Synthesis of Metalated Pseudorotaxane Polymers with Full Control over the Average Linear Density of Threaded Macrocycles

Songsu Kang,[†] M. Mustafa Cetin, Ruiyang Jiang,[‡] Eric S. Clevenger, and Michael F. Mayer*

Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, Texas 79409, United States

Ⓢ *Supporting Information*

ABSTRACT: Here we report the synthesis of metalated main-chain polypseudorotaxanes via ring-opening olefin metathesis copolymerization of macrocycles and metalated [2]catenanes. By varying the feed ratio of the macrocycle and the [2]catenate comonomers, we prepared metalated pseudorotaxane polymers with selected, predictable average linear densities of threaded macrocycles that ranged from 0% to 100%, thus allowing, for the first time, both full and fine control over this key parameter.

Macroscopic materials' properties such as strength and elasticity are emergent manifestations of both the fundamental identity and the arrangement of the material components over many orders of magnitude of scale.[1] Within an organizational hierarchy, the nanoscale offers countless unique structural motifs.[2] For many polymeric materials, among other nanoscopic architectures, both covalent chain cross-links[3] and transient chain entanglements[4] play a vital role in effecting bulk properties.

Of long-standing interest is the development of polymeric materials that possess mobile cross-links, i.e., a permanent, yet dynamic and potentially responsive, entanglement that serves as a chain cross-link.[5] One such mobile cross-link motif is the slip-link, also known as a slide-ring, which is, in the most simplified form, a macrocycle that encircles and maintains association of two (or more) polymer chains. Network materials held together by mobile cross-links have been shown to possess both novel and peculiar viscoelastic properties.[6] Due to the synthetic challenge, examples of introduction of mobile slip-links into polymers are still relatively uncommon;[7] furthermore, the ability to control and measure the quantity and distribution of the slip-links remains limited.

To address these current limitations, we have undertaken methodological development of new synthetic approaches to main-chain metalated pseudorotaxane polymers,[8] which are polymer−macrocycle conjugates wherein many macrocyclic molecules are threaded on polymer chains.[9] Such compounds are approximate one-dimensional analogs of mechanically cross-linked networks (topological gels or slide-ring materials[7a]). Improvement in synthetic control over the average density of macrocycles in polypseudorotaxanes should, by extension, lead to an increased ability to introduce and orchestrate the distribution of slip-links within network materials.

To date, most main-chain polypseudorotaxane syntheses have been performed via either solution-phase treatment of preformed polymers with macrocycles (such as crown ethers or cyclodextrins) or by various polymerizations of monomers in the presence of macrocycles.[9] Important general factors that affect threading/dethreading equilibria have been studied and applied so as to allow observation of a range of threading efficiencies;[10,11] furthermore, mathematical expressions have been derived to predict the extent of threading.[12] With these synthetic approaches, numerous structurally diverse polypseudorotaxanes have been prepared; however, since these methods rely upon the efficiency of threading, most examples generally show a lack of specific control over the ultimate number of macrocycles present per given length of polymer (average linear density of threaded macrocycle, ALDTM[11]). Control over this parameter is of further consequence, beyond the above-mentioned long-term motivation, because physical properties of both polypseudorotaxanes and polyrotaxanes track with changes in the ALDTM.[9c] Thus, selective methods are needed to precisely control the density of threaded macrocycles within polypseudorotaxanes.

Toward this goal, we have previously reported an entropy-driven ring-opening olefin metathesis homopolymerization of a [2]catenate via a novel ring−chain equilibration.[8a] This approach does not depend upon threading efficiency; instead, it benefited from use of prethreaded metalated monomers to provide metalated pseudorotaxane polymers that were essentially saturated with macrocycles, where every monomeric repeat unit of the backbone was encircled by exactly one macrocycle.[13] To gain ALDTM selectivity, we envisioned that use of ring-opening olefin metathesis copolymerizations[14,15] of noncatenated macrocycles with [2]catenates, in specific proportions, could allow access to metalated polypseudorotaxanes with predetermined linear densities of macrocycles threaded upon the formed polymer chains, Scheme 1.

Herein we describe the first study of random ring-opening olefin metathesis copolymerizations of macrocycles and [2]-catenates to provide main-chain metalated polypseudorotax-

Scheme 1. Metalated Pseudorotaxane Polymers via Ring Opening, Copolymerization of a Macrocycle, and a [2]Catenate
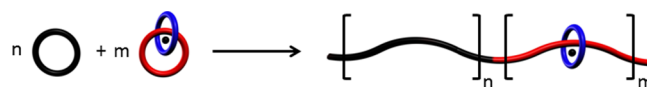
anes. Most importantly, simple adjustment of the monomer feed ratio allows both full and fine control over the ALDTM.

To explore the feasibility of such a copolymerization, we initially sought to copolymerize two custom macrocyclic monomers. The monomers were designed with the following criteria in mind: (1) similar reactivity/polymerizability, (2) the macrocycles need to be large enough and feature a molecular recognition template site so that [2]catenates of the macrocycles may be prepared in high yield, and (3) the monomers should have discernible spectroscopic signatures such that, once incorporated within a copolymer, the relative proportion of each type of monomeric unit may be readily quantified. Thus, we prepared both monomers $\mathbf{1}^{8a}$ and $\mathbf{2}^{16}$ (46-membered rings, shown in Table 2) in divergent five-step syntheses beginning with 1,10-phenanthroline.

Initially, separate ring-opening olefin metathesis homopolymerizations of **1** and **2** were tested under identical conditions. In each case, a highly concentrated CH_2Cl_2 solution of the monomer (200 mM) was treated with 1 mol % Grubbs' second generation catalyst,[17] Table 1, entries 1 and 2. After stirring

Table 1. Homopolymerization and Copolymerization of Macrocycles

entry	ratio **1:2** (%)	polymer (%)	M_n (kDa)^c	DP^c	PDI^c	%^{d}
1	100:0	**3**, 94^a	50	63 ± 1	2.0	0
2	0:100	**4**, 92^a	32	39 ± 1	1.5	100
3	50:50	**5**, 88,^{a} 86^b	32	39 ± 1	1.4	49

^{a}Conversion of monomer (by SEC). ^{b}Isolated yield of copolymer. ^{c}By SEC using PS standards. ^{d}Percent monomers within the polymer derived from monomer **2** (by NMR).

each reaction for 4 h at rt, both monomers were mainly consumed (>90% conversion) as determined by analytical size-exclusion chromatography (SEC). The observed extents of conversion are noteworthy given the entropy-driven ring−chain equilibration mechanism[18] for this polymerization. Interestingly, despite only minor structural differences between monomers **1** and **2**, equilibration beginning with **1** resulted in a polymer (**3**) with a higher degree of polymerization (DP) than equilibration beginning with **2**. Furthermore, monomer **1** resulted in a polymer (**3**) with the thermodynamically expected M_w/M_n ratio (polydispersity index, PDI) of 2.0, thus indicating a more efficient and complete equilibration, compared to the equilibration involving **2**.

Copolymerization of **1** and **2** (1:1 molar feed ratio) was then performed (Table 1, entry 3). In this case, a similarly concentrated CH_2Cl_2 solution of the monomers (200 mM total monomer concentration) was treated with 1 mol % Grubbs' second generation catalyst. After stirring the reaction for 4 h at room temperature, both monomers were again mainly consumed. The resulting copolymer (**5**) was analyzed and found to possess a DP and PDI that were comparable to those observed for homopolymer **4**.

In order to accurately measure the copolymer composition of **5**, i.e., the relative incorporated quantity of the comonomers derived from **1** and **2**, the crude copolymer product mixture was carefully fractionated by preparative SEC. Subsequent analysis of the fractions by analytical SEC allowed for the grouping of fractions according to whether monomer was present. After further fractionation of mixed fractions, ultimately, and with negligible loss of material (~2%), excellent separation of both the oligomer and polymer from monomer

was achieved. The recombined polymer and oligomer, without monomer according to analytical SEC, was then probed by ^1H NMR spectroscopy. Due to the presence of the two methyl substituents of monomer **2** and their absence from monomer **1**, three readily integratable signals in the ^1H NMR spectrum of copolymer **5** allowed for the direct quantification of the relative proportion of both monomeric units within the copolymer. Analysis revealed that copolymer **5** consisted of 51% of a monomer derived from **1** and of 49% of a monomer derived from **2**. Thus, despite some minor differences in the homopolymerizations of **1** and **2**, the incorporation of the two monomers into copolymer **5** closely matched the 1:1 monomer feed ratio.

Given the satisfactory copolymerizability of **1** and **2**, we separately prepared both a Sauvage-type[19] [2]catenate of macrocycle **1** (**6**)[8a] and also the analogous [2]catenate of macrocycle **2** (**7**).[16] Two series of copolymerizations were then performed, namely, copolymerizations of macrocycle **2** with [2]catenate **6** and also copolymerizations of macrocycle **1** with [2]catenate **7**, Table 2. In these two series, the feed ratios of the noncatenated macrocycles (**1** and **2**) to the catenated macrocycles (**6** and **7**) were systematically varied to determine the feasibility of controllably targeting specific ALDTMs for the formed polymer chains.

In the first series of copolymerizations employing monomers **2** and/or **6**, indeed, it was found that as the amount of the [2]catenate comonomer **6** was increased from 0% to 100% in the feed ratio, the ALDTM for the resultant polymers increased, correspondingly, from 0% to 100%. For example, at the opposite limits of this series, the homopolymerization of **2** (Table 2, entry 1) provided bare polymer **4**, i.e., a polymer without any threaded macrocycles (ALDTM = 0%) while the homopolymerization of **6** (Table 2, entry 7) resulted in metalated pseudorotaxane polymer **13**, wherein every monomeric unit of the polymer backbone was encircled by exactly one macrocycle (ALDTM = 100%). Notably, in this latter case, the average molecule of **13** contained ca. 77 threaded macrocycles. In these metalated polypseudorotaxanes (**8−13**, and also **20−23**), the threaded macrocycles (**28**), originating from [2]catenate **6** or **7**, remained bound via the copper(I) ion and thus stably threaded upon the polymer backbone, even without bulky chain termini.[8a]

The copolymerization of macrocycle **2** with varying relative amounts of [2]catenate **6** (10%−90%, where the total monomer concentration was held constant at 200 mM) resulted in metalated pseudorotaxane polymers **8−12**, Table 2, entries 2−6. In order to determine the degree of polymerization for these metalated polypseudorotaxanes as well as the copolymer composition (and thus the ALDTM for the formed polymer chains), the metalated polypseudorotaxanes were quantitatively demetalated via treatment with aq. KCN. Importantly, removal of the copper(I) ions concomitantly induced release of the threaded macrocycles (**28**) from the acyclic polymer chains. Then, as with copolymer **5**, each of the resulting bare copolymers (**14−18**) was carefully isolated by preparative SEC from the unreacted monomers and **28**. Subsequent analysis, by analytical SEC and ^1H NMR spectroscopy, showed that the copolymer composition of **14−18**, again, closely matched the comonomer (**2** and **6**) feed ratios.

Since demetalation of polypseudorotaxanes **8−12** does not affect the copolymer composition or otherwise alter the microstructure or DP of copolymers **14−18**, the ALDTM for

Table 2. Homopolymerization and Copolymerization of Macrocycles and [2]Catenates
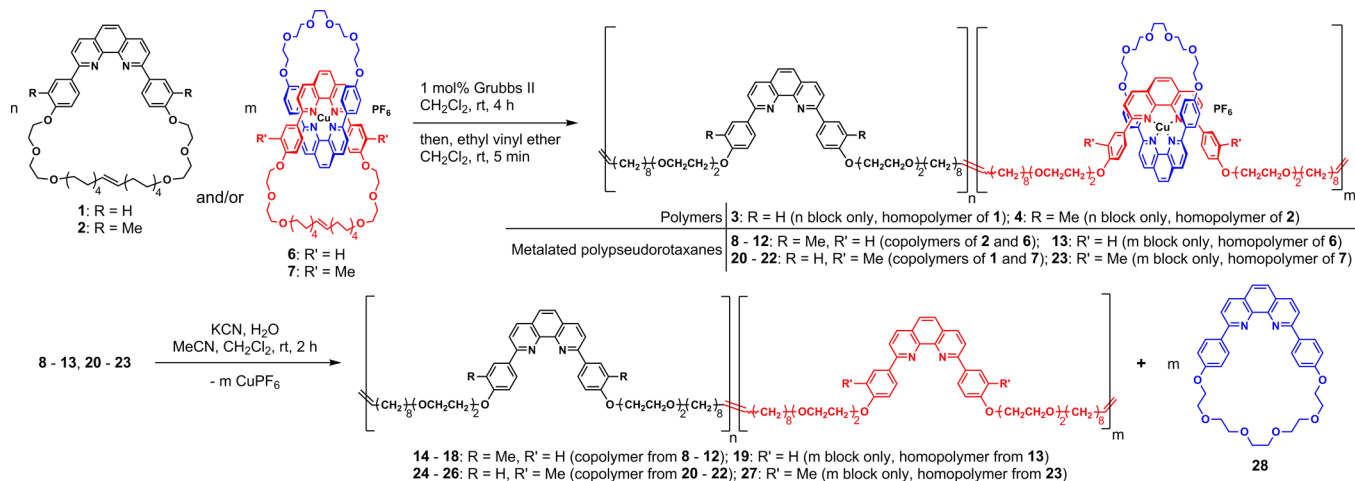
entry	monomer feed ratio (%)	isolated yield (%)[a]	M_n (kDa)[b]	DP[b]	PDI[b]	ALDTM (%)[c]	consecutive macrocycles[d]
1	**2:6** = 100:0	**4**: nd[e]	**4**: 32	**4**: 39 ± 1	**4**: 1.5	**4**: 0	**4**: 0
2	**2:6** = 90:10	**14**: 86	**8**: 22, **14**: 21	**8, 14**: 25 ± 1	**8, 14**: 1.4	**8**: 8.7 ± 5.5	**8**: 1.1 ± 0.8
3	**2:6** = 75:25	**15**: 91	**9**: 28, **15**: 23	**9, 15**: 28 ± 1	**9, 15**: 1.7	**9**: 24.3 ± 4.5	**9**: 1.3 ± 0.3
4	**2:6** = 50:50	**16**: 89	**10**: 43, **16**: 31	**10, 16**: 38 ± 1	**10, 16**: 1.7	**10**: 49.0 ± 3.1	**10**: 2.0 ± 0.2
5	**2:6** = 25:75	**17**: 87	**11**: 51, **17**: 32	**11, 17**: 40 ± 1	**11, 17**: 1.7	**11**: 77.0 ± 4.6	**11**: 4.3 ± 1.1
6	**2:6** = 10:90	**18**: 86	**12**: 83, **18**: 49	**12, 18**: 61 ± 1	**12, 18**: 1.6	**12**: 91.4 ± 5.5	**12**: 12 ± 8
7	**2:6** = 0:100	**19**: nd[e]	**13**: 110, **19**: 61	**13, 19**: 77 ± 2	**13, 19**: 2.0	**13**: 100	**13**: 77 ± 2
8	**1:7** = 100:0	**3**: nd[e]	**3**: 50	**3**: 63 ± 1	**3**: 2.0	**3**: 0	**3**: 0
9	**1:7** = 75:25	**24**: 87	**20**: 46, **24**: 38	**20, 24**: 48 ± 1	**20, 24**: 1.8	**20**: 24.5 ± 4.5	**20**: 1.3 ± 0.3
10	**1:7** = 50:50	**25**: 88	**21**: 45, **25**: 32	**21, 25**: 40 ± 1	**21, 25**: 1.5	**21**: 48.6 ± 3.1	**21**: 1.9 ± 0.2
11	**1:7** = 25:75	**26**: 89	**22**: 46, **26**: 29	**22, 26**: 36 ± 1	**22, 26**: 1.8	**22**: 72.8 ± 4.4	**22**: 3.7 ± 0.8
12	**1:7** = 0:100	**27**: nd[e]	**23**: 53, **27**: 30	**23, 27**: 36 ± 1	**23, 27**: 2.0	**23**: 100	**23**: 36 ± 1

[a]Isolated yield of copolymers (**14−18** and **24−26**) after removal of monomers, $CuPF_6$, and **28**. [b]By SEC in $CHCl_3$, calibrated with PS standards. [c]ALDTM = Average linear density of threaded macrocycles (expressed as percentage), by ^{1}H NMR. [d]Average number of consecutive threaded macrocycles, by ^{1}H NMR. [e]nd = not determined.

the metalated polypseudorotaxanes (**8−12**) can be inferred from the copolymer composition of the corresponding, resulting copolymers (**14−18**). Thus, metalated polypseudorotaxanes (**8−12**) were formed with ALDTMs that ranged from ~9% to 91%, closely matching the percentage of [2]catenate **6** (10%−90%) used in the comonomer feed. Interestingly, as in the case of the homopolymerization of macrocycle **1**, the homopolymerization of **6** (i.e., the [2]catenate of macrocycle **1**) also occurred with a greater degree of polymerization (DP) than the homopolymerization macrocycle **2**.

In the second series of copolymerizations employing monomers **1** and/or **7**, Table 2, entries 8−12, the amount of the [2]catenate comonomer **7** was analogously increased from 0% to 100% in the feed ratio. As with the first series, the ALDTM for the resultant polymers (**3**, **20−23**) likewise increased, correspondingly, from 0% to 100%.

As described above, all of the metalated polypseudorotaxanes possess well-defined predetermined ALDTMs. However, the ALDTM quantity does not provide certain information about the copolymer microstructure, i.e., the average sequence length or, more pertinently, the average number of consecutive macrocycles along the copolymer backbone. Given the dynamic mechanism of olefin metathesis[18] and the use of similar symmetrical macrocyclic olefins, these copolymerizations are expected to yield random (statistical) copolymers, without selectivity for comonomer alternation or block formation. Since statistical copolymer populations possess statistical sequence lengths ranging from 1 to DP, one can readily calculate the average sequence length as a function of monomer feed ratio[3] (or DP[20]). For example, for a 50:50 copolymer with a DP of 40, the average block size is approximately 1.95.[20] Thus, for metalated polypseudorotaxanes **10** and **21**, with average linear macrocycle densities of approximately 50%, the average number of consecutive macrocycles encircling these copolymer backbones is approximately 2. Furthermore, approximately 25% of all threaded macrocycles (**28**) within **10** and **21** can be found within blocks of 2. For the other metalated polypseudorotaxanes, the average number of consecutive threaded macrocycles ranged from ~1 to 77, as listed in Table 2.

In summary, we report a ring-opening olefin metathesis copolymerization of macrocycles and [2]catenates to provide main-chain metalated polypseudorotaxanes. In this approach, metalated polypseudorotaxanes are obtained without any byproduct via an entropy-driven ring−chain equilibration mechanism. Homopolymerization of the noncatenated macrocycles produced polymers with 0% threaded macrocycles

whereas homopolymerization of the catenated macrocycles produced metalated polypseudorotaxanes with 100% threaded macrocycles. Copolymerization of macrocycles and [2]-catenates, in various feed ratios, produced metalated polypseudorotaxanes with average linear macrocycle densities between the two limits, thus demonstrating targeted selectivity for specific macrocycle densities over the full range of possible densities.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Synthetic procedures, characterization data, NMR spectra, and SEC chromatograms. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
mf.mayer@ttu.edu

Present Addresses
[†]Department of Chemistry and Biochemistry, The University of Texas at Austin, Austin, Texas 78712, United States.
[‡]Department of Surgery, Duke University Medical Center, Durham, North Carolina 27710, United States.

Notes
The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

■ REFERENCES

(1) Callister, W. D., Jr.; Rethwisch, D. G. *Materials Science and Engineering: An Introduction*, 8th ed.; Wiley: USA, 2010.
(2) (a) Wang, A.; Huang, J.; Yan, Y. *Soft Matter* **2014**, *10*, 3362. (b) Stupp, S. I.; Zha, R. H.; Palmer, L. C.; Cui, H.; Bitton, R. *Faraday Discuss.* **2013**, *166*, 9.
(3) Hiemenz, P. C.; Lodge, T. P. *Polymer Chemistry*, 2nd ed.; CRC Press: Boca Raton, FL, 2007.
(4) (a) Likhtman, A. E.; Ponmurugan, M. *Macromolecules* **2014**, *47*, 1470. (b) Haas, H. C.; Livingston, D. I. *J. Polym. Sci.* **1955**, *17*, 135.
(5) (a) Granick, S.; Rubinstein, M. *Nat. Mater.* **2004**, *3*, 586. (b) de Gennes, P. G. *Physica A* **1999**, *271*, 231. (c) Ball, R. C.; Doi, M.; Edwards, S. F.; Warner, M. *Polymer* **1981**, *22*, 1010.
(6) (a) Kato, K.; Yasuda, T.; Ito, K. *Polymer* **2014**, *55*, 2614. (b) Mayumi, K.; Tezuka, M.; Bando, A.; Ito, K. *Soft Matter* **2012**, *8*, 8179.
(7) (a) Noda, Y.; Hayashi, Y.; Ito, K. *J. Appl. Polym. Sci.* **2014**, DOI: 10.1002/APP.40509. (b) Wang, Y.; Li, X.; Pan, Y.; Zheng, Z.; Ding, X.; Peng, Y. *RSC Adv.* **2014**, *4*, 17156. (c) Okumura, Y.; Ito, K. *Adv. Mater.* **2001**, *13*, 485.
(8) (a) Kang, S.; Berkshire, B. M.; Xue, Z.; Gupta, M.; Layode, C.; May, P. A.; Mayer, M. F. *J. Am. Chem. Soc.* **2008**, *130*, 15246. (b) Gupta, M.; Kang, S.; Mayer, M. F. *Tetrahedron Lett.* **2008**, *49*, 2946.
(9) (a) Arunachalam, M.; Gibson, H. W. *Prog. Polym. Sci.* **2014**, *39*, 1043. (b) Harada, A.; Hashidzume, A.; Yamaguchi, H.; Takashima, Y. *Chem. Rev.* **2009**, *109*, 5974. (c) Huang, F.; Gibson, H. W. *Prog. Polym. Sci.* **2005**, *30*, 982.
(10) Shen, Y. X.; Xie, D.; Gibson, H. W. *J. Am. Chem. Soc.* **1994**, *116*, 537.
(11) Threading efficiency has been defined as the number of macrocycles present per monomeric repeat unit of the polymer backbone (x/n),[10] and it is numerically equivalent to the average linear density of threaded macrocycle (ALDTM).[16]
(12) Agam, G.; Graiver, D.; Zilkha, A. *J. Am. Chem. Soc.* **1976**, *98*, 5206.
(13) For a related approach to polyrotaxanes via olefin metathesis polymerization, see: Momčilović, N.; Clark, P. G.; Boydston, A. J.; Grubbs, R. H. *J. Am. Chem. Soc.* **2011**, *133*, 19087.
(14) For entropy-driven ring-opening olefin metathesis polymerizations of noncatenated macrocycles, see: (a) Xu, Y.; Xu, W. L.; Smith, M. D.; Shimizu, L. S. *RSC Adv.* **2014**, *4*, 1675. (b) Peng, Y.; Decatur, J.; Meier, M. A. R.; Gross, R. A. *Macromolecules* **2013**, *46*, 3293. (c) Gao, W.; Hagver, R.; Shah, V.; Xie, W.; Gross, R. A.; Ilker, M. F.; Bell, C.; Burke, K. A.; Coughlin, E. B. *Macromolecules* **2007**, *40*, 145. (d) Gautrot, J. E.; Zhu, X. X. *Angew. Chem., Int. Ed.* **2006**, *45*, 6872. (e) Tastard, C. Y.; Hodge, P.; Ben-Haida, A.; Dobinson, M. *React. Funct. Polym.* **2006**, *66*, 93. (f) Marsella, M. J.; Maynard, H. D.; Grubbs, R. H. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1101. For a review, see: (g) Xue, Z.; Mayer, M. F. *Soft Matter* **2009**, *5*, 4600.
(15) For entropy-driven ring-opening olefin metathesis copolymerizations of noncatenated macrocycles, see: (a) Pepels, M. P. F.; Hansen, M. R.; Goossens, H.; Duchateau, R. *Macromolecules* **2013**, *46*, 7668. (b) Xie, M.; Wang, W.; Ding, L.; Liu, J.; Yang, D.; Wei, L.; Zhang, Y. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, *48*, 380. (c) Gautrot, J. E.; Zhu, X. X. *Chem. Commun.* **2008**, 1674. (d) Yang, Y.; Swager, T. M. *Macromolecules* **2007**, *40*, 7437. (e) Hodge, P.; Kamau, S. D. *Angew. Chem., Int. Ed.* **2003**, *42*, 2412. (f) Maynard, H. D.; Grubbs, R. H. *Macromolecules* **1999**, *32*, 6917.
(16) See Supporting Information.
(17) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953.
(18) Monfette, S.; Fogg, D. E. *Chem. Rev.* **2009**, *109*, 3783.
(19) (a) Weck, M.; Mohr, B.; Sauvage, J.-P.; Grubbs, R. H. *J. Org. Chem.* **1999**, *64*, 5463. (b) Dietrich-Buchecker, C.; Sauvage, J.-P. *Tetrahedron* **1990**, *46*, 503.
(20) Clevenger, E. S. Ph.D. Dissertation, Texas Tech University, Lubbock, TX, 2014.