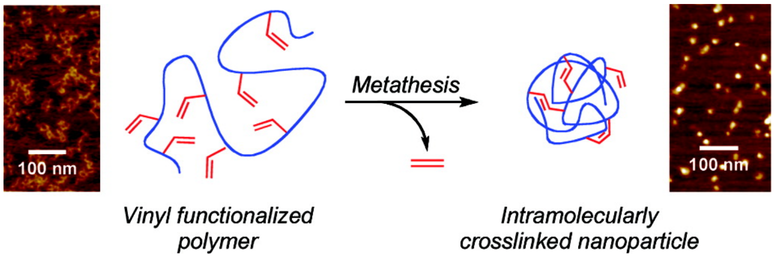
Communication

Formation of Nanoparticles by Intramolecular Cross-Linking: Following the Reaction Progress of Single Polymer Chains by Atomic Force Microscopy

Anna E. Cherian, Frank C. Sun, Sergei S. Sheiko, and Geoffrey W. Coates

J. Am. Chem. Soc., **2007**, 129 (37), 11350-11351• DOI: 10.1021/ja074301l • Publication Date (Web): 28 August 2007



ACS Publications
High quality. High impact.

Journal of the American Chemical Society is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

J|A|C|S
COMMUNICATIONS

Formation of Nanoparticles by Intramolecular Cross-Linking: Following the Reaction Progress of Single Polymer Chains by Atomic Force Microscopy

Anna E. Cherian,[†,‡] Frank C. Sun,[§] Sergei S. Sheiko,*[,§] and Geoffrey W. Coates*[,†]

Department of Chemistry and Chemical Biology, Baker Laboratory, Cornell University, Ithaca, New York 14853-1301, and Department of Chemistry, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599-3290

Received June 13, 2007; E-mail: sergei@email.unc.edu; gc39@cornell.edu

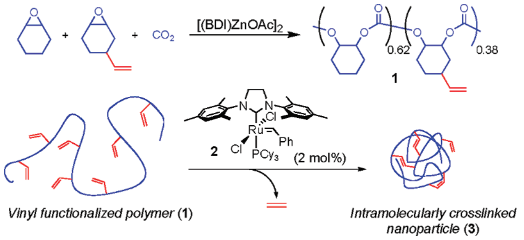
Significant interest in the controlled synthesis of polymeric nanoparticles has developed in the past decade. These small particles have numerous applications, including drug delivery systems,[1] photonic crystals,[2] and nanoporous materials for low dielectric applications.[3] Methods for synthesizing polymeric nanoparticles include several approaches, including generation of micro- and mini-emulsions,[4] self-assembly of amphiphilic diblock copolymers into micelles,[5] synthesis of dendrimers,[6] and chain collapse through intramolecular cross-linking.[7]

Olefin cross-metathesis has been used to cross-link and stabilize supramolecular assemblies, including cylindrical peptide assemblies,[8] the shells of polymeric micelles,[9] and the peripheries of dendrimers.[10] Metathesis reactions of linear polymer chains with pendant vinyls give a range of results, depending on reaction conditions. When the vinyl groups are located at suitable distances for cyclization, as in 1,2-polybutadiene, formation of rings along the chain occurs.[11] When the vinyl groups are spaced too far apart for convenient ring-closing metathesis, as in poly(methylenecyclopentane-*co*-vinyltetramethylene) synthesized from the polymerization of 1,5-hexadiene,[12] functional groups can be attached through olefin cross-metathesis.[13] In the absence of a cross-metathesis partner, the polymer undergoes cross-linking, which can be limited to intramolecular cross-linking under dilute conditions.[14] We reasoned that this intramolecular cross-linking would be effective with any type of linear polymer which contained pendant vinyl groups, including aliphatic polycarbonates. Aliphatic polycarbonates have relatively low and clean thermal decompositions (<250 °C), making them ideal for electronics applications such as nanoporous insulators.

The synthesis of polycarbonates with vinyl functionality was achieved through the terpolymerization of cyclohexene oxide (CHO), vinylcyclohexene oxide (VCHO), and CO_2 with a β-diiminate zinc(II) acetate catalyst ($[(BDI)ZnOAc]_2$) (Scheme 1).[15] Reactivity of CHO and VCHO are comparable, such that reaction of a 70:30 mixture of CHO/VCHO gave a polymer (**1**) with 38 mol % of vinyl-containing polycarbonate units. The polymer had a high molecular weight ($M_n = 54\,100$ g/mol) and narrow molecular weight distribution ($M_w/M_n = 1.20$), representative of the living nature of the polymerization.

Grubbs' catalyst (**2**)[16] effectively cross-metathesized the pendant vinyl groups along the polymer chain, releasing ethylene as a byproduct (Scheme 1). At high concentrations of polymer (>10 mg/mL), cross-linking occurred both intra- and intermolecularly, as exhibited by an increase in the apparent molecular weight (M_n) and a broadening of the molecular weight distribution (M_w/M_n) as observed by gel permeation chromatography (GPC). However, when **2** was added to dilute polymer solutions (1 mg/mL), the apparent molecular weight decreased steadily, and the molecular weight distribution remained narrow, indicating that only intramolecular cross-linking occurred.

Scheme 1. Synthesis of Alkene Cross-Linked Polycarbonate Nanoparticles



A series of cross-metathesis reactions were performed for different amounts of time (Table 1). The cross-metathesis reaction progressed quickly in the beginning, with 42% of the pendant vinyl groups forming cross-links within 15 min, but the metathesis slowed down as the reaction progressed, presumably due to the increasingly constrained movement of the polymer chain. The apparent molecular weight of the polymer also decreased as cross-links were formed, dropping from 54 100 to 31 500 g/mol after 4 h, indicating a decrease of hydrodynamic volume. In addition, the glass transition temperature (T_g) increases as the chain collapses from an initial value of 114 to 194 °C at 76% cross-linking. This is also consistent with cross-linking as it hinders segmental chain mobility.

Formation of molecular nanoparticles was confirmed by atomic force microscopy (AFM) through visualization of individual molecules[17] at different stages of cross-linking. Figure 1a−d shows height images of samples 1−3 and 5 (Table 1) prepared by spin-casting from a dilute solution in 1,2,4-trichlorobenzene on a mica substrate. The unreacted polymer (Table 1, entry 1) in Figure 1a reveals extended molecules that adsorb as either isolated species or clusters of overlapped chains. The number average length of the isolated molecules was measured to be $L_n = 58 \pm 7$ nm. This is about 3 times shorter than $L_0 = 176$ nm, the length of a fully extended polymer chain with a number average degree of polymerization of $N_n = 370$ and indicates a coiled microconformation of the polymer chain. In the course of the cross-linking reaction, molecules became more compact, occupying a smaller area (Figure 1b−d). The majority of the cross-linked molecules were visualized as isolated particles, providing further support, along with the GPC data in Table 1, for predominate intramolecular cross-linking under dilute conditions.

To characterize the change in elasticity of the molecular particles, we measured the number average particle area (Σ) and determined the extension ratio $\lambda = \Sigma/\Sigma_1$, where $\Sigma_1 = 24$ nm^2 (the area occupied by a solid spherical particle with a M_n of 54 100 g/mol and dry volume (V) of 90 nm^3). Figure 1e shows that the extension ratio

---

[†] Cornell University.
[‡] Present address: Novomer, LLC, Ithaca, NY.
[§] University of North Carolina at Chapel Hill.

10.1021/ja074301l CCC: $37.00

Table 1. Intramolecular Cross-Linking of **1** Using **2**[a]

entry	time (h)	M_n[b] (g/mol)	M_w/M_n[b]	% vinyls cross-linked[c]	T_g[d] (°C)
1	0	54 100	1.20	0	114
2	0.25	45 700	1.34	42	157
3	0.50	39 500	1.26	59	167
4	2.0	33 000	1.19	70	185
5	4.0	31 500	1.19	76	194

[a] All reactions were run with 2 mol % of Ru catalyst at 22 °C with 1.0 mg polymer/mL toluene. [b] Determined by GPC in THF at 40 °C versus polystyrene standards. [c] Determined by ^{1}H NMR spectroscopy. [d] Determined by differential scanning calorimetry (second heat).

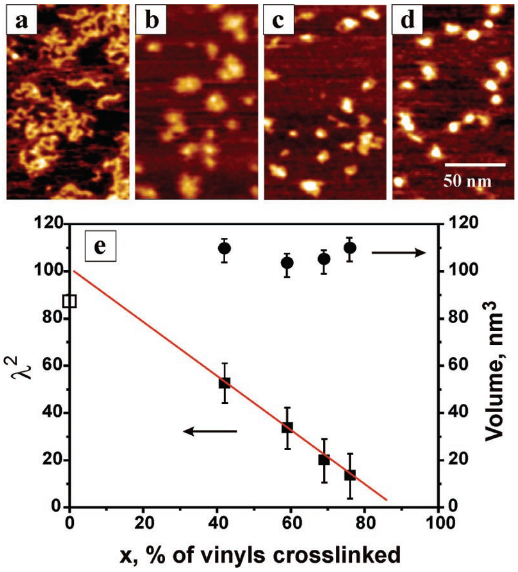


Figure 1. AFM height images for the nanoparticles in Table 1: (a) entry 1, (b) entry 2, (c) entry 3, (d) entry 5. (e) The plot presents the square of the extension ratio $\lambda = \Sigma/\Sigma_1$ and the particle volume $V \cong \Sigma h$ as a function of the percentage of cross-linked vinyl groups. The hollow square symbol corresponds to $\lambda = \Sigma_0/\Sigma_1$ of the uncross-linked molecule (see text). The percent cross-linking was determined using NMR spectroscopy.

decreases with cross-linking, while the volume of the particles remains nearly constant. Furthermore, the square of the extension ratio (λ^2) exhibits linear dependence on the degree of cross-linking. Extrapolation of the line to $x = 0$ gives $\lambda^2 = 102 \pm 3$ and $\Sigma = 242 \pm 7$ nm^2, which is consistent with the calculated area of a flat molecular disk ($\Sigma_0 = V/h = 90$ nm^3/0.4 nm $= 225$ nm^2).

In order to understand the observed linear dependence, we considered a cross-linked molecule as an affine network which was deformed due to attraction to the substrate. Deformation of the network $\lambda = \Sigma/\Sigma_1$ can be determined by minimization of the particle's free energy $F = F_e + F_s + F_{vdw}$. The first term, $F_e = nkT(2\lambda + 1/\lambda^2 - 3)/2$, is the free energy change due to substrate-caused deformation of the molecule, where n is the number of network strands per molecule. The second contribution is the energy decrease due to spreading on the substrate, $F_s = (\gamma_s - \gamma_p - \gamma_{sp})\Sigma$, where γ_s, γ_p, and γ_{sp} are the surface energies of the substrate, polymer, and polymer−substrate interfaces, respectively. The third term represents the long-range van der Waals interactions between the particle and the substrate, $F_{vdw} \cong -A\Sigma/12\pi h^2$, where A is the Hamaker constant and h is the particle thickness. Minimization of the total free energy for $\lambda > 1$ and $V \cong \Sigma h$ gives $\lambda^2 = (S\Sigma_1 - nkT)/3A$, which explains the linear dependence $\lambda^2(x)$ since the number of network strands is linearly proportional to the fraction of cross-linked vinyl groups, $n \sim x$.[18]

In summary, we have demonstrated a unique way to transform linear polymers into nanoparticles of controlled dimensions by the application of olefin metathesis. AFM was demonstrated to be an effective technique to monitor covalent cross-linking reactions in polymers, complementary to other previously demonstrated molecular-scale processes such as formation and scission of covalent bonds, conformational transitions, diffusion, and flow.[19]

Acknowledgment. G.W.C. gratefully acknowledges funding from the NSF (CHE-0243605). This work is supported in part by the New York State Office of Science, Technology, and Research (Grant C020023). This research made use of the Cornell Center for Materials Research Shared Experimental Facilities supported through the NSF MRSEC (DMR-0520404). S.S. thanks CBET and DMR divisions of the NSF as well as Petroleum Research Fund for financial support of this research.

Supporting Information Available: Polymer synthesis and characterization, polymer cross-metathesis data, and nanoparticle characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Benoit, J.-P.; Puisieux, F. In *Polymeric Nanoparticles and Microspheres*; Guiot, P., Couvreur, P., Eds.; CRC Press: Boca Raton, FL, 1986.
(2) Xia, Y.; Gates, B.; Yin, Y.; Lu, Y. *Adv. Mater.* **2000**, *12*, 693−713.
(3) Hedrick, J. L.; Miller, R. D.; Hawker, C. J.; Carter, K. R.; Volksen, W.; Yoon, D. Y.; Trollsås, M. *Adv. Mater.* **1998**, *10*, 1049−1053.
(4) Landfester, K. *Adv. Mater.* **2001**, *13*, 765−768.
(5) (a) Thurmond, K. B., II; Kowalewski, T.; Wooley, K. L. *J. Am. Chem. Soc.* **1997**, *119*, 6656−6665. (b) Bertin, P. A.; Gibbs, J. M.; Shen, C. K.-F.; Thaxton, C. S.; Russin, W. A.; Mirkin, C. A.; Nguyen, S. T. *J. Am. Chem. Soc.* **2006**, *128*, 4168−4169.
(6) (a) Bosman, A. W.; Janssen, H. M.; Meijer, E. W. *Chem. Rev.* **1999**, *99*, 1665−1688. (b) Hecht, S.; Fréchet, J. M. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 74−91. (c) Pyun, J.; Zhou, X.-Z.; Drockenmuller, E.; Hawker, C. J. *J. Mater. Chem.* **2003**, *13*, 2653−2660. (d) Hawker, C. J.; Wooley, K. L. *Science* **2005**, *309*, 1200−1205.
(7) (a) Davankov, V. A.; Ilyin, M. M.; Tsyurupa, M. P.; Timofeeva, G. I.; Dubrovina, L. V. *Macromolecules* **1996**, *29*, 8398−8403. (b) Mecerreyes, D.; Lee, V.; Hawker, C. J.; Hedrick, J. L.; Wursch, A.; Volksen, W.; Magitang, T.; Huang, E.; Miller, R. D. *Adv. Mater.* **2001**, *13*, 204−208. (c) Harth, E.; Van Horn, B.; Lee, V. Y.; Germack, D. S.; Gonzales, C. P.; Miller, R. D.; Hawker, C. J. *J. Am. Chem. Soc.* **2002**, *124*, 8653−8660. (d) Mackay, M. E.; Dao, T. T.; Tuteja, A.; Ho, D. L.; van Horn, B.; Kim, H. C.; Hawker, C. J. *Nat. Mater.* **2003**, *2*, 762−766.
(8) Clark, T. D.; Kobayashi, K.; Ghadiri, M. R. *Chem.*−*Eur. J.* **1999**, *5*, 782−792.
(9) (a) Watson, K. J.; Zhu, J.; Nguyen, S. T.; Mirkin, C. A. *J. Am. Chem. Soc.* **1999**, *121*, 462−463. (b) Beil, J. B.; Zimmerman, S. C. *Macromolecules* **2004**, *37*, 778−787. (c) Skaff, H.; Lin, Y.; Tangirala, R.; Breitenkamp, K.; Böker, A.; Russell, T. P.; Emrick, T. *Adv. Mater.* **2005**, *17*, 2082−2086.
(10) (a) Zimmerman, S. C.; Zharov, I.; Wendland, M. S.; Rakow, N. A.; Suslick, K. S. *J. Am. Chem. Soc.* **2003**, *125*, 13504−13518. (b) Lemcoff, N. G.; Spurlin, T. A.; Gewirth, A. A.; Zimmerman, S. C.; Beil, J. B.; Elmer, S. L.; Vandeveer, H. G. *J. Am. Chem. Soc.* **2004**, *126*, 11420−11421.
(11) Coates, G. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 229−230.
(12) Hustad, P. D.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 11578−11579.
(13) Mathers, R. T.; Coates, G. W. *Chem. Commun.* **2004**, 422−423.
(14) Cherian, A. E.; Lee, H.; Mathers, R. T.; Coates, G. W. Manuscript in preparation.
(15) Moore, D. R.; Cheng, M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2003**, *125*, 11911−11924.
(16) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953−956.
(17) Sheiko, S. S.; Möller, M *Chem. Rev.* **2001**, *101*, 4099−4123.
(18) Even though the assumption of an affine network demonstrates good agreement with experiment, we do not claim that the molecules are affine networks. One should consider other types of network topologies including multiple loops that are typical for intramolecular cross-linking and do not contribute to the network elasticity.
(19) (a) Berge, T.; Haken, E. L.; Waring, M. J.; Henderson, R. M. *J. Struct. Biol.* **2003**, *142*, 241−246. (b) Xu, H.; Shirvaniants, D.; Beers, K.; Matyjaszewski, K.; Rubinstein, M.; Sheiko, S. S. *Phys. Rev. Lett.* **2004**, *93*, 206103/1−4. (c) Roiter, Y.; Minko, S. *J. Am. Chem. Soc.* **2005**, *127*, 15688−15689. (d) Al-ellani, R.; Barner, J.; Rabe, J. P.; Schlueter, A. D. *Chem.*−*Eur. J.* **2006**, *12*, 6542−6551. (e) Sheiko, S. S.; Sun, F.; Randal, A.; Shirvaniants, D.; Matyjaszewski, K.; Rubinstein, M. *Nature* **2006**, *440*, 191−194.

JA074301L