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N-Heterocyclic Carbenes: Versatile Reagents for Postpolymerization Modification

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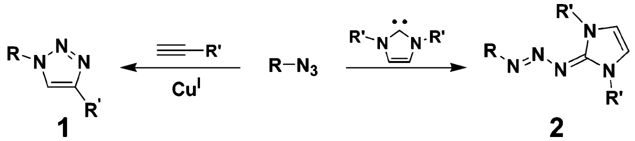
Postpolymerization modification is a powerful method for installing new or altering existing functional groups on macromolecular materials.[1,2] In general, the technique is employed when (1) catalysts or reaction conditions necessary for polymerization are incompatible with the functional groups present on the corresponding monomer(s), (2) polymer isolation and/or processing is inhibited by the desired functionality, or (3) a means to rapidly prepare a diverse library of materials from a single polymeric precursor is desired.[3] This broad range of applications warrants the development of new reactions and protocols for modifying polymeric materials. An ideal reaction for this purpose should adhere to the following criteria: (1) it must not compromise the structural integrity of the polymeric materials (i.e., chain scission and other degradative side reactions should not occur), (2) it should proceed with a high yield and with high atom economy to minimize purification efforts and costs, and (3) to maximize applicability, it should utilize a structurally diverse range of reagents that are commercially or readily available.

Reactions that meet these requirements mirror the conditions necessary to be classified under "click chemistry".[4] The most notable and commonly utilized of the click reactions is the Cu(I)-catalyzed 1,3-dipolar cycloaddition between organic azides and terminal alkynes which affords 1,4-disubstituted triazoles (**1**) (Scheme 1).[5] Indeed, because of the cycloaddition reaction's high functional group tolerance, use of environmentally friendly solvents, and excellent yields, this particular click reaction is gaining widespread use for the synthesis and modification of macromolecular materials.[6]

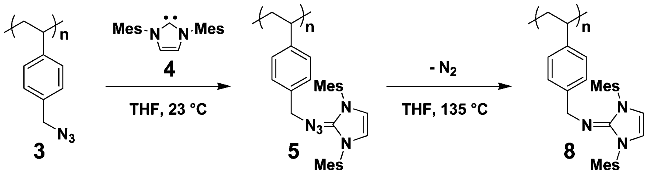
Recently, we found that organic azides react with *N*-heterocyclic carbenes[7] (NHCs) to afford 1,3-disubstituted triazenes (**2**) (Scheme 1).[8] The mechanism of this reaction is believed to proceed via nucleophilic attack of the NHC on the terminal nitrogen of the azide to afford the respective triazeno moiety (**2**), analogous to the Staudinger reaction between phosphines and azides.[9] Notably, this unique reaction proceeds rapidly at ambient temperatures, requires no catalyst, and generally affords excellent yields (>95%) of stable product.[10] Considering the large number of known synthetic protocols (and often commercial availability) of azides[11] and NHCs,[7] the NHC−azide coupling reaction meets the aforementioned criteria for use in postpolymerization modification.

As part of our general program in the study of NHCs as key components in macromolecular synthesis,[12] we investigated the potential of the NHC−azide coupling reaction as a new method for the postpolymerization modification of polymeric materials.[13] Herein, we demonstrate that polystyrenes containing pendent azido moieties may be quantitatively converted to the respective triazeno-functionalized derivatives using a commercially available NHC (Scheme 2). Furthermore, we show that the coupling reaction may be combined with an alkyne−azide cycloaddition (click) reaction to prepare copolymers featuring two distinct functional groups. Finally, by capitalizing on a unique thermally induced nitrogen extrusion process, we show that polystyrenes featuring pendent triazenes may be converted to their respective guanidines.

Scheme 1. Generalized Example of Cu-Catalyzed Cycloaddition between an Azide and an Alkyne to Form a Triazole (1) and Coupling of an Azide to an *N*-Heterocyclic Carbene To Form a Triazene (2)



Scheme 2. Postpolymerization Modification of Poly(*p*-azidomethylstyrene) (3) with an NHC (4) Affords the Respective Triazeno-Functionalized Polymer 5[a]



[a] At elevated temperatures, nitrogen is extruded from polymer **5** which transforms the pendent triazeno moieties into their respective guanidines (**8**).

Following a literature procedure,[14] poly(*p*-azidomethylstyrene) (**3**) ($M_n = 3.8 \times 10^4$ Da, PDI = 1.6; relative to polystyrene standards) was prepared by first polymerizing *p*-chloromethylstyrene (**3**) followed by derivatizing the polymeric product with excess sodium azide. To probe the capacity of the aforementioned NHC−azide coupling reaction as a means to effect postpolymerization modification of this polymer, a 0.1 M THF solution of **3** was treated with a molar equivalent (relative to monomer) of 1,3-dimesitylimidazolylidene (**4**) (as a 0.1 M THF solution) under an atmosphere of nitrogen.[15] After stirring for 4 h at ambient temperature, the reaction solution was evaporated to dryness, and the crude product (**5**) was characterized using a variety of spectroscopic techniques. The pendent benzyl azido moieties along the backbone of polymer **3** appeared to be completely consumed, as determined by the absence of an azide stretching frequency at 2100 cm^{-1} in the IR spectrum of **5**. This was corroborated by ^{1}H NMR spectroscopy which indicated that the signal typically found at $\delta = 4.2$ ppm (attributable to the CH_2 unit of the benzyl azide in $CDCl_3$) was broadened and shifted upfield to $\delta = 3.9$ ppm (CH_2 unit of the respective benzyl triazene). Furthermore, broadened signals were observed at δ = 6.4, 2.2, and 2.1 ppm (attributed to the =CH of the imidazole ring and the mesityl CH_3 groups, respectively, in $CDCl_3$) which provided additional structural characterization. Analysis of polymer **5** using size-exclusion chromatography (SEC) indicated that its M_n was 8.4×10^4 Da with a polydispersity index (PDI) = 1.7. The overall effect of the postpolymerization modification reaction can be seen in Figure 1A, which overlays the size-exclusion chromatograms of polymers **3** and **5** and concisely shows that molecular weight was increased while the polydispersity remained essentially unchanged.

Taken together, these data suggested that the NHC−azide coupling reaction was successfully used as a method for

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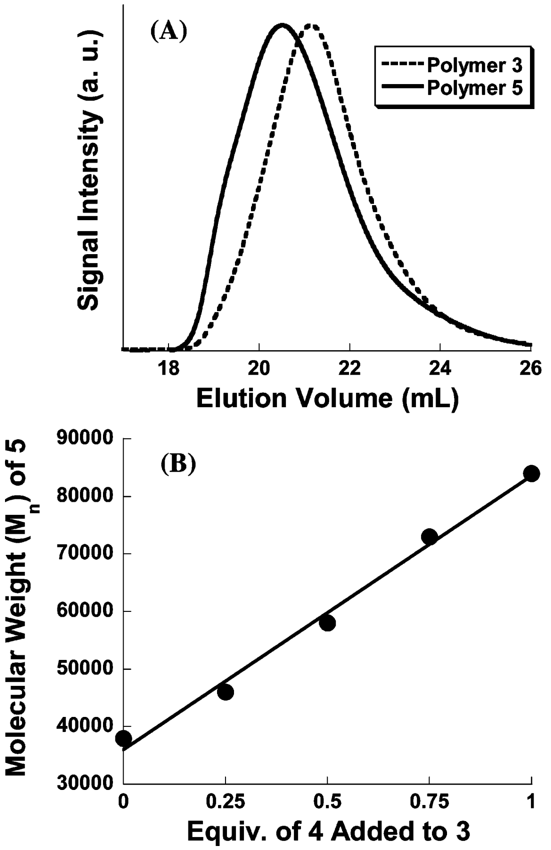
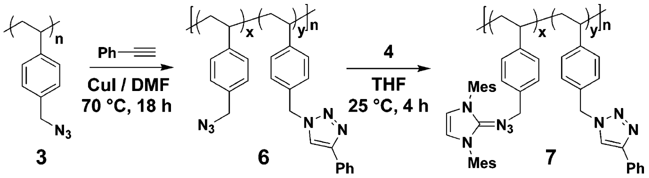


Figure 1. (A) Size-exclusion chromatograms of polymer **3** and its NHC-modified derivative, polymer **5**. (B) A plot of the M_n of the polymer obtained by adding various amounts of NHC **4** to polymer **3**. Data were obtained using SEC (0.01 M LiBr in DMF at 40 °C; all values are reported relative to polystyrene standards).

Scheme 3. A Two-Step Procedure for Preparing Random Copolymers Featuring Pendent Triazole and Triazene Substituents



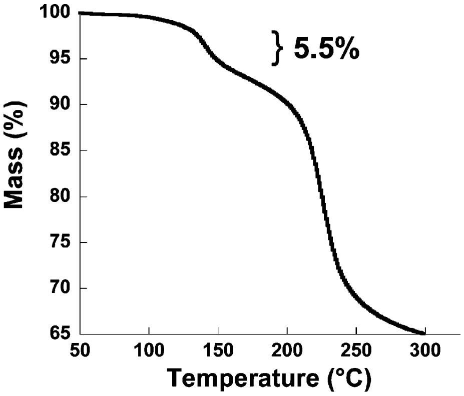


Figure 2. Thermogram of polymer **5** (M_n = 7.9 × 10^4 Da, PDI = 1.7). Data were obtained via TGA at a scan rate of 10 °C/min under an atmosphere of nitrogen.

postpolymerization modification. To assess the fidelity of this reaction, a series of experiments were performed where polymer **3** was reacted with various amounts of **4** (relative to monomer) using the protocol discussed above and analyzed by SEC. As shown in Figure 1B, M_n of the resulting polymers linearly correlated with the amount of NHC added.[16] These results were not only a strong testament of the high efficiency of the NHC−azide coupling reaction but also indicated that partially functionalized polymers were successfully prepared. This effectively creates an opportunity for further postpolymerization modification using other chemical methods that utilize azides.

Thus, in an effort to enhance the scope and applicability of this postpolymerization modification technique, we turned our attention toward combining the NHC−azide coupling reaction with a Cu-catalyzed [3+2] alkyne−azide cycloaddition reaction to prepare random copolymers featuring two different functional groups (Scheme 3). This was accomplished by first partially functionalizing polymer **3** with 0.5 mol equiv of phenylacetylene (relative to monomer) using known[4,17] conditions which facilitate the coupling of these two substrates (CuI, DMF, 70 °C, 18 h). The intermediate copolymer **6** was isolated in 91% yield by precipitation into methanol, followed by filtration. A signal at 2100 cm^{-1} was observed in the IR spectrum of this material which suggested that unreacted azides were present. This amount was quantified using ^{1}H NMR spectroscopy by integrating the signals at δ = 4.2 ppm (benzyl azide) and 5.4 ppm (benzyl triazole) and was found to be 51%. Copolymer **6** was subsequently subjected to the NHC−azide coupling conditions discussed above (0.5 mol equiv of **4** relative to monomer, THF, 23 °C, 4 h) and isolated by precipitation into methanol in 96% yield. NMR and IR spectroscopies revealed that the residual azides in **6** were completely converted to their triazeno derivatives, affording polymer **7**. Furthermore, SEC indicated that polymer **7** showed a higher MW (M_n = 9.0 × 10^4 Da, PDI = 1.9) relative to **6** (M_n = 7.3 × 10^4 Da, PDI = 1.7), as expected. Collectively, these results suggested that random copolymers featuring pendent triazenes and triazoles were successfully prepared using this two-step protocol.

Finally, we turned our attention toward studying the thermal stability of the polystyrenes containing pendent triazeno moieties using thermogravimetric analysis (TGA). Surprisingly, despite the relatively high nitrogen content of polymer **5** (15.1 wt %), the material was found to be stable up to 135 °C (under nitrogen). As shown in Figure 2, a 5.5% weight loss was observed at this temperature which was attributed to the evolution of molecular nitrogen. This was in accord with our small molecule studies where the triazeno groups were found to cleanly decompose to their respective guanidines at 120 °C in solution.[8] Thus, attention shifted toward using this nitrogen-extrusion process as a method for preparing polyolefins containing pendent guanidines. Heating a sealed THF solution of polymer **5** at 135 °C for 6 h followed by evaporation of solvent afforded the corresponding polymer **8**. Although the ^{1}H NMR spectrum of **8** was nearly identical to **5** and molecular weight characteristics were essentially unchanged, evidence for clean decomposition was obtained from elemental analyses which revealed a 5.53% difference in nitrogen content (theoretical: 5.46%) between polymers **5** and **8**.

In summary, the coupling reaction between NHCs and azides to afford triazenes has been shown to be a practical and versatile method for the postpolymerization modification of polyolefins. In particular, we found that polystyrenes containing pendent azides were successfully functionalized upon simple addition of a readily available NHC. The catalyst-free NHC−azide coupling reaction was found to be rapid and quantitative at ambient temperature, manifesting in a linear correlation between polymer modification and quantity of NHC added. The versatility of this postpolymerization modification method was demonstrated by adding free carbenes to a partially modified polystyrene containing pendent triazoles and residual azides which afforded a random copolymer bearing two distinct functional groups. Finally, it was found that heating NHC-modified poly(*p*-azidomethylstyrene)s resulted in nitrogen extrusion and transformed pendent triazeno moieties to their respective guanidines.

We believe this NHC−azide coupling reaction complements click and other emerging reactions that utilize azides to generate new functionalities and unique materials.[18] Considering the large number of biomedical, synthetic, and materials applications for triazenes[19] and guanidines,[20] the use of azides in conjunction with NHCs offers unique avenues to access these important functional groups and creates new opportunities within these respective fields.

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Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) NHC **4** can be generated in situ from its corresponding imidazolium salt and then immediately used to modify polymer **3** (see Supporting Information for additional details). One drawback to this approach, however, is that removal of inorganic salts from the organic product is necessary. This can be accomplished by dissolving polymer **5** in a minimal amount of ethanol, removing the inorganic salts via filtration, and then pouring the filtrate into excess hexanes causing the organic polymer to precipitate.

(16) The polymer obtained after adding 1.25 mol equiv of NHC **4** to **3** showed no appreciable difference in molecular weight when compared to the polymer obtained by using an equimolar amount of these reagents (Figure 1B).

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