Enabling Reversible Addition-Fragmentation Chain-Transfer Polymerization for Brush Copolymers with a Poly(2-oxazoline) Backbone

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ABSTRACT: The combination of different monomer classes has been sought after to access a wider range of brush copolymers owing to their unique properties derived from their dense macromolecular structures. Herein, we report the synthesis of a 2-oxazoline monomer (RAFTOx) containing a chain transfer agent at the 2-position and its subsequent utilization in reversible addition-fragmentation chain-transfer (RAFT) polymerization. With the aim of tuning the brush density in these polymers, homopolymers, block copolymers, and gradient copolymers of various ratios with 2-ethyl-2-oxazoline and RAFTOx have been prepared. Selected brush macroCTAs were then used for the RAFT polymerization of N,N-dimethylacrylamide and 2-ethyhexyl acrylate to prepare brush copolymers of different architectures.

INTRODUCTION

Brush copolymers continue to be of growing importance, with numerous reports from synthesis to application being reported each year.1−7 With the use of controlled radical polymerization (CRP) techniques, it is possible to form complex macromolecular structures with excellent control.5,8 Brush copolymers have been extensively studied for their intriguing properties that are inherently different compared to that of their linear counterpart, highlighting its importance as a macromolecular structure.9 For example, in bottlebrush polymers, where the branches are very densely grafted onto the backbone, steric interactions between side chains result in the backbone being partially or fully extended, leading to unusual rheological behavior.7 This has led to a range of applications of graft copolymers exploiting their mechanical and viscoelastic properties. Numerous synthetic approaches to brush copolymers exist1−5,7 and a plethora of recent literature studies on the grafting-from technique alone highlights the growing importance for well-defined methods.1,5,6,9 While one may argue that a brush copolymer from a single polymerization method enables a facile synthesis,7 the combination of two polymerization techniques can be an advantageous route for incorporating monomer classes, which would otherwise not be compatible, an example being 2-oxazolines and vinyl monomers.10,11 2-Oxazoline is an incredibly powerful and versatile monomer class that has been widely used for biological applications12,13 as well as industrial applications in adhesives14 and lubricants.15

Reversible addition-fragmentation chain-transfer (RAFT) polymerization is a versatile and robust technique in which a wide range of monomers can be polymerized with a good molecular weight distribution under various conditions.16 It has emerged as a powerful polymerization technique owing to the use of a chain transfer agent (CTA, interchangeably referred to as a RAFT agent), and its utilization in both linear and branched architectures highlights the popularity and versatility of this technique.16 The design of the CTA, an integral part of the RAFT mechanism, involves an R and Z group with respect to the thiocarbonyl group and can be

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selected from variations of trithiocarbonates, dithioesters, xanthates, and dithiocarbamates.16,17 The Z group influences reactivity of the C=S bond and the stability of the intermediate radical while the R group affects the fragmentation to form the intermediate radical as well as reinitiating propagation.16,18,19 In brush copolymers utilizing the grafting-from approach, where the CTAs are embedded within the polymeric backbone, both the R and Z groups tethering have been previously demonstrated.5,20,21 Its high tolerance toward functional groups and reaction conditions as well as being a metal free reaction allows for, what one may argue, a facile reaction setup comparable to that of a free radical polymerization.16,17

Poly(2-oxazoline)s (POx) formed via cationic ring opening polymerization (CROP)22 are an incredibly versatile polymer class: the amide functionality on the backbone can be regarded as pseudo-peptides; side chains resulting from the R group of the monomer lead to the overall polymer chain displaying hydrophilic,23 hydrophobic,24 or thermoresponsive25 properties; and ease of end group modification can introduce further functionalities. The living nature of the polymerization provides an elegant approach to well-defined polymers and thus has been widely investigated for their biological applications12,13 as well as industrial applications in adhesives14 and lubricants.15 As macromolecular structures, POx has also shown antifouling properties,26,27 and POx-based graft copolymers have also been used for biolubrication purposes.28

The clear synthetic advantages of both RAFT and CROP as well as the numerous POx-based applications mentioned show the need and motivation for combining the two polymerization methods together. The combination of CROP and RAFT has been reported previously for the synthesis of both diblock copolymers29−31 and brush copolymers.32−34 For brush copolymers, the recent literature includes that of Concilio et al. where poly(2-alkyl-2-oxazoline)s were terminated on a RAFT polymerized methacrylic acid backbone to form brush copolymers exhibiting thermoresponsive behavior in oil.33 Similarly, Floyd et al. synthesized cationic bottlebrush copolymers by grafting through vinyl groups present in poly(2-ethyl-2-oxazoline)-based macromonomers via RAFT.34 It must be noted that while there are literature reports of CROP brush copolymers, there are only a few studies where the oxazoline is on the backbone, not on the brush, and no previous studies on poly(2-oxazoline) backbone-based graft copolymers with RAFT on the side chain to date.

We recently reported the combination of CROP with a metal-mediated controlled radical polymerization (CRP) for the synthesis of brush copolymers via an “inimer” approach.9,35,36 In these studies, the carboxylic acid equivalent of the Cu(0)-mediated reversible deactivation radical polymerization (Cu(0)-RDRP) initiator, α-bromoisobutyric acid, was coupled to a hydroxy-functionalized 2-oxazoline monomer to form a bifunctional compound containing both a monomer for CROP and an initiator for Cu(0)-RDRP. The “inimers” were polymerized by CROP, resulting in well-defined polymers of narrow dispersity, and resultant graft copolymers by Cu(0)-mediated RDRP in organic media produced oxazoline-based graft copolymers of acrylate brushes. Following this synthetic approach, our aim in this study is to expand this toolbox and to determine if the combination of CROP with other CRP techniques, primarily RAFT, would be possible, the use of RAFT opening a metal-free approach to the synthesis of brush copolymers.

In this study, we report the synthesis of a novel 2-RAFT CTA-2-oxazoline hybrid monomer, termed RAFTOx, where a trithiocarbonate-based CTA was modified to contain a 2-oxazoline group that can undergo CROP (Scheme 1, step 1). After establishing optimum reaction conditions for the backbone synthesis via CROP (Scheme 1, step 2), select macroCTAs were then used to yield brush copolymers via RAFT polymerization (Scheme 1, step 3). By changing the backbone composition, from a homopolymer of RAFTOx, to a block and gradient copolymers of RAFTOx and 2-ethyl-2-oxazoline, the brush distribution was modified, resulting in less densely distributed brush copolymers. Multidetector gel permeation chromatography (GPC) analysis was carried out to show the change in the intrinsic viscosity of the brush copolymer compared to that of its linear counterpart. These structures were then visually confirmed by atomic force microscopy (AFM) showing a difference in size and shape of the polymers.
EXPERIMENTAL SECTION

Materials. 2-Ethyl-2-oxazoline (EtOx) (>99%, Sigma-Aldrich) was distilled over calcium hydride prior to use and stored over 3 Å molecular sieves. Methyl p-toluenesulfonate (MeOTs) (>97%, Fisher Scientific), anhydrous acetonitrile (>99.9%, Sigma-Aldrich), dimethylformamide (DMF), (>99%, Fisher Chemical), 2-((butylthio)carbonylthio)propanoic acid (95%, Boron Molecular), N,N′-diisopropylcarbodiimide (DICI) (>98%, Sigma-Aldrich), 4-((dimethylamino)pyridine (DMAP) (>99%, Sigma-Aldrich), dimethyl 2,2′-azobis(2-methylpropion) (V601) (Wako Chemicals Corporation), N,N-dimethylacrylamide (DMA) (99%, Sigma-Aldrich), and 2-ethylhexyl acrylate (EHA) (98%, Sigma-Aldrich) were used as received.

1H NMR Spectroscopy. NMR spectra were recorded either on Bruker Avance III HD 300 or 400 MHz spectrometers at room temperature using deuterated chloroform. The resonance signal of residual CHCl₃ at 7.26 ppm served as a reference for the chemical shift, δ.

Gel Permeation Chromatography (GPC). Three different GPC systems were used in this study due to the solubility differences between the backbone and brush copolymers. The first system was run at 40 °C with an Agilent 1260 infinity system with a THF + 2% TEA (triethylamine) and 0.1% BHT (butylated hydroxytoluene) eluent, equipped with a refractive index detector and variable wavelength detector, 1 × PLgel 5 mm Mixed-C column (300 × 7.5 mm) and autosampler. Narrow linear poly(methyl methacrylate) standards were used for calibration between 12,160 and 550 g mol⁻¹. All samples were filtered through 0.2 μm PTFE filters before injection.

The second GPC system was an Agilent Infinity II MDS instrument that was equipped with differential refractive index (DRI), viscometry (VS), dual angle light scattering (LS), and variable wavelength UV detectors. The system was equipped with 2 × PLgel Mixed D columns (300 × 7.5 mm) and a PLgel 5 μm guard column. The eluent is DMF with 5 mmol of NH₄BF₄ additive. Samples were run at 1 mL/min at 50 °C. Poly(methyl methacrylate) standards (Agilent EasiVials) were used for calibration between 955,000 and 550 g mol⁻¹. All samples were filtered through 0.2 μm nylon filters before injection.

The third GPC system was an Agilent Infinity II MDS instrument that was equipped with differential refractive index (DRI), viscometry (VS), dual angle light scattering (LS), and multiple wavelength UV detectors. The system was equipped with 2 × PLgel Mixed C columns (300 × 7.5 mm) and a PLgel 5 μm guard column. The eluent is THF with 0.01% BHT (butylated hydroxytoluene) as an additive. Samples were run at 1 mL/min at 30 °C. Narrow linear poly(methyl methacrylate) standards were used for calibration between 955,000 and 550 g mol⁻¹. All samples were filtered through 0.2 μm PTFE filters before injection.

Gas Chromatography (GC). An Agilent 7820A system equipped with an Agilent capillary HP-5 column (30 m length × 320 μm ID × 0.25 μm) and a FID detector was used. The inlet was set to 250 °C with a splitless injection mode. Nitrogen was used as carrier gas at a flow rate of 2 mL min⁻¹ with the oven temperature starting at 40 °C and increased to 280 °C at a rate of 20 °C/min.

Thermogravimetric Analysis (TGA). The analyses were performed on a Mettler-Toledo TGA equipped with an autosampler under an air flow of 50 mL min⁻¹ from 25 to 550 °C with a heating rate of 1 °C min⁻¹. The samples (5–10 mg) were prepared using aluminum pans.

Differential Scanning Calorimetry (DSC). Thermal transitions were determined on a Mettler-Toledo DSC1 equipped with a autosampler under a nitrogen atmosphere with a flow of 50 mL min⁻¹ from −80 to 150 °C. A heating/cooling rate of 1 °C min⁻¹ was used, and the values of the glass transition temperature (Tg) were determined from the second heating run. The samples (5–10 mg) were prepared using aluminum pans.

Dynamic Light Scattering (DLS). DLS was carried out on an Anton-Paar Litesizer 500 DLS. All samples were prepared in water with a concentration of 10 mg/mL, then further diluted in water, and filtered through 0.2 μm filters before measurements.

Atomic Force Microscopy (AFM). Samples were prepared by drop-casting a 0.05 mg mL⁻¹ polymer solution prepared in chloroform onto freshly cleaved mica and drying gently under a flow of N₂. Images were collected then using a Bruker Dimension Icon instrument with ScanAsyst in air, and the images were processed with Gwyddion software.

Synthesis of Caprolactone-Derived Hydroxyl Oxazoline (2-n-Pentanol-2-oxazoline). 2-Caprolactone (7.45 g, 648 mmol) was added to a flask and heated at 80 °C under inert conditions. The same equivalent of ethanolamine (39.1 mL, 648 mmol) was then added to the flask and subsequently heated at 120 °C for 2 h. Titanium(IV) butoxide (5.00 mL, 16.2 mmol) was then added to the reaction mixture and heated in vacuo at 230 °C for 2 h. The reaction mixture was then distilled in vacuo four times (distillation temperature of 110 °C) to obtain 2-n-pentanol-2-oxazoline as a clear pale yellow oil (60.4 g, 95%).

1H NMR (400 MHz, CDCl₃) δ 4.23 (t, J = 9.5 Hz, 2H), 3.81 (t, J = 9.4 Hz, 2H), 3.65 (q, J = 5.2 Hz, 2H), 2.29 (t, J = 7.3 Hz, 2H), 1.62 (m, J = 6.0 Hz, 6H), 1.45 (q, J = 7.1 Hz, 2H) ppm; 13C NMR (400 MHz, CDCl₃) δ = 168.93, 167.6, 61.20, 53.50, 31.77, 27.28, 24.22 ppm. ESI-MS (m/z) found 158.1, calc. 158.1176 [M + H].

Synthesis of 2-RAFT-2-Oxazoline Monomer (RAFTOX). 2-n-Pentanol-2-oxazoline (10.8 g, 63.6 mmol) was placed in a round-bottom flask with dry DCM. To this mixture were added DMAP (0.78 g, 6.37 mmol) and (2-((butylthio)carbonylthio)propanoic acid (14.6 g, 63.6 mmol). The solution was then cooled in an ice bath, and DIC (9.15 mL, 63.61 mmol) was slowly added dropwise and left to stand overnight. The crude product was then filtered and the crude was washed with saturated NaHCO₃ and brine. The solvent was then removed in vacuo, and the product was purified by column chromatography (silica gel, ethyl acetate, TEA 2%) to obtain RAFTOX as an orange oil (14.48 g, 60.3%). The monomer was stored over 3 Å molecular sieves under N₂.

1H NMR (400 MHz, CDCl₃) δ = 4.74 (q, J = 7.4 Hz, 1H), 4.15 (t, J = 9.4 Hz, 2H), 4.07 (m, J = 5.1 Hz, 2H), 3.75 (t, J = 9.5 Hz, 2H), 3.29 (t, J = 7.4 Hz, 2H), 2.21 (t, J = 7.5 Hz, 1H), 1.60 (m, J = 7.6 Hz, 1H), 1.52 (d, J = 7.3 Hz, 3H), 1.37 (m, J = 7.2 Hz, 4H), 0.87 (t, J = 7.3 Hz, 3H) ppm; 13C NMR (400 MHz, CDCl₃) δ = 212.99, 170.75, 168.19, 77.11, 67.12, 65.65, 54.45, 47.32, 36.92, 30.00, 28.22, 27.75, 25.44, 22.01 ppm. ESI-MS (m/z) found 378.1, calc. 378.576 [M + H].

Cationic Ring Opening Homopolymerization of RAFTOX. RAFTOX (378 mg, 1.00 mmol) was weighed out onto an oven-dried vial, and the vial was capped. Dry acetonitrile (0.5 mL) was then added into the vial using a syringe. Subsequently, MeOTs (2.50 μL, 0.033 mmol) was injected in using a microsyringe so that the monomer to initiator ratio of 30:1 was obtained. Before starting the reaction, a small amount of aliquot was taken for 1H NMR analysis and the sealed vial was purged with N₂ for several minutes. The reaction mixture was then left to stir for 240 min at 80 °C for P4, 60 min at 100 °C for P3, and 10 min at 140 °C for P1 in an oil bath. Upon completion of the reaction, the vials were cooled down in an ice bath to stop the polymerization. They were then precipitated into cold Et₂O and centrifuged to isolate the purified polymer, which was confirmed by 1H NMR.

Cationic Ring Opening Gradient Copolymerization of RAFTOX and EtOx Monomers. As an example, the experimental procedure of P6 is provided as follows. RAFTOX (604 mg, 1.60 mmol) and EtOx (158.6 mg, 1.60 mmol) were weighed out onto an oven-dried vial and the vial was capped. Dry acetonitrile (0.8 mL, 2 M) was then added into the vial using a syringe. Subsequently, MeOTs (8.00 μL, 0.053 mmol) was injected using a microsyringe so that a total monomer to initiator ratio of 30:30:1 was obtained. A small aliquot was then taken for 1H NMR analysis. The sealed vial was purged with N₂ for several minutes. The reaction mixture was then left to stir for 240 min at 80 °C in an oil bath. Upon reaction completion, the vials were cooled down in an ice bath to stop the polymerization, and a final sample was taken for 1H NMR and GPC
0.133 mmol) were injected and purged with N2 for several minutes. Following a previous study from our group on the functionalization of the ε-caprolactone-derived 2-n-pentanol-2-oxazoline, a similar synthetic strategy was devised to couple a RAFT agent to 2-n-pentanol-2-oxazoline. Therefore, 2-(((butylthio)carbonothiolyl)thio)propanoic acid was selected as it is a well-studied trithiocarbonate-based RAFT agent that mediates the polymerization of acrylamides, acrylates, styrenes, and to a lesser degree, methacrylates and methacrylamides. Utilizing the carboxylic acid on the R end of this RAFT agent, it was coupled to the hydroxyl group of the ε-caprolactone-derived 2-oxazoline monomer by DIC coupling. The product was then purified by column chromatography and thoroughly dried under vacuum to ensure that no side products or nucleophilic species remained. Synthesis of the 2-RAFT-2-oxazoline monomer, which we have termed RAFTOx, was then confirmed by 1H NMR (Figure 1) and 13C NMR (Figure S1).

**Cationic Ring Opening Homopolymerization of RAFTOx.** CROP of RAFTOx was studied to determine optimal polymerization conditions (Table 1). The polymerization of RAFTOx was first carried out under well-established CROP conditions: initiator (in this case, methyl p-toluenesulfonate), dry solvent (acetonitrile), with a reaction temperature of 140 °C. Although these conditions yielded near full monomer conversion in under 10 min, GPC analysis showed relatively high dispersity D = 1.52, which included both a slight high-molecular-weight shoulder and low-molecular-weight tailing (Figure S2). The low-molecular-weight tailing of the GPC trace indicated early termination of the chain, and the presence of a slight high-molecular-weight shoulder showed a potential interference of the CTA part of the monomer during the CROP of the RAFTOx monomer.

Possible side reactions include thermolysis of the RAFT agent at high temperatures or nucleophilic attack of the C–S bond, which can cause coupling of chains or early termination of chains leading to both low- and high-molecular-weight moieties. Thermal analysis of both the RAFTOx monomer and the polymer P4 indicated no thermal degradation taking place.

### RESULTS AND DISCUSSION

**Synthesis of 2-RAFT-2-Oxazoline Monomer (RAFTOx).** Following a previous study from our group on the functionalization of the ε-caprolactone-derived 2-n-pentanol-2-oxazoline, a similar synthetic strategy was devised to couple a RAFT agent to 2-n-pentanol-2-oxazoline. Therefore, 2-(((butylthio)carbonothiolyl)thio)propanoic acid was selected as it is a well-studied trithiocarbonate-based RAFT agent that mediates the polymerization of acrylamides, acrylates, styrenes, and to a lesser degree, methacrylates and methacrylamides. Utilizing the carboxylic acid on the R end of this RAFT agent, it was coupled to the hydroxyl group of the ε-caprolactone-derived 2-oxazoline monomer by DIC coupling. The product was then purified by column chromatography and thoroughly dried under vacuum to ensure that no side products or nucleophilic species remained. Synthesis of the 2-RAFT-2-oxazoline monomer, which we have termed RAFTOx, was then confirmed by 1H NMR (Figure 1) and 13C NMR (Figure S1).

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<th>time (min)</th>
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aDenotes the ratio of RAFTOx to EtOx determined by 1H NMR at the end of the reaction. bTotal monomer conversion calculated by 1H NMR. cFor block copolymer synthesis, the EtOx block was always polymerized first. dAll polymers were analyzed using a GPC with THF as an eluent (2% TEA).
up to 200 °C (Figures S3 and S4). However, it should be noted that even a small percentage of CTA fragmentation or the presence of impurities can result in early termination, or chain−chain coupling. In addition, CROP itself is prone to nucleophilic attacks and so anhydrous conditions are required for obtaining narrowly dispersed polymers. However, because RAFTOx is purified by column chromatography and not vacuum-distilled, which is the common purification method for 2-oxazolines, trace amounts of water can contribute to unwanted side reactions.

In order to avoid the side reactions mentioned above, lower reaction temperatures were screened to determine if side reactions could be minimized and indeed at 80 °C, the polymer (P4) showed relatively narrow dispersity (D = 1.22) with an overall conversion of 88% after 4 h (Figure 2C). Higher conversions were not favored as this led to broader GPC traces, the cause of this potentially being unwanted side reactions due to the prolonged reaction time. Kinetic investigations of the reaction showed that the polymerization followed pseudo-first-order kinetics with the apparent rate of propagation being $k_{app} = 1.494 \times 10^{-4} \text{ s}^{-1}$ (Figure 2A).

Gradient copolymerization of RAFTOx and 2-ethyl-2-oxazoline (EtOx) was carried out to distribute the CTAs less densely along the poly(2-oxazoline) chain (P5). Reaction rates of each component were determined by a combination of gas chromatography (GC) and $^1$H NMR. Individual kinetic investigations of the polymerization of RAFTOx and EtOx showed a similar rate of reaction (Figure 2 and Figure S6), which would indicate that copolymerization of the two monomers would result in a statistical distribution of the RAFT agents. However, upon the kinetic investigation of the copolymerization of RAFTOx and EtOx, it showed that the EtOx monomer polymerized much faster than RAFTOx with the apparent rate of propagation being $k_{app} = 1.559 \times 10^{-4} \text{ s}^{-1}$ and $k_{app} = 0.405 \times 10^{-4} \text{ s}^{-1}$, respectively (Figure 3). As a result, the copolymer is determined to be a gradient copolymer rather than a random copolymer of the two. Following the kinetic investigation of P5, P6 was synthesized and purified to be used.
in the brush copolymer synthesis (Figure S6). It must also be noted that the rate of reaction of both RAFTOx and EtOx is slower during the copolymerization than when they are homopolymerized independently as shown by the large difference in the $k_{ap}$ between the homopolymer and copolymer (Figure S7).

In addition, diblock copolymers were also synthesized where the EtOx block was polymerized first, and subsequently RAFTOx was injected to form the second block (P7 and P8). GPC traces showed clear shift from first block to second block (Figure S8). The synthesis of three different backbone architectures now opens the route to form three separate macromolecular structures via RAFT polymerization of the brushes: bottlebrush, comb-like, and block-brush graft copolymers.

**RAFT Polymerization Using RAFTOx Incorporated macroCTA.** After establishing the CROP conditions of RAFTOx, the synthesis of brush copolymers was established by utilizing the CTAs embedded along the poly(2-oxazoline) backbone (Table 2). The effectiveness of RAFTOx as a CTA, compared to that of the commercially available CTA (with no 2-oxazoline) was first investigated by polymerizing N,N-dimethylacrylamide (DMA) using the thermal initiator dimethyl 2,2'-azobisis(2-methylpropionate) (V601). Direct comparison of the two polymers showed relatively narrow dispersity for both (commercially available CTA $D = 1.16$, RAFTOx CTA $D = 1.24$); however, a slight high-molecular-weight shoulder was observed for RAFTOx, suggesting some side reactions associated with the oxazoline ring (Figure S9). Following the confirmation of RAFTOx as a CTA, the addition of a "shuttle CTA", as reported by Zheng and coworkers, was determined by polymerization of DMA using various RAFTOx containing polymers as the macroCTA.

Regarding the grafting-from approach with RAFT polymerization, there are two distinct mechanistic pathways depending on how the RAFT agent is attached to the backbone. If the Z group (the C=S bond activator and radical stabilizing group) is linked to the backbone, the propagating radicals are leaving the backbone and reattaching to the core again. However, if the R group of the CTA is attached to the backbone, the branch that is forming tethered to the backbone with the active radical transferring to and adjacent CTA or on another backbone. In addition, due to the densely packed nature of radicals that exists when forming graft copolymers, radical brush−brush coupling can be of high occurrence and can lead to unwanted termination. However, previous reports have questioned this reasoning since radical chain−chain coupling seems to be less of an occurrence for Cu(0)-mediated graft copolymer reactions. Indeed, in our inimer approach graft copolymers synthesized via Cu(0)-RDRP, we reported narrow dispersity of brush polymers. Zheng et al. proposed that in the R group approach, the transfer of active radicals is hindered and less efficient in a graft copolymer system (termed the "entrapment effect"), leading to broad molecular weight dispersity, and reported that the addition of a low-molecular-weight CTA (termed "shuttle CTA") can reduce the entrapment effect, thus allowing for better control and higher density graft copolymers.

Following this, Wang et al. and Kerr et al. have also reported well-defined graft copolymers via RAFT also using the "shuttle CTA" approach. More recently, Shamugam et al. reported a photoiniferter approach employing two different light sources to mediate the polymerization, resulting in narrowly dispersed graft copolymers without additional CTA added to the reaction. Tanaka and coworkers also reported a RAFT on RAFT graft copolymer synthesis but terminated the reaction at low conversions to prevent chain−chain coupling.

Using the homopolymer of RAFTOx, P4, two separate graft polymerizations of DMA were carried out with (B1) and without (B2) a shuttle CTA (RAFTOx in 0.3 equiv was used as the shuttle CTA). After a reaction time of 2 h, both resulted in a clear shift in the GPC trace from the backbone to brush. For the reaction containing the shuttle CTA, the GPC trace revealed two distributions as expected: brush copolymer and its linear counterpart (Figure S10). Analysis of the lower-molecular-weight distribution showed that the $M_n$ as determined by GPC matched closely to the initial target DP of the brush (Figure S11). The reaction that contained no shuttle CTA on the other hand showed a high-molecular-weight shoulder indicative of brush−brush coupling. Upon visual inspection, the reaction mixture was more viscous than that of the shuttle CTA containing the reaction mixture. This can be due to two possible reasons that are diradical brush−brush coupling between either adjacent chains or from different backbones leading to higher-molecular-weight structures, or nucleophilic RAFT agent removal, leading to free thiols, which subsequently couple with each other, leading to brush−brush coupling to form disulfide bonds. In order to determine the mechanism in which the brush coupling occurs, a small amount of DTT, a disulfide reducing agent, was added to the polymer solution with the high-molecular-weight shoulder. Interestingly, upon addition of DTT and remeasuring of the polymer by GPC, it showed that the high-molecular-weight species had disappeared, suggesting that the high-molecular-weight shoulder was mainly caused by disulfide bonds (Figure S12). This would indicate that the brush

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<td>82</td>
<td>377.1</td>
<td>143.3</td>
<td>1.55</td>
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<tr>
<td>B5</td>
<td>P6-S</td>
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<td>DMA</td>
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<td>180</td>
<td>90</td>
<td>86.6</td>
<td>66.6</td>
<td>1.16</td>
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<tr>
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<td>P6</td>
<td>comb-like</td>
<td>DMA</td>
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<td>52.4</td>
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<td>B7</td>
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<td>block brush</td>
<td>DMA</td>
<td>63</td>
<td>180</td>
<td>87</td>
<td>42.5</td>
<td>43.0</td>
<td>1.15</td>
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<tr>
<td>B8</td>
<td>P8</td>
<td>block brush</td>
<td>DMA</td>
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<td>88</td>
<td>41.1</td>
<td>34.4</td>
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<tr>
<td>B9</td>
<td>P4</td>
<td>bottle brush</td>
<td>EHA</td>
<td>60</td>
<td>120</td>
<td>64</td>
<td>188.3</td>
<td>217.8</td>
<td>1.16</td>
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"S denotes use of a shuttle CTA in 0.3 equiv. DMA = N,N-dimethylacrylamide and EHA = 2-ethylhexyl acrylate. Monomer conversion was calculated by $^1$H NMR. $^dM_w$, $^dM_n$, and $^dD$ measured by DMF GPC (B1-B8) and THF GPC (B9).
coupling was occurring via reduction of the RAFT agent by a nucleophilic species resulting in chain−chain coupling through disulfide bonds. However, upon repeating the reaction in more dilute conditions (monomer concentration of 2 M as opposed to 10 M, B3), brush copolymers were synthesized with minimized brush−brush coupling. (Figure 4A and Figure S13).

Subsequently, a larger bottlebrush was aimed by increasing the target to DP = 150 per CTA. The final conversion was calculated to be 82% and again, GPC analysis shows a clear shift in the GPC trace from backbone (P4-1) to bottlebrush (B4) with no indication of a leftover backbone (Figure 4B).

Upon further analysis of the GPC data by use of the multidetector GPC analysis, Mark−Houwink plots of log(IV)) and log(MW)) were plotted. With graft copolymers, the intrinsic viscosity of the polymer is lower compared to a linear polymer due to the size of the polymer in solution and therefore, the Mark−Houwink plot shows the difference in the intrinsic viscosity compared to its linear counterpart. The Mark−Houwink plot of B4 (Figure S14) shows an almost horizontal slope in the main polymer peak region, indicating that between log(MW) = 5.5 and 6.0, the intrinsic viscosity does not increase with the increasing molecular weight. This would indicate that it is in fact a brush copolymer structure rather than a linear polymer.

Following the demonstration of bottlebrush formation, other macromolecular architectures were investigated using backbones that incorporated EtOx. The polymer P8, which was a diblock copolymer of EtOx and RAFTOx, would result in brush−block grafting whereas P6, which is a copolymer of EtOx and RAFTOx (where DP of RAFTOx = 12 and EtOx = 18), would form comb-like brush copolymers. Overlaid GPC traces (Figure 5) again show clear shift from the backbone to
brush, albeit with a low-molecular-weight tail prominent in all the GPC traces. The presence of low-molecular-weight tailing could be due to the distribution of RAFT agents per chain, with some backbone chains containing less CTA than others. Last but not least, the RAFT monomer scope was established by using 2-ethylhexyl acrylate (EHA) as the acrylate monomer using P4 as the macroinitiator (Figures S15 and S16), showing that the macroCTA is compatible with acrylates (P9) as well as acrylamides.

Focusing on the three different brush architectures of DMA, mainly B3, B6, and B8, further analysis was carried out in order to determine thermophysical properties and brush size. Differential scanning calorimetry (DSC) showed that the glass transition temperature (Tg) was dependent on the DMA content where the Tg was the highest for B3 at 74.4 °C and the lowest for B8 (Tg = 33.3 °C; Tg B6 = 56.3 °C). Dynamic light scattering (DLS) was performed on the different brush copolymer architectures to determine if there was a difference in particle size depending on backbone composition. Comparison of B3, B6, and B8 showed that the particle sizes decreased from 21.9, 14.7, and 11.8 nm, respectively (Figures S17–S19), confirming that changes in brush density affected the overall size of the graft copolymer.

Atomic force microscopy (AFM) was then used to visually confirm graft copolymer structures. A dilute solution of B4, the largest bottlebrush synthesized, was drop cast onto a mica substrate for analysis. AFM micrographs showed short speckle-like structures visible throughout a wide area of the substrate and had an average contour length of 21 nm (Figure 6B). Comparison of the contour length from the AFM micrograph and the DLS data showed a slight discrepancy between the two, the DLS data showing an average particle size of 30 nm after three runs (Figure 6A). This can be attributed to the fact that the DLS was measured in solution (water), whereas AFM was measured in a dry state. In addition, DLS measurements are under the assumption that the particles are spherical, which, as shown in the AFM micrograph, is not. The AFM micrograph of B6 on the other hand (Figure S21), which we had asserted to be a comb-like brush due to the less densely distributed RAFT agents along the oxazoline backbone, showed no obvious visible structures but rather a few dot-like appearances across the micrograph. The length of the contours could not be accurately determined due to the relatively low resolution of the images.

CONCLUSIONS

A novel trithiocarbonate CTA containing the 2-oxazoline monomer was synthesized that can undergo CROP in a pseudo-living manner while retaining its CTA functionality throughout, resulting in POx-based macroCTAs. Kinetics investigation of the backbone showed that RAFTOx polymerized in a pseudo-living manner and upon copolymerization with EtOx, diblock and gradient distribution of the CTA is possible. We demonstrate that the resulting macroCTAs can form brush copolymers via the grafting-from approach by RAFT polymerization of primarily DMA but also EHA. By varying the CTA distribution on the backbone, the overall macromolecular structure can be altered, from a very dense bottlebrush, to comb-like and block-brush structures. Using DLS, a brush density-dependent particle size was observed and we were then able to visually confirm this using AFM. AFM micrographs showed that when homopolymers of RAFTOx were used as the macroCTA, the elongated backbone resulted in short speckles across the micrograph. However, when fewer CTAs were on the backbone, smaller structures, which appeared more flexible, were visible, indicating the more flexible nature of the backbone from the fewer brushes. While the system mainly focused on DMA to demonstrate brush formation, the CTA is compatible with many other monomer classes, including styrene, showing the versatility of this method to combine 2-oxazolines with other monomers. In addition, our work shows a highly promising method for access to well-defined brush copolymers via a monomer-CTA hybrid compound.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.macromol.2c00497.

Supporting analysis of the monomers (C NMR) and polymers (1H NMR, GPC traces, TGA, DLS, and additional AFM) (PDF)

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Notes

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REFERENCES


