Macromolecules
ARTICLE

DOI: 10.1021/ma902291a

Dynamic Covalent Diblock Copolymers Prepared from RAFT Generated Aldehyde and Alkoxyamine End-Functionalized Polymers

Alexander W. Jackson and David A. Fulton*

Chemical Nanoscience Laboratory, School of Chemistry, Bedson Building, Newcastle University, Newcastle upon Tyne NE1 7RU, U.K.

Received October 15, 2009; Revised Manuscript Received November 13, 2009

ABSTRACT: Aldehyde- or alkoxyamine-containing trithiocarbonate chain transfer agents were prepared and used to mediate the synthesis of a series of polymers end-functionlized with either aldehyde or alkoxyamines functions, utilizing reversible addition−fragmentation polymerization techniques. Aldehyde end-functionalized polymers were shown to link through reversible oxime bond formation with alkoxyamine end-funtionalized polymers forming diblock copolymers. The dynamic nature of the oxime bond linking these polymer blocks together was demonstrated through a simple exchange reaction with a small molecule alkoxyamine. A diblock copolymer prepared from the self-assembly of an aldehyde end-functionalized polyisoprene with an alkoxyamine end-functionalized polystyrene was shown to undergo further hierarchical self-assembly into micellar aggregates in DMF. It was shown that the addition of an excess of a small molecule alkoxyamine triggered the disassembly of these micelles.

Introduction

Block copolymers are building blocks for a large variety of important self-assembled nanoscale objects such as micelles and vesicles in solution or ordered copolymer morphologies such as lamellae in bulk.[1] In the drive toward the development of new "smart" polymer-based systems possessing responsive and adaptable properties, chemists have incorporated dynamic and reversible supramolecular interactions such as H-bonding,[2] metal−ligand interactions,[3] or a combination of both[4] to link polymer blocks together. Recent advances have also seen the utilization of the macrocyclic host cucurbit[8]uril as a supramolcular "handcuff" to link polymer chains into supramolecular diblock copolymers in water,[5] and pseudorotaxane formation has also been utilized[6] to link polymer blocks end-functionalized with either crown ethers or secondary ammonium salts. In addition to facilitating self-assembly, supramolecular interactions can impart dynamic behaviors into the resultant block copolymer assemblies which are also incorporated into supramolecular aggregates formed from their block copolymer components.

We became intrigued by the possibility of using ideas from the field of dynamic covalent chemistry (DCC)[7] to develop new advanced materials with responsive and adaptive properties. DCC uses reversible covalent bond formation to link organic building blocks into larger structures. In addition to facilitating self-assembly, the reversible nature of the dynamic covalent linkages enables product assemblies to modify their constitutions by exchanging and reshuffling their building blocks. Equilibrium perturbations, such as changes in concentration, temperature, or the addition of other molecules, can result in constitutional alterations as the product assemblies re-equilibrate.[8] The reversible nature of the dynamic covalent link instils the "intelligent" virtues of controlled assembly, adaptability, and self-repair into the resultant nanostructures. In effect, dynamic covalent interactions could provide a mechanism for a polymer-based assembly to reconfigure its covalent structure and therefore its functional or material properties. Furthermore, the strength of the covalent bond ensures product assemblies possess chemical robustness, and as reversible covalent reactions are usually performed with the help of a suitable catalyst to aid kinetics, the option exists to halt these reversible processes and kinetically "fix" the products simply by quenching the catalyst.

The groups of Otsuka, Takahara, and Lehn have pioneered the use of reversible covalent reactions in polymer chemistry. Otsuka and Takahara have focused[9] on thermally reversible bonds based on alkoxyamines, using this motif to link monomers into polymer chains or graft components onto preformed polymer scaffolds. Work by Lehn's group on their hydrazone-based systems has demonstrated[9a,10] how the dynamic nature of the linkages can impart adaptive behaviors into polymers or affect their optical or mechanical properties. Recent work by the groups of Sumerlin[11] and Jäkle[12] has focused on polymer blocks terminated with boronic acids and their dynamic covalent self-assembly through boronate ester formation into three-arm star polymers. Here, we report the results of our preliminary studies on the synthesis and supramolecular aggregation of diblock copolymers where the polymer blocks are joined through a *single dynamic covalent bond* and their subsequent aggregation into micellar assemblies. There has been recent impressive work describing micellization of dynamic covalent surfactants;[13] however, to the best of our knowledge this work describes the first examples of dynamic covalent block copolymers of a truly polymeric nature.

Experimental Section

All chemicals were purchased from Sigma-Aldrich or Alfa Aesar and were used as received without further purification. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 spectrometer at 300 and 75 MHz, respectively, with the residual solvent signal as an internal standard. FTIR spectroscopy was performed on a Varian 800 FTIR instrument (Varian Inc.). High-resolution mass spectrometry was performed on a Waters LCT premier mass spectrometer (Waters Inc.). Gel permeation chromatography (GPC) was conducted on a Varian ProStar

*Corresponding author. E-mail: d.a.fulton@ncl.ac.uk.

instrument (Varian Inc.) equipped with a Varian 325 UV−vis dual wavelength detector (254 nm), a Viscotek 3580 differential RI detector, and a pair of PL gel 5 μm Mixed D 300 × 7.5 mm columns with guard column (Polymer Laboratories Inc.) in series. Near monodisperse polystyrene standards (Polymer Laboratories) were used for calibration. Data collection was performed with Galaxie software (Varian Inc.) and chromatograms analyzed with the Cirrus software (Varian Inc.). Dynamic and static light scattering was performed on a Dawn Heleos II instrument (Wyatt Technology Corp.), and data collection and analysis were performed with Astra software (Wyatt Technology Corp.).

2-[2-(2-Hydroxyethoxy)ethoxy]ethyl-4-formylbenzoate. A solution of NEt_3 (6.0 g, 0.059 mol) and triethylene glycol (31.1 g, 0.207 mol) in CH_2Cl_2 (40 mL) was cooled to 0 °C in an ice bath while stirring under a nitrogen atmosphere. To this solution 4-formylbenzoyl chloride (4.99 g, 0.0296 mol) in CH_2Cl_2 (50 mL) was added dropwise over 30 min, and the reaction was left to stir overnight at room temperature. The reaction mixture was evaporated to dryness, and the residue was dissolved in EtOAc (50 mL) and washed with saturated $NaHCO_3$ solution. The organic layer was dried over $MgSO_4$, filtered, and evaporated to dryness to obtain crude oil which was purified by column chromatography [SiO_2, EtOAc−hexane (3:1)] to yield the title product as a pale yellow oil (4.68 g, 50%). ^{1}H NMR ($CDCl_3$): δ 3.57 (m, 2H), 3.67 (m, 6H), 3.82 (m, 2H), 4.49 (m, 2H), 7.91 (d, 2H, J = 8.0 Hz), 8.18 (d, 2H, J = 8.0 Hz), 10.06 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 62.1, 64.8, 69.5, 70.8, 71.1, 72.9, 129.7, 130.2, 135.5, 139.8, 165.8, 191.6. FT-IR (wavenumber, cm^{-1}): 3490 (O−H), 2920 (C−H, alkyl), 2855 (C−H, alkyl), 1702 (C=O), 1453 (C=C, aromatic), 1385 (C=C, aromatic), 1202 (C−H, aromatic). HRMS$^+$ $C_{14}H_{18}O_6$: Theoretical: 283.1182. Actual: 283.1189.

Aldehyde-Functionalized Chain Transfer Agent (1). A solution of *S*-1-dodecyl-*S*′-(α,α-dimethyl-α″-acetic acid)trithiocarbonate (DDMAT, 0.63 g, 1.73 mmol) and 2-[2-(2-hydroxyethoxy)ethoxy]ethyl-4-formylbenzoate (0.49 g, 1.73 mmol) in CH_2Cl_2 (20 mL) was cooled to 0 °C in an ice bath while stirring under a nitrogen atmosphere. A solution of EDC (0.37 g, 1.91 mmol) and DMAP (0.23 g, 1.91 mmol) in CH_2Cl_2 (10 mL) was added dropwise. The reaction mixture was stirred overnight at room temperature and then evaporated to dryness to afford a crude yellow oil which was purified by column chromatography [SiO_2, hexane−EtOAc (3:1)] to yield the title product as a yellow oil (0.65 g, 59%). ^{1}H NMR ($CDCl_3$): δ 0.86 (t, 3H, J = 7 Hz), 1.25 (m, 18H), 1.68 (m, 8H), 3.24 (t, 2H, J = 7.5 Hz), 3.66 (t, 6H), 3.85 (t, 2H, J = 5.0 Hz), 4.24 (t, 2H, J = 5.0 Hz), 4.50 (t, 2H, J = 5.0 Hz), 7.95 (d, 2H, J = 9.0 Hz), 8.21 (d, 2H, 9.0 Hz), 10.10 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 14.2, 22.9, 25.5, 25.7, 28.3, 29.2, 29.4, 29.6, 29.7, 29.8, 29.9, 30.9, 32.2, 37.3, 56.4, 64.9, 65.3, 69.3, 69.5, 71.1, 129.7, 130.6, 135.6, 139.8, 165.8, 172.9, 191.4, 206.1. FT-IR (wavenumber, cm^{-1}): 2981 (C−H, alkyl), 2923 (C−H, alkyl), 1726 (C=O), 1463 (C=C, aromatic), 1383 (C=C, aromatic), 1270 (C−H, aromatic). HRMS$^+$ $C_{31}H_{48}O_7S_3Na$: Theoretical: 651.2460. Actual: 651.2463.

***N*-Boc-6-aminoxyhexan-1-ol.** 1,8-Diazabicyclo[5.4.0]undec-7-ene (0.677 mL, 4.52 mmol) was added dropwise over 10 min to a solution of *N*-Boc-hydroxylamine (0.50 g, 3.75 mmol) and 6-bromohexan-1-ol (0.819 g, 4.52 mmol) in CH_2Cl_2 (20 mL). The reaction mixture was left to stir overnight at room temperature, then transferred into a separating funnel, and CH_2Cl_2 (100 mL) added. The organic layer was washed with 1 M HCl (50 mL) and saturated $NaCl_{(aq)}$ (50 mL) and then dried over $MgSO_4$, filtered, and evaporated to dryness to afford a yellow oil which was purified by column chromatography [SiO_2, hexane−EtOAc (3:2)] to yield the title product as a pale yellow oil (0.565 g, 64%). ^{1}H NMR ($CDCl_3$): δ 1.38 (m, 4H), 1.45 (s, 9H), 1.57 (m, 4H), 3.61 (t, 2H, J = 6.5 Hz), 3.83 (t, 2H, J = 6.5 Hz), 7.28 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 25.3, 28.3, 28.8, 33.1, 60.6, 63.1, 81.8, 157.2, 171.2. FT-IR (wavenumber, cm^{-1}): 3450 (O−H), 3230 (N−H), 2981 (C−H, alkyl), 1716 (C=O). HRMS$^+$ $C_{11}H_{23}NO_3K$: Theoretical: 256.1525. Actual: 256.1529.

Alkoxyamine-Functionalized Chain Transfer Agent (2). A solution of *S*-1-dodecyl-*S*′-(α,α-dimethyl-α″-acetic acid)-trithiocarbonate (DDMAT, 0.78 g, 2.14 mmol) and *N*-Boc-6-aminoxy hexan-1-ol (0.50 g, 2.14 mmol) in CH_2Cl_2 (20 mL) was cooled to 0 °C in an ice bath while stirring under a nitrogen atmosphere. A solution of EDC (0.452 g, 2.35 mmol) and DMAP (0.29 g, 2.35 mmol) in CH_2Cl_2 (10 mL) was added dropwise, and the reaction mixture was stirred overnight at room temperature. The reaction mixture was evaporated to dryness, and the crude yellow oil was purified by column chromatography [SiO_2, hexane−EtOAc (9:1)] to yield the Boc-protected oxylamine chain transfer agent as a yellow oil (0.707 g, 57%). ^{1}H NMR ($CDCl_3$): δ 0.87 (t, 3H, J = 7.0 Hz), 1.36 (m, 18H), 1.48 (s, 9H), 1.64 (m, 16H), 3.26 (t, 2H, J = 7.5 Hz), 3.83 (t, 2H, J = 6.0 Hz), 4.08 (t, 2H, J = 6.5 Hz), 7.10 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 14.2, 22.9, 25.8, 25.9, 26.1, 28.3, 28.6, 28.7, 29.2, 29.4, 29.6, 29.7, 29.8, 29.9, 31.8, 32.2, 37.3, 56.5, 66.2, 77.7, 81.7, 157.1, 173.1. FT-IR (wavenumber, cm^{-1}): 2981 (C−H, alkyl), 2925 (C−H, alkyl), 1733 (C=O).

Boc-protected oxylamine chain transfer agent (0.350 g, 0.60 mmol) was dissolved in CH_2Cl_2 (3 mL) and TFA (3 mL). The reaction mixture was left to stir at room temperature for 30 min, and the solution was evaporated to dryness to afford a yellow oil. The crude product was purified by column chromatography [SiO_2, hexane−EtOAc (4:1)] to yield the title product as a yellow oil (0.158 g, 55%). ^{1}H NMR ($CDCl_3$): δ 0.87 (t, 3H, J = 6.5 Hz), 1.25 (m, 18H), 1.68 (m, 16H), 3.26 (t, 2H, J = 7.5 Hz), 3.64 (t, 2H, J = 6.5 Hz), 4.08 (t, 2H, J = 6 Hz), 5.35 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 14.2, 22.9, 25.8, 26.0, 26.2, 28.2, 28.7, 28.8, 29.2, 29.4, 29.6, 29.7, 29.8, 29.9, 32.2, 37.3, 56.5, 66.2, 76.2, 173.1. HRMS$^+$ $C_{23}H_{45}S_3O_3N$: Theoretical: 480.2640. Actual: 480.2646.

Aldehyde End-Functionalized Poly(styrene) (P1a-d). To a small Schlenk tube the chain transfer agent **1** (1 equiv) and AIBN (0.1−0.2 equiv) was added. Styrene (100−200 equiv) was then added followed by DMF (200 equiv). The reaction mixture was degassed five times, and then the vessel was backfilled with nitrogen, purged with N_2, and allowed to warm to room temperature. The reaction mixture was placed in an oil bath at 70 °C. The polymerization was quenched after a predetermined time, and solvent was removed on the rotary evaporator. The resulting yellow oil was dissolved in a minimal amount of THF and added dropwise to ice cold methanol. The polymer precipitate was then isolated by filtration and dried under high vacuum. Polymers **P1a−d** were obtained as pale yellow solids with yields typically between 60 and 80%. ^{1}H NMR ($CDCl_3$): δ 0.88−1.01 (br, dodecyl of the chain terminus), 1.45 (br, $CHCH_2$, polymer backbone), 1.88 (br, $CHCH_2$, polymer backbone), 3.29 (br, SCH_2, of the chain terminus) 6.59 (br, Ar, polymer backbone), 7.06 (br, Ar, polymer backbone), 7.95 (d, Ar, of the chain terminus), 8.21 (d, Ar, of the chain terminus), 10.12 (s, CHO, of the chain terminus).

Alkoxyamine End-Functionalized Poly(styrene) (P5a−c). To a small Schlenk tube the chain transfer agent **2** (1 equiv) and AIBN (0.1−0.2 equiv) was added. Styrene (100−200 equiv) was then added followed by DMF (200 equiv). The reaction mixture was degassed five times, then the vessel was backfilled with nitrogen, purged with N_2, and allowed to warm to room temperature. The reaction mixture was placed in an oil bath at 70 °C. The polymerization was quenched after a predetermined time, and solvent was removed on the rotary evaporator. The resulting yellow oil was dissolved in minimal amount of THF and added dropwise to ice cold methanol. The polymer precipitate was then isolated by filtration and dried under high vacuum. Polymers **P5a−c** were obtained as pale yellow solids with yields typically between 70 and 80%. ^{1}H NMR ($CDCl_3$): δ 0.88−1.01 (br, dodecyl of the chain terminus), 1.45 (br, $CHCH_2$, polymer backbone), 1.88 (br, $CHCH_2$, polymer backbone), 3.29 (br, SCH_2, of the chain terminus), 5.35 (br, CH_2ONH_2, of the chain terminus) 6.59 (br, Ar, polymer backbone), 7.06 (br, Ar, polymer backbone).

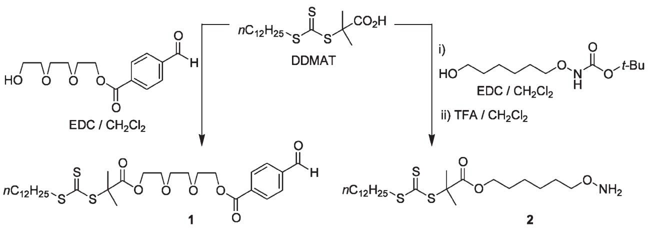
Aldehyde-End-Functionalized Poly(methyl methacrylate) (P2). The chain transfer agent **1** (118 mg, 0.188 mmol) and AIBN (3.08 mg, 18.8 μmol) were added to a small Schlenk tube. Methyl methacrylate (1.88 g, 18.8 mmol) was then added followed by DMF (1.9 mL). The reaction mixture was degassed five times, and then the vessel was backfilled with nitrogen, purged with N_2, and allowed to warm to room temperature. The reaction mixture was placed in an oil bath at 70 °C. The polymerization was quenched after 16 h, and solvent was removed on the rotary evaporator. The resulting yellow oil was dissolved in minimal amount of THF and added dropwise to ice cold hexane. The polymer precipitate was then isolated by filtration and dried under high vacuum. Polymer **P2** was obtained as pale yellow solid in a yield of 81%. ^{1}H NMR ($CDCl_3$): δ 0.92 (br, 3H, $CH_2C(CH_3)C$, polymer backbone), 1.80 (br, 2H, $CH_2C(CH_3)C$, polymer backbone), 3.59 (br, 3H, $C(O)OCH_3$, polymer backbone), 8.01 (d, Ar, of the chain terminus), 8.21 (d, Ar, of the chain terminus), 10.11 (s, C*H*O, of the chain terminus).

Aldehyde-End-Functionalized Poly(isoprene) (P3). The chain transfer agent **1** (94 mg, 0.15 mmol) and *tert*-butyl peroxide (4.4 mg, 0.03 mmol) were placed in a small Schlenk tube fitted with a Young's tap. Isoprene (5.09 g, 0.0748 mol) was then added, the reaction mixture was degassed five times, and the vessel was backfilled with nitrogen, purged with N_2, and allowed to warm to room temperature. The system was then sealed and placed in an oil bath at 125 °C. The polymerization was quenched after 45 h, and the reaction mixture was evaporated to dryness on the rotary evaporator. The resulting yellow oil was dissolved in a minimal amount of CH_2Cl_2 and added dropwise to ice cold methanol. Evaporation to dryness and further drying under high vacuum afforded polymer **P3** as a yellow oil in a yield of 83%. ^{1}H NMR ($CDCl_3$): δ 0.8−1.0 (br, dodecyl of the chain terminus), 1.60 (br, CH_3, polymer backbone), 2.00 (br, CH_2, polymer backbone), 3.35 (br, SCH_2, of the chain terminus), 4.0−4.1 (br, C*H*, polymer backbone), 4.6−4.8 (br, 3,4-C-$(CH_3){-}CH_2$, polymer backbone), 4.8−5.1 (br, 1,2-$CH{=}CH_2$, polymer backbone), 5.1−5.3 (br, 1,4-$CH_2{-}C(CH_3){-}CH{-}CH_2$, polymer backbone) 5.70−5.85 (1,2-$CH{=}CH_2$, polymer backbone), 7.95 (d, Ar, of the chain terminus), 8.22 (d, Ar, of the chain terminus) 10.12 (s, C*H*O, of the chain terminus). ^{1}H NMR spectroscopic analysis confirmed the distribution of monomers units to be 10:19:230 for the 1,2-, 3,4-, and 1,4- conformations, respectively.

Aldehyde-End-Functionalized Poly(ethylene glycol) (P4). Poly(ethylene glycol) monomethyl ether $M_w = 5000$ g mol^{-1} (Sigma-Aldrich) (3.65 g, 0.731 mmol) was dissolved in CH_2Cl_2 (50 mL). 4-Carboxybenzaldehyde (0.548 g, 3.65 mmol), DMAP (0.464 g, 3.80 mmol), and EDC (0.728 g, 3.80 mmol) were added, and the reaction mixture was stirred at room temperature for 72 h and then evaporated to dryness. The crude product was dissolved in CH_2Cl_2 (10 mL), and this solution was added dropwise to ice cold diethyl ether. The precipitated solids were isolated by filtration, the precipitation procedure was repeated another two times, and the product was dried under high vacuum. Polymer **P4** was obtained as a white solid in a 20% yield. ^{1}H NMR ($CDCl_3$): δ 3.61 (br, 4H, $CH_2{-}CH_2O$, polymer backbone), 7.95 (d, Ar, of the chain terminus), 8.21 (d, Ar, of the chain terminus), 10.10 (s, C*H*O, of the chain terminus).

General Procedure for Dynamic Covalent Diblock Copolymers. The appropriate aldehyde-terminated polymer (**P1a−d**, **P2**, **P3**, **P4**) and alkoxyamine-terminated polymer (**P5a,c**) were dissolved in DMF-d_7 (5 mM of each polymer) for ^{1}H NMR spectroscopic analysis or THF (5 mM of each polymer) for GPC analysis. To each solution TFA (10−20 mol %) was added. Samples were analyzed at regular intervals during the dimerization process after predetermined times.

Scheme 1. Synthesis of Modified CTA Agents 1 and 2



Micellization of Dynamic Covalent Diblock Copolymer (P3-Dyn*b*-P5b). **P3** poly(isoprene) (78.8 mg, 1 equiv) and **P5b** poly(styrene) (64.7 mg, 1 equiv) were dissolved in CH_2Cl_2 (2 mL), and TFA (0.25 μL, 0.75 equiv) was added. The reaction mixture was left to stir at room temperature for 24 h. After this time DMF (8 mL) was added dropwise over 10 min. 2 mL of this stock solution (0.4 mM) was filtered through 0.45 μm nylon syringe filter and diluted in DMF to prepare a range of solutions (0.2 mM−4 μM) for DLS and GPC analysis.

Results and Discussion

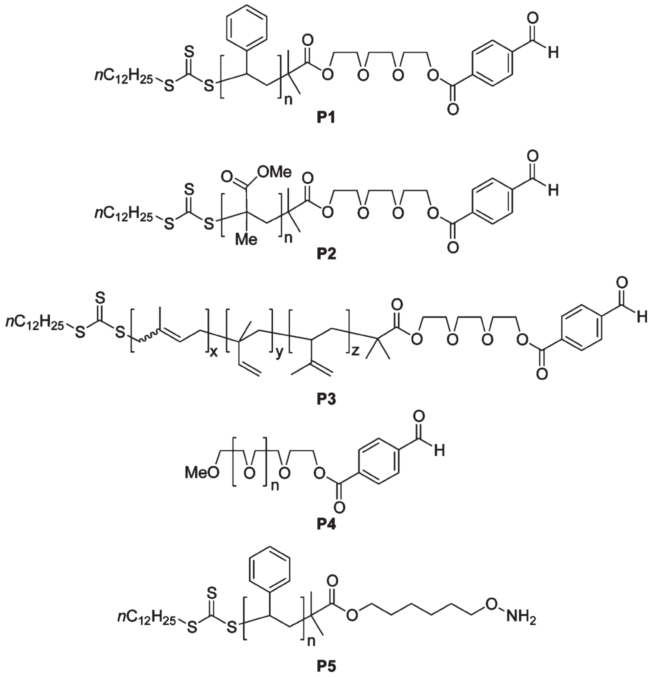
Chain Transfer Agent Syntheses. Oxime exchange was chosen as our dynamic covalent reaction to link preformed polymer blocks into diblock copolymers, as it is a well-studied and successful reaction in dynamic covalent chemistry[7,8b] and one with which we had also gained experience in our own research laboratory from previous projects. To prepare polymer chains end-functionalized with either alkoxyamine or aldehyde groups, we utilized reversible addition−fragmentation transfer (RAFT) polymerization techniques.[14] RAFT is a living radical polymerization technique which allows access to a range of well-defined polymer structures possessing high levels of end-group fidelity and is mediated by a chain transfer agent (CTA) typically based on dithioesters or trithiocarbonates. The use of modified CTAs allows the preparation of polymers end-functionalized with a specific functional group and overcomes the limitations of postpolymerization strategies.[15] Thus, the aldehyde-containing CTA **1** was prepared (Scheme 1) in a yield of 59% via a carbodiimide-mediated coupling between the chain transfer agent (*S*-1-dodecyl-*S*′-(α,α′-dimethyl-α″-acetic acid)trithiocarbonate)[16] (DDMAT) and 2-[2-(2-hydroxyethoxy)ethoxy]-ethyl-4-formylbenzoate. Likewise, the alkoxyamine-containing CTA **2** was prepared from a similar carbodiimide-mediated coupling between DDMAT and *N*-Boc-6-aminoxyhexan-1-ol followed by acid-catalyzed removal of the Boc protecting group, reactions which proceeded in yields of 57% and 55%, respectively. ^{1}H NMR (see Supporting Information) and FTIR spectroscopies and mass spectrometry confirmed the identity of both modified CTAs **1** and **2**.

RAFT Polymerizations. Polymerizations of styrene, isoprene, and methyl methacrylate mediated by RAFT CTAs **1** and **2** afforded a range of formyl or alkoxyamine-terminated[17] polymers (Scheme 2, Table 1). The RAFT polymerizations of styrene were performed in DMF at 70 °C using a range of reagent stiochiometries (Table 1, entries **P1a−P1d** and **P5a−c**) yielding well-defined polymers in all cases. Pseudo-first-order rate plots and plots of molecular weight versus conversion for styrene mediated by CTAs **1** and **2** were performed. The plots obtained (Supporting Information) from this brief kinetic study were linear, suggesting a constant concentration of radicals during the polymerizations. The polymerization of methyl methacrylate to afford **P2** was performed in DMF at 70 °C under near identical conditions to those used for polystyrene **P1**. The RAFT polymerization of isoprene to afford **P3** was performed using the method of

Wooley and co-workers[18] using *tert*-butyl peroxide as initiator at 125 °C in the absence of solvent. All RAFT polymers were characterized by GPC analysis, indicating unimolecular weight distributions and low polydispersities in all cases. The DP values calculated from NMR matched well those found by GPC. Polymer **P4** was prepared by EDC-mediated esterification of commercially available poly(ethylene glycol) monomethyl ether ($M_w = \sim 5000$ Da) with 4-formylbenzoic acid. The presence of the formyl or alkoxyamine end groups in polymers **P1**−**P5** was confirmed by ^{1}H NMR spectroscopy. Polymers possessing formyl end groups (**P1**−**P4**) each displayed singlets at 10.10−10.12 ppm, corresponding to the formyl proton, and triplets at 3.29 ppm, corresponding to the SCH_2 group. Those polymers possessing alkoxyamine end-groups (**P5a**−**c**) each displayed signals at 5.34 ppm corresponding to CH_2ONH_2 and triplets at 3.29 ppm corresponding to SCH_2 group. The degree of end-functionalization of all RAFT polymers (**P1**−**P3**, **P5**) was estimated from ^{1}H NMR spectroscopy to be ∼80−90% and the degree of end-functionalization of polymer **P4** to be ∼95%.

Formation and Characterization of Dynamic Covalent Diblock Copolymers. As a first step toward dynamic covalent diblock copolymers, we studied initially the dimerization of the modified CTAs **1** and **2** to form the oxime-linked dimer **3** (Scheme 3). TFA catalyst (20 mol %) was added to a 1:1 mixture of **1** and **2** ($c = 30$ mM of each component) in $CDCl_3$ and the solution allowed to come to equilibrium (< 30 min). ^{1}H NMR spectroscopy showed (Figure 1a) a significant reduction in the intensity of the signal corresponding to the formyl proton (H_a) of **1** and the appearance of a *trans*-oxime ($H_{a'}$) signal at 8.14 ppm.[19] These changes were accompanied by a reduction in intensity of the aromatic signals (H_c) of **1** at 8.21 and 7.95 ppm and the appearance of signals corresponding to the aromatic moiety of oxime **3** ($H_{c'}$) at 8.03 and 7.66 ppm. Further evidence for the formation of **3** was obtained from electrospray mass spectrometry of this solution, which showed a signal at $m/z = 1090.51$, indicating the presence of the oxime-linked dimer **3** at equilibrium. To demonstrate the dynamic nature of oxime **3**, 4 equiv of 2-aminooxymethynapthalene **4** was added (Scheme 3), and the solution was left to re-equilibrate. ^{1}H NMR spectroscopic analysis (Figure 1b) shows the appearance of a signal at 5.41 ppm, corresponding to the CH_2ON protons of oxime **5** ($H_{e'}$) and an equal increase in the intensity of the signal corresponding to the CH_2ONH_2 protons of **2** ($H_{f,g}$). This observation indicates the presence of oxime **5** and confirms the dynamic nature of the oxime bond.[20] These same experiments were repeated in DMF-d_7 with essentially identical outcomes, and the equilibrium constant in this solvent for the formation of oxime **3** from starting materials **1** and **2** was determined from ^{1}H NMR spectroscopy to be 361.[21]

Scheme 2. Structures of Aldehyde- or Alkoxyamine-End-Functionalized Polymers P1−P5



Scheme 3. Dimerization of Modified CTAs 1 and 2 To Form Oxime 3 and Subsequent Re-equilibration upon the Addition of 1-Aminooxymethylnapthalene into Oxime 5

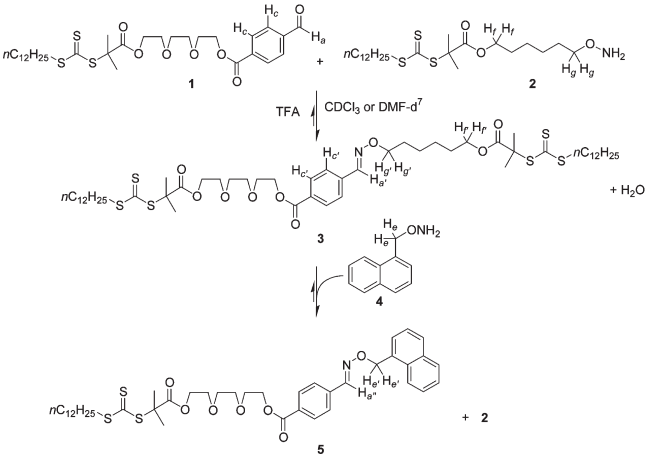


Table 1. Selection of Aldehyde- or Alkoxyamine-End-Functionalized Polymers P1−P5

polymer	chain transfer agent	monomer	initiator	temp (°C)	time (h)	M_n[a] (g mol^{-1})	M_n[b] (g mol^{-1})	M_w[b] (g mol^{-1})	PDI[b] (M_w/M_n)
P1a	**1** (1 equiv)	styrene (100 equiv)	AIBN (0.2 equiv)	70	3	1750	1950	2100	1.08
P1b	**1** (1 equiv)	styrene (100 equiv)	AIBN (0.1 equiv)	70	14	5100	4800	5050	1.05
P1c	**1** (1 equiv)	styrene (100 equiv)	AIBN (0.2 equiv)	70	24	6250	6100	6600	1.08
P1d	**1** (1 equiv)	styrene (200 equiv)	AIBN (0.1 equiv)	70	26	9800	9000	10700	1.19
P2	**1** (1 equiv)	methyl methacrylate (200 equiv)	AIBN (0.1eq)	70	24	13550	11850[c]	16000[c]	1.35
P3	**1** (1 equiv)	isoprene (500 equiv)	*t*-BP (0.2 equiv)	125	45	18300	14 600	19100	1.31
P4						5000	4900[c]	5450[c]	1.11
P5a	**2** (1 equiv)	styrene (100 equiv)	AIBN (0.2 equiv)	70	21	6350	6200	6400	1.03
P5b	**2** (1 equiv)	styrene (300 equiv)	AIBN (0.2 equiv)	70	23	10750	12700	14950	1.18
P5c	**2** (1 equiv)	styrene (200 equiv)	AIBN (0.1 equiv)	70	16	5050	5450	5650	1.04

[a] As determined by ^{1}H NMR spectroscopy. [b] As determined by gel permeation chromatography in THF. [c] Calculated by multiangle light scattering. AIBN: azobis(isobutyronitrile); ^{t}BP: *tert*-butyl peroxide.

To investigate the formation of a dynamic covalent block copolymer, **P1b** ($M_n = 4800$ Da) and **P5a** ($M_n = 6200$ Da) were mixed in DMF-d_7 (5 mM each) and TFA added (10 mol %),

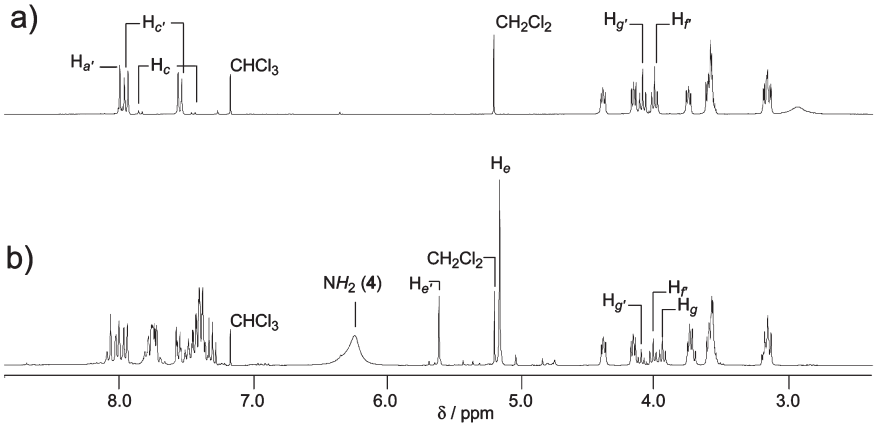


Figure 1. (a) Partial ^{1}H NMR spectra (300 MHz, 298 K, $CDCl_3$) displaying dimerization between modified chain transfer agents **1** + **2** to afford dimer **3** linked via oxime formation. (b) Partial ^{1}H NMR spectra (300 MHz, 298 K, $CDCl_3$) displaying the re-equilibration of oxime **3** to oxime **5** upon the addition of alkoxyamine **4**.

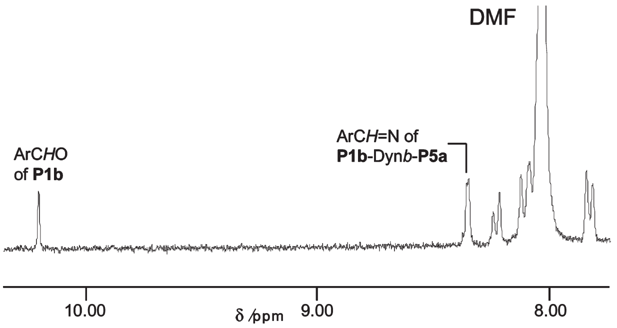


Figure 2. Partial ^{1}H NMR spectra (300 MHz, 298 K, DMF-d_7) displaying dimerization between **P1b** and **P5a** to afford oxime-linked dynamic covalent diblock copolymer **P1b**-Dyn*b*-**P5a**.

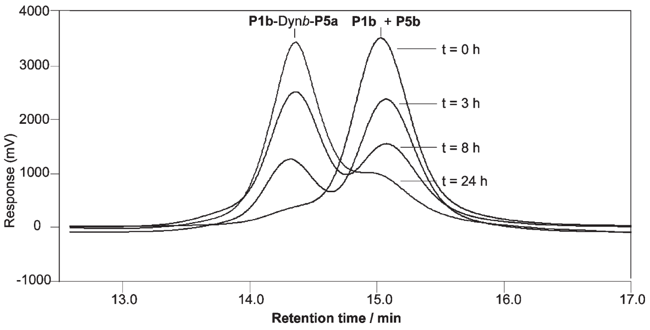


Figure 3. Gel permeation chromatography (THF, 1 mL/min) traces of the dimerization process of **P1b** and **P5a** into **P1b**-Dyn*b*-**P5a** at *t* = 0, 3, 8, and 24 h. Traces were recorded on a UV detector at 254 nm.

Table 2. Preparation of a Selection of Homo- and Heterodynamic Covalent Diblock Copolymers (5 mM of Each Block)

polymer blocks	block copolymers	theoretical M_n (Da) of block copolymer[a]	association constant
P1b + **P5a**	**P1b**-Dyn*b*-**P5a**	11 000	5.44[b]
P1d + **P5b**	**P1c**-Dyn*b*-**P5b**	21 700	2.45[b]
P2 + **P5b**	**P2**-Dyn*b*-**P5b**	24 550	2.66[b]
P3 + **P5b**	**P3**-Dyn*b*-**P5b**	27 300	2.07[c]
P4 + **P5a**	**P4**-Dyn*b*-**P5a**	11 100	6.61[c]

[a] Calculated by addition of the M_n values (as determined by GPC or multiangled light scattering) of each polymer block. [b] Calculated in DMF-d_7. [c] Calculated in THF-d_8.

and the reaction was allowed to reach equilibrium. The solution was analyzed by ^{1}H NMR spectroscopy (Figure 2), which displayed the appearance of a signal at 8.35 ppm corresponding to the oxime linkage of **P1b**-Dyn*b*-**P5a**[22] (M_n = 11 000 Da) and a reduction in the intensity of the signal at 10.21 ppm corresponding to the formyl proton in **P1b**. Under these conditions, equilibrium was reached in ~24 h. Dimerization of **P1b** and **P5a** to form **P1b**-Dyn*b*-**P5a** was also investigated by GPC (Figure 3), which shows the appearance of a peak at 14.29 min, corresponding to the block copolymer **P1b**-Dyn*b*-**P5a** and the reduction in area of the peak at 15.01 min corresponding to both **P1b** and **P5a**. To demonstrate the dynamic and reversible nature of the oxime linkage, excess 1-aminooxyhexane (10 equiv) was added to a solution of **P1b**-Dyn*b*-**P5a** at equilibrium with its component polymer blocks in the presence of TFA. GPC analysis displayed the complete disappearance of the peak at 14.29 min and an increase in the area of the peak at 15.01 min, a process which took 4 days to reach completion. This observation suggests that 1-aminooxyhexane competes with the alkoxyamine end group of **P5a** to form an oxime linkage with **P1b**, resulting in the re-equilibration of the diblock copolymer **P1b**-Dyn*b*-**P5a** into **P5a** and hexyloxime-capped **P1b**. The results of the ^{1}H NMR spectroscopic and GPC analysis suggest that polymer chains can be linked through a dynamic covalent bond to form a diblock copolymer which displays dynamic behavior.

A series of end-functionalized polymer building blocks were reacted to form dynamic covalent diblock copolymers and characterized under equilibrium conditions (Table 2). The equilibrium constants for the dimerization of all polymer blocks were determined from ^{1}H NMR spectroscopy and were found to be considerably lower than those for the dimerization of **1** + **2**. This significant reduction in equilibrium constant is presumably on account of the steric bulk of the polymer blocks hindering the linking of the chain ends and the fact that not all polymer chains contain the desired end-groups as a consequence of less than 100% end-group fidelity in the RAFT process.

Self-Assembly of Micelles. To investigate the potential of dynamic covalent diblock copolymers to form micellar aggregates, we focused on the **P3**-Dyn*b*-**P5b** system formed at equilibrium from the dimerization of the polystyrene block **P5b** and the polyisoprene block **P3** in DMF, which is a selective solvent for the polystyrene block. The self-assembly into micelles of polystyrene-*b*-polyisoprene diblock copolymers in organic solvents which are selective for one of the blocks is well-known,[23] and this aggregation process is thought to be enthalpy-driven.[23b] Under the

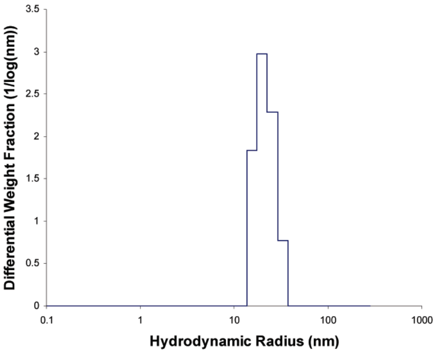


Figure 4. Regularization analysis of DLS data of micelles formed from **P3**-Dyn*b*-**P5b** in DMF.

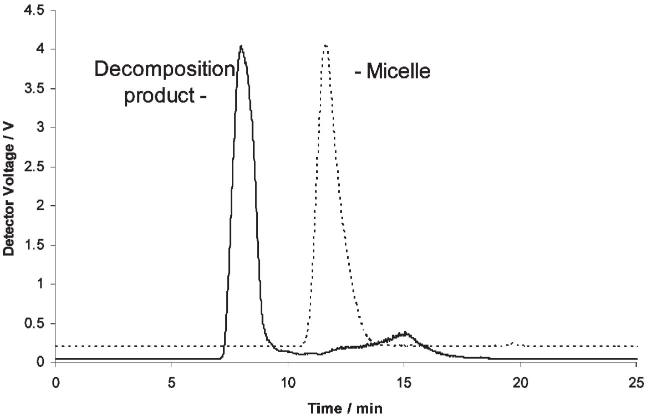


Figure 5. Gel permeation chromatographic traces of the micellar aggregates formed from dynamic covalent diblock copolymer **P3**-Dyn*b*-**P5b** (dotted line) and trace of the decomposition products (solid line). GPC was performed in DMF at 1 mL/min at 40 °C and recorded using a light scattering detector measuring the scattered light at 90°.

conditions studied, any micelles formed should possess polyisoprene chains at their core surrounded by a corona of polystyrene chains. On account of the poor solubility of **P3** in DMF, both **P3** and **P5b** were dissolved in CH_2Cl_2 (concentration of each block = 2 mM) and TFA was added (10 mol %). DMF was added, and a portion of this stock solution was filtered and further diluted in DMF (concentration of each block $\sim 4\,\mu$M). Dynamic light scattering measurements indicated the formation of a tertiary structure with a calculated hydrodynamic radius of 29.6 ± 1.8 nm (by cumulants analysis). Regularization analysis of the light scattering data displays (Figure 4) a narrow monomodal particle size distribution. Control experiments using THF, which is selective for both blocks, revealed a hydrodynamic radius which indicates only the presence of nonaggregated polymer mono- and diblocks. Further evidence for the formation of a tertiary structure was obtained from GPC analysis (Figure 5) at 25 °C, which displayed a peak at 11.04 min, corresponding to a very high molecular weight aggregate. The spreading after the micelle peak may be attributable to the effects of dilution on the micelle/free chain equilibrium and/or the lack of micelle stability.

To trigger the decomposition of the micelles, a large excess of **4** was added, and the re-equilibration process was monitored over the course of several days. GPC analysis (Figure 5) displays a peak at 9.00 min which is indicative of high molecular weight aggregates.[24] This observation was further supported by dynamic light scattering measurements which show an apparent increase in the hydrodynamic radius of the system to 65−70 nm. Furthermore, even after several days no precipitation of the polyisoprene cores was observed. These observations suggest the formation of metastable aggregates of collapsed polyisoprene cores in DMF, which is a poor solvent for polyisoprene, formed when the individual polystyrene and polyisoprene blocks begin to phase separate,[25] and support the hypothesis[26] that the addition of the small molecule alkoxyamine **4** has indeed triggered the decomposition of the micelles.

Summary

In summary, we have utilized RAFT polymerization techniques to prepare a series of polymer building blocks possessing either aldehyde or alkoxyamine functions as end-groups. We have demonstrated that these polymers can link together through dynamic covalent oxime bonds to form dynamic covalent diblock copolymers and highlighted the dynamic nature of these species. The ability of a dynamic covalent diblock copolymer formed from polystyrene and polyisoprene blocks to aggregate into higher order micellar structures has been demonstrated, and we have shown how its disassembly can be triggered by the addition of a small molecule alkoxyamine. We believe that the utilization of dynamic covalent linkages between polymer blocks may lead to the development of new dynamic functional materials and complements alternative systems[2−6] that utilize noncovalent or metal−ligand interactions to link polymer chains together. In particular, our approach may allow for the preparation of kinetically stable micelles which possess the ability to alter the polymer block composition of their coronal polymer chains while their core polymer chains remain within the core.

Acknowledgment. Research Councils UK (fellowship to D.A.F.), Newcastle University (Studentship to A.W.J.), and One North East are gratefully thanked for support.

Supporting Information Available: ^{1}H NMR spectra of the modified chain transfer agents **1** and **2** and kinetic plots demonstrating the controlled nature of the polymerization of styrene mediated by these chain transfer agents. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Förster, S.; Platenberg, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 688–714.
(2) (a) Yang, X.; Hua, F.; Yamato, K.; Ruckstein, E.; Gong, B.; Kim, W.; Ryu, C. Y. *Angew. Chem., Int. Ed.* **2004**, *43*, 6471–6474. (b) Binder, W. H.; Bernstorff, S.; Kluger, C.; Petraru, L.; Kunz, M. J. *Adv. Mater.* **2005**, *17*, 2824–2828. (c) Noro, A.; Nagata, Y.; Takano, A.; Matsushita, Y. *Biomacromolecules* **2006**, *7*, 1696–1699. (d) Feldman, K. E.; Kade, M. J.; de Greef, T. F. A.; Meijer, E. W.; Kramer, E. J.; Hawker, C. J. *Macromolecules* **2008**, *41*, 4694–4700.
(3) (a) Lohmeijer, B. G. G.; Schubert, U. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 3825–3829. (b) Chen, B.; Sleiman, H. F. *Macromolecules* **2004**, *37*, 5866–5872. (c) Zhou, G.; Harruna, I. I. *Macromolecules* **2005**, *38*, 4114–4123. (d) Moughton, A. O.; O'Reilly, R. K. *J. Am. Chem. Soc.* **2008**, *130*, 8714–8725.
(4) Ambade, A. V.; Yang, S. K.; Weck, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 2894–2898.
(5) Rauwald, U.; Scherman, O. A. *Angew. Chem., Int. Ed.* **2008**, *47*, 3950–3953.
(6) Gibson, H. W.; Farcas, A.; Jones, J. W.; Zhongxin, Z.; Huang, F.; Vergne, M.; Hercules, D. M. *J. Polym. Sci., Part A* **2009**, *47*, 3518–3543.
(7) Rowan, S. J.; Cantrill, S. J.; Cousins, G. R. L.; Sanders, J. K. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2002**, *41*, 898–952.
(8) (a) Lehn, J.-M. *Chem. Soc. Chem. Rev.* **2007**, *36*, 151–160. (b) Corbett, P. T.; Leclaire, J.; Vial, L.; West, K. R.; Wietor, J.-L.; Sanders, J. K. M.; Otto, S. *Chem. Rev.* **2006**, *106*, 3652–3711.
(9) (a) Maeda, T.; Otsuka, H.; Takahara, A. *Prog. Polym. Sci.* **2009**, *34*, 681–704. (b) Amamoto, Y.; Maeda, T.; Kikuchi, M.; Otsuka, H.; Takahara, A. *Chem. Commun.* **2009**, 689–691.

(10) (a) Lehn, J.-M. *Prog. Polym. Sci.* **2005**, *30*, 814–830.

(11) De, P.; Gondi, S. R.; Roy, D.; Sumerlin, B. S. *Macromolcules* **2009**, *42*, 5614–5621.

(12) Qin, Y.; Cui, C.; Jäkle, F. *Macromolecules* **2007**, *40*, 1413–1420.

(13) (a) Nguyen, R.; Allouche, L.; Buhler, E.; Giuseppone, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 1093–1096. (b) Minkenberg, C. B.; Florusse, L.; Eelkema, R.; Koper, G. J. M.; van Esch, J. H. *J. Am. Chem. Soc.* **2009**, *131*, 11274–11275.

(14) (a) Moad, G.; Rizzardo, E.; Thang, S. H. *Aust. J. Chem.* **2005**, *58*, 379–410. (b) Perrier, S.; Takolpuckdee, P. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 5347–5393. (c) Moad, G.; Rizzardo, E.; Thang, S. H. *Aust. J. Chem.* **2005**, *59*, 669–692.

(15) For some examples of the utilization of RAFT polymerizations to prepare end-functionalized polymers, see: (a) Gondi, S. R.; Vogt, A. P.; Summerlin, B. S. *Macromolecules* **2007**, *40*, 471–481. (b) Heredia, K. L.; Nguyen, T. H.; Chang, C.-W.; Bulmus, V.; Davis, T. P.; Maynard, H. D. *Chem. Commun.* **2008**, 3245–3247. (c) Hong, C.-Y.; Pan, C.-Y. *Macromolecules* **2006**, *39*, 3517–3524.

(16) Lai, J. T.; Filla, D.; Shea, R. *Macromolecules* **2002**, *35*, 6754–6756.

(17) For an example of an alkoyamine-terminated polystyrene prepared by atom transfer radical polymerization, see: Kopping, J. T.; Tolstyka, Z. P.; Maynard, H. D. *Macromolecules* **2007**, *40*, 8593–8599.

(18) Germack, D. S.; Wooley, K. L. *J. Polym. Sci., Part A: Polym. Chem* **2007**, *45*, 4100–4108.

(19) The ^{1}H NMR signal corresponding to the *cis*-oxime proton overlaps with aromatic signals of compound **3**. It is reasonable to assume that most of the oxime exists as its thermodynamically most stable *trans*-isomer.

(20) The NMR spectroscopic and mass spectrometry studies also indicate that the trithiocarbonate moieties of all species in solution were found to remain intact and appear not to be susceptible to nucleophilic attack by the alkoxyamine nitrogen under the reaction conditions.

(21) Determined by ^{1}H NMR spectroscopy in DMF-d_7 at 298 K assuming the concentration of water equals the concentration of oxime. The water signal unfortunately is obscured by other signals in the spectrum to allow its accurate integration.

(22) We propose the notation "Dyn*b*" to highlight the presence of dynamic covalent bond linking the polymer blocks together.

(23) (a) Booth, C.; Naylor, T. D.; Price, C.; Rajab, N. S.; Stubbersfield, R. B. *J. Chem. Soc., Faraday Trans. 1* **1978**, *74*, 2352–2362. (b) Price, C. *Pure Appl. Chem.* **1983**, *55*, 1563–1572. (c) Bahadur, P.; Sastry, S. V.; Marti, S.; Reiss, G. *Colloids Surf.* **1985**, *16*, 337–346.

(24) Calibration of our GPC system (DMF, 1 mL/min, 40 °C) with polystyrene standards of masses up to 6.3 MDa (retention time 9.20 min) affords a linear calibration curve. The observed decomposition product (retention time 9.00 min) is therefore probably of even higher mass, although it is not known with certainty whether this measurement is within the exclusion limits of our GPC setup.

(25) P.-G. de Gennes *Scaling Concepts in Polymer Physics*; Cornell University Press: Ithaca, NY, 1970; pp 113−123.

(26) To further support this hypothesis, a number of simple control experiments were performed. Following the same procedure for the formation of micelles, a solution of polystyrene and polyisoprene blocks of very similar size which do not contain reactive end-functional group was prepared and analyzed by DLS and GPC. This sample was found to display the same GPC characteristics as the sample prepared by the small molecule-induced decomposition of **P3**-dyn*b*-**P5b**. The same situation was observed when the procedure was repeated with polyisoprene **P3** on its own.