Self-Complementary ABC Triblock Copolymers via Ring-Opening Metathesis Polymerization

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One of the unique features of DNA is its ability to associate with its complementary partner into a well-defined secondary structure.[1] This property, which is unrivalled by synthetic macromolecules, is derived from the placement of a well-defined sequence of hydrogen-bonding units along a regioregular polymer backbone.[1] While DNA has been used as a highly specific building block by a number of laboratories in materials science,[2] the challenges associated with its synthesis and stability have impeded more general use of this molecule. The construction of synthetic polymers which can mimic the specificity of this biopolymer, but can be readily accessed in large quantities, is thus an especially attractive goal.

One approach toward DNA-inspired synthetic polymers is through the use of living polymerization to generate block copolymers containing a well-defined sequence of molecular recognition blocks. While polymers containing molecular recognition units have been previously reported, these were typically generated using nonliving methods or by statistical attachment of these units to a polymer backbone.[3,4] We have recently initiated a research program to examine the synthesis of polymers containing nucleic acid bases or their analogues by living ring-opening metathesis polymerization (ROMP).[5] The ROMP reaction is a highly efficient method to generate polymers and copolymers in a living fashion.[6,7] We here report the synthesis of the first ABC triblock copolymers containing specific sequences of complementary molecular recognition blocks. Importantly, different sequences of these copolymers can be readily constructed by sequential polymerization of the three monomers in different order, and these polymers are nearly monodisperse. Finally, we report the first example of a dramatic change in polymer morphology which is brought about merely by changing the sequence of the molecular recognition blocks in this triblock copolymer.

The ease of synthesis of the building blocks for our polymers was of great importance in our approach. Therefore, monomers **2**−**4** were used. *exo*-7-Oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboximide, **2**[8] (thymine analogue, Chart 1), was readily synthesized by the Diels−Alder reaction of furan and maleimide. The second, hydrophobic monomer *exo*-*N*-butyl-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboximide, **3,**[9] was obtained by reacting **2** with 1-bromobutane and K_2CO_3 in DMF. Our third monomer **4** contains an acetylated diaminopyridine (DAP), which is complementary to the dicarboximide moiety in **2**, through a strong, three-point hydrogen-bonding interation.[10] Monomer **4** was synthesized as shown in Scheme 1. 2-Acetylamino-6-aminopyridine was prepared via the reaction of 2,6-diaminopyridine and acetyl chloride[11] and was then reacted with 6-bromohexanoyl chloride to give **5**. Monomer **4** was obtained in good yield and high purity from the reaction of **5** with monomer **2** and K_2CO_3 in DMF.

We have previously shown that the ROMP reaction of **2** is living and that well-defined polymers and copolymers can be readily generated.[5] The ROMP reaction of monomer **4** was examined in dichloromethane at room temperature using $Cl_2(PCy_3)_2Ru{=}CHPh$, **1**[7] (Scheme 1). Fast initiation was detected,[6,7] and ^1H NMR showed that the monomer consumption was 95% after 30 min. The reaction was quenched with ethyl vinyl ether and precipitated in hexanes. Gel permeation chromatography (GPC) analysis of polymer **6** showed a monomodal and narrow molecular weight distribution (polydispersity index, PDI = 1.11; see Table 1 of the Supporting Information), indicative of a living polymerization.[12] Polymer **6** has a 67:33 trans:cis ratio (^1H NMR)[6,7] and is soluble in common organic solvents but shows some turbidity in non-hydrogen-bonding solvents, such as dichloromethane, likely due to the self-association of the diacetamidopyridine units in the polymer backbone.[10] The UV−vis spectrum[13] of polymer **6** showed absorption peaks similar to those of monomer **4,** with a slight bathochromic shift (6 nm).

Having established that monomers **2** and **4** undergo well-behaved and controlled ROMP, we examined the generation of an ABC-triblock copolymer (Scheme 2) by the sequential addition of monomers **2** (block A), **3** (block B), and **4** (block C). Blocks A and C are complementary to each other through a three-point hydrogen-bonding interaction between their diacetamidopyridine and dicarboximide units (Scheme 2),[10] and block B is relatively hydrophobic, due to the alkyl chains in the repeat units.

The synthesis of the triblock copolymer started with the addition of the Grubbs catalyst **1** to a solution of **2** (10 equiv) in THF (5 mL). ^1H NMR showed that monomer consumption was complete after 5 min. Half of the polymerization solution was taken out, quenched with ethyl vinyl ether, precipitated into hexanes, and dried (polymer **7**). To the remaining half, monomer **3** (50 equiv in 2.5 mL of THF) was added.[9] ^1H NMR analysis showed complete conversion of **3** in 20 min. Again, half of the solution was syringed out, quenched, and precipitated into hexanes (diblock copolymer **8**). Finally, monomer **4** (10 equiv in 2.5 mL of CH_2Cl_2) was added to the polymerization solution. Monomer conversion was complete in 30 min (^1H NMR), after which the reaction mixture was quenched and precipitated into hexanes and the resulting ABC triblock copolymer **9** was collected and dried.

The synthesis and investigation of the rich morphological behavior of ABC triblock copolymers have been the subject of increasing recent interest.[14] However, because of monomer crossover problems, there are very few examples in the literature of the synthesis of triblock copolymers containing different block sequences, merely by changing the order of addition of monomers.[14] In addition, there are very few previously reported examples of the use of ROMP to access ABC triblock copolymers.[15] Because of the highly controlled nature of the ROMP reaction of **2** and **4**, we were thus

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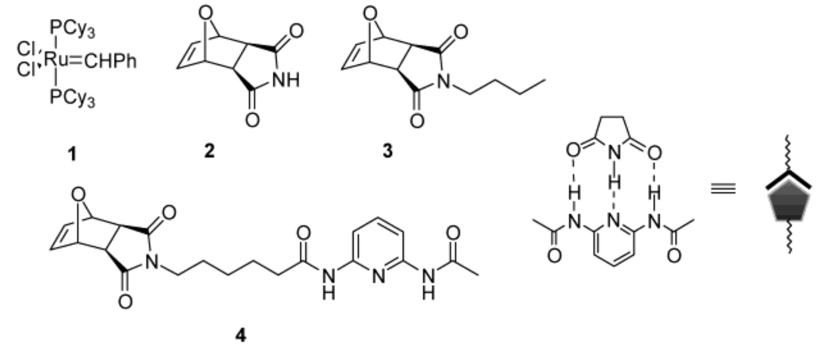
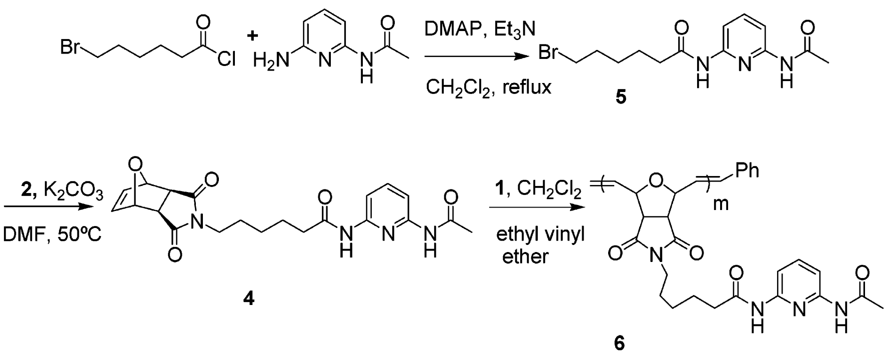
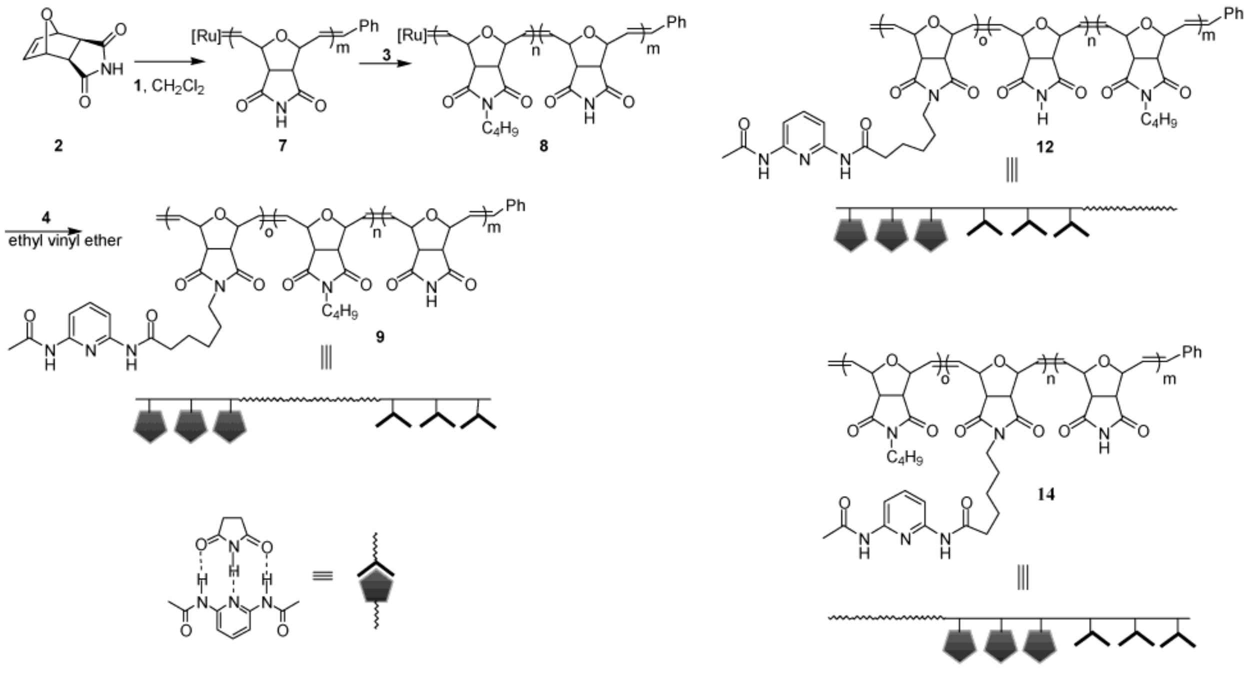
Chart 1



Scheme 1



Scheme 2



intrigued by the possibility of synthesizing different sequences of these triblock copolymers. Thus, we carried out the sequential addition of monomers **3**, **2**, and **4** to the Grubbs catalyst **1**, using a similar procedure to the above synthesis of triblock **9**. Again, conversion of all three monomers was quantitative (^{1}H NMR), and BAC triblock copolymer **12** was obtained in high yield (Scheme 2).

Gel permeation chromatography data of polymers **6**−**12** are shown in Figure 1. All GPC traces displayed monomodal molecular weight distributions with low polydispersity indexes (PDI = 1.08−1.14).[16] Figure 1 shows well-resolved GPC traces for both the ABC triblock copolymer **9** and the BAC triblock copolymer **12**. The absence of traces at higher retention time (lower molecular weight) indicates that there was essentially no chain termination during the sequential addition of the monomers to the polymerization reaction. A slight variation was detected in the observed molecular weights of triblock copolymers **9** and **12** (21.1 and 22.7 × 10^3), although they have the same calculated molecular weights. The different block sequence can account for

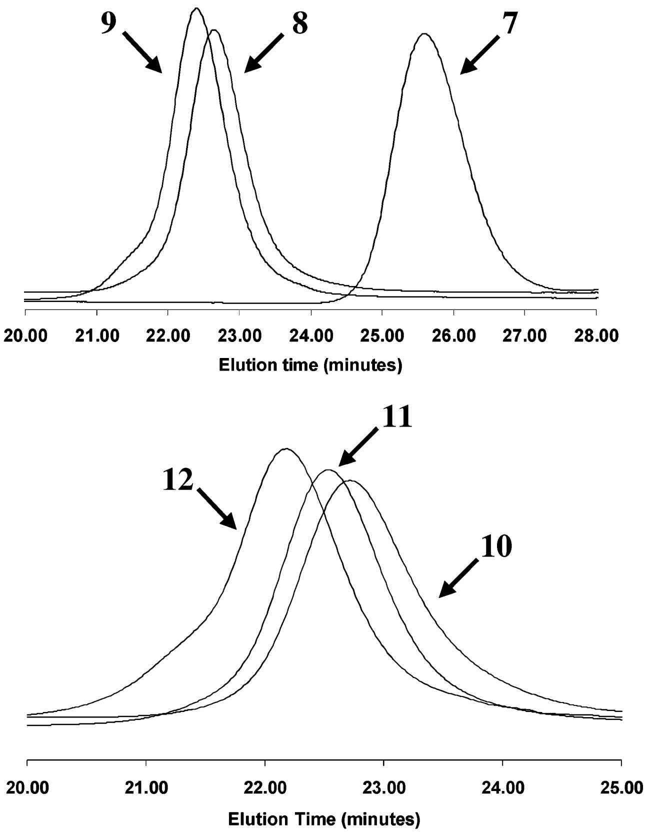


Figure 1. Gel permeation chromatography traces of the triblock copolymers **9** and **12** and their precursors.

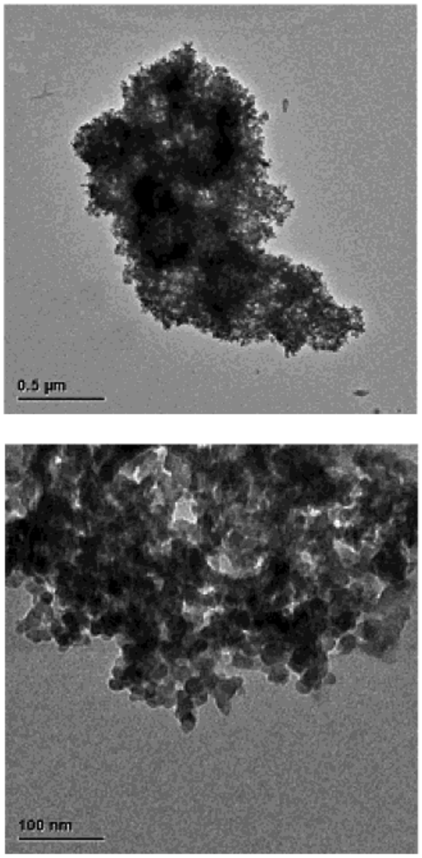


Figure 2. Transmission electron micrographs of copolymer **9** from a $CHCl_3$ solution

this variation, thus likely resulting in different hydrodynamic volumes for the ABC and BAC polymers. The compositions of the triblock copolymers were 10:50:10 for **9** (poly(**2**):poly(**3**):poly(**4**), respectively) and 50:10:10 for **12** (poly(**3**):poly(**2**):poly(**4**), respectively) as confirmed by both NMR and GPC data. In addition, copolymers **9** and **12** showed UV/vis spectra similar to that of the diaminopyridine monomer **4**, with a slight bathochromic shift similar to that of polymer **6**.

Finally, we attempted the synthesis of a triblock copolymer ACB, containing a third sequence of these blocks by the sequential addition of monomers **2**, **4**, and **3** to catalyst **1** (Scheme 2). However, after the complete consumption of monomer **2** and addition of monomer **4**, the solution became turbid, and the conversion of monomer **4** stopped at 70%. Thus, although homopolymers poly(**2**) and poly(**4**) are soluble in THF, their solubility behavior changes dramatically when they are covalently linked in copolymer **13**. This is likely due to the H-bond complementarity of the two molecular recognition units in the adjacent blocks of **13**. Despite the incomplete monomer conversion in the second block, monomer **3** was added to the solution. Interestingly, ^{1}H NMR showed that the polymerization had resumed, and monomer **3** was fully consumed in 30 min. ACB triblock copolymer **14**[17] was thus also obtained, albeit less efficiently than polymers **9** and **12**. Because of its limited solubility in THF, GPC data could not be obtained. However, ^{1}H NMR of **14** after its isolation showed the presence of the three monomeric units (**2**:**4**:**3**) in a 10:8:50 ratio.

The synthesis of different sequences of the triblock copolymers allowed us to address the question of the effect of molecular recognition block sequence on self-assembly properties. Copolymers **9** and **12** are composed of the same building blocks in different sequences. The complementary dicarboximide and diacetamidopyridine units in these copolymers can selectively associate via a hydrogen-bond-mediated interaction[18] (Chart 1). Examination of the self-assembly properties of **9** and **12** revealed dramatic differences. Dynamic light scattering studies (DLS) of a solution of ABC copolymer **9** in $CHCl_3$, taken at multiple angles, showed the presence of a bimodal distribution of small (20−40 nm) and large (200−700 nm) aggregates. A solution of **9** in $CHCl_3$ (1% w/v) was evaporated on a carbon-coated copper grid and examined by transmission electron microscopy (TEM). Large aggregates of small spherical micelles (approximately 20 nm) were observed, in accordance with the DLS results (Figure 2). On the other hand, no aggregates were detected when solutions of BAC copolymer **12** in $CHCl_3$ were examined by DLS and TEM. Thus, mere modification of the sequence of the blocks in copolymers **9** and **12** results in a dramatic change in polymer morphology.[19] While we are examining the mechanism of this self-assembly in more detail, this preliminary study shows the potential of the ROMP reaction with monomers such as **2**, **3**, and **4** to yield novel triblock copolymers with deliberate variation of sequence and self-assembly properties.

In summary, we have shown the synthesis of the first self-complementary triblock copolymers by controlled ring-opening metathesis polymerization. These copolymers possess ordered sequences of complementary molecular recognition blocks and can be synthesized efficiently with deliberate variation of this sequence. Changing the triblock copolymer sequence results in materials with dramatically different self-assembly properties. These novel systems introduce a new parameter to the study of the self-assembly of ABC triblock copolymers, namely molecular recognition and complementarity between the different blocks. Further studies on the interplay of molecular recognition and microphase separation in the self-assembly of these triblock copolymers are underway.

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Supporting Information Available: Full experimental details of the synthesis and characterization of monomers and polymers, ^{1}H NMR monitoring of the polymerization of monomer **4**, and GPC data table of the polymers. This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) We performed a preliminary investigation of the living nature of the ROMP of **4** by monitoring this polymerization by ^{1}H NMR (monomer:initiator 10:1). A linear dependence of the molecular weight of the polymer on the conversion of monomer **4** was observed (see Supporting Information).

(13) See Supporting Information.

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(16) See Table 1 in the Supporting Information.

(17) The ROMP of monomer **3** was complete in approximately 10 min, while the ROMP of monomer **4** took 30 min. This difference in reactivity is expected to result in a block copolymer, rather than a random copolymer in **14**, even though the last polymerization step was carried out in the presence of both monomers **3** and **4.** Indeed, after the polymerization was over, the ^{1}H NMR integration of unreacted monomer **4** (olefinic peaks relative to the aromatic portion of the diaminopyridine unit) did not change significantly, indicating that **4** did not react, while monomer **3** was being consumed in the polymerization. Thus, copolymer **14** is most likely a triblock copolymer, even though we cannot exclude the possibility of some randomness in its last block.

(18) The three blocks in these ABC polymers possess different solubility properties. Poly(**2**) is soluble in THF and insoluble in dichloromethane, poly(**4**) (or **6**) is soluble in THF and gives slightly turbid solutions in dichloromethane, and poly(**3**) is soluble in both THF and dichloromethane.

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