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2. "Cyclic Macromolecules: Dynamics and Nonlinear Rheology"

PI: Gregory B. McKenna

Co-PIs: Robert H. Grubbs, Julia A. Kornfield

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4. Accomplishments:

Introduction: The work described in the present report had the original goal to produce large, entangled, ring polymers that were uncontaminated by linear chains and to characterize by rheological methods the dynamics of these rings. While the work fell short of this specific goal, the outcomes of the research performed under support from this grant provided novel macromolecular synthesis methods, new separation methods for ring and linear chains, and novel rheological data on bottle brush polymers, wedge polymers and dendron-based ring molecules. The grant funded a total of 8 archival manuscripts and one patent, all of which are attached to the present report. In the following paragraphs we highlight the major accomplishments.

Polymer Synthesis

Cyclic polymer topologies remain a synthetic challenge for polymer chemistry, and a region of untapped potential for material engineering. The cyclic macromolecule synthesis related to the present grant was based on a robust platform for cyclic polymer synthesis that had several perceived advantages.^{1,2} These derive from the cyclic nature of all monomers, catalysts and intermediates that participate, leading to a ring-expansion metathesis polymerization (REMP). The technology utilizes ruthenium-based olefin metathesis catalysts with bidentate ligands bearing N-heterocyclic carbene (NHC) and alkylidene moieties that are based on commercially available ruthenium catalysts (Figure 1). Two series of REMP catalysts were synthesized and characterized.³ The first class contains N-mesityl, N-alkyl imidazol-2-ylidene ligands (denoted **UC-#**; the number indicates the length of the alkylidene chain), while the second class contains the dihydro analogs (**SC-#**). The alkylidene-linked chains are varied from four to seven carbons atoms long (Figure 2).

Figure 1. Commercially available ruthenium-based olefin metathesis catalysts

Figure 2. Cyclic ruthenium catalysts for ring-expansion metathesis polymerization (REMP)

The polymerization kinetics for these catalysts were also investigated, with the aim to determine the factors that influence catalyst activity and molecular weight control (Figure 3).⁴ The model that we have developed involves four steps (Figure 3, depicted with a generic REMP catalyst and cyclooctene monomer). As with all living polymerizations, the process contains an initiation step and a propagation step (controlled by rate constants k_i and k_p , respectively). In an initiation kinetics study, the relative observed initiation rates were found to fall in the order SC-5>3>UC-5>SC-6>UC-6. In general, it appears that linker length is the dominant variable in initiation, where the five-carbon linker promotes faster initiation than the six-carbon linker. The propagation rates were found to fall in the order SC-6>UC-7>SC-5>>UC-6>UC-5>>UC-4. Here, the electronic characteristics of the NHC ligand

have a large influence with the saturated **SC** catalysts outperforming the corresponding **UC** analogs. In order to generate the desired cyclic polymer, the catalyst-containing macrocycle can undergo an intramolecular reaction between the proximal olefin and the alkylidene to extrude cyclic polycyclooctene (cPCOE) and release the original catalyst (k_r). Catalyst release can also occur by intramolecular chain transfer, where olefin metathesis occurs between a distal olefin

opening metathesis

and the alkylidene, generating a ruthenium-containing macrocycle and an all-carbon macrocycle (k_t). At low conversion, the relative rates of propagation and catalyst release were found to control molecular weight, whereas at high conversion, the rates of intramolecular and intermolecular chain transfer (k_{ct}) were found to become significant and dominate the molecular weight control. In the case of **UC-5** and **SC-5**, catalyst release is fast compared to propagation and the molecular weight remains low. At high conversion, the molecular weight rapidly increases, likely due to intermolecular chain transfer. For **UC-6** and **SC-6**, the opposite is true. Propagation is faster than catalyst release, leading to large molecular weights at low conversion. The molecular weight is eroded at high conversions of monomer, as intramolecular chain transfer becomes the controlling factor.

Numerous physical, spectroscopic and microscopic techniques were employed to verify the cyclic nature of REMP products. Our initial report demonstrated there are significant differences between cyclic and linear PCOE in their elution volumes, intrinsic viscosities, hydrodynamic radii and calorimetric properties. Further analysis employed melt-state ^{13}C NMR. This method was chosen because recently developed methods offer higher sensitivity than typical ^1H solution-state NMR, especially in the field of polymer chemistry. The spectra for L-PCOE clearly show small additional peaks in the alkyl and olefinic regions that correspond to the end groups of the linear polymer (Figure 4, A and B). For comparison, a cyclic sample was synthesized with **UC-6**, yielded a polymer with $M_w=114$ kDa and DP=1040 (Figure 4, C and D). The sample clearly lacks end groups, indicating a cyclic topology. Considering the known sensitivity of the technique, we estimate

that the purity of the C-PCOE to be at least 90%. However, this level of purity was found to be insufficient for the characterization of cyclic molecules.

With a good understanding of REMP kinetics and the apparent cyclicity of its polymer products, we moved to the next stage of our collaborative project: a study of the fundamental materials properties of cyclic polymers. Owing to the lack of reliable methods for cyclic polymer synthesis, it has been extremely difficult to effectively evaluate their rheological properties and dynamics. Despite their success, the catalysts developed thus far do not provide pure cyclic polymers, owing to catalyst and monomer degradation. The nature of the impurities precludes them from being removed by traditional methods such as fractionation or column chromatography. Therefore, we have undertaken the design and refinement of a novel method for the purification of cyclic polymers., which we now discuss.

Cyclic and Linear Chain Separation: The major topological difference between linear and cyclic polymers is the existence or absence of end groups, respectively. We sought to exploit this difference with rotaxation: the threading of a linear molecule through a macrocycle (Figure 6). The Grubbs group has previously disclosed that specially designed ammonium-based polymers will undergo rotaxation with 24-crown-8 if they possess linear topology (**L-PA** to **T-PA**), but cyclic polymers (**C-PA**) will not.⁵

Initial results have shown that we can use rotaxation to assess the amount of **L-PA** contained within a **C-PA** sample. In these experiments, **C-PA** samples were prepared with various catalyst types and loadings, then treated with 24-crown-8 (Table 1). The ratio of **C-PA** to **L-PA** was measured by ¹H NMR. Much of the **L-PA** is believed to arise from olefin migration by Ru-hydride species and subsequent ring scission by hydrolysis. The evidence for this comes from the inverse relation between reaction time (and thus catalyst degradation to Ru-hydride species) and **C-PA/L-PA** ratio. In order to solve the problem of olefin migration, we added benzoquinone to the reaction mixture because it is known to remove Ru-hydride species. As expected, the **C-PA/L-PA** ratio increased (Table 2). The beauty of these monomers is that they allow a careful analysis and purification through threading, however, they are the poorest performing monomers and appear to produce the highest levels of linear contaminants. Further cyclic polymer synthesis will take these findings into account.

Figure 5. Polyammonium topologies and rotaxation.

Table 1. REMP of **5** and Threading Experiments with **C-PA**

Entry	Catalyst	[1] ₀ (M)	[1/C] ₀	Time (h)	<i>M</i> _w (kDa) ^b	PDI	Cyc/Lin ^c
1	UC-5	2.0	250	23	485	1.21	80/20
2 ^d	UC-5	2.0	250	23+24	481	1.24	61/39
3	UC-5	2.0	500	47	502	1.23	64/36
4	UC-5	2.0	1000	47	633	1.20	70/30
5	UC-5	1.5	250	34	412	1.25	67/33
6	UC-5	1.0	250	34	393	1.25	66/34
7	UC-6	2.0	250	16	237	1.28	45/55
8	SC-5	2	250	8	202	1.30	52/48

^aReaction Conditions: 40 °C in dry C₆D₆ under N₂ atmosphere. ^bMolecular weight data obtained for polycarbamates **2** via GPC with multiangle laser light scattering. ^cCyclic/linear ratios determined by ¹H NMR spectroscopy in the presence of **24C8**, as described in the text. ^dReaction mixture maintained at 40 °C for 24 h after monomer conversion was >95% as determined by ¹H NMR spectroscopy.

Table 2. Data for REMP of **1** in the presence of BQ and threading experiments of the resulting **C-PA**.^a

Entry	Catalyst	M_w (kDa) ^b	PDI	Cyc/Lin ^c
1	UC-5	354	1.16	87/13
2	SC-5	274	1.21	95/5

^aReaction Conditions: $[1]_0 = 2.0$ M, $[1/C]_0 = 250$, $[BQ/C]_0 = 10$, 40 °C in dry C_6D_6 under N_2 atmosphere. ^bMolecular weight data obtained for polycarbamates **2** via GPC with multiangle laser light scattering. ^cCyclic/linear ratios determined by 1H NMR spectroscopy in the presence of **24C8**, as described in the text.

different solubility profiles, due to the ability of the crown ether to mask the polyionic nature of the polymer. Initial results have shown that the polyionic nature of **C-PA** limits its solubility in less polar solvents such as benzene or toluene, whereas **T-PA** shows much greater solubility. Initial attempts at selective precipitation of the **C-PA** have had some success. Current work is focused on optimization of precipitation conditions in order to achieve complete removal of the **T-PA**

(Figure 6).

Should suitable precipitation conditions not be found, we have also attempted to separate **C-PA** and **T-PA** with a resin-bound crown ether. Dibenzo-24-crown-8 (DB24C8) is an analog of 24-crown-8 that also participates in rotaxation, and has the added benefit of modifiable positions its aryl rings. We envision a functionalized DB24C8 that is attached to crosslinked polymer resin beads. A solution of **C-PA** and **T-PA** will be treated with the resin-bound DB24C8. Rotaxation of **T-PA** should bind all the linear contaminants to the beads. Simple filtration of the beads should leave a solution of pure **C-PA** (Figure 6).

Although these methods were used, the ring purity achieved during the present work was never sufficient to give samples that were completely free (>99%) of linear chains. The rheological measurements on these samples are not presented here simply because they showed the presence of contamination by linear chains and inconsistencies in results due to varying amount of contamination. It is recommended that future work on these macrocycles continue with the REMP synthesis and the rotaxation/filtration method of molecular separations. It is a highly promising technique and suggests high purification capability in specialized applications, such as those demanded in ring macromolecule synthesis.

Because of the difficulties in separations just described, the group also examined other routes to ring synthesis and worked with other molecular architectures. The synthesis methods are based on macromonomer approaches⁶ combined with ROMP. This approach to making model bottle-brush molecules is described first followed by discussion of wedge polymers and dendronized rings.

Macromonomer Synthesis of Brush Polymers: The synthesis of high molecular weight brush polymers with good control over side chain lengths, side chain density and backbone lengths is extremely challenging. Of the three current methods to make these molecules (grafting from, grafting onto and grafting through), only the “grafting through” method, which is also called the macromonomer (MM) approach, guarantees complete grafting of the polymer.⁶ Still, the MM approach does not always provide good control over the main chain length and the PDI of the polymer.⁷ One such MM-based method to make brush polymers is by ring-opening metathesis polymerization (ROMP) of a norbornene-based macromonomer functionalized with the desired side chains (Figure 7). Recently, the group reported on a class of pyridine-

containing ruthenium based catalyst (Figure 8) that has shown both high reactivity and fast initiation for ROMP. Using this catalyst, we were able to synthesize brush polymers with a backbone lengths up to 400 units while still maintaining a narrow polydispersity ($PDI < 1.10$).⁸

Figure 7. Synthesis of brush polymer using ROMP.

Figure 8. Pyridine containing Ruthenium based catalyst.

We examined several types of brush polymers with different side chains composed of polylactide, polystyrene, and polyacrylates.^{9,10} So far, we have employed two different approaches to synthesize the macromonomers. The first method uses a norbornene initiator that is used for the direct polymerization of the macromonomer and the second procedure utilizes click chemistry. In the click approach, the azide end-functionalized side chain polymer is first made and subsequently clicked on a norbornene alkyne. The kinetics of these systems have been studied using varying side chain and backbone lengths.^{9,10} Examination of brush copolymers using several different combinations of the above mentioned side chains has also been undertaken.⁹ This study has yielded information on the self-assembly of the brush copolymers based on whether it is a random or a block copolymer (Figure 9).

The characterization methods used include ¹H NMR and gel permeation chromatography (GPC) to analyze the size of the macromonomer, and the subsequent brush polymer has been characterized using GPC and AFM. The AFM images (Figure 10) depict the worm-like structures of the brush polymers and accompanied by the

Figure 9. Schematic of self-assembly of brush random copolymer (top) and brush block copolymer (bottom).

Figure 10. AFM images of (a) polylactide brush polymer and (b) brush block copolymer of polylactide and poly n-butyl acrylate.

GPC results have provided a way to approximate how stretched the backbone is. The brush copolymers were also analyzed using small angle X-ray scattering (SAXS). This method provided a means to look at the size of the domains formed by the different side chains and consequently determine how the brush copolymers self-assemble as previously mentioned (Figure 10).¹⁰ Subsequently, we detail results from the rheological characterization of one series of model bottle-brush polymers.

Macromonomer/ROMP Polymer Syntheses: Clearly, monomer structure can have profound influences on polymer topology, stereochemistry and materials properties. Versatile monomer constructs are valuable tools for the study of polymer behavior, as incremental changes in

pendant functional groups can manifest themselves in macromolecular properties. To further investigate such effects, we designed and synthesized a wedge-shaped monomer (**WM**) that can both influence polymer backbone topology as well as side-group interactions. The synthesis is straightforward (Figure 11) and allows for the incorporation many different functional groups. The first step is the alkylation of methyl gallate to compound **7**. The depicted wedge monomer acquires dodecyl groups from this step, but many electrophiles are suitable and will allow us to easily produce an array of monomers. The remaining two steps are saponification to **8** and a Steglich esterification with norbornene **9** to obtain **WM**. All steps are accomplished in good to excellent yield. Ring-opening metathesis polymerization (ROMP) of **WM** to **PW** is initiated with ruthenium-based catalyst **10**.

Polymers are synthesized on gram-scale with good molecular weight control and low PDIs. Rheological characterization of a series of wedge polymers is described in a later section.

Frechet and coworkers have shown that polymers of dendritic macromonomers such as **4** can be synthesized¹¹ and visualized using atomic force microscopy (AFM). To this end, macromonomer **4** was treated with **UC-6** to obtain a cyclic polymer **C-P4** ($M_w=3790$ kDa, DP=4210, PDI=1.18). Polymer **C-P4** was then applied to freshly-cleaved mica and examined by AFM (Figure 12). It is evident from the obtained images that **C-P4** forms toroidal structures on the mica surface. The line scans also indicated a uniform structure between individual polymer chains. Linear analogs were prepared and demonstrated no toroidal features when visualized by AFM.¹¹ Rheological behavior of a set of synthesized dendron-based rings and linear chains is presented in a later section.

Rheological Characterization of Model Polymers: Three classes of model polymers were synthesized and the dynamic rheology of the systems was measured. These were, first, a series of bottle-brush polymers having different chain length (degree of polymerization) and different side chain length. Second, we examined a set of wedge-type polymers and, finally, we investigated the response of the dendron-based macrocycles.

Bottle Brush Polymers: The polynorbornene-g- poly-(D, L)-lactide brush polymers used in the present study¹⁰ were synthesized by previously described ring-opening metathesis polymerization (ROMP) of norbornenyl macromonomers (MMs) (Figure 13)^{9,10}. The molecular weights of the MMs and the brush polymers were controlled by the ratio of the monomer (or MM) to the initiator. The polylactide side chains had molecular weights from 1.4 kg/mol to 8.7 kg/mol and the backbone DPs were 200, 400 or 800. Table 3 shows the molecular characteristics of the molecules.

Figure 13. Scheme of the synthesis of polynorbornene-g-poly(lactide) brush polymers and schematic of the molecule.

Table 3. Bottle brush polymer molecular characteristics.

sample number	M_{br}^a (kDa)	DP ^b	M_w^c (kDa)	PDI ^d	ϕ_{br}^e
P(PLA1.4)-200	1.4	200	350	1.01	0.893
P(PLA1.4)-400		400	680	1.02	0.898
P(PLA1.4)-800		800	1510	1.04	0.900
P(PLA4.4)-200	4.4	200	840	1.02	0.951
P(PLA4.4)-400		400	2240	1.02	0.956
P(PLA4.4)-800		800	4880	1.03	0.958
P(PLA8.7)-200	8.7	200	1600	1.02	0.970
P(PLA8.7)-400		400	3660	1.08	0.975
P(PLA8.7)-800		800	6050	1.07	0.977

^a M_{br} is the molecular weight of the side chains. ^b DP is the degree of polymerization of the backbone. ^c M_w is the molecular weight of the brush polymer determined by GPC-MALLS in THF. ^d Polydispersity index (PDI) of the brush polymer. ^e ϕ_{br} is the volume fraction of the side chain estimated by the group contribution method.³¹

Dynamic Response of the Brush Polymers

Figure 15 presents dynamic master curves at 80 °C for the brush polymers having a DP of 200 and different side chain molecular weights over the full range from the glassy plateau to the terminal flow region. The curves are vertically shifted to separate the data for each different side chain length. The figure show clearly that from the glassy state to the terminal flow region, several different relaxation behaviors appear in sequence. In the following sections, we plot the dynamic master curves for all of the polymers in different ways and compare the influence of side chain length and backbone DP to the sequential relaxation behaviors

Dilute solution properties

The intrinsic viscosity ($[\eta]$) and molecular weight for these brush polymers with different side chain and backbone lengths were measured using GPC coupled with a light scattering detector and a viscometer. As shown in Figure 14, for the three groups of brush samples with fixed side chain molecular weight but increasing DP, the slope of $\log([\eta])$ vs $\log(M_w)$ decreases from 0.67 to 0.55 as the side chain molecular weight increases.

Figure 14. Intrinsic viscosity versus molecular weight for brush polymers. with fixed side chain molecular weight but increasing DP (in THF at room temperature ≈ 25 °C).

of these densely branched brush polymers. In the terminal zone, most of the densely branched

Figure 15. Comparison of the dynamic responses of the brush polymers with fixed DP of 200 and differing side chain lengths, as indicated..

gradually develops as the DP increases. Such a two plateau region phenomenon is referred to as a double relaxation mechanism which is typical for brush, comb, or star polymers with long side chains^{13,14,15,16,17,18,19,20,21,22,23,24}.

To clarify the attribution of the two plateaus in the dynamic spectrum for the brush polymers with different side chain molecular weight, the dynamic master curves were plotted following the van Gorp-Palmen method²⁵ by plotting the phase angle (δ) vs the logarithm of the complex modulus $|G^*|$. The van Gorp_Palmen plot is sensitive to the molecular weight and molecular architectures of the materials and provides an excellent tool to estimate the value of the plateau modulus²⁶. The van Gorp_Palmen plots for the DP dependence and the side chain molecular weight dependence of several brush samples are shown in Figure 5, parts a and b. Similar to the two plateau phenomenon discussed in relation to the dynamic curves, there are two minima in the phase angle (δ) vs $\log|G^*|$ plot for most of the brush samples. As shown in Figure 16a, for the first minimum in the phase angle (δ) at higher modulus, the $|G^*|$ values and phase angle (δ) values are almost independence of the DP with fixed side chain molecular weight. While in Figure 16b, for fixed backbone DP and increasing side chain molecular weight, the $|G^*|$ values at the first minimum are almost fixed but the δ value decreases. In van Gorp-Palmen plots for linear polymers, as the molecular weight increases, the δ value will decrease and the $|G^*|$ values do not change²⁶. Hence, parts a and b of Figure 16 suggest that the first minimum in the van Gorp-Palmen plot, which corresponds to the first plateau in the dynamic master curve, should be related with the relaxation of the side chains. The plateau modulus of the polylactide is reported to be approximately 5×10^5 Pa and the entanglement molecular weight is approximately 8.7 kDa²⁷. In parts a and b of Figure 16, the corresponding $|G^*|$ values for the first plateau is approximately 6.3×10^5 Pa, which is again near to the plateau modulus value for the polylactide.

Sequential Relaxation

It is expected that branched polymers should relax sequentially. The chain segments should relax first, followed by the side chains, and the whole polymer should be the last to move^{13,15,23}. Rheo-optical study of a similar densely branched polymer shows relaxation that follows the same

sequence as regular branched polymers²⁸. To examine the sequential relaxation behaviors of

Figure 16. van Gurp-Palmen plot for brush polymers with (a) fixed side chain molecular weight and (b) fixed backbone DP.

the brush polymers, we plot the storage modulus (G') master curves of brush polymers having the same side chains shifted horizontally to match in the segmental regime. The slight horizontal

Figure 17. Sequential relaxation of the brush polymers (vertical shift of $C = 0, 1$, and 2 used to separate the respective the curves).

Segmental Regime The segmental regime covers the glassy and glass transition region of the brush polymers. If one compares the curves in Figure 17 and Figure 18, the side chain length and backbone DP have only minor effects on the glassy moduli (G_g). The glassy modulus value of the brush polymer is around 10^9 Pa which is much higher than that of polynorbornene and is closer to that of linear polylactide²⁹.

Arm Regime Figure 18 shows an expanded plot of the arm regime for the brush polymers with shifting

shifting was applied to compensate for the modest differences in glass transition temperatures among the samples. As shown in Figure 17, the master curves can be divided into three regimes: the segmental regime, the arm regime, and the terminal regime. For the brush polymers with the same side chains, when their glass transition regions are shifted together, the arm regimes overlap with each other very well. The length of the arm regime increases with increasing side chain length. In the terminal region, the curves start to deviate from each other moving to lower frequency as the DP of the backbone increases.

Figure 18. Expanded plot of the arm regime and segmental regime for the brush polymers with fixed DP (vertical shift of $C = 0, 1$, and 2 used to separate the respective DP curves).

the polymers with the same DP together. By shifting the samples with the same backbone DP together, the influence of arm length on the relaxation behavior of the brush polymer can be readily demonstrated. For each group of samples with the same backbone DP, a clear plateau is seen for samples with the 4.4 kDa and 8.7 kDa side chain. The plateau values are 6.3×10^5 and 6.2×10^5 Pa, which are independent of the arm length and backbone DP. This regime is missing or difficult to detect in the samples with the 1.4 kDa side chain molecular weight. As shown in Figure 18, the plateau found in the relaxation behaviors of the arm regime are affected by both the faster segmental relaxation and the slower terminal relaxation processes. Rather than using the dynamic data of Figure 18, a better resolution of the arm relaxation can be achieved using the retardation spectra ($L(\tau)$) of the different brush polymers and these were calculated. The retardation spectra of the brush polymers with the same 200 backbone DP but different side chain molecular weight are plotted in Figure 19. Horizontal shifting was applied to

Figure 19. Double logarithmic representation of the retardation spectra from the creep data. ($L(\tau)$) for brush polymers with fixed 200 DP backbone and different side chain molecular

overlap the glassy regions and eliminate the effects of the differences between the glass transition temperatures. According to Plazek^{30,31}, in the retardation spectra of entangled polymers, there are usually two peaks with similar heights. The length between the two peak points corresponds to the length of the rubbery plateau. In Figure 19, only one peak is found in all of the retardation spectra. With the increase of the side chain molecular weight, a shoulder plateau region can be seen and this increases in length with increasing side chain molecular weight. If one integrates the retardation spectrum over the relaxation time (τ), the shoulder region in the spectrum corresponds to the side chain relaxation as seen in the relevant dynamic curves. The length of the shoulder region can be estimated as the distance between the glass transition region and the transition region from arm relaxation to the terminal relaxation. If the side chains are

entangled, then the length of the shoulder plateau should increase with the 3.4 power of molecular weight.¹² However in Figure 19, the relaxation time only scales approximately as the 2.3 power of the side chain molecular weight, which is consistent with the side chains being unentangled, Rouse-like chains. The unentangled nature and Rouse-like behaviors of side chains are similar to the treatment of the side chains in some current model predictions^{13,24,32,33}.

Terminal Regime Figure 20 presents an expanded plot of the terminal regime and shows the relaxation behavior of the backbone. In the plot, a not very obvious plateau in the storage modulus curve can be found for each sample. This plateau corresponds to the second plateau found in the van Gorp-Palmen plot discussed previously. The modulus values for this plateau can be accurately estimated from the van Gorp-Palmen plot (Table 4). In the terminal regime, the whole polymer molecule relaxes. Thus the modulus value should decrease following the same ratio of the increasing DP. If we take the modulus values of the 800DP samples as references and mark them as $G'_{1.4}$, $G'_{4.4}$, and $G'_{8.7}$, respectively, for different side chains, then it is found that the storage modulus values decrease nearly linearly with increasing DP. The plateau shown in Figure 20 looks like a rubbery plateau for the brush polymers. However, for an entangled polymer material, the rubbery plateau modulus should be a constant value and independent of the DP¹². To further examine this, the steady state recoverable compliance (J_s) values for the brush polymers were estimated from the creep data using the equation, $J(t) =$

Figure 20. Expanded plot of the terminal regime for the relaxation of the brush polymer with fixed side chains (vertical shift of $C = 0, 1$, and 2 used to separate the curves).

steady state recoverable compliance ($G_N^0 = 2/J_s$)¹² Thus if the plateau associated with the backbone (G'_b) is not the rubbery plateau, then we expect $\log(J_s) = -\log(G'_b)$. The log values of plateau modulus (G'_b) in the terminal regime estimated from the van Gorp-Palmen plot and steady state recoverable compliance (J_s) obtained from the creep experiments are listed in Table 3. As shown in Table 3, the value of $G'_b J_s$ is generally near to Plazek's prediction of 1 for unentangled polymer chains. Thus, following Plazek, the backbone plateaus found in the dynamic curves reflect the chain orientation for these stiffened polymers and the plateaus observed are not due to entanglements.

Table 4. Estimated backbone plateau modulus (G'_b) and steady state recoverable compliance (J_s) for the brush polymers at 80°C

Polymer	$\log(G'_b)^a$	$\log(J_s)^b$	$G'_b J_s$	$G'_b \text{ ratio}^c$
P(PLA1.4)-200	4.64	-4.55	1.2	$3.3G'_{1.4}$
P(PLA1.4)-400	4.38	-4.26	1.3	$1.8G'_{1.4}$
P(PLA1.4)-800	4.12	-3.96	1.4	$1.0G'_{1.4}$
P(PLA4.4)-200	4.11	-4.08	1.1	$5.2G'_{4.4}$
P(PLA4.4)-400	3.72	-3.62	1.3	$2.1G'_{4.4}$
P(PLA4.4)-800	3.39	-3.24	1.4	$1.0G'_{4.4}$
P(PLA8.7)-200	3.96	-3.94	1.0	$4.6G'_{8.7}$
P(PLA8.7)-400	3.62	-3.24	2.4	$2.1G'_{8.7}$
P(PLA8.7)-800	3.30	-3.07	1.7	$1.0G'_{8.7}$

From the above it is clear that there is no entanglement in either the arm regime or the terminal regime. Then for these brush polymers of very high molecular weight, are they all Rouse chains? We found that for the brush polymers with the same backbone DP, the J_s values increase with side chain length. This shows the increasing dilution effect with side chain length. For the brushes with the same side chain molecular weight but different DP, the steady state recoverable compliance (J_s) increases with DP, and the J_s value is expected to approach a plateau at higher DP. This seems to be the case for the 1.7 kDa and 8.7 kDa side chain brushes, but is less clear for the 4.4 kDa samples. Such a trend is similar to what is expected for linear chains and is consistent with these brushes being in the transition zone from the Rouse like chain to the fully entangled melt.

$J_R(t) + t/\eta$. The $J(t)$ is the shear creep compliance and η is the steady shear viscosity. $J_R(t)$ is the recoverable compliance. According to Plazek^{30,31}, for not well entangled polymers, the plateau or shoulder observed in the dynamic modulus data is not the rubbery plateau. It simply reflects the molecular orientation and is not the entropy due to the deformation of a chain entanglement network. The storage modulus value that appears to be a rubbery response in unentangled or lightly entangled linear polymers is, rather, the inverse value of the steady state recoverable compliance (J_s). The $G'_0 J_s$ is expected to equal 1, and $\log(G'_0)$ is equal to the negative $\log(J_s)$. The value of G'_0 on this lower plateau is readily estimated from the van Gorp-Palmen plot. If it is the rubbery plateau, theoretically it should be twice the reciprocal of the

There are slight differences between the glass transition temperatures (T_g) of these brush polymers. The zero shear viscosities (η_0) at the same experimental temperature therefore do not correctly reflect the viscosity dependence on molecular weight. We used the WLF equation to correct the viscosity values to the same temperature distance from their corresponding glass transition temperatures. To further clarify the entanglement conditions for the brushes in the melt, the zero shear viscosities (η_0) at T_g+30 °C for the three series of samples were determined as a function of weight average molecular weight and it was found that viscosity data follows a power law of approximately 1.7 with M_w , and this is consistent with these brush samples being in the transition zone from the unentangled near linear dependence on M_w toward but not reaching entangled behavior, where the exponent would be 3.4¹².

Macromonomer Systems:

Wedge Polymer: The first macromonomer system that combined ROMP-synthesis was the so-called wedge polymer. Figure 21 shows the structure of this polymer side group on the polynorbornene backbone (see also Figure 11). These can be made at very large DP and good polydispersity control: $M_w/M_n=1.09$. Table 5 shows the properties of the wedge polymers studied here.

Figure 21. Scheme of the synthesis of the wedge polymers.

Table 5. Wedge polymer molecular weight and characterization data.

Sample number	DP ^a	M_w ^b (kDa)	PDI ^c	ϕ_{br} ^d	T_g ^e (°C)
273-1	1001	2815	3.26	0.876	42.8
273-2	699	1164	1.93	0.876	42.2
221A	1406	1347	1.11	0.876	42.9
221B	5314	5713	1.25	0.877	43.4

^aDP is the degree of polymerization of the macromonomers (MMs); ^b M_w is the molecular weight of the wedge polymer determined by GPC-MALLS in THF; ^c Polydispersity index(PDI) of the wedge polymer; ^d ϕ_{br} is the volume fraction of the side chain was estimated by the group contribution method^{34,35}; ^e The glass transition temperature (T_g) of the wedge polymer determined from the dynamic temperature ramp curve.

Chain conformation in solution. The radius of gyration (R_g) of the wedge polymer with different backbone DP was measured using GPC coupled with a light scattering detector. As shown in

Figure 22. The radius of gyration (R_g) change for wedge polymer with different molecular weight in THF at room temperature ($\approx 25^\circ\text{C}$).

relaxation time increases with increasing backbone DP or molecular weight of the wedge polymer.

The wedge polymer is a branched polymer with polynorbornene backbone and a unique branch structure. Within the experimental temperature range, the measured glassy modulus of the wedge polymer is near 10^8Pa . Mather et. al.³⁶ measured the tensile storage modulus (E') and loss modulus (E'') of polynorbornene at different temperatures. At the temperature of -20°C , which is the lowest temperature in our experiments, the E' was found to be $8 \times 10^8\text{Pa}$. Estimating the shear modulus from the tensile modulus, the storage modulus (G') for linear polynorbornene is then approximately $3 \times 10^8\text{Pa}$. Influenced by the bulky side chain structure, the polymer does not densely pack, and the wedge polymer consequently, exhibits a lower glassy modulus than the pure linear polynorbornene.

Figure 24 depicts the shift factors used to construct the dynamic master curves. The shift factors for the four samples are almost the same. The shift factor data at higher temperature can be well fitted by the Williams-Landel-Ferry (WLF)^{12,37} equation. Influenced by the experimental thermal history, after the glass transition region the samples are out of equilibrium and the shift factors deviate from the equilibrium line predicted by the WLF fitting.

Figure 22, the size of the wedge polymer increases with increasing molecular weight and the slope for the $\log(R_g)$ vs $\log(M_w)$ is 0.75, which indicates that the THF is a good solvent for the wedge polymer at room temperature.

Dynamic response of the wedge polymers Figure 23 shows the dynamic master curve for the four wedge polymers at a reference temperature of 80°C . Unlike the brush polymers described above, in the dynamic master curves of the wedge polymers, there is only one rubbery plateau with a magnitude of approximately $(G_N^0) = 1.3 \times 10^4\text{Pa}$, corresponding to an entanglement molecular weight of $M_e = 2.26 \times 10^5\text{g/mol}$. Thus the number of entanglements per chain of the wedge polymers examined in this work is between 4 and 25. In the terminal zone, the

Figure 23. The dynamic master curves for wedge polymers of different backbone DP at a reference temperature of 80°C .

Figure 24. Time-temperature shift factors for wedge polymers of different backbone DP.

Figure 25. The zero shear viscosity for the wedge polymer vs. molecular weight at the reference temperature of 80°C.

Zero shear viscosity of the wedge polymers Finally, Figure 25 shows the increase of the zero shear rate viscosity for the wedge polymers as a function of molecular weight. The scaling of the viscosity with molecular weight follows a power law typical of entangled linear chains, i.e.,

$$\eta_0 \approx M_w^{3.4}$$

Conclusions: In conclusion, a series of wedge polymers with bulky side chains and polynorbornene backbone were synthesized via ROMP of poly(macromonomers). Similar to other branched polymers with bulky side chain structure, the plateau modulus of the wedge polymer is low and due to the difficulty of entanglement of such bulky chains. Affected by the bulky side chain structure, the glass transition temperature of the wedge polymer is higher than for the linear polynorbornene, but the wedge polymer shows a much lower glassy modulus with the value around 10^8 Pa.

Dendron-Based Ring Polymers:

Synthesis of dendronized rings Because of the difficulty in synthesis this complex macromonomer, only one dendronized polymer ring was prepared during the course of the present study. The molecular weight of the dendronized polymer ring was 5.658×10^6 Da and the polydispersity index PDI=1.16. If estimated from the molecular weight of the macromonomer, the DP is around 4740. To compare the viscoelastic properties of the dendronized macrocyclic polymer, we also needed to prepare the dendronized polymer with linear structure. However, limited by the steric hindrance, the ring structure is more favorable for this kind of macromonomer, which is why it is favorable as a candidate for ring polymer synthesis. With ring opening metathesis polymerization (ROMP), it is difficult to obtain linear dendronized polymers with higher backbone degree of polymerization (DP). Hence, to prepare linear dendronized polymers, ultrasound was used to break the high DP dendronized rings into linear chains. As discussed below, this does not result in exactly comparable linear samples to the original ring because large amounts of the dendron side chains are broken along with the cleavage of the backbone of the polymer rings. Hence, the ultrasound prepared linear chain may not bare the same structure as the dendronized macrocyclic polymer. The only linear

sample prepared by the ultrasonication had a molecular weight of 3.23×10^6 Da and the PDI was 1.38 with a corresponding backbone DP of approximately 2230.

Viscoelastic properties of dendronized rings The dynamic master curve of the dendronized polymer ring sample at a reference temperature of 80 °C is shown in Figure 26. The examined temperature range was from 45 °C to 200 °C and was limited at the high end by concerns of sample degradation. Thus in the dynamic master curves, the sample does not quite reach the terminal flow region.

Figure 26. The dynamic master curves of storage (G') and loss (G'') moduli for the dendronized polymer ring sample at a reference temperature of 80 °C.

As shown in Figure 26, the dendronized polymer ring shows a clear glassy plateau with the modulus (G_g) near 10^9 Pa. The rubbery plateau modulus (G_e) is approximately 1.42×10^4 Pa. We also performed a creep experiment at 120 °C and this gives the plateau compliance (J_e) of approximately 7.69×10^{-5} Pa⁻¹, which gives a plateau modulus ($G_e = 1/J_e$) value of approximately 1.3×10^4 Pa. If the plateau found in the dynamic master curve is the entanglement plateau of the macrocyclic polymer, then the estimated number of entanglements per chain for this macrocyclic polymer would be around 27, which would be greater than the entanglement density of any previous synthetic rings investigated, and significantly greater than the recent results for

polystyrene reported by Kapnistos et al¹⁷ which was fewer than 10 even if the entanglement molecular weight of the rings is as small as that for the linear chain, which seems doubtful based on the prior studies from McKenna and co-workers^{38,39} and from Roovers and Toporowski⁴⁰. The zero shear viscosity at 120 °C for the ring polymer was found to be 8.85×10^6 Pa.s. The recoverable compliance $J_R(t)$ was estimated from the creep data with the equation¹² $J_R = J(t) - t/\eta_0$ (see Figure 27). Then, the steady state recoverable compliance J_s could be determined from the long-time limiting value. We found from this procedure that $J_s = 3 \times 10^{-3}$ Pa⁻¹, hence $J_s G_e$ for the ring polymer is 39, which is significantly larger than what is expected for linear chains. If this is a true ring polymer, the high value of $J_s G_e$ remains unexplained by theory. However, at this stage of understanding, it is also possible that the dendronized ring is contaminated by linear chains, which would greatly increase the value of J_s , as shown by McKenna and Plazek^{39,41} in studies of blends of linear and cyclic polymer. Yet, the AFM images (see Figure 12) do not show linear counterparts to the rings. Furthermore, the very low value of the plateau modulus is also suggestive of difficulty in entanglement and a different chain dynamics for rings vis-à-vis linear polymer chains. This avenue of research should be further pursued.

Figure 27. The recoverable compliance of dendronized polymer ring at 120 °C.

From the above, it appears that the dendronized polymer ring shows quite different viscoelastic properties than normal entangled linear polymers. The dendronized polymer ring has a very complex molecular structure. Based on model predictions^{17,42,43,44,45}, the ring structure should not entangle. But in the present data, we see a clear rubbery plateau. Estimating the volume fraction of the dendronized side chains through group contribution methods^{34,35}, the volume fraction of the side chain should account for over 75% of the total volume of the cyclic sample. Hence, the side chains should act as solvent to dilute the backbone and lower the plateau modulus and increase the steady state recoverable compliance value^{13,15,22,24,46,47}.

Summary and Recommendations

The work performed under the present grant, provided novel macromolecular synthesis methods, new separation methods for ring and linear chains, and novel rheological data on bottle brush polymers, wedge polymers and dendron-based ring molecules. The grant funded a total of 8 archival manuscripts and one patent, all of which are attached to the present report.

The outcomes of the work demonstrate the power of ROMP based chemistry to create novel molecular architectures and of rheological methods to characterize those architectures. In fact, the sensitivity of rheological measurements showed that the goal of achieving large macromolecular rings of simple backbone structure remains elusive. However, novel methods of linear chain separation from the rings were developed and novel macromonomer rings were synthesized using ROMP chemistry. It is recommended that the methods developed here be refined and broadened. It is the view of the authors of this report that these methods can eventually achieve large macromolecular rings uncontaminated by linear chains and, consequently, resolve a major outstanding problem in polymer chain dynamics, viz., how do large rings move.

5. Publications in Which DOE Support is Acknowledged

- 1) Y. Xia, B.D. Olsen, J.A. Kornfield and R.H. Grubbs, "Efficient Synthesis of Narrowly Dispersed Brush Copolymers and Study of Their Assemblies: The Importance of Side Chain Arrangement," *J. Am. Chem. Society*, **131**, 18525-18432 (2009).
- 2) Y. Xia, A. J. Boydston and R. H. Grubbs, "Synthesis and Direct Imaging of Ultrahigh Molecular Weight Cyclic Brush Polymers," *Angew. Chem. Int. Ed.*, **50**, 5882-5885 (2011).
- 3) Y. Xia, Y. Li, A.O. Burts, M. F. Ottaviani, D.A. Tirrell, J. A. Johnson, N. J. Turro and R.H. Grubbs, "EPR Study of Spin Labeled Brush Polymers in Organic Solvents," *J. Am. Chem. Society*, **133**, 19953-19959 (2011).
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- 5) M. Hu, Y. Xia, G. B. McKenna, J. A. Kornfield and R. H. Grubbs, "Linear Rheological Response of a Series of Densely Branched Brush Polymers," *Macromolecules*, **44**, 6935-6943 (2011).
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- 8) Y. Xia, A. J. Boydston, Y. Yao, J. A. Kornfield, I. A. Gorodetskaya, H. W. Spiess and R. H. Grubbs, "Ring-Expansion Metathesis Polymerization: Catalyst Dependent Polymerization Profiles," *J. Am. Chem. Soc.*, **131**, 2670-2677 (2009).
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6. People Working on the Project

Texas Tech

Gregory B. McKenna (Professor)
Miao Hu (Graduate Student)
Yanfei Li (Graduate Student)
Xiaoguang Peng (Graduate Student)
Stephen A. Hutcheson (Postdoctoral Researcher)
Paul A. O'Connell (Research Professor)

Caltech

Robert H. Grubbs (Professor)
Julia A. Kornfield (Professor)
Andrew J. Boydston (Postdoctoral Researcher)
Yan Xia (Graduate Student)
Christopher Daeffler (Graduate Student)
Brendan Quigley (Graduate Student)
Meisam (Iman) Hajimorad (GRA)
Rohan Hule (Postdoctoral Researcher)

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Linear Rheological Response of a Series of Densely Branched Brush Polymers

Miao Hu,[†] Yan Xia,[‡] Gregory B. McKenna,^{*,†} Julia A. Kornfield,^{*,‡} and Robert H. Grubbs[‡]

[†]Department of Chemical Engineering, Texas Tech University, Lubbock, Texas 79409, United States

[‡]Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, United States

ABSTRACT: We have examined the linear rheological responses of a series of well-defined, dense, regularly branched brush polymers. These narrow molecular weight distribution brush polymers had polynorbornene backbones with degrees of polymerization (DP) of 200, 400, and 800 and polylactide side chains with molecular weight of 1.4 kDa, 4.4 kDa, and 8.7 kDa. The master curves for these brush polymers were obtained by time temperature superposition (TTS) of the dynamic moduli over the range from the glassy region to the terminal flow region. Similar to other long chain branched polymers, these densely branched brush polymers show a sequence of relaxation. Subsequent to the glassy relaxation, two different relaxation processes can be observed for samples with the high molecular weight (4.4 and 8.7 kDa) side chains, corresponding to the relaxation of the side chains and the brush polymer backbone. Influenced by the large volume fraction of high molecular weight side chains, these brush polymers are unentangled. The lowest plateau observed in the dynamic response is not the rubbery entanglement plateau but is instead associated with the steady state recoverable compliance. Side chain properties affect the rheological responses of these densely branched brush polymers and determine their glassy behaviors.

INTRODUCTION

Polymer architecture has long been known to greatly affect the rheological properties of polymer materials. Brush polymer is a unique type of graft polymers possessing a very high density of regularly spaced side chains along the backbone, and has become a subject of active research in the field of molecular rheology due to its interesting architecture.^{1–20} The grafting density and the molecular weight of the branches affect the movement of the backbone and the rheological responses of these complex macromolecules.

The rheological responses of long chain branched polymers with relatively low grafting density have been well examined.^{1–12} In general, such polymers relax in a sequence with the grafted branches relaxing first, followed by the branching points, and the backbone subsequently reptates in a dilated tube.^{1,3} Side chains act as a solvent and decrease the rubbery modulus of the backbone.^{3,12} For polymers with shorter side chains and extremely high grafting density, similar to the long chain branched polymers, two rubbery plateaus are found in the dynamic master curves.^{14–20} One corresponds to the relaxation of the side chains. A second, lower plateau with modulus value of approximately 1 kPa is usually regarded as the rubbery plateau of the whole polymer.^{13,14,16,19} It is found that the modulus value of the lower plateau decreases with increasing side chain length and the entanglement molecular weights (M_e) of these densely branched brush polymers are extremely high.¹⁶ The very low rubbery modulus is attributed to the interactions between the densely packed side chains which causes the polymer backbones to be stiffened as the persistence length of the brush chain increases with increasing side chain density.^{13,15,16,21–23} A worm-like

conformation is expected for this kind of brush polymer.^{13,24,25}

The stiffened chain conformation affects the inter chain interactions and increases the distance between entanglements. Prior studies were limited by the synthesis methods available to polymers with high backbone degree of polymerization (DP) but side chain length generally lower than 1/4 of the entanglement molecular weight of the corresponding linear polymer.^{14,16,19} There are no prior systematic works investigating how the side chain length and backbone DP affect the rheological responses of the densely branched brush polymers. In the present investigation we take advantage of a new type of densely grafted brush polymer with narrow molecular weight distribution that is synthesized via ring-opening metathesis polymerization (ROMP) of macromonomers (MMs).^{26,27} The resulting brush polymers possess low polydispersities (PDIs) in both backbones and side chains, and very high molecular weights (up to 6000 kDa). The MM synthetic approach ensures that each repeat unit in the backbone is grafted with a side chain, leading to very large branch to backbone ratios and a dense distribution of branching points.^{23,24,26–28} We have synthesized polynorbornene-*g*-polylactide brush polymers with polylactide side chain length of 1/5, 1/2, and 1 entanglement distance of the corresponding linear polymer and the backbone degree of polymerization (DP) of 200, 400, and 800. In the following section, we first present our experimental methods and then show the results of dilute solution characterization of these densely branched brush polymers. This is followed by a presentation of the dynamic moduli

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Figure 1. Scheme of the synthesis of polynorbornene-*g*-poly(lactide) brush polymers and schematic of the resulting brush polymer.

Table 1. Sample Molecular Weight and Characterization Data

sample number	M_{br}^a (kDa)	DP ^b	M_w^c (kDa)	PDI ^d	ϕ_{br}^e
P(PLA1.4)-200	1.4	200	350	1.01	0.893
P(PLA1.4)-400		400	680	1.02	0.898
P(PLA1.4)-800		800	1510	1.04	0.900
P(PLA4.4)-200	4.4	200	840	1.02	0.951
P(PLA4.4)-400		400	2240	1.02	0.956
P(PLA4.4)-800		800	4880	1.03	0.958
P(PLA8.7)-200	8.7	200	1600	1.02	0.970
P(PLA8.7)-400		400	3660	1.08	0.975
P(PLA8.7)-800		800	6050	1.07	0.977

^a M_{br} is the molecular weight of the side chains. ^b DP is the degree of polymerization of the backbone. ^c M_w is the molecular weight of the brush polymer determined by GPC–MALLS in THF. ^d Polydispersity index (PDI) of the brush polymer. ^e ϕ_{br} is the volume fraction of the side chain estimated by the group contribution method.³¹

of the materials and the temperature dependence of the dynamics. We then discuss the sequential relaxation of these densely branched brush polymers covering the three ranges from the glassy relaxation through the Rouse-like relaxation regime of the side chains through the terminal regime which also shows the hallmark of unentangled Rouse-like behavior in spite of the high backbone DP of 800. Similar to what was originally shown by Plazek,^{29,30} the steady state recoverable compliance contributes to the long time dynamics of these unentangled or barely entangled materials.

EXPERIMENT

Polymer Synthesis. The polynorbornene-*g*-poly-(D,L)-lactide brush polymers used in this study were synthesized by previously described ring-opening metathesis polymerization (ROMP) of norbornenyl macromonomers (MMs) (Figure 1).²⁶ The molecular weights of the MMs and the brush polymers were controlled by the ratio of the monomer (or MM) to the initiator (see Table 1).

Gel Permeation Chromatography (GPC). GPC was carried out in THF on two PLgel 10 μ m mixed-B LS columns (Polymer Laboratories) connected in series with a DAWN EOS multiangle laser light scattering (MALLS) detector, an Optilab DSP differential refractometer, and a ViscoStar viscometer (all from Wyatt Technology). No calibration standards were used, and dn/dc values of 0.050 for PLA brush polymers were obtained by assuming 100% mass elution from the columns.

Rheological Measurements. These were carried out using an MCR-501 rheometer (Anton Paar Inc.) with 8 mm parallel plate and approximately 1 mm gap under nitrogen flow over a temperature range from 50 to 140 °C. The measured frequency range is 0.01–100 Hz.

The machine compliance was corrected by setting both the cell compliance and geometry compliance in the instrument software to zero and the raw data were corrected using the measured machine compliance value following Hutcheson and McKenna's method.³² The dynamic responses at different temperature were shifted and the master curve of $G'(\alpha_T\omega)$ and $G''(\alpha_T\omega)$ vs $\alpha_T\omega$ was constructed at a reference temperature of 80 °C. When constructing the master curves, the same shift factors were applied to each group of samples with the same side chain molecular weights. To determine the shift factors for each group of samples, the shift factors for the 400DP polymers were chosen as the reference and modified a little to find the best fit values for the other two samples. For samples with longer side chains, some empirical vertical shifting was applied to shift the dynamic curves at different temperatures together. Creep experiments were performed at 80 °C in the 8 mm parallel plate geometry. The experiments were carried out until steady state was achieved and the viscosity was determined. The steady state recoverable compliance was determined by subtracting time divided by viscosity from the creep compliance.³³

DATA ANALYSIS

Fragility and Glass Transition Temperature. The shift factors with reference temperature at 80 °C were fitted with the WLF equation.³⁴

$$\log(a_T) = \frac{-c_1(T - T_{ref})}{c_2 + T - T_{ref}} \quad (1)$$

The C_1 and C_2 at this reference temperature (T_{ref}) were estimated from the curve fitting. According to the principle of time (frequency)-temperature superposition, the temperature dependence of the $G'(\omega)$ and $G''(\omega)$ ($G'(\omega)$ and $G''(\omega)$ vs T) at the frequency of $\omega = 0.0628$ rad/s was converted from the dynamic master curve ($G'(\omega)$ and $G''(\omega)$ vs ω) with the WLF equation and used to determine the glass transition temperature (T_g). T_g was estimated from the peak of the $\tan(\delta)$ curve in the so-constructed dynamic modulus thermal spectrum. We fit the shift factors with the WLF equation at the reference temperature set to T_g to estimate the C_1^g and C_2^g . The fragility (m)^{35–37} and apparent activation energy (E_g) of the brush samples were estimated with equations,^{38,39}

$$m = \frac{C_1^g T_g}{C_2^g} \quad (2)$$

$$E_g = \ln 10 R \frac{C_1^g}{C_2^g} T_g^2 \quad (3)$$

The change of C_1^g , C_2^g , T_∞ , fragility (m), apparent activation energy (E_g), and glass transition temperature (T_g) of the brush polymers are discussed subsequently.

Retardation Spectrum. According to Plazek,^{29,30} the retardation spectrum ($L(\tau)$) is a very useful tool to examine the relaxation behavior of polymer chains. The retardation spectrum can be calculated from the dynamic results or creep data. To calculate the retardation spectrum ($L(\tau)$) from the dynamic data, the relaxation spectrum ($H(\tau)$) was first estimated from the storage modulus (G') with the equation,³³ for $m < 1$,

$$H(\tau) = AG' d(\log G')/d(\log \omega|_{\omega=\tau}) \quad (4)$$

$$A = \frac{\sin(m\pi/2)}{m\pi/2} \quad (5)$$

Figure 2. Intrinsic viscosity versus molecular weight for brush polymers with fixed side chain molecular weight but increasing DP (in THF at room temperature $\approx 25^\circ\text{C}$).

for $1 < m < 2$,

$$H(\tau) = A'G'(2 - d(\log G')/d(\log \omega)|_{1/\omega=\tau}) \quad (6)$$

$$A = \frac{\sin(m\pi/2)}{\pi(1 - m/2)} \quad (7)$$

Then $L(\tau)$ was calculated from the $H(\tau)$ with

$$L(\tau) = \frac{H(\tau)}{[G'(1/\tau) - G''(1/\tau) + 1.37H(\tau)]^2 + \pi^2 H^2(\tau)} \quad (8)$$

The retardation spectrum ($L(\tau)$) can be directly estimated from the creep data with equation,³³

$$L(\tau) = M(-m) \left[J(t) - \frac{t}{\eta_0} \right] d \left(\log \left[J(t) - \frac{t}{\eta_0} \right] \right) / d(\log(t)|_{t=\tau}) \quad (9)$$

In the present work, because we did not directly obtain the glassy response in creep experiments, the retardation spectrum ($L(\tau)$) curves were constructed by a combination of the dynamic data using eqs 4–8 and the creep response at 80°C less t/η_0 using eq 9.

RESULTS AND DISCUSSION

Intrinsic Viscosity. The intrinsic viscosity ($[\eta]$) and molecular weight for these brush polymers with different side chain and backbone lengths were measured using GPC coupled with a light scattering detector and a viscometer. As shown in Figure 2, for the three groups of brush samples with fixed side chain molecular weight but increasing DP, the slope of $\log([\eta])$ vs $\log(M_w)$ decreases from 0.67 to 0.55 as the side chain molecular weight increases. Tsukahara¹⁵ examined the intrinsic viscosity change for a series of poly(MM)s with different length polystyrene (PS) side chains. On the double logarithmic plot of intrinsic viscosity with the total polymer molecular weight, the intrinsic

Figure 3. Plot of $(M^2/[\eta])^{1/3}$ vs $M^{1/2}$ for the three groups of brush samples of different side chain length (in THF at room temperature $\approx 25^\circ\text{C}$).

viscosity was found to be unchanged until a critical molecular weight value was reached. Then the intrinsic viscosity was found to increase sharply and scale with the same Mark–Houwink parameter as that for PS in the same conditions. The critical molecular weight for the occurrence of this sudden viscosity change increased with side chain molecular weight.¹⁵ In the present study, the slopes of $\log([\eta])$ vs $\log(M_w)$ are near and slightly lower than what is expected for PLA in good solvent,^{40,41} and the values decrease weakly with increasing side chain molecular weight. Though the data are limited, it appears likely that these polymers are above the region of their critical molecular weight.

The chain conformation of the densely grafted brush polymers can be estimated from their intrinsic viscosity data. The model proposed by Yamakawa^{42–44} for the $[\eta]$ and molecular weight of the bottle brush polymers was applied to analyze our data,

$$\left(\frac{M^2}{[\eta]_0} \right)^{1/3} = \Phi_{0,\infty}^{-1/3} A_0 M_L + \Phi_{0,\infty}^{-1/3} B_0 \left(\frac{\lambda^{-1}}{M_L} \right)^{-1/2} M^{1/2} \quad (10)$$

M is the chain molecular weight; $[\eta]_0$ is the intrinsic viscosity for unperturbed conditions; $\Phi_{0,\infty}^{-1/3}$ is a constant; A_0 and B_0 are functions of the reduced hydrodynamic diameter; M_L is equal to M divided by the contour length (L) and λ^{-1} is the Kuhn length. For chains in good solvent, the expansion of the molecular dimension due to the excluded volume effect should be considered. The viscosity expansion factor is defined as $a_\eta^3 = [\eta]/[\eta]_0 = (1 + 3.8z + 1.9z^2)^{0.3}$, where z is the excluded volume parameter. As there is little knowledge about the values of the relevant parameters for the brush polymers used in the present study, we simply plotted the good solvent data of $(M^2/[\eta])^{1/3}$ vs $M^{1/2}$ and from this plot estimated the change of M_L and λ^{-1} from the slope and the intercept (Figure 3).

In Figure 3, the three lines are nearly linear indicating that the influence of the viscosity expansion parameter is not very strong. The intercept ($\Phi_{0,\infty}^{-1/3} A_0 M_L$) values are 3.5×10^{-4} , 7.1×10^{-4} , and 11.3×10^{-4} . Since in the equation $\Phi_{0,\infty}^{-1/3}$ and A_0 are a constant, this indicates that M_L increases with increasing

side chain molecular weight ($M_{w,side} = 1.4, 4.4, \text{ and } 8.7 \text{ kDa}$). As the molecular weight of the brush polymer is determined by the side chain molecular weight multiplied by the degree of polymerization (DP) of the macromonomers ($M_w \approx M_{w,side} \times DP$), the contour length ($L = M/M_L = M_{w,side}/M_L \times DP$) should be a constant value for brush polymers having the same DP. The slope values ($\Phi_{0,\infty}^{-1/3} B_0 ((\lambda^{-1})/(M_L))^{-1/2}$) determined from Figure 3 for the three groups of samples are nearly constant, which implies that the Kuhn length (λ^{-1}) only increases with the side chain molecular weight and has a fixed value for brush polymers with the same side chain. If we assume the Kuhn length for the 1.4k side chain samples to be k_b , then the Kuhn length for the 4.4k and 8.7k side chain samples are $2.0k_b$ and $3.2k_b$, respectively. The results are similar to what has been well discussed in other work^{15,16,21,22,45–47} for brush polymers with densely grafted branches and fixed side chain length. Due to the strong steric interactions between the side chains, the backbone becomes rigid and the Kuhn length of the branched polymer increases.

Dynamic Responses of the Brush Polymers. Figures 4a through 4c present dynamic master curves at 80 °C for the brush polymers having different DPs and side chain molecular weights over the full range from the glassy plateau to the terminal flow region. The master curves are presented as families of fixed backbone DP and varying side chain length. Within a given series of fixed backbone DP the curves are vertically shifted to separate the data for each different side chain length. The figures show clearly that from the glassy state to the terminal flow region, several different relaxation behaviors appear in sequence. In the following sections, we plot the dynamic master curves in different ways and compare the influence of side chain length and backbone DP to the sequential relaxation behaviors of these densely branched brush polymers.

In the terminal zone, most of the densely branched brush samples seem to behave in a Rouse-like manner. There is little evidence of entanglement. For linear polymer materials increasing the backbone length leads to a longer relaxation time and the terminal flow region will move to a lower frequency.³³ On the other hand, in Figure 4, if compare the brush samples with the same backbone DP, the terminal relaxation time not only depends on the DP of the polymer, but also increases with increasing side chain molecular weight. Similar phenomena have been observed for other brush or comb polymers with fixed backbone length and the influence of the side chains on the relaxation of the backbone was invoked to explain this phenomenon.⁵

For the samples with 4.4k and 8.7 kDa side chains, two rubbery plateau regions can be observed in the dynamic master curve. Upon increasing side chain molecular weight, the first plateau from the glassy modulus region at intermediate frequencies becomes more obvious, while the second plateau gradually develops as the DP increases. The two plateau region phenomenon is referred to as a double relaxation mechanism which is typical for brush, comb, or star polymers with long side chains.^{1–12}

To clarify the attribution of the two plateaus in the dynamic spectrum for the brush polymers with different side chain molecular weight, the dynamic master curves were plotted following the van Gorp–Palmen method⁴⁸ by plotting the phase angle (δ°) vs the logarithm of the complex modulus $|G^*|$. The van Gorp–Palmen plot is sensitive to the molecular weight and molecular architectures of the materials and provides an excellent tool to estimate the value of the plateau modulus.⁴⁹ The van

Figure 4. Comparison of the dynamic responses of the investigated brush polymers with fixed DP (200, 400, and 800) (vertical shift of $C = 0, 1, \text{ and } 2$ used to separate the respective the curves).

Gorp–Palmen plots for the DP dependence and the side chain molecular weight dependence of several brush samples are shown in Figure 5, parts a and b. Similar to the two plateau phenomenon discussed in relation to the dynamic curves, there are two minima in the phase angle (δ) vs $\log|G^*|$ plot for most of the brush samples. As shown in Figure 5a, for the first minimum

Figure 5. van Gurp–Palmen plot for brush polymers with (a) fixed side chain molecular weight and (b) fixed backbone DP.

in the phase angle (δ) at higher modulus, the $|G^*|$ values and phase angle (δ) values are almost independent of the DP with fixed side chain molecular weight. While in Figure 5b, for fixed backbone DP and increasing side chain molecular weight, the $|G^*|$ values at the first minimum are almost fixed but the δ value decreases. In van Gurp–Palmen plots for linear polymers, as the molecular weight increases, the δ value will decrease and the $|G^*|$ values do not change.⁴⁹ Hence, parts a and b of Figure 5 suggest that the first minimum in the van Gurp–Palmen plot, which corresponds to the first plateau in the dynamic master curve, should be related with the relaxation of the side chains. The plateau modulus of the polylactide is reported to be approximately 5×10^5 Pa and the entanglement molecular weight is approximately 8.7 kDa.⁵⁰ In parts a and b of Figure 5, the corresponding $|G^*|$ values for the first plateau is approximately 6.3×10^5 Pa, which is near to the plateau modulus value for the polylactide.

The second minimum in the van Gurp–Palmen plot gives a modulus value of approximately 2 to 5 kPa. For brush polymers with the same side chain molecular weight as shown in Figure 5a, the δ value at the second minimum decreases with increasing DP. While for the polymers with the same DP but different side chain molecular weight (Figure 5b), the δ value increases with increasing side chain molecular weight. As discussed before, the side chains stiffen the backbone and increase the Kuhn length. We expect that the effect of the side chain on the conformation of the backbone also occurs in the melt¹⁶ and these brush polymers of the same DP

Figure 6. Sequential relaxation of the brush polymers (vertical shift of $C = 0, 1$, and 2 used to separate the respective the curves).

are unlikely to entangle as the side chain molecular weight increases. The second plateau should, thus, reflect the molecular weight and conformation change of the backbone and it should, consequently, correspond to the relaxation of the whole brush polymer. This lower plateau modulus phenomenon is similar to what has been reported for other poly(macromonomer) brushes^{16,19} with longer backbone but shorter side chain than our samples.

Sequential Relaxation. It is expected that branched polymers should relax sequentially. The chain segments should relax first, followed by the side chains, and the whole polymer should be the last to move.^{1,3,11} Rheo-optical study of a similar densely branched polymer shows relaxation that follows the same sequence as regular branched polymers.⁵¹ To examine the sequential relaxation behaviors of the brush polymers, we plot the storage modulus (G') master curves of brush polymers having the same side chains shifted horizontally to match in the segmental regime. The slight horizontal shifting was applied to compensate for the modest differences in glass transition temperatures among the samples. As shown in Figure 6, the master curves can be divided into three regimes: the segmental regime, the arm regime, and the terminal regime. For the brush polymers with the same side chains, when their glass transition regions are shifted together, the arm regimes overlap with each other very well. The length of the arm regime increases with increasing side chain length. In the terminal region, the curves start to deviate from each other moving to lower frequency as the DP of the backbone increases.

Temperature Dependence of the Dynamic Responses. Figure 7 depicts the temperature shift factors for the three groups of brush polymers with the reference temperature $T_{\text{ref}} = 80^\circ\text{C}$. We fit the shift factors with the WLF equation³⁴ to obtain the fitting parameters C_1 and C_2 at the reference temperature of 80°C .

Following the analysis method discussed before, the values for C_1^g , C_2^g , fragility index (m), apparent activation energy (E_g), and glass transition temperature (T_g) of the brush polymers are estimated and listed in Table 2.

For these brush polymers, the fragility values increase with increasing side chain molecular weight, which means the polymer molecules become less flexible as the side chain length increases.³⁸ As discussed in the section on intrinsic viscosity, the strong

Figure 7. Temperature shift factors for brush polymers with different side chain molecular weight (1.4k, 4.4k, and 8.7k Da) at the reference temperature of 80 °C.

Table 2. WLF Fitting Parameters, Fragility, Apparent Activation Energy, and Glass Transition Temperature Determined from the Dynamic Modulus Data for the Brush Polymers

	C_1^g ^a	C_2^g ^a (K)	m^b	E_g^c (kJ/mol)	T_g^d (K)
P(PLA1.4)-200	11.22	41.58	88.6	556.4	328.2
P(PLA1.4)-400			88.5	556.1	328.1
P(PLA1.4)-800			88.7	557.8	328.6
P(PLA4.4)-200	11.5	36.06	103.7	645.7	325.2
P(PLA4.4)-400			103.8	646.8	325.5
P(PLA4.4)-800			104.0	649.6	326.2
P(PLA8.7)-200	12.05	34.92	112.5	702.5	326.1
P(PLA8.7)-400			112.4	701.2	325.8
P(PLA8.7)-800			112.7	705.1	326.7

^a C_1^g and C_2^g are the WLF fit parameters for the brush samples with reference temperature at the glass transition temperature. ^b m is estimated with eq 2. ^c E_g is estimated with eq 3. ^d T_g is the mechanical glass transition temperature at 100 s relaxation time.

interactions among the side chains stiffen the backbone and increase the Kuhn length.^{15,16} Here in bulk, we see similar influence of the side chain to the conformation of the polymers. Unlike the work done by others on poly(macromonomers)¹⁶ or comb polymers,⁵² the glass transition temperatures (T_g) of our samples are not greatly affected by the side chain length. The glass transition temperature (T_g) and fragility (m) for polylactide are reported to be 323 K and 69.6, respectively.⁵³ The T_g values estimated for these brush polymers are close and within the glass transition temperature range expected for linear polylactide,⁴¹ which seems to confirm that the side chain properties determine the glass transition behaviors of these poly(macromonomers).¹⁶ However, it is worth remarking that there is a large difference in the fragility index m between the brushes and linear polylactide material, which remains an area for further investigation.

Segmental Regime. The segmental regime covers the glassy and glass transition region of the brush polymers. The glass transition behaviors of these brush polymers have been discussed in the previous section. If one compares the curves in Figure 6

Figure 8. Expanded plot of the arm regime and segmental regime for the brush polymers with fixed DP (vertical shift of $C = 0, 1$, and 2 used to separate the respective DP curves).

and Figure 8, the side chain length and backbone DP have only minor effects on the glassy moduli (G_g). The glassy modulus value of the brush polymer is around 10^9 Pa which is much higher than that of polynorbornene and is closer to that of linear polylactide.⁴¹

Arm Regime. Figure 8 shows an expanded plot of the arm regime for the brush polymers with shifting the polymers with the same DP together. By shifting the samples with the same backbone DP together, the influence of arm length on the relaxation behavior of the brush polymer can be readily demonstrated. For each group of samples with the same backbone DP, a clear plateau is seen for samples with the 4.4 kDa and 8.7 kDa side chain. The plateau values are 6.3×10^5 and 6.2×10^5 Pa, which are independent of the arm length and backbone DP. This regime is missing or difficult to detect in the samples with the 1.4 kDa side chain molecular weight.

As shown in Figure 8, the plateau found in the relaxation behaviors of the arm regime are affected by both the faster segmental relaxation and the slower terminal relaxation processes. Rather than using the dynamic data of Figure 8, a better resolution of the arm relaxation can be achieved using the retardation spectra ($L(\tau)$) of the different brush polymers and these were calculated. The retardation spectra of the brush polymers with the same 200 backbone DP but different side chain molecular weight are plotted in Figure 9. Horizontal shifting was applied to overlap the glassy regions and eliminate the effects of the differences between the glass transition temperatures. According to Plazek,^{29,30,33} in the retardation spectra of entangled polymers, there are usually two peaks with similar heights. The length between the two peak points corresponds to the length of the rubbery plateau.

In Figure 9, only one peak is found in all of the retardation spectra. With the increase of the side chain molecular weight, a shoulder plateau region can be seen and this increases in length with increasing side chain molecular weight. If one integrates the retardation spectrum over the relaxation time (τ), the shoulder region in the spectrum corresponds to the side chain relaxation as seen in the relevant dynamic curves. The length of the shoulder region can be estimated as the distance between the glass transition region and the transition region from arm relaxation to the terminal relaxation. If the side chains are entangled, then

Figure 9. Double logarithmic representation of the retardation spectra ($L(\tau)$) for brush polymers with fixed 200 DP backbone and different side chain molecular weights.

Figure 10. Expanded plot of the terminal regime for the relaxation of the brush polymer with fixed side chains (vertical shift of $C = 0, 1$, and 2 used to separate the curves).

the length of the shoulder plateau should increase with the 3.4 power of molecular weight.²⁹ However in Figure 9, the relaxation time only scales approximately as the 2.3 power of the side chain molecular weight, which is consistent with the side chains being unentangled, Rouse-like chains. The unentangled nature and Rouse-like behaviors of side chains are similar to the treatment of the side chains in some current model predictions.^{1,12,54,55}

Terminal Regime. Figure 10 presents an expanded plot of the terminal regime and shows the relaxation behavior of the backbone. In the plot, a not very obvious plateau in the storage modulus curve can be found for each sample. This plateau corresponds to the second plateau found in the van Gurp–Palmen plot discussed previously. The modulus values for this plateau can be accurately estimated from the van Gurp–Palmen plot (Table 3). For a polymer network, the shear modulus can be expressed as⁵⁶

$$G = \nu kT = \frac{\rho RT}{M_s} \quad (11)$$

ν is the number of network strands per unit volume which is the inverse of the molecular weight of the structure (M_s) included in

Table 3. Estimated Backbone Plateau Modulus (G'_b) and Steady State Recoverable Compliance (J_s) for the Brush Polymers at 80 °C

	$\log(G'_b)^a$	$\log(J_s)^b$	$G'_b J_s$	G'_b ratio ^c
P(PLA1.4)-200	4.64	−4.55	1.2	$3.3G'_{1.4}$
P(PLA1.4)-400	4.38	−4.26	1.3	$1.8G'_{1.4}$
P(PLA1.4)-800	4.12	−3.96	1.4	$1.0G'_{1.4}$
P(PLA4.4)-200	4.11	−4.08	1.1	$5.2G'_{4.4}$
P(PLA4.4)-400	3.72	−3.62	1.3	$2.1G'_{4.4}$
P(PLA4.4)-800	3.39	−3.24	1.4	$1.0G'_{4.4}$
P(PLA8.7)-200	3.96	−3.94	1.0	$4.6G'_{8.7}$
P(PLA8.7)-400	3.62	−3.24	2.4	$2.1G'_{8.7}$
P(PLA8.7)-800	3.30	−3.07	1.7	$1.0G'_{8.7}$

^a The plateau modulus in the terminal regime estimated using the van Gurp–Palmen plot. ^b Steady state recoverable compliance estimated from the creep data. ^c The ratio of the plateau modulus with different DP.

the relaxation process. In the terminal regime, the whole polymer molecule relaxes. Thus the modulus value should decrease following the same ratio of the increasing DP. As shown in Table 3, the plateau modulus values decrease with increasing DP. If we take the modulus value of the 800DP samples as the reference and mark it as $G'_{1.4}$, $G'_{4.4}$, and $G'_{8.7}$, respectively for different side chains. Then it can be found that, the storage modulus values decrease nearly linearly with increasing DP.

The plateau shown in Figure 10 looks like a rubbery plateau for the brush polymers. However, for an entangled polymer material, the rubbery plateau modulus should be a constant value and independent of the DP.³³ To further examine this, the steady state recoverable compliance (J_s) values for the brush polymers were estimated from the creep experiment data with the equation, $J(t) = J_R(t) + t/\eta$. The $J(t)$ is the shear creep compliance and η is the steady shear viscosity. $J_R(t)$ is the recoverable compliance. According to Plazek,^{29,30} for not well entangled polymers, the plateau or shoulder observed in the dynamic modulus data is not the rubbery plateau. It simply reflects the molecular orientation and is not the entropy due to the deformation of a chain entanglement network. The storage modulus value that appears to be a rubbery response in unentangled or lightly entangled linear polymers is indeed the inverse value of the steady state recoverable compliance (J_s). The $G'_b J_s$ is expected to equal 1, and $\log(G'_b)$ is equal to the negative $\log(J_s)$. The value of G'_b on this lower plateau is readily estimated from the van Gurp–Palmen plot. If it is the rubbery plateau, theoretically it should be twice the reciprocal of the steady state recoverable compliance ($G_N^0 = 2/J_s$).³³ Thus if the plateau associated with the backbone (G'_b) is not the rubbery plateau, then we expect $\log(J_s) = -\log(G'_b)$. The log values of plateau modulus (G'_b) in the terminal regime estimated from the van Gurp–Palmen plot and steady state recoverable compliance (J_s) obtained from the creep experiments are listed in Table 3.

As shown in Table 3, the value of $G'_b J_s$ is generally near to Plazek's prediction of 1 for unentangled polymer chains. Thus, following Plazek,^{29,30} the backbone plateaus found in the dynamic curves reflect the chain orientation for these stiffened polymers and the plateaus observed are not due to entanglements.

From the above discussion, we did not observe any sign of entanglement in both the arm regime and the terminal regime. Then for these brush polymers of very high molecular weight, are they all Rouse chains? Figure 11 shows the change of the steady

Figure 11. Double logarithmic representation of steady state recoverable compliance (J_s) vs DP for the three groups of brush polymers studied.

Figure 12. Double logarithmic representation of zero shear viscosity (η_0) at $T_g + 30$ °C vs weight average molecular weight (M_w) for the three groups of brush polymer samples with different side chain lengths.

state recoverable compliance with DP on a double logarithmic scale. It is assumed that side chains can act as a solvent to dilute the polymer backbone.^{3,12} While for linear polymers, solvent dilution effect will increase the J_s values.⁵⁷ From Figure 11, we see that for the brush polymers with the same backbone DP, the J_s values increase with side chain length. This shows the increasing dilution effect with side chain length. For the brushes with the same side chain molecular weight but different DP, the steady state recoverable compliance (J_s) increases with DP, and the J_s value is expected to approach a plateau at higher DP. This seems to be the case for the 1.7 kDa and 8.7 kDa side chain brushes, but is less clear for the 4.4 kDa samples. Such a trend is similar to what is expected for linear chains⁵⁸ and is consistent with these brushes being in the transition zone from the Rouse like chain to the fully entangled melt.

There are slight differences between the glass transition temperatures (T_g) of these brush polymers. The zero shear viscosities (η_0) at the same experimental temperature therefore do not correctly reflect the viscosity dependence on molecular weight. We use the WLF equation to correct the viscosity value to the same temperature distance from their corresponding glass transition temperatures. To further clarify the entanglement conditions for the brushes in the melt, the zero shear viscosities

(η_0) at $T_g + 30$ °C for the three series of samples were plotted against their weight average molecular weights (M_w) and this is shown in Figure 12. The viscosity data can be described with a line with a slope of approximately 1.7, which also indicates that these brush samples are in the transition zone from the unentangled near linear dependence on M_w toward but not reaching entangled behavior.³³

SUMMARY AND CONCLUSIONS

In this work, three series of densely branched polymers with uniform side chain length and uniform branching point distribution were synthesized via the polymerization of macromonomers using ROMP. Compared with other brush densely grafted polymers, these novel brush polymers have lower polydispersity and a complete grafting of side chains on every backbone repeat unit. The backbone DP of these special brush polymers is in the intermediate range, but the side chains are longer than what had been examined in others' work. Dilute solution characterization shows that the strong intermolecular forces between the side chains cause the Kuhn length of the polymer backbone to increase as the side chains get longer. The densely branched brush polymers with the same backbone DP have the same contour lengths.

A sequential relaxation framework was applied to analyze the relaxation behaviors of these brush polymers. The dynamic modulus master curves of these dense brush polymers were divided into three regions, the segmental regime, arm regime and the terminal regime. Two plateaus were found in the dynamic master curves for the brush polymer with 4.4 kDa and 8.7 kDa side chain. One is in the arm regime and corresponds to the relaxation of the side chain. The other one is in the terminal regime and is related to the movement of the backbone. This double relaxation process phenomenon with one plateau being much lower than the other one is similar to what had been found in other brush polymers with similar structures.

Side chain properties affect the relaxation behavior of the whole brush polymer. For brush polymers with the same side chains but different backbone DP, their arm and segmental regimes are almost identical. The glassy modulus and glass transition temperature are near to the values for the polylactide side chains. The molecular weights of the brush polymers are huge and the side chains are long, however neither the side chains nor the whole polymer show evidence of entanglement. The Rouse-like behaviors of the side chain in the arm regime are confirmed by analyzing the retardation spectra.

A very low modulus plateau can be found in the terminal zone. Both the backbone DP and the arm length can affect the plateau value. Further analysis shows that the plateau is related to the relaxation of the backbone and is not the entanglement or rubbery plateau. It is the inverse value of the steady state recoverable compliance and only reflects the molecular orientation of these Rouse-like chains. The unentangled nature of these brush polymers was further confirmed by the zero shear viscosity in the melt state. The slope of the zero shear viscosity vs weight average molecular weight is much smaller than 3.4, being 1.7, i.e., although having very large molar masses these brush polymer chains remain unentangled.

AUTHOR INFORMATION

Corresponding Author

*E-mail: (G.B.M.) Greg.mckenna@ttu.edu; (J.A.K.) jak@cheme.caltech.edu.

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(1 of 1)

United States Patent Application**20120035293****Kind Code****A1****Boydston; Andrew J. ; et al.****February 9, 2012**

ON-DEMAND PHOTOINITIATED POLYMERIZATION

Abstract

Compositions and methods for adjustable lenses are provided. In some embodiments, the lenses contain a lens matrix material, a masking compound, and a prepolymer. The lens matrix material provides structure to the lens. The masking compound is capable of blocking polymerization or crosslinking of the prepolymer, until photoisomerization of the compound is triggered, and the compound is converted from a first isomer to a second isomer having a different absorption profile. The prepolymer is a composition that can undergo a polymerization or crosslinking reaction upon photoinitiation to alter one or more of the properties of the lenses.

Inventors: **Boydston; Andrew J.**; (*Seattle, WA*) ; **Grubbs; Robert H.**; (*South Pasadena, CA*) ; **Daeffler; Chris**; (*Pasadena, CA*) ; **Momcilovic; Nebojsa**; (*Vienna, VA*)

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[0002] This invention was made with U.S. Government support under Grant No. DE-FG02-05ER46218 awarded by the Department of Energy and Grant No. GM031332 awarded by the National Institutes of Health. The Government has certain rights in the invention.

Claims

1. A method for modifying a composition, the method comprising: (a) a triggering step, comprising applying electromagnetic energy of a first wavelength and intensity to the composition, wherein the triggering step causes photoisomerization of a masking compound in the composition; and (b) a polymerization or crosslinking step, comprising applying electromagnetic energy of a second wavelength and intensity to the composition, wherein the polymerization or crosslinking step causes polymerization or crosslinking of a prepolymer in the composition.
2. The method of claim 1, wherein the photoisomerization converts the masking compound from a first isomer to a second isomer, wherein the second isomer absorbs less light at the second wavelength compared with the first isomer.
3. The method of claim 2, wherein the photoisomerization is selected from a cis-trans, cyclization, or ring-opening transition.
4. The method of claim 1, wherein the electromagnetic energy at the second wavelength induces polymerization by direct initiation of the prepolymer.
5. The method of claim 1, wherein the electromagnetic energy at the second wavelength induces polymerization indirectly on the prepolymer via activation of a photoinitiator.
6. The method of claim 1, wherein the electromagnetic energy at the second wavelength induces crosslinking of the prepolymer via a cross-linkable monomer or oligomer.
7. The method of claim 2, wherein the method further comprises: (c) waiting for a period of time sufficient to allow the masking compound to

isomerize from the second isomer to the first isomer; and (d) repeating the triggering step and the polymerization or crosslinking step.

8. The method of claim 1, wherein the composition is an intraocular implant and the polymerization or crosslinking step modifies an optical property of the implant.

9. The method of claim 1, wherein the masking compound is described by the structure of formula (I): $(Z^{sup.1})_{sub.n1}-Y-(Z^{sup.2})_{sub.n2}$ (I) wherein Y is a photoisomerizable moiety; $n^{sup.1}$ and $n^{sup.2}$ are each independently 0, 1, 2 or 3; and each $Z^{sup.1}$ and $Z^{sup.2}$ is independently a polymerizable moiety or a crosslinking moiety that is connected to Y via an optional linker.

10. A composition comprising: (a) a masking compound capable of photoisomerization between a first isomer and a second isomer upon absorption of electromagnetic energy at a first wavelength and intensity; and (b) a prepolymer capable of polymerization upon photoinitiation with electromagnetic energy at a second wavelength and intensity.

11. The composition of claim 10, wherein the first isomer of the masking compound absorbs more light at the second wavelength than the second isomer of the masking compound.

12. The composition of claim 10, wherein the prepolymer comprises a photocrosslinker or a photoinitiator.

13. The composition of claim 12, wherein the photocrosslinker or photoinitiator has an absorption maximum that is about 50 nm or less from the absorption maximum of the first isomer of the masking compound.

14. The composition of claim 10, wherein the composition is an intraocular implant further comprising a matrix material.

15. The composition of claim 10, wherein the masking compound is described by the structure of formula (I): $(Z^{sup.1})_{sub.n1}-Y-(Z^{sup.2})_{sub.n2}$ (I) wherein Y is a photoisomerizable moiety; $n^{sup.1}$ and $n^{sup.2}$ are each independently 0, 1, 2 or 3; and each $Z^{sup.1}$ and $Z^{sup.2}$ is independently a polymerizable moiety or a crosslinking moiety that is connected to Y via an optional linker.

16. A method for making an intraocular implant, the method comprising combining: (a) a lens matrix material; (b) a masking compound capable of photoisomerization between a first isomer and a second isomer upon absorption of electromagnetic energy at a first wavelength and intensity; and (c) a prepolymer capable of polymerization or crosslinking upon photoinitiation with electromagnetic energy at a second wavelength and intensity.

17. The method of claim 16, wherein the lens matrix material comprises a polymer selected from a polyacrylate, a polymethacrylate, a silicone, and a polysiloxane.

18. The method of claim 16, wherein the prepolymer comprises a crosslinkable monomer or oligomer and an optional crosslinking moiety.

19. The method of claim 16, wherein the prepolymer comprises a photoinitiator and a polymerizable moiety.

20. The method of claim 16, wherein the masking compound is described by the structure of formula (I): (Z.^{sup.1}).sub.n1-Y-(Z.^{sup.2}).sub.n2 (I) wherein Y is a photoisomerizable moiety; n.^{sup.1} and n.^{sup.2} are each independently 0, 1, 2 or 3; and each Z.^{sup.1} and Z.^{sup.2} is independently a polymerizable moiety or a crosslinking moiety that is connected to Y via an optional linker.

Description

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority under 35 U.S.C. .sectn.119 to U.S. Provisional Application Ser. No. 61/362,249, filed Jul. 7, 2010, the contents of which is incorporated herein by reference in its entirety.

BACKGROUND

[0003] The insertion of an intraocular lens is a common eye surgical procedure for the treatment of cataracts, or as a form of refractive surgery to change the eye's optical power and decrease or eliminate dependency on glasses or contact lenses. Successful refractive eye surgery can reduce or cure common vision disorders such as myopia, hyperopia and astigmatism.

[0004] For certain applications, healing alters the physical environment around the lens. Lens adjustment via photoinitiated polymerization can account for the changes in the physical environment. During the healing time, premature polymerization of the lens material (e.g. from exposure to sunlight) can be detrimental to the procedure.

[0005] As such, lenses and pre-polymer materials that resist polymerization in sunlight during healing but which can be readily polymerized on demand are of interest.

SUMMARY

[0006] Compositions for adjustable lenses are provided, and methods for making and modifying the same. In some embodiments, the lenses contain a lens matrix material, a masking compound, and a prepolymer. The lens matrix material provides structure to the lens. The masking compound is capable of blocking polymerization or crosslinking of the prepolymer, until photoisomerization of the compound is triggered, and the masking compound is converted from a first isomer to a second isomer having a different absorption profile. The prepolymer is a composition that can undergo a polymerization or crosslinking reaction upon photoinitiation, to alter one or more of the properties of the lenses.

[0007] In one aspect, the disclosure provides a method for modifying a composition including: (a) a triggering step, including applying electromagnetic energy of a first wavelength and intensity to the composition, where the triggering step causes photoisomerization of a masking compound in the composition; and (b) a polymerization or crosslinking step, including applying electromagnetic energy of a second wavelength and intensity to the composition, where the polymerization or crosslinking step causes polymerization or crosslinking of a prepolymer in the

composition.

[0008] In some embodiments, the first and second wavelengths are between 1 and 800 nm, and where the electromagnetic energy of the second wavelength is optionally generated from a monochromatic source.

[0009] In some embodiments, photoisomerization converts the masking compound from a first isomer to a second isomer, where the second isomer absorbs less light at the second wavelength compared with the first isomer. In some embodiments, photoisomerization is selected from a cis-trans, cyclization, or ring-opening transition. In some embodiments, the masking compound includes a --C.dbd.C-- or --N.dbd.N-- moiety that undergoes a cis-trans transition. In some embodiments, the masking compound undergoes a cyclization or ring-opening photoisomerization upon absorption of electromagnetic energy at the first wavelength.

[0010] In some embodiments, the electromagnetic energy at the second wavelength induces polymerization by direct initiation of the prepolymer. In some embodiments, the electromagnetic energy at the second wavelength induces polymerization indirectly on the prepolymer via activation of a photoinitiator. In some embodiments, the electromagnetic energy at the second wavelength induces crosslinking of the prepolymer via a cross-linkable monomer or oligomer.

[0011] In some embodiments, the subject method further includes: (c) waiting for a period of time sufficient to allow the masking compound to isomerize from the second isomer to the first isomer; and (d) repeating the triggering step and the polymerization or crosslinking step.

[0012] In some embodiments, the composition is an intraocular implant and the polymerization or crosslinking step modifies an optical property of the implant.

[0013] In another aspect, the disclosure provides a composition including: (a) a masking compound capable of photoisomerization between a first isomer and a second isomer upon absorption of electromagnetic energy at a first wavelength and intensity; and (b) a prepolymer capable of polymerization upon photoinitiation with electromagnetic energy at a second wavelength and intensity.

[0014] In some embodiments, the first isomer of the masking compound absorbs more light at the second wavelength than the second isomer of the masking compound. In some embodiments, the first isomer of the masking compound is capable of blocking photoinitiation of the prepolymer upon application of ambient sunlight. In some embodiments, the prepolymer is capable of polymerization upon photoinitiation with electromagnetic energy at the second wavelength and intensity in the presence of the second isomer of the masking compound. Thus, in some embodiments, the disclosure provides compositions including the prepolymer and the masking compound, wherein the masking compound is present in sufficient quantity to prevent polymerization or crosslinking of the prepolymer upon exposure to ambient sunlight, and wherein isomerization of a sufficient proportion of the masking compound (to the second isomer, e.g. by application of light at the first wavelength described herein) reduces the inhibitory effect of the masking compound to the extent that the prepolymer can polymerize or crosslink (e.g. upon application of light at the second wavelength described herein).

[0015] In some embodiments, the prepolymer includes a photocrosslinker or a photoinitiator. In some embodiments, the photocrosslinker or photoinitiator has an absorption maximum (i.e. a wavelength that causes the photocrosslinker or photoinitiator to initiate crosslinking or

polymerization of a prepolymer) that is about 50 nm or less (e.g., about 40 nm or less, about 30 nm or less, about 20 nm or less, or about 10 nm or less) from a region of substantial absorption (e.g., an absorption maximum) in the absorption spectrum of the first isomer of the masking compound. In some embodiments, the photocrosslinker or photoinitiator has an absorption maximum that is closer to the absorption maximum of the first isomer as compared to the second isomer of the masking compound.

[0016] In some embodiments, the subject composition is an intraocular implant further including a matrix material.

[0017] In another aspect, the disclosure provides a method for implanting an intraocular implant including: (a) inserting the intraocular implant into the eye of a patient; (b) allowing the eye to heal for a period of time; (c) applying electromagnetic energy of a first wavelength and intensity to the intraocular implant to cause photoisomerization of a masking compound; and (d) applying electromagnetic energy of a second wavelength and intensity to the intraocular implant to cause polymerization of a prepolymer.

[0018] In some embodiments, the intraocular implant is a composition including: (a) a masking compound capable of photoisomerization between a first isomer and a second isomer upon absorption of electromagnetic energy at a first wavelength and intensity; (b) a prepolymer capable of polymerization upon photoinitiation with electromagnetic energy at a second wavelength and intensity; and (c) a matrix material.

[0019] In some embodiments, the first wavelength is between about 1 and about 800 nm, such as between about 200 and about 800 nm, between about 250 and about 600 nm, between about 300 and about 400 nm, between about 340 and about 365 nm (e.g., about 365 nm), or between about 340 and about 350 nm. For example, the first wavelength is less than 800 nm, or less than 600 nm, or less than 400 nm, or less than 365 nm. Also for example, the first wavelength is greater than 1 nm, or greater than 200 nm, or greater than 250 nm, or greater than 300 nm, or greater than 340 nm. In some embodiments, the second wavelength is between about 1 and about 800 nm, such as between 200 and 800 nm, between about 300 and about 650 nm, between about 300 and about 500 nm, between about 300 and about 400 nm, between about 340 and about 370 nm (e.g., about 365 nm), or between about 340 and about 350 nm. For example, the second wavelength is less than 800 nm, or less than 600 nm, or less than 400 nm, or less than 365 nm. Also for example, the second wavelength is greater than 1 nm, or greater than 200 nm, or greater than 250 nm, or greater than 300 nm, or greater than 340 nm. In some embodiments, the first and the second wavelengths are the same. In some embodiments, in the subject methods, the steps of applying electromagnetic energy of the first and second wavelengths are performed concurrently, e.g., substantially at the same time. In some embodiments, the electromagnetic energy of the first and second wavelengths is applied from the same light source.

[0020] In some embodiments, the subject method further includes repeating (c) and (d).

[0021] In another aspect, the disclosure provides a method for making an intraocular implant, the method including combining: (a) a lens matrix material; (b) a masking compound capable of photoisomerization between a first isomer and a second isomer upon absorption of electromagnetic energy at a first wavelength and intensity; and (c) a prepolymer capable of polymerization or crosslinking upon photoinitiation with electromagnetic energy at a second wavelength and intensity.

[0022] In some embodiments, the lens matrix material includes a polymer selected from a polyacrylate, a polymethacrylate, a silicone, and a polysiloxane.

[0023] In some embodiments, the prepolymer includes a crosslinkable monomer or oligomer and an optional crosslinking moiety.

[0024] In some embodiments, the prepolymer includes a photoinitiator and a polymerizable moiety.

[0025] In another aspect, the disclosure provides masking compounds for use in the subject methods and compositions, as summarized above and described herein.

[0026] In some embodiments, the masking compound is described by the structure of formula (I):

$(Z^{sup.1})_{sub.n1}-Y-(Z^{sup.2})_{sub.n2}$ (I)

[0027] where [0028] Y is a photoisomerizable moiety; [0029] $n^{sup.1}$ and $n^{sup.2}$ are each independently 0, 1, 2 or 3; and [0030] each $Z^{sup.1}$ and $Z^{sup.2}$ is independently a polymerizable moiety or a crosslinking moiety that is connected to Y via an optional linker.

[0031] In some embodiments, in formula (I), $n^{sup.1}$ is 2 or 3, and each $Z^{sup.1}$ is attached to Y via a branched linker (e.g., an amino or an ammonium containing linker). In some embodiments, in formula (I), $n^{sup.2}$ is 2 or 3, and each $Z^{sup.2}$ is attached to Y via a branched linker (e.g., an amino or an ammonium containing linker). In some embodiments, in formula (I), when $n^{sup.1}$ and/or $n^{sup.2}$ is 2 or 3, then each $Z^{sup.1}$ and/or $Z^{sup.2}$ is independently connected to Y via a linear linker that is not branched.

[0032] In some embodiments, the masking compound is described by the structure of formula (II):

##STR00001##

[0033] where:

[0034] $n^{sup.5}$ and $n^{sup.6}$ are each independently 0, 1, 2, 3, 4 or 5;

[0035] each R is independently selected from the group consisting of hydrogen, a hydrocarbyl (e.g., alkyl, alkenyl, aryl, etc.), a heterocycle, a halogen, a haloalkyl or perhaloalkyl (e.g., trifluoromethyl), an amino, hydroxyl, an ether, nitro, cyano, carboxy, an acyl, an amido, an ester, a thiol, a thioether, a sulfonyl and a sulfonamide; and

[0036] $(Z^{sup.3})_{sub.n3}-L^{sup.3}-$ and $-L^{sup.4}-(Z^{sup.4})_{sub.n4}$ may be independently absent or present, and when present;

[0037] $n^{sup.3}$ and $n^{sup.4}$ are each independently 1, 2 or 3;

[0038] each $Z^{sup.3}$ and $Z^{sup.4}$ is independently a polymerizable moiety or a crosslinking moiety; and

[0039] $L^{sup.3}$ and $L^{sup.4}$ are linkers.

[0040] In some embodiments, the masking compound is described by the structure of formula (III):

##STR00002##

[0041] where

[0042] L^{sup.3} and L^{sup.4} are linkers;

[0043] n^{sup.5} and n^{sup.6} are each independently 0, 1, 2, 3 or 4; and

[0044] each R is independently selected from the group consisting of hydrogen, a hydrocarbyl (e.g., alkyl, alkenyl, aryl, etc.), a heterocycle, a halogen, a haloalkyl or perhaloalkyl (e.g., trifluoromethyl), an amino, hydroxyl, an ether, nitro, cyano, carboxy, an acyl, an amido, an ester, a thiol, a thioether, a sulfonyl and a sulfonamide.

[0045] In some embodiments, the masking compound is described by one of the following structures:

##STR00003##

[0046] In some embodiments, the masking compound is described by the structure of formula (IV) or (V):

##STR00004##

[0047] where R^{sup.1}-R^{sup.8} are each independently selected from the group consisting of hydrogen, a hydrocarbyl (e.g., alkyl, alkenyl, aryl, etc.), a heterocycle, a halogen, a haloalkyl or perhaloalkyl (e.g., trifluoromethyl), an amino, hydroxyl, an ether, nitro, cyano, carboxy, an acyl, an amido, an ester, a thiol, a thioether, a sulfonyl and a sulfonamide. Any convenient counterion may be used for masking compounds described by formula (V). Examples include chloride, iodide, and the like.

[0048] In some embodiments, the masking compound is described by the structure of formula (VI):

##STR00005##

[0049] where

[0050] A is a heterocycle ring;

[0051] n^{sup.7} is 0 or an integer from 1 to 5;

[0052] each R is independently selected from the group consisting of hydrogen, L⁵-(Z⁵)_m where m is 1, 2 or 3, a hydrocarbyl (e.g., alkyl, alkenyl, aryl, etc.), a heterocycle, a halogen, a haloalkyl or perhaloalkyl (e.g., trifluoromethyl), an amino, hydroxyl, an ether, nitro, cyano, carboxy, an acyl, an amido, an ester, a thiol, a thioether, a sulfonyl and a sulfonamide; and

[0053] R¹¹-R¹⁵ are each independently selected from the group consisting of hydrogen, a hydrocarbyl (e.g., alkyl, alkenyl, aryl, etc.), a heterocycle, a halogen, a haloalkyl or perhaloalkyl (e.g., trifluoromethyl), an amino, hydroxyl, an ether, nitro, cyano, carboxy, an acyl, an amido, an ester, a thiol, a thioether, a sulfonyl and a sulfonamide, and L⁵-Z⁵;

[0054] where L⁵ is a linker and each Z⁵ is independently a polymerizable group or a crosslinking group.

[0055] In some embodiments, the masking compound is described by the structure of formula (VII):

##STR00006##

[0056] where Y is O or N--R²¹, where R²¹ is hydrogen, an alkyl, an aryl, an acyl, a heterocycle, or -L⁵-Z⁵; and

[0057] R¹⁶-R²⁰ are each independently selected from the group consisting of hydrogen, a hydrocarbyl (e.g., alkyl, alkenyl, aryl, etc.), a heterocycle, a halogen, a haloalkyl or perhaloalkyl (e.g., trifluoromethyl), an amino, hydroxyl, an ether, nitro, cyano, carboxy, an acyl, an amido, an ester, a thiol, a thioether, a sulfonyl and a sulfonamide, and -L⁵-Z⁵; and

[0058] where each L⁵ is a linker and each Z⁵ is a polymerizable group.

[0059] In some embodiments, the masking compound is described by one of the following structures:

##STR00007##

BRIEF DESCRIPTION OF THE DRAWINGS

[0060] FIG. 1 illustrates a general schematic of an exemplary photopolymerizable prepolymer composition that includes a photoinitiator (star), a masking compound (i.e., blocking chromophore) and a monomer solution, that can resist initiation of polymerization due to sunlight. The first and second panels show the interconversion of some blocking chromophore to non-blocking chromophore (circles and triangles, respectively) in ambient sunlight. The second and third panels shows the complete conversion of masking compound (i.e., blocking chromophore) to a non-blocking form by irradiation with light (e.g., 350 nm). In addition, the third and fourth panels show crosslinking of the unmasked prepolymer solution to a crosslinked material.

[0061] FIG. 2 shows the UV-vis spectra of solutions of an exemplary masking compound 5.

[0062] FIG. 3 illustrates an image of a slab containing an exemplary masking compound 5 that was subjected to a circular pattern of 365 nm light.

DEFINITIONS

[0063] Unless otherwise indicated, the disclosure is not limited to specific procedures, materials, or the like, as such may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting.

[0064] As used in the specification and the appended claims, the singular forms "a," "an," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a compound" includes not only a single compound but also a combination of two or more compounds, reference to "a substituent" includes a single substituent as well as two or more substituents, and the like.

[0065] In describing and claiming the present invention, certain terminology will be used in accordance with the definitions set out below. It will be appreciated that the definitions provided herein are not intended to be mutually exclusive. Accordingly, some chemical moieties may fall within the definition of more than one term.

[0066] As used herein, the phrases "for example," "for instance," "such as," or "including" are meant to introduce examples that further clarify more general subject matter. These examples are provided only as an aid for understanding the disclosure, and are not meant to be limiting in any fashion.

[0067] As used herein, the phrase "having the formula" or "having the structure" is not intended to be limiting and is used in the same way that the term "comprising" is commonly used. The term "independently selected from" is used herein to indicate that the recited elements, e.g., R groups or the like, can be identical or different.

[0068] As used herein, the terms "may," "optional," "optionally," or "may optionally" mean that the subsequently described circumstance may or may not occur, so that the description includes instances where the circumstance occurs and instances where it does not. For example, the phrase "optionally substituted" means that a non-hydrogen substituent may or may not be present on a given atom, and, thus, the description includes structures wherein a non-hydrogen substituent is present and structures wherein a non-hydrogen substituent is not present.

[0069] The term "alkyl" as used herein refers to a branched or unbranched saturated hydrocarbon group (i.e., a mono-radical) typically although not necessarily containing 1 to about 24 carbon atoms, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl, octyl, decyl, and the like, as well as cycloalkyl groups such as cyclopentyl, cyclohexyl and the like. Generally, although not necessarily, alkyl groups herein may contain 1 to about 18 carbon atoms, and such groups may contain 1 to about 12 carbon atoms. The term "lower alkyl" intends an alkyl group of 1 to 6 carbon atoms. "Substituted alkyl" refers to alkyl substituted with one or more substituent groups, and this includes instances wherein two hydrogen atoms from the same carbon atom in an alkyl substituent are replaced, such as in a carbonyl group (i.e., a substituted alkyl group may include a --C(.dbd.O)-- moiety). The terms "heteroatom-containing alkyl" and "heteroalkyl" refer to an alkyl substituent in which at least one carbon atom is replaced with a heteroatom, as described in further detail infra. If not otherwise indicated, the terms "alkyl" and "lower alkyl" include linear, branched, cyclic, unsubstituted, substituted, and/or heteroatom-containing alkyl or lower alkyl, respectively.

[0070] The term "alkenyl" as used herein refers to a linear, branched or cyclic hydrocarbon group of 2 to about 24 carbon atoms containing at least

one double bond, such as ethenyl, n-propenyl, isopropenyl, n-butenyl, isobutenyl, octenyl, decenyl, tetradecenyl, hexadecenyl, eicosenyl, tetracosenyl, and the like. Generally, although again not necessarily, alkenyl groups herein may contain 2 to about 18 carbon atoms, and for example may contain 2 to 12 carbon atoms. The term "lower alkenyl" intends an alkenyl group of 2 to 6 carbon atoms. The term "substituted alkenyl" refers to alkenyl substituted with one or more substituent groups, and the terms "heteroatom-containing alkenyl" and "heteroalkenyl" refer to alkenyl in which at least one carbon atom is replaced with a heteroatom. If not otherwise indicated, the terms "alkenyl" and "lower alkenyl" include linear, branched, cyclic, unsubstituted, substituted, and/or heteroatom-containing alkenyl and lower alkenyl, respectively.

[0071] The term "alkynyl" as used herein refers to a linear or branched hydrocarbon group of 2 to 24 carbon atoms containing at least one triple bond, such as ethynyl, n-propynyl, and the like. Generally, although again not necessarily, alkynyl groups herein may contain 2 to about 18 carbon atoms, and such groups may further contain 2 to 12 carbon atoms. The term "lower alkynyl" intends an alkynyl group of 2 to 6 carbon atoms. The term "substituted alkynyl" refers to alkynyl substituted with one or more substituent groups, and the terms "heteroatom-containing alkynyl" and "heteroalkynyl" refer to alkynyl in which at least one carbon atom is replaced with a heteroatom. If not otherwise indicated, the terms "alkynyl" and "lower alkynyl" include linear, branched, unsubstituted, substituted, and/or heteroatom-containing alkynyl and lower alkynyl, respectively.

[0072] The term "alkoxy" as used herein intends an alkyl group bound through a single, terminal ether linkage; that is, an "alkoxy" group may be represented as --O-alkyl where alkyl is as defined above. A "lower alkoxy" group intends an alkoxy group containing 1 to 6 carbon atoms, and includes, for example, methoxy, ethoxy, n-propoxy, isopropoxy, t-butyloxy, etc. Substituents identified as "C.sub.1-C.sub.6 alkoxy" or "lower alkoxy" herein may, for example, may contain 1 to 3 carbon atoms, and as a further example, such substituents may contain 1 or 2 carbon atoms (i.e., methoxy and ethoxy).

[0073] The term "aryl" as used herein, and unless otherwise specified, refers to an aromatic substituent generally, although not necessarily, containing 5 to 30 carbon atoms and containing a single aromatic ring or multiple aromatic rings that are fused together, directly linked, or indirectly linked (such that the different aromatic rings are bound to a common group such as a methylene or ethylene moiety). Aryl groups may, for example, contain 5 to 20 carbon atoms, and as a further example, aryl groups may contain 5 to 12 carbon atoms. For example, aryl groups may contain one aromatic ring or two or more fused or linked aromatic rings (i.e., biaryl, aryl-substituted aryl, etc.). Examples include phenyl, naphthyl, biphenyl, diphenylether, diphenylamine, benzophenone, and the like. "Substituted aryl" refers to an aryl moiety substituted with one or more substituent groups, and the terms "heteroatom-containing aryl" and "heteroaryl" refer to aryl substituent, in which at least one carbon atom is replaced with a heteroatom, as will be described in further detail infra. If not otherwise indicated, the term "aryl" includes unsubstituted, substituted, and/or heteroatom-containing aromatic substituents.

[0074] The term "aralkyl" refers to an alkyl group with an aryl substituent, and the term "alkaryl" refers to an aryl group with an alkyl substituent, wherein "alkyl" and "aryl" are as defined above. In general, aralkyl and alkaryl groups herein contain 6 to 30 carbon atoms. Aralkyl and alkaryl groups may, for example, contain 6 to 20 carbon atoms, and as a further example, such groups may contain 6 to 12 carbon atoms.

[0075] The term "alkylene" as used herein refers to a di-radical alkyl group. Unless otherwise indicated, such groups include saturated hydrocarbon chains containing from 1 to 24 carbon atoms, which may be substituted or unsubstituted, may contain one or more alicyclic groups, and may be heteroatom-containing. "Lower alkylene" refers to alkylene linkages containing from 1 to 6 carbon atoms. Examples include, methylene (--CH.sub.2--), ethylene (--CH.sub.2CH.sub.2--), propylene (--CH.sub.2CH.sub.2CH.sub.2--), 2-methylpropylene

(--CH.sub.2--CH(CH.sub.3)--CH.sub.2--), hexylene (--(CH.sub.2).sub.6--) and the like.

[0076] Similarly, the terms "alkenylene," "alkynylene," "arylene," "aralkylene," and "alkarylene" as used herein refer to di-radical alkenyl, alkynyl, aryl, aralkyl, and alkaryl groups, respectively.

[0077] The term "amino" is used herein to refer to the group --NZ.sup.1Z.sup.2 wherein Z.sup.1 and Z.sup.2 are hydrogen or nonhydrogen substituents, with nonhydrogen substituents including, for example, alkyl, aryl, alkenyl, aralkyl, and substituted and/or heteroatom-containing variants thereof.

[0078] The terms "halo" and "halogen" are used in the conventional sense to refer to a chloro, bromo, fluoro or iodo substituent.

[0079] The term "heteroatom-containing" as in a "heteroatom-containing alkyl group" (also termed a "heteroalkyl" group) or a "heteroatom-containing aryl group" (also termed a "heteroaryl" group) refers to a molecule, linkage or substituent in which one or more carbon atoms are replaced with an atom other than carbon, e.g., nitrogen, oxygen, sulfur, phosphorus or silicon, typically nitrogen, oxygen or sulfur. Similarly, the term "heteroalkyl" refers to an alkyl substituent that is heteroatom-containing, the term "heterocyclic" refers to a cyclic substituent that is heteroatom-containing, the terms "heteroaryl" and "heteroaromatic" respectively refer to "aryl" and "aromatic" substituents that are heteroatom-containing, and the like. Examples of heteroalkyl groups include alkoxyaryl, alkylsulfanyl-substituted alkyl, N-alkylated amino alkyl, and the like. Examples of heteroaryl substituents include pyrrolyl, pyrrolidinyl, pyridinyl, quinolinyl, indolyl, furyl, pyrimidinyl, imidazolyl, 1,2,4-triazolyl, tetrazolyl, etc., and examples of heteroatom-containing alicyclic groups are pyrrolidino, morpholino, piperazino, piperidino, tetrahydrofuranyl, etc.

[0080] "Hydrocarbyl" refers to univalent hydrocarbyl radicals containing 1 to about 30 carbon atoms, including 1 to about 24 carbon atoms, further including 1 to about 18 carbon atoms, and further including about 1 to 12 carbon atoms, including linear, branched, cyclic, saturated and unsaturated species, such as alkyl groups, alkenyl groups, aryl groups, and the like. "Substituted hydrocarbyl" refers to hydrocarbyl substituted with one or more substituent groups, and the term "heteroatom-containing hydrocarbyl" refers to hydrocarbyl in which at least one carbon atom is replaced with a heteroatom. Unless otherwise indicated, the term "hydrocarbyl" is to be interpreted as including substituted and/or heteroatom-containing hydrocarbyl moieties.

[0081] By "substituted" as in "substituted hydrocarbyl," "substituted alkyl," "substituted aryl," and the like, as alluded to in some of the aforementioned definitions, is meant that in the hydrocarbyl, alkyl, aryl, or other moiety, at least one hydrogen atom bound to a carbon (or other) atom is replaced with one or more non-hydrogen substituents. Examples of such substituents include, without limitation, functional groups, and the hydrocarbyl moieties C.sub.1-C.sub.24 alkyl (including C.sub.1-C.sub.18 alkyl, further including C.sub.1-C.sub.12 alkyl, and further including C.sub.1-C.sub.6 alkyl), C.sub.2-C.sub.24 alkenyl (including C.sub.2-C.sub.18 alkenyl, further including C.sub.2-C.sub.12 alkenyl, and further including C.sub.2-C.sub.6 alkenyl), C.sub.2-C.sub.24 alkynyl (including C.sub.2-C.sub.18 alkynyl, further including C.sub.2-C.sub.12 alkynyl, and further including C.sub.2-C.sub.6 alkynyl), C.sub.5-C.sub.30 aryl (including C.sub.5-C.sub.20 aryl, and further including C.sub.5-C.sub.12 aryl), and C.sub.6-C.sub.30 aralkyl (including C.sub.6-C.sub.20 aralkyl, and further including C.sub.6-C.sub.12 aralkyl). The above-mentioned hydrocarbyl moieties may be further substituted with one or more functional groups or additional hydrocarbyl moieties such as those specifically enumerated.

[0082] By the term "functional groups" is meant chemical groups such as halo, hydroxyl, sulfhydryl, C.sub.1-C.sub.24 alkoxy, C.sub.2-C.sub.24 alkenyloxy, C.sub.2-C.sub.24 alkynyloxy, C.sub.5-C.sub.20 aryloxy, acyl (including C.sub.2-C.sub.24 alkylcarbonyl (--CO-alkyl) and C.sub.6-C.sub.20 arylcarbonyl (--CO-aryl)), acyloxy (--O-acyl), C.sub.2-C.sub.24 alkoxycarbonyl (--(CO)--O-alkyl), C.sub.6-C.sub.20 aryloxycarbonyl (--(CO)--O-aryl), halocarbonyl (--CO)--X where X is halo), C.sub.2-C.sub.24 alkylcarbonato (--O--(CO)--O-alkyl), C.sub.6-C.sub.20 arylcarbonato (--O--(CO)--O-aryl), carboxy (--COOH), carboxylato (--COO.sup.-), carbamoyl (--(CO)--NH.sub.2), mono-substituted C.sub.1-C.sub.24 alkylcarbamoyl (--(CO)--NH(C.sub.1-C.sub.24 alkyl)), di-substituted alkylcarbamoyl (--(CO)--N(C.sub.1-C.sub.24 alkyl).sub.2), mono-substituted arylcarbamoyl (--(CO)--NH-aryl), thiocarbamoyl (--(CS)--NH.sub.2), carbamido (--NH--(CO)--NH.sub.2), cyano (--C.ident.N), isocyano (--N.sup.+ident.C.sup.-), cyanato (--O--C.ident.N), isocyanato (--O--N.sup.+ident.C.sup.-), isothiocyanato (--S--C.ident.N), azido (--N.dbd.N.sup.+dbd.N.sup.-), formyl (--(CO)--H), thioformyl (--(CS)--H), amino (--NH.sub.2), mono- and di-(C.sub.1-C.sub.24 alkyl)-substituted amino, mono- and di-(C.sub.5-C.sub.20 aryl)-substituted amino, C.sub.2-C.sub.24 alkylamido (--NH--(CO)-alkyl), C.sub.5-C.sub.20 arylamido (--NH--(CO)-aryl), imino (--CR.dbd.NH where R=hydrogen, C.sub.1-C.sub.24 alkyl, C.sub.5-C.sub.20 aryl, C.sub.6-C.sub.20 alkaryl, C.sub.6-C.sub.20 aralkyl, etc.), alkylimino (--CR.dbd.N(alkyl), where R=hydrogen, alkyl, aryl, alkaryl, etc.), arylimino (--CR.dbd.N(aryl), where R=hydrogen, alkyl, aryl, alkaryl, etc.), nitro (--NO.sub.2), nitroso (--NO), sulfo (--SO.sub.2--OH), sulfonato (--SO.sub.2--O.sup.-), C.sub.1-C.sub.24 alkylsulfanyl (--S-alkyl; also termed "alkylthio"), arylsulfanyl (--S-aryl; also termed "arylthio"), C.sub.1-C.sub.24 alkylsulfanyl (--SO-alkyl), C.sub.5-C.sub.20 arylsulfanyl (--SO-aryl), C.sub.1-C.sub.24 alkylsulfonyl (--SO.sub.2-alkyl), C.sub.5-C.sub.20 arylsulfonyl (--SO.sub.2-aryl), phosphono (--P(O)(OH).sub.2), phosphonato (--P(O)(O.sup.-).sub.2), phosphinato (--P(O)(O.sup.-)), phospho (--PO.sub.2), and phosphino (--PH.sub.2), mono- and di-(C.sub.1-C.sub.24 alkyl)-substituted phosphino, mono- and di-(C.sub.5-C.sub.20 aryl)-substituted phosphine. In addition, the aforementioned functional groups may, if a particular group permits, be further substituted with one or more additional functional groups or with one or more hydrocarbyl moieties such as those specifically enumerated above.

[0083] By "linking" or "linker" as in "linking group," "linker moiety," etc., is meant a multivalent (e.g., trivalent or bivalent) radical moiety. A linker may be branched or linear, saturated or unsaturated, and of 1 to about 20 atoms in length. Examples of such linking groups include alkylene, alkenylene, alkynylene, arylene, alkarylene, aralkylene, amino, oxy, and linking moieties containing functional groups including, without limitation: amido (--NH--CO--), ureylene (--NH--CO--NH--), imide (--CO--NH--CO--), epoxy (--O--), epithio (--S--), epidioxy (--O--O--), carbonyldioxy (--O--CO--O--), alkyldioxy (--O--(CH.sub.2).sub.n--O--), epoxyimino (--O--NH--), epimino (--NH--), carbonyl (--CO--), etc.

[0084] When the term "substituted" appears prior to a list of possible substituted groups, it is intended that the term apply to every member of that group. For example, the phrase "substituted alkyl and aryl" is to be interpreted as "substituted alkyl and substituted aryl."

[0085] Unless otherwise specified, reference to an atom is meant to include isotopes of that atom. For example, reference to H is meant to include .sup.1H, .sup.2H (i.e., D) and .sup.3H (i.e., T), and reference to C is meant to include .sup.12C and all isotopes of carbon (such as .sup.13C).

[0086] Definitions of other terms and concepts appear throughout the detailed description below.

DETAILED DESCRIPTION

[0087] As summarized above, the present disclosure provides methods of modifying a composition, where the composition includes a masking compound and a prepolymer. The subject compositions and methods find use in adjustable intraocular lenses and the manufacturing, use and

modification thereof. The invention relates to lenses that can be modified post-fabrication using photoinitiated polymerization methodologies.

[0088] The subject lenses provide for on demand polymerization for lens adjustment, following surgical insertion of the lens into the eye of a patient. Lens adjustment may be controlled to account for changes in the physical environment of the eye around the lens that may occur during healing after eye surgery. In some cases, lens adjustment is performed via photoinitiated polymerization or crosslinking after healing has occurred.

[0089] To avoid unwanted photoinitiated polymerization or crosslinking induced by ambient sunlight during healing, masking compounds are included that block such photoinitiation by absorbing light. The photoinitiator and masking compound are selected to have overlapping absorption spectra, such that the masking compound is capable of absorbing sufficient ambient sunlight to prevent activation of the photoinitiator. Upon application of suitable triggering conditions, photoisomerization of the masking compound results in a shift in the absorption maximum of the masking compound away from that of the photoinitiator, such that the absorption spectral overlap of the photoisomerized masking compound and the photoinitiator is substantially reduced at a wavelength suitable for activation of the photoinitiator.

[0090] Polymerization of the subject compositions may then be triggered via photoinitiation when desired, i.e. after post-surgical healing is completed.

[0091] In some embodiments, photoinitiated polymerization may be triggered without the need for a high intensity UV light that could lead to undesirable damaging side effects in a human eye. Potential undesirable damage may occur to the eye when the masking compound and the photoinitiator when a high intensity UV light is needed to surpass the optical density of the masking compound before activating a photoinitiator of polymerization.

[0092] In order to further illustrate certain aspects of the present disclosure, the following specific examples are provided. Before certain embodiments are described in greater detail, it is to be understood that this disclosure is not limited to the certain embodiments described, as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the disclosure will be limited only by the appended claims.

[0093] Where a range of values is provided, it is understood that each intervening value, to the tenth of the unit of the lower limit unless the context clearly dictates otherwise, between the upper and lower limits of that range is also specifically disclosed. Each smaller range between any stated value or intervening value in a stated range and any other stated or intervening value in that stated range is encompassed within the disclosure. The upper and lower limits of these smaller ranges may independently be included or excluded in the range, and each range where either, neither or both limits are included in the smaller ranges is also encompassed within the disclosure, subject to any specifically excluded limit in the stated range. Where the stated range includes one or both of the limits, ranges excluding either or both of those included limits are also included in the disclosure.

Compositions

[0094] In some embodiments, the compositions of interest contain at least three components: a matrix material, a masking compound, and a prepolymer. In some embodiments, the prepolymer includes a photoinitiator and a polymerizable moiety. In some embodiments, the prepolymer

includes a crosslinking moiety (e.g., a photocrosslinker). In some embodiments, the masking compound is linked to a polymerizable moiety or a crosslinking moiety. In some embodiments, the subject compositions find use in an intraocular lens. Any convenient additional ingredients may be included in the subject compositions, such as, structural materials, excipients, fillers, matrix polymers, colorants, anti-reflection compounds, biocompatibility-enhancing agents, anti-bacterial agents, and the like.

Masking Compounds

[0095] The compositions of interest include a masking compound (also referred to herein as a "masking agent" or "masking component"). The masking compound is a molecule that has an absorption spectrum that overlaps that of a prepolymer component, such that the masking compound is capable of blocking the absorption of certain wavelengths of light by prepolymer component (e.g., wavelengths at or near the absorption maximum of the prepolymer component, such as a photoinitiator), until the application of a triggering condition to the masking compound. As used herein, the terms "blocking" and "masking" are used interchangeably. The blocked wavelengths of light may be wavelengths that induce polymerization or crosslinking in the prepolymer (e.g., induce the formation of a polymerization-initiating radical). The masking compound is a molecule that upon application of a suitable triggering condition (e.g., irradiation at a particular wavelength of light, a first wavelength) experiences a change in its absorption spectra—for example, a shift in its absorption maximum. As described above, the masking compound may be referred to as "switchable" because its absorption maximum can be shifted upon application of a triggering condition.

[0096] In some embodiments, the subject masking compounds display switchable absorption maxima (e.g., upon photoisomerization) such that a photoinitiator (described in more detail below) can be masked from, or exposed to, irradiation on demand.

[0097] In some embodiments, the masking compound blocks or prevents polymerization or crosslinking of the prepolymer in ambient sunlight for a period of 12 hours or more, such as 1 day or more, 2 days or more, 3 days or more, 4 days or more, 5 days or more, 6 days or more, 7 days or more, 14 days or more, or even more.

[0098] In some embodiments, the masking compound is a photoisomerizable molecule and application of light of a suitable wavelength to the molecule causes isomerization from a first isomer to a second isomer with a concomitant shift in the absorption maximum. In some embodiments, the application of light to a masking compound to cause photoisomerization is referred to as a "triggering condition", as "triggering" or as "switching" the masking compound. As used herein, the terms "photoisomerizable" and "photoisomerization" refer to a structural change that converts a first isomer of a compound to a second isomer, and which is caused by photoexcitation of the molecule. Photoisomerization may be reversible or irreversible. In some embodiments, thermal relaxation returns the compound to its original state, such that the photoisomerization process can be repeated, e.g., several times.

[0099] In some embodiments, the photoisomerizable masking compound has two isomeric forms (i.e., a first isomer and a second isomer) that have significantly different absorption spectra. By significantly different absorption spectra is meant that the difference in absorption maxima between the first and second isomers is about 10 nm or more, 20 nm or more, 30 nm or more, 40 nm or more, 50 nm or more, 60 nm or more, 70 nm or more, 80 nm or more, 90 nm or more, 100 nm or more, 125 nm or more, 150 nm or more, 175 nm or more, or even about 200 nm or more. In some embodiments, the first isomer has an absorption maximum that does not overlap the absorption spectrum (i.e., the region of significant absorption in the IR, visible, and UV wavelengths) of the second isomer. In some embodiments, the second isomer has an absorption maximum that does not

overlap the absorption spectrum of the first isomer. In some embodiments, the absorption maximum of the second isomer is at a wavelength where there is substantially less (e.g., 20% less, or 30% less, or 40% less, or 50% less, or 60% less, or 70% less, or 75% less, or greater than 75% less) absorption by the first isomer.

[0100] In some embodiments, photoisomerization converts the masking compound from a first isomer to a second isomer, where the second isomer absorbs less light compared with the first isomer at a wavelength that activates a prepolymer component of the subject composition.

[0101] In some embodiments, in qualitative terms, the absorption of the first isomer of the masking compound at the wavelength that causes the photoinitiator or photocrosslinker to initiate polymerization or crosslinking is sufficiently large that the presence of the first isomer in solution prevents photoinitiation or photo-induced crosslinking. In contrast, the second isomer absorbs substantially less at that wavelength, and photoinitiation or photocrosslinking becomes possible when a sufficient quantity of the first isomer is converted to the second isomer. A sufficient quantity of such isomer conversion will depend upon the characteristics of the solution (e.g. concentrations of the various components) but will be apparent by the onset of polymerization or crosslinking of the prepolymer (see below for more details).

[0102] In some embodiments, the masking compound is isomerized from the first to the second isomer solely by the application of electromagnetic radiation--no thermal energy is required to cause the isomerization.

[0103] In some embodiments, as described in more detail herein, after photoisomerization, the masking compound re-isomerizes back to the first isomer over a period of time. The re-isomerization may occur via thermal relaxation (i.e., the rate is a function of the reaction temperature) and/or may be accelerated by application of a stimulus (e.g. electromagnetic radiation). After re-isomerizing back to the first isomer, the masking compound can be isomerized again from the first isomer to the second isomer.

[0104] It will be appreciated that the photoisomerization is a reaction, and as such has an associated reaction rate. Such reaction rate can, in some embodiments, be accelerated by application of additional stimulus (e.g., a more intense electromagnetic radiation source, or a plurality of such sources). Application of light at the second wavelength to initiate reaction of the prepolymer (see discussion below) can, in some embodiments, be carried out after complete isomerization of the masking compound (i.e., substantially 100% reaction). In other embodiments, application of light at the second wavelength can be carried out at less than 100% isomerization of the masking compound--e.g., where the concentration of masking compound present as the first isomer has fallen below the level needed to inhibit initiation of reaction of the prepolymer.

[0105] In some embodiments, photoisomerization is performed in a photoreactor. In some embodiments, photoisomerization is performed using a monochromatic light source.

[0106] In some embodiments, photoisomerization of the masking compound occurs via a cis-trans isomerization, a cyclization reaction, or a ring-opening reaction. Convenient photoisomerizable compounds that may be used as the subject masking compounds include compounds that are capable of blocking absorption of a suitable prepolymer component (e.g., a photoinitiator) and that experience a significant shift in absorption maxima upon application of a suitable triggering condition. In some embodiments, the masking compound undergoes a cyclization or ring-opening photoisomerization upon absorption of electromagnetic energy at the first wavelength (e.g., a triggering condition). In some embodiments, the masking compound includes a photoisomerizable moiety that is a stilbene (e.g., an azastilbene), an azobenzene moiety, an azoarylene, a fulgide, a

spiropyran, a naphthopyran, a quinone, a spiro-oxazine, a nitron, a triaryl methane (e.g., a triphenyl methane), a thioindigo, a diarylethene, a dithienylethene, or an overcrowded alkene. In some embodiments, the masking compound includes an alkenyl (C.dbd.C) or an azo moiety (--N.dbd.N--) moiety that undergoes photoisomerization via a cis-trans transition. In some embodiments, the masking compound includes a diarylethene that undergoes photoisomerization via an electrocyclic cyclization reaction. In some embodiments, the masking compound includes a spiropyran that undergoes photoisomerization via a ring opening transition.

[0107] In some embodiments, the photoisomerizable moiety is selected from an azoarylene, a diarylethene, and a dithienylethene.

[0108] In some embodiments, photoisomerization of the masking compound results in a second isomer that is thermally unstable, e.g., the second isomer will revert to the first isomer when the light source is removed. In such cases, photoisomerization is reversible.

[0109] In some embodiments, the masking compound includes a photoisomerizable moiety linked to one or more polymerizable moieties. In some embodiments, the masking compound is described by the formula:

(Z.sup.1).sub.n1-Y-(Z.sup.2).sub.n2 (I)

[0110] where

[0111] Y is a photoisomerizable moiety (e.g., as described above);

[0112] n.sup.1 and n.sup.2 are each independently 0, 1, 2 or 3; and

[0113] each Z.sup.1 and Z.sup.2 is independently a polymerizable moiety or a crosslinking moiety that is connected to Y via an optional linker.

[0114] In some embodiments, in formula (I), n.sup.1 and n.sup.2 are each 1, and Z.sup.1 and Z.sup.2 are each independently connected to Y via a linker of 1 to 20 atoms in length (e.g., 1 to 6 atoms in length). In some embodiments, in formula (I), Y is an azoarylene, a diarylethene, or a dithienylethene. In some embodiments, in formula (I), each Z.sup.1 and Z.sup.2 is independently selected from a vinyl, a vinylidene, a diene, an olefin, an allyl, an acrylate, an acrylamide and an acrylic acid.

[0115] In some embodiments, the masking compound has the structure Ar.sup.1-N.dbd.N--Ar.sup.2 or Ar.sup.1-C.dbd.C--Ar.sup.2, where Ar.sup.1 and Ar.sup.2 are independently selected from aromatic 6-membered rings that may be substituted or unsubstituted and may include one or more heteroatoms. In some embodiments, the masking compound includes an azobenzene moiety (e.g., where Ar.sup.1 and Ar.sup.2 are phenyl). In some embodiments, the masking compound is capable of photoisomerization from a trans isomer to a cis isomer, e.g., as exemplified for the Ar.sup.1--N.dbd.N--Ar.sup.2 compound below shown below. In some embodiments, the cis isomer of the masking compound spontaneously isomerizes back to the trans isomer.

##STR00008##

[0116] In some embodiments, the azobenzene moiety is a photoisomerizable chromophore having absorption maximum near that of a photoinitiator (such as any of the photoinitiators used and described herein). In some embodiments, the azobenzene moiety has an absorption maximum about 50 nm or less (e.g., about 40 nm or less, about 30 nm or less, about 20 nm or less, or about 10 nm or less) from the absorption maximum of the photoinitiator. In some embodiments, the thermodynamically more stable trans-azobenzene (t-AB) moiety tends to absorb at lower wavelengths than the corresponding cis-azobenzene (c-AB) isomer. Upon irradiation, photoisomerization may be facile and quantitative. In some embodiments, thermal relaxation from the c-AB moiety to the t-AB isomer occurs within hours (e.g., within 12 hours or less, such as 6, 5, 4, 3, 2 or within 1 hour or less) at ambient temperature. Irradiation of the t-AB moiety near its absorption maximum causes isomerization to the cis isomer and a change in the absorption spectrum (e.g., a shift in the absorption maxima).

[0117] In some embodiments, the masking compound further includes a polymerizable moiety, i.e., a functional group capable of polymerization in a prepolymer composition upon application of a suitable stimulus (e.g., activation of a photoinitiator). The polymerizable moiety may include a functional group such as an alkenyl, a vinyl, a vinylidene, a diene, an olefin, an allyl, an acrylate or a (meth)acrylic functional group. In some embodiments, the polymerizable moiety is an allyl or a vinyl group.

[0118] In some embodiments, where the masking compound comprises a polymerizable moiety, the masking compound may be chemically incorporated into another component of the compositions of interest. For example, the masking compound can be incorporated into the backbone of a polymer that is present as a matrix material (see below). Also for example, the masking compound can be incorporated into the backbone or as a sidegroup of the prepolymer (see below). In this way, small molecule masking compounds can be chemically incorporated into polymeric components of the compositions of interest. In some embodiments and for some applications, incorporating masking compounds in this manner makes it less likely for the masking component to diffuse out of the compositions of interest.

[0119] In some embodiments, the masking compound is described by the structure of formula (II):

##STR00009##

[0120] where:

[0121] n^{sup.3} and n^{sup.4} are each independently 0, 1, 2 or 3;

[0122] each Z^{sup.3} and Z^{sup.4} is independently a polymerizable moiety or a crosslinking moiety;

[0123] L^{sup.3} and L^{sup.4} are linkers;

[0124] n^{sup.5} and n^{sup.6} are each independently 0, 1, 2, 3, 4 or 5, provided that when (Z^{sup.3}).sub.n³-L^{sup.3}- is present, n^{sup.5} is not 5, and when -L^{sup.4}-(Z^{sup.4}).sub.n⁴ is present, n^{sup.6} is not 5; and

[0125] each R is independently selected from the group consisting of hydrogen, a hydrocarbyl (e.g., alkyl, alkenyl, aryl, etc.), a heterocycle, a halogen, a haloalkyl or perhaloalkyl (e.g., trifluoromethyl), an amino, hydroxyl, an ether, nitro, cyano, carboxy, an acyl, an amido, an ester, a thiol,

a thioether, a sulfonyl and a sulfonamide.

[0126] In some embodiments, in formula (II), each Z^{sup.3} and Z^{sup.4} is independently selected from a vinyl, a vinylidene, a diene, an olefin, an allyl, an acrylate, an acrylamide and an acrylic acid.

[0127] In some embodiments, in formula (II), L^{sup.3} and L^{sup.4} are each independently a linker of 1 to 20 atoms in length, such as of 1 to 6 atoms in length. In some embodiments, in formula (II), the linker L^{sup.3} and/or L^{sup.4}, when present, may include an amino group that connects to a polymerizable moiety or a crosslinking moiety. In some embodiments, a linker is present and includes a branched amino group (e.g., a trivalent amino or a tetravalent ammonium group) for connecting two or three polymerizable moieties and/or crosslinking moieties to the azobenzene. In some embodiments, in formula (II), L^{sup.3} and/or L^{sup.4} is a branched amino (--N.dbd.) group. In some embodiments, in formula (II), L^{sup.3} and/or L^{sup.4} is a branched ammonium (--N(+).ident.) group. In some embodiments, in formula (II), L^{sup.3} includes a branched amino or ammonium group, n^{sup.3} is 2 or 3, and Z^{sup.3} is an allyl or a vinyl.

[0128] In some embodiments, in formula (II), L^{sup.3} and L^{sup.4}, when present, may be attached to the azobenzene ring at any convenient positions. For example, L^{sup.3} may be attached to the first phenyl ring at the 2, 3 or 4 position relative to the azo substituent. For example, L^{sup.4} may be attached to the second phenyl ring at the 2', 3' or 4' position relative to the azo substituent. All combinations of L^{sup.3} and/or L^{sup.4} positioning around the first and second phenyl rings, respectively, are envisaged. For example, L^{sup.3} and L^{sup.4} may be attached at the 2 and 2' positions, respectively. For example, L^{sup.3} and L^{sup.4} may be attached at the 3 and 3' positions, respectively. For example, L^{sup.3} and L^{sup.4} may be attached at the 4 and 4' positions (i.e., para), respectively. Alternatively, L^{sup.3} may be attached at the 4-position of the first phenyl ring, and L^{sup.4} may be attached at the 2' position of the second phenyl ring. Exemplary arrangements of L^{sup.3} and L^{sup.4} are shown in the compounds described below.

[0129] In some embodiments, the masking compound is described by the structure of Formula (III):

##STR00010##

[0130] where

[0131] L^{sup.3} and L^{sup.4} are linkers;

[0132] n^{sup.5} and n^{sup.6} are each independently 0, 1, 2, 3 or 4; and

[0133] each R is independently selected from the group consisting of hydrogen, a hydrocarbyl (e.g., alkyl, alkenyl, aryl, etc.), a heterocycle, a halogen, a haloalkyl or perhaloalkyl (e.g., trifluoromethyl), an amino, hydroxyl, an ether, nitro, cyano, carboxy, an acyl, an amido, an ester, a thiol, a thioether, a sulfonyl and a sulfonamide.

[0134] In some embodiments, the masking compound is as described by the structure of Formula (III) except that one or both of the terminal allyl groups may be independently replaced with any convenient polymerizable moiety or crosslinking moiety, as described herein.

[0135] In some embodiments, in Formula (III), one or both of L.³ and L.⁴ are connected to the azobenzene via an electron withdrawing substituent, such as, a carbonyl, an ester, an amido, a sulfonyl or a sulfonamide. In some embodiments, in Formula (III), L.³ and L.⁴ are independently --(CH₂)_{m1}--Z⁴--(CH₂)_{m2}-- where m¹ and m² are each independently 0 or an integer from 1 to 6, and Z⁴ is selected from a carbonyl (--C(=O)--), an ester (--C(=O)O--), an amido (e.g., --C(=O)NH--), a carbamate (e.g., --OC(=O)NH--), a sulfonyl (--SO₂--), a sulfonamide (e.g., --SO₂NH--), an ether (--O--), a thioether (--S--), or a urea group (e.g., --NHC(=NH)NH--). In some embodiments, m¹ is 2 and m² is 0. In some embodiments, Z⁴ is --O--.

[0136] In some embodiments, the masking compound is described by one of the following structures:

##STR00011##

[0137] where L.³, L.⁴, (R)_{n5} and (R)_{n6} are defined above for Formula (III). In certain embodiments, L.³ and L.⁴ are independently selected from --O-- and --O(CH₂)_m-- where m is an integer from 1 to 6, (e.g., m is 2). In some embodiments, each R is hydrogen.

[0138] In some embodiments, the masking compound is described by the structure of Formula (IV) or (V):

##STR00012##

[0139] where R¹-R⁸ are each independently selected from the group consisting of hydrogen, a hydrocarbyl (e.g., alkyl, alkenyl, aryl, etc.), a heterocycle, a halogen, a haloalkyl or perhaloalkyl (e.g., trifluoromethyl), an amino, hydroxyl, an ether, nitro, cyano, carboxy, an acyl, an amido, an ester, a thiol, a thioether, a sulfonyl and a sulfonamide.

[0140] In some embodiments, in Formula (IV) or (V), one or more of R¹-R⁸ is -L⁵-O-CH₂CH₂, where L⁵ is an optional linker group. In some embodiments, in Formula (IV) or (V), each L⁵ is a C₁-C₆ alkyl chain (e.g., a C₂ alkyl). In some embodiments, in Formula (IV) or (V), each L⁵ is absent. In some embodiments, in Formula (IV) or (V), R¹-R⁸ are each hydrogen.

[0141] In some embodiments, the masking compound is described by the structure of Formula (VI):

##STR00013##

[0142] where

[0143] A is a heterocycle ring;

[0144] n⁷ is 0 or an integer from 1 to 5;

[0145] each R is independently selected from the group consisting of hydrogen, -L⁵-(Z⁵)_m where m is 1, 2 or 3, a hydrocarbyl (e.g., alkyl, alkenyl, aryl, etc.), a heterocycle, a halogen, a haloalkyl or perhaloalkyl (e.g., trifluoromethyl), an amino, hydroxyl, an ether, nitro, cyano, carboxy, an acyl, an amido, an ester, a thiol, a thioether, a sulfonyl and a sulfonamide; and

[0146] R¹¹-R¹⁵ are each independently selected from the group consisting of hydrogen, a hydrocarbyl (e.g., alkyl, alkenyl, aryl, etc.), a heterocycle, a halogen, a haloalkyl or perhaloalkyl (e.g., trifluoromethyl), an amino, hydroxyl, an ether, nitro, cyano, carboxy, an acyl, an amido, an ester, a thiol, a thioether, a sulfonyl and a sulfonamide, a hydrocarbyl (e.g., alkyl, alkenyl, aryl, etc.), a heterocycle, a halogen, a haloalkyl or perhaloalkyl (e.g., trifluoromethyl), an amino, hydroxyl, an ether, nitro, cyano, carboxy, an acyl, an amido, an ester, a thiol, a thioether, a sulfonyl and a sulfonamide, and -L⁵-Z⁵;

[0147] where L⁵ is a linker and each Z⁵ is independently a polymerizable group or a crosslinking group.

[0148] In some embodiments, in formula (VI), A is a N-linked heterocycle, such as but not limited to, morpholino, thiomorpholino piperidino, piperazino, homopiperazine, azepano, or pyrrolidino.

[0149] In some embodiments, in formula (VI), A is a N-linked heterocycle (e.g., an N-morpholino or a N-piperidinyl). In some embodiments, the masking compound is described by the structure of formula (VII):

##STR00014##

[0150] where Y is O or N--R²¹, where R²¹ is hydrogen, an alkyl, an aryl, an acyl, a heterocycle, or -L³-Z³;

[0151] R¹⁶-R²⁰ are each independently selected from the group consisting of hydrogen, a hydrocarbyl (e.g., alkyl, alkenyl, aryl, etc.), a heterocycle, a halogen, a haloalkyl or perhaloalkyl (e.g., trifluoromethyl), an amino, hydroxyl, an ether, nitro, cyano, carboxy, an acyl, an amido, an ester, a thiol, a thioether, a sulfonyl and a sulfonamide, and -L⁵-Z⁵; and

[0152] where L⁵ is a linker and Z⁵ is a polymerizable group or a crosslinking group.

[0153] In some embodiments, in Formula (VII), each L⁵ is independently a C₁-C₆ alkyl chain (e.g., a C₂ alkyl).

[0154] In some embodiments, in Formula (VII), at least one (e.g., two) of R¹⁶-R²⁰ and R²¹ includes a polymerizable moiety (e.g., an allyl group) or a crosslinking moiety. In some embodiments, in Formula (VII), at least one of R¹⁶-R²⁰ and R²¹ includes an allyl or a vinyl group. In some embodiments, in Formula (VII), R¹⁸ is --(CH₂)_{m1}-L⁶-(CH₂)_{m2}-Z⁶ where m¹ and m² are each independently 0 or an integer from 1 to 6, and L⁶ is selected from a carbonyl (--C(=O)--), an ester (--C(=O)O--), an amido (e.g., --C(=O)NH--), a carbamate (e.g., --OC(=O)NH--), a sulfonyl (--SO₂--), a sulfonamide (e.g., --SO₂NH--), an ether (--O--), a thioether (--S--), or a urea group (e.g., --NHC(=NH)NH--). In some embodiments, m¹ is 2 and m² is 0. In some embodiments, L⁶ is --O--.

[0155] In some embodiments, at least one of R^{sup.16}-R^{sup.20} and R^{sup.21} (e.g., R^{sup.18}, R^{sup.19} or R^{sup.20}) is -L^{sup.7}-O--CH₂CH₂CH₂CH₂, where L^{sup.7} is an optional linker group. In some embodiments, in Formula (VII), each L^{sup.7} is independently a C₁-C₆ alkyl chain (e.g., a C₂ alkyl).

[0156] In some embodiments, in Formula (VII), Y is O. In some embodiments, in Formula (VII), one or more of R^{sup.16}-R^{sup.20} is nitro. In some embodiments, in Formula (V), R^{sup.18} is nitro, and R^{sup.16}, R^{sup.17}, R^{sup.19} and R^{sup.20} are hydrogen.

[0157] In some embodiments, the masking compound is selected from one of the following structures:

##STR00015##

Prepolymer

[0158] The compositions of interest may include a prepolymer. The prepolymer is a material capable of undergoing a reaction (e.g., polymerization, crosslinking, etc.), and capable of modifying one or more properties of the composition via such reaction. In some embodiments, the prepolymer is a single component, whereas in other embodiments, the prepolymer is a composition comprising two or more components. At least one of the components in the prepolymer (or the sole component, where the prepolymer consists of only one component) is a material that can undergo a reaction such as a polymerization or crosslinking reaction. Such component may be a small molecule such as a monomer or oligomer, or may be a polymer.

[0159] In some embodiments where the prepolymer is a single component, the prepolymer is capable of absorbing light that self-initiates the modification reaction (e.g., polymerization, crosslinking, etc.) in the single component. In some embodiments where the prepolymer is a multi-component composition, the prepolymer includes a prepolymer component that is capable of absorbing light to induce the modifying reaction (e.g., polymerization, crosslinking, etc.) in the prepolymer. In some such embodiments, the prepolymer component is a photoinitiator. In some such embodiments, the prepolymer component is crosslinking moiety.

[0160] In some embodiments, the prepolymer includes a photoinitiator and a polymerizable moiety and the modifying reaction is a polymerization reaction. In some embodiments, the polymerization reaction is a radical polymerization. In some embodiments, the prepolymer includes a crosslinking moiety (e.g., a photocrosslinker) and a crosslinkable monomer or oligomer and the modifying reaction is a crosslinking reaction.

[0161] In some embodiments, the shifted absorption maximum of the masking compound (i.e., the maximum of the second isomer) no longer significantly overlaps the absorption spectrum of a photoinitiator present in the subject composition. Because of the reduced absorbance of the masking compound, polymerization of the prepolymer of the subject composition becomes possible upon irradiation with light of a suitable wavelength and intensity. Such application of light to cause polymerization is referred to herein as a polymerization or crosslinking condition or a polymerization or crosslinking step.

[0162] In some embodiments, the electromagnetic energy of the polymerization condition induces polymerization of the prepolymer indirectly via

activation of a photoinitiator (e.g., by the absorption of light of a suitable wavelength and intensity). In some embodiments, the electromagnetic energy of the polymerization condition induces polymerization (e.g., by the absorption of light of a suitable wavelength and intensity) by direct initiation of the prepolymer. By direct initiation is meant that the polymerization condition induces polymerization of a polymerizable moiety directly rather than via contact with a photoinitiator.

[0163] In some embodiments, polymerization is not induced thermally, e.g., by activation of a thermal initiator.

[0164] In some embodiments, suitable polymerization conditions include wavelengths of light of between about 1 and about 800 nm, such as, between about 200 and about 800 nm, between about 300 and about 650 nm, between about 300 and about 500 nm, between about 300 and about 400 nm, between about 340 and about 370 nm (e.g., about 365 nm), or between about 340 and about 350 nm. In some embodiments, the triggering and polymerization conditions are the same. In some embodiments, in the subject methods, the triggering and polymerization steps are performed concurrently, e.g., substantially at the same time. In some embodiments, the triggering and polymerization conditions include applying electromagnetic energy from the same light source. In some embodiments, the triggering and polymerization conditions include applying electromagnetic energy from different light sources. In some embodiments, the electromagnetic energy of the light is optionally generated from a monochromatic source, such as a laser. In other embodiments, the light is generated by a polychromatic source (e.g., ambient sunlight).

[0165] In some embodiments, the photoinitiator is a benzoin-type photoinitiator (e.g., 2,2-dimethoxy-1,2-diphenylethan-1-one). In some embodiments, the photoinitiator is an aryl peroxide (e.g., benzoyl peroxide).

[0166] Exemplary photoinitiators include but are not limited to, 2,2-dimethoxy-1,2-diphenylethan-1-one, benzoyl peroxide, benzoin, benzyl, hydroxyacetophenone, dimethylbenzil, di-tert-butyl peroxide, AIBN and analogues thereof, etc.

[0167] In some embodiments, the polymerizable moiety includes one or more olefinic double bonds. They may be of low (monomeric) or high (oligomeric) molecular mass. In some embodiments, the polymerizable moiety includes a vinyl, a vinylidene, a diene, an olefin, an allyl, an acrylate, an acrylamide or an acrylic acid. In some embodiments, the prepolymer includes a polymerizable monomer--i.e. a monomer containing at least one polymerizable moiety.

[0168] Examples of polymerizable monomers containing a double bond include alkyl, aryl, hydroxyalkyl, cycloalkyl (optionally including an O) or amino acrylates, or alkyl, hydroxyalkyl, cycloalkyl (optionally including an O) or amino methacrylates, for example methyl, ethyl, butyl, 2-ethylhexyl, phenyl or 2-hydroxyethyl acrylate, tetrahydrofurfuryl acrylate, isobornyl acrylate, methyl methacrylate, cyclohexyl methacrylate or ethyl methacrylate, hydroxyalkyl acrylates such as 2-hydroxyethyl acrylate, etheralkyl acrylates such as 2-methoxyethyl acrylate, alkoxy- or aryloxy-poly(alkylene glycol) acrylates such as methoxypoly(ethylene glycol)acrylates, ethoxypoly(ethylene glycol)acrylates, polyethylene glycol diacrylate, methoxypoly(propylene glycol)acrylates, methoxypoly(ethylene glycol)-poly(propylene glycol)acrylates or their mixtures, aminoalkyl acrylates such as 2-(dimethylamino)ethyl acrylate (DMAEA), fluoro acrylates, silyl acrylates, phosphorus acrylates such as alkylene glycol phosphate acrylates, methacrylic monomers such as methacrylic acid or its salts, alkyl, cycloalkyl, alkenyl or aryl methacrylates, such as methyl methacrylate (MMA), lauryl methacrylate, cyclohexyl methacrylate, allyl methacrylate, phenyl methacrylate or naphthyl methacrylate, hydroxyalkyl methacrylates such as 2-hydroxyethyl methacrylate or 2-hydroxypropyl methacrylate, etheralkyl methacrylates such as 2-ethoxyethyl methacrylate, alkoxy- or aryloxy-poly(alkylene glycol) methacrylates such as methoxypoly(ethylene glycol)methacrylates,

ethoxypoly(ethylene glycol)methacrylates, methoxypoly(propylene glycol)methacrylates, methoxypoly(ethylene glycol)-poly(propylene glycol)methacrylates or their mixtures, aminoalkyl methacrylates such as 2-(dimethylamino)ethyl methacrylate (DMAEMA), fluoro methacrylates such as 2,2,2-trifluoroethyl methacrylate, silyl methacrylates such as 3-methacryloylpropyltrimethylsilane, and phosphorus methacrylates such as alkylene glycol phosphate methacrylates, hydroxyethylimidazolidone methacrylate, hydroxyethylimidazolidinone methacrylate, or 2-(2-oxo-1-imidazolidinyl)ethyl methacrylate.

[0169] Silicone acrylates may also be used. Further exemplary polymerizable moieties include acrylonitrile, acrylamide, methacrylamide, N-substituted (meth)acrylamides, vinyl esters such as vinyl acetate, vinyl ethers such as isobutyl vinyl ether, styrene, alkyl- and halostyrenes, N-vinylpyrrolidone, vinyl chloride or vinylidene chloride. Further exemplary polymerizable moieties include: vinylaromatic monomers such as styrene or substituted styrenes, (e.g., alpha-methylstyrene), acrylonitrile, acrylamide or substituted acrylamides, 4-acryloylmorpholine, N-methylolacrylamide, methacrylamide or substituted methacrylamides, trimethylolpropane triacrylate (TPT), acryloyl chloride, N-methylolmethacrylamide, methacrylamidopropyltrimethyl ammonium chloride (MAPTAC), itaconic acid, maleic acid or its salts, maleic anhydride, alkyl or alkoxy- or aryloxy-poly (alkylene glycol) maleates or hemimaleates, vinyl alcohols, vinylpyridine, vinylpyrrolidinone, (alkoxy) poly(alkylene glycol)vinyl ether or divinyl ether, such as methoxy poly(ethylene glycol)vinyl ether, poly(ethylene glycol)divinyl ether, olefin monomers, among which mention may be made of ethylene, butene, hexene and 1-octene and also fluoro olefin monomers, and vinylidene monomers, among which mention may be made of vinylidene fluoride, these monomers being used alone or as a mixture of at least two aforesaid monomers.

[0170] Examples of polymerizable monomers containing two or more double bonds are the diacrylates of ethylene glycol, propylene glycol, neopentyl glycol, hexamethylene glycol or of bisphenol A, and 4,4'-bis(2-acryloyloxyethoxy)diphenylpropane, trimethylolpropane triacrylate, pentaerythritol triacrylate or tetraacrylate, vinyl acrylate, divinylbenzene, divinyl succinate, diallyl phthalate, triallyl phosphate, triallyl isocyanurate or tris(2-acryloylethyl) isocyanurate.

[0171] Examples of polyunsaturated compounds of relatively high molecular mass (polymerizable oligomers) are acrylated epoxy resins, polyesters containing acrylate-, vinyl ether- or epoxy-groups, and also polyurethanes and polyethers. Further examples of unsaturated polymerizable oligomers are unsaturated polyester resins, which are usually prepared from maleic acid, phthalic acid and one or more diols and have molecular weights of from about 500 to 3000. In addition, vinyl ether monomers and oligomers may be used, and also maleate-terminated oligomers with polyester, polyurethane, polyether, polyvinyl ether and epoxy main chains. In some embodiments, copolymers of vinyl ether and maleic acid-functionalized monomers are also suitable.

[0172] Examples are esters of ethylenically unsaturated carboxylic acids and polyols or polyepoxides, and polymers having ethylenically unsaturated groups in the chain or in side groups, for example unsaturated polyesters, polyamides and polyurethanes and copolymers thereof, polymers and copolymers containing (meth)acrylic groups in side chains, and also mixtures of one or more such polymers.

[0173] Examples of unsaturated carboxylic acids are acrylic acid, methacrylic acid, crotonic acid, itaconic acid, cinnamic acid, and unsaturated fatty acids such as linolenic acid or oleic acid. Acrylic and methacrylic acid are preferred.

[0174] In some embodiments, the polyols are aromatic, aliphatic or cycloaliphatic polyols. Examples of aromatic polyols are hydroquinone,

4,4'-dihydroxydiphenyl, 2,2-di(4-hydroxyphenyl)propane, and also novolaks and resols. Examples of polyepoxides are those based on the abovementioned polyols, e.g., the aromatic polyols, and epichlorohydrin. Other suitable polyols are polymers and copolymers containing hydroxyl groups in the polymer chain or in side groups, examples being polyvinyl alcohol and copolymers thereof, or polyhydroxyalkyl methacrylates or copolymers thereof. Further polyols which are suitable are oligoesters having hydroxyl end groups.

[0175] Examples of aliphatic and cycloaliphatic polyols are alkylenediols having e.g., 2 to 12 C atoms, such as ethylene glycol, 1,2- or 1,3-propanediol, 1,2-, 1,3- or 1,4-butanediol, pentanediol, hexanediol, octanediol, dodecanediol, diethylene glycol, triethylene glycol, polyethylene glycols having molecular weights of preferably from 200 to 1500, 1,3-cyclopentanediol, 1,2-, 1,3- or 1,4-cyclohexanediol, 1,4-dihydroxymethylcyclohexane, glycerol, tris(beta-hydroxyethyl)amine, trimethylolethane, trimethylolpropane, pentaerythritol, dipentaerythritol and sorbitol. The polyols may be partially or completely esterified with one carboxylic acid or with different unsaturated carboxylic acids, and in partial esters the free hydroxyl groups may be modified, for example etherified or esterified with other carboxylic acids.

[0176] Examples of esters are: trimethylolpropane triacrylate, trimethylolethane triacrylate, trimethylolpropane trimethacrylate, trimethylolethane trimethacrylate, tetramethylene glycol dimethacrylate, triethylene glycol dimethacrylate, tetraethylene glycol diacrylate, pentaerythritol diacrylate, pentaerythritol triacrylate, pentaerythritol tetraacrylate, dipentaerythritol diacrylate, dipentaerythritol triacrylate, dipentaerythritol tetraacrylate, dipentaerythritol pentaacrylate, dipentaerythritol hexaacrylate, tripentaerythritol octaacrylate, pentaerythritol dimethacrylate, pentaerythritol trimethacrylate, dipentaerythritol dimethacrylate, dipentaerythritol tetramethacrylate, tripentaerythritol octamethacrylate, pentaerythritol diitaconate, dipentaerythritol tris-itaconate, dipentaerythritol pentaitaconate, dipentaerythritol hexaitaconate, ethylene glycol diacrylate, 1,3-butanediol diacrylate, 1,3-butanediol dimethacrylate, 1,4-butanediol diitaconate, sorbitol triacrylate, sorbitol tetraacrylate, pentaerythritol-modified triacrylate, sorbitol tetra methacrylate, sorbitol pentaacrylate, sorbitol hexaacrylate, oligoester acrylates and methacrylates, glycerol diacrylate and triacrylate, 1,4-cyclohexane diacrylate, bisacrylates and bismethacrylates of polyethylene glycol with a molecular weight of from 200 to 1500, or mixtures thereof.

[0177] Also suitable as polymerizable moieties are the amides of identical or different, unsaturated carboxylic acids with aromatic, cycloaliphatic and aliphatic polyamines having preferably 2 to 6, especially 2 to 4, amino groups. Examples of such polyamines are ethylenediamine, 1,2- or 1,3-propylenediamine, 1,2-, 1,3- or 1,4-butylenediamine, 1,5-pentylenediamine, 1,6-hexylenediamine, octylenediamine, dodecylenediamine, 1,4-diaminocyclohexane, isophoronediamine, phenylenediamine, bisphenylenediamine, di-beta-aminoethyl ether, diethylenetriamine, triethylenetetramine, di(beta-aminoethoxy)- or di(beta-aminopropoxy)ethane. Other suitable polyamines are polymers and copolymers, e.g., with additional amino groups in the side chain, and oligoamides having amino end groups. Examples of such unsaturated amides are methylenebisacrylamide, 1,6-hexamethylenebisacrylamide, diethylenetriaminetrismethacrylamide, bis(methacrylamidopropoxy)ethane, beta-methacrylamidoethyl methacrylate and N-[(beta-hydroxyethoxy)ethyl]acrylamide.

[0178] Suitable unsaturated polyesters and polyamides are derived, for example, from maleic acid and from diols or diamines. Some of the maleic acid can be replaced by other dicarboxylic acids. They can be used together with ethylenically unsaturated comonomers, for example styrene. The polyesters and polyamides may also be derived from dicarboxylic acids and from ethylenically unsaturated diols or diamines, e.g., from those with relatively long chains of, for example 6 to 20 C atoms. Examples of polyurethanes are those composed of saturated or unsaturated diisocyanates and of unsaturated or, respectively, saturated diols.

[0179] Polymers with (meth)acrylate groups in the side chain may also be used. They may, for example, be reaction products of epoxy resins based on novolaks with (meth)acrylic acid, or may be homo- or copolymers of vinyl alcohol or hydroxyalkyl derivatives thereof which are esterified with (meth)acrylic acid, or may be homo- and copolymers of (meth)acrylates which are esterified with hydroxyalkyl (meth)acrylates.

[0180] Other suitable polymers with acrylate or methacrylate groups in the side chains are, for example, solvent soluble or alkaline soluble polyimide precursors, for example poly(amic acid ester) compounds, having the photopolymerizable side groups either attached to the backbone or to the ester groups in the molecule.

[0181] In some embodiments, the methods of interest convert the prepolymer to a modified polymer. In some embodiments, the modified polymer is a crosslinked composition. In other embodiments, the modified polymer is not crosslinked but has a molecular weight higher than the prepolymer. The methods of interest may convert the prepolymer to the modified polymer in a single polymerization reaction, or the conversion may occur over the course of several polymerization reactions.

[0182] In some embodiments, the prepolymer includes a crosslinkable monomer or oligomer and an optional crosslinking moiety (e.g., a photocrosslinker). In some embodiments, the crosslinkable monomer or oligomer is selected from acrylates, methacrylates, vinyl alcohols, polyacrylates, polymethacrylates, vinyl polymers, polyalkylene oxides, polysiloxanes, polyvinylpyrroles, polyamino acids, polysaccharides, and polynucleic acids, as well as copolymers thereof. Such crosslinkable monomers and oligomers may be substituted or unsubstituted. Some specific exemplary crosslinkable monomer or oligomers include polymethyl methacrylate (PMMA), polyvinyl alcohol (PVA), polydimethyl siloxane.

Matrix Material

[0183] The compositions of interest contain a matrix material. In some embodiments, the matrix material is a composition containing one or more components and performing one or more functions. For example, components of the matrix material include one or more of matrix polymers, colorants, anti-reflection compounds, biocompatibility-enhancing agents, anti-bacterial agents, and the like.

[0184] The matrix material serves one or more functional roles. In some embodiments, for example, the matrix material serves as a structural material, and may be either flexible or rigid. In some embodiments, prior to polymerization of the prepolymer (discussed herein), the matrix material imparts structural form and stability to the compositions of interest. The matrix material may also serve as a carrier for other components (e.g. the masking component, prepolymer, additives, etc.).

[0185] In some embodiments, the matrix material is a polymer. Example classes of suitable polymer matrix materials include polyacrylates, polymethacrylates, vinyl polymers, polyalkylene oxides, polysiloxanes, polyvinylpyrroles, polyamino acids, polysaccharides, and polynucleic acids, as well as copolymers thereof. Such polymers may be substituted or unsubstituted. Some specific example matrix polymers include polymethyl methacrylate (PMMA), polyvinyl alcohol (PVA), and polydimethyl siloxane.

[0186] Many colorants, anti-reflection compounds, biocompatibility-enhancing agents, anti-bacterial agents, etc. are known and are suitable to be included in the matrix material, and may be incorporated according to the desired application.

[0187] In some embodiments, the matrix material comprises a polymeric material, and the masking compound is chemically incorporated (e.g., via polymerization through a vinyl group attached to the masking compound) into the polymeric material.

Lenses

[0188] Aspects of the disclosure include adjustable lenses. Any of the subject compositions described above may be used in preparing the subject lenses. By adjustable is meant that one or more properties of the lens (e.g., an optical property such as refractive index, or a physical property such as thickness, rigidity, or the like) may be changed or modified in a controlled fashion, e.g., by practicing the subject methods described herein. In some embodiments, the subject lenses are modified in a location specific manner by controlling the exposure of different portions of the lens to electromagnetic energy (e.g., via masking or light directing optics).

[0189] In some embodiments, the subject adjustable lens is an intraocular implant. In some embodiments, the subject lens includes a masking compound and a prepolymer. The masking compound is capable of photoisomerization between a first isomer and a second isomer upon absorption of electromagnetic energy at a first wavelength and intensity (e.g., a triggering condition). The prepolymer is capable of polymerization or crosslinking upon photoinitiation with electromagnetic energy at a second wavelength and intensity (e.g., a polymerization or crosslinking condition).

[0190] In some embodiments, one or more properties (e.g., optical power, refractive index, volume, thickness, etc.) of the subject lenses may be adjusted (e.g., increased or decreased) using the subject methods described herein. In some embodiments, polymerization or crosslinking of the prepolymer in a lens composition can be performed to produce a change in the volume of the lens. For example, the portion of the subject lens that is exposed to a photoinitiating electromagnetic energy to induce polymerization or crosslinking may change the volume of the exposed lens composition. In some embodiments, polymerization or crosslinking in the exposed portion of the lens leads to an increase in volume or a change in composition that causes a decrease in the refractive index. In some embodiments, polymerization or crosslinking in the exposed portion of the lens leads to a decrease in volume or a change in composition that causes an increase in the refractive index. The effects of crosslinking and polymerization on the optical properties of the subject lenses may be determined using any convenient methods, such as the Lorentz-Lorenz equation, which expresses the refractive index in terms of a molar refractivity and molar volume.

[0191] In some embodiments, the subject lens composition does not contain free polymerizable monomer, and upon exposure to ultraviolet radiation, crosslinking occurs between polymers in the exposed portion of the lens.

[0192] In some embodiments, polymerization or crosslinking of the prepolymer in a lens composition can be performed to produce a refractive index change in the lens that was controllable, reproducible, and adjustable.

[0193] As described herein, the masking compound is capable of blocking polymerization or crosslinking of the prepolymer, until photoisomerization of the compound is triggered, and the masking compound is converted from a first isomer to a second isomer having a different absorption profile. In some embodiments, the first isomer of the masking compound absorbs more light at the second wavelength than the second isomer of the masking compound. In such cases, the first isomer of the masking compound can block polymerization of the prepolymer by absorbing ambient sunlight at wavelengths that induce polymerization or crosslinking (e.g., the second wavelength). The absorption maximum of

the second isomer of the masking compound may be sufficiently shifted from that of the first isomer such that the prepolymer is no longer masked (e.g., prevented from undergoing a photoinitiated modifying reaction).

[0194] In some embodiments, the subject lens further includes a matrix material. Any convenient matrix material may be used to provide structure to the subject lenses. In general, the matrix materials of the subject lenses may fall into the following categories: hydrogels; silicones, and non-hydrogel acrylics. In some embodiments, the matrix material of the subject lens is a polymer selected from a polyacrylate, a polymethacrylate and a polysiloxane. In some embodiments, the subject lens includes soft, foldable materials, which are easier to insert into the eye through a small incision in the eye.

Methods

[0195] Aspects of the disclosure include methods of implanting and modifying the subject compositions and lenses.

[0196] In some embodiments, the method is a method for implanting and modifying an intraocular implant, such as a lens. In some embodiments, the subject method includes inserting the intraocular implant into the eye of a patient, allowing the eye to heal for a period of time, applying a triggering step, and applying a polymerization step. In some embodiments, the triggering step includes application of electromagnetic energy of a first wavelength and intensity to the intraocular implant to cause photoisomerization of the masking compound. In some embodiments, polymerization step includes application of electromagnetic energy of a second wavelength and intensity to the intraocular implant to cause polymerization of a prepolymer.

[0197] In some embodiments, the first wavelength is between about 1 and about 800 nm, such as, between about 200 and about 800 nm, between about 250 and about 600 nm, between about 300 and about 500 nm, between about 300 and about 400 nm, between about 340 and about 365 nm (e.g., about 365 nm), or between about 340 and about 350 nm. For example, the first wavelength is less than 800 nm, or less than 600 nm, or less than 400 nm, or less than 365 nm. Also for example, the first wavelength is greater than 1 nm, or greater than 200 nm, or greater than 250 nm, or greater than 300 nm, or greater than 340 nm. In some embodiments, the second wavelength is between about 1 and about 800 nm, such as, between about 200 and about 800 nm, between about 300 and about 650 nm, between about 300 and about 500 nm, between about 300 and about 400 nm, between about 340 and about 370 nm (e.g., about 365 nm), or between about 340 and about 350 nm. For example, the second wavelength is less than 800 nm, or less than 600 nm, or less than 400 nm, or less than 365 nm. Also for example, the second wavelength is greater than 1 nm, or greater than 200 nm, or greater than 250 nm, or greater than 300 nm, or greater than 340 nm. In some embodiments, the first wavelength is about 340 to about 365 nm (e.g., about 350 nm), and the second wavelength is about 365 nm to about 400 nm. In some embodiments, the first and second wavelengths are the same or substantially overlapping ranges. In some embodiments, the first and second wavelengths are applied concurrently from the same light source.

[0198] In some embodiments, the application of a triggering and/or polymerization condition may be using a monochromatic source, such as filtered light, diffraction grating separated light or laser light. In some embodiments, the triggering and polymerization conditions are selected such the eye of the subject is not exposed to damaging high energy UV light. In some embodiments, the triggering and polymerization conditions are applied concurrently by application of light from the same light source.

[0199] In some embodiments, the method further includes waiting for a period of time sufficient to allow the masking compound to isomerize from the second isomer to the first isomer (e.g., reversible photoisomerization); and repeating the triggering step and the polymerization step. By period of time sufficient to allow the masking compound to isomerize from the second isomer to the first isomer is meant a period of time of about 1 minute or more, such as about 2 minutes or more, about 5 minutes or more, about 10 minutes or more, about 15 minutes or more, about 20 minutes or more, about 30 minutes or more, about 60 minutes or more, about 2 hours or more, about 3 hours or more, about 4 hours or more, about 5 hours or more, about 6 hours or more, about 12 hours or more, about 1 day or more, or even more. In some embodiments, the triggering and polymerization steps may be repeated multiple times, such as 2 times or more, 3 times or more, 4 times or more, 5 times or more, or even more.

[0200] In some embodiments, the method further includes determining the optical power of the lens and the eye of the subject and selecting the polymerization condition to produce a desirable change in the optical power of the implanted lens.

[0201] Aspects of the disclosure include methods of preparing the subject compositions and lenses. In some embodiments, the subject lens preparation method includes combining a matrix material, a masking compound, and a prepolymer.

Utility

[0202] The subject compositions and lenses described herein find use in a variety of applications, including but not limited to, ophthalmic devices and intraocular lenses for corrective eye surgery applications, materials applications such as color-changing materials (e.g., sunglasses, safety glasses, etc.), onlays, piggyback lenses and contact lenses. In some embodiments, the subject lenses of are used as intraocular implants, such as lenses that are used to treat vision disorders such as, myopia (nearsightedness), hyperopia (e.g., farsightedness, longsightedness or hypermetropia) and astigmatism. In some embodiments, the subject lenses may be used to treat cataracts, such as senile, morgagnian, secondary, traumatic or congenital cataracts.

[0203] Intraocular lenses can be inserted into various locations of the eye and used to supplement or correct the vision provided by the natural crystalline lens of the eye or can replace the natural crystalline lens of the eye. Lenses that supplement or correct the vision without replacing the natural crystalline lens are typically referred to as Phakic Lenses while lenses that replace the natural crystalline lens are typically referred to as Aphakic lenses. Phakic lenses can be located within the anterior chamber (AC) of the eye (AC Phakic lenses) or the posterior chamber (PC) of the eye (PC Phakic Lenses).

[0204] In some embodiments, the subject compositions find use in materials applications, e.g., applications where controlled modification of a material on demand is desired, such as but not limited to, optical coatings, transparent materials, electronic applications, inks, and the like. In such materials, polymerization of a prepolymer of the subject composition can be controlled on demand, as described herein, to produce a modified material. For example, the subject composition is stable to ambient condition (e.g., sunlight) until subjected to a triggering condition. In some embodiments, the modified material has a desirable property over the starting composition (e.g., an optical property, increased thickness or increased strength). In some embodiments, the subject compositions find use as color-changing materials, such as in sunglasses or lab safety glasses that may block a range of wavelengths of light. For example, in such applications, the subject compositions may provide a large color change upon application of light, that could be used as an indicator of how much light of selected wavelengths and intensities is applied.

EXAMPLES

Example 1

[0205] Solutions of MA, 1,4-butanediol diacrylate (BDDA), IC-651, and trans-azobenzene (t-AB) were prepared with varying ratios of IC-651 (2,2-dimethoxy-1,2-diphenylethane-1-one, Irgacure 651, Ciba Specialty Chemicals) and t-AB. The solutions were exposed to ambient sunlight to determine the time required for a crosslinked gel to form. For solutions having specific ratios of IC-651 and t-AB, no gel formation was observed after 14 days of exposure to sunlight. In these systems, sufficient amounts of t-AB were present such that the majority of the incident light was absorbed by the t-AB and the IC-651 was not able to initiate. Although absorption of sunlight may have caused some photoisomerization of the AB chromophores, thermal relaxation of the c-AB back to the t-AB maintained an equilibrium amount of these species in solution. To initiate polymerization, the solutions were irradiated using 350 nm light which effectively isomerized enough t-AB to cis-azobenzene (c-AB) and shifted the absorption maxima away from that of the IC-651, ultimately resulting in activation of the photoinitiator and polymerization of the MA/BDDA solution.

[0206] Example Type A: Photoinitiated polymerization of a liquid solution of methyl acrylate (MA) using Irgacure 651 (IC-651) as a photoinitiator was performed "on-demand" by using a photoisomerizable azobenzene (AB) UV-Vis absorber that allowed photoinitiation to occur only upon exposure to a specific light source. The absorbing AB dye inhibited photoinitiation in ambient sunlight for several days. Triggering photoinitiated polymerization was achieved by irradiation of solutions containing MA, AB, and IC-651 with 350 nm light which first isomerized trans-AB (t-AB) chromophores to cis-isomers (c-AB), significantly reducing the UV absorption overlap between this species and the IC-651. Thus, the photoisomerization and subsequent photoinitiated polymerization were performed under controlled conditions and premature initiation due to ambient light was avoided.

##STR00016##

[0207] Solutions of MA, 1,4-butanediol diacrylate (BDDA), IC-651, and t-AB were prepared with varying ratios of IC-651 and t-AB. The solutions were exposed to ambient sunlight to determine the time required for a crosslinked gel to form. For solutions having specific ratios of IC-651 and t-AB, no gel formation was observed after 14 days of exposure to sunlight. In these systems, sufficient amounts of t-AB were present such that the majority of the incident light was absorbed by the t-AB and the IC-651 was not able to initiate. Although absorption of sunlight may have caused some photoisomerization of the AB chromophores, thermal relaxation of the c-AB back to the t-AB presumably maintained an equilibrium amount of these species in solution. To initiate polymerization, the solutions were irradiated using 350 nm light which effectively isomerized enough t-AB to c-AB and shifted the absorption maxima away from that of the IC-651, ultimately resulting in activation of the photoinitiator and polymerization of the MA/BDDA solution.

[0208] Experimental: Methyl acrylate and 1,4-butanediol diacrylate were each filtered through a column of activated alumina prior to use. A Pyrex vial was charged with methyl acrylate and 1,4-butanediol diacrylate. Azobenzene was added, followed by IC-651. The solution was divided into two separate Pyrex vials and each was sealed with a Teflon-lined screw cap. One vial was placed in direct sunlight and the other used for irradiation in a Luzchem photoreactor.

Example 2

[0209] Example Type B: A series of polysiloxane slabs were prepared that contained the aforementioned AB and IC-651 so that the photoinitiation would again be controllable "on-demand" upon exposure to a specified light source. The slabs also included Silicon MED 6820, Pt-divinyltetramethyldisiloxane complex, methacrylate-terminated telechelic dimethylsiloxane-co-diphenylsiloxane polymer having M.sub.n of 7-10 kDa. The materials were combined as described below, degassed, and poured into stainless steel molds. The molded mixtures were then held in a Carver press at 1000 psi and 37.degree. C. for 24-48 h. The slabs were then irradiated using laser light, while control slabs were exposed only to sunlight for a period of several days. Overall, certain compositions were found to withstand sunlight without signs of photoinitiated polymerization, whereas rapid photoinitiation was observed upon irradiation with 365 nm laser light even at relatively low power intensities.

[0210] Experimental: A mixture of Silicon MED 6820, Pt-divinyltetramethyldisiloxane complex, methacrylate-terminated telechelic dimethylsiloxane-co-diphenylsiloxane polymer having M.sub.n of 7-10 kDa, azobenzene, and Irgacure 651 was degassed, then poured into stainless steel molds measuring 1.times.1.times.0.1 cm and again degassed. The molds were then placed into a Carver press at 1000 psi and 37.degree. C. for 24 h. Slabs were then irradiated as described above, while duplicate slabs were placed in direct sunlight for comparison.

[0211] "On-demand" photoinitiated polymerization was demonstrated by the use of mixtures containing IC-651 as a photoinitiator for MA and containing BDDA as a crosslinking agent. Solutions of MA containing IC-651 (0.1 wt %) polymerized within minutes upon exposure to sunlight. Lower loadings of IC-651 failed to give complete polymerization, and samples prepared under either N.sub.2 or ambient atmosphere performed similarly. Addition of t-AB was found to significantly delay the gel time depending upon the relative amount of t-AB present; key data are summarized in Table 1. Very low loading of t-AB did not impede the initiation significantly (entry 1), and gel formation occurred in less than 24 h when exposed to sunlight. The amount of t-AB relative to IC-651 was gradually increased until solutions could withstand multiple days in direct sunlight without undergoing polymerization.

[0212] Once resistance to sunlight had been established, polymerization was initiated by photoisomerization of the t-AB and activation of the IC-651 using a photoreactor. The samples were prepared in Pyrex vials and irradiated in a Luzchem LZC-ORG photoreactor equipped with 10 LZC-UVA bulbs (output wavelength centered at 350 nm). Samples with low loadings of t-AB polymerized within a few hours of exposure (entries 1-4), whereas those with at least a 100:1 ratio of t-AB to IC-651 failed to polymerize after 10 h of irradiation. An exemplary working condition included 0.1 wt % loading of IC-651 with 1.0 wt % loading of t-AB (entry 4). This sample withstood polymerization in sunlight for greater than 14 days, but was readily polymerized within 3 h upon exposure to 350 nm light in the photoreactor.

TABLE-US-00001 TABLE 1 Gel times required for samples exposed to sunlight or 350 nm light..^{sup.1} Loading (wt %).^{sup.2} Gel Times.^{sup.3}

Entry	AB	IC-651	Ambient (d)	Irradiated (h)
1	0.001	0.1	<1	<1
2	0.01	0.1	3	<1
3	0.1	0.1	10	1
4	1.0	0.1	>14	3
5	10	0.1	>14	5
6	10	0.1	>14	10
7	30	0.1	>14	>10

^{sup.1}Reactions were conducted in Pyrex vials sealed under ambient atmosphere using methyl acrylate and 1,4-butanediol diacrylate each filtered through activated alumina gel prior to use. ^{sup.2}Solutions were prepared using methyl acrylate containing 5 wt % of 1,4-butanediol diacrylate and the indicated amounts of AB and IC-651. ^{sup.3}Solutions monitored under ambient light were placed outdoors in direct sunlight.

[0213] Slabs were next investigated as model systems for light-adjustable lenses. The slabs were irradiated at 365 nm using a 5.6 mm beam and an

average irradiance of 12 mW/cm² (2.96 mW output power). Each slab was irradiated in four different locations with exposure times ranging from 30-120 s. Identical slabs were also placed outdoors for exposure to sunlight. All slabs were examined using interferometry to determine if photoinitiated polymerization and crosslinking had taken place. Slabs containing the AB molecules resisted polymerization in sunlight for several days. Irradiation using the 365 nm light source resulted in isomerization of the AB as described above and allowed photoinitiation and polymerization to occur. In this way, using low power densities for the controlled irradiation was successful in slabs that fully resisted polymerization in sunlight.

Example 3

Masking Compound Synthesis

[0214] The azobenzene compounds 1-5 and the triazine 6 (see structures below) were synthesized using standard synthetic methods. Compounds 1-5 were prepared to include dialkenes to facilitate the inclusion of the compound into a lens matrix upon polymerization. The synthetic methods are used to prepare azobenzene compounds that include both electron-donating and electron-withdrawing groups, in order to tune the spectral properties of the compounds.

##STR00017##

[0215] UV-Vis Spectroscopy

[0216] Compound 5 was characterized using UV-vis spectroscopy, using the solutions of the dilution series shown in Table 2 below, and found to have $\lambda_{\text{max}}=339$ nm and $\epsilon=29114$ M⁻¹ cm⁻¹. See FIG. 2 for absorption spectra.

TABLE-US-00002 TABLE 2 Stock Solution (1) [Azo] (M) DCM [Azo] (M) 448 nm 339 nm 235 nm A 0.0001 1.00E-04 0.0009 0.00001 0.018 0.443 0.492 B 0.0002 1.00E-04 0.0009 1.81818E-05 0.048 0.693 0.774 C 0.0003 1.00E-04 0.0009 0.000025 0.057 0.889 0.972 D 0.0004 1.00E-04 0.0009 3.07692E-05 0.064 1.048 1.069 E 0.0005 1.00E-04 0.0009 3.57143E-05 0.071 1.196 1.186

[0217] Ambient Condition and Lab Testing

[0218] The compounds were evaluated by inclusion of the compounds into cross-linked poly(dimethylsiloxane) (PDMS) slabs at 0.2% by weight. The slabs also included a macromonomer, Irgacure 651 photoinitiator and Pt catalyst for hydrosilylation. The slabs were then exposed to sunlight for 24 hours, and evaluated colorimetrically.

[0219] The slab containing compound 5 was subjected to 365 nm light in a concentric circle pattern for up to 10 minutes. Visual inspection of the slab (see FIG. 3) showed a dark coloration corresponding to the locations of the concentric circle pattern from application of 365 nm light. The image in FIG. 3, clearly shows the largest circle, and upon close inspection, shows further adjacent circle features corresponding to the pattern. The compound 5 containing slabs showed decreased initiation of the Irgacure compared to control slabs without the masking compound.

[0220] Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it is readily apparent to those of ordinary skill in the art in light of the teachings of this invention that certain changes and modifications may be made thereto without departing from the spirit or scope of the appended claims.

[0221] Accordingly, the preceding merely illustrates the principles of the invention. It will be appreciated that those skilled in the art will be able to devise various arrangements which, although not explicitly described or shown herein, embody the principles of the invention and are included within its spirit and scope. Furthermore, all examples and conditional language recited herein are principally intended to aid the reader in understanding the principles of the invention and the concepts contributed by the inventors to furthering the art, and are to be construed as being without limitation to such specifically recited examples and conditions. Moreover, all statements herein reciting principles, aspects, and embodiments of the invention as well as specific examples thereof, are intended to encompass both structural and functional equivalents thereof. Additionally, it is intended that such equivalents include both currently known equivalents and equivalents developed in the future, i.e., any elements developed that perform the same function, regardless of structure. The scope of the present invention, therefore, is not intended to be limited to the exemplary embodiments shown and described herein. Rather, the scope and spirit of present invention is embodied by the appended claims.

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A Direct Route to Cyclic Organic Nanostructures via Ring-Expansion Metathesis Polymerization of a Dendronized Macromonomer

Andrew J. Boydston^a, Thomas W. Holcombe^b, David A. Unruh^b, Jean M. J. Fréchet^{b,*}, and Robert H. Grubbs^{a,*}

^aArnold and Mabel Beckman Laboratory of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA 91125

^bCollege of Chemistry, University of California, Berkeley, CA 94720

Controlling polymer topology presents challenging synthetic obstacles as well as exciting opportunities for tuning macromolecular properties.¹ In particular, nanoscale molecular architectures with well-defined shapes and dimensions may provide significant advancements in areas such as drug delivery and nanotechnology. Over the last decade, breakthroughs in polymer syntheses have greatly increased the variety of macromolecular architectures that may be obtained, including dendronized, cylindrical, star, hyperbranched, and cyclic polymers as well as various block copolymers.^{2,3} However, the synthesis of circular nanostructures remains challenging due in large part to the difficulty in preparing functionalized cyclic polymers.⁴ Furthermore, reliance on macrocyclization routes to cyclic polymers restricts attachment of large side chains or dendrons to post-polymerization, and an efficient route to cyclic hybrid architectures of high purity is yet to be realized. Following recent developments in ring-expansion metathesis polymerization (REMP)⁵ and linear dendronized polymers,⁶ we aimed to interface these two areas to achieve a direct, efficient route to cyclic organic nanostructures.⁷ Herein, we report the REMP of a dendronized macromonomer (MM) as well as confirmation of cyclic polymer topology via atomic force microscopy (AFM).

REMP utilizes Ru-based metathesis catalysts (Figure 1) capable of producing cyclic polymers directly from cyclic olefin monomers, thus avoiding linear polymeric synthons. Earlier studies revealed that N-heterocyclic carbene backbone saturation greatly increased overall catalyst activity, while tether length influenced the relative rates of propagation vs catalyst release. With access to a range of catalyst activities, we envisioned that REMP of dendronized MMs may achieve dendronized cyclic polymers in a single operation. In addition, REMP can produce high molecular weight (MW) cyclic polymers, a goal not easily accomplished using macrocyclization processes.

While the polymerization of sterically hindered MMs presents an inherent challenge, it was shown that **1** (Figure 1) could be efficiently polymerized via ROMP using a highly active Ru-based metathesis catalyst. This approach to dendritic polymers is particularly attractive, in that post-polymerization modifications are unnecessary, ensuring that complete dendron functionality is present along the polymer backbone.^{2c} Thus, we examined the efficiency of REMP using **1** in combination with cyclic catalysts **SC-5** and **UC-6**.

rhg@caltech.edu and frechet@berkeley.edu.

Supporting Information Available Detailed experimental procedures and AFM images of **P1_{son}**. This materials is available free of charge via the Internet at <http://pubs.acs.org>

Saturated catalyst **SC-5** was found to mediate REMP of **1** and key data are summarized in Table 1. In general, polymerizations required higher temperatures (55 °C) and higher loadings of $[1]_0/[SC-5]_0$ than used in previous studies involving cyclooctene monomers, which is ascribed to the steric bulk of MM **1**. Interestingly, an inverse relationship between reaction concentration and degree of polymerization (DP) of polymer **P1** was observed. Specifically, REMP of **1** ($[1]_0/[SC-5]_0 = 50:1$) at $[1]_0 = 0.05, 0.10, 0.20$, and 0.33 M resulted in polymers having DPs of 5840, 4510, 4330, and 2190, respectively (entries 1, 2, 5, and 6). Since each polymerization reached full monomer conversion, this trend suggests that the initiation rate increases more with increased reaction concentration than does the propagation rate. Additionally, because incomplete initiation is observed with catalyst **SC-5**, the increased reaction concentration essentially led to a greater number of growing polymer rings and therefore a lower average MW.

Increasing the $[1]_0/[SC-5]_0$ resulted in incomplete monomer conversion due to catalyst death over the extended reaction periods. However, as expected, increased $[1]_0/[SC-5]_0$ ratios resulted in higher M_w values. Specifically, using $[1]_0/[SC-5]_0 = 100:1$ polymer **P1** with $M_w = 4.47$ MDa (entry 3) was obtained, whereas $M_w = 5.33$ MDa was obtained with $[1]_0/[SC-5]_0$ (entry 4). Notably, catalyst **UC-6** efficiently polymerized **1** to >95% conversion at $[1]_0/[UC-6]_0 = 250:1$. These conditions provided **P1** with a $M_w = 3.79$ MDa (entry 7).

Catalyst release and reincorporation have been shown to guide the thermodynamically driven MW of REMP polymers. In the present case, catalyst reincorporation and chain transfer are unlikely considering the steric bulk of MM **1**. Notably, the MW of **P1** did not change upon prolonged standing after 100% monomer conversion, or upon injection of fresh catalyst into the reaction mixtures. This indicates that thermodynamic equilibration of ring sizes is not taking place. Furthermore, the MW of isolated **P1** did not increase upon treatment with additional **1**, suggesting that no significant amount of active Ru species remain in the cyclic polymer. Collectively the data suggests efficient, irreversible catalyst release, and an absence of chain transfer events. These experiments provide an initial investigation into the kinetically controlled MW profile of REMP.

We next turned our attention toward visualization of the polymers via AFM.⁸ Samples of **P1** were prepared by spin-coating a 9 ng/mL solution of the polymer in $CHCl_3$ onto freshly cleaved mica. As shown in Figure 2, toroidal features were observed with diameters of ca 35 - 40 nm, heights ranging from 5 - 9 Å, and internal diameters ranging from ca 5 - 7 nm. Multiple rings were observed (Figure 2A) without any detectable linear polymers, and analysis of the line scans of the toroids revealed highly uniform profile features (Figure 2D). Considering the high DP values obtained for **P1**, the dimensions observed via AFM suggested that the polymer backbone is not fully extended and may be adopting a zigzag orientation.

For comparison, we also examined linear analogues via AFM. Because the high DPs obtained via REMP were difficult to achieve using acyclic ROMP catalysts, we investigated ring-opening of **P1** via sonication. Given that polymer chain scission can be induced via ultrasound,⁹ and that the steric congestion may weaken the backbone of **P1**, we subjected a solution of cyclic polymer ($M_w = 2.99$ MDa, 1 mg/mL in THF) to ultrasound irradiation for 30 min to give **P1_{son}**. GPC analysis of **P1_{son}** revealed an $M_w = 959$ kDa, which suggests that chain scission accompanied ring-opening. In addition, **P1_{son}** displayed shorter elution times at the same MW in comparison with **P1**, consistent with linear and cyclic topologies, respectively (Figure 3).¹⁰ AFM imaging of **P1_{son}** revealed features consistent with a linear topology (see the Supporting Information). Notably, some features resembled those of the cyclic polymers in diameter and shape; however these did not appear toroidal as no central void was observed. This may be ascribed to aggregation, which is more commonly observed upon AFM imaging of the linear polymers in comparison with cyclic **P1**.

In conclusion, we have demonstrated the first direct synthesis of cyclic dendronized polymers via REMP of a dendronized macromonomer. AFM imaging has confirmed the cyclic topology, revealing uniform cyclic features with no detectable linear polymer contaminants. The kinetically controlled molecular weight profiles and relative initiation versus propagation rates of REMP resulted in polymer M_w values that increased with decreasing initial concentrations. Despite the steric challenges inherent to the polymerization of these dendronized monomers, very high molecular weights were achieved for this novel class of hybrid macromolecules.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Structures of the cyclic REMP catalysts and dendronized macromonomer used in this study.

Figure 2.
(A) AFM images of **P1** (Table 1, entry 7) on mica. (B) 3-D plot of toroidal feature. (C) Three toroids from image (A). (D) Line scans of toroids in image (C).

Figure 3. GPC data for **P1** (black) and **P1_{son}** (blue): normalized refractive index detector intensities (solid lines) and M_w values (dashed lines) vs retention times.

Table 1

REMP of **1** to give cyclic dendeonized polymer **P1**^a.

Entry	Catalyst	[1] ₀ (M)	[1] ₀ /[C] ₀	<i>M_w</i> (MDa) ^b	DP/1000	PDI ^b
1	SC-5	0.05	50	5.26	5.84	1.29
2	SC-5	0.10	50	4.06	4.51	1.25
3 ^c	SC-5	0.10	100	4.47	4.97	1.51
4 ^d	SC-5	0.10	200	5.33	5.92	1.49
5	SC-5	0.20	50	3.90	4.33	1.33
6	SC-5	0.33	50	1.97	2.19	1.17
7	UC-6	0.10	250	3.79	4.21	1.18

^aUnless noted otherwise, reactions were conducted under dry N₂ and monitored via ¹H NMR spectroscopy until conversions were >90%. [**1**]₀ = initial concentration of **1**; [**C**]₀ = initial catalyst concentration

^bMolecular weight data obtained via GPC with multiangle laser light scattering.

^cMaximum conversion = 60%.

^dMaximum conversion = 39%

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Cyclic Ruthenium-Alkylidene Catalysts for Ring-Expansion Metathesis Polymerization

Andrew J. Boydston, Yan Xia, Julia A. Kornfield, Irina A. Gorodetskaya, and Robert H. Grubbs*

Arnold and Mabel Beckman Laboratory of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125

Abstract

A series of cyclic Ru-alkylidene catalysts have been prepared and evaluated for their efficiency in ring-expansion metathesis polymerization (REMP). The catalyst structures feature chelating tethers extending from one N-atom of an imidazolylidene ligand to the Ru metal center. The catalyst design is modular in nature, which provided access to Ru-complexes having varying tether lengths, as well as electronically different NHC ligands. Structural impacts of the tether length were unveiled through ^1H NMR spectroscopy as well as single-crystal X-ray analyses. Catalyst activities were evaluated via polymerization of cyclooctene and key data are provided regarding propagation rates, intramolecular chain-transfer, and catalyst stabilities, three areas necessary for the efficient synthesis of cyclic poly(olefin)s via REMP. From these studies, it was determined that while increasing the tether length of the catalyst leads to enhanced rates of polymerization, shorter tethers were found to facilitate intramolecular chain-transfer and release of catalyst from the polymer. Electronic modification of the NHC via backbone saturation was found to enhance polymerization rates to a greater extent than did homologation of the tether. Overall, cyclic Ru-complexes bearing 5- or 6-carbon tethers and saturated NHC ligands were found to be readily synthesized, bench-stable, and highly active catalysts for REMP.

Keywords

cyclic polymers; metathesis; ring-opening polymerization; ruthenium

Introduction

The exploration of Ru-based metathesis catalysts has opened doorways to multiple areas of synthetic and polymer chemistry.^{1,2} Advances in these areas have been made possible via development of new catalyst scaffolds based upon bis(phosphine) complex **1** (Figure 1), or those bearing N-heterocyclic carbene (NHC) ligands such as **2** and **3**. The introduction of catalysts based on **1** – **3**, but predisposed for specific tasks, has further expanded the potential of olefin metathesis. For example, areas such as solid-supported catalysis,³ asymmetric olefin metathesis,⁴ tandem catalysis,⁵ living polymerization,^{1a,6} acyclic diene metathesis,⁷ and stereoselective cross-metathesis (CM) have each benefited from breakthroughs in catalyst design, development, and application.⁸

Recently, a Ru-based catalyst design was reported that featured a chelating N-to-Ru tether (Figure 2).⁹ Whereas the catalytic activities of **4_{cyc}** – **6_{cyc}** have not been explored, **7_{cyc}** was

found to mediate the synthesis of cyclic polymers from cyclic monomers (Scheme 1).^{10,11} This ring-*expansion* metathesis polymerization (REMP) afforded the ability to produce cyclic polymers on large scale from diverse, readily-available cyclic monomers.^{12,13} While the high catalytic activity of **7_{cyc}** was desirable, the synthesis and storage of this compound were complicated by instability.

To realize the potential in the area of cyclic polymer chemistry, catalysts should be readily synthesized in good yields, be easily purified to eliminate any acyclic contaminants, and have an appropriate balance of stability (e.g., during storage as well as polymerizations) and activity. To address issues of stability, we envisioned that catalysts with shorter tether lengths, such as **4_{cyc}**, **5_{cyc}**, and **6_{cyc}**, which contain 4-, 5-, and 6-carbon tethers, respectively, may be advantageous. A potential drawback, however, is that this may be accompanied by decreased catalytic activities. Therefore, we designed catalysts to incorporate two key structural features, shortened tether lengths and saturated NHC backbones, expected to synergistically provide REMP catalysts of high stabilities and activities.¹⁴

We also hoped to further elucidate the mechanism by which REMP proceeds through judicious catalyst design. Initially, REMP was proposed to proceed via a ring-expansion initiation event from a cyclic Ru-alkylidene catalyst (Scheme 1) and propagate as cyclic monomers were incorporated into a growing cyclic polymer. Upon consumption of monomer, a final catalyst release step would provide the original catalyst and the desired cyclic polymer. The polymerization mechanism depicted in Scheme 1 has several intriguing features including: 1) opening of a chelated Ru-alkylidene catalyst, 2) propagation with the prospect of competing intramolecular chain-transfer events, and 3) a final release of the original catalyst via intramolecular CM.

Many scenarios are consistent with Scheme 1, depending on the relative rates of initiation, propagation, intramolecular chain-transfer, and catalyst release. Initial studies using catalyst **7_{cyc}** demonstrated the ability to control polymer molecular-weight (MW) using the monomer/catalyst loading.¹¹ This corresponds to a regime in which nearly complete initiation occurs, and catalyst release does not take place prior to complete monomer consumption. Another key observation was that after complete conversion of monomer, the MW of the cyclic polymers progressively decreased in the presence of **7_{cyc}**, indicating significant amounts of intramolecular chain-transfer (Scheme 1). Alternatively, if the rate of propagation is much greater than that of initiation, and the rates of intramolecular chain-transfer and catalyst release are negligible, then all monomer species may be incorporated into a number of macrocycles equal to the number of catalyst molecules that initiated. This latter scenario would yield cyclic polymers in which Ru is incorporated into the backbone. Finally, a catalyst that shows relatively rapid release from a propagating cyclic chain may be expected to initiate, propagate (e.g., oligomerize), and then release, ultimately providing multiple polymer rings from each catalyst complex. Therefore, understanding how the catalyst design influences the relative kinetics of these processes is central to controlling the nature and distribution of products obtained via REMP.

To better understand each of the mechanistic aspects of REMP, and provide guidance for REMP catalyst design, we sought to investigate a homologous series of cyclic catalysts of varying N-to-Ru tether lengths (Figure 2). The tether length may be central in controlling structural features of the catalyst such as: 1) inherent ring-strain in the cyclic Ru-complexes, 2) relative orientations of the NHC and PCy₃ ligands about the metal center, and 3) rotation about the Ru-alkylidene (i.e., Ru=C-R) bond. As will be discussed below, a combination of NMR spectroscopy and single-crystal X-ray analyses of cyclic catalysts ultimately revealed key connections between their structures and activities.

Considering each step in the REMP cycle, it was expected that the tether length ideal for polymerization activity might be unfavorable for catalyst release. Specifically, intramolecular metathesis to reform and release the initial catalyst from the polymer is expected to be most efficient for shorter tether lengths. In contrast, increased tether lengths may be beneficial for polymerization rates, considering longer tethers may increase ring-strain of the catalyst or provide necessary flexibility within the structure. Encouraged by the modular nature of the NHC ligand, and the possibility of controlling REMP catalyst activities via tether length, we prepared and analyzed a homologous series of cyclic REMP catalysts (**4_{cyc}** – **7_{cyc}**, Figure 2), as well as analogues possessing saturated imidazolinyldene ligands. Herein, we report the study of their activities in various steps of the REMP cycle, as well as key structure-activity relationships.

Results and Discussion

Catalyst Syntheses

The syntheses of complexes **4_{cyc}** and **5_{cyc}** were previously described by Fürstner.⁹ To our knowledge, however, their catalytic activity has not been reported. Catalysts **6_{cyc}** and **7_{cyc}** were prepared analogously, as described in Scheme 2. The corresponding imidazolium salts (**8**) were first obtained by alkylation of 1-mesitylimidazole.¹⁵ Ligand exchange was then achieved via deprotonation of the imidazolium salt, followed by addition of bis(phosphine) complex **1** (**8**/**1** molar ratio = 2:1) to give “open” complexes **4_{acyc}** – **7_{acyc}**.^{10, 16} In general, ligand exchange proceeded smoothly and the desired non-chelated complexes were isolated in good yields after chromatography on silica gel.^{17, 18} Intramolecular metathesis/cyclization was conducted in a PhH/pentane mixture (1:15 v/v) at 70 °C and 0.001 M to give the final “closed” complexes **4_{cyc}** – **7_{cyc}**. Each of the catalysts could be purified by chromatography on silica gel, however, purification of **4_{cyc}** – **6_{cyc}** was more efficiently accomplished via recrystallization from Et₂O/pentane.¹⁵

We noted that the efficiency of cyclization of open complexes **4_{acyc}** – **7_{acyc}** to give cyclic catalysts **4_{cyc}** – **7_{cyc}** is highly dependent on the tether length (Table 1). Ostensibly, the ability of an open complex to undergo intra- versus intermolecular metathesis events gives some indication of the tendency for the proposed catalyst release step in Scheme 1. Table 1 summarizes the results of cyclization reactions for each catalyst at 0.01 and 0.001 M. In each case, yields were markedly improved at lower concentration (0.001 M) as determined by ¹H NMR analysis of the crude reaction mixtures. At 0.01 M, additional alkylidene peaks were observed via ¹H NMR spectroscopy that were upfield of signals characteristic of **1**, **4_{acyc}** – **7_{acyc}**, or **4_{cyc}** – **7_{cyc}**. These signals may be attributed to CM products such as those arising from CM involving styrene (formed as a product in the cyclization step), or the terminal olefin on an NHC ligand with another Ru-complex. As expected, these intermolecular metathesis events were significantly diminished at lower concentration. Prolonged reaction times did not result in increased yields of the desired cyclic species, rather decomposition was observed. It is worth noting that in the case of **7_{acyc}**, no product was observed when cyclization was conducted at 0.01 M. Therefore, catalyst release during REMP may be slow in comparison with other chain-transfer events when **7_{cyc}** is employed.¹⁹

Considering the enhanced activity observed from saturation of the NHC backbone (cf. **2** and **3**),¹⁴ we were motivated to investigate cyclic catalysts incorporating this design feature. As depicted in Scheme 3, a PhCH₃ solution of *N*-mesitylethylenediamine (**9**)²⁰ was treated with HC(OEt)₃ in the presence of catalytic PTSA and stoichiometric bromo-olefin at 110 °C. This one-pot procedure effected cyclization and alkylation to provide the imidazolium salts **10** in excellent yields.²¹ Unfortunately, attempts at direct deprotonation of **10** using KHMDS in the presence of bis(phosphine) complex **1** were complicated by NHC dimerization and provided low yields of the desired products.²² Alternatively, treatment of **10** with NaH in CHCl₃ cleanly

provided neutral adducts **11**.²³ Heating THF solutions of **11** (0.001 M) in the presence of **1** (**11**/**1** molar ratio = 2:1) accomplished ligand exchange as well as cyclization to provide the desired cyclic catalysts **5_{cyc}·H₂** and **6_{cyc}·H₂** in 46 and 57% overall yields, respectively.²⁴ Although **5_{cyc}·H₂** and **6_{cyc}·H₂** were each isolable via chromatography on silica gel, both were found to be crystalline solids and were routinely recrystallized by slow addition of pentane into saturated PhH solutions of the complexes. Similar to **5_{cyc}** and **6_{cyc}**, the saturated catalysts **5_{cyc}·H₂** and **6_{cyc}·H₂** displayed good stability both in the solid-state and in solution.²⁵

Structural Analyses

The structural impacts of changing the tether lengths of catalysts **4_{cyc}** – **7_{cyc}** resulted in significant differences in catalyst activities (see polymerization studies below for more discussion). In addition to understanding the structure-activity relationships pertaining to REMP catalysts, a more general understanding of catalyst architecture may lead to breakthroughs in catalyst design as well as fundamental mechanistic insights of olefin metathesis. Cyclic catalysts **4_{cyc}** – **6_{cyc}** were found to show tether length-dependent trends in three key structural parameters summarized in Table 2: 1) rotation about the Ru1-C2 bond, 2) the C1-Ru1-P1 bond angle, and 3) the Ru-C1 bond length (Figure 3).²⁶

Although many structural features of **4_{cyc}** – **7_{cyc}** are best observed via solid-state analysis, rotation about the Ru1-C2 bond is manifested in the coupling constants between the P1 and H2 (i.e., the alkylidene proton, bonded to C2) atoms in the ¹H NMR spectra (Table 2 and Figure 3). Complexes **4_{cyc}** and **5_{cyc}**, which were previously characterized in solution and solid-state,⁹ displayed coupling constants of ³J_{H2,P1} = 14.1 and 10.5 Hz (solvent = C₆D₆), respectively. The smaller coupling constant observed from complex **5_{cyc}**, in comparison with **4_{cyc}**, indicated that the corresponding atoms in the former are closer to a perpendicular arrangement. Consistent with this trend, a smaller coupling constant was observed in the ¹H NMR spectrum of **6_{cyc}** (i.e., ³J_{H2,P1} = 5.1 Hz), indicating that the alkylidene proton (H2) was projected nearly perpendicular to the Ru1-P1 bond. The ¹H NMR spectrum of **7_{cyc}** revealed a coupling constant of ³J_{H2,P1} = 10.2 Hz, which may be ascribed to the increased ring size (cf. **6_{cyc}**) inducing twist about the Ru1-C2 bond.²⁷

To further investigate the structures of the cyclic catalysts, we compared single-crystal X-ray data of **4_{cyc}** – **6_{cyc}**, as well as saturated analogues **5_{cyc}·H₂** and **6_{cyc}·H₂**.²⁶ The crystal structures of these complexes confirmed a variable degree of rotation about the Ru1-C2 bond, as determined from the Cl2-Ru-C2-C3 dihedral angles (Table 2). Overall, for **4_{cyc}** – **6_{cyc}**, decreased ³J_{H2,P1} values corresponded to decreased dihedral angles suggesting that the solution and solid-state structures of the catalysts are similar. It should be noted that while the ³J_{H2,P1} values observed from **5_{cyc}·H₂** and **6_{cyc}·H₂** were consistent with each complex's respective unsaturated analogue, solid-state analysis revealed that the Cl2-Ru-C2-C3 dihedral angles were not consistent with the trend observed from the unsaturated series.

Stepwise increase in the tether lengths was found to cause increasing nonlinearity in the C1-Ru1-P1 bond angles. Specifically, catalysts **4_{cyc}**, **5_{cyc}**, and **6_{cyc}** have C1-Ru1-P1 bond angles of 171.0, 166.0, and 163.3°, respectively. One rationale for this trend may be that increasing the tether length caused the NHC ligand to tilt to accommodate the increased steric demand of the tether. A consequence of this tilt is that the Mes group is forced closer to the PCy₃ group which may facilitate dissociation of the phosphine during initiation (see below for a comparison of catalyst activities).^{14a} In addition, the tilted conformation may be difficult to restore which would hinder catalyst release and thus manifest in more rapid polymerization. Steric demands also resulted in discernable increases in the Ru1-P1 and Ru1-C1 bond lengths as the tether length was increased. For example, upon extension of the tether, the Ru1-C1 bond length increased from 2.076 Å for **4_{cyc}** to 2.113 Å for **6_{cyc}**. The saturated catalysts, **5_{cyc}·H₂** and

6_{cyc}-H₂, showed changes in their Ru1-P1 and Ru1-C1 bond lengths that were consistent with those observed in the unsaturated series.

Ring-Expansion Metathesis Polymerization

To our knowledge, the catalytic activities of complexes **4_{cyc}** – **6_{cyc}** have not been explored in either small-molecule or polymer syntheses. In addition, electronic variants such as saturation of the NHC backbone have not been investigated. To compare the activities of **4_{cyc}** – **7_{cyc}** in REMP, we examined their relative efficiencies in the polymerization of cyclooctene (COE) to poly(cyclooctene) (PCOE). As can be seen from the data presented in Figure 4, the relative efficiencies of the catalysts showed a strong dependence on the length of the chelating tether.²⁸ In general, increased tether length was accompanied by an increase in catalytic activity. For example, comparison of the unsaturated catalysts revealed the time required to reach >95% conversion was nearly 24 h for **4_{cyc}** (green line), approximately 8 h for **5_{cyc}** (purple line) and **6_{cyc}** (blue line), and less than 1 h for **7_{cyc}** (red line).

Saturation of the NHC backbone was found to dramatically increase catalyst activity. As expected, **5_{cyc}-H₂** and **6_{cyc}-H₂** each displayed faster polymerization rates than their unsaturated analogues **5_{cyc}** and **6_{cyc}**, respectively (Figure 4). Surprisingly, the rate acceleration resulting from NHC saturation appeared to be greater than for homologation of the tether length. Specifically, **6_{cyc}-H₂** was found to achieve >95% conversion in shorter reaction times than did **7_{cyc}**. Similarly, **5_{cyc}-H₂** was found to be a more active polymerization catalyst than **6_{cyc}**. Overall, the data revealed that judicious combinations of shorter tether lengths (i.e., 5- or 6-carbon tethers) and NHC backbone saturation (e.g., **5_{cyc}-H₂** and **6_{cyc}-H₂**) provided a desirable balance of catalyst stabilities, synthetic accessibility, and activities.

Catalyst stability takes on particular importance in REMP as decomposition of the catalyst before, during, or after polymerization could potentially lead to linear polymers, instead of the envisioned macrocycles. In addition, relative stabilities are important factors in the general development of new metathesis catalysts, especially considering that catalyst stability and activity are often inversely related.²⁹ To explore the stabilities of REMP catalysts **4_{cyc}** – **7_{cyc}** during polymerization reactions, we plotted the ln([COE]) versus time for REMP of COE (Figure 5). The logarithmic plots were found to be linear (*R*² values ranged from 0.969 – 0.997) between 20 and 80% conversion of COE to PCOE, indicating that catalyst decomposition was negligible in all cases during the time of the polymerization reactions. Closer examination of the plots revealed that the only discernable deviations from linearity (i.e., pseudo-first-order rate kinetics) involved apparent increases in the rate of monomer consumption. This observation can be rationalized by a relatively slow initiation period which would manifest in a gradual increase in the number of propagating polymer chains, and concomitant increase in the rate of conversion.

Catalyst Release

A unique aspect of REMP, in comparison with ring-opening metathesis polymerization (ROMP), is the requirement for an intramolecular chain-transfer event with the olefin nearest to the NHC to release the initial cyclic catalyst and provide a cyclic polymer free of Ru (Scheme 1). While removal of Ru from linear polymers obtained via ROMP can be done efficiently using a terminating agent, such as ethyl vinyl ether, this method is incompatible with REMP as it may result in linear polymer formation.³⁰ Given the importance of catalyst release from the cyclic polymers, we investigated each catalyst's propensity to undergo intramolecular cyclization during polymerization that would be indicative of the catalyst's ability to be released from a polymer.

We envisioned that conducting polymerizations using “open” catalysts **5_{acyc}** – **7_{acyc}** would provide insight into each catalyst’s ability to perform intramolecular CM to release “closed” catalysts **5_{acyc}** – **7_{acyc}**.³¹ Propagation via growing Ru-alkylidene species **A** (Scheme 4) would inherently compete with catalyst cyclization (e.g., **A** → **5_{cyc}** + **B**), and provide an indication of each catalyst’s propensity to be released from the polymer chain.

To investigate, we conducted polymerizations of COE using open catalysts **5_{acyc}** – **7_{acyc}** in CD₂Cl₂ at 40 °C ([M/C]₀ = 250:1, [M]₀ = 0.5 M) and monitored the alkylidene region of the ¹H NMR spectrum as the reactions progressed. Each Ru-complex shown in Scheme 4 was identified by characteristic chemical shifts of the corresponding alkylidene protons. In CD₂Cl₂, complexes **5_{acyc}** – **7_{acyc}** gave sharp benzylidene resonances as singlets at δ = 19.30 ppm, whereas propagating species (**A**) displayed broad multiplets at δ = 18.69 ppm. Cyclic catalysts **5_{cyc}**, **6_{cyc}**, and **7_{cyc}** displayed signals at δ = 20.23, 19.35, and 19.67 ppm, respectively, with multiplicities matching those in Table 2.

We first examined open catalysts **6_{acyc}** and **7_{acyc}** as these were representative of the most active cyclic catalysts (**6_{cyc}** and **7_{cyc}**, respectively) for this series. Catalysts **6_{acyc}** and **7_{acyc}** gave similar results, and polymerization of COE was found to reach completion faster than did cyclization of **6_{acyc}** and **7_{acyc}** to give **6_{cyc}** and **7_{cyc}**, respectively. Specifically, complete conversion of COE was achieved in less than 5 min for each catalyst.³² The mole fraction of cyclic catalyst (**6_{cyc}**/**7_{cyc}**) observed at this point, however, was only ca 10%, relative to **6_{acyc}**/**7_{acyc}** (ca 30%) and **A** (ca 60%). Continued heating resulted in diminished amounts of **6_{acyc}**/**7_{acyc}** and **6_{cyc}**/**7_{cyc}** in each case, with concomitant increases in the relative amounts of **A**. As will be discussed in the next section, the continued progression to form **A** may have been due to incorporation of free cyclic catalyst into the polymer chains. After ca 1 h, only trace amounts of cyclic species **6_{cyc}**/**7_{cyc}** could be observed. Overall, these results suggested that cyclization is not favored over polymerization for catalysts bearing 6- or 7-membered tethers, and that cyclization to release catalyst **6_{cyc}** or **7_{cyc}** after polymerization is not likely.

We next investigated the behavior of **5_{acyc}** under the same conditions as described above. In contrast to the longer tethered analogues **6_{acyc}** and **7_{acyc}**, polymerization reactions using **5_{acyc}** revealed much faster cyclization (to give **5_{cyc}**) relative to polymerization. Figure 6 shows the mole fraction of each catalytic species (**5_{acyc}**, **A**, and **5_{cyc}**) as well as the conversion of COE to PCOE over time. As can be seen, almost complete formation of cyclic catalyst **5_{cyc}** was observed after ca 45 min, at which time the polymerization had reached only 48% conversion. Moreover, the amount of catalytic species within the polymer chains (**A**) quickly diminished to nearly undetectable amounts. The data presented in Figure 6 supports that cyclization to form **5_{cyc}** is favored over propagation and that the background rate of cyclization (i.e., **5_{acyc}** → **5_{cyc}**) is also significant for this catalyst. In addition, the persistent amount of **5_{cyc}** that is observed relative to propagating species (**A**) suggested that incorporation of **5_{cyc}** into existing polymer chains is unlikely. The continued conversion of COE to PCOE, with persistent observation of only **5_{cyc}**, suggested that this cyclic catalyst reached an equilibrium between propagating (e.g., **A**) and resting (i.e., **5_{cyc}**) states that strongly favored the latter.

Collectively, the experiments investigating the behavior of open catalysts **5_{acyc}** – **7_{acyc}** revealed that controlling the tether lengths of cyclic catalysts may dictate polymerization kinetics with regard to polymer MWs and polydispersities. For example, shorter tether lengths may facilitate catalyst release during polymerization (Scheme 1), ultimately leading to multiple macrocycles produced from each catalyst molecule. Alternatively, REMP catalysts displaying little tendency to be released from a cyclic polymer may provide access to cyclic block copolymers or other advanced macrocycles.

Interaction Between Free Catalyst and Polymer

As mentioned previously, it may be possible for a cyclic catalyst to equilibrate with poly(olefin)s and become incorporated (or reincorporated) into a polymer chain. This equilibrium, depicted in Scheme 5, may be tether length-dependent given that ring-opening of the catalyst may be a driving force toward incorporation into the polymer. With regard to REMP, the reversibility of intramolecular chain-transfer and catalyst release (Scheme 1) would result in an equilibrium amount of Ru species contained within the final cyclic polymers. Therefore, understanding each catalyst's affinity toward polymer incorporation is important for understanding the potential purity of the cyclic polymers. To investigate, we prepared linear PCOE via ROMP using acyclic catalyst **3** in the presence of 3-hexene as a chain-transfer agent. This provided a hydrocarbon polymer ($M_n = 150$ kDa, PDI = 2.1) which closely resembled the PCOE obtained via REMP in composition.³³ The linear PCOE was then treated with each of the cyclic catalysts **5_{cyc}**–**7_{cyc}** (olefin/catalyst molar ratio = 100:1) in CD_2Cl_2 at 40 °C. The equilibration of catalyst and polymer was monitored via 1H NMR spectroscopy using anthracene as an internal standard; key NMR signals of the cyclic catalysts and incorporated species were similar to those observed in the previous section (Scheme 4).

As expected, incorporation of cyclic catalyst into the polymer chain was dependent on the tether length of the catalyst. Specifically, after 1 h ca 11% of catalyst **7_{cyc}** had become incorporated into the polymer, whereas catalyst **6_{cyc}** showed only 3% incorporation over the same time period. Catalyst **5_{cyc}**, however, revealed no incorporation even after extended periods (up to 6 h). To compare, catalyst **5_{cyc}**-**H₂** was also studied and gave similar results as **5_{cyc}**. Overall, although the amount of incorporated catalyst was small in each case, there appeared to be some equilibration of free catalyst into the poly(olefin) depending upon the length of the catalyst tether. Notably, equilibration appeared to be slow in comparison with polymerization data presented above. Therefore, avoiding prolonged polymerization reaction times may be sufficient for minimizing the amount of Ru in the resulting polymers.

Conclusions

In summary, we describe the synthesis and characterization of a series of cyclic Ru-alkylidene catalysts with particular focus on their ability to mediate ring-expansion metathesis polymerization. Both catalyst tether length as well as NHC electronics were found to significantly impact different aspects of the polymerization mechanism. Whereas shorter tether lengths were more efficient for catalyst release from the polymer, the caveat for these systems was found to be slower polymerization rates. Saturation of the NHC backbone, however, increased polymerization efficiency and effectively balanced activity loss due to shortening of the tether. Overall, catalyst stabilities were found to be good over the course of the polymerization experiments. The ability to control catalyst activity by a combination of tether length and ligand electronics may lead to new opportunities in olefin metathesis and catalyst design.

Experimental Section

Materials and Methods

1H and ^{13}C NMR spectra were recorded using a Varian Mercury 300 or Varian Inova 500 spectrometer and were routinely run using broadband decoupling. Chemical shifts (δ) are expressed in ppm downfield from tetramethylsilane using the residual protiated solvent as an internal standard ($CDCl_3$ 1H : 7.26 ppm and ^{13}C : 77.0 ppm; C_6D_6 1H : 7.20 ppm and ^{13}C : 128.0 ppm). ^{31}P NMR spectra were externally referenced to 85% H_3PO_4 (0.00 ppm). Coupling constants are expressed in hertz (Hz). THF, CH_2Cl_2 , Et_2O , pentane, PhH, $PhCH_3$, and C_6D_6 were obtained from solvent purification columns.³⁴ CD_2Cl_2 used for NMR-scale experiments

was distilled over CaH₂ under N₂ prior to use. CHCl₃ was distilled over P₂O₅ under N₂ prior to use. Ru-complex **1** was obtained from Materia, Inc. All other solvents and reagents were of reagent quality and used as obtained from commercial sources. Chromatography was performed with neutral silica gel (TSI Scientific, 230–400mesh, pH 6.5–7.0). Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K., and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition numbers 687290 (**5_{cyc}-H₂**), 683585 (**6_{cyc}**), and 687247 (**6_{cyc}-H₂**).

Cyclic complex **5_{cyc}-H₂**

In a Schlenk tube, chloroform adduct **11a** (200 mg, 0.51 mmol) was dissolved in dry THF (515 mL) under an atmosphere of dry N₂. To the solution was added Ru-complex **1** (210 mg, 0.26 mmol). The flask was sealed and the reaction mixture was stirred in an oil bath at 70 °C for 2 h. Afterward, the cooled reaction mixture was concentrated under vacuum, redissolved in a minimal amount of PhH, and treated dropwise with pentane until crystallization ensued (X-ray analysis was performed on crystals obtained in this manner). The solids were collected by vacuum filtration, rinsed with 5% Et₂O/pentane, and dried under vacuum to provide 147 mg (81% yield) of the desired complex as a tan solid. ¹H NMR (500 MHz, C₆D₆): δ 20.39 (dt, 3J_{H,P} = 9.3 Hz, J_{H,H} = 4.5 Hz, 1H), 6.93 (s, 2H), 3.17 (t, J = 10.0 Hz, 2H), 3.10–3.09 (m, 2H), 2.85 (t, J = 10.0 Hz, 2H), 2.75 (br, 2H), 3.71 (s, 6H), 2.60–2.53 (m, 3H), 2.32 (br 2H), 2.23 (s, 3H), 1.95–1.92 (m, 6H), 1.78 (br, 6H), 1.68 (br, 2H), 1.47–1.45 (m, 6H), 1.34–1.29 (m, 10H), 1.19–1.17 (m, 2H). ¹³C NMR (125 MHz, C₆D₆): δ 216.0 (J_{CP} = 85.9 Hz), 138.4, 137.6, 136.6, 129.9, 57.9 (J_{CP} = 4.9 Hz), 51.2 (J_{CP} = 3.5 Hz), 48.5 (J_{CP} = 2.7 Hz), 47.9, 32.1 (J_{CP} = 15.1 Hz), 29.8, 28.2 (J_{CP} = 10.4 Hz), 27.3, 26.8, 26.7, 21.1, 20.0. ³¹P NMR (121 MHz, C₆D₆): δ 27.0. HRMS m/z calcd for C₃₅H₅₇Cl₂N₂PRu [M⁺] 708.2680, found 708.2659.

[1-(6-Heptenyl)-3-mesitylimidazolylidene]RuCl₂(=CHPh) (PCy₃) (**6_{acyc}**)

Imidazolium bromide **8_{n=5}** (400 mg, 1.10 mmol), was suspended in dry PhCH₃ (7 mL) under dry N₂. To the solution was added NaOtBu (106 mg, 1.10 mmol) and the resulting mixture was stirred at RT for 12 h. Ru-complex **1** (453 mg, 0.55 mmol) was then added in a single portion and the resulting mixture was stirred for 1 h during which time a color change from purple to brown was observed. Upon completion, the mixture was filtered through a thin pad of TSI silica gel using Et₂O/pentane (1:4 v/v) as eluent. The filtrate was concentrated under vacuum without heating. Purification by column chromatography on TSI silica gel under N₂ pressure (10% Et₂O/pentane) provided 408 mg (90% yield) of the desired compound as a red-purple powder. ¹H NMR (major isomer) (300 MHz, C₆D₆): δ 19.85 (s, 1H), 7.05–6.94 (m, 2H), 6.56–6.55 (m, 1H), 6.31–6.15 (m, 3H), 5.90–5.76 (m, 1H), 5.15–5.03 (m, 2H), 4.70 (t, J = 7.7 Hz, 2H), 2.65–2.53 (m, 4H), 2.13 (s, 3H), 1.97–1.08 (m, 37H), 1.80 (s, 6H). ³¹P NMR (major isomer) (121 MHz, C₆D₆): δ 34.4. HRMS m/z calcd for C₄₄H₆₅Cl₂N₂PRu [M⁺] 824.3306, found 824.3298.

Cyclic complex **6_{cyc}**

Ru-complex **6_{acyc}** (400 mg, 0.48 mmol), was dissolved in dry PhH (30 mL) and pentane (450 mL) in a Schlenk tube under dry N₂. The mixture was then placed in a oil bath at 70 °C and stirred for 1 h. Upon completion, the solution was cooled to RT, transferred to a round-bottom flask, and concentrated under vacuum without heat. The crude material was triturated with 20% Et₂O/pentane (50 mL) for ca 20 min. The solids were then collected via vacuum filtration, rinsed with pentane, and dried under vacuum to provide 335 mg (96% yield) of the desired compound as a red-brown powder. X-ray quality crystals were obtained by slow addition of pentane to a PhH solution of the complex. ¹H NMR (300 MHz, C₆D₆): δ 19.71 (dt, 3J_{H,P} = 5.1 Hz, J_{H,H} = 5.5 Hz, 1H), 6.90 (s, 2H), 6.35 (d, J = 1.8 Hz, 1H), 6.14 (s, 1H), 2.74–2.51 (m, 3H), 2.51 (s, 6H), 2.23 (s, 3H), 1.99–1.31 (m, 40H). ¹³C NMR (125 MHz, C₆D₆): δ 186.0

($J_{\text{CP}} = 84.7$ Hz), 138.2, 137.1, 129.4, 128.3, 123.6 ($J_{\text{CP}} = 2.3$ Hz), 120.4, 62.9, 47.0, 32.4 ($J_{\text{CP}} = 16.9$ Hz), 31.5, 29.8, 28.1 ($J_{\text{CP}} = 10.0$ Hz), 26.8, 22.9, 21.1, 19.7. ^{31}P NMR (121 MHz, C_6D_6): δ 33.3. HRMS m/z calcd for $\text{C}_{36}\text{H}_{57}\text{Cl}_2\text{N}_2\text{PRu} [\text{M}^+]$ 720.2680, found 720.2671.

Cyclic complex **6_{cyc}-H₂**

This compound was prepared analogously to **5_{cyc}-H₂** from chloroform adduct **11b** (280 mg, 0.69 mmol) and Ru-complex **1** (285 mg, 0.35 mmol) in THF (650 mL) to provide 369 mg (74% yield) of the desired complex as a red-brown solid. X-ray quality crystals were obtained by slow diffusion of pentane into a $\text{Et}_2\text{O}/\text{PhH}$ (20:1 v/v) solution of the complex. ^1H NMR (500 MHz, C_6D_6): δ 19.61 (dt, $3J_{\text{H,P}} = 5.0$ Hz, $J_{\text{H,H}} = 5.7$ Hz, 1H), 6.93 (s, 2H), 3.33-2.83 (m, 4H), 2.70 (s, 6H), 2.63-2.56 (m, 3H), 2.22 (s, 3H), 1.93-1.30 (m, 40H). ^{13}C NMR (125 MHz, C_6D_6): δ 215.3 ($J_{\text{CP}} = 80.1$ Hz) 137.5, 137.0, 129.9, 129.5, 62.8, 51.7 ($J_{\text{CP}} = 3.3$ Hz), 47.7, 46.9, 32.2 ($J_{\text{CP}} = 16.5$ Hz), 29.7, 28.1 ($J_{\text{CP}} = 10.1$ Hz), 27.9, 26.8, 25.6, 23.6, 21.1. ^{31}P NMR (121 MHz, C_6D_6): δ 30.4. HRMS m/z calcd for $\text{C}_{36}\text{H}_{59}\text{Cl}_2\text{N}_2\text{PRu} [\text{M}^+]$ 722.2837, found 722.2808.

Cyclic complex **7_{cyc}**

This compound was prepared analogously to **6_{cyc}** from open complex **7_{acyc}** (150 mg, 0.18 mmol) in PhH (10 mL) and pentane (170 mL). Upon completion, the cooled reaction mixture was concentrated under vacuum without heat, then triturated with 20% Et_2O /pentane (10 mL) for ca 20 min. The solids were collected via vacuum filtration and further purification via column chromatography on TSI silica gel under N_2 pressure (30% Et_2O /pentane) provided 56 mg (42% yield) of the desired compound as a light brown powder. ^1H NMR (500 MHz, C_6D_6): δ 19.37 (dt, $3J_{\text{H,P}} = 10.2$ Hz, $J_{\text{H,H}} = 5.5$ Hz, 1H), 6.92 (s, 2H), 6.38 (d, $J = 1.5$ Hz, 1H), 6.19 (s, 1H), 3.66 (br, 2H), 2.62-2.57 (m, 3H), 2.54 (s, 6H), 2.24 (s, 3H), 2.08-1.61 (m, 24H), 1.50-1.42 (m, 2H), 1.34-1.28 (m, 12H), 1.22-1.17 (m, 2H). ^{13}C NMR (125 MHz, C_6D_6): δ 184.7 ($J_{\text{CP}} = 97.5$ Hz), 138.1, 137.6, 129.2, 128.4, 128.3, 128.1, 127.9, 123.3 ($J_{\text{CP}} = 3.3$ Hz), 119.9, 60.4, 47.1, 32.7 ($J_{\text{CP}} = 16.1$ Hz), 29.9, 28.2 ($J_{\text{CP}} = 9.5$ Hz), 26.8, 26.5, 24.7, 21.1, 20.7, 19.7. ^{31}P NMR (121 MHz, C_6D_6): δ 26.3. HRMS m/z calcd for $\text{C}_{37}\text{H}_{59}\text{Cl}_2\text{N}_2\text{PRu} [\text{M}^+]$ 734.2837, found 734.2814.

1-(6-Heptenyl)-3-mesitylimidazolium bromide (**8_{n=5}**)

This compound was prepared analogously to **8_{n=3,4,6}** from *N*-mesitylimidazole (1.00 g, 5.37 mmol) and 7-bromo-1-heptene (1.0 mL, 6.55 mmol) in PhCH_3 (20 mL).⁹ Upon completion, the reaction mixture was concentrated under vacuum and the crude material was suspended in Et_2O (100 mL) and vigorously stirred for 12 h to produce a fine white suspension. The solids were collected via vacuum filtration under a stream of N_2 to provide 1.81 g (93% yield) of the desired compound as an off-white powder. ^1H NMR (300 MHz, CDCl_3): δ 10.31 (dd appearing as t, $J = 1.5$ Hz, 1H), 7.94 (dd appearing as t, $J = 1.7$ Hz, 1H), 7.21 (dd appearing as t, $J = 1.7$ Hz, 1H), 6.94 (s, 2H), 5.76-5.63 (m, 1H), 4.96-4.84 (m, 2H), 4.67 (t, $J = 7.4$ Hz, 2H), 2.29 (s, 3H), 2.01 (s, 6H), 2.01-1.91 (m, 4H), 1.43-1.30 (m, 4H). ^{13}C NMR (125 MHz, CDCl_3): δ 141.1, 138.1, 137.8, 134.0, 130.6, 129.7, 123.2, 123.1, 114.7, 50.1, 33.2, 30.2, 28.0, 25.3, 21.0, 17.5. HRMS m/z calcd for $\text{C}_{19}\text{H}_{27}\text{N}_2 [\text{M}^+]$ 283.2174, found 283.2186.

1-(5-Hexenyl)-3-mesitylimidazolium bromide (**10a**)

To a solution of $\text{HC}(\text{OEt})_3$ (10 mL) and PhCH_3 (10 mL) in a 50 mL round-bottom flask was added $\text{PTSA} \cdot \text{H}_2\text{O}$ (39 mg, 0.20 mmol), *N*-mesitylethylenediamine (**9**) (729 mg, 4.09 mmol), and 6-bromo-1-hexene (0.66 mL, 4.91 mmol). The flask was fitted with a H_2O -jacketed condenser and the reaction mixture was stirred under N_2 in an oil bath at 110 °C for 10 h. Afterward, the cooled reaction mixture was concentrated under vacuum. The crude product was treated with Et_2O (40 mL) and vigorously stirred for 2 h to produce an off-white slurry. The

solids were collected via vacuum filtration, rinsed with Et₂O, and dried under vacuum to provide 1.31 g (91% yield) of the desired compound. ¹H NMR (300 MHz, CDCl₃): δ 9.50 (s, 1H), 6.87 (s, 2H), 5.80-5.67 (m, 1H), 5.03-4.92 (m, 2H), 4.30-4.11 (m, 4H), 3.94 (t, *J* = 7.2 Hz, 2H), 2.26 (s, 6H), 2.24 (s, 3H), 2.12-2.05 (m, 2H), 1.76-1.66 (m, 2H), 1.49-1.42 (m, 2H). ¹³C NMR (125 MHz, CDCl₃): δ 158.7, 139.9, 137.6, 135.0, 130.4, 129.7, 115.2, 50.9, 48.7, 48.1, 32.8, 26.4, 25.2, 20.8, 17.9. HRMS *m/z* calcd for C₁₈H₂₇N₂ [M⁺] 271.2174, found 271.2161.

1-(6-Heptenyl)-3-mesitylimidazolinium bromide (10b)

This compound was prepared analogously to **10a** from HC(OEt)₃ (7.0 mL), PhCH₃ (7.0 mL), PTSA·H₂O (27 mg, 0.14 mmol), *N*-mesitylethylenediamine (**9**) (500 mg, 2.80 mmol), and 7-bromo-1-heptene (0.51 mL, 3.36 mmol) to provide 951 mg (93% yield) of the desired compound. ¹H NMR (500 MHz, CDCl₃): δ 9.31 (s, 1H), 6.77 (s, 2H), 5.70-5.61 (m, 1H), 4.90-4.81 (m, 2H), 4.20-4.16 (m, 2H), 4.12-4.08 (m, 2H), 3.78 (t, *J* = 7.3 Hz, 2H), 2.16 (s, 3H), 2.15 (s, 6H), 1.96-1.91 (m, 2H), 1.64-1.58 (m, 2H), 1.35-1.30 (m, 2H), 1.27-1.21 (m, 2H). ¹³C NMR (125 MHz, CDCl₃): δ 158.5, 139.7, 138.1, 134.9, 130.3, 129.5, 114.4, 50.8, 48.6, 48.0, 33.1, 27.9, 26.7, 25.3, 20.7, 17.8. HRMS *m/z* calcd for C₁₉H₂₉N₂ [M⁺] 285.2325, found 285.2310.

1-(5-Hexenyl)-3-mesityl-2-(trichloromethyl)imidazolidine (11a)

Under an atmosphere of dry N₂, imidazolinium bromide **10a** (443 mg, 1.26 mmol) was dissolved in dry CHCl₃ (6 mL). NaH (95 wt%, 38 mg, 1.51 mmol) was then added portionwise under a stream of N₂. The resulting mixture was placed in an oil bath at 55 °C and stirred for 10 h. Afterward, the cooled reaction mixture was diluted with Et₂O (100 mL), filtered through a thin pad of silica gel, and concentrated to provide 305 mg (62% yield) of the desired product as a pale yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 6.86 (s, 1H), 6.85 (s, 1H), 5.91-5.78 (m, 1H), 5.07-4.95 (m, 2H), 4.73 (s, 1H), 3.86-3.78 (m, 1H), 3.62-3.55 (m, 1H), 3.41-3.32 (m, 1H), 3.23-3.16 (m, 1H), 3.10-3.02 (m, 1H), 2.98-2.90 (m, 1H), 2.35 (s, 3H), 2.70 (s, 3H), 2.25 (s, 3H), 2.16-2.09 (m, 2H), 1.68-1.43 (m, 4H). ¹³C NMR (75 MHz, CDCl₃): δ 147.8, 147.7, 142.8, 138.8, 138.7, 134.9, 132.6, 129.9, 129.5, 114.5, 108.2, 94.2, 58.2, 52.9, 52.6, 33.7, 29.7, 26.1, 20.7, 19.8, 19.3. HRMS *m/z* calcd for C₁₉H₂₇Cl₃N₂ [M⁺] 388.1240, found 388.1225.

1-(6-Heptenyl)-3-mesityl-2-(trichloromethyl)imidazolidine (11b)

This compound was prepared analogously to **11a** from imidazolinium bromide **10b** (730 mg, 2.0 mmol), CHCl₃ (8 mL), and NaH (95 wt%, 101 mg, 4.00 mmol) to provide 670 mg (83% yield) of the desired product as a pale yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 6.88 (s, 1H), 6.86 (s, 1H), 5.92-5.79 (m, 1H), 5.08-4.96 (m, 2H), 4.75 (2, 1H), 3.87-3.80 (m, 1H), 3.65-3.58 (m, 1H), 3.42-3.33 (m, 1H), 3.25-3.17 (m, 1H), 3.10-3.02 (m, 1H), 3.00-2.92 (m, 1H), 2.37 (s, 3H), 2.29 (s, 3H), 2.27 (s, 3H), 2.14-2.05 (m, 2H), 1.68-1.54 (m, 2H), 1.50-1.38 (m, 4H). ¹³C NMR (75 MHz, CDCl₃): δ 142.8, 139.0, 138.6, 134.8, 132.6, 129.9, 129.4, 114.3, 108.2, 94.2, 58.4, 52.9, 52.6, 33.8, 30.1, 28.8, 26.4, 20.7, 19.8, 19.3. HRMS *m/z* calcd for C₂₀H₂₉Cl₃N₂ [M⁺] 402.1396, found 402.1382.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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- See Supporting Information.
- In solution, complexes $4_{acyc} - 7_{acyc}$ appeared to exist as a mixture of two rotamers as shown by two benzyldiene signals (ratio ca 10:1). The major isomer appeared as a singlet, analogous to complex 2, whereas a second signal was observed further downfield as a doublet (e.g., $^3J_{H,P} = 12.9$ Hz for 6_{cyc}).¹⁵

17. Purchased from TSI Scientific, 230–400 mesh, neutral pH.
18. Notably, “open” complexes $4_{\text{acyc}} - 7_{\text{acyc}}$ were routinely used in subsequent cyclization steps following only filtration through a short silica gel plug and concentration under vacuum. Residual tricyclohexylphosphine was efficiently removed from the cyclized catalysts ($4_{\text{cyc}} - 7_{\text{cyc}}$) during purification.
19. Additional considerations should be noted: 1) intramolecular cyclization may proceed to directly give an acyclic methylenide complex that is identical to the product that would be obtained between CM of styrene and the cyclic catalyst, and 2) in rare cases, olefin isomerization and cyclization to give small amounts of cyclic catalysts bearing a one-carbon shorter tether were observed (e.g., $7_{\text{acyc}} \rightarrow 6_{\text{cyc}}$).
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21. For an alternative, two-step procedure for the synthesis of imidazolinium salts bearing one *N*-aryl and one *N'*-alkyl group, see ref 8d.
22. Attempts at ligand exchange via deprotonation of imidazolinium salts 10 in hexanes were also unsuccessful.
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24. This reaction was found to be solvent-dependent and PhCH_3 , PhH, pentane, and PhH/pentane mixture gave inferior results.
25. Unfortunately, attempts to isolate pure samples of $7_{\text{cyc}}\text{-H}_2$ were unsuccessful.
26. Attempts to obtain X-ray quality crystals of 7_{cyc} were met with limited success.
27. Since single-crystal X-ray data was not obtained for 7_{cyc} , therefore, it was not possible to determine the direction of the rotation about the Ru1-C2 bond with respect to complexes $4_{\text{cyc}} - 6_{\text{cyc}}$. We speculate that the long tether of 7_{cyc} may allow for conformations that collectively frustrate crystallization.
28. Additional representations of the data in Figure 4 are provided.¹⁵
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31. In light of the relatively low activity of 4_{cyc} , 4_{acyc} was not evaluated in these experiments.
32. Under identical conditions, $5_{\text{acyc}} - 7_{\text{acyc}}$ gave faster conversions of COE to PCOE than the corresponding “closed” systems ($5_{\text{cyc}} - 7_{\text{cyc}}$). The higher polymerization activities of $5_{\text{acyc}} - 7_{\text{acyc}}$ versus $5_{\text{cyc}} - 7_{\text{cyc}}$ may reflect restricted conformations of the latter. Further investigations are underway.
33. Molecular-weight data was obtained from triple-angle laser light-scattering and refractive index measurements.
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35. The compound appeared to be hygroscopic, producing a thick, viscous material when collected under air.

Figure 1.
Representative Ru-based metathesis catalysts.

Figure 2.
Cyclic Ru-alkylidene metathesis catalysts.

Figure 3.

(top): X-ray crystal structures of $5_{\text{cyc}}\cdot\text{H}_2$, 6_{cyc} , and $6_{\text{cyc}}\cdot\text{H}_2$. Solvent molecules and hydrogens have been removed for clarity. Ellipsoids are drawn at the 50% probability level.

(bottom): ^1H NMR spectra (C_6D_6) of alkylidene proton of $5_{\text{cyc}}\cdot\text{H}_2$, 6_{cyc} , and $6_{\text{cyc}}\cdot\text{H}_2$.

Figure 4. REMP of COE using catalysts 4_{cyc} (green), 5_{cyc} (purple), $5_{\text{cyc}} \cdot \text{H}_2$ (orange), 6_{cyc} (blue), $6_{\text{cyc}} \cdot \text{H}_2$ (black), and 7_{cyc} (red). Conditions: CD_2Cl_2 , 40 °C, $[\text{M}/\text{C}]_0 = 1000:1$, $[\text{M}]_0 = 0.5 \text{ M}$. Conversion determined by ^1H NMR spectroscopy.

Figure 5.

Log plots for REMP of COE using catalysts 4_{cyc} (green), 5_{cyc} (purple), $5_{cyc} \cdot H_2$ (orange), 6_{cyc} (blue), $6_{cyc} \cdot H_2$ (black), and 7_{cyc} (red). Linear least-squares fitting gave R^2 values of: 4_{cyc} , 0.997; 5_{cyc} , 0.969; $5_{cyc} \cdot H_2$, 0.991; 6_{cyc} , 0.998; $6_{cyc} \cdot H_2$, 0.990; and 7_{cyc} , 0.991. Conditions: CD_2Cl_2 , 40 °C, $[M/C]_0 = 1000:1$, $[M]_0 = 0.5$ M. Data recorded using 1H NMR spectroscopy.

Figure 6. Left axis: Conversion of COE to PCOE using 5_{acyc} (black). Right axis: Mole fraction of 5_{cyc} (red), 5_{acyc} (blue), and A (green). Conditions: CD_2Cl_2 , 40 °C, $[COE/5_{acyc}]_0 = 250:1$, $[COE]_0 = 0.5$ M. Conversion determined by 1H NMR spectroscopy.

Scheme 1.
Proposed REMP catalytic cycle.

Scheme 2.

Synthesis of cyclic REMP catalysts **4_{cyc}** – **7_{cyc}**.

Scheme 3.

Synthesis of “saturated” catalysts **5_{cyc}·H₂** and **6_{cyc}·H₂**.

Scheme 4.

Proposed species observable upon ROMP of COE using open catalysts $5_{\text{acyc}} - 7_{\text{acyc}}$.

Scheme 5.
Equilibration of cyclic catalyst and linear PCOE.

Table 1Cyclization to give cyclic catalysts **4_{cyc}** – **7_{cyc}**.^a

cyclic catalyst	tether length	yield (%) ^b	
		0.01 M	0.001 M
4_{cyc}	4	62	81
5_{cyc}	5	76	97
6_{cyc}	6	81	97
7_{cyc}	7	0	63

^a Reactions conducted in dry C₆D₆ under N₂ atmosphere at 80 °C for 1 h.^b Determined by ¹H NMR spectroscopy.

Table 2
Selected ^1H NMR and single-crystal X-ray data for 4_{cyc} – 6_{cyc} , $5_{\text{cyc}}\cdot\text{H}_2$ and $6_{\text{cyc}}\cdot\text{H}_2$.

Catalyst	4_{cyc}	5_{cyc}	6_{cyc}	$5_{\text{cyc}}\cdot\text{H}_2$	$6_{\text{cyc}}\cdot\text{H}_2$
δH_2 (ppm) ^a	19.70	20.50	19.71	20.39	19.61
$^3J_{\text{H}_2,\text{P1}}$ (Hz) ^a	14.1	10.5	5.1	9.3	5.0
	<i>dihedral angles</i> (°)				
Cl2-Ru1-C2-C3	51.3	26.6	16.2	18.3	21.1
N1-C1-Ru1-C2	156.5	162.2	153.5	160.0	151.2
	<i>bond angles</i> (°)				
Cl1-Ru1-P1	171.0	166.0	163.3	165.3	168.8
N1-C1-Ru1	128.8	127.0	126.6	124.3	124.0
N2-C1-Ru1	127.8	128.9	129.4	128.1	129.5
N1-C1-N2	103.4	104.1	103.6	107.5	107.2
	<i>bond lengths</i> (Å)				
Ru1-Cl1	2.076	2.091	2.113	2.072	2.084
Ru1-C2	1.812	1.806	1.823	1.821	1.800
Ru1-P1	2.402	2.421	2.421	2.417	2.423

^aData taken in C_6D_6 at ambient temperature.

^bSee ref ⁹.

Efficient Synthesis of Narrowly Dispersed Brush Copolymers and Study of Their Assemblies: The Importance of Side Chain Arrangement

Yan Xia, Bradley D. Olsen, Julia A. Kornfield,* and Robert H. Grubbs*

Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125

Received October 2, 2009; E-mail: jak@cheme.caltech.edu; rhg@caltech.edu

Abstract: Efficient, one-pot preparation of synthetically challenging, high molecular weight (MW), narrowly dispersed brush block copolymers and random copolymers in high conversions was achieved by ring-opening metathesis (co)polymerization (ROMP) of various macromonomers (MMs) using the highly active, fast-initiating ruthenium olefin metathesis catalyst (H₂IMes)(pyr)₂(Cl)₂RuCHPh. A series of random and block copolymers were prepared from a pair of MMs containing polylactide (PLA) and poly(*n*-butyl acrylate) (PnBA) side chains at similar MWs. Their self-assembly in the melt state was studied by small-angle X-ray scattering (SAXS) and atomic force microscopy (AFM). In brush random copolymers containing approximately equal volume fractions of PLA and PnBA, the side chains segregate into lamellae with domain spacing of 14 nm as measured by SAXS, which was in good agreement with the lamellar thickness measured by AFM. The domain spacings and order–disorder transition temperatures of brush random copolymers were insensitive to the backbone length. In contrast, brush block copolymers containing approximately equal volume fractions of these MMs self-assembled into highly ordered lamellae with domain spacing over 100 nm. Their assemblies suggested that the brush block copolymer backbone adopted an extended conformation in the ordered state.

Introduction

Brush polymers are a type of high molecular weight (MW) graft polymers with very dense and regularly spaced side chains. They possess an interesting worm-like structure due to the high steric crowding of sides chains.¹ Their nonspherical macromolecular geometries and lengths up to a few hundred nanometers afforded numerous potential applications in nanoscience, such as molecular actuators,² templates for inorganic particles,^{3–5} and as precursors for nanocapsules,⁶ nanotubes,⁷ and other carbon nanostructures.⁸

On the other hand, linear block copolymers have proven to be versatile, powerful tools in the “bottom-up” approach to create nanostructured materials with novel mechanical, optical, and electronic properties and with specific functionalities over

the last few decades.⁹ When two or more different types of side chains are attached to a linear polymer backbone to form brush copolymers, each side chain may behave like a block segment in a block copolymer: they can be long enough to drive segregation, due to selective solubility or enthalpically favored demixing, yet are constrained by covalent attachment onto a single molecule. The spatial arrangement of different types of side chains along the backbone and their relative ratio should dramatically affect the assembly of the copolymers. The assembly of brush copolymers may also be profoundly affected by the limited flexibility of the brush polymer backbone as a result of the high steric hindrance between densely grafted side chains. On the other hand, the densely grafted side chains and extended conformation of brush polymers give them reduced entanglement density compared to their linear analogs. The reduced entanglement is a favorable feature to overcome the kinetic barrier for self-assembly, especially for ultrahigh MW polymers. Bowden and co-workers and Rzaev have recently found that brush–coil and brush–brush block copolymers can self-assemble into exceptionally large structures with domain

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spacing above 100 nm.^{10–12} Large domain structures are scientifically attractive and technically important with the potential to create periodic dielectric media to manipulate and control light, but have been challenging to achieve with linear block copolymers.^{13–16} However, self-assembly of brush copolymers has been much less explored relative to the vast number of reports on their linear copolymer analogs.^{10–12,17,18}

Well-defined macromolecular characteristics, such as the lengths of the backbone and side chains as well as the grafting density, are prerequisites to obtain ordered self-assembled structures. However, due to the complex architectures and demanding steric congestion, brush copolymers with controlled and high MW, low polydispersity (PDI), and complete side chain grafting remain challenging targets for polymer chemists. Current synthetic strategies to approach these targets normally involve multistep reactions and separations.

The most explored method to make brush polymers is “graft from”: the majority of previously reported brush block copolymers were synthesized by polymerizing different monomers from a diblock copolymer backbone using orthogonal polymerization mechanisms (i.e., radical polymerization and ring-opening polymerization).^{10–12,19,20} To grow distinct side chains from a given backbone requires orthogonal polymerization mechanisms and/or selective protection/deprotection and subsequent functionalization of the copolymer backbone. Furthermore, the initiation efficiency of the macroinitiators may be limited,^{12,21,22} and the monomer conversions must be kept low to avoid cross-linking due to the high density of initiating sites.^{2,6–8,10–12,19–22} Alternatively, preformed side chains can be “grafted onto” a polymer backbone to prepare brush polymers.^{23–25} Lanson et al. recently prepared brush block copolymers^{23,26} and random copolymers¹⁸ by grafting anionically prepared side chains onto polymers with pendent functional groups and by a combination of “graft from” and “graft onto” methods. However, purification to remove the unreacted side chains was required in each grafting step and repetitive protection and deprotection

of the backbone functional groups was required to synthesize brush block copolymers.

On the other hand, the macromonomer (MM) approach toward brush copolymers is highly desirable,²⁷ because (1) it does not require orthogonal, noninterfering chemistry for grafting different side chains; (2) the side chain and the graft polymer can be well characterized; and (3) it is the only approach that guarantees complete grafting on every repeating unit. However, the macromonomer (MM) approach toward brush block copolymers is exceedingly challenging due to steric hindrance at the propagating polyMM chain end. Brush-coil block copolymers and brush random copolymers have been reported using uncontrolled metallocene-catalyzed¹⁷ or radical²⁸ polymerizations and polycondensation²⁹ of MMs. As a result, the final graft polymers were polydisperse, and the MM conversion was limited. Neugebauer et al. reported copolymerization of MMs containing poly(ethylene oxide) and poly-(dimethylsiloxane) or octadecane side chains by atom transfer radical polymerization (ATRP) to produce random or gradient brush copolymers depending on the relative polymerization rates of MMs.^{30,31} However, the MMs used in those reports were relatively small and less hindered (MW ≤ 1100) and no brush block copolymers were reported.

Here we show that ring-opening metathesis polymerization (ROMP) can be used to overcome the obstacles to well-defined brush copolymers by taking advantage of the high ring strain of norbornene monomer and the high activity of Ru-based olefin metathesis catalyst. In contrast to prior reports of ROMP synthesis of short graft block copolymers using molybdenum-based catalyst that were limited to oligomers with 5–10 side chains per block (star-like rather than brush-like architectures),^{32,33} the present polymers have DP up to 200 per block. The present method builds on the highly efficient syntheses we recently demonstrated for a variety of ultrahigh MW brush polymers with controlled MW (up to 2600 kg/mol) and very low PDI (1.01–1.07) using the highly active, fast-initiating Ru olefin metathesis catalyst (H₂IMes)(pyr)₂(Cl)₂RuCHPh (**1**). Atomic force microscopy (AFM) revealed their worm-like structure and narrow PDI.³⁴

In this work, we utilized ROMP of MMs to efficiently prepare a library of high MW, narrowly dispersed brush copolymers with different side chains, including brush block copolymers and brush random copolymers, each in one pot. ROMP of MMs allowed for facile control of the side chain and backbone block lengths and virtually arbitrary selection of side chains. To the best of our knowledge, this report contains the first examples of high MW, narrowly dispersed brush block copolymers

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Figure 1. Schematic illustration of the synthesis of brush block copolymer through sequential addition (top) and brush random copolymer through random copolymerization (bottom) of MMs.

Scheme 1. Synthesis of Macromonomers^a

^a Conditions: (a) NaN_3 , DMF, 25 °C. (b) CuBr , PMDETA, THF, 50 °C. (c) $\text{Sn}[\text{CH}_3(\text{CH}_2)_3\text{CH}(\text{C}_2\text{H}_5)\text{CO}_2]_2$, 120 °C.

prepared sequentially via living polymerization of MMs.³⁵ The well-defined molecular characteristics of these brush copolymers provided an excellent model system to study the effect of side chain arrangement on the backbone and the relative ratio of the MMs on the self-assembly of brush copolymers. Specifically, we compared brush block copolymers (Figure 1, top) to brush random copolymers (Figure 1, bottom), showing that they provide convenient routes to self-assembled nanostructures with the backbone either predominantly orthogonal to the “intermaterial dividing surface”³⁶ or localized to the “intermaterial dividing surface”, respectively.

Results and Discussion

Syntheses of Brush Copolymers. We have synthesized ω -norbornenyl MMs containing poly(*n*-butyl acrylate) (PnBA), poly(*t*-butyl acrylate) (PtBA), and polystyrene (PS) side chains, according to our reported procedure.³⁴ “Click” coupling of a norbornenyl group to the chain ends of polymers made by ATRP was used to prevent the unfavorable copolymerization of norbornene during ATRP.^{37,38} ω -Norbornenyl MMs containing polylactide (PLA) side chains were also synthesized from ring-opening polymerization of D,L-lactide using a norbornenyl alcohol as the initiator and stannous octoate as the polymerization catalyst (Scheme 1). All MMs were narrowly dispersed. A high degree of norbornenyl end group functionalization was confirmed from good agreement between the degree of polymerization (DP) calculated by end group analysis using ^1H NMR spectroscopy (DP_{NMR}) and the DP calculated from the absolute

Table 1. Characteristics of ω -Norbornenyl Macromonomers and Their Polymerization Rates

MM ^a	M_n^b (kDa)	PDI ^b	DP_{NMR}^c	DP_{GPC}^d	k_p (min^{-1}) ^e	$k_{p,\text{rel}}^f$
NB(PS)6.6k	6.6	1.02	66	60	0.079	1
NB(PS)2.2k	2.2	1.03	19	17	0.092	1.2
NB(PtBA)4.7k	4.7	1.03	33	33	0.13	1.7
NB(PLA)7.0k	7.0	1.12	46	47	0.24	3.0
NB(PLA)4.7k	4.7	1.06	28	31	0.35	4.4
NB(PnBA)4.0k	4.0	1.06	29	28	0.33	4.2

^a Macromonomers were named using a format of NB(X)Y, with X designating the type of prepolymer and Y designating the M_n of macromonomer. ^b Determined by GPC in THF using refractive index (RI) and MALLS detectors. ^c Calculated by comparing the integrations of the norbornenyl olefin and polymer backbone proton signals from ^1H NMR spectra in CDCl_3 . ^d Calculated by $(M_n - \text{molar mass of norbornenyl end group})/\text{molar mass of monomer}$. ^e Conditions: $[\text{MM}]_0 = 0.05$ M in THF at room temperature, $[\text{MM}/\text{C}]_0 = 200$. ^f $k_{p,\text{rel}}$ is the relative rate constant with respect to k_p of NB(PS)6.6k.

Figure 2. Dependence of $\ln([\text{MM}]_0/[\text{MM}]_t)$ on time for ROMP of MMs. Conditions: $[\text{MM}]_0 = 0.05$ M in THF at room temperature, $[\text{MM}/\text{C}]_0 = 200$. The dashed lines are best-fit lines.

MWs obtained from gel permeation chromatography (GPC) coupled with a multiangle laser light scattering (MALLS) detector (Table 1).

Polymerization of all these MMs using Ru catalyst **1** followed linear first-order kinetics (Figure 2). GPC analyses of the polyMMs each showed narrow, monomodal peaks, and MWs increased linearly with conversion while the PDI remained less than 1.1 throughout the entire polymerization (Supporting Information Figure S2a). Furthermore, all MMs reached greater than 90% conversion within 1 h at room temperature (Supporting Information Figure S2b). Although very weak signals that may correspond to MMs can be observed in the GPC traces of the crude polymer products, NMR spectroscopy of the reaction mixtures revealed the absence of the MM norbornene olefin signal. Therefore, the residual low MW peak may correspond to a small fraction of side chains with unfunctionalized chain ends in the MM. These observations collectively indicated the well-controlled character of ROMP of MMs and the extraordinary activity of catalyst **1**.

Due to the high activity of catalyst **1** and low critical monomer concentration of norbornene, the ROMP of MM can be performed at very low concentration ($[\text{MM}]_0 = 0.05$ M) to keep a relatively low viscosity of the solution throughout the polymerization. This is a distinct advantage over free radical polymerization of MMs.^{39–42} Therefore, the polymerization is unlikely to be diffusion controlled (at least until the very late

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stage of the polymerization), in accord with the approximately linear first-order kinetics up to high conversions (>85%).

The polymerization rates, measured from the kinetic plot, depended weakly on both the MW and the structure of the MM (Table 1). In general, polyacrylate and polylactide MMs polymerized faster than polystyrene MMs. For example, NB(PLA)7.0k polymerized about 3 times faster than NB(PS)6.6k despite their similar MW. The nature of the effects of side chain structure and MW on the polymerization rate of MMs warrants further investigation. It may be the local steric congestion around the propagating metallocycle or different solvent quality for various polymers that is causing the observed difference in the polymerization rate. Although the relative polymerization rates of different MMs varied less than an order of magnitude, they are significant when statistical copolymerization is attempted, since the relative polymerization rates can determine the distribution of side chains along the backbone (i.e., random vs gradient).

The controlled nature of the ROMP of MMs and the very high conversions motivated us to prepare brush block copolymers via simple sequential addition of MMs: Polymerization was initiated by injecting catalyst from a stock solution into a solution of the first type of MM at room temperature. As soon as the MM has been all consumed and only unfunctionalized side chains remained, a solution of a second type of MM was injected into the reaction mixture. GPC was used to analyze the reaction mixtures before the injection of the second MM and after completion of the second block polymerization. The GPC peak had shifted from the first block homopolymer to a shorter elution time corresponding to the brush diblock copolymer. The peak shape remained narrow without significant tailing, and the PDI remained low (≤ 1.10) (Figure 3). The low PDI was also indicated by the complete overlap of the light scattering trace and refractive index trace from GPC. Only very weak signal was observed between 16 and 18 min in elution time, and this may correspond to unfunctionalized side chains in some of the MMs used. For example, in the brush PS and PnBA block copolymer, the intensity of the low MW peak remained similar in the first PS block and the diblock copolymer (Figure 3B), which may correspond to unfunctionalized side chains in the PS MM. The order of addition of different MMs did not affect the MW or the PDI of the final block copolymers. Therefore, different MMs were arbitrarily polymerized sequentially to give various brush block copolymers, and the DP of each block was easily controlled by the ratio of MM to catalyst ([MM]/[C]). With narrow PDIs less than 1.1, regardless of the MW and combination of MMs, the MW of the copolymers measured by GPC-MALLS is close to or slightly higher than the theoretical MW. GPC analysis of the reaction mixture revealed the final conversions of MM to be greater than 90% in all the copolymerizations, while NMR spectroscopy showed no MM norbornene olefin signal.

PnBA side chains in the brush block copolymers can be hydrolyzed into poly(acrylic acid) (PAA) using TFA in CH_2Cl_2 , leaving the other block and the backbone intact, as indicated by NMR spectroscopy (Supporting Information Figure S1). Thus, amphiphilic block brush copolymers were also easily obtained.

Figure 3. Representative GPC RI traces of the first block brush homopolymer (right) and the brush diblock copolymer (left) without any purification. (A) $(\text{PNB-g-PnBA})_{100}\text{-b-(PNB-g-PnBA)}_{100}$; (B) $(\text{PNB-g-PS})_{100}\text{-b-(PNB-g-PnBA)}_{50}$; (C) $(\text{PNB-g-PLA})_{100}\text{-b-(PNB-g-PnBA)}_{100}$.

The side chain distribution along the brush copolymer backbone can dominantly affect the macromolecular packing in order to minimize the interfacial energy while retaining relatively extended backbone conformation. In this report, we focus on the study of the melt state self-assembly of copolymers containing PLA and PnBA side chains. We chose MMs NB(PLA)4.7k and NB(PnBA)4.0k as the side chains, because they possess very similar MWs and polymerization rates, and their copolymers can be thermally annealed relatively easily due to their low T_g 's. These features allowed us to easily prepare a series of brush block and random copolymers with the same pair of side chains and matched backbone length, but varying the relative ratio of the two MMs (Table 2, entry 7–15). Brush block copolymers, $g\text{-[PLA}_x\text{-b-PnBA}_y\text{]}$, with varied block lengths and ratios were synthesized via sequential addition of MMs. Brush random copolymers, $g\text{-[PLA}_x\text{-ran-PnBA}_y\text{]}$, with varied total backbone length and side chain composition were synthesized via initiating a mixture of two MMs (Figure 3). Note that the subscripts x and y represent the number of side chains of each type—not the DP of the side chains, which was held fixed at approximately 30 for both the PLA and PnBA side chains (see the last two rows of Table 1). Since the ROMP of these MMs proceeded to very high conversions (>97%) and only a minute amount of catalyst was used (0.04–0.16 wt % to MMs used), no attempts to purify the polymer products were made. All polymer samples were simply dried under vacuum to remove solvent. These samples provided a model series to study how

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Table 2. Characteristics of Brush Copolymers

entry	MM ₁	MM ₂	type of copolymer	[MM ₁ /C]:[MM ₂ /C] ^a	conv ^b	M _{n,theo} (kDa) ^c	M _{n,GPC} (kDa) ^d	PDI ^d
1	PS6.6k	PnBA4.0k	block	40:70	91%	540	730	1.04
2	PS6.6k	PnBA4.0k	block	40:200	91%	1060	1230	1.04
3	PrBA4.7k	PnBA4.0k	block	100:100	97%	870	890	1.05
4	PrBA4.7k	PnBA4.0k	block	100:200	98%	1270	1260	1.04
5	PS2.2k	PrBA4.7k	block	50:50	96%	345	340	1.03
6	PS2.2k	PrBA4.7k	block	100:50	94%	455	540	1.04
7	PLA4.7k	PnBA4.0k	block	20:180	98%	810	820	1.08
8	PLA4.7k	PnBA4.0k	block	40:160	97%	830	890	1.08
9	PLA4.7k	PnBA4.0k	block	100:100	97%	870	980	1.07
10	PLA4.7k	PnBA4.0k	block	200:200	96%	1740	1770	1.09
11	PLA4.7k	PnBA4.0k	random	50:50	98%	435	450	1.06
12	PLA4.7k	PnBA4.0k	random	100:100	97%	870	1050	1.05
13	PLA4.7k	PnBA4.0k	random	200:200	98%	1740	1880	1.10
14	PLA4.7k	PnBA4.0k	random	160:40	98%	910	1030	1.04
15	PLA4.7k	PnBA4.0k	random	130:70	98%	890	1030	1.05

^a Ratio of each MM to Ru catalyst. ^b Conversion of MM to brush copolymer is determined by comparing the peak areas of brush copolymer and residual MM from GPC measurement of the final crude product without any purification. ^c $M_{n,theo} = M_{n,GPC}(MM_1) \times [MM_1/C] + M_{n,GPC}(MM_2) \times [MM_2/C]$. ^d Determined by THF GPC using RI and MALLS detectors.

Table 3. Molecular and Morphological Characteristics of PLA-PnBA Brush Random and Block Copolymers

	f_{PLA}^a	$T_g, PLA/^\circ C^b$	$d(SAXS)/nm^c$	$d(AFM)/nm^d$	$T_{ODT}/^\circ C^e$
<i>g</i> -[PLA ₅₀ - <i>ran</i> -PnBA ₅₀]	0.49	38	14.2	18	80
<i>g</i> -[PLA ₁₀₀ - <i>ran</i> -PnBA ₁₀₀]	0.49	38	14.0	21	85
<i>g</i> -[PLA ₂₀₀ - <i>ran</i> -PnBA ₂₀₀]	0.49	38	14.6	17	75
<i>g</i> -[PLA ₁₃₀ - <i>ran</i> -PnBA ₇₀]	0.63	39	—	—	—
<i>g</i> -[PLA ₁₆₀ - <i>ran</i> -PnBA ₄₀]	0.79	42	—	—	—
<i>g</i> -[PLA ₁₀₀ - <i>b</i> -PnBA ₁₀₀]	0.49	49	116	—	—
<i>g</i> -[PLA ₄₀ - <i>b</i> -PnBA ₁₆₀]	0.19	49	—	—	—
<i>g</i> -[PLA ₂₀ - <i>b</i> -PnBA ₁₈₀]	0.09	—	64	—	—

^a Volume fraction of PLA calculated using densities $\rho_{PnBA} = 0.99$ g/mL, $\rho_{PLA} = 1.25$ g/mL. ^b T_g of PLA side chain, measured by DSC with heating rate of 15 °C/min. ^c Domain spacing determined by SAXS. ^d Lamellar thickness determined by AFM cross-sectional analysis. ^e Order–disorder transition temperature determined by SAXS.

side chain distribution along the brush copolymer backbone affects brush copolymer self-assembly in the melt state.

Thermal Analyses of Brush (Co)polymers. DSC analysis revealed the architectural effect of brush homopolymers and copolymers on the T_g of their side chains. For a PLA brush homopolymer (backbone DP=200) synthesized using NB(PLA)4.7k, a single thermal transition at 49 °C was observed in the temperature range of 0–200 °C scanned. This temperature corresponded to the T_g of amorphous PLA side chains and is close to the literature values. The T_g of the brush homopolymer was higher than that of the MM (42 °C), due to the increased MW and/or the increased molecular constraint resulting from linking the side chains along the formed polynorbornene backbone.⁴³ The T_g of PLA side chains in brush block copolymers was found to be about 49 °C, close to that of the PLA brush homopolymer, except for PLA₂₀-*b*-PnBA₁₈₀ whose signal was too weak to enable accurate T_g determination (Table 3). This is consistent with phase separation in the block copolymers to form two distinct domains. In contrast, the T_g of PLA was found to be lower in the brush random copolymers, and increasing the PnBA content resulted in further suppression of the T_g of PLA. However, the T_g 's of brush random copolymers were similar to that of the PLA MM, which indicated microphase separation of PLA and PnBA side chains. With equal amounts of PLA and PnBA in the brush random copolymers, the T_g was found to be 38 °C (Table 3). The lower

Figure 4. SAXS curves for brush random copolymers, *g*-[PLA-*ran*-PnBA].

T_g of PLA in random copolymers may be a result of smaller domain sizes than those in brush block copolymers.

Self-Assembly of Brush Copolymers in the Melt State. We investigated the self-assembly of brush copolymers in bulk using small-angle X-ray scattering (SAXS) and in thin films using AFM. These two techniques provide complementary information about the self-assembled morphology and domain spacing.

Brush random copolymers, *g*-[PLA-*ran*-PnBA], were thermally annealed at 100 °C for 12 h in order to achieve equilibrium, and prolonged annealing did not result in any further structural change. Brush random copolymers with an equal number of PLA and PnBA side chains (symmetric) exhibited a sharp principal SAXS peak at wavevector q^* along with peaks at integer multiples of q^* (Figure 4). This is indicative of a lamellar morphology, as expected due to the near symmetric volume fractions of the PLA and PnBA segments ($f_{PLA} = 0.49$). The domain spacing (d) calculated from q^* is very similar, 14.3 ± 0.3 nm, for all three symmetric random copolymers, independent of their backbone length. The inde-

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Figure 5. Inverse intensity of peak heights in the vicinity of the order–disorder transition for brush random copolymers, g -[PLA-*ran*-PnBA]. The arrows mark the T_{ODT} 's.

pendence of d -spacing on backbone length and the lamellar morphology suggests that the polynorbornene backbone is confined at the interface between PLA and PnBA layers, with the PLA and PnBA side chains segregated to opposite sides of the brush polymer backbone to minimize contact between dissimilar chains.

Furthermore, as the symmetric random copolymers were heated, they underwent a transition from an ordered lamellar phase into a microphase disordered regime. The order–disorder transition (ODT) temperature, T_{ODT} , can be evaluated using the discontinuity in the plot of inverse primary peak intensity vs inverse temperature (Figure 5), using SAXS patterns acquired in 5 °C step ramping with 5 min thermal equilibration at each temperature. This was accompanied by the disappearance of higher order peaks. The T_{ODT} was found to hardly change, giving 75–85 °C for g -[PLA₅₀-*ran*-PnBA₅₀], g -[PLA₁₀₀-*ran*-PnBA₁₀₀], and g -[PLA₂₀₀-*ran*-PnBA₂₀₀] as the MW increased from 450 to 1880 kDa. The broad scattering peak in SAXS that remained above the ODT originated from intramolecular correlations of block copolymers.⁴⁴ For a wide range of block copolymers, T_{ODT} is controlled by the product of the Flory–Huggins interaction parameter χ and the total degree of polymerization N .⁴⁴ The similar T_{ODT} 's observed for the brush random copolymers over a wide range of the brush backbone length suggested that the degree of polymerization N of the side chains dictates the T_{ODT} . This is consistent with side chain microphase separation with the backbones localized at interfaces between PLA and PnBA domains (Figure 6, top).

We studied the morphology of brush random copolymers in thin films using AFM. Based on the T_{ODT} determined using SAXS, these samples were annealed at 70 °C, which is below the T_{ODT} but still above the T_g of PLA. AFM showed that the films were featureless before annealing (Figure 7a). After annealing, a layer of islands with very uniform height was clearly observed for each of the symmetric random copolymers (Figure 7b–d). An island layer is formed if the natural repeat spacing of a parallel oriented block copolymer is incommensurate with the film thickness, and the film segregates excess material to the top surface to form an incomplete layer.^{45–47} The height difference between the thicker and thinner regions of the film is equal to the natural period of the block copolymer.

Figure 6. Proposed assembly of symmetric brush random copolymer and block copolymer.

Here the island layers are remarkably uniform across areas of tens of micrometers, with thickness of 17–20 nm for all three samples. The height values are very close to the bulk d -spacings measured by SAXS, indicating that the domain spacing of parallel oriented lamellae in the film is similar to domain spacing in the bulk.

Due to the independence of lamellar thickness on brush polymer MW, we propose that uniform lamellar structures can be obtained using polydisperse brush copolymer samples. Indeed, an indistinguishable “islands and holes” morphology with 17–20 nm in height was obtained from blends of any two of the symmetric random copolymers at arbitrary ratios after annealing. This further supports the complete dominance of the side chains in governing the self-assembly of these brush random copolymers.

In contrast to the symmetric random copolymers, when PLA and PnBA side chains were incorporated in uneven amounts (Table 2, entry 14 and 15), ordered microphase separation of the side chains was not observed: No structural features were observed in thin films by AFM after extensive annealing at temperatures ranging from 75 to 140 °C. SAXS of g -[PLA₁₆₀-*ran*-PnBA₄₀] and g -[PLA₁₃₀-*ran*-PnBA₇₀] showed only one broad peak with no higher order peaks; the single peak corresponds to intramolecular correlations between side chains of the block copolymers. Furthermore, the peak intensity continuously decreased upon heating, and no ODT was observed (Supporting Information Figure S5). As the side chains microphase separate to opposite sides of the backbone, the resulting asymmetric space filling on the backbone makes it impossible to assemble into lamellae. Meanwhile, the backbone of a brush polymer may be more difficult to coil than a linear polymer to adopt other morphologies, as a result of the high congestion of the segregated side chains.

We next investigated the self-assembly of brush block copolymers, g -[PLA-*b*-PnBA]. Due to the very large domain spacing in the assembled brush block copolymers, principal q^* was out of the q range obtainable by SAXS in some samples (Figure 8). For the symmetric block copolymer, g -[PLA₁₀₀-*b*-PnBA₁₀₀], multiple higher-order scattering peaks up to the 12th order were clearly observed. The even distribution of scattering peaks to $12q^*$ indicated remarkably well-ordered lamellar morphology with a d -spacing of 116 nm, consistent with the fact that principal q^* was out of the q range obtainable by SAXS. This length scale is close to the fully extended length of a polynorbornene brush homopolymer with backbone DP = 220

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Figure 7. AFM height images of brush random copolymer thin films (120–150 nm) on silicon wafer and their cross sectional analysis. (a) g -[PLA₁₀₀-*ran*-PnBA₁₀₀] as cast, and after annealing (b) g -[PLA₅₀-*ran*-PnBA₅₀], (c) g -[PLA₁₀₀-*ran*-PnBA₁₀₀], (d) g -[PLA₂₀₀-*ran*-PnBA₂₀₀]. The vertical scale is 30 nm for (a) and 100 nm for (b–d).

Figure 8. SAXS curves for brush block copolymers, g -[PLA-*b*-PnBA].

Figure 9. AFM phase images of (a) individual PLA brush homopolymers ($DP_{\text{backbone}} = 200$, MM NB(PLA)4.7k was used) on mica; (b) brush block copolymer, g -[PLA₁₀₀-*b*-PnBA₁₀₀], morphology in thin film (ca. 120 nm) as cast from 2.5% toluene solution onto silicon wafer.

and PS side chains of 6.6 kDa, as previously observed by AFM.³⁴ Although clear AFM imaging of individual g -[PLA₁₀₀-*b*-PnBA₁₀₀] polymers has been difficult due to the aggregation of molecules, AFM revealed worm-like shapes with contour lengths of ca. 110–130 nm for a PLA brush homopolymer with backbone $DP = 200$ prepared using the same MM as in the block copolymer (Figure 9a). Therefore, the large lamellar d -spacing of g -[PLA₁₀₀-*b*-PnBA₁₀₀] is dictated by the length of its highly extended polynorbornene backbone and suggests interdigitated packing of the molecules in the lamellae (Figure 6 bottom). The highly ordered self-assembly structure also supports the well-controlled macromolecular characteristics of

Figure 10. Photograph of slowly dried g -[PLA₂₀₀-*b*-PnBA₂₀₀] (Table 2, entry 10) showing green color due to reflectance from the large self-assembled domains.

the brush copolymers obtained from ROMP of MMs. Notably, the larger symmetric block copolymer g -[PLA₂₀₀-*b*-PnBA₂₀₀] (Table 2, entry 10) appeared green spontaneously upon slowly evaporating the solvent (Figure 10). This indicates that the domain spacing in this ultrahigh MW sample is large enough to reflect green light.⁴⁸

On the other hand, highly asymmetric block copolymers, g -[PLA₂₀-*b*-PnBA₁₈₀] and g -[PLA₄₀-*b*-PnBA₁₆₀], formed non-lamellar morphologies. Both materials showed scattering peaks at very low q , a feature indicative of microphase separation, with q^* inaccessible for g -[PLA₄₀-*b*-PnBA₁₆₀] and q^* corresponding to a domain spacing of 64 nm for g -[PLA₂₀-*b*-PnBA₁₈₀]. Based on the domain spacing for g -[PLA₂₀-*b*-PnBA₁₈₀], it is clear that the backbone is not fully extended in its highly asymmetric polymer. In addition, both polymers show oscillations at higher q that originate from the form factor of the block copolymer aggregates.⁴⁹ Although the quality of fits is not sufficient to identify the specific shape of the aggregates, the period of the oscillations allows us to identify the characteristic size of the presumably spherical or cylindrical PLA domains with sizes of 38 and 67 nm in diameter, respectively,

(48) The wavelength of the reflected light at the interfaces of multilayer lamellae is governed by: $\lambda = 2(n_1d_1 + n_2d_2)$, where n and d are the refractive index and the thickness of each layer. In a rough estimate, taking $n_1 = n_2 = 1.5$ for both polymer layers and $\lambda = 500$ nm for green light, the domain spacing is calculated to be about 170 nm for a symmetric lamellar morphology presumably formed in the symmetric block copolymer g -[PLA₂₀₀-*b*-PnBA₂₀₀].

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irregularly distributed in a matrix of PnBA. In addition, the PLA domain size is consistent with the calculated result using the domain spacing of 64 nm obtained from q^* and 9% PLA volume fraction in g -[PLA₂₀- b -PnBA₁₈₀]. The nonlamellar morphologies formed from these asymmetric brush block copolymers suggest that the backbone is not as fully extended as in the symmetric brush block copolymer, g -[PLA₁₀₀- b -PnBA₁₀₀]. On the other hand, the decreased ordering in asymmetric block copolymers suggests frustrated packing when the backbone has to adopt nonlamellar morphologies due to its reduced flexibility. Similar packing frustration has also been suggested for asymmetric brush block copolymers with side chains of different MWs.¹²

Thin films of the block copolymer g -[PLA₁₀₀- b -PnBA₁₀₀] after spin-coating from toluene solution showed large cylindrical micellar structures of 200 nm wide and several micrometers long as imaged by AFM (Figure 10b), in sharp contrast to the featureless as-cast film from the random copolymer, g -[PLA₁₀₀- ran -PnBA₁₀₀], at the same MW and composition (Figure 7a). After annealing, the surface topology became rough, but clear phase separation was observed from the sharp contrast in the phase image, which derives from mechanical property differences between the PLA and PnBA blocks in the copolymers (Supporting Information Figure S7). Microphase separation in thin films of the asymmetric brush block copolymers was also observed from the AFM phase images. However, the structural assignment for the thin film morphologies of these brush block copolymers was unclear. This is because the film thickness is similar to the polymer domain spacing in bulk and corresponds to one layer of molecular packing. Therefore, the surface effect on the thin film morphology makes it difficult to correlate to the bulk morphology for large brush block copolymers.

Conclusions

ROMP of various MMs bearing polyacrylate, polystyrene, and polylactide chains using highly active, fast initiating Ru catalyst has shown typical characteristics of a living polymerization, such as first-order kinetics and linear MW growth with increasing conversion. The living nature of ROMP and very high conversion (>90%) of MMs have allowed facile one-pot preparation of a variety of high MW narrowly dispersed brush block and random copolymers in high conversions, which otherwise involve multiple steps to synthesize using different grafting techniques. The length of each block and the overall backbone can be easily controlled by the ratio of MM to catalyst.

By choosing MMs with the similar polymerization rates, we prepared a series of brush block and random copolymers from a pair of MMs, NB(PLA)4.7k and NB(PnBA)4.0k, varying their relative ratios. In symmetric brush random copolymers (equal number of PLA and PnBA side chains), the side chains were found to microphase separate into lamellar morphology with domain spacing of about 14 nm as determined by SAXS. AFM studies of thin film samples also revealed lamellar structures with similar thickness of 17–21 nm. The domain spacing and T_{ODT} were insensitive to the brush copolymer backbone length, suggesting microphase separation of side chains to opposite sides of the brush polymer backbone and that the side chains played a dominant role in the self-assembly. On the other hand, the brush block copolymer with the same number of PLA and PnBA side chains self-assembled into highly ordered, large lamellar domains over 100 nm as revealed by SAXS. The domain size was dictated by the backbone length.

Asymmetric brush copolymers containing different numbers of two types of side chains did not form well-ordered morphologies. This may be attributed to the reduced backbone flexibility of brush polymers and their increased difficulty to adopt coiled conformations.

Controlled ROMP of MMs greatly simplifies the syntheses of brush copolymers. The combination of facile synthesis and good structural control of brush copolymers with the functional group tolerant Ru catalyst opens the door to further studies of the self-assembly of these macromolecular architectures. Brush copolymers provide a unique macromolecular platform for bottom-up assembly to form nanostructures with large domain spacings and controlled intermaterial dividing surfaces.

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Supporting Information Available: Experimental section, ¹H NMR spectra, GPC traces, and DSC traces of MMs and brush copolymers, conversion and MW growth profiles for ROMP of MMs, and additional AFM images. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Synthesis and Direct Imaging of Ultrahigh Molecular Weight Cyclic Brush Polymers**

Yan Xia, Andrew J. Boydston, and Robert H. Grubbs*

Polymer architectures and nanostructures have profound effects on the materials properties, and significant progress has been made in controlling polymer architectures with the development of new polymerization techniques.^[1] Brush polymers or densely grafted polymers represent an important class of nanoscale macromolecular architectures.^[2] The extremely high congestion arising from the high density of side chains forces the macromolecular backbone to adopt an extended conformation that forces brush polymers into worm-like nanoscale structures and bestows unique properties in comparison with conventional coiled polymers.^[3]

Over the past decade, linear and star-shaped brush polymers have been synthesized and molecular imaging has shown their distinct worm-like and star-like nanostructures.^[4] However, cyclic graft polymers that exhibit toroidal nanostructures remain very rare, partly due to the challenging synthesis of high MW cyclic polymers with high grafting density required to achieve nanoscale features. An inspiring example of high MW cyclic brush polymers was recently reported by Deffieux and co-workers.^[5] In their synthesis, an ABC triblock linear copolymer was used in order to prepare high MW cyclic polymer by ring-closing under high dilution conditions, and subsequent grafting of living anionic polystyrene chains to the backbone afforded cyclic brush polymer. Atomic force microscopy (AFM) clearly revealed the toroidal nanostructures of cyclic brush polymers on the surface, but linear, figure-eight, tadpole, and catenane shapes were also observed as a result of side reactions during the ring-closing reaction.^[6] Since the synthesis involved multiple steps and required high dilution and stringent conditions, we sought an alternative route to synthesize high MW brush polymers and achieve cyclic nanostructures. Our group has developed a series of Ru-based catalysts (Scheme 1) that mediate ring-expansion metathesis polymerization (REMP) to produce high MW cyclic polymers under simple experimental conditions without necessitating high dilution conditions by an end-linking approach.^[7] With the Frechét group, we recently showed that cyclic dendronized polymers synthesized using

Scheme 1. Cyclic olefin metathesis catalysts.

these catalysts indeed adopted toroidal shapes with internal diameters of 5–7 nm.^[8] During publication of this manuscript, the Tew group also reported the use of REMP for the synthesis of cyclic polymer templates that were converted to cyclic brush polymers via a “graft-to” approach.^[9] Herein, we report the synthesis of ultrahigh MW cyclic brush polymers by a one-pot “graft through” approach, and direct imaging of their large toroidal nanostructures by AFM.

We investigated direct REMP of macromonomers (MMs) that we have used previously for the synthesis of linear brush polymers.^[10] Initial attempts using less active cyclic catalysts **UC-5** and **UC-6** were unsuccessful, with only minimal conversion of MMs. In contrast, when more active catalysts (**SC-5** and **SC-6**) were used, moderate to high conversions were obtained within a few hours for each of the MMs attempted, giving highly viscous or solidified reaction media. Notably, each of the obtained brush polymers was readily redissolved in good solvents (e.g., CH_2Cl_2 , THF, toluene, etc). Their MWs were all extremely high in the range of 1.9 to 26×10^6 Da and exceeded our GPC separation limit. Thus, absolute MWs were determined by static light scattering and used to calculate the degree of polymerization (DP) of the brush polymer backbones. To our knowledge, the MWs of these cyclic brush polymers are among the highest for any structure of graft/brush polymers reported to date. The MW distribution was broad as a result of slow initiation of REMP catalysts. The MM conversion was dependent on a combination of catalyst activity as well as MM structure and MW. In general, the MM conversion and DP of cyclic brush polymer decreased with increasing MW of the MM. For example, when the MW of ω -norbornenyl polystyrene MM (Scheme 2) increased from 2200 to 6600 Da, the conversion decreased from 93 % to 65 %, with concomitant decrease in DP from 4100 to 880 (Table 1). Notably, the MWs of these cyclic brush polymers significantly exceeded those of the linear brush polymers we previously synthesized using ring-opening metathesis polymerization (ROMP).^[10]

We have previously used AFM to directly image individual linear brush polymers prepared from these MMs, and observed linear, extended worm-like nanostructures.^[10a]

[*] Dr. Y. Xia, Dr. A. J. Boydston, Prof. R. H. Grubbs
Division of Chemistry and Chemical Engineering
California Institute of Technology
Pasadena, CA 91125 (USA)
Fax: (+1) 626-564-9297
E-mail: rhg@caltech.edu

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Scheme 2. Synthesis of cyclic brush polymer from REMP of ω -norbornenyl MM.

Herein, we used identical sample preparation and imaging conditions to image the cyclic brush polymers. Brush polymers with large PS side chains (**NB(PS)6600**) on graphite surface gave the clearest AFM images of individual molecules. As shown in Figure 1, various large ring-shaped nanostructures were clearly observed, either as small aggregates or as individual rings, together with some linear chains. All the observed nanostructures, both cyclic and linear, had uniform width of 30–40 nm and height of 1–2 nm, which are consistent with the linear brush polymer we previously prepared by ROMP of the same MMs. Most cyclic structures have diameters in the range of 100–180 nm, corresponding to contour lengths of 310–560 nm. We have previously measured the average length per monomeric unit to be 0.6 nm,^[10a] using uniform, narrowly dispersed linear brush polymers with the same side chain. Therefore, a contour length of 310–560 nm corresponds to a backbone DP of ca. 500–900, which is close to the calculated backbone DP (880) based on the absolute MW measured by light scattering. Additionally, all the cyclic

Table 1: REMP of Macromonomers.^[a]

No.	Macromonomer ^[b]	Cat.	M_w ($\times 10^6$ Da) ^[c]	PDI ^[d]	DP _{back} ^[e]	Conv. ^[f]
1	NB(PS)2200	SC-5	9.1	1.2	4100	93%
2	NB(PS)3200	SC-5	6.2	1.1	1900	74%
3	NB(PS)6600	SC-5	5.8	1.1	880	67%
4 ^[g]	NB(PS)6600	SC-5	5.7	1.2	860	55%
5	NB(PLA)4400	SC-5	13	1.4	3000	92%
6	NB(PLA)8700	SC-5	26	1.1	3000	79%
7	NB(PS)2200	SC-6	2.4	1.2	1100	89%
8	NB(PS)6600	SC-6	6.5	1.1	1000	78%
9	NB(PnBA)4000	SC-6	4.0	1.3	1000	> 99%
10	NB(PLA)4400	SC-6	1.9	1.5	430	> 99%
11	NB(PLA)8700	SC-6	6.0	1.4	690	98%

[a] Conditions: [MM]/[catalyst] = 50, 55 °C, in benzene unless otherwise noted. [b] MMs were named in a format of NB(X)Y, with X the type of polymer and Y the M_n of MM. [c] Determined by multi-angle laser light scattering, using $dn/dc = 0.180 \text{ mL g}^{-1}$ for PS, 0.049 mL g^{-1} for PLA, and 0.055 mL g^{-1} for PnBA. [d] Determined by GPC in THF. PDI is likely underestimated due to the ultrahigh MWs that exceed the GPC column size exclusion limit. [e] DP of the brush polymer backbones. [f] Conversion of MM is determined by comparing the peak areas of brush polymer and residual MM from GPC measurement of the crude product. [g] THF was used as solvent.

structures exhibited loop-like shapes with large open pores, different from our previously reported cyclic dendronized polymers, which presented as donut-like shapes with small pores of only 5–7 nm.^[8] This is presumably due to the high MWs of both side chain and backbone and the significantly extended backbone conformation. Interestingly, we also observed structures where cyclic loops either partially stacked or crossed (Figure 1e), and the cross-sectional analysis

Figure 1. Topographic AFM images of REMP brush polymer **PNB(PS)6600** (Table 1, entry 3) on graphite: a) spin-coated from 0.01 mg mL^{-1} solution; b,c) spin-coated from 0.001 mg mL^{-1} solution. Inserts are magnified images of individual cyclic brush polymers; d) cross-sectional analysis of a cyclic and a linear brush polymer in the highlighted area in (b); e) cross-sectional analysis of either stacked or crossed rings in the highlighted area in (c).

showed that the stacked portion had a height twice that of the non-overlapping portion. We believe this structure is more likely to be from physically, partially overlapped rings during spin-coating and drying process, as opposed to catenated rings. Formation of catenanes during metathesis polymerization of norbornenyl MMs is very unlikely because chain transfer between greatly hindered polynorbornene backbones should not be possible.

Although of lower imaging quality, we also observed cyclic structures for brush polymers made with other MMs, such as **NB(PLA)8700**, and the largest observed loop contour length was nearly 2.5 μm . The extremely large loop was highly elongated in order to minimize side chain congestion (Figure 2).

Figure 2. Topographic AFM image of REMP brush polymer **NB-(PLA)8700** (Table 1, entry 5) on mica. Arrow points to a cyclic polymer with contour length of nearly 2.5 μm .

In addition to cyclic structures, linear contaminants were observed at variable lengths, some even exceeding 1 μm . Individual brush polymers with lengths more than 1 μm have been rare in the literature, and this length was even unattainable with our previous synthesis of linear brush (co)polymers using living ROMP (Supporting Information, Figure 2S).

Matyjaszewski, Sheiko, and co-workers have recently found that high MW, densely grafted polymers are prone to rapid mechanical degradation through backbone scission.^[11] This spontaneous phenomenon was attributed to the concentrated tension at the backbone due to adsorption of high density, long side chains at surfaces. They observed very rapid degradation of brush polymers that were 500 nm in length within the first hour of adsorption, and degradation rates slowed exponentially as the length reached 100–200 nm. In light of their findings, ultrahigh MW cyclic brush polymers may be even more susceptible to cleavage considering the additional stress in the backbone from the forced curving. In fact, we observed ring scission of individual cyclic brush polymer after leaving on graphite surface for 2 h (Figure 3). This ring scission closely resembles the previously reported cleavage of cyclic DNA plasmid on mica surface.^[12] Additionally, we have also reported rapid mechanical degradation of cyclic dendronized polymers upon sonication.^[8] Collectively, these observations may suggest the vulnerable nature

Figure 3. Topographic AFM images of a cyclic brush polymer **PNB(PS)6600** undergoing ring cleavage on graphite surface after 2 h at room temperature. The arrow points to the cleavage site. The scale bar is 100 nm.

of ultrahigh MW cyclic brush polymers toward mechanical ring-cleavage events.

In conclusion, we have demonstrated the direct synthesis of various ultrahigh molecular weight cyclic brush polymers by using ring-expansion metathesis polymerization of macro-monomers, and toroidal shapes with large opening pores were visualized by AFM. Although we have observed linear contamination (manifesting in linear nanostructures) in our preliminary results, REMP of MMs affords facile access to large cyclic organic nanostructures with different functionalities that would be otherwise challenging to achieve.

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Ring-Expansion Metathesis Polymerization:

Catalyst Dependent Polymerization Profiles

Yan Xia[†], Andrew J. Boydston[†], Yefeng Yao^{‡,§}, Julia A. Kornfield[†], Irina A. Gorodetskaya[†], Hans W. Spiess[‡], and Robert H. Grubbs[†]

[†]Arnold and Mabel Beckman Laboratory of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125

[‡]Max Planck Institute for Polymer Research, Ackermannweg 10, 55128 Mainz, Germany

Abstract

Ring-expansion metathesis polymerization (REMP) mediated by recently developed cyclic Ru catalysts has been studied in detail with a focus on the polymer products obtained under varied reaction conditions and catalyst architectures. Depending upon the nature of the catalyst structure, two distinct molecular weight evolutions were observed. Polymerization conducted with catalysts bearing 6-carbon tethers displayed rapid polymer molecular weight growth which reached a maximum value at ca 70% monomer conversion, resembling chain-growth polymerization mechanism. In contrast, 5-carbon tethered catalysts lead to molecular weight growth that resembled a step-growth mechanism with a steep increase occurring only after 95% monomer conversion. The underlying reason for these mechanistic differences appeared to be ready release of 5-carbon tethered catalysts from growing polymer rings, which competed significantly with propagation. Owing to reversible chain transfer and the lack of end groups in REMP, the final molecular weights of cyclic polymers was controlled by thermodynamic equilibria. Large ring sizes in the range of 60 - 120 kDa were observed at equilibrium for polycyclooctene and polycyclododecatriene, which were found to be independent of catalyst structure and initial monomer/catalyst ratio. While 6-carbon tethered catalysts slowly incorporated into the formed cyclic polymer, the incorporation of 5-carbon tethered catalysts was minimal, as revealed by ICP-MS. Further polymer analysis was conducted using melt-state magic-angle spinning ¹³C NMR spectroscopy of both linear and cyclic polymers, which revealed little or no chain ends for the latter topology.

Keywords

cyclic polymers; metathesis; ring-expansion metathesis polymerization; ruthenium

Introduction

Cyclic polymers have been a fascinating macromolecular architecture for synthetic chemists, as well as materials scientists and physicists, since the discovery of circular DNA.^{1,2} Constraining a macromolecule into a cyclic topology can result in unique properties in comparison with linear analogues such as lower viscosities, smaller hydrodynamic radii, and increased functional group density.¹⁻³ Furthermore, cyclic polymers may challenge and expand fundamental knowledge regarding polymer properties as they relate to the presence

To whom correspondence should be addressed: rhg@caltech.edu.

[§]Current address: Shanghai Key Laboratory of Functional Magnetic Resonance Imaging, East China Normal University, North Zhongshan Road 3663, 200062 Shanghai, P. R. China

and absence of chain ends. These characteristics make cyclic polymers interesting targets for studying fundamental aspects of property-topology relationships as well as new resources in materials science. Despite considerable recent development in the area of cyclic polymers, the full potential of these materials is yet to be realized. Further advancement requires the ability to efficiently prepare large-scale quantities of cyclic polymers spanning a diverse range of functionality and controlled molecular weights.

From a synthetic standpoint, cyclic polymers present a unique challenge in polymer chemistry. Successful production of large macrocycles has traditionally been accomplished by macrocyclization of appropriately end-functionalized telechelic polymers.⁴ Although this approach is compatible with both symmetric⁵⁻¹¹ and unsymmetric¹²⁻¹⁵ telechelic polymers, as well as triblock copolymers,^{16,17} inherent limitations still persist. Specifically, macrocyclization is generally limited to low polymers (i.e., < 10 kDa), and requires high-dilution conditions to suppress intermolecular reaction of end-groups. A recent breakthrough in obtaining high molecular weight cyclic polymers utilized macrocyclization of triblock copolymers under high dilution conditions.^{16,17} Using an ABC triblock system in which the A and C blocks comprised complementary coupling partners, this approach provided a mixture of linear and cyclic polymers of up to 96 kDa. The cyclization efficiency for these high molecular weight triblocks was much greater than that typically observed for traditional macrocyclization of telechelic polymers due to the greatly increased effective concentration of functional groups in the A and C blocks of the former. Other cyclic polymer syntheses include those relying on back-biting events during ring-chain equilibria^{18,19} or linear living polymerizations.²⁰ The scope of such methods, however, remains narrow in comparison with the macrocyclization methods previously mentioned.

Complementary to the “grow-then-cyclize” approach of macrocyclization, an alternative strategy, which may be viewed as a “grow-while-cyclic” method, involves ring-expansion of cyclic monomers.²¹⁻²⁹ For example, Pd-mediated polymerization of methylenecyclopropanes was demonstrated by Osakada, and achieved metallacycles of 5.3 kDa.²⁴ The prospect of high fidelity ring-expansion methodology offers the potential for formation of pure cyclic polymers free of linear contaminants and to improve the efficiency with which such materials are produced.

We recently reported a series of cyclic Ru-alkylidene catalysts (Figure 1) resembling olefin metathesis catalyst **1**, which were able to mediate ring-expansion metathesis polymerization (REMP) of cyclic olefins to produce cyclic polymers.^{21,28,29} Overall, REMP has several distinct advantages, such as: 1) the potential to produce large quantities of cyclic polymers from readily available cyclic monomers; 2) tolerance for high concentration, including bulk polymerizations; 3) the ability to produce homopolymers without linkage groups, including pure hydrocarbon macrocycles; and 4) access to a broad range of molecular weights, extending up to 10⁶ Da.

Capitalizing on the attributes mentioned above requires deeper insights into the mechanism of REMP and an ability to control polymer molecular weights and product distribution by guiding metathesis events within the catalytic cycle. The activities of Ru-based metathesis catalysts can be finely tuned via structural modulation,³⁰⁻³³ and we envisioned that the specific structural differences in cyclic catalysts (Figure 1) may offer a means to guide the relative rates of different metathesis events involved in REMP. The most apparent mechanistic steps involved in REMP include catalyst initiation, propagation, catalyst release, and intramolecular chain transfer (Figure 2). The rate of initiation (given rate constant k_i) determines the number of catalyst molecules which enter the catalytic cycle, and may also influence the total number of polymer rings which are ultimately formed. Chain propagation, represented by the rate constant k_p , is expected to be independent of catalyst tether length and dependent on NHC

electronics (i.e., saturated versus unsaturated backbones). Due to the possibility of catalyst release (with rate constant k_r) and re-incorporation (k_{-r}) during REMP, the value of k_p cannot be directly determined based on the overall polymerization rates alone. Importantly, it is the relative rates of each of these events that will dictate the kinetically controlled product distribution.

In a simplified case, the average degree of polymerization (DP) would be given by:

$$DP = k_p [\text{monomer}] / k_r \quad (1)$$

In such cases, chain growth mechanism would be expected to dominate when $k_p[\text{monomer}] \gg k_r$. In contrast, for $k_p[\text{monomer}] \sim k_r$, step growth molecular weight increase would be expected. Both intra- and intermolecular chain transfer events, however, must also be considered during REMP, and therefore Eq (1) cannot be applied to polymerization involving such events. As depicted in Figure 3, the ability of an incorporated (i.e., propagating) catalyst species to interact with olefins within the polymer backbone, in a manner that does not result in release of the original catalyst, may be regarded as polymer “pinching” and is assigned the rate constant k_i . Polymer pinching would yield two separate macrocycles of reduced, and not necessarily equal, molecular weight. Dependent upon the number and placement of Ru complexes in the initial ring, at least one of the ensuing macrocycles would contain an active catalyst species and could either undergo chain growth or further pinching. Intermolecular chain transfer (k_{-t}), which may be viewed as the reverse of polymer pinching or polymer “fusion”, would result in considerable molecular weight growth since two large ring systems are being combined. Notably, the reversibility of olefin metathesis provides a potential avenue toward thermodynamic molecular weight control over “endless” polymers via polymer pinching and macrocyclic combination.

We envisioned that catalyst structure and reaction conditions could be tuned to control the relative values of k_i , k_p , k_r and k_{-t} and ultimately facilitate access to different kinetically-controlled polymer product distributions. Specifically, we previously observed that NHC saturation (e.g., **SC-5** and **SC-6**) resulted in increased catalyst activity toward polymerization, relative to unsaturated analogues **UC-5** and **UC-6**. The origins of the faster conversions of monomer to polymer, however, may be due to faster initiation, slower catalyst release, faster propagation, or some combination thereof. Additionally, catalysts bearing 5-carbon tethers (e.g., **UC-5** and **SC-5**) showed no incorporation into the polymer during polymerizations, suggesting an equilibrium had been established that strongly favored a non-incorporated resting state of the cyclic catalysts. This observation corresponds to catalyst behavior involving initiation, incorporation of monomer units, and catalyst release all prior to complete consumption of monomer; therefore the catalyst does not reside in the formed polymer. This would be expected to provide multiple polymer macrocycles from each catalyst molecule, and potentially display molecular weight growth reminiscent of step-growth mechanisms.

Herein, predictions regarding polymer structure based on our previous catalyst-focused investigations are tested by examining polymer products during and after polymerization. Collectively, the results demonstrate how different catalyst architectures may be used to control the kinetic profiles of REMP. We report comparative studies of cyclic polymers obtained via REMP of cyclooctene (COE), cyclododecatriene (CDT), and cyclooctene macrocycles (e.g., cyclic cyclooctene trimer), with particular focus on catalyst initiation rates, polymer molecular weight evolution during and after polymerization, quantification of Ru in the cyclic polymer products, and application of melt-state ^{13}C NMR spectroscopy for the characterization of cyclic polymers.

Results and Discussion

Polymer Characterization

A significant challenge in cyclic polymer chemistry is the confirmation of a ring topology. Differences between cyclic and linear analogues are typically elucidated via a combination of solution-state properties, such as different GPC retention times, hydrodynamic radii, viscosities, and mass spectroscopy analysis.^{5-16,19,21-28} In addition to these techniques, which have been conducted on polymers obtained via REMP, we explored melt-state magic-angle spinning (MAS) NMR spectroscopy as a viable method for detecting linear polymer contaminants.

¹³C NMR spectroscopy is one of the few methods that can provide quantitative information about polymer topology and microstructure, and has been widely used for the determination of branch content and tacticity of polyolefins.³⁴⁻³⁸ The sensitivity of solution-state NMR spectroscopy is limited due to the low concentration of ¹³C nuclei, and bulk samples typically suffer severe line broadening. Recently, optimized melt-state MAS NMR methodology has been developed to combine high spin concentrations and motional averaging of line broadening interactions that allows for quantitative analysis of minute chain units (e.g., long-chain branch junctions in polyethylene). Sensitivities for this technique are high, reaching 1 branch per 100,000 CH₂ groups.³⁵

Herein, we extended this highly sensitive technique to compare linear (L) and cyclic (C) PCOE prepared from complex **1** and **UC-6**, respectively. GPC analysis revealed a M_w of 220 kDa for the L-PCOE, corresponding to a DP of 2,000, and a M_w of 114 kDa (DP = 1,040) for the C-PCOE. Notably, the lower DP of the C-PCOE in comparison with the L-PCOE should facilitate the detection of linear contaminants in the former. The polymer samples were melted in a sealed zirconia rotor under N₂ at 70 °C and melt-state MAS ¹³C NMR spectra were recorded using a 7 mm MAS probe at 70 °C for ca. 13 h. The L-PCOE and C-PCOE were found to have similar trans/cis olefin ratios (3.5:1 for L-PCOE and 4.2:1 for C-PCOE), calculated from the intense peaks from the polymer olefinic (δ = 132-129 ppm) and methylene (δ = 34-27 ppm) carbon resonances (Figure 4). These values were consistent with those obtained via solution-state ¹H NMR spectroscopy. End groups in the L-PCOE sample manifested additional peaks in both the olefinic and alkyl regions of the spectrum. In contrast, these signals were not detectable for the C-PCOE, indicating a lack of end groups as expected for the cyclic topology. Considering the sensitivity of this technique, and the DP of the C-PCOE, the results indicate that no greater than 1 in 10 chains contain end groups. In other words, the sample obtained from **UC-6** was found to be > 90% cyclic.

Initiation

Catalyst initiation is an important parameter, governing the amount of catalyst that enters the REMP cycle and thus the number of growing chains in solution. In the case of REMP, catalyst release during polymerization may also influence the overall rate of conversion because it competes with propagation, thus it is important to examine the catalyst initiation rates independently. Furthermore, resting state and propagating REMP catalyst species are different in nature, and it has been observed that initiation rates of Ru complexes are not always directly proportional to their olefin metathesis activities.³²

To investigate REMP catalyst initiation rates, we measured the initiation kinetics by monitoring the stoichiometric metathesis reaction of **1**, **UC-5**, **SC-5**, **UC-6** and **SC-6** each with butyl vinyl ether (BVE).^{32,33} Each catalyst was treated with an excess of BVE (30 equiv relative to [Ru]) in C₆D₆ at 60 °C and the reaction progress was monitored by ¹H NMR spectroscopy. Regioselective conversion of the alkylidene complexes (**A**) to the corresponding Fischer

carbenes (**B**) was observed for each catalyst and key data are summarized in Table 1. All reactions showed clean first-order kinetics over the time investigated (see the Supporting Information).

The initiation rates showed a strong dependence on the catalyst structure (Table 1). Both **UC-5** and **SC-5** displayed dramatically increased initiation rates in comparison with their 6-carbon tether counterparts, **UC-6** and **SC-6**. Specifically, shortening the tether length by one carbon atom increased the initiation rate by 25 and 48 times for catalysts with saturated and unsaturated NHCs, respectively. In addition, saturation of the NHC backbone also improved initiation as reported for other Ru-NHC complexes.³² Notably, **SC-5** was found to initiate slightly faster than complex **1** under identical conditions.

Interestingly, the effects of ligand structure on initiation rates do not correspond directly with previously observed relative rates of polymerization. In particular, the significantly faster initiation of the C-5 catalysts is surprising, considering the observed rates of polymerization were in the order of **SC-6** > **SC-5** > **UC-6** > **UC-5**.²¹ After the insertion of the first monomer, further insertions are not expected to depend on a single carbon difference in the size of the ring. Therefore, slower polymerization for C-5 vs. C-6 analogues is not attributed to a difference in the rate constant for monomer addition. Instead, the decreased polymerization rate of C-5 catalysts—in spite of their faster initiation—supports our previous hypothesis that the catalyst release is strongly favored over polymer propagation for these systems.

Molecular Weight Growth and Decline

The molecular weight evolution during polymerization, and equilibration of the cyclic polymers after complete monomer consumption, can shed light on the relative values of k_p , k_t , and k_i . For a specific monomer, different catalysts may be useful for guiding the molecular weight evolution of the cyclic polymers.

We monitored the molecular weight of PCOE during the REMP of COE using cyclic catalysts **UC-6**, **SC-6**, **UC-5**, and **SC-5**. Tether length was found to strongly affect the molecular weight versus conversion profiles (Figure 5), and in all cases the polydispersity indices (PDIs) ranged from 1.3 to 1.8. Catalysts **UC-6** and **SC-6** each delivered a large increase in molecular weight at the beginning of the polymerizations. Additionally, sharp increases in solution viscosities were observed within 1 h. PCOE obtained using **UC-6** displayed a peak molecular weight of 667 kDa when conversion reached 69%, followed by a drop in molecular weight such that at 100% conversion the molecular weight was found to be 393 kDa. Saturated catalyst **SC-6** displayed rapid molecular weight growth such that aliquots drawn prior to complete consumption of monomer provided polymers of sufficiently high molecular weight that they precluded molecular weight analysis via our GPC instrumentation. Thus, for comparison with the other catalyst systems, we use the first M_w obtained of 1,260 kDa at 100% conversion. The observed molecular weight evolution for **UC-6** and **SC-6** under these conditions corresponds to polymerization rates that are significantly greater than those of catalyst release or other intramolecular chain transfer reactions. As the concentration of monomer decreased and that of polymer increased, propagation slowed sufficiently such that polymer pinching (k_t) became competitive resulting in molecular weight decline, as discussed in the next section.

Interestingly, **UC-5** and **SC-5** were found to give strikingly different molecular weight growth profiles than their homologues **UC-6** and **SC-6** (Figure 5). In addition, the reaction mixtures did not show noticeable increase in viscosity until nearly complete monomer consumption, when rapid increase in viscosity was observed. In each case PCOE molecular weight increased sharply at low conversion (i.e., < 10%) with noticeable amounts of oligomeric species detected by GPC analysis. Following this initial molecular weight increase, more gradual change in molecular weight, and concomitant decrease in the relative amounts of oligomer, were

observed until approximately 90% conversion was achieved. At this point, sharp increases in molecular weight were observed reaching 575 and 717 kDa for **UC-5** and **SC-5**, respectively, at 100% conversion. The molecular weight evolution observed using the C-5 catalysts indicated a greater tendency for catalyst release during polymerization than their C-6 counterparts. Since the relative rates of monomer insertion and catalyst release regulate the kinetic molecular weight in REMP, at high monomer concentrations propagation occurred faster than catalyst release, and thus polymeric species were observed even at low conversions. The rate of catalyst release, however, quickly became dominant as monomer concentration declined. The steep increase in molecular weight at high conversion suggested that macrocycles were combined via intermolecular chain-transfer events while remaining monomer continued to be incorporated. Notably, this data supports the notion that **UC-5** and **SC-5** each established an equilibrium during polymerization that strongly favored a non-incorporated resting state of the catalyst.

Once all of the monomer is consumed during REMP, the catalyst may continue to perform intra- and intermolecular chain transfer events on macrocyclic species, facilitating molecular weight equilibration. In the absence of end groups, the molecular weight of the final polymers at equilibrium should correspond to the ring size having the lowest thermodynamic energy under the experimental conditions. This differs from many linear polymerizations, including ring-opening metathesis polymerization (ROMP) in which the molecular weight is regulated by the amount of end groups present in the system, which are often from the initiator or chain transfer agent.

To investigate the molecular weight equilibration, we monitored the M_w of the polymers after 100% monomer conversion. Each of the catalysts studied eventually arrived at PCOE M_w s ranging from 300 - 500 kDa (Figure 6). The broad range of final M_w s suggested that the equilibration had stopped, for example due to catalyst death. To continue the equilibration, we isolated the cyclic PCOE via precipitation into excess acetone. After redissolving and precipitating the polymer successively three times to remove residual catalyst, the polymer was redissolved in CH_2Cl_2 with an olefin concentration = 0.5 M. Polymer solutions were then treated with REMP catalyst and heated at 40 °C. After 12 h, PCOE was iteratively precipitated three times into acetone and analyzed by GPC to determine the PCOE M_w . The process of polymer isolation, analysis, and subsection to polymerization conditions was repeated three times while maintaining an olefin concentration of 0.5 M in each round, until the change in M_w was minimal. As shown in Figure 7, the PCOE M_w declined rapidly during the first cycle, then more slowly in subsequent cycles, ultimately approaching a value of 60 kDa. The entire process was repeated using PhCH_3 in place of CH_2Cl_2 , which lead to a final M_w of 100 kDa.

As mentioned previously, if the molecular weight evolution in REMP was approaching a thermodynamically stable state, catalyst loading should only impact the rate at which the equilibrium molecular weight is reached. Using similar conditions to those described above, but with varying initial monomer to catalyst ratios ($[\text{M}/\text{Ru}]_0$), we examined the molecular weight dependence on this variable. As shown in Table 2, the $[\text{M}/\text{Ru}]_0$ did not linearly correlate with the final molecular weights obtained from the cyclic PCOE. Specifically, a $[\text{M}/\text{Ru}]_0$ of 1000:1 resulted in a PCOE molecular weight of 380 kDa, reflecting catalyst death prior to complete molecular weight equilibration (see above). Using $[\text{M}/\text{Ru}]_0$ of 300:1 or 100:1, however, resulted in a PCOE molecular weight of 150 and 100 kDa, respectively. Notably, the difference in molecular weights did not directly reflect the difference in $[\text{M}/\text{Ru}]_0$ used. Further reduction of the $[\text{M}/\text{Ru}]_0$ to 33:1 gave PCOE having a molecular weight of 70 kDa. Collectively, the results suggested that in the absence of considerable catalyst death, the final molecular weight more closely reflected thermodynamic equilibration, rather than $[\text{M}/\text{Ru}]_0$.³⁹

We next explored the impact of monomer structure on the molecular weight evolution during REMP. Monomer characteristics, such as ring strain and olefin density, may strongly affect the relative rates of propagation and chain transfer. Therefore, we studied REMP of cyclododecatriene (CDT), which has less strain than COE and twice the olefin density, and would be expected to slow propagation but facilitate chain transfer. To test the hypothesis that REMP of CDT using C-5 catalysts would exhibit efficient catalyst release and as a result more step-like molecular weight growth than REMP of COE, the molecular weight evolution was studied for CDT in CH₂Cl₂ (0.3 M) at 40 °C using [CDT/SC-5]₀ = 500:1. The total monomer concentration was reduced in comparison with the experiments described above using COE ([COE]₀ = 0.5 M). The reduced monomer concentration is also expected to favor catalyst release over propagation.

Strikingly, although the monomer conversion reached completion in 4 h, only oligomeric species were observed suggesting that propagation is slower than catalyst release. Polymeric species were detectable by GPC only when conversion began to approach 90% (Figure 8), and relative amounts were significantly less than that of oligomeric species. Continued GPC analysis revealed that a polymer peak gradually became dominant over lower molecular weight oligomers 8 h after full monomer conversion. After all the monomer was converted to oligomers, these small rings then coalesced into thermodynamically favored cyclic polymers through intermolecular chain transfer. Thus, the propagation of CDT at 0.3 M was sufficiently slower than chain transfer, leading to the observed step-growth type polymerization profile.

In contrast to REMP of CDT using SC-5, SC-6 produced polymeric species even at low conversions, in addition to significant amounts of oligomer. This is in accord with the faster propagation previously observed from SC-6 (cf. SC-5) in combination with sluggish catalyst release. Moreover, intramolecular chain transfer would be expected to occur equally efficiently from either an incorporated SC-5 or SC-6 species. Therefore, the stunted molecular weight growth observed from SC-5 can likely be ascribed specifically to increased catalyst release in comparison with SC-6, as opposed to ring “pinching” via intra-chain metathesis events.

The molecular weight growth observed at high conversion when using UC-5 or SC-5 (Figures 5 and 8) suggested that these catalysts were capable of mediating intermolecular chain transfer between oligomeric macrocycles to achieve polymers of higher molecular weight. This was surprising considering that this required REMP of large, unstrained cyclic olefins. We envisioned REMP of relatively large monomers should then also equilibrate to high molecular weight polymer, despite relatively low disparity in the ring strain of each species.

To obtain appropriate monomers, we took advantage of the entropically driven ring-chain equilibria in ROMP, where unstrained macrocycles are preferentially formed below the critical monomer concentration.^{19,40-44} We prepared COE macrocycles at 0.1 M, using SC-5 as the catalyst to avoid potential linear contamination. Analysis of the product mixture via ¹H NMR spectroscopy, GC-MS, and GPC collectively indicated that no linear contaminants or polymeric species were present. When solutions of COE macrocycles in PhCH₃ (olefin concentration = 0.5 M) were heated at 40 °C in the presence of SC-5, the reaction mixtures became more viscous indicating an increase in molecular weight. After 12 h, the PCOE was isolated in 70% yield via precipitation into acetone. GPC analysis revealed a M_w of 100 kDa, consistent with the results of the molecular weight equilibration starting from high molecular weight PCOE (see above). The same final M_w was obtained for [olefin/Ru]₀ = 500:1 and 150:1, and remained unchanged upon isolation of polymer and re-injection of new catalyst under the same experimental conditions, suggesting that the ring sizes had reached the most thermodynamically stable state under these conditions.

Determination of Residual Ruthenium

As described previously, incomplete catalyst release from cyclic polymers will result in residual Ru within the polymer backbone. In addition to compromising the overall purity of the polymer products, the metal centers may decompose during subsequent workup, processing, or reactions. Unfortunately, catalyst cleavage using terminating agents such as ethyl vinyl ether, which are widely used to cleave catalyst off polymer prepared via ROMP, cannot remove the incorporated catalyst from the polymer and may also introduce linear impurity.

Therefore, the determination of the residual Ru content in the cyclic polymers obtained via REMP is crucial. Our conclusions thus far have been that catalyst release (i.e., to reform the initial cyclic catalyst) is favored for 5-carbon tethered complexes (e.g., **UC-5** and **SC-5**), and disfavored for complexes bearing longer tethers. Although solution NMR spectroscopy and kinetic data corroborate these findings, we sought a more accurate means to determine the amount of residual Ru in the cyclic polymers. Thus, we prepared samples of PCOE from various cyclic catalysts and analyzed the residual Ru content via inductively-coupled plasma mass spectroscopy (ICP-MS). For comparison, linear polymer samples prepared using complex **1** were also analyzed.

Polymerizations were conducted using COE monomer (0.5 M in CH₂Cl₂) and [M/Ru]₀ = 1000:1. Upon completion, reaction mixtures were diluted to half concentration with CH₂Cl₂ and cooled to 0 °C causing crystallization of PCOE out of solution. The PCOE was collected and recrystallized three times from CH₂Cl₂ to remove most of the unbound catalyst. To produce solutions for analysis via ICP-MS, polymer samples were digested in a mixture of concentrated H₂SO₄ and concentrated HNO₃ for 2 days at 70 °C, during which time complete dissolution of polymer was achieved. ICP-MS experiments were conducted in duplicate and a calibration curve was used to determine the amount of Ru in each sample; key data are summarized in Table 3.

The theoretical maximum Ru that could be present in the polymers at a [M/Ru]₀ = 1000:1 is 6,550 ppm. PCOE prepared from **UC-5**, **SC-5** and **UC-6** (entries 3 - 5) were found to contain similar residual Ru content of only ca 230 ppm Ru. In contrast, PCOE prepared using **SC-6** (entry 6) was found to contain 609 ppm Ru. This is consistent with previous NMR spectroscopic experiments which indicated that **SC-6** can gradually incorporate into the polymer backbone, while the incorporation of **UC-5** and **SC-5** was not observed and the incorporation of **UC-6** was only minimal at elevated temperatures. Considering that a small amount of residual Ru was detectable even when complex **1** was used and catalyst cleavage was performed at the end of ROMP (entries 1 and 2), we speculate that the consistent amounts of residual Ru from samples prepared using **UC-5**, **SC-5** and **UC-6** may reflect unbound, physically trapped metal species.

Conclusions

Ring-expansion metathesis polymerization (REMP) has been studied in detail using monomers of varied ring strain and degrees of unsaturation, in combination with cyclic Ru catalysts of varying architecture. Each key step in the proposed REMP catalytic cycle (initiation, propagation, and catalyst release or chain transfer), was probed using different catalysts. The order of initiation rates did not directly correspond to previously observed rates of polymerization, and specifically, C-5 catalysts gave faster initiation than did C-6 analogues. The catalyst tether length was found to have a significant impact on the polymerization profile: REMP using C-5 catalysts showed a step-growth like mechanism, as a result of the fast catalyst release that competed with propagation. In contrast, REMP using C-6 catalysts showed a chain-growth like mechanism and it gave high molecular weight polymer before full monomer

conversion due to significantly faster propagation relative to catalyst release or chain transfer. The catalyst structure controls the kinetic molecular weight of their polymer product, but after full monomer conversion the molecular weight of PCOE was found to approach an equilibrium value that was independent of catalyst structure and initial monomer/catalyst ratios. The cyclic nature of the polymer products was supported by high sensitivity melt-state ^{13}C NMR spectroscopy. ICP-MS analysis concluded that low levels of residual Ru were present in the cyclic polymer samples when either catalyst release was efficient (i.e., **UC-5** or **SC-5**) or catalyst incorporation was slow (i.e., **UC-6**). The reported results provide insights into the mechanism of REMP and will guide the synthesis of functional cyclic polymers and development of novel materials based on such materials.

Experimental Section

Materials and Instrumentation

CH_2Cl_2 , PhCH_3 and C_6D_6 were obtained from solvent purification columns. CD_2Cl_2 used for NMR scale experiments was distilled from CaH_2 under N_2 prior to use. Ru complex **1** was obtained from Materia, Inc. Cyclooctene and *cis*, *trans*, *trans*-cyclododecatiene were fractionally distilled before use. All other solvents and reagents were of reagent quality and used as obtained from commercial sources. Cyclic Ru catalysts were synthesized as described previously and stored in a glove box filled with N_2 .²¹ Solution state ^1H and ^{13}C NMR spectra were recorded using a Varian Mercury 300 or Varian Inova 500 spectrometer and were routinely run using broadband decoupling. Chemical shifts (δ) are expressed in ppm downfield from tetramethylsilane using the residual protiated solvent as an internal standard.

Melt-State ^{13}C NMR spectroscopy was recorded using a Bruker Avance 500 dedicated solid-state NMR spectrometer operating at a proton and carbon Larmor frequency of 500.13 and 125.75 MHz respectively. All measurements were undertaken with a commercial Bruker, ^{13}C - ^1H optimized, high temperature, 7 mm magic-angle spinning (MAS) probehead using zirconia rotors and rotor caps with ca. 200 mg of PCOE packed inside. N_2 gas was used for all pneumatics to limit thermal oxidation. All measurements were conducted at $\omega_r/2\pi = 3$ kHz spinning speed at 70 °C sample temperature, whilst compensating for thermal MAS effects. Single pulse excitation spectra were acquired using 10 μs ^{13}C $\pi/2$ excitation pulses and π pulse-train heteronuclear dipolar decoupling. For both linear and cyclic PCOEs, 200 mg of polymer was used and 21,000 scans were accumulated with a 2 s recycle delay resulting in a measurement time of 13 h 35 min per sample. The spectra were normalized according to the total intensity of olefinic peaks ($\delta = 132\text{--}129$ ppm) to compare the presence of end groups.

Gel permeation chromatography (GPC) was carried out in THF on two PLgel 5 μm mixed-C columns (Polymer Labs) connected in series with a DAWN EOS multi-angle laser light-scattering (MALLS) detector and an Optilab DSP differential refractometer (both from Wyatt Technology). No calibration standards were used, and dn/dc values were obtained for each injection by assuming 100% mass elution from the columns.

Inductively-coupled plasma mass spectroscopy (ICP-MS) was conducted on a Hewlett-Packard 4500 ICP mass spectrometer (Agilent Technologies) with a CETAC ASX-500 auto-sampler (CETAC). PlasmaCal Ru and Rh standard solutions were used for calibration and DigitTUBEs were used for sample digestion. For sample preparation, 25 mg of polymer was accurately weighed using a microbalance and digested in a mixture of 3 mL of concentrated nitric acid and 2 mL of concentrated sulfuric acid at 70 °C for 2 days. To each digested solution was added 1 mL of a 10 ppm Rh solution, used as an internal standard for Ru. Each solution was diluted to 50 mL using DI water before analysis.

NMR Initiation Kinetics

The Ru catalyst (0.0028 mmol) was dissolved in C₆D₆ (0.7 mL) in an NMR tube fitted with a screw cap containing a rubber septum. The resulting solution was equilibrated in the NMR probe at 60 °C, and BVE (30 equiv relative to [Ru]) was injected into the NMR tube. Reactions were monitored by measuring the peak integration of the starting Ru-alkylidene as a function of time.

General Procedure for REMP of Cyclooctene

In a typical experiment, an oven-dried 40 mL vial with a Teflon-lined screw cap was charged with degassed COE (1.0 g, 9.1 mmol) and a stir bar. Under an argon atmosphere, 18 mL (0.5 M for the monomer) of dry, degassed CH₂Cl₂ or PhCH₃ was added via syringe. In a separate oven-dried vial, a catalyst stock solution was prepared in dry, degassed CH₂Cl₂ or PhCH₃ under an atmosphere of argon. The desired amount of catalyst was injected to the monomer solution under argon to initiate the polymerization at 40 °C. Aliquots (0.5 mL) were removed using a degassed syringe at desired time intervals and chilled with dry ice. At the end of polymerization, the solution was diluted to half concentration and was either added dropwise into 300 mL of stirred MeOH or acetone, or cooled to 0 °C in a refrigerator and the resulting precipitate was collected by centrifugation. Isolated polymer was redissolved in THF at room temperature and reprecipitated and collected two additional times. The isolated white polymer was dried under high vacuum.

Synthesis of Macrocyclic Cyclooctene Oligomer Using SC-5

A 50 mL round bottom flask filled with argon was charged with 0.3 g degassed COE and 30 mL degassed PhCH₃ (0.1 M). In a separate vial, an **SC-5** stock solution was prepared in degassed PhCH₃ under an atmosphere of argon. 2 mg **SC-5** ([COE/**SC-5**]₀ = 1000) was injected into the flask. After stirring at 40 °C for 10 h, NMR showed complete conversion, and one drop of ethyl vinyl ether was added to quench the reaction. After 1 h, all the solvent was removed under vacuum and the product passed a short silica plug eluting with hexanes to remove the catalyst. The volatiles were removed in vacuo to yield 0.2 g clear thick oil. ¹H-NMR: δ 5.4-5.2 (m, 2H), 2.1-1.9 (m, 4H), 1.4-1.2 (m, 8H). ¹³C-NMR: δ 130.4, 129.9, 32.8, 30.0, 29.9, 29.4, 29.3, 27.5.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Olefin metathesis catalyst **1** and cyclic REMP catalysts.

Figure 2.
Key mechanistic steps involved in REMP.

Figure 3. Depiction of reversible polymer “pinching” via intramolecular chain transfer and “fusion” via intermolecular chain transfer.

Figure 4. Melt-state ¹³C NMR spectra of linear PCOE olefinic region (top left), linear PCOE aliphatic region (top right), cyclic PCOE olefinic region (bottom left), and cyclic PCOE aliphatic region (bottom right). Linear PCOE $M_w = 220$ kDa; Cyclic PCOE $M_w = 114$ kDa.

Figure 5.

Weight-average molecular weight versus monomer conversion for the polymerization of COE using catalysts **UC-6** (●), **UC-5** (■), and **SC-5** (□). Conditions: [COE]₀ = 0.5 M in CH₂Cl₂ at 40 °C; [COE/Ru]₀ = 1000:1. (Polymer peaks were used to determine the molecular weight when separate oligomer peaks co-existed at low conversions using **UC-5** and **SC-5**.)

Figure 6.

Equilibration of molecular weight of PCOE after 100% monomer conversion was obtained via REMP using catalysts **UC-6** ($\bullet$), **SC-6** ($\circ$), **UC-5** ($\blacksquare$), and **SC-5** ($\square$). Conditions: $[\text{COE}]_0 = 0.5$ M in CH_2Cl_2 at 40°C ; $[\text{COE}/\text{Ru}]_0 = 1000:1$.

Figure 7.

Molecular weight equilibrium of PCOE. Conditions: **SC-5** was repeatedly added at $[\text{olefin}/\text{Ru}] = 500$ to isolated PCOE, PCOE dissolved at 0.5 M (olefin concentration), 12 h, 40 °C in PhCH_3 (■) and in CH_2Cl_2 (□).

Figure 8.

(A) GPC traces of REMP of CDT using **SC-5** at different conversions. (B) molecular weight vs. monomer conversion for REMP of CDT using **SC-5**. $[\text{CDT}]_0 = 0.3 \text{ M}$ in CH_2Cl_2 , $[\text{CDT}/\text{SC-5}]_0 = 500:1$, 40°C . Aliquots were withdrawn at the indicated times and immediately treated with ethyl vinyl ether. Conversions were determined by ^1H NMR spectroscopy prior to GPC analysis. After the formation of polymeric species above 95% conversion, only the polymer peaks were selected to determine the molecular weight in Figure 8B.

Initiation Kinetics via ^1H NMR Spectroscopy^a

k_{rel}^b is the relative rate constant with respect to catalyst **1**.

Table 2Effect of **UC-6** Catalyst Loading on PCOE molecular weight^a

$[M/Ru]_0$	M_w (kDa)	PDI
1000	380	1.6
300	150	1.5
100	100	1.8
33	70	1.6

^a Conditions: $[COE]_0 = 0.5$ M in CH_2Cl_2 at 40 °C for 12 h.

Table 3Residual Ru amounts in PCOE (ppm) prepared by different catalysts after crystallization of polymer from solution^a

Entry	Catalyst	M _w of PCOE (kDa)	[Ru] (ppm) ^b
1	1 ^c	80	151 ± 8
2	1 ^d	80	137 ± 10
3	UC-5	560	236 ± 6
4	SC-5	500	237 ± 37
5	UC-6	340	219 ± 20
6	SC-6	380	609 ± 42

^a Polymerization conditions: CH₂Cl₂, 40 °C, [M/Ru]₀ = 1000:1, [M]₀ = 0.5 M, 12 h. Excess ethyl vinyl ether was added at the end of polymerization only when **1** was used.

^b Analyzed by ICP-MS, experiments conducted in duplicate and averaged.

^c Crystallized once at 0 °C from CH₂Cl₂.

^d Crystallized three times at 0 °C from CH₂Cl₂.

EPR Study of Spin Labeled Brush Polymers in Organic Solvents

Yan Xia,[†] Yongjun Li,[‡] Alan O. Burts,^{||} M. Francesca Ottaviani,[§] David A. Tirrell,[†] Jeremiah A. Johnson,^{*,†,||} Nicholas J. Turro,^{*,‡} and Robert H. Grubbs^{*,†}

[†]Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, United States

[‡]Department of Chemistry, Columbia University, New York, New York 10027, United States

[§]Department of Earth, Life and Environment Sciences, University of Urbino, Loc. Crocicchia -61029 Urbino, Italy

^{||}Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, United States

Supporting Information

ABSTRACT: Spin-labeled polylactide brush polymers were synthesized via ring-opening metathesis polymerization (ROMP), and nitroxide radicals were incorporated at three different locations of brush polymers: the end and the middle of the backbone, and the end of the side chains (periphery). Electron paramagnetic resonance (EPR) was used to quantitatively probe the macromolecular structure of brush polymers in dilute solutions. The peripheral spin-labels showed significantly higher mobility than the backbone labels, and in dimethylsulfoxide (DMSO), the backbone end labels were shown to be more mobile than the middle labels. Reduction of the nitroxide labels by a polymeric reductant revealed location-dependent reactivity of the nitroxide labels: peripheral nitroxides were much more reactive than the backbone nitroxides. In contrast, almost no difference was observed when a small molecule reductant was used. These results reveal that the dense side chains of brush polymers significantly reduce the interaction of the backbone region with external macromolecules, but allow free diffusion of small molecules.

INTRODUCTION

The combination of controlled polymerization techniques with selective, robust, postpolymerization chemistries has greatly improved our ability to control the size and functionality of macromolecular structures on length scales from tens to hundreds of nanometers.^{1–5} Dendrimers, which have a globular shape, a uniform branched structure, and abundant surface functional groups, have been among the most widely studied macromolecular architectures^{6–8} due to their potential in applications that range from nanomedicine to molecular electronics.^{9–14} Despite this potential, the multistep, iterative synthesis of dendrimers limits their industrial application. Hyper-branched polymers represent an alternative to dendrimers with easier synthetic access; typically, their molecular weight (MW) is not easily controlled.^{15–17} Bottle-brush polymers^{18–20} and dendronized polymers,^{21–23} which possess a very high density of polymer side chains or dendrons, uniformly grafted to the backbone of a linear polymer, are another highly branched polymer architecture. Their sterically crowded architecture leads to an extended backbone conformation and a corresponding cylindrical, wormlike nanostructure.^{18–20} This cylindrical structure distinguishes the shape of bottle-brush polymers from the globular shapes of dendrimers and hyperbranched polymers; in applications like solution and bulk self-assembly, where polymer shape is a critical feature, brush polymers behave differently from spherical nanostructures.^{24–33}

Recently, we and other groups have demonstrated that ring-opening metathesis polymerization (ROMP) of norbornene-terminated macromonomers (MMs) initiated by a Ru-based catalyst is a powerful, general approach for the synthesis of brush polymers via the “graft through” method.^{31,33–39} Using this strategy, well-defined brush homopolymers and copolymers with high molecular weights (MWs) and low polydispersities (PDIs) can be easily prepared in high yields. Unlike spherical dendrimers, whose symmetric structures can be divided into two domains typically called the corona (periphery) and core, bottle-brush structures can generally be divided into three domains: periphery, backbone end, and backbone middle. We wondered if functional groups placed in these regions would display unique, location-dependent reactivities and interactions with the outside environment. In particular, we hypothesized that functional groups anywhere along the backbone would be less accessible to the outside medium than peripheral functional groups, and that functional groups located at the ends and in the middle of the backbone would have different mobilities and/or steric environments. Ultimately, these differences could be used for kinetic control of postpolymerization modification, or for controlled self-assembly and interaction with biological systems. Understanding the interactions of pendant functional

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Chart 1. Structures of Norbornene-TEMPO Monomer 2 and TEMPO-Labeled Brush Polymers Used in This Study

groups with local side chains and their reactivity at different locations on a brush polymer is of fundamental importance for applications of brush polymers as well-defined, cylindrical molecular carriers in drug delivery, catalysis, and molecular recognition.

Electron paramagnetic resonance (EPR) spectroscopy is a powerful technique for the study of local structural and dynamic behavior of paramagnetic, spin-labeled polymer chains or molecular assemblies.^{40–42} Common nitroxide free-radical spin-probes can be easily installed into macromolecules; their EPR spectra are very sensitive to local polarity, viscosity, and polymer segmental motion. As a result, EPR has been widely utilized to investigate polymer chain aggregation and segmental mobility as it pertains to phase transition behavior and/or heterogeneity in polymer blends,^{43–45} block copolymers,^{46–49} and polymer solutions^{50,51} or gels,⁵² as well as to obtain solution conformation and dynamic information about macromolecules.^{53–56} Particularly, application of the EPR technique to study the dynamic structure of dendrimers has been actively pursued. For example, poly(amidoamine) (PAMAM) dendrimers have been spin-labeled either covalently at the periphery or noncovalently via encapsulation or diffusion of a spin label inside the dendrimer. EPR studies of these spin-labeled PAMAMs have provided useful information on the structure and dynamic behavior of the dendritic branches,^{57–60} the interaction of dendrimers with surfactants,⁶¹ biomolecules,^{62–64} and surfaces,⁶⁵ and encapsulation of small molecules inside the “dendritic box”.⁶⁶

In this report, living ROMP of MMs has allowed us to easily incorporate spin-labels at desired positions along the backbone of narrowly dispersed brush polymers through sequential copolymerization of a small-molecule norbornene-nitroxide with norbornene-terminated polylactide MMs. EPR analysis of these

brush polymers revealed different steric environments throughout the brush polymers and demonstrated position-dependent reactivity of nitroxide radicals toward a polymeric reactant. To the best of our knowledge, this report represents the first examples of chemically spin-labeled brush polymers and their subsequent study by EPR. These results provide quantitative information on the local environment of a brush polymer in solution.

RESULTS AND DISCUSSION

Synthesis of Spin-Labeled Brush Polymers. Using the fast initiating ruthenium catalyst (IMesH₂)-(PCy₃)(py)₂RuCl₂-(CHPh) **1**, ROMP of MMs with strained olefin end groups can proceed in a living fashion to produce brush block polymers if two types of MMs are polymerized sequentially.^{31,39} We took advantage of this strategy to incorporate nitroxide radical spin-labels into different positions along the backbone. An *exo*-norbornenyl monomer **2** with a pendent 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) group was polymerized in CH₂Cl₂ using **1**. The resulting homopolymer had a very low PDI of 1.08 and a MW that matched the theoretical value as determined by the ratio of monomer to catalyst (Supporting Information Figure S2). This result indicates that the nitroxide radical does not interfere with living ROMP. Metathesis polymerization is particularly attractive, because unlike radical polymerization methods where TEMPO has to be formed by oxidation from tetramethyl-4-piperidinol or attached post polymerization, ROMP allows direct incorporation of TEMPO labels into polymers.

To prepare a brush polymer with TEMPO labels at the end of the backbone, a 5-fold excess of **2** was treated with **1** to form the first pseudo-block, followed by the addition of a MM to grow the brush polymer. Similarly, for the preparation of mid-backbone labeled brush polymer, 5 equiv of **2** was added after the first block of MM had completely reacted, followed by the addition of the third block of MM. Following this strategy, we prepared TEMPO-labeled polylactide (PLA) brush polymers (side chain MW = 4 kDa) with PDIs < 1.1 and high MWs close to the theoretical values (Chart 1, Table 1). A peripherally labeled sample was synthesized by coupling *N*-TEMPO-succinamic acid to ~5% of the hydroxyl end groups of PLA side chains of a PLA brush homopolymer. The same amide linkage to TEMPO was used for all the labeled brush polymers to ensure the same electronic environment of the nitroxide. The number of TEMPO labels per brush polymer chain was measured to be 6, 6, and 4 for the end, middle, and peripherally labeled brush polymers, respectively, against standard TEMPO solutions. The extent of TEMPO labeling in each case was consistent with the target stoichiometry of the labeling reaction.

Table 1. Characteristics of TEMPO-Labeled PLA Brush Polymers

sample name	$M_{w, \text{GPC}}^a$ (kDa)	$M_{w, \text{theo}}^b$ (kDa)	PDI ^c
<i>E</i> -TEMPO-Brush ^d	444	440	1.04
<i>M</i> -TEMPO-Brush ^d	410	440	1.03
<i>P</i> -TEMPO-Brush ^d	474	440	1.01

^a Absolute MW determined by MALLS using $dn/dc = 0.05$, which was determined from the RI measurement. ^b Theoretical MW calculated using $MW = 4400[\text{MM}/\text{Ru}]_0$. ^c Determined by THF GPC using RI and MALLS detectors. ^d PLA brush polymers with TEMPO labels at the end of backbone (*E*-TEMPO-Brush), the middle of backbone (*M*-TEMPO-Brush), and the periphery (*P*-TEMPO-Brush).

EPR of Spin-Labeled Brush Polymers. EPR spectra of various labeled brush polymers were recorded in deoxygenated dichloromethane (DCM), dimethylformamide (DMF), and dimethylsulfoxide (DMSO) at 25 °C. The correlation time for the rotational diffusion motion, τ , was obtained by simulation of the experimental spectra.

In previous EPR studies of dendrimers (e.g., PAMAM), nitroxide radicals were covalently attached at the periphery. Strong spin–spin exchange interactions between spin-labels usually led to significantly broadened peaks in the EPR spectra, and eventually to collapse of the lines into a single exchange-narrowed line, especially for dendrimers with a large number of spin-labels.^{57,58} In contrast, each of the brush polymers studied here displayed characteristic nitroxide 1:1:1 triplet signals in the EPR spectrum regardless of the location of the nitroxide label (Figure 1). This observation suggests that the labels in these brush polymers are well separated; the electron exchange integral J is much less than the ¹⁴N hyperfine coupling constant ($J \ll a_N$). Indeed, even for the polynorbornene-TEMPO homopolymer, triplet signals were observed when DCM, DMF, or DMSO was used as the solvent. When THF was used as the solvent for poly(**2**), we observed a broad, single EPR peak, which suggests a collapsed chain conformation and close proximity of the spin labels in THF (Supporting Information Figure S3A). Therefore, only DCM, DMF, and DMSO were used for our EPR study.

In the range of nitroxide concentration from 0.1 to 0.001 mM, no concentration-dependent EPR line-broadening was observed for spin-labeled brush polymers (Supporting Information Figure S4), which indicates that the polymers are segregated and that nitroxides on different polymers do not interact. Therefore, we used a nitroxide concentration of 0.05 mM for all the brush polymers in the EPR experiments. τ is an important EPR parameter that is sensitive to the change of environment surrounding

Figure 1. EPR spectra of TEMPO-labeled PLA brush polymers in DMSO ([nitroxide] = 0.05 mM).

Table 2. EPR Characteristics of Monomer 2 and Brush Polymers with Spin-Labels at Different Chain Locations in Deoxygenated DCM, DMF, and DMSO at [nitroxide] = 0.05 mM

	solvent	τ /ns	% broad	anisotropy
<i>Monomer 2</i>	DCM	0.005	0	No
	DMF	0.037	0	No
	DMSO	0.095	0	No
<i>E-TEMPO-Brush</i>	DCM	0.235	21	No
	DMF	0.36	25	Yes
	DMSO	0.59	0	Yes
<i>M-TEMPO-Brush</i>	DCM	0.235	19	No
	DMF	0.36	15	Yes
	DMSO	0.81	8	Yes
<i>P-TEMPO-Brush</i>	DCM	0.005	0	No
	DMF	0.033	0	No
	DMSO	0.13	0	No

the radical, such as solvent viscosity and steric hindrance. Computation of the EPR spectra by a well-known procedure reported by Budil et al.⁶⁷ accurately provided the τ values. Brownian rotational diffusion was assumed in the calculation. The τ values increased in the order $\tau_{\text{DCM}} < \tau_{\text{DMF}} < \tau_{\text{DMSO}}$ for the monomer and for each of the spin-labeled brush polymers at the same concentration (Table 2), consistent with the increase of solvent viscosity. As we compared τ for each type of spin-labeled brush polymer in all three solvents, the same trend was observed: peripherally labeled brush polymer (P-TEMPO-Brush) gave the smallest τ , almost the same as that of the monomeric TEMPO, but when the labels were tethered on the backbone, either at the end (E-TEMPO-Brush) or in the middle (M-TEMPO-Brush), considerably larger values of τ were observed (Figure 2 and exemplary spectra in DMSO shown in Figure 1). In DCM and DMF, the τ values for both the end and middle-labeled brush polymers were the same, but accurate simulation of the spectra for these samples required addition of another component, which was termed “broad” (Table 2). This component arises from interaction of adjacent nitroxides, which results in line broadening in the EPR spectrum. In DMF and DCM, the percentage of this broad component is higher for the E-TEMPO-Brush than for the M-TEMPO-Brush, which may be due to the lower steric hindrance and greater flexibility of nitroxides to interact with each other at the end versus the middle of the backbone. In DMSO, there was almost no broad signal contribution, indicating that the EPR signal in DMSO originates only from individual spin-labels. Therefore, DMSO is identified as the best EPR solvent to differentiate steric environments among the different brush polymer regions. In DMSO, the M-TEMPO-Brush had a larger τ than the E-TEMPO-Brush, and labels in both backbone regions had much larger values of τ than labels on the periphery. Since τ is inversely related to the mobility of the spin-label, this result clearly indicates a difference in the mobility of spin-labels at different locations of the brush polymers in DMSO. Considering all the labeled brush polymers had almost the same MW and composition, the difference is attributed to the steric crowding created by dense side chains and the chain mobility of different regions of a brush polymer.

The EPR spectra of M-TEMPO-Brush and E-TEMPO-Brush also exhibited anisotropy in DMF and DMSO, while anisotropy

Figure 2. Rotational correlation times (τ) of TEMPO monomer and brush polymers with spin-labels at different chain locations in deoxygenated DCM, DMF, and DMSO at [nitroxide] = 0.05 mM.

was not observed for the monomeric TEMPO and P-TEMPO-Brush. Anisotropy in the orientation of the rotational main axis of spin labels confirms that steric interactions lead to hindered rotation for the spin labels on the backbone in DMF and DMSO.⁶⁸ In contrast, peripherally labeled samples exhibited no anisotropy, which suggests that the peripheral spin labels freely rotate and are not constrained.

Quenching Experiment. Since dense side chains provide steric shielding to the backbone functional groups, the more shielded areas should be less accessible to external reactants. This effect may be most manifested for a polymeric reactant since the reaction may become diffusion limited in the most hindered sites. Encouraged by the different τ values of labeled brush polymers, we designed a quenching experiment to test our hypotheses on the site dependent reaction accessibility on brush polymer for both small molecules and polymeric reactants. It is well-known that nitroxide radicals can be efficiently reduced to hydroxylamine by phenylhydrazine (PhNHNH₂), leading to quenching of the EPR signal.⁶⁹ Here we used a small molecule quencher, PhNHNH₂, and a polymer-tagged quencher, hydrazine-functionalized polystyrene (PS-NHNH₂), to study the rate of quenching as a function of nitroxide location. The polymeric quencher was prepared by atom-transfer radical polymerization (ATRP) of styrene along with a small amount of *para*-chloro-styrene. The aryl chloride moieties in the copolymer were converted to aryl hydrazines via a recently reported palladium cross-coupling strategy.⁷⁰ The MALDI spectrum of PS-NHNH₂ clearly showed the hydrazine functionality on the polymer (Supporting Information Figure S5).

We compared the quenching of P-TEMPO-Brush, E-TEMPO-Brush, and M-TEMPO-Brush at the same nitroxide concentration and used the same loading for quenchers. The quenching rate was monitored by the intensity of the low-field peak of the EPR spectra as a function of time. When PhNHNH₂ was used, regardless of the position of the TEMPO labels on the brush polymer, the EPR signal was rapidly quenched at almost the same rate; the reaction was almost complete in ~30 min (Figure 3A). In contrast, when the polymeric quencher was used, significantly different quenching rates between spin-labels at different brush locations were observed: more than 90% of P-TEMPO-Brush was quenched after ~3 h, but quenching of the backbone-labeled

Figure 3. Quenching of the EPR signal for brush polymers with TEMPO labels at different positions: (A) quenched by PhNHNH₂; (B) quenched by PS-NHNH₂ (MW = 2400 Da). [nitroxide]₀ = 5×10^{-5} M in air-saturated DMF at room temperature.

samples reached a quasi-plateau after 20 min with ~30% quenching for E-TEMPO-Brush and ~20% quenching for M-TEMPO-Brush (Figure 3B), and prolonged time did not result in increased quenching. This striking difference is attributed to the limited access of polymeric quencher to the core of the brush polymer because it has to penetrate through the dense side chains in order to react with spin-labels at the backbone. A similar quasi-plateau has been reported for quenching of nitroxides by excess ascorbate.⁷¹ This was attributed to the reoxidation of the reduced product of nitroxide, hydroxylamine, by O₂ to regenerate the EPR-active nitroxide.⁷¹ Therefore, an equilibrium exists between the reduction reaction and reoxidation. To keep the same oxygen level in the sample solutions, we used air-saturated solvent for quenching experiments. For peripherally labeled polymer, the reduction rate is much faster than the reverse oxidation rate, leading to almost complete quenching at the end. However, for the middle- and end-labeled polymers, the initial reduction rates were only about 20% of that of the peripheral polymer after addition of PS-NHNH₂. On the other hand, reoxidation involves a small molecule reactant (O₂); because its diffusion should not be substantially affected by the side chains, oxidation becomes competitive with reduction and a dynamic equilibrium characterized by partial quenching is reached. To test this hypothesis, we measured quenching of M-TEMPO-Brush in carefully degassed DMF; 92% quenching was indeed observed after 26 h (Supporting Information Figure S6).

These quenching studies suggest that the brush architecture provides a unimolecular system with distinct core and shell regions. The dense side chains of brush polymers significantly reduce the interaction of the core (backbone) region with external macromolecules (i.e., PS-NHNH₂), but allow free diffusion of small molecules (i.e., phenylhydrazine and O₂).

CONCLUSIONS

We report the EPR study of spin labeled brush polymers, which were efficiently synthesized using ROMP. Living ROMP allowed accurate and convenient incorporation of finite numbers of functionalities (e.g., spin labels) at different positions of brush polymers. The EPR analysis suggests that brush polymers can

possess either two or three distinct domains depending on the solvent: periphery and core, or periphery, backbone end, and backbone middle. Reactions between large external reductants and nitroxide spin-labels bound to brush polymers exhibit location-dependent rates. Peripheral nitroxides react rapidly with both small-molecule and polymeric reductants. Core-bound nitroxides react rapidly with a small reductant, but steric hindrance to the backbone limits their reactivity with a polymeric reductant. Ultimately these differences in reactivity could be exploited for kinetically controlled, orthogonal functionalization of brush polymers. The efficiency of ROMP for the synthesis of multifunctional, narrowly dispersed brush polymers makes it a convenient alternative to widely studied dendritic and hyper-branched polymer structures. The ease of synthesis and the unique properties of brush polymers make them appealing macromolecular structures in a range of applications where nanoscopic structures have great impact. Our future research is focused on the development of brush polymer based drug delivery systems^{36,37,72,73} that take advantage of their unique structural features and modular synthesis. Toward this end, we will report on the EPR study of water-soluble poly(ethylene glycol)-based brush polymers in a subsequent paper.

ASSOCIATED CONTENT

S Supporting Information. Experimental section, ¹H and ¹³C NMR spectra, GPC traces, and additional EPR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Corresponding Author

rhg@caltech.edu; jaj2109@mit.edu; njt3@columbia.edu

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Low Pressure Ethenolysis of Renewable Methyl Oleate in a Microchemical System

Chan Pil Park,[†] Matthew M. Van Wingerden,[‡] So-Yeop Han,[§] Dong-Pyo Kim,^{*,†} and Robert H. Grubbs^{*,‡}

National Creative Research Center of Applied Microfluidic Chemistry, Chungnam National University, Daejeon, 305-764, Korea, The Arnold and Mabel Beckman Laboratory of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, United States, and Center for Catalysis and Synthesis, Ewha Womans University, Seoul, 120-750, Korea
rhg@caltech.edu; dpkim@cnu.ac.kr

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ABSTRACT

A microchemical system for ethenolysis of renewable methyl oleate was developed, in which the dual-phase, microfluidic design enabled efficient diffusion of ethylene gas into liquid methyl oleate through an increased contact area. The increased mass transfer of ethylene favored the formation of desired commodity chemicals with significantly suppressed homometathesis when compared to the bulk system. In addition to higher selectivity and conversion, this system also provides the typical advantages of a microchemical system, including the possibility of convenient scale-up.

The generation of useful, low molecular weight chemicals from renewable natural resources is an important research topic throughout the fields of chemistry and chemical engineering. Because of environmental challenges and potential economic advantages, the search for new feedstock sources and the development of chemical and biological processes to utilize the new feedstocks are the focus of much research.¹ Ruthenium catalysts, which have become useful for organic synthesis and polymer chemistry, have been tested in the olefin metathesis of internal olefins with ethylene, known as

ethenolysis, which can be used to produce the desired low molecular weight products from renewable seed oils (eq 1).²

Early studies of the ethenolysis of natural seed oils showed promise but was limited by the high sensitivity of the traditional molybdenum, tungsten, and rhenium catalysts. The advent of ruthenium catalysts with low sensitivity but high activity has spurred a renewed interest in ethenolysis, but limited selectivity and conversion have hampered progress to commercially viable processes. Homometathesis continues to be a troubling competing reaction which reduces the yield.

Microchemical systems have provided new strategies and new challenges as new process techniques.³ The benefits of precise control of reaction variables and high surface area-to-volume ratios are manifest in reduced

[†] Chungnam National University.

[‡] California Institute of Technology.

[§] Ewha Womans University.

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waste, higher yield, and reduced reaction times. Furthermore, the difficulties of scale-up can largely be avoided by simple parallelization of small-scale microfluidic test reactors. In addition to traditional, one-step microchemical reactions, several consecutive reactions, including separation, purification, and detection, have been successfully integrated as complete microchemical processes.⁴

A particularly challenging type of microchemical system is the heterogeneous reaction involving any combination of the gas, liquid, and solid phases.⁵ The heterogeneous reactions between gas and liquid are mainly conducted with two main modes of contact:⁶ one with the two phases flowing in contact in parallel, the other with alternative bands of gas bubbles and liquid slugs. In a recent report we described a microchemical system with the former mode of contact mediated by a PDMS (polydimethylsiloxane) membrane.⁷ As an alternative to this strategy, however, we feel the segmented mode of contact has its own unique advantages due mainly to the simple, convenient setup and a broader choice of available capillary materials, allowing better chemical stability and mechanical strength even at high pressure. Herein, we report a facile and efficient microchemical ethenolysis under various reaction conditions, through the continuous segmented flow of ethylene and methyl oleate in a capillary tube with a 0.5 mm inner diameter. Moreover, the reaction was performed nearly solvent-free, except for a minimum amount of toluene to dissolve the catalyst (1.0 mg of catalyst in 2.0 mL of toluene), which avoids the use of excess organic solvent to facilitate the dissolution of ethylene gas as has been reported.⁸ The poor solubility of ethylene in methyl oleate (mole fraction of ethylene/methyl oleate = 0.108, 60 psi)^{2a}

and the slow diffusion of ethylene into the solution favor homometathesis instead of the desirable ethenolysis. Overcoming the bias for homometathesis suggests two straightforward strategies: developing catalysts with a high kinetic selectivity for ethenolysis, or engineering processes to drive ethylene into the reaction. The engineering approach was the main strategy of this work and was accomplished by increasing the contact area between methyl oleate and ethylene, thereby maximizing the transfer of the ethylene into the methyl oleate phase with high diffusion efficiency.⁶

Figure 1. (A) Microchemical ethenolysis of methyl oleate (MO) with Ru catalyst (1.0 mg/2 mL toluene). (B) Segmented flow of ethylene and methyl oleate in a capillary microreactor.

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A noticeable shortening of the length of ethylene bubbles was observed through the length of the microreactor, a not unexpected observation as ethylene is consumed during the reaction.⁹ The pressure drop across the length of the microreactor caused by the increased friction of the segmented liquid flow was worrisome because of the potentially variable solubility of ethylene, but the pressure at the exit was measured to be 56 psi when the inlet pressure was set to 60 psi. The pressure differential and corresponding solubility difference were thus concluded to be negligible.

Figure 2. Ethenolysis under different temperature and pressure conditions. Catalyst **6** (300 ppm) was used. (a) Yield (%) = conversion $\times$ selectivity = $(1 - \text{final moles of } \mathbf{1} / \text{initial moles of } \mathbf{1}) \times \{(2 + 3) / (2 + 3 + 4 + 5)\} \times 100$. Conversion and selectivity were determined by GC analysis. (b) Selectivity after 120 min retention time.

As the effects of pressure and temperature in the batch system were well documented in previous reports,² the same variables were carefully studied in the microchemical system. With 300 ppm of catalyst **6**, the pressure was varied from 15 to 60 psi and the temperature was varied from 20 to 40 °C. The results illustrate that the pressure of ethylene has a direct impact on the yield (Figure 2).¹⁰ Elevating the temperature over 30 °C resulted in a 5% loss in the net yield after 120 min, due to the decreased selectivity (30 psi and 30 °C: 48% conversion, 85% selectivity, 30 psi and 40 °C: 50% conversion, 72% selectivity). These good results at low temperature and high pressure are well consistent with the batch studies, where the same factors increase the selectivity and yield of ethenolysis.²

For the ethenolysis of methyl oleate **1**, six ruthenium catalysts were selected: first generation catalysts **6** and **7**; second generation catalysts **8**, **9**, and **10**; and cyclic alkyl-amino carbene (CAAC)-based catalyst **11**¹¹ (Figure 3). Each catalyst was screened at a variety of catalyst loadings, and the results were tabulated (Table 1). When catalyst **6** was used at 0 °C only a negligible amount of product was formed, confirming that no olefin metathesis occurs in the first cooled mixing zone as was expected in the redesigned system (entry 1). When the first mixing section was not

Figure 3. Ruthenium catalysts for ethenolysis of methyl oleate.

cooled, an increase in homometathesis was observed as expected (entry 3). Hoveyda-type catalyst **7** was slightly more effective than catalyst **6** (entries 4 and 5), and the typical second generation catalyst **8** gave the poorest results in selectivity and yield, although the more active catalyst required less time than catalysts **6** and **7** to achieve a similar conversion (entries 6–8). The second generation catalysts **9** and **10**, which contain a sterically hindered NHC ligand, also gave lower yields than PCy₃-based catalysts **6** and **7** (entries 9–12), even though it is known that catalysts with NHC ligands have better stability and activity toward olefin metathesis than catalysts with PCy₃ ligands. In this case the homocoupling reaction, while not significant for phosphine-based catalysts **6** and **7**, accounted for about half the activity of the NHC-based

Table 1. Ethenolyses of Methyl Oleate **1** in the Microchemical System^a

	cat. (ppm)	<i>t</i> (°C)	time (min)	conv (%) ^c	select (%) ^d	yield (%) ^e	TON ^f
1	6 (150)	0	180	3	99	3.0	600
2	6 (300)	30	120	65	96	62.4	5800
3	6 ^b (300)	30	120	66	91	60.1	5600
4	7 (100)	30	120	39	94.8	37.0	7500
5	7 (300)	30	120	69	93.7	64.7	4400
6	8 (50)	40	60	58	45	26.1	11 000
7	8 (100)	30	120	59	43.5	25.7	5400
8	8 (100)	40	60	61	41	25.0	5300
9	9 (50)	40	60	54	52	28.1	13 500
10	9 (100)	40	60	57	50	28.5	6800
11	10 (50)	40	40	61	58	35.4	22 300
12	10 (100)	40	40	63	55	34.7	10 900
13	11 (50)	40	60	80	87	69.6	27 200
14	11 (100)	40	60	81	84	68.0	13 300
15	11 (100)	40	30	72	88	63.4	12 400

^a General reaction conditions: 60 psi ethylene, the microchemical system described in Figure 1A. Conversion and selectivity were determined by GC analysis. ^b No cooling of the mixing zone. ^c Conversion = $(1 - \text{final moles of } \mathbf{1} / \text{initial moles of } \mathbf{1}) \times 100$. ^d Selectivity (%) = $(2 + 3) / (2 + 3 + 4 + 5) \times 100$. ^e Yield (%) = conversion $\times$ selectivity/100. ^f TON = yield $\times$ [(initial moles of **1**)/(moles of cat.)].

(9) In addition to the higher surface area-to-volume ratio, the microfluidic system is free from pressure drop, even though much of the gas is consumed, which is a property not found in batch systems.

(10) Conversion and selectivity for each condition are in the Supporting Information, Table 1S.

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catalysts **8**, **9**, and **10**. The result from catalyst **11** is the most noteworthy as the catalyst is currently the most selective catalyst known for ethenolysis among the NHC-based catalysts. Catalyst **11** gives the highest yield in this study, even when compared with phosphine-based catalysts **6** and **7**. Catalyst **11** gave a 69.6% yield with only 50 ppm catalyst and a 60 min retention time (entry 13). The selectivity is comparable to the result of the batch reaction tested at higher pressure (selectivities up to 83% were measured at 150 psi), but because of the higher conversion the yield was higher in the microchemical system.^{2b} Additionally, the selectivities of catalysts **6**, **7**, **8**, **9**, and **10** are superior in the microchemical system at 60 psi compared to the batch reaction at 150 psi.

In conclusion, a microchemical system for gas–liquid dual-phase reactions was developed which was applied to the ethenolysis of methyl oleate. The results at 60 psi

of ethylene were comparable to the results of batch reactions at 150 psi of ethylene. This is expected to be due to the high surface area-to-volume ratio suitable for fast mass transfer of the gas into the solution phase. The sterically hindered CAAC-based ruthenium catalyst **11** gave 80% conversion and 87% selectivity with only 50 ppm catalyst.

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Supporting Information Available. Experimental procedures. This material is available free of charge via the Internet at <http://pubs.acs.org>.