Vinyl Phenylboronic Acid Controlling Co-monomer for Nitroxide Mediated Synthesis of Thermoresponsive Poly(2-*N* Morpholinoethyl Methacrylate)

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((Additional Supporting Information may be found in the online version of this article.))

ABSTRACT

Low concentrations of 4-vinylphenylboronic acid (VPBA) were copolymerized with 2-*N*-morpholinoethyl methacrylate (MEMA) by nitroxide mediated polymerization using BlocBuilder™ unimolecular initiator at 80 – 90 °C. The MEMA/VPBA copolymerizations were performed at initial feed compositions ($f_{VPBA,0}$) of 0.05 - 0.10 VPBA, with $f_{VPBA,0}$ = 0.10 using dimethylacetamide (DMAc) solvent being most effective, as seen by a linear increase in number average molecular weight, M_n, versus conversion and low dispersity, Đ < 1.40. The copolymers were further chain-extended with a second batch of VPBA, resulting in a block copolymer with monomodal molecular weight distribution and Đ = 1.66. For MEMA/VPBA copolymers, increases in VPBA composition and polymer solution concentration resulted in decreases in the cloud point temperature (CPT, typically varied between 27.4 - 37.8 °C) and CPT increased from 31.2 - 33.8 °C to about 88 °C with decreases in pH from 7 to 4. These copolymers were targeted as models to combine possible glucose-sensing boronic acid functionality the thermoresponsiveness provided by MEMA groups.

KEYWORDS: copolymerization, nitroxide-mediated polymerization, stimuli-sensitive materials, small angle light scattering (SALS)

INTRODUCTION

Controlled radical polymerization (CRP) techniques allow synthesis of polymers with tailored microstructure, previously attainable only by ionic polymerization. CRP techniques, such as nitroxide mediated polymerization (NMP)[1, 2], atom transfer radical polymerization (ATRP)[3], and reversible-addition fragmentation chain transfer polymerization (RAFT)[4,5], combine the simplicity and moderate sensitivity to impurities of free radical polymerization with the livingness of true living polymerization. Since the true living polymerization techniques

are sometimes limited to the types of monomers it can polymerize, particularly the sequence of monomers desired for block copolymers, CRP is an alternative method to prepare polymers with controlled molecular weight and narrow molecular weight distribution, such as required for stimuli-responsive materials (especially for multiple transitions or responses). For example, thermo-responsive polymers such as poly(*N*-isopropylacrylmide) (PNIPAM) are characterized by lower critical solution temperature (LCST) in aqueous solution, where the polymer precipitates from the solution upon heating.[6, 7]

Polymers containing boronic acid moieties have attracted attention as stimuli-responsive materials due to their ability to bind diols, specifically 1,2- and 1,3- diols,[8-10] through reversible boronate ester formation.[11,12] As a result, these polymers switch their solubility in water depending on glucose concentration, which enables their usage as self-regulated drug delivery polymers,[13-17] saccharide sensors,[17] separating agents,[18] and self-healing materials.[19,20] Moreover, the phenylboronic acid moieties lack toxicity and are stable *in vivo*.[17] Conventional radical polymerization of unprotected phenylboronic acid-containing polymers has resulted in ill-defined polymers.[16,21,22] Control over the microstructure and molecular weight is essential for sensing and controlled delivery applications, and CRP techniques enable synthesis of such polymers.

Polymers bearing morpholine functionality, have shown promise in biomedical applications as drug delivery vehicles.[23-25] Using 4-acryloylmorpholine (4AM) as an example, the 4AM containing polymers were applied as next-generation drug delivery vehicles,[24, 26] as chelating agents for wastewater treatment[27] and in sensing applications.[28] Another example of morpholino-functional polymers is 2-*N*-morpholinoethyl methacrylate (MEMA), a methacrylate related to 4AM, and unlike water-soluble 4AM homopolymers, MEMA homopolymers exhibited LCST-type behavior around 37 °C[29], which makes MEMA an interesting candidate for polymers used in controlled release applications. Despite these properties, morpholino-functional polymers have not been as extensively studied as other thermoresponsive polymers and only recently has poly(4AM) been synthesized by controlled radical polymerizations like NMP,[25,30] RAFT,[31-38] and Cu(0)-mediated living radical polymerization (SET-LRP).[39]

In this work, 4-vinylphenyl boronic acid (VPBA), was used to control the NMP of MEMA (Figure 1). MEMA, like many methacrylates, is challenging to synthesize by NMP in a controlled manner due to the high equilibrium constant, K, and propagation rate constant k_p, typically associated with methacrylates. Using the commercially available SG1-based BlocBuilder unimolecular initiator, addition of a small amount of controlling co-monomer however enables NMP methacrylic-rich copolymers (> 90 mol% methacrylate) by lowering the coupled product k_pK, which has been used as one measure of NMP controllability (linear M_n versus conversion, low Đ, chain-end fidelity).[40] Examples of controlling co-monomers for NMP include styrene[40, 41] and many of its derivatives (like sodium 4-styrene sulfonate (SS),[42] pentafluorostyrene (PFS),[43] 2-vinylpyridine (2VP),[44,45] 4-vinylpyridine (4VP),[46,47] 9-(4-vinylbenzyl-9H-carbazole)

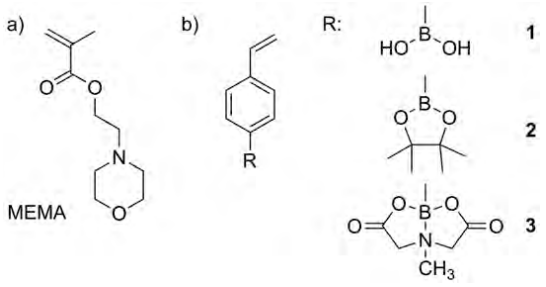

FIGURE 1 Molecular structures for a) 2-*N*-morpholinoethyl methacrylate (MEMA); b) 4-vinylphenylboronic acid monomers where **1** doesn't have protection group (VPBA), **2** is protected with a pinacol ester (pBSt), and **3** is protected with a MIDA ester (VPBAM).

(VBK),[48-53] and acrylonitrile (AN).[54]

MEMA was shown previously to be controllable by NMP using 9-(4-vinylbenzyl-9H-carbazole) (VBK)[51] as a controlling co-monomer, and the final copolymers had LCST behavior in aqueous solution along with hole-transporting and fluorescent functionalities[55] due to incorporation of VBK. The combination of poly(MEMA)'s stimuli-responsive behavior (LCST-type behaviour around psychological temperatures) with sugar sensing (via pH) properties of the VPBA is promising for biomedical applications. The use of ATRP and RAFT can be problematic in some cases, depending on the application, due to presence of metallic species or thiol groups in the product. Using NMP as an alternative CRP synthesis route is advantageous due to its robustness since it often requires only a single initiating species, and in contrast to ATRP and RAFT, NMP enables to reduce a number of possible purification steps of the final polymer. The protected boronic acid monomers, namely 4-vinylphenylboronic acid MIDA ester (VPBAM) and 4-pinacolatoborylstyrene (pBSt), were also tested as a controlling co-monomer for MEMA-rich copolymerization, where the effect of the protecting group on kinetic behavior and molecular weight control was assessed (Figure 1). The chain extension with VPBA was performed to test the ability of the poly(MEMA-*ran*-VPBA) random copolymer to reinitiate a fresh batch of monomer. The solution properties of the resulting random and block copolymers are described in detail as well, where the effect of solution concentration, polymer composition and pH was examined.

EXPERIMENTAL

Materials

4-vinylphenylboronic acid (VPBA, > 95 % Sigma-Aldrich), 4-vinylphenylboronic acid MIDA ester (VPBAM, 97%, Sigma-Aldrich), 4-pinacolatoborylstyrene (pBSt, 97%, AK Scientific, Inc.), 2-*N*-morpholinoethyl methacrylate (MEMA, 95%, MEHQ as inhibitor, Sigma-Aldrich), *N*,*N*-dimethylformamide (DMF, > 95%, certified ACS, Acros Organics), *N*,*N*-dimethylacetamide (DMAc, 99%, Sigma-Aldrich), dichloromethane (DCM, 99.8 %, anhydrous, Sigma-Aldrich), dimethyl sulfoxide-d_6 (DMSO, 100%, 99.96 atom % D, Sigma-Aldrich), tetrahydrofuran (THF, > 99.9%, HPLC grade, Fisher Scientific), anhydrous ethyl ether (> 95%, certified ACS/BHT stabilized, Fisher Scientific), pinacol (98%, Sigma-Aldrich), molecular sieves (3 Å, 1.6 mm, Sigma-Aldrich), basic alumina (Brockmann, type 1, 150 mesh, Sigma-Aldrich), reverse osmosis (RO) H_2O, were used as received. Oligo(ethylene glycol) methyl ether methacrylate ($OEGMA_{8-9}$ or OEGMA, average molecular weight M_n = 475 g·mol^{-1}, contained 100 ppm MEHQ as inhibitor and 300 ppm BHT as inhibitor) and 2-(2-methoxyethoxy)ethyl methacrylate, also known as di(ethylene glycol) methyl ether methacrylate (DEGMA, 188 g·mol^{-1}, 95%, 100 ppm MEHQ as inhibitor) were obtained from Sigma-Aldrich and used as received. 2-([*tert*-butyl[1-(diethoxyphosphoryl)-2,2-dimethylpropyl]amino]oxy)-2-methylpropanoic acid (BlocBuilder, 99%) was obtained from Arkema and used without further purification. (tert-butyl[1-(dithoxyphosphoryl)-2,2-dimethylpropyl]amino)oxidanyl (SG1, > 85%) was kindly donated by Arkema and used as received.

Polymer Synthesis

General

All syntheses of copolymers were performed in a J-Kem Scientific Inc. personal reaction station containing 6 vials. A magnetic stir bar was inserted into each vial, and each vial was capped with a rubber septum through which a temperature well was placed. A thermocouple was inserted through the temperature well and connected to the controller. The controller was used to monitor and control the reaction temperature for several reactors in parallel. The lower portion of the personal reaction station was connected directly to the controller and used for heating. To prevent monomer and

solvent evaporation, the upper portion of the multi-reactor station was connected to a Neslab 740 Chiller unit, where a 50 vol% mixture of water and ethylene glycol was circulated. Prior to heating, the reaction mixture was purged with nitrogen for 30 minutes, and then continued throughout the entirety of the reaction but with a reduced flow once the desired temperature was reached. The rubber septum cap was pierced with a needle to relieve pressure build-up.

Copolymerization of 2-N-morpholino ethyl methacrylate (MEMA) with unprotected 4-vinylphenylboronic acid (VPBA)

In all cases using unprotected VPBA, copolymerizations were performed at 90 °C in a 50 wt% DMF or DMAc solution using the BlocBuilder/SG1 initiating system. The amount of initiator was calculated so that the target molecular weight at complete conversion was 25 kg mol^{-1}, and a molar ratio of SG1 relative to BlocBuilder (r = $[SG1]_0/[BlocBuilder]_0$) was approximately 0.10. The initial feed composition of VPBA relative to MEMA was varied over $f_{VPBA,0}$ = 0.05 - 0.10 to observe the effect on polymerization kinetics and molecular weight control, and each composition was run in both DMF and DMAc solvents separately. The water was added to suppress the formation of a cyclic trimer of boronic acid, boroxine, which would induce network formation.[56] As an example, the formulation for MEMA/VPBA copolymerization in DMAc with $f_{VPBA,0}$ = 0.1 (M/VPBA-10-2) is given: BlocBuilder (0.0495 g, 0.130 mmol), SG1 (0.004 g, 0.013 mmol), MEMA (3.02 g, 15.2 mmol), VPBA (0.24 g, 1.63 mmol), DMAc (3.21 g, 36.8 mmol), water (0.17 g, 9.32 mmol). The solution was stirred and bubbled with a nitrogen purge for 15 minutes. The solution was then heated to 90 °C at a heating rate of approximately 10 °C per minute while continuing the purge, and the start of the polymerization was arbitrarily taken when the set temperature was reached. Samples were periodically withdrawn using a syringe and precipitated in excess diethyl ether for molecular weight analysis. The crude polymer was recovered when the solution became too viscous, and after cooling, was precipitated using excess diethyl ether, then dried in the vacuum oven at 40 °C overnight. For the specific example, the reaction was stopped after 55 minutes. The final yield, after all the samples were drawn, was 0.86 g (63 % conversion according to ^{1}H NMR; final molar composition of VPBA, F_{VPBA} = 0.11 with M_n = 20.1 kg mol^{-1} and Đ = 1.19 by GPC relative to poly(methyl methacrylate) standards in THF at 40 °C). All the formulations for MEMA/VPBA copolymerizations are listed in Table 1.

Copolymerization of 2-N-morpholino ethyl methacrylate (MEMA) with MIDA ester protected 4-vinylphenylboronic acid (VPBAM) or 4-pinacolatoborylstyrene (pBSt)

All of the polymerizations were performed in a solution of 50 wt% DMAc as solvent using 10 mol% additional SG1 (r = 0.10). The feed composition of protected boronic acid monomer was kept at $f_{VPBAM,0}$ *or* $f_{pBSt,0}$ *= 0.10*. The polymerizations were performed at either 90 °C or 80 °C, and no water was added for these reactions as the boronic acid group was protected, thus removing the possibility of cyclic trimer formation. An additional set of reactions was performed at 90 °C only with the addition of water to the reaction mixture to test whether there is any deprotection during at the polymerization conditions. The formulation for MEMA/VPBAM at 90 °C using the MIDA protected boronic acid monomer (M/VPBAM-10-90) is given as an example: BlocBuilder (0.0349 g, 0.092 mmol), SG1 (0.0027 g, 0.009 mmol), MEMA (1.97 g, 9.91 mmol), VPBAM (0.27 g, 1.05 mmol), DMAc (2.18 g, 25.01 mmol). The same nitrogen purging and polymer/sample collection procedure was also followed for this reaction. The reaction given as an example was stopped after 17 minutes and the yield was 0.35 g (75 % conversion according to ^{1}H NMR; final molar composition of VPBAM, F_{VPBAM} = 0.17 with M_n = 10.5 kg mol^{-1} and Đ = 1.49 by GPC relative to poly(methyl

methacrylate) standards in THF at 40 °C). Low yield was attributed to difficulties removing the product from the reaction vial, caused by the high viscosity of the final product solution. All the formulations for MEMA copolymerizations with either VPBAM or pBSt are listed in Table 1.

Terpolymerization of oligo(ethylene glycol) methyl ether methacrylate (OEGMA), 2-(2-methoxyethoxy)ethyl methacrylate (DEGMA), and 4-vinylphenylboronic acid (VPBA)

The terpolymerizations were performed in an identical setup as the MPAM/VPBA copolymerizations, following the identical procedure. The reactions were performed with f_{VPBA} = 0.10 and f_{OEGMA} = 0.09 in both DMF and DMAc solvents at 90 °C. Table 2 lists the formulations for terpolymerizations. These terpolymerizations were done as a comparison to show the effect of non-ionic monomers that provide thermoresponsive polymers in comparison to amine-containing MPAM monomers.

Block copolymer synthesis

To test the ability of MEMA/VPBA copolymers to reinitiate a fresh batch of monomer, a MEMA/VPBA was used as a macroinitiator (M/VPBA-10-2, M_n = 20.1 kg mol^{-1}, Đ = 1.19, F_{VPBA} *= 0.11*) to initiate a new batch of VPBA. The same reaction set-up was used as for the macroinitiator synthesis. The macroinitiator (0.66 g, 0.032 mmol) was dissolved in DMAc (1.46 g, 16.8 mmol) along with water (0.07 g, 4.4 mmol) and VBPA (0.8 g, 5.4 mmol) and then subjected to a nitrogen purge at room temperature for 20 minutes. The reactor was then heated to 90 °C, while maintaining a light nitrogen purge, and the reaction was stopped when the solution became much more viscous. The reaction was stopped after 170 minutes and the polymer was collected by precipitation in excess diethyl ether before being dried in the vacuum oven overnight at 40 °C. The final product was richer in VPBA (F_{VPBA} = 0.41 from ^{1}H NMR) with M_n = 27.9 kg mol^{-1}, and Đ = 1.66.

Polymer Characterization

Gel Permeation Chromatography (GPC)

To determine the number-average molecular weight (M_n) and the dispersity (Đ), gel permeation chromatography GPC (Waters Breeze) was used. The GPC was equipped with both ultra-violet (UV 2487) and differential refractive index (RI 4214) detectors, a guard column and three Waters Styragel® HR columns (HR1, HR2, and HR4) with a particle size of 5 µm which were heated to 40 °C. The HR columns used have molecular weight measurement ranges of 0.1-5 kg mol^{-1}, 0.5-20 kg mol^{-1}, and 5-500 kg mol^{-1}, respectively. The mobile phase was HPLC grade THF, with a flow rate of 0.3 mL min^{-1}. The calibration was done using poly(methyl methacrylate) standards with molecular weights ranging from 1 - 1677 kg mol^{-1} at 40 °C. The Mark-Houwink coefficients, used to correct for the differences in hydrodynamic volume of the actual polymer and PMMA standards used for GPC calibration, are not available, as far as we know, for MEMA polymers, and therefore all molecular weight data was determined based on PMMA calibration. Attempts to use ^{1}H NMR for end-group analysis were subject to high error as the ratio of the initiator proton peak signals to that of the backbone were very low and noisy. We thus report here only the M_n estimated by GPC.

Due to the use of unprotected VPBA as a co-monomer, the MEMA/VPBA copolymers had a tendency to adhere to the column, interfering with the GPC results. To remedy this issue, the copolymers synthesized using unprotected VPBA were protected by esterification with pinacol. The boronic acid groups were protected by adding to the dry sample vials approximately 2 mL of anhydrous dichloromethane, 3 Å molecular sieves, and excess pinacol. The reaction was left for 24 hours to proceed, with periodic agitation of the vial contents. Following this period, basic aluminum oxide was added to the vial and left for 12 hours. The contents of the vial were then filtered using 0.2 µm filters, and the recovered

product was then passed through the GPC column for analysis.

TABLE 1 Experimental formulations for poly(2-N-morpholinoethyl methacrylate-ran-4-vinylphenylboronic acid) (poly(MEMA-ran-VPBA)) copolymerizations performed in 50 wt% DMF or DMAc solution using VPBA with and without protection groups.

Exp. ID[a]	$[BlocBuilder]_0$ (mmol)	$[SG1]_0$ (mmol)	$[MEMA]_0$ (mmol)	$[VPBA]_0$ [b] (mmol)	$[Solvent]_0$ (mmol)	$[H_2O]_0$ (mmol)	$f_{VPBA,0}$[c]
M/VPBA-5-1	0.103	0.010	12.50	0.66	35.40	7.18	0.050
M/VPBA-7.5-1	0.124	0.013	15.18	1.27	44.66	9.10	0.077
M/VPBA-10-1	0.123	0.014	15.14	1.49	43.92	8.87	0.090
M/VPBA-5-2	0.125	0.013	15.39	0.78	36.54	8.09	0.050
M/VPBA-7.5-2	0.122	0.013	15.17	1.23	36.74	9.19	0.075
M/VPBA-10-2	0.130	0.013	15.15	1.63	36.79	9.32	0.10
M/VPBAM-10-90	0.092	0.009	9.91	1.05	25.01	N/A	0.10
M/VPBAM-10-90-W	0.092	0.01	10.02	1.25	26.52	6.11	0.11
M/VPBAM-10-80	0.089	0.009	10.04	1.12	26.34	N/A	0.10
M/pBST-10-90	0.099	0.010	11.31	1.26	29.16	N/A	0.10
M/pBST-10-90-W	0.102	0.011	11.35	1.26	29.04	6.11	0.10
M/pBST-10-80	0.098	0.010	11.31	1.26	29.18	N/A	0.10

[a] Experimental identification (Exp. ID) for MEMA/VPBA copolymerizations is given by M/X-Y-Z, with M representing 2-*N*-morpholinoethyl methacrylate (MEMA), X representing 4-vinylphenylboronic acid without a protection group (VPBA) or with protection groups (VPBAM for MIDA ester and pBST for pinacol ester) as shown in Figure 1, Y representing the initial feed composition of controlling comonomer in mol%, Z representing either the solvent (1 for DMF or 2 for DMAc) for the first six entries or temperature the polymerization was ran at (80 or 90 °C) for the last six entries. The copolymerizations with VPBA were performed at 90 °C. [b] VPBA monomer with and without protective groups (see note a). [c] $f_{VPBA,0}$ is the initial molar fraction of the co-monomer (protected and unprotected VPBA) in the feed.

TABLE 2 Experimental formulations for oligo(ethylene glycol) methyl ether methacrylate (OEGMA), 2-(2-methoxyethoxy)ethyl methacrylate (DEGMA), and 4-vinylphenylboronic acid (VPBA) terpolymerizations.

Exp. ID[a]	$[BlocBuilder]_0$ (mmol)	$[SG1]_0$ (mmol)	$[OEGMA]_0$ (mmol)	$[DEGMA]_0$ (mmol)	$[VPBA]_0$ (mmol)	$[Solvent]_0$ (mmol)	$[H_2O]_0$ (mmol)
OEGMA/DEGMA/ VPBA-1	0.017	0.165	1.76	15.84	1.96	56.18	11.16
OEGMA/DEGMA/ VPBA-2	0.016	0.164	1.75	15.78	1.96	47.17	11.62

[a] Experimental identification (Exp. ID) for OEGMA/DEGMA/VPBA terpolymerizations is given by X/Y/Z-N, with X representing oligo(ethylene glycol) methyl ether methacrylate (OEGMA), Y representing 2-(2-methoxyethoxy)ethyl methacrylate (DEGMA), Z representing 4-vinylphenylboronic acid without a protection group (VPBA), and N representing the solvent (1 for DMF or 2 for DMAc). The terpolymerizations were performed at 90 °C, and the initial molar fraction of the monomers in the feed was kept constant at $f_{VPBA,0}$ =0.10 and $f_{OEGMA,0}$ =0.09.

Nuclear Magnetic Resonance (NMR) Spectroscopy

To determine polymerization progression, monomer conversion was determined with ^{1}H NMR spectroscopy of samples taken at various times during the polymerization. The samples were analyzed using a 300 MHz Varian Mercury NMR using deuterated dimethyl sulfoxide (DMSO) as the solvent. Figure S1 (in the *Supporting Information*) shows the typical spectra obtained by ^{1}H NMR using a crude mixture of M/VPBA-10-2 as an example. The conversion of VPBA was determined by comparing the areas associated with the phenyl proton peaks (H_{1-4}, δ = 7.4, 7.7 ppm for monomer, corresponding to 4H in total and H_{1-2}, δ = 7.6 ppm for polymer, corresponding to 2H). The conversion of MEMA was obtained using the vinylic proton peaks (H_{5-6}, average of δ = 5.7, 6.0 ppm, corresponding to 2H in total) and comparing that to the non-vinylic proton peak (H_{7-8}, δ = 3.8 - 4.2 ppm, corresponding to 2H). Overall conversion of MEMA/VPBA co-polymerizations was calculated according to $X=X_a\ f_{(a,0)} + X_b\ f_{(b,0)}$ where X_a and X_b are the individual monomer conversions and $f_{(a,0)}$ and $f_{(b,0)}$ are the initial molar fractions of monomers a and b, respectively.

TABLE 3 Molecular weight characterization for poly(2-*N*-morpholinoethyl methacrylate-*ran*-4-vinylphenylboronic acid) (poly(MEMA-*ran*-VPBA)) copolymers.

Exp. ID[a]	$f_{B,0}$[b]	F_B[b]	X[c]	M_n[d] (kg mol^{-1})	Đ[d]	Time[e] (min)
M/VPBA-5-1	0.05	0.075	0.68	20.5	1.17	67
M/VPBA-7.5-1	0.077	0.10	0.68	20.8	1.44	17
M/VPBA-10-1	0.09	0.13	0.90	25.5	1.21	55
M/VPBA-5-2	0.05	0.045	0.70	20.1	1.26	24
M/VPBA-7.5-2	0.075	0.075	0.66	20.4	1.10	45
M/VPBA-10-2	0.1	0.11	0.63	20.1	1.19	55
M/VPBAM-10-90	0.1	0.17	0.75	10.5	1.49	17
M/VPBAM-10-90-W	0.11	N/A	0.70	12.9	1.35	35
M/VPBAM-10-80	0.1	0.12	0.80	15.3	1.19	24
M/pBST-10-90	0.1	0.09	0.68	11.9	1.32	72
M/pBST-10-90-W	0.1	N/A	0.71	15.6	1.49	65
M/pBST-10-80	0.1	0.13	0.76	15.8	1.36	70

[a] Experimental identification (Exp. ID) for MEMA/VPBA copolymerizations are given by M/X-Y-Z, with M representing 2-*N*-morpholinoethyl methacrylate (MEMA), X representing 4-vinylphenylboronic acid without a protection group (VPBA) or with protection groups (VPBAM for MIDA ester and pBST for pinacol ester) as shown in Figure 1, Y representing the initial feed composition of controlling comonomer in mol%, Z representing either the solvent (**1** for DMF or **2** for DMAc) for the first six entries or temperature the polymerization was ran at (80 or 90 °C) for the last six entries. The copolymerizations with VPBA were performed at 90 °C. [b] $f_{B,0}$ is the initial molar fraction of the controlling comonomer *B* (4-vinylphenylboronic acid with and without protection groups); F_B is the molar fraction of the controlling comonomer in the final copolymer as determined by ^{1}H NMR spectroscopy. [c] Monomer conversion determined by ^{1}H NMR spectroscopy. Individual monomer conversions are listed in Table S1 in the *Supporting Information*. [d] M_n and Đ were determined by gel permeation chromatography (GPC) relative to poly(methyl methacrylate) standards at 40 °C. [e] The final polymerization time.

TABLE 4 Molecular weight characterization for oligo(ethylene glycol) methyl ether methacrylate (OEGMA), 2-(2-methoxyethoxy)ethyl methacrylate (DEGMA), and 4-vinylphenylboronic acid (VPBA) terpolymerizations.

Exp. ID[a]	$f_{VPBA,0}$[b]	F_{VPBA}[b]	X[c]	M_n[d] (kg mol^{-1})	Đ[d]	Time[e] (min)
OEGMA/DEGMA/VPBA-1	0.10	0.096	0.71	18.6	1.32	80
OEGMA/DEGMA/VPBA-2	0.10	0.120	0.69	20.1	1.20	80

[a] Experimental identification (Exp. ID) for OEGMA/DEGMA/VPBA terpolymerizations is given by X/Y/Z-N, with X representing oligo(ethylene glycol) methyl ether methacrylate (OEGMA), Y representing 2-(2-methoxyethoxy)ethyl methacrylate (DEGMA), Z representing 4-vinylphenylboronic acid without a protection group (VPBA), and N representing the solvent (1 for DMF or 2 for DMAc). The terpolymerizations were performed at 90 °C, and the initial molar fraction of the monomers in the feed was kept constant at $f_{VPBA,0}$ =0.10 and $f_{OEGMA,0}$ =0.09. [b] $f_{VPBA,0}$ is the initial molar fraction of the VPBA controlling comonomer and F_{VPBA} is the molar fraction of the VPBA controlling comonomer in the final copolymer as determined by ^{1}H NMR spectroscopy. [c] Monomer conversion determined by ^{1}H NMR spectroscopy. [d] M_n and Đ were determined by gel permeation chromatography (GPC) relative to poly(methyl methacrylate) standards at 40 °C. [e] The final polymerization time.

Cloud Point Temperature Determination

UV-Vis spectroscopy and dynamic light scattering (DLS) were used to determine cloud point temperature (CPT) of the copolymers in aqueous solution. All samples examined were dissolved in deionized water (DIW) appropriately to obtain the desired compositions by weight. 2-3 heating/cooling cycles were performed for each sample run below 60 °C and 1 heating/cooling cycle was performed for samples ran above 60 °C. This is due to the need to use Teflon caps, which did not provide a perfect seal and thus water was lost when running the samples at higher temperatures. This effectively changed the concentration of samples and thus the results could not be related to those run at lower temperatures.

UV-Vis Spectroscopy

UV-Vis was one of the methods used to determine the cloud point temperatures (CPTs) of the various MEMA/VPBA copolymers. To perform the analysis, a Cary 5000 UV-Vis-NIR spectrometer (Agilent Technologies) equipped with a Peltier thermostatted (6 x 6) multi-cell holder with temperature controller, magnetic stirring and a heating rate of 1 °C min^{-1} was used. A wavelength of 500 nm was used to measure the polymers light absorbance at different temperatures, which was then converted into transmittance and scaled. The CPT was calculated as the temperature at which normalized transmittance was equal to 50 %. Concentration ranges for the copolymers studied spanned 0.25 - 1 wt. % and unprotected copolymers were used.

Dynamic Light Scattering (DLS)

A select few samples were also analyzed using a Malvern Zetasizer Nano ZS equipped with a He-Ne laser at 633 nm. All DLS measurements were performed at a scattering angle (θ) of 173° using the refractive index (RI) of PMMA. The instrument was also equipped with an avalanche photodiode detector and a temperature-controlled cell. In all DLS measurements samples were filtered using 0.2 µm pore size filer and the hydrodynamic radius (R_h) of the copolymers was measured as the temperature increased from 15 °C to 45 °C at a rate of about 1 °C per minute. Unlike the UV-Vis method, where the CPT was determined mid-way through the phase transition, at 50 % transmittance, the CPT by DLS was determined at the end of the phase transition. Figure S2 in the *Supporting Information* shows typical R_h

distributions near the CPT using M/VPBA-5-2 at 0.5 wt% solution concentration. Starting from a unimer peak at room temperature (R_h of about 6 – 10 nm), the concentration of aggregates increased with increasing temperature until the point when the peak corresponding to unimers completely disappeared leaving only the peak corresponding to aggregates (with R_h > 100 nm), which was taken as a CPT (33 °C).

Rheology

Small angle light scattering (SALS) experiments were coupled with rheology measurements and experiments were performed with an Anton Paar MCR 302 Rheometer equipped with a Peltier P-PTD 200 temperature control and Peltier H-PTD 200 temperature controlled hood. Rheological tests consisted of temperature sweep experiments under a constant frequency (1 s^{-1}), and the viscosity of the sample was measured for 0.5 wt% M/VPBA-5-1 polymer solution in DI water as it was heated from 25 to 45 °C in 1 °C min^{-1} intervals. Red laser was used to illuminate the sample and the images were captured by an LU165C-IO Lumenera CCD camera in 30 second intervals.

RESULTS AND DISCUSSION

A series of MEMA/VPBA copolymerizations by NMP using BlocBuilder as the unimolecular initiator and 10 mol% additional SG1 free nitroxide were performed as a function of VPBA composition, VPBA protecting group, solvent, and temperature (see Table 1 for formulations). Controlled homopolymerization of VPBA by NMP has been reported in the presence of BlocBuilder initiator previously.[57] Figure 2 shows the characteristic kinetic plots of log ((1-X)$^{-1}$), versus time and Figures 3 and 4 shows M_n and Đ, respectively, versus conversion for all copolymerizations.

Copolymerization with Unprotected VPBA

The copolymerizations were performed in two solvents, DMF and DMAc, with controlling comonomer compositions $f_{VPBA,0}$ = 0.05, 0.075 or 0.10. Since boronates are known to form cyclic structures in a side reaction, 5 wt% water was added to the reaction mixture to shift the equilibrium and prevent it.[56] Figures 2a and 2b show scaled conversion (ln[(1-X)$^{-1}$]) versus time for copolymerizations done in DMF solvent and DMAc solvent, respectively, at 90 °C. The conversion increased linearly with time for all the polymerizations.

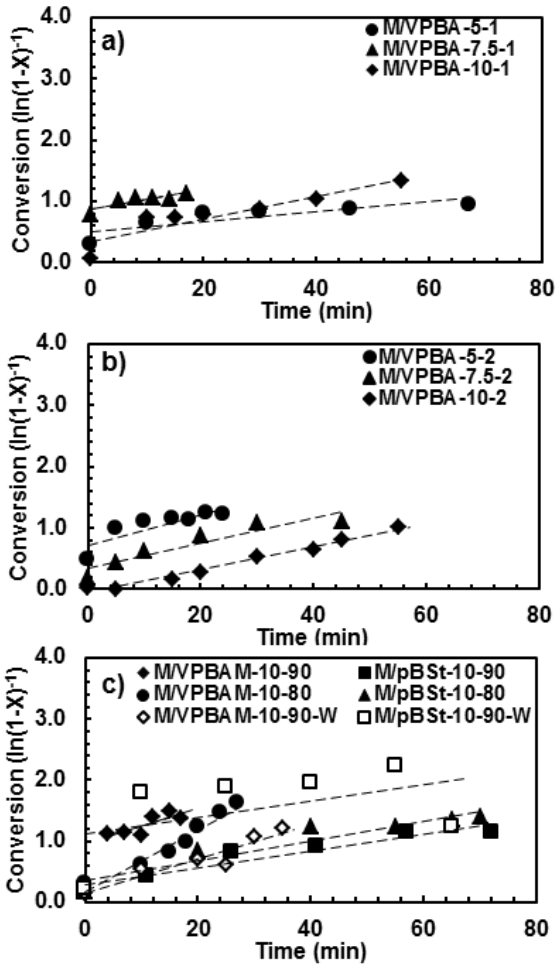

FIGURE 2 The semi-logarithmic plots of scaled conversion (ln[1-X]$^{-1}$]) (X = conversion) versus time for all copolymerizations using a) unprotected VPBA in DMF solvent; b) unprotected VPBA in DMAc solvent; c) protected VPBA in DMAc solvent or in DMAc/water mixture.

Moreover, for $f_{VPBA,0}$ = 0.050 and 0.075, the conversion at time zero was > 40% in both DMF and DMAc solvents, and for $f_{VPBA,0}$ = 0.1 the

conversion at time zero was very low. The start of the reaction was chosen when the set temperature was reached, and some conversion was possible as the nitroxide can begin to decompose at temperatures as low as 60 °C.[58] Figures 3a and 3b show the progression of M_n with conversion for all MEMA/VPBA copolymerizations and Figure 4 shows the molecular weight distributions (MWDs) for some of the experiments. The M_n progresses linearly with increasing conversion for all MEMA/VPBA copolymerizations. The dispersity, Đ, for copolymerizations in either DMF or DMAc solvents is outlined in Figures 5a and 5b, respectively. Đ was between 1.38 – 1.58 throughout the copolymerizations when DMF was used as a solvent, and it was between 1. 38 – 1.26 for copolymerizations performed in DMAc solvent. Table 3 summarizes the molecular weight characterization data for the copolymers.

Solvent played an important role in control of MEMA polymerizations with VPBA. Based on the results presented for copolymerizations performed in both solvents, DMAc was found to be a more suitable solvent for the reaction. The lack of control over the copolymerization, exemplified by non-linear M_n progression with conversion and high Đs when DMF was used as a solvent, might be due to chain transfer to solvent. Previous studies have shown higher probability of chain transfer to solvent when DMF was used as a medium for polymerization for some monomers such as *tert*-butyl acrylate[59] and N-isopropyl acrylamide (NIPAM).[60]

Copolymerization with Protected VPBA

We indicated that MEMA polymerizations are controllable by NMP with addition of VPBA in small quantities, $f_{VPBA,0}$ = 0.05 - 0.10. The CRP of boronic acid containing monomers was reported previously. For instance, ATRP[61] and RAFT[57] polymerizations were successful by protecting the boronic acid groups during the reaction, whereas NMP of VPBA using BlocBuilder initiator was successful without any protection.[57] Although the ability to use the unprotected monomer for the synthesis is desirable to avoid additional protection and de-protection steps, the effect of the protecting group on control of the MEMA polymerization is interesting to study in comparison to VPBA where the OH groups might interact with the carboxylic acid attached to the BlocBuilder initiator. The commercially available monomers, with MIDA ester and pinacol ester protecting groups, were selected for the study, and the formulations are listed in Table 1.

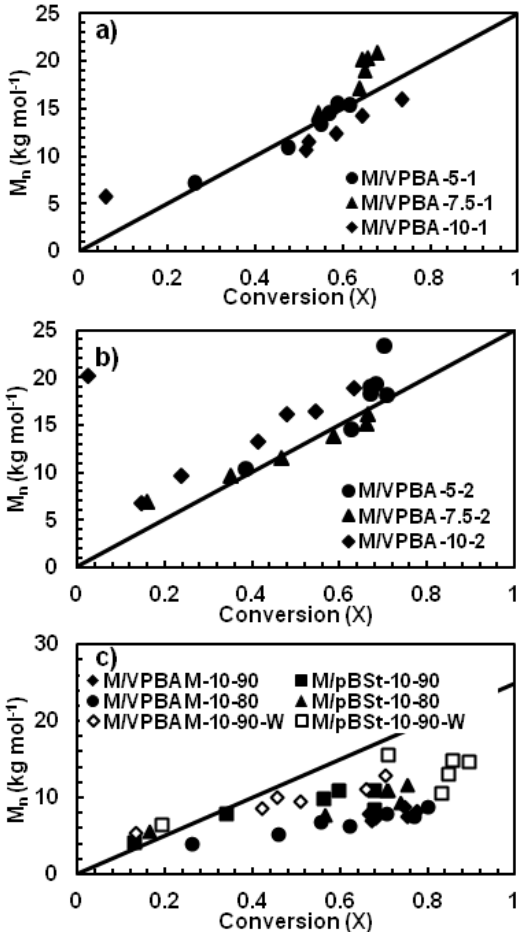

FIGURE 3 The number average molecular weight (M_n) versus conversion (X) for all copolymerizations using a) unprotected VPBA in DMF solvent; b) unprotected VPBA in DMAc solvent; c) protected VPBA in DMAc solvent or in DMAc/water mixture.

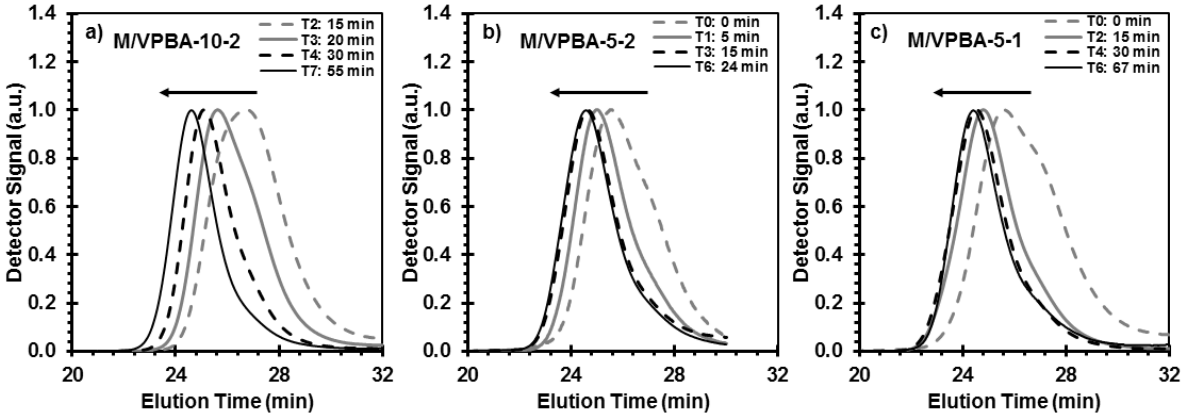

FIGURE 4. GPC chromatograms (molecular weight distributions, MWDs) for characteristic copolymerization of 2-*N*-morpholinoethyl methacrylate with 4-vinylphenylboronic acid (MEMA/VPBA): a) M/VPBA-10-2 was with 10 mol% VPBA in the initial feed in DMAc; b) M/VPBA-5-2 was with 5 mol% VPBA in the initial feed in DMAc; c) M/VPBA-5-1 was with 5 mol% VPBA in the initial feed in DMF.

The polymerizations were conducted at two temperatures: 80 and 90 °C. The scaled conversion progressed linearly with time for all the copolymerizations (Figure 2c) and M_n increased linearly with increasing conversion (Figure 3c). The M_n does not follow the theoretical line precisely, which might be due to differences in hydrodynamic volume between the actual polymer and PMMA standards used for GPC calibration. The downward deviation of M_n from the theoretical line for some of the experiments might be due to the termination reactions. Figure 5c with the dispersity data confirms the presence of the termination reactions for the M/pBSt copolymerizations, where Đ increased from 1.39 to 1.73 and from 1.44 to 2.38 for M/pBSt-10-80 and M/pBSt-10-90, respectively. As a comparison, Đ increased only slightly for M/VPBAM copolymerizations, from 1.35 to 1.51 and from 1.45 to 1.58 for M/VPBAM-10-80 and M/VPBAM-10-90, respectively. From the individual conversions (shown in Table S1 in the *Supporting Information*) for M/VPBAM and M/pBSt experiments, the pBSt seemed to be consumed more preferentially during the course of the polymerization, leaving only MEMA monomer available in the mixture, which is known to be poorly homopolymerized as a typical methacrylate monomer, by NMP.

High Đs might be explained by instability of the protected VPBA and its partial deprotection during the polymerization. The molecular weight characterization of the copolymerizations involving the protected VPBA monomers did not involve an additional protection step, and the MWDs for these copolymers had a characteristic tail, which was due to premature termination of short chains or due to the polymer sticking to a column. The final sample of M/pBSt-10-90 was analyzed by GPC before and after the additional protection with pinacol ester (Figure 6a), and the initially present tailing of the MWD disappeared. The analysis was repeated for the other copolymers, and the effect was identical: MWDs became narrower and Đs decreased, having an effect akin to fractionation.

Addition of water to the reaction (M/VPBAM-10-90-W and M/pBSt-10-90-W) seemed to help to control the polymerization, if compared to the similar experiments without the water. As shown in Figure 5c) the Đs increased from 1.33 to 1.49 for M/pBSt-10-90-W during polymerization and the Đs decreased from 1.42 to 1.35 for M/VPBAM-10-90-W during the course of polymerization. This is in contrast to the generally higher Đs without any water present. The additional water might have helped to prevent the formation of a cyclic trimer of boronic acid, boroxine, between the

unprotected VPBA, in case if there was VPBAM and/or pBSt deprotection during the polymerization. The molecular weight data of the resulting polymers is listed in Table 3.

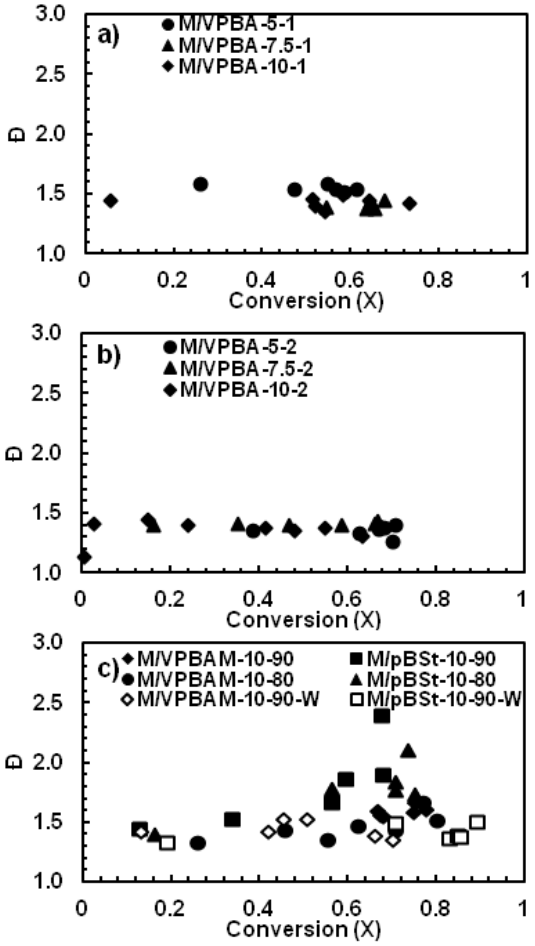

FIGURE 5 The dispersity, Đ, versus conversion (X) for all copolymerizations using a) unprotected VPBA in DMF solvent; b) unprotected VPBA in DMAc solvent; c) protected VPBA in DMAc solvent or in DMAc/water mixture.

Synthesis of block copolymers

The MEMA-rich copolymers were further chain extended with a fresh batch of VPBA monomer in order to assess the copolymer's ability to reinitiate a reaction. The set-up of the reaction and the formulation is covered in the *Experimental section*. Figure 6b shows the MWDs of the final block copolymer (F_{VPBA} = 0.41, M_n = 27.9 kg mol^{-1}, and Đ = 1.66) and its corresponding macroinitiator (M/VPBA-10-2: F_{VPBA} = 0.11, M_n = 20.1 kg mol^{-1}, Đ = 1.19). The shift of MWD to lower elution times signifies chain growth and a combination of low Đ and monomodal MWD signifies successful chain extension of M/VPBA-10-2 macroinitiator.

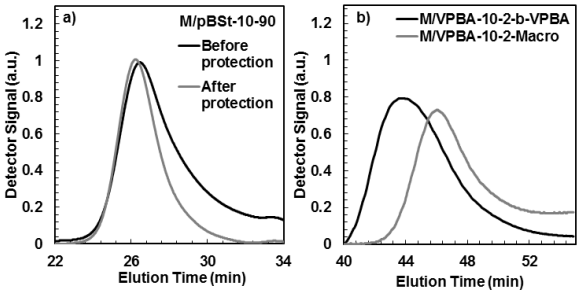

FIGURE 6. GPC chromatograms (molecular weight distributions, MWDs) for a) M/pBSt-10-90 final sample before and after the reprotection; b) MEMA/VPBA chain extension experiment.

Complexation of boron with the tertiary amine

In order to address a possible complexation of boronic acid moiety with a tertiary amine present in MEMA, the unprotected VPBA monomer was used to control the polymerization of non-ionic monomers, such as oligo(ethylene glycol) methyl ether methacrylates with 8-9 ethylene glycol (EG) units (OEGMA) and 2-(2-methoxyethoxy)ethyl methacrylate with 2 EG units (DEGMA). OEGMA/DEGMA containing statistical copolymers exhibit tunable CPTs in water depending on the ratio of OEGMA:DEGMA[62, 63], and these polymers have been synthesized previously by NMP using 9-(4-vinylbenzyl)-9H-carbazole (VBK) as a controlling co-monomer [64].

The characteristic scaled conversion (ln (1-X)$^{-1}$) versus time, M_n versus X, and Đ versus X plots are depicted in Figure 7a, 7c and 7b, respectively. The final terpolymers were characterized by relatively narrow molecular weight distributions with Đ = 1.20, 1.32 and M_n = 20.1, 18.6 kg mol^{-1} (Table 4). These

terpolymerizations did not seem sensitive to the solvents used, as was the case for the MEMA-rich systems studied earlier.

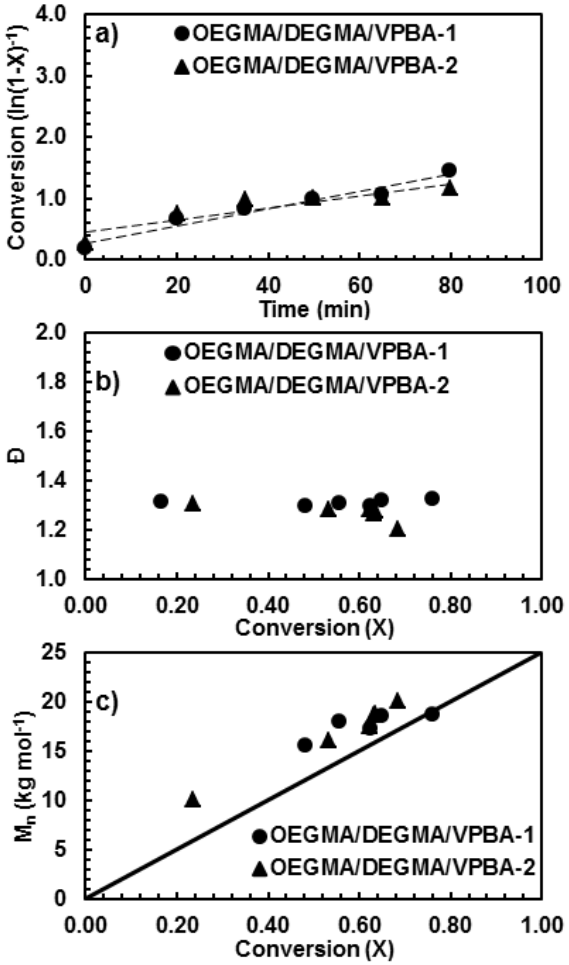

FIGURE 7: a) The semi-logarithmic plots of scaled conversion ($\ln[1-X]^{-1}$]) (X = conversion) versus time; b) the dispersity, Đ, versus conversion (X); c) the number average molecular weight (M_n) versus conversion (X) for OEGMA/DEGMA/VPBA terpolymerizations done in either DMF (1) or DMAc (2) solvent. Please see Table 4 for complete polymer characterization of these two terpolymerizations.

Temperature and pH Sensitivities of Random Copolymers

MEMA homopolymers were shown to have an LCST around 37 °C,[29] making them excellent candidates for targeted drug delivery applications. Water solubility of boronic acids can be altered by changes in both pH and solution diol concentration. The solution behavior of the resulting copolymers is of particular interest, as VPBA not only can serve as a controlling co-monomer for MEMA polymerizations, but also can impart additional solution properties.

A series of MEMA/VPBA copolymers, with a range of VPBA molar compositions F_{VPBA} = 0.045 - 0.13, and molecular weights from M_n = 20.1 - 25.1 kg mol^{-1}, were tested for thermoresponsive behavior as a function of solution composition, copolymer composition and pH. The copolymers were dissolved in either aqueous solution at different concentrations or in buffer solutions from pH 4 to 11 at 0.5 wt% concentration and their temperature response was monitored by UV-Vis spectroscopy (see Tables S2 and S3 in the *Supporting Information).* As a comparison, the corresponding CPTs were plotted as a function of solution concentration (Figure 8a) and pH (Figure 8b). Polymers with controlled structure are suitable for precise LCST determination, and therefore copolymers synthesized with only unprotected VPBA were considered, since in our cases they generally possessed the lowest Đ.

The LCST can be affected by many parameters, such as copolymer composition,[49,65] solution concentration,[65] pH,[65,66] and heating rate.[51,52,67,68] The effect of copolymer composition on CPT was studied since incorporation of VPBA into the copolymer would alter the phase separation temperature. The VPBA segments of the copolymer were not soluble in aqueous solution due to strong hydrogen bonding between the boronic acid moieties and the transition to the tetragonal anionic form that occurs around pH 8-10 in the presence of glucose.[57] As expected, the CPT decreased with an increase of VPBA content in the final copolymer and it was 28.0 - 36.4 °C (at 0.5 wt% solution concentration) with F_{VPBA} = 0.045 - 0.13 (approximately a degree decrease

in CPT per 1 mol% of increase in VPBA content). In previous studies of a similar system where MEMA was copolymerized with VBK via NMP, the CPTs of the resulting copolymers were affected by composition and ranged between 37 and 43 °C.[51]

The effect of solution concentration, ranging from 0.25 - 1 wt%, on CPT was studied as well. As expected, the CPT was found to decrease with an increase in solution concentration. For instance, M/VPBA-5-2 (M_n = 20.1 kg mol^{-1}, Đ = 1.26, F_{VPBA} = 0.045) exhibited an LCST at 37.8 and 35.0 °C for 0.25 and 1.0 wt% solution concentration, respectively. Similar behavior for different polymer systems was observed earlier.[51] The CPTs for solution concentrations above 1 wt% were not determined due to poor solubility of the polymers, resulting from incorporation of VPBA monomer. For instance, M/VPBA-5-1 and M/VPBA-5-2 were the only copolymers found to be soluble at 1 wt%. The CPTs for 0.25 wt% solution concentration of both M/VPBA-10-1 and M/VPBA-10-2 were determined via DLS due to its ability to sense small fluctuations in hydrodynamic diameter, thus giving a more precise CPT value at such low concentrations. At that composition, the CPT was found to be 26 and 27 °C for M/VPBA-10-1 and M/VPBA-10-2 copolymers, respectively. The CPT and hysteresis values are summarized in Table S2 in the *Supporting Information*. The hysteresis was evident for all of the polymer solutions and it was determined by comparing the measured CPT during heating and during cooling.

The effect of changing pH levels on CPT, which can have an effect on solubility when using VPBA as a comonomer, was investigated for M/VPBA-5-1 and M/VPBA-5-2 copolymers at a constant 0.5 wt% concentration as the pH was increased from 4 to 7. As shown in Figure 8b, the CPT decreased sharply from 87 - 88 °C at pH = 4 to 31 - 34 °C at pH 7. The sharp changes in the temperature response are related to the degree of ionization (DI) of the polymer. The pKa for the conjugate acid forms of tertiary amine methacrylate residues in the MEMA homopolymer was found to be 4.9.[29] The hydrolysis of boronate esters is favored at neutral pH conditions[68] and the sugar-responsive behavior occurs at relatively high pH (> 9). For instance, VPBA homopolymer is only soluble in the presence of glucose between pH 9 and 10; otherwise, the polymer is not soluble due to strong hydrogen bonding between the boronic acid moieties.[57]

Protonation of the tertiary amine groups occurs between pH 4-6 for MEMA residues (pK_a 4.9),[29]

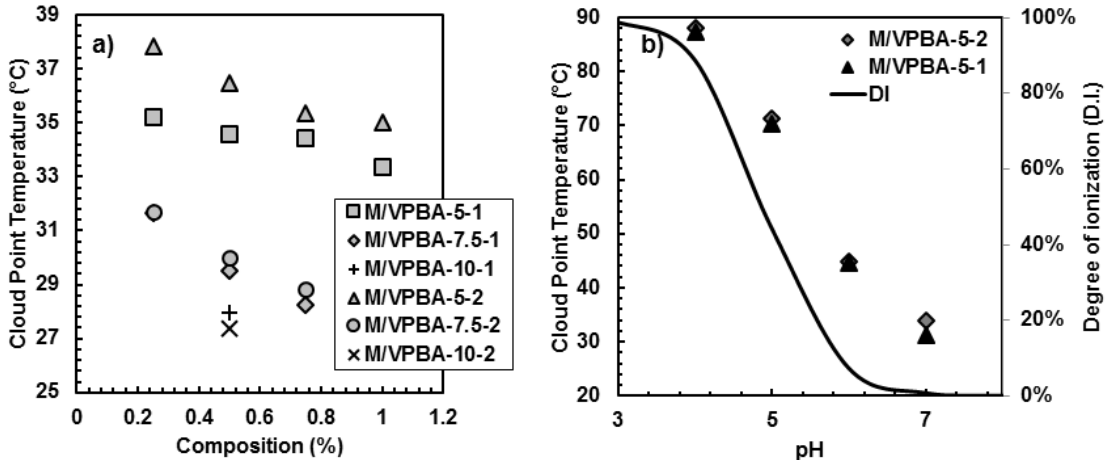

FIGURE 8 a) The CPT dependence of MEMA/VPBA random copolymers on composition and on solution concentration ; b) The CPT dependence of M/VPBA-5-1 (M_n = 20.5 kg mol^{-1}, Đ = 1.17, F_{VPBA} = 0.075) and

M/VPBA-5-2 (M_n = 20.1 kg mol^{-1}, Đ = 1.26, F_{VPBA} = 0.045) samples on pH at 0.5 wt% as measured by UV-Vis spectroscopy with a heating ramp of 1 °C min^{-1}.

and DI decreases from about 89% to 7% with an increase in pH in this range. As the repulsive forces between the charged units become less dominant in the molecule conformation, the chains become more compact and hydrophobic at higher pH, resulting in lowering of the CPT. At pH 7, the DI decreases below 0.1 wt%, a point at which the MEMA residues in the polymer are considered to be neutral. It is interesting to note that the two polymer samples (M/VPBA-5-1 and M/VPBA-5-2) exhibited similar CPTs at pH 4-6. At pH 7, M/VPBA-5-1 had CPT slightly lower than M/VPBA-5-2, which is in part from higher VPBA content in M/VPBA-5-1 (0.075 versus 0.045) since MEMA is considered neutral at this point. With higher VPBA content, the polymer is more hydrophobic, and as a result the CPT is lower as discussed previously. The CPT measured at pH 7 is comparable to the CPT of these two copolymers in aqueous solution at 0.5 wt%. At pH > 7, the MEMA/VPBA copolymers are no longer soluble at room temperature while at pH < 4, the copolymers were completely water-soluble. The CPT values are summarized in Table S3 in the *Supporting Information.* The pH of M/VPBA-5-1 (at 0.5 wt% solution concentration) was 6.7, yielding CPT of 34.6 °C (which is between CPT of 44.6 °C at pH of 6 and 31.2 °C at pH of 7. Solution of M/VPBA-7.5-2 at 0.75 wt% and 0.5 wt% had pH of 7.19 and 7.66 respectively. Based on the pH measurement study performed for two copolymers at 0.5 wt%, M/VPBA-5-1 (which has a similar composition to M/VPBA-7.5-2) had a CPT of about 31 °C at pH 7, and at pH of 7.66, the polymer might not be soluble at room temperature.

Rheology – Small Angle Light Scattering (SALS)

Rheological measurements using SALS under constant shear provided an additional tool in examining temperature-induced phase transitions and provided corroborating evidence for phase transitions measured by DLS and UV-vis. Figure 9 shows scattering images of the sample along with the change in viscosity (Figure 9a) at different temperatures. At low temperatures (points A and B in Figure 9a and

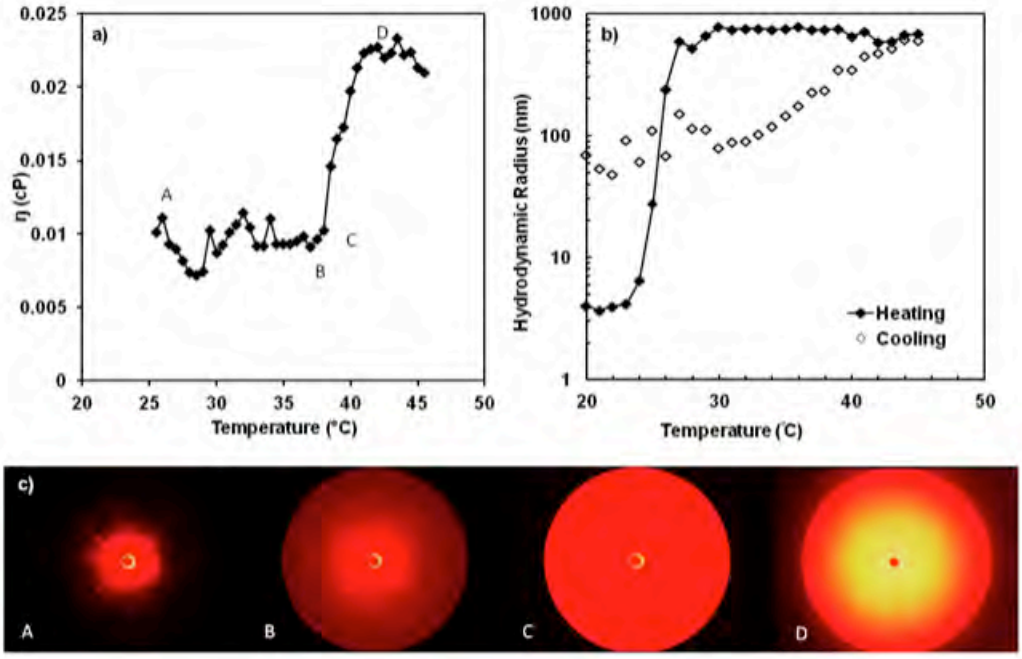

FIGURE 9 a) Viscosity as a function of temperature for 0.5 wt% M/VPBA-5-1 polymer solution in DI water

heated from 25 to 45 °C in 1 °C min^{-1} intervals and measured at constant frequency (1 s^{-1}); b) Average hydrodynamic radius (R_h) as measured by DLS; c) The SALS images correspond to specific temperatures (25, 37, 37.5, and 41.5 °C) as indicated on the curve by points A, B, C, and D, respectively.

in Figure 9c), insignificant scattering is seen from the sample; however, at higher temperatures, the scattering becomes more prominent due to phase separation (points C and D), and an increase in viscosity of the sample is observed. The CPT is around 38 °C which is close to 36.4 °C as measured by UV-vis (Table S2) and to 33 °C as measured by DLS (Figure 9b) for this sample.

CONCLUSIONS

Nitroxide-mediated polymerization (NMP) of 2-N-morpholino ethyl methacrylate (MEMA) was successful in the presence of a styrenic co-monomer, 4-vinylphenylboronic acid (VPBA), at low concentrations (~ 10 mol% VBPA). The effect of varying feed conditions, such as controlling co-monomer (VPBA) composition, solvent type, boronic acid protection group type, and temperature, was studied. The MEMA/VPBA copolymerization using 10 mol% VBPA in dimethylacetamide (DMAc) solvent was deemed successful as evidenced by a linear increase in molecular weight, M_n, versus conversion and low dispersity values (Đ < 1.40). The MEMA/VPBA copolymer was also chain extended with VPBA monomer to assess its ability to reinitiate the polymerization. The resulting block copolymer had a monomodal molecular weight distribution and its molecular weight distribution broadened with Đ = 1.66. The cloud point temperature (CPT) of MEMA/VPBA copolymers was found to be a function of copolymer composition and solution concentration (CPT typically varied between 27.4 - 37.8 °C), as well as pH (CPT increased from 31.2 - 33.8 °C to about 88 °C with a decrease in pH from 7 to 4). The VPBA monomer serves not only as a controlling co-monomer in the polymerization, but the boronic acid functionality is also capable for glucose sensing and thus the combination of these stimuli-sensitive properties in one copolymer is promising for future dual responsive systems.

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GRAPHICAL ABSTRACT

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Vinyl Phenylboronic Acid Controlling Co-monomer for Nitroxide Mediated Synthesis of Thermoresponsive Poly(2-N Morpholinoethyl Methacrylate)

Nitroxide mediated polymerization of N-morpholinoethyl methacrylate (MEMA) was accomplished with small concentrations of vinylphenylboronic acid (VPBA) as a controlling co-monomer. Resulting poly(MEMA-*ran*-VPBA) copolymers were thermoresponsive and the VPBA imparted glucose-sensing functionality. Cloud point temperatures (CPT) varied from about 31-33 °C to 88 °C as pH was altered from 7 to 4. Rheological tests with small angle light scattering (SALS) confirmed CPTs measured by UV-vis and DLS. Chain extensions with a second batch of VPBA resulted in monomodal shifts (SEC) to higher molecular weights, indicating block copolymer formation.