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Solid-Phase Synthesis of Polymers Using the Ring-Opening Metathesis Polymerization

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The ring-opening metathesis polymerization (ROMP) can generate polymers with diverse attributes. The characteristics and therefore function of a polymer can be tailored by altering its length and the substituents displayed on the backbone. Methods for the combinatorial synthesis of polymers using ROMP could accelerate the production of materials with novel properties. To this end, polymer scaffolds that can be readily modified in solution have been devised. The rapid synthesis of polymer libraries from these scaffolds is hindered by purification of the resulting functionalized polymers. Purification methods depend on the physical properties of the reactants used and the polymers that result. The complications of isolating diverse polymers render the solution-phase synthesis of libraries impractical. Solid-phase synthesis has been used to simplify purification steps en route to libraries of small molecules; reaction products remain immobilized, and soluble byproducts are washed away. The application of solid-phase methods to polymer chemistry, however, is more complex. Developing such a strategy involves attaching a soluble polymer to an insoluble one. The immobilized polymer can be derivatized and subsequently released from the resin. To implement such an approach is challenging: an immobilization method that is orthogonal to the polymer modification chemistry is required, as is a process for polymer release that affords minimal byproducts. Here, we report a general method for the solid-phase synthesis of polymers using ROMP that surmounts these barriers.

Immobilized polymers have been synthesized by ROMP from a surface-anchored monomer or catalyst. The kinetics of such polymerization reactions will be complex; consequently, the resulting polymers will be more heterogeneous than those generated in solution. We sought to preserve the high level of control over polymer structure that can be obtained with ROMP in solution. Under these conditions, ROMP effected using metal carbene initiators can be “living”, that is, termination or chain transfer processes do not compete with initiation or propagation. Thus, following monomer consumption, a metathesis-active metal carbene exists at the polymer terminus. The presence of this reactive moiety facilitates the introduction of unique functionality at the terminus or the synthesis of block copolymers by continued polymerization with a different monomer. When the rate of initiation significantly exceeds that of propagation, polymers of defined lengths and narrow polydispersity indices can be generated. Our goal, therefore, was to develop a solid-phase synthetic strategy that would retain these advantages.

Our synthetic strategy has three critical features. First, we wanted to immobilize a polymer that could be readily diversified. We had demonstrated that polymers bearing reactive N-hydroxysuccinimidyl (NHS) esters can be modified using an efficiency of polymer capture by presenting multiple copies of a group that can participate in the immobilization process of a variety of amines (Figure 1). Second, we sought to increase the immobilization efficiency using a short block containing functional groups that can be captured on a reactive resin. Third, we needed an immobilization strategy that allows facile purification of the cleaved polymers. We envisioned that a reversible Diels–Alder reaction could be used to append polymer to resin. The reactivity of NHS esters is orthogonal to that of typical diene/diendophile pairs. Moreover, we anticipated that the linkage between the resin and the polymers could be severed under mild conditions.

To test our synthetic strategy, we generated block copolymers using ROMP. One block was designed for immobilization, the other for presenting functionality of interest. We reacted a ruthenium carbene initiator with a surface-anchored monomer or catalyst. The kinetics of such polymerization reactions can be complex; consequently, the resulting polymers will be more heterogeneous than those generated in solution. We sought to preserve the high level of control over polymer structure that can be obtained with ROMP in solution. Under these conditions, ROMP effected using metal carbene initiators can be “living”, that is, termination or chain transfer processes do not compete with initiation or propagation. Thus, following monomer consumption, a metathesis-active metal carbene exists at the polymer terminus. The presence of this reactive moiety facilitates the introduction of unique functionality at the terminus or the synthesis of block copolymers by continued polymerization with a different monomer. When the rate of initiation significantly exceeds that of propagation, polymers of defined lengths and narrow polydispersity indices can be generated. Our goal, therefore, was to develop a solid-phase synthetic strategy that would retain these advantages.

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To test our synthetic strategy, we generated block copolymers using ROMP. One block was designed for immobilization, the other for presenting functionality of interest. We reacted a ruthenium carbene initiator with a monomer bearing an NHS ester and then with one bearing a maleimide dienophile. The length of the block of activated ester groups was varied by controlling the ratio of NHS ester-substituted monomer to initiator (M:I); 50:1 and 100:1 ratios were employed. When the initial monomer was consumed, a maleimide-substituted norbornene was added (10:1 M:I ratio) to afford polymers 3a,b. This order of monomer polymerization ensures that all living polymer chains possess the key functionality required for immobilization; any chains that have undergone premature termination will remain in solution. To test the Diels–Alder immobilization strategy, we exposed the polymers to Rink amide polystyrene resin substituted with furan groups (4) under microwave irradiation. Microwave irradiation can promote Diels–Alder reactions, and we found that it facilitated the linkage of the polymer to the resin. Indeed, this process resulted in highly efficient polymer immobilization. Over 90% of the polymer was captured. Attempts to immobilize polymers using a single endgroup were inefficient. Specifically, when polymers bearing a single end-group dienophile were exposed to resin, the immobilization yield was only 30%. The excellent yields we obtained for block copolymers attests to the advantages of their use.

With immobilized polymers in hand, we explored conditions for their functionalization. We conjugated two amines with different structures, a mannose derivative and 2,4-dinitrophenyl (DNP) lysine. The amide bond-forming reactions were conducted using a 10:1 ratio of amine to NHS ester in the presence of base. Spectroscopic analysis of the polymer products generated upon

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As discussed, the reactivity of the reaction partners is orthogonal to that of many other functional groups. In addition, the reversibility of the furan Diels—Alder reaction provides a means to release the polymer from the solid support and a handle for further functionalization. We postulate that the strained alkene that results can participate in additional ROMP reactions to build branched copolymers. Alternatively, other reactive species could be used to trap the dienophile (e.g., thioclates) to produce block copolymers that display a range of functionality. We anticipate that the flexibility of this strategy will markedly accelerate the synthesis of soluble polymers with novel functions.

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Supporting Information Available: Synthetic methods and experimental details for the development of the methodology. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(15) For details of analysis, see the Supporting Information.

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