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Boronic Acid-Terminated Polymers: Synthesis by RAFT and Subsequent Supramolecular and Dynamic Covalent Self-Assembly

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ABSTRACT: Well-defined homopolymers and block copolymers with boronic acid-functional end groups were prepared by reversible addition−fragmentation chain transfer (RAFT) polymerization and subsequently investigated for the potential to undergo model supramolecular and dynamic covalent self-assembly in aqueous and organic media. By employing a boronic acid-functionalized RAFT chain transfer agent, end-functional polymers were prepared without recourse to postpolymerization functionalization. The polymerizations of styrene, *N*,*N*-dimethylacrylamide, and *N*-isopropylacrylamide all led to homopolymers of controlled molecular weight that were capable of subsequent chain extension to form well-defined block copolymers. The amphiphilic and stimuli-responsive block copolymers were capable of self-assembly into micellar aggregates. Quantitative retention of the boronic acid chain termini during polymerization was spectroscopically demonstrated, and two types of dynamic covalent transformations involving these moieties were investigated. The formation of boronic esters with a model 1,2-diol proved to be a highly efficient process in nonaqueous media. Additionally, Lewis base-promoted trimerization of the boronic acid end groups led to three-arm star polymers with boroxine junction points. Both of these covalent interactions were readily reversible upon the introduction of water, suggesting the potential application of these polymers to construct dynamic covalent macromolecular assemblies.

Introduction

To compliment the versatility and dynamics of supramolecular polymers, advanced materials can also be constructed via reversible covalent interactions.[1] As compared to supramolecular assemblies that rely on intermolecular forces, dynamic covalent systems have enhanced stability while maintaining the potential for dynamics, self-assembly, and self-repair. The formation of boronic esters by reaction of boronic acids and diols is a classic example of a process that occurs by reversible covalent bond formation.[2] To employ this particular interaction to prepare covalent macromolecular assemblies with the dynamics of supramolecular systems, it is advantageous to incorporate boronic acid moieties within polymeric or monomeric structures to allow subsequent reversible assembly or polymerization with multifunctional diols. For instance, Lavigne and co-workers have prepared self-repairing and blue-emissive poly(dioxaborole)s and other advanced macromolecular structures by the polymerization of multifunctional boronic acid and diol monomers,[3−7] and Mikami and Shinkai[8,9] and Shimizu et al.[10] reported the polymerization of diboronic acids with multisaccharide-containing species to form macromolecules via boronate ester formation.

While there are reports of well-defined, controlled molecular weight polymers containing pendant boronic acid groups,[11−15] fewer have considered the synthesis of polymers with boronic acid end groups.[16] Metallocene,[17] metathesis,[18,19] and living cationic polymerization[20−22] have been employed to incorporate terminal organoboron functionality, generally by initiation with or chain transfer to a boron-containing compound, though few have resulted in specifically boronic acid-terminated polymers.

In addition to providing control over molecular weight, molecular weight distribution, and macromolecular chain topology, controlled radical polymerization (CRP) techniques facilitate the synthesis of a diverse range of (co)polymers with predetermined end groups that are particularly useful for preparing, for example, block copolymers, bioconjugates,[23−27] fluorescently labeled chains,[28,29] and surface-immobilized polymers.[30,31] Two major strategies exist to incorporate or manipulate reactive α- or ω-end groups of polymers prepared by CRP. The first method involves postpolymerization modification of the ω-end groups that inherently result by virtue of the polymerization chemistry being employed. For instance, modification of halogen end groups on polymers prepared by atom transfer radical polymerization[32,33] by nucleophilic substitution or electrophilic addition has proven to be an excellent means to incorporate a range of additional functionality.[34] Similarly, reduction, aminolysis, or hydrolysis of thiocarbonylthio end groups on the end of polymers prepared by reversible addition−fragmentation chain transfer (RAFT) polymerization[35−37] has resulted in thiol-terminated polymers capable of nanoparticle stabilization,[30] protein conjugation,[38] and modular block copolymer formation.[39] While telechelic polymer synthesis via such postpolymerization modification is quite successful and has recently garnered increased attention resulting from the particular utility and application of various "click" chemistry strategies,[40−51] α-end group functionalization can also be rendered highly efficient and perhaps more straightforward. For instance, polymerization from functional ATRP initiators or RAFT chain transfer agents (CTAs) can lead to near-quantitative incorporation of a desired functionality at the α-end of each chain. Provided the functional moiety is compatible with the polymerization conditions, this approach can reduce the number of postpolymerization steps and lead to polymers with higher degrees of chain end functionality. Additionally, highly efficient conversion of the end groups derived from functional initiators to another desired moiety is an excellent means to incorporate

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specific end groups at the α-chain end by postpolymerization modification. For example, Jakle et al. reported a process of this type by developing a pathway to borane telechelic polymers through ATRP with a trimethylsilyl initiator, followed by efficient end group exchange with BBr_3.[52] Hydrolysis of the resulting $-BBr_2$ end groups led to well-defined boronic acid telechelic polymers capable of reversible covalent self-assembly into stars or networks via boroxine formation.

We have previously reported the synthesis of well-defined boron-containing (co)polymers by RAFT, both by polymerization and subsequent deprotection of boronic ester monomers[13] and by direct polymerization of unprotected boronic acid monomers.[14,15] Herein, we capitalize on the ability of RAFT to facilitate the synthesis of telechelic polymers[53] by employing a functional CTA so that boronic acid groups are directly incorporated without postpolymerization strategies. This new boronic acid-functionalized RAFT agent allowed the controlled polymerization of styrene, *N*,*N*-dimethylacrylamide (DMA), and *N*-isopropylacrylamide (NIPAM) to yield well-defined homopolymers and block copolymers. After successfully confirming retention of the boronic acid chain termini, two types of reversible covalent transformations were investigated. The formation of boronic esters with a model 1,2-diol proved to be a highly efficient and readily reversible process that was conveniently and quantitatively monitored spectroscopically. Moreover, trimerization of the boronic acid end groups facilitated by a Lewis base, a process recently elucidated by Iovine and co-workers,[54−58] led to three-arm star polymers with boroxine junction points. These reactions were chosen to demonstrate the possible application of these polymers for construction of dynamic covalent macromolecular assemblies.

Experimental Section

Materials. DMA (Fluka, 98%) and styrene (Aldrich, 99%) were passed through a column of basic alumina prior to polymerization. 2,2′-Azobis(isobutyronitrile) (AIBN, Sigma, 98%) was recrystallized from ethanol, and NIPAM (TCI America) was recrystallized twice from hexanes. Triethylamine (TEA, EMD Chemicals, 99.5+%), piperidine (Aldrich, >99.5%), 3-bromomethylphenylboronic acid (Boron Molecular), phenylboronic acid (TCI, >97%), 1,3,5-trioxane (Acros, 99.5%), alizarin (TCI America), *N*,*N*-dimethylformamide (DMF, Aldrich, 99.9%), $CDCl_3$ (Cambridge Isotope, 99% D), and acetone-d_6 (Acros, 99.5% D) were used as received. 2-Dodecylsulfanylthiocarbonylsulfanyl-2-methylpropionic acid (DMP) was prepared as previously reported.[59] All other chemicals were purchased from VWR and used without further purification.

Synthesis of 2-Dodecylsulfanylthiocarbonylsulfanyl-2-methylpropionic Acid 3-Boronic Benzyl Ester (1). 3-Bromomethylphenylboronic acid (0.60 g, 2.7 mmol) in anhydrous dimethyl sulfoxide (DMSO, 5.0 mL) was added slowly to a mixture of DMP (1.0 g, 2.7 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.42 g, 2.7 mmol) in anhydrous DMSO (10 mL) over a period of 15 min. The reaction mixture was stirred at 65−70 °C under nitrogen until the starting material disappeared (ca. 5 h). The reaction mixture was poured into cold water (100 mL) and extracted with ethyl acetate (100 mL × 2). The combined organic layers were washed with a saturated aqueous sodium bicarbonate solution (100 mL), deionized water (100 mL), and brine (100 mL). The resulting solution was dried over $MgSO_4$ (2.0 g) and filtered to give **1** as a residual oil (1.2 g, 88%). ^1H NMR (400 MHz, $CDCl_3$, ppm): 8.21−8.19 (d, 2H, J = 3.6 Hz, $C2\boldsymbol{H}{-}Ar$ and $C6\boldsymbol{H}{-}Ar$), 7.61−7.59 (d, 1H, J = 7.26 Hz, $C4\boldsymbol{H}{-}Ar$), 7.54−7.52 (d, 1H, J = 7.27 Hz, $C5\boldsymbol{H}{-}Ar$), 5.28 (s, 2H, $Ar{-}C\boldsymbol{H}_2OCO$), 3.26−3.22 (t, 2H, J=7.3 Hz, $-CH_2{-}CH_2{-}S{-}C{=}S$), 1.77 (s, 6H, $-S{-}C(CH_3)_2{-}CO$), 1.66−1.61 (t, 2H, J= 8.10 Hz, $-CH_2{-}CH_2{-}S{-}C{=}S$), 1.24 (s, 18H, $CH_3{-}C_9H_{18}{-}CH_2{-}CH_2S{-}C{=}S$), 0.91−0.87 (t, 3H, J = 6.10 Hz, $CH_3{-}C_9H_{18}{-}CH_2{-}CH_2S{-}C{=}S$). ^{13}C NMR (100.6 MHz, $CDCl_3$, ppm): 172.8 ($C{=}O$), 135.4 ($\mathbf{C}1{-}B{-}Ph$), 135.3 ($\boldsymbol{C}3{-}Ar$), 135.2 ($\mathbf{C}2{-}Ar$), 135.0 ($\boldsymbol{C}6{-}Ar$), 132.4 ($\boldsymbol{C}4{-}Ar$), 128.1 ($\boldsymbol{C}5{-}Ar$), 67.4 ($Ar{-}C\boldsymbol{H}_2OCO$), 55.8 ($-S{-}\boldsymbol{C}(CH_3)_2{-}CO$), 36.8 ($-CH_2{-}\boldsymbol{C(1)}H_2{-}S{-}C{=}S$), 31.8 ($-\boldsymbol{C(2)}H_2{-}CH_2{-}S{-}C{=}S$), 29.6 ($-\boldsymbol{C(3}$ ***and 4)***$H_2{-}CH_2{-}S$), 29.5 ($-\boldsymbol{C(5)}H_2{-}CH_2{-}S$), 29.4 ($-\boldsymbol{C(6)}H_2{-}CH_2{-}S$), 29.3 ($-\boldsymbol{C(7)}H_2{-}CH_2{-}S$), 29.0 ($-\boldsymbol{C(8)}H_2{-}CH_2{-}S$), 28.9 ($-\boldsymbol{C(9)}H_2{-}CH_2{-}S$), 27.8 ($-\boldsymbol{C(10)}H_2{-}CH_2{-}S$), 25.2 ($-S{-}C(\boldsymbol{C}H_3)_2{-}CO$), 22.6 ($-\boldsymbol{C(11)}H_2{-}CH_2{-}S$), 14.0 ($\boldsymbol{C(12)}H_3{-}C_9H_{18}{-}CH_2{-}CH_2S{-}C{=}S$). IR (KBr, cm^{-1}): 3444 (B−OH), 2924 and 2852 (C−C*s*), 1732 (C=O), 1600 and 1463 (Ar−C=C), 1066 (C=S), 1155 and 817 (C−C*b*). Elemental Analysis. Calculated for $C_{24}H_{39}BO_4S_3$: C, 57.82%; H, 7.88%. Found: C, 57.40%; H, 7.94%.

RAFT Polymerization with 1. Polymerizations were conducted under nitrogen at 70 °C in DMF employing **1** as the RAFT agent and AIBN as the initiator. A representative polymerization procedure for DMA or NIPAM was as follows. DMA (0.600 g, 6.05 mmol), **1** (30.2 mg, 60.5 μmol), AIBN [0.50 mg, 3.0 μmol (0.5 mL of a solution of 4.0 mg AIBN in 4.0 mL of DMF)], DMF (2.9 mL), and trioxane (27.3 mg, 0.303 mmol) were sealed in vial equipped with a magnetic stir bar and purged with nitrogen for 30 min. The reaction vial was placed in a preheated reaction block at 70 °C, and samples were removed periodically by syringe to determine molecular weight and polydispersity index by gel permeation chromatography (GPC) and monomer conversion by ^1H NMR spectroscopy. The polymerization was quenched after a predetermined time by removing the polymerization from heat and exposing the reaction solution to air. After concentration under vacuum, the polymer was precipitated into cold hexanes. The polymer was reprecipitated four additional times from tetrahydrofuran (THF) into ether and dried under vacuum at room temperature for 12 h to yield a yellow powder. The procedure for the RAFT polymerization of styrene was similar except that after the reaction mixture was concentrated under vacuum, the polymer was precipitated (×3) from THF into methanol.

RAFT Block Copolymerization. An example RAFT block copolymerization procedure was as follows. DMA (0.850 g, 8.57 mmol), polystyrene (PSt) macro-chain-transfer agent (macro-CTA) (M_n = 3480 g/mol, M_w/M_n = 1.07) (0.298 g, 85.7 μmol), trioxane (38.6 mg, 0.428 mmol), AIBN [0.70 mg, 4.3 μmol (705 μL of a solution of 4.0 mg AIBN in 4.0 mL of DMF)], and DMF (4.15 mL) were sealed in a vial and purged with nitrogen for 30 min. The reaction vial was placed in a preheated reaction block at 70 °C, and samples were removed periodically by syringe to determine molecular weight, polydispersity index, and monomer conversion as described above. The polymerization was quenched after a predetermined time by removing the polymerization from heat and exposing the reaction solution to air. The resulting $(HO)_2B$-PSt-*b*-PDMA (51% conversion; M_n = 9820 g/mol; M_w/M_n = 1.12) was isolated by precipitation (×3) from THF into ether and drying under vacuum.

Binding of Alizarin with Boronic Acid-Terminated Polymer. In a 2 mL glass vial, boronic acid-terminated polymer (8.8 mg, 2.6 μmol, 1 equiv) was dissolved in anhydrous THF (0.7 mL). Alizarin (2 equiv) and triethylamine (10 μL) were added, and after waiting for 60 min, the mixture was excited with long wavelength UV light. Water (2 drops) was added to this vial, and after 5 min the solution was again exposed to long wavelength UV light. The resulting solution was stirred over molecular sieves overnight, and after filtering, the solution was again irradiated.

Spectroscopic Quantification of Boronic Acid Functionality. Solutions for a Beers law calibration curve were prepared by mixing varying ratios of stock solutions of alizarin, triethylamine, and phenylboronic acid in anhydrous THF to yield final solutions with [alizarin] = 0.50 mM, [triethylamine] = 1.5 mM, and [phenylboronic acid] = 0.1−0.5 mM. The reference

Scheme 1. Reversible Addition−Fragmentation Chain Transfer (RAFT) Homopolymerization and Block Copolymerization of *N*,*N*-Dimethylacrylamide (DMA), Styrene (St), and *N*-Isopropylacrylamide (NIPAM) with a Boronic Acid-Functionalized Chain Transfer Agent (1)

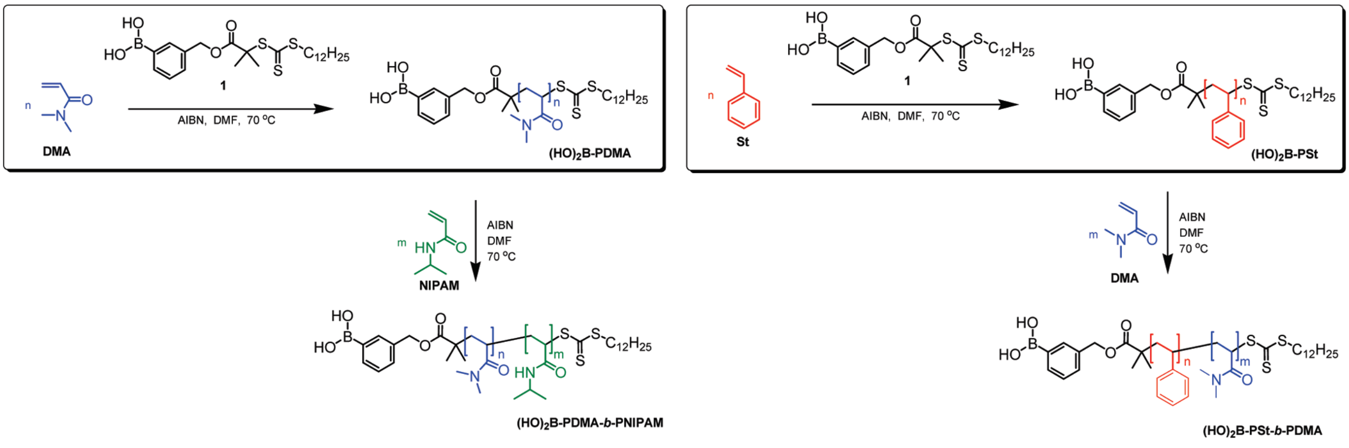


Table 1. Results from Synthesis of (HO)$_2$B-Poly(*N*,*N*-dimethylacrylamide) and (HO)$_2$B-Polystyrene at 70 °C

polymer	[M]/[**1**]/[I][a]	time (min)	conv[b] (%)	$M_{n,GPC}$[c] (g/mol)	M_w/M_n[c]	$M_{n,NMR}$[d] (g/mol)	$M_{n,theo}$[e] (g/mol)
(HO)$_2$B-PDMA	100/1/0.05	250	70.4	7040	1.15	6750	7470
(HO)$_2$B-PDMA	200/1/0.05	250	58.8	11200	1.16	12930	12160
(HO)$_2$B-PDMA	200/1/0.025	420	51.7	9400	1.13	11500	10750
(HO)$_2$B-PSt	100/1/0.3	480	33.8	4420	1.13	3870	4020
(HO)$_2$B-PSt	200/1/0.3	480	23.3	5520	1.12	4950	5350
(HO)$_2$B-PSt	200/1/0.5	420	30.0	7160	1.19	5920	6750

[a] Stoichiometric ratio of monomer/chain transfer agent (**1**)/initiator (AIBN). [b] Monomer conversion as determined by ^{1}H NMR spectroscopy. [c] Determined by gel permeation chromatography. [d] Determined by ^{1}H NMR spectroscopy. [e] $M_{n,theo}$ = ([monomer]$_0$/[**1**]$_0$) × monomer conversion × molecular weight of monomer + molecular weight of **1**). M_n: number-average molecular weight; $M_{n,theo}$: theoretical M_n; M_w: weight-average molecular weight.

spectrum was recorded from a solution of alizarin (0.50 mM) and triethylamine (1.5 mM) in anhydrous THF. Aliquots from the phenylboronic acid stock solutions were added, and after 30 min equilibration, UV−vis spectroscopy was used to measure the absorbance at 495 nm. The measured absorbance and calculated extinction coefficient were used to determine the concentration of boronic acid groups and number-average molecular weight from solutions of known polymer concentration.

Block Copolymer Micellar Solution Preparation. A (HO)$_2$B-PSt-*b*-PDMA block copolymer (25 mg) was dissolved in THF (3.0 mL), and the resulting solution was placed in 1000 molecular weight cutoff dialysis tubing and dialyzed for 42 h against deionized water (18 L) with constant stirring and frequent water changes. The resulting solution was sonicated for 1 h and filtered through a 0.45 μm nylon syringe filter, and dynamic light scattering (DLS) measurements were conducted at 25 °C. (HO)$_2$B-PDMA, (HO)$_2$B-PDMA-*b*-PDMA, and (HO)$_2$B-PDMA-*b*-PNIPAM were dissolved in DI water (1.0 mg/mL) and stirred at room temperature for 24 h to ensure complete dissolution of the polymer. The solutions were transferred to a cuvette, and DLS measurements were carried out.

Boroxine Formation. An example procedure for the formation of boroxine-linked three-armed stars is as follows. (HO)$_2$B-PDMA (M_n = 3580 g/mol; 8.0 mg, 2.2 μmol) was dissolved in a solution of piperidine in acetone-d_6 (0.8 mL, 2.8 mM). The resulting sample was held at room temperature for 1 h before being analyzed by ^{1}H NMR spectroscopy before and after the addition of D_2O (10 μL). The analogous reaction with (HO)$_2$B-PSt was conducted in a similar manner in both acetone-d_6 and $CDCl_3$.

Analyses. GPC was conducted in DMF with 50 mM LiBr at 55 °C with a flow rate of 1.0 mL/min (Viscotek VE 2001 GPCmax; Viscotek VE 3580 (λ = 660 nm), and UV−vis detector (λ = 254 nm); ViscoGel I-series G3000 and G4000 mixed bed columns (0−60 × 10^3 and 0−400 × 10^3 g/mol, respectively). Molecular weight and molecular weight distributions were determined by conventional calibration based on narrow PSt standards. ^{1}H NMR spectroscopy was conducted with a Bruker Avance 400 spectrometer operating at 400 MHz. DLS was conducted with a Malvern Zetasizer Nano-ZS equipped with a 4 mW, 633 nm He−Ne laser and an Avalanche photodiode detector at an angle of 173°. The temperature of the polymer solutions (0.1 wt %) was regulated within an error of ±0.1 °C. UV−vis spectroscopy was conducted with a Beckman Coulter DU 800 spectrophotometer equipped with a Peltier temperature controller. Elemental analysis was conducted with duplicate or triplicate measurements using a ThermoFinnigan CE Elantech model Flash EA1112 elemental analyzer, which was initially calibrated against atropine, acetanilide, nicatinamide, and cyclohexanone−2,4-dinitrophenylhydrazine.

Results and Discussion

RAFT Polymerization of DMA and Styrene. CTA **1** was prepared in high yield by reacting 3-bromomethylphenylboronic acid with DMP. After isolation and purification, the RAFT agent was used to mediate the polymerizations of DMA and St in DMF at 70 °C (Scheme 1). A range of polymerization conditions was employed to determine the effect of reaction stoichiometry on polymerization control (Table 1). In general, the expected relationships were observed, with increasing [monomer]/[**1**] leading to polymers of higher molecular weight and higher concentrations of initiator leading to faster polymerizations. The relative linearity of the pseudo-first-order kinetic plots (Figure 1A,D) indicated a constant concentration of radicals during each polymerization, though polymerizations of styrene demonstrated an induction period that could partially be the result of oxygen or other trace impurities. M_n increased linearly with conversion for all ratios of [monomer]/[**1**]/[AIBN], and

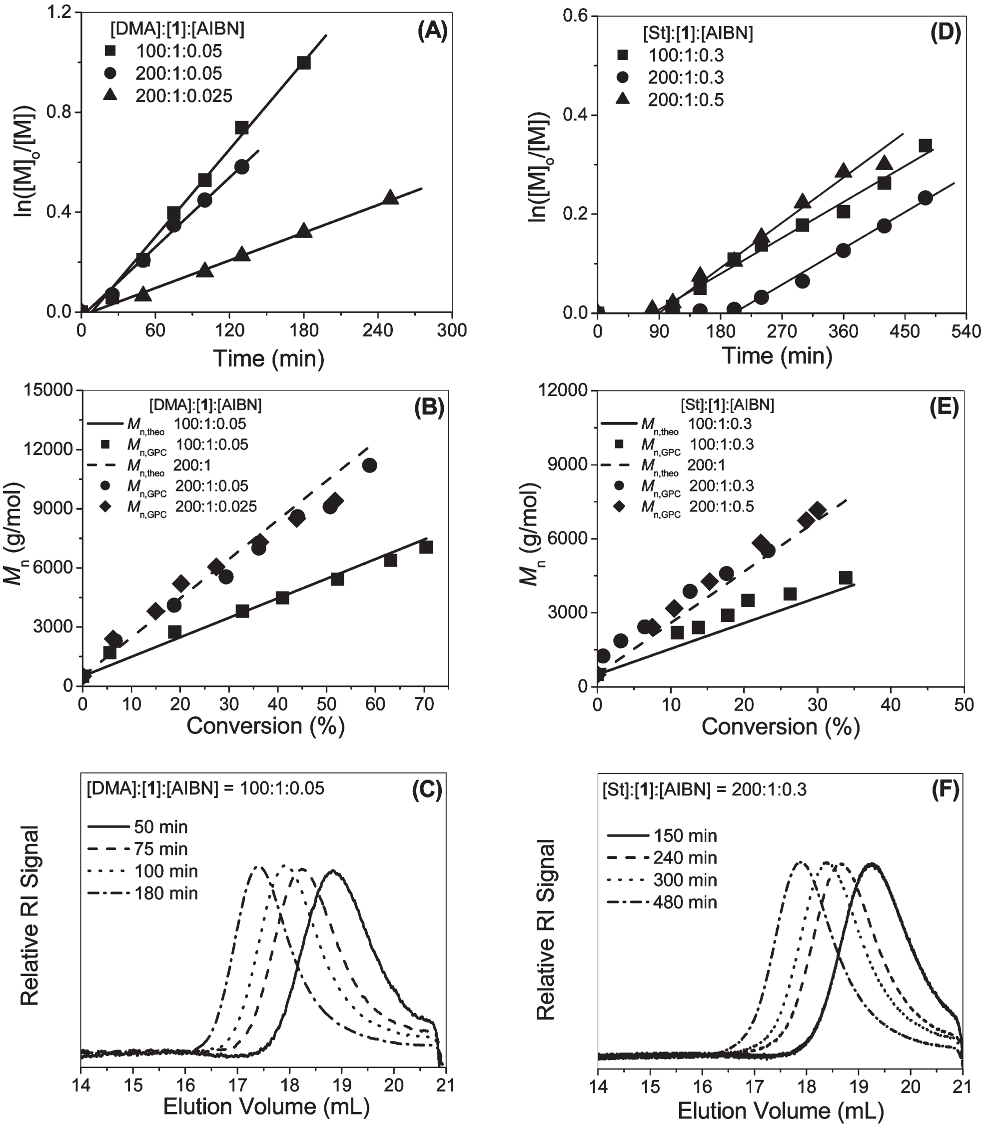


Figure 1. Pseudo-first-order kinetic plot (A, D), number-average molecular weight (M_n) vs monomer conversion (B, E), and gel permeation (GPC) chromatography traces (C, F) for the reversible addition–fragmentation chain transfer (RAFT) polymerization of *N*,*N*-dimethylacrylamide (DMA) (A–C) and styrene (D, F) in the presence of chain transfer agent (CTA) **1**.

the correlation between theoretical and experimental values was excellent throughout the conversion ranges (Figure 1B, E). The homopolymerizations of both monomers resulted in polymer with narrow and unimodal molecular weight distributions, as observed by GPC (Figure 1C,F).

The resulting boronic acid-terminated polymers, $(HO)_2$-B-PDMA and $(HO)_2$B-PSt, were characterized by ^{1}H NMR spectroscopy (Supporting Information). The typical resonance signals for the $-C(=O)-N(CH_3)_2$ protons of PDMA were visible at approximately at 2.8–3.3 ppm, and the main chain $-CH_2-$ and $-CH-$ protons appeared at 1.2–2.1 and 2.3–2.8 ppm, respectively. The dodecyl trithiocarbonate ($-S-C(=S)-S-C_{12}H_{25}$) moiety resulted in characteristic resonances at 0.88 and 3.3 ppm for the terminal $-CH_3$ and the $-S-CH_2-$ protons, respectively. The aromatic protons of the α-terminal phenylboronic acid moiety appeared at 7.3–8.05 ppm. Comparison of the areas from the terminal group and backbone protons allowed calculation of the number-average molecular weight ($M_{n,NMR}$). Similarly, the spectrum of the boronic acid-terminated PSt demonstrated the expected signals with the backbone $-CH_2-$ and $-CH-$ protons appearing at 1.2–2.6 ppm, the monomer unit phenyl signals appearing at 6.3–7.5 ppm, and the terminal phenylboronic acid protons appearing at 7.5–8.3 ppm. Integration of the monomer unit aromatic protons and comparison with the $-S-CH_2-$ signals from the dodecyl end group at 3.29 ppm allowed $M_{n,NMR}$ to be determined. For both polymers, the theoretical, NMR, and GPC molecular weights were in good agreement (Table 1).

Block Copolymerization. To demonstrate ω-chain end retention during the homopolymerizations, block copolymers were prepared by chain extension with a second monomer (Scheme 1). Boronic acid-terminated PSt was copolymerized with DMA. For example, $(HO)_2$B-PSt (M_n = 4950 g/mol, M_w/M_n = 1.13) prepared with CTA **1** was employed as macroCTA for polymerization of DMA with [DMA]/[$(HO)_2$B-PSt macroCTA]/[AIBN] = 100/1/0.05 at 70 °C in DMF. A conversion of 63% was obtained in 5.6 h, resulting in a $(HO)_2$B-PSt-*b*-PDMA block copolymer with M_n = 12 400 g/mol and M_w/M_n = 1.09. GPC analysis of the products demonstrated high blocking efficiency with no evidence of unreacted macroCTA (Figure 2). Extensions of $(HO)_2$B-PDMA with NIPAM and DMA were similarly effective. NMR spectra of the block copolymers demonstrated the expected peaks of each constituent block, but it was difficult to determine an accurate $M_{n,NMR}$ because of significant peak overlap. However, there was reasonable agreement between the theoretical molecular weight and the M_n determined by GPC.

Spectroscopic Analysis of Boronic Acid End Groups. The identity of the end groups were further confirmed by UV−vis spectroscopy. All homopolymers and block copolymers demonstrated the expected absorption at $\lambda_{max} \approx 310$ nm, indicating retention of the ω-trithiocarbonate moiety during polymerization (Supporting Information). Perhaps more importantly, α-chain end identity (i.e., retention of the boronic acid moiety) could be confirmed by reaction with the dye alizarin. In the presence of boronic acids or boronates, the catechol portion of alizarin forms a boronic ester or boronate ester, respectively, which emits orange fluorescence upon excitation with long-wavelength UV irradiation.[60,61] For this reason, it has been employed to detect the presence and concentration of boronic acids in solution. Boronic esters are generally stable in anhydrous organic media but susceptible to hydrolysis in the presence of trace amounts of water. A Lewis base (e.g., triethylamine) is often used to enhance the stability of the boronic acid−alizarin complex.[62,63]

Upon long-wavelength UV irradiation, anhydrous THF solutions of alizarin and polymer prepared from **1** emitted the expected orange fluorescence (Figure 3). This observation both qualitatively confirms the presence of boronic acid moieties and also demonstrates their availability to form boronic esters with diols. Addition of water to these solutions led to loss of fluorescence, indicating the hydrolytic susceptibility of the boronic esters. Interestingly, addition of molecular sieves to the wet THF solutions resulted in fluorescence recovery, thereby demonstrating the ready reversibility of the boronic acid−alizarin covalent complexes.

In addition to having enhanced fluorescence, the boronic acid−alizarin complex demonstrated concentration dependent absorption in the visible wavelength at $\lambda_{max} \approx 495$ nm. Quantification of the boronic acid end groups was possible by first preparing a linear calibration based on standard solutions of known concentration (0.1−0.4 mM) of phenylboronic acid (PBA) and alizarin (Figure 4). The resulting extinction coefficient of $\varepsilon = 996$ L mol^{-1} cm^{-1} for the boronic ester complex was used to quantify the $(HO)_2B-$ end group concentration from a solution of known polymer concentration. Dividing the mass of polymer by the moles of $(HO)_2B-$ end groups allowed calculation of the number-average molecular weight ($M_{n,UV-vis}$), which was in good agreement with the theoretical value and those determined by NMR and GPC (Table 2).

Solution Behavior. Two aspects of the solution behavior of the boronic acid-terminated copolymers were investigated. In addition to the ability of the amphiphilic and double hydrophilic block copolymers to self-assemble into micellar aggregates in aqueous media, the boronic acid-terminated polymers also formed three-arm stars via terminal boroxine formation.[52] First, the supramolecular self-assembly process was studied by DLS and NMR spectroscopy, with these experiments suggesting the amphiphilic block copolymers were capable of forming micelles with hydrophobic cores (PSt) and hydrophilic (PDMA) exterior shells. The glassy nature of the PSt segments necessitated molecular dissolution of the block copolymers in THF before self-assembly was induced by dialyzing against water. Analysis of the hydrophilic homopolymers $(HO)_2B$-PDMA$_{61}$ and $(HO)_2B$-PDMA$_{61}$-*b*-PDMA$_{54}$ yielded solution sizes on the order of unimers (< 10 nm). However, heating a solution of the thermoresponsive[64] $(HO)_2B$-PDMA$_{61}$-*b*-PNIPAM$_{44}$ from room temperature to 50 °C resulted in the formation of stable aggregates of 33 nm at a critical temperature of 36 °C. The hydrodynamic size determined by DLS for each of the (co)polymers is given in Table 3.

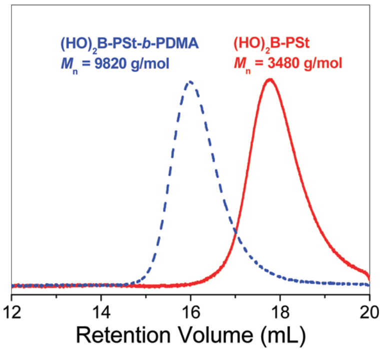


Figure 2. Gel permeation chromatography traces for a boronic acid-terminated polystyrene macro-chain-transfer agent ($(HO)_2$B-PSt) and a $(HO)_2$B-PSt-*b*-poly(*N*,*N*-dimethylacrylamide) ($(HO)_2$B-PSt-*b*-PDMA) block copolymer.

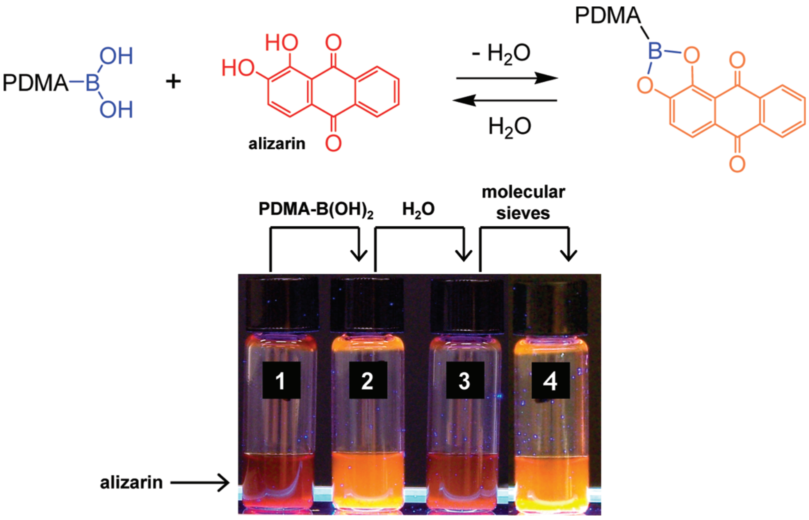


Figure 3. Proposed boronic ester formation between alizarin and boronic acid-terminated polymer. Solutions of alizarin in anhydrous THF/triethylamine solutions (1: alizarin; 2: $(HO)_2$B-PDMA + alizarin; 3: solution from vial 2 after adding two drops of water; 4: solution from vial 3 after stirring over molecular sieves and filtering).

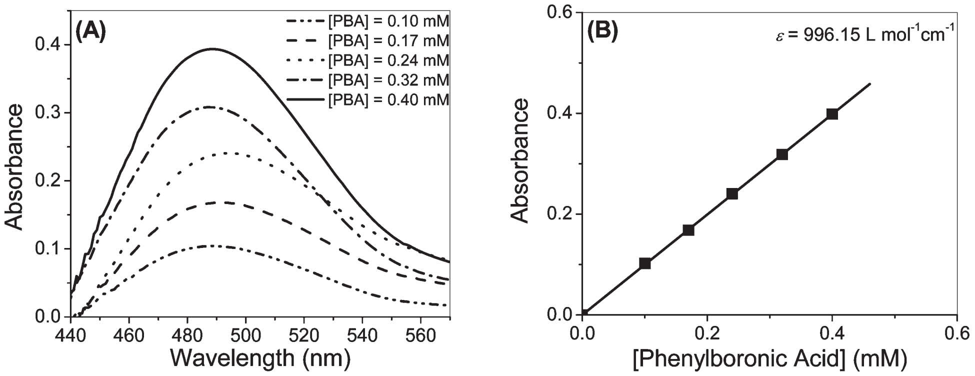


Figure 4. (A) UV−vis spectra from the titration of alizarin (0.5 mM) with phenylboronic acid in THF at room temperature. (B) Absorbance value at different phenylboronic acid concentrations in THF.

Table 2. Results from the Synthesis of Boronic Acid-Terminated Block Copolymers at 70 °C in DMF

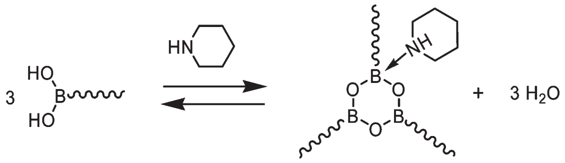
polymer	CTA	[M]:[CTA]:[I][a]	time (min)	conv[b] (%)	$M_{n,GPC}$[c] (g/mol)	M_w/M_n[c]	$M_{n,theo}$[d] (g/mol)	$M_{n,NMR}$[e] (g/mol)	$M_{n,UV-vis}$[f] (g/mol)
$(HO)_2B$-PDMA	**1**	100:1:0.05	80	57	6620	1.12	6110	5840	6280
$(HO)_2B$-PDMA	**1**	200:1:0.05	100	51	11900	1.16	10690	10120	9850
$(HO)_2B$-PSt	**1**	100: 1: 0.3	300	25	3480	1.07	3110	3580	3220
$(HO)_2B$-PSt	**1**	100: 1: 0.3	300	21	4950	1.13	4960	5280	4740
$(HO)_2B$-PDMA-*b*-PNIPAM	$(HO)_2B$-PDMA	100:1:0.07	100	66	11640	1.15	14090		12770
$(HO)_2B$-PDMA-*b*-PDMA	$(HO)_2B$-PDMA	100:1:0.07	75	79	11960	1.16	14410		12890
$(HO)_2B$-PSt-*b*-PDMA	$(HO)_2B$-PSt	100:1:0.05	335	51	9820	1.12	8490		9100
$(HO)_2B$-PSt-*b*-PDMA	$(HO)_2B$-PSt	100:1:0.05	335	63	12400	1.09	11230		

[a] Stoichiometric ratio of monomer/CTA (or macroCTA)/initiator (AIBN). [b] Monomer conversion as determined by ^{1}H NMR spectroscopy. [c] Determined by gel permeation chromatography in *N*,*N*-dimethylformamide. [d] $M_{n,theo}$ = ([monomer]$_0$/[CTA]$_0$) × monomer conversion × molecular weight of monomer + molecular weight of CTA). [e] Determined by ^{1}H NMR spectroscopy. [f] Determined by UV−vis spectroscopy. M_n: number-average molecular weight; $M_{n,theo}$: theoretical M_n; M_w: weight-average molecular weight.

Table 3. Dynamic Light Scattering Results for Boronic Acid-Terminated Homopolymers and Block Copolymers in Water

polymer	temperature (°C)	hydrodynamic diameter (nm)
$(HO)_2B$-PDMA$_{61}$	25	6
$(HO)_2B$-PDMA$_{61}$-*b*-PDMA$_{54}$	25	7
$(HO)_2B$-PDMA$_{61}$-*b*-PNIPAM$_{44}$	36	33
$(HO)_2B$-PSt$_{29}$-*b*-PDMA$_{64}$	25	23
$(HO)_2B$-PSt$_{43}$-*b*-PDMA$_{75}$	25	32

Scheme 2. Proposed Mechanism for Reversible Formation of Three-Arm Star Boroxines by Lewis-Base-Promoted Condensation of Boronic Acid-Terminated Polymers



In addition to the supramolecular self-assembly process, the boronic acid-terminated polymers were capable of forming dynamic covalent macromolecular assemblies. The dehydration of organoboronic acids exclusively produces a six-membered triorganoboroxine ring [$(RBO)_3$]. For example, Jakle and co-workers reported the successful synthesis of stars by azeotropic distillation of a solution of boronic-acid functional PSt prepared by ATRP.[52]

Boroxine formation by condensation of three boronic acids generally requires prolonged heating and/or drying agents; however, in the presence of a nitrogen-containing ligand (e.g., pyridine, piperidine, ammonia, etc.), formation of a 1:1 boroxine·ligand adduct can take place efficiently at low temperatures by complexation of the ligand with one boron atom within the boroxine ring (Scheme 2).[65] The resulting complex demonstrates enhanced hydrolytic stability as a result of its reduced ring strain as compared to the free boroxine.[66]

Piperidine was chosen as the amine ligand for boroxine star formation. Under the conditions employed, less than 2% aminolysis of the trithiocarbonate moieties was observed by UV−vis. A signal arising from two of the aromatic protons of the phenyl boronic acid end group of $(HO)_2B$-PSt was observed at $\delta = 7.83$ ppm in acetone-d_6 (Figure 5). Upon the addition of piperidine, this peak essentially disappeared, and a new signal was observed at $\delta = 7.99$ ppm. This transformation in chemical shifts is consistent with that reported in the literature for the condensation of phenylboronic acid to form phenylboroxine,[52,55,57] which seems to indicate successful formation of three-armed stars via the covalent assembly of $(HO)_2B$-PSt through boroxine linkages. Boroxine ring formation of $(HO)_2B$-PSt in the presence of piperidine was also observed in $CDCl_3$, with the chain end phenylboronic acid ring protons at $\delta = 7.78$ and 7.91 ppm shifting to 8.01 and 8.13 ppm, respectively (Supporting Information). The readily accessible reversibility of the covalent constructs was demonstrated by hydrolysis of the boroxine linkage upon addition of a small amount of D_2O to the acetone-d_6 solution (Figure 5). GPC in dry DMF was also used to investigate the formation of boroxine-linked stars. The polymeric boroxine·piperidine complex remained stable under the conditions of analysis, and a decrease in elution volume was observed for the expected star product. While this increase in apparent molecular weight is qualitative indication of successful star formation, the M_n of 3530 g/mol determined for the boroxine product was less than the predicted value of 6270 g/mol, based on the $(HO)_2B$-PSt starting material having

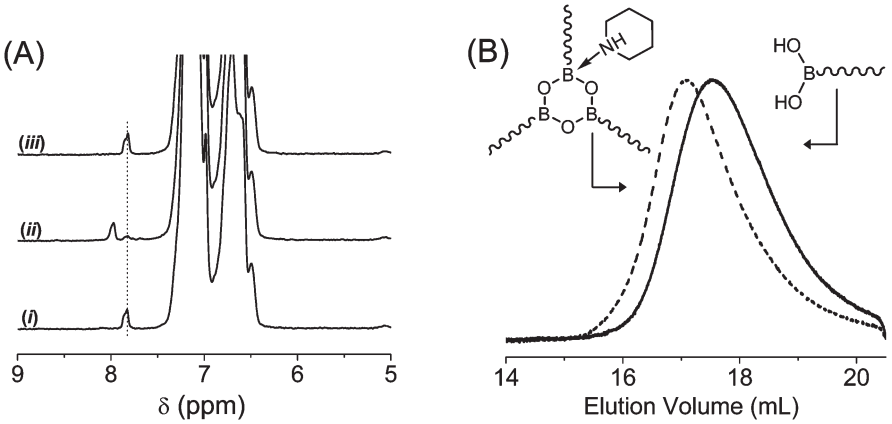


Figure 5. (A) ^{1}H NMR spectra in acetone-d_6 of (i) $(HO)_2B$-PSt, (ii) $(HO)_2B$-PSt and piperidine (1 equiv), and (iii) $(HO)_2B$-PSt and piperidine after the addition of D_2O. (B) Relative refractive index traces from gel permeation chromatography of $(HO)_2B$-PSt (M_n = 2090 g/mol) in DMF and boroxine-linked three-armed stars (M_n = 3530 g/mol) in DMF with piperidine (1 equiv).

M_n=2090 g/mol. This difference is potentially the result of less than quantitative boroxine formation, partial hydrolysis during GPC analysis, or the branched nature of the star not being ideally characterized by conventional column calibration.

Conclusions

Well-defined acrylamide and styrenic (co)polymers containing boronic acid α-chain end functionality were prepared by RAFT without postpolymerization reactions by employing a novel boronic acid-functionalized CTA. Retention of the ω-thiocarbonylthio end groups during the polymerization was demonstrated by the successful macroCTA chain extension to prepare a variety of telechelic block copolymers. Depending on the blocking order during synthesis, self-assembly of these block copolymers can lead to supramolecular micellar aggregates with boronic acid groups distributed along the corona periphery or within the hydrophobic core. The presence and location of these functional groups can be particularly important for applications that capitalize on the inherent reversible covalent chemistry of boronic acids. In this study, the formation of boronic esters with a model diol proved to be a highly efficient and readily reversible process, and Lewis base-promoted trimerization of the boronic acid end groups led to reversible three-arm stars with boroxine junction points. Both of these model reactions occur by way of dynamic covalent interactions, which indicate other polymers prepared in this manner may be capable of forming new dynamic macromolecular architectures.

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Supporting Information Available: Additional NMR and UV–vis spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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