Precise Synthesis of Amphiphilic Polymeric Architectures by Grafting Poly(ethylene glycol) to End-Functionalized Block ROMP Copolymers

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ABSTRACT: Various (linear, triarms, ABA or ABCBA type) amphiphilic multiblock copolymers containing acetal-protected sugars have been prepared by the coupling of an end-functionalized ROMP copolymer with poly(ethylene glycol) (PEG). The synthesis involves three key steps: (i) termination of the block ROMP copolymer prepared by molybdenum−alkylidene initiator, [Mo(CHCMe$_2$Ph)(N-2,6-^{i}Pr$_2$C$_6$H$_3$)-(O^{t}Bu)$_2$] (**1**), with either TMS ($SiMe_3$) protected 4-hydroxy- or 3,5-dihydroxybenzaldehyde; (ii) exclusive removal of the TMS protection from the terminus; and (iii) the potassium hydride mediated attachment of poly(ethylene glycol), PEG (M_n = 2200 or 4600), to the ring-opened polymers. In all cases, M_n values for resultant copolymers estimated by ^{1}H NMR (and by GPC) were very close to those calculated based on the initial monomer/initiator loadings with low polydispersity indices (M_w/M_n = 1.05−1.20 by GPC). The preparation of a multiblock or star-shaped (triarms) amphiphilic copolymer was possible depending on which terminating agent was adopted. The cyclic acetal in the sugar-containing polymers could be hydrolyzed exclusively using a CF_3CO_2H/H_2O mixture (9/1 v/v) affording the corresponding deprotected analogues with the M_n values calculated based on the initial molar ratios.

Introduction

Precise control over macromolecular structure and the resulting material properties has been a central goal in the field of synthetic polymer chemistry, and efforts have thus been directed toward the accomplishment of new synthetic methodologies for precise placement of chemical functionality and monomer composition.[1] Amphiphilic block copolymers (ABCs), consisting of both hydrophobic and hydrophilic parts in the polymer molecule, have attracted considerable attention on account of the ability to exhibit unique structures and properties such as surface activity on the formation of micelles (aggregates) via self-association in both aqueous and hydrophobic media.[2−9] The ability to control the properties by tuning the initial building blocks (hydrophobic/hydrophilic parts) results in the preparation of various well-defined phase-separated microstructures and nanoarchitectures (spheres, rods, vesicles, lamellae, large compound micelles, nanofibers, nanotubes, etc.) for diverse, promising applications. One area in which ABCs have received particular interest is in pharmaceutical applications ranging from sustained-release technologies to gene delivery.[10,11] The ability of ABCs for delivery of therapeutic reagents results from their unique chemical composition, which is characterized by a hydrophilic block that is chemically tethered to a hydrophobic block. Upon micellization, the hydrophobic core regions serve as reservoirs for hydrophobic drugs, which may be loaded by chemical, physical, or electrostatic means, depending on the specific functionalities of the core-forming block and the solubilizate (solubilizer). The most commonly used hydrophilic block in polymeric micelle drug delivery systems is poly(ethylene oxide)/poly(ethylene glycol), PEO/PEG, as the shell-forming material[12] due to its low toxicity as well as its ability to minimize protein adsorption to surfaces.[13] PEO attachment is thus often used to improve the biocompatibility with foreign materials.

We recently demonstrated that new types of amphiphilic poly(macromonomer)s shown in Chart 1 can be prepared by the repetitive ROMP technique using the molybdenum−alkylidene initiator.[14] The key step for this success was the exclusive preparation of end-functionalized ring-opened poly(norbornene)s realized by a living polymerization with quantitative initiation as well as the preparation and purification of the macromonomers. Another important factor for this achievement was that the molybdenum−alkylidene complexes (Chart 2) are useful initiators for the living ring-opening metathesis polymerization (ROMP) of cyclic olefins, especially substituted norbornenes and norbornadienes.[15−18] The absence of chain-transfer and termination reactions in such polymerizations allows for the production of homopolymers and block copolymers with narrow molecular weight distributions as well as enabling the control of terminal groups in both the initiation and the termination sites. Since the reaction of an hydroxyl-terminated ROMP polymer with norbornene carboxylic acid chloride afforded the corresponding macromonomer exclusively in all cases,[14] these results suggest the possibility that the reaction with the chain end of an other polymer will afford the new types of ABCs consisting of different polymer main chains.[19−24]

Preparation of ABCs by sequential addition of norbornene monomers,[20] by a combination of ROMP with ATRP (atom transfer radical polymerization)[21] or group-transfer system,[22] and by using a tandem system incorporating ROMP and ATRP[23] were previously reported. These are synthetic methodologies adopting the so-called "grafting from" approach by propagating another polymer chain from the chain-end of ring-opened poly(norbornene). In contrast, examples of "grafting to" the ROMP polymer by reaction with another polymer chain end have been limited due to the difficulty in achieving complete conversion and also due

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Chart 1

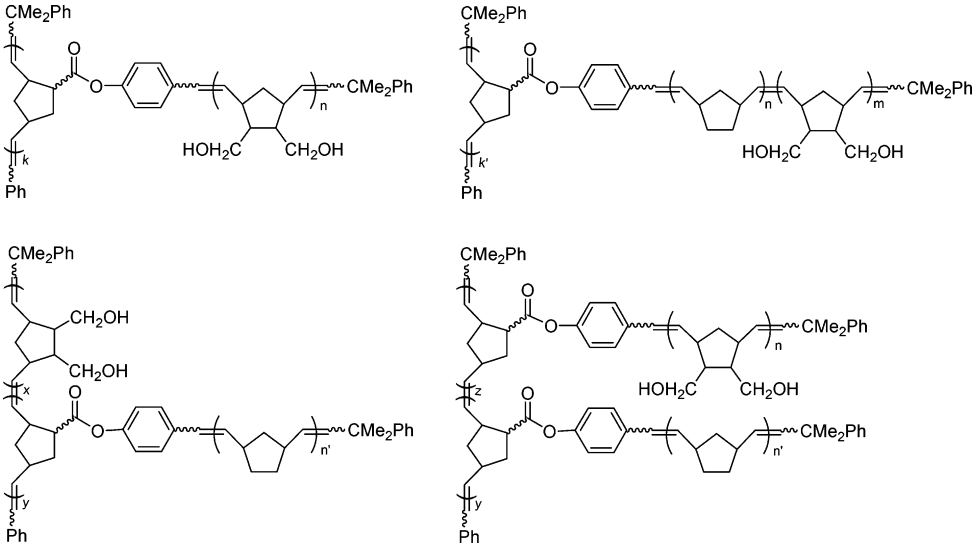
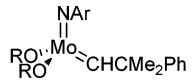
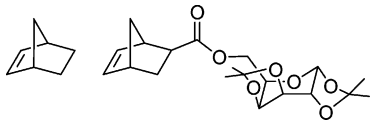


Chart 2



OR = O^{t}Bu, OCMe(CF$_3$)$_2$ etc.
Ar =2,6-^{i}Pr$_2$C$_6$H$_3$ etc.

Chart 3



to the potential difficulty of separation of unreacted polymer by fractionation, etc., because, in previous cases, an excess amount of polystyrene bearing an aldehyde at the chain end was required for the termination of ROMP.[19] Since, as described above, the reaction of the hydroxyl-terminated ROMP polymer with norbornene carboxylic acid chloride afforded the corresponding norbornene-based macromonomer in quantitative yields in all cases,[14] we decided to explore the possibility of establishing new synthetic methodologies to prepare new types of ABCs consisting of different polymer main chains by a "grafting to" approach.[24] In this paper, therefore, we wish to introduce our explored results concerning the synthesis of various amphiphilic multiblock copolymers adopting a "grafting to" approach whereby poly(ethylene glycol) is attached to, in the first instance, a nonpolar ROMP homopolymer of NBE and, second, to a diblock ROMP copolymer containing a sugar functionalized segment prepared by the living technique using the Schrock-type molybdenum initiator.

Results and Discussion

1. Preparation of End-Functionalized ROMP Polymers. Norbornene and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-*O*-yl 5-norbornene-2-carboxylate (*endo*/*exo* = 87/13, Chart 3) were chosen for this study to prepare homopolymers and block copolymers, not only because synthesis and purification procedures for these monomers were already established[25] but also because the resultant polymers containing carbohydrates 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 which led to a greater affinity and specificity than their monovalent counterparts. The tuning of these protein−carbohydrate recognition events is thus potentially one of the most promising routes in cellular specific drug targeting.[26] We also chose the Mo(CHCMe$_2$Ph)(N-2,6-^{i}Pr$_2$C$_6$H$_3$)(O^{t}Bu)$_2$ (**1**) as the initiator due to its ability to prepare multiblock copolymers in a precise manner, as reported recently.[25,27]

Norbornene was polymerized in toluene at 25 °C with **1** at different monomer/initiator molar ratios, and the reactions were terminated by addition of 4-Me$_3$SiO-C$_6$H$_4$CHO to afford poly(**2a**) or by addition of 3,5-(Me$_3$SiO)$_2$-C$_6$H$_3$CHO to afford poly(**2b**) in high isolated yield (>94%) in all cases (Scheme 1, Table 1, runs 1−6). This is the established procedure for cleaving ROMP polymer−metal bonds of this type from the initiator fragment in a Witig-like reaction with an aldehyde. As shown in both Figure 1 and Table 1, the M_n value for resultant ring-opened poly(norbornene) by GPC linearly increased upon increasing the monomer/Mo molar ratios, and the molecular weight distributions for both poly(**2a**) and poly(**2b**) were narrow in all cases (M_w/M_n = 1.05−1.12). These results clearly indicate that these polymerizations took place in a living manner.

As reported previously,[14] the observed M_n value by GPC vs polystyrene standards were relatively larger than those calculated based on the initial monomer/initiator molar ratio, but the M_n values estimated by ^{1}H NMR spectra (integration ratio with SiMe$_3$ group at the polymer chain end) were in good agreement with the calculated values,[14,28] indicating that these polymerizations proceed in a living manner with quantitative initiation as was often seen in the ROMP of norbornene derivatives with **1**.[15−18]

Various block copolymers were also prepared by the sequential addition of norbornene and its derivative (Table 1, runs 7−15). As shown in Figure 2, the M_n value increased linearly upon increasing the added amount of the norbornene derivative containing acetal-protected galactose residue (norbornene/Mo = 50). These results also indicated that these polymerizations took place in a living manner. The low PDI values (M_w/M_n = 1.09−1.12) were additional evidence of a living system under these conditions.

The SiMe$_3$ group of both the above homopolymer and the block ROMP copolymer, poly(**2**), was cleanly re-

Scheme 1

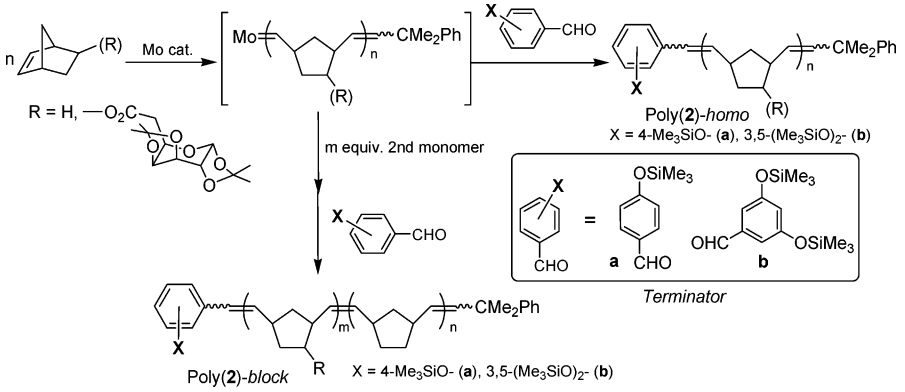


Table 1. Ring-Opening Metathesis Polymerization of Norbornene and Its Carbohydrate Derivative with Mo(N-2,6-^{i}Pr$_2$C$_6$H$_3$)(CHCMe$_2$Ph)(O^{t}Bu)$_2$ (1) in Toluene[a]

run	n/m[b] 1st/2nd	time/min 1st/2nd	poly(**2**)	M_n[c] × 10^{-4}	M_w/M_n[c]	yield[d]/%
1	50/0	30/–	poly(**2a**)	1.03	1.08	99
2	50/0	30/–	poly(**2b**)	1.03	1.12	96
3	50/0	30/–	poly(**2b**)	0.96	1.07	99
4	60/0	30/–	poly(**2a**)	1.07	1.12	99
5	75/0	30/–	poly(**2a**)	1.38	1.10	94
6	100/0	30/–	poly(**2a**)	1.77	1.05	99
7	25/25	20/20	poly(**2a**)	1.38	1.09	99
8	25/25	20/20	poly(**2a**)	1.53	1.11	99
9	25/25	20/20	poly(**2b**)	1.56	1.11	99
10	50/25	40/20	poly(**2a**)	1.51	1.12	99
11	50/25	40/20	poly(**2a**)	1.88	1.07	96
12	50/25	40/20	poly(**2b**)	1.85	1.16	99
13	50/35	40/25	poly(**2a**)	2.10	1.09	99
14	50/40	40/30	poly(**2a**)	2.28	1.12	97
15	50/50	40/30	poly(**2a**)	2.37	1.31	96
16	0/50	–/50	poly(**2b**)	2.28	1.17	94

[a] Preparation of homopolymers and diblock copolymers, poly(**2**). [a] Polymerization conditions: in toluene at room temperature (25 °C). [b] Molar ratio based on Mo (shown in Scheme 1). [c] GPC data in THF vs polystyrene standards. [d] Isolated yield.

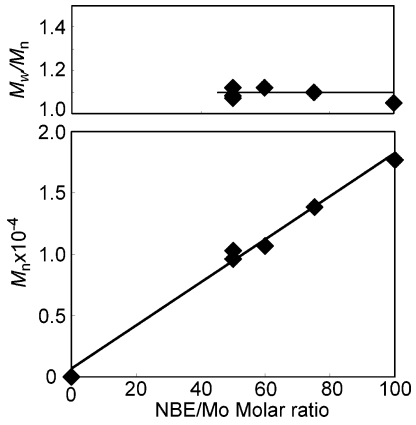


Figure 1. Plots of M_n vs norbornene/Mo molar ratio in the ring-opening metathesis polymerization of norbornene with **1**.

moved by treating the poly(**2**) with aqueous HCl solution, affording the ROMP polymers containing an OH group at the chain end, poly(**3**), in quantitative yields (yield 91–99%, Schemes 2 and 3, and Tables 2–4). In contrast, cyclic acetal groups of the carbohydrate residue in the polymer were not eliminated/deprotected under these weakly acidified conditions. These results clearly indicated that various end-functionalized copolymers with controlled molecular weights (with precisely controlled repeated units) could be easily prepared by this ROMP procedure by the sequential addition of different monomers and/or by varying monomer/initiator molar ratios.

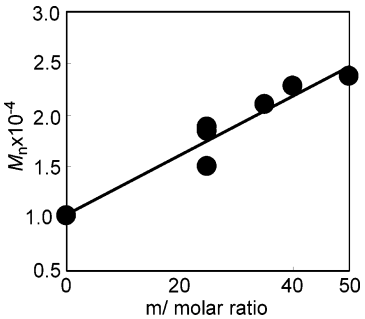
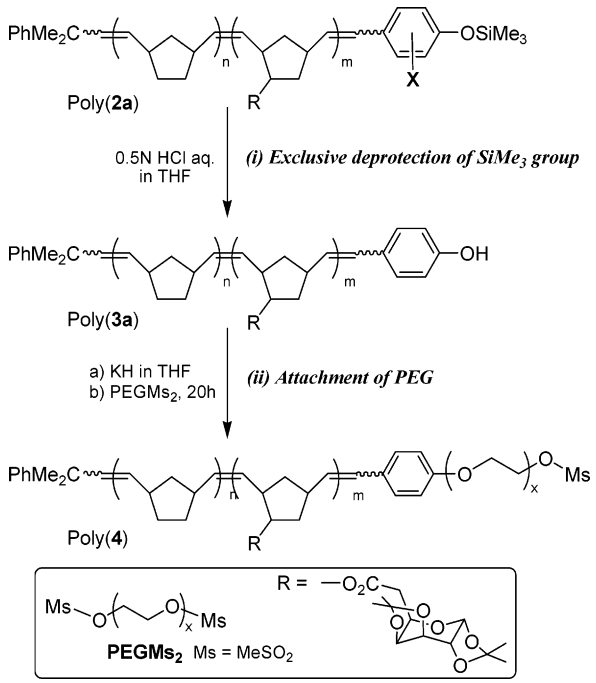


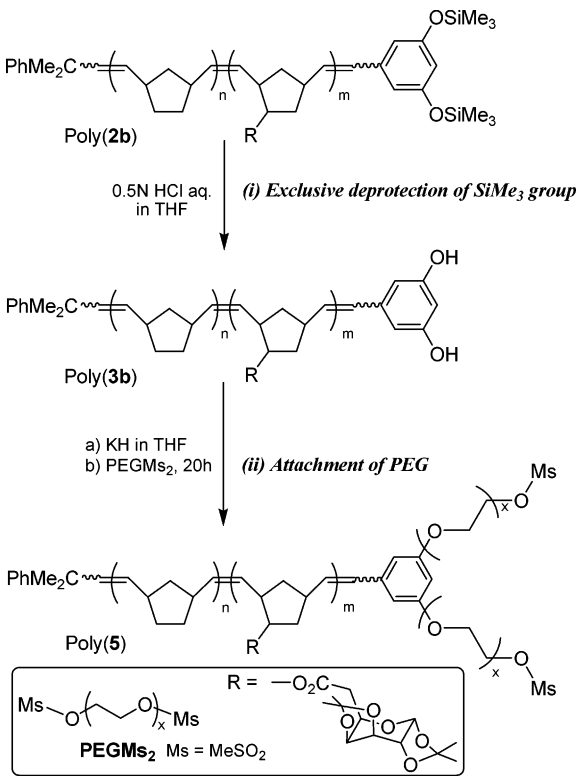
Figure 2. Plots of M_n vs m (molar ratio of norbornene derivative) in addition to 50 equiv of norbornene in the ROMP with **1** (Table 1).

2. Precise Synthesis of Amphiphilic Multiblock Copolymers by Grafting Poly(ethylene glycol) into the ROMP Polymer. Two types of poly(ethylene glycol) (PEG) [M_n = 2200 (PEG_{47}), 4600 (PEG_{110}), M_w/M_n = 1.03] were chosen for attachment with the above hy-

Scheme 2



Scheme 3



droxyl-terminated poly(norbornene)s, not only because these PEGs were commercially available with various molecular weights with low M_w/M_n values but also because PEG is widely used as the hydrophilic segment of amphiphilic block copolymers, especially for drug delivery systems.[10,12−13] In addition, the procedure for preparing the ether linkage through $PEGMs_2$ [$MsO(CH_2CH_2O)_nMs$, Ms = $MeSO_2$] prepared by treating PEG with methane sulfonyl chloride was expected to be suited for this approach.[29]

The hydroxyl group at the polymer chain end in poly(**3a**) was treated with KH in THF, and its subsequent coupling with $PEGMs_2$ [$MsO(CH_2CH_2O)_nMs$, Ms = $MeSO_2$] yielded the diblock linear ABCs consisting of ring-opened poly(norbornene) and PEG, poly(**4**) in high yield (Scheme 2, Table 2, runs 1, 4−6). The GPC traces for the resultant poly(**4**) showed that appropriate increases in the M_n values were observed after the attachment reaction (Figure 3), and the resultant polymers possessed both unimodal and narrow molecular weight distributions in all cases (M_w/M_n = 1.06−1.12). In addition, the M_n values estimated by ^1H NMR (by comparison of olefinic protons vs protons in PEG) were in good agreement with those calculated based on the initial molar ratios in all cases. These results clearly indicate the exclusive formation of PEG-attached ABCs by this approach.

Moreover, the hydroxyl group at the diblock copolymer chain end in poly(**3a**) was treated with KH in THF, and its subsequent coupling with $PEGMs_2$ [$MsO(CH_2CH_2O)_nMs$, Ms = $MeSO_2$] afforded the linear amphiphilic triblock copolymers, poly(**4**) in relatively high yield (Scheme 2, Table 2, runs 7, 8, 10, 11, 13−15). The GPC traces for the resultant poly(**4**) showed both unimodal and narrow molecular weight distributions in all cases (M_w/M_n = 1.06−1.22), and the M_n values estimated by ^1H NMR (by comparison of olefinic protons vs protons in PEG) were the same as those calculated based on the molar ratios. These results also clearly indicated that precise control of each block could be possible by this approach. The reason for the decreased isolation yields in some experimental runs (especially the reaction with PEG_{110}) was due to the difficulty in isolating from the reaction mixture containing the desired poly(**4**) and PEG added in a relatively excess amount. This excess was necessary to obtain the desired poly(**4**) exclusively without accompanying the sandwich (ABA or ABCBA) type copolymer as the byproduct, poly(**6**) described below. The optimization of the molar amount of PEG added under optimized purification procedure would increase the yields because no starting ROMP polymer was remained in the reaction mixture after the attachment procedure (confirmed by GPC). Since it was clear that various linear ABCs will be prepared by varying monomer/Mo molar ratio as well as by varying the repeated unit of PEG, these results clearly indicate that precise control of hydrophobic and hydrophilic segment can be easily achieved by this procedure.

Synthesis of Triarms Amphiphilic Block Copolymers. An additional benefit of the present approach was, we believe, that the polymer termini could be modified by changing the terminating agent, and preparation of the triarms ABCs was thus expected by the analogous procedure. Bifunctionalized ring-opened poly(norbornene), poly(**3b**), was treated with KH in THF, and its subsequent coupling with $PEGMs_2$ [$MsO(CH_2CH_2O)_nMs$, Ms = $MeSO_2$] yielded the triarms ABCs consisting of ring-opened poly(norbornene) and PEG, poly(**5**), in moderate

Table 2. Synthesis of Amphiphilic Block Copolymers, Poly(4)

		poly(**2a**)		poly(**3a**)			PEG	poly(**4**)				
run[a]	n/m[b]	M_n[c](GPC) $\times 10^{-4}$	M_w/M_n[c]	M_n[c](GPC) $\times 10^{-4}$	M_w/M_n[c]	yield/%	M_n[c] $\times 10^{-3}$	M_n[d](calcd) $\times 10^{-4}$	M_n[c](GPC) $\times 10^{-4}$	M_n[e](NMR) $\times 10^{-4}$	M_w/M_n[c]	yield[f]/%
1	50/0	1.03	1.08	0.99	1.09	98	2.20	0.70	1.41	0.69	1.10	86
1	50/0	1.03	1.08	0.99	1.09	98	4.60	0.96	1.61	0.97	1.08	86
4	60/0	1.07	1.12	1.02	1.11	99	2.20	0.79	1.32	0.82	1.12	83
5	75/0	1.38	1.10	1.35	1.09	99	2.20	0.93	1.72	1.07	1.12	90
6	100/0	1.77	1.05	1.82	1.05	98	2.20	1.17	2.15	1.16	1.06	82
7	25/25	1.38	1.09	1.36	1.08	96	2.20	1.37	1.67	1.44	1.10	88
8	25/25	1.53	1.11	1.47	1.08	95	4.60	1.63	2.30	1.62	1.16	68
10	50/25	1.51	1.12	1.49	1.13	98	2.20	1.62	1.95	1.65	1.13	89
11	50/25	1.88	1.07	1.92	1.07	98	4.60	1.86	2.38	1.85	1.06	72
13	50/35	2.10	1.09	2.05	1.08	98	4.60	2.22	2.52	2.32	1.11	77
14	50/40	2.28	1.12	2.25	1.11	99	4.60	2.41	2.69	2.44	1.10	82
15	50/50	2.37	1.31	2.42	1.29	98	4.60	2.75	2.83	2.79	1.22	88

[a] Run no. in Table 1 (sample of ROMP polymer). [b] Molar ratio of based on Mo (shown in Schemes 1 and 2). [c] GPC data in THF vs polystyrene standards. [d] Calculated value based on initial feedstock ratio. [e] Estimated from ^1H NMR data. [f] Isolated yield.

Table 3. Synthesis of Amphiphilic Triarms Block Copolymers, Poly(5)

		poly(**2b**)		poly(**3b**)			PEG	poly(**5**)				
run[a]	*n*/*m*[b]	M_n[c](GPC) × 10^{-4}	M_w/M_n[c]	M_n[c](GPC) × 10^{-4}	M_w/M_n[c]	yield/%	M_n[c] × 10^{-3}	M_n[d](calcd) × 10^{-4}	M_n[e](NMR) × 10^{-4}	M_n[c](GPC) × 10^{-4}	M_w/M_n[c]	yield[f]/%
2	50/0	1.03	1.12	1.02	1.06	96	2.20	0.71	0.72	1.52	1.12	50
3	50/0	0.96	1.07	0.93	1.06	96	4.60	1.38	1.44	1.82	1.11	60
16	0/50	2.28	1.17	2.28	1.13	92	4.60	2.82	2.84	2.82	1.10	86
9	25/25	1.56	1.11	1.42	1.09	91	2.20	1.44	1.48	1.92	1.20	93
12	50/25	1.85	1.16	1.91	1.17	97	2.20	1.84	1.87	2.75	1.12	83

[a] Run no. in Table 1 (sample of ROMP polymer). [b] Molar ratio based on Mo (shown in Schemes 1 and 3). [c] GPC data in THF vs polystyrene standards. [d] Calculated value based on initial feedstock ratio. [e] Estimated from ^{1}H NMR data. [f] Isolated yield.

Table 4. Synthesis of ABA or ABCBA Type Amphiphilic Multiblock Copolymers, Poly(6)

		poly(**2a**)		poly(**3a**)			PEG	poly(**6**)				
run[a]	*n*/*m*[b]	M_n[c](GPC) × 10^{-4}	M_w/M_n[c]	M_n[c](GPC) × 10^{-4}	M_w/M_n[c]	yield/%	M_n[c] × 10^{-3}	M_n[d](calcd) × 10^{-4}	M_n[e](NMR) × 10^{-4}	M_n[c](GPC) × 10^{-4}	M_w/M_n[c]	yield[f]/%
1	50/0	1.03	1.08	0.99	1.09	98	2.20	1.20	1.20	2.19	1.04	85
7	25/25	1.38	1.09	1.36	1.08	96	2.20	2.62	2.67	3.18	1.04	83
10	50/25	1.51	1.12	1.49	1.13	98	2.20	3.10	3.25	4.02	1.01	88

[a] Run no. in Table 1 (sample of ROMP polymer). [b] Molar ratio based on Mo (shown in Schemes 1 and 4). [c] GPC data in THF vs polystyrene standards. [d] Calculated value based on initial feedstock ratio. [e] Estimated from ^{1}H NMR data. [f] Isolated yield.

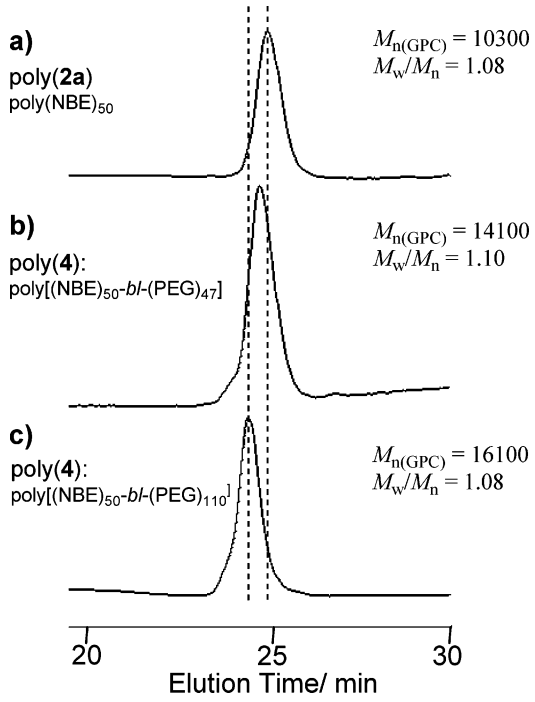


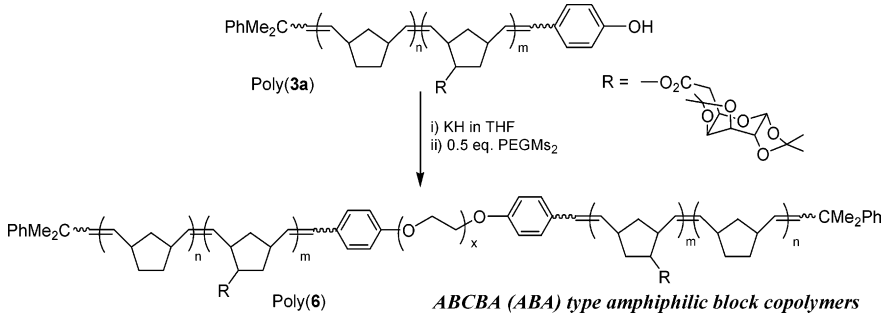
Figure 3. GPC trace for (a) poly(**2a**) (run 1) and PEG attached poly(**4**), (b) poly(**2**)-*bl*-PEG_{47}, and (c) poly(**2**)-*bl*-PEG_{110}.

yields (runs 2 and 3, Scheme 3, Table 3).[30] The GPC traces for the resultant poly(**5**) showed both unimodal and narrow molecular weight distributions in all cases (M_w/M_n = 1.11−1.12), and the M_n values estimated by ^{1}H NMR (by comparison of olefinic protons vs protons in PEG) were in good agreement with those calculated based on the molar ratios. Triarms ABCs consisting of ROMP homopolymer containing acetal-protected galactose residue could also be prepared in the same manner (run 16, Table 3).

The amphiphilic triarms block copolymer consisting of diblock ROMP copolymers and PEG could also be prepared by the analogous procedure; the coupling of diblock copolymer with $PEGMs_2$ afforded (ABC_2 type) poly(**5**) in high yield (Scheme 3, Table 3, runs 9, 12). The M_n values estimated by ^{1}H NMR for resultant poly(**5**) were close to the calculated values and possessed both unimodal and narrow molecular weight distributions. Since precise control of the repeat units of both norbornene (hydrophobic) and the sugar-substituted norbornene derivatives (rather hydrophilic after deprotection) as well as the attached PEG (hydrophilic) could be possible by using this approach, it was thus concluded that the present approach should be very effective for the preparation of new types of ABCs consisting of ROMP and PEG units in a precise manner.

Preparation of ABA or ABCBA Type Amphiphilic Block Copolymers. It was revealed that the reaction of poly(**3a**) with 0.5 equiv of PEG in the presence of KH afforded ABA or ABCBA (sandwich) type amphiphilic multiblock copolymers, poly(**6**), in high yield (Scheme 4, Table 4). The M_n values for resultant polymers were very close to the calculated values based on initial molar ratios. It was noteworthy that the reaction with 0.5 equiv of $PEGMs_2$ completed without remaining poly(**3**)

Scheme 4



Scheme 5

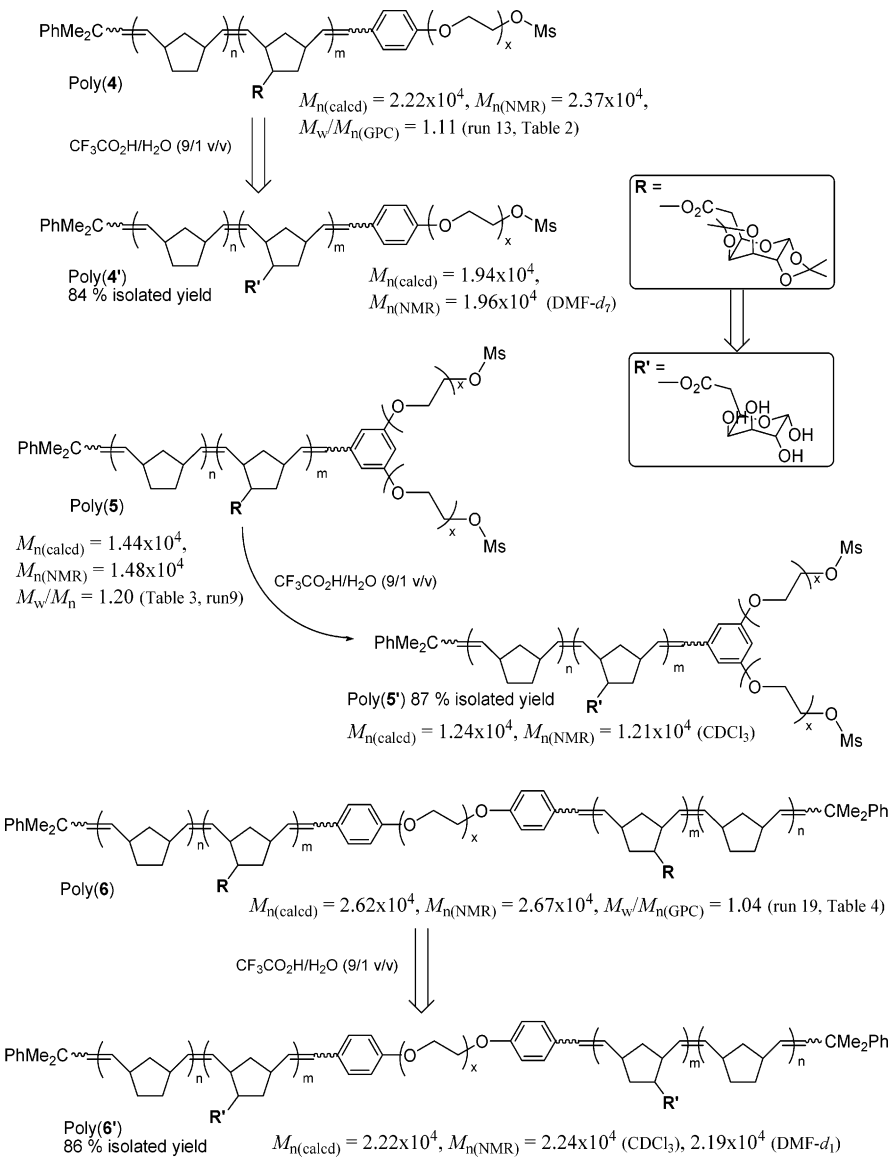


Table 5. Deprotection of Acetal in Poly(4), Poly(5), and Poly(6)[a]

		poly(**4**), poly(**5**), or poly(**6**)					poly(**4′**), poly(**5′**), or poly(**6′**)		proton ratio[h] PEG/sugar/NBE	
run[a]	polymer	*n*/*m*/*x*[b]	M_n[c](calcd) × 10^{-4}	M_n[d](NMR) × 10^{-4}	M_n[e](GPC) × 10^{-4}	yield[f]/%	M_n[c](calcd) × 10^{-4}	M_n[g](NMR) × 10^{-4}	calcd	obsd
10	poly(**4**)	50/25/47	1.62	1.65	1.13	89	1.42	1.41 ($CDCl_3$)	1.50/1.00/4.20	1.60/1.00/4.25
13	poly(**4**)	50/35/110	2.22	2.32	1.11	84	1.94	1.96 (DMF-d_7)	2.51/1.00/3.40	2.31/1.00/3.22
14	poly(**4**)	50/40/110	2.41	2.44	1.10	86	2.09	2.08 (DMF-d_7)	2.20/1.00/2.86	2.35/1.00/3.03
15	poly(**4**)	50/50/110	2.75	2.79	1.22	83	2.35	2.41 (DMF-d_7)	1.76/1.00/2.80	1.75/1.00/2.75
9	poly(**5**)	25/25/47	1.44	1.48	1.20	87	1.24	1.21 ($CDCl_3$)	3.00/1.00/2.80	3.19/1.00/3.01
7	poly(**6**)	25/25/47	2.62	2.67	1.04	86	2.22	2.24 ($CDCl_3$)	0.75/1.00/2.80	0.84/1.00/3.03
								2.19 (DMF-d_7)	0.75/1.00/2.80	0.84/1.00/2.94
10	poly(**6**)	50/25/47	3.10	3.25	1.01	91	2.70	2.78 (DMF-d_7)	0.75/1.00/4.20	0.75/1.00/4.28

[a] Synthesis of amphiphilic block copolymers. [a] Run no. in Table 1 (sample of ROMP polymer). [b] Molar ratio based on Mo (shown in Scheme 5). [c] Calculated value based on initial feedstock ratio. [d] Estimated value from ^{1}H NMR spectrum in $CDCl_3$. [e] GPC data in THF vs polystyrene standards. [f] Isolated yield. [g] Estimated value from ^{1}H NMR spectrum (comparison of PEG with olefinic protons). [h] Proton ratios estimated by ^{1}H NMR spectra.

nor PEG, and these results clearly emphasized the high reactivity of both $PEGMs_2$ and hydroxyl group at the ROMP polymer chain end.

3. Hydrolysis of Acetals in the Carbohydrate Residues. Hydrolysis of cyclic acetals of ketoses by acetic acid, oxalic acid, ion-exchange resin, or mixtures of trifluoroacetic acid and water are well-known, and the deprotection with a mixture of CF_3CO_2H and water (9/1 v/v) has been effective, not only because the reaction requires only 5−10 min at room temperature but also because many functional groups are not attacked.[31] Since the cyclic acetals in the ROMP polymer, poly(**2**), could be removed by using a mixture of CF_3CO_2H and water (9/1 v/v) at room temperature (for 15 min),[25] therefore, we chose this procedure for the present hydrolysis procedure.

The cyclic acetals in the ABC poly(**4**) could be removed according to the same procedure, and the deprotected polymer, poly(**4′**), could be isolated as the white precipitates by adding the reaction mixture into a vigorously stirred cold THF solution (0 °C). Both the ^{1}H and ^{13}C NMR spectrum (in $CDCl_3$-d_1, DMF-d_7) showed that no signals ascribed to the acetal protecting groups remained, but all other characteristic resonances of the intact deprotected sugar bound through an ester linkage to the backbone were present.[33,34] As shown in Table 5, the isolated yields in these hydrolysis procedures were very high, suggesting that these procedures afforded the resultant deprotected polymers without removing the galactose residue from the main chain. FT-IR spectra showed a broad absorption band at 3415 cm^{-1} characteristic of hydroxyl groups but no absorption ascribable to a carboxylic acid. In addition, the proton ratios of PEG/sugar/ring-opened NBE for resultant polymers estimated by ^{1}H NMR spectra were very close to the calculated values.[33,34] These facts clearly indicated that the present hydrolysis procedure efficiently removed the acetal group from the sugar moiety without cleaving the ester functionality connecting it to the ROMP polymer main chain. The deprotected polymers were soluble to varying degrees in dimethyl sulfoxide, dimethylformamide, chloroform, slightly soluble in water, THF at room temperature, and insoluble in hexane and pentane.

Concluding Remarks

We have shown that precise control of amphiphilic block sequences in linear (AB or ABC type), triarms (AB_2 or ABC_2 type), and ABA or ABCBA (sandwich) type polymeric architectures can be possible by grafting PEG to the chain end of the ROMP polymer prepared by the living technique using Mo−alkylidene initiator. Since the precise placement of the functionality as well as the precise control of each repeating unit and degree of hydrophobic and hydrophilic nature can be possible by this method, the present "grafting to" approach should be very useful to prepare the ABCs for desired properties in a precise manner. Moreover, various functionalities can be placed as the side chain in the ROMP polymers; this approach will afford new efficient synthetic methodologies for precisely designing unique polymeric architectures for desired properties.

Experimental Section

General Procedure. All experiments were carried out under a nitrogen atmosphere in a Vacuum Atmospheres drybox or using standard Schlenk techniques. All chemicals used were of reagent grade and were purified by standard purification procedures. Polymerization grade toluene was distilled from sodium and benzophenone, stored over sodium/potassium alloy in a drybox, and was then passed through an alumina short column prior to use. Anhydrous grade diethyl ether, CH_2Cl_2, THF, and *n*-hexane (Kanto Kagaku Co. Ltd.) were transferred into a bottle containing molecular sieves (mixture of 3A, 4A 1/16, and 13X) in the drybox. Mo(CHCMe$_2$Ph)(N-2,6-^{i}Pr$_2$C$_6$H$_4$)(O^{t}Bu)$_2$ (**1**)[15] and 5-norbornenecarboxylic acid chloride[32] were prepared according to the literature. 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranos-6-*O*-yl 5-norbornene-2-carboxylate was synthesized, purified, and recrystallized according to the previous report.[25]

All ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-LA400 spectrometer (^{1}H, 399.65 MHz; ^{13}C, 100.40 MHz), all spectra were obtained in the solvent indicated at 25 °C, and all chemical shifts are given in ppm and are referenced to $SiMe_4$. HPLC grade THF was used for GPC and was degassed prior to use. GPC were performed at 40 °C on a Shimazu SCL-10A using a RID-10A detector (Shimazu 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 mm^2 diameter) were calibrated vs polystyrene standard samples.

Poly(2): Homopolymerization of 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranos-6-*O*-yl 5-Norbornene-2-carboxylate. A toluene solution of Mo(CHCMe$_2$Ph)(N-2,6-^{i}Pr$_2$C$_6$H$_3$)(O^{t}Bu$_2$)$_2$ (**1**, 2.58 μmol/0.7 mL of toluene) was added in one portion to a rapidly stirred toluene solution (4 mL) containing the prescribed amount of the above monomer at room temperature, and the solution was stirred for the prescribed time. The polymerization was quenched by adding 4-Me$_3$Si-C$_6$H$_4$CHO (∼10 mg). The solvents were removed in vacuo after 1 h, and the resultant solid was dissolved in the minimum amount of THF. The solution was poured dropwise into cyclohexane to afford pale white precipitates, and the homopolymer, poly(**2a**), was collected by filtration and dried in vacuo; yield = 94%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.1 (br, olefinic H), 5.1−5.5 (br, olefinic H), 3.95 (br, s), 4.18 (br, d), 4.27 (br, s), 4.58 (br), 3.9−4.1 (br) (sugar group protons), 1.60 (br), 1.92 (br) and 2.31−3.18 (br) (protons of the five-membered ring), 1.48 (s, Me), 1.43 (s, Me), 1.31 (s, Me) (cyclic acetal group). ^{13}C NMR (400 MHz, $CDCl_3$): δ 174.8 (carbonyl), 135.0, 129.9, 129.2, 128.2, 126.3 (olefinic carbon), 109.7, 108.9 (isopropylidene), 96.5, 71.2, 70.9, 70.6, 66.0, 63.4, 63.1 (sugar group), 43.0−43.1, 40.8−41.2, 39.9, 36.0−36.8, 29.1 (five-membered ring), 26.2, 25.2, 24.7, (isopropylidene).

Poly(2a): Synthesis of Block Copolymers of Norbornene (NBE) and 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranos-6-*O*-yl 5-Norbornene-2-carboxylate. A toluene solution of Mo(CHCMe$_2$Ph)(N-2,6-^{i}Pr$_2$C$_6$H$_3$)(O^{t}Bu$_2$)$_2$ (2−7 mg/0.3−1.0 mL of toluene) was added in one portion to a rapidly stirred solution of norbornene in toluene (4 mL) at room temperature, and the solution was stirred for the prescribed time. The second monomer in toluene (1.7 mL) was added in one portion to the reaction mixture, and the solution was stirred for the additional required time. The polymerization was quenched by adding 4-Me$_3$Si-C$_6$H$_4$CHO (∼10 mg). The solvents were removed in vacuo after 1 h, and the resultant solid was dissolved in the minimum amount of THF. The solution was then poured dropwise into methanol to afford pale white precipitates, and the copolymer, poly(**2a**), was collected by filtration and dried in vacuo. Yield >95%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (s), 6.97 (s), 5.58 (br), 5.39 (br) (olefinic end group protons), 5.37−5.18 (br, olefinic H), 5.49 (br s), 4.58 (br s), 4.29−4.21 (br d), 3.97 (br s) (sugar group protons), 2.93 (br), 2.75 (br), 2.40 (br), 1.95−1.74 (br) (protons of the five-membered rings), 1.54 (br s), 1.46 (br s), 1.41 (br s), 1.34 (br s), 1.31 (br s) (isopropylidene), 0.24 (s, trimethylsilyl end group). ^{13}C NMR (400 MHz, $CDCl_3$): δ 174.4 (carbonyl), 133.8−132.8 (olefinic carbon), 109.5, 108.7 (isopropylidene), 96.2, 71.0−70.4, 65.9, 63.2−62.9 (sugar group), 48.4, 45.7, 43.4−42.1, 38.5, 33.1−32.1 (five-membered ring), 26.0, 24.9, 24.5 (isopropylidene).

Poly(3a): Removal of TMS Protection from Copolymer Terminus. Into a rapidly stirred solution of 5−10 mL of THF containing the copolymer was added 0.5 M HCl (1 drop/10 mg poly(**2a**)), and the mixture was stirred for 1 h at room temperature. The reaction solution was then added dropwise into methanol to isolate the hydroxyl group terminated ROMP copolymer, poly(**3**), which was collected by filtration and dried in vacuo. Yield >99%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (s), 6.97 (s), 5.58 (br), 5.39 (br) (olefinic end group H), 5.37−5.17 (br, olefinic H), 5.49 (br s), 4.58 (br s), 4.28−4.20 (br d), 3.97 (br) (sugar group protons), 2.93−2.76 (br d), 2.40 (br s), 1.86−1.74 (br) (protons of the five-membered rings), 1.47 (br s), 1.41 (br s), 1.34 (br s), 1.30 (br s) (isopropylidene). ^{13}C NMR (400 MHz, $CDCl_3$): δ 174.6 (carbonyl), 134.6−129.3 (olefinic carbon), 109.5, 108.7 (isopropylidene), 96.2, 70.9−70.6, 67.9, 65.8, 62.8 (sugar group), 48.3, 45.8, 43.4−42.1, 38.4, 36.0, 32.9−32.2 (five-membered rings), 26.0, 25.6, 25.0, 24.5 (isopropylidene).

Poly(4): Synthesis of Linear Amphiphilic Block Copolymer (ABC). A typical procedure for attachment of PEG with the ROMP polymer is as follows: into a THF solution

containing poly(**3a**) (1 equiv) was added KH (1.1 equiv), and the mixture was stirred for 3 h at room temperature. A THF solution containing the PEG oligomer (1.8 equiv) was then added in one portion, and the mixture was stirred overnight. The reaction solvent was removed in vacuo, and the residual product was washed twice with hexane, then with diethyl ether, and finally with methanol to remove all traces of PEG. The resultant white solid was stirred in methanol for a further 2 h, and the triblock ABC, poly(**4**), was collected by filtration and dried in vacuo. Yield >80%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (s), 6.97 (s), 5.58 (br), 5.39 (br) (olefinic end group protons), 5.37−5.17 (br, olefinic H), 5.49 (br s), 4.58 (br s), 4.28−4.21 (br d), 3.97 (br) (sugar group protons), 3.62 (br s, PEG H), 2.93−2.76 (br d), 2.40 (br s), 1.87−1.74 (br) (protons of five-membered rings), 1.47 (br s), 1.41 (br s), 1.34 (br s) (isopropylidene). ^{13}C NMR (400 MHz, $CDCl_3$): δ 173.5 (carbonyl), 132.7−129.9 (olefinic carbon), 108.5, 107.7 (isopropylidene), 95.2, 75.7, 70.9, 64.9, 61.9 (sugar group), 69.5 (PEG), 47.3, 44.7, 42.2, 41.0, 37.5, 32.0−31.3 (five-membered ring), 25.1, 23.9 (isopropylidene). FT-IR (KBr): 1749 cm^{-1} (br s, carbonyl).

Poly(5): Synthesis of Triarms ABCs. The procedure was analogous to the preparation of the linear amphiphilic block copolymer, with the exception that in the initial copolymer synthesis, poly(**2b**), the polymerization is terminated with trimethylsilyl 3,5-dihydroxybenzaldehyde. These protecting groups are subsequently removed (as described for poly(**3a**) above) to afford poly(**3b**), and the KH (2.2 equiv) mediated attachment of the PEG oligomers (3.6 equiv) afforded the triarms ABC, poly(**5**). Yield >80%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (s), 6.97 (s), 5.58 (br), 5.39 (br) (protons of olefinic end groups), 5.38−5.19 (br olefinic H), 5.49 (br s), 4.58 (br s), 4.29−4.20 (br d), 3.98 (br) (sugar group protons), 3.62 (br s, PEG H), 2.93 2.77 (br d), 2.41 (br s), 1.85−1.74 (br) (protons of the five-membered rings), 1.56 (br s), 1.51 (br s), 1.47 (br s), 1.41 (br s), 1.34 (br s), 1.31 (br s) (isopropylidene). ^{13}C NMR (400 MHz, $CDCl_3$): δ 174.4, 174.3 (carbonyl), 134.1, 133.4−132.4, 128.9 (olefinic carbon), 109.4, 108.5 (isopropylidene), 96.4−95.9, 70.8, 70.3, 65.8, 62.7 (sugar group), 70.7 (PEG), 48.0, 43.4, 42.8, 38.6−38.2, 32.8−31.9 (five-membered ring), 26.1−25.6, 25.0−24.2 (isopropylidene).

Poly(6): Synthesis of ABA or ABCBA Type Amphiphilic Block Copolymer. The procedure was analogous to the preparation of the linear ABCs, poly(**4**), with the exception that only (0.5 equiv) of the PEG oligomer is added to the reaction to afford the sandwich type ABC, poly(**6**). Yield >80%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (s), 6.97 (s), 5.58 (br), 5.39 (br) (protons of olefinic end groups), 5.36−5.17 (br olefinic H), 5.49 (br s), 4.57 (br s), 4.27−4.19 (br d), 3.96 (br) (sugar group protons), 3.61 (br s, PEG H), 2.92−2.75 (br d), 2.39 (br), 1.84−1.73 (br) (protons of the five-membered rings), 1.49 (br s), 1.40 (br s), 1.34 (br s) (isopropylidine). ^{13}C NMR (400 MHz, $CDCl_3$): δ 174.5, 174.4, 173.3, 173.2 (carbonyl), 134.0, 133.3, 132.9 (olefinic carbon), 109.5, 108.7 (isopropylidene), 96.1, 71.9, 70.9, 70.5, 67.8, 65.7 (sugar group), 71.0 (PEG), 41.9−43.4, 32.8, 32.4, 32.1−32.3 (five-membered ring), 26.1, 25.9, 24.6 (isopropylidene). FT-IR (KBr): 1731 cm^{-1} (br s, carbonyl).

Hydrolysis of Triblock Amphiphilic Block Copolymer, Poly(4′). The general hydrolysis procedure for acetal deprotection was as follows: poly(**4**) was added to a solution consisting of CF_3CO_2H/H_2O (9/1, v/v, 1.5 g), and the reaction was stirred at room temperature for 15 min. The homogeneous pale blue solution was then poured dropwise into a vigorously stirred chilled THF solution (~70 mL) at 0 °C. The pale to white precipitates were collected by filtration, washed with cold THF, hexanes, and ether, and then dried in vacuo to afford the deprotected linear ABC, poly(**4′**), as a white solid. Yield = 83−89%. ^{1}H NMR (400 MHz, DMF-d_7): δ 7.74 (br s, olefinic H), 5.19, 5.00, 4.89 (br olefinic H), 4.16 (br), 3.90 (br), 3.81 (br), 3.64 (br) (sugar group protons), 3.33 (br s, PEG H), 2.91−2.27 (br), 1.58 (br), 1.15 (br), 0.86 (br) (protons of the five-membered rings). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (br s, olefinic H), 5.72, 5.64, 5.31, 5.18 (br olefinic H), 4.36 (br), 3.94 (br), 3.42 (br) (sugar group protons), 3.62 (br s, PEG H), 2.75 (br), 2.40 (br), 2.14−1.77 (br), 1.33 (br), 1.01 (br) (protons of the five-membered rings). ^{13}C NMR (400 MHz, DMF-d_7): δ 172.0 (carbonyl), 132.0, 131.0, 129.2, 127.6 (olefinic carbon), 101.3, 96.1, 94.6, 91.4, 82.0−80.6, 76.3−75.8, 74.0, 71.1−70.8, 63.6, 61.7 (sugar group), 70.8 (PEG), 46.4, 43.6, 39.1, 37.6−33.8 (five-membered rings). FT-IR (KBr pellet): 3402 (br, OH), 1724 cm^{-1} (br s, carbonyl).

Hydrolysis of Triarms Amphiphilic Block Copolymer, Poly(5′). The general method of acetal deprotection was as follows: poly(**5**) was added to a solution consisting of CF_3CO_2H/H_2O (9/1, v/v, 1.5 g), and the reaction was stirred at room temperature for 15 min. The homogeneous pale blue solution was then poured dropwise into a vigorously stirred THF solution (~70 mL) at 0 °C. The pale to white precipitates were collected by filtration, washed with THF, hexanes, and ether, and then dried in vacuo to afford the deprotected linear ABC, poly(**4′**), as a white solid. Yield = 87%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.40, 5.27, 4.91 (br olefinic H), 4.22 (br), 3.93 (br), 3.83 (br), 3.65 (br) (sugar group protons), 2.90 (br), 2.49 (br), 1.90 (br), 1.75 (br), 1.57 (br), 1.25 (br), (protons of the five-membered rings). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.32−5.19 (br, olefinic H), 4.26 (br), 3.78 (br), 3.70 (br) (sugar group protons), 3.63 (br s, PEG H), 2.76 (br), 2,35 (br), 2.16 (br), 1.86−1.65 (br), 1.02 (br), (protons of the five-membered rings).

Hydrolysis of ABA or ABCBA Type Amphiphilic Block Copolymer, Poly(6′). Procedure analogous to previous hydrolysis to afford the deprotected sandwich type ABC, poly(**6′**), as a white solid. Yield = 86−91%. ^{1}H NMR (400 MHz, DMF-d_7): δ 7.35 (br, olefinic H) 5.54−5.34 (br, olefinic H) 4.98 (br), 4.88 (br), 4.17 (br) (sugar group protons), 3.70 (br s, PEG H), 3.16−3.07 (br), 3.01 (br), 2.49 (br), 1.94 (br), 1.50 (br) (protons of the five-membered rings). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (br, olefinic H), 5.34−5.11 (br, olefinic H), 4.19 (br), 3.92 (br), 3.64 (br), 3.40 (br) (sugar group protons), 3.82 (br s, PEG H), 2.79 (br), 2.44 (br), 1.90 (br), 1.36 (br), 1.04 (br) (protons of the five-membered rings). ^{13}C NMR (400 MHz, DMSO-d_6): δ 173.1 (carbonyl), 132.9, 132.0, 129.0, 124.5 (olefinic carbon), 101.8, 97.1, 82.1, 76.2, 72.9, 71.7, 67.7, 64.7 (sugar group), 69.4 (PEG), 47.3, 41.7, 32.2, 21.3 (five-membered rings). FT-IR (KBr pellet): 3427 (br, OH), 1732 cm^{-1} (br s, carbonyl).

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-*O*-yl 5-norbornene-2-carboxylate (monomer), poly(**2a**) (block ROMP copolymer), poly(**3a**), poly(**2b**), poly(**3b**) (block ROMP copolymer), poly(**4**), poly(**5**), poly(**6**), poly(**4′**), poly(**5′**), and poly(**6′**); FT-IR spectra for protected polymers, poly(**4**), poly(**6**), and deprotected polymers, poly(**4′**) and poly(**6′**). This material is available free of charge via the Internet at http://pubs.acs.org.

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(28) As reported previously,[14] ^{1}H NMR spectra of the resultant poly(norbornene), poly(**2a**), showed relatively broad resonances at 5.2 and 5.3 ppm due to the olefinic protons (mixture of *cis*- and *trans*-isomer) and broad resonances between 0.9 and 2.0 ppm and between 2.4 and 2.8 ppm characteristic of the ring-opened polymers of norbornene, as reported previously. In addition, a peak attributable to the $SiMe_3$ group was observed at 0.3 ppm, and a number of resonances characteristic to vinyl protons at the polymer chain end group were also observed.[14] Although the observed M_n value determined by GPC vs polystyrene standards were relatively larger than those calculated based on the initial monomer/initiator molar ratios, the M_n values estimated by ^{1}H NMR spectra (integration ratio with $SiMe_3$ group at the polymer chain end) as well as determined by MALDI-TOF spectrometry were in good agreement with the calculated values.[14]
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(30) The reason for the decreased isolation yields in some experimental runs was due to the isolation from the reaction mixture containing the desired poly(**5**) and PEG added in a relatively excess amount to obtain the desired poly(**5**) with high selectivity without accompanying the sandwich type copolymer, poly(**6**) described below. The optimization of reaction conditions would increase the yields as a result of no starting ROMP polymer remaining in the reaction mixture after this attachment procedure (confirmed by GPC).
(31) Christensen, J. E.; Goodman, L. *Carbohydr. Res.* **1968**, *7*, 510.
(32) (a) Komiya, Z.; Pugh, C.; Schrock, R. R. *Macromolecules* **1992**, *25*, 6586−6592. (b) Sinner, F.; Buchmeiser, M. R.; Tessadri, R.; Mupa, M.; Wurst, K.; Bonn, K. *J. Am. Chem. Soc.* **1998**, *120*, 2790−2797.
(33) Since the deprotected polymers, poly(**4′**), poly(**5′**), and poly(**6′**), were soluble in varying degree in chloroform, dimethylformamide, and dimethyl sulfoxide, we measured these ^{1}H NMR spectra in $CDCl_3$, DMF-d_7, and DMSO-d_6. Identifications of each resonance, estimations of molecular weights, and estimations of proton ratios in PEG/sugar/ring-opened NBE were performed in the best suited solvent for each purpose based on results explored in these three solvents. In particular, because of the poor solubility of poly(**5′**) in DMF-d_7, $CDCl_3$, the spectrum was measured in DMSO-d_6, from which was possible to estimate the ratio of protons attributable to the sugar/ring-opened NBE moieties from their respective resonances. In addition, estimation of the ratio of protons the PEG/ring-opened NBE group was possible from the analogous ^{1}H NMR spectrum in $CDCl_3$. The ratio of PEG/sugar/ring-opened NBE shown in Table 5 was thus a combination of these ratios.
(34) More detailed ^{1}H and ^{13}C NMR spectra are shown in the Supporting Information.

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