Step-Growth "Click" Coupling of Telechelic Polymers Prepared by Atom Transfer Radical Polymerization

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Introduction. The methods of controlled/living radical polymerization (CRP)[1] developed in the past decade allow for the preparation of not only polymers with predetermined molecular weight and narrow molecular weight distribution but also a plethora of previously unattainable polymeric materials. Numerous examples of gradient[2] and block[3] copolymers have been reported as well as polymers with complex architectures, including polymer brushes,[4] stars,[5] and hyperbranched[6] polymers. The most widely used CRP methods are atom transfer radical polymerization (ATRP),[7−9] reversible addition−fragmentation chain transfer (RAFT) polymerization,[10,11] nitroxide-mediated polymerization,[12,13] and degenerative transfer polymerization.[14] Importantly, the polymers produced by ATRP contain terminal halogen atom(s) and can be successfully derivatized in various end group transformations, chiefly nucleophilic substitutions. The use of functional initiators makes it possible to prepare either homo- or heterotelechelic polymers.[15] Thus, ATRP is an attractive technique for the synthesis of well-defined end-functionalized polymers.

The nucleophilic substitution of a halogen atom from a polymer chain end by an azide anion[16,17] is very efficient and, when followed by reduction, leads to amino-terminated polymers. Organic azides can be used for a variety of chemical transformations.[18,19] Cycloaddition reactions with alkynes, thoroughly studied by Huisgen,[20,21] produce a mixture of substituted triazoles. When the reaction is carried out in the presence of a catalytic amount of Cu^I complexes, it yields 1,4-disubstituted triazoles exclusively.[22,23] This reaction along with other 1,3-dipolar cycloadditions (such as the reaction between azides and nitriles catalyzed by Lewis acids) and other high-yield reactions are often termed "click reactions".[24] Click-type synthetic procedures are attractive because of their near quantitative yields and low susceptibility to side reactions. As such, they are particularly important in preparative methods in which high conversion of functional groups is desirable, e.g., in step-growth polymerization processes. Some click reactions have already been successfully used in polymer and materials chemistry. The efficient preparation of well-defined polymeric tetrazoles,[25] or dendrimers,[26] amphiphilic block copolymers,[27] cross-linked block copolymer vesicles,[28] and adhesives[29] with triazole units has been reported. Click reactions were also used in the synthesis of functionalized poly(oxynorbornenes)[30] and block copolymers[31] and are a convenient alternative to other coupling reactions applied to polymers prepared by ATRP (such as atom transfer radical coupling[32] or reversible thiol oxidative coupling[33]) for the preparation of high molecular weight polymeric materials.

Herein, we describe the synthesis of homo- or heterotelechelic polymers and their efficient step-growth click coupling in the presence of CuBr. A one-pot ATRP−nucleophilic substitution−click coupling process is reported as well.

Experimental Section. An ATRP initiator containing an acetylene functionality was prepared by reacting propargyl alcohol with 2-bromoisobutyric acid in the presence of dicyclohexyl carbodiimide. The resulting initiator, propargyl 2-bromoisobutyrate (PgBiB), was used to prepare heterotelechelic polystyrene (polySty) by ATRP ([Sty]:[PgBiB]:[CuBr]:[*N,N,N′,N″,N″*-pentamethyldiethylenetriamine (PMDETA)] = 40:1:1:1, 11 vol % phenyl ether, 90 °C, 75 min). The resulting α-alkyne-ω-bromo-terminated polystyrene (M_n = 2590 g/mol, M_w/M_n = 1.12) was reacted with NaN_3 in DMF to yield the corresponding α-alkyne-ω-azido-terminated polystyrene. This "monomer" was then click coupled in DMF at room temperature in the presence of CuBr.

A one-pot ATRP−nucleophilic substitution−click coupling process was achieved by (i) initiating Sty ATRP with PgBiB ([Sty]:[PgBiB]:[CuBr]:[PMDETA] = 76:1:0.25:0.25, 44 vol % toluene, 80 °C, 200 min, M_n = 960 g/mol, M_w/M_n = 1.04), (ii) quenching the polymerization by freezing with liquid nitrogen, (iii) adding NaN_3, ascorbic acid, and DMF, and (iv) equilibrating to room temperature. The monomer conversion of the ATRP reached 13% prior to addition of the subsequent reagents, and the click reaction was allowed to proceed for 116 h.

α,ω-Dibromo-terminated polystyrene was prepared by ATRP of Sty with a difunctional initiator ([Sty]:[dimethyl 2,6-dibromoheptadioate (DM-2,6-DBHD)]:[CuBr]:[PMDETA] = 74:1:0.5:0.5, 40 vol % toluene, 80 °C, 140 min). The resulting polySty (M_n = 1900 g/mol, M_w/M_n = 1.09) was isolated, purified, and reacted with NaN_3 in DMF at room temperature to α,ω-diazido-terminated polystyrene. After purification and isolation, this product was reacted with propargyl ether in DMF at room temperature with a CuBr catalyst.

Results and Discussion. The synthetic strategies used to prepare high molecular weight polystyrene by step-growth click coupling are presented in Scheme 1. Mono- and dibromo-terminated polystyrene of low molecular weight were synthesized by ATRP using CuBr/PMDETA as the catalyst and PgBiB or DM-2,6-DBHD as the initiators, respectively. In the former case, the polymer also contained an acetylene end group, which could be used for further click coupling. The ATRP reactions were stopped at relatively low monomer conversion to ensure a high degree of bromine end-functionality.[34,35] The reactions of the polymers with sodium azide yielded the corresponding azido-terminated polymers. Based on ^{1}H NMR spectroscopy, the nucleophilic substitution was complete within several hours (Figure 1).

The α-alkyne-ω-azido-terminated polystyrene "monomer" was then self-coupled in the presence of CuBr in DMF at room temperature. Since CuBr exhibits sufficient solubility in DMF, addition of no extra ligand was necessary to achieve efficient coupling. The only precaution taken was that the reaction was performed under

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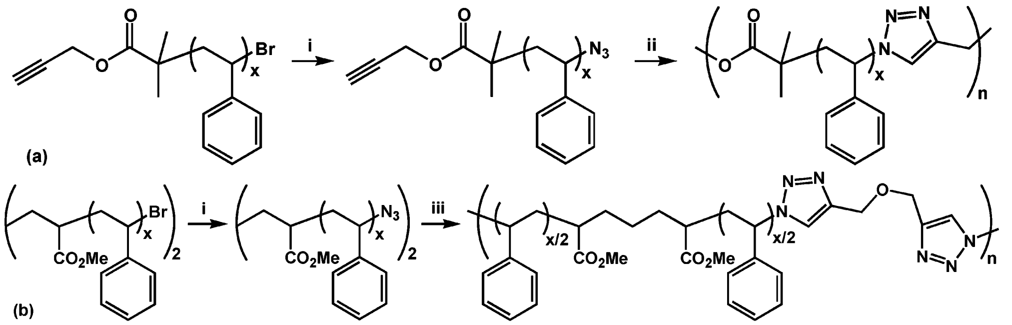
Scheme 1. Click Coupling Reactions Using Telechelic Polymers Prepared by ATRP: (a) Synthesis of α-Acetylene-ω-azido-Terminated Polystyrene and Its Subsequent Homocoupling and (b) Synthesis of Diazido-Terminated Polystyrene and Its Coupling with Propargyl Ether[a]



[a] Reaction conditions: (i) NaN_3 in DMF, room temperature, 4 h; (ii) CuBr in deoxygenated DMF, room temperature; and (iii) propargyl ether and CuBr in deoxygenated DMF, room temperature.

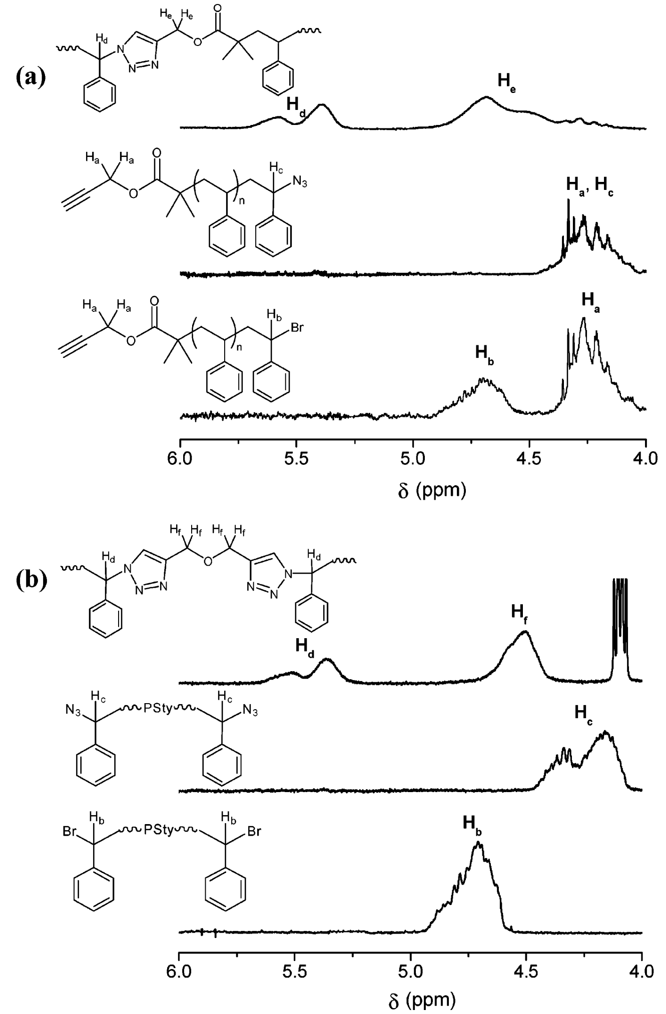


Figure 1. ^{1}H NMR spectra of (a) α,ω-heterotelechelic polystyrene and its click coupled product and (b) α,ω-homotelechelic polystyrene and the corresponding product after click coupling with propargyl ether.

a nitrogen atmosphere in order to avoid air oxidation of the Cu^I compound. Figure 2a shows the evolution of the SEC traces with time.

As seen in Table 1, the click coupling of the parent α-alkyne-ω-azido-terminated polystyrene (M_n = 2590 g/mol, M_w/M_n = 1.11) resulted in a polymer of high molecular weight (M_n = 21 500 g/mol) and broad molecular weight distribution (M_w/M_n = 4.85), as expected for a step-growth process. While the amount of high molecular weight polymer in the mixture increased, not all of the starting material appeared to be consumed. The elution volume of the low molecular weight fraction in the product was slightly higher than the starting material, possibly indicating that cyclization occurred. The hydrodynamic volume of the cyclic product obtained by intramolecular self-coupling should be lower than the parent polymer, and thus a lower apparent SEC molecular weight is expected. The high extent of cyclization may be a result of DMF being a rather poor solvent for polySty,[36] since the propensity for intramolecular reaction is increased for a compact coil. The remaining low molecular weight material present at even long reaction times (Table 1a) served as further evidence of cyclization. After 14.5 h, the low molecular weight peak constituted 18% of the total area of the SEC trace and essentially remained constant even after 89 h of reaction time. Meanwhile, the coupling products continuously increased in molecular weight, indicating that the conditions were still appropriate for the reaction to take place and the activity of the CuBr catalyst was preserved. The reaction was stopped at this point, and the polymer was analyzed by ^{1}H NMR spectroscopy (Figure 1a). The fraction of residual azido groups in the product was very small, indicating essentially complete "monomer" consumption to either high molecular weight polymer or cyclic product. As evidenced by SEC, a small portion of double molecular weight chains was present in the starting material due to radical−radical termination during ATRP. These chains contain two alkyne end groups and potentially limit the degree of polymerization of the click coupled chains. The alkyne at the chain end may also copolymerize during ATRP, and such a branched product can additionally broaden the molecular weight distribution of the final polymer.

This study also considers the possibility of conducting the ATRP of Sty with an alkyne-containing initiator, end-group substitution with NaN_3, and subsequent click coupling of the resulting heterotelechelic polymers as a one-pot procedure. For this purpose, the ATRP reaction mixture of Sty initiated with PgBiB was cooled in liquid nitrogen, and a mixture of sodium azide and ascorbic acid (to reduce the Cu^{II} complexes formed during the polymerization) was added under a nitrogen atmosphere. The one-pot procedure was less efficient than the click coupling reaction of the isolated materials, as judged by SEC analysis (Figure 2b). Because only a limited amount of high molecular weight product was obtained during the coupling process, we were not able to determine an accurate molecular weight for the

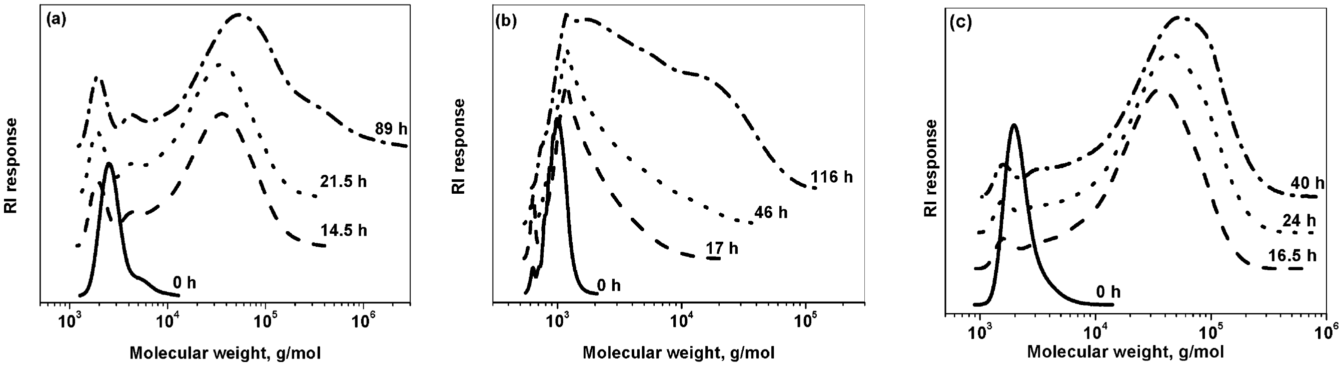


Figure 2. Evolution of the SEC traces during step-growth click coupling of (a) α-alkyne-ω-azido-terminated polySty after its isolation and mixing with CuBr in DMF, (b) the similar reaction performed in one-pot, and (c) a mixture of diazido-terminated polySty with propargyl ether.

Table 1. SEC Data from the Click Coupling of Hetero- and Homotelechelic PolySty

coupling reaction	time (h)	LMW fraction[c] peak area (%)[e]			HMW product[d]	
			$M_{n,app}$[f]	M_w/M_n[f]	M_n[f]	M_w/M_n[f]
a	0	100	2590	1.11		
	14.5	18	1920	1.04	15 500	2.43
	21.5	18	1900	1.04	15 600	2.35
	89	17	1920	1.04	21 500	4.85
b	0	100	2020	1.09		
	16.5	7	1570	1.03	13 700	2.77
	24	7	1540	1.03	14 800	3.15
	40	7	1550	1.03	16 700	3.34

[a] Click coupling of α-alkyne-ω-azido-terminated polySty. [b] Click coupling of α,ω-diazido-terminated polySty with propargyl ether. [c] Low molecular weight fraction of the SEC trace after Gaussian peak fitting. [d] Click coupled polymer—remaining portion of the SEC trace excluding the low molecular weight fraction. [e] Percent of the total SEC trace area. [f] Number-average molecular weight and polydispersity of each molecular weight fraction as determined by SEC (polySty calibration).

coupled products. The decreased rate of reaction in the one-pot process may be a result of competing side reactions between the inorganic azide and the acetylene groups, which would result in N-unsubstituted triazoles and prevent further step growth.[37]

Finally, a click reaction was performed using a 1:1 mixture of diazido-terminated polystyrene and propargyl ether (Table 1b). After the addition of the acetylene derivative to the solution of polymer and CuBr in DMF, the reaction mixture became bright yellow and turbid due to formation of a Cu^I−alkyne complex. After 20−30 h, there was a noticeable increase in solution viscosity. The molecular weight and polydispersity of the polymer (Figure 2c) increased with time, as in the other step-growth-type polymerization processes discussed above. A polymer with an M_n of 16 700 g/mol and $M_w/M_n = 3.34$ was obtained by click coupling of the α,ω-diazido-terminated polySty with an original M_n of 2020 g/mol and M_w/M_n of 1.09. As in the case of coupling of the heterotelechelic polySty in DMF, a small and constant amount (7%) of polymer of lower apparent molecular weight than the starting material remained in the mixture, most likely a product of cyclization. The portion of polySty that reacted with propargyl ether to form cyclic chains is rendered unreactive; therefore, its concentration as determined by SEC does not appear to change with time, despite the step-growth process continuing to higher molecular weight. No unreacted azide could be seen in the ^{1}H NMR spectrum of the final polymer, proving the high efficiency of click coupling and providing evidence that a cyclic product was most likely formed during the reaction.

Conclusions. Homo- and heterotelechelic polySty oligomers prepared by ATRP were coupled via step-growth click coupling to yield polySty containing 1,2,3-triazole linkages. α-Alkyne-ω-azido-terminated polySty was click coupled at room temperature in DMF with a CuBr catalyst. As a result of the click reaction being conducted in DMF, no additional ligand was necessary to solubilize the CuBr catalyst. Additionally, because both ATRP and azide−alkyne click reactions are catalyzed by Cu^I compounds, a one-pot ATRP−nucleophilic substitution−click coupling process was attempted. So far, this approach has led to only moderate success. Another method involved α,ω-diazido-terminated polySty being polymerized with propargyl ether at room temperature to yield higher molecular weight polySty. In all cases, the resulting click coupled polySty was polydisperse with moderate to high molecular weight.

SEC and ^{1}H NMR spectroscopy indicated the possibility of an intramolecular click reaction to yield cyclic polymers in DMF. This phenomenon is currently under further investigation and will be the subject of a future publication.

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Supporting Information Available: Procedures for the preparation of propargyl 2-bromoisobutyrate and homo- and heterotelechelic polystyrenes and their step-growth click coupling. This material is available free of charge via the Internet at http://pubs.acs.org.

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