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A Facile, Controlled Synthesis of Soluble Star Polymers Containing a Sugar Residue by Ring-Opening Metathesis Polymerization (ROMP)

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Summary: Precise syntheses of soluble star polymers containing a sugar residue could be attained by adopting sequential ring-opening metathesis polymerizations of norbornene, 1,4,4a,5,8,8a-hexahydro-1,4,5,8-*exo-endo*-dimethanonaphtalene, and then 1,2:3,4-di-*O*-isopropylidene-α-D-galacto-pyranos-6-*O*-yl 5-norbornene-2-carboxylate using $Mo(CHCMe_2Ph)(N\text{-}2,6\text{-}{}^iPr_2C_6H_3)(O^tBu)_2$. The resultant polymers possessed uniform molecular weight distributions, and the M_n values could be varied by the monomer/Mo molar ratios; their spherical images were observed in the TEM micrographs.

Keywords: carbohydrate; ring-opening metathesis polymerization (ROMP); star polymers; synthesis; TEM

Introduction

Star polymers containing multiple linear arms connected at a central branched core are one of the simplest nonlinear polymers,[1,2] and the synthesis by atom transfer radical polymerization[3] via core-first,[4] coupling-onto,[5] or arm-first [6] approach has been investigated recently. The approach for synthesis of cross-linked polymers by ring-opening metathesis polymerization (ROMP)[7] has also been known,[8–10] especially in terms of application as monolith materials.[9,10] In contrast, examples for syntheses of star polymers with better solubility in common organic solvents were not reported. We recently demonstrated a controlled synthesis of 'soluble' star polymers by adopting the living ROMP technique using the Mo-alkylidene initiator by simple sequential additions of norbornene (NBE) and the cross-linker (CL).[11] We thus herein present a controlled synthesis of the star polymers containing a sugar (hydrophilic) residue by this method.

Results and Discussion

As communicated recently,[11] the method consists of 4 key steps outlined in Scheme 1. $Mo(CHCMe_2Ph)(N\text{-}2,6\text{-}{}^iPr_2C_6H_3)(O^tBu)_2$ was chosen due to its ability to prepare the ROMP (co)polymers in a living manner with the quantitative initiation.[12,13] 1,2:3,4-Di-*O*-isopropylidene-*α-D*-galactopyranos-6-*O*-yl 5-norbornene-2-carboxylate (**2**, *endo*/*exo* = 87/13) was also chosen, not only because the monomer synthesis/purification procedures were established,[13b,c,14] but also because the resultant polymers containing a sugar residue may exhibit both specific and strong affinity with cell surface proteins that can be explained as the result of clustering and binding of the cells by multivalent arrays.[15] 1,4,4a,5,8,8a-Hexahydro-1,4,5,8-*exo-endo*-dimethanonaphtalene (**CL**, *exo*/*endo* = 0.17/1.00)[16] was chosen as a cross-linking reagent, and the polymerization was terminated with $4\text{-}Me_3SiO\text{-}C_6H_4CHO$ (**A**) or 1-pyrenecarboxaldehyde (**B**). The results are summarized in Table 1.

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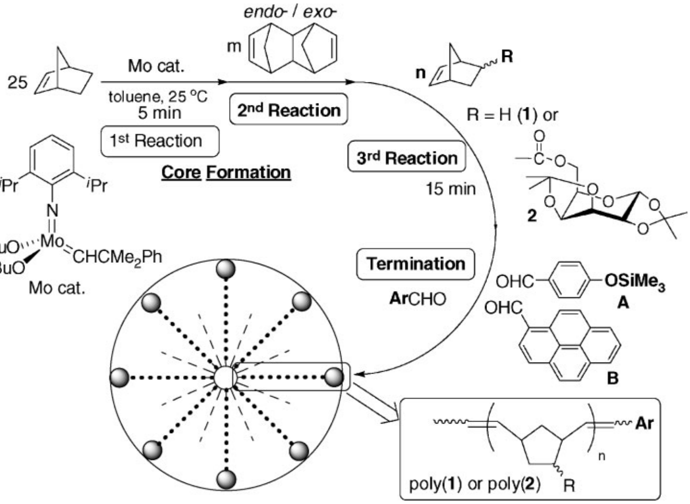

Scheme 1.
Synthesis of soluble star shape ROMP polymers.

It turned out that the resultant polymers were high molecular weight ring-opened polymers, poly(**2**), with uniform molecular weight distributions with good reproducibility under the optimized conditions ($M_n = 1.30–1.40 \times 10^5$, $M_w/M_n = 1.21–1.31$, runs 5,6,9,10), and are highly soluble in ordinary organic solvents such as toluene, THF, dichloromethane, chloroform etc. As seen in the preparation of poly(**1**),[11] optimization of the reaction conditions were required for obtainment of the "soluble" polymers with uniform molecular weight distributions. The reaction time after addition of **CL** (2nd reaction, more than 70 min) as well as after addition of third monomer seemed important to obtain the high molecular weight ROMP polymers with uniform distributions. As reported previously,[13] $SiMe_3$ group in the polymer termini could be cleanly hydrolyzed using 0.5M HCl aq. solution in THF (yield 99%) without any changes in the M_n values by GPC.

Table 1.
Selected results for syntheses of star polymers in the ring-opening metathesis polymerization (ROMP) using $Mo(CHCMe_2Ph)(N\text{-}2,6\text{-}{}^iPr_2C_6H_3)(O^tBu)_2$ in toluene.[a]

run	terminator[b]	2nd reaction		3rd reaction			poly(1) or poly(2)		
		CL/Mo[c]/m	time/min	monomer	NBE/Mo[c]/n	time/min	M_n[d]$\times 10^{-4}$	M_w/M_n [d]	yield[e]/%
1[f]	**A**	10	60	**1**	25	20	9.67	1.44	93
2[f]	**A**	10	50	**1**	25	15	8.97	1.31	95
3[f]	**A**	10	50	**1**	25	30	9.23	1.48	96
4	**A**	10	50	**2**	25	15	12.5	1.52	95
5[g]	**A**	10	70	**2**	25	15	13.9	1.27	88
6	**A**	10	70	**2**	25	15	13.0	1.28	74
7	**B**	10	70	**2**	25	15	14.5	1.27	89
8	**A**	15	70	**2**	25	15	16.5	1.38	88
9	**A**	10	90	**2**	25	15	13.1	1.21	76
10	**A**	10	90	**2**	25	15	14.0	1.31	84
11	**A**	10	70	**2**	50	15	18.2	1.32	94
12	**A**	10	70	**2**	50	30	26.8	1.77[h]	97

[a] Conditions (1st reaction): Mo cat. 1.82×10^{-5} mol, NBE (norbornene) 25 equiv. to Mo, toluene (10.0 g), 25 °C, 5 min. [b] Aldehyde for termination shown in Scheme 1. [c] Starting feedstock ratio (m and n in Scheme 1). [d] GPC data in THF vs. polystyrene standards. [e] Isolated yields. [f] Data cited from reference 11. [g] After deprtection of $SiMe_3$ group, $M_n = 14.0 \times 10^4$, $M_w/M_n = 1.30$ (yield 99%). [h] Bimodal molecular weight distirbutions in the GPC trace.

Note that the M_n values in poly(**2**) increased upon increasing the amount of **2** in the 3rd polymerization (25→50 equiv. to Mo, runs 5,6,9,10 vs run 11). Since the observed increases in the M_n values (ca. 42000–52000, by GPC vs polystyrene standards) were much higher than those in the homopolymer [increased 25 repeating units (9500 by molecular weight)], the results thus suggest that the resultant ROMP polymers are star polymers. As demonstrated in the preparation of poly(**1**) terminated with various aldehydes,[11] the M_n values in the resultant polymers terminated with **A**, **B** were close, suggesting that a fluorescent moiety into the polymer chain end (surface of the star polymers) could be introduced by adopting this approach.

Figure 1 shows selected TEM micrographs of thin films prepared by casting the resultant ROMP polymers, poly(**2**), on a plastic coated copper grid (samples runs 5 and 7).[17] The resulting micrographs depict formation of spherical images, as seen in poly(**1**) reported previously. These also suggest that the observed spherical micrographs should be ascribed to star (ball) shape polymers prepared by adopting the present ROMP methodology. However, diameters in poly(**2**) are not uniform and some of them were apparently longer than those in poly(**1**) (average 52 nm, run 2).[11] The facts are unique contrast to those seen in poly(**1**), and would be assumed as due to that poly(**2**) form aggregates by weak interaction of sugar units (probably hydrogen bonding) even under highly dilute conditions (as seen in Figure 1 bottom, and top middle).

In conclusion, we have shown that soluble star polymers containing a sugar residue could be prepared in a precise manner by the present ROMP methodology. As far as we know, this is a rare successful example for controlled synthesis of carbohydrate coated star polymers, and various applications as novel biomaterials[15] can be highly expected.

Experimental Part

General Procedure

All experiments were carried out under a nitrogen atmosphere in a Vacuum Atmo-

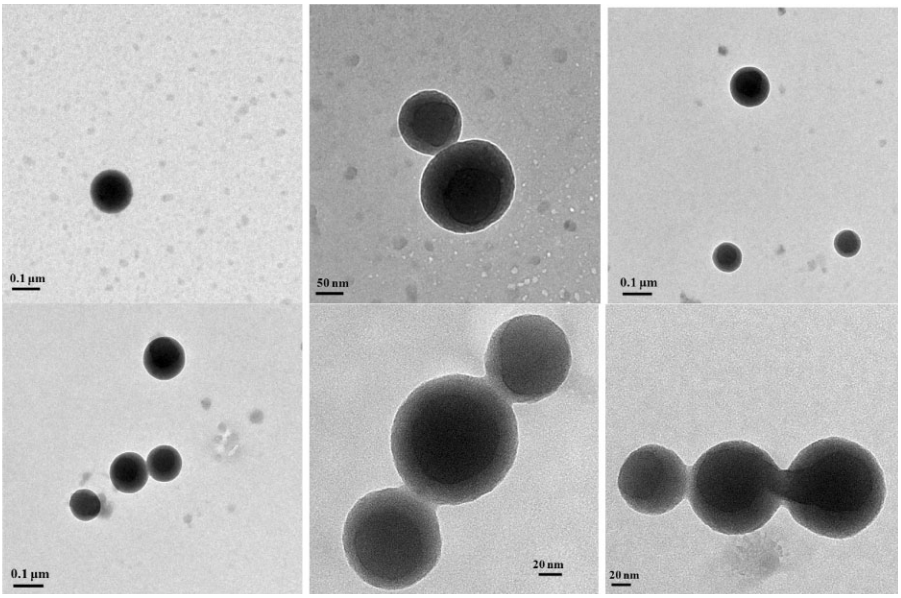

Figure 1.
TEM micrographs of thin film prepared by casting poly(**2**) [run 5 (top left and middle) and run 7 (top right and bottom)] on a plastic coated copper grid at a concentration of 10^{-4} mg/mL at varying magnification.

spheres drybox or using standard Schlenk techniques. All ^{1}H-, ^{13}C-NMR spectra were recorded on a *JEOL* JNM-LA400 spectrometer (^{1}H, 399.65 MHz; ^{13}C, 100.40 MHz), and were obtained in the solvent at 25 °C. HPLC grade THF (Wako Pure Chemical Industries, Inc.) was used for GPC and was degassed prior to use. GPC were performed at 40 °C on a Shimadzu SCL-10A using a RID-10A detector (Shimadzu Co. Ltd.) in THF (containing 0.03 wt% 2,6-di-*tert*-butyl-*p*-cresol, flow rate 1.0 mL/min). GPC columns (ShimPAC GPC-806, 804 and 802, 30 cm × 8.0 mmϕ) were calibrated versus polystyrene standard samples. All chemicals used were of reagent grade and were purified by the standard purification procedures. Polymerization grade toluene was stored over Na/K alloy in the drybox, and was then passed through an alumina short column prior to use. $Mo(CHCMe_2Ph)(N\text{-}2,6\text{-}{}^{i}Pr_2C_6H_3)(O^{t}Bu)_2$,[18] 1,4,4a,5,8,8a-hexahydro-1,4,5,8-*exo*-*endo*-dimethanonaphtalene(*exo*:*endo* = 0.17:1.00),[16] $4\text{-}Me_3SiO\text{-}C_6H_4CHO$,[13a] 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranos-6-*O*-yl 5-norbornene-2-carboxylate[14] were prepared according to the previous reports.

General Polymerization Procedure

A toluene solution (0.5 g) containing $Mo(CHCMe_2Ph)(N\text{-}2,6\text{-}{}^{i}Pr_2C_6H_3)(O^{t}Bu)_2$ (1.82×10^{-5} mol) was added in one portion to a rapidly stirred toluene solution (9.5 g) containing norbornene (25 equiv. to Mo) at 25 °C, and the solution was stirred for 5 min. 1,4,4a,5,8,8a-Hexahydro-1,4,5,8-*exo*-*endo*-dimethanonaphtalene (**CL**, *exo*:*endo* = 0.17:1.00), was then added into the solution, and the mixture was stirred for prescribed time. Prescribed amount of the third monomer in toluene (1.0 g) was then added in one portion and the reaction mixture was further stirred for 15 min. The polymerization was quenched by adding aldehyde (**A** or **B**) (ca. >10 mg, excess), and the solution was stirred for 1 h for completetion. The mixture was then removed *in vacuo*, and the resultant solid was dissolved in the minimum amount of THF. The solution was poured dropwise into methanol to afford pale white precipitates. The polymer was then collected by filtration and dried *in vacuo*. Yield 88% (run 5).[19]

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[19] ^{1}H NMR (400MHz, $CDCl_3$): δ 7.51 (s), 6.77 (s), 5.58 (br), 5.39 (br) (olefinic end group protons), 5.37-5.19 (br, olefinic H), 5.49 (brs), 4.60 (brs), 4.30-4.21 (br d), 3.97 (brs) (sugar group protons), 2.95 (br), 2.78 (br), 2.42 (br), 1.95-1.74 (br) (protons of the fivemembered rings), 1.52 (brs), 1.46 (brs), 1.43 (brs), 1.36 (brs), 1.33 (brs) (isopropylidene), 0.25 (s, $SiMe_3$ end group). The observed resonances were analogous to those in poly(**1**)[11] and homopolymer of monomer **2**.[14]