Macromolecules

Article

pubs.acs.org/Macromolecules

Determining the Regioregularity in Alkyne Polycarbodiimides and Their Orthogonal Modification of Side Chains To Yield Perfectly Alternating Functional Polymers

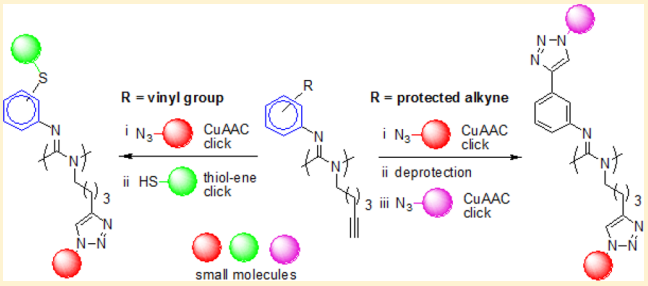
Januka Budhathoki-Uprety,[†] James F. Reuther,[†] and Bruce M. Novak*[,‡]

[†]Department of Chemistry, North Carolina State University, Raleigh, North Carolina 27695, United States

[‡]Department of Chemistry and the Alan G MacDiarmid NanoTech Institute, University of Texas at Dallas, Richardson, Texas 75080-3021, United States

Supporting Information

ABSTRACT: To understand the structure−property relationship in functional macromolecules through side chain modulation, both the accurate determination of the position of modifiable groups along the polymer chain and their subsequent modifications using high fidelity methods are crucial. In this report, the polymer microstructure of a helical alkyne polycarbodiimide has directly been probed through ^{15}N NMR spectroscopy on isotopic labeled poly(*N*-(3-ethynylphenyl)-$^{15}N'$-hexyl)carbodiimide and found to be a highly regioregular polymer structure. This polymer undergoes facile and quantitative CuAAC "click" chemistry, yielding perfectly alternating functional polymers. Advances have been made through the synthesis of new optically active alkyne polycarbodiimides with two independently modifiable pendant groups per repeat unit of polymers. Orthogonal postmodifications of the pendant groups were then performed to incorporate two different sets of small molecules in the repeat unit of polymers in a controlled manner and under mild reaction conditions using either sequential CuAAC "click" reactions when two dissimilar alkyne groups are present or a combination of CuAAC and thiol−ene click chemistries when pendant groups bear alkyne and vinyl moieties.



INTRODUCTION

The synthesis of functional helical polymers has been an active area of research interest due to their wide range of potential applications such as chiral recognition and separation media, asymmetric catalysis, chiral template, chiral amplification, optical displays, and biomimetic materials.[1−8] Polymer properties vastly rely on their microstructures, and in many of those synthetic helical polymers, specific properties have been achieved through versatile side chains. As an example, helical polycarbodiimides have shown many remarkable properties such as thermo- and solvo-controllable chiroptical switching, liquid crystalline structure, and chiral orienting media through modulations of their side chains.[6,9−12] To further expand the properties of these polycarbodiimides with functional side chains, postmodification of a polymer sample is a versatile method. In a previous publication, we demonstrated that a family of alkyne functionalized polycarbodiimides undergo facile and quantitative postmodifications in the copper-catalyzed azide−alkyne cycloaddition (CuAAC) "click" and Sonogashira coupling reactions involving a variety of functional groups along the side chains of polymers.[13] These unprecedented functionalizations of side chains in polycarbodiimides help extend the useful properties of this polymer system, of which antibacterial activity is an example.[14] For fundamental understanding of the structure−property relationship, it is important to ascertain the position of modiafiable alkyne groups along the polymer chain prior to their further modification. As such, for designing new functional polymer derivatives, both the highly efficient functional group modulation and ascertaining the positions of modifiable groups along polymer chains are crucial. Here, we chose poly(*N*-(3-ethynylphenyl)-*N'*-hexyl)carbodiimide, an example of alkyne polycarbodiimide derived from a nonsymmetric monomer, to unravel whether the mode of distribution of alkyne pendant groups along the polymer chain is regioregular or regiorandom.

The coordination−insertion polymerization of carbodiimide monomers using titanium(IV) alkoxide catalysts to obtain polycarbodiimides (including the one mentioned earlier) may yield a multitude of polymer regiostructures.[4] For instance, the use of symmetric carbodiimide monomers in polymerization results in polycarbodiimides with uniform repeat units. On the other hand, polycarbodiimides derived from asymmetric monomers, in principle, can result in a regic (regioregular distribution of pendant groups), syndioregic (alternate

Received: August 3, 2012
Revised: September 25, 2012
Published: October 2, 2012

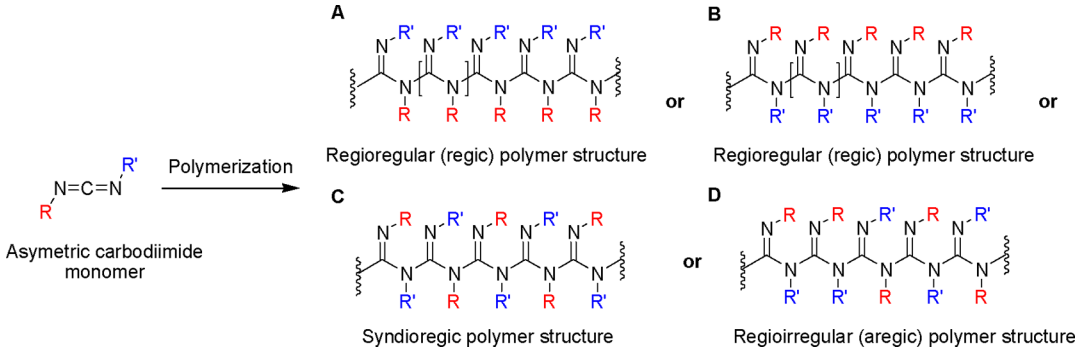


Figure 1. Some of the possible microstructures in polycarbodiimides represented by pentamer structures: **A** and **B** (regic), **C** (syndioregic), and **D** (aregic).

distribution of pendant groups), or aregic (regiorandom distribution of pendant groups) microstructure (Figure 1) due to configurational choices for a side group to bond to either imine nitrogen or amine nitrogen in the repeat unit of the polymer.

To study the regioregularity in polycarbodiimides, ^{13}C NMR signals in polymers can be obtained without isotope enrichment of a polymer sample but are often poorly resolved. IR spectra of polycarbodiimides show strong signals at ca. 1620−1650 cm^{-1} corresponding to imine group in the polymer backbone, but this window of IR absorption (1620−1640 cm^{-1}) has recently been discovered to include a number of stretch and/or bending modes that are associated with conformational changes in some polycarbodiimides.[15] Those limitations stymied the accurate determination of regio(ir)regularity in polycarbodiimides using the aforementioned methods and demand an additional characterization tool. Recently, our group reported ^{15}N NMR spectroscopy as a new characterization method to precisely determine regioiregularity in poly(*N*-*n*-hexyl-*N*′-phenylcarbodiimide), **Poly-2** (Figure 2), a polycarbodiimide sample derived from a nonsymmetric carbodiimide monomer.[16] Although the spectroscopy requires isotopic enrichment of a polymer sample with ^{15}N isotope, the high resolution of the spectral signals and distinct chemical shifts observed for amine nitrogen compared with that of imine nitrogen (separated by ∼100 ppm) in repeat unit of polymers make ^{15}N NMR spectroscopy the most reliable method to date for directly probing regio(ir)regularity in polycarbodiimides involving a wide range of pendant groups.

Here, we use ^{15}N NMR spectroscopy to unravel the regioregularity in an alkyne polycarbodiimide derived from a nonsymmetric carbodiimide monomer. Upon confirmation of regioregularity in polycarbodiimides with aliphatic and directly attached aromatic side chains, of special note is **Poly-1**, we extended our study on functional polycarbodiimides through the synthesis of new alkyne polycarbodiimides with two independently modifiable alkyne functionalities: 1-hexyne and protected phenylacetylene groups in repeat units. The orthogonal postmodification of these alkyne moieties were performed in consecutive "click" reactions in a controlled fashion under mild reaction conditions. In addition, this report also includes the synthesis of an optically active polycarbodiimide with two orthogonal clickable groups, an alkyne and a styrene side chains for the first time, followed by orthogonal side chain modulation in two consecutive click chemistries: azide−alkyne and thiol−ene.

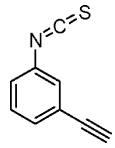
EXPERIMENTAL SECTION

General. Chemicals were purchased from commercial venders—Sigma-Aldrich, Milwaukee, WI; Fisher Scientific, Fair Lawn, NJ; Acros Organics; and Strem Chemicals, Newburyport, MA—and were used as received unless stated otherwise. The certified ACS grade solvents were purchased from Fisher Scientific and used as received except tetrahydrofuran (THF), which was distilled prior to use. Column chromatography on monomers was performed using high purity silica gel, either neutral (purchased) or neutralized with triethylamine. ^{1}H, ^{13}C, and ^{15}N NMR data were recorded on Mercury spectrometers (300 or 400 MHz for ^{1}H NMR, 75 or 100 MHz for ^{13}C NMR, and 40.5 MHz for ^{15}N NMR) at room temperature. The chemical shift values were reported relative to TMS (δ = 0.00 ppm) or corresponding solvents as an internal standard for ^{1}H and ^{13}C NMR and ^{15}N-benzamide (δ = 0.00 ppm) as an external standard for ^{15}N NMR. A small amount (ca. 5 mg) of gadolinium(III) acetylacetate, $Gd(acac)_3$, was added in an ∼35 mg polymer sample in $CDCl_3$ prior to ^{15}N NMR data collection over the period of 8 h. IR spectra were obtained from a JASCO FT/IR-410. Wavenumbers in cm^{-1} are reported for characteristic peaks. Mass spectra (HRMS) were obtained at the NCSU Department of Chemistry Mass Spectrometry Facility using electrospray ionization (ESI) on an Agilent Technologies 6210 LC-TOF mass spectrometer. Specific optical rotation was recorded on a JASCO P-1010 polarimeter. All the manipulations for polymerizations were performed at room temperature inside an MBraun UNIlab drybox under a nitrogen atmosphere. Size exclusion chromatography (SEC) was performed on a Viscotek VE 3580 system equipped with ViscoGEL columns (GMHHR-M) connected to a refractive index (RI) detector at 30 °C using 0.12 M diethanolamine in THF as an eluent to determine relative molecular weights of the polymers. Polystyrene standards were used for the calibration of the instrument. Polymer samples were dissolved in the solvent system containing 0.12 M diethanolamine in THF, and the solutions were filtered through 0.45 μm PTFE filters prior to injection. The flow rate was 1.0 mL/min, and injector volume was 100 μL.

Chemistry. *Synthesis of Isothiocyanate Derivatives from Corresponding Amines.* Isothiocyanate derivatives were prepared with a slight modification in the literature procedure from ref 20. Thiophosgene (1.2 equiv) was added dropwise to a stirred mixture of desired amine (1.0 equiv) and triethylamine (4.0 equiv) in dichloromethane (∼20 mL for the reaction scale mentioned below) at 0 °C under a nitrogen atmosphere. Thiophosgene is toxic and should be handled with care. The reaction mixture was stirred at room temperature overnight, after which the organic layer was washed with DI water (10 mL × 4) and brine (10 mL × 2), separated, dried over anhydrous Na_2SO_4, filtered, and concentrated on a rotary evaporator. A viscous, dark brown liquid thus obtained was purified by column chromatography in silica gel using a mixture of ethyl acetate and hexane (1:1 by volume) to afford desired compound as colorless to light yellow oil.

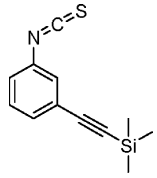
1-Ethynyl-3-isothiocyanatobenzene, Compound ***6****.* Light yellow oil, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm); reference: $CDCl_3$

dx.doi.org/10.1021/ma301639m | *Macromolecules* 2012, 45, 8155−8165



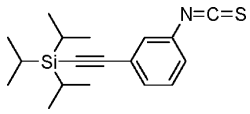
= 7.24 ppm, δ = 7.39−7.21 (m, 4H), 3.13(s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 77.23 ppm, δ = 136.6, 131.6, 130.8, 129.6, 129.0, 126.0, 123.7, 81.8, 78.8. FTIR (KBr thin film, neat, cm^{-1}): 3294, 3064, 2958 (w), 2142 and 2102 (vs, N═C═S), 1591, 1573, 790 (s).

(2-(3-Isothiocyanatophenyl)ethynyl)trimethylsilane, Compound ***10a***. The solvent used in purification by column chromatography



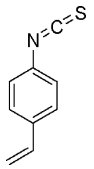
was a mixture of petroleum ether and dichloromethane (3:1 respectively) to afford compound **10a** as light yellow oil (0.41 g, 68% yield). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm); reference: $CDCl_3$ = 7.24 ppm, δ = 7.35−7.25 (m, 3H), 7.16−7.13 (m, 1H), 0.24 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 77.23 ppm, δ = 136.6, 131.6, 130.8, 129.6, 129.2, 125.8, 125.0, 103.2, 96.4, 0.03. FTIR (KBr thin film, neat, cm^{-1}): 3066, 2958 (s, alkyl C−H), 2898 (w), 2051 (vs, N═C═S), 1594, 1573, 1249 (s), 860 (vs), 842 (vs).

Triisopropyl(2-(3-isothiocyanatophenyl)ethynyl)silane, Compound ***10b***. 1.01 g, 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$, δ



ppm); reference TMS = 0.00 ppm, δ = 7.36 (dt, J = 7.6 Hz, 1.2 Hz, 1H), 7.32 (t, J = 1.2 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 7.15 (dq, J = 7.6 Hz, 1.2 Hz, 1H), 1.12 (s, br, 21H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 77.23 ppm, δ = 131.0, 129.6, 129.2, 125.6, 125.3, 105.2, 93.0, 18.8, 11.4. FTIR (KBr thin film, neat, cm^{-1}): 3066, 2942 (s, alkyl C−H), 2890 (w), 2863, 2051 (vs, N═C═S), 1592, 1573, 1469, 881 (m), 833 (m), 678.

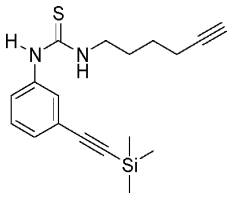
1-Isothiocyanato-4-vinylbenzene, Compound ***15***. 0.982 g, 82% yield (orange oil). ^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm): 7.37 (td, J =



8.0 Hz, J = 1.4 Hz, Ar−H, 2H), 7.19 (td, J = 8.8 Hz, J = 4.0 Hz, Ar−H, 2H), 6.67 (dd, J = 17.6 Hz, J = 11.2 Hz, vinyl−H, 1H), 5.74 (d, J = 18.8 Hz, vinyl−H, 1H), 5.31 (d, J = 11.6 Hz, vinyl−H, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 136.9, 135.8, 127.5, 126.1, 115.5, 94.5. FTIR (KBr salt plate, cm^{-1}): 3087 (w, Ar−H), 3037 (w, Ar−H), 3008 (w, vinyl−H), 2100 (s, S═C═N−), 1598 (C═C aryl, m).

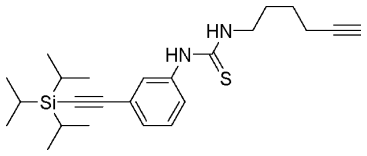
Synthesis of Thiourea Derivatives. Isothiocyanate (1.0 equiv) diluted in dichloromethane (10 mL for 1.0 g isothiocyanate) was added to a stirred solution of desired amine (1.04 equiv) in dichloromethane (20 mL) at 0 °C. The reaction mixture was stirred at room temperature until completion (ca. 1 h for **13a** and **13b**) as observed under FTIR analysis. The solvent was removed in a rotary evaporator, and sticky viscous residue was purified through column chromatography in silica gel using a mixture of hexane and ethyl acetate (2:1 by volume respectively) or CH_2Cl_2: ethyl acetate (6:1 by volume) as mobile phase to afford desired thiourea derivative as off-white solid or thick viscous liquid.

1-(Hex-5-ynyl)-3-(3-(2-(trimethylsilyl)ethynyl)phenyl)thiourea, Compound ***13a***. Thick viscous liquid, 0.50 g, 71% yield (yield varied



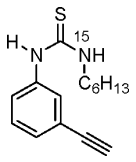
71−85% in different runs). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 7.24 ppm, δ = 7.87(s, 1H), 7.38−7.13 (m, 4H), 6.03 (br, s, 1H), 3.66−3.65 (m, 2H), 2.21 (td, J = 6.8 Hz, 2.8 Hz, 2H), 1.91 (t, J = 2.8 Hz, 1H), 1.72−1.67 (m, 2H), 1.57−1.52 (m, 2H), 0.24 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 77.23 ppm, δ = 180.8, 136.2, 131.0, 130.3, 128.6, 125.6, 125.5, 103.4, 96.6, 84.1, 69.0, 45.1, 28.1, 25.7, 18.2, 0.1. HRMS (ESI) m/z: [M + H]$^+$: calcd for $C_{18}H_{24}N_2SSi$, 329.1502; found, 329.1493. FTIR (KBr thin film, neat, cm^{-1}): 3289 (vs, C≡**C**−**H**), 3062, 2956 (s, alkyl C−H), 2863 (w), 2057 (s, **C**≡**C**−TMS), 2115 (w, **C**≡**C**−H), 1598, 1579, 1538 (s), 1484, 1249 (s), 844 (vs).

1-(Hex-5-ynyl)-3-(3-(2-(triisopropylsilyl)ethynyl)phenyl)thiourea, Compound ***13b***. Off-white solid, 0.99 g, 76% yield (yield varied 76−



97% in different runs) ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): reference TMS = 0.00 ppm, δ = 7.77 (s, br 1H), 7.41−7.31 (m, 3H), 7.15 (d, J = 7.6 Hz, 1H), 6.03 (br, s, 1H), 3.67 (q, J = 6.4 Hz, 2H), 2.22 (td, J = 6.4 Hz, 2.4 Hz, 2H), 1.91 (t, J = 2.4 Hz 1H), 1.75−1.68 (m, 2H), 1.59−1.51 (m, 2H), 1.12 (s, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 77.23 ppm, δ = 180.9, 136.2, 131.0, 130.4, 128.8, 125.9, 125.5, 105.5, 93.2, 84.0, 69.0, 45.1, 28.1, 25.7, 18.8, 18.2, 11.4. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{24}H_{36}N_2SSi$, 413.2441; found, 413.2443. FTIR (KBr thin film, neat, cm^{-1}): 3293 (vs, C≡**C**−**H** and N−H), 3056 (w), 2942 (s, alkyl C−H), 2863 (s), 2054 (s, **C**≡**C**−TMS), 2117 (w, **C**≡**C**−H), 1538 (s), 1484, 1292.

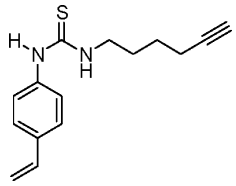
1-(3-Ethynylphenyl)-3-hexylthiourea, Compound ***7***. Sticky viscous mass, 0.65 g, 91% yield. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm):



reference $CDCl_3$ = 7.24 ppm, δ = 7.86 (s, 1H), 7.41−7.20 (m, 4H), 6.03 (dt, J = 6.0 Hz, 87.0 Hz, 1H), 3.65−3.58 (m, 2H), 3.15 (s, 1H), 1.62−1.55 (m, 2H), 1.32−1.28 (m, 6H), 0.87 (t, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 77.23 ppm, δ = 180.4 (d), 180.3, 130.7, 130.2, 128.4, 125.5, 108.5, 82.1, 78.8, 45.6, 31.3, 28.8, 26.5, 22.5, 13.9. FTIR (KBr thin film, neat, cm^{-1}): 3290 (vs), 3062, 2954 (s, alkyl C−H), 2929, 2856 (w), 2107 (w, **C**≡**C**−H), 1598, 1579, 1523 (s), 1336, 1288 (s), 1249 (s), 1249, 647. ^{15}N NMR (40.5 MHz, $CDCl_3$, δ ppm): reference (external standard) ^{15}N-benzamide = 0.00 ppm, δ = 18.93 ppm.

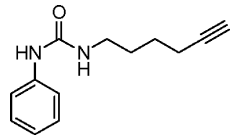
1-(Hex-5-ynyl)-3-(4-vinylphenyl)thiourea, Compound ***16***. Off-white powder, 0.860 g, 61% yield. FTIR (KBr salt plate, cm^{-1}): 3295 (s, N−H and C≡**C**−**H**, overlapped), 3086 (w, Ar−H), 3043 (w, Ar−H), 2979 (s, vinyl−H), 2938 (s, alkyl−H), 2864 (m, alkyl−H), 2115 (m, C≡C), 1538 (s, S═C). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 8.11 (N−H, s, 1H), 7.45 (td, J = 8.8 Hz, J = 2.4 Hz, Ar−H, 2H), 7.16 (d, J = 8.4 Hz, Ar−H, 2H), 6.69 (dd, J = 17.6 Hz, J = 11.2

dx.doi.org/10.1021/ma301639m | *Macromolecules* 2012, 45, 8155−8165



Hz, vinyl−H, 1H), 6.07 (N−H, s, 1H), 5.74 (d, J = 17.6 Hz, vinyl−H, 1H), 5.30 (d, J = 10.4 Hz, vinyl−H, 1H), 3.65 (q, J = 7.2 Hz, N−**CH_2**−, 2H), 2.21 (m, −CH_2**CH_2**CH_2CH_2C≡CH, 2H), 1.89 (t, J = 2.4 Hz, −CH_2C≡**CH**, 1H), 1.71 (m, −CH_2CH_2**CH_2**CH_2C≡CH, 2H), 1.53 (m, −$CH_2CH_2CH_2$**CH_2**C≡CH, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 180.8, 136.8, 135.8, 128.1, 125.5, 115.3, 84.1, 69.1, 45.2, 28.3, 25.8, 18.3.

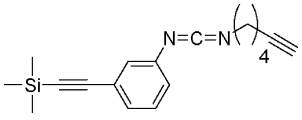
Synthesis of Urea Derivative: 1-(Hex-5-ynyl)-3-phenylurea. Phenyl isocyanate (0.32 g, 2.67 mmol) was added dropwise to a



stirred solution of amine **12** (0.26 g, 2.67 mmol) in dichloromethane (5 mL) at 0 °C. After complete addition, the ice bath was removed, and the reaction mixture in a closed cap vial was stirred at room temperature until completion (ca. 1 h). The reaction mixture was concentrated in a rotary evaporator to remove all the solvent. Recrystallization of the yellow sticky mass at low temperature (−78 °C) afforded 1-(hex-5-ynyl)-3-phenylurea as white solid (0.5 g, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): reference TMS = 0.00 ppm, δ = 7.70 (br, 1H), 7.30−7.20 (m, 4H), 7.00−7.07 (t, 1H), 5.59 (br, 1H), 3.15 (t, J = 6.4 Hz, 2H), 2.13 (td, J = 6.4 Hz, J = 2.8 Hz, 2H), 1.92 (t, J = 2.8 Hz, 1H), 1.52−1.47 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 77.23 ppm, δ = 157.0, 138.8, 129.2, 129.1, 123.5, 120.8, 84.2, 68.8, 39.9, 29.3, 25.8, 18.2. FTIR (KBr thin film, casted from $CHCl_3$, cm^{-1}): 3299 (vs, C≡**C**−**H** and N−H), 3056, 2938 (s, alkyl C−H), 2863 (m), 2115 (w, **C**≡**C**−H), 1644 (vs), 1596, 1523, 1500, 1440, 1313, 1236.

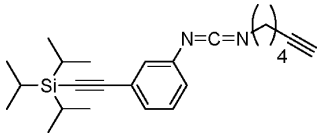
Synthesis of Monomers. Triethylamine (2.5 equiv) was added dropwise to a stirred suspension of PPh_3Br_2 (1.2 equiv) in dichloromethane (10 mL for 1.0 g scale of the reagent) at 0 °C under a nitrogen atmosphere. After 5 min, urea or thiourea derivative (1.0 equiv) was added slowly to the reaction mixture. The reaction was stirred at low temperature for 1 h and then at room temperature until completion. Once the reaction was complete as monitored by FTIR spectroscopy, solvent was removed in a rotary evaporator and the crude monomer product was extracted with pentane from solid residue. The process was repeated to extract all of the crude monomer, and the solution was concentrated in a rotary evaporator. The crude oily product thus received was purified by column chromatography in silica gel using a mixture of ethyl acetate:hexane (1:4 by volume) along with 2% triethylamine to afford desired carbodiimide monomer as oily liquid in all cases.

*N-((Hex-5-ynylimino)methylene)-3-(2-(trimethylsilyl)ethynyl)-benzenamine, Compound **14a**.* Pale yellow oil, 0.236 g, 88% yield.



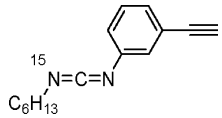
^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 7.24 ppm, δ = 7.18−7.15 (m, 3H), 7.0−6.98 (m, 1H), 3.45 (t, J = 6.8 Hz, 2H), 2.23 (td, J = 6.8 Hz, 2.8 Hz, 2H), 1.95 (t, J = 2.8 Hz 1H), 1.82−1.75 (m, 2H), 1.67−1.60 (m, 2H), 0.22 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 77.23 ppm, δ = 140.8, 129.7, 129.4, 128.4, 126.9, 124.3, 124.0, 104.5, 94.8, 83.9, 69.1, 46.4, 30.3, 25.7, 18.1, 0.1. FTIR (KBr thin film, neat, cm^{-1}): 3301 (s, terminal alkyne C−H), 3062, 2956 (s, alkyl C−H), 2865 (w), 2140 (vs, N=C=N, carbodiimide), 1670, 1596, 1573, 1249 (s), 844 (vs). HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{18}H_{22}N_2Si$, 295.1625; found, 295.1631.

*N-((Hex-5-ynylimino)methylene)-3-(2-(triisopropylsilyl)ethynyl)-benzenamine, Compound **14b**.* Clear oil, 0.63 g, 90% yield. ^{1}H NMR



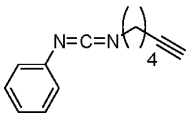
(400 MHz, $CDCl_3$, δ ppm): reference TMS = 0.00 ppm, δ = 7.22−7.17 (m, 3H), 7.03−7.00 (m, 1H), 3.47 (t, J = 6.8 Hz, 2H), 2.25 (td, J = 6.8 Hz, 2.4 Hz, 2H), 1.96 (t, J = 2.4 Hz 1H), 1.85−1.78 (m, 2H), 1.70−1.63 (m, 2H), 1.12 (s, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 77.23 ppm, δ = 140.8, 135.4, 129.4, 128.5, 127.0, 124.8, 123.8, 106.5, 91.3, 83.8, 69.1, 46.4, 30.3, 25.7, 18.8, 18.1, 11.4. FTIR (KBr thin film, casted from $CHCl_3$, cm^{-1}): 3309 (s), 3064 (w), 2942 (s, alkyl C−H), 2890, 2863 (s), 2140 (vs, N=C=N), 1594, 1575, 1463. HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{24}H_{34}N_2Si$, 379.2564; found, 379.2559.

*N-(3-Ethynylphenyl)-^{15}N′-hexylcarbodiimide, Compound **8**.* Colorless oil, 0.39 g, 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm,



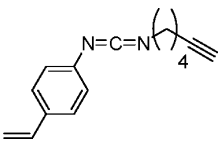
reference TMS = 0 ppm): 7.23−7.20 (m, 3H, Ar−H), 7.07−7.05 (m,1H, Ar−H), 3.41 (t, J = 7.2, 2H), 3.07 (s,1H, sp C−H), 1.70−1.65 (m, 2H), 1.43−1.29 (m, 6H), 0.88 (t, J = 7.2, 3H, −CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm, reference $CDCl_3$ = 77.23 ppm): δ = 141.3, 135.2 (d), 129.5, 128.3, 127.1, 124.2, 123.3, 83.2, 77.7, 46.9 (d), 31.4, 26.6, 22.7, 14.1. FTIR (cm^{-1}): 3294 (terminal alkyne C−H), 3066, 2929, 2858, 2121 (vs, N=C=N), 1594, 1575, 1481, 617; HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{15}H_{18}$[^{15}N], 228.1513; found, 228.1518.

N-Hex-5-yn-1-yl-N′-phenylcarbodiimide. Colorless oil, 0.35 g, 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 7.24



ppm, δ = 7.30−7.25 (m, 2H), 7.10−7.07 (m, 3H), 3.45 (t, J = 6.8 Hz, 2H), 2.25 (td, J = 6.8 Hz, J = 2.8 Hz, 2H), 1.96 (t, J = 2.8 Hz, 1H), 1.84−1.77 (m, 2H), 1.70−1.63 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 77.23 ppm, δ = 140.6, 129.8, 129.5, 124.8, 123.7, 83.9, 69.0, 46.5, 30.4, 25.7, 18.1. FTIR (KBr thin film, casted from $CHCl_3$, cm^{-1}): 3295 (s), 3062 (w), 2944 (m, alkyl C−H), 2865 (w), 2140 (vs, N=C=N), 1698 (w), 1594, 1500.

*N-(4-Ethenylphenyl)-N′-hex-5-yn-1-ylcarbodiimide, Compound **17**.* Pale yellow oil, 0.418 g, 58% yield. FTIR (KBr salt plate, cm^{-1}):



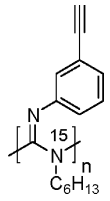
3293 (s, C≡**C**−**H**), 3060 (w, Ar−H), 2954 (m, alkyl−H), 2929 (s, alkyl−H), 2857 (s, alkyl−H), 2140 (s, N=C=N), 1597 (s, C=C_{aryl}). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.33 (td, J = 11.6 Hz, J = 2.8 Hz, Ar−H, 2H), 7.03 (td, J = 11.6 Hz, J = 2.8 Hz, Ar−H, 2H), 6.67 (dd, J = 23.6 Hz, J = 14.8 Hz, vinyl−H, 1H), 5.67 (d, J = 23.2 Hz, vinyl−H, 1H), 5.20 (d, vinyl−H, J = 14.8 Hz, 1H), 3.47 (t, J = 8.4 Hz, N−**CH_2**−, 2H), 2.25 (td, J = 9.2 Hz, J = 3.2 Hz, −CH_2**CH_2**CH_2CH_2C≡CH, 2H), 1.96 (t, J = 3.6 Hz, −CH_2C≡**CH**, 1H), 1.80 (m, −CH_2**CH_2**CH_2C≡CH, 2H), 1.67 (m, −CH_2CH_2**CH_2**C≡CH, 2H).

dx.doi.org/10.1021/ma301639m | *Macromolecules* 2012, 45, 8155−8165

^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 140.2, 136.3, 132.6, 128.8, 127.4, 123.8, 113.4, 69.1, 46.6, 30.5, 25.8, 18.2. HRMS-ESI: $M_{theoretical}$ = 225.1386, M_{sample} = 225.1377, ΔM = 0.92 mass units (4.13 ppm) $C_{15}H_{16}N_2$.

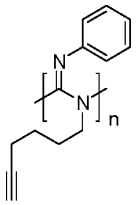
Synthesis of Polymers. All the manipulations for polymerization were performed inside a glovebox under a nitrogen atmosphere and at room temperature. Polymerization catalyst, *R*-BINOL Ti(IV) diisopropoxide, was added to a stirred solution of carbodiimide monomer in the desired monomer to catalyst ratio (~100:1 or 50:1). The reaction mixture was stirred until stir bar seized from stirring (ca. 1−2 h). The reaction mixture was left inside the glovebox for 24 h prior to work up for purification. In FTIR, the complete loss of a very strong band corresponding to carbodiimide functionality (~2140 cm^{-1}) and emergence of strong band at 1620−1650 cm^{-1} corresponding to imine functionality indicates that the polymerization reaction was complete. Resulted pale yellow solid was dissolved in chloroform and precipitated in methanol (a common antisolvent for polycarbodiimides), separated by filtration, washed with methanol, and dried under reduced pressure to afford desired polymer.

Poly(N-(3-ethynylphenyl)-^{15}N′-hexylcarbodiimide), ***Poly-1.*** Pale yellow solid (0.28 g, 80% yield), monomer:catalyst (molar ratio)



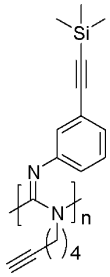
100:1. ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm, reference TMS = 0 ppm): 7.60−6.20 (br, Ar−H), 4.0−2.2 (br), 3.0 (br, s, Sp C−H), 1.8−0 (br). FTIR (cm^{-1}): 3305 (terminal alkyne C−H), 2107 (C≡C), 1629 (imine). ^{15}N NMR (40.5 MHz, $CDCl_3$, δ ppm): reference (external standard) ^{15}*N*-benzamide = 0.00 ppm; δ = 13.91 ppm.

Poly(N-hex-5-yn-1-yl-N′-phenylcarbodiimide), ***Poly-3.*** White fibrous solid (0.18 g, 76% yield). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm):



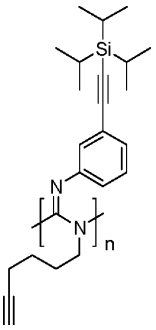
reference $CDCl_3$ = 7.24 ppm, δ = 7.09 (br), 6.85−6.76 (br), 3.53 (br), 2.56 (br), 1.90 (br, C≡C−**H**), 1.59−1.51 (br), 0.83 (br), 0.56 (br). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 77.23 ppm, δ = 148.3, 147.6, 128.8, 121.9, 84.5, 68.4, 46.7, 27.5, 25.3, 18.0. FTIR (KBr thin film, casted from $CHCl_3$, cm^{-1}): 3297 (s, C≡**C**−**H**), 3058 (Ar−H), 3018, 2942 (s, alkyl C−H), 2115 (m, **C**≡**C**−H), 1631 (vs, imine), 1589, 1484, 1375, 1243, 1145, 1083, 630. $[\alpha]_{589}^{21}$ = 365° (*c* = 0.2 in $CHCl_3$, *l* = 0.5 dm).

Poly(N-hex-5-yn-1-yl-N′-(3-(2-trimethylsilyl)ethynylphenyl)-carbodiimide), ***Poly-5.*** White solid (0.436 g, 85% yield). ^{1}H NMR



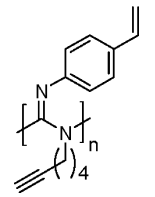
(400 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 7.24 ppm, δ = 7.00 (br), 3.65 (br), 2.40 (br), 1.82 (br, −C≡**C**−**H**), 1.62 (br), 0.85 (br), 0.15−0.13 (br). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 77.23 ppm, δ = 149.2, 147.5, 129.9, 126.9, 125.0, 123.3, 105.1, 94.9, 84.7, 68.5, 48.0, 28.3, 25.7, 18.1, 0.2. FTIR (KBr thin film, cm^{-1}): 3307 (s, −C≡**C**−**H**), 3052 (Ar−H), 2958 (s, alkyl C−H), 2156 (s, −**C**≡**C**−TMS), 2119 (w, −**C**≡**C**−H), 1625 (imine). $[\alpha]_{589}^{21}$ = 367° (*c* = 0.2 in $CHCl_3$, *l* = 0.5 dm).

Poly(N-hex-5-yn-1-yl-N′-(3-(2-triisopropysilyl)ethynylphenyl)-carbodiimide), ***Poly-6.*** White fibrous solid (0.469 g, 80% yield,



monomer:catalyst ratio used (100:1)). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): reference TMS = 0.00 ppm, δ = 7.07 (br), 3.70 (br), 2.45 (br), 1.71−1.61 (br), 1.25, 1.06−1.00 (br). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): reference $CDCl_3$ = 77.23 ppm, δ = 148.3, 147.8, 129.4, 127.7, 123.6, 107.1, 91.5, 84.2, 68.3, 48.0, 29.9, 25.7, 18.8, 11.5. FTIR (KBr thin film, casted from $CHCl_3$, cm^{-1}): 3313 (s, −C≡**C**−**H**), 3060 (w, Ar−H), 2942 (s, alkyl C−H), 2892, 2865 (s), 2152 (s, −**C**≡**C**−TMS), 2121 (w, −**C**≡**C**−H), 1631 (vs, imine), 1587, 1571, 1463, 1384, 1243, 1149, 1130, 663. $[\alpha]_{589}^{21}$ = 125° (*c* = 0.22 in $CHCl_3$, *l* = 0.5 dm).

Poly(N-(4-ethenylphenyl)-N′-hex-5-yn-1-ylcarbodiimide), ***Poly-10.*** Dilute solution of (*S*)-BINOL titanium(IV) diisopropoxide in

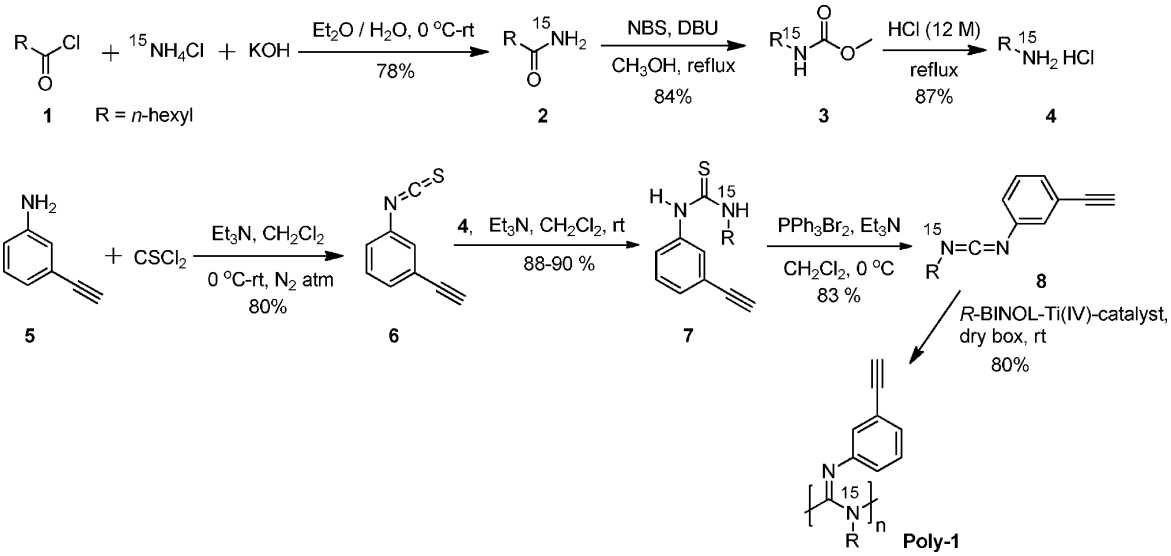


dry $CHCl_3$ (0.100 mL (14.5 μmol, 1.0 equiv)) was used to polymerize 0.404 g (1.80 mmol, 124 equiv) of *N*-(4-ethenylphenyl)-*N*′-hex-5-yn-1-ylcarbodiimide. Polymer: pale-orange solid (0.319 g, 79% yield). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 7.25 (Ar−H, br, d, 2H), 7.67 (Ar−H/vinyl−H, br, d, 3H), 5.59 (vinyl−H, br, s, 1H), 5.12 (vinyl−H, br, s, 1H), 3.54 (N−**CH_2**−, br, s, 1H), 2.56 (N−**CH_2**−, br, s, 1H), 1.90 (C≡C−H, s, 1H), 1.56−0.58 (alkyl-H, br, 6H). FTIR (KBr salt plate, cm^{-1}): 3295 (s, −C≡**C**−**H**), 3083 (w, Ar−H), 3008 (w, vinyl−H), 2944 (m, alkyl−H), 2115 (w, −**C**≡**C**−H), 1623 (s, C=N), 1595 (s, $C{=}C_{aryl}$). $[\alpha]_{435}^{25}$ = (−)128° (*c* = 0.2 in $CHCl_3$, *l* = 0.5 dm).

The CuAAC "click" chemistry was performed using the procedure as reported in ref 13. The thiol−ene reaction was performed using the literature procedure as described in ref 33 (details available in Supporting Information). The alkyne-protected aniline derivative **9a** was synthesized by Sonogashira coupling reaction of trimethylsilylacetylene, TMSA (0.717 g, 7.3 mmol), and 3-iodoaniline (1.0 g, 4.56 mmol) in the presence of $Pd(PPh_3)_4$ (0.26 g, 0.23 mmol), CuI (0.087 g, 0.45 mmol), and PPh_3 (0.12 g, 0.45 mmol) in triethylamine (5.0 mL) under a nitrogen atmosphere, with a slight modification of literature procedure.[17] The synthesis of hex-5-yn-1-amine from commercial 6-chloro-hex-1-yne was performed with a slight modification of the literature procedure.[18] Details on synthesis and characterization of those compounds are available in the Supporting Information.

dx.doi.org/10.1021/ma301639m | *Macromolecules* 2012, 45, 8155−8165

Scheme 1. Synthesis of ^{15}N Labeled Alkyne Polymer, Poly-1



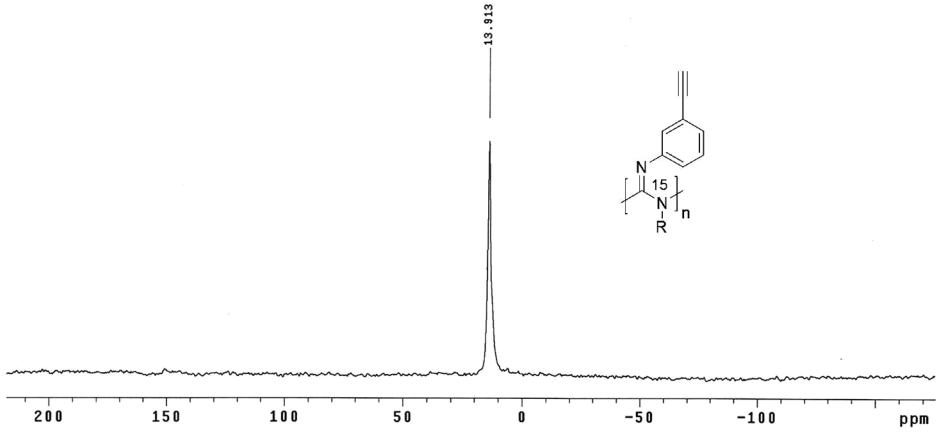


Figure 2. ^{15}N NMR spectrum of poly(*N*-(3-ethynylphenyl)-^{15}*N*′-hexyl)carbodiimide, **Poly-1**, showing a regioregular polymer microstructure.

RESULTS AND DISCUSSION

Determination of Regioregularity in an Alkyne Polycarbodiimide, Poly-1, through ^{15}N NMR Spectroscopy. ^{15}N isotope labeled alkyne polycarbodiimide **Poly-1** has been synthesized from its corresponding ^{15}N labeled carbodiimide monomer **8** as shown in Scheme 1.

Monomer **8** was prepared in five steps starting from commercial heptanoyl chloride **1**. ^{15}N-enriched (99%) ammonium chloride was used to synthesize ^{15}N labeled *n*-hexylamine hydrochloride **4** in three steps following the literature procedure.[16,19] In a separate reaction, commercial 3-aminophenylacetylene **5** was converted into corresponding isothiocyanate **6** using thiophosgene in the presence of triethylamine using the literature procedure[20] with a slight modification. Thiourea derivative **7**, obtained from combination of **7** and **6**, was treated with dibromotriphenylphosphorane in the presence of triethylamine to form monomer **8**. Monomer **8** was polymerized to **Poly-1** using *R*-BINOL Ti(IV) diisopropoxide[21−23] catalyst at room temperature inside a glovebox under a nitrogen atmosphere.

During polymerization, if the mode of monomer insertion is uniform, the resulting polymer will be homogeneous with regioregular polymer chains. ^{15}N NMR spectra of such regioregular polymer would result in a single resonance due to the specified position of isotope labeled (^{15}N) nitrogen. On the other hand, if the mode of monomer insertion is random, a regioirregular polymer structure forms, which would result in at least two separate peaks in ^{15}N NMR spectra of the polymer due to a random distribution of the isotope labeled nitrogen to imine and amine positions along the polymer chain.[16,38]

Figure 2 shows the ^{15}N NMR spectrum of **Poly-1** collected in deuterated chloroform. The spectrum shows just a single peak at 13.9 ppm (relative to external reference ^{15}*N*-benzamide set at 0.00 ppm), which is indicative of a highly regioregular polymer structure ensuing from this polymerization.

Furthermore, this specific regioisomer in the repeat units of polymer with *n*-hexyl group bonded to amine nitrogen, and therefore, the phenylacetylene group bonded to the imine nitrogen was assigned based on FTIR spectral results. The absence of isotopic shifts in the imine absorption in IR spectrum (spectra available in Supporting Information) of **Poly-1** precludes the ^{15}N labeled nitrogen at the imine position. In addition, the observed chemical shift of the peak on ^{15}N NMR spectra is inconsistent with the literature report for the regioisomer specified.[16]

Orthogonal and Site-Specific Pendant Group Modification. With established regioregular microstructure, **Poly-1** is a foundational helical polymer from which functional

dx.doi.org/10.1021/ma301639m | *Macromolecules* 2012, 45, 8155−8165

macromolecules can be derived for potential applications. It is noteworthy that all the previously reported functional derivatives of **Poly-1** with carboxylic acids, protected amines, triazoles, and amino acids in the side chains[13] introduced to the pendant groups are now confirmed uniformly regioregular and new appended functionalities bonded exclusively to imine nitrogen site along the polymer chains. Therefore, these polymer derivatives can be considered as perfectly alternating functional polymers.

In order to alter the position of modifiable alkyne groups along the polymer chain, we installed an alkyne group at a remote carbon in the repeat unit of **Poly-3** (Figure 3 and

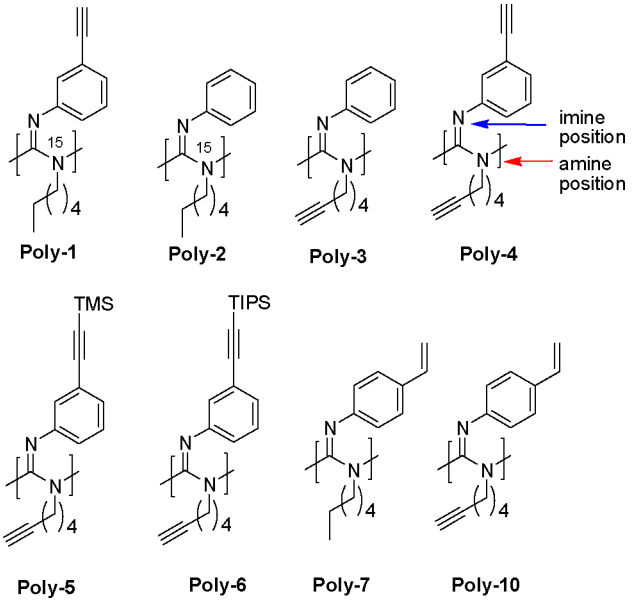


Figure 3. A family of alkyne polycarbodiimides, **Poly-1** and **Poly-3**; dialkynes, **Poly(4–6)**; alkenyl, **Poly-7** and alkene-alkyne, **Poly-10**. Previously reported **Poly-2** is shown for comparison.

Scheme S2). The unprotected terminal alkyne functionality in **Poly-3** linked to the polymer backbone by a longer hydrophobic tether allows synthetic versatilities to obtain regioregular functional polycarbodiimide derivatives. We employed CuAAC ("click") protocol[24−27] with optimized conditions for polycarbodiimides[13] in **Poly-3**. Click chemistry was chosen because of its proven compatibility and efficiency in alkyne polycarbodiimides. The CuAAC reaction of **Poly-3** with benzyl azide and the characterization of the purified polymer product by ^{1}H NMR showed the loss of ^{1}H NMR signal at 1.90 ppm from terminal alkyne proton. In addition, FTIR analysis of the product showed a complete disappearance of IR signals at 3297 cm^{-1} (s), corresponding to terminal alkyne C−H and 2115 cm^{-1} attributed to carbon−carbon triple bond in alkyne groups. This facile and quantitative modification of alkyne side chains in **Poly-3** as in previously reported **Poly-1** demonstrates that alkyne functionalities either bonded to helical polymer backbone via a rigid aromatic tether (**Poly-1**) or through flexible aliphatic linker (**Poly-3**) in repeat units are exposed and easily accessible to the reagents. In addition, highly regioregular structures of **Poly-1** and **Poly-2** coupled with close structural similarities of **Poly-3** with the mentioned polymers suggests a regioregular polymer structure of **Poly-3** with the aliphatic alkyne group bonded to amine nitrogen in the repeat unit.

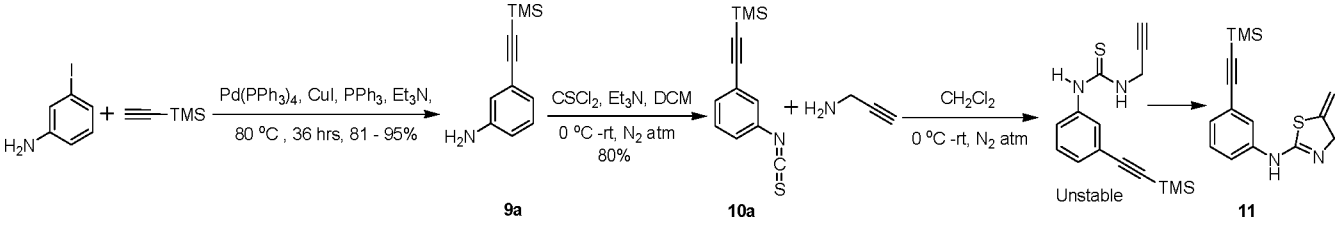
To double the potential appendable functional groups in the repeat unit along the polymer chain, **Poly-4** (Figure 3) has two modifiable alkyne groups per repeat unit. Although the natures of the two alkyne functionalities are different, phenylacetylene and aliphatic alkyne, a selective modification of one alkyne group over the other through "click" chemistry to incorporate two different moieties is not possible in our hands. Therefore, one of the two terminal alkyne groups needs to be rendered inactive for a controlled postfunctionalization.

One of the versatile approaches for orthogonal modification of two alkyne functionalities is to use protection chemistry to mask the activities of one of them. Here, we use a well-known alkyne protecting group, trimethylsilyl (TMS), early in the synthesis of **Poly-5**. Our initial attempt to synthesize an asymmetric polycarbodiimide with two independently modifiable alkyne functionalities—a propargyl group and a TMS protected phenylacetylene in repeat unit—remains unsuccessful. In an attempted synthesis, a TMS protected 3-aminophenylacetylene **9a**, obtained from Sonogashira coupling reaction of 3-iodoaniline and trimethylsilylacetylene,[17] was treated with thiophosgene in the presence of triethylamine as shown in Scheme 2 to obtain a thioisocyanate derivative **10a**. The thiourea derivative formed upon reaction of **10a** with propargylic amine is unstable and undergoes in-situ intramolecular cyclization, resulting in a heterocyclic compound **11** which is comparable to that of the synthesis of heterocyclic derivatives reported by Arya et al.[28] Use of isocyanate, instead of thioisocyanate, would result in a stable urea derivative as carbodiimide monomer precursor. However, the corresponding isocyanate was unstable during aqueous work-up in the attempted synthesis.

In order to overcome this intramolecular cyclization, a higher homologue of alkynylamine, 6-amino-hex-1-yne **12**, was synthesized[18] and used to prepare the thiourea derivative **13a** (Scheme 3). The subsequent protodesulfurization of thiourea **13a** using dibromotriphenylphosphorane in the presence of triethylamine generated carbodiimide monomer **14a**. Monomer **14a** was polymerized under the standard carbodiimide polymerization conditions to obtain **Poly-5** (Scheme 3).

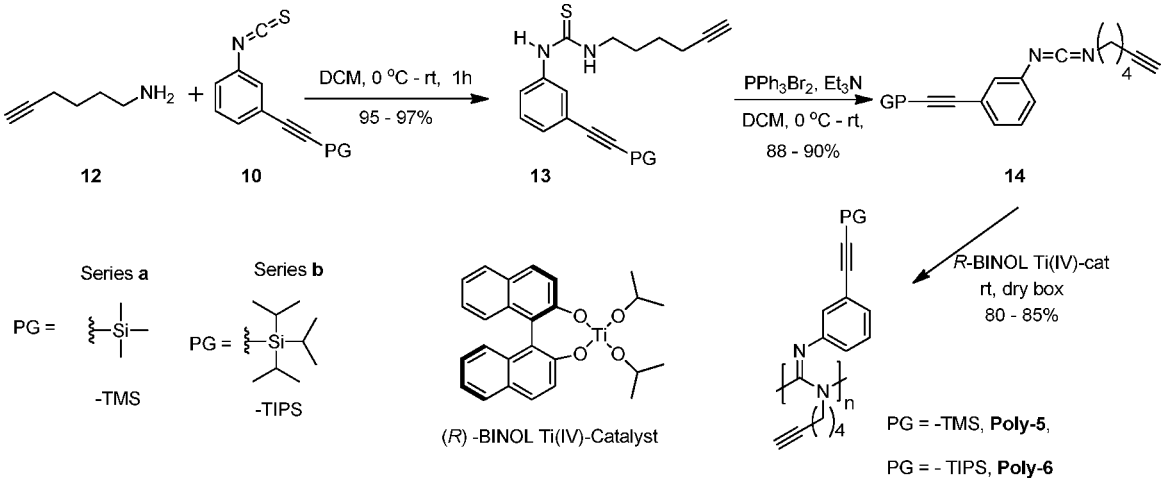
The "click" conditions employed for **Poly-3** were also used in the postmodification of **Poly-5** with commercial benzyl azide. Benzyl azide was chosen once again because it would provide

Scheme 2. Attempted Synthesis of a Dialkyne Thiourea

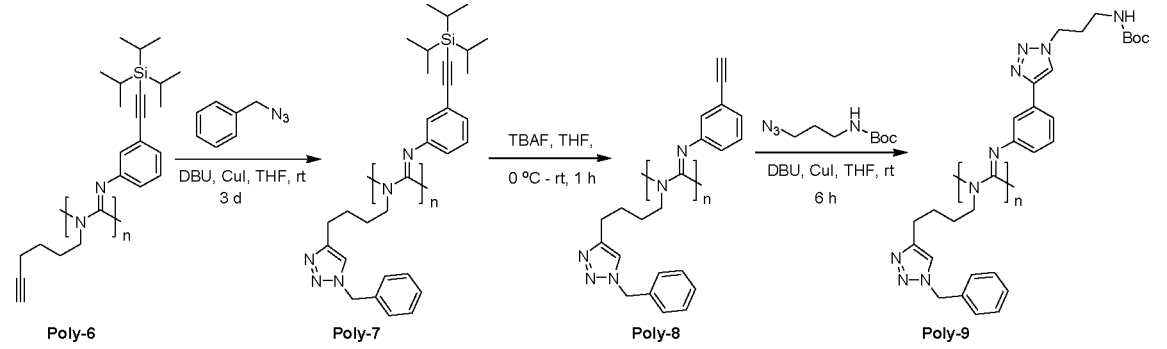


dx.doi.org/10.1021/ma301639m | Macromolecules 2012, 45, 8155−8165

Scheme 3. Synthesis of Monoprotected Dialkyne Polymers Poly-5 and Poly-6



Scheme 4. Orthogonal Functionalization of Alkyne Pendant Groups in Sequential Click Reactions



signals in ^{1}H NMR and IR spectroscopies in the product without any interference from the signals in the parent polymer molecule. Despite protection of the terminal alkyne functionality in phenylacetylene, CuAAC reaction in **Poly-5** did not show any selectivity on reactivity of the two alkynes. The lack of selectivity is most possibly because of DBU-promoted cleavage of acetylenic TMS group.[29] The use of triethylamine as a base in the click reaction instead of DBU gave mono click product while retaining the TMS protected alkyne intact, albeit at a slower rate.

To move forward to be able to carry out control postmodification reactions in dialkyne polymers, a more robust alkyne-protecting group of similar category for clean deprotection was sought. Triisopropylsilyl (TIPS) protected alkynes have been reported to be more robust compared to TMS alkynes in "click reactions".[30] Therefore, the TIPS group was then selected to protect one of the alkyne groups early in the synthesis. Similar to Scheme 2, TIPS protected phenylacetylene **9b** was converted into the corresponding isothiocyanate **10b** that in combination with 6-aminohex-1-yne (**12**) formed thiourea derivative **13b** (Scheme 3). The protodesulfurization of the thiourea derivative using PPh_3Br_2 in the presence of triethylamine resulted in monomer **14b**. When polymerized, monomer **14b** furnished a TIPS alkyne polycarbodiimide, **Poly-6**.

These newly synthesized polymers were characterized by ^{1}H NMR, ^{13}C NMR, FTIR, and polarimetry. Size exclusion chromatography was employed to determine the molecular weight of these polymers relative to polystyrene standards. 0.12 M diethanolamine in THF was used as a mobile phase to reduce the affinity of these polymers toward conventional SEC column matrix.[6,14] Molecular weight and molecular weight distribution of new polymers are as follows: (a) **Poly-1**, M_w = 17 000 Da, M_n = 8007 Da, M_w/M_n = 2.13, (b) **Poly-3**, M_w = 20 000 Da, M_n = 8112 Da, M_w/M_n = 2.49, (c) **Poly-5**, M_w = 23 000 Da, M_n = 9340 Da, M_w/M_n = 2.50, and (d) **Poly-6**, M_w = 24 000 Da, M_n = 8182, M_w/M_n = 3.0.

Scheme 4 shows postmodification of **Poly-6** in a series of chemical transformations. To begin with, CuAAC reaction was performed with benzyl azide (1.2 equiv relative to polymer repeat unit) in the presence of CuI and DBU at room temperature. FTIR analysis of the purified product **Poly-7** showed the absence of strong IR signal at 3313 cm^{-1} attributed to terminal alkyne C−H, demonstrating that all the terminal alkynes were modified (Figure 4). Furthermore, with persistent IR peak at 2152 cm^{-1}, Figure 4 also illustrates that the TIPS protected alkynes remain intact under these conditions. Therefore, the alkyne functionalities in the repeat unit of **Poly-6** were modified in a control fashion in the first step postmodification. The product polymer was characterized by ^{1}H NMR and FTIR spectroscopies.

As shown in Scheme 4, once **Poly-7** was obtained from the first step click reaction, the alkyne protecting group (TIPS) was removed using TBAF, a standard deprotecting reagent,[31] to access a second modifiable conjugation site as a phenylacetylene group in the repeat unit in **Poly-8**. The complete deprotection was confirmed by the appearance of the characteristic IR signal at 3293 cm^{-1} corresponding to alkyne

dx.doi.org/10.1021/ma301639m | Macromolecules 2012, 45, 8155−8165

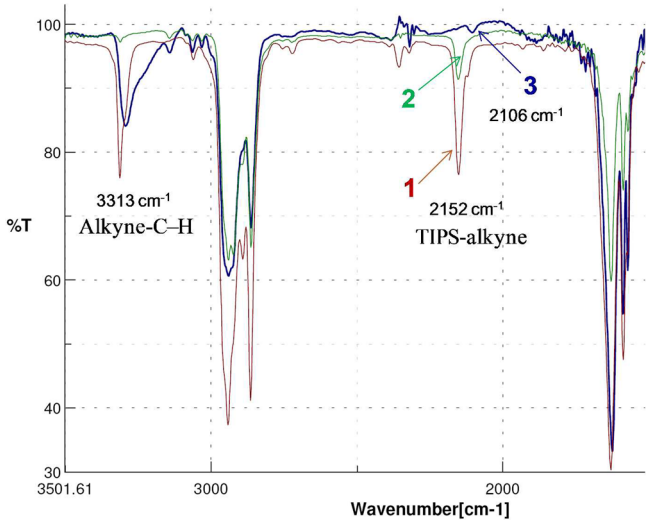


Figure 4. FTIR spectra of **Poly-6** (1), **Poly-7** (2, after click reaction), and **Poly-8** (3, after removal of TIPS groups).

C−H as shown in Figure 4. In addition, the ^{1}H NMR spectrum showed the loss of resonance signals from methyl protons on TIPS group at ca. 1.0 ppm and the appearance of resonance at ca. 2.96 ppm corresponding to phenylacetylene proton. In addition to ^{1}H NMR and FTIR, the resulting polymer (**Poly-8**) was also analyzed by polarimetry. **Poly-8** has specific optical rotation $[\alpha]_{589}^{21}$ = 117° (c = 0.2 in $CHCl_3$, l = 0.5), which is comparable to its parent polymer **Poly-6**, $[\alpha]_{589}^{21}$ = 125° (c = 0.22 in $CHCl_3$, l = 0.5).

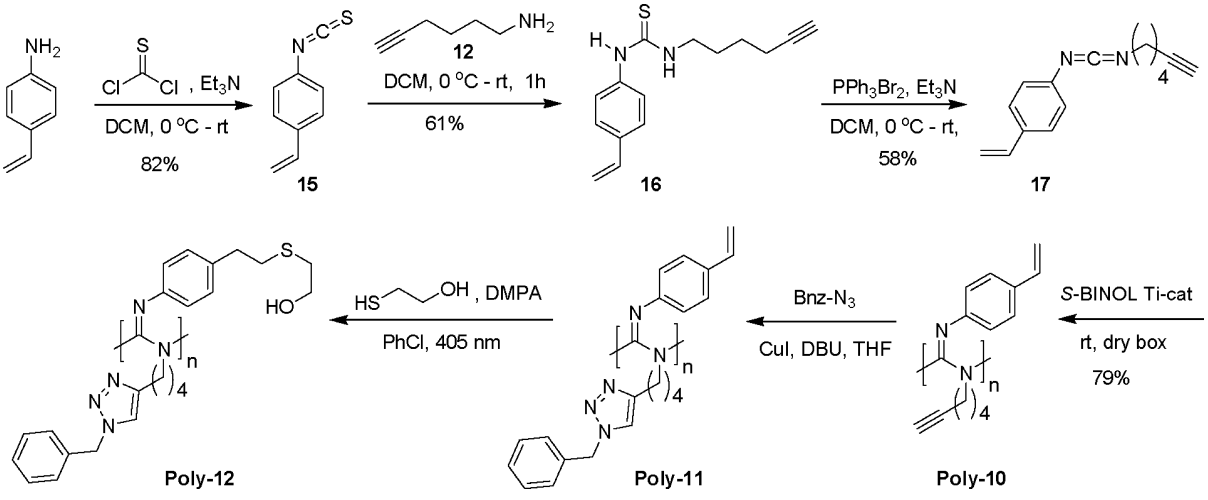
The reactivity of phenylacetylene group in **Poly-8** in CuAAC click reaction was tested through incorporation of Boc-amine as an example of second appended group in the repeat unit in postmodification. This second step click reaction to obtain **Poly-9** took place in relatively short period of time (monitored by IR signals) as compared to the first one. The sequential click reaction in **Poly-6** involving benzyl azide and Boc-amine is the first example and a significant progress toward enriching polycarbodiimide side chains with two dissimilar molecules in postmodification. With desired functionalities in azide molecules, this approach can be extended to incorporate variety of functionalities to optimize polymer properties.

In order to expand the diversity of functionalities that can be incorporated in the side chains of polycarbodiimides and further be explored in postmodification reactions, we synthesized **Poly-10** (Figure 3) with 4-vinylbenzene and 1-hexyne in the repeat unit. Prior to the synthesis of **Poly-10**, the compatibility of 4-vinylbenzene moiety in the standard carbodiimide polymerization system was tested via the synthesis of **Poly-7** (Figure 3), a polymer with 4-vinylbenzene and *n*-hexyl groups in the side chains (Scheme S3). This newly incorporated vinyl functionality in the side chain offers new conjugation reactions for further functionalization of the polymer,[32] especially, conjugation with thiols through thiol−ene click chemistry.[33−36] Further, alkyne−azide click and thiol−ene click are known orthogonal reactions in macromolecules.[33,37] However, to our knowledge, this orthogonal double click chemistry has not yet been explored when applied to the side chains of synthetic helical polycarbodiimides. This orthogonal click approach delivers a higher degree of versatile functionalization compared to functional chain-end polymers. The presence of two pendant groups per repeat unit in polycarbodiimides coupled with the compatibility of both the terminal alkyne and vinyl functionalities in the polymerization reaction lead to the synthesis of **Poly-10** (Scheme 5).

As shown in Scheme 5, the synthesis of **Poly-10** was accomplished in short synthetic route. In brief, isothiocyanate **15** was combined with amine **12** to obtain a thiourea derivative **16** that resulted in monomer **17** upon treating with PPh_3Br_2/Et_3N. Monomer **17** was then polymerized to **Poly-10** under the standard carbodiimide polymerization conditions. The presence of two known versatile groups—vinyl and alkyne functionalities in the repeat unit of **Poly-10**—opens up new opportunities to employ two different well-known click chemistries—azide−alkyne click and thiol−ene click—in a consecutive manner for new functional polycarbodiimides in a short synthetic route.

The efficiency of this new polymer, **Poly-10** in CuAAC click reaction was tested and has been found to be facile as observed in ^{1}H NMR and FTIR spectra of the product (spectra included in Supporting Information). The polymer after click reaction (**Poly-11**) was further modified in a thiol−ene reaction (using the literature procedure as described in ref 33) with

Scheme 5. Synthesis of Poly-10 with Alkyne and Vinyl Functionalities and Modification of Its Side Chains by CuAAC and Thiol−Ene Click Reactions



dx.doi.org/10.1021/ma301639m | *Macromolecules* 2012, 45, 8155−8165

mercaptoethanol to functionalize side chains in our polymer and study a new method to functionalize polycarbodiimides. One of the most commonly used radical-mediated thiol−ene reaction using azobis(isobutyronitrile) (AIBN) at elevated temperature was attempted first. However, the attempted AIBN-mediated thio−ene reaction at the elevated temperatures (ca. 80 °C) for the extended reaction times (ca. 15 h) caused the polymer to decompose back to the carbodiimide monomer due to the thermal decomposition of polycarbodiimides that is accelerated by common radical initiators. In order to overcome this limitation, a photochemical approach was employed. This later approach for thiol−ene reaction using the protocol described in ref 33 ensued without complication and yielded the polymer with newly appended alcohol functionalities in **Poly-12**.

CONCLUSIONS

An ^{15}N isotope labeled alkyne polycarbodiimide, poly(*N*-(3-ethynylphenyl)-$^{15}N'$-hexyl)carbodiimide, has been synthesized to study the polymer microstructure with a focus on its regioregularities. ^{15}N NMR spectroscopy illustrated a highly regioregular distribution of pendant groups along the polymer chain with *n*-hexyl group bonded to amine nitrogen and the phenylacetylene group bonded to imine nitrogen of the repeat unit. Additionally, two independently modifiable alkyne moieties have been incorporated in the repeat unit of an optically active alkyne polycarbodiimide, **Poly-6**. Orthogonal postmodification of these alkyne groups have been performed in consecutive click reactions, demonstrating that two different sets of groups can be incorporated in repeat units of polycarbodiimides in a controlled fashion under mild reaction conditions using this protocol. Furthermore, a combination of alkyne and vinyl groups in the side chains of a polycarbodiimide has been introduced via the synthesis of **Poly-10** that provided an opportunity to employ sequential alkyne−azide and thiol−ene click reactions for new functional polycarbodiimides derivatives. This report on determining the regioregularity of a helical polycarbodiimide and orthogonal side chain modulation in polycarbodiimide system presents a significant advancement and opens up the possibilities for precise functional helical macromolecules that possess perfectly alternating structures.

ASSOCIATED CONTENT

Supporting Information

Further experimental details, NMR and IR spectra of synthesized molecules. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: bruce.novak@utdallas.edu.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

Funding was provided by the Faculty Start up from The University of Texas at Dallas (UTD), the Endowed Chair for Excellence at UTD, and the Howard J. Schaeffer Distinguished Chair at NCSU. We thank NCSU Department of Chemistry Mass Spectrometry Facility funded by the North Carolina Biotechnology Center and the NCSU Department of Chemistry for all HRMS data. We thank Dr. Sabapathy Sankar for his help in ^{15}N NMR spectroscopy. Our special thanks to Dr. Mihaela C. Stefan and Dr. Prakash Sista, Department of Chemistry, The University of Texas at Dallas, for their help in performing GPC on these polymers.

REFERENCES

(1) Nakano, T.; Okamoto, Y. *Chem. Rev.* **2001**, *101*, 4013−4038.
(2) Yashima, E.; Maeda, K.; Iida, H.; Furusho, Y.; Nagai, K. *Chem. Rev.* **2009**, *109*, 6102−6211.
(3) Chen, B.; Deng, J.; Cui, X.; Yang, W. *Macromolecules* **2011**, *44*, 7109−7114.
(4) Kennemur, J. G.; Novak, B. M. *Polymer* **2011**, *52*, 1693−1710.
(5) Kawauchi, T.; Kitaura, A.; Kawauchi, M.; Takeichi, T.; Kumaki, J.; Iida, H.; Yashima, E. *J. Am. Chem. Soc.* **2010**, *132*, 12191−12193.
(6) Arnold, L.; Marx, A.; Thiele, C.; Reggelin, M. *Chem.—Eur. J.* **2010**, *16*, 10342−10346.
(7) Green, M. M.; Park, J. W.; Sato, T.; Teramoto, A.; Lifson, S.; Selinger, R. L. B.; Selinger, J. V. *Angew. Chem., Int. Ed.* **1999**, *38*, 3139−3154.
(8) Miyabe, T.; Hase, Y.; Iida, H.; Maeda, K.; Yashima, E. *Chirality* **2009**, *21*, 44−50.
(9) Tang, H.; Boyle, P.; Novak, B. *J. Am. Chem. Soc.* **2005**, *127*, 2136−2142.
(10) Kennemur, J. G.; Clark, J. B.; Tian, G.; Novak, B. M. *Macromolecules* **2010**, *43*, 1867−1873.
(11) Xue, Q. B.; Kimura, T.; Fukuda, T.; Shimada, S.; Matsuda, H. *Liq. Cryst.* **2004**, *31*, 137−143.
(12) Kim, J.; Novak, B. M.; Waddon, A. *Macromolecules* **2004**, *37*, 8286−8292.
(13) Budhathoki-Uprety, J.; Novak, B. M. *Macromolecules* **2011**, *44*, 5947−5954.
(14) Budhathoki-Uprety, J.; Peng, L.; Melander, C.; Novak, B. M. *ACS Macro Lett.* **2012**, *1*, 370−374.
(15) Kennemur, J. G.; DeSousa, J. D.; Martin, J. D.; Novak, B. M. *Macromolecules* **2011**, *44*, 5064−5067.
(16) DeSousa, J. D.; Novak, B. M. *ACS Macro Lett.* **2012**, *1*, 672−675.
(17) Miyamura, Y.; Kinbara, K.; Yamamoto, Y.; Praveen, V.; Kato, K.; Takata, M.; Takano, A.; Matsushita, Y.; Lee, E.; Lee, M.; Aida, T. *J. Am. Chem. Soc.* **2010**, *132*, 3292−3294.
(18) Crivello, A.; Nervi, C.; Gobetto, R.; Crich, S.; Szabo, I.; Barge, A.; Toppino, A.; Deagostino, A.; Venturello, P.; Aime, S. *J. Biol. Inorg. Chem.* **2009**, *14*, 883−890.
(19) Huang, H.; Seid, M.; Keillor, J. *J. Org. Chem.* **1997**, *62*, 7495−7496.
(20) Nowick, J.; Powell, N.; Nguyen, T.; Noronha, G. *J. Org. Chem.* **1992**, *57*, 7364−7366.
(21) Balsells, J.; Davis, T.; Carroll, P.; Walsh, P. *J. Am. Chem. Soc.* **2002**, *124*, 10336−10348.
(22) Tian, G.; Lu, Y.; Novak, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 4082−4083.
(23) Tang, H.; Garland, E.; Novak, B. M.; He, J.; Polavarapu, P.; Sun, F.; Sheiko, S. *Macromolecules* **2007**, *40*, 3575−3580.
(24) Kolb, H.; Finn, M.; Sharpless, K. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004−2021.
(25) Binder, W.; Sachsenhofer, R. *Macromol. Rapid Commun.* **2007**, *28*, 15−54.
(26) Fournier, D.; Hoogenboom, R.; Schubert, U. *Chem. Soc. Rev.* **2007**, *36*, 1369−1380.
(27) Lutz, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 1018−1025.
(28) Arya, V.; Grewal, R.; Kaul, C.; David, J.; Honkan, V. *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **1977**, *15*, 133−140.
(29) Yeom, C.; Kim, M.; Choi, W.; Kim, B. *Synlett* **2008**, *4*, 565−568.
(30) Cuevas, F.; Oliva, A.; Pericas, M. *Synlett* **2010**, *12*, 1873−1877.
(31) Malkoch, M.; Thibault, R.; Drockenmuller, E.; Messerschmidt, M.; Voit, B.; Russell, T.; Hawker, C. *J. Am. Chem. Soc.* **2005**, *127*, 14942−14949.

(32) Lu, H.; Bai, Y.; Wang, J.; Gabrielson, N.; Wang, F.; Lin, Y.; Cheng, J. *Macromolecules* **2011**, *44*, 6237−6240.
(33) Campos, L. M.; Killops, K. L.; Sakai, R.; Paulusse, J. M. J.; Damiron, D.; Drockenmuller, E.; Messmore, B. W.; Hawker, C. J. *Macromolecules* **2008**, *41*, 7063−7070.
(34) Hoyle, C. E.; Bowman, C. N. *Angew. Chem., Int. Ed.* **2010**, *49*, 1540−1573.
(35) Kade, M. J.; Burke, D. J.; Hawker, C. J. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, *48*, 743−750.
(36) Sumerlin, B. S.; Vogt, A. P. *Macromolecules* **2010**, *43*, 1−13.
(37) Iehl, J.; Nierengarten, J. *Chem. Commun.* **2010**, *46*, 4160−4162.
(38) Reuther, J. F.; DeSousa, J. D.; Novak, B. M. *Macromolecules* **2012**, DOI: 10.1021/ma301448b.