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Communications to the Editor

Benzyl Acetate and Benzyl Ether Groups as Latent Initiator Sites for Atom Transfer Radical Polymerization

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Synthetic approaches to structurally defined, architecturally complex macromolecules usually involve modular synthesis: assembling or constructing individual subunits using a series of separate and controllable steps. Such a process using controlled/living radical polymerizations[1−3] was demonstrated in the synthesis of dendrigraft polymers,[4] in which a nitroxyl radical-mediated polymerization was used to form a copolymer backbone that contained initiator sites for atom transfer radical polymerization (ATRP). The fact that the pendant initiator sites in the monomer were not cross-reactive with the conditions used to prepare the polymer backbone allowed for the modular construction of the macromolecule. A different variant that allowed both the backbone and grafts to be prepared at the same time was the simultaneous use of controlled/living radical and ring-opening polymerizations that did not exhibit cross-reactivity.[5,6] An additional challenge is encountered if one wants to use only one type of controlled/living radical polymerization to construct each part of the macromolecule in a modular fashion. The ATRP of monomers containing pendant ATRP initiation sites leads to branched or hyperbranched polymers.[7,8] To form a graft polymer, the graft initiation sites must be masked in order to prevent premature initiation during the preparation of the parent polymer backbone. These latent initiation sites could be transformed at a later time during the synthetic sequence to provide the desired graft initiation sites. One procedure recently reported involved the polymerization of a monomer containing a protected hydroxyl group, and after formation of the parent backbone the hydroxyl group was deprotected and derivatized to form the ATRP initiation sites.[9] We report the use of benzyl acetates and benzyl ethers as latent initiation sites for ATRP. These functional groups are inert under ATRP conditions, yet can be transformed directly into ATRP initiation sites when needed. To demonstrate this concept, we present an example synthesis of well-defined styrene graft copolymers using sequential ATRP polymerizations.

The monomers used in this study, 4-acetoxymethylstyrene (**1**),[10] and 4-methoxymethylstyrene, (**2**),[11] were selected because the functional groups contained within these monomers are inert under ATRP conditions yet can be transformed into benzyl halide ATRP initiation sites. Monomers **1** and **2** were copolymerized[12] with styrene using typical ATRP conditions (eq 1, Scheme 1): 10−20 mol % of monomer **1** or **2** relative to styrene was heated at 110 °C with 1-phenylethyl bromide (1-PEBr) and the complex of copper(I) bromide with 2 equiv of 2,2′-bipyridine (bipy) or 4,4′-di-(5-nonyl)-2,2′-bipyridine (dNbipy) (Table 1).[13] Upon workup good yields of copolymer were obtained. Molecular weight measurements (GPC)[14] showed that the final molecular weights of the copolymers were close to those expected on the basis of the polymerization conversion and the initial ratio of monomer to initiator ($DP_n = [M]_0/[I]_0 \times p$, where p = conversion), and the molecular weight distributions were narrow: $M_w/M_n < 1.2$. IR spectra of the styrene/monomer **1** copolymer showed signals at the characteristic stretching frequencies for an acetate group ($\nu_{C=O}$ at 1741 cm^{-1}, ν_{C-O} at 1240 cm^{-1}). Also, ^1H NMR spectra of the styrene/monomer **1** copolymer showed diagnostic signals for the acetoxymethyl group at 5.0 ppm ($-CH_2$-$OCOCH_3$) and 2.1 ppm ($-CH_2OCOCH_3$). The ratio of signal integrations for the methylene protons of these groups with those of either the side chain aromatic protons or the backbone methylene and methyne protons corresponded with expected ratios calculated using the polymerization feed ratio. Similar results were

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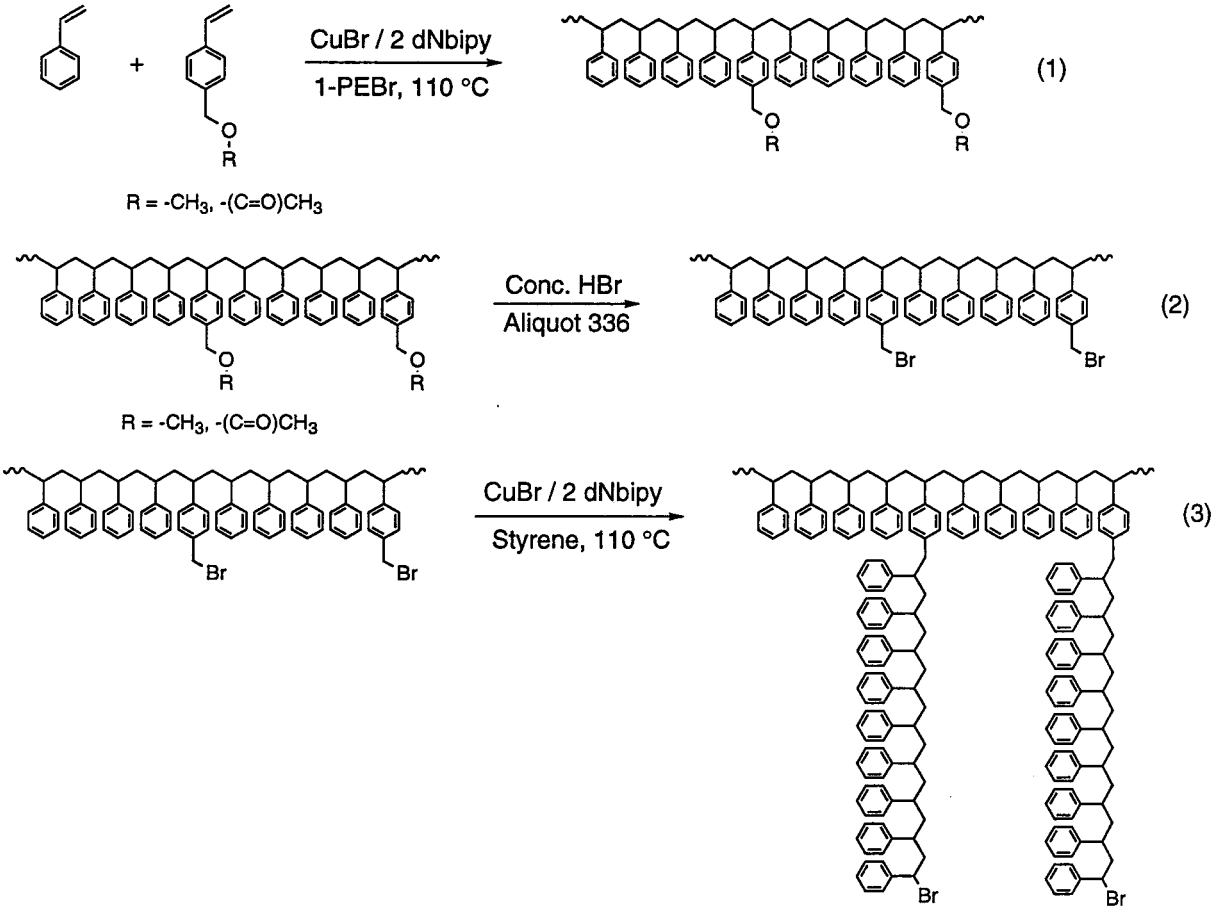
Table 1. Characterization Data for the Copolymerization of Monomers 1 and 2 with Styrene and the Conversion of the Products to the Bromomethyl Group-Containing Copolymers

monomer	mol % monomer in feed	catalyst system	mol % monomer incorporated	M_n	M_w/M_n	M_n after conversion to $-CH_2Br$ groups	M_w/M_n after conversion to $-CH_2Br$ groups
1	10	CuBr/2dNbipy	13	9.80×10^3	1.19	9.60×10^3	1.18
2	15	CuBr/2bipy	16	4.00×10^3	1.20	3.50×10^3	1.21
2	17	CuBr/2dNbipy	16	8.90×10^3	1.08	9.00×10^3	1.08

Scheme 1



obtained for the copolymerization of monomer **2** with styrene. The reactivity ratios of monomers **1** and **2** with styrene were not determined; however, alkyl substitution at the 4-position of styrene results in only a small change in the absolute rate constant of radical propagation ($k_p^\bullet$ styrene (30 °C) = 110 M^{-1} s^{-1}; $k_p^\bullet$ 4-methylstyrene (30 °C) = 84 M^{-1} s^{-1}).[15] With such similar reactivities, these comonomer pairs most likely form a copolymer with a random distribution of the two repeat units.

With the polymer backbone thus formed, the acetoxymethyl or methoxymethyl functional groups were converted to bromomethyl groups (eq 2, Scheme 1).[16] A toluene solution of either copolymer was heated at 70 °C with concentrated HBr and a catalytic amount of Aliquot 336, a phase transfer catalyst that served to transfer HBr and H_2O into the toluene layer. The reaction involving the acetoxymethyl groups could be monitored using IR spectroscopy. Over time the IR signals for the acetate group in the copolymer decreased, and after isolation, the IR spectrum of the product showed no signals corresponding to either an acetate or hydroxyl group. The ^1H NMR spectrum of the product showed that the signals for the acetate methyl and intervening methylene group protons were absent, and a new signal had appeared at 4.4 ppm, corresponding to the chemical shift of the methylene protons in benzyl bromide. Additionally, the ^{13}C $\{^1H\}$ spectrum showed a new signal at 34.3 ppm also diagnostic for the $-CH_2Br$ group. Molecular weight measurements showed that, within experimental error, the number-average molecular weight and molecular weight distribution of the new copolymer were the same as those of the starting copolymer. These data support the conclusion that, within detectable limits, the acetoxymethyl groups of the starting copolymer had been converted to bromomethyl groups. Similar results were obtained starting with methoxymethyl functional groups.

With the latent initiation sites converted to ATRP initiation sites, the copolymers were used to initiate the growth of graft copolymers (eq 3, Scheme 1). Two separate grafting procedures were performed using either CuBr/2 bipy (Figure 1) or CuBr/2 dNbipy as the catalyst system (Figure 2), corresponding to the catalyst system used to prepare the copolymer backbone. To facilitate molecular weight characterization this work was performed using only styrene; however, bromomethylphenyl groups can serve as initiators for methyl

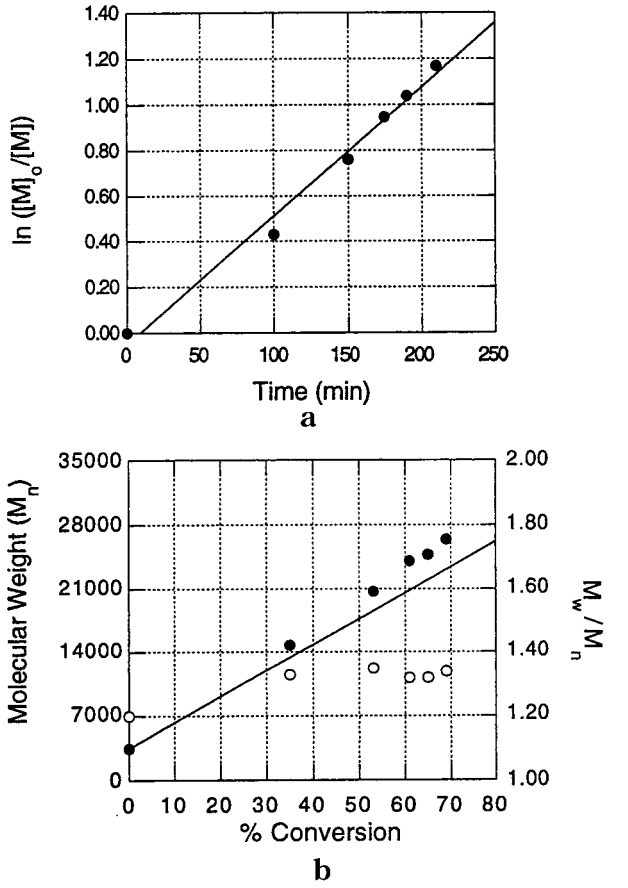


Figure 1. Kinetic and molecular weight plots for the graft polymerization of styrene using CuBr/2bipy. Conditions: temperature = 110 ± 1 °C; solvent = *p*-xylene; $[-CH_2Br]_0 = 0.192$ M; $[\text{styrene}]_0 = 6.5$ M; $[\text{CuBr}]_0 = 0.223$ M; $[\text{bipy}]_0 = 0.475$ M.

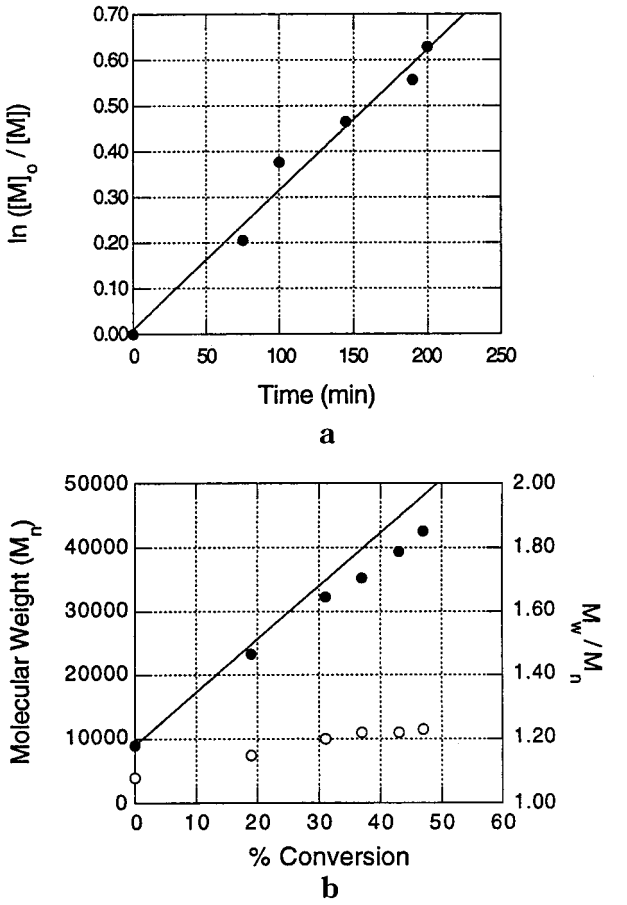


Figure 2. Kinetic and molecular weight plots for the graft polymerization of styrene using CuBr/2dNbipy. Conditions: temperature = 110 ± 1 °C; solvent = *p*-xylene; $[-CH_2Br]_0 = 0.118$ M; $[\text{styrene}]_0 = 6.70$ M; $[\text{CuBr}]_0 = 0.124$ M; $[\text{dNbipy}]_0 = 0.284$ M.

acrylate and methyl methacrylate polymerization.[17,18] Thus, well-defined polystyrene backbones with different graft compositions should be accessible using this method.

In both cases the first-order kinetic plots showed linear fits typical for styrene ATRP, indicating that the concentration of radicals was constant during the course of the polymerization and that chain termination was not prominent. The faster rate of polymerization for the bipy grafting reaction versus the dNbipy reaction is reflective of the differences in initial concentrations of copper(I) and initiator. In both cases the molecular weight (M_n) of the graft polymer increased in a linear fashion as a function of conversion while the molecular weight distributions remained narrow, both hallmarks of a controlled/living polymerization process.

The final graft polymers contained, on average, 8 (bipy) or 14 (dNbipy) branch points and therefore were not densely branched. Still, the molecular weights of these graft polymers should be underestimated somewhat, because the GPC was calibrated using linear polystyrene standards. In the molecular weight versus conversion plots there were two notable differences. First, the molecular weight distributions for the bipy grafting system were higher than those for the dNbipy grafting system. This is typical for the Cu(I)-catalyzed ATRP of styrene and is primarily accounted for by the lower solubility of the Cu(II) deactivator in the monomer.[3] Second, the molecular weights of the graft polymers for the bipy system fall above the expected molecular weight line, whereas for the dNbipy system the data lie somewhat below this line. Considering that the molecular weights are underestimated, the actual molecular weights in the bipy system are even higher than the expected molecular weights, and in the dNbipy system the actual molecular weight are either above or coincidental with the expected molecular weights. Inspection of the individual GPC chromatograms reveals that the signals for the bipy samples clearly contain a high molecular weight shoulder. This shoulder is most likely a result of interpolymer coupling, as observed previously in star polymer syntheses using ATRP.[19,20] Again, this difference in molecular weight behavior can be ascribed to the lower solubility of the copper(II) deactivator in styrene for the bipy versus dNbipy catalyst systems. For the dNbipy samples a much smaller shoulder is observed only at higher conversions. Clearly, the bipy grafting process was less controlled than the dNbipy grafting process even though the latter macroinitiator had a greater number of initiator sites per polymer chain.

In conclusion, monomers **1** and **2** were copolymerized with styrene using ATRP to yield well-defined copolymers. The acetoxymethyl or methoxymethyl functional groups in the copolymer were converted to bromomethyl groups using a phase-transfer catalyzed reaction. The copolymers containing the bromomethyl units were used as macroinitiators for styrene ATRP, and the resulting graft copolymers had narrow molecular weight distributions: $M_w/M_n \leq 1.3$. The use of latent initiation sites for ATRP is a synthetic strategy that may be applied to

the preparation of macromolecules with more complex architectures, such as in the preparation of graft copolymers with arms of two or more different compositions (this work is in progress).

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Supporting Information Available: Experimental procedures and characterization data for the copolymerization of monomer **2** with styrene using bipy or dNbipy, for the conversion of the resulting copolymers to bromomethyl group-containing copolymers, and for the graft polymerization of styrene from both copolymer backbones. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) 4-Acetoxymethylstyrene: 4-vinylbenzyl chloride (5.00 mL, 5.42 g, 35.5 mmol) and 5.11 g (62.3 mmol) of sodium acetate were added to 20 mL of dimethylformamide. The mixture was stirred and heated at 70 °C using an oil bath. After 24 h the solution was diluted with 50 mL of water and 100 mL of diethyl ether. The organic layer was separated and extracted with 3 × 50 mL of water. The organic layer was dried over $MgSO_4$, and volatile materials were removed under vacuum. The crude product was distilled at 55 °C and 20 mTorr, yielding 4.99 g (80%) of a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.29 (m, 4H), 6.65 (dd, J = 17 and 11 Hz, 1H), 5.71 (d, J = 17 Hz, 1H), 5.20 (d, J = 11 Hz. 1H), 5.03 (s, 2H), 2.00 (s, 3H). IR (neat): ν (cm^{-1}) 1742 ($\nu_{C=O}$), 1630 ($\nu_{C=C}$). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 170.1, 137.1, 136.0, 135.2, 128.1, 125.9, 113.7, 65.4, 20.4.
(11) 4-Methoxymethylstyrene: 4-vinylbenzyl chloride (21.0 mL, 22.7 g, 0.149 mol) and 24.4 g (0.452 mol) of sodium methoxide were added to 120 mL of anhydrous dimethylformamide. The mixture was stirred under nitrogen and heated at 70 °C using an oil bath. After 18 h the solution was diluted with 100 mL of water and 100 mL of diethyl ether. The organic layer was separated and extracted with 3 × 100 mL of water. The organic layer was dried over $MgSO_4$, and volatile materials were removed under vacuum. The crude product was distilled at 40 °C and 100 mTorr, yielding 14.6 g (73%) of a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.4 (m, 4H), 6.7 (dd, J = 12 and 9 Hz, 1H), 5.8 (d, J = 15 Hz, 1H), 5.2 (d, J = 9 Hz, 1H), 4.45 (s, 2H), 3.4 (s, 3H). IR (neat): ν (cm^{-1}) 1630 ($\nu_{C=C}$). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 136.9, 136.5, 127.8, 126.1, 125.4, 113.6, 74.3, 57.9.
(12) For example, the ATRP copolymerization of 4-acetoxymethylstyrene with styrene. A 25 mL Schlenk flask was loaded with 4.00 mL (34.9 mmol) of styrene, 10 mol % of 4-acetoxymethylstyrene (0.684 g, 3.88 mmol), 53.0 μL of 1-phenylethyl bromide (0.39 mmol), 56 mg of CuBr (0.39 mmol), and 0.318 g of dNbipy (0.78 mmol). The flask was fitted with a glass stopper, and the solution was degassed by three freeze−pump−thaw degas cycles. The flask was placed in an oil bath thermostated at 110 °C for 16 h Afterward, the contents were dissolved in THF and precipitated using CH_3-OH. The precipitate was filtered, and volatile materials were removed under vacuum yielding 3.19 g (74%) of a colorless solid. SEC (THF): M_n = 9.80 × 10^3, M_w/M_n = 1.19 ($M_{n,calc}$ = 8, 240). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.1 (br, aromatic ring H's), 6.5 (br − 2 maxima signal, aromatic ring H's), 5.11 (br, $-CH_2-$ of acetoxymethyl unit), 2.17 (br, acetate CH_3), 1.8 (br, backbone H's), 1.4 (br, backbone H's). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 145.9, 128.0 (broad signal), 125.9, 66.6 (small signal, $-CH_2O_2CCH_3$), 46.2−40.6 (broad multiline signal), 21.5 (small signal, $-CH_2O_2CCH_3$). IR (neat): ν (cm^{-1}) 1741 ($\nu_{C=O}$), 1240 (ν_{C-O}).
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(14) Number-averaged molecular (M_n), weight-averaged molecular weights (M_w), and molecular weight distributions (M_w/M_n) were determined using gel permeation chromatography in THF at 30 °C (flow rate = 1.00 mL min^{-1}). Three Polymer Standards Services columns (100 Å, 1000 Å, linear) were connected in series to a Thermoseparation Products P-1000 isocratic pump, autosampler, column oven, and a Knauer refractive index detector. Calibration was performed using linear polystyrene standards (Polymer Standard Services; M_p = 300−1 000 000; M_w/M_n < 1.10).
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(16) For example, the conversion of the benzyl acetate-containing copolymer to bromomethyl-containing copolymer (also see Supporting Information): This procedure is based upon: Landini, D.; Montanari, F.; Rolla, F. *Synthesis* **1978**, 771−773. In a 50 mL round-bottom flask with stir bar and West condenser, 1.03 g (1.47 mmol of acetoxymethyl groups) of the 4-acetoxymethylstyrene/styrene copolymer and 57.6 mg (0.143 mmol) of Aliquat 336 were dissolved in 15 mL of toluene. To this solution was added 10 mL (87.8 mmol) of concentrated HBr, and the solution was stirred and heated at reflux. The reaction was monitored by recording IR spectra of aliquots of the toluene layer and observing the disappearance of $\nu_{C=O}$ 1741 cm^{-1}. After 14 h the reaction was complete. The toluene layer was separated and added to 50 mL of CH_3OH. The colorless precipitate was filtered, and volatile materials were removed under vacuum yielding 0.597 g (59% recovery) of a colorless solid. SEC (THF): M_n = 9.60 × 10^3, M_w/M_n = 1.18. ^{1}H NMR ($CDCl_3$): δ (ppm) 7.1 (br, aromatic ring H's), 6.5 (br − 2 maxima signal, aromatic ring H's), 4.4 (br, $-CH_2Br$), 1.8 (br, backbone CH's), 1.4 (br, backbone CH_2's). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ (ppm) 145.3, 129−128 (broad signal) 125.9, 46−40 (broad multiline signal), 34.3 (small signal, $-CH_2Br$). IR (neat): ν (cm^{-1}) 1741 absent, 1240 absent, ν_{O-H} absent).
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