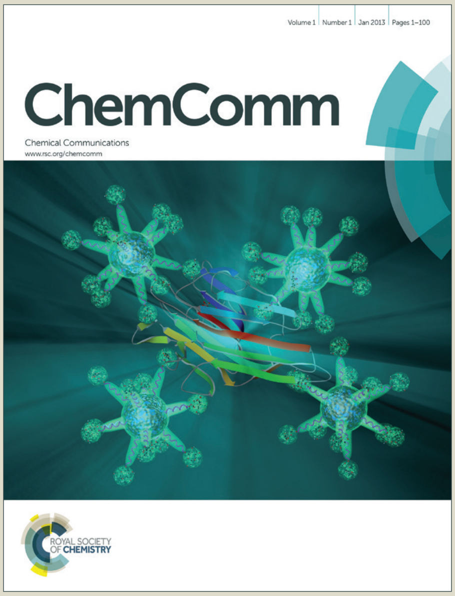
ChemComm

Accepted Manuscript



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/chemcomm

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

Polymeric Catenanes by "Click" Chemistry and Atom Transfer Radical Coupling

Ajaykumar Bunha, Peng-Fei Cao, Joey Mangadlao, Fei-Mo Shi, Edward Foster, Katrina Pangilinan, and Rigoberto Advincula*

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

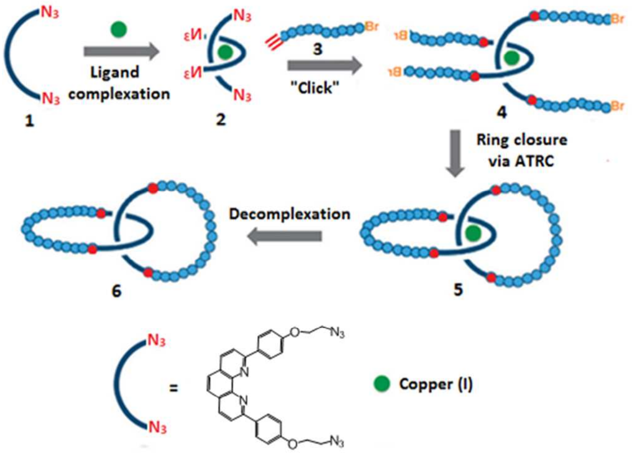
A novel route for the synthesis of polymeric catenanes was demonstrated by grafting alkyne functionalized polymer to supramolecularly templated azide terminated ligand followed by ring closing *via* Atom Transfer Radical Coupling (ATRC). The polymeric catenane was characterized by GPC and AFM imaging.

Over the past few decades, the synthesis of novel polymers has become an interesting topic due to their extraordinary properties for wider applications.[1] The aspects of polymer architecture such as inter-/intra-molecular interactions and chain conformations, play an important role on the fundamental properties of polymers as well as the chemical compositions.[1h] Inspired by synthetic molecular catenanes which exhibit great potential as molecular switches, supramolecular machines, and controlled drug release systems, mechanically interlocking the cyclic polymer chains was also introduced to the polymer systems, known as polymeric catenanes.[1h, 2] Despite the broad exploration of the synthesis of molecular catenanes over the years, polymeric catenanes with relatively high molecular weight are still one of the most challenging targets in synthetic polymer chemistry.[3]

The commonly used synthetic method for polymeric catenanes include threading and subsequent cyclization step wherein a linear polymer threads into a cyclic polymer ring; after which, cyclization of the resulting pseudorotaxane affords polymeric catenanes.[3a-3b] However, the thermodynamically unfavorable statistical threading and difficulties associated with the purification result in low yielding polymeric catenanes. Recently, our group has demonstrated the synthesis of homo- and block- polymeric catenanes *via* controlled radical polymerization from supramolecularly templated atom-transfer radical-polymerization (ATRP) initiators followed by ring closing reaction.[3e,4] The approach not only improves the yield of polymeric catenanes, but also opens the door for the synthesis of wide varieties of structurally different polymeric catenanes.

In our effort to demonstrate other possible efficient method for the synthesis of polymeric catenanes, the utilization of the copper(I)-catalyzed alkyne-azide cycloaddition (CuAAC) reaction also known as "click" reaction was performed. Click chemistry has found extensive use in the design and synthesis of new polymeric materials.[5] In particular, CuAAC reaction has been proven to be a promising tool for the synthesis of mechanically interlocked molecules because it can be performed at room temperature in a variety of solvents, allowing the optimization of non-covalent bonding interactions of the precursors.[6] In this work, we have demonstrated another versatile approach for the synthesis of polymeric catenanes by 1) grafting alkyne functionalized linear polymer to supramolecularly templated azide functionalized ligand *via* CuAAC reaction, and 2) ring closing *via* intramolecular coupling of polymer arms by ATRC as shown in Scheme 1. Compared to our previous report on "grafting" from the catenated ATRP initiator, the pre-synthesized alkyne terminated linear polymer allows better control over the molecular weight, polydispersity, and polymer component. To the best of our knowledge, this is one of the first reports of a synthesized polymeric catenanes *via* "click" reaction.[1h, 6c,7]

Scheme 1. Schematic route for the preparation of polymeric catenanes



The classic strategy of forming tetrahedral complex using two phenanthroline ligands and one Cu(I) metal ion has been successfully utilized in the synthesis of many types of mechanically interlocked molecules.[2a-2b,8] Moreover, with Cu(I)-phenanthroline complex, the CuAAC "click" reaction has been proven as a very effective method to construct functionalized molecular catenanes with high yield.[6d, 7] Based on this concept, the azide functionalized phenanthroline ligand **1** was synthetized by reaction of 2,9-bis(4-(hydroxy)phenyl))-1,10-phenanthroline and 2-azidoethyl 4-methylbenzenesulfonate in basic condition (see Supporting Information). The supramolecular assembly of ligand-N_3 **1** in the presence of $Cu(I)(CH_3CN)_4PF_6$ yields a dark red solid tetrahedral Cu(I)-complex of ligand-N_3 **2**. The UV-Vis analysis of ligand-N_3 Cu(I)-complex **2** (Figure S1) shows intense ligand-centered transition at 283 nm and 321 nm and weaker absorption peak at 437 nm corresponding to metal-to-ligand charge transfer (MLCT), which is consistent with reported literature.[9] The comparative ^1H NMR spectrum of ligand-N_3 (compound **1**) and Cu(I)-complex **2** was shown in Figure 1. The significant chemical shift and complete disappearance of signals corresponding to the ligand-N_3 confirmed the quantitative formation of the complex. The alkyne terminated linear polystyrene (PS) **3** was prepared as a precursor for grafting to a ligand-N_3 Cu(I)-complex **2** *via* CuAAC "click" reaction. The bulk polymerization of styrene using prop-2-ynyl 2-bromo-2-methylpropanoate as initiator and Cu(I)Br/PMDETA as catalyst yield polymers with a low polydispersity and good control over molecular weight (M_n: 3,373 g mol^{-1}, PDI: 1.05).

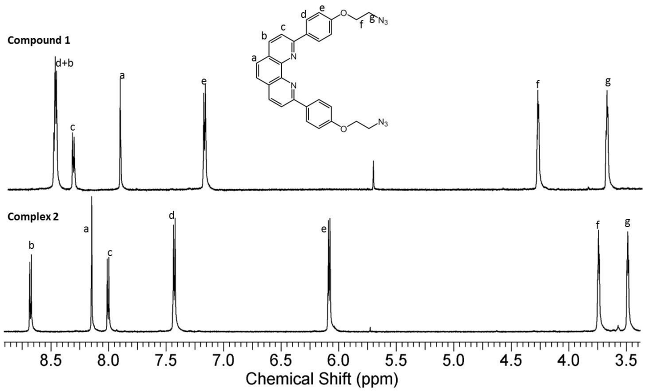


Figure 1. Comparative ^1H NMR spectrum of (a) Ligand-N_3 (**1**) and Ligand-N_3 Cu(I) complex (**2**)

The CuAAC "click" reaction between alkyne-PS **3** and the ligand-N_3 complex **2** in DMF using CuBr/PMDETA as catalyst produced PS Cu(I) complex **4**. The alkyne-PS **3** was used in excess to ensure complete conversion of ligand-N_3 complex **2** to PS Cu(I) complex **4.** The "click" reaction was monitored by GPC analysis at different time intervals, and the reaction was completed after 48 hours. As shown in Figure 2a and 2b, it show a clear shifting of peak corresponding to PS Cu(I) complex **4** toward high molecular weight compared to linear precursor PS-alkyne **3**. On the basis of the calibration curve with linear PS as standard, the apparent molecular weight of PS Cu(I) complex **4** was 4,878 g/mol, which was found to be smaller than the theoretical value. This deviation was perhaps due to the compact structure of PS Cu(I) complex **4** (four arm star-like polymers). UV-vis spectrum analysis confirmed the stability of the complex after "click" reaction (Figure S2). The appearance of new peaks and slight chemical shift of the original signals were observed for the ^1H NMR spectrum of PS Cu(I)-complex (**4**) compared to that of alkyne-PS (**3**) (see Figure S3).[10] Further evidence of efficient "click" reaction was also obtained from Fourier Transform Infrared (FT-IR) analysis (Figure S4) of PS Cu(I) complex **4**, which shows the absence of the azide peak at 2090 cm^{-1} compared to that of ligand-N_3 **1**.[10b]

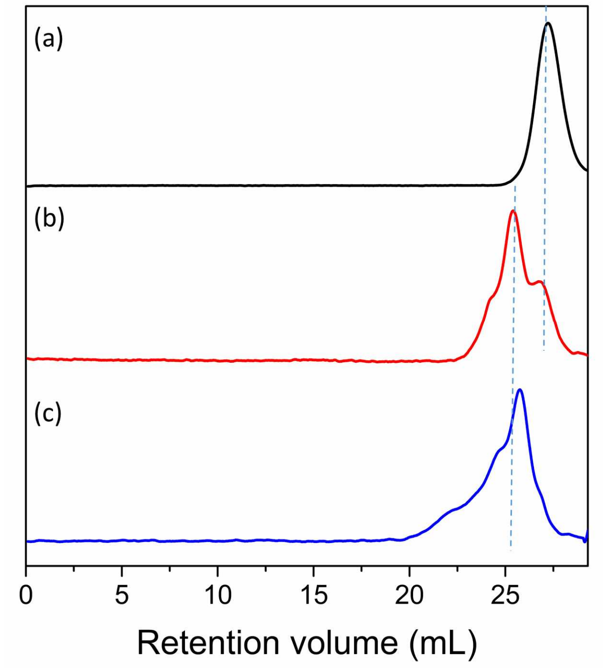


Figure 2. GPC traces of a) PS-alkyne **3**, b) PS-Cu(I) complex **4**, and c) PS-catenane **5**.

The intramolecular ATRC of dibrominated PS (Br-PS-Br) at relatively high temperature have been reported to synthesize macrocyclic polystyrene.[11] Similarly, the formation of PS-catenane **5** can be achieved by intramolecular ATRC of dibrominated PS arms of Cu(I) complex **4** under pseudo-high dilution conditions. Thus, a THF solution of the PS Cu(I) complex **4** was added dropwise at a fairly low rate (0.75 mL h^{-1}), into a refluxing THF solution of catalyst CuBr/Me_6TREN and Cu(0). The GPC trace of resulting PS-catenane **5** (Figure 2c) show slight shifting toward higher retention volume as a result of reduced hydrodynamic radius upon ring closing by ATRC. However, the coexistence of the intermolecularly coupled product was evidenced by a small shoulder at smaller retention volume. The weight percentage of desired polymeric catenane **5** was estimated to be 62.5% as calculated from the area under the curve of the RI signal (Figure S5). Hence, there are around 37.5% of intermolecularly cross-linked products, which are most likely polymeric [n] catenane (n≥3).

The interlocked structure of polymeric catenanes can also be useful to determine the efficiency of ATRC by monitoring the change in hydrodynamic volume of the products after removing the metal from the template. A metal-free PS catenane **6** was obtained by reacting PS catenane **5** with a saturated solution of KCN in THF: methanol (3:1) at room temperature. The GPC traces of the resulting PS catenane **6** (Figure S6) show that the retention volume peak has not shifted to low molecular weight region after removing the copper, indicating an interlocked structure of PS catenane **6**. GPC analysis of PS catenane (**6**) showed some small polymer peaks with higher hydrodynamic volumes. Aside from intermolecular cross-linking, another possible side reaction of ATRC is the formation of a "figure of eight" shaped PS polymers.[12] After the demetallation step, "figure of eight" shaped PS generated cyclic PS with higher hydrodynamic volume compared to its catenated form. In addition, GPC traces also show the low molecular weight peak at a retention volume of 28.9 mL which can be attributed to the acyclic and/or cyclic polymers generated upon demetallation of uncyclized or partially cyclized polymer complex **4** during ATRC. The efficiency of cylization by ATRC was found to be approximately 50.3% by calculating the area under the curve for the polymeric [2]catenanes/cyclic-isomer/[n]catenanes (n≥3) versus uncyclized/partially cyclized polymers. The final polymeric catenanes **6** was purified by dialysis in THF (three times, Sigma/MWCO 2000) to remove the low molecular weight side products from demetallation step and the unreacted alkyne-PS **3**. The GPC traces of purified PS catenane **6** (Figure S7) revealed that most of the low molecular weight fraction was removed.

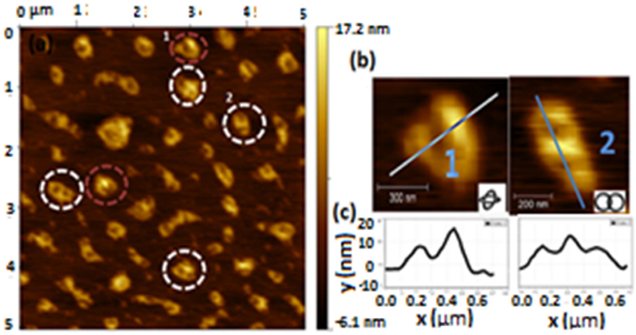


Figure 3. (a) AFM image of the PS catenanes 6 on a 8 x 8 µm scale on mica, (b) magnified images of the representative PS catenanes from (a), and (c) line profile of the PS catenanes.

To test the integrity of Cu(I) complex during click reaction and efficiency of metal removal from the template, a control experiment was performed by demetallation of PS Cu(I) complex **4** using the same reaction conditions. GPC traces (Figure S8) of resulting polymer clearly suggest that the peak of PS Cu(I) complex **4** shifted toward higher retention volume as polymer chains decoupled from metal center, resulting to an overall decrease in the molecular weight of polymers.

To provide direct proof of the formation of polymeric catenanes, AFM imaging was also performed as shown in Figure 3 and Figure S9. The samples of PS-catenanes **6** for AFM analysis were prepared by spin-coating a very dilute solution of the polymer in $CHCl_3$ onto freshly cleaved mica. Interlocked cyclic structures of PS catenanes **6** were statistically observed, exhibiting different orientations on the surface (Figure 3). In addition, the line profile analysis of individual structure revealed the presence of the cavities inside the catenanes and the height doubled at overlapping point of polymer chain. Similarly, a large single cyclic polymer as a topological isomer of catenanes was also observed with the presence of a single cavity as measured by the line profile (Figure S9c). Moreover, the presence of intermolecular coupling product as observed in GPC trace was also supported by AFM image, where it shows interlocked multi-cyclic polymer rings in the form of polymeric [n]catenanes (n≥3) (Figure S9d). More work on separating and analyzing these different polymeric catenanes and cyclic polymers are still underway.

In conclusion, the 'grafting to' approach as a novel route to synthesize polymeric catenanes was demonstrated. The CuAAC "click" reaction has been proven to be an efficient way to couple alkyne functionalized polymers to azide functionalized ligand-Cu(I) complex. The ring closing *via* intramolecular ATRC enables the formation of polymeric catenanes which was further characterized by GPC and AFM to confirm its interlocked structure. The GPC and AFM results suggested the possible presence of polymeric [n]catenanes (n≥3) aside from polymeric [2]catenane due to intermolecular cross-linking. However, more investigation is needed for polymeric [n]catenanes (n≥3). As the alkyne functionality can be easily introduced in a variety of polymers, this approach can be further explored to obtain structurally different homo- and block-polymeric catenanes.

Acknowledgements

The authors acknowledge funding from NSF CHE-10-41300. The authors also acknowledge technical support from Malvern (formerly Viscotek) Inc. and Agilent Technologies (formerly Molecular Imaging).

Notes and references

(1) (a) N. Nasongkla, B. Chen, N. Macaraeg, M. E. Fox, J. M. J. Frechet and F. C. J. Szoka, *J. Am. Chem. Soc.*, 2009, **131**, 3842–3843; (b) D. M. Eugene and S. M. Grayson, *Macromolecules*, 2008, **41**, 5082–5084; (c)Z. J. Guan, *J. Polym. Sci., Part A: Polym. Chem.*, 2003, **41**, 3680–3692; (d) Z. Guan, *Chem.–Eur. J.*, 2002, **8**, 3086–3092; (e) E. M. Harth, S. Hecht, B. Helms, E. E. Maelmstrom, J. M. J. Frechet and C. J. Hawker, *J. Am. Chem. Soc.*, 2002, **124**, 3926–3938. (f) P. F. Cao, R. X. Zhao, L. Li, W. W. Yang, Y. Chen, C. H. Lu, and S. C. Jiang, *J. Polym. Sci., Part A: Polym. Chem.*, 2012, **50**, 227-236. (g) P. F. Cao, Z. Su, Al. Leon, R. C. Advincula, *ACS Macro. Lett.* 2015, **4**, 58-62; (h) Z. Niu, H. W. Gibson, *Chem. Rev.* 2009, **109,** 6024–6046. (i) P. F. Cao, J. Mangadlao, R. Advincula, *Angew. Chem. Int. Ed.*, 2015, **54**, doi: 10.1002/anie.201411623.

(2) (a) C. O. Dietrich-Buchecker, J.-P. Sauvage, *Angew. Chem., Int. Ed. Engl.*, 1989, **28**, 189-192; (b) J. F. Stoddart, *Chem. Soc. Rev.,* 2009, **38**, 1802-1820; (c) K. K. Cotí, M. E. Belowich, M. Liong, M. W. Amgrogio, Y. A. Lau, H. A. Khatib, J. I. Zink, N. M. Khashab and J. F. Stoddart, *Nanoscale*, 2009, **1**, 16-39.

(3) (a) Y. Gan, D. Dong, T. E. Hogen-Esch, *Macromolecules,* 2002, **35**, 6799–6803; (b) Y. Ohta, Y. Kushida, D.

Kawaguchi, Y. Matsushita, A. Takano, *Macromolecules,* 2008, **41**, 3957-3961. (c) K. Ishikawa, T. Yamamoto, M. Asakawa, and Y. Tezuka, *Macromolecules*, 2010, **43**, 168-176; (d) P. F. Cao, A. Bunha, J. Mangadlao, M. J. Felipe, K. I. Mongcopa, and R. Advincula, *Chem. Commnun.*, 2012, **48**, 12094-12096; (e) K. Pangilinan, R. Advincula*, Polym. Int.* 2014, **63**, 803-813.

(4) (a) A. Bunha, C. Tria, R. Advincula, *Chem. Commun.,* 2011, **47**, 9173–9175; (b) A. Bunha, J. Mangadlao, M. Felipe, K. Pangilinan, R. Advincula, *Macromol. Rapid Commun*., 2012, **33**, 1214–1219.

(5) (a) N. V. Tsarevsky, K. V. Bernaerts, B. Dufour, F. E. Du Prez, K. Matyjaszewski, *Macromolecules*, 2004, **37**, 9308–9313; (b) M. B. Steffensen, E. E. Simanek, *Angew. Chem., Int. Ed.*, 2004, **43**, 5178–5180; (c) M. Ergin, B. Kiskan, B. Gacal, Y. Yagci, *Macromolecules,* 2007, **40**, 4724–4727; (d) Q. Liu, P. Zhao, Y. Chen, *J. Polym. Sci. Polym. Chem.*, 2007, **45**, 3330–3341; (e) J. E. Moses, and A. D. Moorhouse, *Chem. Soc. Rev*. 2007, **36**, 1249-1262.

(6) (a) W. R. Dichtel, O.S. Miljanic, J. M. Spruell, J. R. Heath, J. F. Stoddart, *J. Am. Chem. Soc.,* 2006, **128**, 10388–10390; (b) S. Loethen, T. Ooya, H.-S. Choi, N. Yui, D. H. Thompson, *Biomacromolecules,* 2006, **7**, 2501–2506; (c) P. Mobian, J.-P. Collin, J.-P. Sauvage, *Tetrahedron Lett.,* 2006, **47**, 4907–4909; (d) K. D. Hänni, and D. A. Leigh, *Chem. Soc. Rev*. 2010, **39**, 1240-1251.

(7) J. D. Megiatto, D. I. Schuster, *J. Am. Chem. Soc.,* 2008, ***130***, 12872-12873.

(8) (a) B. Mohr, J.-P. Sauvage, R. H. Grubbs, M. Weck, *Angew. Chem. Int. Ed.* 1997, **36**, 1308-1310; (b) L. E. Perret-Aebi, A. Zelewsky, C. Dietrich-Buchecker, and J.-P. Sauvage, *Angew. Chem. Int. Ed.* 2004, **43**, 4482-4485.

(9) P. Yang, X.-J. Yang, and B. Wu, *Eur. J. Inorg. Chem.*, 2009, **20**, 2951-2958.

(10) (a) N. V. Tsarevsky, B. S. Sumerlin, K. Matyjaszewski, *Macromolecules*, 2005, **38**, 3558-3561; (b)B. A. Laurent, S. M. Grayson, *J. Am. Chem. Soc.*, 2006, **128**, 4238-4239.

(11) (a) A. F. Voter, and E. S. Tillman, *Macromolecules* 2010, **43**, 10304-10310; (b) A. F. Voter, E. S. Tillman, P. M. Findeis, and S. C. Radzinski, *ACS Macro lett.*, 2012, **1**, 1066-1070.

(12) N. Belfrekh, C. Dietrich-Buckechker and J.-P. Sauvage, *Inorg. Chem.,* 2000, **39**, 5169-5172.

Department of Macromolecular Science and Engineering, Case Western Reserve University, Cleveland, Ohio 44106,
USA.
E-mail: rca41@case.edu;
Fax: +1 216-368-4202;
Tel: +1 216-368-4566

†Electronic Supplementary Information (ESI) available: Detailed procedures for the chemical synthesis and polymerization, characterization by ^{1}H-NMR, GPC and AFM image analysis. See DOI: 10.1039/b000000x/