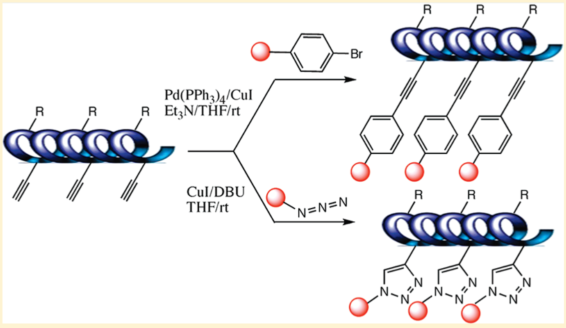
Macromolecules
ARTICLE
pubs.acs.org/Macromolecules

Synthesis of Alkyne-Functionalized Helical Polycarbodiimides and their Ligation to Small Molecules using 'Click' and Sonogashira Reactions

Januka Budhathoki-Uprety and Bruce M. Novak*

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

Supporting Information



ABSTRACT: New terminal alkyne side chain functionalized polycarbodiimides, have been synthesized and "alkyne" ligation tools—"click" (copper-catalyzed Huisgen 1,3-dipolar cycloaddition reaction) and Sonogashira couplings—were utilized to create functional polymers in one step postpolymerization modifications. Polycarbodiimides are interesting synthetic, helical, nanodimensional scaffolds that are capable of presenting a variety of functional groups in highly regular periodic fashion. Herein, we report the synthesis of the first alkyne substituted polycarbodiimides, **Poly-1**, **Poly-2**, and **Poly-3** and the quantitative coupling of functional azides to the alkyne repeat units of these polymers, as evidenced by IR and ^{1}H NMR and ^{13}C NMR spectra. We are able to couple benzyl azide, carboxylic acid azide, and N-Boc amine azide by "click" and *N*-Boc-L-phenylalanine by Sonogashira reactions to the alkyne side chain of **Poly 1** to provide **Poly-1a**, **-1b**, **-1c** and **-1phe**, respectively. **Poly-1b** and **Poly-1c** provide peptide-coupling sites and are precursors for synthetic helical polymer-peptide conjugates. This was demonstrated by coupling L-alanine methylester to **Poly-1b** with excellent conversion. Aliphatic-terminal alkyne functionalized polymer, **Poly-2** with the flexible methylene linker to the backbone provides more degrees of steric freedom for the incorporated groups, fixes the groups closer to the chiral, helical backbone, and reduces the hydrophobic nature of the polymer. However, **Poly-3** offers all of these advantages and with two clickable handles per repeat unit doubles the functional sites along the polymer backbone.

INTRODUCTION

The ability to incorporate functional groups into a polymer system offers the opportunity to vastly expand the properties of macromolecules. The design and successful synthesis of such functionalized polymers depends heavily on the polymerization conditions and reagents, most notably, in transition-mediated polymerizations, on the tolerance of the catalysts to polar functional groups. Post polymerization modifications prove very useful under these catalyst-limiting conditions as long as the polymer backbone is sufficiently stable to the required modification reagents. For complete conversions not only must the reactions prove quantitative but the reagents must have accessibility to all of the modifiable groups along the polymer backbone. Fortunately, the stiff polycarbodiimide backbone assures exposure of all appended groups and the robust nature of the substituted guanidine repeat is resistant to many typical chemical reagents.

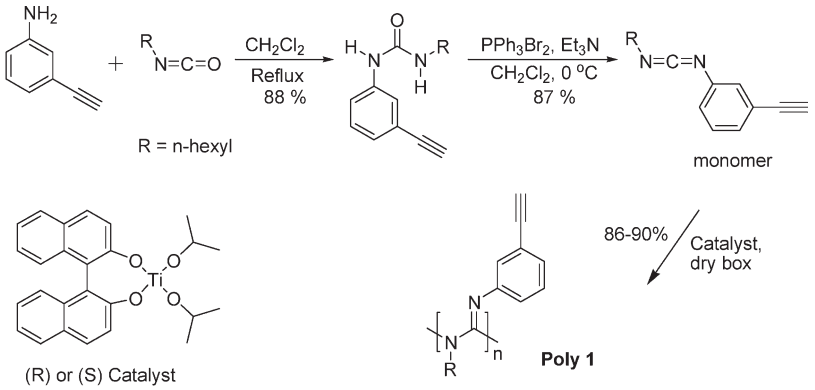
To date, the vast number of polycarbodiimides that have been synthesized possess simple aliphatic and/or aromatic side chains. The reason for this is that the highly Lewis acidic catalysts used to polymerize carbodiimides (e.g., Ti(IV))[1−6] are quickly poisoned by most functional groups. The few successful examples of polymerizable monomers possessing heteroatoms are in the form of the traditionally benign functional groups like ethers, heterocycles, tertiary amines, and bulky esters without enolizable protons. The aromatic substituents, nitro, cyano, and halogens are also tolerated.

The periodic and regular distribution of two tunable pendant groups per repeat unit along the helical backbone make these polycarbodiimides a potential new class of synthetic helical scaffolds for future technologies including optical switches, sensory systems, and advanced chiral materials for biological applications. Even within the existing pool of side chains, many of the previously reported polycarbodiimides have demonstrated many remarkable features including liquid crystalline cholesteric, lyotropic, and thermotrophic phases,[7−9] high racemization barriers,[5] large optical rotatory dispersion, reversible chiroptical switching that is sensitive to temperature and solvents,[10,11] and an efficient and recyclable polymer support for chemical reagents.[12] In order for many of the future applications to move forward, however, the inability to incorporate functional groups must be overcome. A specific prohibition that has stymied us is the synthesis of polycarbodiimide based polymer—peptide and

Received: April 28, 2011
Revised: July 5, 2011
Published: July 18, 2011

dx.doi.org/10.1021/ma200960e | *Macromolecules* 2011, 44, 5947–5954

Scheme 1. Synthesis of Alkyne-Functionalized Polycarbodiimide, Poly 1



other polymer—bioconjugates that would allow for the exploration of the biomedical applications of these polymers.

Herein, we would like to report that nonprotected, terminal alkynes are tolerated by our family of Ti(IV) catalysts. This find now allows us to use well-known and refined protocols to modify the alkyne side chains of these polymers. Specifically we have successfully demonstrated that both "click" reactions and Sonogashira can be used to quantitatively modify the alkynes to incorporate functional side chains that include acids, bases, α-amino acids, and biotin.

EXPERIMENTAL SECTION

General Data. The chemicals were purchased from Sigma-Aldrich, Milwaukee, WI, and Fisher Scientific, Fair Lawn, NJ, and used as received unless stated otherwise. The solvents, tetrahydrofuran (THF) dichloromethane and chloroform were distilled prior to use. 3-Aminophenylacetylene, Boc-4-iodo-L-phenylalanine and dibromotriphenylphosphorane were purchased from Acros Organics, NJ, Chem.-Impex International, IL, and Strem Chemicals, MA, respectively. ^{1}H and ^{13}C NMR data were recorded on a Varian or Mercury 300 or 400 MHz spectrometers (300 or 400 MHz for ^{1}H, 75 or 100 MHz for ^{13}C NMR) at room temperature. The chemical shift values were reported relative to TMS (δ = 0.00 ppm) as an internal standard. IR spectra were obtained from JASCO FT/IR-410. Wave numbers in cm^{-1} are reported for characteristic peaks. Mass spectra 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. UV/vis spectroscopy was performed on a Jasco V-550 UV/vis spectrometer using high-clarity quartz cells. CD data were collected on a Jasco J-815 CD spectrometer. All the manipulations for polymerizations were done inside an MBraun UNIlab drybox under nitrogen atmosphere.

Synthesis of Urea Derivatives. Alkyne amines (ca. 1.0 g) diluted in 10 mL of dichloromethane was added dropwise to the stirring solution of *n*-alkyl isocyanate (1:1 mol equiv) in 25 mL of dichloromethane under nitrogen atmosphere and at low temperature using ice bath. The reaction mixture was then allowed to stir at room temperature for an hour. IR of the reaction mixture showed the complete consumption of isocyanates for those with propargyl amines, and with 3-aminophenyl acetylenes overnight reflux was necessary. The solvent was then removed by rotavap and the resulting urea compound was purified by recrystallization from ethanol at low temperature to obtain urea derivative as a white crystalline solid.

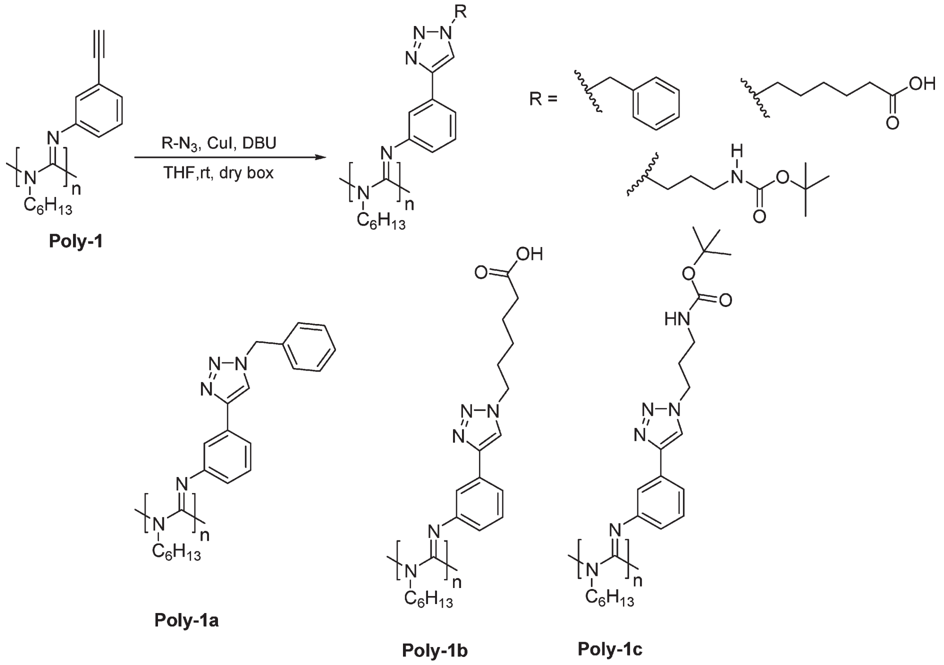
Synthesis of Monomers. Monomer was synthesized as shown in the scheme 1. To the dibromotriphenyl phosphorane and triethyl amine (1.2:2.5 mol equiv relative to the urea compound) suspended in dichloromethane (5 mL for 1.0 g scale of urea derivative) at 0 °C under nitrogen atmosphere, the urea derivative was added in portions. The reaction mixture was allowed to warm to room temperature and stirred until the reaction was finished. The dehydration of the urea compound into the carbodiimide monomer can be monitored by Infrared spectroscopy by the formation of strong absorption band corresponding to N═C═N at 2142 cm^{-1}. After completion, the reaction was quenched by pentane. The resulting monomer was extracted from the solid by pentane. The crude carbodiimide monomer sample was purified by column chromatography on silica gel using ethyl acetate and hexane 1:1 or 1:4 by volume mixture and dried under vacuum to provide colorless oil.

Synthesis of Polymers. A representative polymerization is presented here. Full characterizations and specific yields are provided in Supporting Information. Alkyne functionalized polymer, **Poly-1**, was synthesized as shown in the Scheme 1. All the manipulations for the polymerization were done inside drybox. The monomer sample was mixed with the catalyst (dissolved in 0.2 mL of chloroform) with a monomer to catalyst ratio 100:1. The reaction mixture transformed into a dark red viscous liquid and solidified to light orange solid. The reaction mixture was allowed to remain at room temperature inside the drybox for 24 h. The resulting light orange solid was taken out from drybox, dissolved in wet chloroform and precipitated in methanol to purify the polymer. The light yellow solid polymer thus obtained was washed with several volumes of methanol. The polymer was collected by filtration, dried, redissolved in chloroform and reprecipitated then finally dried under vacuum overnight. Similar procedure was followed for other alkyne polycarbodimides except THF was used while purification for **Poly-3**. These polymerizations were performed on 0.09—1.5 g scale monomers.

Click Reaction with Benzyl Azide (Poly-1a). To the stirring solution of polymer in tetrahydrofuran, benzyl azide and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (1.3:6.0 mol equiv per alkyne unit in the polymer) followed by the catalyst CuI (10 mol %) were added. The reaction mixture was stirred overnight. The reaction can be monitored by disappearance of strong sp C—H absorption band at 3305 cm^{-1} in the infrared spectroscopy. Once completed, the polymer was precipitated in methanol and separated by filtration. For further purification, the polymer was dissolved in dicholoromethane, stirred with aqueous solution of EDTA, separated and reprecipitated in methanol, filtered, and dried under vacuum overnight to obtain a white solid, **Poly-1a** (Scheme 2).

Sonogashira Cross Coupling of Amino Acid (Poly-1-phe). To the stirring solution of polymer, **Poly-1**, in tetrahydrofuran, 4-iodo-*N*-Boc-L-phenylalanine and triethyl amine (1.3:4.0 mol equiv per alkyne unit in the polymer) followed by the catalysts Pd(PPh$_3$)$_4$ (5 mol %) and CuI (10 mol %) were added. The reaction mixture was stirred overnight.

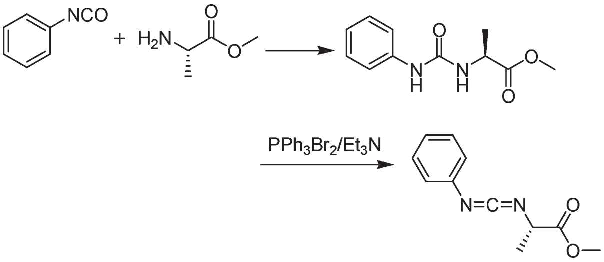
Scheme 2. Click Reactions in Poly-1 and Resulting Polymers Poly-1a, -1b, and -1c



The polymer was precipitated in benzene, separated by filtration, and dried under vacuum to get **Poly-1-phe** (Scheme 4).

RESULTS AND DISCUSSION

The most direct route to incorporate α-amino acid side chains into the polycarbodiimide backbone would be to use the amine to form the carbodiimide as shown in eq 1 utilizing the methyl ester of L-alanine. Ester deprotection of the polymer resulting from such monomers could be used in a C-terminal Merrifield coupling sequences to grow oligopeptides of interest.



(1)

Unfortunately, these ester side-chains bearing enolizable α-protons (p$K_a \approx 24$) completely deactivate the family of Ti(IV) compounds routinely used in carbodiimide polymerizations.[28] These repeated negative results forced us to rethink our strategy and look at postpolymerization approaches. The number possible functional groups that are both amenable to a range of reactions and inert toward the Ti(IV) catalysts are few. Fortunately, we were able to discover that terminal alkynes, despite their potential acidity (p$K_a \approx 25$) were completely tolerated by our catalysts and several new alkyne-containing polymers are reported here. Alkynes can be used in specific coupling reactions to provide diverse polymer-based materials. In fact, alkyne functionalized polymers have been used to create variety of functional polymers by coupling with inorganic particles or small organic molecules containing diverse functional groups.[13−16] Reliable, high yielding couplings reactions with acetylenes include the click reaction (copper-catalyzed Huisgen 1,3-dipolar cycloaddition reaction with an azide),[17−25] and the palladium catalyzed Sonogashira reaction between alkynes and aryl halides.[26]

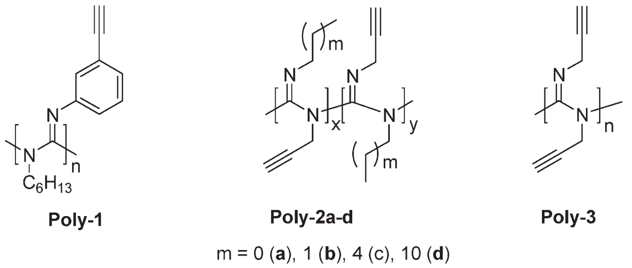


Figure 1. Newly prepared polycarbodiimides having terminal alkyne side chains.

In this current work, a family of alkyne-functionalized polycarbodiimides (Figure 1) have been synthesized from carbodiimides monomers using a chiral BINOL−Ti(IV)−catalyst. We chose this particular catalyst from our library of Ti(IV) catalysts because we have shown that it is extraordinarily potent and providing optically active polymers with a preferred helical sense.[29] The nonsymmetric carbodiimide monomers **1** and **2a**−**d** were prepared from commercial 3-aminophenylacetylene and *n*-hexylisocyanate (**1**) and propargyl amine with ethyl-, propyl-, hexyl- and dodecylisocyanate (**2a**−**d**) as depicted in Scheme 1 for **Poly-1**. The symmetric carbodiimide, **3**, was prepared using 2 equiv of propargyl amine and 1,1′-carbonyldiimidazole. In all cases, the intermediate ureas were dehydrated using $PPh_3Br^+Br^-$ and triethylamine.

The progress of the polymerizations was followed by IR spectroscopy by monitoring the complete disappearance of the

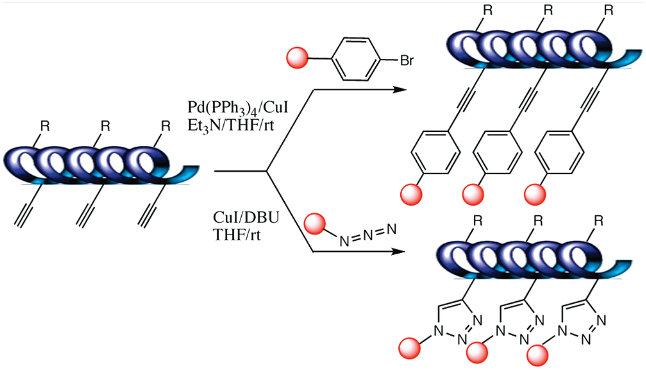


Figure 2. Schematic representation of postpolymerization modifications by both the click and Sonogashira reactions.

strong absorption band corresponding to N=C=N asymmetric stretch at 2142 cm^{-1} (**1**), 2132 cm^{-1} (**2**), and 2134 cm^{-1} (**3**), and formation of strong absorption band near 1630−1640 cm^{-1} corresponding to imine stretch in the polymer backbones. All polymers were further characterized by ^{1}H, ^{13}C nuclear magnetic resonance spectroscopy and polarimetry. The polymerizations were done using the neat liquid monomers except for a minimum amount of chloroform (ca. 0.2 mL) to dissolve the catalyst. All polymerizations are very rapid at room temperature with the mixtures solidifying in 2−3 min for monomers **2a**−**d** and **3** and 15−20 min for monomer **1**. These polymers showed good solubility in various polar organic solvents such as CHCl$_3$, THF, and DMSO. Unfortunately, and as was repeatedly observed in the past, the nitrogen-rich nature of these polycarbodiimides precludes their routine molecular weight measurements by GPC as they strongly adhere to the column. Viscometry is also thwarted by their pronounced liquid crystalline nature. In other studies on polymers possessing long alkyl chains that help to suppress absorption, these catalysts have been shown to produce both living and well-controlled polymerizations. Empirical observations (e.g., solubility) of polycarbodiimides made at different monomer to catalyst ratios support differences in molecular weight that parallel these ratios.[29]

With these new helical polymers in hand postpolymerization studies were investigated. Fortuitously, the terminal alkyne affords an excellent spectroscopic handle to monitor the progress of these reactions. In order to explore an opportunity to synthesize wide variety of new functionalized polymer-based materials with broad applications, postpolymerization modification was performed as depicted in the figure 2.

As a model reaction to test the feasibility and compatibility of reaction conditions with the polycarbodiimide backbone the click reaction was performed using a simple, neutral azide molecule (benzylazide). It should be noted that the insoluble nature of the **Poly-1** in aqueous and any alcoholic media prevents the use of the less precaution-demanding conditions: cupric sulfate and sodium ascorbate in aqueous/alcoholic media or copper turnings in water/alcohol mixtures that are routinely used for the click reaction. After screening, the best conditions for the click reaction were determined to be CuI and DBU as catalysts under anaerobic conditions in THF solvent at room temperature. Under these conditions, quantitative conversion of **Poly-1** to **Poly-1a** possessing the benzyl triazole side chains was observed. Quantitative conversion is evidenced by the complete disappearance of both the alkyne triple bond and C−H IR bands at 2107 cm^{-1} and 3305 cm^{-1}, respectively, and the ^{1}H NMR peak at approx 3.0 ppm, which is assigned as the alkyne C−H resonance, and the appearance of a new peak at approx 5.4 ppm that corresponds to benzylic methylene group (Figure 3).

The uniform periodic distribution of the alkyne pendant groups along the helical backbone seemed to provide sufficient space for coupling of azide molecules to all alkyne functionalities present in the chain. The possible copper catalyzed alkyne homocoupling side reaction often associated with alkyne-rich macromolecular systems was not observed as long as oxygen was excluded from the reaction. This first trial shows that the polymer backbone is completely stable to the click conditions and that the alkyne side-chains are fully accessible to the reagents. Given this we then expanded the polycarbodiimide family by incorporating carboxylic acid and Boc-protected amine side chains in the polycarbodiimide to furnish **Poly-1b** and **Poly-1c**, respectively, via click chemistry (Scheme 2). Clicking the free amine (3-aminopropyl azide) also appeared to work but the resulting polymer proved to be insoluble in all solvents tried.

Facile and quantitative coupling proceeded with all selected molecules as revealed by spectroscopic analysis (see Supporting Information). No racemization appears to have occurred in the chiral, excess single-handed helix sense polymer as evidenced by the retention of the specific optical rotation of the polymer after post polymerization modification. Comparison was made between **Poly-1** ($[\alpha]_{589}{}^{21}$ = +404.20, c = 0.2, in CHCl$_3$); and **Poly-1a** ($[\alpha]_{589}{}^{21}$ = +340.90, c = 0.2, in CHCl$_3$). The decrease in the specific optical rotation in **Poly-1a** compared to **Poly-1** is not surprising due to change in chemical nature of polymer as well as the increase in mass of the polymer repeat units which effectively decreases the relative optically active component per repeat unit in the polymer. Consistent with the polarimetry data, circular dichroism (CD) measurements were also made on the polymers before and after. **Poly-1** made from the *R*-BINOL-Ti catalyst shows a positive Cotton effect absorption at 249 nm corresponding to the amidine backbone chromophore. Consistently, **Poly-1** prepared using the *S*-BINOL-Ti shows an equal but oppositely signed Cotton effect. Upon performing the click modification to form **Poly-1a** (*R*-BINOL-Ti), shows the same positive Cotton effect for the backbone absorption. These data are consistent with the polymers maintaining the persistent secondary structure of the polymers even after click reaction. (CD spectra are available in the Supporting Information.)

The newly created polymers, **Poly-1b** and **Poly-1c** possessing carboxylic acids and Boc protected amines offer sites for direct peptide coupling onto these side chains. In principle, any desired amino acid sequence can be grown or grafted onto the side chain using a variety of well-known Merrifield type peptide coupling reactions. To demonstrate this fact, **Poly-1b-ala** was prepared in a very efficient manner through coupling of L-alanine methylester hydrochloride with the carboxylic acid of **Poly-1b** after *in situ* activation of the acid functionality with *N*-hydroxysuccinimide as depicted in Scheme 3.

Facile transformation of **Poly-1b** to **Poly-1b-ala** is the first of a new hybrid polymer-bio conjugate that opens a new avenue to explore the use of polycarbodiimides as robust helical scaffolds that can present specific amino acids sequences/polypeptides with highly regular spacing and orientations.

To further expand the scope of these postpolymerization modification reactions to allow us to present useful functional

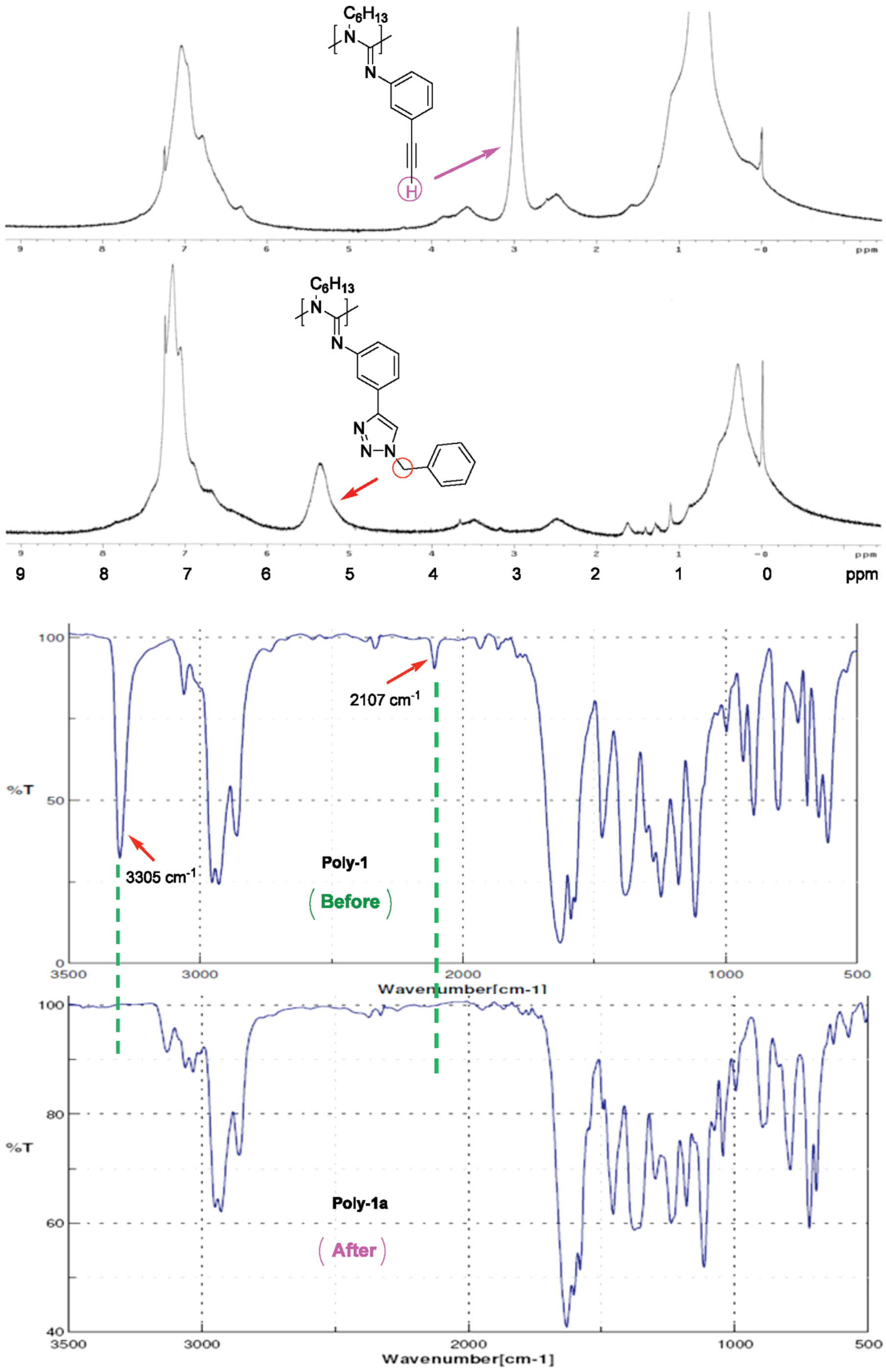


Figure 3. ^{1}H NMR and IR spectra of both **Poly-1** and **Poly-1a** showing quantitative postmodification by the click reaction.

groups tethered with alternative linker sites, we explored the Sonogashira reaction. **Poly-1b**, as shown in Scheme 3 can be used to couple amino acids via C-terminus peptide growth, while **Poly-1c**, with its amine functionality would allow for N-terminus peptide growth. In both cases the peptide chains radiate out from the helical scaffold. Another potential presentation of an amino acid is creating a linkage that allows for exposure of either the N-, or C-terminus, or both. With this in mind, we employed the Sonogashira reaction to couple an N-Boc protected amino acid, N-Boc-L-phenylalanine through the modified side chain (*p*-iodobenzyl) to the alkyne of **Poly-1**, thus leaving the N- and C-terminus free for further reaction (Scheme 4). This Sonogashira reaction also proved to be quantitative between this modified phenylalanine and the alkynes projecting from helical **Poly-1**.

Unfortunately, not every reaction proved to be successful, but in all unsuccessful cases, the reactions appear to be thwarted by solubility problems of the products. For example, click reactions between biotin or thymidine azide derivatives and **Poly-1** resulted in products that were insoluble in all common organic solvents and aqueous media. These failures emphasized the importance of developing new alkyne-appended polycarbodiimide backbones (*vide infra*).

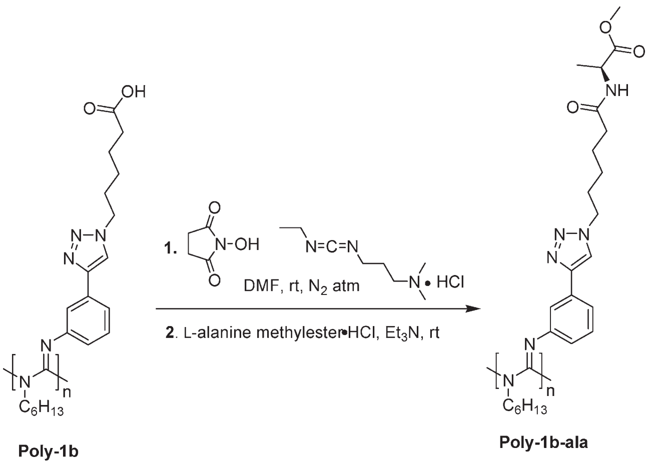
In both the above click and Sonogashira coupling reactions, the functional groups are separated from the backbone by either a triazole ring or a diphenylacetylene linker. Without bias, these extended spacers may or may not provide benefits in designing polymer—bioconjugates. In principle, the longer tethers provide better access of the biomoiety to the surrounding environment but they do increase the hydrophobicity of the polymer itself and separate the active moiety from the intrinsic chirality of the helical polymer backbone. Hence, we designed systems based on the propargyl side-chain that places the added functionality substantially closer to the chirality of the single-sense helix.

In accordance with the analysis above, and bolstered by the success of polymerizing monomer **1** and its subsequent modifications, we prepared five additional alkyne monomers, **2a**—**d** and **3** (Scheme 5) that possess a single methylene group between the alkyne and the carbodiimide group that will be converted into the substituted guanidine backbone. **Poly-2** derivatives were prepared having side chains that include ethyl (**2a**), propyl (**2b**), hexyl (**2c**), and dodecyl (**2d**). Of special note, **Poly-3** offers two alkyne (modifiable groups) per repeat unit, whereas **Poly-1** and **-2a**—**d** provide one.

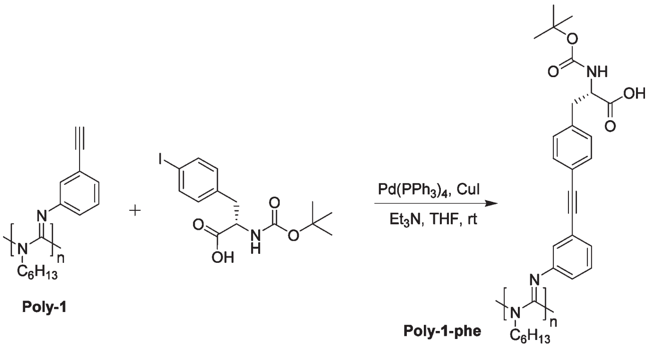
The monomers **2a**—**d** and **3** proved to be very active monomers when polymerized with the Ti(IV) catalysts. As liquid monomers they can be polymerized neat at room temperature. The monomers solidified at room temperature within 2—3 min when contacted with the BINOL—Ti(IV) catalysts (shown in Scheme 1). The **Poly-2** family with two groups of similar steric and electronic character shows two regioisomers brought about by nondiscriminate insertions of the monomer by the catalyst during polymerization. This regio-illregularity is qualitatively but not quantitatively evidenced by the appearance of two imine carbons in the ^{13}C NMR at 150 and 146 ppm and four alkyne signals at 83.9 and 80.4 (internal alkyne carbons) and 73.3 and 69.0 (terminal alkyne carbons) for **Poly-2d**. The carbon NMR's collected on the other two **Poly-2b-c** derivatives show similar patterns in the alkyne region but are less resolved in the imine window. If we assume similar relaxation delays for the same carbons in the two environments, the regioregularity of **Poly-2d** is nearly 50/50. In contrast, our evidence collected using ^{15}N NMR indicates that aromatic—aliphatic monomers such as **1** show regioregular insertions through the imine possessing the aromatic group.[30] Fortunately, the shorter chains of these propargylic polymers were also accessible to the click reagents and catalysts, and again, quantitative conversions were observed, even on **Poly-3** which presents two alkynes in close proximity in each repeat unit. To demonstrate this we returned to the simple benzyl azide as a model compound. Again for solubility reasons the click reaction was run in THF (Scheme 6).

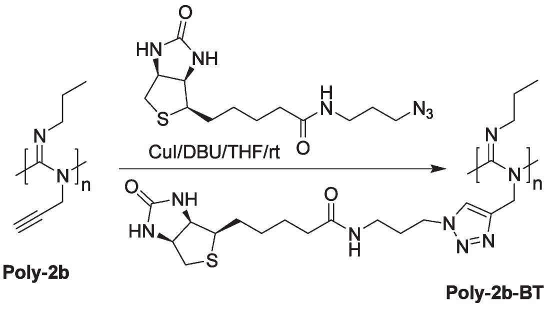
As a proof of concept and to expand our pool of bioconjugates, we successfully incorporated biotin moieties along the side chains via click chemistry (eq 2).

Scheme 3. Amino Acid Coupling to Side Chain in Poly-1b Resulting in the Amino Acid Conjugate Poly-1b-ala



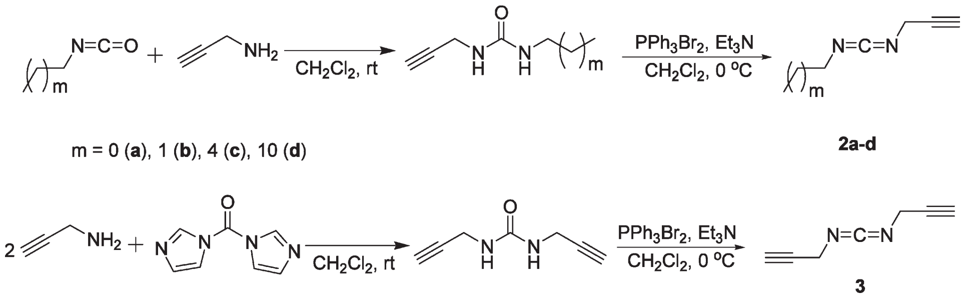
Scheme 4. Sonogashira Reaction between Poly-1 and Boc-4-iodo-L-phenylalanine To Form Poly-1-Phe



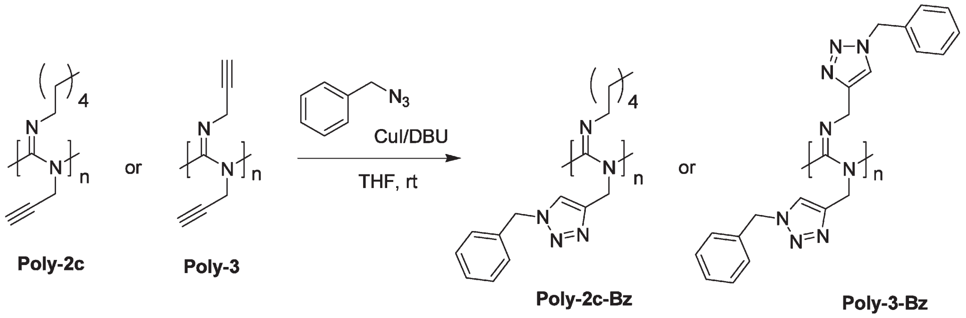


(2)

Scheme 5. Preparation of Propargylic Monomers 2a—d and 3



Scheme 6. Model Click Reactions on Poly-2c and Poly-3 Using Benzylazide



In contrast to the insoluble polymeric product derived from the biotin azide used in eq 2 and **Poly-1**, **Poly-2b-BT** is soluble in DMSO and the material was characterized using both IR and NMR. Overlapping peaks, both in the IR and NMR, from the biotin unit prevent us from stating definitively that this reaction was quantitative, however, based on the benzylazide results we are fairly confident that this is the case.

A short, versatile, and mild synthetic route to produce highly functionalized and complex polycarbodiimides through an efficient pathway has the following implications. First, this grafting strategy allowed the formation of new polymer–amino acid conjugates with high density of amino acids along the polymer side chain in well-defined local and global conformations of polycarbodiimides. Second, the carboxylic acid side chain in the functionalized polymer, **Poly-1b**, has been demonstrated as a peptide coupling site. Suitable peptides when coupled to this polymer may be explored as synthetic peptide mimics for drug delivery and gene therapy.[26,27] Third, oligopeptides with control over chain length and monomer sequence can be developed along the side chains in a step growth fashion in **Poly-1b** or **Poly-1c** (after deprotection) to develop polymer-peptide conjugates presenting the amino acids in regular, repeating positions. Fourth, due to the presence of another inherent tunable side chain, these polymers can offer the advantages of both solution and solid phase chemistry for biomedical applications.

CONCLUSION

We have synthesized and characterized a family of polycarbodiimides with alkyne side-chains and shown that these could be coupled to functional molecules presenting neutral, acidic, and basic groups including biotin and α-amino acids. Coupling reactions used included the click reaction and Sonogashira couplings. The quantitative and facile conversion took place without racemization of the excess single-handed helix sense polymer. Furthermore, these new functional side chains can undergo further modification with quantitative yields (e.g., peptide coupling). The uniform periodic distribution of pendant groups along the helical backbone and their efficient transformation to new functionalities produces these polycarbodiimides as a unique class of synthetic helical scaffolds for uses in future technologies. This new synthetic approach help explore broad applications of these polycarbodiimides. Currently work is in progress to anchor biofunctionalities and biological evaluation of the resulting polymers.

ASSOCIATED CONTENT

Ⓢ **Supporting Information.** Further experimental details and characterization data for the presented compounds. This material is available free of charge via Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: Bruce_Novak@ncsu.edu.

ACKNOWLEDGMENT

Funding was provided by the Howard J. Schaeffer Distinguished University Chair endowment. We also thank NCSU Department of Chemistry Mass Spectrometry Facility.

REFERENCES

(1) Goodwin, A.; Novak, B. M. *Macromolecules* **1994**, *27*, 5520–5522.

(2) Shibayama, K.; Seidel, S. W.; Novak, B. M. *Macromolecules* **1997**, *30*, 3159–3163.

(3) Schlitzer, D. S.; Novak, B. M. *J. Am. Chem. Soc.* **1998**, *120*, 2196–2197.

(4) Lu, Y.; Tian, G.; Novak, B. M. *Polym. Prepr.* **2003**, *44*, 693–694.

(5) Tang, H. Z.; Lu, Y. J.; Tian, G. L.; Capracotta, M. D.; Novak, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 3722–3723.

(6) Tang, H. Z.; Garland, E. R.; Novak, B. M.; He, J. T.; Polavarapu, P. L.; Sun, F. C.; Sheiko, S. S. *Macromolecules* **2007**, *40*, 3575–3580.

(7) Tian, G.; Lu, Y.; Novak, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 4082–4083.

(8) Kim, J.; Novak, B. M.; Waddon, A. J. *Macromolecules* **2004**, *37*, 1660–1662.

(9) Kim, J.; Novak, B. M.; Waddon, A. J. *Macromolecules* **2004**, *37*, 8286–8292.

(10) Tang, H. Z.; Boyle, P. D.; Novak, B. M. *J. Am. Chem. Soc.* **2005**, *127*, 2136–2142.

(11) Kennumer, J. G.; Clark, J. B., IV; Tian, G.; Novak, B. M. *Macromolecules* **2010**, *43*, 1867–1873.

(12) Budhathoki-Uprety, J.; Novak, B. M. *Polymer* **2010**, *51*, 2140–2146.

(13) Scholz, S.; Leech, P. J.; Englert, B. C.; Sommer, W.; Weck, M.; Bunz, U. H. F. *Adv. Mater.* **2005**, *17*, 1052–1055.

(14) Allen, C. W.; Bahadur, M. *J. Inorg. Organomet. Polym.* **1998**, *8*, 23–31.

(15) Grubbs, R. B. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 4323–4336.

(16) Chan, W. Y.; Clendenning, S. B.; Berenbaum, A.; Lough, A. J.; Aouba, S.; Ruda, H. E.; Manners, I. *J. Am. Chem. Soc.* **2005**, *127*, 1765–1772.

(17) Huisgen, R. *Angew. Chem., Int. Ed.* **1963**, *2*, 565–632.

(18) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004–2021.

(19) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596–2599.

(20) (a) Binder, W. H.; Sachsenhofer, R. *Macromol. Rapid Commun.* **2007**, *28*, 15–54. (b) Binder, W. H.; Sachsenhofer, R. *Macromol. Rapid Commun.* **2008**, *29*, 952–981.

(21) Antoni, P.; Hed, Y.; Nordberg, A.; Nystörm, D.; von Holst, H.; Hult, A.; Malkoch, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 2126–2130.

(22) Fournier, D.; Du Prez, F. *Macromolecules* **2008**, *41*, 4622–4630.

(23) Opsteen, J. A.; van Hest, J. C. M. *Chem. Commun.* **2005**, 57–59.

(24) Bock, V. D.; Hiemstra, H.; van Maarseveen, J. H. *Eur. J. Org. Chem.* **2006**, 51–68.

(25) Chinchilla, R; Nájera, C. *Chem. Rev.* **2007**, *107*, 874–922.

(26) Funhoff, A. M.; van Nostrum, C. F.; Lok, M. C.; Fretz, M. M.; Crommelin, D. J. A.; Hennink, W. E. *Bioconjugate Chem.* **2004**, *15*, 1212–1220.

(27) Wender, P. A.; Rothbard, J. B.; Jessop, T. C.; Kreider, E. L.; Wylie, B. L. *J. Am. Chem. Soc.* **2002**, *124*, 13382–13383.

(28) Unpublished results from the Novak group, Department of Chemistry, North Carolina State University.

(29) Kennemur, J. G.; Novak, B. M. Advances in Polycarbodiimide Chemistry. *Polymer* **2011**, *52*, 1693–1710.

(30) DeSousa, J. D.; Novak, B. M. Manuscript in preparation.