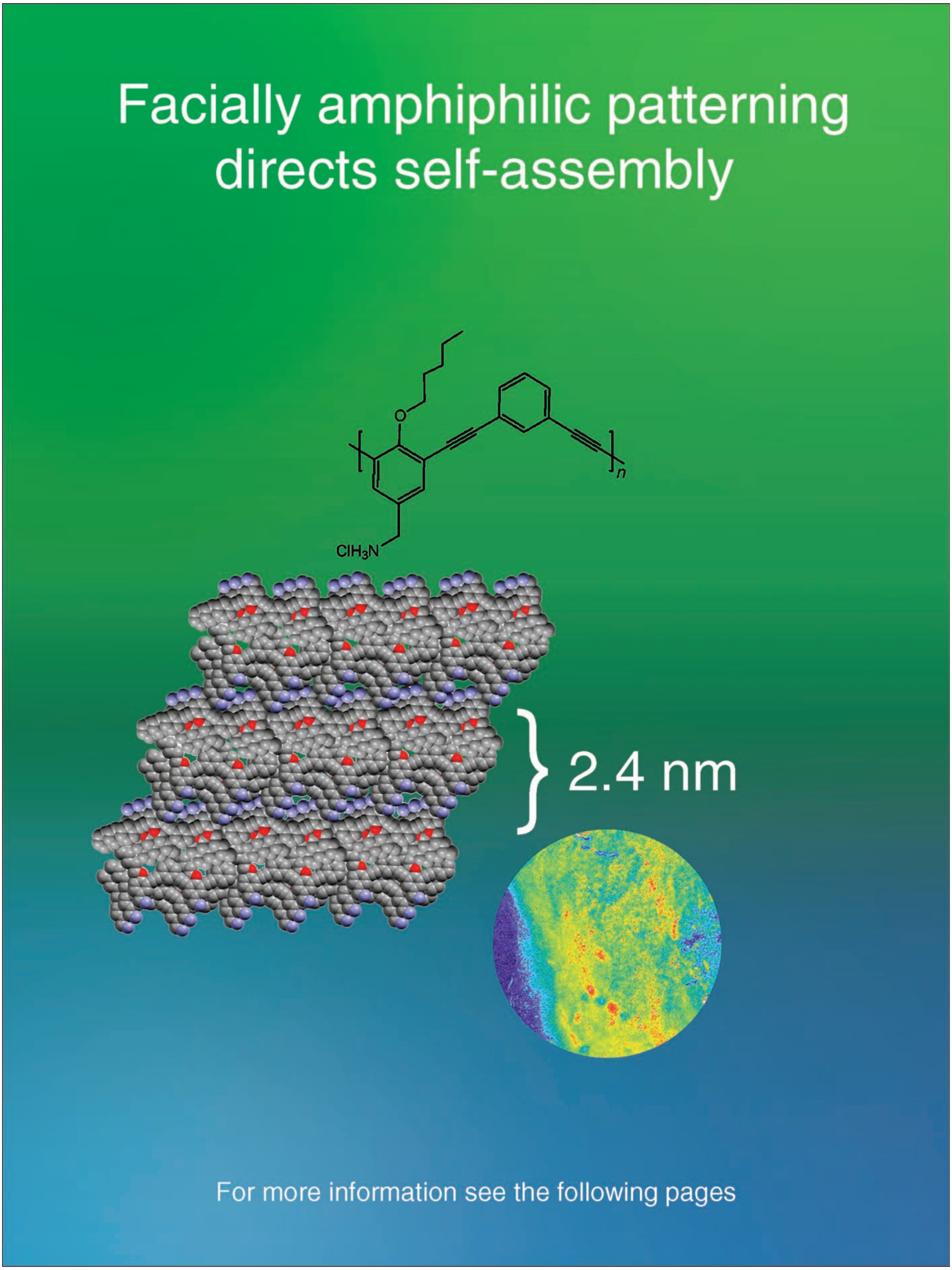

Facially amphiphilic patterning directs self-assembly
ClH3N
O
n
2.4 nm
For more information see the following pages

DOI: 10.1002/chem.200501283

Self-Assembled Structures with Liquid-Crystalline Order in Aqueous Solution by Patterning Poly(phenylene ethynylene)s

Taehyung Kim, Lachelle Arnt, Edward Atkins, and Gregory N. Tew*[a]

Abstract: Facially amphiphilic (FA) phenylene ethynylene (PE) polymers that self-assemble in aqueous solution were studied by small-angle X-ray diffraction (SAXD) and found to self-assemble into bilayers with a fully extended backbone. The resulting bilayers have long-range liquid-crystalline order. This self-assembly is programmed into the molecule by placing polar and nonpolar groups at precise locations so that they segregate onto opposite sides of the molecular structure. The absence of FA patterning generated an amorphous sample confirming the importance of this programmed amphiphilicity in the self-assembly process. Facially amphiphilic patterning represents a new design criterion for supramolecular chemistry, illustrated here in the observation of molecular ordering into bilayers reminiscent of self-assembled structures commonly found in biology, including amphiphilic β-sheet polypeptides and phospholipid bilayers.

Keywords: amphiphiles • bilayers • phenylene ethynylene • polymers • self-assembly • X-ray diffraction

Introduction

Synthetic biomimetic polymers have attracted attention as useful model materials for understanding parameters affecting the folded structure of proteins. Phenylene ethynylene (PE) polymers are of interest owing to their unique photophysical properties, supramolecular organization, and conformational diversity.[1,2] Their structures include rigid *para*-substituted polymers,[3] oligomers and macrocycles[4,5] as well as more conformationally flexible *meta*-[6,7] and *ortho*-linked[8,9] molecules. Polymeric *para*-derivatives have been characterized with respect to their optical properties and, more recently, their liquid-crystalline organization.[10,11] These molecules organize into lamellar structures with interdigitated alkyl side chains, in which the spacing between chains is controlled by the length of the side chain in one direction and π–π stacking of the aromatic backbone in the other. Moore and co-workers[6] have characterized *meta*-derivatives with short ethylene glycol chains that undergo random coil-to-springlike helical conformational modifications as the solvent is changed from chlorohydrocarbons to those with higher dielectric constants. Solid-state characterization showed that these oligomers unfold into extended structures with lamellar packing.[12] However, filling the interior cavity of the helices with methyl groups, to reduce free volume, stabilized the helix in the solid state.[13] Single-crystal structures of *ortho*-substituted oligomers indicate the adoption of a helical conformation with a helical repeat of three aromatic rings.[8]

The study of facially amphiphilic (FA) molecules in which the side chains attached to the backbone are polar (P) and nonpolar (NP) has been more limited.[14–17,7] However, our research group has recently reported structures in which the PE backbone was patterned with P cationic and NP alkyl groups that project from opposite sides of the extended structures.[7] Langmuir experiments showed that these molecules adopt stable monolayers with extended conformations at the air–water interface owing to their FA nature.[18] This structure is similar to that adopted by peptides designed to form amphiphilic β-sheets at the air–water interface.[19] The FA PE structures were also shown to disrupt phospholipid vesicles[7] and exhibited antibacterial activity.[20] It was speculated that the FA patterning could provide instructions for molecular self-assemble into ordered structures.

In this report, we describe the structure of organized assemblies formed when the polymers were dissolved in a polar aprotic solvent and then diluted with water. Small-angle X-ray diffraction (SAXD) experiments revealed that

---

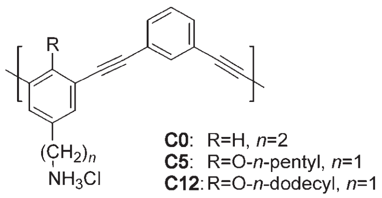
[a] T. Kim, L. Arnt, Prof. E. Atkins, Prof. Dr. G. N. Tew
Polymer Science and Engineering Department
University of Massachusetts
120 Governors Drive, Amherst, MA 01003 (USA)
Fax: (+1)413-545-0082
E-mail: tew@mail.pse.umass.edu

Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author.

these self-assembled structures organized into bilayers with a fully extended backbone and the resulting bilayers further assembled with long-range liquid-crystalline order.

Results and Discussion

The patterning of PE structures shown here (**C0**, **C5**, and **C12** containing sides chains with NP chain lengths of zero, five, and twelve carbon atoms, respectively) leads to a strong facial preference in the structure. When these materials were precipitated from dioxane and examined in the solid-phase state by SAXD, ordered structures were observed. Figure 1 shows the X-ray diffraction traces obtained from powders of the three polymers. Diffraction peaks corresponding to *d* spacings of 2.0, 2.4, and 3.1 nm are observed for the structures **C0**, **C5**, and **C12**, respectively. These spacings are consistent with a bilayer structure in which P cationic groups and NP alkyl side chains segregate to opposite sides of an extended conformation. For example, Figure 2 shows a model of the **C5** structure with a bilayer spacing of 2.4 nm and NP groups in the interior. Assemblies from dioxane may expose the NP groups to the exterior; however, in aqueous solution, discussed below, the P groups will be displayed to the solvent. In either case, the bilayer spacing remains the same and only the chemical functionality exposed to the solvent changes.



C0: R=H, *n*=2
C5: R=O-*n*-pentyl, *n*=1
C12: R=O-*n*-dodecyl, *n*=1

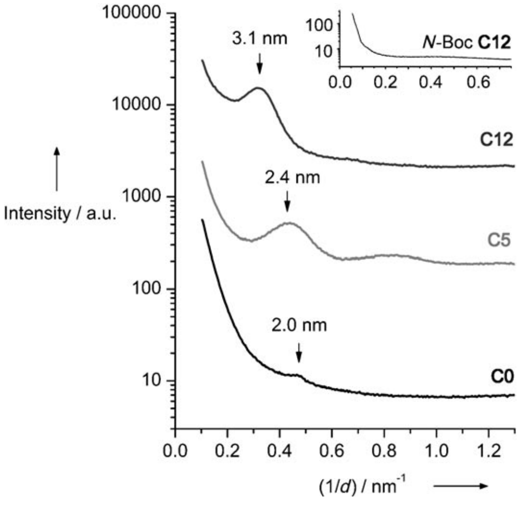


Figure 1. SAXD of **C0**, **C5**, and **C12** with diffraction peaks that correspond to *d* spacings of 2.0, 2.4, and 3.1 nm, respectively. The inset shows the diffraction curve for the **C12** polymer before removal of the *N*-Boc protecting group. This material is not facially amphiphilic and therefore it is not programmed to self-organize; thus the absence of diffraction peaks.

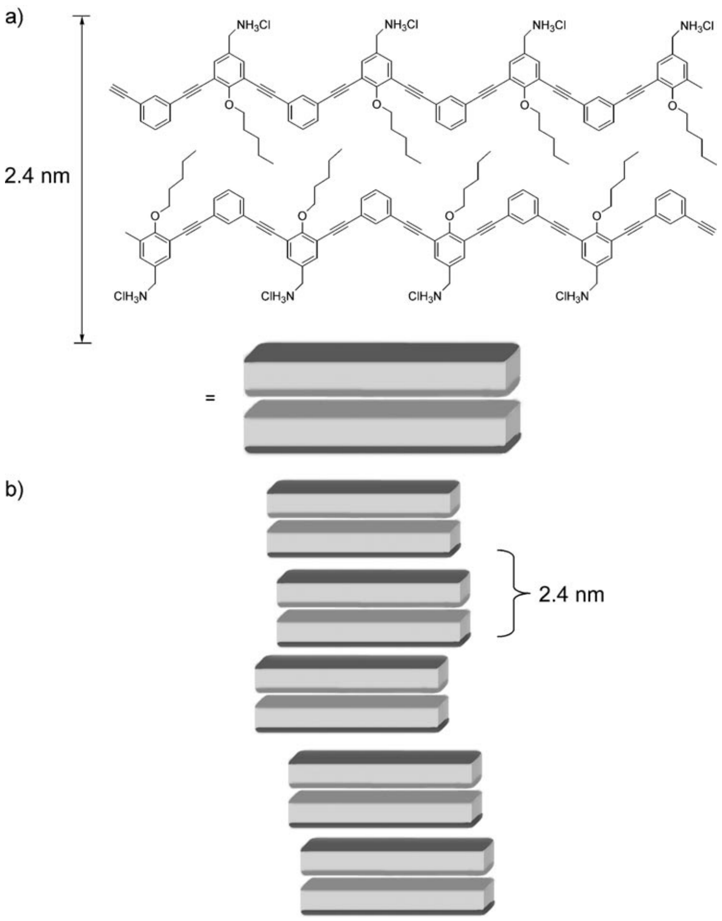


Figure 2. a) Model for the lamellar structure formed by **C5** in which two molecules form a bilayer by associating nonpolar surfaces together. This bilayer is represented schematically with the P and NP groups in black and dark gray, respectively. The molecular backbone is shown in light gray. b) These bilayers then act as rigid entities, or mesogens, and further organize with long-range liquid-crystalline order.

Molecular models of **C5** with a fully extended NP side chain indicate a width of ~1.3 nm. The measured interbilayer spacing of 2.4 nm is 7.7 % less than the value of 2.6 nm (the bilayer is twice 1.3 nm) suggested from models incorporating side chains in an extended conformation. This slight reduction in bilayer width likely arises from interdigitation of the side chains or a larger tilt angle of the NP side chains as they pack. When the **C5** NP chains are extended by seven carbon atoms, the observed diffraction peak spacing increases to 3.1 nm; when the NP side chain is removed, this spacing decreases to 2.0 nm consistent with expectations. Most importantly, when the nonamphiphilic precursor to **C12**, a polymer containing *N*-Boc protecting groups and therefore not FA, was studied under identical conditions no diffraction peaks were observed (inset Figure 1). The lack of order observed for the non-FA molecule in conjunction with the diffraction data from **C0**, **C5**, and **C12** supports the importance of the FA patterning in directing the self-organization of this family of polymers into ordered materials.

The SAXD trace of **C5** in Figure 1 also shows a weaker second-order peak, and the wide-angle X-ray diffraction (WAXD) of **C5** showed diffraction peaks at spacing corresponding to 1.19, 0.78, and 0.55 nm (Figure S1 in the Supporting Information). These peaks are consistent with a lamellar structure in which each lamella is composed of two fully extended backbones as illustrated in Figure 2. These lamellae, or bilayers of rigid rods, self-organize with liquid-crystalline-like order (see Figure S2 in the Supporting Information) based on the diffraction patterns expected from disordered structures.[21] Figure 2 shows a model of the **C5** polymer with the lamellar structure as well as how these lamellae act as mesogens and organize into layers with liquid-crystalline order.

Observations from fluorescence spectroscopy in aqueous solution[7] and the presence of organization in condensed matter suggested the possibility that these soft systems form ordered assemblies in aqueous solutions. Polarized optical microscopy studies shown in Figure 3 support the formation of ordered assemblies in aqueous solution. This image, collected under cross-polarized microscopy, shows that the sample is birefringent at room temperature. No changes in the birefringence were observed upon heating to 90 °C, suggesting that the ordered phase does not undergo a phase transition within this temperature range.

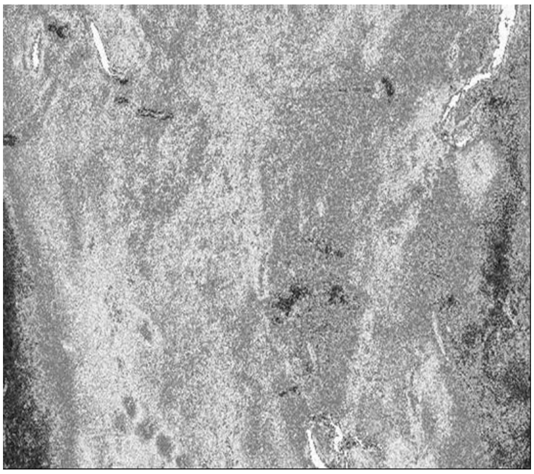


Figure 3. Polarized optical microscopy image of the self-assemble of **C12** in aqueous solution at room temperature. The strong birefringence is consistent with an ordered material as opposed to random precipitation.

To better characterize the ordered assemblies formed from solutions of **C12** in 10 % DMSO/water, SAXD was collected and a typical powder diffraction trace from this sample is shown in Figure 4. The curve obtained has a strong diffraction peak corresponding to a spacing of 3.6 nm for the wet powder, shown in the inset of Figure 4. The structure is consistent with that observed for **C12** in the condensed matter state; however, the spacing is increased by 0.5 nm. This increase in spacing results from hydration of the P cationic ammonium ions in the structure. Indeed, when this same sample was dried to remove all visible DMSO and water, the SAXD spacing matches exactly the value obtained for **C12** in Figure 1. As a result, it is shown that this material self-organizes into ordered structures in aqueous solution excluding the possibility of random chain collapse into an amorphous state due to poor solvent conditions, which might be expected. These results further support the importance of the strongly programmed FA patterning. The molecular architecture and self-assembled structures of these polymers are reminiscent of structures formed by amphiphilic β-sheet polypeptides in which P and NP amino acid side chains extend from opposite faces of the polypeptide backbone.[19] In addition, many β-sheet-forming polypeptides adopt amphiphilic, ordered conformations only when two or more strands self-assemble. Individual strands in solution typically adopt random coil conformations. Further, amphiphilic β-sheet peptides studied in the absence of larger structures (like other protein domains) often associate into larger structures and precipitate from solution.

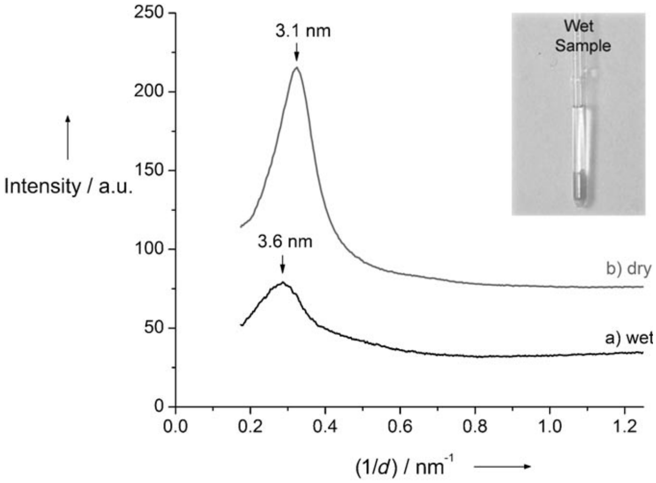


Figure 4. SAXD obtained from a) the self-assembly of **C12** in aqueous solution, and b) after solvent removal in vacuum.

In conclusion, we have characterized the structures formed by FA PE materials in aqueous solution by SAXD and found that they self-assemble into ordered bilayers, in which the molecular backbone is extended with P and NP groups segregated onto opposite faces. This structure is supported by SAXD data obtained from the solid state and aqueous solutions. WAXD data supports bilayer or lamellae organization in layered liquid-crystalline structures. The absence of FA patterning generated an amorphous sample and confirms the importance of this programmed amphiphilicity in self-assembly. These self-assembled structures mimic those found for amphiphilic β-sheet polypeptides; however, intrastrand associations in these samples consist of strong van der Waals and π–π stacking interactions as opposed to hydrogen bonding found in polypeptides. In addition, analogy to the layered assemblies observed for phospholipid molecules are easily envisaged, providing further interest in these novel FA macromolecules. The FA patterning of molecular backbones imparts ordering in these structures and represents a new design criterion for supramolecular chemistry.

Experimental Section

The syntheses of **C0**, **C5**, and **C12** have been described elsewhere, as have the NMR, GPC, and UV data.[7] Final deprotection of the nitrogen protection group results in 80% yield after precipitation and repeated washing with ethyl ether.

Sample preparation: Powder samples were prepared of all polymers by precipitation from dioxane during the deprotection of the Boc protecting group. These dried powders were annealed at 100°C for 8 h. Powders that were not annealed showed similar peak position and widths and thus annealing is not absolutely essential. To study assembly in aqueous solutions, solutions in DMSO were prepared at 1 $\mathrm{mg\,mL^{-1}}$ of all polymers and added to water so that the final concentration was 90% water/10% DMSO (v/v). These samples were allowed to stand overnight followed by centrifugation at 7000 rpm for five minutes to collect the material at the bottom of a glass capillary.

X-ray diffraction: Dried and wet powder samples were placed into HR6-122 glass capillaries with 1.0 mm diameter purchased from Hampton Research. SAXD and WAXD data were collected by using a point-collimated incident beam and the patterns were collected on an image plate in an evacuated camera to reduce air scatter. The image plates were recorded and read using a Fujifilm BAS-2500 imaging analyzer. The incident beam wavelength was 0.154 nm, corresponding to $\mathrm{Cu_{K\alpha}}$ radiation.

Acknowledgements

The authors thank NIH, ONR (GM065803–01 and N00140310503 to GNT), and the MRSEC on Polymers at UMass funded by NSF (DMR-9400488). G.N.T. thanks the PECASE program, ARO and ONR for Young Investigator Awards, 3M for a nontenured faculty grant and DuPont's Young Faculty program.

[1] J. M. Tour, *Chem. Rev.* **1996**, *96*, 537.
[2] J. S. Moore, *Acc. Chem. Res.* **1997**, *30*, 402.
[3] U. H. F. Bunz, *Chem. Rev.* **2000**, *100*, 1605.
[4] J. S. Zhang, J. S. Moore, Z. F. Xu, R. A. Aguirre, *J. Am. Chem. Soc.* **1992**, *114*, 2273.
[5] S. Hoger, J. Spickermann, D. L. Morrison, P. Dziezok, H. J. Ruder, *Macromolecules* **1997**, *30*, 3110.
[6] J. C. Nelson, J. G. Saven, J. S. Moore, P. G. Wolynes, *Science* **1997**, *277*, 1793.
[7] L. Arnt, G. N. Tew, *J. Am. Chem. Soc.* **2002**, *124*, 7664.
[8] R. H. Grubbs, D. Kratz, *Chem. Ber.* **1993**, *126*, 149.
[9] a) A. Orita, E. Alonso, J. Yaruva, J. Otera, *Synlett* **2000**, 1333; b) T. V. Jones, R. A. Blatchly, G. N. Tew, *Org. Lett.* **2003**, *5*, 3297; c) T. V. Jones, M. M. Slutsky, R. Laos, T. F. A. de Greef, G. N. Tew, *J. Am. Chem. Soc.* **2005**, *127*, 17235.
[10] D. Ofer, T. M. Swager, M. S. Wrighton, *Chem. Mater.* **1995**, *7*, 418.
[11] L. Kloppenburg, D. Jones, J. B. Claridge, H. C. zur Loye, U. H. F. Bunz, *Macromolecules* **1999**, *32*, 4460.
[12] P. J. Prest, R. B. Prince, J. S. Moore, *J. Am. Chem. Soc.* **1999**, *121*, 5933.
[13] C. Kubel, M. J. Mio, J. S. Moore, D. C. Martin, *J. Am. Chem. Soc.* **2002**, *124*, 8605.
[14] Z. S. Bo, J. P. Rabe, A. D. Schluter, *Angew. Chem.* **1999**, *111*, 2540–2542; *Angew. Chem. Int. Ed.* **1999**, *38*, 2370.
[15] E. Arias-Marin, J. C. Arnault, D. Guillon, T. Maillou, J. Le Moigne, B. Geffroy, J. M. Nunzi, *Langmuir* **2000**, *16*, 4309.
[16] N. Reitzel, D. R. Greve, K. Kjaer, P. B. Hows, M. Jayaraman, S. Savoy, R. D. McCullough, J. T. McDevitt, T. Bjornholm, *J. Am. Chem. Soc.* **2000**, *122*, 5788.
[17] J. Kim, T. M. Swager, *Nature* **2001**, *411*, 1030.
[18] L. Arnt, G. N. Tew, *Langmuir* **2003**, *19*, 2404.
[19] H. Rapaport, K. Kjaer, T. R. Jensen, L. Leiserowitz, D. A. Tirrell, *J. Am. Chem. Soc.* **2000**, *122*, 12523.
[20] L. Arnt, K. Nusslein, G. N. Tew, *J. Polym. Sci. Part A* **2004**, *42*, 3860.
[21] R. Hosemann, S. N. Bacghi, *Direct Analysis of Diffraction by Matter*, North-Holland, Amsterdam, **1962**.

Received: October 17, 2005