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Synthesis of a Molecular Charm Bracelet via Click Cyclization and Olefin Metathesis Clipping

Paul G. Clark,[†] Erin N. Guidry,[†] Wing Yan Chan,[†] Wayne E. Steinmetz,[‡] and Robert H. Grubbs*[,†]

The Arnold and Mabel Beckman Laboratory of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, and Chemistry Department, Pomona College, 645 North College Avenue, Claremont, California 91711

Received October 22, 2009; E-mail: rhg@caltech.edu

Abstract: We describe the synthesis of a polycatenated cyclic polymer, a structure that resembles a molecular charm bracelet. Ruthenium-catalyzed ring-opening metathesis polymerization of an amino-containing cyclic olefin monomer in the presence of a chain transfer agent generated an α,ω-diazide functionalized polyamine. Cyclization of the resulting linear polyamine using pseudo-high-dilution copper-catalyzed click cyclization produced a cyclic polymer in 19% yield. The click reaction was then further employed to remove linear contaminants from the cyclic polymer using azide- and alkyne-functionalized scavenging resins, and the purified cyclic polymer product was characterized by gel permeation chromatography, ^{1}H NMR spectroscopy, and IR spectroscopy. Polymer hydrogenation and conversion to the corresponding polyammonium species enabled coordination and interlocking of diolefin polyether fragments around the cyclic polymer backbone using ruthenium-catalyzed ring-closing olefin metathesis to afford a molecular charm bracelet structure. This charm bracelet complex was characterized by ^{1}H NMR spectroscopy, and the catenated nature of the small rings was confirmed using two-dimensional diffusion-ordered NMR spectroscopy.

Introduction

Novel polymer architectures have attracted significant interest from scientists in an unceasing quest to tailor the structural attributes of a material for specific applications. Cyclic polymers (CPs) have garnered particular attention due to a number of attractive traits, including desirable physical properties, increased functional group density, and smaller hydrodynamic radii relative to linear polymer analogues.[1−7] Recent work by Fréchet, Szoka, and co-workers[8] has also indicated that CPs have potential biological applications, displaying better circulation half-lives than their linear counterparts and thus making them attractive candidates as possible drug carriers.

In addition to their intriguing properties, CPs also present a unique challenge to synthetic chemists, as there are few procedures that favor the formation of these "endless" polymers in high purity.[9−12] Traditionally, CPs have been synthesized via high-dilution cyclization of dianionic linear polymers and a two-site coupling agent. However, due to issues associated with polymer purity using this technique, modern efforts have focused on the development of a number of new routes to cyclic architectures, including macrocyclization of α,ω-heterotelechelic linear polymers (Figure 1)[13−15] or olefin-terminated polymers,[16,17] cyclization of electrostatically templated telechelic polymers,[18−25] and ring-expansion reactions of cyclic species, including lac-

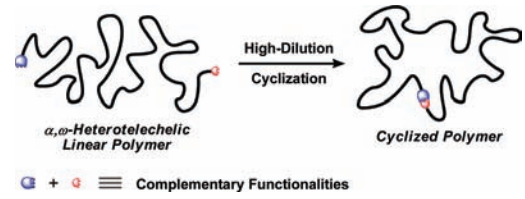

Figure 1. Macrocyclization of an α,ω-heterotelechelic polymer under high-dilution conditions.

[†] California Institute of Technology.
[‡] Chemistry Department, Pomona College.

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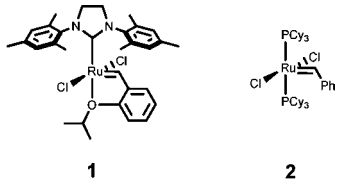

Figure 2. Ruthenium olefin metathesis catalysts **1** and **2**.

tides[26] and olefin monomers.[27−30] Macrocyclization reactions of α,ω-heterotelechelic polymers often employ high-fidelity, high-conversion "click" reactions,[31−36] such as the Huisgen 1,3-dipolar cycloaddition between an alkyne and an azide, but necessitate high-dilution or pseudo-high-dilution conditions to favor cycles rather than oligomers. In contrast, reactions such as ring-expansion metathesis polymerization[27−30] (REMP), catalyzed by cyclic ruthenium alkylidene species, overcome this limitation and enable rapid synthesis of multigram quantities of pure cyclic polymer. In addition to the cyclic ruthenium catalysts used in REMP, a number of other functional-group-tolerant ruthenium alkylidene catalysts, for example, catalysts **1** and **2** (Figure 2), have seen broad application in polymer synthesis.[37−40]

Another intriguing and challenging area of research is the synthesis of mechanically interlocked molecules.[41−44] Such structures contain two or more molecules that cannot be separated without covalent bond cleavage but that do not contain any covalent bonds between them. Utilizing a combination of

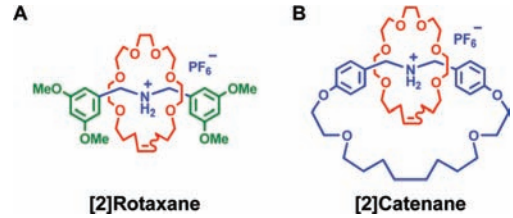

Figure 3. Mechanically interlocked structures synthesized by olefin metathesis. A rodlike structure, with bulky terminal "stopper" units, encircled by a ring (A) is termed a [2]rotaxane, while two interlocked rings (B) are designated a [2]catenane.

supramolecular chemistry[45−47] (often involving hydrogen-bonding interactions between crown ether-type species and secondary ammonium ions) to template the formation of preorganized structures and dynamic covalent chemistry[48−54] to induce interlocking of the resulting complex, high-yielding syntheses of rotaxanes[55−58] and catenanes[59−65] (Figure 3), as well as a variety of other, more complex architectures,[66−72] have been realized. One particularly effective strategy to synthesize mechanically interlocked molecules employs the dynamic, ruthenium-catalyzed ring-closing metathesis (RCM) reaction, whereby a diolefin polyether fragment is subjected to RCM conditions and "clipped" around a disubstituted ammonium ion.[56,63,69]

Due to the complexity of mechanically linked structures, confirmation of the interlocked nature of the products can often prove difficult via standard characterization techniques. However, the use of two-dimensional diffusion-ordered NMR

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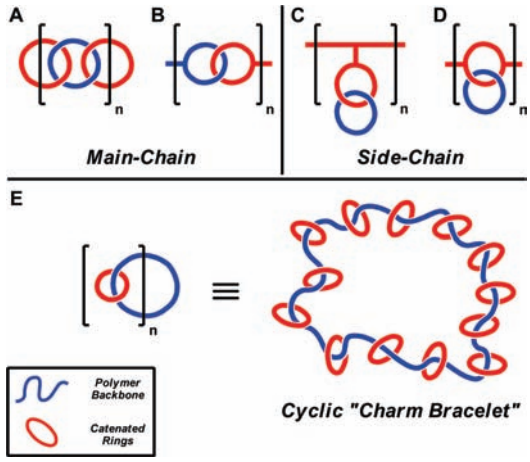

Figure 4. Graphic representation of various polycatenane structures, including main-chain polycatenanes (A and B), side-chain polycatenanes (C and D), and the targeted cyclic interlocked charm bracelet polycatenane (E).

spectroscopy[73−79] (2D-DOSY) facilitates the analysis of distinct complexes in solution on the basis of their unique diffusion rate. Using this technique, small molecules with fast diffusion rates that are intimately associated (either covalently or mechanically) with a slowly diffusing macromolecule will diffuse at the speed of the larger structure to which they are appended. The application of this technique to linear polymers with threaded rings has been demonstrated previously.[80]

The inclusion of interlocked moieties as a part of a larger macromolecular structure[43,81] has been shown to have an impact on both the solution state and bulk properties[82−85] of the resulting material, and to this end, researchers have synthesized a number of polyrotaxanes,[82,83] as well as polycatenane species (Figure 4A−D).[72,84,85] The polycatenane charm bracelet structure (Figure 4E), however, has been particularly elusive.[9−11,45,70] Recently, a few reports have emerged describing smaller cyclic complexes containing threaded moieties,[86−91] and Harada has reported the cyclization of a threaded, capped polyrotaxane.[92]

In complement to these reports, we wanted to explore a "clipping" approach to such a polycatenated molecular charm bracelet. We synthesized a CP architecture via a pseudo-high-dilution, two-component click macrocyclization and subsequently converted this species to the polyammonium analogue. We were then able to clip diolefin crown ether-type rings around the ammonium sites of the polymer scaffold using RCM. Confirmation of the interlocked nature of the charm bracelet product was achieved via 2D-DOSY NMR.

Results and Discussion

Monomer Design and Synthesis. We believed the nine-membered cyclic boc-amine compound **3** (Scheme 1)[93] possessed sufficient ring strain energy to be a suitable metathesis polymerization monomer and would afford the desired polyammonium polymer upon removal of the Boc-protecting group.

Synthesis of **3** was readily achieved in eight steps and 31% overall yield. *cis*-1,5-Cyclooctadiene (**4**) was treated with *m*-3-chloroperoxybenzoic acid to afford the monoepoxidized cyclooctene species **5**. Reduction of **5** with lithium aluminum hydride opened the epoxide to the corresponding alcohol **6**, which was subjected to Swern oxidation conditions, giving ketone **7**. Refluxing **7** in the presence of hydroxylamine hydrochloride generated oxime **8**, which was transiently converted to the tosyl oxime intermediate prior to undergoing a base-promoted Beckmann rearrangement that produced a regioisomeric mixture of lactams **9a** and **9b**. By ^{1}H NMR spectroscopic analysis, isomer **9b** appeared to dominate the product mixture, which is not entirely surprising given that, in **8**, the ratio of oxime *anti* to H_a versus *syn* to H_a was approximately 6:1, respectively. The mixture of lactams was reduced to the cyclic amine by lithium aluminum hydride, and the amine was subsequently Boc-protected to yield the desired unsaturated nine-membered cyclic Boc-amine monomer **3**. Interestingly, despite the mixture of starting materials, only the nonsymmetric regioisomer of **3** was isolated.

Polymer Synthesis and Characterization. Unfortunately, initial efforts to utilize REMP as the polymerization method proved challenging with monomer **3**. Thus, we turned our attention to ring-opening metathesis polymerization (ROMP) in the presence of a chain-transfer agent (CTA),[94−98] as a

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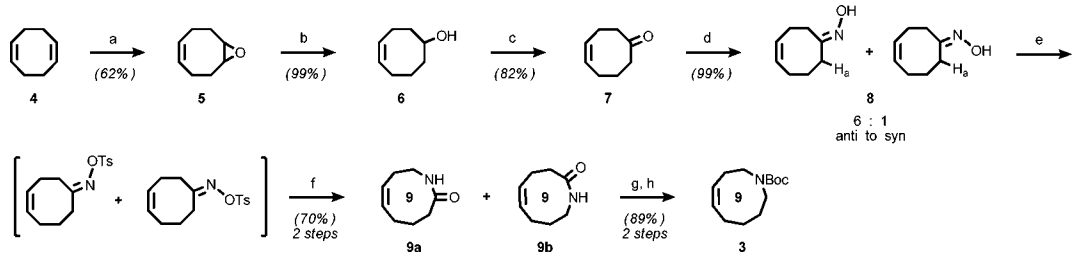
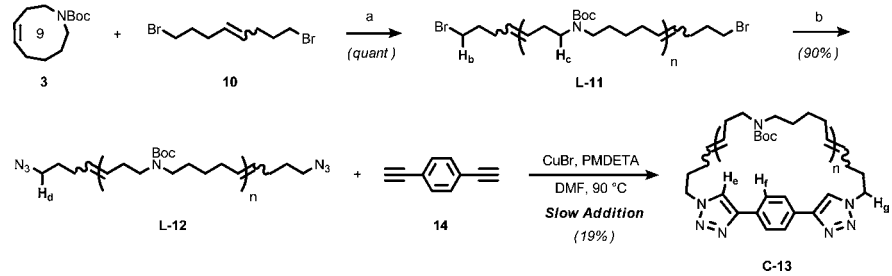
Scheme 1. Synthesis of Nine-Membered Cyclic Boc-amine Monomer **3**[a]



[a] Reagents and conditions: (a) *m*-CPBA, $CHCl_3$, 0 °C to room temperature, 12 h; (b) LAH, THF, 0 °C to reflux, 4 h; (c) oxalyl chloride, DMSO, TEA, −78 °C to room temperature, 4 h; (d) $NH_2OH \cdot HCl$, $NaHCO_3$, MeOH, reflux, 4 h; (e) TsCl, Pyr, DCM, 0 °C to room temperature, 12 h; (f) K_2CO_3, H_2O, THF, room temperature, 12 h; (g) LAH, THF, reflux, 4 h; (h) Boc_2O, TEA, DMAP, DCM, room temperature, 24 h.

Scheme 2. Synthesis of Linear Telechelic Dibromide Polymer **L-11**, Diazide Polymer **L-12**, and Cyclic Polymer **C-13**[a]



[a] Reagents and conditions: (a) catalyst **1**, 1.0 M DCM, 43 °C, 1 day; (b) NaN_3, DMF, 50 °C, 12 h.

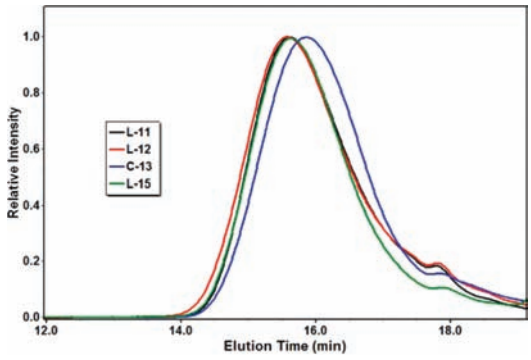


Figure 5. GPC traces of linear bromide polymer **L-11** (black), linear azide polymer **L-12** (red), doubly clicked linear polymer **L-15** (green), and cyclic polymer **C-13** (blue).

suitably functionalized telechelic polymer would be structurally analogous to early dianionic polymers used in the synthesis of CPs.[9,99]

Given the successful application of the alkyne−azide click reaction to the synthesis of CPs,[13−15] we employed this procedure to cyclize our linear polymer. Though our efforts to use a diazide CTA during ROMP to monomer **3** were unsuccessful, we readily accessed the dibromo telechelic polymer **L-11** upon treatment of a solution of **3** and dibromo CTA **10**[100] with catalyst **1** (Scheme 2). Gel permeation chromatography (GPC, Figure 5) analysis of **L-11** revealed that the polymer had an M_n value of 4.1 kDa, correlating to a degree of polymerization (DP) of 17, and a polydispersity index (PDI) of 1.49. By ^{1}H NMR end-group analysis (Figure 6A), the DP of **L-11** was found to be 19, in close agreement with the GPC results. Synthesis of the desired diazide telechelic polymer **L-12** was accomplished by treating dibromotelechelic polymer **L-11** with sodium azide (Scheme 2). The GPC traces for **L-11** and **L-12** overlapped closely (Figure 5), and polymer end-group conversion from bromide to azide was monitored by ^{1}H NMR spectroscopy (Figure 6B), which showed an upfield shift of the bromomethylene protons (from 3.37 to 3.23 ppm) after substitution with sodium azide. To verify that **L-12** contained azide functionalities, we studied polymers **L-11** and **L-12** by FT-IR (Figure 7). As expected, the spectrum of **L-12** contained a strong band at 2096 cm^{-1}, while no azide peak was observed in the spectrum of **L-11**.

We effected the cyclization of the linear diazide polymer **L-12** to the targeted CP **C-13** via a slow-addition, pseudo-high-dilution process[13−15] (Scheme 2), whereby a solution of diazide linear polymer **L-12** and 1,4-diethynylbenzene (**14**) was added by syringe pump over several days to a well-stirred DMF reservoir containing Cu catalyst and *N*,*N*,*N*′,*N*″,*N*″-pentamethyl-diethylenetriamine (PMDETA) ligand. Rather than attempt to fractionally precipitate linear polymer impurities[99] from **C-13**, we instead utilized the high fidelity of the click reaction. Since any linear polymer contaminants would likely contain either an azide or an alkyne chain-end functionality, we subjected the crude cyclization products to a more concentrated click reaction in the presence of alkyne-functionalized polymer beads and azide-functionalized Merrifield resin (Scheme 3).[100] Filtration of the solid beads resulted in the concomitant removal of all linear contaminants from solution and afforded a solution of pure cylic polymer **C-13**.

The cyclic topology of **C-13** was confirmed by ^{1}H NMR end-group analysis and shifting of GPC peak elution volume. Evidence for the success of the click reaction could be readily observed in the dramatic downfield shift of the azidomethylene proton (H_d) signal from 3.23 to 4.37 ppm (Figure 6C), indicating conversion of the azides to triazole functionalities. IR spectroscopy of **C-13** (Figure 7) also showed that the strong azide band in the spectrum of **L-12** was no longer present. Inclusion of the 1,4-diethynylbenzene unit within the backbone of **C-13** was

(99) Gan, Y.; Dong, D.; Hogen-Esch, T. E. *Macromolecules* **2002**, *35*, 6799.
(100) See the Supporting Information for full details.

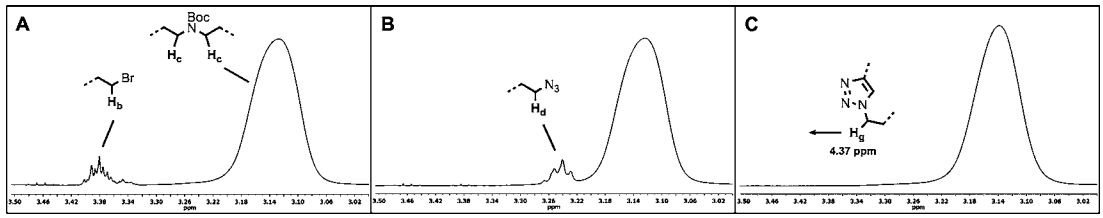


Figure 6. Partial 600 MHz ^{1}H NMR spectra at 25 °C in $CDCl_3$ of polymer end-group resonances, showing conversion of telechelic bromide **L-11** (A) to diazide **L-12** (B) to post-click cyclic species **C-13** (C). After cyclization, the end-group signal shifts downfield to 4.37 ppm. Full spectra can be seen in the Supporting Information.

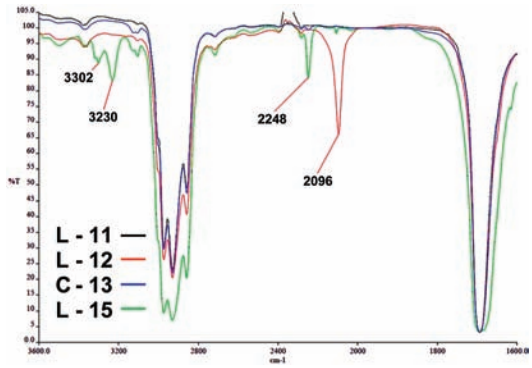


Figure 7. FT-IR spectra for linear bromide polymer **L-11** (black), linear azide polymer **L-12** (red), cyclic polymer **C-13** (blue), and doubly clicked linear polymer **L-15** (green).

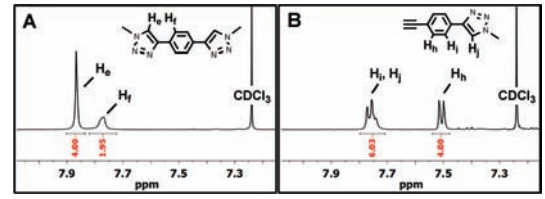


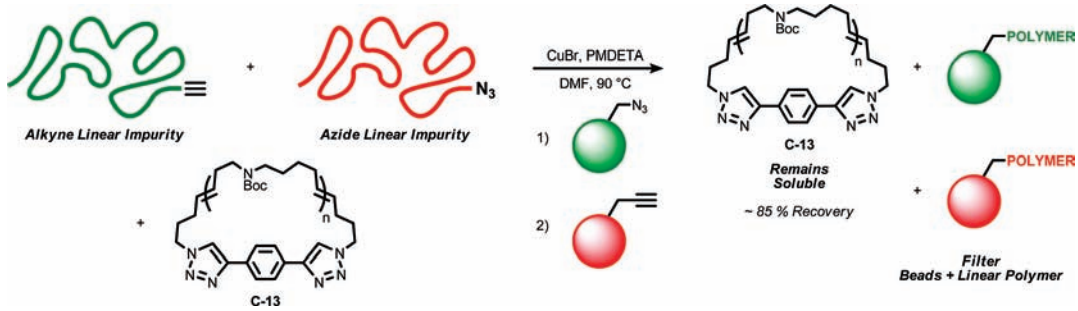
Figure 8. Partial 600 MHz ^{1}H NMR spectra at 25 °C in $CDCl_3$ of the clicked end-groups of symmetric cyclic polymer **C-13** (A) and nonsymmetric double-clicked linear polymer analogue **L-15** (B). Integration values in red were obtained by assigning the end group signal from H_g an integration value of 4.

readily apparent in the ^{1}H NMR spectrum (Figure 8A), with the phenyl protons of the linker (H_f) generating a sharp singlet at 7.88 ppm that integrated to four protons upon assigning the end-group signal from the α-triazole methylene proton H_g an integration value of four (Scheme 2). Absence of splitting of the aromatic signal indicated the symmetric nature of the clicked unit and implied click coupling at both ends of the 1,4-diethynylbenzene. The triazole moiety also produced a broad singlet at 7.78 ppm (Figure 8) that integrated to two protons. GPC analysis of **C-13** (Figure 5) showed the expected increase in peak retention time characteristic of cyclic polymers,[9] with no appreciable change in molecular weight (MW) except for the addition of the diethynylbenzene unit (M_n = 4.4 kDa).[101] Additionally, ^{1}H NMR end group integration values remained identical to the linear species **L-11** and **L-12**. Though we attempted to confirm the MW of the polymers by matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI TOF MS), the lability of the boc groups, as well as the lability of the bromide and azide end groups of the linear precursors, prevented accurate mass analysis due to complex and intractable fragmentation patterns.

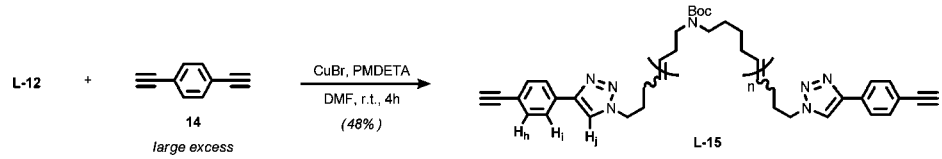
To confirm that the observed increase in retention time upon cyclization was not an artifact of the click reaction, we synthesized a control polymer using the original diazide polymer **L-12**. We again subjected **L-12** to click conditions, but in the presence of a significant excess of dialkyne **14** to give linear, doubly clicked analogue **L-15** (Scheme 4). The GPC trace for **L-15** (Figure 5) overlapped identically with both **L-11** and **L-12**, again with only a slight MW increase (M_n = 4.4 kDa) due to the addition of the clicked units. In contrast to the symmetric singlet of the phenyl clicked end group of **C-13**, the signal from H_h and H_i of the phenyl group of the clicked units of **L-15** produced two doublets (Figure 8) with coincidental overlap of the triazole signal from H_j with the downfield doublet. When the signal from H_g was assigned a value of four protons, each of the doublets from H_h and H_i integrated to four protons with an additional two protons from the triazole, confirming the clicking of two 1,4-diethynylbenzene units per polymer chain. IR spectroscopy (Figure 7) also showed no remaining azide resonance after the "click" reaction, though peaks at 3300 and 2200 cm^{-1} indicated the presence of remaining alkyne functionality. The alkyne protons, too, could be observed in the ^{1}H NMR spectrum (3.10 ppm) as a sharp singlet extending above the broad signal from H_c.[100]

Polymer Functionalization. Once we had confirmed the cyclic structure of **C-13**, we began the process of functionalizing the polymer in preparation for the desired interlocking reaction. The use of the ruthenium olefin metathesis catalyst **1** to affect the final clipping RCM reaction necessitated hydrogenation of all olefin residues within the cyclic polymer backbone,

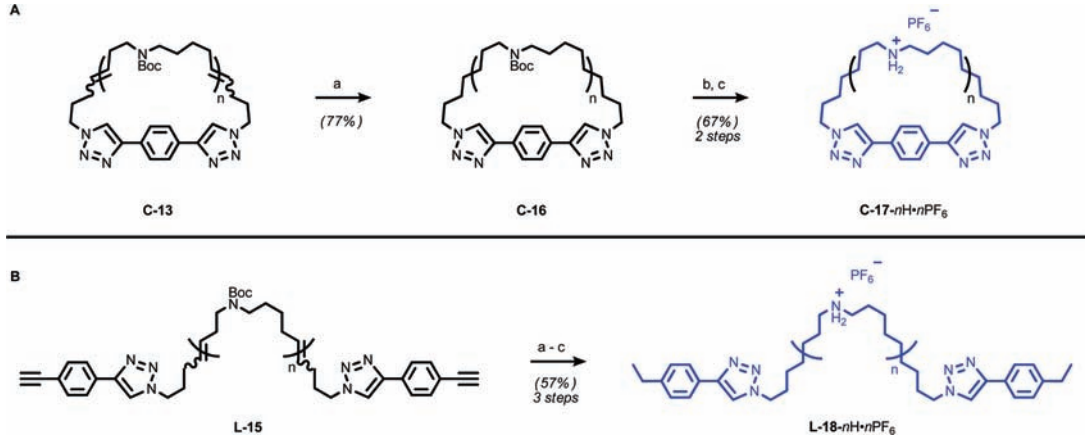
Scheme 3. Click Removal of Linear Contaminants from Cyclic Polymer **C-13** Using Azide- and Alkyne-Functionalized Beads



Scheme 4. Synthesis of Doubly Clicked Linear Polymer **L-15**



Scheme 5. Synthesis of (A) Cyclic Polyammonium **C-17-***n*H·*n*PF_6 and (B) Linear Polyammonium **L-18-***n*H·*n*PF_6[a]



[a] Reagents and conditions: (a) Wilkinson's catalyst ($Rh(PPh_3)_3Cl$), 800 psi of H_2, THF, 50 °C, 24 h; (b) TFA, DCM, room temperature, 4 h; (c) NH_4PF_6, MeOH, room temperature, 12 h.

and this was achieved by treating **C-13** with Wilkinson's catalyst under high-pressure hydrogenation conditions (Scheme 5A) to give **C-16**. No remaining olefin residues at 5.40 ppm were observed by ^{1}H NMR spectroscopy, indicating saturation of **C-13**.

To reveal the coordinating ammonium sites within the backbone of the polymer, we treated **C-16** with trifluoroacetic acid (TFA), removing the Boc protecting group. The ammonium−TFA adduct was then subjected to counterion exchange with ammonium hexafluorophosphate to produce **C-17-***n*H·*n*PF_6. Hexafluorophosphate counterions have been shown to increase the binding constant between crown ether-type species and ammonium ions and also enhance the solubility of the charged complex in organic solvents.[102−105] The ^{1}H NMR spectrum of **C-17-***n*H·*n*PF_6 contained a broad singlet (6.45 ppm) corresponding to the ammonium residues, and the sharp signal at 1.4 ppm corresponding to protons on the Boc-group was no longer present. Additionally the α-ammonium methylene proton signal from H_c (Scheme 2) shifted upfield to 2.96 ppm (originally 3.13 ppm), an effect of the conversion of the Boc-amine to an ammonium salt. Broadening and shifting of the triazole resonance (from 7.80 ppm to 8.14 ppm) suggested that the acidic conditions of the deprotection may have resulted in protonation of the triazole.

The linear doubly clicked analogue **L-15** was subjected to the same hydrogenation conditions (Scheme 5B) as **C-13** to give the saturated product. Deprotection and anion exchange were also performed, generating the linear polyammonium adduct **L-18-***n*H·*n*PF_6.

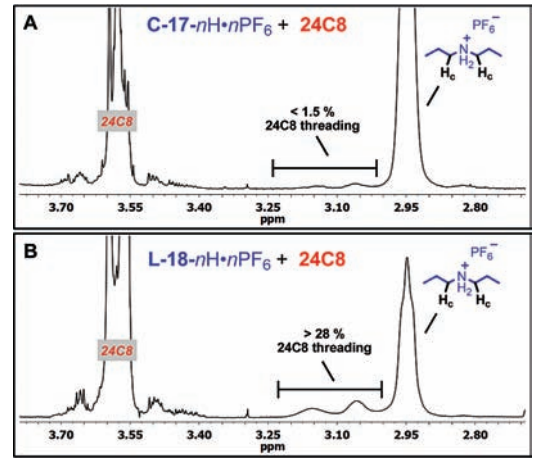


Figure 9. Partial 600 MHz ^{1}H NMR spectra at 25 °C in CD_3CN of (A) cyclic polyammonium **C-17-**nH_2·nPF_6 with 24-crown-8 ether (24C8) showing less than 1.5% threading and (B) linear double-clicked polyammonium **L-18-**nH_2·nPF_6 with 24C8 showing more than 28% threading. (Note: approximately 0.5 equiv of 24C8 per ammonium; see the Supporting Information for complete details.)

Unfortunately, none of the charged polymers were amenable to GPC analysis, due to challenges associated with solubility. As an alternate method for cyclic/linear topology confirmation, we exploited the well-known hydrogen-bonding association between 24-crown-8 ether (24C8) and dialkylammonium ions. Upon encircling a dialkylammonium ion, the strongly coordinating 24C8 causes a downfield shift of the signal from the protons on the carbons adjacent to that ammonium site. Correlating the integration value of the original signal with the shifted signal enables quantitation of the threading of the polymeric chains by 24C8. When a solution of the "endless" **C-17-***n*H·*n*PF_6 was mixed with 24C8 (0.5 equiv per ammonium site), barely detectable threading (<2%) was observed by ^{1}H NMR spec-

(101) All GPC MW measurements were obtained through multiangle laser light scattering detection, giving the absolute molecular weight of the polymer.
(102) Ashton, P. R.; Cantrill, S. J.; Preece, J. A.; Stoddart, J. F.; Wang, Z.-H.; White, A. J. P.; Williams, D. J. *Org. Lett.* **1999**, *1*, 1917.
(103) Montalti, M. *Chem. Commun.* **1998**, 1461.
(104) Doxsee, K. M. *J. Org. Chem.* **1989**, *54*, 4712.
(105) Jones, J. W.; Gibson, H. W. *J. Am. Chem. Soc.* **2003**, *125*, 7001.

Scheme 6. Screen Reaction To Determine Effect of Nitromethane Concentration on RCM Olefin Conversion

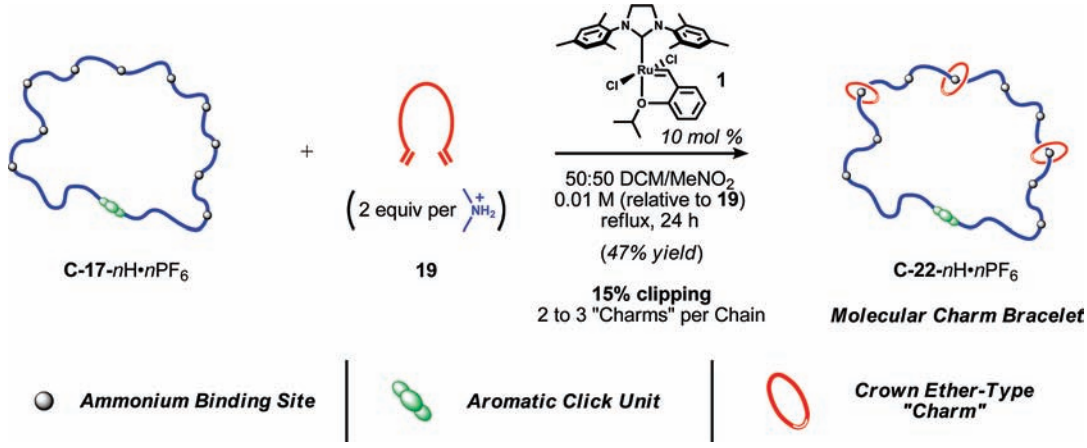
troscopy (Figure 9A; see the Supporting Information for full details). However, the linear analogue **L-18-***n*H·*n*PF_6 engaged in significant threading interactions upon addition of the same amount of 24C8 (nearly 30% threading, Figure 9B). As expected, introduction of additional 24C8 (total of 2.0 equiv per ammonium site) resulted in increased threading for both polymers, with coordination remaining low for **C-17-***n*H·*n*PF_6 (∼10%) while **L-18-***n*H·*n*PF_6 threaded to ∼45%. It is worth noting that, due to the dominance of cyclic architectures in the sample of **C-17-***n*H·*n*PF_6, the effective concentration of available 24C8 would be much higher per ammonium site for any linear, threadable polymers, and could explain the proportionally greater increase in threading upon introduction of additional crown. This topologically based threading technique was particularly valuable, as it enabled quantitative determination that the presence of linear contaminants **C-17-***n*H·*n*PF_6 was very low and unambiguously showed that the sample contained near or above 90% cyclic polymer.

Molecular Charm Bracelet Synthesis and Analysis. To enable "clipping" of CP **C-17-***n*H·*n*PF_6, we had to develop a suitable solvent system that would both solubilize the highly charged polymer and facilitate the olefin metathesis reaction. Because the polymer displayed good solubility in nitromethane, we explored the possibility of using this as our RCM solvent. To test the efficacy of this system, we monitored the effect of nitromethane concentration on the conversion of protons H_k and H_m to H_n upon clipping of the diolefin crown ether-type fragment **19** around the template **20**-H·PF_6 to form the pseudorotaxane **21**-H·PF_6 (Scheme 6).[100] We observed that an increased nitromethane volume fraction (relative to DCM) led to decreased olefin conversion. Consequently, we concluded that a 1:1 mixture (v/v) of dichloromethane to nitromethane would maximize the solubility of the polymer while still enabling reasonable olefin conversion.

Synthesis of the molecular charm bracelet polymer was achieved via addition of catalyst **1** to a solution of **C-17-**nH_2·*n*PF_6 and **19** in the 1:1 dichloromethane/nitromethane (v/v) solvent mixture. Simple precipitation of the polymer into pure dichloromethane and isolation of the insoluble material afforded the desired interlocked charm bracelet **C-22-***n*H·*n*PF_6 (Scheme 7). By ^{1}H NMR spectroscopic analysis, ∼15% of the ammonium sites were clipped, indicating that each polymer chain contained approximately two to three interlocked "charms". We believe there are several factors that resulted in this low clipping percent. Because of the limited solubility of the polymer, the charged ammonium residues were likely concentrated in a dense core surrounded by the more soluble alkyl components, severely limiting access of **19** and catalyst to the polymer binding sites and preventing extensive clipping. Also, the large amount of nitromethane solvent required to dissolve **C-17-**nH_2·*n*PF_6 would significantly decrease the association constant governing coordination of **19** to the ammonium sites, a phenomenon further compounded by the inherently lower binding constant of dialkylammonium species relative to their dibenzyl counterparts.[45]

Though efforts to neutralize **C-22-***n*H·*n*PF_6 were unsuccessful, conclusive evidence for the interlocked nature of the molecular charm bracelet was obtained using ^{1}H and 2D-DOSY NMR spectroscopy. Analysis of the proton signals of the interlocked crown showed significant line broadening[100] relative to the free, noninterlocked ring-closed analogue, a phenomenon that is commonly observed for interlocked complexes[56,63,69] and arises from an increase in the rotational correlation time of the interlocked crown as a result of increased MW and volume (due to interlocking of the small ring with the large polymer). Additionally, a downfield shift in the primary $-CH_2-$ crown proton signals from 3.57 ppm to 3.64 ppm was observed, a phenomenon attributed to subtle electron-withdrawing effects from hydrogen-bonding interactions occurring between the ammonium protons and crown oxygens. Though one-dimensional ^{1}H NMR analysis suggested the interlocked nature of **C-22-***n*H·*n*PF_6, 2D-DOSY NMR provided convincing evidence. This technique enabled the direct detection of the diffusion rates of ring-closed product **23** after RCM in the absence and presence of polymer (Figure 10A and 10B, respectively). Typically, the diffusion values obtained from 2D-DOSY NMR are reported as log *D*, where the diffusion constant, *D*, has units of $m^2\ s^{-1}$. Thus, a smaller (more negative) diffusion value implies a slower diffusion rate. For example, the large macromolecular template **C-17-***n*H·*n*PF_6 had a diffusion value of log $D = -8.83$ (slow),[100] while free crown **23** had a faster diffusion value of

Scheme 7. Graphical Representation of the Synthesis of Molecular Charm Bracelet **C-22-***n*H·*n*PF_6



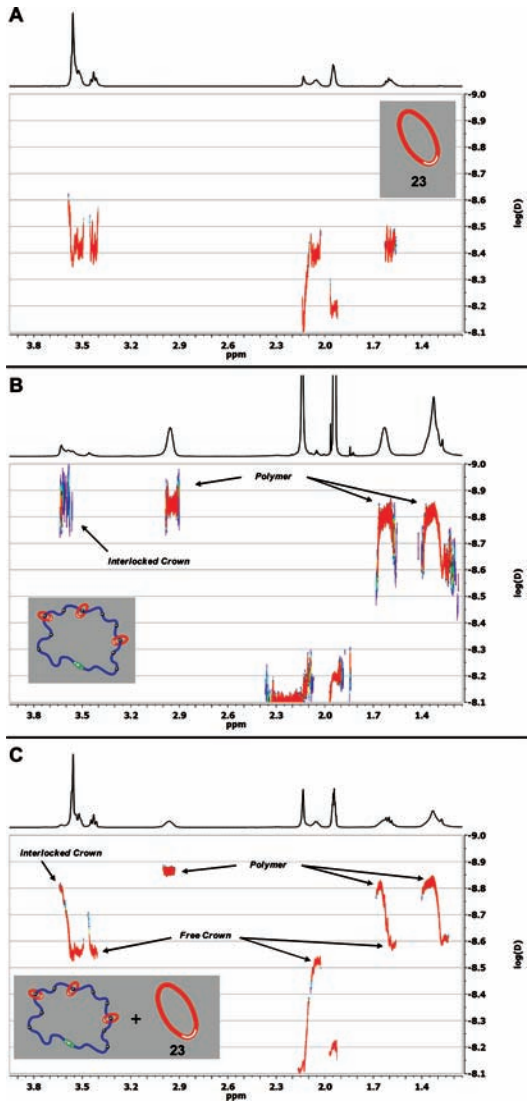


Figure 10. 2D-DOSY ^{1}H NMR spectra at 400 MHz and 25 °C in CD_3CN of free ring-closed crown **23** (A), purified molecular "charm bracelet" **C-22-***n*H·*n*PF_6 (B), and a physical mixture of **C-22-***n*H·*n*PF_6 and **23** (C). The units of the diffusion constant D are $m^2\ s^{-1}$.

log $D = -8.45$ (Figure 10A), expected behavior for a small molecule. However, when the crown signals from **C-22-***n*H·*n*PF_6 were analyzed by 2D-DOSY NMR, a significant reduction in crown diffusion speed (log $D = -8.85$) was observed (Figure 10B). The alignment of crown and polymer signals at the same diffusion rate indicated an intimate association between the two species, only possible if **23** was interlocked around the cyclic polymer framework. To rule out the possibility of coincidental overlap between crown and polymer diffusion values observed in Figure 10B, a sample of **C-22-***n*H·*n*PF_6 was spiked with noninterlocked **23**. If the slow diffusion rate of crown signals in the 2D-DOSY NMR of **C-22-***n*H·*n*PF_6 (Figure 10B) originated from hydrogen-bonding interactions between the crown and polymer and not from interlocking of the crown around the polymer backbone, we would expect to see the introduced, noninterlocked crown diffuse at a similarly slow rate as the interlocked crown in **C-22-***n*H·*n*PF_6. However, 2D-DOSY NMR analysis of a physical mixture of **C-22-***n*H·*n*PF_6 and **23** (Figure 10C) revealed a distinct difference between diffusion rates of the two types of crown (log $D = -8.80$ and -8.52, bound and free, respectively), confirming the interlocked nature of the crown in the molecular charm bracelet **C-22-***n*H·*n*PF_6.

Conclusions

We have described a clipping approach to a polycatenated cyclic polymer, a structure that resembles a molecular charm bracelet. We have shown that the use of ring-opening metathesis polymerization of a Boc-amine macromer in the presence of a chain transfer agent allows for the synthesis of a linear polymer that could be subsequently functionalized and cyclized to the corresponding cyclic analogue. This cyclic polymer was characterized through a variety of techniques and subjected to further functionalization reactions, affording a cyclic polyammonium scaffold. Diolefin polyether fragments were coordinated and clipped around the ammonium sites within the polymer backbone using ring-closing olefin metathesis, giving the molecular charm bracelet. Confirmation of the interlocked nature of the product was achieved via ^{1}H NMR spectroscopy and two-dimensional diffusion-ordered NMR spectroscopy.

Acknowledgment. We thank Professor Daniel J. O'Leary, Dr. David VanderVelde, Dr. Andrew J. Boydston, Dr. John. B. Matson, and Yan Xia for helpful discussions. The work was supported by the Office of Naval Research through its MURI program and the NSF (NSF CHE-0809418). W.Y.C. acknowledges the NSERC of Canada for a postdoctoral fellowship.

Supporting Information Available: Figures, tables, and text giving complete experimental procedures as well as full characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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