Knotted Polymers

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A Trefoil Knotted Polymer Produced through Ring Expansion[**]

Peng-Fei Cao, Joey Mangadlao, and Rigoberto Advincula[*]

Abstract: *A synthetic strategy is reported for the production of a trefoil knotted polymer from a copper(I)-templated helical knot precursor through ring expansion. The expected changes in the properties of the knotted polymer compared to a linear analogue, for example, reduced hydrodynamic radius and lower intrinsic viscosity, together with an atomic force microscopy (AFM) image of individual molecular knots, confirmed the formation of the resulting trefoil knotted polymer. The strategies employed here could be utilized to enrich the variety of available polymers with new architectures.*

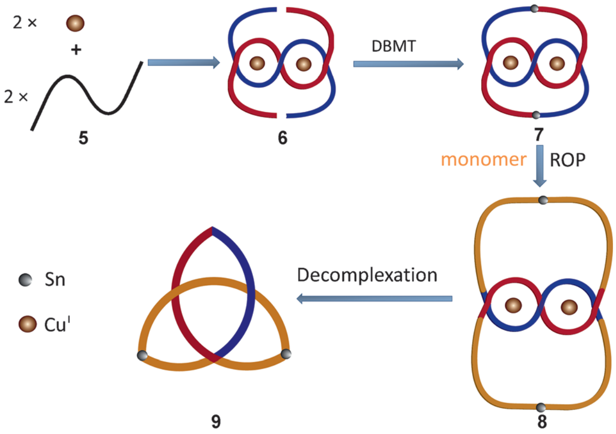
Knots, which initially gained interest in the fields of art and mathematics because of their attractive and fascinating structures,[1] have been found in DNA[2] and in proteins.[3] In the last decades, chemists have been attracted by the synthetic challenges they pose and their inherent structural beauty, as well the potential for special properties arising from their compact twisted forms, reduced entanglement, and topological chirality.[4] Thanks to the development of coordination chemistry, supramolecular chemistry, and new methods of covalent bond formation, successful syntheses of molecular trefoil knots[5] and even pentafoil knots[6] have been achieved. Recently, Sanders and co-workers reported the near quantitative self-assembly of trefoil knots or meso figure-of-eight knots from naphthalenediimide-based ligands in aqueous solution with the hydrophobic effect as the driving force.[5l,7] However, the synthesis of molecular knots with large molecular weights, such as knotted polymers, remains elusive, although theoretical calculations indicate that their unique topologies would have a significant effect on the physical properties of the polymers.[8]

Polymers with topologically interesting structures, such as cyclic polymers[9] and catenated polymers,[10] have been synthesized by different strategies. Their distinct properties, such as reduced hydrodynamic radii and lower viscosity compared to their linear analogues, have been well studied. However, mathematically speaking, none of these polymers are genuine knots since a cyclic polymer is a trivial knot (unknot) and a catenated polymer is a Hopf link (a type of two-component link).[4a] Truly knotted polymers represent a challenging chemical target for which no rational synthesis has been reported to date, although their formation has been claimed in polymer systems, often through creativity and luck during end-to-end ring closure of a linear chain precursor.[11] Herein, a rational access to knotted polymers is reported, which combines a highly successful templated synthesis with ring expansion.

To date, the fabrication of Cu^{I}-templated knot precursors by Sauvage et al. remains one of the most successful examples of the synthesis of molecular knots (especially for the trefoil knot, the simplest and yet perhaps most beautiful one). This method involves the quantitative formation of a helical knot precursor, readily modifiable terminal groups, and a facile decomplexation method.[5a–c] Moreover, progress in polymer science has produced the ring-expansion technique for the fabrication of cyclic polymers, and this technique allows concentrated synthesis and facile product isolation.[9a,b] Through utilizing ring expansion, Kricheldorf et al. successfully prepared cyclic polymers by inserting lactones or lactides into the Sn–O bonds of cyclic dibutyltin alkylene oxides, where the macrocycles were prepared under kinetic control with no side reactions observed.[12]

Based on the successes in these fields, we designed a novel synthetic route (Scheme 1) to address the challenge of trefoil knotted polymer synthesis: ring closing of the Cu^{I}-templated helical knot precursor affords a trefoil knot initiator, into which monomer units are inserted to generate the polymer chains, and a final decomplexation results in a trefoil knotted polymer. To our knowledge, this is the first report of a rational synthesis of knotted polymers. This method could potentially afford a new polymer family with unique properties and hence novel polymeric materials.[8a,11]

The rational design of a Cu^{I}-templated trefoil precursor not only concerns the yield of desired complex formation, but



Scheme 1. Synthetic scheme for the production of trefoil knotted polymers through templating and ring expansion. DBMT = dibutyldimethoxy-tin), ROP = ring-opening polymerization.

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[*] P.-F. Cao, J. Mangadlao, Prof. R. Advincula
Department of Macromolecular Science and Engineering
Case Western Reserve University
Cleveland, Ohio 44106 (USA)
E-mail: rca41@case.edu

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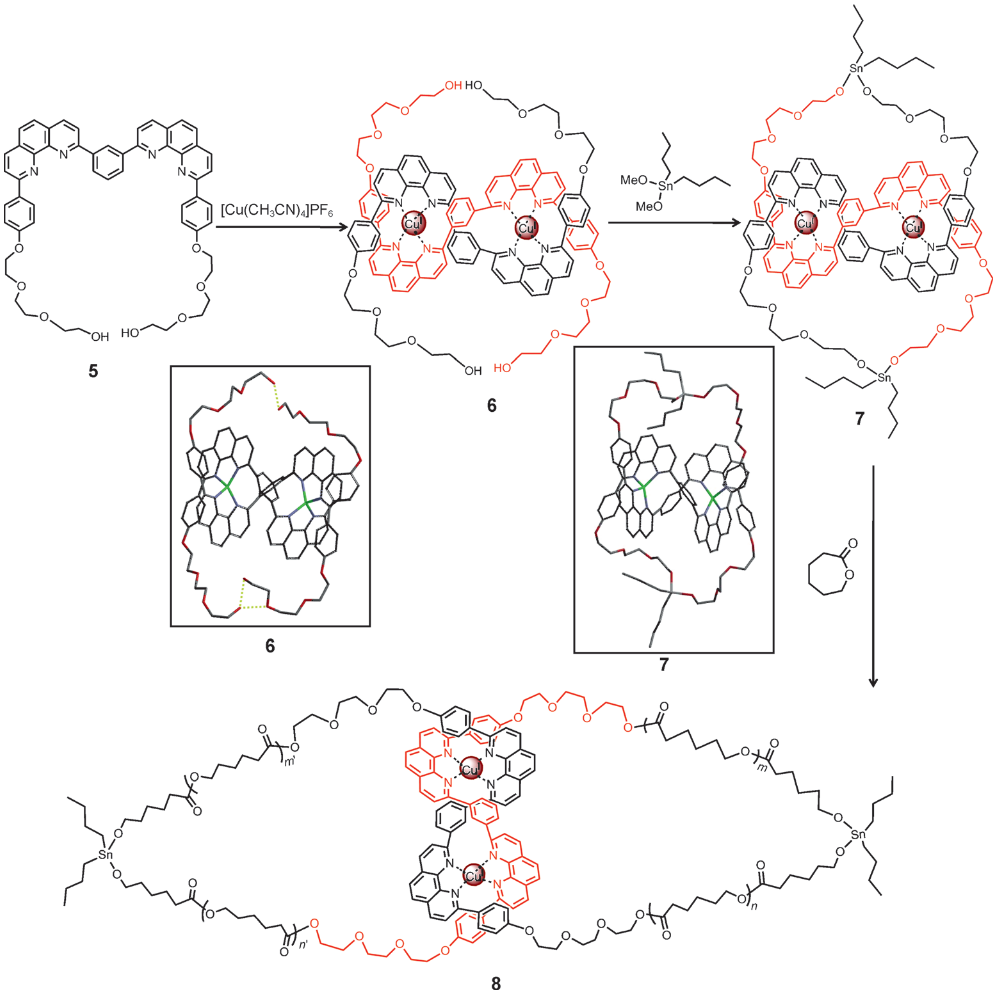
also needs to favor the bond formation in the next step. Compound **5** was synthesized accordingly with an overall yield of 32% (Scheme S1 in the Supporting Information). The helical knot precursor **6** was obtained quantitatively by slowly transferring the acetonitrile (CH$_3$CN) solution of Cu(CH$_3$N)$_4$PF$_6$ to the dichloromethane solution of **5**. The formation of the complex was confirmed by UV/Vis spectrometry (see the Supporting Information), which showed absorption peaks in the visible region at 427 nm and 515 nm, which correspond to the metal-to-ligand transition (MLCT) and the ligand-to-metal transition (LMCT), respectively.[13] The significant upfield shifts in the ^{1}H NMR spectrum of the resulting knot precursor complex **6** compared to that of **5** (Figure S6 in the Supporting Information) can also ascribed to the quantitative formation of the copper(I)–phenanthroline complex and secondary interactions.[4c]



Scheme 2. Synthesis of Cu^{I}-templated helical knot precursor **6**, trefoil knot initiator **7**, and Cu^{I}-templated trefoil knotted polymer **8**. The insets show compounds **6** and **7** modeled by using semi-empirical PM3 (tm).

Preorganized stable conformation with two reactive groups positioned close together will greatly favor the formation of the desired product, and utilizing secondary interactions is one important approach to achieving this target.[4c] In the Cu^{I}-templated knot complex, the favorable conformation, where the two reactive hydroxyl groups are positioned close together, was not only supported by previous reports[14] but also confirmed by theoretical calculations (the calculated structure of **6** (Scheme 2, inset) shows a very stable conformation with a heat of formation value $H_f = -733\ \mathrm{kJ\,mol^{-1}}$). The aromatic CH···O interactions and gauche effect play an important role in this favorable conformation.[4c] Cu^{I}-templated trefoil knot initiator **7** was synthesized by refluxing the chloroform solution of **6** with dibutyldimethoxyl tin (DBMT). UV/Vis analysis indicated the presence of the Cu^{I}–phenanthroline complex, whereas the NMR spectrum and X-ray photoelectron spectroscopy (XPS) analysis suggested the insertion of Sn (see the Supporting Information). According to theoretical calculations, the formation energy of Cu^{I}-templated trefoil knot initiator **7** ($H_f = -867\ \mathrm{kJ\,mol^{-1}}$) is even lower than that of complex **6** ($H_f = -733\ \mathrm{kJ\,mol^{-1}}$). As shown in Scheme 2, the optimized conformation of compound **7** is a bridged structure with twisting phenanthroline moieties and a tetrahedral metal–ligand conformation.

By adopting a similar method to that reported by Kricheldorf et al.,[12] caprolactone was utilized as the monomer to afford Cu^{I}-templated knot polymer **8** through kinetically controlled ring expansion (Scheme 1 and Scheme 2). After 18 h of bulk polymerization, crude product was obtained with monomer conversion calculated to be 75% (see the Supporting information). The ^{1}H NMR spectrum of product purified by dialysis showed relatively strong typical poly(ε-caprolactone) resonances at 4.05 ppm and 2.10 ppm, which suggested successful coordination–insertion polymerization.[15] Moreover, the presence of absorption peaks at 427 nm and 515 nm in the UV/Vis spectrum of **8** indicate stability of the Cu^{I}–phenanthroline complex during the polymerization process (see the Supporting Information). The ^{1}H NMR spectrum of the Cu^{I}-templated trefoil knotted polymer also confirmed the stability of the complex (see the Supporting Information). These two factors are important in maintaining the trefoil knot structure during the polymerization process.

To obtain the genuine trefoil knotted polymer without copper, decomplexation was performed by adding 10 equivalents of KCN to the polymer solution stirring the mixture overnight.[10d] An obvious color change (from reddish to yellow) and the disappearance of the absorption peaks in the visible region suggested successful decomplexation (see the Supporting Information). Additional evidence was provided by downfield shifts of the peaks corresponding to the aromatic segment in the ^{1}H NMR spectrum of trefoil knotted polymer (Figure 1 A and the Supporting Information). After decomplexation, the GPC curve of the trefoil knotted polymer showed a broader peak and smaller hydrodynamic diameter compared to that of the Cu^I-templated trefoil knotted polymer (see the Supporting Information). This is perhaps due to the relatively high conformational freedom and more compact structure after removing the Cu^I template. It is worth noting that each trefoil knotted polymer had four poly(ε-caprolactone) chains derived from two Sn atoms. Here, the average degree of polymerization (DP_n) was defined as the sum of two poly(ε-caprolactone) chains derived from the same Sn atom ($m+n$; Figure 1 A). From the integrations of the methylene groups next to the -OOC (v; Figure 1 A) in the polymer chains and the methylene groups in the triethylene glycol segments (l + q or m), the average degree of polymerization ($m+n$) was calculated to be 83, which suggested 166 monomers per trefoil knotted polymer. Hence, the absolute molecular weight ($M_{n(absolute)}$) of the trefoil knotted polymer was calculated to be 21.3 kDa. Another interesting observation from the ^{1}H NMR spectrum of the trefoil knotted polymer (**9**) is its well-resolved features compared to phenanthroline-based trefoil knotted molecules with low molecular weight.[5m] This could be due to the more flexible structure of the trefoil knotted polymer and hence faster intramolecular reptation process.

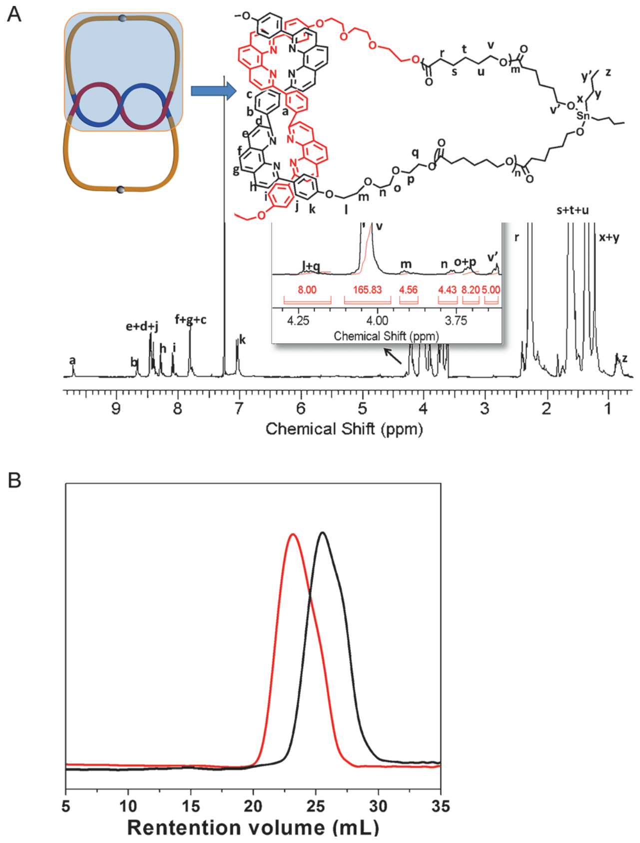


Figure 1. A) ^{1}H NMR spectrum for trefoil knotted polymer **9**. The chemical structure of **9** is not an actual representation because the two bis-phenanthroline groups are probably far away from each other. B) Comparative gel permeation chromatography (GPC) curves for the trefoil knotted polymer and linear polymer with the same absolute molecular weight. Linear polymer(red curve): $M_{n(apparent)} = 15.5$ kDa, PDI = 1.795, IV = 0.2678 dL g^{-1}; trefoil knotted polymer (black curve)0: $M_{n(apparent)} = 6.99$ kDa, PDI = 1.966, IV = 0.1025 dL g^{-1}.

To confirm the structure of the trefoil knotted polymer from its predicted properties, linear poly(ε-caprolactone) with the same $M_{n(absolute)}$ was synthesized as a control. As expected, the trefoil knotted polymer showed a much smaller hydrodynamic diameter than its linear analogue as a result of its compact structure (Figure 1 B).[11c] Moreover, less inter- and intramolecular interaction lead to a much lower intrinsic viscosity (IV): 0.1025 dL g^{-1} for the trefoil knotted polymer and 0.2678 dL g^{-1} for the linear polymer analogue.[8a]

To provide direct evidence of the structure, atomic force microscopy (AFM) was also employed to capture an image of the trefoil knotted polymer. The topography images of the target molecules in a large area did not provide the necessary structural information and only showed individual spots. This is perhaps due to the flexible polymer chains and the compact polymer structures. However, the phase image afforded more useful structural information (Figure 2 A). The broad size distribution is attributed to the high polydispersity index of the poly(ε-capralactone). The AFM image of the Cu^I-templated trefoil knotted polymer (**8**) exhibited similar architecture to a catenated polymer owing to the presence of the template (see the Supporting Information).[10e] It is worth noting that after decomplexation, the polymer (**9**) appears to adapt a topological C_3 symmetry rather than the previous C_2 symmetry shown by **8**, in spite of the fact that absolute C_3 symmetry is impossible owing to the presence of phenanthroline groups. This result suggests an increase in the degree of freedom, which allows the polymer chains to relax and transform to give a topological C_3 symmetry. This transformation further indicates successful decomplexation to afford a genuine trefoil knotted polymer. Among many topography images of the individual polymers, only very few of these exhibited an ideal trefoil knot (Figure 2 B), perhaps owing to the relatively large sizes. Basic analysis of the obtained polymers indicated the successful synthesis of trefoil knotted polymers. More studies on the properties derived from this unique structure are still underway.

In conclusion, although the formation of knotted polymers has previously been claimed, this work represents the first rational synthesis of a knotted polymer. The trefoil knotted polymer was synthesized (yield of isolated product: 65 %) through ring expansion of the trefoil knot initiator, which was formed through a ring-closing reaction of the Cu^I-templated helical knot precursor. Rational design of the helical knot ligand (**5**) not only provided quantitative formation of trefoil knot complex but also favored the ring-closing reaction of the trefoil knot initiator. Through insertion of the monomer, the trefoil knotted initiator grows into the Cu^I-templated trefoil knotted polymer, from which decom-

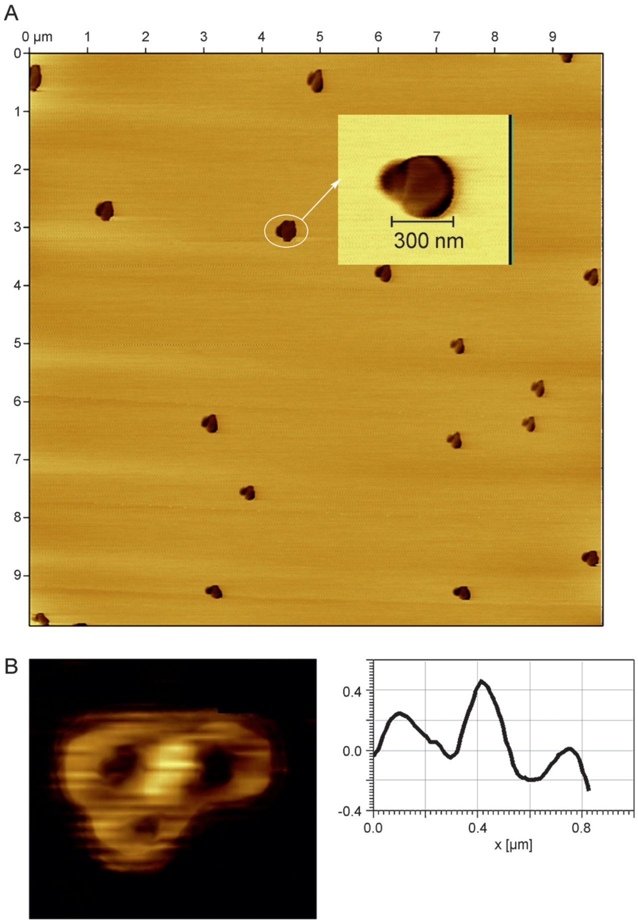


Figure 2. A) AFM image of the trefoil knotted polymer on mica substrate. Inset: Enlarged phase image of a trefoil knotted polymer. B) Topography image of one of the largest trefoil knotted polymers and its height profile.

plexation renders the genuine trefoil knotted polymer. The trefoil knotted polymer showed the expected property changes compared to its linear analogue, namely reduced hydrodynamic radius and lower intrinsic viscosity. Moreover, AFM images provide direct evidence for the structure of the trefoil knotted polymer. We expect that the strategies employed herein will be useful for the synthesis of polymers with various types of architectures, and the special properties of the trefoil knotted polymer may expand the potential applications of polymer materials. Moreover, new opportunities have been provided to study the effects of topology on polymer properties.[8a]

Keywords: copper(I) · knotted polymers · ring expansion · supramolecular chemistry · templated complexes

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