Synthesis and Characterization of Well-Defined Optically Active Methacrylic Diblock Copolymers

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Received 18 April 2012; accepted 13 June 2012; published online
DOI: 10.1002/pola.26223

ABSTRACT: A new, simple, and cost-effective approach toward the development of well-defined optically active diblock copolymers based on methacrylate monomers is described for the first time. Starting from the low-cost optically active (*S*)-(−)-2-methyl-1-butanol, a new optically active methacrylic monomer, namely, (*S*)-(+)-2-methyl-1-butyl methacrylate [(*S*)-(+)-MBuMA], was synthesized. Reversible addition fragmentation chain transfer polymerization was then used for preparing well-defined poly[(*S*)-(+)-MBuMA] homopolymers and water-soluble diblock copolymers based on [(*S*)-(+)-MBuMA] and the hydrophilic and ionizable monomer 2-(dimethyl amino)ethyl methacrylate (DMAEMA). The respective homopolymers and diblock copolymers were characterized in terms of their molecular weights, polydispersity indices, and compositions by size exclusion chromatography and ^{1}H NMR spectroscopy. Polarimetry measurements were used to determine the specific optical rotations of these systems. The structural and compositional characteristics of micellar nanostructures possessing an optically active core generated by p((*S*)-(+)-MBuMA)-*b*-p(DMAEMA) chains characterized by predetermined molecular characteristics may be easily tuned to match biological constructs. Consequently, the aggregation behavior of the p[(*S*)-(+)-MBuMA]-*b*-p[DMAEMA] diblock copolymers was investigated in aqueous media by means of dynamic light scattering and atomic force microscopy, which revealed the formation of micelles in neutral and acidified aqueous solutions. © 2012 Wiley Periodicals, Inc. J Polym Sci Part A: Polym Chem 000: 000–000, 2012

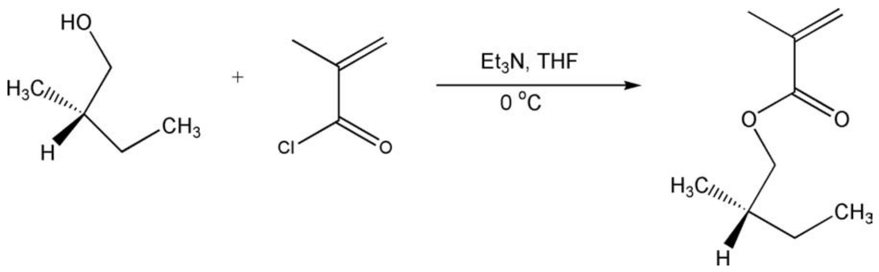
KEYWORDS: block copolymers; chiral; micelles; reversible addition fragmentation chain transfer (RAFT)

INTRODUCTION Nature routinely uses optically active molecules such as D-sugars and L-amino acids to build up chiral biopolymers such as proteins and DNA.[1,2] The specific chiral configuration of such macromolecules imparts unique properties to these materials such as molecular recognition capability and highly efficient catalytic action toward asymmetric catalysis.[2] The significance of the aforementioned chiral biopolymers in biological processes such as self-replication, protein synthesis, regulation, and gene expression cannot be understated,[3–6] and in contrary, racemic molecules have been proved to be inefficient in these processes.

Inspired by naturally occurring optically active polymers, chiral polymeric materials obtained synthetically[7–11] have been of particular interest in the area of modern polymer science because of their fascinating applicability in chiral and molecular recognition,[12–14] enantiomeric separation,[15,16] chiroptical switching,[17,18] nonlinear optics,[19,20] circular photoluminescence and electroluminescence,[21,22] and so forth. However, most of the developed systems are characterized by structural complexity and/or demanding synthetic methodologies toward their preparation. Moreover, a limited number of reports appear in the literature dealing with the synthesis of well-defined optically active polymers characterized by predetermined molecular weights (MWs) and narrow molecular weight distributions (MWDs).[23–31] The aforementioned characteristics are highly desirable, as they allow for their structural characteristics to be correlated to the properties of the materials.

As far as methacrylate-based polymers are concerned, relatively complex functional moieties such as amino acids,[32] 1,1′-binaphthyl,[33] urea,[34] cyclic pyrrolidinyl moieties or succinimide[35] and cholesteryl groups[36] have been introduced as side chains to induce optical activity. The synthesis of optically active methacrylic monomers characterized by structural simplicity has not yet been reported.

Herein, we report for the first time the synthesis of a new, simple, and optically active methacrylic monomer by following an easy and cost-effective synthetic approach, that is, by using a cheap optically active methacrylic alcohol as a starting material. For the synthesis of the respective homopolymers, reversible addition fragmentation chain transfer (RAFT) polymerization was used, which is a versatile



SCHEME 1 One-step synthetic methodology followed for the preparation of (*S*)-(+)-MBuMA optically active monomer.

polymerization technique, allowing for the preparation of well-defined polymers of various architectures such as block copolymers, star polymers, graft polymers, hyperbranched polymers, and polymer (co)networks.[37,38]

The RAFT process was readily used to prepare well-defined poly((S)-(+)-2-methyl-1-butyl methacrylate) p((S)-(+)-MBuMA) homopolymers as well as diblock copolymers with the water-soluble and ionizable 2-(dimethyl amino)ethyl methacrylate (DMAEMA) on sequential chain growth, using p((*S*)-(+)-MBuMA) as the macro-chain transfer agents (macro-CTAs). The molecular and compositional characteristics of the resulting homopolymers and diblock copolymers were determined by size exclusion chromatography (SEC) and ^{1}H NMR spectroscopy, respectively.

The aggregation behavior of the p((*S*)-(+)-MBuMA)-*b*-p(DMAEMA) diblock copolymers was investigated by dynamic light scattering (DLS). In aqueous media, micelles are generated consisting of a hydrophobic, optically active core comprised of p((*S*)-(+)-MBuMA) chains and a hydrophilic, ionizable (depending on the pH) p(DMAEMA) corona. Micellization of diblock copolymers possessing an optically active block segment may lead to nanoparticles with size and shape that can be tuned to match biological constructs.[39] They may also have applications in the selective uptake of chiral molecules for enantiomeric separations. Hence, the preparation and characterization of optically active methacrylate-based micelles consisting of simple optically active methacrylates as well as their evaluation as effective chiral recognition systems will be a highly promising research direction.

RESULTS AND DISCUSSION

Poly((*S*)-(+)-MBuMA) Homopolymers

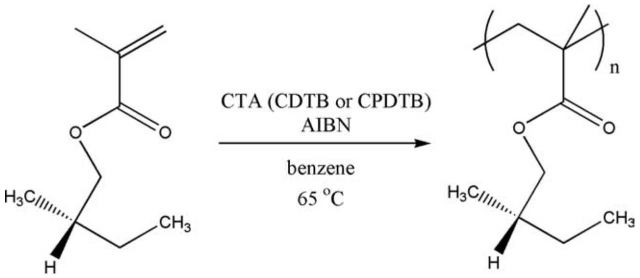
In this work, for the first time, a new optically active monomer, namely, (*S*)-(+)-MBuMA, was synthesized via a typical esterification methodology reported in the literature,[40] involving the reaction of the low-cost optically active (*S*)-(−)-2-methyl-1-butanol with methacryloyl chloride in the presence of triethylamine, as illustrated in Scheme 1.

RAFT polymerization was then used to prepare a series of well-defined optically active p((*S*)-(+)-MBuMA) homopolymers, as shown in Scheme 2.

Two monofunctional CTAs were used in polymer synthesis, namely, cumyl dithiobenzoate (CDTB, CTA 1) and 2-cyano-2-propyl benzodithioate (CPDTB, CTA 2), with 2,2′-azobis(isobutylnitrile) (AIBN) serving as the radical source. All polymers were obtained as pink gum-like solids, which are soluble in most common organic solvents used to dissolve *n*-butyl methacrylate such as tetrahydrofuran (THF), benzene, ethyl acetate, and toluene. To demonstrate the controlled character of the RAFT process in the polymerization of the (*S*)-(+)-MBuMA, p((*S*)-(+)-MBuMA) homopolymers were prepared in the presence (RAFT polymerization) and absence (conventional free radical polymerization) of a CTA under identical experimental conditions (entries 1 and 6 in Table 1). The SEC traces of the two homopolymers prepared by RAFT and conventional free radical polymerization are plotted in Figure 1. The RAFT homopolymer was characterized by low polydispersity index (PDI = 1.16) and unimodal MWD, whereas the homopolymer prepared via the conventional free radical process exhibited broad MWD (2.0).

The MW parameters (number-average MWs and PDIs) along with the polymerization yield of the synthesized homopolymers are summarized in Table 1. As can be seen from the table, all polymers synthesized by RAFT were characterized by unimodal, narrow MWDs and low PDIs (<1.25).

Even though in the literature it is reported that there is no difference in the effectiveness and reactivity of the CDTB and CPDTB toward methacrylate-based monomers,[38] in our case, the latter was proved to be more effective in terms of polymerization yield by following exactly the same experimental conditions (i.e., reaction time, solution concentration, and temperature), as p(*S*)-(+)-MBuMA) homopolymers synthesized using CTA 2 (CPDTB) were obtained in a much higher yield (∼65%) when compared with those obtained in the presence of CTA 1 (CDTB; ∼35%).



SCHEME 2 RAFT-controlled radical polymerization of (*S*)-(+)-MBuMA carried out in solution in the presence of either CDTB or CPDTB and AIBN.

TABLE 1 Yield and Molecular Weight Parameters of Homopolymers Based on (*S*)-(+)-MBuMA Obtained by RAFT and FRP

Entry	Experimental Structure[a]	Yield (%)	Theoretical Molecular Weight (g mol^{-1})[b]	SEC Results	
				M_n	PDI
1	(*S*)-(+)-MBuMA$_{55}$ (CDTB)	35	5,750	8,135	1.16
2	(*S*)-(+)-MBuMA$_{85}$ (CDTB)	30	9,650	12,600	1.25
3	(*S*)-(+)-MBuMA$_{55}$ (CDTB)	33	5,450	8,800	1.12
4	(*S*)-(+)-MBuMA$_{70}$ (CPDTB)	65	15,500	11,000	1.13
5	(*S*)-(+)-MBuMA$_{75}$ (CPDTB)	68	16,150	11,750	1.15
6	(*S*)-(+)-MBuMA$_{100}$ (FRP)	95	15,600	14,750	2.00

[a] Determined by SEC.

[b] [(g monomer)/(mol RAFT agent)] × (polymerization yield) + MW of CTA; M_n, number-average molecular weight; PDI, polydispersity index; (*S*)-(+)-MBuMA, (*S*)-(+)-2-methyl-1-butyl methacrylate; CDTB, cumyl dithiobenzoate; CPDTB, 2-cyano-2-propyl benzodithioate; FRP, free radical polymerization.

Optical rotation measurements were carried out in chloroform for the (*S*)-(+)-MBuMA monomer and two p((*S*)-(+)-MBuMA) homopolymers characterized by different average MWs. More precisely, the specific optical rotation value obtained for the (*S*)-(+)-MBuMA monomer was $[\alpha]_D^{21}$ (°) +3.17 ± 0.1. The optical rotation values for the (*S*)-(+)-MBuMA$_{55}$ ($M_n = 5{,}750$ g mol^{-1}; entry 1 in Table 1) and the (*S*)-(+)-MBuMA$_{70}$ ($M_n = 15{,}500$ g mol^{-1}; entry 4 in Table 1) homopolymers were determined to be $[\alpha]_D^{24}$ (°) +3.3 ± 1.6 and $[\alpha]_D^{24}$ (°) +3.4 ± 0.75, respectively. Even though the aforementioned homopolymers were characterized by different MW parameters, no significant variations in the values of the specific optical rotations were observed, demonstrating the independency of the latter on the molecular weight. This result is in agreement with previously reported work by Skey and O'Reilly[23] and Endo and coworkers.[41] Moreover, the similarity of the optical rotation values of the two homopolymers to that of the monomer suggests that no cooperative effect exists between the polymer units within the homopolymers (i.e., no helix formation).

Unfortunately, attempts to record circular dichroism (CD) spectra were hampered by the ester chromophore transitions having absorptions in the far-UV region and small extinction coefficients; typically for esters, these can be expected to be $\lambda_{max} = 190$–215 nm and $\varepsilon = 50$–500 mol^{-1} dm^{-3} cm^{-1}. The far-UV region is notoriously difficult to access for weak chromophores because of the limited range of solvents with no significant absorption in this range. Homopolymer **4** was not soluble in pentane, acetonitrile, water, or trifluoroethanol or mixtures of these solvents. A 2:1 ratio of cyclohexane and propanol did dissolve the polymer though significant absorption for the solvent was observed from 240 nm and lower. Therefore, no absolutely distinct Cotton effects could be observed in the range of 200–300 nm. As can be seen from Figure 2, weak possible Cotton effects were visible in the CD spectrum in the region 200–300 nm that overlap with absorptions visible in the UV–vis spectra. The far-UV absorptions in the UV spectrum (Fig. 2) could be deconvolved into three major peaks at 209, 224, and 255 nm, tentatively assigned to the π–π^* and n–π^* transitions of the carbonyl

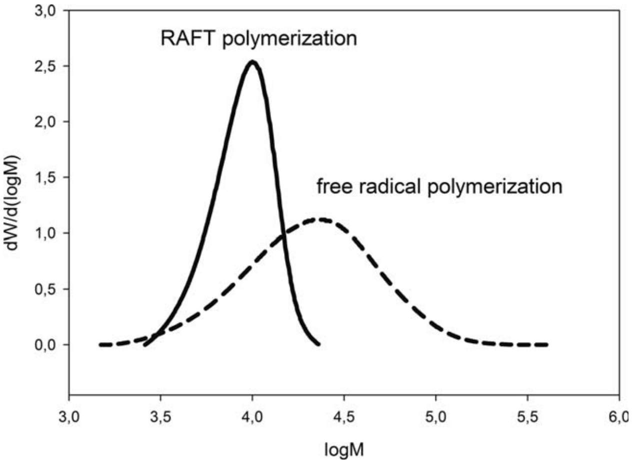


FIGURE 1 SEC traces of the p((*S*)-(+)-MBuMA) homopolymer synthesized by RAFT polymerization and the respective one synthesized by conventional free radical polymerization.

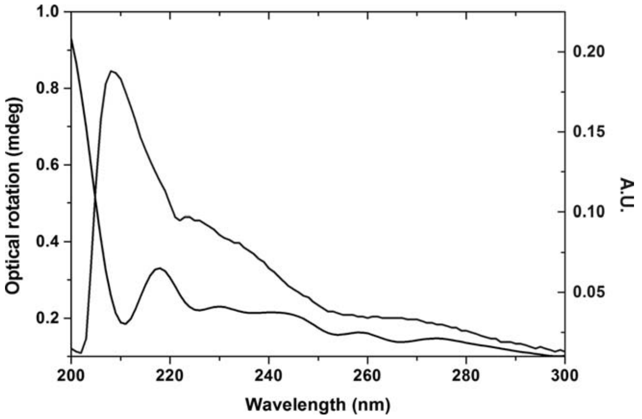


FIGURE 2 UV–vis absorption spectrum (upper line) and circular dichroism spectrum (lower line) of homopolymer **4** in cyclohexane:1-propanol (2:1) at 21 °C.

TABLE 2 Yield and Molecular Weight Parameters of p((*S*)-(+)-MBuMA)-*b*-p(DMAEMA) Copolymers

Entry	Experimental Structure[a]	Yield (%)	Theoretical Molecular Weight (g mol^{-1})[b]	SEC Results M_n (g mol^{-1})	PDI
1	(*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{104}$	65	23,500	24,500	1.15
2	(*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{230}$	72	37,100	45,000	1.15
3	(*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{475}$	60	56,000	83,500	1.35

[a] Determined by SEC and ^{1}H NMR.

[b] [(g monomer)/(mol RAFT agent)] × (polymerization yield) + M_n of macro-CTA 1; M_n, number-average molecular weight; PDI, polydispersity index; (*S*)-(+)-MBuMA, (*S*)-(+)-2-methyl-1-butyl methacrylate; DMAEMA, 2-(dimethyl amino)ethyl methacrylate.

and the π–π* transition of the aromatic chain ends from the CTDB. It is apparent that better solvent systems and possibly synchrotron CD measurements will be necessary to conclusively observe the electronic optical activity of these polymers.

p((*S*)-(+)-MBuMA)-*b*-p(DMAEMA) Diblock Copolymers

Amphiphilic diblock copolymers were synthesized through chain growth of the p((*S*)-(+)-MBuMA) (macro-CTA 1) via the addition of the hydrophilic and ionizable DMAEMA. The degree of polymerization (DP) of the presynthesized p((*S*)-(+)-MBuMA) was 55 in all cases, whereas the DP of the DMAEMA block segment varied (104, 230, and 475; entries 1–3 in Table 2). The polymerization yield, the theoretical and experimental MWs, and the PDIs of the obtained p((*S*)-(+)-MBuMA)-*b*-p(DMAEMA) diblock copolymers are summarized in Table 2.

All diblock copolymers received as orange solids were obtained in good yield (60–72%). The PDIs were relatively low (1.15–1.35), with the highest value corresponding to the (*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{475}$ having the highest MW. Moreover, the MWD of the diblock copolymers is shifted toward higher MWs when compared with that of the (*S*)-(+)-MBuMA$_{55}$ homopolymer (Fig. 3), demonstrating the block efficiency from homopolymer to block copolymer[42,43] and thus providing further evidence for the "living" nature of the polymerization under these conditions.[23,38]

The specific optical rotation of (*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{475}$ (M_n = 83,500 g mol^{-1}; entry 3 in Table 2) in chloroform was determined to be $[\alpha]_D^{21}$ (°) +5.1 ± 0.6, demonstrating the preservation of optical activity of the (*S*)-(+)-MBuMA units in the block copolymer structure.

Aggregation Behavior in Aqueous Media

Because of their amphiphilic character, the p((*S*)-(+)-MBuMA)-*b*-p(DMAEMA) diblock copolymers are expected to self-assemble in selective for one of the block solvents generating well-organized nanomorphologies in solution. The aggregation behavior of the p((*S*)-(+)-MBuMA)-*b*-p(DMAEMA) diblock copolymers was investigated in aqueous media. Water is a good solvent for the p(DMAEMA) block segment, and therefore, micelles are generated in aqueous solutions consisting of a p(DMAEMA) solvating corona and a p((*S*)-(+)-MBuMA) optically active core. The hydrodynamic diameters (D_H) of the resulting macromolecular aggregates were determined by DLS and atomic force microscopy (AFM). The experimental D_H values for the p((*S*)-(+)-MBuMA)-*b*-p(DMAEMA) micelles generated in water at pH = 2.54 and 5.5 are summarized in Table 3. From the obtained data, it can be clearly seen that under acidified conditions, the hydrodynamic diameter or the micellar aggregates increases as expected, because on protonation of the DMAEMA units found on the micellar exterior, chain extension is caused through electrostatic repulsion.[44,45] At a pH of 2.54, the DMAEMA block can be considered fully charged ($\alpha \approx 1$),[46] and dramatic expansions in the size micelles with poly(DMAEMA) coronae have been previously recorded on decreasing the pH to similar values.[47,48] In some cases, the obtained D_Hs values exceed the maximum theoretical micelle diameters calculated assuming spherical morphology and fully extended chains (see Table 3), suggesting the presence of micellar aggregates in solution.

Figure 4 illustrates sample AFM micrographs of spherical block copolymer micelles of (a) (*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{104}$ and (b) (*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{230}$ generated in water at pH 2.54 and 5.5, respectively. It is noteworthy that the D_H values from the AFM measurements are in

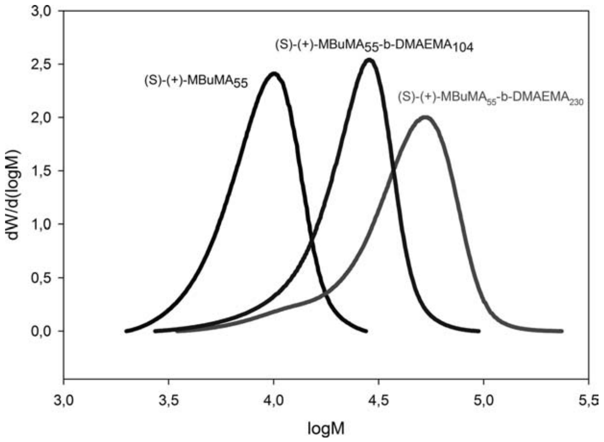


FIGURE 3 SEC traces of the (*S*)-(+)-MBuMA$_{55}$ homopolymer and the corresponding (*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{104}$ and (*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{230}$ diblock copolymers prepared via chain growth of the former with DMAEMA.

TABLE 3 Experimental Hydrodynamic Diameters (D_Hs) Obtained by DLS for the p((*S*)-(+)-MBuMA)-*b*-p(DMAEMA) Diblock Copolymer Micelles Formed in Aqueous Solutions at Different pH

Entry	Experimental Structure[a]	pH	D_H (Theoretical) (nm)[b]	D_H (DLS) (nm)	Polydispersity (DLS)	D_H (AFM) (nm)
1	(*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{104}$	5.5	80	N.D.	N.D.	N.D.
2	(*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{104}$	2.54	80	68	0.323	74
3	(*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{230}$	5.5	144	70	0.210	98
4	(*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{230}$	2.54	144	199	0.282	122
5	(*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{475}$	5.5	267	116	0.333	137
6	(*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{475}$	2.54	267	300	0.361	230

[a] Determined by SEC and ^{1}H NMR.

[b] Calculated assuming a spherical morphology and fully extended chains; (*S*)-(+)-MBuMA, (*S*)-(+)-2-methyl-1-butyl methacrylate; DMAEMA, 2-(dimethyl amino)ethyl methacrylate.

closer agreement with the D_H values from DLS in pH 5.5 solutions; this is a result of AFM measurement of the largely dehydrated micelles with collapsed coronae.

As seen from the images, spherical micelles are present in both cases, whereas the existence of micellar aggregates is suggested for the sample from the pH 2.54 solution. The latter supports the supposition from the DLS data that some micellar aggregation occurs for the pH 2.54 solutions.

EXPERIMENTAL

Materials and Methods

THF (HPLC grade; Scharlau) and benzene (99%; Fluka) were stored over CaH_2 before distillation under reduced pressure immediately prior to the reactions. DMAEMA (99%; Merck) was passed through basic alumina column (Activated, basic, Brockmann I, ~150 mesh, pore size = 58 Å), stored over CaH_2 (99.99%; Aldrich), followed by distillation under reduced pressure, and storage under nitrogen atmosphere before use. Triethylamine (99.5%; Scharlau) was stored under anhydrous $MgSO_4$ (98%; Scharlau), followed by filtration before use. AIBN (95%; Sigma-Aldrich) was recrystallized twice from ethanol. (*S*)-(−)-2-Methyl-1-butanol (99%; Sigma-Aldrich), methacryloyl chloride (97%; Fluka), methanol (99.9%; Scharlau), ethanol (99.9%; Scharlau), and *n*-hexane (96%; Scharlau) were used as received.

Syntheses

Synthesis of CDTB

CDTB was synthesized in two steps, following a procedure reported by Rizzardo et al.[49] Briefly, the first step involved the preparation of dithiobenzoic acid via the reaction of sulfur, sodium methoxide, and benzyl chloride in methanol at room temperature for 18 h. Subsequently, dithiobenzoic acid was left to react with α-methylstyrene in carbon tetrachloride at 70 °C for 18 h to obtain CDTB in 19.3% yield after purification by column chromatography (silica gel) using *n*-hexane as solvent.

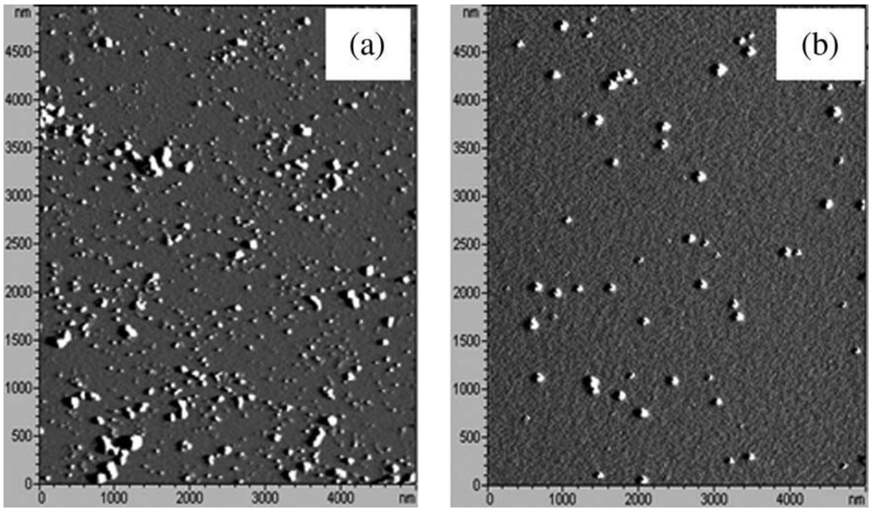


FIGURE 4 AFM (topography/derivative) images of the diblock copolymer micelles formed in aqueous media: (a) (*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{104}$ at pH = 2.54 and (b) (*S*)-(+)-MBuMA$_{55}$-*b*-DMAEMA$_{230}$ at pH = 5.5. Scale: 5 μm × 5 μm.

^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.87 (d, 2H), 7.58–7.22 (m, 8H), 2.01 (s, —CH_3).

Synthesis of (S)-(+)-2-MBuMA

A typical procedure for the synthesis of the (*S*)-(+)-2-MBuMA is described.[38] To a round-bottomed flask (100 mL) equipped with an egg-shaped polytetrafluoroethylene (PTFE) stirring bar, methacryloyl chloride (3.5 g, 35.5 mmol) was added dropwise into a mixture of (*S*)-(−)-2-methyl-1-butanol (2.46 g, 27.9 mmol) and triethylamine (19.4 mL) in freshly distilled THF (19 mL) at 0 °C. After the addition was completed, the mixture was left to stir for 1 h until it reached room temperature. The whole mixture was then placed in the refrigerator (to assist precipitation of the reaction byproduct, namely, triethylamine hydrochloride salt) for 1 day. The mixture was then left to reach room temperature followed by filtration to remove the salt. Subsequently, basic alumina was added into the filtrate and left to stir at room temperature for 1 h. The basic alumina was then filtered off, and the filtrate was passed through a basic alumina column followed by washing of the latter with THF. The volatiles were removed under vacuum with the aid of a rotary evaporator, and the product was further dried in the vacuum oven at room temperature for 1 day. Yield: 30% wt.

^{1}H NMR ($CDCl_3$): δ (ppm): 1.96 ($\mathbf{CH_3}$—C), 5.52 and 6.07 (C**H**=C**H**), respectively, 4.11 ($\mathbf{CH_2}$—O), 2.02 (C**H**—CH_3), 1.09 (CH—$\mathbf{CH_3}$), 1.31 ($\mathbf{CH_2}$—CH), 0.88 (CH_2—$\mathbf{CH_3}$).

Synthesis of p((S)-(+)-MBuMA) by RAFT Polymerization

A typical procedure for the synthesis of the p((*S*)-(+)-MBuMA) is described. To a round-bottomed flask (25 mL) equipped with an egg-shaped PTFE stirring bar and maintained under nitrogen atmosphere, (*S*)-(+)-2-MBuMA (1.5 g, 10 mmol) was added using Schlenk-line techniques. CDTB (0.027 g, 0.1 mmol) and AIBN (0.01 g, 0.06 mmol) were dissolved in benzene (1.7 mL), and the monomer was added via the aid of a syringe. The reaction mixture was stirred rapidly at room temperature, degassed by three freeze-evacuate-thaw cycles, and heated at 65 °C for 20 h. The polymerization was terminated by cooling the reaction mixture to room temperature. The produced *p*((S)-(+)-MBuMA) was retrieved by precipitation in methanol (10 mL).

^{1}H NMR ($CDCl_3$): δ (ppm): 3.95 ($\mathbf{CH_2}$—O), 1.91 (C**H**—CH_2—CH_3), 1.81 ($\mathbf{CH_2}$—C), 1.25 ($\mathbf{CH_3}$—C and CH—$\mathbf{CH_2}$—CH_3), 1.024 (CH—$\mathbf{CH_3}$), 0.90 (CH—CH_2—$\mathbf{CH_3}$) [tacticity (calculated based on —$\mathbf{CH_3}$ backbone protons): 75% rr, syndiotactic ($\delta \sim 0.8$ ppm); 14% mr, heterotactic ($\delta \sim 1.0$ ppm); 11% mm, isotactic ($\delta \sim 1.2$ ppm)].

Synthesis of p((S)-(+)-MBuMA) by Free Radical Polymerization

To a round-bottomed flask (25 mL) equipped with an egg-shaped PTFE stirring bar and maintained under nitrogen atmosphere, (*S*)-(+)-2-MBuMA (1 g, 6.4 mmol) was added using Schlenk-line techniques. AIBN (0.01 g, 0.064 mmol) was dissolved in benzene and was added to the monomer with the aid of a syringe. The reaction mixture was stirred rapidly at room temperature, degassed by three freeze-evacuate-thaw cycles, and heated at 65 °C for 20 h. The polymerization was terminated by cooling the reaction mixture to room temperature. The produced p((S)-(+)-MBuMA) was retrieved by precipitation in methanol (5 mL).

Synthesis of p((S)-(+)-MBuMA)-b-p(DMAEMA) Block Copolymer

A typical procedure for the synthesis of the p((*S*)-(+)-MBuMA)-*b*-p(DMAEMA) diblock copolymer is described. To a round-bottomed flask (25 mL) equipped with an egg-shaped PTFE stirring bar and maintained under nitrogen atmosphere, p((*S*)-(+)-MBuMA) (M_n = 8135 g mol^{-1}, 0.1103 g, 0.0136 mmol of the macro-CTA) and DMAEMA (0.32 g, 2.04 mmol) were added using Schlenk-line techniques. AIBN (0.0013 g, 0.00816 mmol) was dissolved in benzene (0.7 mL) and was added into the reactor via the aid of a syringe. The reaction mixture was stirred rapidly at room temperature, degassed by three freeze-evacuate-thaw cycles, and heated at 65 °C for 20 h. The polymerization was terminated by cooling the reaction mixture to room temperature. The produced p((S)-(+)-MBuMA)-*b*-p(DMAEMA) was retrieved by precipitation in *n*-hexane (10 mL).

^{1}H NMR ($CDCl_3$): δ (ppm): 4.05 ($\mathbf{CH_2}$—O), 1.91 (C**H**—CH_2—CH_3), 1.81 ($\mathbf{CH_2}$—C), 1.25 ($\mathbf{CH_3}$—C and CH—$\mathbf{CH_2}$—CH_3), 1.024 (CH—$\mathbf{CH_3}$), 0.90 (CH—CH_2—$\mathbf{CH_3}$), 2.60 ($\mathbf{CH_2}$—N), 2.06 ($\mathbf{CH_3}$—N—$\mathbf{CH_3}$).

Micellization

Micellar solutions of the p((*S*)-(+)-MBuMA)-*b*-p(DMAEMA) block copolymers were prepared in aqueous media. Each block copolymer was placed in water and stirred at room temperature until complete dissolution. In the case of the acidified solutions, the pH was adjusted on adding one drop of HCl (10% w/w).

Characterization

NMR spectra were recorded in $CDCl_3$ with tetramethylsilane used as an internal standard using an Avance Brucker 300 MHz spectrometer equipped with an Ultrashield magnet. The MWs and PDIs of the polymers were determined by SEC using equipment supplied by Polymer Standards Service (PSS). All measurements were carried out at room temperature using Styragel HR 3 and Styragel HR 4 columns. The mobile phase was THF delivered at a flow rate of 1 mLmin^{-1} using a Waters 515 isocratic pump. The refractive index was measured with a Waters 2414 refractive index detector supplied by PSS. The instrumentation was calibrated using poly(methyl methacrylate) standards with low PDI [MWs of 739,000, 446,000, 270,000, 126,000, 65,000, 31,000, 14,400, 4200, 1580, 670, 450, and 102 (methyl isobutyrate) g mol^{-1}] supplied by PSS.

The specific optical rotation of the monomer (*S*)-(+)-MBuMA and of the homopolymers **4** and **5** in chloroform (AR) solutions were recorded in a 5-cm sample tube on an Optical Activity AA-5 polarimeter at 21 and 24 °C, respectively, with the instrument zeroed with the chloroform solvent.

CD spectra were recorded on a JASCO J-715 Spectropolarimeter with a PTC-4235/15 Peltier heating attachment. The final

CD spectrum obtained from a solution of homopolymer **4** in cyclohexane/1-propanol (2:1) at 20 °C was the average of three separate measurements of 32 accumulations each, with the cyclohexane/propanol solvent subtracted.

The UV–vis spectrum was recorded on a Unicam UV-500 UV–Visible Spectrometer and obtained from homopolymer **4** in a cyclohexane:1-propanol (2:1) solution with the solvent as the baseline.

DLS measurements were carried out using a 90Plus Brookhaven DLS spectrometer equipped with a 30-mW laser operating at 633 nm. DLS experiments were performed at 90° scattering angle. Solution concentrations were maintained at $\sim$0.1 g L^{-1}. The high quality of the scattering curves was ensured by repeating the measurements several times. All polymer solutions were filtered through cellulose acetate microfilters (pore size: 0.45 μm) prior to the measurements.

AFM measurements were performed on a PicoPlus scanning probe microscope from Molecular Imaging (Agilent) using a cantilever (length: 125 mm; width: 45 mm; resonant frequency: 200–400 kHz; force constant: 25–75 N m^{-1}; tip radius <10 nm, height: 12–16 mm; Applied Nanostructures). Dilute solutions of the p((*S*)-(+)-2-MBuMA)-*b*-p(DMAEMA) diblock copolymers (0.1 g L^{-1}) prepared in aqueous media (at pH 2.54 and 5.5) were spin coated on a mica substrate and visualized by AFM. All measurements were carried out with tapping mode at room temperature in the air.

CONCLUSIONS

Conclusively, we have presented for the first time the synthesis of a new, simple, and optically active methacrylic monomer (*S*)-(+)-2-MBuMA by following an easy and cost-effective synthetic methodology, thus creating a straightforward and undemanding approach toward the design and synthesis of optically active monomers characterized by structural simplicity.

RAFT-controlled radical polymerization has been successfully used for the preparation of well-defined homopolymers and water-soluble diblock copolymers based on this monomer. The latter demonstrated the ability to self-organize in aqueous solutions creating well-defined macromolecular aggregates (i.e., micelles) of tunable diameters possessing a hydrophilic and ionizable corona and an optically active hydrophobic core. Such optically active micellar nanostructures are expected to act as effective chiral recognition systems. Future work involves the evaluation of the p((*S*)-(+)-2-MBuMA)-*b*-p(DMAEMA) diblock copolymer micelles for the separation of enantiomeric molecules by using the micellar electrokinetic chromatography (MEKC) technique. The latter is the second most commonly used capillary electrochromatography method, in which the separation mechanism is based on the electrophoretic mobility and the partitioning of the analytes between the mobile phase and the micellar aggregates that are present, acting as a moving stationary phase or else a pseudo-stationary phase. It is expected that the tunable design of the aforementioned micellar systems in terms of size, morphology, hydrophobic/hydrophilic content, and charge combined with the MEKC method will lead to the development of highly efficient optically active polymeric materials with potential use in chiral separation processes.

ACKNOWLEDGMENTS

This work was financially supported by the University of Cyprus. The authors are grateful to Costas S. Patrickios for providing access to the DLS and AFM apparatus. They also thank the A. G. Leventis Foundation for a generous donation that enabled the purchase of the NMR spectrometer of the University of Cyprus.

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