Synthesis of End-Functionalized Polymers by Means of Living Anionic Polymerization. 9. Synthesis of Well-Defined End-Functionalized Polymers with One, Two, Three, or Four Monosaccharide Residues

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ABSTRACT: Well-defined end-functionalized polystyrenes and polyisoprenes with monosaccharide residues were synthesized by the termination reactions of the anionic living polymer of styrene or isoprene with benzyl chloride derivatives containing acetal-protected glucofuranose (**1**), fructopyranose (**2**), galactopyranose (**3**), and sorbofuranose (**4**). Furthermore, novel well-defined end-functionalized polymers with two, three, and four monosaccharide residues were successfully synthesized by reacting polystyryllithium with 1,1-bis{3′-[(1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose-*O*-3-yl)methyl]phenyl}ethylene (**5**), followed by treating with methanol, **1** (or **3**), and the octyliodide containing two acetal-protected glucofuranoses (**6**), respectively. The end-functionalized polystyrenes with one and two glucose residues thus synthesized were found by static light scattering measurements to form reverse micelles in cyclohexane by aggregating several polymer chains.

Introduction

Synthetic polymers with mono- and/or oligosaccharide residues as side chains are attractive materials with a variety of potential applications. They could be particularly interesting from the viewpoints of solubility in water, hydrophilicity, high water-absorptivity, biodegradability, specific cell adhesion, and pharmacological activity.[1−5] They might also be of interest as chiral templates for asymmetric synthesis and optical resolution of organic compounds.[6,7] Chain structures of these polymers used are mainly linear homopolymers and random copolymers, which are prepared by radical polymerization of vinyl monomers containing saccharide moieties and by chemical modification of conventional polymers.[5]

Very recently, the synthesis of monosaccharide-containing polymers with well-defined structures by means of living polymerization have been reported. For example, Schrock and Nomura have synthesized new norbornene derivatives containing protected monosaccharides and polymerized them successfully in a living manner to prepare homo- and block poly(norbornene)s having monosaccharide residues as side chains by a Mo-catalyzed ROMP technique.[8] Miyamoto and co-workers have applied the method of living cationic polymerization to prepare poly(vinyl ether)s with pendant glucose residues and amphiphilic block copolymers.[9] Thus, molecular architectures of such polymers can be realized to a certain extent as the need arises.

Little attention has been, however, paid to synthesis and application of end-functionalized polymers with saccharide residues.[10] This is rather surprising in view of the consideration that these end-functionalized polymers may also exhibit the above-mentioned specific characters originated from monosaccharide molecules that have strong hydrogen-bonding abilities and hydrophilicities. Furthermore, it is expected that the incorporation of terminal saccharide residues at polymer chain ends may possibly cause dramatic changes in their morphologies, similar to the cases observed in some end-functionalized polymers.[11−13]

We present here a general, versatile synthetic procedures for well-defined end-functionalized polymers with monosaccharide residues by the reaction of anionic living polymers with specially designed terminators containing acetal-protected monosaccharide derivatives, followed by deprotection. We are also reporting in this paper the first successful synthesis of novel well-defined end-functionalized polymers with two, three, and four monosaccharide residues. Finally, the results of light scattering measurements of the end-functionalized polystyrenes with one and two glucose residues synthesized here illustrate their micellization behaviors in cyclohexane.

Experimental Section

Materials. Monomers were purified according to the usual procedures. Styrene and isoprene were finally distilled over C_6H_5MgCl and *n*-butyllithium, respectively, on the vacuum line into ampules with break-seals that were prewashed with (1,1-diphenylhexyl)lithium in heptane.

3-(4′-Chloromethylbenzyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1). To a stirred solution of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1.04 g, 3.85 mmol) in 2.6 mL of dimethyl sulfoxide (DMSO) was added sodium hydride (0.183 g, 7.63 mmol) in small portions at 0 °C, and the mixture was stirred for 30 min at 25 °C. α,α′-Dichloro-*p*-xylene (1.69 g, 9.64 mmol) in 3.0 mL of DMSO was then added dropwise to the mixture at 0 °C, and the resulting suspension was stirred for an additional 1 h at 25 °C, quenched with 15 mL of water, and extracted with ether (3 × 20 mL). The combined organic layer was washed with water, dried over $MgSO_4$, and concentrated. **1** was isolated as a colorless syrup by flash column chromatography (hexanes/EtOAc, 9:1) to afford 1.21 g (79%). **1** thus obtained was carefully freeze-dried several times to remove water from the benzene solution: $[\alpha]_D^{28}$ −15.5 (*C* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.35 (m, 4H, C_6H_4), 5.90 (d, 1H, J = 5.0 Hz, α-furanose H-1), 4.65 (s, 2H, CH_2−O), 4.60 (s, 2H, CH_2Cl) 4.60−4.01 (m, 6H, H-2 − H-6), 1.50, 1.44, 1.38, and 1.31 (four singlets, 12H, CH_3); ^{13}C NMR ($CDCl_3$) δ 137.8, 136.9, 128.5, 128.2, 111.7, 108.9, 105.1, 82.5, 81.6, 81.2, 72.3, 67.3, 71.7, 45.8, 26.7, 26.1, 25.3.

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3-(4′-Chloromethylbenzyl)-1,2:4,5-di-*O*-isopropylidene-*β*-D-fructopyranose (2), 6-(4′-chloromethylbenzyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (3), and 1-(4′-chloromethylbenzyl)-2,3:4,6-di-*O*-isopropylidene-*β*-L-sorbofuranose (4). **2**, **3**, and **4** were synthesized in good yields by the similar procedure used in the case of **1**. 1,2:4,5-Di-*O*-isopropylidene-*β*-D-fructopyranose, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose, or 2,3:4,6-di-*O*-isopropylidene-*β*-L-sorbofuranose was used in each of the reactions. After the usual workup, flash column chromatography on silica gel (hexanes/EtOAc, 9:1) afforded **2**, **3**, or **4** as a pale yellow syrup.

2: $[\alpha]_D^{28}$ −85.2 (*C* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.36 (m, 4H, C_6H_4), 4.65 (s, 2H, CH_2−O), 4.58 (s, 2H, CH_2Cl), 4.98−3.49 (m, 7H, H-2−H-6), 1.58, 1.54, 1.50, and 1.42 (four singlets, 12H, CH_3); ^{13}C NMR ($CDCl_3$) δ 138.7, 136.4, 128.2, 127.5, 111.8, 108.6, 104.0, 76.3, 75.9, 73.4, 72.2, 71.5, 59.8, 45.6, 27.8, 26.5, 25.8, 25.7.

3: $[\alpha]_D^{28}$ −49.6 (*C* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.38 (m, 4H, C_6H_4), 5.55 (d, 1H, J = 4.7 Hz, α-pyranose H-1), 4.61 (s, 2H, CH_2−O), 4.58 (s, 2H, CH_2Cl), 4.33−3.63 (m, 6H, H-2−H-6), 1.49, 1.44, 1.44, and 1.34 (four singlets, 12H, CH_3); ^{13}C NMR ($CDCl_3$) δ 138.7, 136.8, 128.7, 128.0, 109.3, 108.6, 96.4, 72.9, 71.2, 70.7, 70.6, 69.1, 66.9, 46.1, 26.1, 25.0, 24.5.

4: $[\alpha]_D^{30}$ −22.7 (*C* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.32 (m, 4H, C_6H_4), 4.60 (s, 2H, CH_2Cl), 4.50 (s, 2H, CH_2−O), 4.75−3.73 (m, 7H, H-2−H-6), 1.49, 1.38, 1.38, and 1.28 (four singlets, 12H, CH_3); ^{13}C NMR ($CDCl_3$) δ 138.4, 136.5, 128.4, 127.7, 113.9, 112.1, 97.1, 84.1, 76.5, 73.0, 72.0, 69.9, 60.2, 45.9, 28.8, 27.4, 26.4, 18.5.

1,1-[Bis(3′-chloromethyl)phenyl]ethylene. 1,1-[Bis(3′-methoxymethyl)phenyl]ethylene was synthesized by the Grignard reaction of ethyl acetate and (3-methoxymethyl)phenylmagnesium bromide, followed by dehydration with *p*-toluenesulfonic acid, according to the previous procedure described for 1,1-diphenylethylene (DPE) derivatives.[14] The methoxy groups of the resulting DPE derivative were chlorinated by BCl_3 as follows: To a CCl_4 (23 mL) solution of 1,1-[bis(3′-methoxymethyl)phenyl]ethylene (4.37 g, 16.3 mmol) at 0 °C was added BCl_3 (18.2 mL of a 1.0 M solution of CH_2Cl_2, 18.2 mmol) dropwise with stirring. After 2 h of stirring at 0 °C, the reaction was quenched with methanol. The reaction mixture was basified with aqueous NaOH, extracted with CCl_4, dried ($MgSO_4$), and concentrated. Flash column chromatography using hexanes as eluents afforded 4.22 g (95%) of 1,1-[bis(3′-chloromethyl)phenyl]ethylene as a colorless liquid: ^{1}H NMR ($CDCl_3$) δ 7.32 (m, 8H, C_6H_4), 5.49 (s, 2H, C=CH_2), 4.56 (s, 4H, CH_2Cl).

1,1-Bis{3′-[(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-*O*-3-yl)methyl]phenyl}ethylene (5). **5** was synthesized by reacting 1,1-[bis(3′-chloromethyl)phenyl]ethylene (1.00 g, 3.61 mmol) with the sodium salt of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (2.63 g, 9.73 mmol) in DMSO (7 mL), similar to the procedure described for **1**. After usual workup, flash column chromatography (hexanes/EtOAc, 8:2) afford 2.48 g (95%) as a pale yellow syrup. It was freeze-dried several times from the benzene solution prior to use: $[\alpha]_D^{29}$ −28.4 (C 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.31 (m, 8H, C_6H_4), 5.89 (d, 2H, J = 3.7 Hz, α-furanose, H-1), 5.47 (s, 2H, C=CH_2), 4.65 (s, 4H, CH_2−O), 4.60−4.00 (m, 12H, H-2 − H-6), 1.50, 1.32, 1.31, and 1.28 (four singlets, 12H, CH_3); ^{13}C NMR ($CDCl_3$) δ 149.7, 141.6, 137.7, 128.4, 127.9, 127.5, 127.2, 114.8, 111.9, 109.1, 105.4, 82.7, 82.1, 81.9, 81.4, 72.6, 72.5, 72.4, 67.4, 26.9, 26.3, 25.4.

3-Methyl-5,5-bis{3′-[(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-*O*-3-yl)methyl]phenyl}octyl Iodide (6). *sec*-BuLi (2.91 mL of a 1.05 M solution in heptane, 3.06 mmol) was added to a solution of **5** (32.7 mL of a 0.0635 M solution in THF, 2.08 mmol) at −78 °C and the resulting deep red mixture was stirred for 70 min at −78 °C. To a solution of 1,3-diiodopropane (2.63 g, 8.87 mmol) in THF (15 mL) was added the mixture dropwise at −78 °C. The dark red color turned to a light yellow on mixing. After the mixture had been warmed to 25 °C, it was stirred at 25 °C for an additional 1 h. After the usual workup, flash column chromatography (hexanes/EtOAc, 7:3) afforded 1.01 g (52%) of **6** as a pale yellow syrup. It was freeze-dried several times to remove water from the benzene solution prior to use: ^{1}H NMR ($CDCl_3$) δ 7.25 (m, 8H, C_6H_4), 5.54 (d, 2H, J = 3.3 Hz, α-furanose, H-1), 4.60 (s, 4H, CH_2−O), 4.53−3.97 (m, 12H, H-2 − H-6), 3.08 (t, 2H, J = 6.6 Hz, CH_2I), 2.00 (m, 1H, CH), 1.49, 1.43, 1.36, and 1.30 (four singlets, 12H, CH_3), 1.50−0.76 (m, 8H, CH_2), 0.69, 0.53 (m, 6H, CH_3).

Anionic Polymerizations and Reactions of Anionic Living Polymers with 1−4. The polymerizations and the reactions were carried out under high vacuum conditions (10^{-6} Torr) in sealed glass reactors with break-seals. The reactors were always prewashed with initiator solutions after being sealed off from the vacuum line. The anionic polymerizations of styrene and isoprene were performed with *sec*-BuLi in THF at −78 °C for 10 min and in heptane at 40 °C for 4 h, respectively. In the case using polyisoprenyllithium as an living polymer, the polymerization mixture was cooled to −78 °C after the polymerization and then an equal volume of THF was added to the mixture prior to the reaction. The reactions of polyisoprenyllithium with the terminators were therefore carried out in a mixture of heptane and THF (1/1, v/v) at −78 °C.

The living polymer solution was added dropwise to each of the terminators (**1**−**4**) in THF at −78 °C over a period of 10 min, and the mixtures were allowed to stand at −78 °C for additional 20 min.

Deprotection of the Protected Monosaccharides Introduced at Polymer Chain Ends. A typical procedure is as follows: A solution of polystyrene end-functionalized with acetal-protected glucofuranose (500 mg, 0.21 mmol for glucose unit, M_n = 2400) and 1.5 mL of concentrated HCl in 20 mL of 1,4-dioxane was stirred at room temperature for 24 h. The polymer was precipitated in methanol, reprecipitated twice from THF to methanol, and freeze-dried from the benzene solution. It was analyzed by ^{1}H and ^{13}C NMR and TLC−FID measurements. The acetals were deprotected in 93−99% yields.

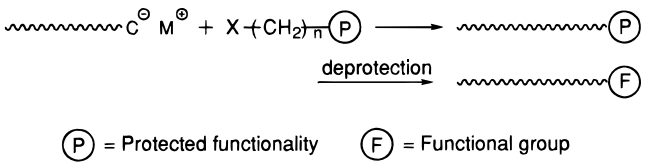
Measurements. ^{1}H and ^{13}C NMR spectra were recorded on a BRUKER DPX spectrometer operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C. Optical rotations were measured in $CHCl_3$ solutions on a JASCO-DIP 370 polarimeter at the sodium D line. Size-exclusion chromatography (SEC) was performed on a TOSOH HLC 8020 instrument with UV (254 nm) and refractive index detection. THF was used as a carrier solvent at a flow rate of 1.0 mL/min. Three polystyrene gel columns (TSKgelG4000H_{XL}, G3000H_{XL}, and G2000H_{XL}) were used. Calibration curves were made to determine M_n and M_w/M_n values with standard polystyrene and polyisoprene samples. For thin-layer chromatography, Merck Kieselgel 60 F_{254} was used as an absorbent. The TLC−FID instrument was an IATROSCAN New MK-5 TS equipped with IATROCORDER TC-21 from Iatron Co., Ltd. Specially designed quartz rods (150 mm × 2.0 mm) were used on which silica gel was sintered. Laser light scattering (LS) measurements were performed with an Ootsuka Electronics DSL-600R instrument in cyclohexane. X-ray photoelectron spectroscopy (XPS) was performed on a Perkin-Elmer 5500MT with a monochromatic Al Kα X-ray source. The polymer films for XPS measurement were prepared by spin coating (4000 rpm, 20 s) onto a cover glass from a 3 wt % of polymer solution in benzene−methanol (4/1, v/v). The samples were dried at room temperature for overnight and annealed for 2 h at 110 °C in vacuo.

Results and Discussion

Synthesis of Well-Defined End-Functionalized Polystyrenes and Polyisoprenes with Monosaccharide Residues. The main synthetic interest of this study is the synthesis of well-defined end-functionalized polymers with monosaccharide residues which possess a quantitative degree of end functionalities, well-controllable molecular weights, and nearly uniform distributions of molecular weight. Another interest is

to establish adequate, general synthetic procedures to introduce two, three, and four monosaccharide residues into polymer termini. Well-defined structures of these end-functionalized polymers are particularly suitable to obtain fundamental understanding regarding the effect of terminal monosaccharide residues on the polymer properties in solution and in solid state.

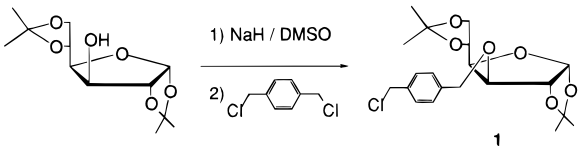
In a recent few years, we have been developing a general, versatile methodology for the synthesis of well-defined end-functionalized polymers. The method involves the termination reaction of anionic living polymer of styrene or isoprene with the alkyl halide containing protected functionality followed by deprotection as shown below:



By means of this method, a variety of end-functionalized polymers with hydroxy,[15] mercapto,[15] amino,[16] and carboxyl groups[17] were successfully synthesized. These polymers usually possessed excellent to quantitative degrees of end functionalities (>95%) and well-controlled molecular weights and narrow molecular weight distributions (M_w/M_n < 1.1).

In this section, we have extended this approach for the synthesis of polymers end-functionalized with monosaccharide residues. For this purpose, it is necessary for us to synthesize new alkyl halides containing acetal-protected monosaccharide moieties as terminators in the reactions with anionic living polymer of either styrene or isoprene. The synthesis of such alkyl halides was first attempted by reacting the sodium salt of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose with several α,*ω*-dihaloalkanes under various conditions. Unfortunately, all the reactions with dibromides or diiodides having different methylene lengths from three to five proceeded sluggishly in DMF or DMSO. The yields were always very low even at higher temperatures up to 80 °C and for longer reaction times to 100 h.

On the other hand, α,α′-dichloroxylene reacted efficiently to afford 3-(4′-chloromethylbenzyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**) in an isolated yield of 81% as shown below:



Similarly, another three chloromethylbenzylated monosaccharide derivatives of **2**−**4** were synthesized in good yields by reacting the sodium salt of 1,2:4,5-di-*O*-isopropylidene-*β*-D-fructopyranose, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose, or 2,3:4,6-di-*O*-isopropylidene-*β*-L-sorbofuranose with α,α′-dichloroxylene.

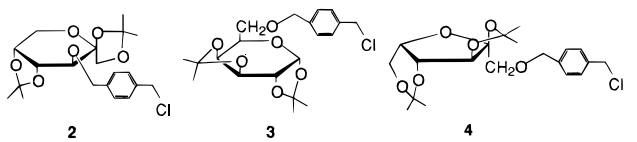


Table 1. Reactions of Living Polymers with 1−4[a]

terminating agent	living polymer[b]	$M_n \times 10^{-3}$ calcd	$M_n \times 10^{-3}$ obsd (SEC)[c]	functionality ^{1}H NMR	functionality TLC−FID
1	PS-Li	2.6	2.4	1.0_0	0.99
1	PS-Li	10.6	12.0		0.93
2	PS-Li	2.6	2.4	1.0_0	1.0_0
2	PS-Li	12.4	11.7		0.99
3	PS-Li	2.6	2.6	1.0_0	0.98
4	PS-Li	2.6	2.6	0.84	1.0_0
1	PI-Li	2.6	2.9	1.0_0	1.0_0
2	PI-Li	11.3	12.6		1.0_0

[a] Reactions were carried out in THF or THF−heptane mixtures at −78 °C for 20 min. About 1.5-fold excesses of **1**−**4** were used. [b] PS-Li and PI-Li indicate poly(styryllithium) and poly(isoprenyllithium), respectively. [c] M_w/M_n values were <1.10 in all polymer samples.

The new terminators, **1**−**4**, thus synthesized were reacted with polystyryllithium in THF at −78 °C by adding the polymeric anion dropwise into each of the terminators. A reddish orange color characteristic for polystyryllithium disappeared instantaneously on mixing, indicating that the reactions proceeded very rapidly even at −78 °C. The results are summarized in Table 1.

The SEC analysis of the resulting polymers usually showed unimodal peaks with narrow distributions. The M_n values observed by SEC are agreed well with those calculated in the range of 2400−12000 as can be seen in Table 1. The values of M_w/M_n are less than 1.1 in all cases. Unfortunately, small but detectable amounts (ca. 5−10%) of dimeric products of the starting living polystyrenes were sometimes formed under the condition employed here, for example, in the reactions with **1** and **3**.[18]

The degrees of end-functionalization were determined by ^{1}H NMR peak intensities to be nearly quantitative in all polymer samples within the accuracy of the analysis (± 5%). Use of small excesses (1.1−1.2-fold) of the terminators is enough for the introduction of protected monosaccharides. Similarly, polyisoprenyllithium was reacted efficiently with either **1** or **2**.

It was observed that all the polymers that were end-functionalized with protected monosaccharides were separated completely from unfunctionalized polystyrene or polyisoprene by TLC using SiO_2 plate with toluene or hexanes as a mobile phase. Under the conditions developed, the polystyrenes or polyisoprenes with monosaccharides always gave spots that remained near the spotting points (R_f = ca. 0), whereas unfunctionalized polystyrene or polyisoprene was quite mobile up to near the top (R_f = 0.9). Since the amount of each spot is detected quantitatively by a flame ionization detector (FID), the degree of end-functionalization can be determined by comparing each peak areas. Accordingly, the method of TLC coupled with FID becomes very effective for quantitative analysis of the end-functionalized polymers. The experimental error of this method is as much as 3 wt %. The degrees of end-functionalization by the analysis of TLC−FID method are also indicated to be nearly quantitative in all polymer samples, again as can be seen in Table 1.

On the basis of these analytical results, it is obvious that the termination reactions of anionic living polymers of styrene and isoprene with each of **1**−**4** proceed satisfactorily to afford the well-defined end-functional-

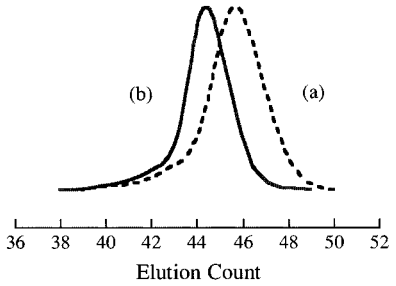


Figure 1. SEC curves of the polymers before and after the reaction with **5**: (a) polystyrene (M_n = 2600) obtained before the reaction. (b) functionally terminated polystyrene (M_n = 3300) obtained by the reaction with **5**.

ized polymers with various monosaccharide residues. However, small amounts of dimers were sometimes but not always formed in 5−10% yields in the reactions. More optimization of the reaction condition should be therefore needed to suppress such dimer formation in some cases.

Synthesis of End-Functionalized Polymers with Two Monosaccharide Residues. The reaction of anionic living polymers of styrene and dienic monomers with 1,1-diphenylethylene (DPE) is known to proceed only in a monoaddition manner of DPE at the living polymer chain ends. Neither oligomerization nor polymerization of DPE usually takes place. Accordingly, this reaction is expected to be an excellent system for development of an end-functionalization reaction. In fact, several successful examples have been recently reported independently by Heiz and Hocker[19] and Quirk and co-workers[20−22] in the end-functionalization reactions of anionic living polymers by the DPE derivatives with protected functionalities, followed by deprotection.

Here we have also utilized the monoaddition nature of DPE to anionic living polymers for the synthesis of end-functionalized polymers with two monosaccharides. Fortunately, 1,1-bis{3′-[(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-*O*-3-yl)methyl]phenyl}ethylene (**5**) as an essential DPE derivative for our purpose could be obtained in a very high yield of 95% by reacting 1,1-[bis(3′-chloromethyl)phenyl]ethylene with the sodium salt of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose. The reaction of polystyryllithium with a slight excess molar of **5** (a 1.3-fold excess) was carried out in THF at −78 °C for 70 min. On mixing, the orange color of polystyryllithium changed immediately to a dark red color characteristic of the 1,1-diphenylalkyl anion derived from **5**. The red color appears to be stable at −78 °C for several hours, indicating that the diisopropylidene glucofuranose skeleton is compatible with the 1,1-diphenylalkyl anion generated under the conditions.

Figure 1 is an overlay of SEC curves of the polystyrene (M_n = 2600) prior to the reaction and the functionally terminated polystyrene (M_n(calcd) = 3300) by the reaction with **5**. As can be seen, the shift to higher molecular weight side is obviously observed in the polymer sample obtained by the reaction. The SEC peak was symmetrically narrow without any shoulders and tailings. The degree of functionality measured by ^{1}H NMR was 1.88. It was observed from TLC−FID analysis that as little as 3 wt % of unfunctionalized polystyrene was present in this polymer sample. Accordingly, a functionality of 0.97 (or 1.94 (0.97 × 2) for glucose residues) was indicated by the TLC−FID method. These results are listed in Table 2.

Table 2. Reactions of Living Polymers with 5[a]

living polymer[b]	time (min)	$M_n \times 10^{-3}$ calcd	$M_n \times 10^{-3}$ obsd (SEC)[c]	functionality ^{1}H NMR	functionality TLC−FID
PS-Li	70	3.3	3.1	1.8_8	1.9_4
PS-Li	70	12.4	12.8	1.7_4	1.9_4
PI-Li	270	2.7	2.7	2.0_0	2.0_0

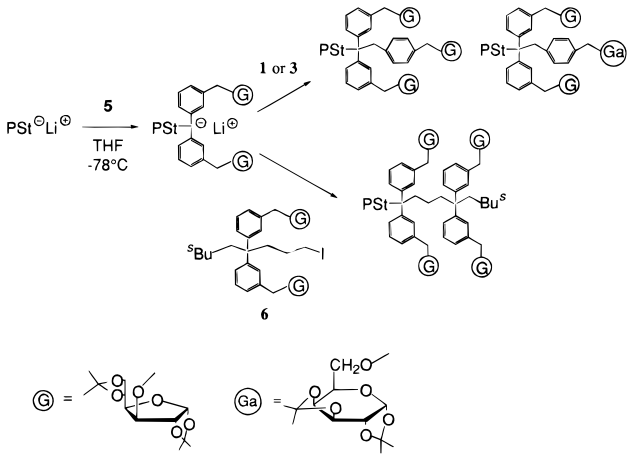
[a] Reactions were carried out in THF or THF−heptane mixtures at −78 °C. About 1.3-fold excesses of 5 was used. [b] PS-Li and PI-Li indicate poly(styryllithium) and poly(isoprenyllithium), respectively. [c] M_w/M_n values were <1.08 in all polymer samples.

A similar result was obtained in the reaction of the polystyryllithium of a higher molecular weight (M_n = 12 000) with **5**. In this case, the end-functionalization was also observed to not be completed from analytical results of both ^{1}H NMR and TLC−FID measurements. The presence of small amounts of unfunctionalized polystyrene in both polymer samples may possibly be caused by the reaction of living polymer with only traces of remaining impurities in **5**. Fortunately, quantitative end-functionalization of polystyryllithium with **5** could be in practice achieved by a further addition of *sec*-BuLi to **5** prior to the reaction.[23] As expected, the polymer thus obtained showed no unfunctionalized polystyrene by TLC−FID analysis.

Polyisoprenyllithium was reacted with **5** in a THF-heptane mixture (1/1, v/v) at −78 °C for 270 min. The ^{1}H NMR spectrum of the resulting polymer showed that two glucofuranoses were introduced in 100% yield. No unfunctionalized polyisoprene was detected by TLC−FID analysis in the functionalized polymer sample. Thus, this end-functionalization reaction with the use of a DPE derivative like **5** offers the potential of providing a general procedures for the synthesis of well-defined end-functionalized polymers with two monosaccharide residues.

Synthesis of End-Functionalized Polystyrene with Three or Four Monosaccharide Residues. As mentioned in the preceding section, the substituted DPE with two acetal-protected glucofuranoses, **5**, was reacted quantitatively with polystyryllithium in a monoaddition manner to afford the end-functionalized polystyrene, while a new carbanion of 1,1-diphenylalkyl-type was generated from polystyrylanion in this reaction. The carbanion thus generated can be used in the further reactions with suitable electrophiles. This procedure, called as a living functionalization reaction by Quirk, has been recently developed to introduce functional groups at any position within the polymer chain.[24]

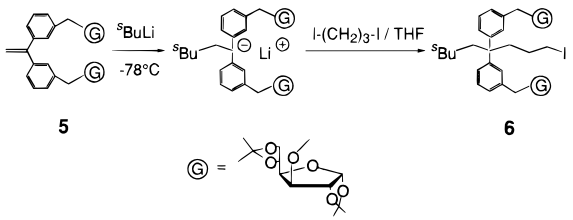
We have applied this living functionalization reaction to the synthesis of end-functionalized polymers with three or four monosaccharide residues. For the synthesis of polymers with three monosaccharide residues, either **1** or **3** as an electrophile was reacted with the carbanion generated by the reaction of polystyryllithium with **5**. By analogy with the synthesis as described above, we synthesized an end-functionalized polystyrene with four glucose residues by reacting the carbanion derived from **5** with a new terminator containing two acetal-protected glucofuranoses (**6**) according to the scheme as shown below:



The reaction with **1** proceeded rapidly, as it was observed that the characteristic dark red color faded immediately to pale yellow on mixing. The resulting polymer was found to possess a symmetrically unimodal SEC peak with a narrow molecular weight distribution. The peak was shifted to higher molecular weight side compared to that of the polymer sample before the reaction. The ^{1}H NMR spectrum indicated a quantitative introduction of three protected glucofuranoses in the polystyrene. The TLC−FID analysis showed that only 1% of unfunctionalized polystyrene was detected, indicating 99% yield of end-functionalization. The results are summarized in Table 3.

Similarly, the reaction with **3** was found to proceeded satisfactorily as indicated by all the analytical data (Table 3). Thus, a new type end-functionalized polystyrene with two glucoses and galactose could be successfully obtained. The ^{1}H NMR spectrum of this polymer is shown in Figure 2. Accordingly, not only the same three monosaccharide residues but also different ones can be introduced at the polymer chain ends by changing the electrophile to be terminated in this method.

For the synthesis of polymer with four glucose residues, we have synthesized a new terminator having two protected glucofuranoses **6** by reacting **5** with *sec*-BuLi, followed by the reaction with an excess amount of 1,3-diiodopropane as shown below:



The **6** thus synthesized reacted as expected with the carbanion from polystyryllithium and **5** as mentioned above. The results are also summarized in Table 3. The resulting polymer had a predictable M_n value as well as a narrow molecular weight distribution, the M_w/M_n value being 1.06. The degree of end-functionality measured by ^{1}H NMR was quantitative. Furthermore, TLC of this polymer sample showed only one spot, the R_f value of which was different from those of unfunctionalized polystyrene and the functionalized polystyrene only with **5**. This clearly indicates that the resulting polymer is pure and free of side products. This implies that the two step end-functionalization reactions

Table 3. Synthesis of Polystyrenes End-Functionalized with Three or Four Monosaccharide Residues[a]

terminating agent	$M_n \times 10^{-3}$ calcd	$M_n \times 10^{-3}$ obsd (SEC)[b]	functionality ^{1}H NMR	functionality TLC-FID
5, **1**	4.0	3.6	2.7_6	2.9_7
5, **3**	3.2	3.1	3.0_9[c]	3.0_0[c]
5, **6**	6.6	6.9	4.0_0	4.0_0

[a] **5** was reacted with poly(styryllithium) in THF at −78 °C for 70 min, followed by treating with **1**, **3**, or **6** for 20 min in THF at −78 °C. [b] M_w/M_n values were <1.06. [c] Two glucose and one galactose residues at the polymer chain end.

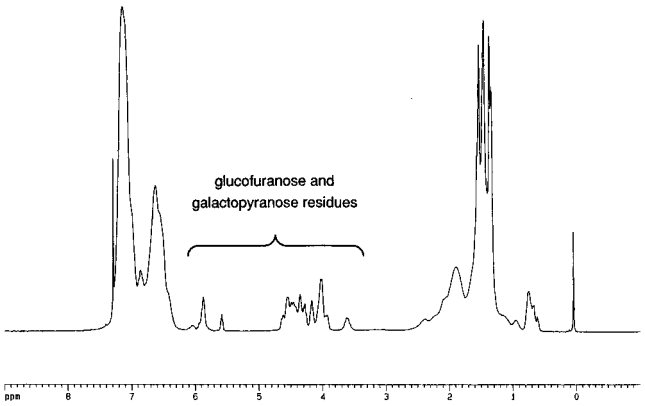


Figure 2. ^{1}H NMR spectrum of end-functionalized polystyrene with two glucofuranose and one galactopyranose acetal-protected residues.

with **5** and then **6** proceed quantitatively to afford a well-defined polystyrene end-functionalized with four glucose residues. Thus, new types of well-defined end-functionalized polymers with three and four of the same or different monosaccharide residues could be synthesized by means of the living end-functionalization reaction with the use of **5**. A further application by this method will be the subject of a future work.

Interestingly, we have found that the R_f values of the end-functionalized polystyrenes by TLC are different as a result of the number of protected glucofuranose at the chain end. Using SiO_2 plate with a toluene-THF mixed solvent (95/5, v/v), for example, the R_f values were 0.90, 0.56, 0.56, 0.22, and 0.16 which corresponded to the polystyrene samples with zero (unfunctionalized sample), one, two, three, and four protected glucofuranoses, respectively. Accordingly, we can readily distinguish to each other by TLC among unfunctionalized polystyrene, the polystyrenes with one and two glucofuranoses, the polystyrene with three glucofuranoses, and the polystyrene with four glucofuranoses. It should be however noted that these R_f values shown here depend to some extent on the molecular weight of polystyrene. With increasing molecular weight, the R_f value becomes higher, although not too significantly. The R_f value should be therefore compared among the polymer samples with comparable M_n values. In the polymer samples used here, their polystyrene main chains had the M_n values of around 2.5×10^3. After hydrolysis of the glucofuranoses at the polymer termini, the resulting polymers were developed with the same mixed solvent as a mobile phase. As a result, the polystyrene with one glucose was mobile to some extent ($R_f = 0.27$), while the polymer samples with two or more glucoses remained near the spotting points (R_f = ca. 0). The polystyrene with one glucose was thus distinguishable from that with two (or more) glucoses.

Static Light Scattering Measurement of Polystyrenes End-Functionalized with One and Two Glucose Residues in Cyclohexane. It has been recently reported that some end-functionalized polymers with either perfluoro groups or ionic functions can behave similar to block copolymers in the solid state and in solution. For example, DeSimone et al.[11] and we[12] have observed that terminal perfluoro groups segregate facilely from the main chain to be remarkably enriched at the film surfaces. Eisenberg and Zong have demonstrated that sodium carboxylates (COO^-Na^+) of hydrophilic terminal groups are separated from hydrophobic polystyrene main chains to form reverse micelles in cyclohexane by aggregating several polymer chains.[13] These observations suggest that the morphology of polymer can be dramatically changed even by only one or two terminal functions of the polymer chain.

The terminal monosaccharide residues are also expected to have an affect on morphology in solution as well as in the solid state, since they show strong hydrogen-bonding abilities and hydrophilicities as described in the Introduction. In this section, behaviors of end-functionalized polystyrenes with glucose residues in solution and in the cast film will be examined by static light scattering (SLS) and XPS measurements.

To examine micellization behavior, two polystyrene samples with one and two glucose residues were characterized by SLS. Their M_w values were measured by SLS in cyclohexane at 25 and 42 °C, respectively. A concentration effect on the M_w value was not observed in the concentration range (2.0−10 g/L). The aggregation number can be therefore calculated from the M_w values determined by light scattering divided by those determined by SEC.

At first, the M_w value of polystyrene itself was measured to be 10 500 in cyclohexane at 25 °C by light scattering. This agreed very well with the M_w value of 10 600 determined by SEC. Under the same condition, the observed M_w value of the end-functionalized polystyrene with one glucose residue was 51 800. The aggregation number was therefore calculated to be 4.1 by dividing 51 800 by the M_w value of 12 500 determined by SEC.

Since 25 °C is lower than the Θ temperature (38 °C) for polystyrene in cyclohexane, the measurement by light scattering is also carried out at 42 °C which is slightly higher than the Θ temperature. The aggregation number determined at 42 °C is 3.6 (45 400 vs 12 500) and close to 4.1 at 25 °C. Similarly, the M_w value of the same molecular weight polystyrene end-functionalized with two glucose residues was measured in cyclohexane at 42 °C by light scattering. The M_w value and aggregation number of this sample were 92 500 and 7.0, respectively (92 500 vs 13 300).

It is obvious on the basis of these results that the polystyrenes end-functionalized with one and two glucose residues are aggregated in cyclohexane. They would possibly form reverse micelles in cyclohexane, similar to the cases of amphiphilic block copolymers and of the polystyrene end-functionalized COO^-Na^+ groups reported by Eisenberg and Zhong.[13] Moreover, it is interesting that the aggregation number increases from 3.6 to 7.0 when the number of glucose residues in the polymer chain end is raised from one to two. However, the experimental conditions, for example, temperature and concentration, should be more optimized for discussion of the effect of the number of glucose on the aggregation and the micelle size. More detailed and systematic work using the polymer samples with monosaccharides will be performed.

Since it is expected that the film surface composition of the end-functionalized polystyrene with glucose residue can be changed as a function of depth, we have measured angle-dependent XPS of the film of the polystyrene end-functionalized with one glucose residue (M_n = 2400). The quantities of glucose from the outermost surface (takeoff angle = 10°) to a depth of about 15 Å were very similar to that of the bulk in any conditions such as a sample annealed at 100 °C for 2 h under vacuum and/or soaked in water. This indicates that the glucose molecule is homogeneously distributed in this range and possibly in the whole range. Thus, unfortunately, the enrichment of the hydrophilic glucose molecule on the film surface was not observed in this sample under the conditions employed. It is considered that the presence of more glucose molecules in one polymer chain would be needed for the segregation of glucose molecules from main chain to aggregate at the surface.

Conclusion

We have developed here general, versatile synthetic methods for the well-defined end-functionalized polymers with one, two, three, and four monosaccharide residues by means of anionic living polymerization. Excellent control of the molecular weight and molecular weight distribution as well as end-functionality is realized in each of all the polymer samples synthesized here. It is observed that the polystyrenes with one and two glucose residues at their chain ends are aggregated, possibly to form reverse micelles in cyclohexane.

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(18) It is presumed that the dimers result from either a lithium−chloride exchange followed by the coupling between the chlorinated polystyrene thus generated and polystyryllithium or a single-electron transfer (SET) pathway followed by the coupling between the generated polymer radicals. Yields of dimers in our termination reactions are as follows: 5% in the reactions of polystyryllithium with **1** and polyisoprenyllithium with **2**; 10% in the reactions of polystyryllithium with **3** and polyisoprenyllithium with **1**, respectively. More complicately, the amount of dimer or even dimer formation is not reproducible in the same reaction. It was also observed under the conditions employed here that dimeric product was not always but often formed in yields of around 3% even by quenching with degassed methanol. This is possibly produced as a result of an elimination of LiH from the living polymer to afford the polymer with C=C end group, followed by the reaction with another living polymer to produce the dimeric product. Amounts of the dimers produced in the reactions should be therefore evaluated to take this into consideration.
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