

**Investigating the fundamentals of ring-opening metathesis
polymerization to synthesize large, well-defined, bottlebrush polymers**

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ABSTRACT

Ring-opening metathesis polymerization (ROMP) is a robust synthetic technique for synthesizing complex polymer architectures (topologies). To achieve complex architectures, specifically bottlebrush polymers, using ROMP, attaining the highest degree of living character is essential. As the molecular weight of the side chain or backbone increases, the “livingness” of the polymerization suffers due to premature catalyst degradation. Attaining large, well-defined, bottlebrush polymers requires precision so it was our goal to determine how seemingly simple reaction variables could affect the rates of propagation and achievable conversion, as well as why these variables have these effects.

We tested several reaction parameters to understand how they affect the rate of polymerization, the rate of catalyst degradation, and the conversion that can be reached. We performed a systematic study using six organic solvents to determine the propagation rate of three macromonomers (MMs), one polystyrene and two poly(*n*-butyl acrylate) MMs, in ROMP with varying side chain chemistries and end groups, as well as rate of catalyst degradation in each of the solvents. We determined that solvent affected that rate of propagation primarily by interacting with the catalyst, while there was some evidence of polymer sidechain chemistry affecting the rate. We found that ethyl acetate (EtOAc) and CH₂Cl₂ had the highest rates of propagation compared to the other solvents, while DMF and THF were the slowest. UV-Vis testing on the catalyst in each solvent revealed that

DMF and THF had fast rates of catalyst decomposition, while toluene was much slower to decompose. From these experiments we learned that toluene, despite its slower propagation rate, has the most living character, due to its slower rate of decomposition. We also learned that purification greatly affects the propagation rate, with THF requiring purification to have any conversion to bottlebrush polymer, while purification of EtOAc slows the rate of propagation almost 2-fold. From the decrease in rate after purification, and the conclusion that it was due to an acetic acid impurity in the impure EtOAc, we decided to systematically test small molecule additives and found that acids can increase the propagation rate and the conversion of the polynorbornene backbone achievable in ROMP reactions. Notably, in reactions performed in DMF with added CF_3COOH we were able to polymerize a norbornene-functionalized unprotected peptide, which was insoluble in most organic solvents, to a higher conversion than in DMF without the added acid.

We learned from our research that changing reaction variables can lead to substantial changes in the rate of propagation as well as the achievable conversion in bottlebrush polymer synthesis. By understanding this we can further test other reaction variables and do systematic studies on atmosphere and temperature. We hope this research and future fundamental research can guide scientists toward synthesizing large, well-defined, complex polymer architectures using ROMP.

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GENERAL AUDIENCE ABSTRACT

Nature has shown that complex molecular architectures lead to unique material properties. This has inspired scientists to synthetically mimic nature to create these polymer architectures in an effort to obtain novel material properties. Ring-opening metathesis polymerization (ROMP) has become a powerful synthetic method for synthesizing complex polymer architectures. Specifically, ROMP has been used to synthesize bottlebrush polymers, so named due to the polymer backbone with long, densely grafted, polymer side chains attached. These materials exhibit very interesting properties compared to their linear polymer counterparts. Using ROMP to synthesize bottlebrush polymers is not uncommon; however, difficulties can arise if trying to use sidechains that are very long or bulky.

We have worked to understand how manipulating some of the reaction parameters can allow us, and other researchers, to synthesize bottlebrush polymers that contain long and/or bulky polymer side chains. We tested the purity and type of solvent that the reaction was performed in on one polystyrene macromonomer and two poly(*n*-butyl acrylate) macromonomers, as well as adding small molecules, including acids, bases, and salts, to determine if these variables could improve the synthesis of bottlebrush polymers. What we found was that all of the tested variables, solvent, purity, additives, and combinations of all of these variables, did have an effect on the synthesis of these materials. This fundamental

information will assist our lab, and many others, in efficiently synthesizing complex architectures, thus achieving unique material properties.

Dedication

This dissertation is dedicated to my mom, Ann Blosch. Your hard work and sacrifice not only contributed to me attaining this degree, but to the woman I have become. I love you and no amount of thanks will ever be enough.

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Attributions

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Chapter 1

Sarah E. Blosch provided authorship of sections 1.2, 1.4, 1.5, 1.8, 1.10, and 1.11, and edited most figures, as well as providing editing to sections written by coauthors. Mohammed Alaboalirat and Samantha J. Scannelli contributed greatly to the writing of this chapter, with Samantha authoring sections 1.6, 1.9, and 1.13 and Mohammed authoring sections 1.7 and 1.12. Prof. John Matson is the advisor and committee chair and authored sections 1.3 and 1.14, while also providing a large amount of editing assistance.

Chapter 2

Sarah E. Blosch provided the majority of the writing of this manuscript as well as the synthesis and characterization of all bottlebrush polymers as well as the catalyst studies. Mohammed Alaboalirat performed the synthesis of the **PS_{Br}** macromonomer. Cabell B. Eades, as an undergraduate researcher, assisted in the ROMP reactions and kinetics of the small molecule norbornene. Samantha J. Scannelli synthesized the small molecule

norbornene monomer. Prof. John Matson is the advisor and committee chair and provided guidance, writing, and editing assistance.

Chapter 3

Sarah E. Blossch provided the primary writing of the manuscript as well as the synthesis and characterization of all macromonomers and bottlebrush polymers. Yumeng Zhu assisted in the synthesis of **Nb-YIGSR-NH₂** and performed all purification of the peptide. Prof. John Matson is the advisor and committee chair and provided guidance, writing, and editing assistance.

Chapter 1: Complex polymer architectures using ring-opening metathesis polymerization: synthesis, applications, and practical considerations

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1.2 Abstract

Nature shows us that complex molecular architectures lead to unique material properties, and these observations have driven polymer scientists to synthesize complex architectures in an effort to discover how topology influences properties in synthetic polymers. In this Perspective we discuss a variety of complex architectures synthesized using ring-opening metathesis polymerization (ROMP), including multiblock linear polymers, bottlebrush homopolymers and (multi)block copolymers, dendronized polymers, star polymers, and polymer-biomolecule conjugates. Traditional and recently developed synthetic methods including polymerization-induced self-assembly, copolymerization to create gradient structures, and engineering approaches to making complex topologies using ROMP are also reviewed. In this context we highlight emerging applications stemming from these materials, including drug delivery vehicles, nanoscale

constructs, and components in light refraction or energy storage, among others. Finally, we conclude with an in-depth discussion on practical considerations in ROMP that enable the highest level of control when synthesizing complex polymer topologies from sterically demanding or otherwise challenging (macro)monomers. Our hope is that this Perspective will guide scientists synthesizing complex polymer architectures toward new and innovative materials with the potential for unique properties and applications.

1.3 Introduction

Polymers with non-linear architectures (topologies) have fascinated polymer scientists for decades and continue to do so well into the 21st century. Interest in this field is driven largely by the opportunity for complex polymer architectures to reveal how topological changes influence properties. Fundamental questions include how the star architecture influences crystallinity, how lack of entanglements in densely grafted comb polymers (aka, bottlebrush polymers) influences elasticity, and how block copolymer topology influences phase diagrams. These questions are inspired in part by complex polymer architectures that appear in nature, such as many proteoglycans (comb or bottlebrush). In these complex biopolymers, polymer architecture drives function, and polymer scientists aim to follow nature's blueprints to study how synthetic polymers with complex architectures can afford properties and functions inaccessible in linear polymers. However, before new properties and applications can be manifested, precise methods for controlled synthesis of complex polymer architectures are needed.

Early efforts to synthesize polymers with complex architectures focused on comb polymers and star polymers, where a comb polymer contains linear chains emanating from a main chain (sometimes called a backbone chain) and a star polymer is composed of linear chains (arms) emanating from a single branch point.¹ Houtz and Adkins were the first to detect the presence of

comb polymers in 1933 when they polymerized styrene in the presence of polystyrene and observed an increase in viscosity.² A few years later in 1937, Flory proposed that some vinyl monomers could lead to the formation of polymer grafts through chain transfer to polymer reactions, explaining the phenomenon observed by Houtz and Adkins.³ In 1950 at an ACS meeting, Bandel and Alfrey⁴ introduced the idea of graft copolymerization, i.e., a chemically distinct backbone and side chains, with their discovery that vinyl acetate polymerizes in the presence of styrene-vinylidene chloride copolymers to create a graft copolymer.⁵ Star polymers first appeared in 1948 when Schaefgen and Flory reported the first systematic study of 4- and 8-arm poly(caprolactam) star polymers made using core molecules containing 4 or 8 carboxylic acid units, respectively.⁶ This landmark study showed that rational molecular design could be applied to synthesize star polymers with well-defined numbers of arms without crosslinking. Overall, these early efforts laid the groundwork for the complex polymer topologies we know today.

Although methods have existed to synthesize complex polymer architectures for the better part of a century, only in the past few decades has it become possible to synthesize them with a wide range of monomer types and a high level of control over molecular weights, end-group functionalities, and (multi)block structures. Precise structural control has begun to enable careful studies on structure-property relationships. This synthetic success has relied largely on living or controlled polymerization methods, including anionic polymerization, various reversible deactivation radical polymerization (RDRP) methods [primarily nitroxide-mediated radical polymerization (NMRP), atom-transfer radical polymerization (ATRP), and reversible addition-fragmentation chain transfer (RAFT) polymerization], ring-opening polymerization (ROP), and ring-opening metathesis polymerization (ROMP). In many cases, two or more of these polymerization methods can be

combined for rapid synthetic access to complex polymer topologies, sometimes in one pot, eliminating the need for any protection/deprotection schemes.

In this Perspective, we focus on the role of ROMP in making complex polymer topologies. These include (multi)block copolymers, star polymers, biomolecule-polymer conjugates, graft/comb/bottlebrush polymers, dendronized polymers, and other related topologies. We do not discuss cyclic polymers made by ring-expansion metathesis polymerization (REMP),⁷ which is related to ROMP but fundamentally different because the catalysts employed must be designed for REMP to enable both polymer growth and extrusion of the cyclic products. While ROMP is not the only method to make complex polymer topologies, it often has advantages over other methods, such as increased air, water, and functional group tolerance compared with anionic polymerization and a lack of concern for polymer–polymer coupling reactions as can occur in RDRP techniques. We also discuss emerging synthetic strategies, for example, methods where a change in topology occurs, termed macromolecular metamorphosis. Some current and envisioned applications of these polymers are also briefly detailed. Throughout, we discuss how specific choices influence the structure and purity in the final polymer product, including choice of catalyst, monomer type, solvent, and other design or reaction parameters. Finally, we summarize these findings in a section focusing specifically on practical considerations.

1.4 ROMP Catalysts

ROMP is a polymerization method that is typically driven by the relief of ring strain in cyclic olefin monomers⁸ or in some cases by entropy for very large, unstrained cyclic olefins.⁹ The most common ROMP catalysts are the Ru complexes developed by Grubbs (Figure 1.1A-D) and the primarily Mo-based catalysts introduced by Schrock (Figure 1.1E). All of these catalysts are transition metal complexes that contain a carbon–metal double bond. We note that these transition

metal (pre)catalysts may be more accurately referred to as ROMP initiators in many contexts, but we use the more common term catalyst throughout for sake of ease, clarity, and in an attempt to reduce potential confusion. The main practical distinction between these two main classes of catalysts is that the Mo catalysts are somewhat more active, but they are limited by air and moisture sensitivity and react with some common functional groups. In contrast, the Grubbs' catalysts are generally bench stable and tolerate air and water. Additionally, these Ru catalysts have specificity for the C=C bond, which allows for polymerization of monomers with pendant functional groups that often cannot be polymerized by other methods (i.e., those that are sensitive to radicals or anions).

Due to this high functional group tolerance and ease of handling, the Grubbs' catalysts are used widely in ROMP. Of these, Grubbs' 3rd generation catalyst [G3, (H₂IMes)(Cl)₂(pyr)₂RuCHPh] is most commonly used in the synthesis of complex polymer architectures by ROMP due to its fast initiation and propagation kinetics.¹⁰ G3 is the catalyst used in many of the examples discussed here. Either unsubstituted pyridine ligands can be used, or they can be substituted at the 3-position with a halogen, usually Br. Here we do not distinguish between unsubstituted and halogen-substituted versions of G3, referring to both types simply as G3. The G3 catalyst can be easily prepared from commercially available Grubbs 2nd generation catalyst [G2, (H₂IMes)(Cl)₂(PCy₃)RuCHPh] by treatment with pyridine or a substituted pyridine.^{11,12} G2 is itself not typically used in ROMP when living characteristics are needed due to its slow initiation compared to propagation rate; Hoveyda-Grubbs G2 catalyst [HG2, (H₂IMes)(Cl)₂(*o*-OiPrC₆H₄)RuCHPh] exhibits similarly slow initiation.¹³ Grubbs 1st generation catalyst [G1, (PCy₃)₂(Cl)₂RuCHPh] is also used to some extent to make complex polymer architectures by

ROMP because it also exhibits fast initiation related to propagation, enabling living characteristics. However, G1 propagates a few orders of magnitude slower than G2/G3 catalysts.¹⁴

Beyond catalysts capable of mediating ROMP with living characteristics, there exist ROMP catalysts capable of controlling *cis/trans* stereochemistry in the resulting polymer. Some catalysts can also control tacticity in ROMP. Many of these catalysts are based on Mo or W transition metals, although some Ru-based catalysts with control over polymer microstructure have been developed. These topics were recently reviewed by Buchmeiser.¹⁵ In figures here we do not intend to imply control over backbone olefin stereochemistry. Attributes of specific catalysts are discussed in further detail in the Practical Considerations section.

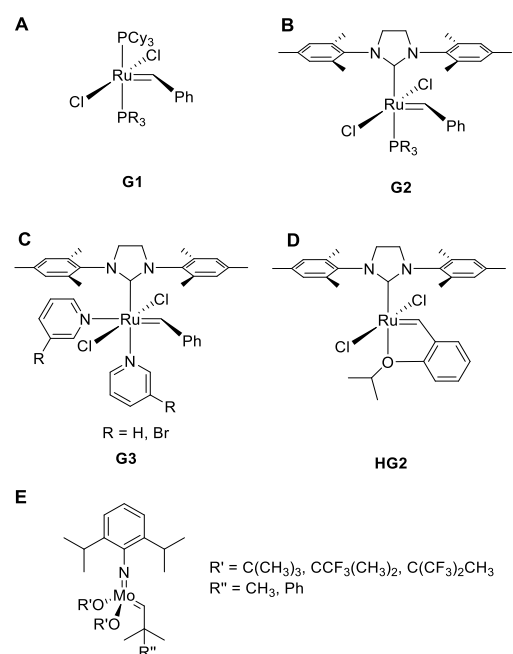


Figure 1.1. Commonly used catalysts for ROMP A) Grubbs' 1st generation (G1), B) Grubbs' 2nd generation (G2), C) Grubbs' 3rd generation (G3), D) Hoveyda-Grubbs' 2nd generation (HG2), and E) Schrock Mo-based catalysts.

1.5 Block and Multiblock Copolymers

Block copolymers (BCPs) have been investigated extensively since their introduction in the early 1950s.¹⁶ Most BCPs to date have been made using anionic or RDRP methods using vinyl

monomers. An advantage of using ROMP for the synthesis of BCPs is the straightforward functionalization of strained cyclic olefin monomers such as norbornenes coupled with the high functional group tolerance of ROMP.¹⁴ Synthesizing BCPs and multiblock (i.e., those with more than 2 blocks) copolymers via ROMP is operationally simple because each monomer can be consecutively polymerized to full conversion, avoiding intermediate workup steps that are required in most RDRP BCP syntheses. BCP synthesis by ROMP dates back to the 1990s using Ru- and Mo-based catalysts and has been reviewed recently.¹⁷ ROMP can also be paired with other polymerization techniques, such as silyl aldol condensation polymerization as early as the late 1980s,¹⁸ and more recently ATRP, RAFT, or ROP, to create BCPs and multiblock copolymers from different monomer classes.^{19–21}

While BCP synthesis via ROMP is relatively straightforward, catalyst death (the main form of chain termination in ROMP), makes the preparation of triblock, tetrablock, or higher multiblock copolymers challenging. The catalyst death is a result of the monomer-starved conditions that occur as monomer concentration drops toward the end of each block addition, increasing the polymerization time, allowing for catalyst decomposition.²² Regardless of these challenges, synthesis of BCPs and multiblock copolymers by ROMP has enabled the creation of unique polymer structures, supramolecular aggregates, and applications.²³

1.5.1 Linear multiblock copolymers

Triblock copolymers have been synthesized using ROMP to achieve telechelic materials for achieving specific endgroups.²⁴ Kilbinger and coworkers developed a strategy for synthesizing these difunctional telechelic polymers with low dispersities using ROMP and termed the method “sacrificial synthesis”.²⁵ This synthetic technique involves chain-extending a polymer with a polymer block that is eventually cleaved, or sacrificed, to leave a specific end group on the first

polymer. Their first example of sacrificial synthesis involved BCP synthesis by chain extending a poly(*exo-N*-phenylnorbornene-2,3-dicarboximide) (PNI) with a dioxepine monomer (a 7-membered cyclic olefin containing a degradable acetal linkage). The poly(dioxepine) block in the resulting diblock copolymer was sacrificed via acid-catalyzed degradation of the acetal units to leave a single hydroxyl group attached to the PNI homopolymer ω chain end, which was used to install a number of different functional groups onto the PNI chain end (Figure 1.2A). While this method enabled simple functionalization of the ω end of the PNI homopolymer, the α chain end remained a phenyl group left behind from initiation with the ruthenium catalyst. In follow-up work, Kilbinger and coworkers made an ABA triblock copolymer of the structure poly(dioxepine)-*b*-PNI-*b*-poly(dioxepine) with two different types of poly(dioxepines) cleavable under different conditions.²⁴ Sequential degradation of the poly(dioxepine) blocks followed by chain end modification reactions allowed them to tune both of the PNI chain ends independently (Figure 1.2B). While this method was successful, a drawback was the consumption of one equivalent of catalyst for every telechelic PNI chain. The authors found that if they synthesized ABABA pentablock or even ABABABA heptablock copolymers with alternating poly(dioxepine) and PNI blocks, followed by acid hydrolysis, they could synthesize two or even three telechelic PNIs per equivalent of catalyst.

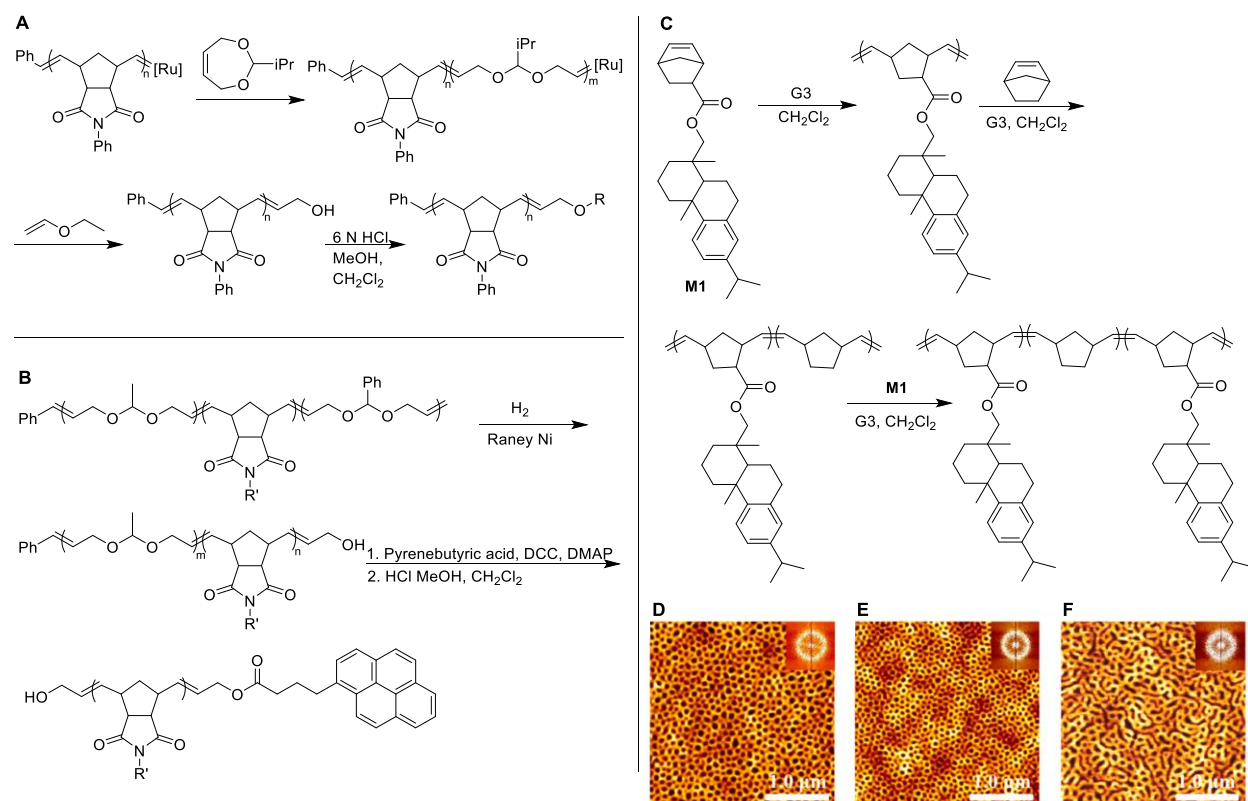


Figure 1.2 Synthesis of A) Di- and B) ABC triblock polymers by ROP to create telechelic polymers via sacrificial synthesis. C) Synthetic scheme for ABA triblock copolymer synthesis, D-F) atomic force microscopy (AFM) images of microphase separated films created by ABA triblock copolymers for different block molecular weights. Adapted with permission from references ^{24–26}.

The synthesis of multiblock copolymers by ROMP is not limited to sacrificial synthesis. An early example of multiblock copolymer synthesis by ROMP reported in 2004 involved the polymerization of norbornene monomers containing acetyl-protected carbohydrates.²⁷ In this work, G1 catalyst mediated the synthesis of tetrablock copolymers with high conversions and low dispersities (usually within the range of 1.10-1.20), although block lengths were generally small with overall molecular weights limited to ~30 kg/mol. Astruc and coworkers took a similar approach, using G3 catalyst to initiate the polymerization of multiple different monomers in sequence to make electrochromic triblock and tetrablock copolymers with side-chain metallocene units.^{28,29} Recently, Tang and coworkers reported the synthesis of tri- and pentablock copolymers

with high molecular weights using sequential ROMP to create tough bioplastic films.²⁶ Here, G3 catalyst was used to prepare ABA and ABABA copolymers from a dehydroabietic acid-derived norbornene monomer (natural rosin functionalized with a norbornene unit, shown in Figure 1.2C) and norbornene. Molecular weights ranged from 100–200 kg/mol, and these copolymers created microphase-separated materials that were molded into stiff yet tough films (Figure 1.2D-F). This example highlights how ROMP can be used to synthesize well-defined multiblock linear copolymers from renewable sources that exhibit microphase separation, leading to high toughness that is difficult to achieve in many bio-derived polymers.

1.5.2 Ring-opening metathesis polymerization-induced self-assembly

Polymer-induced self-assembly (PISA) is a method of producing BCP nanomaterials with high solids contents (often >10%) that avoids isolation and dialysis steps traditionally required in making these materials. This process begins with a homopolymer that is chain-extended with a second monomer and is highly dependent on the solubility of this second monomer and its polymer in the chosen solvent in this chain-extension step. The original homopolymer is soluble in the solvent, as is the monomer for the chain-extension step; however, as the second monomer polymerizes, the polymer becomes insoluble in the solvent, driving self-assembly into nanostructures.³⁰ RDRPs are often used for PISA, specifically RAFT as it offers an extensive breadth of functional monomers.^{31–33} In the past decade, ring-opening metathesis polymerization-induced self-assembly (ROMPISA) has been implemented to complement RAFT PISA approaches. Unlike traditional PISA by RAFT, ROMPISA allows for materials that can be synthesized at room temperature under air while also incorporating complex monomers.³⁴ Additionally, ROMPISA can be carried out using backbone chemistries that could not be implemented using traditional RAFT or other radical strategies (i.e., degradable linkages).³⁵

ROMPISA was first introduced as an *in situ* polymerization method in 2010.³⁶ G1 catalyst mediated the polymerization of a norbornene monomer to make a homopolymer that was soluble in toluene; next, an oxanorbornene monomer that was soluble in toluene was added, forming a block copolymer with a toluene-soluble polynorbornene (PNb) block and a toluene-insoluble polyoxanorbornene (PONb) block. Using this one-pot ROMPISA strategy, nanospheres ranging in size from 136 to 210 nm were synthesized. This work paved a path for synthesizing more complex BCP assemblies by ROMPPISA. For example, Choi and coworkers used ROMPISA to make self-assembled, semi-conducting “nanocaterpillars” containing a polyacetylene core block and a PNb outer soluble block.³⁷ These materials were created by first polymerizing a norbornene monomer in CH₂Cl₂ then chain extending with cyclooctatetraene using G3 catalyst. The formation of the “nanocaterpillar” morphology, which resembles a string of pearls, was attributed to the π - π interactions in the polyacetylene block. A major advantage of the using ROMPISA approach here was that it limited the depolymerization of polyacetylene to form benzene, a problem commonly encountered in ROMP approaches to make this structurally simple but unstable conjugated polymer.

Early research on ROMPISA was performed in nonpolar solvents, but more recently, advances in ROMPISA using polar solvents have been achieved in efforts to make nanostructures with applications in biomedicine. Gianneschi and coworkers utilized a norbornenyl oligo-(ethylene glycol) monomer to form the soluble block and a norbornene-capped protected peptide as the monomer to form the insoluble, chain-extended polymer in a ROMPISA approach (Figure 1.3).³⁴ Solvent studies revealed that a mixture of dimethylformamide and methanol in a ratio of 1:2 was ideal for this PISA synthesis to form a variety of nanostructures depending on the length of the peptide-containing block.

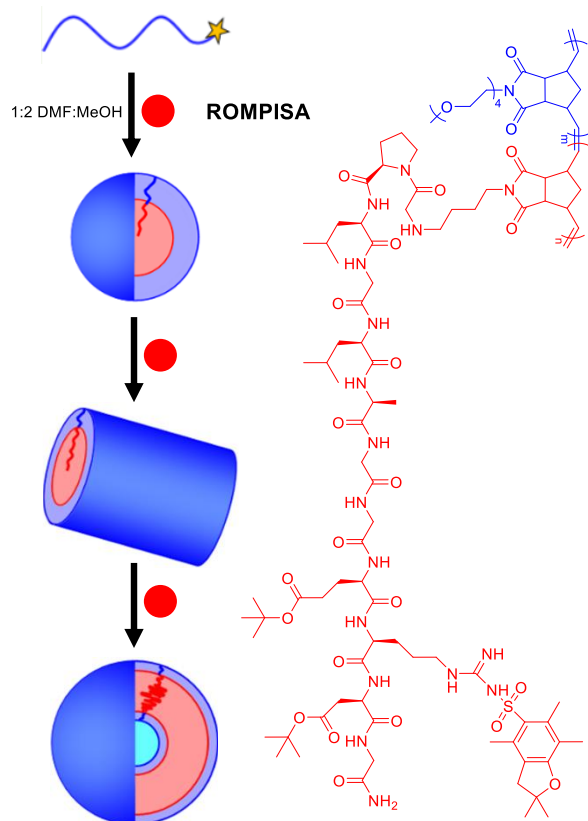


Figure 1.3 Schematic illustration of ROMPISA using a polymer peptide amphiphile. The polymer blue is hydrophilic while the red polymer is a hydrophobic polymer with a pendant peptide. Adapted with permission from reference ³⁴.

The ultimate goal in PISA for biological applications is to conduct the polymerization entirely in water. In the case of ROMPISA, this is difficult due to the insolubility and low activity of most ROMP catalysts in water. Gianneschi and coworkers addressed this problem by using a water-soluble, quaternary amine-based HG2-type second-generation catalyst.³⁸ In this work, a charged, norbornene-capped peptide was used to make the water-soluble block, followed by chain-extension with a quaternary amine-based phenyl norbornene dicarboximide to make the water-insoluble block. The final block copolymer formed spheres for shorter peptide chain lengths and vesicles for larger peptide chain lengths, and cleavage of part of the peptide sequence using the

proteolytic enzyme thermolysin led to the formation of larger aggregates. A related aqueous ROMPISA strategy was applied by the same group to make cisplatin-loaded nanoparticles that displayed cytotoxicity behavior toward human ovarian and cervical cancers.³⁹ Finally, O'Reilly and coworkers have addressed the catalyst solubility problem by first preparing a water-soluble PNb block in organic solvent using the G3 catalyst, then transitioning the water-soluble PNb block into water, with the catalyst still on the chain end, to make the water-insoluble block.⁴⁰ They also discovered that controlling the concentration of Cl^- can increase control over the polymerization, leading to higher conversion in the aqueous ROMP step.⁴¹ As evidenced by the recent work, ROMPISA is a new field that broadens the outlook for potential nanostructures, applications, and capabilities of ROMP.

1.6 Bottlebrush homopolymers

Bottlebrush polymers, also termed molecular brushes, are graft polymers with densely grafted side chains attached to a linear polymer backbone.^{42–44} Many polymerization techniques are suitable for the synthesis of bottlebrush polymer backbones, side chains, or both, using the synthetic strategies detailed below. Historically, anionic polymerization was preferred because it enabled precise control over molecular weight and end group functionality needed to make bottlebrush polymers.⁴⁵ More recently, RDRP techniques as well as ROP and ROMP methods have gained popularity in bottlebrush polymer synthesis. In many cases, more than one type of polymerization technique is used. The general goal is to synthesize bottlebrush polymers with tunable chemical composition, controllable and high grafting density, and tunable side chain and backbone degrees of polymerization (N_{sc} and N_{bb} , respectively). The dense packing and steric repulsion of polymer side chains along the backbone hinders entanglement and forces extension of the backbone chain, forming stiff cylindrical nanostructures in many cases.⁴⁶ The high molecular weight but

unentangled nature of bottlebrush polymers generates interesting mechanical and rheological properties, which are altered by the composition and the N_{sc} and N_{bb} of the bottlebrush polymer.⁴⁷

There exist four general strategies to synthesize bottlebrush polymers, grafting-to, grafting-from, transfer-to, and grafting-through, which differ in how the side chains are connected to the backbone chain.⁴⁸ Grafting-to requires separate polymerization reactions to generate the backbone and the side chains, followed by efficient reactions to attach the side chains to the backbone. The grafting-from method requires the polymerization of a monomer with a pendant functional group to make the backbone chain. Next, initiation sites are attached to the backbone (if they were not already pre-installed on the monomer), which are then used in a subsequent polymerization step to initiate the synthesis of the sidechains. The transfer-to strategy is a hybrid of grafting-to and grafting-from that is less widely used. It involves the synthesis of a polymer backbone with a pendant chain transfer agent attached via the Z-group in the case of RAFT. The side chains are synthesized in a process where propagation occurs free in solution, and the growing side chains return to the backbone via a chain transfer reaction.⁴⁹ Lastly, the grafting-through method involves the synthesis of a monotelechelic polymer with a polymerizable group on one chain end, called a macromonomer (MM). Polymerization of the MM end-groups creates the bottlebrush polymer backbone in a second step. While all four methods have advantages and disadvantages and various potential side products, grafting-through holds the potential for the greatest level of control over grafting density, N_{sc} , and N_{bb} . Although ROMP can be used in all four methods, it is most commonly applied in the grafting-through of MMs, with early reports from Bowden in 2004,⁵⁰ and later Grubbs in 2009,⁵¹ highlighting the capability of ROMP grafting-through to make long cylindrical bottlebrush polymers. ROMP has advantages in the polymerization of MMs over the RDRP methods, which can be hampered by low equilibrium monomer concentrations under

standard conditions, even using low molecular weight macromonomers.⁵² In this section we discuss the use of ROMP in making bottlebrush homopolymers using the grafting-through method, focusing on how different approaches to MM synthesis influence the purity of the ultimate bottlebrush polymer product.

1.6.1 Direct-growth vs. growth-then-coupling

ROMP grafting-through involves the polymerization of MMs, which are made using controlled or living polymerization techniques. MMs used in ROMP grafting-through most often contain a norbornene functional group due to its high ring strain and fast polymerization by ROMP. Here we discuss norbornene-based MMs for the sake of simplicity, but other strained cyclic olefins have been used as well. The release of ring strain in the norbornene unit provides the driving force for the polymerization, and fast initiation rates and even faster propagation rates in ROMP can afford bottlebrush polymers in minutes.¹⁰ The norbornene groups can be present during side chain synthesis or added in a post-polymerization modification reaction, and these approaches are referred to as direct-growth and growth-then-coupling, respectively (Figure 1.4).⁵³

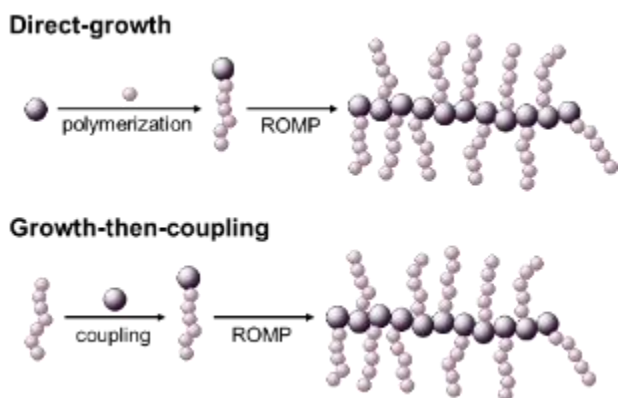


Figure 1.4 Schematic representation of bottlebrush polymer synthesis via the direct-growth and growth-then-coupling strategies.

Direct-growth is most commonly used in making bottlebrush polymers due to the more straightforward synthetic approach. This method relies on the use of a norbornene functionalized with an initiator or chain transfer agent for a different polymerization technique, often ROP or an RDRP technique. Polymerization is carried out from this norbornene-functionalized unit to generate an MM, and then ROMP is used in the second step to form the backbone without any modification. The MM is typically isolated before the ROMP reaction, but one-pot syntheses using the direct-growth method are possible, as detailed below. Bowden and coworkers were the first to synthesize bottlebrush polymers using ROMP in the direct-growth method, achieving narrowly disperse polymers with molecular weights exceeding 60,000 kg/mol.^{54,55} Since then, others have been able to successfully achieve large degrees of polymerization of the backbone using this method, although such enormous molecular weights remain difficult to access for most MMs.

RDRPs are typically used to make MMs to ensure low dispersities and the high chain end fidelity necessary for the subsequent ROMP step. A variety of dual-functionalized small molecules have been made that carry a norbornene (or similar) unit and an initiator or chain-transfer agent (CTA) for the RDRP step. The RDRP techniques most commonly used to make MMs are ATRP⁵⁶ and RAFT.⁵⁷ With these techniques, MMs of polystyrene (PS), poly(methyl methacrylate) (PMMA), poly(methyl acrylate) (PMA),⁵⁸ poly(*tert*-butyl acrylate) (PtBA),⁵⁹ and poly(*N*-isopropylacrylamide)⁶⁰ have been made and used to synthesize bottlebrush polymers via ROMP. In one of the first reports on this topic in 2006, Patton and Advincula showed that the direct-growth method enabled the synthesis of well-defined PS and PMMA MMs using a combination of RAFT and ROMP, with efficient ROMP to generate small BB polymers ($N_{bb} = 8$).⁵⁸

One important consideration in the synthesis of BB polymers using the direct-growth approach is the potential for copolymerization of the norbornene unit in the RDRP reaction. For example, some

studies have shown bimodal MW distributions for the resulting bottlebrush polymers, specifically those where polyacrylates were prepared in the RDRP step.^{56,58,61} Xia and Grubbs noticed this problem in 2009 in the synthesis of MMs using both ATRP and RAFT of acrylates, suggesting that the norbornene can interfere with the initial polymerization of the sidechain.⁵¹ Keddie and coworkers recently reported a systematic study on this problem and suggest some methods to limit it, such as running RDRP reactions to low monomer conversion.⁶¹ However, to avoid this problem entirely, the growth-then-coupling method can be used.

Initially used as early as 1994 by Feast and coworkers with Mo-based catalysts⁶² and later coined by Xia in 2015,⁵³ the growth-then-coupling method involves the synthesis of the side chains followed by a chain end modification reaction to install the norbornene unit (Figure 1.5). Although the growth-then-coupling approach lengthens the synthesis with the addition of intermediate reactions and purification steps, it removes any interference of the sidechain polymerization with the norbornene unit, allowing for the synthesis of well-defined bottlebrush polymers.⁵¹ This synthetic strategy can accommodate a broader scope of monomers and polymerization techniques than the direct-growth strategy but is limited by the intermediate modification step.

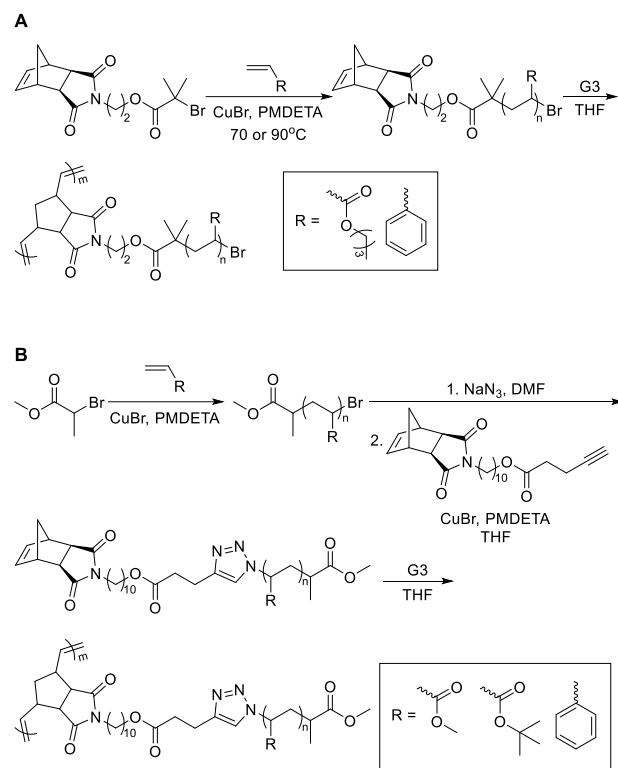


Figure 1.5. Synthesis of various MMs via the A) direct-growth and B) growth-then-coupling approaches. Adapted with permission from references ^{51,53}.

In order for the growth-then-coupling strategy to be successful, highly efficient intermediate reactions need to be used to ensure full functionalization of the sidechains, which typically include “click” reactions⁵³ or carbodiimide couplings.⁶³ Anionic polymerization, RAFT, ATRP, and ROP have been used to polymerize well-defined side chains of PMA, PtBA, PS,⁵¹ PMMA,⁵³ polycaprolactone, and poly(ethylene oxide) (PEO)⁶³ with one end group capable of further reaction. A high-yielding coupling reaction, potentially followed by purification, enables the synthesis of the MM. If done correctly, the growth-then-coupling strategy ensures bottlebrush polymer formation via grafting-through without branching. However, care must be taken to confirm that MMs are fully functionalized with a norbornene or similar unit; MMs lacking a polymerizable unit are simply side chains that do not attach to the backbone in the grafting-through

step. Ultimately, assuming high purity MMs in both cases, when comparing identical MMs made by the direct-growth and growth-then-coupling approaches, those made by growth-then-coupling achieve bottlebrush polymers of higher molecular weight and lower dispersity than those made by direct-growth.⁵³

1.6.2 Purity Considerations

As alluded to above, an important factor to consider when performing the grafting-through method is the intermediate purification of the MM, which tends to be extensive. For direct-growth, these purifications generally include multiple precipitation steps to remove residual monomer, requiring large amounts of solvent and are tedious for polymers with low glass transition temperatures (T_g 's). If vinyl monomers are used to make the MM, exhaustive removal is usually required because even very small amounts of residual monomers such as acrylates can act as chain transfer agents or terminators in ROMP, especially when targeting large DPs or when making bottlebrush polymers using the grafting-through process.⁶⁴ In addition to precipitation steps and residual monomer removal, growth-then-coupling also requires purification after the post-polymerization modification reaction to attach the norbornene. Removal of residual impurities from previous reactions is crucial in order to achieve bottlebrush polymers of high MW and low dispersity. Even after exhaustive removal of any vinyl monomer, small amounts of other impurities (e.g., alkynes) can be detrimental in the ROMP step due to the small amount of catalyst needed in comparison to the MM. Bang and coworkers investigated how residual impurities in MMs made via “click” reactions through the growth-then-coupling method affected ROMP.⁶⁵ They observed higher conversion and lower dispersities for MMs that were rigorously purified compared to MMs with residual impurities, confirming the importance of purity to produce well-defined bottlebrush polymers.

Although impurities can be detrimental to the ROMP step of the grafting-through method, several groups have avoided this problem in developing one-pot syntheses of bottlebrush polymers. One-pot processes simplify the synthesis of bottlebrush polymers by removing intermediate purification steps, although they are limited in scope. The first attempt at a one-pot bottlebrush polymer synthesis by ROMP grafting-through was in 2009 by Cheng and coworkers,⁶⁶ but was reported as uncontrolled with large dispersities compared to a similar grafting-from one-pot method. A successful attempt at a one-pot synthesis was performed in 2012 by Wooley and coworkers using RAFT to make a PMMA MM followed by ROMP with an intermediate cooling step to quench the RAFT reaction (Figure 1.6).⁶⁷ This synthesis was successful despite residual vinyl monomer because MMA does not react with Grubbs' catalysts,⁶⁸ but most other vinyl monomers are metathesis active and therefore cannot be easily used in one-pot syntheses. To broaden the scope of monomers available for a one-step procedure, our group used ROP to make MMs of poly(lactic acid) (PLA) followed by ROMP. The choice of a 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) cocatalyst system for the ROP step based on its ability to maintain high end group fidelity enabled a high degree of control over the ROP, creating MMs of low dispersity and only required the addition of trifluoroacetic acid to terminate the ROP step before moving forward with the ROMP step.⁶⁹ Klapper and coworkers recently extended this ROP/ROMP concept to make BB polymers using a simultaneous polymerization approach, where the ROP and ROMP steps can occur in the same pot at the same time in a hybrid of grafting-through and grafting-from.⁷⁰

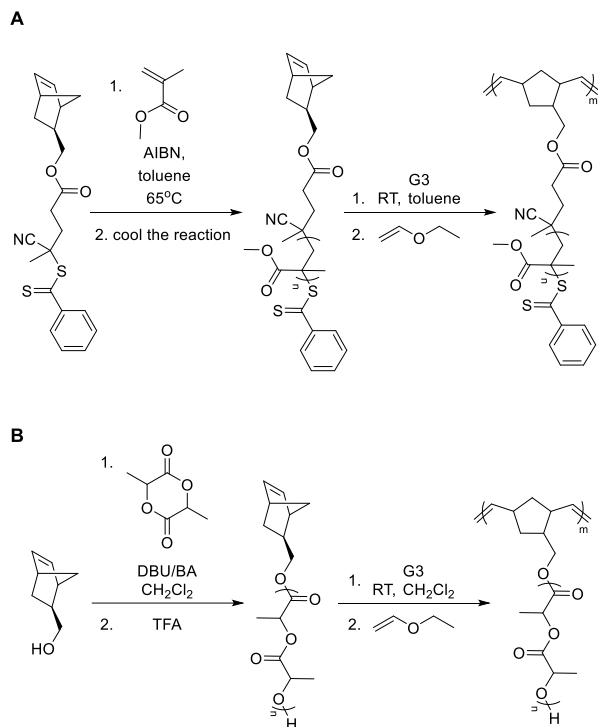


Figure 1.6 Synthesis of bottlebrush polymers with (A) PMMA side chains and (B) PLAside chains via a one-pot method. Adapted with permission from references ^{67,69}.

1.7 Bottlebrush (Multi)Block Copolymers

1.7.1 Diblock and triblock bottlebrush BCPs

Along with bottlebrush homopolymers, ROMP enables the synthesis of bottlebrush BCPs, adding another dimension of complexity to this topology. Bowden and coworkers reported the first synthesis of a series of BCPs that included one linear block and one bottlebrush block (i.e., linear-*block*-bottlebrush copolymers) in a pair of reports in 2007 and 2008.^{55,71} In a large systematic study of 32 polymers, they highlighted how N_{bb} and N_{sc} of the bottlebrush component and the DP of the linear component influenced solid-state morphology.⁵⁵ Grubbs and coworkers reported the first synthesis of a bottlebrush BCP with two bottlebrush blocks by ROMP in 2009.⁷² In this work, the growth-then-coupling method was used for the preparation of PS, PtBA, and poly(*n*-butyl acrylate) (PnBA) MMs, which were synthesized using ATRP followed by coupling a norbornene to the MM

chain end, while a PLA MM was synthesized using the direct-growth method. A series of bottlebrush BCPs were then prepared using sequential ROMP of different combinations of two MMs (Figure 1.7A). This method enabled the synthesis of a variety of bottlebrush BCPs with variable side chain chemistry, N_{sc} , and N_{bb} values. Small-angle X-ray scattering (SAXS) and AFM studies on these polymers showed self-assembly as evidenced by a bright green color due to the reflectance of light from the nanosized self-assembled domains (Figure 1.7B).

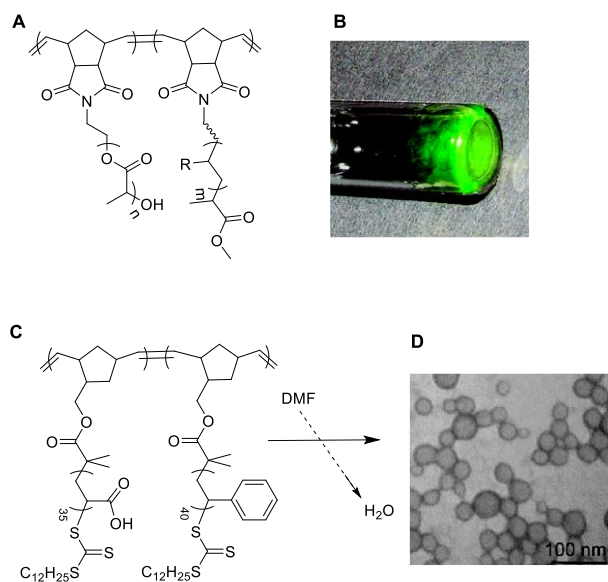


Figure 1.7 (A) Chemical structure of bottlebrush BCP based on PLA, PtBA, and PnBA side chains. (B) Photograph of bottlebrush BCP after drying showing green color due to reflectance from the large self-assembled domains. (C) Synthesis of bottlebrush BCP based on PAA and PS side chains. (D) TEM image of self-assembled bottlebrush BCP in aqueous solution into micelles. Adapted with permission from references ^{72,73}.

In related work, Wooley and coworkers synthesized bottlebrush BCPs using PS and PtBA MMs prepared by RAFT polymerization. Sequential ROMP afforded a bottlebrush BCP of the structure (PNb-graft-PS)-*block*-(PNb-graft-PtBA). Hydrolysis of the *tert*-butyl esters in the PtBA side chains afforded an amphiphilic bottlebrush BCP of the structure (PNb-graft-PS)-*block*-(PNb-

graft-PAA), where PAA = poly(acrylic acid) (Figure 1.7C). These polymers self-assembled in aqueous solution, forming micellar structures (Figure 1.7D).⁷³

The versatility of ROMP grafting-through enables the preparation of bottlebrush multiblock copolymers. The same principle of using sequential polymerizations can be utilized to prepare ABA or ABC triblock or even ABCD tetrablock copolymers, where a PNb backbone is typically used while the variation occurs on the side chains. For example, Wooley and coworkers prepared two different types of ABC bottlebrush triblock copolymers using the grafting-through method with the structures (PNb-*graft*-PEG)-*block*-(PNb-*graft*-PLA)-*block*-(PNb-*graft*-PBAEAM) (B1 and B2) and (PNb-*graft*-PEG)-*block*-(PNb-*graft*-(PHS-*co*-PNPM))-*block*-(PNb-*graft*-PBAEAM) (B3), where PBAEAM = poly(*N*-*tert*-butyloxycarbonyl-*N'*-acryl-1,2-diamino-ethane) and PHS-*co*-PNPM = poly(*p*-hydroxystyrene-*co*-*N*-phenylmaleimide) (Figure 1.8).⁷⁴ Removal of the Boc groups on the PBAEAM side chains afforded a cationic, water-soluble side chain. The self-assembly of these triblock copolymers in aqueous solutions exhibited micellar or vesicular structures.

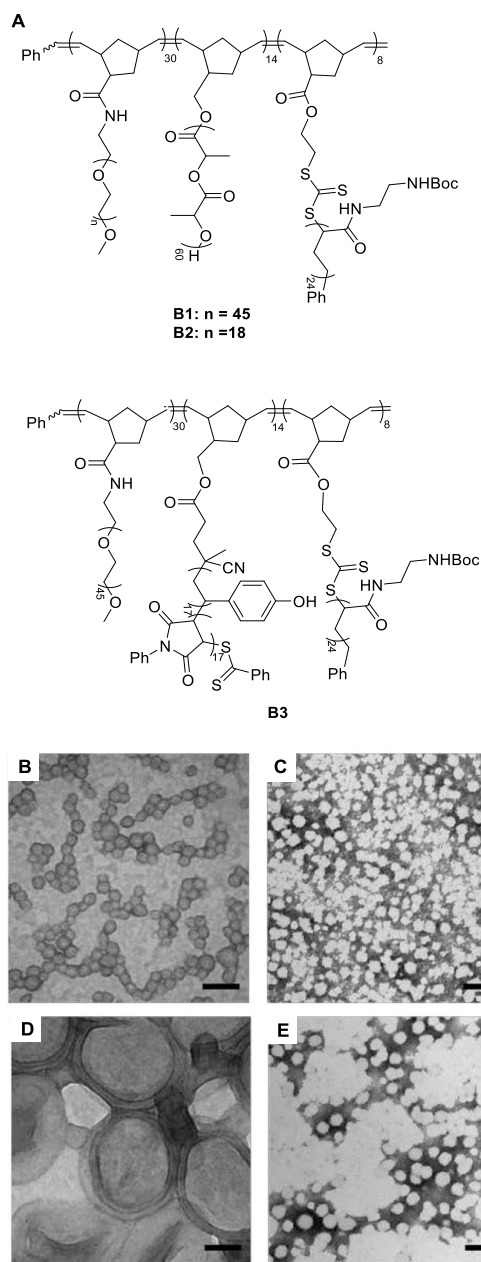


Figure 1.8 (A) Chemical structures of ABC triblock copolymers. TEM images of self-assembly in aqueous solution of (B) B1 protected with Boc (C) B1 with Boc removed (D) B2 protected with Boc (E) B2 with Boc removed. All scale bars are equal to 100 nm. Adapted with permission from reference ⁷⁴.

1.7.2 Core-shell bottlebrush BCPs

Beyond the block copolymers discussed above, another type of bottlebrush BCP is a core-shell bottlebrush BCP. In this case, the macromonomer is a BCP or triblock copolymer with a

norbornene on one end. ROMP grafting-through of this type of MM results in a core-shell structure or core-shell-corona structure. A particularly interesting example by Rzayev and Onbulak involved the preparation of core-shell bottlebrush triblock copolymer where the inner block consisted of PLA, the middle block consisted of poly(*tert*-butyl methacrylate) (PtBMA), and the outer block was a statistical copolymer of the structure POEGMA-*stat*-PCEM where POEGMA = poly(oligoethyleneglycol methacrylate) and PCEM = poly(coumarin ethyl methacrylate) (Figure 1.9A).⁷⁵ Once in solution, UV light was used to crosslink the coumarin groups in the corona. Aqueous NaOH was then added to degrade the PLA inner block to create nanotubes. Finally, trifluoroacetic acid was added to the polymer to hydrolyze the *tert*-butyl esters to create a PAA shell (middle block). Nanotubes were observed by transmission electron microscopy (TEM) both in CH₂Cl₂ before the hydrolysis steps and in aqueous solution after the hydrolysis steps, and the cylindrical nanostructures were larger in water likely due to hydrogen bonding, which induced end-to-end anisotropic aggregation (Figure 1.9B-C).

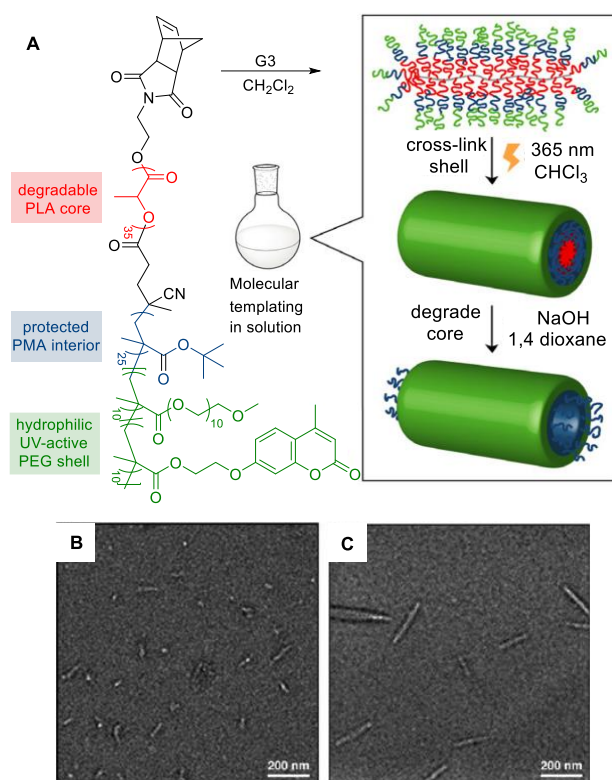


Figure 1.9 (A) Synthesis of PEG nanotubes with inner functionalities from tricomponent core-shell bottlebrush copolymers. TEM images of core-shell bottlebrush block copolymer (B) PLA degradation and (C) tert-butyl group removal. Adapted with permission from reference ⁷⁵.

1.7.3 Janus bottlebrush BCPs

Finally, there is one more type of bottlebrush BCP: Janus bottlebrush BCP synthesis involves ROMP grafting-through of a norbornene connected to two different polymer side chains. Multiple clever methodologies have been used to achieve this type of topology. Johnson and coworkers prepared Janus bottlebrush BCPs using a norbornene-based MM precursor.⁷⁶ This precursor contained two orthogonal functional groups, an alkyne for CuAAC coupling and an alcohol for 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) coupling. In this example, an azide-functionalized PS MM prepared by ATRP was attached to the norbornene, as well as PLA prepared by ROP. An example of an MM with a clicked PS and PLA prepared by ROP is shown in Figure

1.10A. SAXS of these materials revealed that while the Janus MM was disordered, the Janus bottlebrush BCPs were ordered and had bicontinuous gyroid morphology.

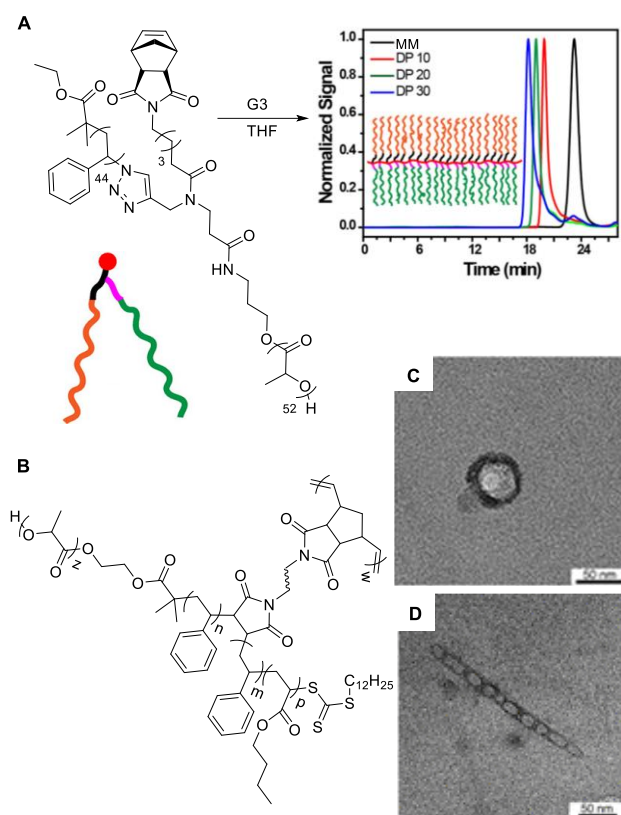


Figure 1.10 (A) Chemical structure of the norbornene functionalized Janus MM and SEC traces of the MM and resulting bottlebrush polymers at different DPs. (B) Chemical structure of Janus core-shell bottlebrush copolymer. TEM images of Janus core-shell bottlebrush block copolymer in CH₃CN resulting in (C) vesicles (D) a row of vesicles after 7 days of aging. Adapted with permission from references ^{76,77}.

Seo and coworkers prepared an even more complex Janus core-shell bottlebrush block copolymer composed of three types of polymer blocks.⁷⁷ Their synthetic method utilized a RAFT chain transfer agent with an alcohol end group, which initiated the polymerization of lactide to make PLA through an ROP step. Next, the authors generated a PS block mediated by the RAFT CTA component. During the synthesis of the PS component, a single unit monomer insertion step was used to introduce a norbornene functionalized maleimide. After the insertion, the RAFT

polymerization continued with another PS block and PnBA block. ROMP of this macromonomer with two diblock copolymer side chains (PS-*block*-PLA and PS-*block*-PnBA) resulted in a bottlebrush block copolymer with both core-shell and Janus structure (Figure 1.10B). Self-assembly of this Janus core-shell bottlebrush block copolymer in CH₃CN resulted in vesicles as shown by TEM imaging (Figure 1.10C). After 7 days of aging, the vesicles aggregated into a row of vesicles due to intervesicle adhesion (Figure 1.10D).

1.7.4 Engineered Bottlebrush Polymer Structures

Recently, the precision that the grafting-through method by ROMP provides has been exploited to engineer bottlebrush polymers with non-linear and in some cases non-centrosymmetric structures. In other words, the customizability of this method enables the synthesis of bottlebrush polymers where the side chain lengths are varied to generate a targeted shape. A comprehensive example of these types of bottlebrush polymers was demonstrated in a 2019 study published by Guironnet and coworkers where they utilized computer simulations and automated flow synthesis to feed MMs prepared *in situ* immediately into the ROMP reaction.⁷⁸ The MMs contained PLA and poly(valerolactone) (PVL) side chains prepared through ROP. The authors conducted the ROP reaction in one reactor and continuously added it to another reactor containing G3 catalyst such that the side chains increased in molecular weight along the polymer backbone, generating a cone-shaped tapered bottlebrush polymer. This methodology was also utilized in another study where PLA and polydimethylsiloxane (PDMS) were utilized as the side chains on the MMs.⁷⁹ Further extension of the methodology allowed for even greater control over the molecular geometry of these bottlebrush polymers, with architectures including bowtie, hourglass, and football shapes (Figure 1.11A). The AFM image of the hourglass shapes is shown in Figure 1.11B.

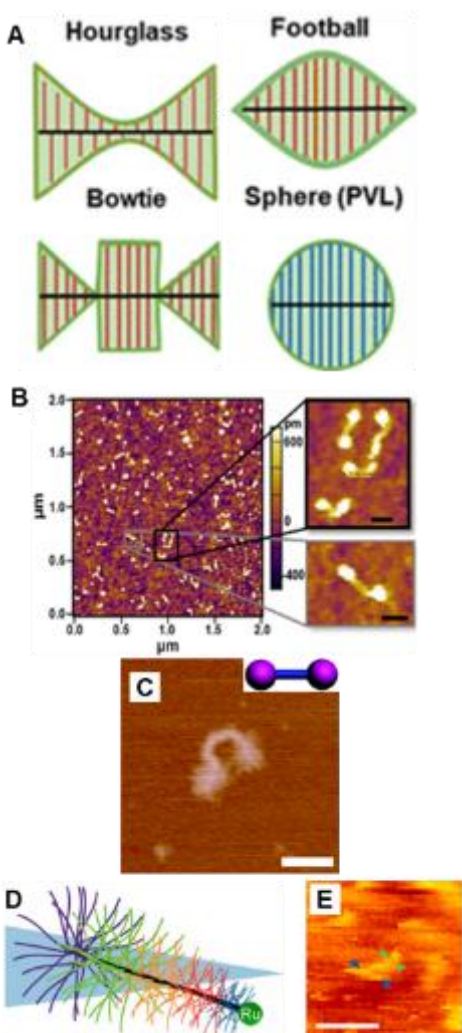


Figure 1.11 (A) Schematic illustrations of targeted engineered bottlebrush polymers architectures using a continuous flow method. (B) AFM image of hourglass shaped bottlebrush polymers (scale bar = 50 nm). (C) AFM image of dumbbell shaped bottlebrush polymers (scale bar = 50 nm). (D) Schematic illustration of cone-shaped tapered bottlebrush block copolymer and (E) AFM image of tapered bottlebrush block copolymer with PS side chains (scale bar = 20 nm). Reproduced with permission from references ^{78,80,81}.

The sequential addition of macromonomer ROMP (SAM-ROMP) method is another way to prepare bottlebrush polymers with non-cylindrical morphologies. This method involves the ROMP of MMs that have varied molecular weights in sequence, with the advantage that each MM can be fully characterized and purified before use in the ROMP grafting-through step. Early work

utilizing this method was carried out by Wooley and coworkers in 2012 in their synthesis of dumbbell-shaped bottlebrush polymers from an ABA triblock bottlebrush BCP where the side chains on the first and third blocks were much longer than those on the middle block (Figure 1.11C).⁸⁰ More recently, this method was utilized by our group in 2017 to prepare tapered bottlebrush polymers that have a cone shape.⁸¹ In this work, five polystyrene MMs were prepared by ATRP with M_n values ranging from 1–10 kg/mol. The SAM-ROMP of the five MMs in descending order allowed for good control over the polymerizations. The cartoon shape of the tapered bottlebrush and AFM image are shown in Figures 1.11D and 1.11E, respectively.

1.7.5 Linear-block-bottlebrush BCPs

A related class of polymers is linear-*block*-bottlebrush BCPs, as pioneered by Bowden.⁵⁵ These polymers involve the sequential ROMP of a small molecule norbornene monomer and an MM. An interesting example is the combination of linear liquid crystalline (LC) and bottlebrush PLA components as reported by Kasi and coworkers in 2020.⁸² In this study, the authors explored the effects of varying the block ratios and the total molecular weight of BCPs of the structure P(Nb-CB12)-*block*-(PNb-*graft*-PLA) where Nb-CB12 = norbornene-*n*-dodecyloxycyanobiphenyl. Figure 1.12A shows the chemical structure and the different colors produced after processing films prepared by sequential addition of the LC monomer, where the color differences were attributed to different sizes of the photonic bandgaps as a result of self-assembly.

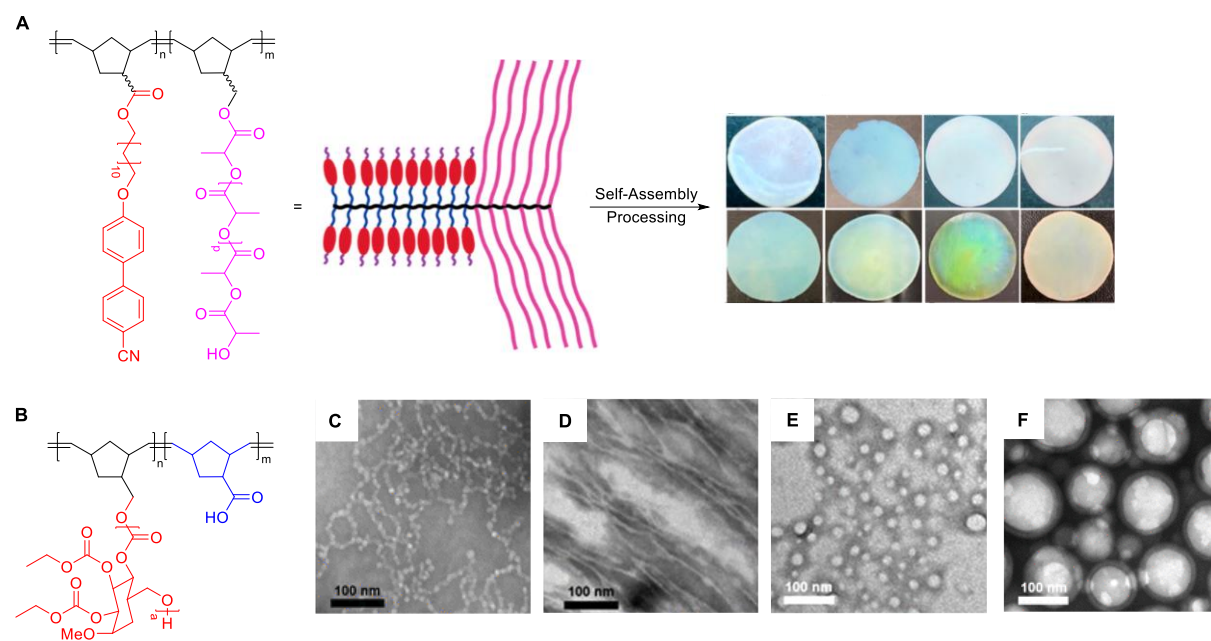


Figure 1.12. (A) Chemical structure of linear-*block*-bottlebrush BCP showing the self-assembly and different colors resulting from varying the block ratios. (B) Chemical structure of BCP of linear poly(acrylic acid) and bottlebrush with PCG side chains. TEM images of linear-*block*-bottlebrush BCP assemblies that form (C) elongated cylinders (D) pearl and necklace (E) spherical micelles and (F) vesicles. Adapted with permission from references ^{82,83}.

Wooley and coworkers reported another example of linear-*block*-bottlebrush BCPs where the linear block contained norbornene carboxylic acid (Nb-COOH) and the bottlebrush block was prepared from an acetylated poly(glucose carbonate) (PGC) MM (Figure 1.12B).⁸³ The structure of the BCP, P(Nb-COOH)-*block*-(PNb-*graft*-PGC), was varied by changing N_{bb} , block ratios, and N_{sc} for the PGC bottlebrush component. In aqueous solution, the polymer assembled into different shapes including spheres, vesicles, and cylinders as shown in Figures 1.12C-F. The ability of the PGC component in this work to degrade into natural metabolites may enable applications of this type of structure in biomedicine, although the PNb backbone remains non-biodegradable. More broadly, with many tunable variables in linear-*block*-bottlebrush BCPs (including block ratios,

N_{bb} , N_{sc} , and rigidity of the linear block and the BB block), there remains much more to explore in the self-assembly of these structures.

1.8 Dendronized polymers

ROMP has been used since the 1990s to synthesize dendronized polymers, a class of polymers typically made from MMs that consist of dendrons attached to polymer backbones.⁸⁴ Dendronized polymers are similar to bottlebrush polymers in that the sterically demanding dendritic unit forces an extension of the polymer backbone. However, MMs used in making dendronized polymers are monodisperse, globular structures rather than the polydisperse MMs with linear side chains used in making bottlebrush polymers. ROMP is used widely in making dendronized polymers, along with related cyclopolymerization strategies, topics that were recently reviewed by Gu.⁸⁵ Early successes in synthesizing dendronized polymers by ROMP included dendritic side chains containing up to third generation (Gen-3) dendrons.^{86–89} More recent reports by Choi and coworkers have demonstrated the ability to synthesize dendronized polymers with side chain dendrons reaching up to Gen-4, Gen-5,⁹⁰ and even Gen-6.⁹¹

To synthesize Gen-4 and Gen-5 dendronized polymers, Choi and coworkers utilized grafting-through ROMP with MMs containing a norbornene unit linked to various amino acids. With the norbornene unit as the focal point of the dendron, the authors synthesized ester-based MMs up to Gen-2 and Gen-3⁹⁰ that underwent ROMP cleanly. However, when attempting the synthesis of a Gen-4 side chain, a temperature of 50 °C was required for the ROMP grafting-through step, which was slower and generated dendronized polymers with higher dispersity than those with only Gen-2 or Gen-3 units. This was due to the steric bulk of the dendron close to the norbornene unit, preventing efficient ROMP. The authors then examined two linkers between the norbornene unit and the dendron: an ethylene linker and a more rigid biphenyl linker (Figure 1.13). The ethylene

linker enabled a smoother synthesis of the Gen-4 dendronized polymer with a lower dispersity than before, but a temperature of 40 °C was still required in the ROMP grafting-through step. The biphenyl linker showed the most success, and they were able to achieve a Gen-5 dendronized polymer at room temperature with low dispersity and control over the molecular weight.⁹⁰

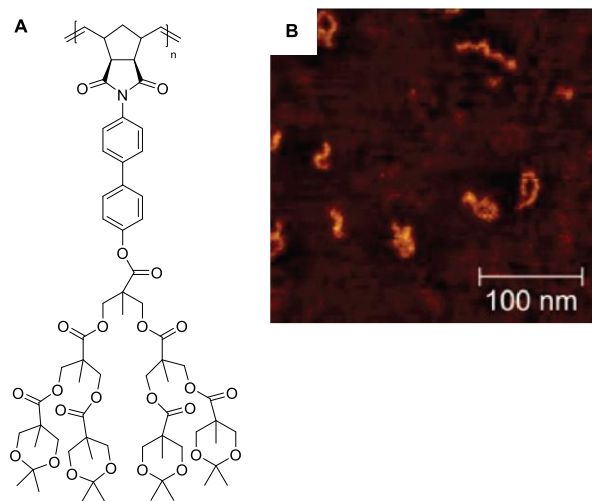


Figure 1.13. A) Structure of Gen-3 dendronized polymer with a biphenyl linker and B) AFM image of the Gen-3 dendronized polymer. Reproduced with permission from reference ⁹⁰.

More recently, Choi and coworkers successfully synthesized a Gen-6 dendronized polymer, the largest ever achieved using the ROMP grafting-through method. Their method employed the G2 catalyst, which initiates much slower than the G3 catalyst but has similar propagation kinetics. The use of the G2 catalyst, with a monomer to initiator ratio of 100:1, enabled ROMP grafting-through at 70 °C, at which point the initiation rate was fast enough to achieve some living character. However, a maximum N_{bb} of 78 was achieved with a dispersity value of 1.45, suggesting that some catalyst death occurred or that the initiation rate remained slower than the propagation rate. The authors also synthesized the Gen-6 dendronized polymer using an Ru olefin metathesis catalyst containing a cyclic (alkyl)-(amino)carbene, which reached a higher N_{bb} . With purification by

preparative SEC, they isolated a Gen-6 dendron with $N_{bb} = 220$ and a dispersity of 1.33.⁹¹ Continued efforts from the Choi lab and others in making dendronized polymers, as well as dendronized BCPs and star polymers,^{92–95} highlight the capabilities of the grafting-through ROMP method in polymerizing sterically bulky MMs but also reveal limitations that need to be addressed to achieve higher molecular weight and lower dispersity dendronized polymers.

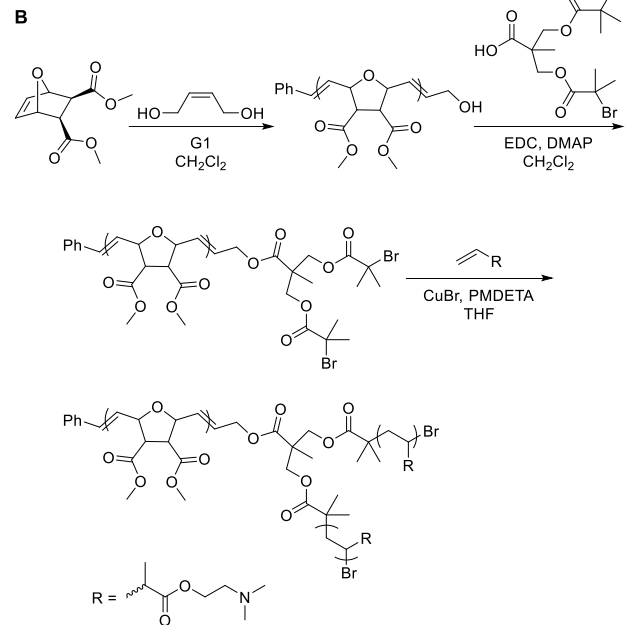
1.9 Star polymers

A few different synthetic approaches are used to make star polymers. The core-first approach utilizes a macroinitiator as the core, and three or more arms are grown from this core. In contrast, the arm-first approach involves the synthesis of the arms followed by crosslinking to make the core. Finally, the grafting-onto approach involves the efficient coupling of the arms to a core molecule.⁹⁶ All three synthetic approaches can utilize ROMP to achieve star polymer architectures, but arm-first is most commonly used. When the arms are bottlebrush polymers, the arm-first method can be called the brush-first method, and brush-arm-star polymers (BASPs) form. BASPs, discussed below, are star polymers with bottlebrush polymer arms instead of linear arms.

Schrock and coworkers published the first few ROMP syntheses of star polymers in the early 1990s using the arm-first approach, where living PNb chains were crosslinked with a bis(norbornene species) using Mo-based ROMP catalysts.⁹⁷ The same synthetic method was later used to polymerize amphiphilic diblock arms that were then crosslinked at the end of the ROMP step to afford star BCPs, albeit with broad dispersities.⁹⁸ Although operationally straightforward, this method is typically limited to only a few arms and suffers from lack of complete control. The number of arms can be increased by increasing the ratio of crosslinking agent to the catalyst, resulting in star polymers of high MW, but excessive crosslinking can lead to gel formation.⁹⁹

Therefore, synthetic strategies involving various growth steps have been developed to maintain solubility and avoid gelation.

One interesting approach from Xia and coworkers in 2020 utilized a rigid, ladder-shaped bis(norbornene) crosslinker to form star polymers from PLA-based MMs.¹⁰⁰ Acidic degradation of the arms allowed for characterization of the remaining core (Figure 1.14), and the authors found that these rigid crosslinked cores were soluble microporous polymer nanoparticles. ROMP has also been successfully incorporated into the synthesis of miktoarm star polymers. For example, Zhang and coworkers showed in 2009 that ATRP and ROMP could be combined to make AB₂ star polymers using a core with dual functionality.¹⁰¹ In this work, they polymerized an oxanorbornene monomer that could be functionalized after ROMP with an initiator species to be used in ATRP. The subsequent polymerization introduced the two additional arms to afford the AB₂ star polymer. Miktoarm star polymers have also been made by introducing a macroterminator to a solution of MMs at the end of the ROMP step.¹⁰²



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using dendritic cores,¹⁰⁸ a γ -cyclodextrin core was functionalized with 8 norbornene units that were used to grow bottlebrush polymer arms via ROMP. This method relies on equal reactivity of the initiating sites and a fast initiation using G3 catalyst to ensure a high level of control over arm number and length.

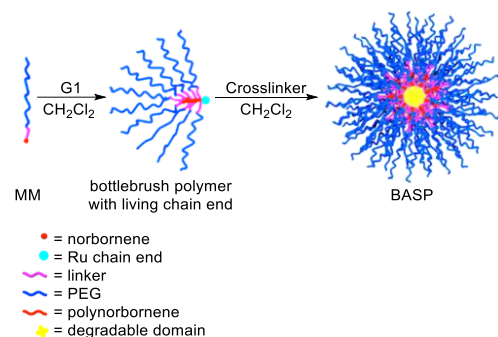


Figure 1.15 Synthesis of BASPs containing PEG arms and a degradable core. Reproduced with permission from reference ¹⁰³.

1.10 Biomolecule-polymer conjugates

Star polymers synthesized using the core-first method utilize a macroinitiator, often generated *in situ* from a core with several norbornene or related groups, to create the unique star-shaped architecture. Using a similar macroinitiator approach, this method can be extended to use ROMP in the construction of biomolecule-polymer conjugates. Proteins used as biotherapeutics are often conjugated to polymers to increase the circulation lifetime of the protein, as well as to decrease protein degradation.¹⁰⁹ Most protein-polymer conjugates utilize the grafting-onto approach, where prepared arms such as PEG are attached to proteins, typically through surface cysteine thiols or lysine amines. ROMP enables other methods to synthesize these conjugates that may offer advantages over the grafting-onto approach. Similarly, ROMP has been used to create DNA-polymer conjugates. We discuss a few important examples of protein-polymer and DNA-polymer conjugates below that highlight the utility of ROMP in making these complex structures. Many

other types of biomolecule-polymer conjugates have also been reported that involve ROMP, including many examples where a norbornene-functionalized oligopeptide is polymerized by ROMP to make a polymer with protein-like folding, enzymatic activity, or other properties.^{110–112} For the interested reader, we recommend an excellent recent review by Maynard on this topic.¹¹³ The grafting-to approach to create traditional biomolecule-polymer conjugates is kinetically and thermodynamically unfavorable,¹¹⁴ so Isarov and Pokorski developed a grafting-from strategy using a protein-based ROMP macroinitiator in an attempt to mitigate the traditional unfavorable conditions.¹¹⁵ By functionalizing lysozyme with a water-soluble Ru catalyst, they were able to grow PNB-*graft*-PEG arms from the surface of the protein (Figure 1.16). While this method worked, a drawback was the need for high monomer loadings due to limited access to the catalytic site on the protein, limiting control over the graft chain length.¹¹³ In follow-up work, Pokorski and coworkers developed a grafting-to approach that attached a synthesized polymer or BCP to the protein, eliminating some of the drawbacks created in their previous work.¹¹⁶

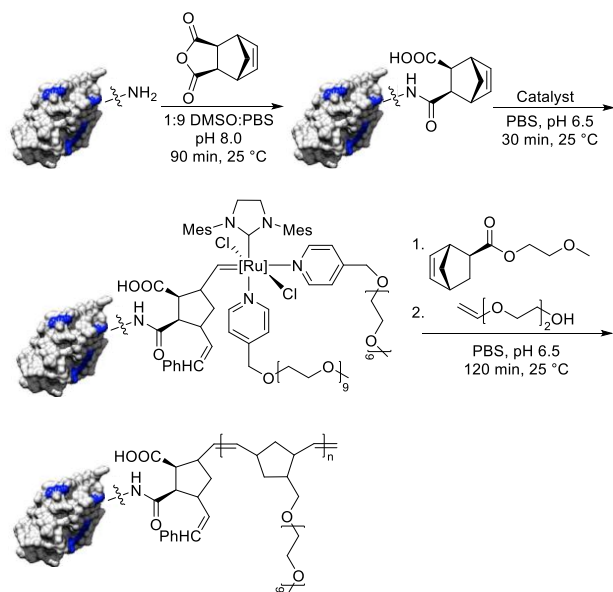


Figure 1.16 Synthesis of PNB-*graft*-PEG attached to a lysozyme. Adapted with permission from reference

While the Pokorski group used grafting-from and grafting-to to synthesize protein-polymer conjugates, many others use the grafting-through technique to prepare biomolecule-polymer conjugates. In a 2014 example of a DNA-polymer conjugate, Zhang and coworkers used a ROMP grafting-through synthesis to make an ABA triblock copolymer of the structure (PNb-NHS)-*block*-(PNb-graft-PEG)-*block*-(PNb-NHS) (NHS = *N*-hydroxysuccinimidyl ester).¹¹⁷ They then displaced the NHS groups with amine-modified DNA to create an ABA bottlebrush block copolymer with the outer blocks containing DNA side chains surrounding a central solubilizing PEG bottlebrush block. Interactions between the DNA units on different polymers led to a step-growth-type supramolecular polymerization in water, generating worm-like aggregates. In a 2019 study from the same group, they developed methods to directly polymerize MMs with DNA side chains using ROMP grafting-through in organic solvents by protecting the DNA. This strategy opened up synthetic access to a number of different types of complex topologies, including the direct synthesis of DNA bottlebrush BCPs of the structure (PNb-graft-PEG)-*block*-(PNb-DNA).¹¹⁸

1.11 Other ROMP Approaches to Complex Architectures

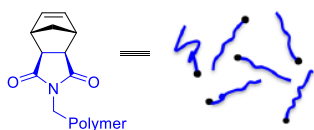
Beyond traditional methods to make homopolymers, BCPs, and multiblock copolymers, a variety of new ROMP-based methods have emerged recently that provide additional structural control, dynamics, or other advantages not available in traditional synthetic methods. Some of these methods are highlighted below.

1.11.1 Controlling Grafting Density and Distribution

Bottlebrush polymers have unique physical properties deriving from the densely grafted side chains, which produce a chain-extended conformation and a lack of chain entanglements.⁴⁶ While advantageous in some respects (lower viscosities at high molecular weights,¹¹⁹ use as pressure-sensitive adhesives,¹²⁰ surface coatings,¹²¹ etc.), controlling the grafting density can fundamentally

change the structure-property relationship and lead to new mechanical properties,¹²² physical properties,¹²³ and self-assembly motifs.¹²⁴ Early efforts to control grafting density utilized ATRP¹²⁵ or other RDRP copolymerizations.¹²⁶ In 2017, Grubbs and coworkers introduced a ROMP method to control grafting density and distribution with a high level of control.¹²⁷ The method relied on the copolymerization of MMs with diluent small molecule monomers with careful tuning of the reactivity ratios (Figure 1.17). For example, matched reactivity ratios ($r_{\text{MM}} \sim 1$, $r_{\text{diluent}} \sim 1$) afforded evenly spaced polymer grafts, while disparate reactivity ratios ($r_{\text{MM}} > 1$, $r_{\text{diluent}} < 1$ or $r_{\text{MM}} < 1$, $r_{\text{diluent}} > 1$) favored grafts on each end of the backbone chain. This method greatly expanded the tunability of bottlebrush polymer structures by enabling fine control over grafting density and distribution for a wide range of MMs and diluent monomers. A subsequent paper focusing on SAXS studies of films of these materials showed quantitatively how grafting density influences backbone stiffness.¹²⁸

Macromonomer:



Example Diluent Monomer:

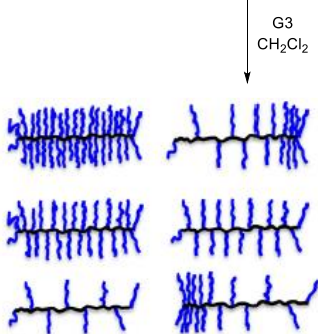
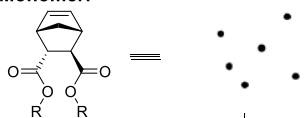


Figure 1.17 Schematic illustration depicting the synthesis of bottlebrush polymers with varying grafting densities made from a mixture of MMs and diluent monomers. Adapted with permission from reference ¹²⁷.

1.11.2 Gradient BB copolymers

While bottlebrush BCPs have been discussed extensively, a unique bottlebrush copolymer includes a gradient between two different side chain polymers. In 2018, Rzaev and coworkers introduced gradient bottlebrush polymers containing PS and PLA pendant chains by taking advantage of the reactivity differences between *exo*- and *endo*-norbornene groups.¹²⁹ Typical ROMP reactions involving norbornene-functionalized monomers utilize *exo*-norbornenes because the *exo*-isomer reacts substantially faster than the *endo*-isomer (see further discussion on *endo/exo* norbornenes in the Practical Considerations section). When performing a homopolymerization with ROMP using a PS MM with an *exo*-norbornene, the reaction proceeded with a rate almost 30 times higher than a similar homopolymerization performed using an *endo*-functionalized PLA MM. By using predetermined feed ratios of the *endo*-Nb-PLA MM and the *exo*-Nb-PS MM, they made gradient bottlebrush polymers with differing concentrations of each side chain attached to the PNB backbone. SAXS analysis of films of these bottlebrush copolymers revealed different morphologies depending on whether the bottlebrush polymer had a block, gradient, or statistical distribution (Figure 1.18).¹³⁰

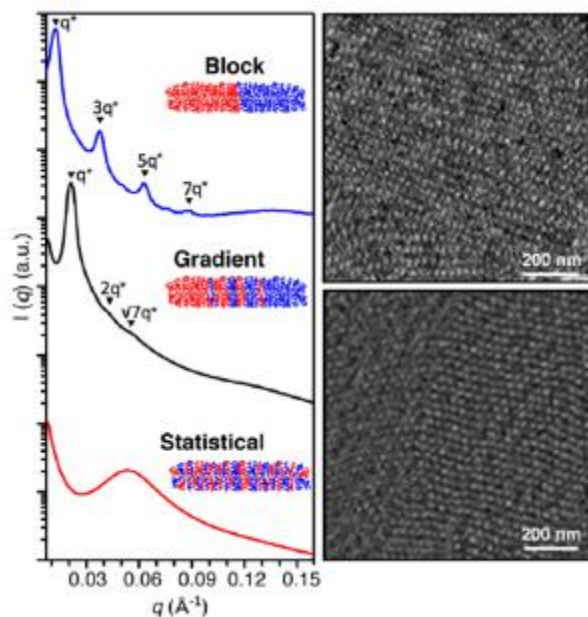


Figure 1.18 SAXS results (left) of block, gradient, and statistical BB copolymers and TEM images (right) of gradient bottlebrush copolymer. Reproduced with permission from reference ¹³⁰.

1.11.3 ROMP of Polymers that Undergo Macromolecular Metamorphosis

Most polymers maintain a static topology through the end-use applications, but there is a desire to create materials with dynamic properties that change upon adjusting the environment or exposure to various stimuli.¹³¹ Recently, Sumerlin and coworkers developed a method termed macromolecular metamorphosis for transforming a covalent polymer from one topology to a different one.¹³² This work showed the transformation of amphiphilic linear block copolymers into comb polymers, hydrophobic block copolymers, and star polymers via diene displacement reactions. The residual unsaturation in polymers made by ROMP is ideal for macromolecular metamorphosis because no additional functionality is required.

Kennemur and coworkers transformed a bottlebrush polymer with a backbone made by ROMP into a linear or star polymer, highlighting the power of olefin metathesis in macromolecular metamorphosis.¹³³ To employ this concept, variable temperature ROMP (VT-ROMP), a method

developed by the same group,¹³⁴ was used to synthesize a linear poly(cyclopentene) (PCP) with pendant bromoisobutyl groups. ATRP was then utilized in a grafting-from reaction to make bottlebrush polymers of the structure PCP-*graft*-PS or PCP-*graft*-(PS-*block*-PMMA).¹³⁵ Addition of olefin metathesis catalyst then induced end-to-end depolymerization and ring-closing metathesis, forming linear polymers with a cyclopentenyl end group.¹³³ This transformation was interesting because depolymerization actually led to an increase in viscosity, consistent with the lack of entanglements in bottlebrush polymers. This transformation also exposed the reactive cyclopentenyl end group, which reacted with a trithiol species in a thiol-ene reaction, transforming bottlebrush polymers into star polymers (Figure 1.19).

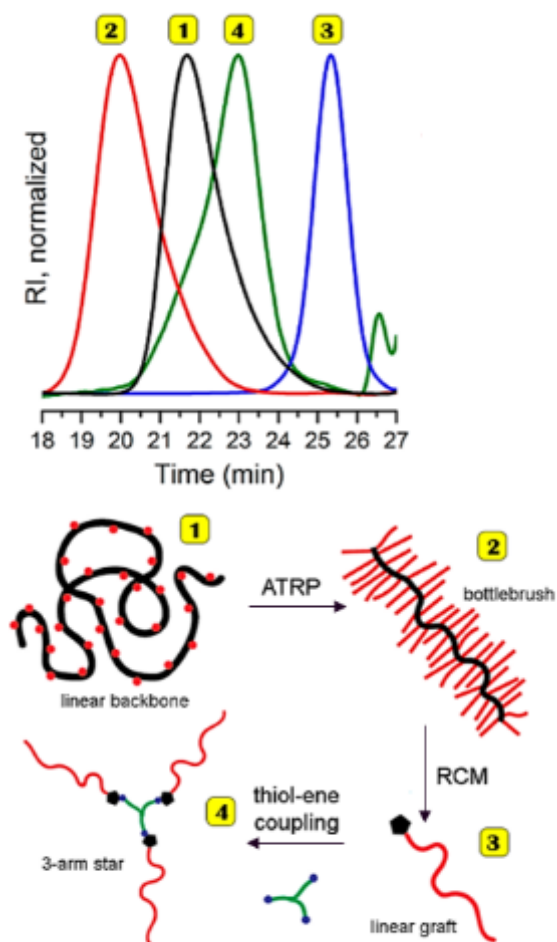


Figure 1.19 SEC confirmation of molecular weight changes through different stages of macromolecular metamorphosis. Adapted with permission from reference ¹³³.

1.11.4 Catalytic ROMP

A drawback to performing ROMP under living conditions, regardless of the monomer, homogeneity, architecture, or morphology, is the necessity of using one catalyst equivalent for every growing polymer chain. The catalysts are expensive and present environmental and human health concerns at moderate levels, so reducing economic, environmental, and health impacts is critical. While methods involving irreversible chain transfer agents (CTAs) have been utilized to address this problem, they can lead to large molecular weight distributions due to the intentional introduction of an irreversible terminating species.^{136,137} Robotic methods utilizing linear olefin reversible CTAs have been reported, but these require specialized equipment.¹³⁸ In 2019, Kilbinger and coworkers introduced what they term “catalytic ROMP,” a synthetic method that uses a reversible CTA to allow each catalyst equivalent to make more than one polymer chain.¹³⁹ Using G3 as the ruthenium catalyst, an oxanorbornene monomer, and a pyran-based reversible CTA, they were able to successfully synthesize moderately low dispersity monomers using as little as 2% of the amount of catalyst that would normally be used in non-catalytic ROMP. BCPs could also be formed this way. This method may enable new applications for materials synthesized by ROMP where contamination with residual catalyst is a concern.

1.12 Applications of Complex Polymer Topologies made by ROMP

ROMP has been cleverly used to synthesize several types of complex polymer topologies. In many cases, the particular topology was chosen to provide specific properties for a desired application. While applications of linear polymers prepared by ROMP have been reviewed elsewhere,^{140–144} we focus here on complex topologies. Of the complex topologies discussed here, bottlebrush

polymers seem to have the most potential applications due to three factors: 1) They generally do not entangle, which most linear polymers do; 2) They can exhibit shape persistence, which is also unusual in other topologies; 3) They are easily tunable, where N_{bb} , N_{sc} , graft density and distribution, and side chain chemistry can be tuned in a relatively straightforward manner. Thus, we focus in this section on emerging applications of bottlebrush polymers prepared by ROMP. For the interested reader, a few of the major potential applications with critical references include photonic crystals,^{145–154} biomedicine/drug delivery,^{155–165} electronic and transport materials,^{166–168} elastomers^{120,169–180} and nanoporous materials.^{181–192} Below, we discuss specific examples of some of these applications.

Photonic crystals result when there is a periodic variation in the dielectric constant in nanostructured materials. To study this phenomenon in bottlebrush polymers, Grubbs and coworkers prepared a series of bottlebrush BCPs with side chains made of poly(isocyanate) (PI) (Figure 1.20A).¹⁴⁷ The PI side chains led to rapid self-assembly due to their rigidity. The authors tuned the photonic crystal color reflection by blending two bottlebrush BCPs with different N_{bb} values. The small and large molecular weight bottlebrush BCPs alone afforded photonic crystals with reflection bands of 360 nm and 785 nm, respectively. Blends of these two polymers with varying ratios gave photonic crystals with reflective bands that varied linearly with the blend composition between these two extremes (Figure 1.20B).

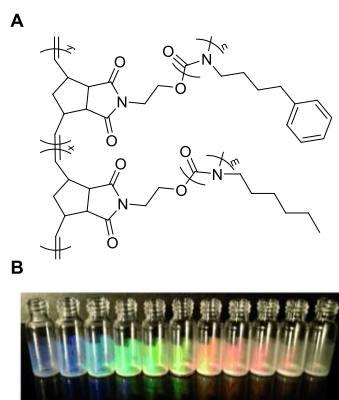


Figure 1.20 (A) Chemical structure of PI-based bottlebrush BCPs. (B) Photograph of brush block copolymer blends reflecting light across the visible spectrum. Adapted with permission from reference ¹⁴⁷.

Bottlebrush homopolymers and BCPs are of interest as circulating nanocarriers due to their persistent cylindrical nanostructure, which often results in more effective drug delivery than spherical carriers.¹⁹³ Johnson and coworkers prepared water-soluble bottlebrush polymers of the general structure PNB-*graft*-PEG with the anticancer drugs doxorubicin and camptothecin covalently attached to the PNB backbone through a branch and a photodegradable linker (Figure 1.21A).¹⁶³ The bottlebrush BCP protected the drugs in solution, with release after UV light exposure, although the need for UV light to trigger release was noted as a downside of this system. In addition to bottlebrush polymers, doxorubicin was incorporated into the polymeric structure of BASPs (Figure 1.21B), for therapeutic release in response to light, similar to the bottlebrush polymers, or pH.¹⁰⁵ Photoinduced degradation of the BASPs displayed similar toxicity of that of free doxorubicin towards cancerous cells. Further adaptation to these structures allowed for BASPs designed to release doxorubicin through hydrolysis rather than irradiation.¹⁰⁶ *In vitro* studies at physiological pH showed higher toxicity than that of free doxorubicin in cancer cells, indicating therapeutically active doxorubicin. Finally, an extension of the BASP-based nanocarriers to include three separate drugs with orthogonal release triggers showed how the molecular design of

complex polymer topologies can be used to deliver chemotherapeutics with precise control over dose.¹⁶⁵

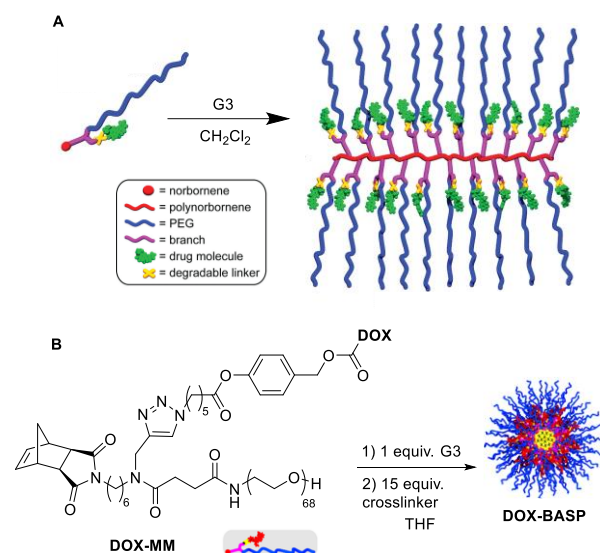


Figure 1.21 (A) Schematic illustration showing the components of the MM and resulting bottlebrush homopolymer with attached drug molecules. Reproduced with permission from reference ¹⁶³. (B) Chemical structure of the MM and schematic representation of the synthesis of doxorubicin-loaded BASPs. Adapted with permission from reference ¹⁰⁶.

The absence of entanglements is a unique feature of the bottlebrush polymer topology due to their densely grafted side chains, making them super-soft elastomers upon chemical or physical crosslinking.¹⁹⁴ Bates and coworkers prepared elastomers based on dynamically crosslinked bottlebrush polymers of the structure *PNb-graft-P4MCL* [P4MCL = poly(4-methylcaprolactone)] crosslinked with a bislactone species at different molecular weights and crosslinking densities.¹⁸⁰ Associative transesterification reactions between the P4MCL ester units and residual hydroxyl groups in the crosslinked bottlebrush polymers allowed for self-healing and dynamic stress relaxation at elevated temperatures (Figure 1.22). Overall, the crosslinked bottlebrush polymers

reached an elongation at break of 350% and retained 85% of their toughness after two cycles of fracture and annealing.

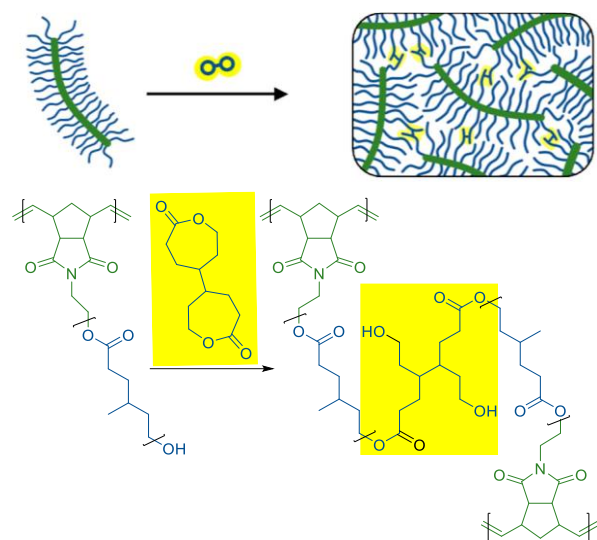


Figure 1.22 Reaction scheme and schematic illustration for generating dynamically crosslinked bottlebrush polymers through associative transesterification. Adapted with permission from reference ¹⁸⁰.

The preparation of ordered porous carbon materials is of significant interest. In particular, it is difficult to create pores in the range of ~35-100 nm in diameter. Watkins and coworkers used bottlebrush BCPs of the structure (PNb-*graft*-PEG)-*block*-(PNb-*graft*-PDMS) to prepare porous carbon materials with pore sizes ranging from 16–108 nm.¹⁹² In the bulk, the bottlebrush BCPs formed a uniform spherical morphology with the PDMS block forming the core and PEG block forming the corona. The creation of a blend of these bottlebrush BCPs with a phenol-formaldehyde resin (resol) provided a precursor to porous carbon materials after crosslinking. Finally, pyrolysis and carbonization resulted in porous carbon materials with pores that varied in size linearly with the molecular weight of the bottlebrush BCP (Figure 1.23).

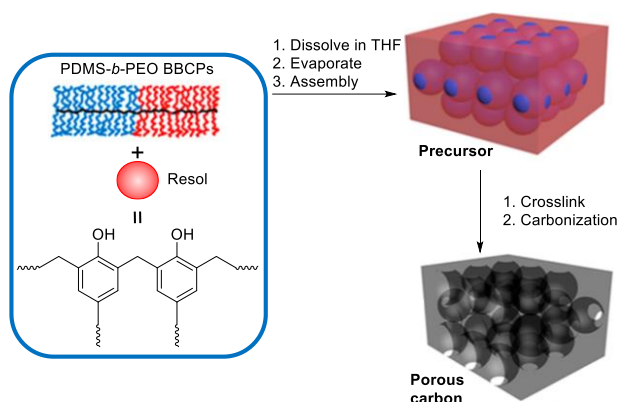


Figure 1.23 Schematic illustration showing the molecular structure, self-assembly, and carbonization leading to nanoporous carbon materials. Adapted with permission from reference ¹⁹².

Finally, nanoscale electronic devices have emerged as applications of bottlebrush multiblock copolymers. Hudson and coworkers recently prepared a series of multiblock bottlebrush copolymers made from ordered sequences of polyacrylate MMs using ATRP followed by ROMP grafting-through.¹⁶⁷ The polymers reached molecular weights exceeding 2,000 kg/mol, and the authors attributed these high molecular weights to a C11 spacer between the norbornene and the polyacrylate side chains. The bottlebrush ABC triblock copolymer imitated the design of a four-component organic light emitting diode (OLED). The three blocks included four different semiconducting components, including an electron-transport layer (ETL), an emissive layer (EML) copolymerized with another phosphorescent macromonomer that contains 8% iridium (Ir), and a hole-transport layer (HTL) (Figure 1.24A). This ABC bottlebrush triblock copolymer of the structure poly(Nb-*graft*-ETL)-*block*-poly(Nb-*graft*[EML-co-Ir])-*block*-poly(Nb-*graft*-HTL) formed cylindrical nanofibers (Figure 1.24B) without the need for crystallization, selective solvation, or supramolecular interactions. Interestingly, this nanoscale phosphorescent OLED exhibited the photophysical characteristics of each of the four organic semiconductors independently.

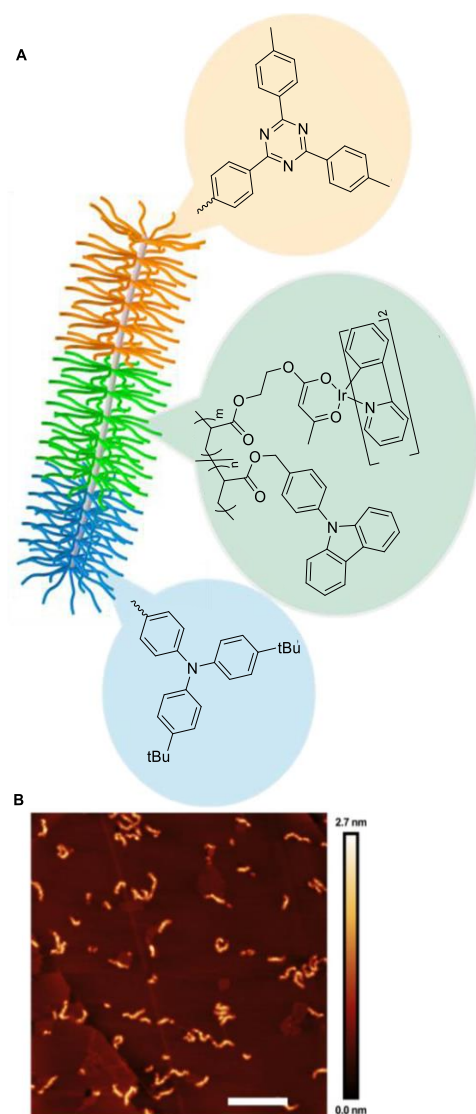


Figure 1.24 (A) Schematic illustration of the color-coded ABC bottlebrush triblock copolymer where ETL is orange, EML is green, and HTL is blue. (B) AFM image of bottlebrush triblock copolymer with scale bar = 200 nm. Adapted with permission from reference ¹⁶⁷.

1.13 Practical Considerations

ROMP is a powerful method capable of producing several different complex polymer topologies. In many methods, ROMP works in tandem with other polymerization techniques, where ROMP is often the final step in the synthesis. ROMP is well-known for its functional group tolerance and

ability to polymerize MMs quickly, enabling the construction of complex topologies displaying a wide variety of functional groups. However, limitations remain. For example, in bottlebrush polymer synthesis, ROMP of even moderate molecular weight MMs ($N_{sc} \sim 50$) can be challenging, as can even relatively low target N_{bb} values ($N_{bb} \sim 100$), where broadening of SEC traces compared to smaller bottlebrush polymers is regularly observed. This difficulty is amplified in bottlebrush multiblock copolymer synthesis and the construction of non-centrosymmetric structures such as tapered bottlebrush polymers. Similar challenges exist in the synthesis of dendronized polymers and BASPs. Control over grafting density may appear straightforward through copolymerization of MMs and diluent (small-molecule) monomers, but careful attention must be paid to the reactivity ratios of the two monomers types.¹²⁷ Recent advances in alternating ROMP by Xia¹⁹⁵ and Sampson¹⁹⁶ may enable precise control over the spacing of side chains at intervals greater than those typically achievable in ROMP of norbornene-based MMs. Altogether, the synthesis of complex polymer topologies while controlling parameters including N_{sc} , N_{bb} , and grafting density requires highly tuned polymerizations. Figure 1.25 highlights some of the elements of the MM and the ROMP reaction conditions that influence the outcome of the polymerization.

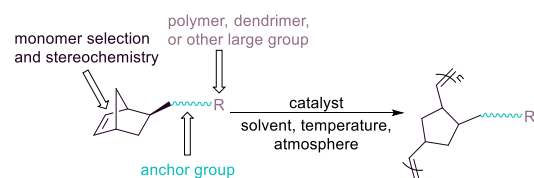


Figure 1.25 Schematic representation of the factors that influence the rate of ROMP.

The efficiency of ROMP relies heavily on the particular catalyst; therefore, extensive research has been done on the various catalysts as well as the invention of new catalysts to fit more specific reaction conditions. Rates of initiation and propagation dramatically influence the precision of the final polymers. The most commonly used catalysts for ROMP are the Ru-based Grubbs' catalysts.

Of these, G3 catalyst (either with pyridine or bromopyridine ligands) is the most widely used catalyst, especially for norbornene species, as it has the fastest initiation and propagation rates of the common Grubbs' catalysts.^{13,197,198} However, G3 catalyst is less stable in solution than other ROMP catalysts and may not be the best option for polymerizations requiring reaction times of more than a few hours. G1 catalyst propagates slower than G3 catalyst by a factor of 10-100, but it also initiates quickly and lives longer in solution than G3 catalyst, making G1 catalyst still a widely used catalyst for ROMP. Unlike G1 catalyst and G3 catalyst, G2 catalyst and common variations of the G2 catalyst (e.g. HG2) rarely work well for polymerizations where living characteristics are needed, including molecular weight control and the capacity for chain extension, because the rate of initiation is slower than the rate of propagation.¹⁹⁹ In fact, in extreme scenarios where initiation is very slow compared with propagation, i.e., in latent catalysts at certain temperatures,²⁰⁰ the monomer/initiator ratio plays no role in controlling molecular weight. In some cases, however, G2 catalyst can be effective for ROMP with living characteristics when monomers or MMs propagate slowly enough that control over the polymerization is maintained. In addition to the widely used Ru catalysts, Mo-based Schrock catalysts are also used in some cases due to their high activity and tacticity control,²⁰¹ although care must be taken to avoid oxygen, water, and certain functional groups.²⁰² Additional catalysts have been synthesized for use in more niche conditions of ROMP (e.g., aqueous ROMP), generally stemming from already published catalyst structures.

In addition to catalyst choice, investigations into optimizing the conditions of ROMP (e.g., atmosphere, temperature, solvent, concentration) have been mostly geared toward the synthesis of bottlebrush polymers. However, lessons learned in bottlebrush polymer synthesis can be applied to a variety of the architectures discussed. As mentioned, the stability of the catalyst may determine

the atmosphere needed to carry out ROMP. Although many opt for the air-stable Ru catalysts, extensive research into catalysts requiring an inert atmosphere has compelled many researchers to continue using dry and air-free conditions. This is despite many examples of ROMP reactions reaching high conversion and producing well-defined polymers while open to air using Ru catalysts. At this point, we are unaware of any systematic studies comparing ROMP carried out under air to those conducted in an inert-atmosphere glovebox. Recent work by Fogg and coworkers on ring-closing metathesis revealed O₂-dependent decomposition mechanisms,²⁰³ but whether these would be active in ROMP is unclear because of the different propagating species (methylidene versus alkylidene). Choice of catalyst can also determine the best temperature to use for ROMP. Most of the syntheses discussed carry out ROMP at room temperature; however, a few studies suggest that elevated temperatures are preferable, mostly in the case of G2 and G1 catalysts. For example, G1 was used at 80 °C to synthesize a core-shell bottlebrush BCP.²⁰⁴ In another recent example, G3 was used at temperatures up to 55°C to increase the rate of initiation for monomers with low ring strain, then the reaction mixtures were cooled in a VT-ROMP process.¹³⁴

Solvent and (macro)monomer concentration have emerged as crucial variables regardless of the choice of catalyst for achieving well-defined polymers by ROMP. Studies have been conducted on both Schrock's and Grubbs' catalysts to determine their behavior in various organic solvents. Fontanille and coworkers investigated solvent effects on a Schrock-type catalyst, finding that cyclohexane and toluene proceeded with high rates of propagation while THF formed a complex with the Mo-based catalyst decreasing the rate of propagation by over ~4-fold.²⁰⁵ In terms of Grubbs' catalysts, Sanford, Love, and Grubbs determined that the initiation rates of G1 and G2 were roughly proportional to the dielectric constant of the solvent.¹¹ However, Percy and coworkers measured the rate of initiation of G2 and HG-2 catalysts in nine different organic

solvents and found only a slight relationship between initiation rate and solvent dielectric constant.²⁰⁶ Focusing on G3, a recent study from our lab compared solvent type and purity for the synthesis of bottlebrush polymers using grafting-through ROMP studying six commonly used solvents (Figure 1.26). We found several key factors in selecting a solvent for a G3-catalyzed ROMP: First, purification of the solvent is unnecessary in most cases, although it was required for THF. Second, solvent influences the rate of propagation and the rate of catalyst decomposition, with EtOAc leading to a propagation rate ~2-4 times faster than the other tested solvents. Third, in terms of livingness, toluene was the best solvent in these studies due to its very low decomposition rate compared to all of the other solvents, but EtOAc and CH₂Cl₂ also show good living behavior during ROMP.²⁰⁷ In terms of monomer concentration, we generally find that ROMP improves (i.e., highest achievable N_{bb} increases and dispersity decreases) with increasing initial MM concentration, up to a point where the reaction mixture becomes highly viscous. However, others have noted no improvement in ROMP with increased (macro)monomer concentration.⁹¹ We speculate that the optimal concentration for a ROMP reaction depends greatly on the specific system.

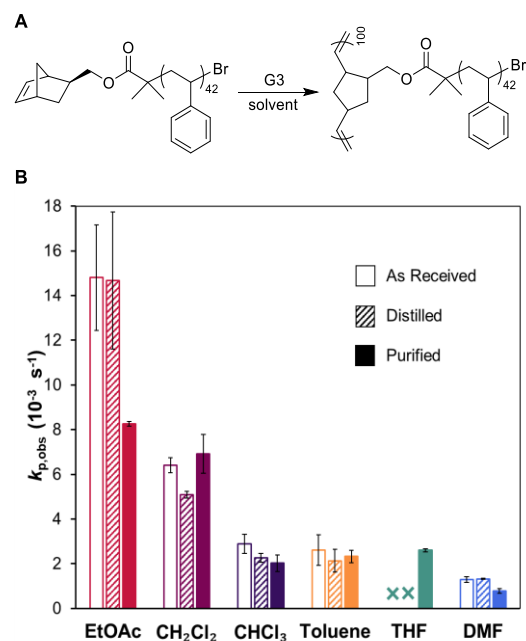


Figure 1.26 A) Reaction scheme of the ROMP grafting-through reaction used in the solvent studies. B) Measured first-order $k_{p,obs}$ values for this ROMP grafting through reaction in six organic solvents with differing levels of purity (as received, distilled, and purified). The $k_{p,obs}$ value for ROMP in EtOAc actually decreases with purification due to removal of an acetic acid impurity. The as received and distilled THF showed <3% conversion to BB polymer, so $k_{p,obs}$ could not be determined in these two cases. Reproduced with permission from reference ²⁰⁷.

Finally, the (macro)monomer structure makes a dramatic difference in the rate of propagation in ROMP and thus the “livingness” of the polymerization. Norbornenes are used widely because of their ease of synthesis and functionalization, high ring strain, and fast propagation kinetics. Oxanorbornenes are sometimes favored over norbornenes because the backbone of the resulting polymer is somewhat less hydrophobic, however, they suffer from low thermal stability due to their tendency to undergo retro-Diels-Alder reactions, generating furan.²⁰⁸ Therefore, we focus here on norbornene-based monomers, where the main factors are 1) the stereochemistry at the 5 and/or 6 positions (the two carbons opposite the carbon-carbon double bond), which can be either

endo or *exo*, 2) the choice of anchor group, which describes the atoms connecting the norbornene unit to the ‘R’ group in Figure 1.25, where R can be a biomolecule, dendron, polymer, or other units, and 3) the size of the R group.

Substituted norbornenes are used widely in ROMP, specifically 5-substituted or 5,6-substituted, and the factor that influences the propagation rate the most is the *endo/exo* stereochemistry. It has been known for decades that *exo*-norbornene monomers polymerize faster than the equivalent *endo* structures by a factor of 20–100.^{209,210} This phenomenon has been validated across various catalysts, solvents, and substituents, and it is largely attributed to steric effects and the fact that Lewis basic units such as esters can coordinate to the catalyst in *endo* monomers.^{10,211–213} Therefore, *exo* monomers are used much more widely than *endo* monomers, despite their substantially higher cost and need for extended synthetic procedures and purifications compared with the cheaper and more widely available *endo* monomers.^{214,215} However, *endo* monomers remain useful in specific scenarios, including as diluent monomers and in cases where gradient structures are targeted.¹²⁷

Beyond the *endo/exo* stereochemistry, our group found in 2016 that the rate of ROMP in a series of *exo* MMs depends on the choice of anchor group, a term originally coined by Slugovc,²¹⁶ which describes the atoms connecting the norbornene unit to a functional group or polymer side chain.²¹⁷ We observed a ~5-fold difference in propagation rates between different sets of three MMs with different anchor groups, and we determined that the effect appears to be related to the HOMO energy of the (macro)monomer. The choice of anchor group dramatically affected the ultimate N_{bb} achievable for MMs with similar molecular weights, from ~140 for an imide anchor group to >800 for a specific ester anchor group. Further investigations into the mechanism of ROMP by Guironnet confirmed that the rate-determining step is the formation of the metallocyclobutane ring

when using norbornene based monomers, which further highlights the importance of monomer/anchor group choice.²¹⁴

Lastly, varying the molecular weight of the monomer, specifically referring to the N_{sc} of MMs used for the synthesis of bottlebrush polymers, affects the dispersity of the resulting polymer and the maximum conversion or maximum N_{bb} under a given set of conditions. In fact, this effect was observed by Khosravi and coworkers in 1997 in a study involving ROMP of MMs using a Schrock Mo catalyst.²¹⁸ The authors noted differences in ultimate conversion for MMs of various molecular weights and suggested that there is an N_{bb} limit that varies inversely with N_{sc} . This result is consistent with observations in our lab and others, but the N_{bb} limit appears to depend not only on N_{sc} but also on the other structural and reaction condition parameters discussed here. We attribute this effect to the ratio of propagation rate (k_p) to termination rate (k_t , i.e., catalyst decomposition rate), which Matyjaszewski has shown is a measure of “livingness”.²¹⁹ In the case of ROMP, k_t appears to depend mostly on the specific catalyst and solvent, while k_p depends on these factors in addition to (macro)monomer structure. Therefore, optimization of structural features and reaction conditions in ROMP to achieve a high k_p/k_t ratio is needed to encourage high conversion for challenging (macro)monomers.

1.14 Challenges, Opportunities, and Future Outlook

ROMP has enabled the synthesis of a dizzying array of complex polymer topologies over the past few decades. Catalyst development in the 1990s and early 2000s directly led to these advances, with the fast initiation and slow termination (catalyst decomposition) rates of the Mo- and Ru-based catalysts providing synthetic access to multi-block polymers, star polymers, dendronized polymers, and many types of bottlebrush (co)polymers, among others. It may seem that we are only constrained by our imagination at this point, and that any envisioned structure can be

synthesized. In many cases this is true, as evidenced by the array of structures and potential uses of these polymers detailed above. However, limitations remain, particularly in the synthesis of complex bottlebrush and dendronized (co)polymer topologies by ROMP grafting-through. For example, bottlebrush polymer syntheses are generally limited to relatively low N_{sc} or N_{bb} values due to the trade-off between these two elements. This limitation becomes particularly important when high aspect ratio nanostructures (i.e., worm-shaped polymers) are desired because the globular to worm transition happens near $N_{bb} \sim 120$.²²⁰ High N_{bb} values are also needed in many materials applications of bottlebrush polymers, such as super-soft elastomers. Dendronized polymers and BASPs also are limited to low N_{bb} values with N_{sc} values or high generation number dendrons.

Several ways can be envisioned to address these current limitations. First, improved catalyst design is a potential avenue for innovation. Olefin metathesis catalysts have typically been developed and tested with a focus on pharmaceutically relevant ring-closing metathesis reactions.²²¹ Rarely are they designed with ROMP in mind because most olefin metathesis catalysts can easily and quickly complete many turnovers of small, high-strain monomers such as cyclooctadiene or norbornene. In fact, G3 with two pyridine ligands, the catalyst used most widely in ROMP to make complex polymer architectures, was developed as a precursor to other catalysts, not as a catalyst by itself.¹¹ It was 18 months later when the bromo-pyridine version of G3 was established as a fast-initiating catalyst for ROMP.¹⁹⁸ These two versions of the G3 catalyst remain the standard today for ROMP with living characteristics, over 20 years after their first report. Despite the high activity of these catalysts, there seems to be room for the development of catalysts optimized for ROMP of large MMs and other sterically demanding monomers.

Second, best practices for optimizing “livingness” in ROMP mediated by existing catalysts such as G3 continue to be discovered. For example, a handful of papers address optimizing monomer type, reaction solvent, anchor group, linker length and rigidity, or reaction conditions (concentration, temperature, atmosphere) in the construction of complex topologies by ROMP. Many such best practices are detailed in the Practical Considerations sections above. However, few conclusions on optimal reaction conditions are derived from broad, systematic studies. In most cases, optimal conditions are empirically determined for a specific system, and it is unclear how such conditions might translate to other systems. Thus, there remains more to do and discover in order to synthesize larger (co)polymers with narrower dispersity values than currently accessible. In this respect, ROMP lags well behind other polymerization techniques such as ATRP, where many careful and thorough studies on ligands, solvents, initiators and other factors form a solid foundation of understanding. This knowledge foundation is critical for especially demanding structures such as tapered bottlebrush polymers, where the catalyst is repeatedly under monomer starved conditions.

Beyond making larger structures, the lack of (bio)degradability and the potential toxicity resulting from catalyst residue has always been a concern in ROMP polymers, whether simple or complex. Polymers made by ROMP such as bottlebrush polymers and BASPs hold potential as drug delivery vehicles, but both concerns need to be addressed before any such polymers can be translated into the clinic. Fortunately, two recent discoveries may help. First, Xia and coworkers showed in 2020 that cyclic enol ethers could be polymerized by ROMP, upending the long-held belief that Fischer carbenes were metathesis inactive.²²² The resulting poly(enol ethers) are degradable under acidic conditions. This group also showed in 2021 that enol ethers such as 2,3-dihydrofuran can be copolymerized with norbornene-based monomers, including even a small MM, opening a synthetic

route to degradable bottlebrush polymers.²²³ Other advances in monomers with acetal linkages^{25,224} and silyl ether linkages²²⁵ also are poised to increase applications of ROMP in biomedicine. Related to these materials are ROMP polymers that can be depolymerized via olefin metathesis routes, such as those developed by Wang,^{226,227} Register,²²⁸ and Kennemur,^{133,229} which may find use as materials with on-demand degradability. Second, Boydston and coworkers developed the first example of metal-free ROMP in 2015, relying on an organic photoredox mediator to conduct ROMP with radical cations as the propagating species.²³⁰ Advances over the past few years from this group have increased the substrate scope and molecular weight control for metal-free ROMP, even providing synthetic access in some cases to polymers that are difficult to make using traditional catalysts.²³¹ Further development of this wholly organic form of ROMP may address concerns over residual metal toxicity.

As synthetic limitations decrease and the versatility of ROMP continues to increase, we see several application areas that are ripe for future advances in ROMP of complex topologies. Already mentioned is the use of ROMP in the construction of vehicles for drug delivery, where new innovations should eliminate long-standing problems in lack of degradability and toxicity, driving growth in this area. Another area that we expect will see increased attention in the near future is self-assembly. Bottlebrush and dendronized BCPs assembled in the solid-state can create photonic crystals, where control over N_{sc} and N_{bb} and grafting density in both blocks in these architectures allows the researcher to tune domain spacing and color. In addition, the creation of these types of nanostructured films from polymers made by ROMP grafting-through offers a level of tunability not accessible through other polymerization routes. Solution self-assembly studies of bottlebrush BCPs and multiblock copolymers are also beginning to reveal how the many tunable variables in these complex topologies influence self-assembled morphology. We anticipate that studies on

assemblies of bottlebrush and dendronized BCPs and multiblock copolymers in solution will continue to emerge, demonstrating how complex polymer topologies can enable access to nanostructured assemblies inaccessible with linear BCPs and multiblock copolymers. Finally, applications of complex nanostructures prepared by ROMP seem poised to make inroads in electronic applications, again as a result of the capacity for high levels of structural control. Further along the horizon are fundamental studies and potential applications of asymmetric or non-centrosymmetric materials prepared by ROMP. This includes tapered bottlebrush polymers, where three-dimensional nanostructured cones, hourglasses, and other shapes are difficult to attain via other routes, and ROMP provides a modular platform for innovation.

In summary, ROMP has emerged as a powerful tool over the past few decades for synthesizing complex polymer topologies. Unbound by the undesired radical-radical side reactions that limit RDRP methods and the stringent conditions and functional group restrictions imposed by anionic polymerization, ROMP in many cases provides the simplest route to star, BASP, dendronized, and bottlebrush homopolymers, BCPs, and multi-block copolymers. These complex polymer topologies are well suited to find uses as drug delivery vehicles, in nanoscale constructs, as elastomers with unusual properties, and as high-value components in devices requiring light manipulation or energy storage/conversion. Further development of the field will require innovations in catalyst and monomer design, as well as careful and systematic studies on how reaction parameters influence rates and polymer structures. Ultimately, continued efforts will broaden the scope and size of polymers and topologies achievable by ROMP, driving fundamental studies on how polymer topology influences properties and encouraging new applications.

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Chapter 2: Solvent effects in grafting-through ring-opening metathesis polymerization

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2.2 Abstract

Ring-opening metathesis polymerization (ROMP) utilizing Grubbs' third-generation catalyst ((H₂IMes)(Cl)₂(pyr)₂RuCHPh) shows characteristics of living polymerizations, including molecular weights increasing with monomer conversion and the ability to make (multi)block copolymers. However, irreversible termination reactions still occur due to catalyst decomposition, leading to terminated chains, especially in the context of sterically demanding monomers such as macromonomers (MM). In this work, we performed identical ROMP reactions on three different MMs in six solvents commonly used in ROMP with varying levels of purity. The solvents included ethyl acetate (EtOAc), dichloromethane (CH₂Cl₂), chloroform (CHCl₃), toluene, tetrahydrofuran (THF), and *N,N*-dimethylformamide (DMF). All polymerizations were conducted under air targeting a bottlebrush polymer backbone degree of polymerization (*N*_{bb}) of 100. All three MMs included a norbornene on the α chain end and had molecular weights (*M*_n) of ~4 kg/mol. They included one polystyrene MM with a bromine on the ω chain end and two poly(*n*-butyl acrylate) MMs with either a bromine or a trithiocarbonate group on the ω chain end. Solvent choice, and in

some cases level of purity, led to significant differences in the propagation rate in these ROMP grafting-through reactions. Of the solvents tested, propagation rates in EtOAc and CH₂Cl₂ were approximately 4-fold and 2-fold faster, respectively, than CHCl₃, toluene, and THF for all MMs. Propagation was much slower in DMF for the polystyrene MM than all the other solvents, and on par with the slower solvents for the two poly(*n*-butyl acrylate) MMs tested. The purity of the solvent in some cases had a profound effect on the propagation rate: In the case of EtOAc, purification led to a 2-fold decrease in propagation rate; in contrast, purification of THF was required to observe full conversion of MM to bottlebrush polymer. The functional group on the ω chain end did not influence the rate of ROMP. Utilizing UV-Vis spectroscopy to measure catalyst decomposition, the main polymer termination route in ROMP, we uncovered dramatic solvent effects, where the catalyst decomposed over ten times faster in THF and DMF than in toluene. Finally, studies targeting $N_{bb} = 500$ or 1000 revealed that toluene, EtOAc, and CH₂Cl₂ demonstrated the highest degree of “livingness” in ROMP. These results will enable the synthesis of complex polymer architectures using ROMP with a high degree of living character.

2.3 Introduction

Ring-opening metathesis polymerization (ROMP) has become a powerful tool for polymer synthesis, especially in constructing complex polymer architectures (i.e., topologies).^{1,2} High strain, cyclic olefin monomers combined with the fast-initiating catalyst (H₂IMes)(Cl)₂(pyr)₂RuCHPh (Grubbs’ third-generation catalyst, G3) are widely used in ROMP,³ but catalyst decomposition (also called catalyst death or catalyst degradation), even at a slow rate, leads to irreversible termination, preventing classification as a living polymerization.⁴ ROMP, nonetheless, can have low enough rates of termination that it often exhibits the characteristics of living polymerizations, including molecular weights that increase linearly with conversion and the

possibility for chain extension to make block copolymers. These traits enable the synthesis of well-defined polymers using a variety of monomers containing a large breadth of functional groups with precise topologies, such as star polymers,^{5–8} hyperbranched polymers,^{9–11} single chain nanoparticles,^{12–14} polymers with bulky side chains,^{15–18} and densely grafted bottlebrush (BB) polymers,^{19–21} among others. However, in particularly challenging polymerizations, including ROMP of monomers with large substituents or synthesis of multiblock copolymers, termination via catalyst decomposition can lead to broader than expected molecular weight distributions and/or mixtures of products. Many experimental factors influence the efficiency of ROMP in the synthesis of complex polymer topologies, and despite widespread use of this polymerization method, studies are remarkably lacking on how reaction parameters such as solvent influence ROMP.

Solvent effects in olefin metathesis have been studied in small molecule reactions such as ring-closing metathesis,^{22–24} acyclic diene metathesis (ADMET) polymerization,²⁵ and ROMP, focusing mostly on initiation rates or using catalysts other than G3.^{26–31} For example, Thompson and coworkers found that when performing ROMP using noble metal halide catalysts, solvents that can complex to the propagating species via hydrogen bonding or via Lewis acid/Lewis base interactions resulted in dramatic changes in the tacticity of the polymer products and in the reactivity ratios in copolymerizations.³¹ In ADMET, Schulz and Wagener showed that solvent choice greatly affected the maximum molecular weight achievable, with molecular weights almost an order of magnitude higher in dichloromethane (CH_2Cl_2) than the same polymerization performed in tetrahydrofuran (THF).²⁵ They concluded that the rate of catalyst decomposition played the most significant role in achieving high molecular weights. However, to our knowledge

no systematic solvent studies have been reported for ROMP using the fast-initiating and widely used G3 catalyst.

We sought to evaluate how common organic solvents affect the rate of propagation (k_p) and the rate of termination (k_t) in ROMP. Knowledge of both rates is critical because the k_p/k_t ratio is the primary factor influencing the “livingness” of a particular polymerization.³² Small molecule monomers can be investigated to determine these effects; however, knowledge of solvent effects on rates is more important for larger macromonomers (MMs) because k_p decreases as the molar mass of the MM increases,³³ decreasing the k_p/k_t ratio and the degree of “livingness”. MMs with even moderate molecular weights can lead to low polymer backbone degrees of polymerization (DP) in the grafting-through step due to the steric hindrance around the propagating site.^{34–36} Beyond BB polymers, both a high k_p and a high k_p/k_t ratio are critical for any ROMP reaction with sterically demanding pendant groups (e.g., sugars, peptides, dendrons), side chains requiring specific solvents (e.g., polar side chains), or even in the synthesis of high molecular weight linear homopolymers and block copolymers.

Herein we aimed to compare propagation rates in the ROMP of various MMs in six organic solvents commonly used in ROMP and other olefin metathesis reactions. These include ethyl acetate (EtOAc), CH_2Cl_2 , chloroform (CHCl_3), toluene, THF, and *N,N*-dimethylformamide (DMF). Additionally, we varied the purification methods for each solvent, while also investigating three different MMs with varied side chain structures and/or end groups. In all cases, we conducted ROMP reactions in capped vials under air rather than in a glovebox in order to measure solvent effects under these minimally stringent and widely used conditions. We hypothesized that solvent type and purification method would affect both k_p and k_t in ROMP and thus influence the

“livingness” of the polymerization. Ultimately, we envisioned that these results would guide researchers in choosing the optimal solvent to synthesize well-defined polymers using ROMP.

2.4 Experimental

2.4.1 Materials

All reagents were obtained from commercial vendors and used as received unless otherwise stated. The six solvents used in the study were EtOAc (VWR BDH Chemicals, ACS grade, $\geq 99.5\%$) CH_2Cl_2 (Fischer, certified ACS grade, $\geq 99.5\%$), CHCl_3 (Fischer, HPLC grade, $\geq 99.5\%$), toluene (Fischer, ACS grade, $\geq 99.5\%$), THF (Fischer, HPLC grade, $\geq 99.9\%$, uninhibited), and DMF (Fischer, HPLC grade, $\geq 99.7\%$). Toluene and THF were stored on a column of activated alumina under nitrogen in a solvent purification system (MBraun). *Exo*-norbornene-methanol was prepared as described previously.³⁷ G3 catalyst was prepared as previously described.^{28,38} Each batch of G3 was only used for 48 h after synthesis due to observations of lower conversions if used after this period of time.

2.4.2 Characterization

Size-exclusion chromatography (SEC) was performed in THF containing 0.025 wt% butylated hydroxytoluene (BHT) at a rate of 1 mL/min at 30 °C, on two MIXED-B Agilent PLgel 10 μm columns connected in a series with a Wyatt Optilab Rex refractive index detector and a Wyatt Dawn Heleos 2 multi-angle light scattering detector. UV-Vis measurements were performed using a Cary 60 UV-Vis and fiber optic dip probe. NMR spectroscopy was performed using an Agilent 400 MHz spectrometer with spectra referenced to internal solvent resonances.

2.4.3 Synthesis of *exo*-norbornene-methyl 2-bromo-2-methylpropanoate (NBMP)

The norbornene-functionalized atom transfer radical polymerization (ATRP) initiator, **NBMP**, was synthesized according to the procedure reported in a recent study (Scheme S1).³⁷ NMR spectra were consistent with literature reports. ¹H NMR (CDCl₃): δ 6.16 (m, 1H), 5.95 (m, 2H), 4.72 (m, 1H), 2.92 (s, 1H), 2.87 (s, 2H), 1.90 (s, 3H, CH₃), 1.75-1.42 (m, 10H). ¹³C NMR (CDCl₃): δ 171.6, 141.6, 132.4, 76.9, 56.3, 47.7, 47.1, 46.4, 45.7, 42.3, 40.7, 34.5, 34.4, 30.8, 30.7.

2.4.4 Synthesis *exo*-norbornene-methyl 2-(((dodecylthio)carbonothioyl)thio)-2-methylpropanoate (NDTMP)

The norbornene-functionalized photoiniferter, **NDTMP**, was synthesized according to the procedure reported in a recent study (Scheme 2.S2).³⁷ NMR spectra were consistent with literature reports. ¹H NMR (CDCl₃): δ 6.07 (m, 2H), 4.22 (dd, *J* = 10.8 Hz, 6.4 Hz, 1H), 3.95 (dd, *J* = 10.8 Hz, 9.2 Hz, 1H), 3.27 (td, *J* = 7.4 Hz, 2.1 Hz, 2H), 2.82 (s, 1H), 2.66 (s, 1H), 1.70 (s, 6H), 1.31 (m, 3H), 1.25 (m, 20H), 0.88 (t, *J* = 7 Hz, 3H). ¹³C NMR (CDCl₃): δ 221.6, 173.2, 137.0, 136.5, 70.2, 56.2, 45.1, 43.8, 41.8, 37.9, 37.0, 32.1, 29.8, 29.7, 29.6, 29.5, 29.3, 29.1, 28.1, 25.6, 25.6, 22.9, 14.3.

2.4.5 Synthesis of PS_{Br}

A polystyrene MM containing a Br end group (**PS_{Br}**) was synthesized using atom-transfer radical polymerization (ATRP). Styrene (30 mL, 358 equiv, 262 mmol) was added to an oven-dried 100 mL Schlenk tube containing a magnetic stir bar, followed by **NBMP** (0.20 g, 1 equiv, 0.73 mmol), CuBr (52 mg, 0.5 equiv, 0.37 mmol), and CuBr₂ (82 mg, 0.5 equiv, 0.37 mmol). The mixture was deoxygenated using three freeze-pump-thaw cycles, then heated in a 90 °C oil bath for ~10 min before *N,N,N',N'',N''*-pentamethyldiethylenetriamine (PMDETA) (0.15 mL, 1 equiv, 0.73 mmol) was added via syringe. The reaction mixture was allowed to stir for 3 h, then the Schlenk tube was

removed from the oil bath, and the valve was removed to expose the contents to air to terminate the reaction. The MM was then purified and isolated by adding approximately 150 mL EtOAc and washing with 150 mL of water in a separatory funnel. The organic layer was then washed with brine (150 mL) and dried over MgSO₄. The EtOAc was removed by rotary evaporation, and the resulting clear, viscous solution was dissolved in approximately 50 mL of CH₂Cl₂. Next, this solution was precipitated by dropwise addition to 1 L of stirring CH₃OH. The solid was recovered by filtration, redissolved in CH₂Cl₂, and precipitated again. This precipitation process was performed three times in total with the final white solid recovered by filtration and dried overnight, yielding 2.8 g **PS_{Br}** (Scheme 2.S3). The molecular weight was estimated using end-group analysis by ¹H NMR spectroscopy and found to be 4400 g/mol (Figure 2.S1), and by SEC and found to have a number average molecular weight (*M_n*) of 4500 g/mol and *D* = 1.03 (Figure 2.S2).

2.4.6 Synthesis of **PnBA_{Br}**

ATRP was used to synthesize a poly(*n*-butyl acrylate) MM containing a Br end group (**PnBA_{Br}**). CuBr (26 mg, 0.5 equiv, 0.18 mmol), **NBMP** (0.10 g, 1 equiv, 0.37 mmol), *n*-butyl acrylate (4.0 mL, 75 equiv, 27 mmol), and acetone (1.4 mL) were added to an oven-dried 100 mL Schlenk tube containing a magnetic stir bar. The Schlenk tube was deoxygenated by three freeze-pump thaw cycles and backfilled with N₂. The reaction mixture was stirred at 60 °C for ~10 min before PMDETA (0.15 mL, 0.5 eq, 0.18 mmol) was added via syringe, and then the mixture was heated and stirred for 12 h. The Schlenk tube was removed from the oil bath, and the valve was removed to expose the contents to air to terminate the reaction. An aliquot was removed for analysis of monomer conversion; ¹H NMR spectroscopy showed 48% conversion of *n*-butyl acrylate to poly(*n*-butyl acrylate). The MM was then purified and isolated by adding approximately 150 mL EtOAc and washing with 150 mL of water in a separatory funnel. The organic layer was then

washed with brine (150 mL) and dried with MgSO₄. The EtOAc was removed via rotary evaporation, and the residual *n*-butyl acrylate was removed by adding around 20 mL DMF and drying by blowing air overnight. The crude product was then dissolved in around 100 mL THF and passed through basic alumina. The THF was removed by rotary evaporation, and the semi-translucent, viscous liquid was dried under vacuum yielding 1.3 g of **PnBA_{Br}** with an expected molecular weight (by conversion) of 4700 g/mol (Scheme 2.S4). The molecular weight was estimated using end-group analysis by ¹H NMR spectroscopy and found to be 4000 g/mol (Figure 2.S4) and by SEC and found to have an *M_n* of 4200 g/mol and *D* of 1.14 (Figure 2.S5).

2.4.7 Synthesis of **PnBA_{TTC}**

The synthesis of the **PnBA_{TTC}** MM utilized photoiniferter polymerization using a photoreactor similar to that previously reported.³⁹ *n*-Butyl acrylate (3.4 mL, 50 equiv, 23.4 mmol) was passed through three basic alumina plugs, then added to an oven-dried 100 mL Schlenk tube containing a magnetic stir bar, along with **NDTMP** (168 mg, 1 equiv, 0.47 mmol) 2,2'-azobis(2-methylpropionitrile) (AIBN) (0.77 mg, 0.01 equiv, 4.7 μmol), and THF (13.4 mL). The mixture was deoxygenated by five freeze-pump-thaw cycles before being placed into the photoreactor containing a blue LED light ($\lambda = 450$ nm) and stirred for 6.5 h at room temperature. The Schlenk tube was removed from the reactor, and the valve was removed to expose the contents to air to terminate the reaction. An aliquot was removed for analysis of monomer conversion; ¹H NMR spectroscopy showed 47% conversion of *n*-butyl acrylate to poly(*n*-butyl acrylate). The excess nBA and THF were removed from the mixture by adding around 20 mL DMF and overnight evaporation by blow-drying with air, followed by overnight drying under vacuum yielding 1.6 g of a yellow, viscous liquid with an expected molecular weight, based on conversion, of 3300 g/mol (Scheme 2.S5). The molecular weight was estimated using end-group analysis by ¹H NMR

spectroscopy and found to be 3900 g/mol (Figure 2.S7) and by SEC and found to have an M_n of 3900 g/mol and D of 1.10 (Figure 2.S8).

2.4.8 Synthesis of NMB

A small molecule norbornene, *exo*-norbornene-5-methyl benzoate (**NMB**), was prepared using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) coupling (Scheme 2.S6). *Exo*-norbornene-methanol (1.0 g, 8.05 mmol) and EDC (1.63 g, 10.5 mmol) were dissolved in CH_2Cl_2 (25 mL) in a round bottom flask equipped with a stir bar. The contents were stirred until the solids had completely dissolved (~5 min). A second flask was charged with benzoic acid (1.28 g, 10.5 mmol), *N,N*-dimethylpyridin-4-amine (DMAP) (0.492 g, 4.03 mmol), and 25 mL CH_2Cl_2 . This second solution was added dropwise into the flask containing *exo*-norbornene-methanol while stirring. After complete addition, the reaction mixture was stirred at room temperature for 12 h, monitoring conversion by TLC with CH_2Cl_2 as the mobile phase and a potassium permanganate stain. The reaction mixture was transferred to a separatory funnel and washed three times with saturated sodium carbonate and once with brine, dried over sodium sulfate, and concentrated by rotary evaporation. The concentrated crude product was purified by a silica column, eluting with 5% EtOAc in hexanes. The product was obtained as a colorless oil (0.96 g, 52% yield). ^1H NMR (CDCl_3): δ 8.11–8.02 (m, 2H), 7.60–7.53 (m, 1H), 7.49–7.40 (m, 2H), 6.12 (m, 2H), 4.42 (m, 1H), 4.22 (m, 1H), 2.91–2.78 (m, 2H), 1.96–1.83 (m, 1H), 1.45–1.22 (m, 5H). ^{13}C NMR (CDCl_3): δ 166.38, 136.72, 135.98, 132.58, 130.21, 129.31, 128.08, 68.74, 44.75, 43.46, 41.37, 37.84, 29.33. Both ^{13}C and ^1H NMR spectra match literature values.⁴⁰

2.4.9 Purification methods for solvents

Three different purity conditions were used to test the effects of potential impurities in each solvent. The “as received” solvents were obtained from commercial vendors (specific vendor and grade are highlighted in the materials section) and used straight from the bottle. The “distilled” solvents were distilled at atmospheric pressure, except for DMF which was distilled at reduced pressure, and stored in an inert atmosphere over 3 Å molecular sieves. The “purified” solvents were purified either using solvent purification columns or following detailed procedures from *Purification of Laboratory Chemicals*.⁴¹ These methods are as follows:

EtOAc was purified by washing with equal volumes of saturated aqueous sodium carbonate in a separatory funnel, followed by brine, before removing the organic layer and drying over MgSO_4 . The solvent was then distilled onto molecular sieves and was stored in a Strauss flask under nitrogen protected from the light. CH_2Cl_2 was first shaken with portions of concentrated sulfuric acid (around 15 mL per 200 mL of CH_2Cl_2) in a separatory funnel until the slightly yellow H_2SO_4 layer turned and remained colorless. The solvent was then washed with water in a separatory funnel, then washed with 5 w/v % NaOH in water, followed by a final wash with water. The CH_2Cl_2 was then dried over MgSO_4 and stirred with 10 w/v % CaCl_2 overnight. The solution was filtered to remove CaCl_2 and then distilled from 10 w/v % CaSO_4 onto molecular sieves. The purified solvent was stored on sieves in a nitrogen-filled Strauss flask protected from the light. CHCl_3 was washed with water using a separatory funnel before drying over 5 w/v% CaCl_2 for 3 h. The CaCl_2 was filtered off, fresh CaCl_2 (5 w/v %) was added, and the solution was refluxed for 4–6 h. The solution was filtered, then distilled onto molecular sieves and was stored in a Strauss flask under nitrogen protected from the light. DMF was stirred over 5 w/v % CaH_2 overnight, then filtered. The DMF was then distilled at reduced pressure onto molecular sieves and was stored in

a Strauss flask under nitrogen protected from the light. Both toluene and THF were taken from solvent drying columns charged with activated alumina and used immediately after removal from the column.

2.4.10 Evaluation of propagation rates of MMs

A representative method for the ROMP of each MM under air is as follows: The MM (40 mg, 100 equiv, 8.9 μmol) was added to a 1-dram vial at a concentration of 50 mg/mL in the chosen solvent. Grubbs' third generation catalyst (G3, 2.0 mg) was dissolved in 0.9 mL of the solvent, and 30 μL of the solution was added rapidly to the stirring MM solution via a 100 μL syringe at a molar ratio of 100:1 MM:G3. The vial was capped, and at specific timepoints throughout the polymerization, 50 μL aliquots were removed via syringe and added to vials containing a few drops of ethyl vinyl ether (EVE) to terminate the reaction. The solutions were allowed to dry by leaving the vials open to the air overnight, then the residual solids were dissolved in THF for SEC analysis to measure MM conversion to BB polymer, molecular weight, and $\bar{D}$. This process was repeated in triplicate for each solvent type and level of purity for **PS_{Br}**, and for each pure solvent for **PnBA_{Br}** and **PnBA_{TTC}**.

2.4.11 Kinetic Analysis of BB Polymers by SEC

To determine conversion, molecular weight, and dispersity at each timepoint during the polymerization of **PS_{Br}**, **PnBA_{Br}**, and **PnBA_{TTC}**, samples were prepared for analysis by SEC. The dried polymer mixture, taken at each timepoint during the course of the reaction, was dissolved in 1 mL THF inhibited by 0.025 wt% butylated hydroxytoluene (BHT) and filtered into an SEC vial and analyzed by SEC. Molecular weights were obtained using a dn/dc value of 0.185 and 0.074 for PS and PnBA, respectively. Polymerization conversion was measured by comparing the relative integrations of the MM and BB polymer peaks in the RI traces using these dn/dc values

for both peaks. Propagation rate constants and half-lives were calculated by fitting conversion data to a first-order kinetics plot. A maximum conversion of less than 100% was used for each of the MMs (94% for **PS_{Br}**, 90% for **PnBA_{Br}**, and 88% for **PnBA_{TTc}**) due to a small amount of the MM lacking a norbornene functional group, as we have seen previously in MMs prepared using reversible-deactivation radical polymerization (RDRP) methods.^{39,42} SEC traces for polymerization of each MM in each solvent with different purities, as well as the rate graphs, can be found in Appendix A (Figures 2.S10-2.S33).

2.4.12 Kinetics of ROMP of NMB

Small molecule norbornene, **NMB**, was polymerized via ROMP, and the kinetics were determined using ¹H NMR spectroscopy. A representative procedure is as follows: **NMB** (40 mg, 100 equiv, 181 μmol) was added to a scintillation vial containing a magnetic stir bar and enough solvent for a 20 mM concentration (8.8 mL). A solution of pyridine was created by adding 0.2 mL pyridine to 1.4 mL of the chosen solvent and injecting 10 μL into the **NMB** solution (final amount added was 1.5 μL, 10 equiv, 18 μmol). A G3 solution was made by adding 2.5 mg of G3 into 0.12 mL of solvent, then a portion of this solution (60 μL, final amount added of solution was 1.28 mg, 1 equiv, 1.8 μmol) was injected rapidly via syringe into the stirring **NMB** solution to make a final reaction mixture containing 100 equiv NMB, 10 equiv pyridine, and 1 equiv G3. Several 500 μL aliquots were taken throughout the 20 min polymerization and added into vials containing a few drops of EVE. The resulting solutions were allowed to air dry for 24–48 h before dissolving in CDCl₃ and analyzing using ¹H NMR spectroscopy (16 scans, 2 s relaxation delay). Monomer conversion was determined by integrating the norbornene olefin proton peaks (around 6.2 ppm) and the norbornene polymer peaks (broad peak around 5.2 ppm) (Figure 2.S34) and comparing the

polymer proton peaks' integration values to the integration value of the norbornene protons. Half-life values were calculated from first-order kinetics fits using these conversions.

2.4.13 Tracking catalyst decomposition via UV-Vis

To monitor catalyst decomposition over time, a fiber optic dip probe was attached to the UV-Vis spectrometer. G3 was dissolved in solvent at a concentration of 0.075 mg/mL at a volume of around 10–12 mL in a 20 mL scintillation vial containing a magnetic stir bar. The vial was placed onto a stir plate, the dip probe was inserted into the vial, and parafilm was wrapped around the top of the vial to limit evaporation of the solvent. Spectra were collected from 250 to 500 nm (2 nm step) every 30 sec with timepoints starting approximately 5–10 seconds after the G3 was added to the solvent (lamp crossover was set to 350 nm). This was repeated in triplicate for each of the six pure solvents. To accurately determine rate constants for each solvent, the decomposition profiles were normalized to the maximum absorption for each sample at 344 nm, and a first-order kinetic analysis was applied (see Figures 2.S35-2.S40 and discussion in Appendix A for details).

2.5 Results and Discussion

BB polymers contain a polymer backbone with pendant polymer side chains that can take on various shapes depending on pendant chain grafting density and chemistry, backbone chemistry, and the DPs of both (N_{bb} and N_{sc} , respectively). The grafting-through synthetic method allows for the best control over grafting density uniformity, allowing for “perfect” grafting density. This is achieved by polymerizing an MM, which is a homotelechelic polymer containing a polymerizable group (e.g., a norbornene) on one chain end.⁴³ This “perfect” grafting density is important because it significantly affects the conformation of the polymer, causing backbone chain extension and essentially eliminating entanglements within the pendant chains and between BB polymers.⁴⁴ The unique properties and topologies of BB polymers make them an exciting topic in polymer science

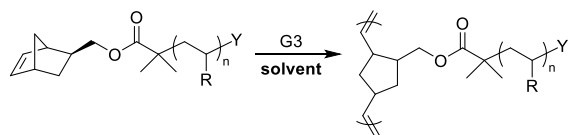
that has gained attention in the past few decades as nanoscale materials with unique shapes and properties that can be applied as drug delivery agents,^{45–48} photonic crystals,^{49–52} interfacially active agents,^{53–55} nanomaterials with tunable sizes and shapes,^{56,57} and in the creation of elastomers with unique properties.^{58–60} Likewise, synthesizing BB polymers enables further understanding of the optimal reaction conditions in ROMP.

Our laboratory, along with others, has sought to create large, well-defined BB polymers, some with unique architectures such as tapered BB polymers.^{37,42,61,62} In these efforts we aim to optimize “livingness” in ROMP to achieve well-defined, low $\bar{D}$ polymers. In 2016 we discovered that the choice of anchor group, the series of atoms connecting the norbornene to the polymer chain in an MM, significantly affects the rate of propagation in ROMP.³⁴ We have also noticed that the choice of solvent affects the propagation rate in ROMP, as well as the maximum conversion that can be achieved during the synthesis of BB polymers. While anecdotal mentions of solvent effects in ROMP in the context of complex polymer topologies have appeared in a few papers from our group and others,^{34,42,63} no systematic studies have been conducted. In addition to differences in propagation rates depending on solvent choice, we have also observed that the method of purification of the chosen solvent can sometimes make a difference in the efficiency of ROMP. Here we set out to systematically study these phenomena.

2.5.1 Solvent type and purity effects on ROMP propagation rate

To investigate the effect that solvent choice and purity have on the propagation rate of ROMP, we first employed ATRP to synthesize a polystyrene MM on the 3 g scale (**PS_{Br}**) with an M_n of 4500 g/mol ($N_{sc} = 40$) and a $\bar{D}$ of 1.03 (Scheme 2.1). We targeted an M_n of less than 5000 g/mol because we have observed a substantial decrease in monomer conversion if N_{sc} exceeds ~50. This batch of

PS_{Br} MM was used throughout the entirety of this portion of the study to measure k_p for six solvents with differing levels of purity.



PS_{Br}: R = Ph, Y = Br (M_n = 4500 g/mol, $\bar{D}$ = 1.03)

PnBA_{Br}: R = C(O)OnBu Y = Br (M_n = 4200 g/mol, $\bar{D}$ = 1.14)

PnBA_{TTc}: R = C(O)OnBu Y = SC(S)SC₁₂H₂₅ (M_n = 3900 g/mol, $\bar{D}$ = 1.10)

Scheme 2.1. Representative scheme of the grafting-through ROMP of the three MMs used in this study.

We chose six solvents based on their wide use in ROMP: EtOAc, CH₂Cl₂, CHCl₃, toluene, THF (uninhibited), and DMF. We hypothesized that purification of each solvent might increase k_p by removing impurities that could hinder the activity of the catalyst. To investigate purification effects on k_p , we used three different categories of purification. The first was the “as received” category, in which we took the solvent directly from the bottle. The second and third categories involved performing simple distillations as well as more rigorous purifications for each solvent, which we term “distilled” and “purified,” respectively. In this third category, each solvent was purified either by passage through solvent purification columns or by following procedures outlined in *Purification of Laboratory Chemicals*,⁴¹ as discussed in the experimental section.

To experimentally measure $k_{p,obs}$, we polymerized **PS_{Br}** MM with a ratio of 100:1 MM:G3 (i.e., target N_{bb} = 100), at a concentration of 50 mg/mL in each solvent (Scheme 2.1). Reactions were performed in capped vials under air at room temperature. Aliquots were removed at pre-determined timepoints and added to vials containing EVE to terminate the polymerization. Solvents were removed, then MM conversion and molecular weight at each timepoint were determined via SEC analysis by comparing the integrations of the MM and BB polymer peaks using the known dn/dc value for polystyrene in THF (0.185 mL/g) for both. After plotting conversion versus time using these experimental conversion results, the data were fitted to a first-

order kinetic model, from which $k_{p,obs}$ values were determined. Each polymerization of **PS_{Br}** was performed three to four times in each of the different solvents (six solvents with three different purification methods each).

First-order kinetics fits are shown in Figure 2.1A for a representative solvent (CH₂Cl₂) for all three purity levels. Similar graphs for the other five solvents are shown in Appendix A (Figures 2.S13, 2.S21, 2.S25, 2.S29, and 2.S33). While ¹H NMR spectroscopy confirmed complete consumption of the norbornene end group, SEC appeared to show only 94% MM conversion to BB polymer. We attribute this discrepancy to 6% of the MM sample that lacks the norbornene end group, as we have seen before in similar MMs.⁴² We therefore adjusted all conversion values to account for this 6% residual PS MM. We also noticed that the experimental points fall slightly below the first order fit above ~60% conversion in all polymerizations. We attribute this decrease in k_p at moderate to high conversions to a small but observable dependence of k_p on N_{bb} in the growing BB polymer chain. This behavior is consistent with reports suggesting that steric hindrance near the chain end of the propagating species slows the propagation rate,³⁵ with the MM being hindered by the brush as it approaches the reactive chain end.⁶⁴ The results for each solvent at each purity level are shown in Figure 2.1B and Table 2.S1, revealing several interesting and some unexpected results.

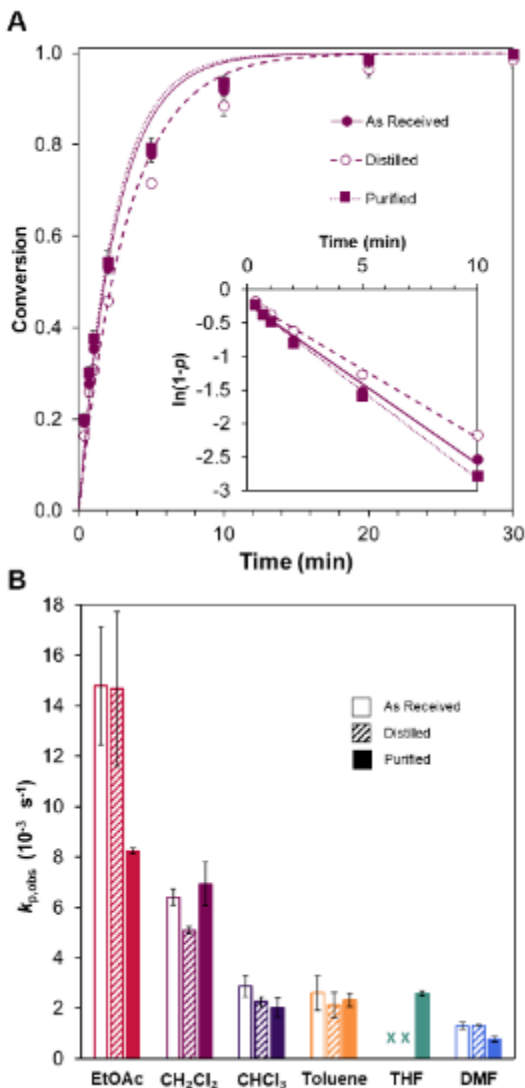


Figure 2.1. (A) Conversion versus time plot for ROMP of PS_{Br} MM in CH_2Cl_2 (50 mg/mL) at three different purity levels. Lines show first-order kinetics fits for each series. Error bars at each data point represent the standard deviation at each time point in 3–4 ROMP experiments for each purity category. Inset shows $\ln(1-p)$ versus time (p = MM conversion), where lines show first-order kinetics fits for each series. Similar plots for the other five solvents are shown in Figures 2.S13, 2.S21, 2.S25, 2.S29, and 2.S33, and $k_{p,obs}$ and half-life values, MM conversion values, and polymer characterization results are shown in Table 2.S1. (B) Measured first-order $k_{p,obs}$ values for ROMP of PS_{Br} in all six solvents with each different method of purification. Empty bars represent the as received solvents, lined bars represent distilled solvents, and solid bars represent purified solvents. The as received and distilled THF showed <3% conversion to

BB polymer, so $k_{p,obs}$ could not be determined in these two cases. Error bars represent the standard deviation in 3–4 ROMP experiments for each solvent.

First, EtOAc, regardless of whether it was used as received, distilled, or more rigorously purified, led to the highest $k_{p,obs}$ among all solvents. CH_2Cl_2 was the next fastest solvent and polymerized **PS_Br** more than twice as fast as CHCl_3 , toluene, and THF. DMF was the slowest solvent regardless of the purification method and was about 6-fold slower than EtOAc. Second, our hypothesis that $k_{p,obs}$ would increase with distillation or purification was disproven—the purified solvents mostly decreased or had little impact on $k_{p,obs}$. Purified EtOAc showed the most significant change in rate, with an almost 50% reduction in $k_{p,obs}$ after purification. We speculate that this could be due to the presence of acetic acid in as received EtOAc. Acetic acid likely protonates the labile pyridine ligands in G3, preventing them from re-binding to the active site on the Ru complex, allowing for faster MM addition, thus an increased polymerization rate. We experimentally tested this hypothesis by performing ROMP reactions in purified EtOAc spiked with 20 equiv acetic acid relative to catalyst (Figure 2.S41) and found that k_p increased to a similar level to that of the as received EtOAc. Support for this conclusion comes from recent work by Guirronet and coworkers that showed that ROMP using G3 is -1 order in pyridine, meaning that k_p is inversely proportional to pyridine concentration.⁶³

THF was an interesting case, as we saw little ROMP (less than 3% conversion) with the as received and distilled levels of purity. Purified THF was taken from solvent drying columns charged with activated alumina, and polymerization with THF from this source went to full conversion at a rate similar to CHCl_3 and toluene. We speculate that low levels of peroxides in as received and even in distilled uninhibited THF cause almost instantaneous catalyst decomposition, although we could not conclusively confirm this. However, rapid catalyst decomposition was obvious based on the

change in the color of the G3 solution from green to brown upon dissolution in as received or distilled THF; this color change did not occur with purified THF or any of the other solvents.

In the case of DMF, which was the slowest solvent in all cases, MM conversion values were lower (84–89%) compared with the other solvents (97–99%), and dispersity values were generally higher ($\mathcal{D} = 1.2\text{--}1.4$ for DMF, and ~ 1.1 for all other solvents). Interestingly, we observed a similar trend to EtOAc when comparing $k_{p,obs}$ values across solvents with different levels of purity, where purification actually reduced $k_{p,obs}$ by about 50%. Typical impurities in DMF include dimethylamine and formic acid,⁶⁵ so the enhanced rate of ROMP in the as received DMF (and even distilled DMF, where these impurities likely remain) may be attributed to the formic acid, which boils nearly 100 °C higher than dimethylamine so is likely present in higher concentrations than dimethylamine.

Finally, we note that these trends for as received solvents may depend on levels of impurities present in the as received forms, which may vary between suppliers and batches of solvents, causing variance in the rate of propagation.

2.5.2 Macromonomer and end group effects on ROMP propagation rate

We next asked whether the rate effects were similar when using different MMs or whether our observations were specific to PS MMs prepared by ATRP. Therefore, we synthesized two PnBA MMs using ATRP and photoiniferter polymerization with molecular weights similar to **PS_{Br}** (Scheme 2.1); these were named **PnBA_{Br}** and **PnBA_{TTC}**, where TTC indicates the trithiocarbonate end group. The goal in creating these two additional MMs was to determine whether the side chain chemistry (PS or PnBA) or side chain end group (Br or trithiocarbonate) affected $k_{p,obs}$. With these two additional MMs in hand, we again performed a series of ROMP reactions to measure $k_{p,obs}$ in

the six selected solvents, this time using only the purified solvents. Again, we targeted $N_{bb} = 100$ by conducting ROMP at a 100:1 MM:G3 ratio for each reaction. Aliquots were removed and analyzed by SEC, and first-order kinetics fits were determined using the same methods as used for **PS_{Br}**. A summary of results highlighting $k_{p,obs}$ values for **PS_{Br}**, **PnBA_{Br}**, and **PnBA_{TTC}** in each of the six purified solvents is shown in Figure 2.2.

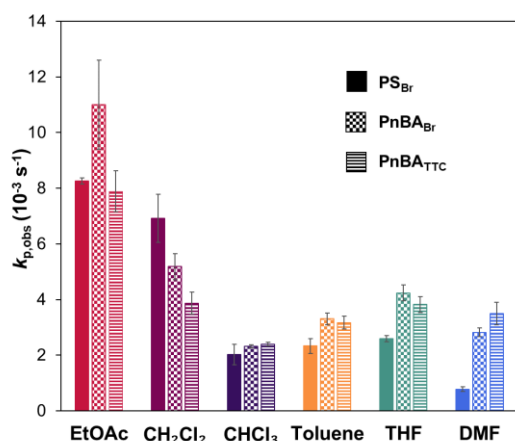


Figure 2.2. Measured $k_{p,obs}$ values based on first-order kinetics fits for the ROMP of **PS_{Br}** (filled bar), **PnBA_{Br}** (checked bar), and **PnBA_{TTC}** (lined bar) in purified solvents. Error bars represent the standard deviation in 3–4 ROMP experiments for each solvent.

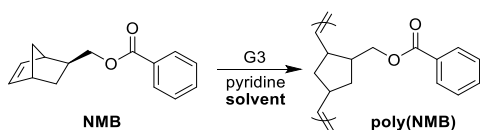
Overall, changes to the polymer side chain and end groups caused only small perturbations in the $k_{p,obs}$ values. However, the PnBA side chains in **PnBA_{Br}** and **PnBA_{TTC}** reduced $k_{p,obs}$ by about 50% compared with **PS_{Br}** in CH₂Cl₂ and increased $k_{p,obs}$ about 4-fold compared with **PS_{Br}** in DMF. These two results may be associated with the behavior of the MM in the solvent, where PS has a less extended conformation in DMF than PnBA does, while the opposite effect occurs in CH₂Cl₂ (see below for further discussion). With these measurements regarding the effect of MM molecular structure on the relative rate of propagation for grafting-through ROMP, further investigations were made into not only the differences in these two solvents as it relates to MMs, but also into the substantial difference between the propagation rate in the six different solvents.

We next set out to explain why k_p varied across the different solvents. Others have considered similar questions: For example, Grubbs and coworkers found that the initiation rate of G3 varied directly with the dielectric constant of the solvent,²⁸ and Matyjaszewski and coworkers discovered a relationship between the enthalpy of grafting-through ATRP reactions and the Hansen solubility parameters.⁶⁶ With this precedent established, we investigated numerous parameters describing the solvents themselves and compared them to the measured $k_{p,obs}$ values for **PSBr** and **PnBA_{ITC}**. These parameters included solubility parameters, solvent dielectric constant, and the viscosity of each solvent (Figure 2.S42). None of these properties showed a discernible relationship with the measured $k_{p,obs}$ values for **PSBr**. We also compared the polymer-solvent interaction parameters for PS with each solvent to the $k_{p,obs}$ values and saw no correlation. Finally, we experimentally compared the polymer behavior in solution for each solvent. To do this, we performed static light scattering (SLS) experiments on high molecular weight linear PS ($M_w = 200$ kg/mol) and PnBA ($M_w = 180$ kg/mol) in each of the six pure solvents. We highlight the experimental methods and results of these experiments in the supporting information (Figure 2.S43, Table 2.S4, and Table 2.S5). While we identified a possible relationship in the propagation rate decrease from PnBA to PS in DMF, there was no clear trend or conclusions for all of the solvents from these experiments.

2.5.3 Propagation rate of ROMP for a small molecule norbornene

In order to compare our results on MMs with a small molecule norbornene, we measured $k_{p,obs}$ values of *exo*-norbornene-5-methyl benzoate (**NMB**) in the same purified solvents (Scheme 2.2). In these experiments, we used a monomer concentration of 20 mM and targeted a backbone DP of 100. As in the kinetics experiments with the MMs, aliquots were taken at timepoints throughout the polymerization and added to vials containing EVE to terminate the reaction. The solvent was removed, and the conversion at each timepoint was determined using ¹H NMR spectroscopy by

comparing the integral areas of the olefin proton peaks of the **NMB** to the olefin proton peaks of **poly(NMB)** (Figure 2.S34). We initially found that polymerizations were too fast to measure effectively using our typical methods (half-lives were <5 s in several solvents). Therefore, we performed these studies with 10 equiv of added pyridine, which slowed the reaction enough to obtain measurable reaction rates. Figure 2.3A and Table 2.S6 show the $k_{p,obs}$ values for each polymerization, while figures 2.3B-D compares **poly(NMB)** $k_{p,obs}$ values to the $k_{p,obs}$ values of the **PS_{Br}** (B), **PnBA_{Br}** (C), and the **PnBA_{TTC}** (D) MMs.



Scheme 2.2. ROMP of small molecule **NMB** used for comparison of $k_{p,obs}$ values with and without polymer pendant side chains.

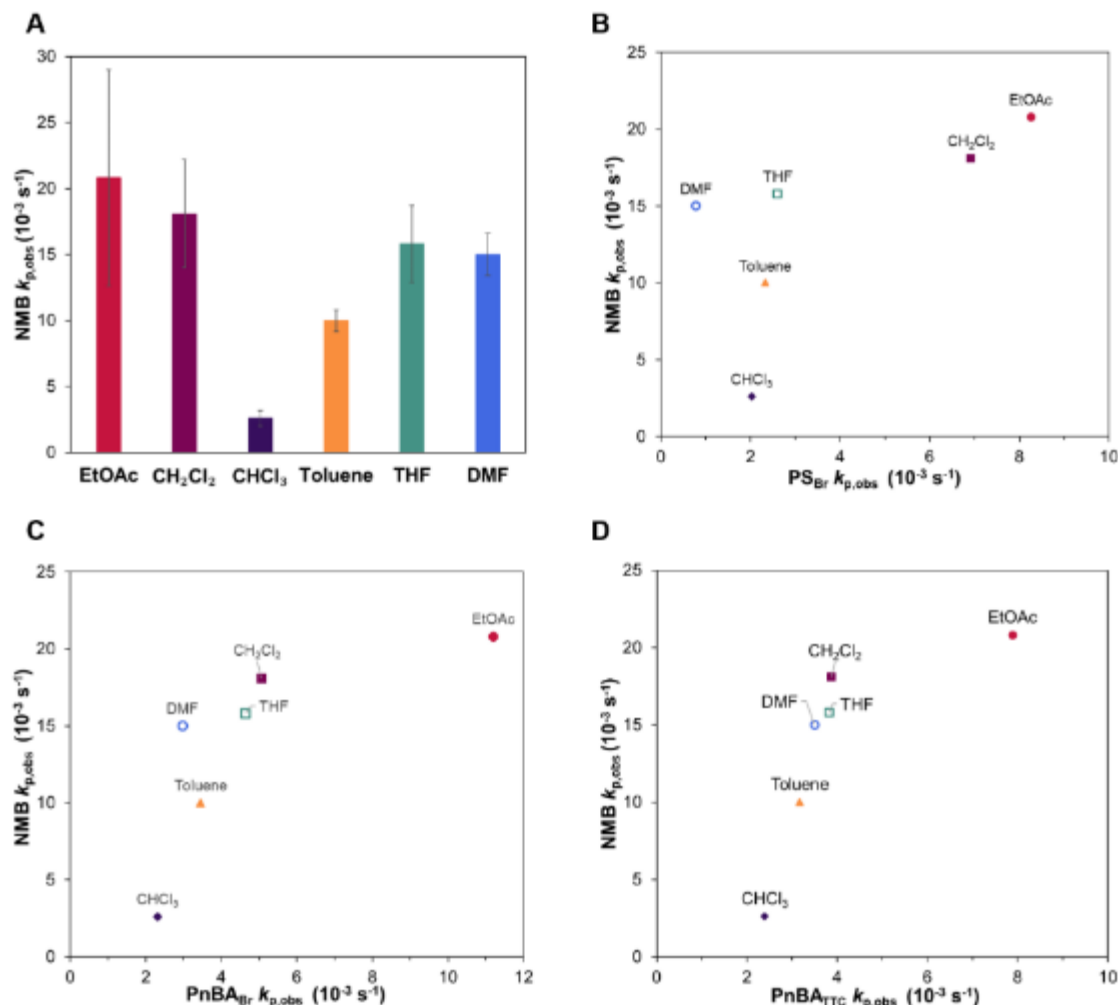


Figure 2.3. A) Graph showing $k_{p,obs}$ values for the ROMP of **NMB** in six purified solvents. The error bars represent the standard deviation in three independent experiments. B–D) Graphs comparing the **NMB** $k_{p,obs}$ to the MM $k_{p,obs}$ for B) **PS_{Br}**, C) **PnBA_{Br}**, and D) **PnBA_{TTC}**.

Figures 2.3B-D reveal that the $k_{p,obs}$ values for **NMB** and the three MMs show an approximately linear relationship in the different solvents (i.e., EtOAc has the highest rate for both **NMB** and the MMs). The $k_{p,obs}$ value in CHCl_3 for **NMB** was much lower than expected and substantially slower than the polymerizations performed in the other solvents. When adding pyridine to CHCl_3 prior to starting the reaction, we noticed the formation of an opaque solution. We believe this could be associated with a complexation between pyridine and CHCl_3 ,⁶⁷ which appears to hinder the activity

of the G3 catalyst. The combined data provide evidence that ROMP propagation rate is more affected by the activity and stability of the G3 catalyst in the particular solvent than it is by the nature or presence of a polymer pendant chain. While EtOAc and CH₂Cl₂ generally promoted faster ROMP propagation than other solvents, the differences are consistent between both **NMB** and the three MMs tested here. The differences in propagation rates are larger when using MMs versus a small molecule norbornene, highlighting the importance of solvent choice when making complex polymer topologies such as BB polymers using ROMP.

2.5.4 Rate of catalyst decomposition

To estimate the rate of catalyst decomposition, we explored the stability of the catalyst itself, without considering the MM or the ROMP grafting-through step. We used UV-Vis spectroscopy to monitor the decrease in the absorption of the metal-ligand charge transfer (MLCT) band associated with the Ru-benzylidene in G3, implying catalyst decomposition over time.^{28,68} In these experiments, G3 was dissolved in each solvent at the same concentration as used during the ROMP kinetics experiments. We measured the absorbance change over time at the MLCT wavelength of 344 nm and fit the results to a first-order kinetics plot (Figure 2.4). We note that these decomposition experiments were not done in the presence of monomer because the catalyst spectrum becomes featureless after initiation. We also could not monitor decomposition in the presence MM by NMR spectroscopy because there is so little catalyst mass added with respect to MM such that we could not see a benzylidene or alkylidene peak.

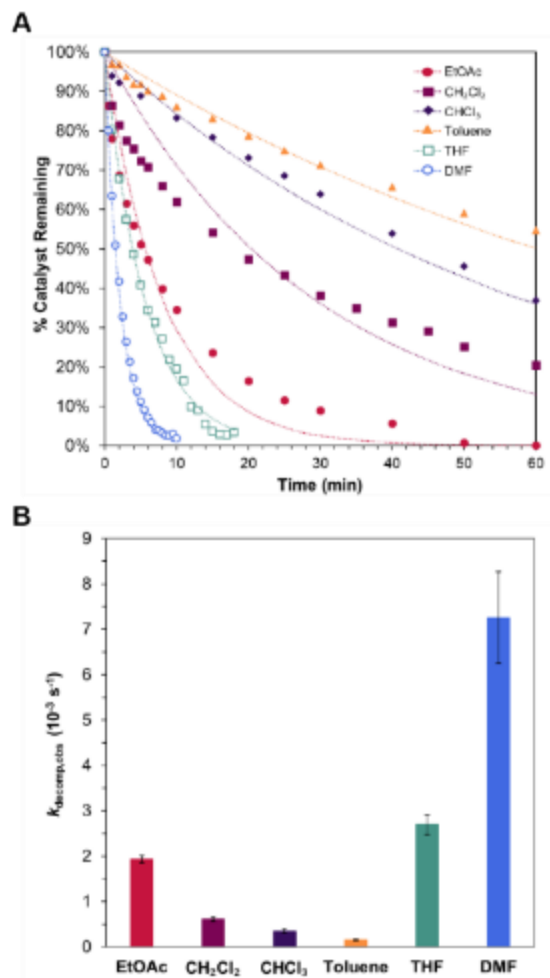


Figure 3.4. A) Change in % catalyst remaining over time in each solvent, as determined by monitoring absorbance of the MLCT peak (344 nm). Studies were performed in covered vessels under air with a concentration of 0.075 mg/mL G3 (0.10 mM) in solvent. B) Measured first-order rates of catalyst decomposition in each purified solvent in triplicate (Table 2.S7). The error bars represent the standard deviation from three independent experiments.

While each solvent showed catalyst decomposition over time, toluene showed the slowest decomposition rate, while DMF and THF showed the fastest decomposition rates, with half-lives on the order of a few minutes. These rates were surprisingly fast considering that ROMP reactions on MMs in these solvents take longer than a few minutes, indicating that catalyst decomposition is slower in the presence of monomer than in its absence. These two solvents also showed the best

fits to first-order kinetics, suggesting a single primary decomposition pathway in these solvents and multiple pathways or higher-order processes in the other solvents. Fast decomposition in THF and DMF is consistent with work from Grubbs and coworkers comparing the rate of initiation of ruthenium olefin metathesis catalysts in different solvents.²⁸ They noted that the solvent dielectric constant was roughly proportional to the rate of initiation in various solvents. It is likely that these moderately polar, coordinating solvents interact with the catalyst in a way that favors decomposition pathways more than less polar solvents incapable of coordination. In our experiments, solvent dielectric constant did not vary linearly with our measured $k_{p,obs}$ values, but the theory behind why THF and DMF led to the fastest catalyst decomposition is still comparable to Grubbs's explanation of results: The state of the G3 ruthenium complex, when the catalyst has an available coordination site, is electron-deficient and could be available for coordination by more polar solvents (i.e., those with higher dielectric constants), which would inhibit the coordination of the monomer. Our results suggest that solvent coordination leads to faster decomposition. This also tracks with studies showing that less polar solvents generally favor productive olefin metathesis, while highly polar solvents instead promote higher levels of olefin isomerization and catalyst decomposition.⁶⁹ Finally, this conclusion is also supported by studies showing that some Ru catalysts have unusual decomposition pathways in solvents with high dielectric constants.⁷⁰

In the case of EtOAc, which could presumably coordinate to the catalyst through its ester linkage, the decomposition rate aligns with previous reports;²⁸ however, the rate of propagation was much faster in EtOAc than in any other solvent. Future computational work may be able to shed some light on specific interactions between the catalyst and EtOAc that enhance catalytic activity. Another explanation for these results could be related to the behavior of the pyridines that are in equilibrium at the active site on the ruthenium complex.⁶³ If pyridine has higher solubility in a

specific solvent, it may drive the equilibrium toward the free pyridine and the active 14-electron catalyst species, enabling monomer binding to the active site.

2.5.5 Macromonomer conversion at high target N_{bb} values

Our ultimate goal in this work was to evaluate “livingness” in ROMP grafting-through in each of these solvents. A good method to assess “livingness” is to target a high DP to see if the targeted molecular weight can be reached at high monomer conversion levels while maintaining low $\bar{D}$. Therefore, we prepared a new PS MM by ATRP with $M_n = 3.0$ kg/mol and subjected it to ROMP when targeting an N_{bb} of 1000 (instead of 100 as in the earlier experiments) in each purified solvent. The reactions were set up in a similar way to the kinetics experiments, but each polymerization was allowed to run for 24 h. After quenching the reaction, we used SEC to estimate the MM conversion to BB polymer in each polymerization by comparing the area of the BB polymer peak to the residual MM peak, both using the data obtained from the differential refractive index detector. We also compared expected molecular weight based on measured conversion values and a target $N_{bb} = 1000$ with observed molecular weight by SEC.

The results of the experiments are shown in Figure 2.5 and in Table 2.S8. DMF and THF reached the lowest conversions, with less than 15% for both, while the other solvents reached >80% conversion. Toluene was the solvent that showed the lowest $k_{decomp,obs}$ when probing catalyst decomposition in each solvent, consistent with its ability in this experiment to achieve the highest conversion over a long reaction time (24 h). Observed and expected M_n values based on its 97% conversion were also quite close in toluene (2750 kg/mol versus 2820 kg/mol, respectively), and toluene was also the solvent leading to the BB polymer with the lowest $\bar{D}$ of 1.44 ($\bar{D}$ values between 1.47 and 1.60 were observed for the other solvents). Therefore, we conclude that toluene, despite its relatively low $k_{p,obs}$, provided the most living system for this MM due to its very low

$k_{\text{decomp,obs}}$. However, dispersity still suffered at this high targeted N_{bb} due to some catalyst decomposition. EtOAc, CH_2Cl_2 , and CHCl_3 also reached high conversions (87%, 94%, and 81%, respectively), with M_n values also within 20% of expected values based on conversion. $\bar{D}$ values for EtOAc, CH_2Cl_2 , and CHCl_3 in this experiment were 1.55, 1.52, and 1.47, respectively. Therefore, these three solvents with the highest $k_{\text{p,obs}}$ values and relatively low $k_{\text{decomp,obs}}$ values also provide a relatively high degree of livingness (Figure 2.S45). THF and DMF did not perform as well, with conversion values reaching 13% and 5%, respectively. Finally, we ran a similar experiment on a PnBA MM ($M_n = 4.8 \text{ kg/mol}$), in this case targeting $N_{\text{bb}}=500$ due to the larger size of this MM. The results were similar to the PS MM, where toluene showed the highest conversion and M_n close to the expected value; EtOAc, CH_2Cl_2 , and CHCl_3 showed somewhat lower conversions, and THF and DMF showed very little conversion (Figure 2.S46, Table 2.S9).

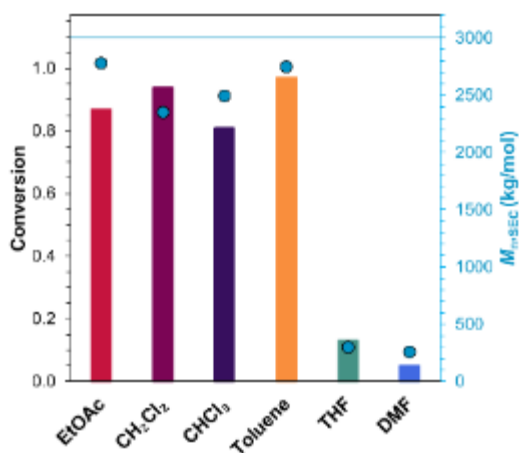


Figure 2.5. MM conversion to BB polymer (bars) and final BB polymer M_n (dots) in the grafting-through ROMP of PS_{Br} (3 kg/mol) in six purified solvents at a $\text{PS}_{\text{Br}}/\text{G3}$ ratio of 1000:1 (target $N_{\text{bb}} = 1000$) over 24 h. The horizontal bar represents the theoretical M_n at full conversion.

These results on high target N_{bb} values for both PS and PnBA MMs correlate with the catalyst decomposition results and suggest that catalyst decomposition plays the primary role in limiting

ultimate N_{bb} in DMF and THF. In other words, in the synthesis of BB polymers, the rate of catalyst decomposition plays a critical role, especially in THF and DMF, because it begins to approach the rate of propagation for even moderately sized MMs.

2.6 Conclusions

In this study, we observed the effects of solvent choice and purity on the rate of propagation and decomposition in ROMP. By measuring propagation kinetics of three MMs of similar molecular weights (**PS_{Br}**, **PnBA_{Br}**, and **PnBA_{TTC}**) and **NMB**, a small molecule norbornene, in multiple solvents and purities, we found that solvent choice heavily influences “livingness” in ROMP. Depending on impurities present in the solvent, purification can have either a positive or negative impact, or in some cases no impact at all, on the rate of ROMP propagation. This was particularly evident in the almost two-fold decrease in propagation rate for polymerizations performed in as received EtOAc compared to purified EtOAc, which has led to current studies in our group on how small molecule additives affect the rate of propagation in ROMP. We also measured a noticeable difference between the solvents themselves, whether purified or not, which we attribute to specific catalyst–solvent effects. This is supported by our observations of the same general trends in $k_{p,obs}$ in a small molecule norbornene (**NMB**) compared to the three MMs. The different MMs tested here revealed polymer effects in some cases, such as **PS_{Br}** having a lower $k_{p,obs}$ in DMF than in any of the other solvents, which could be attributed to the collapsed conformation of PS in DMF. We found that the catalyst decomposition rate plays the largest role in the ultimate conversion that can be achieved in a given solvent when targeting high N_{bb} values, where among purified solvents, toluene outperformed all other solvents with the highest conversion, lowest dispersity, and M_n matching the expected value, with EtOAc and CH_2Cl_2 not too far behind. Future studies on

additives may reveal better solvent/additive combinations, and systematic studies on ROMP in an air-free environment compared with polymerizations under air could reveal more insights.

Overall, these results have produced several important conclusions. 1) Solvent purification is unnecessary in most situations, unless the chosen solvent is THF, in which case purification through activated alumina is required. 2) Solvent choice impacts the rate of propagation; for example, $k_{p,obs}$ in EtOAc is 2–4 times faster than most other solvents tested for all three MMs and nearly an order of magnitude faster than DMF for PS MMs. 3) Among purified solvents, high “livingness” is best achieved with toluene, at least with these MMs, but EtOAc and CH₂Cl₂ also perform well and have higher $k_{p,obs}$ values than toluene. Together, these results will be useful for future efforts in ROMP, especially in the context of sterically demanding or otherwise challenging monomers, helping researchers select the best reaction conditions for achieving well-defined and low dispersity ROMP polymers.

2.7 Acknowledgements

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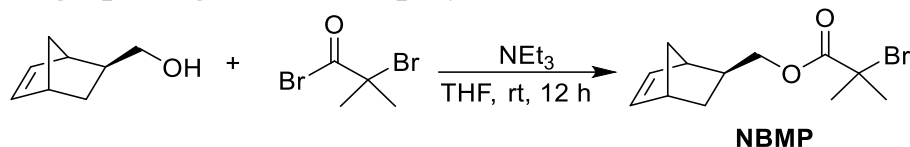
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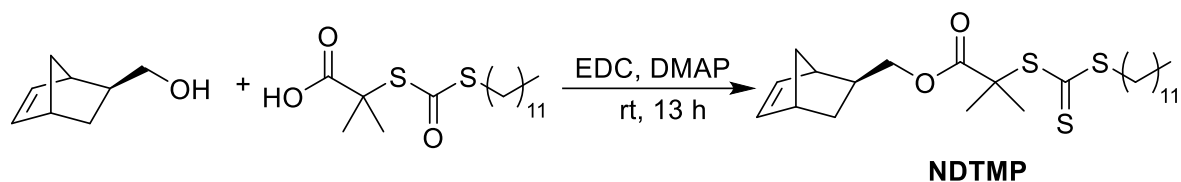
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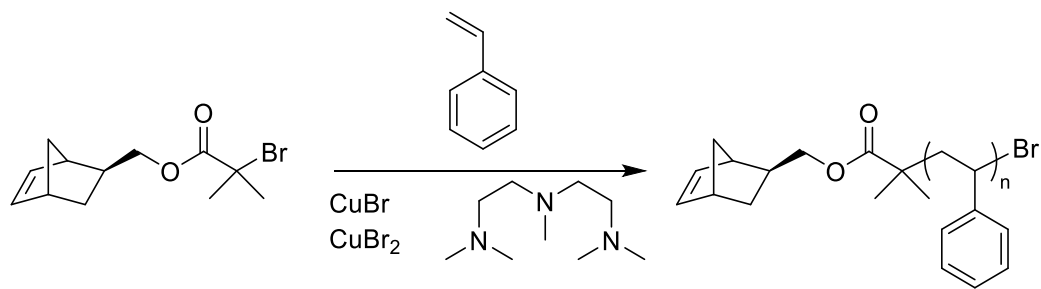
Appendix A: Supporting information for “Solvent effects in grafting-through ring-opening metathesis polymerization”



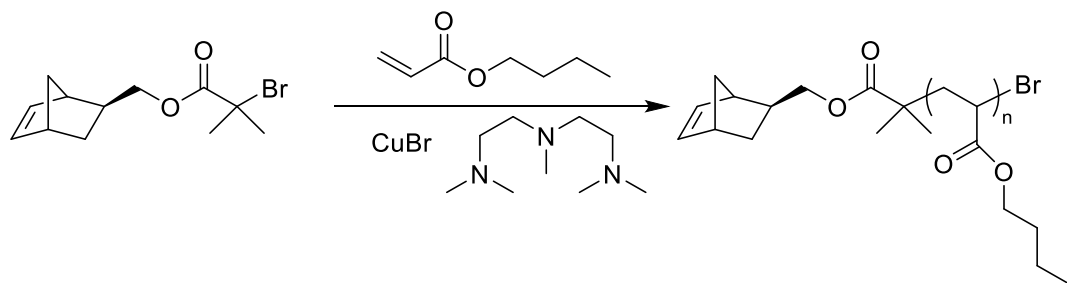
Scheme 2.S1. Synthesis of the *exo*-norbornene-methyl 2-bromo-2-methylpropanoate (**NBMP**), ATRP initiator, prepared as previously described.¹



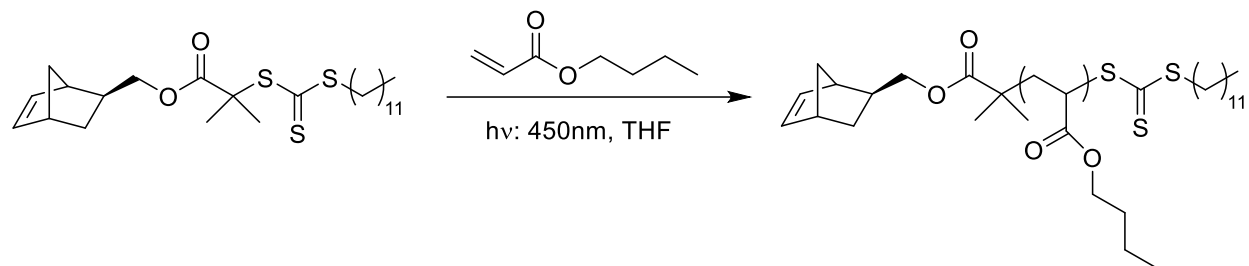
Scheme 2.S2. Synthesis of the *exo*-norbornene-methyl 2-(((dodecylthio)carbonothioyl)thio)-2-methylpropanoate (**NDTMP**) photoiniferter chain-transfer agent, prepared as previously described.¹



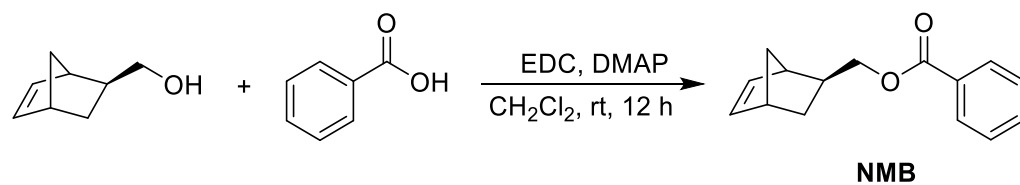
Scheme 2.S3. Synthesis of **PS_{Br} MM**.



Scheme 2.S4. Synthesis of **PnBA_{Br} MM**.



Scheme 2.S5. Synthesis of **PnBA_{TTC} MM**.



Scheme 2.S6. Synthesis of small molecule analog, exo-norbornene-5-methyl benzoate (**NMB**).

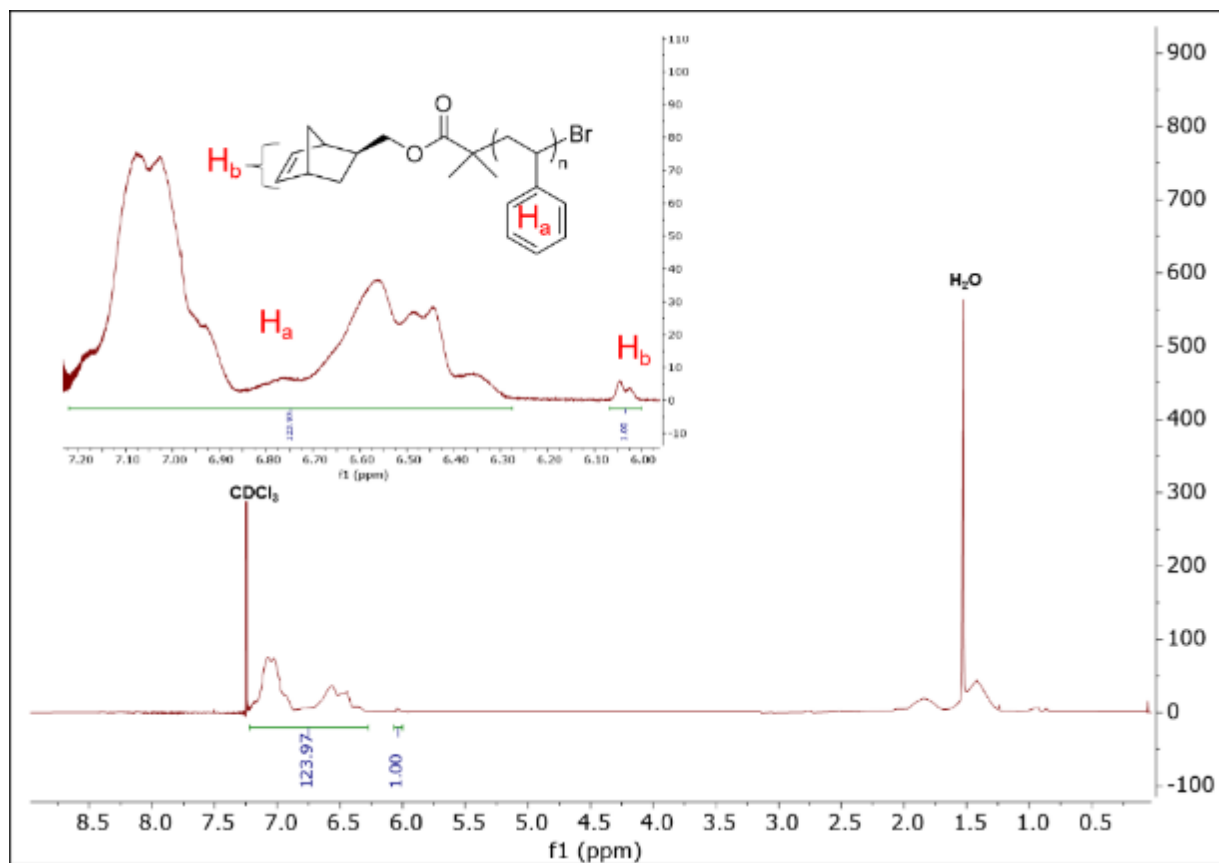


Figure 2.S1. ¹H NMR spectrum of pure **PS_{Br}** in CDCl_3 .

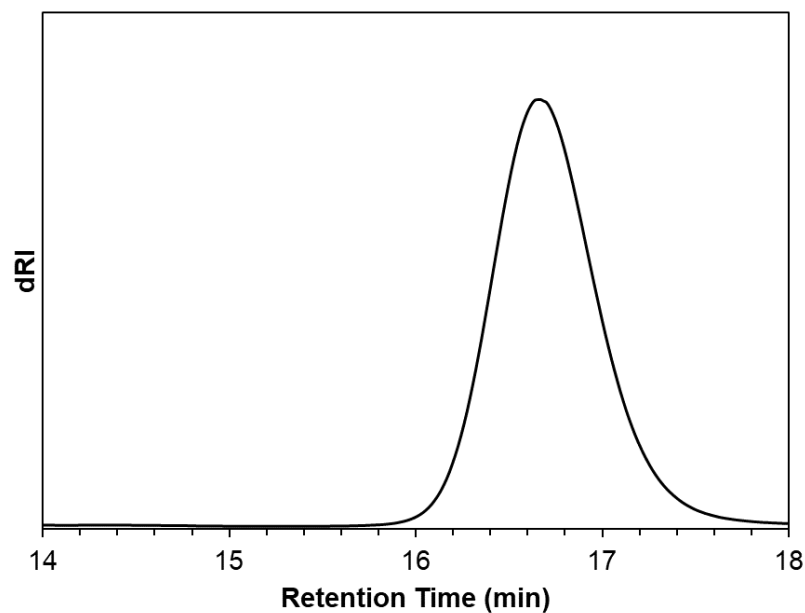


Figure 2.S2: SEC trace of **PS_{Br}** MM synthesized by ATRP. M_n : 4500 g/mol $\bar{D}$: 1.03.

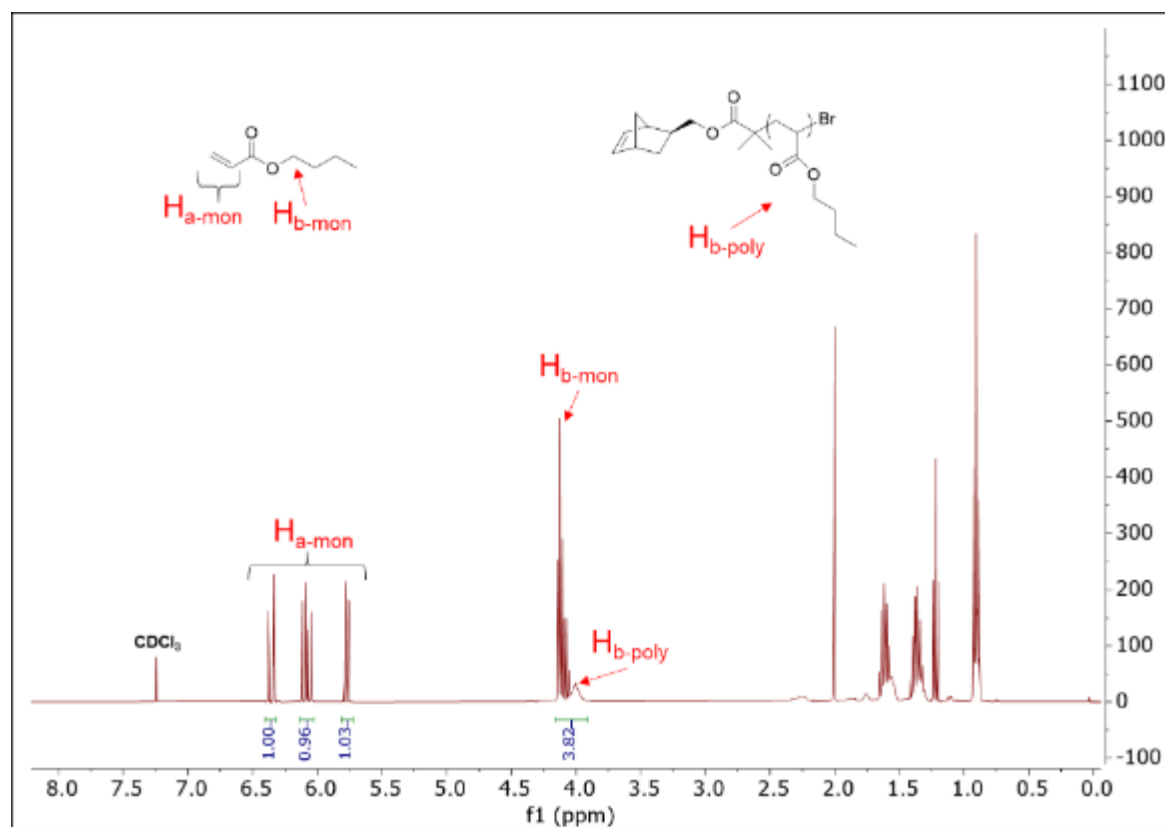


Figure 2.S3. ^1H NMR spectrum of **PnBA_{Br}** reaction mixture after 12 h (reached 48% conversion) in CDCl_3 .

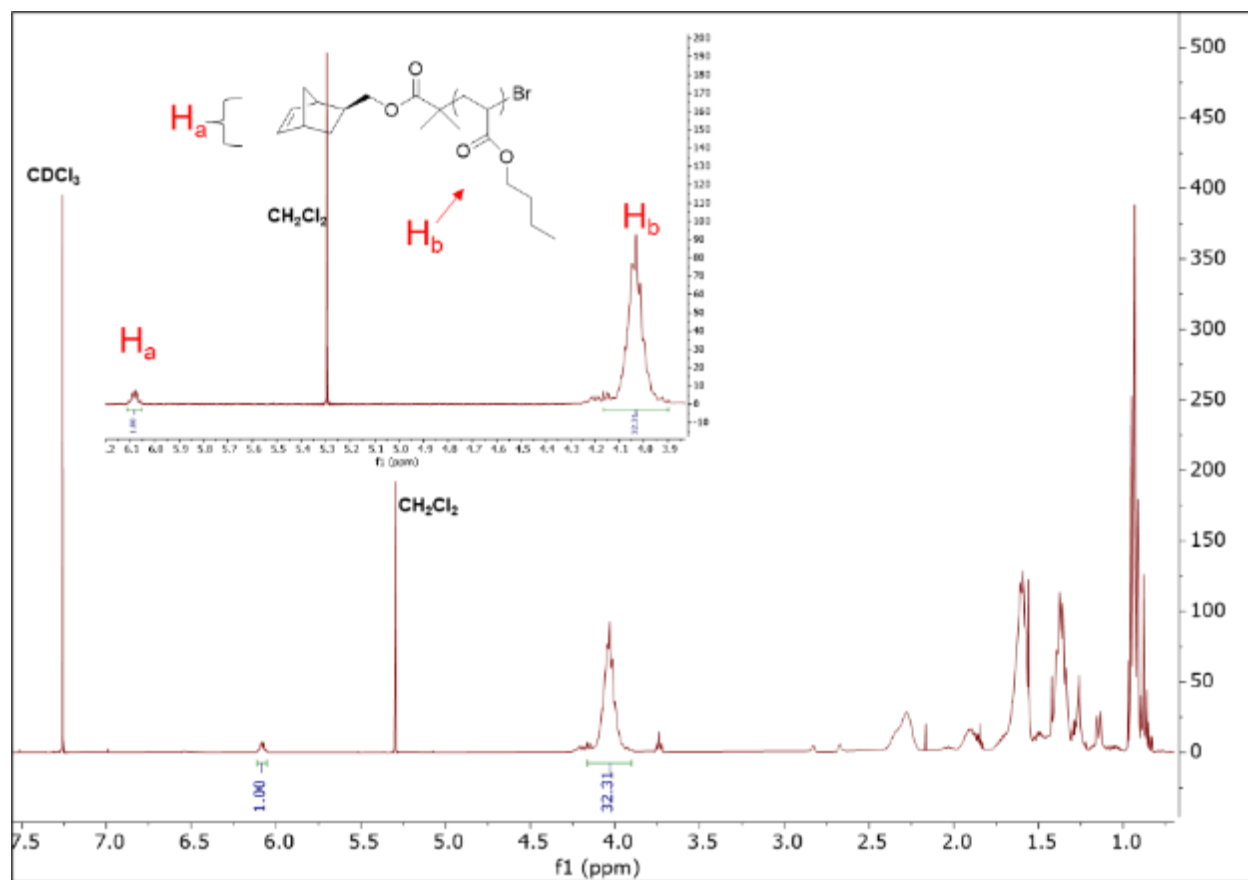


Figure 2.S4. ^1H NMR spectrum of pure **PnBA_{Br}** MM in CDCl_3 .

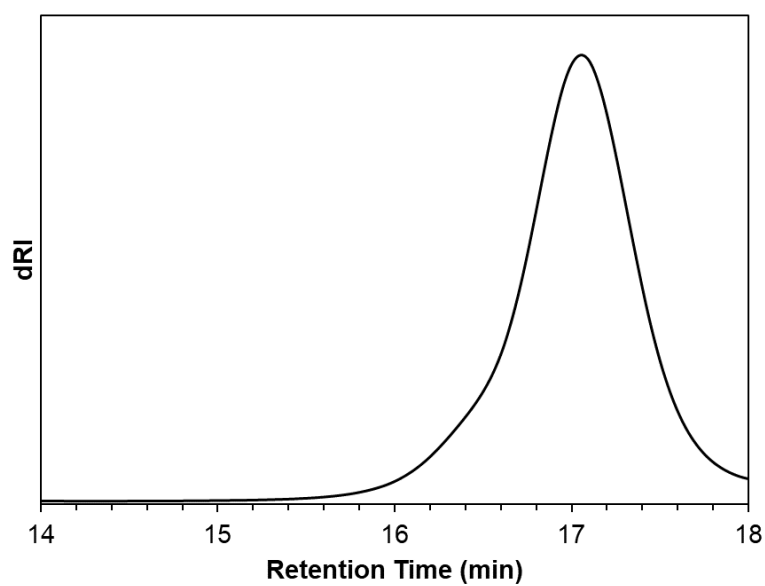


Figure 2.S5: SEC trace of **PnBA_{Br}** MM synthesized by ATRP. M_n : 4200 g/mol $\bar{D}$: 1.14.

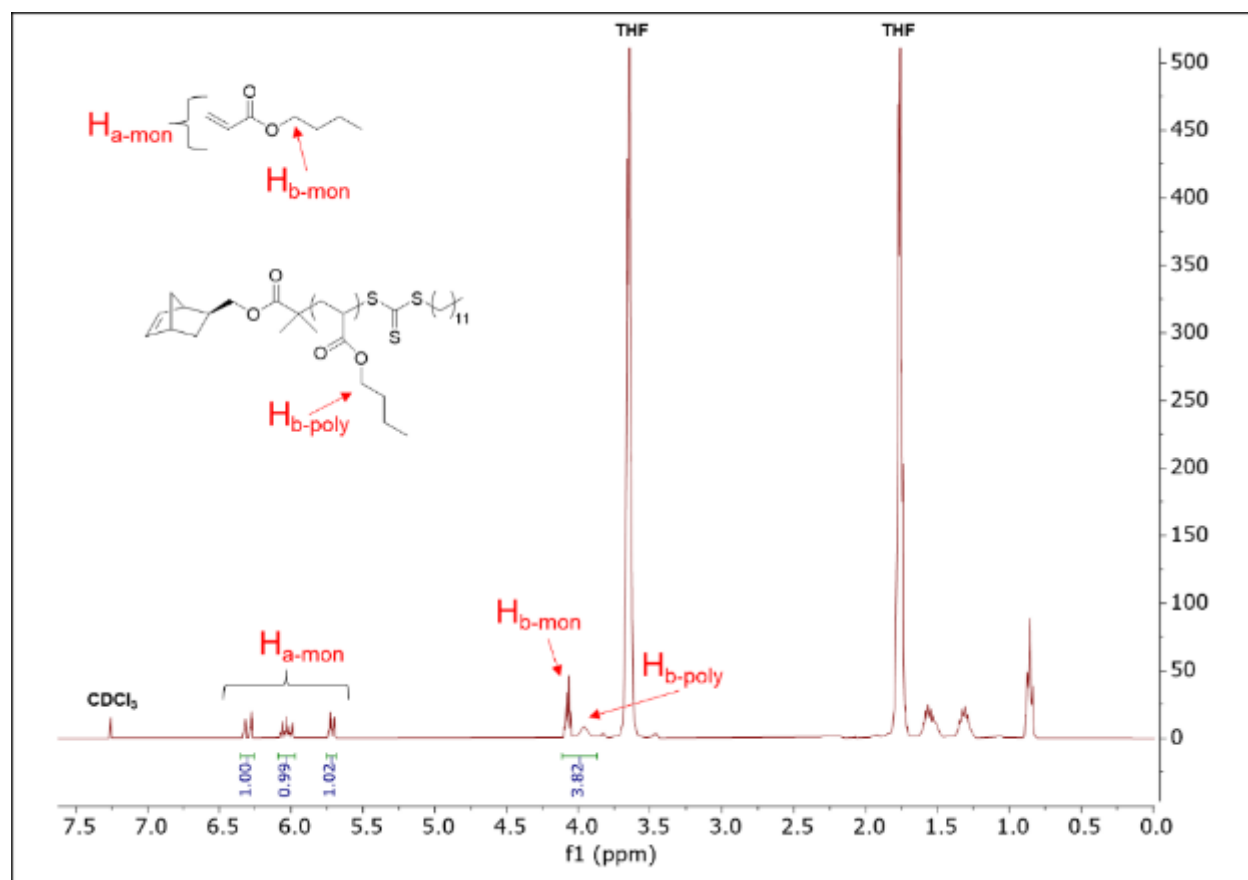


Figure 2.S6. ^1H NMR spectrum of PnBA_{TTC} reaction mixture after 6.5 h (reached 47% conversion) in CDCl_3 .

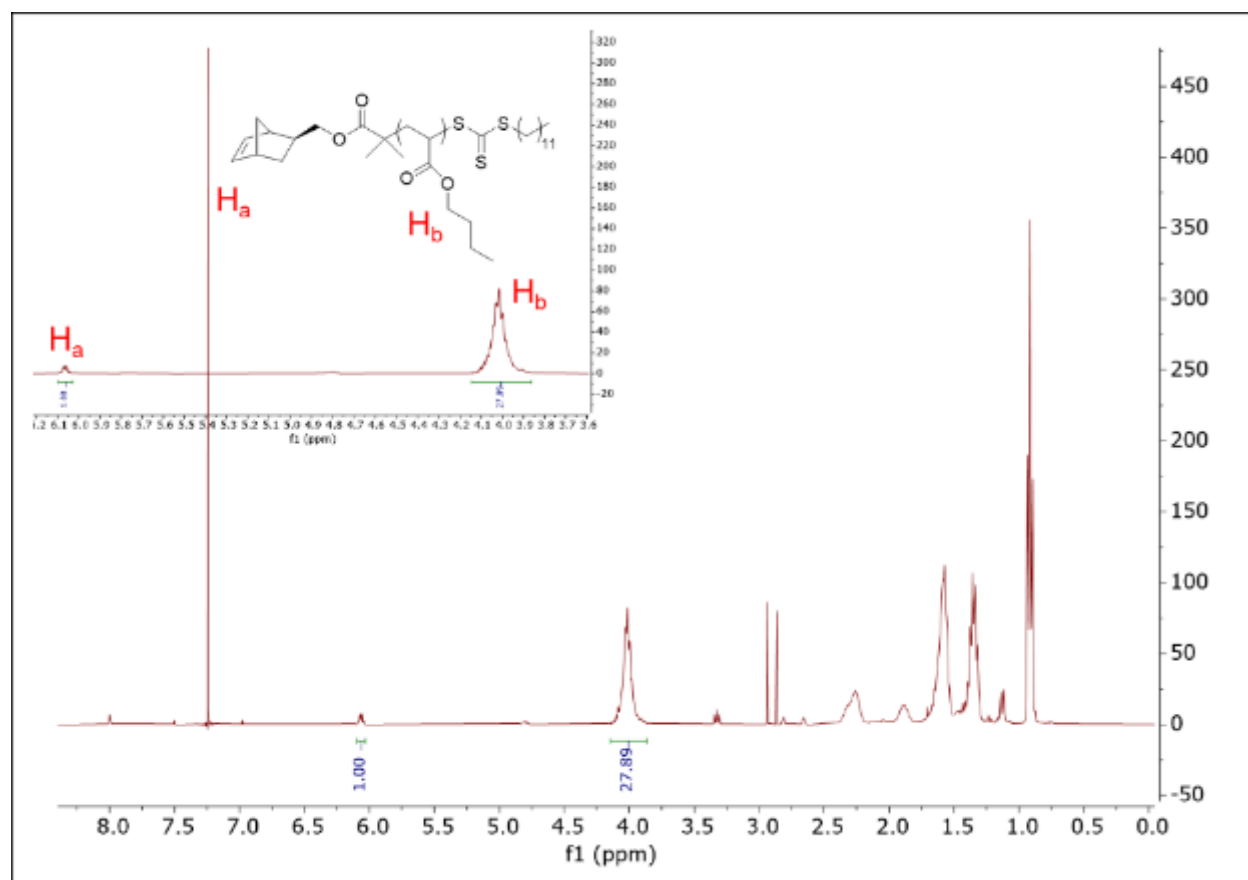


Figure 2.S7. ^1H NMR spectrum of pure **PnBA_{TTC}** in CDCl_3 .

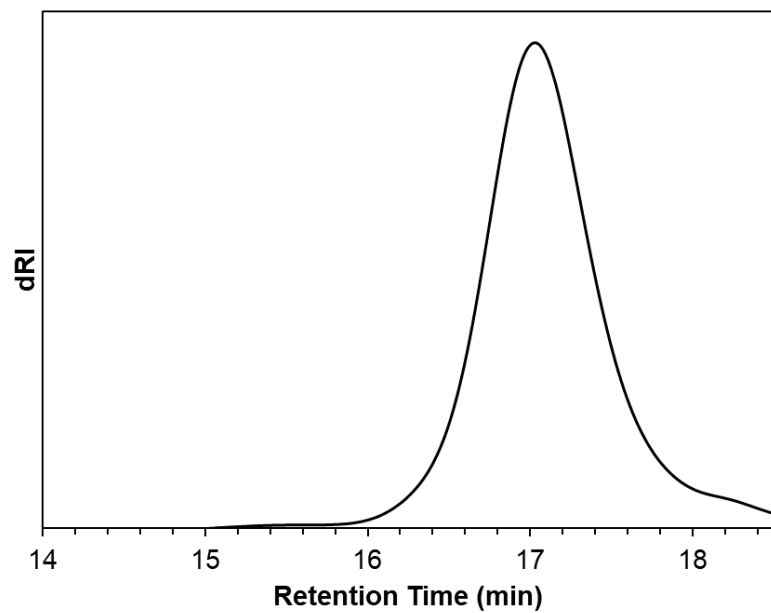


Figure 2.S8: SEC trace of **PnBA_{TTC}** MM synthesized by photoiniferter polymerization. M_n : 3800 g/mol
 $\bar{D}$: 1.10.

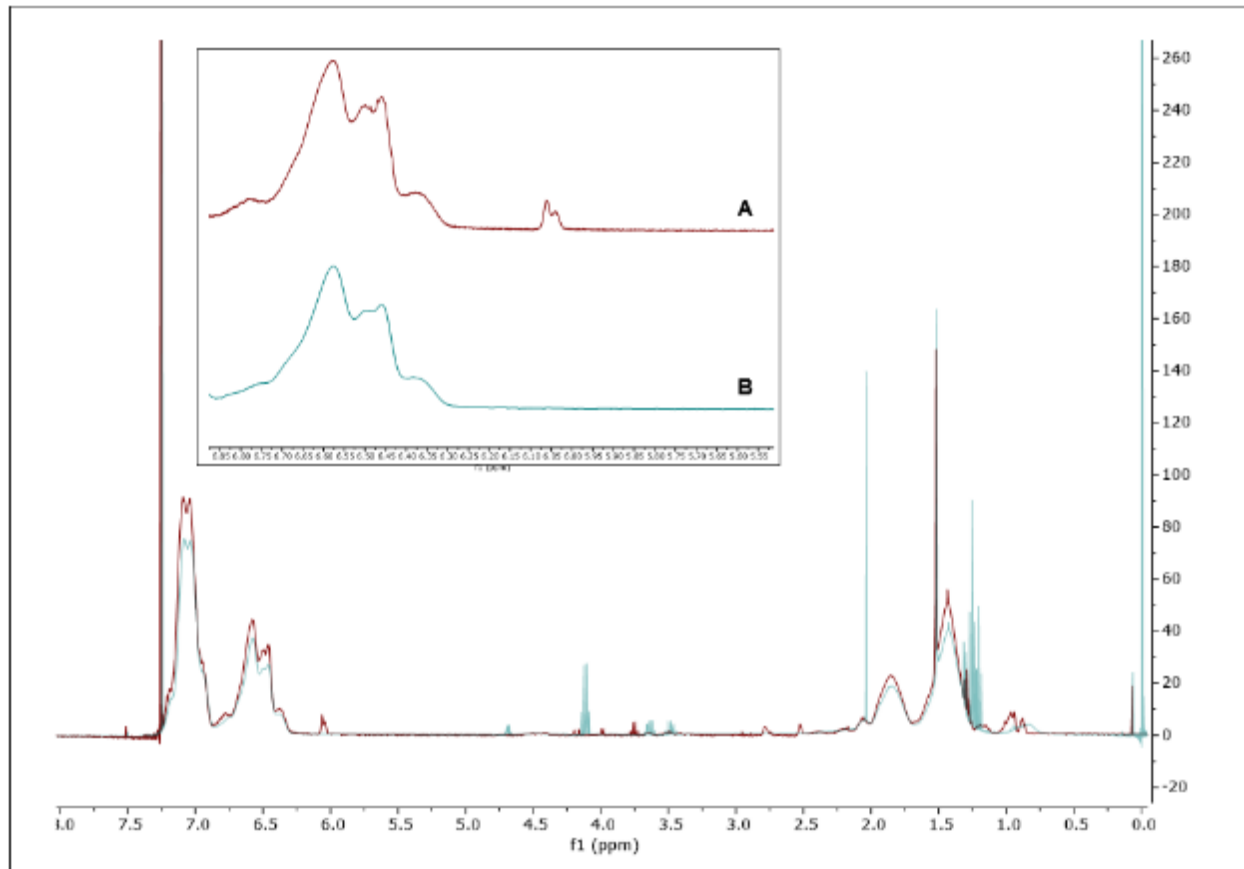


Figure 2.S9. Representative ^1H NMR spectra for A) PS_{Br} MM (red) and B) $\text{poly}(\text{PS}_{\text{Br}})$ bottlebrush polymer at a G3/ PS_{Br} ratio of 100:1 polymer (blue) showing complete disappearance of the norbornene protons at 6.1 ppm, confirming full conversion of the MM in the ROMP reaction.

PS_{Br}, PnBA_{Br}, and PnBA_{ATTC} ROMP kinetics in ethyl acetate:

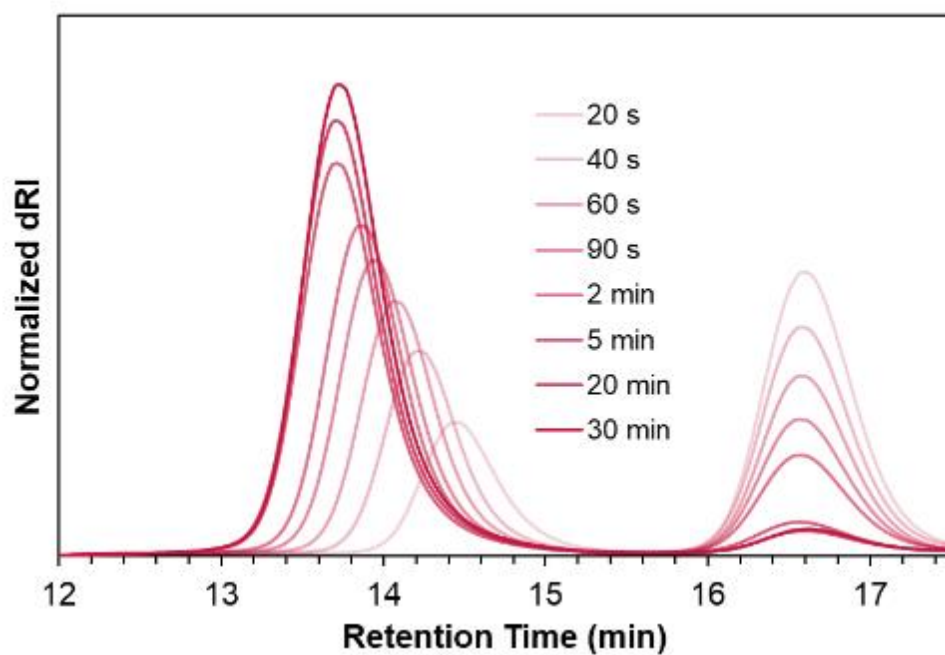


Figure 2.S10: Representative SEC traces for the kinetic study of **PS_{Br}** ROMP in purified EtOAc.

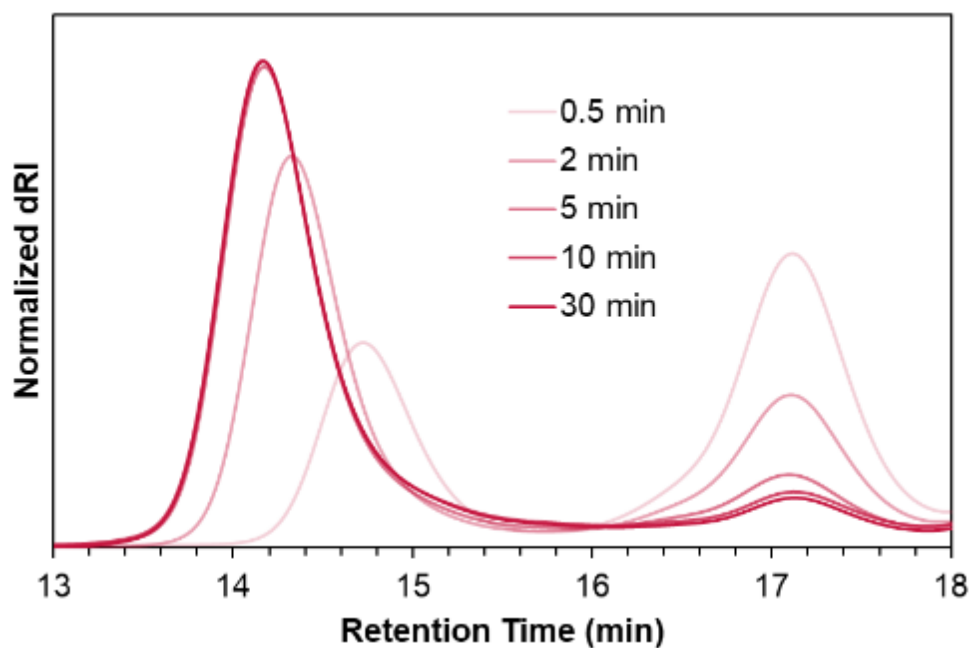


Figure 2.S11: Representative SEC traces for the kinetic study of **PnBA_{Br}** ROMP in purified EtOAc.

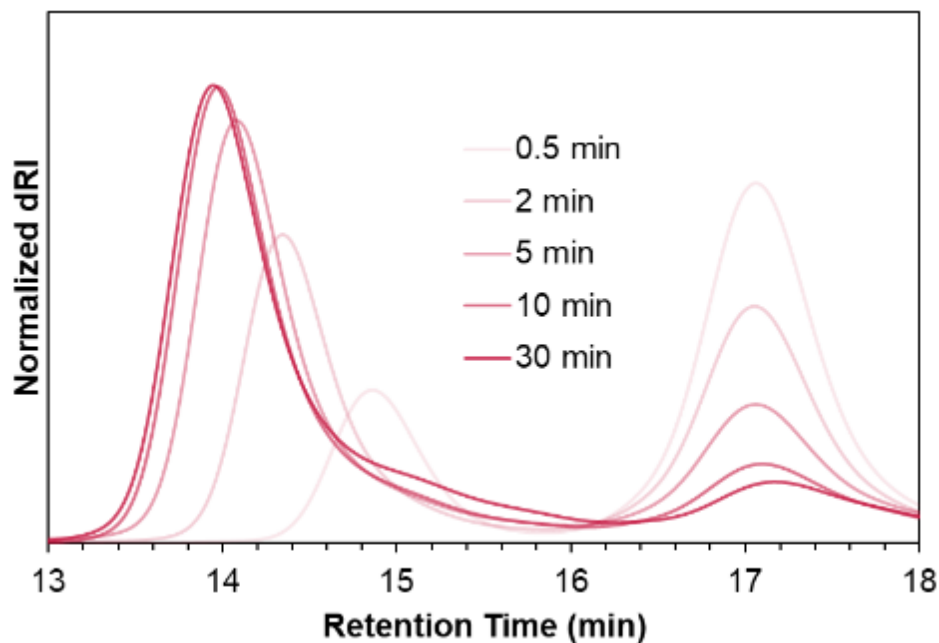


Figure 2.S12: Representative SEC traces for the kinetic study of **PnBA_{TTC}** ROMP in purified EtOAc.

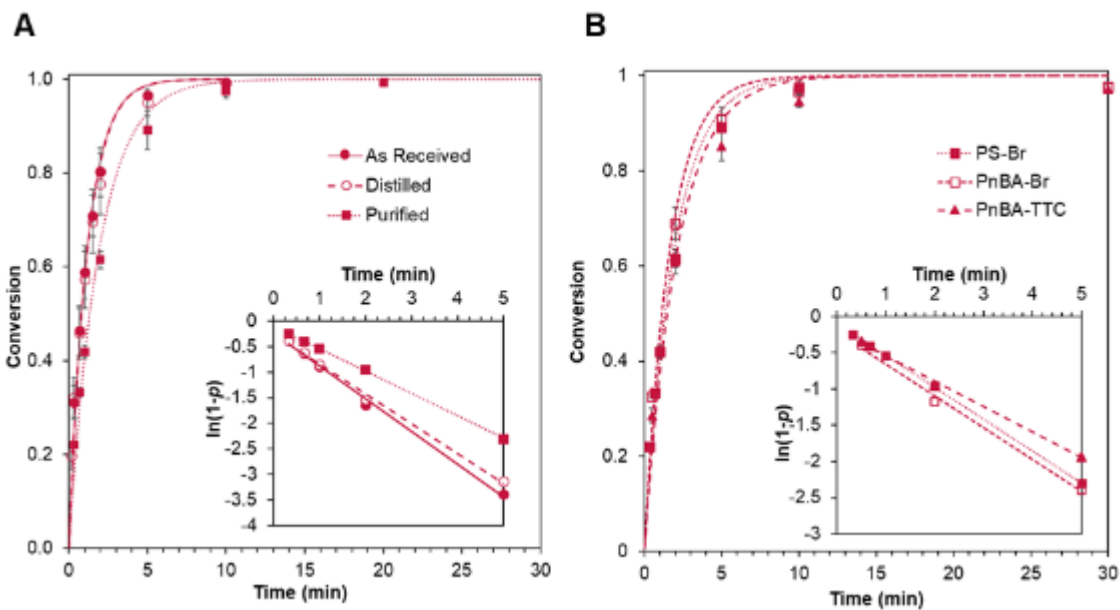


Figure 2.S13: Conversion versus time plots for ROMP of MMs in EtOAc. A) ROMP of **PS_{Br}** in EtOAc with different purity levels; B) ROMP of **PS_{Br}**, **PnBA_{Br}**, **PnBA_{TTC}** in purified EtOAc. Markers are experimental results, lines are first-order kinetic fits. Insets show the same data for $\ln(1-p)$ with the lines depicting the first-order fits.

PS_{Br}, PnBA_{Br}, and PnBA_{TTC} ROMP kinetics in CH₂Cl₂:

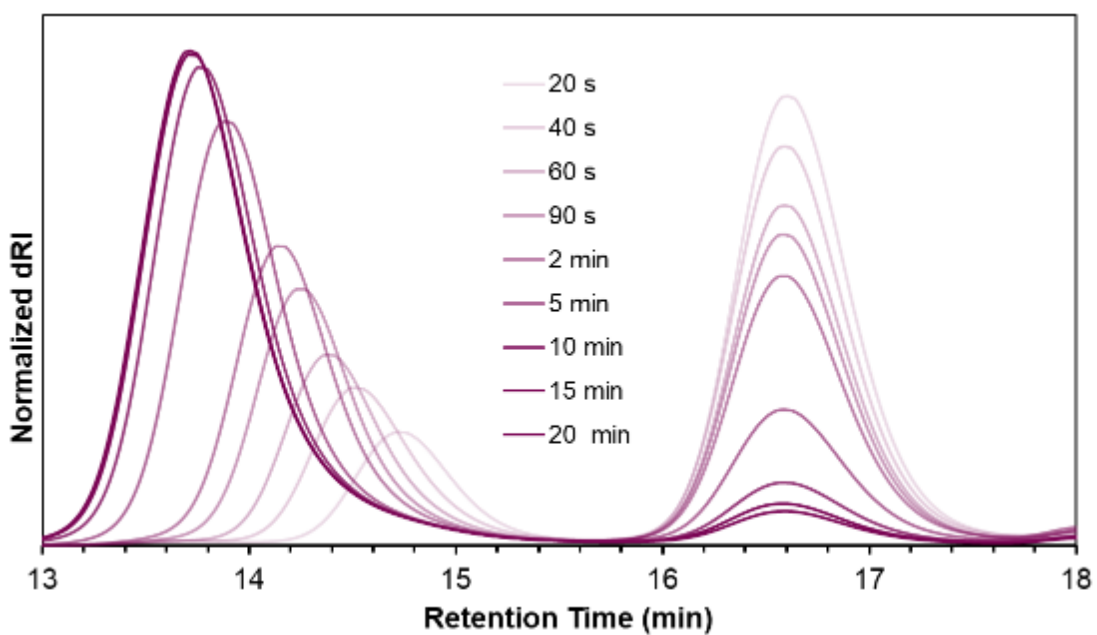


Figure 2.S14: Representative SEC traces for the kinetic study of **PS_{Br}** ROMP in CH₂Cl₂.

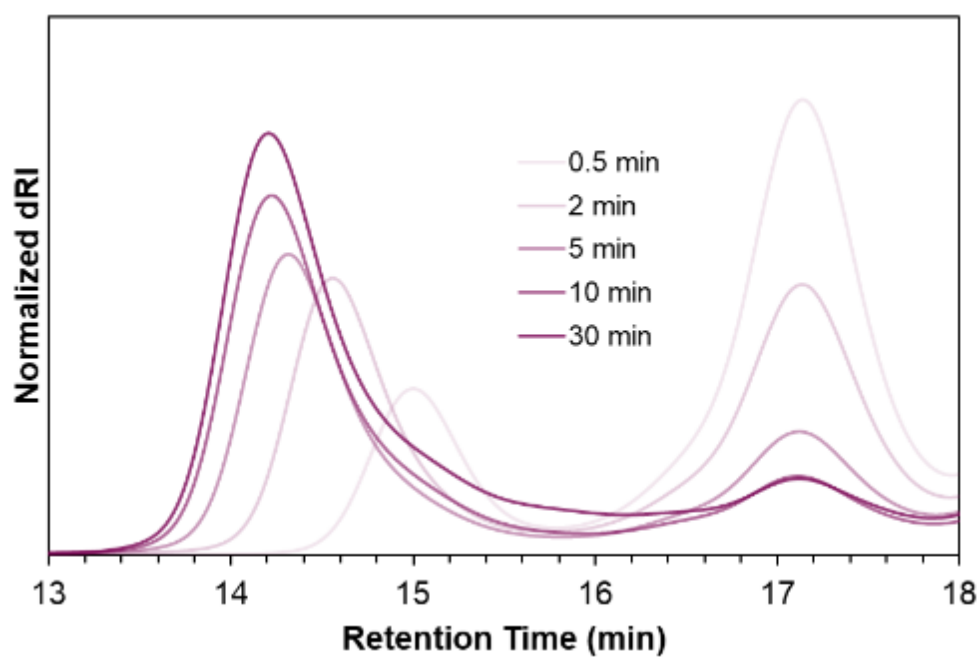


Figure 2.S15: Representative SEC traces for the kinetic study of **PnBA_{Br}** ROMP in CH₂Cl₂.

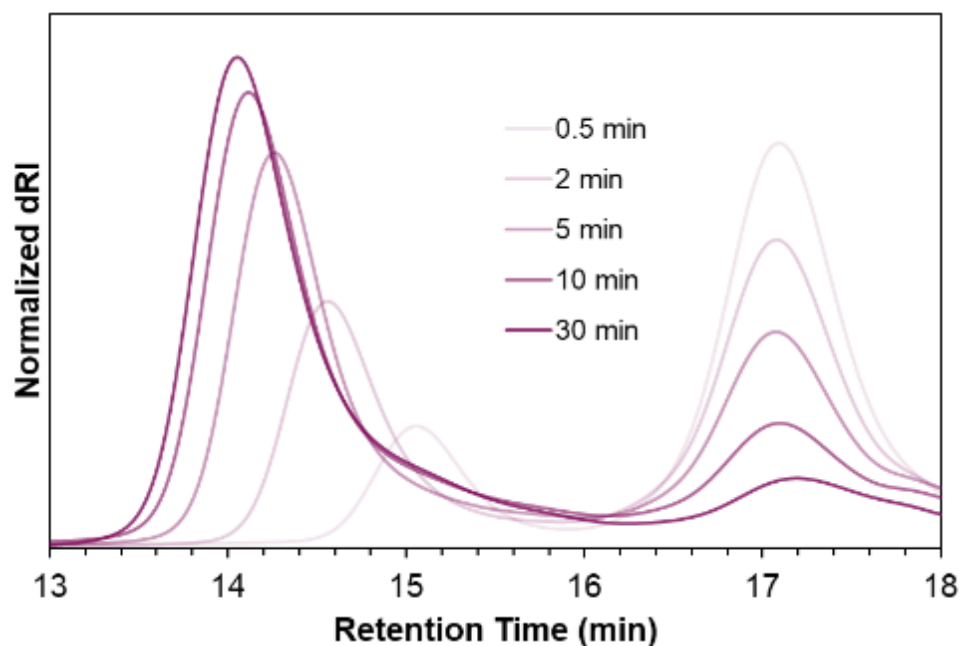


Figure 2.S16: Representative SEC traces for the kinetic study of **PnBA_{TTC}** ROMP in CH_2Cl_2 .

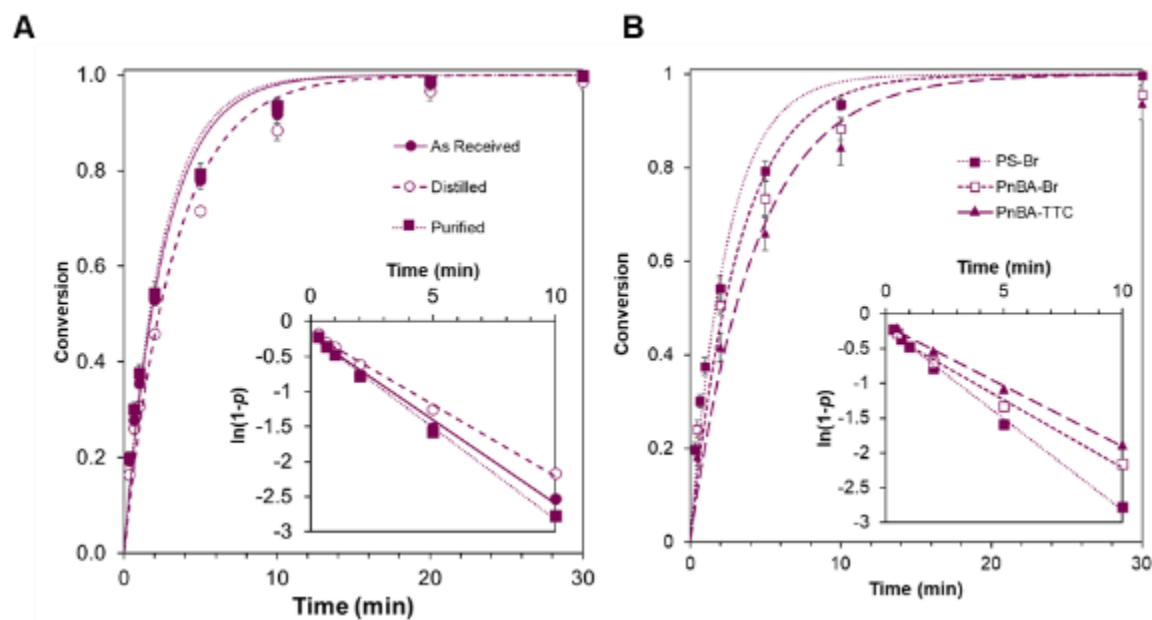


Figure 2.S17: Conversion versus time plots for ROMP of MMs in CH_2Cl_2 . A) ROMP of **PS_{Br}** in CH_2Cl_2 with different purity levels; B) ROMP of **PS_{Br}**, **PnBA_{Br}**, **PnBA_{TTC}** in purified CH_2Cl_2 . Markers are experimental results, lines are first-order kinetic fits. Insets show the same data for $\ln(1-p)$ with the lines depicting the first-order fits.

PS_{Br}, PnBA_{Br}, and PnBA_{TTC} ROMP kinetics in chloroform:

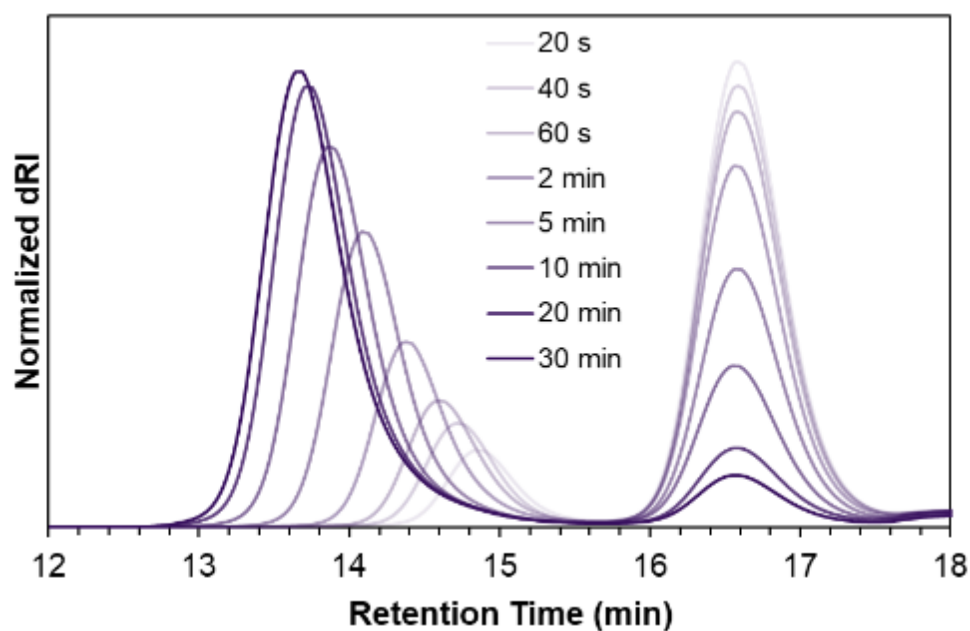


Figure 2.S18: Representative SEC traces for the kinetic study of **PS_{Br}** ROMP in CHCl₃.

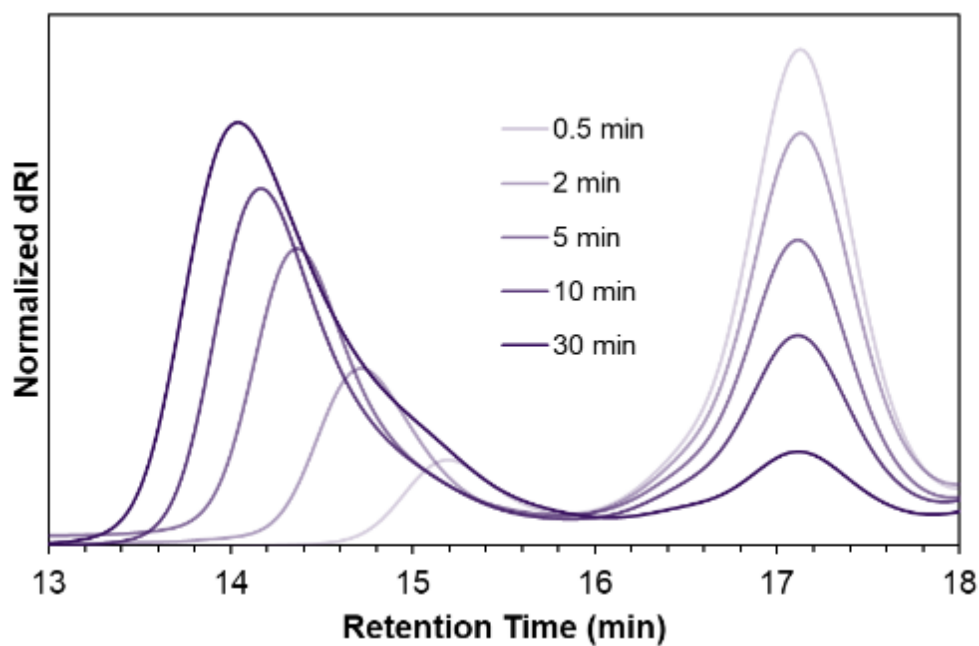


Figure 2.S19: Representative SEC traces for the kinetic study of **PnBA_{Br}** ROMP in CHCl₃.

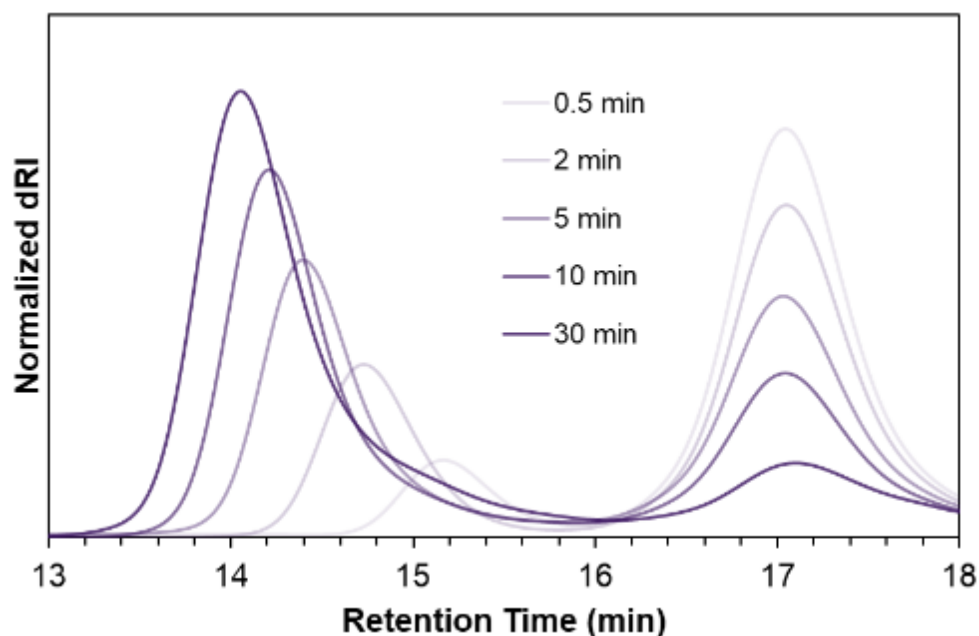


Figure 2.S20: Representative SEC traces for the kinetic study of **PnBA_{TTC}** ROMP in CHCl_3 .

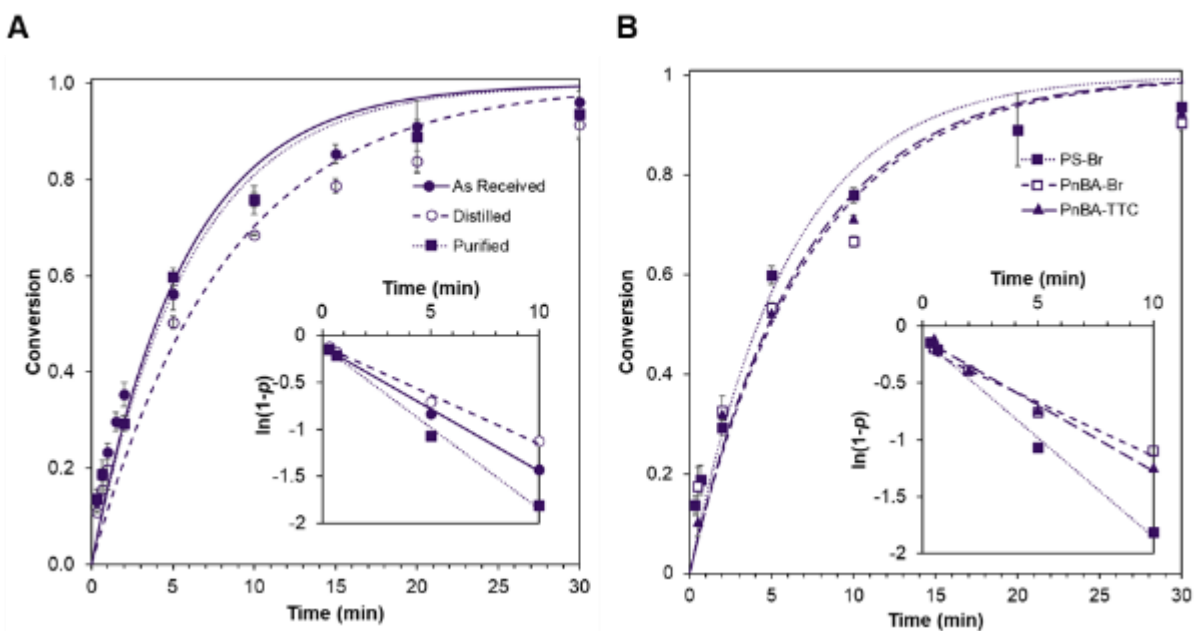


Figure 2.S21: Conversion versus time plots for ROMP of MMs in CHCl_3 . A) ROMP of **PS_{Br}** in CHCl_3 with different purity levels; B) ROMP of **PS_{Br}**, **PnBA_{Br}**, **PnBA_{TTC}** in purified CHCl_3 . Markers are experimental results, lines are first-order kinetic fits. Insets show the same data for $\ln(1-p)$ with the lines depicting the first-order fits.

PS_{Br}, PnBA_{Br}, and PnBA_{ATTC} ROMP kinetics in toluene:

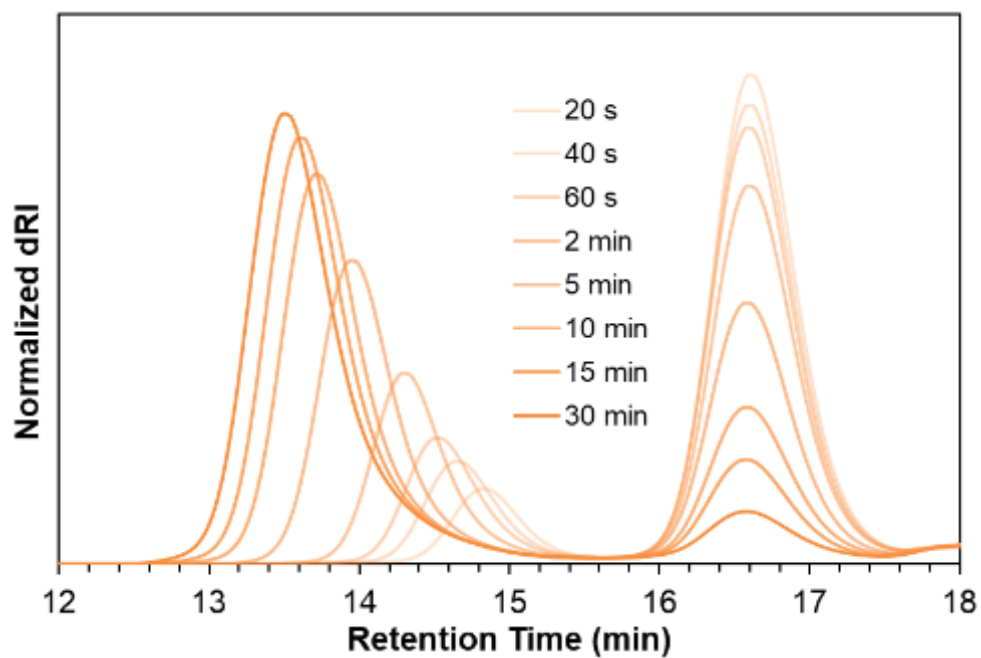


Figure 2.S22: Representative SEC traces for the kinetic study of **PS_{Br}** ROMP in toluene.

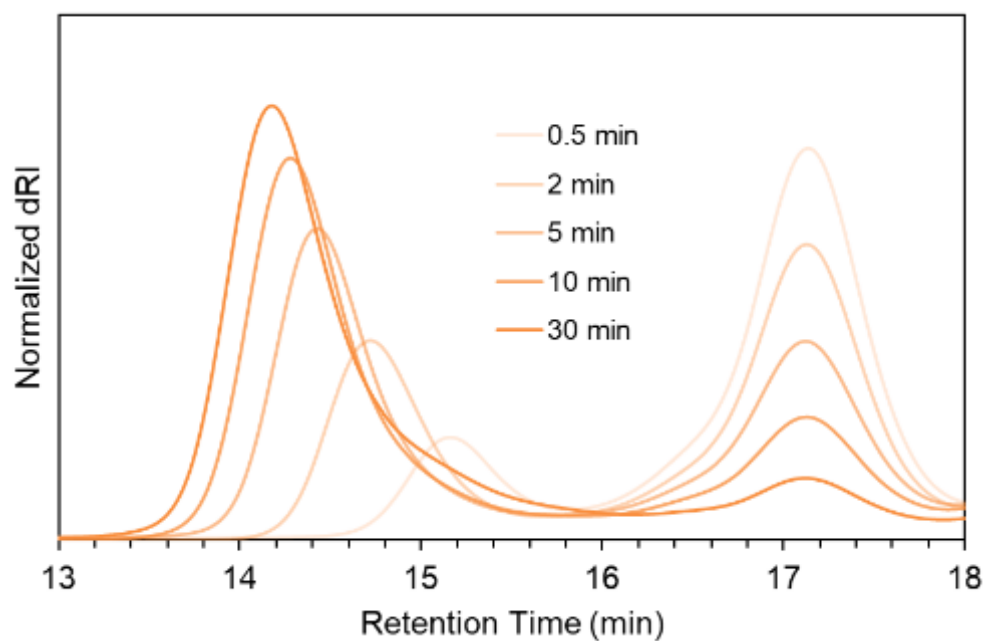


Figure 2.S23: Representative SEC traces for the kinetic study of **PnBA_{Br}** ROMP in toluene.

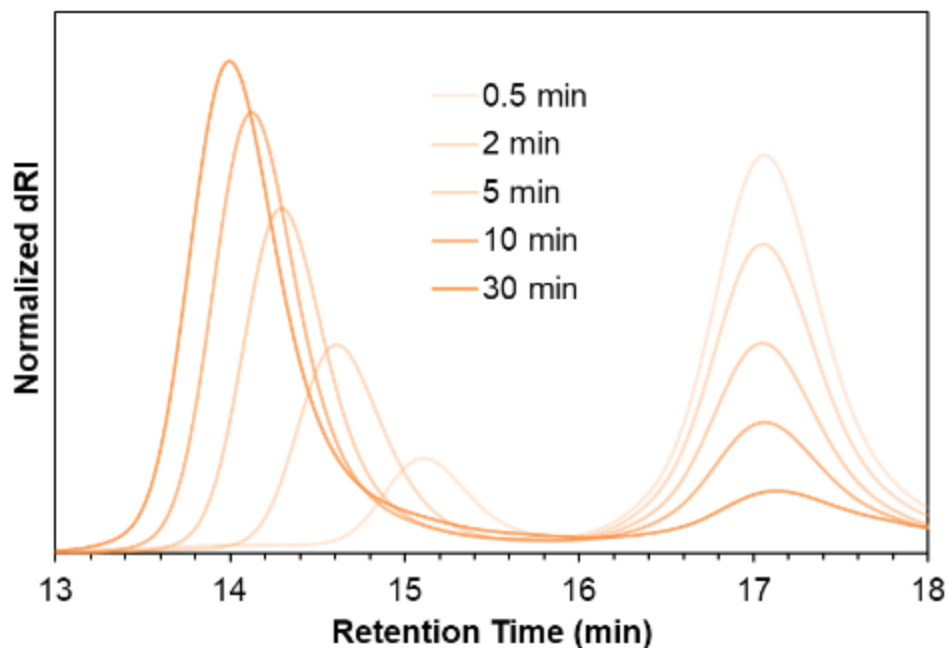


Figure 2.S24: Representative SEC traces for the kinetic study of **PnBA_{TTC}** ROMP in toluene.

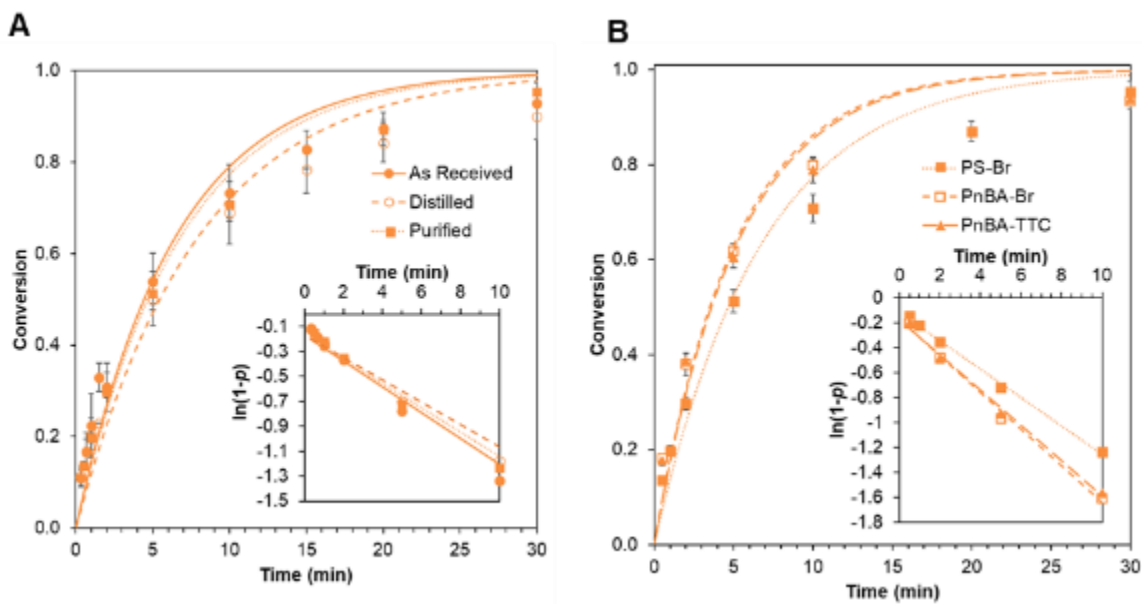


Figure 2.S25: Conversion versus time plots for ROMP of MMs in toluene. A) ROMP of **PS_{Br}** in toluene with different purity levels; B) ROMP of **PS_{Br}**, **PnBA_{Br}**, **PnBA_{TTC}** in purified toluene. Markers are experimental results, lines are first-order kinetic fits. Insets show the same data for $\ln(1-p)$ with the lines depicting the first-order fits.

PS_{Br}, PnBA_{Br}, and PnBA_{ATTC} ROMP kinetics in tetrahydrofuran:

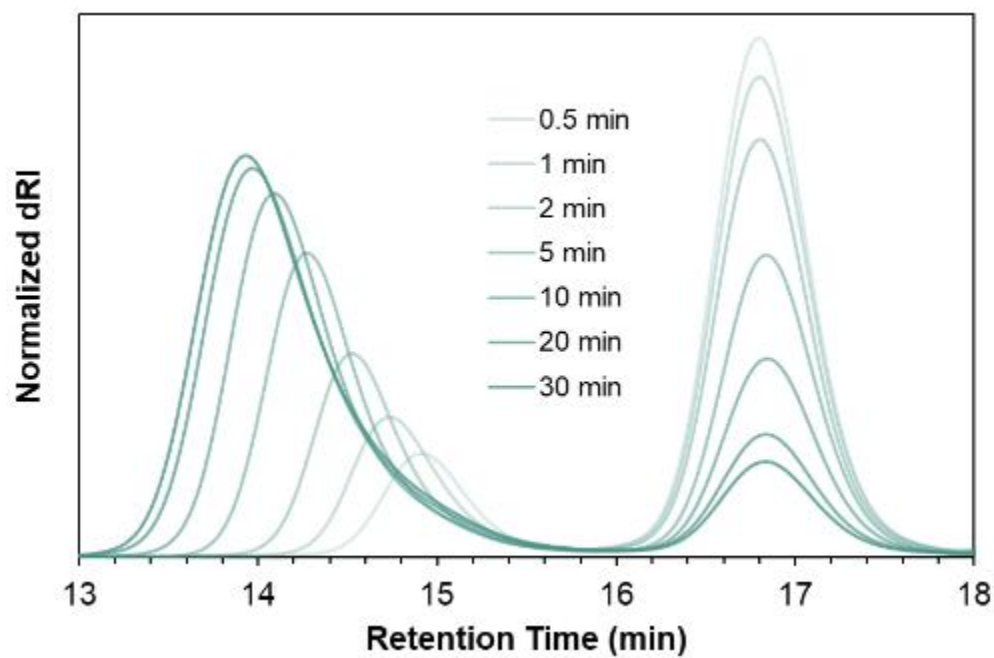


Figure 2.S26: Representative SEC traces for the kinetic study of **PS_{Br}** ROMP in THF.

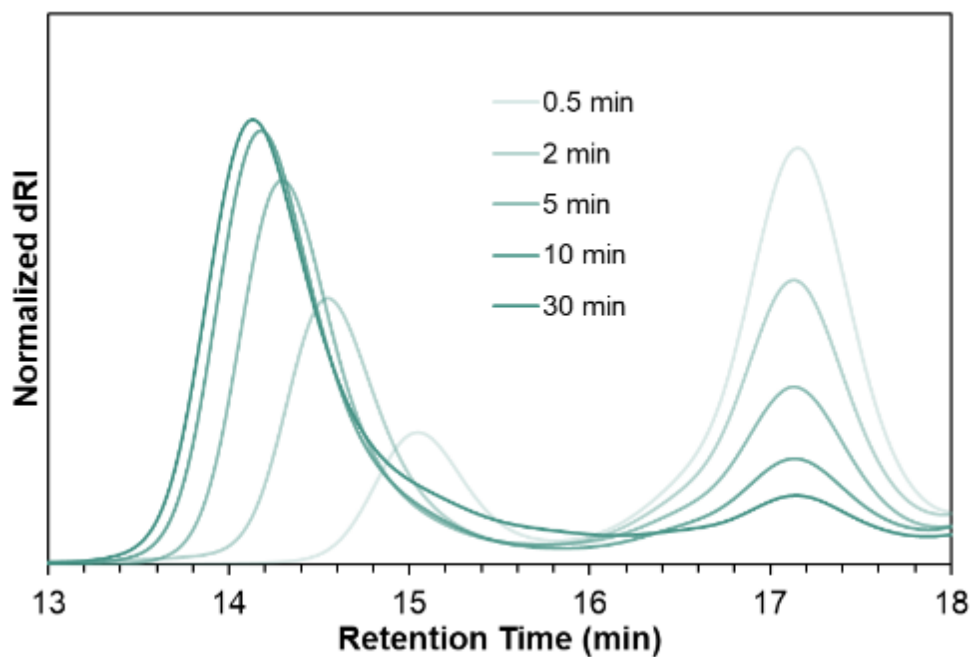


Figure 2.S27: Representative SEC traces for the kinetic study of **PnBA_{Br}** ROMP in THF.

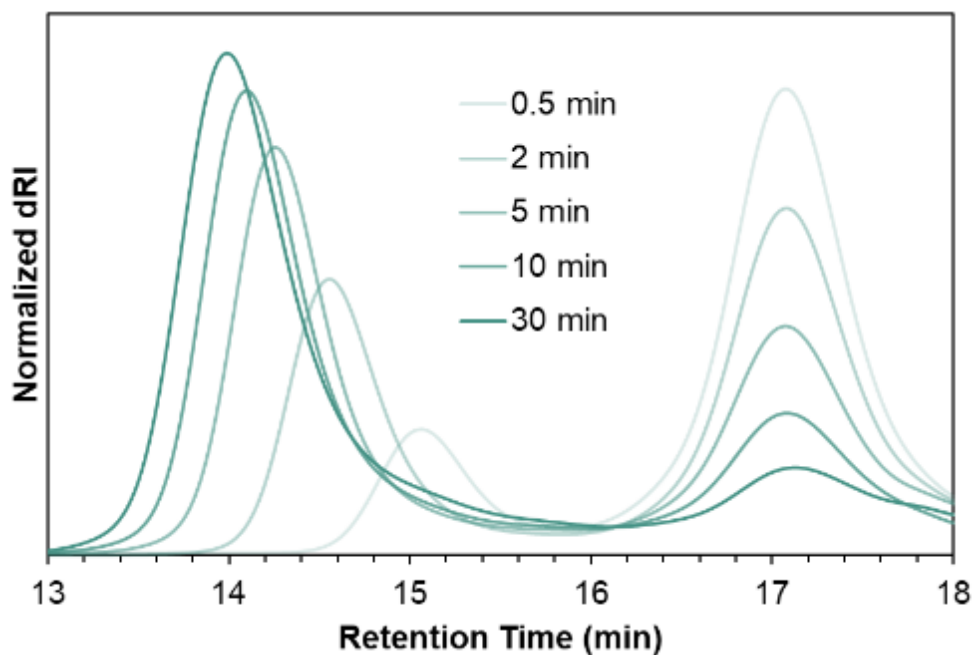


Figure 2.S28: Representative SEC traces for the kinetic study of **PnBA_{TTC}** ROMP in THF.

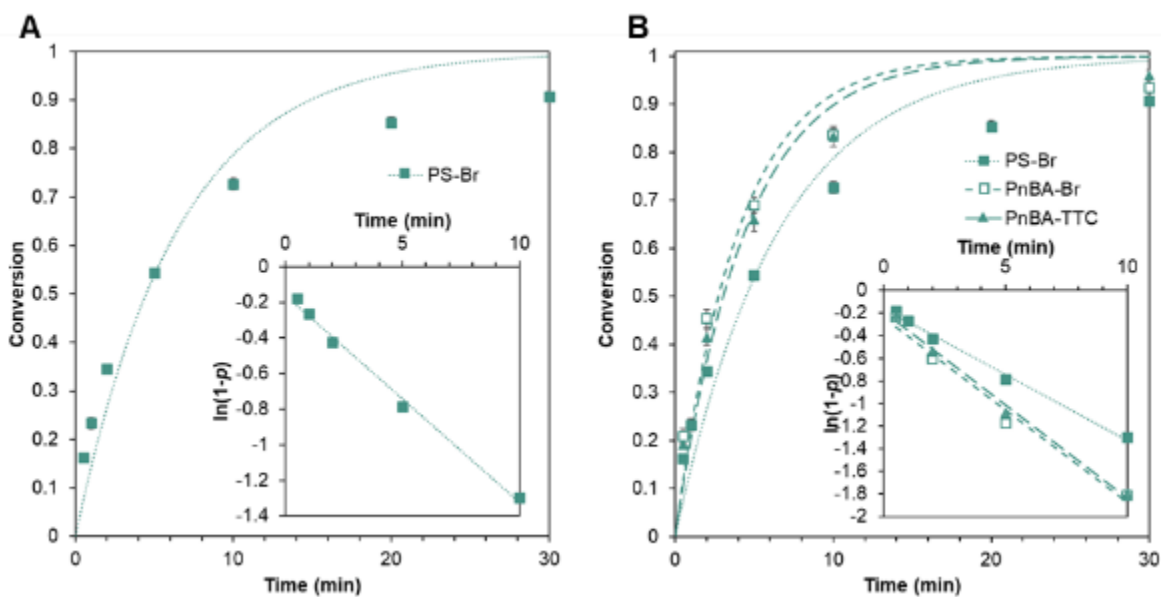


Figure 2.S29: Conversion versus time plots for ROMP of MMs in THF. A) ROMP of **PS_{Br}** in pure THF (negligible ROMP was observed in as received and distilled THF); B) ROMP of **PS_{Br}**, **PnBA_{Br}**, **PnBA_{TTC}** in purified THF. Markers are experimental results, lines are first-order kinetic fits. Insets show the same data for $\ln(1-p)$ with the lines depicting the first-order fits.

PS_{Br}, PnBA_{Br}, and PnBA_{ATTC} ROMP kinetics in *N,N*-dimethylformamide:

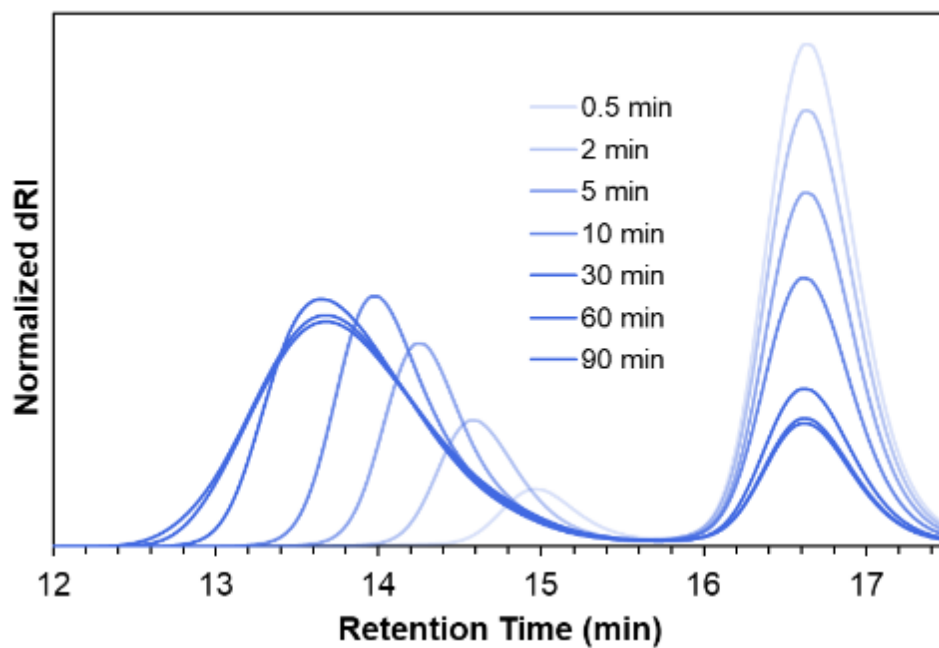


Figure 2.S30: Representative GPC traces for the kinetic study of **PS_{Br}** ROMP in DMF.

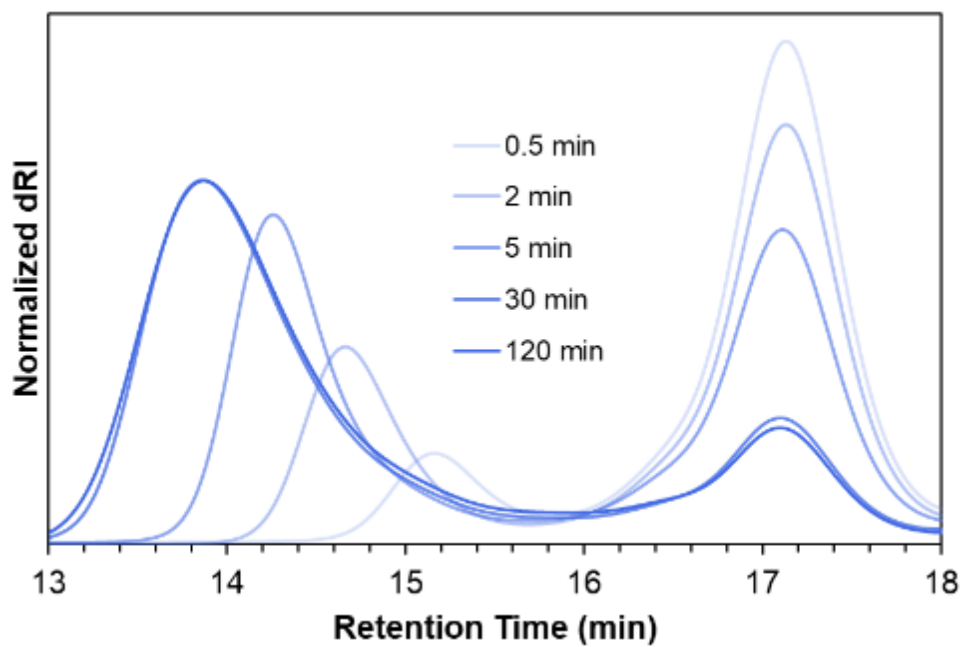


Figure 2.S31: Representative SEC traces for the kinetic study of **PnBA_{Br}** ROMP in DMF.

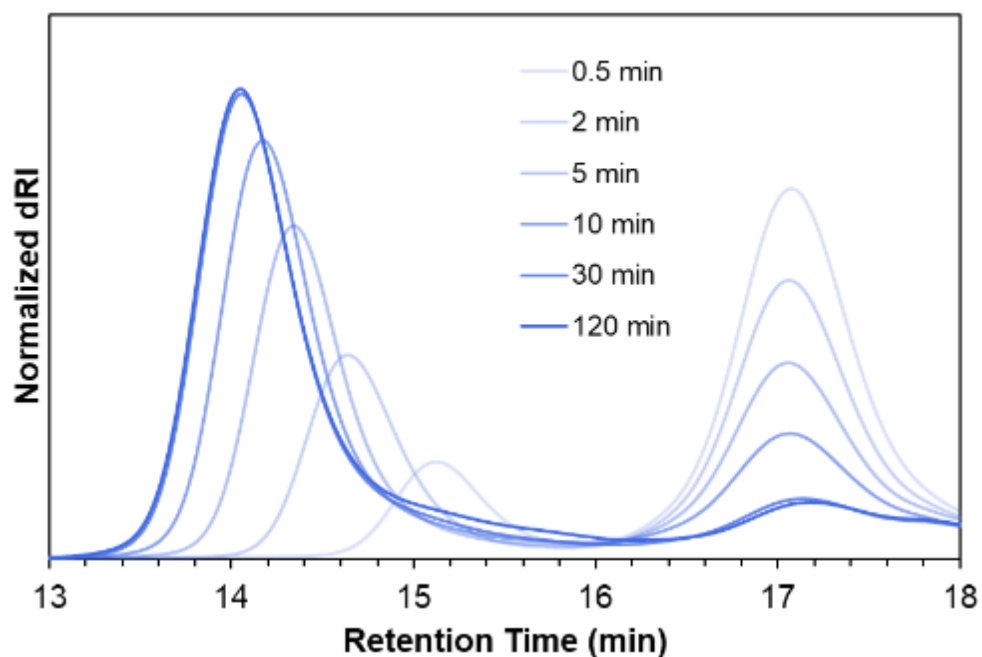


Figure 2.S32: Representative SEC traces for the kinetic study of **PnBA_{TTC}** ROMP in DMF.

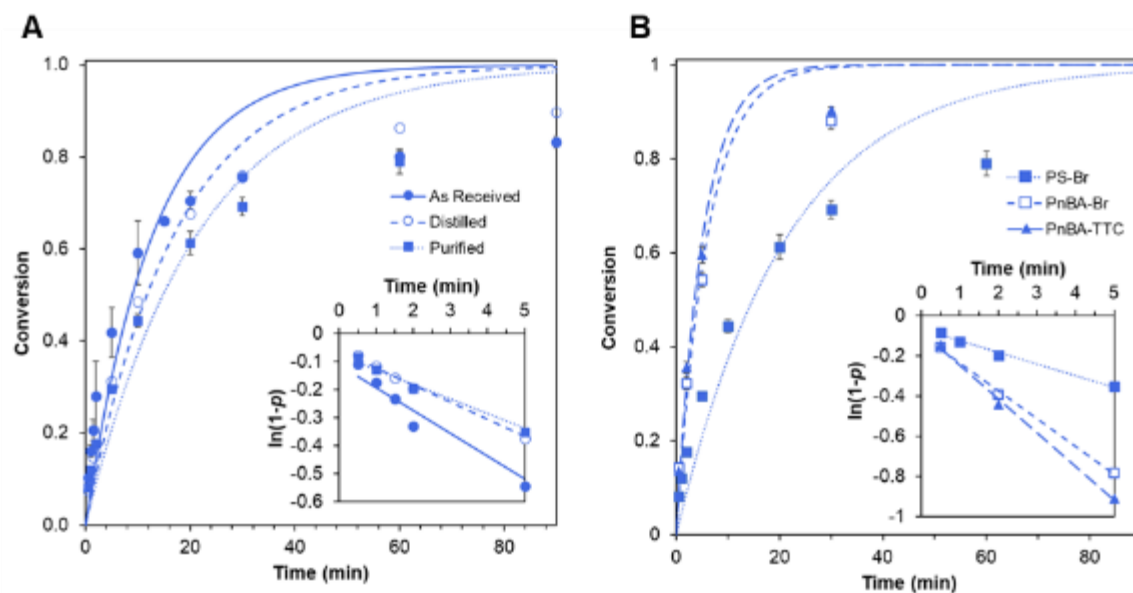


Figure 2.S33: Conversion versus time plots for ROMP of MMs in DMF. A) ROMP of **PS_{Br}** in DMF with different purity levels; B) ROMP of **PS_{Br}**, **PnBA_{Br}**, **PnBA_{TTC}** in purified DMF. Markers are experimental results, lines are first-order kinetic fits. Deviation from first-order kinetics becomes prevalent above ~50%

conversion likely due to catalyst death. Insets show the same data for $\ln(1-p)$ with the lines depicting the first-order fits.

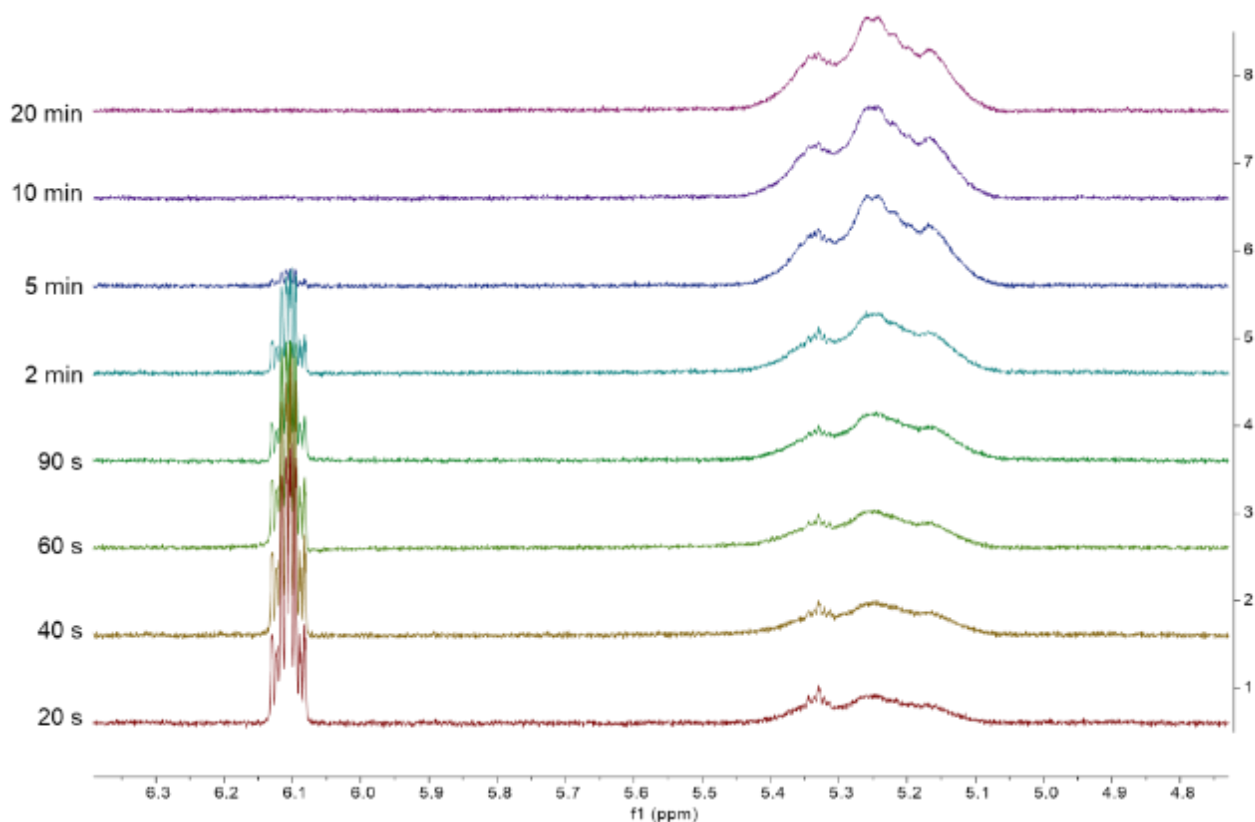


Figure 2.S34. Representative NMR spectra for small molecule kinetics tests. The peak at around 6.1 ppm is the vinyl peak in the **NMB** monomer, while the broad peak around 5.1-5.4 ppm is the growing polymer peak in the polynorbornene backbone.

Measuring catalyst decomposition using UV-Vis:

Description of data workbook for catalyst decomposition experiments using UV-vis spectrometry

UV-vis scans were taken every 30 seconds for each solvent (with the exception of every 1 min for CHCl_3 and toluene), for up to 4 h. An explanation for the data workbook in Excel is as follows: The absorbances for all of the traces were normalized to the peak maximum (344 nm) at the zero

timepoint by dividing each absorbance value by the maximum value at 344 nm (usually between 1.1 and 1.3). These graphs allowed for an initial estimation of the absorbance at 344 nm at 100% catalyst decomposition based on the presence of a straight line with negative slope through 344 nm; this absorbance value was between 0.3 and 0.5 depending on the solvent. The normalized absorbance value at 344 nm at each timepoint was then used to create plots of normalized absorbance versus time. The estimated absorbance at 100% decomposition was subtracted from the normalized absorbance at 344 nm at each time point. To convert the normalized-and-subtracted absorbance versus time graphs to % catalyst remaining versus time graphs, normalized-and-subtracted absorbance at each time point was divided by the estimated normalized absorbance value at $t=0$. By graphing $\ln(\% \text{ catalyst remaining})$ versus time, the slope produced an initial estimate of $k_{\text{decomp,obs}}$.

$$\% \text{ catalyst remaining} = e^{-k_{\text{decomp,obs}}t} \quad \text{Equation 2.1}$$

Next, using Equation 2.1, a first-order fit curve was generated and graphed on top of the experimental data. The differences in % catalyst remaining between the experimental data and the fit were squared and summed across all timepoints. Finally, the Excel Solver function was used to minimize the sum of the squares using the variables of $k_{\text{decomp,obs}}$ and normalized absorbance at 100% catalyst decomposition, where the 100% catalyst decomposition value was constrained in some cases. The $k_{\text{decomp,obs}}$ value determined using this Solver procedure is the value that is reported in the catalyst decomposition studies (Figure 2.5).

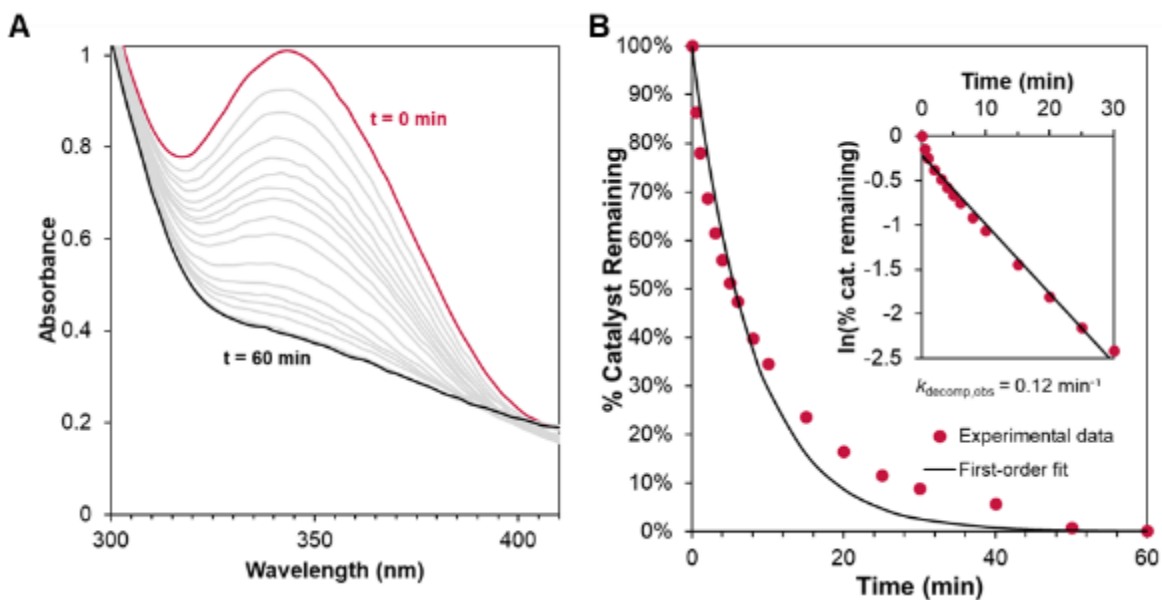


Figure 2.S35. UV-Vis spectra showing decomposition of G3 catalyst in EtOAc over time with a concentration of 0.075 mg/mL catalyst in solvent, at room temperature, open to air. A) Absorbance spectra were obtained between 300 and 420 nm (red line is 0 min and black line is 60 min). B) Graph of % catalyst remaining versus time and first-order curve fit used to calculate the rate of decomposition ($k_{\text{decomp,obs}}$). Inset shows the same data for $\ln(\% \text{ catalyst remaining})$ with the line depicting the first-order fit.

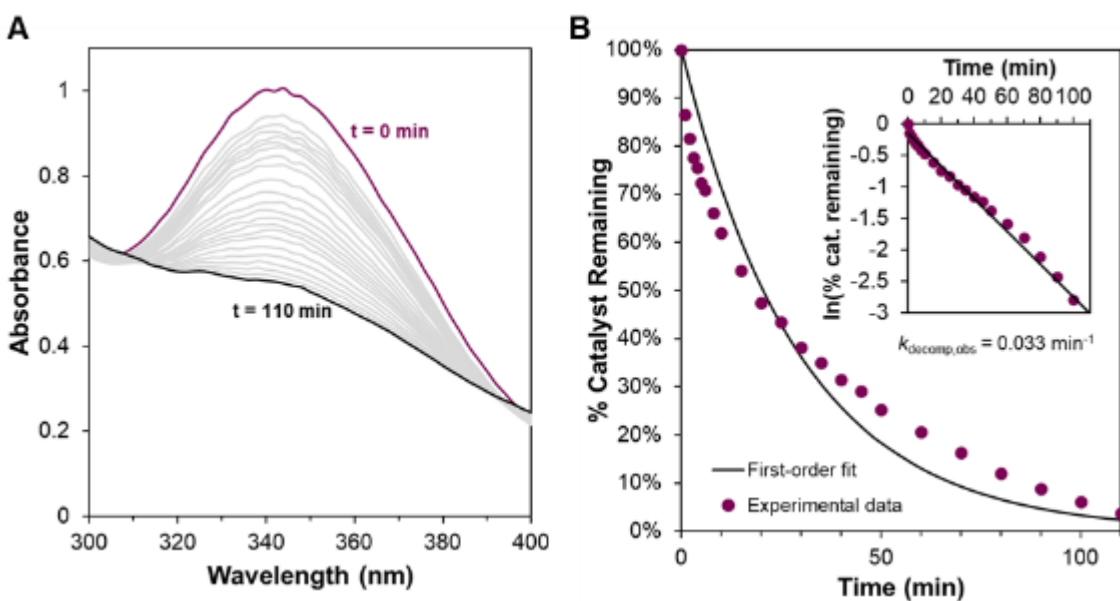


Figure 2.S36. UV-Vis spectra showing decomposition of G3 catalyst in CH_2Cl_2 over time with a concentration of 0.075 mg/mL catalyst in solvent, at room temperature, open to air. A) Absorbance spectra were obtained between 300 and 400 nm (purple line is 0 min and black line is 110 min). B) Graph of % catalyst remaining versus time and first-order curve fit used to calculate the rate of decomposition ($k_{\text{decomp,obs}}$). Inset shows the same data for $\ln(\% \text{ catalyst remaining})$ with the line depicting the first-order fit. The deviation from first-order indicates that the decomposition of G3 in CH_2Cl_2 is likely not a perfect first-order process.

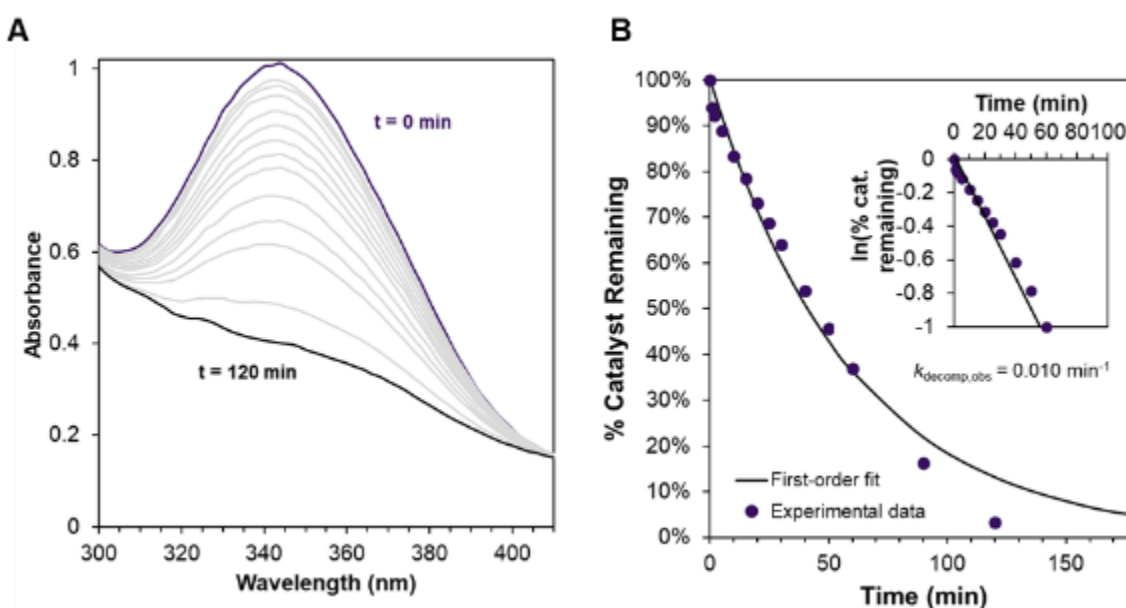


Figure 2.S37. UV-Vis spectra showing decomposition of G3 catalyst in CHCl_3 over time with a concentration of 0.075 mg/mL catalyst in solvent, at room temperature, open to air. A) Absorbance spectra were obtained between 300 and 420 nm (dark purple line is 0 min and black line is 120 min). B) Graph of % catalyst remaining versus time and first-order curve fit used to calculate the rate of decomposition ($k_{\text{obs, decomp}}$). Inset shows the same data for $\ln(\% \text{ catalyst remaining})$ with the line depicting the first-order fit.

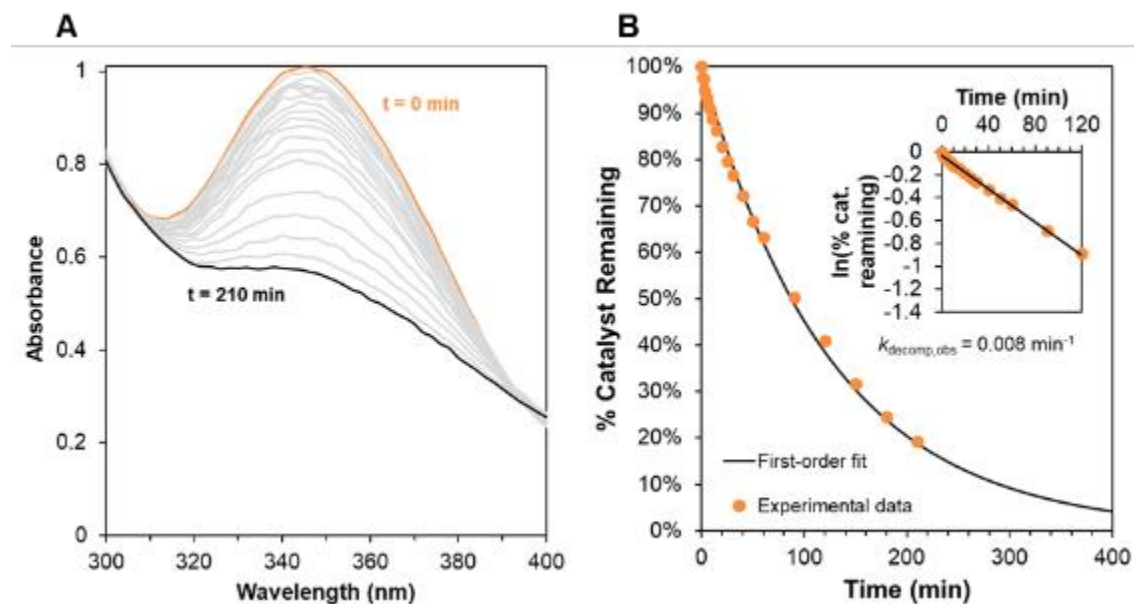


Figure 2.S38. UV-Vis spectra showing decomposition of G3 catalyst in toluene over time with a concentration of 0.075 mg/mL catalyst in solvent, at room temperature, open to air. A) Absorbance spectra were obtained between 300 and 400 nm (orange line is 0 min and black line is 210 min). B) Graph of % catalyst remaining versus time and first-order curve fit used to calculate the rate of decomposition ($k_{\text{decomp, obs}}$). Inset shows the same data for $\ln(\% \text{ catalyst remaining})$ with the line depicting the first-order fit.

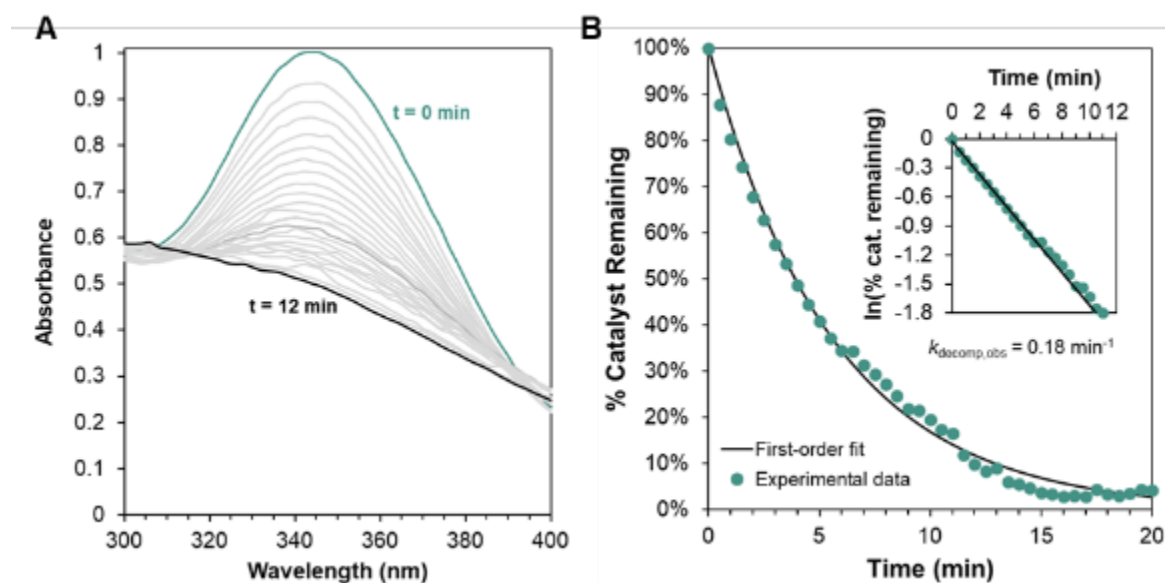


Figure 2.S39. UV-Vis spectra showing decomposition of G3 catalyst in THF over time with a concentration of 0.075 mg/mL catalyst in solvent, at room temperature, open to air. A) Absorbance spectra were obtained between 300 and 400 nm (teal line is 0 min and black line is 12 min). B) Graph of % catalyst remaining versus time and first-order curve fit used to calculate the rate of decomposition ($k_{\text{decomp,obs}}$). Inset shows the same data for $\ln(\% \text{ catalyst remaining})$ with the line depicting the first-order fit.

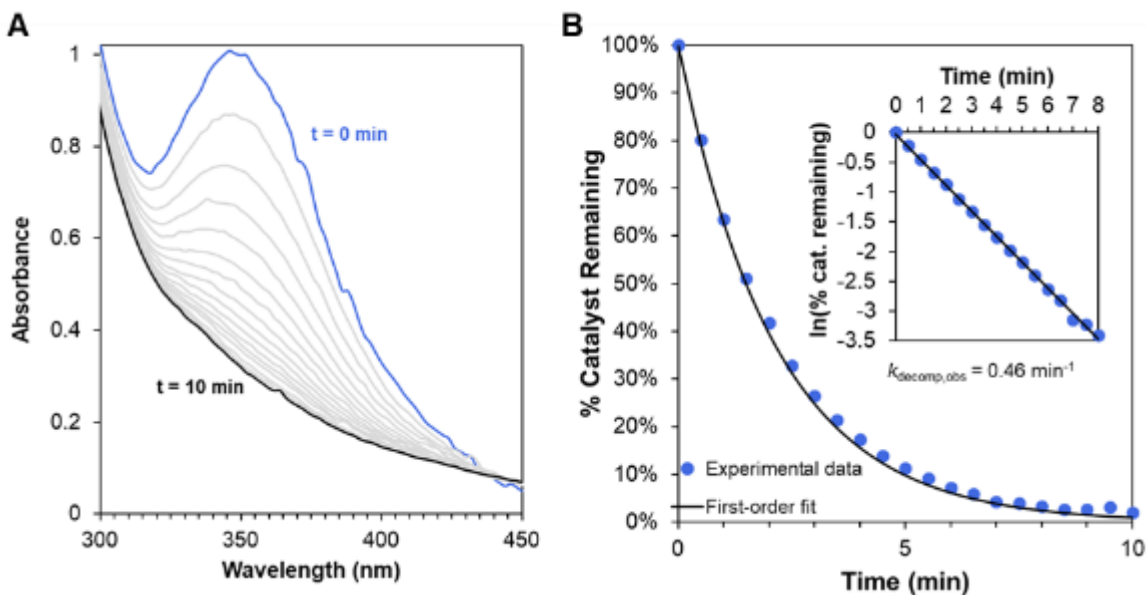


Figure 2.S40. UV-Vis spectra showing decomposition of G3 catalyst in DMF over time with a concentration of 0.075 mg/mL catalyst in solvent, at room temperature, open to air. A) Absorbance spectra were obtained between 300 and 450 nm (blue line is 0 min and black line is 10 min). B) Graph of % catalyst remaining versus time and first-order curve fit used to calculate the rate of decomposition ($k_{\text{decomp,obs}}$). Inset shows the same data for $\ln(\% \text{ catalyst remaining})$ with the line depicting the first-order fit.

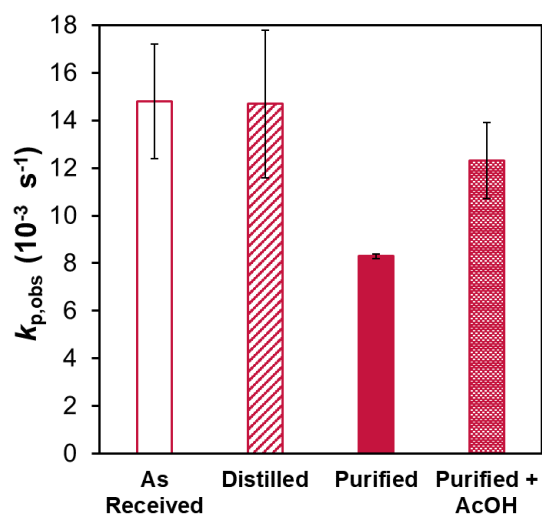


Figure 2.S41. Measured first-order $k_{p,obs}$ values for ROMP of PS_{Br} ($M_n = 4500 \text{ g/mol}$, $D = 1.03$) performed in EtOAc of differing purity levels. The “purified + AcOH” ROMP was performed using 20 equiv acetic acid relative to the G3 catalyst. Error bars represent the standard deviation between three repetitions.

First order kinetics results

Table 2.S1. First order kinetics of **PS_{Br}** ROMP in chosen solvents and levels of purity.

Solvent	Purification State	Conversion ^a	$k_{p,obs}$ (10^{-3} s^{-1}) ^b	$t_{1/2}$ (s) ^b	M_n , SEC (kg/mol) ^c	M_n , expected (kg/mol) ^d	$\bar{D}$ ^c
EtOAc	As Received	0.99	15 ± 2	48 ± 8	440	430	1.04
CH ₂ Cl ₂		0.99	6.4 ± 0.3	110 ± 6	400	430	1.07
CHCl ₃		0.99	2.9 ± 0.4	240 ± 30	440	430	1.11
Toluene		0.97	2.6 ± 0.7	280 ± 80	480	420	1.06
THF		-----No ROMP-----					
DMF	Distilled	0.84	1.3 ± 0.1	540 ± 60	370	360	1.36
EtOAc		0.99	15 ± 3	49 ± 9	430	430	1.07
CH ₂ Cl ₂		0.99	5.1 ± 0.1	140 ± 4	420	430	1.19
CHCl ₃		0.98	2.3 ± 0.2	310 ± 30	410	420	1.21
Toluene		0.98	2.1 ± 0.5	330 ± 80	420	420	1.12
THF	Purified	-----No ROMP-----					
DMF		0.89	1.3 ± 0.2	520 ± 9	440	390	1.18
EtOAc		0.99	8.3 ± 0.1	80 ± 1	430	430	1.07
CH ₂ Cl ₂		0.99	6.9 ± 0.9	100 ± 10	420	430	1.12
CHCl ₃		0.99	2.0 ± 0.4	350 ± 60	410	430	1.21
Toluene		0.99	2.3 ± 0.3	300 ± 30	450	430	1.14
THF		0.97	2.6 ± 0.1	270 ± 10	430	420	1.13
DMF		0.88	0.78 ± 0.08	890 ± 90	350	380	1.28

^aConversion from MM to BB polymer was measured using SEC and comparing the relative integrations of the MM and BB polymer peaks in the RI traces using a dn/dc value of 0.185. ^b $k_{p,obs}$ and $t_{1/2}$ were calculated by fitting conversion data to a first-order kinetics plot. ^c M_n and $\bar{D}$ values were determined by SEC in THF

containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors. ^dExpected M_n values were calculated based on measured conversion values (p) based on the equation: expected $M_n = (p)(\text{monomer molar mass})([\text{MM}]/[\text{G3}])$. Error ranges indicate standard deviation for $n=3-4$ separate experiments.

Table 2.S2: First-order kinetics of **PnBA_{Br}** ROMP in purified solvents

Solvent	Conversion ^a	$k_{p,\text{obs}}$ (10^{-3} s^{-1}) ^b	$t_{1/2}$ (s) ^b	M_n , SEC (kg/mol) ^c	M_n , expected (kg/mol) ^d	$\bar{D}$ ^c
EtOAc	0.99	11 ± 2	64 ± 9	300	370	1.06
CH ₂ Cl ₂	0.98	5.2 ± 0.5	130 ± 120	310	370	1.09
CHCl ₃	0.97	2.3 ± 0.1	300 ± 10	360	360	1.12
Toluene	0.97	3.3 ± 0.2	210 ± 20	300	360	1.11
THF	0.97	4.2 ± 0.3	160 ± 10	360	360	1.12
DMF	0.91	2.8 ± 0.2	250 ± 10	320	340	1.19

^aConversion from MM to BB polymer was measured using SEC and comparing the relative integrations of the MM and BB polymer peaks in the RI traces using a dn/dc value of 0.074. ^b $k_{p,\text{obs}}$ and $t_{1/2}$ were calculated by fitting conversion data to a first-order kinetics plot. ^c M_n and $\bar{D}$ values were determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors. ^dExpected values were calculated based on measured conversion values (p) based on the equation: expected $M_n = (p)(\text{monomer molar mass})([\text{MM}]/[\text{G3}])$. All error ranges indicate standard deviation for $n=3-4$ separate experiments.

Table 2.S3. First-order kinetics of **PnBA_{TTc}** ROMP in pure solvents

Solvent	Conversion ^a	$k_{p,obs}$ (10^{-3} s^{-1}) ^b	$t_{1/2}$ (s) ^b	M_n , (kDa) ^c	SEC M_n , (kDa) ^d	$\bar{D}$ ^c
EtOAc	0.99	8.4 ± 0.1	80 ± 10	390	340	1.11
CH ₂ Cl ₂	0.99	3.9 ± 0.4	180 ± 20	390	340	1.08
CHCl ₃	0.97	2.4 ± 0.1	290 ± 10	320	330	1.10
Toluene	0.98	3.2 ± 0.3	220 ± 20	360	330	1.11
THF	0.99	3.8 ± 0.3	180 ± 10	340	340	1.08
DMF	0.93	3.5 ± 0.4	200 ± 20	340	320	1.12

^aConversion from MM to BB polymer was measured using SEC and comparing the relative integrations of the MM and BB polymer peaks in the RI traces using a dn/dc value of 0.074. ^b $k_{p,obs}$ and $t_{1/2}$ were calculated by fitting conversion data to a first-order kinetics plot. ^c M_n and $\bar{D}$ values were determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors. ^dExpected values were calculated based on measured conversion values (p) based on the equation: expected $M_n = (p)(\text{monomer molar mass})([MM]/[G3])$. All error ranges indicate standard deviation for n=3–4 separate experiments.

Comparing solvent and polystyrene interactions to PS_{Br} rate of propagation:

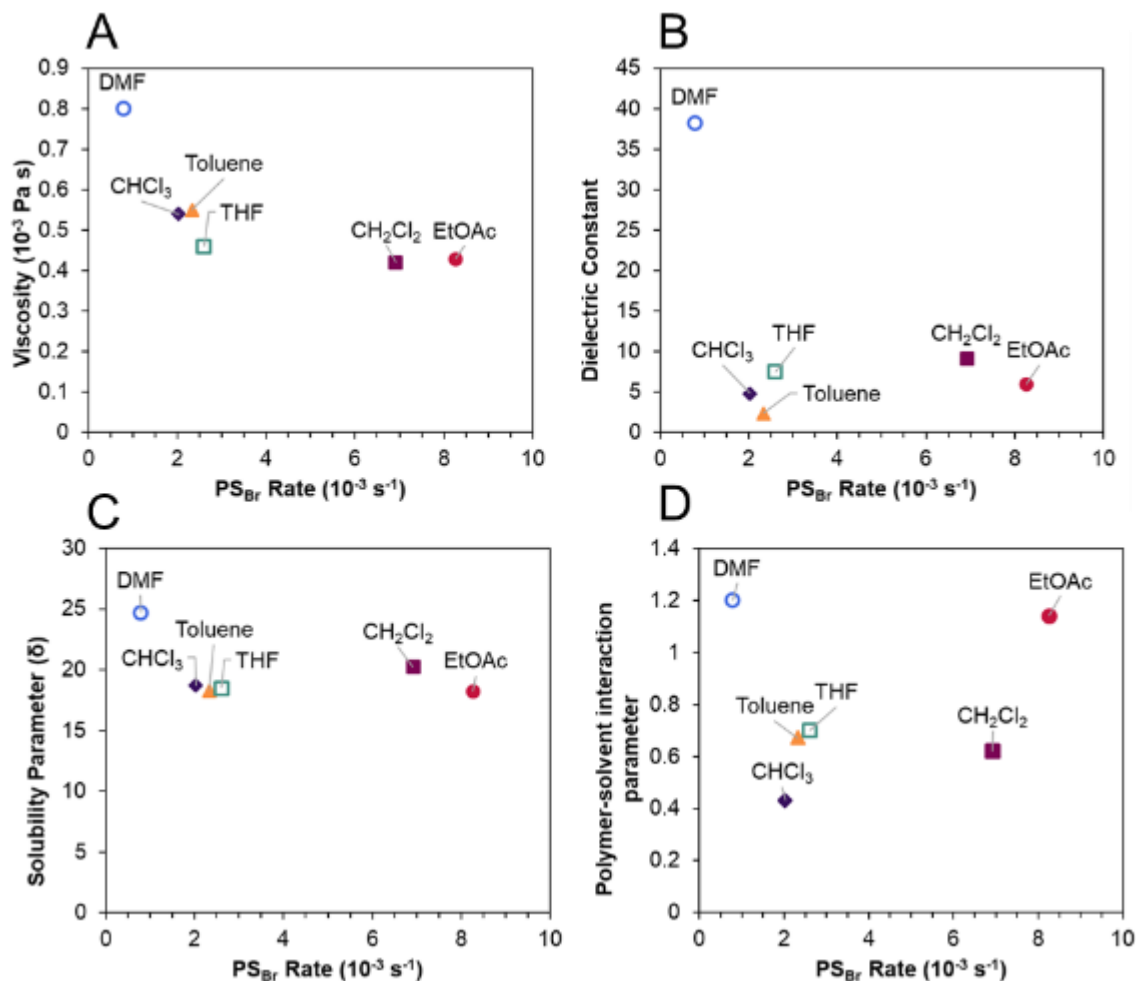


Figure 2.S42: Comparing PS_{Br} ROMP propagation to published values for A) solvent viscosity,² B) solvent dielectric constant,² C) Hildebrand solubility parameter,³ and D) the polymer–solvent interaction parameter.⁴

Measuring R_g of PS and PnBA in each solvent

Synthesis of linear PnBA for radius of gyration (R_g) measurements

A high molecular weight PnBA polymer sample was synthesized by thermal reversible addition-fragmentation chain-transfer (RAFT) polymerization. *n*-Butyl acrylate (17.6 mL, 1800 equiv, 122

mmol) was passed through a basic alumina plug, then added to an oven-dried 100 mL Schlenk tube containing a magnetic stir bar, along with **NDTMP** (28 mg, 1 equiv, 68 μ mol), prepared as previously reported.³⁷ AIBN (2.22 mg, 0.2 equiv, 14 μ mol) was dissolved in DMF (1 mL), then 100 μ L was added to 17.5 mL DMF, to obtain a total volume of DMF equal to 17.6 mL. The reaction mixture was deoxygenated by three freeze-pump-thaw cycles before the Schlenk tube was placed into an oil bath set to a temperature of 80 °C and then heated and stirred for 18 h. The Schlenk tube was removed from the oil bath, and the valve was removed to expose the contents to air to terminate the reaction. An aliquot was removed for analysis of monomer conversion; ¹H NMR spectroscopy showed 60% conversion of *n*-butyl acrylate to poly(*n*-butyl acrylate). The excess nBA and DMF were removed from the reaction mixture by blow-drying with air for 12 h, followed by drying under vacuum for 12 h, yielding a thick, yellow, viscous fluid. Based on conversion, the expected molecular weight was 140 kg/mol. The molecular weight of the sample was determined by SEC and found to have an M_n of 112 kg/mol, an M_w of 180 kg/mol and D of 1.65.

Determining R_g of PS and PnBA in each solvent

A PS standard from Wyatt (PS 50912, M_w of 200,000 g/mol) was used for all PS tests, while the synthesized linear PnBA was used for the PnBA tests. For the static light scattering measurements, batch mode data collection was performed on a Wyatt Dawn Heleos 2 multi-angle light scattering detector. Each solvent (10 mL) in the study was added to a clean 20 mL scintillation vial after passing through a 0.45 μ m syringe filter. The PS sample was dissolved in each solvent at a concentration of 1 mg/mL, and this solution was added to a clean scintillation vial after passing through a 0.45 μ m syringe filter. The PnBA was dissolved in each solvent at a concentration of 20 mg/mL, and this solution was added to a clean scintillation vial after passing through a 0.45 μ m

syringe filter. Batch mode analysis using the Zimm model was performed to obtain an average R_g measurement for both polymers in each solvent.

PS, dissolved in each solvent at a concentration of 1 mg/mL, generated sufficient light scattering angular dependence to afford R_g values in all six solvents (Table 2.S4). PnBA required a concentration of 20 mg/mL in each solvent due to a lack of angular dependence found at lower concentrations (Table 2.S5). Because of the differences in molecular weights and concentrations between these two polymers, we compared the results of both polymers in all six solvents by normalizing R_g values to the highest measured value for each polymer (Figure 2.S43).

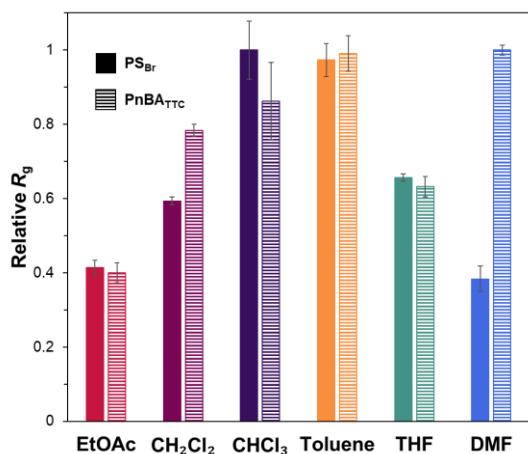


Figure 2.S43. Relative R_g measured by SLS of a $M_w = 200$ kg/mol PS standard and a $M_w = 180$ kg/mol PnBA synthesized by thermal RAFT polymerization. R_g values were measured in pure solvents (1 mg/mL for PS and 20 mg/mL for PnBA) and normalized to the highest measured value for each polymer. Actual R_g values are shown in Tables 2.S4 and 2.S5. Error bars represent the standard deviation in R_g measured over several minutes in one tested solution.

We found that for five of the six solvents, the measured relative R_g was similar for both PS and PnBA, while DMF resulted in a much lower R_g for PS than it did for PnBA. As mentioned in the manuscript, when comparing $k_{p,obs}$ for **PnBA_{Br}** and **PS_{Br}** MMs in CH₂Cl₂ and DMF, we noticed

that the rate decreased for **PnBA_{Br}** in CH₂Cl₂ relative to the rate of **PS_{Br}**, while the opposite was true in DMF. We theorized that this could be due to the behavior of the polymer in each solvent, and while not entirely conclusive, the R_g results do show trends consistent with the rate results we obtained for the polymers in DMF: The $k_{p,obs}$ of **PS_{Br}** in DMF was 3–4x lower than the $k_{p,obs}$ we measured for both PnBA MMs, and the R_g of PS in DMF is around 60% lower than the R_g of PnBA in the same solvent. These results indicate that the polymer conformation in DMF could be playing a role in the rate of ROMP, since a less extended MM would likely be more sterically hindered near the reactive norbornene, thus favoring a lower reaction rate. However, the case of CH₂Cl₂ is less clear when comparing the R_g results to the rate results, but the differences in the reaction rates between PS and PnBA MMs are also much smaller. Another observation from this analysis is that both polymers had a lower R_g in EtOAc compared with all other solvents. This is surprising because EtOAc provides the fastest $k_{p,obs}$ for all three MMs relative to the other solvents. Therefore, the relative R_g values may explain the differences in $k_{p,obs}$ for the PS and PnBA MMs in DMF, but the reason for the differences in $k_{p,obs}$ in the other solvents remains unclear.

Table 2.S4. R_g of a 200 kg/mol PS standard in six organic solvents

Solvent	R_g (nm) ^a
CHCl ₃	18 ± 7
CH ₂ Cl ₂	16 ± 1
DMF	11 ± 1
EtOAc	11 ± 2
THF	19 ± 1
Toluene	35 ± 2

^aStatic light scattering and batch mode data collection using a Zimm model was used to measure R_g . The solution was measured at a concentration of 1 mg/mL and at room temperature.

Table 2.S5. R_g of a 180 kg/mol prepared PnBA sample in six organic solvents

Solvent	R_g (nm) ^b
EtOAc	75 ± 9
CH ₂ Cl ₂	68 ± 2
CHCl ₃	87 ± 1
Toluene	35 ± 2
THF	55 ± 2
DMF	86 ± 4

^bStatic light scattering and batch mode data collection using a Zimm model was used to measure R_g . The solution was measured at a concentration of 20 mg/mL and at room temperature.

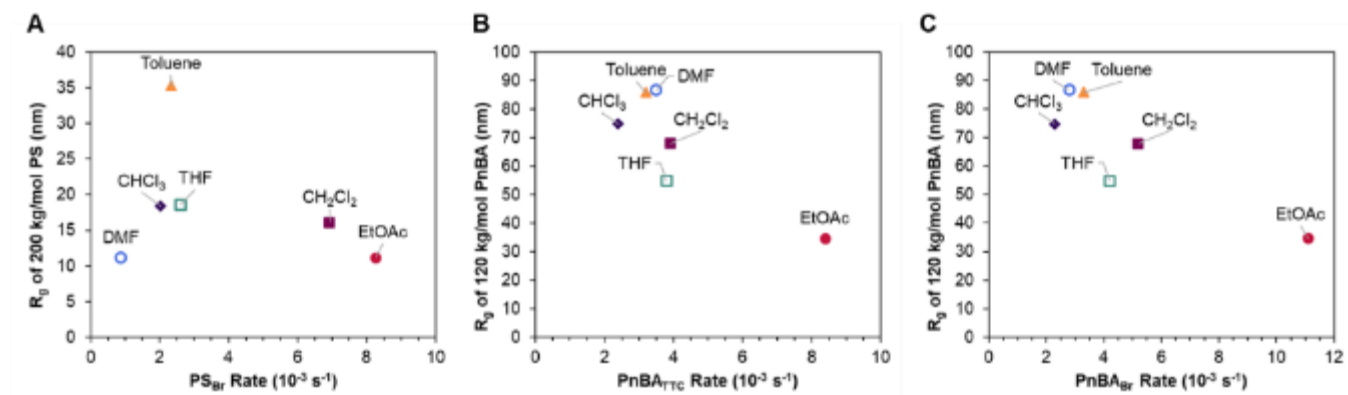


Figure 2.S44. R_g values determined using static light scattering compared with measured $k_{p,obs}$ values for the three MMs. A) R_g value of a 200 kg/mol PS polymer (room temperature, 1 mg/mL) compared to $k_{p,obs}$ of **PS_{Br}** ROMP. B and C) R_g value of a 180 kg/mol PnBA polymer (room temperature, 20 mg/mL) compared to $k_{p,obs}$ of B) **PnBA_{TTC}** ROMP and C) **PnBA_{Br}** ROMP.

Table 2.S6. Propagation rates for the ROMP of **NMB** in six purified solvents.

Solvent	$k_{p,obs}$ ($10^{-3} s^{-1}$) ^a
EtOAc	21 ± 8
CH ₂ Cl ₂	18 ± 4
CHCl ₃	2.6 ± 0.6
Toluene	10 ± 1
THF	16 ± 3
DMF	15 ± 2

^a $k_{p,obs}$ was calculated by fitting experimental data obtained from ¹H NMR spectroscopy experiments to a first-order fit plot. Error represents the standard deviation in three independent experiments. Note that the value for k_p in CHCl₃ is likely underestimated due to the complexation of CHCl₃ with added pyridine.

Table 2.S7. Catalyst decomposition rate ($10^{-3} s^{-1}$) in six organic solvents

Solvent	$k_{decomp,obs}$ ($10^{-3} s^{-1}$) ^a
EtOAc	1.9 ± 0.1
CH ₂ Cl ₂	0.61 ± 0.04
CHCl ₃	0.35 ± 0.05
Toluene	0.15 ± 0.02
THF	2.7 ± 0.2
DMF	7.3 ± 1.0

^a $k_{decomp,obs}$ was calculated by fitting % catalyst remaining data to a first-order kinetic plot.

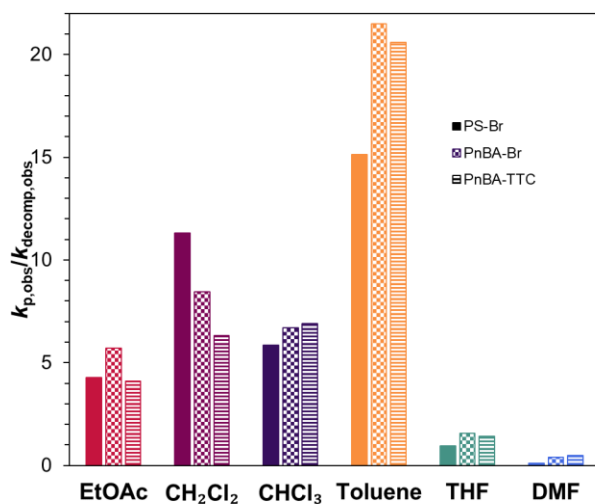


Figure 2.S45. Relative values for "livingness" of ROMP for the three MMs in six different organic solvents calculated by dividing $k_{p,obs}$ by $k_{decomp,obs}$. Note that this is not a true comparison of k_p/k_t because these rates were measured under different conditions. This is a qualitative comparison of relative values among the different solvents.

Table 2.S8. Conversion of **PS_{Br}** ($M_n = 3.0$ kg/mol) with target $N_{bb} = 1000$

Solvent	Conversion ^a	M_n , (kg/mol) ^b	SEC M_n , expected (kg/mol) ^c	$\bar{D}$ ^b
EtOAc	0.87	2780	2530	1.55
CH ₂ Cl ₂	0.94	2350	2730	1.52
CHCl ₃	0.81	2495	2360	1.47
Toluene	0.97	2750	2820	1.44
THF	0.13	298	380	1.60
DMF	0.05	257	150	1.35

^aConversion from MM to BB polymer was measured using SEC and comparing the relative integrations of the MM and BB polymer peaks in the RI traces using a dn/dc value of 0.185. ^b M_n and $\bar{D}$ values were determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive

index and light scattering detectors. ^cExpected M_n values were calculated based on measured conversion values (p) based on the equation: expected $M_n = (p)(\text{monomer molar mass})([\text{MM}]/[\text{G3}])$.

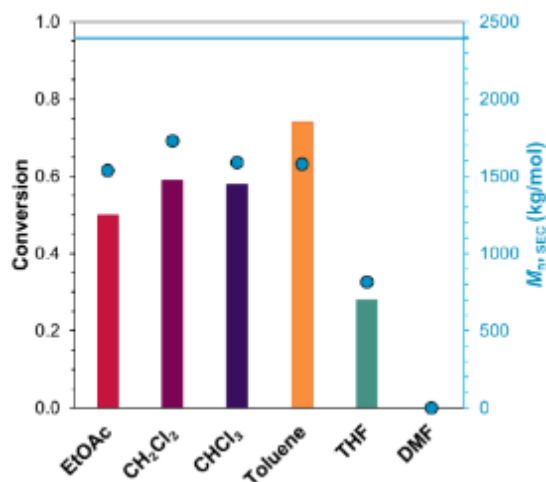


Figure 2.S46. MM conversion to BB polymer (bars) and final BB polymer M_n (dots) in the grafting-through ROMP of **PnBA_{TTC}** (4.8 kg/mol) in six purified solvents at a **PnBA_{TTC}**/G3 ratio of 500:1 (target $N_{\text{bb}} = 500$) over 24 h.

Table 2.S9. Conversion of **PnBA_{TTC}** ($M_n = 4.8$ kg/mol) with target $N_{\text{bb}} = 500$

Solvent	Conversion ^a	$M_{n, \text{SEC}}$ (kg/mol) ^b	$M_{n, \text{expected}}$ (kg/mol) ^c	$\bar{D}$ ^b
EtOAc	0.50	1530	1200	1.47
CH_2Cl_2	0.59	1730	1420	1.51
CHCl_3	0.58	1590	1390	1.67
Toluene	0.74	1580	1780	1.69
THF	0.28	820	670	1.61
DMF	0.00	0	0	---

^aConversion from MM to BB polymer was measured using SEC and comparing the relative integrations of the MM and BB polymer peaks in the RI traces using a dn/dc value of 0.074. ^b M_n and $\bar{D}$ values were determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive

index and light scattering detectors. ^cExpected M_n values were calculated based on measured conversion values (p) based on the equation: expected $M_n = (p)(\text{monomer molar mass})([MM]/[G3])$.

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Chapter 3: Synthesis of bottlebrush polymers by grafting-through ring-opening metathesis polymerization: Effect of additives

Manuscript is *in revision*.

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3.2 Abstract

Ring-opening metathesis polymerization (ROMP) is a powerful synthetic method capable of producing complex polymer architectures. Improving the “livingness” of ROMP by enabling efficient polymerization of bulky (macro)monomers can enhance the size and complexity of these polymer architectures. We tested the effects of small molecule additives in the ROMP of two different macromonomers (MMs) of differing molecular weights in three organic solvents: ethyl acetate (EtOAc), toluene, and *N,N*-dimethylformamide (DMF). Acids tended to improve conversion of MMs to bottlebrush polymer in all solvents, most profoundly in DMF. Other types of additives mostly decreased MM conversion. Based on these findings, we improved conversion in the ROMP of an unprotected, norbornene-functionalized peptide in DMF by adding trifluoroacetic acid. These results indicate that low loadings of acid additives can improve conversion in the ROMP of bulky or otherwise challenging (macro)monomers.

3.3 Introduction

Ring-opening metathesis polymerization (ROMP) has become a robust technique for synthesizing polymers with complex architectures, such as bottlebrush polymers,¹⁻⁴ star polymers,⁵⁻⁷ and dendronized polymers,⁸⁻¹⁰ among others.¹¹ One particular feature of ROMP that enables rapid and efficient synthesis of complex architectures is that it often exhibits living characteristics, including increasing molecular weight with increasing conversion and the ability to form block copolymers.¹² Thus, while ROMP is not characterized as living due to termination that arises *via* catalyst decomposition (also termed catalyst degradation or catalyst death),¹³ it remains a robust and widely used technique for the synthesis of large and well-defined polymer architectures.¹⁴ Key to many modern ROMP reactions is Grubbs' third generation catalyst, $(\text{H}_2\text{IMes})(\text{Cl})_2(\text{pyr})_2\text{RuCHPh}$ (G3), which provides fast initiation (k_i) and propagation (k_p) rates relative to termination (k_t),^{15,16} giving a high degree of living character. However, when the (macro)monomer has high molecular weight, is sterically bulky, or is otherwise slow to propagate, termination due to catalyst decomposition can lead to a loss in living character.¹⁷⁻¹⁹ Even in cases where high molecular weight materials can be achieved, dispersity can still broaden due to premature catalyst decomposition.^{20,21} Circumventing this decrease in living character when polymerizing bulky (macro)monomers by ROMP could enable the synthesis of polymers with even larger backbones/side chains and more elaborate architectures than those currently accessible.

One common architecture synthesized using ROMP is a densely grafted comb polymer, more typically referred to as a bottlebrush polymer. Bottlebrush polymers contain a polymer backbone with densely grafted side chains extending from the backbone, leading to a stiff backbone and a lack of entanglements.^{22,23} These structural traits lead to a variety of potential applications, including drug delivery agents,²⁴⁻²⁶ elastomers with unique properties,^{27,28} nanomaterials with

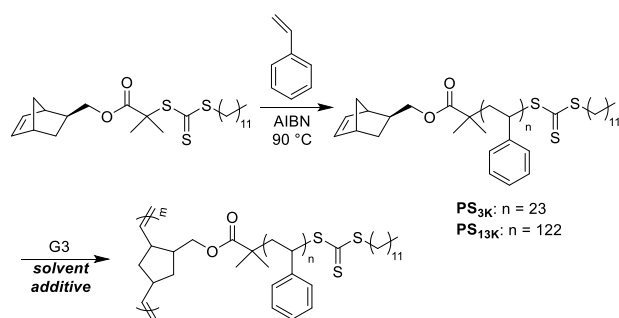
precisely controlled dimensions,^{29,30} miniaturized electronic materials,³¹ and photonic crystals.^{32–}
³⁴ The variety of chemistries, physical/chemical properties, and 3D nanostructures that can be realized by synthesizing bottlebrush polymers is extensive due to the range of backbone and side chain functionalities and the variability in the length of the backbone (N_{bb}) and side chains (N_{sc}). The grafting-through method for synthesizing bottlebrush polymers involves polymerizing a homotelechelic macromonomer (MM), often containing a norbornene derivative on one end, then performing ROMP to form a polynorbornene or other unsaturated polymer backbone. While other methods exist to synthesize bottlebrush polymers, the grafting-through method gives the most control over grafting density uniformity and is the only method that gives “perfect” grafting density.¹ A drawback of using the grafting-through method is that as the molecular weight of the MM increases, it becomes difficult to achieve high N_{bb} values due to steric hindrance around the propagating site.^{17,35,36} Therefore, methods to improve the conversion and “livingness” in ROMP of challenging (macro)monomers are still needed.

Our group and many others have attempted to improve the efficiency of ROMP for challenging MMs by investigating solvent,³⁷ the anchor group (series of atoms connecting the norbornene to the side chain),¹⁸ and altering the temperature,^{38,39} among others. Each of these critical variables can affect k_p and/or the MM conversion in a given ROMP reaction. Of particular importance for this work is our recent finding that solvent quality can profoundly affect k_p in ROMP.³⁷ Notably, we discovered that impure ethyl acetate (EtOAc) exhibited an almost two-fold faster k_p compared with purified EtOAc, and we deduced that this was related to a CH_3COOH impurity. We attributed this effect to protonation of the labile pyridine ligands, where an inverse proportional relationship between ROMP k_p and pyridine concentration was recently identified.⁴⁰ In contrast, in other solvents such as THF, purification was critical to achieving high conversion in ROMP, suggesting

the presence of a deleterious impurity in the as-received solvent. Based on these discoveries, we decided to investigate how other small molecule additives could affect ROMP reactions. Additive effects have been well documented in olefin cross metathesis^{41–43} ring-closing metathesis,⁴⁴ and using solvents as additives for ROMP^{45,46} but we have found few studies on other small molecule additives included in G3-initiated ROMP reactions. One example of a small molecule contributing to ROMP comes from O'Reilly and coworkers, where they found that the addition of chloride in aqueous ROMP improved conversion and control over polymerization.⁴⁷ However, studies on a variety of additives in ROMP under otherwise identical conditions have not been reported.

3.4 Results and Discussion

Motivated by these discoveries on small molecule additives in olefin cross metathesis, RCM, and ROMP, we aimed here to systematically identify small molecule additives that could improve conversion of MMs to make bottlebrush polymers. To determine how various additives influence the ROMP of MMs, we synthesized two polystyrene (PS) MMs via the direct-growth method with different N_{sc} values: **PS_{3K}** ($N_{sc} = 23$, $M_n = 3$ kg/mol) and **PS_{13K}** ($N_{sc} = 122$, $M_n = 13$ kg/mol) (Scheme 3.1) using reversible addition–fragmentation chain-transfer (RAFT) polymerization. MM **PS_{3K}** was utilized to ascertain whether small molecule additives would affect conversion at high N_{bb} values (up to 2000), whereas MM **PS_{13K}** was evaluated to confirm if we could achieve at least moderate N_{bb} values (up to 50) using this very challenging MM with a substantially higher N_{sc} .



Scheme 3.1. RAFT and ROMP scheme for the synthesis of **PS_{3K}** and **PS_{13K}**.

We set out to test the potential effects of small molecule additives on the conversion in ROMP using three purified solvents (purification methods are described in the SI): EtOAc, toluene, and *N,N*-dimethylformamide (DMF). We chose these solvents to span a variety of functional groups and dielectric constants, and also based on results in our previous study where we observed that EtOAc has a high k_p and relatively high k_t , DMF has a very low k_p and a high k_t , and toluene has a k_p in between the other two solvents, but a very low k_t .³⁷ We chose twelve different small molecule additives including six acids (HCl, CF₃COOH, H₃PO₄, CH₃COOH, HCOOH, and H₃BO₃), some of which were examined by Wagener in acyclic diene metathesis polymerization (ADMET),⁴⁸ one strong base (NaOH), and five other compounds that are relevant to either MM syntheses or olefin metathesis, including CuBr, CuI, NaI, triphenylphosphine oxide (Ph₃PO), and titanium tetrakisopropoxide (Ti(*i*OPr)₄). We chose the six acids to gather information on a wide range of pK_a values (around -7 to 9), as well as a strong base to complement the acids. CuI and NaI were chosen based on their use as promoters of metathesis reactions in small molecules,^{43,49} while CuBr was chosen based on its wide use in atom transfer radical polymerization (ATRP) reactions, which is a common method for synthesizing MMs used in ROMP. Ph₃PO has been used for the removal of ruthenium byproducts in metathesis reactions⁵⁰ and Ti(*i*OPr)₄ has been previously tested by our lab for its effect on k_p changes,¹⁸ making them both interesting additives to test in challenging ROMP reactions.

To determine the effects of small molecule additives on ROMP reactions, we first aimed to find a target N_{bb} value that achieved ~50% conversion for both MMs in each of the three solvents so that we could observe whether additives would increase or decrease conversion. We tested multiple MM:G3 ratios for each solvent, and we chose ratios that led to bottlebrush polymer conversions around 25-75% (see SI for further explanation of this process and Figures 3.S3 and 3.S7 for the

results). Based on these experiments, for MM **PS**_{3K} we chose a target N_{bb} of 2000 for EtOAc and toluene, while for DMF our target N_{bb} was 250. For MM **PS**_{13K}, target N_{bb} values were 50 for EtOAc and toluene and 25 for DMF.

From our previous work, we found that 20 equiv of additive with respect to G3 catalyst was enough to change the k_p of a PS MM,³⁷ so we used 20 equiv of each additive for these experiments. For each ROMP test in each solvent, a separate polymerization was carried out under air using each of the twelve additives and one ‘no additive’ control. After 24 h, each ROMP reaction was terminated with ethyl vinyl ether, the solvent was removed under air flow, and then M_n , N_{bb} , and $\bar{D}$ of the crude products were determined by size exclusion chromatography (SEC). Conversion was determined using the SEC results by comparing the areas of the MM and bottlebrush polymer peaks using the known dn/dc value for PS in tetrahydrofuran (THF) (0.185 mL/g). For both MMs (**PS**_{3K} and **PS**_{13K}), each of the three solvents, and each of the 12 additives, all experiments were performed 3–4 times.

Figure 3.1 shows the conversion and N_{bb} results of the ROMPs using the 12 additives and the no-additive control for the polymerization of MM **PS**_{3K}. MM conversion and N_{bb} had similar trends, as expected. For the experiments performed in EtOAc (Figure 3.1A) and toluene (Figure 3.1B), numerous additives caused a decrease in conversion and N_{bb} compared to the control polymerization. The most deleterious additive was NaOH, which showed less than 2% conversion for all solvents. Other deleterious additives for both solvents included CF₃COOH, CuBr, CuI, and NaI, all of which decreased conversion and N_{bb} . HCl decreased both conversion of MM to bottlebrush polymer and N_{bb} in EtOAc, but it had no effect on either conversion or N_{bb} in toluene.

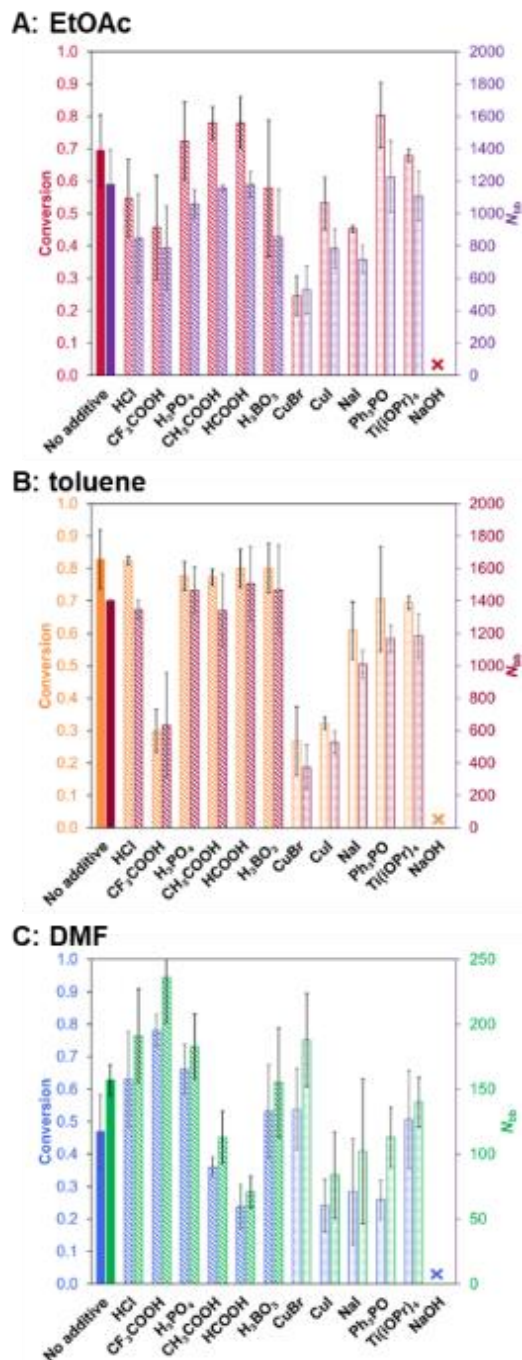


Figure 3.1. MM conversion to bottlebrush polymer and N_{bb} (as measured by SEC) in ROMP of PS_{3K} for 24 h in (A) EtOAc, (B) toluene, and (C) DMF. PS_{3K} :G3 ratio was 2000 for EtOAc and toluene and 250 for DMF. Solid bars represent reactions with no additives, striped bars represent reactions containing acid additives, and spotted bars include a variety of other additives. Error bars represent the standard deviation over three replicates. NaOH showed $< 2\%$ conversion for every reaction, so the data were not plotted.

Interestingly, CuBr also substantially decreased conversion and N_{bb} in both EtOAc and toluene. This is especially relevant in syntheses using atom transfer radical polymerization (ATRP) prior to ROMP (to synthesize MMs), which often uses CuBr as the activator. Thus, incomplete removal of residual Cu(I) species after ATRP may impede the subsequent ROMP reaction in a bottlebrush polymer synthesis, demonstrating the necessity of the MM purification process. In contrast, H_3PO_4 , CH_3COOH , $HCOOH$, Ph_3PO , and $Ti(iOPr)_4$ showed similar or minor increases in conversion and N_{bb} compared to the no-additive control in both EtOAc and toluene. As mentioned previously, we noticed in an earlier report that CH_3COOH increased k_p in ROMP of MMs in EtOAc.³⁷ We observed a similar effect here, with the average conversion increasing from 70% to 78% upon addition of CH_3COOH .

Additives had the greatest effects on polymerizations of MM **PS_{3K}** performed in DMF, with some improving ROMP and some hindering propagation (Figure 3.1C). As mentioned above, we used a target N_{bb} for DMF of 250 due to the very low MM conversion observed in DMF at the higher targeted values (Figure 3.S3C). Not only did we observe a much larger variation in conversion, the acids increased conversion to >60%, considerably higher than the no-additive control polymerization (47% conversion). Interestingly, the acid additives showed varying effects: HCl, CF_3COOH , H_3PO_4 , and H_3BO_3 improved conversion in DMF, while CH_3COOH and $HCOOH$ both decreased conversion. The results did not trend with acid pK_a , suggesting that the conjugate base may also influence catalyst activity. CuI, NaI, and Ph_3PO also hindered ROMP, lowering conversion to 20–25% with similar lowering effects on N_{bb} . Another interesting observation was that CuBr did not lower MM conversion in DMF, as it did in the other solvents, showing instead a slight enhancing effect. This is likely related to the coordination of CuBr in DMF,^{51,52} which is

lacking in EtOAc and toluene. Overall, the best additive for ROMP of **PS**_{3K} in DMF was CF₃COOH.

The enhanced conversion and higher N_{bb} with acid additives in DMF could be related to the protonation of the labile pyridine ligands, as mentioned before. However, this hypothesis creates a question about why the acids showed a less pronounced effect in toluene and EtOAc. We hypothesize that when targeting very high N_{bb} values ($N_{bb} = 2000$), the steric hindrance around the propagating site becomes too great to overcome, even with higher k_p values generated by acid additives. Therefore, since the target N_{bb} was lower for DMF, the acids improved conversion, but the high target N_{bb} values in EtOAc and toluene attenuated this improvement.

We also attempted polymerizations using MM **PS**_{13K} in the same solvents, testing the same small molecule additives (excluding NaOH in these experiments because it inhibited ROMP) at a **PS**_{13K}:G3 ratio of 50 for EtOAc and toluene and 25 for DMF. The results of these reactions are shown in Figure 2. ROMP reactions of **PS**_{13K} in EtOAc generally reached 75–85% conversion and were impeded by NaI but were unaffected by the other additives (Figure 3.2A). In toluene, the high molecular weight MM **PS**_{13K} appeared to create a great deal of steric hindrance around the propagating site, resulting in the polymerization reaching relatively low conversions (Figure 3.2B) of ~40% even at an N_{bb} value as low as 50. This result suggests that when polymerizing very bulky (macro)monomers, EtOAc, which gives high ROMP k_p values, can be used to improve conversion. This outcome was different than the result we observed using MM **PS**_{3K}, where MM conversion in toluene was higher than in EtOAc. We hypothesize that the **PS**_{3K} ROMP reactions went to higher conversions in toluene than the **PS**_{13K} reactions because k_p is too low for MM **PS**_{13K} to overcome the steric hindrance present at the propagating site using the higher molecular weight MM. This allowed termination due to catalyst decomposition to impact the reaction, even with the

relatively slow k_t seen in toluene.³⁷ However, k_p is high enough in EtOAc to “outrun” k_t and for the ROMP reaction to still achieve high conversion.

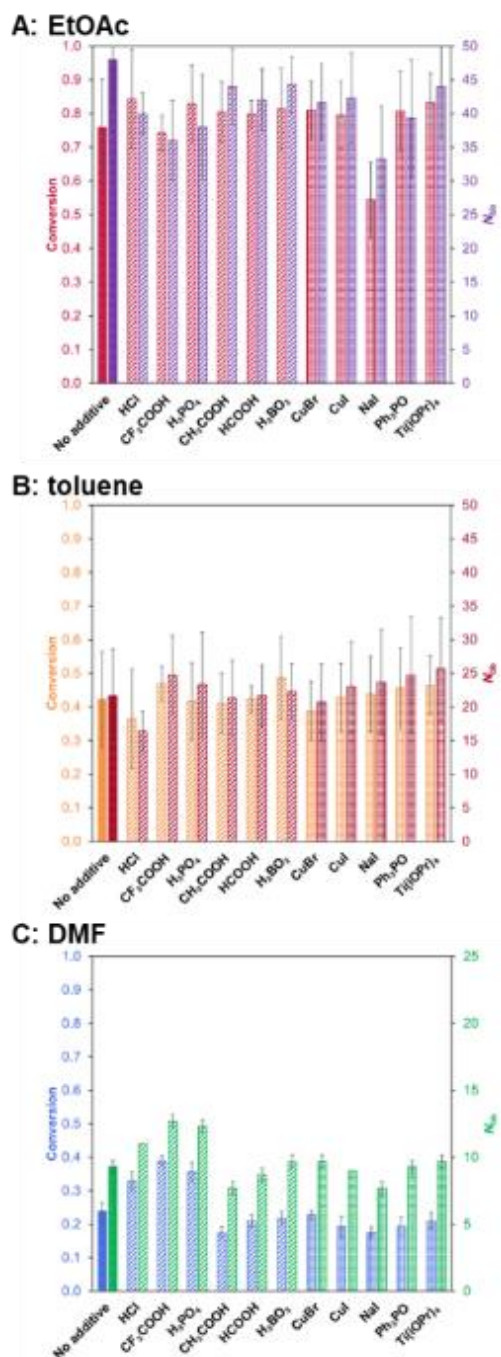


Figure 3.2. MM conversion to bottlebrush polymer and N_{bb} (as measured by SEC) in ROMP of **PS**_{13K} for 24 h in (A) EtOAc, (B) toluene, and (C) DMF. **PS**_{13K}:G3 ratio was 50 for EtOAc and toluene and 25 for

DMF. Solid bars represent reactions with no additives, striped bars represent reactions containing acid additives, and spotted bars include a variety of other additives. Error bars represent the standard deviation over three replicates.

Similar to what we observed for **PS_{3K}**, ROMP reactions performed in DMF at a **PS_{13K}**:G3 ratio of 25:1 were the most significantly affected by the small molecule additives (Figure 3.2C). Once again, acid additives improved conversion and N_{bb} compared to the control polymerization, with CF_3COOH increasing MM conversion from 25% to 40%. While DMF still led to low conversions overall, the fact that adding a small quantity of acid to the polymerization can improve conversion and increase N_{bb} is an important finding. This could lead to improved ROMP of challenging (macro)monomers that are only soluble in DMF.

Finally, following up on these results showing improved ROMP in DMF with a CF_3COOH additive, we asked whether this additive could improve ROMP of other challenging monomers that require polar solvents like DMF. One class of monomers that is typically only soluble in DMF (not EtOAc or toluene) is peptide-based monomers. ROMP of peptide-based monomers, especially unprotected peptides, is often limited to low N_{bb} due to the need for polar solvents such as DMF.⁵³ We hypothesized that CF_3COOH could improve the ROMP of a peptide-based monomer.

In order to test this hypothesis, we synthesized a norbornene-functionalized peptide (Figure 3.3A) and performed ROMP reactions in DMF with and without an acid additive. For this study, we chose Tyr-Ile-Gly-Ser-Arg (YIGSR), a pentapeptide derived from laminin that improves cell adhesion and promotes cell spreading.⁵⁴ We synthesized the peptide monomer using Fmoc-based solid-phase peptide synthesis (SPPS), adding the norbornene to the N-terminus on-resin, and finally cleaving the peptide monomer from the resin and removing all protecting groups under

acidic conditions. Purification by preparative-scale HPLC afforded the desired unprotected peptide monomer, **Nb-YIGSR-NH₂**, which was soluble in DMF but not EtOAc or toluene.

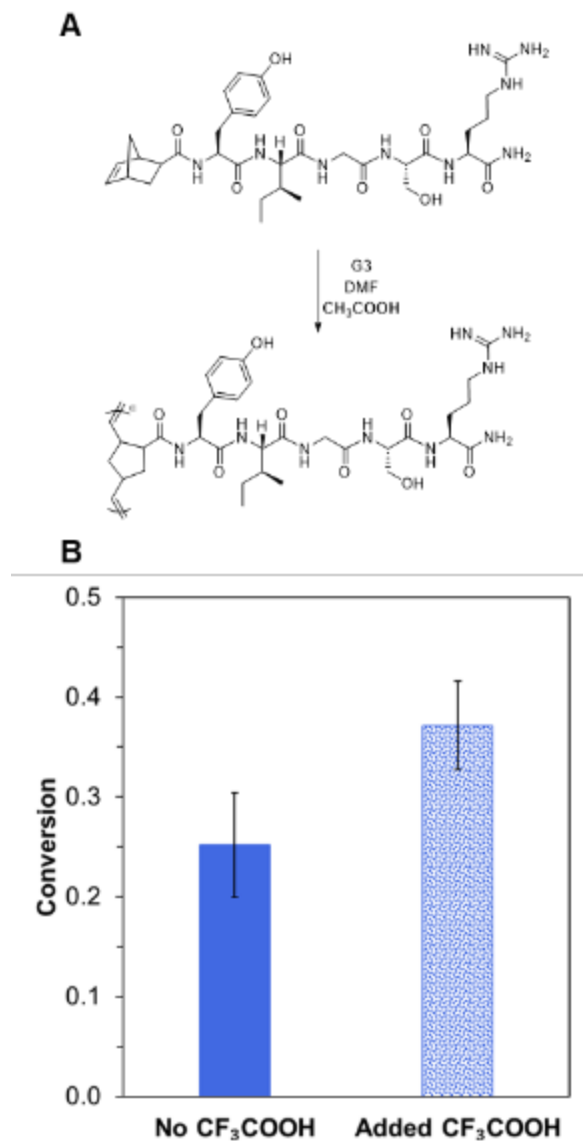


Figure 3.3. (A) Scheme of the ROMP of **Nb-YIGSR-NH₂** with 20 equiv CF₃COOH and a monomer/G3 ratio of 25:1. (B) Conversion results for the ROMP of **Nb-YIGSR-NH₂** with and without added CF₃COOH.

Using 20 equiv of CF₃COOH and a **Nb-YIGSR-NH₂**:G3 ratio of 25:1, conversion of this challenging polar monomer increased from 25% to 37% (Figure 3.3B). The degree of polymerization also increased from 6 to 9. This result was a change in conversion slightly lower

than seen in **PS**_{3K} (~35% increase when adding CF₃COOH), but similar to the conversion increase observed for **PS**_{13K}. Therefore, CF₃COOH may be a broadly useful additive in the ROMP of challenging (macro)monomers that require dissolution in DMF.

3.5 Conclusions

In summary, we found that small molecule additives can either improve or reduce the conversion of norbornene-based MMs in ROMP. Specifically, acid additives tended to increase conversion, especially in DMF. We observed increases in conversion and N_{bb} upon addition of certain acid additives in two polystyrene MMs with differing molecular weights, as well as in a norbornene-functionalized peptide. Other MMs or challenging (macro)monomers with significant steric bulk, high polarity, or both may also benefit from inclusion of small molecule acids in the ROMP reaction, such as HCl, CF₃COOH, or H₃PO₄. We anticipate that this work will guide attempts to synthesize large, well-defined, and complex polymeric materials.

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Appendix B: Supporting information for “*Synthesis of bottlebrush polymers by grafting-through ring-opening metathesis polymerization: Effect of additives*”

Materials and Characterization

All reagents were obtained from commercial vendors and used as received unless otherwise stated. EtOAc (VWR BDH Chemicals, ACS grade, $\geq 99.5\%$) was purified by washing with equal volumes of saturated aqueous sodium carbonate in a separatory funnel, followed by brine, before removing the organic layer and drying over MgSO_4 . The solvent was then distilled onto molecular sieves and was stored in a Strauss flask under nitrogen protected from the light. Toluene (Fischer, ACS grade, $\geq 99.5\%$) was stored on a column of activated alumina under nitrogen in a solvent purification system (MBraun). DMF (Fischer, HPLC grade, $\geq 99.7\%$) was stirred over 5 w/v % CaH_2 overnight, then filtered. The DMF was then distilled at reduced pressure onto molecular sieves and was stored in a Strauss flask under nitrogen protected from the light. The G3 catalyst was prepared as previous described,^{1,2} and each batch of G3 was only used for 48 h after synthesis. For analysis of MMs and bottlebrush polymers, size exclusion chromatography (SEC) was performed using THF containing 0.025 wt% butylated hydroxytoluene at a rate of 1 mL/min at 30 °C on two MIXED-B Agilent PLgel 10 μm columns connected in a series with a Wyatt Optilab rEX refractive index detector and a Wyatt Dawn Heleos 2 multi-angle light scattering detector. The polypeptide was characterized by SEC using a mobile phase consisting of *N,N*-dimethylacetamide containing 50 mM LiCl at a rate of 1 mL/min at 50 °C on two Agilent Technologies PLgel 10 μm mixed-bed columns connected in series with Wyatt Technologies TRIOS II light scattering and Optilab T-REX refractive index detectors.

Preparation of additives for ROMP reactions

For each small molecule additive that was a solid, H_3BO_3 , CuBr , CuI , NaI , NaOH , triphenylphosphine oxide (Ph_3PO), and titanium(IV) tetraisopropoxide ($\text{Ti}(\text{iOPr})_4$), 2000, 250, 50, or 25 equiv (relative to catalyst and depending on the solvent used and M_n of the MM) of each additive was dissolved in distilled water (100 mL), and 0.1 mL of the solution was injected into a 1-dram vial for a resulting amount of 20 equiv. These 1-dram vials were then lyophilized and used within four weeks for the polymerizations.

For the liquid additives, HCl , CF_3COOH , H_3PO_4 , CH_3COOH , and HCOOH , stock solutions were made to the proper concentration needed to add 20 equiv of the additive.

Synthesis of *exo*-norbornene-methyl 2-(((dodecylthio)carbonothioyl)thio)-2-methylpropanoate (NDTMP)

The norbornene-functionalized photoiniferter, **NDTMP**, was synthesized according to the procedure reported in a recent study. NMR spectra were consistent with literature reports.³ ^1H NMR (CDCl_3): δ 6.07 (m, 2H), 4.22 (dd, $J = 10.8$ Hz, 6.4 Hz, 1H), 3.95 (dd, $J = 10.8$ Hz, 9.2 Hz, 1H), 3.27 (td, $J = 7.4$ Hz, 2.1 Hz, 2H), 2.82 (s, 1H), 2.66 (s, 1H), 1.70 (s, 6H), 1.31 (m, 3H), 1.25 (m, 20H), 0.88 (t, $J = 7$ Hz, 3H). ^{13}C NMR (CDCl_3): δ 221.6, 173.2, 137.0, 136.5, 70.2, 56.2, 45.1, 43.8, 41.8, 37.9, 37.0, 32.1, 29.8, 29.7, 29.6, 29.5, 29.3, 29.1, 28.1, 25.6, 25.6, 22.9, 14.3.

Synthesis of polystyrene MMs by RAFT

Radical addition-fragmentation chain-transfer (RAFT) polymerization was used to synthesize two polystyrene MMs with targeted molecular weights of 3 kg/mol and 13 kg/mol. For the MM with a target of 3 kg/mol, styrene (31.8 mL, 290 equiv, 277 mmol), **NDTMP** (450 mg, 1 equiv, 0.96 mmol), and AIBN (1.57 mg, 0.01 equiv, 0.096 mmol) were combined and added to an oven-dried 100 mL Schlenk tube containing a magnetic stir bar. The mixture was deoxygenated using three

freeze-pump-thaw cycles, then heated and stirred using an oil bath at 90 °C. After 2.5 h the cap was removed and the mixture was exposed to air to terminate the reaction. The mixture was precipitated twice into methanol, then the solids were dissolved in CH₂Cl₂ and purified by automated silica gel column chromatography using a gradient of 100% hexanes to 50/50 hexanes/CH₂Cl₂ on a Biotage Selekt. Product-containing fractions were concentrated using rotary evaporation, and then the products were isolated by precipitation into methanol once more. The light-yellow powder was filtered and dried under vacuum overnight. The molecular weight for the 3k MM (**PS_{3k}**) was confirmed by SEC (Figure 3.S2A) to have a number average molecular weight (M_n) of 2900 g/mol and $\bar{D} = 1.08$. For the targeted 13 kg/mol MM a similar procedure was performed but with changes to the amount of each chemical added and the time it was heated and stirred in the oil bath. Those changes are as follows: styrene (27.4 mL, 675 equiv, 239 mmol), **NDTMP** (167 mg, 1 equiv, 0.36 mmol), AIBN (0.58 mg, 0.01 equiv, 0.036 mmol) and a stirring/heating time of 6.5 h. The M_n was determined by SEC (Figure 3.S2B) for this MM (**PS_{13k}**) and was 13,200 g/mol and $\bar{D} = 1.09$.

Determination of target N_{bb} for PS ROMPs in three organic solvents

Each solvent (EtOAc, toluene, and DMF) was tested separately to determine the target N_{bb} value in the additive studies using **PS_{3k}**. The reactions performed in EtOAc and toluene were prepared similarly: 10 mg of **PS_{3k}** was added to three 1-dram vials equipped with stir bars and dissolved in 0.2 mL of the selected solvent. G3 (2 mg) was added to a 25 mL beaker along with 6 mL of the solvent to create a solution with a concentration of 0.335 mg/mL. Adding 15 μ L of this solution to one of the MM solutions afforded an MM:G3 ratio of 500:1. The G3 solution was then diluted 2-fold, and 15 μ L was added to the second MM solution, to give an MM:G3 ratio of 1000:1. The dilution was performed again for the third vial, to give an MM:G3 ratio of 2000:1. The three

samples were allowed to polymerize overnight, then terminated by adding a few drops of ethyl vinyl ether (EVE) to each vial. The synthesis in DMF differed slightly: 10 mg of **PS_{3K}** was added to three 1-dram vials equipped with stir bars and dissolved in 0.2 mL DMF. G3 (2 mg) was added to a 25 mL beaker and 3 mL of DMF was added to give a concentration of 0.670 mg/mL. The same procedure was used to add the G3 solution to the MM solution and to dilute the G3 solution. However, the MM:G3 ratios for the DMF samples were 250:1, 500:1, and 1000:1. The terminated reaction mixtures for all solvents were concentrated under air flow, and then SEC was used to determine the conversion from MM to BB by comparing the integrations of the MM and BB polymer peaks in the RI traces using a dn/dc value of 0.185 (Figure 3.S3). A similar procedure was followed for the **PS_{13K}** MM; however, the MM:G3 values were 25:1, 50:1, and 100:1 (Figure 3.S7).

ROMP of MM in the presence of small molecule additives

A representative ROMP reaction of **PS_{3K}** in toluene is as follows. To a 1-dram vial equipped with a magnetic stir bar, 10 mg (2000 equiv, 3.4 μ mol) of **PS_{3K}** was added along with 0.2 mL toluene (to achieve a concentration of 50 mg/mL). If using a solid additive, the additive was already present in the 1-dram vial (preparation outlined above), but if using a liquid additive 10 μ L of the prepared stock solution was added to the 1-dram vial containing the MM and solvent. To a separate vial, 2 mg G3 catalyst was dissolved in 16 mL of toluene, then 10 μ L of the solution was quickly injected into the MM solution (to achieve a molar ratio of 2000:1 MM/G3). The reaction was stirred at room temperature for 24 h, and then a few drops of ethyl vinyl ether (EVE) were added to terminate the reaction. The solution was dried in air overnight before dissolving the residual solids in THF for SEC analysis, and the conversion from MM to bottlebrush polymer was determined by dividing the peak area of MM by the combined peak areas of the MM and bottlebrush polymer (Figures

3.S4, 3.S5, and 3.S6). This process was repeated in triplicate for each additive. Reactions performed in EtOAc were set up identically, only altering the solvent, while reactions performed in DMF were performed similarly but the molar ratio of MM to G3 was 250:1 because 2000:1 led to little to no conversion.

Reactions performed using the **PS_{13K}** MM were performed similarly to the **PS_{3K}** MM; however, lower backbone N_{bb} values were targeted. For EtOAc and toluene, an N_{bb} of 50 was targeted, while for DMF the target was an N_{bb} value of 25. Otherwise, additive preparation, reaction conditions, and conversion calculations (Figures S8, S9, S10) were identical.

Synthesis and ROMP of **Nb-YIGSR-NH₂**

The synthesis of the *exo*-5-norbornene-2-carboxylic acid (**Nb**) followed procedures from a previously published report.³ ¹H NMR (CDCl₃): δ 6.15 (qd, J = 5.6, 2.9 Hz, 2H), 3.11 (ddt, J = 3.1, 1.6, 0.8 Hz, 1H), 2.94 (d, J = 3.2 Hz, 1H), 2.32-2.23 (m, 1H), 1.95 (ddd, J = 11.9, 4.6, 3.5 Hz, 1H), 1.58-1.35 (m, 4H). ¹³C NMR (CDCl₃): δ 182.3, 138.1, 135.7, 49.7, 46.7, 45.7, 43.0, 29.0.

Peptide monomer Nb-Tyr-Ile-Gly-Ser-Arg-NH₂ (**Nb-YIGSR-NH₂**) was manually synthesized using standard 9-fluorenylmethoxycarbonyl (Fmoc) solid phase synthesis techniques at a 0.5 mmol scale. Fmoc deprotection steps were carried out by treating the Rink amide MBHA resin with 4-methylpiperidine in DMF (20% v/v) for 15 min (2 times). Amino acid coupling steps were performed following Fmoc deprotection by treating the resin with Fmoc-amino acid, *O*-benzotriazole-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HBTU), and diisopropylethylamine (DIEA) (4:3.96:10 molar ratio to amine groups on resin) in DMF for 2 h. After coupling of the final amino acid, **Nb** was then coupled to the Tyr N-terminus using the same coupling conditions as noted above for the Fmoc amino acids. Finally, **Nb-YIGSR-NH₂** was

cleaved from the resin by treatment with a TFA/triisopropylsilane (TIPS)/H₂O (95:2.5:2.5) solution (15 mL) for 3 h. The solution was concentrated in vacuo and triturated with cold diethyl ether to precipitate the crude peptide. Following centrifugation to remove the supernatant liquid, the crude product was dissolved in a 50/50 mixture of water and acetonitrile containing 0.1% TFA for purification.

Nb-YIGSR-NH₂ was then purified by preparative RP-HPLC using an Agilent Technologies 1260 Infinity HPLC system (Agilent Technologies, Santa Clara, CA) equipped with a fraction collector. Separations were performed using an Agilent PLRP-S column (100 Å, 10 µm, 150 × 25 mm) monitoring at 220 nm. The expected mass was confirmed using ESI-MS (Advion Expression Compact Mass Spectrometer). Fractions containing pure products were combined and lyophilized (FreeZone -105 °C, Labconco, Kansas City, MO), and then stored at -20 °C until needed.

Mass spectrometry results

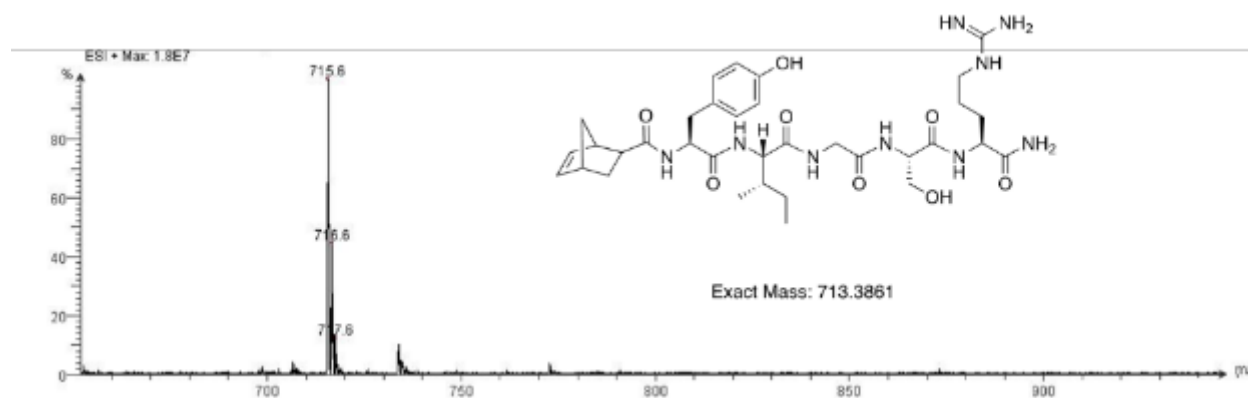


Figure 3.S1. ESI mass spectrum of **Nb-YIGSR-NH₂**.

SEC Traces

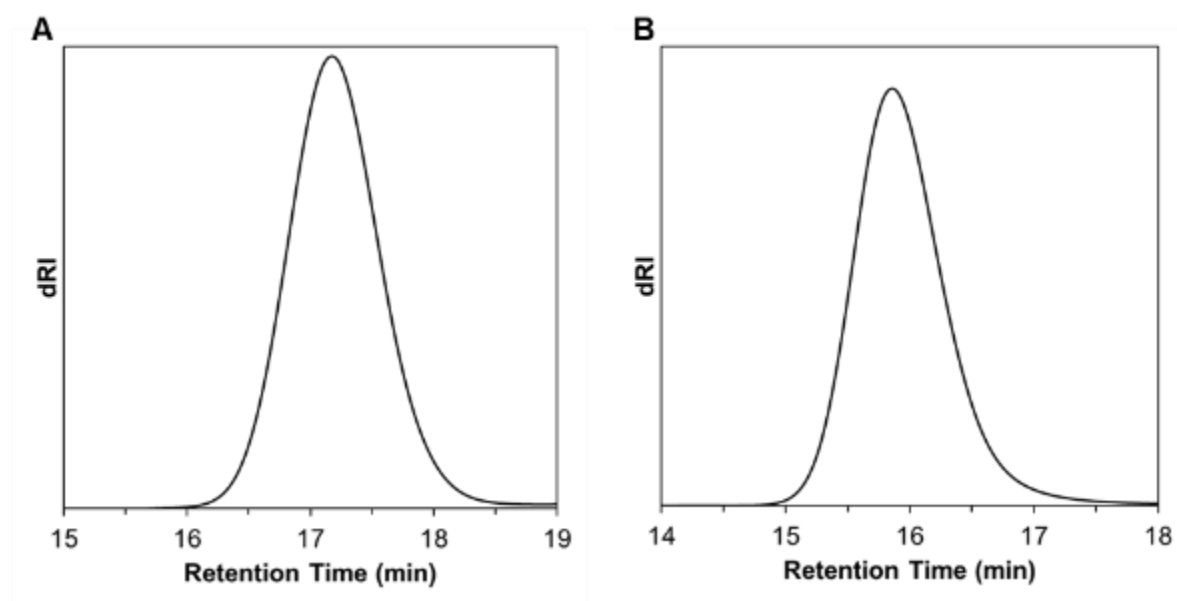


Figure 3.S2. SEC traces (RI detector) for (A) PS_{3K} and (B) PS_{13K}.

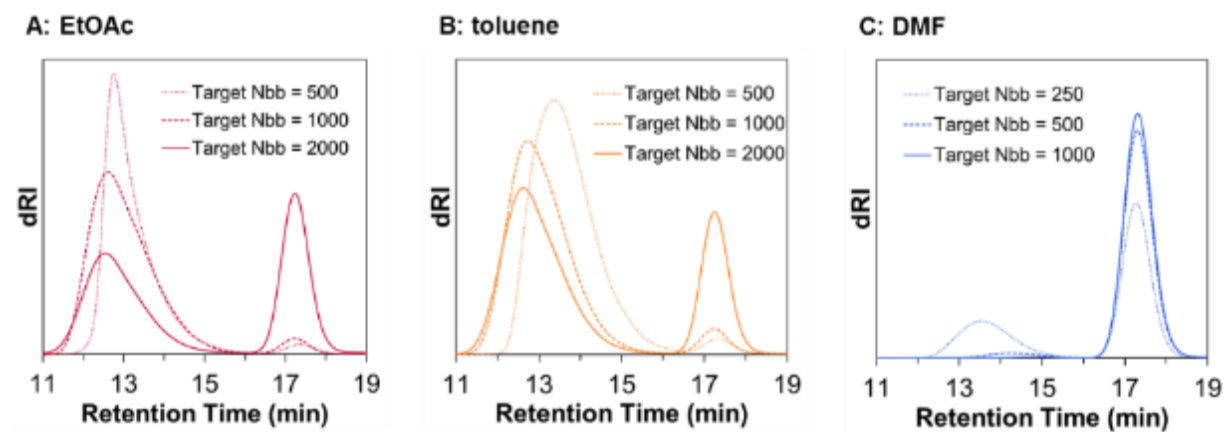


Figure 3.S3. SEC traces (RI detector) of ROMPs used to determine the target N_{bb} for PS_{3K} in (A) EtOAc, (B) toluene, and (C) DMF.

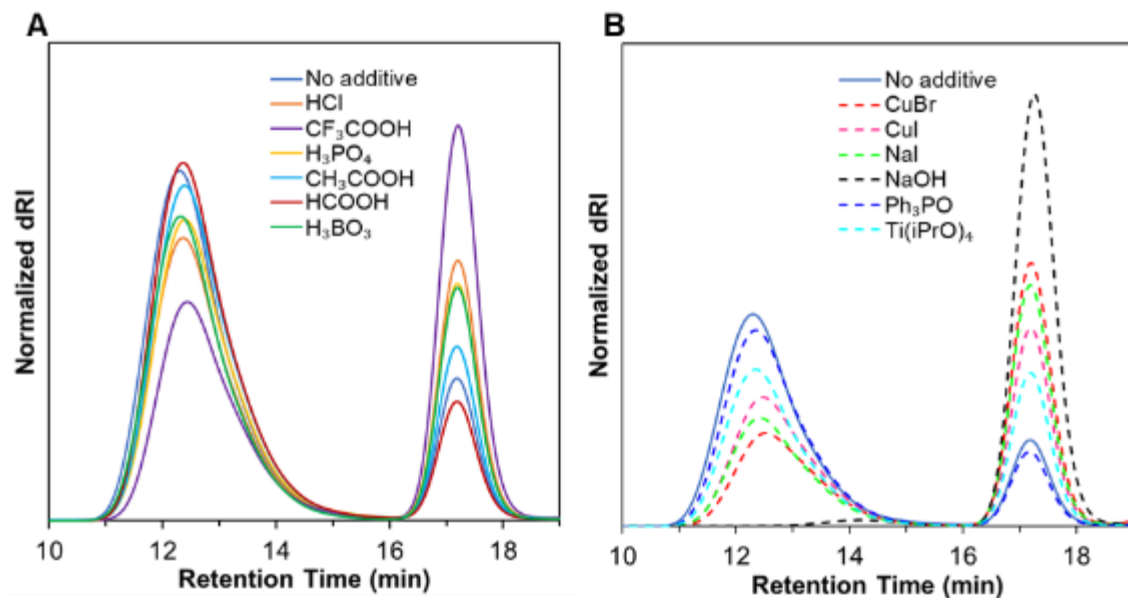


Figure 3.S4. Representative SEC traces (RI detector) for ROMP of $\text{PS}_{3\text{K}}$ in EtOAc (target $N_{\text{bb}} = 2000$) with (A) acid additives and (B) other additives.

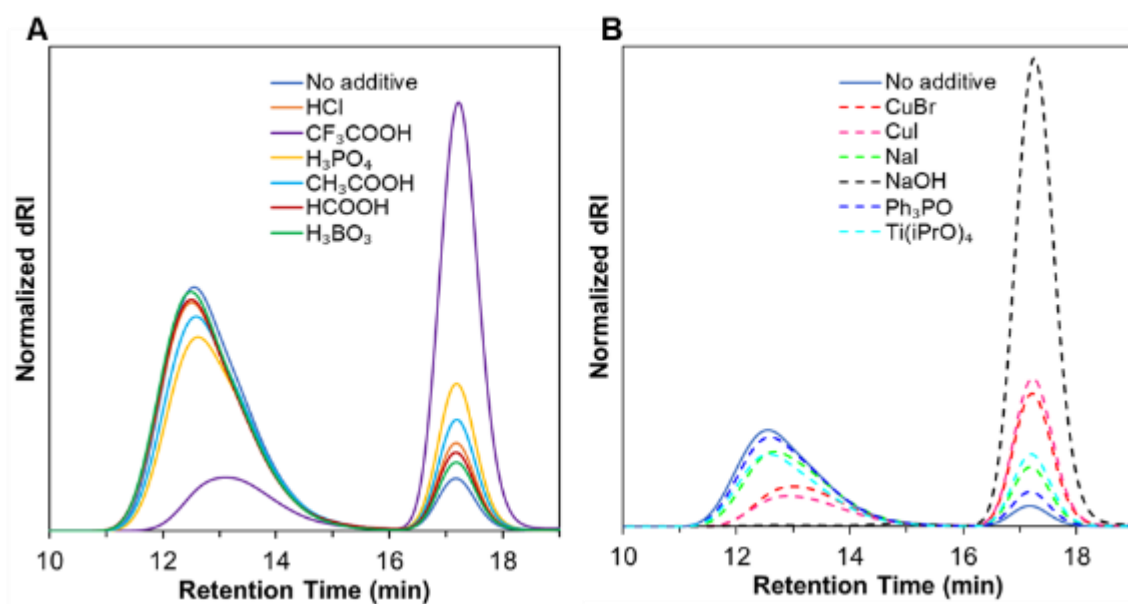


Figure 3.S5. Representative SEC traces (RI detector) of $\text{PS}_{3\text{K}}$ in toluene (target $N_{\text{bb}} = 2000$) with (A) acid additives and (B) other additives.

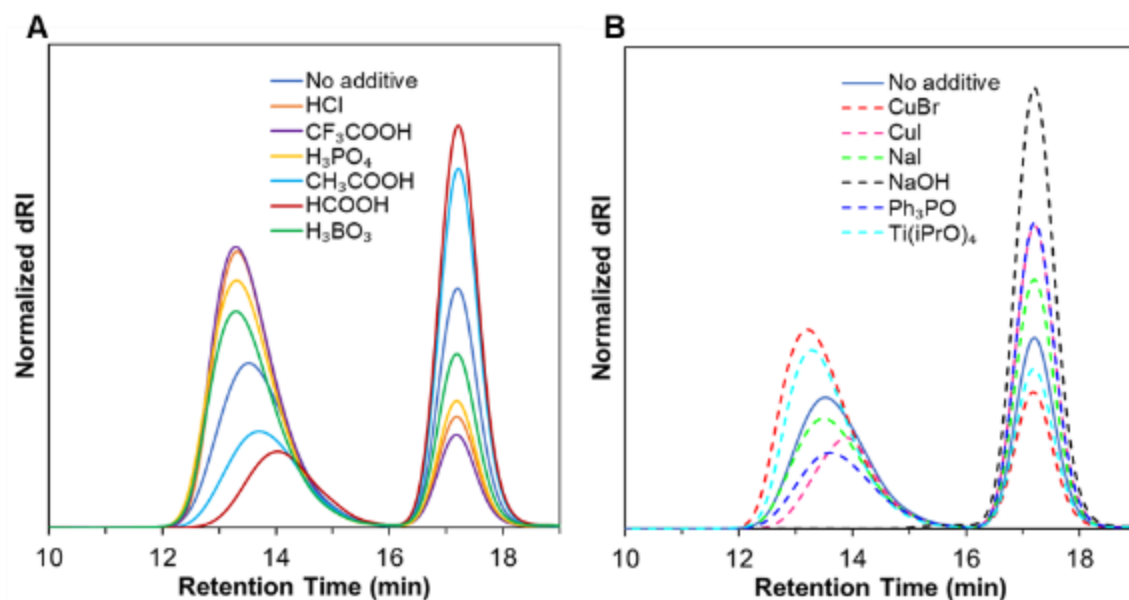


Figure 3.S6. Representative SEC traces (RI detector) of $\text{PS}_{3\text{K}}$ in DMF (target $N_{\text{bb}} = 250$) with (A) acid additives and (B) other additives.

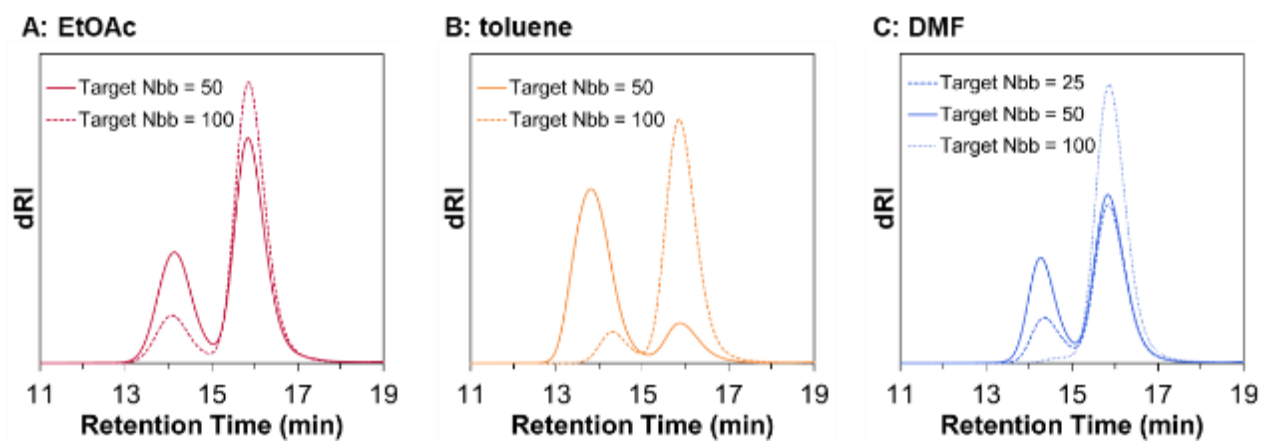


Figure 3.S7. SEC traces (RI detector) of ROMPs used to determine the target N_{bb} for $\text{PS}_{13\text{K}}$ in (A) EtOAc, (B) toluene, and (C) DMF.

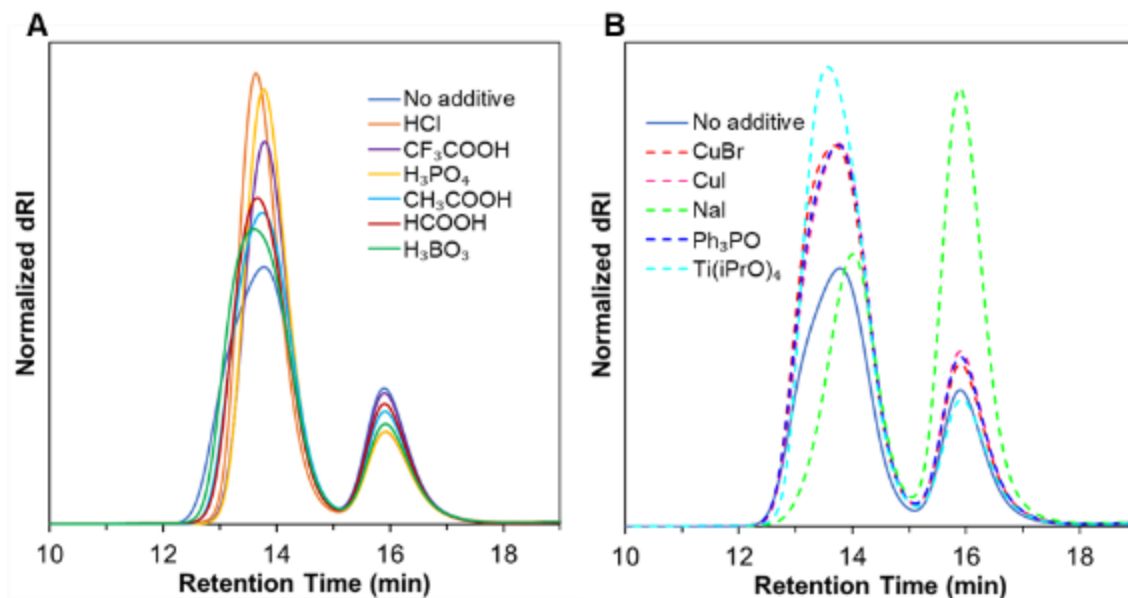


Figure 3.S8. Representative SEC traces (RI detector) of $\text{PS}_{13\text{K}}$ in EtOAc (target $N_{\text{bb}} = 50$) with (A) acid additives and (B) other additives.

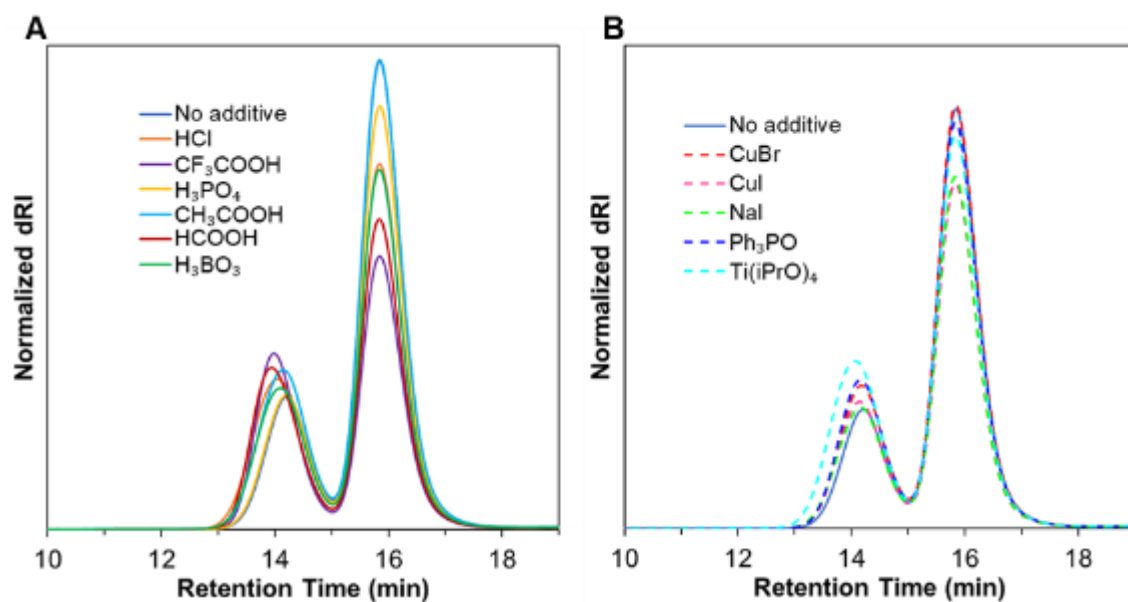


Figure 3.S9. Representative SEC traces (RI detector) of $\text{PS}_{13\text{K}}$ in toluene (target $N_{\text{bb}} = 50$) with (A) acid additives and (B) other additives.

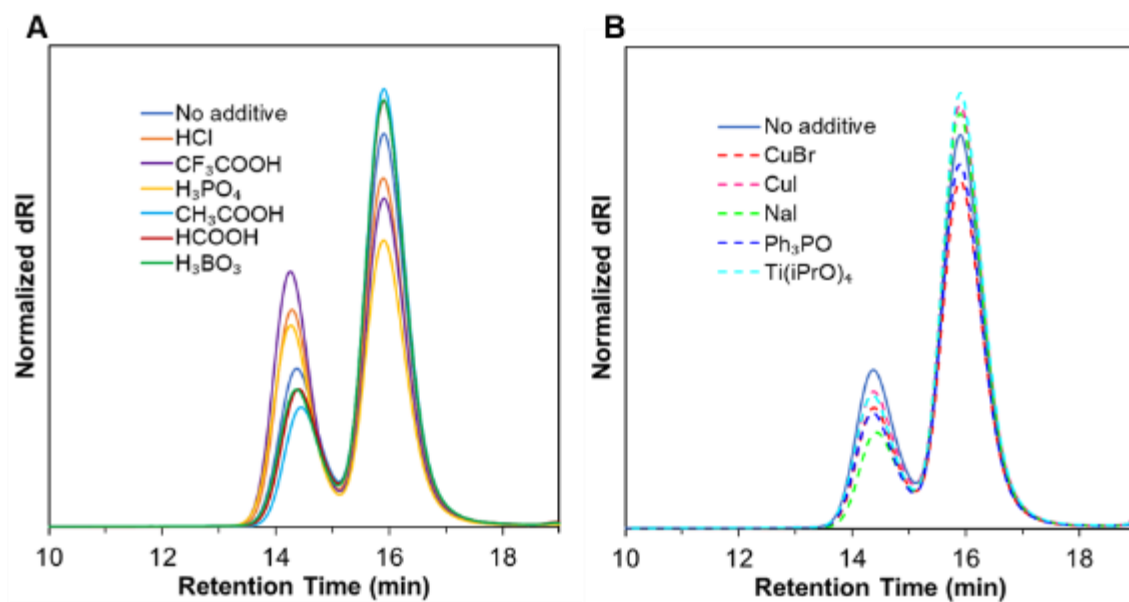


Figure 3.S10. Representative SEC traces (RI detector) of **PS_{13K}** in DMF (target $N_{bb} = 25$) with (A) acid additives and (B) other additives.

Table 3.S1. Conversion of **PS_{3K}** in EtOAc with additives targeting $N_{bb} = 2000$

Solvent	Conversion ^a	$N_{bb,SEC}$ ^b	$N_{bb,expected}$ ^c	$\bar{D}$ ^d
No additive	0.70 ± 0.10	1200 ± 200	1400 ± 200	1.55 ± 0.01
HCl	0.55 ± 0.10	900 ± 300	1100 ± 300	1.56 ± 0.03
CF ₃ COOH	0.46 ± 0.20	800 ± 200	900 ± 300	1.40 ± 0.10
H ₃ PO ₄	0.72 ± 0.10	1060 ± 90	1400 ± 200	1.54 ± 0.01
CH ₃ COOH	0.78 ± 0.05	1160 ± 20	1560 ± 90	1.49 ± 0.07
HCOOH	0.78 ± 0.08	1180 ± 80	1600 ± 200	1.54 ± 0.02
H ₃ BO ₃	0.58 ± 0.20	900 ± 300	1200 ± 400	1.55 ± 0.02
CuBr	0.25 ± 0.06	500 ± 100	500 ± 100	1.51 ± 0.04
CuI	0.53 ± 0.08	800 ± 100	1100 ± 200	1.56 ± 0.03
NaI	0.45 ± 0.01	700 ± 80	910 ± 10	1.49 ± 0.03
NaOH	0	0	0	0
Ti(<i>i</i> OPr) ₄	0.68 ± 0.02	1100 ± 200	1360 ± 40	1.55 ± 0.01
Ph ₃ PO	0.80 ± 0.10	1200 ± 200	1600 ± 200	1.56 ± 0.02

^aConversion from MM to BB polymer was measured using SEC, comparing the relative areas of the MM and BB polymer peaks in the RI traces using a dn/dc value of 0.185. ^b N_{bb} was calculated using M_n values for the bottlebrush polymer peaks determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors using the equation $N_{bb,SEC} = (M_{n,SEC})/(\text{MM molar mass})$. ^cExpected N_{bb} values were calculated based on measured conversion values (p) based on the equation: $\text{expected } N_{bb,expected} = (p)([\text{MM}]/[\text{G3}])/(\text{monomer molar mass})$. ^d $\bar{D}$ values were determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors.

Table 3.S2. Conversion of **PS_{3K}** in toluene with additives targeting $N_{bb} = 2000$

Solvent	Conversion ^a	$N_{bb,SEC}$ ^b	$N_{bb,expected}$ ^c	$\bar{D}$ ^d
No additive	0.83 ± 0.09	1400 ± 10	1600 ± 200	1.62 ± 0.02
HCl	0.82 ± 0.01	1350 ± 60	1650 ± 30	1.61 ± 0.01
CF ₃ COOH	0.30 ± 0.07	600 ± 300	500 ± 100	1.56 ± 0.01
H ₃ PO ₄	0.78 ± 0.04	1500 ± 100	1550 ± 90	1.59 ± 0.02
CH ₃ COOH	0.77 ± 0.03	1300 ± 200	1550 ± 50	1.62 ± 0.01
HCOOH	0.80 ± 0.06	1500 ± 200	1600 ± 100	1.61 ± 0.02
H ₃ BO ₃	0.80 ± 0.08	1500 ± 300	1600 ± 100	1.57 ± 0.02
CuBr	0.30 ± 0.10	400 ± 100	500 ± 200	1.49 ± 0.03
CuI	0.32 ± 0.02	530 ± 70	640 ± 40	1.57 ± 0.01
NaI	0.61 ± 0.09	1010 ± 90	1200 ± 200	1.62 ± 0.02
NaOH	0	0	0	0
Ti(<i>i</i> OPr) ₄	0.69 ± 0.02	1200 ± 100	1390 ± 40	1.60 ± 0.02
Ph ₃ PO	0.70 ± 0.10	1180 ± 80	1400 ± 300	1.60 ± 0.04

^aConversion from MM to BB polymer was measured using SEC, comparing the relative areas of the MM and BB polymer peaks in the RI traces using a dn/dc value of 0.185. ^b N_{bb} was calculated using M_n values for the bottlebrush polymer peaks determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors using the equation $N_{bb,SEC} = (M_{n,SEC})/(\text{MM molar mass})$. ^cExpected N_{bb} values were calculated based on measured conversion values (p) based on the equation: $\text{expected } N_{bb,expected} = (p)([\text{MM}]/[\text{G3}])/(\text{monomer molar mass})$. ^d $\bar{D}$ values were determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors.

Table 3.S3. Conversion of **PS_{3K}** in DMF with additives targeting $N_{bb} = 250$

Solvent	Conversion ^a	$N_{bb,SEC}$ ^b	$N_{bb,expected}$ ^c	$\bar{D}$ ^d
No additive	0.50 ± 0.10	160 ± 10	120 ± 30	1.42 ± 0.02
HCl	0.60 ± 0.10	190 ± 40	160 ± 40	1.36 ± 0.08
CF ₃ COOH	0.78 ± 0.05	200 ± 40	200 ± 10	1.30 ± 0.02
H ₃ PO ₄	0.66 ± 0.08	180 ± 20	170 ± 20	1.42 ± 0.10
CH ₃ COOH	0.36 ± 0.03	110 ± 20	90 ± 10	1.43 ± 0.01
HCOOH	0.24 ± 0.07	70 ± 10	60 ± 20	1.44 ± 0.05
H ₃ BO ₃	0.50 ± 0.10	150 ± 40	130 ± 30	1.46 ± 0.09
CuBr	0.50 ± 0.10	190 ± 30	130 ± 30	1.37 ± 0.07
CuI	0.24 ± 0.08	80 ± 30	60 ± 20	1.45 ± 0.07
NaI	0.30 ± 0.10	100 ± 50	70 ± 40	1.50 ± 0.05
NaOH	0	0	0	0
Ti(<i>i</i> OPr) ₄	0.50 ± 0.10	140 ± 20	130 ± 40	1.40 ± 0.07
Ph ₃ PO	0.26 ± 0.06	110 ± 20	70 ± 20	1.55 ± 0.03

^aConversion from MM to BB polymer was measured using SEC, comparing the relative areas of the MM and BB polymer peaks in the RI traces using a dn/dc value of 0.185. ^b N_{bb} was calculated using M_n values for the bottlebrush polymer peaks determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors using the equation $N_{bb,SEC} = (M_{n,SEC})/(\text{MM molar mass})$. ^cExpected N_{bb} values were calculated based on measured conversion values (p) based on the equation: expected $N_{bb,expected} = (p)([\text{MM}]/[\text{G3}])/(\text{monomer molar mass})$. ^d $\bar{D}$ values were determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors.

Table 3.S4. Conversion of **PS_{13K}** in EtOAc with additives targeting $N_{bb} = 50$

Solvent	Conversion ^a	$N_{bb,SEC}$ ^b	$N_{bb,expected}$ ^c	$\bar{D}$ ^d
No additive	0.76 ± 0.05	50 ± 10	38 ± 2	1.47 ± 0.08
HCl	0.84 ± 0.02	40 ± 5	42 ± 1	1.14 ± 0.02
CF ₃ COOH	0.74 ± 0.02	36 ± 5	37 ± 1	1.22 ± 0.02
H ₃ PO ₄	0.83 ± 0.01	38 ± 5	41 ± 1	1.18 ± 0.02
CH ₃ COOH	0.80 ± 0.02	44 ± 9	40 ± 1	1.35 ± 0.06
HCOOH	0.80 ± 0.03	42 ± 6	40 ± 1	1.27 ± 0.05
H ₃ BO ₃	0.81 ± 0.01	44 ± 6	41 ± 1	1.35 ± 0.05
CuBr	0.81 ± 0.03	42 ± 9	40 ± 1	1.38 ± 0.07
CuI	0.80 ± 0.04	40 ± 10	40 ± 2	1.40 ± 0.08
NaI	0.54 ± 0.08	33 ± 9	27 ± 4	1.50 ± 0.04
Ti(<i>i</i> OPr) ₄	0.83 ± 0.01	44 ± 6	42 ± 1	1.30 ± 0.04
Ph ₃ PO	0.81 ± 0.03	39 ± 3	40 ± 2	1.38 ± 0.07

^aConversion from MM to BB polymer was measured using SEC, comparing the relative areas of the MM and BB polymer peaks in the RI traces using a dn/dc value of 0.185. ^b N_{bb} was calculated using M_n values for the bottlebrush polymer peaks determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors using the equation $N_{bb,SEC} = (M_{n,SEC})/(\text{MM molar mass})$. ^cExpected N_{bb} values were calculated based on measured conversion values (p) based on the equation: $\text{expected } N_{bb,expected} = (p)([\text{MM}]/[\text{G3}])/(\text{monomer molar mass})$. ^d $\bar{D}$ values were determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors.

Table 3.S5. Conversion of **PS_{13K}** in toluene with additives targeting $N_{bb} = 50$

Solvent	Conversion ^a	$N_{bb,SEC}$ ^b	$N_{bb,expected}$ ^c	$\bar{D}$ ^d
No additive	0.40 ± 0.10	22 ± 7	22 ± 7	1.36 ± 0.01
HCl	0.40 ± 0.10	16 ± 3	18 ± 3	1.30 ± 0.10
CF ₃ COOH	0.47 ± 0.05	25 ± 6	23 ± 3	1.27 ± 0.01
H ₃ PO ₄	0.40 ± 0.10	23 ± 8	21 ± 6	1.38 ± 0.02
CH ₃ COOH	0.41 ± 0.09	21 ± 6	21 ± 4	1.37 ± 0.04
HCOOH	0.42 ± 0.04	22 ± 5	21 ± 2	1.30 ± 0.02
H ₃ BO ₃	0.50 ± 0.10	22 ± 4	24 ± 6	1.35 ± 0.05
CuBr	0.39 ± 0.09	21 ± 6	19 ± 4	1.34 ± 0.02
CuI	0.43 ± 0.09	23 ± 7	22 ± 5	1.35 ± 0.01
NaI	0.40 ± 0.10	24 ± 8	22 ± 6	1.34 ± 0.01
Ti(<i>i</i> OPr) ₄	0.46 ± 0.08	26 ± 8	23 ± 4	1.39 ± 0.04
Ph ₃ PO	0.50 ± 0.10	25 ± 9	23 ± 6	1.39 ± 0.02

^aConversion from MM to BB polymer was measured using SEC, comparing the relative areas of the MM and BB polymer peaks in the RI traces using a dn/dc value of 0.185. ^b N_{bb} was calculated using M_n values for the bottlebrush polymer peaks determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors using the equation $N_{bb,SEC} = (M_{n,SEC})/(\text{MM molar mass})$. ^cExpected N_{bb} values were calculated based on measured conversion values (p) based on the equation: $\text{expected } N_{bb,expected} = (p)([\text{MM}]/[\text{G3}])/(\text{monomer molar mass})$. ^d $\bar{D}$ values were determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors.

Table 3.S6. Conversion of **PS_{13K}** in DMF with additives targeting $N_{bb} = 25$

Solvent	Conversion ^a	$N_{bb,SEC}$ ^b	$N_{bb,expected}$ ^c	$\bar{D}$ ^d
No additive	0.24 ± 0.03	9.0 ± 0.5	6.0 ± 0.6	1.20 ± 0.01
HCl	0.33 ± 0.02	11 ± 1	8.0 ± 0.5	1.19 ± 0.01
CF ₃ COOH	0.39 ± 0.02	13 ± 1	10 ± 1	1.21 ± 0.01
H ₃ PO ₄	0.36 ± 0.03	12 ± 1	9.1 ± 0.7	1.22 ± 0.01
CH ₃ COOH	0.18 ± 0.02	8.0 ± 0.5	4.5 ± 0.5	1.18 ± 0.01
HCOOH	0.21 ± 0.02	8.7 ± 0.6	5.2 ± 0.5	1.20 ± 0.01
H ₃ BO ₃	0.22 ± 0.02	9.7 ± 0.5	5.4 ± 0.5	1.20 ± 0.01
CuBr	0.19 ± 0.03	9.7 ± 0.4	5.7 ± 0.4	1.22 ± 0.01
CuI	0.19 ± 0.02	9.0 ± 0.1	4.8 ± 0.8	1.20 ± 0.01
NaI	0.18 ± 0.02	7.7 ± 0.5	4.4 ± 0.4	1.16 ± 0.01
Ti(<i>i</i> OPr) ₄	0.21 ± 0.03	9.7 ± 0.3	5.3 ± 0.6	1.21 ± 0.01
Ph ₃ PO	0.19 ± 0.03	9.3 ± 0.4	4.9 ± 0.7	1.19 ± 0.01

^aConversion from MM to BB polymer was measured using SEC, comparing the relative areas of the MM and BB polymer peaks in the RI traces using a dn/dc value of 0.185. ^b N_{bb} was calculated using M_n values for the bottlebrush polymer peaks determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors using the equation $N_{bb,SEC} = (M_{n,SEC})/(\text{MM molar mass})$. ^cExpected N_{bb} values were calculated based on measured conversion values (p) based on the equation: expected $N_{bb,expected} = (p)([\text{MM}]/[\text{G3}])/(\text{monomer molar mass})$. ^d $\bar{D}$ values were determined by SEC in THF containing 0.025 wt% BHT at a rate of 1 mL/min at 30 °C using refractive index and light scattering detectors.

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Chapter 4: Conclusions and Future Work

Ring-opening metathesis polymerization (ROMP) is a powerful tool for the synthesis of complex polymer architectures. It is an advantageous synthetic method due to its controlled molecular weight increase over time, the multitude of monomer functionalities that can be used, and the stability of the catalyst, allowing for room temperature reactions that can be performed in air. While all of these traits make it an attractive polymerization technique for synthesizing complex architectures, bulky (macro)monomers can make polymerization to high conversions difficult.

Our research has been focused on the fundamentals of ROMP to improve the efficiency of the reaction when polymerizing generally difficult monomers. We are not the first group to do this, and others have made great strides in exploring the effects of temperature, catalysts, and chemical changes to the monomer. We have strived to determine how seemingly simple reaction variables can be changed to influence the rate of reaction and the conversion that can be reached in grafting-through ROMP. By testing solvents and small molecule additives, we found that not only can we improve propagation rates, but we can improve the conversion of bulky macromonomers at high degrees of polymerization.

Solvent choice can make or break a ROMP reaction. Many groups have published research on ROMP using tetrahydrofuran (THF) as the reaction solvent. While successful, high levels of solvent purification or an inert atmosphere is required to successfully perform ROMP with THF as the solvent. We found that even when highly purified, THF still doesn't lead to as fast propagation rates or as high conversion as some of the other solvents examined. Conversely, ethyl acetate (EtOAc), if used straight from the bottle can achieve extremely high propagation rates and high conversion with no purification required. Interestingly purifying EtOAc slows the

propagation rate. We associate this decrease in propagation rate to residual CH_3COOH in impure EtOAc, but that will be discussed more later. *N,N*-Dimethylformamide (DMF) was also highly influential on the propagation rate and achievable conversion for polystyrene macromonomers (MMs). However, unlike EtOAc, the rates of the ROMP reactions in DMF were low at rates almost 2-fold slower than the next slowest reaction. CH_2Cl_2 , toluene, and chloroform were also measured for reaction rate and conversion at high degrees of polymerization. Notably, CH_2Cl_2 had the second highest rate, following EtOAc, while toluene and chloroform were slightly slower, but still faster than DMF. If only inspecting the rates of polymerization, toluene can get “lost in the shuffle”, however, after thorough inspection of the rate of catalyst decomposition (also referred to as catalyst death or degradation) using UV-Vis, toluene becomes a much more interesting solvent choice.

To improve the ROMP of difficult (macro)monomers, improving the “livingness” of the polymerization is imperative. ROMP behaves like a living polymerization, but termination by catalyst decomposition leads to decreased conversion at high degrees of polymerization and when using bulky or difficult to polymerize monomers. This is why investigating catalyst decomposition in each of the solvents was incredibly relevant to our research. What we discovered was that DMF and THF had fast rates of decomposition, while toluene was by far the slowest to decompose. “Livingness” can be measured by dividing the rate of propagation by the rate of termination. Using our rates of propagation for each solvent and the rate of catalyst decomposition we could qualitatively determine the “livingness” of the ROMP reaction. While having a relatively slower rate of propagation, compared to reactions run in EtOAc and CH_2Cl_2 , the incredibly slow rate of catalyst decomposition in toluene made it the solvent that that allowed for the most living character in ROMP.

Revisiting the interesting results we observed with EtOAc purification and how that affects the propagation rate, as mentioned, the reactions performed in impure EtOAc were almost 2-fold faster than the reactions performed in the pure solvent. A common impurity in EtOAc is CH_3COOH and we hypothesize that the residual acid can protonate the labile pyridine ligands allowing monomer to add to the coordination site at a faster rate, thus increasing the rate of propagation in the solvent. We experimentally confirmed this result by adding 20 equiv of CH_3COOH to purified EtOAc and achieved a higher rate of propagation than was observed for the purified EtOAc.

From this result and some previous observations in our lab we wanted to experimentally test how small molecule additives would affect the conversion in ROMP at high degrees of polymerization. To do this we tested 12 different additives including acids, bases, and salts. We observed that acids were the most effective at improving conversion in the three tested solvents, EtOAc, toluene, and DMF. The most profound effect was observed in DMF where HCl , CF_3COOH , and H_3PO_4 all increased the conversion, with CF_3COOH increasing conversion over from around 47% to almost 80% for a polystyrene (PS) MM with a molecular weight of 3000 g/mol. We also tested a PS MM with a molecular weight of 13000 g/mol and saw a smaller but still promising increase in conversion. Using these results, we also tested a norbornene-functionalized peptide that was only soluble in DMF, not in EtOAc or toluene. This molecule would normally be very difficult to ROMP, and once tested, we observed only a 25% conversion in DMF at a target degree of polymerization of 25. We added 20 equiv of CF_3COOH and observed an almost 20% increase in conversion. While still lower than 50% total, this result does indicate that there are variables that we can manipulate to improve the ROMP of this incredibly difficult monomer.

What we have learned is that we can improve propagation rate and achievable conversion by simply choosing the correct solvent, purifying that solvent (or leaving it impure), or adding small

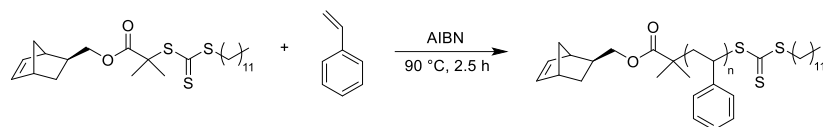
molecule additives. These results will hopefully greatly improve the ROMP research that is performed, not only in our research group, but those that do ROMP globally. We have strived to lay further foundations for this powerful polymerization technique that allows for controlled polymerizations and the formation of complex polymer architectures. Further experimentation is being performed in our research group related to the anchor group that connects the norbornene to the polymer side chain as well as in depth experimentation related to MM synthesis and purification. Future work related to ROMP fundamentals should include performing solvent and additive studies on other difficult to polymerize (macro)monomers. Also, using what we have learned to study the synthesis of other polymer architectures, such as tapered bottlebrush polymers, hourglass shaped materials, or “bowtie” shapes, among others. Lastly a systematic study determining the influence of atmosphere on ROMP is a critical missing piece of the “ROMP fundamentals” puzzle. While we have observed in our lab that performing ROMP in an inert atmosphere doesn’t make much of a difference in terms of propagation rate for reactions we performed, we have not performed a systematic study to determine if there is any influence on the reactions. This experiment would be crucial in understanding what we can achieve using this powerful polymerization technique.

Appendix C: Macromonomer purification

The grafting-through synthesis of bottlebrush polymers requires the synthesis of a homotelechelic macromonomer (MM), in which the end group can be further polymerized. When paired with ring-opening metathesis polymerization (ROMP), the homotelechelic end is often a norbornene derivative due to its high ring strain. In many cases the MM is synthesized using a reversible-deactivation radical polymerization (RDRP) method such as atom-transfer radical polymerization (ATRP), or reversible addition-fragmentation chain-transfer (RAFT) polymerization. These controlled polymerizations are ideal because they give MMs with controlled molecular weights and low molecular weight distributions.

In our lab, we have found that the purity of these materials is paramount to achieving a bottlebrush polymer with high conversion and low dispersity. With the recent acquisition of a Biotage Selekt flash chromatography system, we have found that not only can we remove any impurities from the synthesized MM (namely residual monomer), but we can also remove high molecular weight shoulders that can occur from coupling reactions, as well as separate different molecular weights of materials.

We synthesized a polystyrene (PS) MM (Scheme 5.1) using RAFT polymerization targeting a molecular weight of 3000 g/mol. We typically attempt to achieve a conversion of around 10% during the RAFT polymerization, as coupling reactions are common which can lead to high molecular weight shoulders in the MM synthesis, and even more noticeable shoulders in the bottlebrush polymer after ROMP has been completed. The PS MM resulting from the RAFT polymerization was characterized using size-exclusion chromatography (SEC) and the resulting trace is shown in Figure 5.1. This material was precipitated three times in methanol prior to characterization, yet there is still an obvious high molecular weight shoulder between 15-16 min.



Scheme 5.1. RAFT polymerization of PS MM.

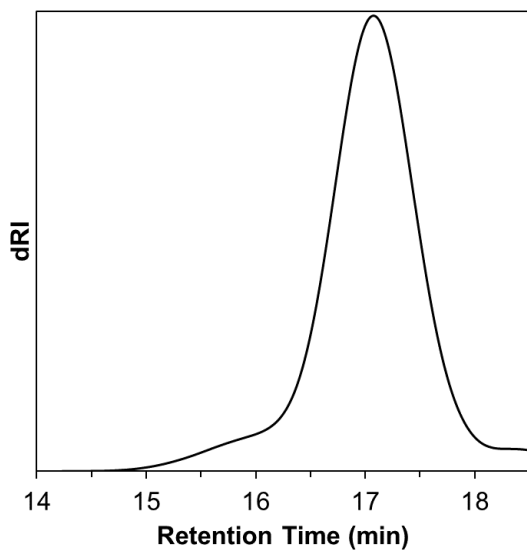


Figure 5.1. SEC trace of PS MM purified with three precipitations in methanol.

In an attempt to remove the high molecular weight shoulder, we performed flash chromatography using a Biotage Selekt instrument and eluted with a gradient of 100% hexanes to 50% CH_2Cl_2 in hexanes. The instrument shows visuals on the different fractions eluted based on the wavelength measured by a UV detector (wavelength range of 190 – 810 nm). Figure 5.2 shows the different fractions with the related sample rack image, using colors to match fractions separated by UV absorbance to the test tubes that the fractions eluted into.

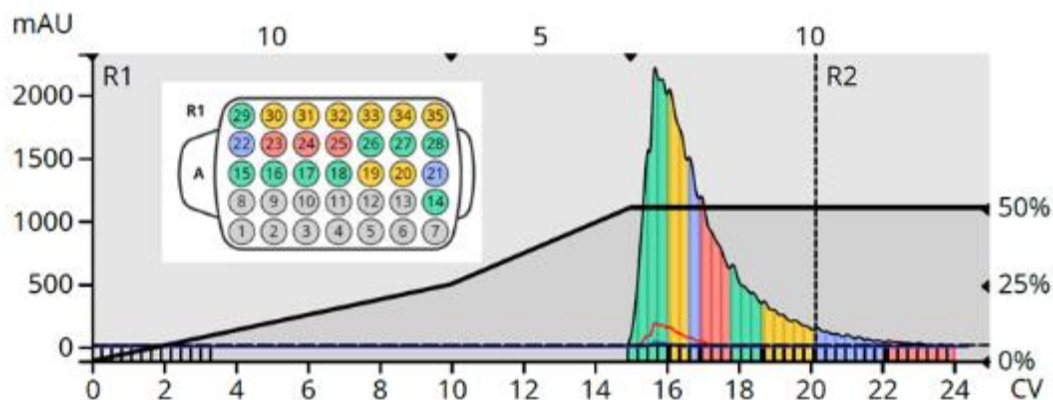


Figure 5.2. Image depicting the trace of the flash chromatography experiment. The thick black line shows the increase in the percentage of CH_2Cl_2 (in hexanes) in the solvent gradient. The inset is the image of the sample rack and the colors matching the chromatography trace.

After performing chromatography on the sample, the first fraction from each new color (fractions 15, 19, 21, 23, and 26) were evaporated using rotary evaporation and separately dissolved in small amounts of CH_2Cl_2 then precipitated in methanol. Each of these precipitated fractions was then characterized with SEC (Figure 5.3), and each molecular weight and dispersity value was obtained (Table 5.1).

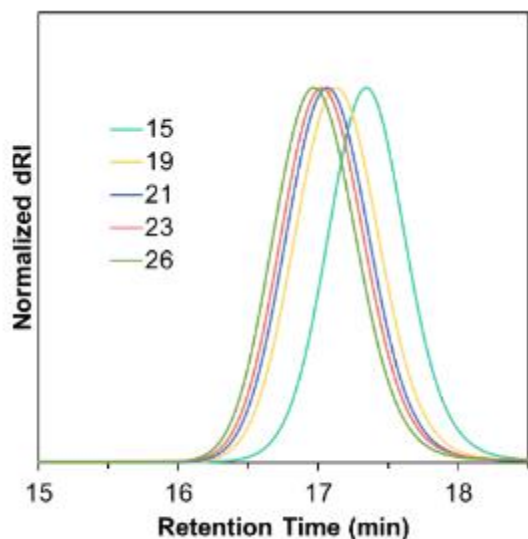


Figure 5.3. SEC traces of each fraction separated by flash chromatography. The traces were normalized by assigning the maximum peak height in each trace equal to 1.

Table 5.1. Molecular weight and dispersity of each fraction for purified MM

Fraction	$M_{n, SEC}$ (kg/mol) ^a	$\bar{D}$ ^a
15	2.6	1.09
19	3.2	1.10
21	3.6	1.09
23	3.7	1.08
26	3.9	1.09

^a M_n and $\bar{D}$ were calculated using SEC and a dn/dc of 0.185 mL/g

The SEC traces clearly show that the high molecular weight shoulder has been completely removed. We also achieved very low dispersities and increasingly higher molecular weights for each fraction. This indicates that we can potentially use this instrument isolate a specific molecular weight of MM. To further test that no high molecular weight shoulder is seen in the bottlebrush polymer, ROMP was performed on each of the fractions (Scheme 5.2), except for fraction 26 due to an inadequate amount of sample. Figure 5.4 shows the SEC traces from these ROMP reactions

and table 5.2 shows the conversion of MM to bottlebrush polymer (with a target degree of polymerization of 500), and the dispersity of each bottlebrush polymer.



Scheme 5.2. ROMP of PS bottlebrush polymer targeting a backbone degree of polymerization equal to 500.

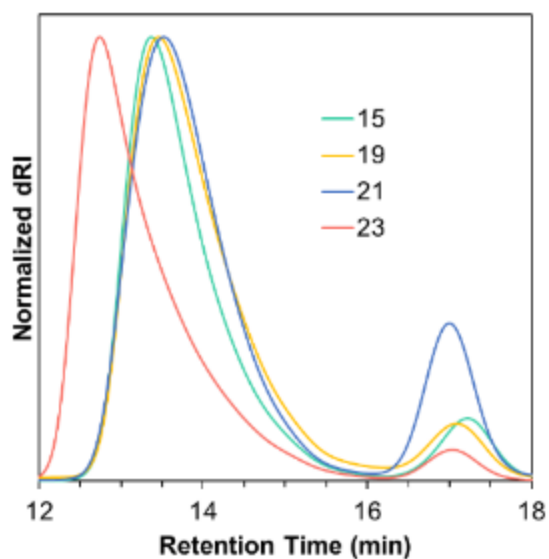


Figure 5.4. SEC traces of bottlebrush polymers following the ROMP of individual MM fractions.

Table 5.2. Molecular weight and dispersity of each fraction for purified MM

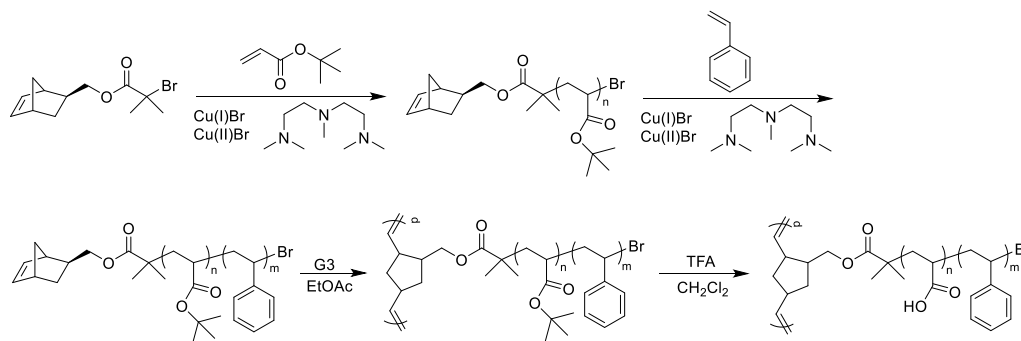
Fraction	Conversion ^a	$\bar{D}^b$
15	0.91	1.24
19	0.93	1.47
21	0.83	1.39
23	0.96	1.46

^aConversion from MM to bottlebrush polymer was measured using SEC and comparing the relative integrations of the MM and bottlebrush polymer peaks in the RI traces using a dn/dc value of 0.185. ^b $\bar{D}$ was calculated using SEC and a dn/dc of 0.185

This work is beneficial to not only our research group, but to others attempting to purify MMs for synthesis into bottlebrush polymers. It is also a potential method for isolating specific MM molecular weights. It has already become common practice in our lab to purify MMs using the Biotage and will hopefully improve future research in our lab and many others.

Appendix D: Gold nanoparticle synthesis using a cylindrical bottlebrush polymer as a template

To synthesize nanoparticles with unique shapes a polymer ‘nanoreactor’ template can be synthesized. To create novel shapes of nanoparticles, bottlebrush polymers with block copolymer pendant chains were prepared (Scheme 6.1). Lin and coworkers developed an initial strategy for preparing these bottlebrush polymer ‘nanoreactors’ using a cellulose backbone and grafting-from ATRP to create the sidechains.¹ With a hydrophilic core and a hydrophobic outer block, nanoparticles can grow within the core and hold their shape due to the hydrophobicity of the outer block. Gold nanoparticles (AuNPs) were chosen for these experiments, following the example from the Lin publication.



Scheme 6.1: Synthesis of block copolymer bottlebrush with subsequent ROMP and hydrolysis shown

The ‘normal’ preparation (following the procedure outline by Lin¹) for AuNPs involved dissolving 1 mg of the bottlebrush polymer in 1 mL of DMF then stirring for 1 h at room temperature. Borane tert-butyl amine (TBAB) was then added as a reducing agent and the solution was stirred for 2 h at 60 °C. The resulting solution was expected to be a dark red in color, but a clear solution with a

dark red precipitate was formed. The procedure was altered in various ways in an attempt to achieve this color and produce rod-shaped nanomaterials, as determined by transmission electron microscopy (TEM). A selection of procedures and their resulting solutions are shown in Figure 6.1. Figures 6.2 and 6.3 show TEM images of two of the solutions, one of which contains nanospheres of pure AuNPs and the other shows largely aggregated nanoparticles. Efforts continue to determine the proper conditions needed to grow the AuNPs within the bottlebrush polymer.

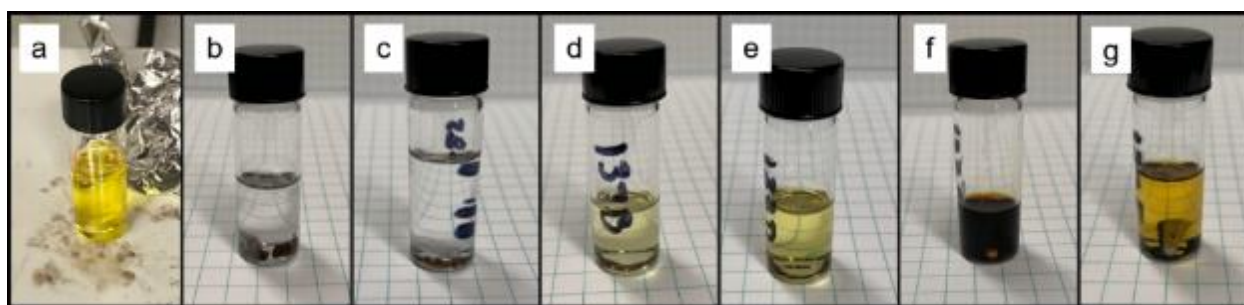


Figure 6.1: Photos of vials containing AuNPs in different testing conditions (A) $\text{HAuCl}_4 \cdot \text{H}_2\text{O}$ with DMF and BB, prior to stirring and addition of base, (B) ‘normal’ conditions, (C) 100 μl TFA added prior to heating, (D) 100 μl DIEA added prior to heating, (E) 10 μl DIEA added prior to heating, (F) DIEA added in place of TBAB, (G) 100 μl DIEA added after 1 h of heat.

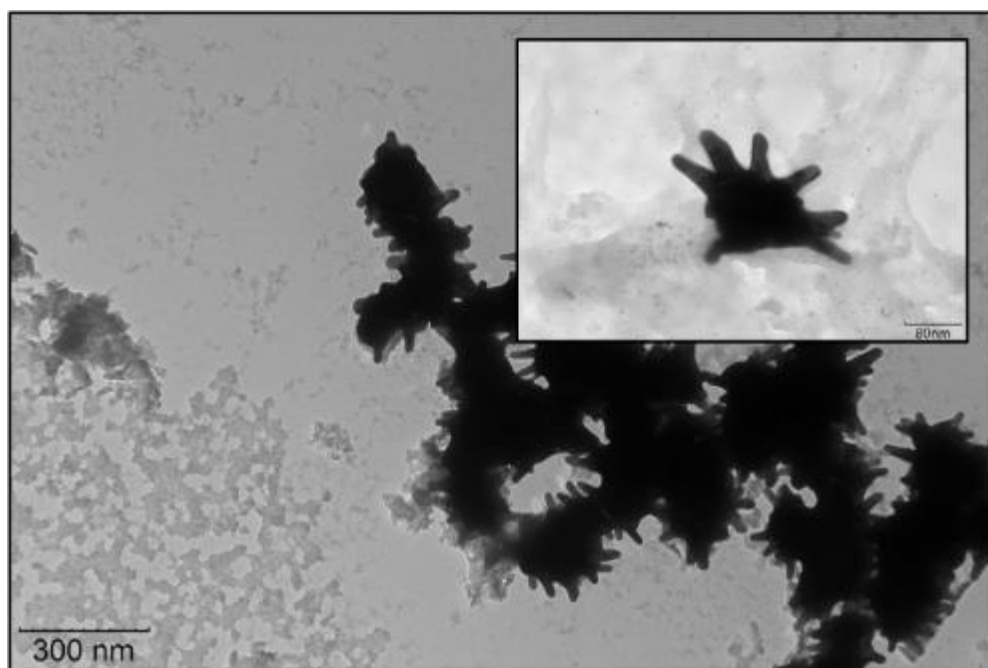


Figure 6.2: TEM of AuNPs under normal conditions

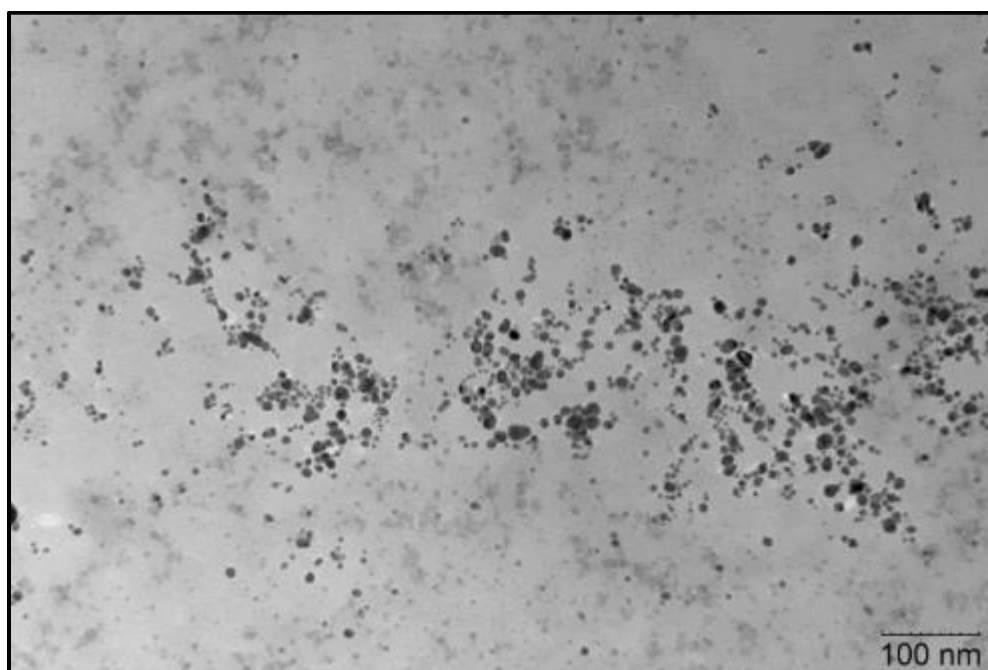


Figure 6.3: TEM of AuNPs using DIEA as the reducing agent

While we were unable to achieve the cylindrical nanoparticles that we had been aiming for, we learned a great deal about the synthetic process of the bottlebrush polymer, as well as the

components of the nanoparticle synthesis. Future work includes further optimization of the bottlebrush polymer synthesis and understanding the proper conditions for creating the nanomaterials and the conditions for TEM grid preparation. Once all synthetic procedures have been developed, creating bottlebrush polymers with unique architectures could lead to nanoparticles with structures never achieved before. Additionally, silver nanoparticles, or other interesting materials could be tested to create a wide library of nanoparticles with unique architectures.

References

- (1) Pang, X.; He, Y.; Jung, J.; Lin, Z. 1D Nanocrystals with Precisely Controlled Dimensions, Compositions, and Architectures. *Science* **2016**, 353, 1268–1272.