Macromolecules
COMMUNICATION TO THE EDITOR

Macromolecules **2010**, *43*, 4829–4832 **4829**
DOI: 10.1021/ma100367q

Cascade Chain-Walking Polymerization to Generate Large Dendritic Nanoparticles

Guobin Sun and Zhibin Guan*

Department of Chemistry, University of California, 1102 Natural Sciences 2, Irvine, California 92697-2025

Received February 15, 2010
Revised Manuscript Received April 19, 2010

This communication reports an efficient catalytic synthesis of large dendritic polymer nanoparticles as fully soluble polymer species. Soft organic/polymeric nanoparticles have received much attention recently because they have many potential applications including bioconjugation, catalysis, multivalent interactions, nanomedicines, and as nanobuilding blocks for constructing new materials.[1] Current methods for generating organic/polymeric nanoparticles can be broadly categorized into physical and chemical approaches. Physical methods include mini-emulsion polymerization[2] and laser techniques.[3] One major limitation of these physical methods is that the nanoparticles so prepared are not soluble molecular species, and they are generally only applicable to applications in which the nanoparticles remain insoluble in the media. For many applications, however, it is desirable to have soft nanoparticles as soluble molecular species because they have better mobility in solution and are more versatile for further functionalizations. Chemical synthesis, in principle, can circumvent these limitations. As an example, dendrimers are ideally suited for this purpose. The unique physical and chemical properties of dendrimers have been capitalized in the preparation of nanomaterials for a wide variety of applications.[4] They can be prepared with precise control through either a convergent or divergent multistep iterative synthesis.[5] However, construction of large size (> 10 nm), high-generation dendrimers using multistep iterative strategies is problematic because of synthesis difficulty. Furthermore, theoretical consideration based on steric congestion predicts the maximal generation of classical dendrimers to be ~10.[6,7] There is a fundamental gap in preparing soluble soft nanoparticles with size in the range of 10−100 nm, the size range of particular interest for many nanoparticle-based applications. Herein we wish to report a method to access efficiently dendritic soft nanoparticles with diameter > 100 nm directly by the catalytic ethylene polymerization based on a newly designed multivalent chain-walking catalyst (MVCWC) (Scheme 1).

A few methods have been previously reported toward the synthesis of large dendritic nanoparticles. For example, Tomalia et al. utilized low-generation dendrimers as building blocks to synthesize large core−shell tecto(dendrimers) nanostructures.[7] Gnanou, Hedrick, and Taton et al. prepared large dendrimer-like homopolymers and block copolymers with highly branched and globular structures through a multistep iterative approach based on "controlled/living" polymerization.[8] Despite the elegance of these approaches, no catalytic polymerization methods have been reported for efficient generation of large soluble dendritic nanoparticles.

Our approach is based on the chain-walking polymerization (CWP) using the Brookhart-type Pd(II)-α-diimine catalyst[9] for one-pot synthesis of dendritic polyethylenes (PEs).[10] Benefiting from good functional-group tolerance of the catalyst, a broad range of functional dendritic PEs were also prepared by chain-walking copolymerization of ethylene and polar olefins.[11,12] One limitation is that because of the inherent chain transfer process of the catalysts,[9b] the dendritic PEs are limited with maximal molecular weight of ~300 kDa (M_n) and radius of gyration (R_g) of ~15 nm. To circumvent this limitation, we recently developed a method based on CWP for directly making much larger soluble dendritic nanoparticles (Scheme 1).

In our first step, copolymerization of ethylene and a comonomer **2** (TBDPS-protected 2,2-dimethyl-pent-4-en-1-ol) using the standard Brookhart -type chain walking catalyst (**Pd-1**), followed by deprotection of TBDPS, afforded a dendritic copolymer **1b** carrying multiple hydroxyl groups, onto which multiple butenoate moieties functional groups were grafted. Treating the copolymer **1c** with the precursor of chain walking catalyst, **Pd-2**, in the presence of NaB(Ar′)$_4$ (Ar′ = 3,5-bis(trifluoromethyl)phenyl), led to activation of the catalyst onto the dendritic scaffold and formation of a multivalent chain walking catalyst (**1d**) having multiple activated catalytic sites covalently attached to the surface of the dendritic PE. Subsequent exposure of the MVCWC **1d** to low pressure of ethylene starts a subsequent CWP from multiple catalytic sites simultaneously, resulting in large dendritic PE nanoparticles having a dendrimer-on-dendrimer architecture. Furthermore, through the copolymerization of ethylene and functionalized olefins, large dendritic nanoparticles with a broad range of functionalities can be prepared for various soft nanoparticle-based applications.[13−16]

Initially, we attempted to prepare MVCWC using a dendritic PE functionalized with multiple acrylate groups on surface, which we prepared by treating the hydroxyl functionalized dendritic PEs **1b**[11b] with acryloyl chloride. However, because of high reactivity to radicals and nucleophiles, gelation always occurred during workup of this reaction. When 3-butenoyl chloride was used instead of acrylyl chloride, dendritic PEs **1c** with multiple 3-butenoate moieties was formed with good yield (Scheme 1). Apparently, separation of the double bond from the ester carbonyl by a methylene group significantly reduced the reactivity of the vinyl group toward radical or nucleophilic addition. To confirm the effectiveness of the 3-butenoate moiety for activating the palladium catalyst precursor (**Pd-2**) as well as the efficacy of so-formed catalyst in initiating CWP, methyl 3-butenoate was used for the synthesis of a model catalyst. The model catalyst is analogous to the standard chain walking catalyst (**Pd-1**) made from acrylate, differing only by an additional methyl group in the β-position of the chelating six-member ring (Scheme 1 and Figure S1 of the Supporting Information). Polymerization of ethylene at 0.1 atm using this model catalyst yielded dendritic PEs having similar molecular weight (M_n 3.30 × 10^5, PDI 1.71) and molecular size (R_g 14.6 nm) by size exclusion chromatography using multi-angle light scattering detector (SEC-MALLS) compared with PEs made by standard catalyst **Pd-1** (M_n 2.87 × 10^5, PDI 1.60, R_g 14.3 nm) under the same polymerization condition, and both have similar branch density (~100 branch per 1000 carbons), indicating that its catalytic properties are equivalent to the standard catalyst. This confirmed that Pd(II) catalyst prepared from 3-butenoate moiety is a competent chain walking catalyst for making dendritic PEs.

Therefore, MVCWC was prepared from dendritic PEs using the following procedures (Scheme 1). The initial hydroxyl functionalized dendritic PE (**1b**, M_n = 3.00 × 10^5 g/mol by

---

*Corresponding author. E-mail: zguan@uci.edu.

SEC-MALLS, ~300 hydroxyl groups/molecule) was treated with an excess amount of 3-butenoyl chloride to afford a 3-butenoate-functionalized polymer (**1c**, M_n = 3.13 × 10^5 g/mol, ~276 3-butenoate groups). Treating polymer **1c** with the Pd catalyst precursor **Pd-2** in the presence of NaB(Ar′)$_4$ gave the desired MVCWC (**1d**, M_n = 3.18 × 10^5 g/mol, ~174 Pd(II) catalytic sites). During the catalyst activation step, the number of covalently linked catalytic sites per molecule is ~63% of the number of 3-butenoate groups on the polymer precursor. A few possibilities could have contributed to the lower catalyst loading. First, because of the proximity of some attached olefin groups, it is possible to have multiple olefin insertion per catalyst activation, which will result in lower number of catalytic sites. Second, the activated catalytic sites may partially decompose during the reaction and workup. Nevertheless, the dendritic core contains a sufficient number of catalytic sites for subsequent CWP.

Exposure to ethylene at 0.1 atm, the MVCWC initiates a subsequent CWP at multiple catalytic sites simultaneously, leading to the formation of dendrimer-on-dendrimer type of dendritic nanoparticle (**PE-1**). After purification, the polymer was characterized by ^{1}H NMR, SEC-MALLS, and dynamic light scattering (DLS). The ^{1}H NMR spectrum shows that **PE-1** has branch density of ~100 per 1000 carbon atoms, similar to that of normal dendritic PE made with single-site chain walking catalyst,[10] indicating similar chain-walking behavior for MVCWC. SEC-MALLS provides absolute molecular weight and molecular size (R_g). As shown in Figure 1 and Table 1, the newly formed denditic naoparticle has a very high molecular weight (M_n = 3.60 × 10^7 g/mol), narrow PDI (1.11), and an average R_g of 48.1 nm. The much narrower polydispersity can be ascribed to the simple statistic effects: the combination of multiple dendritic polymers with broader PDI should result in larger polymers with narrower PDI. On the basis of molecular weight increase, it is estimated that ~71 individual dendritic PEs are covalently attached during the chain walking polymerization.

For a linear flexible polymer forming a random coil in good solvent, R_g scales as $M_w^{0.589}$.[17] Therefore, an increase in M_w by a factor of ~71 would result in an ~8 times increase in R_g for a linear polymer. However, the R_g for the dendritic nanoparticles only increases by a factor of 3.3 compared with the size of the individual dendritic PEs. This strongly supports the dendrimer-on-dendrimer kind of globular architecture. Additional evidence of molecular topology was provided by DLS studies. The hydrodynamic radius (R_h) of the nanoparticles was measured to be 59.6 nm by DLS. According to classical polymer solution theory, the ratio R_g/R_h reflects polymer chain architecture and segment density.[18] In general, value of R_g/R_h 0.78 in good solvents is predicted for a sphere. For our dendritic nanoparticles, this ratio is 0.81, supporting a globular spherical molecular architecture for our polymer. To confirm the dendrimer-on-dendrimer architecture further, we have conducted hydrolysis studies. After full hydrolysis of the ester linkages, the giant nanoparticles are cleaved into smaller dendritic PEs formed from each CWP catalytic site, as confirmed by the SEC characterization (Figure S6 in the Supporting Information).

The dendritic nanoparticles (**PE-1**) were directly imaged by atomic force microscopy (AFM). Samples were prepared by casting polymer solution on mica substrates, which were imaged

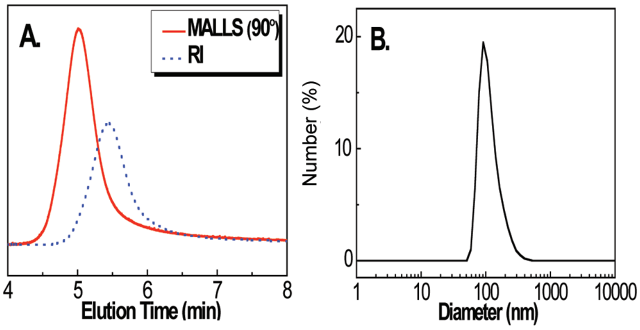


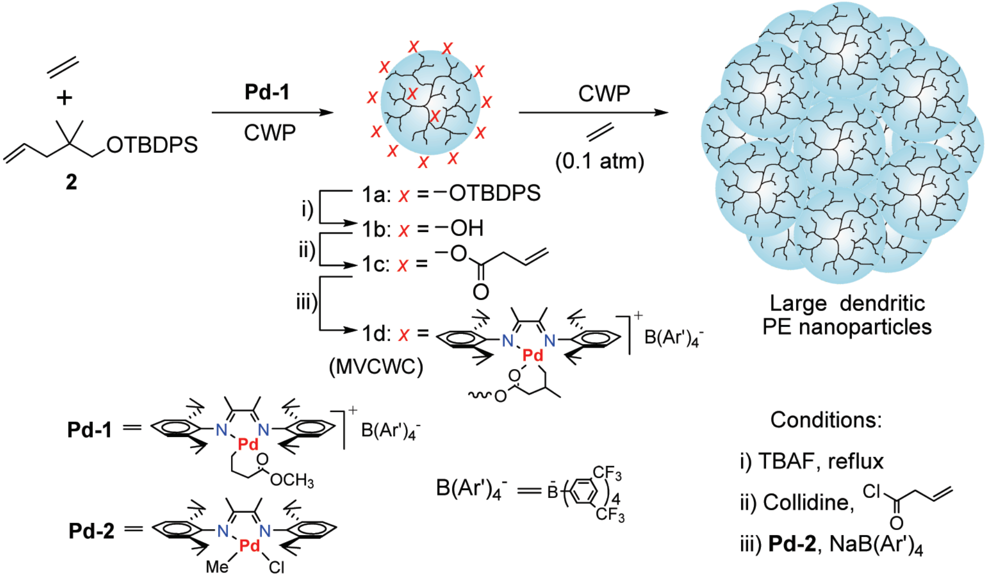
Figure 1. (A) Size exclusion chromatography (SEC) of **PE-1** in THF (1.0 mL/min) equipped with multi-angle laser light scattering (MALLS) detector (scattering angle 90°) and refractometric index (RI) detector and (B) particle size measurement by dynamic light scattering (DLS) of **PE-1** in THF.

Table 1. Characterization of Dendritic PE Nanoparticles and Functional Nanoparticles via Catalytic Chain-Walking Polymerization[a,b]

polymer	condition	M_n (10^6 g/mol)[c]	R_g (nm)[c]	PDI[c]	R_h (nm)[d]
PE-1	a	36.0	48.1	1.11	59.6
PE-2	b	63.4	54.7	1.08	59.0

[a] 0.1 atm of ethylene at r.t. for 2 days. [b] 0.1 atm of ethylene at r.t., copolymerizing with comonomer **2** (0.22 M) for 2 days. [c] Measured by SEC coupled to MALLS detector in THF (1 mL/min). [d] Measured by DLS.

Scheme 1. Synthesis of the Large Dendritic PEs by CWP



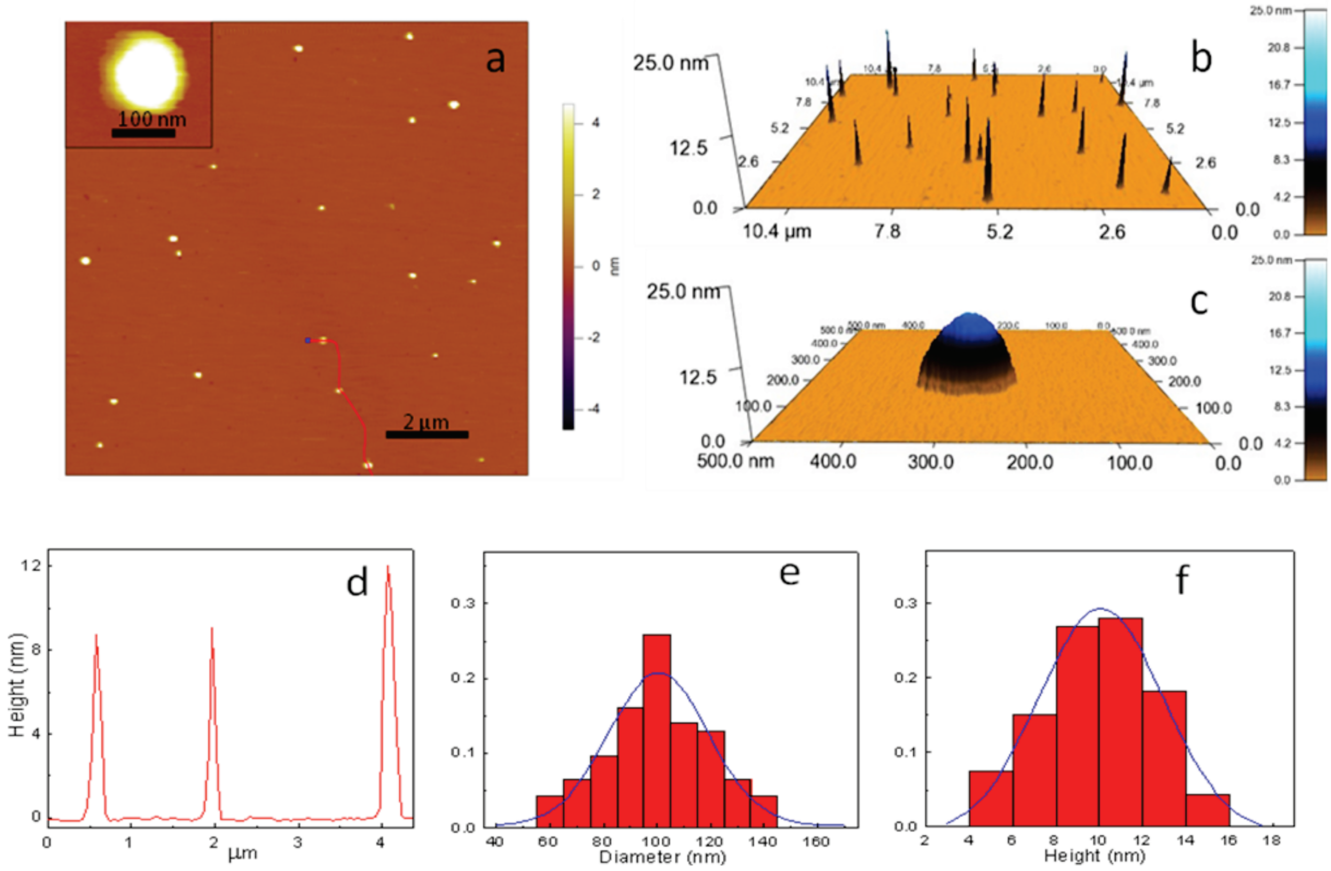


Figure 2. AFM imaging analysis of polymer **PE-1**. (a) 2D image of **PE-1** on a freshly cleaved mica (insert is the image of a single nanoparticle); (b,c) 3D images of **PE-1** on mica; (d) height distribution along the detour of the particles shown in part a; (e) histogram of particle diameter; (f) histogram of fraction particle height. (Parts e and f are based on the statistic analysis of 100 nanoparticles.)

in tapping mode (Figure 2). Many spherical nanoparticles were observed, strongly confirming spherical architecture of the polymer. On the basis of the histograms constructed from the AFM images, the average diameter is ~100.5 nm, and the height is ~10 nm (Figure 2). The height/diameter ratio suggests that the dendritic **PE-1** nanoparticles become flattened on the substrate surface. This is reasonable because the dendritic PE has a very low glass-transition temperature ($T_g = -60$ °C). At room temperature, the nanoparticles are extremely soft and can deform from its globular shape on flat surface of hard substrate. Previous AFM studies also showed similar deformation when dendrimers are deposited on the flat surface.[19,20]

For many functional applications of soft nanoparticles, it is desirable to have soluble nanoparticles carrying multiple functional groups. To demonstrate the capability of our method for making functional dendritic nanoparticles, chain-walking copolymerization of ethylene and a model polar olefin was also tested. Our previous studies have shown that the Pd(II)-α-diimine catalyst is versatile for copolymerization to yield functionalized dendritic PEs.[11] For concept demonstration, the MVCWC was used to initiate chain-walking copolymerization of ethylene and an α-olefin containing a terminal TBDPS-protected alcohol **2** to afford functional dendritic **PE-2** having many TBDPS-protected alcohols.

Calculation based on M_n and ^{1}H NMR data (Table 1 and the Supporting Information) showed on average that there are $\sim 8.6 \times 10^4$ TBDPS-protected alcohol groups per polymer nanoparticle, with an average diameter of 109.4 nm measured by MALLS. The R_g/R_h value for **PE-2** also confirms the globular architecture of the dendritic nanoparticle.[18] AFM imaging of **PE-2** further confirmed its spherical shape. (See Figure S4 of the Supporting Information.) Upon the removal of the TBDPS protection groups, the free hydroxyl groups can be used for conjugating various functional moieties for specific nanopartile-based applications. By repeating the procedure used for preparing MVCWC, the surface hydroxyl groups of deprotected **PE-2** might be utilized to prepare a second-generation MVCWC that can initiate another subsequent CWP to build gigantic dendritic nanoparticles as fully soluble molecular species. Furthermore, by varying the pressure of ethylene from low to high, the morphology of the newly formed polyethylenes on the surface of the dendritic core can also be tuned.[10]

In summary, we have developed a new approach for facile synthesis of large dendritic nanoparticles as fully soluble molecular species. The synthesis is achieved in a one-pot CWP of ethylene with or without a polar comonomer catalyzed by MVCWC. The MVCWC was conveniently prepared from functional dendritic PEs made by CWP.[10,11] The resulting polymers have a spherical architecture with very high molecular weight, narrow polydispersity, and size >100 nm in diameter. Large functional dendritic nanoparticles can also be prepared via one-pot copolymerization of ethylene with a polar monomer. In principle, iteration of surface catalyst loading, followed by a subsequent CWP, should lend a powerful method for preparing giant dendritic polymer nanoparticles with increasing dimension and complexity. Importantly, these dendritic nanoparticles are fully soluble in organic solvents such as molecular species and can be easily characterized and functionalized. This method expands the scope of current CWP and offers a novel catalytic method for constructing soft nanoparticles with many potential applications.

Acknowledgment. We thank the National Science Foundation (CHE-0456719, CHE-0723497, and DMR-0703988) for the financial support. We also thank Dr. Phil Dennison and Dr. John Grave for valuable assistance of NMR and mass spectrum measurement. Z.G. acknowledges a Camille Dreyfus Teacher-Scholar Award.

Supporting Information Available: Experimental details, including catalyst synthesis and characterizations, polymerization and polymer purification procedures, polymer characterizations by SEC coupled to MALLS, NMR spectra, DLS, and polymer morphology study results by AFM. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Functional Nanomaterials, Nanoparticles, and Polymer Design. In *Handbook of Theoretical and Computational Nanotechnology*; Rieth, M., Schommers, W., Eds.; American Scientific Publishers: Stevenson Ranch, CA, 2006; Vol. *8*.
(2) Landfester, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 4488–4507.
(3) Asahi, T.; Sugiyama, T.; Masuhara, H. *Acc. Chem. Res.* **2008**, *41*, 1790–1798.
(4) *Dendrimers and Other Dendritic Polymers*; Frechet, J. M. J., Tomalia, D. A., Eds.; John Wiley & Sons: Hoboken, NJ, 2001.
(5) (a) Tomalia, D. A.; Baker, H. D.; Dewald, J.; Hall, J. M.; Kallos, G.; Martin, R.; Ryder, J. *Polym. J.* **1985**, *17*, 117–132. (b) Newkome, G. R.; Yao, Z.; Baker, G. R.; Gupta, V. K. *J. Org. Chem.* **1985**, *50*, 2003–2004. (c) Hawker, C. J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1990**, *112*, 7638–7647.
(6) Lothian-Tomalia, M. K.; Hedstrand, D. M.; Tomalia, D. A. *Tetrahedron* **1997**, *53*, 15495–15513.
(7) Tomalia, D. A. *Prog. Polym. Sci.* **2005**, *30*, 294–324.
(8) (a) Hedrick, J. L.; Magbitang, T.; Connor, E. F.; Glauser, T.; Volksen, W.; Hawker, C. J.; Lee, V. Y.; Miller, R. D. *Chem.—Eur. J.* **2002**, *8*, 3308–3319. (b) Taton, D.; Feng, X.; Gnanou, Y. *New J. Chem.* **2007**, *31*, 1097–1110.
(9) (a) Ittel, S. D.; Johnson, L. K.; Brookhart, M. *Chem. Rev.* **2000**, *100*, 1169–1203. (b) Tempel, D. J.; Johnson, L. K.; Huff, R. L.; White, P. S.; Brookhart, M. *J. Am. Chem. Soc.* **2000**, *122*, 6686–6700. (c) Domski, G. J.; Rose, J. M.; Coates, G. W.; Bolig, A. D.; Brookhart, M. *Prog. Polym. Sci.* **2007**, *32*, 30–92.
(10) (a) Guan, Z.; Cotts, P. M.; McCord, E. F.; McLain, S. J. *Science* **1999**, *283*, 2059–2062. (b) Guan, Z. *Chem.—Eur. J.* **2002**, *8*, 3087–3092.
(11) (a) Chen, G.; Ma, X. S.; Guan, Z. *J. Am. Chem. Soc.* **2003**, *125*, 6697–6704. (b) Chen, G.; Guan, Z. *J. Am. Chem. Soc.* **2004**, *126*, 2662–2663. (c) Chen, G.; Huynh, D.; Felgner, P. L.; Guan, Z. *J. Am. Chem. Soc.* **2006**, *128*, 4298–4302.
(12) Mecking, S.; Johnson, L. K.; Wang, L.; Brookhart, M. *J. Am. Chem. Soc.* **1998**, *120*, 888–899.
(13) (a) Wang, J.; Ye, Z.; Zhu, S. *Ind. Eng. Chem. Res.* **2007**, *46*, 1174–1178. (b) Ye, J.; Ye, Z.; Zhu, S. *Polymer* **2008**, *49*, 3382–3392.
(14) Soussan, E.; Cassel, S.; Blanzat, M.; Rico-Lattes, I. *Angew. Chem., Int. Ed.* **2009**, *48*, 274–288.
(15) (a) Mackay, M. E.; Tuteja, A.; Duxbury, P. M.; Hawker, C. J.; Van Horn, B.; Guan, Z.; Chen, G.; Krishnan, R. S. *Science* **2006**, *311*, 1740–1743. (b) Meyers, M. A.; Chen, P. Y.; Lin, A. Y. M.; Seki, Y. *Prog. Mater. Sci.* **2008**, *53*, 1–206.
(16) Turner, J. L.; Chen, Z.; Wooley, K. L. *J. Controlled Release* **2005**, *109*, 189.
(17) Flory, P. J. *Principles of Polymer Chemistry*; Cornell University Press: Ithaca, NY, 1953.
(18) (a) Burchard, W. *Adv. Polym. Sci.* **1983**, *48*, 1–124. (b) Burchard, W. *Adv. Polym. Sci.* **1999**, *143*, 113–194.
(19) (a) Hierlemann, A.; Campbell, J. K.; Baker, L. A.; Crooks, R. M.; Rico, A. J. *J. Am. Chem. Soc.* **1998**, *120*, 5323–5324. (b) Zhang, H.; Grim, P. C. M.; Vosch, T.; Wiesler, U. M.; Berresheim, A. J.; Müllen, K.; De Schryver, F. C. *Langmuir* **2000**, *16*, 9294–9298.
(20) Ornelas, C.; Ruiz, J.; Belin, C.; Astruc, D. *J. Am. Chem. Soc.* **2009**, *131*, 590–631.