation of SCO-methacrylate
- Identify minimum local concentration of polymer bound SCO units for effective intrachain ROMP

Acknowledgements

The authors would like to graciously thank both the Army Research Office and the Army Educational Outreach Program for the support, as well as the program for its funding which allowed research to be conducted and presented. We would also like to thank Dr. Erik Berda, for sharing his time and expertise.

References

1. Lyon, C. K., Prasher, A., Hanlon, A. M., Tuten, B. T., Tooley, C. A., Frank, P. G., & Berda, E. B. (2015). A brief user's guide to single-chain nanoparticles. *Polymer Chemistry*, *6*(2), 181-197.