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Synthesis of bottlebrush polymers *via* transfer-to and grafting-through approaches using a RAFT chain transfer agent with a ROMP-active Z-group†

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A novel dithiocarbamate chain transfer agent (**CTA1**) with a directly polymerizable Z-group was synthesized for use in reversible addition–fragmentation chain transfer polymerization (RAFT). This CTA effectively mediated RAFT polymerization of styrenic and acrylic monomers with dispersities (*Đ*) < 1.08. Utilizing the polymerizable Z-group on the ω-chain end that is inherited from the RAFT process, bottlebrush polymers were synthesized *via* ring-opening metathesis polymerization (ROMP) in a grafting-through process. The effect of a number of parameters on the grafting process was studied, and optimized conditions yielded bottlebrush polymers of controllable molecular weights, narrow molecular weight distributions, and high conversions (>90%). Bottlebrush polymers made by a transfer-to strategy were also synthesized from **CTA1**. In this case, ROMP was first carried out to produce poly(**CTA1**) (**PCTA1**), then RAFT was performed from the **PCTA1** backbone. This technique allows for the preparation of high molecular weight bottlebrush polymers without radical coupling between bottlebrush polymers. Lastly, regardless of the synthetic method, all bottlebrush polymers produced using **CTA1** are composed of polymeric side chains that are attached to the bottlebrush backbone through a labile dithiocarbamate linkage that can be cleaved in the presence of nucleophiles such as amines. The unique combination of these capabilities allows for the study of bottlebrush polymer formation by both transfer-to and grafting-through strategies using a single agent.

Introduction

Over the past two decades, bottlebrush polymers have become an increasingly relevant polymer topology as a result of their well-defined structures, shape persistence, nanoscopic dimensions, and unique mechanical and rheological properties.[1] Bottlebrush polymers are comprised of polymeric side-chains grafted to a polymer backbone, and given sufficient grafting density, steric repulsion between polymeric neighbors causes the backbone to adopt a chain-extended conformation.[2,3] Consequently, cylindrical,[4,5] spherical,[6,7] or worm-like,[8] morphologies can be realized in single macromolecules by tuning polymer composition, grafting density, or side-chain molecular weight. Additionally, important polymeric properties, such as amphiphilicity or stimuli-responsiveness, can be extrapolated to bottlebrush systems by tuning the chemical composition of the polymeric side-chains.[9–11] In terms of mechanical pro-

perties, bottlebrush polymers differ from linear polymers primarily due to their inability to interact *via* chain entanglements—a phenomenon from which many of the physical properties of linear polymers arise. Therefore, bottlebrush polymers have garnered interest for use in applications such as rheology modifiers and super-soft elastomers.[12] Lastly, their size and shape-persistence makes bottlebrush polymers well suited for the *in vivo* delivery of therapeutic agents.[13]

Bottlebrush polymers can be prepared *via* one of four approaches: (1) the grafting-from strategy, whereby polymer side chains are grown from a polymeric backbone decorated with initiating functionalities; (2) the grafting-to methodology involving the attachment of pre-formed polymers to reactive sites on a polymer backbone; (3) the grafting-through or macromonomer (MM) approach, in which polymers fitted with a polymerizable moiety are utilized as MMs in an subsequent polymerization; and, (4) the transfer-to strategy (sometimes called the RAFT Z-group approach). Transfer-to is a unique hybrid of the grafting-from and grafting-to strategies in which polymeric radicals detach from the bottlebrush backbone, propagate freely in solution, and return to the backbone through a chain-transfer reaction with a pendant CTA.[14] While the grafting-from, grafting-to, and transfer-to strategies yield

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macromolecules with a bottlebrush topology, the grafting process is hindered by steric interactions between adjacent polymer chains, resulting in low grafting densities.[15] However, despite this shortcoming, grafting-from (and to a greater extent transfer-to) can be employed to synthesize bottlebrush polymers with relatively higher molecular weights (on the order of $\geq 10^6$ Da) than are possible with grafting-through. In contrast, grafting-through results in "perfectly grafted" (i.e. the highest possible grafting density) bottlebrush polymers, as each repeat unit bears a polymeric side chain. In view of the high grafting density and synthetic versatility of the grafting-through technique, recent efforts have focused on its application.[11,16–31]

To prepare well-defined bottlebrush polymers via the grafting-through strategy, reversible-deactivation radical polymerization techniques such as atom transfer radical polymerization (ATRP) and reversible addition–fragmentation chain transfer polymerization (RAFT) are often employed.[1] Generally, semitelechelic MMs of predefined MW and low dispersity (Đ) are synthesized via one of these techniques. In a second step, the resulting MMs are functionalized with a polymerizable moiety in a post polymerization reaction, and the MMs are subsequently polymerized using an additional polymerization method in the third and final step.[20,23] Alternatively, in a two-step method, MM synthesis can be conducted in the presence of an initiator or chain-transfer agent (CTA) containing an orthogonal functionality.[17,21,22] For example, norbornene and derivatives thereof have been coupled to dithioester and trithiocarbonate CTAs.[19] In this case, RAFT was utilized to prepare the MM grafts, and ring-opening metathesis polymerization (ROMP) was employed in a subsequent grafting-through step. ROMP is particularly well suited for this purpose because of the high functional group tolerance and rapid propagation rate of several ruthenium-based olefin metathesis catalysts (Fig. 1).[16] Bottlebrush polymers have been prepared via a combination of these two polymerization techniques in separate steps as described above, or more simply via a one-pot strategy wherein a ROMP catalyst is added to a terminated RAFT reaction mixture.[18]
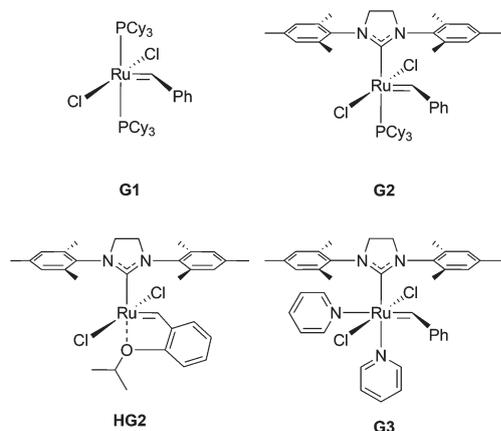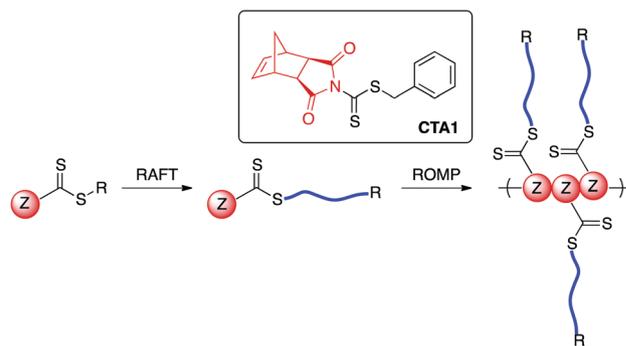

Scheme 1 Proposed CTA structure with directly polymerizable Z-group.

RAFT polymerization is mediated by a thiocarbonylthio-containing agent with an activating Z-group and a leaving group (R-group) that is comparable in radical stability to that of the monomer-derived radical. A number of R- and Z-groups have been utilized to gain control over the RAFT polymerization of a wide range of vinyl monomers.[32] However, to our knowledge, there exists no report in the literature on the incorporation of a directly polymerizable Z-group such as exo-norbornene imide into a RAFT agent (Scheme 1). We envisioned that such a CTA (**CTA1**) could be employed in both RAFT transfer-to and ROMP grafting-through methodologies.

While directly polymerizable R-groups have been incorporated into RAFT CTAs,[18,19] a directly polymerizable Z-group would experience the benefits inherent in the Z-group, or transfer-to, approach.[33–36] Such benefits are a result of the RAFT mechanism when applied in a graft polymerization. During a RAFT transfer-to polymerization, growing polymer chains detach from the bottlebrush polymer backbone during propagation and then add back to the backbone through reaction with a pendant thiocarbonylthio group. Because the growing "arms" are free in solution, coupling between growing adjacent "arms" attached to the bottlebrush backbone does not occur. In addition, radical coupling between growing bottlebrush polymers cannot occur, as the propagating radical resides on the detached polymeric side chains. As a result, the transfer-to approach affords bottlebrush polymers with lower dispersities and higher possible conversions relative to conventional RAFT grafting-from using the R group approach.[36,37] An additional advantage of the incorporation of a directly polymerizable Z-group is the location of the thiocarbonylthio group in the bottlebrush polymer. In the case of bottlebrush polymers prepared from **CTA1**, the thiocarbonylthio group would link the polymeric arms to the backbone polymer, in contrast to systems using directly polymerizable R-groups, which leave the thiocarbonylthio group on the bottlebrush surface. Given the wealth of literature concerning the post-polymerization removal of RAFT end groups,[38] we envisioned the possibility of thiocarbonylthio degradation-driven side chain dissociation. Herein, we investigate the efficacy of **CTA1** as a mediator of RAFT polymerization and the availability of the norbornene functionality for ROMP. Additionally, we evalu-

Fig. 1 ROMP catalysts used in this work.

ate the preparation of bottlebrush polymers *via* both transfer-to and grafting-through strategies. Finally, we explore side-chain cleavage by aminolysis to investigate side chain molecular weights and molecular weight distributions.

Materials and methods

Materials

All reagents were obtained from commercial vendors and used as received unless otherwise stated. Styrene and *n*-butyl acrylate were passed through small columns of basic alumina prior to use. ROMP catalysts $(PCy_3)_2(Cl)_2Ru=CHPh$ (**G1**), $(H_2IMes)(Cl)_2(PCy_3)Ru=CHPh$ (**G2**) and $(H_2IMes)(Cl)_2(PCy_3)$-$Ru=CH(2\text{-}OiPrPh)$ (**HG2**) were obtained as a generous gift from Materia. ROMP catalyst $(H_2IMes)(pyr)_2(Cl)_2Ru=CHPh$ (**G3**) was prepared from **G2** according to literature procedures.[39,40]

Methods

NMR spectra were measured on Agilent 400 MHz or Bruker 500 MHz spectrometers. ^{1}H and ^{13}C NMR chemical shifts are reported in ppm relative to internal solvent resonances. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise stated. Size exclusion chromatography (SEC) was carried out in THF at 1 mL min^{-1} at 30 °C on two Agilent PLgel 10 μm MIXED-B columns connected in series with a Wyatt Dawn Helios 2 light scattering detector and a Wyatt Optilab Rex refractive index detector. No calibration standards were used, and dn/dc values were obtained by assuming 100% mass elution from the columns. Atomic force microscopy (AFM) was conducted using a Veeco BioScope II AFM in tapping mode in air at room temperature using Nano World Pointprobe-silicon SPM Sensor tips (spring constant = 7.4 N m^{-1}, resonance frequency = 160 kHz). Dynamic light scattering (DLS) was conducted using a Malvern Zetasizer Nano operating at 25 °C. Polymer solutions were prepared at 1 mg mL^{-1} and were filtered with a 0.25 μm filter prior to scanning. The calculations of the particle size distributions and distribution averages were conducted using CONTIN particle size distribution analysis routines. All measurements were made in triplicate and errors reflect standard deviations.

Synthesis of CTA1

KOH (0.60 g, 10.7 mmol) was ground to a fine powder with a mortar and pestle and placed in a 100 mL round bottom flask. To the flask was added *exo*-norbornene imide (1.33 g, 8.15 mmol) followed by 30 mL of DMF. This mixture was stirred for 5 min, followed by dropwise addition of CS_2 (2.46 mL, 40.8 mmol). The solution developed a deep red color. After an additional 3 h of stirring, benzyl bromide (4.84 mL, 40.8 mmol) was added dropwise, and the reaction mixture was stirred at rt for 12 h. The following day, the reaction mixture was diluted with diethyl ether (~50 mL) and

washed with H_2O (3 × 150 mL) and brine. The organic layer was dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was purified on a silica gel column, eluting with 1 : 1 CH_2Cl_2–hexanes, to give 1.30 g of **CTA1** as a yellow solid (48% yield). ^{1}H NMR (CDCl$_3$): δ 1.57 (m, 2H), 2.82 (s, 2H), 3.39 (s, 2H), 4.50 (s, 2H), 6.33 (s, 2H), 7.35 (m, 5H). ^{13}C NMR (CDCl$_3$): δ 199.31, 173.75, 138.29, 132.93, 129.34, 128.95, 128.26, 48.27, 46.47, 43.62, 43.22. HRMS (m/z): calculated 330.0617, found 330.0627.

Synthesis of polystyrene MMs

A typical polymerization procedure of styrene is as follows: to an oven-dried Schlenk tube equipped with a magnetic stir bar was added **CTA1** (29.0 mg, 87.0 μmol), 2,2′-azobis(2-methylpropionitrile) (AIBN) (1.43 mg, 8.73 μmol), styrene (1 mL, 8.7 mmol), and 1 mL of THF. The reaction mixture was deoxygenated by three freeze–pump–thaw cycles. The Schlenk tube was then backfilled with N_2 and submerged in an oil bath maintained at 75 °C. Samples were removed periodically by N_2-purged syringe to monitor molecular weight evolution by SEC and conversion by ^{1}H NMR spectroscopy. The polymerization was quenched by submerging the tube into liquid N_2 and exposing the reaction mixture to air. The resulting polystyrene was purified *via* precipitation from MeOH (3×).

Synthesis of poly(*n*-butyl acrylate) (*n*BA) MMs

A typical polymerization procedure of *n*BA is as follows: to an oven-dried Schlenk tube equipped with a magnetic stir bar was added **CTA1** (46.0 mg, 140 μmol), AIBN (2.29 mg, 14.0 μmol), *n*BA (2 mL, 14 mmol), and 2 mL of THF. The reaction mixture was deoxygenated by three freeze–pump–thaw cycles. The Schlenk tube was then backfilled with N_2 and submerged in an oil bath maintained at 60 °C. Samples were removed periodically by N_2-purged syringe to monitor molecular weight evolution by SEC and conversion by ^{1}H NMR spectroscopy. The polymerization was quenched by submerging the tube into liquid N_2 and exposing the reaction solution to air. The resulting poly(*n*BA) was purified *via* precipitation from hexanes (3×).

Synthesis of poly(CTA1) (PCTA1)

A typical polymerization procedure of **CTA1** is as follows: **CTA1** (109 mg, 329 μmol) was dissolved in 1.5 mL of anhydrous CH_2Cl_2 in a 1-dram vial. A solution of **G3** in anhydrous CH_2Cl_2 was prepared at 9.6 mg mL^{-1} in a second vial. 0.5 mL of this **G3** soln was added rapidly to the vial containing **CTA1**. The polymerization was quenched after 20 min by adding 1–3 drops of ethyl vinyl ether. The polymer was isolated *via* precipitation from hexanes and dried under vacuum to yield 93 mg of pure polymer as an off-white powder (85% yield).

Synthesis of poly(CTA1-*g*-styrene) by RAFT transfer-to

To an oven-dried Schlenk tube equipped with a magnetic stir bar was added poly(**CTA1**) (22.0 mg, 873 μmol, M_n = 25 100 g mol^{-1}), AIBN (0.014 mg, 0.087 μmol), styrene (5 mL, 43 mmol), and 5 mL of THF. The reaction mixture was

deoxygenated by three freeze–pump–thaw cycles. The Schlenk tube was then backfilled with N_2 and submerged in an oil bath maintained at 75 °C. Samples were removed periodically by N_2-purged syringe to monitor molecular weight evolution by SEC and conversion by ^{1}H NMR spectroscopy. The polymerization was quenched by submerging the tube into liquid N_2 and exposing the reaction solution to air. The resulting poly(**CTA1**-*g*-styrene) was purified *via* precipitation from MeOH.

Synthesis of poly(CTA1-*g*-styrene) by RAFT grafting-through

A typical grafting-through polymerization procedure is as follows: to a vial containing **MM** in anhydrous CH_2Cl_2 was added rapidly a soln of **G3** in anhydrous CH_2Cl_2 to make a final polymer concentration of 100 mg mL^{-1}. The polymerization was stirred at rt. After 1 h, the polymerization was quenched by adding 1–3 drops of ethyl vinyl ether. The resulting bottlebrush polymer was isolated *via* precipitation from a MeOH–H_2O mixture and dried under vacuum.

Aminolysis of bottlebrush polymers

Bottlebrush polymer was dissolved in 0.3 mL of THF in a 1-dram vial equipped with a stir bar. To the vial was added 0.3 mL of a 40 w/v% soln of methylamine in H_2O. The reaction mixture was stirred at rt in air for 72 h to ensure complete thiol oxidation. A few drops of THF were added to dissolve the precipitated solids, and the resulting aminolyzed side chains were isolated *via* precipitation from MeOH and were dried under vacuum overnight.

Results and discussion

CTA1 synthesis

CTA1 was synthesized in one-pot starting from *exo*-norbornene imide (see ESI† for further details) as shown in Scheme 2. The reaction proceeds *via* the potassium hydroxide-assisted attack of the imide nitrogen on carbon disulfide, forming a dithiocarbamate salt. In the second step, the dithiocarbamate intermediate reacts with benzyl bromide in a substitution reaction to yield the desired product.

Column purification was required to remove unreacted starting materials, and isolated yields ranged from 35–48%. While this range is lower than reported values for the synthesis of other dithiocarbamates,[41,42] many such CTAs are derived from electron-rich secondary amines in contrast to the relatively electron-deficient imide employed in our study. This electron-deficiency results in the limited nucleophilicity of the

imide nitrogen,[43] hindering its addition to electrophiles such as CS_2. Longer reaction times or increased temperatures were not found to increase yields.
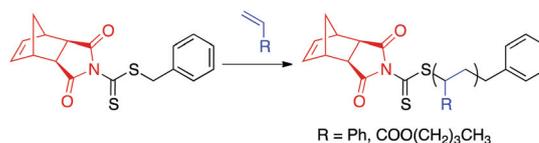
RAFT polymerization

The success of a RAFT polymerization is tied to many factors, chief among which is the matching of monomer reactivity to that of the CTA.[44–48] More activated monomers (MAMs) (*i.e.*, methacrylates, acrylates, styrenes) require electron deficient C=S bonds, such as those present in dithioester and trithiocarbonate RAFT agents, while less activated monomers (LAMs) (*i.e.*, vinyl esters and amides) can only be polymerized in the presence of more electron rich thiocarbonyl-containing compounds such as xanthates. In fact, reaction of LAMs with dithiobenzoate or certain trithiocarbonate CTAs can result in complete inhibition of polymerization.[49] The use of *N*-pyrrolyl and *N*-phthalimidyl moieties as Z-groups in dithiocarbamate RAFT CTAs was first reported by Cheifari and coworkers.[50] These CTAs are suitable for controlling the polymerization of many MAMs.[47,51–53] Therefore, we envisioned that **CTA1** could be employed to mediate the polymerization of this class of vinyl monomers.

To evaluate our hypothesis, RAFT polymerizations of styrene and *n*-butyl acrylate (*n*BA) were carried out in the presence of **CTA1** (Scheme 3). The polymerizations were conducted in THF (1 : 1 v/v% THF–monomer) at 75 °C for styrene or 60 °C for *n*BA in the presence of 2,2′-azobis(isobutyronitrile) (AIBN). To maintain a high level of chain end fidelity, a [CTA]/[AIBN] ratio of 10 : 1 was chosen.[54] Kinetic analysis was performed by removing aliquots of the polymerization solution at various time points *via* N_2-purged syringe. The polymerizations were quenched by exposing the reaction mixture to air and submerging the reaction vessel into liquid N_2. Molecular weight (MW) and dispersity (*Đ*) were determined by size-exclusion chromatography (SEC), and conversions were measured by ^{1}H NMR spectroscopy. **CTA1**-mediated RAFT polymerization of styrene and *n*BA yielded polymers of controllable molecular weights with narrow molecular weight distributions (*Đ* < 1.08). As previously reported for similar dithiocarbamate CTAs,[55] polymerization of methyl methacrylate was uncontrolled. On the opposite end of the monomer reactivity spectrum, polymerization of vinyl acetate was completely inhibited in the presence of **CTA1**.

Kinetic analysis of **CTA1**-mediated polymerization of styrene and *n*BA is shown in Fig. 2. Molecular weight distributions determined by SEC were monomodal with low *Đ*, indicative of a well-controlled polymerization and a high chain
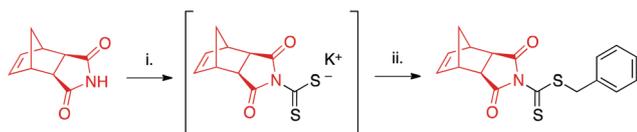
Scheme 2 One-pot synthesis of **CTA1**. ªExperimental conditions: (i) CS_2, KOH, DMF; (ii) benzyl bromide.

R = Ph, COO(CH$_2$)$_3$CH$_3$

Scheme 3 **CTA1**-mediated RAFT polymerization of styrene or *n*BA. ªExperimental conditions: AIBN, THF, 75 °C for styrene or 60 °C for *n*BA.
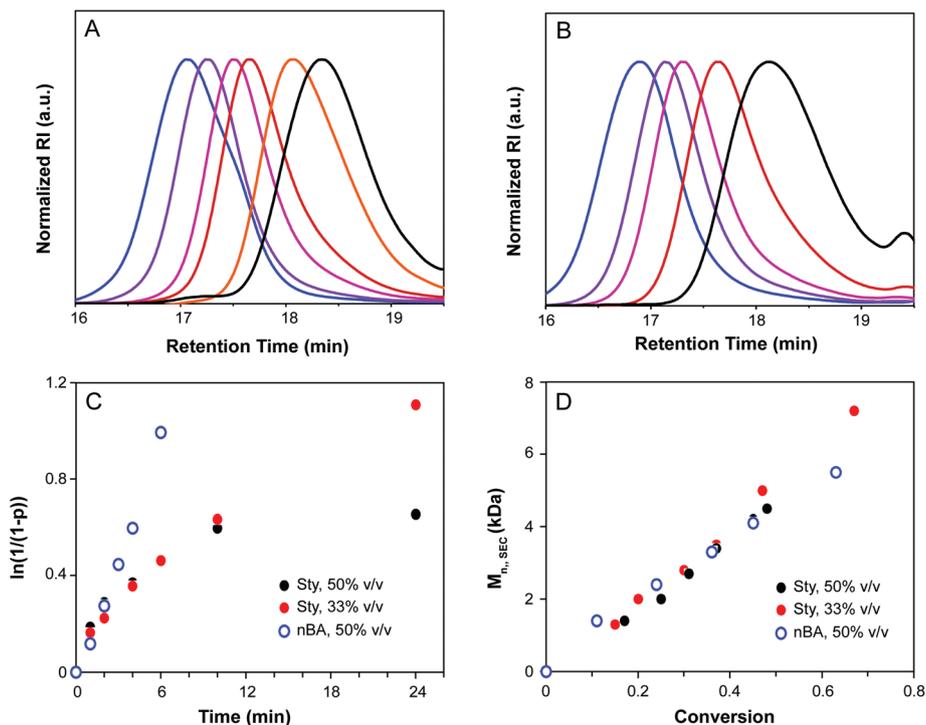
Fig. 2 Kinetic analysis of **CTA1**-mediated RAFT polymerization. (A and B) SEC traces show evolution of MW during the polymerizations of styrene (A) and nBA (B). (C) $\ln(1/(1 − p))$ vs. time for the polymerization of styrene ([styrene]/[CTA]/[I] = 100 : 1 : 0.1, 50% v/v in THF, 75 °C, black circles; [styrene]/[CTA]/[I] = 100 : 1 : 0.1, 33% v/v in THF, 75 °C, red circles) and nBA ([nBA]/[CTA]/[I] = 100 : 1 : 0.1, 50% v/v in THF, 60 °C, blue open circles). (D) M_n as a function of conversion for the polymerization of styrene and nBA.

transfer efficiency of **CTA1** under the conditions investigated. Conversion increased linearly with time for nBA, and $Đ$ decreased over the course of the reaction for both nBA and styrene. In the case of styrene, a non-linear relationship was observed in the semi-logarithmic plot (Fig. 2C) and a maximum conversion of only 48% was obtained after 24 h, indicative of the occurrence of termination reactions during the polymerization. The polymerization was repeated under more dilute conditions (2 : 1 v/v% THF–styrene), resulting in a reduction of termination reactions and a higher terminal conversion (81% after 24 h). For both monomers, the linear relationship between MW and conversion corroborated the controlled nature of the polymerization (Fig. 2D).

Chain extension of a polymer prepared using **CTA1** was attempted to further validate its capability to mediate controlled RAFT polymerization. For the first block, poly(nBA) of MW = 6900 Da ($Đ$ = 1.06) was synthesized using **CTA1**. This polymerization yielded a macroCTA with a dithiocarbamate at the ω-chain end. The poly(nBA) macroCTA was utilized in a second step to control the polymerization of styrene ([M]/[CTA]/[AIBN] = 1000 : 1 : 0.1), ultimately resulting in the formation of a block copolymer. After 4 h, the polymer had grown to 27.0 kDa as measured by SEC ($Đ$ = 1.05) (Fig. S9†). This measured MW agreed with the expected value of 26.6 kDa based on conversion as measured by ^{1}H NMR spectroscopy.

To prepare macromonomers for ROMP grafting-through, a series of polymers of differential MW were synthesized, and

Table 1 Polystyrene MMs prepared by RAFT polymerization

Polymer[a]	$M_{n\,(SEC)}$ (Da)[b]	$M_{n\,(theo)}$[c] (Da)	$Đ$[b]
MM$_{29}$	3300	3100	1.05
MM$_{52}$	5700	6000	1.02
MM$_{113}$	12 100	13 300	1.04

[a] Average degree of polymerization shown as a subscript calculated from SEC data using the formula DP = (M_n − MW$_{CTA}$)/MW$_{styrene}$. [b] Measured by SEC using absolute MW determined by light scattering. [c] Determined by ^{1}H NMR spectroscopy using the formula $M_{n\,(theo)}$ = MW$_{styrene}$ × ([styrene]/[CTA]) × % conv.

the isolated polymers were characterized by SEC and ^{1}H NMR spectroscopy (Fig. S8 and S10†). A summary of our analysis is provided in Table 1. The subscripts in the polymer name assignments refer to the degree of polymerization of the polystyrene component of the macromonomers. Polymers with relatively narrow molecular weight distributions were obtained. In addition, MWs measured by SEC were in good agreement with those calculated from conversion using ^{1}H NMR spectroscopy.

An important outcome of **CTA1**-mediated RAFT polymerization is the preservation of the reactive norbornene olefin moiety on the ω-end of the resulting polymer chain, allowing for subsequent bottlebrush formation via ROMP grafting-through. The orthogonality of the norbornene olefin with reversible-deactivation radical polymerization has been previously shown.[56] The poor reactivity of the internal norbornene

olefin in RAFT relative to the terminal, vinyl groups of acrylic monomers is attributed to their differences in electronics. ^{1}H NMR spectroscopic analysis of the pure MMs confirmed the preservation of the norbornene olefin, evident as a singlet at 6.2 ppm (Fig. S8†).

RAFT transfer-to

There exist four methodologies for preparing bottlebrush polymers, and careful consideration is warranted to select the best strategy for a given system. For example, adoption of a grafting-through approach is appropriate when high grafting density is needed. However, bottlebrush formation *via* grafting-through is hindered by high MW macromonomers, limiting the use of this strategy to applications in which bottlebrushes with relatively short side chains are acceptable.[57] In contrast, the transfer-to technique allows for the synthesis of bottlebrush polymers with high MW side chains, but can potentially suffer from broad side chain dispersities and lower than "perfect" grafting densities due to termination reactions during the polymerization.[58]

CTA1 can be utilized for both transfer-to and grafting-through strategies, creating a unique opportunity to evaluate the differences between these two techniques while using identical chemistry. To evaluate the ability of CTA1 to control the growth of high MW side chains from a polymeric backbone by RAFT transfer-to polymerization, CTA1 was first polymerized by ROMP (Scheme 4 left) using Grubbs' 3rd generation catalyst ((H$_2$IMes)(Cl)$_2$(pyr)$_2$Ru=CHPh) (G3) (50 : 1 [CTA1]/[G3]) to yield a poly(CTA1) (PCTA1) consisting of a poly(norbornene) backbone with a dithiocarbamate group on each repeat unit (Fig. S7†). Following our characterization of the resulting polymeric CTA, PCTA1 was then subjected to RAFT polymerization con-
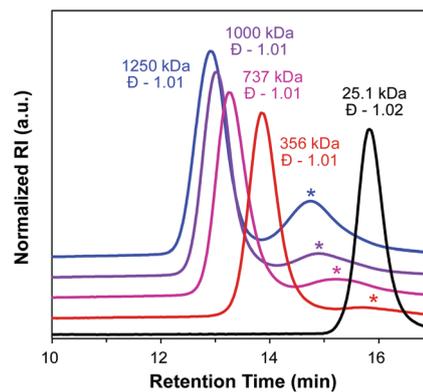

Fig. 3 RAFT transfer-to mediated by **PCTA1** (black trace), sampled at 19 h (red trace), 42 h (magenta trace), 67 h (purple trace), and 91 h (blue trace). Starred peaks correspond to "dead" polymer. Baselines are shifted for clarity.

ditions ([styrene]/[macroCTA]/[AIBN] = 50 000 : 1 : 0.1, THF, 75 °C), and the progress of the reaction was monitored by SEC (Fig. 3). Molecular weight distributions of the growing bottlebrush polymer were monomodal, and the corresponding polymers exhibited successively shorter retention times, indicative of increasing MW. After 91 h, the polymer had grown from 25.1 kDa (for **PCTA1**) to 1250 kDa, with Đ remaining low (<1.02) throughout the course of the polymerization. A second peak in the SEC traces at ~15 min corresponds to dead polymer arising from termination reactions between detached polymeric radicals. This phenomenon is discussed in further detail below.

ROMP grafting-through

The presence of a strained, cyclic olefin at the ω-chain end of polymers prepared *via* RAFT using CTA1 allows for the direct synthesis of bottlebrush polymers by ROMP. In order to prepare bottlebrush polymers by ROMP, polystyrene MMs were precipitated three times from THF into methanol to ensure the complete removal of styrene, which can participate in olefin metathesis in the presence of Ru catalysts.[59] The existence of residual styrene during ROMP has been shown to result in chain transfer and a broadening of the molecular weight distribution.[60] Therefore, MM purity was confirmed by monitoring the disappearance of styrene olefin peaks at 5.5 and 5.0 ppm by ^{1}H NMR spectroscopy between precipitations.

A series of Ru-based metathesis catalysts were evaluated for their efficacy towards the grafting-through polymerization of CTA1-derived polystyrene (MM$_{29}$) (Scheme 4 right). Toward this end, ROMP of MM$_{29}$ was conducted in the presence of various ROMP catalysts at a [MM]/[catalyst] ratio of 50 : 1 (Fig. S11†). Grafting-through polymerizations initiated by Grubbs' 1st ((PCy$_3$)$_2$(Cl)$_2$Ru=CHPh) (G1) and 2nd generation ((H$_2$IMes)-(Cl)$_2$(PCy$_3$)Ru=CHPh) (G2) catalysts showed poor conversion to the corresponding bottlebrush polymer after 1 h in CH$_2$Cl$_2$ (Table 2, entries 1 and 2, respectively). The Hoveyda-Grubbs' 2nd generation catalyst ((H$_2$IMes)(Cl)$_2$(PCy$_3$)Ru=CH(2-OiPrPh)) (HG2) effected higher conversion to bottlebrush polymer
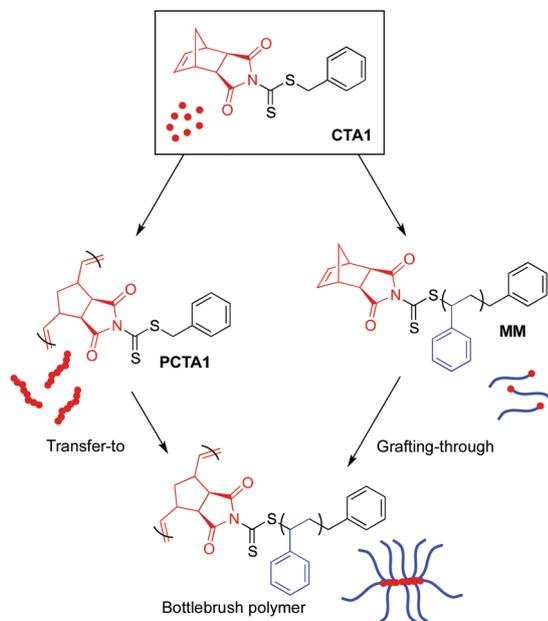
Scheme 4 Preparation of bottlebrush polymers from **CTA1** by transfer-to or grafting-through.

Table 2 Investigation of the effect of catalyst, MW, and MM concentration on conversion to bottlebrush

Entry	MM	MM $M_{n,SEC}$ [a] (kDa)	Cat.	[MM]/[I]	[MM] (mg mL^{-1})	% Conv. to BB [b]	BB $M_{n,theo}$ [c] (kDa)	BB $M_{n,SEC}$ [a] (kDa)	BB $Đ$ [a]
1	MM$_{29}$	3.3	G1	50 : 1	100	8	13.2	21.1	1.11
2	MM$_{29}$	3.3	G2	50 : 1	100	16	26.4	353	1.48
3	MM$_{29}$	3.3	HG2	50 : 1	100	78	129	334	1.50
4	MM$_{29}$	3.3	G3	25 : 1	100	91	75.0	85.6	1.04
5	MM$_{29}$	3.3	G3	50 : 1	100	91	150	152	1.03
6	MM$_{29}$	3.3	G3	75 : 1	100	89	220	240	1.14
7	MM$_{29}$	3.3	G3	100 : 1	100	87	330	340	1.25
8	MM$_{29}$	3.3	G3	50 : 1	25	70	116	100	1.10
9	MM$_{29}$	3.3	G3	50 : 1	50	80	132	125	1.09
10	MM$_{52}$	5.6	G3	50 : 1	100	65	182	190	1.09
11	MM$_{113}$	12.1	G3	50 : 1	100	40	242	180	1.16

[a] Measured by SEC using absolute MW determination by light scattering. [b] Determined from SEC by comparing the integrations of BB and MM peaks. [c] Calculated using the formula % conv. × ([M]/[I]) × $M_{n,MM}$. All polymerizations were conducted for 1 h in CH_2Cl_2.

(78%); however, the resulting polymer had a broad molecular weight distribution ($Đ$ = 1.50) (Table 2, entry 3). Grafting-through by the modified Grubbs' 2nd generation catalyst (G3) showed 91% conversion to bottlebrush polymer with $Đ$ = 1.03 and a monomodal molecular weight distribution (Table 2, entry 5). Based on this analysis, G3 was utilized for further experiments.

Macromonomer MW was found to influence ROMP grafting-through polymerization (Table 2, entries 5, 10–11, Fig. S12†). Comparing the grafting-through polymerization of three MMs of differing MW (3.3 KDa, 5.6 KDa, and 12 KDa) revealed an inverse correlation between MW and conversion. This observed dependence of conversion on MW is attributed to steric factors.[57] The MW of the isolated bottlebrush polymer made from MM$_{29}$ was 152 kDa (Table 2, entry 5), which is in good agreement with the expected molecular weight of 150 kDa. Despite lower conversions, polymerizations of MM$_{52}$ and MM$_{113}$ showed reasonable agreement between theoretical and observed M_n values and maintained fairly low dispersities.

To further confirm the livingness of grafting-through polymerization of CTA1-derived MMs, the [MM$_{29}$]/[G3] ratio was varied from 25 : 1 to 100 : 1 (Table 2, entries 4–7). The resulting bottlebrush polymers were monomodal and their SEC traces exhibited the expected inverse relationship between MW and retention time (Fig. 4A). M_n values determined by SEC are in good agreement with theoretical MWs. A plot of M_n vs. [M]/[I] showed the anticipated linear trend (Fig. 4B).[61] Additionally, dispersity values were low, ranging from 1.04–1.25 throughout the series.

Macromonomer concentration had a small but significant influence on the conversion to bottlebrush polymer (Table 2, entries 5, 8–9, Fig. S13†). Measured conversions varied from 70% to 80% to 91% for the evaluated concentration range (25 mg mL^{-1} to 100 mg mL^{-1}), with increasing concentration resulting in higher conversion to BB.

It is important to note that MM conversion could not be increased beyond 91%, even under optimized conditions. Given the wealth of literature regarding the dependence of RAFT chain-end fidelity on a number of factors including
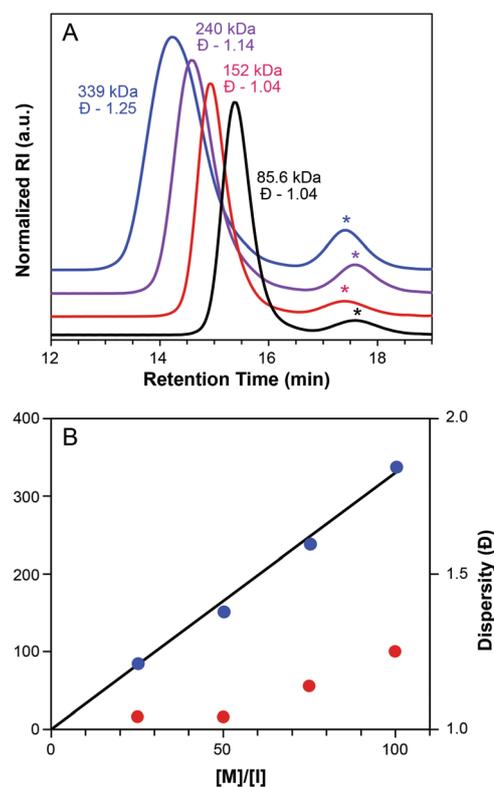

Fig. 4 Assessment of the livingness of ROMP grafting-through of MM$_{29}$. (A) SEC traces illustrating the increase in MW with increasing [MM]/[G3] ratio (black = [25] : [1], red = [50] : [1], purple = [75] : [1], blue = [100] : [1]). Starred peaks are assigned to residual MMs. Baselines are shifted for clarity. (B) Plot of MW vs. [M]/[I] ratio. The black line represents the theoretical MW for each [MM]/[G3].

[M]/[I] and [CTA]/[I] ratios,[49] it can be hypothesized that the observed conversion limit of 91% originates from the existence of "non-living" chains, or those that do not possesses a thiocarbonylthio group on the ω-chain end, in the MM samples. It has been shown that ca. 8% of polymer chains prepared by RAFT polymerization under similar conditions are of this
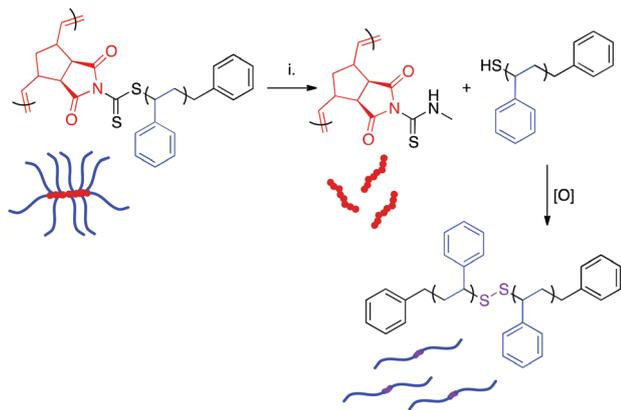
Scheme 5 Displacement of polymeric side chains by methylamine. Experimental conditions: (i) CH_3NH_2, $H_2O–THF$.

"non-living" type.[54,62] Polymers of this "non-living" variety do not possess a norbornene on the chain end and thus will not polymerize during ROMP grafting-through.

Aminolysis of bottlebrush polymers

The dithiocarbamate linkage is susceptible to reaction with nucleophiles such as amines.[38] Reaction of this functional group proceeds *via* an addition-elimination mechanism, resulting in detachment of polymeric side chains and their replacement by the nucleophile. The displaced side chains bear thiol groups at their ω-chain ends, which oxidize in air to form disulfide linkages between polymer chains.[38,63] Therefore, nucleophilic displacement initially yields a mixture of free side chains, side chain dimers, and the poly(norbornene) bottlebrush backbone. Over time, the remaining thiol-terminated polymers become quantitatively oxidized. Disulfide reduction is possible, but this process generally requires elevated temperatures and long reaction times.[64]

The presence of the dithiocarbamate moiety adjacent to the bottlebrush backbone allowed for the cleavage of the polystyrene side chains (Scheme 5). A series of bottlebrush polymers prepared by RAFT transfer-to were dissolved in THF and exposed to a 40% w/v solution of methylamine in H_2O for 72 h. The resulting mixture of backbone and dimerized side chain polymers was separated from residual reactants *via* precipitation. SEC analysis of the aminolyzed bottlebrush poly-

mers showed a clean shift of the molecular weight distribution to a longer retention time, indicating that the side chains had been quantitatively cleaved (Fig. S14†). Interestingly, the measured MWs of the dissociated side chains were higher than the expected values calculated by dividing the experimental BB MW by the DP of **PCTA1** (Table 3). We attribute this deviation to three independent phenomena. First, oxidation of ω-chain end thiols liberated during aminolysis resulted in disulfide bond formation, as has been previously reported.[63] This reaction doubles the observed molecular weight of the side chains. Second, increased steric crowding of the dithiocarbamate CTAs near the bottlebrush backbone by the attached polystyrene sidechains likely led to radical termination reactions between detached polymeric radicals during the transfer-to process, as has also been observed.[65,66] This side reaction not only yielded a significant amount of dead polymer, evident as a low MW peak in the SEC trace (Fig. 3), but also likely resulted in lower than perfect grafting density and a higher than expected average side chain MW. Lastly, "dead" polymer arising during the RAFT polymerization is also incorporated into this sample. Although the concentration of "dead" polymer is surely eclipsed by the more abundant aminolyzed sidechains, these "dead" polymer chains could explain the observed broadening of the molecular weight distributions of the aminolyzed polymers relative to those of the bottlebrush polymers prior to aminolysis. While ultrahigh MW polymers can be obtained *via* RAFT transfer-to, the limitations of this methodology (*i.e.*, limited control over grafting density) are made clear by this aminolysis experiment.

To further evaluate bottlebrush polymers prepared by the grafting-through approach, we subjected these polymers to aminolysis as well. ROMP of **MM29** at a [MM]/[I] ratio of 50 : 1 was carried out to give a BB with degradable side chain linkages. A MW of 164 kDa was determined for the BB, with Đ = 1.07. Aminolysis of the BB proceeded rapidly and quantitatively at rt in the presence of an excess of methylamine in THF–H_2O. SEC analysis of the precipitated reaction mixture revealed a narrow molecular weight distribution and a MW approximately double that of the starting MM (5400 Da, Đ = 1.01), as expected for polystyrene side chain disulfide dimers (Fig. 5). Quantitative aminolysis was confirmed by the complete disappearance of the bottlebrush peak in the SEC trace. Additionally, DLS analysis of the cleaved bottlebrushes exhibited a shift in the size of the macromolecules from 11.8 ± 3.1 nm for

Table 3 RAFT transfer-to polymerization mediated by **PCTA1** and subsequent aminolysis

Polymerization time (h)	$M_{n,SEC}$[a] (kDa)	$Đ$[a]	$M_{n,sidechains\ theo}$[b] (kDa)	$M_{n,sidechains\ SEC}$[a] (kDa)	$Đ_{aminolysis}$[a]
0	25.1	1.02	—	—	—
19	356	1.01	4.7	19.5	1.15
42	737	1.01	9.9	35.5	1.21
67	1000	1.01	13.2	47.4	1.23
91	1250	1.01	16.5	56.9	1.28

[a] Measured by SEC using absolute MW by light scattering. [b] Determined using the formula: $M_{n,sidechains} = M_{n,BB}/DP_{MCTA1}$.
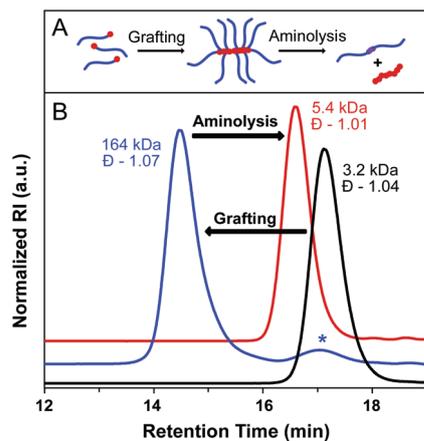
Fig. 5 (A) Graphical representation of grafting-through and aminolysis. (B) BB synthesis by ROMP grafting-through (blue trace) from **MM$_{29}$** (black trace) and subsequent aminolysis with methylamine (red trace). The starred peak corresponds to residual MM. Baselines are shifted for clarity.

the BB to 2.6 ± 0.4 nm for the dissociated side chain dimers (original **MM$_{29}$** = 2.0 ± 0.5 nm) (Fig. S15†).

Conclusions

A novel RAFT CTA with a directly polymerizable Z-group was prepared in a one-pot synthesis from an *exo*-norbornene imide. **CTA1**-mediated RAFT polymerizations of styrene and *n*BA were conducted successfully, yielding polymers of controllable MW and low dispersity bearing a polymerizable norbornene moiety on the ω-chain end. We demonstrated that **CTA1** could be utilized effectively for transfer-to and grafting-through methodologies, with the former resulting in high MW bottlebrush polymers (1250 kDa). Polystyrene MMs prepared using **CTA1** were polymerized by ROMP *via* a grafting-through strategy. In general, ROMP polymerization of **CTA1**-derived MMs proceeded efficiently when catalyzed by Grubbs' 3rd generation catalyst, with conversions on the order of 70–90%. Macromonomer MW, concentration, and the [MM]/[catalyst] ratio of the polymerization were found to influence the conversion to BB. In general, an inverse relationship between MW of the MM and the conversion to BB was observed, with the smallest MM (3300 Da) resulting in the highest conversion. Increasing the MM concentration from 25 to 100 mg mL^{-1} also enhanced conversion, while increasing the [MM]/[G3] ratio from 25 : 1 to 100 : 1 resulted in decreased conversion and a broadening of the molecular weight distribution. Side chain scission *via* aminolysis was quantitative and revealed significant differences between the bottlebrush polymers prepared by the two different approaches. **CTA1** is unique in that it allows for the preparation of bottlebrush polymers utilizing functionality built into the chain-transfer agent. We expect **CTA1** will prove to be useful for the facile preparation of bottlebrush polymers possessing inherent side chain lability *via* the transfer-to or grafting-through approach.

Acknowledgements

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