Protection and Polymerization of Functional Monomers. 30. Anionic Living Polymerization of 4-Alkylstyrenes Containing Acetal-Protected Monosaccharide Residues

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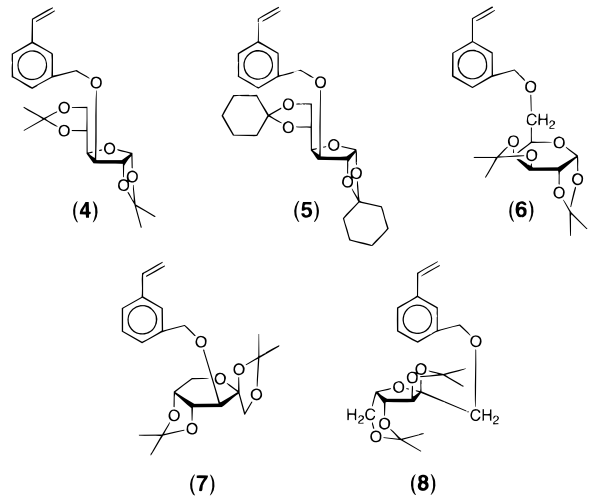
ABSTRACT: Three new para-substituted styrene derivatives, *p*-[3-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-3-oxy)propyl]styrene (**1**), *p*-[3-(1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose-6-oxy)propyl]-styrene (**2**), and *p*-[11-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-3-oxy)undecyl]styrene (**3**) were synthesized by phase transfer catalyzed etherifications. Their anionic polymerizations proceed in a living manner in THF at −78 °C using *sec*-BuLi as the initiator to quantitatively afford polymers with well-controlled molecular weights (6.7−42K) and narrow molecular weight distributions (M_w/M_n < 1.06). Novel AB and BA diblock copolymers of **1** and styrene were also successfully synthesized. The stabilities of the living polymer of **1** and the already reported living polymer of *m*-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-3-oxymethyl)styrene (**4**) were examined under the polymerization conditions at −78 °C for 22 h and −30 °C for 0.5 h.

Introduction

A variety of synthetic polymers containing saccharide residues have been reported.[1−3] They should be useful functional materials due to their solubility in water, high hydrophilicity, strong hydrogen bonding ability, and the presence of many chiral centers. Moreover, they may find biochemical and pharmacological uses based on the bioactivity of saccharide derivatives.[4−8] At the present time, most saccharide-containing polymers are prepared by radical polymerization and polymer analogous reactions, and therefore, they are not well-defined with respect to chain structures.

Several researchers have recently attempted to synthesize polymers containing monosaccharide or even disaccharide residues by living polymerizations.[9−14] With living polymerizations, one can design and synthesize high-performance polymeric materials such as well-controlled homopolymers and block copolymers with desired structures. Successful examples for such attempts include the ring-opening polymerization of a glucose-substituted L-serine *N*-carboxyanhydride,[9] the Ru-initiated ring-opening metathesis polymerization (ROMP) of norbornenes substituted with protected glucopyranoses,[10] the Mo-initiated ROMP of norbornenes substituted with protected-monosaccharides,[11] and the HI/ZnI_2-initiated cationic polymerization of vinyl ethers containing protected glucose residues.[12,13] Very recently, the nitroxide-controlled free radical polymerization of disaccharide containing styrene was reported.[14] Although several living polymerization systems have thus been demonstrated, each of these systems have inherent limitations in the polymerization conditions and the kinds of monomers that can be used. Therefore, the attempt to synthesize well-defined polymers by means of living polymerization is still an important challenging subject.

Our preceding paper[15] reported the successful anionic living polymerization of the following meta-substituted styrene derivatives containing acetal-protected monosaccharide residues, namely *m*-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-3-oxymethyl)styrene (**4**), *m*-(1,2:5,6-di-*O*-cyclohexylidene-α-D-glucofuranose-3-oxymethyl)-styrene (**5**), *m*-(1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose-3-oxymethyl)styrene (**6**), *m*-(1,2:4,5-di-*O*-isopropylidene-*β*-D-fructopyranose-3-oxymethyl)styrene (**7**), and *m*-(2,3:4,6-di-*O*-isopropylidene-*β*-L-sorbofuranose-3-oxymethyl)styrene (**8**).



Using *s*-BuLi as the initiator in THF at −78 °C, polymers of predictable molecular weights and narrow molecular weight distributions were quantitatively obtained. Novel well-defined AB and BA diblock copolymers of **4** and styrene were also obtained using this living polymerization system.

Although the living polymerization of **4** was successful, the anionic polymerization of the corresponding para-substituted styrene, *p*-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-3-oxymethyl)styrene (**9**) did not polymerize well under identical conditions. More surprisingly, attempts to synthesize a block copolymer by reacting **9** with difunctional living polystyrene produced an insoluble gelatinous material along with a small

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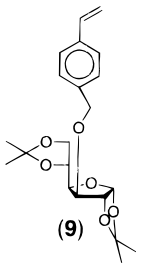
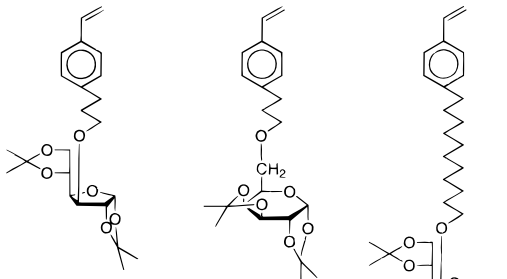
amount of THF-soluble polymer with a very broad molecular weight distribution. In this case, unreacted **9** was recovered nearly quantitatively from the reaction mixture. The insoluble material is apparently a cross-linked polystyrene containing a few units of **9**; it is insoluble in a number of common organic solvents, and has an IR spectrum very similar to that of polystyrene with small absorption peaks corresponding to the acetal-protected glucofuranose moiety. Therefore, **9** essentially does not participate in the anionic polymerization, but does contribute to cross-linking.



(**9**)

On the basis of the discrepancy in the polymerizability of **4** and **9**, we studied the anionic polymerization of additional styrene derivatives structurally similar to **9**. In this study, we will explore anionic polymerization of the following three new para-substituted styrene derivatives, *p*-[3-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-3-oxy)propyl]styrene (**1**), *p*-[3-(1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose-6-oxy)propyl]styrene (**2**), and *p*-[11-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-3-oxy)undecyl]styrene (**3**), whose monosaccharide residues are separated from styrene by 3 or 11 methylenic units.



(**1**) (**2**) (**3**)

Experimental Section

Materials. 4-Chlorostyrene was kindly supplied by Hokko Chemical Industry Co., Ltd. and 4-(chloromethyl)styrene was purchased from Seimi Chemical Co., Ltd. They were distilled from calcium hydride and used for the synthesis of **1**−**3**. Commercially available 1,3-dibromopropane (98%) from Tokyo Kasei Kogyo Co., Ltd., and 1,10-dibromodecane (>97%) from Merck were distilled over calcium hydride under reduced pressures, and magnesium (turnings) from Nacalai Tesque, Inc., was used without purification. A THF solution of Li_2CuCl_4 was synthesized by the reaction of LiCl and $CuCl_2$ according to the literature.[16] Styrene was washed with 10% NaOH and H_2O and dried over $CaCl_2$. Then it was distilled from calcium hydride, and further purified by distillation in the presence of phenylmagnesium chloride (THF solution) on a vacuum line. THF used as a polymerization solvent was refluxed over sodium wire for 5 h and distilled from lithium aluminum hydride and finally through a vacuum line from the sodium naphthalenide solution. Commercially available *s*-BuLi as a 1.3 M solution in cyclohexane from Aldrich was used without purification and diluted with *n*-heptane.

Measurements. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX spectrometer operating at 300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR in $CDCl_3$. Chemical shifts were reported in ppm downfield relative to tetramethylsilane (δ 0) for ^{1}H NMR and to $CDCl_3$ (δ 77.1) for ^{13}C NMR as standard. Size-exclusion chromatography (SEC) relative to polystyrene 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 (measurable molecular weight range: 1×10^4 to 4×10^6) were used.

4-(3′-Bromopropyl)styrene. A solution of the Grignard reagent from 4-chlorostyrene (12.0 g, 86.7 mmol) and Mg (3.16 g, 130 mmol) in THF (70 mL) was carefully added dropwise to a mixture of 1,3-dibromopropane (34.5 g, 171 mmol) and Li_2CuCl_4 (0.149 M THF solution, 7.21 mL, 1.08 mmol) at 0 °C. The solution was allowed to warm to room temperature and was stirred for an additional 15 h. After removal of the solvent under vacuum, 2 N HCl was added to the residue. It was extracted with ether three times and the organic phase was washed with water and dried over anhydrous $MgSO_4$. After concentration of the ethereal solution, fractional distillation of the crude product at 93 °C (0.15 Torr) gave 4-(3′-bromopropyl)styrene as a colorless liquid (8.92 g, 39.6 mmol, 46%). ^{1}H NMR: δ 7.35 and 7.16 (2 d, 4H, J = 7.80 Hz, Ar), 6.70 (dd, 1H, −C*H*═), 5.72 and 5.21 (2d, 2H, J = 17.4 and 10.8 Hz, CH_2═), 3.40 (t, 2H, J = 6.00 Hz, CH_2Br), 2.77 (t, 2H, J = 7.20 Hz, ArCH_2−), 2.16 (m, 2H, $CH_2CH_2CH_2$).

***p*-[3-(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose-3-oxy)propyl]styrene (1).** A mixture of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (9.72 g, 37.4 mmol) dispersed in 50% aqueous NaOH (70 mL) was added to a solution of tetrabutylammonium hydrogen sulfate (1.28 g, 3.74 mmol) in CH_2Cl_2 (70 mL). 4-(3′-Bromopropyl)styrene (7.66 g, 34.0 mmol) was then added at room temperature, and the mixture was stirred at 40 °C for 4 days. The organic layer was washed with water, dried over $MgSO_4$, and concentrated. Flash chromatography on silica gel (hexanes/EtOAc, 9/1 v/v) afforded 7.86 g (19.5 mmol, 57%) of **1** as a colorless syrup. It was carefully freeze-dried from benzene several times to remove a trace of water. ^{1}H NMR: δ 7.30 and 7.16 (2 d, 4H, J = 8.10 Hz, Ar), 6.69 (dd, 1H, −C*H*═), 5.88 (d, 1H, J = 3.60 Hz, α-furanose H-1), 5.70 and 5.20 (2 d, 2H, J = 17.7 and 10.8 Hz, CH_2═), 4.50−3.85 (m, 6H, H-2−H-6), 3.62 and 3.50 (2 m, 2H, CH_2-CH_2CH_2O), 2.69 (t, 2H, J = 7.20 Hz, ArCH_2−), 1.88 (m, 2H, $CH_2CH_2CH_2CH_2$), 1.49 1.43, 1.35, and 1.31 (four singlets, 12H, CH_3). ^{13}C NMR: δ 141.55, 135.45, 128.79, and 126.29 (Ar), 136.70 (−*C*H═), 113.13 (*C*H_2═), 111.82 and 109.06 (>*C* (O)(O)), 105.38 (C-1), 82.43, 82.21, 81.35, 72.53, and 67.44 (C-2−C-6), 69.35 ($CH_2CH_2CH_2$O), 31.91 (Ar*C*H_2), 31.27 (CH_2CH_2-CH_2), 26.92, 26.90, 26.32, and 25.48 (*C*H_3).

***p*-[3-(1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose-6-oxy)propyl]styrene (2).** Monomer **2** was synthesized in 61% yield by a similar procedure used in the case of **1** starting from 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose. Purification by flash chromatography on silica gel (hexanes/EtOAc, 9/1 v/v) afforded **2** as a white solid. ^{1}H NMR: δ 7.32 and 7.15 (2 d, 4H, J = 8.10 Hz, Ar), 6.69 (dd, 1H, −C*H*═), 5.55 (d, 1H, J = 5.10 Hz, α-pyranose H-1), 5.70 and 5.19 (2 d, 2H, J = 17.7 and 11.1 Hz, CH_2═), 4.63−3.48 (m, 8H, H-2−H-6, and $CH_2CH_2CH_2$O), 2.68 (t, 2H, J = 7.50 Hz, ArCH_2), 1.89 (m, 2H, $CH_2CH_2CH_2CH_2$), 1.54 1.46, 1.35, and 1.34 (four singlets, 12H, CH_3). ^{13}C NMR: δ 141.93, 135.24, 128.78, and 126.24 (Ar), 136.76 (−*C*H═), 112.99 (*C*H_2═), 109.28 and 108.61 (>*C* (O)(O)), 96.45 (C-1), 77.30, 71.25, 70.48, 69.38, and 66.72 (C-2−C-6), 70.71 ($CH_2CH_2CH_2$O), 32.02 (Ar*C*H_2), 31.24 (CH_2CH_2-CH_2), 26.18, 26.08, 25.04, and 24.52 (*C*H_3).

4-(11′-Bromoundecyl)styrene. A solution of Grignard reagent from 4-chloromethylstyrene (5.60 g, 36.8 mmol) and Mg (1.10 g, 45.5 mmol) in diethyl ether (25 mL) was added dropwise to a mixture of 1,10-dibromodecane (8.47 g, 28.3 mmol) and Li_2CuCl_4 (0.149 M THF solution, 2.50 mL, 0.37 mmol) at 0 °C. The solution was allowed to warm to room

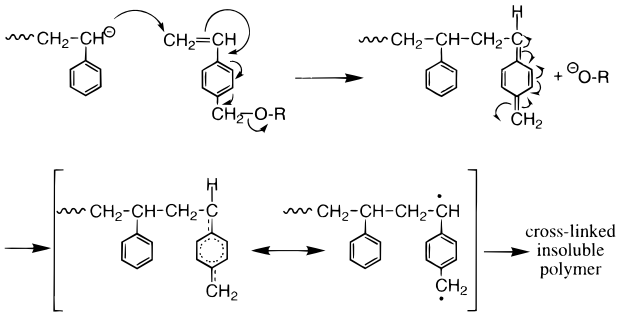
temperature and stirred for an additional 3 h. After removal of the solvent under vacuum, 2 N HCl was added to the residue. It was extracted with ether three times and the organic phase was washed with water and dried over anhydrous $MgSO_4$. After concentration of ethereal solution, flash chromatography on silica gel (hexane solvent) afforded 4-(11′-bromoundecyl)styrene as a colorless liquid (5.03 g, 14.9 mmol, 53%). ^{1}H NMR: δ 7.32 and 7.13 (2 d, 4H, J = 7.80 Hz, Ar), 6.69 (dd, 1H, −C*H*═), 5.70 and 5.18 (2d, 2H, J = 17.7 and 11.1 Hz, CH_2═), 3.40 (t, 2H, J = 6.90 Hz, CH_2Br), 2.58 (t, 2H, J = 7.50 Hz, ArCH_2−), 1.85 (m, 2H, CH_2CH$_2$Br), 1.60 (m, 2H, ArCH$_2$CH_2), 1.42−1.27 (m, 14H, CH$_2$ (CH_2) $_7$CH$_2$).

***p*-[11-(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose-3-oxy)undecyl]styrene (3).** A mixture of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (5.20 g, 20.0 mmol) dispersed in 50% aqueous NaOH (50 mL) was added to a solution of tetrabutylammonium hydrogensulfate (0.69 g, 2.00 mmol) in CH_2Cl_2 (50 mL). 4-(11′-Bromopropyl)styrene (5.03 g, 14.9 mmol) was then added at room temperature, and the mixture was stirred at 40 °C for 2 weeks. The organic layer was washed with water, dried over $MgSO_4$, and concentrated. Flash chromatography on silica gel (hexanes/EtOAc, 9/1 v/v) afforded 2.57 g (4.98 mmol, 33%) of **3** as a colorless syrup. Monomer **3** was carefully freeze-dried from benzene several times to remove a trace of water. ^{1}H NMR: δ 7.32 and 7.13 (2 d, 4H, J = 8.04 Hz, Ar), 6.69 (dd, 1H, −C*H*═), 5.87 (d, 1H, J = 3.66 Hz, α-furanose H-1), 5.70 and 5.18 (2d, 2H, J = 17.6 and 10.9 Hz, CH_2═), 4.53−3.84 (m, 6H, H-2−H-6), 3.58 and 3.51 (2m, 2H, CH$_2$CH$_2$CH_2O), 2.58 (t, 2H, J = 7.44 Hz, ArCH_2−), 1.59−1.26 (m, 30H, CH$_2$ (CH_2) $_9$CH$_2$ and CH_3). ^{13}C NMR: δ 142.80, 135.12, 128.64, and 126.19 (Ar), 136.82 (−*C*H═), 112.87 (*C*H$_2$═), 111.79 and 108.95 (>*C* (O) (O)), 105.37 (C-1), 82.65, 82.18, 81.30, 72.64, and 67.31 (C-2−C-6), 70.80 (CH$_2$CH$_2$*C*H$_2$O), 35.78 (Ar*C*H$_2$), 31.53, 29.82, 29.67, 29.59, 29.49, 29.38, 26.94, 26.80, 26.35, 26.15, and 25.50 (CH$_2$(*C*H$_2$)$_9$CH$_2$, and *C*H$_3$).

Polymerization Procedures. All polymerizations were carried out in THF at −78 °C in an all-glass apparatus equipped with break-seals with vigorous shaking under high vacuum conditions as previously reported.[17] The polymerization was terminated in situ with methanol at −78 °C. The polymer was obtained by evaporation and purified by reprecipitation in diethyl ether/methanol and by freeze-drying from the benzene solution. In a typical polymerization procedure, a solution of **1** (768 mg, 1.90 mmol) in THF (9.50 mL) chilled to −78 °C was added at once to *s*-BuLi (0.117 mmol in heptane 3.15 mL) at −78 °C with stirring. After 30 min, the polymerization was terminated in situ with methanol at −78 °C. The poly(**1**) was obtained as white powder (762 mg, 99% yield) by evaporation and purified by reprecipitation in diethyl ether/methanol and by freeze-drying from the benzene solution. The M_n value determined by comparing the ^{1}H NMR peak intensity of the initiator fragment with that of main chain or side chain was 6700. The M_w/M_n value estimated from SEC calibration using polystyrene standards in THF was 1.05.

Block Copolymerization. The first-stage polymerization of **1** was carried out with *s*-BuLi in THF at −78 °C. After 30 min, a small portion of the living poly(**1**) was withdrawn to determine the characteristics of the first-stage polymer. To the residue of the polymerization system was added styrene as a second monomer at −78 °C in one portion with vigorous stirring, and the second-stage polymerization was continued for additional 30 min. After the reaction was quenched with degassed methanol, both polymers were quantitatively obtained by pouring the mixtures into methanol. Similarly, the sequential copolymerization of styrene and **1** by the reversed addition of both monomers was also carried out under the same condition. In a typical copolymerization procedure, a solution of styrene (478 mg, 4.60 mmol) in THF (9.20 mL) chilled to −78 °C was added at once to *s*-BuLi (0.103 mmol in heptane 2.77 mL) at −78 °C with stirring. After 30 min, monomer **1** (513 mg, 1.27 mmol in THF 6.35 mL) as a second monomer was added at −78 °C in one portion with stirring and the second-stage polymerization was continued for additional 30 min. After being quenched with degassed methanol at −78 °C, the mixture was poured into a large amount of methanol to precipitate the polymer. Reprecipitation twice from the THF solution to methanol and freeze-dried from the benzene solution gave 992 mg (100% yield) of poly(styrene-*b*-**1**) as white powder. The M_n value determined by using the molecular weight of the homopolymer and the molar ratio of monomer units in the block copolymer analyzed by ^{1}H NMR was 9900. The M_w/M_n value estimated from SEC calibration using polystyrene standards in THF was 1.07.

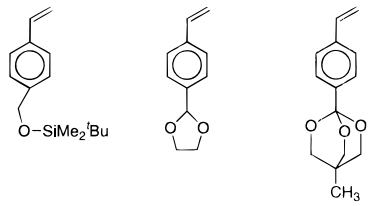
Scheme 1



Reaction of Poly(4) with Polystyryllithium. Poly(**4**) (0.220 mmol, M_n SEC = 4 600, M_w/M_n = 1.06), which was synthesized by the polymerization of **4** according to the preceding paper,[15] was mixed with polystyryllithium (0.218 mmol, M_n SEC = 4500) in THF (18.1 mL) at −78 °C, and the mixture was further stirred for 22 h. After being quenched with degassed methanol at −78 °C, the mixture was concentrated and analyzed by SEC. M_n and M_w/M_n values estimated from SEC calibration using polystyrene standards in THF were 4500 and 1.07, respectively.

Results and Discussion

Reaction Mechanism in Anionic Polymerization of 9. As mentioned in the Introduction, there is a significant difference in the anionic polymerizability of **4** and **9**, although they are structurally the same except for the substituent position. However, this is not a very special case. Our previous papers reported the same difference between meta- and para-substituted monomers in the anionic polymerizations of styrene derivatives (**10**−**12**).[18−20]



(**10**) (**11**) (**12**)

Namely, the meta-substituted styrenes all undergo anionic living polymerization, whereas the corresponding para-substituted monomers do not. In addition, gelation always occurred by reacting each of the para-substituted monomers with difunctional living polystyrene. Monomers **9**−**12** all bear the *p*-vinylbenzyl alkyl (or silyl) ether moiety.

We explained the cross-linking behavior of the para-substituted monomers by the proposed reaction mechanism outline in Scheme 1.

After a few monomers add normally to the polystyryl-anion, the terminal carbanion derived from **9** or the related styrenes undergoes a 1,6-elimination reaction to generate a very reactive *p*-xylylene or biradical intermediate. The biradical intermediates could react with each other at both chain ends to form a cross-linked

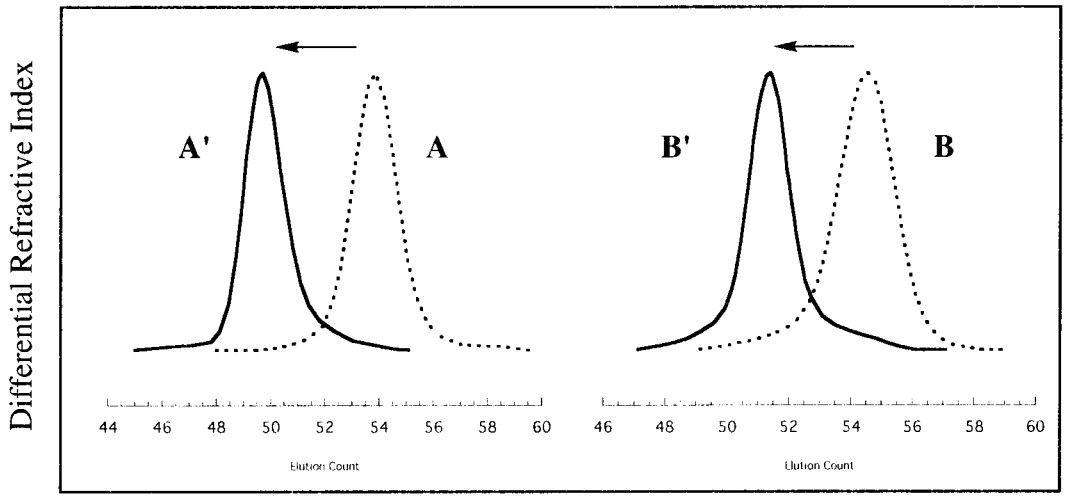


Figure 1. SEC curves of poly(**1**) (A), polystyrene (B) at the first-stage polymerization and poly(**1**-*b*-styrene) (A′) and poly(styrene-*b*-**1**) (B′) obtained by the second-stage polymerization (block copolymerization): peak A, M_n(calcd) = 7800, M_n(obsd) = 7800, M_w/M_n = 1.06; peak A′, M_n(calcd) = 18 000, M_n(obsd) = 20 000, M_w/M_n = 1.07; peak B, M_n(calcd) = 4700, M_n(obsd) = 4700, M_w/M_n = 1.07; peak B′, M_n(calcd) = 9700, M_n(obsd) = 9900, M_w/M_n = 1.07. (The second monomer was added after the first-stage polymerization for 0.5 h.)

insoluble polymer. In the homopolymerizations, if these reactions occur at the early stage of the polymerization, they would explain why no polymer was obtained, and instead, most of the monomer was recovered.

In this pathway, the terminal carbanions with para-substituted benzyl alkyl (or silyl) ether moieties are the key intermediates that cause 1,6-elimination and prevent polymerization. A similar elimination reaction may occur with the corresponding ortho-substituted styrenes. Indeed, the ortho-substituted analogues of monomers **10** and **11** also fail to polymerize anionically.[17,18] In contrast, the terminal carbanion derived from the corresponding meta-substituted styrene cannot form a *m*-xylylene intermediate and therefore does not undergo elimination.

On the basis of this proposed mechanism, we have designed and synthesized **1** and **2** as anionically polymerizable para-substituted styrene monomers with a 3-(*p*-vinylphenyl)propyl alkyl ether moiety, thereby avoiding the structure of *p*-vinylbenzyl alkyl ether. The para-substituted styrene derivative **3** was also synthesized based on the same concept.

Monomer Synthesis. We first attempted to synthesize **1** by reacting *p*-bromopropylstyrene with the sodium salt of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose in DMF, as in the synthesis of **4**−**9**. However, this produced the expected product in less than 10% yield. The yield was not improved by modification of the solvent, temperature, or time.

The yield of **1** was improved significantly by using a phase transfer catalyzed Williamson etherification. The reaction of *p*-bromopropylstyrene with 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose in 50% aqueous NaOH−CH_2Cl_2 in the presence of tetrabutylammonium hydrogensulfate produced pure **1** in 57% yield after the usual workup and column chromatography. Similarly, **2** and **3** were obtained in 61 and 33% yields, respectively.

Anionic Polymerization of 1. The anionic polymerization of **1** was carried out in THF at −78 °C using *s*-BuLi as the initiator for 0.5 h, which are the exact conditions used to polymerize **4** and **9**. Addition of **1** to *s*-BuLi immediately produced an intense reddish orange color, which remained unchanged during the polymerization, but disappeared with methanol. The yield of polymer was quantitative.

Table 1. Anionic Polymerization of 1 in THF at −78 °C for 0.5 h

		$M_n \times 10^{-3}$		
$[\mathbf{1}]_0/[s\text{-BuLi}]_0$	yield, %	calcd[a]	obsd[b]	M_w/M_n[c]
16.2	∼100	6.6	6.7	1.05
36.8	∼100	15	15	1.06
99.1[d]	∼100	40	42	1.04

[a] M_n (calcd) = ([monomer] × (MW of monomer)/[initiator]) + MW of initiator. [b] M_ns(obsd) of the polymers were estimated by ^{1}H NMR area ratio of signals corresponding to main chain and initiator fragment. [c] M_w/M_ns were estimated from SEC calibration using polystyrene standards in THF. [d] Bu_2Mg (0.0615 mmol) was added prior to the polymerization and the polymerization time was 24 h.

Table 2. Anionic Polymerization of 2 and 3 in THF at −78 °C for 0.5 h

			$M_n \times 10^{-3}$		
monomer	$[\text{monomer}]_0/[s\text{-BuLi}]_0$	yield, %	calcd[a]	obsd[b]	M_w/M_n[c]
2	16.6	∼100	6.8	7.4	1.05
	24.7	∼100	10	12	1.04
	79.2[d]	∼100	32	31	1.04
3	15.6	∼100	8.1	9.2	1.05

[a] M_n(calcd) = ([monomer] × (MW of monomer)/[initiator]) + MW of initiator. [b] M_n(obsd)s of the polymers were estimated by ^{1}H NMR area ratio of signals corresponding to main chain and initiator fragment. [c] M_w/M_ns were estimated from SEC calibration using polystyrene standards in THF. [d] Bu_2Mg (0.0561 mmol) was added prior to the polymerization and the polymerization time was 24 h.

The SEC trace revealed that the resulting polymer possessed a symmetrical unimodal peak and a quite narrow molecular weight distribution (M_w/M_n = 1.05). The M_n value (6600) calculated from a $[M]_0/[I]_0$ ratio agreed well with the value of 6700 determined by comparing the ^{1}H NMR peak intensity of the methyl proton of the *s*-BuLi fragment with that of the main chain. These results are summarized in Table 1.

Similarly, a polymer with a predictable molecular weight (M_n = 15 000) was obtained. However, M_n values higher than 15 000 deviated from those calculated. Since monomer **1** was a very viscous liquid, it could be neither

Table 3. Block Copolymerization of 1 with Styrene in THF at −78 °C

first monomer	second monomer	$[M_1]_0/[s\text{-BuLi}]_0$	$[M_2]_0/[s\text{-BuLi}]_0$	yield, %	$M_n \times 10^{-3}$ calcd[a]	$M_n \times 10^{-3}$ obsd[b]	M_w/M_n[c]
1	styrene	19.1	100	∼100	18	20	1.07
styrene	**1**	44.7	12.3	∼100	9.7	9.9	1.07

[a] M_n (calcd) = ([monomer] × (MW of monomer)/[initiator]) + MW of initiator. [b] The molecular weights of the block copolymers were determined by using the molecular weights of the homopolymers and the molar ratios of monomer units in the block copolymers analyzed by ^{1}H NMR. [c] M_w/M_n was estimated from SEC calibration using polystyrene standards in THF.

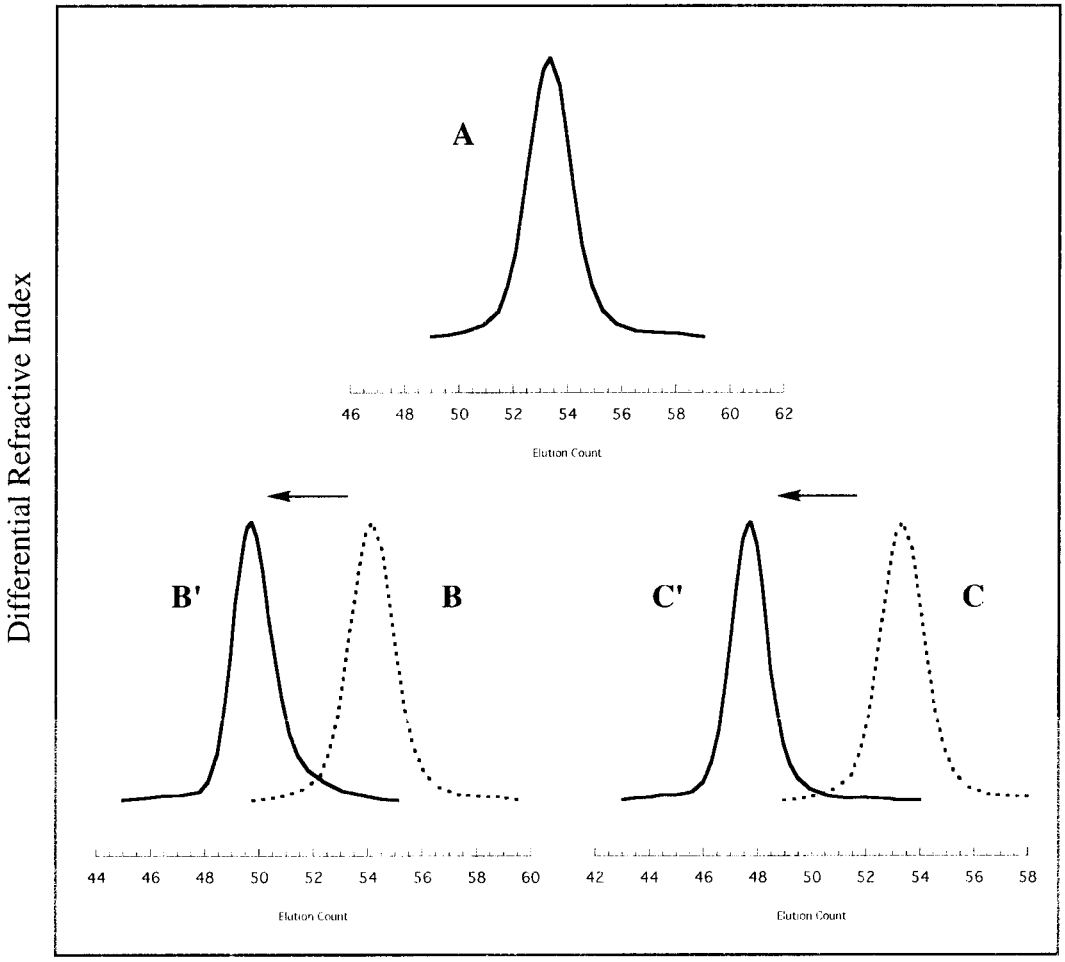


Figure 2. SEC curves: poly(**1**) obtained at −78 °C for 0.5 h (A), M_n(calcd) = 6600, M_n(obsd) = 6700, M_w/M_n = 1.05; poly(**1**-*b*-styrene) obtained by addition of styrene to living poly(**1**) (B), M_n(calcd) = 7400, M_n(obsd) = 7100, M_w/M_n = 1.05, after allowing it to stand at −78 °C for 22 h (B′), M_n(calcd) = 18 000, M_n(obsd) = 20 000, M_w/M_n = 1.07; poly(**1**-*b*-styrene) obtained by addition of styrene to living poly(**1**) (C), M_n(calcd) = 8400, M_n(obsd) = 8900, M_w/M_n = 1.06, after allowing it to stand at −30 °C for 0.5 h (C′), M_n(calcd) = 20 300, M_n(obsd) = 23 000, M_w/M_n = 1.08.

distilled nor recrystallized. Trace amounts of impurities such as water were difficult to remove completely from **1**. This difficulty was overcome by the addition of 3 mol % of dibutylmagnesium (Bu_2Mg) to **1** and allowing the mixture to stand further for 1 h at room temperature prior to the polymerization. By this treatment, a polymer of predictable molecular weight (M_n = 42 000) and of very narrow molecular weight distribution (M_w/M_n = 1.04) was quantitatively obtained under the same conditions. Bu_2Mg *is thus effective to purify* **1**.[21]

The results of the polymerization and appearance of the reddish orange coloration clearly indicate the living character of the anionic polymerization of **1**. The proposed mechanism as illustrated in Scheme 1 is also supported by the success of the anionic living polymerization of **1** bearing a 3-(*p*-vinylphenyl)propyl alkyl moiety but not a *p*-benzyl alkyl one.

The anionic polymerization of **1** was also attempted using *s*-BuLi in benzene for 1 h at either 0 or 30 °C. In each case, the mixture showed an intense red color, which faded with time. This suggests that the carbanion at the propagating chain end is deactivated under these conditions. In both cases, polymers of broad molecular weight distributions were obtained in 16% yield at 0 °C and 25% yield at 30 °C, respectively. *s*-BuLi and/or the chain-end carbanion might attack the acetals under the conditions. Thus, the anionic polymerization of **1** using *s*-BuLi in benzene failed and is far from a complete conversion.

Anionic Polymerization of 2 and 3. To establish the more generality of anionic living polymerization of para-substituted styrenes containing monosaccharide residues, another two monomers, **2** and **3** were polymerized in THF using *s*-BuLi at −78 °C. A reddish orange

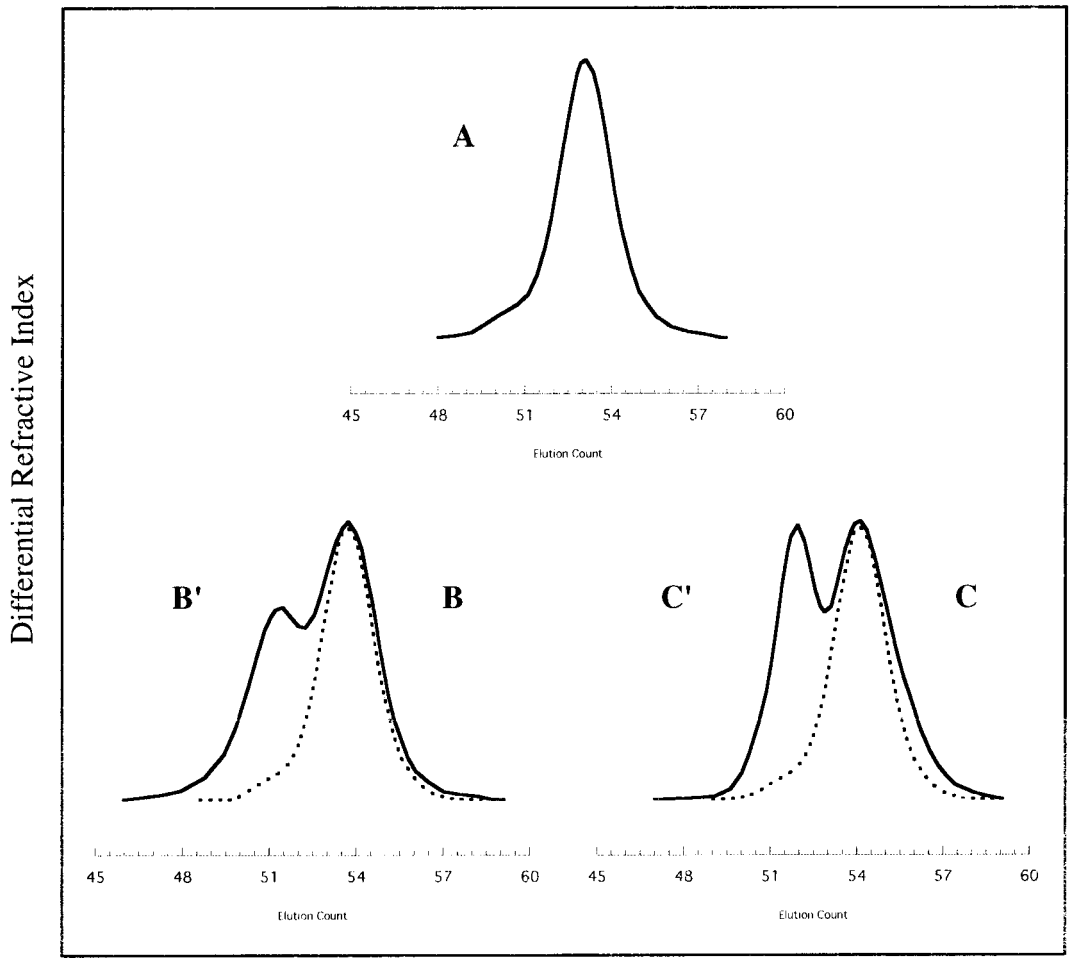


Figure 3. SEC curves of poly(**4**) obtained as follows: at −78 °C for 0.5 h (A) M_n(calcd) = 11 000, M_n(obsd) = 9300, M_w/M_n = 1.07; (B) M_n(calcd) = 8400, M_n(obsd) = 8900, M_w/M_n = 1.07; (C) M_n(calcd) = 7400, M_n(obsd) = 7700, M_w/M_n = 1.07; at −78 °C for 22 h (B′), M_n(calcd) = 8400, M_n(obsd) = 12 000, M_w/M_n = 1.16; at −30 °C for 0.5 h (**C′**), M_n(calcd) = 7400, M_n(obsd) = 11 000, M_w/M_n = 1.16.

color was also observed in each polymerization mixture. Yields of polymers were quantitative under the conditions. The results are summarized in Table 2.

There is a good agreement between M_n values calculated and observed in all cases. The resulting polymers all had symmetrical SEC distributions composed of unimodal peaks and were very narrow in molecular weight. The addition of Bu_2Mg was needed in the case where the target molecular weight was 32 000. Otherwise, no polymer was obtained under the same conditions without addition of Bu_2Mg. The living character of the anionic polymerizations of **2** and **3** is evident from the results in Table 2. Thus, we have also succeeded in achieving the anionic living polymerization of *p*-substituted styrenes by introducing 3 or 11 methylenic units between the protected monosaccharide residue and styrene, thereby avoiding the structure of *p*-vinylbenzyl alkyl ether.

Block Copolymerization of 1 with Styrene. One of the best advantages in living polymerization is to create well-defined block copolymers with precisely controlled chain structures and compositions. Furthermore, the results of the block copolymerization provide direct evidence on the stability of the produced living polymer at the first stage as well as relative reactivities of both monomers and the living polymer chain ends.

The block copolymerizations were carried out by the sequential addition of **1** and styrene in this order or vice versa. In both cases, the block copolymers were obtained quantitatively. The SEC peaks of the resulting copolymers were symmetrically unimodal and completely shifted to higher molecular weight sides as shown in Figure 1. No peaks corresponding to the homopolymers produced at the first stage were observed at all. Their *M*n values and compositions determined by SEC and ^{1}H NMR agreed with those calculated by feed ratios. Accordingly, new well-defined AB and BA diblock copolymers could be successfully synthesized. These results are summarized in Table 3. Their expected amphiphilic characters and precisely controlled structures are especially attractive for examining the micelle formation in selective solvents.

Quantitative formation of the AB block copolymer where A and B were poly(**1**) and polystyrene segments provides a direct evidence that the living polymer produced from **1** is completely stable in THF at −78 °C for 0.5 h. The success of both block copolymerizations indicates that monomer reactivities of styrene and **1** and nucleophilicities of their living polymers are nearly equal.

Stabilities of Anionic Living Polymers Produced from 1 and 4. In the preceding sections, we confirmed the living character of the anionic polymerization of **1** from the results of homopolymerization and block copolymerization. Since the living polymer of **1** possesses the acetals and glucofuranose moieties susceptible to

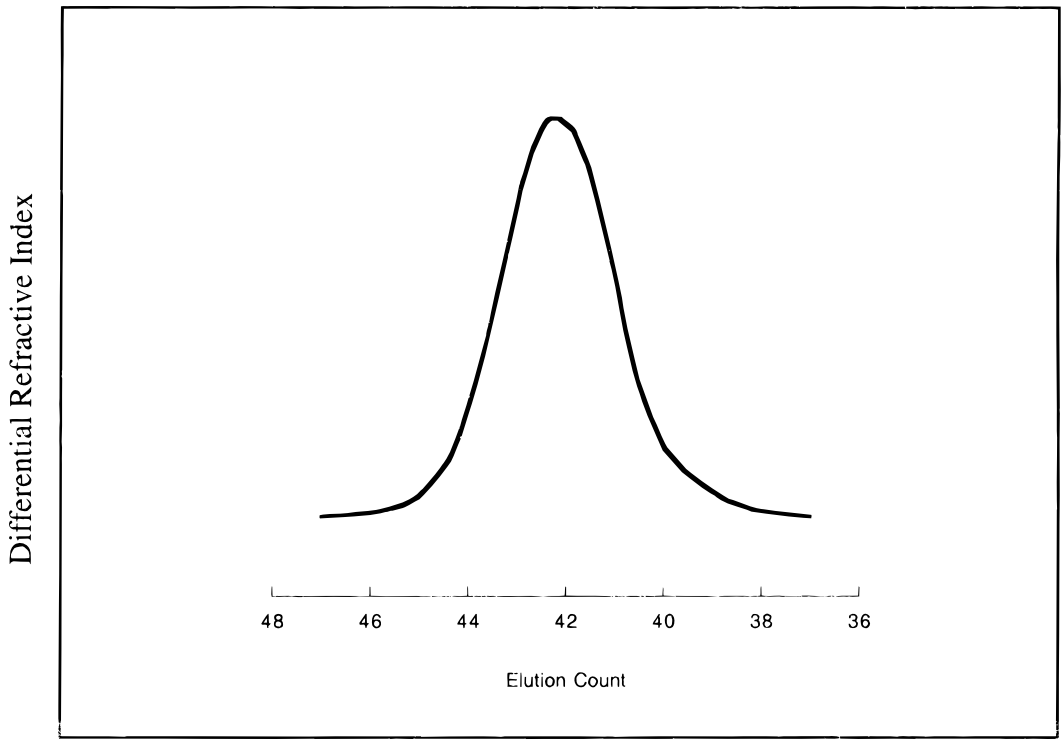


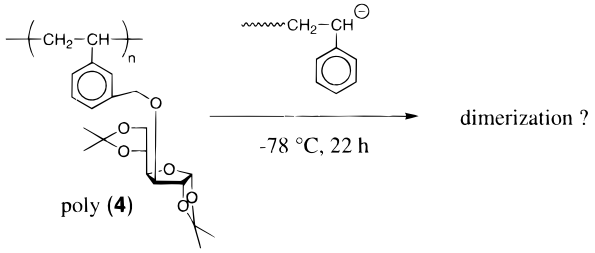
Figure 4. SEC curves of a mixture of poly(**4**) and polystyrene obtained by mixing poly(**4**) (M_n(obsd by SEC) = 4600) with polystyryllithium (M_n(obsd by SEC) = 4500) at −78 °C for 22 h.

attack by the chain-end carbanion, it is important to examine the stability under more severe conditions. As mentioned before, the SEC peak of the polymer obtained at −78 °C after 0.5 h was a symmetrical unimodal peak as shown in Figure 2A. On allowing the living polymer to stand for a longer time of 22 h or at a higher temperature of −30 °C, no change in the SEC peaks was observed (see Figure 2, parts B and C). Furthermore, the addition of styrene to both living polymers gave quantitative formation of the expected block copolymers, showing that their chain-end carbanions all retained activity and could initiate the polymerization of styrene quantitatively (see Figure 2, parts B′ and C′). These results show that the living polymer of **1** is completely stable either in THF at −78 °C for 22 h or at −30 °C for 0.5 h.

On the other hand, the living polymer of **4** was unstable when it allowed to stand at −78 °C for 22 h or at −30 °C for 0.5 h. The molecular weight distribution of the polymer obtained at −78 °C after 0.5 h is unimodal as shown in Figure 3A. However, a significant amount of dimer was formed in the polymer obtained after 22 h (see Figure 3, parts B and B′). It was estimated from both peak areas that ca. 40% of the starting living polymer was dimerized. Similarly, the dimer was formed in ca. 50% yield at −30 °C after 0.5 h (see Figure 3, parts C and C′). Thus, even the living polymer produced from a meta-substituted styrene like **4** was not as stable as we thought previously, and it deactivated gradually along with dimerization, possibly after the conclusion of the polymerization.

The benzyl proton abstraction by the chain-end carbanion often observed in this kind of reaction was ruled out, because the dimer could not be formed by this mechanism. To check the possibility of the intermolecular polymer reaction between poly(**4**) and the chain-end carbanion, a model reaction using polystyryllithium instead of the unstable living polymer of **4** was carried out (Scheme 2).[23]

Scheme 2



The poly(**4**) was mixed with a newly prepared polystyryllithium in THF at −78 °C and the mixture was stirred for additional 22 h at −78 °C. After quenching with methanol, the reaction mixture was analyzed by SEC. No reaction between them was suggested from the SEC trace as was seen in Figure 4. In other words, any reactions between poly(**4**) and the chain-end carbanion did not occur intermolecularly.

The dimer formation must be considered from yet another perspective. We are tentatively considering that reactive species such as radical and carbene may be produced from the chain-end carbanion by migration via an electron-transfer pathway. One candidate is a similar mechanism occurring in the polymerization of **9** illustrated in Scheme 1. Namely, the generation of *m*-xylylene or a biradical intermediate by a 1,5-elimination reaction of the chain-end carbanion and coupling with each other to form the dimer are considered. A problem is that this mechanism is difficult to apply to **4** of the meta-substituted styrene as mentioned before. Furthermore, the stabilities of the already reported anionic living polymers derived from the meta-substituted styrenes of **10**−**13** should be reexamined in more detail.

Conclusions

The anionic living polymerizations of three para-substituted alkyl styrenes containing acetal-protected monosaccharide residues, **1**−**3**, were successfully achieved in THF at −78 °C using *s*-BuLi. The living polymer derived from **1** was stable in THF either at −78 °C for 22 h or at −30 °C for 0.5 h, while the living polymer of **4** was not stable under those two conditions. It was deactivated gradually along with the dimerization of the starting living polymer.

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(21) The addition of Bu_2Mg significantly influences the BuLi-initiated anionic polymerization of styrene in cyclohexane.[22] On the other hand, no effect was observed in our polymerization system carried out in THF at −78 °C, at least with respect to molecular weight and molecular weight distribution of the resulting poly(**1**). However, the rate of polymerization of **1** decreased. For example, only 50% poly(**1**) yield was realized in the presence of Bu_2Mg in the polymerization in THF at −78 °C for 1 h, while the polymerization proceeded quantitatively within 0.5 h in the absence of Bu_2Mg. Work is now in progress to examine in more detail the effect of Bu_2Mg on anionic living polymerizations of styrene and 1,3-dienes by changing several variables such as amount of Bu_2Mg, temperature, etc. The results will be published in the near future.
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(23) In our previous paper, we demonstrated that both AB and BA diblock copolymers with the expected structures were obtained quantitatively by the sequential addition of styrene and **4** in this order or vice versa. These results indicate that both living polymers of styrene and **4** have very similar reactivities.

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