# A Modular Approach toward Functionalized Three-Dimensional Macromolecules: From Synthetic Concepts to Practical Applications

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***Abstract:*** A new strategy for the preparation of functional, multiarm star polymers via nitroxide-mediated "living" radical polymerization has been explored. The generality of this approach to the synthesis of three-dimensional macromolecular architectures allows for the construction of nanoscopically defined materials from a wide range of different homo, block, and random copolymers combining both apolar and polar vinylic repeat units. Functional groups can also be included along the backbone or as peripheral/chain end groups, thereby modulating the reactivity and polarity of defined portions of the stars. This modular approach to the synthesis of three-dimensional macromolecules permits the application of these tailored materials as multifunctional hosts for hydrogen bonding, nanoparticle formation, and as scaffolds for catalytic groups. Examples of applications of the functional stars in catalysis include their use in a Heck-type coupling as well as an enantioselective addition reaction.

## Introduction

The growing demand for well-defined and functional soft materials in nanoscale applications has led to a dramatic increase in the development of procedures that combine architectural control with flexibility in the incorporation of functional groups.[1-4] The unusual solution and interfacial properties of these tailor-made macromolecules make them suitable as active materials in nanotechnology with recent examples including shell cross-linked nanoparticles,[5] hyperbranched macromolecules,[6] dendrimers,[7] etc. While not as highly branched as these three-dimensional polymeric architectures, star polymers have recently experienced a renewed interest due to their potential for greater accessibility by living free radical procedures.[8]

Previously, multiarm star polymers have been prepared by living ionic procedures;[9] however, the synthetically demanding nature of this approach and its lack of compatibility with a variety of functional groups have limited the applicability of

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(1) (a) Kato, T. *Science* **2002**, *295*, 2414. (b) Yu, S. M.; Soto, C. M.; Tirrell, D. A. *J. Am. Chem. Soc.* **2000**, *122*, 6552. (c) Farrer, R. A.; Copeland, G. T.; Previte, M. J. R.; Okamoto, M. M.; Miller, S. J.; Fourkas, J. T. *J. Am. Chem. Soc.* **2002**, *124*, 1994. (d) Peerlings, H. W. I.; Van Benthem, R. A. T. M.; Meijer, E. W. *J. Polym. Sci., Polym. Chem.* **2001**, *39*, 3112. (e) Wooley, K. L.; Clark, C. *J. Polym. Sci., Polym. Chem.* **2000**, *38*, 1397. (f) Nishinaga, T.; Tanatani, A.; Oh, K.; Moore, J. S. *J. Am. Chem. Soc.* **2002**, *124*, 5934.

(2) (a) Percec, V.; Cho, W. D.; Ungar, G.; Yeardley, D. J. P. *Angew. Chem., Int. Ed.* **2000**, *39*, 1597. (b) Ma, H.; Jen, A. K. Y. *Adv. Mater.* **2001**, *13*, 1201. (c) Ma, Q.; Remsen, E. E.; Kowalewski, T.; Wooley, K. L. *J. Am. Chem. Soc.* **2001**, *123*, 4627. (d) Nam, J. M.; Park, S. J.; Mirkin, C. A. *J. Am. Chem. Soc.* **2002**, *124*, 3820.

(3) (a) Zubarev, E.; Stupp, S. I. *J. Am. Chem. Soc.* **2002**, *124*, 5762. (b) Weil, T.; Wiesler, U. M.; Herrmann, A.; Bauer, R.; Hofkens, J.; De Schryver, F.; Müllen, K. *J. Am. Chem. Soc.* **2001**, *123*, 8101. (c) Tew, G. N.; Pralle, M. U.; Stupp, S. I. *J. Am. Chem. Soc.* **1999**, *121*, 9852. (d) Hill, D. J.; Mio, M. J.; Prince, R. B.; Hughes, T. S.; Moore, J. S. *Chem. Rev.* **2001**, *101*, 3893−4012.

(4) (a) Liu, S.; O'Brien, D. F. *J. Am. Chem. Soc.* **2002**, *124*, 6037. (b) Brunsveld, L.; Meijer, E. W.; Prince, R. B.; Moore, J. S. *J. Am. Chem. Soc.* **2001**, *123*, 7978. (c) Gossl, I.; Shu, L.; Schluter, A. D.; Rabe, J. P. *J. Am. Chem. Soc.* **2002**, *124*, 6860. (d) El-Ghayoury, A.; Schenning, A. P. H. J.; Meijer, E. W. *J. Polym. Sci., Polym. Chem.* **2002**, *40*, 4020. (e) Zheng, H.; Lee, I.; Rubner, M. F.; Hammond, P. T. *Adv. Mater.* **2002**, *14*, 569.

(5) (a) Ma, Q. G.; Remsen, E. E.; Clark, C. G.; Kowalewski, T.; Wooley, K. L. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 5058−5063. (b) Huang, H.; Remsen, E. E.; Kowalewski, T.; Wooley, K. L. *J. Am. Chem. Soc.* **1999**, *121*, 3805. (c) Becker, M. L.; Remsen, E. E.; Wooley, K. L. *J. Polym. Sci., Polym. Chem.* **2001**, *39*, 4152. (d) Bütün, V.; Wang, X. S.; de Paz Báñez, M. V.; Robinson, K. L.; Billingham, N. C.; Armes, S. P.; Tuzar, Z. *Macromolecules* **2000**, *33*, 1. (e) Liu, S.; Armes, S. P. *J. Am. Chem. Soc.* **2001**, *123*, 9910.

(6) (a) Guan, Z. B. *J. Am. Chem. Soc.* **2002**, *124*, 5616. (b) Bolton, D. H.; Wooley, K. L. *J. Polym. Sci., Polym. Chem.* **2002**, *40*, 823. (c) Sunder, A.; Quincy, M. F.; Mulhaupt, R.; Frey, H. *Angew. Chem., Int. Ed.* **1999**, *38*, 2928. (d) Jikei, M.; Fujii, K.; Kakimoto, M. *J. Polym. Sci., Polym. Chem.* **2001**, *39*, 3304. (e) Bernal, D. P.; Bankey, N.; Cockayne, R. C.; Fossum, E. J. *Polym. Sci., Polym. Chem.* **2002**, *40*, 1456. (f) Thompson, D. S.; Markoski, L. J.; Moore, J. S.; Sendijarevic, I.; Lee, A.; McHugh, A. J. *Macromolecules* **2000**, *33*, 6412. (g) Simon, P. F. W.; Müller, A. H. E. *Macromolecules* **2001**, *34*, 6206. (h) Hawker, C. J.; Lee, R.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1991**, *113*, 4583.

(7) (a) Stiriba, S. E.; Frey, H.; Haag, R. *Angew. Chem., Int. Ed.* **2002**, *41*, 1329. (b) Gibson, H. W.; Yamaguchi, N.; Hamilton, L.; Jones, J. W. *J. Am. Chem. Soc.* **2002**, *124*, 4653. (c) Bosman, A. W.; Jansen, H. M.; Meijer, E. W. *Chem. Rev.* **1999**, *99*, 1665. (d) Devadoss, C.; Bharathi, P.; Moore, J. S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1633. (e) Vetter, S.; Koch, S.; Schluter, A. D. *J. Polym. Sci., Polym. Chem.* **2001**, *39*, 1940. (f) Percec, V.; Obata, M.; Rudick, J. G.; De, B. B.; Glodde, M.; Bera, T. K.; Magonov, S. N.; Balagurusamy, V. S. K.; Heiney, P. A. *J. Polym. Sci., Polym. Chem.* **2002**, *40*, 3509. (g) Marsitzky, D.; Vestberg, R.; Blainey, P.; Tang, B. T.; Hawker, C. J.; Carter, K. R. *J. Am. Chem. Soc.* **2001**, *123*, 6965. (h) Piotti, M. E.; Rivera, F.; Bond, R.; Hawker, C. J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1999**, *121*, 9471−9472. (i) Tomalia, D. A.; Fréchet, J. M. J. *J. Polym. Sci., Polym. Chem.* **2002**, *40*, 2719.

(8) (a) Hawker, C. J.; Bosman, A. W.; Harth, E. *Chem. Rev.* **2001**, *101*, 3661−3688. (b) Kamigaito, M.; Ando, T.; Sawamoto, M. *Chem. Rev.* **2001**, *101*, 3689−3746. (c) Matyjaszewski, K.; Xia, J. *Chem. Rev.* **2001**, *101*, 2921−2990.
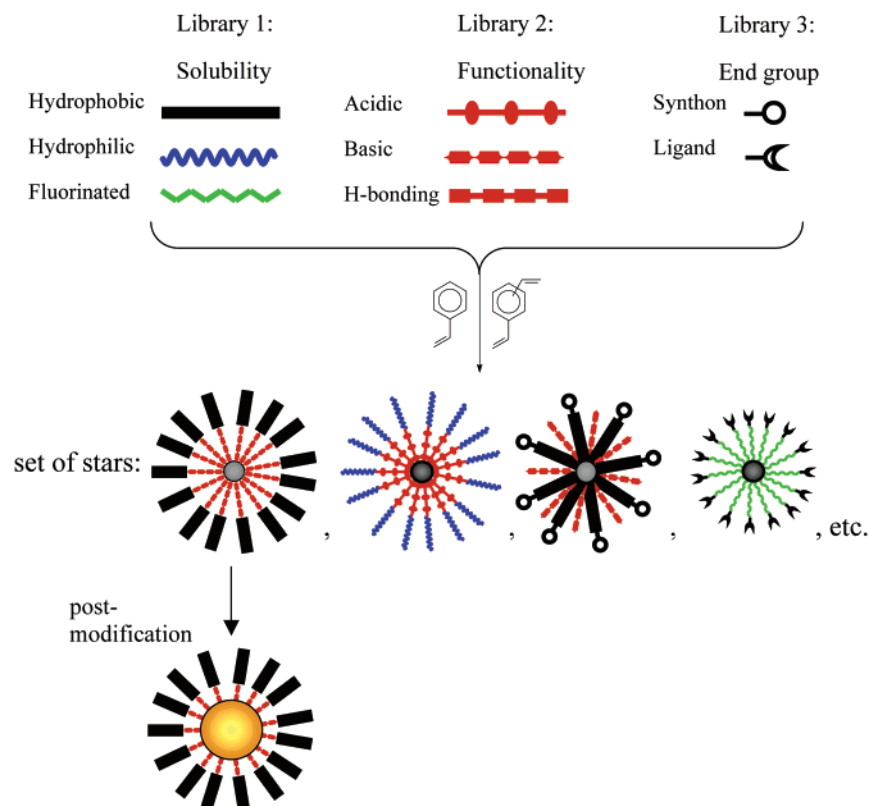
**Figure 1.** Schematic representation of the modular approach to star polymers.

this strategy. In contrast, recent reports from a number of groups[10] have detailed the application of nitroxide[11] or ATRP[12] living radical polymerizations to the synthesis of star polymers, which overcomes many of these limitations. While a number of approaches are possible, the most promising involves the coupling of preformed linear chains, containing a dormant chain end, with a cross-linkable monomer such as divinylbenzene. Traditionally, such an approach has been complicated by the large number of reaction and structure variables that limits the ability to optimize and control the structure of the resulting star polymers. This deficiency has recently been overcome by employing high-throughput "combinatorial" techniques for the rapid screening and optimization of these multivariable systems and has permitted the synthesis of well-defined three-dimensional star polymers by living free radical techniques.[13]

In this report, we describe the development of a modular approach for the preparation of functionalized star polymers, which permits the custom synthesis of a wide variety of

functionalized materials. As shown in Figure 1, the applicability of living free radical procedures to the preparation of functionalized block and random copolymers from hydrophilic, hydrophobic, or fluorinated segments, potentially containing acidic, basic, or H-bonding groups, enables the production of libraries of linear polymers incorporating combinations of these features. While this structural diversity is important, a critical feature of our approach is the incorporation of a dormant initiating group at one of the chain ends of these linear polymers.[14] Activation of these chain ends, followed by their coupling under conditions optimized for star polymer formation, then leads to a myriad of functionalized three-dimensional star polymers with accurate control over molecular weight, arm length, and both the nature and the placement of functional groups. These unique structures are useful in a range of applications as supramolecular hosts, catalytic scaffolds, or substrates for nanoparticle formation.

## Experimental Section

**General Methods.** DMF, technical grade DVB (55% *m*- and *p*-divinylbenzene, with the remainder consisting mostly *m*- and *p*-ethylstyrene), all monomers, and reagents were used as obtained (Aldrich), except for 2- and 4-vinylpyridine, which were purified over alumina. Toluene and THF were distilled from sodium under a nitrogen atmosphere. The CDCl₃ employed in the hydrogen-bonding experiments was dried by passing over alumina before use. Nitroxide **1** and alkoxyamines **2** and **3** were prepared as described by Hawker et al.[15,16] The ʟ-Tyr-based ligand **4**,[17] dendritic initiator **5**,[18] and 2,6-bis-(acetylamino)pyridine **6**[19] were synthesized according to literature

(9) (a) Tsoukatos, T.; Hadjichristidis, N. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 2575. (b) Al-Muallem, H. A.; Knauss, D. M. *J. Polym. Sci., Polym. Chem.* **2001**, *39*, 3547. (c) Hull, D. L.; Kennedy, J. P. *J. Polym. Sci., Polym. Chem.* **2001**, *39*, 1525. (d) Moschogianni, P.; Pispas, S.; Hadjichristidis, N. *J. Polym. Sci., Polym. Chem.* **2001**, *39*, 650.

(10) (a) Narrainen, A. P.; Pascual, S.; Haddleton, D. M. *J. Polym. Sci., Polym. Chem.* **2002**, *40*, 439. (b) Stenzel-Rosenbaum, M.; Davis, T. P.; Chen, V.; Fane, A. G. *J. Polym. Sci., Polym. Chem.* **2001**, *39*, 2777. (c) Quinn, J. F.; Chaplin, R. P.; Davis, T. P. *J. Polym. Sci., Polym. Chem.* **2002**, *40*, 2956.

(11) (a) Tsoukatos, T.; Pispas, S.; Hadjichristidis, N. *J. Polym. Sci., Polym. Chem.* **2001**, *39*, 320. (b) Pasquale, A. J.; Long, T. E. *J. Polym. Sci., Polym. Chem.* **2001**, *39*, 216. (c) Hawker, C. J. *Angew Chem., Int. Ed. Engl.* **1995**, *34*, 1456.

(12) (a) Baek, K. Y.; Kamigaito, M.; Sawamoto, M. *J. Polym. Sci., Polym. Chem.* **2002**, *40*, 1972. (b) Baek, K. Y.; Kamigaito, M.; Sawamoto, M. *J. Polym. Sci., Polym. Chem.* **2002**, *40*, 2245. (c) Baek, K. Y.; Kamigaito, M.; Sawamoto, M. *J. Polym. Sci., Polym. Chem.* **2002**, *40*, 633. (d) Zhang, X.; Xia, J. H.; Matyjaszewski, K. *Macromolecules* **2000**, *33*, 2340.

(13) Bosman, A. W.; Heumann, A.; Klaerner, G.; Fréchet, J. M. J.; Hawker, C. J. *J. Am. Chem. Soc.* **2001**, *123*, 6461.

(14) (a) Burguiere, C.; Dourges, M. A.; Charleux, B.; Varion, J. P. *Macromolecules* **1999**, *32*, 3883−3890. (b) Hawker, C. J.; Hedrick, J. L. *Macromolecules* **1995**, *28*, 2993. (c) Hawker, C. J. *J. Am. Chem. Soc.* **1994**, *116*, 11185.

(15) Dao, J.; Benoit, D.; Hawker, C. J. *J. Polym. Sci., Part A: Polym. Chem.* **1998**, *36*, 2161−67.

procedures. Column chromatography was carried out with Merck silica gel, 230−400 mesh. NMR spectra were recorded on a Bruker AM 250 (250 MHz) spectrometer with the residual protonated solvent peak as internal standard. GPC was carried out on a Waters chromatograph connected to a Waters 410 differential refractometer with THF as the carrier solvent. Absorption spectra were recorded in degassed THF solution (containing no stabilizers) on a Cary 50 UV−visible spectrophotometer. Optical rotation was measured on a Jasco DIP-370 digital polarimeter. MALDI-TOF mass spectrometry was performed on a PerSeptive Biosystems Voyager DE mass spectrometer operating in linear mode, using dithranol in combination with silver trifluoroacetate as matrix. Transmission electron micrographs of unstained samples were recorded on a JEOL JEM 2000 FX at 80 kV. Transmission electron microscopy grids were prepared by placing one drop of a toluene solution (0.5 mg/mL) on a carbon-covered copper grid followed by immediate drainage.

**2,2,5-Trimethyl-3-(4′-$p$-acetoxymethylphenylethoxy)-4-phenyl-3-azahexane, 7.** The chloromethyl substituted alkoxyamine,[15] **3** (14.0 g, 37.5 mmol), and potassium acetate (9.20 g, 93.8 mmol) were stirred at room temperature in hexamethylphosphorus triamide (HMPT, 100 mL) for 48 h. After being diluted with dichloromethane (400 mL) and washed with water (4 × 250 mL), the organic fraction was concentrated and passed through a short silica column eluting with dichloromethane/hexane, 9:1, gradually increasing to dichloromethane/hexane, 1:1. This gave the acetoxymethyl derivative, **7**, as a colorless gum (13.7 g, 91.8%). ^{1}H NMR both diastereomers (250 MHz, CDCl$_3$): $\delta$ 7.10−7.40 ppm (m, 18H), 5.12 ppm (d, 2H, $J$ = 9.3 Hz), 4.91 ppm (ds, 4H, $J$ = 3.2 Hz), 3.45 ppm (d, 1H, $J$ = 10.8 Hz), 3.31 ppm (d, 1H, $J$ = 10.8 Hz), 2.44 ppm (m, 1H), 1.60 ppm (d, 3H, $J$ = 6.3 Hz), 1.52 ppm (d, 3H, $J$ = 6.3 Hz), 1.41 ppm (m, 1H), 1.28 ppm (d, 3H, $J$ = 6.3 Hz), 1.07 ppm (s, 9H), 0.88 ppm (d, 3H, $J$ = 6.3 Hz), 0.81 ppm (s, 9H), 0.60 ppm (d, 3H, $J$ = 6.6 Hz), 0.21 ppm (d, 3H, $J$ = 6.6 Hz). ^{13}C NMR (APT) (63 MHz, CDCl$_3$, both diastereomers): $\delta$ 172.54 (s), 146.03 (s), 145.27 (s), 142.80 (s), 142.35 (s), 135.78 (d), 131.04 (d), 128.51 (d), 127.36 (d), 127.31 (d), 127.19 (d), 127.05 (d), 126.50 (d), 126.37 (d), 126.23 (d), 83.23 (d), 82.30 (d), 72.12 (d), 72.10 (d), 63.20 (t), 60.55 (s), 60.48 (s), 46.20 (d), 32.07 (d), 31.77 (d), 28.45 (q), 28.23 (q), 25.48 (q), 24.70 (q), 23.08 (q), 23.01 (q), 22.12 (q), 21.30 (q), 21.19 (q). Anal. Calcd for C$_{25}$H$_{35}$NO$_3$: C, 75.5; H, 8.87; N, 3.52. Found: C, 75.3; H, 8.82; N, 3.70.

**2,2,5-Trimethyl-3-(4′-$p$-hydroxymethylphenylethoxy)-4-phenyl-3-azahexane, 8.** 2,2,5-Trimethyl-3-(1′-$p$-acetoxymethylphenylethoxy)-4-phenyl-3-azahexane, **7** (19.9 g, 50.0 mmol), was mixed with water (100 mL), ethanol (30 mL), 18-crown-6 (0.20 g, 0.76 mmol), and sodium hydroxide (5.00 g, 125 mmol). The two-phase system was vigorously stirred and heated at reflux for 18 h. The reaction mixture was then cooled, extracted with dichloromethane, dried over magnesium sulfate, and concentrated. The crude product was purified by column chromatography eluting with dichloromethane/petroleum ether 3:2, gradually increasing to dichloromethane to give the hydroxyl-functionalized alkoxyamine, **8**, as a colorless oil (15.8 g, 89.1% yield). ^{1}H NMR both diastereomers (250 MHz, CDCl$_3$): $\delta$ 7.10−7.40 ppm (m, 18H), 4.96 ppm (m, 2H), 4.74 ppm (m, 4H), 3.40 ppm (d, 1H, $J$ = 10.8 Hz), 3.31 ppm (d, 1H, $J$ = 10.8 Hz), 2.42 ppm (m, 1H), 1.59 ppm (d, 3H, $J$ = 6.3 Hz), 1.50 ppm (d, 3H, $J$ = 6.3 Hz), 1.41 ppm (m, 1H), 1.32 ppm (d, 3H, $J$ = 6.3 Hz), 1.05 ppm (s, 9H), 0.93 ppm (d, 3H, $J$ = 6.3 Hz), 0.78 ppm (s, 9H), 0.61 ppm (d, 3H, $J$ = 6.6 Hz), 0.19 ppm (d, 3H, $J$ = 6.6 Hz). ^{13}C NMR (APT) (63 MHz, CDCl$_3$, both diastereomers): $\delta$ 146.11 (s), 145.24 (s), 142.55 (s), 135.67 (d),

131.12 (d), 128.43 (d), 127.33 (d), 127.16 (d), 127.03 (d), 126.42 (d), 126.21 (d), 83.19 (d), 82.34 (d), 72.10 (d), 63.05 (t), 60.68 (s), 60.52 (s), 32.17 (d), 31.70 (d), 28.50 (q), 28.24 (q), 24.73 (q), 23.09 (q), 22.10 (q), 21.19 (q). Anal. Calcd for C$_{23}$H$_{33}$NO$_2$: C, 77.7; H, 9.35; N, 3.94. Found: C, 77.6; H, 9.13; N, 3.68.

**2,2,5-Trimethyl-3-(1′-$p$-azidomethylphenylethoxy)-4-phenyl-3-azahexane, 9.** A mixture of the alkoxyamine, **3** (8.74 g, 23.0 mmol), sodium azide (4.40 g, 68.0 mmol), and 18-crown-6 (100 mg) was stirred in dimethyl sulfoxide (60 mL) at 60 °C for 16 h. The reaction mixture was then poured into water (600 mL) and extracted with dichloromethane (3 × 150 mL). The combined organic fractions were dried on MgSO$_4$, evaporated to dryness, and purified by flash chromatography eluting with dichloromethane. The azido derivative, **9**, was obtained as a colorless gum (7.38 g, 83.4%). IR (film): 2098 cm$^{-1}$ (azide). ^{1}H NMR both diastereomers (250 MHz, CDCl$_3$): $\delta$ 7.10−7.40 ppm (m, 18H), 4.73 ppm (q, 2H), 4.16 ppm (d, 4H), 3.44 ppm (d, 1H, $J$ = 10.8 Hz), 3.30 ppm (d, 1H, $J$ = 10.8 Hz), 2.39 ppm (m, 1H), 1.60 ppm (d, 3H, $J$ = 6.3 Hz), 1.49 ppm (d, 3H, $J$ = 6.3 Hz), 1.40 ppm (m, 1H), 1.28 ppm (d, 3H, $J$ = 6.3 Hz), 1.03 ppm (s, 9H), 0.90 ppm (d, 3H, $J$ = 6.3 Hz), 0.82 ppm (s, 9H), 0.63 ppm (d, 3H, $J$ = 6.6 Hz), 0.24 ppm (d, 3H, $J$ = 6.6 Hz). ^{13}C NMR (APT) (63 MHz, CDCl$_3$, both diastereomers): $\delta$ 146.28 (s), 145.25 (s), 142.63 (s), 135.56 (d), 131.10 (d), 128.43 (d), 128.30 (d), 127.28 (d), 127.11 (d), 127.00 (d), 126.53 (d), 126.25 (d), 83.25 (d), 82.21 (d), 72.09 (d), 63.13 (t), 60.70 (s), 60.58 (s), 50.35 (t), 32.23 (d), 31.76 (d), 28.46 (q), 28.19 (q), 24.82 (q), 23.13 (q), 22.09 (q), 21.27 (q). Anal. Calcd for C$_{23}$H$_{33}$N$_4$O: C, 72.6; H, 8.46; N, 14.72. Found: C, 72.6; H, 8.58; N, 14.93.

**2,2,5-Trimethyl-3-(1′-$p$-aminomethylphenylethoxy)-4-phenyl-3-azahexane, 10.** Lithium aluminum hydride (920 mg, 25.0 mmol) was slowly added to 2,2,5-trimethyl-3-(1′-$p$-azidomethylphenylethoxy)-4-phenyl-3-azahexane, **9** (7.90 g, 25.0 mmol), dissolved in dry THF (150 mL), and cooled to 0 °C. After being stirred under argon for 16 h, water (1 mL) was slowly added to the reaction mixture, followed by filtration and concentration by rotary evaporation. The crude product was purified by column chromatography eluting with dichloromethane, gradually increasing to 10% methanol/dichloromethane to give the amino derivative, **10**, as a colorless gum (6.70 g, 91.0%). ^{1}H NMR both diastereomers (250 MHz, CDCl$_3$): $\delta$ 7.10−7.40 ppm (m, 18H), 4.93 ppm (q, 2H, $J$ = 6 Hz), 3.89 ppm (d, 4H, $J$ = 9.6 Hz), 3.41 ppm (d, 1H, $J$ = 10.8 Hz), 3.28 ppm (d, 1H, $J$ = 10.8 Hz), 2.40 ppm (m, 1H), 1.61 ppm (d, 3H, $J$ = 6.3 Hz), 1.48 ppm (d, 3H, $J$ = 6.3 Hz), 1.40 ppm (m, 1H), 1.27 ppm (d, 3H, $J$ = 6.3 Hz), 1.02 ppm (s, 9H), 0.90 ppm (d, 3H, $J$ = 6.3 Hz), 0.81 ppm (s, 9H), 0.57 ppm (d, 3H, $J$ = 6.6 Hz), 0.22 ppm (d, 3H, $J$ = 6.6 Hz). ^{13}C NMR (APT) (63 MHz, CDCl$_3$, both diastereomers): $\delta$ 146.31 (s), 145.37 (s), 142.80 (s), 135.67 (d), 131.22 (d), 128.56 (d), 128.45 (d), 128.31 (d), 127.32 (d), 127.08 (d), 127.04 (d), 126.62 (d), 126.29 (d), 83.32 (d), 82.28 (d), 72.16 (d), 63.21 (t), 60.71 (s), 60.46 (s), 56.32 (t), 32.15 (d), 31.69 (d), 28.51 (q), 28.30 (q), 24.80 (q), 23.17 (q), 22.13 (q), 21.32 (q). Anal. Calcd for C$_{23}$H$_{34}$N$_2$O: C, 77.92; H, 9.67; N, 7.90. Found: C, 77.80; H, 9.43; N, 8.03.

**2,2,5-Trimethyl-3-(1′-$p$-($t$-butyloxycarbonylamidomethylphenylethoxy)-4-phenyl-3-azahexane, 11.** Di-$tert$-butyl dicarbonate (0.89 g, 4.10 mmol) was slowly added to 2,2,5-trimethyl-3-(1′-$p$-aminomethylphenylethoxy)-4-phenyl-3-azahexane, **10** (1.20 g, 3.40 mmol), and triethylamine (500 mg, 4.95 mmol) dissolved in dry dichloromethane (10 mL). After being stirred at room temperature under argon for 12 h, the reaction mixture was washed with saturated NaHCO$_3$ (25 mL), followed by water (25 mL). The organic fraction was evaporated to dryness and purified by flash chromatography using dichloromethane as eluent to give the protected amino derivative, **11**, as a colorless gum (1.50 g, 94.9%). IR (film): 3352 cm$^{-1}$ (N−H), 1704 cm$^{-1}$ (amide). ^{1}H NMR both diastereomers (250 MHz, CDCl$_3$): $\delta$ 7.10−7.40 ppm (m, 18H), 4.88 ppm (m, 2H), 4.74 ppm (br, 2H), 4.22 ppm (m, 4H), 3.41 ppm (d, 1H, $J$ = 10.8 Hz), 3.30 ppm (d, 1H, $J$ = 10.8 Hz), 2.43 ppm (m, 1H), 1.60 ppm (d, 3H, $J$ = 6.3 Hz), 1.49 ppm (d, 3H, $J$ = 6.3

(16) (a) Harth, E.; Hawker, C. J.; Fan, W.; Waymouth, R. M. *Macromolecules* **2001**, *34*, 3856. (b) Hawker, C. J.; Barclay, G. G.; Orellana, A.; Dao, J.; Devonport, W. *Macromolecules* **1996**, *29*, 5245.
(17) Itsuno, S.; Nakano, M.; Ito, K.; Hirao, A.; Owa, M.; Kanda, N.; Nakahama, S. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2615.
(18) Leduc, M. R.; Hawker, C. J.; Dao, J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1996**, *118*, 11111.
(19) Feibush, B.; Figueroa, A.; Charles, R.; Onan, K. D.; Feibush, P.; Karger, B. L. *J. Am. Chem. Soc.* **1986**, *108*, 3310.

Hz), 1.41 ppm (m, 1H), 1.32 ppm (d, 3H, $J = 6.3$ Hz), 1.20 ppm (s, 18H), 1.02 ppm (s, 9H), 0.88 ppm (d, 3H, $J = 6.3$ Hz), 0.81 ppm (s, 9H), 0.60 ppm (d, 3H, $J = 6.6$ Hz), 0.21 ppm (d, 3H, $J = 6.6$ Hz). ^{13}C NMR (APT) (63 MHz, CDCl$_3$, both diastereomers): $\delta$ 173.54 (s), 146.65 (s), 145.44 (s), 142.72 (s), 135.51 (d), 132.13 (d), 128.62 (d), 128.50 (d), 128.45 (d), 128.28 (d), 127.40 (d), 127.11 (d), 127.01 (d), 126.24 (d), 83.25 (d), 82.34 (d), 74.17 (s), 72.20 (d), 63.34 (t), 60.82 (s), 60.45 (s), 54.45 (t), 33.10 (q), 32.10 (d), 31.78 (d), 28.45 (q), 28.23 (q), 24.81 (q), 23.33 (q), 22.16 (q), 21.36 (q). Anal. Calcd for C$_{29}$H$_{42}$N$_2$O$_3$: C, 74.64; H, 9.07; N, 6.00. Found: C, 74.31; H, 8.89; N, 5.78.

**2,2,5-Trimethyl-3-(1′-*p*-((S)-(−)-2″-amino-3″-*p*-oxyphenyl)-1″,1″-diphenylpropan-1″-ol)-benzylethoxy)-4-phenyl-3-azahexane, 12.** NaH (0.23 g, 6.30 mmol) was slowly added to a mixture of **4**[17] (0.50 g, 1.57 mmol) and 18-crown-6 (10 mg) dissolved in THF (10 mL) under a constant argon flow. After 15 min, alkoxyamine, **3** (0.58 g, 1.57 mmol), was added to the reaction mixture, which was subsequently heated at reflux under argon for 16 h. After the addition of a few drops of water to neutralize the excess NaH, the reaction mixture was concentrated, dissolved in dichloromethane (50 mL), and washed with water (2 × 50 mL). The crude product was obtained after drying with Na$_2$SO$_4$ and evaporation to dryness. The pure compound, **12**, was obtained as a yellowish solid after flash chromatography eluting with dichloromethane gradually increasing to 10% methanol/dichloromethane (903 mg, 86.2%). IR (KBr): 3439 cm$^{-1}$ (NH). ^{1}H NMR both diastereomers (250 MHz, CDCl$_3$): $\delta$ 6.80−7.70 ppm (m, 46H), 4.93 ppm (m, 2H), 4.84 ppm (m, 2H), 4.05 ppm (m, 2H), 3.41 ppm (d, 1H, $J = 10.8$ Hz), 3.30 ppm (d, 1H, $J = 10.8$ Hz), 2.42 ppm (m, 1H), 1.63 ppm (d, 3H, $J = 6.3$ Hz), 1.52 ppm (d, 3H, $J = 6.3$ Hz), 1.39 ppm (m, 1H), 1.30 ppm (d, 3H, $J = 6.3$ Hz), 1.04 ppm (s, 9H), 0.92 ppm (d, 3H, $J = 6.3$ Hz), 0.80 ppm (s, 9H), 0.61 ppm (d, 3H, $J = 6.6$ Hz), 0.20 ppm (d, 3H, $J = 6.6$ Hz). Anal. Calcd for C$_{44}$H$_{52}$N$_2$O$_3$: C, 80.45; H, 7.98; N, 4.26. Found: C, 80.56; H, 7.74; N, 3.97.

**2,2,5-Trimethyl-3-(1′-*p*-((S)-(−)-2″-(*t*-butyl-oxy-carbonylamide)-3″-*p*-oxyphenyl)-1″,1″-diphenylpropan-1″-ol)-benzylethoxy)-4-phenyl-3-azahexane, 13.** Di-*tert*-butyl dicarbonate (6.04 g, 27.0 mmol) was slowly added to a mixture of 2,2,5-trimethyl-3-(1′-*p*-((S)-(−)-2″-amino-3″-*p*-oxyphenyl)-1″,1″-diphenylpropan-1″-ol)-benzylethoxy)-4-phenyl-3-azahexane, **12** (7.89 g, 11.7 mmol), and triethylamine (3.75 g, 37 mmol) dissolved in dry THF (75 mL). After being stirred for 2 h at room temperature, the solvent was evaporated, and the crude product was dissolved in ethyl acetate (200 mL), followed by washing with saturated NaHCO$_3$ (2 × 100 mL). Drying and evaporation to dryness gave the crude product, which was purified by flash chromatography eluting with dichloromethane gradually increasing to 10% diethyl ether/dichloromethane to give the carbamate, **13**, as a yellow gum (4.98 g, 56.2%). IR (KBr): 3439 cm$^{-1}$ (NH), 1645 cm$^{-1}$ (carbamate). ^{1}H NMR both diastereomers (250 MHz, CDCl$_3$): $\delta$ 7.7−6.8 ppm (m, 46H), 4.94 ppm (m, 2H), 4.81 ppm (m, 2H), 4.63 (br, 2H), 3.70 ppm (m, 2H), 3.27 ppm (d, 1H, $J = 10.8$ Hz), 3.10 ppm (d, 1H, $J = 10.8$ Hz), 2.69 ppm (m, 4H), 2.42 ppm (m, 1H), 1.61 ppm (d, 3H, $J = 6.3$ Hz), 1.48 ppm (d, 3H, $J = 6.3$ Hz), 1.40 ppm (m, 1H), 1.32 ppm (d, 3H, $J = 6.3$ Hz), 1.24 ppm (s, 18H), 1.05 ppm (s, 9H), 0.91 ppm (d, 3H, $J = 6.3$ Hz), 0.80 ppm (s, 9H), 0.59 ppm (d, 3H, $J = 6.6$ Hz), 0.23 ppm (d, 3H, $J = 6.6$ Hz). Anal. Calcd for C$_{49}$H$_{60}$N$_2$O$_5$: C, 77.75; H, 7.99; N, 3.70. Found: C, 77.62; H, 7.89; N, 3.46.

**Macroinitiators. General Procedure for Styrene Polymerization, 14−23.** A mixture of styrene (11.5 g, 111 mmol) and the alkoxyamine, **2** (601 mg, 1.80 mmol), was degassed by three freeze/thaw cycles, sealed under argon, and heated at 125 °C for 8 h. The viscous reaction mixture was then dissolved in dichloromethane (25 mL) and precipitated in methanol (1 L). The white powder was filtered, and then dried in vacuo to give the alkoxyamine-terminated polystyrene (10.0 g, 82.5%).

**General Procedure for Acrylate Polymerization, 24, 25.** A mixture of *n*-butyl acrylate (7.36 g, 58.0 mmol), the alkoxyamine **2** (348 mg, 1.10 mmol), and nitroxide **1** (13 mg, 58 $\mu$mol) was degassed by three

freeze/thaw cycles, sealed under argon, and heated at 125 °C for 16 h. The reaction mixture was then diluted with dichloromethane (20 mL) and precipitated in methanol (500 mL). The colorless gum was collected and dried in vacuo to give the poly(*n*-butyl acrylate) derivative (6.01 g, 78.0%).

**General Procedure for *N*-Isopropylacrylamide Polymerization, 26.** A mixture of *N*-isopropylacrylamide (8.40 g, 74.0 mmol), alkoxyamine **2** (476 mg, 1.50 mmol), nitroxide **1** (17 mg, 78 $\mu$mol), and DMF (9 mL) was degassed by three freeze/thaw cycles, sealed under argon, and heated at 125 °C for 48 h. The reaction mixture was then diluted with dichloromethane (25 mL) and precipitated in diethyl ether (500 mL). The white powder was filtered, and then dried in vacuo to give the desired poly(*N*-isopropylacrylamide) linear polymer, **26** (5.71 g, 64.3%).

**General Procedure for *N,N*-Dimethylacrylamide Polymerization, 27−29.** A mixture of *N,N*-dimethylacrylamide (3.38 g, 34.0 mmol), alkoxyamine **2** (264 mg, 0.81 mmol), and nitroxide **1** (9.0 mg, 41 $\mu$mol) was degassed by three freeze/thaw cycles, sealed under argon, and heated at 125 °C for 16 h. The reaction mixture was then diluted with dichloromethane (20 mL) and precipitated in hexanes (500 mL). The white powder was filtered, and then dried in vacuo to give the alkoxyamine-terminated poly(*N,N*-dimethylacrylamide) derivative (2.62 g, 72.0%).

**General Procedure for 2-Vinylpyridine Polymerization, 30.** A mixture of 2-vinylpyridine (10.0 g, 95.0 mmol) and the alkoxyamine **2** (746 mg, 2.3 mmol) was degassed by three freeze/thaw cycles, sealed under argon, and heated at 125 °C for 5 h. The reaction mixture was then diluted with dichloromethane (30 mL) and precipitated in hexanes (500 mL). The yellowish powder was filtered, and then dried in vacuo to give the desired alkoxyamine-terminated poly(2-vinylpyridine), **30** (8.87 g, 82.5%).

**General Procedure for Formation of Star Polymers, 31−47.** A mixture of the polymeric macroinitiator, **16** (2.07 g, 0.36 mmol, $M_n =$ 5700, PDI = 1.08), styrene (315 mg, 3.03 mmol), and divinylbenzene (156 mg, 1.20 mmol) was dissolved in DMF (8.0 mL), degassed by three freeze/thaw cycles, and sealed under argon. The polymerization mixture was then stirred at 125 °C for 16 h, allowed to cool, and the star polymer, **33**, was obtained after precipitation using propan-2-ol (2.08 g, 82%, $M_n = 74\,000$, PDI = 1.19). Poly(*N*-isopropylacrylamide)-containing stars were precipitated with diethyl ether as nonsolvent at 0 °C, whereas hexanes were used as nonsolvent for the poly(*N,N*-dimethylacrylamide)-containing stars.

**General Procedure for Block Copolymer Formation: Preparation of Poly(*n*-butyl Acrylate)-*b*-polystyrene, 48−59.** A mixture of the alkoxyamine-terminated poly(*n*-butyl acrylate) starting block, **24** (2.00 g, 0.40 mmol, $M_n = 5000$, PDI = 1.09), was dissolved in styrene (2.50 g, 24.0 mmol), degassed by three freeze/thaw cycles, sealed under argon, and the polymerization reaction was heated at 125 °C for 8 h. The solidified reaction mixture was then dissolved in dichloromethane (20 mL) and precipitated (2×) into methanol (500 mL). The precipitate was then collected by vacuum filtration and dried to give the desired block copolymer, **53**, as a white solid (4.06 g, 90.2%, $M_n = 9700$, PDI = 1.12).

**X-ray Analysis.** Crystals were obtained after separation of both diastereoisomers of **3** with flash chromatography on silica using petroleum ether/dichloromethane 10:1 as eluent, followed by crystallization from a mixture of dichloromethane/hexane. The X-ray structure analyses data were collected with a Bruker SMART CCD area-detector diffractometer using graphite monochromated Mo Kα radiation ($T = -119 \pm 1$ °C). Data were corrected for Lorentz and polarization effects. The structure was solved by direct methods[20] and expanded using Fourier techniques.[21] The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. Crystal data:

(20) Altomare, A.; Cascarano, M.; Giacovazzo, C.; Guagliardi, A. *J. Appl. Crystallogr.* **1993**, *26*, 343.

$C_{23}H_{32}NOCl$, $M_r$ = 373.96, colorless prismatic crystal (0.22 × 0.21 × 0.19 mm), primitive monoclinic cell, $P2_1/n$ (no. 14) with $a$ = 8.7967(4) Å, $b$ = 8.8891(2) Å, $c$ = 27.195(2) Å, $\beta$ = 96.139(2)°, $V$ = 2114.3(2) Å$^3$, $Z$ = 4, $D_c$ = 1.17 g/cm$^3$, $\mu$(Mo Kα) = 15.89 cm$^{-1}$, 9091 reflections measured (3.50 < $2\theta$ < 45.00°), 3772 unique ($R_{int}$ = 0.032), $R_1$ = 0.031 (for 1842 $I$ > 3.00 $\sigma(I)$). No residual density outside −0.16 and 0.25 e Å$^{-3}$.

**Dye Complexation Studies.** To a solution of the PSt-P(4VP-*r*-St) star, **72** (50 mg, 0.06 mmol 4VP), in a mixture of toluene (5 mL) and chloroform (1 mL) was added coumarin-3-carboxylic acid, **60** (6.0 mg, 0.032 mmol), or Zn(II) protoporphyrin IX, **61** (9.0 mg, 0.014 mmol). After being stirred overnight, a deeply colored solution was obtained that was subsequently filtered over Celite, concentrated, and evaporated to dryness. The complexation behavior of the dye was studied by a range of spectroscopic techniques.

**H-Bonded Complexes with Maleimide-Functionalized Stars.** FT-IR spectra were obtained in deuterated chloroform (5−10 mM) using NaCl cells with a 1 mm path length. $^1$H NMR titration experiments were performed by portionwise addition of the maleimide-functionalized star, **73**, to a solution of 2,6-bis(acetylamino)pyridine, **6** (17 mM), in deuterated chloroform. The association constant was determined using a nonlinear least-squares fitting procedure.[55]

**Enantioselective Addition of Et$_2$Zn to Benzaldehyde.** To a solution of tyrosine-functionalized star, **39** (220 mg), deprotected with trifluo-

roacetic acid under standard conditions, in dry toluene (1.5 mL) was added benzaldehyde (120 $\mu$L, 20 mol equiv with respect to each Tyr-end group). After being stirred for 16 h under an argon atmosphere, the reaction mixture was cooled to 0 °C, and a 1 M solution of Et$_2$Zn in hexane (2.7 mL, 3 mol equiv to benzaldehyde) was added. After 8 h, the reaction was quenched with 1 M HCl and extracted with dichloromethane. GC-MS and $^1$H NMR analysis of the extract showed quantitative conversion to 1-phenylpropanol. GC analysis with a chiral stationary phase ($\beta$-Dex capillary column, Supelco Co.) gave an ee of 71%, whereas the negative sign of the optical rotation showed predominant formation of the *S*-configuration.

**Pd-Nanoparticle Formation and Catalysis.** The palladium nano-particle was prepared by dissolving the PSt-P2VP star, **71** (200 mg, 0.27 mmol equiv of 2VP), in toluene (10 mL) and subsequent addition of palladium acetate (15 mg, 0.25 mol Pd(OAc)$_2$ per mol 2VP). After the mixture was stirred at room temperature for 4 h under an argon atmosphere, complete dissolution of the palladium salts was observed, and a clear light orange solution was obtained. The solution was diluted with ethanol (5 mL) followed by heating to 80 °C for 16 h. The resulting dark brown solution was concentrated followed by precipitation in methanol. After being dried in vacuo, the Pd(0)-containing star, **78**, was obtained as a dark brown precipitate.

Hydrogenation experiments were performed by dissolving the Pd-containing star, **78** (10 mg, 0.007 mmol of Pd), in THF (15 mL) in an argon atmosphere. The reaction mixture was purged with hydrogen, and subsequently 0.5 mL (4.9 mmol) of cyclohexene was added while a hydrogen atmosphere was maintained at a pressure of 1 atm. After 1 h at 30 °C, a sample was taken from the reaction mixture, precipitated in methanol, filtered through a microfilter, and analyzed with GC-MS.

The Heck coupling was performed by dissolving the Pd-containing star, **78** (28 mg, 0.019 mmol of Pd), in xylenes (10 mL) followed by the addition of 1-bromo-4-nitrobenzene (788 mg, 3.9 mmol), *n*-butyl acrylate (2.5 g, 20 mmol), tri-*n*-butylamine (1.1 g, 5.9 mmol), and tetradecane (200 mg) as internal standard. After the mixture was heated to 125 °C, aliquots were taken from the reaction mixture, precipitated in methanol, filtered through a microfilter, and analyzed with GC. After 2 h, the reaction was washed with water (3 × 20 mL), evaporated to dryness, and analyzed by $^1$H NMR.

(21) Beurskens, P. T.; Admiraal, G.; Beurskens, G.; Bosman, W. P.; de Gelder, R.; Israel, R.; Smits, J. M. M. *The DIRDIF-94 Program System*; Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands, 1994.
(22) (a) Sawamoto, M.; Kamigaito, M. *CHEMTECH* **1999**, *29*, 30−38. (b) Malmstrom, E. E.; Hawker, C. J. *Macromol. Chem. Phys.* **1998**, *199*, 923. (c) Matyjaszewski, K. *Controlled Radical Polymerization ACS Symposium Series 685*; Matyjaszewski, K., Ed.; American Chemical Society: Washington, DC, 1998; pp 1−25. (d) Hawker, C. J. *Acc. Chem. Res.* **1997**, *30*, 373.
(23) (a) Baek, K. Y.; Kamigaito, M.; Sawamoto, M. *Macromolecules* **2001**, *34*, 7629. (b) Matyjaszewski, K.; Miller, P. J.; Pyun, J.; Kickelbick, G.; Diamanti, S. *Macromolecules* **1999**, *32*, 6526.
(24) (a) Benoit, D.; Grimaldi, S.; Robin, S.; Finet, J. P.; Tordo, P.; Gnanou, Y. *J. Am. Chem. Soc.* **2000**, *122*, 5929. (b) Benoit, D.; Chaplinski, V.; Braslau, R.; Hawker, C. J. *J. Am. Chem. Soc.* **1999**, *121*, 3904.
(25) Benoit, D.; Harth, E.; Fox, P.; Waymouth, R. M.; Hawker, C. J. *Macromolecules* **2000**, *33*, 363.
(26) Husemann, M.; Malmstrom, E.; McNamara, M.; Mate, M.; Mecerreyes, D.; Benoit, D.; Hedrick, J.; Mansky, P.; Huang, E.; Russell, T.; Hawker, C. J. *Macromolecules* **1999**, *32*, 1424.
(27) Bignozzi, M. C.; Ober, C. K.; Laus, M. *Macromol. Rapid Commun.* **1999**, *20*, 622.
(28) (a) Ananchenko, G. S.; Souaille, M.; Fischer, H.; LeMercier, C.; Tordo, P. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 3264. (b) Ananchenko, G. S.; Fischer, H. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 3604. (c) Fischer, H. *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37*, 1885.
(29) Götz, H.; Harth, E.; Schiller, S. M.; Frank, C. W.; Knoll, W.; Hawker, C. J. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 3379.
(30) Skene, W. G.; Scaiano, J. C.; Yap, G. P. A. *Macromolecules* **2000**, *33*, 3536.
(31) Bowman, D. F.; Gillan, T.; Ingold, K. U. *J. Am. Chem. Soc.* **1971**, *93*, 6555.
(32) Spek, A. L. *PLUTON. A Program for Plotting Molecules and Crystal Structures*; University of Utrecht, Utrecht, Netherlands, 1995.
(33) Li, D.; Brittain, W. J. *Macromolecules* **1998**, *31*, 3852.
(34) Rodlert, M.; Harth, E.; Rees, I.; Hawker, C. J. *J. Polym. Sci., Polym. Chem.* **2000**, *38*, 4749.
(35) The number of arms was estimated by determining the absolute molecular weight of the star polymer by either MALLS or viscosity experiments, and, after assuming that 90% of the mass of the star polymer is due to the arms (10% is due to the core), it was estimated by dividing this final molecular weight by the molecular weight of the starting linear polymer.
(36) (a) Grubbs, R. B.; Dean, J. M.; Broz, M. E.; Bates, F. S. *Macromolecules* **2000**, *33*, 9522. (b) Hawker, C. J.; Hedrick, J. L.; Malmstrom, E. E.; Trollsas, M.; Mecerreys, D.; Dubois, P.; Jerome, R. *Macromolecules* **1998**, *31*, 213.
(37) (a) Hedrick, J. L.; Miller, R. D.; Hawker, C. J.; Carter, K. R.; Volksen, W.; Yoon, D. Y.; Trollsas, M. *Adv. Mater.* **1998**, *10*, 1049. (b) Hawker, C. J.; Hedrick, J. L.; Miller, R. D.; Volksen, W. *MRS Bull.* **2000**, *25*, 54. (c) Yang, S.; Mirau, P. A.; Pai, C. S.; Nalamasu, O.; Reichmanis, E.; Lin, E. K.; Lee, H. J.; Gidley, D. W.; Sun, J. N. *Chem. Mater.* **2001**, *13*, 2762.
(38) Itsuno, S.; Fréchet, J. M. J. *J. Org. Chem.* **1987**, *52*, 4140.
(39) Chung, Y. M.; Rhee, H. K. *Chem. Commun.* **2002**, 238.
(40) Peerlings, H. W. I.; Meijer, E. W. *Chem.-Eur. J.* **1997**, *3*, 1563.
(41) Itsuno, S.; Sakurai, Y.; Ito, K.; Maruyama, T.; Nakahama, S.; Fréchet, J. M. J. *J. Org. Chem.* **1990**, *55*, 304.

(42) Kragl, U.; Dreisbach, C. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 642. Hovestad, N. J.; Eggeling, E. B.; Heidbüchel, H. J.; Jastrzebski, J. T. B. H.; Kragl, U.; Keim, W.; Vogt, D.; van Koten, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 1655.
(43) Jung, M. E.; Lyster, M. A. *J. Am. Chem. Soc.* **1977**, *99*, 968. Zhang, Q.; Remsen, E. E.; Wooley, K. L. *J. Am. Chem. Soc.* **2000**, *122*, 3642.
(44) Kline, S. R. *Langmuir* **1999**, *15*, 2726−2732.
(45) Benoit, D.; Hawker, C. J.; Huang, E. E.; Lin, Z.; Russell, T. P. *Macromolecules* **2000**, *33*, 1505.
(46) (a) Hawker, C. J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1990**, *112*, 7638. (b) Hawker, C. J.; Fréchet, J. M. J. *J. Chem. Soc., Chem. Commun.* **1990**, 1010. (c) Wooley, K. L.; Hawker, C. J.; Frechet, J. M. J. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1059.
(47) Jeong, M.; Mackay, M. E.; Vestberg, R.; Hawker, C. J. *Macromolecules* **2001**, *34*, 4927.
(48) Leduc, M. R.; Hayes, W.; Fréchet, J. M. J. *J. Polym. Sci., Polym. Chem.* **1998**, *36*, 1.
(49) (a) Kumar, U.; Kato, T.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1996**, *118*, 11111. (b) Kato, T.; Kihara, H.; Ujiie, S.; Uryu, S.; Fréchet, J. M. J. *Macromolecules* **1996**, *29*, 8734. (c) Kihara, H.; Kato, T.; Uryu, S.; Fréchet, J. M. J. *Chem. Mater.* **1996**, *8*, 961. (d) Kato, T.; Fréchet, J. M. J. *Macromolecules* **1989**, *22*, 3818.
(50) Hecht, S.; Vladimirov, N.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **2001**, *123*, 18.
(51) (a) Abraham, R. J.; Fell, S. C. M.; Pearson, H. *Tetrahedron* **1979**, *35*, 1759. (b) Dolphin, D., Ed. *The Porphyrins*; Academic Press: New York, 1978.
(52) (a) Sijbesma, R. P.; Beijer, F. H.; Brunsveld, L.; Folmer, B. J. B.; Hirschberg, J. J. K. K.; Lange, R. F. M.; Lowe, J. K. L.; Meijer, E. W. *Science* **1997**, *278*, 1601. (b) Sherrington, D. C.; Taskinen, K. A. *Chem. Soc. Rev.* **2001**, *30*, 83. (c) Sherrington, D. C. *J. Polym. Sci., Polym. Chem.* **2001**, *39*, 2364.
(53) Lange, R. F. M.; Meijer, E. W. *Macromolecules* **1995**, *28*, 782.
(54) Lange, R. F. M.; Beijer, F. H.; Sijbesma, R. P.; Hooft, R. W. W.; Kooijman, H.; Spek, A. L.; Kroon, J.; Meijer, E. W. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 969.
(55) Beijer, F. H.; Sijbesma, R. P.; Vekemans, J. A. J. M.; Meijer, E. W.; Kooijman, H.; Spek, A. L. *J. Org. Chem.* **1996**, *61*, 6371.

## Results and Discussion

One of the attractive features of living free radical polymerizations, which makes these procedures applicable for the formation of star polymers, is the presence of a dormant initiating group at one of the polymer chain ends.[22] This dormant chain end, an alkoxyamine functionality in the case of nitroxide-mediated living free radical polymerization, is obtained as a direct result of the mechanism of the polymerization in which the mediating nitroxide radical is continually cleaved and reinserted at the growing chain end. Under the appropriate conditions, reactivation of this dormant chain end in the presence of a cross-linking monomer, such as divinylbenzene, leads to the coupling of a multiplicity of these starting linear chains to give a highly branched star polymer in a single step.[23] Obviously, the ultimate structure of this star polymer is dictated to a large extent by the structure of the starting linear polymer. However, the versatility of the living free radical approach enabling not only the preparation of chains functionalized either at the chain end or along the backbone, but also that of random copolymers or block copolymers, can lead to a wealth of different functionalized star polymers.

**End Group Functionality.** These synthetic possibilities were initially examined by introducing the functional groups specifically at the multiple chain ends of the star polymers in a controlled fashion. To succeed in the preparation of chain-end-functionalized star polymers, it is critical to have access to the corresponding functionalized initiators while also ensuring that the telechelic polymers derived from these initiators have a high degree of chain end retention (ca. 95–100%). One family of alkoxyamine initiators that fulfills both of these criteria is the recently introduced α-hydrido alkoxyamines[24] that contain a hydrogen atom attached to a carbon located α to the nitroxide nitrogen. Experimental results have proven the applicability of this family of initiators to the controlled polymerization of a wide variety of monomers,[25–27] while combined kinetic and theoretical studies have highlighted their usefulness in procedures where the persistent radical effect (PRE) is operative.[28] This ability to control polymerizations is a surprising result given the general lack of stability of nitroxides with hydrogen atoms in the α-position and their propensity toward decomposition, for example, by disproportionation.[31] To better understand this important new family of alkoxyamine-based initiators, the crystal structure of the *p*-chloromethyl derivative, **3**,[15,29] has been resolved by X-ray spectroscopy.

Depicted in Figure 2 is the *SS*-diastereoisomer, present together with its enantiomer in the crystal. The N−O−C bond lengths and angles are comparable to those found in the crystal structures of other alkoxyamines.[30] However, the most intriguing aspect of the structure is the O(1)−N(1)−C(10)−H(11) torsion angle of 167.54°. This results in an almost transoid orientation of the proton with respect to the oxygen and is most likely a direct result of steric hindrance between the *tert*-butyl group on the nitrogen and the isopropyl and phenyl moieties on the adjacent carbon C(10). Because disproportionation is thought to occur via a five-membered transition state with the O and the H-atoms cisoid,[31] the tendency of nitroxides, such as **1**, to undergo disproportionation is significantly reduced and may explain their significantly improved performance in living free radical polymerizations as compared to traditional TEMPO (2,2,6,6-tetramethylpiperidinyloxy) systems.
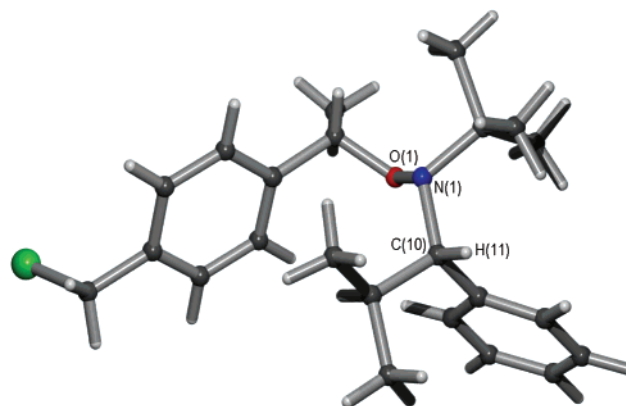
**Figure 2.** X-ray structure[32] of **3**.

**Table 1.** Molecular Weight Data for Alkoxyamine-Terminated Homopolymers[a]

| | | | | | | |
|---|---|---|---|---|---|---|
| | | alkoxyamine-terminated homopolymers | | | | |
| entry | initiator | monomer | DP[b] | $M_{n,NMR}$[b] (kDa) | $M_{n,GPC}$ (kDa) | $M_w/M_n$ |
| **14** | **2** | St | 48 | 5.3 | 5.5 | 1.09 |
| **15** | **2** | St | 84 | 9.0 | 9.1 | 1.07 |
| **16** | **3** | St | 57 | 5.7 | 5.8 | 1.08 |
| **17** | **3** | St | 96 | 10.3 | 9.9 | 1.10 |
| **18** | **8** | St | 45 | 4.8 | 4.4 | 1.06 |
| **19** | **8** | St | 55 | 5.5 | 5.1 | 1.08 |
| **20** | **8** | St | 65 | 7.1 | 7.2 | 1.10 |
| **21** | **11** | St | 47 | 5.2 | 4.3 | 1.08 |
| **22** | **13** | St | 44 | 5.2 | 4.7 | 1.12 |
| **23** | **13** | St | 55 | 6.3 | 6.0 | 1.14 |
| **24** | **2** | *n*BA | 45 | 5.4 | 5.0 | 1.09 |
| **25** | **2** | *t*BA | 40 | 5.5 | 4.6 | 1.12 |
| **26** | **8** | NIPAM | 31 | 3.9 | 2.6 | 1.12 |
| **27** | **2** | DMA | 44 | 5.2 | 8.9 | 1.09 |
| **28** | **8** | DMA | 55 | 7.1 | 10.3 | 1.06 |
| **29** | **8** | DMA | 90 | 10.2 | 14.4 | 1.12 |
| **30** | **2** | 2VP | 34 | 3.6 | 5.5 | 1.14 |

[a] Molecular weight data after purification; GPC data relative to PS-standards. [b] Obtained by integration of $^1$H NMR signals.

The conversion of the *p*-chloromethyl functionality into a variety of other functional groups is facilitated by the inertness of the alkoxyamine group to basic and reducing reaction conditions (see Scheme 1).[29] For example, substitution of the chloromethyl functionality with sodium azide followed by reduction with lithium aluminum hydride gives **10** containing a benzylic amine. Alternatively, substitution with potassium acetate followed by basic hydrolysis resulted in a molecule, **8**, with a benzylic alcohol functionality. More complex functional groups such as the L-Tyr-based ligand,[17] **4**, could also be introduced using nucleophilic displacement.

The compatibility of these functional groups with living free radical procedures was then demonstrated by the polymerization of a variety of vinyl monomers from these functionalized initiators. As shown in Tables 1–4, in each case, the polymerization proved to be successful, although it was necessary to protect the amine function with a Boc-group, **11**, to prevent formation of a small (approximately 2–5%) amount of higher molecular weight coupled product. Of particular note is the ability to control the polymerization of functionalized monomers such as *N,N*-dimethylacrylamide (DMA) and *N*-isopropylacrylamide (NIPAM), both of which are difficult to polymerize in a controlled fashion under typical ATRP conditions.[33]

**Scheme 1.** Synthesis of Functionalized Initiators, **8**, **11**, and **13**, from the Chloromethyl Alkoxyamine, **3**
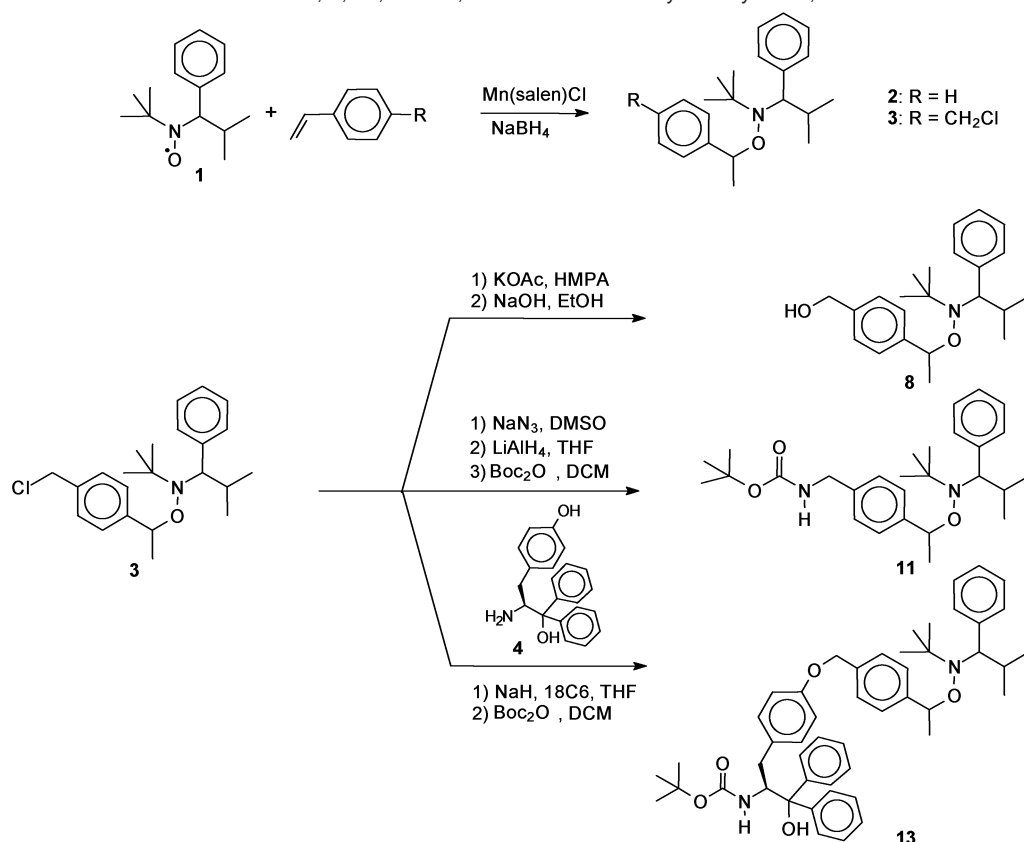


**Table 2.** Molecular Weight Data for Homopolymer Stars[a]

| | | star polymers | | |
| --- | --- | --- | --- | --- |
| macroinitiator | star no. | $M_{n,GPC}$ (kDa) | $M_w/M_n$ | conversion (%) |
| **14** | **31** | 56 | 1.35 | 85 |
| **15** | **32** | 106 | 1.22 | 87 |
| **16** | **33** | 74 (195)[c] | 1.19 | 82 |
| **17** | **34** | 117 | 1.20 | 79 |
| **18** | **35** | 72 | 1.22 | 83 |
| **19** | **36** | 76 | 1.16 | 85 |
| **20** | **37** | 67 | 1.26 | 90 |
| **21** | **38** | 58 | 1.21 | 92 |
| **22** | **39** | 73 | 1.28 | 83 |
| **23** | **40** | 70 | 1.19 | 78 |
| **24** | **41** | 102 (142)[b] | 1.24 (1.95)[b] | 76 (81)[b] |
| **25** | **42** | 89 (160)[b] | 1.27 (2.10)[b] | 85 (80)[b] |
| **26** | **43** | 73 | 1.21 | 66 |
| **27** | **44** | 69 | 1.30 | 86 |
| **28** | **45** | 83 | 1.19 | 79 |
| 1:1 **27**+**28** | **46** | 98 | 1.24 | 64 |
| **30** | **47** | 38 | 1.14 | 43 |

[a] Molecular weight data for star polymers after purification; GPC data relative to PS-standards. [b] GPC data in brackets are for optimized conditions for polystyrene star formation. [c] Absolute molecular weight by light scattering.

The resulting polymers were fully characterized by ${}^1$H NMR, FT-IR, and MALDI-TOF measurements, which showed greater than 95% incorporation of the desired α-functional end group and greater than 95% retention of the ω-nitroxide end group (Figure 3). These results confirm the high degree of end group fidelity previously observed for polymers prepared using derivatives of **2** and are in accord with previous work that showed better than 95% retention of chain end groups for polymers with molecular weights <25 000 amu.[34]

**Table 3.** Molecular Weight Data for Block Copolymers

| entry | macroinitiator | block copolymer | $M_{n,GPC}$ (kDa)[a] | $M_w/M_n$ |
| --- | --- | --- | --- | --- |
| **48** | **25** | P*t*BA-*b*-PSt | 12.1 | 1.24 |
| **49** | **24** | P*n*BA-*b*-PSt | 9.7 | 1.12 |
| **50** | **27** | PDMA-*b*-PSt | 9.3 | 1.14 |
| **51** | **26** | PNIPAAm-*b*-PSt | 6.5 | 1.33 |
| **52** | **14** | PSt-*b*-P*t*BA | 7.6 | 1.18 |
| **53** | **14** | PSt-*b*-PDMA | 7.3 | 1.17 |
| **54** | **14** | PSt-*b*-P4VBA | 7.4 | 1.20 |
| **55** | **14** | PSt-*b*-P2VP | 8.2 | 1.11 |
| **56** | **14** | PSt-*b*-P(4VP-*r*-St) | 8.0 | 1.06 |
| **57** | **14** | PSt-*b*-P(St-*r*-MI)-*b*-PSt | 11.1 | 1.16 |
| **58** | **77** | dendron-*b*-PSt | 6.8 | 1.07 |
| **59** | **77** | dendron-*b*-PSt | 9.2 | 1.09 |

[a] SEC data relative to PS-standards.

The high level of alkoxyamine chain end retention was further confirmed by the efficiency achieved in forming well-defined polystyrene stars from these chain-end-functionalized linear polymers. Employing the optimized reaction conditions obtained from previous combinatorial, high-throughput studies,[13] we heated a mixture of the functionalized linear polystyrenes, **14**−**23**, with molecular weights in the 3000−10 000 amu range, divinylbenzene (DVB), and styrene in the ratio 1/4/10 at 125 °C in DMF (30 wt %) for 16 h. Highly branched polystyrene stars, **31**−**40**, with 40−50 arms[35] and a narrow polydispersity (PDI < 1.2), were obtained with no significant amount of starting macromonomer remaining (Table 1). The globular, three-dimensional nature of these star polymers is apparent from the difference in polystyrene equivalent molecular weights as determined by GPC and the absolute molecular weights as determined by either viscosimetry or light scattering. For

**Table 4.** Molecular Weight Data for Star Block Copolymers[a]

| entry | starting block copolymer | $M_{n,GPC}$ (kDa)[b] | $M_w/M_n$ | conversion (%) |
|---|---|---|---|---|
| 64 | P*t*BA-*b*-PSt | 102 | 1.19 | 76 |
| 65 | P*n*BA-*b*-PSt | 88 | 1.17 | 81 |
| 66 | PDMA-*b*-PSt | 90 | 1.37 | 83 |
| 67 | PNIPAAm-*b*-PSt | 89 | 1.24 | 72 |
| 68 | PSt-*b*-P*t*BA[c] | 68 | 1.26 | 74 |
| 69 | PSt-*b*-PDMA | 66 | 1.27 | 63 |
| 70 | PSt-*b*-P4VBA | 61 | 1.24 | 58 |
| 71 | PSt-*b*-P2VP | 69 | 1.14 | 66 |
| 72 | PSt-*b*-P(4VP-*r*-St) | 57 | 1.14 | 82 |
| 73 | PSt-*b*-P(St-*r*-MI)-*b*-PSt | 65 | 1.21 | 76 |
| 74 | dendron-*b*-PSt | 61 | 1.14 | 87 |
| 75 | dendron-*b*-PSt | 83 | 1.11 | 89 |

[a] Molecular weight data for star polymers after purification. [b] SEC data relative to PS-standards. [c] Conditions for star polymer formation are the same as those for the homopolyacrylate example.
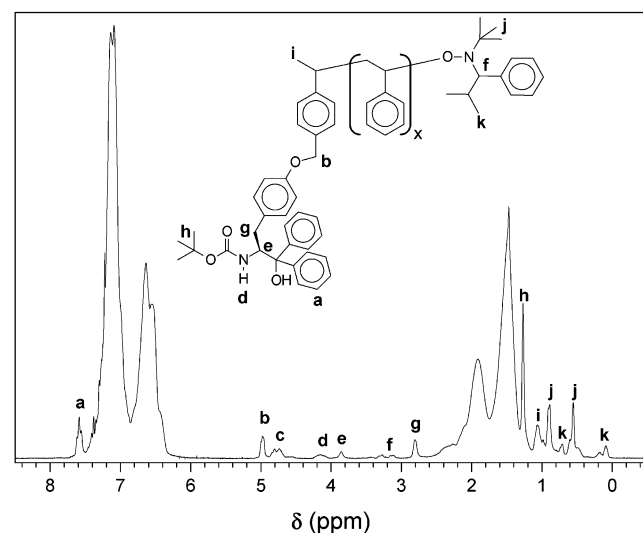


**Figure 3.** ^{1}H NMR spectrum of tyrosine chain-end-functionalized polystyrene, **22**.

example, the polystyrene star, **33**, was shown to have an absolute molecular weight of 195 000, which contrasts with the GPC molecular weight of 74 000, while the absolute molecular weight of the poly(*N,N*-dimethylacrylamide) star (220 000), **44**, was significantly greater than the molecular weight measured by GPC of 69 000. In both cases, a comparison of the absolute molecular weight with the molecular weight determined by NMR for the starting linear polymers (relative weight % in star polymer was ca. 90%) allowed the number of arms per chain to be calculated, ranging from 30 to 40 arms.

The generality of this approach for the formation of star polymers was examined in detail by exploring functionalized macroinitiators based on nonstyrenic monomers. As previously shown,[25-27] α-hydrido initiators, such as **2**, are capable of polymerizing a variety of non styrenic monomers such as *tert*-butyl acrylate (*t*BA), *N,N*-dimethylacrylamide (DMA), *N*-isopropylacrylamide (NIPAM), and 2-vinylpyridine (2VP) with the acrylamide and acrylate derivatives requiring the presence of 5 mol % of the corresponding nitroxide, **1**, for controlled polymerization.[25] In each case, formation of the macroinitiators, **25−30**, was a controlled process leading to low polydispersity materials (PDI = 1.09−1.18) with greater than 98% retention of the dormant alkoxyamine group at the chain end (Table 1). Using the optimized procedures developed for polystyrene stars,

we obtained high molecular weight star polymers, **42−47**, after heating these homopolymers with divinylbenzene and styrene in a 1/4/10 ratio at 125 °C. For the acrylamide and 2-vinyl pyridine derivatives, excellent control over the coupling reaction is observed leading to low polydispersity materials (Table 1). In the case of the acrylate-based macroinitiators, these conditions resulted in a poorly controlled coupling reaction, and multimodal, high molecular weight star polymers were obtained with a significantly increased polydispersity (PDI = 1.95−2.10). High-throughput optimization of the acrylate reaction system then revealed that well-defined polyacrylate stars could be formed by reducing the DVB and styrene concentrations from 1/4/10 to 1/3.4/8.2.

From Table 1, it is apparent that the presence or absence of functional groups attached to the initiating molecule had no detectable effect on the structural control of the resulting star copolymer. This is in agreement with earlier work[36] for linear polymers, which showed the compatibility of nitroxide-mediated living free radical polymerization with a wide variety of functional groups. As a consequence, formation of star polymers by the coupling procedure described above should have a wide tolerance of different functional groups resulting in the ability to readily prepare functionalized, three-dimensional star polymers. The modular nature of this approach also allows for excellent control over the number, nature, and placement of these functional groups.

A further benefit of this modular approach for the synthesis of these star polymers is that it enables the preparation of star polymers from mixtures of starting linear polymers. For example, a 1:1 mixture of hydroxy-functionalized poly(*N,N*-dimethylacrylamide), **28** ($M_n$ = 7100; PDI = 1.06), initiated with alkoxyamine, **8**, and unfunctionalized poly(*N,N*-dimethyl-acrylamide), **27** ($M_n$ = 5200; PDI = 1.09), initiated with **2**, could be "knitted" together with divinylbenzene to give a "mixed" star polymer, **46**, with a degree of control similar to that obtained with the homogeneous examples, **44** and **45** (Scheme 2).

The accessibility of these chain end functional groups was demonstrated by the quantitative postfunctionalization of the hydroxymethyl groups of **46** with the chromophore, 4-pyrene-butyryl chloride. By comparing the extinction coefficients for the chromophore-functionalized derivative of **46** with the corresponding chromophore-functionalized derivatives of **45** and **44**, we determined that approximately 50% of the chain ends of **46** contain a hydroxyl group, in agreement with the synthetic strategy. The synthesis of **46** is an excellent illustration of the power of this modular approach when combined with the ability to use dormant linear chains prepared by living free radical procedures. By simply mixing two starting linear polymers, each having dormant chain ends of essentially similar reactivity, we obtained a complex macromolecular architecture in which the number of chain end functional groups is controlled. It should be noted that chains of different lengths or monomer composition can also be used, which leads to further possible structural refinement. One potential application of these functionalized star polymers is as pore generating materials for the preparation of nanoporous thin films as low dielectric constant layers in advanced microelectronic devices.[37]

The presence of the chain end functional groups at the periphery of these star architectures, combined with their

**Scheme 2.** Graphical Representation of the Synthesis of a Poly(*N,N*-dimethylacrylamide) Star, **46**, with 50% of the Chain Ends Functionalized with Hydroxy Groups
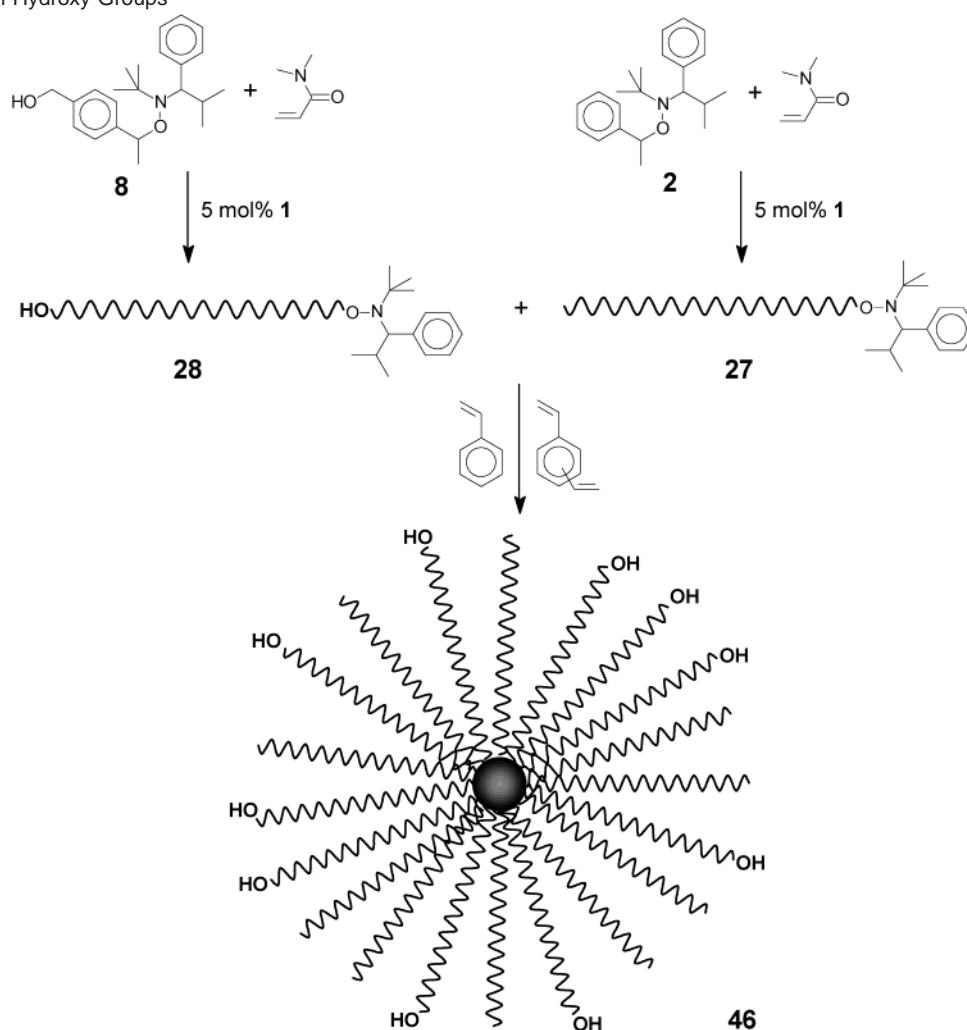


multifunctional nature and nanoscale size, also suggests the use of these structures as polymer supports for homogeneous catalysis. On the basis of the synthetic strategy of Itsuno and Fréchet,[38] the protected tyrosine initiator, **13**, was prepared as shown in Scheme 1 and used to initiate the polymerization of styrene. The resulting telechelic polystyrene, **22** ($M_n$ = 5200, PDI = 1.12), contains both a chiral ligand and an α-hydrido alkoxyamine as end groups and could therefore be used to prepare the star polymer, **39**, under standard conditions. This gave a soluble, three-dimensional macromolecule, which, after deprotection with trifluoroacetic acid, has ca. 40−50 L-tyrosine-based ligands located at its periphery. These functionalized stars could then be investigated as multifunctional chiral auxiliaries for the catalytic alkylation of benzaldehyde with diethylzinc (Scheme 3).[39] Indeed, quantitative formation of the enantiomeric alcohols, **62** and **63**, was observed after stirring a mixture of benzaldehyde and diethylzinc in the presence of deprotected **39** (0.05 mol equiv) for 8 h at 0 °C. Significantly, the use of deprotected **39** led to stereoselective alkylation with an observed enantiomeric excess, ee, of 71%, as compared to 18% for a peripherally substituted dendrimer analogue[40] and 77% for a low molecular weight linear PS-analogue.[41] The increased ee as compared to the dendritic analogue which is due to functional group accessibility and the ability to easily recycle these three-dimensional structures when compared to short linear polymers

**Scheme 3.** Enantiomeric Alkylation of Benzaldehyde Catalyzed by the L-Tyrosine-Functionalized Star Polystyrene, **39**
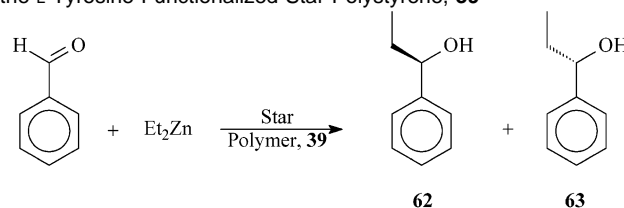


demonstrate the viability of these chain-end-functionalized star polymers as catalytic scaffolds. The high molecular weight and branched nature of the scaffolds permit increased solubility and functionality, leading to an efficient homogeneous system while at the same time permitting the use of nanoseparation/filtration techniques for catalyst recycling.[42]

**Block Copolymer Stars.** The great potential of the modular approach to star polymers was further demonstrated by employing block copolymers as starting materials. In analogy with the homopolymers studies described above, the presence of the dormant alkoxyamine group at the chain end of a diblock copolymer can be used as an initiating site for star formation via chain coupling in the presence of divinylbenzene. The added dimension afforded by block copolymers leads to a number of potential advantages; for example, the use of an amphiphilic

**Scheme 4.** Synthesis of Poly(NIPAM)-*b*-polystyrene Star Block Copolymer, **67**
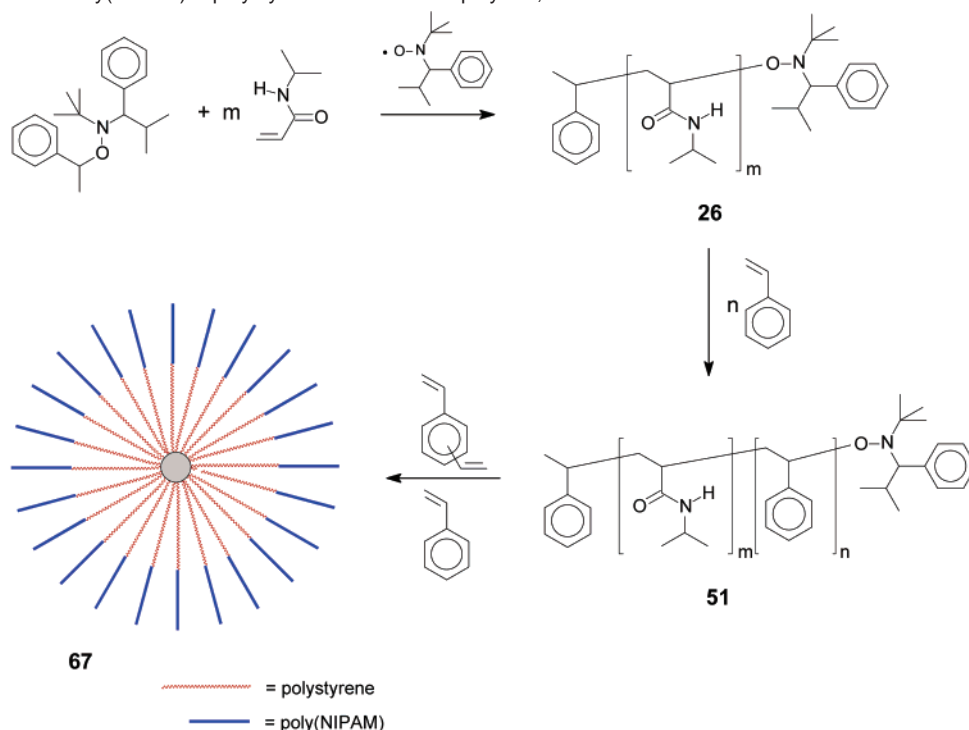


diblock leads to a core−shell-type morphology with an apolar interior and a polar corona or vice versa.

A series of diblock copolymers were prepared by reaction of the appropriate macroinitiators with styrene at 120 °C. This gave the resulting block copolymers PBA-*b*-PS **48**, **49**, PDMA-*b*-PS **50**, and PNIPAM-*b*-PS **51** as low polydispersity materials with little or no detectable homopolymer contamination. As anticipated, coupling of these block copolymers with divinylbenzene and styrene under the conditions defined above proceeded smoothly in each case to give the corresponding star polymers, **64**−**67**, in a controlled fashion (Scheme 4).

In contrast, the use of the reverse diblock copolymers as starting materials would result in inverted materials in which the polar core is surrounded by an apolar exterior. To achieve these structures, the initial macroinitiator should be polystyrene from which either *t*BA or DMA would subsequently be grown. Although it has previously been reported[24b] that the polymerization of acrylates from a polystyrene macroinitiator is problematic, no difficulties were observed at these low molecular weights, and well-defined block copolymers, such as **53**, were obtained. Subsequent coupling of **53** ($M_n = 7300$, PDI = 1.17) gave the desired star block copolymer, **69** ($M_n$ (abs) = 175 000, $M_n$ (GPC) = 66 000, PDI = 1.17), in which a hydrophobic polystyrene shell surrounds a hydrophilic DMA core. As was the case with homopolymer examples, the polystyrene equivalent molecular weights, as determined by GPC, were significantly lower than their absolute molecular weights with the final star polymers containing an average of 30−40 chains.

The reactivity of the internal functional groups was demonstrated for the PS-P*t*BA star, **68**, where hydrolysis of the *tert*-butyl esters in the interior of the star with trimethylsilyliodide[43] gives the amphiphilic polystyrene-*b*-poly(acrylic acid) star, **76**, in which a PSt-corona surrounds a polycarboxylic acid interior. ^{1}H NMR and IR spectroscopy confirmed complete deprotection of the *tert*-butyl groups, while the solubility of **76** in aqueous

base demonstrated its amphiphilic nature. Alternatively, the acid groups could be introduced directly into the star structure by polymerizing the cetyltrimethylammonium salt of 4-vinyl-benzoic acid (4VBA),[44] with a PS-macroinitiator, **14**, followed by coupling of the resulting block copolymer, **54**, with divinyl benzene and neutralization of the carboxylate salt to give a similar star, **70**, with carboxylic groups in the core.

For the introduction of basic or chelating functionalities, either 2-vinyl pyridine or 4-vinyl pyridine was employed as monomers. In the case of 2-vinyl pyridine, well-defined block copolymers could be prepared from the polystyrene macroinitiator ($M_n$ = 5300; PDI = 1.09), **14**, and the resulting diblock copolymer ($M_n$ = 8200; PDI = 1.11), **55**, subsequently coupled with divinyl benzene to give a PS-*b*-P2VP star, **71**. Alternatively, the poly-(2-vinylpyridine) block could be replaced with a random block of styrene and 4-vinylpyridine (4VP) to give a polystyrene-*b*-(styrene-*r*-4-vinylpyridine) copolymer, **56**. Coupling of **56** then leads to the star polymer, **72**, in which the nanoenvironment of the interior can be controlled by the percent incorporation of 4-vinylpyridine in the original block copolymer. By increasing the amount of 4-vinyl pyridine in the core, both the number of chelating or H-bond acceptor sites as well as the polarity of the core increases.

The concept of a structured core can be further amplified by introducing acceptor−donor−acceptor H-bonding arrays into the star structure. These were introduced by copolymerizing a mixture of maleimide and styrene from a PS-macroinitiator, **14**, using a high feed ratio of styrene to maleimide (9/1 St/MI).[45] The resulting block copolymer, **57**, consists of an initial PS-block followed by a gradient styrene-maleimide copolymer and a final PS-block. This copolymer was subsequently coupled with DVB to give the functionalized star copolymer, **73**, having a polystyrene core surrounded by a shell of H-bonding units that, in turn, is surrounded by a PS-corona.

The sophistication of the structural control during the

**Scheme 5.** Schematic Representation of the Synthesis of the Dendritic Star Block Copolymer, **75**
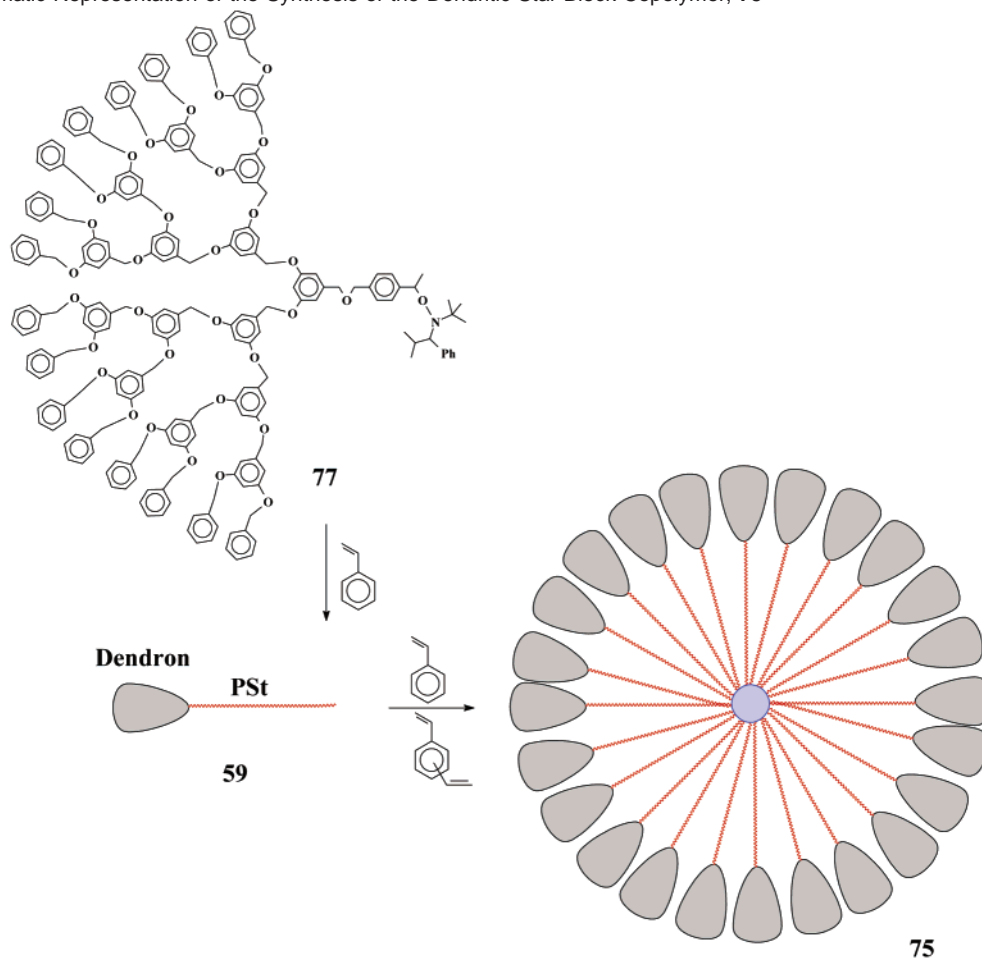


synthesis of the above block copolymer stars demonstrates the potential of this modular approach for the fabrication of functionalized three-dimensional macromolecules. However, the modular nature permits other, more complex, macromolecular architectures to be employed as starting materials; the only criteria is that an alkoxyamine group must be present at one of the chain ends. Perhaps the best example of this structural diversity is the synthesis and application of dendritic linear block copolymers, **58** and **59**, as starting materials for the preparation of star polymers. A series of such hybrid structures were then prepared by reaction of a fourth generation Fréchet-type dendron,[46] **77**, containing an alkoxyamine group at the focal point, with styrene under living free radical conditions to give the hybrid linear-dendritic block copolymers, **59** (Scheme 5).[18,47,48]

The presence of an alkoxyamine chain end at one chain end of the hybrid block copolymer, **59**, then permits the coupling of **59** with divinylbenzene, and, interestingly, this reaction was not retarded by the presence of the sterically large dendritic fragments. As a result, novel star structures, such as **75**, decorated with numerous dendron end groups on the periphery were obtained. Monitoring the progress of this transformation from dendritic initiator, **77**, to block copolymer, **59**, to star, **75**, could be conveniently accomplished by gel permeation chromatography, which shows the expected increase in molecular weight and the associated low polydispersity of the products (Figure 4).

**Host−Guest Interaction Stars.** The presence of the 4-vinylpyridine units in the interior of the PSt-P(4VP-*r*-St) stars, **72**, makes it possible to use these entities as supramolecular scaffolds for guests containing hydrogen bond donors, that is, carboxylic acid functions. The driving force for formation of these polymeric complexes[49] is a combination of H-bonding and the increased polarity of the nanoenvironment in the interior of the polymer. Indeed, the chromophore, coumarin-3-carboxylic acid, **60**, which was practically insoluble in toluene, could be solubilized in deuterated toluene upon addition of **72**, as
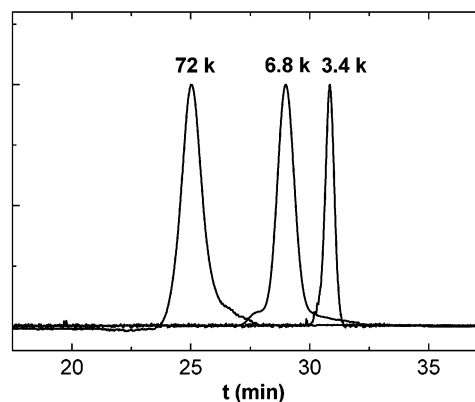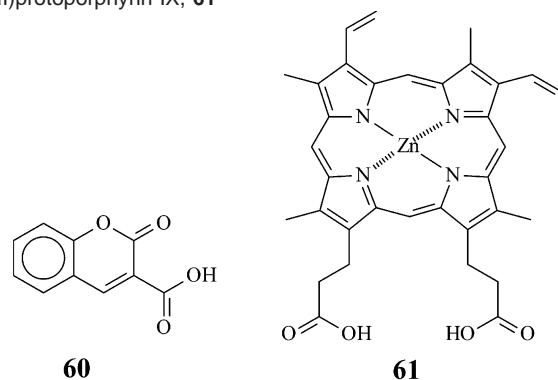


**Figure 4.** GPC traces for the starting dendritic initiator, **77** ($M_n$ = 3400, PDI = 1.002), intermediate dendritic-polystyrene block copolymer, **59** ($M_n$ = 6800, PDI = 1.07), and the final dendritic star block copolymer, **75** ($M_n$ = 72 000, PDI = 1.19).

**Scheme 6.** Structure of Coumarin-3-carboxylic Acid, **60**, and Zn(II)protoporphyrin IX, **61**
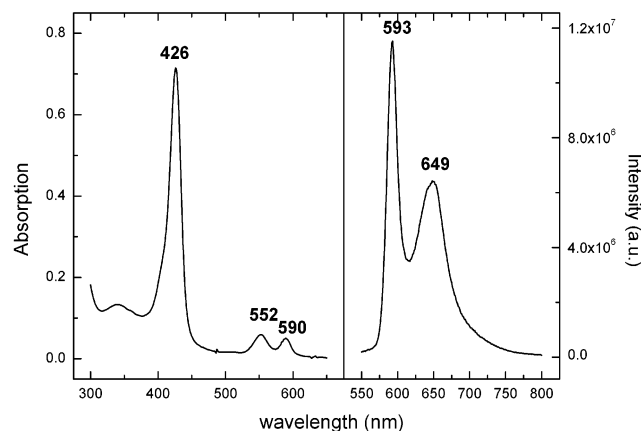
**60**          **61**

**Figure 5.** UV–vis (left) and fluorescence (right) spectra of star **72** loaded with Zn(II) protoporphyrin, **61**, dissolved in toluene, excitation at $\lambda = 430$ nm.

evidenced by ^{1}H NMR spectroscopy. Significantly, the UV–vis ($\lambda_{max} = 290$ and 340 nm) and fluorescence ($\lambda_{em} = 420$ nm) spectra for this host–guest complex in toluene demonstrated that **60** was in a nonaggregated state, which suggests molecular complexation of the coumarin carboxylic acid with the vinyl pyridine moieties located within the star polymer.[50] That H-bonding is a driving force for this complex formation was evident from FT-IR measurements which showed that the O–H stretching band of the carboxylic acid for **60** shifts to lower energies (broad absorption around 2507 cm$^{-1}$), accompanied by a shift in the carbonyl band from 1740 to 1757 cm$^{-1}$.[49]

Alternatively, the ligating ability of the 4-vinylpyridine-functionalized stars, **72**, could be used to solubilize organometallic systems such as zinc(II) protoporphyrin IX, **61** (ZnP-PIX, Scheme 6). In this case, metal ligand interactions as well as H-bonding are responsible for complex formation and solubilization, with the signals belonging to the ZnPPIX nucleus being clearly visible in the ^{1}H NMR spectrum and the extreme broadening of the resonances for the pyridine groups indicating coordinative interaction of the pyridine nitrogens with the Zn(II)-site in the protoporphyrins.[51] UV–vis and fluorescence studies of mixtures of ZnPPIX (**61**) and **72** (15 wt % of dye) in toluene were in agreement with the pyridine coordination observed in NMR experiments, as comparable UV–vis and fluorescence spectra were obtained from a model system consisting of native Zn-porphyrin, **61**, dissolved in toluene containing 1 M pyridine.

This supports the formation of a host–guest system (Figure 5).[51] Moreover, the exact overlay of the SEC traces recorded with dual RI and UV detection (420 nm, Soret band of the porphyrin) confirmed the presence of the low molecular weight dye in the star-shaped macromolecule and the strong degree of encapsulation. Consequently, functionalized star polymers such as **72** can be used to entrap a variety of interacting guest molecules using a combination of H-bonding and metal–ligand interactions.

This concept of using the interior of the star as a nanoscale supramolecular environment was further investigated with a more selective host–guest system based on the maleimide-containing star **73**. The acceptor–donor–acceptor (ADA) array present in the maleimide repeat units makes it possible to use multiple H-bonding as a directional and selective tool for molecular recognition, and this behavior was investigated with 2,6-bis(acetylamino)pyridine, **6**, as the complementary guest.[19,52–54] Initial analysis of a mixture of **73** and **6** in deuterated chloroform (1:1 molar ratio of guest:maleimide repeat
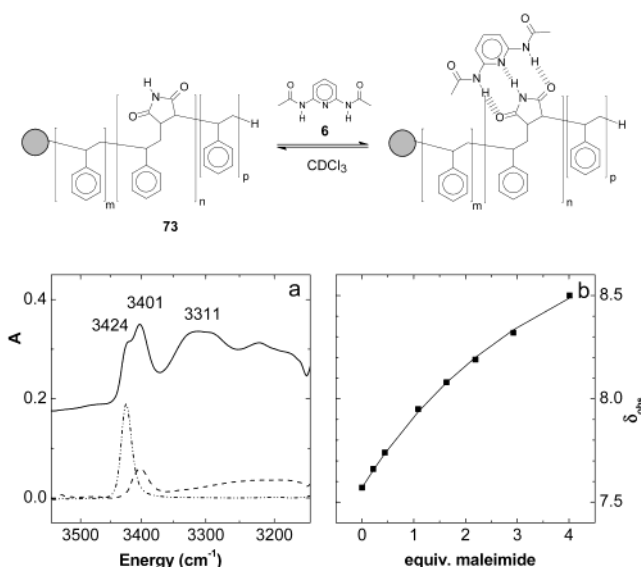
**Figure 6.** (a) Infrared spectra of 2,6-bis(acetylamino)pyridine **6** (dot–dashed), star **73** (dashed), and a 1:1 mixture of **6** and **73** in CDCl₃ (8 mM) (solid). (b) NMR titration curve obtained by addition of **73** to a 17 mM solution of **6** in CDCl₃.

unit) revealed a new broad absorption band in the amide-stretch region of the infrared spectrum (Figure 6a). The appearance of this band at lower energy (3311 cm$^{-1}$) than those for the non-H-bonded amides of the starting individual host and guest (3401 and 3424 cm$^{-1}$, respectively) is indicative of the formation of the targeted hydrogen bonded complex.

These findings were confirmed by ^{1}H NMR titration of 2,6-bis(acetylamino)pyridine, **6**, with **73** in deuterated chloroform via monitoring of the change in the chemical shift of the amide protons of the guest being followed. Assuming that all maleimide sites interact independently, we obtained an association constant, $K_a$, of $14 \pm 1$ M$^{-1}$ which is comparable to the reported $K_a$ for a small molecule model system with maleimide as the ADA unit of 131 M$^{-1}$ (Figure 6b).[55,56] These results clearly indicate that functionalized star polymers can be used as scaffolds for the encapsulation and chelation of a variety of guests.

(56) Lange, R. F. M. Ph.D. Thesis, Eindhoven University of Technology, November, 1997.
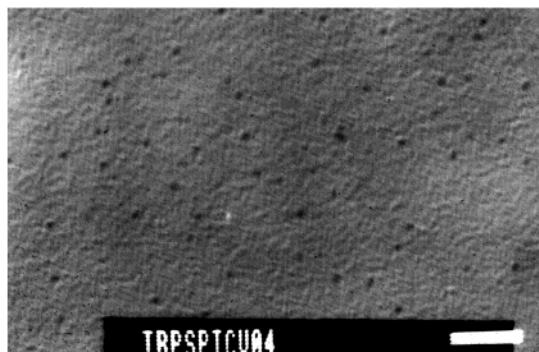
**Figure 7.** TEM micrograph of palladium-functionalized star, **78**, dropcast from toluene solution (0.5 mg/mL); white bar represents 20 nm.

**Catalysis.** As detailed above for chain-end-modified star polymers, the use of the star architecture as a scaffold for the placement of numerous catalytic sites is an exciting avenue of research. However, the star architecture can also serve as a stabilizing environment for the fabrication of catalytically active metallic nanoparticles. Previously, poly(vinylpyridine)-containing block copolymer micelles have been utilized to stabilize Pd-nanoclusters;[57] however, the dynamic nature of polymeric micelles makes them sensitive to environmental conditions. To address this issue, covalent systems such as dendrimers,[58] hyperbranched polymers,[59] and star copolymers[60] have recently been employed as templates for nanoparticle formation, although the challenges inherent to the use of large quantities of dendritic macromolecules are a concern.[7c] To overcome this difficulty, the 2-vinylpyridine-functionalized star polymer, PS-*b*-P2VP **71**, was investigated as a more readily available scaffold for the preparation and stabilization of metallic nanoparticles. Addition of Pd(OAc)$_2$ to a toluene solution of **71** resulted in slow solvation of the metal with formation of a clear light-orange solution (broad absorptions at $\lambda_{max}$ = 325 and 365 nm). Subsequent reduction of the bound palladium cations was performed using ethanol at elevated temperatures and could be followed by a color change to dark brown. After being precipitated in methanol, the star-stabilized palladium nanoparticles, **78**, were obtained as a dark brown solid, and TEM analysis confirmed the formation of isolated Pd-nanoparticles with diameters of 2−3 nm (Figure 7). Furthermore, SEC analysis of these Pd-containing stars, **78**, showed that they were almost identical to the starting PS-*b*-P2VP star **71**, demonstrating that formation of the palladium nanoparticles did not induce agglomeration of the star polymer. This lack of association provides further support for the concept of using three-dimensional star polymers to provide a sterically isolated internal nanoenvironment in which a variety of reactions can take place.

To investigate the possibility of using these nanoparticles in catalysis, initial studies were performed on the hydrogenation reaction of cyclohexene. Indeed, cyclohexene conversion into cyclohexane was catalyzed by the Pd-loaded star **78**, with an observed TOF (turnover frequency) of 138 h$^{-1}$ atm (H$_2$)$^{-1}$. This is comparable to the activity of other polymer stabilized Pd-

(57) (a) Antonietti, M.; Wenz, E.; Bronstein, L.; Seregina, M. *Adv. Mater.* **1995**, *7*, 1000. (b) Klingelhöfer, S.; Heitz, W.; Greiner, A.; Oestreich, S.; Förster, S.; Antonietti, M. *J. Am. Chem. Soc.* **1997**, *119*, 10116.
(58) Zhao, M.; Crooks, R. M. *Angew. Chem., Int. Ed.* **1999**, *38*, 364.
(59) Mecking, S.; Thomann, R.; Frey, H.; Sunder, A. *Macromolecules* **2000**, *33*, 3958.
(60) Youk, J. H.; Park, M. K.; Locklin, J.; Advincula, R.; Yang, J.; Mays, J. *Langmuir* **2002**, *18*, 2455.
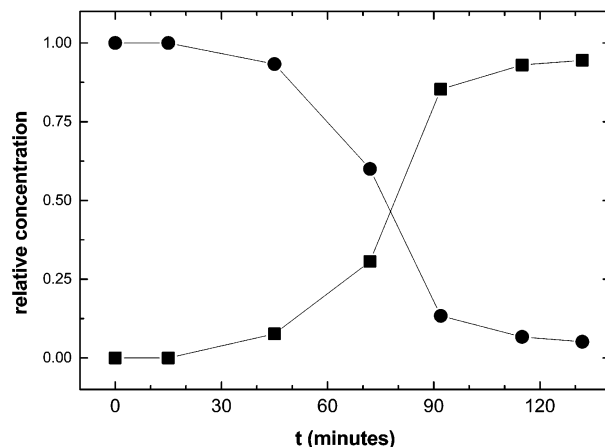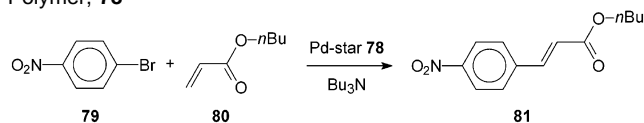


**Figure 8.** GC conversion of 1-bromo-4-nitro benzene, **79** (●), to the corresponding cinnamate derivative, **81** (■), catalyzed by the Pd-containing star **78**.

**Scheme 7.** Heck Reaction of 1-Bromo-4-nitrobenzene, **79**, with *n*-Butyl Acrylate, **80**, Catalyzed by the Pd-Containing Star Polymer, **78**



nanoparticles and demonstrates the potential for these materials.[57] This was further tested by examining the ability of these palladium-containing stars, **78**, to catalyze more demanding transformations such as the Heck reaction (Scheme 7). Heating a mixture of 1-bromo-4-nitrobenzene, **79**, and *n*-butyl acrylate, **80**, in xylene at 125 °C in the presence of 0.5 mol % of Pd encapsulated in star **78**, with tributylamine as base,[57] led to almost quantitative formation (96%) of the trans cinnamate, **81**, in 2 h after a short induction period, resulting in a TOF (turnover frequency) of 95 h$^{-1}$ (Figure 8).

Significantly, no formation of palladium black was observed during the reaction, demonstrating the steric stabilization of the nanoparticles. Of equal significance is the ability to perform the reaction in nonpolar solvents such as xylene, instead of the traditional polar amidic solvents. This illustrates the utility of these functionalized three-dimensional macromolecules in creating a defined nanoenvironment, in this case, a nonpolar polystyrene corona, soluble in xylene, surrounding the catalytically active interior. Precipitation of the reaction mixture in methanol leads to recovery of the Pd-containing star catalyst, **82**, which was reused five times without any observable degradation in performance.

## Conclusions

The ready availability of telechelic linear polymers from nitroxide-mediated living free radical polymerizations has permitted the development of a modular approach to functionalized star macromolecules in which the nature, number, and location of the functional groups can be varied to an unprecedented degree. As a consequence, libraries of linear polymeric starting materials with different backbones and end groups can be prepared and combined to give functionalized star architectures with tailor-made physical and chemical properties. The generality of this modular approach has been demonstrated by the synthesis of three-dimensional nanomaterials from a wide

range of different block copolymers and random copolymers, optionally with end group functionalities. These materials are active as supramolecular hosts for the encapsulation of a variety of guests, and as scaffolds for catalytic sites, which can be located at either the periphery or the interior of the stars. The diverse nature of these applications demonstrates the utility of this modular, library-based approach to functionalized three-dimensional macromolecules.

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