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Nitroxide-mediated polymerization to form symmetrical ABA triblock copolymers from a bidirectional alkoxyamine initiator

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Abstract

Bidirectional alkoxyamine **2** was synthesized and used as the initiator in the polymerization of styrene (S), *n*-butyl acrylate (*n*BA), *t*-butyl acrylate (*t*BA), isoprene (I), and dimethylacrylamide (DMA). A variety of symmetrical ABA triblock copolymers were prepared, ranging in size from 5 to 59 kDa. Kinetics studies and gel permeation chromatography (GPC) confirmed the ‘‘living’’ nature of these polymerizations. Trifluoroacetic acid was used to convert the P*t*BA blocks of these polymers into poly(acrylic acid) (PAA) blocks, forming ABA amphiphilic triblock copolymers. AFM images of PAA-*b*-P*n*BA-*b*-PAA and PAA-*b*-PS-*b*-PAA triblock copolymers ionized by the addition of 2,2′-(ethylenedioxy)-bis(ethylamine) show evidence of self-assembly.

Keywords: Nitroxide-mediated polymerization; Alkoxyamine; Bidirectional

1. Introduction

Nitroxide-mediated living free radical polymerization (NMRP) can be used to form polymers with well-controlled chain lengths and low polydispersities [1]. Typically an alkoxyamine is used as a unimolecular initiator in the polymerization process (Fig. 1). At elevated temperatures, homolysis of the C−O bond forms a stable nitroxide radical and an active alkyl radical. Monomer units add to this alkyl radical to form a growing polymer chain. Throughout the polymerization, the persistent nitroxide radical reversibly caps and uncaps the active radical chain terminus, converting it to either the dormant or active state. Because most polymer chains exist in the dormant state at any given time, termination events are rare; hence, polymers with low polydispersities are formed.

Early work in this field employed TEMPO (Fig. 2) as the mediating nitroxide [2−4]; this effected the controlled polymerization of styrenes. Well-controlled polymerization of other monomers was not possible with TEMPO, but second-generation nitroxides such as TIPNO [5,6] and DEPN [7,8] have been used to polymerize acrylates, acrylamides, acrylonitrile, and 1,3-dienes.

Unlike conventional free radical polymerization, NMRP is a ‘‘living’’ process. Following polymerization, the resultant polymers can be isolated. At a later time, polymerization can be reinitiated by heating in the presence of monomer. This technique lends itself well for the synthesis of block copolymers. Various polymer morphologies, such as AB diblock, ABA triblock, and ABC triblock copolymers have been made using NMRP. ABA triblock copolymers have been used in a variety of biomedical, nanotechnical, and material applications [9−11]. The unique structure of amphiphilic ABA triblock copolymers has been utilized to form self-assembled structures such as micelles [12,13], vesicles [14,15], and membranes [16,17].

Although it is possible to grow ABA triblock copolymers from monodirectional initiator **1** (Fig. 3), use of a bidirectional initiator has several advantages. In this paper, bidirectional

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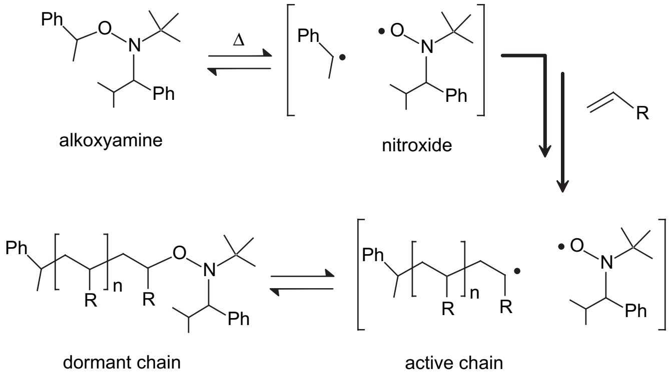


Fig. 1. General mechanism for nitroxide-mediated radical polymerization.

initiator **2** is introduced, in which the polymer is grown from the center outward. This allows three blocks to be grown in only two steps. The simultaneous growth of the outer A blocks ensures that they are identical in length, forming symmetrical ABA triblocks. A variety of multidirectional initiators based on TEMPO [18–25], TIPNO [26–28], and DEPN [29] have been synthesized, but their use in forming ABA triblock copolymers has been limited. Herein is reported the synthesis of bidirectional alkoxyamine initiator **2** based on TIPNO as the mediating nitroxide. The preparation of a wide range of ABA triblock copolymers from this initiator is demonstrated; subsequent conversion of selected ABA triblocks into amphiphilic copolymers is reported.

2. Experimental section

2.1. Materials

Styrene (99%, Acros Organics), *t*-butyl acrylate (98%, Aldrich), *n*-butyl acrylate (99+%, Acros Organics), and *N*,*N*-dimethylacrylamide (99%, Aldrich) were vacuum distilled prior to use. Isoprene (99+%, Acros Organics) was distilled at atmospheric pressure. Dimethylsulfoxide (DMSO) was distilled from calcium hydride and stored over molecular sieves. Water was deionized. All other reagents were used without further purification. Both 1,4-diacetylbenzene (99%) and *p*-toluenesulfonic acid monohydrate (99%) were purchased from Aldrich. Jacobsen's catalyst (98%), sodium borohydride (98+%), and *p*-anisaldehyde (99+%) were purchased from Acros Organics. Trifluoroacetic acid and hydroquinone were purchased from Fisher Scientific. 2,2′-(Ethylenedioxy)bis(ethylamine) was purchased from Alfa Aesar (97+%). Flash chromatography was performed using EM Science Silica Gel 60. Analytical TLC was performed using commercial Whatman plates coated with silica gel (0.25 mm thick). PAA stain was made from a mixture of ethanol (37.5 mL), concentrated sulfuric acid (2.08 mL), glacial acetic acid (0.427 mL), and *p*-anisaldehyde (2.5 mL). Initiator **1** and TIPNO were prepared according to the published procedures [5].

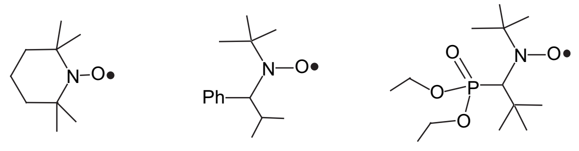


Fig. 2. Common nitroxides used in NMRP.

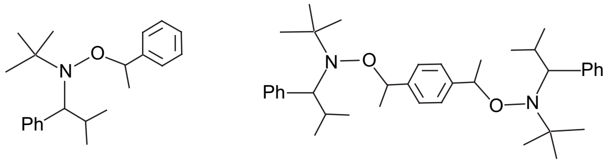


Fig. 3. Mono- and bidirectional TIPNO-based initiators for nitroxide-mediated polymerization.

2.2. Measurements

NMR spectra were collected on a Varian 500 MHz spectrometer in $CDCl_3$ at ambient temperature. HRMS were obtained on an electrospray ionization time of flight (ESITOF) mass spectrometer (Mariner Biospectrometry workstation from Applied Biosciences). FTIR spectra were recorded in chloroform on a Perkin–Elmer 1600 FTIR spectrometer. AFM images were collected using a PicoSPM LE instrument (Molecular Imaging Inc.) in the tapping mode. The resulting images were flattened and plane-fitted using Molecular Imaging software. Samples were prepared by drop-casting dilute polymer solutions onto a freshly cleaved mica substrate and drying before imaging. Polymer molecular weights and polydispersities were measured by gel permeation chromatography (GPC) using a Waters apparatus equipped with five Styragel columns (300 × 4.6 mm, 5 μm bead size), HR 0.5 (pore size 50 Å, 0–1000 Da), HR 1 (pore size 100 Å, 100–5000 Da), HR 2 (pore size 500 Å, 500–20 000 Da), HR 4 (pore size 10 000 Å, 50–100 000 Da), HR 5E (linear bed, mixed pore sizes, $2000–4 \times 10^6$ Da). Tetrahydrofuran was used as the eluent at a flow rate of 0.35 mL/min at ambient temperature. A refractive index detector was used, and the molecular weights were calibrated against seven polystyrene standards ranging from 2000 to 156 000 Da. Percent conversions of polymerizations were calculated in two ways. From ^{1}H NMR integrations of aliquots of crude polymer mixtures, the ratio of polymerized to remaining monomer was determined. This was used to calculate a percent conversion and a theoretical molecular weight, $M_{n,NMR}$. The mass of precipitated polymers was compared to the mass of the crude polymer mixture in order to calculate a gravimetric percent conversion and a theoretical molecular weight, $M_{n,grav}$.

2.3. Synthesis of bidirectional initiator

2.3.1. 1,4-Bis(1-hydroxyethyl)benzene (*3*)

Following the procedure of Smejkal et al. [30], 1,4-diacetylbenzene (5.041 g, 31.08 mmol) was dissolved in 240 mL of isopropyl alcohol at rt. After 20 min, most of the solute was dissolved, and sodium borohydride (3.314 g, 87.60 mmol) was added. The mixture was stirred for 21 h, then quenched with 50 mL of 5% aqueous NaOH. The reaction mixture was concentrated and dissolved in 50 mL of dichloromethane and 50 mL of deionized water. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 × 50 mL). The organic layers were combined, washed with 50 mL of brine, and dried over potassium carbonate. The solution was filtered and concentrated to give the crude product as a yellowish-white powder. Purification by flash chromatography using 70:30 dichloromethane/acetone as the eluent yielded the pure product (4.572 g, 88% yield) as an off-white powder. This was a mixture of two diastereomers, even though the diastereomers are not discernible by ^{1}H NMR [31]. TLC 80:20 ethyl acetate/hexanes, UV and PAA stain, $R_f = 0.62$; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.36 (s, 4H, Ar H), 4.89 (q, 2H, $J = 6$ Hz, benzylic H), 1.88 (br s, 2H, $-OH$), 1.49 (d, 6H, $J = 6$ Hz, $-CH_3$).

2.3.2. 1,4-Divinylbenzene (**4**)

Following the procedure of Smejkal et al. [30], a two-necked round bottom flask fitted with a condenser was flushed with argon. Through a septum was added bisalcohol **3** (3.053 g, 18.36 mmol), *p*-toluenesulfonic acid (0.229 g, 1.20 mmol), hydroquinone (0.697 g, 6.33 mmol), and 30 mL of DMSO. The reaction mixture was stirred and heated at 120 °C for 2 h. After cooling to rt, 50 mL of 2% hydroquinone (w/w in water) was added. This mixture was extracted with pentane (4 × 20 mL), washed with brine, dried over magnesium sulfate, filtered, and concentrated to afford a yellow oil. The crude product was run through a short silica column using pentane. The eluent was concentrated to give a pure, colorless oil (1.130 g, 47% yield). This compound was not very stable; thus it was converted immediately into alkoxyamine **2**. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.38 (s, 4H, Ar H), 6.71 (dd, 2H, $J = 11$ Hz and 18 Hz, benzylic H), 5.76 (dd, 2H, $J = 18$ Hz and 0.8 Hz, vinylic H), 5.25 (dd, 2H, $J = 11$ Hz and 0.8 Hz, vinylic H).

2.3.3. 1,4-Bis[1-2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide)ethyl]benzene (**2**)

Following a modified procedure of Hawker et al. [5], to a round bottom flask were added 1,4-divinylbenzene **4** (1.130 g, 8.680 mmol), TIPNO (4.821 g, 21.91 mmol), 65 mL of toluene, and 80 mL of ethanol. Jacobsen's catalyst (1.254 g, 1.974 mmol) was then added, followed by sodium borohydride (0.670 g, 17.7 mmol). The reaction mixture was stirred while open to air and monitored by TLC (2.5% ethyl acetate/hexanes). After 48 h, the reaction mixture was concentrated, and then partitioned between 100 mL of dichloromethane and 100 mL of water. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (2 × 50 mL). The organic layers were combined and run through a silica plug using dichloromethane in order to remove some of the brown manganese catalyst. The crude product was concentrated to give a brown oil, and was purified by flash chromatography using 80:20 hexanes/dichloromethane as the eluent. The pure product was an off-white sticky wax, isolated as a mixture of multiple diastereomers (3.111 g, 63% yield). TLC 40:60 dichloromethane/hexanes, UV and PAA stain, $R_f = 0.78$; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.5–7.1 (m, 14H, Ar H), 5.0–4.8 (mixture of q, 2H, $J = 7$ Hz), 3.42–3.23 (several d, 2H, $J = 11$ Hz, $-ONCH-$), 2.35 and 1.25 (several m, 2H, $-CH(CH_3)_2$), 1.65–1.5 (several d, 6H, $J = 7$ Hz, benzylic CH_3), 1.3–0.12 (several d, 12H, $J = 7$ Hz, isopropyl $-CH_3$), 1.1–0.7 (several s, 18H, *t*-butyl CH_3); ^{13}C NMR (500 MHz, CDCl$_3$) δ 145.1, 145.1, 144.1, 144.1, 143.5, 142.7, 142.6, 142.4, 142.4, 131.1, 128.9, 127.5, 127.37, 127.3, 127.2, 127.1, 127.1, 127.0, 126.7, 126.4, 126.3, 126.2, 126.0, 125.9, 125.9, 83.7, 83.7, 83.4, 83.2, 82.5, 72.4, 72.3, 72.1, 60.7, 60.5, 60.4, 60.3, 32.1, 31.9, 31.5, 28.6, 28.5, 28.4, 27.4, 25.1, 25.0, 24.4, 23.5, 23.2, 23.1, 22.3, 22.2, 22.1, 21.3, 21.0; Elemental analysis calcd for $C_{38}H_{56}N_2O_2$ C = 79.67, H = 9.85, N = 4.89, found C = 79.80, H = 9.68, N = 4.89.

2.4. Polymerizations

2.4.1. General procedure for the polymerization of styrene to form PS (***PS-2***)

Bidirectional initiator **2** (58.9 mg, 0.101 mmol) was dissolved in styrene (1.0597 g, 10.175 mmol) in a 5 mL glass ampoule. A stir bar was added and the ampoule was sealed under argon after three cycles of freeze-pump-thaw. It was suspended in a 125 °C oil bath for 2 h. A ^{1}H NMR spectrum of an aliquot of the crude mixture was taken to determine percent conversion. The polymer was precipitated three times by dissolving it in 2 mL of dichloromethane, adding 50 mL of cold methanol, and filtering. After drying in vacuo, the purified poly(styrene) was isolated as a white powder (0.735 g, 64% conversion, $M_{n,grav} = 7300$). ^{1}H NMR: 70% conversion, $M_{n,NMR} = 7900$; GPC: $M_{n,GPC} = 7300$; PDI = 1.11; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.3–6.3 (two br s, 5H, Ar H), 2.4–1.2 (several br, 3H, $-CH_2-$ and $-CH-$ in polymer backbone).

2.4.2. General procedure for the polymerization of t-butyl acrylate to form PtBA (***PtBA-1***)

TIPNO (6.48 mg, 0.0294 mmol) and bidirectional initiator **2** (169.9 mg, 0.2966 mmol) were dissolved in *t*-butyl acrylate (1.9028 g, 14.846 mmol) in a 5 mL glass ampoule. A stir bar was added and the ampoule was sealed under argon after three cycles of freeze-pump-thaw. It was suspended in a 122 °C oil bath for 13.3 h. A ^{1}H NMR spectrum of an aliquot of the crude mixture was taken to determine percent conversion. The polymer was precipitated three times by dissolving it in 2 mL of tetrahydrofuran, adding a cold mixture of 50 mL of methanol/50 mL of water, and decanting the supernatant. After drying in vacuo, the purified poly(*t*-butyl acrylate) was isolated as a white powder (1.123 g, 50% conversion, $M_{n,grav} = 3800$). ^{1}H NMR: 60% conversion, $M_{n,NMR} = 4400$; GPC: $M_{n,GPC} = 3700$; PDI = 1.17; ^{1}H NMR (500 MHz, CDCl$_3$) δ 2.35–2.1

(br, 1H, $-\mathrm{C}H-$ in polymer backbone), 1.9−1.4 (two br, 2H, $-\mathrm{C}H_2-$ in polymer backbone), 1.42 (br s, 9H, $-\mathrm{C}(\mathrm{C}H_3)_3$).

*2.4.3. General procedure for the polymerization of n-butyl acrylate to form PnBA (**PnBA-2**)*

TIPNO (5.6 mg, 0.025 mmol) and bidirectional initiator **2** (0.2946 g, 0.4619 mmol) were dissolved in *n*-butyl acrylate (2.5081 g, 19.569 mmol) in a 10 mL glass ampoule. A stir bar was added and the ampoule was sealed under argon after three cycles of freeze-pump-thaw. It was suspended in a 125 °C oil bath for 13 h. A ^{1}H NMR spectrum of an aliquot of the crude mixture was taken to determine percent conversion. The polymer was difficult to precipitate because it is a liquid at room temperature; thus, the unreacted monomer was removed in vacuo while gently warming and rotating the sample in a Kugelrohr apparatus. The poly(*n*-butyl acrylate) thus obtained was a viscous yellow liquid (2.396 g, 84% conversion, $M_{\mathrm{n,grav}} = 5100$). ^{1}H NMR: 84% conversion, $M_{\mathrm{n,NMR}} = 5100$; GPC: $M_{\mathrm{n,GPC}} = 5000$; PDI = 1.15; ^{1}H NMR (500 MHz, $\mathrm{CDCl_3}$) δ 4.2−3.8 (br, 2H, $-\mathrm{OC}H_2\mathrm{CH_2CH_2CH_3}$), 2.4−2.1 (br, 1H, $-\mathrm{C}H-$ in polymer backbone), 2.0−1.3 (two br, 2H, $-\mathrm{C}H_2-$ in polymer backbone), 1.8−1.5 (br, 2H, $-\mathrm{OCH_2C}H_2\mathrm{CH_2CH_3}$), 1.5−1.2 (br, 2H, $-\mathrm{OCH_2CH_2C}H_2\mathrm{CH_3}$), 1.0−0.8 (br, 3H, $-\mathrm{OCH_2CH_2CH_2C}H_3$).

*2.4.4. General procedure for the polymerization of isoprene to form PI (**PI-1**)*

Note: Polymerization of isoprene using standard glass ampoules is dangerous; a vessel made to withstand high pressures must be used to avoid explosion! Bidirectional initiator **2** (0.2256 g, 0.3938 mmol) and isoprene (1.3505 g, 19.828 mmol) were mixed in a two-necked flask. After three cycles of freeze-pump-thaw, the mixture was transferred via syringe under argon into a 15 mL pressure vessel equipped with a stir bar. The pressure vessel was sealed and suspended in a 124 °C oil bath for 38 h. A ^{1}H NMR spectrum of an aliquot of the crude mixture was taken to determine percent conversion. The polymer was difficult to precipitate; thus, the unreacted isoprene was removed in vacuo while gently warming and rotating the sample on a Kugelrohr apparatus. The resulting poly(isoprene) was isolated as a viscous liquid (0.593 g, 27% conversion, $M_{\mathrm{n,grav}} = 1500$). ^{1}H NMR: 53% conversion, $M_{\mathrm{n,NMR}} = 2400$; GPC: $M_{\mathrm{n,GPC}} = 1500$; PDI = 1.10; ^{1}H NMR (500 MHz, $\mathrm{CDCl_3}$) δ 5.2−5.0 (br, 1H, vinylic H), 2.2−1.8 (br, 4H, $-\mathrm{C}H_2-$ from polymer backbone), 1.8−1.5 (br, 3H, $-\mathrm{C}H_3$).

2.4.5. General procedure for the polymerization of N,N-dimethylacrylamide to form PDMA-b-PS-b-PDMA

TIPNO (1.3 g, 0.0060 mmol), poly(isoprene) macroinitiator **PI-1** ($M_{\mathrm{n,GPC}} = 1500$, 0.2003 g, 0.13 mmol) and *N*,*N*-dimethylacrylamide (0.9344 g, 9.426 mmol) were added to a 5 mL glass ampoule along with a stir bar. The ampoule was sealed under argon after three cycles of freeze-pump-thaw and suspended in a 123 °C oil bath for 12 h. A ^{1}H NMR spectrum of an aliquot of the crude mixture was taken to determine percent conversion. The polymer was precipitated three times by dissolving it in 2 mL of dichloromethane, adding 50 mL of cold methanol, and decanting the supernatant. After drying in vacuo, the purified poly(dimethylacrylamide)-*b*-poly(isoprene)-*b*-poly(dimethylacrylamide) was isolated as a white solid (0.627 g, 46% conversion, $M_{\mathrm{n,grav}} = 4800$). ^{1}H NMR: 57% conversion, $M_{\mathrm{n,NMR}} = 6600$; GPC: $M_{\mathrm{n,GPC}} = 7000$; PDI = 1.23; ^{1}H NMR (500 MHz, $\mathrm{CDCl_3}$) δ 5.2−5.0 (br, vinylic H in PI), 3.2−2.8 (br, $-\mathrm{C}H_3$ from PDMA), 2.8−1.0 (br, $-\mathrm{C}H-$ and $-\mathrm{C}H_2-$ from polymer backbone and $-\mathrm{C}H_3$ from PI).

2.4.6. General procedure for the hydrolysis of PtBA blocks with trifluoroacetic acid to form PAA blocks

Following the procedure of O'Reilly et al. [32], P*t*BA$_{14}$-*b*-P*n*BA$_{36}$-*b*-P*t*BA$_{14}$ triblock copolymer (0.920 g, 0.11 mmol, 3.0 mmol of *t*-butyl ester) was dissolved in 6.5 mL of dichloromethane. Trifluoroacetic acid (2.95 mL, 39.7 mmol) was added, and the resulting mixture was allowed to stir under argon for 2 h. The reaction mixture was then concentrated and dried in vacuo to give a sticky white solid that did not dissolve in chloroform, but did dissolve in a mixture of methanol and chloroform (0.799 g, 106%). ^{1}H NMR (500 MHz, MeOH-d_4/$\mathrm{CDCl_3}$) δ 4.2−3.8 (br, $-\mathrm{OC}H_2\mathrm{CH_2CH_2CH_3}$), 2.7−2.1 (br, $-\mathrm{C}H-$ in polymer backbone), 2.0−1.3 (br, $-\mathrm{C}H_2-$ in polymer backbone), 1.8−1.5 (br, $-\mathrm{OCH_2C}H_2\mathrm{CH_2CH_3}$), 1.5−1.2 (br, $-\mathrm{OCH_2CH_2C}H_2\mathrm{CH_3}$), 1.0−0.8 (br, $-\mathrm{OCH_2CH_2CH_2C}H_3$).

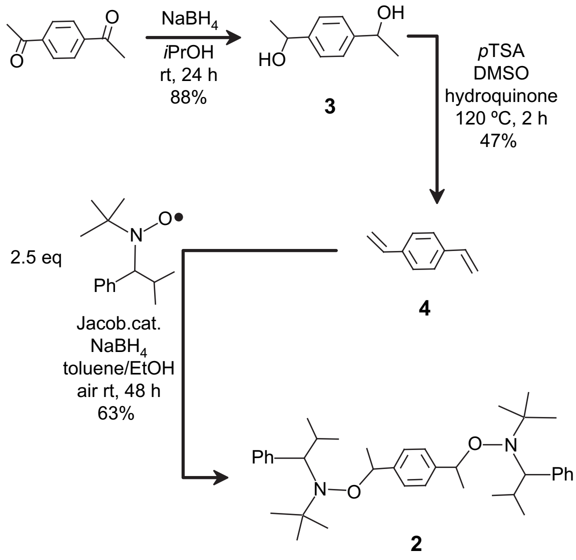
2.4.7. General procedure for self-assembly of ABA triblock copolymers

Following the procedure of Wooley et al. [33], 0.020 g of polymer was dissolved in 2 mL of tetrahydrofuran. 2,2′-(Ethylenedioxy)bis(ethylamine) was added so as to maintain a 2:1 ratio of amine/carboxylic acid functionality. This mixture was sonicated for several minutes in order to dissolve the polymer, and a mixture of 8 mL of tetrahydrofuran and 10 mL of nanopure water was added. The solution was stored at room temperature in a vial wrapped in parafilm for two weeks prior to imaging.

3. Results and discussion

3.1. Synthesis of the bidirectional initiator

Bidirectional initiator **2** was synthesized as shown in Scheme 1. Commercially available 1,4-divinylbenzene was not used as it consists of a mixture of regioisomers as well as a large amount of ethylvinyl benzene. Instead, clean 1,4-divinylbenzene was synthesized according to the published procedure [30]. Briefly, 1,4-diacetylbenzene was reduced with sodium borohydride to yield 1,4-bis(1-hydroxyethyl)benzene **3**, which was treated with *p*-toluenesulfonic acid in DMSO to yield 1,4-divinylbenzene **4**. When reacted with excess TIPNO, Jacobsen's Mn(salen) catalyst, and sodium borohydride, bidirectional alkoxyamine **2** was obtained in 63% yield.



Scheme 1. Synthesis of bidirectional alkoxyamine initiator.

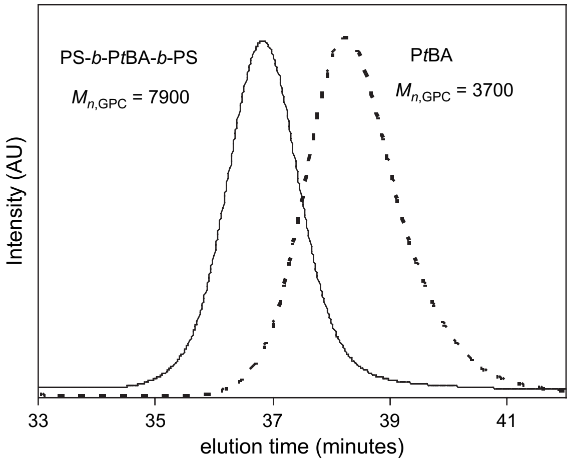


Fig. 4. Comparison of GPC traces of the starting P*t*BA homopolymer (- - -) and the PS-*b*-P*t*BA-*b*-PS triblock copolymer (—). The homopolymer was prepared by heating 1 eq of initiator **2**, 50 eq of *t*BA, and 0.1 eq of TIPNO at 120 °C for 13 h. The triblock copolymer was prepared by heating 1 eq of the homopolymer and 100 eq of styrene at 120 °C for 2 h.

3.2. Proof of "livingness"

Initiator **2** was used in the polymerization of neat styrene, *t*-butyl acrylate, *n*-butyl acrylate, and isoprene (Table 1). In all cases, the polymerizations were well controlled, resulting in polydispersities of less than 1.3. The theoretical molecular weights, which were calculated both gravimetrically ($M_{n,grav}$) and from ^{1}H NMR integration ($M_{n,NMR}$), are in close agreement with the molecular weights determined by GPC ($M_{n,GPC}$). In some cases where poly(*t*-butyl acrylate) was purified by precipitation, $M_{n,grav}$ is slightly lower than $M_{n,NMR}$ and $M_{n,GPC}$. This difference can be attributed to the loss of material during precipitation. For poly(*n*-butyl acrylate), unreacted monomer was removed in vacuo, and $M_{n,grav}$ values are in closer agreement with $M_{n,NMR}$ and $M_{n,GPC}$ values. In the case of poly(isoprene), the large difference between $M_{n,NMR}$ and $M_{n,GPC}$ is most likely due to the loss of volatile isoprene when preparing the crude ^{1}H NMR sample.

Table 1
Homopolymers made from bidirectional initiator **2** at 120–125 °C

Polymer	$M_{n,grav}$[a]	$M_{n,NMR}$[b]	$M_{n,GPC}$[c]	PDI[d]	DP[e]
PS-1	2800	2800	2200	1.27	19
PS-2	7300	7900	7300	1.11	67
P*n*BA-1	4400	4400	4900	1.16	31
P*n*BA-2	5100	5100	5000	1.15	35
P*n*BA-3	8400	5900	7200	1.12	51
P*n*BA-4	10 200	8500	10 400	1.12	71
P*n*BA-5	Not measured	11 600	13 700	1.15	102
P*t*BA-1	3800	4400	3700	1.17	26
P*t*BA-2	14 000	15 100	17 500	1.15	117
P*t*BA-3	16 600	19 700	19 600	1.18	141
P*t*BA-4	25 700	31 100	26 800	1.19	213
P*t*BA-5	37 700	35 200	41 900	1.20	294
P*t*BA-6	42 400	51 900	44 800	1.20	357
P*t*BA-7	46 700	60 900	47 300	1.21	398
P*t*BA-8	55 200	57 000	56 600	1.20	435
P*t*BA-9	66 200	68 100	58 200	1.23	496
P*t*BA-10	68 000	66 800	63 800	1.23	512
P*t*BA-11	85 900	83 900	72 200	1.26	625
PI-1	1500	2400	1500	1.10	18
PI-2	Not measured	16 400	10 100	1.18	186

PS = poly(styrene), P*t*BA = poly(*t*-butyl acrylate), P*n*BA = poly(*n*-butyl acrylate), PI = poly(isoprene).

[a] Theoretical molecular weight determined gravimetrically.

[b] Theoretical molecular weight determined from ^{1}H NMR integration.

[c] Number average molecular weight determined from gel permeation chromatography.

[d] Polydispersity determined from gel permeation chromatography.

[e] Degree of polymerization, based on the average of $M_{n,grav}$, $M_{n,NMR}$, and $M_{n,GPC}$.

The living nature of these polymers was further verified by growing external second blocks. As an example, macroinitiator **P*t*BA-1** was used to polymerize styrene, forming PS-*b*-PtBA-*b*-PS. The GPC traces of the macroinitiator ($M_{n,GPC} = 3700$; PDI = 1.17) and block copolymer ($M_{n,GPC} = 7900$; PDI = 1.13) show monomodal peaks and an increase in molecular weight (Fig. 4). This chain extension experiment verifies the fidelity of the nitroxide caps on both ends of the polymer chain. Table 2 shows a variety of triblock copolymers prepared using bidirectional initiator **2**.

Time studies were carried out for the polymerization of both homopolymers and ABA triblock copolymers. The initiator (or macroinitiator) was dissolved in monomer and divided amongst several ampoules. The ampoules were suspended in a 125 °C oil bath, and removed at scheduled intervals. Percent conversions were calculated from the precipitated masses of the polymers and molecular weights were determined by GPC. Fig. 5 shows the results of two such studies. The linear relationship between molecular weight and percent conversion confirms that there are no significant chain transfer events. The kinetic plots of monomer consumption are also linear, verifying that chain termination events are rare.

Table 2
Molecular weights and polydispersities of ABA triblock copolymers obtained after chain extension of the corresponding bidirectional homopolymers

Homopolymer	$M_{\text{n,GPC}}$	PDI	Triblock copolymer	$M_{\text{n,GPC}}$	PDI
P*n*BA-6	2300	1.44	P*t*BA-*b*-P*n*BA-*b*-P*t*BA	5900	1.51
			P*t*BA-*b*-P*n*BA-*b*-P*t*BA	6800	1.30
			P*t*BA-*b*-P*n*BA-*b*-P*t*BA	7100	1.38
			P*t*BA-*b*-P*n*BA-*b*-P*t*BA	7700	1.34
P*n*BA-2	5000	1.15	P*t*BA-*b*-P*n*BA-*b*-P*t*BA	6200	1.15
			P*t*BA-*b*-P*n*BA-*b*-P*t*BA	6800	1.16
			P*t*BA-*b*-P*n*BA-*b*-P*t*BA	8100	1.15
			P*t*BA-*b*-P*n*BA-*b*-P*t*BA	8600	1.19
P*n*BA-5	13 700	1.15	P*t*BA-*b*-P*n*BA-*b*-P*t*BA	15 000	1.15
			P*t*BA-*b*-P*n*BA-*b*-P*t*BA	16 200	1.16
PS-1	2200	1.27	P*t*BA-*b*-PS-*b*-P*t*BA	4500	1.17
			P*t*BA-*b*-PS-*b*-P*t*BA	5100	1.16
			P*t*BA-*b*-PS-*b*-P*t*BA	6700	1.14
			P*t*BA-*b*-PS-*b*-P*t*BA	7300	1.13
PS-2	7300	1.11	P*t*BA-*b*-PS-*b*-P*t*BA	13 200	1.15
			P*t*BA-*b*-PS-*b*-P*t*BA	16 900	1.16
			P*t*BA-*b*-PS-*b*-P*t*BA	20 800	1.17
P*t*BA-1	3700	1.17	PS-*b*-P*t*BA-*b*-PS	7900	1.13
			P*n*BA-*b*-P*t*BA-*b*-P*n*BA	10 400	1.14
			PI-*b*-P*t*BA-*b*-PI	6600	1.18
P*t*BA-2	17 500	1.15	P*n*BA-*b*-P*t*BA-*b*-P*n*BA	20 700	1.15
			P*n*BA-*b*-P*t*BA-*b*-P*n*BA	21 200	1.16
			P*n*BA-*b*-P*t*BA-*b*-P*n*BA	23 000	1.18
			P*n*BA-*b*-P*t*BA-*b*-P*n*BA	26 200	1.19
			P*n*BA-*b*-P*t*BA-*b*-P*n*BA	28 500	1.21
			P*n*BA-*b*-P*t*BA-*b*-P*n*BA	31 200	1.24
			P*n*BA-*b*-P*t*BA-*b*-P*n*BA	36 300	1.27
			P*n*BA-*b*-P*t*BA-*b*-P*n*BA	40 400	1.28
			P*n*BA-*b*-P*t*BA-*b*-P*n*BA	43 500	1.33
P*t*BA-3	19 600	1.18	PS-*b*-P*t*BA-*b*-PS	59 100	1.24
P*t*BA-4	26 800	1.19	PS-*b*-P*t*BA-*b*-PS	42 400	1.27
			P*n*BA-*b*-P*t*BA-*b*-P*n*BA	45 200	1.27
			PI-*b*-P*t*BA-*b*-PI	29 800	1.15
PI-1	1500	1.10	PDMA-*b*-PI-*b*-PDMA	7000	1.23
PI-2	10 100	1.18	PDMA-*b*-PI-*b*-PDMA	40 000	1.26

3.3. Proof of bidirectionality

In order to prove that alkoxyamine **2** functions as a *bidirectional* initiator, a competition experiment was carried out [22,26,29]. One equivalent of bidirectional initiator **2** was mixed with 2 eq of monodirectional initiator **1**; this mixture was used to polymerize styrene. An ampoule containing only monodirectional initiator **1** and styrene, and a separate ampoule containing only bidirectional initiator **2** and styrene were used as controls. The molar ratio of styrene to alkoxyamine functionality was 200:1 in all three ampoules. The GPC traces of the resulting polymers are shown in Fig. 6. The control experiments using only **1** and only **2** produced polymers with molecular weights of 10 200 and 22 600, respectively. While these GPC peaks were monomodal, the polystyrene that was made from a mixture of **1** and **2** shows a bimodal distribution. Furthermore, the two peaks in the bimodal distribution occur at the same elution times as each of the control peaks. This indicates that the mixture of initiators led to a mixture of polymers whose molecular weights are in a ratio of 1:2, confirming that initiator **2** does indeed effect polymerization from both ends.

3.4. Amphiphilic ABA triblock copolymers

A variety of amphiphilic ABA triblock copolymers were prepared (Table 3). The center block was polymerized directly from bidirectional initiator **2** using a hydrophobic monomer (styrene or *n*-butyl acrylate). The hydrophilic outer blocks were prepared by using this macroinitiator to polymerize *t*-butyl acrylate, followed by selective deprotection of the *t*-butyl esters with trifluoroacetic acid [32,34]. The disappearance of the *t*-butyl peak at 1.45 ppm in the ^{1}H NMR spectra confirms that the P*t*BA blocks were converted to poly(acrylic acid) (PAA) blocks.

3.5. AFM images

Wooley et al. [33,35−37] have shown that mixing AB and ABC amphiphilic block copolymers containing PAA blocks with diamines results in the formation of diverse self-assembled morphologies. The resulting carboxylate salts made of bridging ammonium ions impart dynamic intermolecular crosslinks. This procedure was applied to the ABA triblock copolymers reported here.

Each polymer was dissolved in a 0.1 wt% solution of 50:50 water/tetrahydrofuran at room temperature. Organic diamine 2,2′-(ethylenedioxy)bis(ethylamine) was added in a 2:1 ratio of amine-to-carboxylic acid functionality. Fig. 7 shows AFM images of several triblock copolymers that exhibited evidence of self-assembly. PAA_8-*b*-PS_{19}-*b*-PAA_8 forms toroid-shaped structures, while both PAA_{24}-*b*-PS_{67}-*b*-PAA_{24} and PAA_{17}-*b*-PnBA_{19}-*b*-PAA_{17} form spherical morphologies.

4. Conclusion

Bidirectional alkoxyamine initiator **2** was synthesized. The bidirectionality and living nature of polymerizations using this initiator were confirmed, and controlled polymerizations using a variety of monomers have been demonstrated. Well-defined symmetrical ABA triblock copolymers of styrene, acrylates, isoprene, and dimethylacrylamide have been prepared. Deprotection of the P*t*BA A blocks afforded a variety of amphiphilic ABA triblock copolymers. AFM images of some of these polymers in the presence of an organic diamine show that they assemble into torodial and spherical morphologies. The properties and self-assembly of these amphiphilic triblock copolymers are currently under investigation in this laboratory.

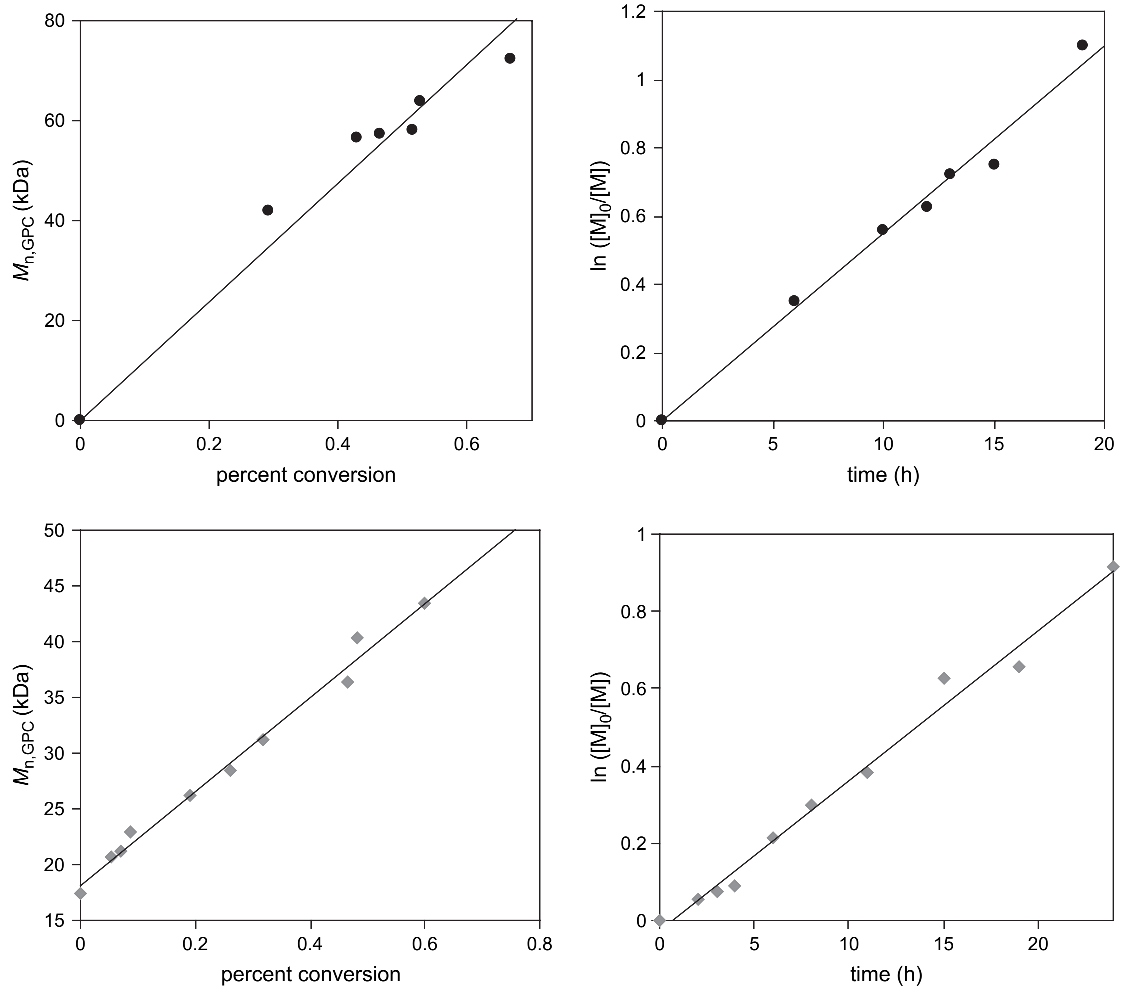


Fig. 5. Time studies of homopolymer P*t*BA (●) and triblock copolymer P*n*BA-*b*-P*t*BA-*b*-P*n*BA (◆) formation. The P*t*BA homopolymer was grown from bidirectional initiator **2**. The P*n*BA blocks of the triblock copolymer were grown from bidirectional macroinitiator **P*t*BA-2** ($M_{n,GPC} = 17\,500$; PDI = 1.15).

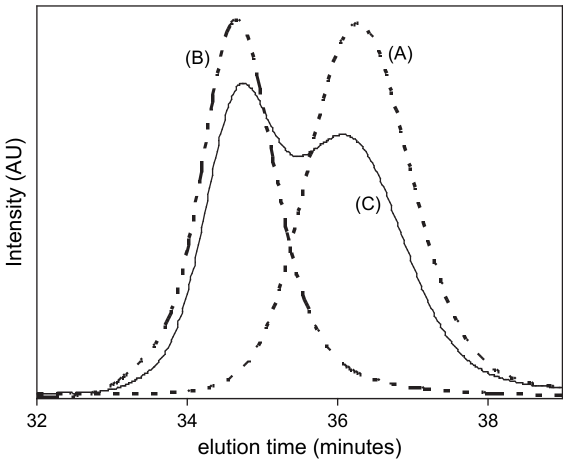


Fig. 6. GPC overlay of poly(styrene) made from (A) monodirectional initiator **1** only (- - -), (B) bidirectional initiator **2** only (— - -), and (C) a 2:1 mole ratio of mono- and bidirectional initiators **1** and **2** (—). All polymerizations were conducted in bulk at 125 °C for 2 h, and the ratio of styrene to alkoxyamine functionality was 200:1.

Table 3
Amphiphilic ABA triblock copolymers

Polymer	Average number of repeat units in hydrophobic B block[a]	Average number of repeat units in hydrophilic A block[a]	Ratio of repeat units (A:B)
PAA-*b*-P*n*BA-*b*-PAA	36	9	0.25
PAA-*b*-P*n*BA-*b*-PAA	36	13	0.36
PAA-*b*-P*n*BA-*b*-PAA	36	23	0.64
PAA-*b*-P*n*BA-*b*-PAA	36	28	0.78
PAA-*b*-P*n*BA-*b*-PAA	19	27	1.4
PAA-*b*-P*n*BA-*b*-PAA	19	27	1.4
PAA-*b*-P*n*BA-*b*-PAA	19	33	1.7
PAA-*b*-P*n*BA-*b*-PAA	19	35	1.8
PAA-*b*-P*n*BA-*b*-PAA	94	17	0.18
PAA-*b*-P*n*BA-*b*-PAA	94	25	0.27
PAA-*b*-PS-*b*-PAA	67	47	0.70
PAA-*b*-PS-*b*-PAA	67	79	1.2
PAA-*b*-PS-*b*-PAA	67	105	1.6
PAA-*b*-PS-*b*-PAA	19	16	0.84
PAA-*b*-PS-*b*-PAA	19	19	1.0
PAA-*b*-PS-*b*-PAA	19	29	1.5
PAA-*b*-PS-*b*-PAA	19	32	1.7

[a] Number of repeat units is based on an average of the gravimetric, ^{1}H NMR, and GPC molecular weights.

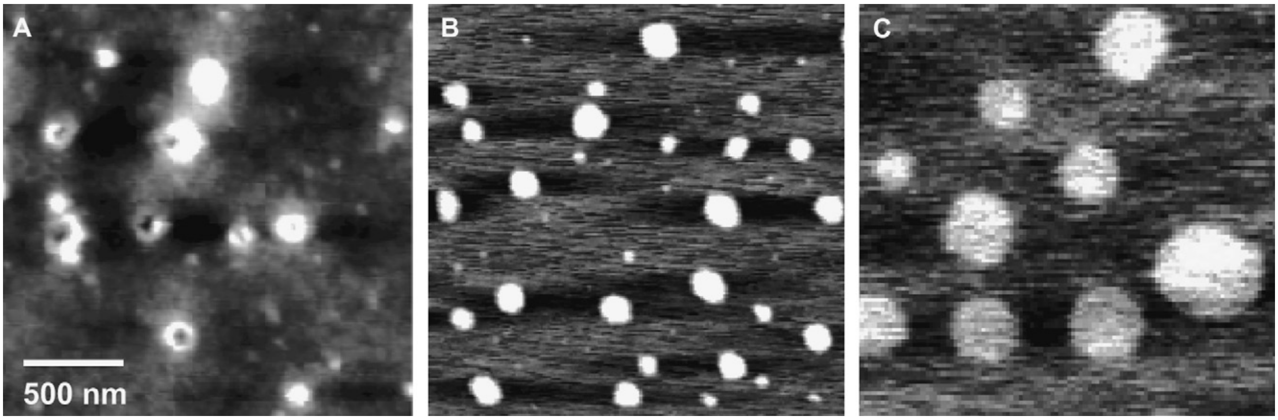


Fig. 7. AFM images of (A) PAA_8-*b*-PS_{19}-*b*-PAA_8, (B) PAA_{24}-*b*-PS_{67}-*b*-PAA_{24}, and (C) PAA_{17}-*b*-$PnBA_{19}$-*b*-PAA_{17}. Scan rate: 1.8 lines/s.

References

[1] Hawker CJ, Bosman AW, Harth E. Chem Rev 2001;101:3661.

[2] Georges MK, Veregin RPN, Kazmaier PM, Hamer GK. Macromolecules 1993;26:2987.

[3] Hawker CJ. J Am Chem Soc 1994;116:11185.

[4] Hawker CJ, Barclay GG, Orellana A, Dao J, Devonport W. Macromolecules 1996;29:5245.

[5] Benoit D, Chaplinski V, Braslau R, Hawker CJ. J Am Chem Soc 1999; 121:3904.

[6] Benoit D, Harth E, Fox P, Waymouth RM, Hawker CJ. Macromolecules 2000;33:363.

[7] Benoit D, Grimaldi S, Robin S, Finet JP, Tordo P, Gnanou Y. J Am Chem Soc 2000;122:5929.

[8] Grimaldi S, Finet J-P, Zeghdaoui A, Tordo P, Benoit D, Gnanou Y, et al. Polym Prepr (Am Chem Soc Div Polym Chem) 1997;38:651.

[9] Li CM, Tang YQ, Armes SP, Morris CJ, Rose SF, Lloyd AW, et al. Biomacromolecules 2005;6:994.

[10] Kuo WF, Tong SN, Pearce EM, Kwei TK. J Appl Polym Sci 1993; 48:1297.

[11] Pyun J, Matyjaszewski K, Wu J, Kim GM, Chun SB, Mather PT. Polymer 2003;44:2739.

[12] Meier MAR, Wouters D, Ott C, Guillet P, Fustin CA, Gohy JF, et al. Macromolecules 2006;39:1569.

[13] Wang CH, Hsiue GH. J Control Release 2005;108:140.

[14] Nardin C, Hirt T, Leukel J, Meier W. Langmuir 2000;16:1035.

[15] Schillen K, Bryskhe K, Mel'nikova YS. Macromolecules 1999;32:6885.

[16] Nardin C, Winterhalter M, Meier W. Langmuir 2000;16:7708.

[17] Napoli A, Tirelli N, Wehrli E, Hubbell JA. Langmuir 2002;18:8324.

[18] Li IQ, Howell BA, Koster RA, Priddy DB. Macromolecules 1996; 29:8554.

[19] Li IQ, Knauss DM, Priddy DB, Howell BA. Polym Int 2003;52:805.

[20] Huang WL, Chiarelli R, Charleux B, Rassat A, Vairon JP. Macromolecules 2002;35:2305.

[21] Beil JB, Zimmerman SC. Macromolecules 2004;37:778.

[22] Miura Y, Yoshida Y. Macromol Chem Phys 2002;203:879.

[23] Lizotte JR, Anderson SG, Long TE. J Polym Sci Part A Polym Chem 2004;42:1547.

[24] Zhang ZB, Zhu XL, Zhu J, Cheng ZP, Lu JM. J Appl Polym Sci 2006;100:1137.

[25] Hawker CJ. Angew Chem Int Ed Engl 1995;34:1456.

[26] Bothe M, Schmidt-Naake G. Macromol Chem Phys 2004;205:208.

[27] Husemann M, Dollase T. Eur Pat Appl (TESA AG, Germany): Ep; 2006. 20 pp.

[28] Husemann M, Dollase T, Kummer AB. Ger Offen (Tesa AG, Germany; Beiersdorf AG): De; 2003. 10 pp.

[29] Robin S, Guerret O, Couturier JL, Gnanou Y. Macromolecules 2002; 35:2481.

[30] Smejkal J, Kopecky J, Linhart I. Z Chem 1986;26:397.

[31] Wallace JS, Baldwin BW, Morrow CJ. J Org Chem 1992;57:5231.

[32] O'Reilly RK, Joralemon MJ, Wooley KL, Hawker CJ. Chem Mater 2005;17:5976.

[33] Li ZB, Chen ZY, Cui HG, Hales K, Qi K, Wooley KL, et al. Langmuir 2005;21:7533.

[34] Mehta A, Jaouhari R, Benson TJ, Douglas KT. Tetrahedron Lett 1992; 33:5441.

[35] Cui HG, Chen ZY, Wooley KL, Pochan DJ. Macromolecules 2006; 39:6599.

[36] Pochan DJ, Chen ZY, Cui HG, Hales K, Qi K, Wooley KL. Science 2004;306:94.

[37] Chen ZY, Cui HG, Hales K, Li ZB, Qi K, Pochan DJ, et al. J Am Chem Soc 2005;127:8592.